doi.org/10.26434/chemrxiv.8346107.v1

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Submitted date: 28/06/2019 • Posted date: 01/07/2019

Citation information: Li, Qi; Pellegrino, Jenna; Lee, D. John; Tran, Arthur; Wang, Ruoxi; Park, Jesslyn; et al. (2019): Synthesis and Mechanism of Action of Group a Streptogramin Antibiotics That Overcome Resistance. ChemRxiv. Preprint.

Natural products serve as chemical blueprints for the majority of classes of antibiotics in our clinical arsenal. The evolutionary process by which these molecules arise is inherently accompanied by the co-evolution of resistance mechanisms that shorten the clinical lifetime of any given class. Virginiamycin acetyltransferases (Vats) are resistance proteins that provide protection against streptogramins, potent Gram-positive antibiotics that inhibit the bacterial ribosome. Due to the challenge of selectively modifying the chemically complex, 23-membered macrocyclic scaffold of group A streptogramins, analogs that overcome Vat resistance have not been previously accessible. Here we report the design, synthesis, and antibacterial evaluation of group A streptogramin antibiotics with unprecedented structural variability. Using cryo-electron microscopy and forcefield-based refinement, we characterize the binding of eight analogs to the bacterial ribosome at high resolution (2.4-2.8 Å), revealing new binding interactions that extend into the peptidyl tRNA binding site and towards synergistic binders that occupy the nascent peptide exit tunnel. Two of these analogs have excellent activity against a streptogramin-resistant strain of S. aureus expressing VatA and exhibit decreased acetylation rates in vitro. Our results demonstrate that the combination of rational design and modular chemical synthesis can revitalize classes of antibiotics that are limited by naturally arising resistance mechanisms.

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Synthesis and mechanism of action of group A streptogramin antibiotics that overcome resistance

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Abstract

Natural products serve as chemical blueprints for the majority of classes of antibiotics in our clinical arsenal. The evolutionary process by which these molecules arise is inherently accompanied by the co-evolution of resistance mechanisms that shorten the clinical lifetime of any given class. Virginiamycin acetyltransferases (Vats) are resistance proteins that provide protection against streptogramins, potent Gram-positive antibiotics that inhibit the bacterial ribosome. Due to the challenge of selectively modifying the chemically complex, 23-membered macrocyclic scaffold of group A streptogramins, analogs that overcome Vat resistance have not been previously accessible. Here we report the design, synthesis, and antibacterial evaluation of group A streptogramin antibiotics with unprecedented structural variability. Using cryo-electron microscopy and forcefield-based refinement, we characterize the binding of eight analogs to the bacterial ribosome at high resolution (2.4-2.8 Å), revealing new binding interactions that extend into the peptidyl tRNA binding site and towards synergistic binders that occupy the nascent peptide exit tunnel. Two of these analogs have excellent activity against a streptogramin-resistant strain of *S. aureus* expressing VatA and exhibit decreased acetylation rates *in vitro*. Our results demonstrate that the combination of rational design and modular chemical synthesis can revitalize classes of antibiotics that are limited by naturally arising resistance mechanisms.

Natural antibiotics and limitations of semisynthesis

Natural product antibiotics are secondary metabolites that have arisen through millions of years of evolutionary optimization and are often favored with excellent antimicrobial activity. This evolutionary process selects for properties that are beneficial for the producing organisms in their native environment; however, these selected properties are not necessarily transferable to therapeutics due to attributes such as solubility and bioavailability[1]. Furthermore, the evolution of natural product antibiotics is inherently coupled with the evolution of resistance mechanisms, both to protect the producing organism and to provide defenses for competing organisms[2]. These resistance mechanisms can be passed to progeny and to other species by horizontal gene transfer. As a result, many potent antimicrobial natural products are poorly suited for clinical use. A primary means by which researchers have sought to overcome poor therapeutic attributes or resistance is semisynthesis: the chemical modification of natural products that are obtained through fermentation[1]. Semisynthesis has been effective to improve the pharmacological properties of myriad natural product classes, such as β-lactams (e.g., amoxicillin), macrolides (e.g., azithromycin), and lincosamides (e.g., clindamycin). In overcoming natural resistance mechanisms, however, semisynthesis has been met with limited success. Often researchers are forced to implement other therapeutic modalities, such as combination therapy with inhibitors of resistance proteins, as in β-lactams/β-lactamase inhibitors[3]. Recently, advances in chemistry have enabled several classes of antibiotics to be accessed by fully synthetic routes, greatly expanding structural variability compared to semisynthesis and providing a renewed avenue to overcome resistance[1].

For many antibiotic classes, methods to overcome resistance mechanisms have yet to be discovered. A salient example is the streptogramin class, which comprises two structurally disparate components (A and B) that are produced by *Streptomyces* spp. (**Figure 1a**)[4]. Group A and group B streptogramins work in concert to inhibit protein synthesis by binding to adjacent sites in the catalytic center of the bacterial ribosome[5]. Group A binding to the peptidyl transferase center (PTC) is associated with an increase in affinity of the group B component to the adjacent nascent peptide exit tunnel (NPET)[6]. Together, the two components act synergistically, achieving bactericidal activity in many organisms[7]. Like many antibiotics that target the PTC, resistance to streptogramins can be mediated by ABC-F family proteins that dislodge antibiotics[8] or by Cfr methylase that directly interfere with binding by modifying A2503 of the 23S RNA[9]. An additional and specific resistance mechanism for group A streptogramins is deactivation by acetyltransferases of the Vat family[10]. These proteins function by transferring an acetyl group to the C14 alcohol, disrupting a hydrogen bond to the phosphodiester backbone at residue G2505 in the PTC and sterically interfering with binding to the ribosome.

Despite resistance liabilities and limited water solubility, streptogramins are attractive antibiotics because they exhibit potent activity against several species of Gram-positive bacteria[11]. While semisynthesis has aided in solubility, it has not yet been effective in overcoming resistance in streptogramins. For example, Rhône-Poulenc developed the water-soluble streptogramin combination quinupristin/dalfopristin (**1**/**2**, trade name: Synercid) by semisynthesis from the natural products pristinamycin IA (**3**) and virginiamycin M1 (**VM1**)[12]. Quinupristin/dalfopristin was approved in the United States in 1999 and served as a valuable weapon against bacteremia caused by vancomycin-resistant *E. faecium* (VRE). However, its use quickly dwindled due to several drawbacks, including common side effects (e.g., venous irritation, arthralgias, myalgias)[13] and extensive clinical resistance[14]. In the two decades following, the only other streptogramin combination to enter the clinic was NXL-103, an orally administered combination of semisynthetic streptogramins flopristin (**4**) and linopristin (**5**)[15]. NXL-103 failed to overcome any of the streptogramin resistance mechanisms and was not available in an IV formulation; further clinical development has not been reported since a successful phase-II trial in 2010. Quinupristin/dalfopristin and NXL-103 are accessed by semisynthetic modifications at only three positions on the two components (see blue highlights in **Figure 1a**): C16 and C26 in group A compounds, and the pipecolic acid residue in group B compounds. These positions were likely selected in part due to their chemical accessibility. We recently reported a modular, fully synthetic route to group A streptogramins that enables modification at sites that are not practical to modify with semisynthesis[16]. Herein we report the application of this route to the synthesis of analogs designed to overcome streptogramin resistance.

Rational design of fully synthetic streptogramins informed by CryoEM

We chose the natural product virginiamycin M2 (**VM2**) as a parent scaffold for our study due to its ease of access by our synthetic route (*vide infra*) and to its ability to be converted to more active analogs (e.g., flopristin, **4**) by C16 fluorination. Co-crystallographic data for other related group A streptogramins bound to bacterial[6,17,18] and archeal[19,20] ribosomes have revealed general binding determinants, but no prior structural data for **VM2** bound to bacterial ribosomes exists. To guide the design of analogs that maintain ribosomal activity while overcoming binding to Vat proteins, we obtained a 2.5-Å resolution CryoEM structure of fully synthetic **VM2** bound to the large subunit of the *E. coli* ribosome (**Figure 1b**, atom coloring in **VM2** mirrors building blocks used in the synthesis[16]). Consistent with the characterized binding of other group A streptogramins, we observed high quality density corresponding to a single binding site for **VM2** in the PTC. For model refinement, we used *phenix.real_space_refine*[21] interfaced with the OPLS3e/VSGB-2.1 forcefield[22] to generate low energy conformations that are consistent with the Coulomb potential density (**Extended Data Figure 1**). Both the quality of the density, enabled by the advantageous properties of the ribosome as a CryoEM sample, and the model, enabled by the forcefield-guided refinement, are sufficient to guide subsequent alterations of the molecule.

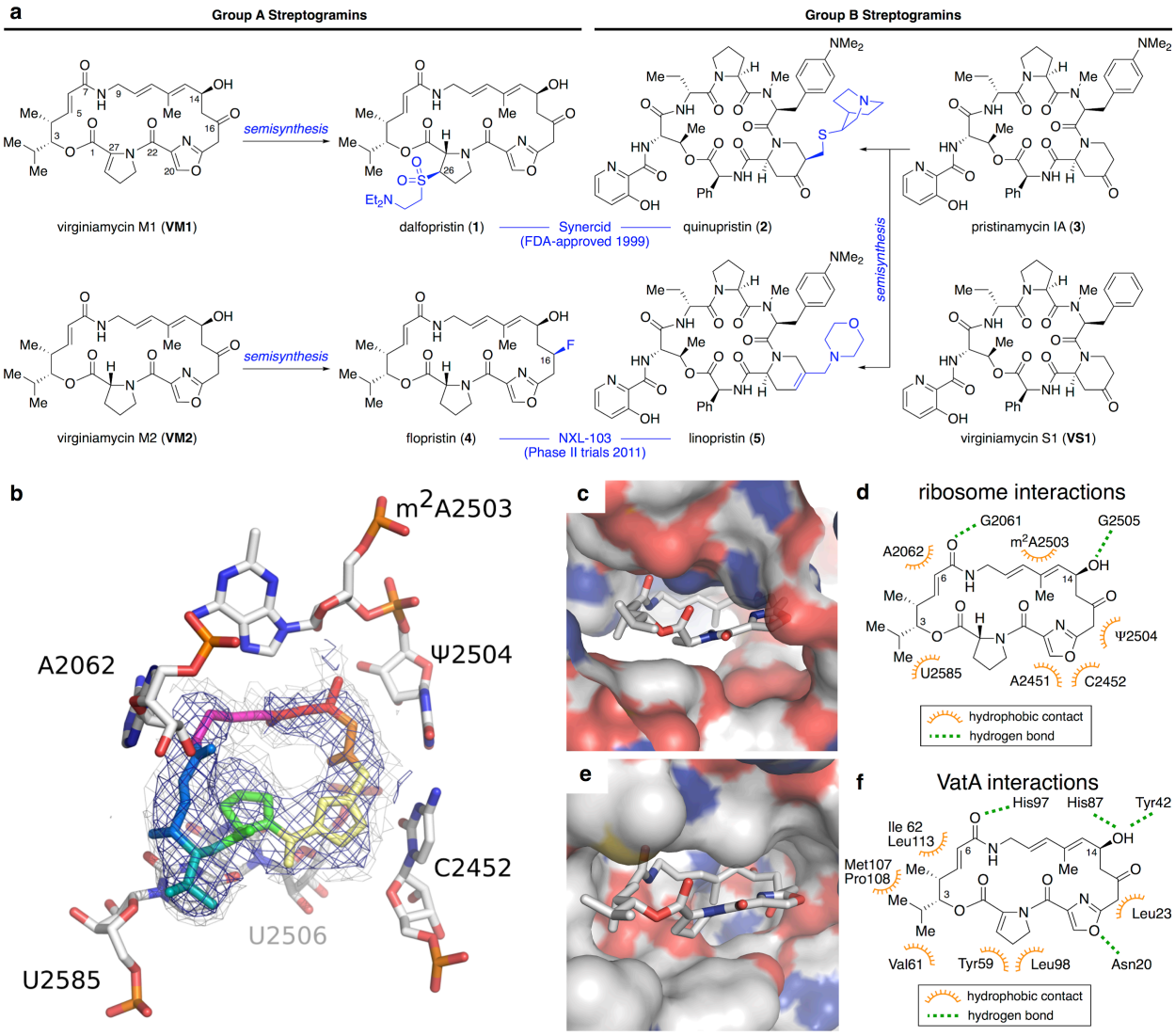


Figure 1 | Natural and semisynthetic streptogramins and their molecular mechanisms of action and resistance. a, Selected natural and semisynthetic streptogramin analogs. Group A streptogramins (left) are 23-membered macrolactones; group B streptogramins (right) are 19-membered cyclic depsipeptides. Modifications installed by semisynthesis are highlighted in blue. **b**, 2.5-Å CryoEM structure of **VM2** bound to the 50S subunit of the *E. coli* ribosome. Coulomb potential density is contoured in dark blue at 4.0 and light gray at 1.0 . **c**, Surface rendering of the peptidyl transferase center of the ribosome with **VM2** bound. Surface coloring is according to heavy atom type (gray = carbon, red = oxygen, blue = nitrogen, orange = sulfur). **d**, Graphical representation of interactions between **VM2** and residues in the ribosomal binding site. **e**, Surface rendering of the binding site in the resistance protein virginiamycin acetyltransferase A (VatA) with **VM1** bound (PDB ID: 4HUS). **f**, Graphical representation of the binding interactions between **VM1** and VatA, highlighting the extensive hydrophobic interactions at C3-C6 (acetylation occurs at the C14 alcohol).

Similar to other group A streptogramins[6,17–20], **VM2** binds to the PTC with its oxazole positioned in the A-site crevice formed by A2451 and C2452, and the remainder of the macrocycle projecting into the P-site. The positioning of the C14 alcohol in **VM2** is consistent with a hydrogen bond to the phosphodiester backbone at G2505, an interaction that would be disrupted by acetylation (**Figure 1b,c,d**). The C3 isopropyl group participates in hydrophobic interactions with the face of U2585, but it otherwise appears to lack binding interactions, suggesting that modifications off of this position would be tolerated. Similarly, the C4 methyl group does not appear to make binding interactions and is angled towards the group B streptogramin binding site in the exit tunnel. In the resistance enzyme VatA (PDB ID: 4HUS), by contrast, mutagenesis and crystallography revealed how contacts between binding site residues (Val61, Ile62, Met107, and Pro108) and the C3 isopropyl group, the C4 methyl group, and the C6 proton are required for drug deactivation by acetylation[10] (**Figure 1e,f**). Structural modifications to these positions might disrupt VatA binding and overcome Vat resistance, but only one semisynthetic streptogramin with modifications at one of these locations has been reported, resulting from hydrogenation of the C5-C6 double bond[10,23]. Broader semisynthetic modifications of these positions are restricted by the lack of proximal functional groups for chemoselective activation. These analyses suggested that modifications to the C3 and C4 groups on **VM2** might disrupt binding to VatA while maintaining ribosomal activity.

Modular synthesis enables access to a diverse library of group A streptogramin analogs

To directly test the hypothesis that structural modifications at these positions could overcome resistance to Vat enzymes, we first developed a pipeline for the synthesis of group A streptogramins possessing unprecedented structural diversity. Our route to group A streptogramins (e.g., **VM2** in **Figure 2a**) comprises the convergent assembly of seven simple, individually diversifiable chemical building blocks, enabling a high level of flexibility in the generation of analogs by building block exchange[16]. Before outlining the details of our synthesis, our general design strategy merits brief discussion: We synthesize two halves of similar complexity; the halves are joined by amide bond coupling, and macrocyclization is accomplished by means of a Stille cross-coupling reaction. Removal of the silyl groups is the only step required after macrocyclization to complete the synthesis. Overall, the route is seven linear steps (11 total steps) from the starting building blocks, facilitating rapid generation of analogs. Importantly, the synthesis of the left and right halves are highly scalable. By pooling decagram quantities of each half, we are able to rapidly synthesize analogs with modifications on the complimentary half without repeating the entire synthesis. This benefit of convergency enables new building blocks to be incorporated in seven total steps, provided sufficient quantities of the complementary half are available.

We first applied our strategy to the natural product virginiamycin M2 (**VM2**), which serves as the parent scaffold for the present study (**Figure 2a**). There are several notable modifications and improvements compared to our original report[16]. The synthesis of the left half (**13**) proceeds in 74%

overall yield from building blocks **7** and **8**. Our previous synthesis delivered the right half (**19**) in three steps and 42% overall yield from **14** and **15**, but we found that purification of **19** was challenging on >1-g scale due to the presence of several contaminants including unreacted thiazole **18**, cleaved thiazolidinethione auxiliary, and a byproduct resulting from nucleophilic ring opening of the thazolidinethione present in **17**. We avoided this complication by first converting **17** to a Weinreb amide[24] followed by treatment with the dianion of oxazole **18** to deliver right half **19**. Although this operational change adds a step, it results in higher overall yield (90% over 2 steps compared to 71% over one step) and simplifies purification of **19**. The two halves are coupled by means of HATU in the presence of Hünig's base in 91% yield, and the resulting macrocycle precursor **20** is cyclized in the presence of $Pd_2(dba)_3$ and JackiePhos[10] (65% yield on 1-g scale). Removal of the silyl groups with buffered tetrabutylammonium fluoride delivers virginiamycin M2 (**VM2**) in 90% yield. The yields of these three final steps improved with the larger scales used in this study (all reactions conducted on >1 mmol scale). The modified synthesis of **VM2** proceeds with an overall yield of 40% through the left half sequence and 28% yield through the right half sequence, and is seven linear steps in each case.

We next sought to systematically modify structural features of group A streptogramins by exchanging building blocks. To inform structure–activity relationships, we varied positions on the scaffold that had not previously been explored with semisynthetic approaches, such as the C3 and C4 positions. We prioritized building blocks that were readily available, would be compatible with the chemistry for assembly, and would avoid steric clashes in the binding site. We were readily able to prepare 18 streptogramins by building block variation, including the natural products virginiamycin M2 (**VM2**, parent scaffold), virginiamycin M1 (**VM1**), madumycin I (**33**), and madumycin II (**34**, **Figure 2b**). The overall yields for each analog from the starting building blocks are displayed in blue for the left half sequence (top) and right half sequence (bottom). The template synthesis of **VM2** (**Figure 2a**) was used directly or with trivial modifications (e.g., addition of a deprotection step for a Boc or PMB group) in most cases to deliver analogs in good yield (10-40% overall). For certain analogs, overall efficiency was impacted by functional group incompatibilities with the chemistry for assembly. For example, the Stille reaction en route to analog **21**, which contains a monosubstituted alkene, proceeded in low yield (20%). In rare cases, a substantially modified route was required to complete the synthesis, exemplified by the oxadiazole-containing analog **28**, which was assembled with a 6-step route to the right half to accommodate the instability of the oxadiazole in strongly basic conditions (see Supporting Information for details).

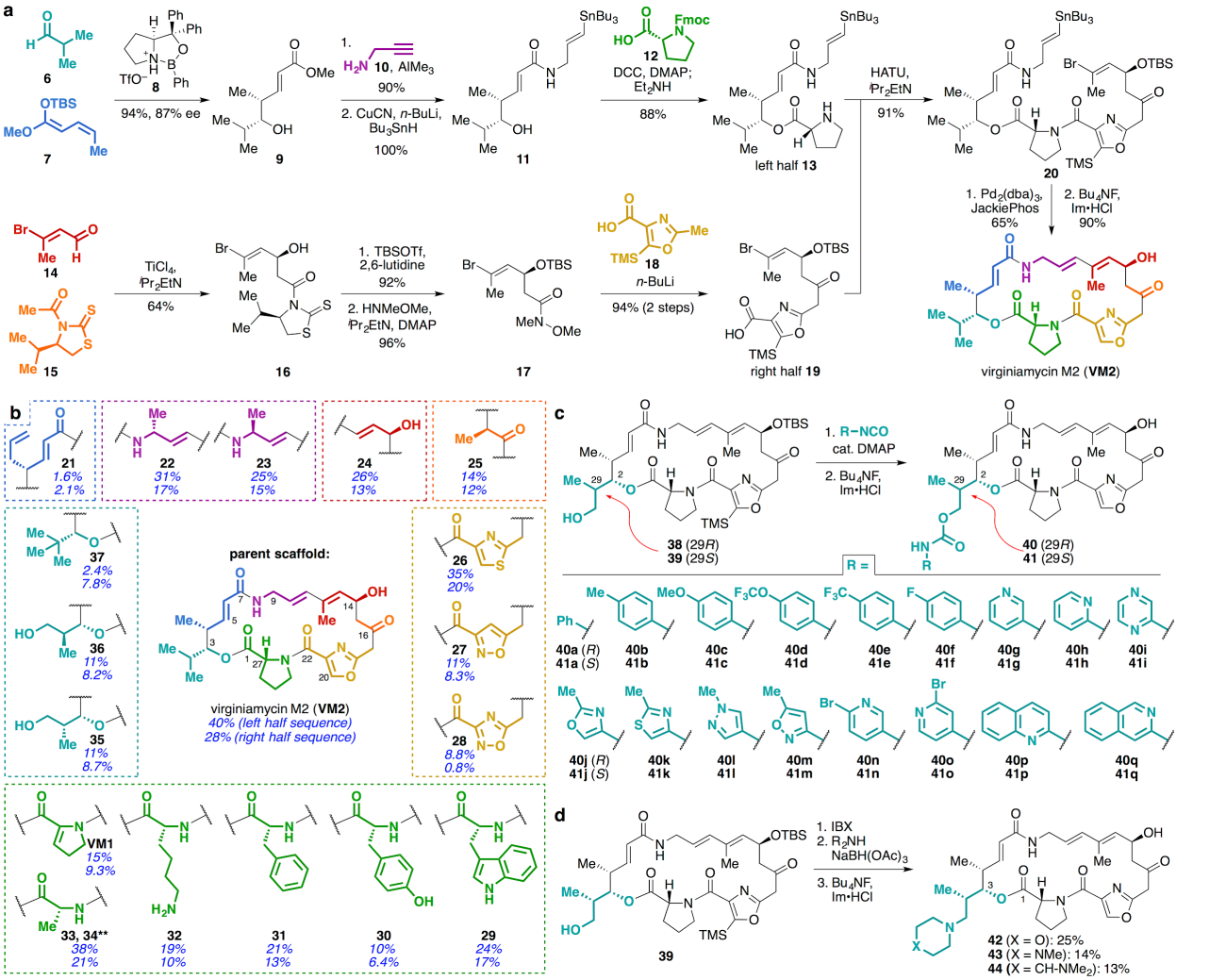


Figure 2 | Modular synthesis enables access to >60 fully synthetic group A streptogramins. a, Convergent route to **VM2** from seven building blocks, slightly modified from reference[16]. This route serves as the template for the synthesis of analogs herein, with route modifications when necessary to accommodate unusual building blocks. **b**, Eighteen group A streptogramins accessed by building block variation. The fragments displayed in the dashed boxes represent the structural variability within each analog compared to the parent scaffold (**VM2**, center). Overall yields for the synthesis of each analog are displayed for the left half sequence (top number) and for the right half sequence (bottom number). ** Instead of a ketone, madumycin II (**34**) contains the following substitution at C16: α-H, β-OH. **c**, Access to 34 analogs (17 in each diastereomeric series) with variability on the C3 side chain by means of carbamate formation followed by desilylation. **d**, Synthesis of tertiary-amine containing analogs by oxidation and reductive amination.

The incorporation of modified building blocks represents an effective approach to access novel analogs, but this approach is burdened by a requisite multistep synthesis for each new analog. In order to efficiently increase the diversity of our library, we incorporated building blocks with functional groups that serve as handles for late-stage diversification. By means of example, replacement of isobutyraldehyde (**7**) with para-methoxybenzyl-protected (*R*)- or (*S*)-3-hydroxy-2-methylpropanal in the left half sequence enabled access to C3-isopropyl-modified analogs **38** and **39** (**Figure 2c**, >1 g

of each prepared). Each of these alcohol-appended streptogramins was allowed to react with 17 commercially available arylisocyanates in the presence of catalytic DMAP followed by subsequent desilylation with buffered fluoride. Thus, from two building block substitutions we were able to access 34 novel streptogramin analogs with arylcarbamate side chains at the C3 position (**40a-q** and **41a-q**). The alcohols in **38** and **39** also served as effective precursors for the installation of secondary amines by oxidation/reductive amination (**42**-**44**, **Figure 2d**) and for incorporation of fluorine by treatment with diethylaminosulfur trifluoride (see Supporting Information). Additionally, we were able to install a fluorine at C16 by a 4-step sequence (see Supporting Information), providing the clinical candidate flopristin (**4**) and several fluorinated analogs (*vide infra*).

Targeted modifications at C3 and C4 show promise against VatA resistance

Our platform has provided 62 new group A streptogramin analogs, four natural products, and the first fully synthetic sample of the clinical candidate flopristin (**4**). We evaluated the activity of each analog against a strain of *S. aureus* expressing the VatA resistance protein[10], using wild type (WT) *S. aureus* (ATCC 29213) as a comparator (**Figure 3a** and **Extended Data Figure 2**). Several structural modifications proved deleterious to activity in both strains. For example, installation of a methyl group at C9 (**23**) or a primary or tertiary amine (**32** and **42**, respectively) resulted in complete loss of activity in WT *S. aureus*. Removal of the C12 methyl group (**24**) also resulted in loss of activity, which may provide biological rationale for the four additional biosynthetic steps required for its installation by means of a SAM methylase[25]. Some structural modifications resulted in no statistically significant change in activity, such as the replacement of the oxazole heterocycle with a thiazole (**45**). Certain modifications to the C3 and C4 side chains, however, granted increased activity against WT and VatA-expressing *S. aureus*. The C4-modified, C29-(*R*) analogs **40e** and **40q** had 2-4-fold decreases in minimum inhibitory concentrations (MIC) against WT *S. aureus* (16 → 4-8 μg/mL) and >4-fold decreases in MICs against the VatA strain (>64 → 16 μg/mL). Interestingly, the C29-(*S*) diastereomer **41q** showed improved activity in WT *S. aureus* (>64 → 8 μg/mL) but was inactive (>64 μg/mL) against the VatA strain, suggesting that the stereochemistry at C29 plays an important role in avoiding Vat resistance. The C4 allyl-containing analog **21** also showed significant improvements in both WT and VatA strains. Further decreases in MIC values were achieved by installing a fluorine at C16, which had previously been shown to improve activity of the semisynthetic streptogramin flopristin (**4**). Thiazole-containing C16-fluoro analog **45** displayed identical activity to flopristin (0.5 μg/mL in WT, 8 μg/mL in VatA). Notably, C3-modified, C16-fluoro analog **46** showed a 2-fold improvement of activity in the WT strain (4 → 2 μg/mL) and a 16-fold improvement in the VatA strain (16 → 1 μg/mL). It is interesting to note that the activity of this analog in the streptogramin-resistant strain is actually better than its activity in the WT strain. Finally, C4-allyl, C16-fluoro analog **47** exhibited a 32-fold decrease

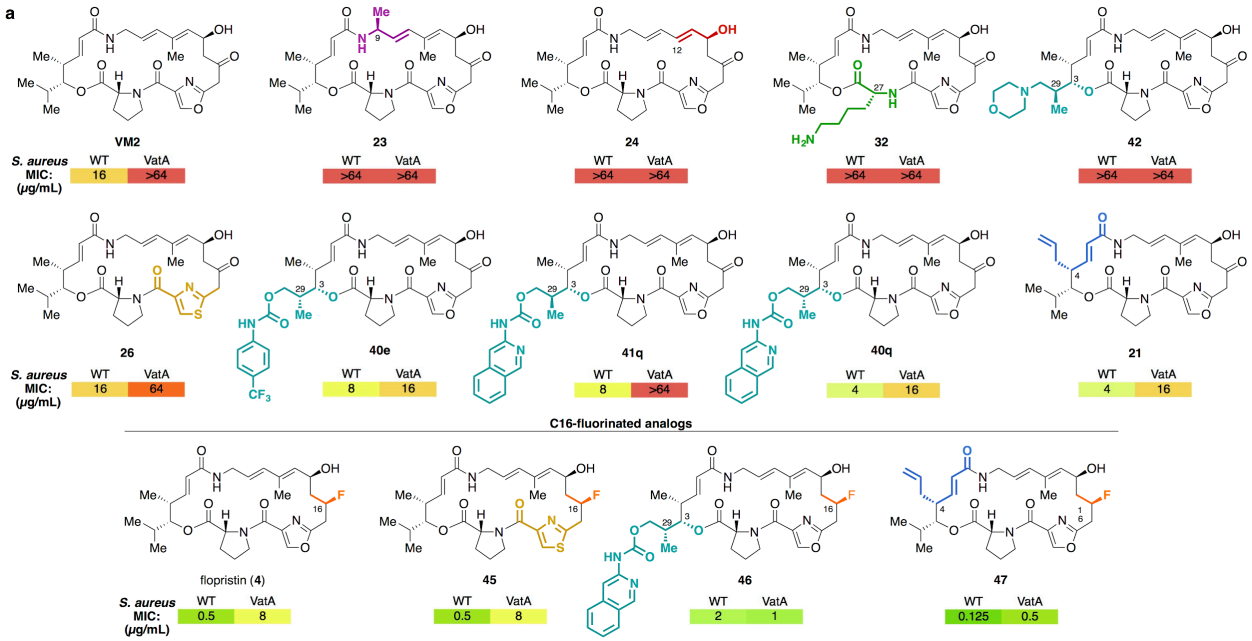
in MIC against both the WT strain (4 → 0.125 μg/mL) and the VatA strain (16 → 0.5 μg/mL). Taken together, these results support the structure-based hypothesis that modifications to C3 and C4 of the group A streptogramin scaffold can overcome resistance caused by Vat proteins. It is likely that modification at these two positions is very difficult to acquire within the biosynthetic pathway of these macrocycles[25], potentially explaining the lack of natural streptogramins with C3 and C4 extensions.

Expanded antibacterial evaluation and *in vitro* analysis of ribosome inhibition and VatA acetylation

To further explore the activities of our fully synthetic group A streptogramins, we tested each of our analogs against a panel of 20 bacterial pathogens (**Figure 3b** and **Extended Data Figures 3 and 4**), including three strains with well-characterized mechanisms of resistance to the class (VatA and Cfr in *S. aureus*, ABC-F in *E. faecalis*). Additionally, we measured cell-free inhibitory activities for selected analogs using an *in vitro* translation (IVT) assay at 10 μM. Despite significantly improved activity in WT and VatA *S. aureus*, non-fluorinated analogs **26**, **40q**, and **21** displayed approximately equal activity to virginiamycin M2 (**VM2**) in *E. faecium* and *S. pneumoniae*. analogs **23**, **24**, **32**, and **42** had little to no cellular activity in all strains, but interestingly, **42** inhibited translation *in vitro* as effectively **VM2**. The poor cellular activity likely results from decreased entry or increased efflux, highlighting the challenge of designing antibiotics with both high on-target activity and high cellular accumulation[26]. C16-fluorinated analogs **45**, **46**, and **47** displayed increased potency compared to their non-fluorinated counterparts against most strains, which was accompanied by improved inhibition of translation *in vitro*. Notably, the C4-allyl, C16-fluoro analog **47** was more potent than flopristin (**4**) in many strains and showed moderate activity (32 μg/mL) against *E. faecalis*, which intrinsically expresses ABC-F proteins[8,27] that mediate high-level resistance to group A streptogramins. Furthermore, although Gram-negative pathogens are usually highly resistant to streptogramins, **47** had moderate activity against *E. coli* (16 μg/mL).

We were interested in the ability of our streptogramin analogs to synergize with group B streptogramins, which has been shown to greatly improve activity against many Gram-positive pathogens and, in some cases, grant bactericidal activity[7]. It is conceivable that modifications that improve the activity of the group A component would be deleterious for synergy with the B component. Conversely, it is possible that modifications that do not increase the activity of a single component could bolster synergy. We measured the activity of virginiamycin S1 (**VS1**) against the panel of pathogens in the presence and absence of its natural partner, **VM1**. Unsurprisingly, the combination of **VM1** and **VS1** (7:3 weight by weight, the ratio naturally produced by *Streptomyces* spp.[6]) was significantly more potent than **VS1** alone against strains that do not harbor resistance mechanisms to either component. We were delighted to find that the combination of C3-modified **46** or C4-modified **47** with **VS1** resulted in improved activity in many strains, and in many cases growth was completely

inhibited even at the lowest concentration tested (0.06 μg/mL). In *E. faecalis*, an organism that is inherently resistant to group A streptogramins, significant reductions in MIC were observed for the **46**/**VS1** combination (>64, 2 μg/mL → 0.5 μg/mL) and the **47**/**VS1** combination (32, 2 μg/mL → 0.25 μg/mL). These results showcase the utility of synergistic streptogramin combinations and demonstrate that modifications to the group A streptogramin scaffold can facilitate improved activity of the combination.



	kcat (s^{-1})	K_{half} (mM)	IC_{50}
VM2	10.3 ± 0.6	0.026 ± 0.004	3.87 ± 0.1
4	6.1 ± 0.2	0.011 ± 0.001	3.79 ± 0.05
40q	8.3 ± 0.4	0.031 ± 0.004	3.9 ± 0.2
46	5 ± 1	0.01 ± 0.01	3.66 ± 0.04
47	4.7 ± 0.2	0.009 ± 0.001	2.8 ± 0.1

Figure 3 | Antibiotic activity and VatA acetylation rates of selected group A streptogramins. a, MIC values for 10 fully synthetic group A streptogramins against two strains of *S. aureus*. "WT" denotes ATCC 29213, "VatA" denotes VatA-expressing strain[10]. Structural differences compared to **VM2** are highlighted by building block according to the color scheme in Figure 2. **b**, MIC values against an expanded panel of pathogens for the analogs in panel (**a**) and for combinations with the synergistic group B streptogramin **VS1**. *In vitro* translation data for each analog or combination at 10 μM is shown in the bar chart to the right of the table relative to a DMSO control. **c**, *In vitro* acetylation rates of selected analogs by VatA. **d**, Summary of *in vitro* acetylation by VatA and inhibition of the *E. coli* ribosome.

To assess the origins of the increased potency of several of our analogs, we measured the *in vitro* translation inhibition for these compounds using the *E. coli* ribosome. We observed only subtle changes in IC50 (**Figure 3d**), suggesting that the major effects are due to other factors such as improved accumulation inside the bacteria or reduced binding to resistance proteins. Next, to determine the effect of structural modifications on deactivation by VatA, we measured the rate of C14 acetylation using purified VatA for **VM2**, flopristin (**4**), and three analogs (**40q**, **46**, **47**) (**Figure 3c,d**). **VM2** is rapidly acetylated *in vitro* (kcat = 10.3 s^{-1}), which likely accounts for its lack of activity in the VatA-containing strain of *S. aureus*. Flopristin (**4**) and C3-modified **40q** are acetylated at a slightly decreased rate compared to **VM2** (kcat = 6.1 and 8.3 s^{-1}, respectively). The fluorinated analogs **46** and **47** are significantly worse substrates for acetylation (kcat = 5 and 4.7 s^{-1}, respectively). This ~2-fold reduction in acetylation rate is unlikely to completely account for the >64-fold reduction in MIC in the VatA expressing strain of *S. aureus*. It is likely that decreased acetylation, increased ribosomal inhibition, and altered cellular accumulation all contribute to the dramatically improved activity.

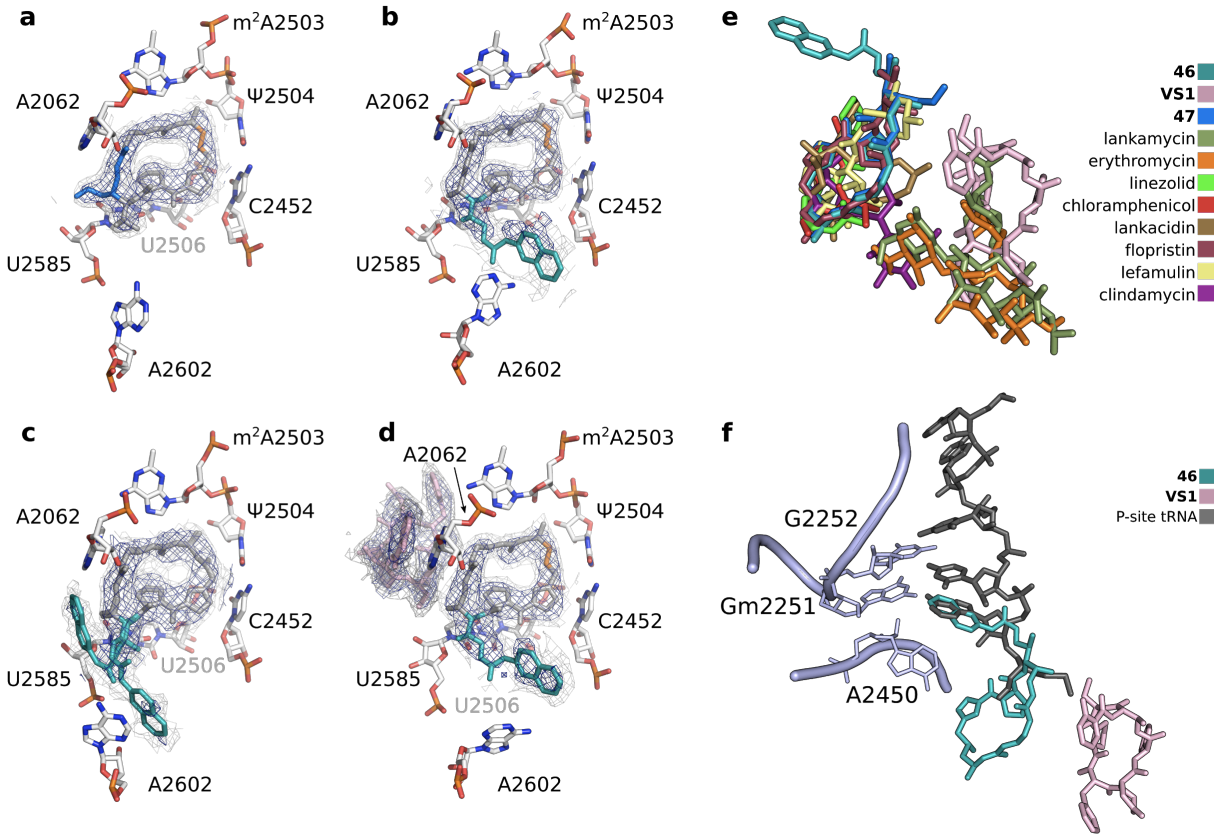
Ribosome-bound structures of modified compounds

To gain insight into the structural basis for antimicrobial activity, we characterized the binding of several of our analogs to the *E. coli* ribosome using CryoEM (**Figure 4** and **Extended Data Figure 5 and 6**). The PTC is highly conserved across pathogenic species of bacteria, and the *E. coli* ribosome has been shown to be a good model for group A streptogramin binding in both Gram-negative organisms and Gram-positive organisms such as *S. aureus*[5]. Compared to **VM2**, analogs **46** and **47** have extensions off of C3 and C4 on the macrocycle, respectively. The 2.6-Å structure of analog **47** bound to the ribosome clearly reveals the position of the C4 allyl extension, which points towards the streptogramin B binding site in the exit tunnel (**Figure 4a**). This extension appears to make contacts with A2062 and with the ribose residues U2585 and U2586. Modeling this conformation of **47** into the VatA crystal structure reveals a steric clash that explains its reduced preference as a substrate (**Extended Data Figure X1a**).

Predicted low energy conformations of **46** position the arylcarbamate extension directly over the macrocycle (**Extended Data Figure 7**); however, the the 2.5-Å structure of **46** showed density for the extension reaching into peptidyl tRNA binding site (P-site, **Figure 4b**). The isoquinoline portion of the side chain sits between A2602 and C2452, although it does not appear to make specific contacts with either of these residues. The proximity of C29 on the side chain to U2585 may explain the difference in activity between the two diastereomeric series (**40a-q** and **41a-q**) at this position. Consistent with this idea, the structure of **41q** had poor density for the extension and was modeled in multiple conformations (**Figure 4b**). Similarly, structures with distinct side chains (**40e, 40o**) had poorer density in the P-site (**Extended Data Figure 5**). In addition, **41q** has poor activity against the strain expressing VatA (**Figure 3a**), further reflecting the importance of this stereocenter for binding to both

targets. Interestingly, unlike **47,** the modeled position of **46** doesn't clash with VatA when superposed in the crystal structure (**Extended Data Figure 8**). However, the low energy conformations that position the side chain over the macrocycle lead to multiple clashes with VatA (**Extended Data Figure 8**). Collectively, these results suggest that the ligands adopt distinct conformations when bound to the ribosome and or VatA. Future efforts to increase effectiveness against the ribosome and decrease binding to VatA will likely be highly dependent on the stereochemistry and rigidity of the arylcarbamate extension. Finally, we characterized the structure of a potent complex, containing **46** and group B streptogramin **VS1 (Figure 4d)**. This structure reveals that A2062 is sandwiched between C5-N8 of **46** and the hydroxypyridine group on **VS1**, as observed previously by crystallography[6,17,20]. The positioning of the arylcarbamate side chain in the **46/VS1** co-bound structure is identical to its position when only **46** is bound, indicating a strong preference for its projection into the P-site in both the presence and absence of the group B streptogramin component.

The bacterial PTC is a privileged binding site for antibiotics, including oxazolidinones (e.g., linezolid), lincomycins (e.g., clindamycin), phenicols (e.g., chloramphenicol), pleuromutilins (e.g., lefamulin), and many others (e.g., lankacidin) (**Figure 4e**). It is striking that the arylcarbamate side chain in **46** and the allyl side chain in **47** do not significantly overlap with other ligands and that they maintain synergy with **VS1**. The position of the arylcarbamate side chain in **46** extends into the P-site (**Figure 4f**). By overlaying the 5-terminal bases of P-site bound tRNA into the structure with **46** and **VS1** bound to the catalytic center (from PDB 1VY4[28]), we discovered that the isoquinoline group in **46** overlaps substantially with the terminal adenosine that is conserved in all tRNAs. Only the non-selective inhibitor blasticidin, which inhibits both eukaryotic and prokaryotic ribosomes, binds this deeply into the P-site by mimicking the cytosines in the CCA tail[19]. To the best of our knowledge, no other antibiotics that mimic the terminal adenosine have been reported. It is likely that the 23-membered macrocyclic core of the group A streptogramins will provide a basis for selectivity for prokaryotic ribosomes over eukaryotic ribosomes which has not been achieved by tRNA mimics such as blasticidin. Further optimization of the C3 side chain, guided by CryoEM structure determination, may provide a new avenue into extremely potent, selective inhibitors of bacterial protein synthesis.



370 **Figure 4 | High resolution CryoEM reveals occupancy of a novel antibiotic binding pocket. a,** 2.5-Å CryoEM Coulomb potential density map (contoured in dark blue at 4.0 and light gray at 1.0) for ribosomes bound to **47** reveal an extension towards the VS1 binding site. **b,** 2.5-Å CryoEM Coulomb potential density map for ribosomes bound to **46** reveal that the side chain extends towards A2602; base U2506 is hidden behind the arylcarbamate side chain. **c,** 2.6-Å CryoEM Coulomb potential density map for ribosomes bound to **41q** reveals
375 poor density for the side chain and is modeled in dual conformations with equal occupancy. **d,** 2.7-Å CryoEM Coulomb potential density map for ribosomes bound to **46** and **VS1** show tight packing of both compounds around A2062. **e**, An overlay of known PTC-site antibiotics shows how the side chain of **46** and the extension of **47** occupy areas distinct to previously characterized antibiotics. The compatibility of **47** with **VS1** (Figure 3b) suggests that the area between these two compounds is a site for future optimization. **f**, The side chain of **46**
380 extends into the P-site and mimics the terminal A of the P-site tRNA.

Conclusion

By combining modular chemical synthesis, antibacterial evaluation, *in vitro* analysis, and high-resolution cryo-electron microscopy, we have developed a pipeline for the synthesis and optimization
385 of group A streptogramin antibiotics. Our approach enabled the preparation of >60 novel analogs by means of building block variation and late-stage diversification, providing valuable structure–activity relationships for the class. Moreover, this work highlights how cryoelectron microscopy is contributing to the elucidation of structure activity relationships[29,30]. Modifications at two previously unexplored positions on the scaffold resulted in the first members of the streptogramin class to overcome
390 resistance caused by virginiamycin acetyltransferase enzymes. These C3- and C4-modified analogs

can serve as templates for optimization of both group A streptogramins and other PTC-binding antibiotics, potentially leading to candidates that overcome resistance caused by binding site modifications such as methylation of A2503 by Cfr methylase. An analogy can be drawn to ketolides, such as telithromycin and solithromycin, which possess biaryl side chains that enhance activity against ribosomes modified by erythromycin methyltransferases (erm resistance) at residue A2058 in the exit tunnel[31]. Although emergence of other resistance mechanisms is inevitable, this approach may permit chemical adaptations to extend the clinical longevity of the streptogramin class.

Acknowledgements

We thank Fred Ward and Jamie Cate for initial advice on ribosome purifications and translation assays, Eva Nogales and a UCSF-UCB Sackler Sabbatical Exchange Fellowship (J.S.F.) for initial CryoEM access and training. A.A.T. and J.P. were supported by the National Science Foundation Graduate Research Fellowship Program under Grant No. 1650113. This project was funded by the UCSF Program for Breakthrough Biomedical Research, funded in part by the Sandler Foundation (J.S.F. and I.B.S.), a Sangvhi-Agarwal Innovation Award (J.S.F.), Packard Fellowships from the David and Lucile Packard Foundation (J.S.F. and I.B.S.), NIH GM123159 (J.S.F.), and NIH GM128656 (I.B.S.). We thank Alex Myasnikov and David Bulkley for technical support at the UCSF Center for Advanced CryoEM, which is supported by NIH grants S10OD020054 and S10OD021741 and the Howard Hughes Medical Institute (HHMI). We thank Ed Eng and Elina Kopylov for technical support at the National Center for CryoEM Access and Training (NCCAT) and the Simons Electron Microscopy Center located at the New York Structural Biology Center, which is supported by the NIH Common Fund Transformative High Resolution Cryo-Electron Microscopy program (U24 GM129539,) and by grants from the Simons Foundation (SF349247) and NY State.

Author Contributions

Q.L. and I.B.S. determined analogues for synthesis and designed the synthetic routes; Q.L. executed and optimized the syntheses of analogues, with assistance from A.A.T. (analogues **29**–**32**), R.W. (analogue **21**), K.J. (analogues **27** and **28**), and D.C. (analogue **26**); J.P. and D.J.L. prepared samples and collected CryoEM data; J.P. and A.F.B calculated CryoEM reconstructions; J.E.P. and J.P. performed the VatA acetylation assay; G.v.Z. and K.B. developed new tools for cryoEM model refinement; J.P., K.B., and J.T.B performed cryoEM model refinements; G.v.Z., N.Z., and M.P.J. determined relative energies of macrocycle confirmations; D.S., C.W., and B.M. designed and executed the MIC assays; Q.L., J.P., I.B.S., and J.S.F. wrote the manuscript. All authors discussed the results and commented on the manuscript.

Methods

Minimum Inhibitory Concentration (MIC) testing

Compounds were evaluated by Micromyx LLC for Minimum Inhibitory Concentration (MIC) activity against a variety of Gram-negative and Gram-positive pathogens, using the broth microdilution method as recommended by the Clinical and Laboratory Standards Institute (CLSI). Pre-weighed vials of the test agents were stored at -20°C until testing. On the day of the assay, the compounds were dissolved in 100% DMSO (Sigma 472301, Lot No. SHBH5551V) to a stock concentration of 6,464 µg/mL. The concentration range tested for each of the compounds was 64–0.06 µg/mL, and each compound was tested in triplicate. Levofloxacin was used as the quality control agent. For more details on test organisms, media, and methods, see the Supporting Information.

In vitro translation assays

The ability of novel group A streptogramin analogs to inhibit the 70S *E. coli* ribosome was tested *in vitro* using the PURExpress® *In Vitro* Protein Synthesis Kit (NEB), murine RNAse inhibitor (NEB), and 10 ng/µl of template DNA encoding the fluorescent protein mEGFP. The volumes of each component in the reaction mixture were scaled down 5-fold from the NEB protocol for a final reaction volume of 5 µL. analogs were either initially screened at a concentration of 10 µM, with a final concentration of 10% DMSO. To measure the IC_{50}, measurements at concentrations between 0.01 and 80 µM in 10% DMSO were performed. All reactions were performed in triplicate. Translation reactions were carried out at 37°C for 1 hour. To assist in the transfer of reactions to 96-well half-area NBS microplates (Corning 3993) for final measurements, the volume was increased to 50 µL by adding buffer C (20 mM Tris-HCl pH 7.5, 60 mM NH_4Cl, 6 mM $MgCl_2$, 0.5 mM EDTA). mEGFP was excited at 485 nm; its emission was recorded at 535 nm. For comparison of analog activities across multiple initial screens, fluorescence readouts were normalized to the blank. The IC_{50} was interpreted by fitting the dose response curve to the following equation, where *Top* and *Bottom* are the values of the plateaus and *H* is the Hill slope: $Y = Bottom + (Top - Bottom) / (1 + (X^H / IC_{50}{}^H))$.

VatA acetylation assay

Acetylation assays were performed in 96-well clear polystyrene flat-bottom NBS plates (Corning 3641) at 50 µL of 50 mM Tris-HCl pH 8.0, 1 mM acetyl-CoA (AcCoA), 53 nM enzyme, and analog ranging from 0 - 1 mM[10,32] which contributed a final ethanol concentration of 2% per reaction. Analogs were diluted from stock solutions prepared at 35 mM compound in 80% ethanol. Reaction mixtures were incubated at 37°C for 10 min and then quenched with 50 µL of stopping solution (100 mM Tris-HCl pH 8.0 and 6 M guanidine HCl). To measure the amount of CoA generated as a byproduct of acetylation, 200 µL of 0.2 mM 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB; Ellman's Reagent), 100 mM Tris-HCl pH 8.0, and 1 mM EDTA were added to the reaction mixtures, which were then incubated at room temperature for 10 min. DTNB reacts 1:1 with the free sulfhydryl of CoA, producing the yellow

TNB, which was measured at 415 nm using a Tecan Spark 10M plate reader. The quantity of CoA produced was determined relative to a CoA standard curve prepared in duplicate. All reactions were carried out in duplicate and corrected against a blank containing enzyme and AcCoA without substrate, as well as corresponding absorbances from a control plate using identical assay conditions without enzyme to detect spontaneous hydrolysis of AcCoA. The reactions lacking enzyme were also corrected against a blank with AcCoA without enzyme nor substrate. VatA activity was measured at µmol CoA/min/mg enzyme. Kinetic information was derived using *scipy.optimize.curve_fit* to fit the data to the allosteric sigmoidal model: $Y = Vmax * X^H / (Km^H + X^H)$, where *H* is the Hill slope.

CryoEM data collection and image processing

All images were collected using 400 mesh 1.2/1.3 or 400 mesh 2/2 Cu Quantifoil grids with purified ribosomes from *E coli* strain MRE600[33]. All data sets were collected on Titan Krios electron microscope (FEI) instruments operating at 300 kV, located at either UCSF or NCCAT, with the exception of **40q**, which was collected on a Talos Arctica electron microscope (FEI) at UCSF operating at 200 kV. Automated data collection at UCSF was facilitated by SerialEM[34]; collection at NCCAT was via Leginon[35]. All images were collected on K2 summit direct electron detectors (Gatan). Pixel sizes, number of images in dose-fractionated micrographs, dose rates, and defocus ranges varied slightly and are reported in Table 1. Images acquired at UCSF were on-axis, while those collected at NCCAT used a four-shot beam-image shift approach with coma compensation[36]. All image stacks were collected in super-resolution mode.

CryoEM data processing

Super-resolution image stacks were binned by a factor of 2, corrected for beam-induced motion, and dose-weighted using MotionCor2.[37] All structures were generated in cisTEM using dose-weighted micrographs. CTF parameters were determined using CTFFIND4, included as part of the cisTEM package, with the resolution range between 30 and 4 Å included in the fitting. Bad micrographs were excluded from processing through visual inspection. Particles were picked in cisTEM by matching to a soft-edged disk template with a maximum particle radius of 110 Å and a characteristic particle radius of 90 Å. The number of particles picked from all micrographs and from good micrographs are found in Table 1. CisTEM refinement packages were made using a particle molecular weight of 1800 kDa. Particles were 2D-classified into 50 classes with a mask radius of 150 Å. Classes containing the 50S ribosome were carried forward into single-class auto refinement with an outer mask radius of 125 Å and a default starting resolution of 20 Å. A filtered volume was used to make a binary mask; Chimera's volume eraser tool was used to exclude the mobile L1 stalk from the mask. This mask was used in single-class manual refinement with a final high-resolution limit of either 3.50 or 3.00 Å (see Table 1). Unsharpened maps were used in model refinement and for all figures.

Model building and refinement with OPLS3e

We used chimera to rigid body align a high resolution X-ray structure of the *E. coli* ribosome (PDB ID: 4YBB[38]) into our maps. Initially, the ligand restraints files (CIF files) were generated with *phenix.eLBOW*[39] using the analog's SMILES string and a "final geometry" reference pdb of the analog that was derived from the pose of flopristin bound to the *E. coli* ribosome (PDB ID: 4U20[6]). These ligands were superimposed into 4YBB based on the binding pose of flopristin in 4U20, and manual edits to the surrounding structure were performed in Coot.

After constructing these initial models, structures were refined using *phenix.real_space_refine* using the default protocol, initially with CIF restraints files from *phenix.eLBOW*. These resulted, however, in non-physical high energy conformations of the ligands (Extended Data Y1). To improve the models of the ligands, we used a new version of `phenix.real_space_refine` interfaced with the OPLS3e/VSGB2.1 force field, a high quality force field for ligands [40]. This approach allows obtaining physics based energies and gradients for either the whole or part of the structure without resorting to accurate manual CIF restraint generation. Standard PHENIX restraints were used for the macromolecule, while the ligand was governed by the OPLS3e/VSGB2.1 force field. Precisely, the unliganded complex and ligand were individually prepped using `phenix.ready_set` and `prepwizard`, respectively, and subsequently recombined. The recombined complex served as input for refinement using the additional Schrodinger dependent options `use_schrodinger=True maestro_file=ligand.mae schrodinger.selection="resname LIG"`, where `ligand.mae` describes the ligand structure in Maestro format and `LIG` is the residue 3-letter code, and otherwise default parameters. The PHENIX - OPLS3e/VSGB2.1 interface works as follows: the PHENIX refinement engine spawns an external process serving as an energy server, initialized with the ligand structure present in the provided `maestro_file` option. When the refinement engine requests energies and gradients, the ligand's internal coordinates are written to file and read in by the external server. After updating ligand coordinates on the server side, the energy and gradients are calculated and exchanged with the refinement engine. The refinement engine on its side updates the ligand energy and gradients contribution in its energy function using a default weight factor of 10 for the OPLS3e/VSGB2.1 energies. Refinement with the OPLS3e/VSGB2.1 force field reduced the energy for all ligands compared to the conformations refined using CIF based restraints calculated by *phenix.eLBOW* **(Extended Data Table 1**).

For all figures, the full, unsharpened density maps and full pdb models were boxed using *phenix.map_box* with a selection radius of 20 Å around the ligand. Boxed map and model were loaded into PyMol with *set normalize_ccp4_maps, off*. Maps were contoured at 4 for tight density (dark blue) and 1 for loose density (light gray), both centered around the ligand with a carve of 1.8.

QM calculations

Calculations were based on the scaffold of flopristin (**4**) from the crystal structure bound to the ribosome[6]. Compound **46** was constructed using LigPrep tool of Maestro (Schrodinger Inc.). First, the macrocycle conformation sampling method[41] was validated by comparison to the low energy pose as that of the co-crystal structure of flopristin (**4**). By using the thorough sampling intensity strategy, 1000 conformations of **46** were obtained, and the lower prime energy pose with the RMSD <2 Å (scaffold atoms of **4** as reference atoms) was regarded as the preferred conformation. Finally, the C3 side chain of this preferred conformation was further optimized using Jaguar software[42] by imposing the constraints on the scaffold atoms.

Code Availability

Forcefield-based refinement is available in Phenix (versions 1.15 and later) using beta features available in Schrodinger 2019-3. Python code for analyzing IVT data and VatA data are available on github: https://github.com/fraser-lab/streptogramin

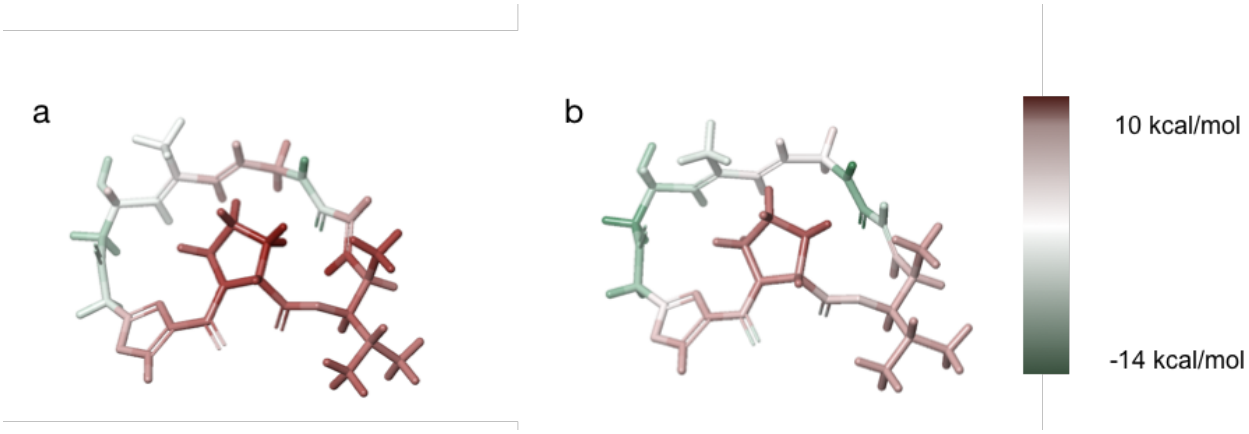
Data Availability

Models and maps generated during this study are available in the EMDB and PDB (accessions are listed in Table 1). We plan to upload all raw data to EMPIAR.

Extended Data

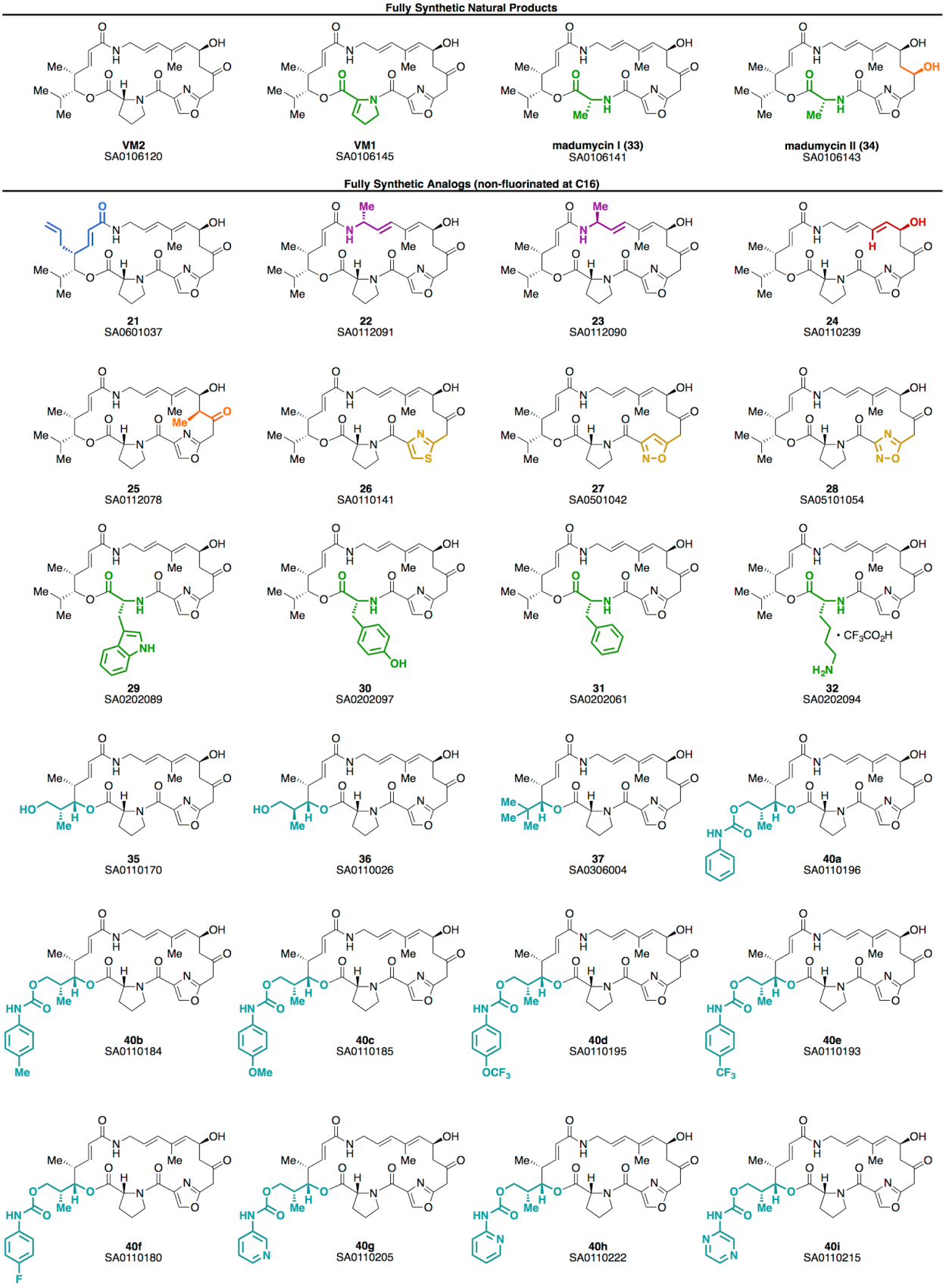
Extended Data Figure 1 - Conformational strain comparison of VM2 with different refinement protocols.

Conformational energy of VM2 showing contributions on a per atom basis when refined with PHENIX interfaced with OPLS3e/VSGB2.1 force field (left) and standard CIF based restraints (right). Color indicates low strain (green, -14 kcal/mol) up to high strain (red, 10 kcal/mol), with total conformational energy of -88.3 (left) and 39.5 kcal/mol (right). Hydrogens were added and optimized with fixed heavy atoms for the CIF based refined conformation using `prepwizard`; the PHENIX-OPLS3e/VSBG2.1 refined conformation was taken as is. Energies were calculated using Prime and per atom contribution visualized using Maestro's Prime Energy Visualization.



Extended Data Figure 2: List of streptogramins tested for inhibitory activity (Page 1 out of 3)

A comprehensive list of all streptogramin antibiotics that were tested for inhibitory activity against 21 strains of bacteria (see **Extended Data Figures 3 and 4**). All compounds except for **VS1** are fully synthetic.



Extended Data Figure 2: List of streptogramins tested for inhibitory activity (Page 2 out of 3)

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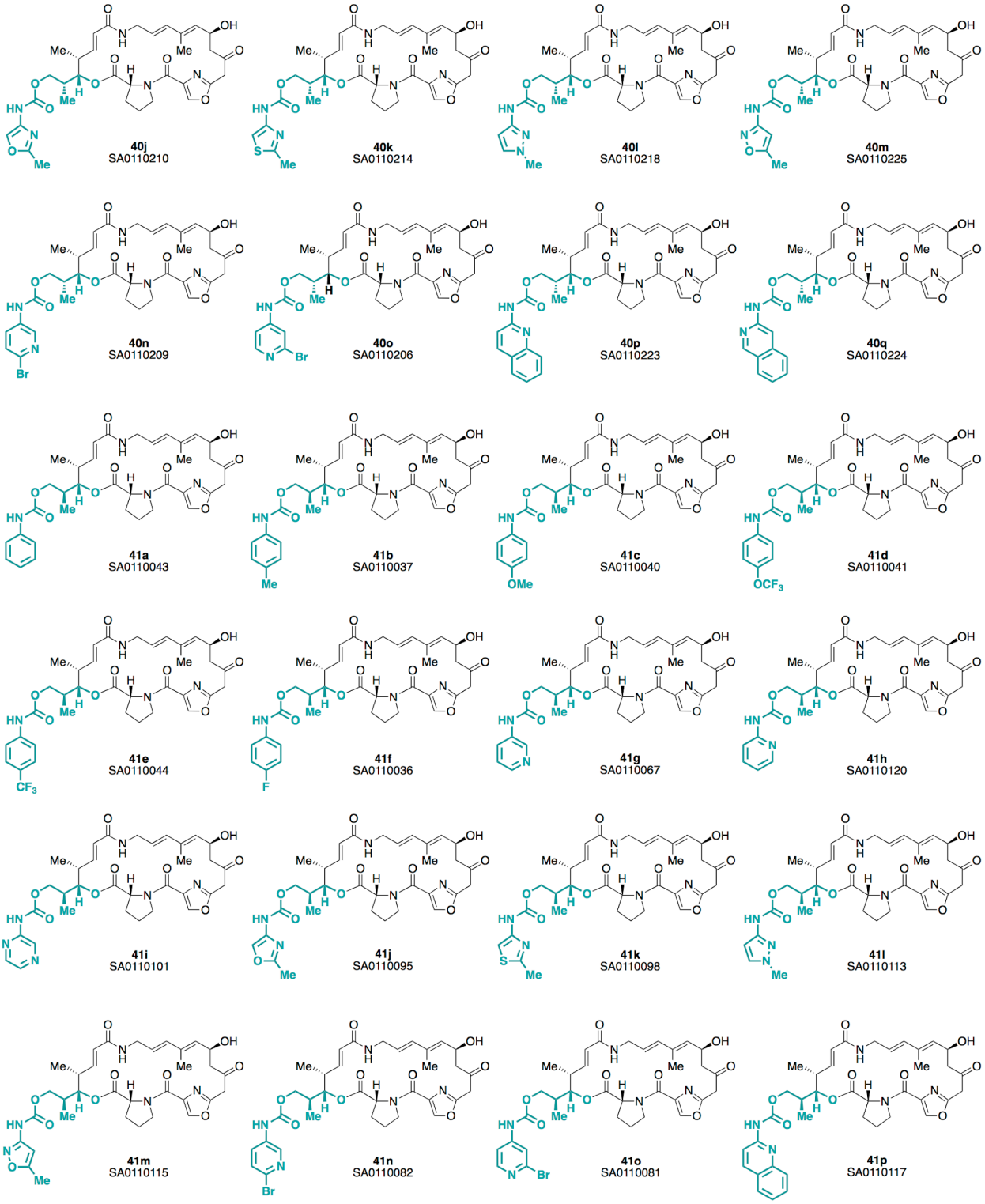

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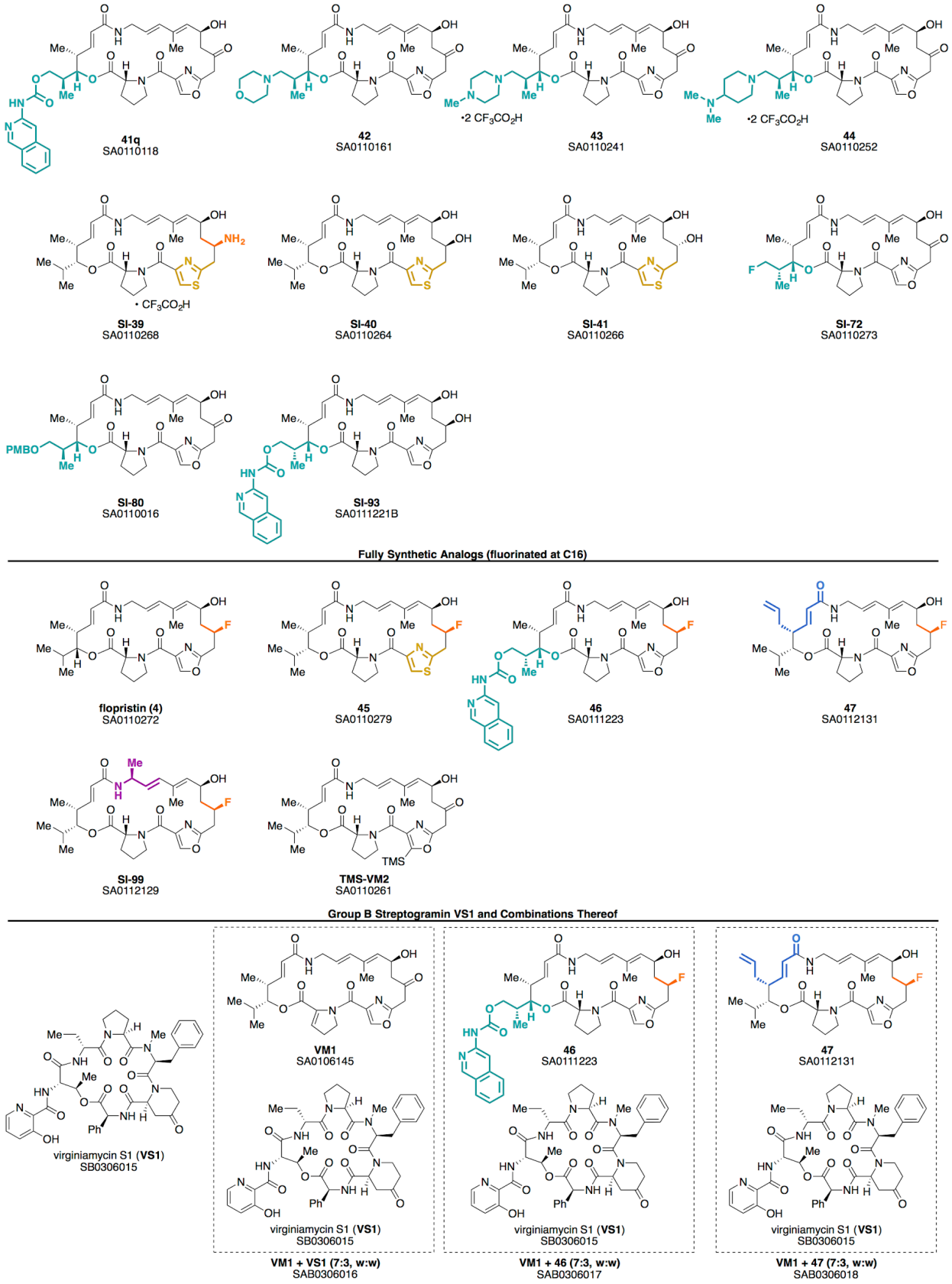


Extended Data Figure 3 - Inhibitory activity against Gram-positive organisms

Minimum inhibitory concentrations (MICs) for streptogramin antibiotics against a panel of 10 Gram-positive organisms. For further details, see the Methods and Supporting Information sections.

Minimal Inhibitory Concentration (MIC) Values (μg/mL)

Compound ID	SA Barcode	*E. faecalis* CLSI QC, *In vivo* strain MMX[2] 0101; ATCC[1] 29212	*E. faecium* ATCC isolate; VSE MMX 709; ATCC 35667	*E. faecium* VRE; vanA MMX 0752	*S. aureus* CLSI QC MMX 100; ATCC 29213	*S. aureus* VatA streptogramin acetyltransferase-mediated resistance Pasteur institute; MMX 10227	*S. aureus* MRSA MMX 2001; ATCC 33591	*S. aureus* MLSb ErmA resistance; inducible MMX 2321; BAA-977	*S. aureus* MLSb ErmA resistance; constitutive MMX 3035	*S. aureus* Linezolid-resistant; cfr MMX 3067	*S. pneumoniae* PSSP; CLSI QC MMX 1195; ATCC 49619
VM2	SA0106120	>64	4	8	16	>64	16	32	8	>64	8
VM1	SA0106145	64	2	8	4	32	2	8	2	>64	8
madumycin I (33)	SA0106141	32	2	4	8	64	8	8	4	64	4
madumycin II (34)	SA0106143	>64	0.5	8	8	>64	8	16	8	>64	4
21	SA0601037	64	2	4	4	16	4	4	2	>64	8
22	SA0112091	>64	>64	>64	>64	>64	>64	>64	>64	>64	64
23	SA0112090	64	>64	>64	>64	>64	>64	>64	>64	>64	64
24	SA0110239	>64	>64	>64	>64	>64	>64	>64	>64	>64	64
25	SA0112078	64	64	>64	64	64	64	>64	64	>64	64
26	SA0110141	>64	4	8	16	64	16	16	8	>64	8
27	SA05101042	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
28	SA05101054	>64	>64	>64	>64	>64	>64	>64	>64	>64	64
29	SA0202089	>64	32	32	32	64	32	32	32	>64	32
30	SA0202097	>64	>64	>64	>64	>64	>64	>64	>64	>64	64
31	SA0202061	32	32	64	64	64	64	64	64	>64	16
32	SA0202094	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
35	SA0110170	>64	>64	>64	>64	>64	>64	>64	>64	>64	64
36	SA0110026	>64	64	>64	>64	>64	>64	>64	>64	>64	64
37	SA0306004	>64	32	>64	32	>64	64	64	32	>64	64
42	SA0110161	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
43	SA0110241	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
44	SA0110252	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
40a	SA0110196	>64	16	64	32	>64	32	64	16	>64	32
40b	SA0110184	>64	16	16	16	>64	16	32	16	>64	32
40c	SA0110185	>64	16	32	32	>64	16	32	16	>64	32
40d	SA0110195	>64	8	>64	16	>64	16	16	8	>64	>64
40e	SA0110193	>64	8	>64	8	16	8	16	8	>64	>64
40f	SA0110180	>64	16	16	32	>64	16	32	16	>64	32
40g	SA0110205	>64	32	64	>64	>64	>64	>64	>64	>64	32
40h	SA0110222	>64	32	64	>64	>64	>64	>64	64	>64	32
40i	SA0110215	>64	64	>64	>64	>64	>64	>64	>64	>64	64
40j	SA0110210	>64	64	64	>64	>64	>64	>64	>64	>64	64
40k	SA0110214	>64	32	64	64	>64	64	>64	64	>64	32
40l	SA0110218	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
40m	SA0110225	>64	32	64	>64	>64	64	>64	64	>64	32
40n	SA0110209	>64	16	>64	16	>64	16	>64	16	>64	16
40o	SA0110206	>64	8	16	16	>64	16	32	16	>64	8
40p	SA0110223	>64	4	16	8	32	8	16	4	>64	32
40q	SA0110224	>64	4	8	4	16	4	8	4	>64	16
41a	SA0110043	>64	16	64	32	>64	32	64	32	>64	16
41b	SA0110037	>64	16	64	32	>64	32	64	16	>64	16
41c	SA0110040	>64	16	64	32	>64	32	64	16	>64	16
41d	SA0110041	>64	8	>64	>64	>64	>64	>64	32	>64	>64
41e	SA0110044	>64	16	>64	>64	>64	>64	>64	32	>64	>64
41e	SA0111044	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
41f	SA0110036	>64	8	32	32	>64	32	>64	16	>64	16
41g	SA0110067	>64	32	>64	>64	>64	>64	>64	64	>64	32
41h	SA0110120	>64	32	64	64	>64	64	>64	32	>64	16
41i	SA0110101	>64	64	>64	>64	>64	>64	>64	>64	>64	32
41j	SA0110095	>64	32	>64	>64	>64	>64	>64	64	>64	16
41k	SA0110098	>64	16	64	64	>64	32	64	32	>64	16
41l	SA0110113	>64	64	>64	>64	>64	>64	>64	>64	>64	8
41m	SA0110115	>64	32	>64	>64	>64	>64	>64	64	>64	16
41n	SA0110082	>64	32	>64	>64	>64	>64	>64	32	>64	8
41o	SA0110081	>64	32	>64	>64	>64	>64	>64	32	>64	32
41p	SA0110117	>64	16	32	16	>64	16	32	16	>64	4
41q	SA0110118	>64	4	16	8	>64	8	16	8	>64	2
SI-39	SA0110268	>64	64	>64	>64	>64	>64	>64	>64	>64	32
SI-40	SA0110264	>64	1	4	8	>64	16	16	8	>64	2
SI-41	SA0110266	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
SI-72	SA0110273	>64	16	64	64	>64	64	64	32	>64	16
SI-80	SA0110016	32	32	64	64	64	64	64	64	64	16
SI-93	SA0111221B	>64	8	>64	16	>64	16	32	16	>64[a]	8
SI-99	SA0112129	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
TMS-VM2	SA0110261	>64	64	>64	>64	>64	64	>64	64	>64	64
flopristin (4)	SA0110272	>64	0.5	2	0.5	8	0.5	1	0.5	>64	2
45	SA0110279	>64	0.5	1	0.5	8	0.5	1	0.5	>64	1
46	SA0111223	>64	2	2	2	1	0.5	0.5	0.25	>64	2
47	SA0112131	32	0.12	0.5	0.12	0.5	0.25	0.25	0.12	>64	1
VS1	SB0306015	2	2	64	8	16	8	4	8	8	1
VM1 + VS1	SAB0306016	1	≤0.06	0.25	0.12	16	12	0.25	1	8	0.12
46 + VS1	SAB0306017	0.5	≤0.06	0.12	0.25	1	0.25	0.25	0.12	4	≤0.06
47 + VS1	SAB0306018	0.25	≤0.06	≤0.06	≤0.06	1	0.5	≤0.06	0.12	4	≤0.06

[1] American Type Culture Collection [2] Micromyx Isolate Number

Extended Data Figure 4 - Inhibitory activity against Gram-negative organisms

Minimum inhibitory concentrations (MICs) for streptogramin antibiotics against a panel of 11 Gram-negative organisms. For further details, see the Methods and Supporting Information sections.

Minimal Inhibitory Concentration (MIC) Values (μg/mL)

Compound ID	SA Barcode	*A. baumannii* In vivo strain MMX[2] 1630; ATCC[1] 19606	*E. coli* CLSI QC, In vivo strain MMX 102; ATCC 25922	*E. coli* TolC efflux defective MMX 121	*E. coli* permeability mutant BAS1314;IMP4213ZAB::T N10 MMX 206	*E. coli* permeability mutant; BAS2006, OMP C, OMP F MMX 207	E. coli ΔompC768; KanR insert MMX 9658	*K. pneumoniae* ATCC isolate MMX 4972; ATCC 43816	*K. pneumoniae* MMX 8438	*P. aeruginosa* CLSI QC, *In vivo* strain MMX 103; ATCC 27853	*P. aeruginosa* MDR clinical isolate MMX 8799	*H. influenzae* In vivo strain MMX 1224; ATCC 49247
VM2	SA0106120	>64	>64	2	2	2	nt	>64	>64	>64	>64	16
VM1	SA0106145	>64	>64	2	0.25	1	>64	>64	>64	>64	>64	2
madumycin I (33)	SA0106141	>64	>64	2	0.25	0.5	nt	>64	>64	>64	>64	8
madumycin II (34)	SA0106143	>64	>64	2	0.5	1	nt	>64	>64	>64	>64	1
21	SA0601037	>64	>64	4	0.25	0.25	>64	>64	>64	>64	>64	2
22	SA0112091	>64	>64	8	8	8	>64	>64	>64	>64	>64	>64
23	SA0112090	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
24	SA0110239	>64	>64	8	8	64	>64	>64	>64	>64	>64	>64
25	SA0112078	>64	>64	32	>64	32	>64	>64	>64	>64	>64	>64
26	SA0110141	>64	>64	2	1	1	nt	>64	>64	>64	>64	32
27	SA05101042	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	1
28	SA05101054	>64	>64	32	32	>64	>64	>64	>64	>64	>64	>64
29	SA0202089	>64	>64	16	8	32	nt	>64	>64	>64	>64	>64
30	SA0202097	>64	>64	32	32	>64	>64	>64	>64	>64	>64	>64
31	SA0202061	>64	>64	4	4	16	nt	>64	>64	>64	>64	>64
32	SA0202094	>64	>64	>64	32	>64	>64	>64	>64	>64	>64	>64
35	SA0110170	>64	>64	32	32	>64	>64	>64	>64	>64	>64	32
36	SA0110026	>64	>64	32	64	64	nt	>64	>64	>64	>64	64
37	SA0306004	>64	>64	4	4	4	nt	>64	>64	>64	>64	>64
42	SA0110161	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
43	SA0110241	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
44	SA0110252	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
40a	SA0110196	>64	>64	2	8	32	>64	>64	>64	>64	>64	16
40b	SA0110184	>64	>64	4	2	>64	>64	>64	>64	>64	>64	16
40c	SA0110185	>64	>64	2	4	64	>64	>64	>64	>64	>64	16
40d	SA0110195	>64	>64	8	8	>64	>64	>64	>64	>64	>64	>64
40e	SA0110193	>64	>64	8	4	>64	>64	>64	>64	>64	>64	>64
40f	SA0110180	>64	>64	4	4	>64	>64	>64	>64	>64	>64	16
40g	SA0110205	>64	>64	8	16	>64	>64	>64	>64	>64	>64	32
40h	SA0110222	>64	>64	4	16	64	>64	>64	>64	>64	>64	16
40i	SA0110215	>64	>64	8	16	>64	>64	>64	>64	>64	>64	16
40j	SA0110210	>64	>64	8	8	>64	>64	>64	>64	>64	>64	16
40k	SA0110214	>64	>64	8	8	64	>64	>64	>64	>64	>64	16
40l	SA0110218	>64	>64	16	32	>64	>64	>64	>64	>64	>64	32
40m	SA0110225	>64	>64	4	8	>64	>64	>64	>64	>64	>64	16
40n	SA0110209	>64	>64	2	2	>64	>64	>64	>64	>64	>64	8
40o	SA0110206	>64	>64	2	2	16	>64	>64	>64	>64	>64	4
40p	SA0110223	>64	>64	2	2	16	>64	>64	>64	>64	>64	8
40q	SA0110224	>64	>64	1	1	8	>64	>64	>64	>64	>64	2
41a	SA0110043	>64	>64	2	8	16	nt	>64	>64	>64	>64	32
41b	SA0110037	>64	>64	4	8	16	nt	>64	>64	>64	>64	>64
41c	SA0110040	>64	>64	2	8	16	nt	>64	>64	>64	>64	16
41d	SA0110041	>64	>64	8	8	>64	nt	>64	>64	>64	>64	>64
41e	SA0110044	>64	>64	16	16	>64	nt	>64	>64	>64	>64	>64
41e	SA0111044	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64	>64
41f	SA0110036	>64	>64	2	8	8	nt	>64	>64	>64	>64	>64
41g	SA0110067	>64	>64	8	32	64	nt	>64	>64	>64	>64	>64
41h	SA0110120	>64	>64	4	8	32	nt	>64	>64	>64	>64	32
41i	SA0110101	>64	>64	8	16	64	nt	>64	>64	>64	>64	64
41j	SA0110095	>64	>64	8	16	32	nt	>64	>64	>64	>64	64
41k	SA0110098	>64	>64	2	8	16	nt	>64	>64	>64	>64	32
41l	SA0110113	>64	>64	8	16	64	nt	>64	>64	>64	>64	64
41m	SA0110115	>64	>64	8	16	64	nt	>64	>64	>64	>64	64
41n	SA0110082	>64	>64	4	16	32	nt	>64	>64	>64	>64	64
41o	SA0110081	>64	>64	4	32	32	nt	>64	>64	>64	>64	>64
41p	SA0110117	>64	>64	2	4	8	nt	>64	>64	>64	>64	>64
41q	SA0110118	>64	>64	2	2	8	nt	>64	>64	>64	>64	>64
SI-39	SA0110268	>64	>64	2	2	16	>64	>64	>64	>64	>64	64
SI-40	SA0110264	>64	>64	2	1	4	>64	>64	>64	>64	>64	1
SI-41	SA0110266	>64	>64	64	16	>64	>64	>64	>64	>64	>64	64
SI-72	SA0110273	>64	>64	4	8	16	>64	>64	>64	>64	>64	8
SI-80	SA0110016	>64	>64	8	16	>64	nt	>64	>64	>64	>64	>64
SI-93	SA0111221B	>64	>64	2	8	>64	>64	>64	>64	>64	>64	4
SI-99	SA0112129	>64	>64	8	16	>64	>64	>64	>64	>64	>64	>64
TMS-VM2	SA0110261	>64	>64	64	16	>64	>64	>64	>64	>64	>64	>64
flopristin (4)	SA0110272	>64	32	1	≤0.06	0.25	64	>64	>64	>64	>64	0.25
45	SA0110279	>64	32	1	≤0.06	0.25	329	>64	>64	>64	>64	0.25
46	SA0111223	>64	>64	1	0.5	>64	>64	>64	>64	>64	>64	1
47	SA0112131	>64	16	1	≤0.06	0.25	32	>64	>64	>64	>64	0.25
VS1	SB0306015	>64	>64	8	8	>64	>64	>64	>64	>64	>64	>64
VM1 + VS1	SAB0306016	>64	64	4	≤0.06	1	64	>64	>64	>64	>64	1
46 + VS1	SAB0306017	64	>64	1	0.12	2	>64	>64	>64	>64	>64	0.25
47 + VS1	SAB0306018	64	16	1	≤0.06	0.5	32	64	64	64	>64	0.25

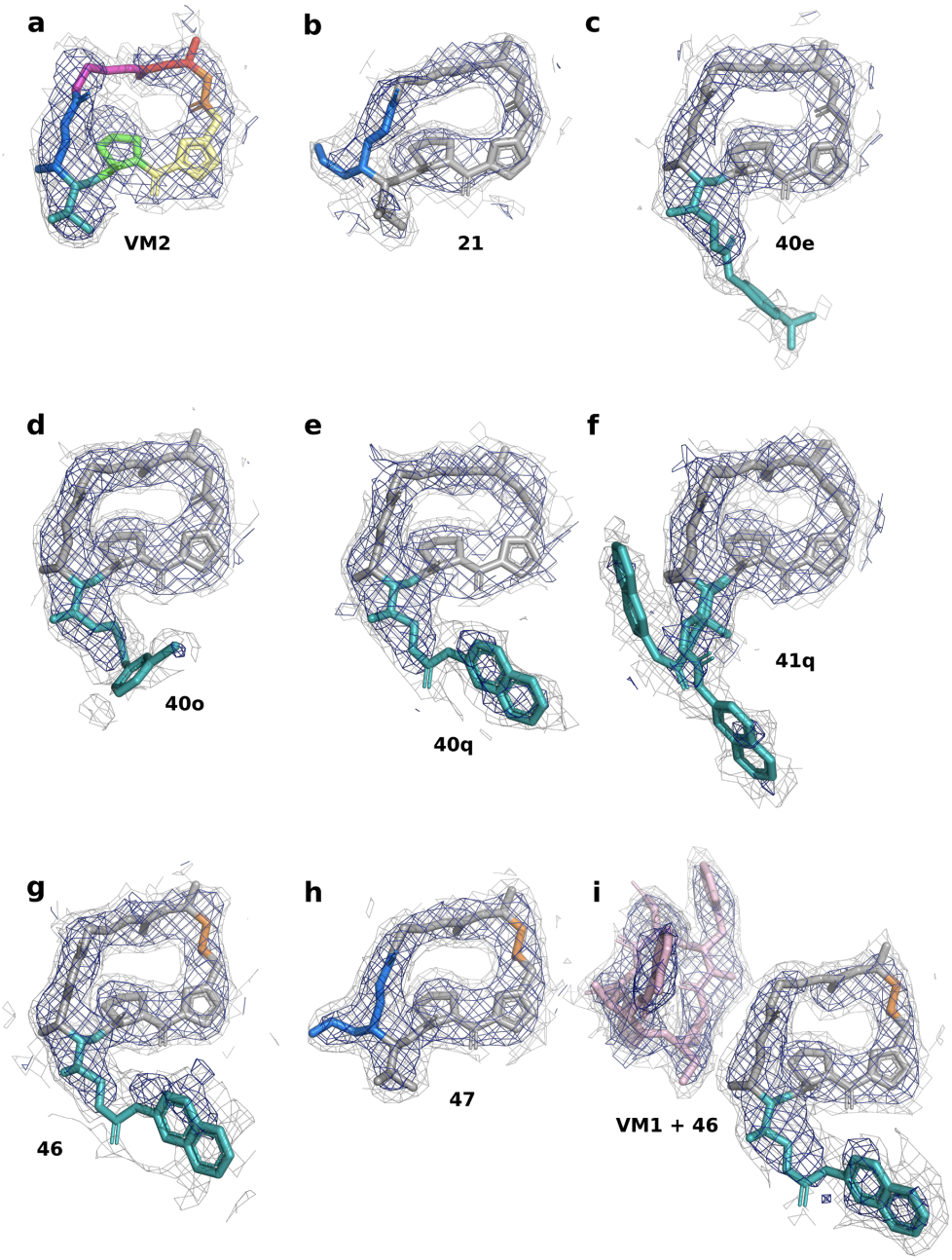
nt = not tested

[1] American Type Culture Collection

[2] Micromyx Isolate Number

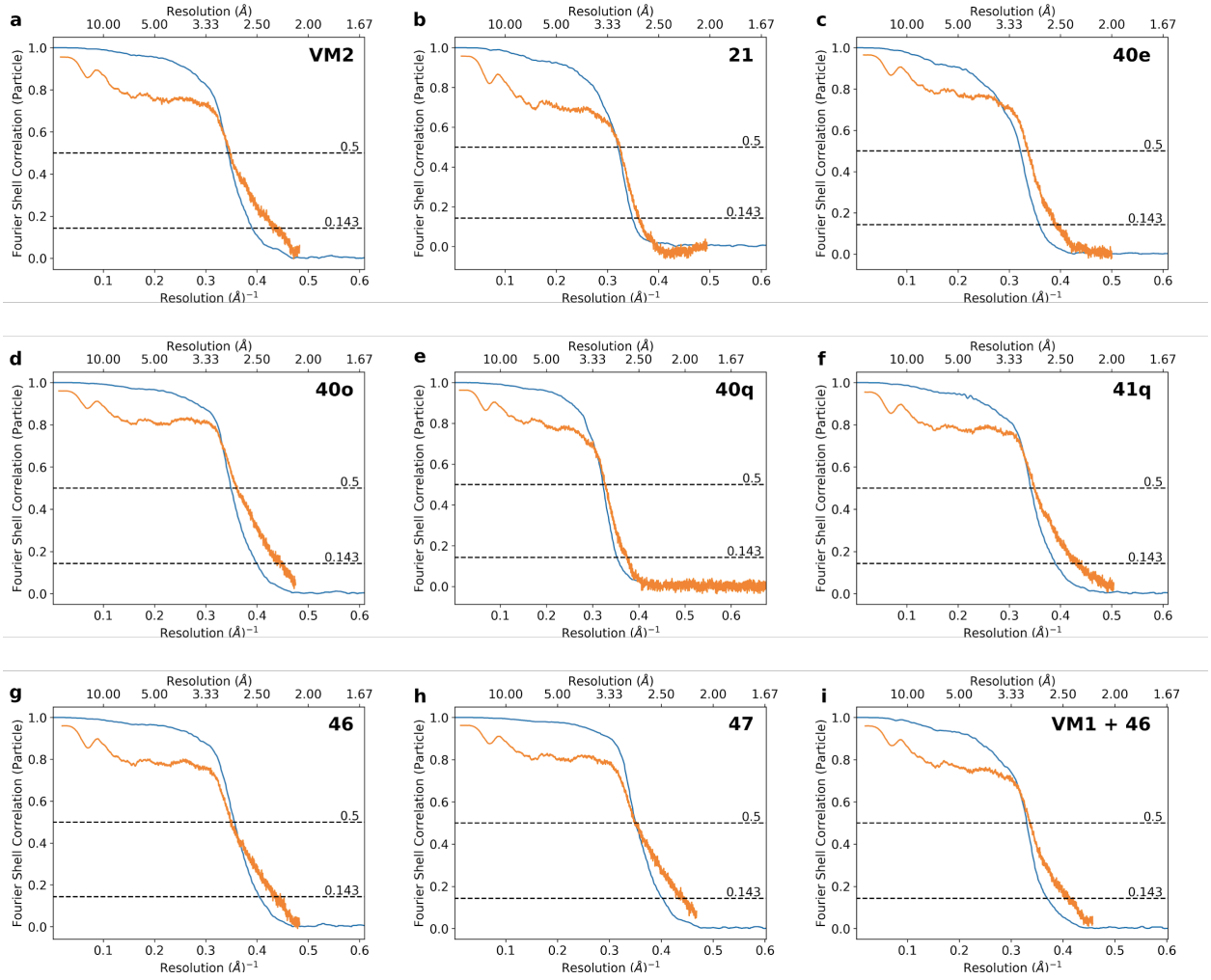
Extended Data Figure 5 - CryoEM Density for all compounds bound to the E coli ribosome

a) 2.6-Å CryoEM structure of **VM2** bound to the 50S subunit of the *E. coli* ribosome. Coulomb potential density is contoured in dark blue at 4.0 and light gray at 1.0 for entire figure. b) 2.8-Å CryoEM structure of **21** bound to the 50S subunit of the *E. coli* ribosome. c) 2.8-Å CryoEM structure of **40e** bound to the 50S subunit of the *E. coli* ribosome. d) 2.5-Å CryoEM structure of **40o** bound to the 50S subunit of the *E. coli* ribosome. e) 2.8-Å CryoEM structure of **40q** bound to the 50S subunit of the *E. coli* ribosome. f) 2.6-Å CryoEM structure of **41q** bound to the 50S subunit of the *E. coli* ribosome. g) 2.5-Å CryoEM structure of **46** bound to the 50S subunit of the *E. coli* ribosome. h) 2.5-Å CryoEM structure of **47** bound to the 50S subunit of the *E. coli* ribosome. i) 2.7-Å CryoEM structure of **VM1 + 46** bound to the 50S subunit of the *E. coli* ribosome.



Extended Data 6 - Gold Standard and Map to Model Fourier Shell Correlation plots

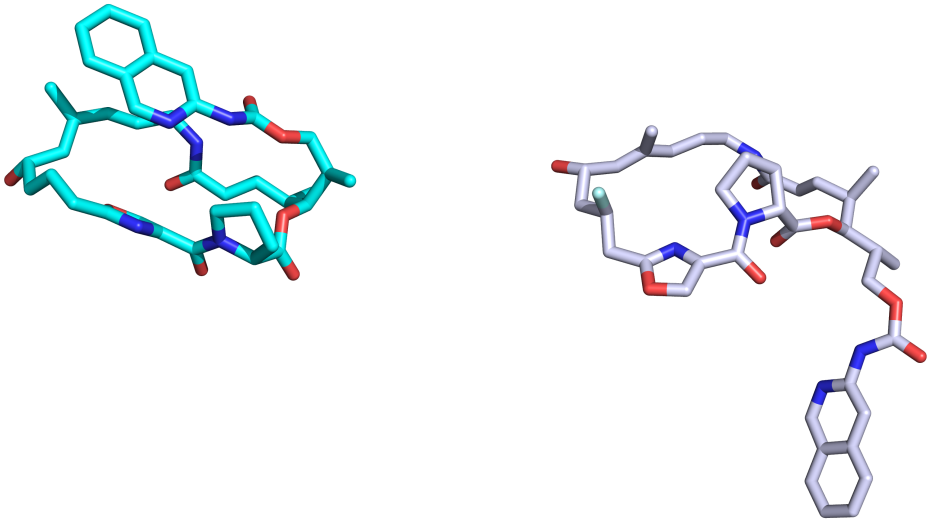
a-i) The Fourier Shell Correlation (FSC) curves for reconstructions obtained by cisTEM using a molecular weight of 1.8MDa, are shown in blue, with masked Map to Model FSC curves obtained from *phenix.mtriage* shown in orange. Dashed lines indicate FSC of 0.143 for estimating Gold Standard resolution and FSC of 0.5 for estimating Map to Model resolution.



Extended Data Figure 7 - The Low Energy Conformations of 46 position the side chain over the macrocycle

a) The conformation of **46** minimized by QM methods in low dielectric, shows how the isoquinoline side chain packs over the macrocycle. b) In contrast, the ribosome bound conformations of **46** determined by CryoEM, the side chain extends away from the macrocycle due to interactions formed in the binding site.

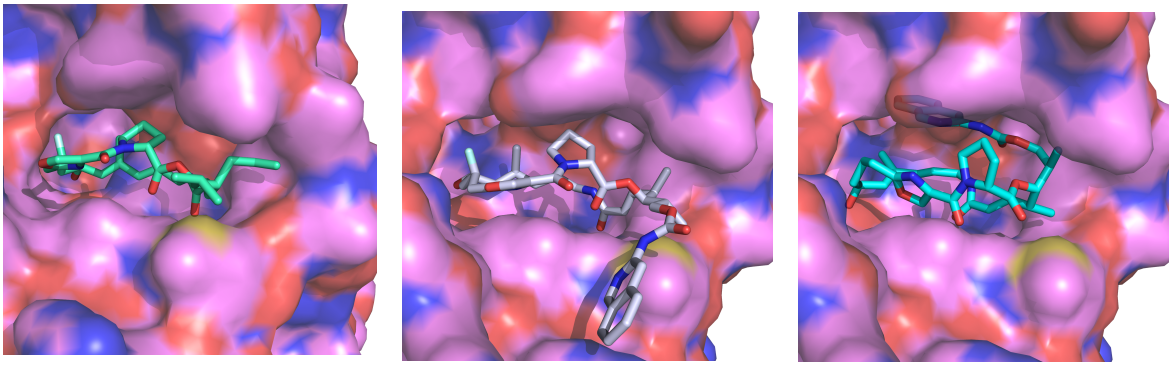
a b



Extended Data Figure 8 - Modeling conformations of 46 and 47 into the VatA active site

a) Model of **47** in the conformation bound to the ribosome modeled into the active site of VatA (shown in surface), b) Model of **46** in the conformation bound to the ribosome modeled into the active site of VatA c) Low energy model of **46** modeled into the active site of VatA

a b c



Extended Data Table 1 – Ligand Energies by different refinement schemes. Table of ligand energies (decoupled from receptor environment as evaluated by Prime with OPLS3e and VSGB2.1

Compound	Energy CIF refinement (kcal/mol)	Energy OPLS3e/VSGB2.1 (kcal/mol)	Delta (kcal/mol)
41q, conf A	**66.3**	**-115**	**-181.3**
41q, conf B	**99.2**	**-112.6**	**-211.8**
40e	**77.9**	**-112.7**	**-190.6**
40o	**20.1**	**-121.7**	**-141.8**
40q	**127.6**	**-109.1**	**-236.7**
21	**103.9**	**-80.4**	**-184.3**
46	**50.2**	**-78.6**	**-128.8**
47	**79.5**	**-64.8**	**-144.3**
VM2	**39.5**	**-88.3**	**-127.8**

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Synthesis and Mechanism of Action of Group A Streptogramin Antibiotics That Overcome Resistance

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Supporting Information

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General Experimental Procedures: All reactions were performed in oven-dried glassware fitted with rubber septa under a positive pressure of nitrogen or argon, unless otherwise noted. Procedures were conducted at 23 ºC unless otherwise noted. All reaction mixtures were stirred throughout the duration of each procedure using Teflon-coated magnetic stir bars. Air- and moisture-sensitive liquids were transferred by means of syringe or stainless steel cannula. Solutions were concentrated by rotary evaporation at or below 35 °C. Analytical thin-layer chromatography (TLC) was performed using glass plates pre-coated with silica gel (0.25-mm, 60-Å pore size, 230−400 mesh, SILICYCLE INC) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV), and then were stained by submersion in a basic aqueous solution of potassium permanganate or with an acidic ethanolic solution of anisaldehyde, followed by brief heating.

Materials: Dichlorometane (DCM), tetrahydrofuran (THF), and acetonitrile to be used in anhydrous reaction mixtures were dried by passage through activated alumina columns immediately prior to use. Other commercial solvents and reagents were used as received, unless otherwise noted. Anhydrous toluene, 2-propanol, and acetone were purchased from Fisher Chemical in Acroseal™ bottles. Anhydrous $^{i}Pr_2EtN$ and Et_3N were purchased from Sigma Aldrich in Sure/Seal™ bottles. Hexanes used were ≥85% *n*-hexane.

Instrumentation: Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 300 or 400 MHz Bruker Avance III HD 2-channel instrument NMR spectrometers at 23 °C or 50 ºC. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual protium in the NMR solvent ($CHC1_3$: δ 7.26, $CHDCl_2$: δ 5.32, CHD_2SOCD_3: δ 2.50 and CHD_2OD: δ 3.31). Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to the carbon resonance of the NMR solvent ($CDC1_3$: δ 77.0, CD_2Cl_2: δ 53.8 and CD_3OD: δ 49.0). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, m = multiplet, br = broad, app = apparent), integration, and coupling constant (*J*) in hertz (Hz). Optical rotations were measured using a JASCO P-2000 polarimeter. High-resolution mass spectra (HRMS) were obtained at the QB3/Chemistry Mass Spectrometry Facility at University of California, Berkeley using a Thermo LTQ-FT mass spectrometer or a Waters Acquity UPLC/Xevo G2-XS QTOF mass spectrometer (special thanks to Dr. Ziyang Zhang in the Shokat Laboratory for assistance). Melting points were recorded on an Electrothermal IA6304 Melting Point Apparatus. HPLC purification was conducted on a Waters Delta Prep 4000 preparative HPLC using a Gemini®-NX (5µm, C18, 110Å, 30.00 mm i.d. x 100 mm) column at a flow rate of 45 mL/min.

Methods for measuring minimum inhibitory concentrations (MICs)

Compounds were evaluated by Micromyx LLC for Minimum Inhibitory Concentration (MIC) activity using the broth microdilution method as recommended by the Clinical and Laboratory Standards Institute (CLSI)[1,2]. Pre-weighed vials of the test agents were stored at -20 °C until testing. On the day of the assay, the compounds were dissolved in 100% DMSO (Sigma 472301, Lot No. SHBH5551V) to a stock concentration of 6,464 µg/mL. The concentration range tested for each of the compounds was 64–0.06 µg/mL. Levofloxacin was used as the quality control agent. For more details on test organisms, media, and methods, see the Supporting Information.

Test Organisms

The organisms in the study were a combination of in vivo strains, clinical isolates and strains with different permeability or resistance phenotypes. Test organisms consisted of reference strains from the American Type Culture Collection (ATCC; Manassas, VA) and clinical isolates from the Micromyx repository (MMX; Kalamazoo, MI). Organisms were initially received at Micromyx and were streaked for isolation. Colonies were picked by sterile swab and suspended in the appropriate broth containing cryoprotectant. The suspensions were aliquoted into cryogenic vials and maintained at -80ºC.

Prior to testing, all isolates except for *H. influenzae* and the *S. aureus vatA* strain were streaked from frozen vials onto Trypticase Soy agar plates with 5% sheep blood (BBL Ref. No. 221261, Lot 7292618) and incubated overnight at 35ºC. The *S. pneumoniae* strain was incubated in the presence of 3% CO_2.

H. influenzae was streaked onto chocolate agar (BBL Ref. No. 221267, Lot 7299878) and incubated overnight at 35ºC in the presence of 3% CO_2.

The *S. aureus vatA* strain was streaked onto Mueller-Hinton agar containing 2, 10, 20, and 40 µg/mL of virginiamycin M1. Colonies growing on 10 µg/mL of virginiamycin M1 were selected for use in the assay.

Test Media

The medium employed for testing in the broth microdilution MIC assay for all organisms except *S. pneumoniae* and *H. influenzae* was cation-adjusted Mueller Hinton broth (MHBII; Becton Dickenson 212322; Lot 7143896) prepared according to CLSI guidelines (1). *S. pneumoniae* was tested in MHBII supplemented with 3% lysed horse blood (LHB; Hemostat, Lot 399694) and *H. influenzae* was tested in Haemophilus Test Medium (Remel Ref. No. R112380, Lot 106403).

Broth Microdilution Susceptibility Testing

The MIC assay method followed the procedure described by the Clinical and Laboratory Standards Institute[1,2] and employed automated liquid handlers (Multidrop 384, Labsystems, Helsinki, Finland; Biomek 2000 and Biomek FX, Beckman Coulter, Fullerton CA) to conduct serial dilutions and liquid transfers. The wells in columns 2-12 in a standard 96-well microdilution plate (Costar) were filled with 150 µL of the appropriate solvent (DMSO for the test agents and water for levofloxacin). These would become the 'mother plates' from which 'daughter' or test plates

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[1] Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Eleventh Edition. CLSI document M07-A11. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087 USA, 2018.

[2] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing—27th Edition: CLSI supplement M100-S27. CLSI, Wayne, PA, USA, 2017.

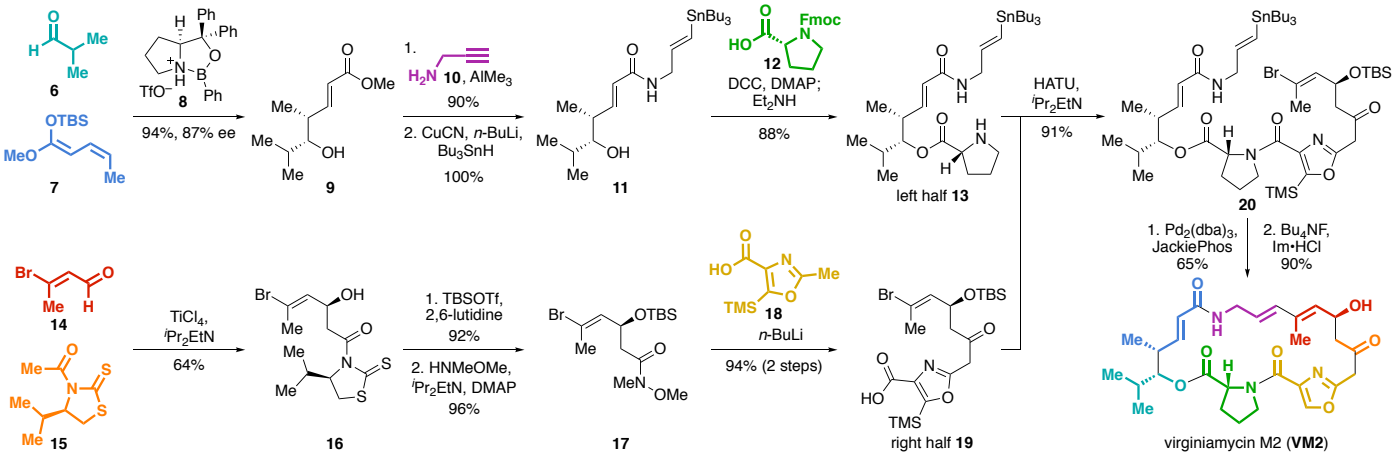
would be prepared. The drugs (300 µL at 101X the desired top concentration in the test plates) were dispensed into the appropriate well in Column 1 of the mother plates. The Biomek 2000 was used to make serial 2-fold dilutions through Column 11 in the "mother plate". The wells of Column 12 contained no drug and were the organism growth control wells.

The daughter plates were loaded with 190 µL per well of MHBII using the Multidrop 384. Plates for testing of *S. pneumoniae* were loaded with MHBII + LHB and those for testing of *H. influenzae* with HTM using a multi-channel pipet. The daughter plates were prepared on the Biomek FX instrument which transferred 2 µL of 101X drug solution from each well of a mother plate to the corresponding well of each daughter plate in a single step. The wells of the daughter plates ultimately contained 190 µL of medium, 2 µL of drug solution, and 10 µL of bacterial inoculum prepared in broth.

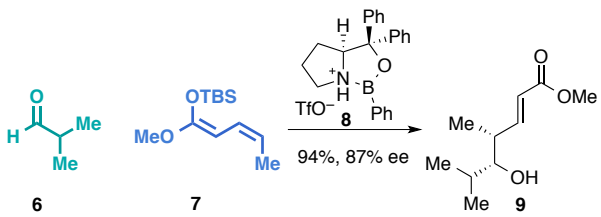
A standardized inoculum of each organism was prepared per CLSI methods[1,2]. Suspensions were prepared in MHBII to equal a turbidity of a 0.5 McFarland standard. The 0.5 McFarland suspensions were diluted 1:20 in the appropriate media. The inoculum for each organism was dispensed into sterile reservoirs divided by length (Beckman Coulter), and the Biomek 2000 was used to inoculate the plates. Daughter plates were placed on the Biomek 2000 work surface in reverse orientation so that inoculation took place from low to high drug concentration. The Biomek 2000 delivered 10 µL of standardized inoculum into each well. This yielded a final cell density in the daughter plates of approximately 5×10^5 CFU/mL.

Plates were stacked 3-4 high, covered with a lid on the top plate, placed in plastic bags and incubated for approximately 20 h at 35ºC. The microplates were viewed from the bottom using a plate viewer. The MIC was read and recorded as the lowest concentration of drug that inhibited visible growth of the organism. Some of the test agents showed precipitation at 32-64 µg/mL; however, the precipitation did not interfere with reading of the MIC values. The MIC values for levofloxacin were within CLSI established QC ranges[2], thus validating the study.

Scheme I Convergent route to virginiamycin M2 (VM2) from seven simple building blocks



Mukaiyama aldol product 9[3]



A 250-mL round-bottom flask was charged with phenylboronic acid (1.22 g, 10.0 mmol, 0.5 equiv) and (*S*)-diphenyl(pyrrolidin-2-yl)methanol (2.53 g, 10.0 mmol, 0.5 equiv). The vessel was equipped with a reflux condenser and the system was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (50 mL) was added, and the resulting clear solution was brought to reflux by means of a 145 ºC oil bath. After 12 h, the mixture was allowed to cool to 23 ºC and was concentrated. The resulting white solid was dried at ≤1 Torr for 1 h. The vessel was flushed with nitrogen, and DCM (80 mL) was added. The resulting colorless solution was cooled to -78 °C, and TfOH (0.80 mL, 8.99 mmol, 0.45 equiv) was added dropwise over 5 min by means of glass syringe (CAUTION: TfOH rapidly corrodes most plastic syringes!). Some of the TfOH froze upon contact with the solution. After 1 h, the solids had dissolved, and a mixture of isobutyraldehyde (**6**, 1.82 mL, 20.0 mmol, 1 equiv), silyl dienolether **7** (5.70 g, 25.0 mmol, 1.25 equiv), and 2-propanol (1.68 mL, 22.0 mmol, 1.1 equiv) in DCM (20 mL) was added dropwise over 2 h by means of syringe pump. The mixture was stirred at -78 °C for another 1.5 h, and saturated aqueous $NaHCO_3$ solution (50 mL) was added in one portion. The vessel was removed from the cooling bath and was allowed to warm to 23 ºC while it was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:10 to 1:6) to afford Mukaiyama aldol product **9** (3.48 g, 94% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:6): R_f = 0.25 (UV, $KMnO_4$).

$[\alpha]^{23}_D$ = +23.5 (*c* = 1.0, $CHCl_3$).

[3] Simsek, S.; Kalesse, M. *Tetrahedron Lett.* **2009**, *50*, 3485–3488.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.92 (dd, *J* = 15.7, 8.1 Hz, 1H), 5.86 (dd, *J* = 15.7, 1.2 Hz, 1H), 3.72 (s, 3H), 3.26 (t, *J* = 5.8 Hz, 1H), 2.59 – 2.39 (m, 1H), 1.78 – 1.64 (m, 1H), 1.59 (br s, 1H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 152.2, 120.4, 80.0, 51.4, 39.9, 30.9, 19.6, 16.5, 13.9.

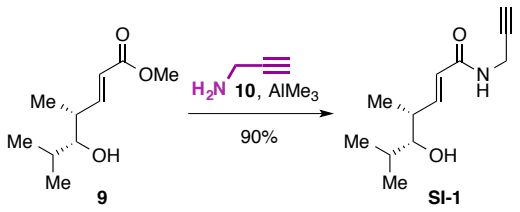
HRMS-EI m/z calcd for $C_{10}H_{19}O_3^+$ $[M + H]^+$ 187.1329, found 187.1331.

Determination of enantiomeric excess: To a solution of **9** (20 mg, 0.11 mmol, 1 equiv) in DCM (2 mL) was added successively Et_3N (0.12 mL, 0.86 mmol, 8.0 equiv), DMAP (18 mg, 0.15 mmol, 1.4 equiv) and (S) or (R)-Mosher acid chloride (80 µL, 0.43 mmol, 4.0 equiv). After 2 h, the mixture was diluted with EtOAc (15 mL). The mixture was transferred to a separatory funnel and was washed successively with 1 M aqueous $KHSO_4$ solution (3 x 5 mL), 1 M aqueous NaOH solution (5 mL) and saturated aqueous $NaHCO_3$ solution (3 x 5 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate concentrated. The resulting residue was analyzed by ^{1}H-NMR withour further purification.

For (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride: the enantiomeric excess (ee) was calculated from integration of the double dublet at 5.82 ppm (major), 5.84 ppm (minor). The ee was 87%.

For (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoyl chloride: the enantiomeric excess (ee) was calculated from integration of the double dublet at 5.84 ppm (major), 5.82 ppm (minor). The ee was 87%.

Amide SI-1



A 500-mL round-bottom flask was charged with propargylamine (**10**, 4.40 mL, 68.7 mmol, 4.0 equiv) and dry DCM (115 mL) under nitrogen. The resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (1 M, 68.7 mL, 68.7 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!). The mixture was allowed to warm to 23 ºC. After 30 min, a solution of **9** (3.20 g, 17.2 mmol, 1 equiv) in DCM (20 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 3 h, the mixture was cooled to 0 °C by means of an ice/water bath, and MeOH (10 mL) was added dropwise (CAUTION: Gas evolution!). Once gas evolution ceased, saturated aqueous potassium sodium tartrate solution (100 mL) was added. After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-1** (3.22 g, 90% yield) as a white solid.

m. p. 88 – 90 ºC (Hexanes).

TLC (EtOAc:hexanes = 1:1): R_f = 0.15 (UV).

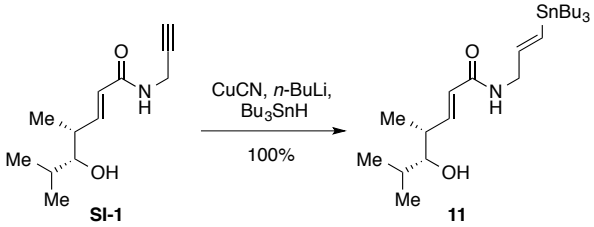
$[\alpha]^{24}_D$ = +29.7 (*c* = 1.0, DCM).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (dd, *J* = 15.4, 7.9 Hz, 1H), 5.82 (dd, *J* = 15.4, 1.2 Hz, 1H), 5.78 (s, 1H), 4.12 (dd, J = 5.3, 2.6 Hz, 2H), 3.30 – 3.22 (m, 1H), 2.56 – 2.43 (m, 1H), 2.24 (t, *J* = 2.6 Hz, 1H), 1.80 – 1.65 (m, 1H), 1.59 (d, *J* = 5.1 Hz, 1H), 1.08 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 148.4, 122.6, 79.4, 79.2, 71.7, 39.6, 30.8, 29.2, 19.7, 16.7, 13.9.

HRMS-ESI m/z calcd for $C_{12}H_{20}NO_2^+$ $[M + H]^+$ 210.1489, found 210.1487.

Vinyl stannane 11[4]



A 500-mL round-bottom flask containing CuCN (2.65 g, 29.6 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (200 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 24.9 mL, 62.2 mmol, 4.2 equiv) was added dropwise over 10 min, and the resulting light-yellow solution was stirred for 30 min. Bu_3SnH (16.8 mL, 62.2 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 min, a solution of **SI-1** (3.10 g, 14.8 mmol, 1 equiv) in THF (15 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (100 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **11** (7.4 g, 100% yield, ≥20:1 E:Z) as a colorless oil.

TLC (EtOAc:hexanes = 1:3): R_f = 0.25 (UV).

$[\alpha]^{24}_D$ = +10.6 (*c* = 1.0, $CHCl_3$).

Note regarding NMR spectra: Satellite peaks caused by geminal coupling between the vinyl proton and ^{117}Sn/^{119}Sn isotopes appear in the spectra[5]. Only the major peaks and ^{1}H-^{1}H coupling constants are reported below. In the spectra section (vide infra), we provide inset spectra highlighting the peaks in question in two solvents as well as a reference that supports the minor peaks arising due to geminal ^{1}H/Sn coupling. Additionally, we provide variable temperature ^{1}H-NMR data that supports the hypothesis that these are not amide rotamers (the ratio does not change even at 140 ºC in DMSO-d*6*). These peaks are present only for the intermediates in the synthesis that contain vinyl tin functionality.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dd, *J* = 15.4, 7.9 Hz, 1H), 6.12 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.97 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.83 (dd, *J* = 15.4, 1.2 Hz, 1H), 5.58 (br s, 1H), 4.04 – 3.94 (m, 2H), 3.26 (q, *J* = 5.6 Hz, 1H), 2.56 – 2.42 (m, 1H), 1.80 – 1.67 (m, 1H), 1.53 – 1.40 (m, 6H), 1.29 (m, 6H), 1.09 (d, *J* = 6.6 Hz, 3H), 0.94 – 0.83 (m, 21H).

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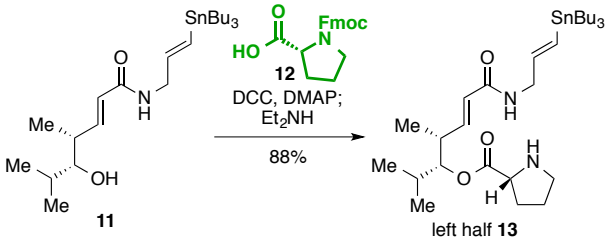
[4] Entwistle, D. A.; Jordan, S. I.; Montgomery, J.; Pattenden, G. *Synthesis* **1998**, 603–612.

[5] Cochran, J. C.; Bayef, S. C.; Bolbo, J. T.; Brown, M. S.; Colen, L. B.; Gaspirini, F. J.; Goldsmith, D. W.; Jamin, M. D.; Nealy, K. A.; Resnick, C. T.; Schwartz, G. J. ; Short, W. M.; Skarda, K. R.; Spring, J. P.; Strause, W. L. *Organometallics* **1982**, *1,* 586–590.

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 147.4, 143.4, 130.4, 123.3, 79.2, 44.9, 39.6, 30.8, 29.0, 27.2, 19.7, 16.7, 14.0, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{24}H_{47}NNaO_2Sn^+$ $[M + Na]^+$ 524.2521, found 524.2515.

Left half 13



A 100-mL round-bottom flask was charged with Fmoc-D-Pro-OH (**12**, 2.00 g, 5.94 mmol, 1.35 equiv), DMAP (0.11 g, 0.88 mmol, 0.2 equiv) and **11** (2.20 g, 4.40 mmol, 1 equiv). DCM (44 mL) was added, resulting in a colorless solution. DCC (1.36 g, 6.60 mmol, 1.5 equiv) was added in one portion. resulting in a white suspension. After 5 h, alcohol **11** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and diethylamine (22 mL) was added. After, 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 20 mL). The combined filtrates were concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford left half **13** (2.32 g, 88% yield) as light-yellow oil.

TLC (MeOH:DCM = 1:20): R_f = 0.20 (UV).

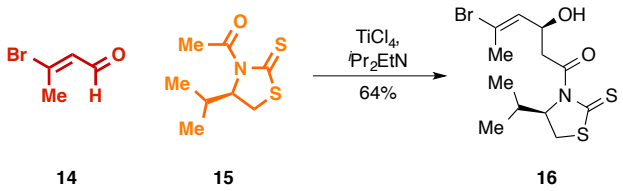
$[\alpha]^{24}_D$ = +13.9 (*c* = 0.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (dd, *J* = 15.4, 7.8 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.96 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.82 (dd, *J* = 15.4, 1.2 Hz, 1H), 5.59 (t, *J* = 5.9 Hz, 1H), 4.81 (dd, *J* = 6.9, 5.4 Hz, 1H), 4.03 – 3.89 (m, 2H), 3.76 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.07 (ddd, *J* = 10.2, 7.4, 6.1 Hz, 1H), 2.89 (ddd, *J* = 10.2, 7.1, 6.2 Hz, 1H), 2.65 (dtd, *J* = 8.0, 6.8, 1.2 Hz, 1H), 2.13 (dtd, *J* = 12.3, 8.1, 6.6 Hz, 1H), 2.07 (s, 1H), 1.94 – 1.79 (m, 2H), 1.80 – 1.65 (m, 2H), 1.56 – 1.39 (m, 6H), 1.35 – 1.21 (m, 6H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.95 – 0.80 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 165.2, 145.2, 143.4, 130.4, 123.8, 80.3, 59.9, 46.9, 44.9, 38.2, 30.5, 29.8, 29.0, 27.2, 25.4, 19.6, 16.8, 14.7, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{29}H_{55}N_2O_3Sn^+$ $[M + H]^+$ 599.3229, found 599.3219.

***β*-hydroxyl amide 16**[6]



A 250-mL round-bottom flask containing **15** (7.96 g, 39.1 mmol, 1.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (80 mL) was added, resulting in a yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of $TiCl_4$ in DCM (1 M, 42.7 mL, 42.7

[6] Romo, D.; Choi, N. S.; Li, S.; Buchler, I.; Shi, Z.; Liu, J. O. *J. Am. Chem. Soc.* **2004**, *34*, 10582–10588.

mmol, 1.2 equiv) was added dropwise, resulting in a deep yellow solution. After 5 min, $^{i}Pr_2EtN$ (7.46 mL, 42.7 mmol, 1.2 equiv) was added over 30 min by means of syringe pump, and the resulting deep red solution was stirred for 2 h at -78 ºC. A solution of aldehyde **14**[7,8] (5.30 g, 35.6 mmol, 1 equiv) in DCM (10 mL) was added by means of syringe pump over 30 min. After 30 min, water (100 mL) was added. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc: hexanes = 1:10 to 1:2.5) to afford *β*-hydroxyl amide **16** (8.3 g, 64% yield) as a yellow oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.25 (UV and $KMnO_4$).

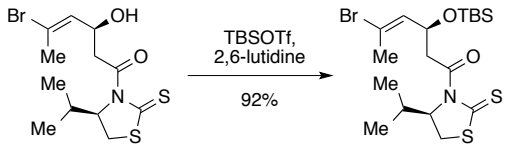
[α]$^{24}_{D}$ = –320 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (dq, *J* = 8.9, 1.3 Hz, 1H), 5.14 (ddd, *J* = 7.7, 6.3, 1.1 Hz, 1H), 4.80 (tdd, *J* = 8.4, 4.4, 3.3 Hz, 1H), 3.59 (dd, *J* = 17.6, 3.3 Hz, 1H), 3.53 (dd, *J* = 11.5, 8.0 Hz, 1H), 3.32 (dd, *J* = 17.7, 8.4 Hz, 1H), 3.03 (dd, *J* = 11.5, 1.1 Hz, 1H), 2.98 (d, *J* = 4.6 Hz, 1H), 2.45 – 2.25 (m, 1H), 2.32 (d, *J* = 1.4 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 171.8, 132.4, 124.2, 71.3, 65.7, 44.8, 30.7, 30.6, 24.1, 19.0, 17.7.

HRMS-ESI m/z calcd for $C_{12}H_{17}BrNO_2S_2^-$ $[M - H]^-$ 349.9890, found 349.9886.

TBS ether SI-2



16 **SI-2**

A 250-mL round-bottom flask containing *β*-hydroxyl amide **16** (4.71 g, 13.4 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (134 mL) was added, followed by 2,6-lutidine (3.1 mL, 26.8 mmol, 2.0 equiv), resulting in a yellow solution. The vessel and its contents were cooled to 0 ºC by means of an ice/water bath, and TBSOTf (3.69 mL, 16.0 mmol, 1.2 equiv) was added dropwise over 10 min. After 30 min, the mixture was transferred to a separatory funnel and washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtrated, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:20) to afford TBS ether **SI-2** (5.76 g, 92% yield) as a light-yellow oil.

TLC (EtOAc:hexanes = 1:50): R_f = 0.20 (UV).

[α]$^{24}_{D}$ = –479 (*c* = 1.0, $CHCl_3$).

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[7] Ghosh, A. K.; Li, J. *Org. Lett.* **2009**, *11*, 4164–4167.

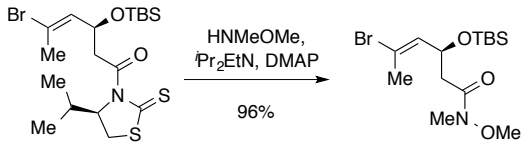
[8] Entwistle, D. A.; Jordan, S. I.; Montgomery, J.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1315–1317.

^{1}H NMR (400 MHz, $CDCl_3$) δ5.87 (dq, *J* = 8.9, 1.3 Hz, 1H), 5.03 (ddd, *J* = 7.6, 6.2, 1.1 Hz, 1H), 4.96 – 4.86 (m, 1H), 3.63 (dd, *J* = 16.5, 8.3 Hz, 1H), 3.47 (dd, *J* = 11.5, 7.9 Hz, 1H), 3.18 (dd, *J* = 16.5, 4.3 Hz, 1H), 3.03 (dd, *J* = 11.4, 1.1 Hz, 1H), 2.36 (dq, *J* = 13.5, 6.8 Hz, 1H), 2.31 (d, *J* = 1.3 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.84 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, CDCl3) δ 202.8, 170.7, 134.5, 121.7, 71.7, 67.2, 45.6, 30.9, 30.8, 25.7, 24.1, 19.1, 18.0, 17.8, –4.5, –5.0.

HRMS-EI m/z calcd for $C_{18}H_{32}BrNO_2S_2Si^+$ $[M]^+$ 465.0827, found 465.0819.

Weinreb amide 17



SI-2 **17**

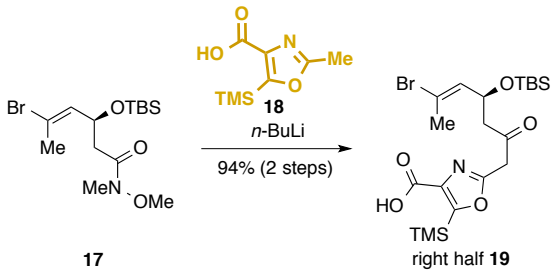
A 500-mL round-bottom flask containing HN(OMe)Me•HCl (2.26 g, 23.1 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (115 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to 0 ºC by means of an ice/water bath. ^{i}Pr$_2$EtN (4.01 mL, 28.9 mmol, 2.5 equiv) was added. After 30 min, a solution of **SI-2** (5.40 g, 11.6 mmol, 1 equiv) and DMAP (0.141 g, 1.16 mmol, 0.1 equiv) in DCM (15 mL) was added. The mixture was allowed to warm to 23 ºC. After 12 h, water (150 mL) was added. The resulting biphasic mixture was transferred to a separatory funnel, and the layers were separated. The organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:15) to afford Weinreb amide **17** (4.06 g, 96% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (dq, *J* = 9.0, 1.3 Hz, 1H), 4.84 (ddd, *J* = 9.0, 7.9, 5.3 Hz, 1H), 3.69 (s, 3H), 3.17 (s, 3H), 2.83 (dd, *J* = 14.8, 8.0 Hz, 1H), 2.41 (dd, *J* = 14.7, 5.3 Hz, 1H), 2.30 (d, *J* = 1.3 Hz, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 135.0, 121.4, 67.5, 61.4, 40.0, 32.0, 25.7, 24.1, 18.0, –4.6, –5.1.

Right half 19



17 right half **19**

A 250-mL round-bottom flask containing acid **18**[9] (1.76 g, 8.19 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (82 mL) was added, resulting in a light-yellow solution, and

[9] Wood, R. D.; Ganem, B. *Tetrahedron Lett.* **1983**, *24*, 4391–4392.

the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 6.55 mL, 16.4 mmol, 4.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, a solution of Weinreb amide **17** (1.50 g, 4.09 mmol, 1 equiv) in THF (10 mL) was added over 30 min by means of syringe pump. After an additional 30 min, water (50 mL) was added, followed by 1 M aqueous $KHSO_4$ solution (20 mL). The system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:70) to afford right half **19** (2.00 g, 94% yield) as a yellow solid.

m. p. 143 – 146 ºC (DCM).

TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

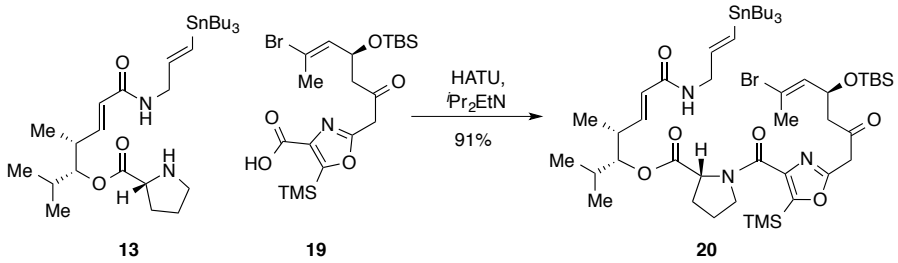
$[\alpha]^{24}_D$ = –24.5 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (dq, *J* = 9.0, 1.3 Hz, 1H), 4.79 (ddd, *J* = 9.1, 8.2, 4.6 Hz, 1H), 4.13 (d, *J* = 17.1 Hz, 1H), 4.05 (d, *J* = 17.1 Hz, 1H), 2.86 (dd, *J* = 15.6, 8.1 Hz, 1H), 2.55 (dd, *J* = 15.6, 4.6 Hz, 1H), 2.27 (d, *J* = 1.3 Hz, 3H), 0.84 (s, 9H), 0.37 (s, 9H), 0.04 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 165.4, 165.3, 161.1, 140.7, 134.2, 121.8, 66.9, 49.7, 43.7, 25.7, 24.0, 18.9, 18.0, –2.1, –4.6, –5.1.

HRMS-ESI m/z calcd for $C_{20}H_{35}BrNO_5Si_2$ $[M + H]^+$ 504.1232, found 504.1227.

Stille coupling precursor 20



A 50-mL round-bottom flask was charged with ^{i}Pr$_2$EtN (0.39 mL, 2.24 mmol, 2.0 equiv), amine **13** (0.67 g, 1.12 mmol, 1 equiv), and acid **19** (0.62 g, 1.23 mmol, 1.1 equiv). DCM (12 mL) was added, resulting in a colorless solution. HATU (0.53 g, 1.40 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (30 mL). The resulting solution was transferred to a separatory funnel and was washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **20** (1.10 g, 91% yield) as a light-yellow oil.

TLC (EtOAc:hexanes = 1:4): R_f = 0.30 (UV).

$[\alpha]^{24}_D$ = –10.7 (*c* = 1.0, $CHCl_3$).

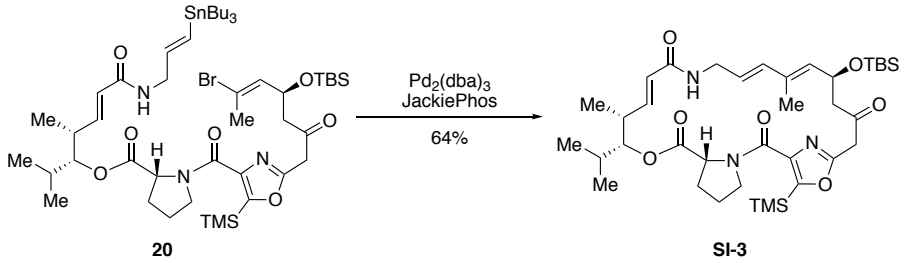
^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.76 – 6.53 (m, 1H), 6.11 (dd, *J* = 18.9, 1.6 Hz, 1H), 6.03 – 5.90 (m, 1H), 5.89 – 5.71 (m, 2H), 5.70 – 5.54 (m, 1H), 4.86 – 4.55 (m, 3H), 4.14 – 3.82 (m, 5H), 3.81 – 3.61 (m, 1H), 2.90 – 2.75

(m, 1H), 2.68 – 2.45 (m, 2H), 2.35 – 2.22 (m, 4H), 2.09 – 1.75 (m, 4H), 1.52 – 1.42 (m, J = 8.3, 6.0 Hz, 6H), 1.35 – 1.22 (dq, J = 13.3, 6.6, 6.0 Hz, 6H), 1.08 – 0.99 (m, 3H), 0.99 – 0.78 (m, 30H), 0.37 – 0.26 (m, 9H), 0.11 – 0.01 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.1, 200.7, 172.34 165.4, 165.1, 163.2, 162.5, 161.5, 159.1, 145.4, 145.2, 145.1, 143.4, 143.3, 134.2, 130.4, 130.2, 123.9, 123.8, 121.8, 80.8, 80.4, 67.0, 66.9, 60.5, 59.9, 49.6, 48.8, 47.1, 44.91, 44.86, 44.2, 44.0, 38.4, 38.1, 31.6, 29.9, 29.8, 29.7, 29.1, 29.0, 28.9, 27.5, 27.2, 27.0, 25.69, 25.67, 25.6, 25.2, 24.00, 23.99, 21.5, 19.7, 19.5, 18.0, 17.0, 16.8, 14.9, 14.6, 13.7, 11.14, 11.06, 9.4, 7.8, 7.7, –1.77, –1.79, –4.57, –5.13, –5.15.

HRMS-ESI m/z calcd for $C_{49}H_{87}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1084.4282, found 1084.4275.

Stille coupling product SI-3



20 **SI-3**

A 500-mL round-bottom flask was charged with JackiePhos (0.16 g, 0.20 mmol, 0.2 equiv), Stille coupling precursor **20** (1.10 g, 1.02 mmol, 1 equiv), and $Pd_2(dba)_3$ (93 mg, 0.10 mmol, 0.1 equiv). The system was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (200 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by means of a 50 ºC oil bath. After 3 h, **SI-3** was entirely consumed by TLC analysis, and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2.5 to 1:2) to afford Stille coupling product **SI-3** (0.46 g, 64% yield) as a white solid.

m. p. 105 – 110 ºC (Hexanes).

TLC (EtOAc:hexanes = 1:2): R_f = 0.20 (UV).

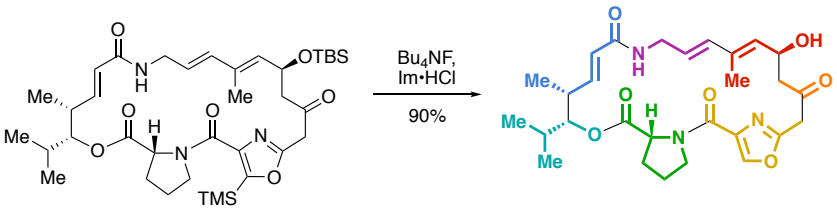
$[\alpha]^{24}_D$ = –57.1 (c = 1.0, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (dd, J = 16.3, 4.2 Hz, 1H), 6.19 – 6.10 (m, 1H), 6.07 (dd, J = 9.2, 3.2 Hz, 1H), 5.77 (dd, J = 16.4, 2.0 Hz, 1H), 5.57 (ddd, J = 15.5, 9.4, 4.2 Hz, 1H), 5.42 (d, J = 8.9 Hz, 1H), 5.00 (ddd, J = 8.9, 7.0, 5.9 Hz, 1H), 4.85 – 4.72 (m, 2H), 4.57 – 4.43 (m, 1H), 3.89 (d, J = 17.2 Hz, 1H), 3.78 – 3.69 (m, 3H), 3.39 (ddd, J = 14.8, 9.5, 3.3 Hz, 1H), 2.92 (dd, J = 15.9, 7.0 Hz, 1H), 2.79 – 2.68 (m, 2H), 2.18 – 2.04 (m, 1H), 1.90 (dddd, J = 24.9, 15.9, 11.3, 6.8 Hz, 3H), 1.77 – 1.68 (m, 1H), 1.66 (d, J = 1.2 Hz, 3H), 1.08 (d, J = 6.9 Hz, 3H), 0.99 (d, J = 6.5 Hz, 3H), 0.94 (d, J = 6.8 Hz, 3H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 172.1, 166.4, 161.8, 161.3, 159.6, 145.1, 144.8, 136.7, 134.7, 132.4, 124.9, 123.7, 81.1, 65.4, 58.7, 50.6, 48.4, 43.7, 41.3, 36.7, 29.3, 28.2, 25.7, 24.8, 19.9, 18.6, 18.1, 12.67, 9.9, –1.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{37}H_{60}N_3O_7Si_2^+$ $[M + H]^+$ 714.3964, found 714.3968.

Virginiamycin M2



SI-3 virginiamycin M2 (**VM2**)

A 100-mL round-bottom flask containing Stille coupling product **SI-3** (0.46 g, 0.64 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.6 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (0.67 g, 6.44 mmol, 10.0 equiv) that had been previously dried at >100 ºC under vacuum for 10 minutes was added to a solution of tetrabutylammonium fluoride in THF (1 M, 6.44 mL, 6.44 mmol, 10.0 equiv)[10]. The resulting colorless solution was added dropwise to the solution of **SI-3**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (3 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford virginiamycin M2 (**VM2**, 0.31 g, 90% yield) as a light-yellow solid.

m. p. 120 – 125 ºC (DCM).

TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

[α]$^{25}_D$ = –67.4 (*c* = 0.3, DCM).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 6.47 (dd, *J* = 16.4, 5.0 Hz, 1H), 6.39 (dd, *J* = 9.0, 3.7 Hz, 1H), 6.11 (m, *J* = 15.6 Hz, 1H), 5.78 (dd, *J* = 16.4, 1.9 Hz, 1H), 5.69 (ddd, *J* = 15.6, 9.2, 4.6 Hz, 1H), 5.41 (d, *J* = 8.8 Hz, 1H), 4.90 (dt, *J* = 8.9, 5.6 Hz, 1H), 4.73 (dd, *J* = 10.1, 2.0 Hz, 1H), 4.70 (dd, *J* = 8.9, 3.2 Hz, 1H), 4.45 (ddd, *J* = 13.9, 8.9, 4.6 Hz, 1H), 4.00 – 3.92 (m, 1H), 3.82 (s, 2H), 3.79 – 3.70 (m, 1H), 3.39 (ddd, *J* = 14.0, 9.2, 3.6 Hz, 1H), 3.05 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.89 (dd, *J* = 17.0, 5.2 Hz, 1H), 2.74 (ddt, *J* = 6.9, 4.9, 2.0 Hz, 1H), 2.60 (br s, 1H), 2.24 – 2.08 (m, 1H), 2.01 – 1.88 (m, 3H), 1.88 – 1.75 (m, 1H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 171.6, 166.5, 160.2, 156.9, 144.5, 143.9, 136.92, 136.86, 134.3, 132.7, 125.2, 124.0, 81.4, 65.0, 59.6, 48.9, 48.4, 43.3, 40.9, 36.6, 29.4, 28.3, 25.0, 19.7, 18.7, 12.6, 10.4.

HRMS-ESI m/z calcd for $C_{28}H_{38}N_3O_7^+$ $[M + H]^+$ 528.2704, found 528.2703.

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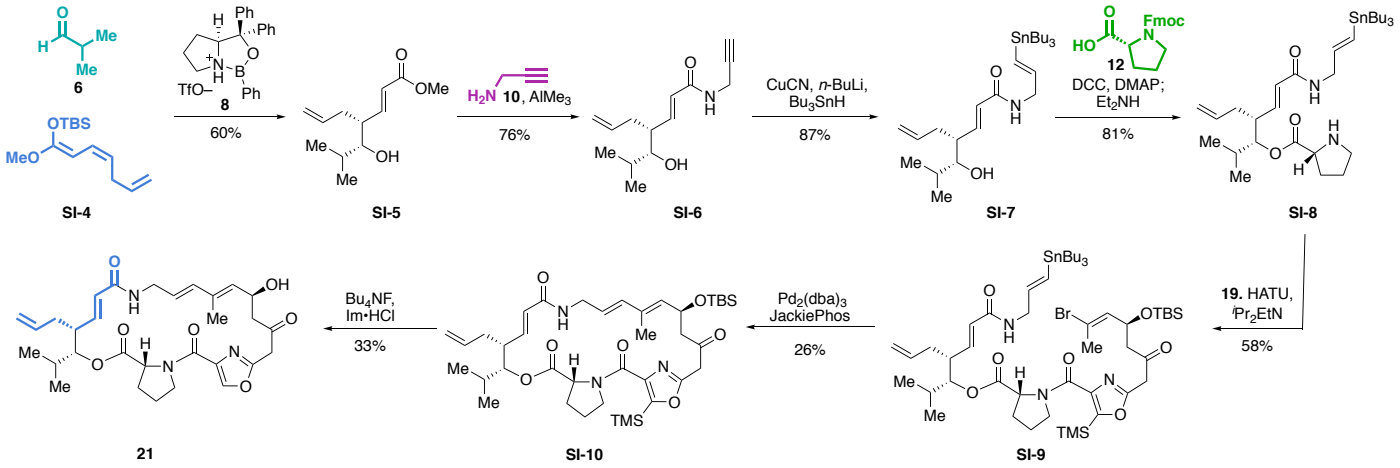
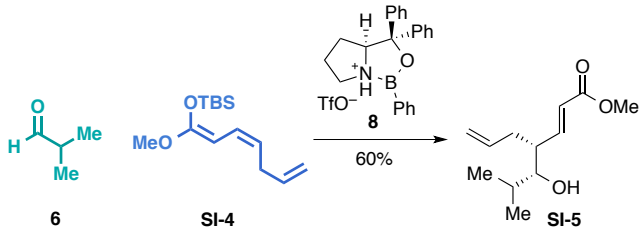
[10] Austad, B. A.; Calkins, T. L.; Chase, C. E.; Fang, F. G.; Horstmann, T. E.; Hu, Y.; Lewis, B. M.; Niu, X.; Noland, T. A.; Orr, J. D.; Schnaderbeck, M. J.; Zhang, H.; Asakawa, N.; Asai, N.; Chiba, H.; Hasebe, T.; Hoshino, Y.; Ishizuka, H.; Kajima, T.; Kayano, A.; Komatsu, Y.; Kubota, M.; Kuroda, H.; Miyazawa, M. Tagami K.; Watanabe, T. *Synlett*, **2013**, *24*, 333–337.

Scheme II Synthesis of 21



Mukaiyama aldol product SI-5



Preparation of SI-4: A 250-mL round-bottome flask was charged with anhydrous $^{i}Pr_2NH$ (3.30 mL, 23.0 mmol, 1.28 equiv) and THF ((46 mL), and the vessel and its contents were cooled to 0 ºC by means of an ice/water bath. A solution of n-butyllithium in hexanes (1.60 M, 14.4 mL, 23.0 mmol, 1.28 equiv) was added. After 30 min, the mixture was cooled to -78°C by means of a dry ice/acetone bath, and DMPU (3.20 mL, 27.0 mmol, 1.50 equiv) was added dropwise. After 15 min, a solution of methyl (*E*)-hepta-2,6-dienoate[11] (2.50 g, 18.0 mmol, 1 equiv) in THF (5 mL) was added dropwise. After a further 15 min, a solution of TBSCl (3.30 g, 22.0 mmol, 1.23 equiv) in THF (8 mL) was added dropwise. After stirring for 30 min, the vessel was removed from the bath and was allowed to warm to 23 °C. After 1.5 h at this temperature, saturated aqueous $NaHCO_3$ solution (50 mL) was added, and the mixture was extracted with hexanes (2 x 70 mL), and the organic extracts were washed with saturated aqueous $NaHCO_3$ (3 x 50 mL) and brine (35 mL). The washed solution was dried ($MgSO_4$), and the dried solution was filtered. The filtrate was concentrated, and the crude mixture was purified by distillation at reduced pressure (b.p. = 71.0-74.0 °C, ~0.5 torr) to afford the product **SI-4** (2.15 g, 47% yield) as light yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.23 (tt, *J* = 10.9, 1.6 Hz, 1H), 5.93 – 5.76 (m, 1H), 5.13 – 4.92 (m, 3H), 4.56 – 4.39 (m, 1H), 3.59 (s, 3H), 2.89 – 2.76 (m, 2H), 0.95 (s, 9H), 0.17 (s, 6H).

Preparation of SI-5: A 100-mL round-bottom flask was charged with phenylboronic acid (0.41 g, 3.36 mmol, 0.50 equiv) and (*S*)-diphenyl(pyrrolidin-2-yl)methanol (0.85 g, 3.36 mmol, 0.50 equiv). The vessel was equipped with a reflux condenser, and the system was evacuated and flushed with nitrogen (this was repeated a total of 3 times). Toluene (25 mL) was added, and the resulting solution was brought to reflux by means of a 145 °C oil bath. After 12 h, the mixture was allowed to cool to 23 °C and was concentrated in vacuum. The resulting white solid was dried at ≤ 1 Torr for 1 h. The vessel was flushed with nitrogen, and DCM (26 mL) was added. The vessel and its contents (a colorless solution) were cooled to -78 °C by means of a dry ice/acetone bath and TfOH (0.27 mL, 3.03 mmol, 0.45 equiv) was

[11] Davies, S. G.; Fletcher, A. M.; Roberts, P. M.; Smith, A. D. *Tetahedron* **2009**, *65*, 10192–10213.

added dropwise over 5 min by glass syringe (CAUTION: TfOH rapidly corrodes most plastic syringes!). NOTE: Some of TfOH froze upon contact with the solution. After 1.5 h the solids had completely dissolved, and a mixture of isobutyraldehyde (**6**, 0.62 mL, 6.72 mmol, 1 equiv), silyl trienolether **SI-4** (2.14 g, 8.40 mmol, 1.25 equiv) and 2-propanol (0.57 mL, 7.39 mmol, 1.1 equiv) in DCM (7 mL) was added dropwise into the solution over 2 h by syringe pump. The mixture was stirred at -78 °C for another 2.5 h, and saturated aqueous $NaHCO_3$ solution (17 mL) was added in one portion. The vessel was removed from the cooling bath and the system was allowed to warm to 23 °C. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with DCM (2 × 15 mL). The organic layers were combined, and the resulting solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:10 to 1:6) to afford Mukaiyama aldol product **SI-5** (0.85 g, 60% yield) as colorless oil.

TLC (EtOAc: hexanes = 1:6): R_f = 0.2 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (dd, *J* = 15.7, 9.6 Hz, 1H), 5.84 (dd, *J* = 15.7, 0.8 Hz, 1H), 5.80 – 5.61 (m, 1H), 5.09 – 4.99 (m, 2H), 3.73 (s, 3H), 3.41 – 3.33 (m, 1H), 2.58 – 2.31 (m, 2H), 2.25 – 2.12 (m, 1H), 1.79 – 1.66 (m, 1H), 1.47 (d, *J* = 5.7 Hz, 1H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 149.5, 136.9, 122.11, 116.9, 77.9, 51.5, 46.5, 34.5, 30.8, 20.1, 15.1.

Amide SI-6

SI-5 **SI-6**

A 250-mL round-bottom flask was charged with propargylamine (**10**, 1.00 mL, 16.0 mmol, 4.0 equiv) and DCM (27 mL). The vessel and its contents (a colorless solution) were cooled to 0 °C by means of an ice/water bath. A solution of $AlMe_3$ in heptane (1.00 M, 16.0 mL, 16.0 mmol, 4.0 equiv) was added dropwise over 30 min (Caution: Gas evolution!). The mixture was allowed to cool to 23 °C. After 30 min, a solution of Mukaiyama aldol product **SI-5** (0.85 g, 4.00 mmol, 1 equiv) in DCM (4.8 mL) was added over 10 min (Caution: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 °C oil bath. After 3 h, the system was cooled to 0 °C by means of an ice/water bath, and MeOH (3.0 mL) was added dropwise (Caution: Gas evolution!). Once gas evolution ceased, saturated aqueous potassium sodium tartrate solution (30 mL) was added. After 1 h, the biphasic mixture was transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with DCM (2 × 10 mL). The combined organic layers were washed with water (30 mL) and brine (30 mL), and the organic extracts were dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-6** (0.71 g, 76% yield) as a white solid.

TLC (EtOAc: hexanes = 1:1): R_f = 0.40 (UV).

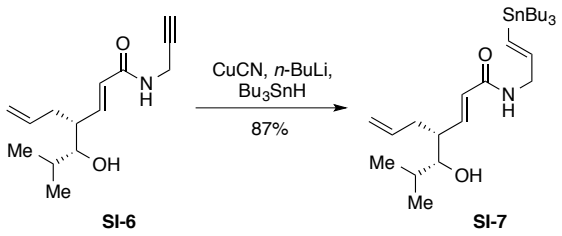
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.70 (ddd, *J* = 15.3, 9.6, 1.6 Hz, 1H), 5.81 (d, *J* = 1.5 Hz, 1H), 5.79 – 5.65 (m, 1H), 5.62 (br s, 1H), 5.10 – 4.98 (m, 2H), 4.13 (m, 2H), 3.40 – 3.34 (m, 1H), 2.49 (d, *J* = 6.0 Hz, 1H), 2.39 (q, *J* = 9.5 Hz, 1H), 2.26

(q, J = 2.3 Hz, 1H), 2.18 (dt, J = 15.2, 8.3 Hz, 1H), 1.73 (m, 1H), 1.57 (s, 1H), 0.95 (dd, J = 6.9, 1.5 Hz, 3H), 0.86 (dd, J = 6.8, 1.6 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.4, 146.2, 136.5, 124.2, 117.1, 79.7, 78.4, 72.1, 46.7, 34.8, 31.0, 29.6, 20.4, 15.6.

HRMS-ESI m/z calcd for $C_{14}H_{21}NNaO_2^+$ $[M + Na]^+$ 258.1465, found 258.1458.

Vinyl stannane SI-7



A 250-mL round-bottom flask charged with CuCN (0.54 g, 6.07 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (40.0 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to -78 °C by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.50 M, 5.1 mL, 12.7 mmol, 4.2 equiv) was added dropwise over 10 min, and the resulting solution was stirred for 30 min. Bu_3SnH (3.43 mL, 12.7 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 minutes, a solution of amide **SI-6** (0.71 g, 3.03 mmol, 1 equiv) in THF (3.2 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (25 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm 23 °C while the mixture was rapidly stirring. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layers were extracted with EtOAc (2 × 25 mL). The combined organic layers were washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-7** (1.38 g, 87% yield) as a colorless oil.

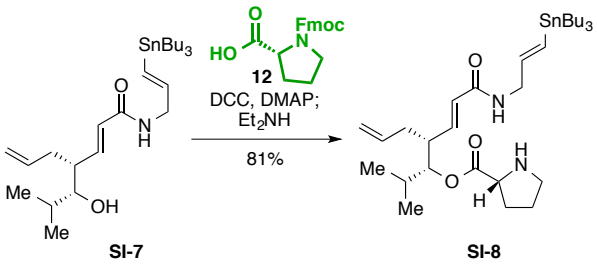
TLC (EtOAc:hexanes = 1:3): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (dd, J = 15.3, 9.6 Hz, 1H), 6.12 (dt, J = 18.9, 1.5 Hz, 1H), 5.98 (dt, J = 19.0, 5.1 Hz, 1H), 5.83 – 5.69 (m, 2H), 5.52 (t, J = 5.9 Hz, 1H), 5.10 – 4.96 (m, 2H), 4.04 – 3.95 (m, 2H), 3.41 – 3.34 (m, 1H), 2.55 – 2.47 (m, 1H), 2.44 – 2.32 (m, 1H), 2.24 – 2.12 (m, 1H), 1.80 – 1.70 (m, 1H), 1.59 – 1.36 (m, 6H), 1.34 – 1.26 (m, 6H), 0.99 – 0.77 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 144.8, 143.4, 136.3, 130.5, 124.7, 116.6, 78.1, 46.3, 45.0, 34.6, 30.7, 29.1, 27.3, 20.1, 15.2, 13.7, 9.5.

HRMS-ESI m/z calcd for $C_{26}H_{50}NO_2Sn^+$ $[M + H]^+$ 528.2858 found 528.2866.

Amine SI-8



A 100-mL round-bottom flask was charged with Fmoc-D-Pro-OH (**12**, 1.16 g, 3.42 mmol, 1.35 equiv), DMAP (62.0 mg, 0.51 mmol, 0.2 equiv) and vinyl stannane **SI-7** (1.34 g, 2.54 mmol, 1 equiv). DCM (25 mL) was added, resulting in a colorless solution. DCC (0.79 g, 3.81 mmol, 1.50 equiv) was added in one portion at 23 °C, resulting in a white suspension. After 5 h, **SI-7** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and diethyl amine (13.0 mL) was added. After 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 20 mL). The combined filtrates were concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-8** (1.28 g, 81% yield) as a light-yellow oil.

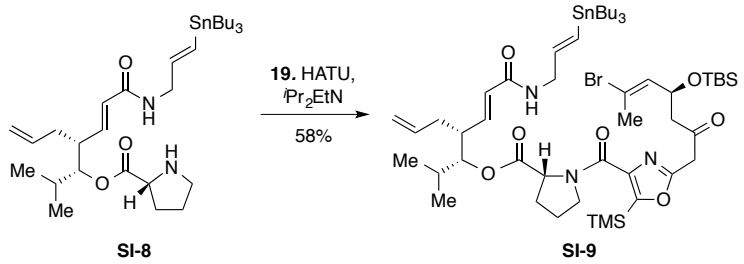
TLC (MeOH:DCM = 1:20) : R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (dd, *J* = 15.3, 9.5 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.96 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.81 (d, *J* = 15.3 Hz, 1H), 5.72 – 5.60 (m, 1H), 5.57 (br, 1H), 5.03 – 4.95 (m, 2H), 4.89 (dd, *J* = 8.1, 4.2 Hz, 1H), 4.01 – 3.95 (m, 2H), 3.80 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.09 (dt, *J* = 10.2, 6.8 Hz, 1H), 2.92 (dt, *J* = 10.2, 6.6 Hz, 1H), 2.55 (m, 1H), 2.38 (s, 1H), 2.28 – 2.02 (m, 3H), 1.94 – 1.72 (m, 4H), 1.54 – 1.40 (m, 6H), 1.33 – 1.24 (m, 6H), 0.91 – 0.83 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 164.8, 143.3, 142.9, 135.3, 130.5, 125.5, 117.1, 79.2, 59.9, 46.9, 45.0, 44.5, 34.4, 30.5, 29.9, 29.0, 27.3, 25.5, 19.8, 15.9, 13.7, 9.5.

HRMS-ESI m/z calcd for $C_{31}H_{57}N_2O_3Sn^+$ $[M + H]^+$ 625.3386 found 625.3390.

Stille coupling precursor SI-9



A 50-mL round-bottom flask was charged with ^{i}Pr$_2$EtN (0.18 mL, 1.06 mmol, 2.0 equiv), amine **SI-8** (0.33 g, 0.53 mmol, 1 equiv) and acid **19** (0.29 g, 0.58 mmol, 1.1 equiv). DCM (6 mL) was added, resulting in colorless solution. HATU (0.25 g, 0.66 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (22 mL). The resulting solution was transferred to a separatory funnel and was washed with water (2 × 28 mL) and brine (18 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-9** (0.34 g, 58% yield) as a light-yellow foam.

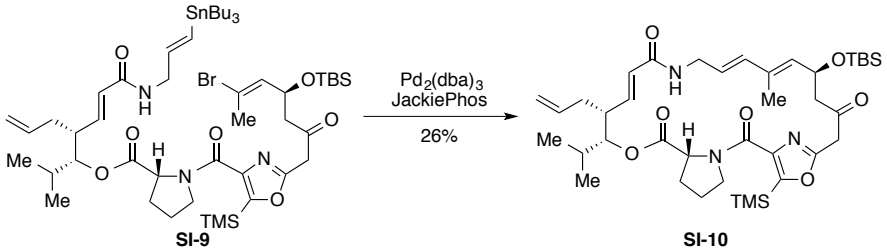
TLC (EtOAc:hexanes = 1:4) : R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.56 (ddd, *J* = 20.2, 15.3, 9.5 Hz, 1H), 6.20 – 6.07 (m, 1H), 6.05 – 5.90 (m, 1H), 5.87 – 5.79 (m, 1H), 5.77 – 5.59 (m, 2H), 5.00 – 4.87 (m, 3H), 4.87 – 4.76 (m, 1H), 4.14 – 3.90 (m, 4H), 3.89 – 3.69 (m, 2H), 2.85 (dt, *J* = 16.3, 8.3 Hz, 1H), 2.55 (pd, *J* = 9.2, 4.5 Hz, 1H), 2.34 – 2.24 (m, 4H), 2.17 – 1.79 (m, 2H), 1.56 – 1.42 (m, 6H), 1.38 – 1.26 (m, 9H), 0.96 – 0.82 (m, 30H), 0.38 – 0.30 (m, 9H), 0.08 – 0.03 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.1, 200.7, 172.4, 172.2, 165.1, 164.8, 163.3, 162.5, 161.5, 159.2, 159.1, 145.2, 145.1, 143.4, 143.3, 143.1, 142.8, 135.6, 135.4, 134.3, 130.4, 130.2, 125.6, 121.8, 117.0, 116.9, 79.5, 79.4, 67.1, 66.9, 60.7, 59.9, 49.7, 49.6, 48.8, 47.1, 44.96, 45.0, 44.7, 44.3, 44.2, 44.0, 34.3, 33.9, 31.7, 30.1, 29.9, 29.0, 27.8, 27.3, 26.8, 25.7, 25.7, 25.3, 24.0, 23.9, 21.6, 20.0, 19.6, 18.0, 17.5, 16.4, 16.2, 13.7, 13.6, 9.5, –1.73, –1.75, –4.5, –5.10, –5.12.

HRMS-ESI m/z calcd for $C_{51}H_{89}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1110.4439 found 1110.4449.

Stille coupling product SI-10



SI-9 **SI-10**

A 100-mL round-bottom flask containing JackiePhos (23.0 mg, 29.0 μmol, 0.2 equiv), Stille coupling precursor **SI-9** (0.16 g, 0.15 mmol, 1 equiv) and $Pd_2(dba)_3$ (13.4 mg, 14.6 μmol, 0.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (30 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by means of an 80 ºC oil bath. After 16 h, **SI-9** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2.5 to 1:2) to afford Stille coupling product **SI-10** (28.6 mg, 26% yield) as a white foam.

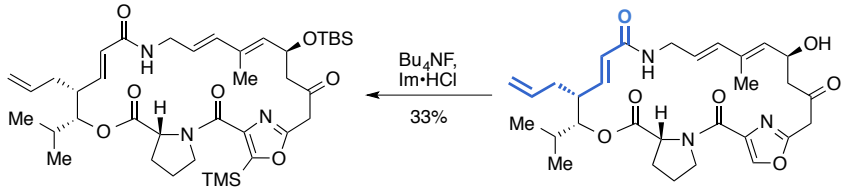
TLC (EtOAc:hexanes = 1:2) : R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (dd, *J* = 16.2, 5.1 Hz, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 6.10 – 6.00 (m, 1H), 5.93 – 5.76 (m, 2H), 5.62 (ddd, *J* = 15.6, 9.1, 4.3 Hz, 1H), 5.42 (d, *J* = 8.8 Hz, 1H), 5.19 – 4.98 (m, 3H), 4.87 (ddd, *J* = 15.3, 9.3, 2.7 Hz, 2H), 4.50 (ddd, *J* = 14.1, 8.8, 4.4 Hz, 1H), 3.97 – 3.86 (m, 1H), 3.86 – 3.72 (m, 2H), 3.67 (dd, *J* = 4.1, 2.1 Hz, 1H), 3.42 (ddd, *J* = 14.9, 9.1, 3.1 Hz, 1H), 3.00 – 2.89 (m, 1H), 2.78 (dd, *J* = 15.9, 6.0 Hz, 1H), 2.44 (d, *J* = 14.5 Hz, 1H), 2.30 – 2.11 (m, 2H), 2.08 – 1.83 (m, 2H), 1.84 – 1.71 (m, 1H), 1.02 – 0.85 (m, 18H), 0.33 (s, 9H), 0.06 (d, *J* = 12.7 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 171.9, 166.0, 161.9, 161.3, 160.9, 159.7, 145.1, 142.9, 136.6, 135.8, 134.7, 132.5, 124.8, 117.1, 81.5, 65.5, 58.9, 50.5, 48.5, 43.8, 41.7, 41.2, 30.4, 29.4, 28.3, 25.8, 24.9, 19.9, 18.7, 12.8, –1.8, –4.5, –4.9.

HRMS-ESI m/z calcd for $C_{39}H_{62}N_3O_7Si_2^+$ $[M + H]^+$ 740.4121 found 740.4116.

Analogue 21



SI-10 **21**

A 50 mL round-bottom flask containing Stille coupling product **SI-10** (30 mg, 41 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (0.8 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (43 mg, 0.41 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.41 mL, 0.41 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-10**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (30 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 15 mL) and brine (15 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **21** (7.3 mg, 33% yield) as a white solid.

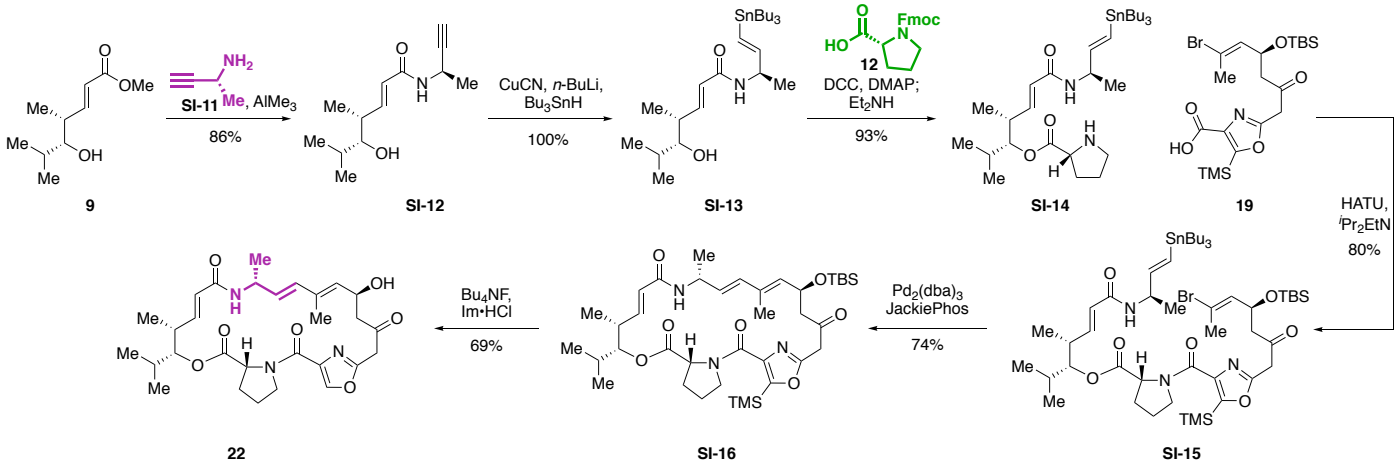
TLC (MeOH:DCM = 1:20) : R_f = 0.15 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 6.69 (dd, *J* = 10.1 Hz, 1H), 6.38 (dd, *J* = 16.3, 6.7 Hz, 1H), 6.06 (d, *J* = 15.7 Hz, 1H), 5.86 (dd, *J* = 16.2, 1.4 Hz, 1H), 5.71 (ddt, *J* = 14.3, 9.8, 5.9 Hz, 2H), 5.25 (d, *J* = 8.8 Hz, 1H), 5.04 – 4.96 (m, 2H), 4.90 (td, *J* = 7.2, 5.0 Hz, 1H), 4.80 (dd, *J* = 9.8, 2.2 Hz, 1H), 4.69 (dd, *J* = 8.8, 3.3 Hz, 1H), 4.46 (ddd, *J* = 14.2, 8.8, 4.9 Hz, 1H), 3.93 – 3.86 (m, 1H), 3.82 (d, *J* = 15.4 Hz, 1H), 3.78 – 3.70 (m, 1H), 3.65 (dd, *J* = 4.0, 1.9 Hz, 1H), 3.44 – 3.34 (m, 1H), 3.04 (dd, *J* = 16.3, 6.8 Hz, 1H), 2.91 – 2.81 (m, 1H), 2.69 – 2.61 (m, 1H), 2.44 – 2.31 (m, 2H), 2.28 – 2.17 (m, 1H), 2.16 – 2.06 (m, 1H), 2.06 – 1.85 (m, 3H), 0.95 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.89, 171.44, 166.31, 160.51, 156.61, 143.95, 141.77, 137.03, 136.86, 135.77, 134.75, 132.21, 126.07, 125.44, 116.91, 81.83, 65.45, 60.05, 48.52, 43.94, 41.97, 41.27, 40.67, 30.99, 29.61, 28.54, 25.15, 19.69, 18.97, 12.80.

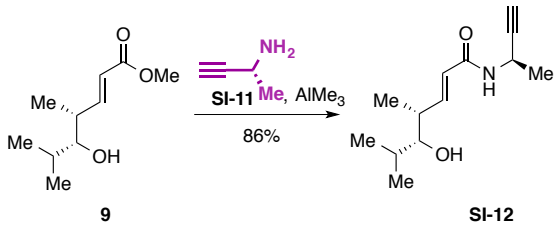
HRMS-ESI m/z calcd for $C_{30}H_{39}N_3NaO_7^+$ $[M + H]^+$ 576.2680, found 576.2678.

Scheme III Synthesis of 22



9 **SI-12** **SI-13** **SI-14** **19** **SI-15** **SI-16** **22**

Amide SI-12



A 200-mL round-bottom flask was charged with (*R*)-but-3-yn-2-amine[12] (**SI-11**, 1.04 g, 15.0 mmol, 4.0 equiv) and dry DCM (25 mL). The resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (2 M, 7.5 mL, 15.0 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!). The mixture was allowed to warm to 23 ºC. After 30 min, a solution of **9** (3.20 g, 17.2 mmol, 1 equiv) in DCM (20 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 12 h, the mixture was cooled to 0 °C by means of an ice/water bath, and MeOH (5 mL) was added (CAUTION: Gas evolution!). Once gas evolution ceased, saturated aqueous potassium sodium tartrate solution (50 mL) was added. After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (60 mL) and brine (60 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-12** (0.72 g, 86% yield) as a white solid.

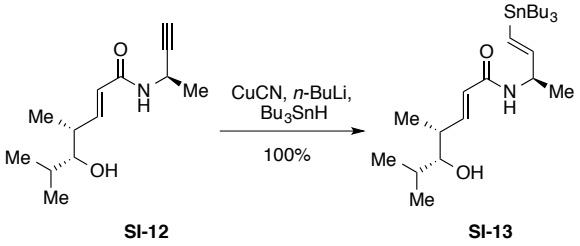
TLC (EtOAc:hexanes = 1:1) : R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (dd, *J* = 15.4, 7.8 Hz, 1H), 6.30 (d, *J* = 8.0 Hz, 1H), 5.81 (dd, *J* = 15.5, 1.2 Hz, 1H), 4.91 – 4.76 (m, 1H), 3.22 (t, *J* = 5.8 Hz, 1H), 2.46 (dddd, *J* = 8.0, 6.9, 5.6, 1.3 Hz, 1H), 2.24 (d, *J* = 2.4 Hz, 2H), 1.69 (dq, *J* = 13.2, 6.6 Hz, 1H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 148.2, 122.8, 84.1, 79.0, 70.3, 39.5, 36.7, 30.8, 22.1, 19.6, 17.0, 13.6.

HRMS-ESI m/z calcd for $C_{13}H_{22}NO_2^+$ $[M + H]^+$ 224.1645, found 224.1648.

Vinyl stannane SI-13



A 200-mL round-bottom flask containing CuCN (0.56 g, 6.27 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (63 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. To this suspension was added a solution of *n*-BuLi in hexanes (2.5 M, 5.27 mL, 13.2 mmol, 4.2 equiv) dropwise over 10 min, and the resulting light-yellow

[12] Rajagopal, B.; Chen, Y.-Y.; Chen, C.-C.; Liu, X.-Y.; Wang, H.-R.; Lin, P.-C. *J. Org. Chem.* **2014**, *79*, 1254–1264.

solution was stirred for 30 min. Bu_3SnH (3.55 mL, 13.2 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 min, a solution of **SI-12** (0.70 g, 3.13 mmol, 1 equiv) in THF (5 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (50 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-13** (1.61 g, 100% yield, ≥20:1 E:Z) as a colorless oil.

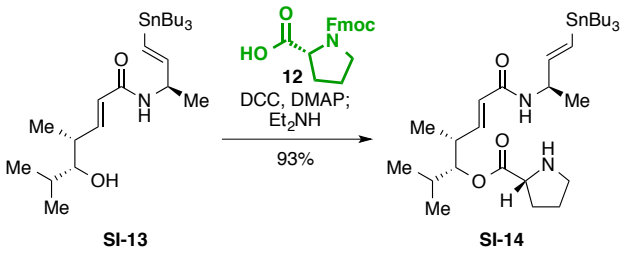
TLC (EtOAc:hexanes = 1:3): R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (dd, *J* = 15.3, 7.8 Hz, 1H), 6.06 (dd, *J* = 19.1, 1.5 Hz, 1H), 5.95 (dd, *J* = 19.2, 4.1 Hz, 1H), 5.81 (dd, *J* = 15.3, 1.2 Hz, 1H), 5.48 (d, *J* = 8.6 Hz, 1H), 4.70 – 4.57 (m, 1H), 3.25 (q, *J* = 5.6 Hz, 1H), 2.48 (dddd, *J* = 8.0, 7.0, 5.9, 1.2 Hz, 1H), 1.80 (d, *J* = 5.1 Hz, 1H), 1.78 – 1.68 (m, 1H), 1.55 – 1.41 (m, 6H), 1.34 – 1.25 (m, 6H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.97 – 0.77 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 148.6, 147.3, 127.1, 123.5, 79.1, 48.8, 39.6, 30.7, 29.0, 27.2, 20.4, 19.7, 16.8, 13.9, 13.6, 9.4.

HRMS-ESI m/z calcd for $C_{25}H_{50}NO_2Sn^+$ $[M + H]^+$ 516.2858, found 516.2863.

Amine SI-14



A 100-mL round-bottom flask was charged with Fmoc-D-Pro-OH (**12**, 0.89 g, 2.62 mmol, 1.35 equiv), DMAP (48 mg, 0.39 mmol, 0.2 equiv) and **SI-13** (1.00 g, 1.94 mmol, 1 equiv). DCM (20 mL) was added, resulting in a colorless solution. DCC (0.60 g, 2.92 mmol, 1.5 equiv) was added in one portion. resulting in a white suspension. After 5 h, the alcohol **SI-13** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and diethyl amine (11 mL) was added. After 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 10 mL). The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-14** (1.10 g, 93% yield) as light-yellow oil.

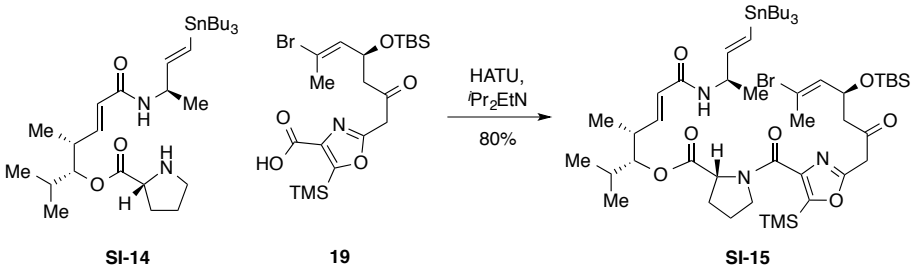
TLC (MeOH:DCM= 1:20): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (dd, *J* = 15.4, 7.7 Hz, 1H), 6.06 (dd, *J* = 19.2, 1.5 Hz, 1H), 5.94 (dd, *J* = 19.1, 4.1 Hz, 1H), 5.81 (dd, *J* = 15.4, 1.2 Hz, 1H), 5.48 (d, *J* = 8.6 Hz, 1H), 4.82 (dd, *J* = 6.7, 5.6 Hz, 1H), 4.68 – 4.56 (m, 1H), 4.02 (br s, 1H), 3.89 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.14 (ddd, *J* = 10.4, 7.5, 6.1 Hz, 1H), 3.05 – 2.95 (m, 1H), 2.70 – 2.60 (m, 1H), 2.25 – 2.15 (m, 1H), 1.97 – 1.87 (m, 2H), 1.85 – 1.71 (m, 2H), 1.53 – 1.40 (m, 6H), 1.34 – 1.24 (m, 6H), 1.23 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.92 – 0.79 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 164.5, 148.5, 144.9, 127.1, 124.2, 80.9, 59.7, 48.8, 46.7, 38.0, 30.2, 29.7, 29.0, 27.2, 25.1, 20.4, 19.5, 16.9, 14.6, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{30}H_{57}N_2O_3Sn^+$ $[M + H]^+$ 613.3386, found 613.3380.

Stille coupling precursor SI-15



A 100-mL round-bottom flask was charged with $^iPr_2EtN$ (0.63 mL, 3.60 mmol, 2.0 equiv), amine **SI-14** (1.10 g, 1.80 mmol, 1 equiv) and acid **19** (1.00 g, 1.98 mmol, 1.1 equiv). DCM (18 mL) was added, resulting in a colorless solution. HATU (0.86 g, 2.25 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (30 mL), and the diluted solution was transferred to a separatory funnel and was washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-15** (1.58 g, 80% yield) as a light-yellow oil.

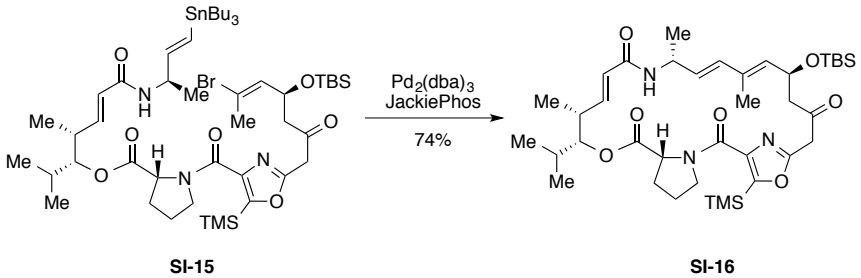
TLC (EtOAc:hexanes = 1:4): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.70 – 6.56 (m, 1H), 6.09 – 5.99 (m, 1H), 5.97 – 5.87 (m, 1H), 5.86 – 5.68 (m, 2H), 5.61 – 5.46 (m, 1H), 4.84 – 4.68 (m, 2H), 4.67 – 4.51 (m, 2H), 4.13 – 3.90 (m, 1H), 3.92 – 3.80 (m, 2H), 3.80 – 3.58 (m, 1H), 2.90 – 2.70 (m, 1H), 2.68 – 2.41 (m, 2H), 2.31 – 2.10 (m, 4H), 1.95 – 1.72 (m, 4H), 1.54 – 1.35 (m, 6H), 1.35 – 1.15 (m, 9H), 0.97 – 0.72 (m, 33H), 0.38 – 0.21 (m, 9H), 0.06 – –0.03 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.0, 200.6, 172.30, 172.29, 164.71, 164.69, 164.4, 163.1, 162.4, 161.5, 161.4, 159.0, 148.57, 148.53, 145.24, 145.12, 145.10, 144.8, 134.2, 126.97, 126.86, 124.16, 124.11, 121.73, 121.71, 80.8, 80.4, 67.0, 66.8, 60.4, 59.8, 49.58, 49.55, 48.74, 48.70, 48.66, 47.0, 44.2, 44.0, 38.3, 37.9, 29.85, 29.73, 28.96, 28.85, 27.2, 25.64, 25.59, 23.95, 23.93, 20.38, 20.35, 19.58, 19.38, 17.9, 17.0, 16.9, 14.7, 14.4, 13.6, 9.4, –1.81, –1.82, –4.6, –4.7, –5.18, –5.20.

HRMS-ESI m/z calcd for $C_{50}H_{89}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1098.4439, found 1098.4455.

Stille coupling product SI-16



A 500-mL round-bottom flask containing JackiePhos (0.22 g, 0.27 mmol, 0.2 equiv), Stille coupling precursor **SI-15** (1.50 g, 1.02 mmol, 1 equiv) and $Pd_2(dba)_3$ (0.13 g, 0.14 mmol, 0.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (270 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by

means of a 50 ºC oil bath. After 3 h, **SI-15** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2.5 to 1:2) to afford Stille coupling product **SI-16** (0.71 g, 74% yield) as a white solid.

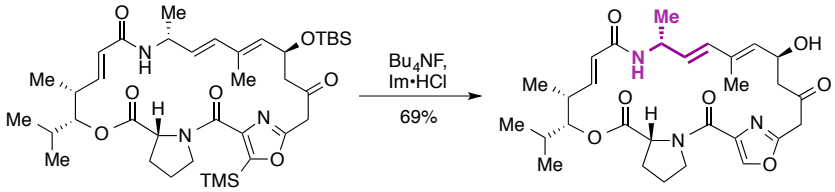
TLC (EtOAc:hexanes = 1:2): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (dd, *J* = 15.5, 4.3 Hz, 1H), 6.22 (d, *J* = 15.4 Hz, 1H), 5.67 – 5.55 (m, 2H), 5.45 (d, *J* = 8.6 Hz, 1H), 5.32 (dd, *J* = 15.4, 8.6 Hz, 1H), 5.05 (td, *J* = 8.4, 3.2 Hz, 1H), 4.85 – 4.70 (m, 2H), 4.62 – 4.50 (m, 1H), 3.82 (d, *J* = 17.3 Hz, 1H), 3.78 – 3.71 (m, 1H), 3.68 (d, *J* = 17.3 Hz, 1H), 3.56 (ddd, *J* = 11.4, 8.8, 3.1 Hz, 1H), 2.97 (dd, *J* = 18.4, 3.2 Hz, 1H), 2.75 – 2.63 (m, 1H), 2.64 (dd, *J* = 18.4, 8.2 Hz, 1H), 2.02 – 1.81 (m, 5H), 1.66 (d, *J* = 1.2 Hz, 3H), 1.23 (d, *J* = 6.7 Hz, 3H), 1.04 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.82 (s, 9H), 0.29 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 169.8, 164.1, 161.54, 161.48, 159.8, 147.5, 145.1, 136.2, 135.3, 130.9, 129.3, 122.6, 80.4, 64.5, 58.9, 50.5, 48.2, 47.4, 43.1, 36.9, 29.3, 28.5, 25.7, 24.4, 21.1, 19.7, 18.5, 18.0, 12.5, 9.2, –1.9, –4.6, –5.0.

HRMS-ESI m/z calcd for $C_{38}H_{62}N_3O_7Si_2^+$ $[M + H]^+$ 728.4121, found 728.4127.

Analogue 22



SI-16 **22**

A 100-mL round-bottom flask containing Stille coupling product **SI-16** (0.70 g, 0.96 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (9.6 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (1.01 g, 9.60 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 9.60 mL, 9.60 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-16**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (100 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **22** (0.36 g, 69% yield) as a light-yellow solid.

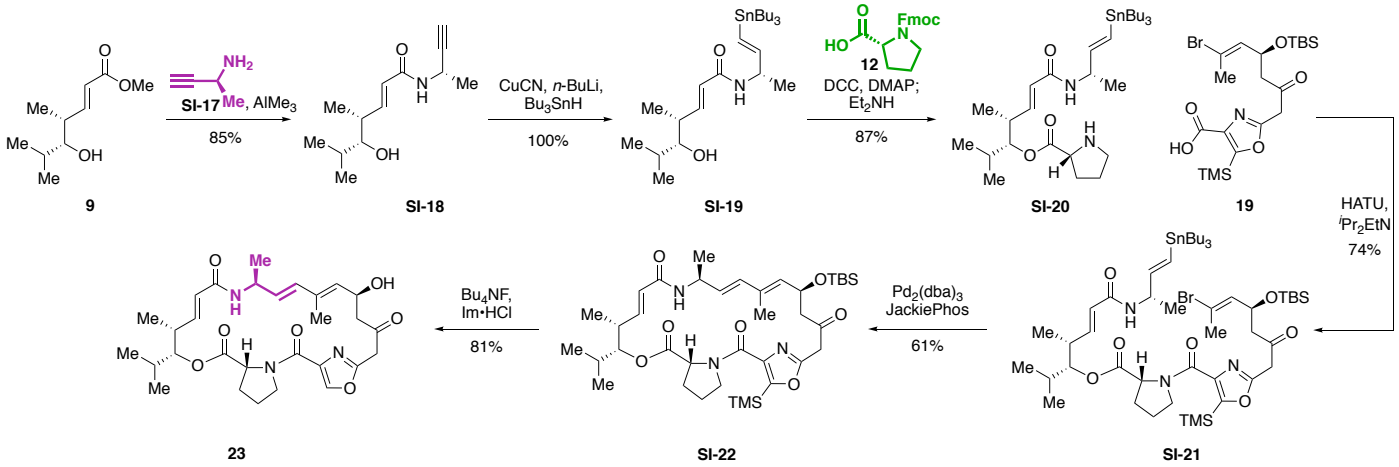
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 6.87 (dd, *J* = 15.5, 4.2 Hz, 1H), 6.29 (d, *J* = 15.4 Hz, 1H), 5.66 – 5.53 (m, 3H), 5.40 (dd, *J* = 15.4, 8.9 Hz, 1H), 4.99 (td, *J* = 8.3, 3.5 Hz, 1H), 4.82 (dd, *J* = 10.3, 1.9 Hz, 1H), 4.77 (dd, *J* = 8.3, 2.5 Hz, 1H), 4.62 – 4.52 (m, 1H), 3.84 (d, *J* = 17.4 Hz, 1H), 3.80 – 3.70 (m, 2H), 3.77 (d, *J* = 17.4 Hz, 1H), 3.29 (dd, *J* = 18.4, 3.4 Hz, 1H), 2.79 – 2.67 (m, 2H), 2.08 – 1.99 (m, 1H), 1.99 – 1.86 (m, 3H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.60 – 1.45 (m, 1H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H).

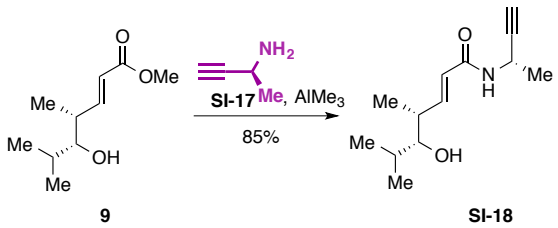
^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 169.6, 164.1, 159.9, 157.4, 147.9, 143.8, 137.2, 135.5, 133.7, 133.3, 130.0, 122.3, 80.6, 64.4, 59.1, 49.1, 48.4, 47.7, 42.6, 36.9, 29.3, 28.3, 24.6, 21.0, 19.7, 18.5, 12.6, 9.2.

HRMS-ESI m/z calcd for $C_{29}H_{39}N_3NaO_7^+$ $[M + Na]^+$ 564.2680, found 564.2678.

Scheme IV Synthesis of 23



Amide SI-18



A 100-mL round-bottom flask was charged with (*S*)-but-3-yn-2-amine[12] (**SI-17**, 1.04 g, 15.0 mmol, 4.0 equiv) and dry DCM (25 mL) under nitrogen. The resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (2 M, 7.5 mL, 15.0 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!). The mixture was allowed to warm to 23 ºC. After 30 min, a solution of **9** (3.20 g, 17.2 mmol, 1 equiv) in DCM (10 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 12 h, the mixture was cooled to 0 °C by means of an ice/water bath, and MeOH (10 mL) was added (CAUTION: Gas evolution!). Once gas evolution ceased, saturated aqueous potassium sodium tartrate solution (50 mL) was added. After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (60 mL) and brine (60 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-18** (0.71 g, 85% yield) as a white solid.

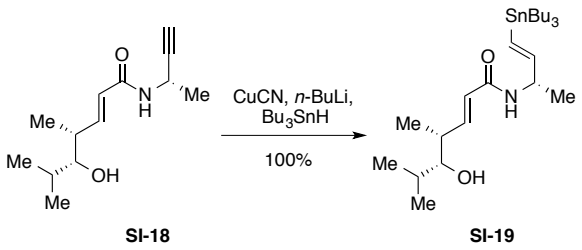
TLC (EtOAc:hexanes = 1:1) : R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dd, *J* = 15.4, 7.8 Hz, 1H), 6.06 (d, *J* = 8.1 Hz, 1H), 5.80 (dd, *J* = 15.4, 0.8 Hz, 1H), 4.94 – 4.80 (m, 1H), 3.23 (t, *J* = 5.8 Hz, 1H), 2.52 – 2.42 (m, 1H), 2.26 (d, *J* = 2.3 Hz, 1H), 1.97 (s, 1H), 1.71 (dq, *J* = 13.2, 6.6 Hz, 1H), 1.42 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 148.3, 122.8, 84.1, 79.1, 70.4, 39.5, 36.8, 30.8, 22.2, 19.7, 16.9, 13.7.

HRMS-ESI m/z calcd for $C_{13}H_{22}NO_2^+$ $[M + H]^+$ 224.1645, found 224.1648.

Vinyl stannane SI-19



SI-18 **SI-19**

A 200-mL round-bottom flask containing CuCN (0.56 g, 6.27 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Dry THF (63 mL) was added, resulting in a white suspension and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 5.27 mL, 13.2 mmol, 4.2 equiv) was added dropwise over 10 min, and the resulting light-yellow solution was stirred for 30 min. Bu_3SnH (3.55 mL, 13.2 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 min, a solution of **SI-18** (0.70 g, 3.13 mmol, 1 equiv) in THF (5 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (50 mL) was added in one portion. The vessel was removed from the cooling bath and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-19** (1.61 g, 100% yield, ≥20:1 E:Z) as a colorless oil.

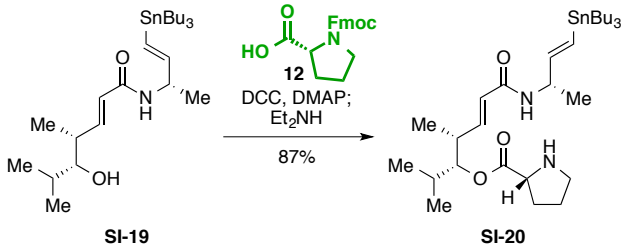
TLC (EtOAc:hexanes = 1:3): R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dd, *J* = 15.3, 7.8 Hz, 1H), 6.07 (dd, *J* = 19.1, 1.5 Hz, 1H), 5.96 (dd, *J* = 19.1, 4.1 Hz, 1H), 5.81 (dd, *J* = 15.3, 1.2 Hz, 1H), 5.43 (d, *J* = 8.6 Hz, 1H), 4.70 – 4.55 (m, 1H), 3.26 (q, *J* = 5.6 Hz, 1H), 2.49 (dddd, *J* = 8.0, 7.0, 5.8, 1.3 Hz, 1H), 1.74 (dq, *J* = 13.3, 6.6 Hz, 1H), 1.64 (d, *J* = 5.1 Hz, 1H), 1.52 – 1.42 (m, 6H), 1.34 – 1.26 (m, 6H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 2.0 Hz, 3H), 0.91 (d, *J* = 2.1 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 15H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 148.6, 147.2, 127.1, 123.5, 79.2, 48.8, 39.5, 30.8, 29.0, 27.2, 20.4, 19.7, 16.8, 13.8, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{25}H_{50}NO_2Sn^+$ $[M + H]^+$ 516.2858, found 516.2863.

Amine SI-20



SI-19 **SI-20**

A 100-mL round-bottom flask was charged with **12** (0.73 g, 2.15 mmol, 1.35 equiv), DMAP (39 mg, 0.32 mmol, 0.2 equiv) and **SI-19** (0.82 g, 1.59 mmol, 1 equiv). DCM (16 mL) was added, resulting in a colorless solution. DCC (0.49 g,

2.39 mmol, 1.5 equiv) was added in one portion. resulting in a white suspension. After 5 h, the alcohol **SI-19** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and diethyl amine (8 mL) was added. After 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 20 mL). The combined filtrates were concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-20** (0.85 g, 87% yield) as light-yellow oil.

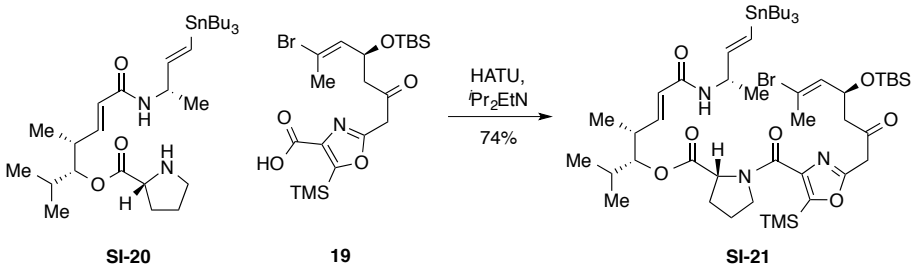
TLC (MeOH:DCM= 1:20): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.69 (dd, *J* = 15.4, 7.6 Hz, 1H), 6.06 (dd, *J* = 19.2, 1.5 Hz, 1H), 5.95 (dd, *J* = 19.2, 4.2 Hz, 1H), 5.81 (dd, *J* = 15.5, 1.2 Hz, 1H), 5.53 (d, *J* = 8.6 Hz, 1H), 4.82 (t, *J* = 6.1 Hz, 1H), 4.67 – 4.56 (m, 1H), 4.52 (br s, 1H), 3.93 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.16 (ddd, *J* = 10.6, 7.5, 6.1 Hz, 1H), 3.03 (dt, *J* = 10.5, 6.8 Hz, 1H), 2.66 (q, *J* = 6.4 Hz, 1H), 2.31 – 2.07 (m, 1H), 2.01 – 1.69 (m, 4H), 1.54 – 1.37 (m, 6H), 1.35 – 1.20 (m, 6H), 1.23 (d, *J* = 6.7 Hz, 4H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.95 – 0.75 (m, 22H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 164.5, 148.5, 144.9, 127.2, 124.1, 81.1, 59.7, 48.8, 46.6, 38.0, 30.1, 29.7, 29.0, 27.2, 24.9, 20.4, 19.5, 16.9, 14.5, 13.6, 9.4.

HRMS-ESI m/z calcd for $C_{30}H_{57}N_2O_3Sn^+$ $[M + H]^+$ 613.3386, found 613.3380.

Stille coupling precursor SI-21



A 100-mL round-bottom flask was charged with ^{i}Pr$_2$EtN (0.34 mL, 1.96 mmol, 2.0 equiv), amine **SI-20** (0.60 g, 0.98 mmol, 1 equiv) and acid **19** (0.55 g, 1.08 mmol, 1.1 equiv). DCM (10 mL) was added, resulting in a colorless solution. HATU (0.47 g, 1.23 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (30 mL). The resulting solution was transferred to a separatory funnel and was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-21** (0.80 g, 74% yield) as a light-yellow oil.

TLC (EtOAc:hexanes = 1:4): R_f = 0.30 (UV).

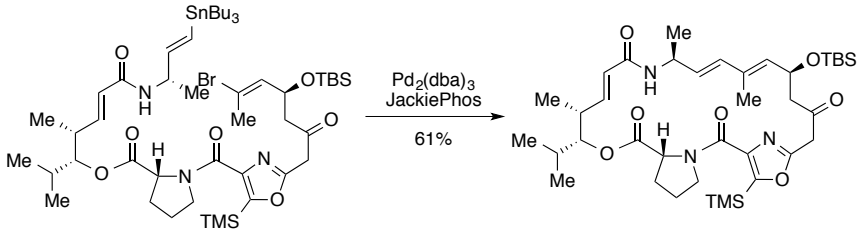
^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.75 – 6.57 (m, 1H), 6.13 – 6.04 (m, 1H), 6.01 – 5.93 (m, 1H), 5.84 – 5.70 (m, 2H), 5.51 – 5.38 (m, 1H), 4.86 – 4.69 (m, 2H), 4.63 (ddd, *J* = 11.6, 8.3, 3.2 Hz, 2H), 4.17 – 3.93 (m, 1H), 3.93 – 3.82 (m, 2H), 3.82 – 3.61 (m, 1H), 2.90 – 2.75 (m, 1H), 2.68 – 2.43 (m, 2H), 2.33 – 2.19 (m, 3H), 2.24 – 2.14 (m, 1H), 2.15 – 1.75 (m, 4H), 1.70 – 1.57 (m, 1H), 1.54 – 1.40 (m, 6H), 1.38 – 1.18 (m, 9H), 1.07 – 0.66 (m, 33H), 0.41 – 0.21 (m, 9H), 0.10 – –0.05 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.1, 200.6, 172.33, 172.31, 164.65, 164.63, 164.41, 163.2, 162.5, 161.52, 161.42, 159.07, 159.03, 148.59, 148.52, 145.37, 145.30, 145.2, 145.0, 134.2, 127.19, 127.11, 124.09, 124.03, 121.79, 121.78, 80.8, 80.3, 67.0, 66.9, 60.5, 59.8, 49.64, 49.62, 48.85, 48.80, 48.74, 47.1, 44.2, 44.0, 38.5, 38.1,

30.0, 29.8, 29.0, 28.9, 27.2, 25.7, 25.6, 20.41, 20.38, 19.7, 19.5, 18.0, 17.5, 16.82, 16.78, 15.1, 14.7, 13.7, 13.6, 9.4, –1.76, –1.77, –4.6, –5.13, –5.14.

HRMS-ESI m/z calcd for $C_{50}H_{89}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1098.4439, found 1098.4455.

Stille coupling product SI-22



SI-21 **SI-22**

A 250-mL round-bottom flask containing JackiePhos (0.12 g, 0.15 mmol, 0.2 equiv), Stille coupling precursor **SI-21** (0.80 g, 0.73 mmol, 1 equiv) and $Pd_2(dba)_3$ (67 mg, 0.073 mmol, 0.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (146 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by means of a 50 ºC oil bath. After 3 h, **SI-21** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2.5 to 1:2) to afford Stille coupling product **SI-22** (0.35 g, 61% yield) as a white solid.

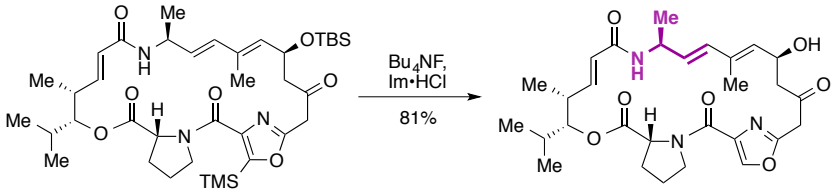
TLC (EtOAc:hexanes = 1:2): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.46 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.07 (dd, *J* = 16.1, 1.6 Hz, 1H), 5.83 – 5.73 (m, 2H), 5.68 (dd, *J* = 16.0, 4.4 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 5.00 (dt, *J* = 8.7, 6.4 Hz, 1H), 4.82 – 4.69 (m, 3H), 3.86 (d, *J* = 17.0 Hz, 1H), 3.79 – 3.73 (m, 2H), 3.70 (d, *J* = 17.0 Hz, 1H), 2.89 (dd, *J* = 16.2, 6.6 Hz, 1H), 2.78 (dd, *J* = 16.2, 6.2 Hz, 1H), 2.76 – 2.66 (m, 1H), 2.14 – 2.02 (m, 1H), 2.00 – 1.80 (m, 3H), 1.78 – 1.69 (m, 1H), 1.67 (s, 3H), 1.28 (d, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.84 (s, 9H), 0.29 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 172.0, 165.6, 161.6, 161.4, 159.7, 145.1, 144.6, 134.5, 132.5, 132.4, 129.6, 123.9, 80.9, 65.4, 58.9, 50.2, 48.4, 44.3, 43.5, 36.5, 29.3, 28.2, 25.7, 24.8, 19.8, 18.8, 18.6, 18.04, 12.8, 10.2, –1.9, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{38}H_{62}N_3O_7Si_2^+$ $[M + H]^+$ 728.4121, found 728.4127.

Analogue 23



SI-22 **23**

A 100-mL round-bottom flask containing Stille coupling product **SI-22** (0.30 g, 0.41 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (4.1 mL) was added, resulting in a light-yellow

solution. In a separate flask, Im•HCl (0.43 g, 4.1 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 4.1 mL, 4.1 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-22**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (100 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **23** (0.18 g, 81% yield) as a light-yellow solid.

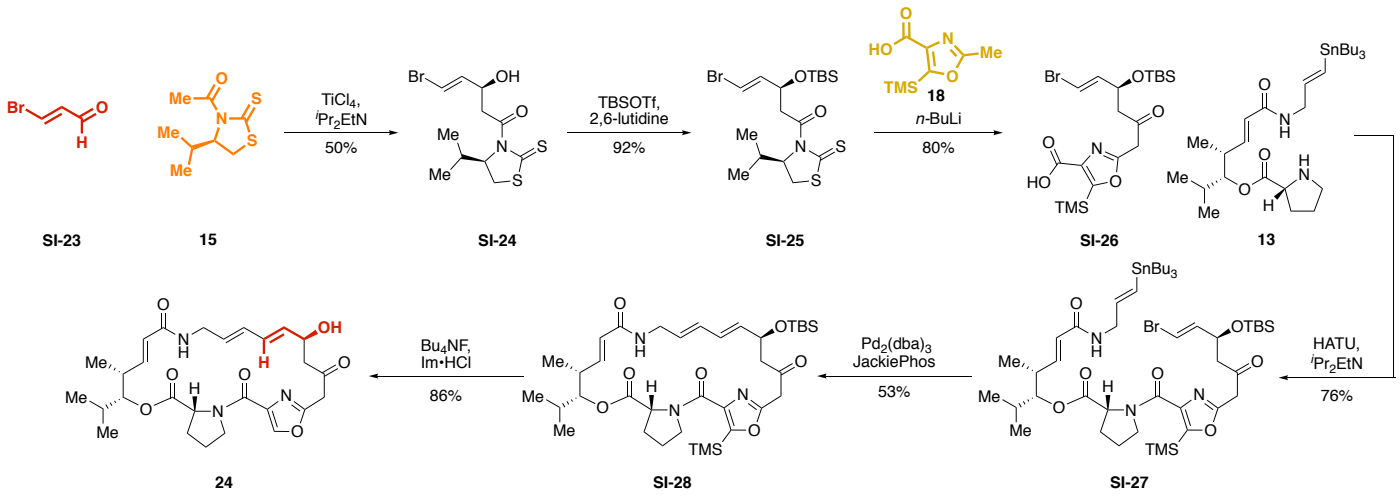
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 6.46 (dd, *J* = 16.3, 5.1 Hz, 1H), 6.20 (d, *J* = 9.0 Hz, 1H), 6.06 (dd, *J* = 16.1, 1.5 Hz, 1H), 5.85 – 5.75 (m, 2H), 5.32 (d, *J* = 8.6 Hz, 1H), 4.89 (dt, *J* = 8.7, 5.8 Hz, 1H), 4.81 – 4.66 (m, 3H), 3.97 (dt, *J* = 10.9, 7.2 Hz, 1H), 3.84 (d, *J* = 15.6 Hz, 1H), 3.84 – 3.74 (m, 1H), 3.78 (d, *J* = 15.5 Hz, 1H), 3.00 (dd, *J* = 16.6, 6.4 Hz, 1H), 2.87 (dd, *J* = 16.6, 5.3 Hz, 1H), 2.77 – 2.67 (m, 1H), 2.21 – 2.11 (m, 1H), 2.02 – 1.78 (m, 4H), 1.71 (s, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H).

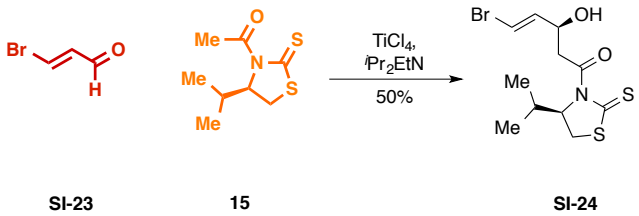
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 171.7, 165.9, 160.2, 156.9, 144.1, 143.9, 137.0, 135.0, 132.4, 131.8, 130.5, 124.4, 81.3, 65.2, 59.7, 48.48, 48.46, 44.3, 43.5, 36.5, 29.5, 28.4, 25.0, 19.7, 19.2, 18.8, 12.9, 10.9.

HRMS-ESI m/z calcd for $C_{29}H_{39}N_3NaO_7^+$ $[M + Na]^+$ 564.2680, found 564.2678.

Scheme V Synthesis of 24



***β*-hydroxyl amide SI-24**



A 250-mL round-bottom flask containing **15** (1.94 g, 9.54 mmol, 1.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (50 mL) was added, resulting in a yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of $TiCl_4$ in DCM (1 M, 10.4 mL, 10.4

mmol, 1.2 equiv) was added dropwise, resulting in a deep yellow solution. After 5 min, $^{i}Pr_2EtN$ (1.80 mL, 10.4 mmol, 1.2 equiv) was added over 30 min by means of syringe pump, and the resulting deep red solution was stirred for 2 h at -78 ºC. A solution of aldehyde **SI-23** (1.17 g, 8.67 mmol, 1 equiv) in DCM (10 mL) was added over 30 min by means of syringe pump. After 30 min, water (100 mL) was added. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:5 to 1:2) to afford *β*-hydroxyl amide **SI-24** (1.46 g, 50% yield) as a yellow oil.

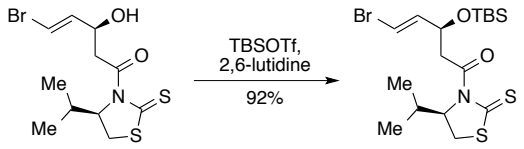
TLC (EtOAc:hexanes = 1:4): R_f = 0.25 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (dd, *J* = 13.5, 1.4 Hz, 1H), 6.28 (dd, *J* = 13.6, 5.6 Hz, 1H), 5.15 (ddd, *J* = 7.7, 6.2, 1.1 Hz, 1H), 4.72 – 4.62 (m, 1H), 3.69 (dd, *J* = 17.7, 3.1 Hz, 1H), 3.54 (dd, *J* = 11.5, 7.9 Hz, 1H), 3.29 (dd, *J* = 17.7, 8.6 Hz, 1H), 3.06 (br s, 1H), 3.04 (dd, *J* = 11.4, 1.1 Hz, 1H), 2.45 – 2.25 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 171.8, 137.7, 108.1, 71.3, 68.5, 44.6, 30.8, 30.7, 19.1, 17.8.

HRMS-ESI m/z calcd for $C_{11}H_{15}BrNOS_2^+$ $[M - OH]^+$ 319.9773, found 319.9777.

TBS ether SI-25



SI-24 **SI-25**

A 250-mL round-bottom flask containing *β*-hydroxyl amide **SI-24** (1.45 g, 4.29 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (43 mL) was added, followed by 2,6-lutidine (1.0 mL, 8.57 mmol, 2.0 equiv), resulting in a yellow solution. The vessel and its contents were cooled to 0 ºC by means of an ice/water bath. TBSOTf (1.48 mL, 6.43 mmol, 1.2 equiv) was added dropwise over 10 min. After 30 min, the mixture was transferred to a separatory funnel and was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtrated, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:20) to afford TBS ether **SI-25** (1.79 g, 92% yield) as a light-yellow oil.

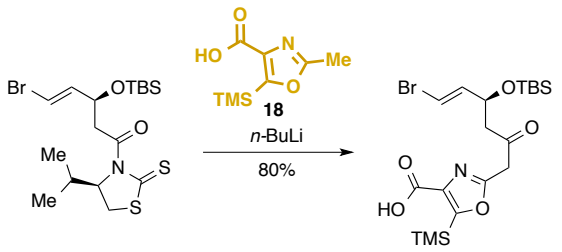
TLC (EtOAc:hexanes = 1:50): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 – 6.23 (m, 2H), 5.04 (ddd, *J* = 7.7, 6.3, 1.1 Hz, 1H), 4.73 (ddd, *J* = 7.7, 5.9, 4.6 Hz, 1H), 3.61 (dd, *J* = 16.8, 7.8 Hz, 1H), 3.48 (dd, *J* = 11.5, 7.8 Hz, 1H), 3.26 (dd, *J* = 16.8, 4.6 Hz, 1H), 3.03 (dd, *J* = 11.5, 1.1 Hz, 1H), 2.42 – 2.28 (m, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.86 (s, 9H), 0.05 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 170.5, 139.5, 107.1, 71.6, 70.0, 45.8, 30.8, 30.7, 25.7, 19.1, 18.0, 17.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{17}H_{30}BrNNaO_2S_2Si^+$ $[M + Na]^+$ 474.0563, found 474.0569.

Acid SI-26



SI-25 **SI-26**

A 100-mL round-bottom flask containing **18** (0.34 g, 1.68 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (17 mL) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 1.34 mL, 3.36 mmol, 4.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, a solution of **SI-25** (0.38 g, 0.84 mmol, 1 equiv) in THF (5.0 mL) was added over 30 min by means of syringe pump. After an additional 30 min, water (100 mL) was added, followed by 1 M aqueous $KHSO_4$ solution (5 mL). The system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 40 mL). The combined organic layers were washed with water (2 × 70 mL) and brine (70 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: AcOH:EtOAc:hexanes = 0.5:50:50) to afford carboxylic acid **SI-26** (0.33 g, 80% yield) as a yellow solid.

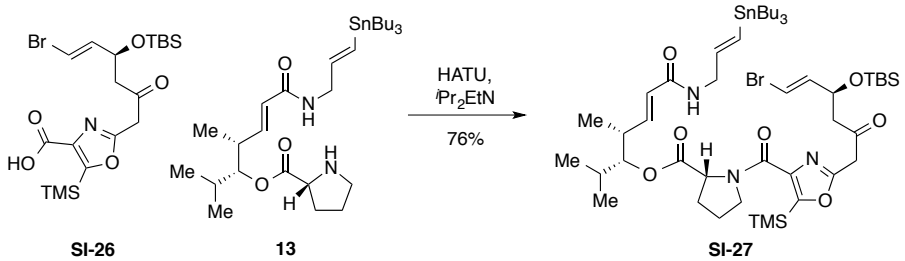
TLC (MeOH:DCM = 1:20): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (s, 1H), 6.31 (dd, *J* = 13.5, 1.0 Hz, 1H), 6.19 (dd, *J* = 13.6, 6.3 Hz, 1H), 4.64 (dddd, *J* = 7.5, 6.1, 4.9, 1.1 Hz, 1H), 4.15 (d, *J* = 17.0 Hz, 1H), 4.06 (d, *J* = 17.0 Hz, 1H), 2.84 (dd, *J* = 15.9, 7.6 Hz, 1H), 2.64 (dd, *J* = 15.9, 4.9 Hz, 1H), 0.86 (s, 9H), 0.37 (s, 9H), 0.04 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 165.3, 165.2, 161.0, 140.8, 139.1, 107.3, 69.5, 49.9, 43.5, 25.7, 18.0, –2.2, –4.6, –5.1.

HRMS-ESI m/z calcd for $C_{19}H_{32}BrNNaO_5Si_2^+$ $[M + Na]^+$ 512.0895, found 512.0920

Stille coupling precursor SI-27



SI-26 **13** **SI-27**

A 50-mL round-bottom flask was charged with ^{i}Pr$_2$EtN (0.11 mL, 0.64 mmol, 2.0 equiv), amine **13** (0.19 g, 0.32 mmol, 1 equiv) and acid **SI-26** (0.17 g, 0.33 mmol, 1.1 equiv). DCM (6.5 mL) was added, resulting in a colorless solution. HATU (0.15 g, 0.40 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (30 mL), and the diluted solution was transferred to a separatory funnel and was washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The

resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3) to afford Stille coupling precursor **SI-27** (0.26 g, 76% yield) as a light-yellow oil.

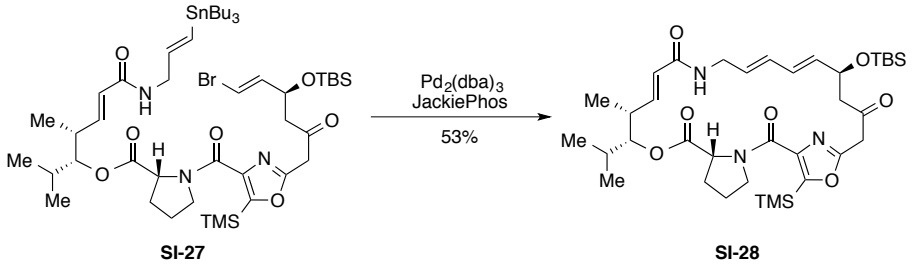
TLC (EtOAc:hexanes = 1:2): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.76 – 6.56 (m, 1H), 6.35 – 6.25 (m, 1H), 6.25 – 6.16 (m, 1H), 6.11 (dq, *J* = 19.0, 1.5 Hz, 1H), 5.96 (dt, *J* = 19.1, 5.1 Hz, 1H), 5.87 – 5.72 (m, 1H), 5.72 – 5.55 (m, 1H), 4.80 (t, *J* = 6.2 Hz, 0.6H), 4.73 (t, *J* = 6.2 Hz, 0.4H), 4.66 – 4.46 (m, 2H), 4.15 – 3.64 (m, 6H), 2.88 – 2.74 (m, 1H), 2.71 – 2.40 (m, 2H), 2.33 – 2.15 (m, 1H), 2.10 – 1.82 (m, 4H), 1.57 – 1.37 (m, 6H), 1.35 – 1.32 (m, 6H), 1.07 – 0.92 (m, 6H), 0.92 – 0.77 (m, 27H), 0.37 – 0.27 (m, 9H), 0.07 – 0.01 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.0, 200.5, 172.34, 172.32, 165.4, 165.1, 163.2, 162.5, 161.5, 161.4, 159.01, 158.97, 145.37, 145.26, 145.22, 145.13, 143.4, 143.3, 139.23, 139.20, 130.4, 130.2, 123.9, 123.8, 107.3, 80.8, 80.4, 69.6, 69.5, 60.5, 59.9, 49.8, 48.8, 47.1, 44.9, 44.9, 44.1, 43.8, 38.4, 38.1, 31.6, 29.9, 29.8, 29.1, 29.0, 28.9, 27.2, 25.73, 25.68, 25.2, 21.5, 19.7, 19.5, 18.0, 17.0, 16.9, 14.9, 14.6, 13.7, 9.4, –1.74, –1.77, –1.79, –4.6, –5.10, –5.13.

HRMS-ESI m/z calcd for $C_{48}H_{85}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1070.4126, found 1070.4136.

Stille coupling product SI-28



A 100-mL round-bottom flask containing JackiePhos (15 mg, 19 μmol, 0.2 equiv), Stille coupling precursor **SI-27** (100 mg, 94 μmol, 1 equiv) and $Pd_2(dba)_3$ (9 mg, 9 μmol, 0.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (19 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by means of a 50 ºC oil bath. After 3 h, **SI-27** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash cheomatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille coupling product **SI-28** (35 mg, 53% yield) as a white solid.

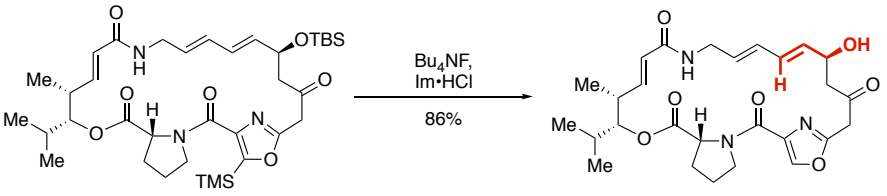
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (dd, *J* = 16.3, 4.6 Hz, 1H), 6.19 – 6.03 (m, 2H), 5.99 (dd, *J* = 7.5, 3.6 Hz, 1H), 5.78 (dd, *J* = 16.3, 1.9 Hz, 1H), 5.72 – 5.56 (m, 2H), 4.84 – 4.70 (m, 3H), 4.26 (dt, *J* = 14.3, 6.5 Hz, 1H), 3.90 (d, *J* = 16.4 Hz, 1H), 3.85 – 3.80 (m, 2H), 3.73 (d, *J* = 16.4 Hz, 1H), 3.56 (ddd, *J* = 15.2, 7.5, 3.5 Hz, 1H), 2.86 (dd, *J* = 16.3, 7.0 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.70 (dd, *J* = 16.3, 5.7 Hz, 1H), 2.20 – 2.06 (m, 1H), 2.03 – 1.77 (m, 4H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.30 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 172.4, 166.7, 161.7, 161.6, 159.6, 145.2, 144.7, 135.5, 131.9, 129.0, 128.9, 123.8, 81.3, 69.0, 59.1, 50.8, 48.5, 43.3 41.1, 36.7, 29.4, 28.29, 25.8, 25.1, 19.8, 18.6, 18.1, 9.9, –1.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{36}H_{58}N_3O_7Si_2^+$ $[M + H]^+$ 700.3808, found 700.3816.

Analogue 24



SI-28 **24**

A 100-mL round-bottom flask containing **SI-28** (35 mg, 50 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.0 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (52 mg, 0.50 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.50 mL, 0.50 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-28**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (25 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 40 mL) and brine (40 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **24** (22 mg, 86% yield) as a light-yellow solid.

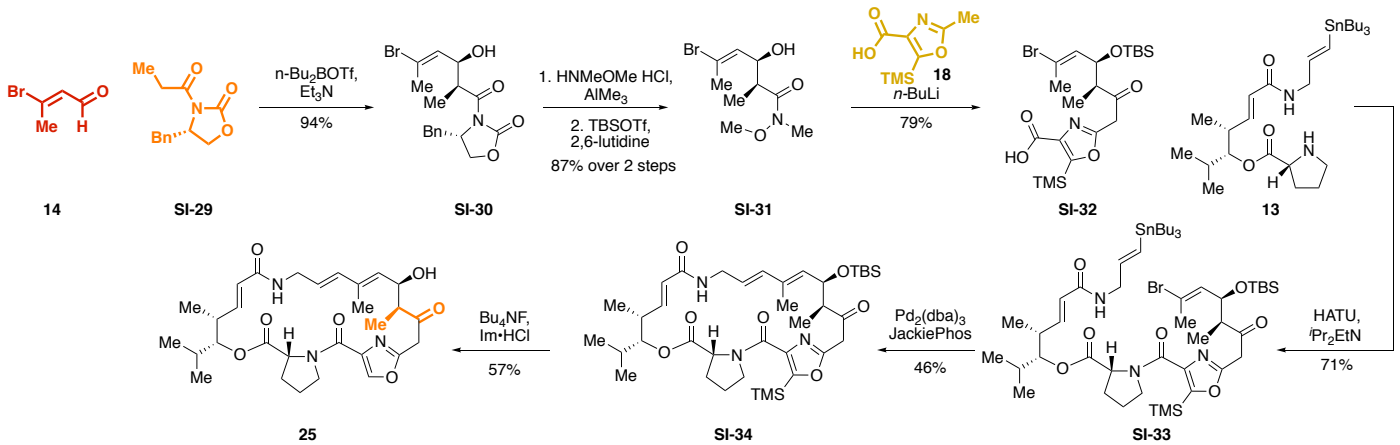
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 6.48 (dd, *J* = 16.4, 4.8 Hz, 1H), 6.27 – 6.15 (m, 1H), 6.15 – 6.04 (m, 2H), 5.78 (dd, *J* = 16.4, 2.1 Hz, 1H), 5.73 – 5.58 (m, 2H), 4.71 (ddd, *J* = 12.7, 9.3, 2.8 Hz, 2H), 4.60 (q, *J* = 6.3 Hz, 1H), 4.33 (ddd, *J* = 14.4, 8.1, 5.0 Hz, 1H), 4.10 – 3.96 (m, 1H), 3.95 – 3.85 (m, 1H), 3.84 (s, 2H), 3.48 (ddd, *J* = 15.0, 7.9, 3.5 Hz, 1H), 3.01 (dd, *J* = 16.8, 5.4 Hz, 1H), 2.91 (dd, *J* = 16.9, 5.7 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.68 (br s, 1H), 2.23 – 2.10 (m, 1H), 2.01 – 1.79 (m, 4H), 1.05 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H).

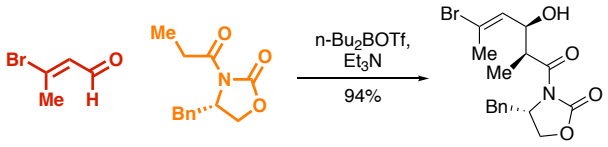
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 171.7, 166.7, 160.1, 157.0, 144.6, 144.1, 137.2, 133.9, 131.6, 130.4, 130.1, 124.1, 81.6, 69.0, 59.6, 48.9, 48.6, 43.1, 40.9, 36.7, 29.4, 28.4, 25.1, 19.7, 18.7, 10.2

HRMS-ESI m/z calcd for $C_{27}H_{34}N_3O_6^+$ $[M - OH]^+$ 496.2442, found 496.2454.

Scheme VI Synthesis of 25



β-hydroxyl Amide SI-30



14 **SI-29** **SI-30**

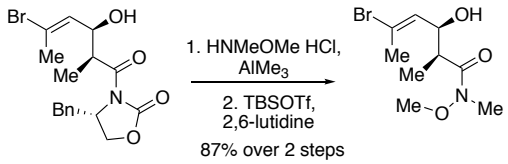
A 250-mL round-bottom flask containing **SI-29** (0.38 g, 1.61 mmol, 1.2 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (8 mL) was added, resulting in a colorless solution, and the vessel and its contents were cooled to 0 ºC by means of an ice/water bath. A solution of *n*-Bu_2BOTf in DCM (1 M, 1.88 mL, 1.88 mmol, 1.2 equiv) was added dropwise, resulting in a pink solution. After 5 min, Et_3N (0.28 mL, 2.01 mmol, 1.5 equiv) was added dropwise over 15 min, and the resulting colorless solution was stirred at 0 ºC for 1 h. Then the flask was cooled to -78 ºC by means of a dry ice/acetone bath, and a solution of aldehyde **14** (0.20 g, 1.34 mmol, 1 equiv) in DCM (2 mL) was added over 30 min by means of syringe pump. After 3 h, the mixture was warmed to 0 ºC by means of an ice/water bath, and pH = 7 phosphate buffer (10 mL), MeOH (20 mL) and 30% H_2O_2 (10 mL) were cautiously added with maintaining the internal temperature between 0-5 ºC. The resulting cloudy mixture was stirred for 1 h and was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:5 to 1:2) to afford *β*-hydroxyl amide **SI-30** (0.48 g, 94% yield, dr > 20:1) as a yellow oil.

TLC (EtOAc:hexanes = 1:4): R_f = 0.25 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.17 (m, 3H), 7.15 – 7.08 (m, 2H), 5.90 (dq, *J* = 8.9, 1.3 Hz, 1H), 4.61 (ddt, *J* = 9.4, 7.6, 3.2 Hz, 1H), 4.51 (dd, *J* = 8.9, 5.1 Hz, 1H), 4.17 (dd, *J* = 9.1, 7.6 Hz, 1H), 4.11 (dd, *J* = 9.1, 2.9 Hz, 1H), 3.84 (qd, *J* = 7.0, 5.0 Hz, 1H), 3.16 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.72 (dd, *J* = 13.4, 9.4 Hz, 1H), 2.58 (br s, 1H), 2.24 (d, *J* = 1.4 Hz, 3H), 1.23 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4, 153.1, 134.9, 131.4, 129.3, 128.9, 127.4, 124.6, 69.9, 66.2, 55.1, 42.8, 37.7, 24.2, 12.1.

Weinreb amide SI-31



SI-30 **SI-31**

A 250-mL round-bottom flask containing HN(OMe)Me•HCl (0.84 g, 8.58 mmol, 4.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (43 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (2.0 M, 4.18 mL, 8.37 mmol, 3.9 equiv) was added dropwise. The mixture was maintained at 0 °C for 30 min and then at 23 ºC for 90 min. The mixture was cooled to -10 °C by means of an ice/acetone bath, and a solution of *β*-hydroxyl amide **SI-30** (0.82 g, 2.15 mmol, 1 equiv) in THF (10 mL) was added by cannula. The mixture was warmed to 0 °C by means of an ice/water bath. After 90 min, 1.0 M aqueous HCl solution (30 mL) was carefully added, followed by DCM (50 mL) at 0

ºC. After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was used for next step without further purification.

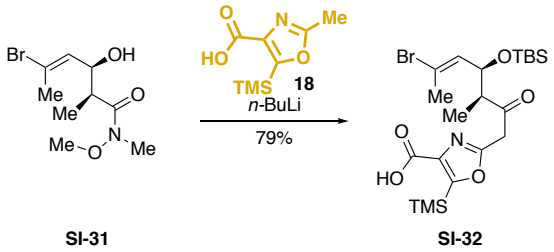
DCM (22 mL) was added to the above residue, and the resulting solution was cooled to 0 ºC by means of an ice/water bath. Then 2,6-lutidine (1.00 mL, 8.58 mmol, 4.0 equiv) was added, followed by TBSOTf (0.99 mL, 4.29 mmol, 2.0 equiv). After 15 min, DCM (50 mL) was added, and the resulting solution was transferred to a separatory funnel and was washed with cold $KHSO_4$ (0.5 M, 20 mL), water (2 × 70 mL) and brine (70 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:40) to afford Weinreb amide **SI-31** (0.71 g, 87% yield) as a yellow oil.

TLC (EtOAc:hexanes = 1:10): R_f = 0.25 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (dt, *J* = 9.3, 1.4 Hz, 1H), 4.34 (t, *J* = 9.1 Hz, 1H), 3.66 (s, 3H), 3.13 (s, 3H), 3.01 (br s, 1H), 2.23 (d, *J* = 1.3 Hz, 3H), 1.18 (d, *J* = 6.8 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 134.3, 122.0, 72.1, 61.6, 42.1, 32.0, 25.7, 24.2, 18.1, 14.3, –4.4, –5.0.

Acid SI-32



SI-31 **SI-32**

A 100-mL round-bottom flask containing **18** (0.52 g, 2.63 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (26 mL) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 2.10 mL, 5.26 mmol, 4.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, a solution of **SI-31** (0.50 g, 1.31 mmol, 1 equiv) in THF (5.0 mL) was added over 30 min by means of syringe pump. After an additional 30 min, water (100 mL) was added, followed by 1 M aqueous $KHSO_4$ solution (7 mL). The system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 40 mL). The combined organic layers were washed with water (2 × 70 mL) and brine (70 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:75) to afford carboxylic acid **SI-32** (0.54 g, 79% yield) as a yellow solid.

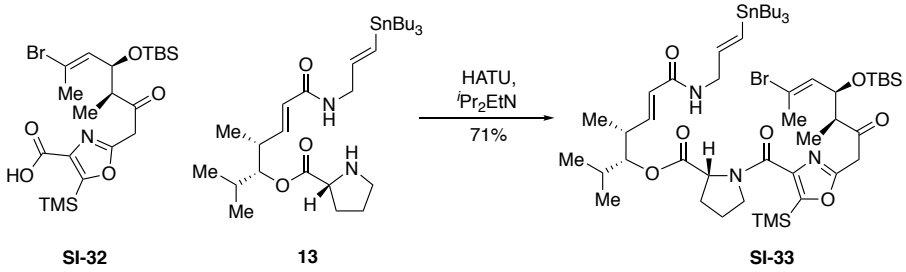
TLC (MeOH:DCM = 1:20): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (dd, *J* = 9.4, 1.4 Hz, 1H), 4.44 (dd, *J* = 9.4, 6.8 Hz, 1H), 4.19 (d, *J* = 17.1 Hz, 1H), 4.14 (d, *J* = 17.1 Hz, 1H), 2.88 (p, *J* = 6.9 Hz, 1H), 2.23 (d, *J* = 1.4 Hz, 3H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 10H), 0.38 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8, 165.3, 165.0, 161.3, 140.7, 133.0, 122.5, 71.5, 52.2, 43.0, 25.7, 24.1, 18.1, 12.5, –2.1, –4.4, –5.1.

HRMS-ESI m/z calcd for $C_{21}H_{37}BrNO_5Si_2^+$ $[M + H]^+$ 518.1388, found 518.1392.

Stille coupling precursor SI-33



SI-32 **13** **SI-33**

A 50-mL round-bottom flask was charged with $^{i}Pr_2EtN$ (0.32 mL, 1.84 mmol, 2.0 equiv), amine **13** (0.55 g, 0.92 mmol, 1 equiv) and acid **SI-32** (0.53 g, 1.01 mmol, 1.1 equiv). DCM (9.2 mL) was added, resulting in a colorless solution. HATU (0.44 g, 1.15 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3) to afford Stille coupling precursor **SI-33** (0.72 g, 71% yield) as a light-yellow oil.

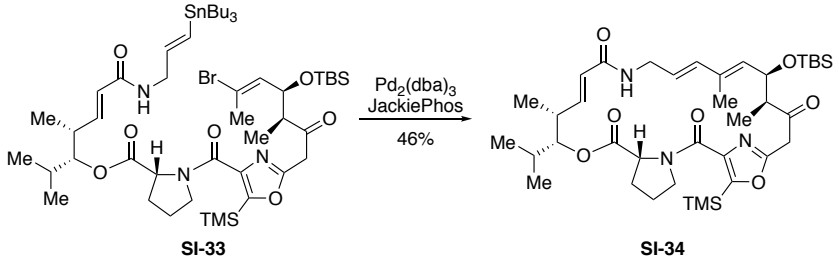
TLC (EtOAc:hexanes = 1:2): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.75 – 6.55 (m, 1H), 6.16 – 6.05 (m, 1H), 5.95 (dt, *J* = 19.1, 5.1 Hz, 1H), 5.87 – 5.73 (m, 2H), 5.73 – 5.58 (m, 1H), 4.84 – 4.59 (m, 2H), 4.54 – 4.34 (m, 1H), 4.13 – 3.83 (m, 5H), 3.83 – 3.61 (m, 1H), 2.84 (dp, *J* = 27.1, 6.9 Hz, 1H), 2.71 – 2.44 (m, 1H), 2.43 – 2.11 (m, 4H), 2.13 – 1.82 (m, 3H), 1.60 – 1.35 (m, 6H), 1.35 – 1.23 (m, 6H), 1.23 – 0.98 (m, 6H), 0.99 – 0.75 (m, 30H), 0.39 – 0.23 (m, 9H), 0.09 – –0.04 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 205.3, 205.0, 172.37, 172.33, 165.43, 165.39, 165.1, 163.1, 162.4, 161.6, 161.5, 159.31, 159.29, 145.35, 145.30, 145.25, 145.15, 143.44, 143.42, 143.32, 132.92, 132.91, 130.4, 130.1, 123.9, 123.9, 122.56, 122.50, 80.7, 80.4, 71.61, 71.57, 60.4, 59.93, 59.89, 51.94, 51.89, 48.8, 47.0, 46.2, 44.89, 44.86, 43.52, 43.49, 38.4, 38.09, 38.05, 31.6, 29.93, 29.81, 29.0, 27.2, 25.70, 25.68, 24.05, 19.7, 19.5, 18.10, 18.04, 16.95, 16.92, 15.0, 14.6, 13.7, 12.6, 9.4, –1.76, –1.78, –4.4, –4.5, –5.11, –5.16.

HRMS-ESI m/z calcd for $C_{50}H_{89}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1098.4439, found 1098.4455.

Stille coupling product SI-34



SI-33 **SI-34**

A 250-mL round-bottom flask containing JackiePhos (97 mg, 0.12 mmol, 0.2 equiv), Stille coupling precursor **SI-33** (0.67 g, 0.61 mmol, 1 equiv) and $Pd_2(dba)_3$ (56 mg, 61 μmol, 0.1 equiv) was evacuated and flushed with nitrogen (this

process was repeated a total of 3 times). Toluene (122 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 12 h, **SI-33** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille coupling product **SI-34** (0.21 g, 46% yield) as a white solid.

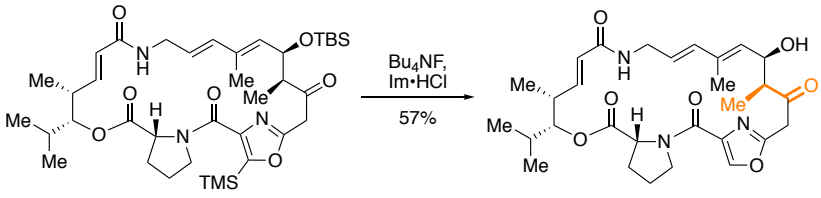
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (dd, *J* = 9.5, 2.9 Hz, 1H), 6.49 (dd, *J* = 16.4, 3.8 Hz, 1H), 6.16 (d, *J* = 16.0 Hz, 1H), 5.78 (dd, *J* = 16.4, 2.1 Hz, 1H), 5.52 (ddd, *J* = 15.5, 10.0, 3.8 Hz, 1H), 5.35 (d, *J* = 8.9 Hz, 1H), 4.90 (dd, *J* = 8.9, 4.1 Hz, 1H), 4.82 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.69 – 4.56 (m, 1H), 4.41 (t, *J* = 9.2 Hz, 1H), 3.95 (d, *J* = 18.0 Hz, 1H), 3.87 – 3.77 (m, 1H), 3.82 (d, *J* = 18.0 Hz, 1H), 3.48 (dt, *J* = 11.2, 7.0 Hz, 1H), 3.34 (ddd, *J* = 14.7, 10.0, 2.8 Hz, 1H), 2.83 (dd, *J* = 9.1, 6.8 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.14 (dq, *J* = 12.9, 8.3 Hz, 1H), 1.99 – 1.86 (m, 2H), 1.86 – 1.77 (m, 1H), 1.77 – 1.66 (m, 1H), 1.57 (d, *J* = 1.2 Hz, 3H), 1.22 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.86 (s, 9H), 0.29 (s, 9H), 0.03 (s, 3H), –0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 206.0, 172.1, 166.6, 162.4, 160.0, 159.4, 145.0, 144.6, 136.2, 133.9, 133.1, 126.0, 123.4, 80.9, 70.7, 58.0, 52.8, 48.5, 43.9, 41.6, 36.7, 29.3, 28.2, 25.8, 25.7, 24.7, 19.9, 18.6, 18.1, 14.2, 12.7, 10.3, –1.8, –4.3, –5.0.

HRMS-ESI m/z calcd for $C_{38}H_{62}N_3O_7Si_2^+$ $[M + H]^+$ 728.4121, found 728.4127.

Analogue 25



SI-34 **25**

A 100-mL round-bottom flask containing Stille coupling product **SI-34** (0.19 g, 0.26 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (5.2 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (0.55 g, 5.22 mmol, 20.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 5.2 mL, 5.22 mmol, 20.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-34**. After 24 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 40 mL) and brine (40 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **25** (80 mg, 57% yield) as a light-yellow solid.

TLC (MeOH:DCM = 1:20): R_f = 0.25 (UV, *p*-anisaldehyde).

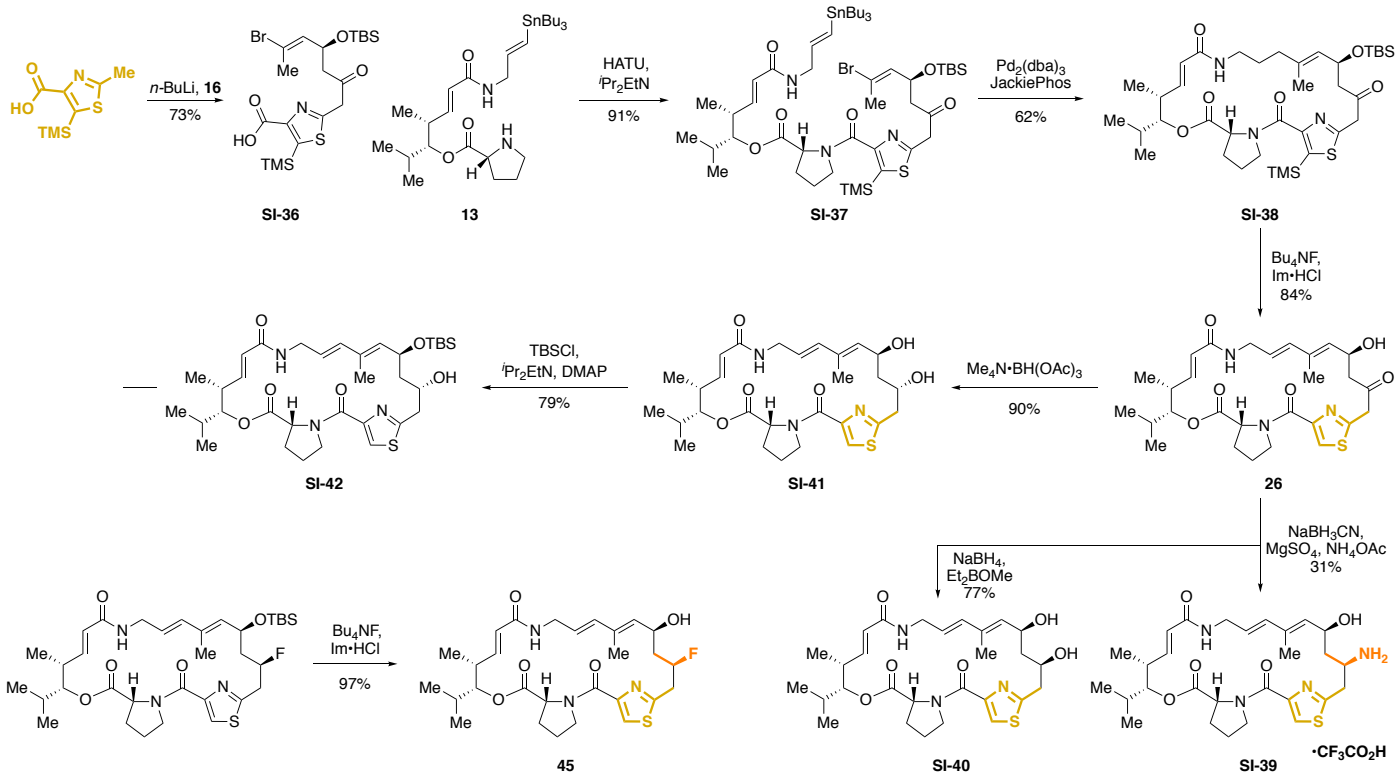
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 6.47 (dd, *J* = 16.4, 5.4 Hz, 1H), 6.09 (d, *J* = 15.7 Hz, 1H), 5.82 (dd, *J* = 16.4, 1.7 Hz, 1H), 5.69 (ddd, *J* = 15.6, 8.5, 4.7 Hz, 1H), 5.16 (d, *J* = 9.2 Hz, 1H), 4.74 (ddd, *J* = 11.3, 9.5, 2.9 Hz, 2H), 4.56 (t, *J* = 8.7 Hz, 1H), 4.48 (td, *J* = 9.0, 8.4, 4.0 Hz, 1H), 3.99 (d, *J* = 15.7 Hz, 1H), 3.92 (dt, *J* = 11.0, 7.0 Hz, 1H), 3.83 – 3.73 (m, 1H), 3.75 (d, *J* = 15.7 Hz, 1H), 3.41 (ddd, *J* = 15.1, 8.6, 3.3 Hz, 1H), 2.97 – 2.80 (m, 1H),

2.73 (dtd, J = 8.9, 7.0, 5.1 Hz, 1H), 2.30 – 2.06 (m, 2H), 2.04 – 1.81 (m, 4H), 1.70 (d, J = 1.2 Hz, 3H), 1.24 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 6.9 Hz, 3H), 0.94 (d, J = 6.7 Hz, 6H).

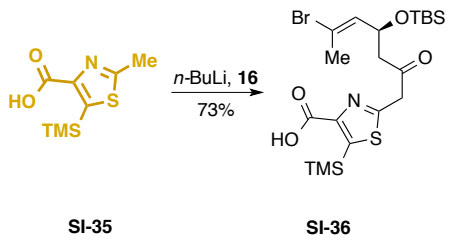
^{13}C NMR (100 MHz, $CDCl_3$) δ 205.0, 171.6, 166.9, 160.8, 156.7, 144.1, 143.4, 136.8, 136.8, 136.2, 131.1, 125.9, 124.4, 81.4, 69.2, 59.7, 51.7, 48.5, 42.8, 40.8, 36.6, 29.5, 28.4, 25.0, 19.6, 18.9, 13.4, 12.8, 11.1.

HRMS-ESI m/z calcd for $C_{29}H_{39}N_3NaO_7^+$ $[M + Na]^+$ 564.2680, found 564.2678.

Scheme VII Synthesis of 26 and derivatives thereof



Acid SI-36



Synthesis of SI-35: A 250-mL round-bottom flask containing 5-methylthiazole-3-carboxylic acid (3.80 g, 26.5 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (135 mL) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-butyllithium in hexanes (2.5 M, 31.9 mL, 79.6 mmol, 3.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, chlorotrimethylsilane (17.0 mL, 133.0 mmol, 5.0 equiv) was added over 30 min by syringe pump. After 1 h, water (100 mL) was added, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the

filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:100 to 1:50) to afford acid **SI-35** (5.02 g, 88% yield) as a yellow solid.

TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (s, 1H), 2.74 (s, 3H), 0.38 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 164.5, 149.7, 145.6, 18.6, -0.5.

Synthesis of SI-36: A 100-mL round-bottom flask containing **SI-35** (0.46 g, 2.15 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (20 mL) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (1.6 M, 2.70 mL, 4.30 mmol, 4.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, a solution of **16** (0.50 g, 1.10 mmol, 1 equiv) in THF (5 mL) was added over 30 min by means of syringe pump. After an additional 30 min, water (30 mL) was added, followed by 1 M aqueous $KHSO_4$ solution (6 mL). The system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: AcOH:EtOAc:hexanes = 0.5:50:50) to afford carboxylic acid **SI-36** (0.41 g, 73% yield) as a yellow solid.

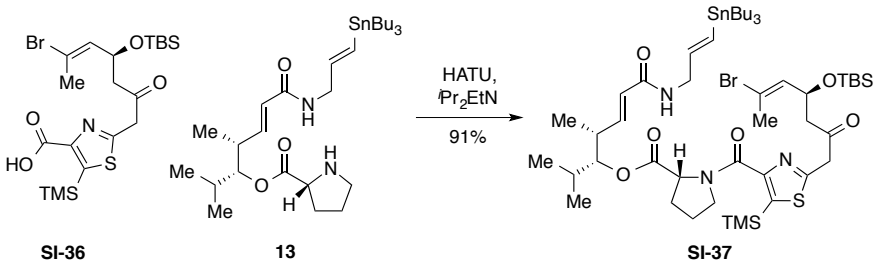
TLC (MeOH:DCM = 1:25): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (br s, 1H), 5.82 (dd, *J* = 9.1, 1.4 Hz, 1H), 4.82 (ddd, *J* = 9.1, 8.0, 4.8 Hz, 1H), 4.36 (d, *J* = 18.2 Hz, 1H), 4.27 (d, *J* = 18.2 Hz, 1H), 2.89 (dd, *J* = 15.6, 8.0 Hz, 1H), 2.60 (dd, *J* = 15.6, 4.8 Hz, 1H), 2.28 (d, *J* = 1.3 Hz, 3H), 0.83 (s, 9H), 0.40 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 165.0, 164.3, 149.6, 146.8, 134.2, 121.8, 66.9, 50.1, 47.4, 25.7, 24.0, 18.0, –0.5, –4.5, –5.1.

HRMS-ESI m/z calcd for $C_{20}H_{33}BrNO_4SSi_2^-$ $[M - H]^-$ 518.0858, found 518.0868.

Stille coupling precursor SI-37



SI-36 **13** **SI-37**

A 50-mL round-bottom flask was charged with ^{i}Pr$_2$EtN (0.51 mL, 2.85 mmol, 2.0 equiv), amine **13** (0.85 g, 1.42 mmol, 1 equiv) and acid **SI-36** (0.82 g, 1.56 mmol, 1.1 equiv). DCM (14 mL) was added, resulting in a colorless solution. HATU (0.68 g, 1.78 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:5) to afford Stille coupling precursor **SI-37** (1.42 g, 91% yield) as a light-yellow oil.

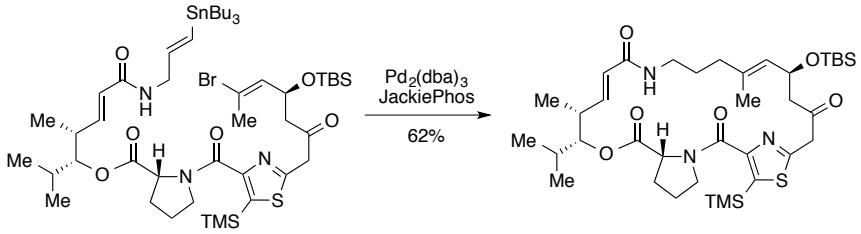
TLC (EtOAc:hexanes = 1:5): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.74 – 6.55 (m, 1H), 6.10 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.95 (dtd, *J* = 19.0, 5.0, 2.1 Hz, 1H), 5.89 – 5.77 (m, 2H), 5.77 – 5.59 (m, 1H), 4.87 – 4.75 (m, 2H), 4.75 – 4.58 (m, 1H), 4.21 – 3.62 (m, 6H), 2.87 (ddd, *J* = 15.5, 8.0, 2.3 Hz, 1H), 2.73 – 2.40 (m, 2H), 2.41 – 2.14 (m, 5H), 2.12 – 1.87 (m, 3H), 1.60 – 1.35 (m, 6H), 1.35 – 1.22 (m, 6H), 1.09 – 0.92 (m, 6H), 0.92 – 0.70 (m, 27H), 0.40 – 0.28 (m, 9H), 0.08 – –0.02 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 202.4, 202.2, 172.5, 172.1, 172.0, 165.42, 165.37, 165.0, 163.1, 163.0, 162.9, 162.8, 161.7, 155.0, 154.3, 145.4, 145.2, 145.0, 143.4, 143.3, 142.7, 141.0, 135.2, 134.3, 134.3, 130.3, 130.2, 130.1, 124.0, 123.9, 121.7, 80.7, 80.4, 67.9, 66.94, 66.86, 61.3, 59.8, 49.9, 49.8, 49.2, 48.03, 47.7, 47.4, 44.8, 38.4, 38.1, 31.7, 29.9, 29.8, 29.7, 29.0, 27.2, 25.7, 25.1, 24.00, 23.98, 23.89, 21.9, 19.7, 19.4, 18.0, 17.0, 16.8, 15.1, 14.5, 13.7, 9.4, 0.2, 0.1, –4.6, –5.1.

HRMS-ESI m/z calcd for $C_{49}H_{87}BrN_3O_6SSi_2Sn^+$ $[M + H]^+$ 1100.4054, found 1100.4078.

Stille coupling product SI-38



SI-37 **SI-38**

A 500-mL round-bottom flask containing JackiePhos (0.21 g, 0.26 mmol, 0.2 equiv), Stille coupling precursor **SI-37** (1.42 g, 1.29 mmol, 1 equiv) and $Pd_2(dba)_3$ (0.12 g, 1.13 mmol, 0.1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (258 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The vessel and its contents were then heated by means of a 50 ºC oil bath. After 3 h, **SI-37** was entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille couping product **SI-38** (0.58 g, 62% yield) as a white solid.

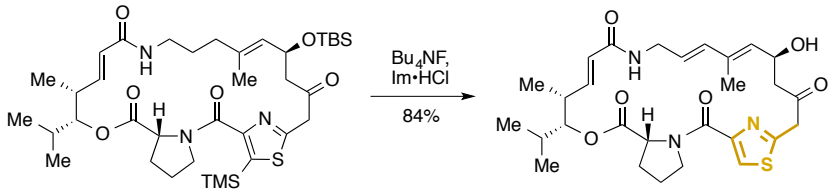
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (dd, *J* = 16.3, 4.1 Hz, 1H), 6.13 (d, *J* = 15.6 Hz, 1H), 6.00 (dd, *J* = 8.8, 2.9 Hz, 1H), 5.77 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.55 (ddd, *J* = 15.5, 9.5, 4.3 Hz, 1H), 5.39 (d, *J* = 9.0 Hz, 1H), 4.97 (ddd, *J* = 9.0, 7.8, 5.3 Hz, 1H), 4.77 (ddd, *J* = 8.7, 6.6, 2.9 Hz, 2H), 4.48 (ddd, *J* = 13.4, 8.9, 4.1 Hz, 1H), 4.10 (d, *J* = 17.2 Hz, 1H), 3.90 (d, *J* = 17.2 Hz, 1H), 3.68 – 3.50 (m, 2H), 3.39 (ddd, *J* = 14.7, 9.5, 3.3 Hz, 1H), 2.89 (dd, *J* = 16.1, 7.8 Hz, 1H), 2.75 (dd, *J* = 16.0, 5.3 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.19 – 2.05 (m, 2H), 1.99 – 1.89 (m, 1H), 1.89 – 1.68 (m, 2H), 1.64 (d, *J* = 1.2 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.84 (s, 9H), 0.31 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 172.2, 166.4, 163.3, 163.2, 155.4, 144.8, 140.1, 137.0, 134.7, 132.5, 124.7, 123.7, 80.9, 65.3, 58.8, 50.8, 48.8, 47.4, 41.3, 36.6, 29.3, 28.6, 25.7, 25.0, 19.9, 18.6, 18.0, 12.7, 9.7, 0.0, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{37}H_{60}N_3O_6SSi_2^+$ $[M + H]^+$ 730.3736, found 730.3758.

Analogue 26



SI-38 **26**

A 100-mL round-bottom flask containing **SI-38** (0.30 g, 0.41 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (4.1 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (0.43 g, 4.11 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 4.11 mL, 4.11 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-38**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40) to afford analogue **26** (0.19 g, 84% yield) as a light-yellow solid.

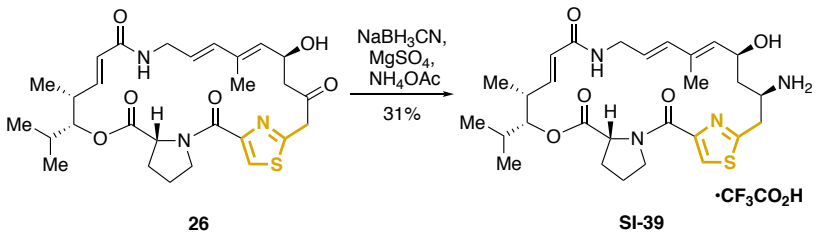
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 6.53 (dd, *J* = 16.3, 4.7 Hz, 1H), 6.40 (dd, *J* = 8.4, 4.1 Hz, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 5.76 (dd, *J* = 16.2, 1.9 Hz, 1H), 5.61 (ddd, *J* = 15.6, 8.9, 4.4 Hz, 1H), 5.40 (d, *J* = 8.9 Hz, 1H), 4.91 (dt, *J* = 8.7, 6.1 Hz, 1H), 4.82 – 4.64 (m, 2H), 4.32 (ddd, *J* = 13.7, 8.5, 4.6 Hz, 1H), 3.98 (d, *J* = 2.3 Hz, 2H), 3.85 (dt, *J* = 10.9, 7.3 Hz, 1H), 3.71 (ddd, *J* = 11.1, 7.8, 4.9 Hz, 1H), 3.45 (ddd, *J* = 14.8, 9.0, 4.0 Hz, 1H), 3.05 (dd, *J* = 16.8, 6.6 Hz, 2H), 2.82 (dd, *J* = 16.8, 5.7 Hz, 1H), 2.73 (ddq, *J* = 6.9, 4.4, 2.3 Hz, 1H), 2.14 (dtd, *J* = 13.2, 9.4, 7.4 Hz, 1H), 1.99 – 1.71 (m, 4H), 1.68 (d, *J* = 1.2 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 171.7, 166.4, 161.4, 160.6, 150.6, 144.9, 136.5, 134.4, 132.7, 126.1, 125.2, 123.9, 81.2, 64.7, 59.6, 49.4, 49.1, 47.5, 40.9, 36.57, 29.4, 28.5, 25.1, 19.7, 18.6, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{28}H_{38}N_3O_6S^+$ $[M + H]^+$ 544.2476, found 544.2480.

Analogue SI-39



26 **SI-39**

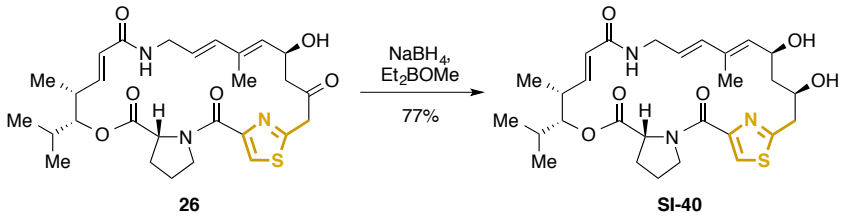
A 50-mL round-bottom flask containing anhydrous $MgSO_4$ (60 mg, 0.50 mmol, 10.0 equiv), NH_4OAc (19 mg, 0.25 mmol, 5.0 equiv) and $NaBH_3CN$ (7.5 mg, 0.12 mmol, 2.4 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). MeOH (5 mL) was added, resulting in a white suspension. After 30 min, a solution of compound **26** (27 mg, 50 µmol, 1 equiv) in MeOH (1 mL) was added. After 20 h, the mixture was filtered through a pad of celite, and the filter cake was washed with MeOH (2 × 10 mL). The combined filtrates were concentrated. The resulting crude residue was purified by preparative HPLC (eluent: H_2O:acetonitrile = 95:5 to 5:95 over 15 min) to afford analogue **SI-39** TFA salt (10 mg, 31 % yield) as a white solid.

^{1}H NMR (400 MHz, MeOD) δ 8.12 (s, 1H), 6.83 (dd, *J* = 15.7, 4.4 Hz, 1H), 6.31 (dd, *J* = 15.5, 1.0 Hz, 1H), 5.88 (dd, *J* = 15.7, 2.0 Hz, 1H), 5.77 – 5.66 (m, 1H), 5.50 (d, *J* = 8.6 Hz, 1H), 4.90 – 4.80 (m, 1H), 4.82 – 4.71 (m, 2H), 4.11 (dd, *J* = 14.3, 9.1 Hz, 1H), 3.92 – 3.82 (m, 2H), 3.77 (dt, *J* = 11.2, 7.6 Hz, 1H), 3.61 – 3.48 (m, 2H), 3.37 (dd, *J* = 15.6, 6.9 Hz, 1H), 2.89 – 2.77 (m, 1H), 2.45 (ddd, *J* = 14.7, 5.1, 3.1 Hz, 1H), 2.22 – 2.07 (m, 1H), 2.03 – 1.90 (m, 3H), 1.83 (d, *J* = 1.2 Hz, 3H), 1.81 – 1.72 (m, 2H), 1.63 – 1.50 (m, 1H), 1.14 (d, *J* = 6.8 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, MeOD) δ 172.1, 167.5, 164.0, 163.0, 151.9, 148.34 138.7, 136.3, 134.9, 128.0, 126.3, 124.2, 82.4, 67.0, 61.1, 50.98, 50.95, 41.3, 39.8, 38.0, 35.5, 30.7, 29.8, 26.4, 20.2, 18.8, 13.2, 9.6.

HRMS-ESI m/z calcd for $C_{28}H_{39}N_4O_4S^+$ $[M - OH]^+$ 527.2687, found 527.2708.

Analogue SI-40



A 50-mL round-bottom flask containing analogue **26** (27 mg, 50 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1 mL) and MeOH (4 mL) were added, and the resulting colorless solution was cooled to -78 ºC by means of a dry ice/acetone bath. A solution of Et_2BOMe in THF (1.0 M, 60 µL, 60 µmol, 1.2 equiv) was added dropwise over 5 min at -78 ºC. After 30 min, $NaBH_4$ (2.8 mg, 74 µmol, 1.5 equiv) was added in one portion at -78 ºC. After additional 3 h, acetic acid (1 mL) and EtOAc (25 mL) were added, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The solution was transferred to a separatory funnel and was washed with saturated aqueous $NaHCO_3$ solution (20 mL), water (3 × 40 mL) and brine (40 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:40 to 1:20) to afford analogue **SI-40** (21 mg, 77% yield) as a white solid.

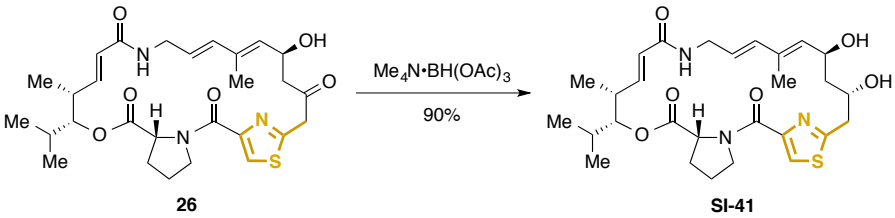
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, KMnO4).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 6.52 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.19 (d, *J* = 15.5 Hz, 1H), 5.93 (dd, *J* = 8.7, 3.9 Hz, 1H), 5.80 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.65 (ddd, *J* = 15.5, 9.4, 4.1 Hz, 1H), 5.38 (d, *J* = 9.2 Hz, 1H), 4.95 – 4.71 (m, 3H), 4.46 (ddd, *J* = 13.5, 8.6, 4.1 Hz, 1H), 4.33 (td, *J* = 8.1, 4.0 Hz, 1H), 4.07 (ddd, *J* = 12.5, 8.0, 4.5 Hz, 1H), 3.86 (dt, *J* = 11.1, 7.2 Hz, 1H), 3.44 (ddd, *J* = 14.2, 9.4, 3.8 Hz, 1H), 3.17 (dd, *J* = 16.3, 7.5 Hz, 1H), 3.04 (dd, *J* = 16.3, 3.7 Hz, 1H), 2.97 (br s, 1H), 2.83 – 2.68 (m, 1H), 2.20 – 2.05 (m, 2H), 2.05 – 1.83 (m, 3H), 1.78 (s, 3H), 1.76 – 1.60 (m, 2H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 166.4, 166.3, 161.0, 149.7, 145.0, 136.6, 134.8, 134.0, 126.6, 125.2, 123.7, 81.0, 68.4, 66.9, 59.7, 49.3, 42.6, 41.4, 40.8, 36.6, 29.4, 28.4, 25.3, 19.9, 18.6, 13.0,10.0.

HRMS-ESI m/z calcd for $C_{28}H_{39}N_3NaO_6S^+$ $[M + Na]^+$ 568.2452, found 568.2473.

Analogue SI-41



A 50-mL round-bottom flask containing $Me_4N•BH(OAc)_3$ (0.12 g, 0.46 mmol, 5.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Acetonitrile (5 mL) and acetic acid (5 mL) were added, and the resulting colorless solution was cooled to -10 ºC by means of an ice/acetone bath. A solution of **26** (50 mg, 0.093 mmol, 1 equiv) in acetonitrile (2.5 mL) was added dropwise (the syringe was rinsed with acetonitrile (1 mL)). The mixture was allowed to warm to 23 ºC slowly. After 5 h, saturated aqueous $NaHCO_3$ solution (50 mL) was added (CAUTION: Gas evolution!), followed by EtOAc (50 mL). The resulting biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH: DCM = 1:30) to afford analogue **SI-41** (45 mg, 90% yield) as a white solid.

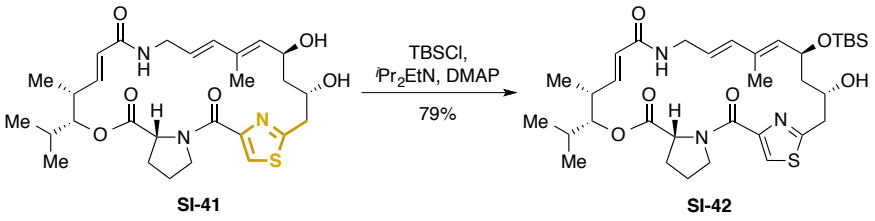
TLC (MeOH:DCM = 1:20): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 6.51 (dd, *J* = 16.2, 4.5 Hz, 1H), 6.20 (dd, *J* = 15.6, 1.1 Hz, 1H), 6.14 (dd, *J* = 8.6, 4.0 Hz, 1H), 5.76 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.72 – 5.66 (m, 1H), 5.66 – 5.59 (m, 1H), 4.86 (dt, *J* = 9.6, 4.9 Hz, 1H), 4.77 – 4.66 (m, 2H), 4.42 – 4.28 (m, 2H), 4.04 (br s, 1H), 3.92 – 3.72 (m, 2H), 3.44 (ddd, *J* = 14.0, 9.4, 4.1 Hz, 1H), 3.23 – 3.02 (m, 3H), 2.74 (dqd, *J* = 7.4, 4.8, 2.6 Hz, 1H), 2.12 (dq, *J* = 13.2, 8.1, 7.3 Hz, 1H), 2.05 – 1.86 (m, 4H), 1.85 – 1.78 (m, 2H), 1.77 (d, *J* = 1.2 Hz, 3H), 1.07 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 166.5, 166.1, 161.3, 150.3, 145.1, 137.3, 133.9, 133.4, 125.8, 125.0, 123.7, 81.3, 68.6, 66.7, 59.6, 49.2, 41.9, 41.1, 40.47, 36.7, 29.4, 28.5, 25.5, 19.8, 18.6, 12.8, 9.7.

HRMS-ESI m/z calcd for $C_{28}H_{39}N_3NaO_6S^+$ $[M + Na]^+$ 568.2452, found 568.2473.

Mono-TBS ether SI-42



To a solution of anti-diol **SI-41** (45 mg, 82 µmol, 1 equiv) and DMAP (1 mg, 8 µmol, 0.1 equiv) in DCM (8 mL) was added $^iPr_2NEt$ (0.22 mL, 1.20 mmol, 15.0 equiv), followed by TBS-Cl (0.19 g, 1.2 mmol, 15.0 equiv). After 24 h, the mixture was concentrated, and the resulting residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:4) to afford mono-TBS ether **SI-42** (43 mg, 79% yield) as a white solid.

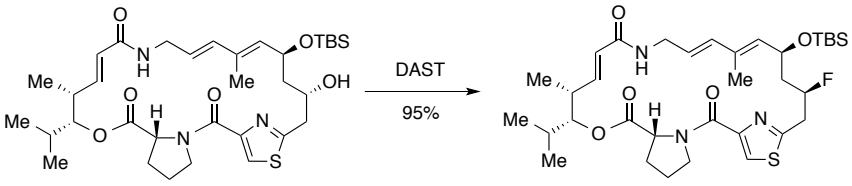
TLC (acetone:hexanes = 1:2): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 6.44 (dd, *J* = 16.4, 4.5 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 6.05 (dd, *J* = 9.3, 3.5 Hz, 1H), 5.76 (dd, *J* = 16.4, 2.0 Hz, 1H), 5.73 – 5.62 (m, 2H), 4.93 (ddd, *J* = 9.4, 4.9, 2.8 Hz, 1H), 4.73 – 4.64 (m, 2H), 4.55 – 4.42 (m, 2H), 4.37 (br s, 1H), 3.84 (dt, *J* = 11.1, 6.6 Hz, 1H), 3.72 (dt, *J* = 11.5, 6.8 Hz, 1H), 3.32 (ddd, *J* = 13.9, 10.2, 3.5 Hz, 1H), 3.23 (dd, *J* = 16.0, 3.1 Hz, 1H), 3.06 (dd, *J* = 16.1, 8.8 Hz, 1H), 2.75 (ddt, *J* = 6.7, 4.3, 2.0 Hz, 1H), 2.13 (dtd, *J* = 16.4, 5.7, 4.7, 2.1 Hz, 1H), 1.96 (tt, *J* = 11.0, 4.7 Hz, 2H), 1.85 – 1.75 (m, 4H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.06 (d, *J* = 5.8 Hz, 3H), 1.04 (d, *J* = 5.4 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 167.1, 166.3, 161.3, 150.5, 144.4, 137.2, 133.6, 132.0, 125.7, 125.2, 123.9, 81.5, 69.2, 68.1, 59.8, 49.0, 43.3, 41.4, 40.7, 36.8, 29.4, 28.4, 25.8, 25.71, 19.9, 18.6, 17.92, 12.7, 9.37, –4.4, –5.3.

HRMS-ESI m/z calcd for $C_{34}H_{54}N_3O_6SSi^+$ $[M + H]^+$ 660.3497, found 660.3521.

Fluorinated compound SI-43



SI-42 **SI-43**

A 50-mL round-bottom flask containing mono-TBS ether **SI-42** (42 mg, 64 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (5 mL) was added, and the resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. DAST (21 μL, 0.16 mmol, 2.50 equiv) was added dropwise, and the vessel and its contents were allowed to warm to 23 ºC. After 3 h, aqueous saturate solution of $NaHCO_3$ (10 mL) was added, followed by DCM (20 mL), and the resulting biphasic solution was transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4), and the dried solution was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:5) to afford fluorinated compound **SI-43** (40 mg, 95 % yield) as a white solid.

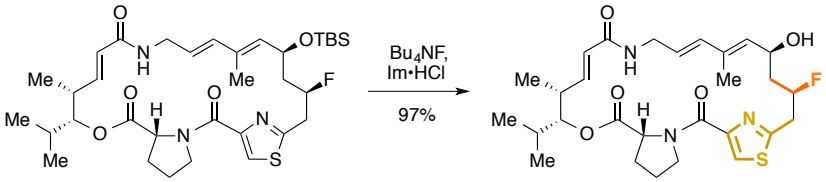
TLC (acetone:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 6.49 (dd, *J* = 16.4, 4.1 Hz, 1H), 6.21 (dd, *J* = 15.5, 1.4 Hz, 1H), 5.91 (dd, *J* = 9.4, 3.2 Hz, 1H), 5.80 (dd, *J* = 16.4, 2.0 Hz, 1H), 5.61 (ddd, *J* = 15.5, 9.6, 4.0 Hz, 1H), 5.34 (d, *J* = 9.2 Hz, 1H), 5.20 (dtt, *J* = 49.7, 11.6, 3.0 Hz, 1H), 4.85 – 4.70 (m, 3H), 4.59 (ddd, *J* = 13.4, 8.4, 3.3 Hz, 1H), 4.06 (dt, *J* = 11.7, 6.9 Hz, 1H), 3.76 (dt, *J* = 11.7, 6.4 Hz, 1H), 3.45 – 3.24 (m, 2H), 3.04 (ddd, *J* = 30.6, 16.5, 3.5 Hz, 1H), 2.75 (ddt, *J* = 7.2, 5.0, 2.4 Hz, 1H), 2.15 (dtd, *J* = 13.6, 6.7, 3.8 Hz, 2H), 2.03 – 1.77 (m, 5H), 1.73 (s, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 166.5, 164.1 (d, $^3J_{CF}$ = 3.5 Hz), 161.5, 150.1, 144.6, 137.0, 134.9, 133.4, 124.9, 124.7, 123.9, 89.9 (d, $^1J_{CF}$ = 169.5 Hz), 80.8, 66.4, 59.1, 49.3, 43.6 (d, $^2J_{CF}$ = 20.0 Hz), 41.5, 38.7 (d, $^2J_{CF}$ = 22.8 Hz), 36.6, 29.3, 28.5, 25.78, 25.75, 25.4, 19.9, 18.5, 18.1, 12.62, 12.60, 9.8, –4.4, –4.9.

HRMS-ESI m/z calcd for $C_{34}H_{53}FN_3O_5SSi^+$ $[M + H]^+$ 662.3454, found 662.3482.

Analogue 45



SI-43 45

A 100-mL round-bottom flask containing **SI-43** (20 mg, 30 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (3 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (32 mg, 0.30 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.30 mL, 0.30 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the above solution of **SI-43**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:100 to 1:50) to afford analogue **45** (16 mg, 97 % yield) as a light-yellow solid.

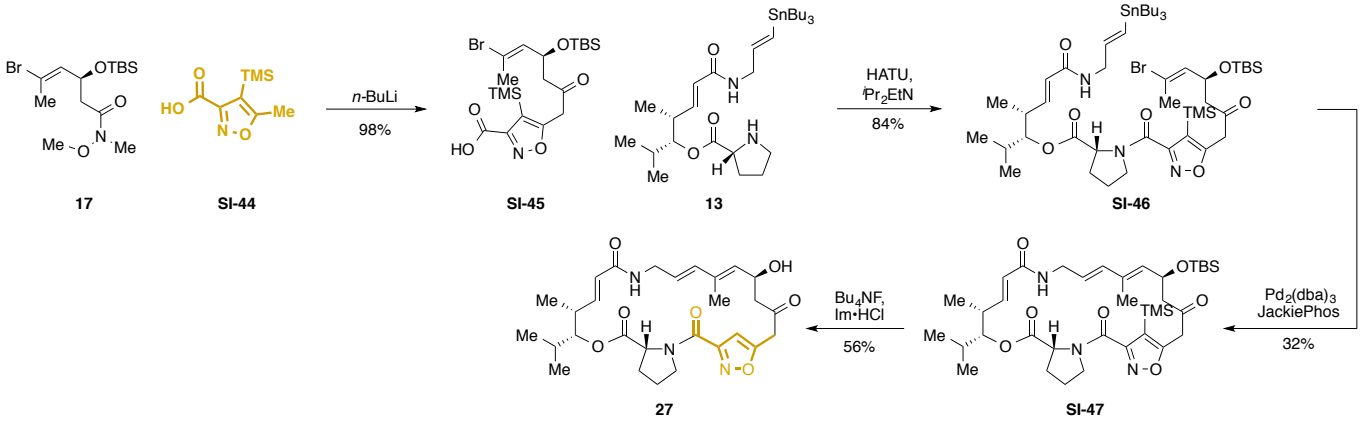
TLC (MeOH:DCM = 1:30): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 6.51 (dd, *J* = 16.4, 4.2 Hz, 1H), 6.23 (d, *J* = 15.7 Hz, 1H), 5.96 (dd, *J* = 8.9, 3.5 Hz, 1H), 5.81 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.9, 9.3, 4.1 Hz, 1H), 5.39 (d, *J* = 9.2 Hz, 1H), 5.34 – 5.10 (dm, $^2J_{HF}$ = 47.9, 1H), 4.88 – 4.71 (m, 3H), 4.55 (ddd, *J* = 14.2, 9.0, 4.0 Hz, 1H), 4.06 (dt, *J* = 11.6, 6.4 Hz, 1H), 3.78 (dt, *J* = 11.6, 6.3 Hz, 1H), 3.52 – 3.31 (m, 2H), 3.10 (ddd, *J* = 27.6, 16.4, 4.1 Hz, 1H), 2.82 – 2.68 (m, 1H), 2.29 – 2.09 (m, 2H), 2.00 – 1.80 (m, 5H), 1.78 (s, 3H), 1.10 (d, *J* = 6.7 Hz, 3H), 1.02 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 166.5, 163.9 (d, $^3J_{CF}$ = 4.3 Hz), 161.5, 150.1, 144.8, 136.2, 135.8, 133.4, 125.48, 125.2, 123.8, 90.0 (d, $^1J_{CF}$ = 169.9 Hz), 80.9, 65.6, 59.2, 49.3, 42.1 (d, $^2J_{CF}$ = 20.6 Hz), 41.3, 38.5 (d, $^2J_{CF}$ = 22.8 Hz), 36.6, 29.4, 28.5, 25.4, 19.9, 18.5, 12.8, 9.8.

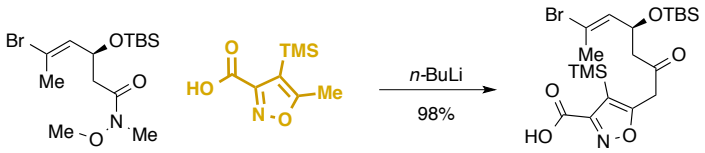
HRMS-ESI m/z calcd for $C_{28}H_{39}FN_3O_5S^+$ $[M + H]^+$ 548.2589, found 548.2593.

Scheme VIII Synthesis of 27



17 SI-44 SI-45 13 SI-46 SI-47 27

Acid SI-45



17 SI-44 SI-45

Preparation of SI-44: A 250-mL round-bottom flask containing 5-methylisoxazole-3-carboxylic acid (0.64 g, 5.04 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (56 mL) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-butyllithium in hexanes (2.5 M, 5.04 mL, 12.6 mmol, 2.5 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, chlorotrimethylsilane (3.2 mL, 25.2 mmol, 5.0 equiv) was added over 30 min by syringe pump. After 1 h, water (50 mL) was added, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:150 to 1:120) to afford acid **SI-44** (0.49 g, 49.2 %) as a yellow solid.

TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 2.53 (s, 3H), 0.33 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 164.8, 159.1, 109.1, 13.6, -0.1.

Preparation of SI-45: A 100-mL round-bottom flask containing acid **SI-44** (0.21 g, 1.06 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (12 ml) was added, resulting in a light-yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 0.85 mL, 2.13 mmol, 4.0 equiv) was added dropwise over 15 min, resulting in a deep red solution. After 30 min, a solution of **17** (0.20 g, 0.53 mmol, 1 equiv) in THF (2 mL) was added over 30 min by means of syringe pump. After an additional 30 min, water (40 mL) was added, followed by 1 M aqueous $KHSO_4$ solution (3 mL). The system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 30 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: DCM:MeOH=150:1 to 100:1) afford acid **SI-45** (0.26 g, 98% yield).

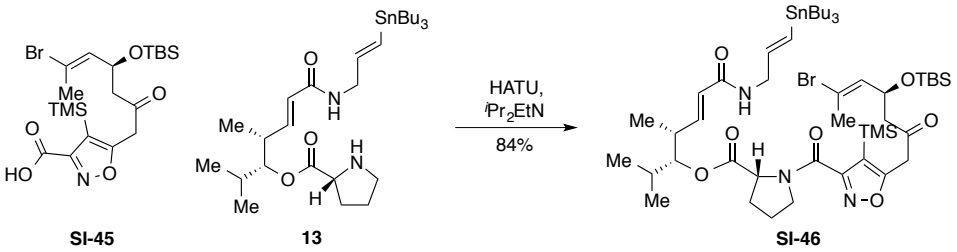
TLC (MeOH:DCM = 1:5): R_f = 0.45 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (s, 1H), 5.83 (dd, J = 9.1, 1.2 Hz, 1H), 4.83 (ddd, J = 9.0, 7.9, 4.9 Hz, 1H), 4.00 (d, J = 7.6 Hz, 2H), 2.90 – 2.80 (m, 1H), 2.56 (dd, J = 16.0, 4.9 Hz, 1H), 2.30 (d, J = 1.1 Hz, 3H), 0.86 (d, J = 8.6 Hz, 9H), 0.31 (s, 9H), 0.07 (t, J = 3.5 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 171.3, 163.6, 159.6, 134.2, 122.0, 112.1, 66.7, 50.0, 42.8, 25.7, 24.0, 18.0, –0.4, –4.6, –5.1.

HRMS-ESI m/z calcd for $C_{20}H_{33}BrNO_5Si_2^-$ $[M - H]^-$ 502.1086, found 502.1091.

Stille coupling precursor SI-46



A 25-mL round-bottom flask was charged with amine **13** (0.31 g, 0.52 mmol 2.6 equiv), $^{i}Pr_2EtN$ (0.18 mL, 1.03 mmol, 5.2 equiv) and acid **SI-45** (0.10 g, 0.20 mmol, 1 equiv). DCM (5 mL) was added, resulting in a clear, colorless solution, and HATU (0.24 g, 0.64 mmol, 3.2 equiv) was added to this solution in one portion. After 5 h, the mixture was diluted with DCM (30 mL). The solution was transferred to a separatory funnel and was washed with water (2 × 30 mL) and brine (30 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-46** (0.18 g, 84% yield) as a light-yellow foam.

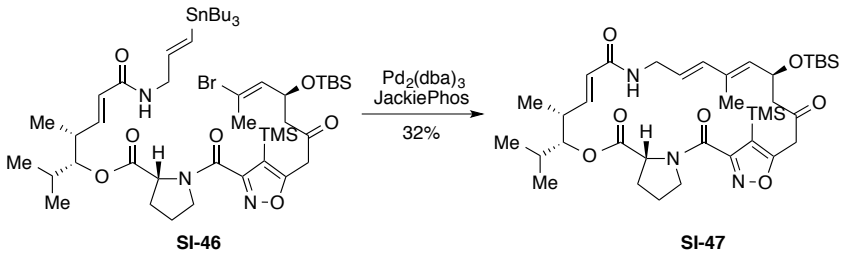
TLC (EtOAc:hexanes = 1:4): R_f = 0.3 (UV)

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 6.70 (dt, *J* = 16.6, 8.4 Hz, 1H), 6.25 – 6.04 (m, 1H), 5.98 (dt, *J* = 19.0, 5.0 Hz, 1H), 5.82 (ddd, *J* = 10.6, 9.2, 6.6 Hz, 2H), 5.68 (dt, *J* = 41.8, 5.6 Hz, 1H), 5.19 (dd, *J* = 8.5, 2.5 Hz, 1H), 4.90 – 4.70 (m, 2H), 4.64 (dd, *J* = 8.6, 3.2 Hz, 1H), 4.09 – 3.78 (m, 6H), 3.78 – 3.67 (m, 1H), 2.80 (ddd, *J* = 15.8, 11.5, 7.8 Hz, 1H), 2.72 – 2.58 (m, 1H), 2.51 (ddd, *J* = 15.8, 11.8, 4.9 Hz, 1H), 2.38 – 2.25 (m, 4H), 2.25 – 2.02 (m, 2H), 1.97 (ddd, *J* = 22.8, 12.9, 6.3 Hz, 2H), 1.80 – 1.73 (m, 1H), 1.61 – 1.40 (m, 7H), 1.31 (dq, *J* = 14.3, 7.1 Hz, 7H), 1.10 – 0.75 (m, 35H), 0.28 (dd, *J* = 18.5, 6.7 Hz, 9H), 0.14 – 0.02 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 200.9, 171.7, 169.3, 169.2, 165.4, 165.2, 162.6, 162.5, 160.5, 145.2, 143.5, 143.4, 134.2, 130.4, 130.2, 124.1, 123.9, 121.9, 112.0, 111.4, 81.1, 80.8, 66.7, 66.6, 60.8, 59.5, 49.9, 49.7, 49.1, 47.2, 44.9, 42.8, 38.2, 38.1, 31.6, 29.9, 29.7, 29.4, 29.1, 29.0, 28.9, 27.3, 27.0, 25.7, 24.8, 24.0, 22.1, 19.5, 19.4, 18.0, 17.0, 16.6, 14.8, 14.6, 13.7, 11.1, 9.5, 7.7, –0.2, –0.3, –4.5, –5.06, –5.08.

HRMS-ESI m/z calcd for $C_{49}H_{87}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1084.4282 found 1084.4292.

Stille coupling product SI-47



A 100-mL round-bottom flask containing JackiePhos (13.2 mg, 16.6 μmol, 0.2 equiv), $Pd_2(dba)_3$ (7.6 mg, 8.3 μmol, 0.1 equiv) and Stille coupling precursor **SI-46** (90.0 mg, 83.0 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (17 ml) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 15 h, **SI-46** was entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:2), and the mixture was cooled to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash

chromatography (silica gel, eluent: EtOAc:hexanes =1:3 to 1:1.5) to afford Stille coupling product **SI-47** (19.2 mg, 32% yield) as a light-yellow solid.

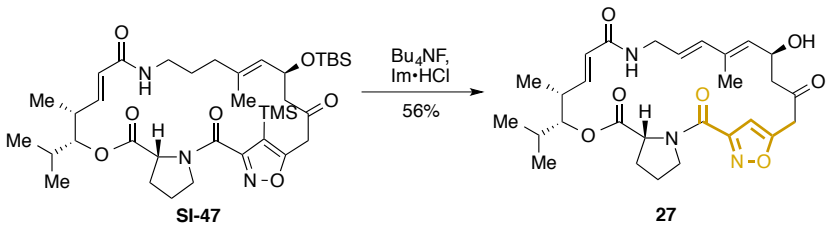
TLC (EtOAc:hexanes = 1:2): R_f = 0.15 (UV)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (d, *J* = 7.1 Hz, 1H), 6.67 (dd, *J* = 15.6, 8.2 Hz, 1H), 6.28 (d, *J* = 15.5 Hz, 1H), 5.92 (dd, *J* = 15.7, 0.9 Hz, 1H), 5.77 – 5.65 (m, 1H), 5.52 (d, *J* = 9.3 Hz, 1H), 4.97 – 4.83 (m, 2H), 4.61 (dd, *J* = 8.3, 5.5 Hz, 1H), 4.48 – 4.38 (m, 1H), 4.05 (d, *J* = 17.4 Hz, 1H), 3.75 – 3.61 (m, 2H), 3.60 – 3.49 (m, 1H), 3.39 (dd, *J* = 13.3, 8.9 Hz, 1H), 2.98 – 2.89 (m, 1H), 2.80 (dd, *J* = 11.9, 5.8 Hz, 1H), 2.63 – 2.53 (m, 1H), 2.36 (dd, *J* = 15.0, 7.3 Hz, 1H), 2.14 (ddd, *J* = 16.1, 9.5, 4.6 Hz, 2H), 2.03 – 1.91 (m, 2H), 1.73 (s, 1H), 1.56 (d, *J* = 15.1 Hz, 3H), 1.29 – 1.24 (m, 1H), 1.15 (d, *J* = 7.3 Hz, 3H), 1.02 – 0.82 (m, 21H), 0.33 – 0.15 (m, 12H), 0.12 – –0.04 (m, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 170.4, 169.7, 166.0, 161.9, 161.6, 142.5, 138.1, 134.6, 132.4, 125.9, 125.2, 110.4, 82.3, 66.8, 60.4, 51.2, 49.0, 43.6, 41.9, 40.6, 29.5, 28.9, 25.7, 25.1, 20.8, 19.6, 18.1, 16.5, 13.2, –0.7, –0.9, –4.5, –4.9.

HRMS-ESI m/z calcd for $C_{37}H_{59}N_3NaO_7Si_2^+$ $[M + Na]^+$ 736.3784, found 736.3791.

Analogue 27



A 25-mL round-bottom flask containing **SI-47** (60 mg, 84.0 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.5 ml) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (0.13 g, 1.30 mmol, 15.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 1.30 mL, 1.30 mmol, 15.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-47**. After 7 d, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **27** (25 mg, 56%, yield).

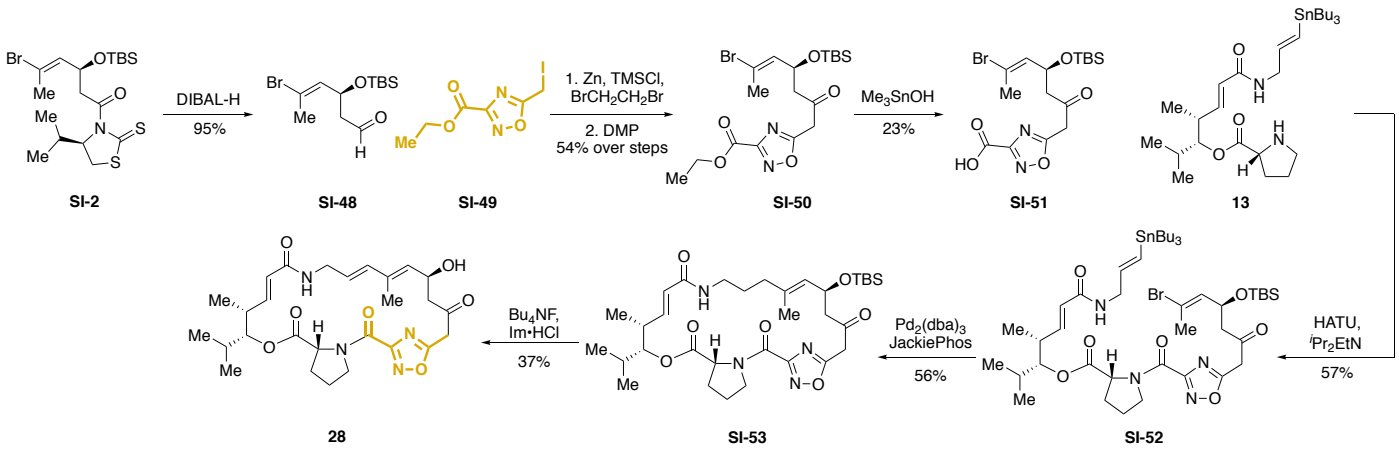
TLC (MeOH:DCM = 1:20): R_f = 0.40 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 8.8, 3.6 Hz, 1H), 6.18 (dd, *J* = 16.4, 8.1 Hz, 1H), 6.13 (d, *J* = 15.2 Hz, 1H), 5.90 – 5.72 (m, 2H), 5.19 (d, *J* = 8.9 Hz, 1H), 4.97 (td, *J* = 8.7, 4.6 Hz, 1H), 4.75 (dd, *J* = 9.9, 2.4 Hz, 1H), 4.69 (dd, *J* = 8.8, 3.0 Hz, 1H), 4.48 (ddd, *J* = 13.9, 8.8, 5.0 Hz, 1H), 4.15 – 3.95 (m, 2H), 3.92 (d, *J* = 16.0 Hz, 1H), 3.69 (d, *J* = 16.0 Hz, 1H), 3.33 (ddd, *J* = 13.4, 9.1, 3.6 Hz, 1H), 2.91 (dd, *J* = 15.3, 4.6 Hz, 1H), 2.81 (dd, *J* = 15.2, 8.6 Hz, 1H), 2.61 – 2.51 (m, 1H), 2.48 (br s, 1H), 2.40 – 2.20 (m, 1H), 2.17 – 2.02 (m, 3H), 1.94 – 1.83 (m, 1H), 1.78 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H).

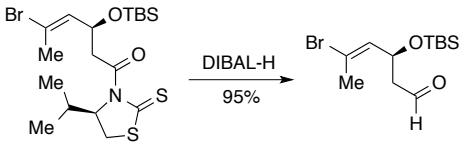
^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 171.0, 166.8, 166.0, 159.3, 158.9, 142.8, 136.7, 136.1, 131.7, 127.1, 125.8, 104.1, 82.2, 65.1, 61.1, 49.5, 49.3, 41.9, 40.6, 36.9, 29.7, 29.1, 25.1, 19.4, 18.8, 13.3, 12.4.

HRMS-ESI m/z calcd for $C_{28}H_{37}N_3NaO_7^+$ $[M + Na]^+$ 550.2524, found 550.2515.

Scheme IX synthesis of 28



Aldehyde SI-48



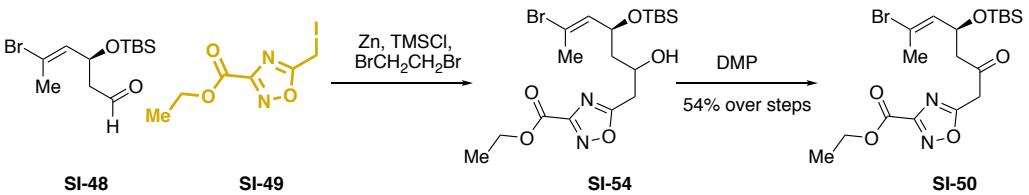
A 250-mL round-bottom flask containing TBS ether **SI-2** (3.00 g, 6.43mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (65 ml) was added, resulting in a light-yellow solution. The vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath, and a solution of DIBAL-H in hexanes (1.0 M, 12.86 mL, 12.86 mmol, 2.0 equiv) was added dropwise over 10 min. After 1 h, MeOH (5 mL) was carefully added, followed saturated aqueous solution of potassium sodium tartrate (50 mL). The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:15) to afford aldehyde **SI-48** (1.87 g, 95% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.4 ($KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (t, *J* = 2.1 Hz, 1H), 5.88 (dq, *J* = 9.0, 1.3 Hz, 1H), 4.82 (ddd, *J* = 9.0, 7.7, 4.8 Hz, 1H), 2.69 (ddd, *J* = 16.1, 7.7, 2.3 Hz, 1H), 2.57 – 2.47 (m, 1H), 2.30 (d, *J* = 1.3 Hz, 3H), 0.86 (s, 9H), 0.06 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4, 134.3, 121.6, 65.9, 51.2, 25.6, 24.0, 18.0, –4.4, –5.1.

Keto ester SI-50



Preparation of SI-49: A 100-mL round-bottom flask was charged with ethyl 5-(chloromethyl)-1,2,4-oxadizaole-3-carboxylate (3.20 g, 16.8 mmol, 1 equiv) and sodium iodide (12.60 g, 84.0 mmol, 5.0 equiv). Acetone (50 mL) was added, resulting a white suspension. After 3 h, the solvent was removed under vacuum, and EtOAc (100 mL) and water (100 mL) were added. The resulting biphasic mixture was transferred to separatory funnel, and the layers were separated. The organic layer was washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was concentrated, the resulting crude residue was purified by flash chromatography (EtOAc:hexanes = 1:3) to afford **SI-49** (3.56 g, 75% yield) as a white solid.

TLC (EtOAc:hexanes = 1:3): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.49 (d, *J* = 7.1 Hz, 2H), 4.48 (s, 2H), 1.43 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 177.9, 162.3, 157.1, 63.2, 14.0, -17.8.

Preparation of SI-50: A 250-mL round-bottom flask containing activated zinc powder (2.80 g, 42.0 mmol, 20.0 equiv) was heated to ≥ 100 ºC at ≤ 1 Torr by means of a heat gun for 1 min and was then flushed with nitrogen (this process was repeated a total of 3 times). After cooling to 23 ºC. THF (42 mL) was added, resulting in a grey suspension. 1,2-dibromoethane (0.36 mL, 4.20 mmol, 2.0 equiv) was added, and the mixture was then heated to reflux by means of an 80 ºC oil bath for 30 min. After cooling to 23 ºC. TMSCl (0.27 mL, 2.10 mmol, 1 equiv) was added. After 15 min, the vessel and its contents were cooled to 0 ºC by means of an ice/water bath, and BF_3•Et_2O (0.52 mL, 4.20 mmol, 2.0 equiv) was added, followed by a solution of **SI-48** (0.65 g, 2.10 mmol, 1 equiv) in THF (8 mL). Then a solution of iodide compound **SI-49** in THF (8 mL) was added dropwise in 10 min, resulting in a deep green solution. After 1.5 h, the aldehyde is entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:2, R_f = 0.85), and saturated aqueous ammonium chloride solution (30 mL) was added. The resulting biphasic solution was transferred to a separated funnel, and the layers were separated. The aqueous phase was extracted with EtOAc (2 × 50 ml), and the combined organic layers were washed with water (100 mL) and brine (100 ml). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:7 to 1:9) to afford Reformatsky product **SI-54** (1:1 mixture, 0.81 g, 83% yield) as a colorless oil.

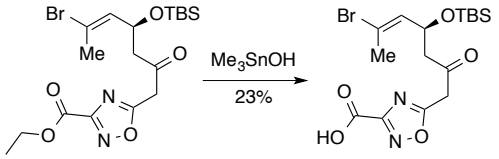
A 1000-mL round-bottom flask containing **SI-54** (0.81 g, 1.75 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (480 mL) was added, resulting in a colorless solution, and a solution of Dess–Martin periodinane (3.71 g, 8.74 mmol, 5.0 equiv) in CH_2Cl_2 (120 mL) was added. After 1 h, saturated aqueous $Na_2S_2O_3$ solution (50 mL) and saturated aqueous $NaHCO_3$ solution (50 mL) were added, and the mixture was stirred for 1 h. The resulting biphasic mixture was transferred to separatory funnel, and the layers were separated. The organic layer was washed with water (200 mL) and brine (200 ml), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: eluent: EtOAc:hexanes = 1:7 to 1:9) afford keto ester **SI-50** (0.52 g, 65% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:3): R_f = 0.7 (UV).

^{1}H NMR (400 MHz, MeOD) δ 5.87 (dd, *J* = 9.1, 1.3 Hz, 1H), 4.93 – 4.88 (m, 1H), 4.48 (q, *J* = 7.1 Hz, 2H), 3.33 (dt, *J* = 3.2, 1.6 Hz, 1H), 2.97 (dd, *J* = 15.9, 7.9 Hz, 1H), 2.77 (dd, *J* = 15.9, 4.7 Hz, 1H), 2.32 (d, *J* = 1.3 Hz, 3H), 1.43 (t, *J* = 7.1 Hz, 3H), 0.88 (d, *J* = 11.9 Hz, 9H), 0.11 – 0.04 (m, 6H).

^{13}C NMR (100 MHz, MeOD) δ 199.8, 175.4, 161.9, 157.5, 134.2, 121.6, 67.7, 66.7, 62.5, 49.4, 24.9, 22.9, 17.5, 12.9, –5.8, –6.2.

Acid SI-51



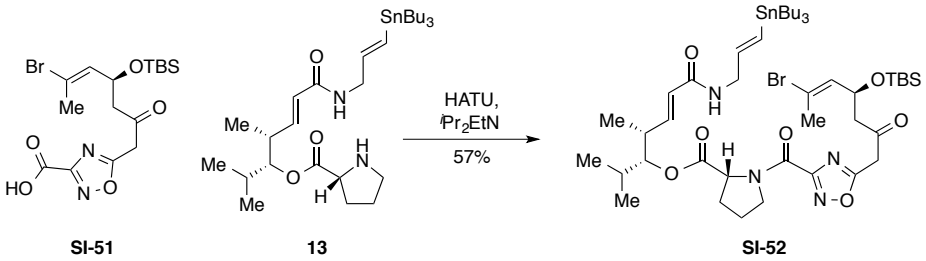
A 100-mL round-bottom flask equipped condenser was charged with ethyl ester **SI-50** (0.13 g, 0.27 mmol, 1 equiv). The vessel was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCE (5.4 mL) was added, resulting in a colorless solution. Me_3SnOH (0.25 g, 1.36 mmol, 5.0 equiv) was added, and the vessel and its contents were heated by means of an 80 ºC oil bath for 1 h. After cooling to 23 ºC. the mixture was concentrated and the resulting residue was dissolved with EtOAc (50 mL). Then the solution was washed with 0.1 N $KHSO_4$ (30 mL), water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAC:hexanes =1:2.5) to afford acid **SI-51** (27.0 mg, 23% yield) as a colorless oil which showed a mixture of keto-enol tautomers (2:1) in NMR spectra.

TLC (EtOAc:hexanes = 1:1): R_f = 0.3 (UV).

Keto-form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (d, *J* = 8.9 Hz, 1H), 4.84 – 4.72 (m, 1H), 3.53 (s, 2H), 2.83 (dd, *J* = 15.7, 8.0 Hz, 1H), 2.56 (dd, *J* = 15.5, 4.7 Hz, 1H), 2.30 (s, 3H), 0.84 (s, 9H), 0.04 (s, 6H).

Enol-form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.77 (s, 1H), 5.82 (d, *J* = 8.9 Hz, 1H), 4.98 (s, 1H), 4.71 – 4.61 (m, 1H), 2.27 (s, 3H), 0.84 (s, 9H), 0.04 (s, 6H).

Stille coupling precursor SI-52



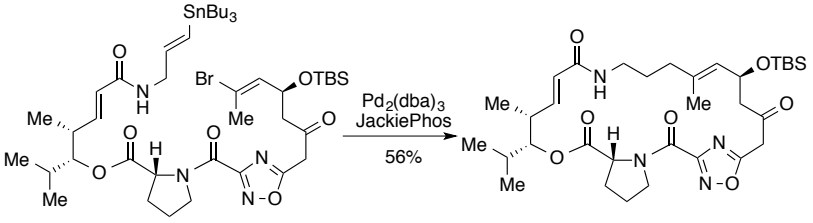
A 25-mL round-bottom flask was charged with amine **13** (32.6 mg, 54.6 µmol, 1 equiv), acid **SI-51** (26.0 mg, 60.0 µmol, 1.1 equiv) and ^{i}Pr$_2$EtN (19.7 µL, 0.11 mmol, 2.0 equiv). DCM (5 mL) was added, resulting in a colorless solution. HATU (25.9 mg, 68.2 µmol, 1.25 equiv) was added to this solution in one portion. After 5 h, the mixture was diluted with DCM (20 mL), and the diluted solution was transferred to a separatory funnel and was washed with water (2 × 20 mL) and brine (20 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to Stille coupling precursor **SI-52** (27 mg, 57% yield) as a light-yellow foam.

TLC (EtOAc:hexanes = 1:3): R_f = 0.3 (UV).

^{1}H NMR (300 MHz, $CDCl_3$, mixtures of rotamers) δ 6.67 (dd, *J* = 15.5, 8.0 Hz, 1H), 6.16 – 6.07 (m, 1H), 5.96 (dt, *J* = 19.0, 5.0 Hz, 1H), 5.90 – 5.57 (m, 3H), 4.88 – 4.73 (m, 2H), 4.53 (ddd, *J* = 10.1, 8.3, 3.2 Hz, 1H), 4.08 – 3.87 (m, 2H), 3.62 – 3.54 (m, 1H), 3.47 (dq, *J* = 13.0, 3.9, 3.3 Hz, 2H), 2.87 (dd, *J* = 16.2, 7.8 Hz, 1H), 2.70 – 2.50 (m, 2H), 2.34 – 2.15

(m, 4H), 2.12 – 1.83 (m, 4H), 1.58 – 1.42 (m, 6H), 1.37 – 1.17 (m, 9H), 1.10 – 1.00 (m, 3H), 1.00 – 0.77 (m, 27H), 0.10 – 0.00 (m, 6H).

Stille coupling product SI-53



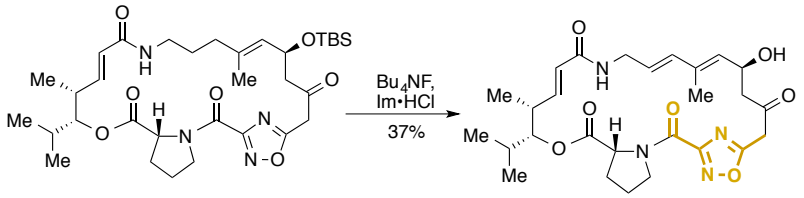
SI-52 **SI-53**

A 25-mL round-bottom flask containing JackiePhos (4.1 mg, 5.1 µmol, 0.2 equiv), $Pd_2(dba)_3$ (2.4 mg, 2.6 µmol, 0.1 equiv) and Stille coupling precursor **SI-52** (26 mg, 26 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (5.2 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 15 h, **SI-52** was entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:1), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2 to to 1:1) to afford Stille coupling product **SI-53** (9.3 mg, 56% yield).

TLC (EtOAc:hexanes = 1:1): R_f = 0.15 (UV).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (dd, *J* = 16.2, 5.6 Hz, 1H), 6.13 (d, *J* = 16.2 Hz, 1H), 5.97 – 5.78 (m, 2H), 5.78 – 5.58 (m, 2H), 4.99 (td, *J* = 10.2, 3.4 Hz, 1H), 4.83 (dd, *J* = 10.4, 2.3 Hz, 1H), 4.60 -4.40 (m, 2H), 3.55 (d, *J* = 18.9 Hz, 1H), 3.44 – 3.18 (m, 4H), 3.12 – 2.95 (m, 1H), 2.84 – 2.68 (m, 1H), 2.58 (dd, *J* = 17.5, 3.4 Hz, 1H), 2.20 – 1.70 (m, 5H), 1.82 (s, 3H), 1.08 (d, *J* = 6.7 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H).

Analogue 28



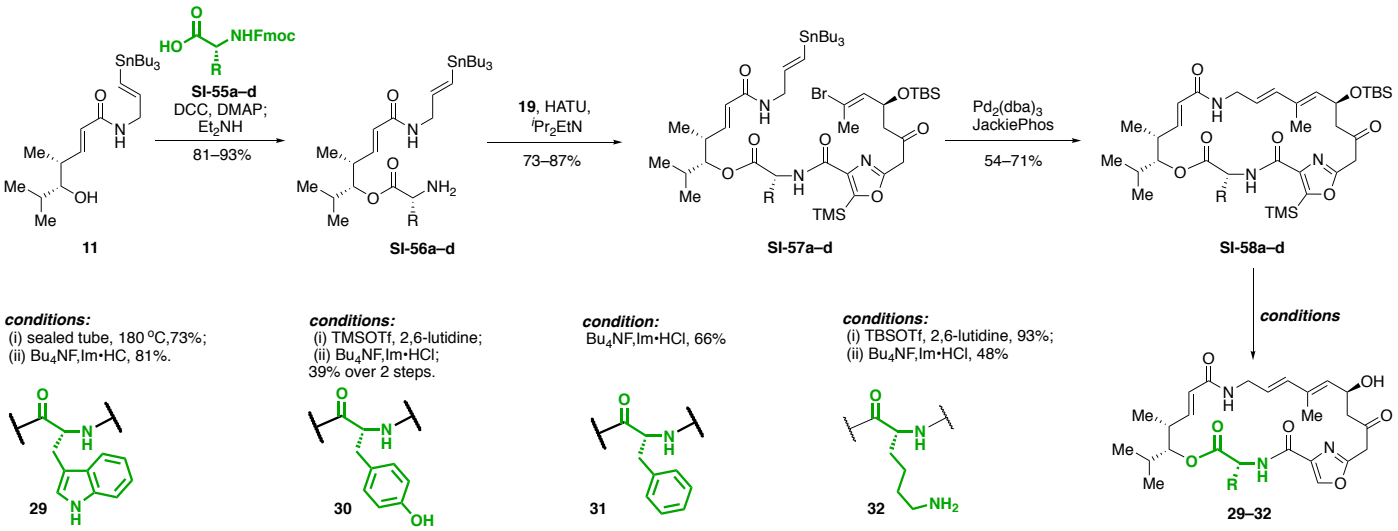
SI-53 **28**

A 25-mL round-bottom flask containing Stille coupling product **SI-53** (9.3 mg, 14.5 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2 ml) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (30 mg, 0.29 mmol, 20.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.29 mL, 0.29 mmol, 20.0 equiv). The resulting colorless solution was added to the solution of **SI-53**. After 72 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **28** (2.8 mg, 37% yield) as a white solid.

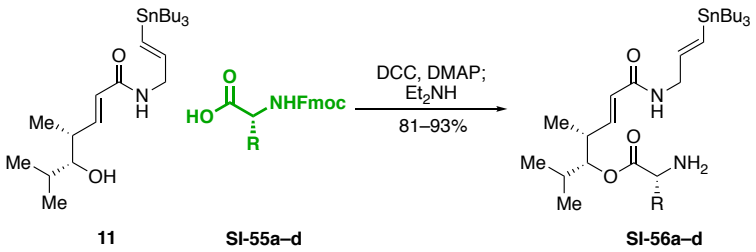
TLC (MeOH:DCM = 1:20): R_f = 0.40 (UV).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.57 (dd, *J* = 16.3, 5.6 Hz, 1H), 6.12 (dt, *J* = 15.7, 2.0 Hz, 1H), 5.98 – 5.82 (m, 3H), 5.71 (dt, *J* = 16.2, 3.3 Hz, 1H), 4.98 (dd, *J* = 10.2, 6.9 Hz, 1H), 4.81 (dd, *J* = 10.4, 2.2 Hz, 1H), 4.61 – 4.44 (m, 2H), 3.56 (d, *J* = 18.8 Hz, 1H), 3.43 (d, *J* = 12.6 Hz, 1H), 3.35 (d, *J* = 12.7 Hz, 1H), 3.28 (ddd, *J* = 10.7, 7.1, 4.1 Hz, 1H), 3.09 (td, *J* = 9.9, 8.7, 4.9 Hz, 1H), 3.01 – 2.89 (m, 2H), 2.82 – 2.67 (m, 1H), 2.73 (dd, *J* = 17.0, 3.4 Hz, 1H), 2.20 – 2.03 (m, 1H), 2.03 – 1.90 (m, 2H), 1.87 (d, *J* = 1.2 Hz, 3H), 1.84 – 1.72 (m, 2H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H).

Scheme X General route to 29–32

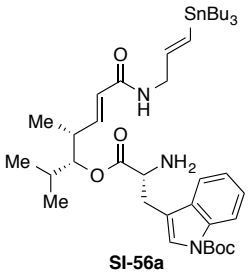


Scheme X-1 General procedure A for preparation of amines SI-56a–d



A 50-mL round-bottom flask was charged with vinyl stannane **11** (0.20 g, 0.40 mmol, 1 equiv), Fmoc-D-amino acid **SI-55a**–**d** (0.60 mmol, 1.5 equiv) and DMAP (10 mg, 80 μmol, 0.2 equiv). DCM (4 mL) was added, resulting in a colorless solution. DCC (0.13 g, 0.64 mmol, 1.6 equiv) was added in one portion, resulting in a white suspension. After 5 h, the alcohol **11** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:3), and diethyl amine (2 mL) was added. After an additional 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 20 mL). The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-56a**–**d** as a light-yellow oil.

Amine SI-56a



SI-56a

Prepared according to general procedure A from alcohol **11** (0.20 g, 0.40 mmol, 1 equiv), Fmoc-D-Trp(Boc)-OH (**SI-55a**, 0.32 g, 0.60 mmol, 1.5 equiv), DMAP (10 mg, 80 μmol, 0.2 equiv) and DCC (0.13 g, 0.64 mmol, 1.6 equiv). Amine **SI-56a** (0.28 g, 89% yield) was obtained as a light-yellow oil.

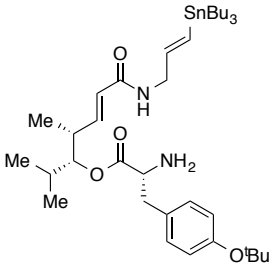
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.2 Hz, 1H), 7.60 – 7.53 (m, 1H), 7.49 (s, 1H), 7.32 (ddd, *J* = 8.4, 7.2, 1.3 Hz, 1H), 7.29 – 7.21 (m, 2H), 6.72 (dd, *J* = 15.4, 8.2 Hz, 1H), 6.12 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.96 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.79 (dd, *J* = 15.4, 1.1 Hz, 1H), 5.54 (t, *J* = 5.9 Hz, 1H), 4.86 (dd, *J* = 7.4, 4.7 Hz, 1H), 4.03 – 3.95 (m, 2H), 3.87 (dd, *J* = 8.9, 4.8 Hz, 1H), 3.26 (dd, *J* = 14.5, 4.7 Hz, 1H), 2.86 (dd, *J* = 14.4, 8.9 Hz, 1H), 2.68 – 2.58 (m, 1H), 1.99 – 1.85 (m, 1H), 1.66 (s, 9H), 1.53 – 1.43 (m, 6H), 1.35 – 1.23 (m, 6H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.95 – 0.75 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 165.1, 149.6, 145.1, 143.3, 135.6, 130.6, 130.3, 124.5, 124.1, 124.0, 122.5, 118.9, 116.3, 115.4, 83.6, 80.7, 54.6, 44.9, 38.4, 30.9, 29.9, 29.0, 28.2, 27.2, 19.8, 16.5, 15.4, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{40}H_{66}N_3O_5Sn^+$ $[M + H]^+$ 788.4019, found 788.4017.

Amine SI-56b



SI-56b

Prepared according to general procedure A from alcohol **11** (0.20 g, 0.40 mmol, 1 equiv), Fmoc-D-Tyr(tBu)-OH (**SI-55b**, 0.28 g, 0.60 mmol, 1.5 equiv), DMAP (0.010 g, 0.080 mmol, 0.2 equiv) and DCC (0.13 g, 0.64 mmol, 1.6 equiv). Amine **SI-56b** (0.23 g, 79% yield) was obtained as a light-yellow oil.

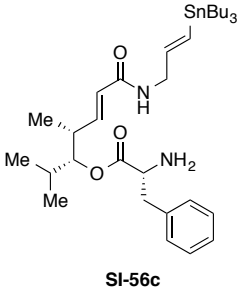
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.69 (dd, *J* = 15.4, 8.2 Hz, 1H), 6.12 (d, *J* = 19.0 Hz, 1H), 5.96 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.77 (dd, *J* = 15.3, 1.1 Hz, 1H), 5.62 (t, *J* = 5.3 Hz, 1H), 4.81 (dd, *J* = 7.2, 4.9 Hz, 1H), 3.98 (t, *J* = 4.8 Hz, 2H), 3.72 (dd, *J* = 8.2, 5.5 Hz, 1H), 3.10 (dd, *J* = 13.7, 5.5 Hz, 1H), 2.74 (dd, *J* = 13.7, 8.4 Hz, 1H), 2.66 – 2.49 (m, 1H), 1.96 – 1.82 (m, 1H), 1.56 – 1.41 (m, 6H), 1.32 (s, 9H), 1.36 – 1.22 (m, 6H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.93 – 0.78 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 165.2, 154.1, 145.0, 143.4, 132.2, 130.4, 129.7, 124.3, 123.9, 80.6, 78.4, 56.1, 44.9, 40.5, 38.4, 29.8, 29.0, 28.8, 27.2, 19.8, 16.5, 15.4, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{37}H_{64}N_2NaO_4Sn^+$ $[M + Na]^+$ 743.3780, found 743.3776.

Amine SI-56c



SI-56c

Prepared according to general procedure A from alcohol **11** (0.20 g, 0.40 mmol, 1 equiv), Fmoc-D-Phe-OH (**SI-55c**, 0.23 g, 0.60 mmol, 1.5 equiv), DMAP (0.010 g, 0.080 mmol, 0.2 equiv) and DCC (0.13 g, 0.64 mmol, 1.6 equiv). Amine **SI-56c** (0.21 g, 81% yield) was obtained as a light-yellow oil.

TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

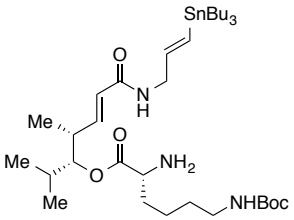
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 6.70 (dd, *J* = 15.4, 8.0

Hz, 1H), 6.12 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.97 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.81 (dd, *J* = 15.4, 1.2 Hz, 1H), 5.56 (t, *J* = 5.9 Hz, 1H), 4.83 (dd, *J* = 7.2, 4.9 Hz, 1H), 4.02 – 3.95 (m, 2H), 3.75 (dd, *J* = 8.9, 5.0 Hz, 1H), 3.16 (dd, *J* = 13.6, 5.0 Hz, 1H), 2.76 (dd, *J* = 13.6, 8.9 Hz, 1H), 2.68 – 2.56 (m, 1H), 1.98 – 1.82 (m, 1H), 1.57 (br s, 2H), 1.55 – 1.41 (m, 6H), 1.36 – 1.22 (m, 7.3 Hz, 6H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.95 – 0.77 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 165.2, 145.1, 143.3, 137.5, 130.5, 129.3, 128.6, 126.8, 123.9, 80.6, 56.1, 44.9, 41.2, 38.3, 29.9, 29.0, 27.2, 19.7, 16.6, 15.2, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{33}H_{57}N_2O_3Sn^+$ $[M + H]^+$ 649.3386, found 649.3378.

Amine SI-56d



SI-56d

Prepared according to general procedure A from alcohol **11** (0.20 g, 0.40 mmol, 1 equiv), Fmoc-D-Lys(Boc)-OH (**SI-55d**, 0.28 g, 0.60 mmol, 1.5 equiv), DMAP (0.010 g, 0.080 mmol, 0.2 equiv) and DCC (0.13 g, 0.64 mmol, 1.6 equiv). Amine **SI-56d** (0.27 g, 93% yield) was obtained as a light-yellow oil.

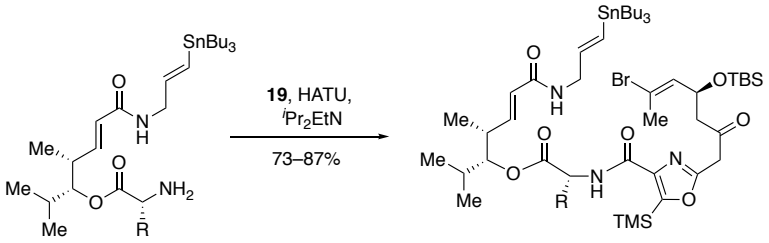
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.73 (dd, *J* = 15.2, 7.5 Hz, 1H), 6.09 (d, *J* = 19.0 Hz, 1H), 6.02 – 5.88 (m, 2H), 5.84 (d, *J* = 15.4 Hz, 1H), 4.79 (q, *J* = 6.2 Hz, 2H), 3.97 (t, *J* = 5.4 Hz, 2H), 3.47 (s, 1H), 3.09 (q, *J* = 7.3, 6.7 Hz, 2H), 2.71 – 2.55 (m, 1H), 1.97 – 1.84 (m, 1H), 1.67 – 1.34 (m, 21H), 1.35 – 1.22 (m, 6H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.97 – 0.77 (m, 21H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 165.2, 156.1, 145.4, 143.5, 130.1, 123.8, 80.5, 79.0, 54.4, 44.9, 40.3, 38.0, 34.6, 29.8, 29.1, 29.0, 28.4, 27.2, 22.9, 19.6, 17.2, 14.3, 13.6, 9.4.

HRMS-ESI m/z calcd for $C_{35}H_{68}N_3O_5Sn^+$ $[M + H]^+$ 730.4175, found 730.4164.

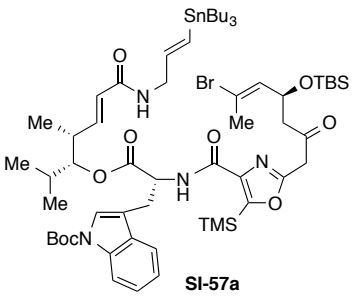
Scheme X-2 General procedure B for preparation of Stille coupling precursors SI-57a–d



SI-56a–d **SI-57a–d**

A 50-mL round-bottom flask was charged with amine **SI-56a–d** (1 equiv), ^{i}Pr$_2$EtN (2.0 equiv) and acid **19 (**1.1 equiv). DCM (about 0.1 M) was added, resulting in a clear, colorless solution, and HATU (1.25 equiv) was added to this solution in one portion. After 5 h, the mixture was diluted with DCM (50 mL). The solution was transferred to a separatory funnel and was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-57a–d** as a light-yellow foam.

Stille coupling precursor SI-57a



SI-57a

Prepared according to general procedure B from amine **SI-56a** (0.28 g, 0.36 mmol, 1 equiv), acid **19** (0.20 g, 0.39 mmol, 1.1 equiv), $^{i}Pr_2EtN$ (0.12 mL, 0.71 mmol, 2.0 equiv) and HATU (0.17 g, 0.45 mmol, 1.25 equiv). Stille coupling precursor **SI-57a** (0.35 g, 77% yield) was obtained as a light-yellow oil.

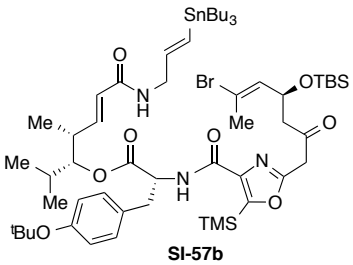
TLC (EtOAc:hexanes = 1:3): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.2 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.47 (s, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.29 (t, *J* = 7.7 Hz, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 6.66 (dd, *J* = 15.3, 8.1 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.4 Hz, 1H), 5.96 (dt, *J* = 19.1, 5.0 Hz, 1H), 5.85 – 5.78 (m, 1H), 5.78 – 5.65 (m, 2H), 5.11 (dt, *J* = 8.9, 6.4 Hz, 1H), 4.86 – 4.71 (m, 2H), 3.97 (t, *J* = 5.3 Hz, 2H), 3.88 (s, 2H), 3.32 (dd, *J* = 15.0, 6.1 Hz, 1H), 3.24 (dd, *J* = 14.8, 6.7 Hz, 1H), 2.80 (dd, *J* = 15.3, 8.2 Hz, 1H), 2.55 – 2.43 (m, 2H), 2.27 (d, *J* = 1.3 Hz, 3H), 1.89 – 1.76 (m, 1H), 1.64 (s, 9H), 1.56 – 1.40 (m, 6H), 1.35 – 1.20 (m, 6H), 0.99 – 0.82 (m, 27H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.7 Hz, 3H), 0.34 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 171.3, 165.3, 161.2, 161.1, 159.6, 149.5, 144.7, 143.5, 135.4, 134.2, 130.4, 130.3, 130.2, 124.5, 124.2, 124.1, 122.6, 121.8, 119.1, 115.2, 115.1, 83.5, 81.6, 67.0, 52.1, 49.6, 44.9, 44.1, 38.1, 29.7, 29.0, 28.2, 27.9, 27.3, 25.7, 24.0, 19.5, 18.0, 16.6, 14.9, 13.7, 9.4, –2.0, –4.6, –5.1.

HRMS-ESI m/z calcd for $C_{48}H_{72}BrN_4O_9Si_2^+$ $[M - SnBu_3 + H]^+$ 983.4016, found 983.4026.

Stille coupling precursor SI-57b



SI-57b

Prepared according to general procedure B from amine **SI-56b** (0.23 g, 0.32 mmol, 1 equiv), acid **19** (0.18 g, 0.35 mmol, 1.1 equiv), $^{i}Pr_2EtN$ (0.11 mL, 0.64 mmol, 2.0 equiv) and HATU (0.15 g, 0.40 mmol, 1.25 equiv). Stille coupling precursor **SI-57b** (0.28 g, 73% yield) was obtained as a light-yellow oil.

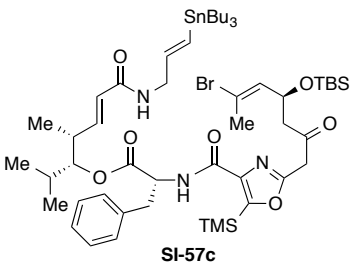
TLC (EtOAc:hexanes = 1:3): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.9 Hz, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.66 (dd, *J* = 15.4, 8.2 Hz, 1H), 6.12 (d, *J* = 19.0 Hz, 1H), 5.97 (dt, *J* = 19.0, 5.0 Hz, 1H), 5.90 – 5.70 (m, 3H), 5.05 – 4.95 (m, 1H), 4.83 – 4.72 (m, 2H), 3.98 (t, *J* = 4.7 Hz, 2H), 3.91 (s, 2H), 3.17 (dd, *J* = 14.3, 6.5 Hz, 1H), 3.08 (dd, *J* = 14.0, 6.9 Hz, 1H), 2.83 (dd, *J* = 15.2, 8.2 Hz, 1H), 2.58 – 2.48 (m, 2H), 2.28 (d, *J* = 1.3 Hz, 3H), 1.90 -1.75 (m, 1H), 1.56 – 1.41 (m, 6H), 1.30 (s, 9H), 1.30 – 1.22 (m, 6H), 0.92 – 0.83 (m, 27H), 0.80 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 6.7 Hz, 3H), 0.33 (s, 9H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 171.3, 165.3, 161.1, 160.9, 159.6, 154.2, 144.8, 143.5, 143.5, 134.2, 131.0, 130.2, 129.8, 124.3, 124.2, 121.8, 81.4, 78.4, 67.1, 52.9, 49.7, 44.9, 44.1, 38.1, 37.5, 29.8, 29.0, 28.8, 27.2, 25.7, 24.0, 19.6, 18.0, 16.6, 15.1, 13.7, 9.4, -2.0, -4.6, -5.1.

HRMS-ESI m/z calcd for $C_{57}H_{97}BrN_3O_8Si_2Sn^+$ $[M + H]^+$ 1206.5014, found 1206.5034.

Stille coupling precursor SI-57c



SI-57c

Prepared according to general procedure B from amine **SI-56c** (0.18 g, 0.28 mmol, 1 equiv), acid **19** (0.16 g, 0.31 mmol, 1.1 equiv), $^{i}Pr_2EtN$ (0.10 mL, 0.56 mmol, 2.0 equiv) and HATU (0.13 g, 0.35 mmol, 1.25 equiv). Stille coupling precursor **SI-57c** (0.28 g, 80% yield) was obtained as a light-yellow oil.

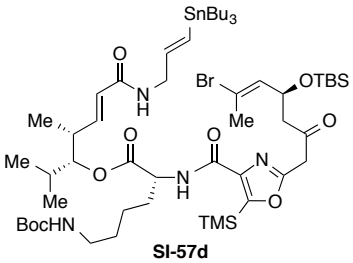
TLC (EtOAc:hexanes = 1:3): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.16 (m, 6H), 6.67 (dd, *J* = 15.4, 8.0 Hz, 1H), 6.13 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.97 (dt, *J* = 18.9, 5.0 Hz, 1H), 5.86 – 5.74 (m, 3H), 5.08 – 4.98 (m, 1H), 4.82 – 4.74 (m, 2H), 3.99 (t, *J* = 5.2 Hz, 2H), 3.91 (s, 2H), 3.24 (dd, *J* = 14.1, 6.1 Hz, 1H), 3.11 (dd, *J* = 14.0, 7.4 Hz, 1H), 2.83 (dd, *J* = 15.2, 8.2 Hz, 1H), 2.62 – 2.48 (m, 2H), 2.28 (d, *J* = 1.3 Hz, 3H), 1.91 – 1.79 (m, 1H), 1.60 – 1.36 (m, 6H), 1.36 – 1.24 (m, 6H), 1.07 – 0.73 (m, 33H), 0.33 (s, 9H), 0.053 (s, 6H), 0.050 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 171.2, 165.3, 161.1, 160.9, 159.6, 144.8, 143.5, 143.4, 136.0, 134.2, 130.2, 129.3, 128.5, 126.9, 124.2, 121.8, 81.4, 67.1, 52.8, 49.6, 44.9, 44.1, 38.1, 37.9, 29.8, 29.0, 27.2, 25.7, 24.0, 19.5, 18.0, 16.6, 14.8, 13.7, 9.4, –2.0, –4.6, –5.2.

HRMS-ESI m/z calcd for $C_{53}H_{89}BrN_3O_7Si_2Sn^+$ $[M + H]^+$ 1134.4439, found 1134.4455.

Stille coupling precursor SI-57d



SI-57d

Prepared according to general procedure B from amine **SI-56d** (0.27 g, 0.37 mmol, 1 equiv), acid **19** (0.21 g, 0.41 mmol, 1.1 equiv), $^{i}Pr_2EtN$ (0.13 mL, 0.74 mmol, 2.0 equiv) and HATU (0.18 g, 0.46 mmol, 1.25 equiv). Stille coupling precursor **SI-57d** (0.39 g, 87% yield) yield was obtained as a light-yellow oil.

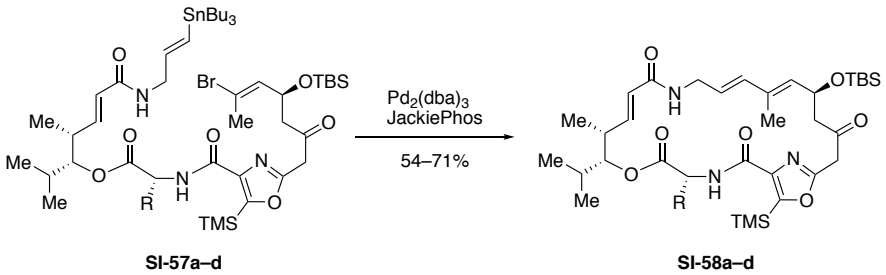
TLC (EtOAc:hexanes = 1:3): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.6 Hz, 1H), 6.75 (dd, *J* = 15.3, 7.4 Hz, 1H), 6.10 (dt, *J* = 18.9, 1.5 Hz, 1H), 6.05 (s, 1H), 5.96 (dt, *J* = 19.1, 5.1 Hz, 1H), 5.91 – 5.76 (m, 2H), 4.91 – 4.62 (m, 4H), 3.98 (t, *J* = 5.1 Hz, 2H), 3.93 (s, 2H), 3.18 – 3.02 (m, 2H), 2.84 (dd, *J* = 15.3, 8.2 Hz, 1H), 2.71 – 2.60 (m, 1H), 2.53 (dd, *J* = 15.3, 4.6 Hz, 1H), 2.28 (d, *J* = 1.3 Hz, 3H), 2.01 – 1.84 (m, 2H), 1.84 – 1.66 (m, 1H), 1.60 – 1.36 (m, 19H), 1.34 – 1.21 (m, 6H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.99 – 0.70 (m, 30H), 0.34 (s, 9H), 0.05 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 171.8, 165.2, 161.1, 161.0, 159.6, 156.1, 145.3, 143.6, 143.5, 134.2, 130.2, 124.0, 121.8, 81.3, 79.1, 67.0, 51.8, 49.7, 44.9, 44.1, 40.3, 37.8, 32.4, 29.8, 29.6, 29.0, 28.4, 27.2, 25.7, 24.0, 22.7, 19.5, 18.0, 17.3, 14.0, 13.7, 9.4, –2.0, –4.6, –5.1.

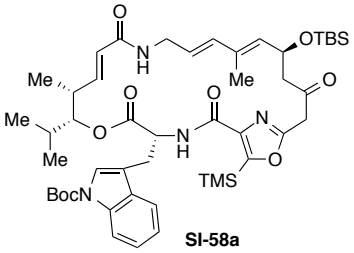
HRMS-ESI m/z calcd for $C_{55}H_{100}BrN_4O_9Si_2Sn^+$ $[M + H]^+$ 1215.5229, found 1215.5249.

Scheme X-3 General procedure C for preparation of Stille coupling products SI-58a–d



A round-bottom flask containing JackiePhos (0.2 equiv), $Pd_2(dba)_3$ (0.1 equiv) and Stille coupling precursor **SI-57a–d** (1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (about 0.005 M) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 3 – 12 h, **SI-57a–d** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille coupling product **SI-58a–d** as a light-yellow foam.

Stille coupling product SI-58a



SI-58a

Prepared according to general procedure C from JackiePhos (44 mg, 55 μmol, 0.2 equiv), $Pd_2(dba)_3$ (25 mg, 28 μmol, 0.1 equiv) and Stille couping precursor **SI-57a** (0.35 g, 0.28 mmol, 1 equiv). Stille coupling product **SI-58a** (0.18 g, 71% yield) was obtained as a light-yellow foam.

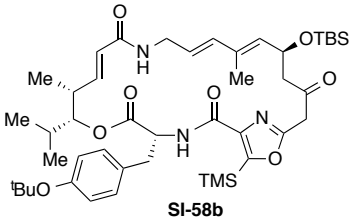
TLC (EtOAc:hexanes = 1:2): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.37 (m, 3H), 7.27 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 6.45 (dd, *J* = 16.2, 5.5 Hz, 1H), 6.19 (d, *J* = 15.7 Hz, 1H), 5.87 (dd, *J* = 7.9, 4.0 Hz, 1H), 5.79 (dd, *J* = 16.2, 1.7 Hz, 1H), 5.60 (ddd, *J* = 15.7, 7.9, 3.7 Hz, 1H), 5.45 (d, *J* = 8.9 Hz, 1H), 5.13 (td, *J* = 8.7, 4.7 Hz, 1H), 4.93 (td, *J* = 8.7, 5.3 Hz, 1H), 4.76 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.44 – 4.30 (m, 1H), 3.88 (d, *J* = 17.4 Hz, 1H), 3.71 (d, *J* = 17.4 Hz, 1H), 3.64 (ddd, *J* = 11.6, 7.8, 3.9 Hz, 1H), 3.32 (dd, *J* = 15.2, 4.8 Hz, 1H), 2.93 (dt, *J* = 14.4, 8.8 Hz, 2H), 2.82 (dd, *J* = 14.4, 5.3 Hz, 1H), 2.78 – 2.68 (m, 1H), 2.04 – 1.92 (m, 1H), 1.63 (s, 9H), 1.63 (s, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 2H), 0.94 (d, *J* = 6.7 Hz, 4H), 0.85 (s, 9H), 0.27 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 172.6, 166.7, 161.0, 160.5, 159.9, 149.5, 144.2, 143.4, 135.2, 133.6, 133.4, 130.3, 125.1, 124.5, 124.4, 123.7, 122.6, 118.9, 115.4, 115.2, 83.6, 83.3, 66.3, 51.4, 50.2, 43.9, 41.1, 37.0, 29.5, 29.0, 28.2, 25.8, 19.9, 18.7, 18.1, 13.0, 10.1, –2.1,– 4.5, –5.0.

HRMS-ESI m/z calcd for $C_{48}H_{71}N_4O_9Si_2^+$ $[M + H]^+$ 903.4754, found 903.4737.

Stille coupling product SI-58b



SI-58b

Prepared according to general procedure C from JackiePhos (37 mg, 47 μmol, 0.2 equiv), $Pd_2(dba)_3$ (22 mg, 24 μmol, 0.1 equiv) and Stille coupling precursor **SI-57b** (0.28 g, 0.24 mmol, 1 equiv). Stille coupling product **SI-58b** (0.11 g, 54% yield) was obtained as a light-yellow foam.

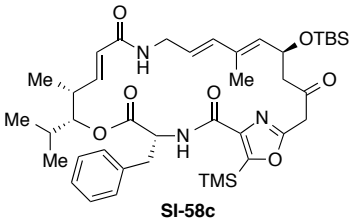
TLC (EtOAc:hexanes = 1:2): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.9 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.40 (dd, *J* = 16.2, 5.2 Hz, 1H), 6.20 (d, *J* = 15.8 Hz, 1H), 5.83 (dd, *J* = 8.1, 3.9 Hz, 1H), 5.78 (dd, *J* = 16.2, 1.8 Hz, 1H), 5.64 (ddd, *J* = 15.7, 8.2, 3.8 Hz, 1H), 5.45 (d, *J* = 8.9 Hz, 1H), 5.04 (td, *J* = 8.3, 5.1 Hz, 1H), 4.95 (td, *J* = 8.6, 5.6 Hz, 1H), 4.75 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.47 – 4.33 (m, 1H), 3.90 (d, *J* = 17.4 Hz, 1H), 3.73 (d, *J* = 17.4 Hz, 1H), 3.64 (ddd, *J* = 15.7, 8.2, 3.8 Hz, 1H), 3.23 (dd, *J* = 14.4, 5.2 Hz, 1H), 2.94 – 2.67 (m, 4H), 2.03 – 1.90 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.28 (s, 9H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.86 (s, 9H), 0.29 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 172.5, 166.6, 160.7, 160.4, 159.8, 154.2, 144.2, 143.4, 135.4, 133.6, 133.5, 130.7, 129.6, 125.3, 124.4, 124.1, 83.1, 78.3, 66.3, 52.1, 50.2, 44.0, 41.1, 38.0, 36.9, 29.5, 28.8, 25.8, 19.9, 18.7, 18.1, 13.0, 10.2, –2.1, –4.4, –5.0.

HRMS-ESI m/z calcd for $C_{45}H_{70}N_3O_8Si_2^+$ $[M + H]^+$ 836.4696, found 836.4712.

Stille coupling product SI-58c



SI-58c

Prepared according to general procedure C from JackiePhos (28 mg, 35 μmol, 0.2 equiv), $Pd_2(dba)_3$ (16 mg, 18 μmol, 0.1 equiv) and Stille coupling precursor **SI-57c** (0.20 g, 0.18 mmol, 1 equiv). Stille coupling product **SI-58c** (77 mg, 57% yield) was obtained as a light-yellow foam.

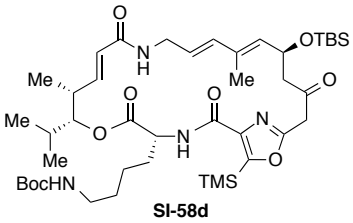
TLC (EtOAc:hexanes = 1:2): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.9 Hz, 1H), 7.25 – 7.15 (m, 3H), 7.12 (dd, *J* = 7.8, 1.7 Hz, 2H), 6.42 (dd, *J* = 16.3, 5.0 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 5.86 – 5.74 (m, 2H), 5.52 (ddd, *J* = 15.2, 8.2, 3.5 Hz, 1H), 5.43 (d, *J* = 8.9 Hz, 1H), 5.06 (ddd, *J* = 9.0, 7.5, 5.2 Hz, 1H), 4.93 (td, *J* = 8.8, 5.3 Hz, 1H), 4.75 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.52 – 4.35 (m, 1H), 3.89 (d, *J* = 17.5 Hz, 1H), 3.73 (d, *J* = 17.6 Hz, 1H), 3.56 (ddd, *J* = 15.8, 8.4, 3.4 Hz, 1H), 3.29 (dd, *J* = 14.2, 5.3 Hz, 1H), 2.94 – 2.68 (m, 4H), 2.06 – 1.94 (m, 6.6 Hz, 1H), 1.67 (s, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.85 (s, 9H), 0.29 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 172.5, 166.7, 160.7, 160.5, 159.8, 144.1, 143.3, 135.7, 135.4, 133.6, 133.4, 129.3, 128.4, 126.9, 125.4, 124.5, 83.5, 66.4, 52.1, 50.2, 44.1, 41.1, 38.5, 36.8, 29.5, 25.7, 19.9, 18.7, 18.1, 13.1, 10.1, –2.1, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{41}H_{61}N_3NaO_7Si_2^+$ $[M + Na]^+$ 786.3940, found 786.3914.

Stille coupling product SI-58d



SI-58d

Prepared according to general procedure C from JackiePhos (0.052 g, 0.065 mmol, 0.2 equiv), $Pd_2(dba)_3$ (0.030 g, 0.033 mmol, 0.1 equiv) and Stille coupling precursor **SI-57d** (0.39 g, 0.33 mmol, 1 equiv). Stille coupling product **SI-58d** (0.17 g, 62% yield) was obtained as a light-yellow foam.

TLC (EtOAc:hexanes = 1:2): R_f = 0.2 (UV).

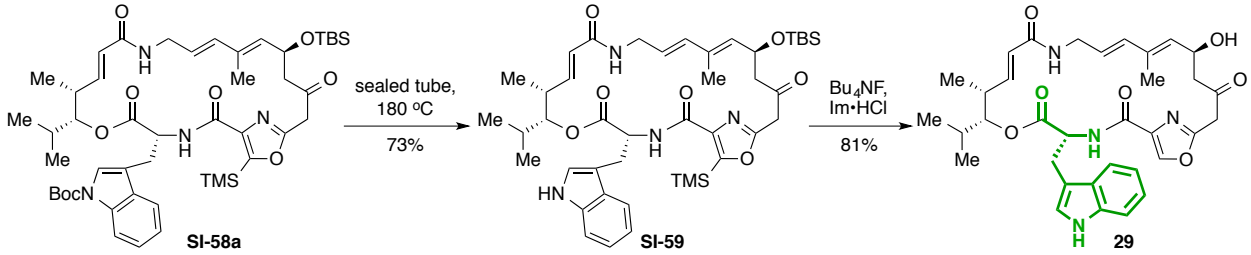
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 9.0 Hz, 1H), 6.65 (dd, *J* = 15.8, 4.5 Hz, 1H), 6.47 (s, 1H), 6.22 (d, *J* = 15.6 Hz, 1H), 5.86 (dd, *J* = 16.0, 1.9 Hz, 1H), 5.64 – 5.51 (m, 1H), 5.47 (d, *J* = 9.0 Hz, 1H), 5.07 – 4.90 (m, 2H), 4.82 (d, *J* = 10.2 Hz, 1H), 4.80 – 4.70 (m, 1H), 4.25 – 4.11 (m, 1H), 3.91 (d, *J* = 17.2 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.74 (d, *J* = 17.1 Hz, 1H), 3.10 (dt, *J* = 13.2, 6.6 Hz, 1H), 3.05 – 2.91 (m, 2H), 2.85 (dd, *J* = 15.0, 5.6 Hz, 1H), 2.80 – 2.67 (m, 1H), 2.25 – 2.05

(m, 1H), 2.02 – 1.84 (m, 2H), 1.68 (s, 3H), 1.65 – 1.47 (m, 3H), 1.42 (s, 9H), 1.09 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 6.8 Hz, 3H), 0.89 (d, J = 6.3 Hz, 3H), 0.85 (s, 9H), 0.34 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 172.2, 166.1, 160.9, 160.2, 159.9, 156.2, 145.4, 143.6, 135.4, 133.9, 133.0, 125.2, 124.0, 82.2, 79.1, 66.1, 50.9, 50.3, 43.9, 40.9, 40.3, 36.6, 32.6, 29.8, 29.5, 28.4, 25.8, 22.2, 19.8, 18.7, 18.1, 13.0, 10.0, –2.0, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{43}H_{72}N_4NaO_9Si_2^+$ $[M + Na]^+$ 867.4730, found 867.4721.

Analogue 29



A 25-mL sealed tube containing Stille coupling product **SI-58a** (40 mg, 45 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). *O*-dichlorobenzene (4.5 mL) was added, resulting in a colorless solution, and the sealed tube was quickly sealed with a TFP cap. The sealed tube and its contents were heated by means of a 180 ºC oil bath, After 2 h, **SI-58a** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was directly purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2) to afford compound **SI-59** (26 mg, 73% yield) as a white solid.

TLC (EtOAc:hexanes = 1:2): R_f = 0.1 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.53 (d, J = 8.5 Hz, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.25 (d, J = 7.9 Hz, 1H), 7.10 (t, J = 7.5 Hz, 1H), 7.03 – 6.93 (m, 2H), 6.42 (dd, J = 16.1, 5.2 Hz, 1H), 6.11 (d, J = 15.7 Hz, 1H), 5.77 (dd, J = 8.0, 4.1 Hz, 1H), 5.68 (dd, J = 16.2, 1.8 Hz, 1H), 5.58 (ddd, J = 15.8, 7.2, 3.8 Hz, 1H), 5.35 (d, J = 9.0 Hz, 1H), 5.13 (dt, J = 8.5, 5.3 Hz, 1H), 4.88 (ddd, J = 8.8, 7.5, 6.2 Hz, 1H), 4.81 (dd, J = 10.1, 1.8 Hz, 1H), 4.40 (dd, J = 14.8, 7.9 Hz, 1H), 3.84 (d, J = 17.2 Hz, 1H), 3.69 (d, J = 17.2 Hz, 1H), 3.66 – 3.58 (m, 1H), 3.50 (dd, J = 15.3, 4.8 Hz, 1H), 3.19 (dd, J = 15.3, 5.8 Hz, 1H), 2.86 (dd, J = 14.4, 6.3 Hz, 1H), 2.78 – 2.66 (m, 1H), 2.56 (dd, J = 14.4, 7.6 Hz, 1H), 2.07 – 1.89 (m, 1H), 1.61 (s, 3H), 1.00 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 6.9 Hz, 3H), 0.93 (d, J = 6.7 Hz, 3H), 0.83 (s, 9H), 0.33 (s, 9H), 0.02 (s, 3H), -0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.5, 172.4, 166.7, 161.0, 160.2, 159.7, 145.3, 143.6, 135.9, 134.9, 134.0, 132.8, 127.7, 125.0, 124.3, 123.0, 122.0, 119.3, 118.7, 111.0, 109.7, 83.4, 66.3, 52.3, 49.6, 44.1, 40.9, 36.6, 29.7, 27.8, 25.7, 19.9, 18.8, 18.1, 13.0, 10.4, –2.0, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{43}H_{63}N_4O_7Si_2^+$ $[M + H]^+$ 803.4230, found 803.4214.

A 50-mL round-bottom flask containing **SI-59** (13 mg, 16 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.6 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (17 mg, 0.16 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.16 mL, 0.16 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-59**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with

water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (silica gel, eluent: MeOH:DCM = 1:20) to afford analogue **29** (8 mg, 81% yield) as a white solid.

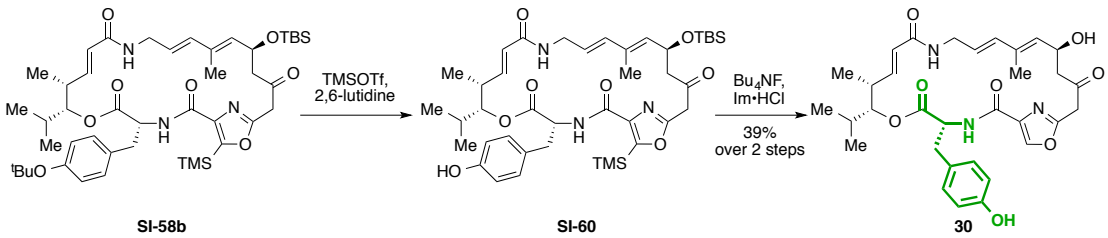
TLC (MeOH:DCM = 1:20): R_f = 0.1 (UV).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.35 (s, 1H), 8.05 (s, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 8.4 Hz, 1H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.05 (d, *J* = 2.2 Hz, 1H), 6.99 (t, *J* = 7.2 Hz, 1H), 6.58 (dd, *J* = 16.0, 5.6 Hz, 1H), 6.01 (d, *J* = 15.9 Hz, 1H), 5.98 – 5.93 (m, 1H), 5.84 (dd, *J* = 16.0, 1.8 Hz, 1H), 5.70 (ddd, *J* = 15.8, 6.2, 3.6 Hz, 1H), 5.17 (d, *J* = 8.5 Hz, 1H), 5.02 (ddd, *J* = 8.5, 6.5, 4.7 Hz, 1H), 4.86 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.82 – 4.72 (m, 1H), 4.40 – 4.27 (m, 1H), 3.80 (d, *J* = 16.9 Hz, 1H), 3.72 (d, *J* = 16.9 Hz, 1H), 3.76 – 3.69 (m, 1H), 3.49 (dd, *J* = 15.1, 4.7 Hz, 1H), 3.20 (dd, *J* = 15.2, 6.5 Hz, 1H), 2.80 – 2.71 (m, 1H), 2.76 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.62 (dd, *J* = 16.1, 6.1 Hz, 1H), 2.36 (br s, 1H), 2.09 – 1.95 (m, 1H), 1.70 (s, 3H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, CD_2Cl_2) δ 202.4, 172.1, 166.6, 163.2, 160.1, 158.3, 146.2, 141.6, 136.5, 135.4, 134.3, 132.7, 128.0, 126.2, 124.8, 124.0, 122.2, 119.6, 118.9, 111.6, 109.9, 83.8, 65.3, 53.0, 48.8, 43.8, 40.8, 37.0, 30.2, 27.9, 19.9, 18.9, 13.1, 11.0.

HRMS-ESI m/z calcd for $C_{34}H_{40}N_4NaO_7^+$ $[M + Na]^+$ 639.2789, found 639.2790.

Analogue 30



A 25-mL round-bottom flask containing Stille coupling product **SI-58b** (10 mg, 12 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (1 mL) was added, resulting in a colorless solution. After cooling to 0 ºC. 2,6-lutidine (33 µL, 287 µmol, 24.0 equiv) was added, followed by TMSOTf (43 µL, 239 µmol, 20.0 equiv). Then the mixture was allowed to warm to 23 ºC. After 36 h, DCM (30 mL) was added, and the resulting solution was transferred to a separatory funnel and was washed with water (3 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue **SI-60** was used for next step without further purification.

A 50-mL round-bottom flask containing **SI-60** was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.6 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (13 mg, 0.12 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.12 mL, 0.12 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-60**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (silica gel, eluent: MeOH:DCM = 1:20) to afford **30** (2.8 mg, 39% yield over 2 steps) as a white solid.

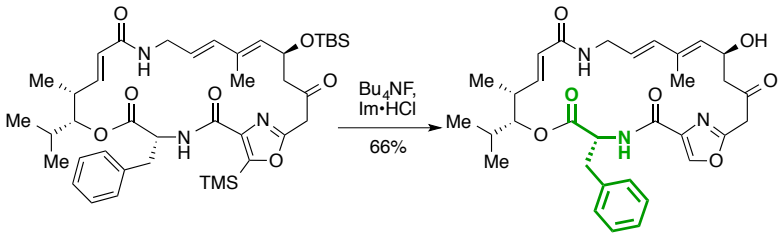
TLC (MeOH:DCM = 1:20): R_f = 0.1 (UV).

^{1}H NMR (400 MHz, CD_2Cl_2)) δ 8.07 (s, 1H), 7.22 (d, *J* = 8.5 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 6.55 (dd, *J* = 16.2, 5.0 Hz, 1H), 6.11 (d, *J* = 15.5 Hz, 1H), 6.10 (br s, 1H), 5.84 (m, 1H), 5.54 (ddd, *J* = 15.7, 8.0, 3.6 Hz, 1H), 5.40 (d, *J* = 8.9 Hz, 1H), 4.95 – 4.84 (m, 2H), 4.78 (dd, *J* = 10.1, 1.9 Hz, 1H), 4.35 – 4.20 (m, 1H), 3.89 (d, *J* = 17.3 Hz, 1H), 3.80 (d, *J* = 17.2 Hz, 1H), 3.61 (ddd, *J* = 16.0, 8.2, 4.2 Hz, 1H), 3.24 (dd, *J* = 14.3, 4.9 Hz, 1H), 2.97 – 2.77 (m, 4H), 2.10 – 1.90 (m, 1H), 1.67 (s, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.4 Hz, 3H).

^{13}C NMR (100 MHz, CD_2Cl_2) δ 202.1, 172.4, 167.3, 160.3, 158.4, 156.01 145.6, 142.1, 136.2, 135.7, 135.6, 132.6, 130.8, 127.3, 126.3, 124.6, 115.9, 84.0, 65.7, 49.4, 44.1, 41.4, 37.3, 37.2, 30.0, 29.0, 20.0, 18.9, 13.2, 10.5.

HRMS-ESI m/z calcd for $C_{32}H_{39}N_3NaO_8^+$ $[M + Na]^+$ 616.2969, found 616.2969.

Analogue 31



SI-58c **31**

A 50-mL round-bottom flask containing **SI-58c** (40 mg, 52 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (5.2 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (55 mg, 0.52 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.52 mL, 0.52 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-58c**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH:DCM = 1:100 to 1:50) to afford analogue **31** (20 mg, 66% yield) as a light-yellow solid.

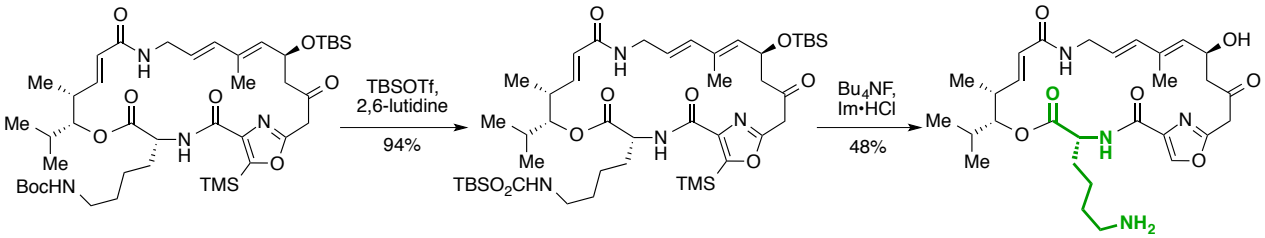
TLC (MeOH:DCM = 1:20): R_f = 0.2 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.26 – 7.11 (m, 5H), 6.50 (dd, *J* = 16.2, 5.6 Hz, 1H), 6.11 (d, *J* = 15.7 Hz, 1H), 6.01 (dd, *J* = 7.8, 4.4 Hz, 1H), 5.84 (dd, *J* = 16.1, 1.7 Hz, 1H), 5.69 – 5.59 (m, 1H), 5.43 (d, *J* = 8.8 Hz, 1H), 5.01 – 4.86 (m, 2H), 4.78 (dd, *J* = 10.2, 1.9 Hz, 1H), 4.42 – 4.23 (m, 1H), 3.86 (d, *J* = 16.8 Hz, 1H), 3.77 (d, *J* = 16.8 Hz, 1H), 3.69 (ddd, *J* = 16.5, 7.5, 4.4 Hz, 1H), 3.32 (dd, *J* = 14.3, 5.1 Hz, 1H), 3.05 – 2.85 (m, 3H), 2.83 – 2.72 (m, 1H), 2.55 (br s, 1H), 2.08 – 1.92 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.6, 171.8, 166.5, 159.9, 157.6, 144.5, 141.7, 135.8, 135.8, 135.2, 134.9, 132.0, 129.1, 128.6, 127.0, 125.7, 124.5, 83.5, 65.3, 52.7, 48.7, 43.6, 40.7, 37.9, 36.9, 29.5, 19.8, 18.7, 13.0, 10.4.

HRMS-ESI m/z calcd for $C_{32}H_{39}N_3NaO_7^+$ $[M + Na]^+$ 600.2680, found 600.2654.

Analogue 32



A 25-mL round-bottom flask containing **SI-58d** (16 mg, 19 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (2 mL) was added, resulting in a colorless solution. After cooling to 0 ºC. 2,6-lutidine (11 µL, 96 µmol, 4.0 equiv) was added, followed by TBSOTf (18 µL, 96 µmol, 5.0 equiv). Then the mixture was allowed to warm to 23 ºC. After 12 h, the mixture was diluted with DCM (30 mL), and the resulting solution was transferred to a separatory funnel and was washed with water (3 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2) to afford TBS carbamate **SI-61** (16 mg, 94% yield) as a white solid.

TLC (EtOAc:hexanes = 1:2): R_f = 0.25 (UV).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.9 Hz, 1H), 6.66 (dd, *J* = 16.1, 4.4 Hz, 1H), 6.52 – 6.40 (m, 1H), 6.22 (d, *J* = 15.8 Hz, 1H), 5.86 (d, *J* = 16.0 Hz, 1H), 5.70 – 5.50 (m, 1H), 5.47 (d, *J* = 9.0 Hz, 1H), 5.37 – 5.27 (m, 1H), 4.94 (q, *J* = 7.9 Hz, 1H), 4.89 – 4.68 (m, 2H), 4.27 – 4.10 (m, 1H), 3.92 (d, *J* = 17.2 Hz, 1H), 3.86 – 3.70 (m, 1H), 3.75 (d, *J* = 17.0 Hz, 1H), 3.24 – 3.08 (m, 1H), 3.07 – 2.90 (m, 2H), 2.86 (dd, *J* = 15.1, 5.4 Hz, 1H), 2.76 (s, 1H), 2.05 – 1.80 (m, 2H), 1.78 – 1.58 (m, 1H), 1.68 (s, 3H), 1.59 – 1.44 (m, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.92 – 0.87 (m, 3H), 0.91 (s, 9H), 0.85 (s, 9H), 0.34 (s, 9H), 0.25 (s, 6H), 0.04 (s, 3H), 0.02 (s, 3H).

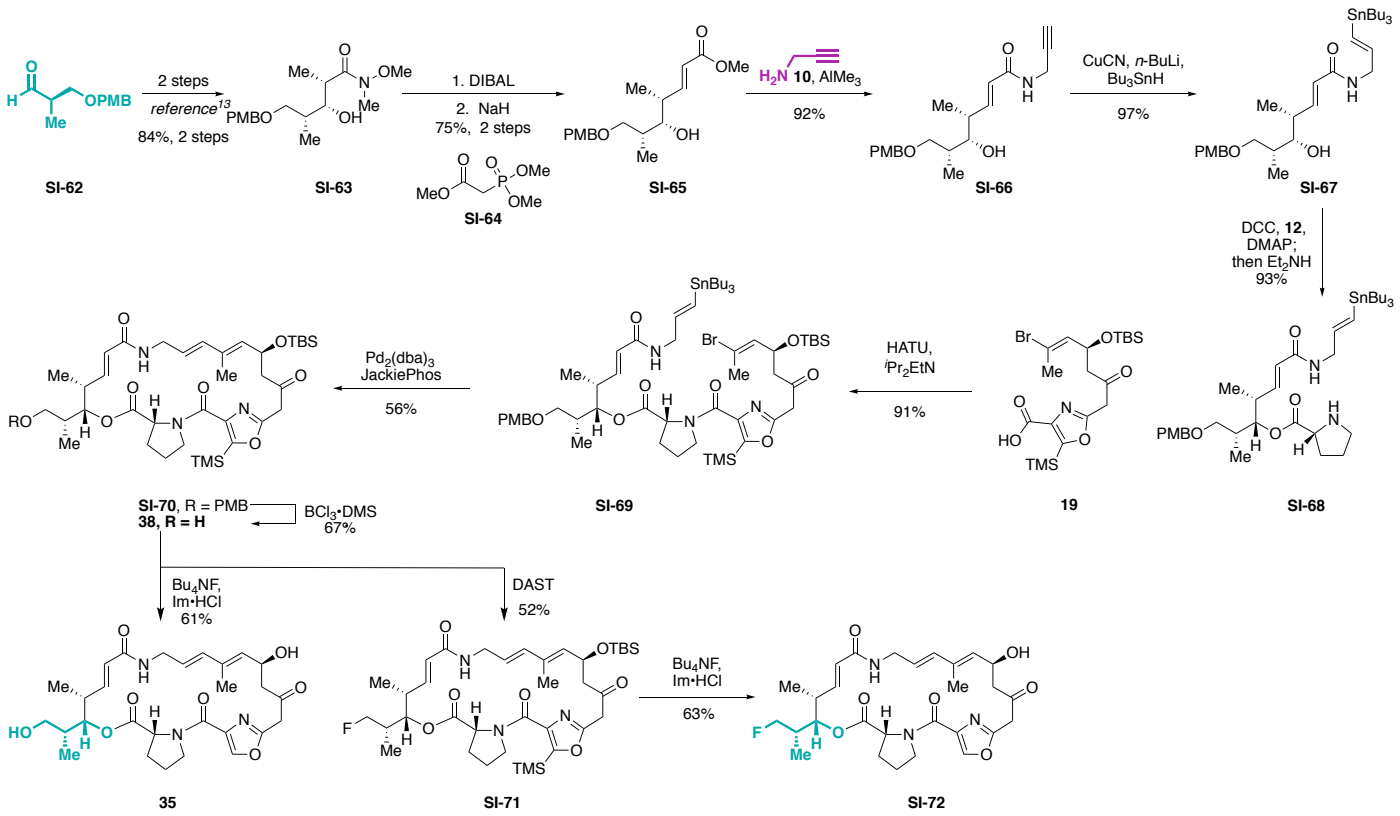
A 50-mL round-bottom flask containing TBS carbamate **SI-61** (42 mg, 46 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.3 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (98 mg, 920 µmol, 20.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.92 mL, 920 µmol, 20.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-61**. After 12 h, the mixture was concentrated, and the resulting residue was purified with preparative HPLC (eluent: H_2O:acetonitrile = 95:5 to 5:95 over 15 min) to afford analogue **32** (15 mg, 48% yield) as a white solid.

^{1}H NMR (400 MHz, MeOD) δ 8.34 (s, 1H), 6.64 (dd, *J* = 15.9, 6.1 Hz, 1H), 6.14 (d, *J* = 15.7 Hz, 1H), 5.98 (dd, *J* = 15.9, 1.6 Hz, 1H), 5.73 (ddd, *J* = 15.8, 6.5, 3.7 Hz, 1H), 5.42 (d, *J* = 9.1 Hz, 1H), 5.25 – 4.75 (m, 2H), 4.74 – 4.65 (m, 1H), 4.20 (d, *J* = 17.1 Hz, 1H), 4.07 (d, *J* = 17.2 Hz, 1H), 3.87 (d, *J* = 17.3 Hz, 1H), 3.73 – 3.60 (m, 1H), 3.01 (dd, *J* = 16.3, 8.2 Hz, 1H), 2.97 – 2.88 (m, 3H), 2.88 – 2.79 (m, 1H), 2.13 – 1.95 (m, 3H), 1.80 (s, 3H), 1.70 (q, *J* = 7.8 Hz, 2H), 1.43 (q, *J* = 7.9 Hz, 2H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H).

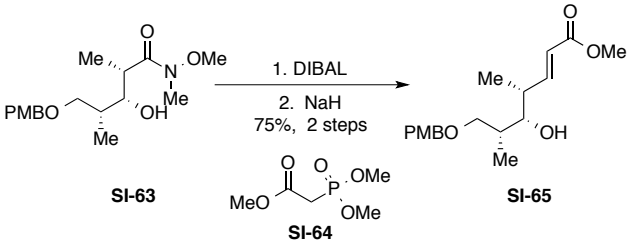
^{13}C NMR (100 MHz, MeOD) δ 203.1, 172.5, 168.4, 162.5, 160.5, 147.8, 143.3, 136.9, 136.0, 135.5, 133.8, 126.4, 125.0, 84.4, 65.2, 52.6, 50.3, 41.4, 40.5, 40.4, 37.8, 32.5, 30.7, 28.1, 23.4, 20.0, 18.9, 13.3, 11.5.

HRMS-ESI m/z calcd for $C_{29}H_{43}N_4O_7^+$ $[M + H]^+$ 559.3126, found 559.3096.

Scheme XI Synthesis of 35 and derivatives thereof



Methyl acrylate SI-65



A 100-mL round-bottom flask containing Weinreb amide **SI-63**[13] (0.35 g, 1.10 mmol, 1 equiv) was evacuated and flushed with nitrogen (the process of nitrogen exchange was repeated a total of 3 times). Dry DCM (11 mL) was added, and the resulting clear solution was cooled to -78 ºC by means of a dry ice/acetone bath. A solution of DIBAL-H in toluene (1.2 M, 2.70 mL, 3.20 mmol, 3.0 equiv) was added dropwise to this solution. After 1 h, **SI-63** was consumed as indicated by TLC analysis, and MeOH (1 mL) was carefylly added (CAUTION: Gas evolution!), followed by saturated aqueous potassium sodium tartrate solution (50 ml). The mixture was allowed to warm to 23 ºC. After 1.5 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The crude aldehyde was used for next step immediately without further purification.

A separate oven-dried 50-mL round-bottom flask containing 60% NaH (0.13 g, 3.20 mmol, 3.0 equiv) was evacuated and flushed with nitrogen (the process of nitrogen exchange was repeated a total of 3 times). THF (11 mL) was added, and the resulting suspension was cooled to 0 ºC by means of an ice/water bath. A solution of **SI-64** (0.52 mL, 3.20 mmol,

13 Dias, L. C.; Perez, C. C. *Eur. J. Org. Chem.* **2013**, *2013*, 2930–2939.

3.0 equiv) in THF (2 mL) was added dropwise at 0 ºC. After 1 h, a solution of the above aldehyde in THF (2 mL) was added. After 2 h, the saturated aqueous ammonium chloride solution (25 mL) was carefully added, and the resulting biphasic mixture was transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (2 × 30 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:5) to afford methyl ester **SI-65** (0.26 g, 75% yield over 2 steps) as a colorless oil.

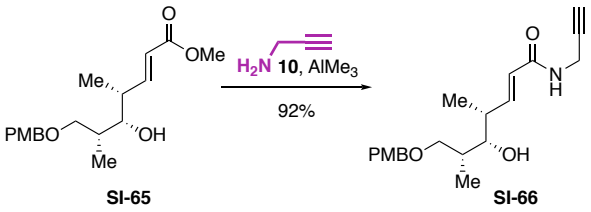
TLC (EtOAc:hexanes = 1:4): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 7.00 (dd, *J* = 15.8, 7.7 Hz, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.82 (dd, *J* = 15.8, 1.3 Hz, 1H), 4.43 (s, 2H), 3.81 (s, 3H), 3.72 (s, 3H), 3.63 (dd, *J* = 10.2, 3.8 Hz, 1H), 3.53 (d, *J* = 4.3 Hz, 1H), 3.47 (dt, *J* = 7.0, 4.5 Hz, 1H), 3.42 (dd, *J* = 9.2, 6.8 Hz, 1H), 2.50 – 2.34 (m, 1H), 1.95 – 1.85 (m, 1H), 1.09 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 159.4, 152.6, 129.5, 129.4, 120.4, 113.9, 78.9, 74.6, 73.3, 55.3, 51.4, 40.1, 35.7, 14.3, 13.0.

HRMS-ESI m/z calcd for $C_{36}H_{52}NaO_{10}^+$ $[2M + Na]^+$ 667.3453, found 667.3456.

Amide SI-66



A 200-mL round-bottom flask was charged with propargylamine (**10**, 2.30 mL, 36.0 mmol, 4.0 equiv) and DCM (60 mL) under nitrogen. The solution was cooled to 0 ºC by means of an ice/water bath, and a solution of $AlMe_3$ in heptane (1 M, 36.0 mL, 36.0 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!). The mixture was allowed to warm to 23 ºC. After 30 min, a solution of **SI-65** (2.90 g, 9.0 mmol, 1 equiv) in DCM (9 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 3 h, **SI-65** was entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:1.5), and the mixture was cooled to 0 °C by means of an ice/water bath. Then MeOH (10 mL) was carefully added (CAUTION: Gas evolution!), followed by saturated aqueous potassium sodium tartrate solution (100 mL). After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-66** (2.86 g, 92% yield) as a white, waxy solid.

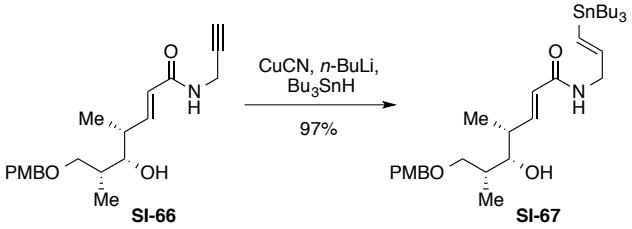
TLC (EtOAc:hexanes = 1:1): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.84 (dd, *J* = 15.5, 1.3 Hz, 1H), 5.86 (s, 1H), 5.76 (dd, *J* = 15.5, 1.3 Hz, 1H), 4.42 (s, 2H), 4.09 (dd, *J* = 5.3, 2.6 Hz, 2H), 3.80 (s, 3H), 3.61 (dd, *J* = 9.2, 3.9 Hz, 1H), 3.54 – 3.39 (m, 3H), 2.49 – 2.36 (m, 1H), 2.22 (t, *J* = 2.6 Hz, 1H), 1.89 (m, 2H), 1.07 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.3, 148.4, 129.6, 129.39, 129.36, 122.5, 113.8, 99.9, 79.6, 78.6, 77.3, 77.0, 76.7, 74.4, 73.2, 71.5, 55.3, 39.7, 35.6, 29.1, 14.4, 12.9.

HRMS-ESI m/z calcd for $C_{20}H_{28}NO_4^+$ $[M + H]^+$ 346.2013, found 346.2012.

Vinyl stannane SI-67



A 500-mL round-bottom flask containing CuCN (1.56 g, 17.4 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (120 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 14.6 mL, 36.5 mmol, 4.2 equiv) was added dropwise over 10 min, resulting in a light-yellow solution, and the mixture was stirred for 30 min. Bu_3SnH (9.83 mL, 36.5 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 min, a solution of **SI-66** (3.00 g, 8.68 mmol, 1 equiv) in THF (17 m) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (100 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 75 mL), and the combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-67** (5.38 g, 97% yield) as a colorless oil.

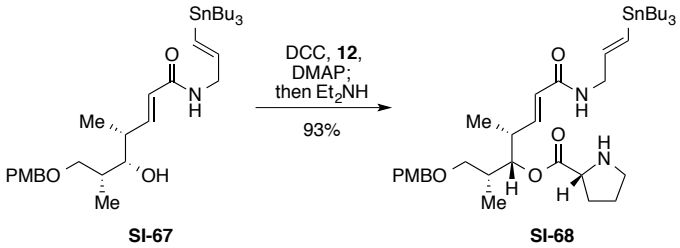
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.83 (dd, *J* = 15.5, 7.5 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.4 Hz, 1H), 5.97 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.79 (dd, *J* = 15.5, 1.3 Hz, 1H), 5.54 (br t, *J* = 5.9 Hz, 1H), 4.43 (s, 2H), 4.00 – 3.93 (m, 2H), 3.80 (s, 3H), 3.62 (dd, *J* = 9.2, 3.9 Hz, 1H), 3.50 – 3.40 (m, 3H), 2.49 – 2.37 (m, 1H), 1.95 – 1.85 (m, 1H), 1.54 – 1.41 (m, 6H), 1.37 – 1.24 (m, 6H), 1.08 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H), 0.91 – 0.77 (m, 15H)..

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6, 159.3, 147.5, 143.5, 130.3, 129.6, 129.4, 123.2, 113.8, 78.7, 74.4, 73.2, 55.3, 44.9, 39.7, 35.6, 29.0, 27.3, 14.4, 13.7, 13.1, 9.4.

HRMS-ESI m/z calcd for $C_{32}H_{56}NO_4Sn^+$ $[M + H]^+$ 638.3226, found 638.3219.

Amine SI-68



A 250-mL round-bottom flask was charged with Fmoc-D-Pro-OH (**12**, 1.34 g, 3.96 mmol, 1.5 equiv), alcohol **SI-67** (1.68 g, 2.64 mmol, 1 equiv) and DMAP (0.065 g, 0.53 mmol, 0.2 equiv). DCM (26 mL) was added, resulting in a colorless solution. DCC (0.87 g, 4.22 mmol, 1.6 equiv) was added in one portion, resulting in a white suspension. After 5 h, the alcohol **SI-67** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:3), and diethyl amine (13 mL) was added. After 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 30 mL). The combined filtrates were concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-68** (1.80 g, 93% yield) as a light-yellow oil.

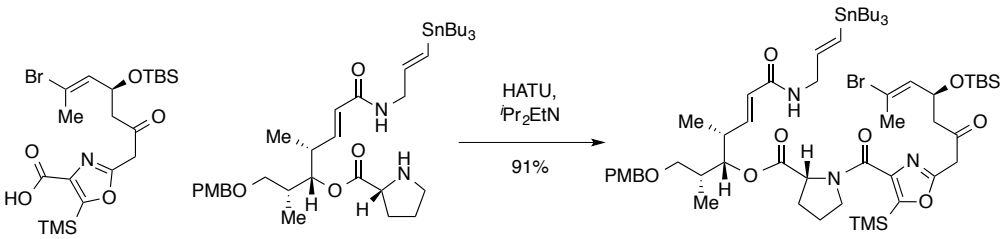
TLC (MeOH: DCM = 1:20): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.67 (dd, *J* = 15.5, 7.4 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.95 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.74 (dd, *J* = 15.5, 1.3 Hz, 1H), 5.54 (br t, *J* = 5.9 Hz, 1H), 4.97 (t, *J* = 6.2 Hz, 1H), 4.37 (s, 2H), 4.03 – 3.90 (m, 2H), 3.79 (s, 3H), 3.70 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.45 (dd, *J* = 9.2, 5.0 Hz, 1H), 3.21 (dd, *J* = 9.2, 6.4 Hz, 1H), 3.03 (ddd, *J* = 10.2, 7.5, 6.2 Hz, 1H), 2.87 (ddd, *J* = 10.2, 7.0, 6.2 Hz, 1H), 2.80 – 2.67 (m, 1H), 2.19 – 2.05 (m, 2H), 1.90 – 1.64 (m, 3H), 1.57 – 1.36 (m, 6H), 1.36 – 1.22 (m, 6H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 0.91 – 0.77 (m, 15H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 165.3, 159.1, 145.1, 143.4, 130.4, 130.3, 129.3, 124.2, 113.7, 77.7, 72.8, 71.3, 59.9, 55.2, 46.9, 44.9, 37.8, 35.4, 30.4, 29.0, 27.2, 25.4, 14.8, 13.9, 13.7, 9.4.

HRMS-ESI m/z calcd for $C_{37}H_{63}N_2O_5Sn^+$ $[M + H]^+$ 735.3753, found 735.3740.

Stille precursor SI-69



A 250-mL round-bottom flask was charged with amine **SI-68** (1.80 g, 2.45 mmol, 1 equiv), ^{i}Pr$_2$EtN (0.86 mL, 4.91mmol, 2.0 equiv) and acid **19** (1.36 g, 2.70 mmol, 1.1 equiv). DCM (45 mL) was added, resulting in a colorless solution, and HATU (1.17 g, 3.07 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (100 mL). The solution was transferred to a separatory funnel and was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-69** (2.72 g, 91% yield) as a light-yellow foam.

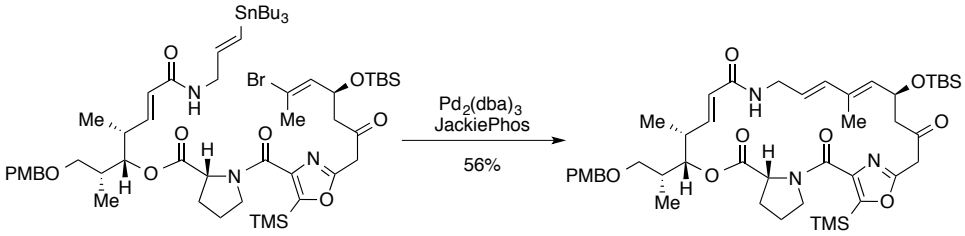
TLC (EtOAc:Hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 7.26 – 7.16 (m, 2H), 6.85 (dt, *J* = 8.9, 2.0 Hz, 2H), 6.70 – 6.52 (m, 1H), 6.18 – 6.00 (m, 1H), 6.03 – 5.90 (m, 1H), 5.84 – 5.70 (m, 2H), 5.68 – 5.50 (m, 2H), 4.97 – 4.83 (m, 1H), 4.82 – 4.65 (m, 1H), 4.59 (td, *J* = 8.6, 3.5 Hz, 1H), 4.40 (s, 1H), 4.31 (s, 1H), 4.15 – 3.85 (m, 5H), 3.85 – 3.59 (m, 5H), 3.31 – 3.10 (m, 1H), 2.89 – 2.32 (m, 3H), 2.32 – 2.25 (m, 3H), 2.24 – 1.70 (m, 2H), 1.60 – 1.37 (m, 6H), 1.29 (h, *J* = 6.7, 6.1 Hz, 6H), 1.01 (ddd, *J* = 6.9, 5.5, 2.3 Hz, 4H), 0.97 – 0.71 (m, 26H), 0.42 – 0.23 (m, 9H), 0.10 – 0.01 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.0, 200.7, 172.3, 172.0, 171.8, 165.4, 165.0, 164.6, 163.8, 163.3, 162.3, 161.5, 161.4, 159.20, 159.08, 159.05, 158.96, 145.2, 145.1, 145.03, 143.5, 143.3, 142.8, 135.0, 134.2, 134.2, 130.9, 130.8, 130.4, 130.3, 130.0, 129.3, 129.3, 129.2, 124.4, 124.3, 121.8, 121.7, 121.0, 113.7, 113.7, 113.6, 78.4, 77.7, 72.7, 72.6, 71.5, 70.9, 67.8, 67.0, 66.1, 60.5, 59.8, 55.2, 55.2, 49.6, 49.5, 48.8, 48.70 47.1, 44.9, 44.8, 44.18, 43.9, 38.1, 37.8, 35.7, 35.6, 31.6, 29.0, 27.2, 25.7, 25.6, 25.2, 24.0, 21.5, 17.9, 14.9, 14.8, 14.76, 14.0, 13.6, 9.4, –1.75, –1.78, –4.6, –5.15, –5.17.

HRMS-ESI m/z calcd for $C_{57}H_{95}BrN_3O_9Si_2Sn^+$ $[M + H]^+$ 1220.4807, found 1220.4827.

Stille coupling product SI-70



SI-69 **SI-70**

A 1000-mL round-bottom flask containing JackiePhos (0.36 g, 0.45 mmol, 0.2 equiv), $Pd_2(dba)_3$ (0.20 g, 0.22 mmol, 0.1 equiv) and Stille coupling precursor **SI-69** (2.72 g, 2.23 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (446 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 12 h, the mixture was allowed to cool to 23 ºC and was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille coupling product **SI-70** (1.0 g, 56% yield) as a light-yellow foam.

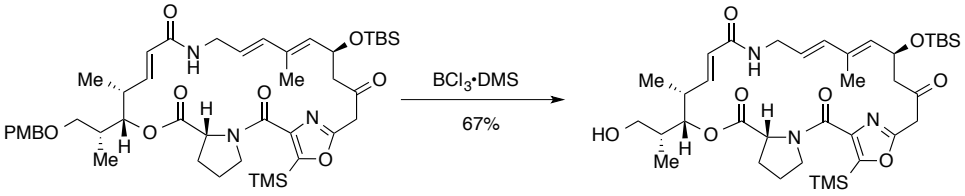
TLC (EtOAc:Hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.49 (dd, *J* = 16.4, 4.1 Hz, 1H), 6.14 (dd, *J* = 15.5, 1.3 Hz, 1H), 6.09 (dd, *J* = 9.0, 3.4 Hz, 1H), 5.77 (dd, *J* = 16.4, 2.1 Hz, 1H), 5.57 (ddd, *J* = 15.5, 9.5, 4.2 Hz, 1H), 5.43 (d, *J* = 8.8 Hz, 1H), 5.11 (dd, *J* = 10.5, 1.8 Hz, 1H), 5.02 (ddd, *J* = 9.0, 6.9, 5.8 Hz, 1H), 4.78 (dd, *J* = 8.8, 3.3 Hz, 1H), 4.56 – 4.36 (m, 3H), 3.89 (d, *J* = 17.1 Hz, 1H), 3.83 – 3.68 (m, 7H), 3.51 (dd, *J* = 9.1, 3.1 Hz, 1H), 3.39 (ddd, *J* = 14.9, 9.7, 3.5 Hz, 1H), 3.31 (dd, *J* = 9.1, 5.6 Hz, 1H), 2.94 (dd, *J* = 16.1, 7.0 Hz, 1H), 2.76 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.75 – 2.65 (m, 1H), 2.16 – 2.10 (m, 2H), 1.91 – 1.80 (m, 2H), 1.76 – 1.69 (m, 1H), 1.68 (d, *J* = 1.2 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 171.9, 166.5, 161.5, 161.5, 159.5, 158.9, 145.1, 144.5, 136.7, 134.8, 132.4, 130.9, 129.4, 124.9 123.8, 113.6, 76.2, 73.0, 71.6, 65.3, 58.8, 55.2, 50.8, 48.5, 43.5, 41.3, 36.4, 35.4, 28.3, 25.7, 24.9, 18.0, 13.9, 12.7, 9.6, –1.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{45}H_{67}N_3NaO_9Si_2^+$ $[M + Na]^+$ 872.4308, found 872.4348.

Primary alcohol 38[14]



SI-70 38

A 200-mL round-bottom charged with compound **SI-70** (0.57 g, 0.67 mmol, 1 equiv) was evacuated and reflushed with nitrogen (this process was repeated 3 times). DCM (67 mL) was added, resulting in a yellow solution. The mixture was cooled to 0 ºC by means of an ice/water bath, and a solution of BCl_3•DMS in DCM (2 M, 0.54 mL, 1.07 mmol, 1.6 equiv) was added dropwise. After 20 min, saturated aqueous $NaHCO_3$ solution (20 mL) was added. The resulting biphasic mixture was stirred for 1 h at 0 ºC and was transferred to a separatory funnel. The organic layer was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:3.5 to 1:2.5) to afford primary alcohol **38** (0.33 g, 67% yield) as a light-yellow solid.

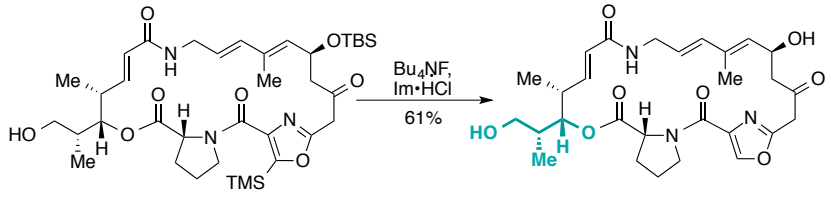
TLC (acetone:hexanes = 1:2.5): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (dd, *J* = 16.4, 4.4 Hz, 1H), 6.16 (d, *J* = 15.7 Hz, 1H), 6.05 (dd, *J* = 9.0, 2.8 Hz, 1H), 5.75 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.58 (ddd, *J* = 15.6, 9.0, 4.4 Hz, 1H), 5.43 (d, *J* = 8.8 Hz, 1H), 5.09 – 4.94 (m, 2H), 4.58 (dd, *J* = 8.4, 5.2 Hz, 1H), 4.50 (ddd, *J* = 14.1, 8.7, 4.2 Hz, 1H), 3.91 – 3.78 (m, 4H), 3.69 (d, *J* = 16.9 Hz, 1H), 3.52 (dd, *J* = 11.6, 3.2 Hz, 1H), 3.40 (ddd, *J* = 15.3, 9.0, 2.8 Hz, 1H), 2.93 (dd, *J* = 16.8, 6.2 Hz, 1H), 2.79 (dd, *J* = 16.9, 5.8 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.21 – 2.07 (m, 1H), 2.05 – 1.95 (m, 1H), 1.90 – 1.80 (m, 2H), 1.81 – 1.71 (m, 1H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.07 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.84 (s, 9H), 0.30 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 172.8, 166.9, 162.3, 161.8, 159.8, 144.6, 144.5, 136.8, 135.1, 132.0, 124.2, 123.6, 77.5, 65.0, 64.6, 59.5, 50.8, 49.1, 43.1, 41.1, 36.4, 36.2, 28.1, 25.7, 25.5, 18.0, 14.0, 12.7, 9.4, –1.9, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{37}H_{59}N_3NaO_8Si_2^+$ $[M + Na]^+$ 752.3733, found 752.3731.

Analogue 35



38 35

A 25-mL round-bottom flask containing compound **38** (36 mg, 49 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.0 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (0.010 g, 0.10 mmol, 2.0 equiv)that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.15 mL, 0.15 mmol, 3.0 equiv). The resulting colorless solution was added dropwise to the above solution of **38** at 0 ºC by means of an ice/water bath. After

[14] Congreve, M. S.; Davision, E. C.; Fuhry, M. A.; Holmes, A. B.; Payne, A. N.; Robinson, R. A.; Ward, S. E. *Synlett*, **1993**, 663–664.

1 h, the mixture was concentrated, and the residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **35** (0.016 g, 61% yield) as a light-yellow solid.

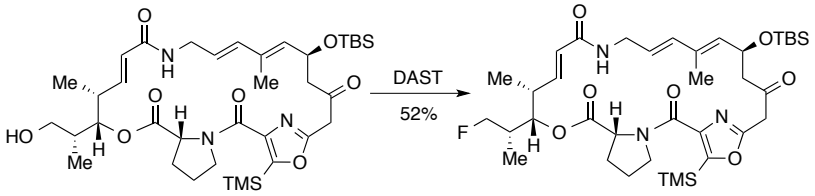
TLC (acetone:hexanes = 1:2.5): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 6.48 (dd, *J* = 16.4, 5.0 Hz, 1H), 6.40 – 6.30 (m, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 5.78 (dd, *J* = 16.4, 1.8 Hz, 1H), 5.69 (ddd, *J* = 14.7, 9.1, 4.8 Hz, 1H), 5.42 (d, *J* = 8.7 Hz, 1H), 5.03 (dd, *J* = 10.7, 1.8 Hz, 1H), 4.90 (dt, *J* = 9.1, 5.7 Hz, 1H), 4.60 (dd, *J* = 8.6, 4.3 Hz, 1H), 4.48 (ddd, *J* = 14.1, 8.9, 4.7 Hz, 1H), 4.02 (dt, *J* = 11.2, 6.8 Hz, 1H), 3.84 – 3.73 (m, 4H), 3.53 (dd, *J* = 11.4, 2.9 Hz, 1H), 3.37 (ddd, *J* = 14.8, 9.0, 3.1 Hz, 1H), 3.01 (dd, *J* = 17.3, 5.6 Hz, 1H), 2.89 (dd, *J* = 17.2, 5.4 Hz, 1H), 2.77 – 2.66 (m, 1H), 2.27 – 2.15 (m, 1H), 1.99 – 1.78 (m, 4H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 172.6, 166.9, 160.4, 157.1, 145.6, 144.3, 137.0, 136.8, 134.2, 132.7, 125.1, 124.1, 77.6, 65.1, 64.2, 60.0, 48.9, 48.7, 43.1, 40.8, 36.5, 36.2, 28.2, 25.5, 14.0, 12.7, 9.9.

HRMS-ESI m/z calcd for $C_{28}H_{38}N_3O_8^+$ $[M + H]^+$ 544.2653, found 544.2651.

Fluorinated product SI-71



A 25-mL round-bottom flask containing of alcohol **38** (25 mg, 34 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (3.4 mL) was added, resulting in a light-yellow solution. The vessel and its contents were cooled to 0 ºC by means of an ice/water bath, and DAST (12 μL, 89 μmol, 2.6 equiv) was added dropwise. The mixture was allowed to warm to 23 ºC. After 3 h, saturated aqueous $NaHCO_3$ solution (20 mL) and DCM (20 mL) were added. After stirring for 30 min, the biphasic solution was transferred to a separatory funnel, and the layers were separated. The organic layer was washed with water (2 × 25 mL) and brine (25 mL). The washed solution was dried (Na_2SO_4), and the dried solution was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:5) to afford fluorinated product **SI-71** (13 mg, 52% yield) as a white solid.

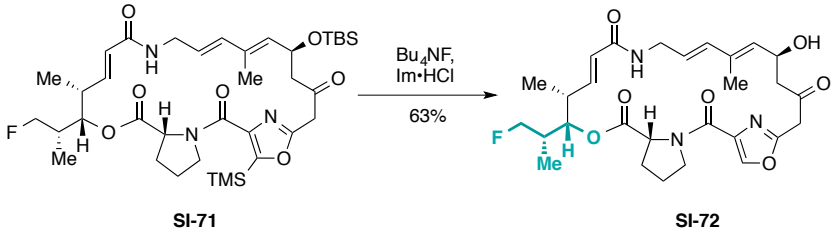
TLC (acetone:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.48 (dd, *J* = 16.4, 4.1 Hz, 1H), 6.14 (d, *J* = 15.7 Hz, 1H), 6.09 (dd, *J* = 8.8, 2.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.57 (ddd, *J* = 15.5, 9.3, 4.3 Hz, 1H), 5.42 (d, *J* = 8.9 Hz, 1H), 5.07 (dd, *J* = 10.5, 1.8 Hz, 1H), 5.01 (dt, *J* = 8.9, 6.4 Hz, 1H), 4.75 (dd, *J* = 8.9, 3.5 Hz, 1H), 4.57 – 4.41 (m, 2H), 4.38 (ddd, *J* = 47.5, 9.2, 5.2 Hz 1H), 3.88 (d, *J* = 17.1 Hz, 1H), 3.81 – 3.70 (m, 2H), 3.73 (d, *J* = 17.1 Hz, 1H), 3.39 (ddd, *J* = 14.9, 9.4, 3.2 Hz, 1H), 2.91 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.80 – 2.69 (m, 1H), 2.91 (dd, *J* = 16.0, 5.9 Hz, 1H), 2.20 – 2.05 (m, 2H), 1.90 – 1.80 (m, 3H), 1.67 (d, *J* = 1.2 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 9H), 0.31 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 172.1, 166.3, 161.8, 161.7, 159.7, 144.9, 144.0, 136.7, 134.9, 132.3, 124.7, 124.1, 85.05 (d, $^1J_{CF}$ = 169.7 Hz), 75.1 (d, $^3J_{CF}$ = 5.2 Hz), 65.3, 58.8, 50.6, 48.5, 43.6, 41.3, 36.3, 35.8 (d, $^2J_{CF}$ = 19.2 Hz), 28.2, 25.7, 25.0, 18.1, 12.9 (d, $^3J_{CF}$ = 4.7 Hz), 12.7, 9.7, –1.9, –4.50, –4.96.

HRMS-ESI m/z calcd for $C_{37}H_{59}FN_3O_7Si_2^+$ [M + H]$^+$ 732.3870, found 732.3905.

Analogue SI-72



A 25-mL round-bottom flask containing fluorinated compound **SI-71** (13 mg, 18 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.6 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (19 mg, 0.18 mmoL, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.18 mL, 0.18 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the above solution of **SI-71**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (30 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **SI-72** (6.1 mg, 63% yield) as a light-yellow solid.

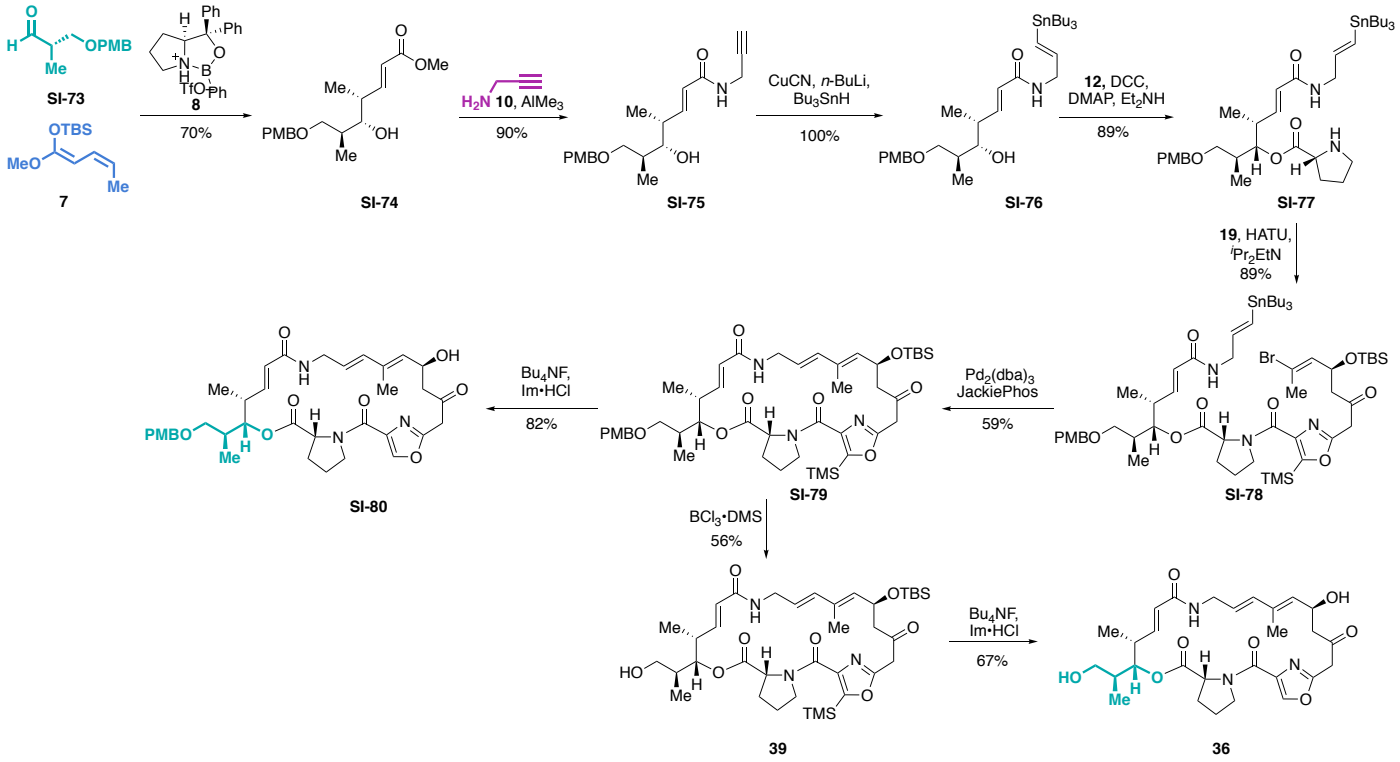
TLC (acetone:hexanes = 1:2): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.49 (dd, *J* = 16.4, 5.0 Hz, 1H), 6.48 – 6.40 (m, 1H), 6.13 (d, *J* = 15.7 Hz, 1H), 5.83 (d, *J* = 16.4 Hz, 1H), 5.72 (ddd, *J* = 14.8, 9.1, 4.6 Hz, 1H), 5.42 (d, *J* = 8.8 Hz, 1H), 5.03 (d, *J* = 10.4 Hz, 1H), 4.93 (dt, *J* = 9.6, 5.6 Hz, 1H), 4.69 (dd, *J* = 8.9, 3.2 Hz, 1H), 4.55 – 4.30 (m, 3H), 4.01 (dt, *J* = 11.5, 7.2 Hz, 1H), 3.84 (s, 2H), 3.81 – 3.71 (m, 1H), 3.41 (ddd, *J* = 13.8, 9.2, 3.7 Hz, 1H), 3.07 (dd, *J* = 17.0, 5.9 Hz, 1H), 3.03 – 2.95 (m, 1H), 2.90 (dd, *J* = 17.0, 5.1 Hz, 1H), 2.75 (br t, *J* = 6.6 Hz, 1H), 2.25 – 2.11 (m, 2H), 2.00 – 1.84 (m, 3H), 1.74 (s, 3H), 1.09 (d, *J* = 6.9 Hz, 6H).

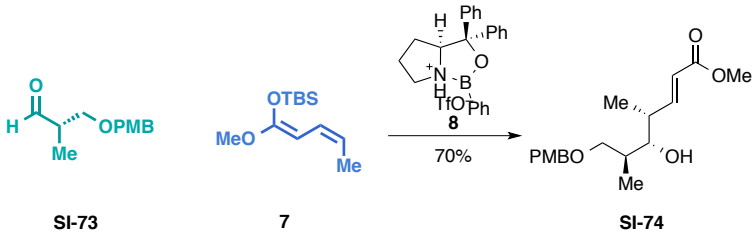
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3, 171.6, 166.5, 160.2, 156.8, 144.0, 143.6, 137.0, 134.4, 132.6, 125.3, 125.3, 124.6, 85.3 (d, $^1J_{CF}$ = 170.4 Hz), 76.1 (d, $^3J_{CF}$ = 4.8 Hz), 65.2, 59.6, 52.1, 48.8, 48.5, 43.3, 40.9, 36.4, 35.8 (d, $^2J_{CF}$ = 19.1 Hz), 29.7, 28.3, 25.13, 25.11, 20.2, 13.5, 13.0 (d, $^3J_{CF}$ = 5.2 Hz), 12.7, 10.1.

HRMS-ESI m/z calcd for $C_{28}H_{37}FN_3O_7^+$ [M + H]$^+$ 546.2610, found 546.2630.

Scheme XII Synthesis of 36 and SI-80



Mukaiyama aldol product SI-74



A 250-mL round-bottom flask was charged with phenylboronic acid (1.22 g, 9.99 mmol, 0.5 equiv) and (S)-diphenyl(pyrrolidin-2-yl)methanol (2.53 g, 9.99 mmol, 0.5 equiv). The vessel was equipped with a Dean-Stark apparatus and a reflux condenser, evacuated and flushed with nitrogen (the process of nitrogen exchange was repeated a total of 3 times). Toluene (50 mL) was added, and the resulting colorless solution was brought to reflux by means of a 145 ºC oil bath. After 12 h, the mixture was allowed to cool to 23 ºC and was concentrated. The resulting white solid was dried at ≤1 Torr for 1 h. The vessel was flushed with nitrogen, and DCM (80 mL) was added. The resulting colorless solution was cooled to -78 °C by means of a dry ice/acetone bath, and TfOH (0.79 mL, 8.99 mmol, 0.45 equiv) was added dropwise over 5 min by means of glass syringe (CAUTION: TfOH rapidly corrodes most plastic syringes!). Some of the TfOH froze upon contact with the solution. After 1 h, the solids had dissolved, and a solution of aldehyde **SI-73** (4.16 g, 20.0 mmol, 1 equiv), TBS ether **7** (5.70 g, 25.0 mmol 1.25 equiv) and 2-propanol (1.91 mL, 25.0 mmol, 1.25 equiv) in DCM (20 mL) was added dropwise over 2 h by means of syringe pump. The mixture was stirred at -78 °C for another 1.5 h, and saturated aqueous $NaHCO_3$ solution (50 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while it was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford aldol product **SI-74** (4.52 g, 70% yield, dr > 20:1) as a colorless oil.

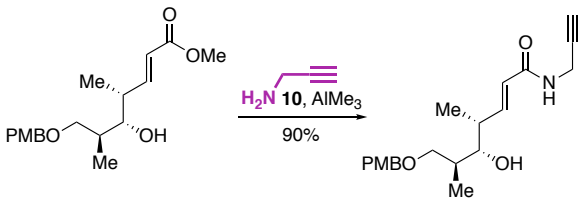
TLC (EtOAc:hexanes = 1:4): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.79 (dd, *J* = 15.7, 9.3 Hz, 1H), 5.85 (dd, *J* = 15.7, 0.7 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.41 (d, *J* = 11.6 Hz, 1H), 3.80 (s, 3H), 3.72 (s, 3H), 3.63 (dt, *J* = 9.0, 2.3 Hz, 1H), 3.52 (dd, *J* = 9.0, 3.9 Hz, 1H), 3.46 (dd, *J* = 9.0, 4.9 Hz, 1H), 2.85 (d, *J* = 2.9 Hz, 1H), 2.51 – 2.38 (m, 1H), 1.78 (dddd, *J* = 7.9, 7.0, 6.1, 2.6 Hz, 1H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 159.2, 151.1, 129.9, 129.2, 120.8, 113.8, 76.9, 75.2, 73.2, 55.3, 51.5, 40.8, 35.8, 16.7, 9.7.

HRMS-ESI m/z calcd for $C_{36}H_{52}NaO_{10}^+$ $[2M + Na]^+$ 667.3453, found 667.3456.

Amide SI-75



SI-74 **SI-75**

A 250-mL round-bottom flask was charged with propargylamine (**10**, 3.10 mL, 48.0 mmol, 4.0 equiv) and DCM (80 mL) under nitrogen. The resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (1 M, 48.0 mL, 48.0 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!). The mixture was allowed to warm to 23 ºC. After 30 min, a solution of **SI-74** (3.50 g, 12.0 mmol, 1 equiv) in DCM (20 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 3 h, **SI-74** was entirely consumed as indicated by TLC analysis, and the mixture was cooled to 0 °C by means of an ice/water bath. MeOH (10 mL) was added (CAUTION: Gas evolution!), followed by saturated aqueous potassium sodium tartrate solution (100 mL). After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-75** (3.22 g, 90% yield) as a white, waxy solid.

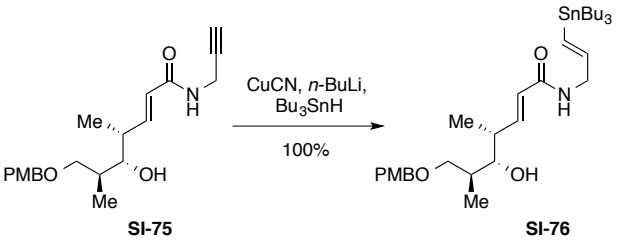
TLC (EtOAc:hexanes = 1:1): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.70 (dd, *J* = 15.3, 9.2 Hz, 1H), 5.92 (t, *J* = 5.2 Hz, 1H), 5.79 (dd, *J* = 15.3, 0.9 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 4.09 (dd, *J* = 5.3, 2.6 Hz, 2H), 3.79 (s, 3H), 3.61 (dt, *J* = 9.0, 2.2 Hz, 1H), 3.51 (dd, *J* = 9.0, 3.9 Hz, 1H), 3.45 (dd, *J* = 9.0, 4.8 Hz, 1H), 2.95 (d, *J* = 2.8 Hz, 1H), 2.47 – 2.34 (m, 1H), 2.23 (t, *J* = 2.6 Hz, 1H), 1.84 – 1.71 (m, 1H), 1.12 (d, *J* = 6.6 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.2, 147.4, 129.9, 129.2, 122.6, 113.8, 79.4, 76.94, 76.7, 75.2, 73.1, 71.6, 55.2, 40.5, 35.7, 29.1, 16.8, 9.8.

HRMS-ESI m/z calcd for $C_{20}H_{28}NO_4^+$ $[M + H]^+$ 346.2013, found 346.2012.

Vinyl stannane SI-76



A 500-mL round-bottom flask containing CuCN (1.92 g, 21.4 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (140 mL) was added, resulting in a white suspension. The vessel and its contents were allowed cool to -78 ºC by means of a dry ice/acetone bath, and a solution of *n*-BuLi in hexanes (2.5 M, 18 mL, 45.0 mmol, 4.2 equiv) was added dropwise over 10 min, resulting in a light-yellow solution. After 30 min, Bu_3SnH (12.1 mL, 45.0 mmol, 4.2 equiv) was added dropwise over 5 min. After 30 min, a solution of amide **SI-75** (3.70 g, 10.7 mmol, 1 equiv) in THF (10 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (100 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 100 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-76** (6.80 g, 100% yield, ≥20:1 E:Z) as a colorless oil.

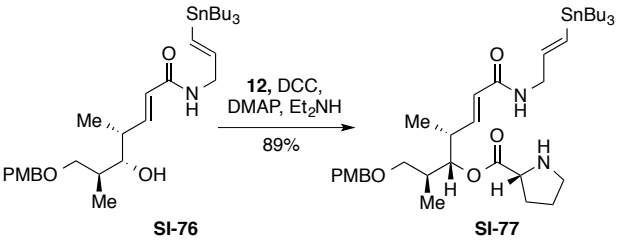
TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.69 (dd, *J* = 15.2, 9.2 Hz, 1H), 6.12 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.97 (dt, *J* = 19.0, 5.1 Hz, 1H), 5.81 (dd, *J* = 15.3, 0.8 Hz, 1H), 5.50 (t, *J* = 5.9 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 4.40 (d, *J* = 11.6 Hz, 1H), 4.04 – 3.92 (m, 2H), 3.80 (s, 3H), 3.63 (dt, *J* = 9.0, 2.4 Hz, 1H), 3.53 (dd, *J* = 9.0, 3.8 Hz, 1H), 3.46 (dd, *J* = 9.0, 4.6 Hz, 1H), 2.91 (d, *J* = 2.6 Hz, 1H), 2.50 – 2.35 (m, 1H), 1.88 – 1.76 (m, 1H), 1.54 – 1.41 (m, 6H), 1.30 (h, *J* = 7.3 Hz, 6H), 1.14 (d, *J* = 6.6 Hz, 3H), 0.95 (d, *J* = 7.1 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 15H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 159.2, 146.5, 143.4, 130.5, 130.0, 129.2, 123.4, 113.8, 77.2, 75.4, 73.2, 55.3, 44.9, 40.6, 35.66, 29.0, 27.2, 16.9, 13.7, 9.8, 9.4.

HRMS-ESI m/z calcd for $C_{32}H_{56}NO_4Sn^+$ $[M + H]^+$ 638.3226, found 638.3219.

Amine SI-77



A 500-mL round-bottom flask was charged with **12** (5.40 g, 16.0 mmol, 1.5 equiv), **SI-76** (6.80 g, 10.7 mmol, 1 equiv) and DMAP (0.26 g, 2.14 mmol, 0.2 equiv). DCM (160 mL) was added, resulting in a colorless solution. DCC (3.53 g, 17.1 mmol, 1.6 equiv) was added in one portion, resulting in a white suspension. After 5 h, the alcohol **SI-76** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:3), and diethyl amine (80 mL) was

added. After an additional 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed with DCM (2 × 30 mL). The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-77** (6.96 g, 89% yield) as a light-yellow oil.

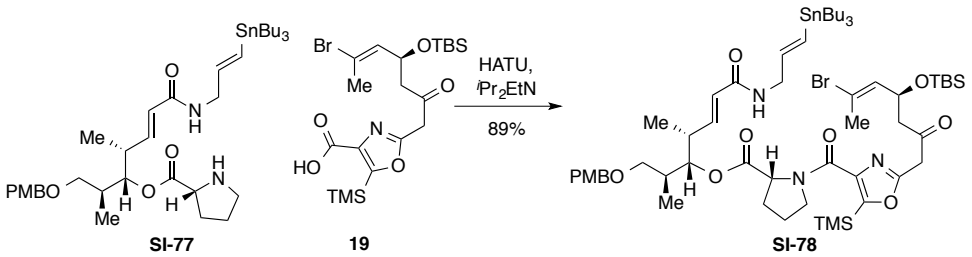
TLC (MeOH: DCM = 1:20): R_f = 0.20 (UV, $KMnO_4$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.68 (dd, *J* = 15.4, 8.2 Hz, 1H), 6.11 (dt, *J* = 19.0, 1.5 Hz, 1H), 5.95 (dt, *J* = 18.9, 5.1 Hz, 1H), 5.81 (dd, *J* = 15.5, 1.1 Hz, 1H), 5.55 (br s, 1H), 5.11 (dd, *J* = 8.1, 3.6 Hz, 1H), 4.38 (d, *J* = 11.5 Hz, 1H), 4.34 (d, *J* = 11.5 Hz, 1H), 4.00 – 3.90 (m, 2H), 3.79 (s, 3H), 3.72 (dd, *J* = 8.5, 5.6 Hz, 1H), 3.34 – 3.17 (m, 2H), 3.12 – 2.99 (m, 1H), 2.88 (ddd, *J* = 10.2, 7.1, 6.2 Hz, 1H), 2.73 – 2.59 (m, 1H), 2.18 – 1.95 (m, 4H), 1.93 – 1.75 (m, 1H), 1.75 – 1.61 (m, 1H), 1.57 – 1.38 (m, 6H), 1.38 – 1.24 (m, 6H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.96 – 0.81 (m, 18H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 165.1, 159.1, 144.7, 143.4, 130.4, 130.3, 129.3, 124.1, 113.7, 76.5, 72.9, 72.5, 59.9, 55.2, 46.9, 44.9, 38.5, 35.5, 30.4, 29.0, 27.2, 25.4, 15.8, 13.7, 11.2, 9.4.

HRMS-ESI m/z calcd for $C_{37}H_{63}N_2O_5Sn^+$ $[M + H]^+$ 735.3753, found 735.3740.

Stille coupling precursor SI-78



A 250-mL round-bottom flask was charged with amine **SI-77** (6.76 g, 9.21 mmol, 1 equiv), ^{i}Pr$_2$EtN (3.22 mL, 18.4 mmol, 2.0 equiv) and acid **19** (5.11 g, 10.1 mmol, 1.1 equiv). DCM (92 mL) was added, resulting in a colorless solution, and HATU (4.38 g, 11.5 mmol, 1.25 equiv) was added to this solution in one portion. After 5 h, the mixture was diluted with DCM (100 mL). The solution was transferred to a separatory funnel and was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-78** (10.0 g, 89% yield) as a light-yellow foam.

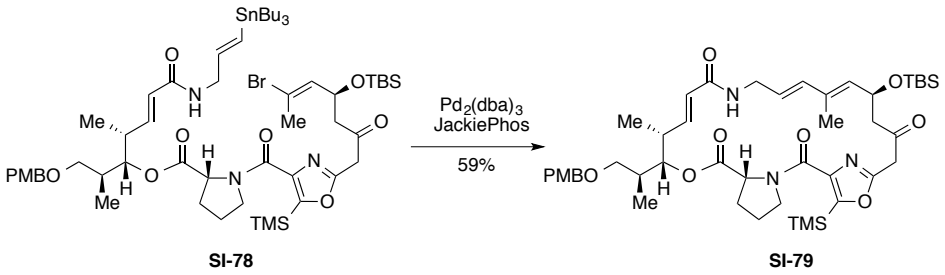
TLC (EtOAc:hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$, mixtures of rotamers) δ 7.26 – 7.15 (m, 2H), 6.91 – 6.78 (m, 2H), 6.63 (m, 1H), 6.10 (m, 1H), 6.01 – 5.91 (m, 1H), 5.85 – 5.68 (m, 2H), 5.68 – 5.53 (m, 1H), 5.05 (m, 1H), 4.82 – 4.71 (m, 1H), 4.64 (m, 1H), 4.45 – 4.22 (m, 2H), 4.11 – 3.64 (m, 9H), 3.33 (m, 1H), 3.17 (d, *J* = 6.6 Hz, 1H), 2.81 (m, 1H), 2.69 – 2.42 (m, 2H), 2.26 (m, 3H), 2.22 – 1.84 (m, 5H), 1.47 (m, 6H), 1.29 (m, 6H), 1.08 – 0.73 (m, 30H), 0.39 – 0.25 (m, 9H), 0.08 – 0 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$, mixtures of rotamers) δ 201.1, 200.6, 172.1, 171.9, 165.3, 165.1, 163.4, 162.3, 161.5, 161.4, 159.2, 159.1, 159.04, 159.00, 145.2, 145.1, 144.8, 144.6, 143.43, 143.35, 134.2, 130.7, 130.31, 130.3, 130.2, 129.3, 129.2, 124.19, 124.15, 121.8, 113.70, 113.65, 72.8, 72.7, 72.6, 72.3, 67.0, 66.8, 60.6, 59.8, 55.2, 49.6, 48.8, 47.1, 44.9, 44.2, 43.9, 38.7, 38.5, 35.8, 35.4, 31.6, 29.0, 27.2, 25.7, 25.7, 25.6, 25.2, 24.0, 21.5, 18.0, 15.7, 13.7, 11.4, 11.3, 9.4, –1.73, –1.77, –4.6, –5.14, –5.16.

HRMS-ESI m/z calcd for $C_{57}H_{95}BrN_3O_9Si_2Sn^+$ $[M + H]^+$ 1220.4807, found 1220.4827.

Stille coupling product SI-79



A round-bottom flask containing JackiePhos (0.54 g, 0.67 mmol, 0.2 equiv), $Pd_2(dba)_3$ (0.31 g, 0.34 mmol, 0.1 equiv) and Stille coupling precursor **SI-78** (4.10 g, 3.36 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (672 mL) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50 ºC oil bath. After 12 h, **SI-78** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and the mixture was allowed to cool to 23 ºC. The mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:3 to 1:1.5) to afford Stille coupling product **SI-79** (1.68 g, 59%) as a light-yellow foam.

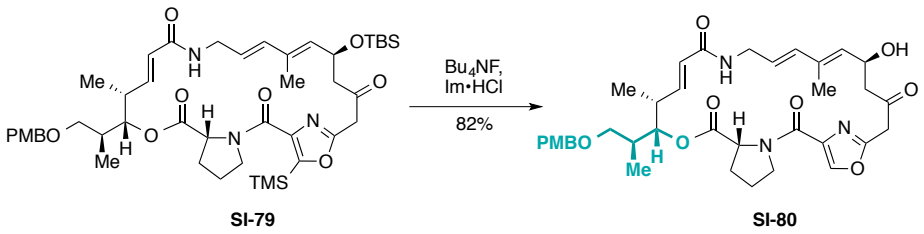
TLC (EtOAc:hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 7.21 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.47 (dd, *J* = 16.3, 4.1 Hz, 1H), 6.20 – 6.10 (m, 2H), 5.75 (dd, *J* = 16.3, 2.1 Hz, 1H), 5.56 (ddd, *J* = 15.5, 9.5, 4.2 Hz, 1H), 5.41 (d, *J* = 8.9 Hz, 1H), 5.08 (dd, *J* = 9.6, 1.8 Hz, 1H), 5.00 (ddd, *J* = 8.9, 7.1, 5.8 Hz, 1H), 4.80 (dd, *J* = 8.6, 3.3 Hz, 1H), 4.51 (ddd, *J* = 13.9, 9.0, 4.1 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 3.89 (d, *J* = 17.2 Hz, 1H), 3.80 (s, 3H), 3.74 (d, *J* = 17.2 Hz, 1H), 3.74 – 3.68 (m, 2H), 3.37 (qt, *J* = 9.4, 4.1 Hz, 3H), 2.91 (dd, *J* = 15.7, 7.2 Hz, 1H), 2.73 (dd, *J* = 15.7, 7.2 Hz, 1H), 2.80 – 2.69 (m, 1H), 2.17 – 2.03 (m, 2H), 1.91 – 1.78 (m, 2H), 1.78 – 1.67 (m, 1H), 1.65 (d, *J* = 1.2 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H), 1.04 (s, 3H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 172.0, 166.5, 161.8, 161.3, 159.6, 159.2, 145.0, 144.8, 136.6, 134.6, 132.5, 130.2, 129.1, 125.0, 123.5, 113.8, 78.1, 72.9, 71.9, 65.4, 58.7, 55.3, 50.6, 48.4, 43.8, 41.3, 37.2, 35.1, 28.3, 25.7, 24.8, 18.1, 14.9, 12.7, 10.6, –1.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{45}H_{67}N_3NaO_9Si_2^+$ $[M + Na]^+$ 872.4308, found 872.4348.

Analogue SI-80



A 25-mL round-bottom flask containing compound **SI-79** (30 mg, 38 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (4 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (40 mg, 0.38 mmol, 10.0 equiv) was added to a tetrabutylammonium fluoride solution in THF (1 M, 0.38 mL, 0.38 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-79**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (30 mL). The resulting solution was

transferred to a separatory funnel and was washed with water (5 × 30 mL) and brine (30 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **SI-80** (21 mg, 82% yield) as a light-yellow solid.

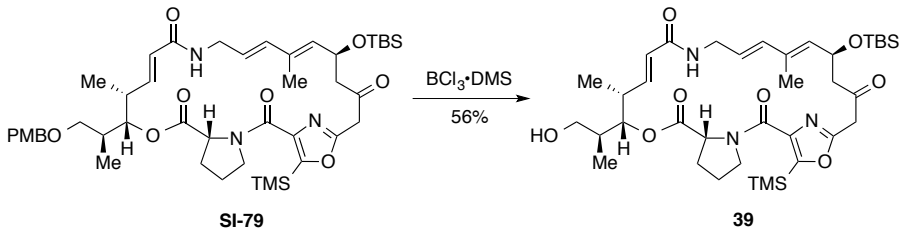
TLC (MeOH:DCM = 1:25): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.21 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.48 (dd, *J* = 16.3, 5.0 Hz, 1H), 6.41 (dd, *J* = 8.9, 3.6 Hz, 1H), 6.09 (d, *J* = 15.6 Hz, 1H), 5.76 (dd, *J* = 16.4, 1.8 Hz, 1H), 5.72 – 5.63 (m, 1H), 5.36 (d, *J* = 8.7 Hz, 1H), 5.01 (dd, *J* = 9.1, 2.0 Hz, 1H), 4.90 (dt, *J* = 8.9, 5.8 Hz, 1H), 4.69 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.52 – 4.32 (m, 3H), 3.97 (dt, *J* = 11.2, 7.6 Hz, 1H), 3.86 – 3.68 (m, 7H), 3.44 – 3.30 (m, 3H), 3.04 (dd, *J* = 16.8, 6.2 Hz, 1H), 2.87 (dd, *J* = 16.8, 5.1 Hz, 1H), 2.76 (ddd, *J* = 9.1, 4.6, 2.0 Hz, 1H), 2.22 – 2.04 (m, 2H), 1.91 (m, 2H), 1.81 (m, 1H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 171.6, 166.7, 160.3, 159.2, 156.8, 144.4, 143.9, 137.0, 136.7, 134.4, 132.4, 130.1, 129.1, 125.4, 124.1, 113.8, 78.5, 72.9, 71.9, 65.2, 59.6, 55.3, 48.7, 48.41, 43.4, 40.9, 37.2, 34.9, 28.4, 25.0, 14.7, 12.7, 11.1.

HRMS-EI m/z calcd for $C_{36}H_{46}N_3O_9^+$ $[M + H]^+$ 664.3229, found 664.3251.

Primary alcohol 39



A round-bottom flak containing compound **SI-79** (0.83 g, 0.98 mmol, 1 equiv) was evacuated and reflushed with nitrogen (this process was repeated 3 times). DCM (98 mL) was added, resulting in a yellow solution. The mixture was cooled down to 0 ºC. and a solution of BCl_3•DMS in DCM (2 M, 0.78 mL, 1.56 mmol, 1.6 equiv) was added dropwise. After 20 min, saturated aqueous $NaHCO_3$ (20 mL) was added. The resulting biphasic mixture was stirred at 0 ºC for 1 h and was transferred to a separatory funnel. The organic layer was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:3.5 to 1:2.5) to afford primary alcohol **39** (0.40 g, 56 % yield) as a light-yellow solid.

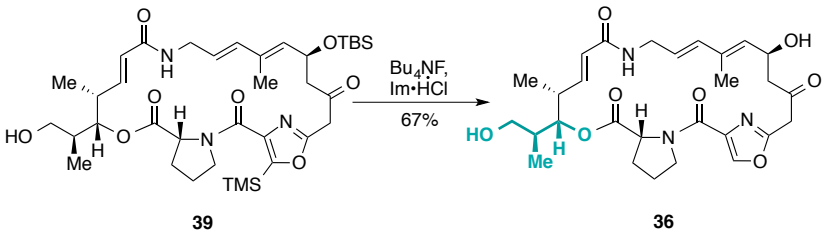
TLC (acetone:hexanes = 1:2.5): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.19 (dd, *J* = 8.9, 3.2 Hz, 1H), 6.14 (d, *J* = 15.7 Hz, 1H), 5.77 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.56 (ddd, *J* = 15.5, 9.3, 4.2 Hz, 1H), 5.41 (d, *J* = 8.9 Hz, 1H), 5.16 (dd, *J* = 8.6, 1.9 Hz, 1H), 4.99 (ddd, *J* = 8.9, 7.2, 5.8 Hz, 1H), 4.79 (dd, *J* = 8.6, 3.5 Hz, 1H), 4.49 (ddd, *J* = 13.6, 8.8, 4.2 Hz, 1H), 3.89 (d, *J* = 17.2 Hz, 1H), 3.74 (d, *J* = 17.2 Hz, 1H), 3.82 – 3.67 (m, 3H), 3.59 (d, *J* = 5.0 Hz, 2H), 3.39 (ddd, *J* = 14.8, 9.4, 3.2 Hz, 1H), 2.91 (dd, *J* = 15.7, 7.2 Hz, 1H), 2.83 (ddq, *J* = 6.6, 4.3, 2.3 Hz, 1H), 2.74 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.20 – 2.06 (m, 2H), 2.06 – 1.96 (m, 1H), 1.94 – 1.80 (m, 2H), 1.65 (d, *J* = 1.2 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 172.1, 166.4, 161.9, 161.3, 159.7, 144.94, 144.85, 136.6, 134.6, 132.5, 124.9, 123.6, 77.0, 65.4, 64.6, 58.8, 50.6, 48.5, 43.7, 41.3, 37.4, 37.0, 28.3, 25.7, 24.9, 18.1, 13.9, 12.7, 11.0, –1.8, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{37}H_{59}N_3NaO_8Si_2^+$ $[M + Na]^+$ 752.3733, found 752.3731.

Analogue 36



A 25-mL round-bottom flask containing compound **39** (36 mg, 49 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.0 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (10 mg, 0.10 mmol, 2.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.15 mL, 0.15 mmol, 3.0 equiv). The resulting colorless solution was added dropwise to the above solution of **39** at 0 ºC. After 1 h, the mixture was concentrated, and the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **36** (18 mg, 67% yield) as a light-yellow solid.

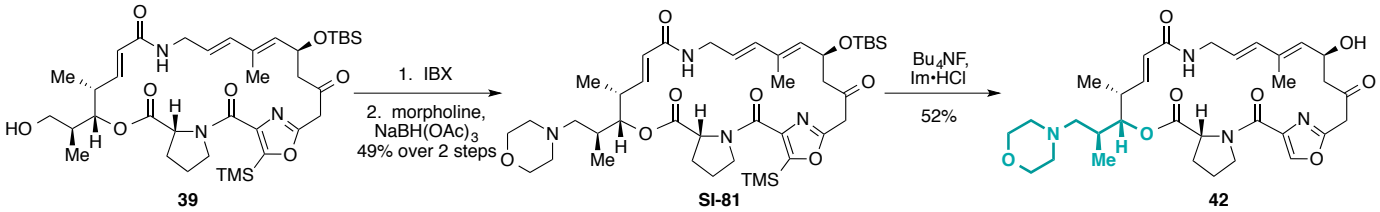
TLC (acetone:hexanes = 1:2.5): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 6.82 – 6.63 (m, 1H), 6.52 (dd, J = 16.3, 5.1 Hz, 1H), 6.08 (d, J = 15.7 Hz, 1H), 5.80 (dd, J = 16.3, 1.8 Hz, 1H), 5.75 – 5.62 (m, 1H), 5.34 (d, J = 8.6 Hz, 1H), 5.09 (d, J = 9.1 Hz, 1H), 4.90 (dt, J = 8.8, 5.8 Hz, 1H), 4.70 (dd, J = 8.8, 3.3 Hz, 1H), 4.48 – 4.32 (m, 1H), 4.01 – 3.88 (m, 1H), 3.88 – 3.72 (m, 3H), 3.64 – 3.50 (m, 2H), 3.41 (ddd, J = 15.0, 8.4, 3.7 Hz, 1H), 3.30 (br s, 2H), 3.00 (dd, J = 16.5, 6.2 Hz, 1H), 2.94 – 2.78 (m, 2H), 2.24 – 2.11 (m, 1H), 2.05 – 1.74 (m, 4H), 1.70 (s, 3H), 1.07 (d, J = 6.8 Hz, 3H), 0.99 (d, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.2, 171.7, 166.6, 160.4, 157.0, 144.6, 143.9, 136.9, 136.3, 134.4, 132.6, 125.3, 124.1, 77.8, 65.1, 64.4, 59.0, 48.7, 48.6, 43.4, 40.8, 37.3, 36.8, 28.5, 25.0, 13.8, 12.7, 11.4.

HRMS-ESI m/z calcd for $C_{28}H_{38}N_3O_8^+$ $[M + H]^+$ 544.2653, found 544.2651.

Scheme XIII Synthesis of 42



To a solution of alcohol **39** (30 mg, 41 μmol, 1 equiv) in EtOAc (2 mL) was added IBX (35 mg, 0.12 mmol, 3.0 equiv), and the resulting suspension was heated by means of an 80 ºC oil bath for 3 h. The mixture was allowed to cool to 23 ºC and was filtered through a pad of celite. The filter cake was washed with ethyl acetate (3 × 2 mL), and the combined filtrates were concentrated to yield a crude aldehyde which was used without further purification.

A 25-mL round-bottom flask containing $NaBH(OAc)_3$ (17 mg, 82 μmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCE (2 mL) and morpholine (7 μL, 82 μmol, 2.0 equiv) was

added, resulting in a light-yellow solution, and a solution of the above crude aldehyde in DCE (2 mL) was added. After 3 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added, followed by EtOAc (50 mL). The resulting biphasic mixture was transferred to separatory funnel, and the layers were separated. The organic layer was washed with water (2 × 20 mL) and brine (20 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:3) to afford **SI-81** (16 mg, 49%, 2 steps) as a light-yellow solid.

TLC (acetone:hexanes = 1:4): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.50 (dd, *J* = 16.3, 4.1 Hz, 1H), 6.20 – 6.05 (m, 2H), 5.77 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.56 (ddd, *J* = 14.8, 9.5, 4.1 Hz, 1H), 5.41 (d, *J* = 8.9 Hz, 1H), 5.05 – 4.95 (m, 2H), 4.80 (dd, *J* = 8.7, 3.3 Hz, 1H), 4.49 (ddd, *J* = 14.1, 9.0, 4.1 Hz, 1H), 3.88 (d, *J* = 17.2 Hz, 1H), 3.81 – 3.56 (m, 7H), 3.40 (ddd, *J* = 13.5, 9.7, 3.1 Hz, 1H), 2.91 (dd, *J* = 15.8, 5.8 Hz, 1H), 2.95 – 2.80 (m, 1H), 2.73 (dd, *J* = 15.7, 5.8 Hz, 1H), 2.52 – 2.29 (m, 6H), 2.29 – 1.75 (m, 5H), 1.65 (s, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 171.9, 166.4, 161.8, 161.3, 159.6, 145.0, 144.8, 136.7, 134.7, 132.5, 124.9, 123.6, 79.1, 67.0, 65.4, 62.6, 58.7, 54.1, 50.6, 48.4, 43.7, 41.3, 37.6, 31.7, 28.3, 25.7, 24.8, 18.1, 15.8, 12.7, 10.9, –1.9, –4.5, –5.0.

HRMS-ESI m/z calcd for $C_{41}H_{67}N_4O_8Si_2^+$ $[M + H]^+$ 799.4492, found 799.4499.

A 25-mL round-bottom flask containing **SI-81** (16 mg, 20 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.0 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (21 mg, 0.20 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.20 mL, 0.20 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the above solution of **SI-81**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (30 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 30 mL) and brine (30 mL). The washed solution was dried (Na_2SO_4), ans the dried solution was filtered. The filtrate was concentrated, the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **42** (6.4 mg, 52% yield) as a light-yellow solid.

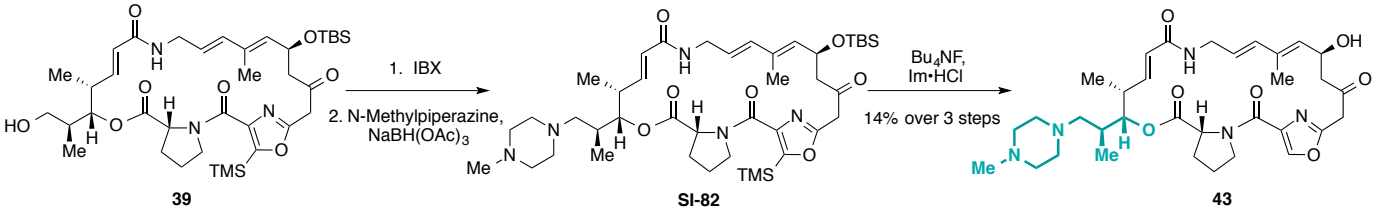
TLC (MeOH:DCM = 1:25): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 6.51 (dd, *J* = 16.3, 5.1 Hz, 1H), 6.45 (dd, *J* = 8.9, 3.7 Hz, 1H), 6.09 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.6, 8.8, 4.6 Hz, 1H), 5.34 (d, *J* = 8.8 Hz, 1H), 5.00 – 4.84 (m, 2H), 4.70 (dd, *J* = 8.9, 3.1 Hz, 1H), 4.45 (ddd, *J* = 14.0, 8.7, 4.6 Hz, 1H), 3.98 (dt, *J* = 11.3, 7.5 Hz, 1H), 3.84 (d, *J* = 15.5 Hz, 1H), 3.79 (d, *J* = 15.7 Hz, 1H), 3.77 – 3.60 (m, 5H), 3.40 (ddd, *J* = 14.9, 8.9, 3.6 Hz, 1H), 3.05 (dd, *J* = 16.7, 6.4 Hz, 1H), 3.01 – 2.90 (m, 1H), 2.87 (dd, *J* = 16.8, 5.0 Hz, 1H), 2.52 – 2.29 (m, 4H), 2.29 – 1.75 (m, 7H), 1.71 (d, *J* = 1.2 Hz, 3H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.5 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 171.6, 166.6, 160.3, 156.7, 144.3, 143.9, 137.0, 136.7, 134.5, 132.4, 125.4, 124.2, 79.6, 66.9, 65.3, 62.7, 59.7, 54.1, 48.7, 48.43, 43.5, 40.9, 37.5, 31.5, 28.5, 25.0, 15.7, 12.7, 11.4.

HRMS-ESI m/z calcd for $C_{32}H_{44}N_4NaO_8^+$ $[M + Na]^+$ 635.3051, found 635.3054.

Scheme XIV Synthesis of 43



To a solution of alcohol **39** (30 mg, 41 μmol, 1 equiv) in EtOAc (2 mL) was added IBX (35 mg, 0.12 mmol, 3.0 equiv), and the resulting suspension was heated by means of an 80 ºC oil bath for 3 h. The mixture was allowed to cool to 23 ºC and was filtered through a pad of celite. The filter cake was washed with ethyl acetate (3 × 2 mL), and the combined filtrates were concentrated to yield a crude aldehyde which was used for next step without further purification.

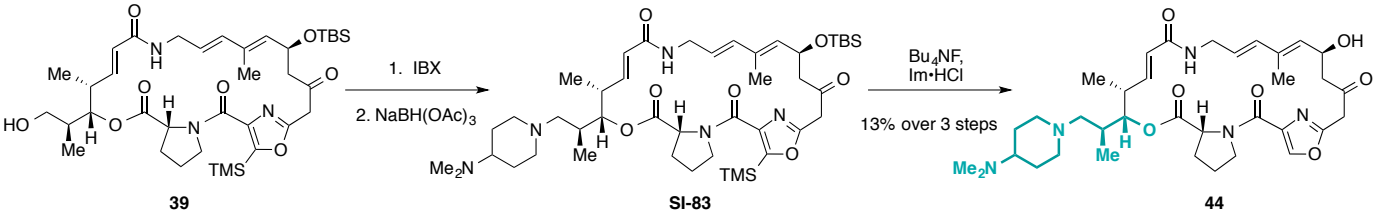
A 25-mL round-bottom flask containing $NaBH(OAc)_3$ (17 mg, 82 μmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCE (2 mL) and N-methylpiperazine (9 μL, 82 μmol, 2.0 equiv) was added, resulting in a light-yellow solution, and the above crude aldehyde solution in DCE (2 mL) was added. After 3 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added, followed by EtOAc (50 mL). The resulting biphasic mixture was transferred to separatory funnel, and the layers were separated. The organic layer was washed with water (2 × 20 mL) and brine (20 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:1) to afford **SI-82** (14 mg, 41% yield over 2 steps) as a white solid.

A 25-mL round-bottom flask containing **SI-82** (14 mg, 17 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (1.7 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (17 mg, 0.17 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.17 mL, 0.17 mmol, 10.0 equiv). The mixture was concentrated and the resulting crude residue was purified by preparative HPLC (eluent: H_2O:acetonitrile = 95:5 to 5:95 over 15 min) to afford analogue **43** (5 mg, 31% yield) as a white solid.

^{1}H NMR (300 MHz, MeOD) δ 8.29 (s, 1H), 6.76 (dd, *J* = 15.9, 4.7 Hz, 1H), 6.22 (d, *J* = 15.9 Hz, 1H), 5.89 (d, *J* = 15.7 Hz, 1H), 5.68 (dd, *J* = 14.8, 7.5 Hz, 1H), 5.43 (d, *J* = 9.3 Hz, 1H), 5.15 – 5.05 (m, 1H), 5.05 – 4.95 (m, 1H), 4.85- 4.75 (m, 2H), 4.05 – 3.80 (m, 5H), 3.78 – 3.65 (m, 1H), 3.60 – 3.40 (m, 1H), 3.24 – 2.68 (m, 14H), 2.50 – 2.25 (m, 4H), 2.25 – 2.00 (m, 4H), 1.95 – 1.85 (m, 1H), 1.78 (d, *J* = 1.7 Hz, 3H), 1.19 (d, *J* = 6.7 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H).

HRMS-ESI m/z calcd for $C_{35}H_{52}N_5O_7^+$ $[M + H]^+$ 654.3861, found 654.3867.

Scheme XV Synthesis of 44



To a solution of alcohol **39** (30 mg, 41 μmol, 1 equiv) in EtOAc (2 mL) was added IBX (35 mg, 0.12 mmol, 3.0 equiv), and the resulting suspension was heated by means of an 80 ºC oil bath for 3 h. The mixture was allowed to cool to 23 ºC and was filtered through a pad of celite. The filter cake was washed with ethyl acetate (3 × 2 mL), and

the combined filtrates were concentrated to yield a crude aldehyde which was used for next step without further purification.

A 25-mL round-bottom flask containing sodium $NaBH(OAc)_3$ (17 mg, 82 μmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCE (2 mL), $^{i}Pr_2EtN$ (29 μL, 0.16 mmol, 4.0 equiv) and 4-(dimethylammonio)piperidinium dichloride (33 μg, 0.16 mmol, 4.0 equiv) were added, resulting in a light-yellow solution. After 30 min, to this solution was added a solution of the above crude aldehyde in DCE (2 mL). After 3 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added, followed by EtOAc (50 mL). The resulting biphasic mixture was transferred to separatory funnel, and the layers were separated. The organic layer was washed with water (2 × 20 mL) and brine (20 mL). The organic layer was washed with water (2 × 20 mL) and brine (20 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:1) to afford **SI-83** (15 mg, 45% yield over 2 steps) as a white solid.

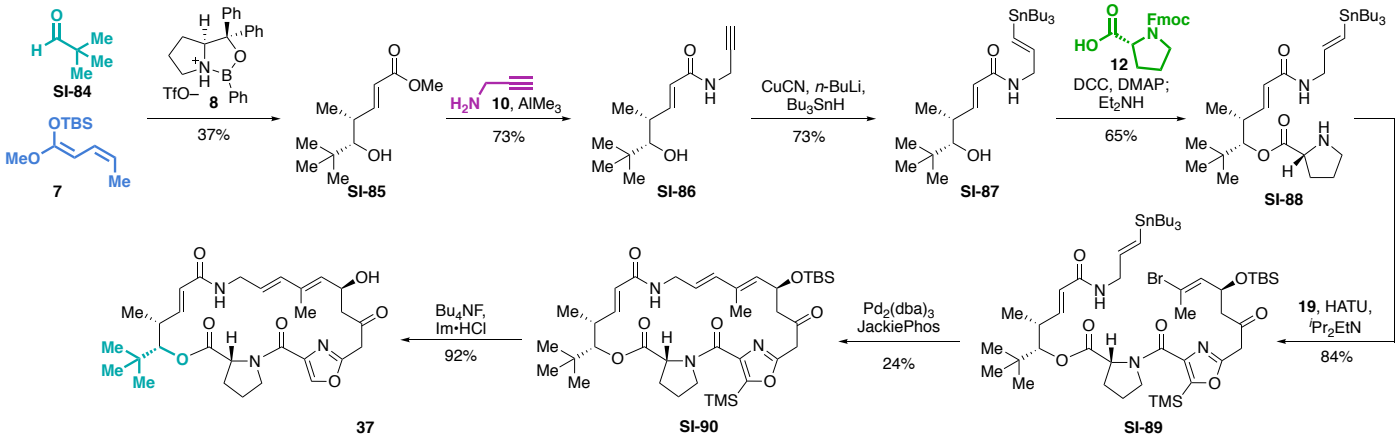
A 25-mL round-bottom flask containing **SI-83** (15 mg, 18 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (2.0 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (19 mg, 0.18 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.18 mL, 0.18 mmol, 10.0 equiv). The mixture was concentrated and the resulting crude residue was purified by preparative HPLC (eluent: H_2O:acetonitrile = 95:5 to 5:95 over 15 min) to afford analogue **44** (5 mg, 32% yield) as a light-yellow solid.

TLC (MeOH:DCM = 1:25): R_f = 0.30 (UV, *p*-anisaldehyde).

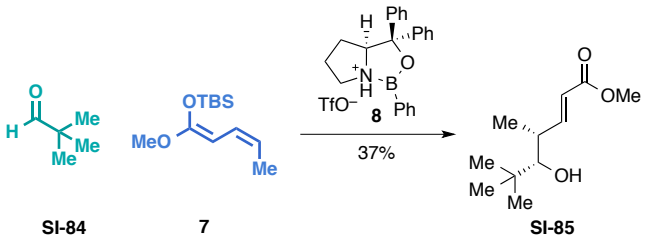
^{1}H NMR (300 MHz, MeOD) δ 8.28 (s, 1H), 6.79 (dd, *J* = 15.8, 4.7 Hz, 1H), 6.21 (d, *J* = 15.9 Hz, 1H), 5.86 (d, *J* = 16.2 Hz, 1H), 5.67 (d, *J* = 14.3 Hz, 1H), 5.41 (d, *J* = 9.1 Hz, 1H), 5.20 – 5.10 (m, 1H), 5.00 (d, *J* = 8.3 Hz, 1H), 4.85 – 4.75 m, 1H), 4.75 (d, *J* = 9.9 Hz, 1H), 4.00 (d, *J* = 16.8 Hz, 1H), 3.95 – 3.80 (m, 3H), 3.27 – 2.68 (m, 14H), 2.50 – 2.35 (m, 1H), 2.35 – 2.25 (m, 2H), 2.15 – 2.00 (s, 2H), 1.78 (s, 3H), 1.16 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H).

HRMS-ESI m/z calcd for $C_{33}H_{48}N_5O_7^+$ $[M + H]^+$ 626.3548, found 626.3552.

Scheme XVI Synthesis of 37

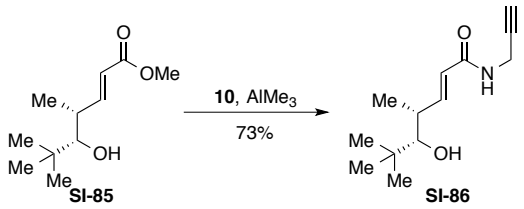


Mukaiyama aldol product SI-85



A 100-mL round-bottom flask was charged with phenylboronic acid (0.30 g, 2.50 mmol, 0.5 equiv) and (S)-diphenyl(pyrrolidin-2-yl)methanol (0.63 g, 2.50 mmol, 0.5 equiv). The vessel was equipped with a Dean-Stark apparatus and a reflux condenser, evacuated and flushed with nitrogen (the process of nitrogen exchange was repeated a total of 3 times). Toluene (25 mL) was added, and the resulting clear solution was brought to reflux by means of a 145 ºC oil bath. After 12 h, the mixture was allowed to cool to 23 ºC and was concentrated. The resulting white solid was dried at ≤1 Torr for 1 h. The vessel was flushed with nitrogen, and DCM (25 mL) was added. The resulting colorless solution was cooled to -78 °C by means of a dry ice-acetone, and TfOH (0.20 mL, 2.25 mmol, 0.45 equiv) was added dropwise over 5 min by means of glass syringe (CAUTION: TfOH rapidly corrodes most plastic syringes!). Some of the TfOH froze upon contact with the solution. After 1 h, the solids had dissolved, and a solution of aldehyde **SI-84** (0.43 g, 5.00 mmol, 1 equiv), TBS dienol ether **8** (1.43 g, 6.24 mmol 1.25 equiv) and isopropanol (0.48 mL, 6.24 mmol, 1.25 equiv) in DCM (10 mL) was added dropwise over 2 h by means of syringe pump. The mixture was stirred at -78 °C for another 1.5 h, and saturated aqueous $NaHCO_3$ solution (50 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while it was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 30 mL). The combined organic layers were dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Mukaiyama aldol product **SI-85** (0.37 g, 37% yield) as a colorless oil.

Amide SI-86

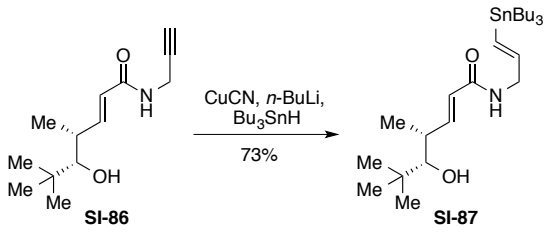


A 100-mL round-bottom flask was charged with propargylamine (**10**, 0.47 mL, 7.40 mmol, 4.0 equiv) and DCM (15 mL) under nitrogen. The resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of $AlMe_3$ in heptane (1 M, 7.40 mL, 7.40 mmol, 4.0 equiv) was added dropwise over 30 min (CAUTION: Gas evolution!), and then the mixture was allowed to warm to 23 ºC. After 30 min, a solution of **SI-85** (0.37 g, 1.85 mmol, 1 equiv) in DCM (5 mL) was added over 10 min (CAUTION: Gas evolution!). The vessel was equipped with a reflux condenser, and the solution was brought to reflux by means of a 50 ºC oil bath. After 3 h, the mixture was cooled to 0 °C by means of an ice/water bath, and MeOH (3 mL) was added (CAUTION: Gas evolution!), followed by saturated aqueous potassium sodium tartrate solution (50 mL). After 1 h, the biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:1) to afford amide **SI-86** (0.30 g, 73% yield) as a white, waxy solid.

TLC (EtOAc:hexanes = 1:1): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (dd, *J* = 15.4, 8.1 Hz, 1H), 5.75 (dd, *J* = 15.4, 1.1 Hz, 1H), 5.61 (s, 1H), 4.13 (dd, *J* = 5.4, 2.5 Hz, 2H), 3.29 (d, *J* = 4.2 Hz, 1H), 2.71 – 2.53 (m, 1H), 2.25 (t, *J* = 2.5 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.95 (s, 9H).

Vinyl stannane SI-87

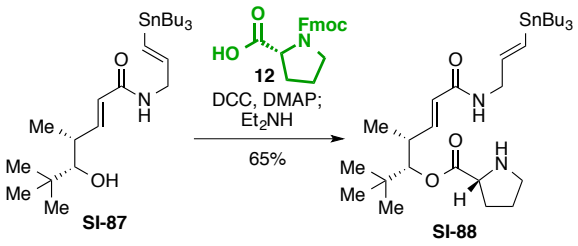


A 100-mL round-bottom flask containing CuCN (0.30 g, 1.35 mmol, 2.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Dry THF (14 mL) was added, resulting in a white suspension, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of *n*-BuLi in hexanes (2.5 M, 2.30 mL, 5.66 mmol, 4.2 equiv) was added dropwise over 10 min, resulting in a light-yellow solution. After 30 min, Bu_3SnH (1.53 mL, 5.66 mmol, 4.2 equiv) was added dropwise over 5 min. The resulting yellow solution was stirred at -78 ºC for 30 min, and a solution of amide **SI-86** (0.30 g, 1.35 mmol, 1 equiv) in THF (5 mL) was added dropwise over 15 min. After 1 h, saturated aqueous ammonium chloride solution (100 mL) was added in one portion. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 0:1 to 1:3) to afford vinyl stannane **SI-87** (0.50 g, 73% yield, ≥20:1 E:Z) **a**s a colorless oil.

TLC (EtOAc:hexanes = 1:2.5): R_f = 0.30 (UV, $KMnO_4$).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (dd, *J* = 15.7, 8.0 Hz, 1H), 6.12 (d, *J* = 19.1 Hz, 1H), 5.97 (dt, *J* = 18.6, 5.5 Hz, 1H),), 5.84 – 5.70 (m, 1H), 5.54 – 5.40 (m, 1H), 4.04 – 3.94 (m, 2H), 3.36 – 3.26 (m, 1H), 2.67 – 2.54 (m, 1H), 1.54 – 1.40 (m, 6H), 1.38 – 1.20 (m, 6H), 1.11 (d, *J* = 6.7 Hz, 3H), 0.95 (s, 9H), 1.00 – 0.80 (m, 15H).

Amine SI-88



A 100-mL round-bottom flask was charged with Fmoc-D-Pro-OH (**12,** 0.11 g, 0.32 mmol, 1.5 equiv), DMAP (5.2 mg, 0.042 mmol, 0.2 equiv) and **SI-87** (0.11 g, 0.21 mmol, 1 equiv). DCM (3 mL) was added, resulting in a colorless solution. DCC (0.071 g, 0.34 mmol, 1.6 equiv) was added in one portion. resulting in a white suspension. After 5 h, the alcohol **SI-87** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:2), and then diethyl amine (1.5 mL) was added. After 3 h, the mixture was filtered through a pad of celite, and the filter cake was washed

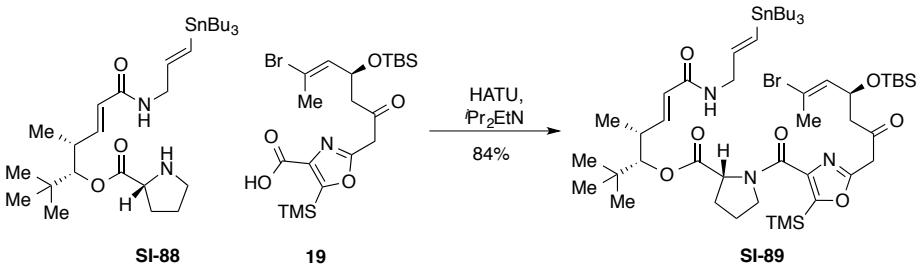
with DCM (2 × 5 mL). The combined filtrates were concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: NH_4OH:MeOH:DCM = 0.2:1:100 to 0.2:1:50) to afford amine **SI-88** (85 mg, 65% yield) as a light-yellow oil.

TLC (MeOH:DCM= 1:20): R_f = 0.20 (UV).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (dd, *J* = 15.4, 8.3 Hz, 1H), 6.10 (dt, *J* = 18.9, 1.4 Hz, 1H), 5.95 (dt, *J* = 19.0, 4.9 Hz, 1H), 5.78 (dd, *J* = 15.4, 1.0 Hz, 1H), 5.62 (t, *J* = 5.8 Hz, 1H), 4.75 (d, *J* = 5.7 Hz, 1H), 3.97 (t, *J* = 5.3 Hz, 2H), 3.77 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.07 (dt, *J* = 10.2, 6.8 Hz, 1H), 2.89 (dt, *J* = 10.3, 6.6 Hz, 1H), 2.78 – 2.62 (m, 1H), 2.22 (br s, 1H), 2.19 – 2.05 (m, 1H), 1.97 – 1.79 (m, 1H), 1.80 – 1.66 (m, 2H), 1.57 – 1.39 (m, 6H), 1.38 – 1.19 (m, 6H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.92 (s, 9H), 0.92 – 0.82 (m, 15H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.0, 165.4, 147.3, 143.4, 130.3, 122.7, 82.0, 59.9, 46.9, 44.9, 37.5, 35.7, 30.4, 29.0, 27.2, 26.6, 25.5, 16.5, 13.7, 9.4.

Stille coupling precursor SI-89



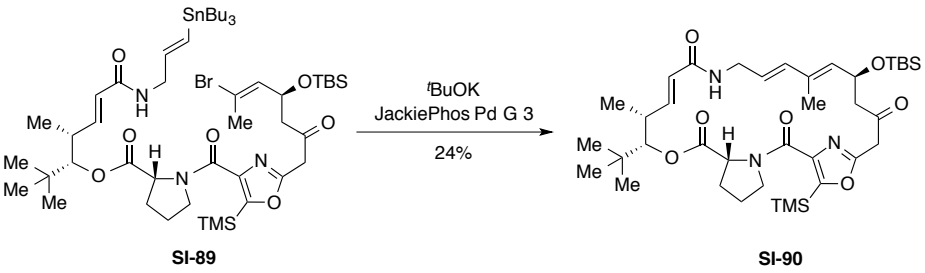
A 50-mL round-bottom flask was charged with amine **SI-88** (80 mg, 0.13 mmol, 1 equiv), ^{i}Pr$_2$EtN (46 μL, 0.26 mmol, 2.0 equiv) and acid **19** (73 mg, 0.14 mmol, 1.1 equiv). DCM (1.3 mL) was added, resulting in a clear, colorless solution, and HATU (62 mg, 0.16 mmol, 1.25 equiv) was added to this solution in one portion. After 5 h, the mixture was diluted with DCM (10 mL). The solution was transferred to a separatory funnel and was washed with water (2 × 10 mL) and brine (10 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-89**(0.12 g, 84% yield) as a light-yellow foam.

TLC (EtOAc:Hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (300 MHz, $CDCl_3$, mixtures of rotamers) δ 6.80 – 6.58 (m, 1H), 6.09 (d, *J* = 19.0 Hz, 1H), 5.93 (dt, *J* = 19.0, 5.0 Hz, 1H), 5.86 – 5.60 (m, 3H), 4.85 – 4.58 (m, 3H), 4.15 – 3.63 (m, 6H), 2.91 – 2.71 (m, 1H), 2.75 – 2.57 (m, 1H), 2.56 – 2.43 (m, 1H), 2.31 – 2.20 (m, 1H), 2.26 (s, 3H), 2.09 – 1.85 (m, 3H), 1.55 – 1.35 (m, 6H), 1.35 – 1.15 (m, 9H), 1.05 – 0.73 (m, 33H), 0.36 – 0.23 (m, 9H), 0.09 – -0.05 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$, mixtures of rotamers) δ 201.1, 200.8, 172.15, 172.06, 165.7, 165.3, 163.2, 162.5, 161.4, 159.11, 159.05, 147.3, 147.2, 145.2, 145.0, 143.45, 143.35, 134.2, 130.2, 123.0, 122.9, 122.6, 121.7, 82.3, 81.8, 67.0, 66.8, 60.4, 59.8, 49.6, 49.5, 48.7, 47.0, 44.8, 44.2, 43.9, 37.5, 37.4, 36.6, 35.73, 35.68, 29.0, 27.2, 26.77, 26.70, 25.6, 23.95, 23.93, 17.9, 16.2, 16.0, 13.6, 9.4, –1.3, –4.6, –5.18, –5.21.

Stille coupling product SI-90



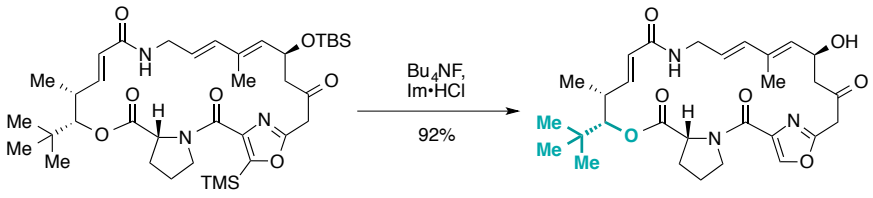
SI-89 **SI-90**

A 25-mL round-bottom flask containing JackiePhos Pd G3 (16 mg, 14 µmol, 0.3 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (8 mL) was added, and a stream of argon was passed through the solution by means of a stainless steel needle for 30 min. A solution of KOtBu in THF (1.6 M, 8.5 µL, 14 µmol, 0.3 equiv) was added, and the resulting orange mixture was heated by means of an 80 ºC oil bath for 5 minutes, during which time the mixture turned deep brown-red. In a scintillation vial, a stream of argon was passed through a solution of Stille coupling precursor **SI-89** (50 mg, 46 µmol, 1 equiv) in Toluene (2 mL) for 5 minutes. The resulting degassed solution was added dropwise over 1 min to the solution of catalyst, which was already stirring at 80 ºC. The mixture was stirred under a positive pressure of nitrogen for 40 h, after which time **SI-89** was completely consumed by TLC analysis (eluent: EtOAc:hexanes = 1:2, stain: anisaldehyde). The mixture was allowed to cool to 23 ºC and was concentrated. The resulting residue was purified by column chromatography (silica gel, eluent: EtOAc:hexanes = 1:2) to afford **SI-90** (8.0 mg, 24% yield) as a light-yellow oil.

TLC (EtOAc:Hexanes = 1:3): R_f = 0.20 (UV, *p*-Anisaldehyde).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.45 (dd, *J* = 16.3, 4.4 Hz, 1H), 6.14 (d, *J* = 15.7 Hz, 1H), 6.08 (s, 1H), 5.75 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.56 (ddd, *J* = 15.0, 9.6, 4.2 Hz, 1H), 5.41 (d, *J* = 8.8 Hz, 1H), 5.08 – 4.95 (m, 1H), 4.88 (d, *J* = 1.5 Hz, 1H), 4.84 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.50 (ddd, *J* = 13.8, 9.0, 4.2 Hz, 1H), 3.89 (d, *J* = 17.2 Hz, 1H), 3.82 – 3.69 (m, 3H), 3.38 (ddd, *J* = 13.9, 9.6, 3.0 Hz, 1H), 2.89 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.88 – 2.78 (m, 1H), 2.73 (dd, *J* = 16.0, 6.0 Hz, 1H), 2.20 – 2.10 (m, 1H), 2.17 (s, 3H), 1.95 – 1.85 (m, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.03 (s, 9H), 0.85 (s, 9H), 0.30 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H).

Analogue 37



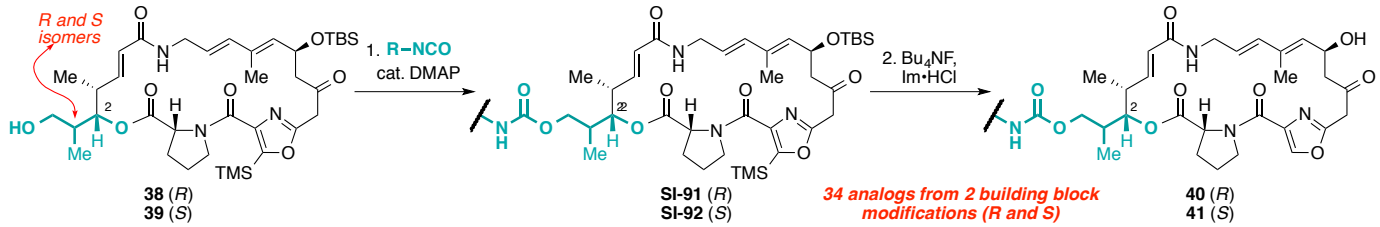
SI-90 **37**

A 10-mL round-bottom flask containing compound **SI-90** (8 mg, 11 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (0.5 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (23 mg, 0.22 mmol, 20.0 equiv) was added to a tetrabutylammonium fluoride solution in THF (1 M, 0.22 mL, 0.22 mmol, 20.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-90**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (30 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 30 mL) and brine (30 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **37** (5.5 mg, 92% yield) as a light-yellow solid.

TLC (MeOH:DCM = 1:25): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (s, 1H), 6.44 (dd, *J* = 16.3, 5.2 Hz, 1H), 6.19 (d, *J* = 7.0 Hz, 1H), 6.11 (d, *J* = 15.5 Hz, 1H), 5.85 – 5.71 (m, 1H), 5.71 – 5.60 (m, 1H), 5.44 (d, *J* = 8.7 Hz, 1H), 4.91 (dt, *J* = 9.1, 5.4 Hz, 1H), 4.81 (d, *J* = 1.5 Hz, 1H), 4.72 (dd, *J* = 8.6, 3.1 Hz, 1H), 4.45 (ddd, *J* = 13.9, 9.0, 4.6 Hz, 1H), 3.98 (dt, *J* = 11.3, 7.1 Hz, 1H), 3.82 (s, 3H), 3.48 (s, 1H), 3.37 (ddd, *J* = 13.8, 9.2, 3.4 Hz, 1H), 3.00 (dd, *J* = 17.4, 5.3 Hz, 1H), 2.92 – 2.75 (m, 2H), 2.63 (s, 1H), 2.28 – 2.12 (m, 1H), 1.91 (dtt, *J* = 12.2, 7.6, 4.3 Hz, 3H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 1.03 (s, 9H).

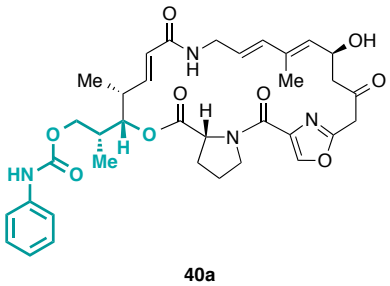
Scheme XVII General procedure D for preparation of carbamate analogues 40a–q and 41a–q



(1) A 50-mL round-bottom containing primary alcohol **38 or 39** (1 equiv) and DMAP (0.1 equiv) was evacuated and reflushed with nitrogen (this process was repeated 3 times). Toluene or DCM (0.01 M) was added, followed by aryl isocyanate or a solution of heteroaryl isocyanate in toluene (0.1 M, 2.0–10.0 equiv), resulting in a yellow solution. The mixture was stirred at 23 ºC or 80 ºC for 12 h. After cooling to 23 ºC (if necessary), the mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:5) to afford cabamate **SI-91** or **SI-92** as a white solid.

(2) A 50-mL round-bottom flask containing carbamate **SI-92** or **SI-92** (1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (0.01 M) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (15.0 equiv) was added to a solution of 1 M tetrabutylammonium fluoride in THF (15.0 equiv). The resulting colorless solution was added dropwise to the solution of **SI-91** or **SI-92**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:20) to afford carbamate analogues **40** or **41** as a white solid.

Analogue 40a



40a

Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and phenyl isocyanate (9 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **40a** (10 mg, 54% yield over 2 steps) was obtained as a white solid.

TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

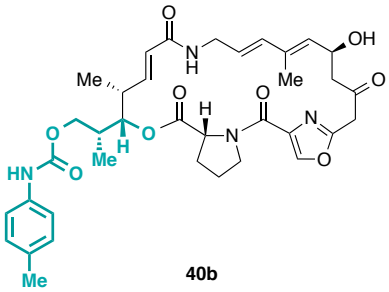
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (br s, 1H), 8.20 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.32 – 7.20 (m, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.54 (dd, *J* = 16.2, 4.2 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 6.00 (dd, *J* = 8.4, 4.3 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.69 (ddd, *J* = 15.6, 9.3, 4.4 Hz, 1H), 5.57 (d, *J* = 8.7 Hz, 1H), 5.17 (dd, *J* = 9.7, 1.9 Hz, 1H), 4.96 (dt, *J* = 9.0, 5.6 Hz, 1H), 4.77 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.58 (dd, *J* = 11.6, 3.7 Hz, 1H), 4.37 (ddd, *J* = 13.6, 8.3, 4.4 Hz, 1H), 4.00 – 3.80 (m, 2H), 3.84 (s, 2H), 3.75 (dd, *J* = 11.6, 9.5 Hz, 1H), 3.48 (ddd, *J* = 14.0, 9.3, 4.2 Hz, 1H), 3.13 (dd, *J* = 17.7, 4.9 Hz, 1H), 2.92 (dd, *J* = 17.7, 6.1 Hz, 1H), 2.78 (br s, 1H), 2.76 – 2.66 (m, 1H), 2.40 – 2.25

(m, 1H), 2.17 – 2.03 (m, 1H), 2.00 – 1.80 (m, 2H), 1.74 (d, J = 1.1 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H), 0.97 (d, J = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.8, 165.9, 160.2, 157.3, 153.7, 144.5, 139.1, 137.1, 136.7, 134.1, 132.9, 128.8, 125.1, 124.2, 122.7, 118.4, 79.2, 68.4, 64.9, 59.9, 49.2, 48.7, 42.6, 41.1, 37.1, 33.8, 28.5, 24.7, 13.5, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{35}H_{43}N_4O_9^+$ $[M + H]^+$ 663.3025, found 663.3021.

Analog 40b



40b

Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and 4-fluorodephenyl isocyanate (10 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analog **40b** (6.8 mg, 36% yield over 2 steps) was obtained as a white solid.

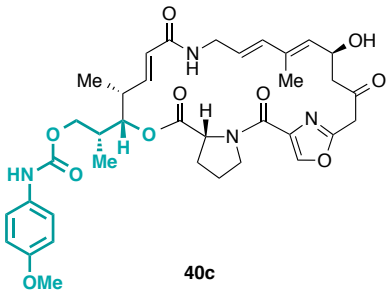
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (br s, 1H), 8.18 (s, 1H), 7.36 (d, J = 8.5 Hz, 2H), 7.05 (d, J = 8.2 Hz, 2H), 6.53 (dd, J = 16.2, 4.2 Hz, 1H), 6.17 (d, J = 15.6 Hz, 1H), 6.04 (d, J = 7.8 Hz, 1H), 5.79 (dd, J = 16.2, 2.0 Hz, 1H), 5.67 (ddd, J = 14.9, 9.3, 4.4 Hz, 1H), 5.55 (d, J = 8.7 Hz, 1H), 5.15 (dd, J = 9.7, 1.9 Hz, 1H), 4.95 (dt, J = 9.0, 5.6 Hz, 1H), 4.75 (dd, J = 8.7, 2.7 Hz, 1H), 4.54 (dd, J = 11.5, 3.8 Hz, 1H), 4.36 (ddd, J = 13.5, 8.2, 4.5 Hz, 1H), 4.01 – 3.84 (m, 2H), 3.83 (s, 2H), 3.74 (dd, J = 11.5, 9.3 Hz, 1H), 3.48 (ddd, J = 14.2, 9.3, 4.2 Hz, 1H), 3.12 (dd, J = 17.6, 5.0 Hz, 1H), 2.91 (dd, J = 17.6, 6.1 Hz, 1H), 2.83 (br s, 1H), 2.77 – 2.67 (m, 1H), 2.40 – 2.31 (m, 1H), 2.27 (s, 3H), 2.15 – 2.00 (m, 1H), 1.99 – 1.80 (m, 3H), 1.73 (d, J = 1.2 Hz, 3H), 1.10 (d, J = 6.8 Hz, 3H), 0.95 (d, J = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.8, 165.9, 160.2, 157.3, 153.8, 144.5, 144.5, 137.5, 136.7, 136.5, 134.10 132.9, 132.1, 129.3, 125.1, 124.2, 118.4, 79.1, 68.7, 64.9, 59.8, 49.3, 48.6, 42.67 41.1, 37.0, 33.8, 28.5, 24.7, 20.7, 13.3, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{36}H_{45}N_4O_9^+$ $[M + H]^+$ 677.3181, found 677.3190.

Analog 40c



40c

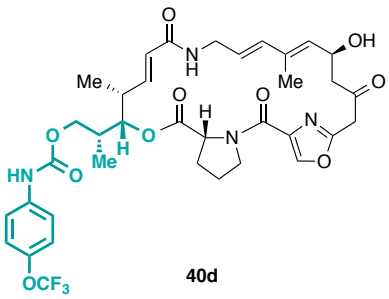
Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and 4-methoxyphenyl isocyanate (11 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **40c** (3.2 mg, 17% yield over 2 steps) was obtained as a white solid.

TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 8.17 (s, 1H), 7.39 (d, J = 9.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 2H), 6.54 (dd, J = 16.2, 4.2 Hz, 1H), 6.17 (d, J = 15.6 Hz, 1H), 6.12 – 5.98 (m, 1H), 5.79 (dd, J = 16.2, 2.0 Hz, 1H), 5.67 (ddd, J = 15.5, 9.3, 4.4 Hz, 1H), 5.55 (d, J = 8.7 Hz, 1H), 5.15 (dd, J = 9.6, 1.9 Hz, 1H), 4.95 (dt, J = 8.6, 5.6 Hz, 1H), 4.76 (dd, J = 8.8, 2.7 Hz, 1H), 4.54 (dd, J = 11.6, 3.7 Hz, 1H), 4.35 (ddd, J = 13.6, 8.3, 4.5 Hz, 1H), 3.98 – 3.84 (m, 2H), 3.82 (s, 2H), 3.76 (s, 3H), 3.80 – 3.68 (m, 1H), 3.49 (ddd, J = 14.2, 9.4, 4.2 Hz, 1H), 3.12 (dd, J = 17.6, 5.0 Hz, 1H), 2.91 (dd, J = 17.6, 6.1 Hz, 1H), 2.86 (br s, 1H), 2.72 (ddt, J = 6.7, 4.3, 2.2 Hz, 1H), 2.40 – 2.24 (m, 1H), 2.16 – 2.02 (m, 1H), 2.00 – 1.81 (m, 3H), 1.73 (s, 3H), 1.10 (d, J = 6.9 Hz, 3H), 0.95 (d, J = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.8, 165.9, 160.2, 157.4, 155.3, 154.0, 144.5, 144.4, 137.0, 136.7, 134.1, 132.9, 132.3, 125.1, 124.2, 112.0, 114.0, 79.1, 68.7, 64.9, 59.8, 55.5, 49.2, 48.6, 42.7, 41.1, 37.0, 33.8, 28.5, 24.7, 13.3, 12.7, 10.2.

Analogue 40d



40d

Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and 4-trifluoromethoxyphenyl isocyanate (12 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **40d** (11 mg, 52% yield over 2 steps) was obtained as a white solid.

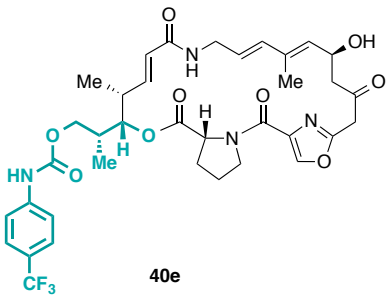
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (br s, 1H), 8.19 (s, 1H), 7.52 (d, *J* = 9.1 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.54 (dd, *J* = 16.2, 4.2 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 5.96 (dd, *J* = 8.2, 4.3 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.6, 9.3, 4.4 Hz, 1H), 5.57 (d, *J* = 8.6 Hz, 1H), 5.17 (dd, *J* = 9.6, 1.9 Hz, 1H), 4.96 (q, *J* = 7.0, 6.5 Hz, 1H), 4.74 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.61 (dd, *J* = 11.5, 3.5 Hz, 1H), 4.36 (ddd, *J* = 13.7, 8.3, 4.5 Hz, 1H), 4.02 – 3.85 (m, 2H), 3.84 (s, 2H), 3.72 (dd, *J* = 11.6, 9.8 Hz, 1H), 3.50 (ddd, *J* = 14.2, 9.2, 4.3 Hz, 1H), 3.13 (dd, *J* = 17.7, 4.9 Hz, 1H), 2.91 (dd, *J* = 17.7, 6.2 Hz, 1H), 2.82 – 2.62 (m, 2H), 2.40 – 2.25 (m, 1H), 2.16 – 2.04 (m, 1H), 2.02 – 1.81 (m, 3H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.6, 165.8, 160.3, 157.5, 153.7, 151.2, 144.5, 144.5, 137.9, 137.0, 136.7, 134.1, 132.9, 125.1, 124.2, 121.6, 119.3, 79.3, 69.1, 64.9, 59.9, 49.2, 48.7, 42.6, 41.1, 37.1, 33.8, 28.5, 24.7, 13.2, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{36}H_{42}F_3N_4O_{10}^+$ $[M + H]^+$ 747.2848, found 747.2838.

Analogue 40e



40e

Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and 4-trifluoromethylphenyl isocyanate (12 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **40e** (12 mg, 59% yield over 2 steps) was obtained as a white solid.

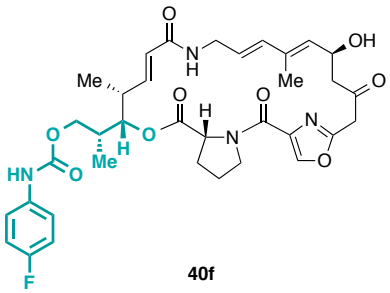
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.40 (s, 1H), 8.20 (s, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 6.54 (dd, *J* = 16.2, 4.2 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 5.98 (dd, *J* = 8.3, 4.4 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.6, 9.3, 4.4 Hz, 1H), 5.57 (d, *J* = 8.6 Hz, 1H), 5.18 (dd, *J* = 9.6, 2.0 Hz, 1H), 4.96 (dt, *J* = 9.3, 5.6 Hz, 1H), 4.73 (dd, *J* = 8.7, 2.6 Hz, 1H), 4.62 (dd, *J* = 11.6, 3.6 Hz, 1H), 4.35 (ddd, *J* = 13.7, 8.2, 4.5 Hz, 1H), 3.98 – 3.86 (m, 2H), 3.84 (s, 2H), 3.73 (dd, *J* = 11.6, 9.8 Hz, 1H), 3.50 (ddd, *J* = 14.2, 9.3, 4.3 Hz, 1H), 3.13 (dd, *J* = 17.7, 4.9 Hz, 1H), 2.92 (dd, *J* = 17.7, 6.1 Hz, 1H), 2.80 (br s, 1H), 2.80 – 2.65 (m, 1H), 2.40 – 2.25 (m, 1H), 2.18 – 2.05 (m, 1H), 2.00 – 1.80 (m, 3H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.6, 165.7, 160.3, 157.5, 153.5, 144.6, 144.4, 142.3, 137.0, 136.7, 134.1, 133.0, 126.0 (q, ^3J = 4.2 Hz), 125.1, 124.2, 117.9, 79.3, 69.2, 64.9, 59.9, 49.2, 48.7, 42.6, 41.1, 37.1, 33.7, 28.5, 24.7, 13.2, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{36}H_{41}F_3N_4NaO^+$ $[M + Na]^+$ 753.2718, found 753.2717.

Analogue 40f



40f

Prepared according to general procedure D from primary alcohol **38** (20 mg, 27 µmol, 1 equiv), DMAP (0.3 mg, 3 µmol, 0.1 equiv) and 4-fluorodephenyl isocyanate (9 µL, 82 µmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **40f** (7.3 mg, 39% yield over 2 steps) was obtained as a white solid.

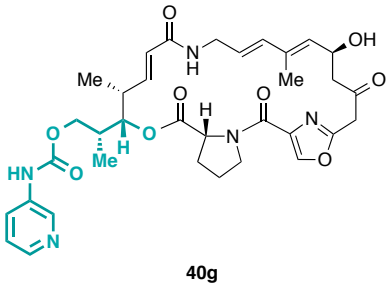
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (br s, 1H), 8.19 (s, 1H), 7.50 – 7.41 (m, 2H), 6.94 (t, *J* = 8.7 Hz, 2H), 6.53 (dd, *J* = 16.2, 4.2 Hz, 1H), 6.17 (d, *J* = 15.6 Hz, 1H), 5.99 – 5.91 (m, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.69 (ddd, *J* = 15.7, 9.3, 4.5 Hz, 1H), 5.56 (d, *J* = 8.8 Hz, 1H), 5.16 (dd, *J* = 9.6, 1.9 Hz, 1H), 5.03 – 4.90 (m, 1H), 4.75 (dd, *J* = 8.7, 2.6 Hz, 1H), 4.58 (dd, *J* = 11.6, 3.7 Hz, 1H), 4.36 (td, *J* = 8.6, 8.2, 4.0 Hz, 1H), 3.98 – 3.85 (m, 2H), 3.84 (s, 2H), 3.76 – 3.68 (m, 1H), 3.48 (ddd, *J* = 14.1, 9.3, 4.2 Hz, 1H), 3.12 (dd, *J* = 17.7, 4.9 Hz, 1H), 2.91 (dd, *J* = 17.7, 6.1 Hz, 1H), 2.80 -2.60 (m, 2H), 2.40 – 2.25 (m, 1H), 2.20 – 2.03 (m, 2H), 2.00 -1.80 (m, 2H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 170.7, 165.8, 160.3, 157.5, 153.8, 144.6, 144.4, 137.0, 136.7, 135.1, 134.1, 133.0, 125.1, 124.2, 119.9 (d, $^3J_{CF}$ = 7.7 Hz), 115.3 (d, $^2J_{CF}$ = 22.3 Hz), 79.2, 68.9, 64.8, 59.8, 49.2, 48.7, 42.6, 41.1, 37.0, 33.8, 28.5, 24.7, 13.2, 12.7, 10.3.

HRMS-ESI m/z calcd for $C_{35}H_{42}FN_4O_9^+$ $[M + H]^+$ 681.2930, found 681.2935.

Analogue 40g



40g

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanatopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40g** (12 mg, 53% yield over 2 steps) was obtained as a white solid.

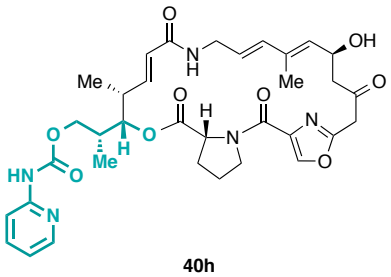
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.38 (br s, 1H), 8.54 (d, *J* = 2.6 Hz, 1H), 8.22 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.20 (s, 1H), 8.11 (ddd, *J* = 8.4, 2.6, 1.5 Hz, 1H), 7.21 (dd, *J* = 8.4, 4.7 Hz, 1H), 6.54 (dd, *J* = 16.2, 4.1 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 6.06 (dd, *J* = 8.3, 4.4 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.67 (ddd, *J* = 15.6, 9.2, 4.4 Hz, 1H), 5.57 (d, *J* = 8.7 Hz, 1H), 5.17 (dd, *J* = 9.5, 1.9 Hz, 1H), 4.95 (dt, *J* = 8.7, 5.6 Hz, 1H), 4.74 (dd, *J* = 8.7, 2.7 Hz, 1H), 4.61 (dd, *J* = 11.6, 3.7 Hz, 1H), 4.34 (ddd, *J* = 13.6, 8.2, 4.4 Hz, 1H), 3.90 (dd, *J* = 8.5, 5.6 Hz, 2H), 3.83 (d, *J* = 1.5 Hz, 2H), 3.74 (dd, *J* = 11.6, 9.7 Hz, 1H), 3.50 (td, *J* = 9.6, 4.6 Hz, 1H), 3.12 (dd, *J* = 17.5, 5.1 Hz, 1H), 2.93 (dd, *J* = 17.5, 6.0 Hz, 1H), 2.80 – 2.65 (m, 1H), 2.40 – 2.25 (m, 1H), 2.20 – 2.00 (m, 1H), 2.00 – 1.80 m, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 170.6, 165.8, 160.4, 157.5, 153.8, 144.5, 144.5, 143.6, 140.3, 136.9, 136.6, 136.1, 134.0, 133.1 125.3, 125.0, 124.2, 123.5, 79.2, 69.2, 64.8, 59.8, 49.2, 48.8, 42.6, 41.1, 37.0, 33.7, 28.5, 24.7, 13.3, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{34}H_{42}N_5O_9^+$ $[M + H]^+$ 664.2977, found 664.2988.

Analogue 40h



40h

Prepared according to general procedure D from primary alcohol **38** (21 mg, 29 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 2-isocyanatopyridine in toluene (0.1 M, 0.86 mL, 0.086 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40h** (10 mg, 57% yield over 2 steps) was obtained as a white solid.

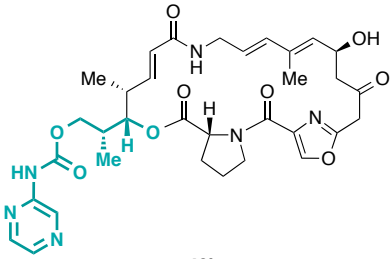
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.34 (s, 1H), 8.23 (dd, *J* = 5.1, 1.8 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.64 (td, *J* = 8.0, 2.0 Hz, 1H), 6.94 (dd, *J* = 7.3, 5.0 Hz, 1H), 6.49 (dd, *J* = 16.3, 4.6 Hz, 1H), 6.18 (dd, *J* = 8.7, 3.7 Hz, 1H), 6.13 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.9 Hz, 1H), 5.67 (ddd, *J* = 15.0, 9.3, 4.4 Hz, 1H), 5.49 (d, *J* = 8.7 Hz, 1H), 5.07 (dd, *J* = 10.0, 1.8 Hz, 1H), 4.91 (dt, *J* = 9.3, 5.5 Hz, 1H), 4.74 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.42 (ddd, *J* = 13.9, 8.7, 4.5 Hz, 1H), 4.27 (dd, *J* = 11.2, 4.6 Hz, 1H), 4.15 (dd, *J* = 11.2, 5.7 Hz, 1H), 3.97 (dt, *J* = 11.4, 7.3 Hz, 1H), 3.85 – 3.75 (m, 1H), 3.83 (d, *J* = 16.1 Hz, 1H), 3.78 (d, *J* = 16.2 Hz, 1H), 3.40 (ddd, *J* = 13.8, 9.3, 3.7 Hz, 1H), 3.05 (dd, *J* = 17.6, 5.2 Hz, 1H), 2.91 (dd, *J* = 17.5, 5.8 Hz, 1H), 2.73 (ddd, *J* = 9.1, 4.6, 2.2 Hz, 1H), 2.37 – 2.21 (m, 1H), 2.21 – 2.04 (m, 1H), 1.90 (qq, *J* = 7.4, 3.2 Hz, 2H), 1.84 – 1.70 (m, 1H), 1.72 (s, 3H), 1.08 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.5, 166.4, 160.2, 157.0, 153.7, 152.1, 147.8, 145.1, 144.1, 138.0, 137.0, 136.3, 134.0, 132.9, 125.1, 124.2, 118.5, 112.6, 77.8, 67.8, 65.0, 59.8, 48.9, 48.5, 42.8, 41.0, 36.7, 34.1, 28.2, 25.0, 14.1, 12.7, 10.0.

HRMS-ESI m/z calcd for $C_{34}H_{42}N_5O_9^+$ $[M + H]^+$ 664.2977, found 664.2988.

Analogue 40i



40i

Prepared according to general procedure D from primary alcohol **38** (21 mg, 29 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 2-isocyanatopyrazine in toluene (0.1 M 0.86 mL, 0.086 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40i** (10 mg, 43% yield over 2 steps) was obtained as a white solid.

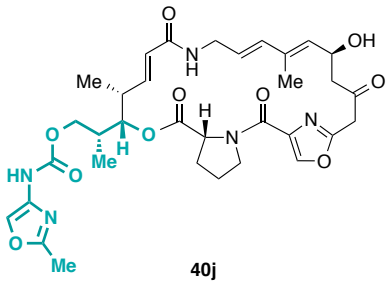
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41 (br s, 1H), 9.28 (d, *J* = 1.5 Hz, 1H), 8.36 (s, 1H), 8.23 (d, *J* = 2.7 Hz, 1H), 8.19 (dd, *J* = 2.6, 1.5 Hz, 1H), 6.50 (dd, *J* = 16.3, 4.5 Hz, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 6.05 (dd, *J* = 9.0, 3.8 Hz, 1H), 5.80 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.6, 9.2, 4.5 Hz, 1H), 5.53 (d, *J* = 8.6 Hz, 1H), 5.11 (dd, *J* = 9.9, 1.9 Hz, 1H), 4.93 (q, *J* = 6.2 Hz, 1H), 4.74 (dd, *J* = 8.9, 3.0 Hz, 1H), 4.50 – 4.35 (m, 2H), 4.09 (dd, *J* = 11.3, 6.9 Hz, 1H), 3.98 (dd, *J* = 11.5, 7.3 Hz, 1H), 3.90 – 3.75 (m, 3H), 3.42 (ddd, *J* = 14.0, 9.3, 3.8 Hz, 1H), 3.07 (dd, *J* = 17.6, 5.0 Hz, 1H), 2.92 (dd, *J* = 17.7, 5.8 Hz, 1H), 2.86 (br s, 1H), 2.78 – 2.68 (m, 1H), 2.40 – 2.25 (m 1H), 2.20 – 2.07 (m, 1H), 1.97 – 1.85 (m, 2H), 1.84 – 1.74 (m, 1H), 1.73 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 171.3, 166.2, 160.3, 157.2, 153.4, 149.0, 145.1, 144.1, 141.9, 138.8, 137.0, 136.7, 136.2, 134.0, 132.9, 125.1, 124.2, 78.2, 68.6, 65.0, 59.8, 49.0 48.6, 42.7, 41.1, 36.8, 33.9, 28.3, 25.0, 14.0, 12.7, 10.0.

HRMS-ESI m/z calcd for $C_{33}H_{41}N_6O_9^+$ $[M + Na]^+$ 687.2749, found 687.2744.

Analogue 40j



40j

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methyloxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40j** (12 mg, 52% yield over 2 steps) was obtained as a white solid.

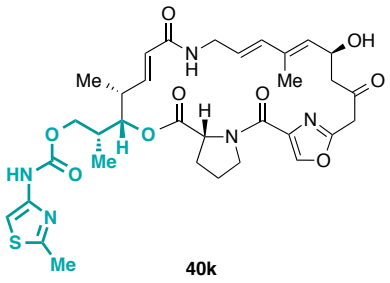
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (br s, 1H), 8.53 (s, 1H), 7.67 (s, 1H), 6.49 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.15 (d, *J* = 15.6 Hz, 1H), 6.04 (d, *J* = 9.4 Hz, 1H), 5.79 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.68 (ddd, *J* = 14.9, 9.2, 4.4 Hz, 1H), 5.54 (d, *J* = 8.7 Hz, 1H), 5.10 (d, *J* = 9.4 Hz, 1H), 4.93 (q, *J* = 6.4 Hz, 1H), 4.76 (dd, *J* = 9.1, 2.8 Hz, 1H), 4.49 – 4.29 (m, 2H), 4.06 – 3.70 (m, 5H), 3.42 (ddd, *J* = 14.1, 9.3, 3.8 Hz, 1H), 3.09 (dd, *J* = 17.7, 4.9 Hz, 1H), 2.91 (dd, *J* = 17.8, 6.0 Hz, 1H), 2.87 (br s, 1H), 2.77 – 2.66 (m, 1H), 2.37 (s, 3H), 2.34 – 2.24 (m, 1H), 2.20 – 2.06 (m, 1H), 1.95 – 1.85 (m, 3H), 1.73 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.2, 166.1, 160.3, 159.2, 157.12 153.5, 145.53 144.3, 137.5, 137.0, 136.7, 134.0, 133.0, 125.1, 124.2, 123.9, 78.5, 69.0, 64.9, 59.8, 49.0, 48.5, 42.7, 41.1, 36.9, 33.9, 28.3, 24.9, 14.0, 13.7, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{33}H_{42}N_5O_{10}^+$ $[M + H]^+$ 668.2926, found 668.2932.

Analogue 40k



40k

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methylthiazole in toluene (0.1 M 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40k** (11 mg, 47% yield over 2 steps) was obtained as a white solid.

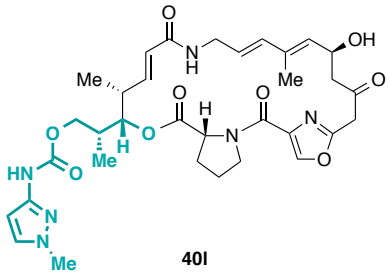
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.32 (br s, 1H), 8.55 (s, 1H), 7.07 (s, 1H), 6.48 (dd, *J* = 16.3, 4.4 Hz, 1H), 6.14 (d, *J* = 15.6 Hz, 1H), 6.07 (d, *J* = 8.3 Hz, 1H), 5.79 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.5, 9.3, 4.4 Hz, 1H), 5.52 (d, *J* = 8.7 Hz, 1H), 5.07 (dd, *J* = 9.8, 1.8 Hz, 1H), 4.92 (dt, *J* = 9.1, 5.4 Hz, 1H), 4.74 (dd, *J* = 8.7, 3.1 Hz, 1H), 4.44 (ddd, *J* = 13.8, 8.8, 4.5 Hz, 1H), 4.32 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.08 (dd, *J* = 11.3, 6.8 Hz, 1H), 4.05 – 3.93 (m, 1H), 3.91 – 3.74 (m, 3H), 3.39 (ddd, *J* = 13.9, 9.4, 3.7 Hz, 1H), 3.06 (dd, *J* = 17.7, 5.0 Hz, 1H), 2.92 (dd, *J* = 17.7, 5.8 Hz, 1H), 2.79 (s, 1H), 2.76 – 2.6 (m, 1H), 2.61 (s, 3H), 2.37 – 2.23 (m, 1H), 2.22 – 2.08 (m, 1H), 1.98 – 1.80 (m, 2H), 1.84 – 1.76 (m, 1H), 1.73 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 171.4, 166.4, 163.5, 160.2, 157.0, 153.9, 147.3, 145.6, 144.2, 137.0, 136.8, 134.0, 132.9, 125.1, 124.2, 98.0, 78.01 68.3, 65.0, 59.8, 48.9, 48.45 42.7, 41.1, 36.9, 34.0, 28.2, 25.0, 19.0, 14.1, 12.7, 10.0.

HRMS-ESI m/z calcd for $C_{33}H_{42}N_5O_9S^+$ $[M + H]^+$ 684.2698, found 684.2726.

Analogue 40l



40l

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methyloxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40l** (12 mg, 52% yield over 2 steps) was obtained as a white solid.

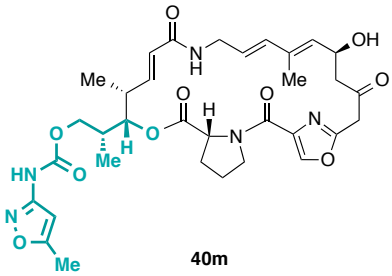
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (br s, 1H), 8.43 (s, 1H), 7.19 (d, *J* = 2.3 Hz, 1H), 6.50 (dd, *J* = 16.3, 4.4 Hz, 1H), 6.42 (s, 1H), 6.14 (d, *J* = 15.4 Hz, 2H), 5.79 (dd, *J* = 16.3, 1.9 Hz, 1H), 5.67 (ddd, *J* = 15.6, 9.3, 4.5 Hz, 1H), 5.51 (d, *J* = 8.6 Hz, 1H), 5.09 (dd, *J* = 9.7, 1.8 Hz, 1H), 4.93 (dd, *J* = 8.8, 5.2 Hz, 1H), 4.77 (dd, *J* = 8.9, 2.8 Hz, 1H), 4.46 – 4.26 (m, 2H), 4.05 – 3.87 (m, 2H), 3.88 – 3.77 (m, 3H), 3.75 (s, 3H), 3.42 (ddd, *J* = 14.0, 9.2, 3.9 Hz, 1H), 3.07 (dd, *J* = 17.6, 5.1 Hz, 1H), 2.92 (br s, 1H), 2.91 (dd, *J* = 17.5, 5.9 Hz, 1H), 2.76 – 2.66 (m, 1H), 2.40 – 2.20 (m, 1H), 2.20 – 2.01 (m, 1H), 2.00 – 1.80 (m, 3H), 1.72 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.3, 166.2, 160.2, 157.0, 153.9, 147.6, 145.3 144.3, 137.0, 136.7, 134.0, 133.0, 130.6, 125.1, 124.2, 96.1, 78.3, 68.4, 65.0, 59.8, 49.0, 48.5, 42.8, 41.0, 38.7, 36.9, 33.9, 28.3, 24.9, 13.8, 12.7, 10.2.

HRMS-ESI m/z calcd for $C_{33}H_{42}N_6NaO_9^+$ $[M + Na]^+$ 689.2905, found 689.2935.

Analogue 40m



40m

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanato-5-methylisoxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40m** (2.6 mg, 13% yield over 2 steps) was obtained as a white solid.

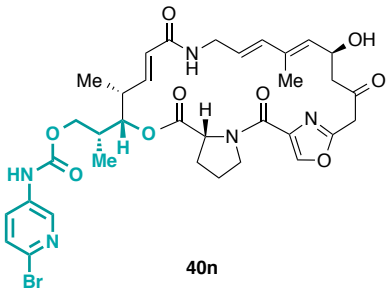
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 8.46 (s, 1H), 6.54 – 6.44 (m, 2H), 6.16 (d, *J* = 15.6 Hz, 1H), 6.03 (dd, *J* = 8.6, 4.0 Hz, 1H), 5.79 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.67 (ddd, *J* = 15.6, 9.3, 4.4 Hz, 1H), 5.56 (d, *J* = 8.6 Hz, 1H), 5.11 (dd, *J* = 9.6, 1.8 Hz, 1H), 4.93 (dt, *J* = 8.7, 5.4 Hz, 1H), 4.72 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.44 (dd, *J* = 11.3, 3.9 Hz, 1H), 4.39 (td, *J* = 8.7, 4.1 Hz, 1H), 4.02 – 3.89 (m, 2H), 3.90 – 3.80 (m, 1H), 3.84 (d, *J* = 16.6 Hz, 1H), 3.78 (d, *J* = 16.6 Hz, 1H), 3.43 (ddd, *J* = 14.1, 9.4, 3.9 Hz, 1H), 3.10 (dd, *J* = 17.8, 4.9 Hz, 1H), 2.93 (dd, *J* = 17.8, 5.9 Hz, 2H), 2.90 (br s,1H), 2.77 – 2.66 (m, 1H), 2.36 (d, *J* = 0.9 Hz, 3H), 2.35 – 2.25 (m, 1H), 2.20 – 2.05 (m, 1H), 1.97 – 1.80 (m, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 171.2, 169.3, 166.1, 160.3, 158.9, 157.2, 153.5, 145.6, 144.2, 136.8, 136.8, 133.9, 133.1, 125.0, 124.2, 95.7, 78.6, 69.2, 64.9, 59.8, 49.1, 48.6, 42.6, 41.1, 37.0, 33.7, 28.3, 24.9, 13.6, 12.7, 12.6, 10.0.

HRMS-ESI m/z calcd for $C_{33}H_{40}N_5O_9^+$ $[M - OH]^+$ 650.2821, found 650.2822.

Analogue 40n



40n

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanato-6-bromopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40n** (11 mg, 43% yield over 2 steps) was obtained as a white solid.

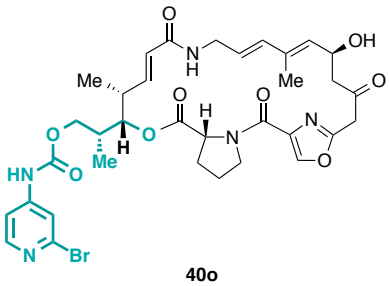
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.50 (br s, 1H), 8.37 (d, *J* = 2.8 Hz, 1H), 8.19 (s, 1H), 8.02 (dd, *J* = 8.7, 2.9 Hz, 1H), 7.36 (d, *J* = 8.7 Hz, 1H), 6.54 (dd, *J* = 16.2, 4.1 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 5.93 (dd, *J* = 8.2, 4.4 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.68 (ddd, *J* = 15.6, 9.2, 4.4 Hz, 1H), 5.57 (d, *J* = 8.7 Hz, 1H), 5.17 (dd, *J* = 9.5, 1.9 Hz, 1H), 4.95 (dt, *J* = 8.7, 5.5 Hz, 1H), 4.71 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.63 (dd, *J* = 11.6, 3.7 Hz, 1H), 4.35 (ddd, *J* = 13.5, 8.1, 4.6 Hz, 1H), 3.95 – 3.85 (m, 2H), 3.84 (d, *J* = 2.6 Hz, 2H), 3.71 (dd, *J* = 11.6, 10.0 Hz, 1H), 3.51 (ddd, *J* = 14.2, 9.2, 4.4 Hz, 1H), 3.13 (dd, *J* = 17.7, 5.0 Hz, 1H), 2.93 (dd, *J* = 17.7, 6.0 Hz, 1H), 2.83 – 2.68 (m, 2H), 2.40 – 2.22 (m, 1H), 2.16 – 2.04 (m, 1H), 1.98 – 1.83 (m, 2H), 1.74 (d, *J* = 1.3 Hz, 3H), 1.72 – 1.62 (m, 1H), 1.12 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 170.5, 165.8, 160.4, 157.5, 153.6, 144.6, 144.5, 140.4, 136.9, 136.6, 135.8, 134.1, 134.0, 133.0, 128.1, 127.7, 125.1, 124.2, 79.3, 69.4, 64.9, 59.9, 49.2, 48.8, 42.6, 41.1, 37.1, 33.7, 28.5, 24.7, 13.3, 12.8, 10.2.

HRMS-ESI m/z calcd for $C_{34}H_{39}BrN_5O_8^+$ $[M - OH]^+$ 724.1977, found 724.1988.

Analogue 40o



40o

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-bromopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40o** (17 mg, 67% yield over 2 steps) was obtained as a white solid.

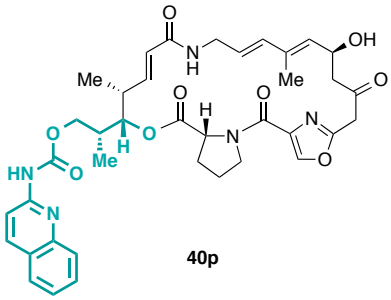
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.65 (br s, 1H), 8.22 (s, 1H), 8.12 (d, *J* = 5.6 Hz, 1H), 7.73 (d, *J* = 1.9 Hz, 1H), 7.43 (dd, *J* = 5.7, 1.9 Hz, 1H), 6.54 (dd, *J* = 16.2, 4.1 Hz, 1H), 6.18 (d, *J* = 15.6 Hz, 1H), 6.01 (dd, *J* = 8.1, 4.5 Hz, 1H), 5.80 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.67 (ddd, *J* = 15.6, 9.1, 4.4 Hz, 1H), 5.58 (d, *J* = 8.7 Hz, 1H), 5.17 (dd, *J* = 9.4, 1.9 Hz, 1H), 4.96 (dt, *J* = 8.8, 5.6 Hz, 1H), 4.70 (dd, *J* = 8.8, 2.6 Hz, 1H), 4.61 (dd, *J* = 11.6, 3.6 Hz, 1H), 4.33 (ddd, *J* = 13.6, 8.0, 4.4 Hz, 1H), 3.91 (dd, *J* = 8.6, 5.5 Hz, 2H), 3.84 (s, 2H), 3.73 (dd, *J* = 11.6, 9.9 Hz, 1H), 3.52 (ddd, *J* = 14.2, 9.2, 4.4 Hz, 1H), 3.14 (dd, *J* = 17.6, 5.0 Hz, 1H), 3.00 – 2.80, (m, 1H), 2.93 (dd, *J* = 17.6, 6.1 Hz, 1H), 2.78 – 2.66 (m, 1H), 2.40 – 2.20 (m, 1H), 2.20 – 2.00 (m, 1H), 1.99 – 1.81 (m, 3H), 1.74 (d, *J* = 1.1 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 170.4, 165.6, 160.3, 157.7, 153.0, 150.2, 148.2, 144.6, 144.4, 142.5, 136.9, 136.6, 134.13 133.0, 125.01 124.2, 116.2, 112.0, 79.2, 69.5, 64.8, 59.8, 49.3, 48.8, 42.6, 41.1, 37.0, 33.7, 28.4, 24.6, 13.3, 12.7, 10.3.

HRMS-ESI m/z calcd for $C_{34}H_{39}BrN_5O_8^+$ $[M - OH]^+$ 724.1977, found 724.1988.

Analogue 40p



40p

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 2-isocyanatoquinoline in toluene (0.1 M, 3.0 mL, 0.34 mmol, 10.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40p** (12 mg, 49% yield over 2 steps) was obtained as a white solid.

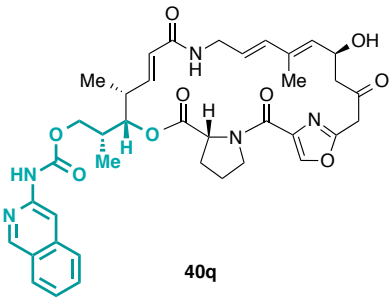
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.08 (br s, 1H), 8.20 (d, *J* = 9.0 Hz, 1H), 8.11 (d, *J* = 9.0 Hz, 1H), 7.77 (d, *J* = 8.5 Hz, 1H), 7.74 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.63 (ddd, *J* = 8.5, 6.8, 1.5 Hz, 1H), 7.40 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.48 (dd, *J* = 16.3, 4.6 Hz, 1H), 6.24 – 6.16 (m, 1H), 6.13 (d, *J* = 15.7 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.9 Hz, 1H), 5.67 (ddd, *J* = 15.6, 9.3, 4.5 Hz, 1H), 5.50 (d, *J* = 8.7 Hz, 1H), 5.06 (dd, *J* = 10.1, 1.8 Hz, 1H), 4.91 (dt, *J* = 9.3, 5.4 Hz, 1H), 4.74 (dd, *J* = 8.7, 3.2 Hz, 1H), 4.45 (ddd, *J* = 13.9, 8.8, 4.5 Hz, 1H), 4.27 (d, *J* = 4.8 Hz, 2H), 4.01 (dt, *J* = 11.3, 7.3 Hz, 1H), 3.92 – 3.73 (m, 3H), 3.38 (ddd, *J* = 14.6, 9.4, 3.6 Hz, 1H), 3.04 (dd, *J* = 17.6, 5.1 Hz, 1H), 2.94 (dd, *J* = 17.6, 5.6 Hz, 1H), 2.89 (s, 1H), 2.79 – 2.63 (m, 1H), 2.38 – 2.23 (m, 1H), 2.20 – 2.10 (m, 1H), 2.01 – 1.82 (m, 3H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.13 – 1.07 (m, 3H), 1.06 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.6, 166.6, 160.2, 157.0, 154.0, 151.5, 146.8, 145.5, 144.0, 138.2, 137.0, 136.9, 133.9, 132.9, 129.7, 127.5, 127.14 125.7, 125.1, 124.6, 124.2, 113.3, 77.6, 67.6, 65.1, 59.8, 48.9, 48.5, 42.8, 41.1, 36.7, 34.1, 28.2, 25.2, 14.4, 12.7, 9.9.

HRMS-ESI m/z calcd for $C_{38}H_{43}N_5NaO_9^+$ $[M + Na]^+$ 736.2953, found 736.2957.

Analogue 40q



40q

Prepared according to general procedure D from primary alcohol **38** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanatoisoquinoline in toluene (0.1 M, 3.0 mL, 0.34 mmol, 10.0 equiv).. Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **40q** (16 mg, 65% yield over 2 steps) was obtained as a white solid.

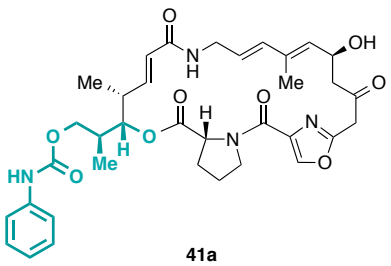
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, p-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.98 (s, 1H), 8.95 (s, 1H), 8.39 (s, 1H), 8.28 (s, 1H), 7.89 – 7.83 (m, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 6.50 (dd, *J* = 16.3, 4.6 Hz, 1H), 6.15 (broad t, *J* = 4.7 Hz, 1H), 6.12 (d, *J* = 8.2 Hz, 1H), 5.80 (dd, *J* = 16.3, 1.9 Hz, 1H), 5.68 (ddd, *J* = 15.5, 9.3, 4.5 Hz, 1H), 5.50 (d, *J* = 8.7 Hz, 1H), 5.10 (dd, *J* = 10.0, 1.8 Hz, 1H), 4.92 (dt, *J* = 8.6, 5.4 Hz, 1H), 4.78 (dd, *J* = 8.8, 3.1 Hz, 1H), 4.44 (ddd, *J* = 14.0, 8.9, 4.5 Hz, 1H), 4.32 (dd, *J* = 11.2, 4.7 Hz, 1H), 4.22 (dd, *J* = 11.2, 5.6 Hz, 1H), 3.99 (dt, *J* = 11.4, 7.4 Hz, 1H), 3.89 – 3.73 (m, 3H), 3.39 (ddd, *J* = 14.1, 9.3, 3.6 Hz, 1H), 3.06 (dd, *J* = 17.6, 5.1 Hz, 1H), 2.92 (dd, *J* = 17.6, 5.7 Hz, 1H), 2.74 (ddt, *J* = 6.9, 4.5, 2.1 Hz, 1H), 2.41 – 2.26 (m, 1H), 2.23 – 2.10 (m, 1H), 2.01 – 1.75 (m, 4H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.07 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.6, 166.4, 160.2, 157.0, 153.8, 151.0, 147.2, 145.19, 144.1, 138.0, 137.1, 136.8, 134.0, 132.9, 130.5, 127.4, 126.5, 125.90, 125.2, 125.1, 124.2, 106.2, 77.9, 67.8, 65.1, 59.8, 48.9, 48.5, 42.8, 41.1, 36.7, 34.2, 28.3, 25.1, 14.2, 12.7, 10.03.

HRMS-ESI m/z calcd for $C_{38}H_{43}N_5NaO_9^+$ $[M + Na]^+$ 736.2953, found 736.2957.

Analog 41a



41a

Prepared according to general procedure D from primary alcohol **39** (40 mg, 55 µmol, 1 equiv), DMAP (0.7 mg, 6 µmol, 0.1 equiv) and phenyl isocyanate (18 µL, 0.16 mmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41a** (18 mg, 50% yield over 2 steps) was obtained as a white solid.

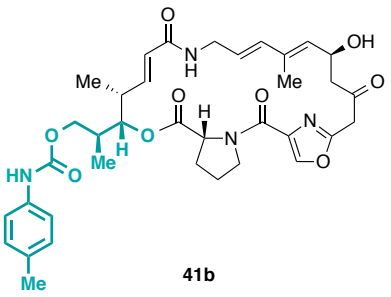
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.06 (s, 1H), 7.54 (br s, 1H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.36 – 7.26 (m, 2H), 7.05 (tt, *J* = 7.4, 1.2 Hz, 1H), 6.50 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.24 (dd, *J* = 8.2, 2.9 Hz, 1H), 6.11 (d, *J* = 15.7 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.6, 9.0, 4.5 Hz, 1H), 5.42 (d, *J* = 8.6 Hz, 1H), 5.17 (d, *J* = 4.3 Hz, 1H), 4.91 (d, *J* = 7.6 Hz, 1H), 4.74 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.44 (ddd, *J* = 13.9, 8.7, 4.6 Hz, 1H), 4.24 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.08 (dd, *J* = 10.9, 4.3 Hz, 1H), 3.99 (dt, *J* = 11.2, 7.4 Hz, 1H), 3.82 (s, 2H), 3.81 – 3.73 (m, 1H), 3.40 (ddd, *J* = 14.5, 9.1, 3.8 Hz, 1H), 3.04 (dd, *J* = 17.2, 5.7 Hz, 1H), 2.89 (dd, *J* = 17.2, 5.4 Hz, 1H), 2.81 – 2.71 (m, 1H), 2.58 (br s, 1H), 2.20 (td, *J* = 8.9, 3.7 Hz, 2H), 1.94 (ddt, *J* = 11.9, 7.3, 3.7 Hz, 2H), 1.88 – 1.76 (m, 1H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 171.3, 166.4, 160.2, 157.0, 153.7, 144.1, 143.8, 138.2, 137.0, 136.5, 134.3, 132.6, 128.9, 125.3, 124.3, 123.3, 118.9, 76.8, 67.8, 65.1, 59.7, 48.8, 48.5, 43.1, 41.0, 36.5, 35.0, 28.4, 25.0, 13.8, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{35}H_{42}N_4NaO_9^+$ $[M + Na]^+$ 685.2844, found 685.2850.

Analog 41b



41b

Prepared according to general procedure D from primary alcohol **39** (50 mg, 68 µmol, 1 equiv), DMAP (0.9 mg, 7 µmol, 0.1 equiv) and 4-methylphenyl isocyanate (17 µL, 0.14 mmol, 2.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41b** (22 mg, 47% yield over 2 steps) was obtained as a white solid.

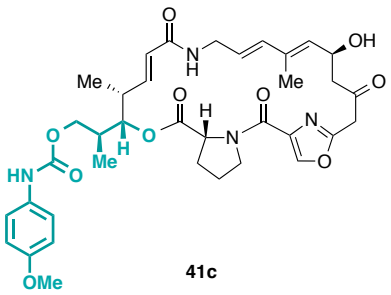
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.05 (s, 1H), 7.48 (br s, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.1 Hz, 2H), 6.50 (dd, J = 16.3, 5.0 Hz, 1H), 6.33 (br s, 1H), 6.10 (d, J = 15.6 Hz, 1H), 5.79 (dd, J = 16.3, 1.8 Hz, 1H), 5.68 (ddd, J = 15.6, 8.9, 4.5 Hz, 1H), 5.41 (d, J = 8.7 Hz, 1H), 5.14 (d, J = 6.5 Hz, 1H), 4.91 (dt, J = 8.8, 5.7 Hz, 1H), 4.73 (dd, J = 9.0, 3.1 Hz, 1H), 4.42 (ddd, J = 14.1, 8.6, 4.7 Hz, 1H), 4.21 (dd, J = 11.0, 3.8 Hz, 1H), 4.07 (dd, J = 11.0, 4.3 Hz, 1H), 3.97 (dt, J = 11.4, 7.5 Hz, 1H), 3.87 – 3.72 (m, 1H), 3.81 (s, 2H), 3.46 – 3.36 (m, 1H), 3.03 (dd, J = 17.0, 5.8 Hz, 1H), 2.89 (dd, J = 17.0, 5.5 Hz, 1H), 2.76 (td, J = 6.2, 5.3, 2.7 Hz, 1H), 2.29 (s, 3H), 2.24 – 2.10 (m, 2H), 1.99 – 1.89 (m, 2H), 1.85 – 1.75 (m, 1H), 1.71 (d, J = 1.2 Hz, 3H), 1.12 (d, J = 7.0 Hz, 3H), 1.11 (d, J = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, CDCl3) δ 202.38, 171.3, 166.4, 160.2, 157.0, 153.8, 144.0, 143.9, 137.0, 136.5, 135.5, 134.3, 132.9, 132.6, 129.4, 125.3, 124.3, 119.0, 76.7, 67.6, 65.1, 59.7, 48.8, 48.53, 43.1, 41.0, 38.6, 34.9, 28.4, 25.0, 20.7, 13.8, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{36}H_{45}N_4O_9^+$ $[M + H]^+$ 677.3181, found 677.3190.

Analog 41c



41c

Prepared according to general procedure D from primary alcohol **39** (50 mg, 68 µmol, 1 equiv), DMAP (0.9 mg, 7 µmol, 0.1 equiv) and 4-methoxyphenyl isocyanate (28 µL, 0.21 mmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41c** (25 mg, 53% yield over 2 steps) was obtained as a white solid.

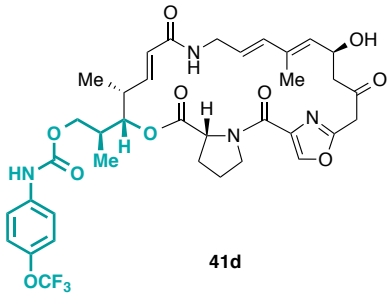
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.04 (br s, 1H), 7.43 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 9.0 Hz, 2H), 6.50 (d, *J* = 16.4 Hz, 1H), 6.28 (s, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.79 (d, *J* = 16.3 Hz, 1H), 5.69 (ddd, *J* = 15.5, 8.9, 4.5 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 5.16 (s, 1H), 4.91 (dt, *J* = 8.6, 5.6 Hz, 1H), 4.80 – 4.67 (m, 1H), 4.43 (ddd, *J* = 14.0, 8.7, 4.6 Hz, 1H), 4.21 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.07 (dd, *J* = 11.0, 4.3 Hz, 1H), 3.98 (dt, *J* = 11.3, 7.5 Hz, 1H), 3.81 (s, 2H), 3.78 (s, 3H), 3.41 (ddd, *J* = 14.6, 8.9, 3.7 Hz, 1H), 3.03 (dd, *J* = 17.1, 5.8 Hz, 1H), 2.89 (dd, *J* = 17.1, 5.4 Hz, 1H), 2.76 (s, 1H), 2.64 (s, 1H), 2.25 – 2.10 (m, 2H), 2.00 – 1.83 (m, 2H), 1.87 – 1.79 (m, 1H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.40, 171.34, 166.46, 160.22, 157.02, 144.08, 143.86, 137.05, 136.56, 134.35, 132.56, 131.19, 125.34, 124.33, 120.87, 114.13, 76.86, 67.73, 65.14, 59.67, 55.49, 48.80, 48.53, 43.13, 41.00, 38.76, 34.97, 28.42, 25.03, 13.82, 12.73, 10.99.

HRMS-ESI m/z calcd for $C_{36}H_{45}N_4O_{10}^+$ $[M + H]^+$ 693.3130, found 693.3138.

Analog 41d



41d

Prepared according to general procedure D from primary alcohol **39** (50 mg, 68 µmol, 1 equiv), DMAP (0.9 mg, 7 µmol, 0.1 equiv) and 4-trifluoromethoxyphenyl isocyanate (31 µL, 0.21 mmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41d** (15 mg, 30% yield over 2 steps) was obtained as a white solid.

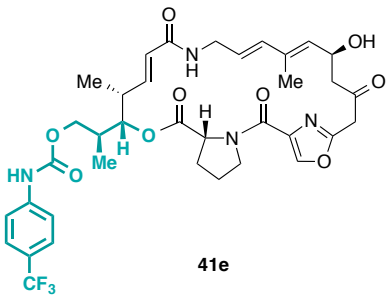
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.05 (s, 1H), 7.92 (br s, 1H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.50 (dd, *J* = 16.3, 4.8 Hz, 1H), 6.16 (s, 1H), 6.12 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.75 – 5.63 (m, 1H), 5.45 (d, *J* = 8.7 Hz, 1H), 5.22 (d, *J* = 4.8 Hz, 1H), 4.91 (q, *J* = 7.6, 6.6 Hz, 1H), 4.75 (dd, *J* = 9.0, 3.0 Hz, 1H), 4.43 (ddd, *J* = 14.0, 8.7, 4.6 Hz, 1H), 4.30 (dd, *J* = 10.9, 3.3 Hz, 1H), 4.07 (dd, *J* = 10.9, 3.9 Hz, 1H), 3.98 (dt, *J* = 11.4, 7.5 Hz, 2H), 3.83 (s, 2H), 3.83 – 3.74 (m, 1H), 3.41 (ddd, *J* = 13.7, 9.0, 3.7 Hz, 1H), 3.04 (dd, *J* = 17.3, 5.6 Hz, 1H), 2.90 (dd, *J* = 17.2, 5.5 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.56 (br s, 1H), 2.30 – 2.13 (m, 2H), 2.00 – 1.88 (m, 2H), 1.87 – 1.75 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.16 (d, *J* = 2.8 Hz, 3H), 1.14 (d, *J* = 2.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.39, 171.20, 166.41, 160.24, 157.18, 153.76, 144.56, 144.01, 143.84, 137.16, 137.09, 136.59, 134.31, 132.64, 125.29, 124.30, 121.65, 119.93, 76.58, 68.59, 65.10, 59.67, 48.87, 48.59, 43.02, 41.08, 39.49, 35.27, 28.43, 25.01, 13.51, 12.73, 11.01.

HRMS-ESI m/z calcd for $C_{36}H_{40}F_3N_4O_9^+$ $[M - H_2O]^+$ 729.2742, found 729.2754.

Analog 41e



41e

Prepared according to general procedure D from primary alcohol **39** (40 mg, 55 µmol, 1 equiv), DMAP (0.7 mg, 6 µmol, 0.1 equiv) and 4-trifluoromethylphenyl isocyanate (18 µL, 0.16 mmol, 3.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41e** (19 mg, 47% yield over 2 steps) was obtained as a white solid.

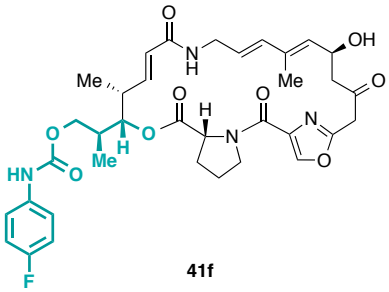
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.18 (br s, 1H), 8.06 (s, 1H), 7.62 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 6.50 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.18 – 6.10 (m, 1H), 6.12 (d, *J* = 15.4 Hz, 1H), 5.80 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.5, 9.1, 4.4 Hz, 1H), 5.46 (d, *J* = 8.7 Hz, 1H), 5.25 (dd, *J* = 4.7, 2.2 Hz, 1H), 4.92 (d, *J* = 7.7 Hz, 1H), 4.75 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.42 (ddd, *J* = 13.7, 8.5, 4.4 Hz, 1H), 4.33 (dd, *J* = 10.9, 3.2 Hz, 1H), 4.08 (dd, *J* = 11.0, 3.7 Hz, 1H), 4.04 – 3.91 (m, 1H), 3.83 (s, 2H), 3.82 – 3.76 (m, 1H), 3.42 (ddd, *J* = 15.0, 9.1, 3.8 Hz, 1H), 3.04 (dd, *J* = 17.3, 5.6 Hz, 1H), 2.91 (dd, *J* = 17.3, 5.5 Hz, 1H), 2.79 – 2.69 (m, 1H), 2.60 (br s, 1H), 2.24 – 2.14 (m, 2H), 2.00 – 1.90 (m, 2H), 1.85 – 1.76 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.17 (d, *J* = 4.2 Hz, 3H), 1.15 (d, *J* = 4.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 171.2, 166.4, 160.3, 157.3, 153.6, 144.0, 141.7, 137.1, 136.6, 134.3, 132.69, 126.1 (q, $^3J_{CF}$ = 3.6 Hz), 125.3, 124.3, 118.4, 76.5, 68.8, 65.0, 59.7, 48.9, 48.6, 43.0, 41.1, 35.3, 31.6, 25.0, 22.6, 14.1, 12.72, 11.0.

HRMS-ESI m/z calcd for $C_{36}H_{41}F_3N_4NaO_9^+$ $[M + Na]^+$ 753,2718, found 753.2717.

Analogue 41f



41f

Prepared according to general procedure D from primary alcohol **39** (50 mg, 68 µmol, 1 equiv), DMAP (0.9 mg, 7 µmol, 0.1 equiv) and 4-fluorodephenyl isocyanate (16 µL, 0.14 mmol, 2.0 equiv). DCM was employed as solvent, and the procedure was performed at 23 ºC. Analogue **41f** (18 mg, 39% yield over 2 steps) was obtained as a white solid.

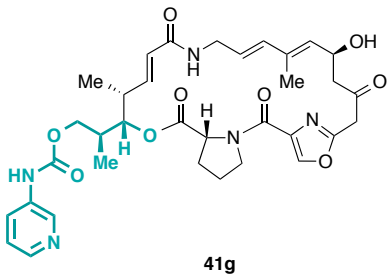
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.04 (s, 1H), 7.73 (br s, 1H), 7.42 (br s, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.50 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.19 (d, *J* = 8.6 Hz, 1H), 6.11 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.5, 9.0, 4.5 Hz, 1H), 5.43 (d, *J* = 8.7 Hz, 1H), 5.19 (d, *J* = 3.0 Hz, 1H), 4.95 – 4.85 (m, 1H), 4.74 (dd, *J* = 8.9, 3.0 Hz, 1H), 4.43 (ddd, *J* = 14.1, 8.9, 4.7 Hz, 1H), 4.25 (dd, *J* = 10.9, 3.4 Hz, 1H), 4.07 (dd, *J* = 10.9, 4.0 Hz, 1H), 3.98 (dt, *J* = 11.4, 7.5 Hz, 1H), 3.82 (s, 2H), 3.80 – 3.72 (m, 1H), 3.41 (ddd, *J* = 15.0, 9.1, 3.8 Hz, 1H), 3.04 (dd, *J* = 17.2, 5.6 Hz, 1H), 2.90 (dd, *J* = 17.2, 5.5 Hz, 1H), 2.79 – 2.72 (m, 1H), 2.60 (br s, 1H), 2.26 – 2.12 (m, 2H), 1.94 (dp, *J* = 11.2, 3.8 Hz, 2H), 1.87 – 1.77 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.14 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 171.3, 166.4, 160.2, 157.1, 153.9, 144.1, 143.8, 137.1, 136.6, 134.3, 132.6, 125.3, 124.3, 120.7 (d, $^3J_{CF}$ = 7.7 Hz), 115.5 (d, $^2J_{CF}$ = 22.6 Hz), 76.7, 68.3, 65.1, 59.7, 48.8, 48.6, 43.0, 41.06, 39.3, 35.2, 28.42, 25.0, 13.6, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{35}H_{42}FN_4O_9^+$ $[M + H]^+$ 681.2930, found 681.2935.

Analogue 41g



41g

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanatopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41g** (10 mg, 44% yield over 2 steps) was obtained as a white solid.

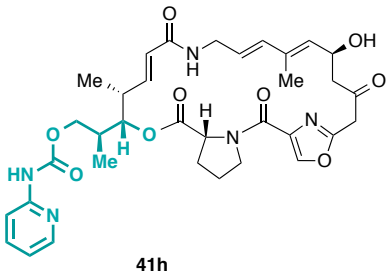
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.52 (d, *J* = 2.6 Hz, 1H), 8.37 (br s, 1H), 8.24 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.09 (br s, 1H), 8.08 (s, 1H), 7.23 (dd, *J* = 8.4, 4.8 Hz, 1H), 6.49 (dd, *J* = 16.3, 4.8 Hz, 1H), 6.15 (d, *J* = 9.5 Hz, 1H), 6.11 (d, *J* = 15.8 Hz, 1H), 5.80 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.68 (ddd, *J* = 15.7, 8.7, 4.3 Hz, 1H), 5.46 (d, *J* = 8.7 Hz, 1H), 5.25 (dd, *J* = 4.2, 2.2 Hz, 1H), 4.91 (dt, *J* = 8.7, 5.7 Hz, 1H), 4.76 (dd, *J* = 9.0, 3.2 Hz, 1H), 4.41 (ddd, *J* = 13.7, 8.1, 4.0 Hz, 1H), 4.26 (dd, *J* = 10.9, 2.9 Hz, 1H), 4.15 (dd, *J* = 10.9, 3.7 Hz, 1H), 3.98 (dt, *J* = 11.5, 7.4 Hz, 1H), 3.88 (td, *J* = 7.5, 7.0, 3.8 Hz, 1H), 3.82 (s, 2H), 3.44 (ddd, *J* = 15.2, 8.7, 3.8 Hz, 1H), 3.07 – 2.91 (m, 2H), 2.76 – 2.66 (m, 1H), 2.28 – 2.08 (m, 2H), 2.00 – 1.90 (m, 2H), 1.89 – 1.75 (m, 1H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.18 (d, *J* = 7.9 Hz, 3H), 1.16 (d, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 171.1, 166.4, 160.4, 157.4, 154.1, 144.2, 144.0, 143.8, 140.8, 137.0, 136.1, 135.6, 134.2, 132.8, 126.3, 125.2, 124.4, 123.6, 76.2, 69.3, 65.1, 59.7, 48.8, 48.7, 43.1, 41.0, 40.1, 35.5, 28.5, 25.0, 13.5, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{34}H_{42}N_5O_9^+$ $[M + H]^+$ 664.2977, found 664.2988.

Analogue 41h



41h

Prepared according to general procedure D from primary alcohol **39** (35 mg, 40 µmol, 1 equiv), DMAP (0.5 mg, 4 µmol, 0.1 equiv) and a solution of 2-isocyanatopyridine in toluene (0.1 M, 4.0 mL, 0.40 mmol, 10.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41h** (11 mg, 31% yield over 2 steps) was obtained as a white solid.

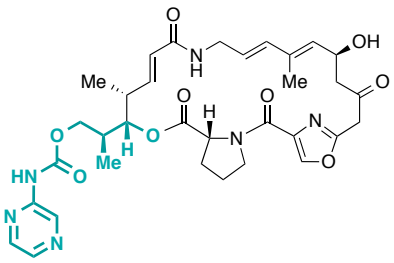
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.52 (s, 1H), 8.32 (s, 1H), 8.29 – 8.21 (m, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.68 (ddd, *J* = 8.7, 7.4, 1.9 Hz, 1H), 6.99 (ddd, *J* = 7.3, 4.9, 1.0 Hz, 1H), 6.55 – 6.44 (m, 1H), 6.37 (dd, *J* = 8.9, 3.6 Hz, 1H), 6.11 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.6, 8.9, 4.6 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 5.11 (dd, *J* = 7.3, 2.2 Hz, 1H), 4.92 (dt, *J* = 8.7, 5.6 Hz, 1H), 4.71 (dd, *J* = 8.7, 3.3 Hz, 1H), 4.45 (ddd, *J* = 14.1, 8.9, 4.6 Hz, 1H), 4.21 (dd, *J* = 11.1, 4.1 Hz, 1H), 4.12 (dd, *J* = 11.1, 4.7 Hz, 1H), 4.05 – 3.97 (m, 1H), 3.84 – 3.74 (m, 1H), 3.81 (s, 2H), 3.39 (ddd, *J* = 14.9, 8.9, 3.6 Hz, 1H), 3.05 (dd, *J* = 17.2, 5.7 Hz, 1H), 2.89 (dd, *J* = 17.3, 5.3 Hz, 1H), 2.82 – 2.70 (m, 1H), 2.27 – 2.11 (m, 2H), 1.98 – 1.78 (m, 3H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 171.6, 166.5, 160.3, 157.0, 153.4, 151.6, 147.6, 144.7, 143.7, 138.4, 136.9, 136.6, 134.2, 132.7, 125.3, 124.4, 119.0, 112.6, 76.9, 67.7, 65.1, 59.7, 48.7, 48.5, 43.2, 40.9, 38.2, 34.7, 28.3, 25.1, 14.03, 12.7, 10.9.

HRMS-ESI m/z calcd for $C_{34}H_{42}N_5O_9^+$ $[M + H]^+$ 664.2977, found 681.2988.

Analogue 41i



41i

Prepared according to general procedure D from primary alcohol **39** (21 mg, 29 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 2-isocyanatopyrazine in toluene (0.1 M, 0.86 mL, 0.086 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41i** (7.3 mg, 43% yield over 2 steps) was obtained as a white solid.

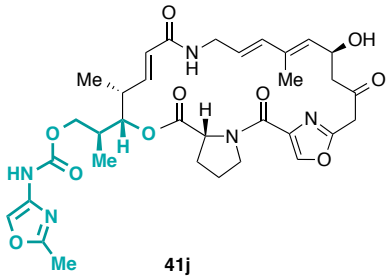
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.31 (br s, 1H), 8.84 (s, 1H), 8.38 (d, *J* = 3.5 Hz, 1H), 8.28 (d, *J* = 2.6 Hz, 1H), 8.22 (t, *J* = 2.0 Hz, 1H), 6.49 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.29 (d, *J* = 8.7 Hz, 1H), 6.10 (d, *J* = 15.7 Hz, 1H), 5.79 (dd, *J* = 16.2, 1.8 Hz, 1H), 5.68 (ddd, *J* = 15.6, 8.8, 4.5 Hz, 1H), 5.43 (d, *J* = 8.7 Hz, 1H), 5.17 (dd, *J* = 6.1, 2.1 Hz, 1H), 4.91 (dt, *J* = 8.7, 5.5 Hz, 1H), 4.71 (dd, *J* = 8.6, 3.3 Hz, 1H), 4.43 (dd, *J* = 11.7, 6.4 Hz, 1H), 4.27 (dd, *J* = 11.0, 3.6 Hz, 1H), 4.15 (dd, *J* = 11.0, 4.2 Hz, 1H), 4.07 – 3.96 (m, 1H), 3.89 – 3.83 (m, 1H), 3.81 (s, 2H), 3.39 (ddd, *J* = 14.9, 8.9, 3.6 Hz, 1H), 3.03 (dd, *J* = 17.1, 5.5 Hz, 1H), 2.91 (dd, *J* = 17.1, 5.5 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.27 – 2.14 (m, 2H), 1.90 (ddd, *J* = 18.9, 10.3, 4.4 Hz, 3H), 1.72 (s, 3H), 1.15 (d, *J* = 6.5 Hz, 3H), 1.13 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 171.6, 166.5, 160.3, 157.1, 153.2, 148.5, 145.0, 143.6, 141.7, 139.3, 136.9, 136.51 136.1, 134.2, 132.8, 125.2, 124.4, 76.4, 68.9, 65.1, 59.7, 48.8, 48.6, 43.1, 40.9, 39.0, 34.9, 28.3, 25.2, 13.7, 12.7, 10.8.

HRMS-ESI m/z calcd for $C_{33}H_{41}N_6O_9^+$ $[M + H]^+$ 665.2930, found 665.2963.

Analogue 41j



41j

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methyloxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41j** (11 mg, 33% yield over 2 steps) was obtained as a white solid.

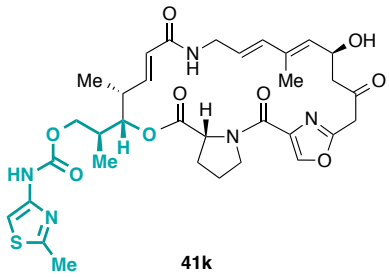
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.89 (s, 1H), 8.65 (s, 1H), 7.67 (s, 1H), 6.46 (dd, *J* = 16.4, 4.8 Hz, 1H), 6.21 – 6.07 (m, 2H), 5.78 (dd, *J* = 16.4, 1.9 Hz, 1H), 5.68 (ddd, *J* = 15.6, 9.2, 4.5 Hz, 1H), 5.47 (d, *J* = 8.6 Hz, 1H), 5.24 – 5.13 (m, 1H), 4.91 (dt, *J* = 8.9, 5.3 Hz, 1H), 4.71 (dd, *J* = 8.7, 3.2 Hz, 1H), 4.47 (ddd, *J* = 13.9, 9.0, 4.6 Hz, 1H), 4.18 (dd, *J* = 10.7, 2.9 Hz, 1H), 4.15 – 3.99 (m, 2H), 3.90 – 3.75 (m, 3H), 3.35 (ddd, *J* = 13.8, 9.1, 3.5 Hz, 1H), 3.04 (dd, *J* = 17.7, 5.0 Hz, 1H), 2.91 (dd, *J* = 17.6, 5.7 Hz, 1H), 2.2.80 – 2.60 (m, 2H), 2.40 (s, 3H), 2.27 – 2.14 (m, 2H), 1.98 – 1.78 (m, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.16 (d, *J* = 7.0 Hz, 3H), 1.14 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8, 171.5, 166.5, 160.2, 159.3, 157.0, 153.5, 146.1, 143.7, 137.2, 136.9, 136.7, 134.0, 132.9, 125.1, 124.3, 123.9, 76.2, 69.4, 65.0, 59.7, 48.8, 48.5, 42.9, 41.0, 40.0 35.2, 28.3, 25.2, 13.9, 13.6, 12.7, 10.6.

HRMS-ESI m/z calcd for $C_{33}H_{41}N_5NaO_{10}^+$ $[M + Na]^+$ 690.2746, found 690.2773.

Analogue 41k



Prepared according to general procedure D from primary alcohol **39** (38 mg, 52 µmol, 1 equiv), DMAP (0.6 mg, 5 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methylthiazole in toluene (0.1 M, 1.60 mL, 0.16 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41k** (17 mg, 52% yield over 2 steps) was obtained as a white solid.

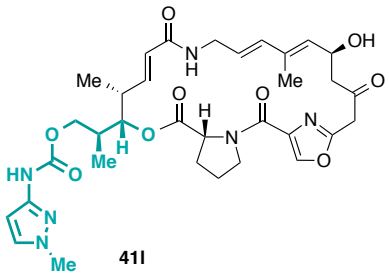
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.81 (s, 1H), 8.66 (s, 1H), 7.08 (s, 1H), 6.47 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.37 – 6.18 (m, 1H), 6.10 (d, *J* = 15.7 Hz, 1H), 5.78 (dd, *J* = 16.4, 1.8 Hz, 1H), 5.68 (ddd, *J* = 15.5, 9.0, 4.5 Hz, 1H), 5.44 (d, *J* = 8.7 Hz, 1H), 5.14 (dd, *J* = 5.8, 2.1 Hz, 1H), 4.91 (dt, *J* = 9.6, 5.6 Hz, 1H), 4.70 (dd, *J* = 8.8, 3.2 Hz, 1H), 4.45 (ddd, *J* = 14.2, 9.0, 4.7 Hz, 1H), 4.19 (dd, *J* = 10.9, 3.5 Hz, 1H), 4.10 (dd, *J* = 10.9, 4.2 Hz, 1H), 4.01 (dt, *J* = 11.1, 7.1 Hz, 1H), 3.87 – 3.71 (m, 1H), 3.81 (s, 2H), 3.36 (ddd, *J* = 14.8, 9.1, 3.5 Hz, 1H), 3.04 (dd, *J* = 17.4, 5.3 Hz, 1H), 2.91 (dd, *J* = 17.4, 5.3 Hz, 1H), 2.85 (br s, 1H), 2.76- 2.67 (m, 1H), 2.63 (s, 3H), 2.26 – 2.10 (m, 2H), 2.01 – 1.82 (m, 3H), 1.72 (s, 3H), 1.14 (d, *J* = 3.7 Hz, 3H), 1.12 (d, *J* = 3.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 171.5, 166.6, 163.7, 160.2, 157.0, 153.7, 146.8, 145.6, 143.7, 136.9, 136.7, 134.1, 132.8, 125.2, 124.3, 98.2, 76.5, 68.67 65.1, 59.7, 48.8, 48.5, 43.0, 41.0, 39.4, 35.0, 28.3, 25.2, 18.9, 13.8, 12.7, 10.7.

HRMS-ESI m/z calcd for $C_{33}H_{42}N_5O_9S^+$ $[M + H]^+$ 684.2698, found 684.2726.

Analogue 41l



Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-methyloxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41l** (11 mg, 48% yield over 2 steps) was obtained as a white solid.

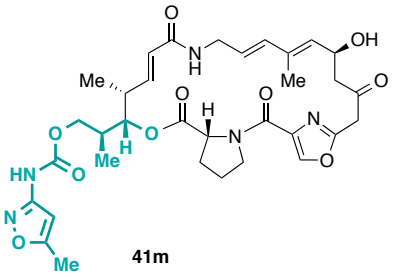
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.57 (s, 1H), 8.44 (s, 1H), 7.21 (d, *J* = 2.3 Hz, 1H), 6.47 (dd, *J* = 16.4, 5.0 Hz, 1H), 6.44 (br s, 1H), 6.31 (brs, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.77 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.6, 9.0, 4.5 Hz, 1H), 5.42 (d, *J* = 8.6 Hz, 1H), 5.18 – 5.01 (m, 1H), 4.91 (q, *J* = 6.4 Hz, 1H), 4.71 (dd, *J* = 8.7, 3.2 Hz, 1H), 4.45 (ddd, *J* = 14.1, 8.8, 4.6 Hz, 1H), 4.13 (qd, *J* = 11.0, 4.0 Hz, 2H), 4.00 (dt, *J* = 11.3, 7.1 Hz, 1H), 3.85 -3.75 (m, 1H), 3.81 (s, 2H), 3.78 (s, 3H), 3.37 (ddd, *J* = 14.3, 9.1, 3.5 Hz, 1H), 3.03 (dd, *J* = 17.3, 5.4 Hz, 1H), 2.90 (dd, *J* = 17.3, 5.6 Hz, 1H), 2.83 (br s, 1H), 2.72 (br t, *J* = 6.5 Hz, 1H), 2.25 – 2.10 (m, 2H), 1.99 – 1.82 (m, 3H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.12 (d, *J* = 6.6 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 171.5, 166.5, 160.2, 157.0, 153.8, 147.3, 145.4, 143.8, 136.9, 136.6, 134.1, 132.7, 130.8, 125.3, 124.3, 96.1, 76.7, 68.2, 65.1, 59.7, 48.7, 48.5, 43.1, 41.0, 39.1, 38.7, 35.0, 28.3, 25.1, 13.9, 12.7, 10.8.

HRMS-ESI m/z calcd for $C_{33}H_{43}N_6O_9^+$ $[M + H]^+$ 667.3086, found 667.3093.

Analogue 41m



41m

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanato-5-methylisoxazole in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41m** (11 mg, 48% yield over 2 steps) was obtained as a white solid.

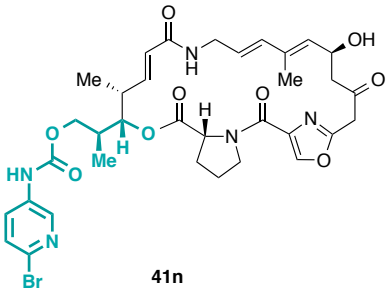
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.35 (s, 1H), 8.85 (s, 1H), 6.52 (s, 1H), 6.45 (dd, *J* = 16.3, 4.7 Hz, 1H), 6.11 (d, *J* = 15.7 Hz, 2H), 5.78 (dd, *J* = 16.4, 1.8 Hz, 1H), 5.68 (ddd, *J* = 14.9, 9.3, 4.5 Hz, 1H), 5.49 (d, *J* = 8.7 Hz, 1H), 5.23 (s, 1H), 4.95 – 4.85 (m, 1H), 4.70 (dd, *J* = 8.7, 3.3 Hz, 1H), 4.52 – 4.42 (m, 1H), 4.21 (dd, *J* = 10.8, 2.6 Hz, 1H), 4.10 (dd, *J* = 10.8, 3.6 Hz, 1H), 4.10 – 4.00 (m, 1H), 3.88 – 3.75 (m, 3H), 3.34 (ddd, *J* = 13.8, 9.3, 3.4 Hz, 1H), 3.05 (dd, *J* = 17.2, 4.9 Hz, 1H), 2.91 (dd, *J* = 17.8, 5.7 Hz, 1H), 2.78 (br s, 1H), 2.72 – 2.63 (m, 1H), 2.37 (d, *J* = 0.9 Hz, 2H), 2.23 – 2.12 (m, 2H), 1.98 – 1.89 (m, 1H), 1.91 – 1.79 (m, 2H), 1.73 (d, *J* = 1.1 Hz, 3H), 1.18 (s, 3H), 1.15 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 171.5, 169.4, 166.6, 160.3, 158.79, 157.0, 153.7, 146.6, 143.5, 136.8, 136.7, 133.9, 133.0, 125.1, 124.3, 95.6, 75.9, 70.3, 65.0, 59.8, 48.8, 48.6, 42.7, 41.1, 40.8, 35.41, 28.2, 25.3, 13.4, 12.7, 12.6, 10.5.

HRMS-ESI m/z calcd for $C_{33}H_{40}N_5O_9^+$ $[M - H_2O]^+$ 650.2821, found 650.2822.

Analogue 41n



41n

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 3-isocyanato-6-brolmopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41n** (11 mg, 40% yield over 2 steps) was obtained as a white solid.

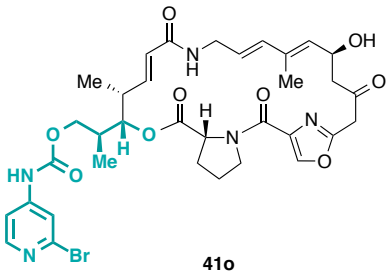
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.66 (br s, 1H), 8.41 (d, *J* = 2.8 Hz, 1H), 8.15 – 7.95 (m, 1H), 8.07 (s, 1H), 7.23 (d, *J* = 8.7 Hz, 1H), 6.51 (dd, *J* = 16.2, 4.8 Hz, 1H), 6.19 (br s, 1H), 6.11 (d, *J* = 15.6 Hz, 1H), 5.79 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.67 (ddd, *J* = 15.6, 8.9, 4.4 Hz, 1H), 5.46 (d, *J* = 8.7 Hz, 1H), 5.27 (dd, *J* = 3.9, 2.2 Hz, 1H), 4.91 (dt, *J* = 9.1, 5.7 Hz, 1H), 4.76 (dd, *J* = 8.9, 3.1 Hz, 1H), 4.37 (ddd, *J* = 14.0, 8.1, 4.3 Hz, 1H), 4.30 (dd, *J* = 11.0, 2.7 Hz, 1H), 4.09 (dd, *J* = 10.9, 3.4 Hz, 1H), 3.93 (dt, *J* = 11.7, 7.6 Hz, 1H), 3.89 – 3.78 (m, 1H), 3.82 (s, 2H), 3.46 (ddd, *J* = 15.0, 9.0, 4.0 Hz, 1H), 3.02 (dd, *J* = 17.1, 5.6 Hz, 1H), 2.97 – 2.83 (m, 2H), 2.75 – 2.58 (m, 1H), 2.30 – 2.10 (m, 1H), 2.00 – 1.86 (m, 2H), 1.84 – 1.74 (m, 2H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.16 (dd, *J* = 6.9, 3.5 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 170.9, 166.3, 160.4, 157.4, 153.9, 144.0, 144.0, 140.2, 136.9, 136.4, 134.9, 134.3, 132.8, 128.9, 127.7, 125.2, 124.2, 124.0, 76.2, 69.6, 65.0, 59.6, 48.9, 48.7, 42.9, 41.1, 40.2, 35.5, 28.4, 24.9, 13.3, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{34}H_{40}BrN_5NaO_9^+$ $[M + Na]^+$ 764.1902, found 764.1928

Analogue 41o



41o

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 4-isocyanato-2-bromopyridine in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41o** (13 mg, 53% yield over 2 steps) was obtained as a white solid.

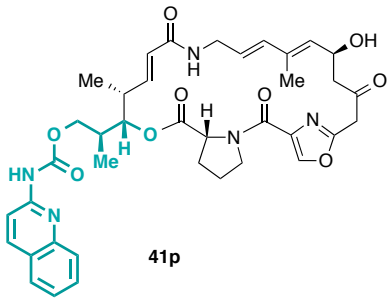
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.91 (s, 1H), 8.20 – 8.10 (m, 2H), 7.71 (d, *J* = 1.9 Hz, 1H), 7.63 – 7.52 (m, 1H), 6.50 (dd, *J* = 16.2, 4.7 Hz, 1H), 6.13 (d, *J* = 15.8 Hz, 2H), 6.09 (d, *J* = 3.8 Hz, 1H), 5.78 (dd, *J* = 16.2, 1.9 Hz, 1H), 5.73 – 5.65 (m, 1H), 5.50 (d, *J* = 8.7 Hz, 1H), 5.30 (t, *J* = 2.7 Hz, 1H), 4.92 (dt, *J* = 8.7, 5.5 Hz, 1H), 4.75 (dd, *J* = 8.9, 3.1 Hz, 1H), 4.47 – 4.36 (m, 1H), 4.34 (dd, *J* = 10.8, 2.6 Hz, 1H), 4.09 (dd, *J* = 10.9, 3.1 Hz, 1H), 3.99 – 3.85 (m, 2H), 3.84 (s, 2H), 3.45 (ddd, *J* = 14.2, 9.1, 4.0 Hz, 1H), 3.04 (dd, *J* = 17.3, 5.6 Hz, 1H), 2.93 (dd, *J* = 17.2, 5.5 Hz, 1H), 2.75 – 2.65 (m, 1H), 2.27 – 2.08 (m, 2H), 1.99 – 1.89 (m, 2H), 1.87 – 1.76 (m, 1H), 1.73 (d, *J* = 1.2 Hz, 6H), 1.17 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.4, 170.8, 166.3, 160.4, 157.5, 153.2, 150.3, 148.1, 144.0, 143.9 142.4, 137.0, 136.5, 134.3, 132.8, 125.2, 124.2, 116.4, 112.1, 76.0, 70.3, 65.0, 59.6, 49.0, 48.8, 42.8, 41.2, 40.7, 35.5, 28.5, 24.94 13.1, 12.7, 11.0.

HRMS-ESI m/z calcd for $C_{34}H_{40}BrN_5NaO_9^+$ $[M + Na]^+$ 764.1902, found 764.1928.

Analogue 41p



41p

Prepared according to general procedure D from primary alcohol **39** (25 mg, 34 µmol, 1 equiv), DMAP (0.4 mg, 3 µmol, 0.1 equiv) and a solution of 2-isocyanatoquinoline in toluene (0.1 M, 1.0 mL, 0.10 mmol, 3.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41p** (10 mg, 46% yield over 2 steps) was obtained as a white solid.

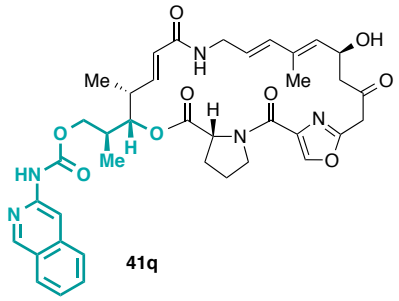
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 8.61 (br s, 1H), 8.43 (s, 1H), 8.18 (q, *J* = 9.0 Hz, 2H), 7.84 – 7.72 (m, 2H), 7.65 (ddd, *J* = 8.5, 6.9, 1.5 Hz, 1H), 7.44 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.49 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.35 (d, *J* = 6.0 Hz, 1H), 6.12 (d, *J* = 15.7 Hz, 1H), 5.81 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.70 (ddd, *J* = 15.6, 8.9, 4.5 Hz, 1H), 5.43 (d, *J* = 8.7 Hz, 1H), 5.13 (dd, *J* = 7.1, 2.1 Hz, 1H), 4.93 (dt, *J* = 8.7, 5.5 Hz, 1H), 4.72 (dd, *J* = 8.6, 3.3 Hz, 1H), 4.47 (ddd, *J* = 14.3, 9.1, 4.7 Hz, 1H), 4.25 (dd, *J* = 11.0, 4.1 Hz, 1H), 4.15 (dd, *J* = 11.0, 4.6 Hz, 1H), 4.00 (dt, *J* = 11.3, 7.2 Hz, 1H), 3.87 – 3.75 (m, 1H), 3.82 (s, 2H), 3.38 (ddd, *J* = 14.8, 9.0, 3.6 Hz, 1H), 3.06 (dd, *J* = 17.3, 5.5 Hz, 1H), 2.90 (dd, *J* = 17.2, 5.5 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.30 – 2.11 (m, 2H), 2.02 – 1.78 (m, 3H), 1.73 (d, *J* = 1.2 Hz, 3H), 1.14 (d, *J* = 3.2 Hz, 3H), 1.13 (d, *J* = 3.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 171.6, 166.5, 160.2, 157.0, 153.6, 151.0, 146.5, 144.9, 143.7, 138.7, 137.0, 136.6, 134.2, 132.7, 130.1, 127.6, 126.9, 125.9, 125.3, 125.0 124.45 113.1, 76.7, 68.0, 65.1, 59.7, 48.7, 48.5, 43.1, 41.0, 38.4, 34.8, 28.3, 25.2, 14.0, 12.8, 10.8.

HRMS-ESI m/z calcd for $C_{38}H_{43}N_5NaO_9^+$ $[M + Na]^+$ 736.2953, found 736.2957.

Analogue 41q



Prepared according to general procedure D from primary alcohol **39** (35 mg, 34 µmol, 1 equiv), DMAP (0.6 mg, 5 µmol, 0.1 equiv) and a solution of 2-isocyanatoisoquinoline in toluene (0.1 M, 3.40 mL, 0.34 mmol, 10.0 equiv). Toluene was employed as solvent, and the procedure was performed at 80 ºC. Analogue **41q** (11 mg, 31% yield over 2 steps) was obtained as a white solid.

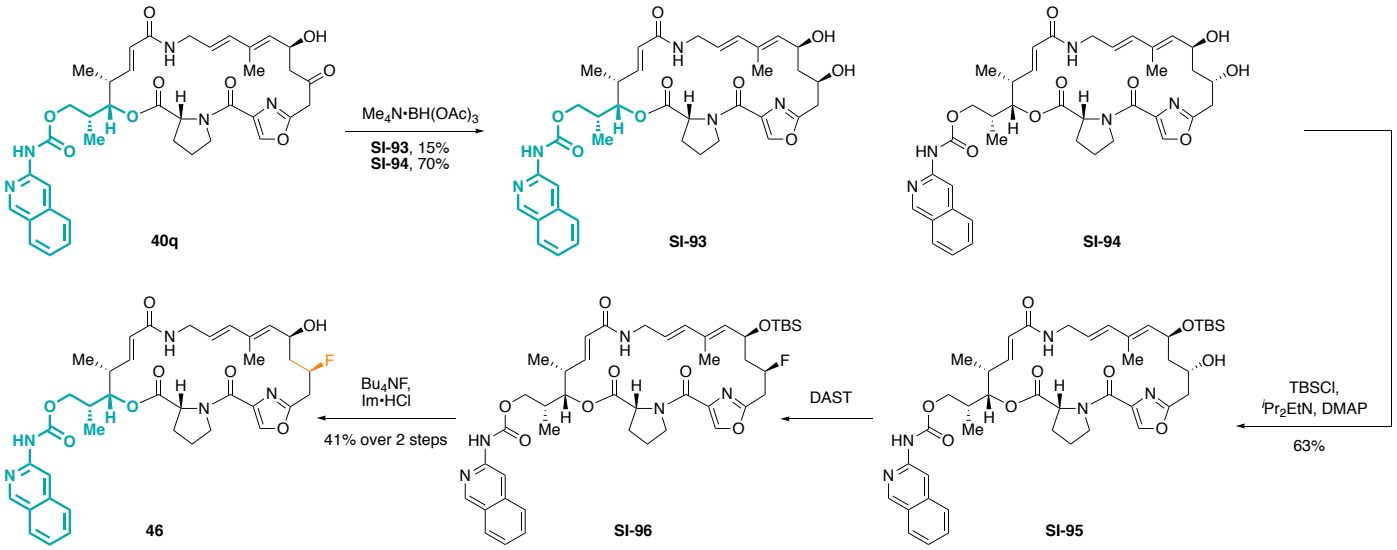
TLC (MeOH;DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.46 (s, 1H), 8.32 (s, 1H), 8.25 (s, 1H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.62 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.45 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 6.50 (dd, *J* = 16.3, 4.9 Hz, 1H), 6.36 (dd, *J* = 8.8, 3.7 Hz, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.80 (dd, *J* = 16.3, 1.8 Hz, 1H), 5.69 (ddd, *J* = 15.6, 8.9, 4.5 Hz, 1H), 5.41 (d, *J* = 8.7 Hz, 1H), 5.14 (dd, *J* = 7.4, 2.2 Hz, 1H), 4.92 (dt, *J* = 8.8, 5.5 Hz, 1H), 4.72 (dd, *J* = 8.7, 3.3 Hz, 1H), 4.26 (dd, *J* = 11.0, 4.1 Hz, 1H), 4.17 (dd, *J* = 11.0, 4.8 Hz, 1H), 3.99 (dt, *J* = 11.3, 7.1 Hz, 1H), 3.81 (s, 3H), 3.37 (ddd, *J* = 14.9, 8.9, 3.6 Hz, 1H), 3.05 (dd, *J* = 17.1, 5.7 Hz, 1H), 2.89 (dd, *J* = 17.1, 5.5 Hz, 1H), 2.80 (ddt, *J* = 7.3, 4.9, 2.2 Hz, 1H), 2.37 – 2.08 (m, 2H), 2.00 – 1.74 (m, 4H), 1.72 (d, *J* = 1.2 Hz, 3H), 1.19 – 1.14 (m, 3H), 1.13 (s, 3H).

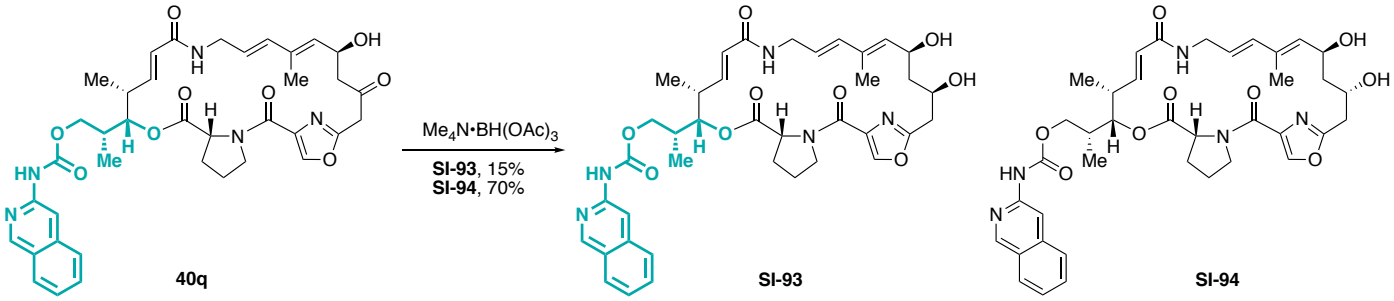
^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 171.6, 166.5, 160.3, 157.0, 153.4, 151.0, 146.5, 144.67, 143.7, 138.0, 137.0, 136.6, 134.2, 132.7, 130.8, 127.5, 126.6, 126.1, 125.5, 125.3, 124.5, 106.3, 77.0, 67.6, 65.1, 59.7, 48.7, 48.5, 43.2, 40.9, 38.2, 34.7, 28.4, 25.1, 14.1, 12.7, 10.9.

HRMS-ESI m/z calcd for $C_{38}H_{43}N_5NaO_9^+$ $[M + Na]^+$ 736.2953, found 736.2957.

Scheme XVIII Synthesis of SI-93, SI-94 and 46



Analogues SI-93 and SI-94



A 50-mL round-bottom flask containing $Me_4N{\cdot}BH(OAc)_3$ (87 mg, 0.33 mmol, 5.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Acetonitrile (6.6 mL) and acetic acid (1.3 mL) was added, and the resulting colorless solution was cooled to -10 ºC by means of an ice-acetone bath. A solution of **40q** (47 mg, 66 µmol, 1 equiv) in acetonitrile (1.2 mL) was added dropwise (the syringe was rinsed with acetonitrile (2 × 0.6 mL) twice), and the mixture was allowed to warm to 23 ºC. After 5 h, saturated aqueous $NaHCO_3$ solution (30 mL) was carefully added (CAUTION: Gas evolution!), followed by EtOAc (50 mL), and the resulting biphasic mixture was transferred to a separatory funnel. Then layers were separated, and the aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH: DCM = 1:30) to afford **SI-93** (7 mg, 15% yield) and **SI-94** (33 mg, 70 % yield) as a white solid.

SI-93: TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.94 (s, 1H), 8.32 (s, 1H), 8.28 (s, 1H), 7.85 (d, *J* = 8.2 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.60 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 6.53 (dd, *J* = 16.2, 4.2 Hz, 1H), 6.18 (d, *J* = 15.7 Hz, 1H), 5.98 (dd, *J* = 8.9, 3.8 Hz, 1H), 5.82 (dd, *J* = 16.2, 2.0 Hz, 1H), 5.65 (ddd, *J* = 15.6, 9.3, 4.2 Hz, 1H), 5.45 (d, *J* = 9.0 Hz, 1H), 5.17 (dd, *J* = 10.0, 1.9 Hz, 1H), 4.95 – 4.80 (m, 2H), 4.46 (ddd, *J* = 14.0, 8.1, 4.3 Hz, 1H), 4.38 (dd, *J* = 11.3, 4.2 Hz, 1H), 4.32 – 4.24 (m, 1H), 4.14 (dd, *J* = 11.3, 6.5 Hz, 2H), 4.05 (ddd, *J* = 12.2, 8.2, 4.1 Hz, 2H), 3.91 (dt, *J* = 11.6, 7.5 Hz, 1H), 3.43 (ddd, *J* = 14.7, 9.3, 3.7 Hz, 1H), 3.00 (dd, *J* = 16.6, 6.1 Hz, 1H), 2.81 (dd, *J* = 16.6, 5.7 Hz, 1H), 2.77 – 2.65 (m, 1H), 2.40 – 2.25 (m, 2H), 2.20 – 2.04 (m, 2H), 1.97 – 1.80 (m 4H), 1.79 (s, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.04 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 165.9, 161.8, 160.5, 153.9, 151.0, 147.3, 144.8, 144.6, 138.0, 136.7, 136.3, 134.4, 134.3, 130.5, 127.4, 126.5, 125.9, 125.2, 125.0, 124.1, 106.3, 77.9, 68.3, 68.1, 67.6, 59.7, 48.7, 42.9, 41.2, 36.6, 35.6, 34.2, 28.2, 24.9, 13.89, 13.1, 10.6.

HRMS-ESI m/z calcd for $C_{38}H_{44}N_5O_8^+$ $[M - OH]^+$ 698.3184, found 698.3190.

SI-94: TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

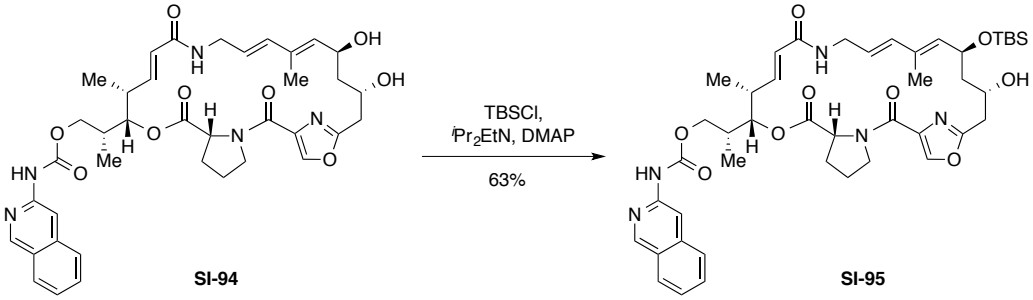
^{1}H NMR (400 MHz, CDCl3) δ 9.16 (s, 1H), 8.93 (s, 1H), 8.28 (s, 1H), 8.26 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.3 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 1H), 6.46 (dd, *J* = 16.4, 4.1 Hz, 1H), 6.21 – 6.09 (m, 2H), 5.82 – 5.76 (m, 1H), 5.75 (t, *J* = 2.2 Hz, 1H), 5.67 (ddd, *J* = 15.0, 9.8, 4.5 Hz, 1H), 5.09 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.97 (dt, *J* = 8.6, 4.0 Hz, 1H), 4.77 (dd, *J* = 8.7, 3.5 Hz, 1H), 4.43 (td, *J* = 14.1, 11.7, 5.9 Hz, 2H), 4.34 (dd, *J* = 11.2, 4.5 Hz, 1H), 4.18 (dd, *J* = 11.2, 5.9 Hz, 1H), 3.88 – 3.73 (m, 2H), 3.35 (ddd, *J* = 14.0, 9.8, 3.8 Hz, 1H), 3.04 (dd, *J* = 16.4, 3.0 Hz, 1H), 2.88 (dd, *J* = 16.5, 9.8 Hz, 1H), 2.95 – 2.80 (m, 2H), 2.77- 2.67 (m, 1H), 2.31 (ddd, *J* = 10.7, 6.8,

4.5 Hz, 1H), 2.20 (ddd, *J* = 14.4, 3.8, 2.0 Hz, 1H), 2.14 – 2.04 (m, 2H), 1.93 (ddd, *J* = 14.0, 9.3, 4.4 Hz, 1H), 1.88 – 1.76 (m, 2H), 1.72 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 166.5, 161.1, 160.5, 153.9, 151.0, 147.12, 144.3, 144.2, 138.0, 137.2, 136.4, 133.7, 133.3, 130.6, 127.3, 126.5, 125.9, 125.2, 124.9, 124.1, 106.3, 77.8, 67.9, 67.5, 66.8, 59.5, 48.3, 41.6, 41.3, 36.7, 35.2, 34.1, 28.1, 25.4, 13.9, 12.5, 9.7.

HRMS-ESI m/z calcd for $C_{38}H_{44}N_5O_8^+$ $[M - OH]^+$ 698.3184, found 698.3190.

Mono-TBS ether SI-95



To a solution of anit-diol **SI-94** (45 mg, 82 µmol, 1 equiv) and DMAP (1 mg, 8 µmol, 0.10 equiv) in DCM (8 mL) was added $^{i}Pr_2NEt$ (0.22 mL, 1.20 mmol, 15.0 equiv), followed by TBS-Cl (0.19 g, 1.2 mmol, 15.0 equiv). After 24 h, the mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:4) to afford mono-TBS ether **SI-95** (43 mg, 79% yield) as a white solid.

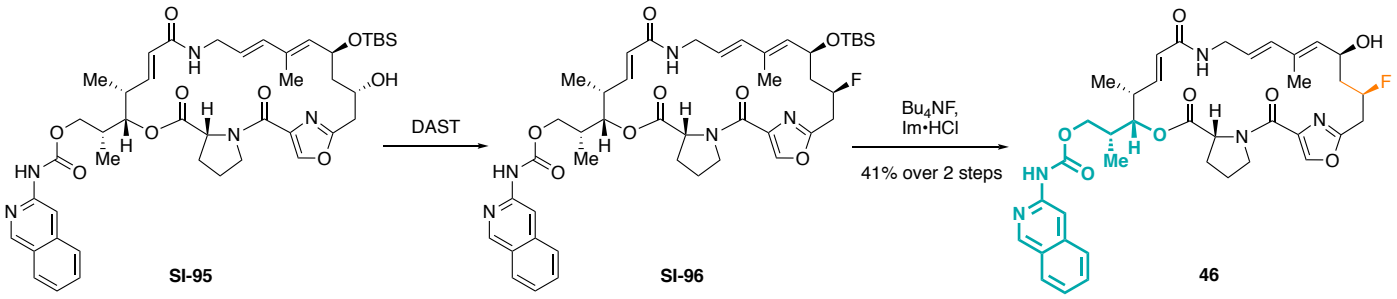
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.13 (s, 1H), 8.93 (s, 1H), 8.37 (s, 1H), 8.27 (s, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.59 (ddd, *J* = 8.2, 6.8, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.0, 6.7, 1.1 Hz, 1H), 6.44 (dd, *J* = 16.4, 4.1 Hz, 1H), 6.17 (s, 1H), 6.07 – 5.93 (m, 1H), 5.82 – 5.72 (m, 2H), 5.67 (ddd, *J* = 15.1, 10.3, 4.2 Hz, 1H), 5.07 (dd, *J* = 10.1, 1.8 Hz, 1H), 4.99 (ddd, *J* = 9.6, 4.9, 2.2 Hz, 1H), 4.76 (dd, *J* = 8.7, 3.7 Hz, 1H), 4.60 – 4.44 (m, 2H), 4.46 – 4.29 (m, 2H), 4.20 (dd, *J* = 11.3, 6.0 Hz, 1H), 3.92 – 3.72 (m, 2H), 3.29 (ddd, *J* = 13.9, 10.4, 3.4 Hz, 1H), 3.03 (d, *J* = 2.4 Hz, 1H), 2.86 – 2.67 (m, 2H), 2.35 (d, *J* = 13.4 Hz, 2H), 2.14 – 2.06 (m, 1H), 2.00 – 1.85 (m, 2H), 1.90 – 1.73 (m, 2H), 1.70 (s, 3H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.06 (d, *J* = 7.0 Hz, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 166.9, 161.1, 160.5, 153.9, 151.0, 147.3, 144.5, 143.7, 138.0, 137.2, 136.5, 134.1, 131.62, 130.4, 127.3, 126.5, 125.9, 125.1, 125.0, 124.2, 106.1, 77.9, 69.8, 67.9, 66.7, 59.6, 48.1, 42.9, 41.6, 36.9, 35.0, 34.0, 28.1, 25.7, 25.6, 17.9, 14.1, 12.4, 9.4, -4.5, -5.3.

HRMS-ESI m/z calcd for $C_{44}H_{60}N_5O_9Si^+$ $[M + H]^+$ 830.4155, found 830.4159.

Analogue 46



A 50-mL round-bottom flask containing mono-TBS ether **SI-95** (42 mg, 64 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (6.4 mL) was added, and the resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of DAST in DCM (2 M, 0.13 mL, 0.27mmol, 10.0 equiv) was added dropwise, and the resulting yellow solution was allowed to warm to 23 ºC. After 3 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added, followed by DCM (20 mL). After stirring for 30 min, the resulting biphasic mixture was transferred to a separatory funnel, and the layers were separated. The organic layer was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was concentrated. The resulting crude residue **SI-96** (22 mg, 100%) was used without further purification.

A 100-mL round-bottom flask containing crude **SI-96** (22 mg, 26 μmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (3 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (28 mg, 0.26 mmol, 10.0 equiv) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.26 mL, 0.26 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the above solution of **SI-96**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (silica gel, eluent: MeOH:DCM = 1:20) to afford analogue **46** (6.5 mg, 34% yield) as a white solid.

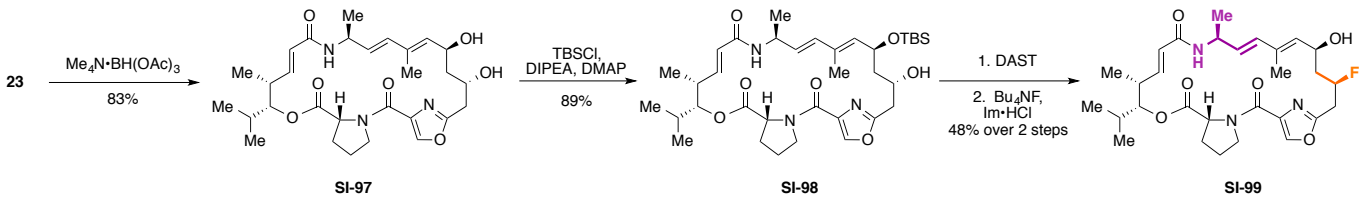
TLC (MeOH:DCM = 1:20): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, CDCl3) δ 9.16 (s, 1H), 8.94 (s, 1H), 8.35 – 8.21 (m, 2H), 7.85 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.59 (ddd, *J* = 8.3, 6.9, 1.2 Hz, 1H), 7.41 (ddd, *J* = 8.1, 6.9, 1.1 Hz, 1H), 6.52 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.19 (d, *J* = 15.7 Hz, 1H), 6.06 – 5.96 (m, 1H), 5.84 (dd, *J* = 16.3, 2.0 Hz, 1H), 5.69 (ddd, *J* = 15.3, 8.5, 4.1 Hz, 1H), 5.40 (d, *J* = 9.0 Hz, 1H), 5.16 (dd, *J* = 10.1, 1.9 Hz, 1H), 5.11 (dm, $^2J_{HF}$ = 41.8 Hz, 1H), 4.88 (dd, *J* = 8.7, 3.4 Hz, 1H), 4.79 (td, *J* = 9.0, 4.4 Hz, 1H), 4.61 – 4.46 (m, 1H), 4.39 (ddd, *J* = 11.3, 4.4, 1.8 Hz, 1H), 4.19 – 4.05 (m, 2H), 3.87 (dt, *J* = 11.4, 6.9 Hz, 1H), 3.45 (ddd, *J* = 15.5, 8.6, 3.1 Hz, 1H), 3.19 (ddd, *J* = 18.9, 16.6, 5.8 Hz, 1H), 3.03 – 2.87 (m, 1H), 2.82 – 2.66 (m, 1H), 2.46 – 2.26 (m, 2H), 2.27 – 2.07 (m, 3H), 1.95 – 1.80 (m, 2H), 1.81 (d, *J* = 1.3 Hz, 3H), 1.13 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H).

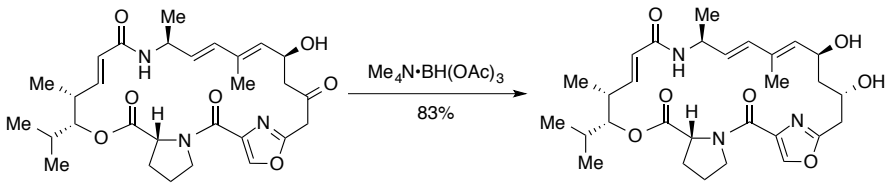
^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 166.1, 160.5, 159.8 (d, $^3J_{CF}$ = 8.2 Hz), 153.8, 151.0, 147.2, 144.4, 144.3, 138.0, 136.6, 135.9, 135.6, 133.5, 130.5, 127.4, 126.5, 125.9, 125.2, 125.2, 124.1, 106.3, 89.3 (d, $^1J_{CF}$ = 169.9 Hz), 77.9, 68.2, 65.7, 59.4, 48.7, 42.3 (d, $^2J_{CF}$ = 20.1 Hz), 41.0, 36.6, 34.1, 33.6 (d, $^2J_{CF}$ = 25.2 Hz), 28.2, 24.9, 13.8, 12.9, 10.3.

HRMS-ESI m/z calcd for $C_{38}H_{44}FN_5NaO_8^+$ $[M + Na]^+$ 740.3066, found 740.3058.

Scheme XIX Synthesis of SI-99



Anti-diol SI-97



23 SI-97

A 50-mL round-bottom flask containing $Me_4N•BH(OAc)_3$ (0.13 g, 0.50 mmol, 5.0 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Acetonitrile (5 mL) and acetic acid (5 mL) was added, and the resulting colorless solution was cooled to -10 ºC by means of an ice-acetone bath. A solution of **23** (54 mg, 0.10 mmol, 1 equiv) in acetonitrile (2.5 mL) was added dropwise (the syringe was rinsed with acetonitrile (2 × 1 mL) twice). The mixture was allowed to warm to 23 ºC slowly. After 5 h, saturated aqueous $NaHCO_3$ solution was added (CAUTION: Gas evolution!), followed by EtOAc (50 mL), and the biphasic mixture was transferred to a separatory funnel. The layers were separated, and aqueous layer was extracted with EtOAc (2 × 10 mL). The combined organic layers were washed with water (50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: MeOH: DCM = 1:30) to afford anti-diol **SI-97** (45 mg, 83% yield) as a white solid.

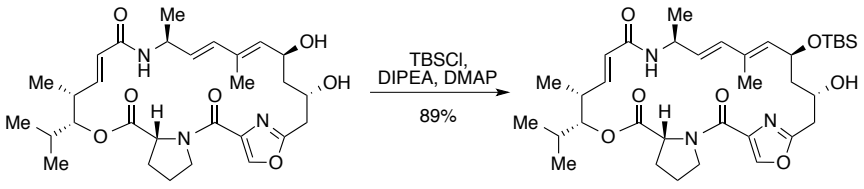
TLC (MeOH:DCM = 1:20): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.42 (dd, *J* = 16.4, 4.3 Hz, 1H), 6.14 (d, *J* = 16.1 Hz, 1H), 5.82 (dd, *J* = 16.1, 4.8 Hz, 1H), 5.79 – 5.71 (m, 3H), 4.98 (dt, *J* = 8.6, 4.0 Hz, 1H), 4.82 – 4.73 (m, 1H), 4.73 – 4.66 (m, 2H), 4.46 (tt, *J* = 9.6, 2.6 Hz, 1H), 3.81 (ddd, *J* = 13.7, 7.2, 4.7 Hz, 2H), 3.05 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.89 (dd, *J* = 16.4, 9.8 Hz, 1H), 2.80 – 2.68 (m, 1H), 2.25 – 2.19 (m, 1H), 2.09 (dtd, *J* = 11.3, 6.4, 5.8, 2.9 Hz, 1H), 2.00 – 1.76 (m, 5H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.31 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 166.2, 161.2, 160.3, 144.5, 143.3, 136.6, 133.7, 133.1, 132.5, 129.8, 123.8, 81.4, 67.6, 66.8, 59.3, 48.3, 44.0, 41.5, 36.6, 35.1, 29.3, 28.2, 25.3, 19.8, 18.6, 17.9, 12.8, 9.7.

HRMS-ESI m/z calcd for $C_{29}H_{42}N_3O_7^+$ $[M + H]^+$ 544.3017, found 544.3020.

Mono-TBS ether SI-98



SI-97 SI-98

To a solution of anti-diol **SI-97** (40 mg, 74 μmol, 1 equiv) and DMAP (0.9 mg, 7.4 μmol, 0.1 equiv) in DCM (7.4 mL) was added ^{i}Pr$_2$NEt (0.19 mL, 1.10 mmol, 15.0 equiv), followed by TBS-Cl (0.17 g, 1.10 mmol, 15.0 equiv). After 24 h, the mixture was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: ethyl acetate:hexanes = 1:3 to 1:1) to afford mono-TBS ether **SI-98** (43 mg, 89% yield) as a white solid.

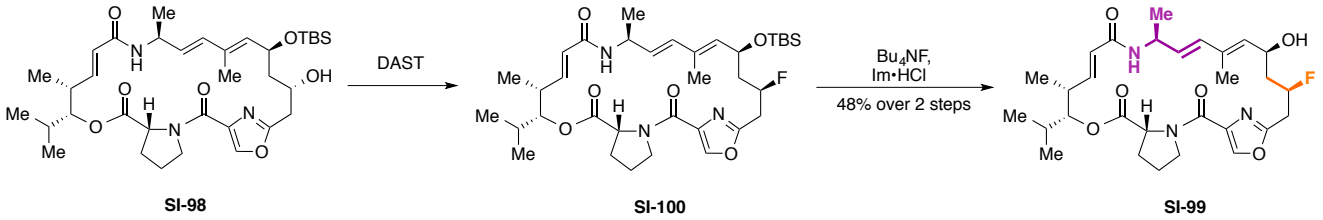
TLC (EtOAc:hexanes = 1:1): R_f = 0.10 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 6.39 (dd, *J* = 16.4, 4.3 Hz, 1H), 6.15 (d, *J* = 16.2 Hz, 1H), 5.81 (dd, *J* = 16.1, 4.6 Hz, 1H), 5.79 – 5.63 (m, 3H), 5.02 – 4.94 (m, 1H), 4.86 – 4.72 (m, 1H), 4.72 – 4.64 (m, 2H), 4.51 (s, 1H), 4.45 (t, *J* = 10.0 Hz, 1H), 3.85 – 3.71 (m, 2H), 3.05 (dd, *J* = 16.8, 2.5 Hz, 1H), 2.80 (dd, *J* = 16.8, 10.3 Hz, 1H), 2.76 – 2.67 (m, 1H), 2.31 (d, *J* = 14.3 Hz, 1H), 2.16 – 2.02 (m, 1H), 1.99 – 1.72 (m, 5H), 1.70 (d, *J* = 1.2 Hz, 3H), 1.34 (d, *J* = 6.9 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 166.4, 161.1, 160.3, 144.2, 143.3, 136.6, 133.6, 132.4, 131.9, 129.5, 123.8, 81.4, 69.9, 66.6, 59.2, 48.1, 43.8, 42.4, 36.7, 35.1, 29.3, 28.1, 25.7, 25.5, 19.9, 18.6, 17.9, 17.2, 12.5, 9.4, –4.5, –5.3.

HRMS-ESI m/z calcd for $C_{35}H_{56}N_3O_7Si^+$ $[M + H]^+$ 658.3882, found 658.3890.

Analogue SI-99



SI-98 **SI-100** **SI-99**

A 50-mL round-bottom flask containing mono-TBS ether **SI-98** (42 mg, 64 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (5 mL) was added, and the resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. DAST (21 µL, 0.16 mmol, 2.50 equiv) was added, and then the mixture was allowed to warm to 23 ºC. After 3 h, saturated aqueous $NaHCO_3$ solution (10 mL) was added, followd by DCM (20 mL), and the resulting biphasic mixture was transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water (50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: acetone:hexanes = 1:5) to afford fluorinated compound **SI-100** (40 mg, 95% yield) as a white solid.

TLC (acetone:hexanes = 1:2.5): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 6.50 (dd, *J* = 16.3, 4.3 Hz, 1H), 6.14 (d, *J* = 16.1 Hz, 1H), 5.93 – 5.68 (m, 3H), 5.34 (d, *J* = 9.0 Hz, 1H), 5.06 (dm, $^1J_{HF}$ = 48.8 Hz, 1H), 4.91 – 4.78 (m, 3H), 4.73 (td, *J* = 9.6, 3.8 Hz, 1H), 4.10 (ddd, *J* = 12.3, 8.1, 4.9 Hz, 1H), 3.83 (dt, *J* = 11.2, 6.9 Hz, 1H), 3.16 (td, *J* = 16.8, 6.5 Hz, 1H), 2.91 (ddd, *J* = 21.5, 16.4, 5.6 Hz, 1H), 2.81 – 2.66 (m, 1H), 2.20 – 2.03 (m, 2H), 1.92 (ddq, *J* = 12.0, 7.7, 4.9, 3.4 Hz, 4H), 1.78 (s, 4H), 1.71 – 1.51 (m, 1H), 1.31 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 165.6, 160.0 (d, $^3J_{CF}$ = 7.8 Hz), 144.7, 143.2, 136.8, 134.3, 133.7, 132.6, 129.6, 124.0, 89.1 (d, $^1J_{CF}$ = 169.0 Hz), 66.5, 59.0, 48.6, 44.6, 43.5 (d, $^2J_{CF}$ = 20.5 Hz), 36.4, 33.8 (d, $^2J_{CF}$ = 25.3 Hz), 29.4, 28.2, 25.8, 24.8, 19.8, 19.2, 18.6, 18.1, 13.1, 10.7, –4.4, –4.9.

A 100-mL round-bottom flask containing **SI-100** (20 mg, 30 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (3 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (32 mg, 0.30 mmol, 10.0 equiv,) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.30 mL, 0.30 mmol, 10.0 equiv). The resulting colorless solution was added dropwise to the above solution. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with

water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **SI-99** (16 mg, 97% yield) as a light-yellow solid.

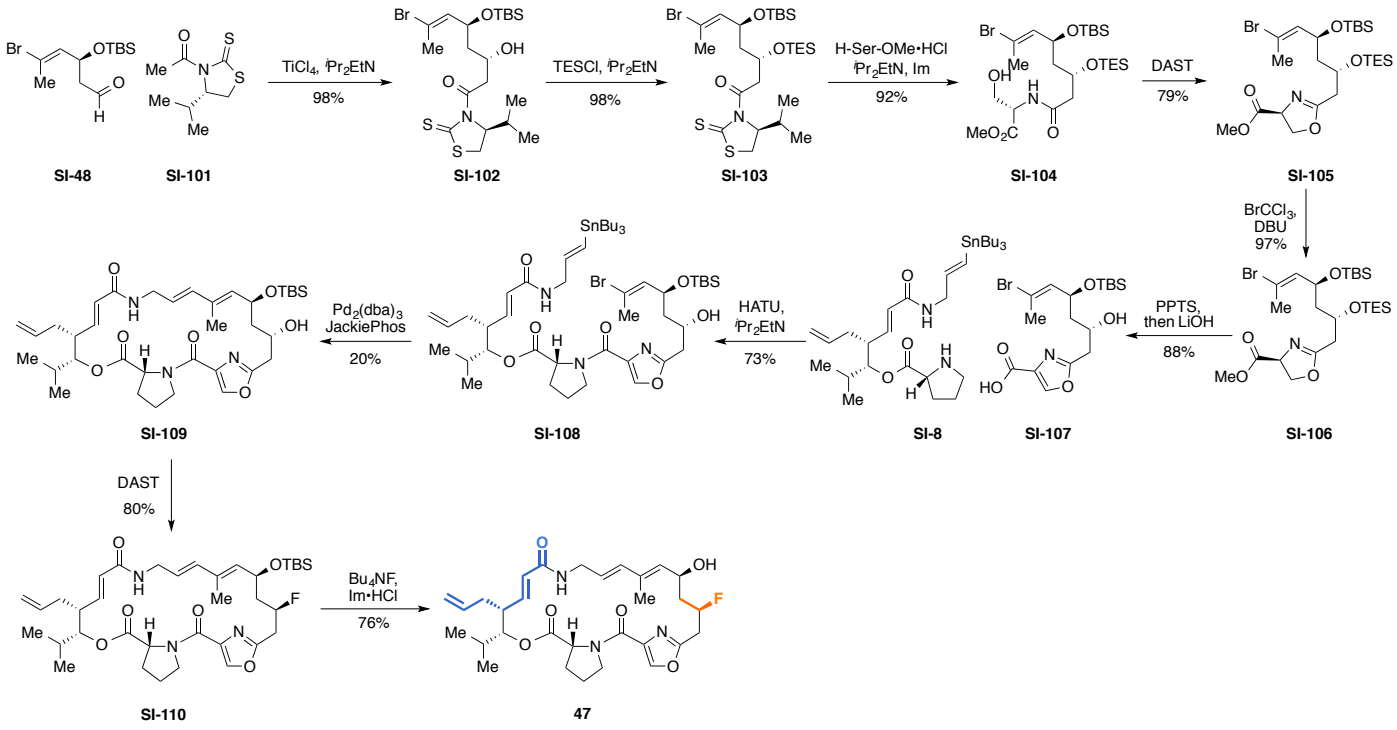
TLC (MeOH:DCM = 1:30): R_f = 0.20 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.51 (dd, *J* = 16.3, 4.5 Hz, 1H), 6.15 (d, *J* = 16.1 Hz, 1H), 5.92 – 5.72 (m, 3H), 5.38 (d, *J* = 8.9 Hz, 1H), 5.06 (dm, $^2J_{HF}$ = 48.0 Hz, 1H), 4.89 – 4.69 (m, 4H), 4.08 (ddd, *J* = 12.5, 8.4, 4.7 Hz, 1H), 3.81 (dt, *J* = 11.4, 7.1 Hz, 1H), 3.21 (td, *J* = 16.7, 5.4 Hz, 1H), 2.99 (td, *J* = 15.9, 7.0 Hz, 1H), 2.81 – 2.67 (m, 1H), 2.25 – 2.05 (m, 2H), 2.05 – 1.75 (m, 4H), 1.83 (s, 3H), 1.75 – 1.53 (m, 1H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H).

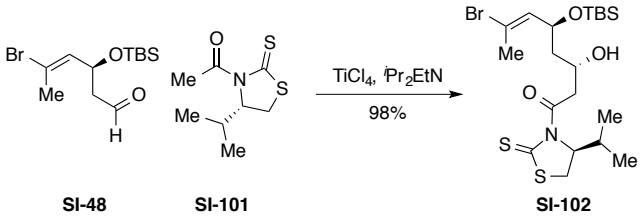
^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 165.6, 160.4, 159.7 (d, $^3J_{CF}$ = 10.7 Hz), 144.7, 143.2, 136.8, 136.4, 132.7, 132.0, 130.8, 124.1, 89.1 (d, $^1J_{CF}$ = 169.8 Hz), 81.0, 65.7, 59.1, 48.6, 44.6, 42.3 (d, $^2J_{CF}$ = 20.3 Hz), 36.4, 33.7 (d, $^2J_{CF}$ = 25.7 Hz), 29.4, 28.3, 24.8, 19.9, 19.8, 18.6, 13.2, 10.7.

HRMS-ESI m/z calcd for $C_{29}H_{41}FN_3O_6^+$ $[M + H]^+$ 546.2974, found 546.2964.

Scheme XX Synthesis of 47



***β*-hydroxyl amide SI-102**



A 500-mL round-bottom flask containing **SI-101** (4.37 g, 21.5 mmol, 1.2 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (110 mL) was added, resulting in a yellow solution, and the vessel and its contents were cooled to -78 ºC by means of a dry ice/acetone bath. A solution of $TiCl_4$ in DCM (1 M, 23.3

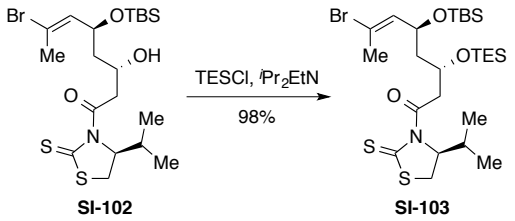
mL, 23.3 mmol, 1.3 equiv) was added dropwise over 5 min, resulting in a deep yellow solution. After 5 min, $^{i}Pr_2EtN$ (4.06 mL, 23.3 mmol, 1.3 equiv) was added over 30 min by means of syringe pump, and the resulting deep red solution was stirred for 2 h at -78 ºC. A solution of aldehyde **SI-48** (5.50 g, 17.9 mmol, 1 equiv) in DCM (18 mL) was added over 30 min by means of syringe pump. After 30 min, **SI-48** was entirely comsumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:4), and then water (150 mL) was added. The vessel was removed from the cooling bath, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with DCM (2 × 50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc: hexanes = 1:10 to 1:2.5) to afford *β*-hydroxyl amide **SI-102** (9.0 g, 98% yield) as a yellow oil.

TLC (EtOAc:hexanes = 1:3): R_f = 0.25 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.92 (dq, *J* = 8.8, 1.3 Hz, 1H), 5.21 – 5.10 (m, 1H), 4.67 – 4.57 (m, 1H), 4.38 (dddd, *J* = 10.7, 5.4, 4.2, 2.8 Hz, 1H), 3.56 – 3.47 (m, 2H), 3.23 (dd, *J* = 17.7, 9.1 Hz, 1H), 3.03 (dd, *J* = 11.5, 1.1 Hz, 1H), 2.37 (dq, *J* = 13.5, 6.8 Hz, 1H), 2.26 (d, *J* = 1.3 Hz, 3H), 1.70 – 1.56 (m, 2H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.88 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 172.6, 135.6, 120.2, 71.4, 67.6, 64.5, 45.9, 43.5, 30.9, 30.6, 25.8, 23.9, 19.1, 18.07, 17.8, –4.5, –5.1.

TES ether SI-103



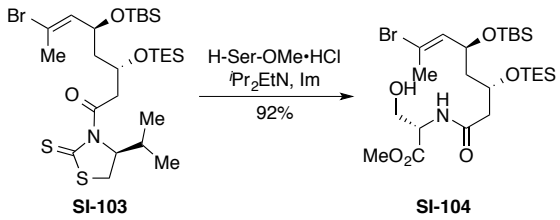
A 250-mL round-bottom flask containing *β*-hydroxyl amide **SI-102** (7.00 g, 13.7 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (140 mL) was added, followed by $^{i}Pr_2EtN$ (7.20 mL, 41.1 mmol, 3.0 equiv), resulting in a colorless solution. The vessel and its contents were cooled to 0 ºC by means of an ice/water bath. TESCl (3.50 mL, 20.6 mmol, 1.5 equiv) was added dropwise over 10 min, and the mixture was allowed to warm to 23 ºC. After 3 h, the mixture was transferred to a separatory funnel and was washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtrated. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:50) to afford TES ether **SI-103** (8.45 g, 98% yield) as a light-yellow oil.

TLC (EtOAc:hexanes = 1:10): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (d, *J* = 9.2 Hz, 1H), 5.07 (t, *J* = 7.0 Hz, 1H), 4.52 – 4.32 (m, 2H), 3.59 (dd, *J* = 17.2, 7.3 Hz, 1H), 3.46 (dd, *J* = 11.4, 7.8 Hz, 1H), 3.29 (dd, *J* = 17.2, 4.6 Hz, 1H), 3.02 (d, *J* = 11.5 Hz, 1H), 2.37 (dq, *J* = 13.5, 6.8 Hz, 1H), 2.25 (s, 3H), 1.81 (ddd, *J* = 13.7, 7.9, 5.8 Hz, 1H), 1.62 (dt, *J* = 13.9, 5.4 Hz, 1H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.94 (t, *J* = 8.1 Hz, 9H), 0.87 (s, 9H), 0.60 (q, *J* = 7.8 Hz, 6H), 0.05 (s, 3H), 0.05 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 202.6, 171.3, 136.1, 120.7, 71.5, 67.5, 66.2, 46.5, 46.2, 30.8, 30.8, 25.9, 23.86, 19.1, 18.1, 17.9, 7.0, 5.2, –4.0, –4.7.

Amide SI-104



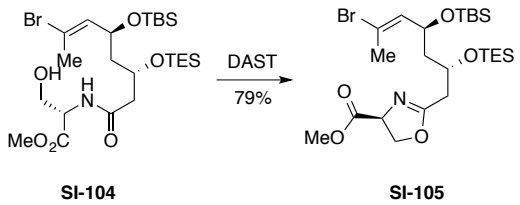
A 500-mL round-bottom flask containing H-Ser-OMe•HCl (3.36 g, 21.6 mmol, 1.5 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (110 mL) was added, followed by $^{i}Pr_2EtN$ (5.01 mL, 28.8 mmol, 2.0 equiv). After 30 min, the resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. A solution of **SI-103** (9.00 g, 14.4 mmol, 1 equiv) in THF (15 mL) was added, followed by Imidazole (2.94 g, 43.2 mmol, 3.0 equiv), and the vessel and its contents were allowed to warm to 23 ºC. After 12 h, the mixture was concentrated, and the residue was dissolved with DCM (150 mL) and water (150 mL). The resulting biphasic mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extract with DCM (50 mL), and the combined layers were washed with water (100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:10 to 1:1) to afford amide **SI-104** (7.75 g, 92% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 7.4 Hz, 1H), 5.79 (dt, *J* = 9.0, 1.4 Hz, 1H), 4.62 (dt, *J* = 7.5, 3.8 Hz, 1H), 4.36 (ddd, *J* = 9.4, 7.5, 5.4 Hz, 1H), 4.17 – 4.07 (m, 1H), 3.96 – 3.82 (m, 2H), 3.74 (s, 3H), 3.01 (br s, 1H), 2.51 (dd, *J* = 14.7, 4.8 Hz, 1H), 2.32 (dd, *J* = 14.7, 5.0 Hz, 1H), 2.24 (s, 3H), 1.79 (ddd, *J* = 13.7, 7.5, 6.0 Hz, 1H), 1.64 (dt, *J* = 13.9, 5.7 Hz, 1H), 0.93 (t, *J* = 7.9 Hz, 9H), 0.84 (s, 9H), 0.61 (q, *J* = 8.1 Hz, 6H), 0.02 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.7, 135.6, 121.1, 67.3, 66.3, 63.3, 54.7, 52.5, 45.2, 44.3, 25.7, 23.8, 18.0, 6.7, 4.8, –4.0, –4.7.

Oxazoline 105



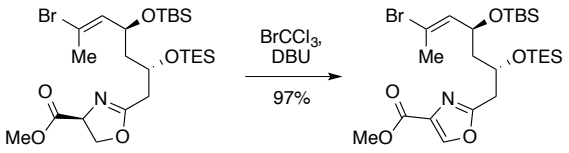
A 250-mL round-bottom flask containing amide **SI-104** (7.60 g, 13.0 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (130 mL) was added, and the resulting colorless solution was cooled to -78 ºC by means of a dry ice/acetone bath. DAST (2.15 mL, 16.3mmol, 1.25 equiv) was added dropwise at -78 ºC under nitrogen. After 3 h, saturated aqueous $NaHCO_3$ solution (50 mL) was added, and the system was allowed to warm to 23 ºC while the mixture was rapidly stirred. The resulting biphasic solution was transferred to a separatory funnel. The organic layer was washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:8) to afford oxazoline **SI-105** (5.78 g, 79% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (dq, *J* = 9.3, 1.4 Hz, 1H), 4.71 (dd, *J* = 10.6, 8.0 Hz, 1H), 4.48 – 4.34 (m, 3H), 4.18 (tdd, *J* = 7.0, 5.9, 4.1 Hz, 1H), 3.78 (s, 3H), 2.52 (ddd, *J* = 8.1, 6.5, 1.0 Hz, 1H), 2.25 (d, *J* = 1.4 Hz, 3H), 1.76 (ddd, *J* = 14.0, 8.5, 4.0 Hz, 1H), 1.60 – 1.53 (m, 1H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.86 (s, 9H), 0.59 (q, *J* = 8.0 Hz, 6H), 0.03 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 167.9, 136.0, 120.8, 69.2, 68.1, 67.1, 66.5, 52.6, 46.1, 37.2, 25.8, 23.8, 18.0, 6.8, 5.1, –3.8, –4.7.

Oxazole SI-106



SI-105 **SI-106**

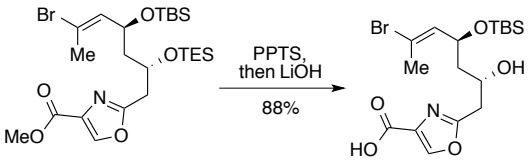
A 250-mL round-bottom flask containing oxazoline **SI-105** (5.78 g, 10.2 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (130 mL) and $BrCCl_3$ (5.04 mL, 51.2 mmol, 5.0 equiv) were added, and the resulting colorless solution was cooled to 0 ºC by means of an ice/water bath. DBU (7.71 mL, 51.2 mmol, 5.0 equiv) was added dropwise at 0 ºC. After 24 h, saturated aqueous ammonium chloride solution (100 mL) was added, and the biphasic mixture was transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with DCM (50 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL). The washed solution was dried (Na_2SO_4), and the dried solution was concentrated. The residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:10) to afford oxazole **SI-106** (5.57 g, 97% yield) as a colorless oil.

TLC (EtOAc:hexanes = 1:5): R_f = 0.20 (UV).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.16 (s, 1H), 5.81 (dt, *J* = 9.3, 1.5 Hz, 1H), 4.44 (td, *J* = 8.9, 4.0 Hz, 1H), 4.29 (qd, *J* = 6.5, 4.1 Hz, 1H), 3.91 (d, *J* = 0.7 Hz, 3H), 2.99 (d, *J* = 6.3 Hz, 2H), 2.26 (d, *J* = 1.3 Hz, 3H), 1.78 – 1.66 (m, 1H), 1.63 – 1.53 (m, 1H), 0.93 (t, *J* = 8.0 Hz, 9H), 0.85 (s, 9H), 0.57 (q, *J* = 8.0 Hz, 6H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 161.7, 143.9, 135.9, 133.3, 120.9, 67.3, 67.1, 52.1, 46.0, 37.2, 25.8, 23.8, 18.0, 6.8, 5.0, –3.7, –4.7.

Acid SI-107

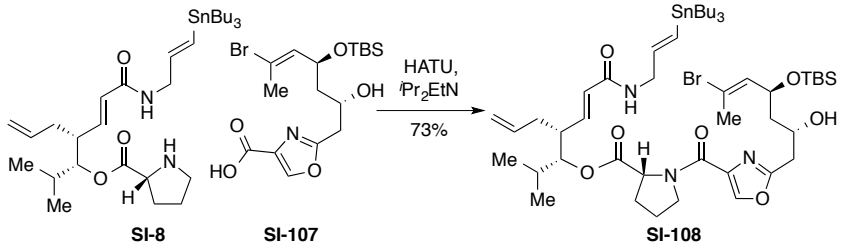


SI-106 **SI-107**

To a solution of oxazole **SI-106** (5.57 g, 9.90 mmol, 1 equiv) in MeOH (100 mL) was added PPTS (0.25 g, 0.99 mmol, 0.1 equiv). After 1 h, **SI-106** was entirely consumed as indicated by TLC analysis (EtOAc:hexanes = 1:3), and then a solution of LiOH in water (1 M, 29.7 mL, 29.7 mmol, 3.0 equiv) was added. After 12 h, the mixture was concentrated, and then water (200 mL) and EtOAc (200 mL) were added, followed by aqueous 1.0 N HCl solution (40 mL) to adjust the pH to 3. The resulting biphasic mixture was transferred to a separatory funnel, and the layers were separated. The

organic layer was washed with water (100 mL) and brine (100 mL), and the washed solution was dried (Na_2SO_4). The dried solution was filtered, and the filtrate was concentrated. The resulting crude residue (3.80 g, 88% yield) was used for next step without further purification.

Stille coupling precursor SI-108



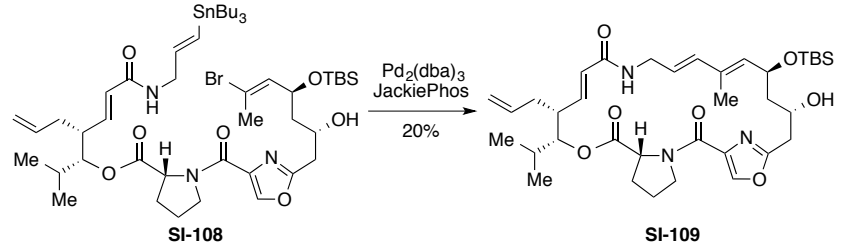
A 50-mL round-bottom flask was charged with acid **SI-107** (0.40 g, 0.92 mmol 1 equiv), $^{i}Pr_2EtN$ (0.32 mL, 1.84 mmol, 2.0 equiv) and amine **SI-8** (0.57 g, 0.92 mmol, 1 equiv). DCM (10 mL) was added, resulting in a clear, colorless solution, and HATU (0.44 g, 1.15 mmol, 1.25 equiv) was added in one portion. After 5 h, the mixture was diluted with DCM (30 mL), and the solution was transferred to a separatory funnel and was washed with water (2 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:6 to 1:4) to afford Stille coupling precursor **SI-108** (0.70 g, 73% yield) as a light-yellow foam.

TLC (EtOAc:hexanes = 1:4): R_f = 0.3 (UV)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 6.49 (dt, *J* = 15.3, 9.6 Hz, 1H), 6.18 – 6.05 (m, 1H), 6.07 – 5.95 (m, 1H), 5.91 (dq, *J* = 8.7, 1.3 Hz, 1H), 5.84 – 5.41 (m, 3H), 4.97 – 4.82 (m, 3H), 4.66 (dp, *J* = 8.4, 4.3 Hz, 2H), 4.43 – 4.19 (m, 1H), 4.09 (tt, *J* = 6.8, 3.1 Hz, 1H), 3.96 (dtt, *J* = 7.1, 5.5, 2.7 Hz, 2H), 3.83 – 3.61 (m, 2H), 2.97 – 2.79 (m, 2H), 2.52 (tdd, *J* = 9.8, 6.7, 3.7 Hz, 1H), 2.33 – 2.19 (m, 4H), 2.15 – 1.84 (m, 6H), 1.66 (dq, *J* = 8.5, 4.6, 3.7 Hz, 2H), 1.53 – 1.38 (m, 6H), 1.33 – 1.15 (m, 6H), 0.99 – 0.77 (m, 30H), 0.15 – –0.04 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.7, 165.3, 164.7, 162.12, 162.11, 160.3, 160.1, 143.58, 143.55, 143.50, 143.3, 142.7, 142.4, 136.73, 136.67, 135.54, 135.29, 135.25, 130.4, 130.2, 125.9, 125.6, 120.4, 120.3, 116.9, 116.8, 80.0, 79.9, 67.7, 65.6, 65.2, 60.9, 60.3, 48.8, 47.3, 50.0, 44.9, 44.7, 43.95, 43.90, 43.5, 36.1, 35.8, 33.98, 33.93, 33.7, 30.0, 29.0, 28.8, 27.2, 25.8, 25.7, 23.87, 23.84, 19.9, 19.6, 18.0, 16.8, 16.6, 13.7, 9.42, 9.40, –4.46, –4.50, –5.0, –5.2.

Stille coupling product SI-109



A 500-mL round-bottom flask containing JackiePhos (92 mg, 0.12 mmol, 0.2 equiv), $Pd_2(dba)_3$ (53 mg, 53 μmol, 0.1 equiv) and Stille coupling precursor **SI-108** (0.60 g, 0.58 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). Toluene (115 ml) was added, resulting in a red suspension. A stream of argon was passed through the solution by a stainless steel needle for 30 min. The mixture was heated by means of a 50^{o} C oil bath. After 60 h, **SI-108** was entirely consumed as indicated by TLC analysis (eluent: EtOAc:hexanes = 1:1), and the mixture was allowed to cool to 23 ^{o}C. The mixture was concentrated, and the resulting crude residue was

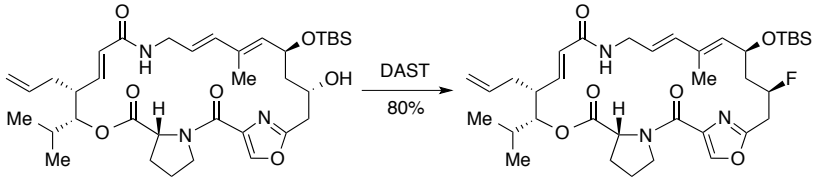
purified by flash chromatography (silica gel, eluent: EtOAc:hexanes =1:3 to 1:1) to afford Stille coupling product **SI-109** (76 mg, 20% yield) as a light-yellow solid.

TLC (EtOAc:hexanes = 1:1): R_f = 0.15 (UV)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 6.28 (dd, *J* = 16.3, 5.3 Hz, 1H), 6.18 (d, *J* = 15.5 Hz, 1H), 5.96 (d, *J* = 8.6 Hz, 1H), 5.84 (d, *J* = 16.3 Hz, 1H), 5.81 – 5.63 (m, 3H), 5.14 – 5.01 (m, 2H), 4.96 (ddt, *J* = 9.2, 4.5, 2.0 Hz, 1H), 4.72 (tt, *J* = 7.4, 2.2 Hz, 2H), 4.57 – 4.36 (m, 3H), 3.79 (t, *J* = 6.0 Hz, 2H), 3.29 (ddd, *J* = 13.9, 10.3, 3.3 Hz, 1H), 3.04 (d, *J* = 16.8 Hz, 1H), 2.79 (dd, *J* = 16.7, 10.4 Hz, 1H), 2.69 – 2.58 (m, 1H), 2.45 – 2.33 (m, 1H), 2.29 (d, *J* = 13.8 Hz, 1H), 2.21 – 2.08 (m, 2H), 2.08 – 1.73 (m, 4H), 1.70 (s, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.88 (s, 9H), 0.08 (s, 3H), 0.03 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 166.8, 161.1, 160.3, 143.2, 142.0, 137.4, 136.6, 135.7, 134.0, 131.6, 125.2, 124.8, 116.9, 81.9, 69.8, 66.6, 59.2, 48.1, 42.8, 41.9, 41.6, 35.1, 29.6, 29.3, 28.1, 25.7, 25.6, 19.9, 18.6, 17.9, 12.4, –4.5, –5.3.

Fluorinated product SI-110



SI-109 **SI-110**

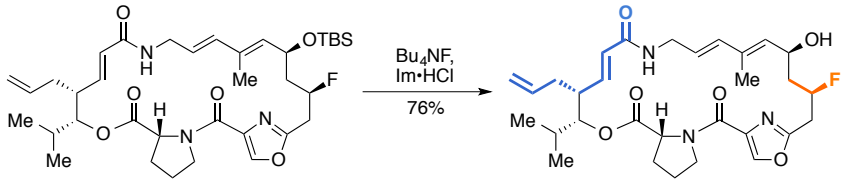
A 50-mL round-bottom flask containing Stille product **SI-109** (70 mg, 0.10 mmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). DCM (5 mL) was added, and the resulting colorless solution was cooled to -78 ºC by means of a dry ice/acetone bath. DAST (34 μL, 0.26 mmol, 2.50 equiv) was added dropwise, and the vessel and its contents were warmed to 0 ºC by means of an ice/water bath. After 3 h, saturated aqueous $NaHCO_3$ solution (30 mL) and DCM (30 mL) were added. After stirring for 30 min, the biphasic mixture was transferred to a separatory funnel, the layers were separated. The organic layer was washed with water (50 mL) and brine (50 mL), and the washed solution was dried (Na_2SO_4). The dried solution was concentrated, and the residue was purified by flash chromatography (silica gel, eluent: EtOAc:hexanes = 1:2) to afford fluorinated product **SI-110** (56 mg, 80% yield) as a white solid.

TLC (EtOAc:hexanes = 1:1): R_f = 0.30 (UV, *p*-anisaldehyde).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 6.50 (dd, *J* = 16.3, 5.2 Hz, 1H), 6.17 (d, *J* = 15.5 Hz, 1H), 6.02 (d, *J* = 8.5 Hz, 1H), 5.89 (d, *J* = 16.2 Hz, 1H), 5.80 – 5.70 (m, 1H), 5.72 – 5.58 (m, 1H), 5.36 – 5.19 (m, 1H), 5.18 – 5.02 (m, 2H), 5.02 – 4.76 (m, 2H), 4.72 (td, *J* = 10.1, 3.8 Hz, 1H), 4.63 – 4.41 (m, 1H), 4.15 – 4.00 (m, 1H), 3.94 – 3.78 (m, 1H), 3.65 (s, 2H), 3.54 – 3.34 (m, 1H), 3.15 (td, *J* = 16.9, 7.0 Hz, 1H), 3.02 – 2.82 (m, 1H), 2.73 – 2.59 (m, 1H), 2.50 – 2.35 (m, 1H), 2.28 – 2.11 (m, 3H), 2.09 – 1.93 (m, 3H), 1.77 (s, 3H), 1.71 – 1.53 (m, 1H), 0.97 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 7.4 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 166.0, 160.6, 160.1 (d, $^3J_{CF}$ = 7.2 Hz), 143.2, 142.8, 136.7, 136.5, 135.8, 134.7, 133.4, 125.0, 124.5, 117.1, 89.1 (d, $^1J_{CF}$ = 169.5 Hz), 81.4, 66.5, 59.0, 48.6, 43.6 (d, $^2J_{CF}$ = 20.5 Hz), 41.5, 41.2, 33.9 (d, $^2J_{CF}$ = 205.2 Hz), 30.6, 29.4, 28.2, 25.8, 24.9, 19.8, 18.7, 18.1, 12.9, –4.4, –4.9.

Analogue 47



SI-110 **47**

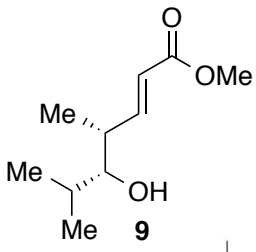
A 50-mL round-bottom flask containing **SI-110** (35 mg, 52 µmol, 1 equiv) was evacuated and flushed with nitrogen (this process was repeated a total of 3 times). THF (5.2 mL) was added, resulting in a light-yellow solution. In a separate flask, Im•HCl (82 mg, 0.78 mmol, 15.0 equiv,) that had previously been dried at >100 ºC for 10 minutes under vacuum was added to a solution of tetrabutylammonium fluoride in THF (1 M, 0.78 mL, 0.78 mmol, 15.0 equiv). The resulting colorless solution was added dropwise to the above solution of **SI-110**. After 12 h, the mixture was concentrated, and the residue was dissolved in DCM (50 mL). The resulting solution was transferred to a separatory funnel and was washed with water (5 × 50 mL) and brine (50 mL). The washed solution was dried (Na_2SO_4), and the dried solution was filtered. The filtrate was concentrated, and the resulting crude residue was purified by preparative TLC (eluent: MeOH:DCM = 1:25) to afford analogue **47** (22 mg, 76 % yield) as a white solid.

TLC (MeOH:DCM = 1:25): R_f = 0.10 (UV, *p*-anisaldehyde).

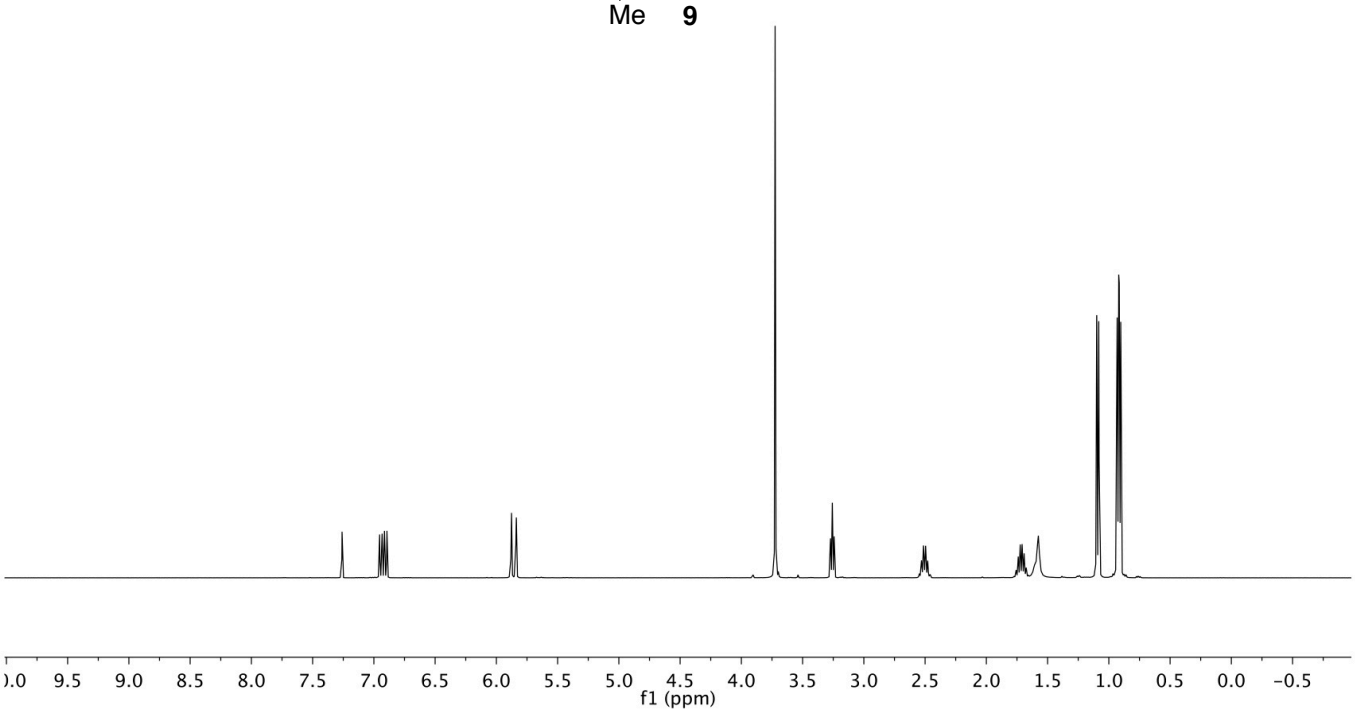
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 6.50 (dd, *J* = 16.2, 5.4 Hz, 1H), 6.16 (d, *J* = 15.7 Hz, 1H), 6.10 (d, *J* = 6.0 Hz, 1H), 5.88 (dd, *J* = 16.2, 1.7 Hz, 1H), 5.85 – 5.65 (m, 2H), 5.32 (d, *J* = 9.0 Hz, 1H), 5.16 – 4.93 (m, 3H), 4.91 – 4.71 (m, 3H), 4.50 (ddd, *J* = 14.5, 8.7, 4.3 Hz, 1H), 4.04 (ddd, *J* = 11.9, 8.0, 4.8 Hz, 1H), 3.84 (dt, *J* = 11.4, 7.2 Hz, 1H), 3.46 (ddd, *J* = 15.9, 8.1, 3.2 Hz, 1H), 3.19 (td, *J* = 16.9, 5.8 Hz, 1H), 2.96 (td, *J* = 17.1, 6.4 Hz, 1H), 2.72 – 2.60 (m, 1H), 2.47 – 2.35 (m, 1H), 2.25 – 2.10 (m, 3H), 2.10 – 1.87 (m, 5H), 1.80 (s, 3H), 1.73 – 1.52 (m, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 165.9, 160.5, 159.8 (d, $^3J_{CF}$ = 9.4 Hz), 143.3, 143.0, 136.7, 135.8, 135.73, 135.69, 133.1, 125.4, 125.0, 117.1, 89.1 (d, $^1J_{CF}$ = 169.9 Hz), 81.6, 65.7 (d, $^3J_{CF}$ = 2.4 Hz), 59.1, 48.6, 42.3 (d, $^2J_{CF}$ = 20.5 Hz), 41.5, 40.8, 33.7 (d, $^2J_{CF}$ = 25.5 Hz), 30.6, 29.4, 28.2, 24.9, 19.8, 18.7, 13.0.

HRMS-ESI m/z calcd for $C_{30}H_{40}FN_3NaO_6^+$ $[M + Na]^+$ 580.2793, found 580.2794.


O
OMe
Me
Me
OH
Me

9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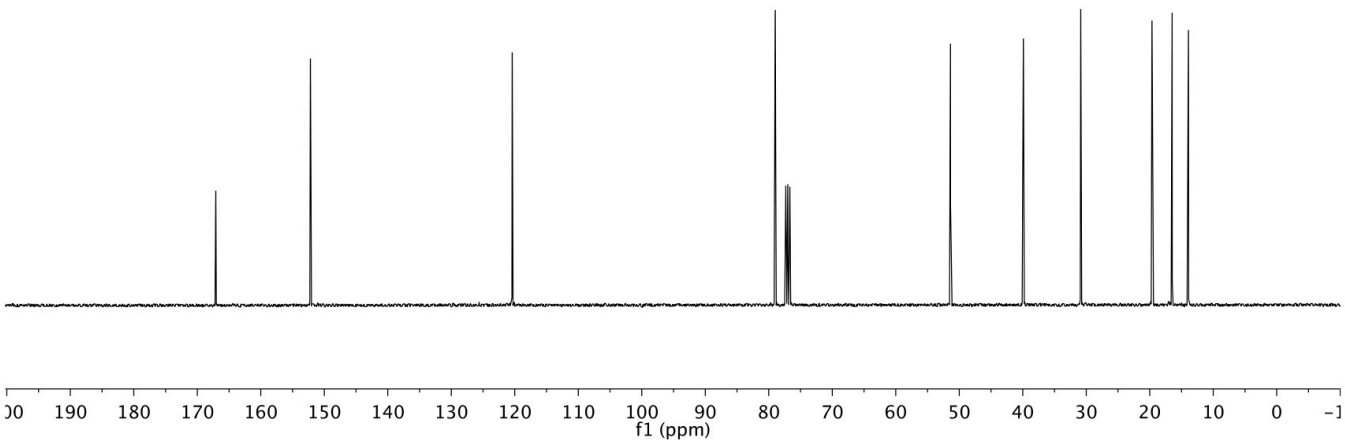
f1 (ppm)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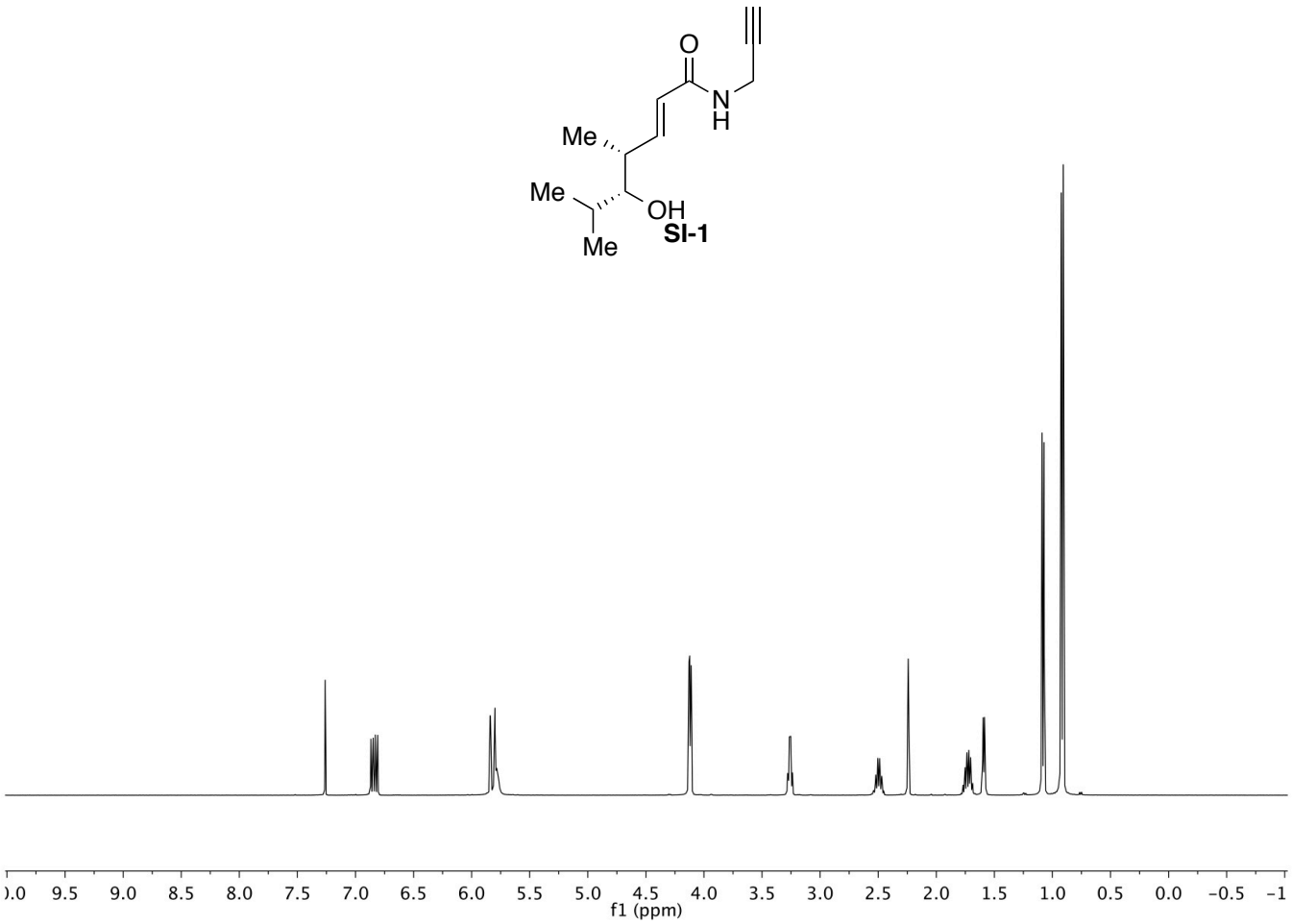
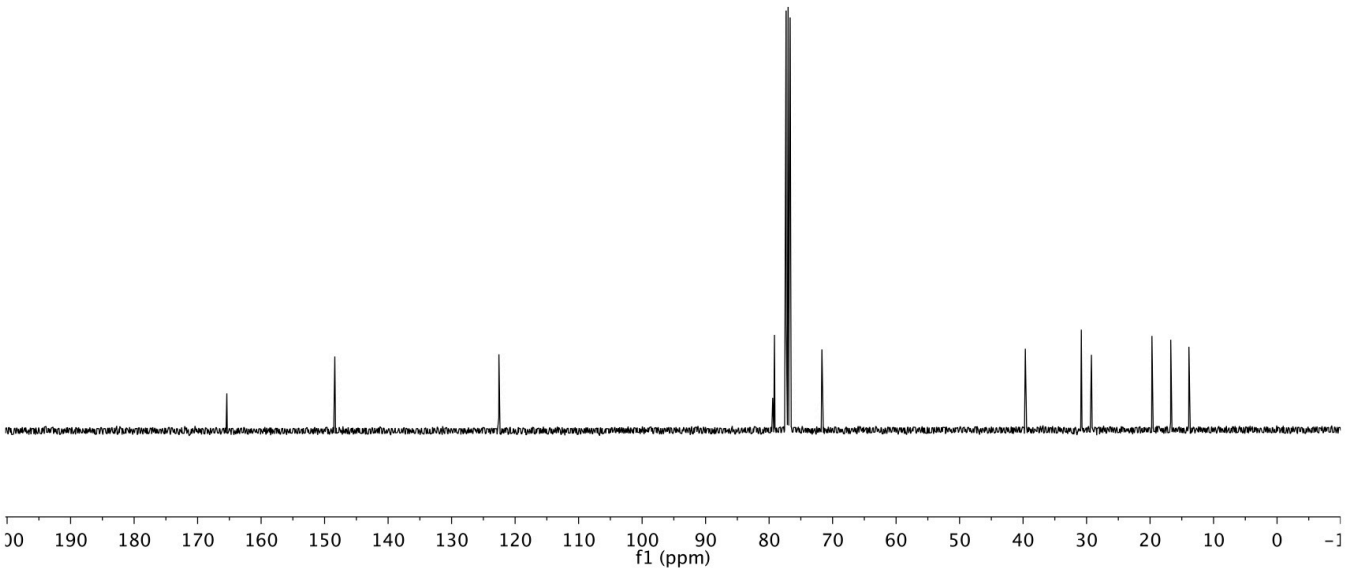
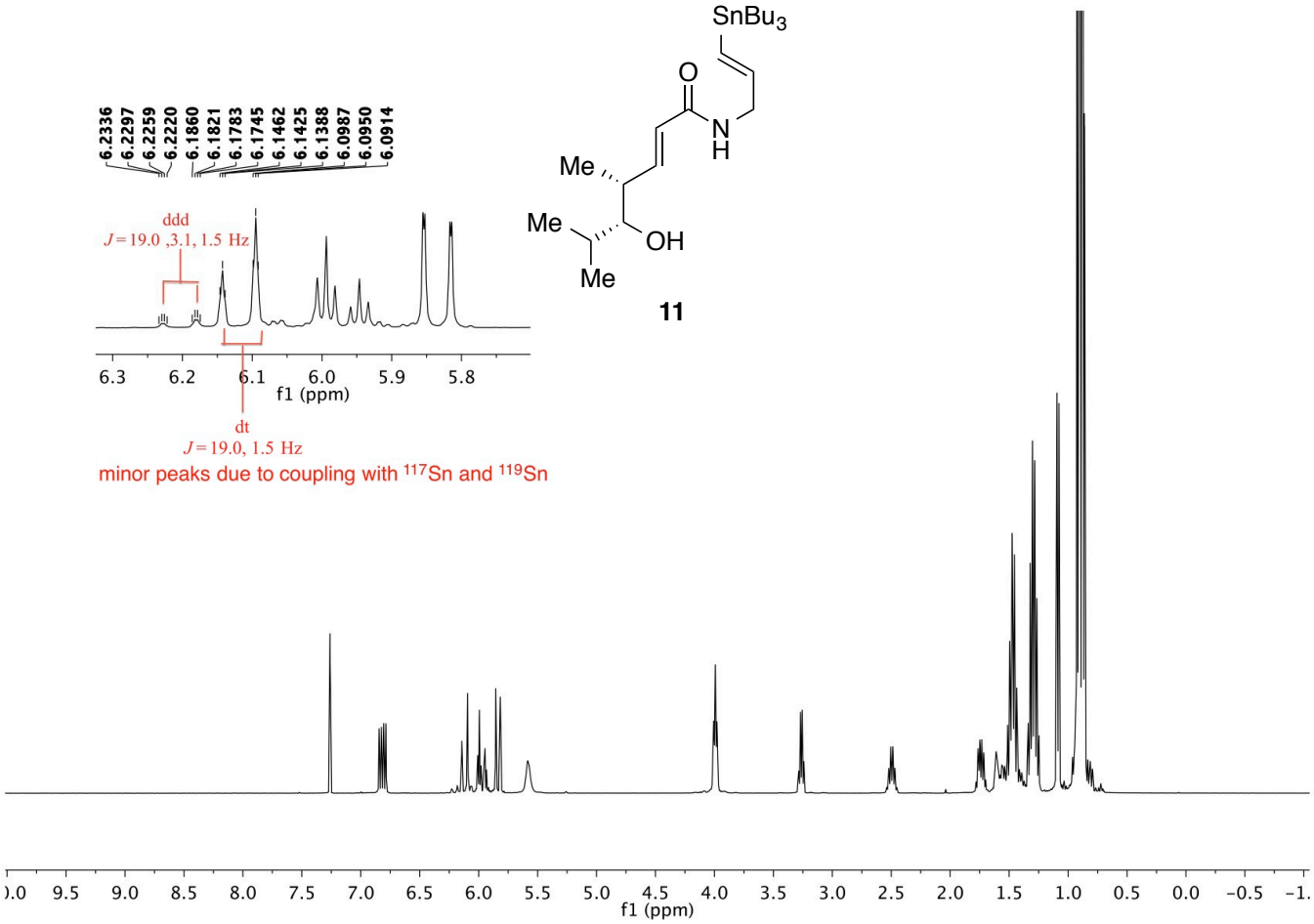
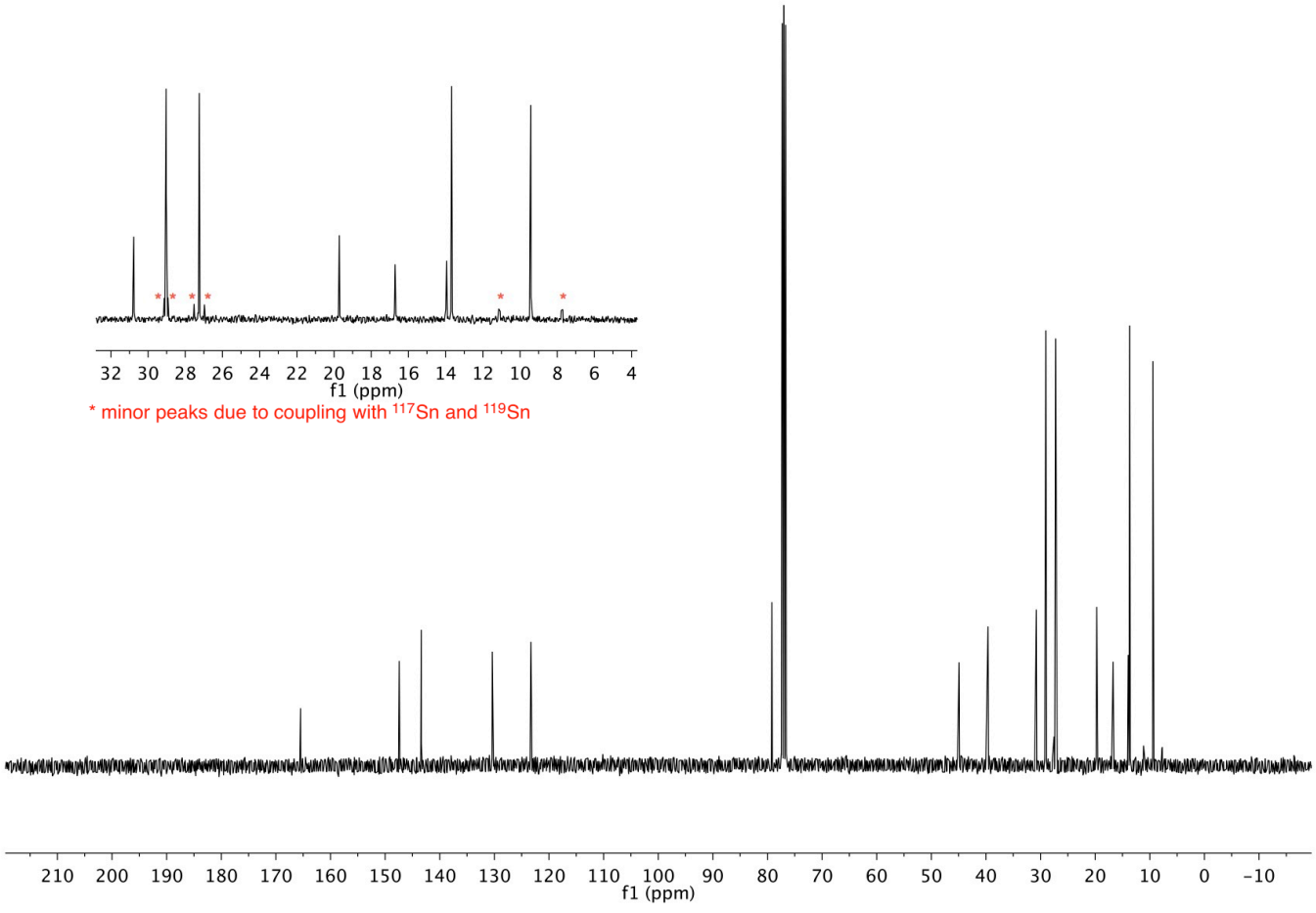
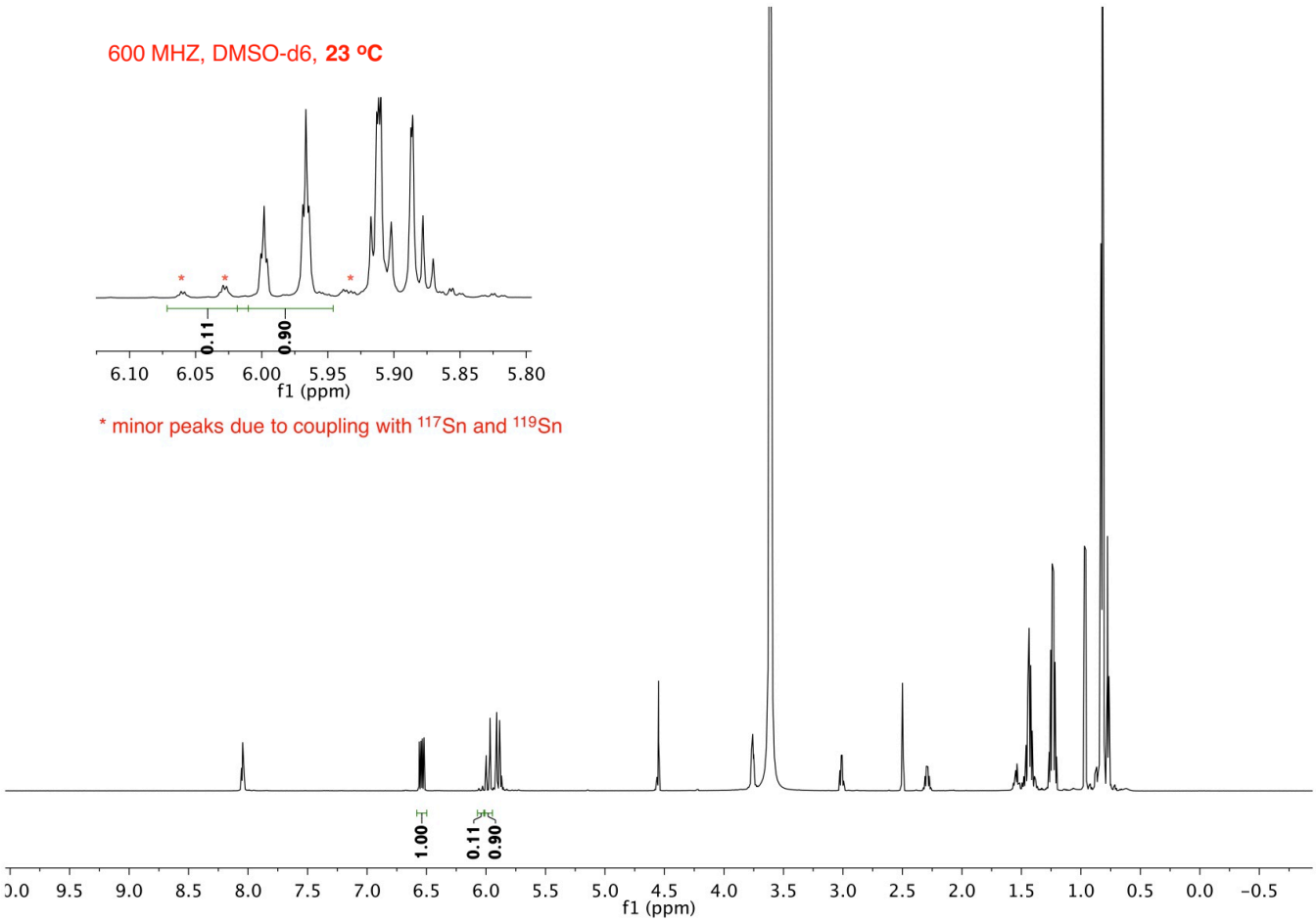
f1 (ppm)

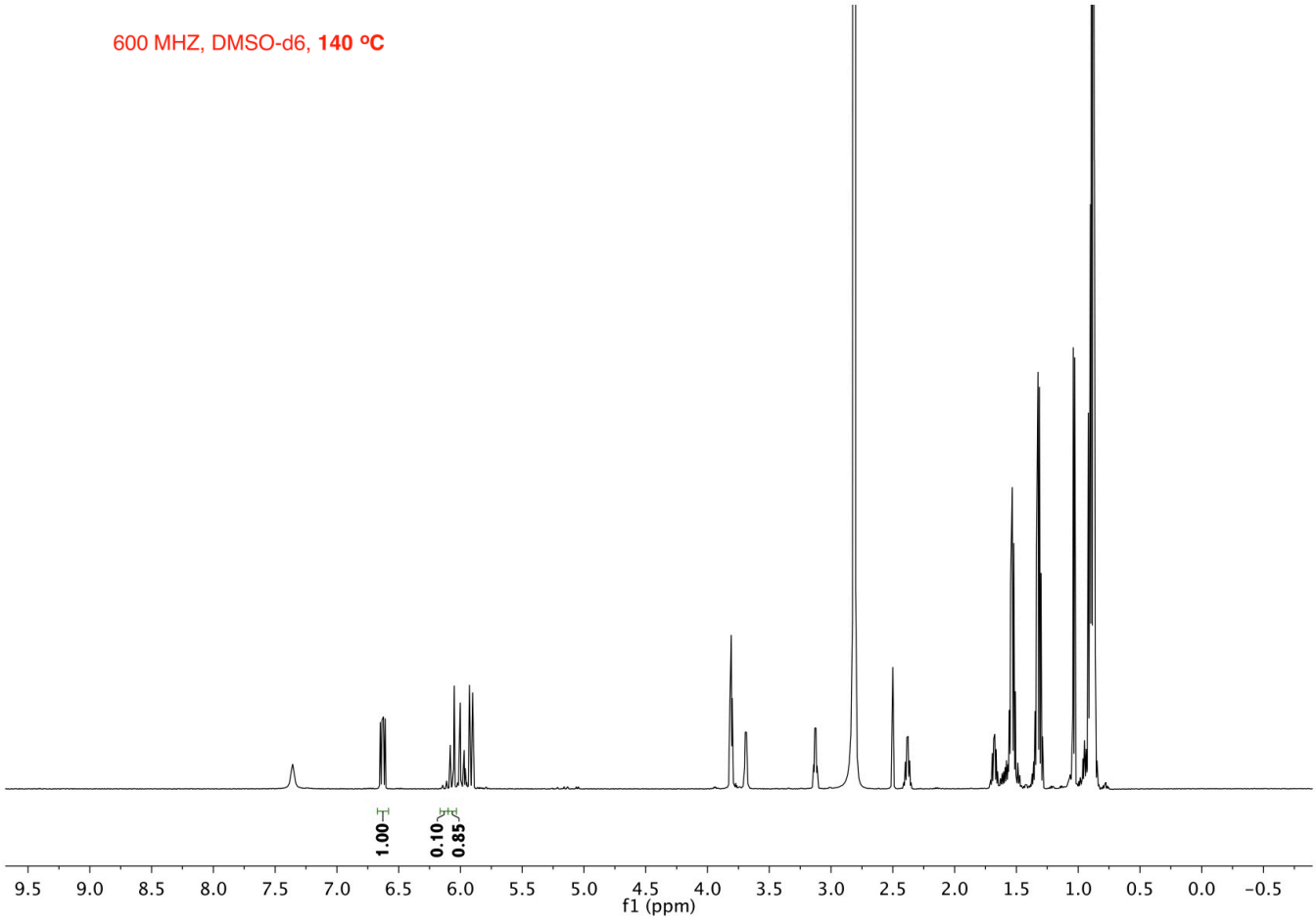

O
N
H
Me
Me
OH
Me
SI-1
f1 (ppm)

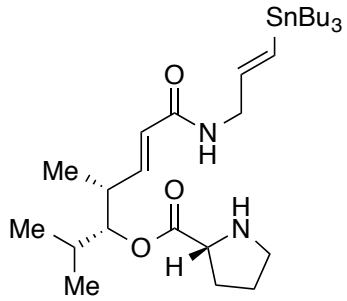

f1 (ppm)


6.2336
6.2297
6.2259
6.2220
6.1860
6.1821
6.1783
6.1745
6.1462
6.1425
6.1388
6.0987
6.0950
6.0914
ddd
J = 19.0 ,3.1, 1.5 Hz
dt
J = 19.0, 1.5 Hz
f1 (ppm)
minor peaks due to coupling with 117Sn and 119Sn
SnBu3
O
N
H
Me
Me
Me
OH
11
f1 (ppm)


* minor peaks due to coupling with 117Sn and 119Sn
f1 (ppm)
f1 (ppm)

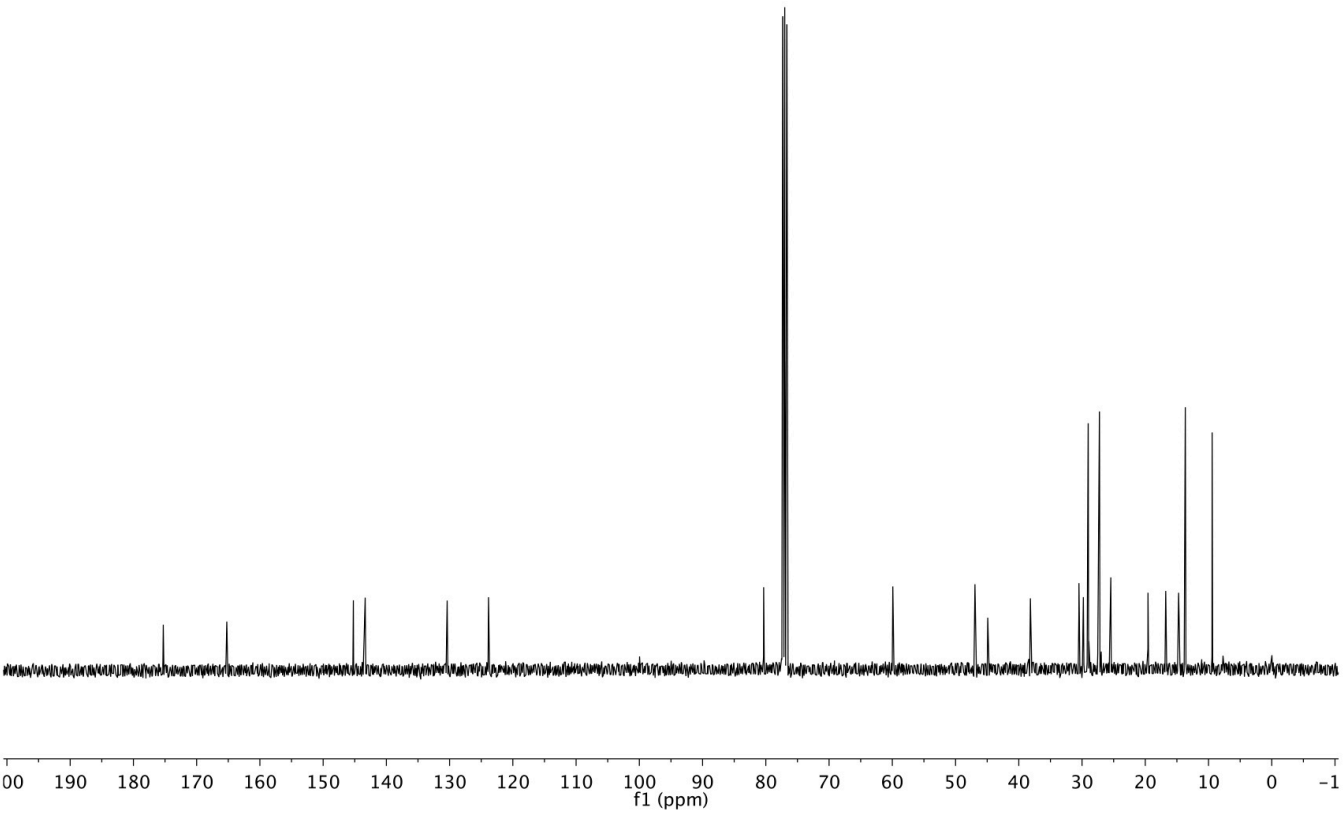

600 MHZ, DMSO-d6, 23 ºC
0.11
0.90
6.10 6.05 6.00 5.95 5.90 5.85 5.80
f1 (ppm)
* minor peaks due to coupling with 117Sn and 119Sn
1.00
0.11
0.90
f1 (ppm)

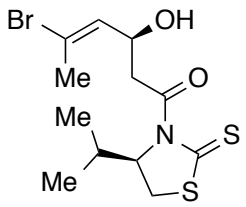

600 MHZ, DMSO-d6, 140 ºC
1.00
0.10
0.85
f1 (ppm)


SnBu3
O
N
H
Me
O
H
N
Me
O
H
Me

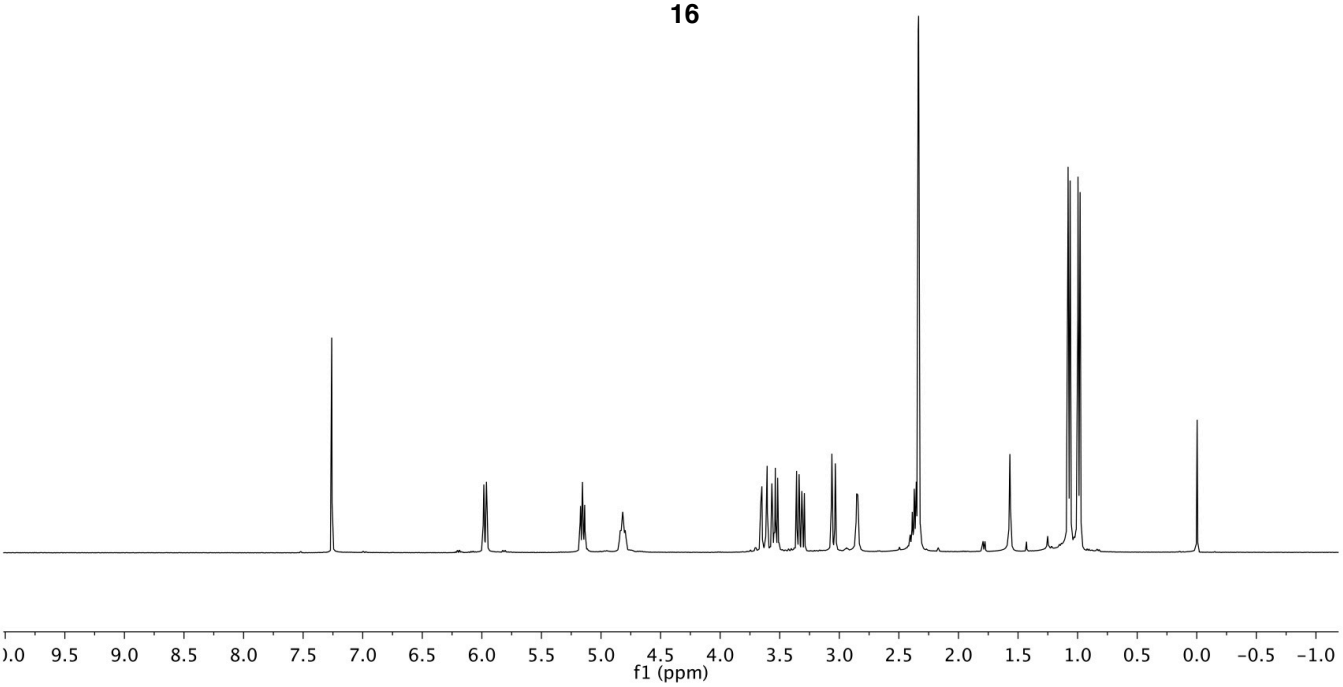
13

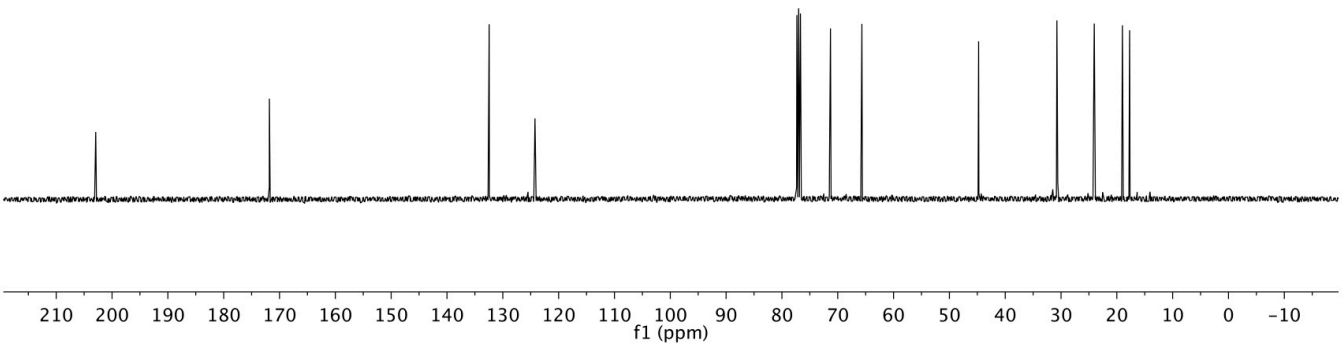
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)

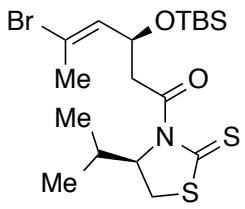

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −1
f1 (ppm)


Br
OH
Me
O
Me
N
S
Me
S

16

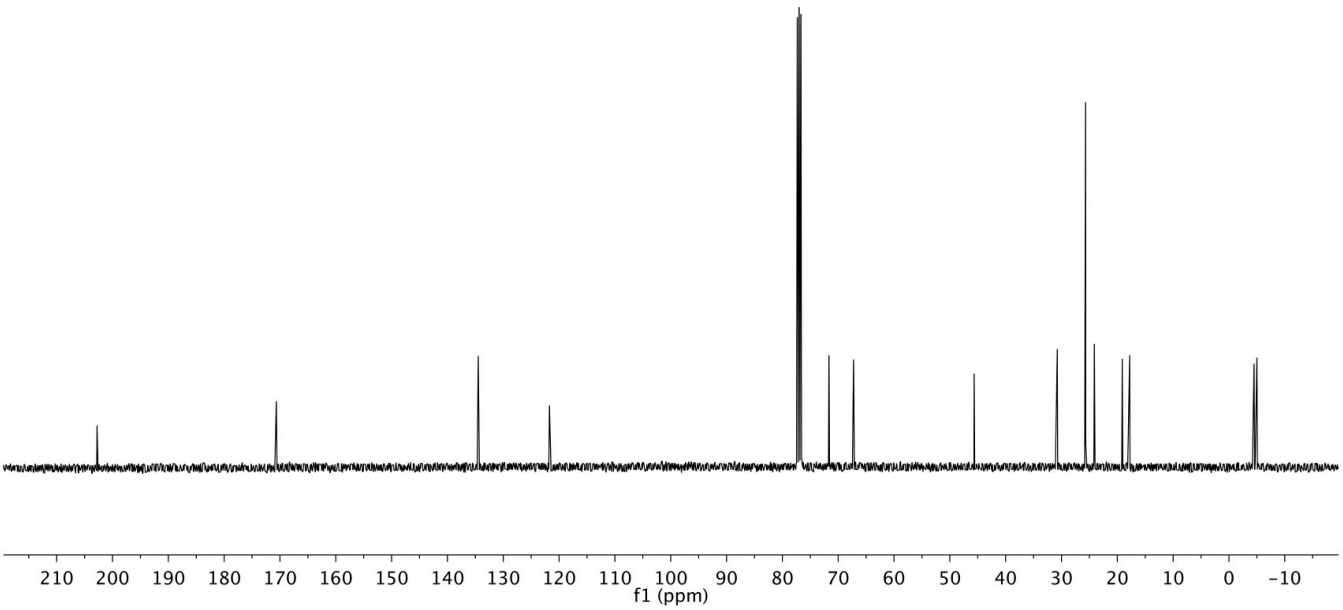

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

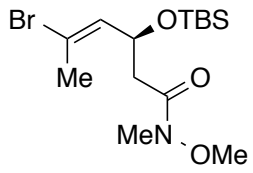

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
Me
N
S
Me
S

SI-2

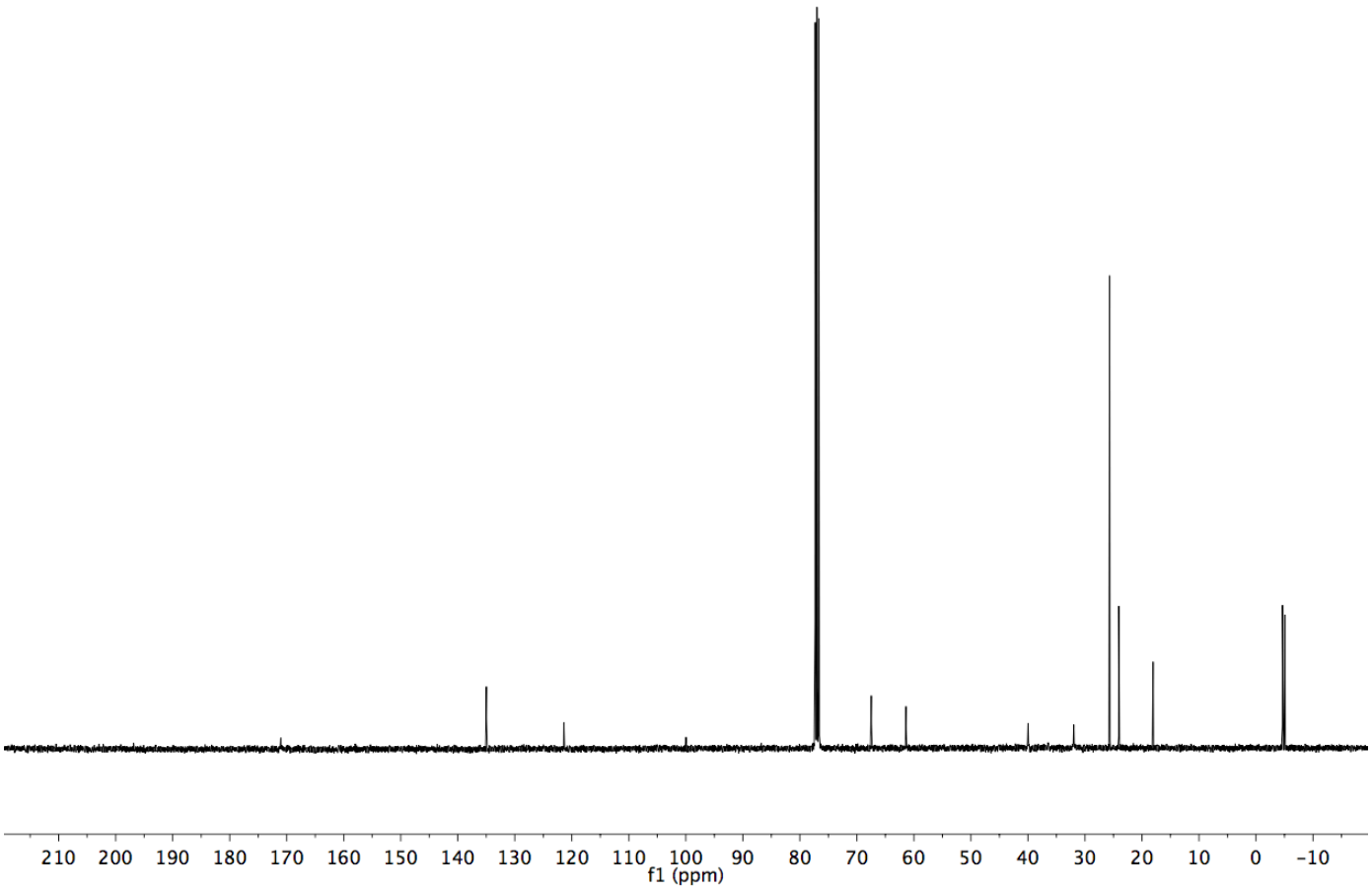
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

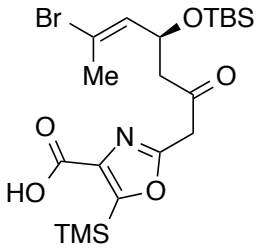

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
MeN
OMe

17

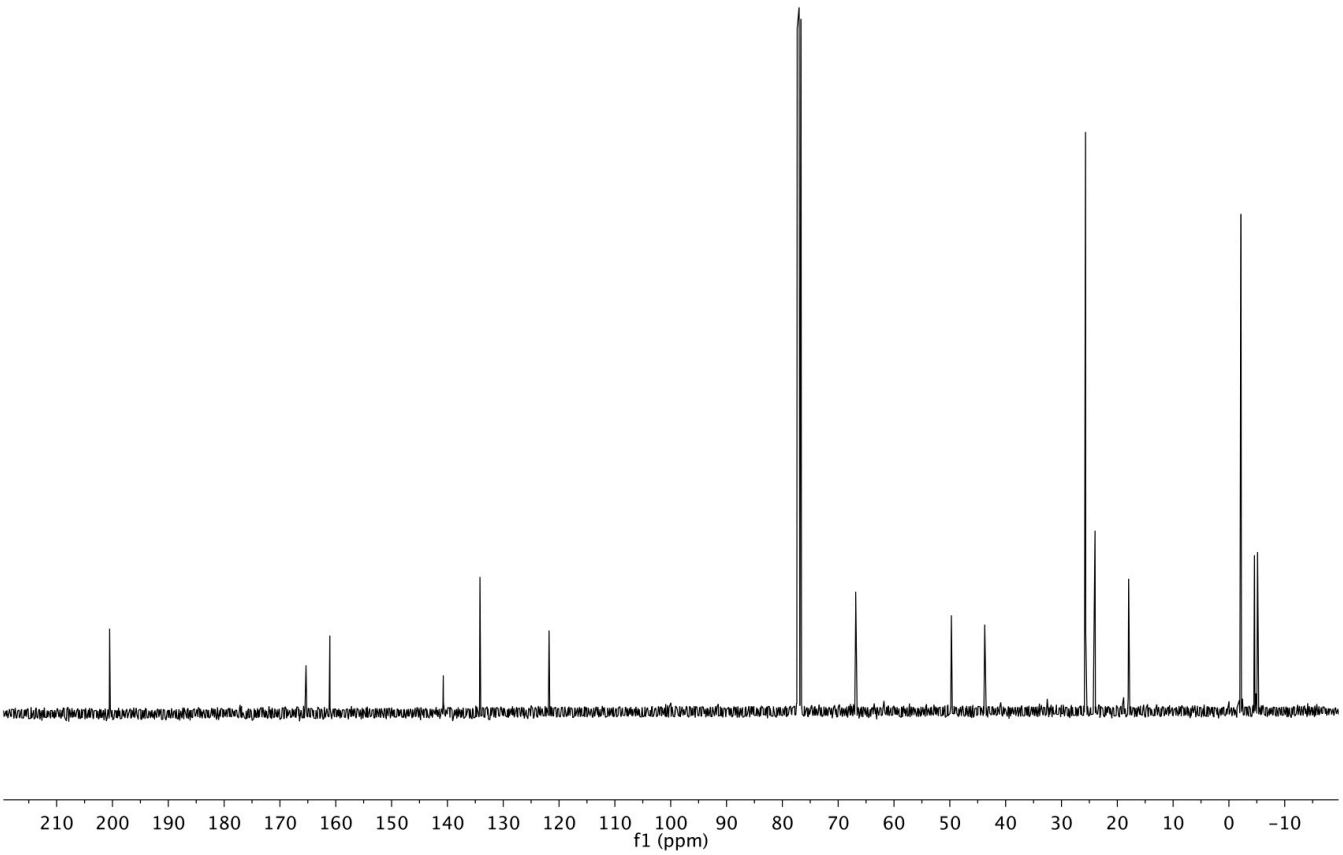
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

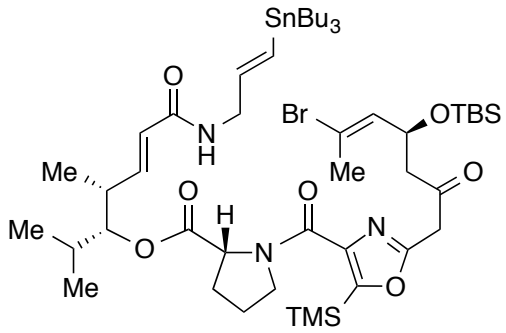

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
O
N
HO
O
TMS

19

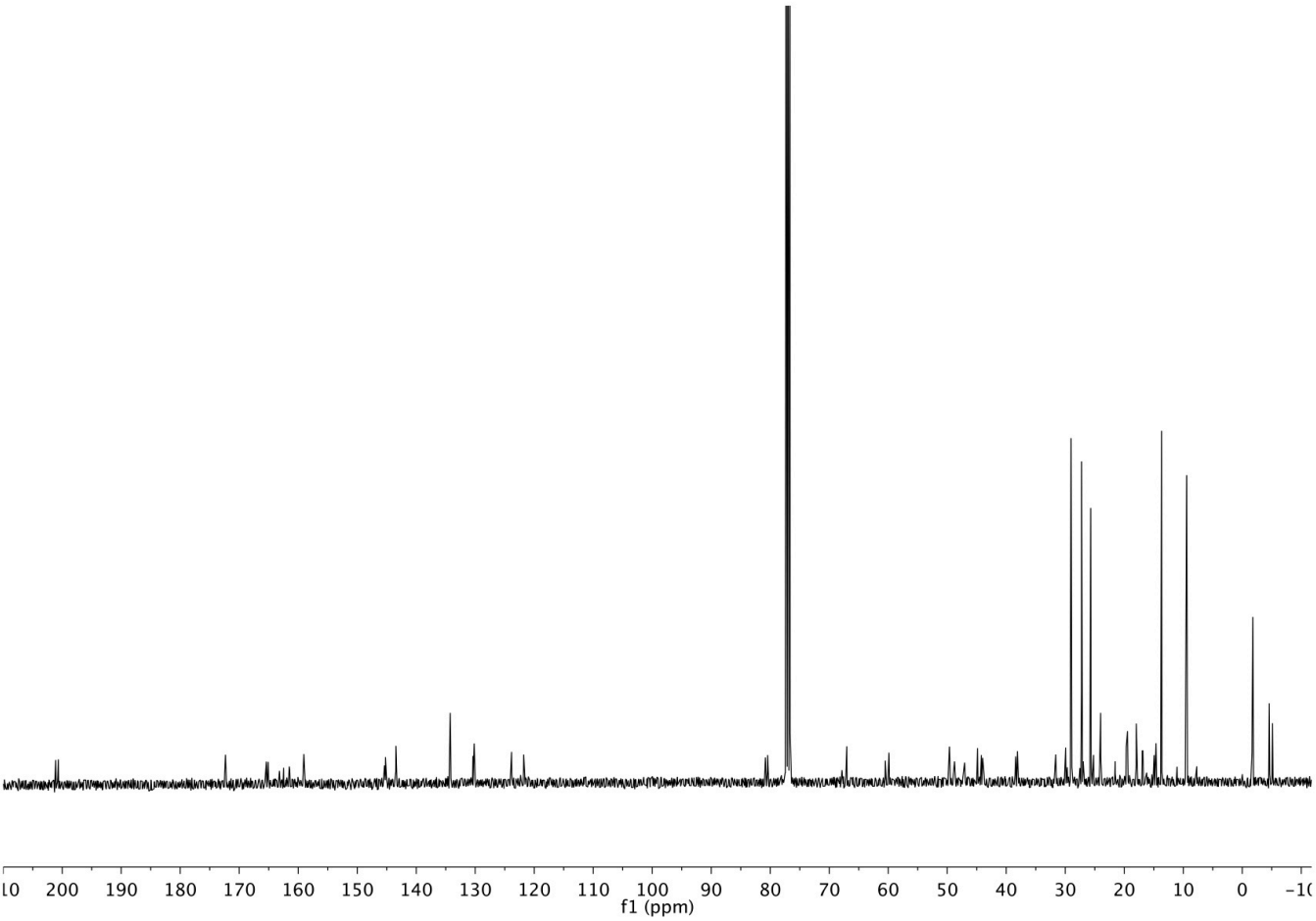
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

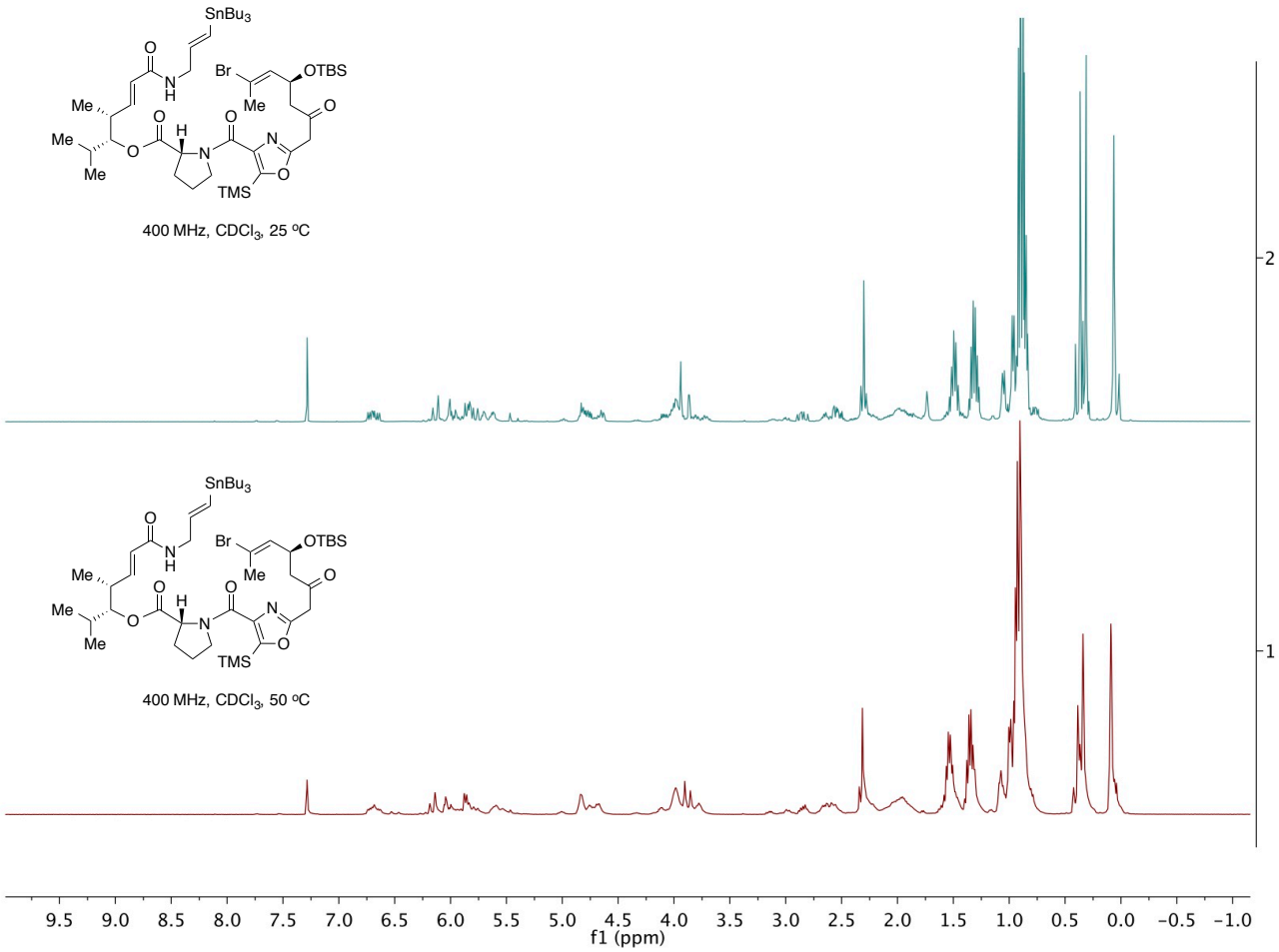

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

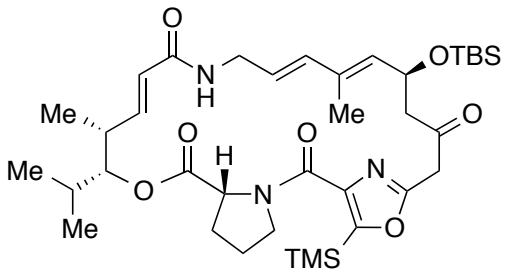

SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
H
Me
O
N
N
O
Me
O
TMS

20

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

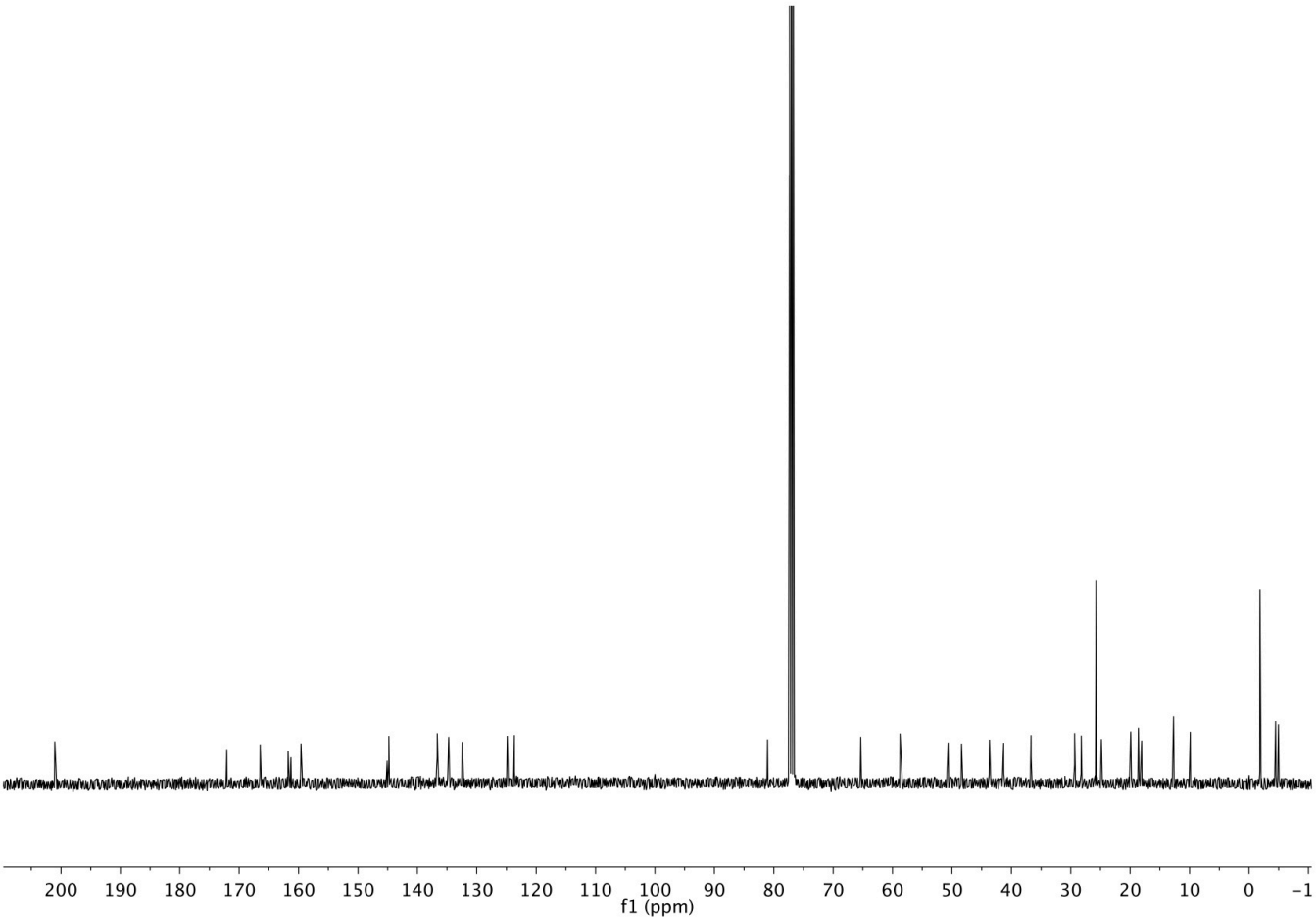

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

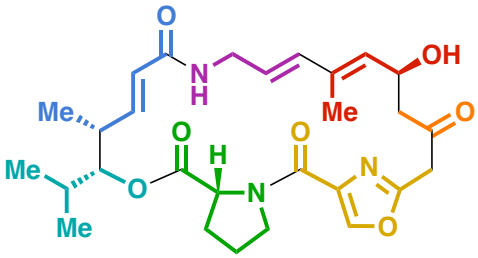

SnBu3
Br
OTBS
Me
Me
Me
Me
O
N
H
TMS
400 MHz, CDCl3, 25 ºC
2
SnBu3
Br
OTBS
Me
Me
Me
Me
O
N
H
TMS
400 MHz, CDCl3, 50 ºC
1
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
H
O
Me
O
N
N
O
Me
TMS

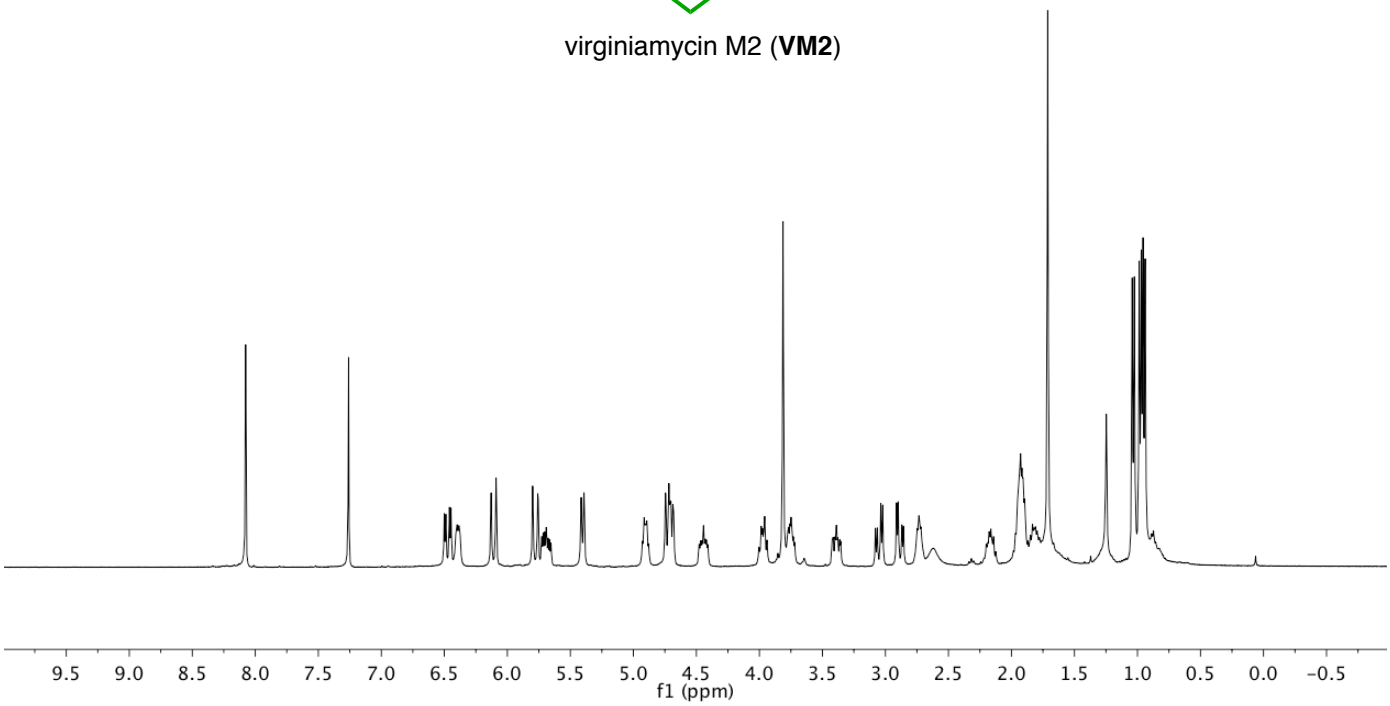
SI-3

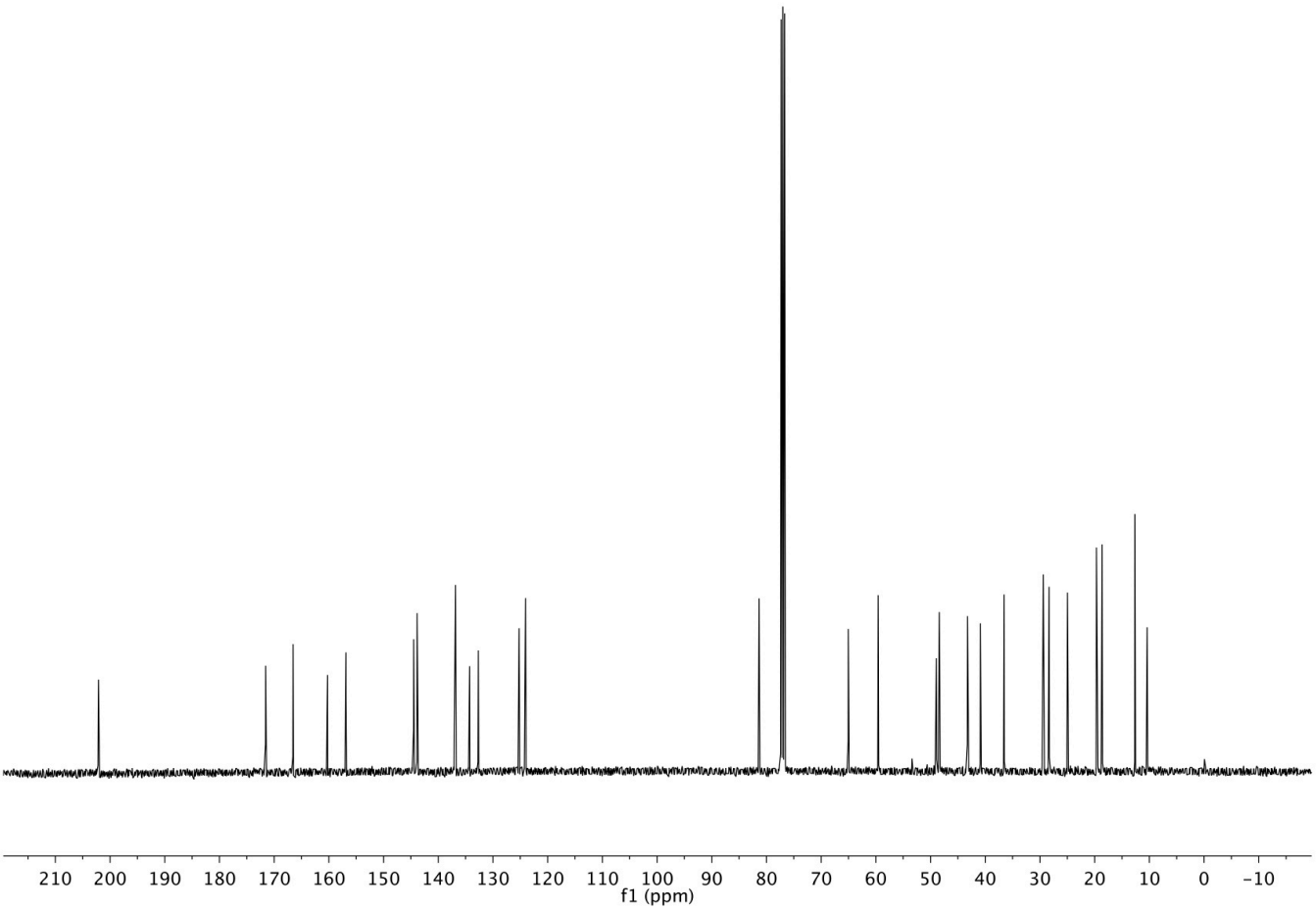
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

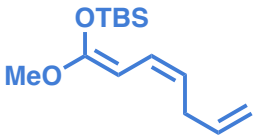

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



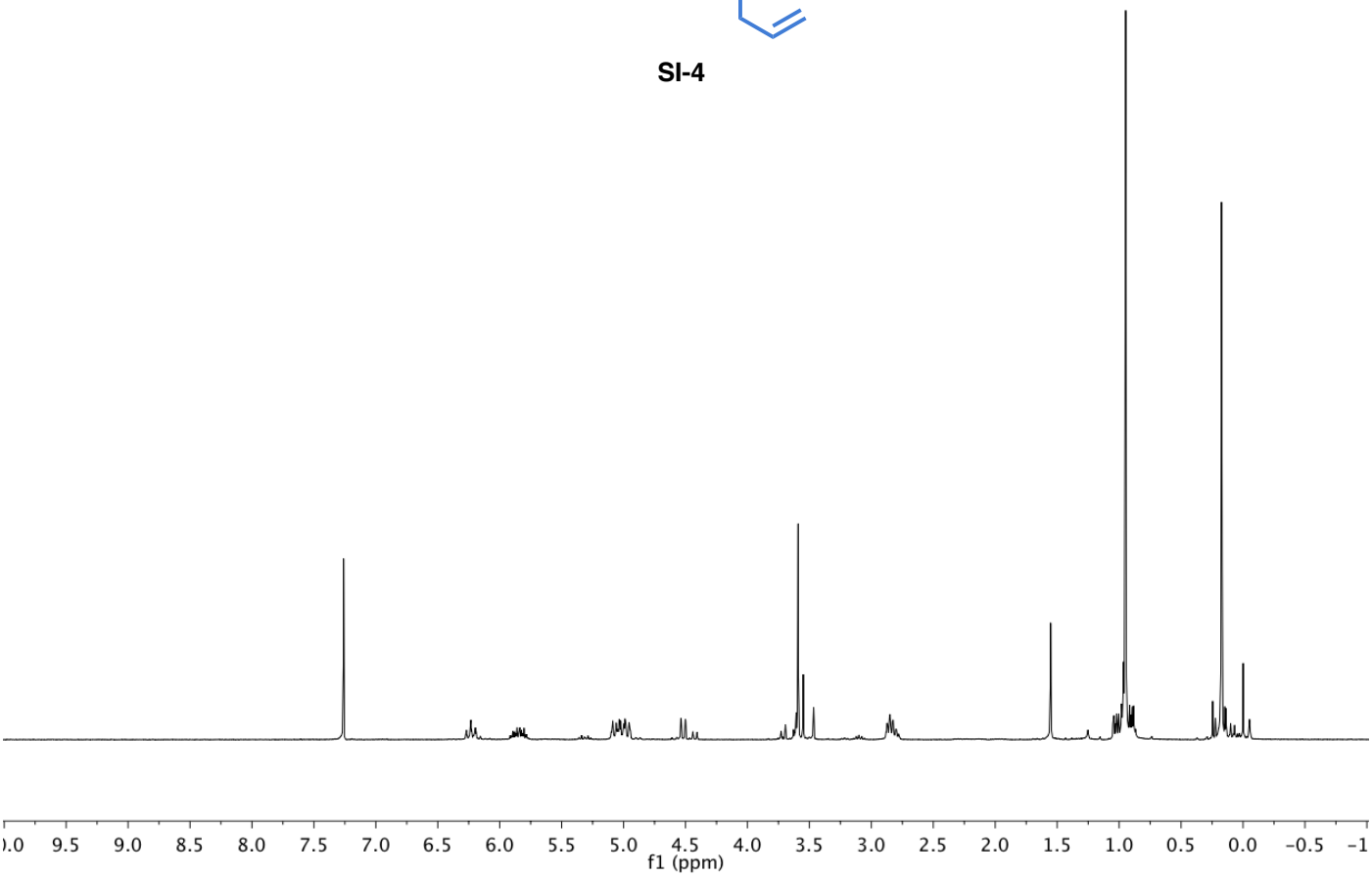
virginiamycin M2 (**VM2**)

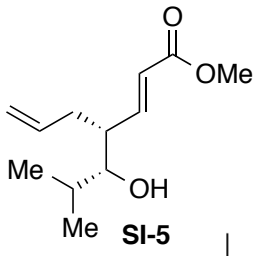




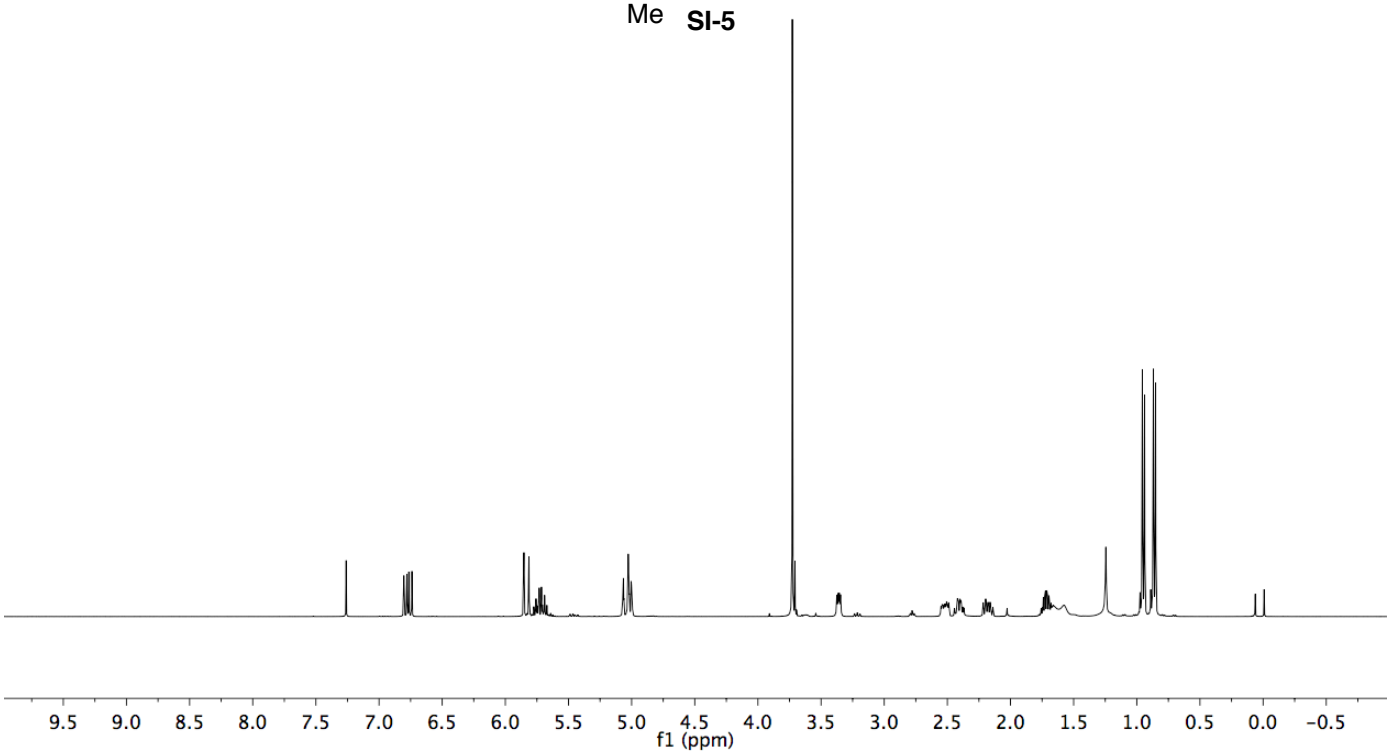

OTBS
MeO

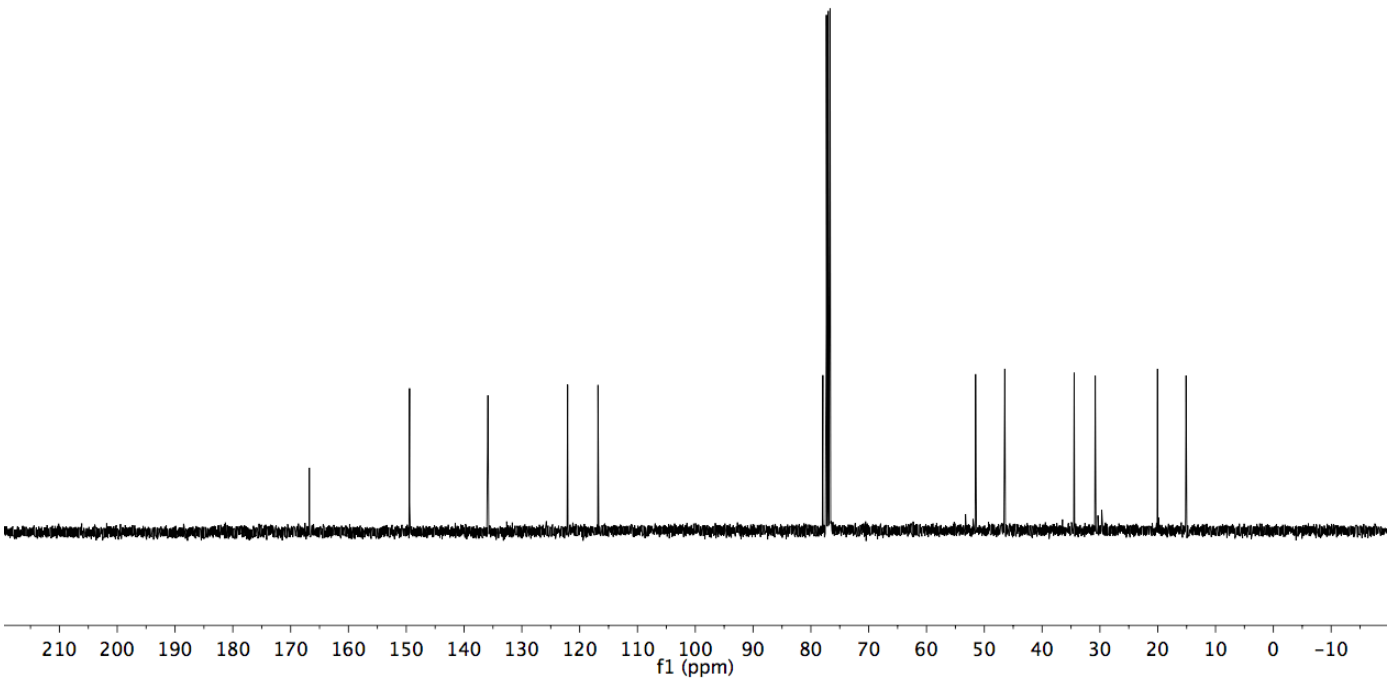
SI-4

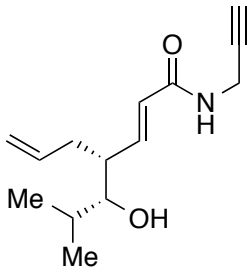

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


O
OMe
Me
OH
Me

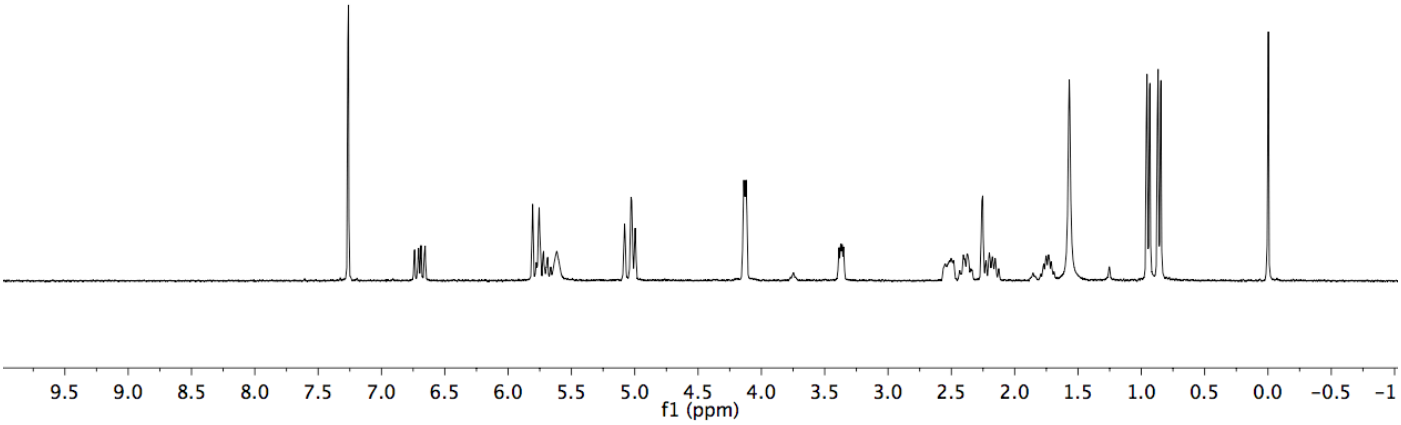
SI-5

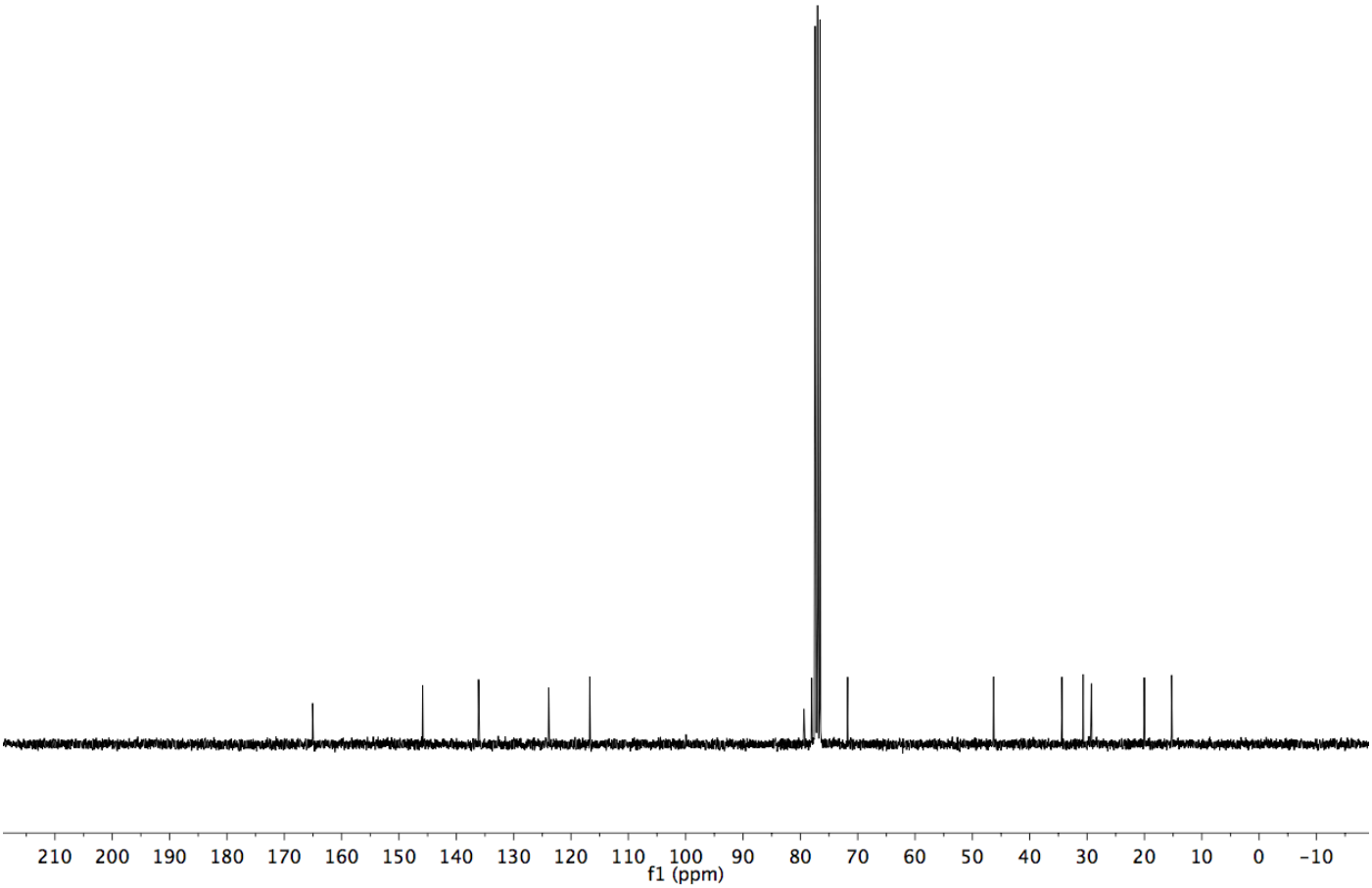

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

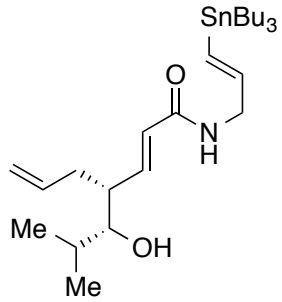

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
Me
OH
Me

SI-6

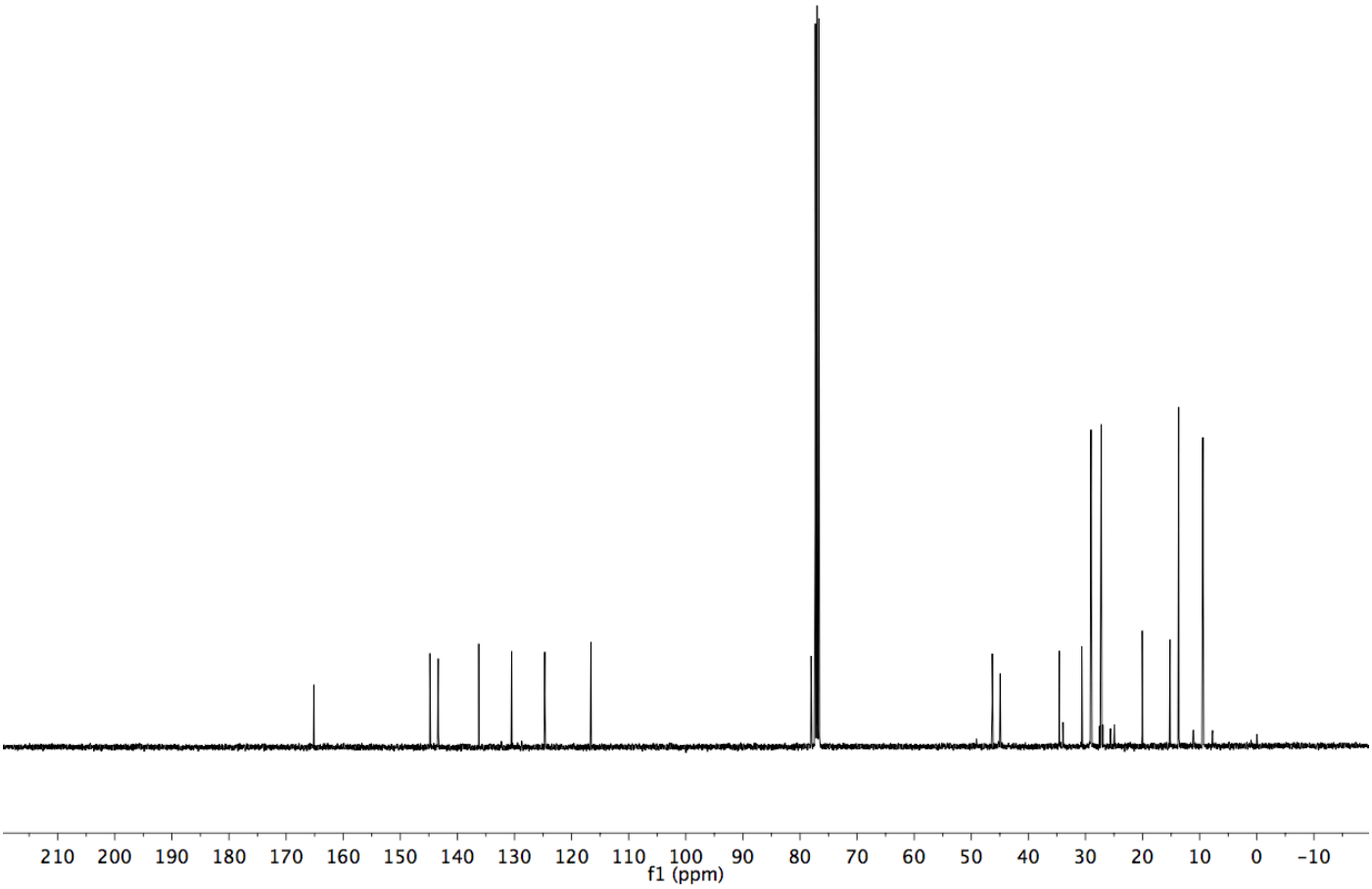

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

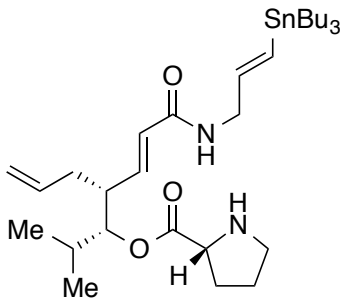

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
OH
Me

SI-7

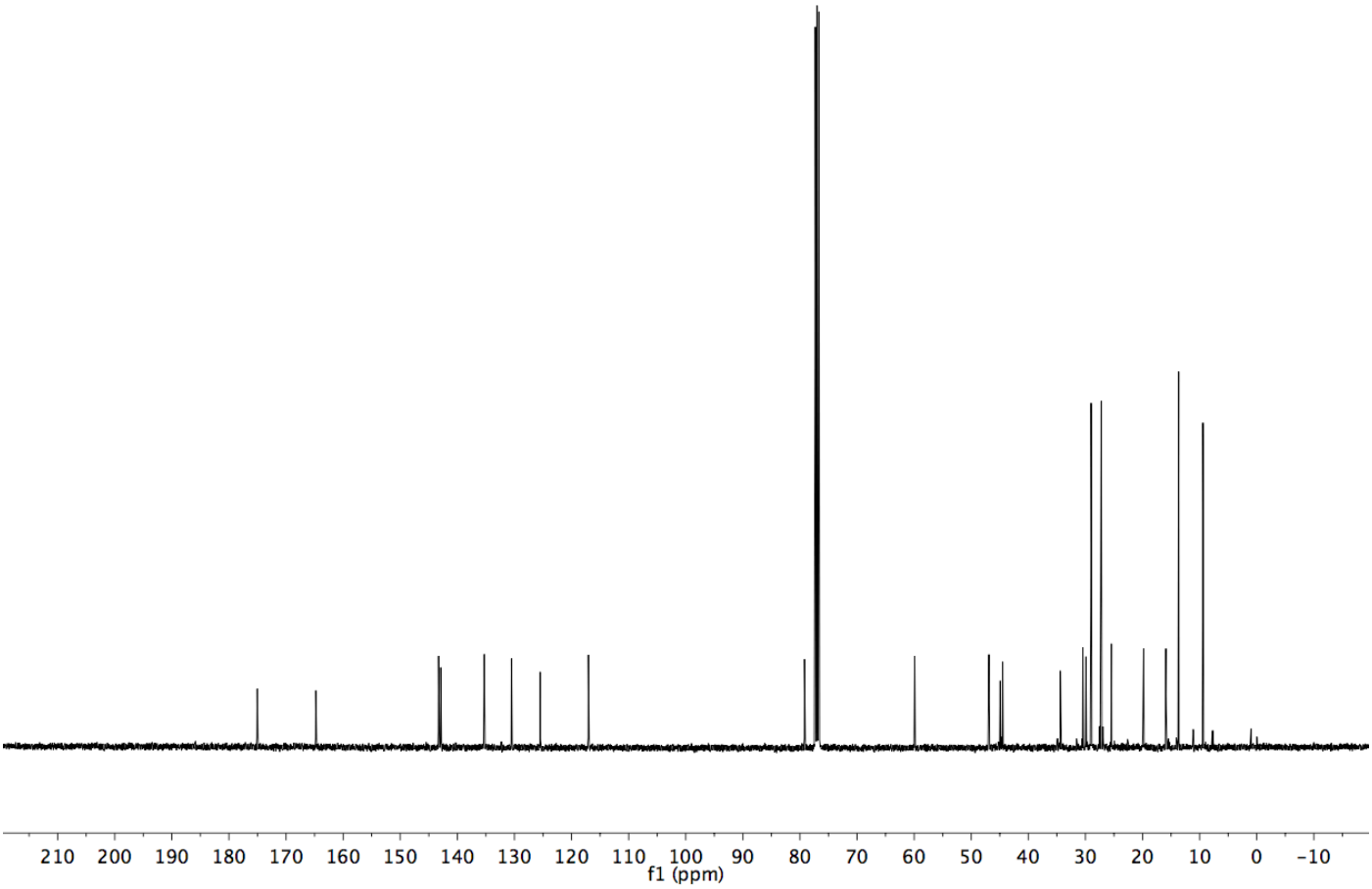
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

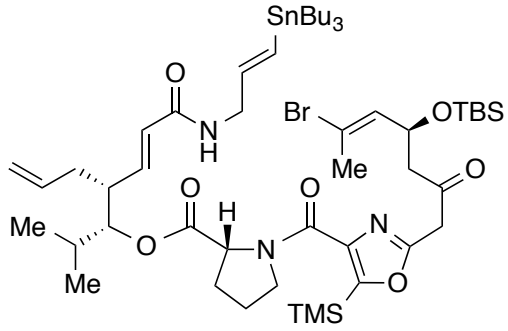

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
O
H
N
Me
O
H
Me

SI-8

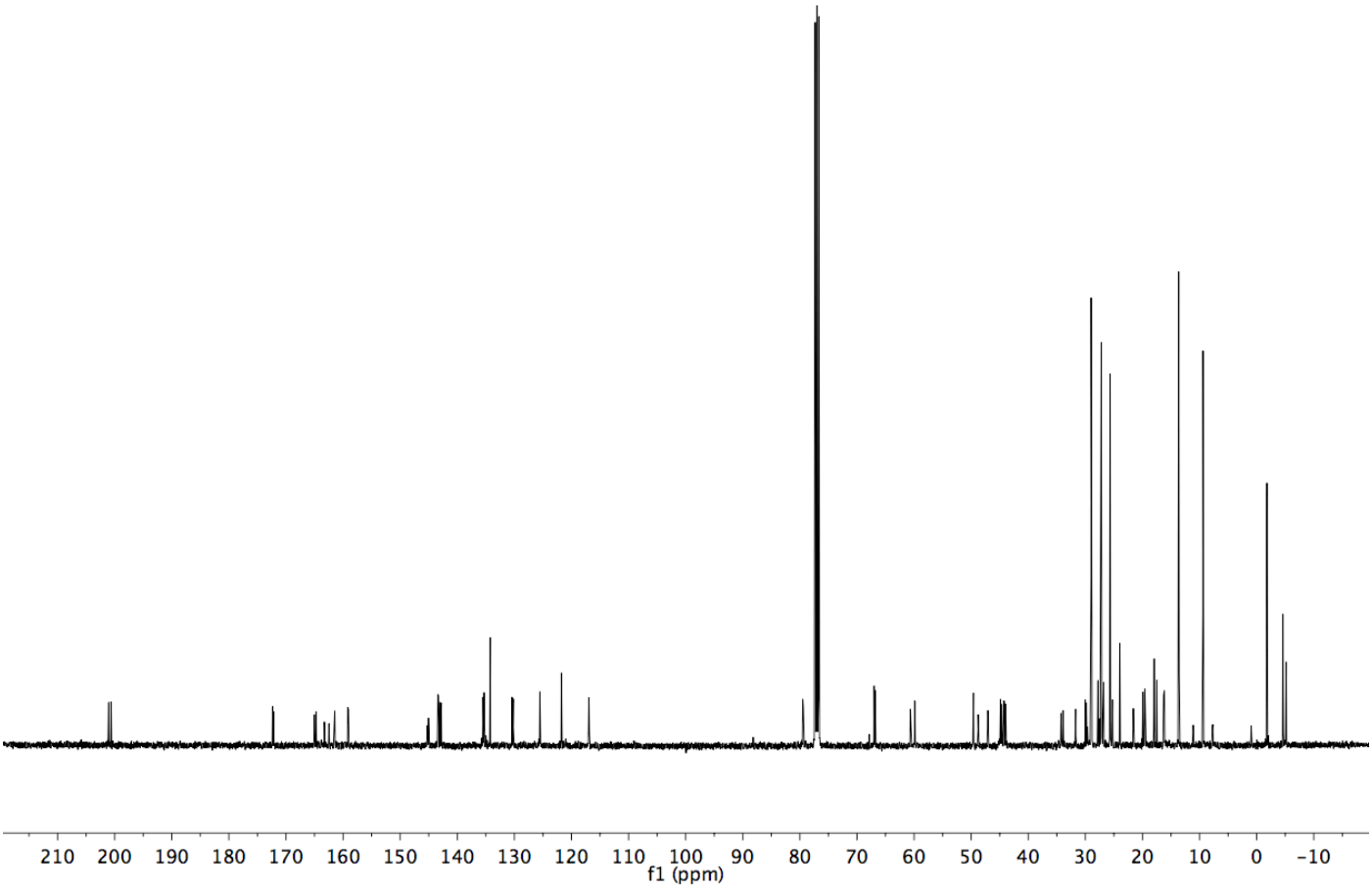
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

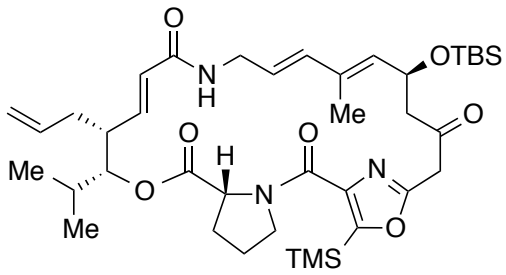

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
O
O
O
H
Me
O
N
N
O
Me
TMS

SI-9

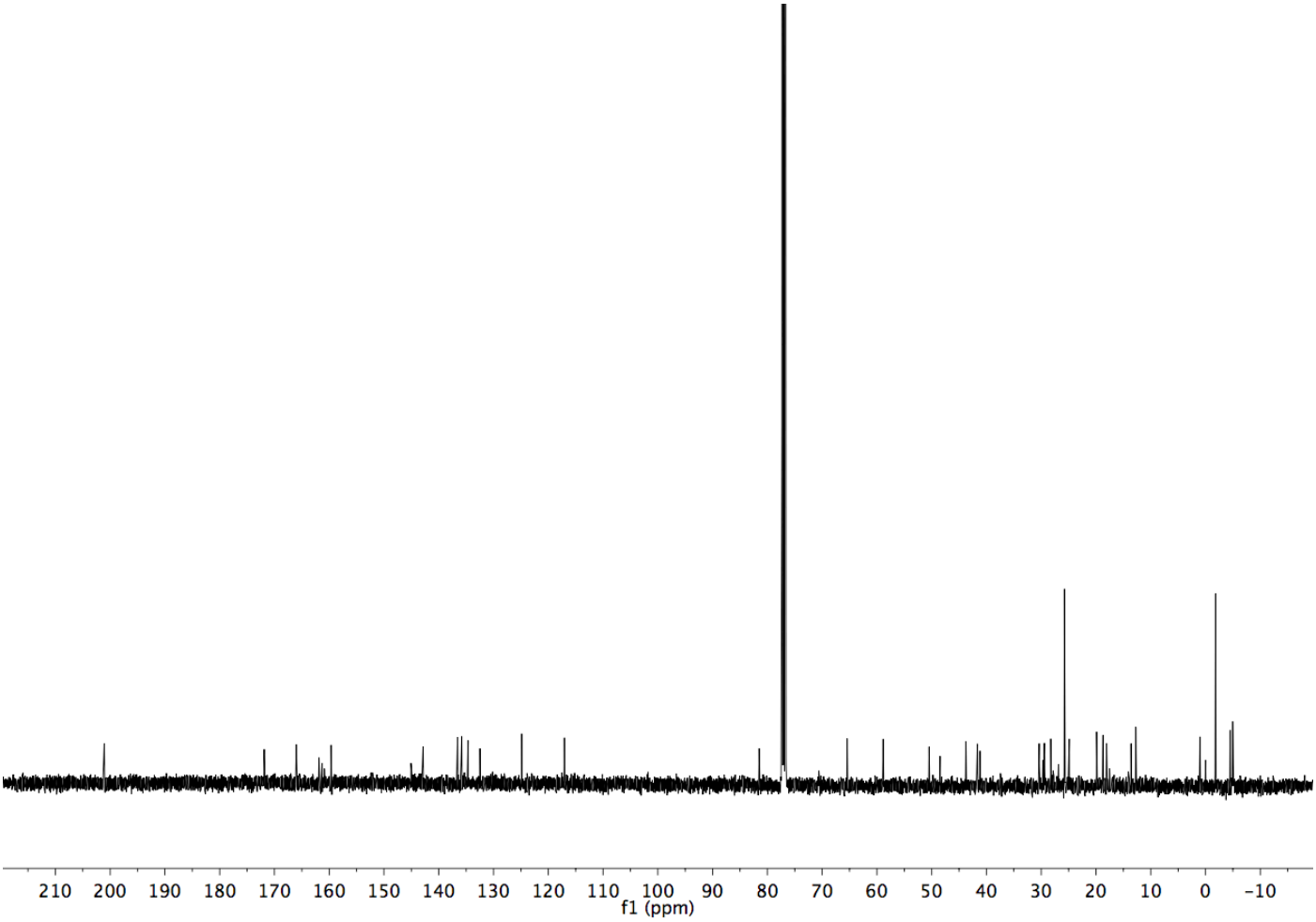
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

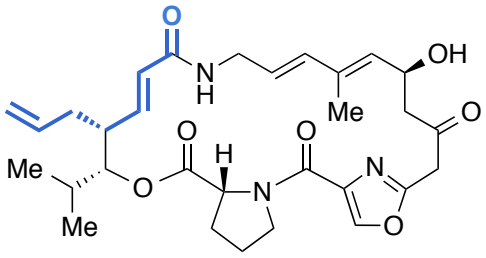

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
O
Me
O
O
H
N
N
O
O
Me
TMS

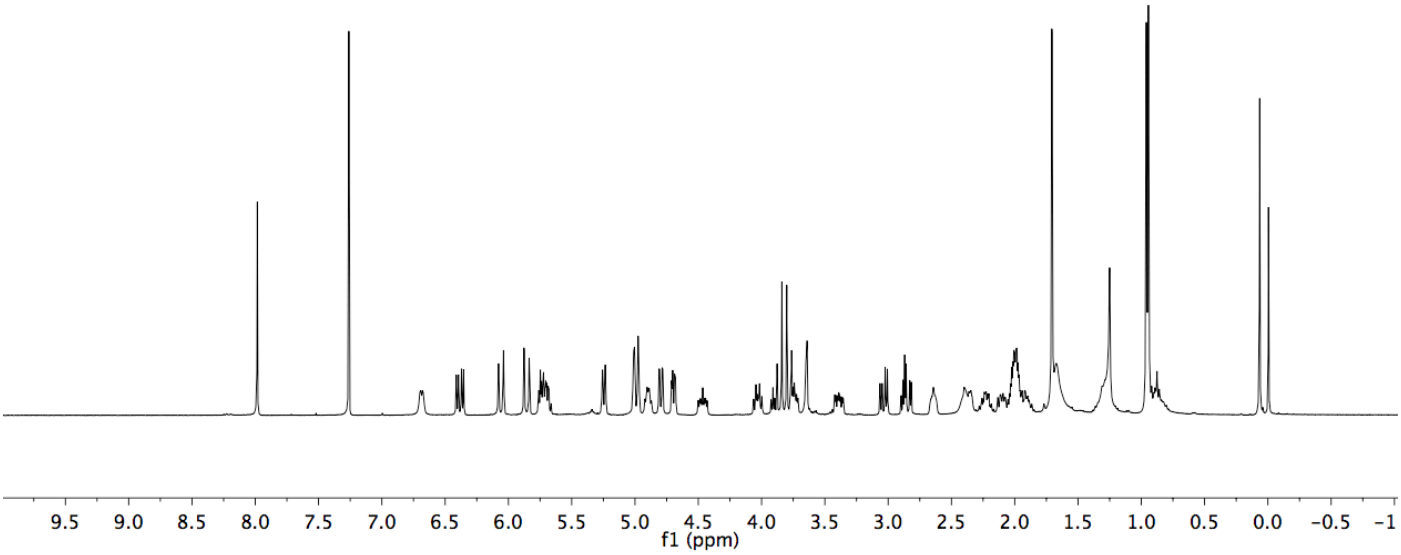
SI-10

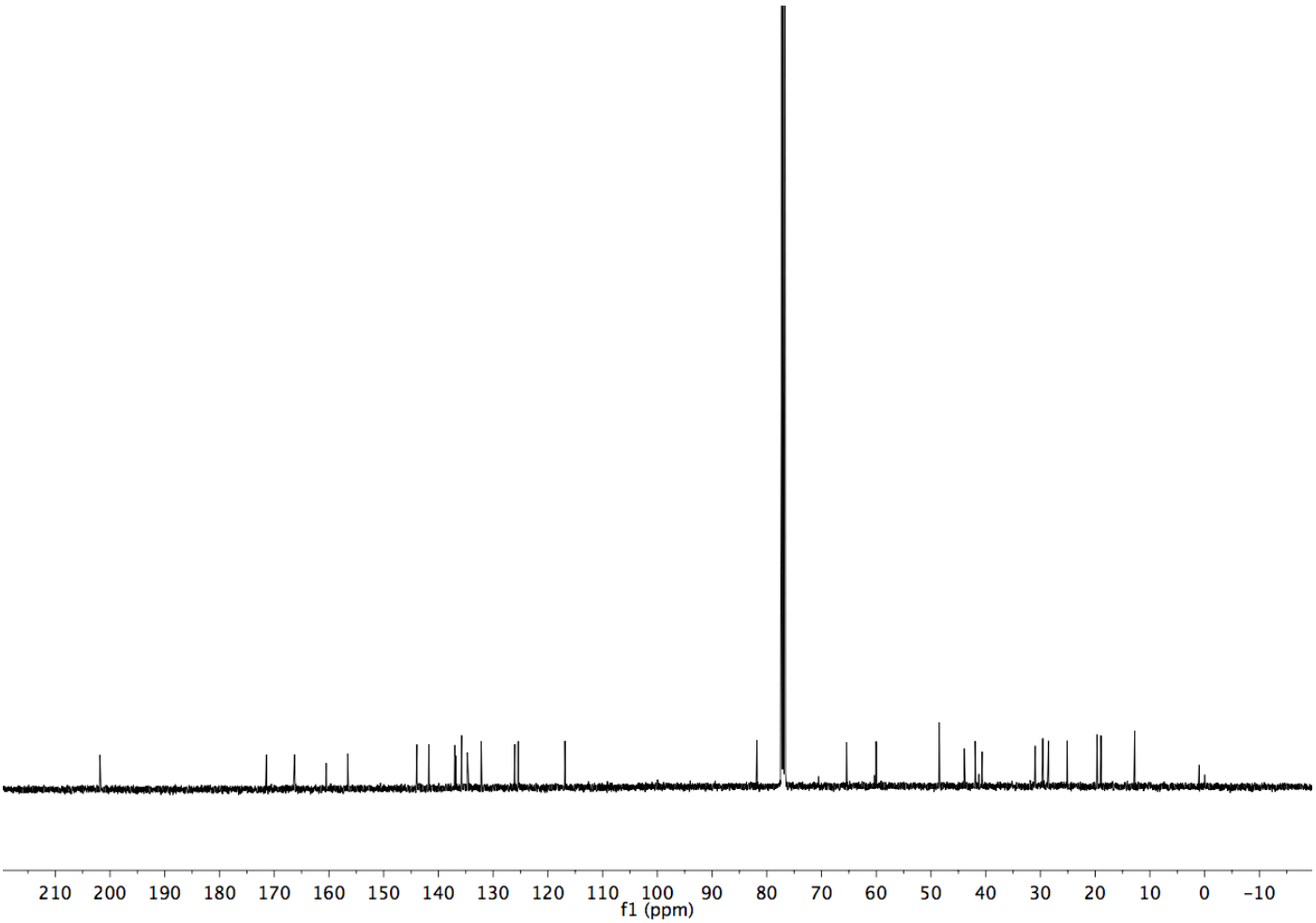
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

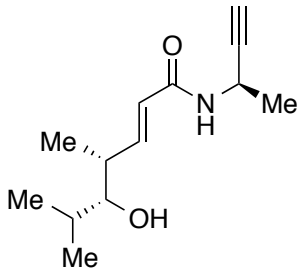

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
O
O
O
H
Me
O
N
N
Me
O

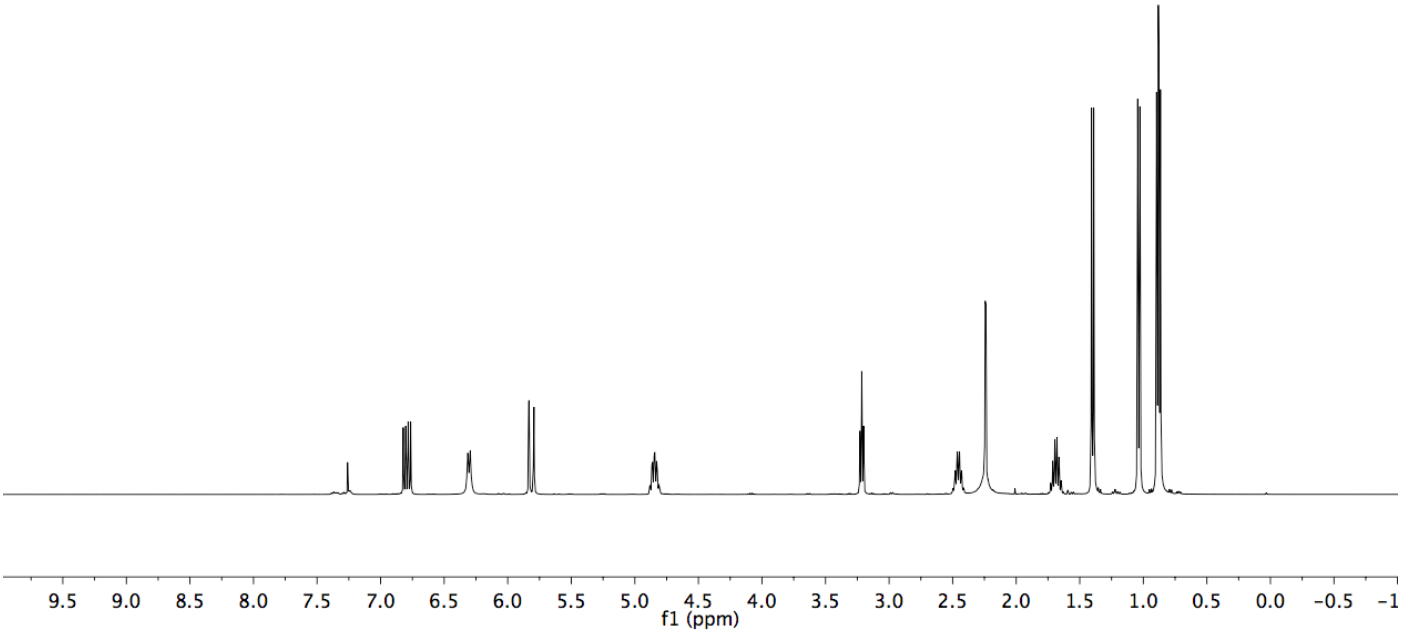
21

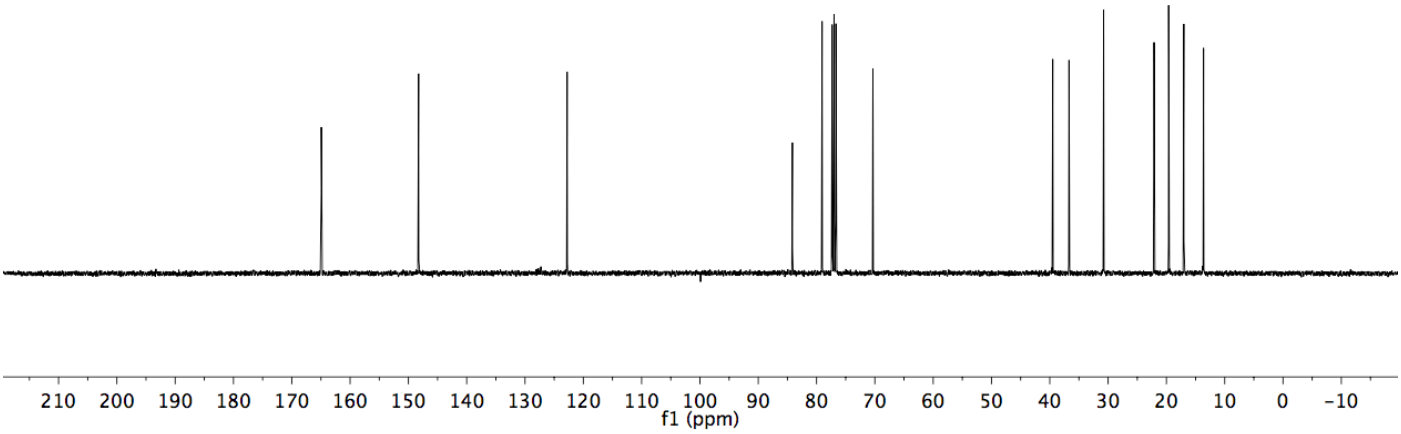

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

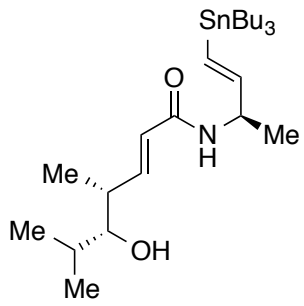

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
Me
Me
Me
OH
Me

SI-12

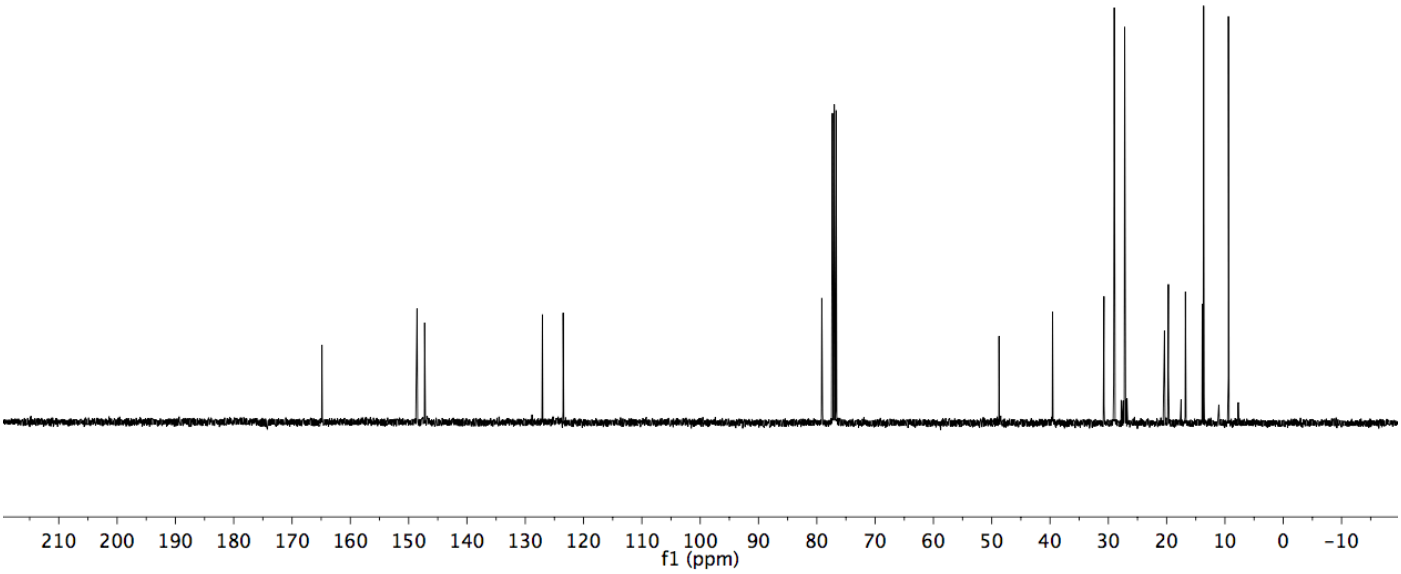

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

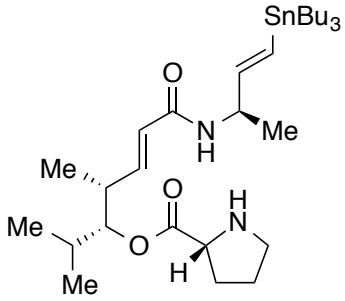

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Me
Me
OH
Me

SI-13

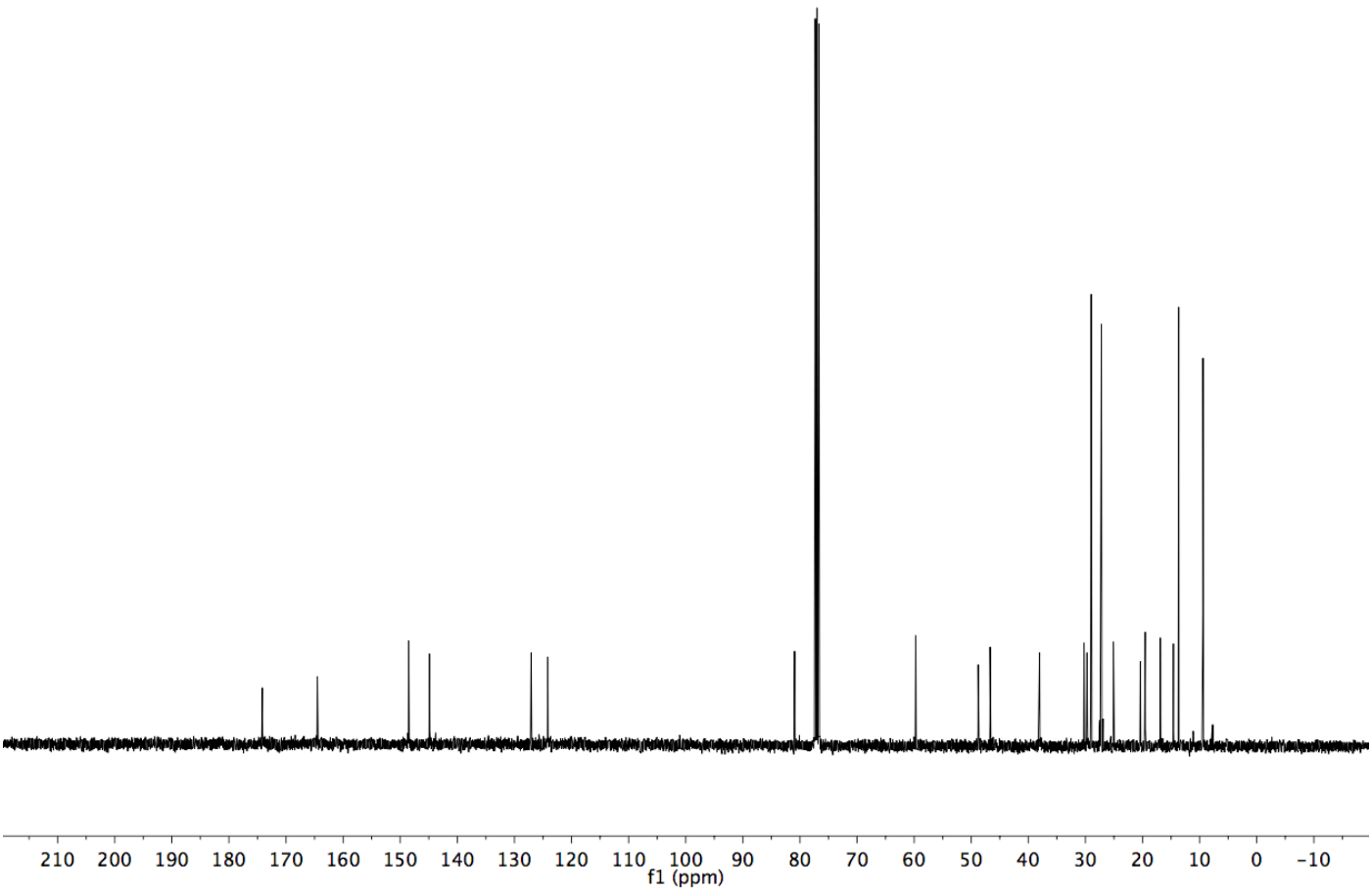
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

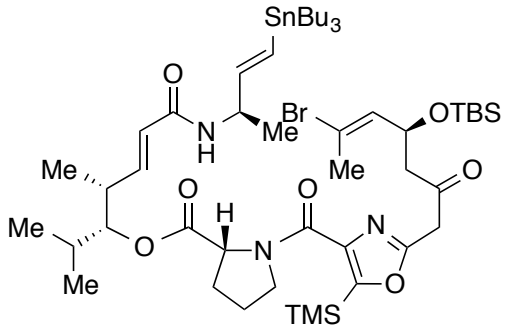

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Me
O
H
N
O
H
Me
Me

SI-14

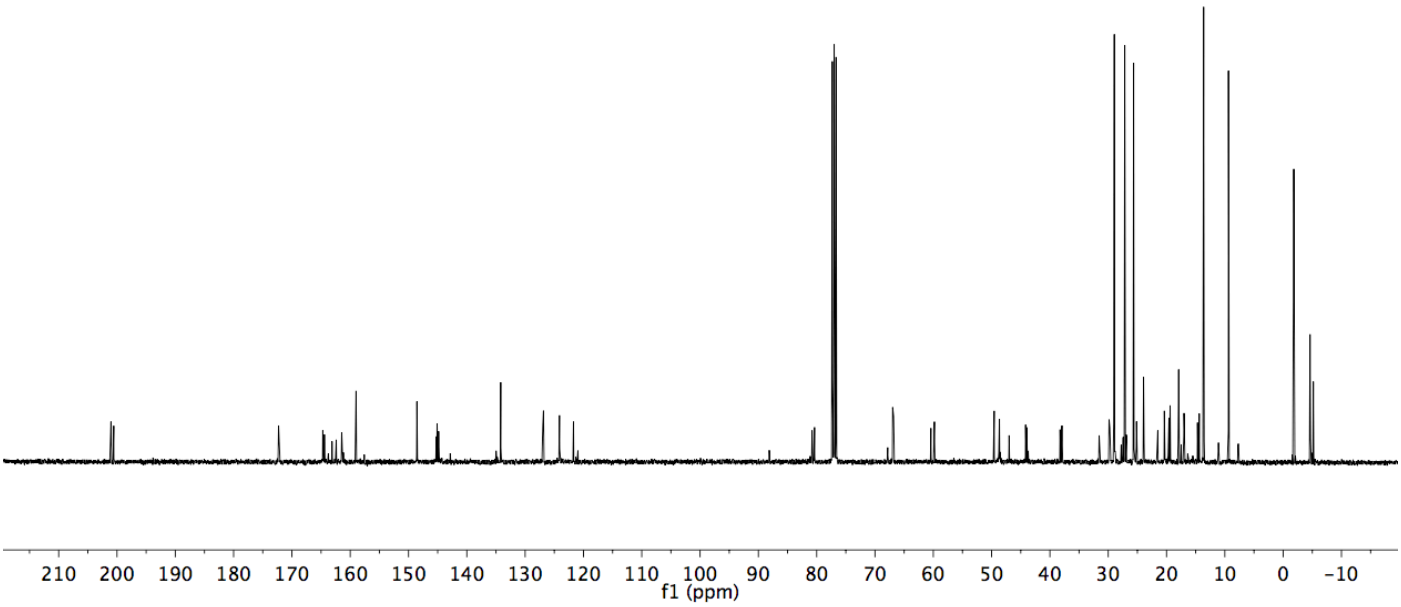
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

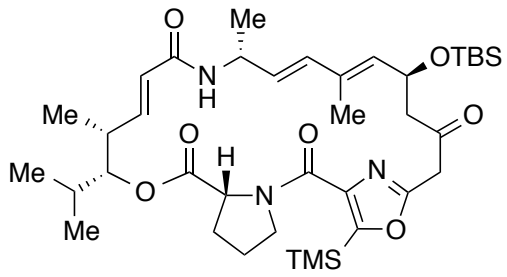

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Br
OTBS
Me
Me
O
O
O
H
Me
O
N
N
Me
O
TMS

SI-15

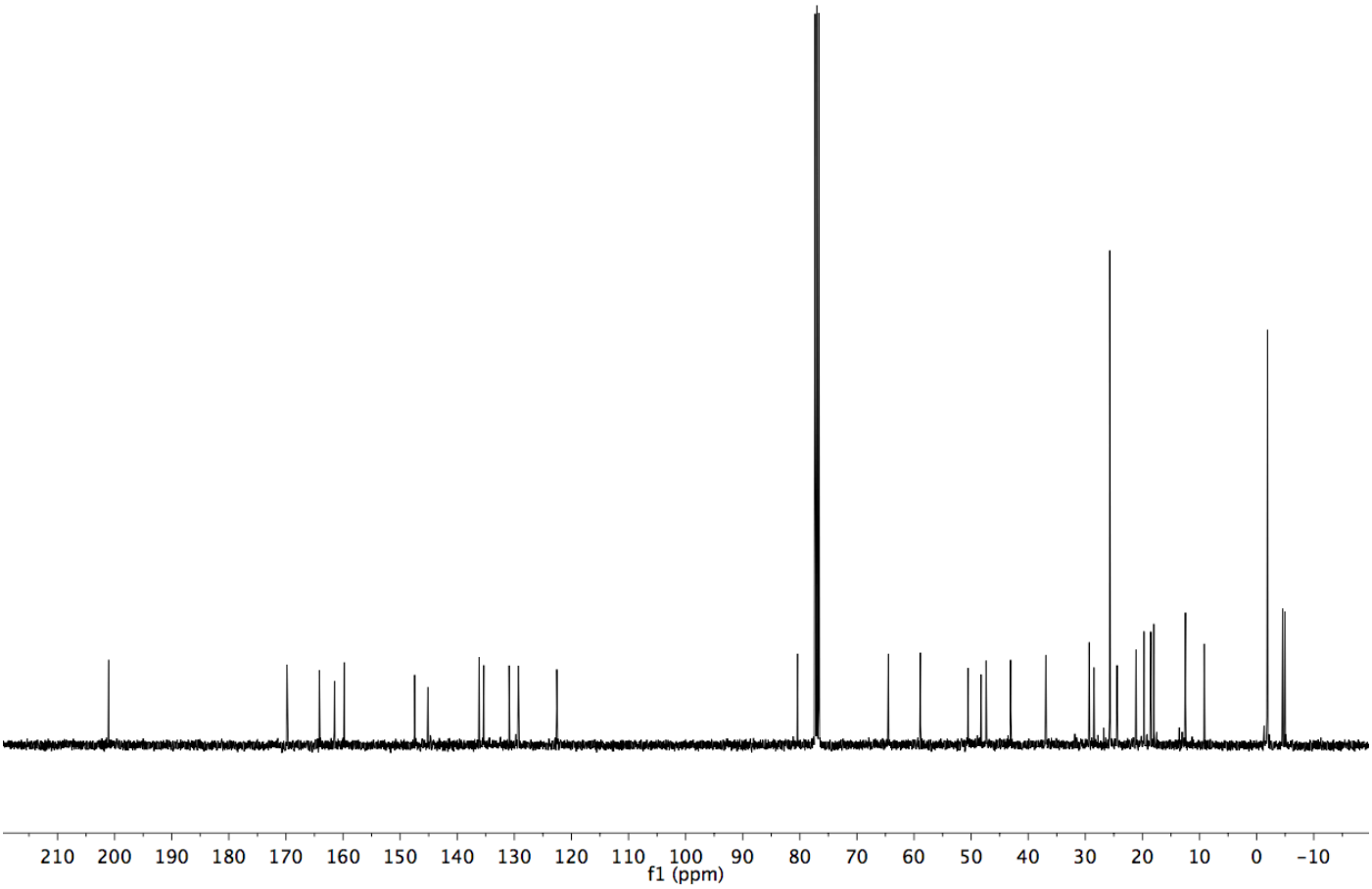
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

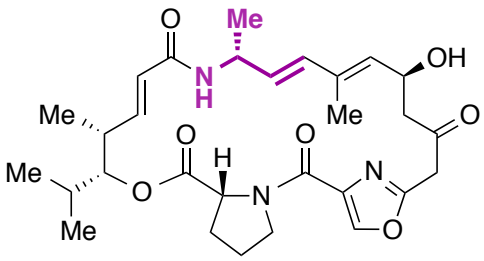

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OTBS
Me
Me
O
O
H
O
Me
O
N
N
Me
O
TMS

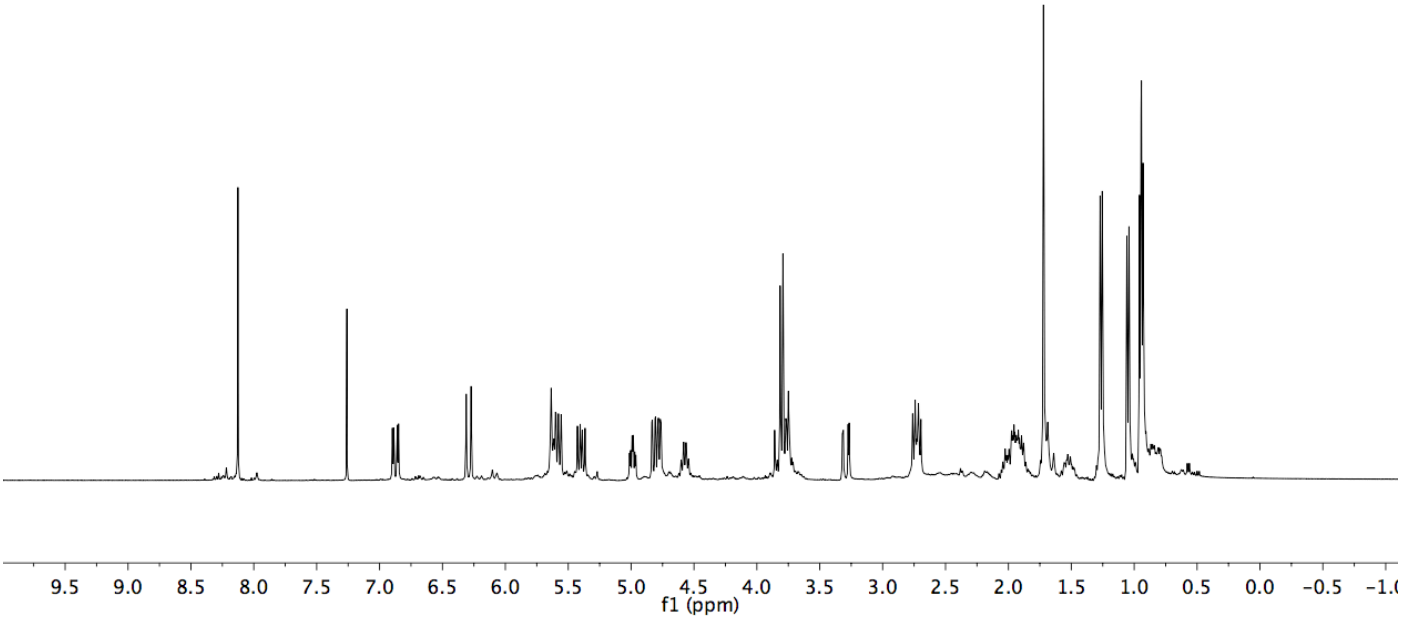
SI-16

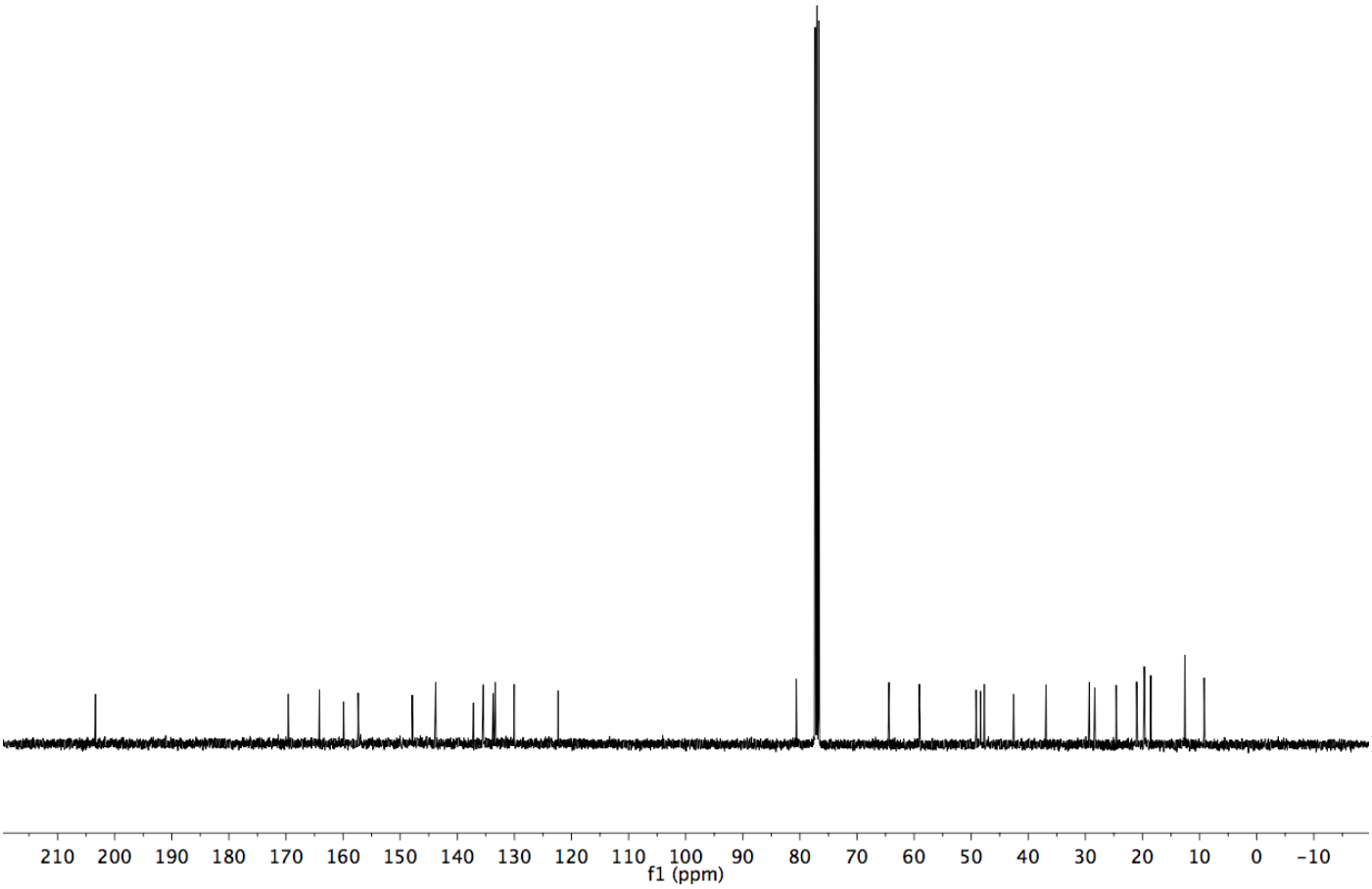
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

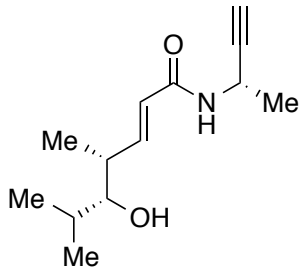

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OH
Me
Me
O
O
O
H
Me
O
N
N
Me
O

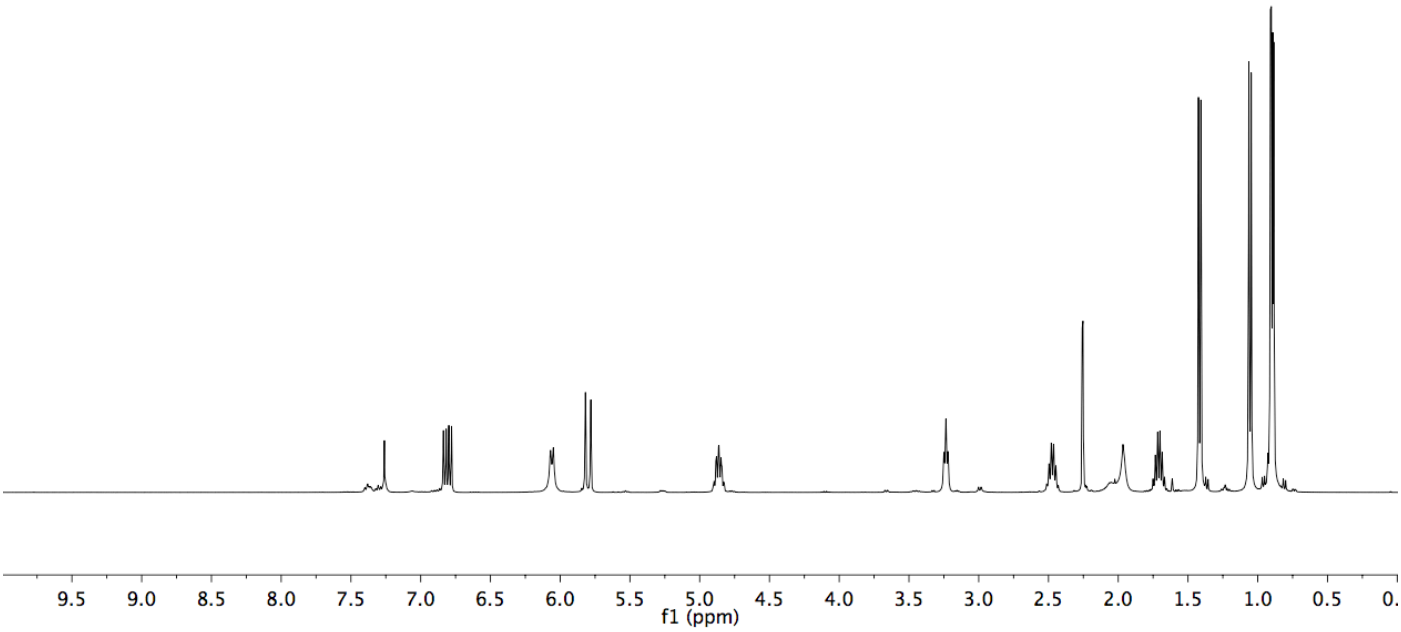
22

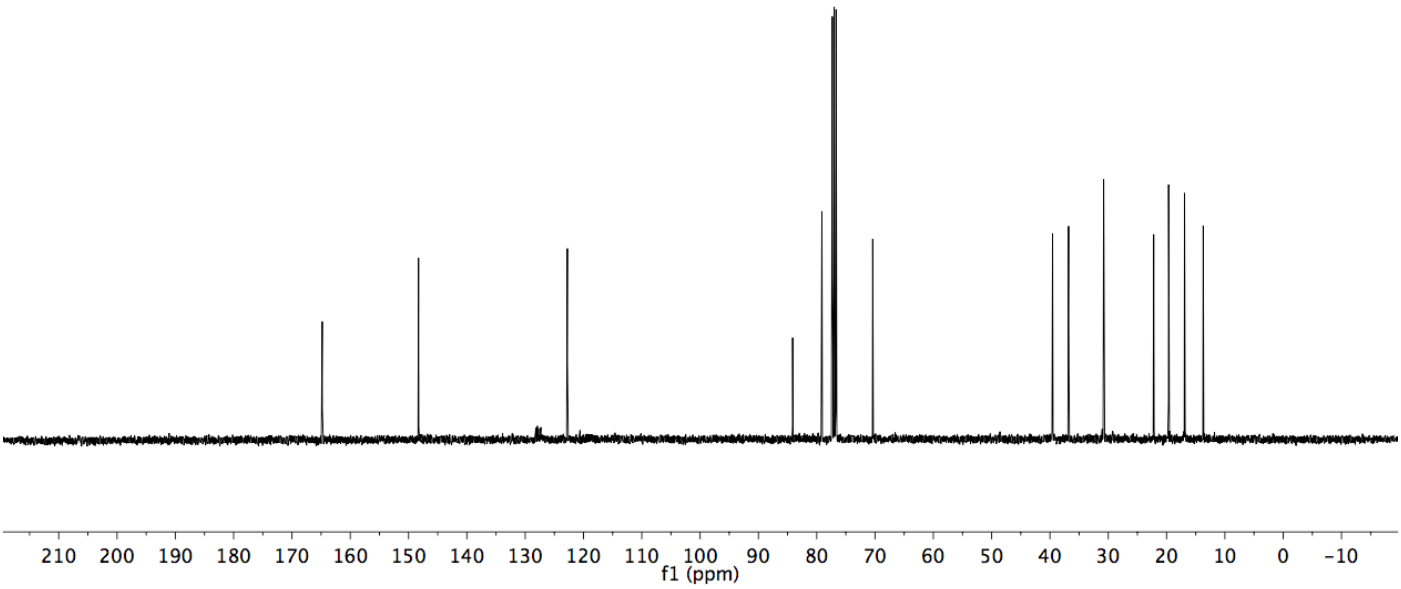

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

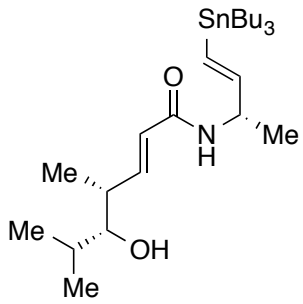

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
Me
Me
Me
OH
Me

SI-18

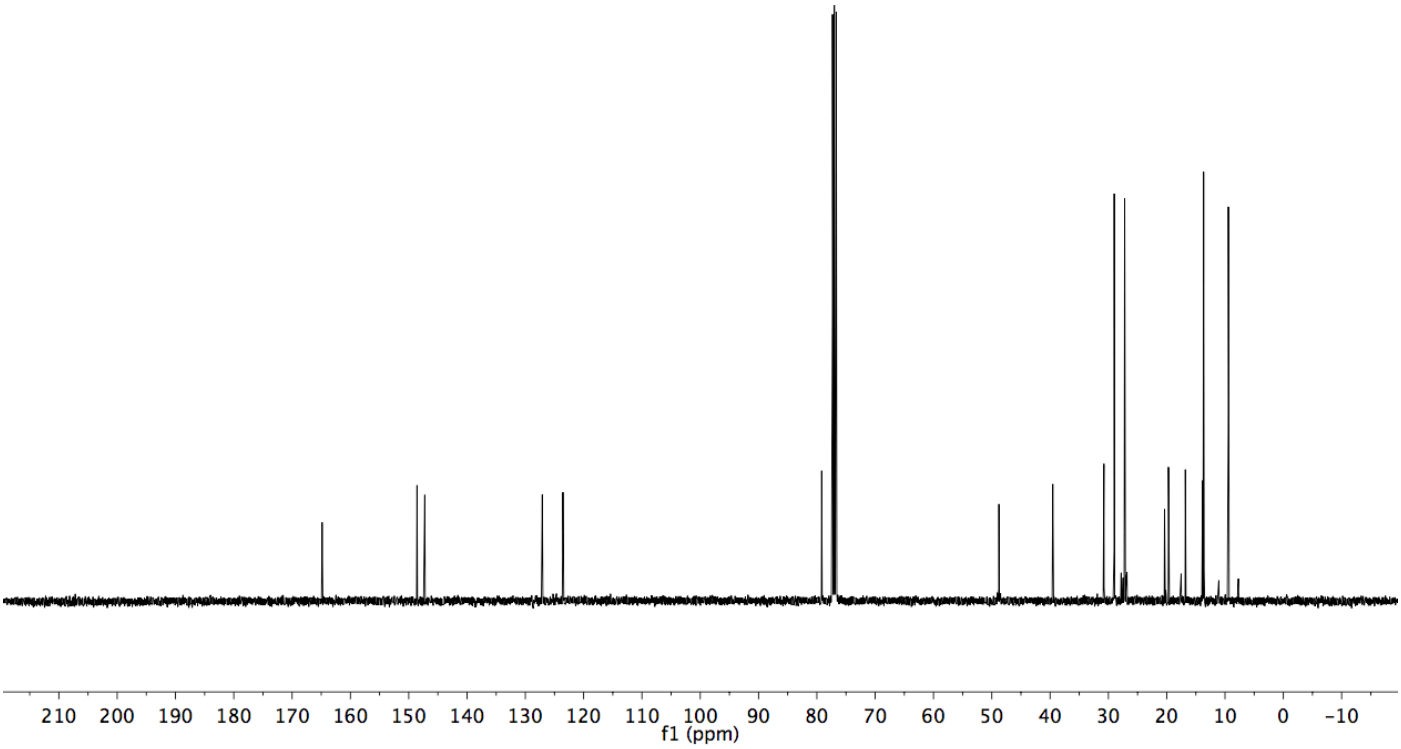

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

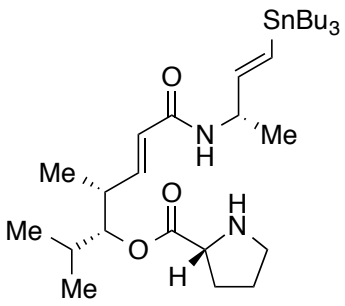

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Me
Me
OH
Me

SI-19

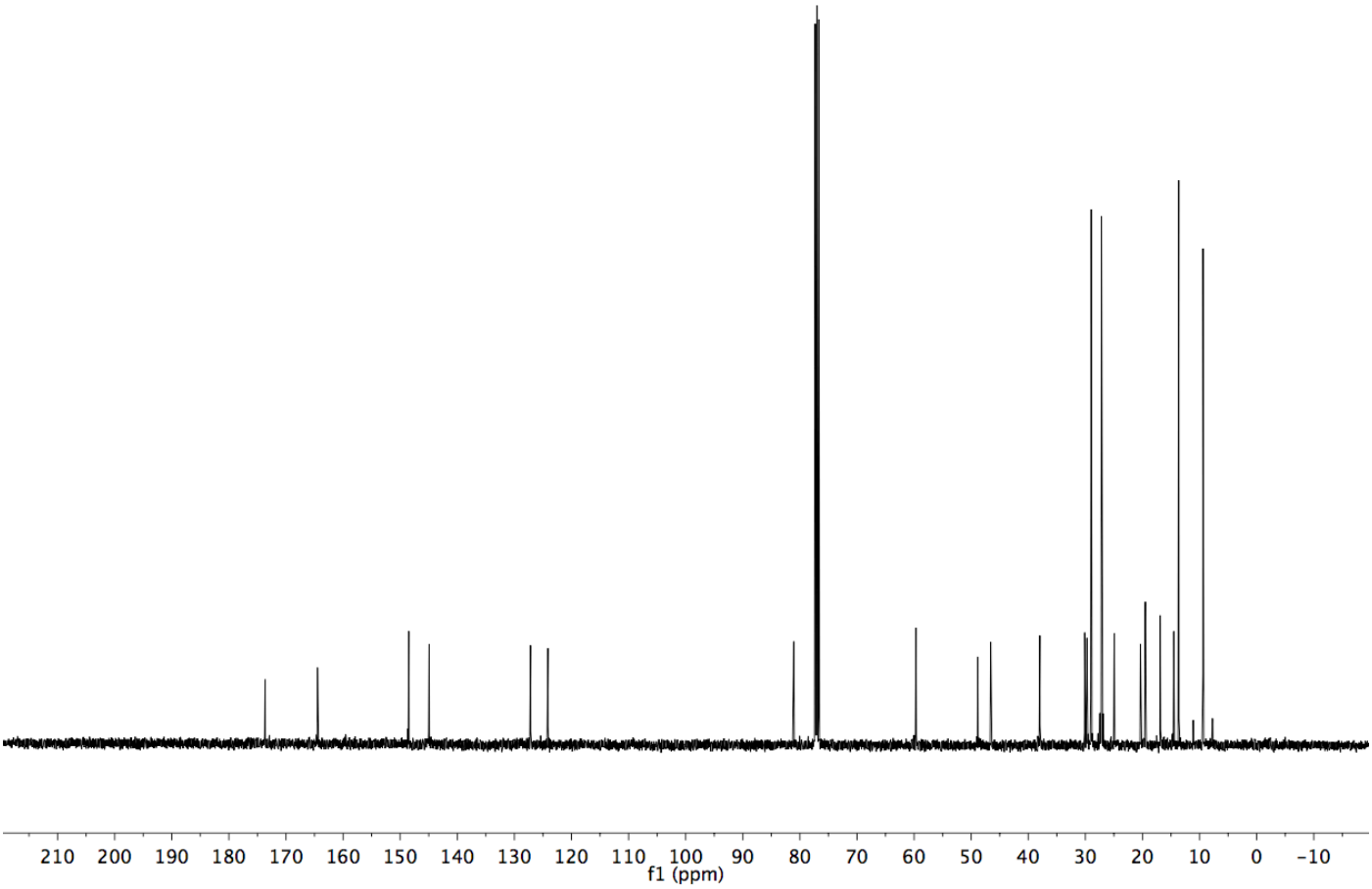
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

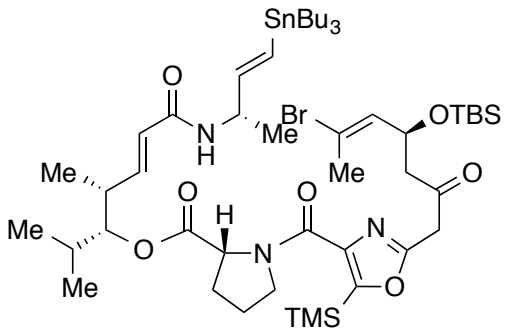

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Me
O
H
N
Me
O
H
Me

SI-20

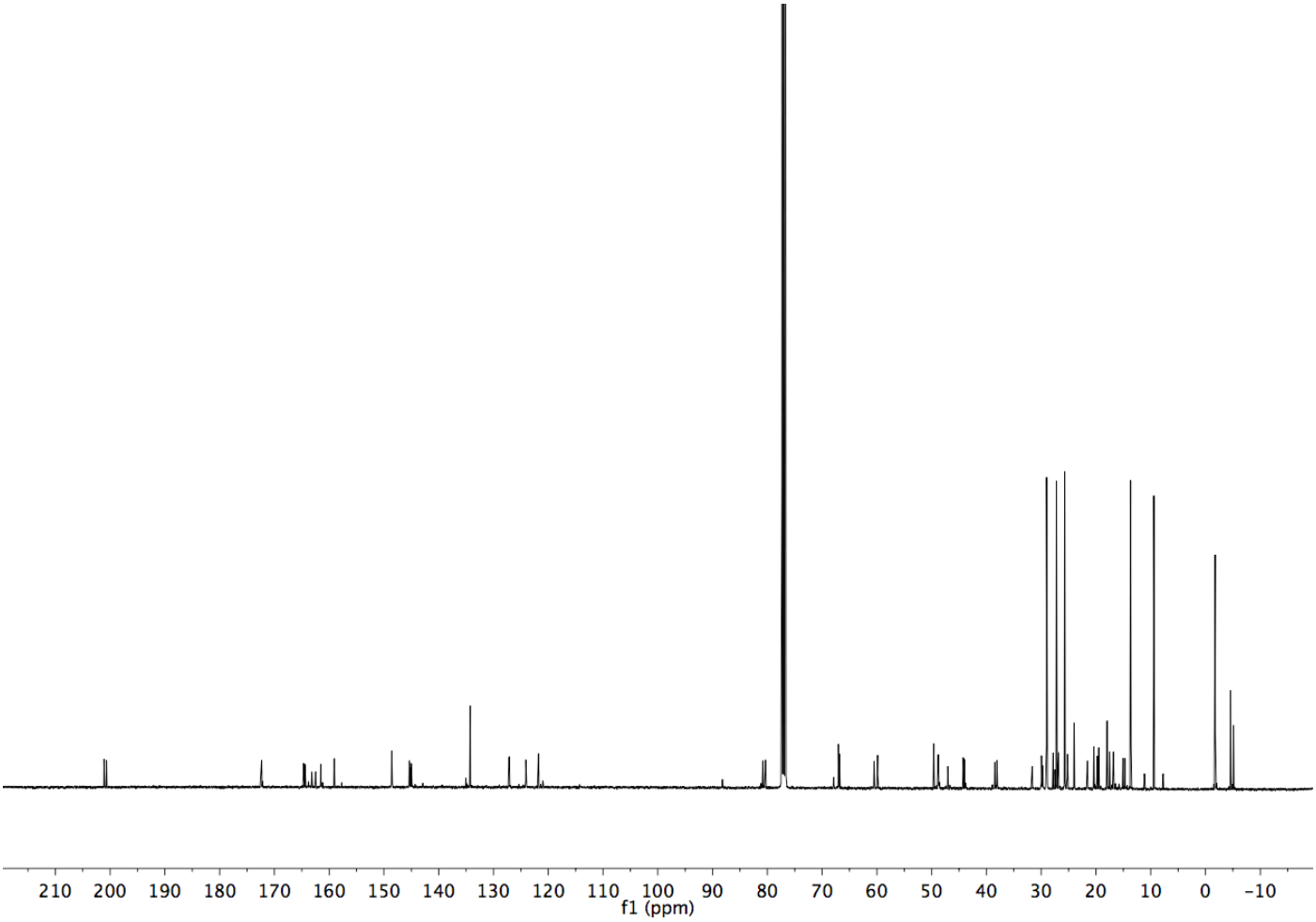
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

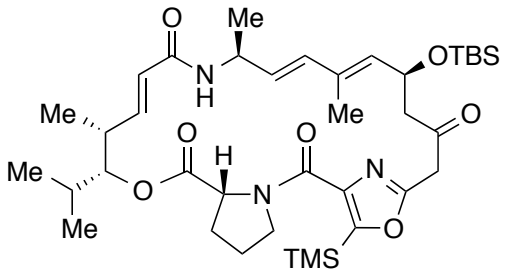

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
Me
OTBS
Me
Me
O
O
O
H
Me
O
N
N
O
Me
TMS

SI-21

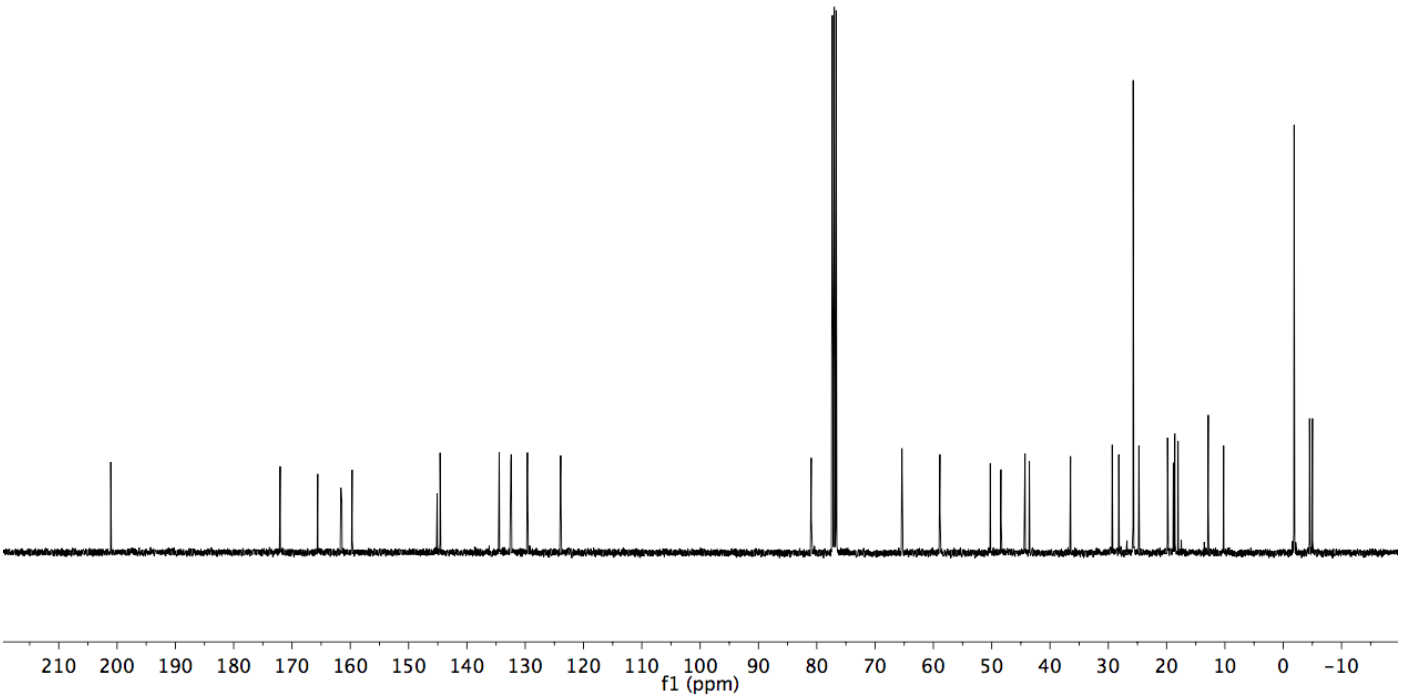
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

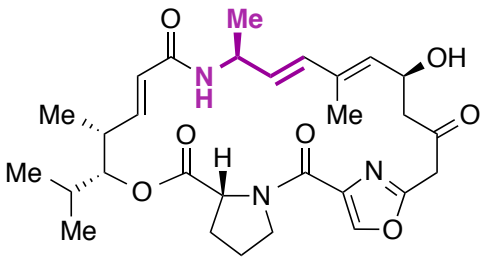

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OTBS
Me
Me
O
O
H
O
Me
O
N
N
O
Me
TMS

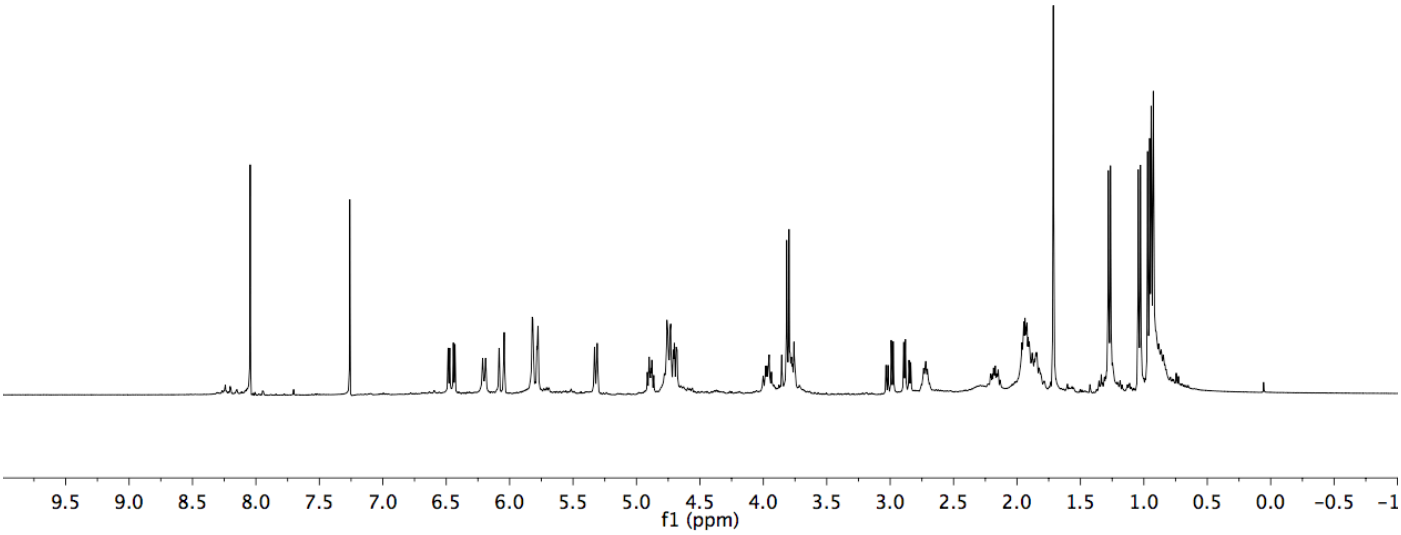
SI-22

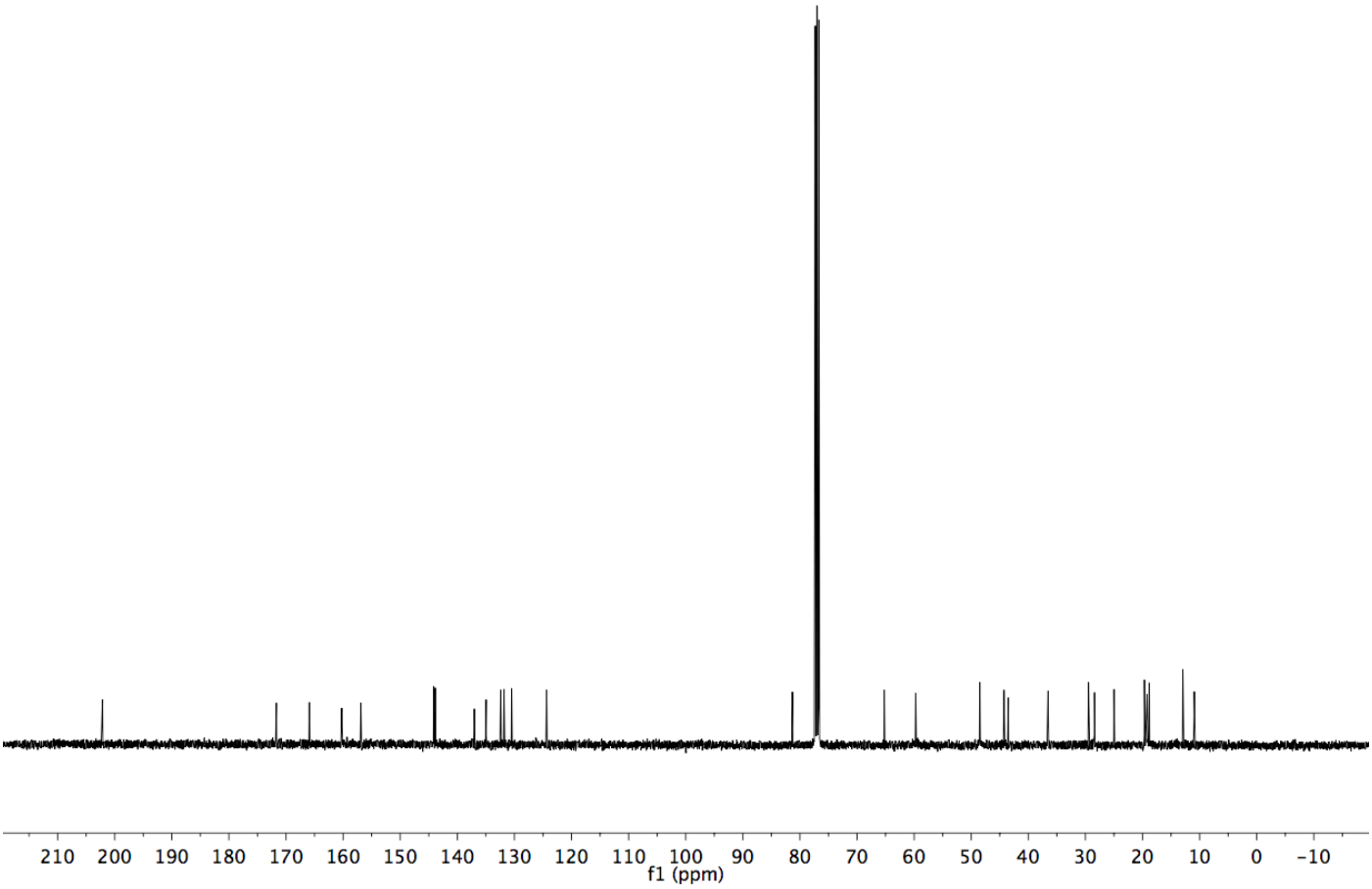
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

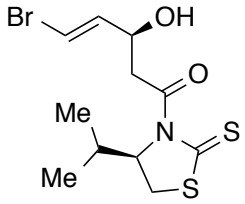

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OH
Me
Me
O
O
H
O
Me
O
N
N
Me
O

23

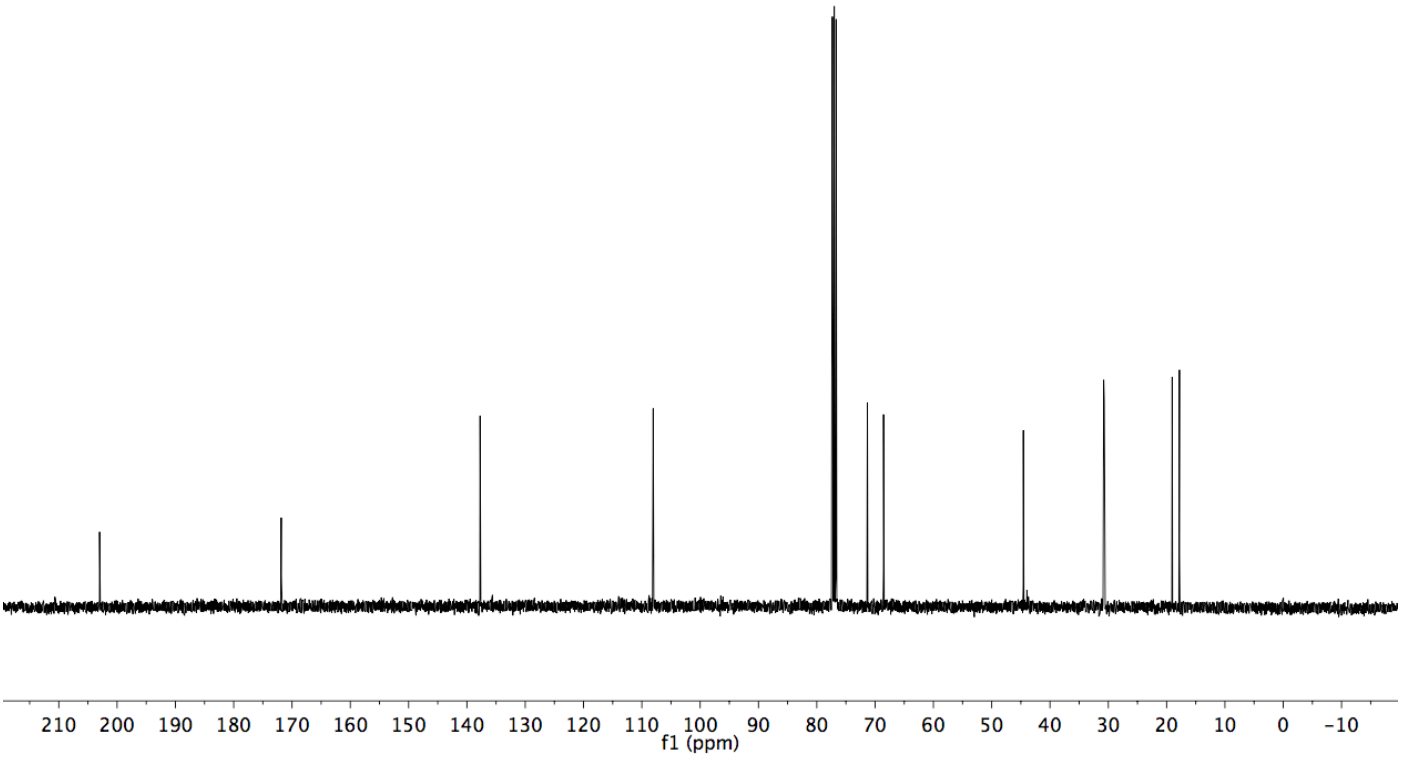

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

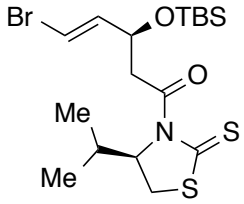

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OH
O
Me
N
S
Me
S

SI-24

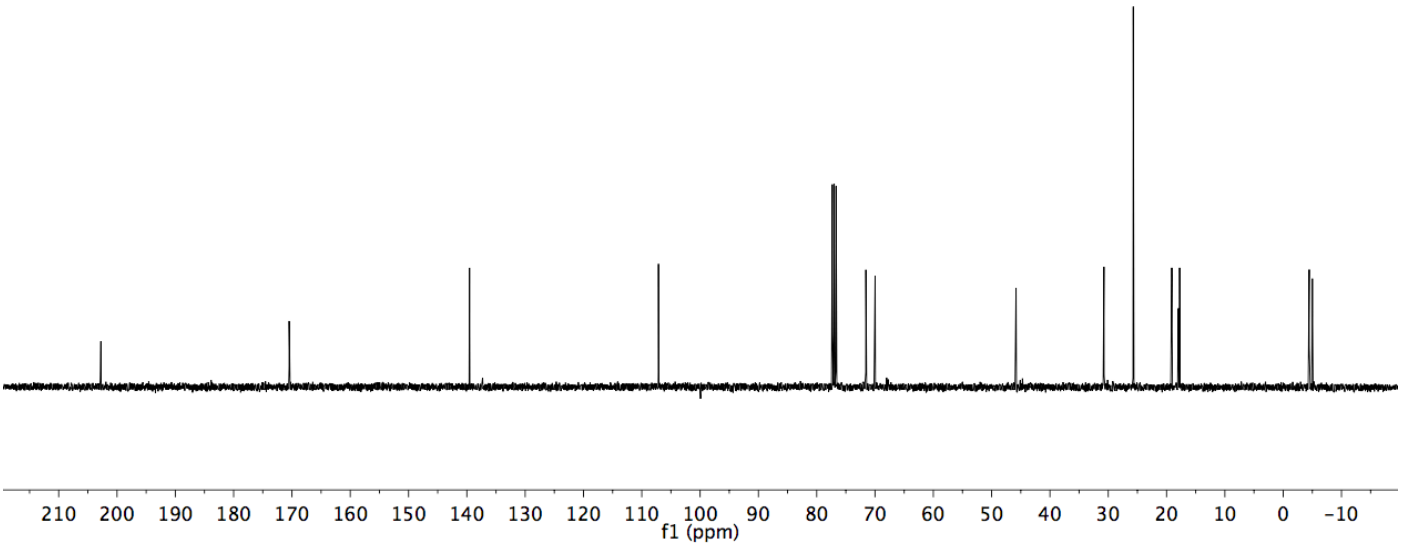
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

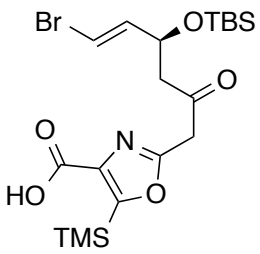

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
O
Me
N
S
Me
S

SI-25

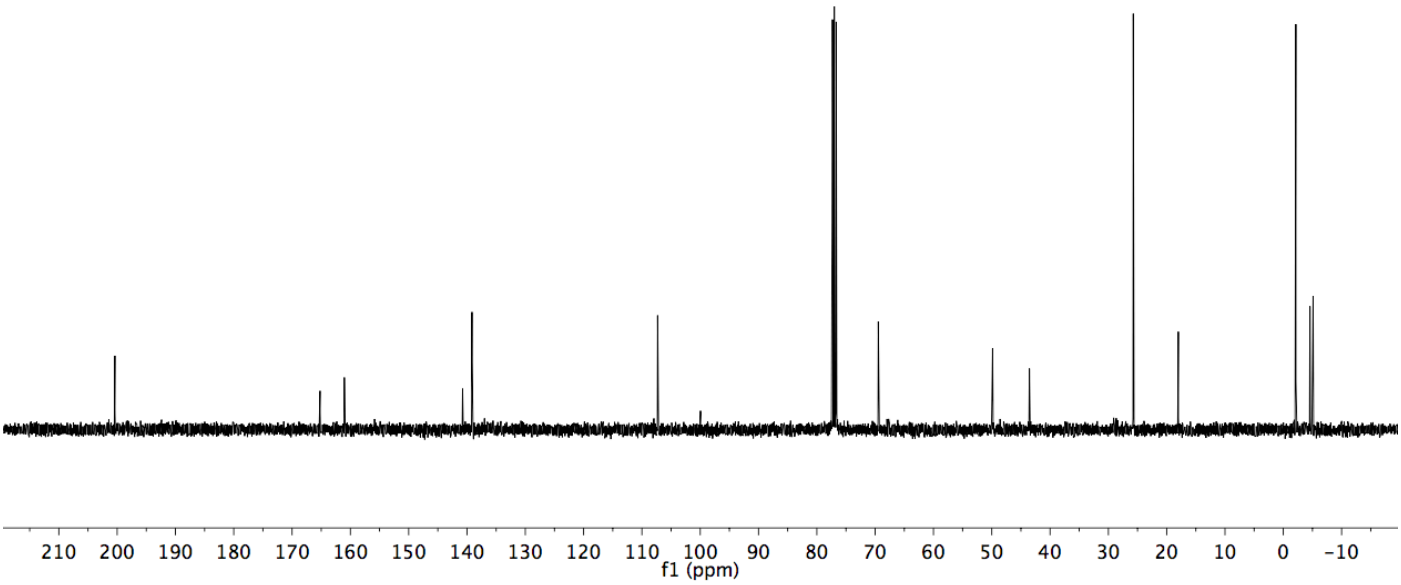
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

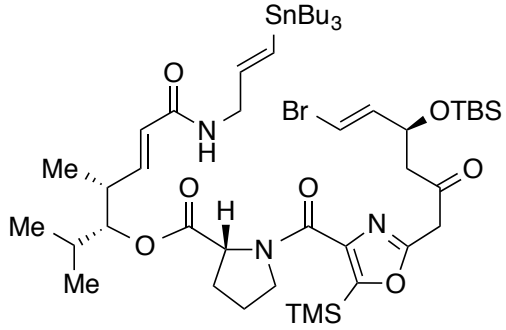

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
O
O
N
HO
O
TMS

SI-26

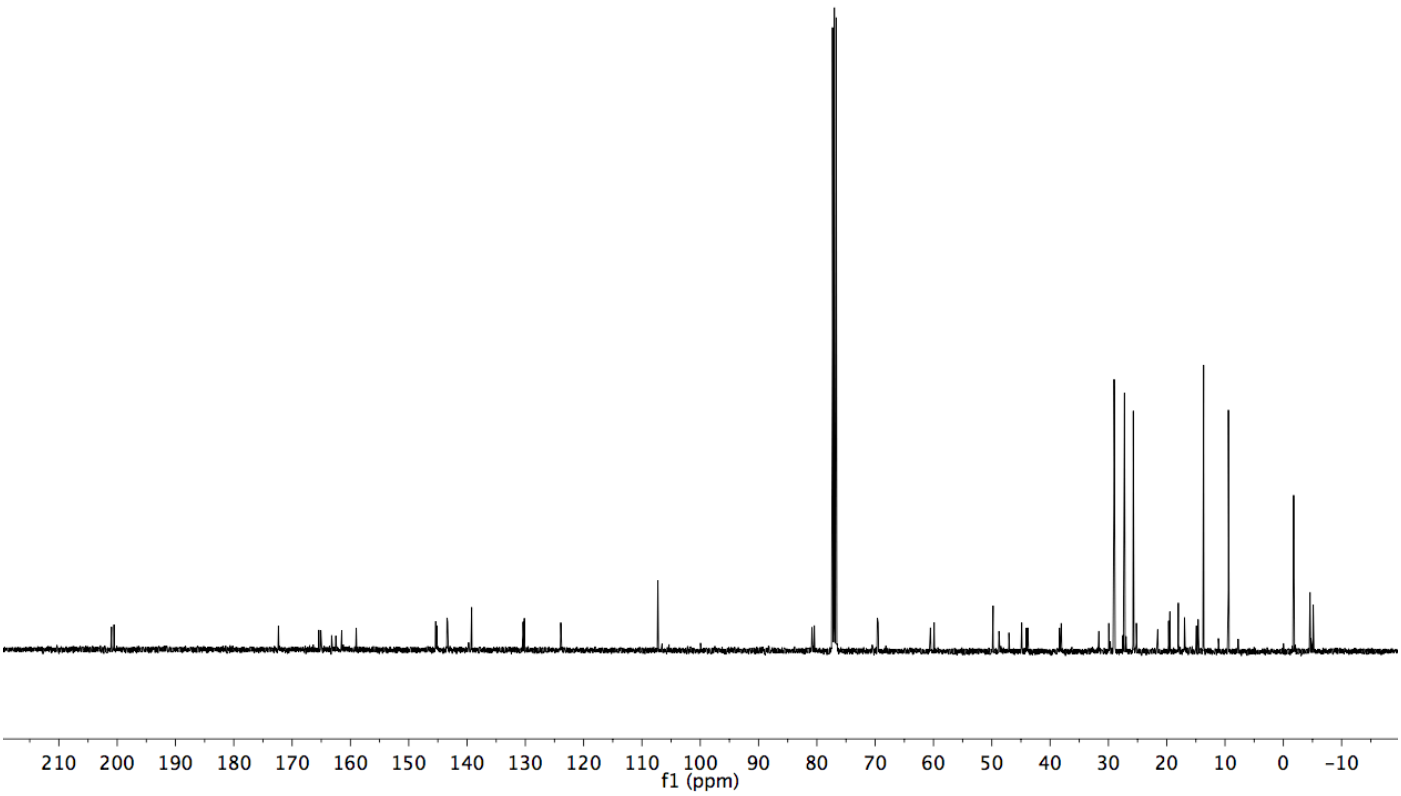
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

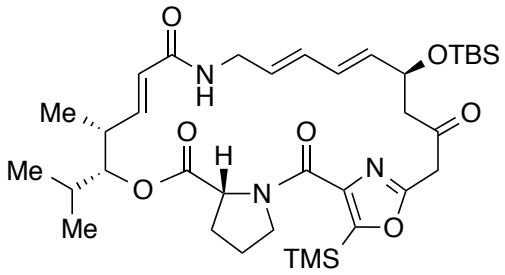

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
O
O
H
O
N
N
Me
O
O
Me
TMS

SI-27

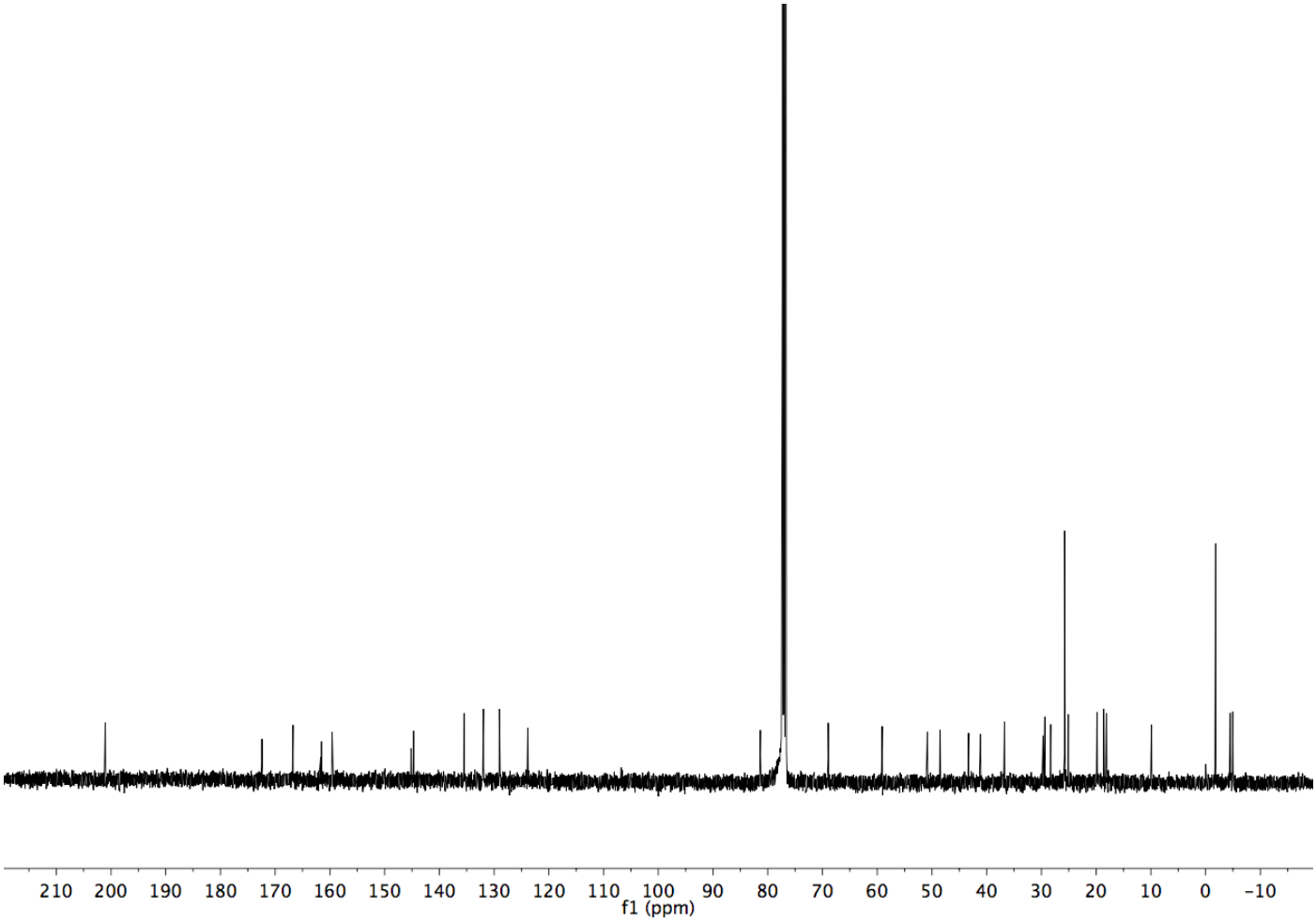
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

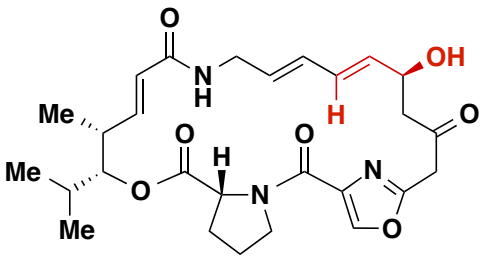

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
O
O
Me
O
H
N
N
O
O
Me
TMS

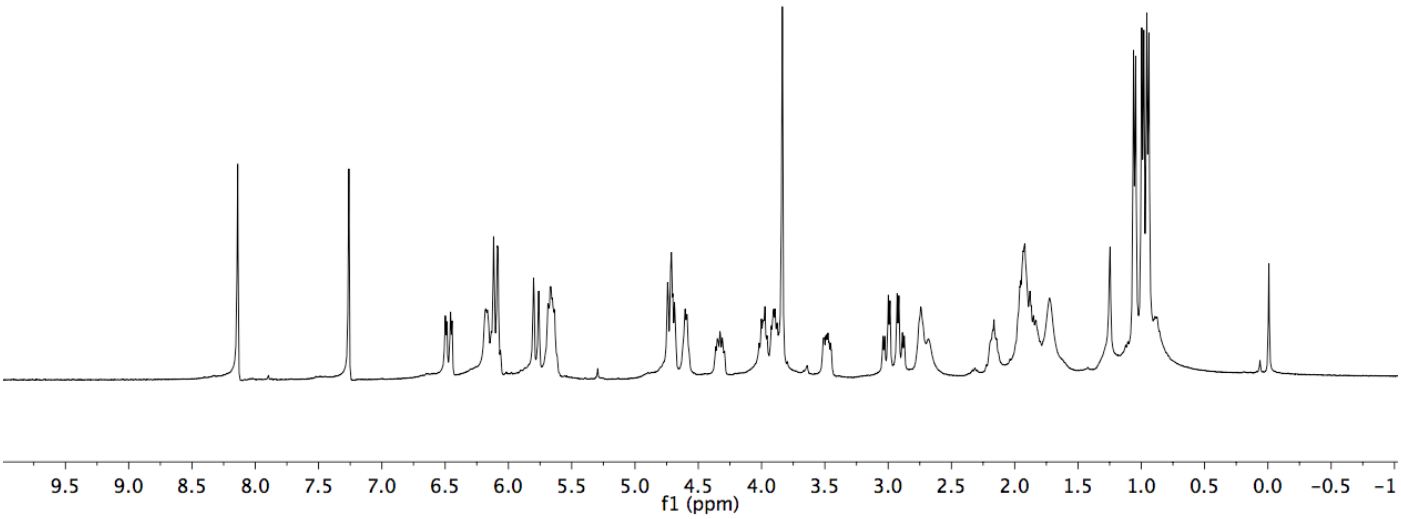
SI-28

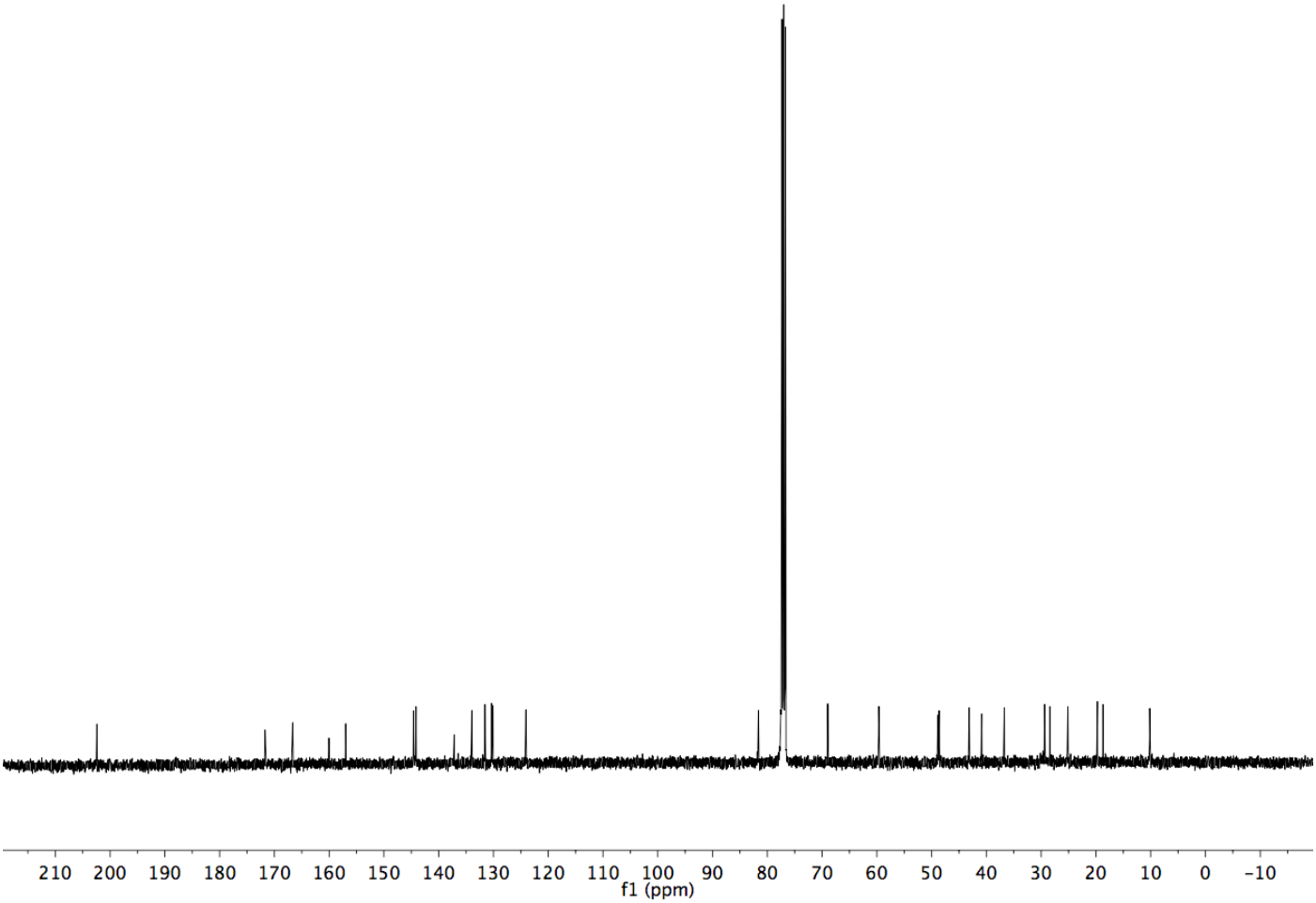
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

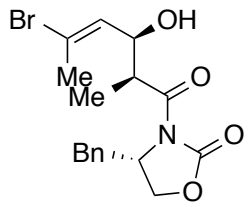

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
H
O
Me
O
H
O
Me
O
N
N
Me
O

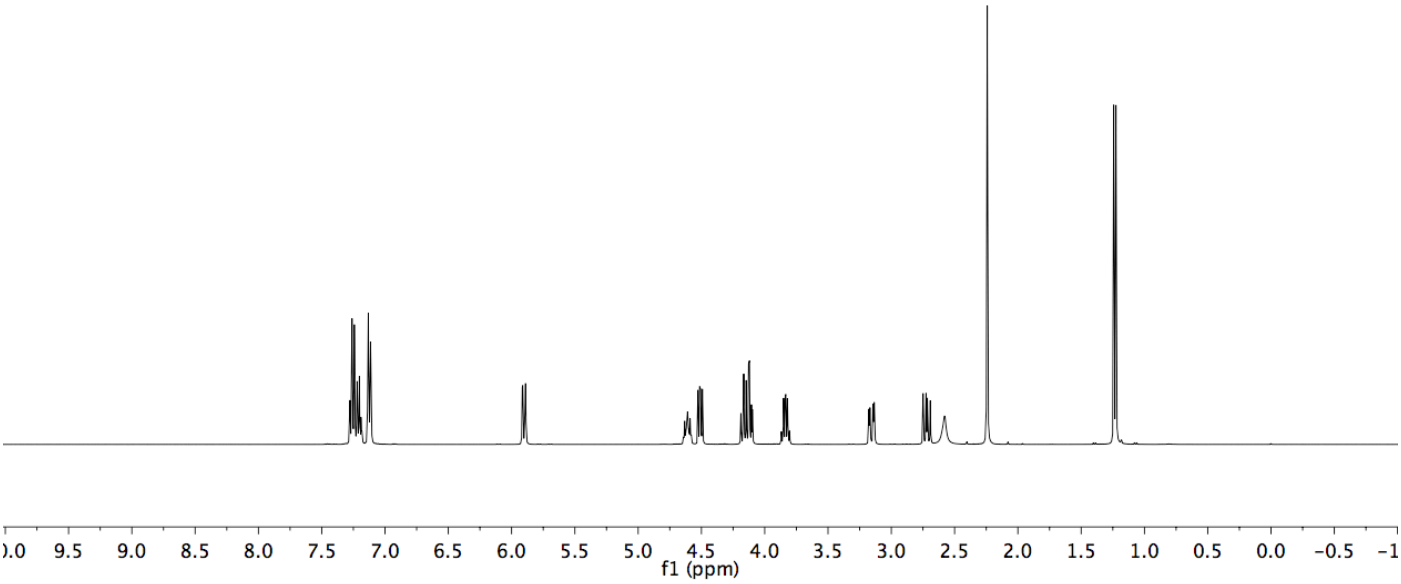
24

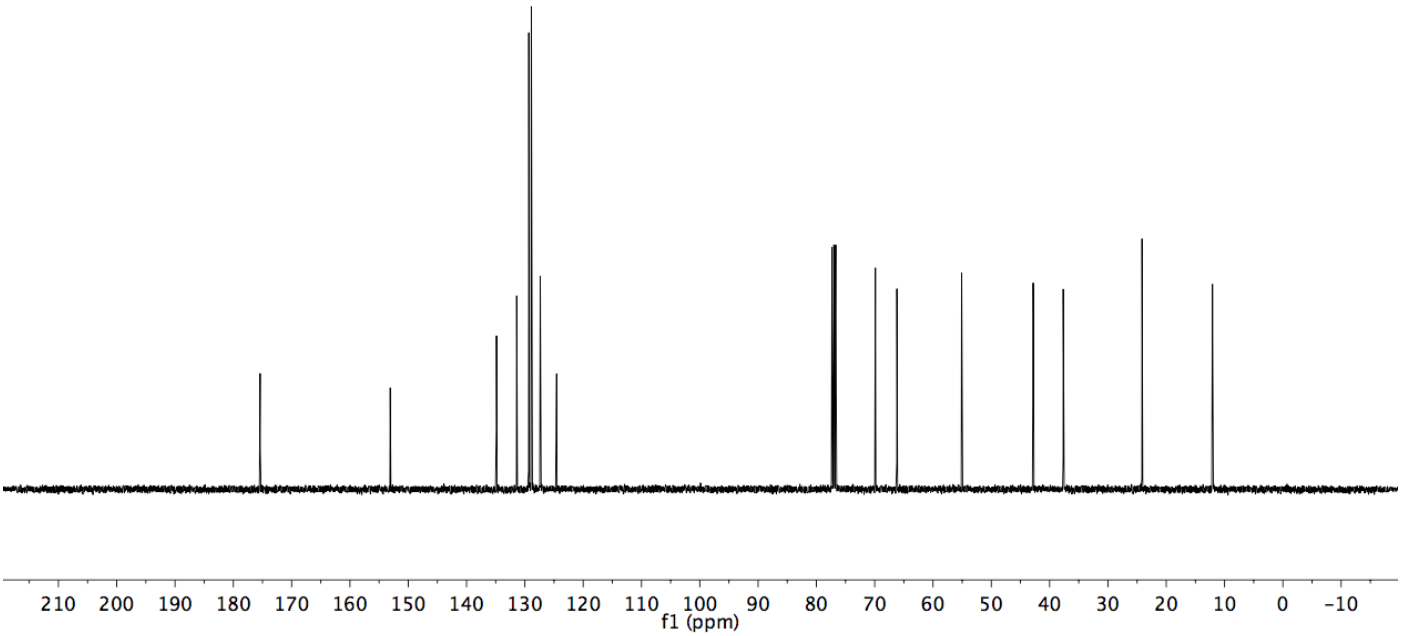

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

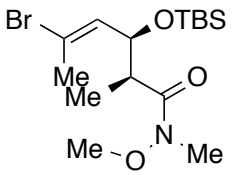

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OH
Me
Me
O
N
O
Bn
O

SI-30

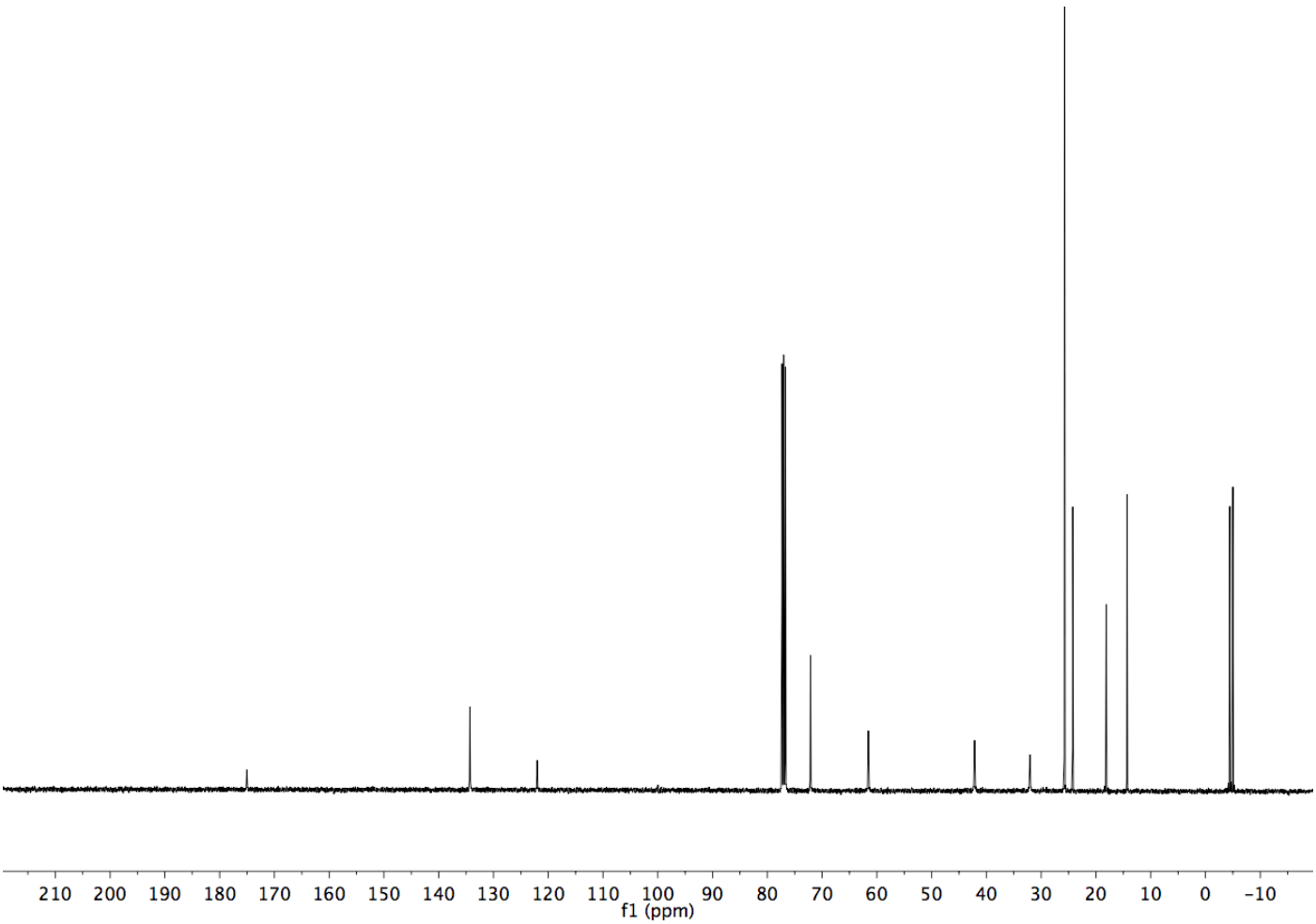

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

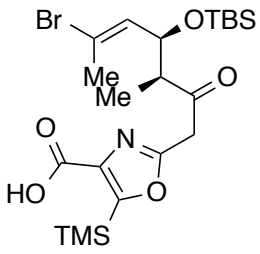

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
Me
O
N
Me
O
Me

SI-31

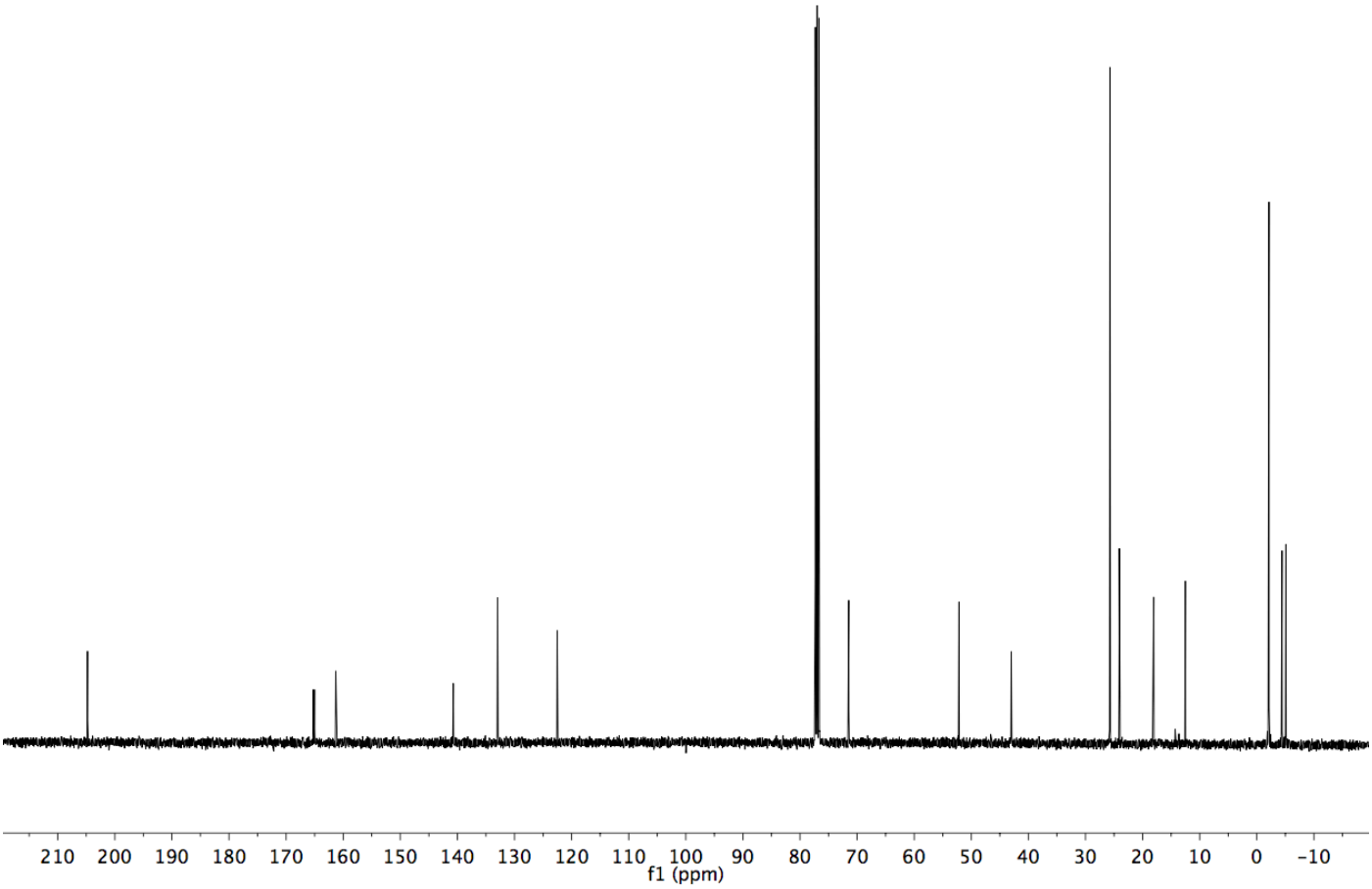
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

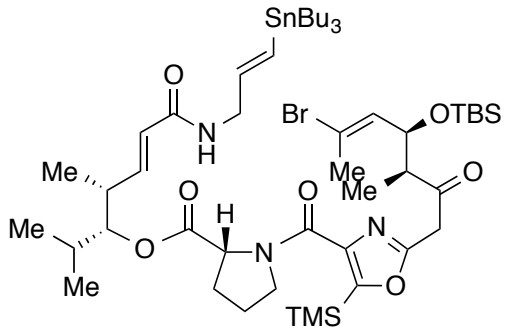

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
Me
O
O
N
HO
O
TMS

SI-32

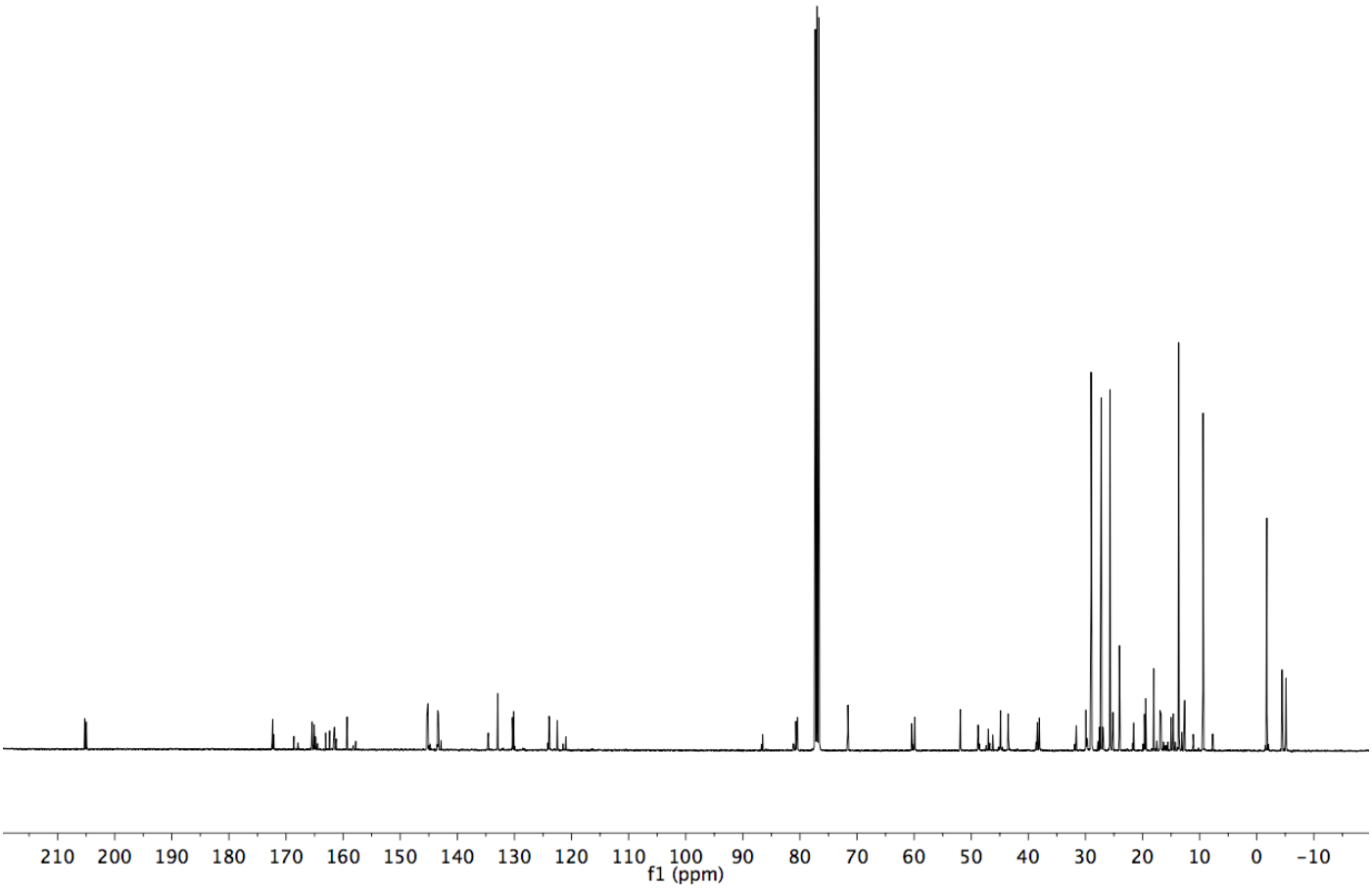
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

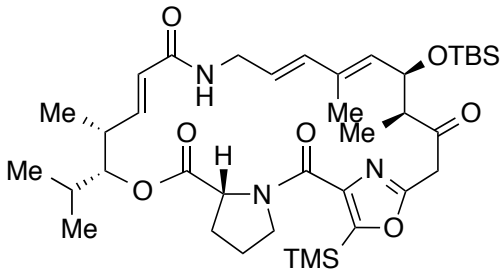

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
Me
O
O
O
H
Me
O
N
N
O
Me
TMS

SI-33

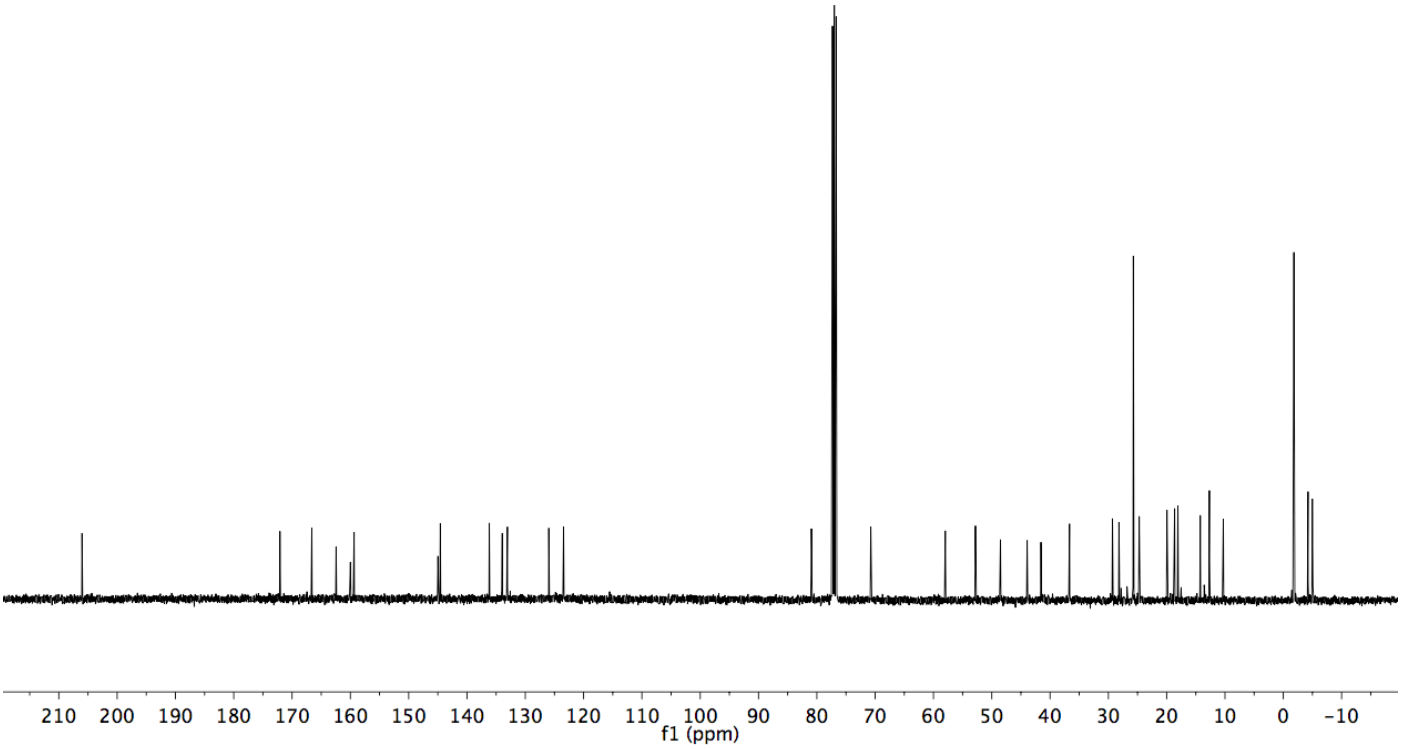
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

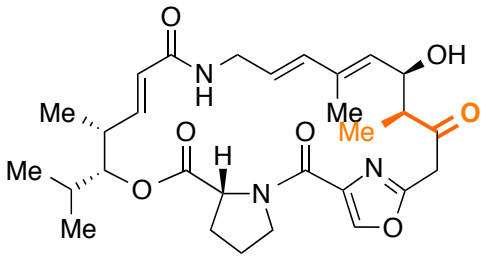

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
Me
O
O
O
H
Me
O
N
N
O
Me
TMS

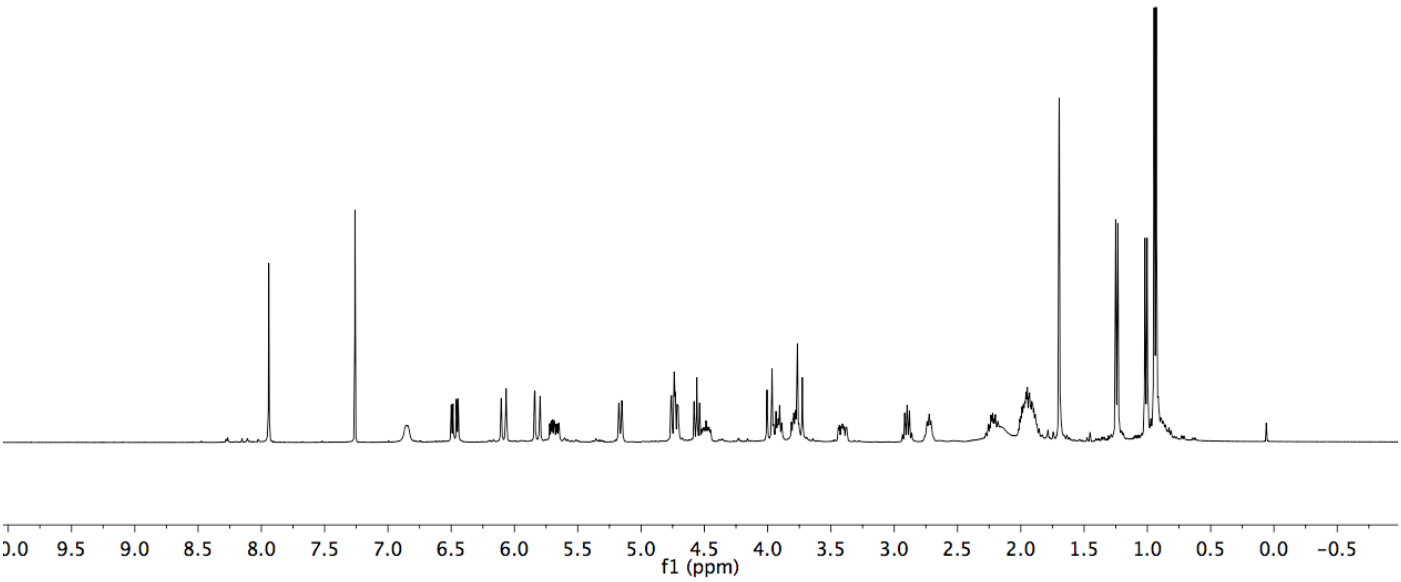
SI-34

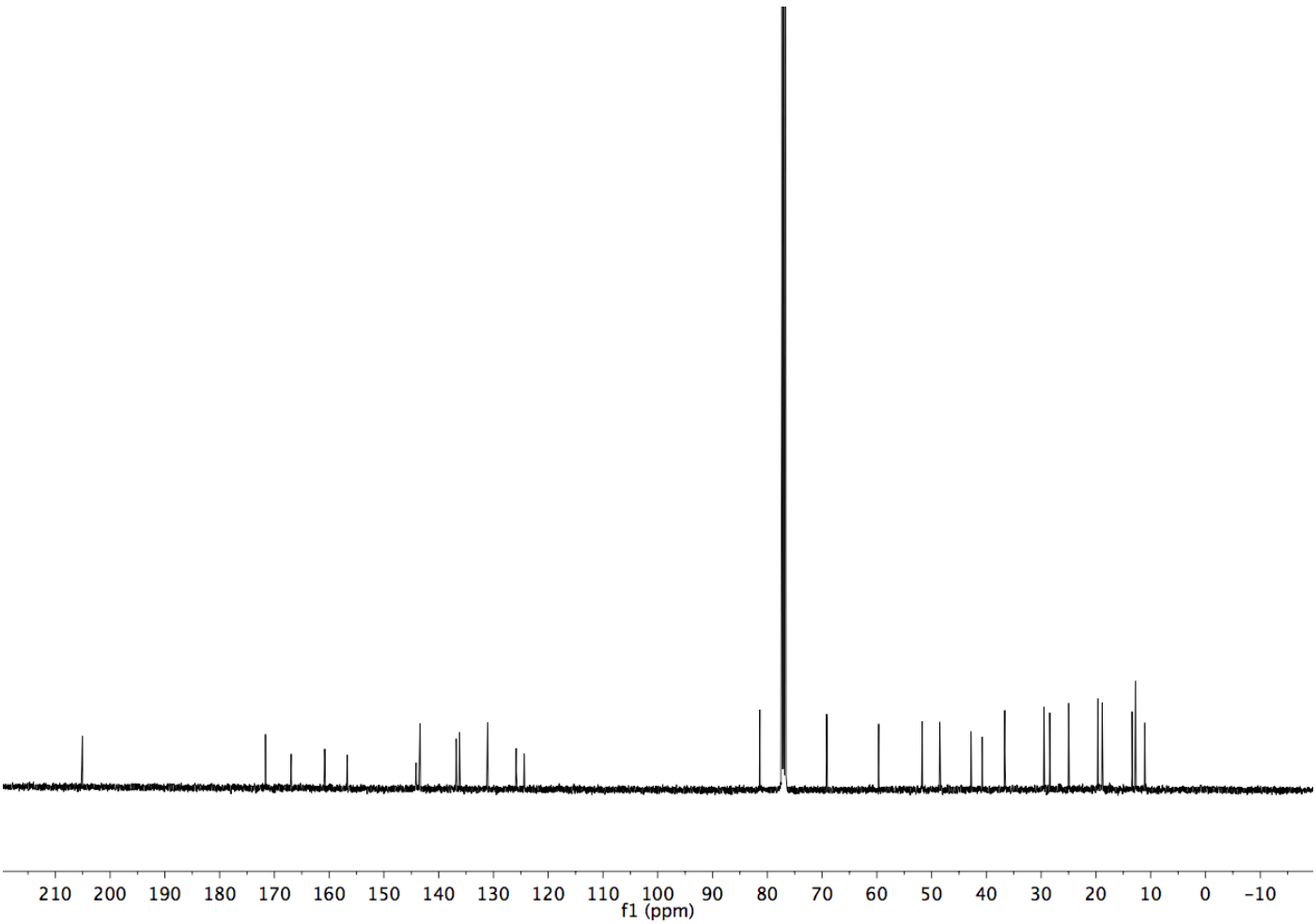
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

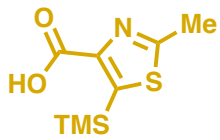

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
Me
O
O
O
H
Me
O
N
N
Me
O

25

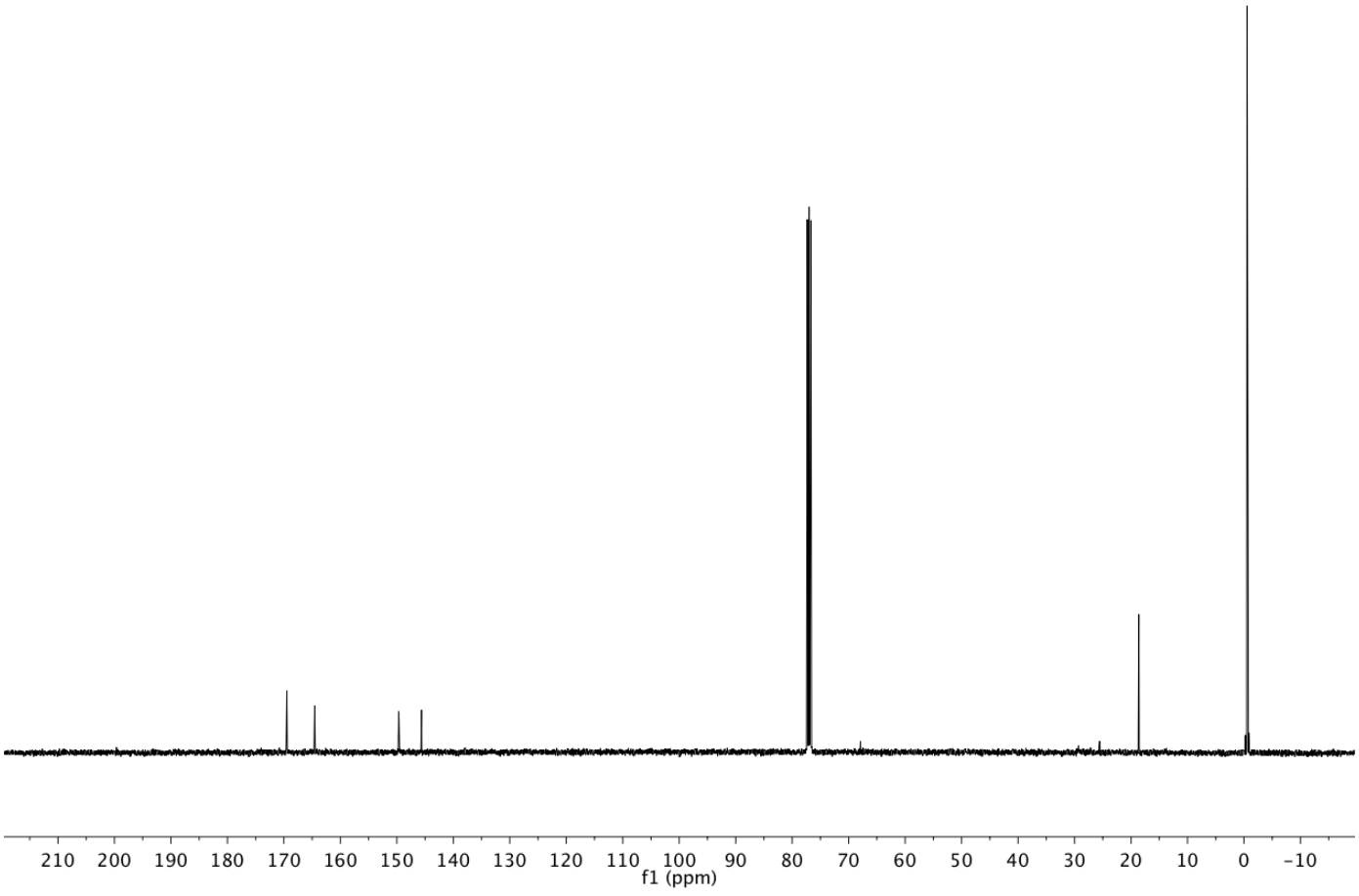

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

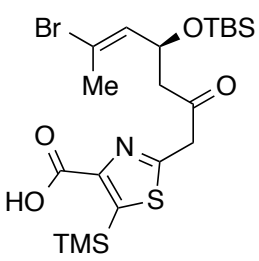

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
HO
N
Me
S
TMS

SI-35

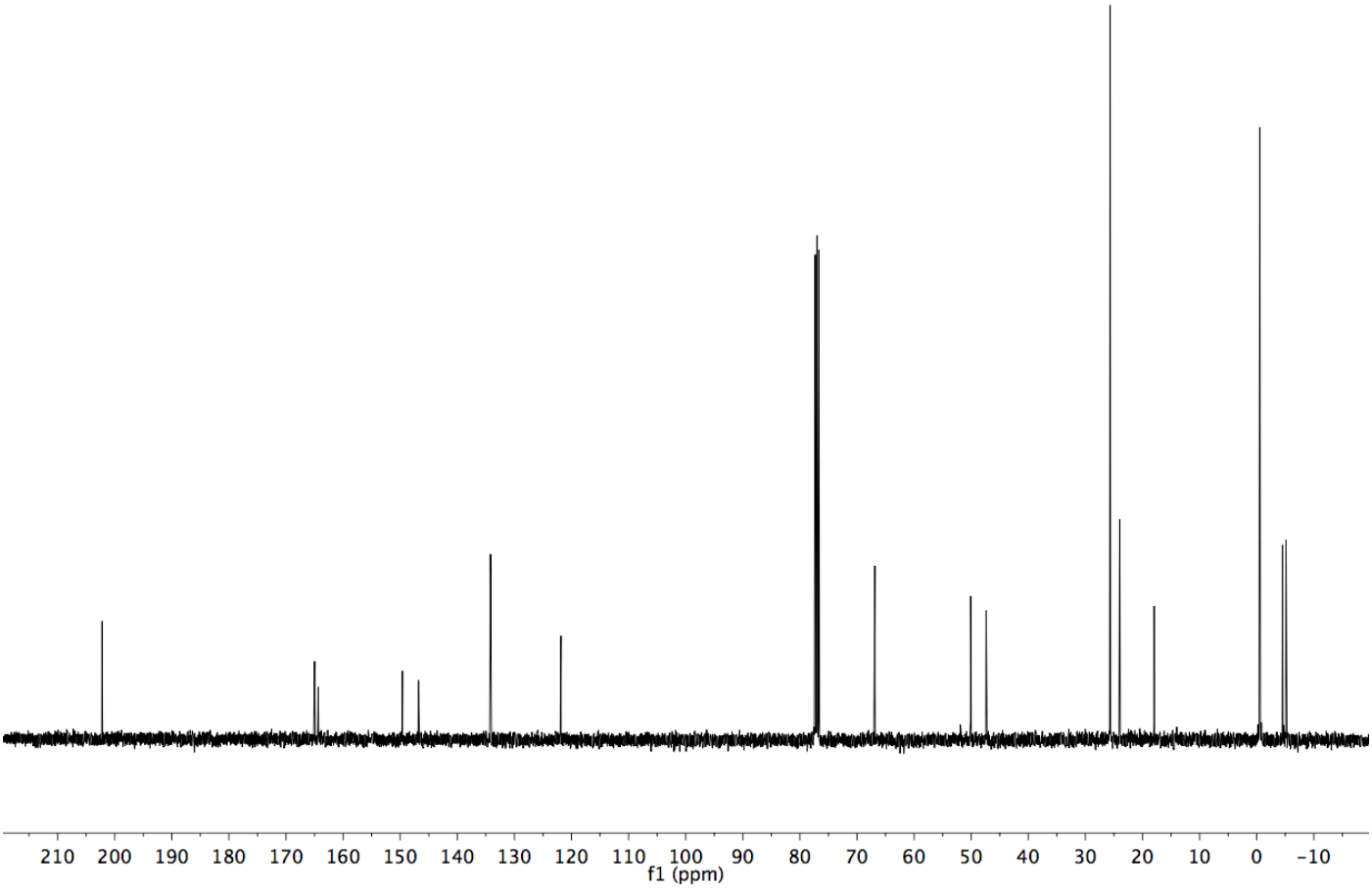
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

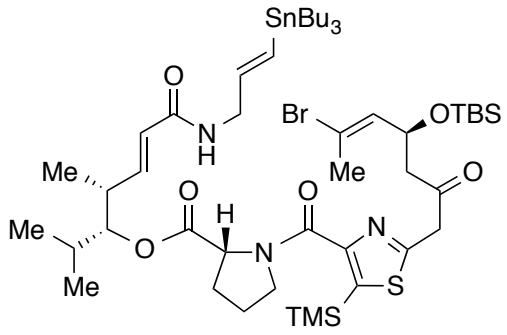

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
O
N
HO
S
TMS

SI-36

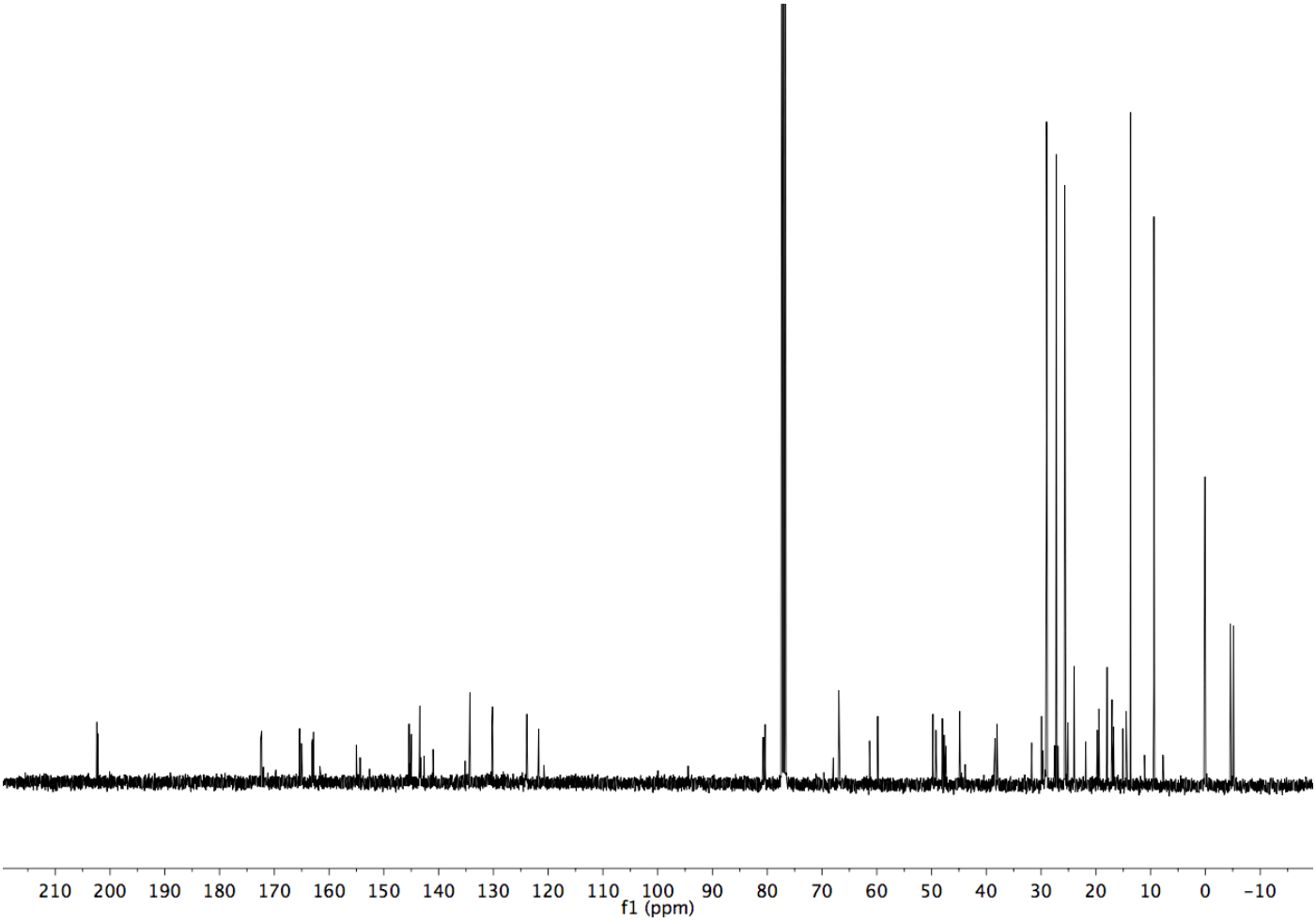
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

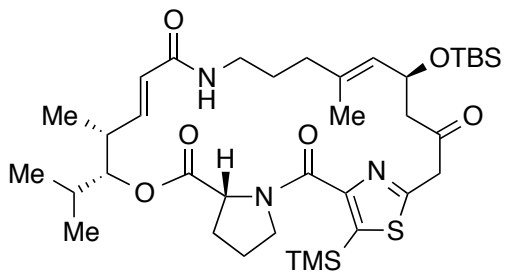

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
O
H
Me
O
N
N
S
Me
TMS

SI-37

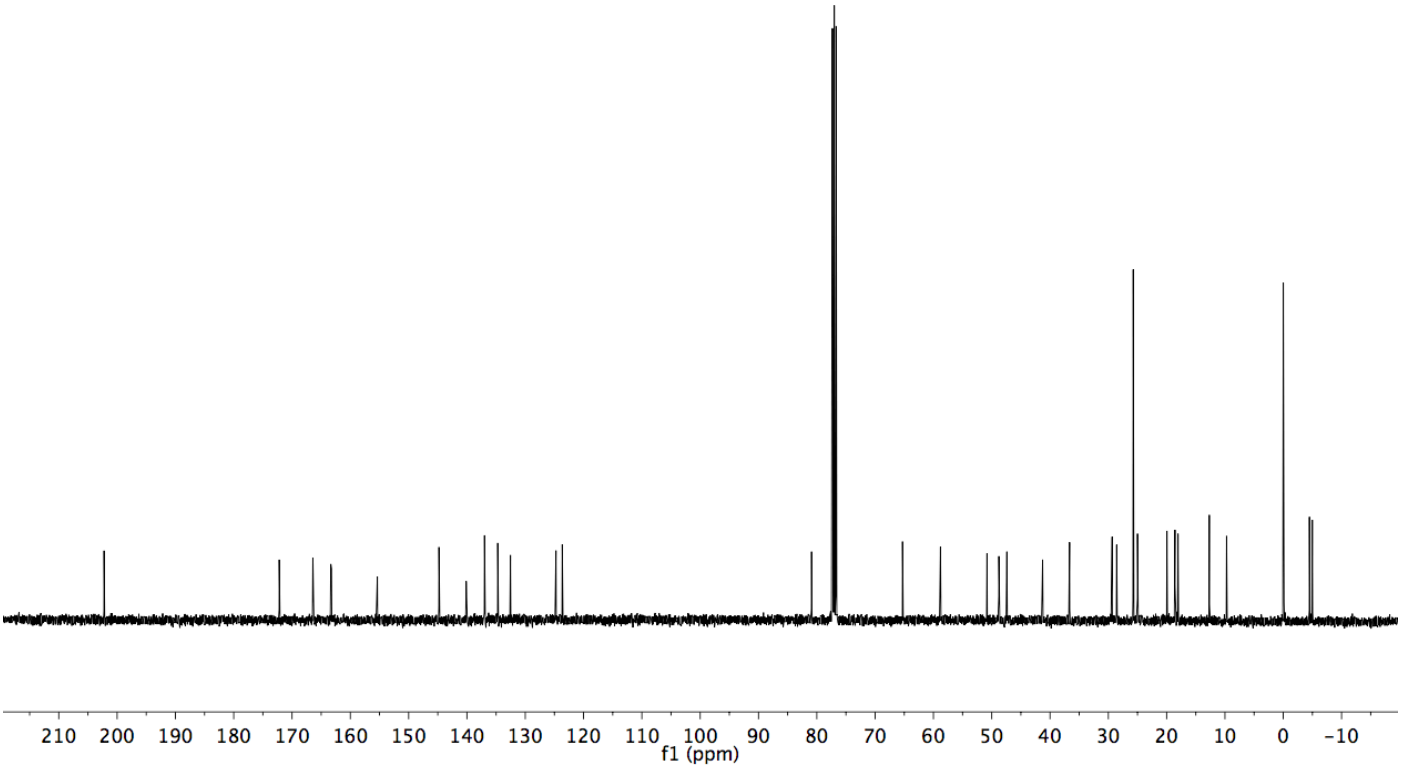
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

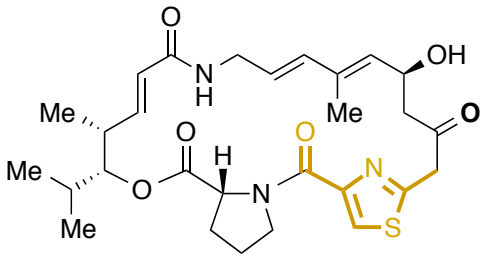

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
Me
O
N
N
Me
S
TMS

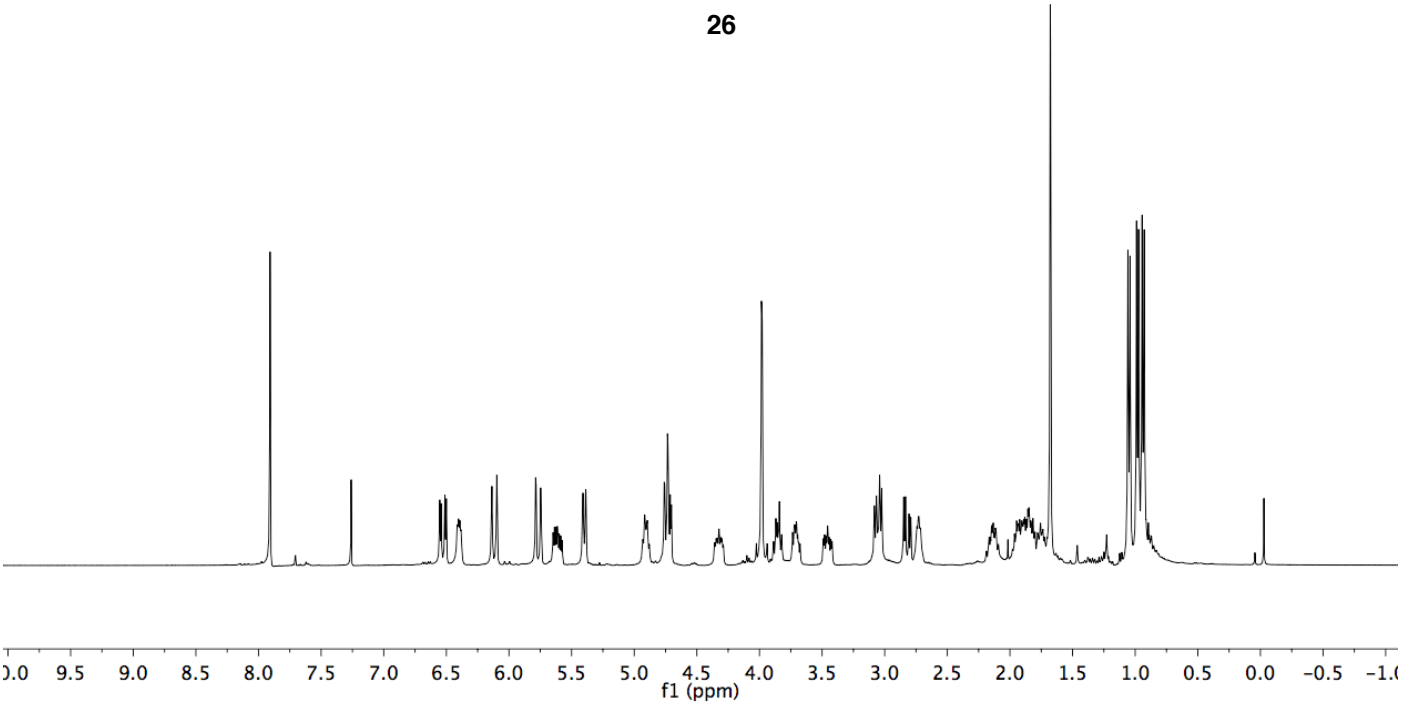
SI-38

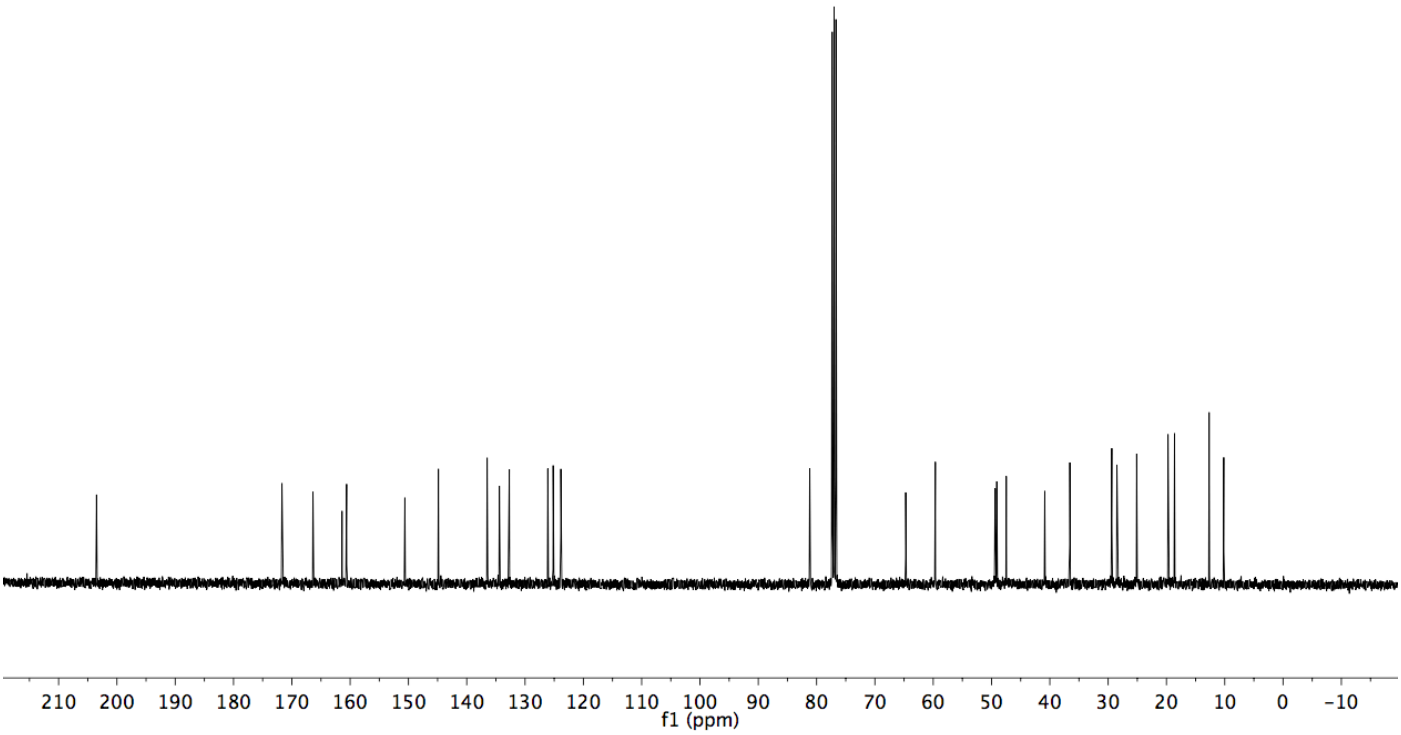
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

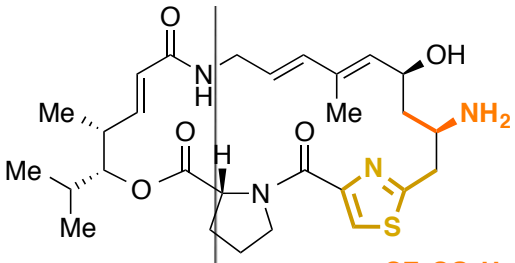

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
Me
O
H
O
N
N
S
Me

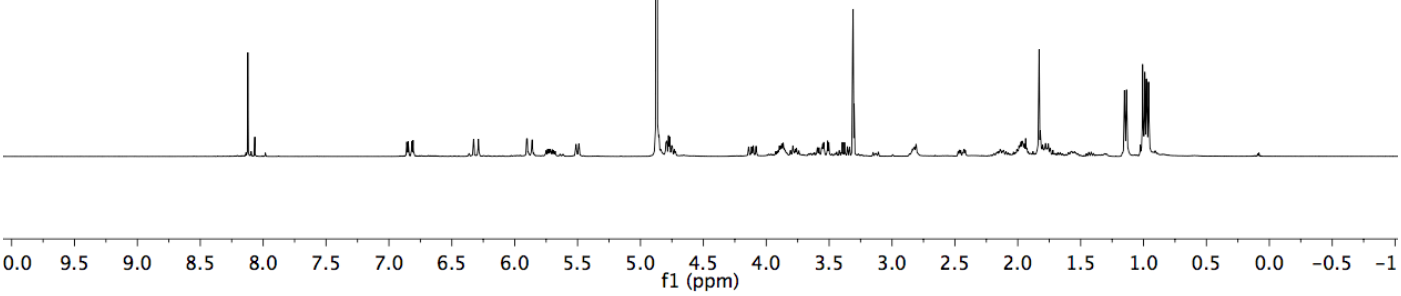
26


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

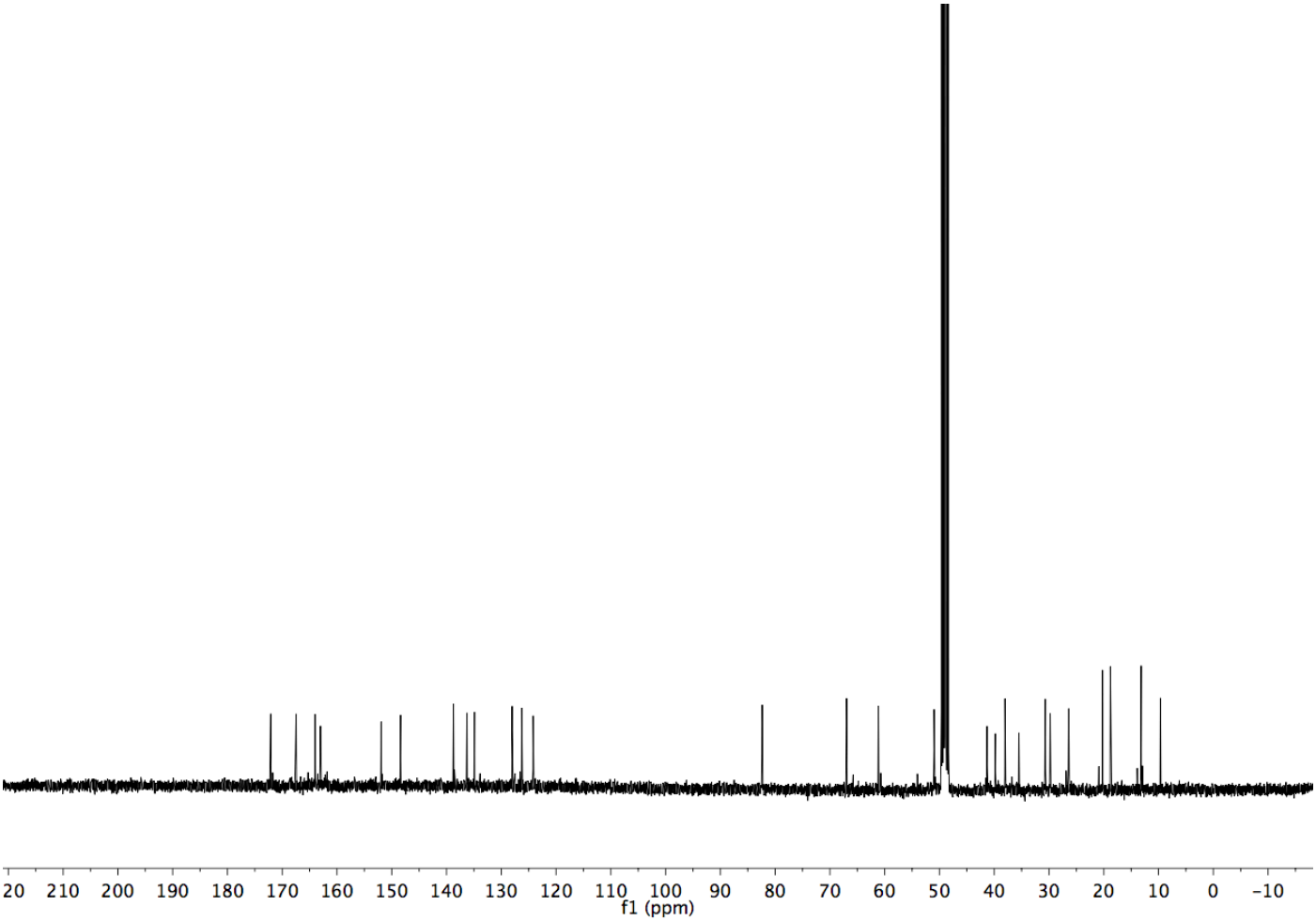

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
NH2
O
O
H
Me
O
N
N
S
Me
CF3CO2H

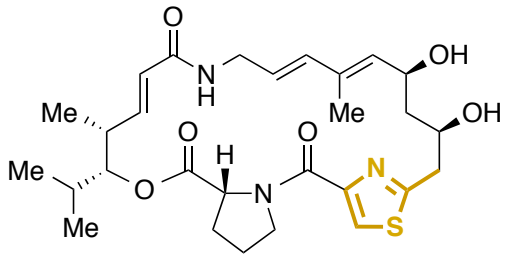
SI-39



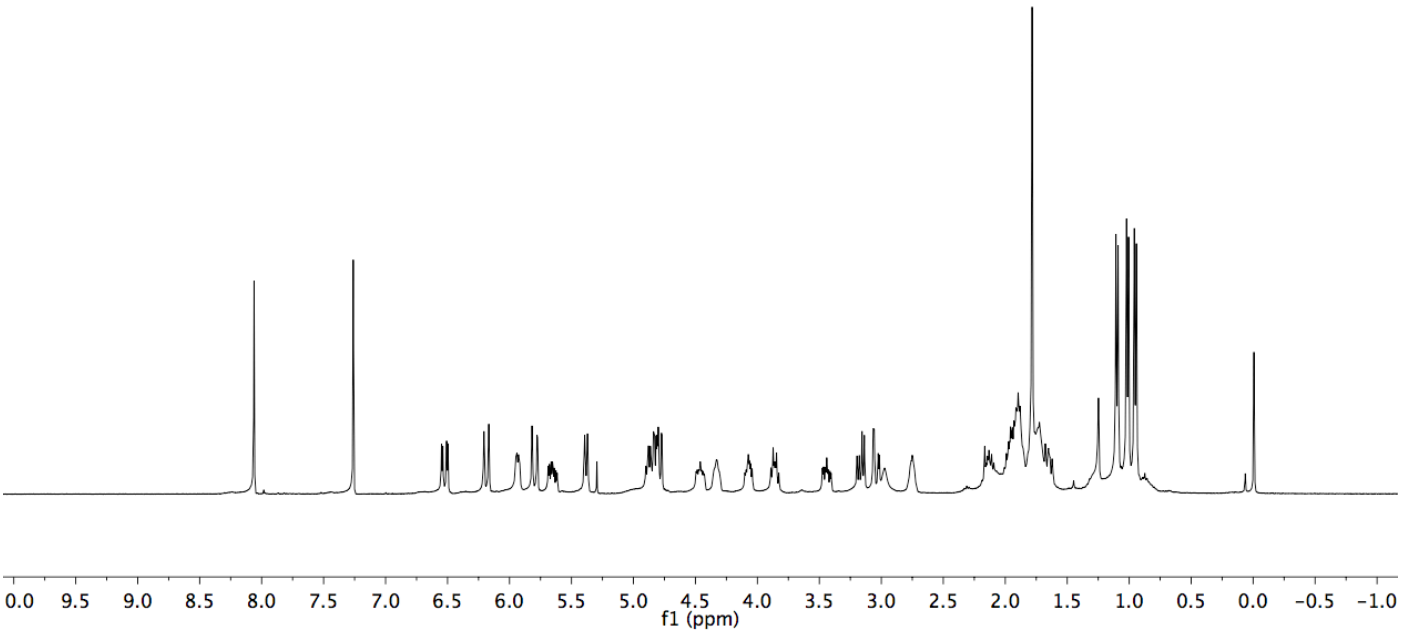
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

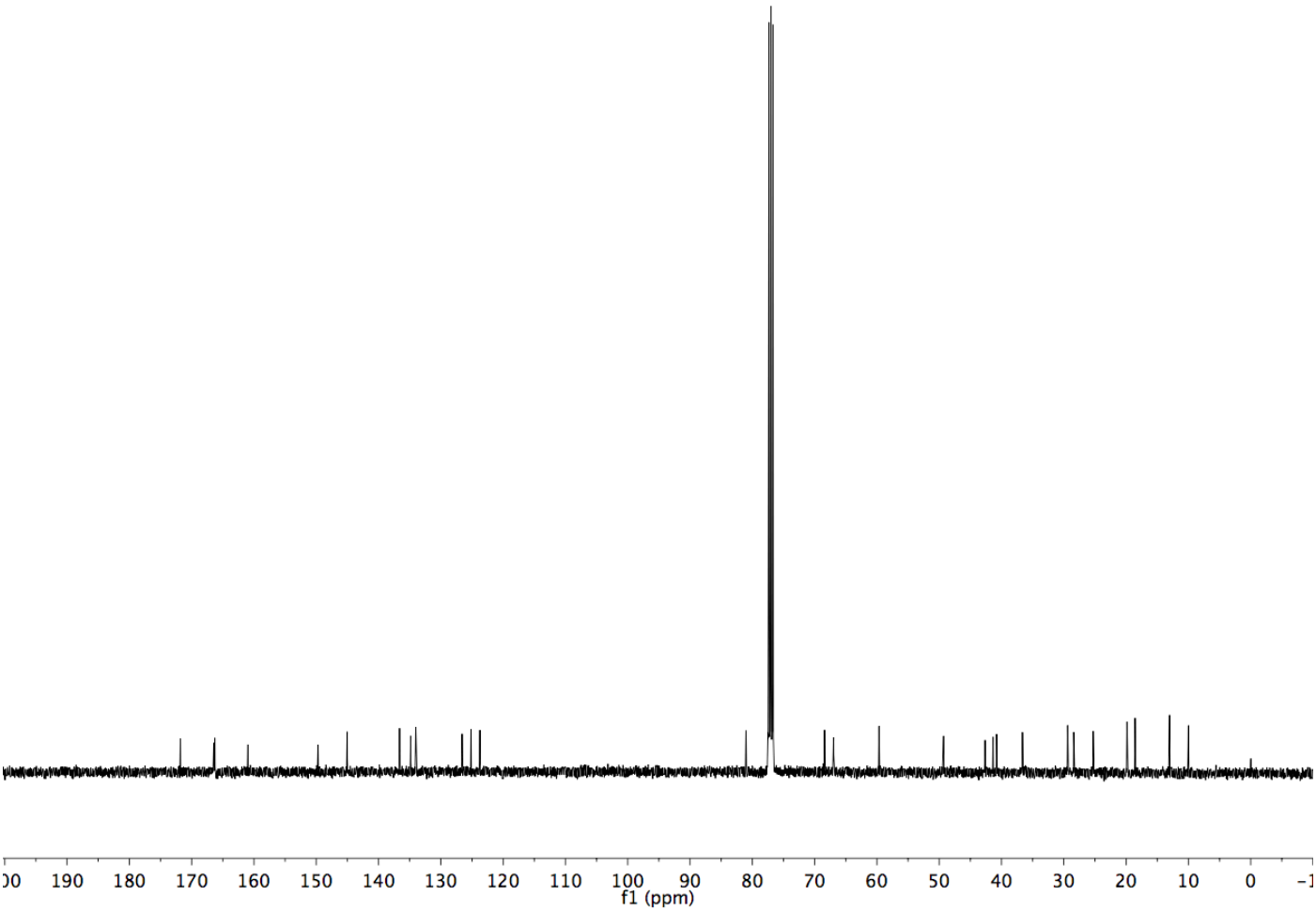


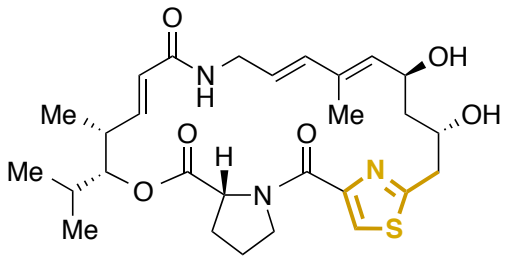
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
OH
O
H
O
Me
O
N
N
S
Me

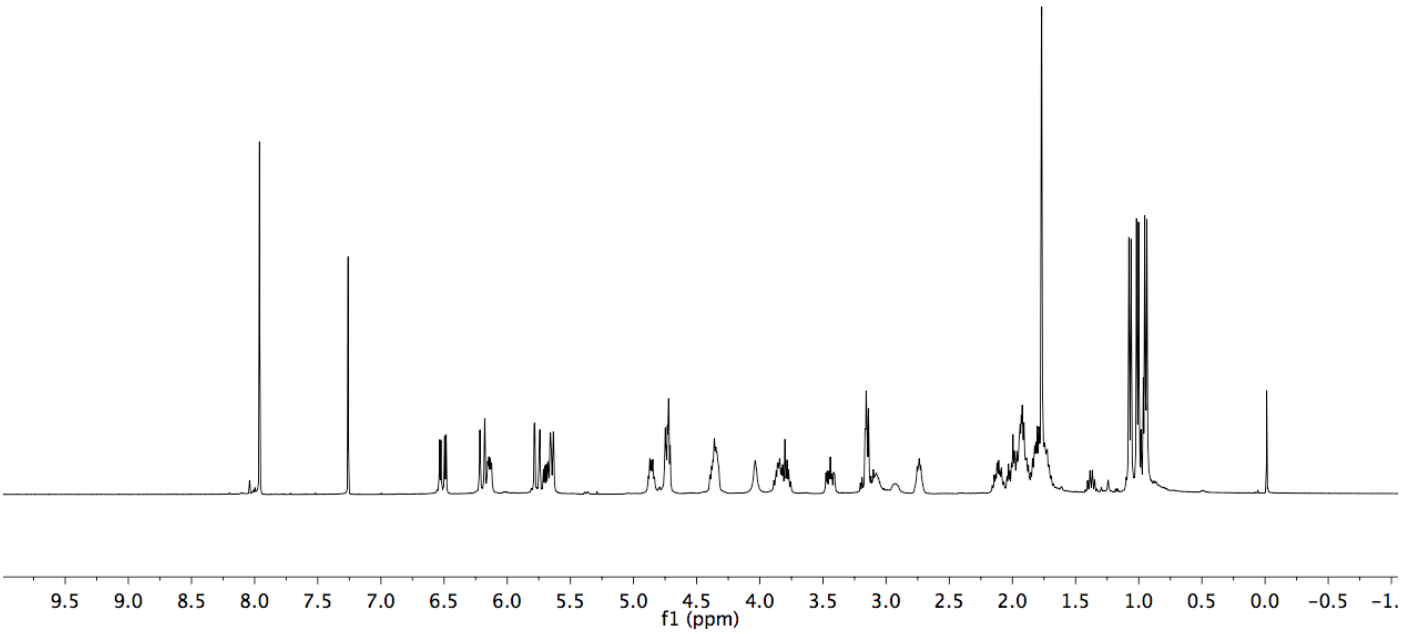
SI-40

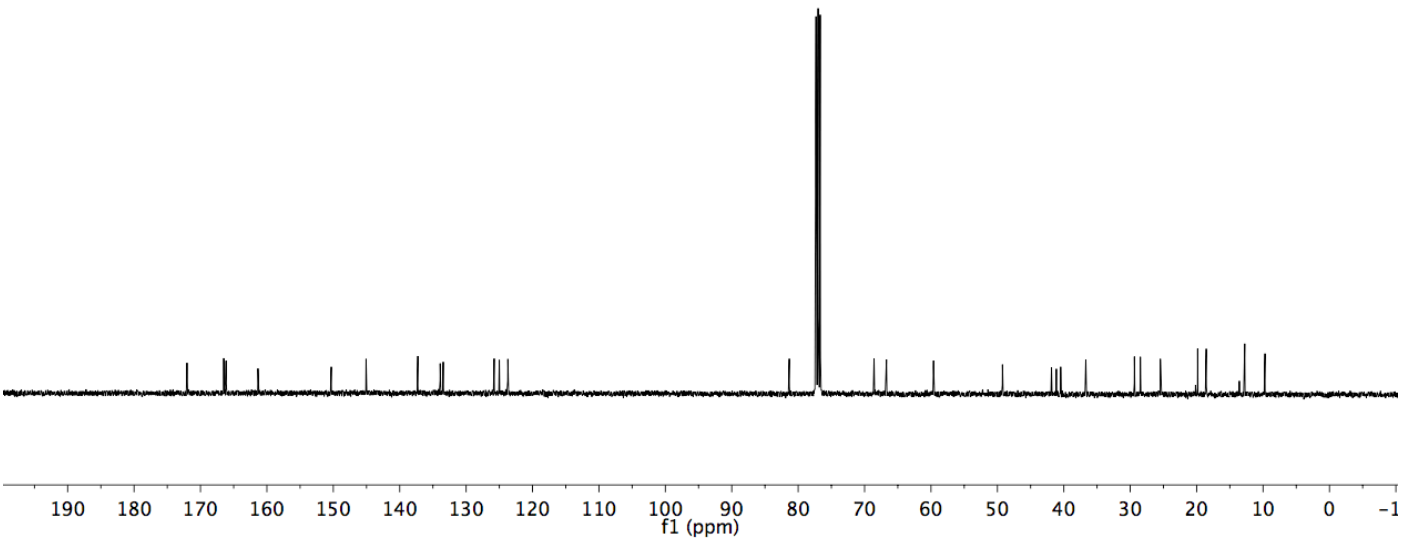

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

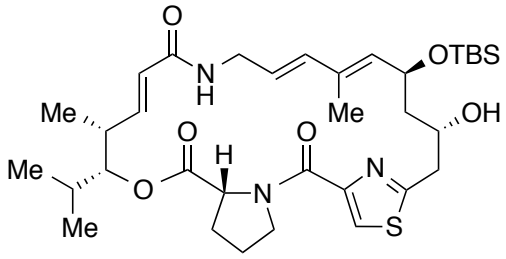

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



SI-41

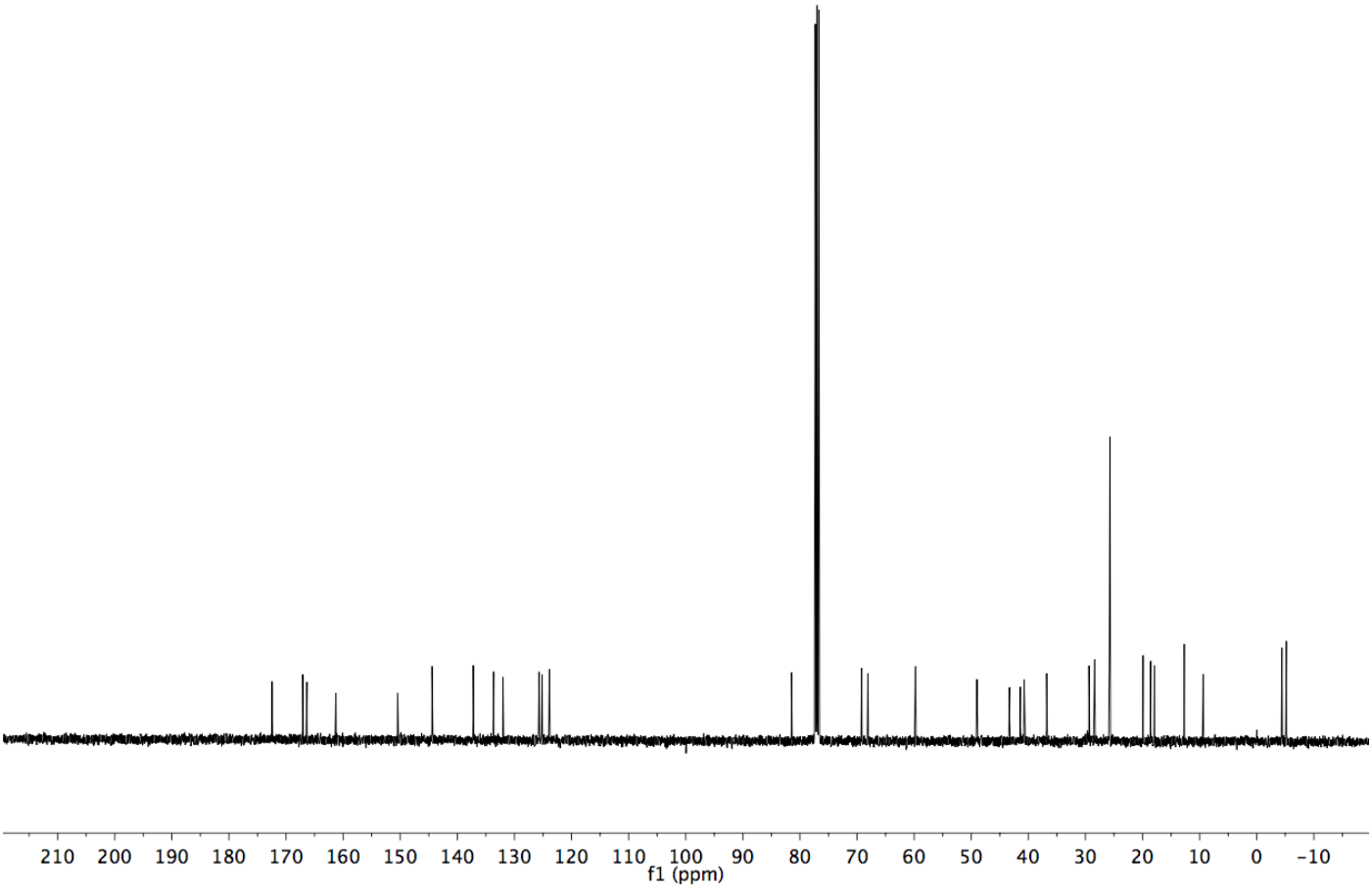

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

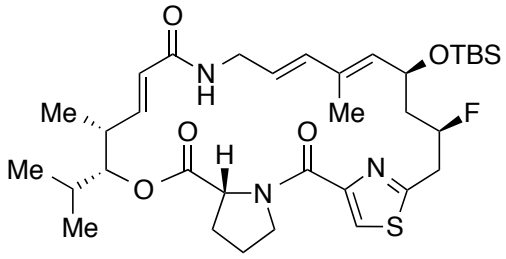

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


O
N
H
OTBS
Me
Me
OH
O
O
H
Me
O
N
N
Me
S

SI-42

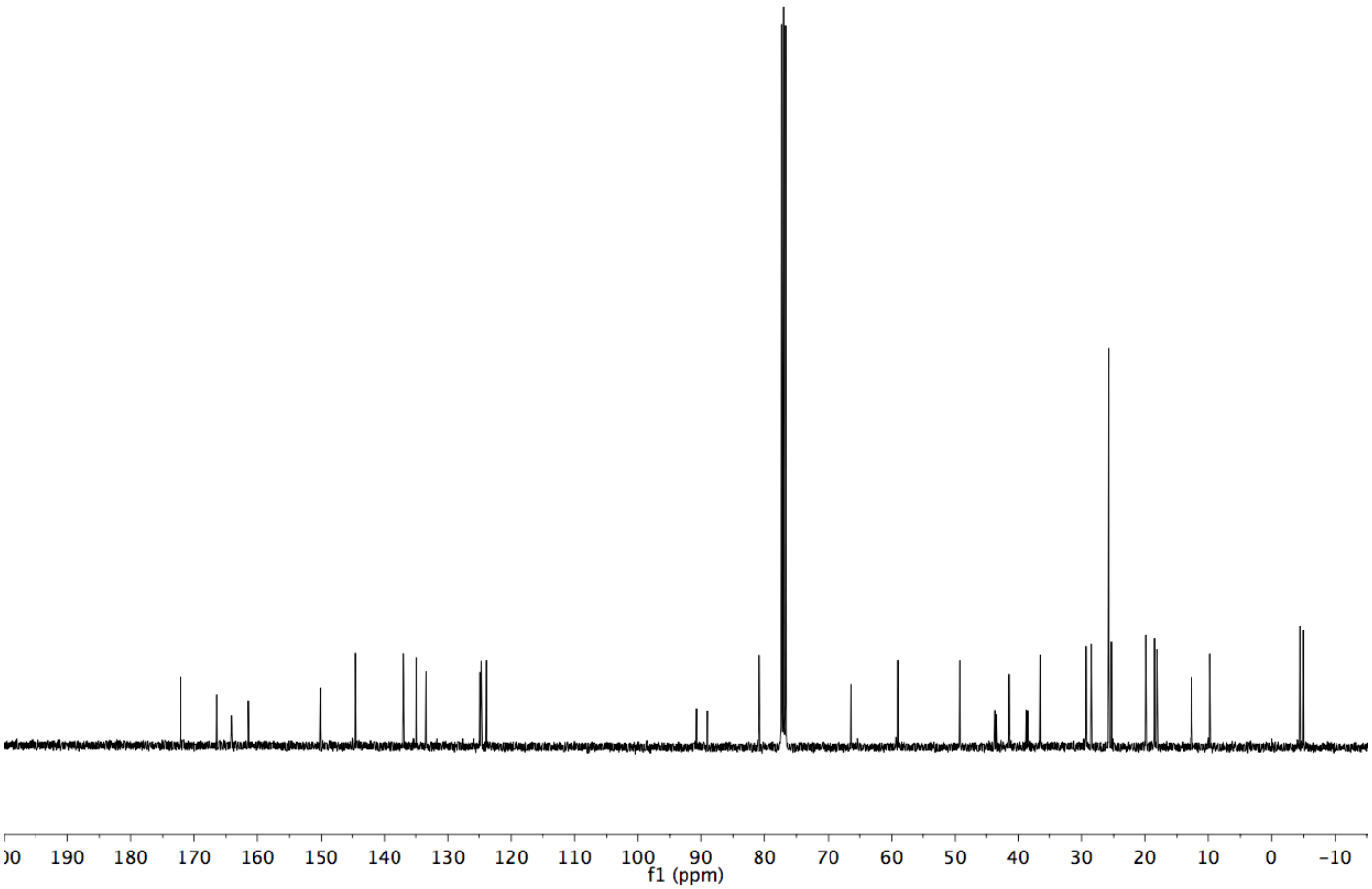
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

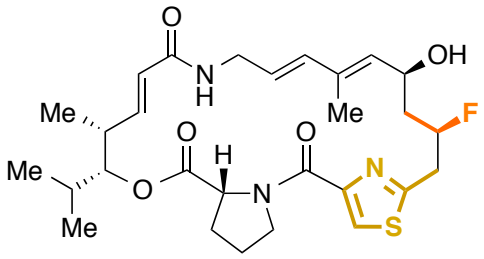

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
F
O
O
H
Me
O
N
N
Me
S

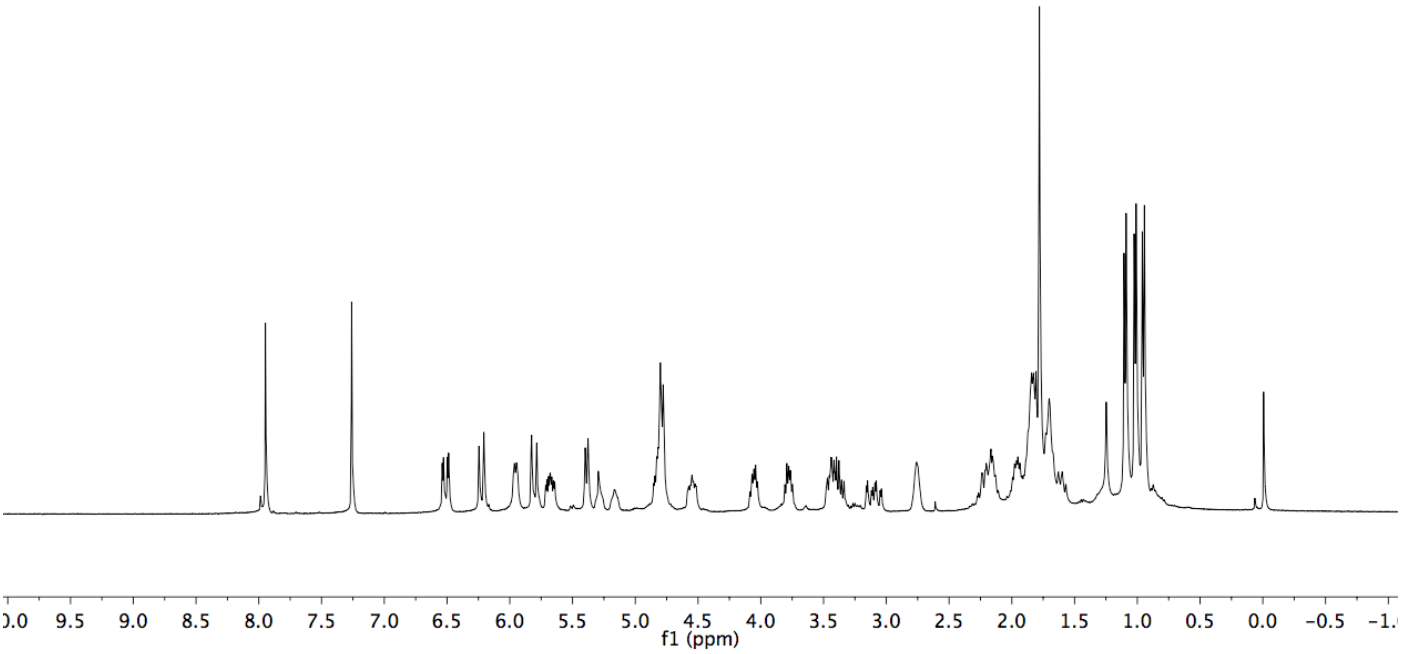
SI-43

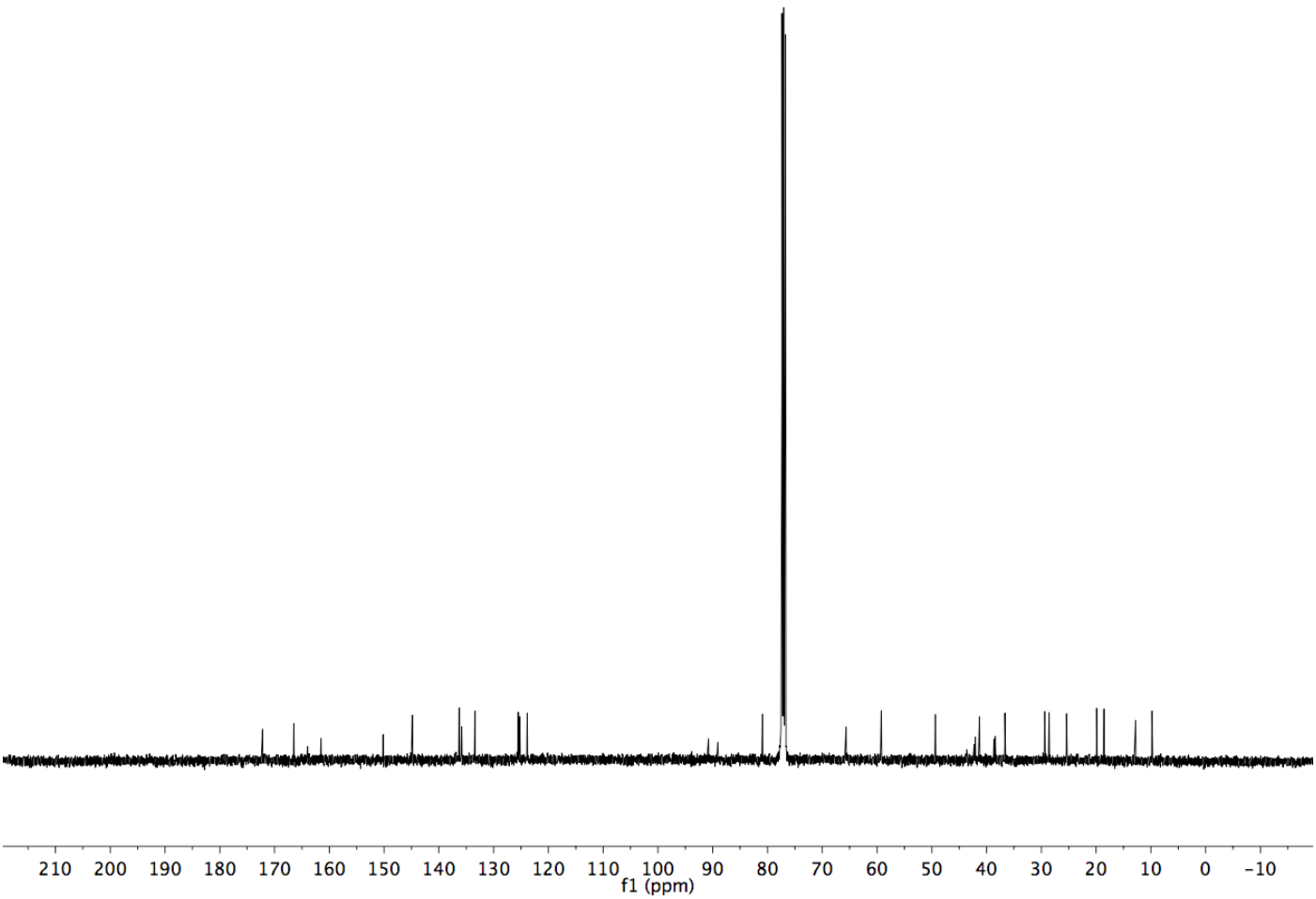
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

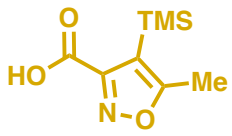

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
F
O
O
H
Me
O
N
N
S
Me

45

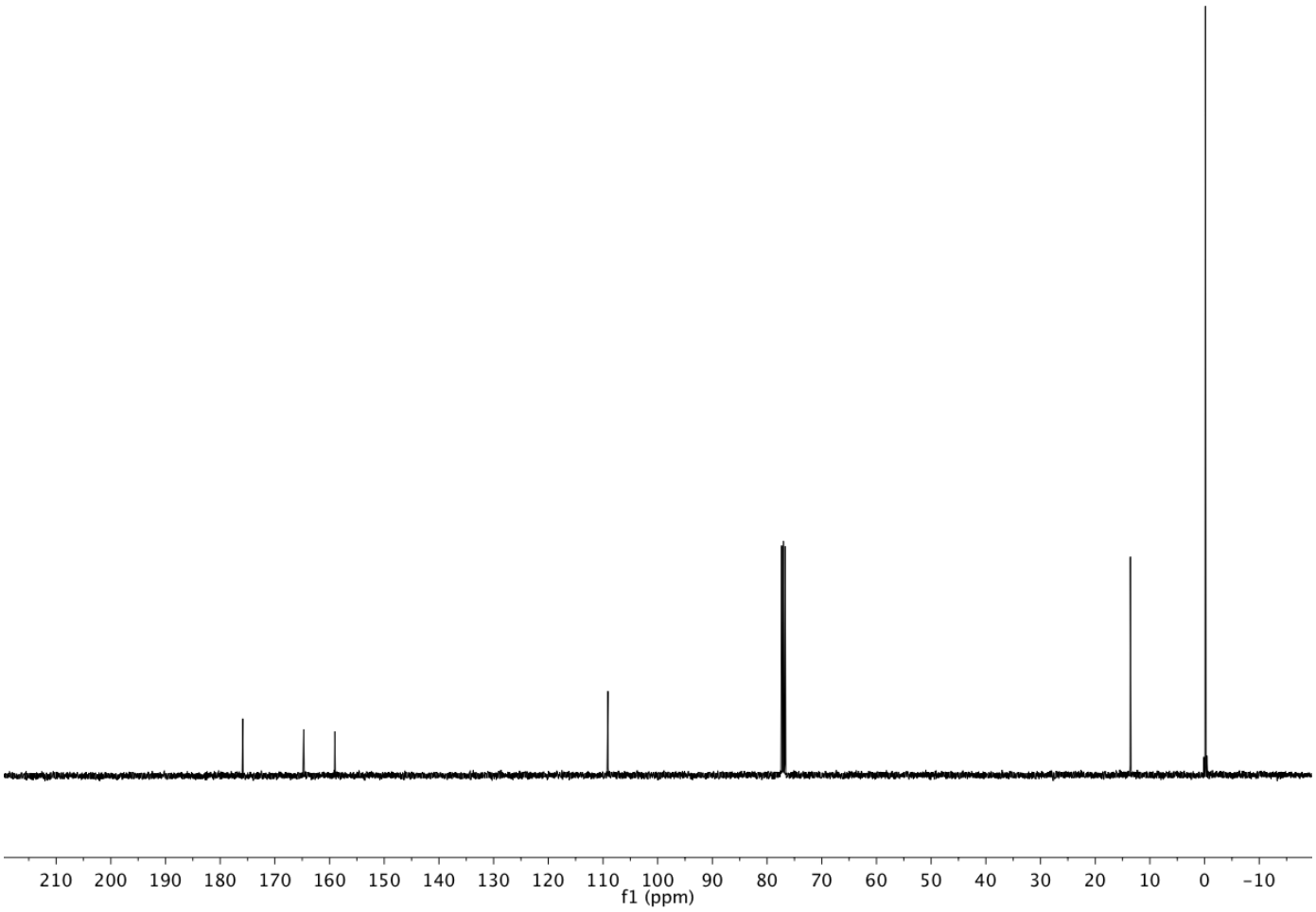

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

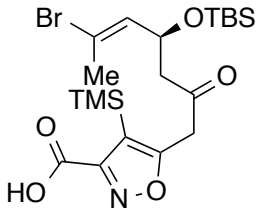

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
TMS
HO
Me
N
O

SI-44

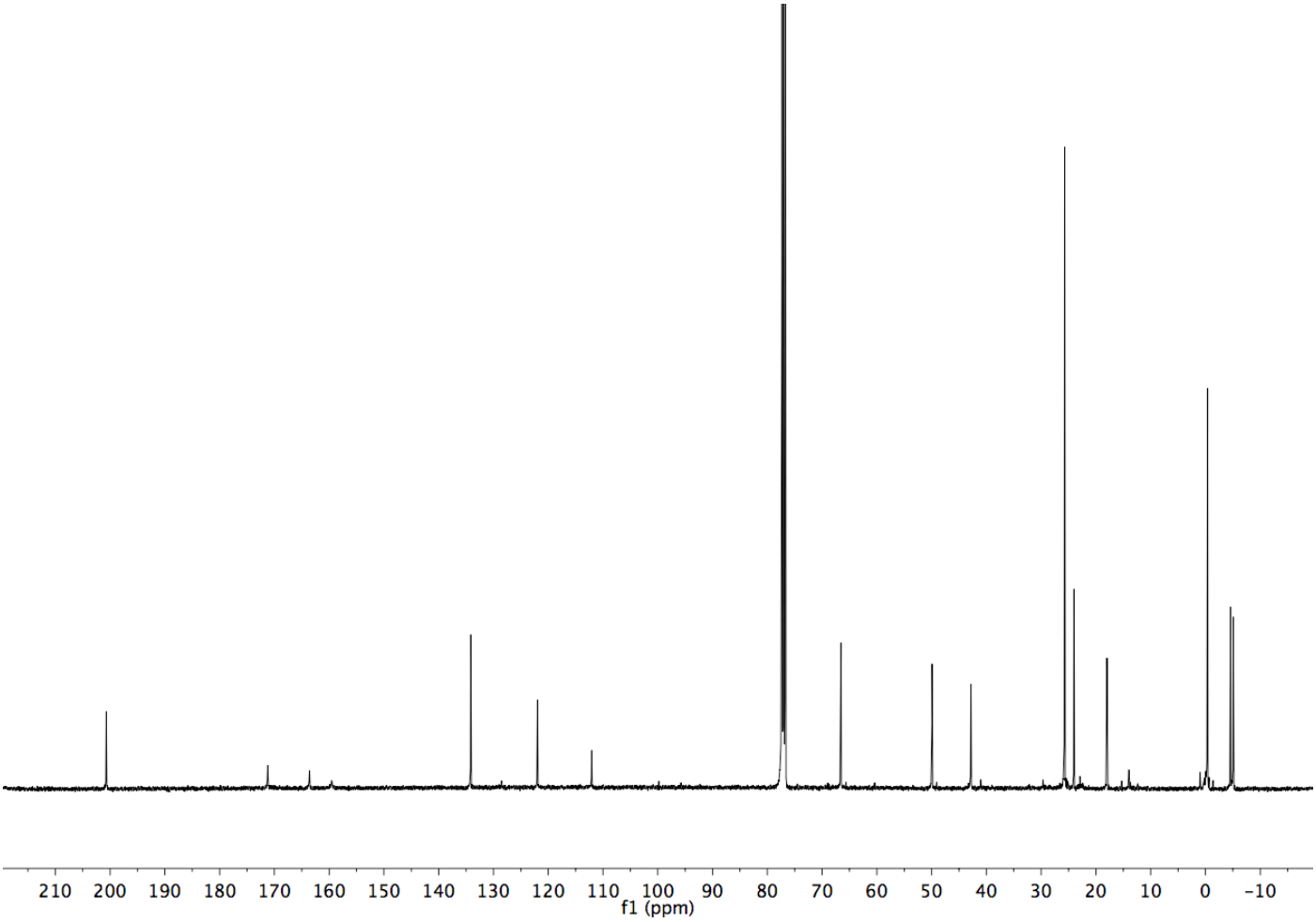
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

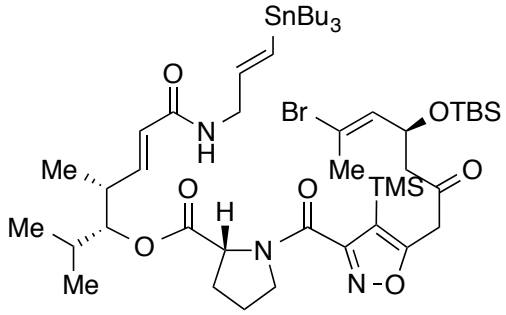

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
TMS
O
O
HO
N
O

SI-45

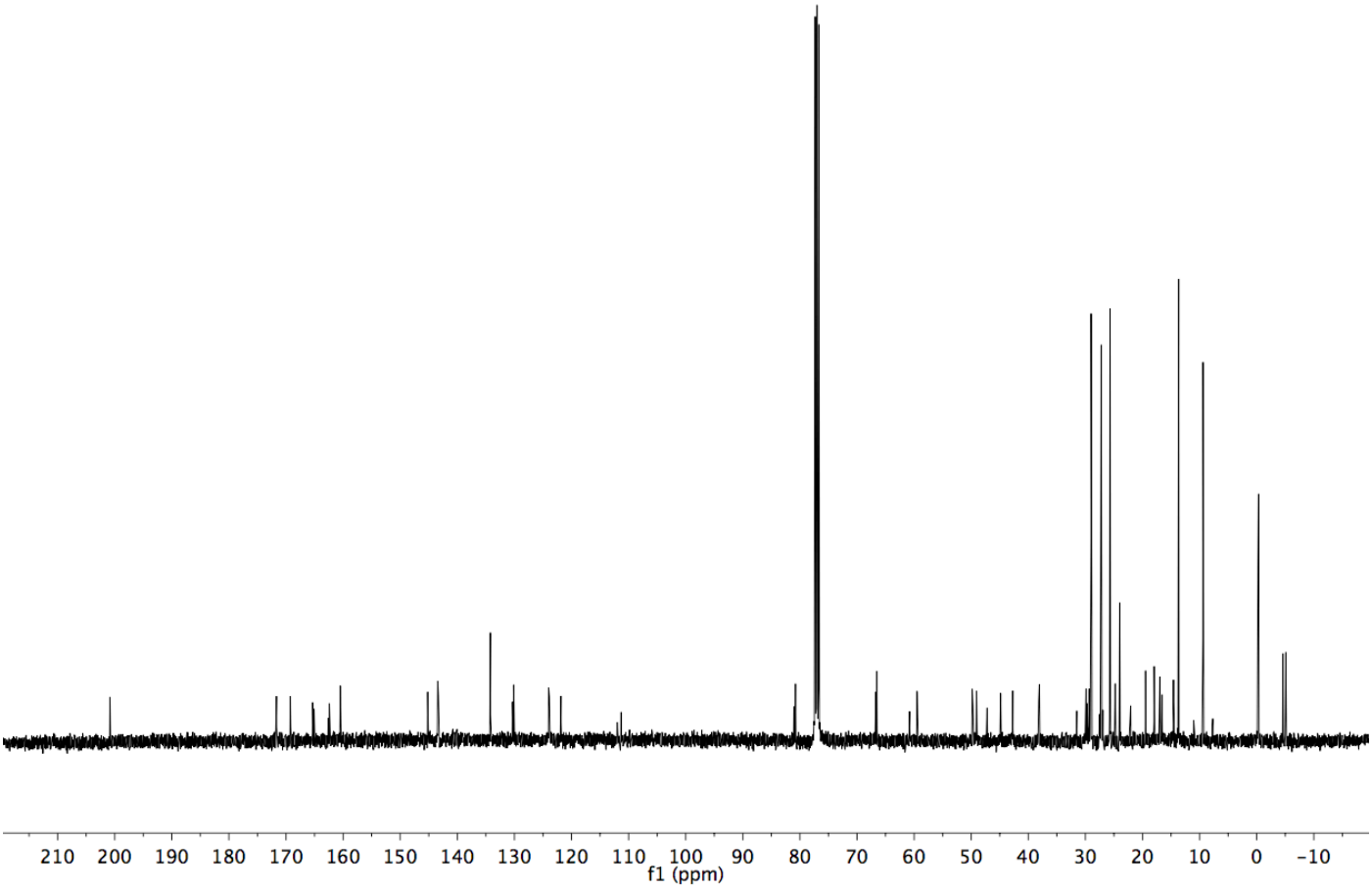
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

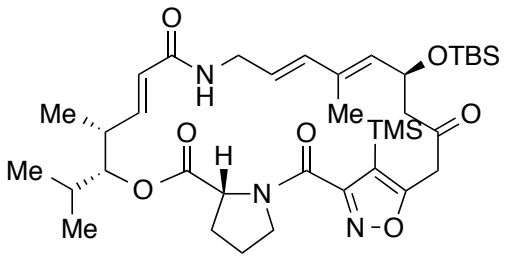

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
TMS
O
O
O
H
Me
O
N
N
O
Me

SI-46

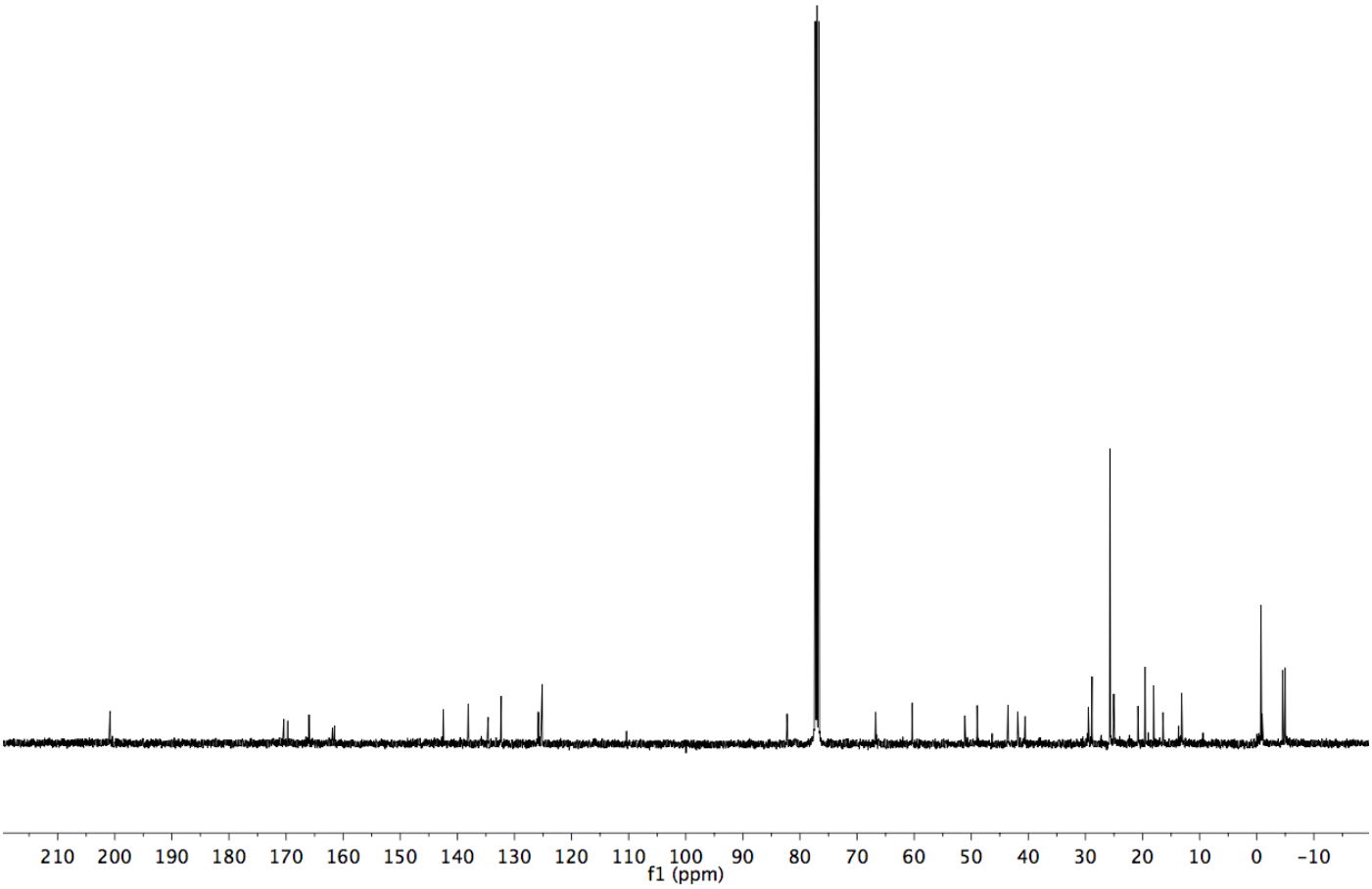
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

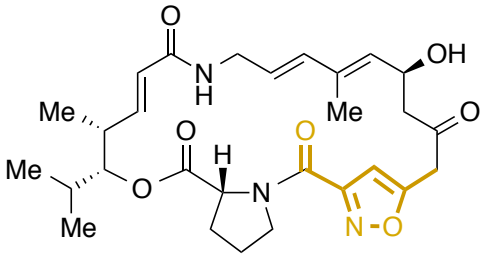

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
TMS
O
O
O
H
Me
O
N
Me
N
O

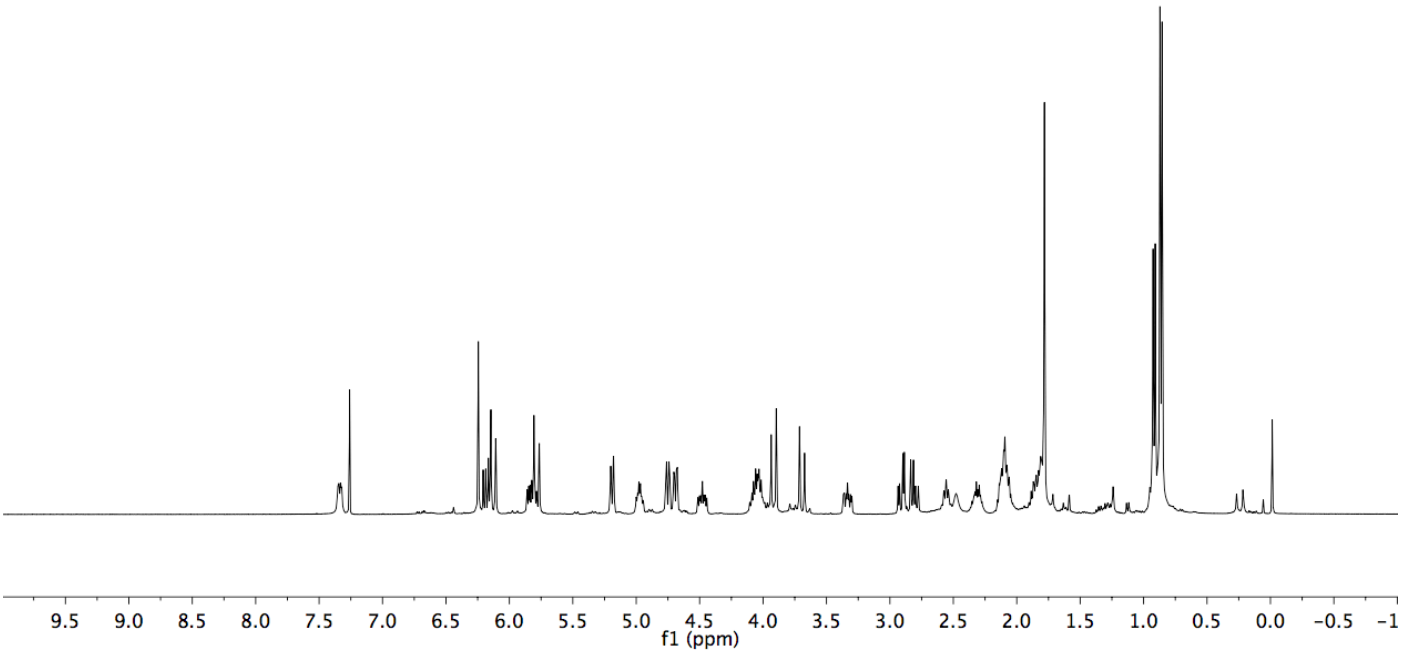
SI-47

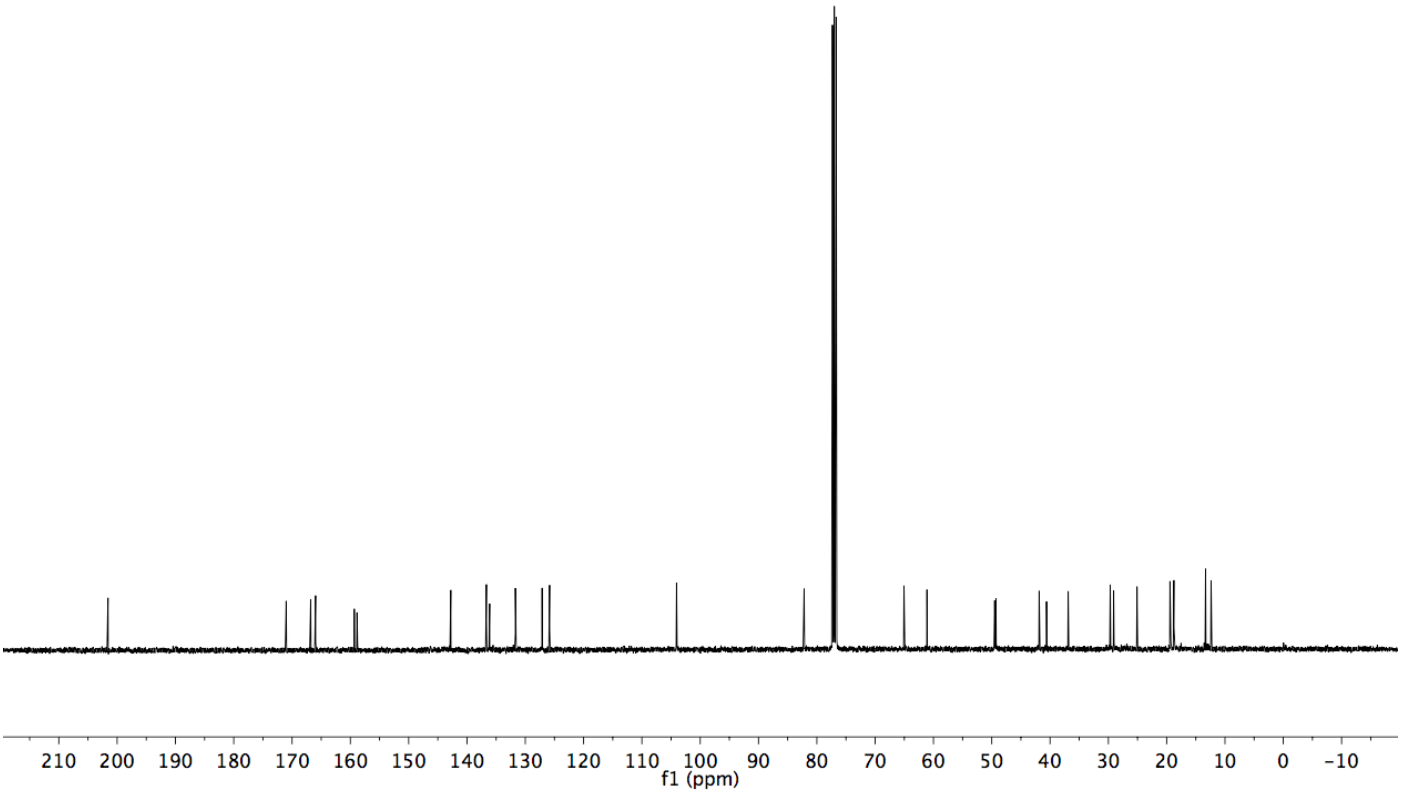
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

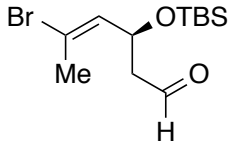

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
H
Me
O
N
O
N-O
Me

27

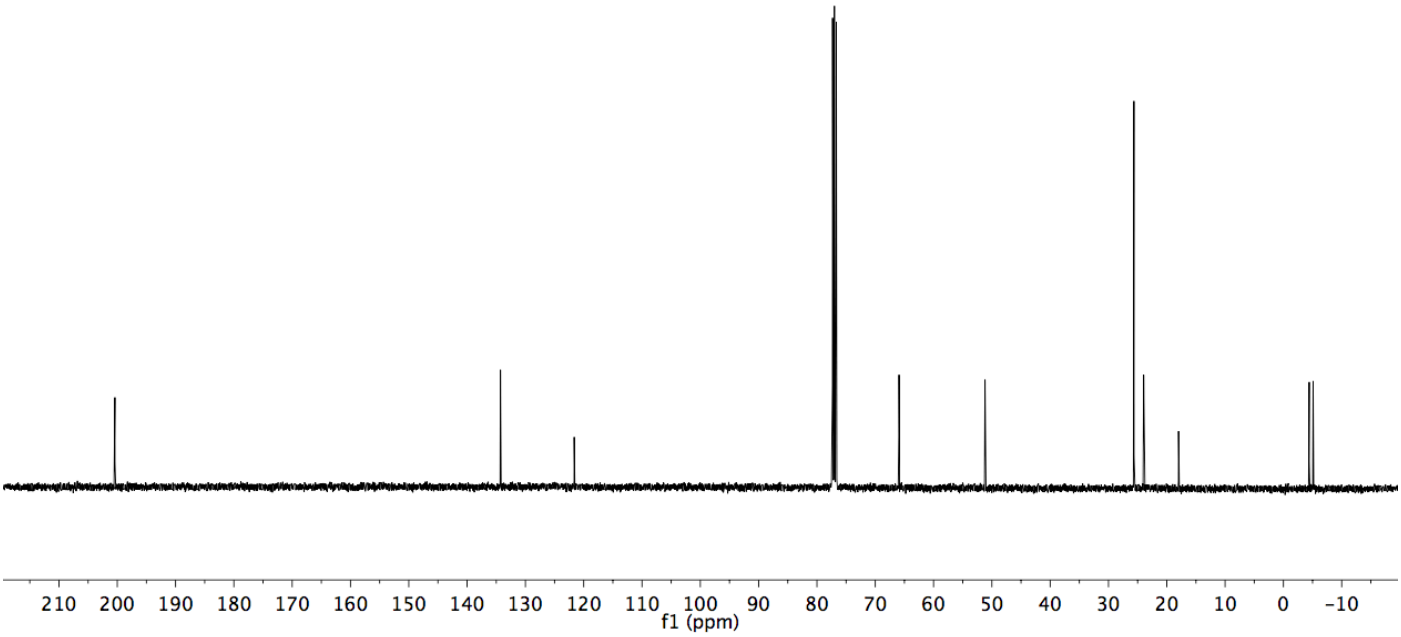

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

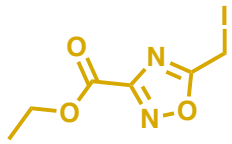

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
H

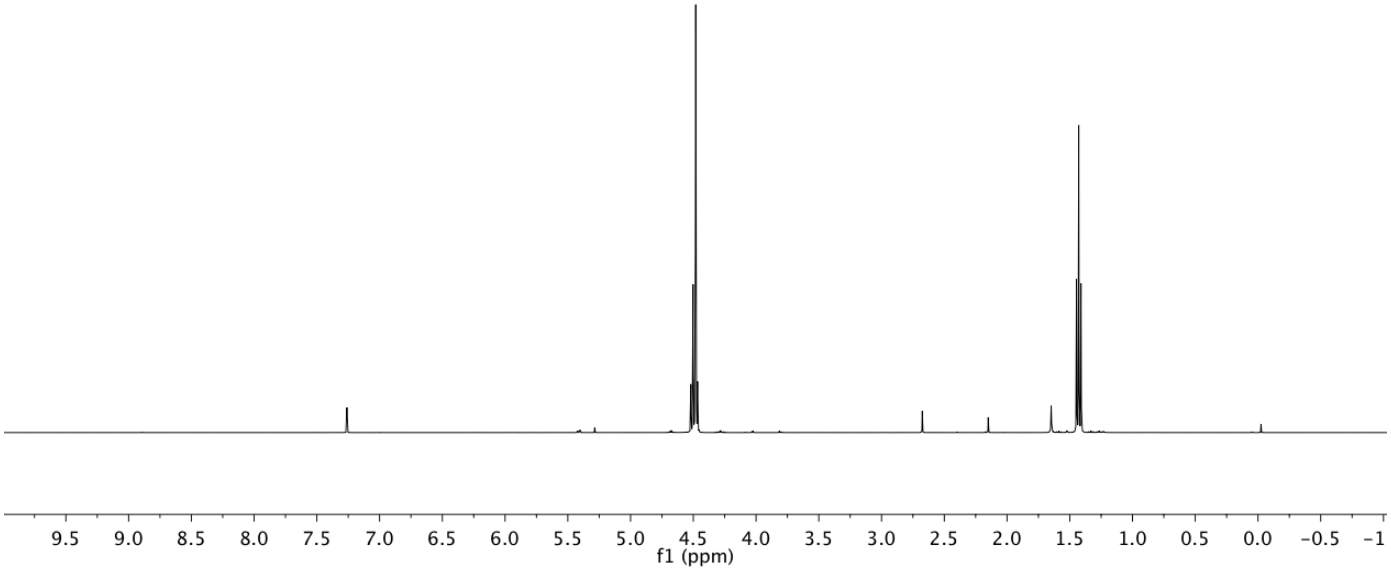
SI-48

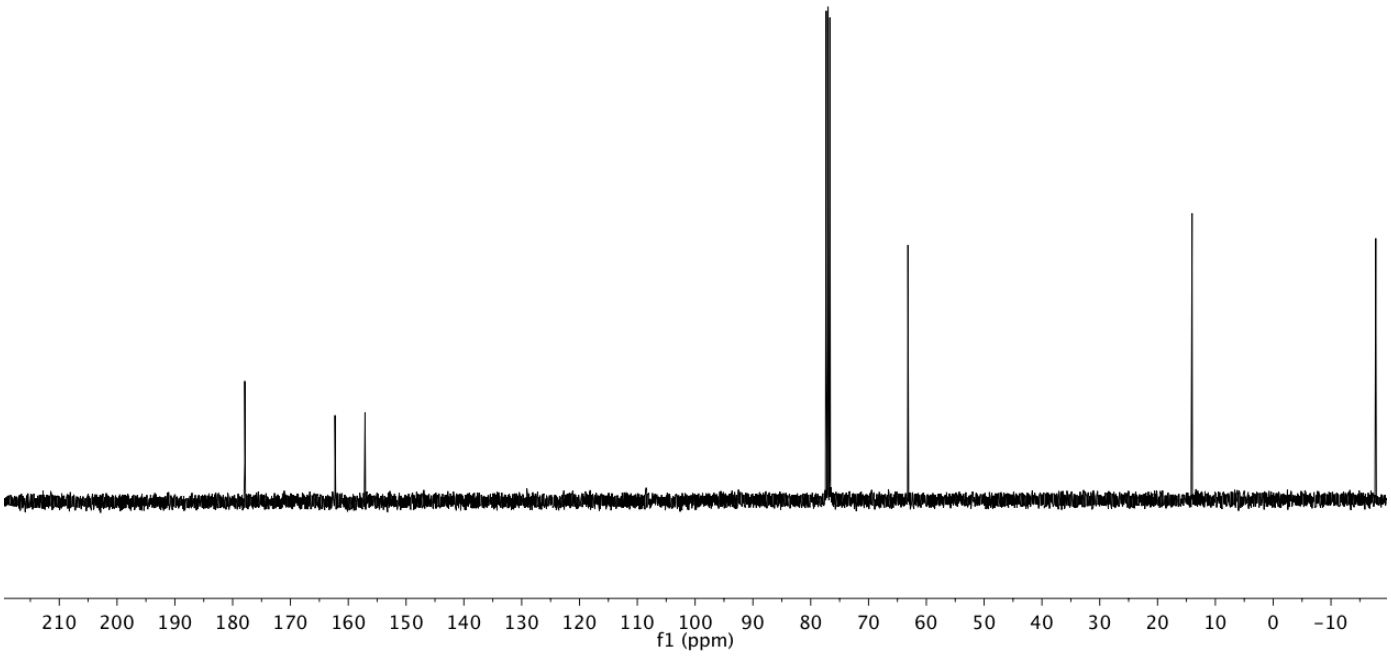
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

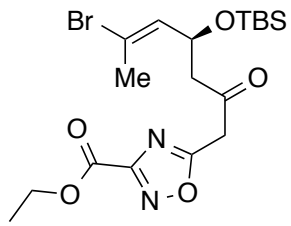

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
O
N
N
O
I

SI-49

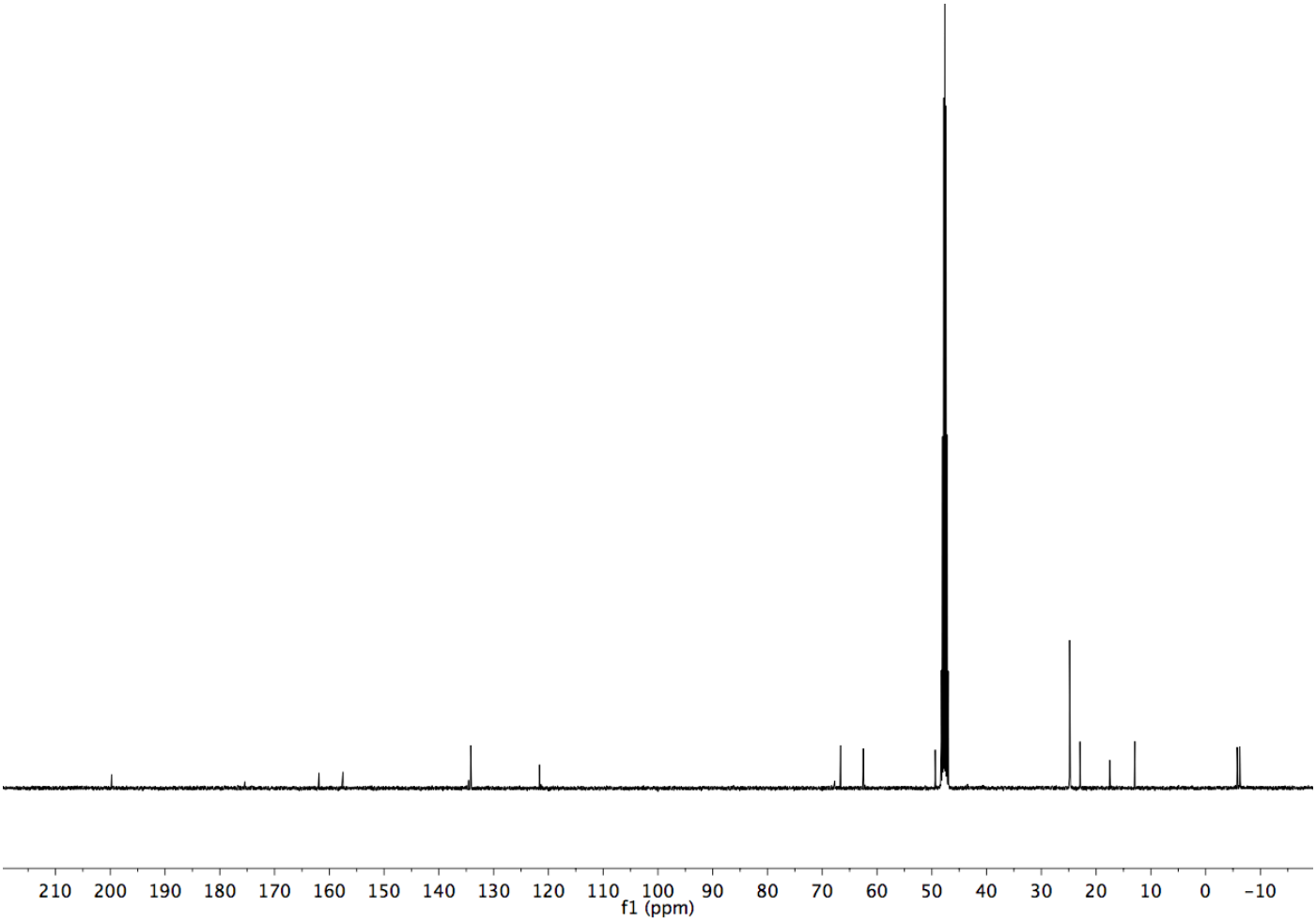

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

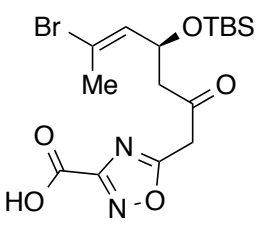

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
O
O
N
O
N
O

SI-50

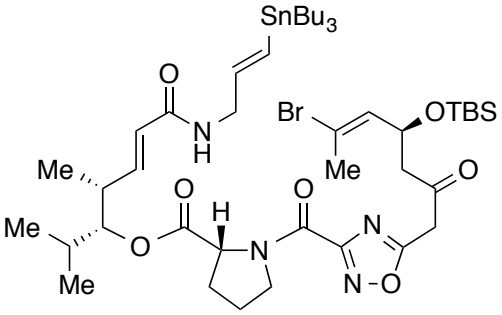
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

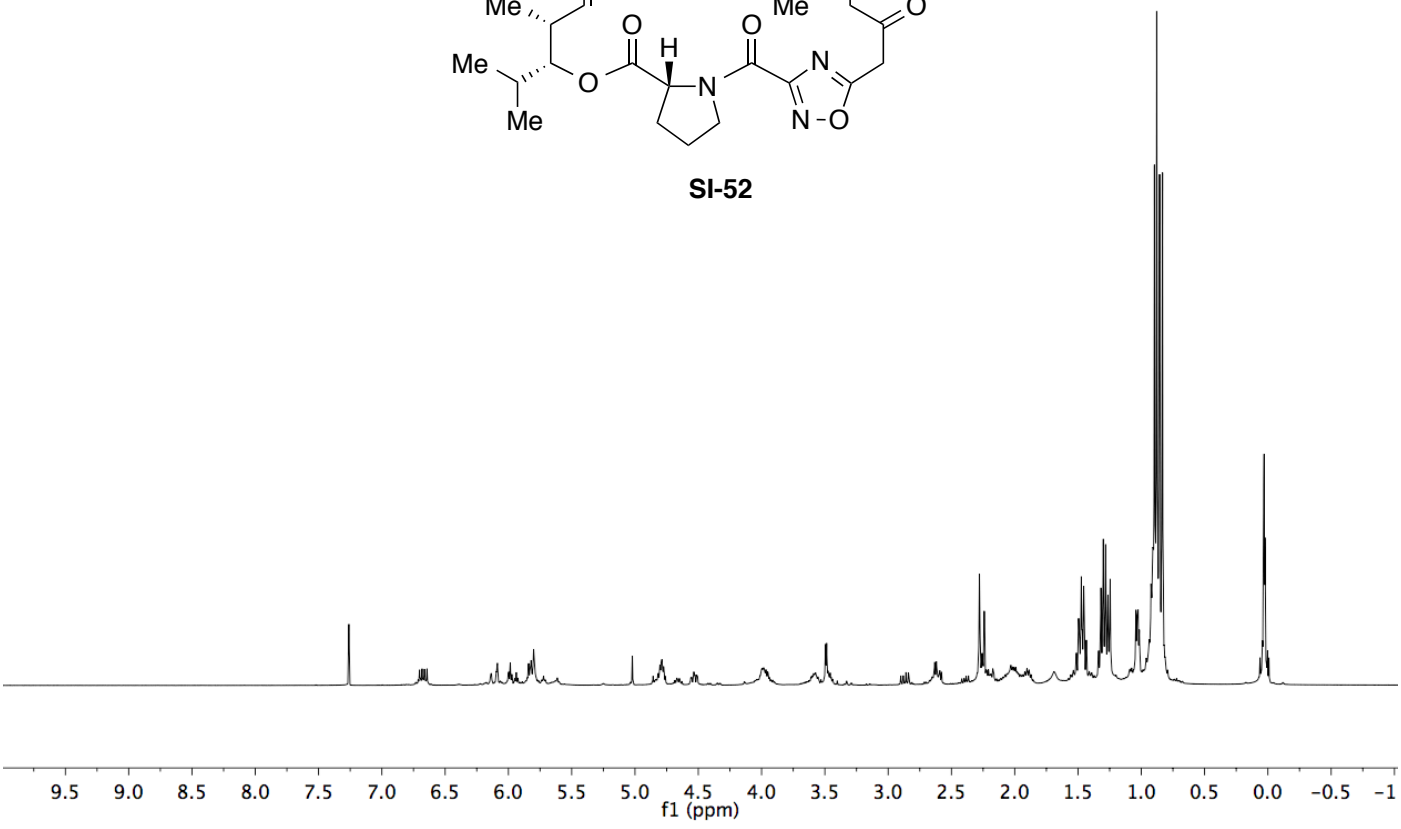

Br
OTBS
Me
O
O
N
HO
N
O

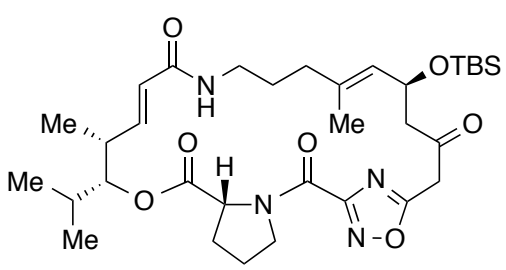
SI-51

16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
H
O
Me
O
N
N
Me
N
O

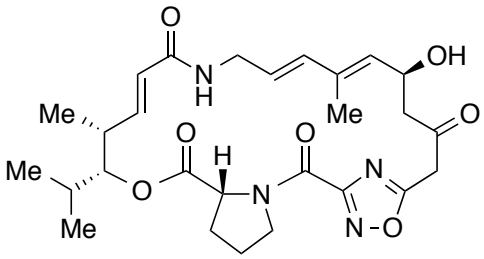
SI-52


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

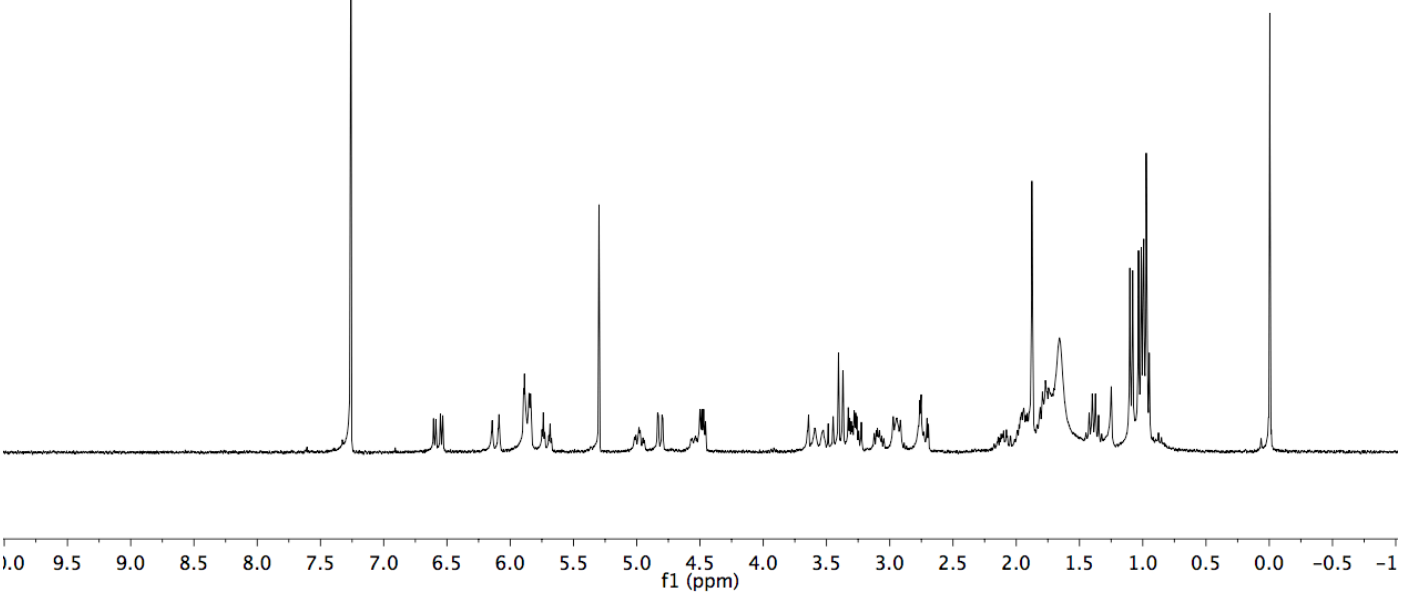

O
N
H
OTBS
Me
Me
O
O
O
H
Me
O
N
N
Me
N
O

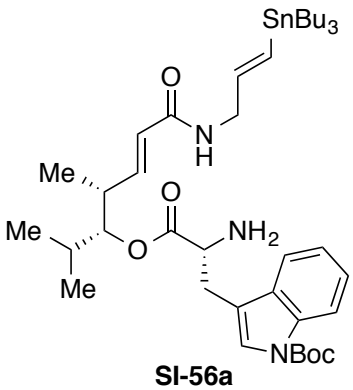
SI-53

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
Me
O
N
N
Me
N
O

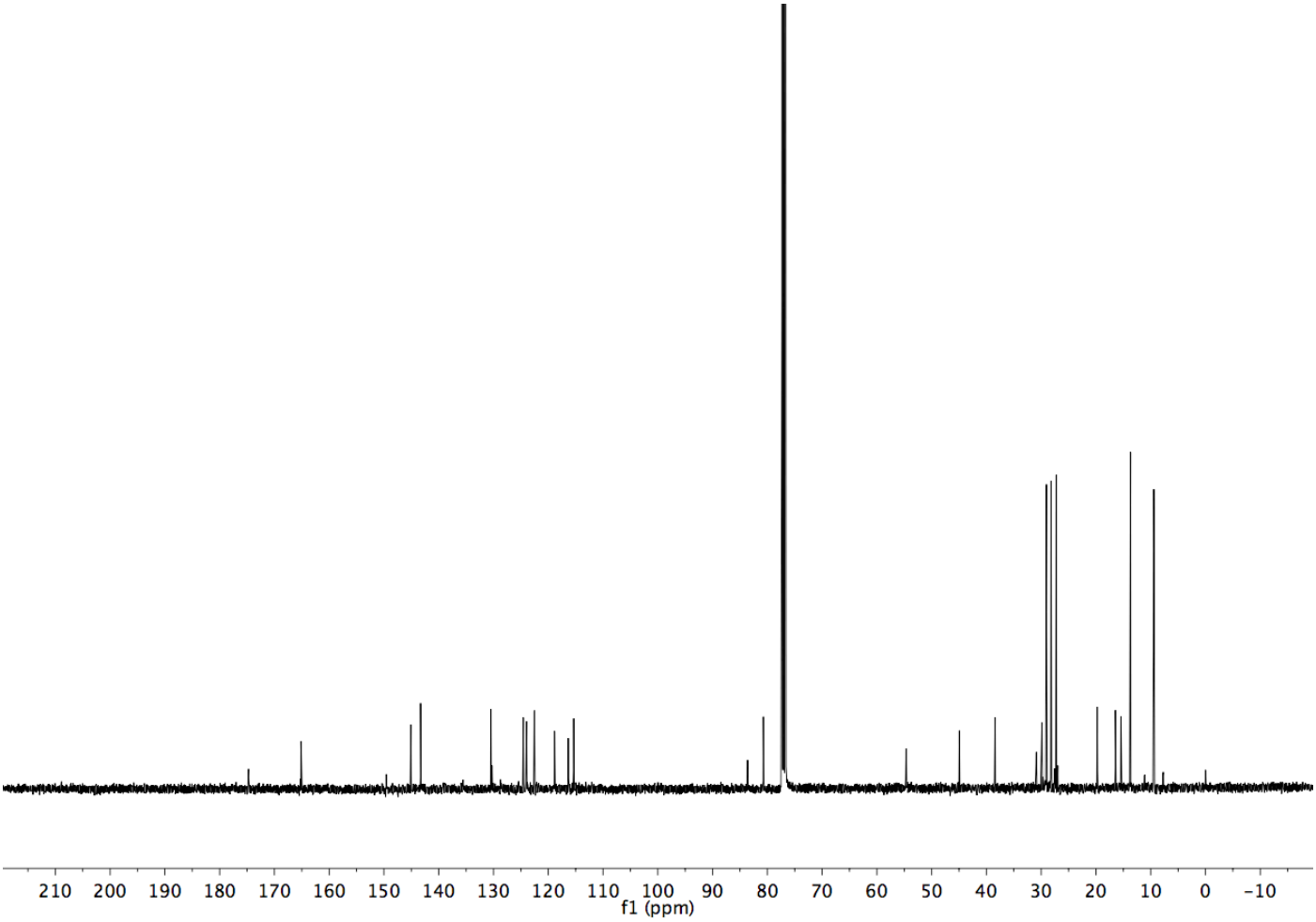
28

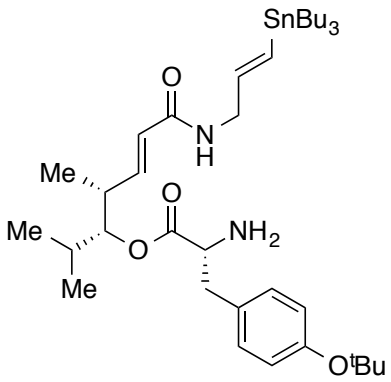

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


SnBu3
O
N
H
Me
O
Me
O
NH2
Me
NBoc

SI-56a

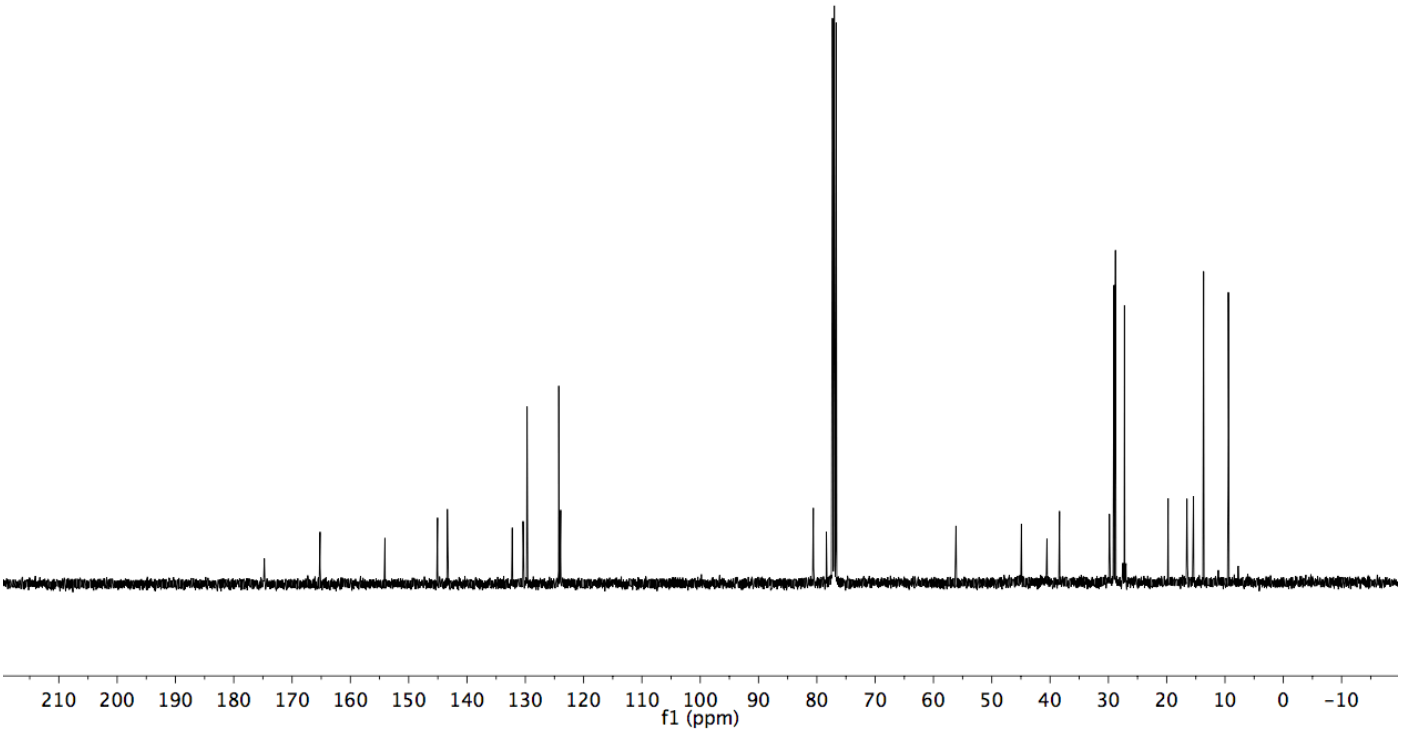
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

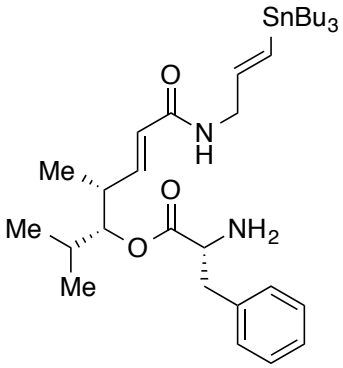

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
O
Me
O
NH2
Me
OtBu

SI-56b

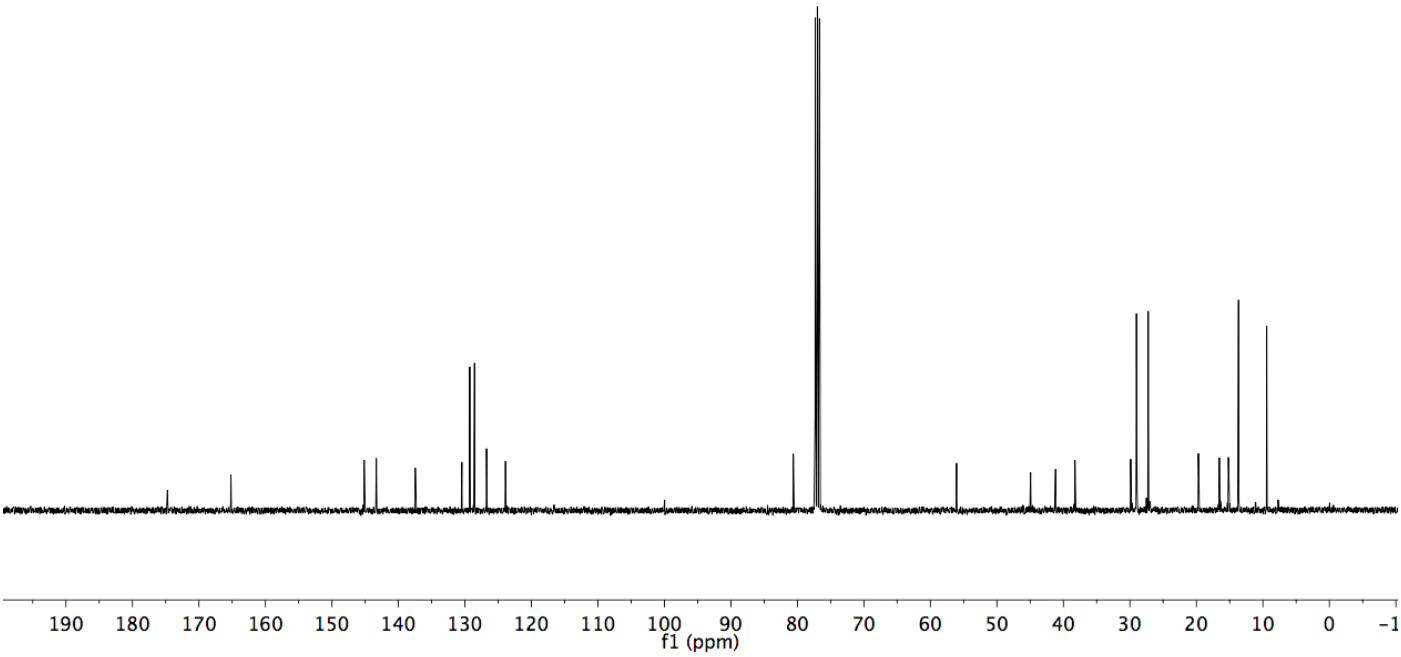
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

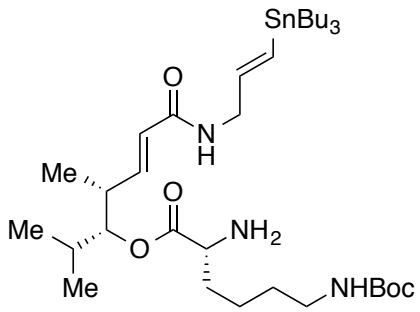

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
Me
Me
O
O
NH2

SI-56c

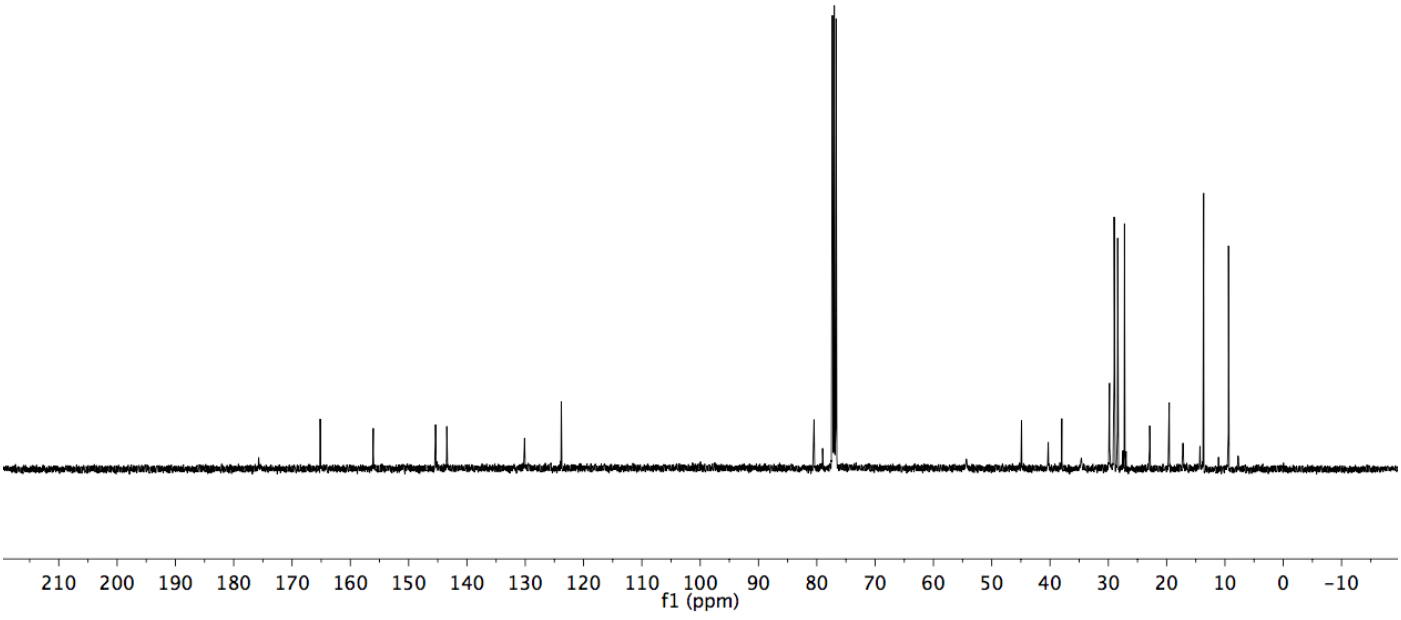
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

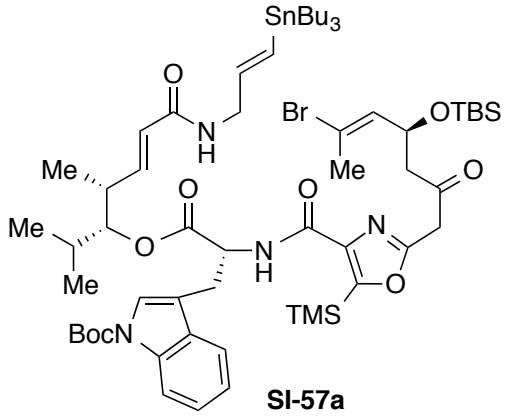

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


SnBu3
O
N
H
Me
O
Me
O
NH2
Me
NHBoc

SI-56d

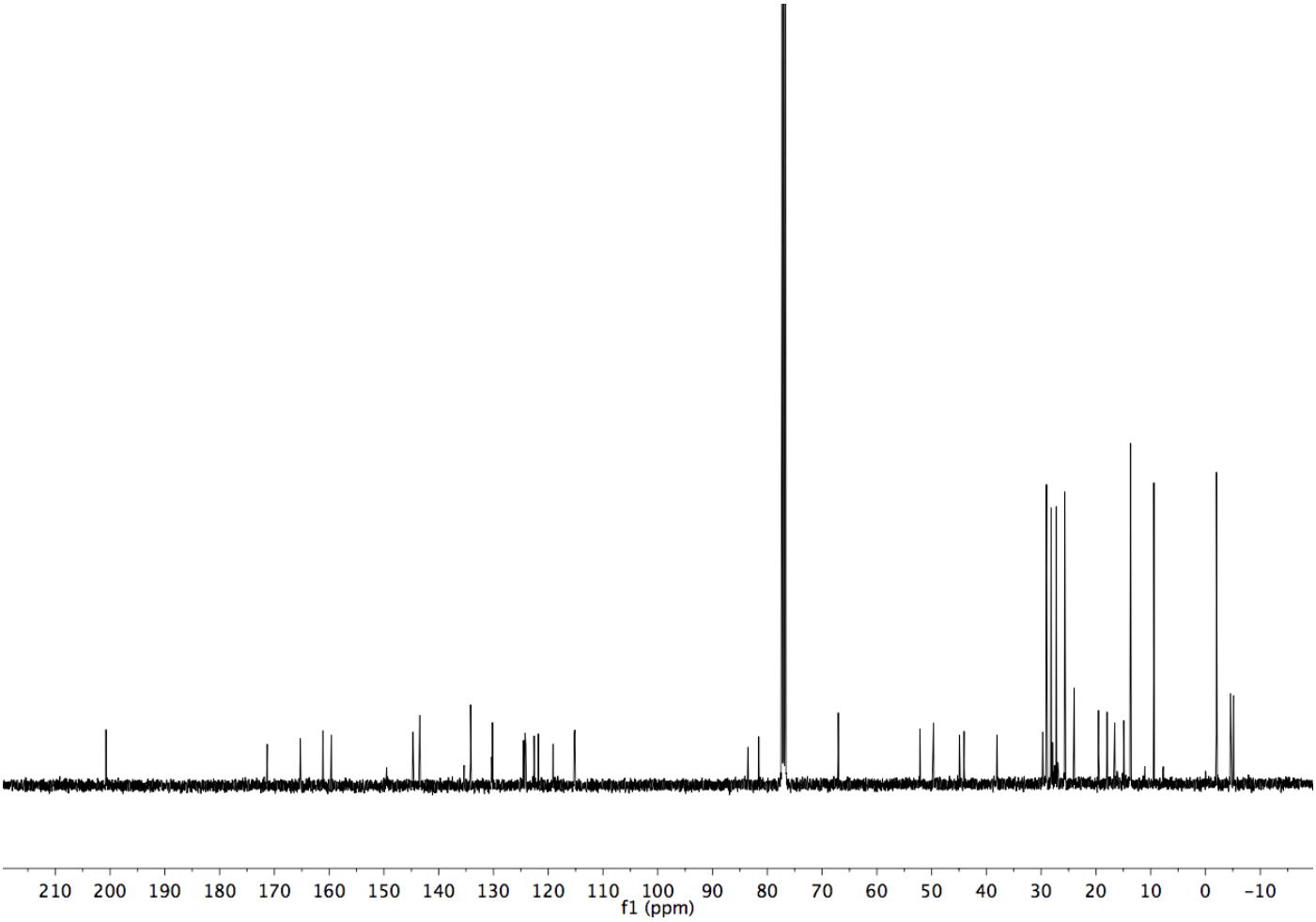
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

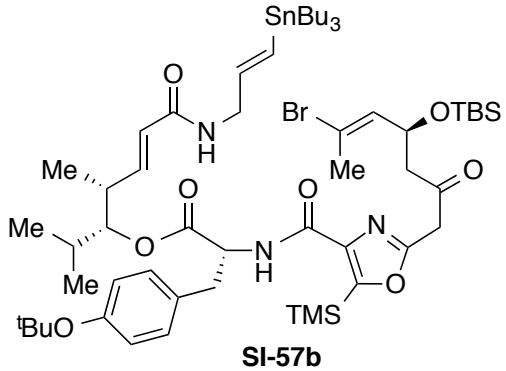

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
O
Me
O
N
H
N
Me
O
TMS
BocN

SI-57a

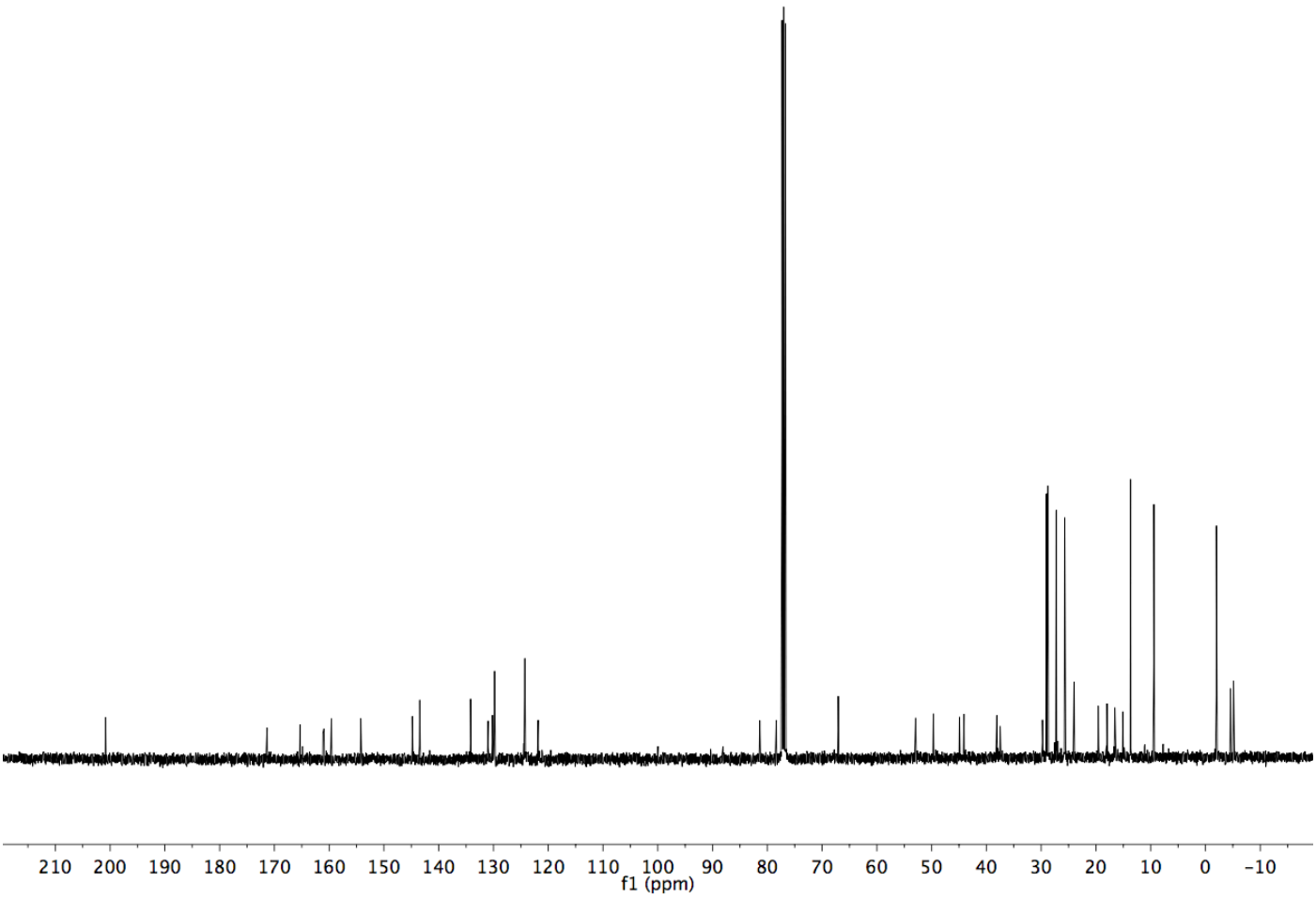
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

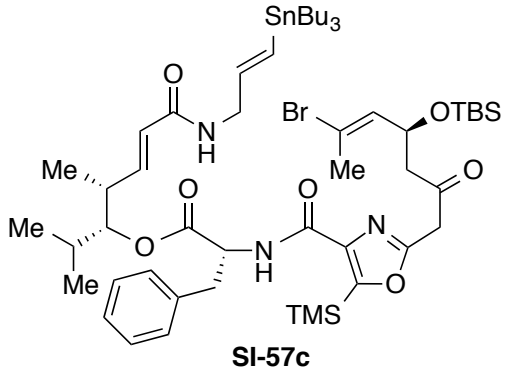

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
O
Me
O
N
H
N
Me
O
tBuO
TMS

SI-57b

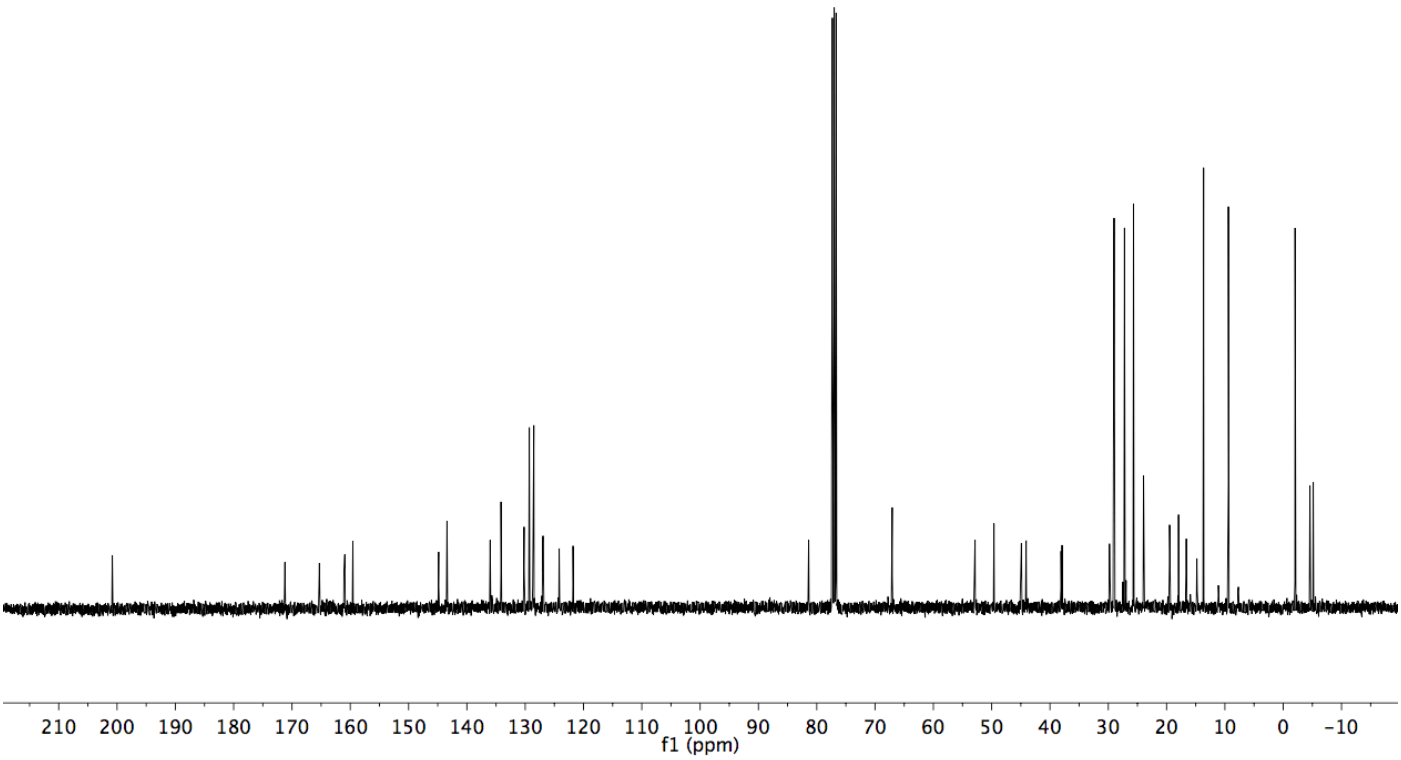
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

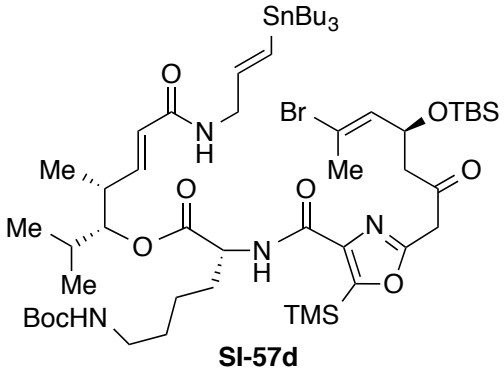

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
O
Me
O
N
H
N
Me
O
TMS

SI-57c

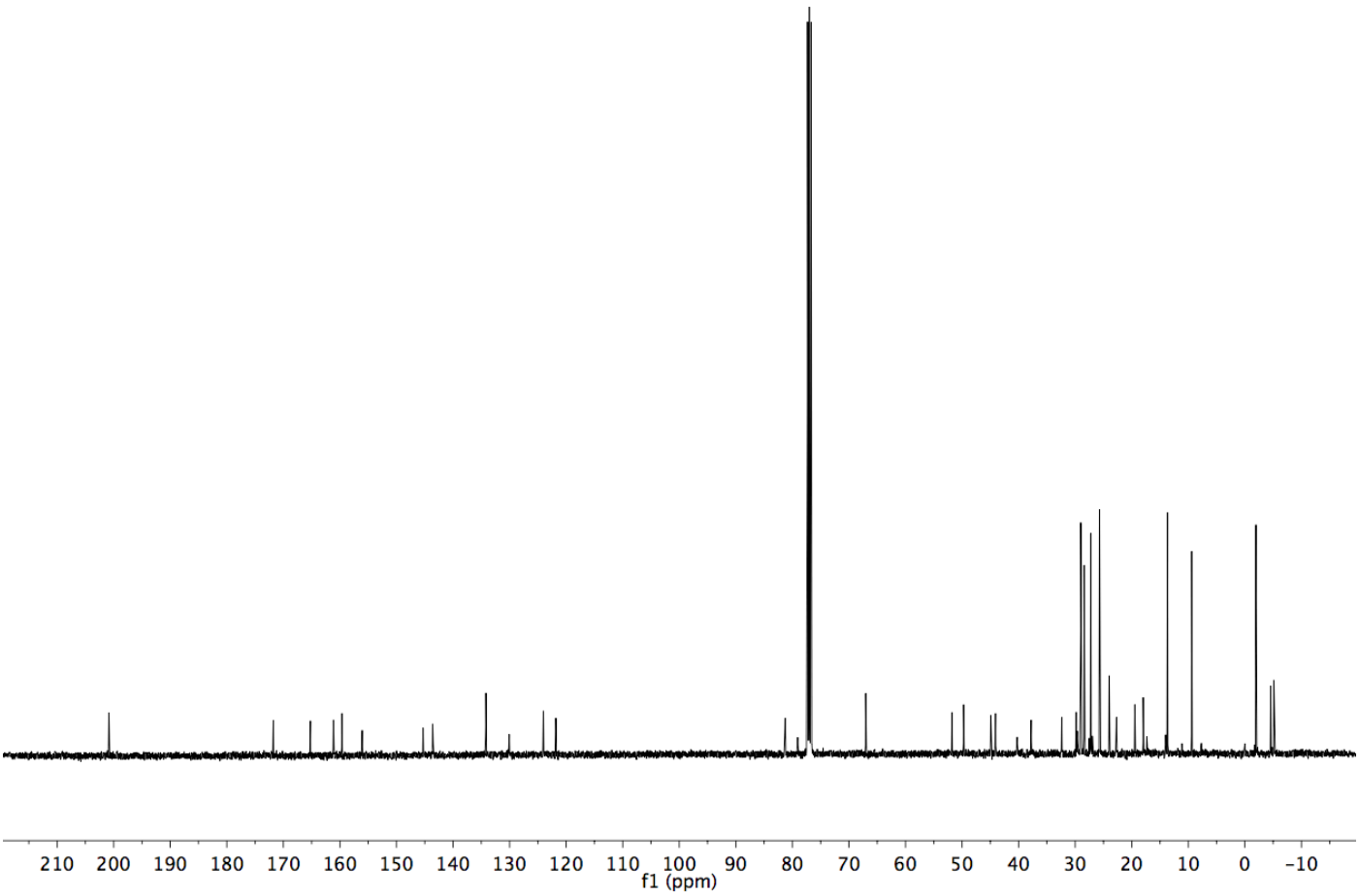
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

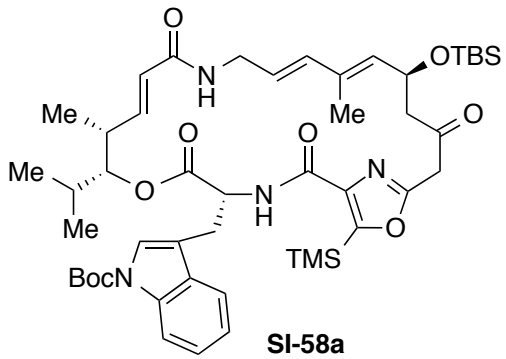

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
O
Me
O
N
H
N
Me
O
BocHN
TMS

SI-57d

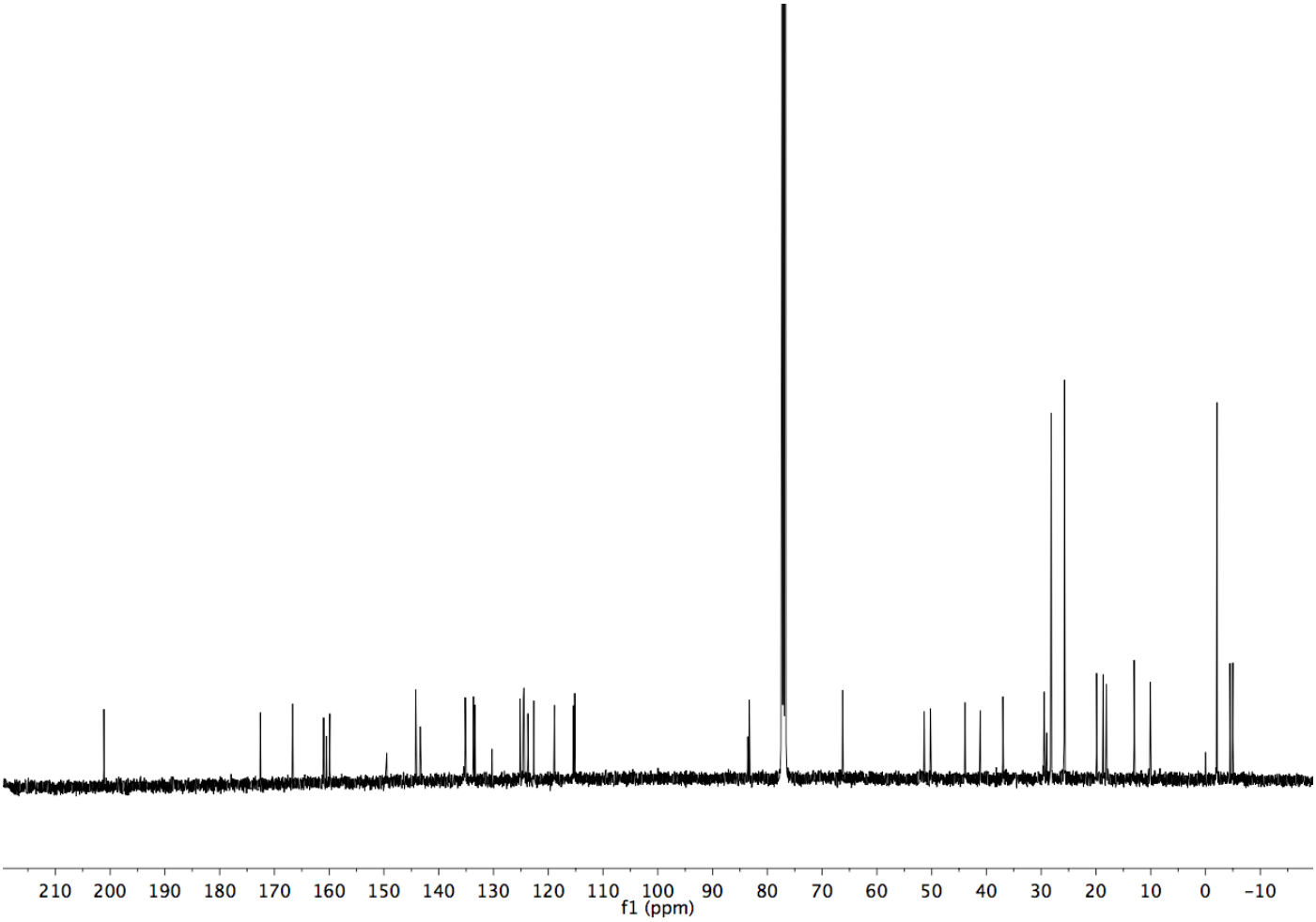
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

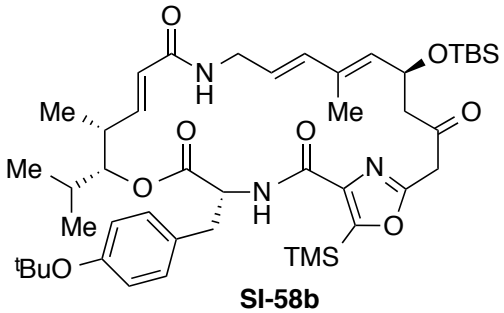

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
Me
O
N
H
N
Me
O
TMS
BocN

SI-58a

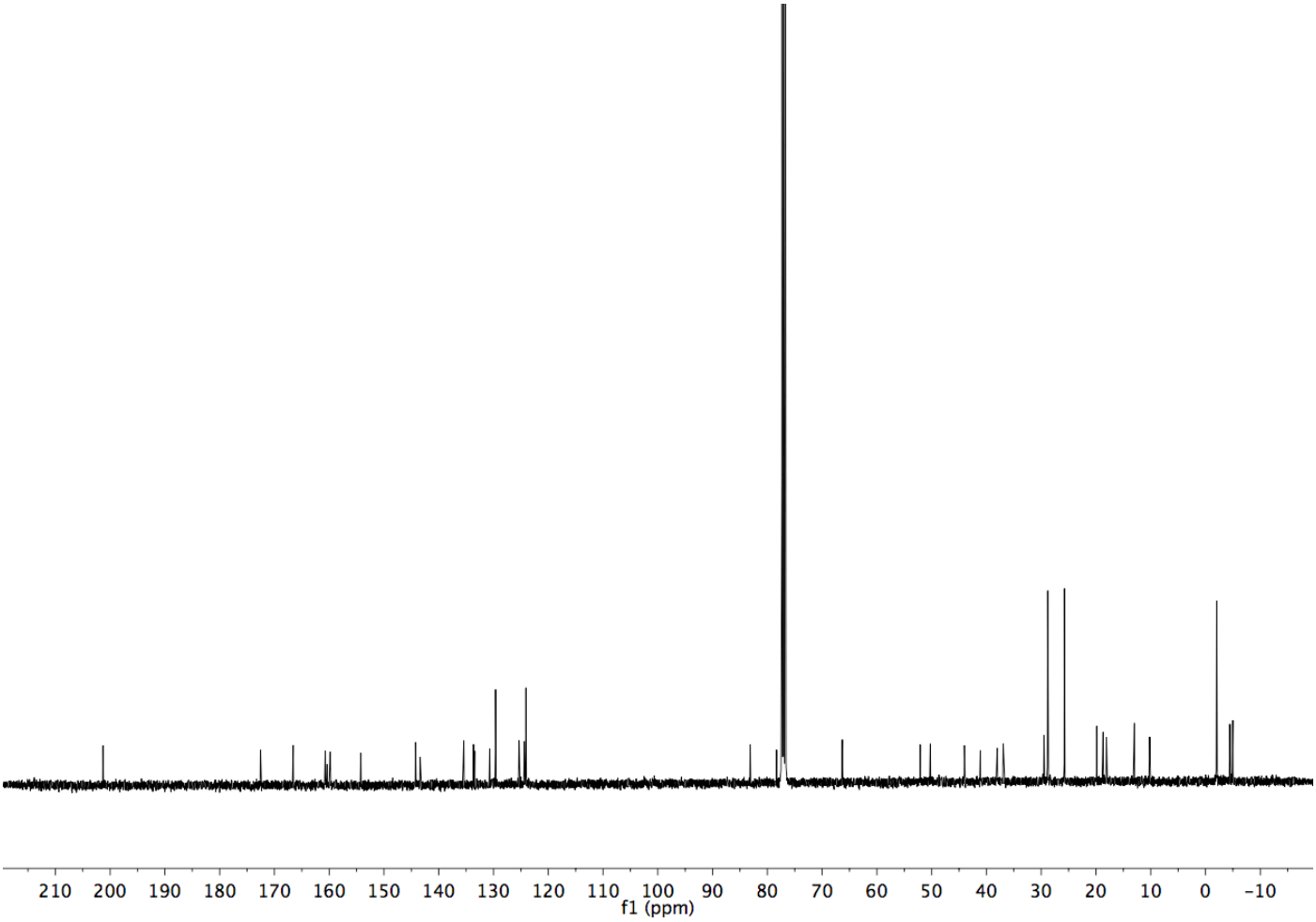
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

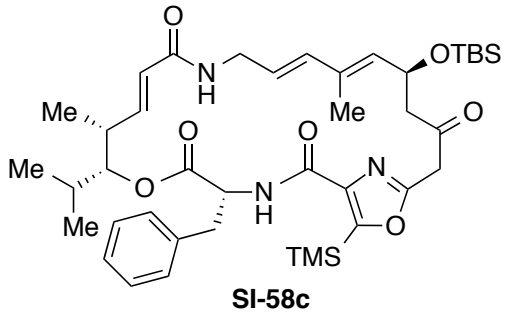

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
Me
O
N
H
O
Me
TMS
tBuO

SI-58b

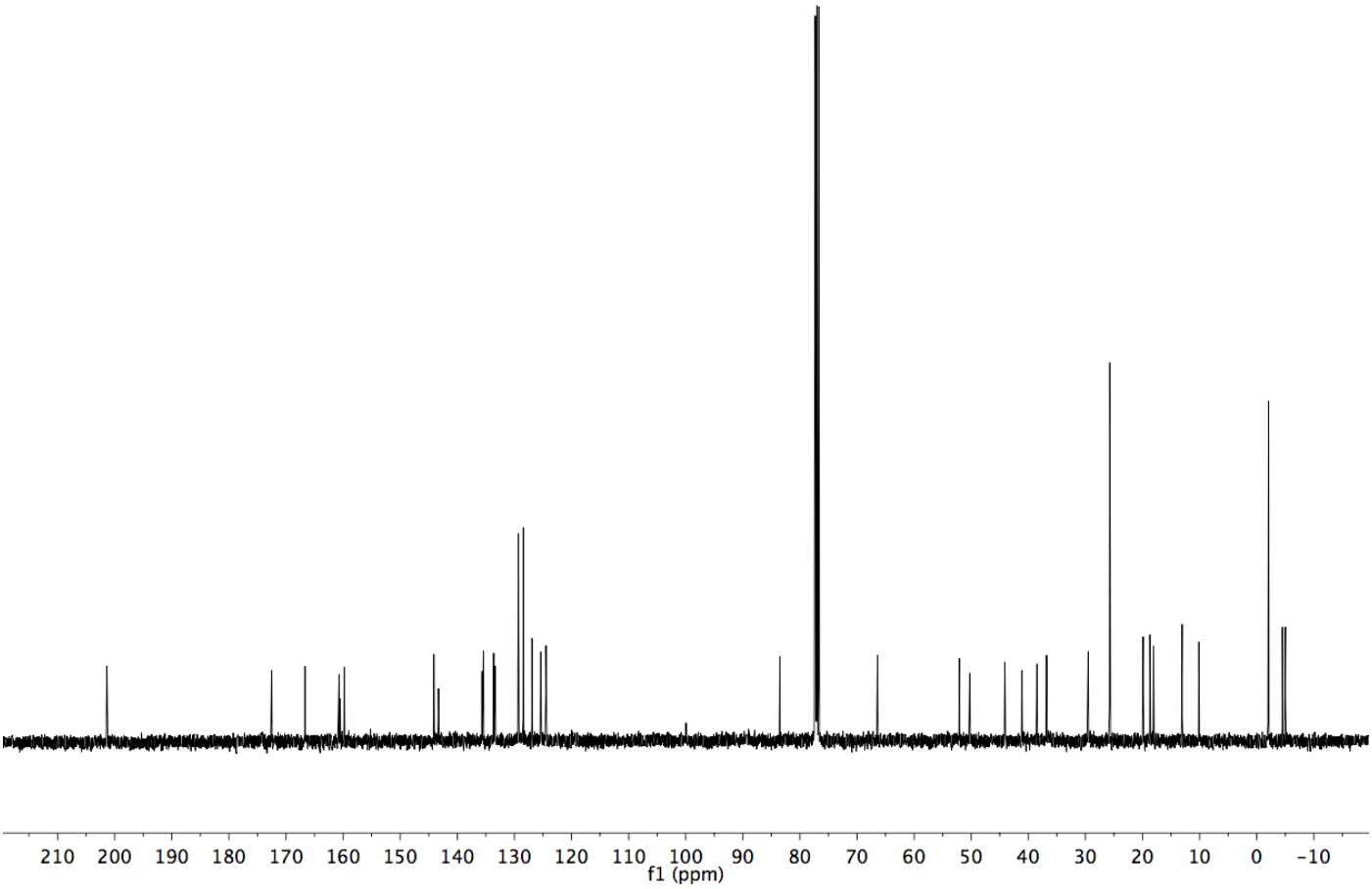
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

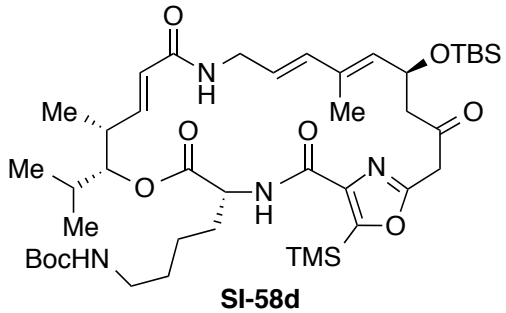

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
Me
O
N
H
O
Me
TMS

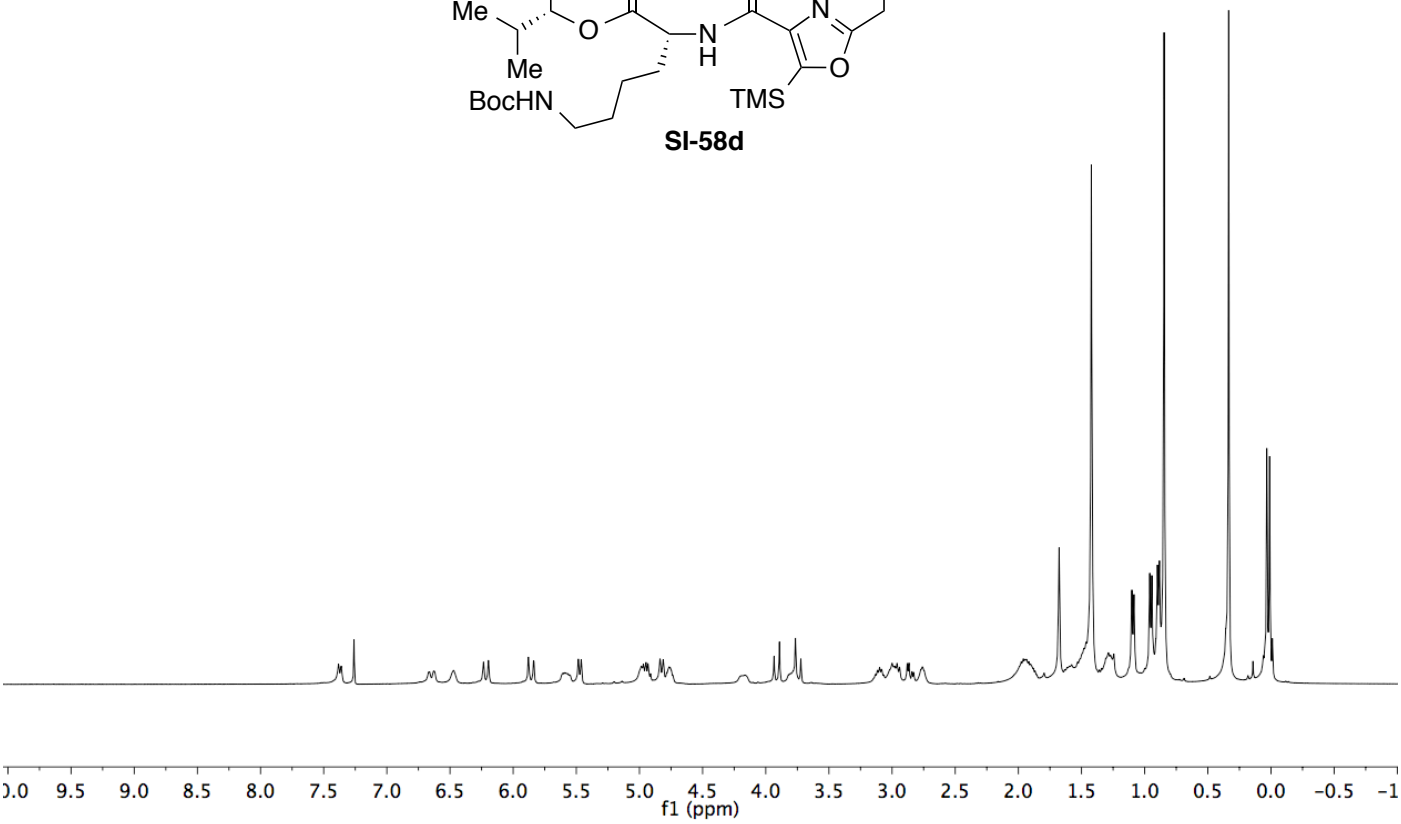
SI-58c

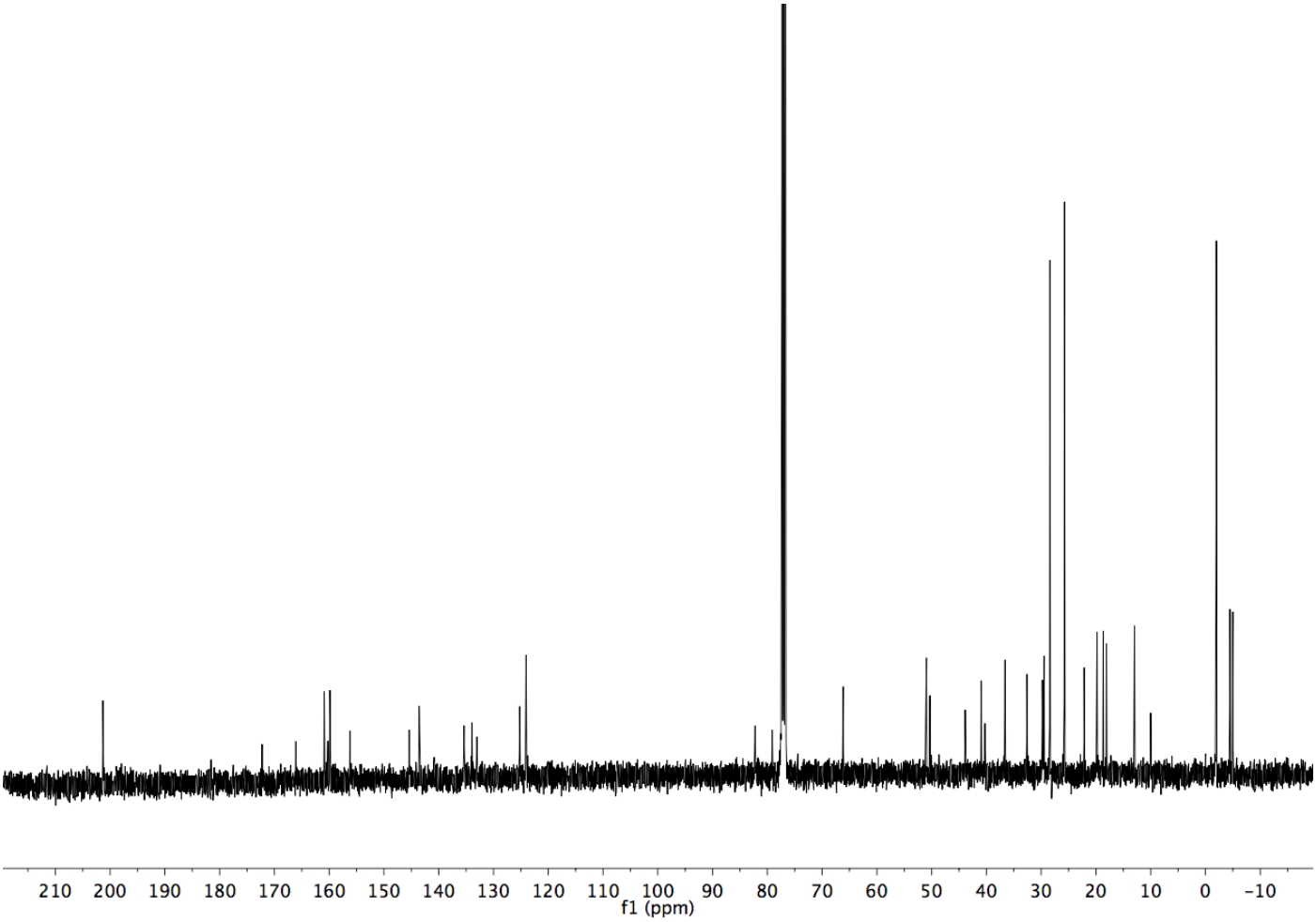
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

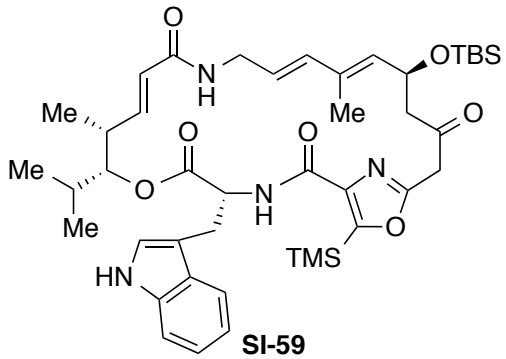

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
Me
O
N
H
O
Me
BocHN
TMS

SI-58d

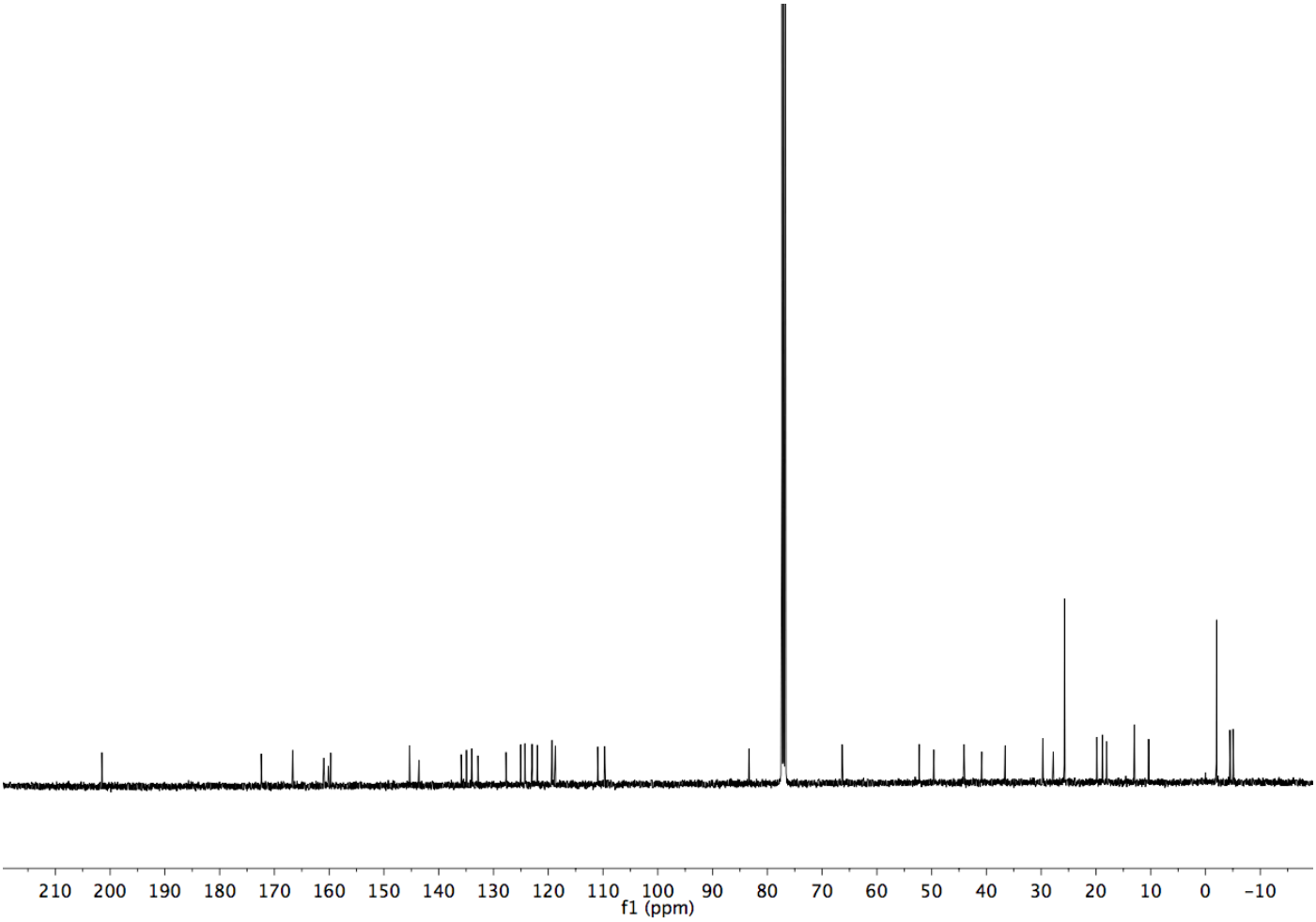

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

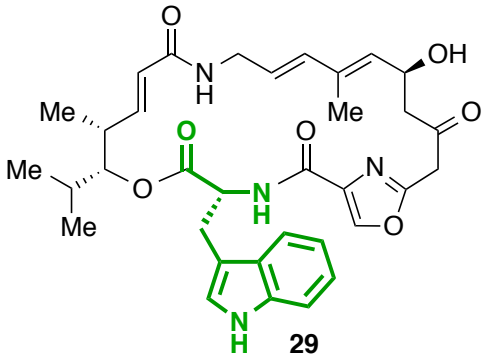

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
Me
O
N
H
N
O
Me
TMS
HN

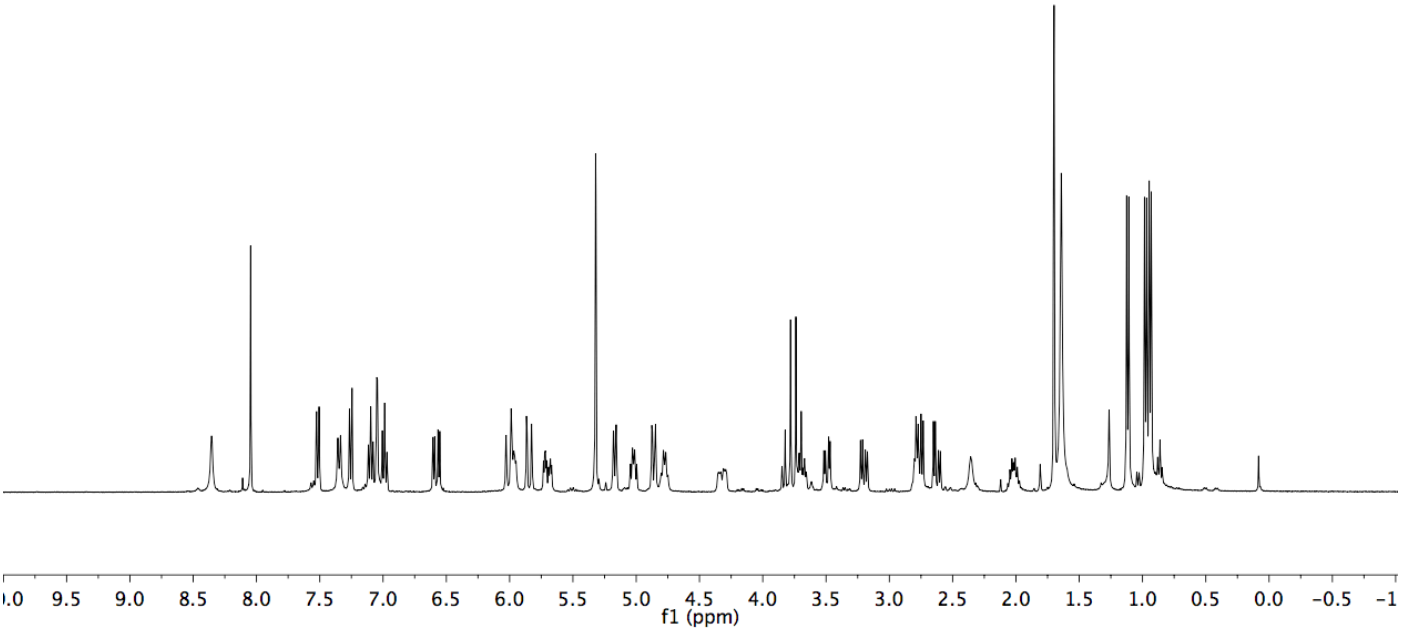
SI-59

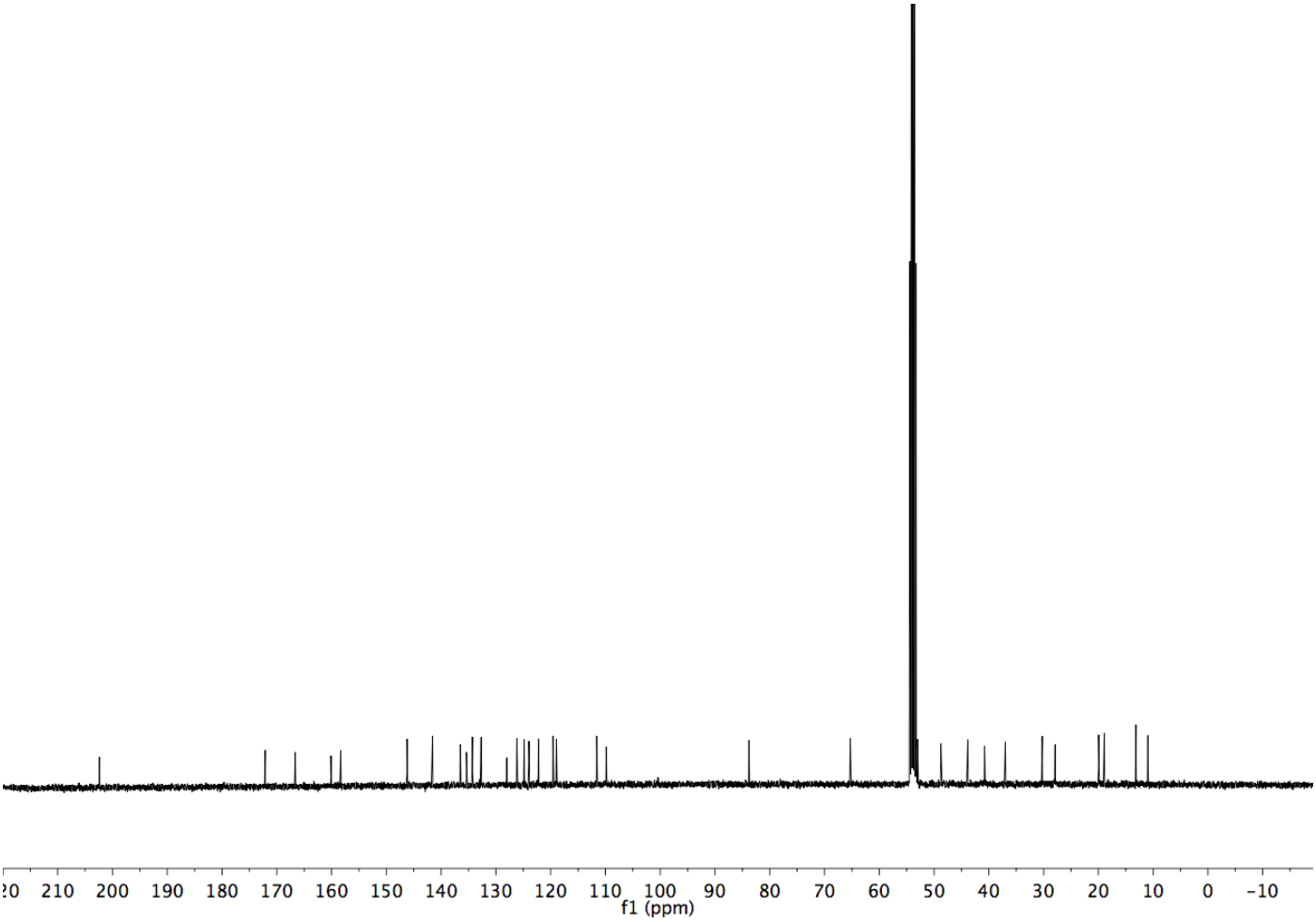
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

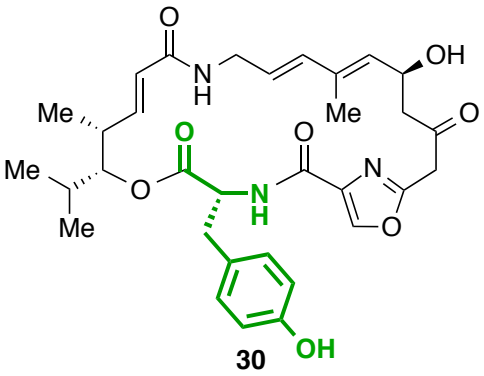

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
Me
O
N
H
N
O
Me
N
H

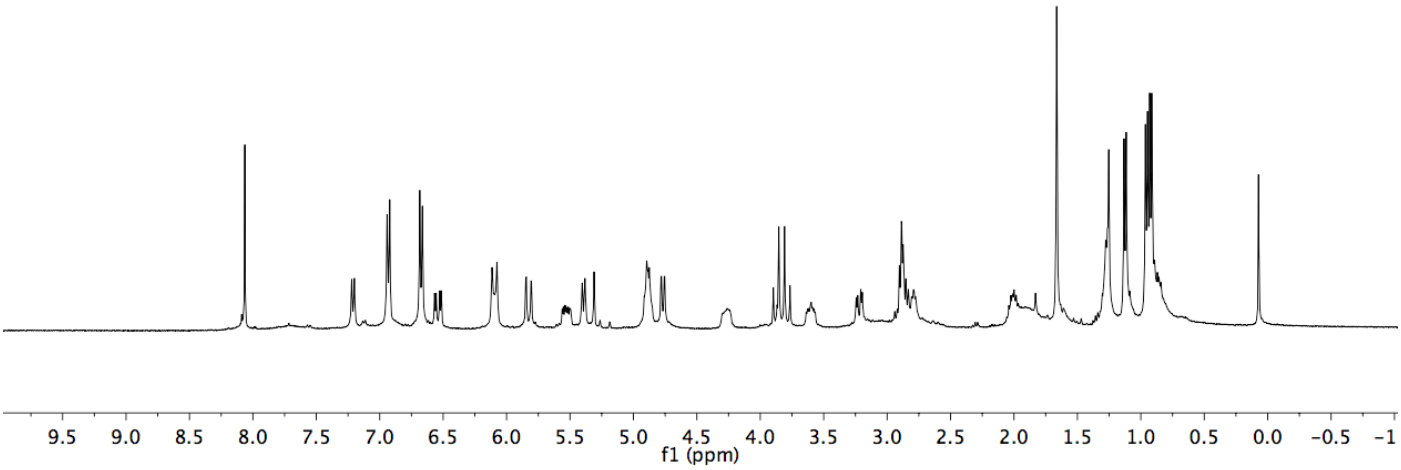
29

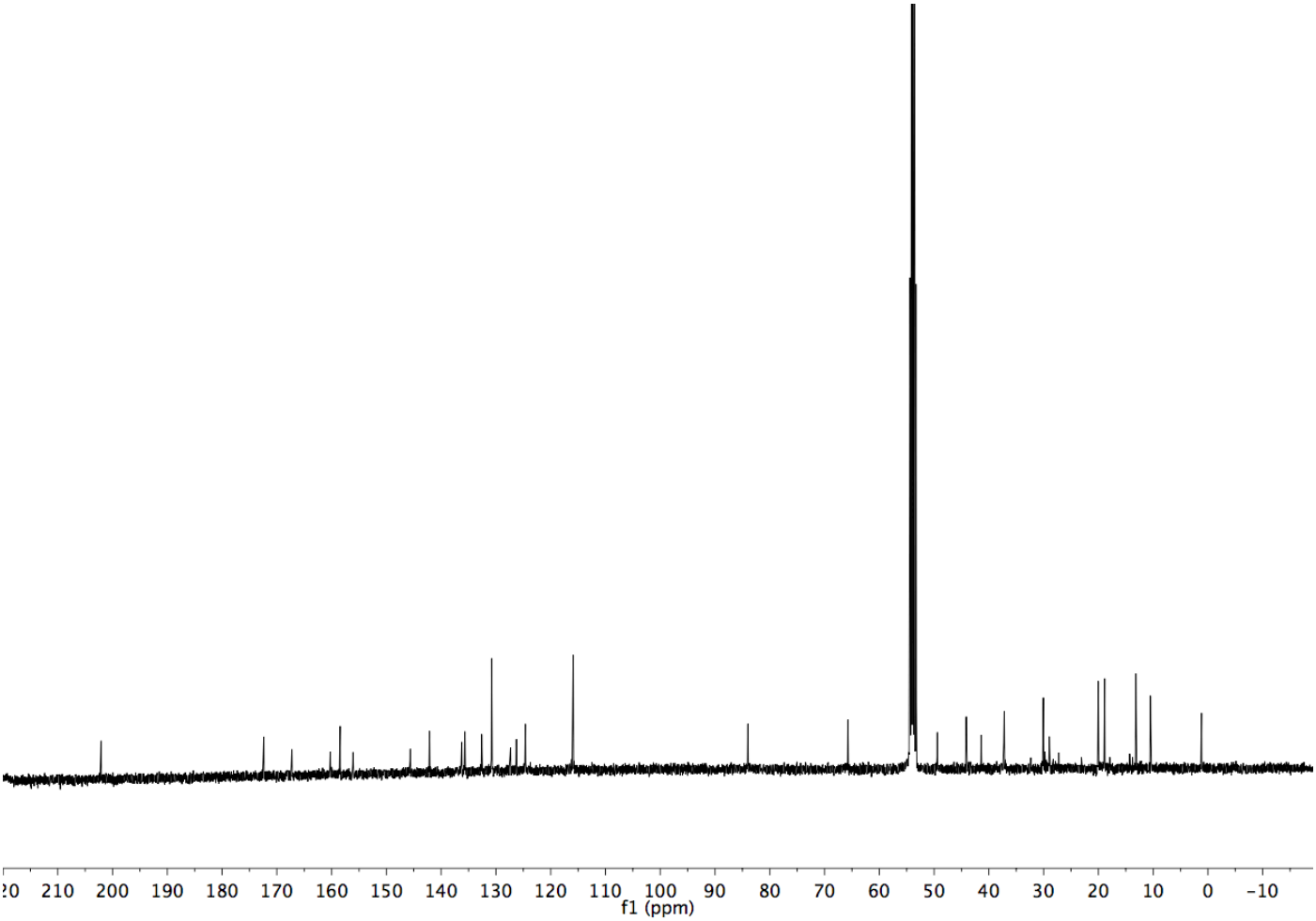

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

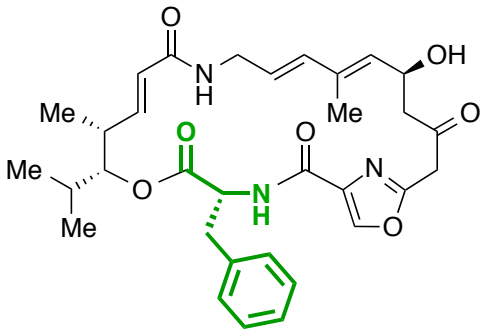

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
Me
O
O
N
O
O
N
H
Me
O
OH

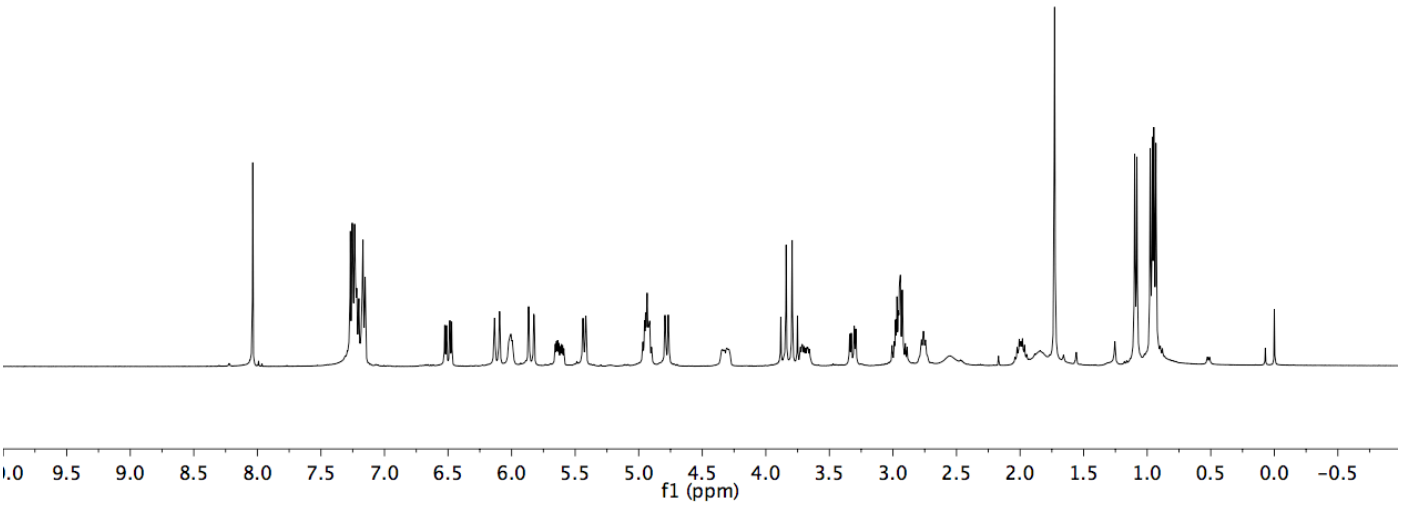
30

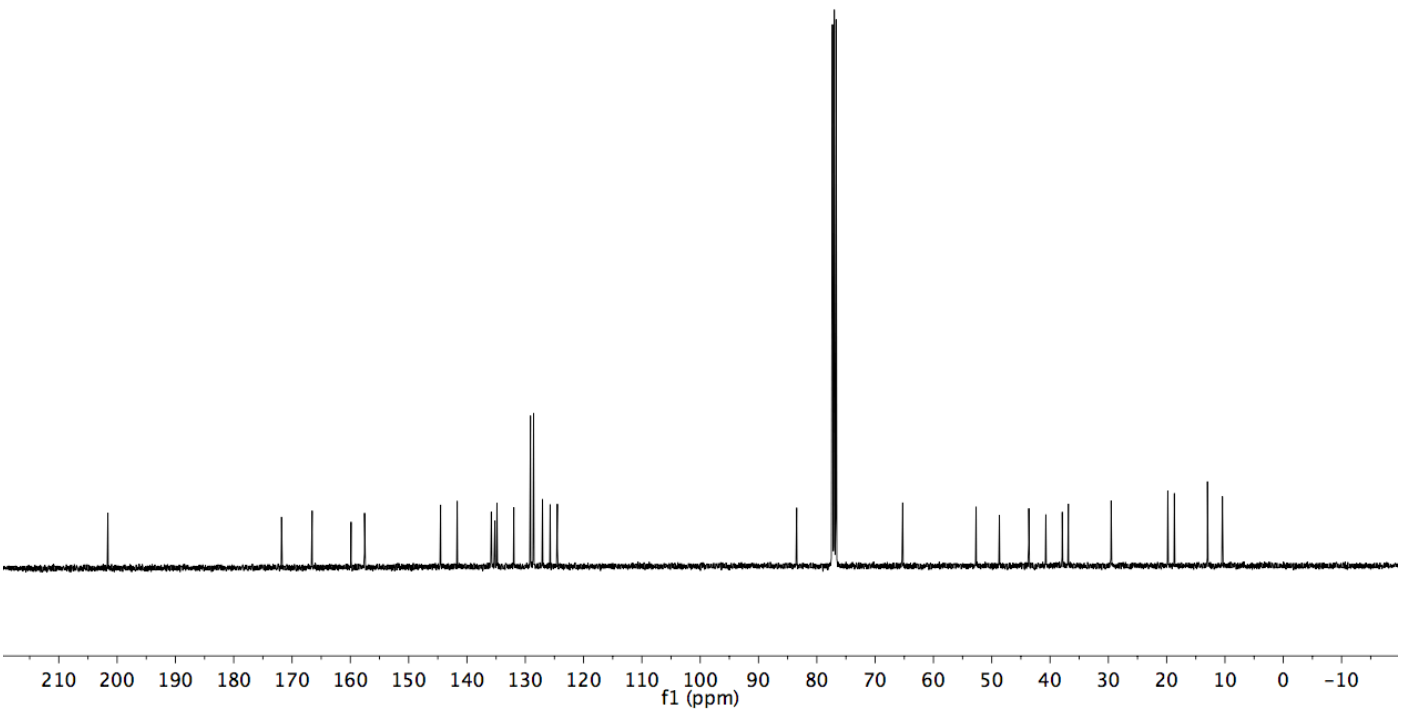

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

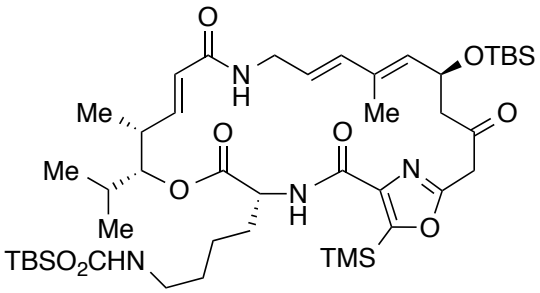

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
Me
O
N
N
H
O
Me

31

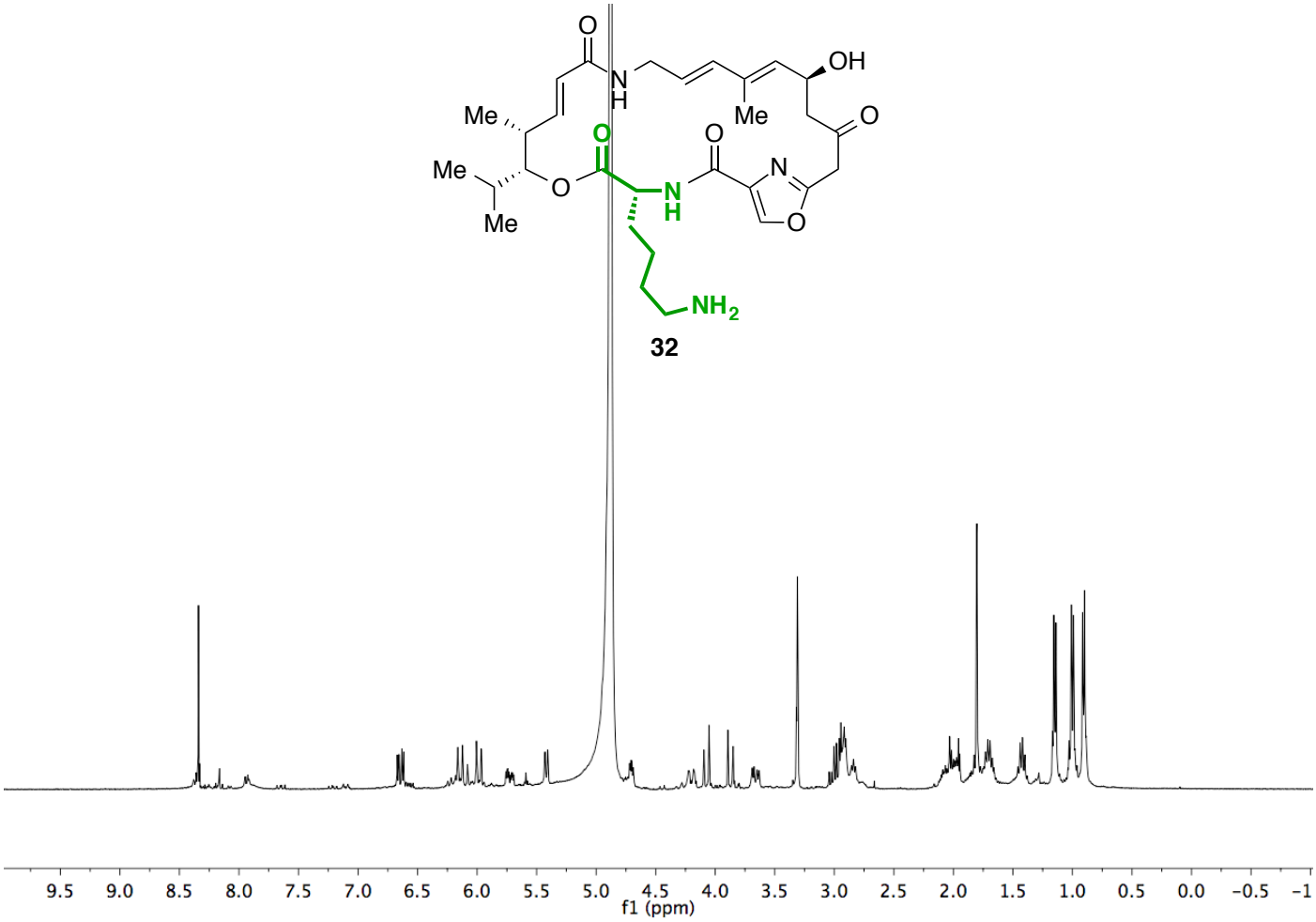

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

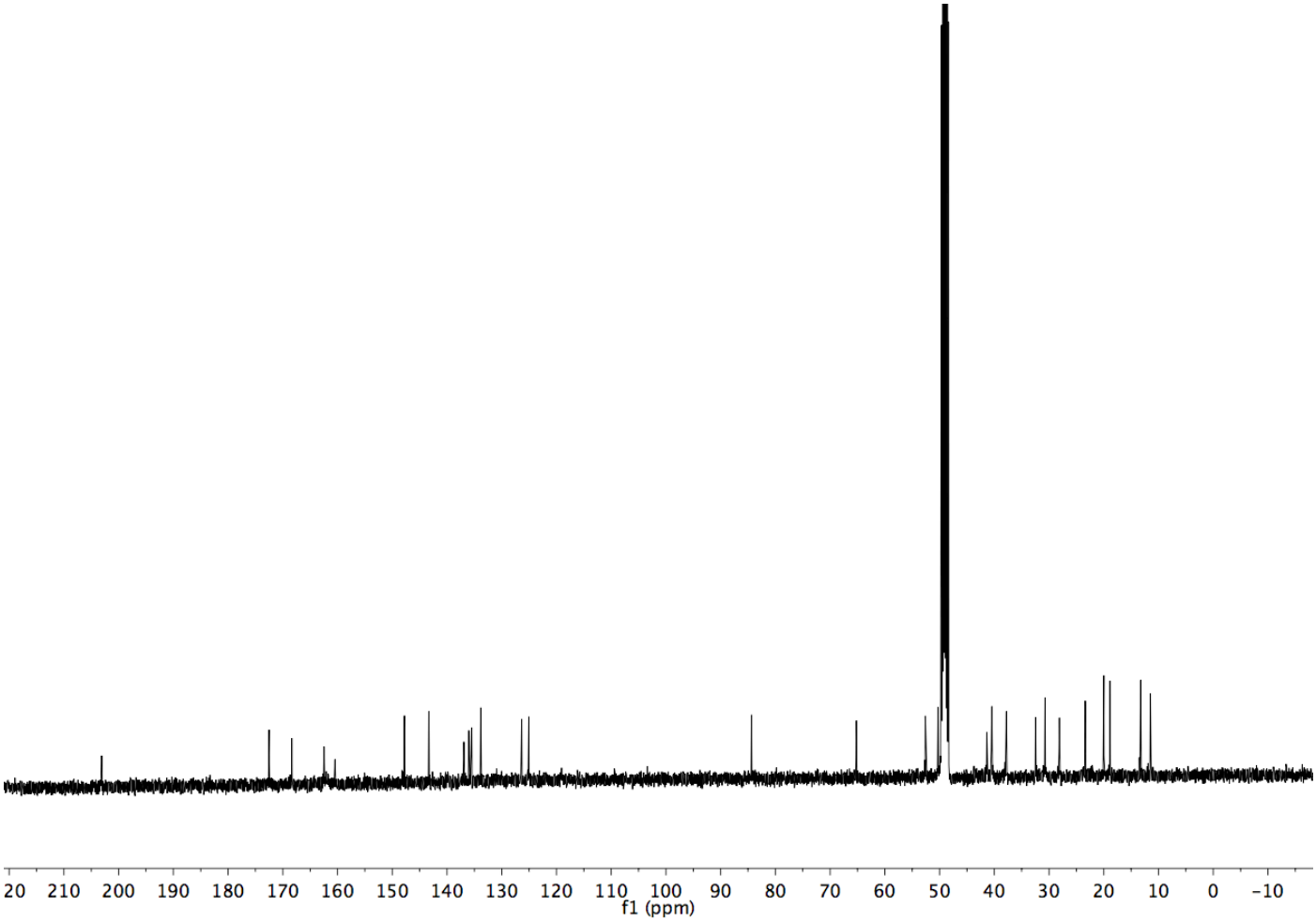

O
N
H
OTBS
Me
Me
O
O
Me
O
N
H
O
Me
TBSO2CHN
TMS

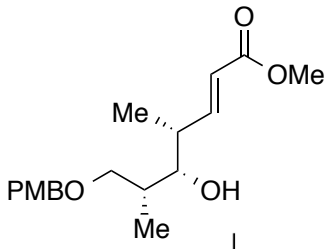
SI-61

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

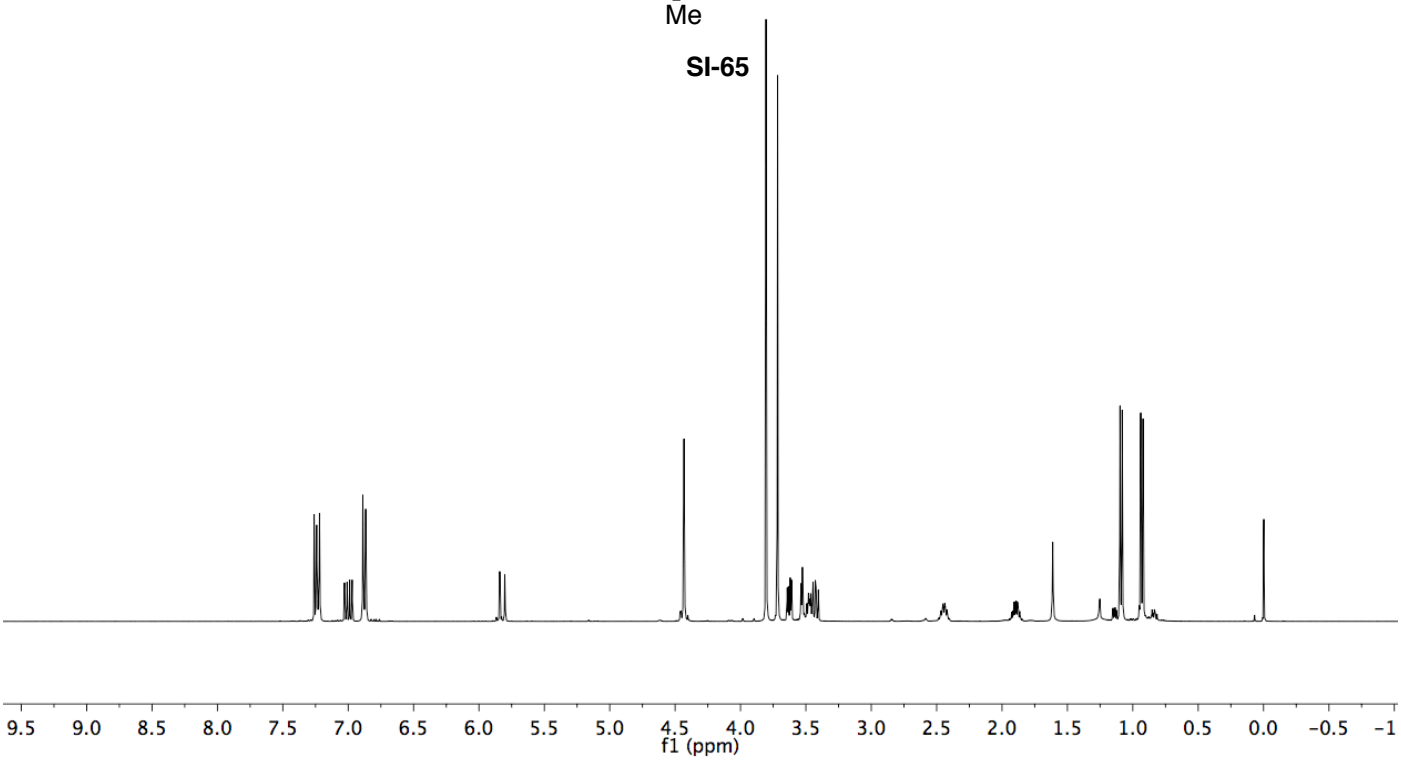

O
N
H
OH
Me
Me
O
Me
O
O
O
N
O
N
H
Me
O
NH2
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

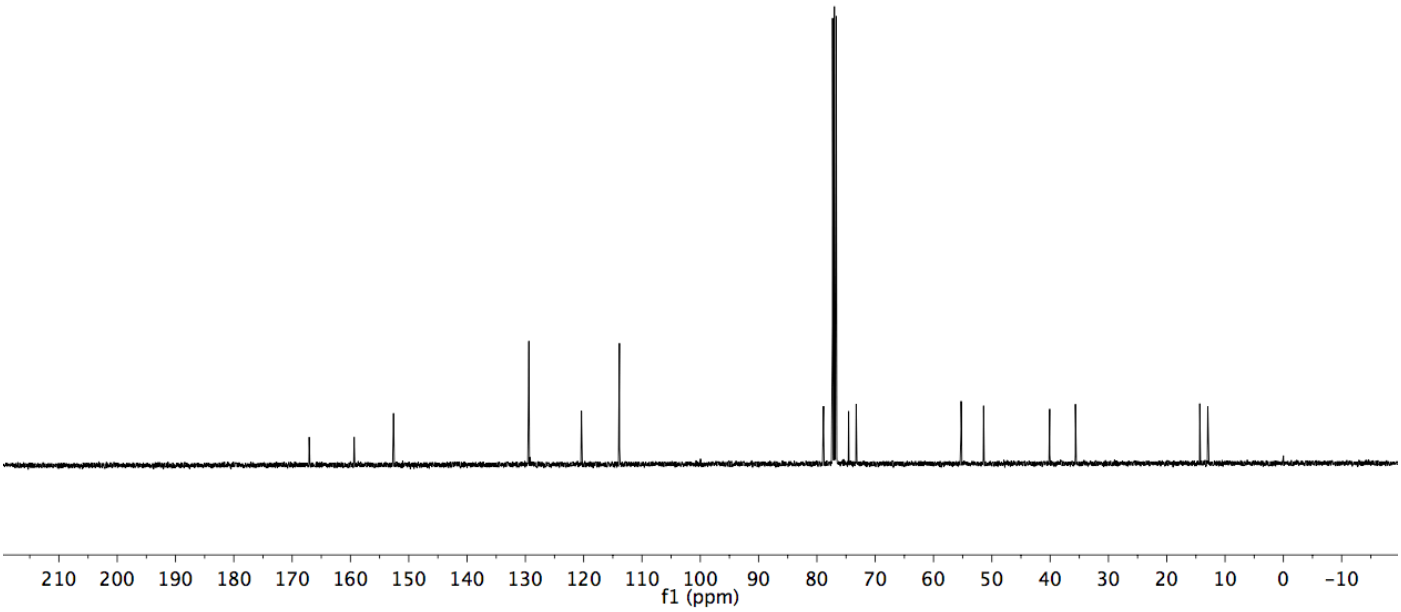
32

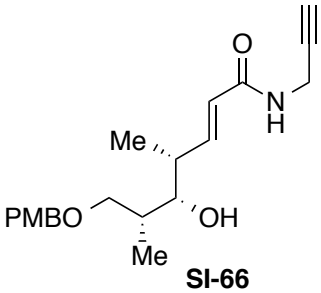

20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
Me
PMBO
OH
Me

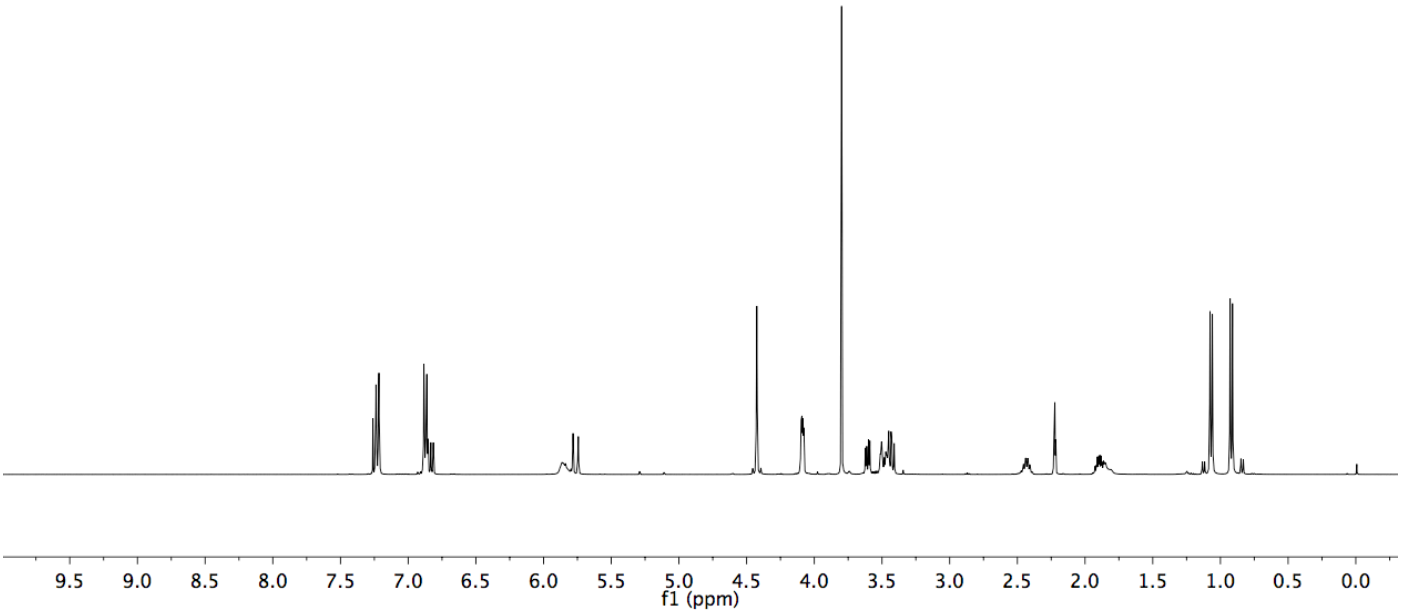
SI-65

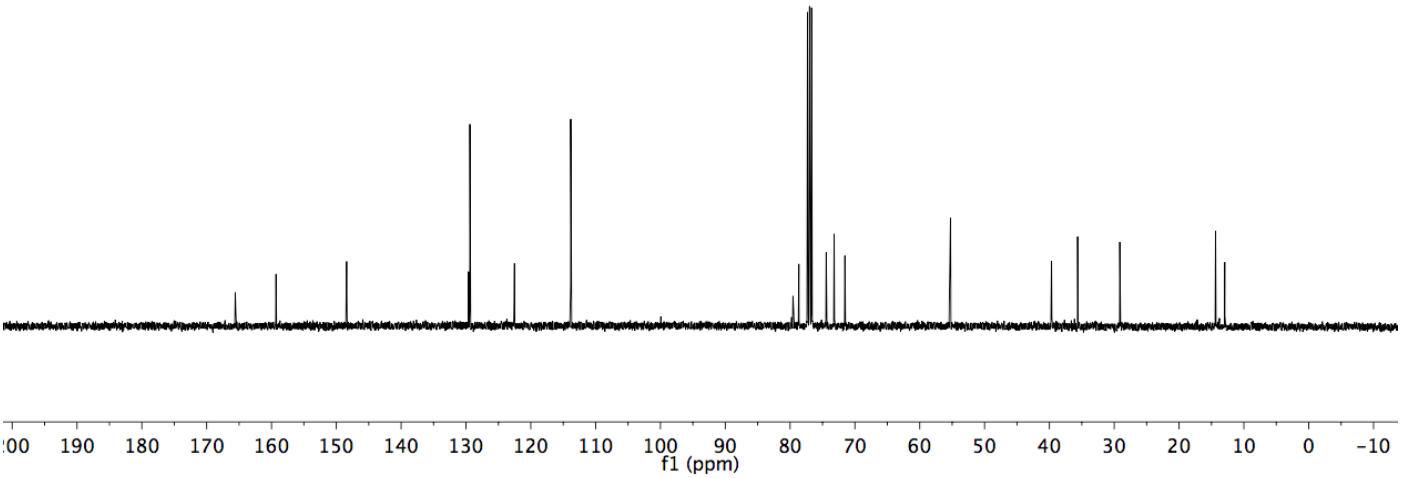

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

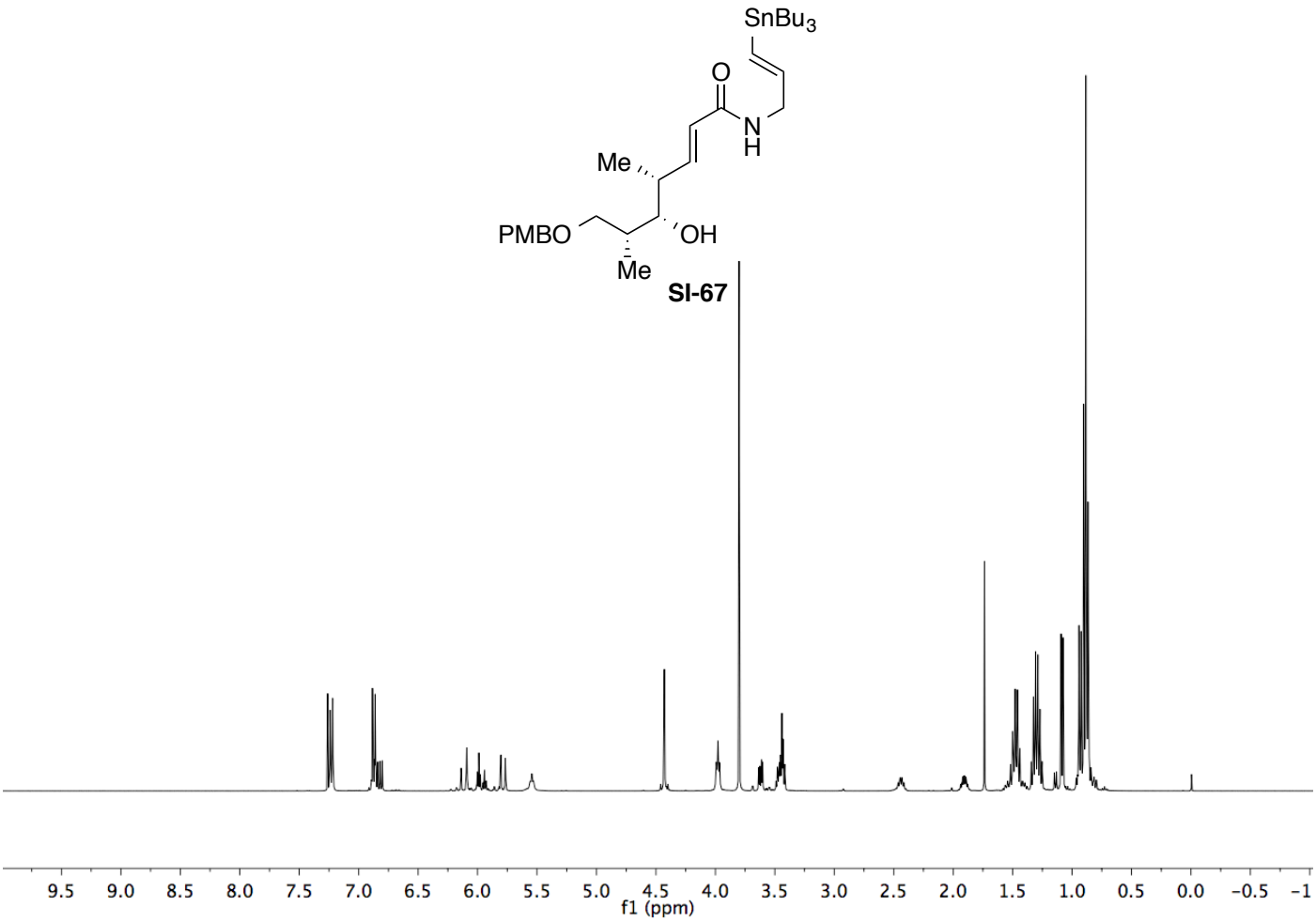

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

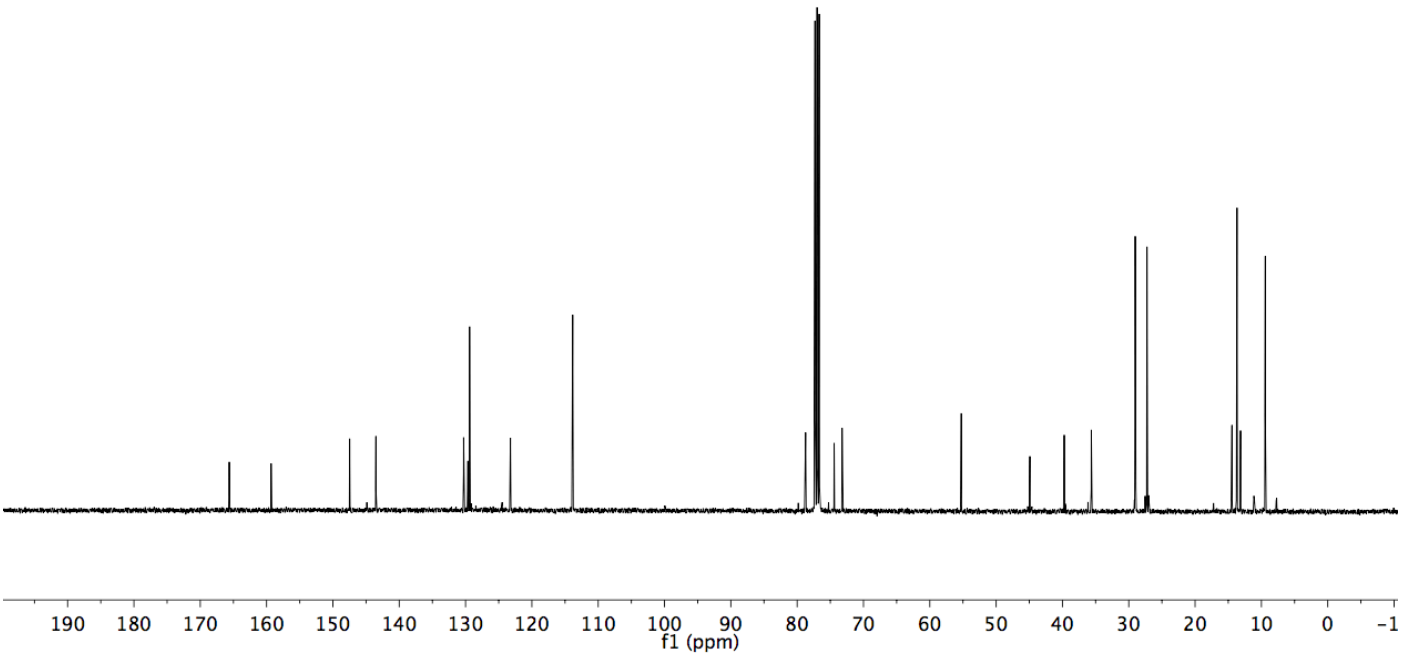

O
N
H
Me
PMBO
OH
Me

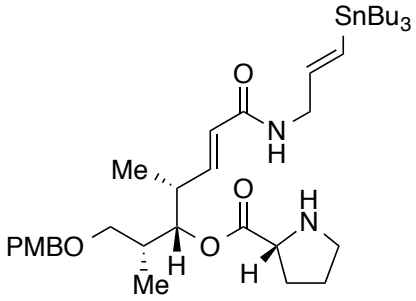
SI-66


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


:00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

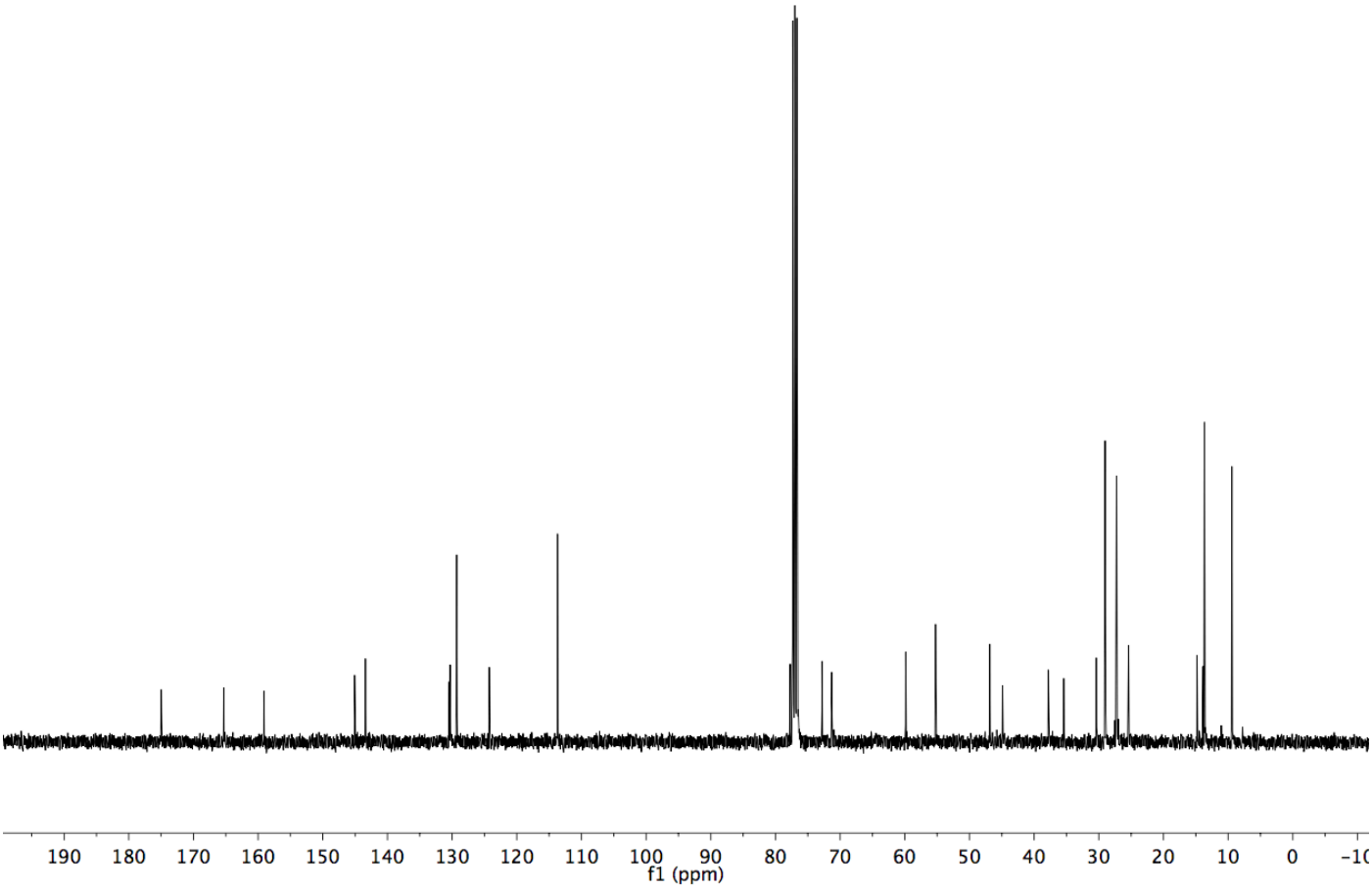

SnBu3
O
N
H
Me
PMBO
OH
Me
SI-67
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

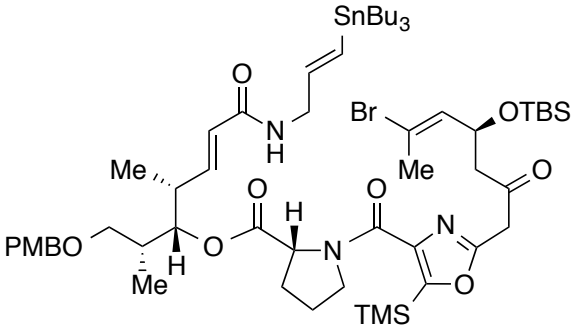

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


SnBu3
O
N
H
Me
O
H
N
PMBO
O
H
H
Me

SI-68

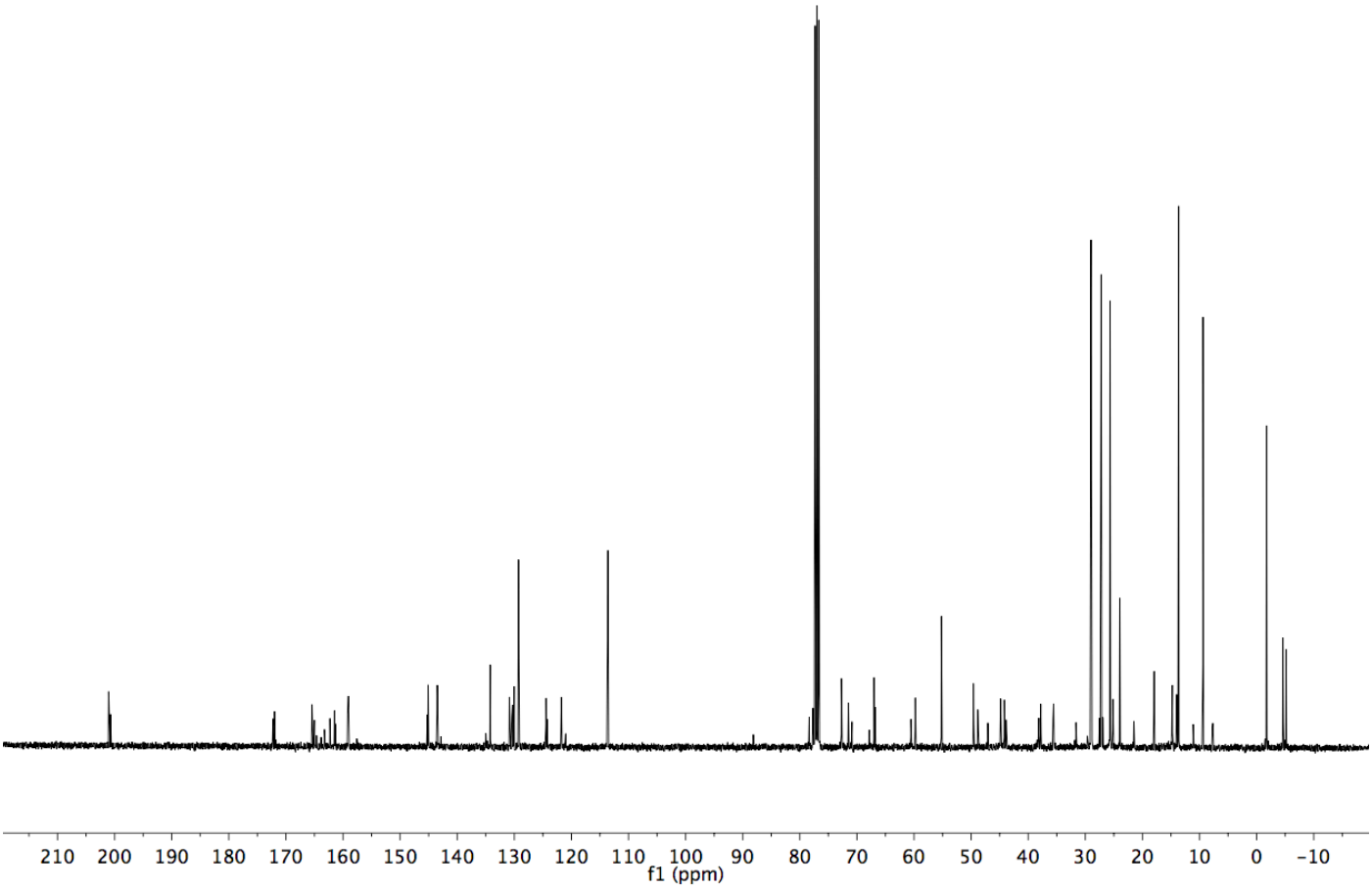
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

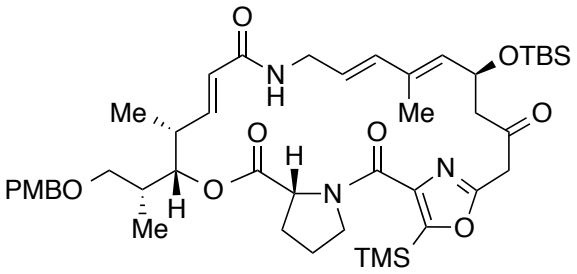

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
H
O
PMBO
O
N
N
H
Me
O
TMS

SI-69

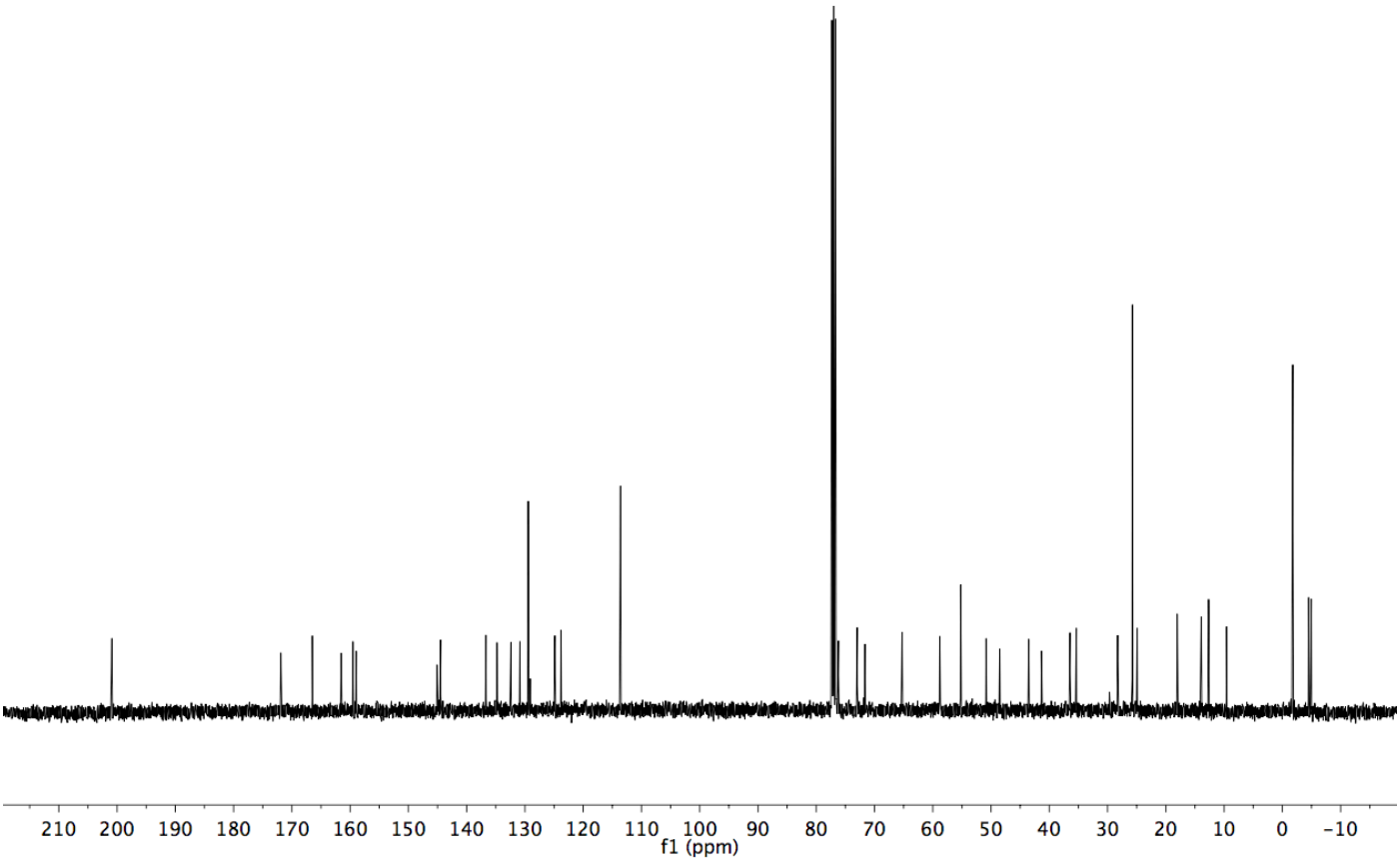
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

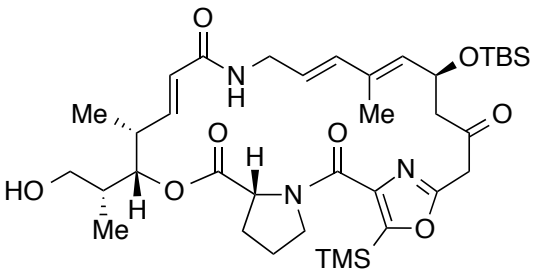

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
PMBO
O
N
N
H
Me
O
TMS

SI-70

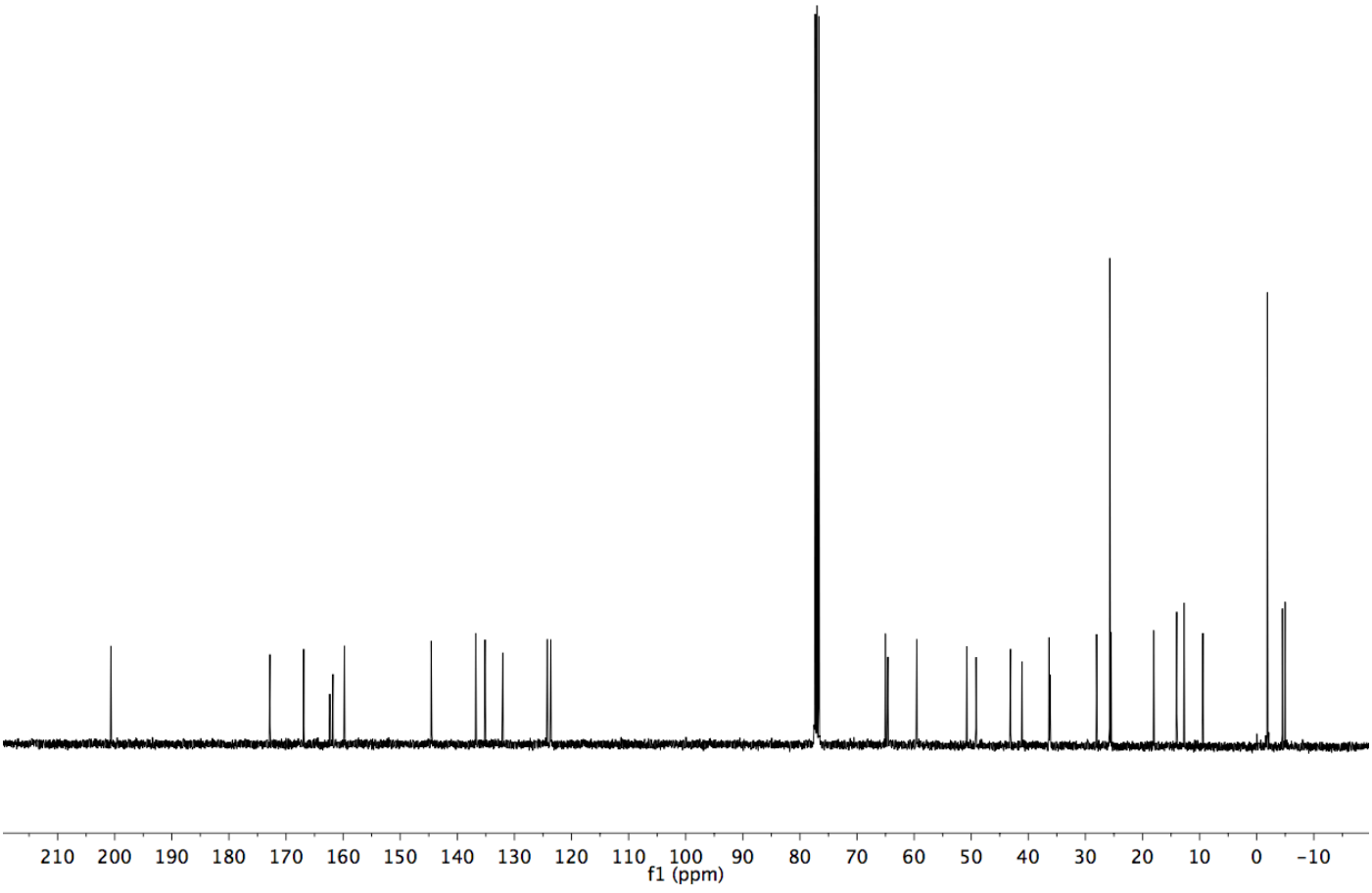
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

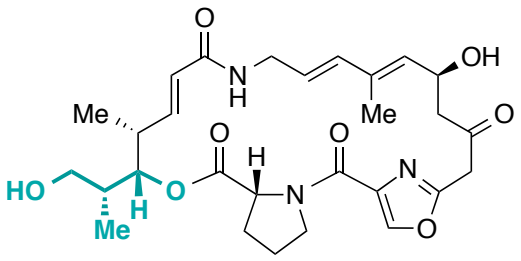

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
HO
O
N
N
H
Me
O
TMS

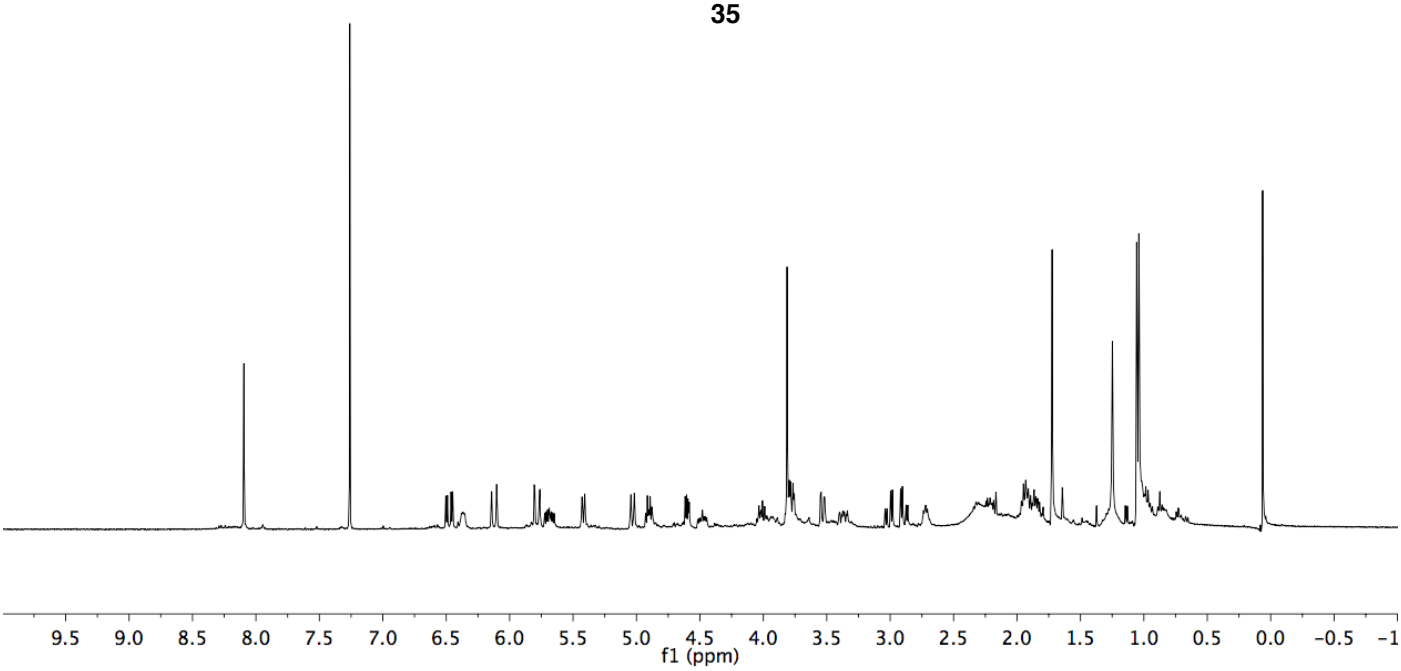
38

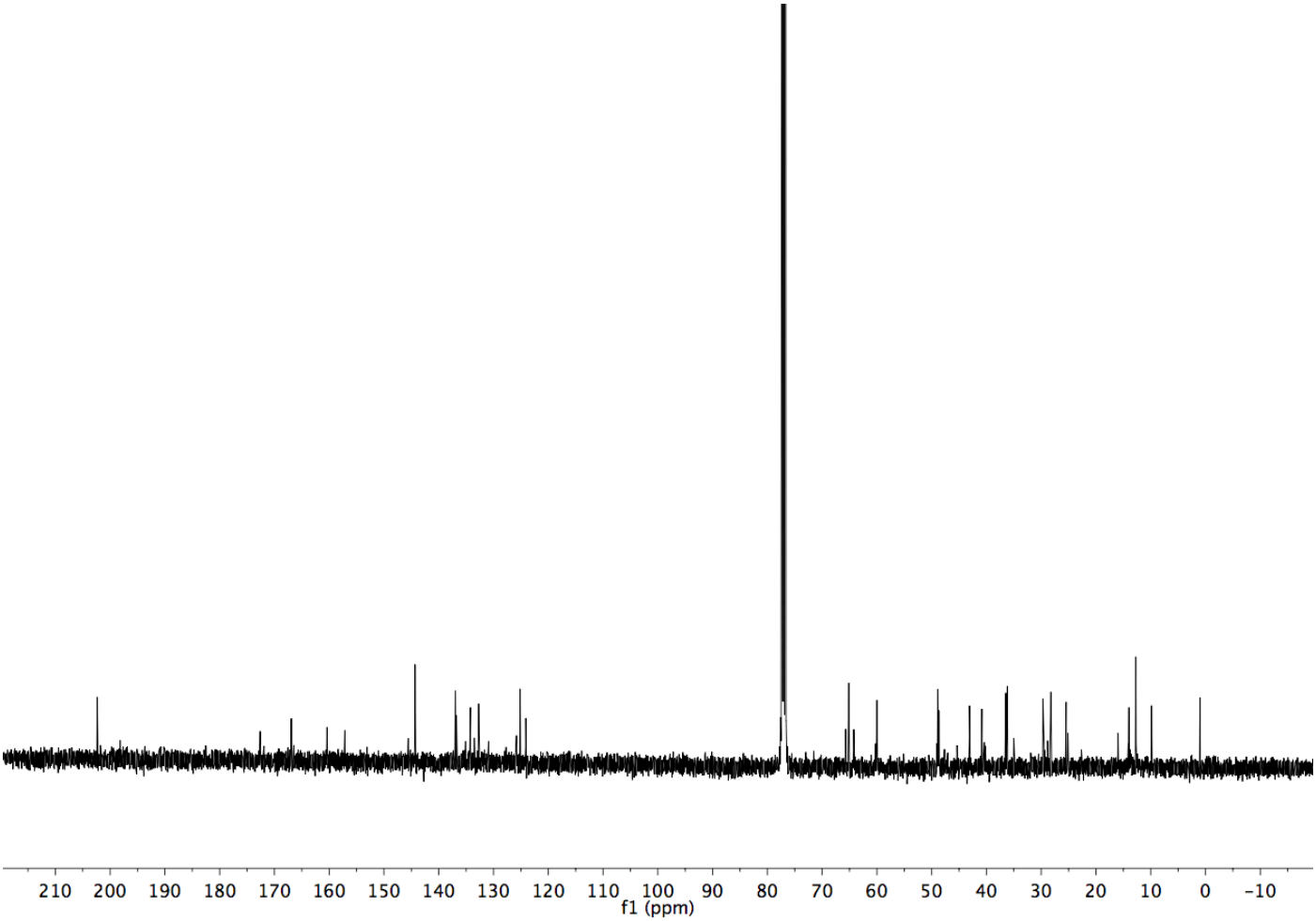
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

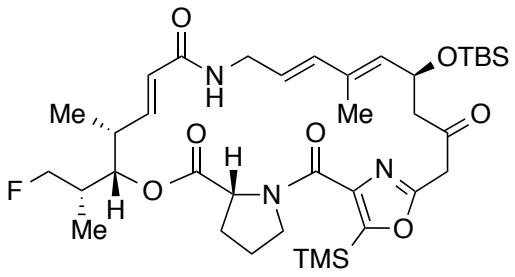

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
HO
O
N
N
Me
H
O

35

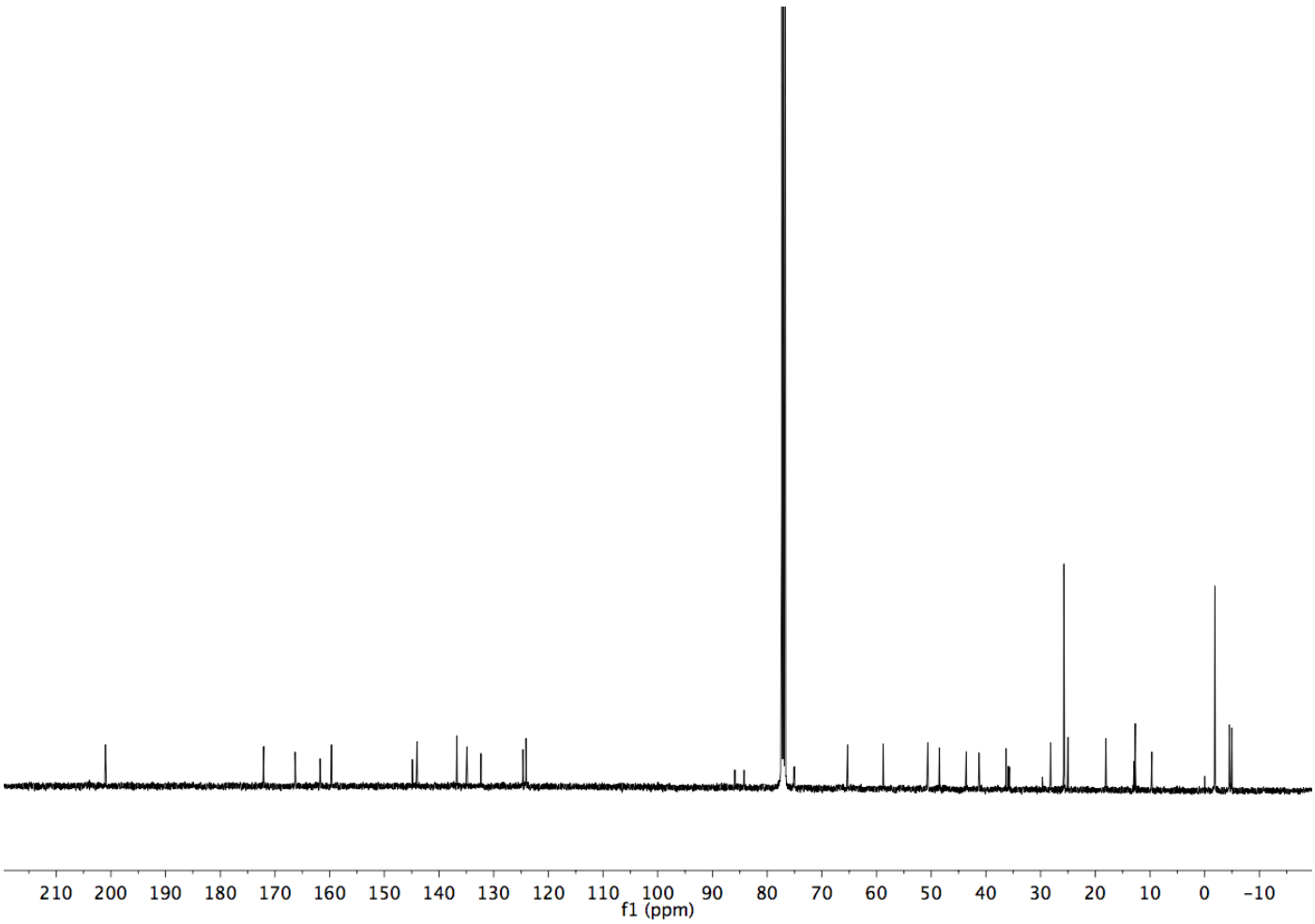

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

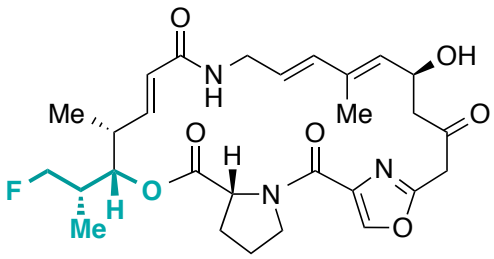

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
F
O
N
N
O
H
Me
TMS

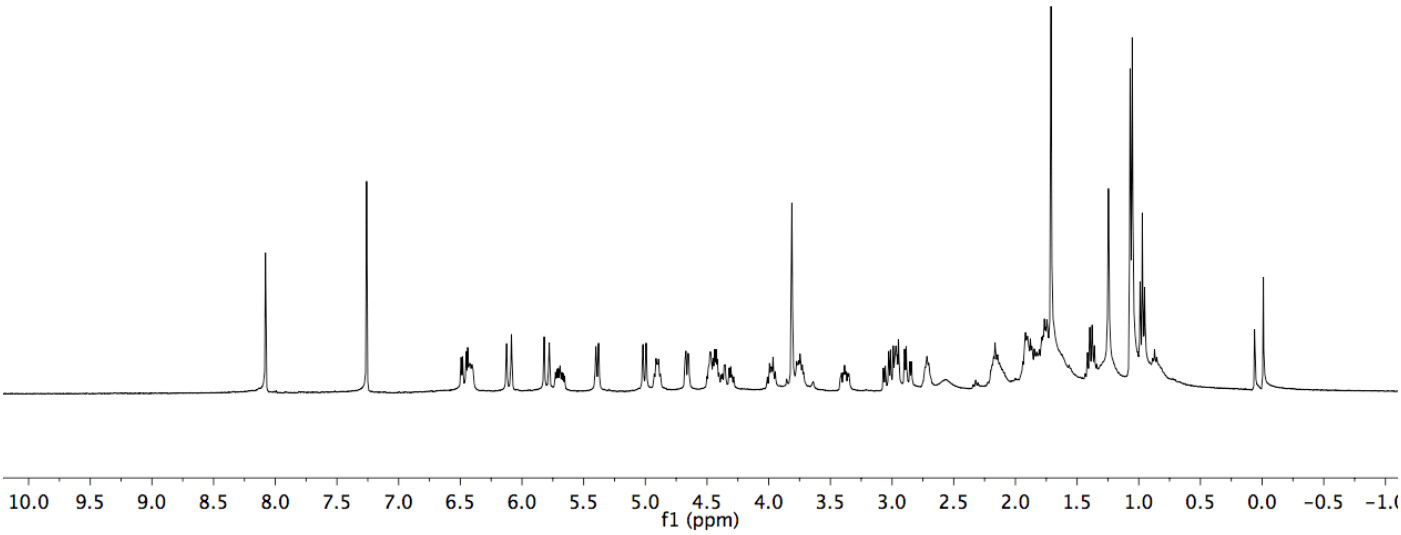
SI-71

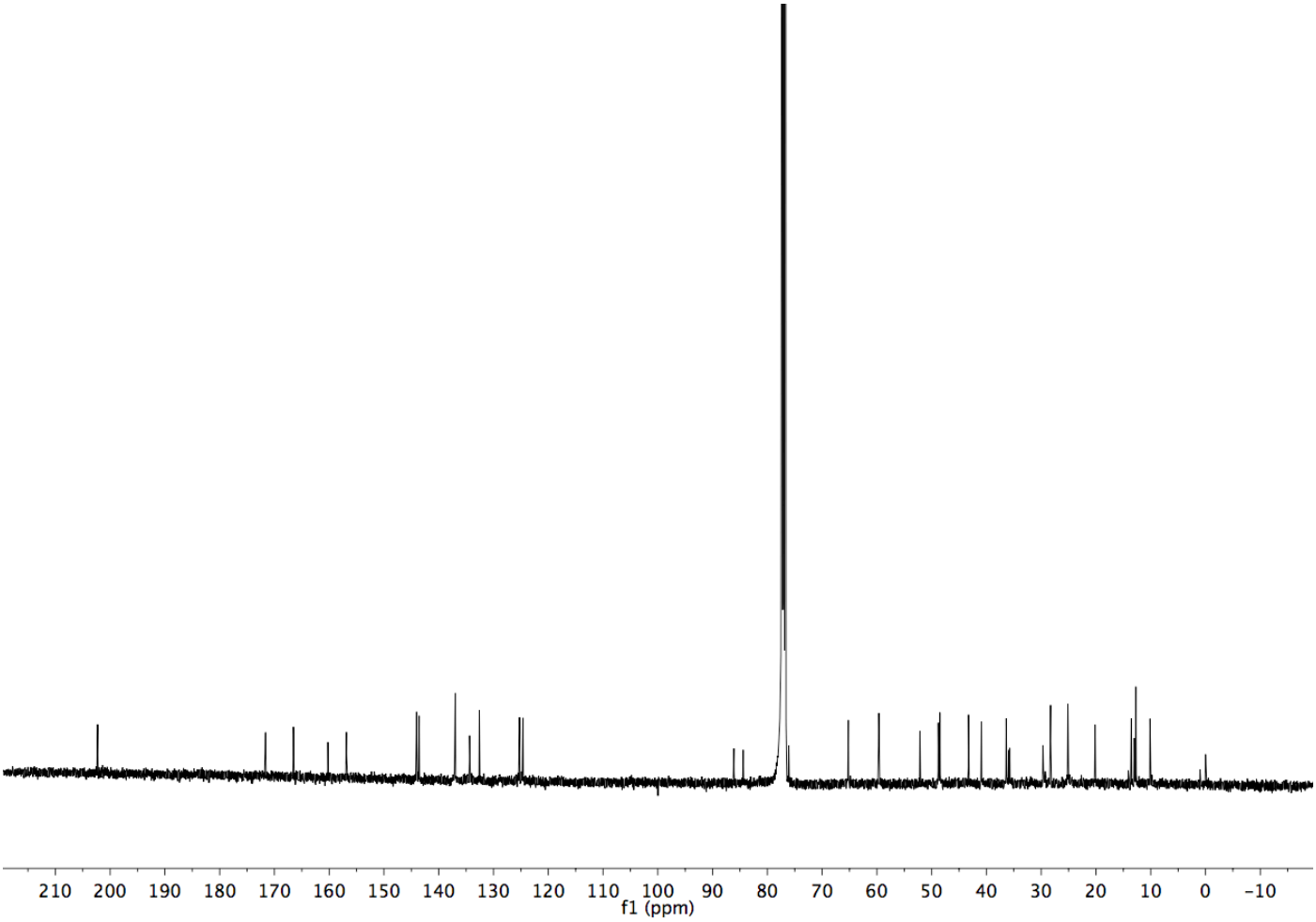
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

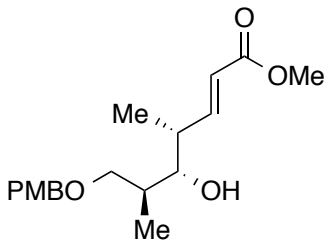

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
N
N
O
F
O
H
Me

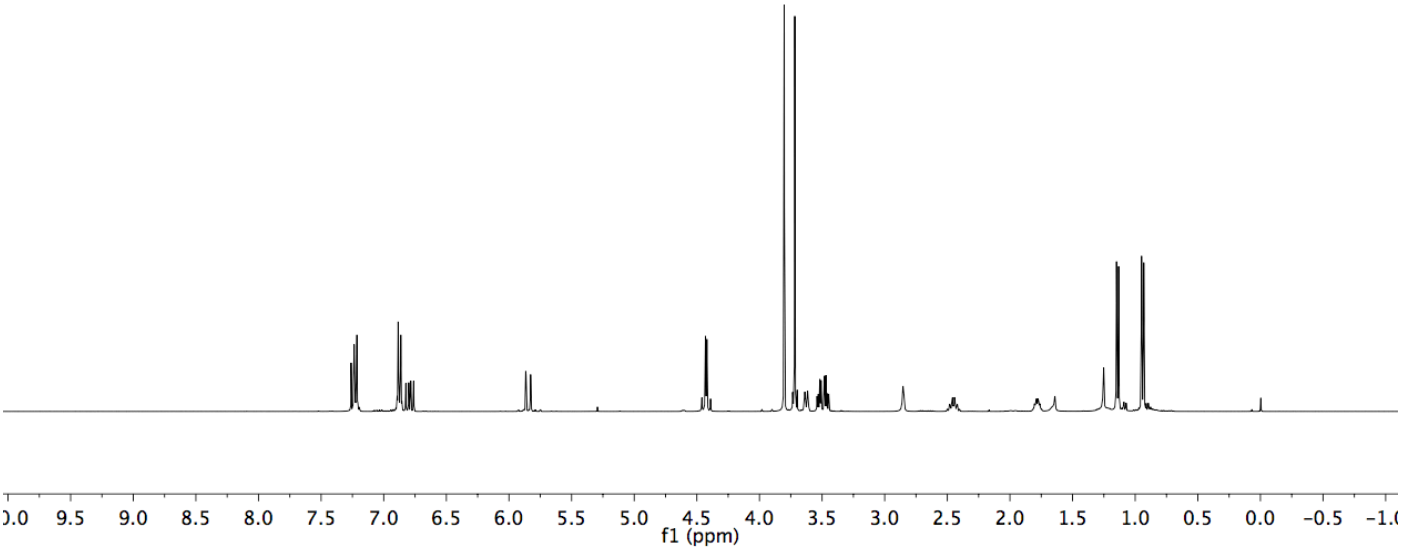
SI-72

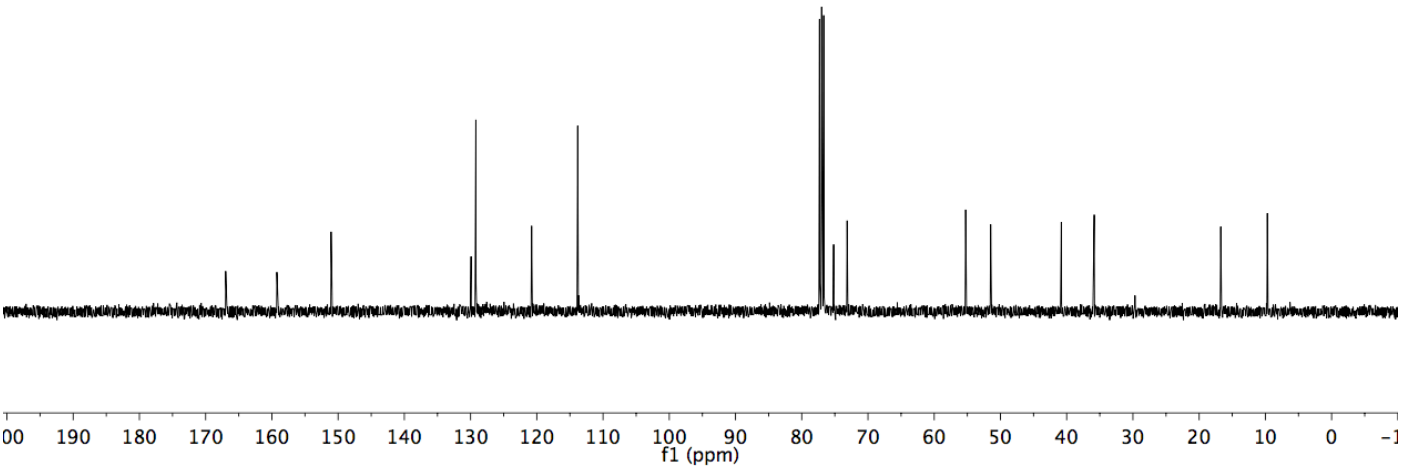

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

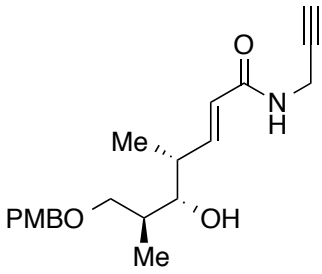

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
OMe
Me
PMBO
OH
Me

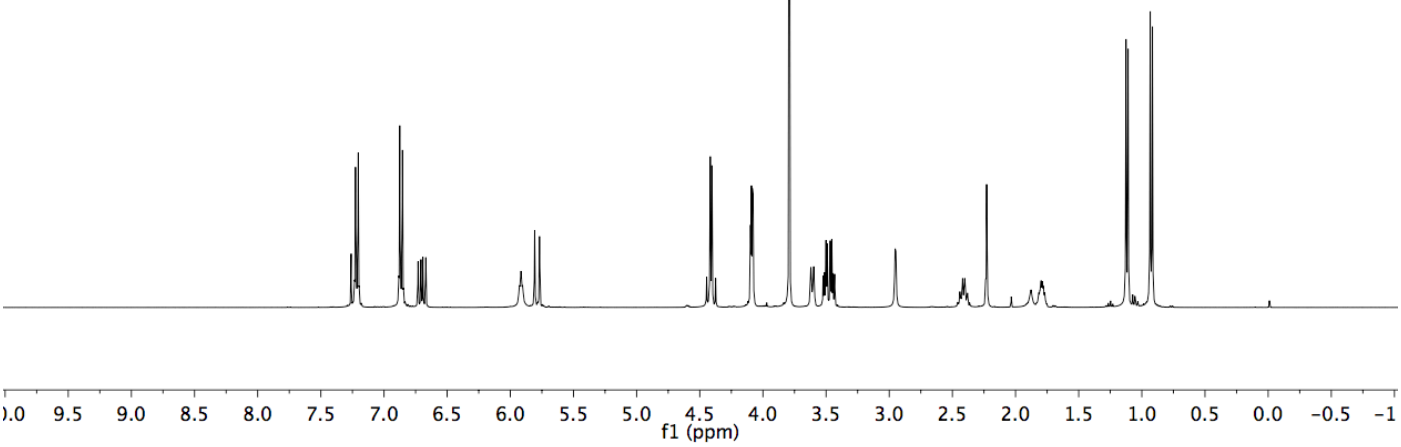
SI-74

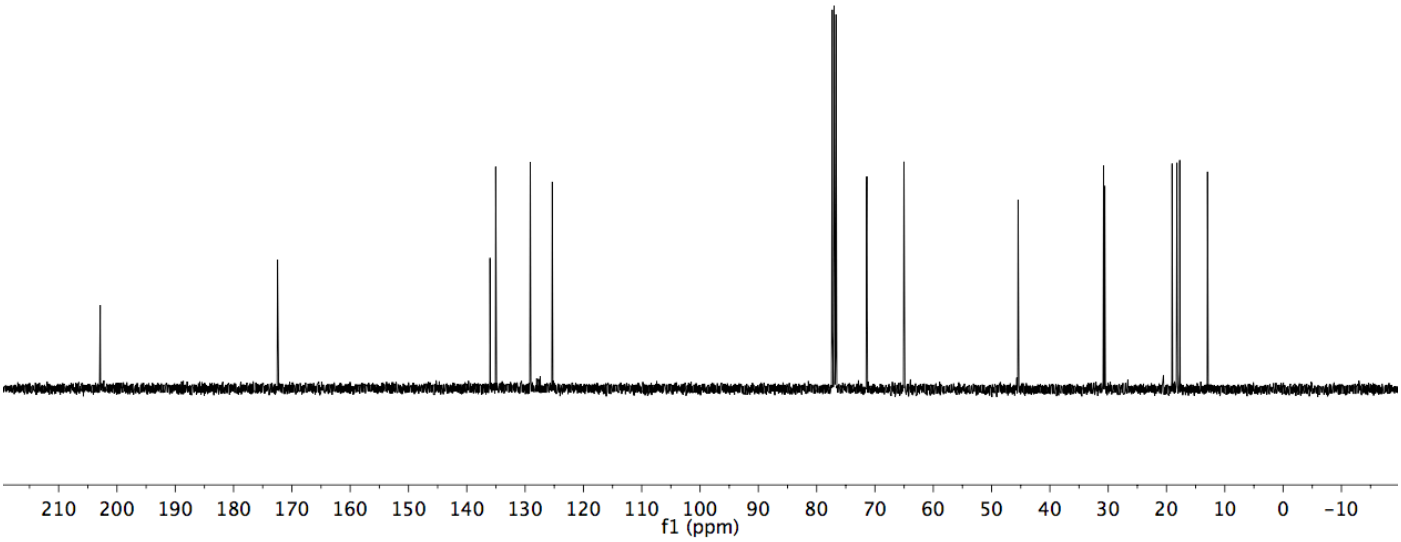

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

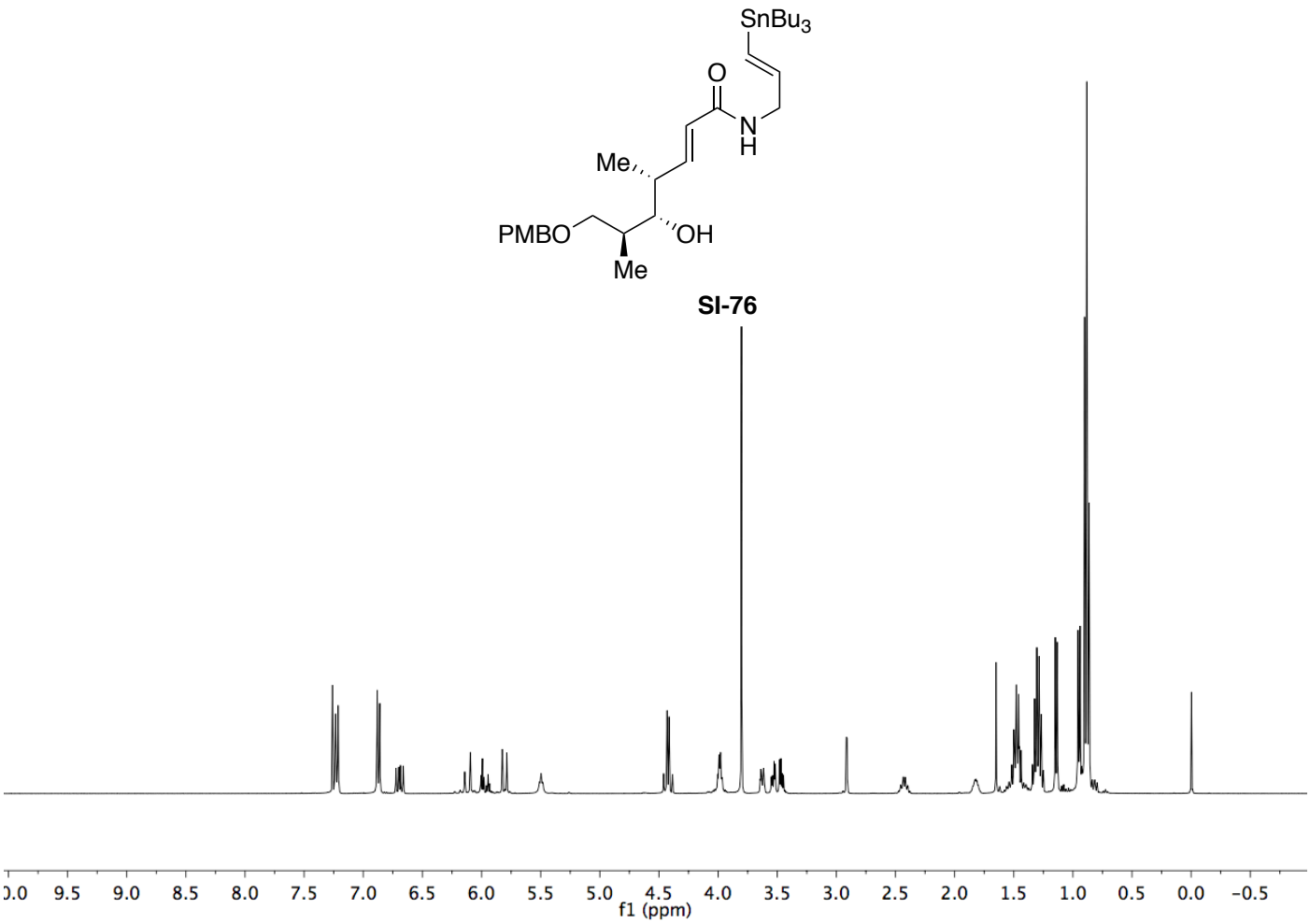

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

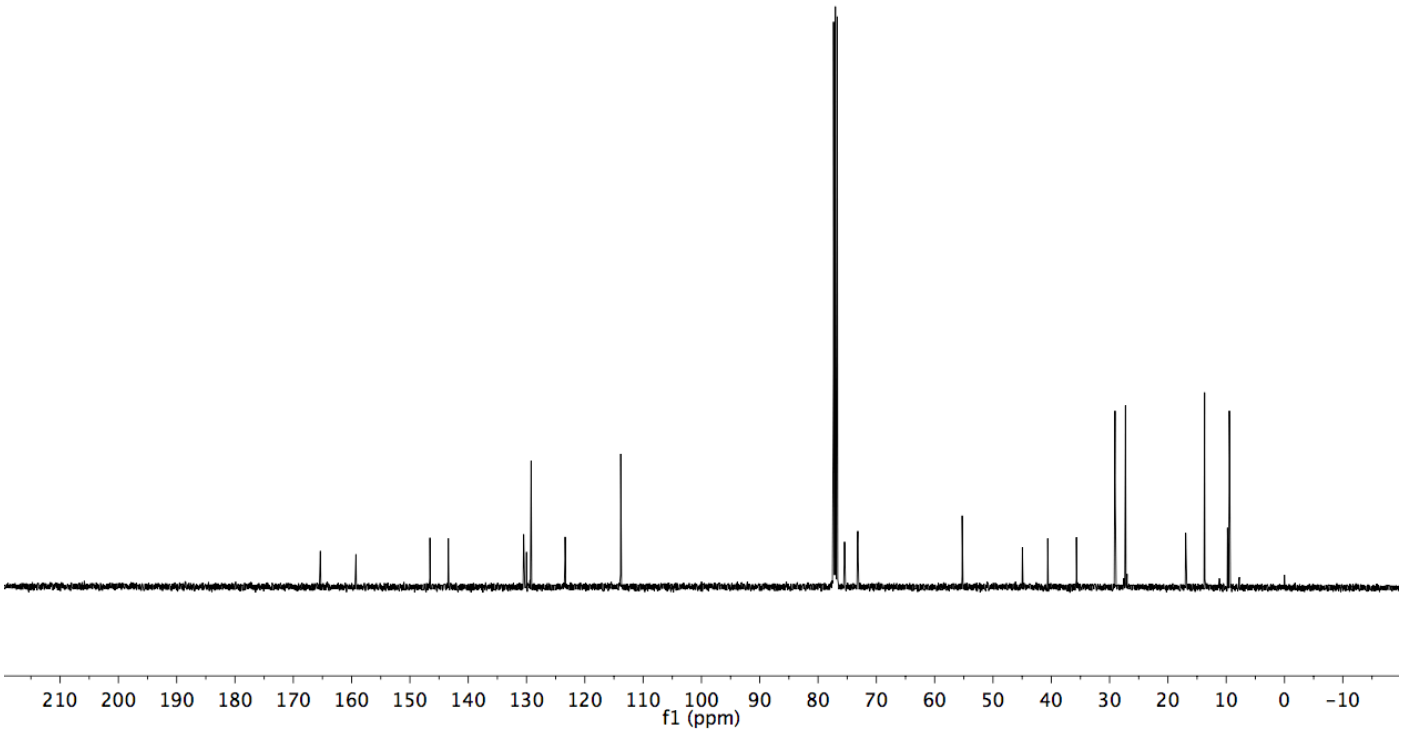

O
N
H
Me
PMBO
OH
Me

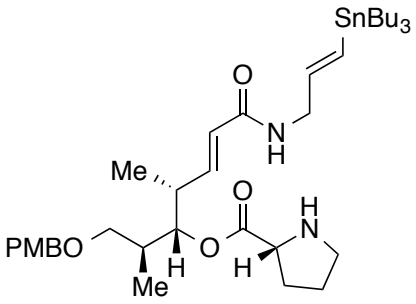
SI-75


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

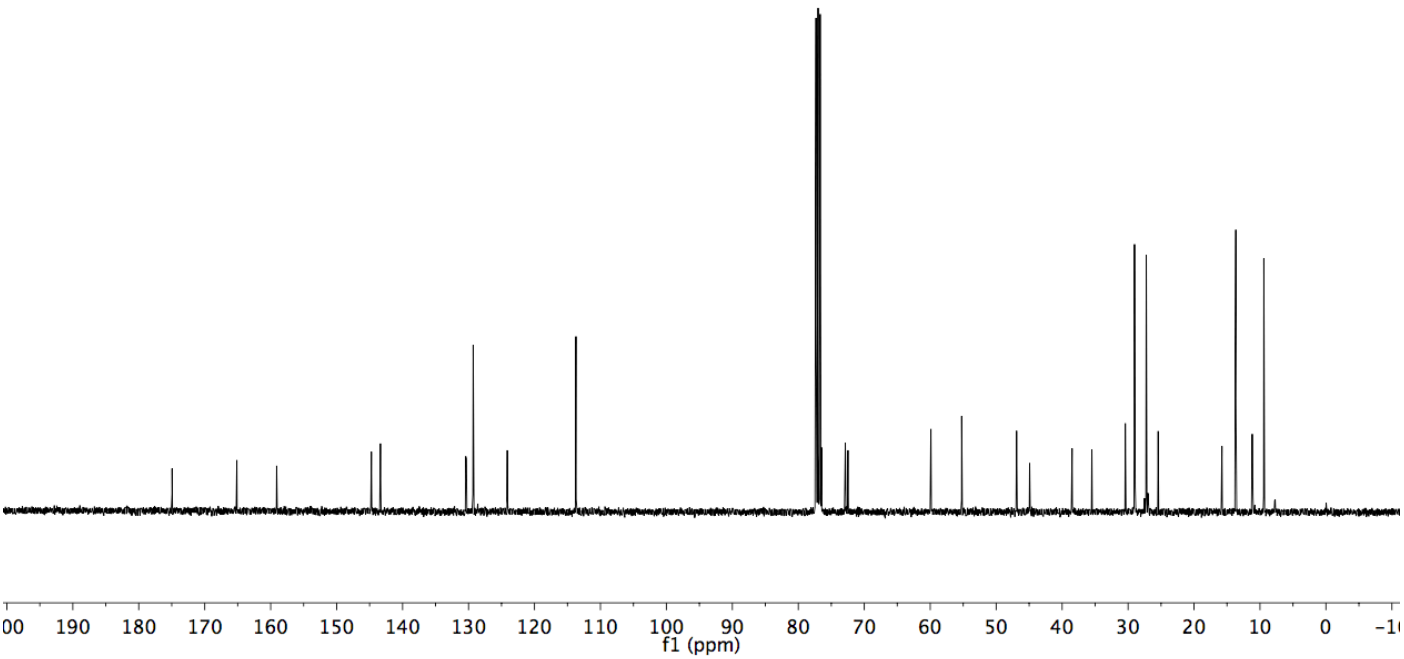

SnBu3
O
N
H
Me
PMBO
OH
Me
SI-76
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

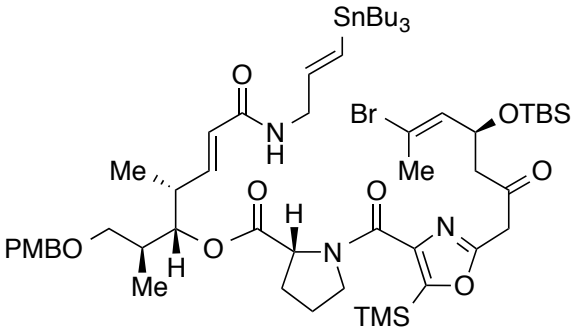

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Me
O
H
N
PMBO
O
H
H
Me

SI-77

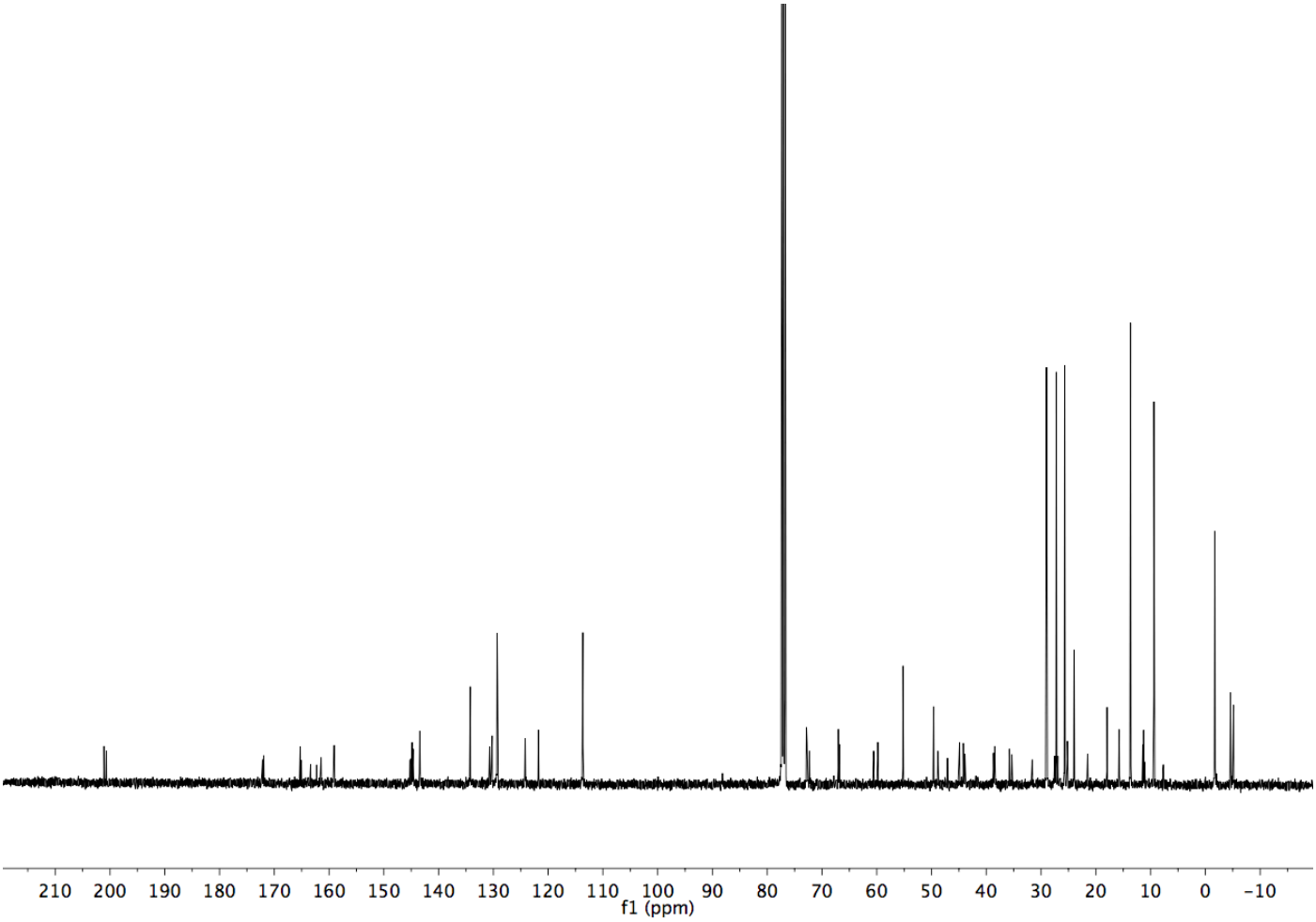
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

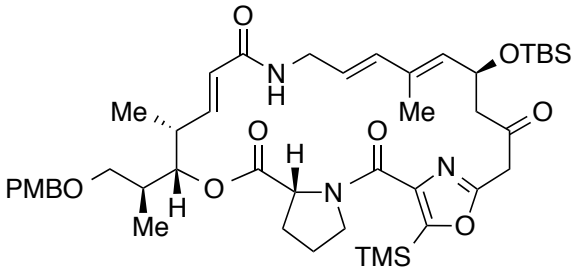

00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
H
O
PMBO
O
N
N
H
Me
O
TMS

SI-78

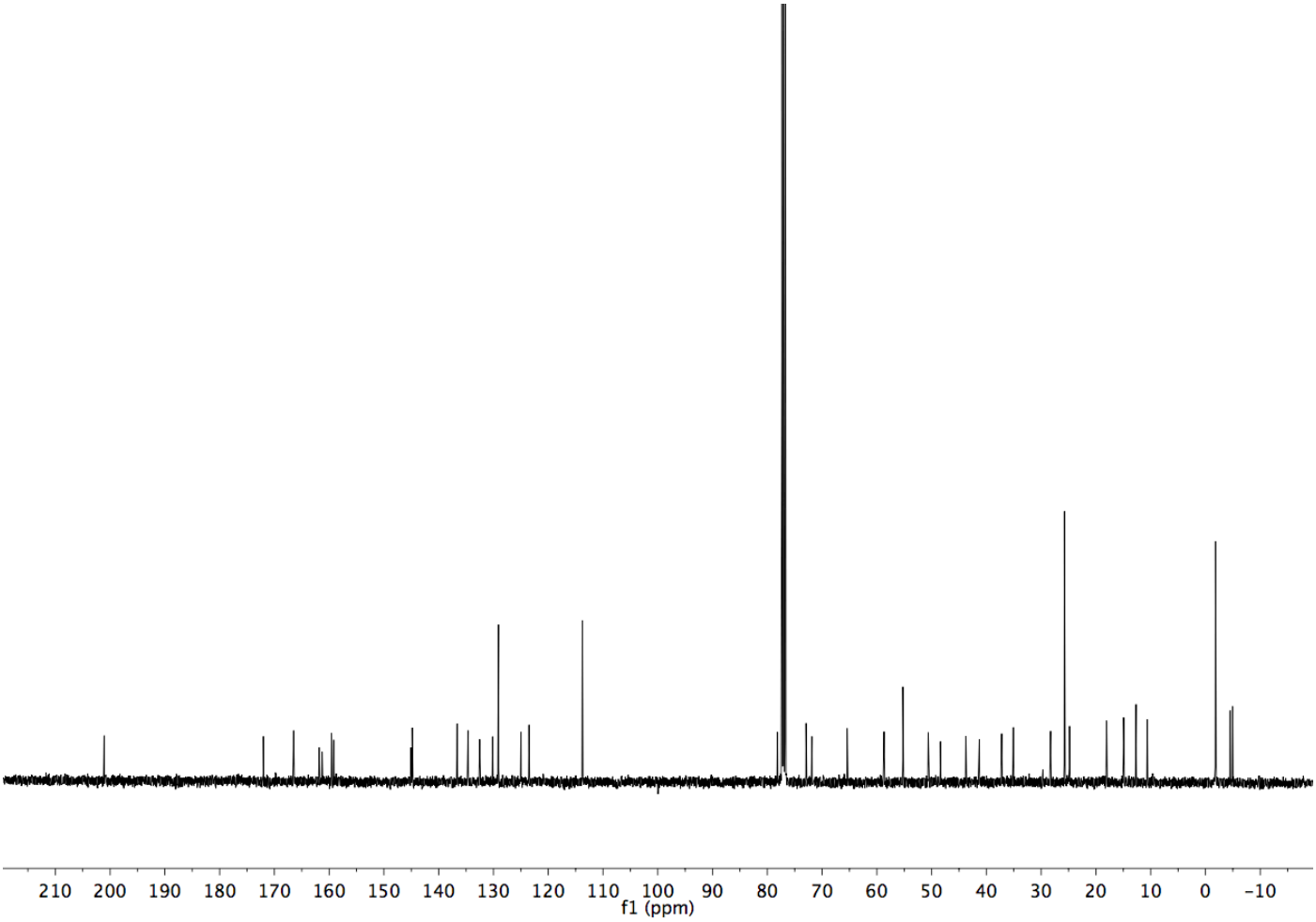
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

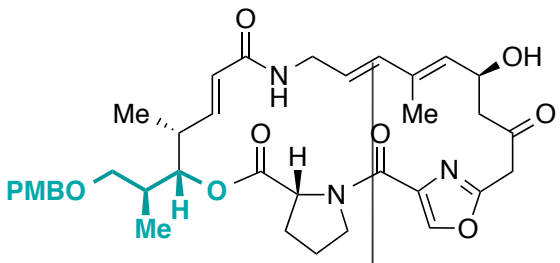

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
H
O
PMBO
O
N
N
H
Me
O
TMS

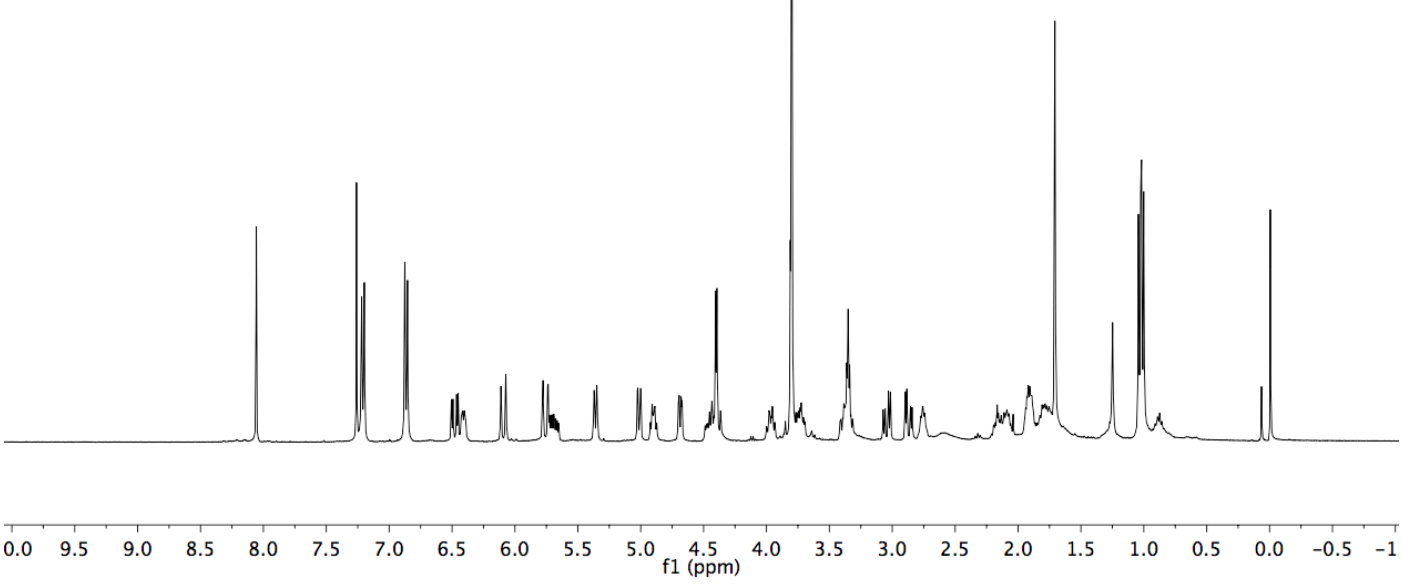
SI-79

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

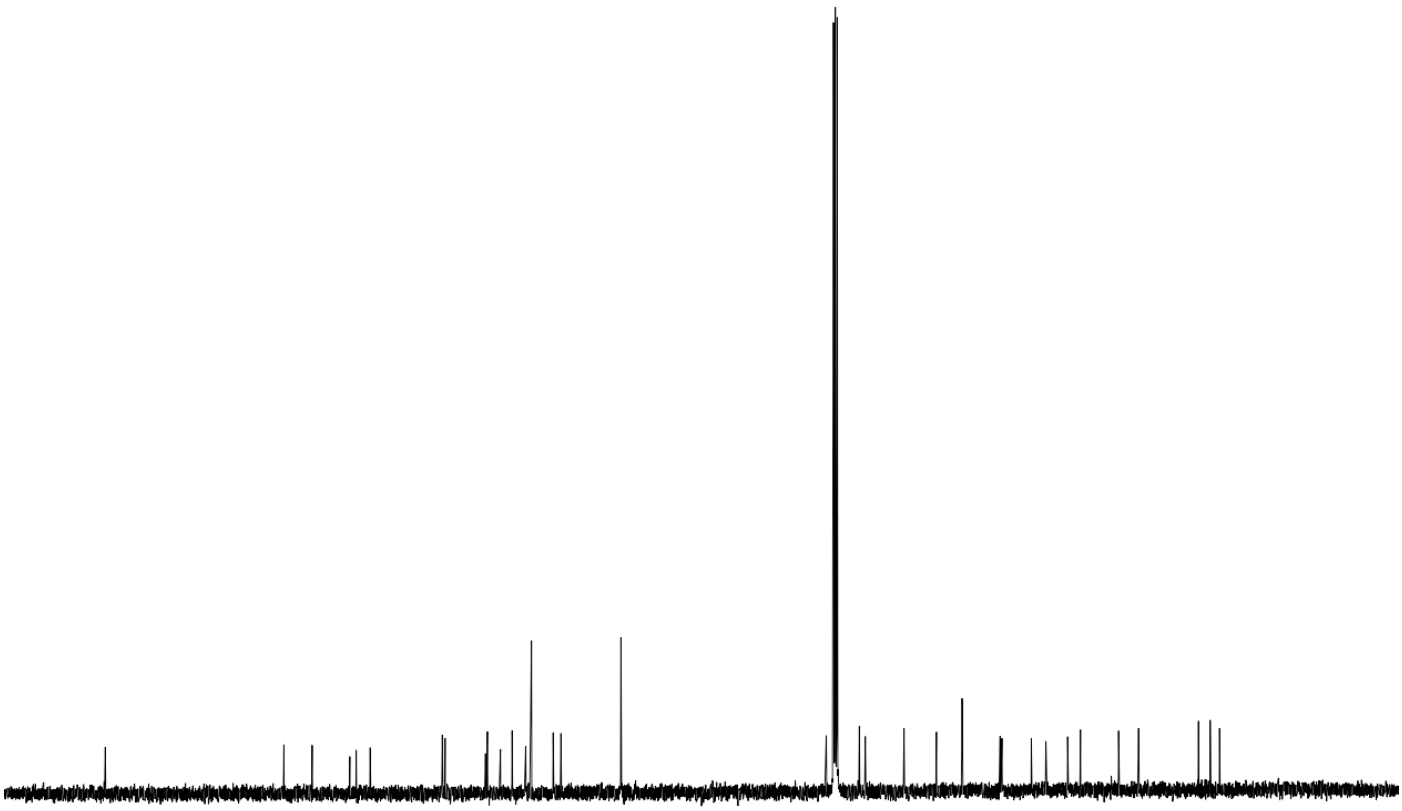

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

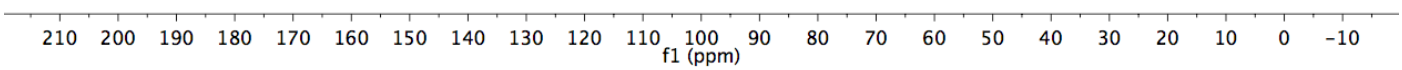

O
N
H
OH
Me
Me
O
O
O
H
O
PMBO
O
N
N
Me
H
O

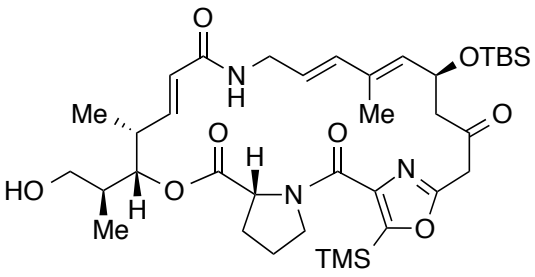
SI-80



0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

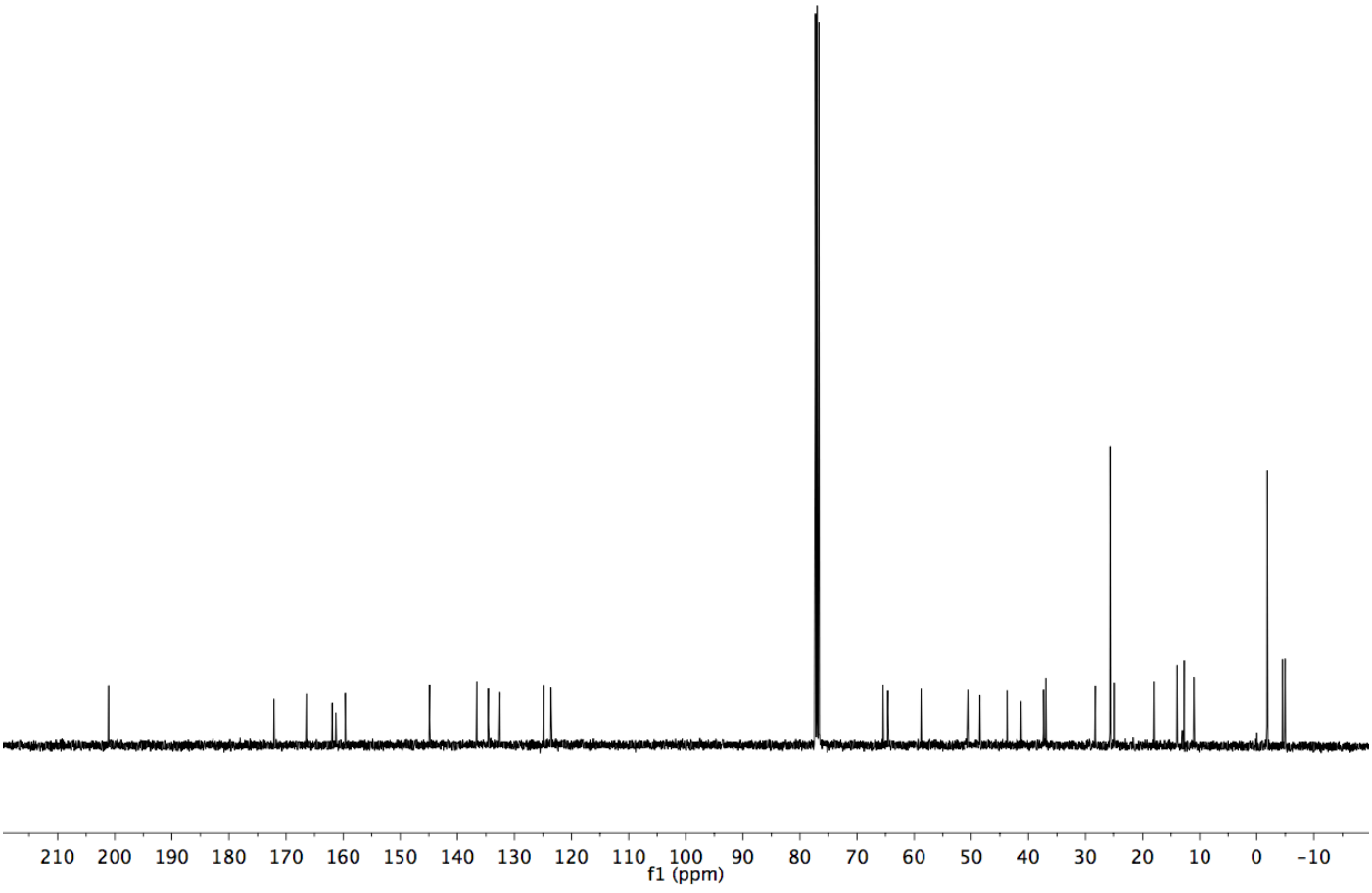


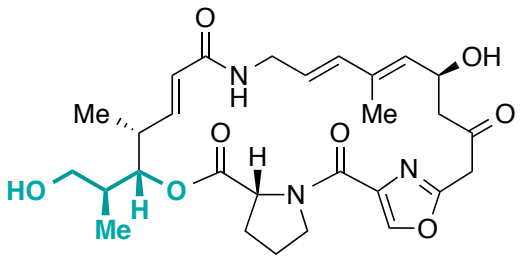

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
HO
O
N
N
H
Me
O
TMS

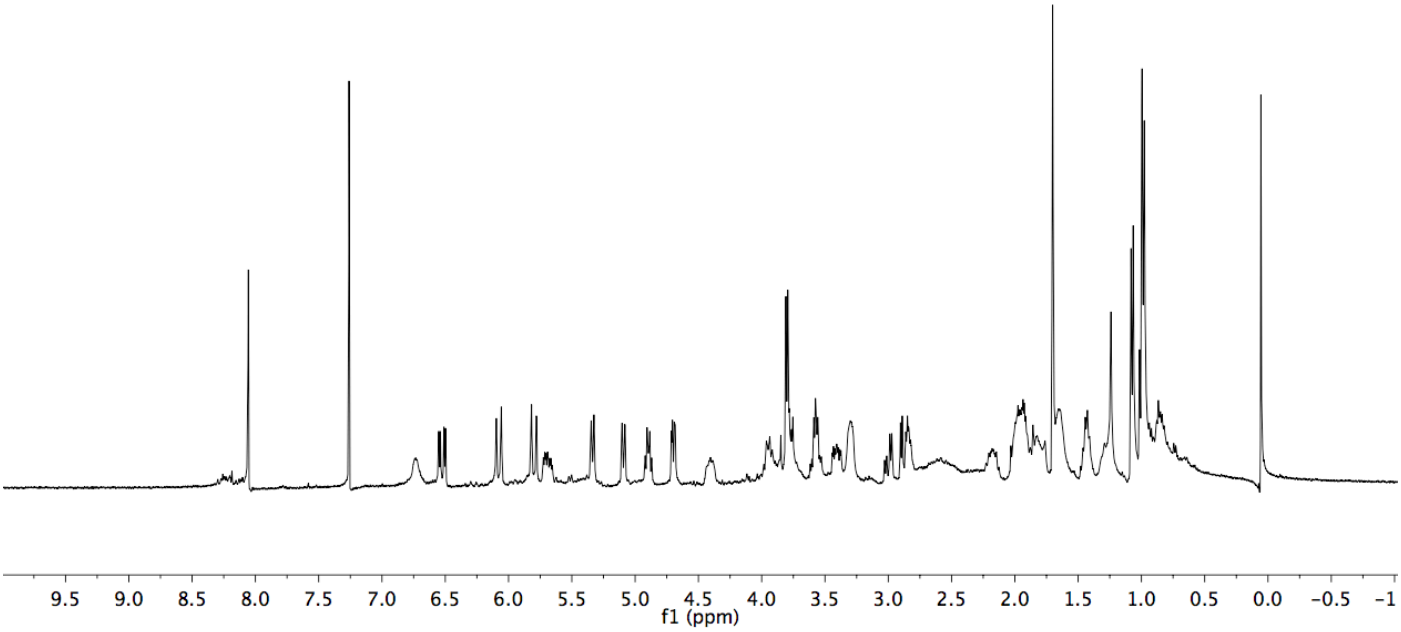
39

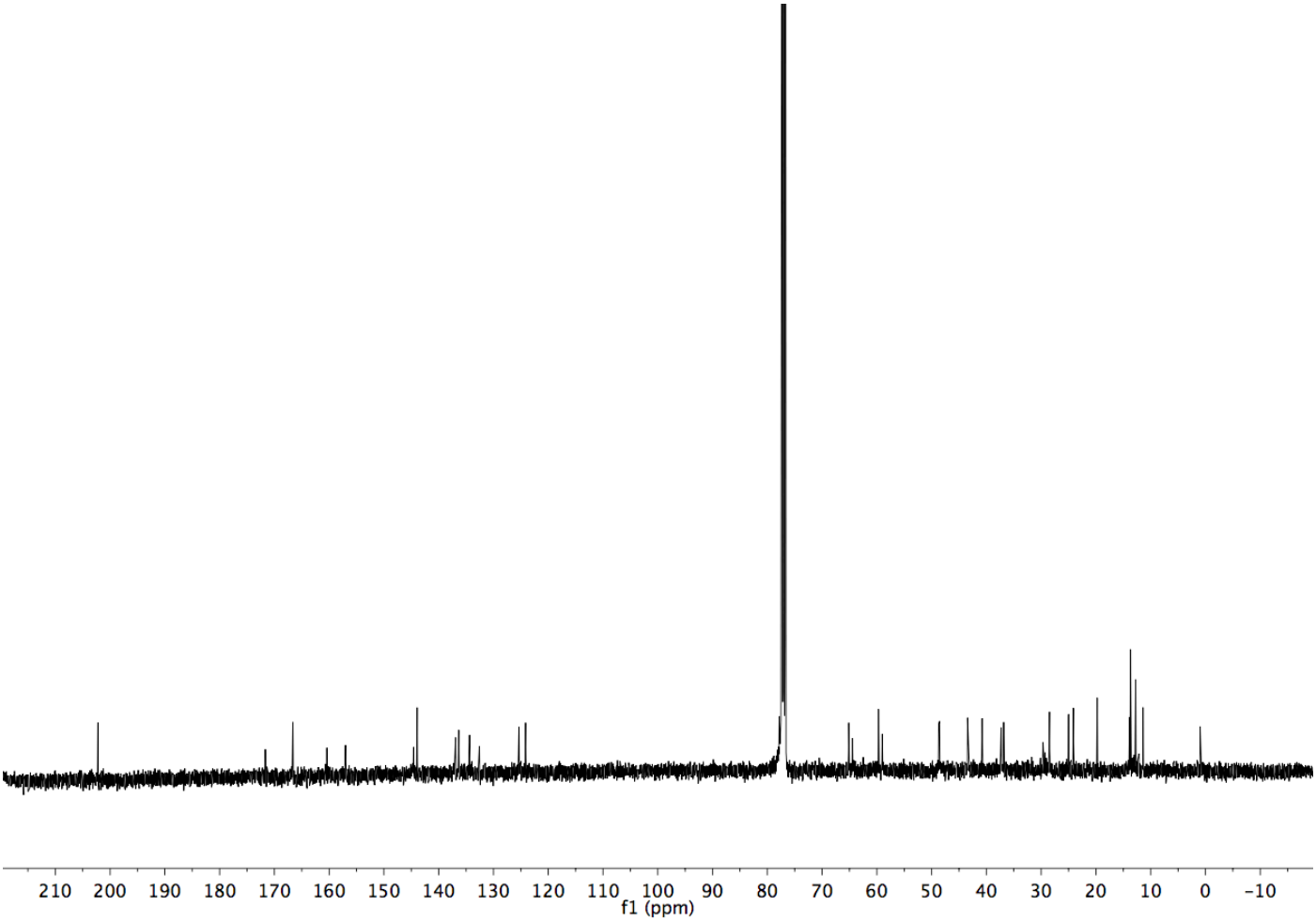
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

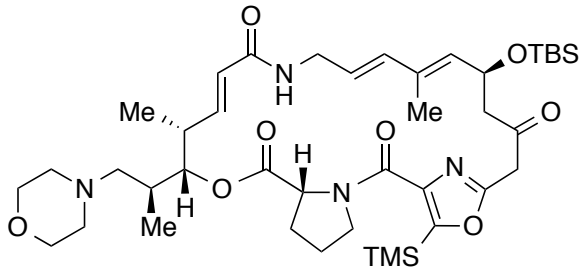

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
HO
O
N
N
Me
H
O

36

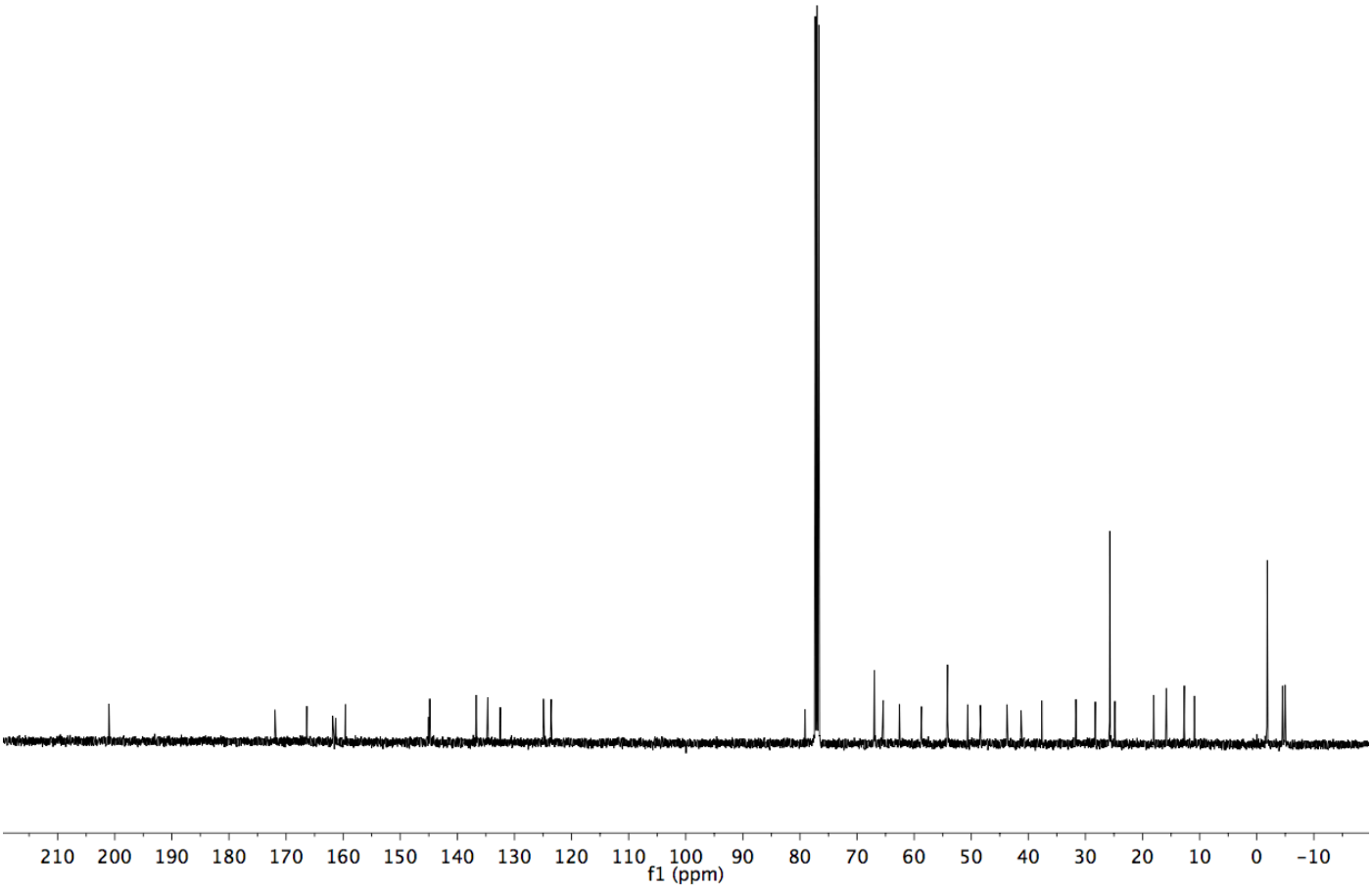

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

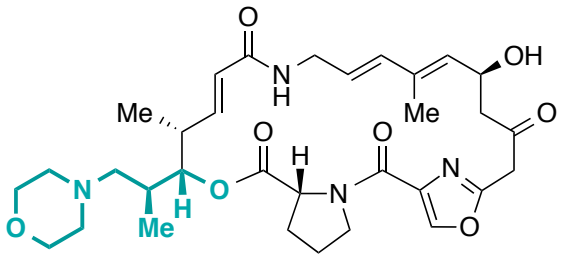

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
Me
O
O
O
H
N
N
O
O
N
O
Me
H
O
TMS

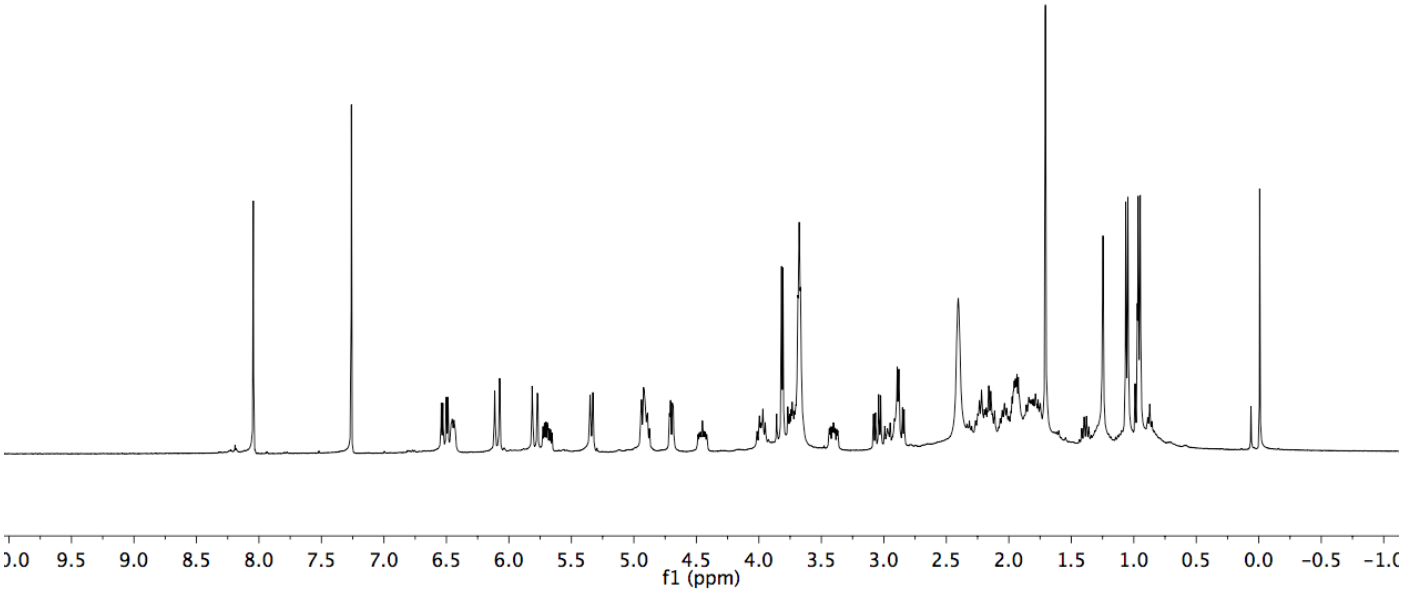
SI-81

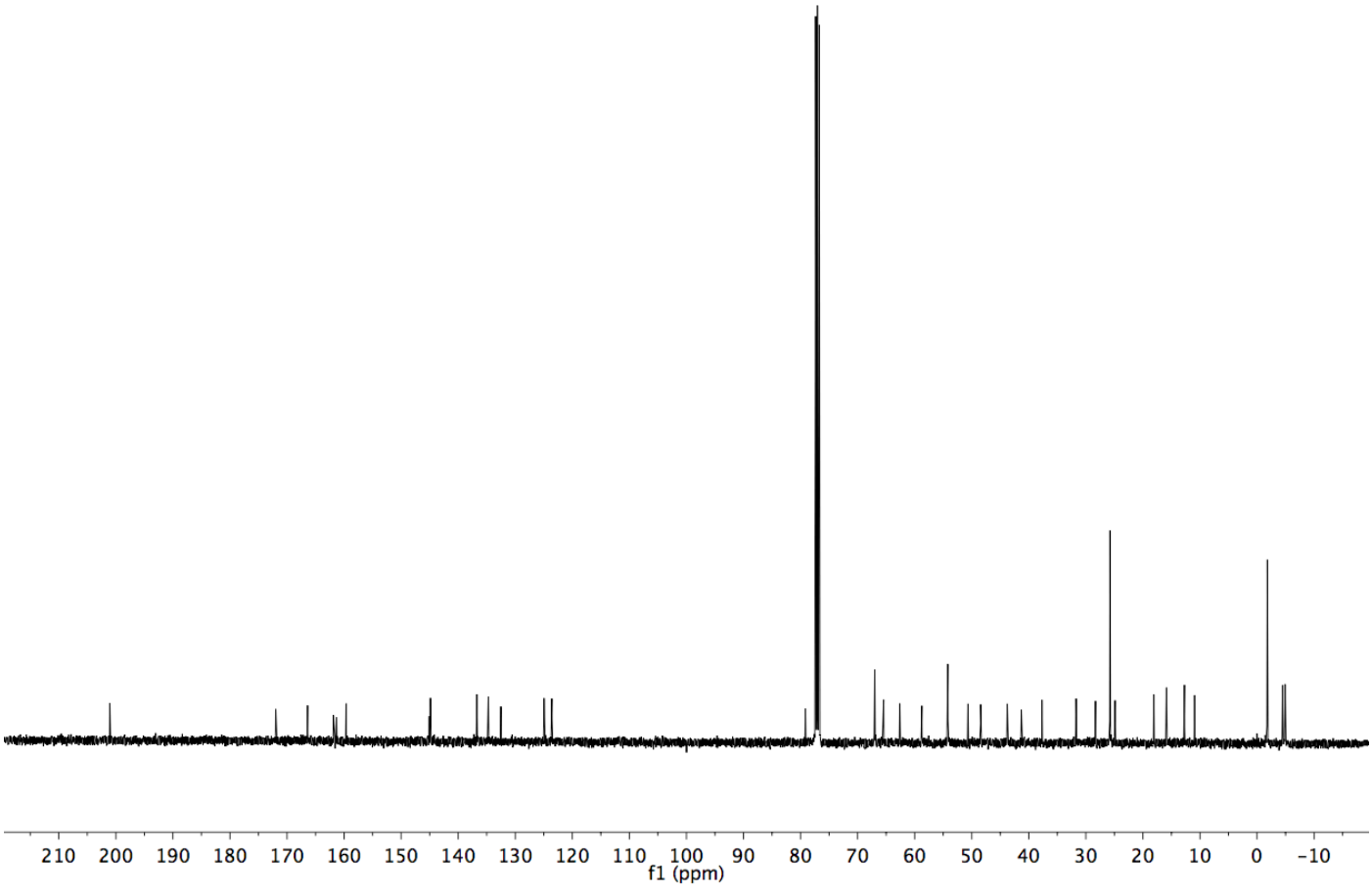
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

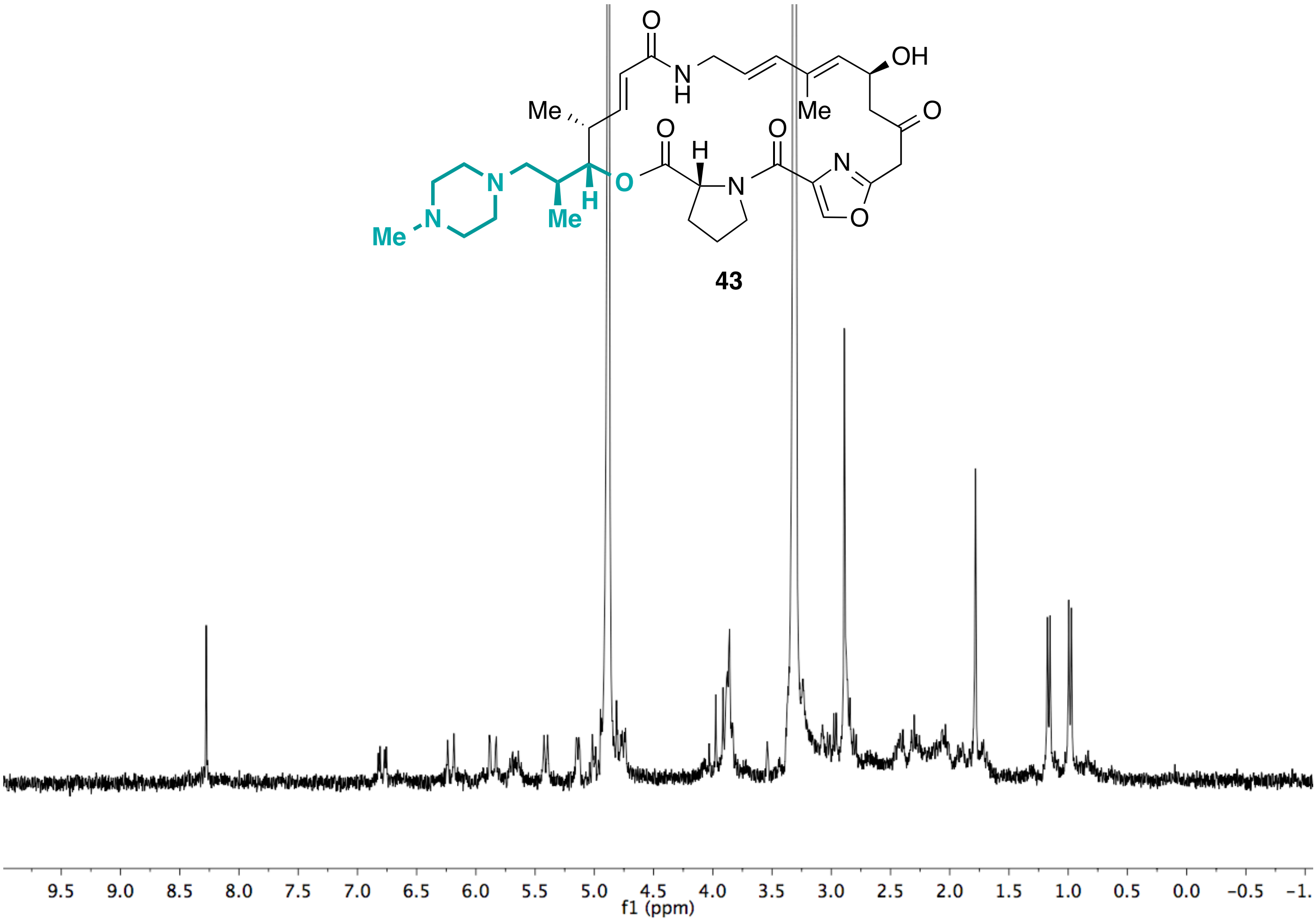

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

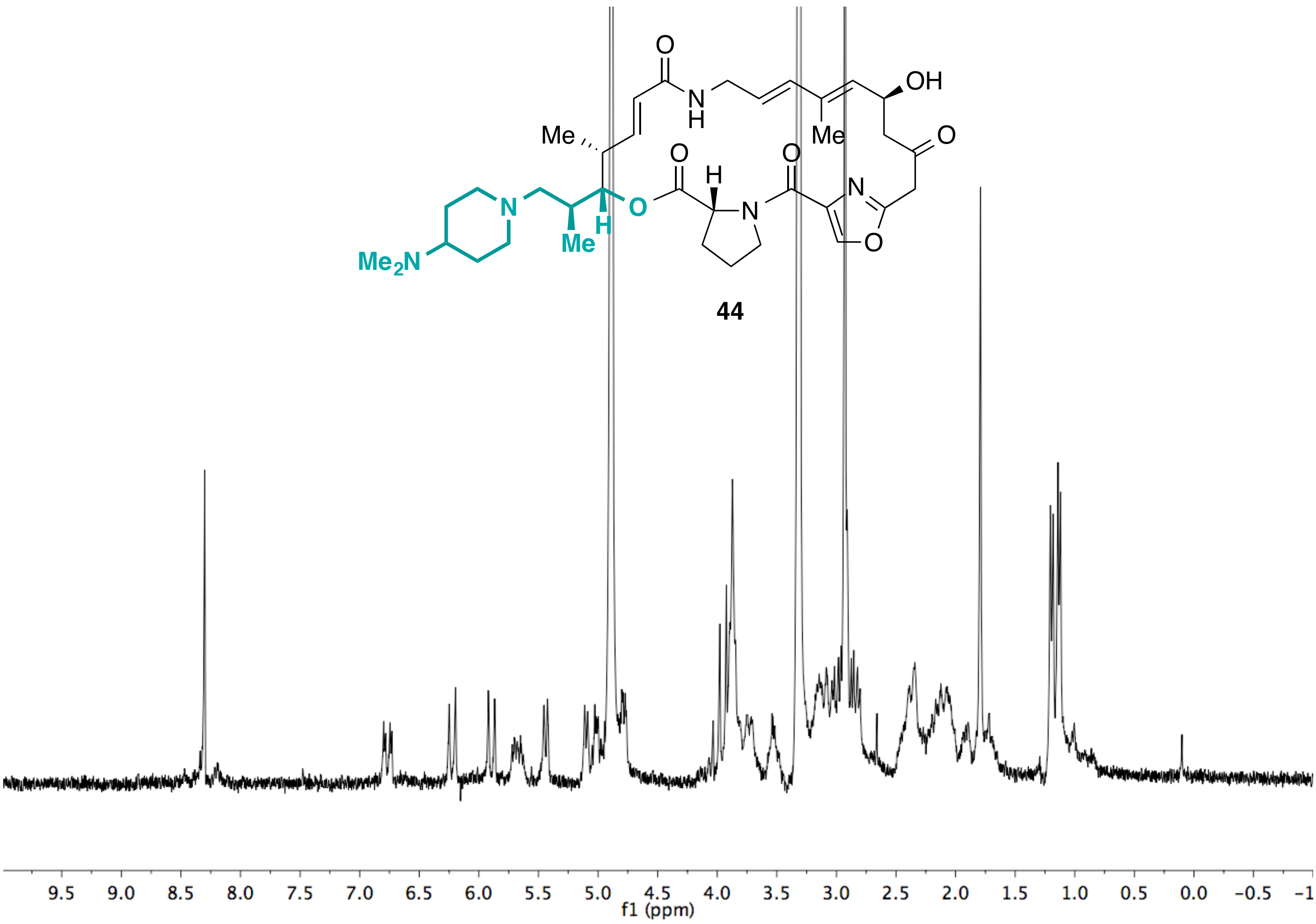


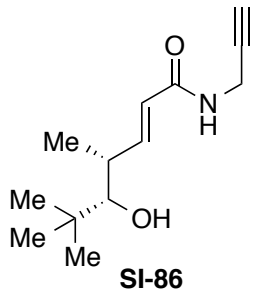
42


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

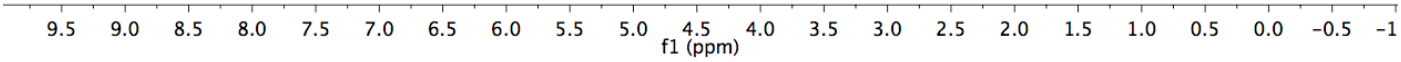

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

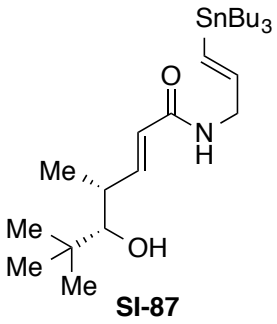

Me
N
N
Me
H
O
O
N
H
O
N
OH
Me
O
O
H
N
O
N
O
43
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)


Me2N
N
Me
H
O
O
N
H
O
N
OH
Me
O
O
H
N
O
N
O
44
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)

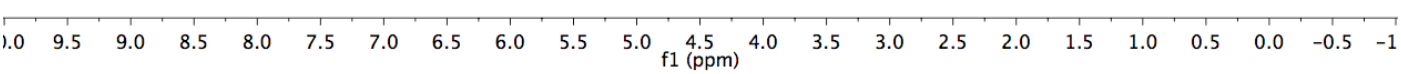

O
N
H
Me
Me
Me
OH

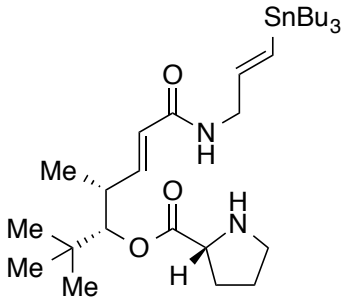
SI-86


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


SnBu3
O
N
H
Me
Me
Me
OH

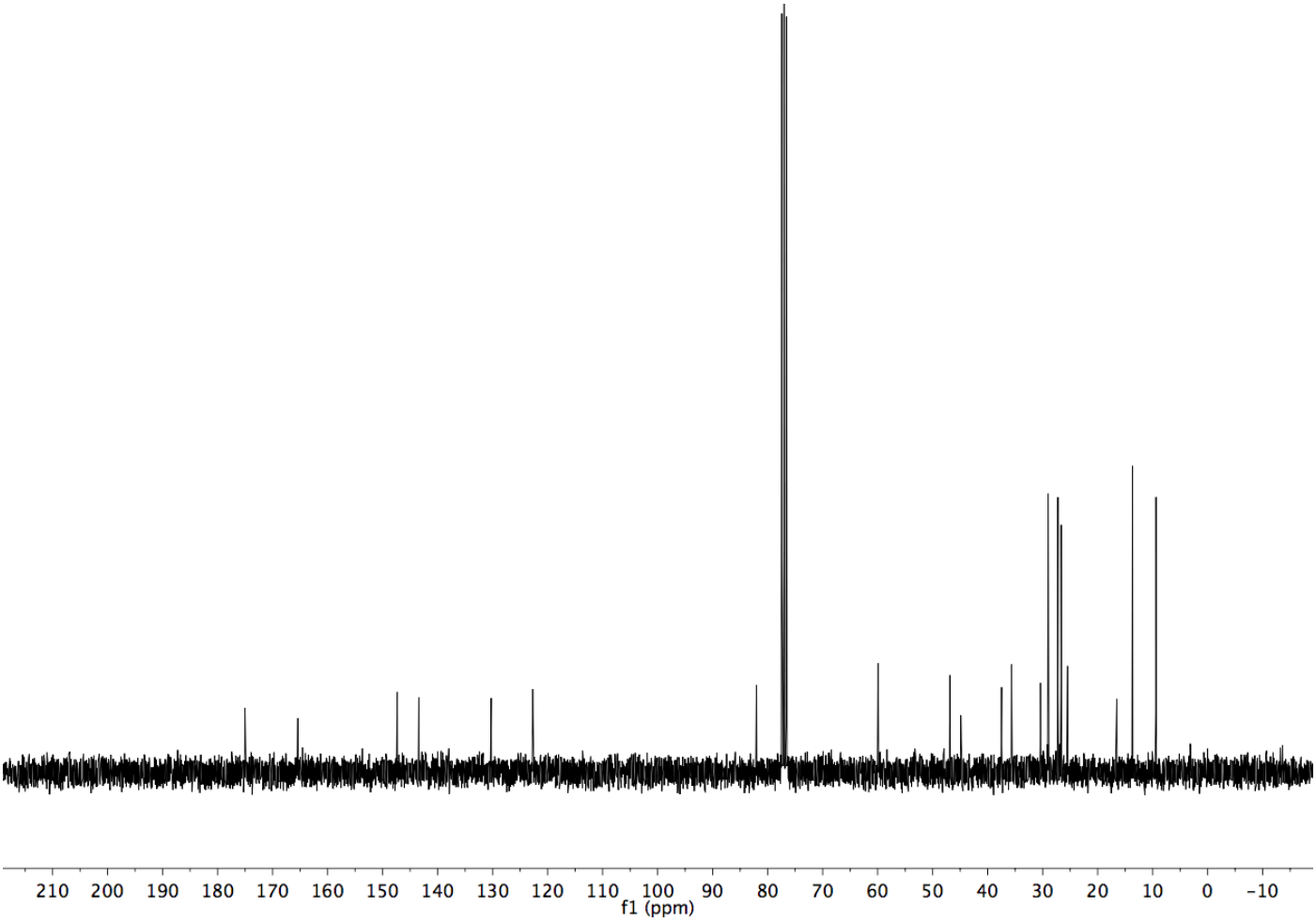
SI-87

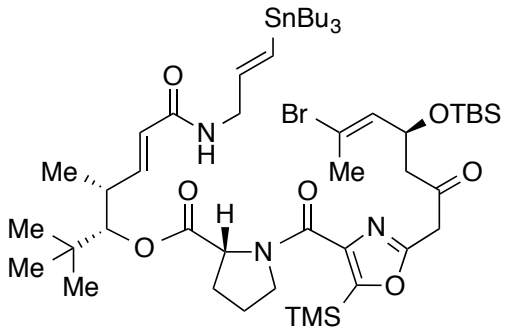

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


SnBu3
O
N
H
Me
O
H
N
Me
O
Me
H
Me

SI-88

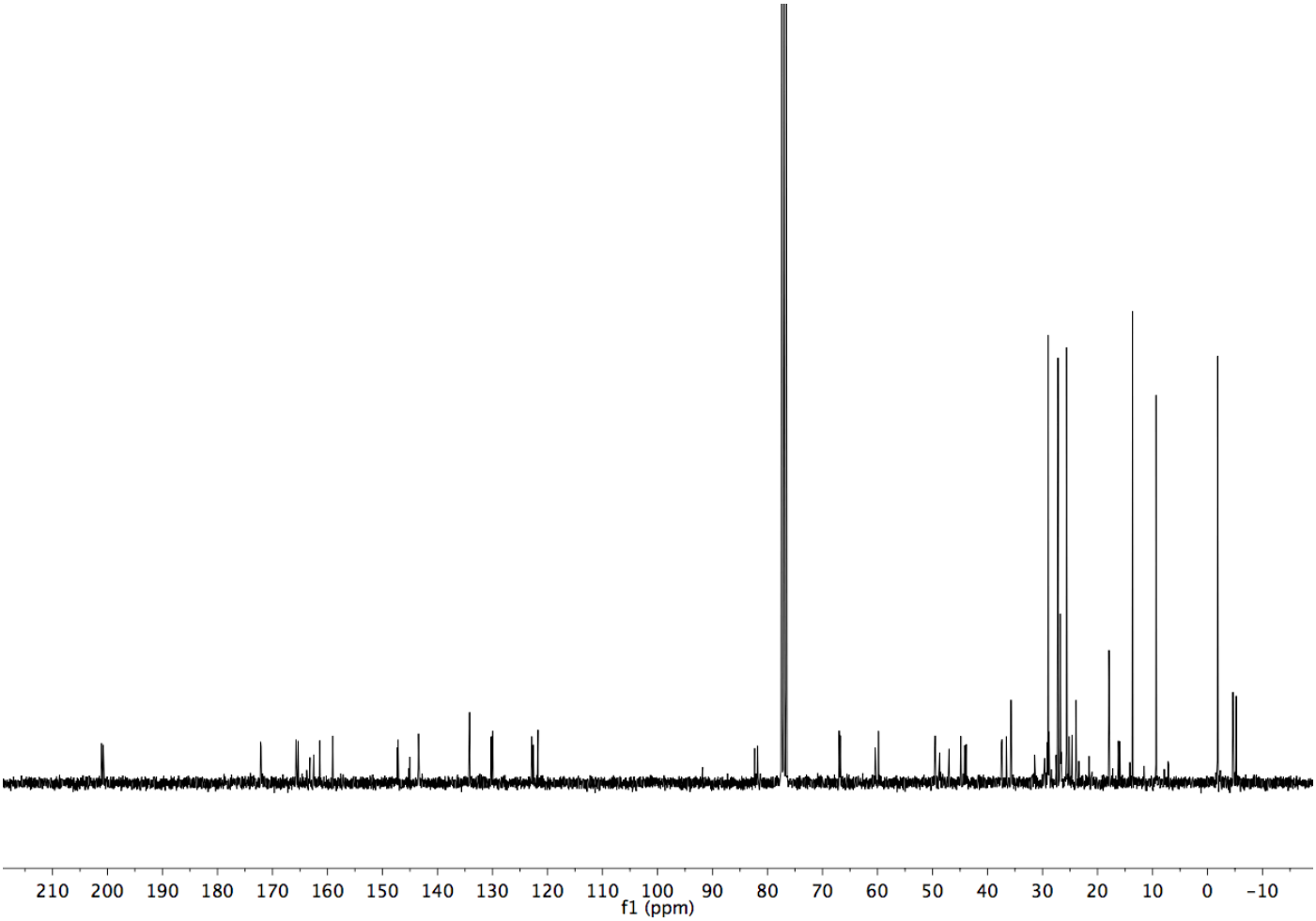
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

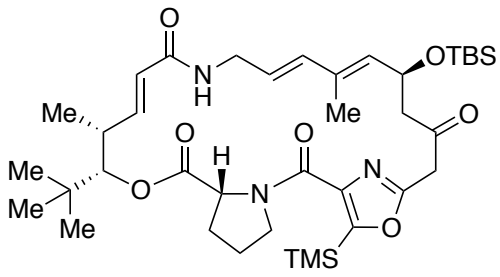

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
Me
O
O
H
O
N
N
Me
Me
Me
O
O
TMS

SI-89

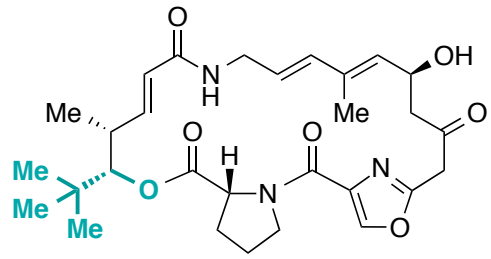
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

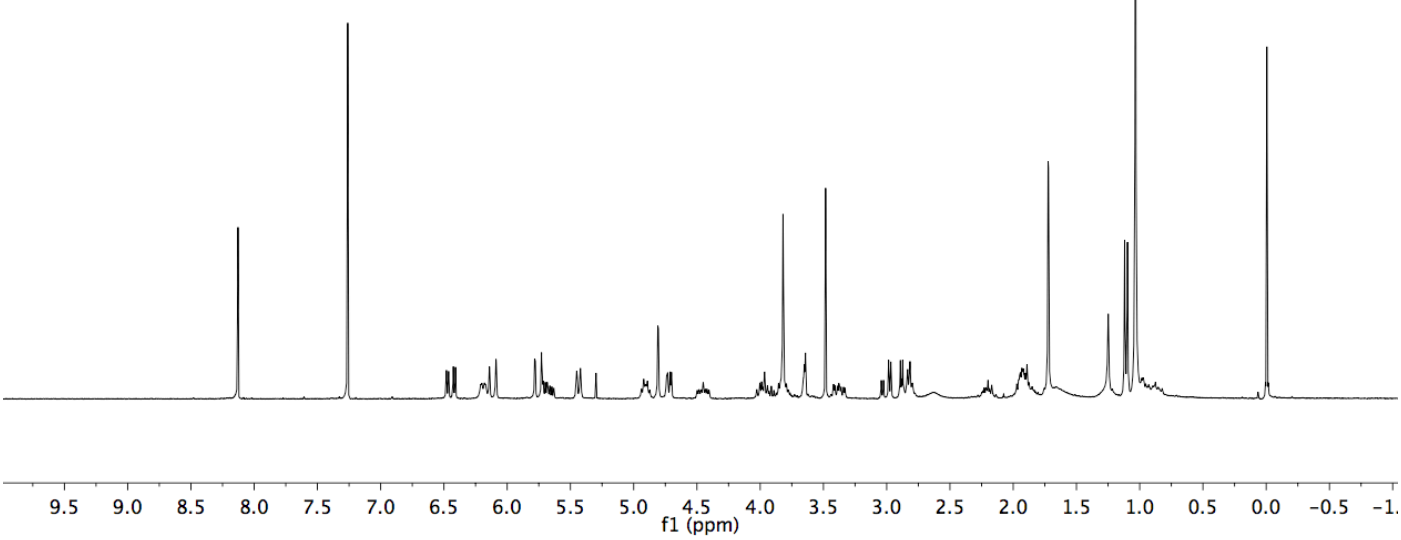

O
N
H
OTBS
Me
Me
O
O
H
O
Me
Me
Me
O
N
N
O
TMS

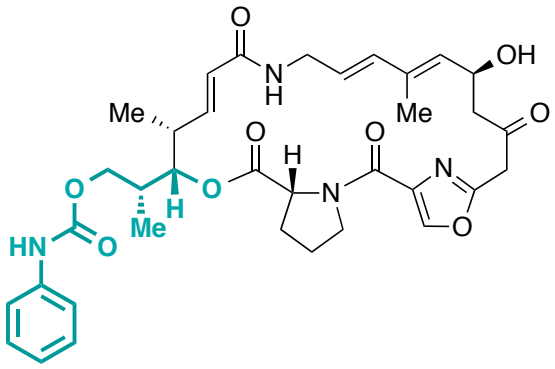
SI-90

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

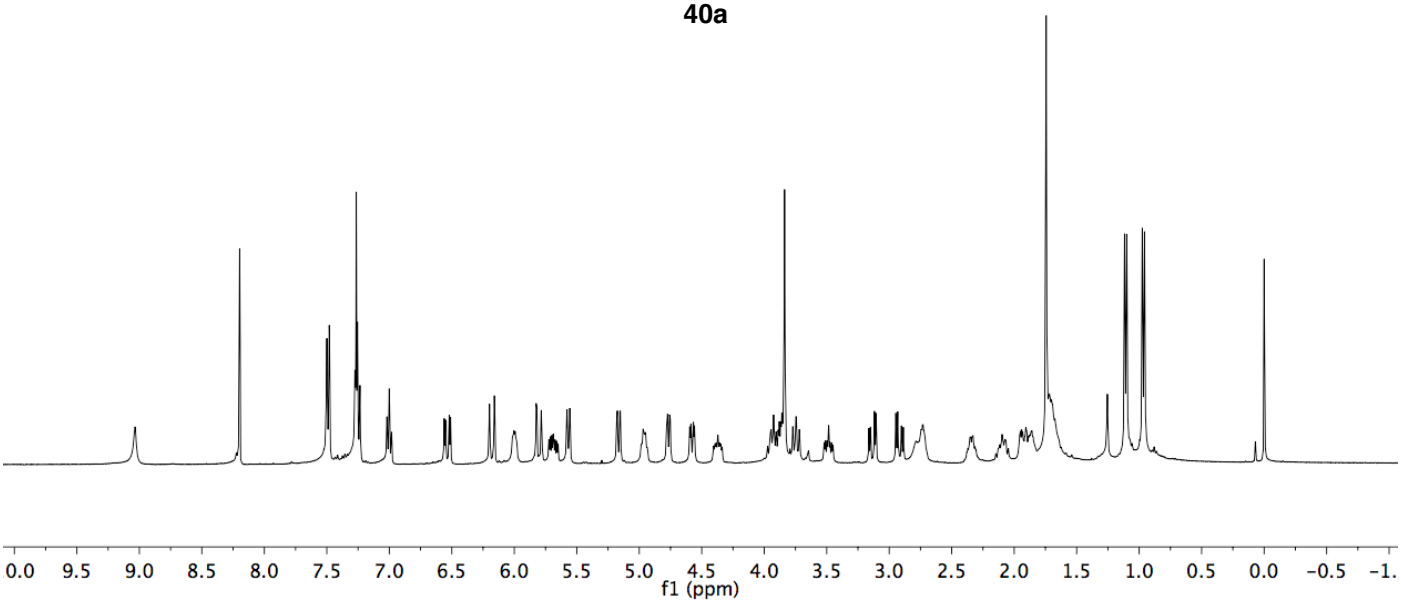

O
N
H
OH
Me
Me
O
O
H
O
Me
Me
Me
O
N
N
O

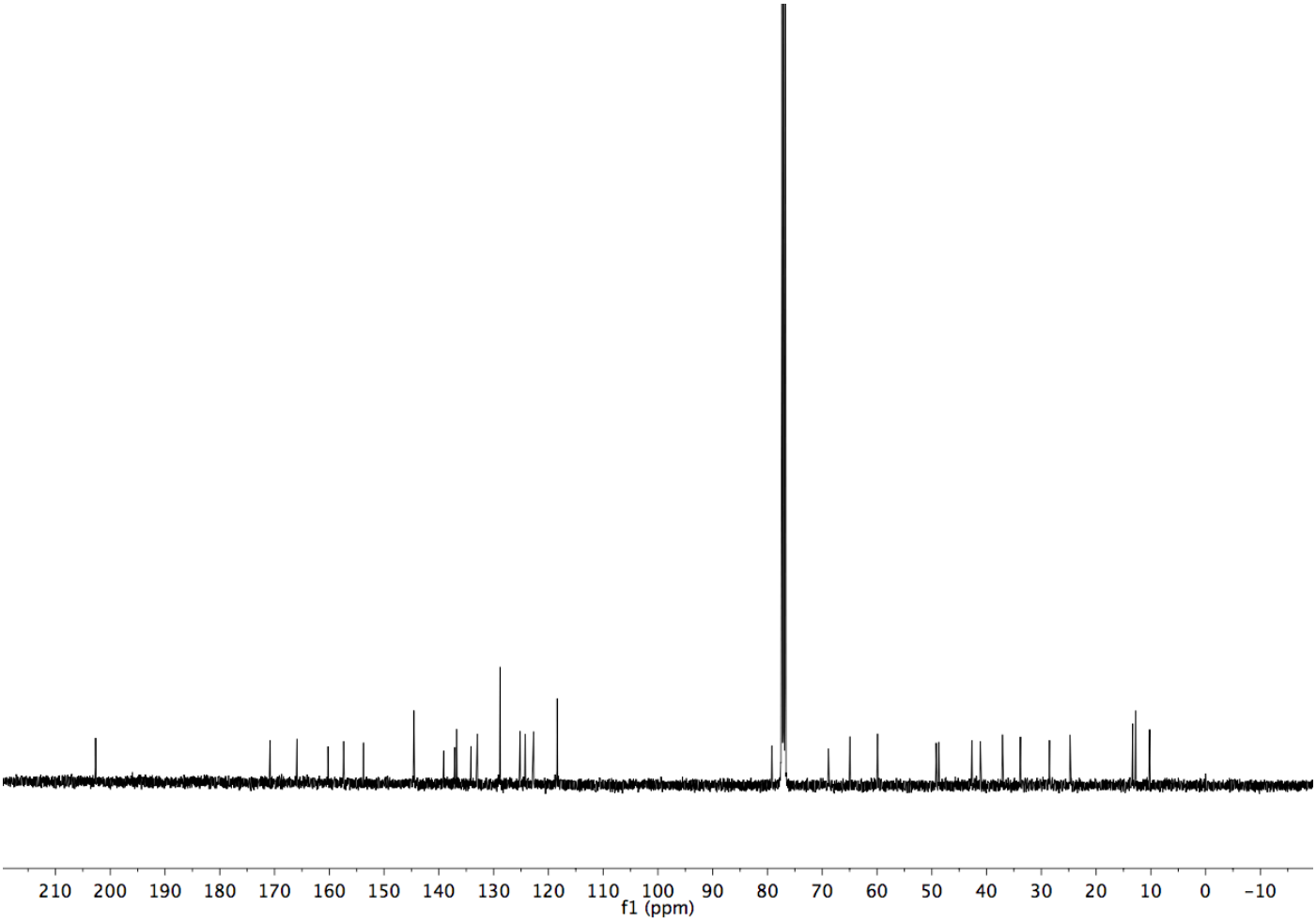
37

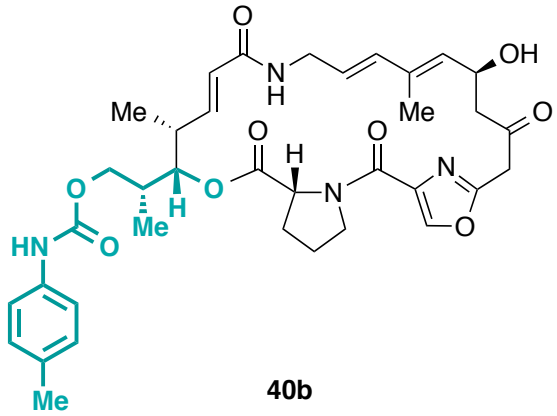

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O

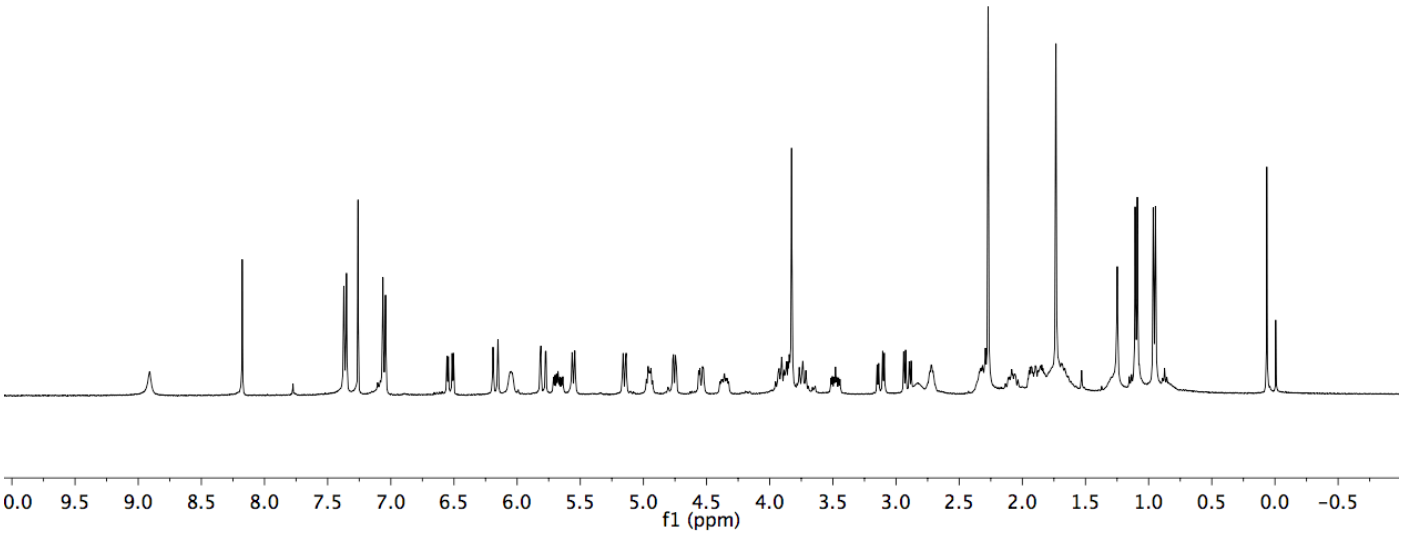
40a

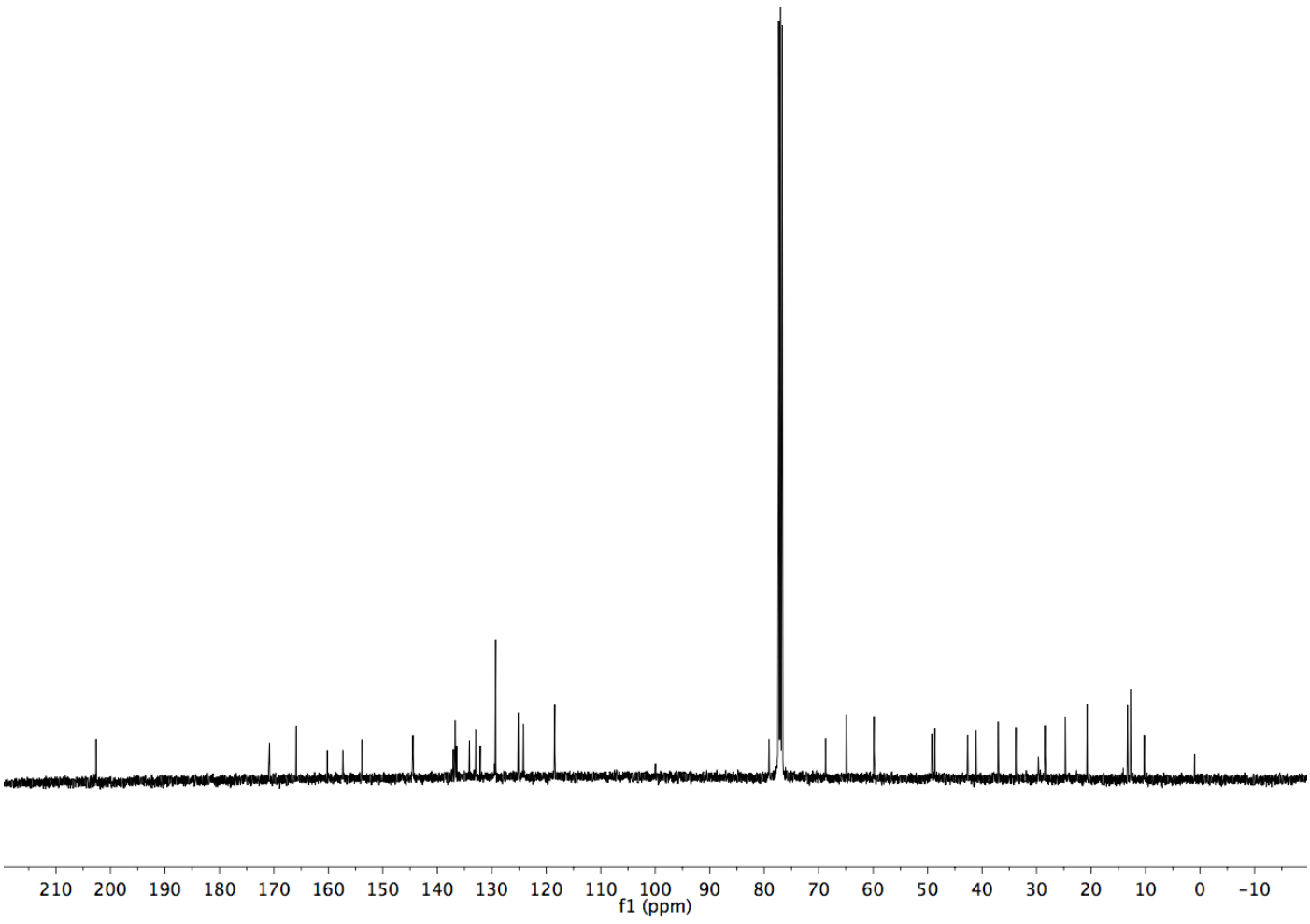

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

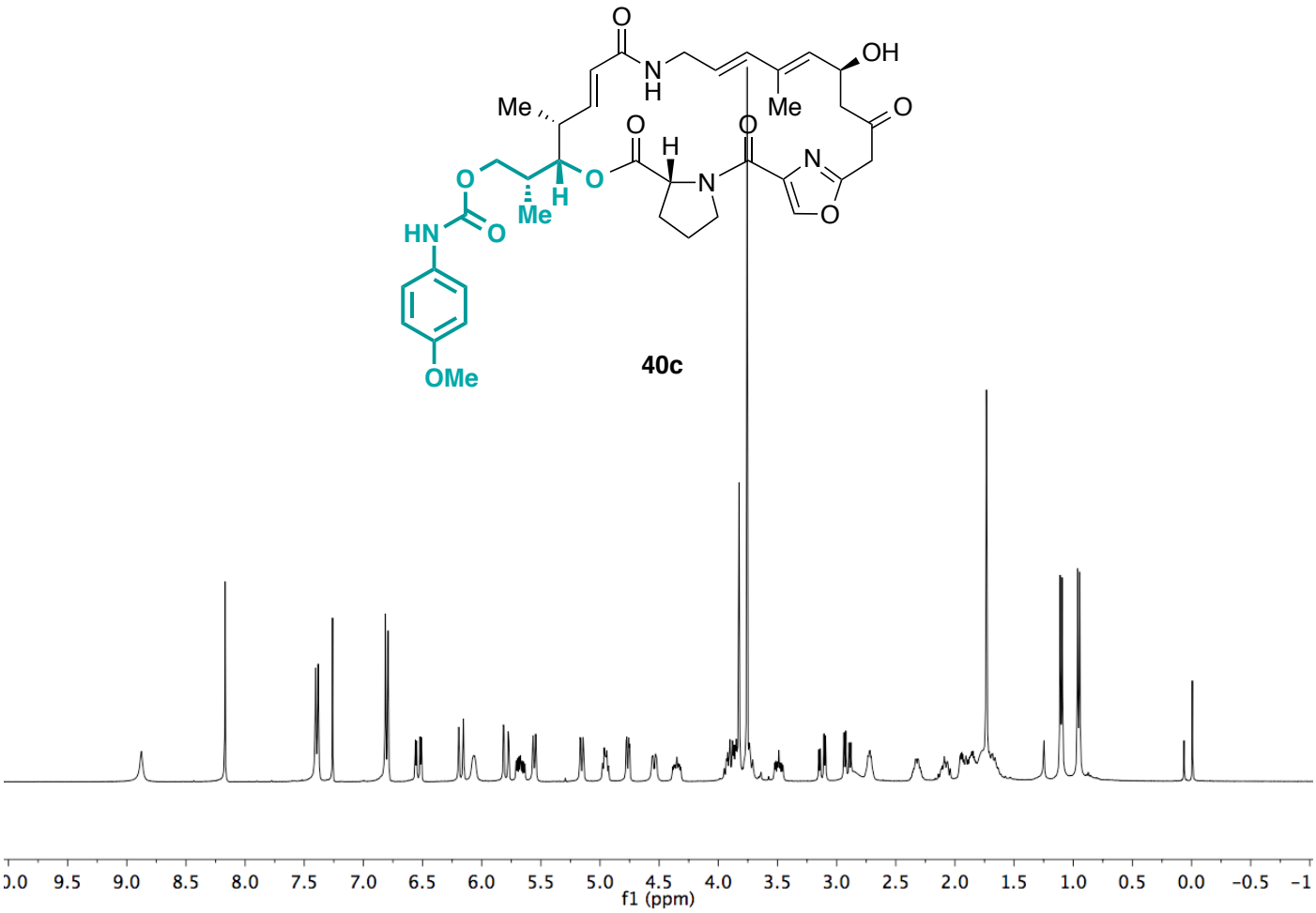

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
H
O
N
N
O
O
H
Me
O
HN
O
Me

40b

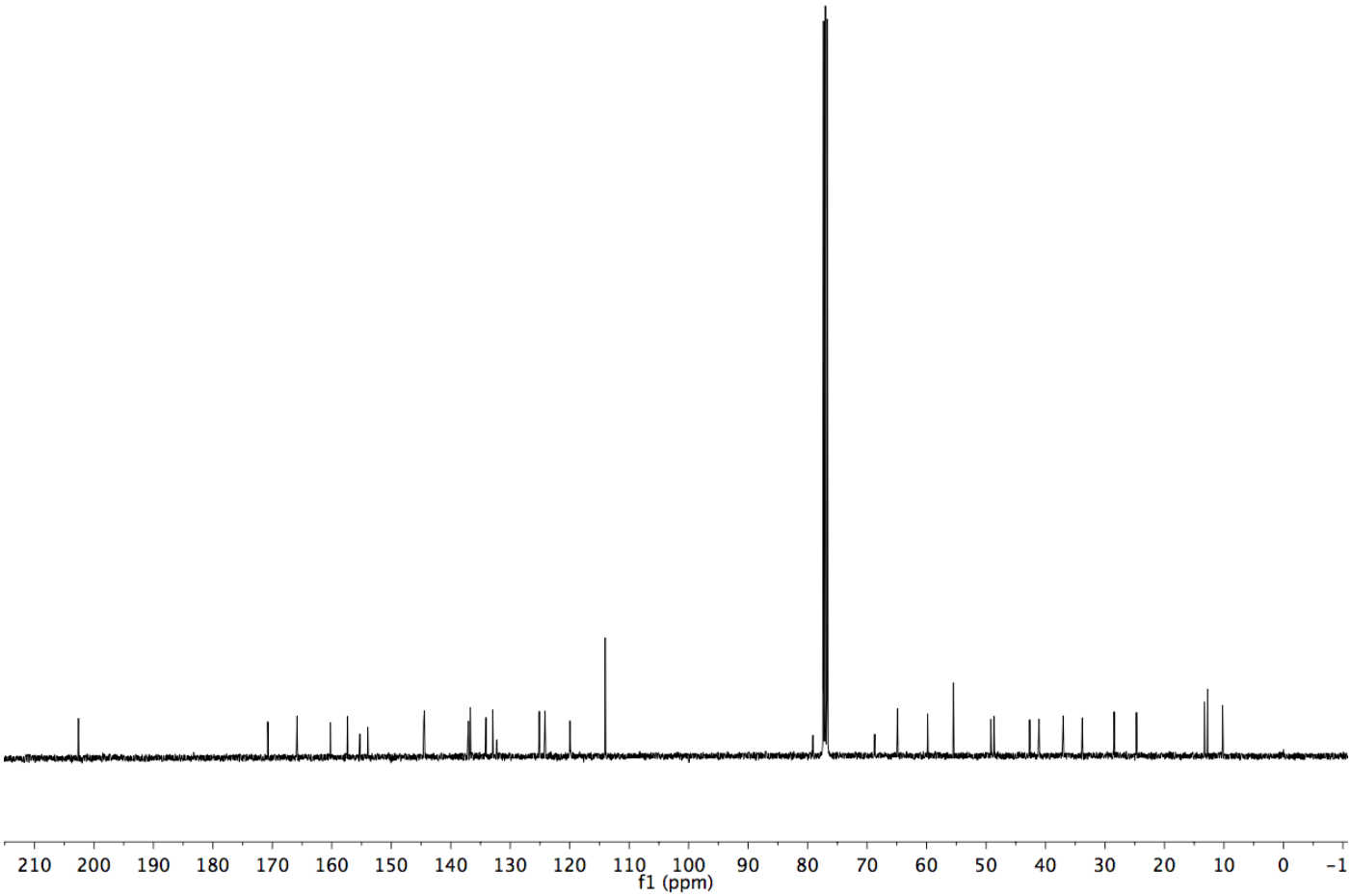

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

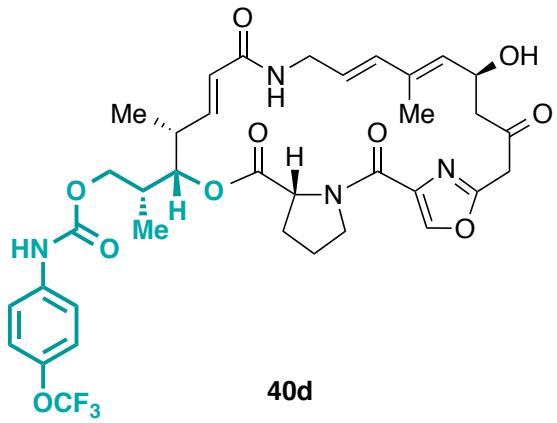

O
N
H
OH
Me
Me
O
O
O
H
N
N
O
O
O
Me
H
HN
O
OMe

40c

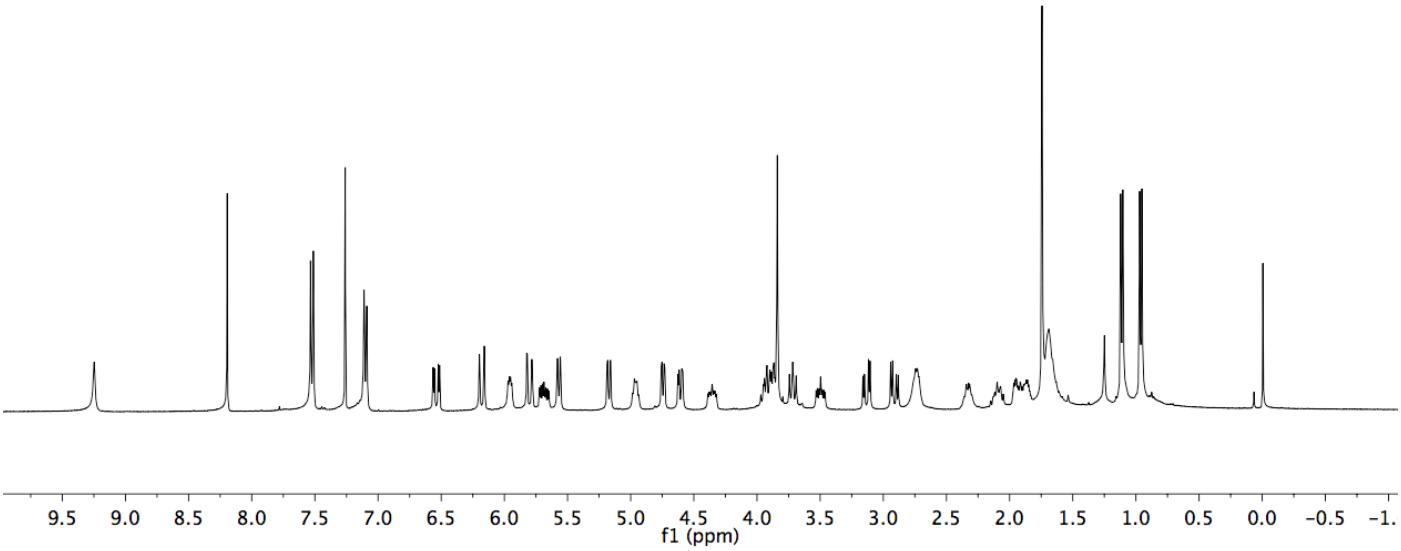
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

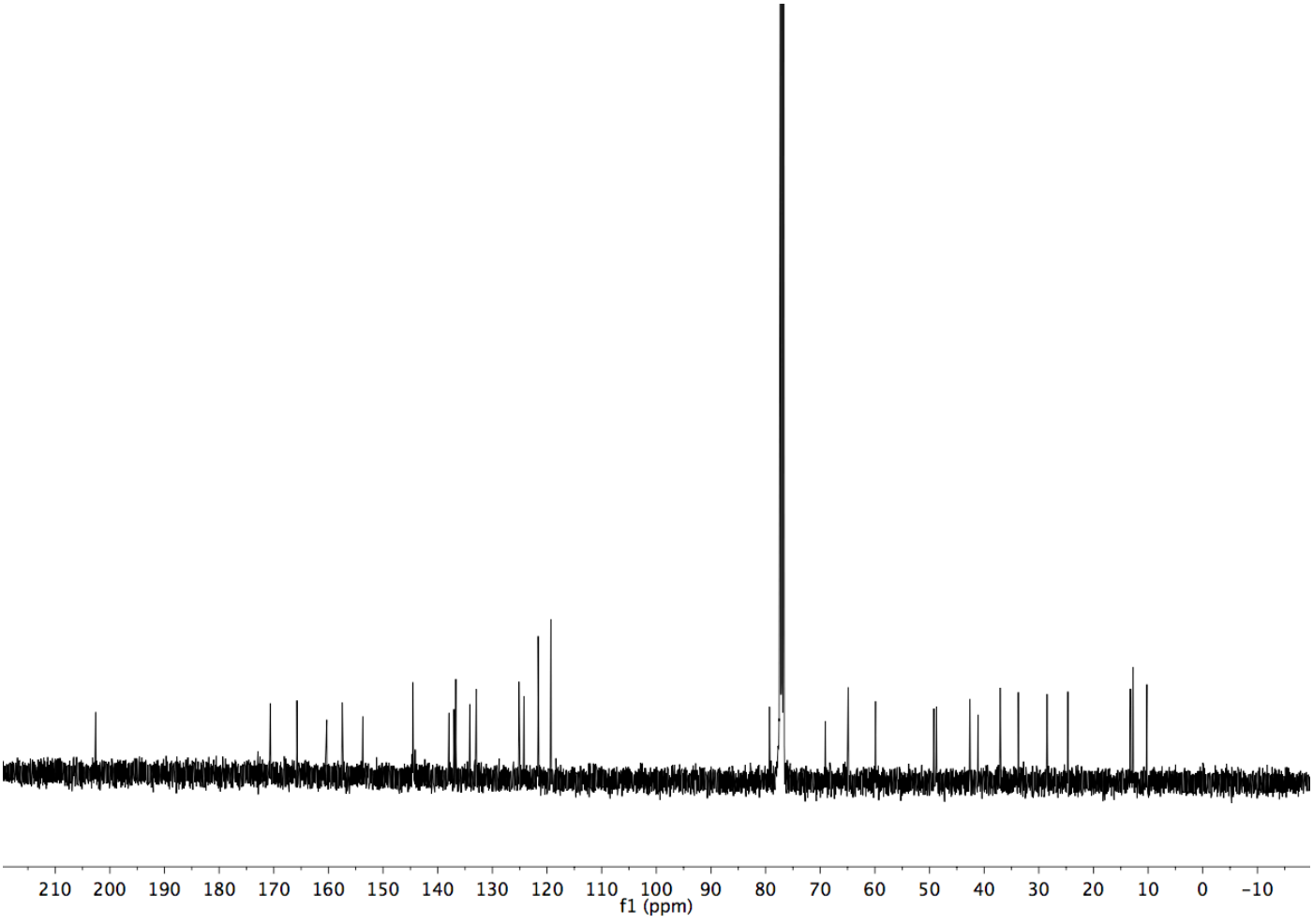


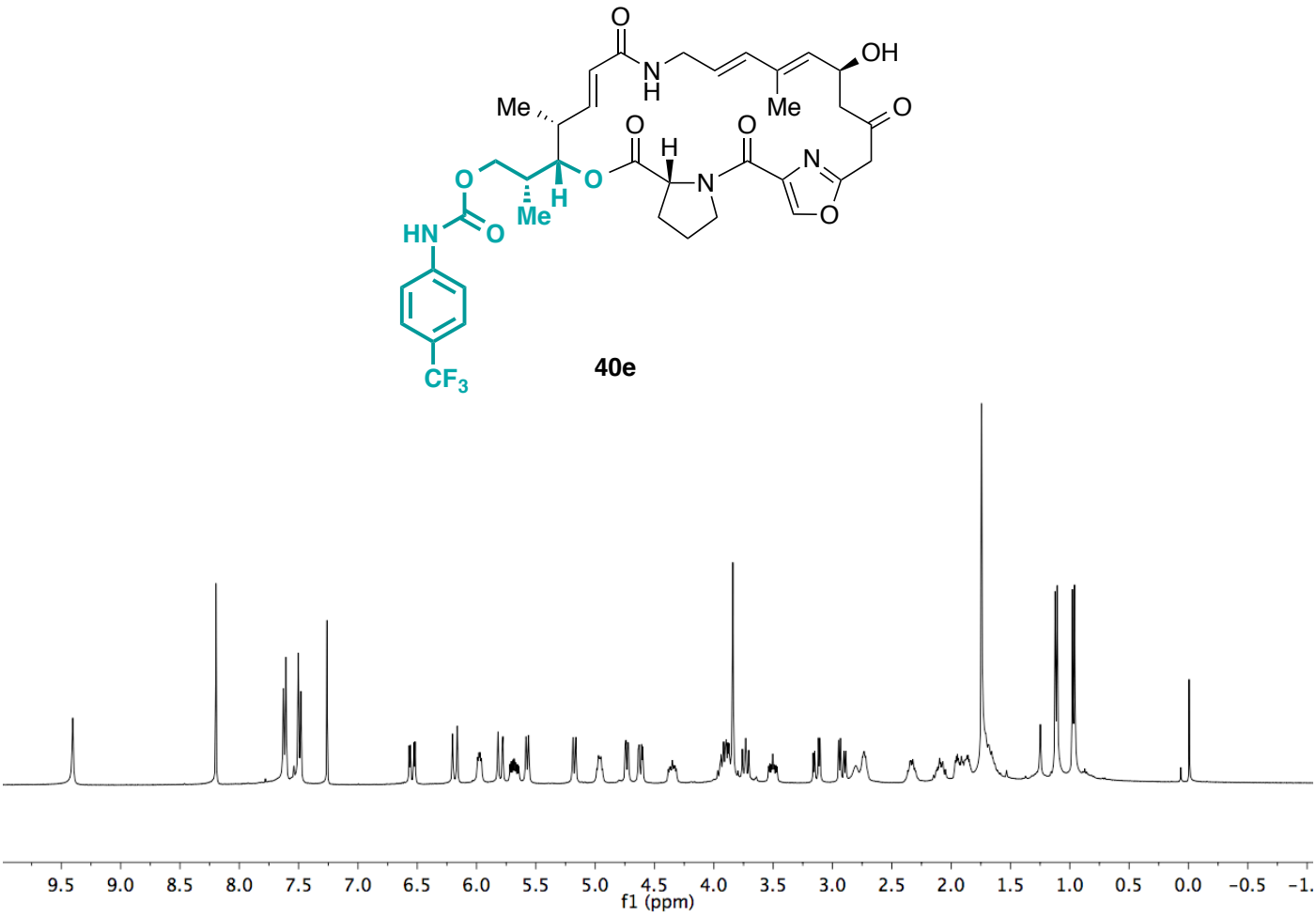
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
OCF3

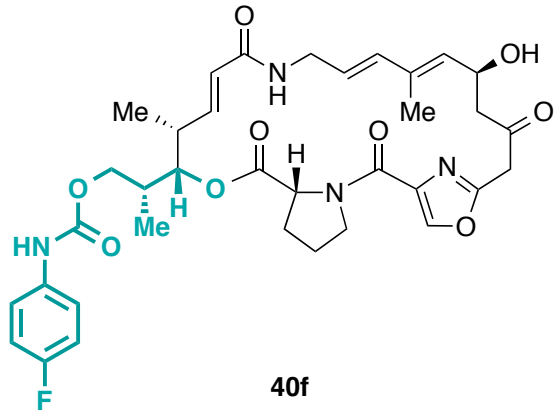
40d


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

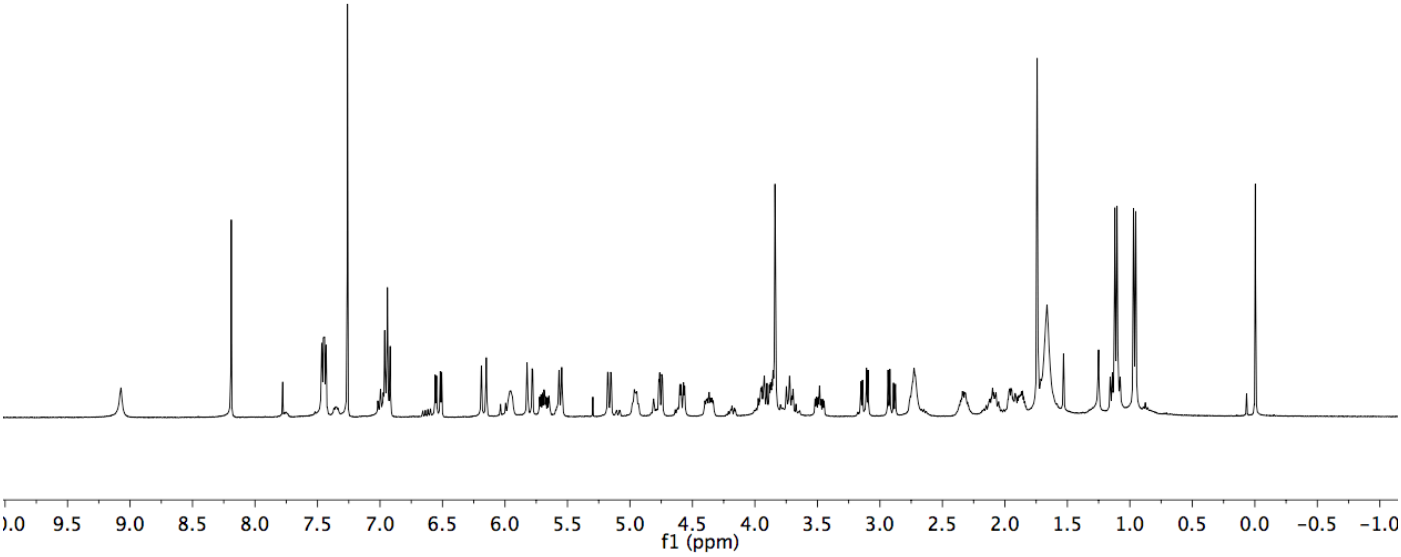

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

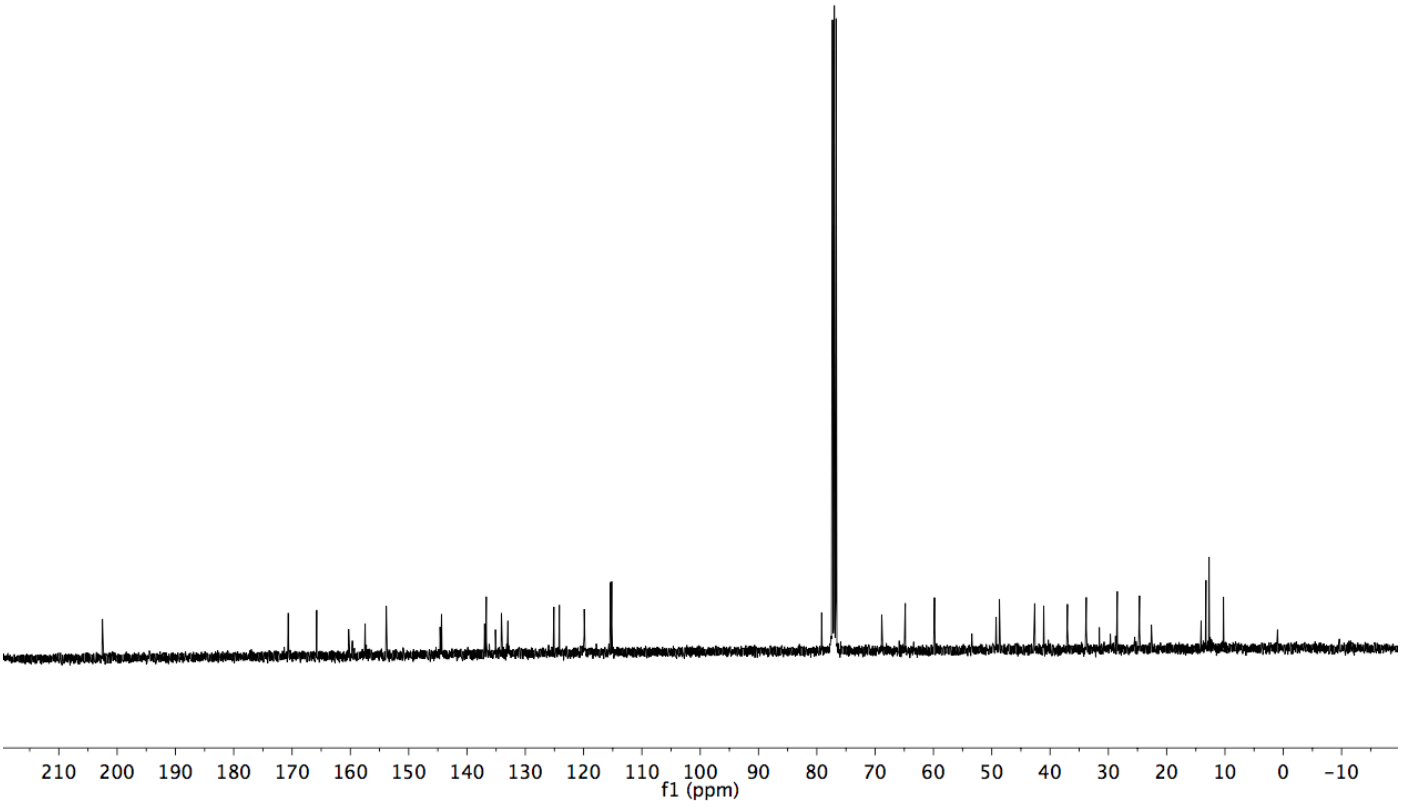

O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
CF3
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

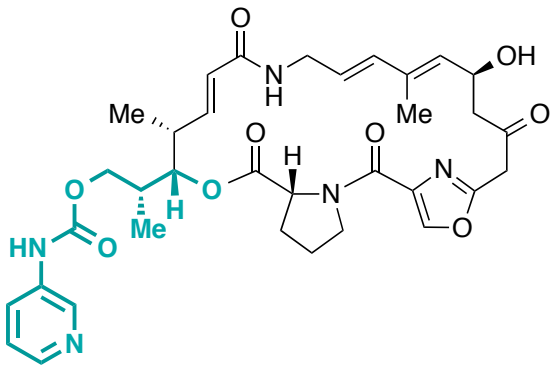
40e



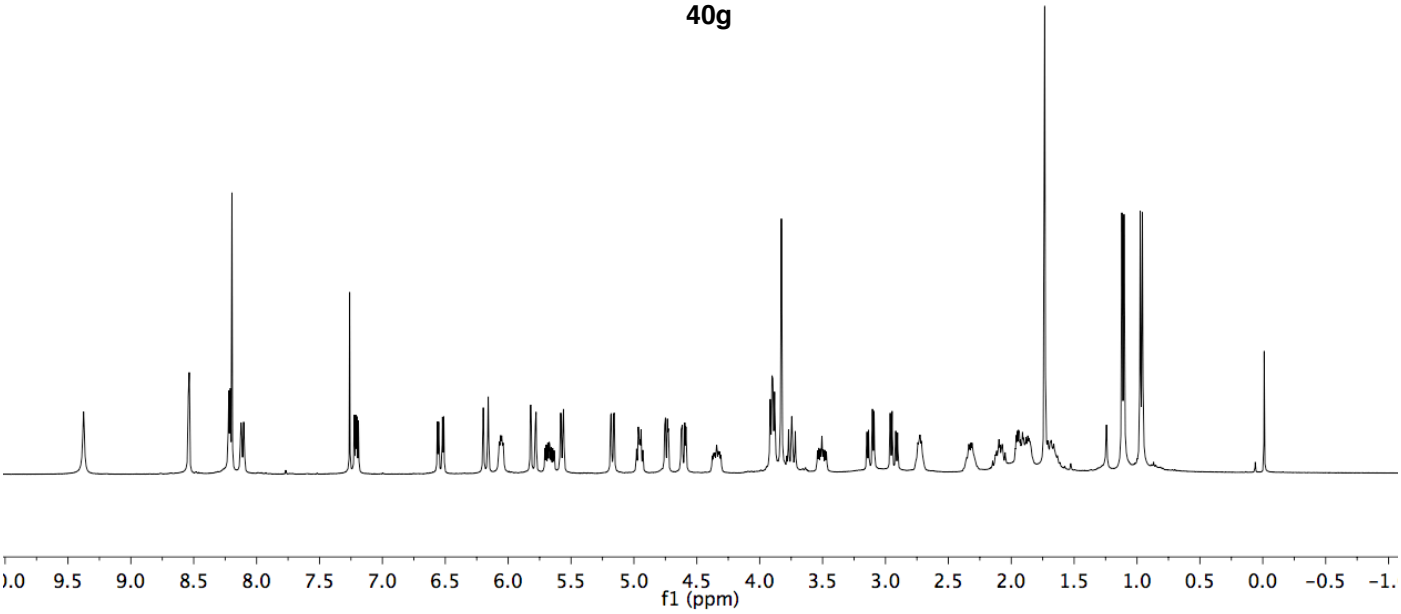
40f

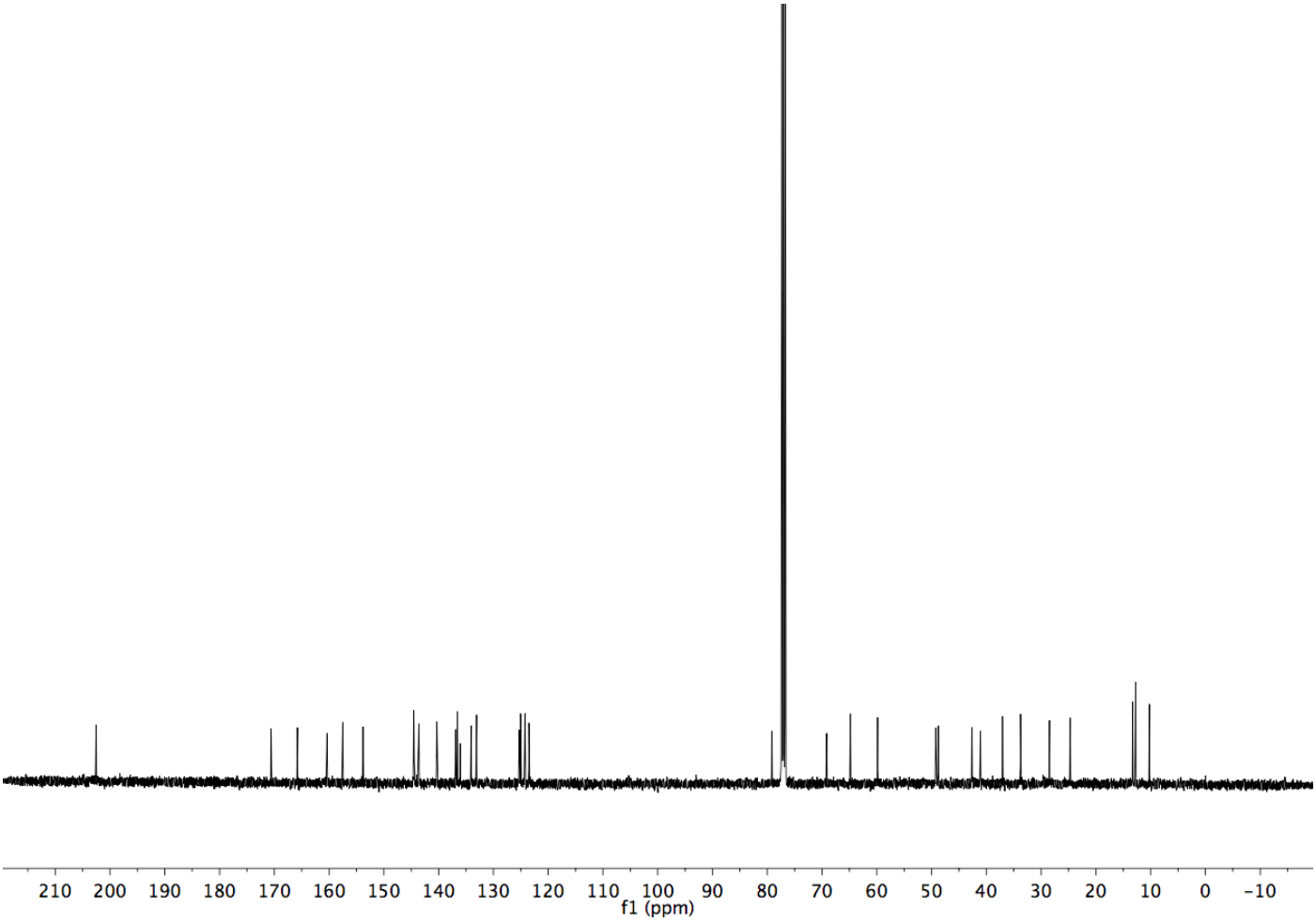

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

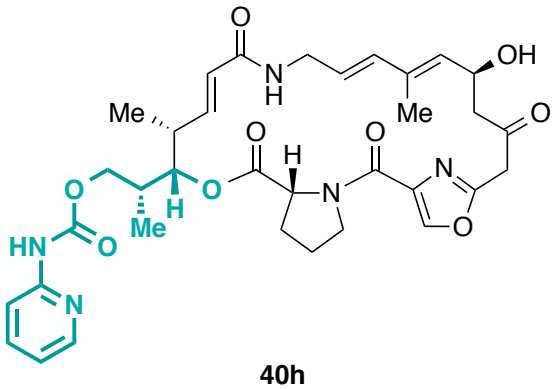

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N

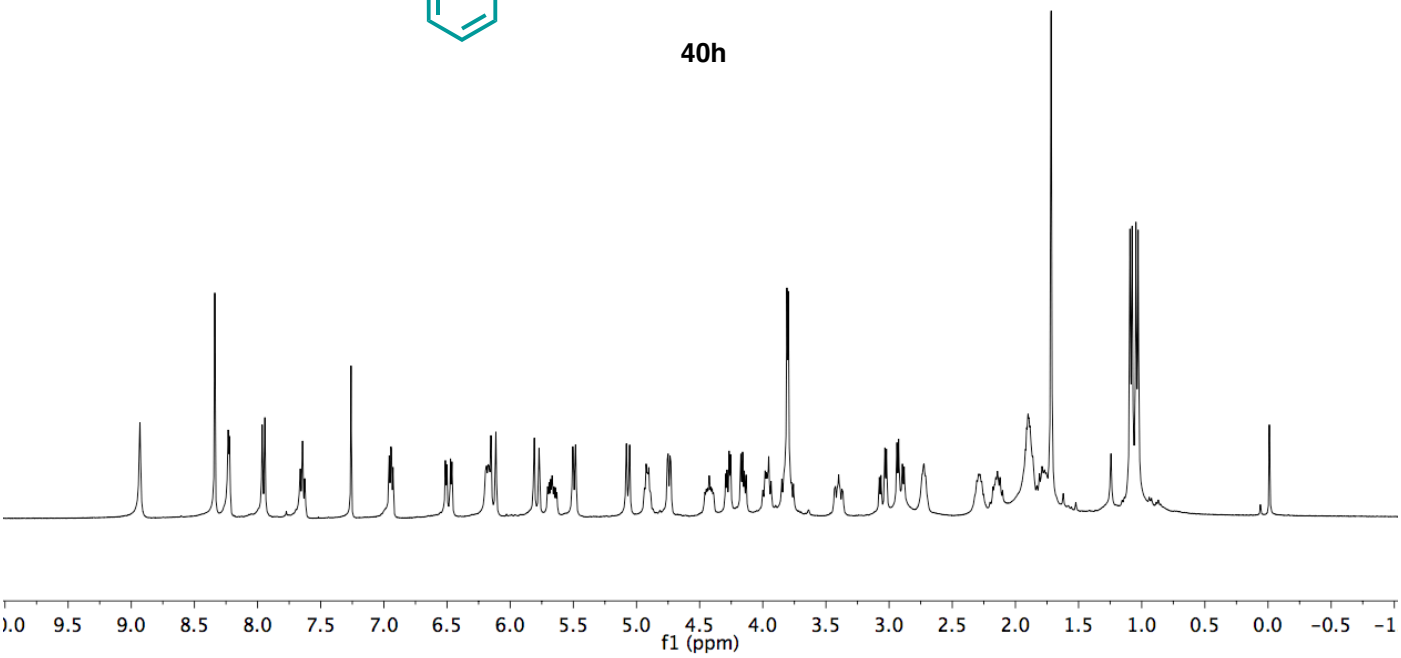
40g

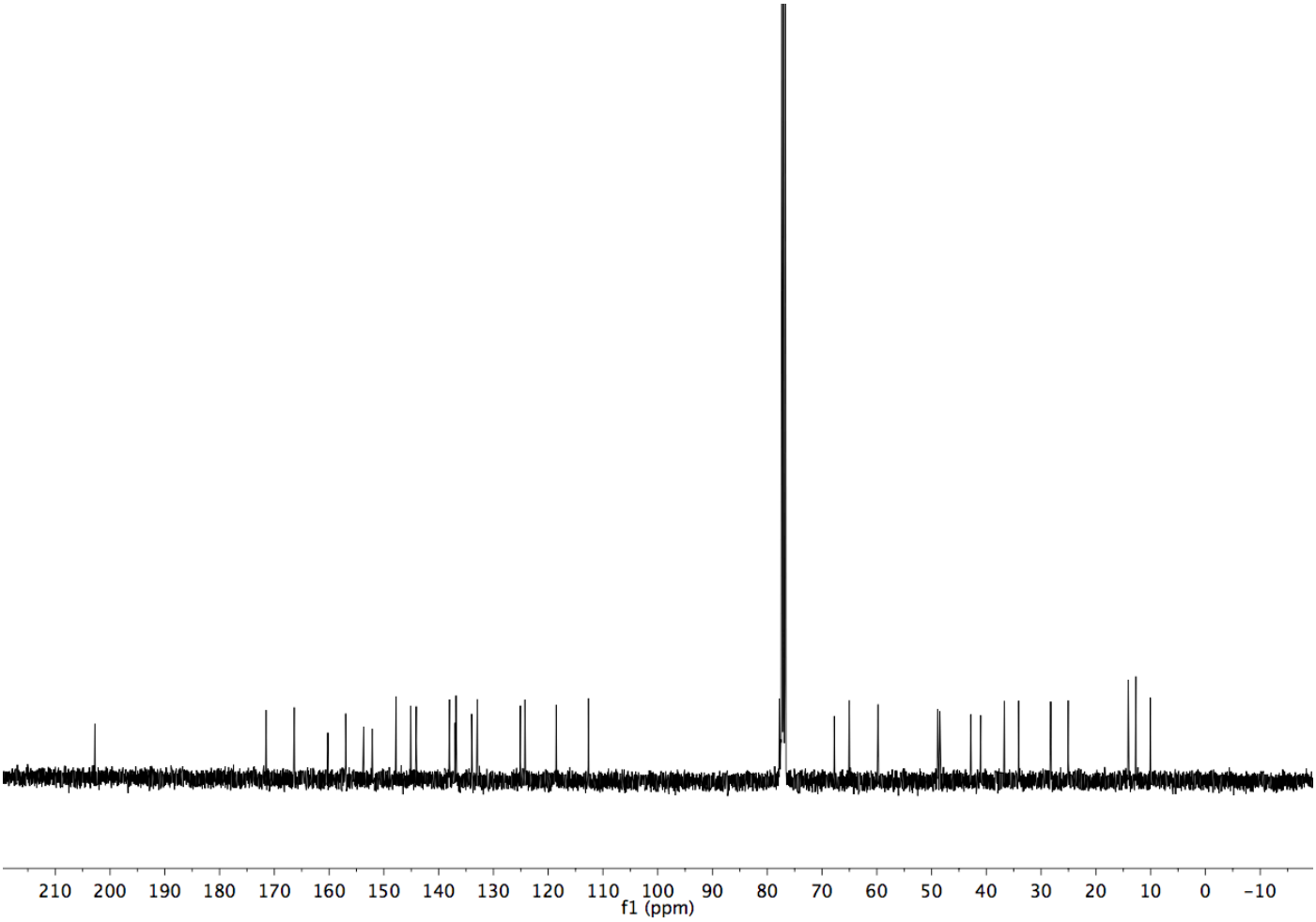

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

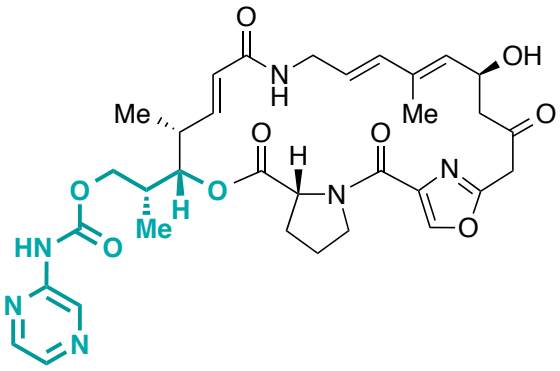

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



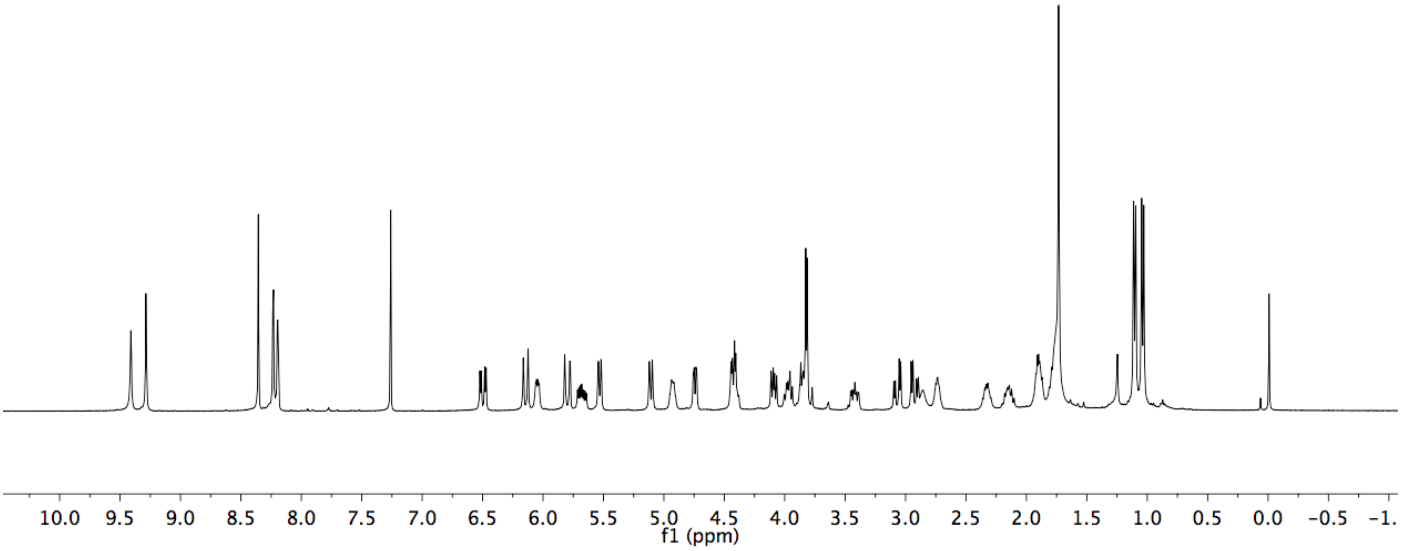
40h

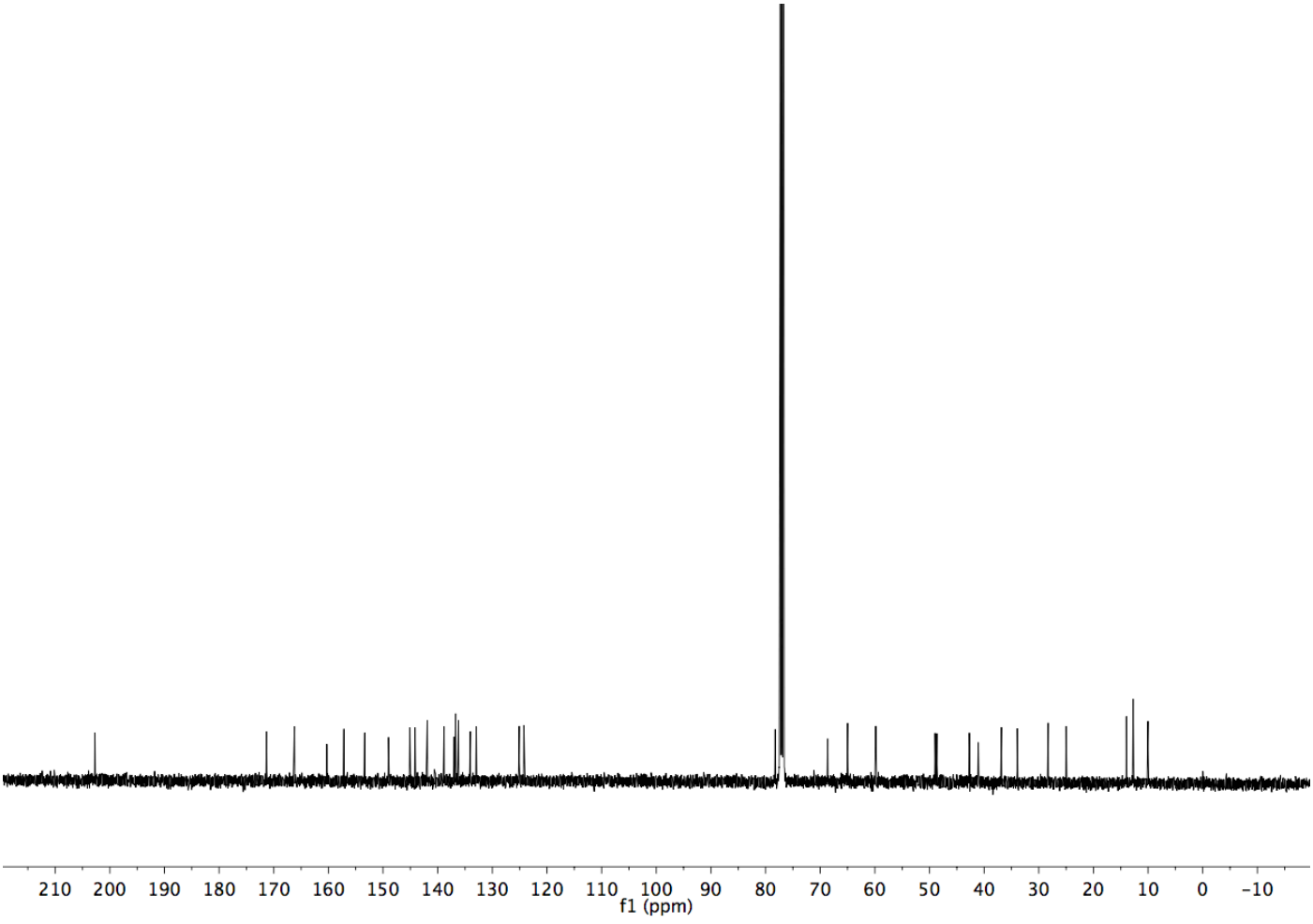

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

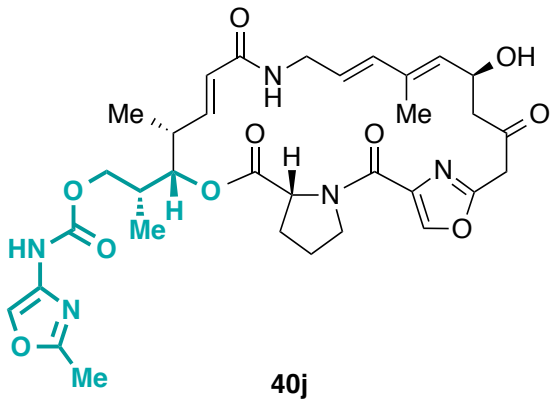

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
O
Me
H
HN
O
N
N

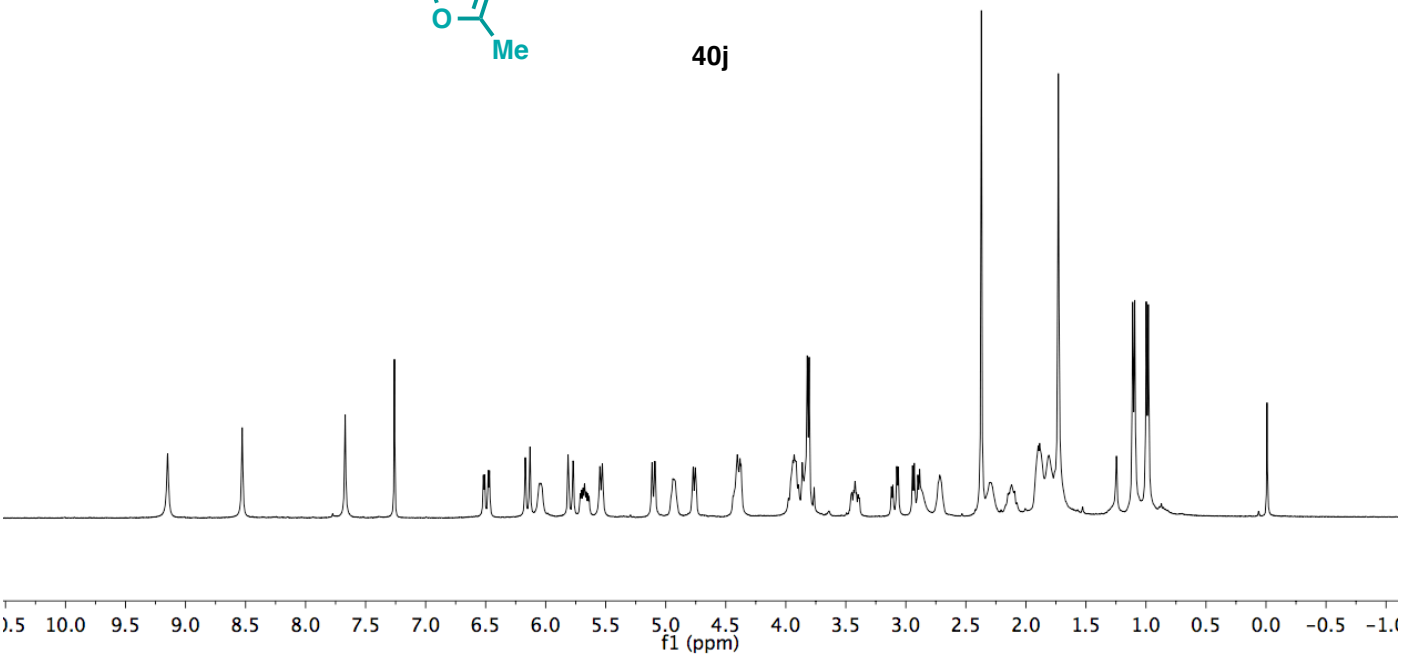
40i

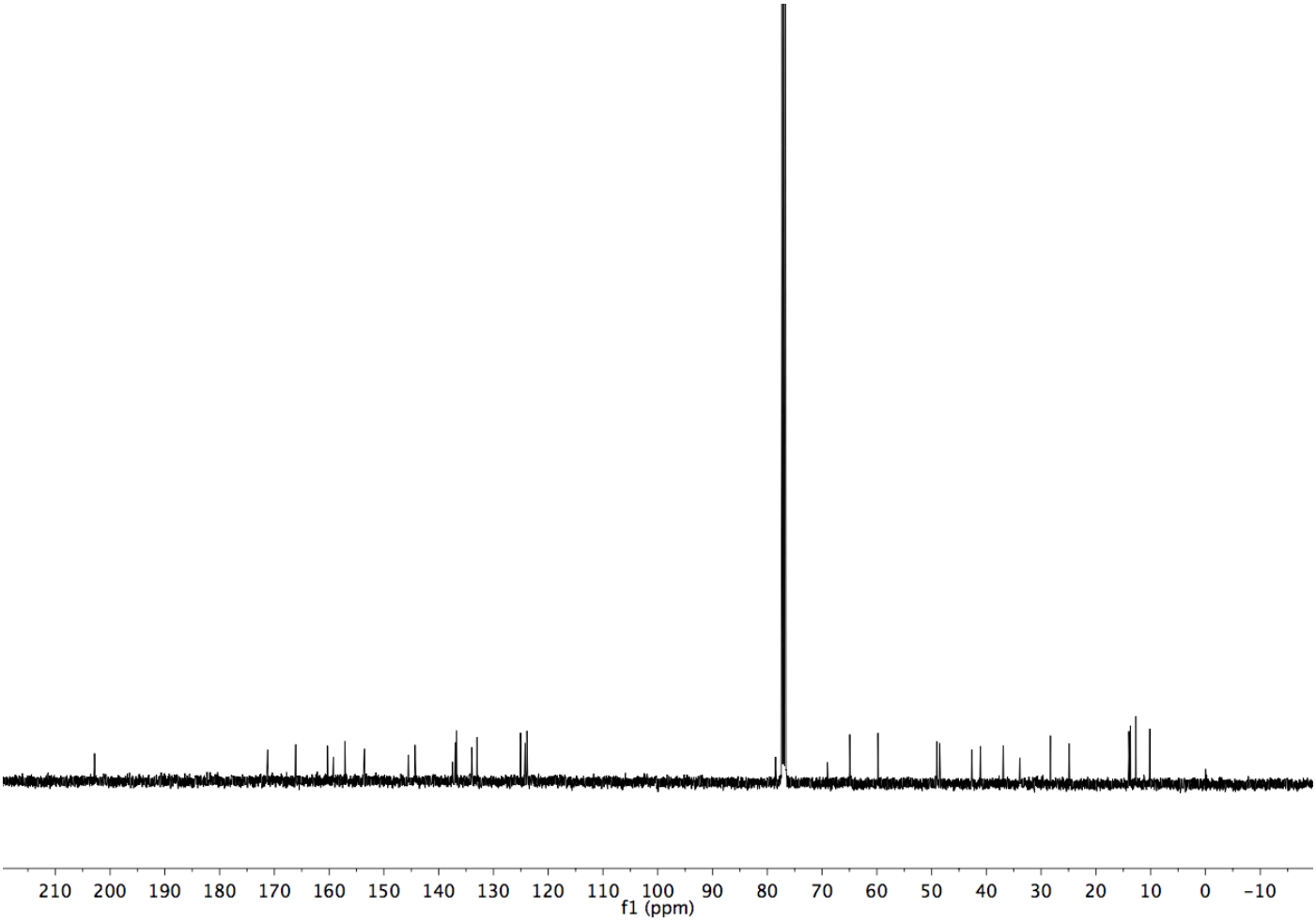

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

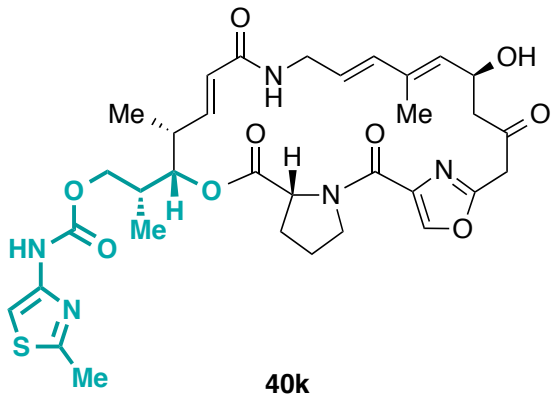

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
H
O
N
N
O
O
H
Me
O
HN
O
N
O
Me

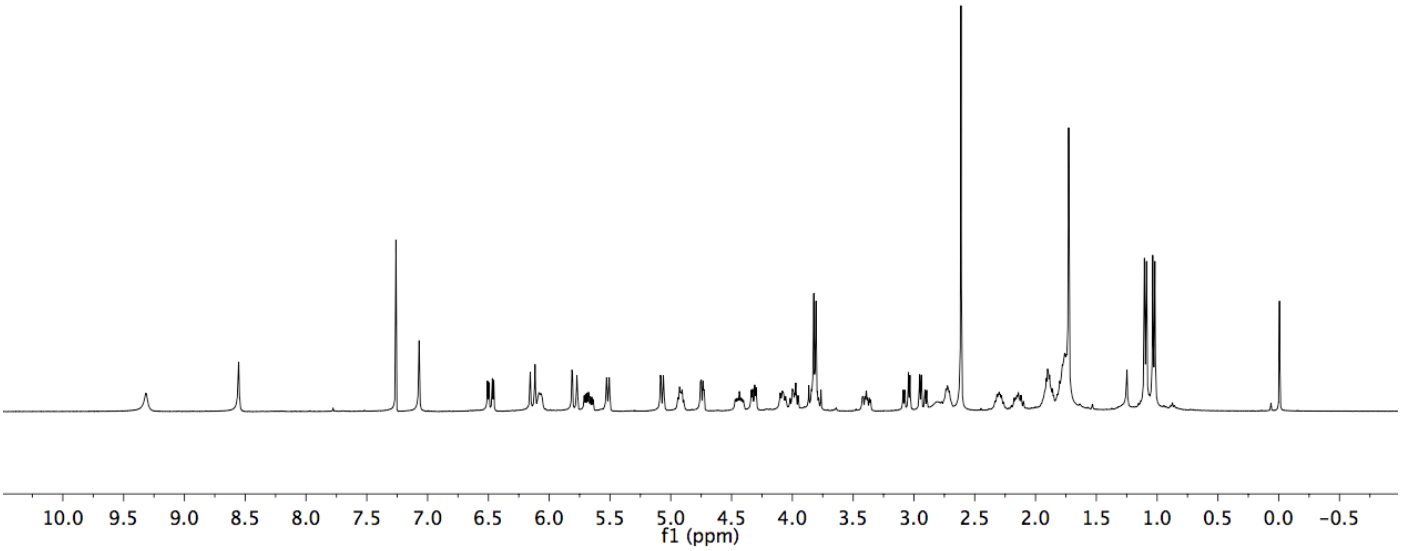
40j

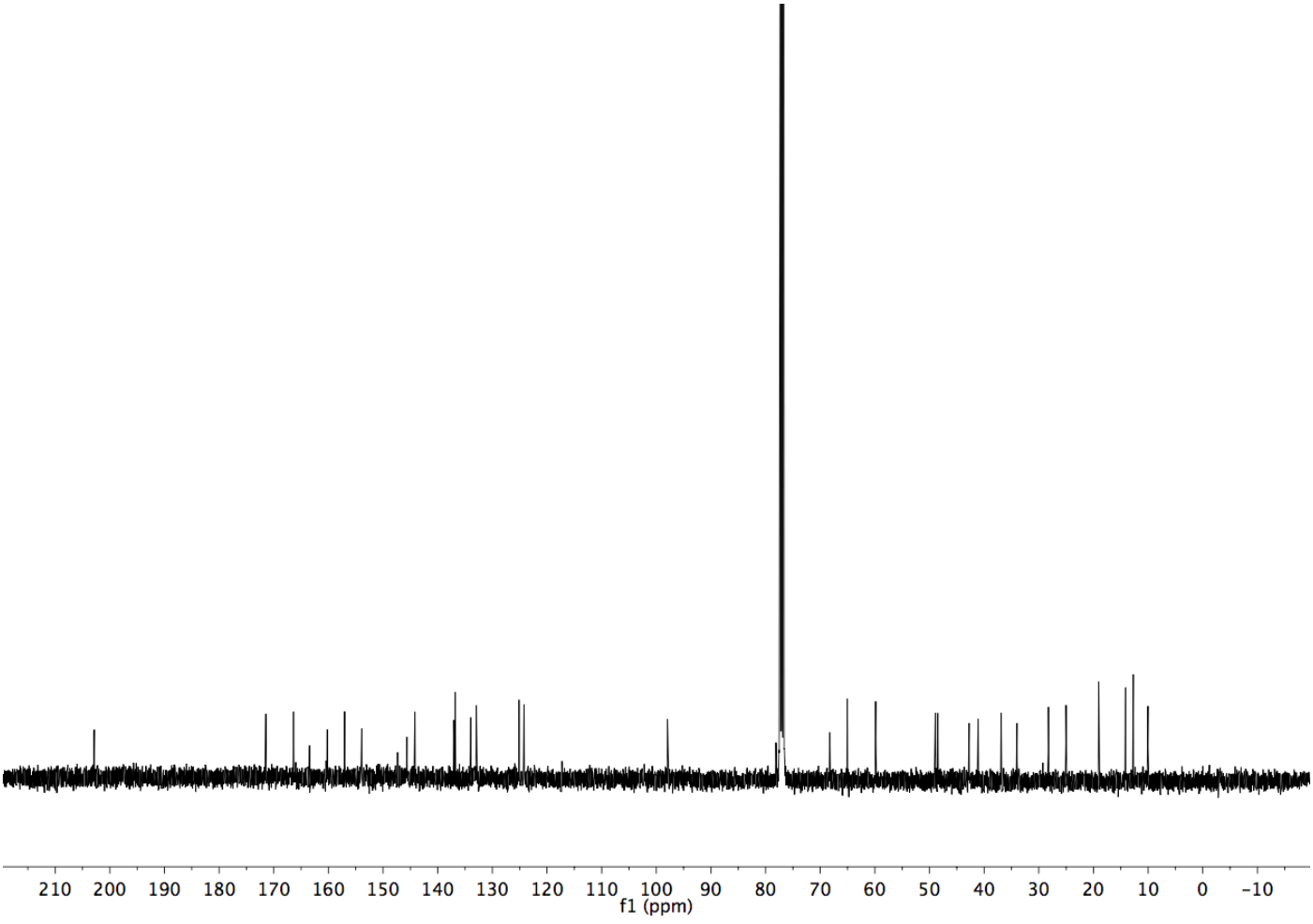

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

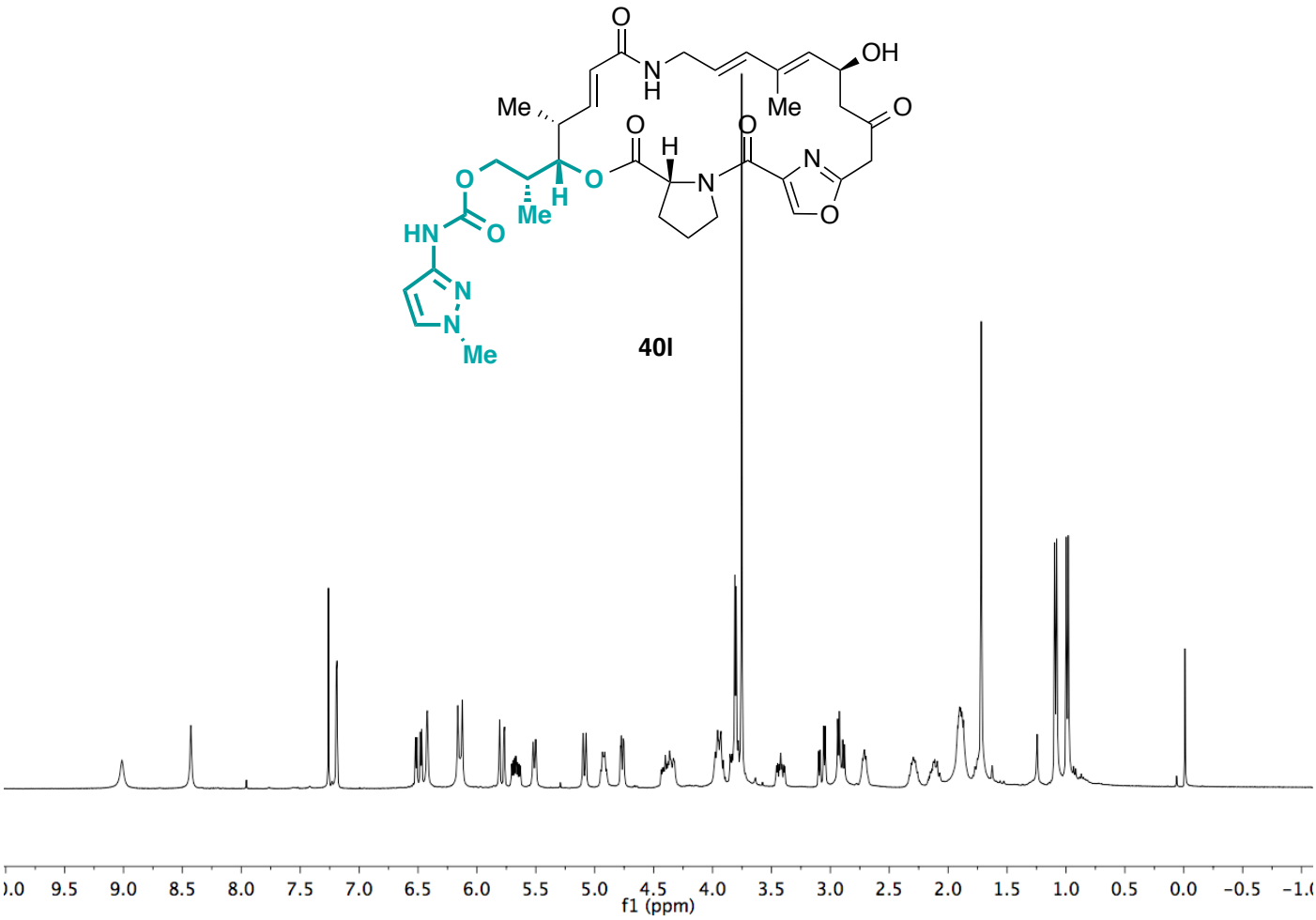

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
S
Me

40k

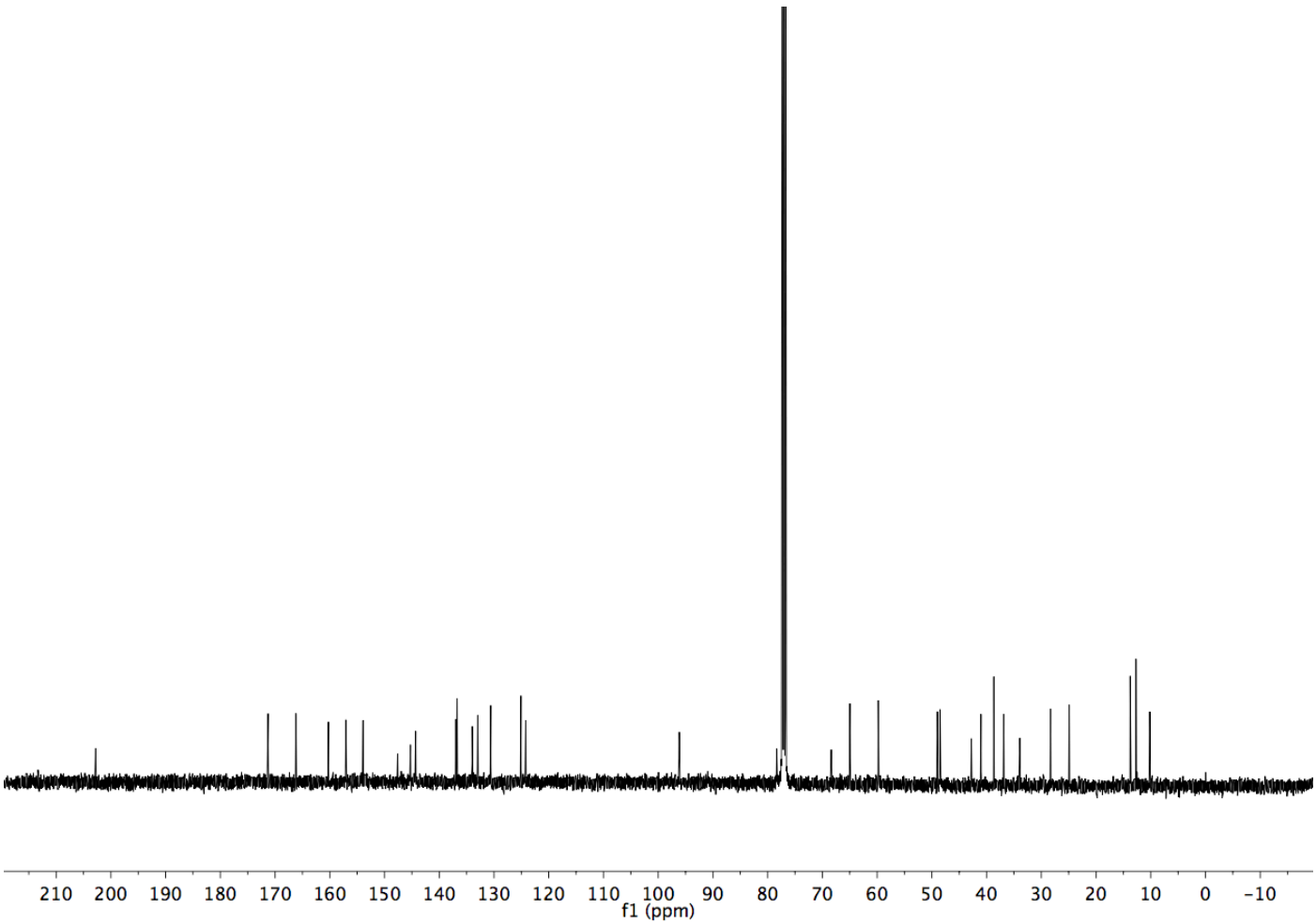

10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

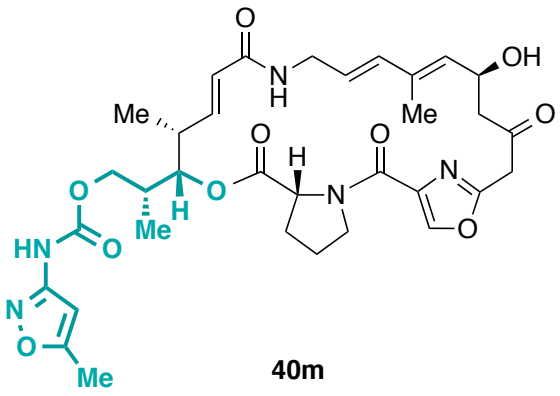

O
N
H
OH
Me
Me
O
O
H
O
N
N
O
O
O
H
Me
HN
O
N
N
Me

40l

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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N
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OH
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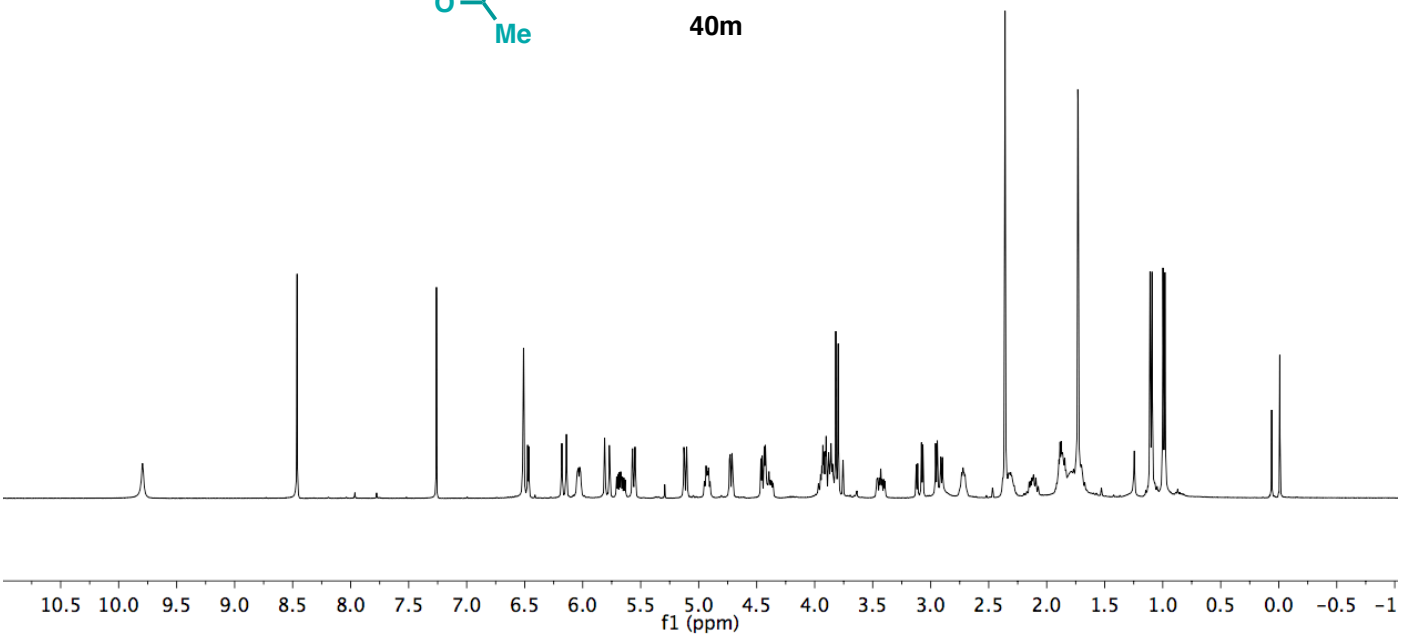
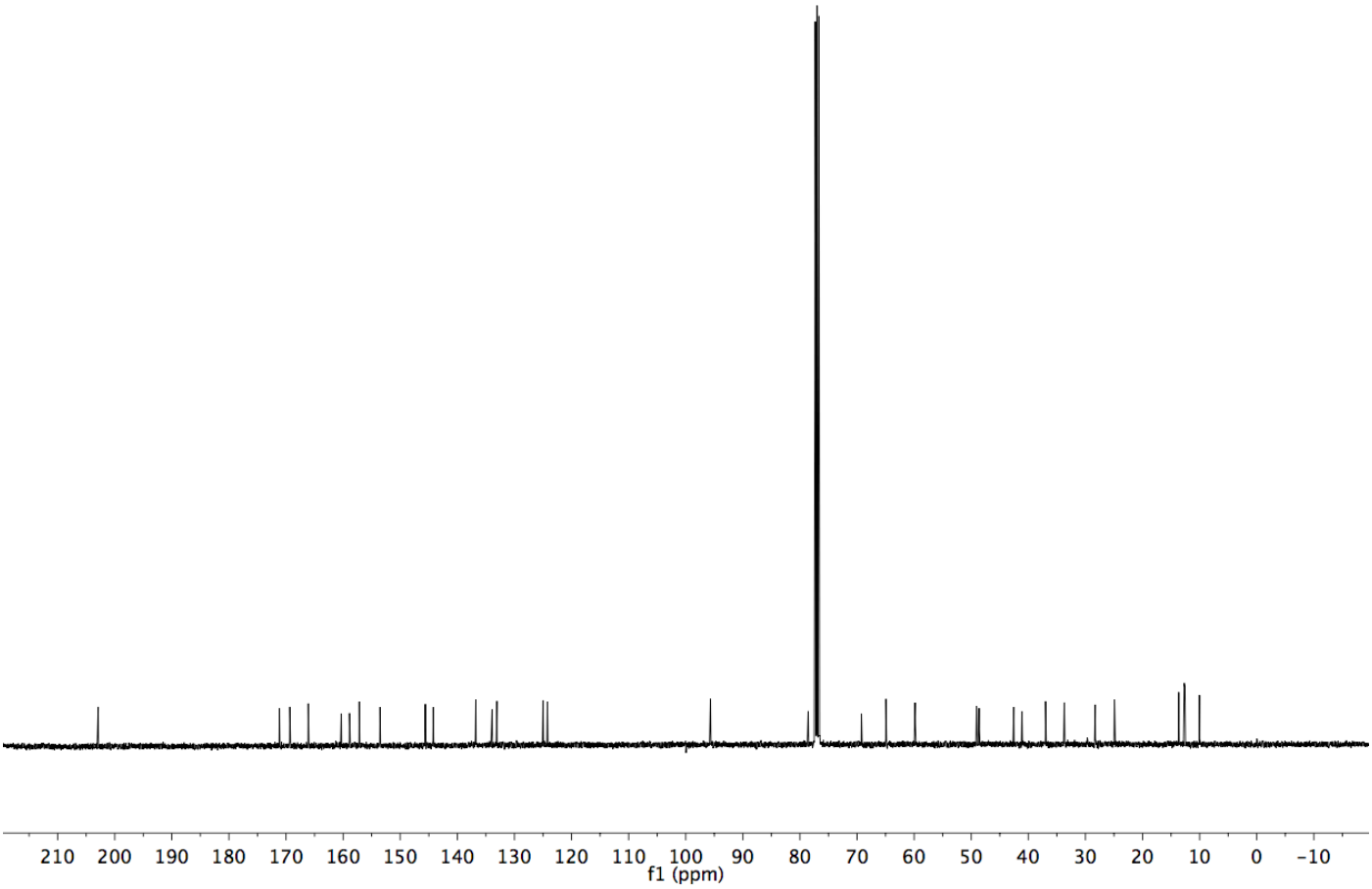
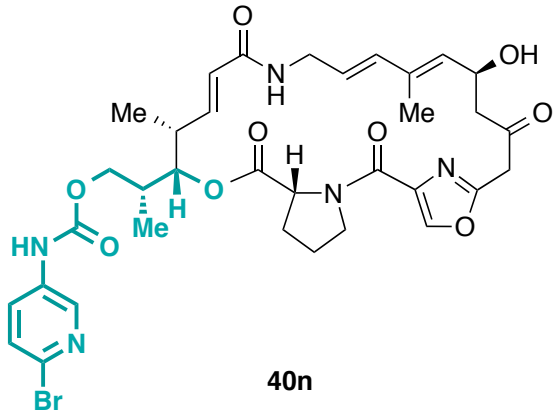
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
O
Me

40m


10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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N
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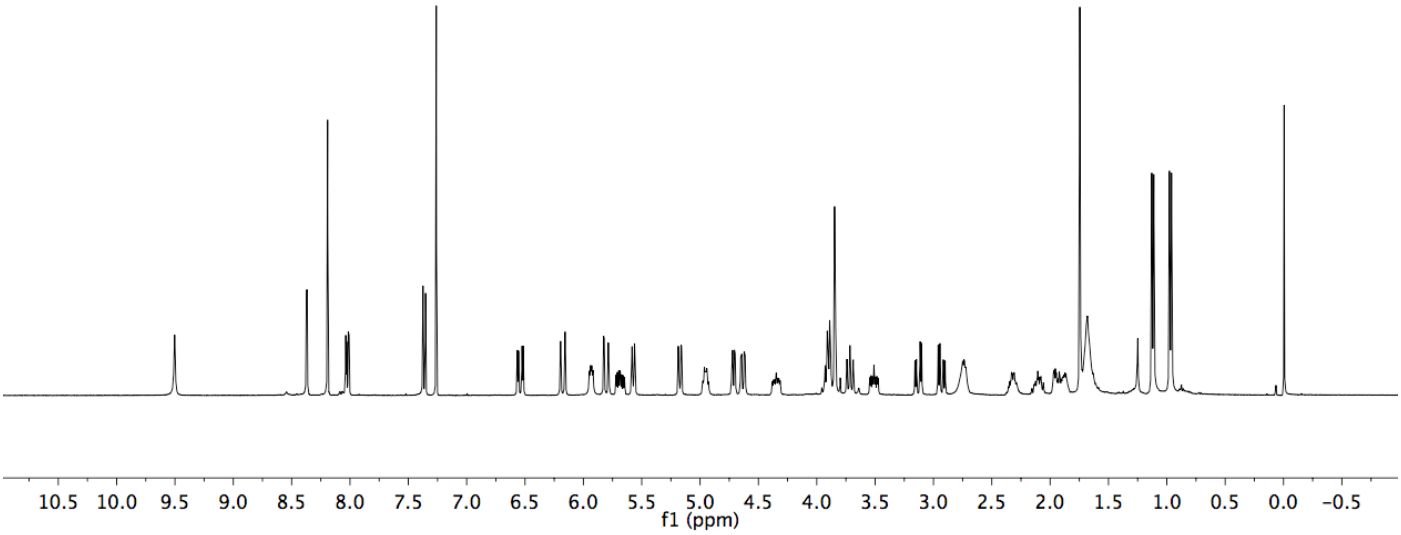
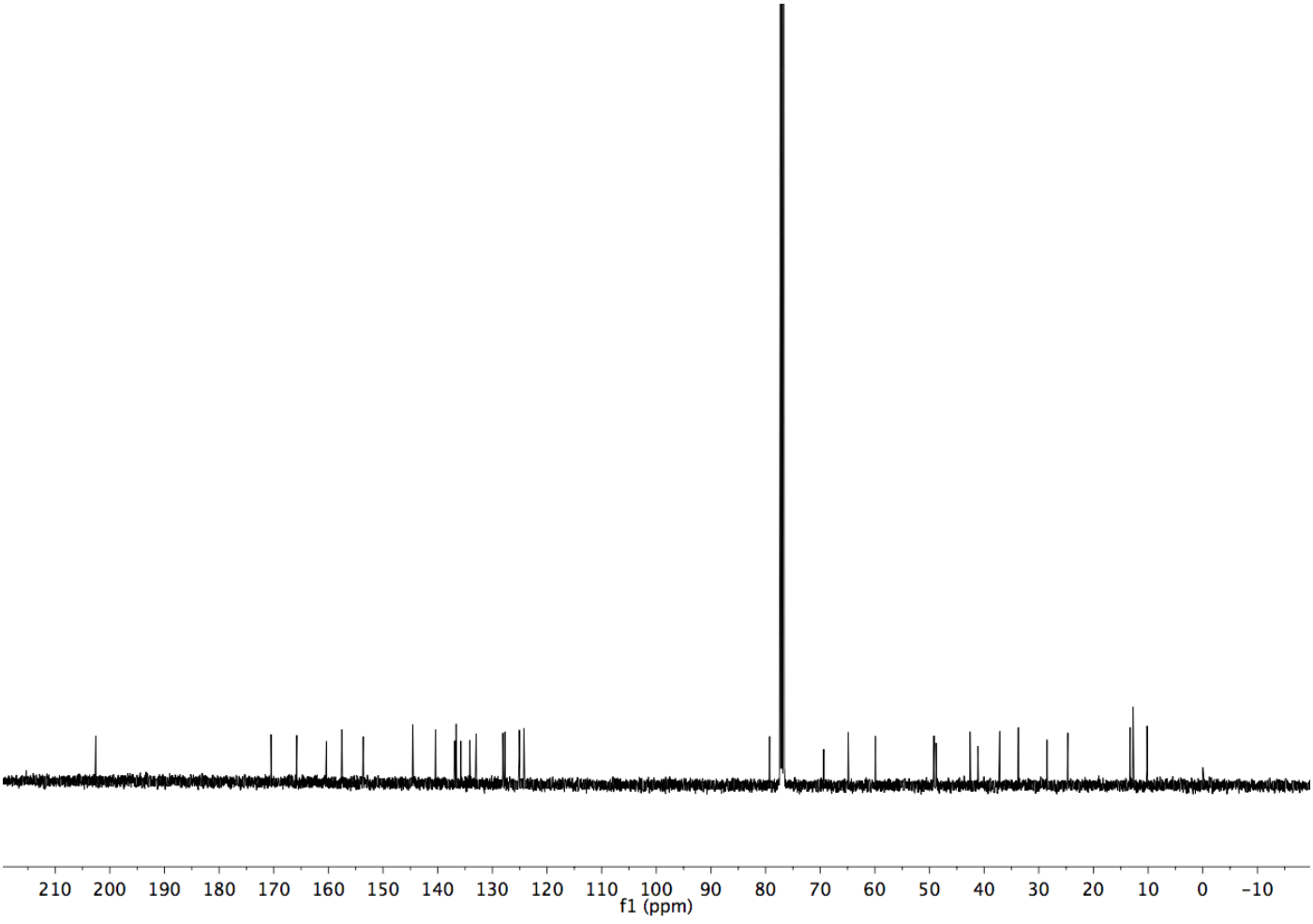
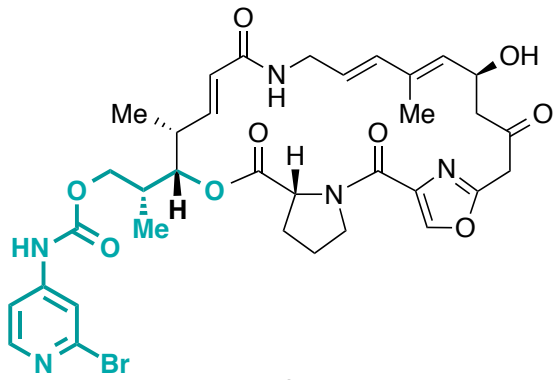
OH
Me
Me
O
O
H
O
N
N
O
O
H
Me
O
HN
O
N
Br

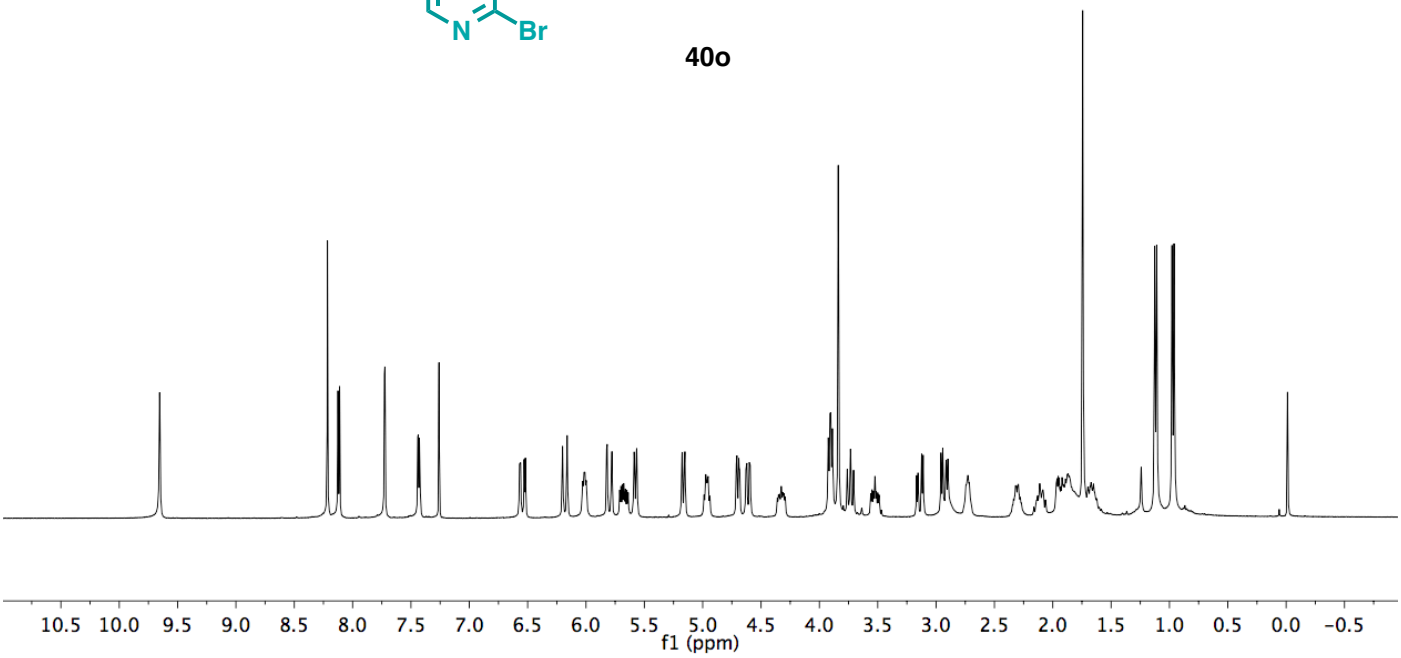
40n

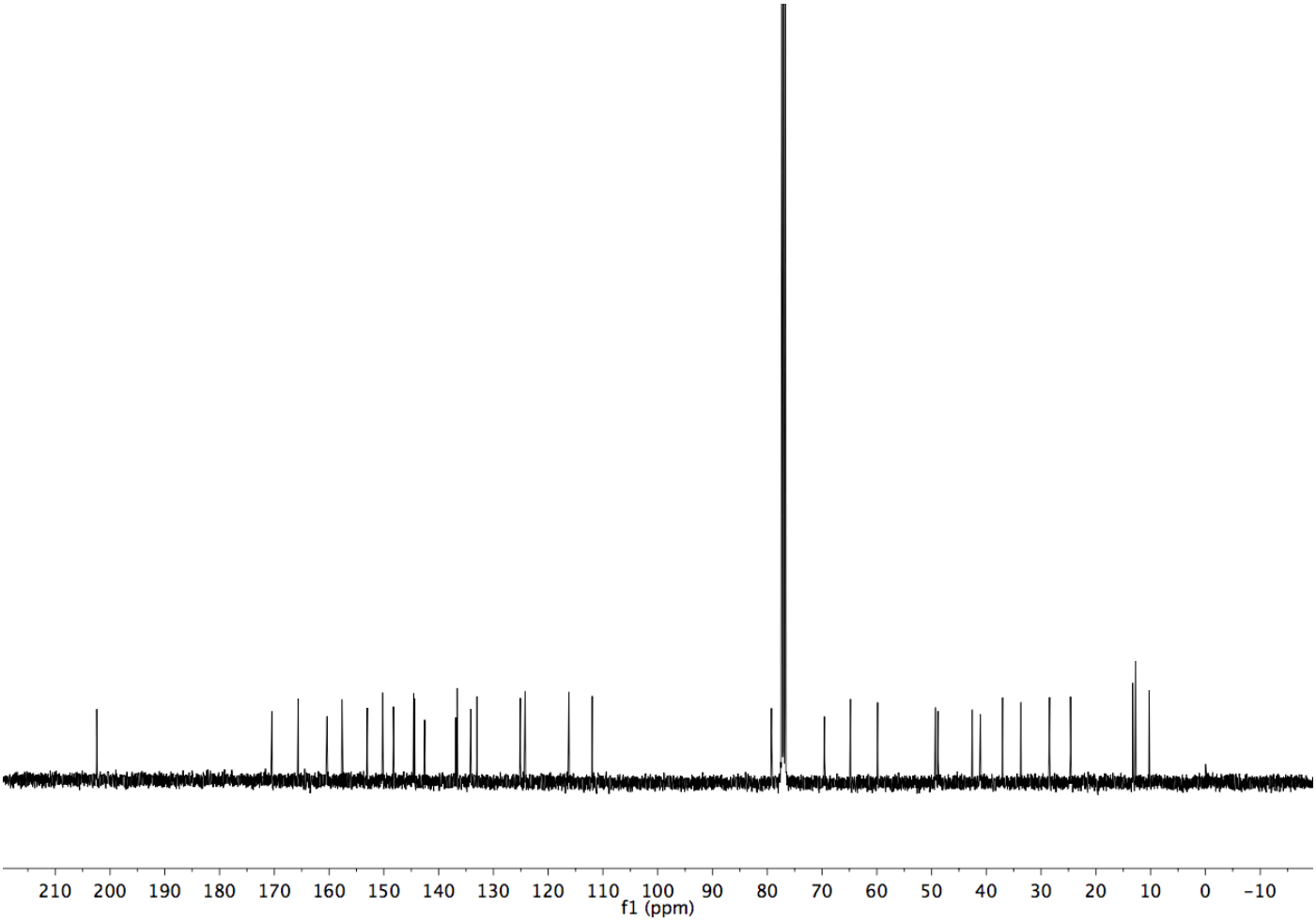

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

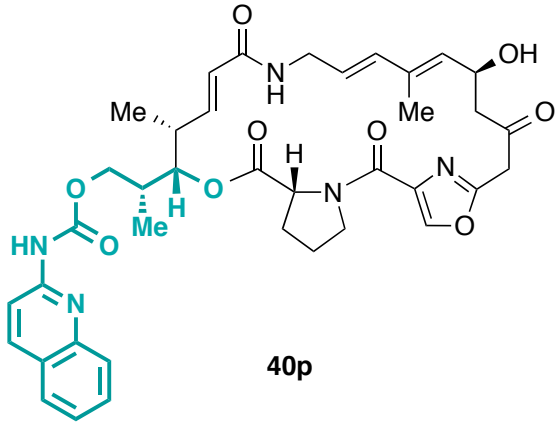

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
Br

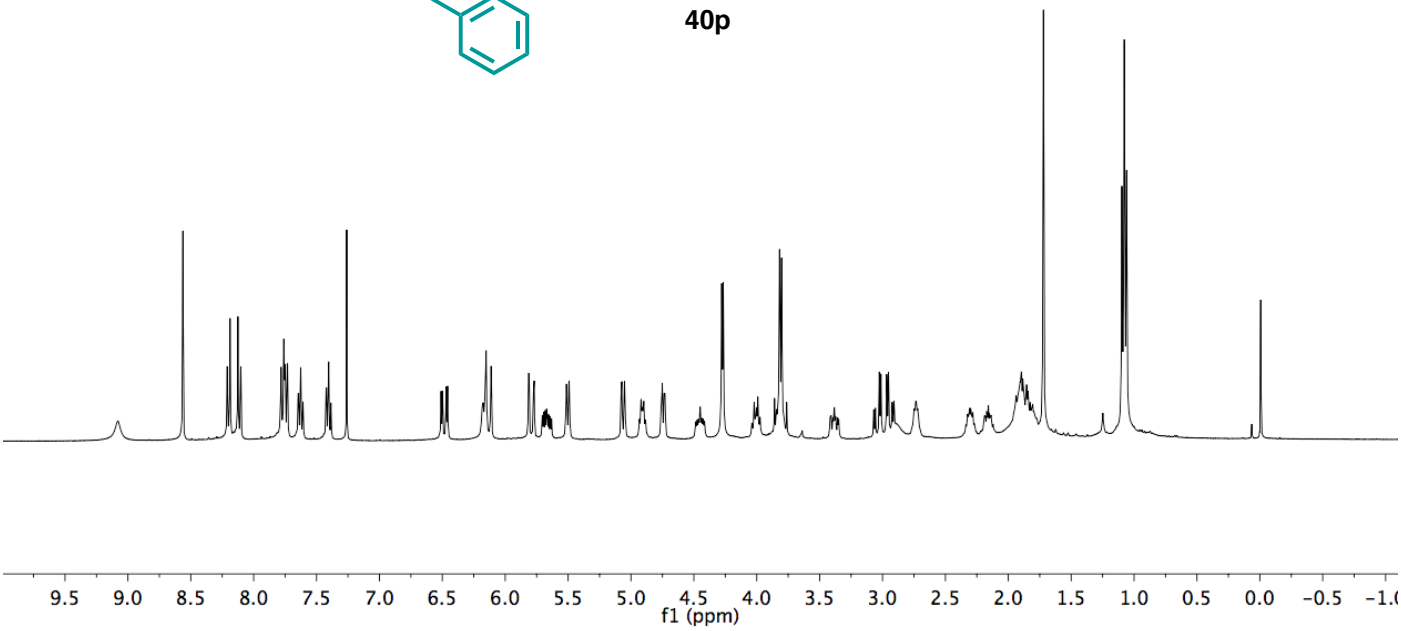
40o

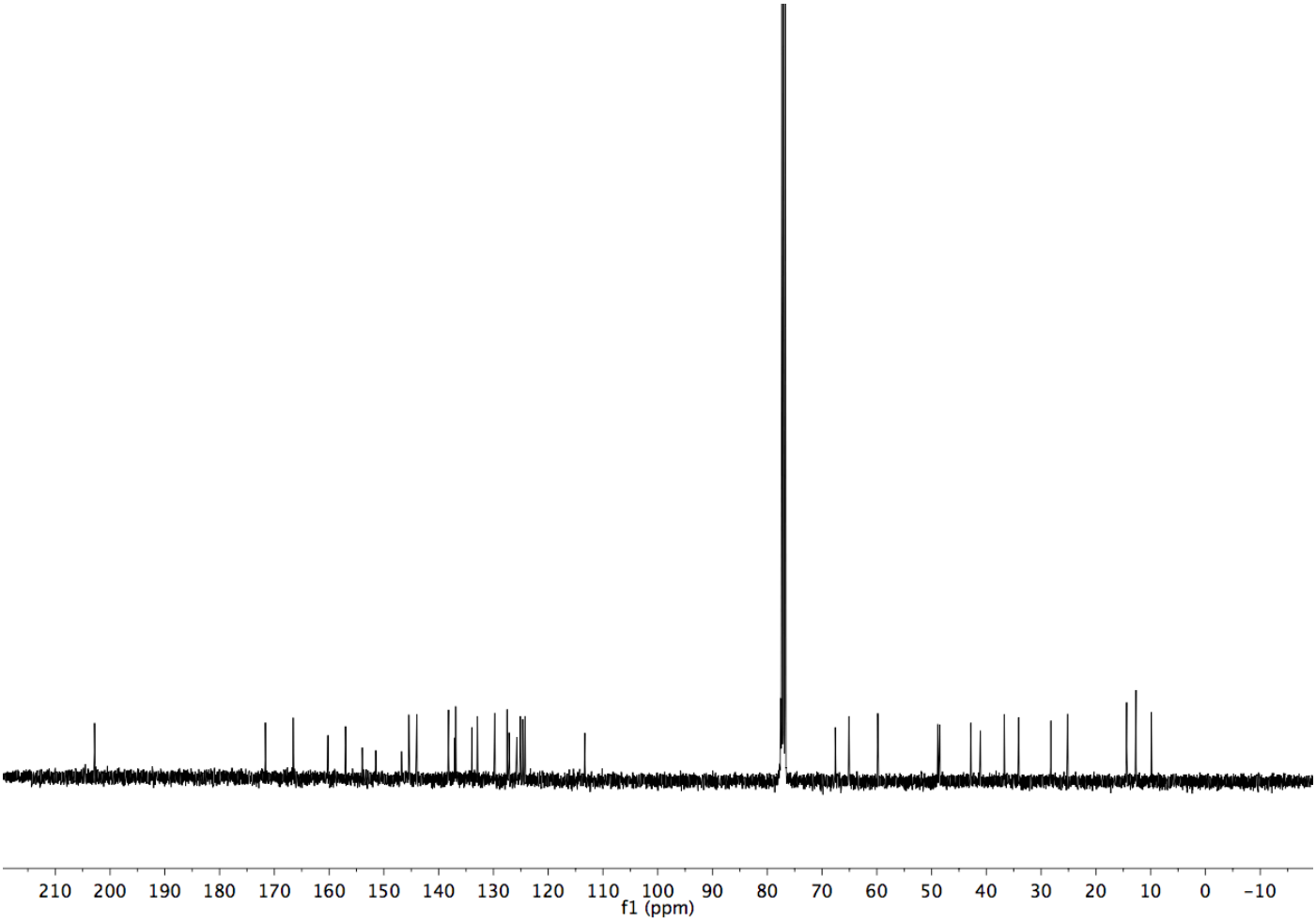

10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

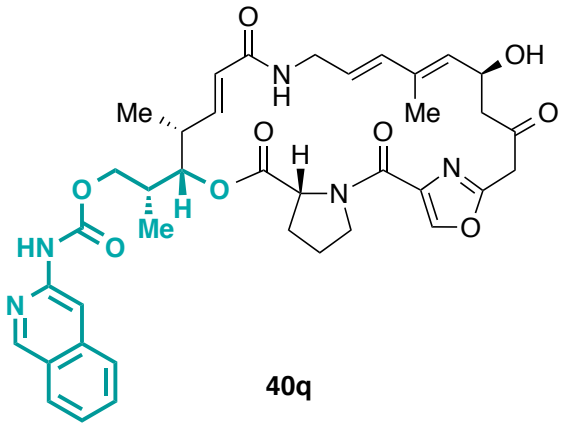

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



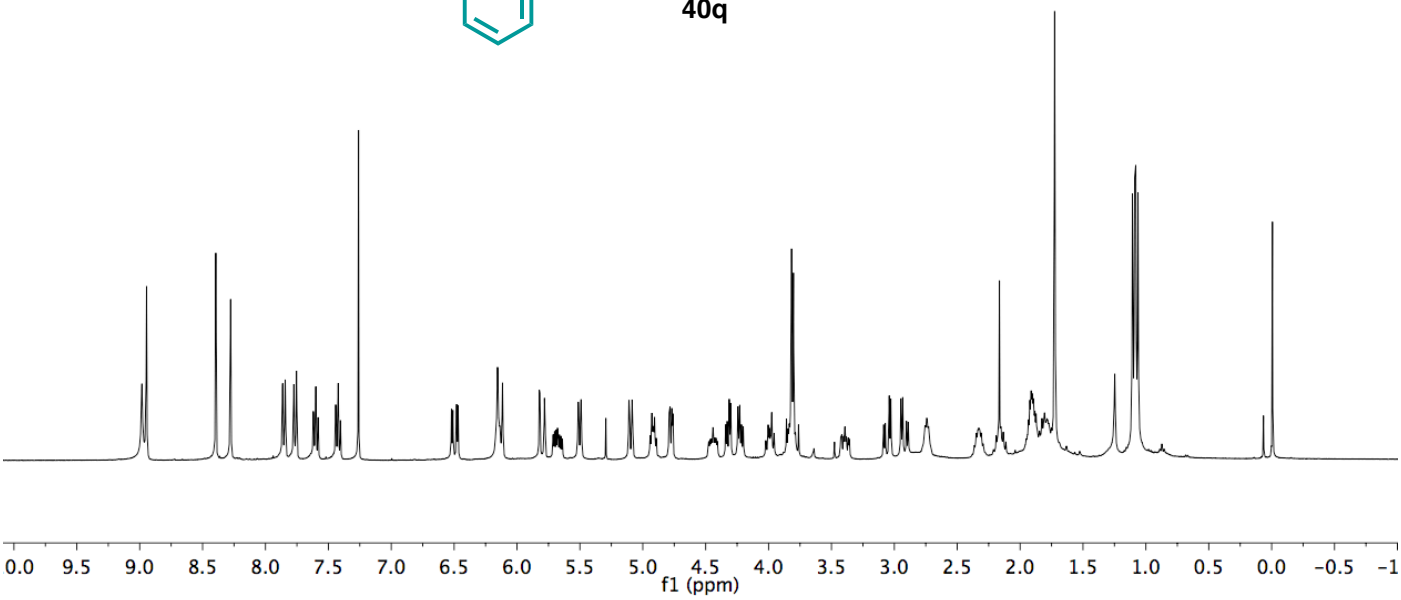
40p

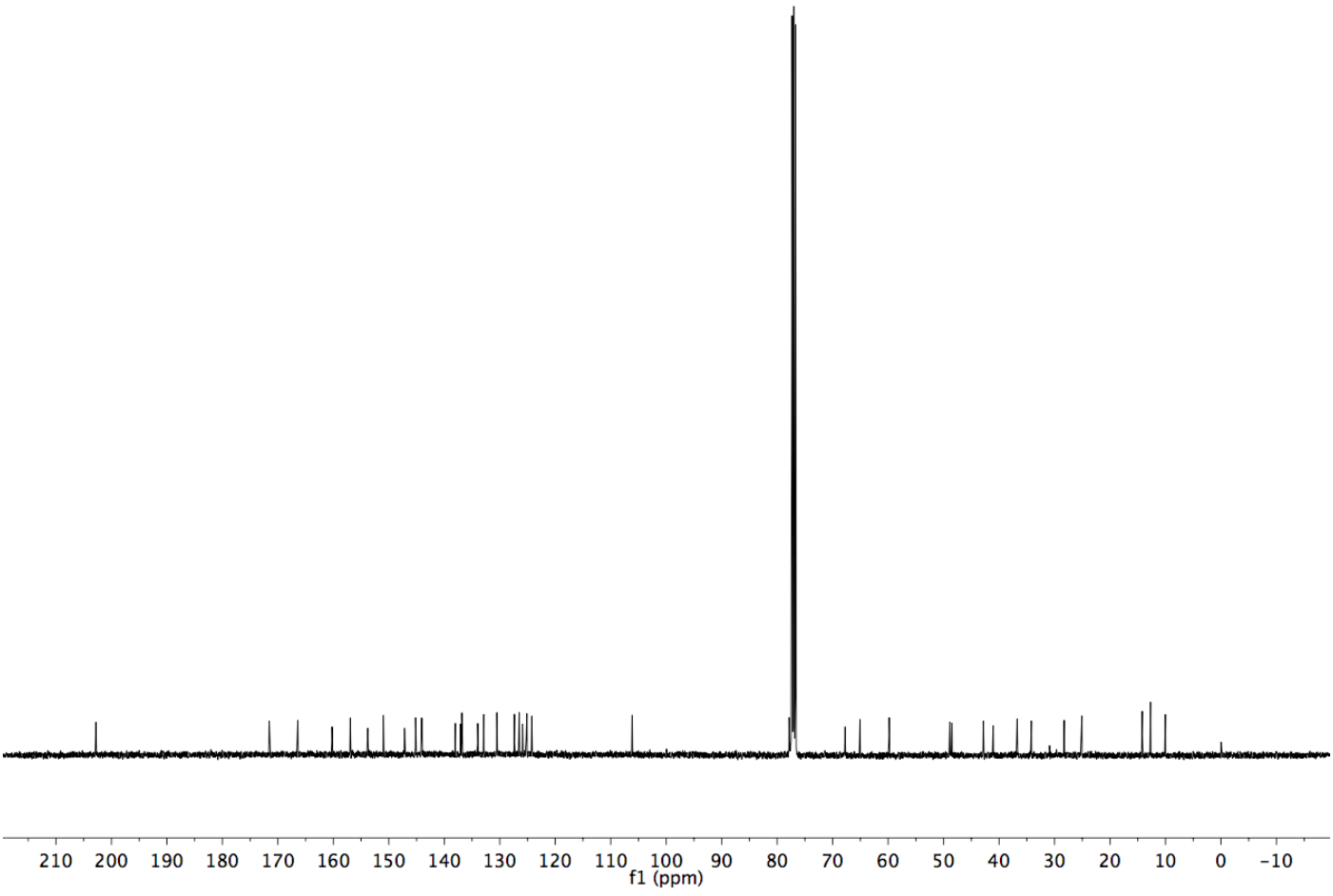

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

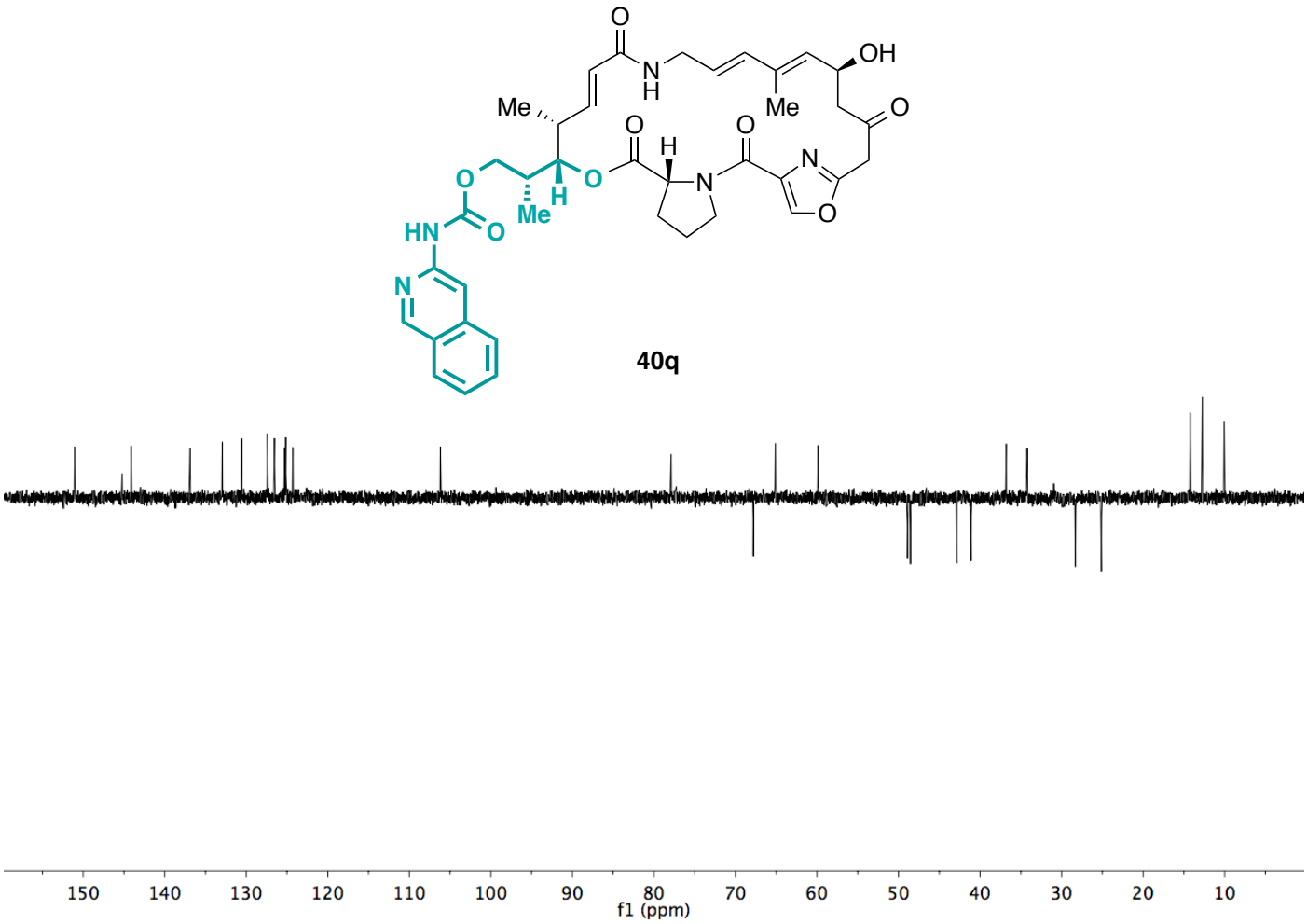

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
H
O
O
N
N
O
O
H
Me
HN
O
N

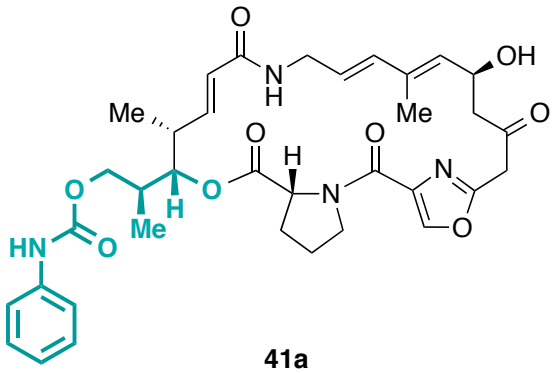
40q


0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

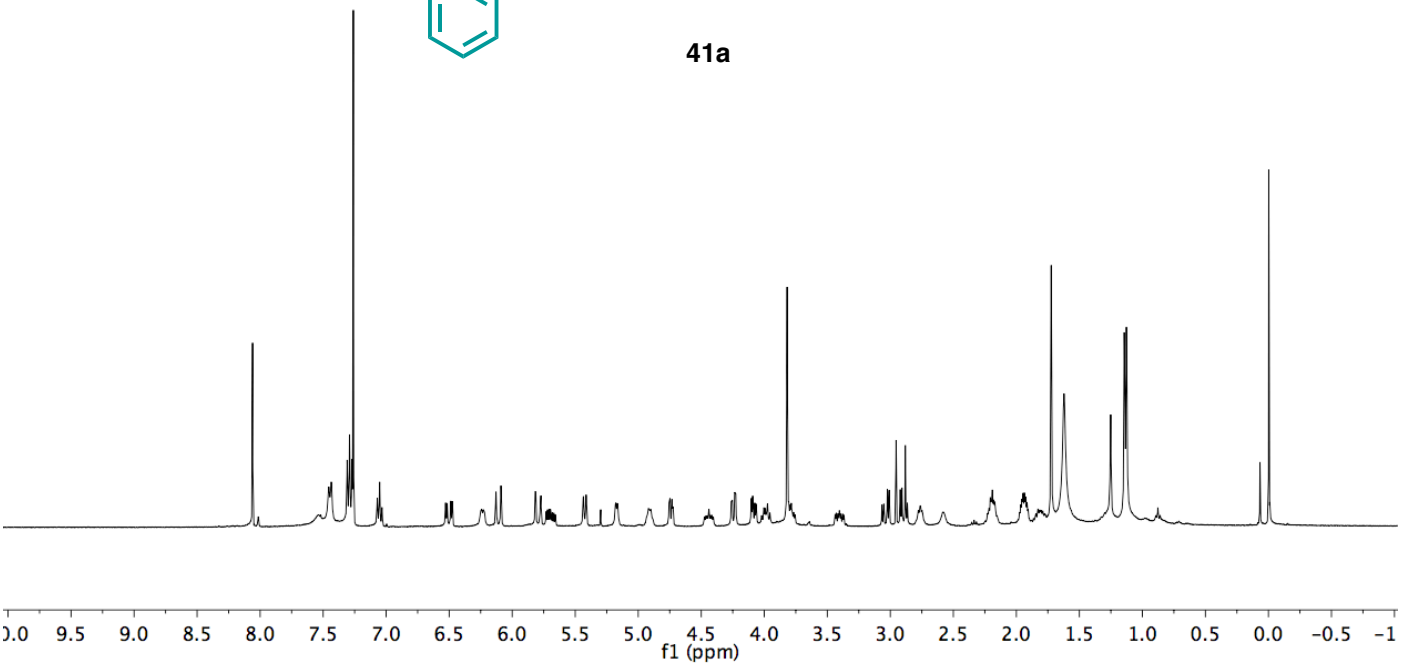

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

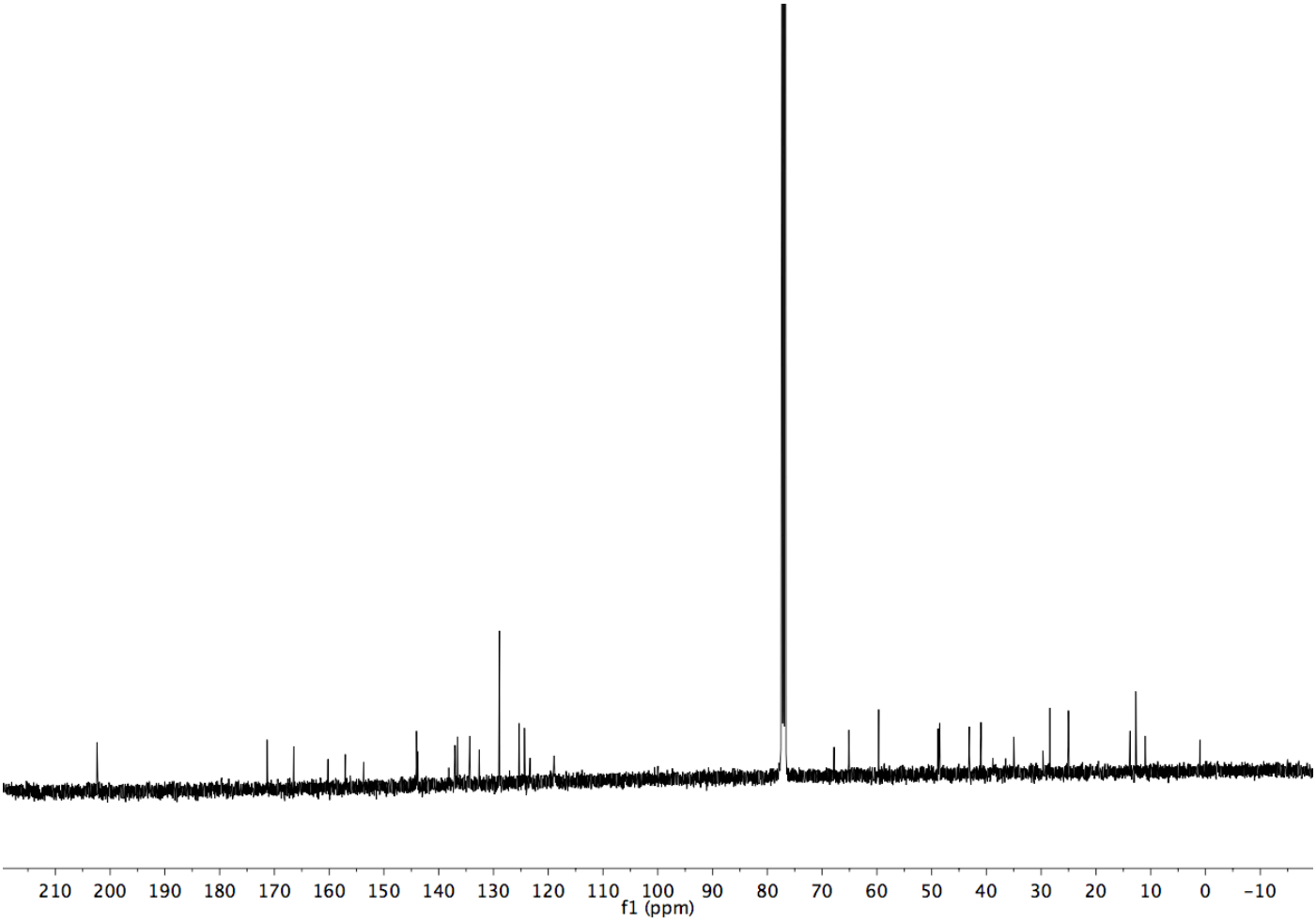

O
N
H
OH
Me
Me
O
O
O
H
O
N
O
Me
H
O
HN
O
N
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

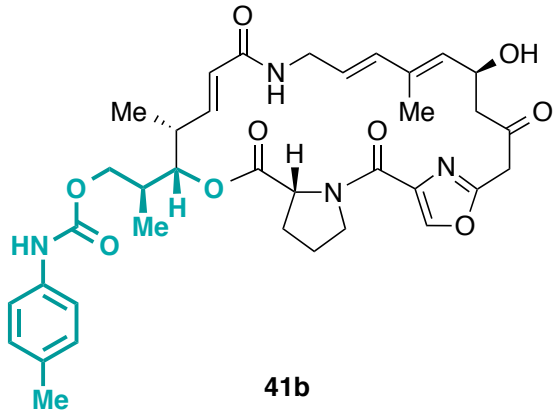
40q



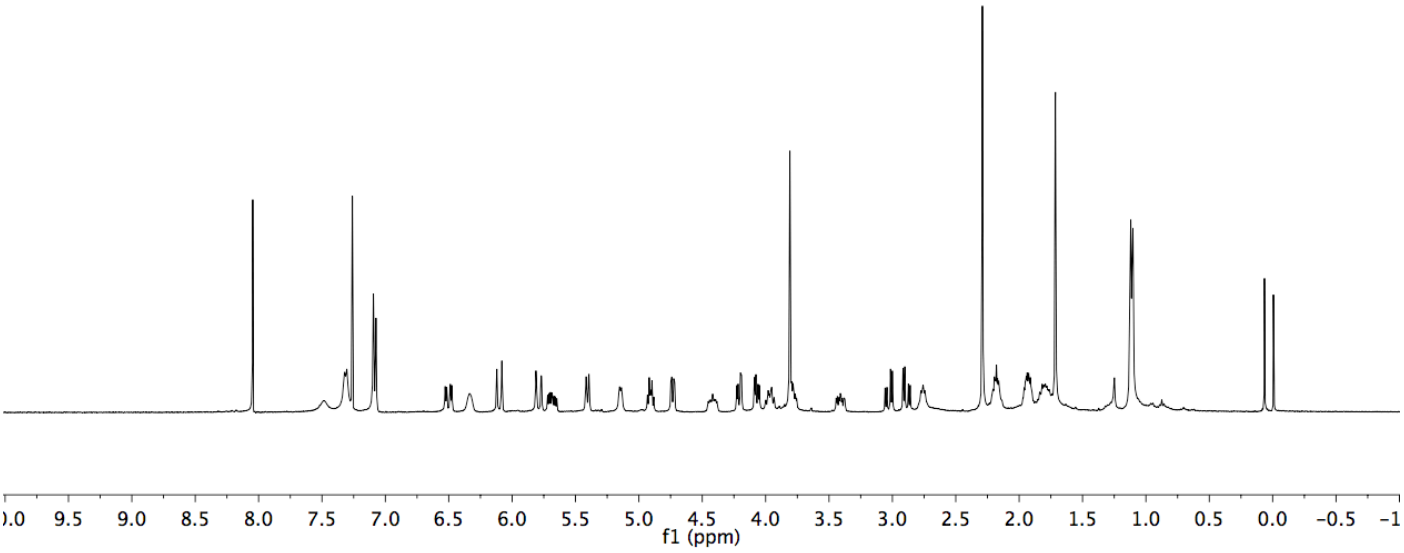
41a

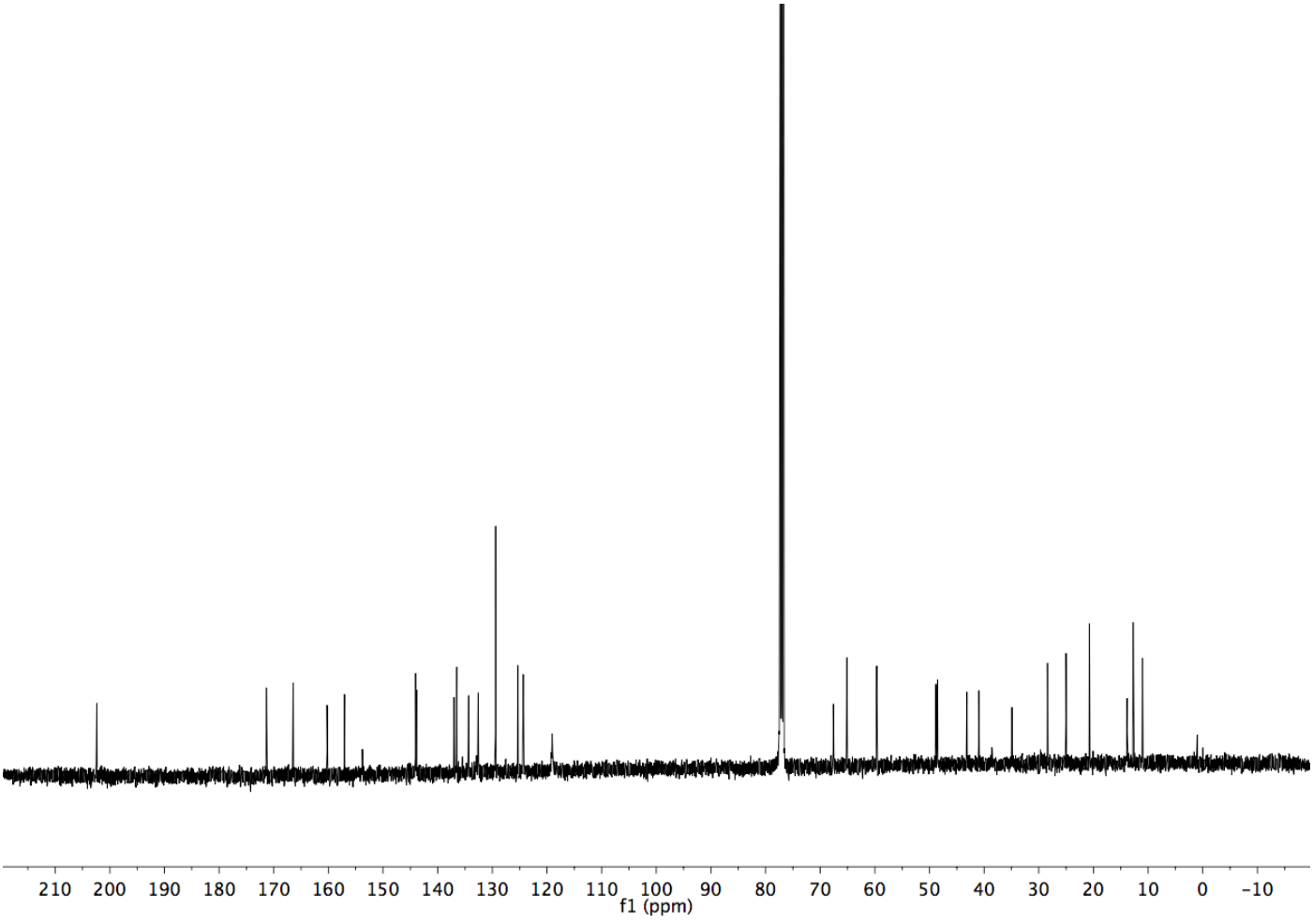

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

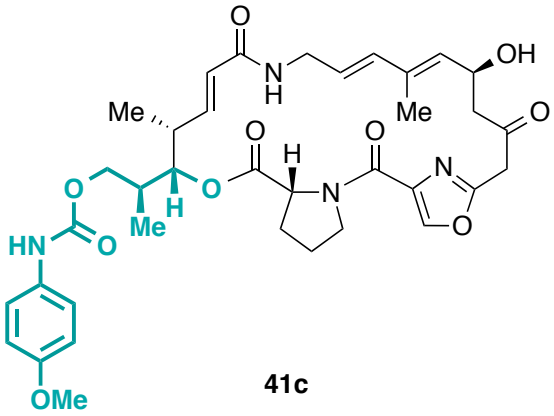

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
Me

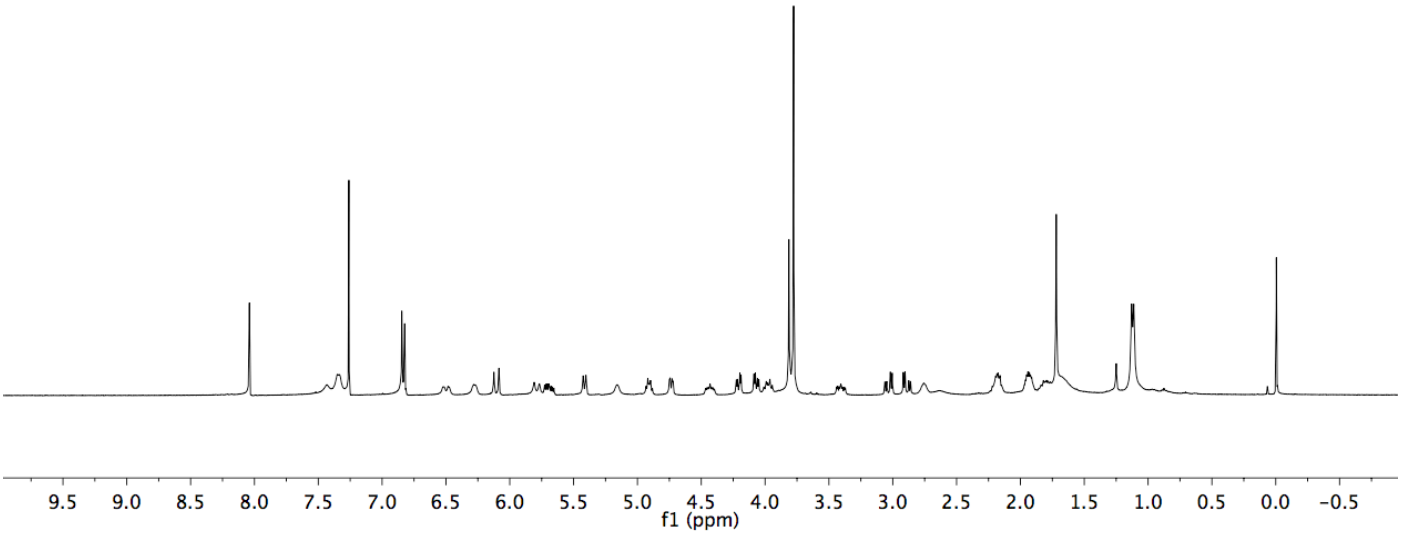
41b

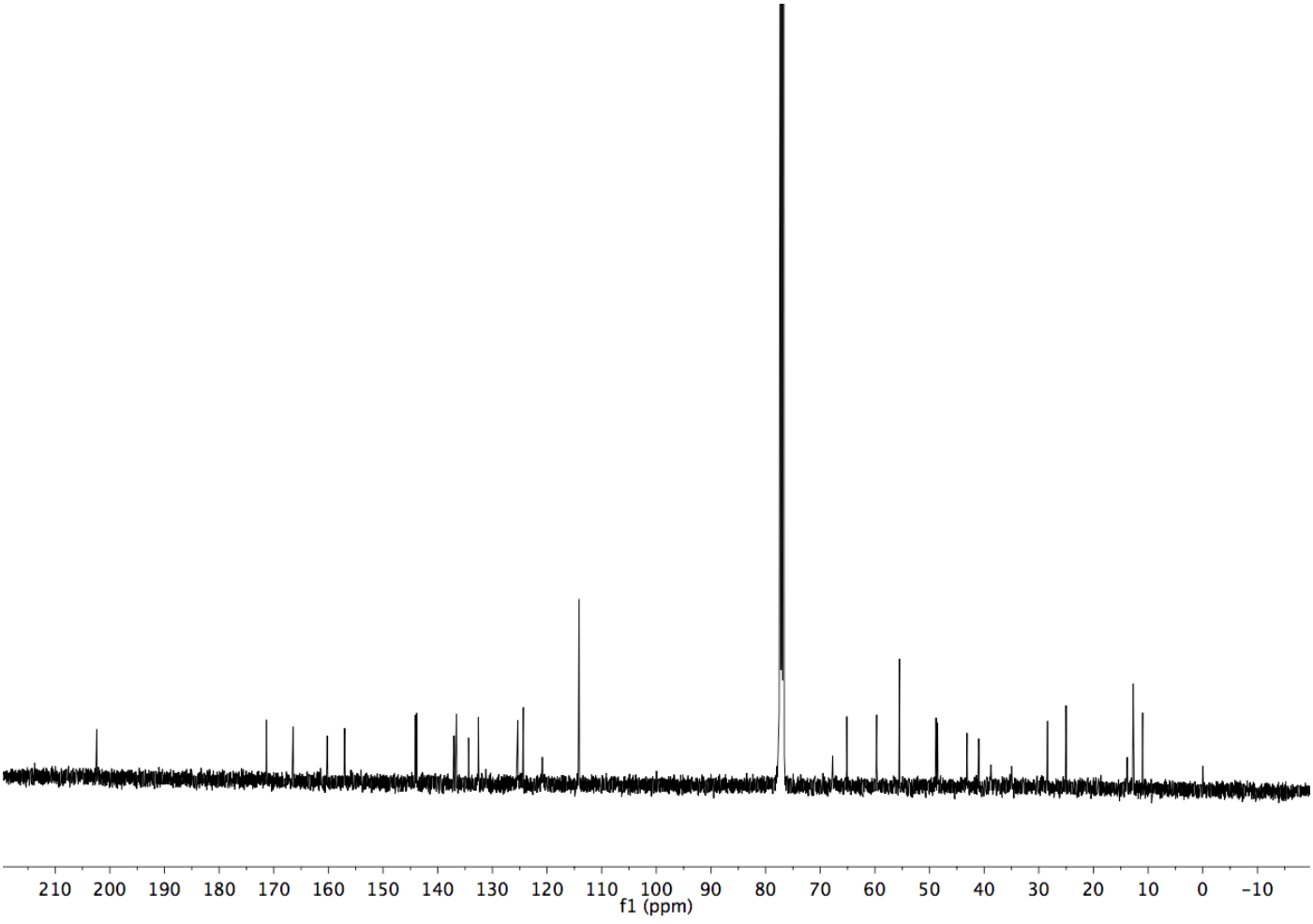

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

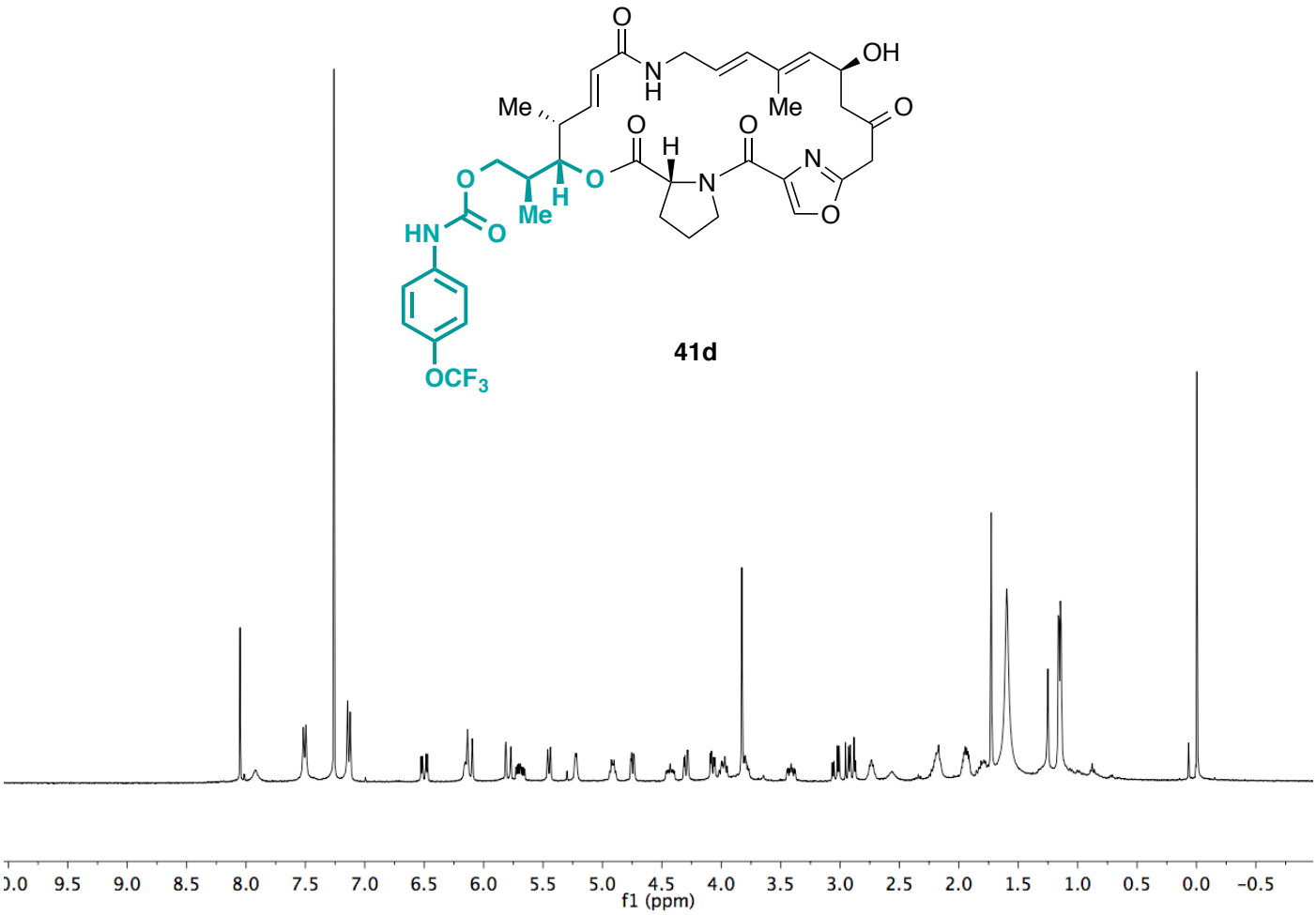

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
OMe

41c

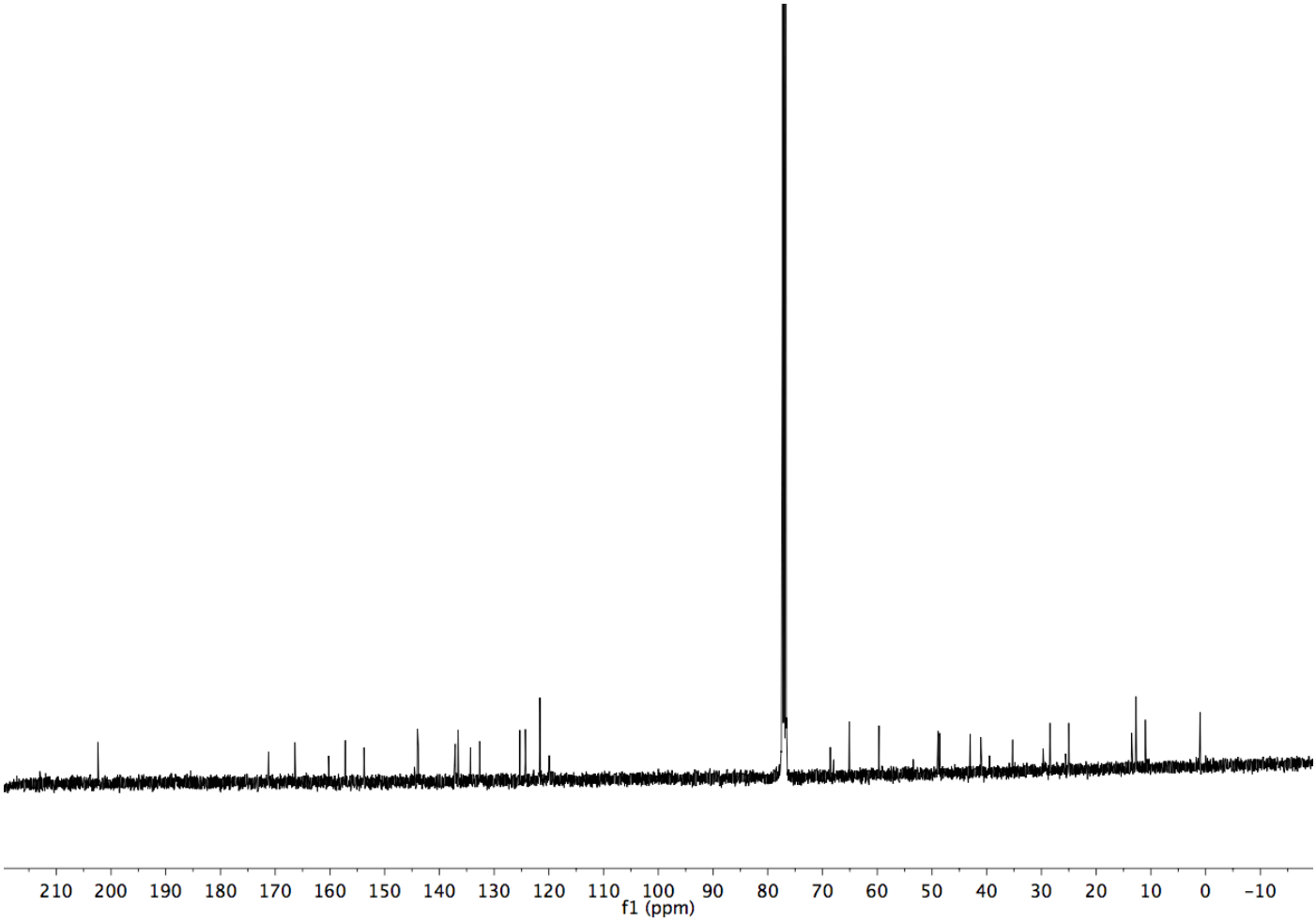

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

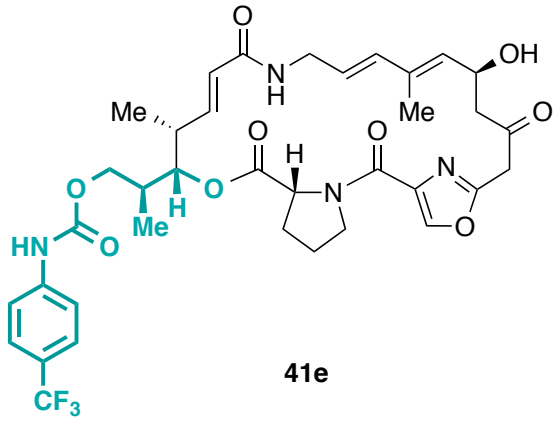

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
H
O
O
N
O
H
Me
HN
O
OCF3

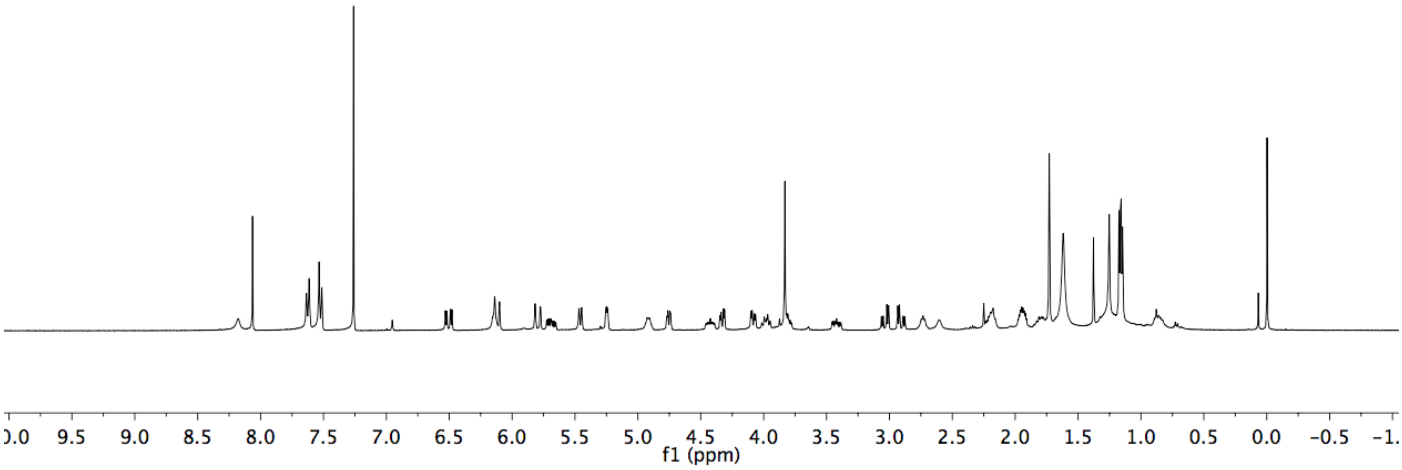
41d

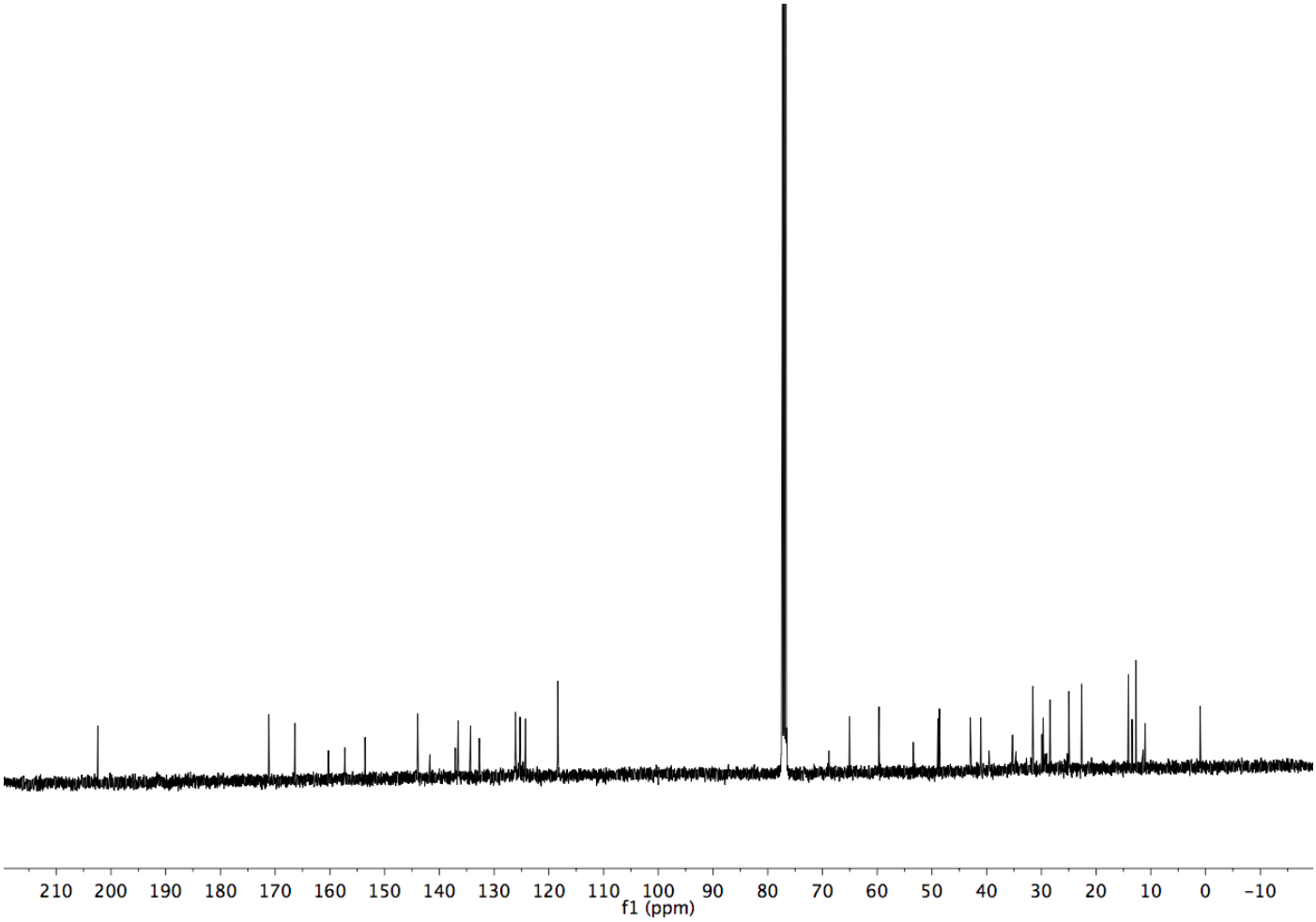
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

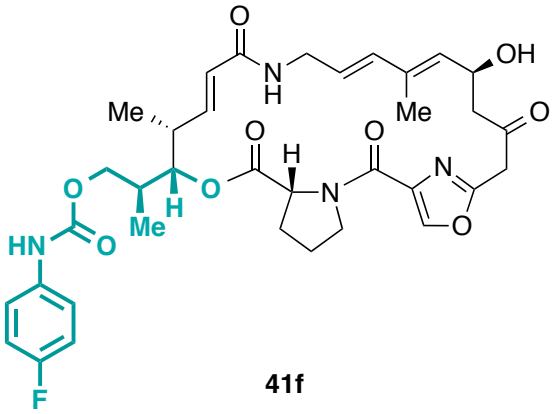

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



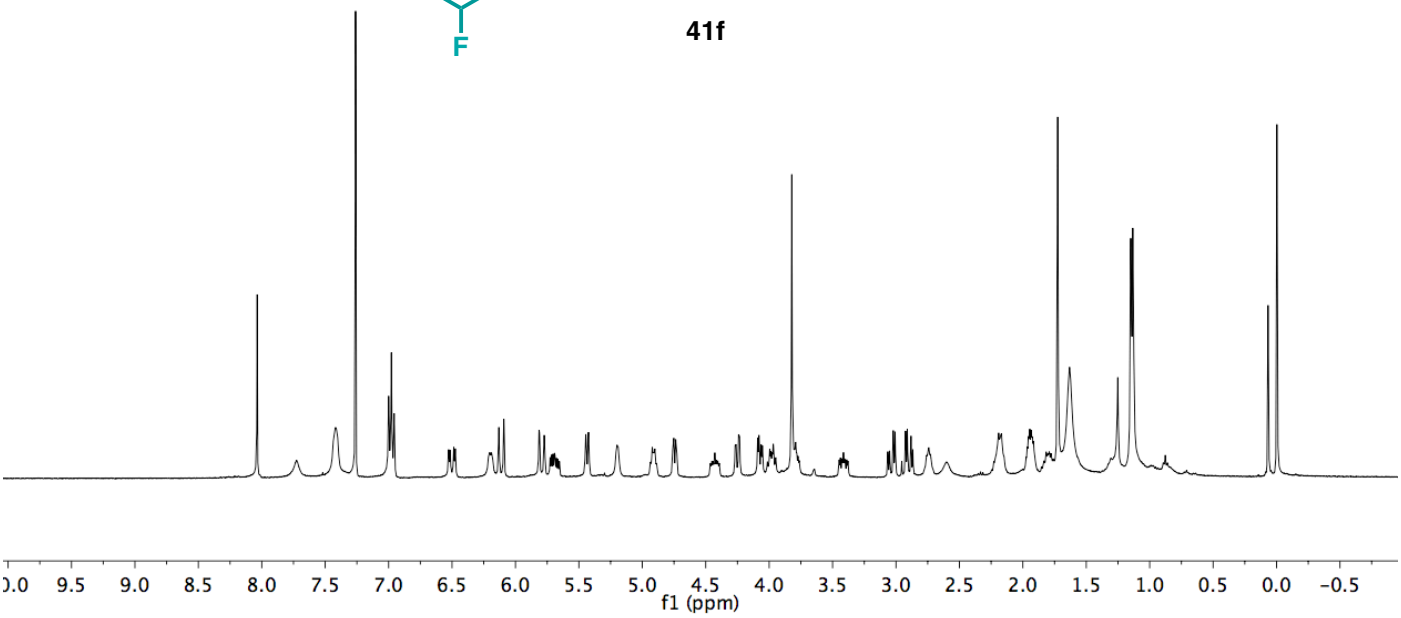
41e

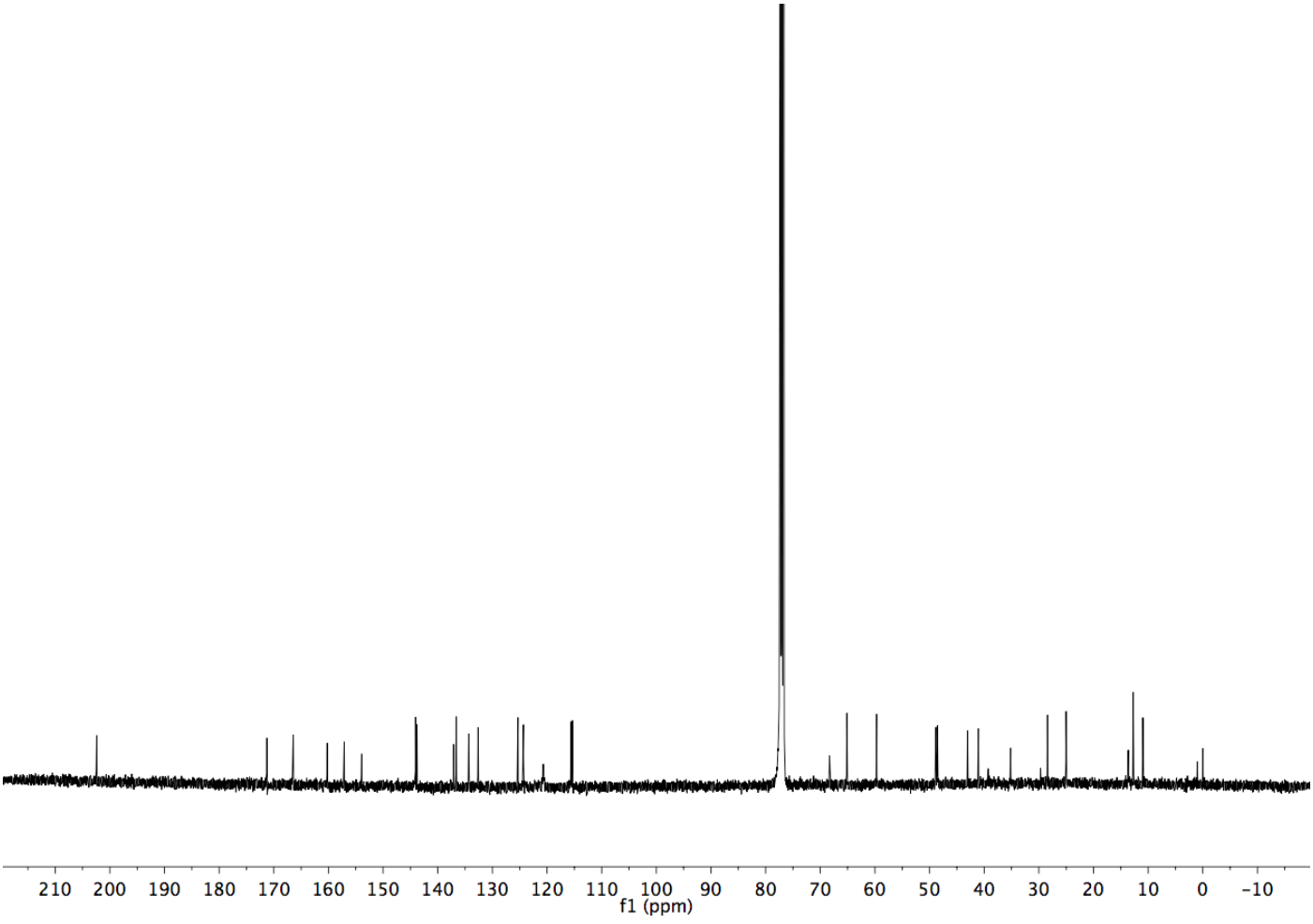

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

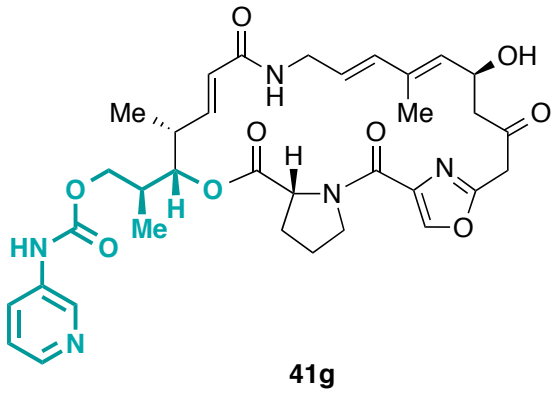

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



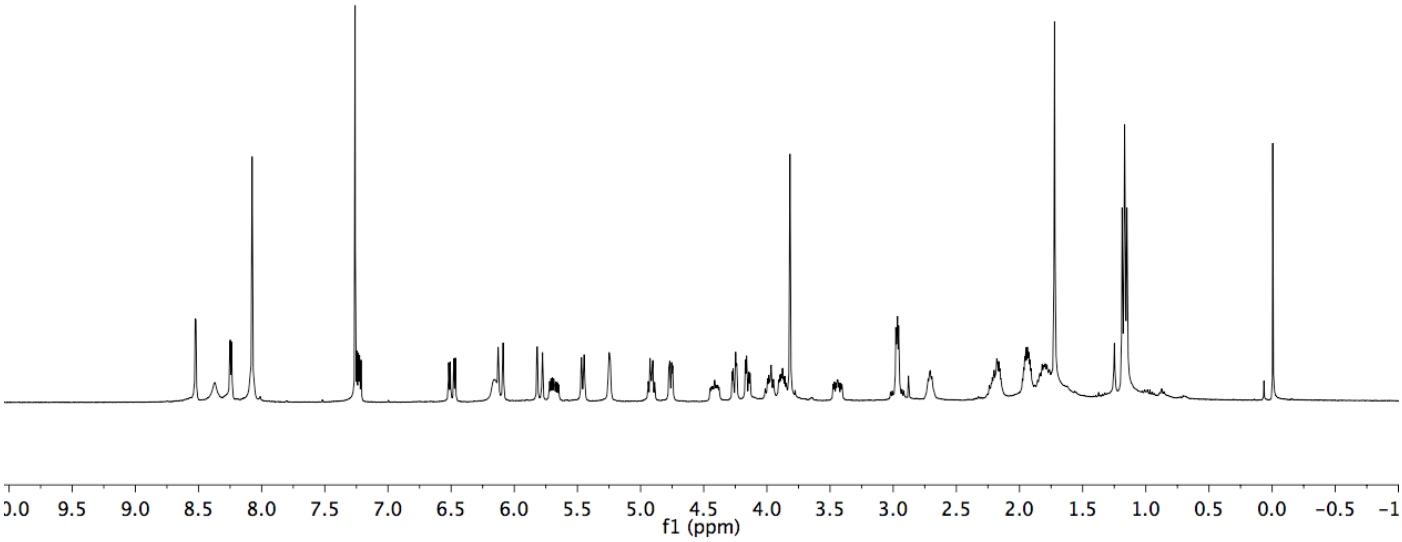
41f

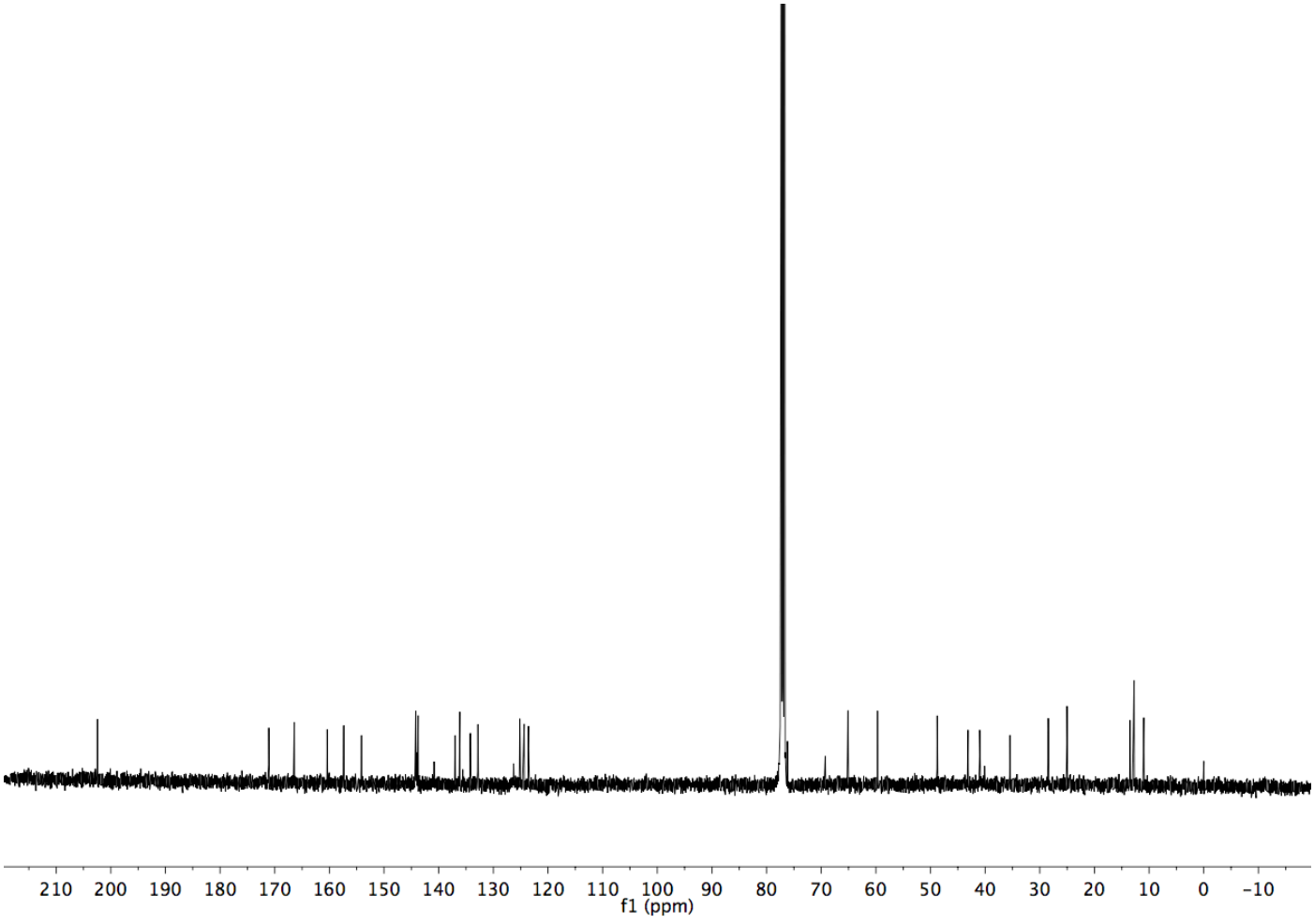


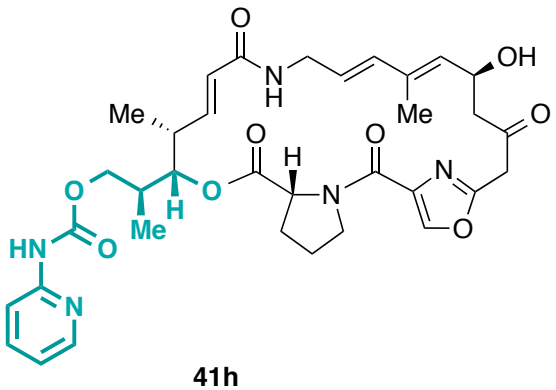



O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N

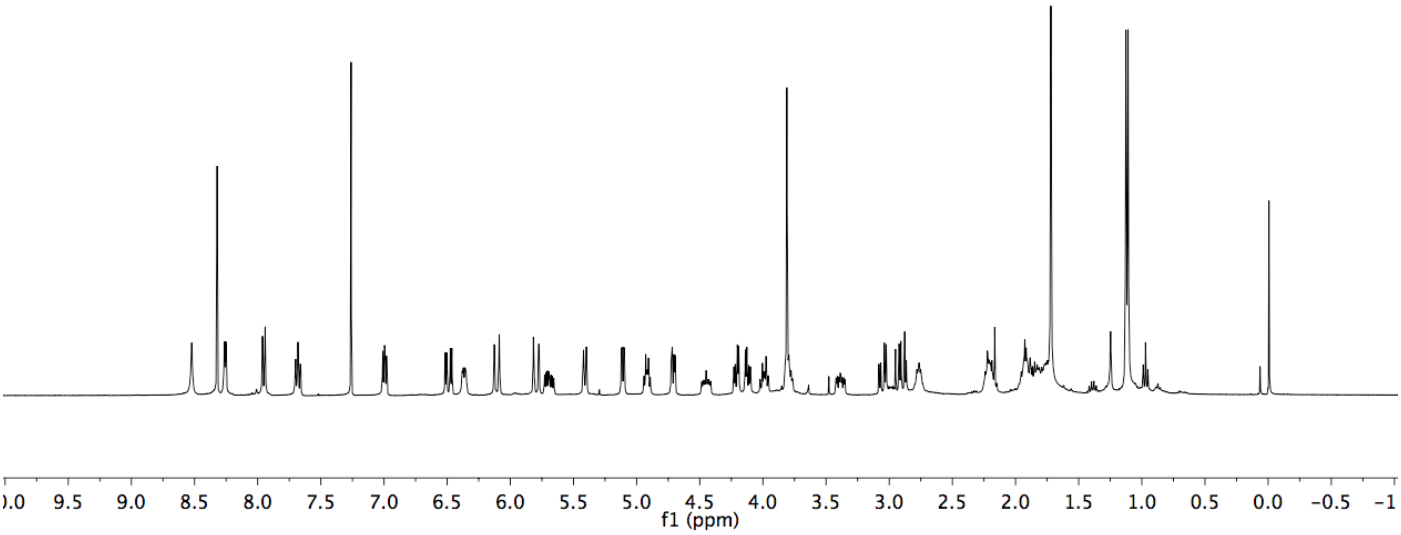
41g

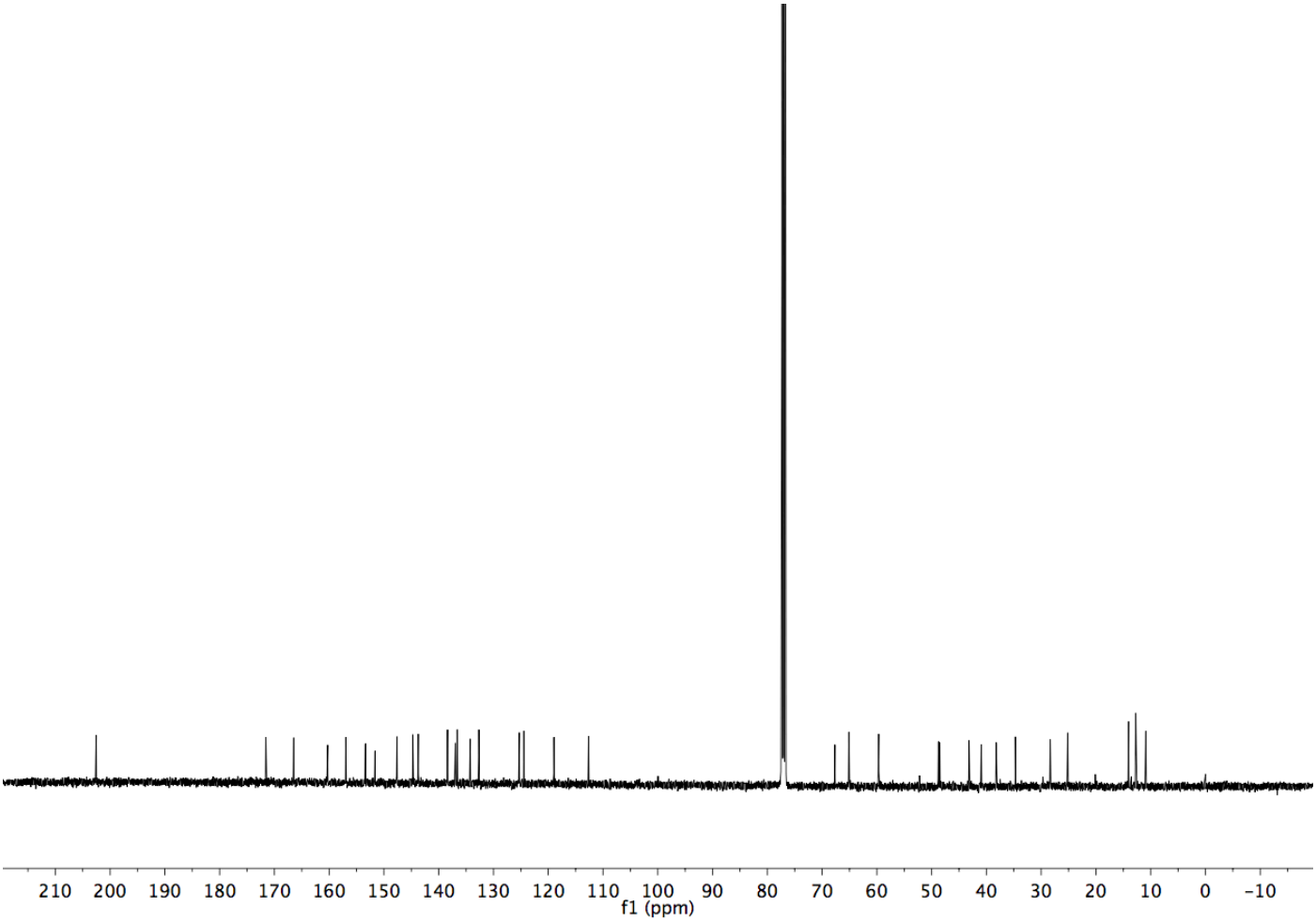

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

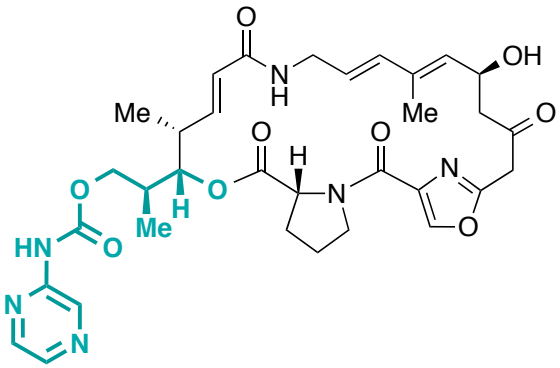

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N

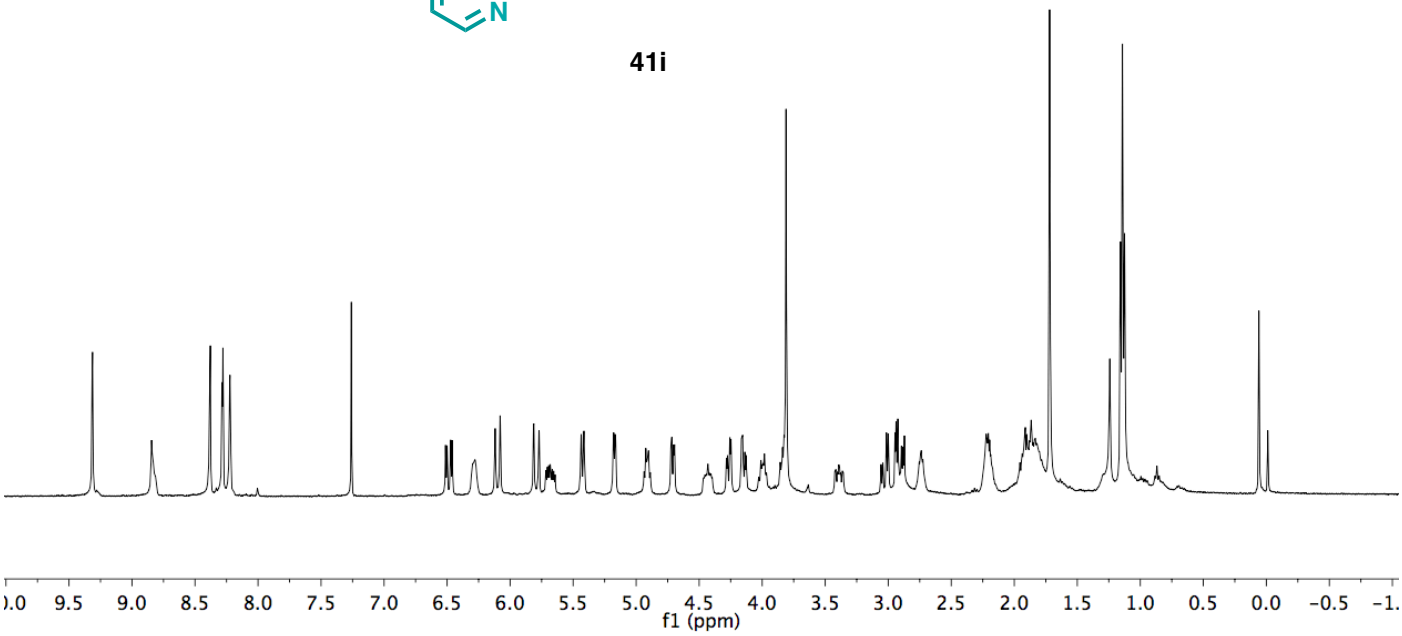
41h

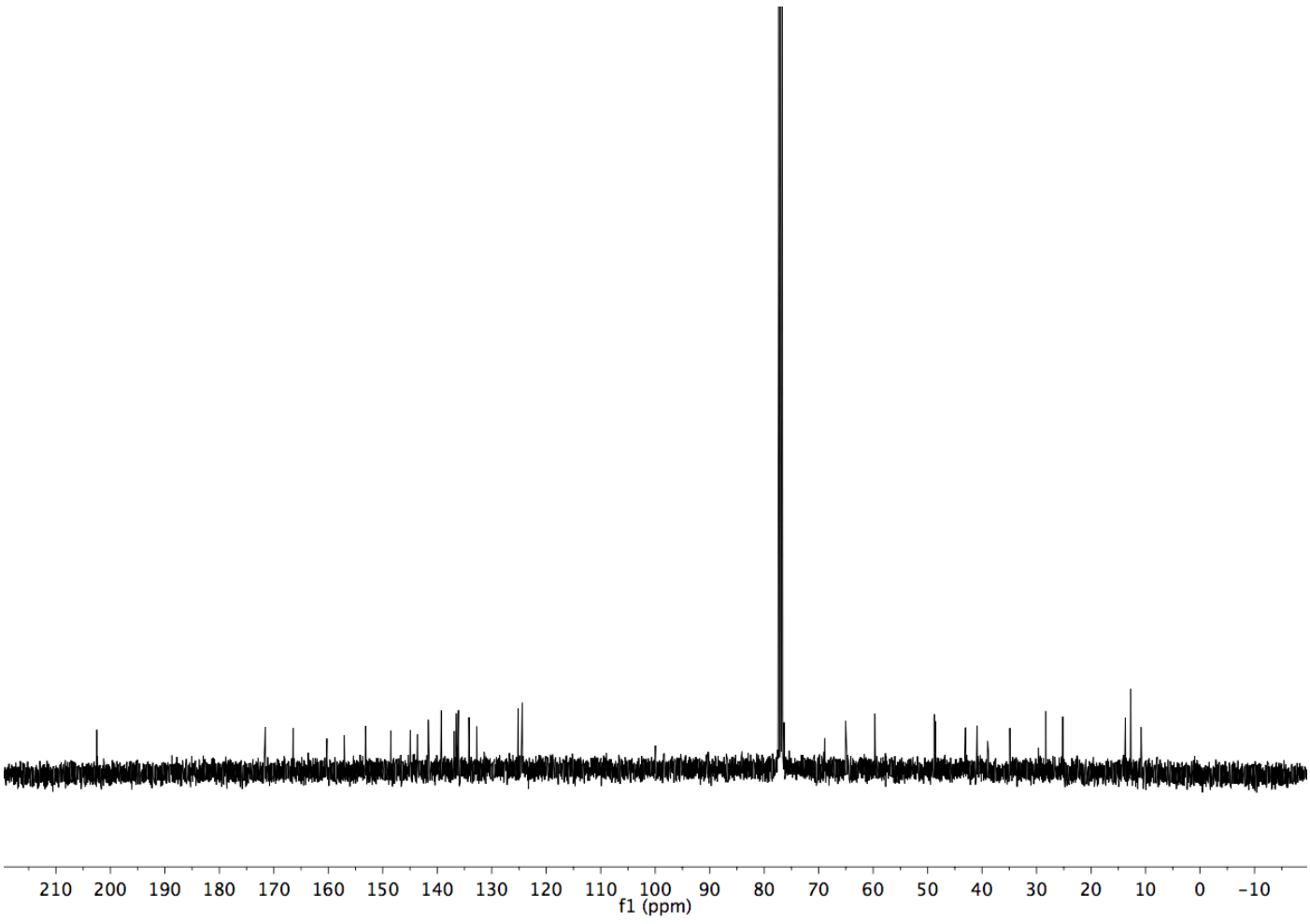

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

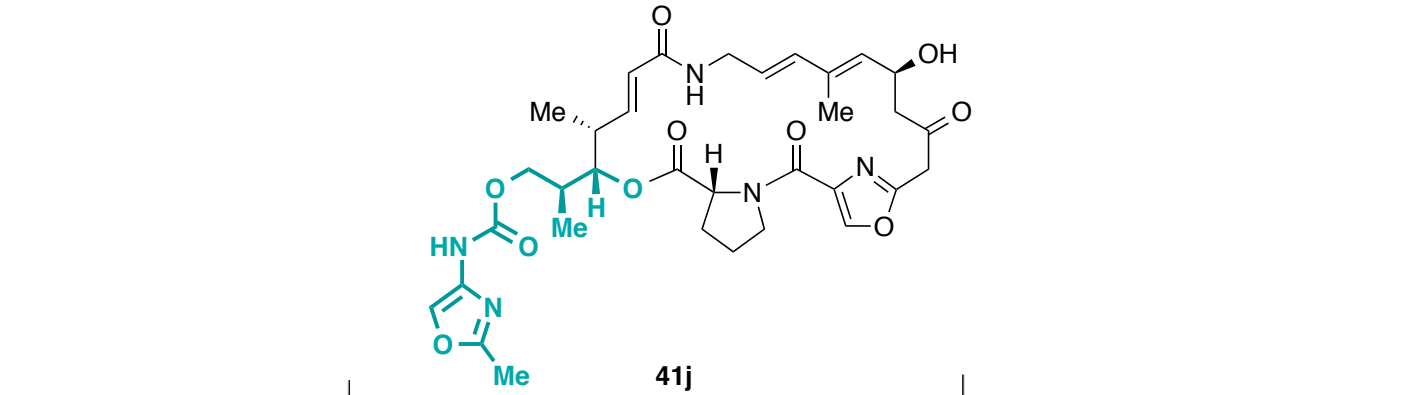

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
N

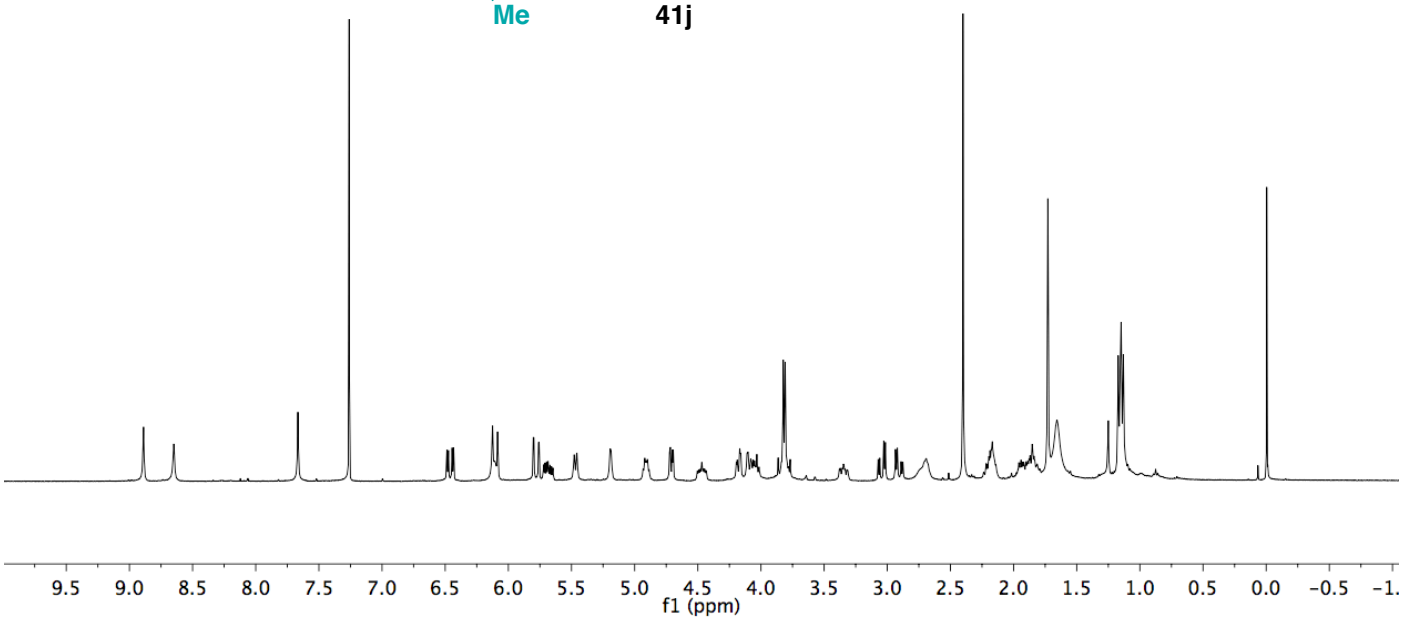
41i

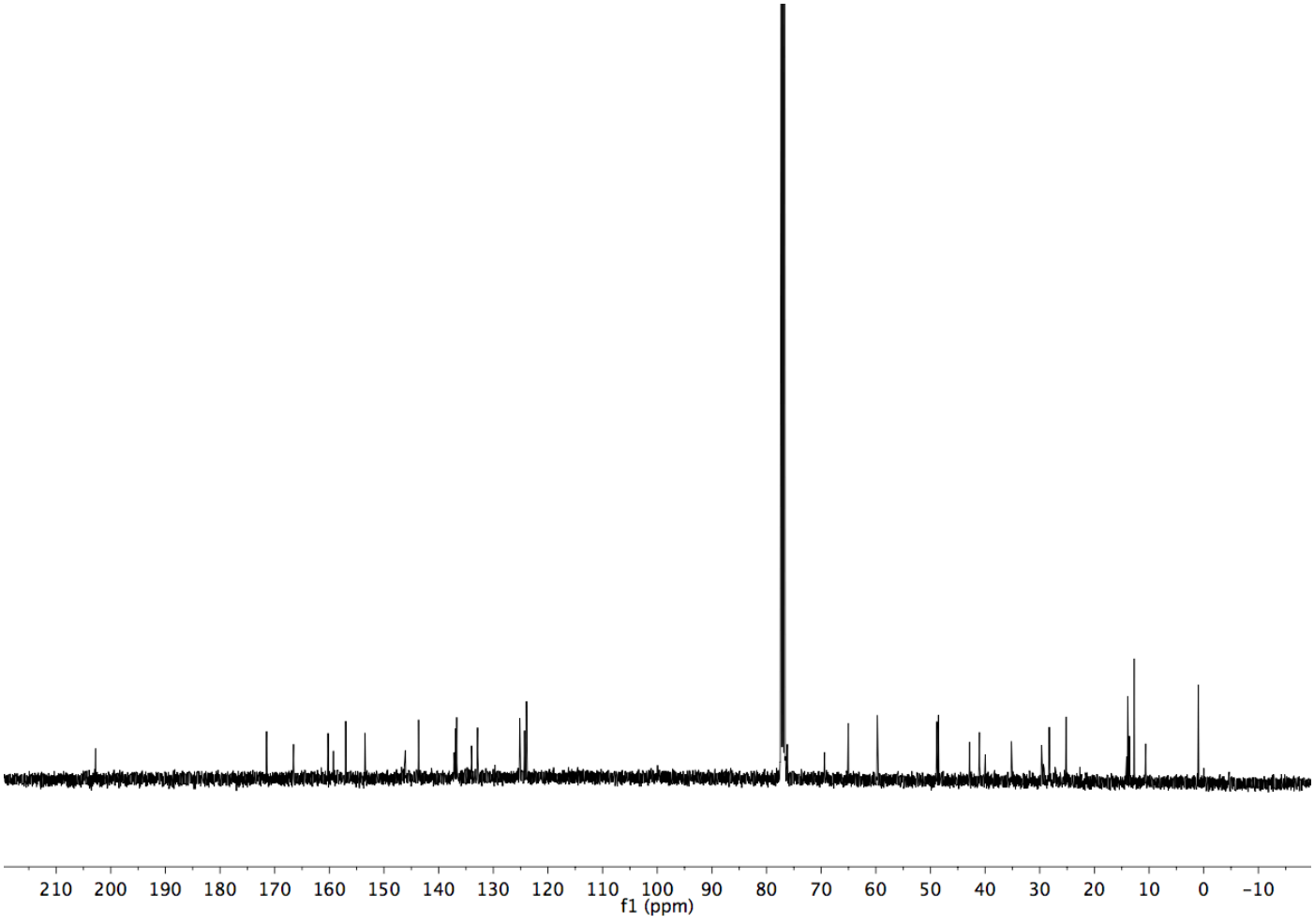

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

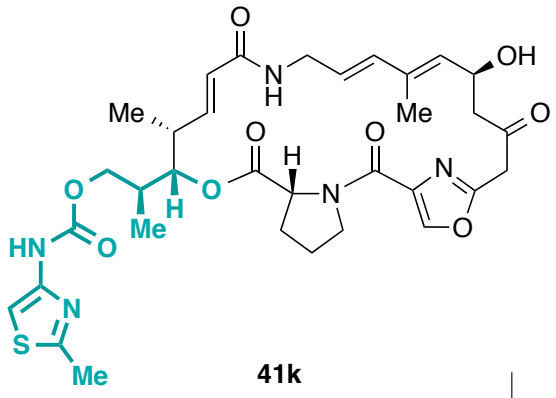

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
O
Me

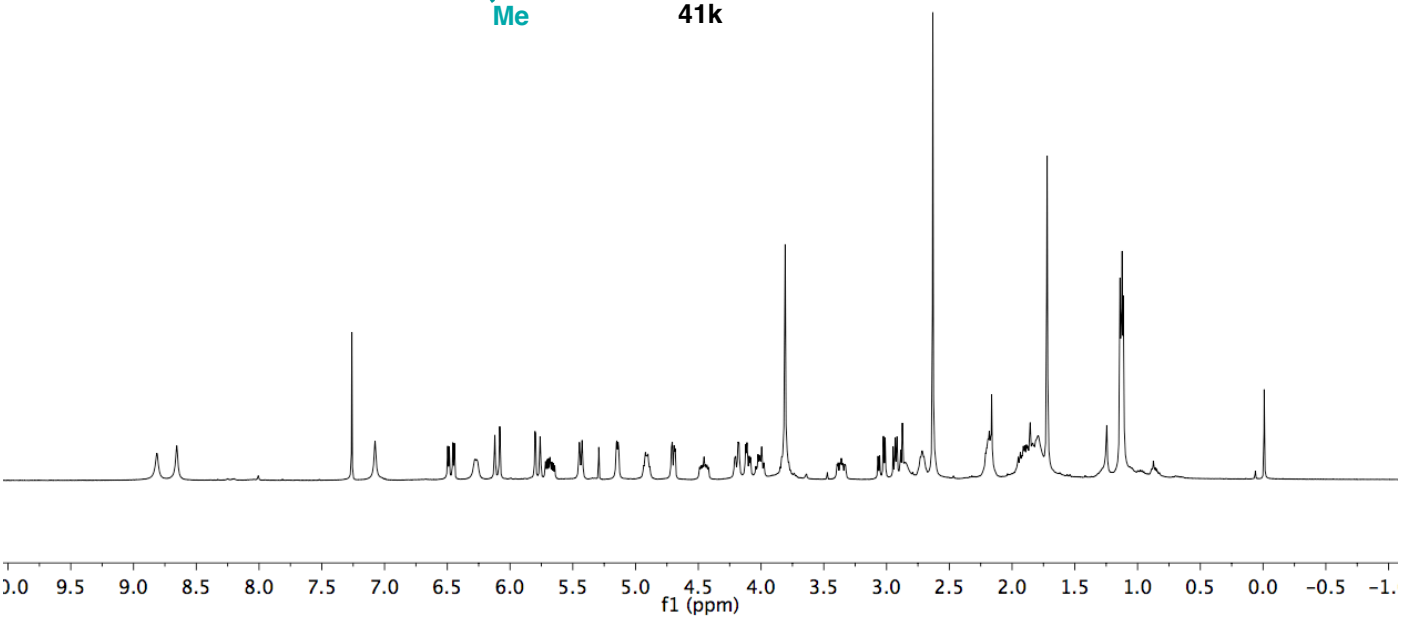
41j

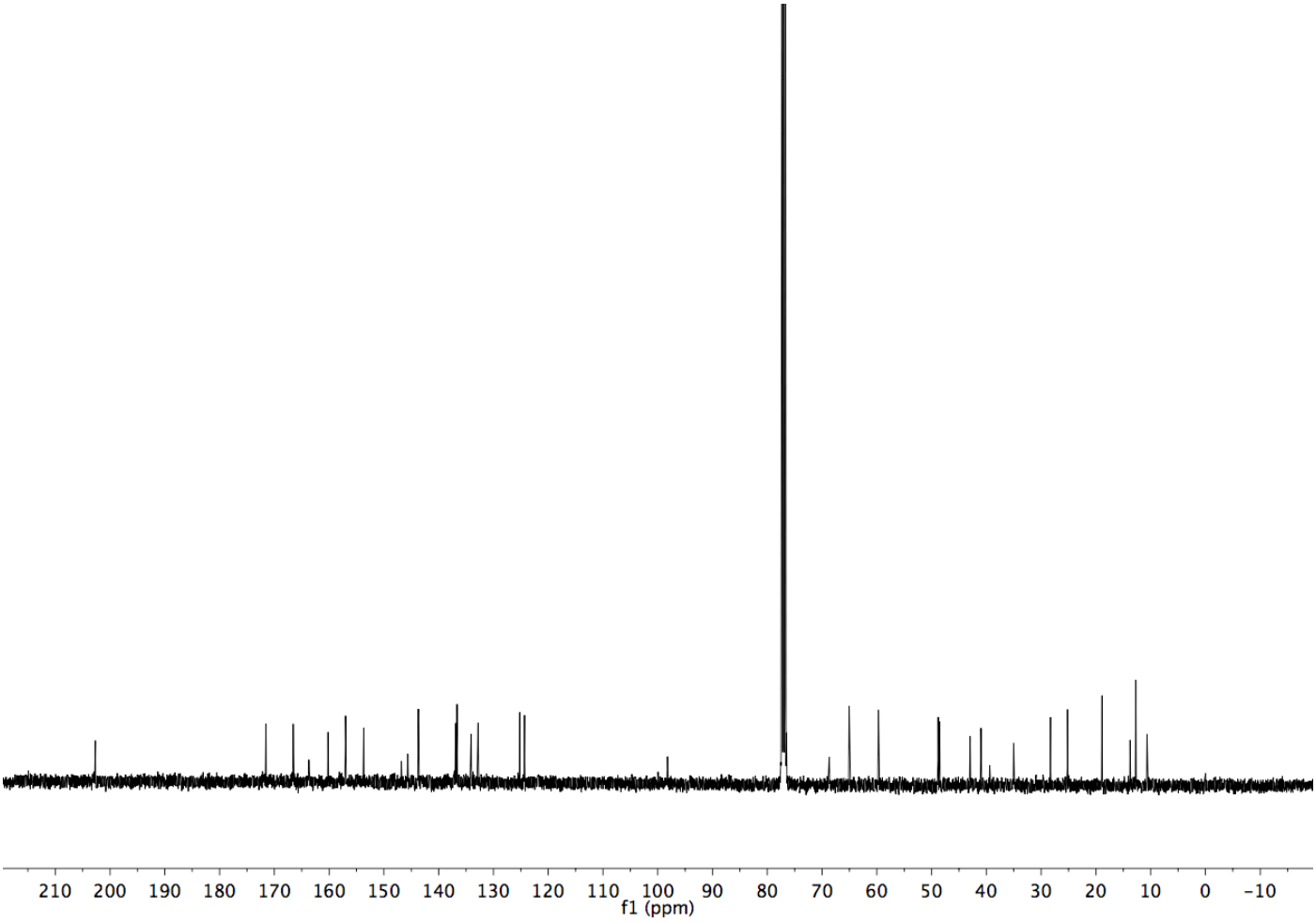

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

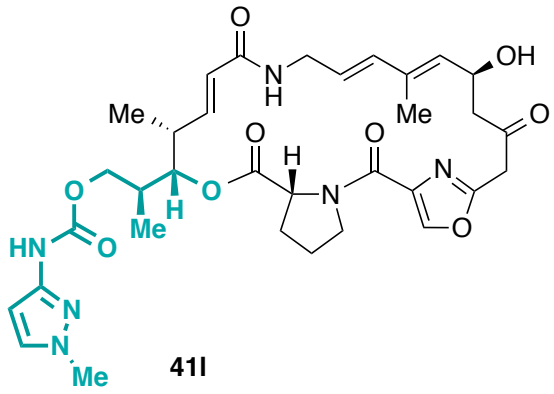

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
S
Me

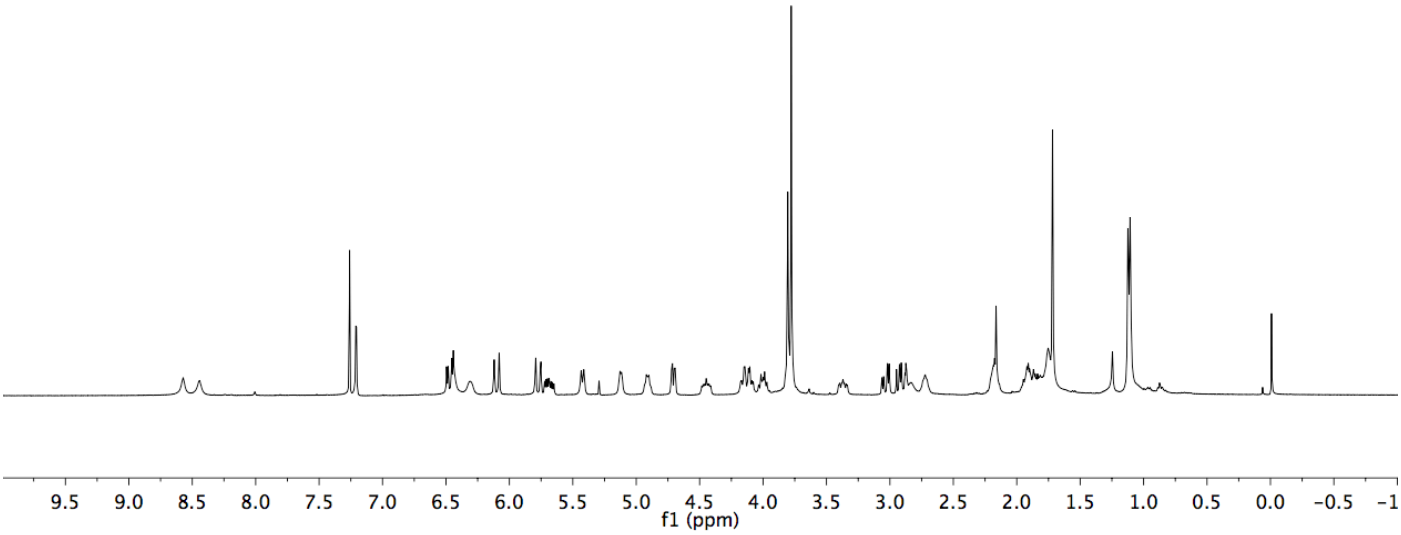
41k

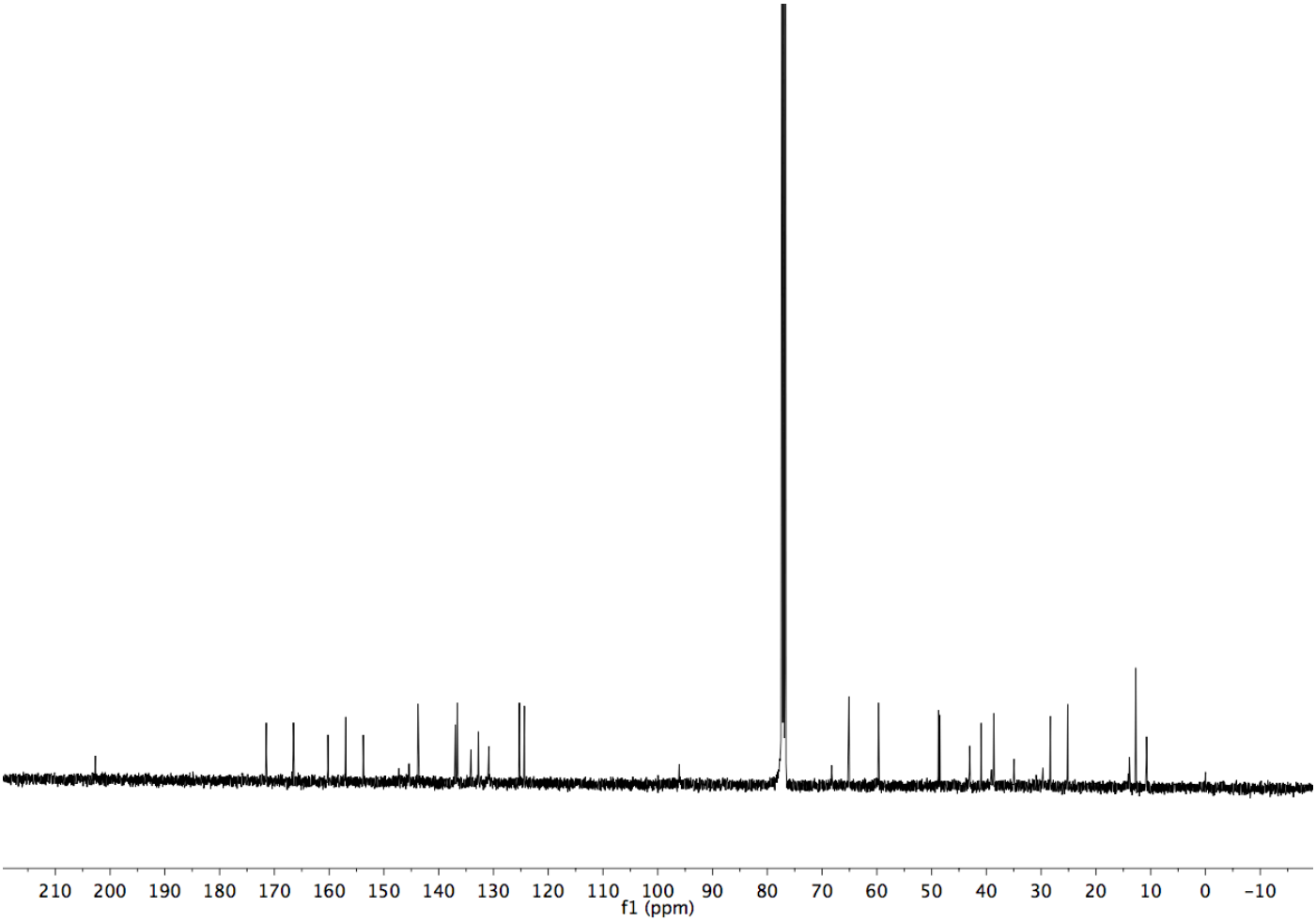

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

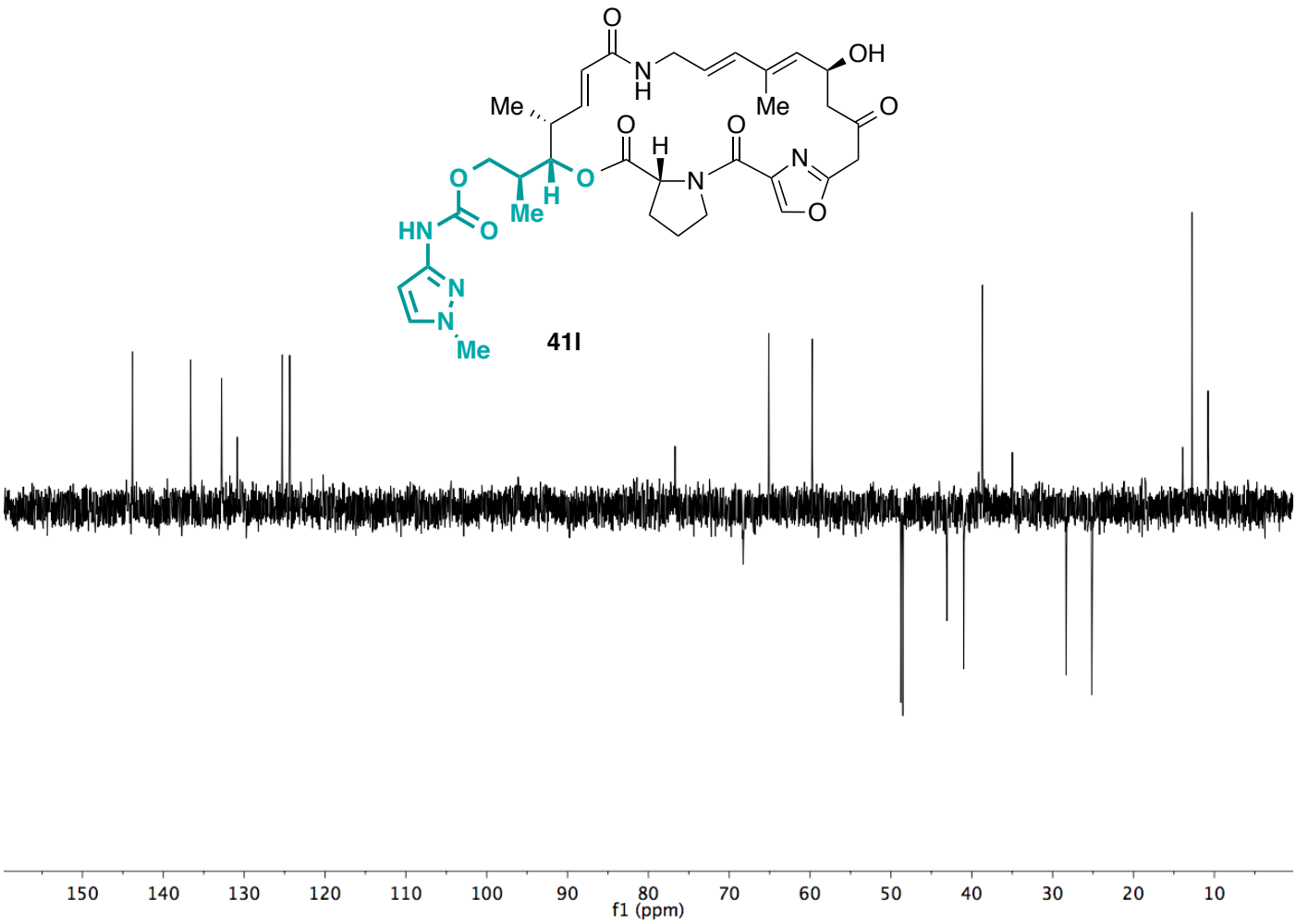

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
N
Me

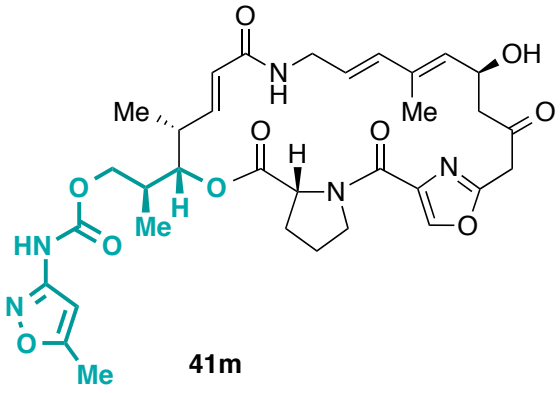
41l


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

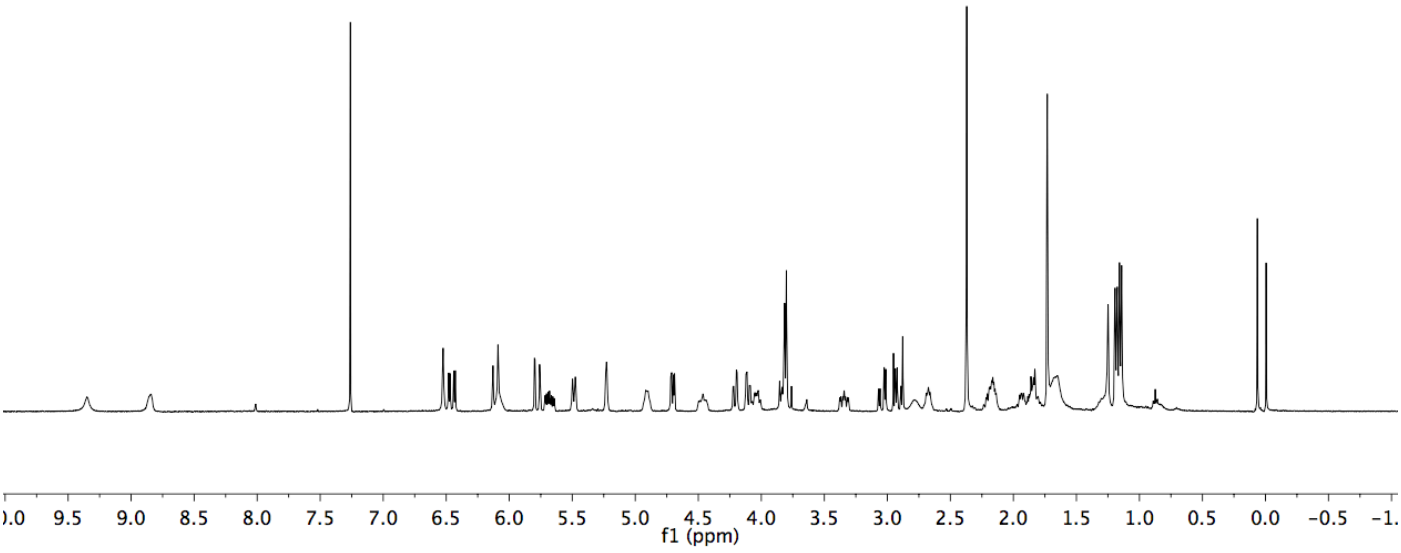

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

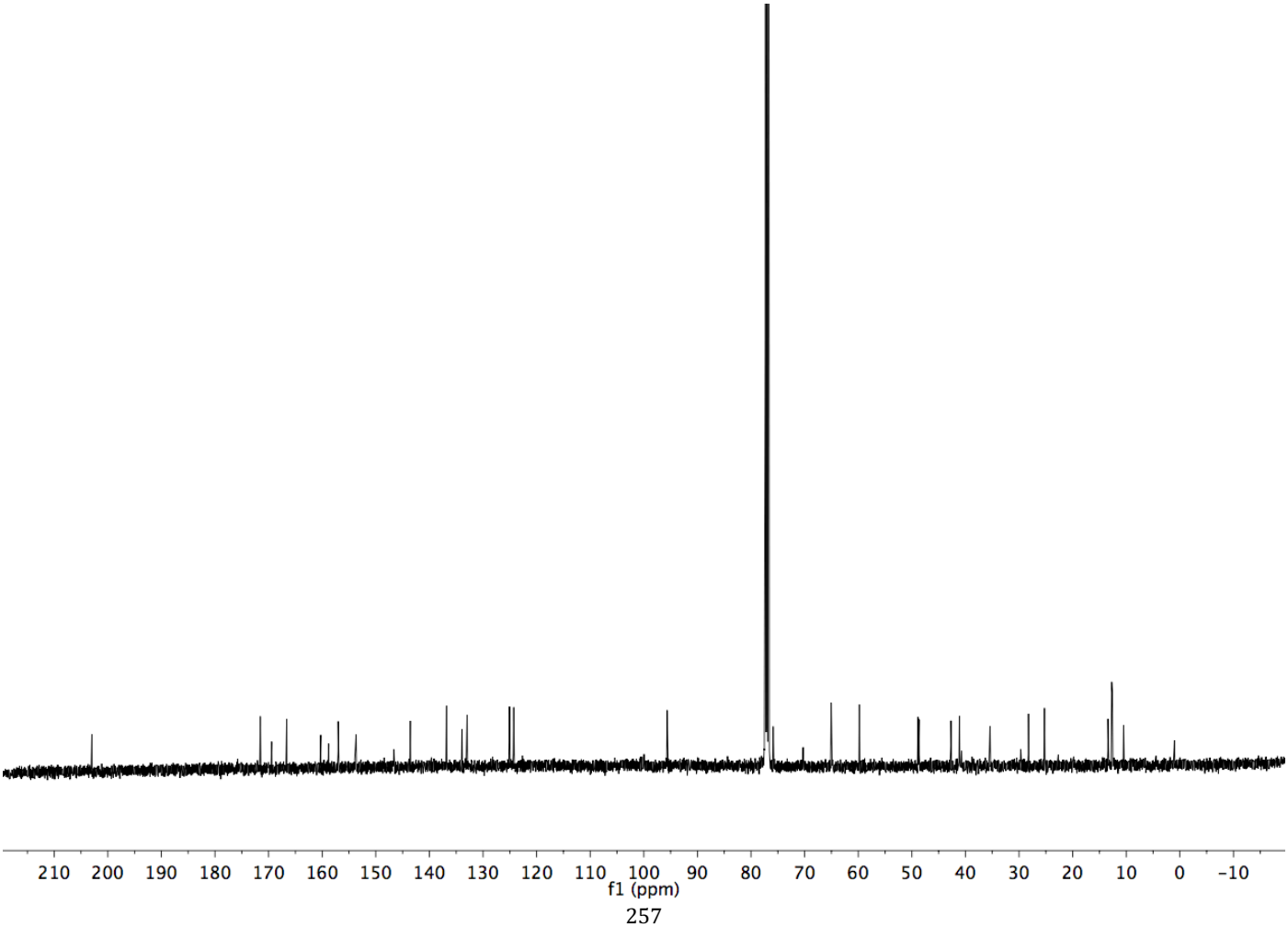

O
N
H
OH
Me
Me
O
O
H
O
N
N
O
O
O
H
Me
HN
O
N
N
Me
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

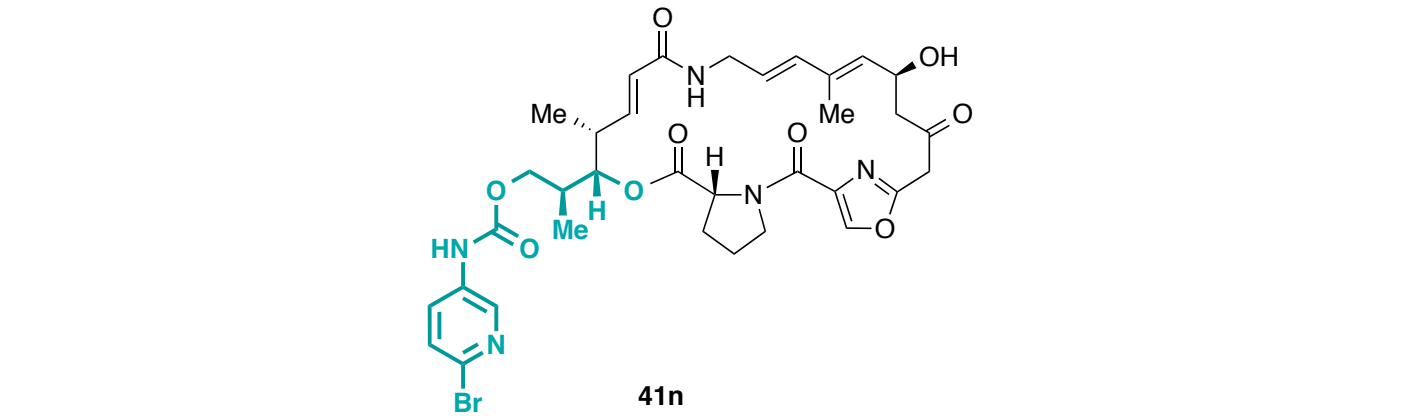
41l


O
N
H
OH
Me
Me
O
O
H
O
N
N
O
O
Me
H
HN
O
N
O
Me

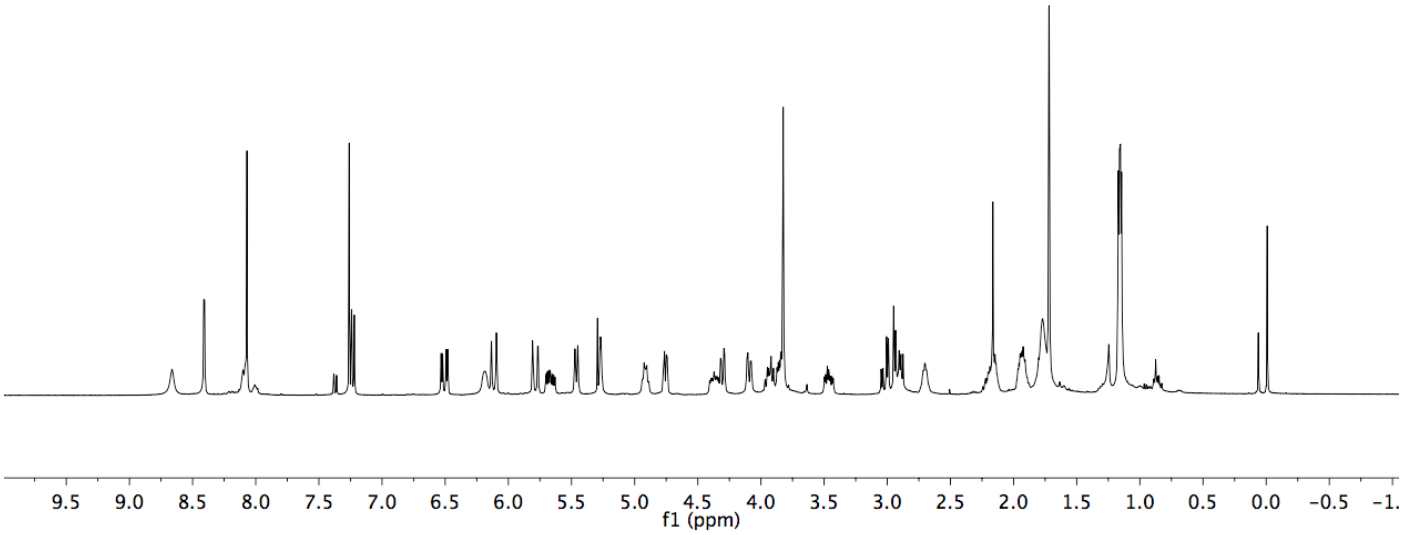
41m

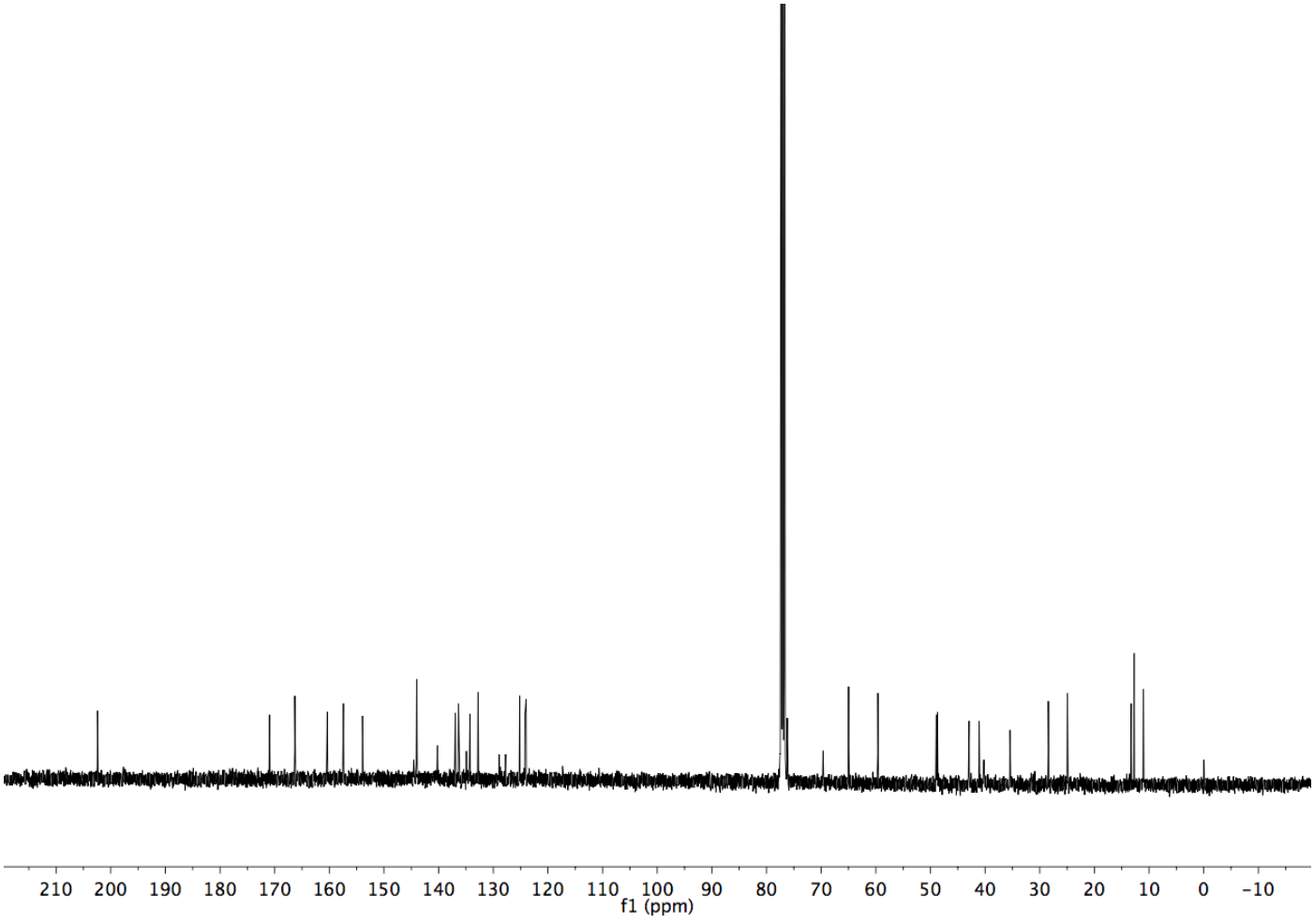

9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

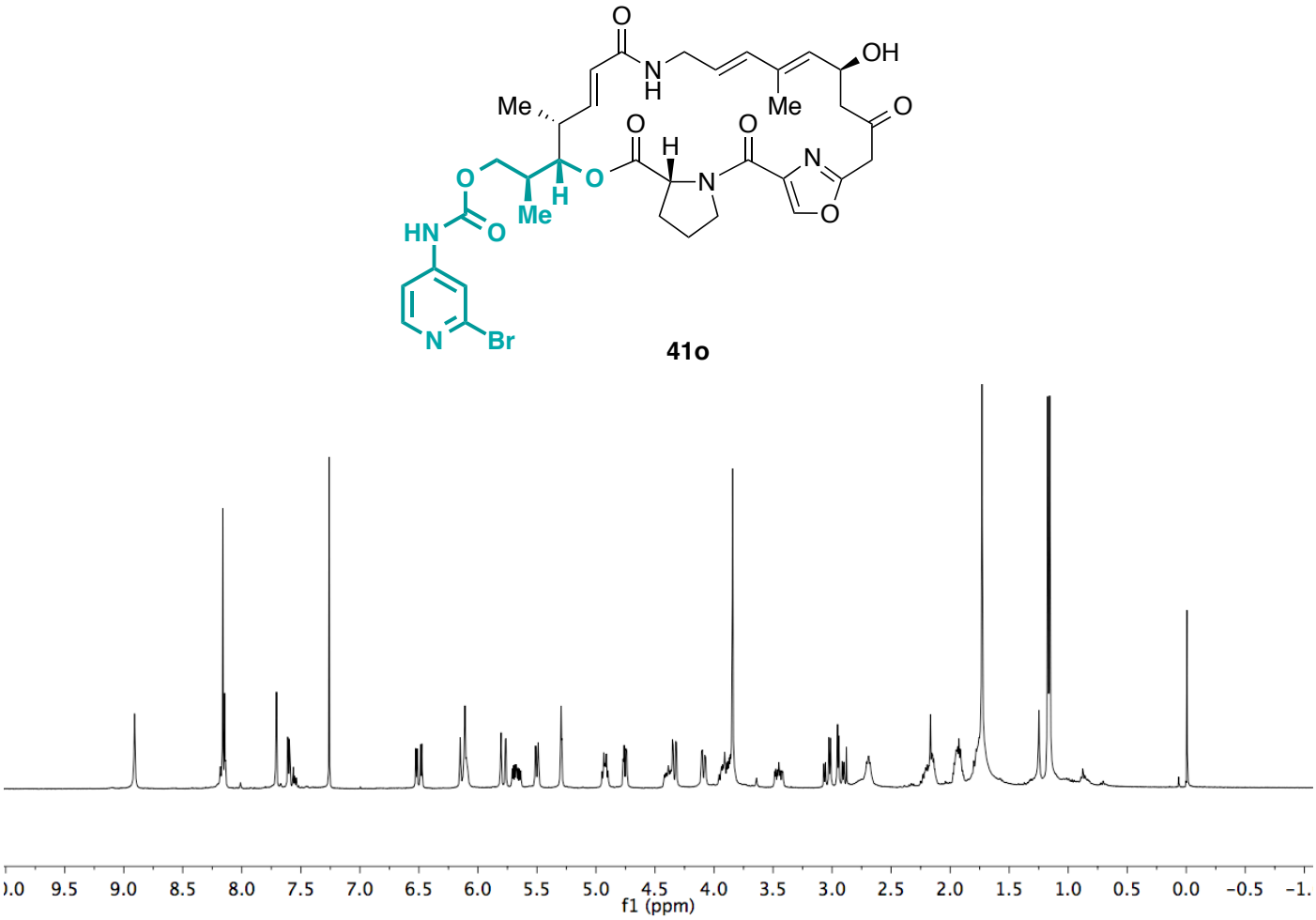

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
H
Me
HN
O
N
Br

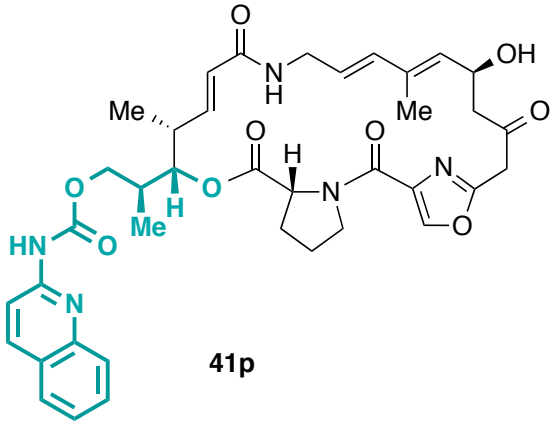
41n


9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

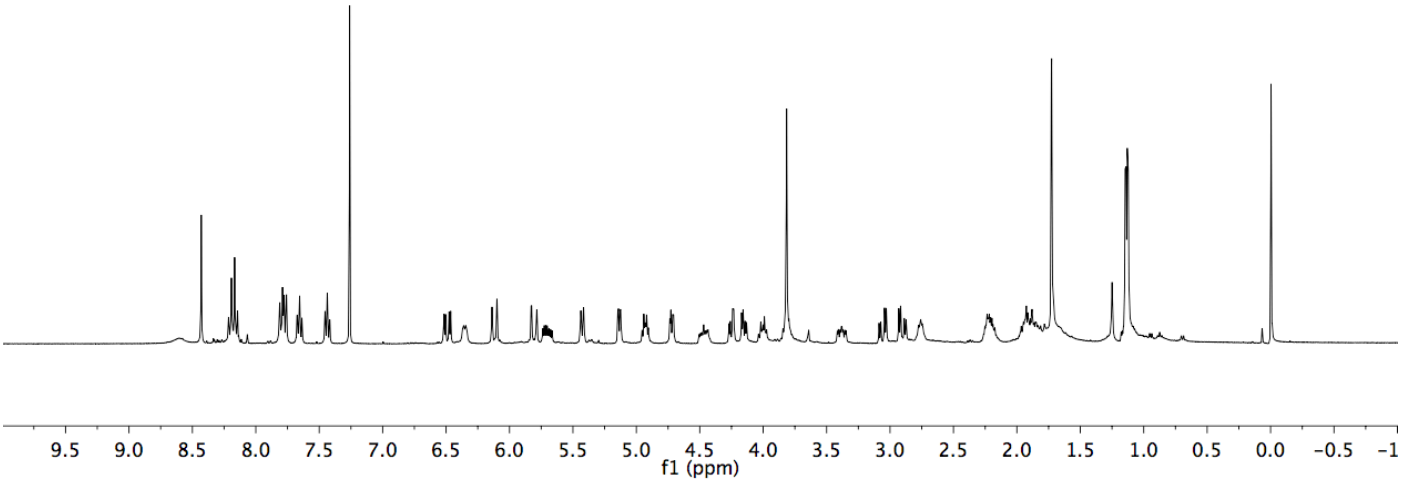

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

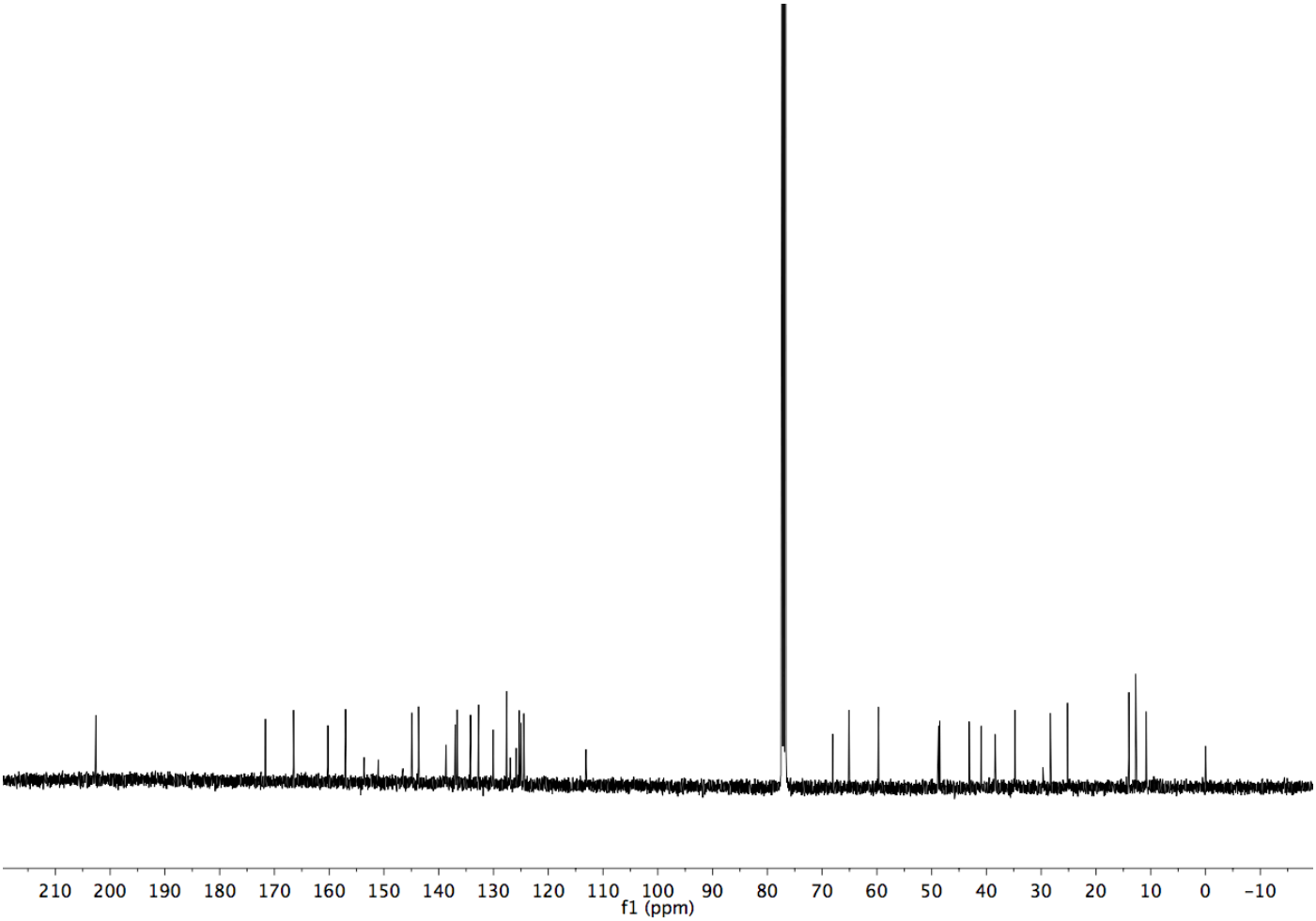


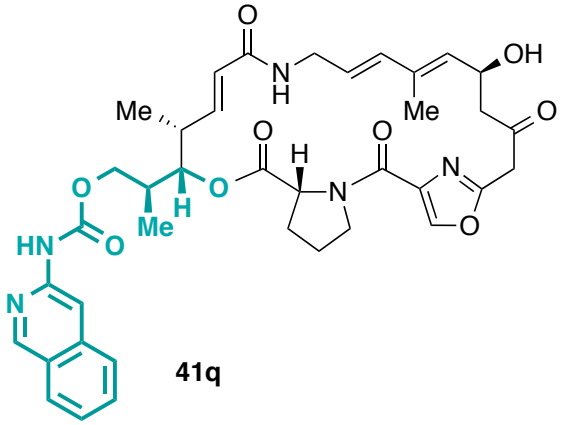
41o



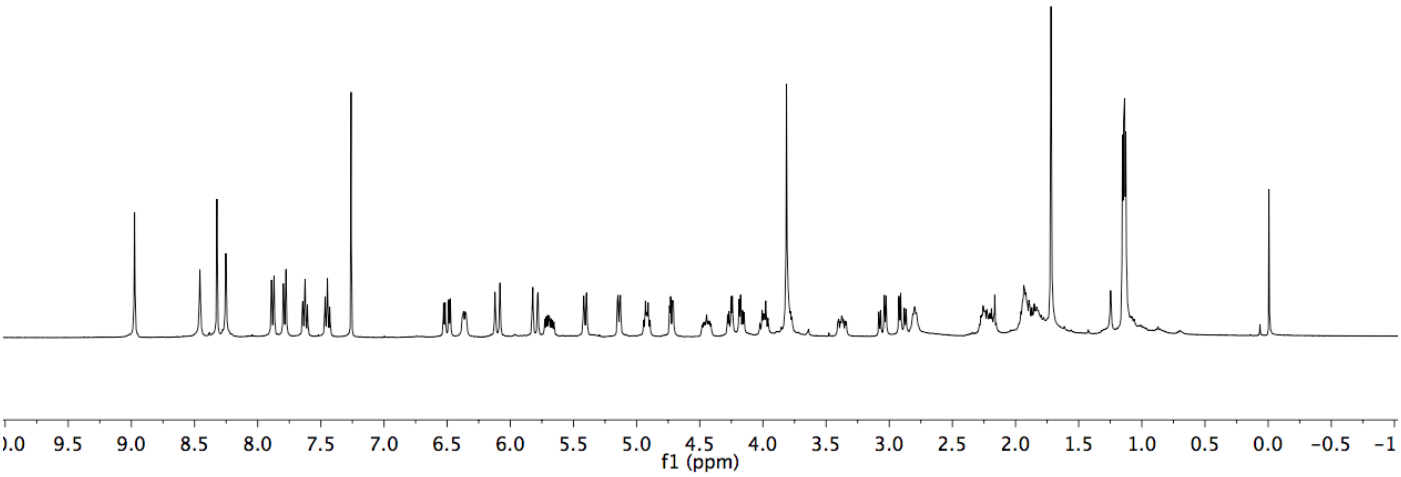
41p

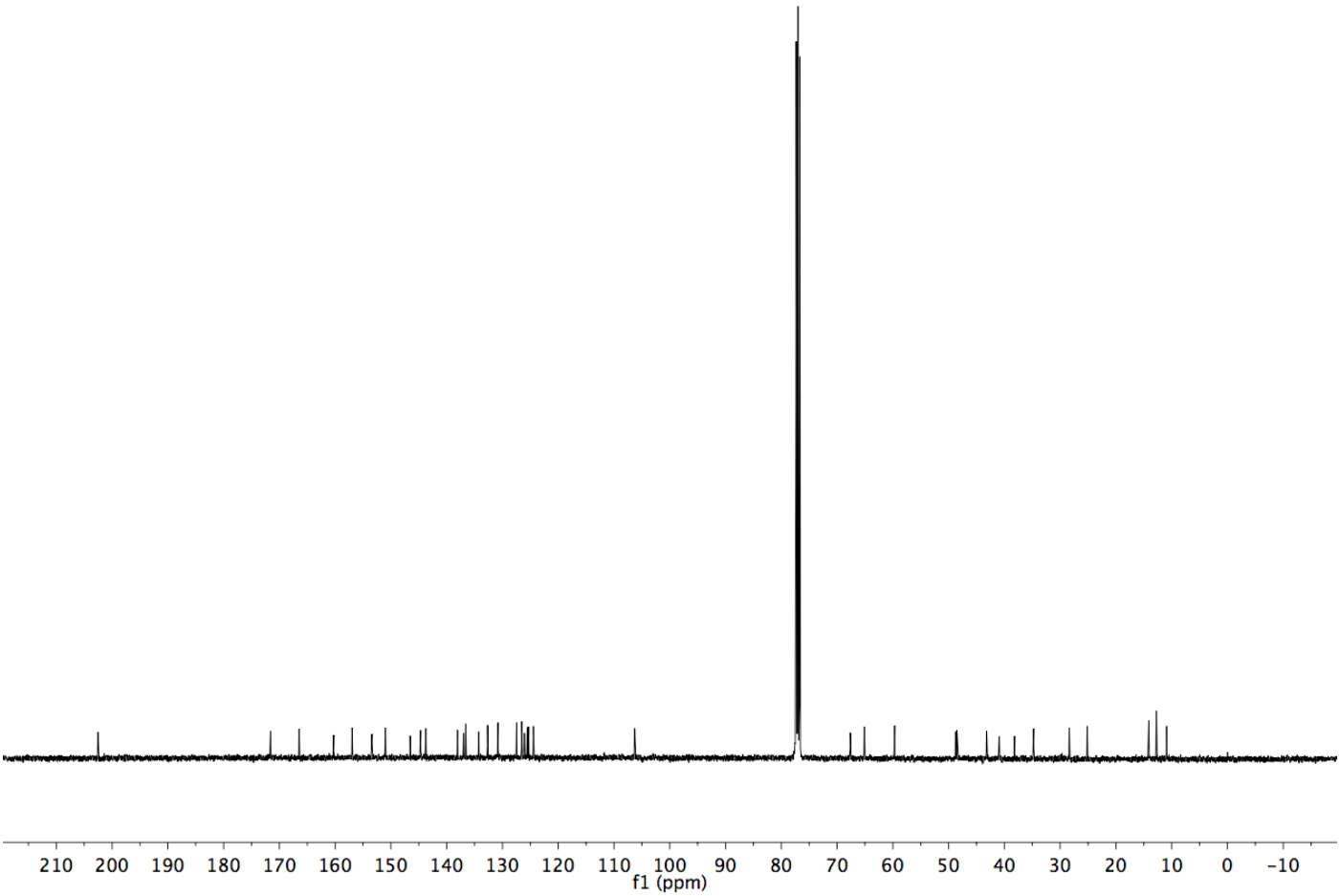

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

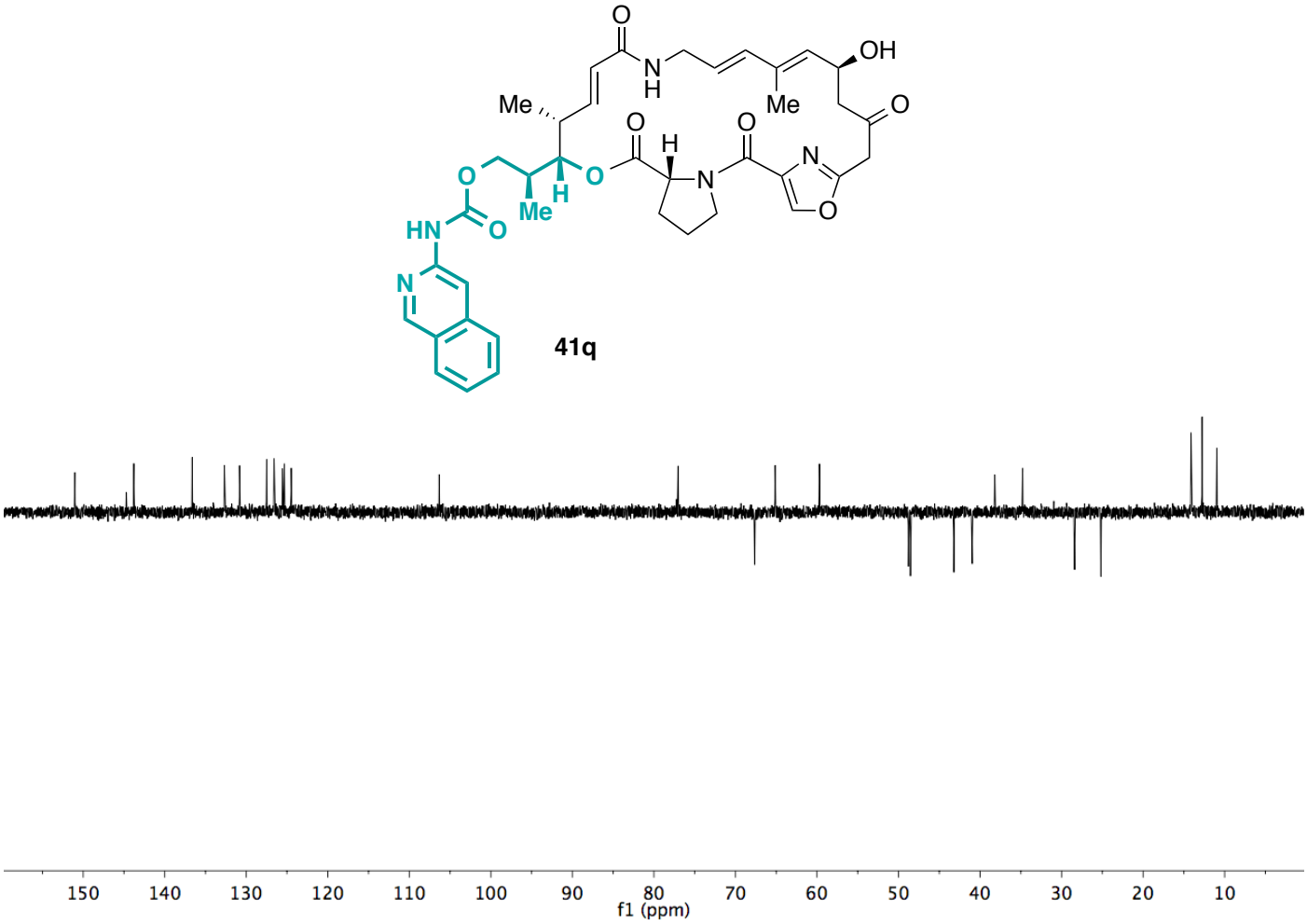

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



41q

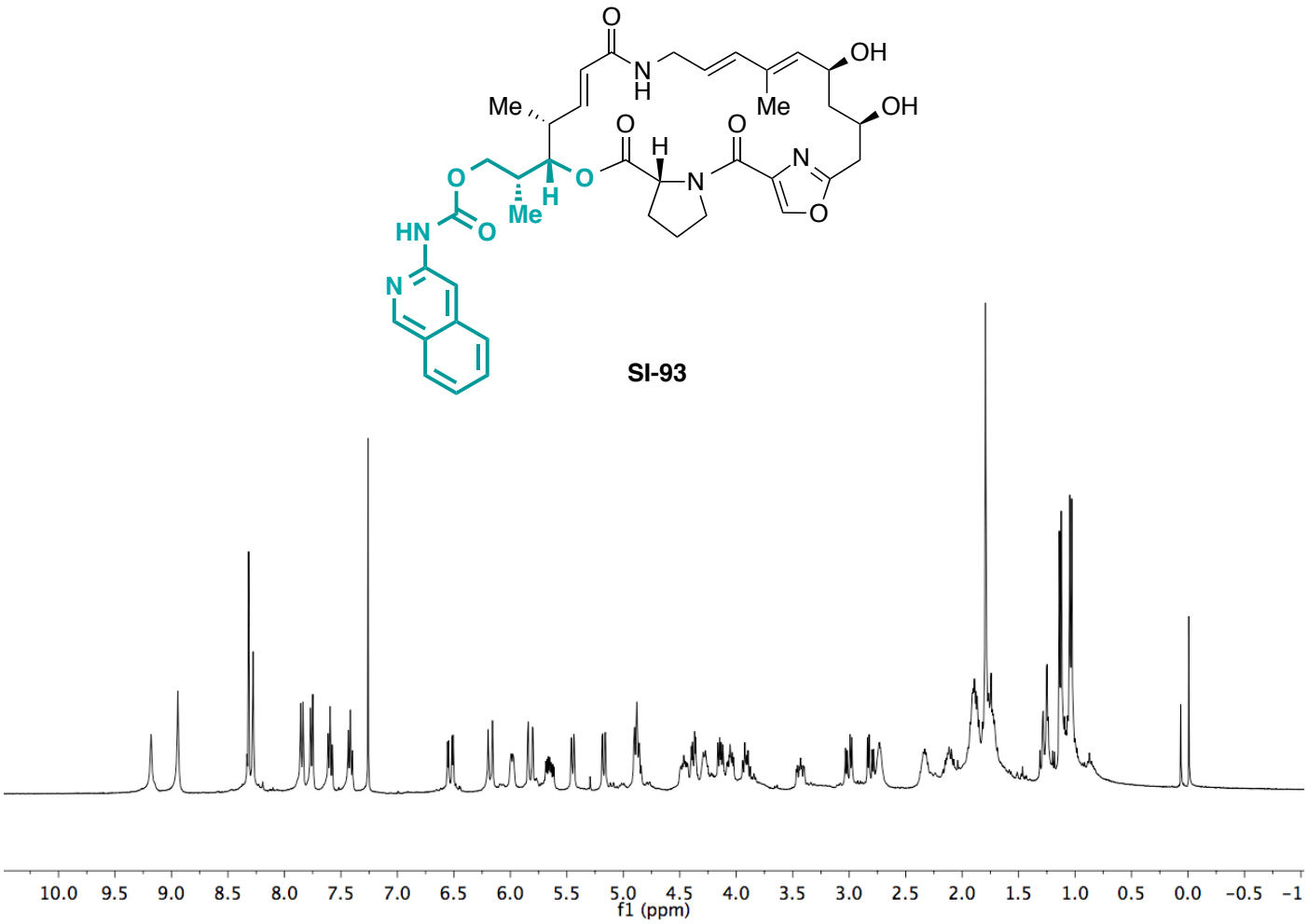

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
O
O
O
H
O
N
N
O
O
Me
H
HN
O
N

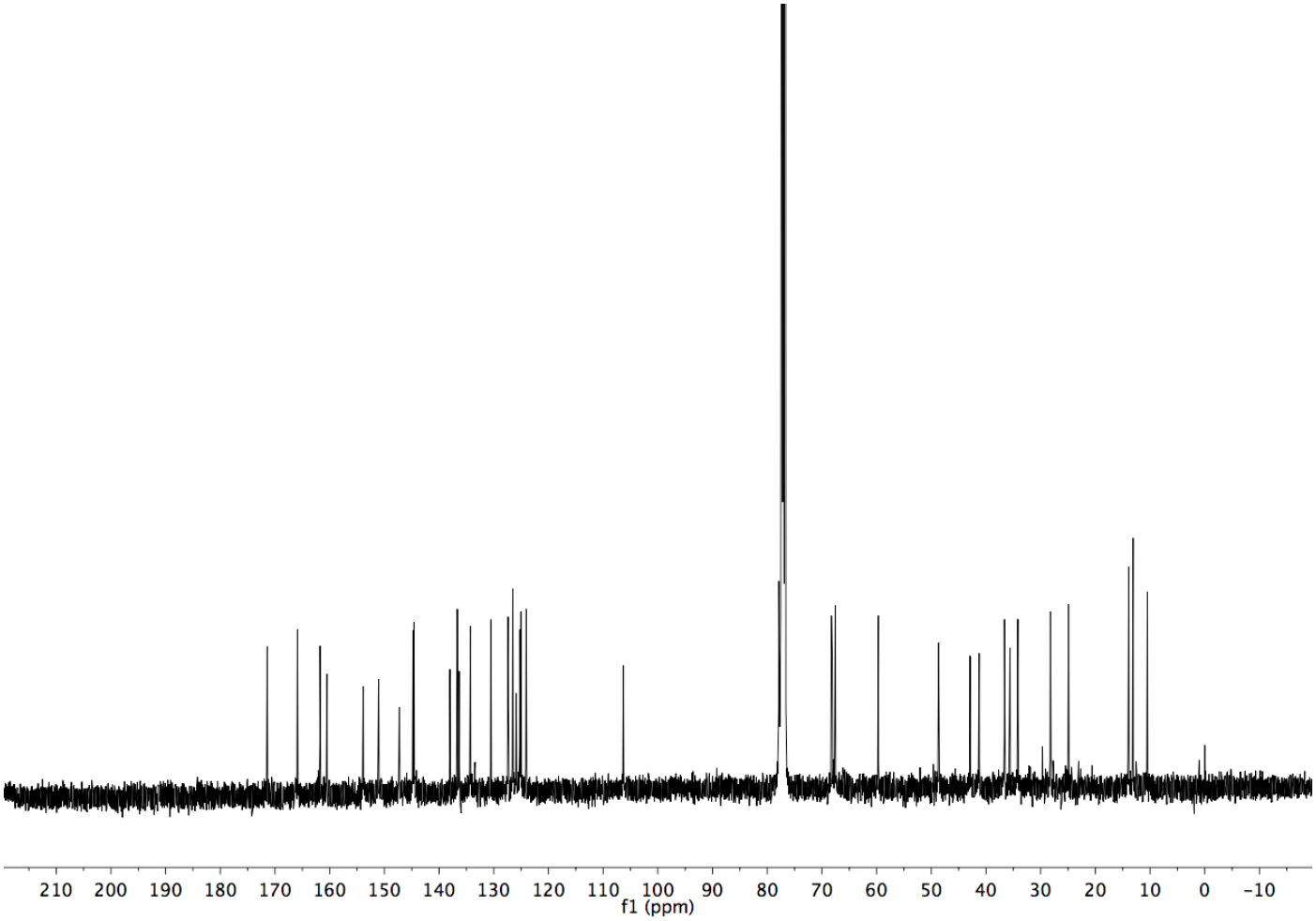
41q

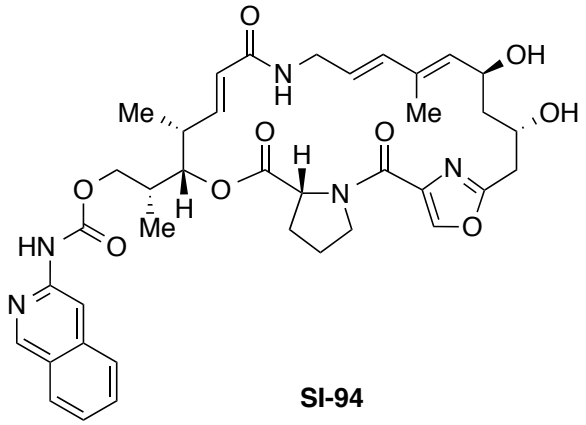
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O
N
H
OH
Me
Me
OH
O
H
O
N
O
O
O
Me
H
HN
O
N

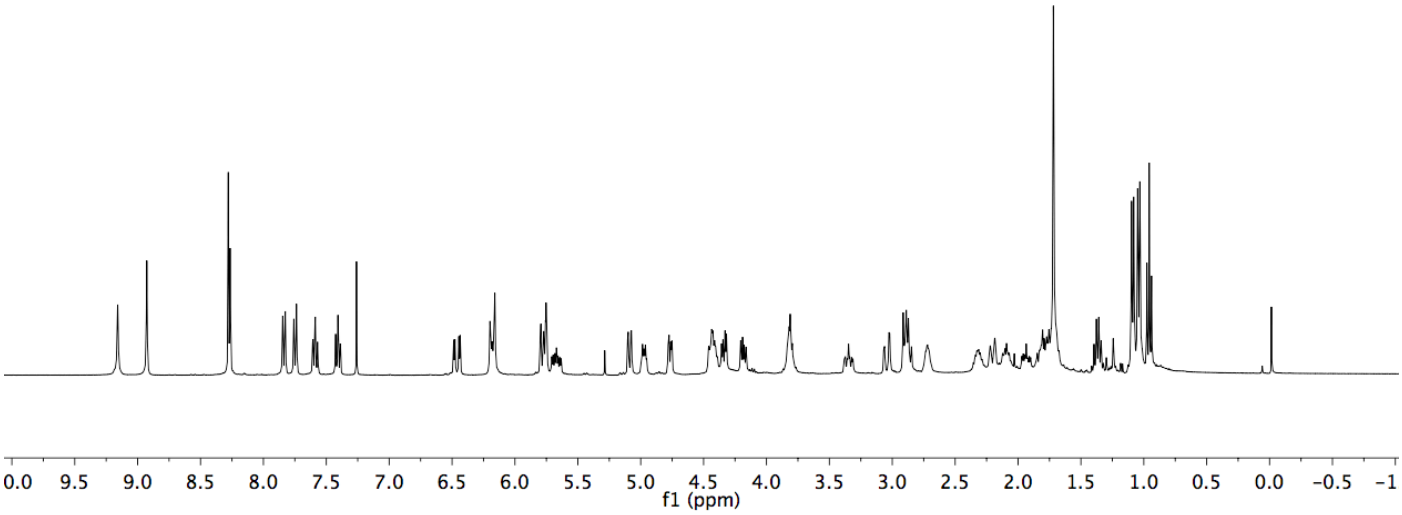
SI-93

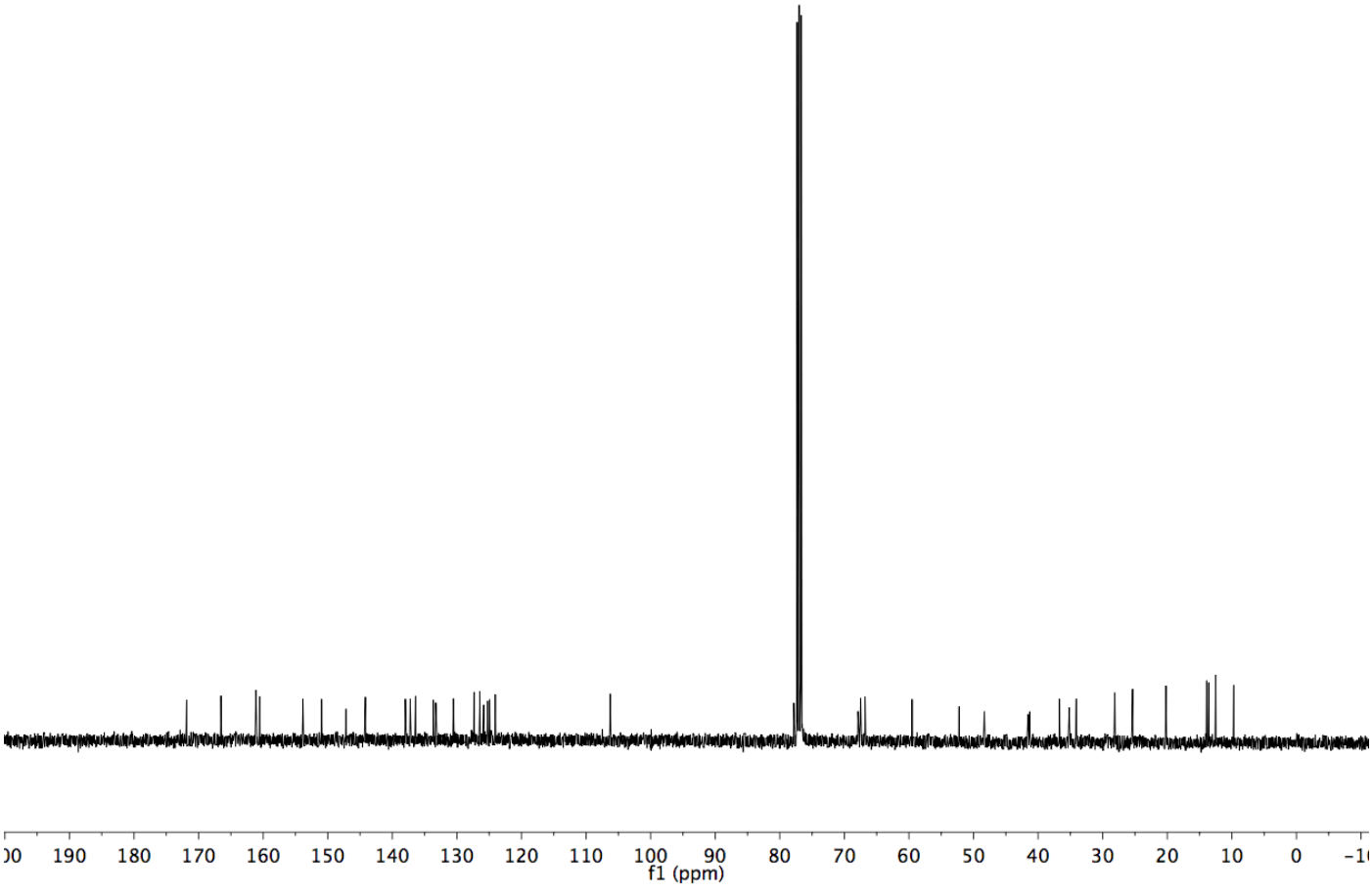
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

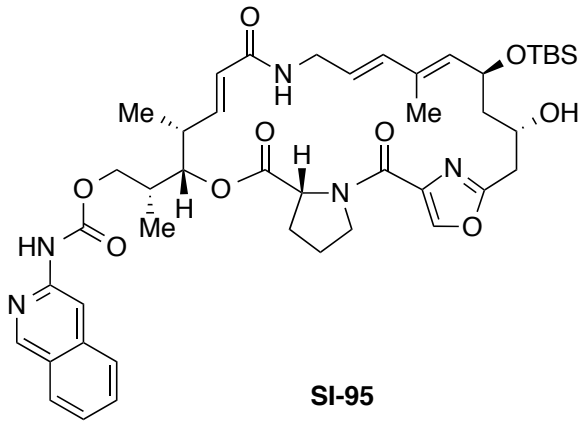

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



SI-94

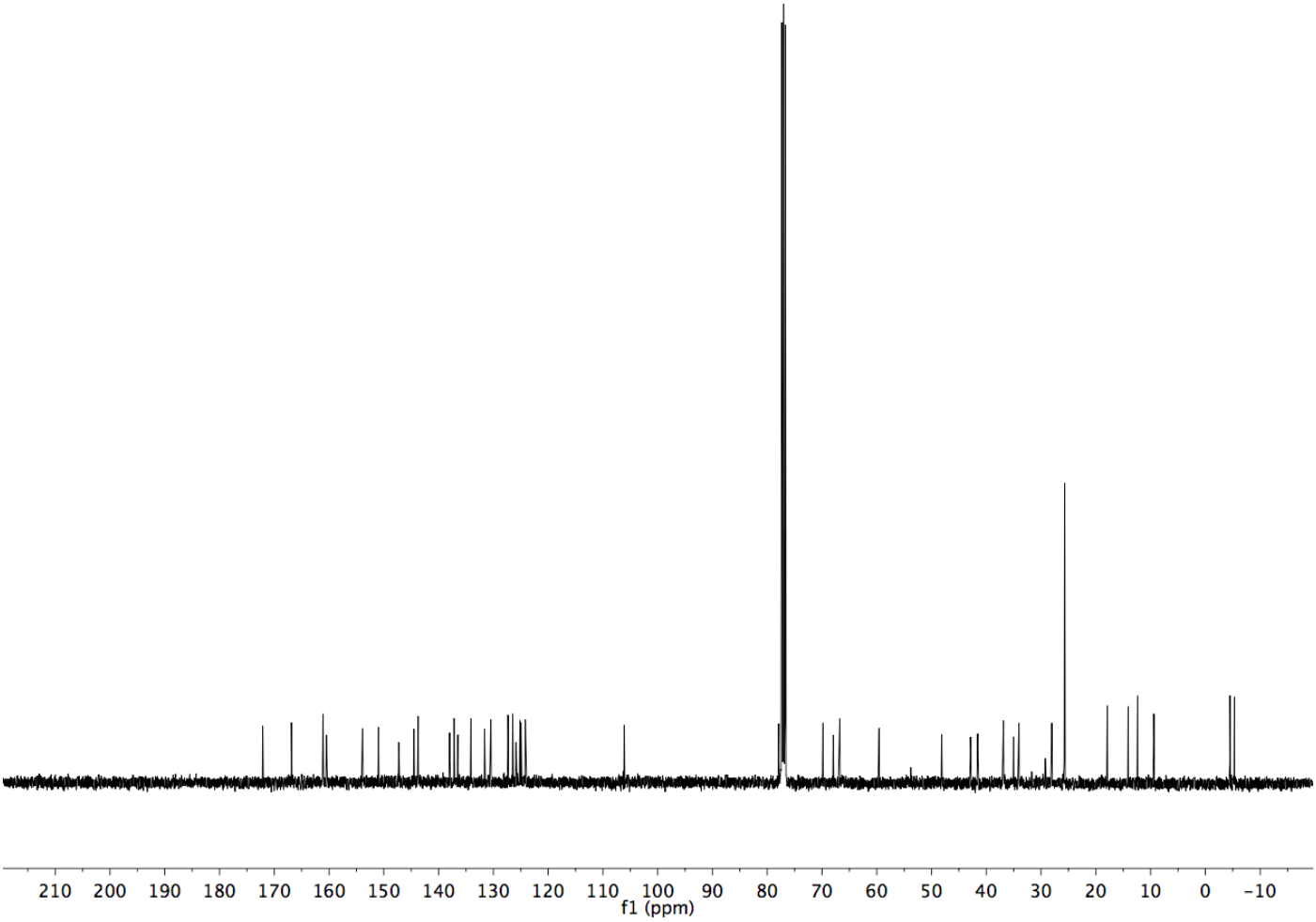

0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

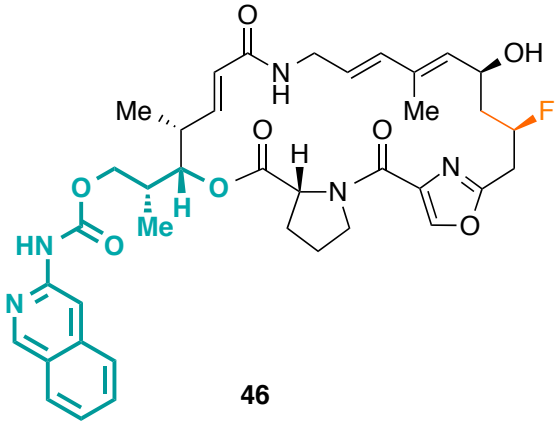

)0 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


O
N
H
OTBS
Me
Me
OH
O
O
H
O
N
O
H
Me
HN
O
N

SI-95

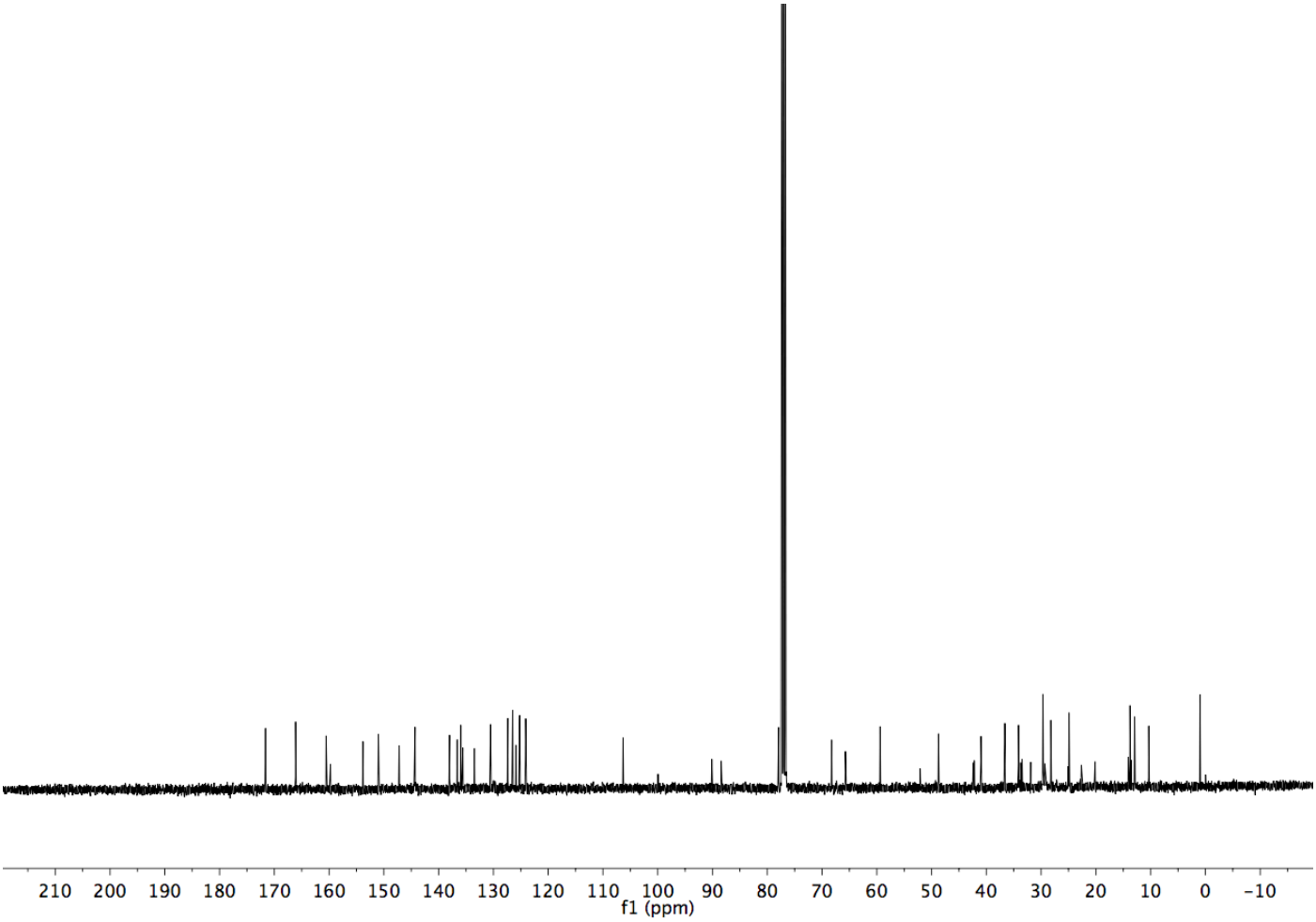
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

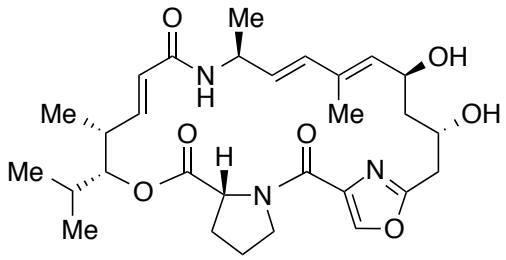

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
Me
F
O
H
O
N
O
N
O
O
Me
H
HN
O
N

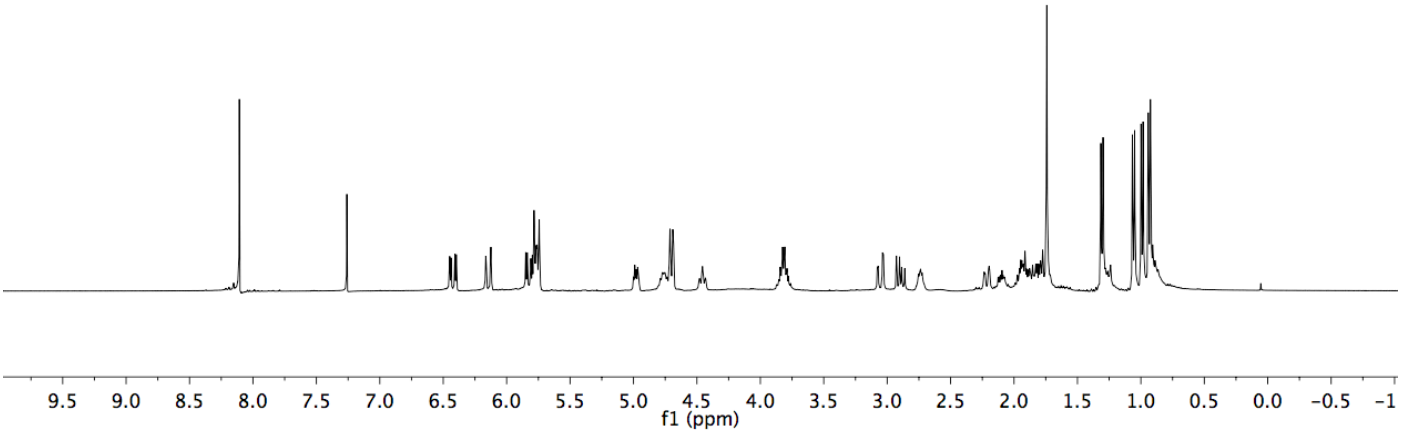
46

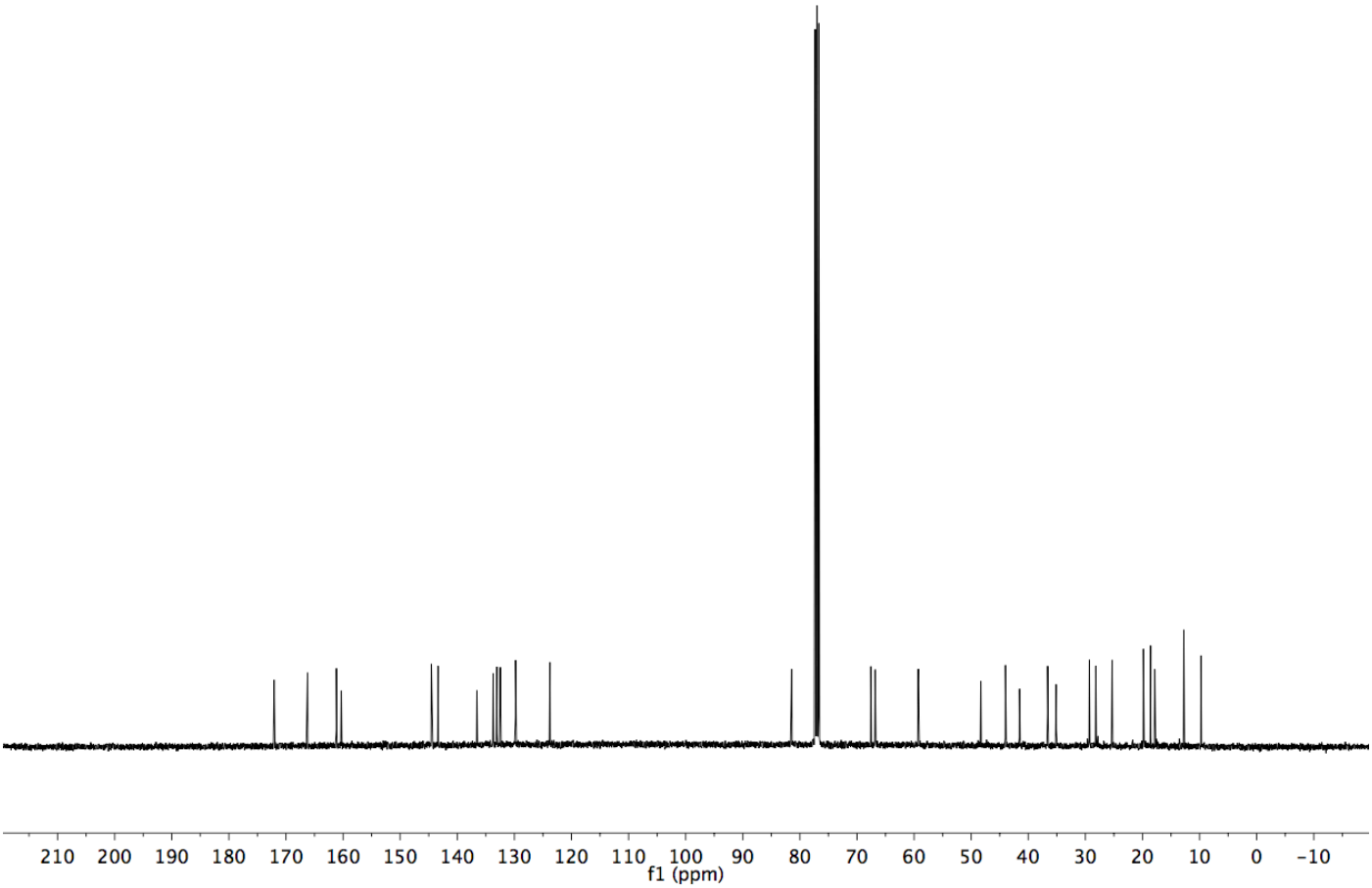
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

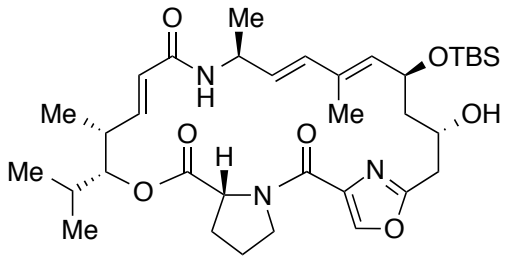

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OH
Me
Me
OH
O
H
O
Me
O
N
N
Me
O

SI-97

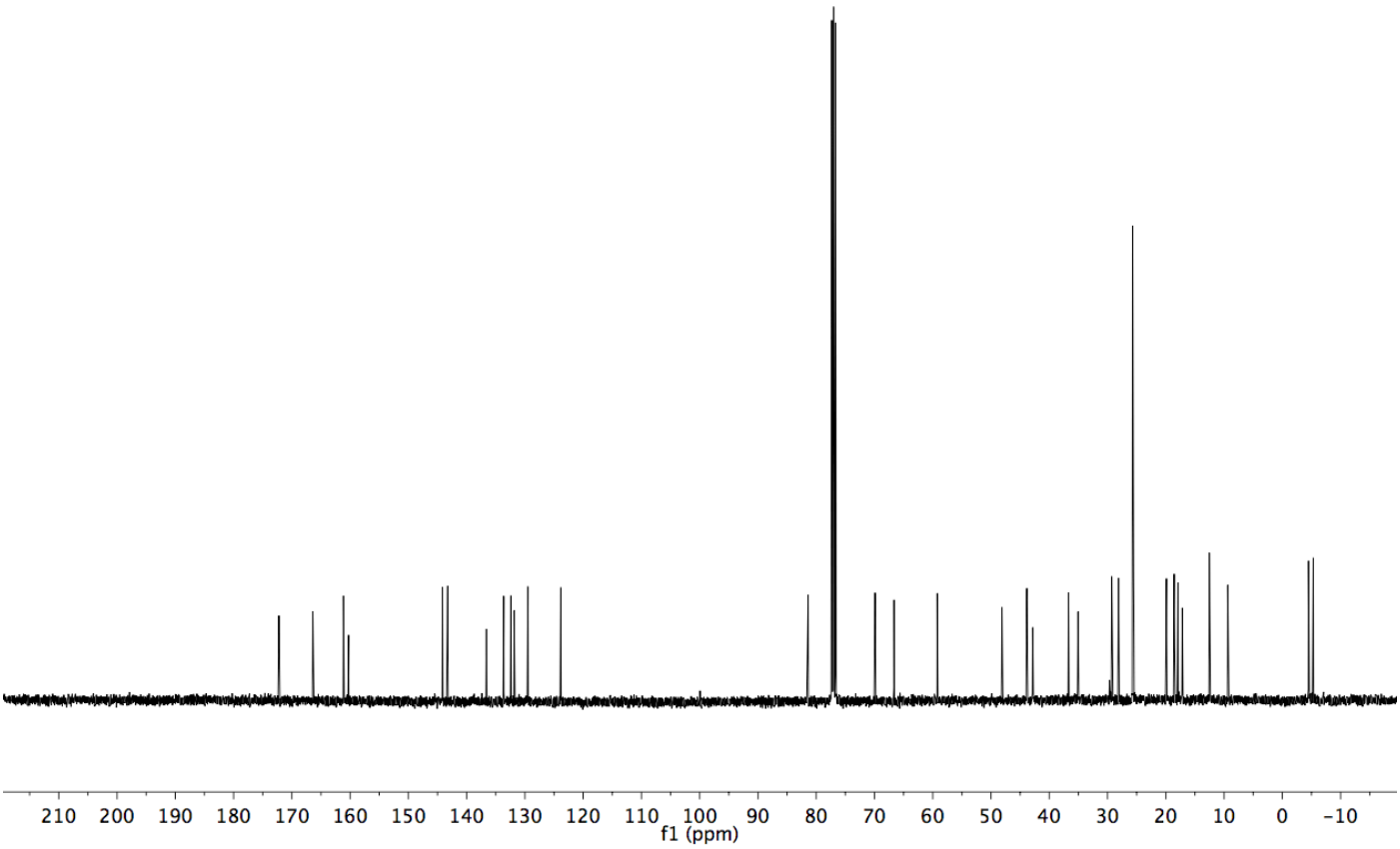

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

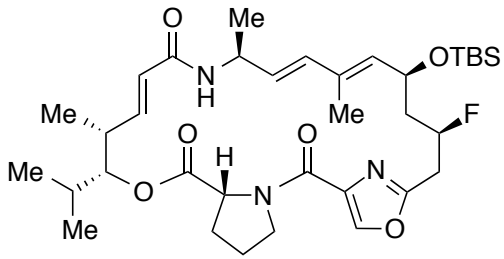

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OTBS
Me
Me
OH
O
H
O
Me
O
N
N
Me
O

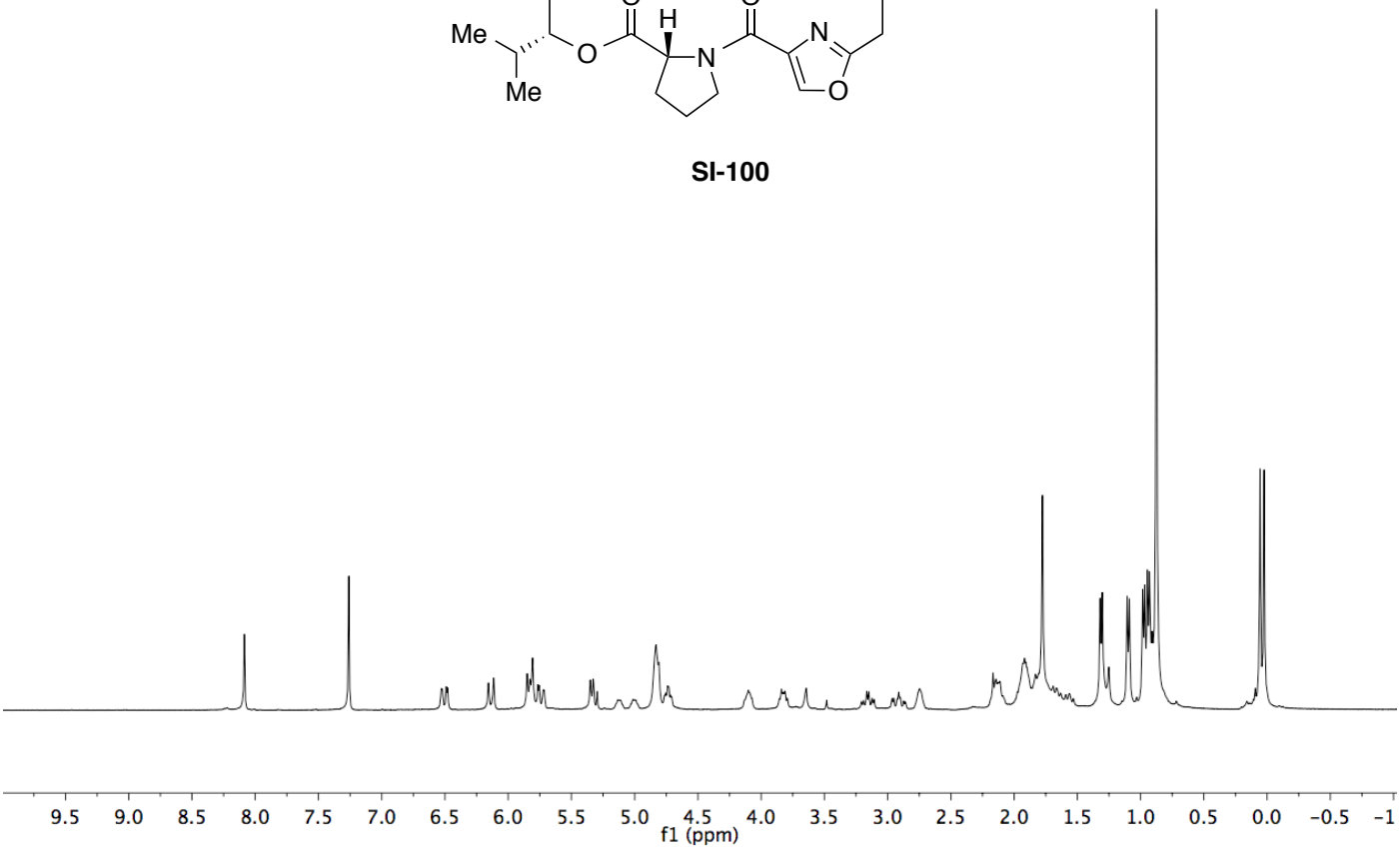
SI-98

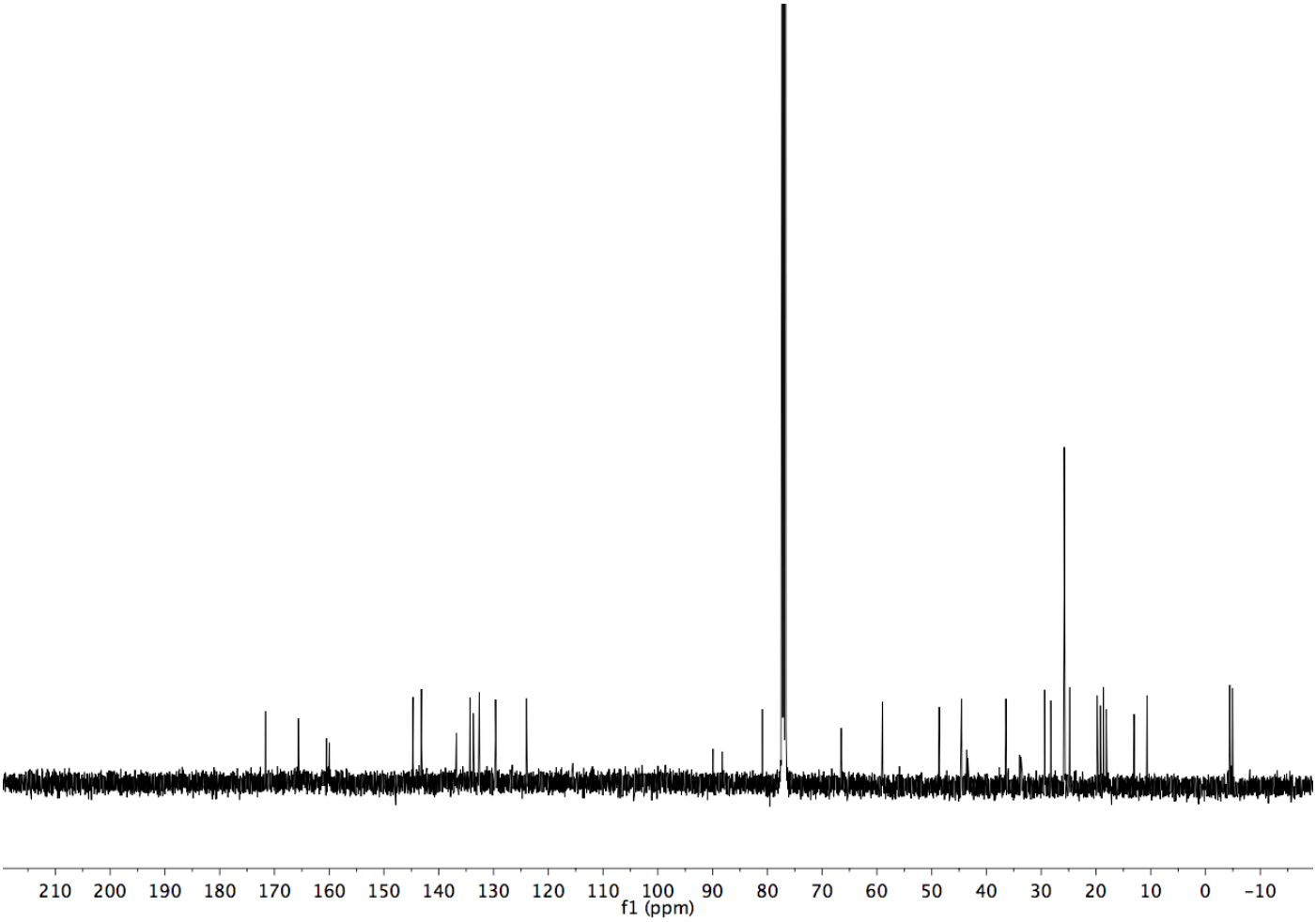
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

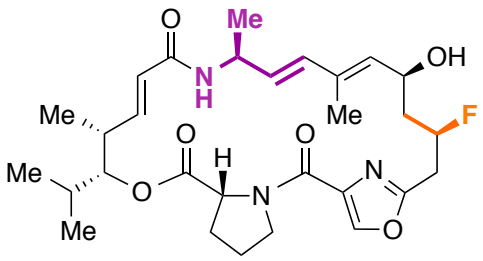

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OTBS
Me
Me
F
O
H
O
Me
O
N
N
Me
O

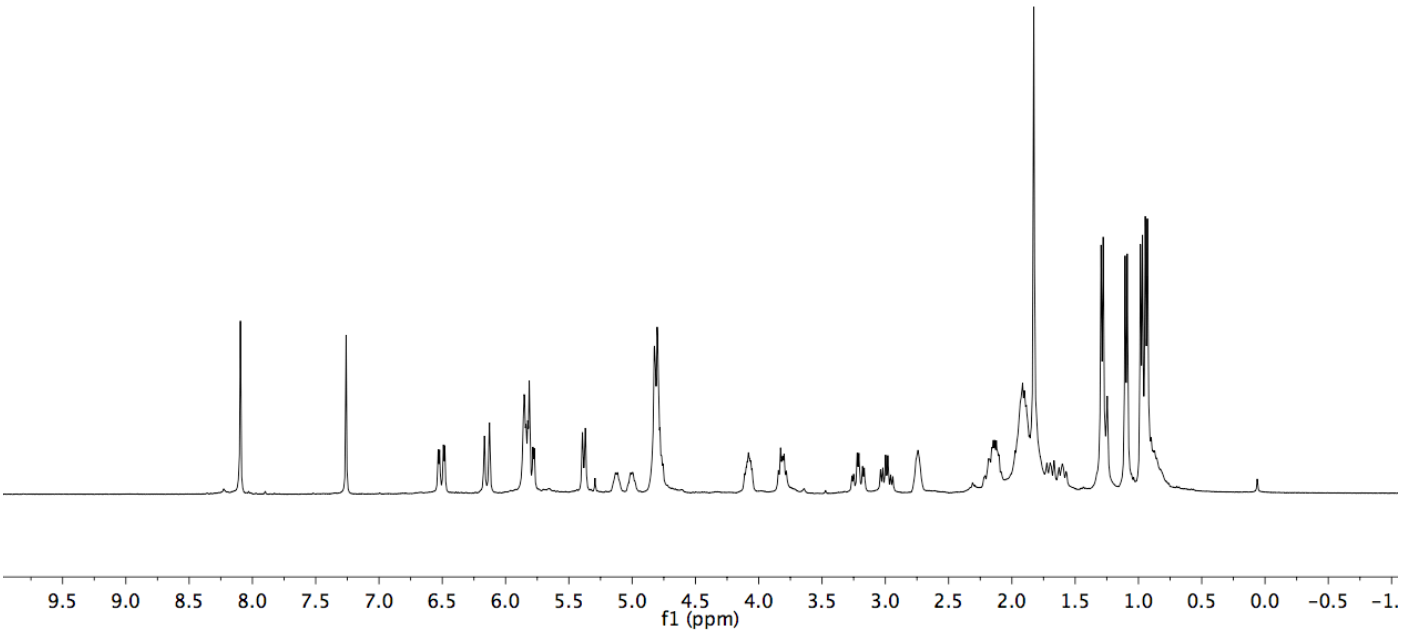
SI-100

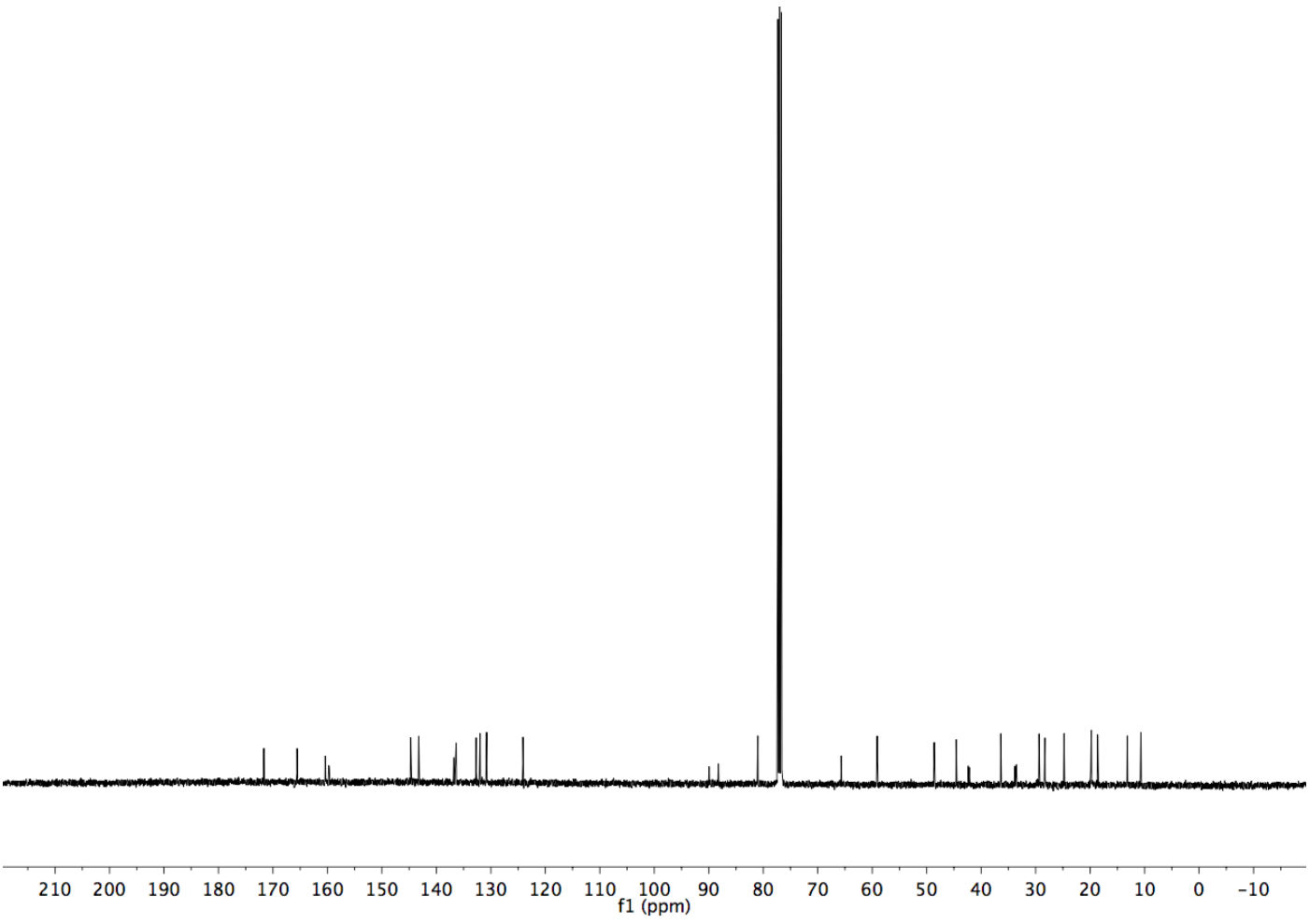

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

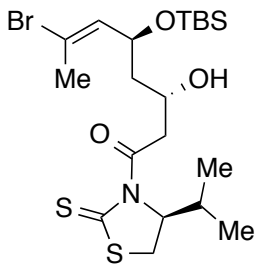

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
Me
N
H
OH
Me
Me
F
O
H
O
Me
O
N
N
Me
O

SI-99

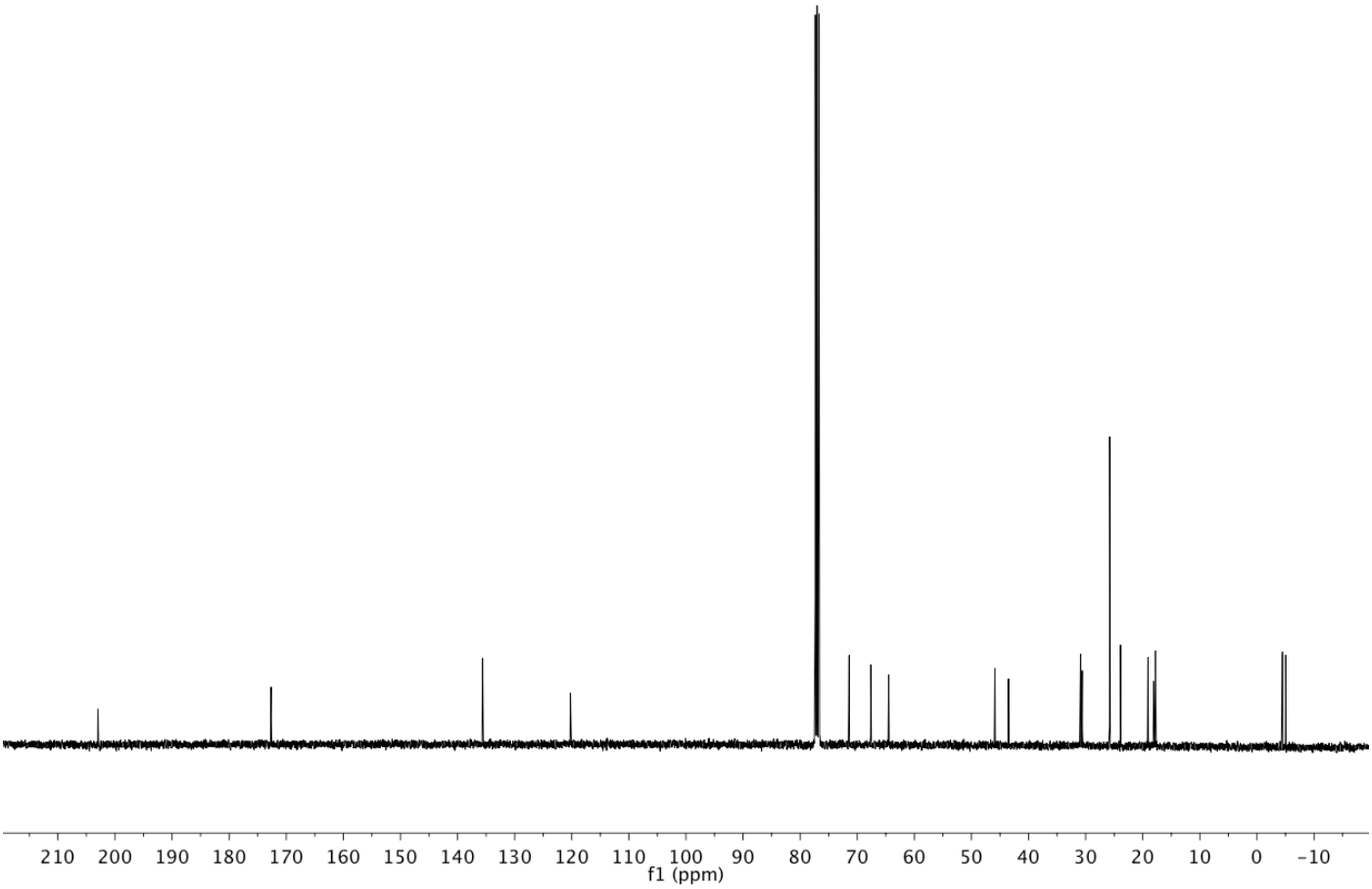

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

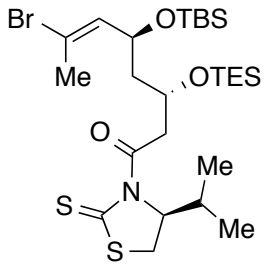

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
OH
O
Me
N
S
Me
S

SI-102

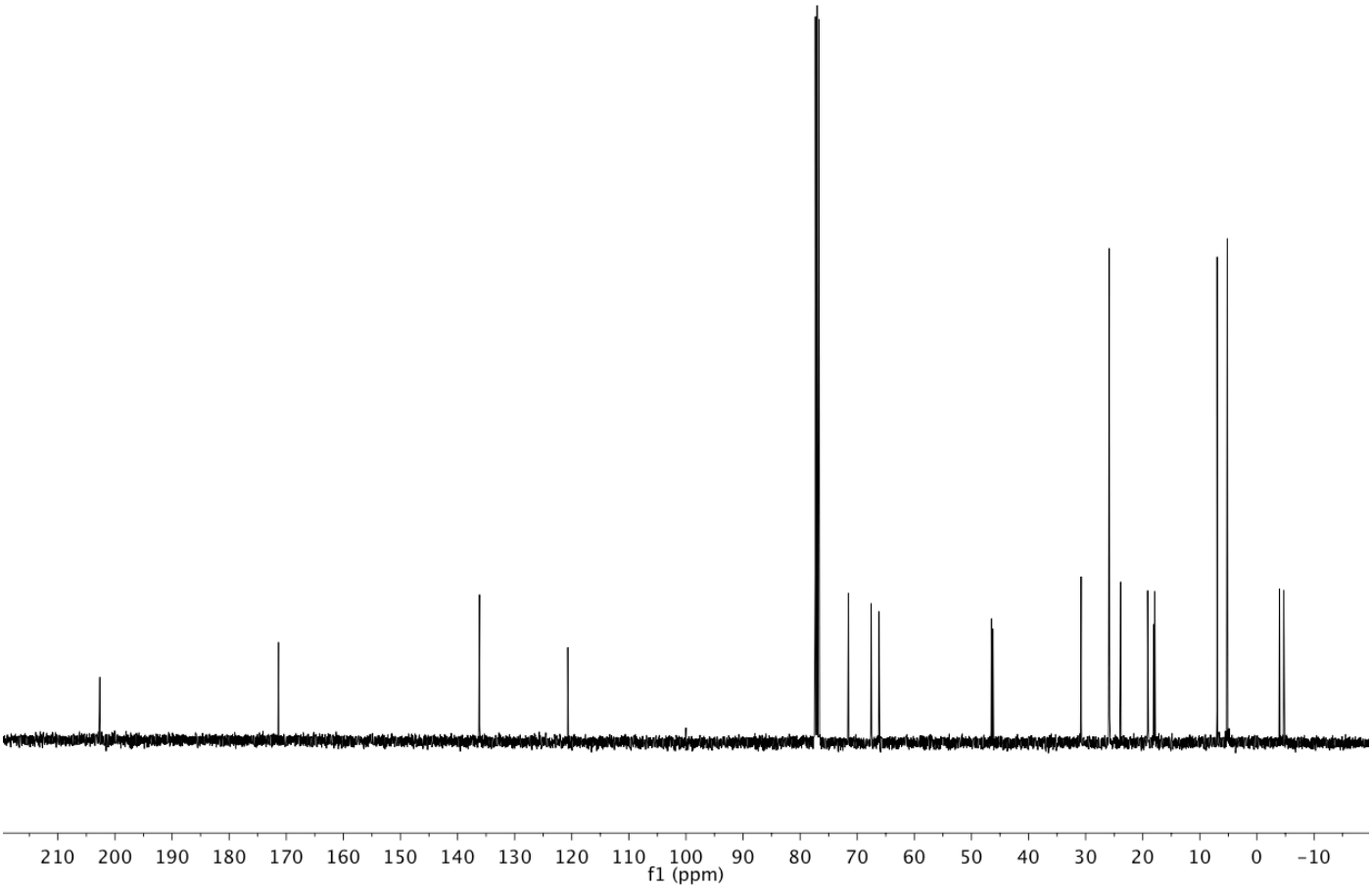
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

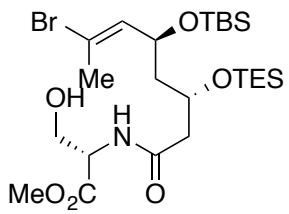

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
OTES
O
Me
N
S
Me
S

SI-103

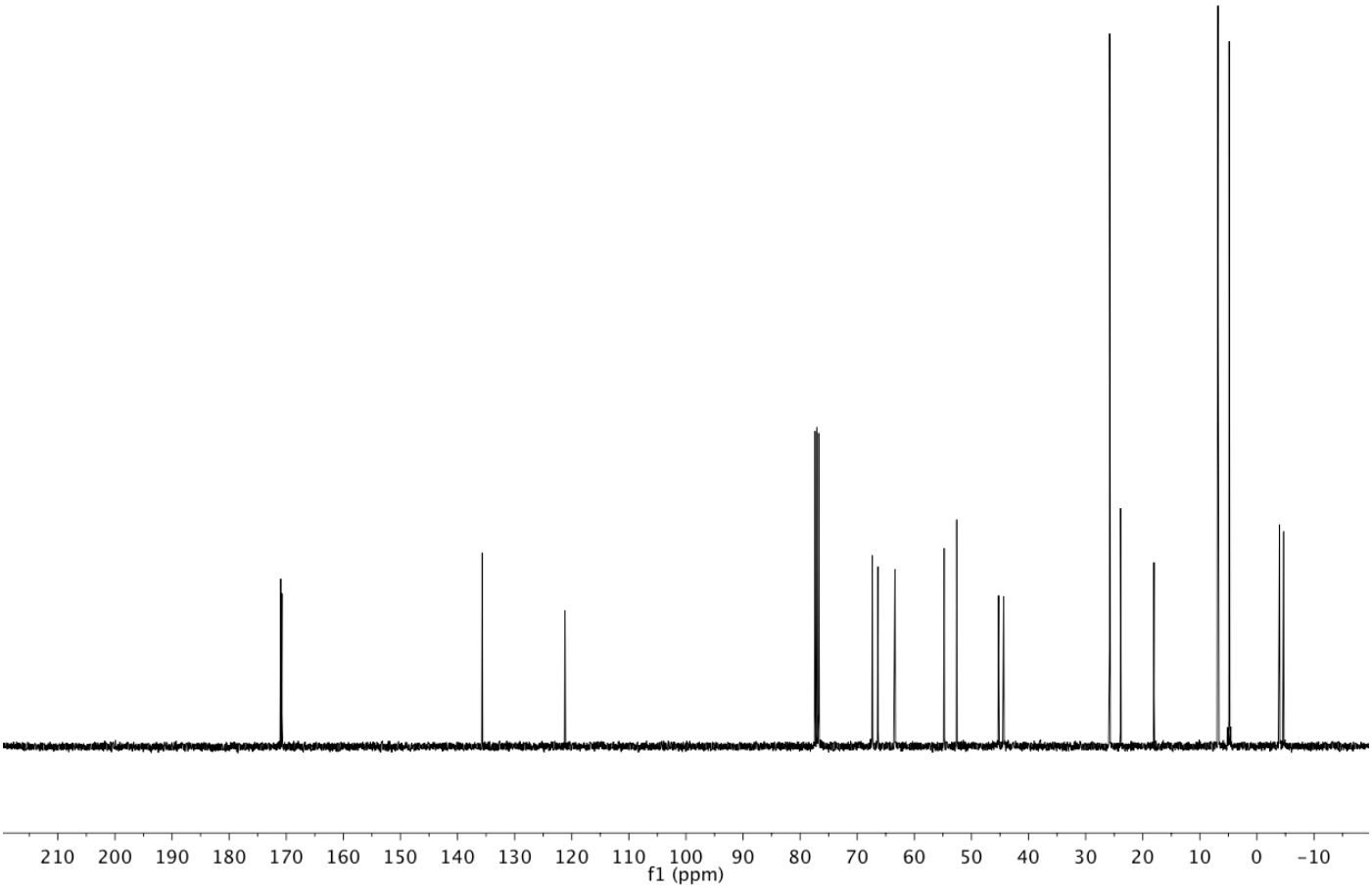
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

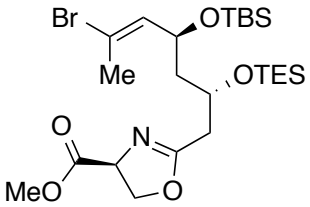

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
OTES
OH
H
N
MeO2C
O

SI-104

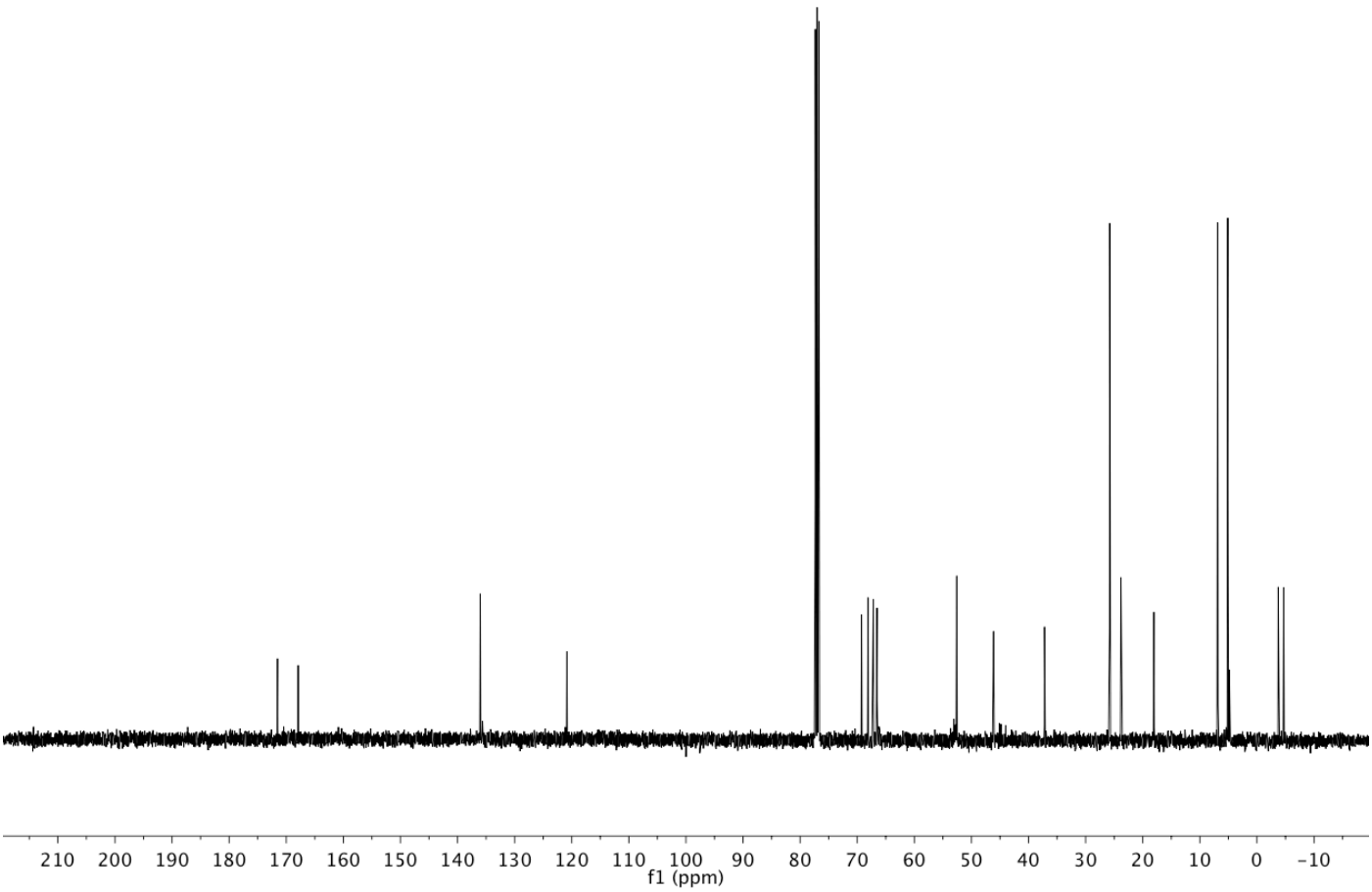
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

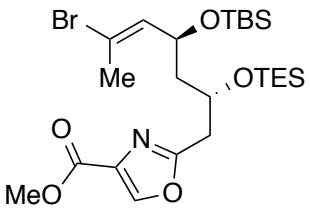

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
OTES
O
N
MeO
O

SI-105

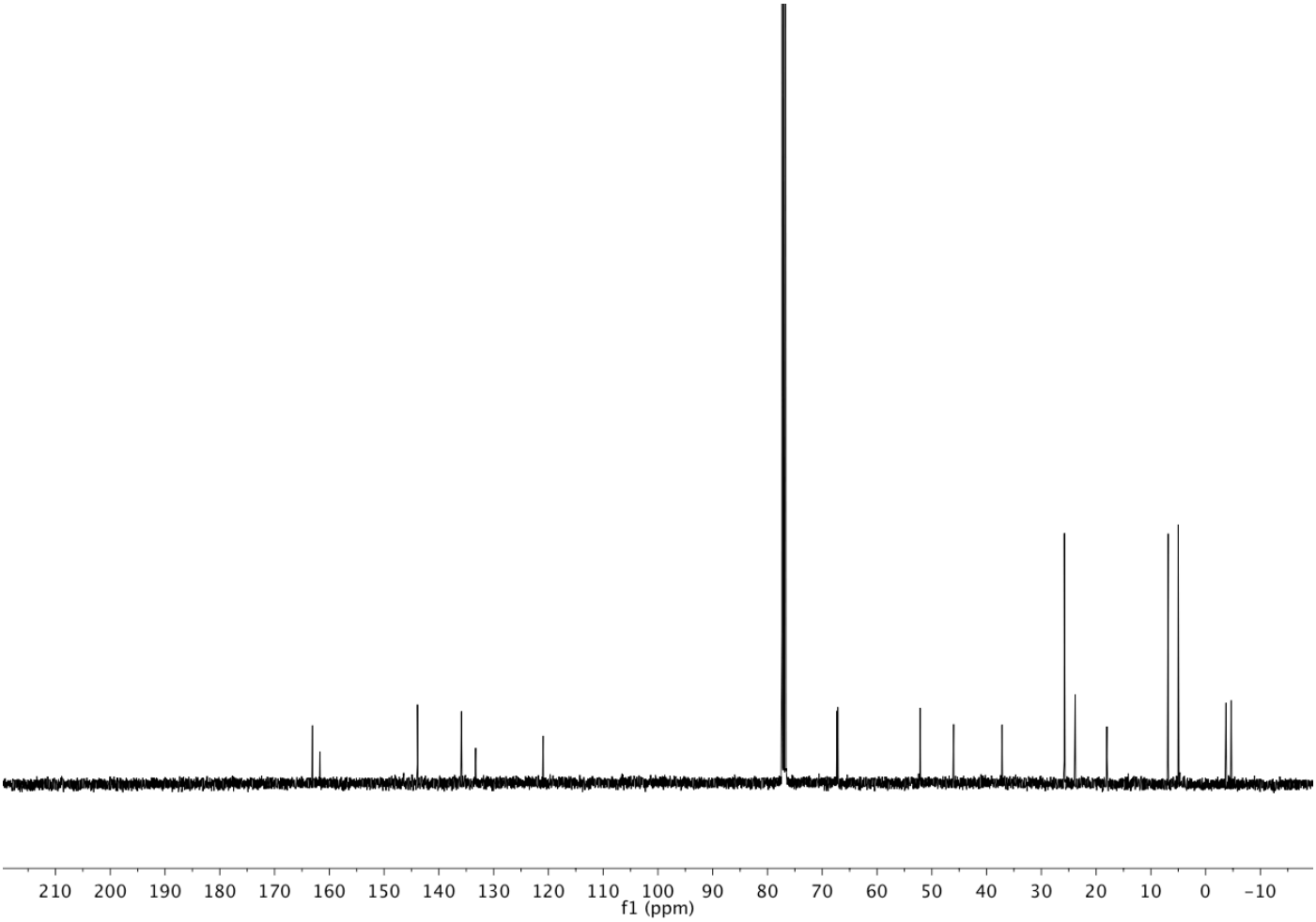
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

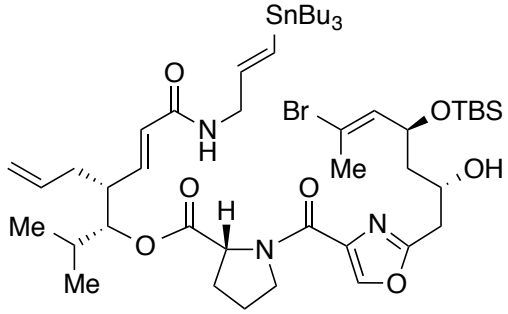

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
OTBS
Me
OTES
O
N
MeO
O

SI-106

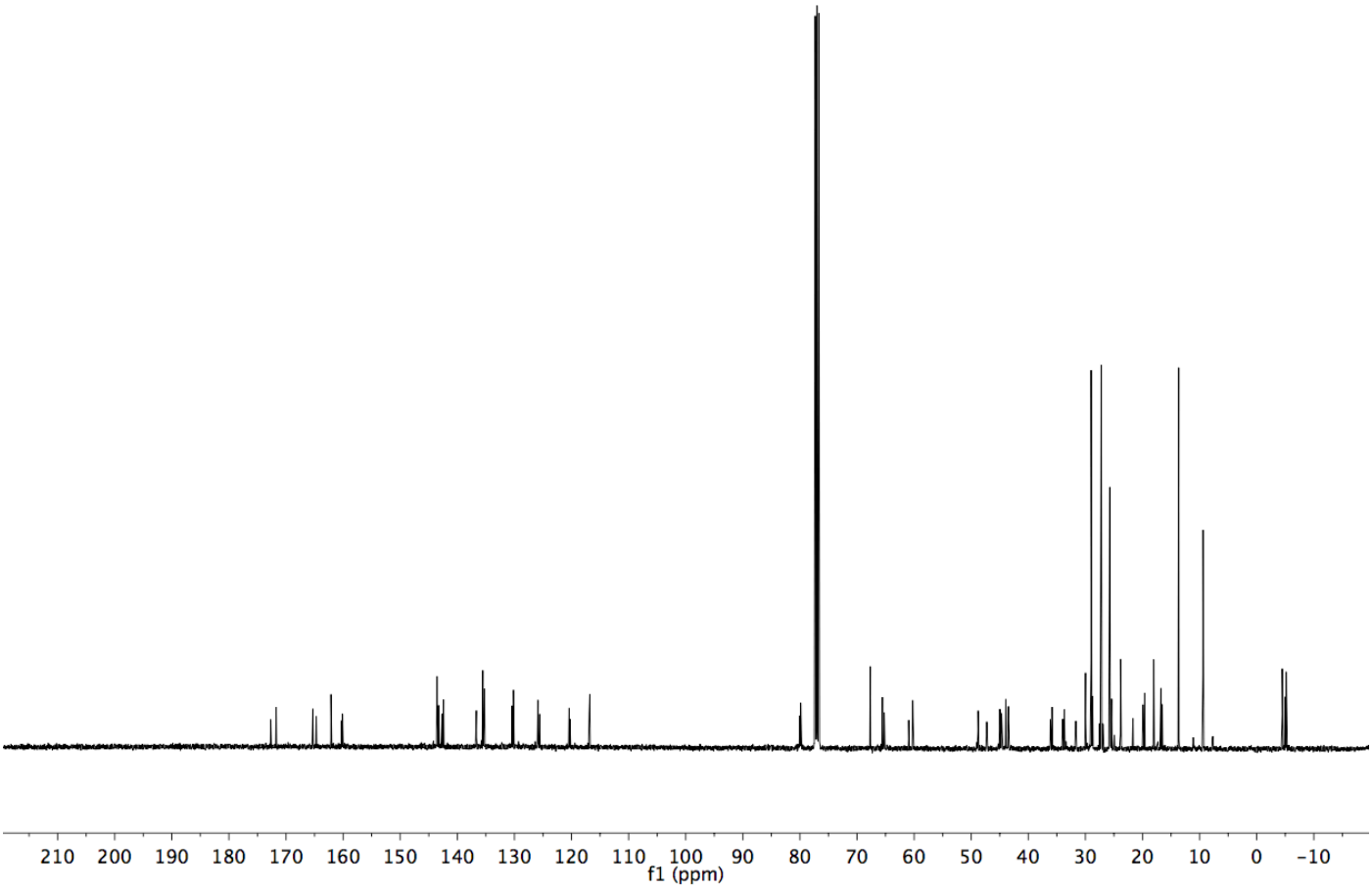
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

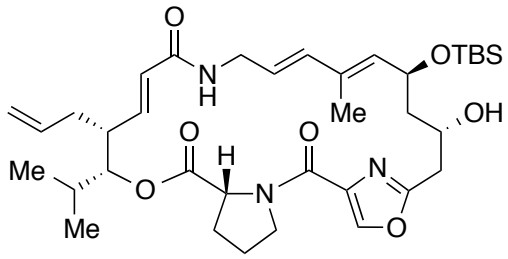

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


SnBu3
O
N
H
Br
OTBS
Me
OH
O
H
O
Me
O
N
N
O
Me

SI-108

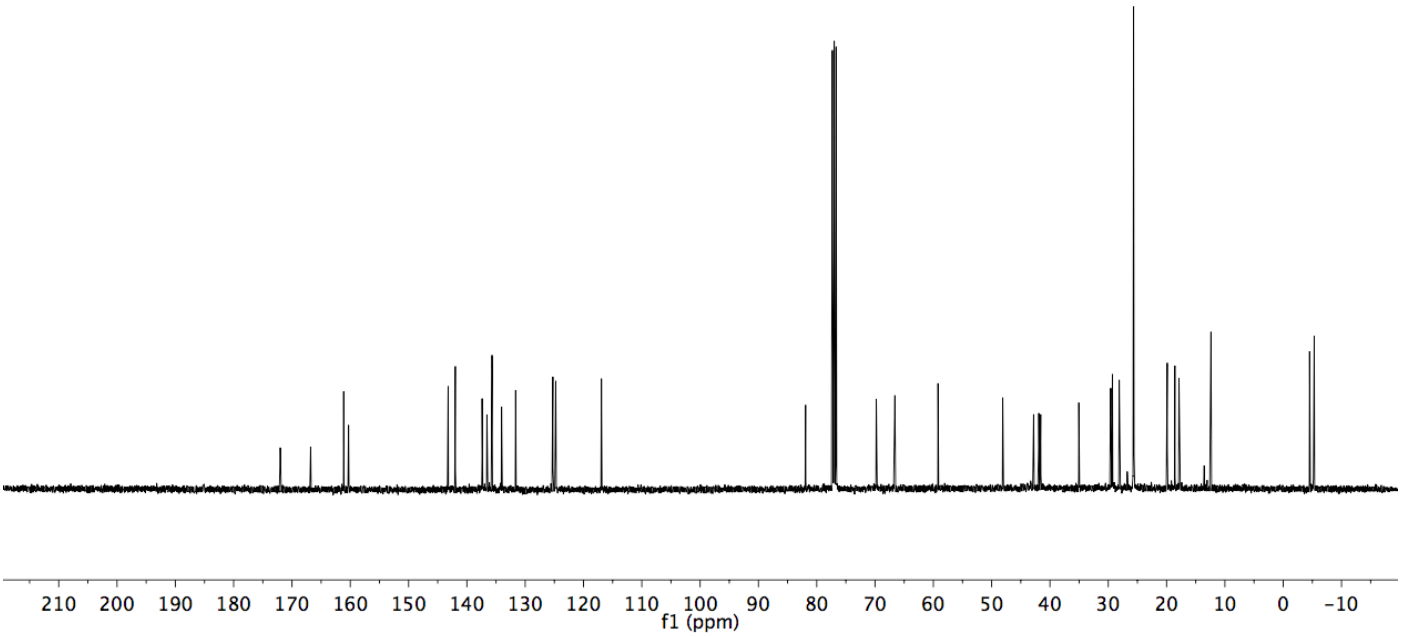
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

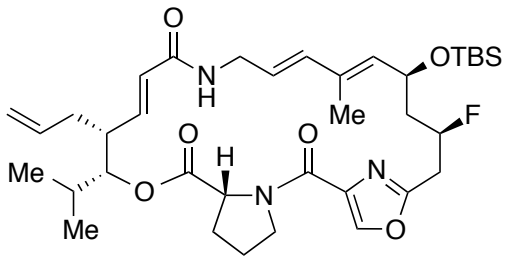

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
OH
O
H
O
Me
O
N
N
Me
O

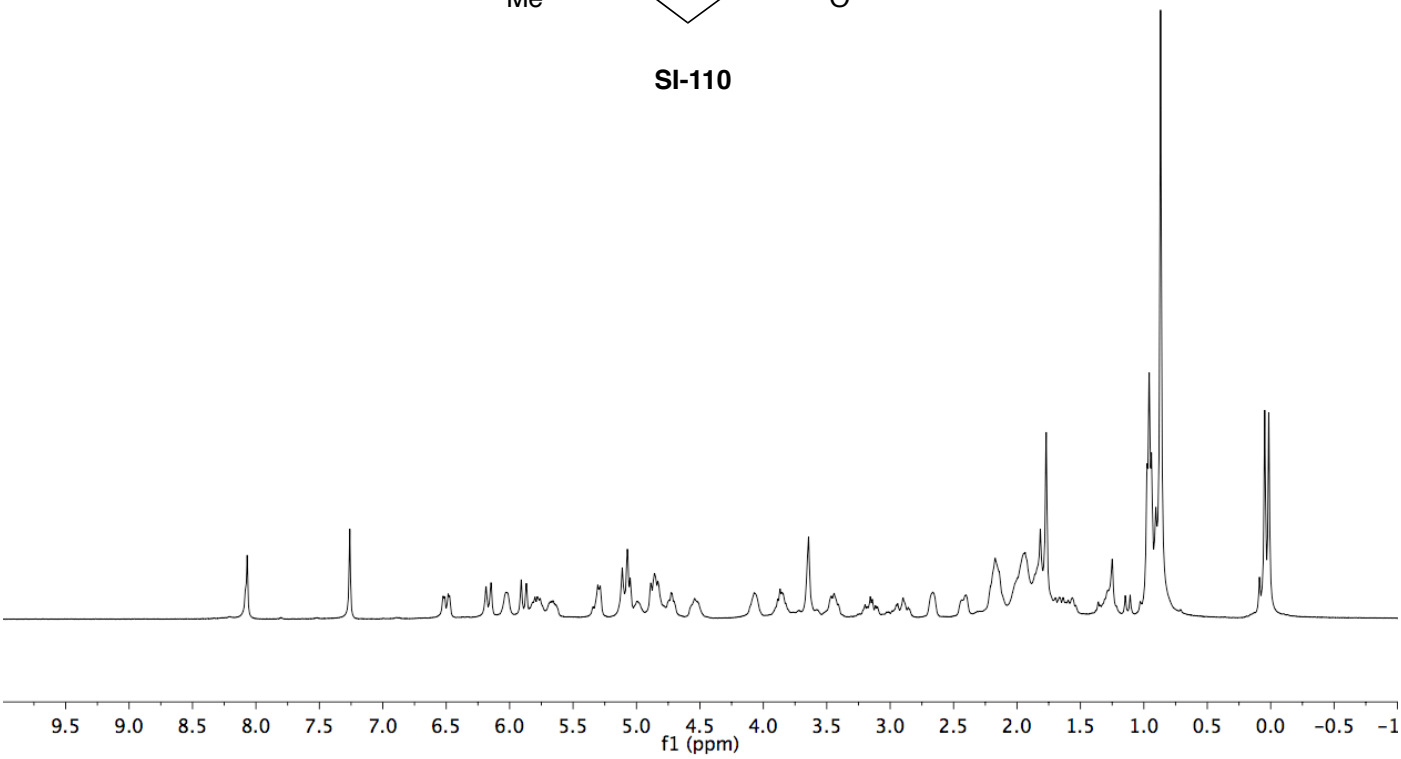
SI-109

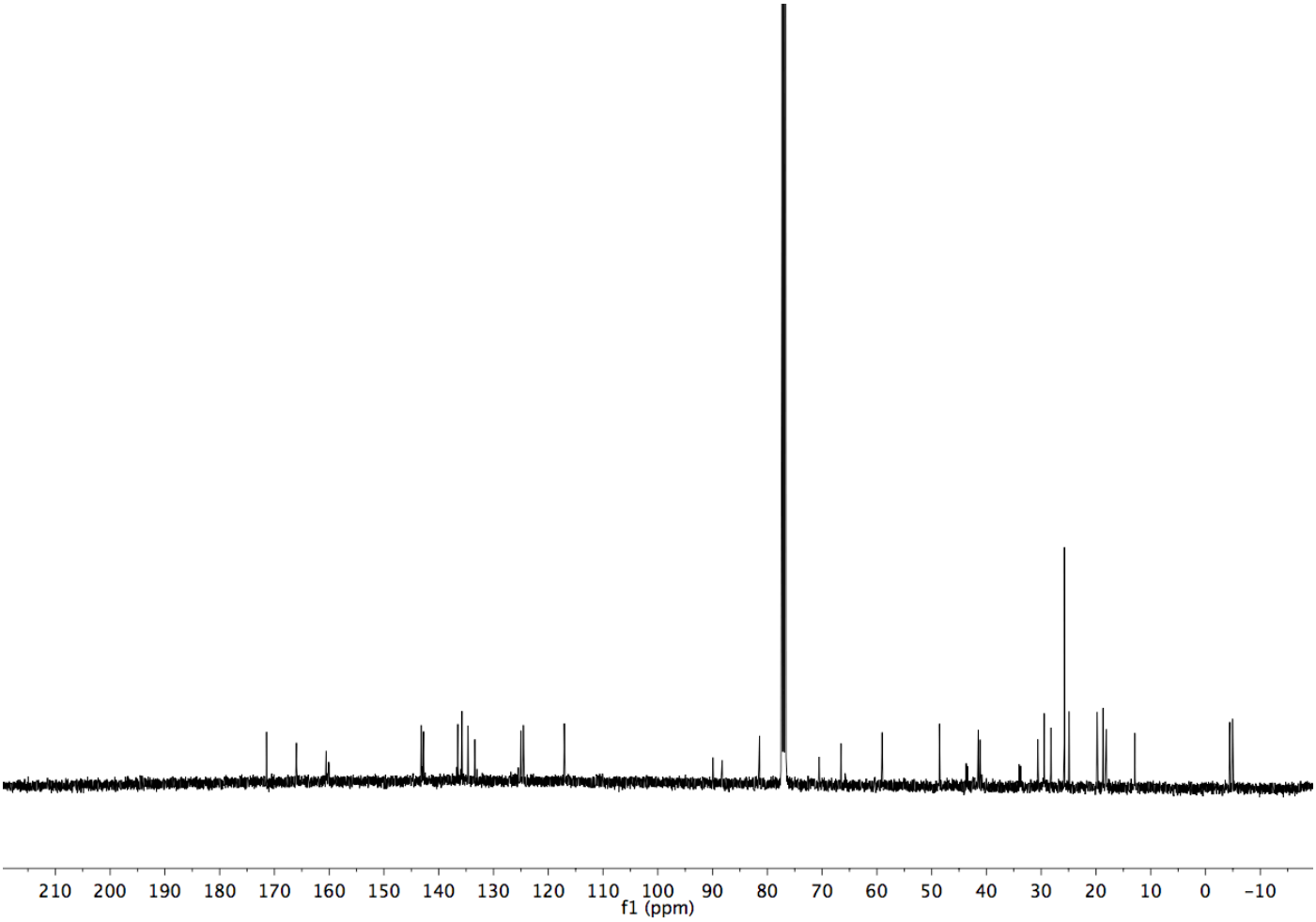
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

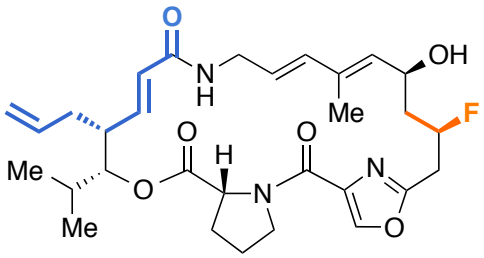

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OTBS
Me
F
O
H
O
Me
O
N
N
Me
O

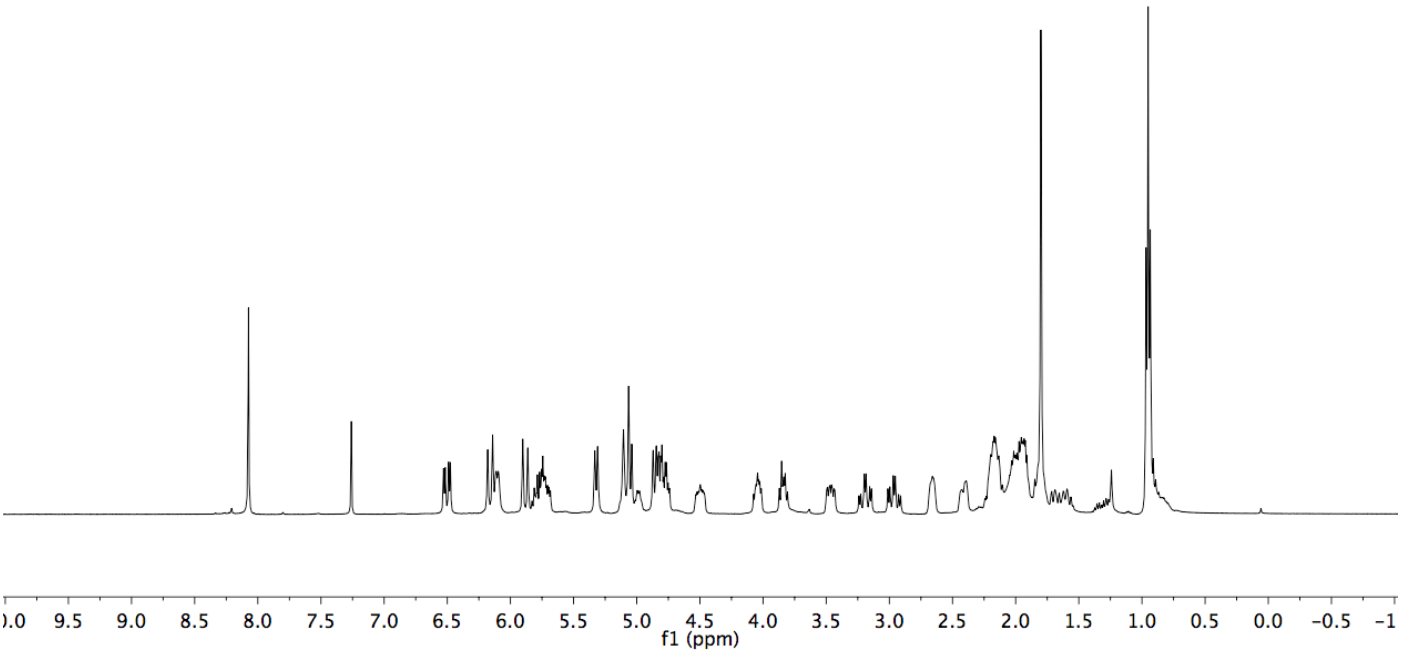
SI-110

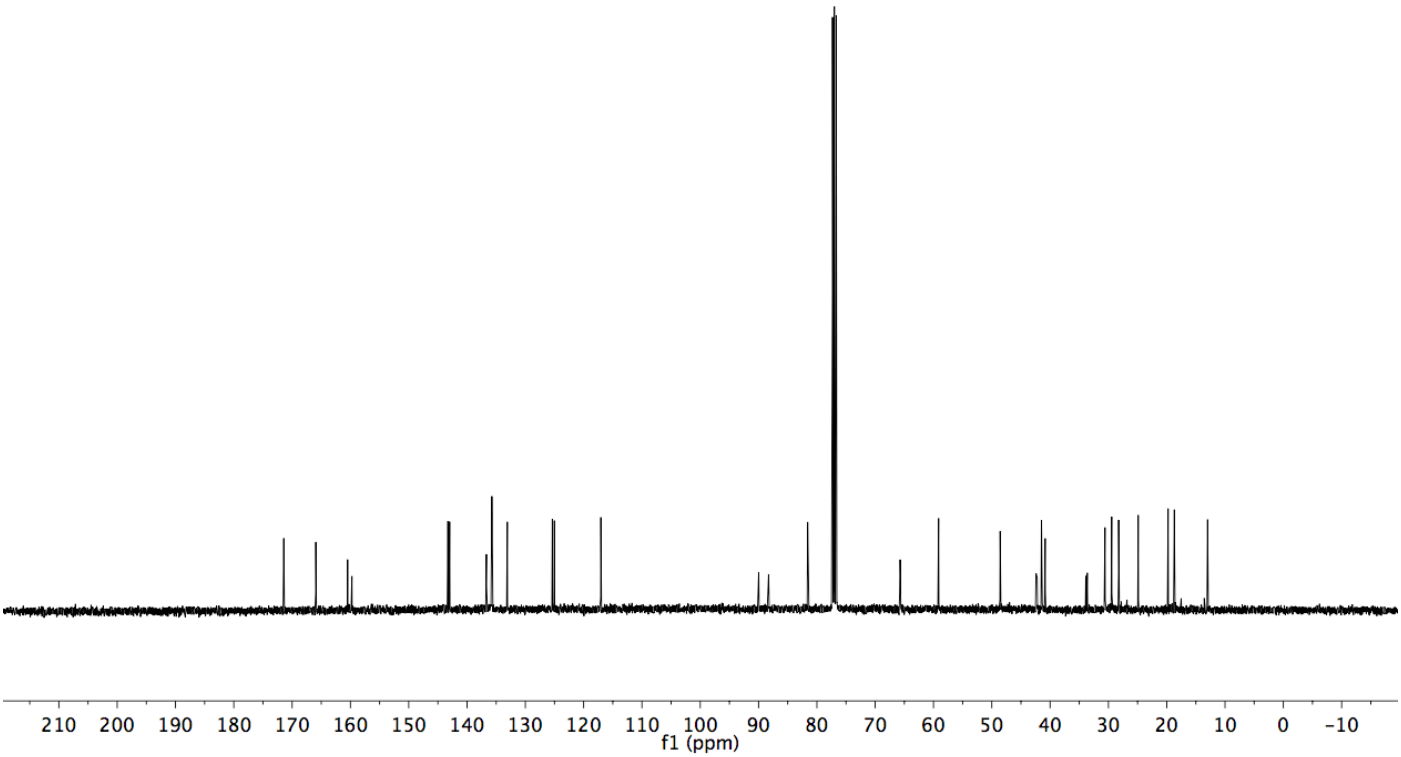

9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
N
H
OH
Me
F
O
H
O
Me
O
N
N
Me
O

47


9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)