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Electronic Supporting Information

Highly Efficient Synthesis of Maleimide-braced Peptide Macrocycles and Their Potential Anti-SARS-CoV-2 Mechanisms

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1. General information

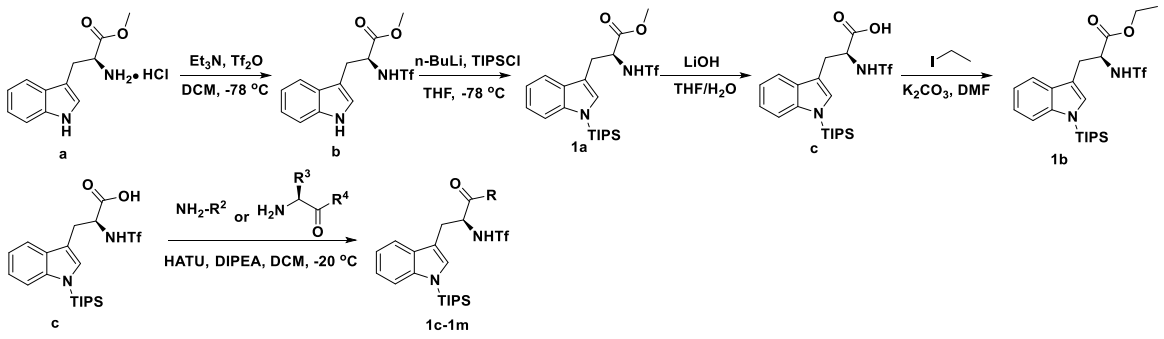
All reagents and solvents were purchased from commercial sources (J&K, Bidepharm, Sinopharm, Adamas-beta, etc.) and used as received without further purification. ^{1}H and ^{13}C nuclear magnetic resonance spectra (NMR) were acquired on a Bruker 400 MHz or 500 MHz or 600 MHz NMR spectrometer. Chemical shifts (δ) were expressed in ppm using tetramethylsilane as an internal reference and the coupling constants (J) were indicated in Hz. The coupling constants were described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), broad (br) or multiplet (m). LRMS data was tested on a Thermo Fisher Finnigan LTQ with Electrospray Ionization (ESI). HRMS data was obtained on an Agilent G6520 Q-TOF with Electrospray Ionization (ESI).

2. General experimental procedures

General procedure for Pd-catalyzed macrocyclization of peptide substrates

To a Shlenk tube was added **4** (0.1 mmol), $Pd(OAc)_2$ (20 mol%), $Cu(OAc)_2$ (0.2 mmol) and 1-adamantanecarboxylic acid (0.2 mmol) under air, and trifluoroethanol (TFE, 4 mL) was added subsequently. The resulting mixture was stirred at 100 ℃ for 12 h. After completion of the reaction, the mixture was filtered through a celite pad and washed with dichloromethane (10 mL × 3). The combined organic layer was concentrated under reduced pressure and the crude residue was purified by flash chromatography to give the desired product **5**.

2.1 General procedure for the synthesis of substrates (1a-1m)



A solution of compound **a** (0.10 mol) in CH_2Cl_2 (250 mL) at –78 ºC was treated with triethylamine (0.25 mmol) and trifluoromethanesulfonic anhydride (0.11 mmol) slowly. After stirring for 2 h at -78 °C, the mixture was quenched by the addition of saturated $NaHCO_3$ and then extracted with CH_2Cl_2 for three times. The combined organic layer was washed by brine (3 x 200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/ethyl acetate) to afford the desired product **b** (21.3 g, 61%).

A solution of compound **b** (50.0 mmol) in dry THF (250 mL) at –78 ºC was treated with 2.5 M n-BuLi (4.6 mL, 102.5 mmol) dropwise by syringe. The mixture was stirred at –78 ºC for 30 min before TIPSCl (40.0 mmol) was added. After stirring for 2 h at -78 °C, the mixture was quenched by the addition of aqueous NH_4Cl solution and then extracted with EtOAc for three times. The combined organic layer was washed by brine (3 x 200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/ethyl acetate) to afford the desired product **1a** (13.2 g, 52%).

A solution of compound **1a** (10.0 mmol) in THF (50 mL) and H_2O (25 mL) was treated with LiOH (20.0 mmol). After stirring at room temperature for 36 h, the reaction mixture was acidified to pH 6-7 by slow addition of aqueous 1N HCl in ice bath and extracted with EtOAc for three times. The combined organic layer was washed by brine (3 x 200 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/ethyl acetate) to afford the desired product **c** (8.5 g, 86%).

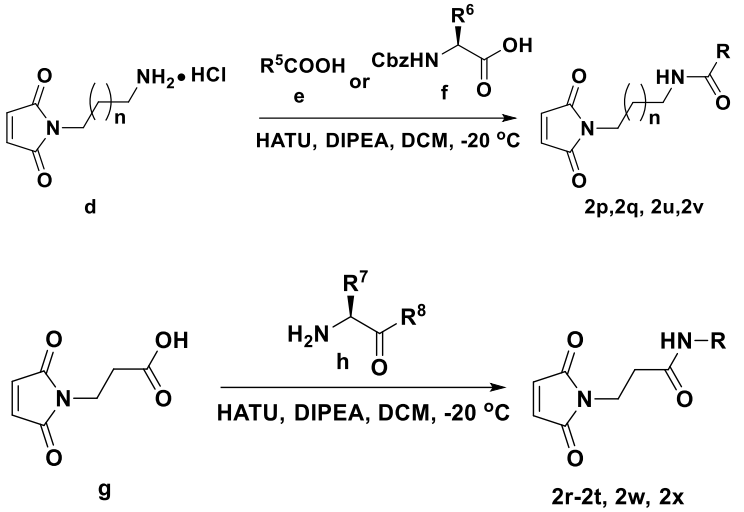
Compound **c** (0.50 mmol) was dissolved in DMF (10 mL) in a round bottom flask, alkyl iodide (0.60 mmol) and K_2CO_3 (0.75 mmol) were then added to the reaction mixture, and the mixture was stirred at room temperature for 12h. Afterwards, the mixture was diluted with EtOAc (60 mL), the mixture was washed by brine (3 x 30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/ethyl acetate) to afford the desired product (**1b**).

Compound **c** (0.50 mmol) was dissolved in CH_2Cl_2 (15 mL) in a round bottom flask at –20 ºC, to the mixture was added DIPEA (1.5 mmol), HATU (0.75 mmol) and substituted amine or C-protected amino acid (0.65 mmol), and the reaction mixture was stirred at –20 ºC overnight. Afterwards, the mixture was diluted with CH_2Cl_2 (30 mL), the mixture was successively washed with water (30 mL), 1N HCl (30 mL), saturated $NaHCO_3$ (30 mL) and brine (30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the desired product (**1c-1m**).

2.2 General procedure for the synthesis of dipeptides

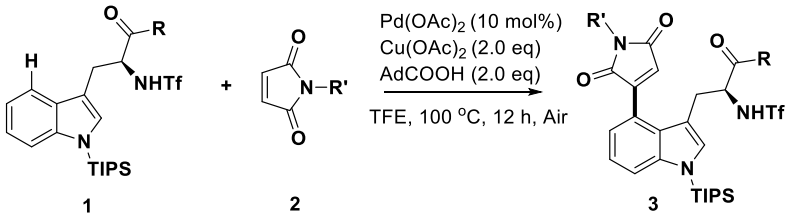
The *N*-protected amino acid (2.0 mmol) and C-protected amino acid (2.6 mmol) were dissolved in CH_2Cl_2 (30 mL) in a round bottom flask at –20 ºC, to the mixture was added DIPEA (6.0 mmol), HATU (3.0 mmol), and the reaction mixture was stirred at –20 ºC overnight. Afterwards, the mixture was diluted with CH_2Cl_2 (50 mL), the mixture was successively washed with water (40 mL), 1N HCl (40 mL), saturated $NaHCO_3$ (40 mL) and brine (40 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the desired dipeptides.

2.3 General procedure for the synthesis of substrates (2p-2x)



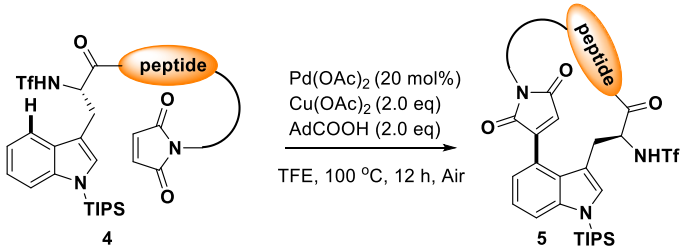
Compound **e** or **f** or **g** (2.0 mmol) and compound **d** or **h** (2.6 mmol) were dissolved in CH_2Cl_2 (30 mL) in a round bottom flask at –20 ºC, to the mixture was added DIPEA (6.0 mmol), HATU (3.0 mmol), and the reaction mixture was stirred at –20 ºC overnight. Afterwards, the mixture was diluted with CH_2Cl_2 (50 mL), the mixture was successively washed with water (40 mL), 1N HCl (40 mL), saturated $NaHCO_3$ (40 mL) and brine (40 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography to afford the desired product (**2p-2x**).

2.4 General procedure for late-stage C–H alkenylation on tryptophan and tryptophan containing peptides



To a Shlenk tube was added **1** (0.1 mmol), **2** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (0.2 mmol) and AdCOOH (0.2 mmol) under air, and trifluoroethanol (TFE, 2 mL) was added subsequently. The resulting mixture was stirred at 100 ℃ for 12 h. After completion of the reaction, the mixture was filtered through a celite pad and washed with DCM (10 mL × 3). The combined organic layer was concentrated under reduced pressure and the crude residue was purified by flash chromatography to give the desired product **3**.

2.5 General procedure for Pd-catalyzed macrocyclization of peptide substrates



To a Shlenk tube was added **4** (0.1 mmol), $Pd(OAc)_2$ (20 mol%), $Cu(OAc)_2$ (0.2 mmol) and AdCOOH (0.2 mmol) under air, and trifluoroethanol (TFE, 4 mL) was added subsequently. The resulting mixture was stirred at 100 ℃ for 12 h. After completion of the reaction, the mixture was filtered through a celite pad and washed with DCM (10 mL × 3). The combined organic layer was concentrated under reduced pressure and the crude residue was purified by flash chromatography to give the desired product **5**.

2.6 Gram-scale experiment for the synthesis of 3aa.

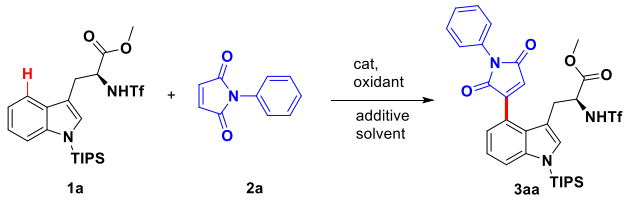
To a 250 mL round bottom flask was added **1a** (1.01 g, 2.0 mmol), **2a** (690.4 mg, 4.0 mmol), $Pd(OAc)_2$ (44.9 mg, 0.2 mmol), $Cu(OAc)_2$ (726.4 mg, 4.0 mmol) and AdCOOH (720.8 mg, 4.0 mmol) under air, and trifluoroethanol (40 mL) was added subsequently. The resulting mixture was stirred at 100 ℃ for 12 h. After completion of the reaction, the mixture was filtered through a celite pad and washed with DCM (50 mL × 3). The organic layer was collected and concentrated under vacuum to yield the crude product which was further purified by flash chromatography eluting with Hexane/EA to afford the pure desired product **3aa** (0.96 g, 71% yield).

3. Optimization of the reaction conditions

The TIPS-protected tryptophan was used as the substrate because this bulky group can enhance the site selectivity at the Trp C4 position by blocking the C-H activation at C2 position. We commenced our study with a comprehensive exploration of the reaction parameters. Initially, Trp (**1a**) and maleimide (**2a**) were mixed in 1,2-dichloroethane (DCE) in the presence of $Pd(OAc)_2$ (20 mol%) and $Cu(OAc)_2$ (2.0 equiv), and the resulting mixture was stirred at 100°C for 12 h. We were pleased to find that the desired compound **3aa** could be isolated in 11% yield (Table S1, entry 1), and its structure was further verified by X-ray crystallography. In order to improve the yield of **3aa**, a series of oxidants, including a multiple of Cu(II) or Ag(I) salt, was independently screened at first. However, the results revealed that only $Cu(OAc)_2$ could trigger the reaction (Table S1, entries 2 - 9). In contrast, the desired product **3aa** could be isolated in low yield or even in trace yield when treated with other Pd(II) catalyst or pre-catalyst (Table S1, entries 10–12). To further explore the optimal reaction conditions, we subsequently investigated different solvents. Among all the selected solvents, **3aa** could be attained in $PhCF_3$ or THF with limited yield (Table S1, entries 13 and 14). However, when treated with 2,2,2-trifluoroethanol

(TFE), the desired compound **3aa** was afforded with an isolated yield of 46% (Table S1, entry 15). To further promote the conversion of the reaction, we next explored various additives; the results indicated that addition of AcOH could further improve the yield of **3aa** to 62% (Table S1, entry 25). On the contrary, the yield of **3aa** was diminished to 38% when $NaHCO_3$ was added (Table S1, entry 26). In later studies, more protic acids were investigated (Table S1, entry 27–32) and it was demonstrated that 1-adamantanecarboxylic acid (AdCOOH) was the optimal additive that could well promote the transformation by attaining the desired product in 73% isolated yield (Table S1, entry 27). Additionally, when investigating the loading of $Pd(OAc)_2$ (Table S1, entries 37 and 38), we were delighted to find that 10 mol% of the Pd(II) salts resulted in a comparable yield of **3aa** (77%, Table 1, entry 38). Therefore, the optimal condition for this transformation is $Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (2.0 equiv), and AdCOOH (2.0 equiv) in TFE at 100°C for 12 h in air.

Table S1. The optimization of the reaction conditions[a]



entry	catalyst (mol%)	oxidant (2.0 equiv)	additive (2.0 equiv)	solvent	temp	yield[b] (%)
1	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	DCE	100	11%
2	$Pd(OAc)_2$ (20)	AgOAc	-	DCE	100	N.R.
3	$Pd(OAc)_2$ (20)	Ag_2O		DCE	100	N.R.
4	$Pd(OAc)_2$ (20)	$Cu(AcAc)_2$	-	DCE	100	trace
5	$Pd(OAc)_2$ (20)	$Cu(OTf)_2$	-	DCE	100	N.R.
6	$Pd(OAc)_2$ (20)	Ag_2CO_3	-	DCE	100	N.R.
7	$Pd(OAc)_2$ (20)	$AgSbF_6$	-	DCE	100	N.R.
8	$Pd(OAc)_2$ (20)	$AgBF_4$	-	DCE	100	N.R.
9	$Pd(OAc)_2$ (20)	AgOTf	-	DCE	100	N.R.
10	$Pd(PhCN)_2Cl_2$(20)	$Cu(OAc)_2$	-	DCE	100	8%
11	$P(Cy_3)$Pd G3 (20)	$Cu(OAc)_2$		DCE	100	N.R.
12	XPhos Pd G2(20)	$Cu(OAc)_2$	-	DCE	100	N.R.
13	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	$PhCF_3$	100	8%
14	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	THF	100	6%
15	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	TFE	100	46%
16	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	DMSO	100	N.R.
17	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	EtOAc	100	5

18	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	PhMe	100	trace
19	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	Dioxane	100	N.R.
20	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	CH_3CN	100	N.R.
21	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	EtOH	100	N.R.
22	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	HFIP	100	trace
23	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	DMA	100	N.R.
24	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	-	DME	100	N.R.
25	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	AcOH	TFE	100	62%
26	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	$NaHCO_3$	TFE	100	38%
27	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	AdCOOH	TFE	100	73%
28	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	Na_2HPO_4	TFE	100	60
29	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	PivOH	TFE	100	66
30	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	TsOH	TFE	100	N.R.
31	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	NaH_2PO_4	TFE	100	54
32	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	*o*-NO_2PhCOOH	TFE	100	61
33	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$ (1.0 equiv)	AdCOOH	TFE	100	67
34	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$ (4.0 equiv)	AdCOOH	TFE	100	66
35	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	AdCOOH (1.0 equiv)	TFE	100	69
36	$Pd(OAc)_2$ (20)	$Cu(OAc)_2$	AdCOOH (3.0 equiv)	TFE	100	70
37	$Pd(OAc)_2$ (5)	$Cu(OAc)_2$	AdCOOH	TFE	100	71%
38	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	AdCOOH	TFE	100	77%

[a]Reaction conditions: **1a** (0.1 mmol) and **2a** (0.2 mmol) with catalyst in the presence of oxidant (2.0 equiv) and additive (2.0 equiv) in solvent (2 mL) at 100 °C for 12 h in the air. [b]Isolated yield.

4. Transformative C−H fusion with different molecules and chemical ligation with amino acids and peptides.

Based on the efficiency of this C–H alkenylation reaction, we further focused on complexity-increasing transformations with different molecular architectures. The C4 alkenylation proved effective for conjugating with small drug molecular to amino acid–drug hybrids in a chemo- and site-selective manner (Fig. S1A). Hybrid conjugates **3ap** and **3aq** with ibuprofen and probenecid acid were selectively assembled in moderate yields (48% and 43%, respectively). This transformation was further applied to the direct conjugation of Trp and maleimide-linked amino acid and peptide (Fig. S1B). Maleimide-modified amino acids and dipeptide by either N-terminal or C-terminal protection all reacted efficiently with substrate (**1a**), affording the corresponding ligation products (**3ar**–**3ax**) in desirable yields ranging from 40% to 56%, respectively. These results indicated the potential application of this method in the direct preparation of complex peptide conjugates in a chemo- and site-selective manner.

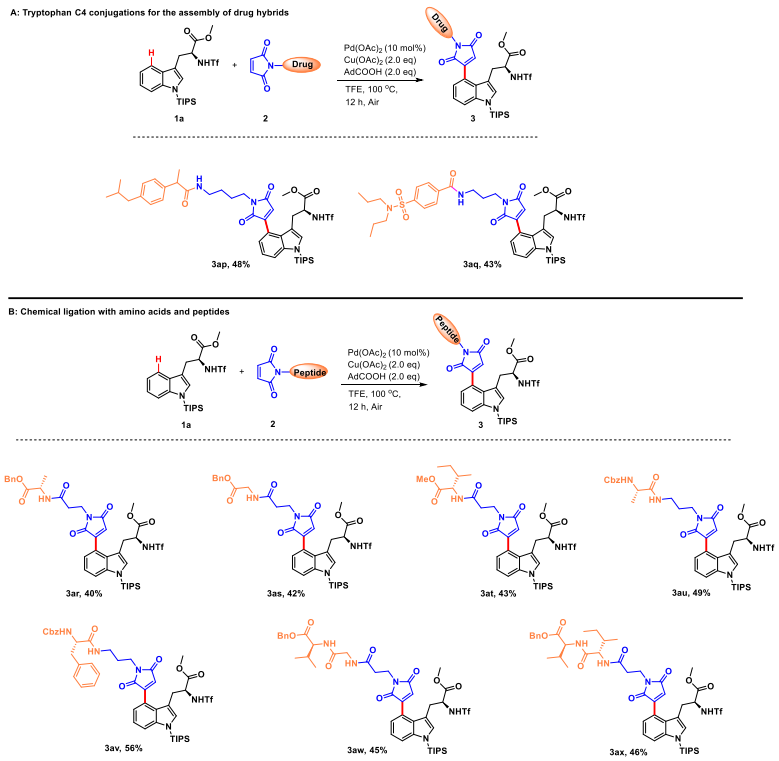


Fig. S1 Transformative C−H fusion with different molecules and chemical ligation with amino acids and peptides.

5. Biological Methods

5.1 Cell-based antiviral activity assay

Vero-E6 cells were maintained in DMEM supplemented with 10% FBS at 37 ℃ and humidified 5% CO_2. Before infection, 10,0000 Vero-E6 cells were seeded into 48-well plates in DMES (10% FBS) and incubated at 37 ℃ and humidified 5% CO_2. After 12h, the medium was replaced with 200 μl of DMEM (2% FBS) per well containing the compound at 10 μM (for primary screen) or one concentration within six gradients (for EC_{50} determination) to incubate for 2 h, then SARS-CoV-2 was added at a MOI of 0.01 and then plates were incubated at 37 ℃ and humidified 5% CO_2. At 24 hours post-infection, the supernatants were collected and the viral RNA in supernatants was extracted and then in reverse transcription using PrimeScript RT reagent Kit with gDNA Eraser (TaKaRa). For determining the viral copies, absolute quantitative RT-PCR was performed with TB Green® Premix Ex Taq™ II (TaKaRa). The primers used for qRT-PCR were RBD-qF1: 5′-CAATGGTTTAACAGGCACAGG-3′ and RBD-qR1:5′-CTCAAGTGTCTGTGGATCACG-3’. All experiments involving SARS-CoV-2 were conducted in BSL3 facility of Wuhan Institute of Virology, Chinese Academy of Sciences. Three independent experiments of each compound which was for determining EC_{50} values were performed, and EC_{50} values were fitted and calculated in GraphPad Prism software version 8 (GraphPad Software Inc., San Diego, CA).

5.2 Reverse docking

The candidate protein structures for reverse docking were prepared by one-step protein preparation panel of Schrödinger2021-1. The compound **5e** was prepared by LigPrep of Schrödinger2021-1, and the designed reverse docking-based target identification workflow is consisted of three steps, including searching druggable binding site on the surface of a protein by SiteMap, a followed grid generation as well as molecular docking simulation performed by using Glide. An in-house script, named as XDOCK and open source at GitHub (https://github.com/Wang-Lin-boop/Schrodinger-Script/blob/main/XDock), was used to perform this pipeline. The structure refinement and MM/GBSA calculation were performed by prime module of Schrödinger2021-1. The subsequent docking for **5a**, **5b**, **5c**, **5f** and **5i** was performed using the binding pose of **5e** and N protein as a reference. The obtained binding poses were further refined by prime module of Schrödinger2021-1.

5.3 Protein expression and purification

The pET28a expression vectors encoding wild type and mutated SARS-CoV-2 nucleocapsid protein (residues 1−419) with N-terminal His_6 tag was transformed into Rosetta™ 2(DE3) Competent Cells. Cells were grown in LB medium at 37 ℃ until an OD_{600} of 0.8 and protein expression was induced by adding IPTG to a concentration of 0.2 mM, and cultures were incubated for 18 h at 16 ℃. After collecting by centrifuge, cells were suspended with lysis buffer (25 mM Tris-HCl pH 7.5, 1M NaCl, 10 mM imidazole, 0.5 mM TCEP, 1x EDTA-free protease inhibitor cocktails, 5% glycerol, 0.1% Triton X-100). After high pressure crushing, the lysate was cleared by centrifugation at 4 ℃, and the supernatant was collected and incubated with Ni^{2+}-NTA beads for 30 min. The mixture was loaded into column and washed with lysis buffer, and eluted with buffer containing 300 mM imidazole. Fractions were further purified using size exclusion chromatography (Superdex 200 Increase 10/300) with buffer of 25 mM HEPES pH 7.5, 300 mM NaCl, 0.5 mM TCEP, 5% glycerol.

5.4 Surface plasmon resonance (SPR) analysis

All SPR experiments were performed at 25 ℃ in HBS-EP buffer (10 mM HEPES, pH 7.4, 150 mM NaCl, 3.0 mM EDTA, and 0.05% (v/v) Tween-20) containing 5% DMSO with Biacore 8K (GE Healthcare). The data were analyzed using Biacore 8K Evaluation Software. The sensorgrams were reference and blank subtracted. Running buffer was used for blank injections, and bulk effects were corrected using 8 cycles of solvent correction.

Prior to determine the binding affinity of each compound, SARS-CoV-2 nucleocapsid protein was diluted to 10 μg/mL in sodium acetate pH 4.5 and immobilized on CM5 chip using standard amine coupling to a level of 5500−6000 response units (RU). 10 mM compound stock solutions were diluted with 1x HBS-EP buffer in a nine-concentration series ranging from 0.195 μM to 100 μM with final DMSO concentration of 5%. Three startup cycles with running buffer were performed first, and analyte was injected and run through the chip with association time of 120 s and disassociation time of 100 s

and washed with 50% DMSO in each cycle. Solvent correction with different DMSO concentration varying from 4.5% to 5.8% was performed every 48th cycle. Raw data were reduced, double-referenced, and solvent-corrected using Biacore 8K Evaluation Software and K_D values of each compound were calculated using steady-state affinity model with a constant R_{max}.

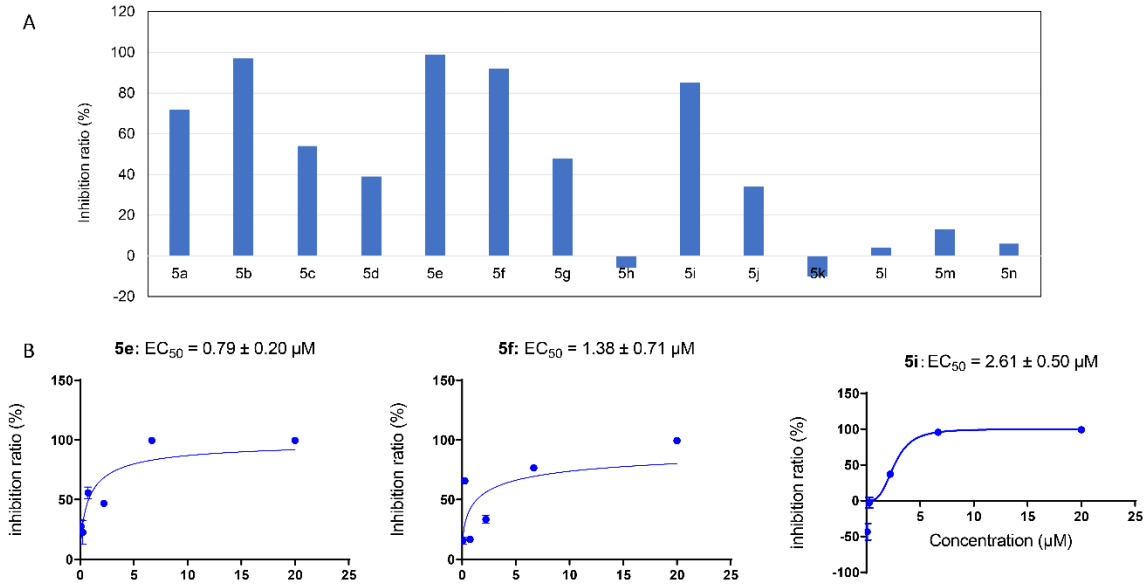


Fig. S2. Anti-SARS-CoV-2 infection activity of the macrocycles in Vero-E6 cell lines. (A)The inhibition rate at a concentration of 10 μM. (B) Inhibition activity of **5e**, **5f** and **5i** against SARS-CoV-2.

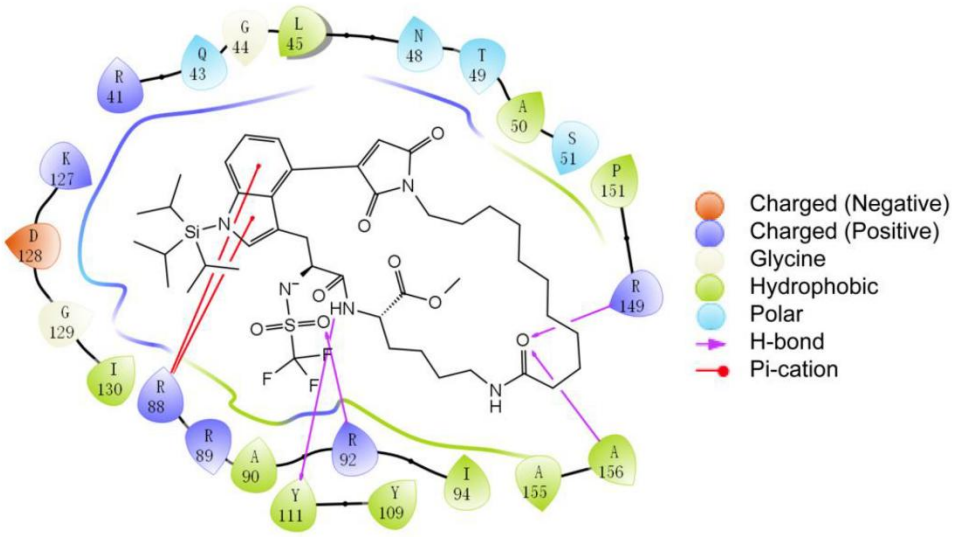


Fig. S3. The 2D interaction diagram of compound 5e with N protein of SARS-CoV-2.

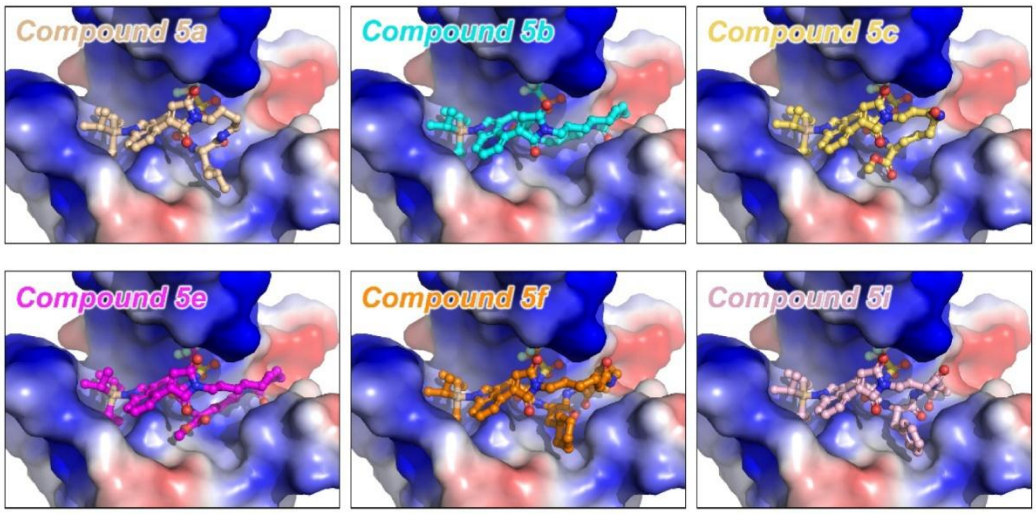


Fig. S4. The predicted binding poses of compound 5a, 5b, 5c, 5e, 5f, and 5h with NTD of N protein (shown in electrostatic potential surface with red as negative charged and blue as positive charged)**.**

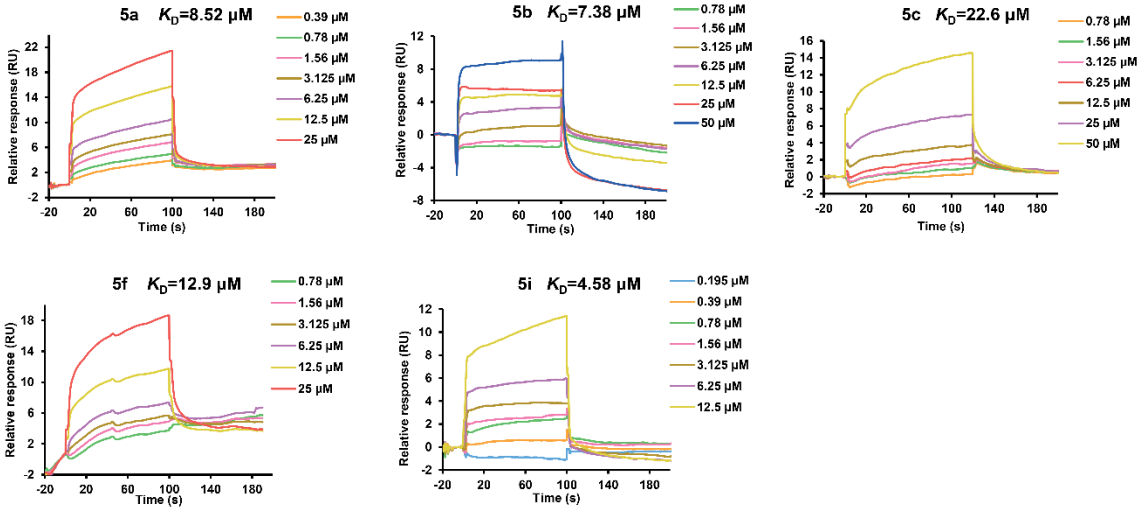


Fig. S5. Macrocycles bind to the nucleocapsid protein of SARS-CoV-2 (SARS-CoV-2-N). SPR sensorgrams of tested compounds bound to wild type SARS-CoV-2-N with concentrations varying from 0.195-50 μM. Experiments were performed with Biacore 8K (GE Healthcare) and data were analyzed using Biacore 8K evaluation software.

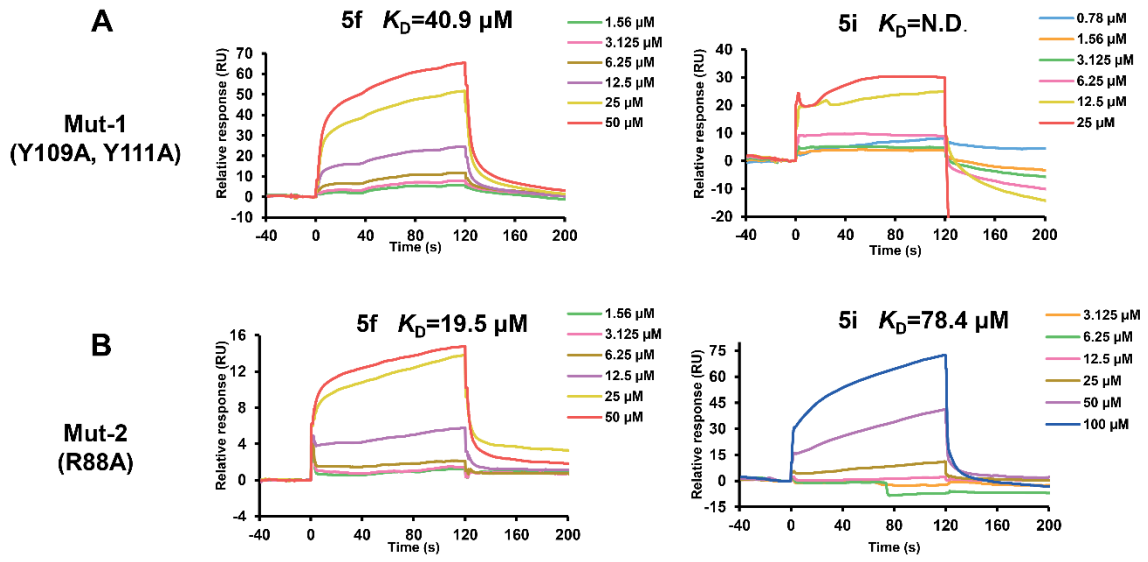
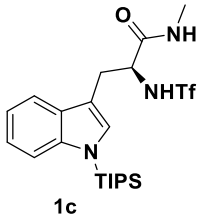


Fig. S6. The binding affinities of compounds **5e**, **5f** and **5i** to designed SARS-Cov-2-N mutants. SPR sensorgrams of compounds **5e**, **5f**, **5i** bound to Mut-1 (A) and Mut-2 (B) with ligand concentrations ranging from 0.78−100 μM. All experiments were performed with Biacore 8K (GE Healthcare).

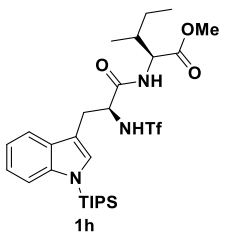
6. Characterization data



1c

(S)-N-methyl-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propenamide ***(1c)***

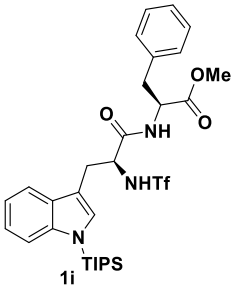
Compound **1c** was synthesized according to the general procedure and purified by flash column chromatography to afford **1c** as a white foam; m.p.: 70.6 – 71.7 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.65 – 7.59 (m, 1H), 7.52 – 7.48 (m, 1H), 7.26 – 7.14 (m, 3H), 7.10 (d, J = 3.4 Hz, 1H), 5.44 – 5.32 (m, 1H), 4.33 – 4.25 (m, 1H), 3.46 – 3.26 (m, 2H), 2.59 (d, J = 4.9 Hz, 3H), 1.72 – 1.64 (m, 3H), 1.18 – 1.05 (m, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.1, 141.4, 130.5, 130.0, 122.1, 121.0, 120.2, 118.4, 118.3, 114.3, 111.2, 58.3, 30.9, 26.3, 18.1, 12.7; LRMS (ESI): *m/z* 504.4 $[M - H]^-$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{22}H_{35}F_3N_3O_3SSi$ 506.2115; found 506.2115.



1h

*Methyl N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-alloisoleucinate (**1h**)*

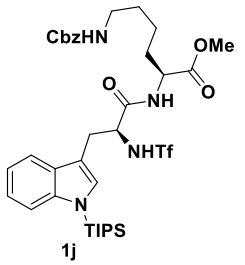
Compound **1h** was synthesized according to the general procedure and purified by flash column chromatography to afford **1h** as a white foam; m.p.: 149.8 – 150.4 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.84 (d, J = 8.9 Hz, 1H), 8.66 (d, J = 8.1 Hz, 1H), 7.71 (d, J = 7.7 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.32 (s, 1H), 7.16 – 7.03 (m, 2H), 4.51 – 4.42 (m, 1H), 4.36 – 4.29 (m, 1H), 3.66 (s, 3H), 3.14 – 2.82 (m, 2H), 1.90 – 1.80 (m, 1H), 1.75 – 1.64 (m, 3H), 1.46 – 1.36 (m, 1H), 1.32 – 1.18 (m, 1H), 1.09 (dd, J = 7.6, 2.9 Hz, 18H), 0.92 – 0.84 (m, 6H); ^{13}C{^{1}H} NMR (DMSO-d_6, 151 MHz): δ 171.8, 170.8, 140.5, 130.6, 130.2, 121.4, 119.0, 118.8, 113.5, 112.1, 57.2, 56.5, 51.8, 36.3, 28.4, 24.6, 18.0, 17.9, 15.3, 12.2, 11.1; LRMS (ESI): *m/z* 618.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{28}H_{45}F_3N_3O_5SSi$ 620.2796; found 620.2792.



1i

*Methyl N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalaninate (**1i**)*

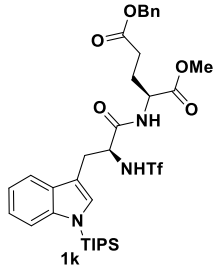
Compound **1i** was synthesized according to the general procedure and purified by flash column chromatography to afford **1i** as a white foam; m.p.: 73.5 – 74.8 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.80 (d, J = 8.8 Hz, 1H), 8.86 (d, J = 7.5 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.34 – 7.18 (m, 6H), 7.15 – 7.03 (m, 2H), 4.62 – 4.52 (m, 1H), 4.36 – 4.26 (m, 1H), 3.62 (s, 3H), 3.17 – 2.85 (m, 4H), 1.76 – 1.61 (m, 3H), 1.08 (dd, J = 7.5, 3.1 Hz, 18H); ^{13}C{^{1}H} NMR (DMSO-d_6, 151 MHz): δ 171.7, 170.5, 140.5, 137.0, 130.5, 130.3, 128.9, 128.3, 126.6, 121.3, 120.1, 119.1, 118.7, 117.9, 113.5, 112.0, 57.4, 53.5, 51.9, 36.4, 28.4, 17.9, 17.9, 12.1; LRMS (ESI): *m/z* 652.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{31}H_{43}F_3N_3O_5SSi$ 654.2639; found 654.2635.



1j

*Methyl N^6-((benzyloxy)carbonyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**1j**)*

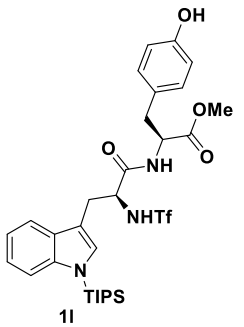
Compound **1j** was synthesized according to the general procedure and purified by flash column chromatography to afford **1j**as a white foam; m.p.: 81.9 – 83.3 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.86 (d, J = 8.8 Hz, 1H), 8.75 (d, J = 7.5 Hz, 1H), 7.75 – 7.68 (m, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.37 – 7.28 (m, 6H), 7.25 (t, J = 5.8 Hz, 1H), 7.14 – 7.05 (m, 2H), 5.00 (s, 2H), 4.40 – 4.27 (m, 2H), 3.64 (s, 3H), 3.15 – 2.89 (m, 4H), 1.80 – 1.64 (m, 5H), 1.47 – 1.39 (m, 2H), 1.36 – 1.27 (m, 2H), 1.09 (dd, J = 7.5, 3.9 Hz, 18H); ^{13}C{^{1}H} NMR (DMSO-d_6, 151 MHz): δ 172.3, 170.7, 156.1, 140.5, 137.3, 130.5, 130.3, 128.3, 127.7, 121.4, 120.2, 119.1, 118.7, 118.0, 113.5, 112.0, 65.1, 57.4, 52.0, 51.9, 40.0, 30.5, 28.9, 28.3, 22.5, 18.0, 17.9, 12.2; LRMS (ESI): *m/z* 767.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{36}H_{52}F_3N_4O_7SSi$ 769.3273; found 769.3273.



1k

*5-Benzyl 1-methyl N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-glutamate (**1k**)*

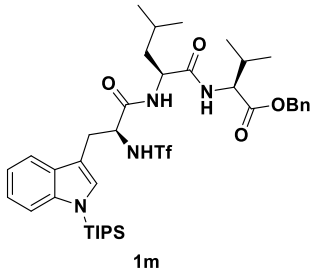
Compound **1k** was synthesized according to the general procedure and purified by flash column chromatography to afford **1k** as an oil; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.89 (d, J = 8.7 Hz, 1H), 8.80 (d, J = 7.6 Hz, 1H), 7.70 (d, J = 7.7 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.39 – 7.30 (m, 6H), 7.15 – 7.05 (m, 2H), 5.11 (s, 2H), 4.44 – 4.38 (m, 1H), 4.37 – 4.30 (m, 1H), 3.64 (s, 3H), 3.14 – 2.90 (m, 2H), 2.50 – 2.43 (m, 2H), 2.14 – 2.01 (m, 1H), 1.93 – 1.83 (m, 1H), 1.73 – 1.63 (m, 3H), 1.09 (dd, J = 7.5, 4.2 Hz, 18H); ^{13}C{^{1}H} NMR (DMSO-d_6, 151 MHz): δ 171.9, 171.8, 170.8, 140.5, 136.1, 130.5, 130.4, 128.4, 128.0, 127.9, 121.4, 119.1, 118.6, 113.5, 112.0, 65.6, 57.4, 52.1, 51.2, 29.7, 28.2, 26.0, 18.0, 17.9, 12.1; LRMS (ESI): *m/z* 724.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{34}H_{47}F_3N_3O_7SSi$ 726.2851; found 726.2852.



1l

*Methyl N^{a}-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-tyrosinate (**1l**)*

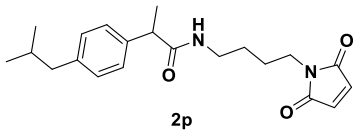
Compound **1l** was synthesized according to the general procedure and purified by flash column chromatography to afford **1l** as a white solid; m.p.: 89.6 – 90.5 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.80 (d, J = 8.8 Hz, 1H), 9.22 (s, 1H), 8.79 (d, J = 7.4 Hz, 1H), 7.69 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 8.2 Hz, 1H), 7.30 (s, 1H), 7.16 – 6.97 (m, 4H), 6.67 (d, J = 7.9 Hz, 2H), 4.44 – 4.52 (m, 1H), 4.36 – 4.28 (m, 1H), 3.61 (s, 3H), 3.11 – 2.86 (m, 4H), 1.73 – 1.63 (m, 3H), 1.09 (dd, J = 7.4, 3.2 Hz, 18H); ^{13}C{^{1}H} NMR (DMSO-d_6, 151 MHz): δ 171.8, 170.5, 156.1, 140.5, 130.5, 130.3, 129.9, 126.9, 121.3, 120.1, 119.1, 118.7, 118.0, 115.0, 113.5, 112.1, 57.4, 53.9, 51.9, 35.7, 28.4, 17.9, 17.9, 12.2; LRMS (ESI): *m/z* 668.5 [M – H]$^{-}$; HRMS (ESI) m/z: [M + H]$^{+}$ calcd for $C_{31}H_{43}F_3N_3O_6SSi$ 670.2588; found 670.2590.



1m

*Benzyl N^{a}-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl-L-valinate (**1m**)*

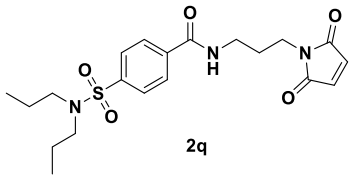
Compound **1m** was synthesized according to the general procedure and purified by flash column chromatography to afford **1m** as a white solid; m.p.: 92.3 – 93.1 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.57 (dd, J = 7.7, 1.4 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.36 – 7.26 (m, 6H), 7.25 (s, 1H), 7.16 – 7.07 (m, 2H), 6.95 – 6.84 (m, 1H), 5.25 – 5.08 (m, 2H), 4.84 – 4.76 (m, 1H), 4.64 (dd, J = 9.0, 5.4 Hz, 1H), 4.45 – 4.38 (m, 1H), 3.24 – 3.17 (m, 2H), 2.21 – 2.12 (m, 1H), 1.73 – 1.58 (m, 4H), 1.52 – 1.40 (m, 2H), 1.12 (dd, J = 10.9, 7.5 Hz, 18H), 0.89 (dd, J = 20.9, 6.9 Hz, 6H), 0.78 (dd, J = 8.9, 6.5 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.0, 171.7, 170.4, 141.3, 135.1, 130.5, 128.6, 128.5, 121.8, 120.7, 119.9, 118.3, 118.2, 114.1, 111.2, 67.3, 58.6, 57.3, 52.2, 41.4, 31.6, 30.0, 24.6, 22.4, 22.4, 18.9, 18.1, 18.1, 17.8, 12.8; LRMS (ESI): *m/z* 793.6 [M – H]$^{-}$; HRMS (ESI) m/z: [M + H]$^{+}$ calcd for $C_{39}H_{58}F_3N_4O_6SSi$ 795.3793; found 795.3794.



2p

*N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-2-(4-isobutylphenyl)propenamide (**2p**)*

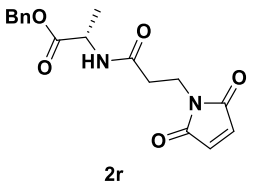
Compound **2p** was synthesized according to the general to afford **2p** as a white solid; m.p.: 109.1 – 110.1 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.23 – 7.18 (m, 2H), 7.16 – 7.07 (m, 2H), 6.68 (s, 2H), 5.39 (s, 1H), 3.57 – 3.43 (m, 3H), 3.27 – 3.14 (m, 2H), 2.46 (d, J = 7.2 Hz, 2H), 1.92 – 1.81 (m, 1H), 1.56 – 1.47 (m, 5H), 1.44 – 1.35 (m, 2H), 0.91 (d, J = 6.6 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 174.5, 170.8, 140.7, 138.6, 134.1, 129.6, 127.4, 46.8, 45.0, 39.0, 37.3, 30.2, 26.7, 25.9, 22.4, 18.5; LRMS (ESI): *m/z* 357.4 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{21}H_{29}N_2O_3$ 357.2173; found 357.2174.



2q

*N-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-4-(N,N-dipropylsulfamoyl)benzamide (**2q**)*

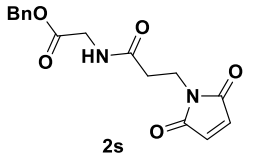
Compound **2q** was synthesized according to the general procedure to afford **2q** as a white solid; m.p.: 78.5 – 79.4 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.02 – 7.92 (m, 2H), 7.93 – 7.78 (m, 2H), 7.17 – 7.05 (m, 1H), 6.77 (s, 2H), 3.68 (t, J = 6.3 Hz, 2H), 3.42 (q, J = 6.2 Hz, 2H), 3.17 – 2.99 (m, 4H), 1.91 (p, J = 6.3 Hz, 2H), 1.61 – 1.45 (m, 4H), 0.88 (t, J = 7.4 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.3, 165.9, 142.9, 137.8, 134.3, 127.7, 127.3, 50.0, 36.4, 34.7, 28.0, 22.0, 11.2; LRMS (ESI): *m/z* 422.3 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{28}N_3O_5S$ 422.1744; found 422.1736.



2r

*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alaninate (**2r**)*

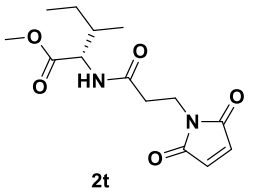
Compound **2r** was synthesized according to the general procedure to afford **2r** as a white solid; m.p.: 101.7 – 103.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41 – 7.31 (m, 5H), 6.69 (s, 2H), 6.17 (d, J = 7.3 Hz, 1H), 5.29 – 5.09 (m, 2H), 4.69 – 4.57 (m, 1H), 3.98 – 3.78 (m, 2H), 2.70 – 2.44 (m, 2H), 1.41 (d, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 172.8, 170.5, 169.1, 135.3, 134.2, 128.7, 128.5, 128.1, 67.2, 48.1, 34.5, 34.1, 18.4; LRMS (ESI): *m/z* 331.3 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{19}N_2O_5$ 331.1288; found 331.1286.



2s

*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycinate (**2s**)*

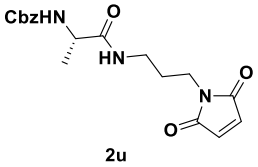
Compound **2s** was synthesized according to the general procedure to afford **2s** as a white solid; m.p.: 122.1 – 123.8 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.42 – 7.32 (m, 5H), 6.70 (s, 2H), 6.14 (s, 1H), 5.19 (s, 2H), 4.08 (d, J = 5.2 Hz, 2H), 3.86 (t, J = 7.1 Hz, 2H), 2.61 (t, J = 7.1 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 170.5, 169.8, 169.7, 135.1, 134.2, 128.7, 128.6, 128.4, 67.3, 41.4, 34.4, 34.1; LRMS (ESI): *m/z* 317.2 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{16}H_{17}N_2O_5$ 317.1132; found 317.1126.



2t

*Methyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucinate (**2t**)*

Compound **2t** was synthesized according to the general procedure to afford **2t** as a white solid; m.p.: 103.5 – 105.1 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 6.71 (s, 2H), 6.07 (d, J = 8.9 Hz, 1H), 4.58 (dd, J = 8.6, 5.0 Hz, 1H), 3.93 – 3.83 (m, 2H), 3.74 (s, 3H), 2.60 (t, J = 7.2 Hz, 2H), 1.91 – 1.81 (m, 1H), 1.48 – 1.38 (m, 1H), 1.22 – 1.12 (m, 1H), 0.96 – 0.86 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 172.4, 170.5, 169.4, 134.2, 56.4, 52.1, 37.9, 34.6, 34.2, 25.2, 15.4, 11.6; LRMS (ESI): *m/z* 297.2 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{14}H_{21}N_2O_5$ 297.1445; found 297.1442.

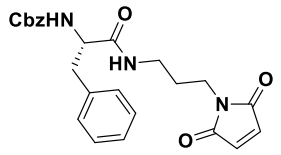


2u

*Benzyl (S)-(1-((3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)amino)-1-oxopropan-2-yl)carbamate (**2u**)*

Compound **2u** was synthesized according to the general procedure to afford **2u** as a white solid; m.p.: 128.9 – 130.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.44 – 7.29 (m, 5H), 6.71 (s, 2H), 6.64 (s, 1H), 5.43 – 5.30 (m, 1H), 5.13 (s, 2H), 4.30 – 4.15 (m, 1H), 3.61 – 3.48 (m, 2H), 3.32 – 3.09 (m, 2H), 1.85 – 1.65 (m, 2H), 1.42 (d, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 172.3, 171.0, 156.0, 136.2,

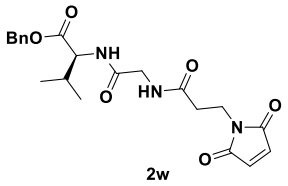
134.2, 128.5, 128.2, 67.1, 50.8, 36.0, 34.6, 28.1, 18.6; LRMS (ESI): *m/z* 360.2 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{22}N_3O_5$ 360.1554; found 360.1554.



2v

*Benzyl (S)-(1-((3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**2v**)*

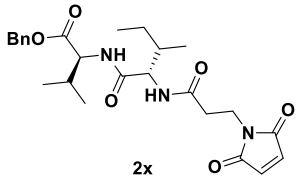
Compound **2v** was synthesized according to the general procedure to afford **2v** as a white solid; m.p.: 134.2 – 134.8 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.38 – 7.29 (m, 6H), 7.26 – 7.09 (m, 4H), 6.68 (d, J = 2.8 Hz, 2H), 6.39 (dd, J = 15.6, 9.2 Hz, 1H), 5.46 – 5.31 (d, J = 23.3 Hz, 1H), 5.10 (s, 2H), 4.44 – 4.33 (m, 1H), 3.41 – 3.30 (m, 1H), 3.27 – 3.10 (m, 3H), 3.09 – 2.96 (m, 2H), 1.62 (q, J = 6.7 Hz, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.0, 170.8, 155.9, 136.5, 136.2, 134.2, 129.3, 128.8, 128.5, 128.2, 128.2, 127.1, 67.1, 56.5, 38.6, 35.9, 34.5, 28.0; LRMS (ESI): *m/z* 436.2 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{24}H_{26}N_3O_5$ 436.1867; found 436.1865.



2w

*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycyl-L-valinate (**2w**)*

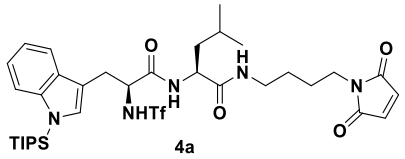
Compound **2w** was synthesized according to the general procedure to afford **2w** as a white solid; m.p.: 148.1 – 149.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.41 – 7.31 (m, 5H), 6.83 (d, J = 8.7 Hz, 1H), 6.73 – 6.64 (m, 3H), 5.26 – 5.10 (m, 2H), 4.57 (dd, J = 8.7, 5.0 Hz, 1H), 4.06 – 3.91 (m, 2H), 3.85 (t, J = 7.1 Hz, 2H), 2.58 (t, J = 7.1 Hz, 2H), 2.26 – 2.13 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.6, 170.5, 170.4, 168.9, 135.3, 134.2, 128.6, 128.5, 128.4, 67.1, 57.4, 43.2, 34.5, 34.2, 31.1, 19.0, 17.7; LRMS (ESI): *m/z* 416.3 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{21}H_{26}N_3O_6$ 416.1816; found 416.1810.



2x

*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucyl-L-valinate (**2x**)*

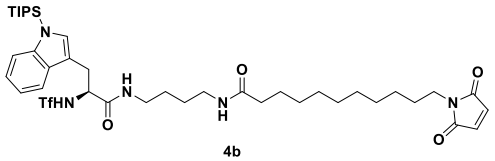
Compound **2x** was synthesized according to the general procedure to afford **2x** as a white solid; m.p.: 136.6 – 138.2 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40 – 7.30 (m, 5H), 6.72 – 6.66 (m, 2H), 6.57 – 6.42 (m, 1H), 6.33 – 6.20 (m, 1H), 5.23 – 5.08 (m, 2H), 4.58 – 4.51 (m, 1H), 4.36 – 4.27 (m, 1H), 3.89 – 3.78 (m, 2H), 2.57 (td, J = 7.2, 4.2 Hz, 2H), 2.25 – 2.14 (m, 1H), 1.86 – 1.72 (m, 1H), 1.55 – 1.43 (m, 1H), 1.18 – 1.07 (m, 1H), 0.94 – 0.82 (m, 12H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.3, 170.9, 170.4, 169.6, 135.2, 134.2, 128.6, 128.5, 128.4, 67.1, 57.7, 57.2, 37.4, 34.6, 34.2, 31.1, 25.1, 18.9, 17.7, 15.2, 11.3; LRMS (ESI): *m/z* 472.3 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{34}N_3O_6$ 472.2442; found 472.2441.



4a

*(S)-N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-4-methyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)pentanamide (**4a**)*

Compound **4a** was synthesized according to the general procedure to afford **4a** as a yellow solid; m.p.: 90.3 – 91.6 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 – 7.53 (m, 1H), 7.48 – 7.45 (m, 1H), 7.21 (s, 1H), 7.16 – 6.81 (m, 4H), 6.64 (d, J = 6.5 Hz, 2H), 6.29 (d, J = 56.4 Hz, 1H), 4.50 – 4.33 (m, 2H), 3.51 – 3.45 (m, 2H), 3.31 – 3.08 (m, 4H), 1.95 – 1.83 (m, 1H), 1.72 – 1.60 (m, 4H), 1.56 – 1.40 (m, 5H), 1.15 – 1.09 (m, 18H), 0.86 – 0.82 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 171.4, 171.3, 170.9, 170.1, 170.0, 141.3, 134.1, 130.5, 121.9, 120.8, 119.9, 118.3, 118.2, 114.2, 111.0, 58.4, 58.4, 52.5, 41.2, 41.2, 38.9, 37.3, 30.0, 26.3, 25.8, 24.7, 22.6, 22.2, 18.1, 12.8; LRMS (ESI): *m/z* 756.4 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{35}H_{53}F_3N_5O_6SSi$ 756.3432; found 756.3445.

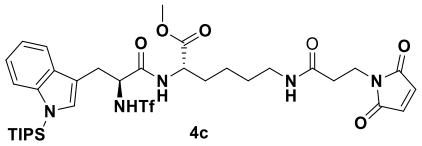


4b

*(S)-11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-(4-(2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)butyl)undecanamide (**4b**)*

Compound **4b** was synthesized according to the general procedure to afford **4b** as a yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (dd, J = 7.5, 1.6 Hz, 1H), 7.47 (d, J = 8.0 Hz, 1H), 7.20 – 7.05 (m, 4H), 6.66 (s, 2H), 6.54 (t, J = 5.5 Hz, 1H), 5.75 (s, 1H), 4.40 – 4.30 (m, 1H), 3.49 (t, J = 7.3 Hz, 2H), 3.42 – 3.20 (m, 3H), 3.07 – 2.93 (m, 3H), 2.11 (t, J = 7.7 Hz, 2H), 1.72 – 1.62 (m, 3H), 1.60 – 1.51 (m, 4H), 1.38 –

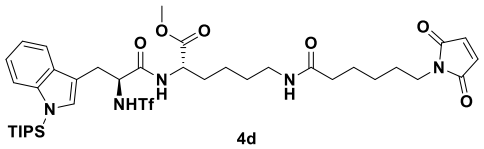
1.21 (m, 16H), 1.12 (dd, *J* = 7.6, 2.0 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): *δ* 173.9, 170.9, 169.9, 141.3, 134.0, 130.5, 121.8, 120.9, 119.9, 118.6, 118.3, 114.1, 111.2, 58.7, 39.6, 38.5, 37.9, 36.6, 30.3, 29.3, 29.3, 29.2, 29.2, 29.0, 28.5, 27.3, 26.7, 25.6, 25.3, 18.1, 12.8; LRMS (ESI): *m/z* 826.6 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{40}H_{63}F_3N_5O_6SSi$ 826.4215; found 826.4229.



4c

*Methyl N^6-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4c**)*

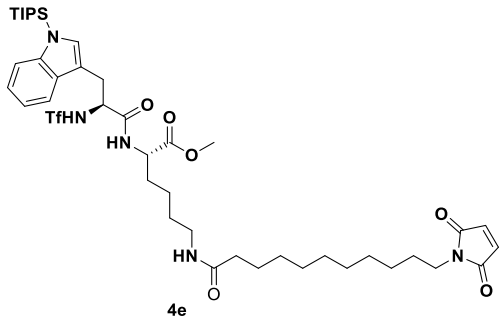
Compound **4c** was synthesized according to the general procedure to afford **4c** as a yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): *δ* 7.60 – 7.53 (m, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.33 (d, *J* = 9.0 Hz, 1H), 7.18 (s, 1H), 7.16 – 7.07 (m, 2H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.64 (s, 2H), 6.14 – 6.07 m, 1H), 4.52 – 4.36 (m, 2H), 3.85 – 3.73 (m, 2H), 3.65 (s, 3H), 3.34 (ddd, *J* = 46.5, 14.6, 6.8 Hz, 2H), 3.42– 3.25 (m, 2H), 2.47 (t, *J* = 7.0 Hz, 2H), 1.98 – 1.90 (m, 1H), 1.84 – 1.75 (m, 1H), 1.70 – 1.64 (m, 3H), 1.47 – 1.40 (m, 2H), 1.31 – 1.20 (m, 2H), 1.12 (d, *J* = 7.5 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): *δ* 171.8, 170.7, 170.3, 170.1, 141.3, 134.2, 130.7, 130.6, 123.3, 121.7, 120.8, 119.8, 118.3, 115.7, 114.1, 111.0, 58.8, 52.4, 52.1, 38.6, 34.8, 34.4, 31.5, 29.7, 28.5, 21.8, 18.1, 12.8; LRMS (ESI): *m/z* 786.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{35}H_{51}F_3N_5O_8SSi$ 786.3174; found 786.3163.



4d

*Methyl N^6-(6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4d**)*

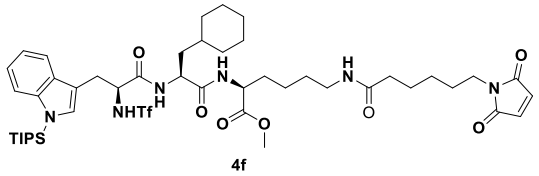
Compound **4d** was synthesized according to the general procedure to afford **4d** as a yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): *δ* 7.58 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.41 (d, *J* = 9.2 Hz, 1H), 7.18 (s, 1H), 7.15 – 7.05 (m, 3H), 6.63 (s, 2H), 5.88 (s, 1H), 4.53 – 4.40 (m, 2H), 3.67 (s, 3H), 3.50 – 3.43 (m, 2H), 3.41 – 3.03 (m, 4H), 2.14 – 2.00 (m, 3H), 1.84 – 1.76 (m, 1H), 1.73 – 1.65 (m, 4H), 1.61 – 1.50 (m, 3H), 1.48 – 1.40 (m, 2H), 1.31 – 1.20 (m, 4H), 1.12 (dd, *J* = 7.6, 1.3 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): *δ* 174.1, 171.8, 171.0, 170.1, 141.3, 134.0, 130.8, 130.7, 121.6, 120.8, 119.8, 118.4, 118.3, 114.1, 111.1, 58.8, 52.3, 38.2, 37.6, 36.3, 30.8, 29.9, 29.1, 28.1, 26.1, 25.1, 21.6, 18.1, 12.8; LRMS (ESI): *m/z* 828.6 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{38}H_{57}F_3N_5O_8SSi$ 828.3644; found 828.3647.



4e

*Methyl N^6-(11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)undecanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4e**)*

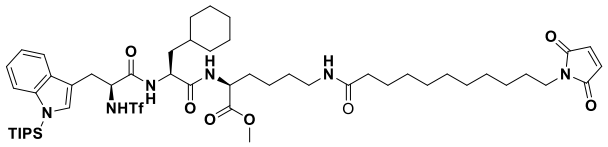
Compound **4e** was synthesized according to the general procedure to afford **4e** as a yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 – 7.57 (m, 1H), 7.46 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 9.2 Hz, 1H), 7.18 (s, 1H), 7.16 – 7.07 (m, 2H), 7.00 (d, J = 7.2 Hz, 1H), 6.67 (s, 2H), 5.79 – 5.71 (m, 1H), 4.48 – 4.40 (m, 2H), 3.67 (s, 3H), 3.49 (t, J = 7.3 Hz, 2H), 3.41 – 3.05 (m, 4H), 2.11 – 2.04 (m, 2H), 1.87 – 1.81 (m, 1H), 1.77 – 1.72 (m, 1H), 1.71 – 1.64 (m, 3H), 1.59 – 1.49 (m, 4H), 1.45 – 1.38 (m, 2H), 1.31 – 1.20 (m, 14H), 1.12 (d, J = 7.5 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.5, 171.8, 170.9, 169.9, 141.2, 134.0, 130.8, 130.7, 121.6, 120.8, 119.8, 118.4, 118.3, 114.0, 111.1, 58.8, 52.3, 52.3, 38.0, 37.9, 36.8, 30.5, 30.0, 29.3, 29.3, 29.1, 29.0, 28.5, 26.7, 25.8, 21.5, 18.1, 12.8; LRMS (ESI): *m/z* 898.7 [M + H]$^+$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{43}H_{67}F_3N_5O_8SSi$ 898.4426; found 898.4419.



4f

*Methyl N^2-((S)-3-cyclohexyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanoyl)-N^6-(6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl)-L-lysinate (**4f**)*

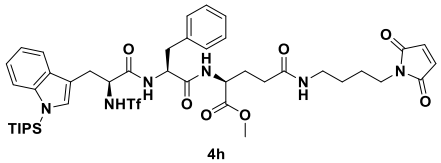
Compound **4f** was synthesized according to the general procedure to afford **4f** as a yellow solid; m.p.: 90.5 – 91.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 – 7.57 (m, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.25 (s, 1H), 7.18 – 6.85 (m, 5H), 6.64 (s, 2H), 6.03 – 5.90 (m, 1H), 4.61 – 4.36 (m, 3H), 3.72 (s, 3H), 3.49 (t, J = 7.1 Hz, 2H), 3.41 – 3.06 (m, 4H), 2.19 (t, J = 7.6 Hz, 2H), 1.89 – 1.81 (m, 1H), 1.74 – 1.25 (m, 22H), 1.18 – 1.08 (m, 21H), 0.93 – 0.80 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 173.9, 172.4, 171.8, 171.0, 170.1, 141.3, 134.0, 130.6, 130.5, 121.8, 120.8, 119.8, 118.3, 118.2, 114.2, 111.2, 58.4, 52.4, 52.2, 51.5, 39.7, 38.5, 37.6, 36.5, 33.9, 33.5, 32.5, 31.0, 30.0, 29.1, 28.1, 26.3, 26.2, 26.1, 25.9, 25.2, 22.2, 18.1, 12.8; LRMS (ESI): *m/z* 981.7 [M + H]$^+$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{47}H_{72}F_3N_6O_9SSi$ 981.4797; found 981.4808.



4g

Methyl N^2-((S)-3-cyclohexyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanoyl)-N^6-(11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)undecanoyl)-L-lysinate ***(4g)***

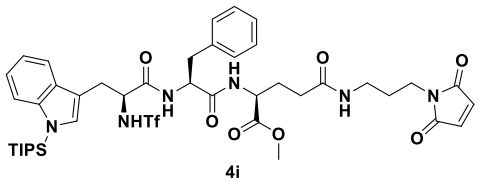
Compound **4g** was synthesized according to the general procedure to afford **4g** as a yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.24 (s, 1H), 7.16 – 7.02 (m, 4H), 6.91 (d, J = 7.7 Hz, 1H), 6.67 (s, 2H), 6.01 – 5.87 (m, 1H), 4.60 – 4.38 (m, 3H), 3.72 (s, 3H), 3.49 (t, J = 7.3 Hz, 2H), 3.40 – 3.11 (m, 4H), 2.19 (t, J = 7.7 Hz, 2H), 1.89 – 1.82 (m, 1H), 1.76 – 1.34 (m, 20H), 1.30 – 1.20 (m, 12H), 1.16 – 1.08 (m, 21H), 0.93 – 0.80 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.5, 172.4, 171.7, 170.9, 170.2, 141.3, 134.0, 130.6, 130.5, 121.8, 120.8, 119.8, 118.3, 118.2, 114.1, 111.3, 58.6, 52.4, 52.2, 51.5, 39.6, 38.6, 37.9, 36.8, 34.0, 33.6, 32.5, 31.0, 30.0, 29.3, 29.2, 29.0, 28.5, 26.7, 26.3, 26.1, 25.9, 25.9, 22.2, 18.1, 12.8; LRMS (ESI): *m/z* 1051.8 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{52}H_{82}F_3N_6O_9SSi$ 1051.5580; found 1051.5594.



4h

*Methyl N^5-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (****4h****)*

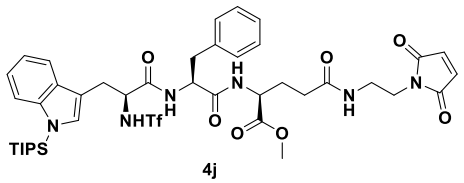
Compound **4h** was synthesized according to the general procedure to afford **4h** as a yellow solid; m.p.: 113.6 – 114.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 – 7.52 (m, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.22 – 7.12 (m, 5H), 7.12 – 6.98 (m, 5H), 6.96 – 6.68 (m, 2H), 6.53 (s, 2H), 4.75 – 4.66 (m, 1H), 4.48 – 4.39 (m, 2H), 3.70 (s, 3H), 3.49 (td, J = 7.2, 1.7 Hz, 2H), 3.34 – 3.17 (m, 4H), 3.01 (d, J = 6.8 Hz, 2H), 2.28 – 2.11 (m, 3H), 1.92 – 1.82 (m, 1H), 1.72 – 1.58 (m, 5H), 1.54 – 1.46 (m, 2H), 1.12 (dd, J = 7.5, 1.4 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.7, 171.5, 171.0, 170.7, 170.0, 141.4, 135.9, 134.0, 130.7, 130.5, 129.3, 128.6, 127.1, 121.9, 120.7, 119.9, 118.3, 118.1, 114.2, 110.9, 58.5, 54.9, 52.6, 51.9, 39.3, 38.0, 37.4, 31.8, 29.6, 28.4, 26.1, 25.9, 18.1, 12.8; LRMS (ESI): *m/z* 933.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{44}H_{60}F_3N_6O_9SSi$ 933.3858; found 933.3847.



4i

*Methyl N^5-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (**4i**)*

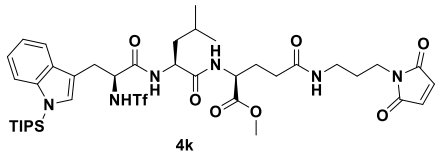
Compound **4i** was synthesized according to the general procedure to afford **4i** as a yellow solid; m.p.: 108.6 – 109.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.53 (d, J = 7.8 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.21 (s, 1H), 7.20 – 7.10 (m, 6H), 7.08 (t, J = 7.4 Hz, 1H), 7.03 (d, J = 6.9 Hz, 2H), 6.99 – 6.90 (m, 1H), 6.74 – 6.66 (m, 1H), 6.62 (d, J = 1.8 Hz, 2H), 4.75 – 4.65 (m, 1H), 4.50 – 4.41 (m, 2H), 3.70 (s, 3H), 3.61 – 3.49 (m, 2H), 3.31 – 3.10 (m, 4H), 3.04 – 2.93 (m, 2H), 2.29 – 2.17 (m, 3H), 1.95 – 1.85 (m, 1H), 1.79 – 1.63 (m, 5H), 1.12 (dd, J = 7.5, 3.6 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.6, 171.7, 171.3, 170.4, 170.1, 141.3, 135.8, 134.1, 130.7, 130.5, 129.3, 128.6, 127.0, 121.9, 120.7, 119.9, 118.3, 118.1, 114.2, 111.0, 58.4, 55.1, 52.6, 51.9, 37.9, 36.4, 34.9, 32.0, 29.9, 28.0, 27.9, 18.1, 12.8; LRMS (ESI): *m/z* 919.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{43}H_{58}F_3N_6O_9SSi$ 919.3702; found 919.3700.



4j

*Methyl N^5-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (**4j**)*

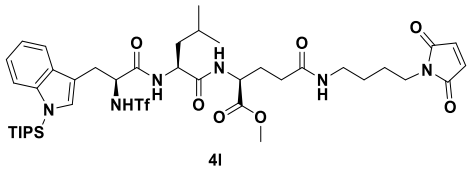
Compound **4j** was synthesized according to the general procedure to afford **4j** as a yellow solid; m.p.: 117.4 – 118.9 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.56 (d, J = 7.6 Hz, 1H), 7.49 (d, J = 8.3 Hz, 1H), 7.23 (s, 1H), 7.20 – 7.14 (m, 4H), 7.14 – 7.09 (m, 1H), 7.06 – 6.96 (m, 3H), 6.92 – 6.87 (m, 1H), 6.77 – 6.72 (m, 1H), 6.58 (s, 2H), 6.44 – 6.38 (m, 1H), 4.65 – 4.57 (m, 1H), 4.51 – 4.37 (m, 2H), 3.72 – 3.59 (m, 5H), 3.51 – 3.21 (m, 4H), 3.03 – 2.90 (m, 2H), 2.20 – 2.09 (m, 3H), 1.90 – 1.80 (m, 1H), 1.73 – 1.63 (m, 3H), 1.12 (dd, J = 7.6, 2.7 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.7, 171.7, 171.2, 170.3, 170.1, 141.4, 135.8, 134.2, 130.8, 130.3, 129.2, 128.6, 127.1, 122.0, 120.7, 120.0, 118.4, 118.1, 114.3, 111.0, 58.2, 55.2, 52.5, 51.8, 38.8, 37.8, 37.5, 31.8, 29.8, 27.7, 18.1, 12.8; LRMS (ESI): *m/z* 905.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{42}H_{56}F_3N_6O_9SSi$ 905.3545; found 905.3553.



4k

*Methyl N^5-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4k**)*

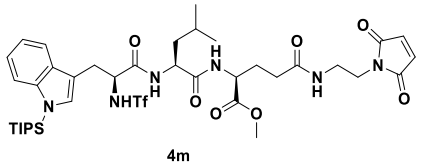
Compound **4k** was synthesized according to the general procedure to afford **4k** as a yellow solid; m.p.: 220.1 – 221.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 – 7.57 (m, 1H), 7.48 (d, J = 8.2 Hz, 1H), 7.27 (s, 1H), 7.25 – 7.03 (m, 4H), 6.72 – 6.40 (m, 4H), 4.61 – 4.40 (m, 3H), 3.77 – 3.70 (m, 3H), 3.63 – 3.52 (m, 2H), 3.33 – 3.25 (m, 2H), 3.21 – 3.12 (m, 2H), 2.35 – 2.25 (m, 3H), 2.00 – 1.93 (m, 1H), 1.81 – 1.74 (m, 2H), 1.73 – 1.65 (m, 3H), 1.63 – 1.50 (m, 2H), 1.46 – 1.38 (m, 1H), 1.13 (t, J = 7.4 Hz, 18H), 0.86 (dd, J = 11.5, 6.4 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.4, 172.1, 171.5, 171.4, 170.3, 141.3, 134.1, 130.6, 130.4, 121.9, 120.8, 119.9, 118.4, 118.2, 114.2, 111.2, 111.1, 58.2, 52.7, 52.6, 51.8, 40.9, 40.9, 36.2, 34.9, 32.0, 32.0, 30.1, 30.1, 27.9, 27.9, 24.6, 22.6, 22.0, 18.1, 12.8; LRMS (ESI): *m/z* 885.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{40}H_{60}F_3N_6O_9SSi$ 885.3858; found 885.3865.



4l

*Methyl N^5-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4l**)*

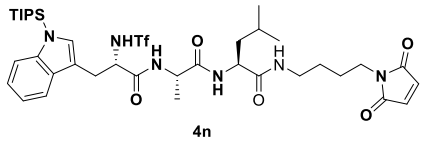
Compound **4l** was synthesized according to the general procedure to afford **4l** as a yellow solid; m.p.: 214.2 – 215.1 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 – 7.37 (m, 3H), 7.25 (s, 1H), 7.21 – 6.78 (m, 4H), 6.79 – 6.44 (m, 3H), 4.66 – 4.40 (m, 3H), 3.79 – 3.70 (m, 3H), 3.55 – 3.45 (m, 2H), 3.35 – 3.15 (m, 4H), 2.31 – 2.17 (m, 3H), 1.98 – 1.90 (m, 1H), 1.72 – 1.42 (m, 10H), 1.18 – 1.06 (m, 18H), 0.91 – 0.79 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.4, 172.1, 172.0, 171.0, 170.2, 141.3, 134.0, 130.6, 130.4, 121.9, 120.7, 119.9, 118.2, 114.2, 111.0, 58.4, 58.3, 52.6, 52.5, 52.4, 51.9, 41.3, 41.2, 39.1, 39.1, 37.4, 32.1, 32.0, 29.6, 28.2, 28.2, 26.2, 25.9, 24.6, 22.6, 22.1, 18.1, 12.8; LRMS (ESI): *m/z* 899.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{41}H_{62}F_3N_6O_9SSi$ 899.4015; found 899.4015.



4m

*Methyl N^5-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4m**)*

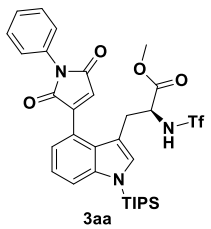
Compound **4m** was synthesized according to the general procedure to afford **4m** as a yellow solid; m.p.: 198.8 – 199.9 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (dd, J = 7.7, 1.4 Hz, 1H), 7.49 (d, J = 8.2 Hz, 1H), 7.29 (s, 1H), 7.25 – 7.00 (m, 4H), 6.62 (s, 2H), 6.56 – 6.48 (m, 2H), 4.59 – 4.39 (m, 3H), 3.73 (s, 3H), 3.69 – 3.60 (m, 2H), 3.49 – 3.25 (m, 4H), 2.27 – 2.16 (m, 3H), 1.95 – 1.88 (m, 1H), 1.73 – 1.65 (m, 3H), 1.62 – 1.38 (m, 3H), 1.13 (dd, J = 7.6, 5.7 Hz, 18H), 0.88 – 0.81 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.7, 172.1, 171.6, 171.3, 170.4, 141.3, 134.2, 130.7, 130.3, 122.0, 120.7, 120.0, 118.4, 118.2, 114.2, 111.2, 58.1, 52.7, 52.6, 51.7, 40.8, 38.8, 37.6, 31.9, 29.9, 27.7, 24.6, 22.5, 22.1, 18.1, 12.8; LRMS (ESI): *m/z* 871.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{39}H_{58}F_3N_6O_9SSi$ 871.3702; found 871.3693.



4n

*(S)-N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-4-methyl-2-((S)-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanamido)pentanamide (**4n**)*

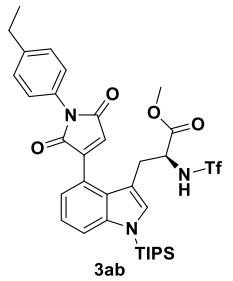
Compound **4n** was synthesized according to the general procedure to afford **4n** as a yellow solid; m.p.: 235.2 – 236.7 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.95 – 8.50 (m, 1H), 8.47 – 7.76 (m, 2H), 7.72 – 7.30 (m, 3H), 7.23 (s, 1H), 7.08 (t, J = 7.7 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H), 6.55 (s, 2H), 5.29 – 5.16 (m, 1H), 4.74 – 4.51 (m, 2H), 3.38 – 3.17 (m, 4H), 3.13 – 2.89 (m, 2H), 1.70 – 1.63 (m, 4H), 1.59 – 1.48 (m, 2H), 1.40 (d, J = 6.5 Hz, 3H), 1.36 – 1.24 (m, 4H), 1.11 (d, J = 7.5 Hz, 18H), 0.92 – 0.81 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.2, 172.2, 170.9, 170.5, 141.1, 133.9, 130.7, 130.1, 121.7, 120.8, 119.6, 118.3, 118.2, 114.0, 111.5, 58.8, 51.8, 48.8, 42.4, 39.0, 36.9, 29.8, 25.8, 25.8, 24.9, 22.7, 22.3, 19.9, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 827.5 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{38}H_{58}F_3N_6O_7SSi$ 827.3804; found 827.3811.



3aa

*Methyl (S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3aa**)*

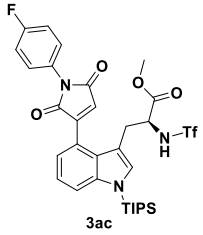
Orange solid (52.1 mg, 77% yield); m.p.: 95.3 – 96.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (dd, J = 8.2, 1.1 Hz, 1H), 7.53 – 7.46 (m, 4H), 7.41 – 7.37 (m, 1H), 7.27 – 7.21 (m, 3H), 6.73 (s, 1H), 5.71 – 5.64 (m, 1H), 4.29 – 4.23 (m, 1H), 3.55 (s, 3H), 3.34 (dd, J = 15.1, 5.2 Hz, 1H), 3.12 (dd, J = 15.1, 8.5 Hz, 1H), 1.73 – 1.67 (m, 3H), 1.16 (dd, J = 7.6, 4.1 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.9, 170.0, 169.4, 146.3, 142.3, 133.2, 131.8, 129.1, 128.1, 127.8, 127.5, 126.2, 123.4, 121.4, 120.6, 120.6, 118.0, 116.6, 110.3, 57.5, 53.0, 31.5, 18.1, 18.1, 12.9; LRMS (ESI): *m/z* 676.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{32}H_{37}F_3N_3O_6SSi$ 676.2130; found 676.2125.



3ab

*Methyl (S)-3-(4-(1-(4-ethylphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ab**)*

Orange solid (45.8 mg, 65% yield); m.p.: 93.7 – 95.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (dd, J = 8.2, 1.1 Hz, 1H), 7.38 – 7.31 (m, 4H), 7.27 – 7.20 (m, 3H), 6.72 (s, 1H), 5.66 – 5.60 (m, 1H), 4.30 – 4.23 (m, 1H), 3.57 (s, 3H), 3.34 (dd, J = 15.1, 5.1 Hz, 1H), 3.11 (dd, J = 15.1, 8.5 Hz, 1H), 2.70 (q, J = 7.6 Hz, 2H), 1.74 – 1.65 (m, 3H), 1.27 (t, J = 7.6 Hz, 3H), 1.16 (dd, J = 7.6, 4.4 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.8, 170.2, 169.5, 146.3, 144.1, 142.2, 133.1, 129.2, 128.6, 128.1, 127.5, 126.1, 123.4, 121.4, 120.7, 120.6, 118.0, 116.5, 110.3, 57.5, 53.1, 31.5, 28.6, 18.1, 18.1, 15.4, 12.9; LRMS (ESI): *m/z* 704.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{34}H_{41}F_3N_3O_6SSi$ 704.2443; found 704.2433.

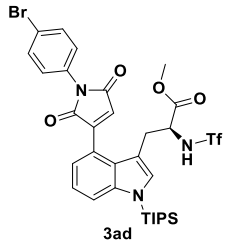


3ac

*Methyl (S)-3-(4-(1-(4-fluorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ac**)*

Orange solid (43.5 mg, 63% yield); m.p.: 100.5 – 101.5 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.64 (dd, J = 8.2, 1.2 Hz, 1H), 7.49 – 7.43 (m, 2H), 7.28 – 7.15 (m, 5H), 6.71 (s, 1H), 5.56 (d, J = 9.3 Hz, 1H), 4.29 – 4.21 (m, 1H), 3.55 (s, 3H), 3.33 (dd, J = 15.0, 5.5 Hz, 1H), 3.14 (dd, J = 15.1, 8.0 Hz, 1H), 1.74 – 1.66

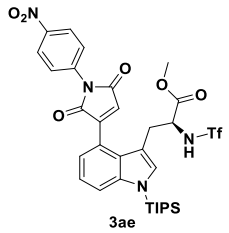
(m, 3H), 1.16 (dd, *J* = 7.5, 2.3 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): δ 170.7, 170.0, 169.2, 161.8 (d, *J* = 247.7 Hz), 146.2, 142.3, 133.2, 128.1 (d, *J* = 8.6 Hz), 128.0, 127.7 (d, *J* = 3.2 Hz), 127.4, 123.5, 121.5, 120.6, 120.5, 118.0, 116.7, 116.1 (d, *J* = 22.8 Hz), 110.1, 57.5, 53.0, 31.6, 18.1, 18.1, 12.9; LRMS (ESI): *m/z* 694.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{32}H_{36}F_4N_3O_6SSi$ 694.2036; found 694.2030.



3ad

*Methyl (S)-3-(4-(1-(4-bromophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ad**)*

Orange solid (60.3 mg, 80% yield); m.p.: 103.8 – 104.7 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (dd, *J* = 12.3, 8.5 Hz, 3H), 7.41 – 7.38 (m, 2H), 7.27 – 7.20 (m, 3H), 6.72 (s, 1H), 5.61 (d, *J* = 9.3 Hz, 1H), 4.27 – 4.21 (m, 1H), 3.55 (s, 3H), 3.32 (dd, *J* = 15.1, 5.5 Hz, 1H), 3.14 (dd, *J* = 15.1, 8.0 Hz, 1H), 1.73 – 1.65 (m, 3H), 1.16 (dd, *J* = 7.5, 2.7 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): δ 170.6, 169.7, 168.9, 146.3, 142.3, 133.2, 132.2, 130.8, 128.0, 127.5, 127.4, 123.5, 121.5, 121.4, 120.5, 120.4, 118.0, 116.7, 110.1, 57.5, 53.0, 31.6, 18.1, 18.0, 12.8; LRMS (ESI): *m/z* 754.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{32}H_{36}BrF_3N_3O_6SSi$ 754.1235; found 754.1230.

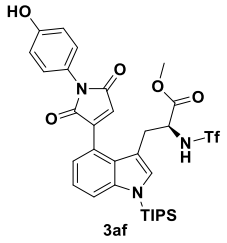


3ae

*Methyl (S)-3-(4-(1-(4-nitrophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ae**)*

Orange solid (36.1 mg, 50% yield); m.p.: 211.4 – 212.5 °C;^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.41 – 8.33 (m, 2H), 7.84 – 7.77 (m, 2H), 7.67 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.22 (s, 1H), 6.76 (s, 1H), 5.50 (d, *J* = 9.3 Hz, 1H), 4.29 – 4.21 (m, 1H), 3.54 (s, 3H), 3.32 (dd, *J* = 15.0, 5.9 Hz, 1H), 3.19 (dd, *J* = 15.0, 7.3 Hz, 1H), 1.76 – 1.66 (m, 3H), 1.16 (d, *J* = 7.5 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): δ 170.5, 169.2, 168.3, 146.4, 146.2, 142.4, 137.6, 133.5, 128.2, 127.3, 125.8, 124.4, 123.7, 121.5,

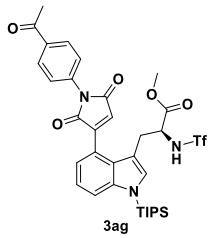
120.5, 120.1, 118.0, 117.0, 110.0, 57.6, 53.0, 31.8, 18.1, 12.9; LRMS (ESI): *m/z* 721.4 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{32}H_{36}F_3N_4O_8SSi$ 721.1981; found 721.1976.



3af

*methyl (S)-3-(4-(1-(4-hydroxyphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3af**)*

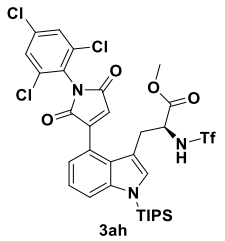
Orange solid (29.4 mg, 42% yield); m.p.: 113.9 – 114.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 8.1 Hz, 1H), 7.28 – 7.25 (m, 3H), 7.24 – 7.20 (m, 2H), 6.91 – 6.85 (m, 2H), 6.71 (s, 1H), 5.88 – 5.73 (m, 1H), 4.29 – 4.23 (m, 1H), 3.56 (s, 3H), 3.32 (dd, J = 15.1, 5.5 Hz, 1H), 3.12 (dd, J = 15.1, 8.3 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.15 (dd, J = 7.6, 3.5 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.9, 170.5, 169.8, 155.4, 146.2, 142.2, 133.1, 128.0, 127.4, 124.2, 123.4, 121.4, 120.6, 120.6, 118.0, 116.6, 116.0, 110.2, 57.5, 53.1, 31.5, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 692.4 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{32}H_{37}F_3N_3O_7SSi$ 692.2079; found 692.2078.



3ag

*Methyl (S)-3-(4-(1-(4-acetylphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ag**)*

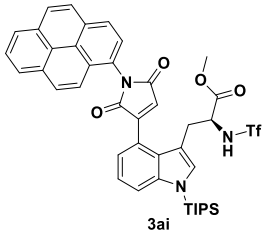
Orange solid (35.5 mg, 49% yield); m.p.: 100.3 – 101.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.12 – 8.08 (m, 2H), 7.69 – 7.63 (m, 3H), 7.28 – 7.23 (m, 3H), 6.75 (s, 1H), 5.72 (d, J = 8.8 Hz, 1H), 4.28 – 4.21 (m, 1H), 3.54 (s, 3H), 3.33 (dd, J = 15.0, 5.5 Hz, 1H), 3.15 (dd, J = 15.1, 8.0 Hz, 1H), 2.64 (s, 3H), 1.73 – 1.67 (m, 3H), 1.16 (dd, J = 7.5, 2.8 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 197.2, 170.7, 169.6, 168.7, 146.4, 142.3, 136.1, 135.8, 133.3, 129.2, 128.2, 127.4, 125.5, 123.5, 121.5, 120.6, 120.3, 118.0, 116.8, 110.1, 57.5, 53.0, 31.6, 26.7, 18.1, 18.1, 12.9; LRMS (ESI): *m/z* 718.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{34}H_{39}F_3N_3O_7SSi$ 718.2236; found 718.2234.



3ah

*Methyl (S)-3-(4-(2,5-dioxo-1-(2,4,6-trichlorophenyl)-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ah**)*

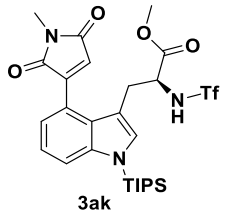
Orange solid (29.7 mg, 38% yield); m.p.: 102.5 – 104.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.66 (d, J = 7.8 Hz, 1H), 7.53 – 7.48 (m, 2H), 7.28 – 7.22 (m, 3H), 6.81 (s, 1H), 5.52 (d, J = 9.3 Hz, 1H), 4.36 – 4.29 (m, 1H), 3.68 (s, 3H), 3.37 (dd, J = 15.5, 4.2 Hz, 1H), 3.10 (dd, J = 15.5, 9.2 Hz, 1H), 1.73 – 1.68 (m, 3H), 1.16 (dd, J = 7.6, 5.7 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.9, 168.1, 167.3, 147.1, 142.2, 136.5, 136.3, 136.2, 132.8, 128.9, 128.8, 128.1, 127.5, 126.8, 123.5, 121.4, 120.5, 120.2, 118.0, 116.9, 110.3, 57.2, 53.1, 31.3, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 780.3 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{32}H_{34}Cl_3F_3N_3O_6SSi$ 778.0961; found 778.0956.



3ai

*Methyl (S)-3-(4-(2,5-dioxo-1-(pyren-1-yl)-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ai**)*

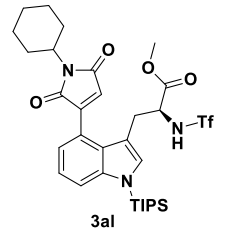
Orange solid (37.8 mg, 47% yield); m.p.: 174.8 – 175.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.31 – 8.21 (m, 3H), 8.19 – 8.11 (m, 3H), 8.08 – 8.00 (m, 2H), 7.97 – 7.90 (m, 1H), 7.70 – 7.64 (m, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.32 – 7.26 (m, 2H), 6.90 (s, 1H), 5.69, 5.61 (2 × d, J = 9.3 Hz, 1H), 4.45 – 4.35 (m, 1H), 3.57, 3.55 (2 × s, 3H), 3.50, 3.47 (2 × d, J = 4.9 Hz, 1H), 3.34 – 3.29, 3.26 – 3.20 (2 × m, 1H), 1.75 – 1.66 (m, 3H), 1.19 – 1.12 (m, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.4, 172.2, 172.1, 172.0, 171.6, 171.5, 147.7, 147.5, 143.9, 143.8, 134.9, 134.6, 133.4, 133.4, 132.5, 132.5, 132.3, 132.2, 130.3, 130.3, 130.0, 130.0, 129.9, 129.9, 129.7, 129.6, 128.9, 128.8, 128.6, 128.6, 127.8, 127.8, 127.4, 127.4, 127.3, 127.3, 126.9, 126.7, 126.6, 126.5, 125.9, 125.3, 125.3, 123.3, 123.2, 123.0, 122.2, 122.1, 122.1, 122.0, 119.5, 119.5, 118.2, 118.1, 111.7, 111.6, 59.0, 58.9, 54.7, 54.6, 33.2, 33.1, 19.5, 19.5, 14.3; LRMS (ESI): *m/z* 800.4 $[M - H]^-$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{42}H_{43}F_3N_3O_6SSi$ 802.2588; found 802.2598.



3ak

*Methyl (S)-3-(4-(1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ak**)*

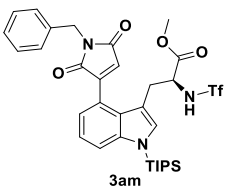
Orange solid (45.6 mg, 74% yield); m.p.: 91.2 – 92.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 (d, J = 8.3 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.12 (d, J = 7.3 Hz, 1H), 6.59 (s, 1H), 6.04 – 5.97 (m, 1H), 4.23 – 4.17 (m, 1H), 3.62 (s, 3H), 3.26 (dd, J = 15.1, 5.5 Hz, 1H), 3.15 (s, 3H), 3.04 (dd, J = 15.1, 8.6 Hz, 1H), 1.74 – 1.66 (m, 3H), 1.15 (dd, J = 7.6, 3.3 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.9, 172.5, 172.2, 148.1, 143.6, 134.5, 129.6, 128.9, 124.6, 122.8, 122.2, 122.0, 119.5, 117.8, 111.8, 58.9, 54.4, 32.7, 25.6, 19.5, 19.5, 14.3; LRMS (ESI): *m/z* 614.4 $[M - H]^-$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{27}H_{37}F_3N_3O_6SSi$ 616.2119; found 616.2117.



3al

*Methyl (S)-3-(4-(1-cyclohexyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3al**)*

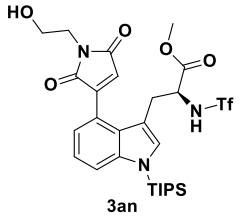
Orange solid (41.7 mg, 61% yield); m.p.: 91.9 – 92.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (d, J = 8.3 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.11 (d, J = 7.3 Hz, 1H), 6.53 (s, 1H), 5.63 (d, J = 9.3 Hz, 1H), 4.27 – 4.21 (m, 1H), 4.07 – 3.99 (m, 1H), 3.65 (s, 3H), 3.25 (dd, J = 15.2, 5.0 Hz, 1H), 3.01 (dd, J = 15.2, 8.9 Hz, 1H), 2.20 – 2.09 (m, 2H), 1.90 – 1.83 (m, 2H), 1.77 – 1.65 (m, 6H), 1.41 – 1.32 (m, 2H), 1.28 – 1.22 (m, 1H), 1.15 (dd, J = 7.6, 4.6 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.9, 170.3, 170.1, 145.6, 141.5, 132.1, 127.4, 127.1, 122.7, 120.8, 120.5, 120.1, 117.5, 115.8, 109.8, 57.0, 52.4, 50.6, 30.5, 29.5, 29.5, 25.5, 24.6, 17.6, 17.6, 12.3; LRMS (ESI): *m/z* 682.5 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{32}H_{43}F_3N_3O_6SSi$ 682.2599; found 682.2587.



3am

*Methyl (S)-3-(4-(1-benzyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3am**)*

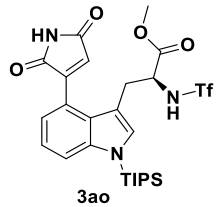
Orange solid (39.6 mg, 57% yield); m.p.: 95.9 – 97.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 (d, J = 8.3 Hz, 1H), 7.43 (d, J = 7.2 Hz, 2H), 7.33 (dd, J = 8.2, 6.6 Hz, 2H), 7.31 – 7.27 (m, 1H), 7.24 – 7.19 (m, 2H), 7.13 (d, J = 7.3 Hz, 1H), 6.58 (s, 1H), 5.51 (d, J = 9.2 Hz, 1H), 4.86 – 4.74 (m, 2H), 4.16 – 4.10 (m, 1H), 3.43 (s, 3H), 3.21 (dd, J = 15.2, 5.0 Hz, 1H), 2.97 (dd, J = 15.2, 8.7 Hz, 1H), 1.72 – 1.64 (m, 3H), 1.15 (dd, J = 7.6, 4.1 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.5, 170.3, 169.6, 145.8, 141.6, 136.0, 132.4, 128.2, 128.1, 127.4, 127.4, 126.9, 122.7, 120.9, 120.2, 120.0, 117.5, 115.9, 109.7, 56.8, 52.3, 41.4, 30.8, 17.6, 17.6, 12.3; LRMS (ESI): *m/z* 690.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{33}H_{39}F_3N_3O_6SSi$ 690.2286; found 690.2281.



3an

*Methyl (S)-3-(4-(1-(2-hydroxyethyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3an**)*

Orange solid (37.3 mg, 58% yield); m.p.: 88.5 – 90.0 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.63 (d, J = 8.3 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.12 (d, J = 7.3 Hz, 1H), 6.63 (s, 1H), 6.24 (d, J = 9.2 Hz, 1H), 4.35 – 4.28 (m, 1H), 3.96 – 3.85 (m, 4H), 3.60 (s, 3H), 3.27 (dd, J = 15.1, 6.8 Hz, 1H), 3.12 (dd, J = 15.1, 7.7 Hz, 1H), 1.77 – 1.67 (m, 3H), 1.18 (dd, J = 7.6, 2.9 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 171.9, 171.0, 170.7, 147.1, 141.9, 132.5, 128.2, 127.6, 122.9, 121.4, 120.7, 120.6, 118.1, 116.4, 110.3, 60.6, 57.5, 52.9, 40.9, 31.1, 18.1, 12.8; LRMS (ESI): *m/z* 644.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$ calcd for $C_{28}H_{37}F_3N_3O_7SSi$ 644.2079; found 644.2070.

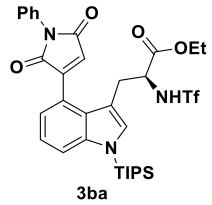


3ao

*Methyl (S)-3-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ao**)*

Orange solid (10.2 mg, 17% yield); m.p.: 92.9 – 94.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.89 (s, 1H), 7.62 (d, J = 8.3 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.14 (d, J = 7.3 Hz, 1H), 6.58 (s, 1H), 6.19 (d, J = 9.3 Hz,

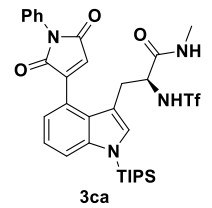
1H), 4.26 – 4.20 (m, 1H), 3.61 (s, 3H), 3.29 (dd, *J* = 15.1, 5.6 Hz, 1H), 3.09 (dd, *J* = 15.1, 8.5 Hz, 1H), 1.73 – 1.66 (m, 3H), 1.15 (dd, *J* = 7.6, 4.3 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): *δ* 171.2, 171.1, 170.3, 147.4, 142.1, 133.0, 128.9, 127.4, 123.2, 121.3, 120.6, 120.3, 118.0, 116.5, 110.3, 57.5, 53.0, 31.3, 18.1, 18.0, 12.8; LRMS (ESI): *m/z* 600.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$ calcd for $C_{26}H_{33}F_3N_3O_6SSi$ 600.1817; found 600.1814.



3ba

*Ethyl (S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate(**3ba**)*

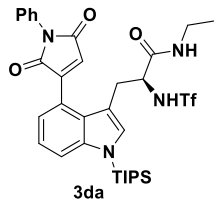
Orange solid (43.1 mg, 62% yield); m.p.: 94.8 – 95.3 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): *δ* 7.64 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.51 – 7.47 (m, 4H), 7.40 – 7.36 (m, 1H), 7.28 – 7.21 (m, 3H), 6.71 (s, 1H), 5.74 – 5.68 (m, 1H), 4.29 – 4.23 (m, 1H), 4.08 – 4.02 (m, 1H), 3.95 – 3.92 (m, 1H), 3.32 (dd, *J* = 15.1, 5.5 Hz, 1H), 3.15 (dd, *J* = 15.1, 8.2 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.15 (dd, *J* = 7.6, 3.4 Hz, 18H), 1.00 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz): *δ* 170.2, 170.0, 169.3, 146.2, 142.2, 133.2, 131.8, 129.1, 128.0, 127.8, 127.6, 126.2, 123.5, 121.4, 120.7, 120.4, 118.5, 116.6, 110.3, 62.4, 57.6, 31.5, 18.1, 18.1, 13.7, 12.8; LRMS (ESI): *m/z* 690.4 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$ calcd for $C_{33}H_{39}F_3N_3O_6SSi$ 690.2286; found 690.2283.



3ca

*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-methyl-2-((trifluoromethyl)sulfonamido)propenamide(**3ca**)*

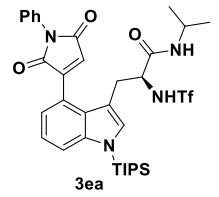
Orange solid (23.5 mg, 35% yield); m.p.: 120.1 – 121.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): *δ* 7.64 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.52 – 7.48 (m, 4H), 7.42 – 7.37 (m, 1H), 7.27 – 7.22 (m, 3H), 6.70 (s, 1H), 6.68 – 6.65 (m, 1H), 5.33 – 5.29 (m, 1H), 3.96 – 3.85 (m, 1H), 3.24 – 3.16 (m, 2H), 2.36 (d, *J* = 4.8 Hz, 3H), 1.75 – 1.67 (m, 3H), 1.14 (dd, *J* = 9.2, 7.5 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz): *δ* 170.7, 169.6, 169.0, 145.6, 142.2, 134.0, 131.6, 129.1, 128.4, 127.9, 127.0, 126.3, 123.6, 121.3, 120.5, 116.6, 110.7, 58.2, 32.7, 26.1, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 675.5 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$ calcd for $C_{32}H_{38}F_3N_4O_5SSi$ 675.2290; found 675.2289.



3da

*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-ethyl-2-((trifluoromethyl)sulfonamido)propenamide(**3da**)*

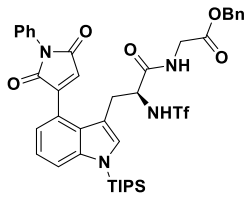
Orange solid (21.4 mg, 31% yield); m.p.: 120.3 – 121.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 7.9 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.41 – 7.37 (m, 1H), 7.26 – 7.22 (m, 3H), 6.70 – 6.68 (m, 2H), 5.31 – 5.26 (m, 1H), 3.92 – 3.87 (m, 1H), 3.24 (dd, J = 14.6, 9.2 Hz, 1H), 3.18 (dd, J = 14.6, 6.6 Hz, 1H), 3.09 – 3.09 (m, 1H), 2.65 – 2.58 (m, 1H), 1.74 – 1.67 (m, 3H), 1.14 (dd, J = 7.5, 5.9 Hz, 18H), 0.75 – 0.66 (m, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 170.7, 169.0, 168.7, 145.6, 142.2, 133.9, 131.6, 129.1, 128.3, 127.9, 127.2, 126.4, 123.6, 121.3, 120.5, 118.4, 116.6, 110.8, 58.4, 34.4, 32.6, 18.1, 18.1, 13.9, 12.8; LRMS (ESI): *m/z* 689.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{33}H_{40}F_3N_4O_5SSi$ 689.2446; found 689.2445.



3ea

*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-isopropyl-2-((trifluoromethyl)sulfonamido)propenamide(**3ea**)*

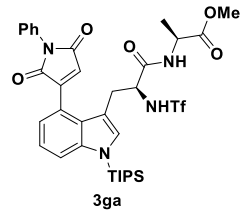
Orange solid (23.3 mg, 33% yield); m.p.: 113.8 – 114.9 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (dd, J = 8.0, 1.3 Hz, 1H), 7.52 – 7.48 (m, 4H), 7.42 – 7.37 (m, 1H), 7.26 – 7.21 (m, 3H), 6.70 (s, 1H), 6.55 (d, J = 8.5 Hz, 1H), 5.08 – 5.12 (m, 1H), 3.92 – 3.85 (m, 1H), 3.66 – 3.57 (m, 1H), 3.25 (dd, J = 14.6, 9.3 Hz, 1H), 3.18 (dd, J = 14.6, 6.7 Hz, 1H), 1.68 – 1.72 (m, 3H), 1.15 (d, J = 7.5 Hz, 18H), 0.88 (d, J = 6.5 Hz, 3H), 0.51 (d, J = 6.6 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 170.7, 169.1, 167.6, 145.6, 142.3, 133.9, 131.6, 129.1, 128.2, 127.9, 127.4, 126.4, 123.5, 121.3, 120.4, 116.6, 110.8, 58.5, 41.8, 32.6, 22.0, 21.6, 18.1, 12.8; LRMS (ESI): *m/z* 703.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{34}H_{42}F_3N_4O_5SSi$ 703.2603; found 703.2604.



3fa

*Benzyl (S)-(3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)glycinate(**3fa**)*

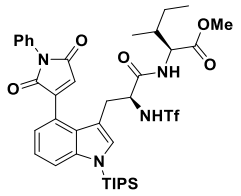
Orange solid (38.3 mg, 47% yield); m.p.: 105.3 – 107.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (dd, J = 8.1, 1.2 Hz, 1H), 7.50 – 7.45 (m, 2H), 7.44 – 7.41 (m, 2H), 7.37 – 7.32 (m, 4H), 7.30 (s, 1H), 7.29 – 7.27 (m, 2H), 7.24 – 7.18 (m, 2H), 6.68 (s, 1H), 6.45 (d, J = 8.7 Hz, 1H), 6.06 – 6.01 (m, 1H), 5.10 – 4.99 (m, 2H), 4.11 – 4.16 (m, 1H), 3.66 (dd, J = 18.3, 5.7 Hz, 1H), 3.49 (dd, J = 18.3, 4.8 Hz, 1H), 3.23 (dd, J = 14.9, 7.4 Hz, 1H), 3.19 – 3.11 (m, 1H), 1.73 – 1.65 (m, 3H), 1.13 (t, J = 7.2 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.7, 169.6, 169.0, 168.5, 146.5, 142.0, 134.9, 133.6, 131.6, 129.1, 128.6, 128.6, 128.5, 128.4, 127.8, 127.5, 126.2, 123.7, 121.3, 120.7, 120.6, 116.7, 110.7, 67.3, 58.4, 41.1, 32.1, 18.1, 12.8; LRMS (ESI): *m/z* 809.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{40}H_{44}F_3N_4O_7SSi$ 809.2658; found 809.2657.



3ga

*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-alaninate (**3ga**)*

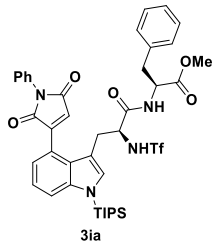
Orange solid (31.9 mg, 43% yield); m.p.: 119.8 – 120.9 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.66 (dd, J = 6.1, 3.3 Hz, 1H), 7.53 – 7.52 (m, 4H), 7.43 – 7.41 (m, 1H), 7.34 (s, 1H), 7.26 (d, J = 3.3 Hz, 2H), 6.73 (s, 1H), 6.57 (d, J = 8.8 Hz, 1H), 6.10 (d, J = 7.0 Hz, 1H), 4.31 – 4.26 (m, 1H), 4.16 – 4.10 (m, 1H), 3.59 (s, 3H), 3.32 (dd, J = 15.0, 7.9 Hz, 1H), 3.21 (dd, J = 15.0, 7.2 Hz, 1H), 1.74 – 1.69 (m, 3H), 1.22 (d, J = 7.1 Hz, 3H), 1.16 (dd, J = 7.6, 3.2 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 171.9, 170.5, 169.2, 168.6, 146.2, 142.2, 133.4, 131.7, 129.0, 128.1, 127.8, 127.5, 126.5, 123.7, 121.2, 120.7, 120.6, 118.1, 116.6, 110.7, 58.6, 52.5, 48.3, 32.0, 18.1, 17.8, 12.8; LRMS (ESI): *m/z* 747.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{35}H_{42}F_3N_4O_7SSi$ 747.2501; found 747.2501.



3ha

*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-alloisoleucinate(**3ha**)*

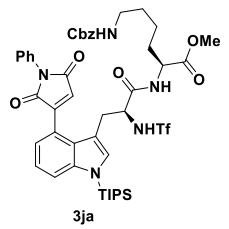
Orange solid (32.7 mg, 41% yield); m.p.: 116.3 – 118.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 (dd, J = 5.7, 3.6 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.40 – 7.35 (m, 1H), 7.32 (s, 1H), 7.23 – 7.19 (m, 2H), 6.71 (d, J = 8.8 Hz, 1H), 6.67 (s, 1H), 6.10 (d, J = 8.0 Hz, 1H), 4.31 (dd, J = 8.1, 4.2 Hz, 1H), 4.16 – 4.08 (m, 1H), 3.50 (s, 3H), 3.31 (dd, J = 15.0, 7.9 Hz, 1H), 3.21 (dd, J = 15.0, 6.9 Hz, 1H), 1.72 – 1.67 (m , 4H), 1.29 – 1.20 (m, 1H), 1.13 (dd, J = 7.6, 3.5 Hz, 18H), 1.04 – 0.97 (m, 1H), 0.82 (t, J = 7.4 Hz, 3H), 0.70 (d, J = 6.9 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.4, 170.1, 168.9, 168.3, 145.5, 141.7, 133.0, 131.3, 128.5, 127.6, 127.3, 127.1, 126.1, 123.2, 120.7, 120.2, 116.1, 110.2, 58.3, 56.1, 51.6, 37.4, 31.7, 24.6, 17.6, 14.5, 12.3, 11.0; LRMS (ESI): *m/z* 789.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{38}H_{48}F_3N_4O_7SSi$ 789.2971; found 789.2972.



3ia

*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-phenylalaninate (**3ia**)*

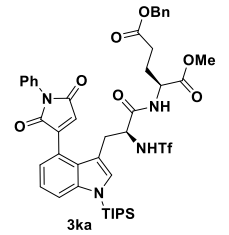
Orange solid (38.3 mg, 46% yield); m.p.: 112.3 – 113.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 (d, J = 7.9 Hz, 1H), 7.49 (m, 4H), 7.40 – 7.37 (m, 1H), 7.29 (s, 1H), 7.22 – 7.17 (m, 5H), 6.92 – 6.89 (m, 2H), 6.66 (s, 1H), 6.25 (d, J = 8.5 Hz, 1H), 5.95 (d, J = 7.4 Hz, 1H), 4.59 – 4.56 (m, 1H), 4.10 – 4.06 (m, 1H), 3.51 (s, 3H), 3.27 (dd, J = 15.1, 7.4 Hz, 1H), 3.17 (dd, J = 15.1, 7.2 Hz, 1H), 2.95 (dd, J = 14.0, 5.7 Hz, 1H), 2.80 (dd, J = 14.1, 6.0 Hz, 1H), 1.71 – 1.67 (m, 3H), 1.15 – 1.11 (m, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.1, 172.0, 170.7, 170.0, 147.8, 143.6, 136.7, 134.8, 133.2, 130.5, 130.0, 129.6, 129.3, 129.1, 128.6, 127.9, 125.1, 122.6, 122.1, 118.0, 112.1, 60.1, 54.8, 53.8, 38.9, 33.5, 19.5, 14.3; LRMS (ESI): *m/z* 823.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{41}H_{48}F_3N_4O_7SSi$ 825.2960; found 825.2946.



3ja

*Methyl N^6-((benzyloxy)carbonyl)-N^2-((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-lysinate (**3ja**)*

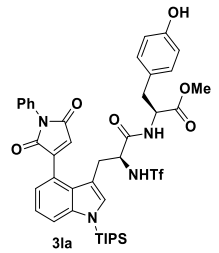
Orange solid (30.5 mg, 32% yield); m.p.: 103.5 – 104.8 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.66 – 7.62 (m, 1H), 7.53 – 7.46 (m, 4H), 7.40 – 7.34 (m, 3H), 7.34 – 7.29 (m, 3H), 7.28 – 7.20 (m, 4H), 6.74 – 6.64 (m, 2H), 6.49 – 6.43 (m, 1H), 5.08 – 4.92 (m, 2H), 4.39 – 4.32 (m, 1H), 4.26 – 4.19 (m, 1H), 3.57 (s, 3H), 3.40 (dd, J = 15.2, 6.3 Hz, 1H), 3.23 – 2.98 (m, 3H), 1.74 – 1.68 (m, 4H), 1.61 – 1.53 (m, 1H), 1.46 – 1.37 (m, 2H), 1.26 – 1.21 (m, 2H), 1.15 (dd, J = 7.5, 2.8 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 171.5, 170.4, 169.3, 169.2, 157.0, 146.3, 142.1, 136.2, 133.1, 131.8, 129.0, 128.5, 128.1, 127.7, 126.4, 123.4, 121.1, 120.7, 118.2, 116.5, 111.0, 66.9, 58.7, 52.4, 52.1, 39.9, 31.9, 30.9, 29.1, 21.6, 18.1, 12.8; LRMS (ESI): *m/z* 938.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{46}H_{55}F_3N_5O_9SSi$ 938.3447; found 938.3444.



3ka

*5-Benzyl 1-methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-glutamate (**3ka**)*

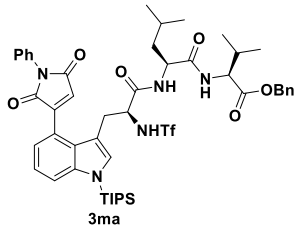
Orange solid (32.4 mg, 36% yield); m.p.: 96.4 – 98.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.62 (dd, J = 7.1, 2.0 Hz, 1H), 7.50 – 7.44 (m, 4H), 7.37 – 7.33 (m, 2H), 7.33 – 7.28 (m, 5H), 7.23 – 7.19 (m, 2H), 6.68 (s, 1H), 6.36 (d, J = 7.4 Hz, 1H), 6.25 (d, J = 8.8 Hz, 1H), 5.05 (s, 2H), 4.37 – 4.32 (m, 1H), 4.16 – 4.11 (m, 1H), 3.52 (s, 3H), 3.29 (dd, J = 15.2, 7.1 Hz, 1H), 3.17 (dd, J = 15.2, 7.4 Hz, 1H), 2.34 – 2.28 (m, 1H), 2.24 – 2.19 (m, 1H), 2.06 – 2.00 (m, 1H), 1.82 – 1.77 (m, 1H), 1.73 – 1.68 (m, 3H), 1.14 (dd, J = 7.5, 4.1 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.0, 172.3, 172.0, 170.7, 170.6, 147.7, 143.6, 137.1, 134.7, 133.2, 130.5, 130.0, 129.8, 129.7, 129.6, 129.2, 129.1, 127.9, 125.1, 122.6, 122.1, 118.0, 112.1, 68.1, 60.1, 54.0, 53.3, 33.3, 31.3, 28.1, 19.5, 14.3; LRMS (ESI): *m/z* 895.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{44}H_{50}F_3N_4O_9SSi$ 895.3025; found 895.3027.



3la

*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-tyrosinate (**3la**)*

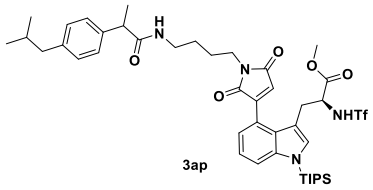
Orange solid (30.8 mg, 37% yield); m.p.: 128.6 – 129.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (dd, J = 7.9, 1.4 Hz, 1H), 7.48 – 7.46 (m, 4H), 7.39 – 7.35 (m, 1H), 7.27 (s, 1H), 7.22 – 7.17 (m, 2H), 6.75 (d, J = 8.5 Hz, 2H), 6.64 (s, 1H), 6.59 (d, J = 8.5 Hz, 2H), 6.47 (d, J = 8.6 Hz, 1H), 6.10 (d, J = 7.6 Hz, 1H), 4.56 – 4.52 (m, 1H), 4.11 – 4.08 (m, 1H), 3.52 (s, 3H), 3.27 (dd, J = 15.1, 7.6 Hz, 1H), 3.14 (dd, J = 15.0, 7.2 Hz, 1H), 2.89 (dd, J = 14.1, 5.4 Hz, 1H), 2.75 (dd, J = 14.1, 6.1 Hz, 1H), 1.70 – 1.65 (m, 3H), 1.12 (dd, J = 7.5, 4.2 Hz, 18H), 1.05 (s, 1H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.3, 170.1, 169.0, 168.2, 154.4, 145.7, 141.7, 133.0, 131.2, 129.8, 128.6, 127.6, 127.4, 127.1, 126.6, 126.0, 123.2, 120.7, 120.1, 116.1, 115.1, 110.2, 58.3, 53.1, 51.9, 36.4, 31.4, 17.6, 17.2, 12.3; LRMS (ESI): *m/z* 839.5 $[M - H]^-$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{41}H_{48}F_3N_4O_8SSi$ 841.2909; found 841.2904.



3ma

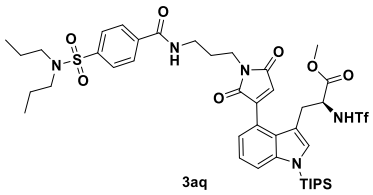
*Benzyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-leucyl-L-valinate (**3ma**)*

Orange solid (26.4 mg, 27% yield); m.p.: 99.5 – 100.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (dd, J = 8.3, 1.0 Hz, 1H), 7.56 – 7.52 (m, 2H), 7.48 (dd, J = 8.6, 7.2 Hz, 2H), 7.40 – 7.28 (m, 7H), 7.22 – 7.13 (m, 2H), 6.68 (s, 1H), 6.42 (s, 1H), 6.28 (d, J = 8.0 Hz, 1H), 6.12 (s, 1H), 5.17 – 5.04 (m, 2H), 4.31 – 4.21 (m, 2H), 4.09 – 4.03 (m, 1H), 3.31 – 3.14 (m, 2H), 2.09 – 2.00 (m, 1H), 1.75 – 1.67 (m, 4H), 1.48 – 1.37 (m, 2H), 1.16 (dd, J = 7.6, 2.9 Hz, 18H), 0.85 – 0.73 (m, 12H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.2, 171.0, 170.8, 169.6, 169.1, 146.3, 142.1, 135.2, 133.5, 131.7, 129.1, 128.6, 128.5, 128.4, 128.0, 127.6, 126.7, 123.6, 121.1, 120.6, 116.5, 110.8, 67.0, 59.3, 57.4, 52.2, 41.4, 31.3, 31.0, 24.5, 22.4, 22.1, 18.7, 18.1, 18.1, 17.9, 12.8; LRMS (ESI): *m/z* 964.6 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{49}H_{61}F_3N_5O_8SSi$ 964.3968; found 964.3969.



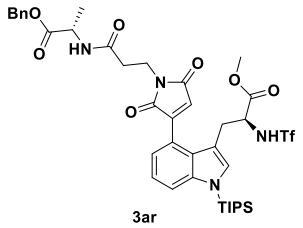
*Methyl (2S)-3-(4-(1-(4-(2-(4-isobutylphenyl)propanamido)butyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ap**)*

Orange solid (41.3 mg, 48% yield); m.p.: 97.4 – 98.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (dd, J = 8.4, 0.9 Hz, 1H), 7.44 (d, J = 8.9 Hz, 1H), 7.22 – 7.16 (m, 4H), 7.13 – 7.09 (m, 2H), 7.07 (dd, J = 7.3, 0.8 Hz, 1H), 6.60 (s, 1H), 5.60 – 5.51 (m, 1H), 4.28 – 4.22 (m, 1H), 3.67 – 3.58 (m, 2H), 3.57 (s, 3H), 3.55 – 3.50 (m, 1H), 3.27 (dd, J = 15.0, 7.5 Hz, 1H), 3.24 – 3.11 (m, 2H), 3.04 (dd, J = 15.0, 7.0 Hz, 1H), 2.44 (d, J = 7.2 Hz, 2H), 1.88 – 1.80 (m, 1H), 1.74 – 1.66 (m, 3H), 1.66 – 1.61 (m, 2H), 1.56 – 1.46 (m, 5H), 1.15 (dd, J = 7.5, 2.5 Hz, 18H), 0.89 (d, J = 6.6 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.7, 171.0, 170.4, 170.0, 146.2, 141.5, 140.3, 137.9, 131.8, 129.2, 127.6, 127.2, 127.0, 122.4, 120.8, 120.5, 115.8, 110.5, 57.2, 52.2, 46.2, 44.6, 39.1, 37.4, 30.7, 29.7, 26.2, 25.3, 21.9, 17.9, 17.6, 12.4; LRMS (ESI): *m/z* 859.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{43}H_{58}F_3N_4O_7SSi$ 859.3753; found 859.3754.



*Methyl (S)-3-(4-(1-(3-(4-(N,N-dipropylsulfamoyl)benzamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3aq**)*

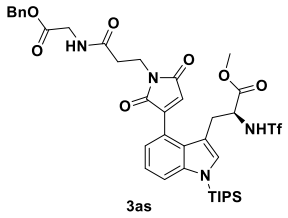
Orange solid (39.6 mg, 43% yield); m.p.: 95.3 – 95.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.98 – 7.93 (m, 2H), 7.87 – 7.83 (m, 2H), 7.62 (d, J = 8.2 Hz, 1H), 7.26 – 7.21 (m, 2H), 7.13 (d, J = 7.3 Hz, 1H), 7.08 (t, J = 6.2 Hz, 1H), 6.89 (d, J = 9.2 Hz, 1H), 6.60 (s, 1H), 4.28 – 4.21 (m, 1H), 3.84 – 3.72 (m, 2H), 3.64 – 3.57 (m, 1H), 3.52 (s, 3H), 3.46 – 3.40 (m, 1H), 3.31 (dd, J = 14.9, 7.1 Hz, 1H), 3.16 (dd, J = 15.0, 7.4 Hz, 1H), 3.12 – 3.02 (m, 4H), 2.10 – 1.96 (m, 2H), 1.74 – 1.66 (m, 3H), 1.58 – 1.50 (m, 4H), 1.15 (dd, J = 7.5, 2.4 Hz, 18H), 0.86 (t, J = 7.4 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 171.4, 170.4, 170.3, 166.0, 146.0, 142.3, 141.7, 137.3, 132.4, 127.5, 127.4, 127.0, 126.8, 122.7, 120.9, 120.1, 116.1, 110.0, 57.2, 52.3, 49.6, 36.2, 34.6, 30.9, 27.5, 21.5, 17.6, 12.4, 10.7; LRMS (ESI): *m/z* 924.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{42}H_{57}F_3N_5O_9S_2Si$ 924.3325; found 924.3327.



3ar

*Methyl (S)-3-(4-(1-(3-(((S)-1-(benzyloxy)-1-oxopropan-2-yl)amino)-3-oxopropyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ar**)*

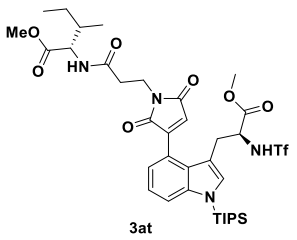
Orange solid (33.5 mg, 40% yield); m.p.: 97.0 – 98.1 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.70 (d, J = 8.4 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.38 – 7.30 (m, 5H), 7.22 (s, 1H), 7.20 – 7.15 (m, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.58 (s, 1H), 6.50 (d, J = 7.5 Hz, 1H), 5.23 – 5.13 (m, 2H), 4.70 – 4.62 (m, 1H), 4.36 – 4.30 (m, 1H), 3.99 – 3.89 (m, 2H), 3.45 (s, 3H), 3.23 (dd, J = 15.1, 9.4 Hz, 1H), 3.13 (dd, J = 15.1, 6.1 Hz, 1H), 2.71 – 2.65 (m, 2H), 1.73 – 1.66 (m, 3H), 1.43 (d, J = 7.1 Hz, 3H), 1.15 (dd, J = 7.6, 3.4 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.5, 170.7, 170.4, 169.7, 169.6, 147.2, 141.2, 134.8, 131.4, 128.2, 128.0, 127.9, 127.7, 127.4, 122.2, 120.8, 120.4, 115.8, 110.6, 66.9, 57.1, 52.0, 47.8, 34.3, 34.2, 30.4, 17.9, 17.6, 12.4; LRMS (ESI): *m/z* 833.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{39}H_{48}F_3N_4O_9SSi$ 833.2869; found 833.2868.



3as

*Methyl (S)-3-(4-(1-(3-((2-(benzyloxy)-2-oxoethyl)amino)-3-oxopropyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3as**)*

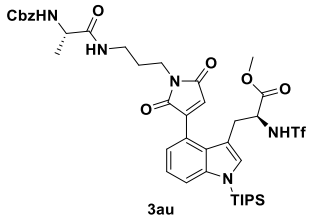
Orange solid (34.7 mg, 42% yield); m.p.: 96.6 – 97.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.71 (d, J = 8.6 Hz, 1H), 7.59 (d, J = 8.4 Hz, 1H), 7.37 – 7.31 (m, 5H), 7.24 (s, 1H), 7.18 (dd, J = 8.4, 7.3 Hz, 1H), 7.02 (d, J = 7.2 Hz, 1H), 6.56 (s, 1H), 6.48 – 6.42 (m, 1H), 5.24 – 5.15 (m, 2H), 4.35 – 4.29 (m, 1H), 4.20 – 4.07 (m, 2H), 4.03 – 3.88 (m, 2H), 3.44 (s, 3H), 3.27 – 3.11 (m, 2H), 2.79 – 2.63 (m, 2H), 1.73 – 1.64 (m, 3H), 1.15 (dd, J = 7.5, 3.2 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 170.7, 170.6, 170.5, 169.6, 169.6, 146.9, 141.3, 134.6, 131.4, 128.2, 128.1, 127.9, 127.4, 122.3, 120.8, 120.4, 120.4, 117.8, 115.8, 110.6, 67.0, 57.1, 52.1, 41.2, 34.2, 34.0, 30.5, 17.6, 12.4; LRMS (ESI): *m/z* 819.4 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{38}H_{46}F_3N_4O_9SSi$ 819.2712; found 819.2710.



3at

*Methyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucinate (**3at**)*

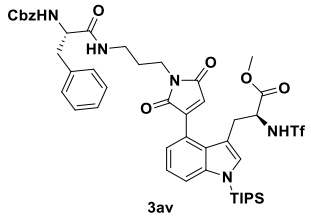
Orange solid (34.6 mg, 43% yield); m.p.: 96.6 – 97.4 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.59 (dd, J = 8.5, 0.9 Hz, 1H), 7.49 (d, J = 8.5 Hz, 1H), 7.22 (s, 1H), 7.18 (dd, J = 8.4, 7.2 Hz, 1H), 7.02 (dd, J = 7.2, 0.8 Hz, 1H), 6.59 (s, 1H), 6.40 (d, J = 8.8 Hz, 1H), 4.64 – 4.58 (m, 1H), 4.36 – 4.29 (m, 1H), 4.01 – 3.88 (m, 2H), 3.73 (s, 3H), 3.49 (s, 3H), 3.26 – 3.21 (m, 1H), 3.15 – 3.09 (m, 1H), 2.70 (t, J = 6.4 Hz, 2H), 1.94 – 1.86 (m, 1H), 1.72 – 1.66 (m, 3H), 1.47 – 1.39 (m, 1H), 1.22 – 1.77 (m, 1H), 1.15 (dd, J = 7.5, 3.3 Hz, 18H), 0.95 – 0.88 (m, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.1, 170.7, 170.4, 170.0, 169.5, 147.1, 141.2, 131.4, 127.9, 127.4, 122.2, 120.8, 120.4, 115.8, 110.5, 57.0, 56.1, 52.1, 51.8, 37.4, 34.4, 34.3, 30.3, 24.7, 17.6, 14.8, 12.4, 11.1; LRMS (ESI): *m/z* 799.5 [M – H]$^-$; HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_{36}H_{52}F_3N_4O_9SSi$ 801.3171; found 801.3171.



3au

*Methyl (S)-3-(4-(1-(3-((S)-2-(((benzyloxy)carbonyl)amino)propanamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3au**)*

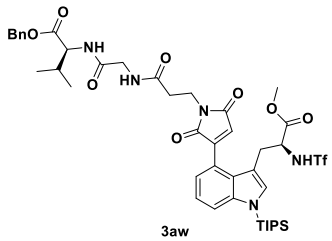
Orange solid (42.2 mg, 49% yield); m.p.: 99.6 – 100.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.67 (d, J = 9.1 Hz, 1H), 7.60 (dd, J = 8.4, 0.9 Hz, 1H), 7.36 – 7.28 (m, 5H), 7.24 (s, 1H), 7.20 (dd, J = 8.4, 7.3 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 6.63 – 6.58 (m, 1H), 6.57 (s, 1H), 5.47 – 5.40 (m, 1H), 5.11 (s, 2H), 4.30 – 4.19 (m, 2H), 3.71 – 3.58 (m, 2H), 3.46 (s, 3H), 3.43 – 3.76 (m, 1H), 3.29 – 3.18 (m, 2H), 3.16 – 3.10 (m, 1H), 1.98 – 1.81 (m, 2H), 1.72 – 1.67 (m, 3H), 1.37 (d, J = 7.1 Hz, 3H), 1.14 (dd, J = 7.5, 2.5 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 172.8, 171.5, 170.8, 170.5, 156.3, 146.6, 142.0, 136.2, 132.3, 128.5, 128.2, 128.1, 128.1, 127.6, 122.9, 121.2, 120.8, 120.5, 118.4, 116.3, 110.9, 67.1, 57.7, 52.6, 36.1, 34.9, 31.1, 27.9, 18.1, 12.8; LRMS (ESI): *m/z* 862.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{40}H_{51}F_3N_5O_9SSi$ 862.3134; found 862.3137.



3av

*Methyl (S)-3-(4-(1-(3-((S)-2-(((benzyloxy)carbonyl)amino)-3-phenylpropanamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3av**)*

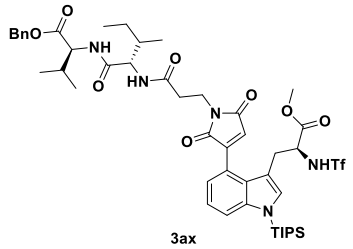
Orange solid (52.3 mg, 56% yield); m.p.: 98.3 – 99.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 – 7.56 (m, 2H), 7.34 – 7.26 (m, 8H), 7.23 – 7.16 (m, 4H), 7.07 (d, J = 7.3 Hz, 1H), 6.56 (s, 1H), 6.38 – 6.30 (m, 1H), 5.51 – 5.42 (m, 1H), 5.06 (s, 2H), 4.41 – 4.21 (m, 2H), 3.53 – 3.48 (m, 2H), 3.47 (s, 3H), 3.30 – 2.99 (m, 6H), 1.83 – 1.76 (m, 1H), 1.71 – 1.66 (m, 4H), 1.15 (dd, J = 7.6, 1.9 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.5, 171.4, 170.8, 170.5, 156.1, 146.6, 142.0, 136.6, 136.2, 132.4, 129.3, 128.7, 128.5, 128.1, 128.0, 128.0, 127.6, 127.0, 123.0, 121.2, 120.7, 120.6, 118.4, 116.4, 110.9, 67.1, 57.7, 56.6, 52.6, 38.2, 36.2, 34.9, 31.3, 28.0, 18.1, 12.8; LRMS (ESI): *m/z* 938.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{46}H_{55}F_3N_5O_9SSi$ 938.3447; found 938.3447.



3aw

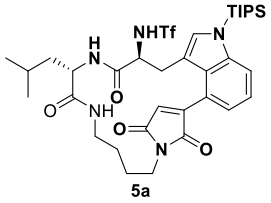
*Benzyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycyl-L-valinate (**3aw**)*

Orange solid (41.3 mg, 45% yield); m.p.: 101.2 – 103.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 9.32 – 9.02 (m, 1H), 7.59 (dd, J = 8.4, 0.9 Hz, 1H), 7.38 – 7.29 (m, 5H), 7.28 (s, 1H), 7.19 (dd, J = 8.4, 7.3 Hz, 1H), 7.10 – 7.03 (m, 2H), 6.86 – 6.78 (m, 1H), 6.47 (s, 1H), 5.23 – 5.13 (m, 2H), 4.61 – 4.57 (m, 1H), 4.25 – 4.17 (m, 2H), 4.05 – 3.97 (m, 1H), 3.92 – 3.80 (m, 2H), 3.34 – 3.18 (m, 5H), 2.74 – 2.65 (m, 1H), 2.63 – 2.54 (m, 1H), 2.22 – 2.14 (m, 1H), 1.75 – 1.69 (m, 3H), 1.16 (dd, J = 7.6, 5.0 Hz, 18H), 0.89 (dd, J = 20.5, 6.9 Hz, 6H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 172.3, 171.4, 171.1, 171.0, 169.7, 169.2, 141.8, 135.4, 132.3, 128.6, 128.5, 128.4, 128.1, 127.5, 123.1, 121.1, 120.7, 120.7, 118.6, 116.2, 111.3, 67.1, 58.3, 57.6, 52.7, 43.0, 35.1, 35.0, 31.4, 30.7, 18.8, 18.1, 17.7, 12.8; LRMS (ESI): *m/z* 918.5 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{43}H_{55}F_3N_5O_{10}SSi$ 918.3396; found 918.3395.



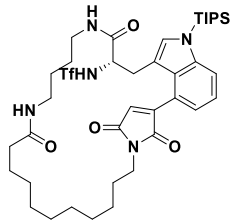
*Benzyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucyl-L-valinate (**3ax**)*

Orange solid (44.6 mg, 46% yield); m.p.: 109.8 – 110.6 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.65 (d, J = 7.9 Hz, 1H), 7.57 (dd, J = 8.5, 0.8 Hz, 1H), 7.36 – 7.29 (m, 5H), 7.23 (s, 1H), 7.16 (dd, J = 8.4, 7.2 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.88 (d, J = 9.2 Hz, 1H), 6.56 (s, 1H), 6.53 (d, J = 8.2 Hz, 1H), 5.23 – 5.08 (m, 2H), 4.52 – 4.46 (m, 1H), 4.37 – 4.28 (m, 2H), 3.96 – 3.83 (m, 2H), 3.46 (s, 3H), 3.30 – 3.22 (m, 1H), 3.17 – 3.11 (m, 1H), 2.79 – 2.66 (m, 2H), 2.21 – 2.13 (m, 1H), 1.81 – 1.65 (m, 5H), 1.55 – 1.47 (m, 1H), 1.15 (dd, J = 7.6, 1.9 Hz, 18H), 0.92 – 0.83 (m, 12H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 171.5, 171.1, 171.0, 170.8, 170.6, 170.0, 147.7, 141.6, 135.4, 131.5, 128.6, 128.5, 128.4, 128.4, 128.0, 122.4, 121.2, 121.0, 120.6, 118.5, 116.1, 111.4, 67.0, 57.8, 57.7, 57.5, 52.4, 37.9, 34.8, 33.9, 30.7, 30.6, 24.8, 18.7, 18.1, 18.1, 17.6, 14.9, 12.8, 11.2; LRMS (ESI): *m/z* 974.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{47}H_{63}F_3N_5O_{10}SSi$ 974.4022; found 974.4027.



*1,1,1-Trifluoro-N-((9S,12S)-9-isobutyl-2^2,2^5,8,11-tetraoxo-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,10-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclotridecaphane-12-yl)methanesulfonamide (**5a**)*

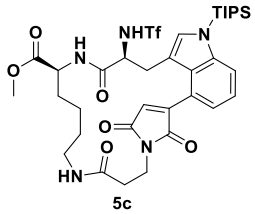
Orange solid (12.9 mg, 17% yield); m.p.: 287.8 – 288.9 °C; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.78 (d, J = 9.0 Hz, 1H), 8.67 (d, J = 8.4 Hz, 1H), 8.01 (dd, J = 8.7, 3.4 Hz, 1H), 7.67 (d, J = 8.4 Hz, 1H), 7.35 (s, 1H), 7.21 (dd, J = 8.4, 7.2 Hz, 1H), 7.01 (d, J = 7.3 Hz, 1H), 6.95 (s, 1H), 4.73 – 4.64 (m, 1H), 4.35 – 4.27 (m, 1H), 3.63 – 3.50 (m, 3H), 2.80 – 2.69 (m, 3H), 1.81 – 1.69 (m, 3H), 1.61 – 1.44 (m, 6H), 1.39 – 1.31 (m, 1H), 1.13 (dd, J = 17.2, 7.5 Hz, 18H), 0.91 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz): δ 172.4, 171.5, 170.7, 170.7, 147.8, 141.3, 130.2, 129.0, 128.8, 122.1, 121.9, 121.5, 121.0, 118.5, 116.2, 113.2, 56.0, 51.5, 40.3, 37.5, 36.9, 31.0, 26.7, 24.6, 24.5, 23.4, 21.7, 18.4, 18.4, 12.6; LRMS (ESI): *m/z* 752.7 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{35}H_{49}F_3N_5O_6SSi$ 752.3130; found 752.3120.



5b

*1,1,1-Trifluoro-N-((21S)-2^2,2^5,13,20-tetraoxo-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-14,19-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclodocosaphane-21-yl)methanesulfonamide (**5b**)*

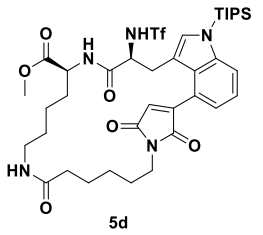
Orange solid (18.3 mg, 22% yield); m.p.: 121.7 – 122.5 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.58 (d, J = 8.3 Hz, 1H), 7.23 – 7.18 (m, 2H), 7.06 (d, J = 7.2 Hz, 1H), 6.95 – 6.88 (m, 1H), 6.58 (s, 1H), 5.90 – 5.76 (m, 2H), 3.98 – 3.89 (m, 1H), 3.68 – 3.59 (m, 2H), 3.20 – 3.11 (m, 2H), 3.10 – 2.92 (m, 3H), 2.79 – 2.68 (m, 1H), 2.17 (t, J = 7.3 Hz, 2H), 1.72 – 1.57 (m, 7H), 1.37 – 1.22 (m, 13H), 1.18 – 1.04 (m, 21H); ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz): δ 174.0, 172.5, 170.4, 168.8, 145.7, 142.1, 133.9, 128.2, 127.4, 122.7, 121.1, 120.6, 120.5, 118.4, 116.3, 110.7, 58.4, 38.8, 38.7, 38.2, 36.5, 32.3, 28.0, 27.9, 27.8, 27.7, 27.7, 26.1, 25.8, 25.6, 25.3, 18.1, 12.8; LRMS (ESI): *m/z* 822.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{40}H_{59}F_3N_5O_6SSi$ 822.3913; found 822.3913.



5c

*Methyl (11S,14S)-2^2,2^5,5,13-tetraoxo-14-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-6,12-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclopentadecaphane-11-carboxylate (**5c**)*

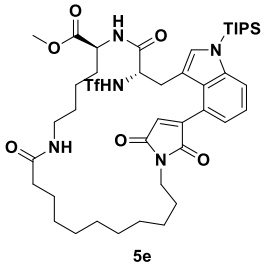
Orange solid (16.8 mg, 21% yield); m.p.: 141.8 – 143.0 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.61 (d, J = 8.2 Hz, 1H), 7.36 (s, 1H), 7.32 – 7.27 (m, 1H), 7.20 (t, J = 7.8 Hz, 1H), 7.12 (d, J = 7.3 Hz, 1H), 6.67 – 6.47 (m, 2H), 4.56 – 4.41 (m, 1H), 4.21 – 4.10 (m, 1H), 3.93 (t, J = 5.7 Hz, 2H), 3.64 (s, 3H), 3.41 – 3.09 (m, 4H), 2.65 – 2.47 (m, 2H), 2.07 – 1.96 (m, 1H), 1.82 – 1.69 (m, 4H), 1.56 – 1.44 (m, 2H), 1.38 – 1.28 (m, 2H), 1.16 (dd, J = 7.6, 1.8 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.6, 171.7, 170.7, 170.4, 170.2, 146.3, 142.2, 133.5, 127.7, 127.6, 123.1, 120.8, 120.5, 118.0, 116.3, 112.3, 60.7, 52.3, 52.0, 38.2, 35.4, 34.9, 31.5, 30.2, 28.8, 21.3, 18.1, 12.8; LRMS (ESI): *m/z* 782.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{35}H_{47}F_3N_5O_8SSi$ 782.2872; found 782.2870.



5d

*Methyl (14S,17S)-2²,2⁵,8,16-tetraoxo-17-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-9,15-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-14-carboxylate (**5d**)*

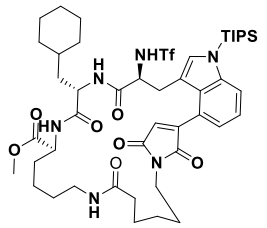
Orange solid (21.5 mg, 26% yield); m.p.: 111.5 – 113.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.59 (d, J = 8.4 Hz, 1H), 7.53 – 7.43 (m, 1H), 7.36 (s, 1H), 7.15 (t, J = 7.8 Hz, 1H), 6.97 (d, J = 7.2 Hz, 1H), 6.81 – 6.68 (m, 1H), 6.64 (s, 1H), 6.06 – 5.93 (m, 1H), 4.45 – 4.38 (m, 1H), 4.36 – 4.30 (m, 1H), 3.68 – 3.61 (m, 5H), 3.38 – 3.28 (m, 2H), 3.26 – 3.13 (m, 2H), 2.34 – 2.28 (m, 1H), 2.26 – 2.20 (m, 1H), 1.88 – 1.76 (m, 4H), 1.88 – 1.64 (m, 5H), 1.53 – 1.31 (m, 6H), 1.14 (t, J = 7.4 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.8, 172.0, 171.9, 170.7, 169.6, 148.3, 141.5, 132.8, 128.7, 128.2, 122.6, 121.0, 120.9, 120.8, 118.2, 116.3, 110.3, 57.9, 52.1, 52.0, 37.8, 37.5, 35.6, 31.3, 29.9, 28.8, 27.5, 25.4, 25.1, 21.2, 18.1, 12.8; LRMS (ESI): *m/z* 824.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{38}H_{53}F_3N_5O_8SSi$ 824.3342; found 824.3349.



5e

*Methyl (19S,22S)-2²,2⁵,13,21-tetraoxo-22-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-14,20-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclotricosaphane-19-carboxylate (**5e**)*

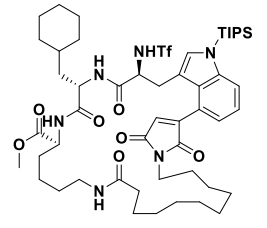
Orange solid (18.2 mg, 20% yield); m.p.: 128.5 – 130.4 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.58 (d, J = 8.3 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.21 – 7.15 (m, 1H), 7.10 (d, J = 7.2 Hz, 1H), 6.76 (d, J = 7.4 Hz, 1H), 6.58 (s, 1H), 6.03 (s, 1H), 4.39 – 4.32 (m, 1H), 4.18 – 4.12 (m, 1H), 3.67 – 3.57 (m, 5H), 3.30 – 3.12 (m, 4H), 2.23 – 2.16 (m, 2H), 1.85 – 1.76 (m, 1H), 1.70 – 1.66 (m, 4H), 1.65 – 1.59 (m, 2H), 1.48 – 1.41 (m, 2H), 1.21 – 1.39 (m, 16H), 1.12 (dd, J = 7.5, 4.3 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.5, 171.8, 171.7, 170.7, 169.1, 146.5, 142.0, 133.3, 127.9, 127.8, 123.2, 121.1, 121.0, 120.8, 118.2, 116.3, 110.7, 58.7, 52.4, 52.2, 38.4, 38.3, 36.5, 31.3, 31.3, 29.0, 28.2, 28.2, 28.0, 28.0, 27.9, 27.8, 26.2, 25.3, 21.9, 18.1, 12.8; LRMS (ESI): *m/z* 894.7 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{43}H_{63}F_3N_5O_8SSi$ 894.4124; found 894.4130.



5f

*Methyl (14S,17S,20S)-17-(cyclohexylmethyl)-2²,2⁵,8,16,19-pentaoxo-20-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-9,15,18-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohenicosaphane-14-carboxylate (**5f**)*

Orange solid (24.3 mg, 25% yield); m.p.: 122.3 – 123.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.60 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.25 – 7.21 (m, 1H), 7.17 (dd, J = 8.4, 7.3 Hz, 2H), 7.01 (d, J = 7.3 Hz, 1H), 6.81 – 6.71 (m, 1H), 6.59 (s, 1H), 5.95 – 5.60 (m, 1H), 4.63 – 4.50 (m, 1H), 4.35 – 4.30 (m, 1H), 4.20 – 4.13 (m, 1H), 3.72 – 3.56 (m, 6H), 3.22 – 3.14 (m, 1H), 3.00 – 2.89 (m, 2H), 2.35 – 2.23 (m, 1H), 2.24 – 2.16 (m, 1H), 2.03 – 1.95 (m, 1H), 1.84 – 1.77 (m, 4H), 1.73 – 1.60 (m, 10H), 1.46 – 1.31 (m, 7H), 1.20 – 1.10 (m, 22H), 0.93 – 0.83 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.9, 172.4, 172.0, 170.5, 169.0, 147.6, 141.8, 132.3, 128.5, 128.1, 123.0, 121.1, 121.0, 120.6, 118.1, 116.4, 111.2, 59.4, 52.5, 52.3, 51.1, 40.9, 38.1, 37.3, 36.3, 33.8, 33.4, 32.7, 30.8, 29.7, 29.3, 28.1, 26.4, 26.2, 26.1, 26.0, 25.3, 21.6, 18.2, 18.1, 12.9; LRMS (ESI): *m/z* 977.6 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{47}H_{68}F_3N_6O_9SSi$ 977.4495; found 977.4489.

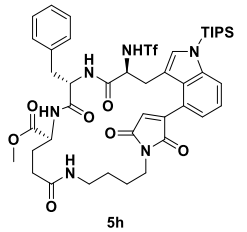


5g

*Methyl (19S,22S,25S)-22-(cyclohexylmethyl)-2²,2⁵,13,21,24-pentaoxo-25-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-14,20,23-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexacosaphane-19-carboxylate (**5g**)*

Orange solid (17.7 mg, 17% yield); m.p.: 104.4 – 105.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.61 (d, J = 8.3 Hz, 1H), 7.32 (s, 1H), 7.21 – 7.16 (m, 1H), 7.09 (d, J = 7.2 Hz, 1H), 6.91 – 6.85 (m, 1H), 6.73 – 6.64 (m, 1H), 6.62 – 6.50 (m, 2H), 6.12 – 5.91 (m, 1H), 4.51 – 4.41 (m, 1H), 4.40 – 4.34 (m, 1H), 4.20 – 4.13 (m, 1H), 3.78 – 3.57 (m, 6H), 3.44 – 3.36 (m, 1H), 3.31 – 3.23 (m, 1H), 3.17 – 3.06 (m, 2H), 2.26 – 2.15 (m, 2H), 1.85 – 1.60 (m, 18H), 1.57 – 1.48 (m, 2H), 1.42 – 1.29 (m, 15H), 1.15 (dd, J = 10.8, 7.5 Hz, 18H), 0.92 – 0.82 (m, 2H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.6, 172.4, 171.9, 171.7,

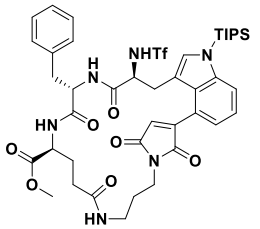
170.8, 169.2, 146.8, 141.9, 133.0, 128.0, 127.8, 123.3, 121.1, 120.9, 116.4, 110.8, 59.2, 52.3, 51.4, 40.4, 38.3, 38.2, 36.7, 33.9, 33.6, 32.7, 31.0, 30.7, 29.7, 29.1, 28.2, 28.1, 28.0, 28.0, 27.9, 26.4, 26.2, 26.2, 25.9, 25.5, 22.0, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 1047.7 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$calcd for $C_{52}H_{78}F_3N_6O_9SSi$ 1047.5278; found 1047.5289.



5h

*Methyl (11S,14S,17S)-14-benzyl-2^2,2^5,8,13,16-pentaoxo-17-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,12,15-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-11-carboxylate (**5h**)*

Orange solid (23.9 mg, 26% yield); m.p.: 126.9 – 127.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (dd, *J* = 8.4, 0.9 Hz, 1H), 7.41 – 7.36 (m, 1H), 7.34 – 7.29 (m, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.07 (m, 4H), 6.94 (d, *J* = 7.0 Hz, 2H), 6.56 (s, 1H), 6.45 – 6.26 (m, 2H), 4.67 – 4.60 (m, 1H), 4.47 – 4.24 (m, 2H), 3.73 – 3.65 (m, 5H), 3.45 – 3.37 (m, 1H), 3.12 – 3.06 (m, 1H), 3.05 – 2.97 (m, 3H), 2.78 – 2.71 (m, 1H), 2.29 – 2.22 (m, 1H), 2.12 – 2.05 (m, 1H), 2.01 – 1.93 (m, 2H), 1.90 – 1.78 (m, 2H), 1.74 – 1.67 (m, 3H), 1.62 – 1.49 (m, 2H), 1.16 (t, *J* = 7.2 Hz, 18H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 173.6, 171.7, 171.5, 170.5, 170.2, 168.9, 147.4, 141.9, 135.7, 131.9, 129.4, 128.6, 128.2, 127.7, 127.0, 123.2, 121.6, 121.0, 120.6, 118.0, 116.6, 110.9, 58.8, 54.0, 52.7, 52.5, 40.1, 37.7, 37.3, 32.2, 31.2, 26.2, 26.1, 18.1, 18.1, 12.8; LRMS (ESI): *m/z* 931.4 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{44}H_{58}F_3N_6O_9SSi$ 931.3702; found 931.3706.

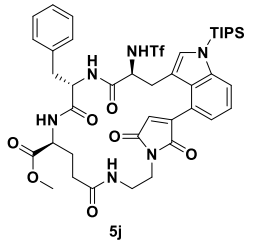


5i

*Methyl (10S,13S,16S)-13-benzyl-2^2,2^5,7,12,15-pentaoxo-16-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-6,11,14-triaza-1(4,3)-indola-2(3,1)-pyrrolacycloheptadecaphane-10-carboxylate (**5i**)*

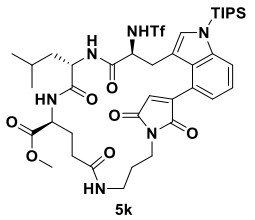
Orange solid (16.5 mg, 18% yield); m.p.: 150.4 – 151.2 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, *J* = 8.4 Hz, 1H), 7.36 (s, 1H), 7.24 – 7.17 (m, 4H), 7.07 – 7.01 (m, 3H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.78 –

6.68 (m, 2H), 6.62 (s, 1H), 6.29 – 6.20 (m, 1H), 4.70 – 4.62 (m, 1H), 4.55 – 4.49 (m, 1H), 4.42 – 4.37 (m, 1H), 3.72 – 3.65 (m, 4H), 3.62 – 3.56 (m, 1H), 3.51 – 3.44 (m, 1H), 3.19 – 3.06 (m, 2H), 2.96 – 2.80 (m, 3H), 2.37 – 2.29 (m, 1H), 2.20 – 2.02 (m, 3H), 1.86 – 1.82 (m, 2H), 1.75 – 1.68 (m, 3H), 1.16 (dd, J = 12.8, 7.5 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): δ 174.8, 173.7, 172.7, 171.5, 171.5, 170.4, 149.4, 143.3, 136.9, 132.7, 130.9, 130.1, 130.0, 129.3, 128.5, 124.5, 122.8, 122.1, 122.0, 119.4, 118.0, 112.4, 59.6, 55.5, 54.0, 53.9, 39.7, 38.0, 36.4, 34.1, 33.4, 29.3, 27.6, 19.6, 19.5, 14.3; LRMS (ESI): *m/z* 917.4 $[M + H]^+$; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{43}H_{56}F_3N_6O_9SSi$ 917.3545; found 917.3553.



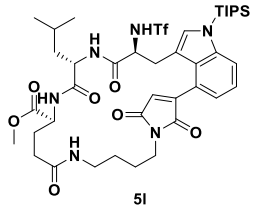
*Methyl (9S,12S,15S)-12-benzyl-2^2,2^5,6,11,14-pentaoxo-15-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-5,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-9-carboxylate (**5j**)*

Orange solid (22.1 mg, 24% yield); m.p.: 152.3 – 153.2 °C; ^1H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 8.4 Hz, 1H), 7.33 (s, 1H), 7.29 – 7.27 (m, 1H), 7.22 – 7.13 (m, 4H), 7.04 – 7.00 (m, 2H), 6.83 – 6.66 (m, 2H), 6.47 (s, 1H), 6.29 – 6.08 (m, 2H), 4.35 – 4.19 (m, 3H), 3.94 – 3.78 (m, 2H), 3.73 – 3.63 (m, 4H), 3.36 – 3.24 (m, 2H), 3.21 – 3.14 (m, 1H), 2.81 – 2.70 (m, 1H), 2.52 – 2.36 (m, 1H), 2.32 – 2.14 (m, 2H), 2.10 – 1.95 (m, 2H), 1.75 – 1.68 (m, 3H), 1.17 (d, J = 7.5 Hz, 18H); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 126 MHz): δ 172.9, 171.8, 171.6, 170.8, 169.8, 146.8, 142.2, 135.2, 132.0, 129.1, 128.7, 127.9, 127.6, 127.1, 123.4, 121.7, 121.1, 120.6, 118.0, 116.5, 110.8, 58.0, 55.2, 52.6, 51.8, 38.4, 38.1, 36.8, 31.7, 30.4, 30.0, 26.5, 18.1, 12.8; LRMS (ESI): *m/z* 901.5 $[M - H]^-$; HRMS (ESI) m/z: $[M - H]^-$ calcd for $C_{42}H_{52}F_3N_6O_9SSi$ 901.3243; found 901.3232.



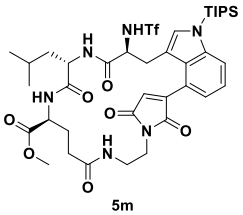
*Methyl (10S,13S,16S)-13-isobutyl-2^2,2^5,7,12,15-pentaoxo-16-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-6,11,14-triaza-1(4,3)-indola-2(3,1)-pyrrolacycloheptadecaphane-10-carboxylate (**5k**)*

Orange solid (24.2 mg, 27% yield); m.p.: 152.3 – 153.0 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (dd, J = 8.4, 0.9 Hz, 1H), 7.36 (s, 1H), 7.19 (dd, J = 8.4, 7.2 Hz, 1H), 7.13 – 7.05 (m, 2H), 7.01 – 6.97 (m, 1H), 6.79 – 6.72 (m, 1H), 6.65 (s, 1H), 6.47 – 6.39 (m, 1H), 4.60 – 4.49 (m, 1H), 4.43 – 4.29 (m, 2H), 3.75 – 3.59 (m, 5H), 3.48 – 3.38 (m, 1H), 3.19 – 3.12 (m, 1H), 3.05 – 2.92 (m, 2H), 2.45 – 2.37 (m, 1H), 2.24 – 2.12 (m, 3H), 1.94 – 1.82 (m, 2H), 1.77 – 1.65 (m, 3H), 1.59 – 1.53 (m, 1H), 1.45 – 1.34 (m, 2H), 1.16 (dd, J = 8.9, 7.5 Hz, 18H), 0.82 (d, J = 6.5 Hz, 3H), 0.77 (d, J = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.9, 173.9, 173.1, 173.1, 171.7, 170.5, 149.7, 143.3, 132.9, 130.2, 129.3, 124.6, 122.8, 122.1, 122.0, 119.5, 118.0, 112.5, 59.8, 53.9, 53.4, 43.1, 38.1, 36.6, 34.3, 32.9, 29.2, 27.6, 25.8, 24.1, 23.5, 19.6, 19.5, 14.3; LRMS (ESI): *m/z* 881.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{40}H_{56}F_3N_6O_9SSi$ 881.3556; found 881.3562.



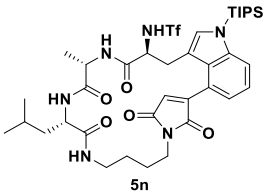
*Methyl (11S,14S,17S)-14-isobutyl-2^2,2^5,8,13,16-pentaoxo-17-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,12,15-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-11-carboxylate (**5l**)*

Orange solid (29.7 mg, 33% yield); m.p.: 157.0 – 158.1 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.62 (dd, J = 8.4, 0.8 Hz, 1H), 7.40 – 7.30 (m, 3H), 7.21 (dd, J = 8.4, 7.3 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 6.57 (s, 1H), 6.52 – 6.37 (m, 2H), 4.47 – 4.40 (m, 1H), 4.30 – 4.24 (m, 1H), 4.23 – 4.15 (m, 1H), 3.75 – 3.63 (m, 5H), 3.49 – 3.40 (m, 1H), 3.19 – 3.07 (m, 3H), 2.39 – 2.31 (m, 1H), 2.28 – 2.08 (m, 4H), 1.89 – 1.80 (m, 1H), 1.74 – 1.68 (m, 3H), 1.62 – 1.50 (m, 3H), 1.40 – 1.31 (m, 1H), 1.28 – 1.22 (m, 1H), 1.15 (dd, J = 7.6, 3.5 Hz, 18H), 0.80 (d, J = 6.6 Hz, 3H), 0.77 (d, J = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 174.8, 173.3, 173.2, 173.0, 172.1, 170.7, 148.4, 143.4, 133.9, 129.3, 129.0, 124.7, 122.8, 122.2, 122.0, 119.4, 117.9, 112.3, 60.5, 53.9, 53.9, 53.5, 42.3, 41.3, 39.2, 33.6, 32.1, 27.7, 27.5, 27.3, 25.9, 24.1, 23.3, 19.5, 19.5, 14.3; LRMS (ESI): *m/z* 895.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{41}H_{58}F_3N_6O_9SSi$ 895.3713; found 895.3717.



*Methyl (9S,12S,15S)-12-isobutyl-2^2,2^5,6,11,14-pentaoxo-15-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^1H,2^1H-5,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-9-carboxylate (**5m**)*

Orange solid (24.6 mg, 28% yield); m.p.: 123.3 – 123.8 °C; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.64 (d, J = 8.3 Hz, 1H), 7.35 (s, 1H), 7.24 (dd, J = 8.4, 7.3 Hz, 1H), 7.13 (d, J = 7.3 Hz, 1H), 7.05 – 6.84 (m, 2H), 6.50 (s, 1H), 6.29 – 6.18 (m, 1H), 5.97 – 5.74 (m, 1H), 4.46 – 4.38 (m, 1H), 4.30 – 4.20 (m, 1H), 4.08 – 3.99 (m, 1H), 3.98 – 3.84 (m, 2H), 3.80 – 3.68 (m, 4H), 3.43 – 3.28 (m, 2H), 3.21 – 3.15 (m, 1H), 2.40 – 2.30 (m, 1H), 2.28 – 2.00 (m, 3H), 1.75 – 1.71 (m, 4H), 1.48 – 1.39 (m, 1H), 1.29 – 1.23 (m, 1H), 1.17 (dd, J = 7.5, 2.5 Hz, 18H), 0.78 (d, J = 6.5 Hz, 3H), 0.74 (d, J = 6.5 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 126 MHz): δ 172.8, 172.1, 171.8, 170.8, 170.8, 169.6, 146.7, 142.2, 132.0, 127.6, 127.4, 123.6, 121.8, 121.0, 120.6, 118.1, 116.5, 110.6, 57.9, 53.4, 52.8, 52.7, 52.0, 40.2, 38.5, 37.9, 31.7, 30.3, 24.4, 22.4, 22.3, 18.1, 12.8; LRMS (ESI): *m/z* 867.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$ calcd for $C_{39}H_{54}F_3N_6O_9SSi$ 867.3400; found 867.3401.



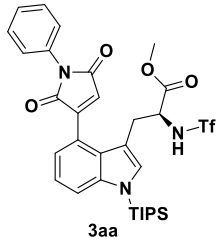
5n

*1,1,1-trifluoro-N-((9S,12S,15S)-9-isobutyl-12-methyl-2^2,2^5,8,11,14-pentaoxo-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^1H,2^1H-7,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-15-yl)methanesulfonamide (**5n**)*

Orange solid (20.8 mg, 25% yield); m.p.: 203.8 – 204.7 °C; ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.89 (s, 1H), 8.55 (s, 1H), 7.83 (s, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.47 (s, 1H), 7.32 – 7.23 (m, 1H), 7.22 – 7.17 (m, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.94 (s, 1H), 4.47 – 4.37 (m, 1H), 4.07 – 3.92 (m, 2H), 3.48 (t, J = 6.7 Hz, 2H), 3.33 – 3.28 (m, 1H), 3.10 – 3.02 (m, 1H), 2.91 – 2.78 (m, 2H), 1.80 – 1.72 (m, 3H), 1.67 – 1.50 (m, 5H), 1.33 – 1.42 (m, 2H), 1.29 (d, J = 7.3 Hz, 3H), 1.12 (dd, J = 11.5, 7.5 Hz, 18H), 0.88 (d, J = 5.9 Hz, 3H), 0.83 (d, J = 5.7 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d_6, 126 MHz): δ 172.3, 171.7, 171.4, 171.3, 171.0, 146.2, 141.5, 131.5, 129.0, 128.6, 122.9, 121.8, 121.3, 120.9, 118.4, 116.1, 113.5, 58.1, 52.3, 50.7, 39.5, 38.4, 37.7, 29.6, 26.8, 25.5, 24.9, 23.5, 21.7, 18.4, 18.4, 17.9, 12.6; LRMS (ESI): *m/z* 823.6 [M – H]$^-$; HRMS (ESI) m/z: [M – H]$^-$calcd for $C_{38}H_{54}F_3N_6O_7SSi$ 823.3502; found 823.3490.

7. X-ray crystallography data

Structural data for 3aa (CCDC 2150681)



3aa

Sample preparation: Compound **3aa** (20 mg) was dissolved in DCM (2 mL), the solution was filtered through a nylon-membrane syringe filter (13 mm*0.22 μm, purchased from ANPEL Laboratory Tech. Shanghai, Inc.) and transferred into a clean tube. The solvent was slowly violated at room temperature to afford the single crystal **3aa**.

Single crystal structure of 3aa: X-ray crystal structure of **3aa** was determined at 170 K with the ellipsoid contour at 50% probability levels.

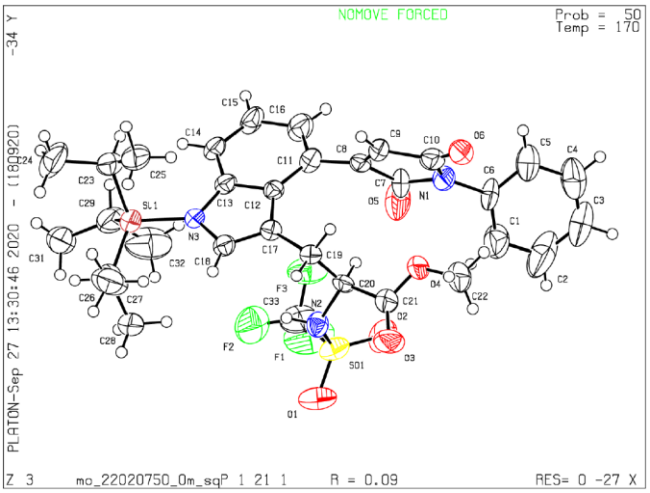


Fig. S7. X-ray crystal structure of **3aa**.

Crystal structure determination of **3aa** (mo_22020750_0m_sq)

Crystal Data for $C_{32}H_{38}F_3N_3O_6SSi$ (M =677.80 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 11.5652(9) Å, b = 14.6334(11) Å, c = 12.0301(11) Å, β = 112.076(2)°, V = 1886.7(3) Å^3, Z = 2, T = 170.0 K, μ(MoKα) = 0.174 mm^{-1}, *Dcalc* = 1.193 g/cm^3, 14406 reflections measured (4.594° ≤ 2Θ ≤ 52.832°), 6469 unique (R_{int} = 0.0927, R_{sigma} = 0.1237) which were used in all calculations. The final R_1 was 0.0857 (I > 2σ(I)) and wR_2 was 0.2526 (all data).

Table S2. Crystal data and structure refinement for **3aa**

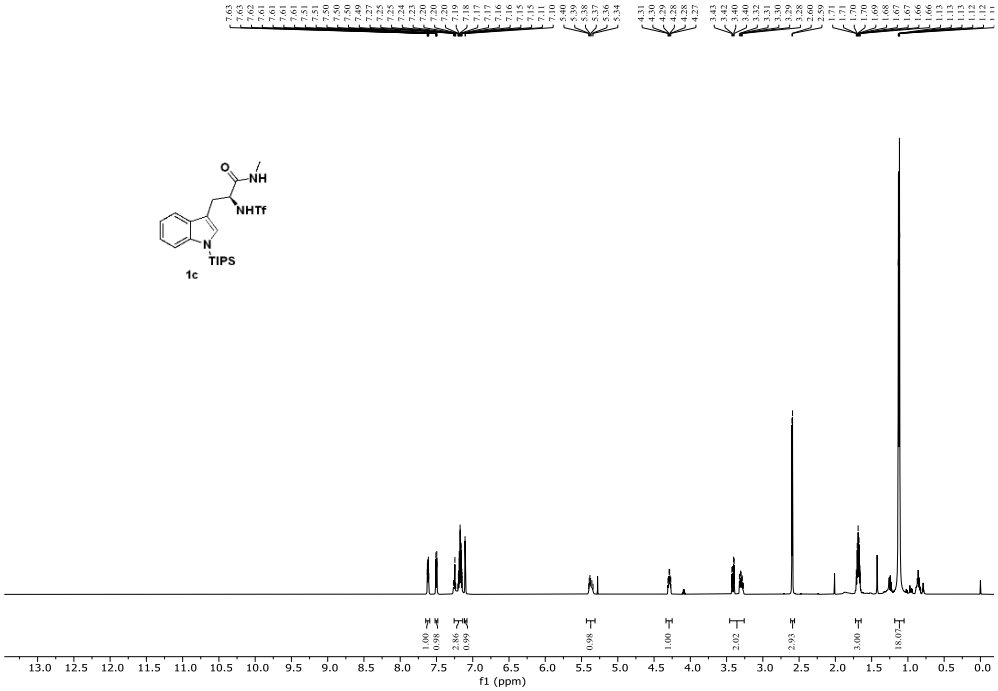
Identification code	**3aa**(mo_22020750_0m_sq)

Empirical formula	$C_{32}H_{38}F_3N_3O_6SSi$
Formula weight	677.80
Temperature/K	170.0
Crystal system	monoclinic
Space group	$P2_1$
a/Å	11.5652(9)
b/Å	14.6334(11)
c/Å	12.0301(11)
α/°	90
β/°	112.076(2)
γ/°	90
Volume/Å^3	1886.7(3)
Z	2
ρ_{calc}g/cm^3	1.193
μ/mm^{-1}	0.174
F(000)	712.0
Crystal size/mm^3	0.15 × 0.08 × 0.05
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.594 to 52.832
Index ranges	$-14 \leq h \leq 14$, $-18 \leq k \leq 17$, $-14 \leq l \leq 13$
Reflections collected	14406
Independent reflections	6469 [R_{int} = 0.0927, R_{sigma} = 0.1237]
Data/restraints/parameters	6469/1/422
Goodness-of-fit on F^2	1.017
Final R indexes [I>=2σ (I)]	R_1 = 0.0857, wR_2 = 0.2045
Final R indexes [all data]	R_1 = 0.1539, wR_2 = 0.2526
Largest diff. peak/hole / e Å^{-3}	0.67/-0.33
Flack parameter	-0.01(10)

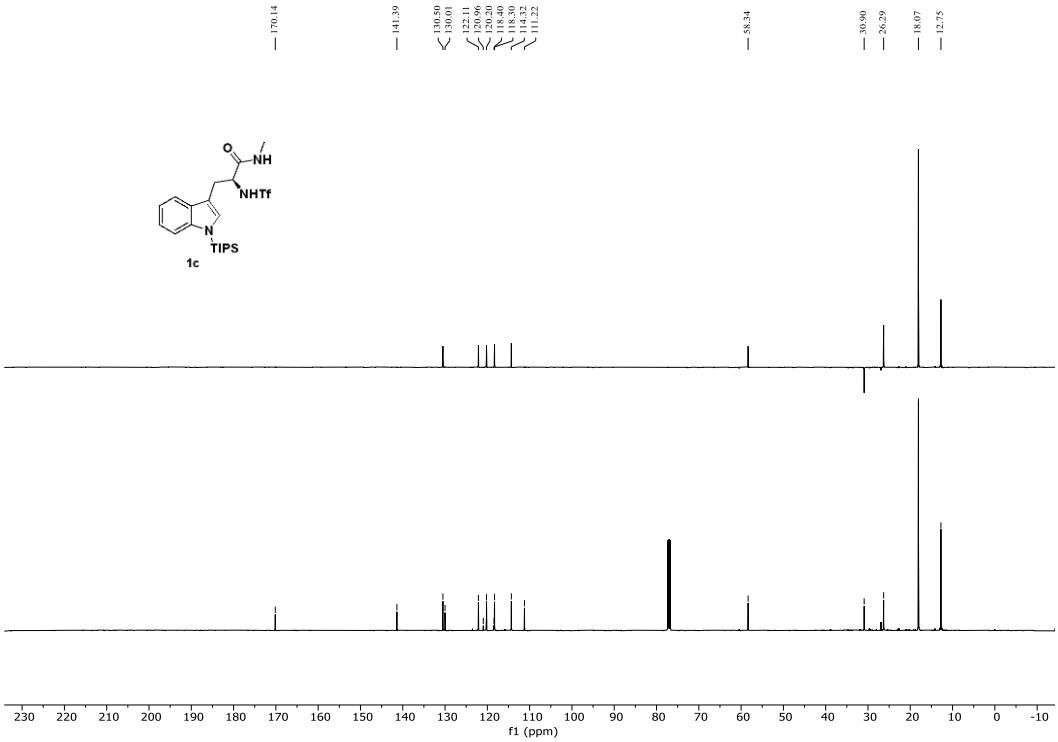
8. NMR spectra data

*(S)-N-methyl-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propenamide (**1c**)*

^{1}H NMR of **1c** (600 MHz, $CDCl_3$)

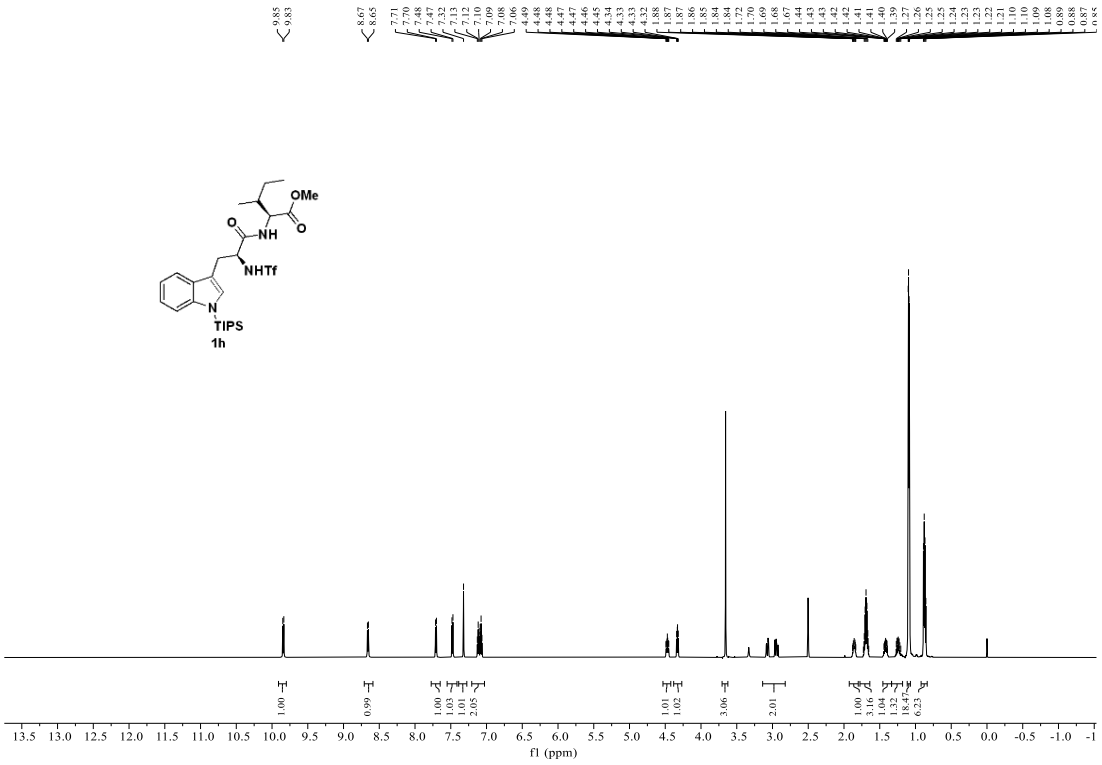


^{13}C{^{1}H} NMR of **1c** (126 MHz, $CDCl_3$)

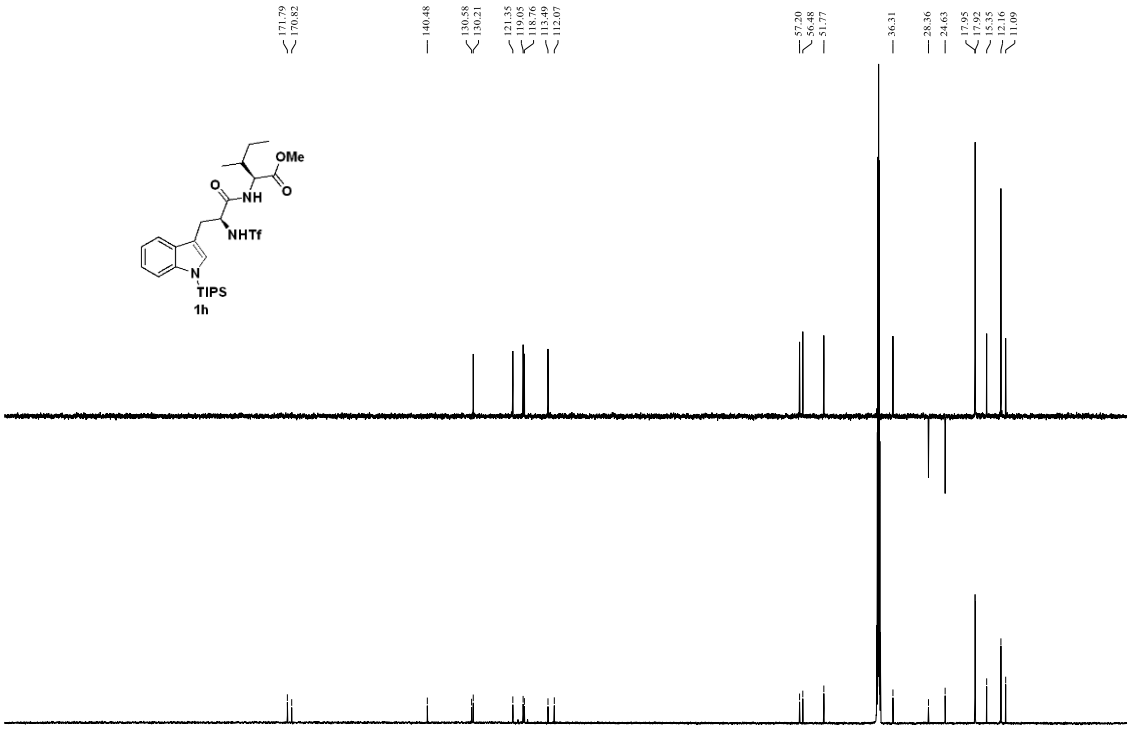


*Methyl Nᵅ-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-alloisoleucinate (**1h**)*

^{1}H NMR of **1h** (600 MHz, DMSO-*d6*)

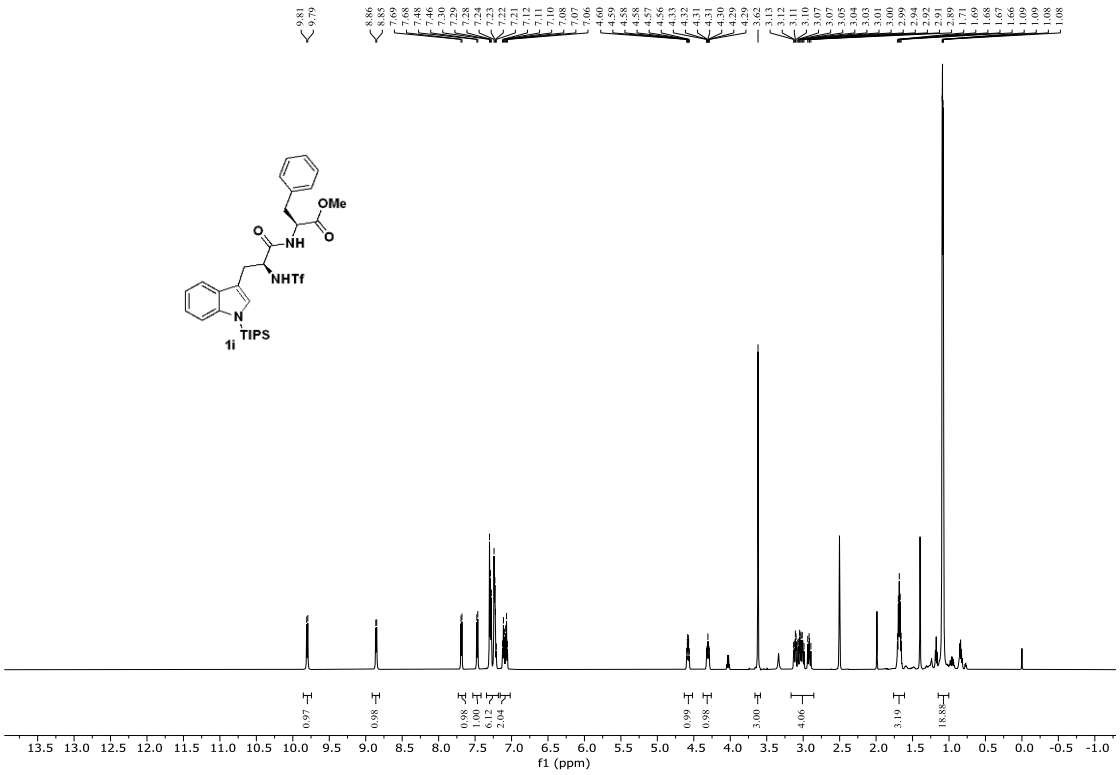


^{13}C{^{1}H} NMR of **1h** (151 MHz, DMSO-*d6*)

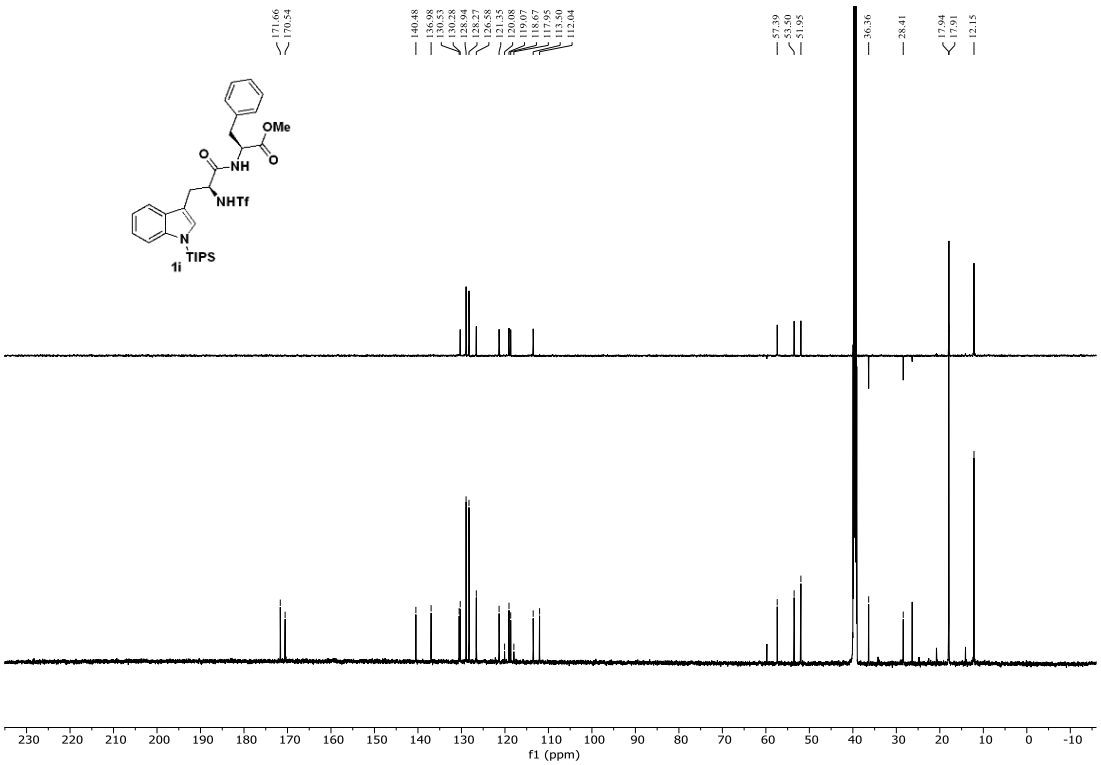


*Methyl N$^{\alpha}$-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalaninate (**1i**)*

^{1}H NMR of **1i** (600 MHz, DMSO-*d6*)

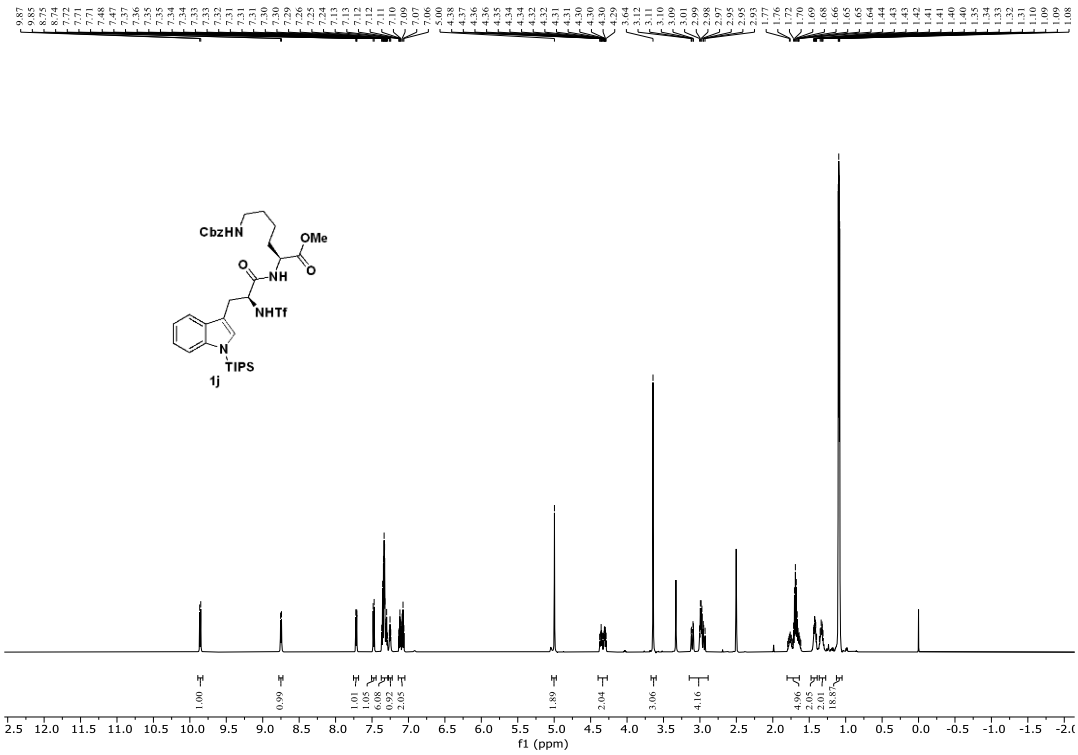


^{13}C{^{1}H} NMR of **1i** (151 MHz, DMSO-*d6*)

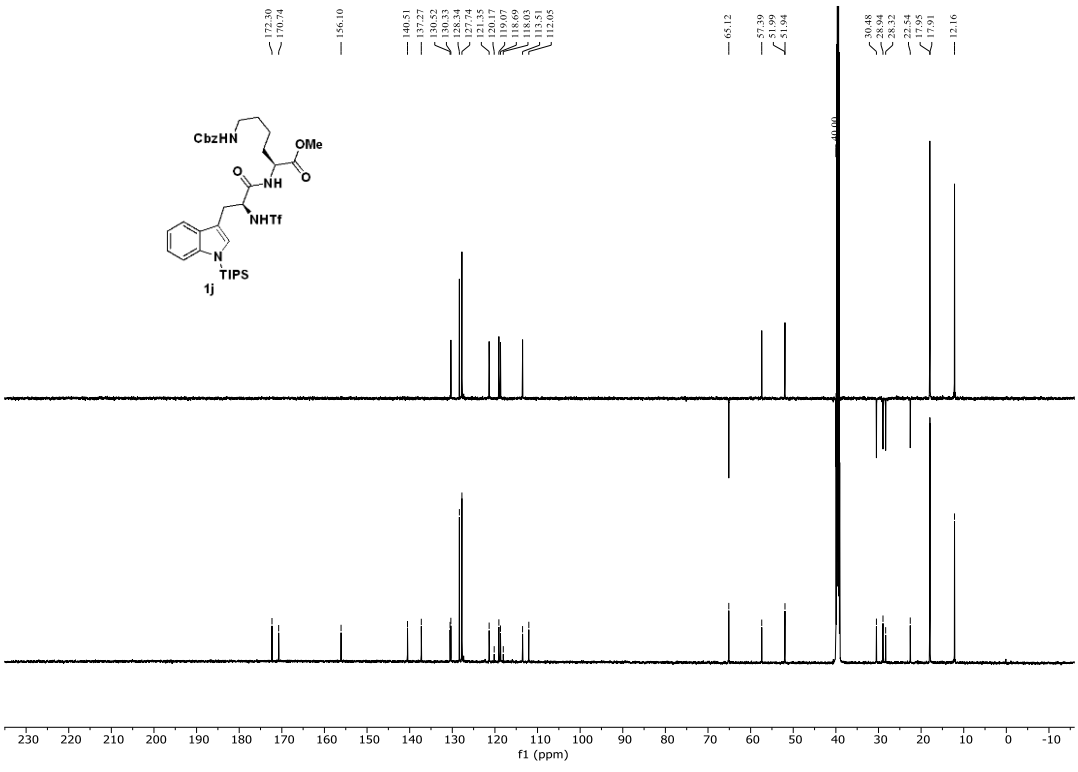


*Methyl N^6-((benzyloxy)carbonyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**1j**)*

^{1}H NMR of **1j** (600 MHz, DMSO-*d6*)

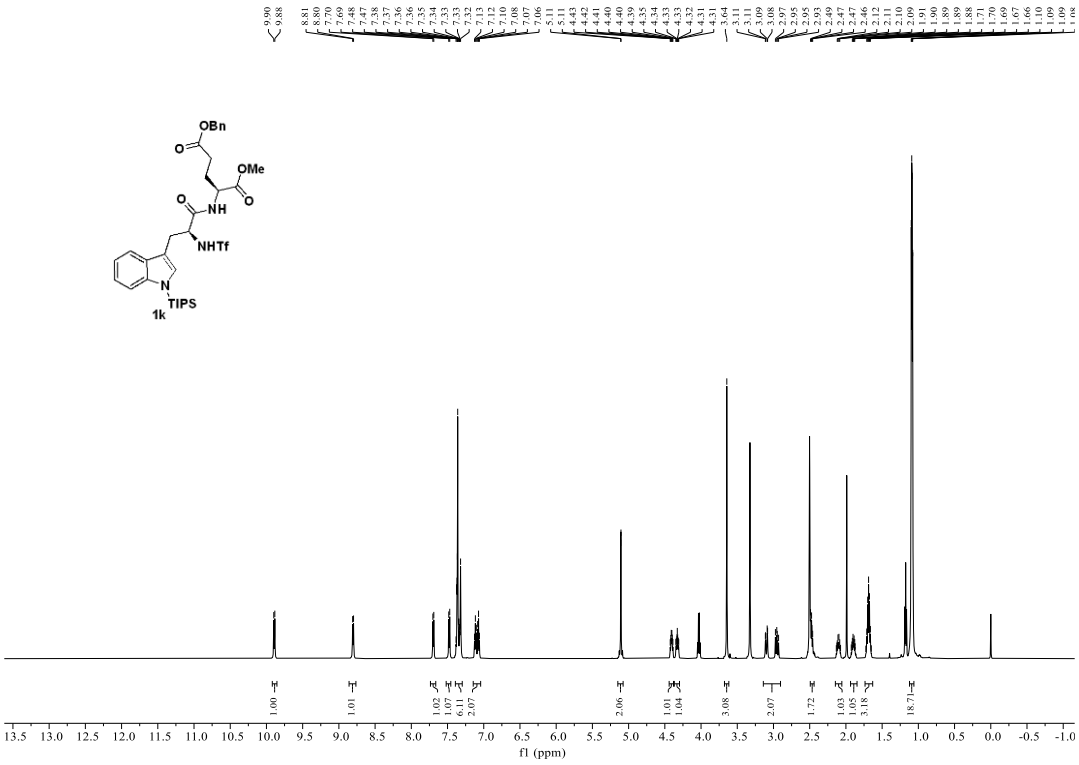


^{13}C{^{1}H} NMR of **1j** (151 MHz, DMSO-*d6*)

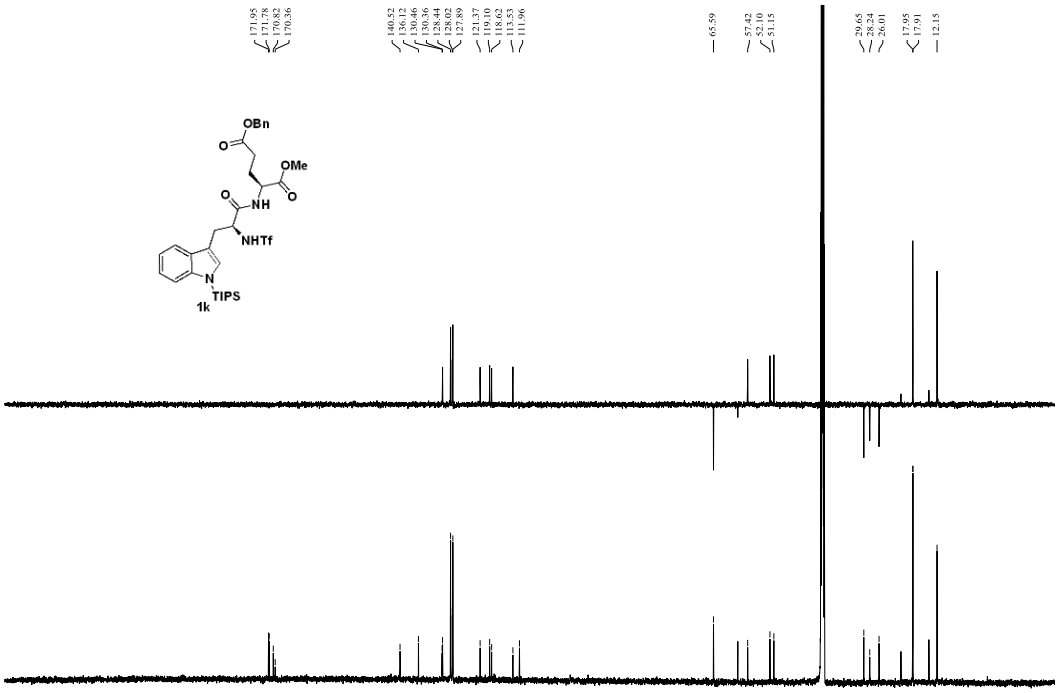


*5-Benzyl 1-methyl N^{a}-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-glutamate (**1k**)*

^{1}H NMR of **1k** (600 MHz, DMSO-*d6*)

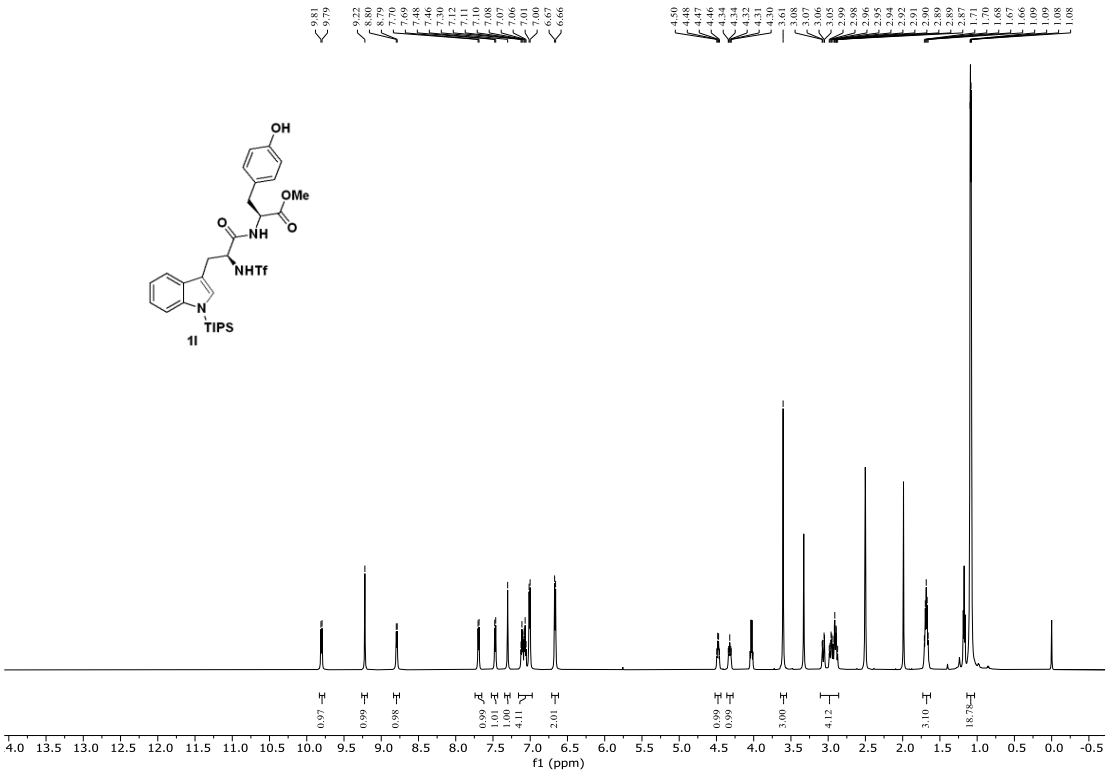


^{13}C{^{1}H} NMR of **1k** (151 MHz, DMSO-*d6*)

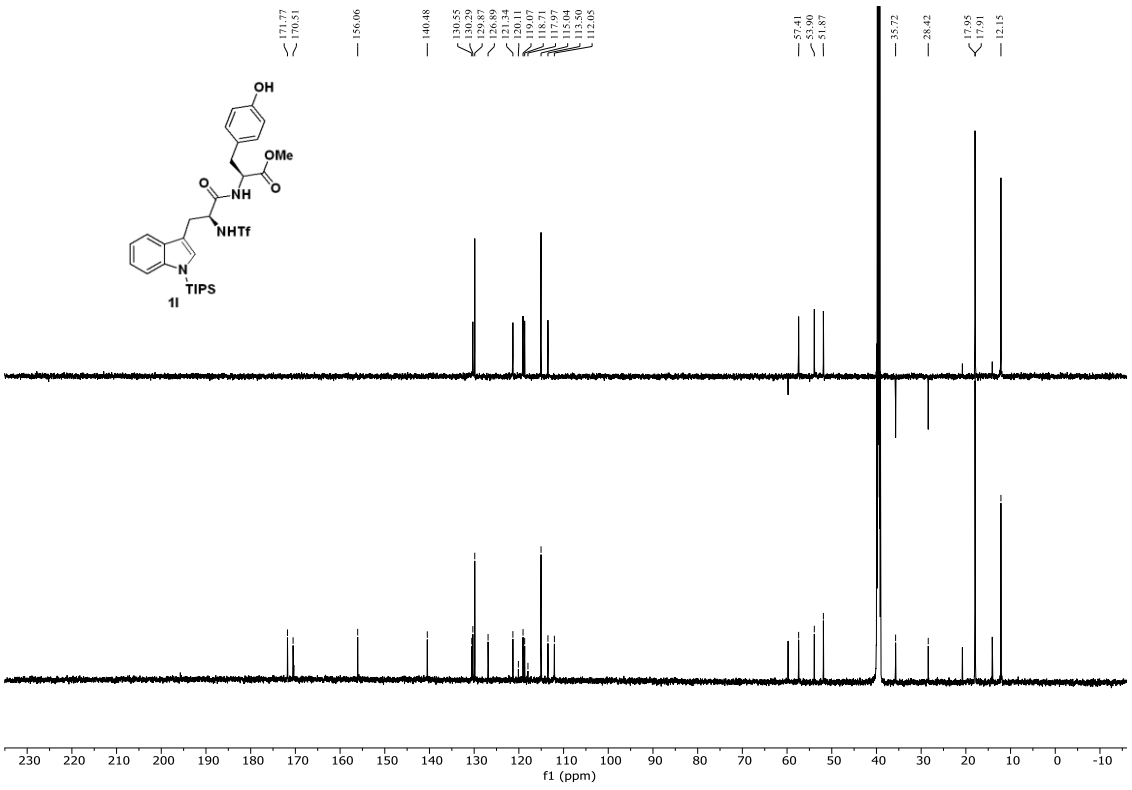


*Methyl N$^{\alpha}$-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-tyrosinate (**1l**)*

^{1}H NMR of **1l** (600 MHz, DMSO-*d6*)

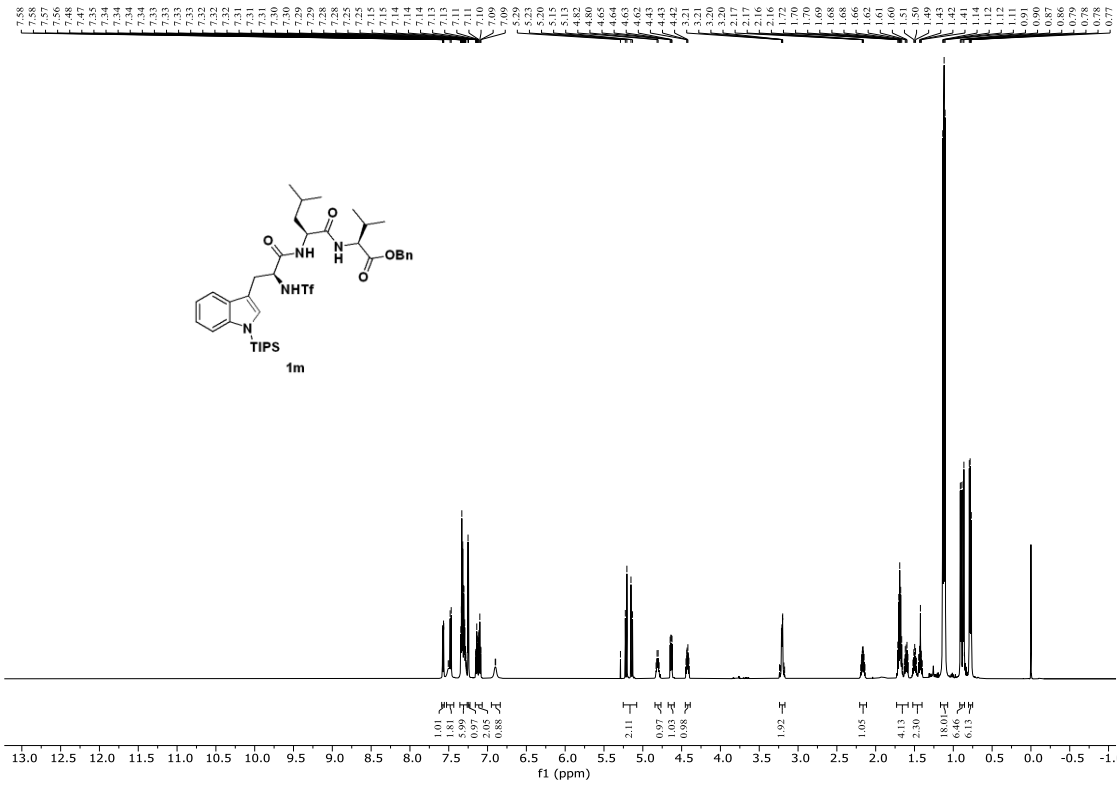


^{13}C{^{1}H} NMR of **1l** (151 MHz, DMSO-*d6*)

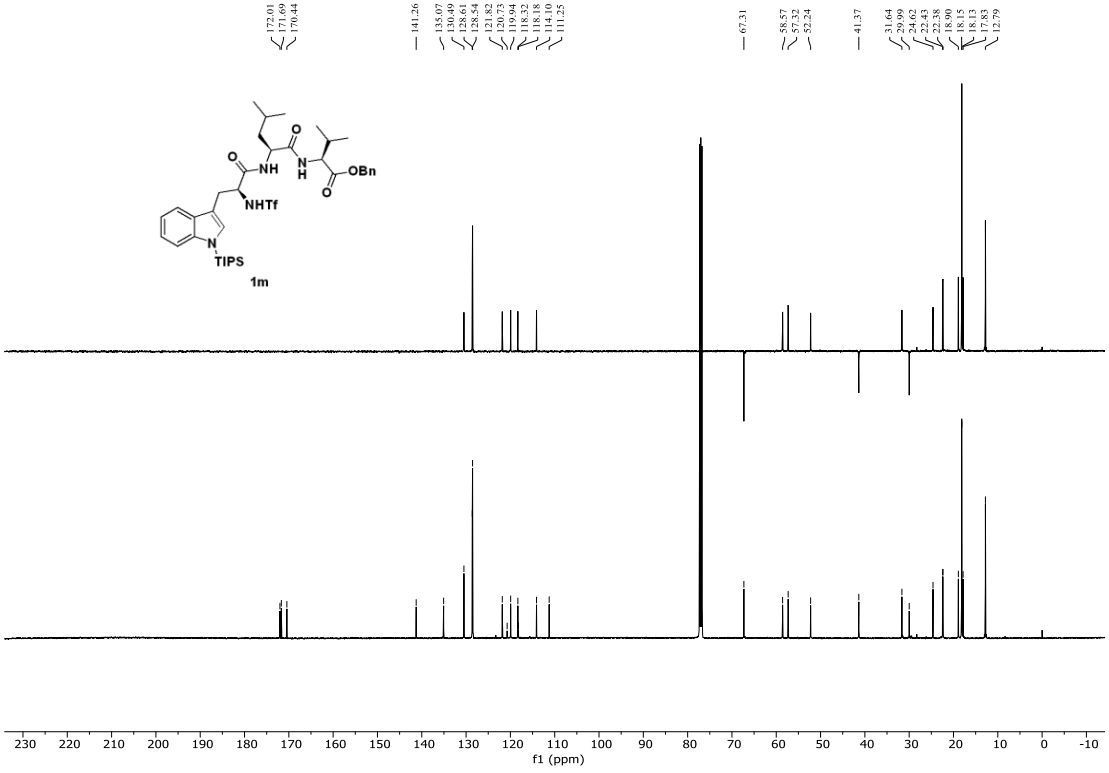


*Benzyl N$^{\alpha}$-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl-L-valinate (**1m**)*

^{1}H NMR of **1m** (600 MHz, $CDCl_3$)

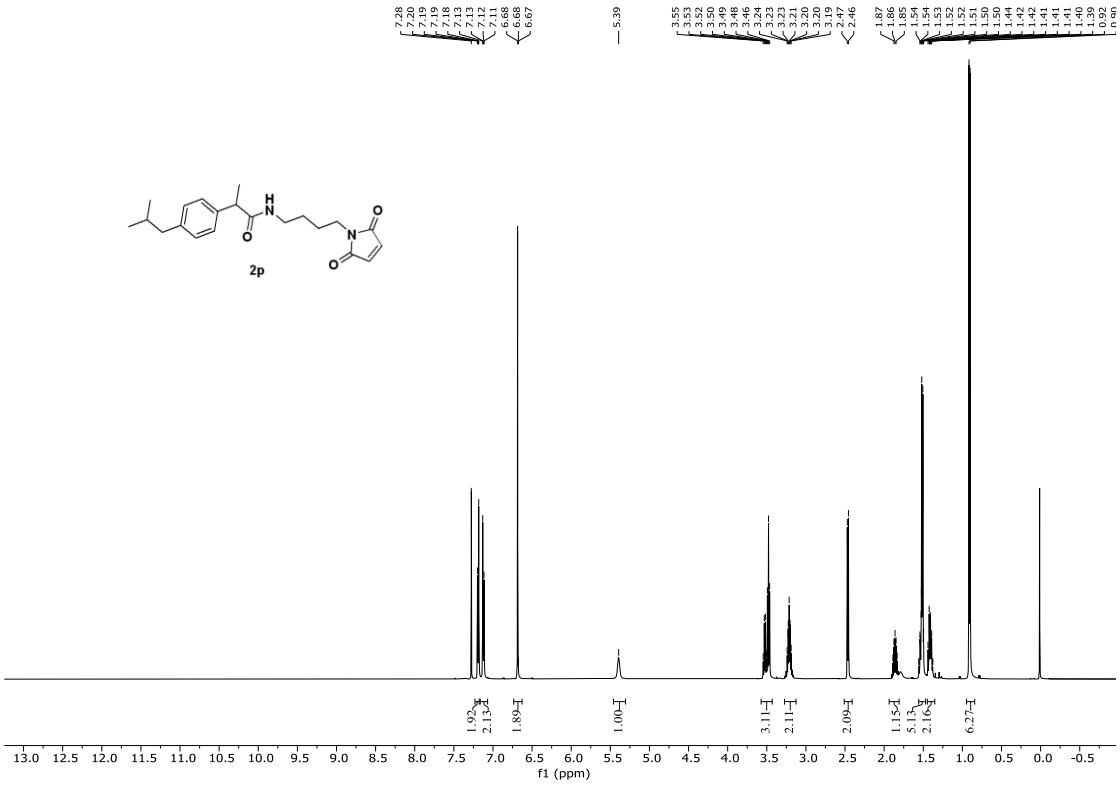


^{13}C{^{1}H} NMR of **1m** (126 MHz, $CDCl_3$)

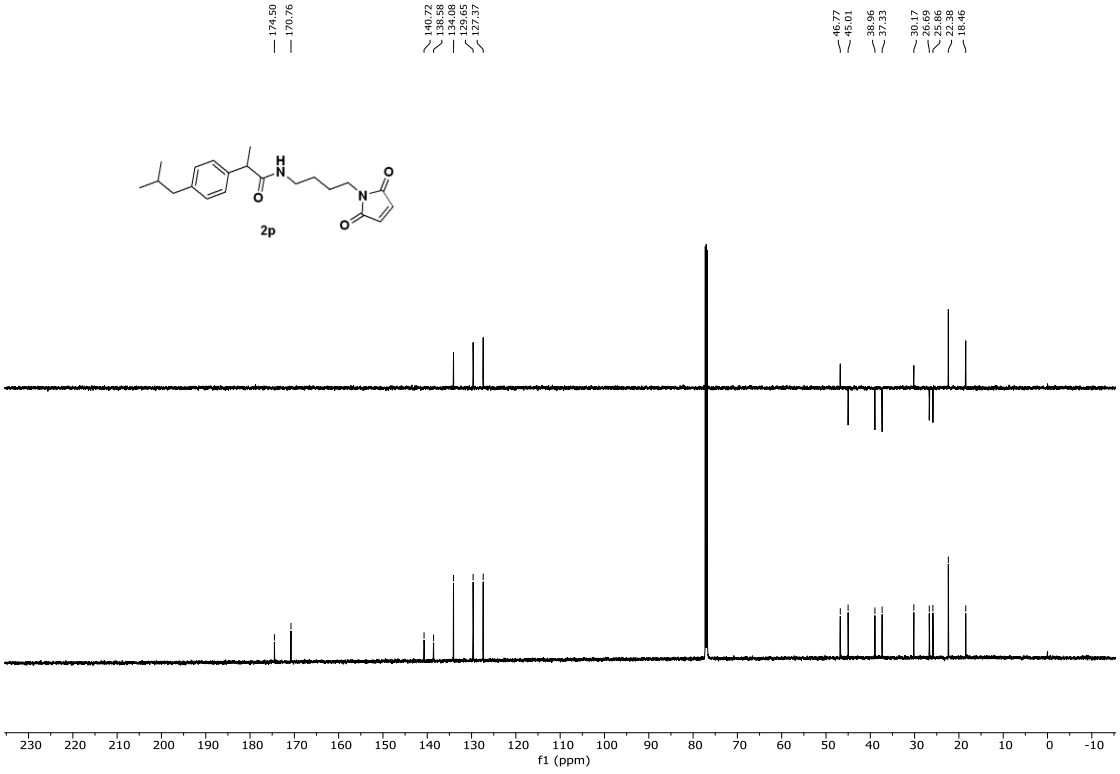


*N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-2-(4-isobutylphenyl)propenamide (**2p**)*

^{1}H NMR of **2p** (500 MHz, $CDCl_3$)

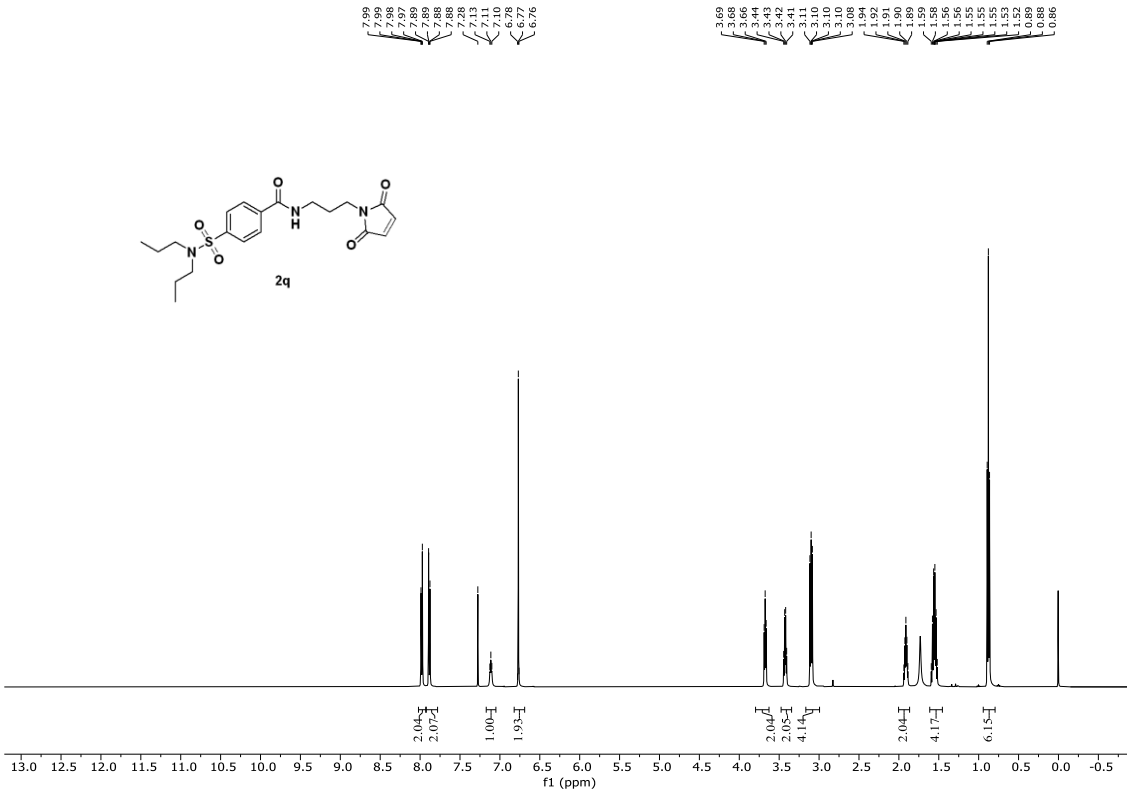


^{13}C{^{1}H} NMR of **2p** (151 MHz, $CDCl_3$)

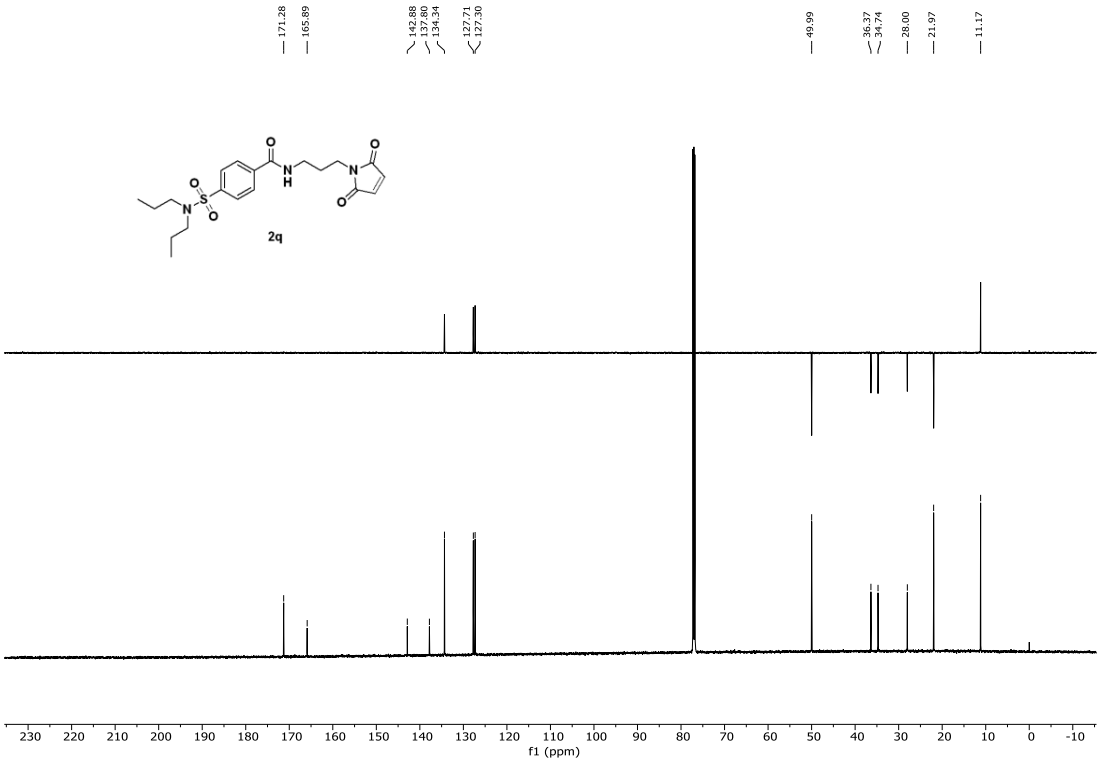


*N-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-4-(N,N-dipropylsulfamoyl)benzamide (**2q**)*

^{1}H NMR of **2q** (500 MHz, $CDCl_3$)

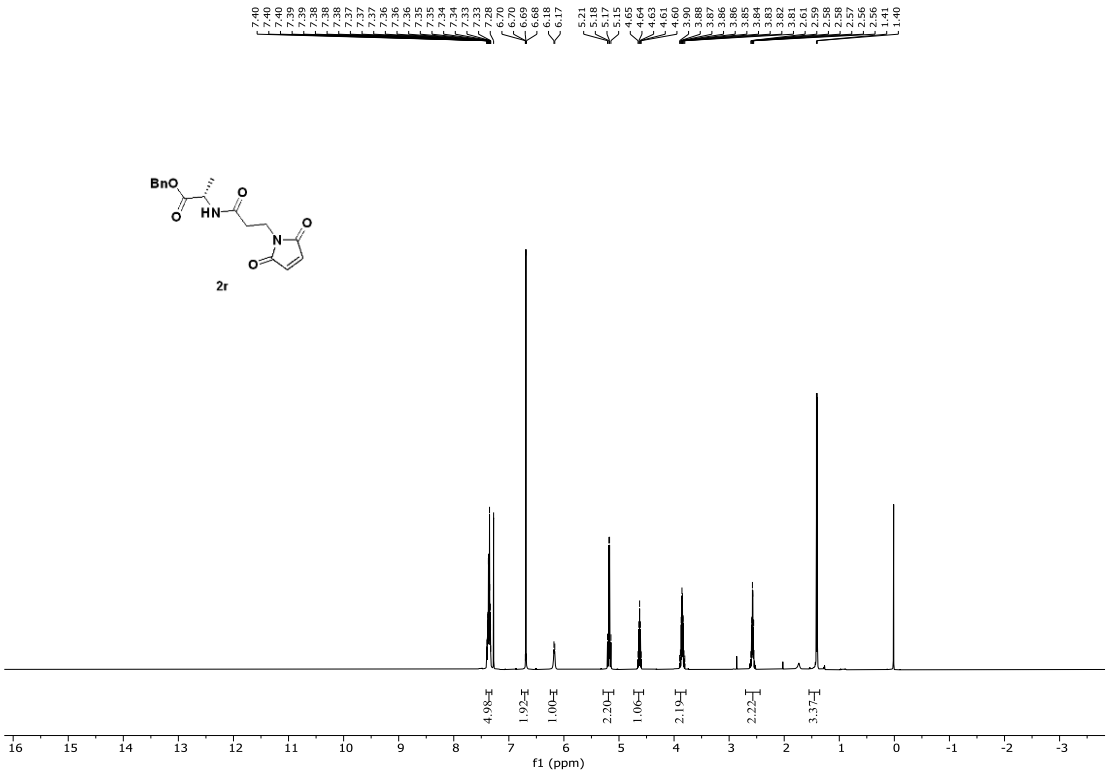


^{13}C{^{1}H} NMR of **2q** (151 MHz, $CDCl_3$)

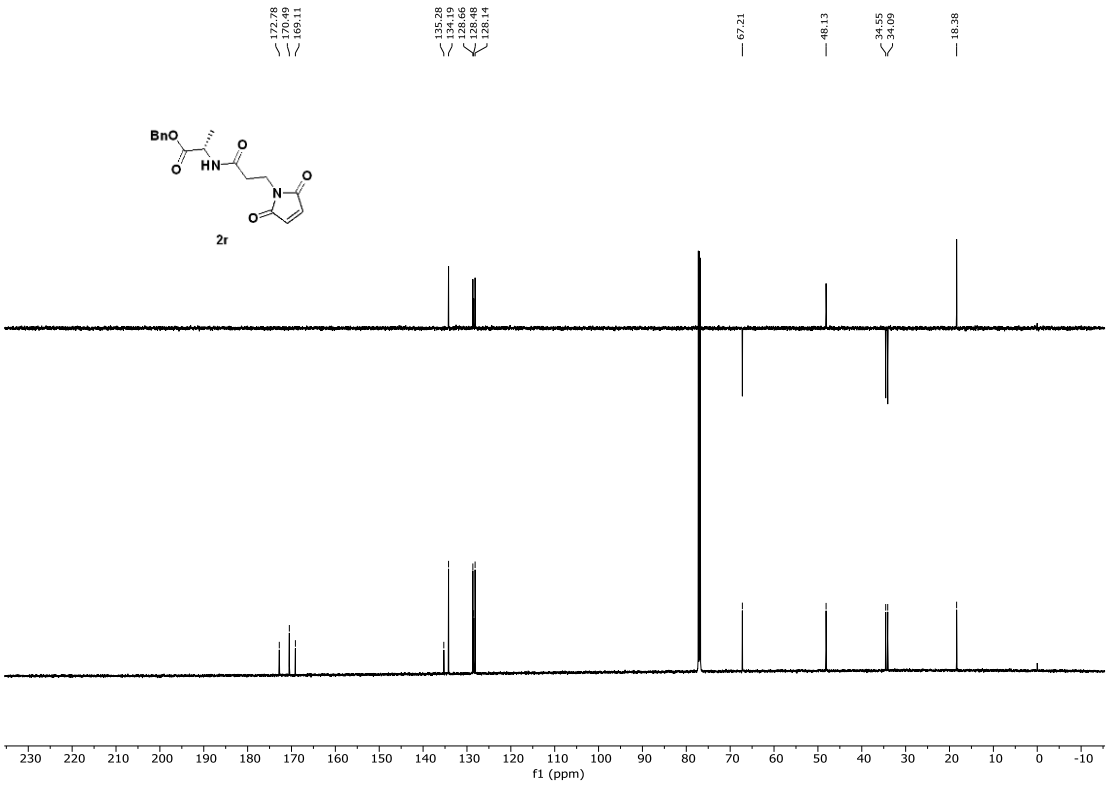


*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alaninate (**2r**)*

^{1}H NMR of **2r** (500 MHz, $CDCl_3$)

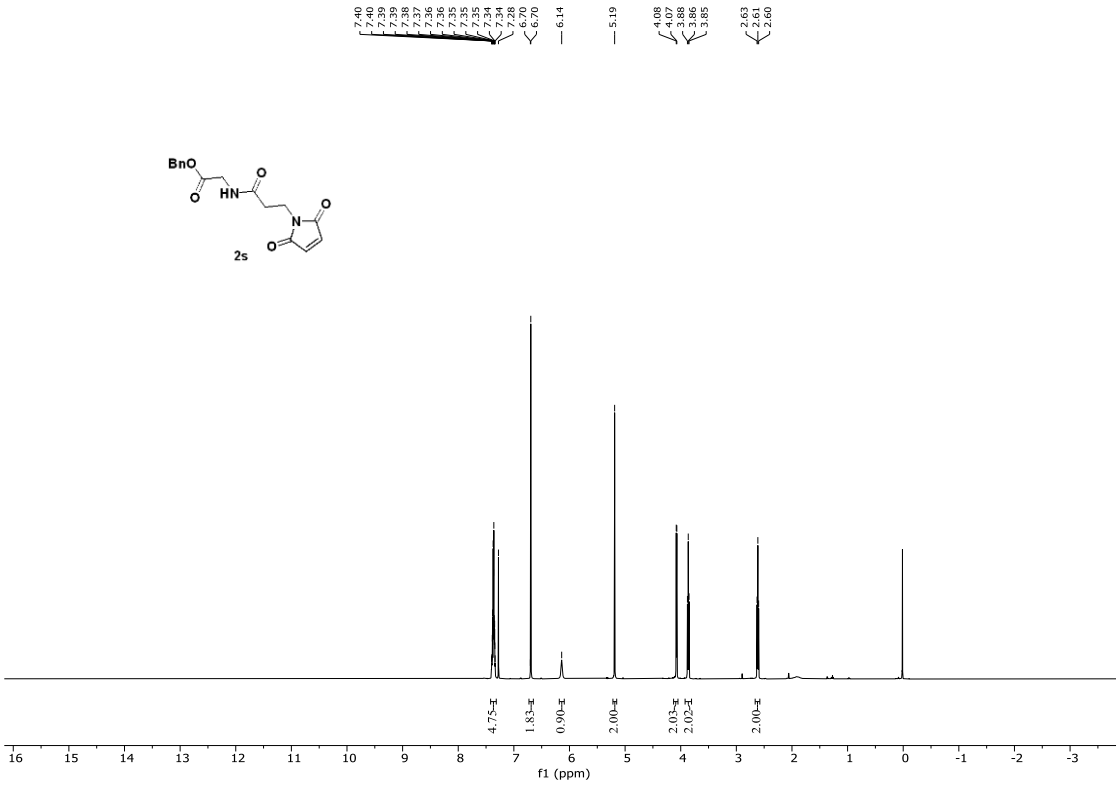


^{13}C{^{1}H} NMR of **2r** (151 MHz, $CDCl_3$)

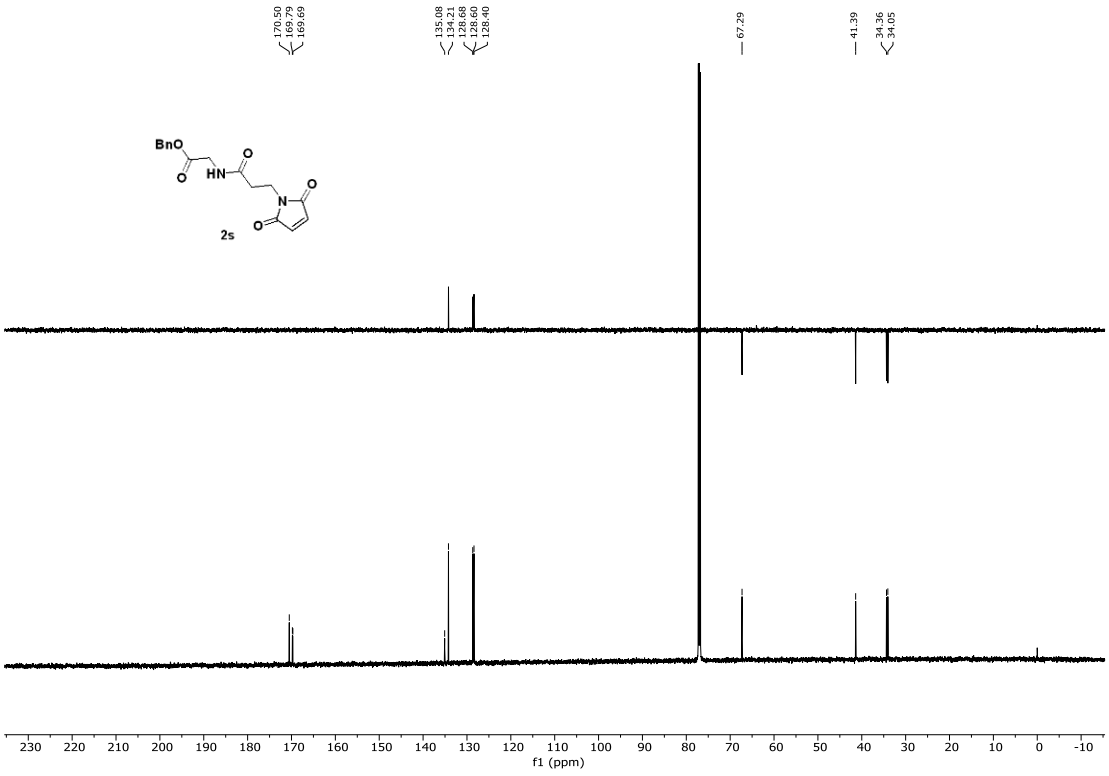


*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycinate (**2s**)*

^{1}H NMR of **2s** (500 MHz, $CDCl_3$)

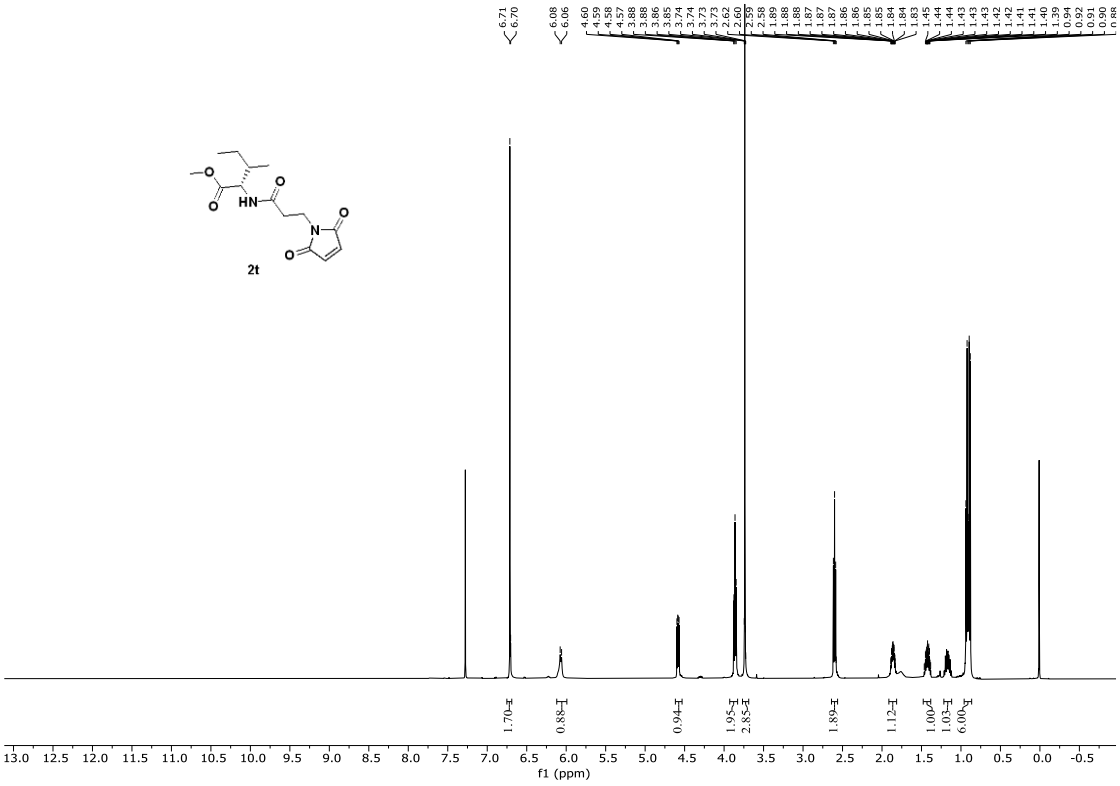


^{13}C{^{1}H} NMR of **2s** (151 MHz, $CDCl_3$)

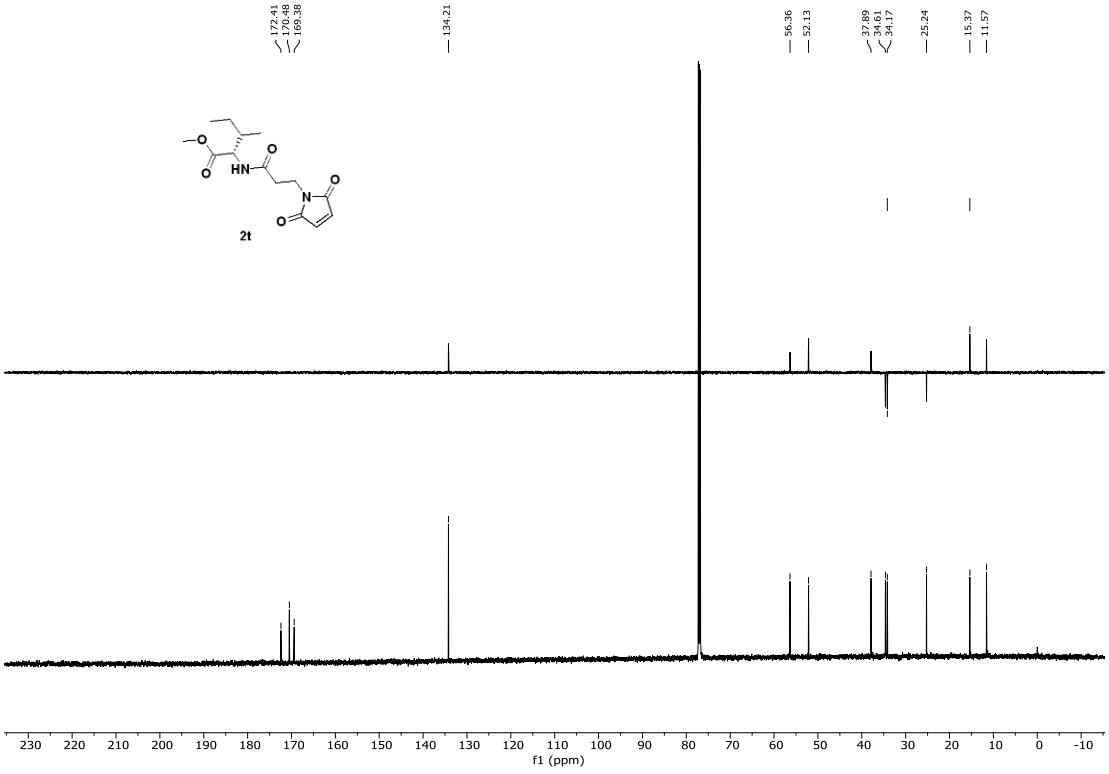


*Methyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucinate (**2t**)*

^{1}H NMR of **2t** (500 MHz, $CDCl_3$)

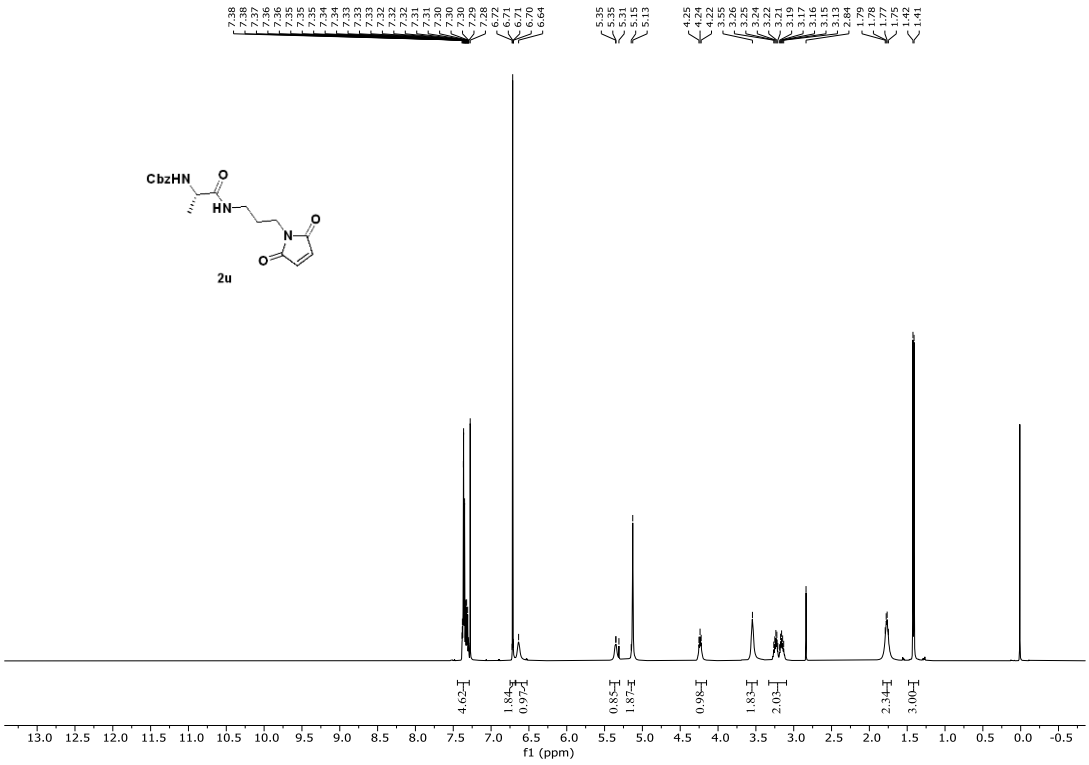


^{13}C{^{1}H} NMR of **2t** (151 MHz, $CDCl_3$)

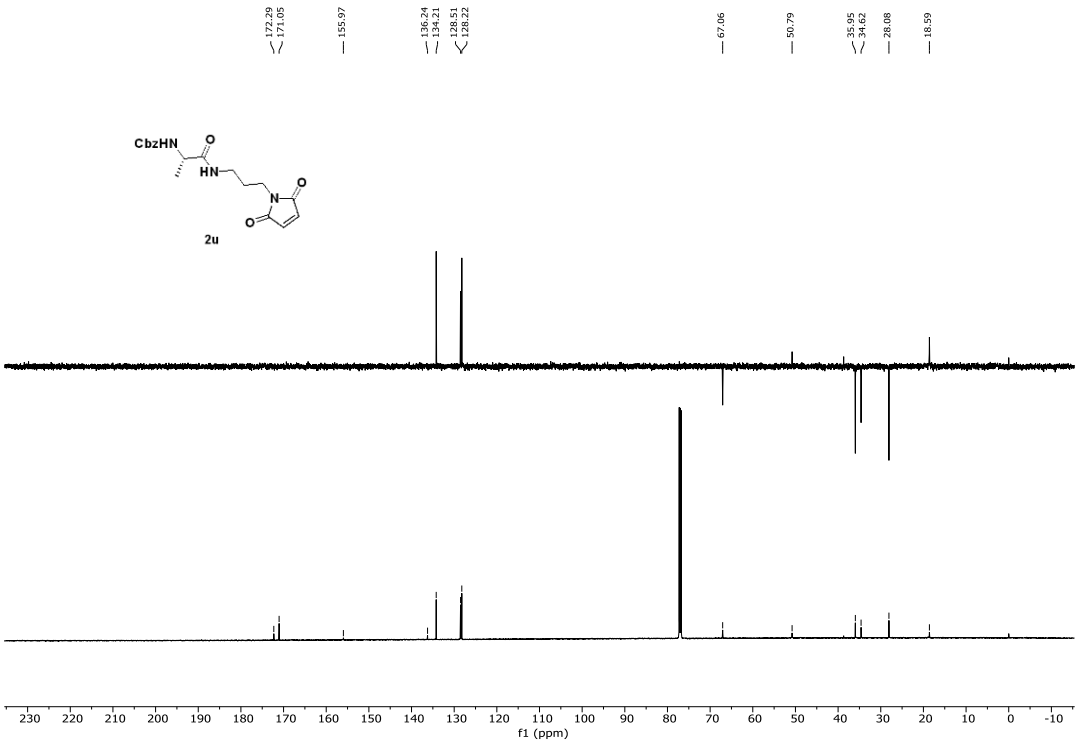


Benzyl (S)-(1-((3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)amino)-1-oxopropan-2-yl)carbamate ***(2u)***

^{1}H NMR of **2u** (500 MHz, $CDCl_3$)

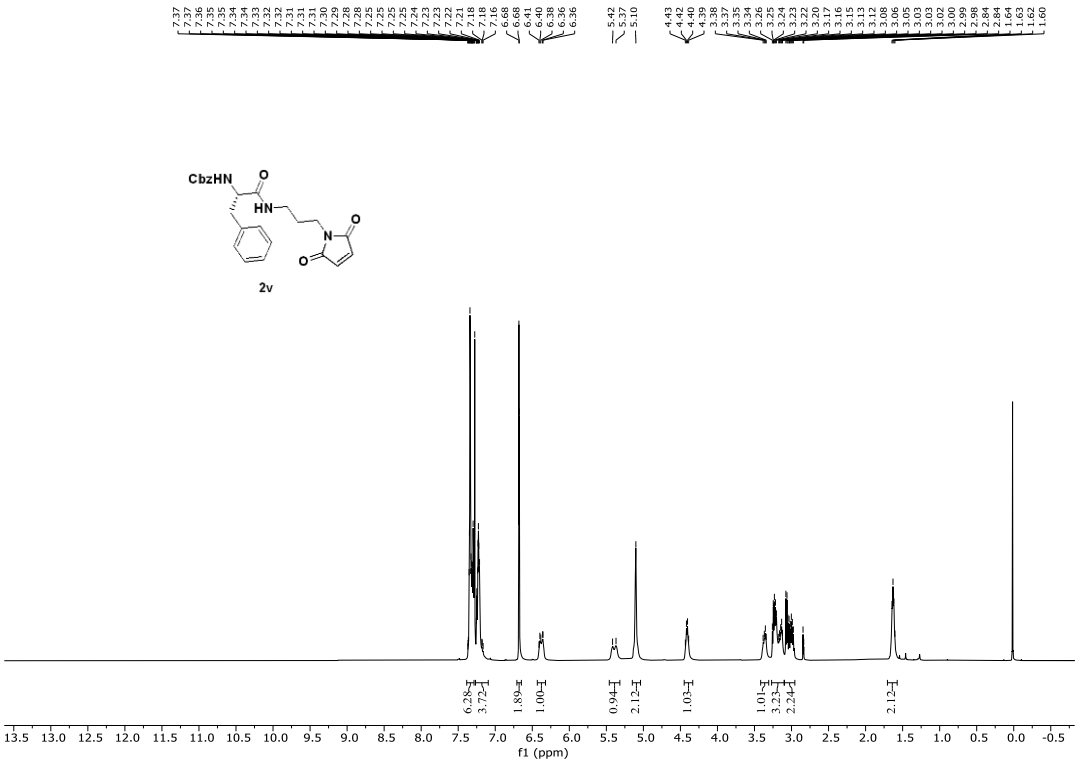


^{13}C{^{1}H} NMR of **2u** (151 MHz, $CDCl_3$)

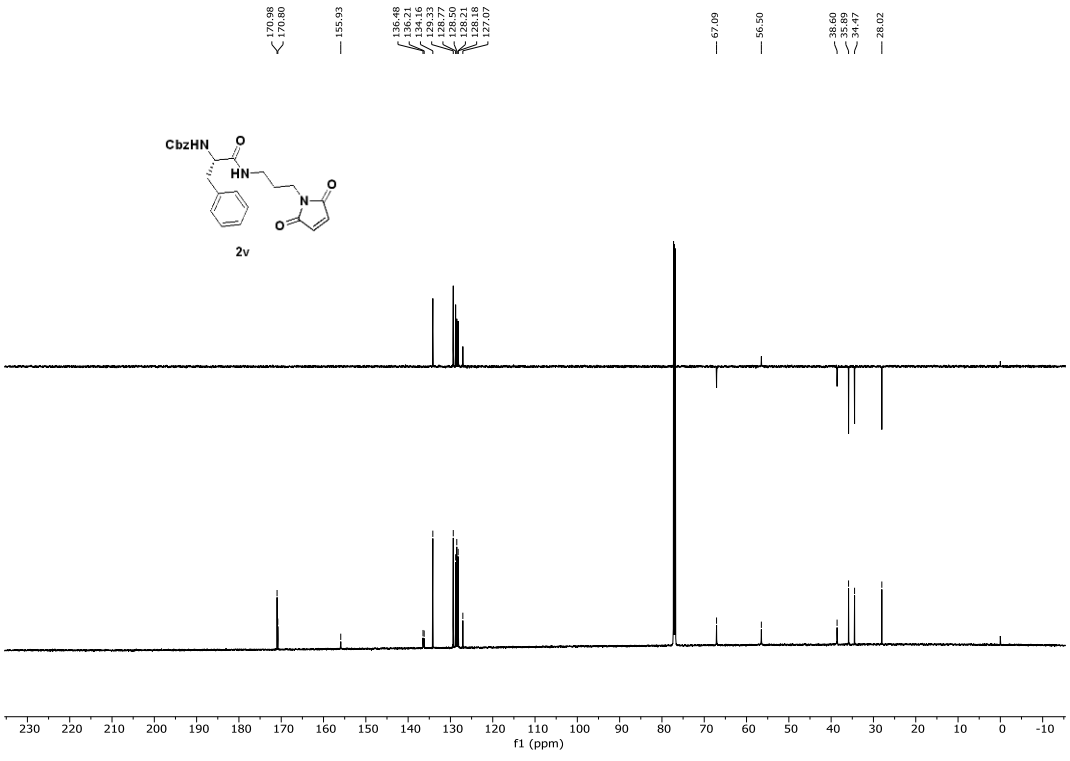


*Benzyl (S)-(1-((3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (**2v**)*

^{1}H NMR of **2v** (500 MHz, $CDCl_3$)

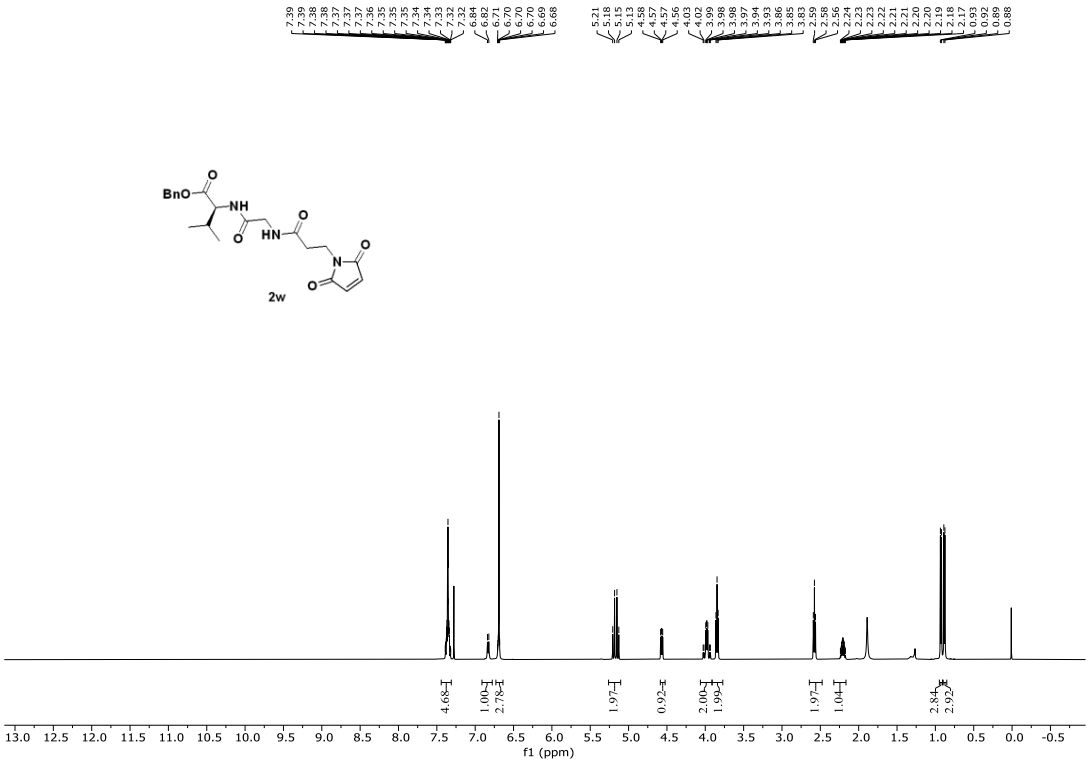


^{13}C{^{1}H} NMR of **2v** (151 MHz, $CDCl_3$)

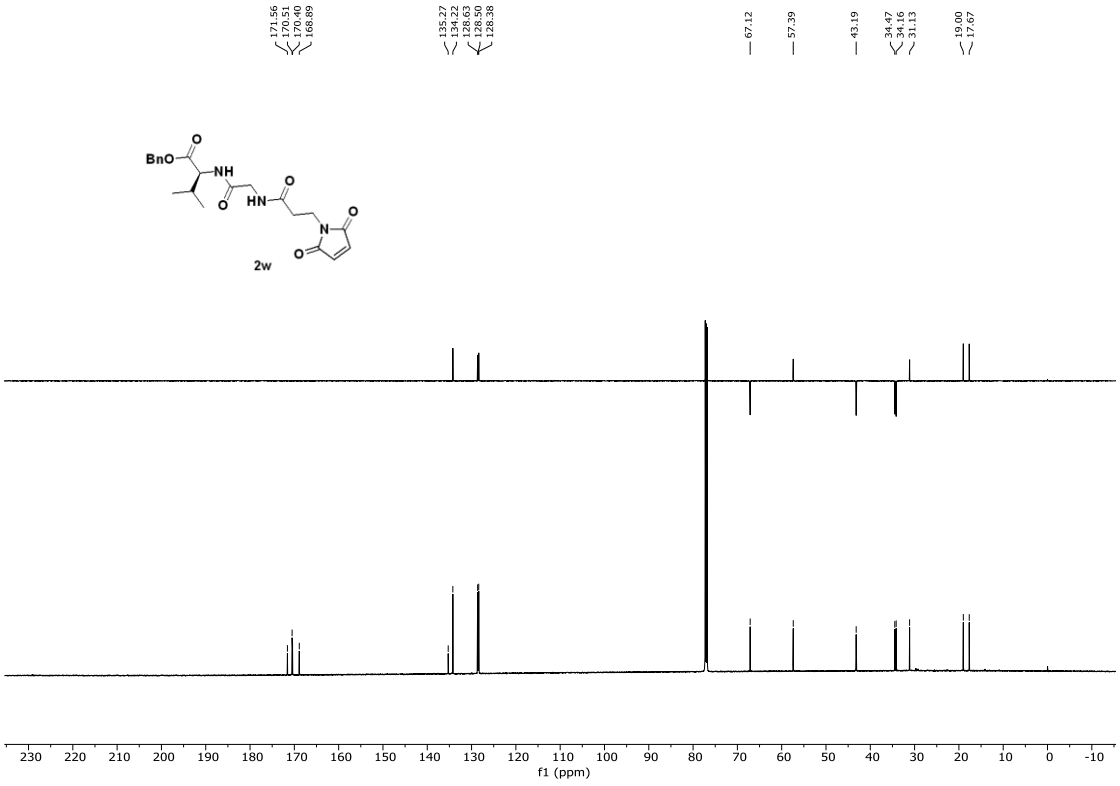


*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycyl-L-valinate (**2w**)*

^{1}H NMR of **2w** (500 MHz, $CDCl_3$)

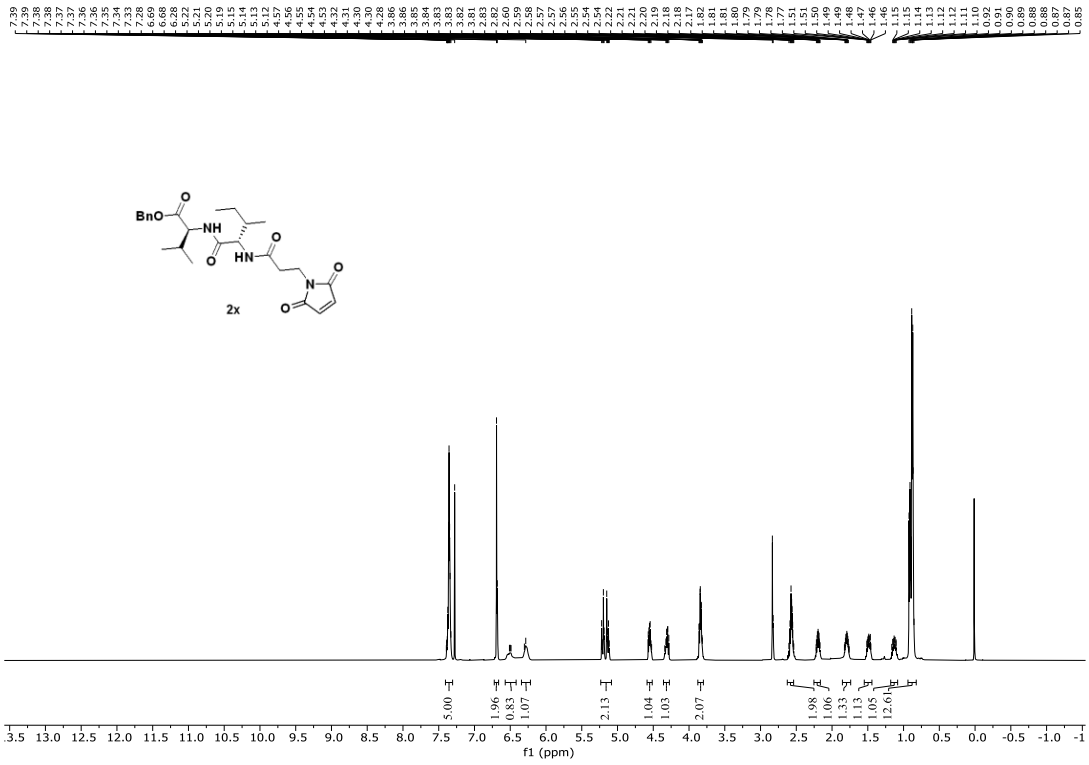


^{13}C{^{1}H} NMR of **2w** (151 MHz, $CDCl_3$)

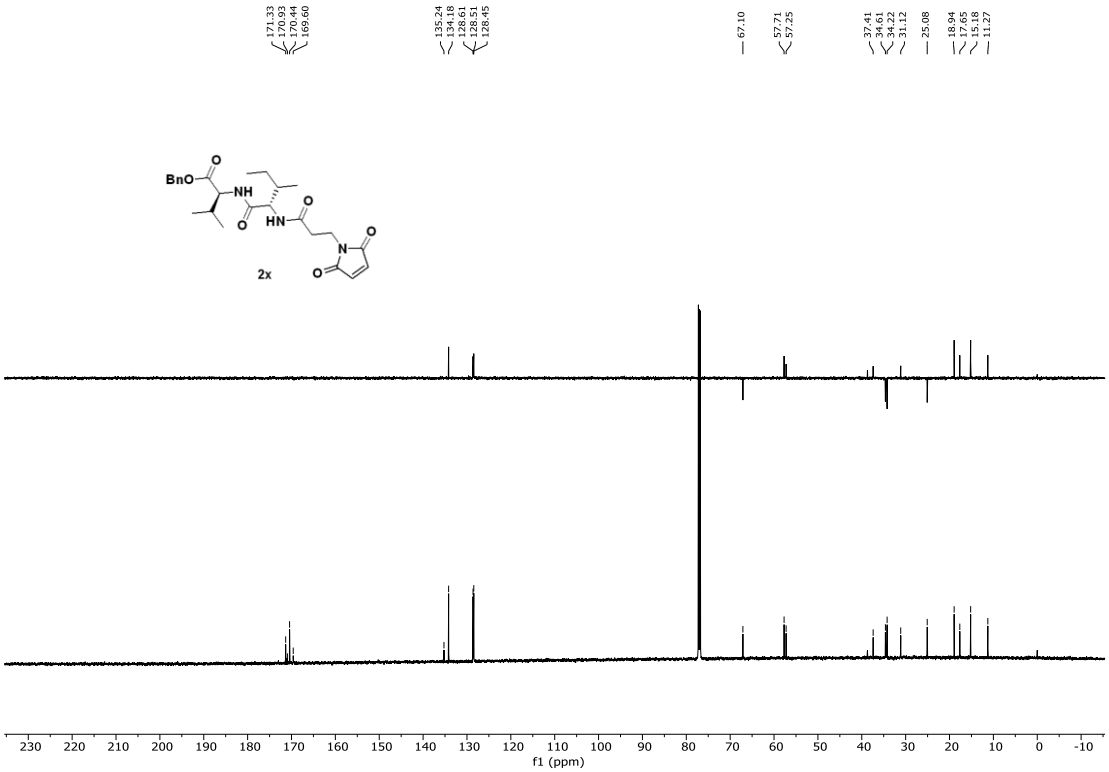


*Benzyl (3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucyl-L-valinate (**2x**)*

^{1}H NMR of **2x** (500 MHz, $CDCl_3$)

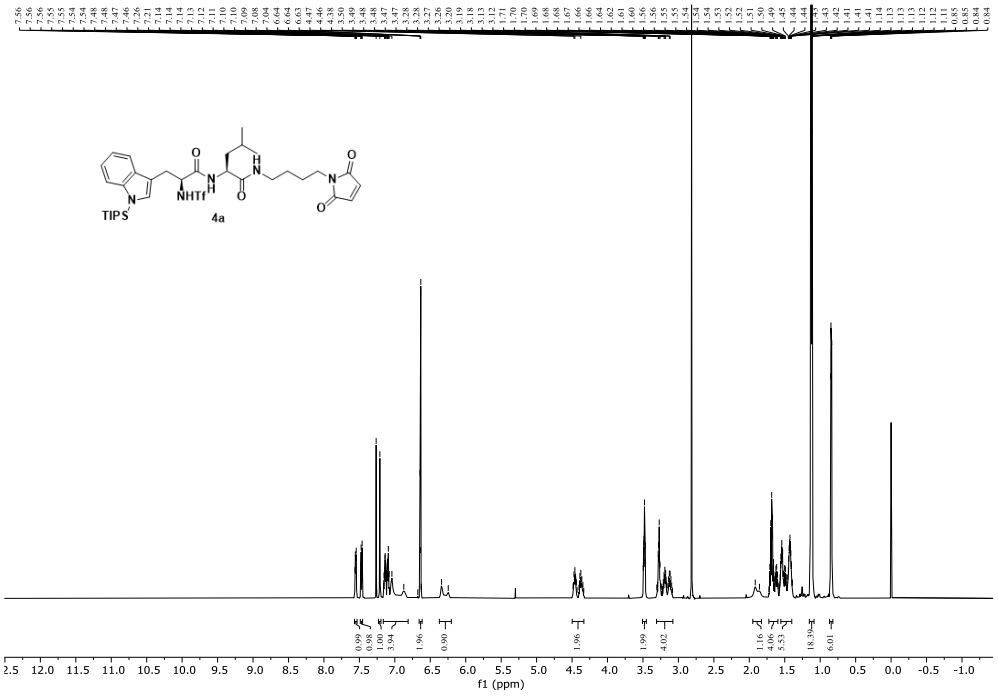


^{13}C{^{1}H} NMR of **2x** (151 MHz, $CDCl_3$)

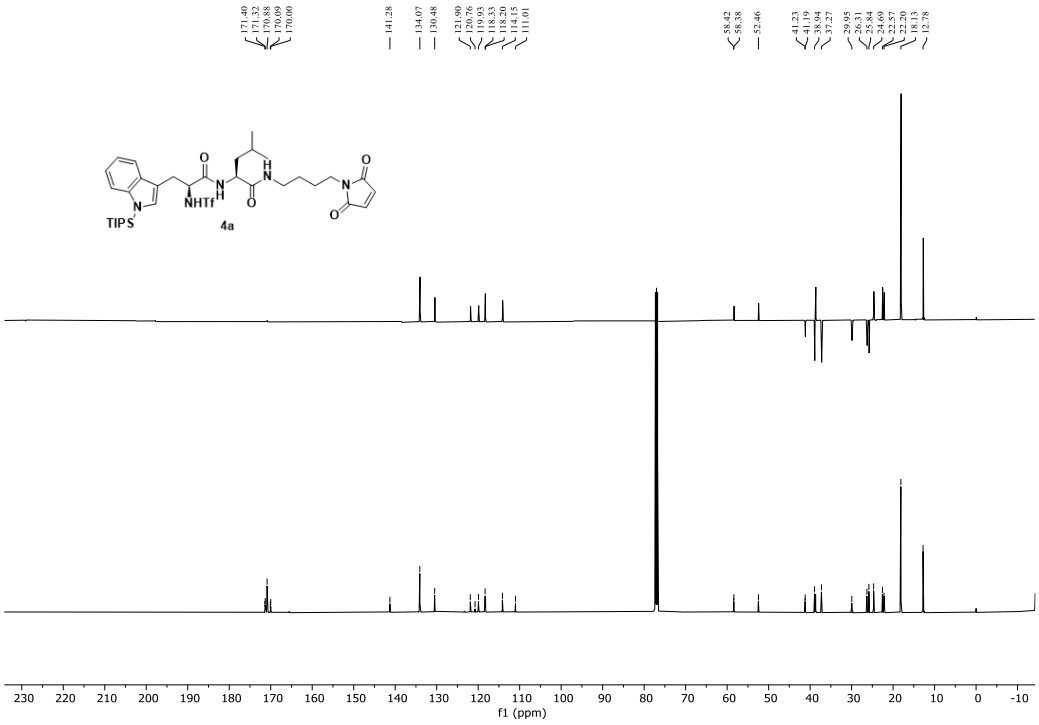


*(S)-N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-4-methyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)pentanamide (**4a**)*

^{1}H NMR of **4a** (600 MHz, $CDCl_3$)

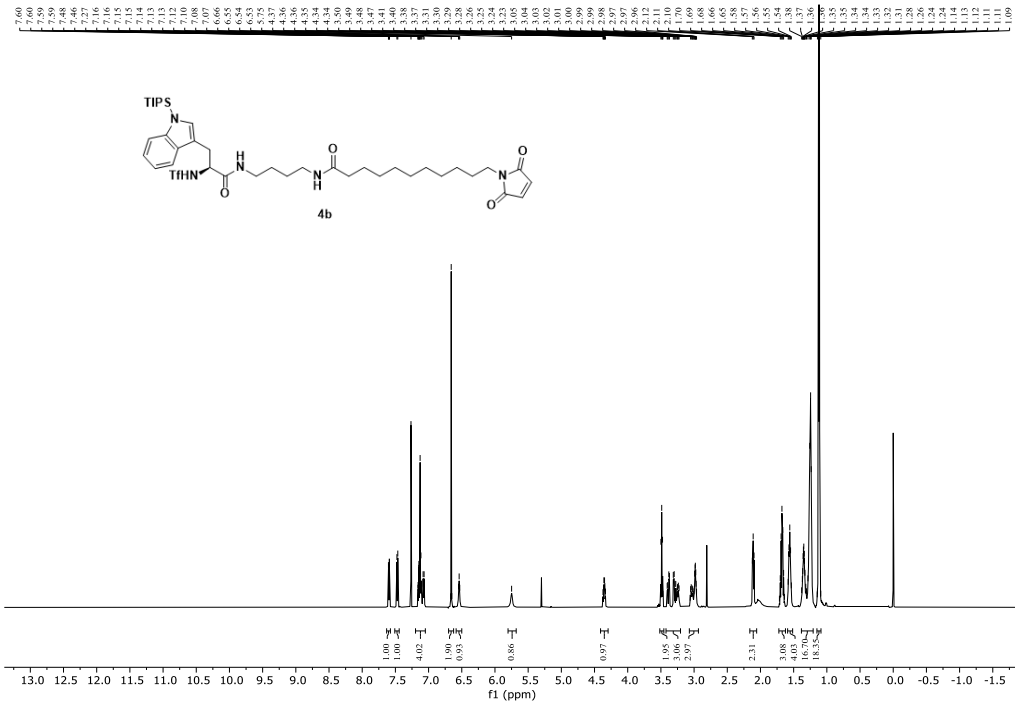


^{13}C{^{1}H} NMR of **4a** (126 MHz, $CDCl_3$)

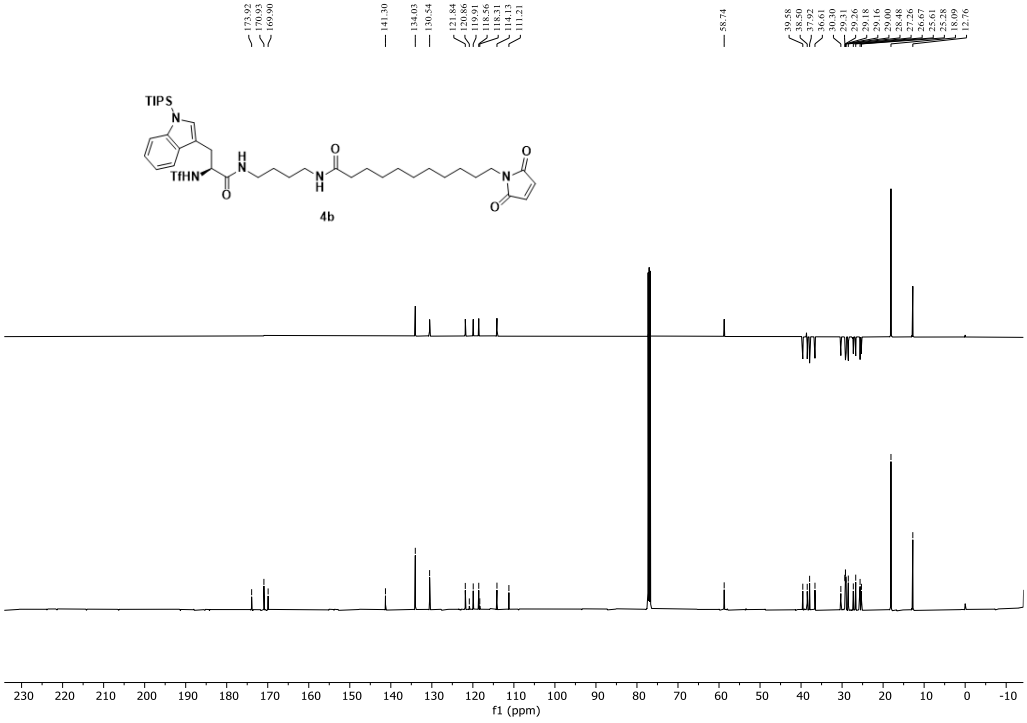


*(S)-11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-N-(4-(2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)butyl)undecanamide (**4b**)*

^{1}H NMR of **4b** (600 MHz, $CDCl_3$)

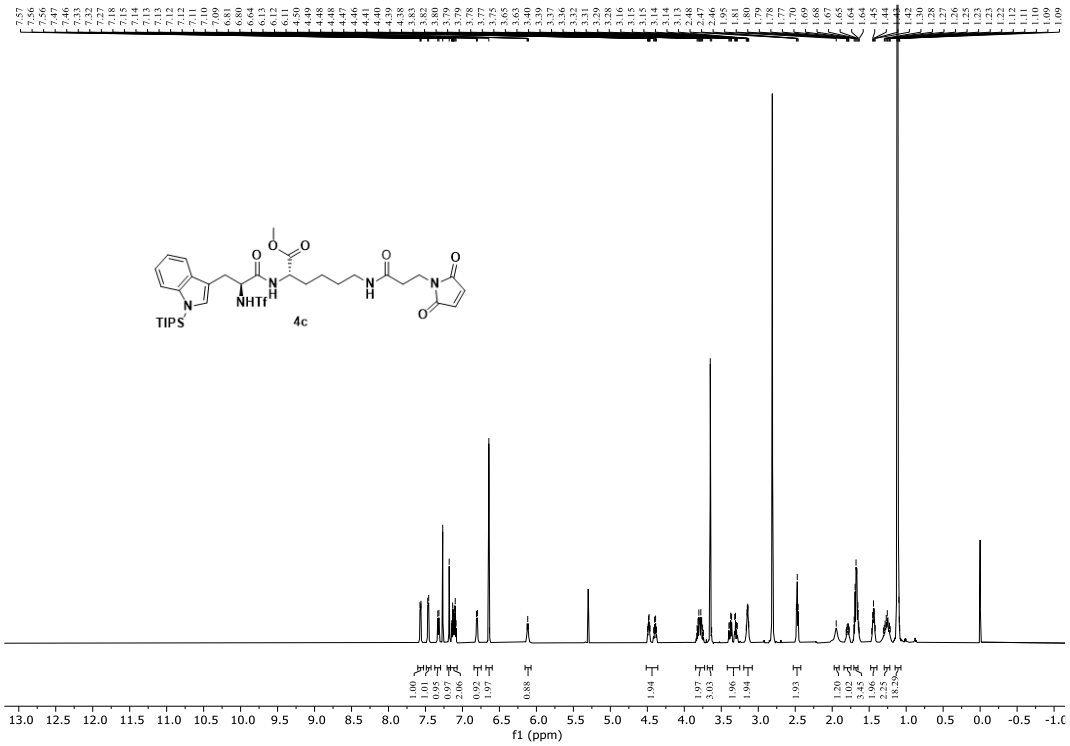


^{13}C{^{1}H} NMR of **4b** (126 MHz, $CDCl_3$)

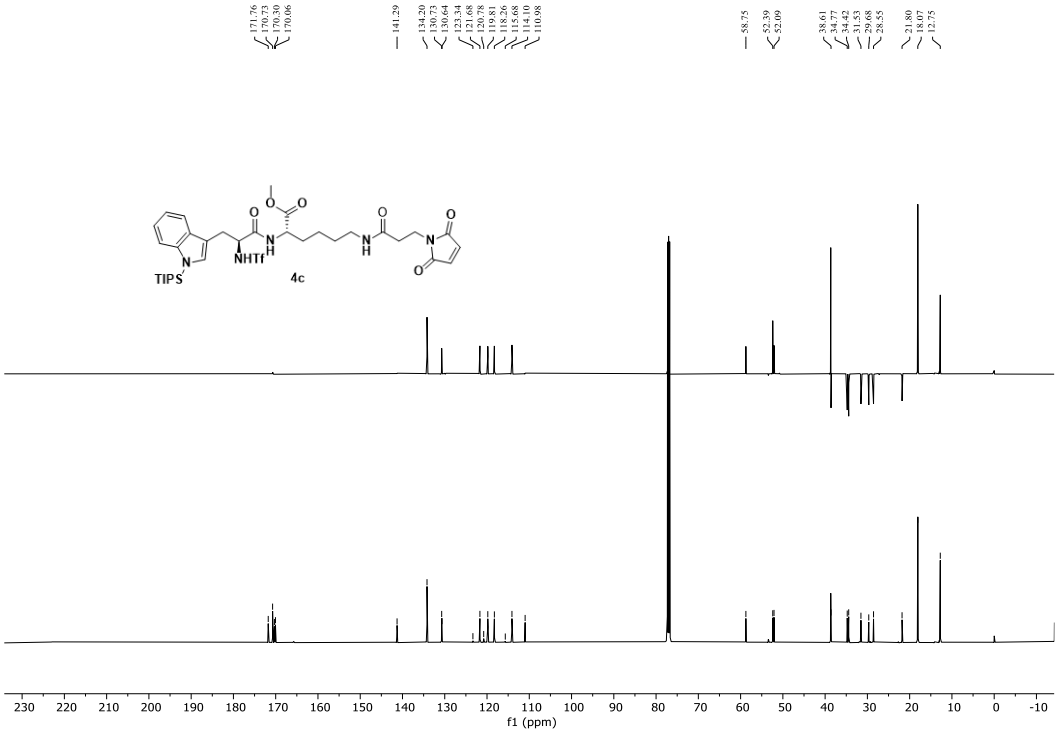


*Methyl N^6-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4c**)*

^{1}H NMR of **4c** (600 MHz, $CDCl_3$)

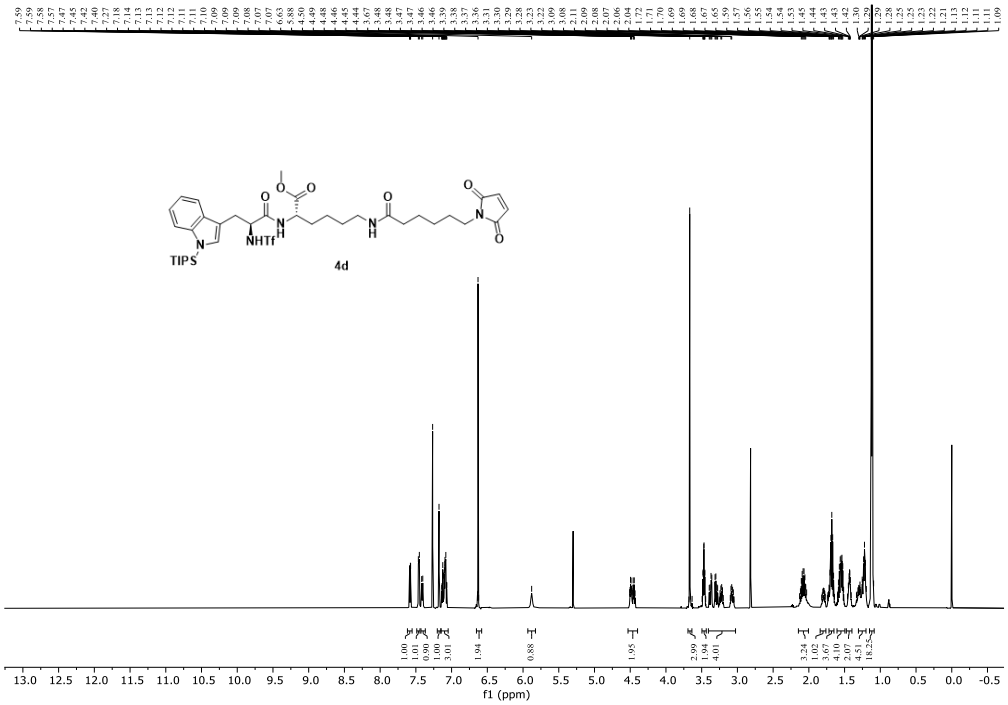


^{13}C{^{1}H} NMR of **4c** (126 MHz, $CDCl_3$)

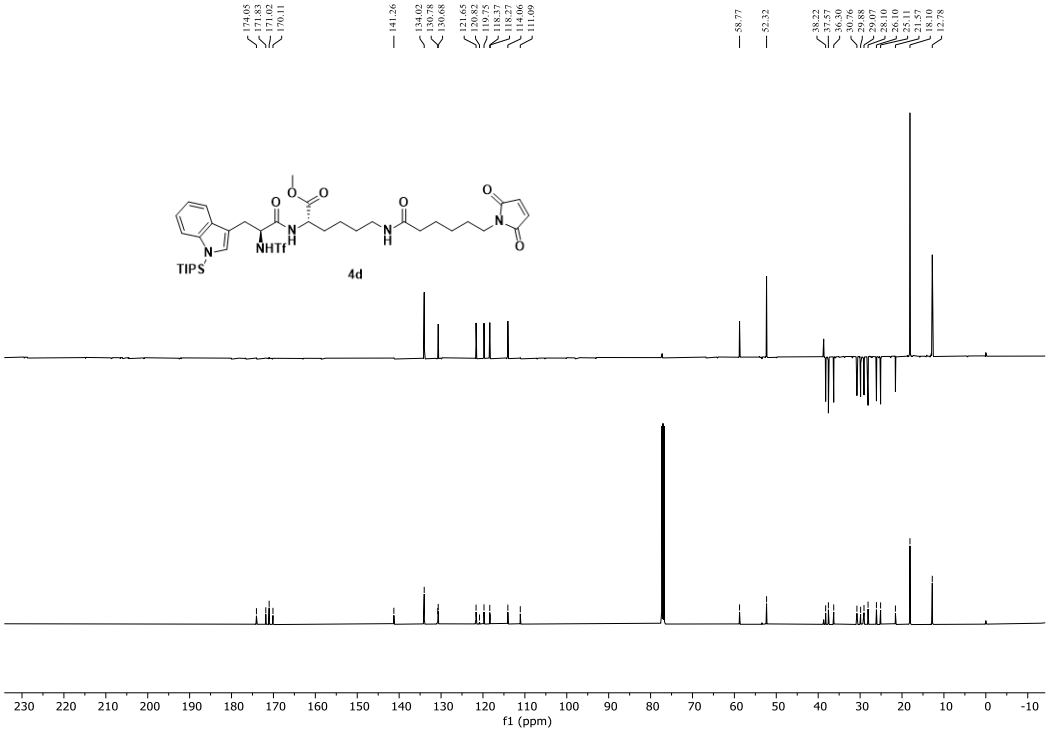


*Methyl N^6-(6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4d**)*

^{1}H NMR of **4d** (600 MHz, $CDCl_3$)

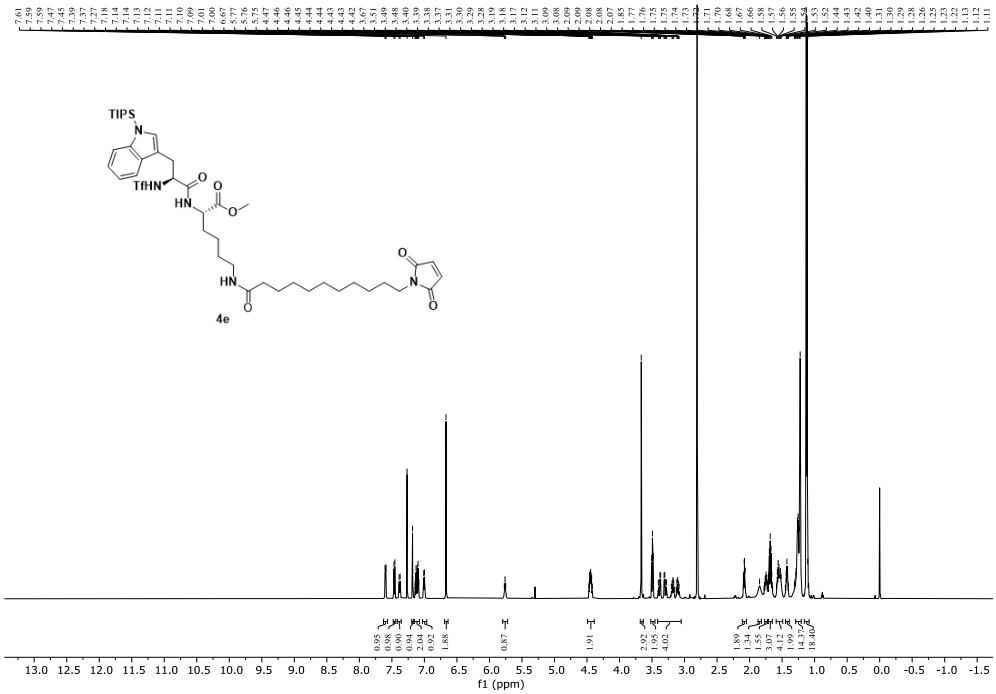


^{13}C{^{1}H} NMR of **4d** (126 MHz, $CDCl_3$)

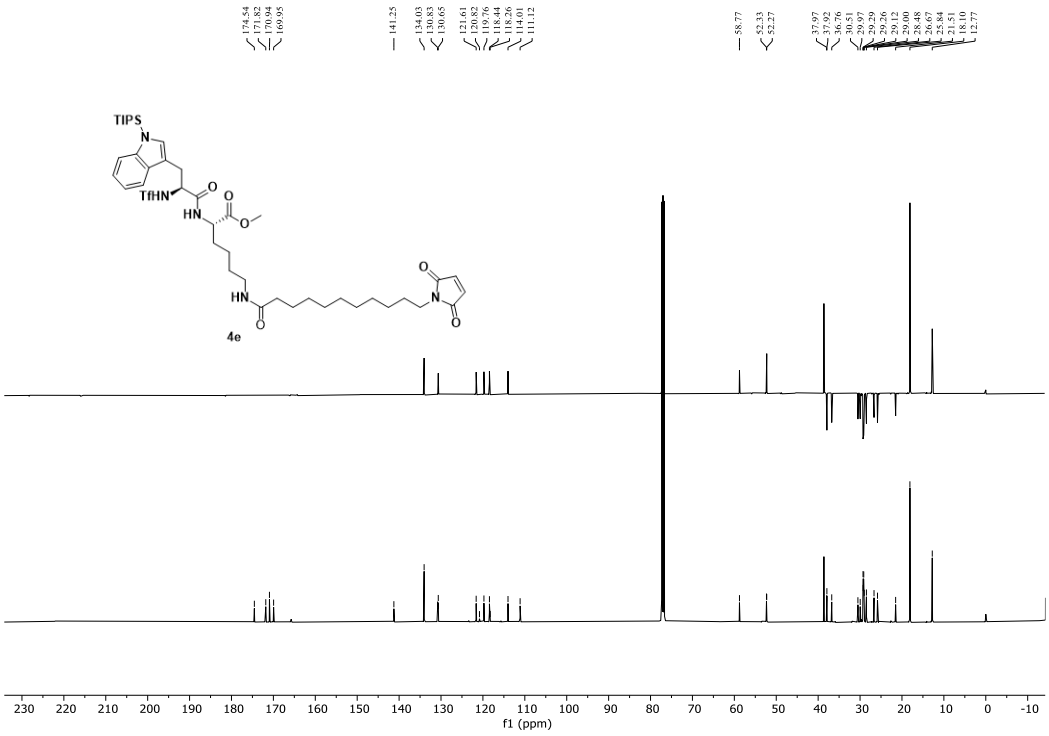


*Methyl N^6-(11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)undecanoyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl)-L-lysinate (**4e**)*

^{1}H NMR of **4e** (600 MHz, $CDCl_3$)

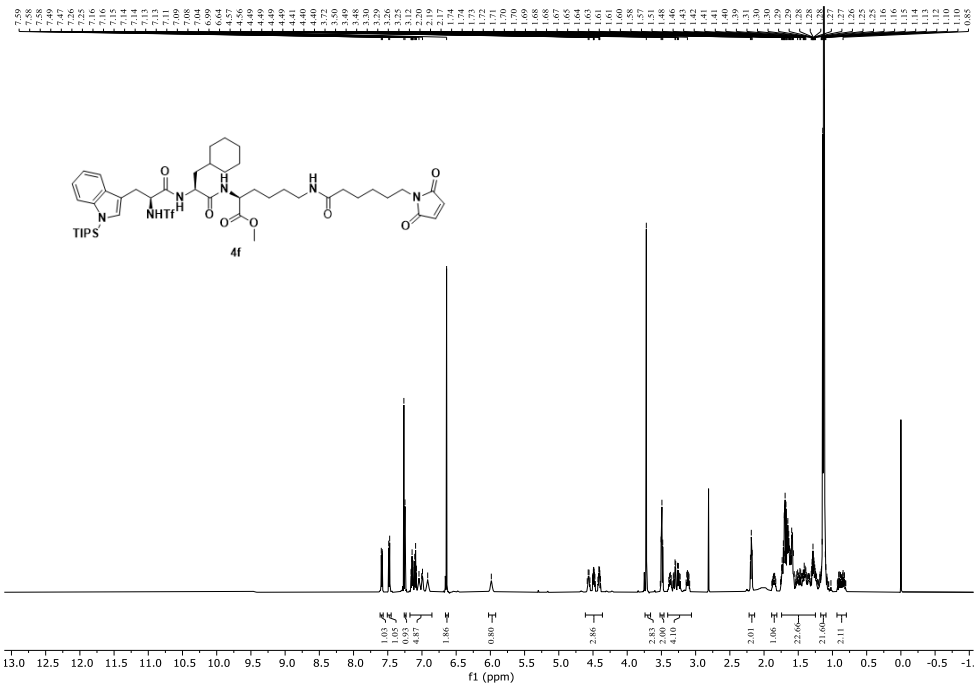


^{13}C{^{1}H} NMR of **4e** (126 MHz, $CDCl_3$)

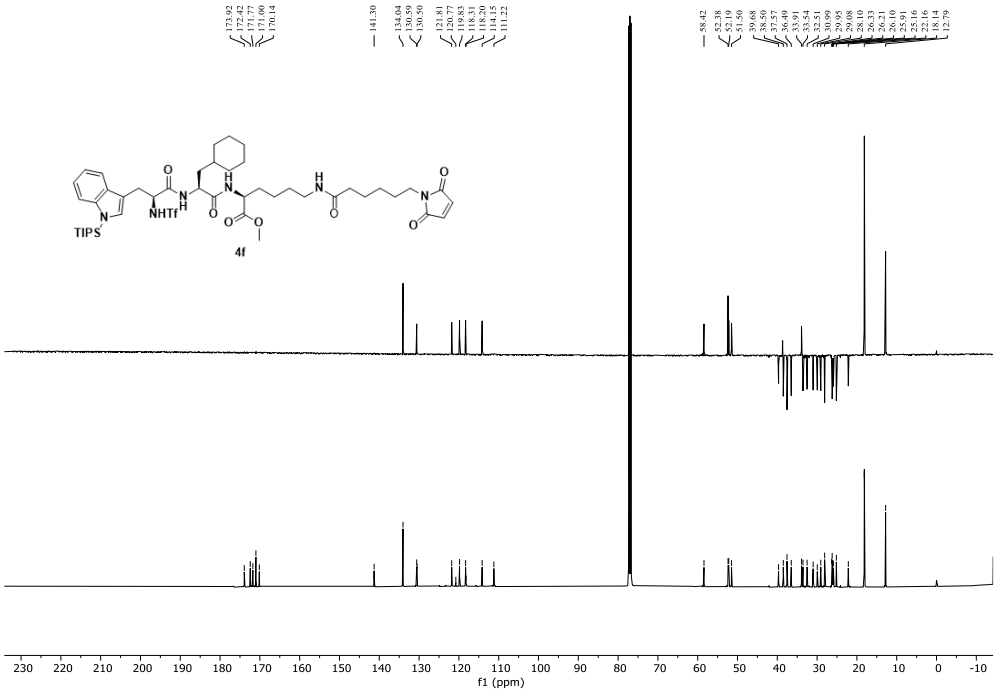


*Methyl N^2-((S)-3-cyclohexyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanoyl)-N^6-(6-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)hexanoyl)-L-lysinate (**4f**)*

^{1}H NMR of **4f** (600 MHz, $CDCl_3$)

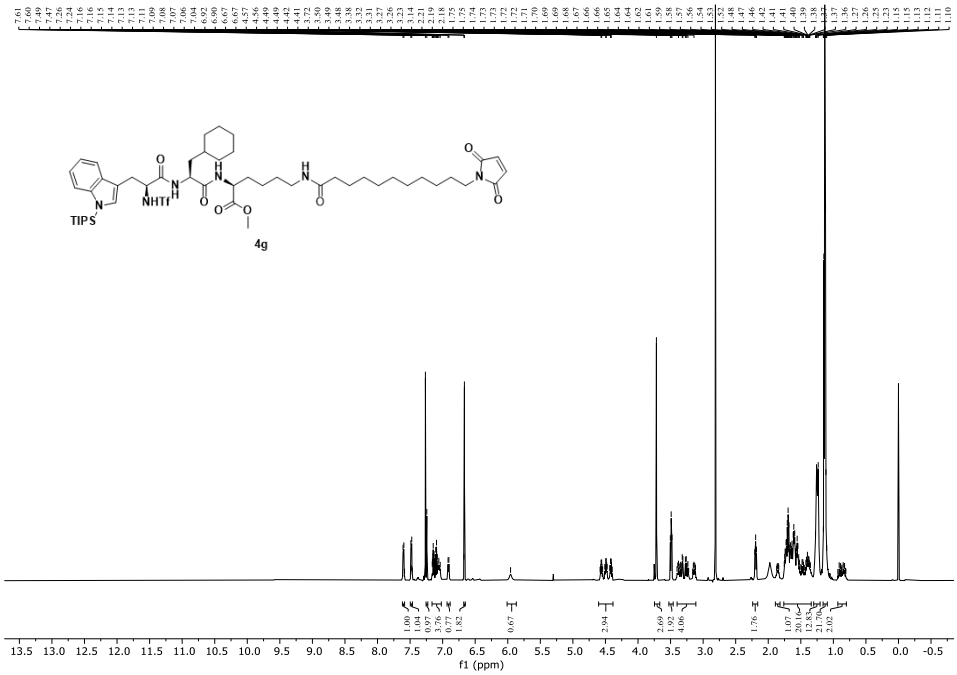


^{13}C{^{1}H} NMR of **4f** (126 MHz, $CDCl_3$)

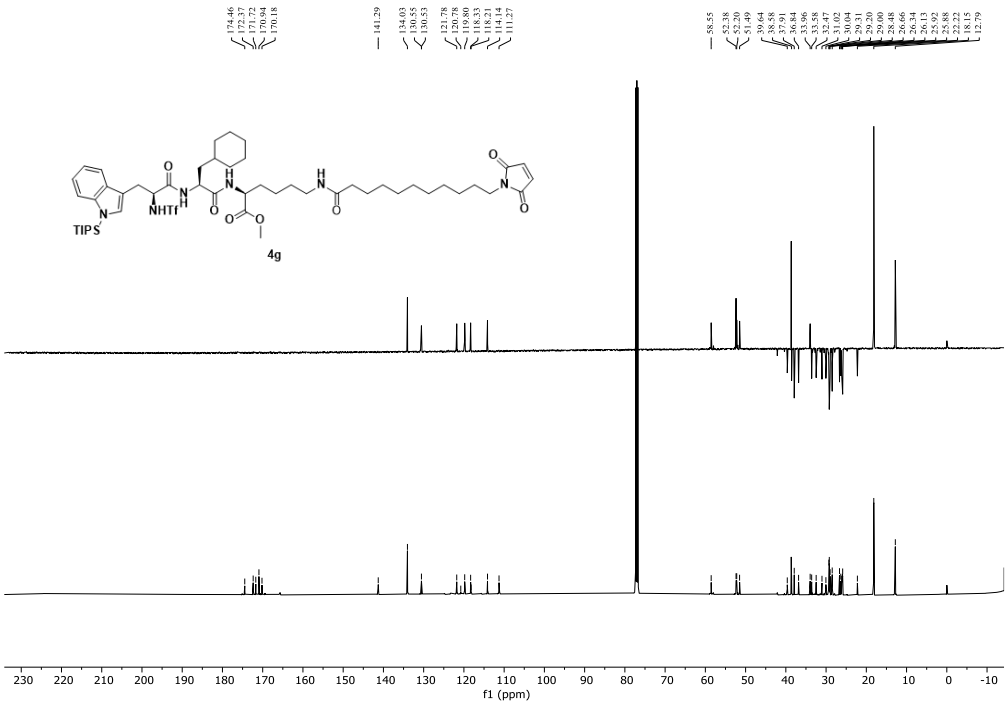


Methyl N^2-((S)-3-cyclohexyl-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanoyl)-N^6-(11-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)undecanoyl)-L-lysinate ***(4g)***

^{1}H NMR of **4g** (600 MHz, $CDCl_3$)

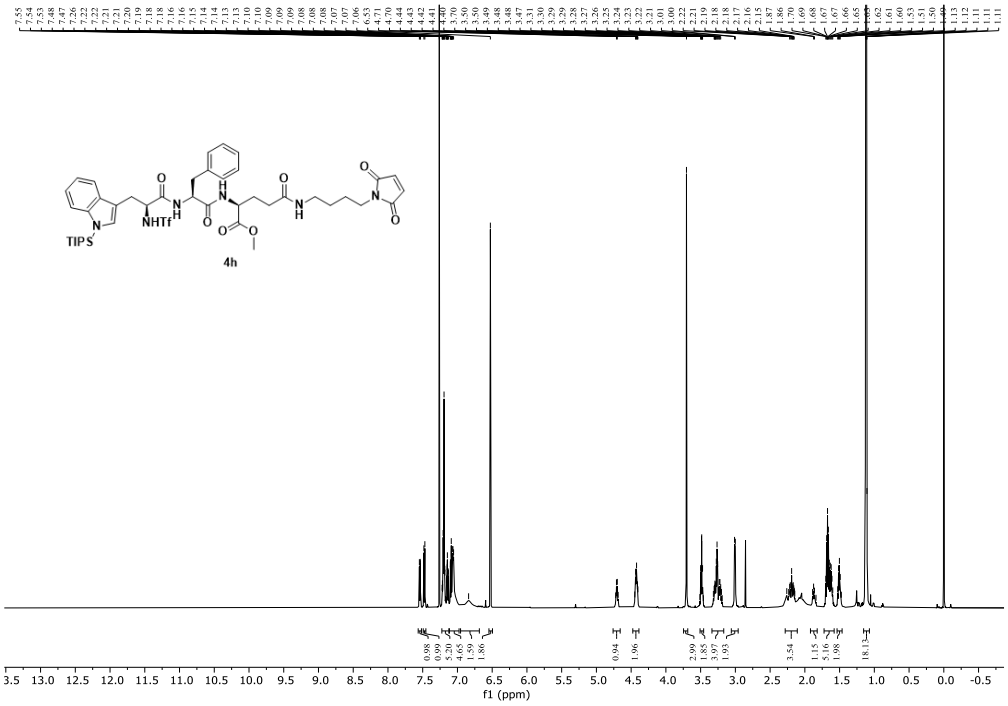


^{13}C{^{1}H} NMR of **4g** (126 MHz, $CDCl_3$)

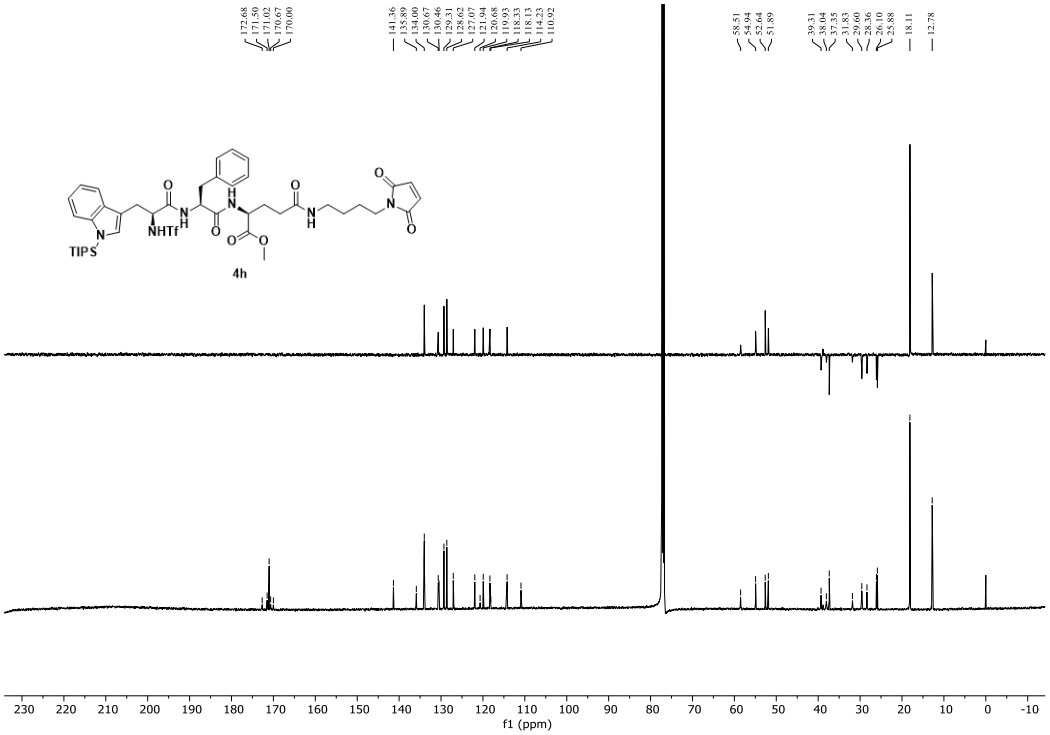


Methyl N^5*-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-*N^2*-(*N^a*-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (**4h**)*

^{1}H NMR of **4h** (600 MHz, $CDCl_3$)

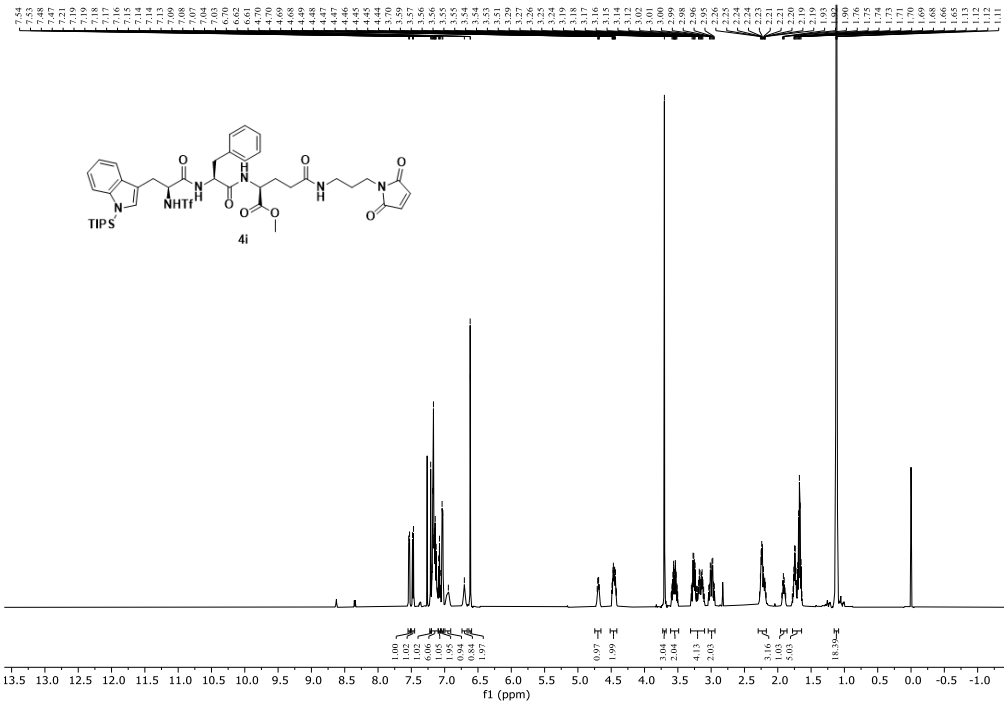


^{13}C{^{1}H} NMR of **4h** (126 MHz, $CDCl_3$)

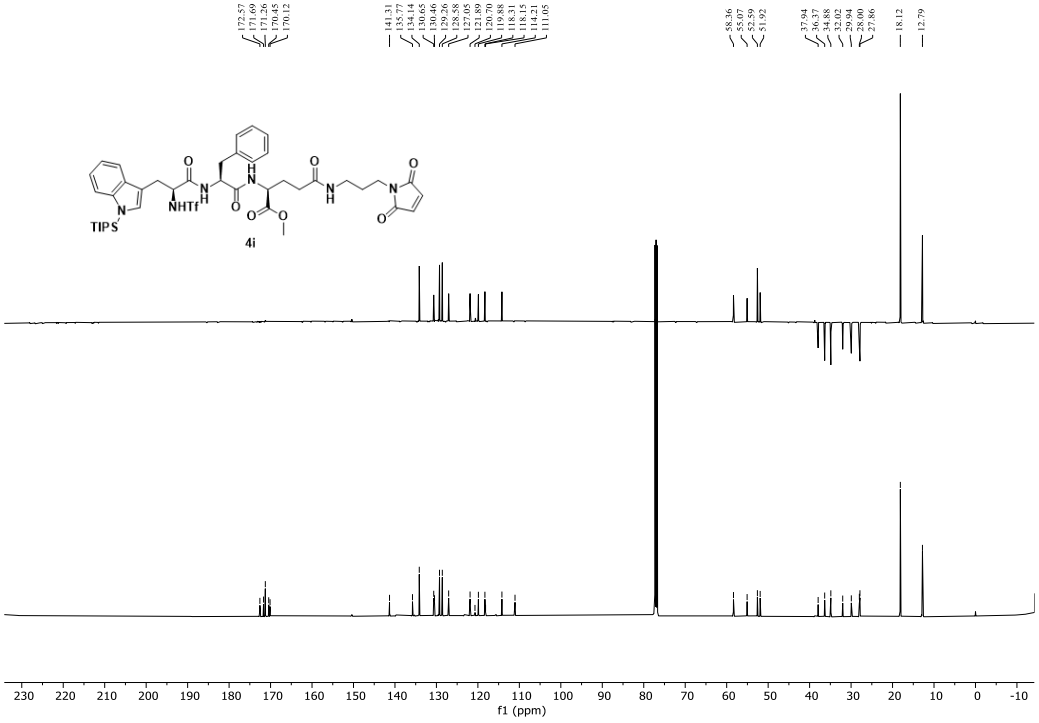


*Methyl N^5-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (**4i**)*

^{1}H NMR of **4i** (600 MHz, $CDCl_3$)

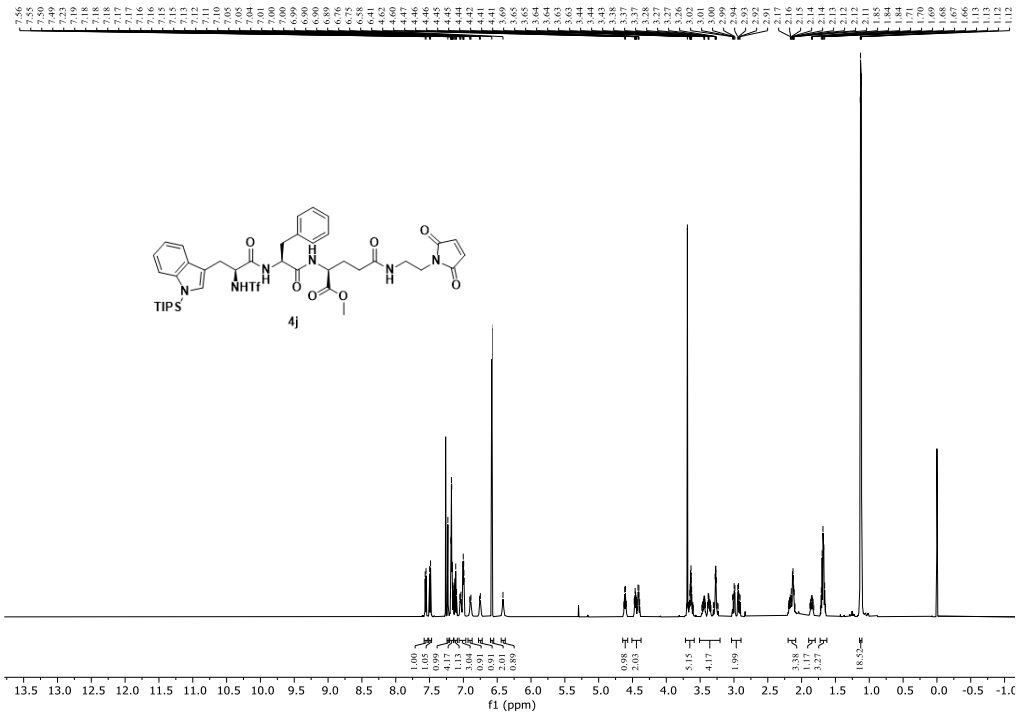


^{13}C{^{1}H} NMR of **4i** (126 MHz, $CDCl_3$)

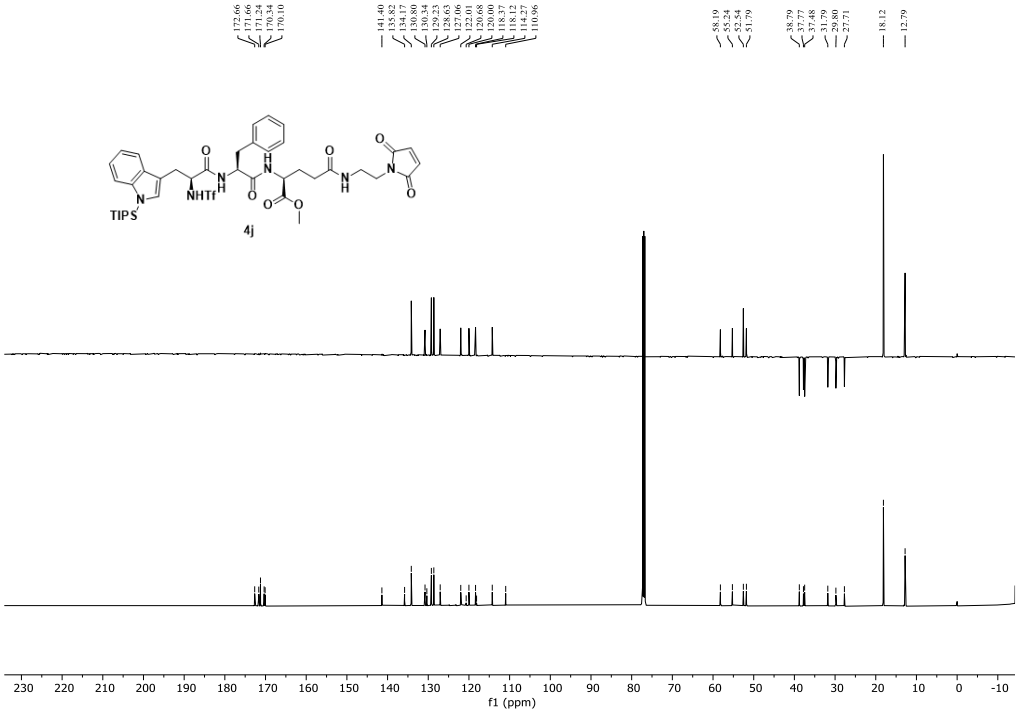


Methyl N^5*-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-*N^2*-(*N^a*-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-phenylalanyl)-L-glutaminate (**4j**)*

^{1}H NMR of **4j** (600 MHz, $CDCl_3$)

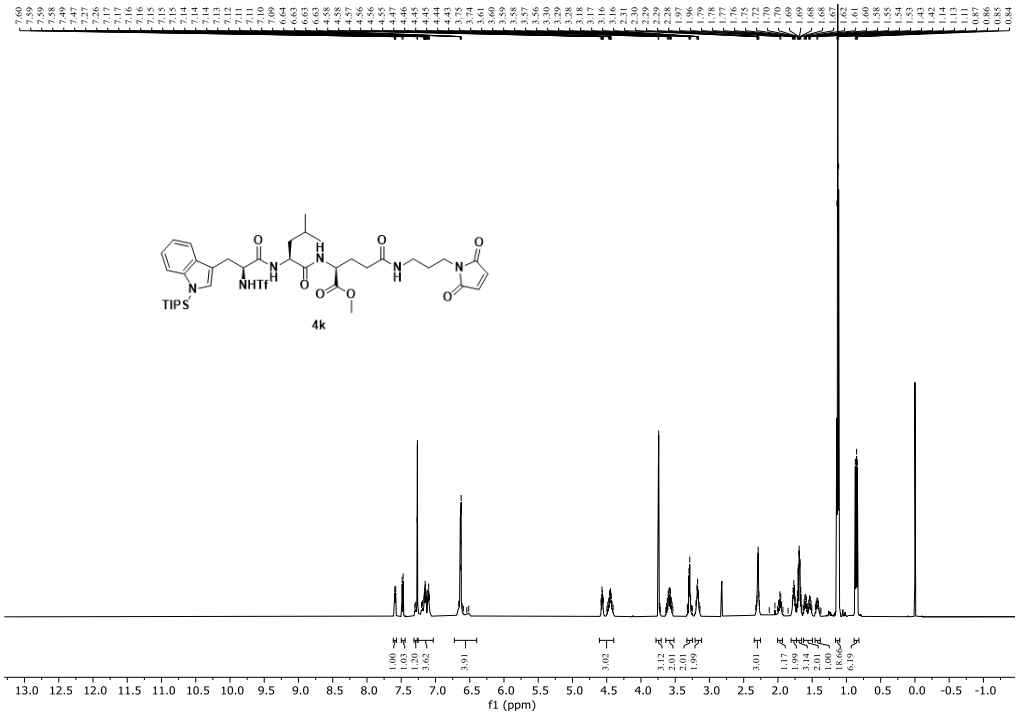


^{13}C{^{1}H} NMR of **4j** (126 MHz, $CDCl_3$)

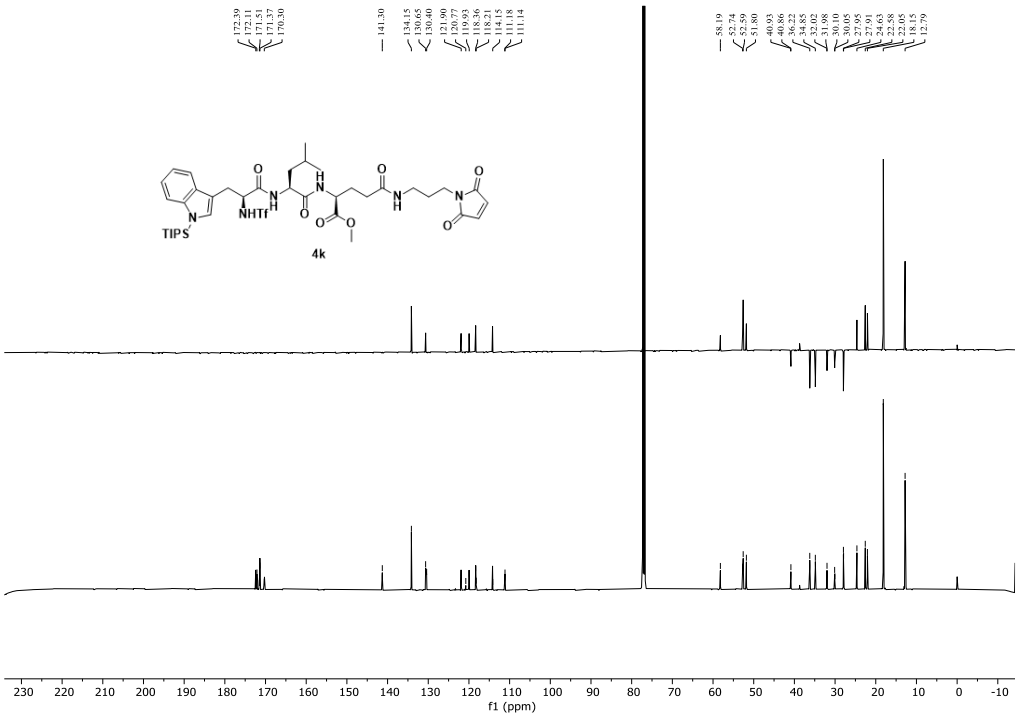


*Methyl N^5-(3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propyl)-N^2-(N^a-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4k**)*

^{1}H NMR of **4k** (600 MHz, $CDCl_3$)

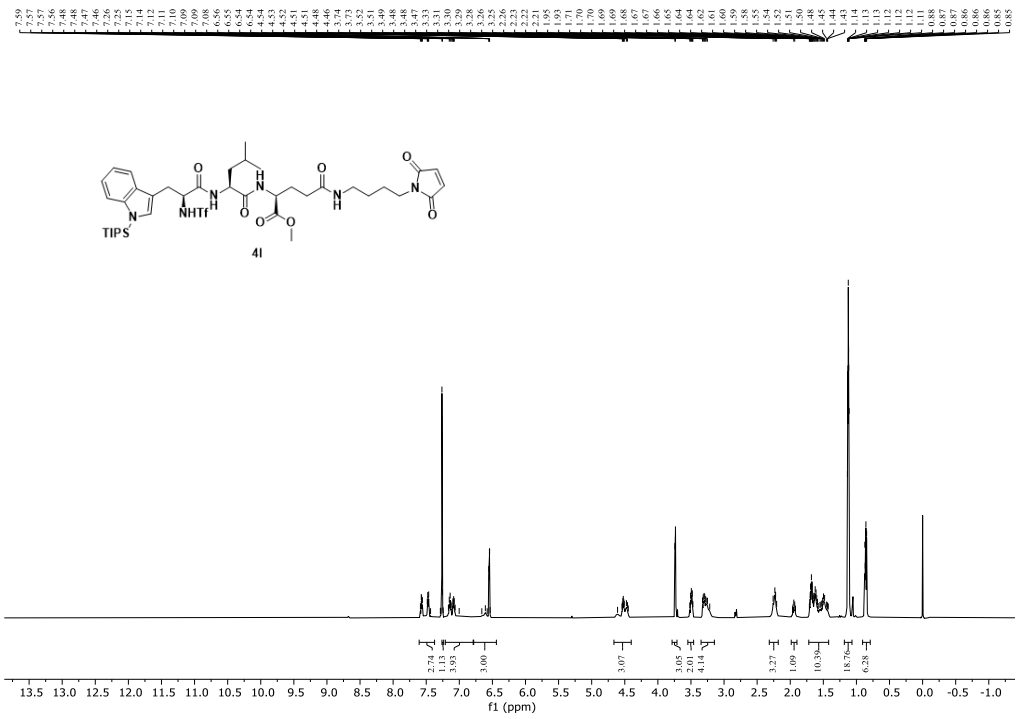


^{13}C{^{1}H} NMR of **4k** (126 MHz, $CDCl_3$)

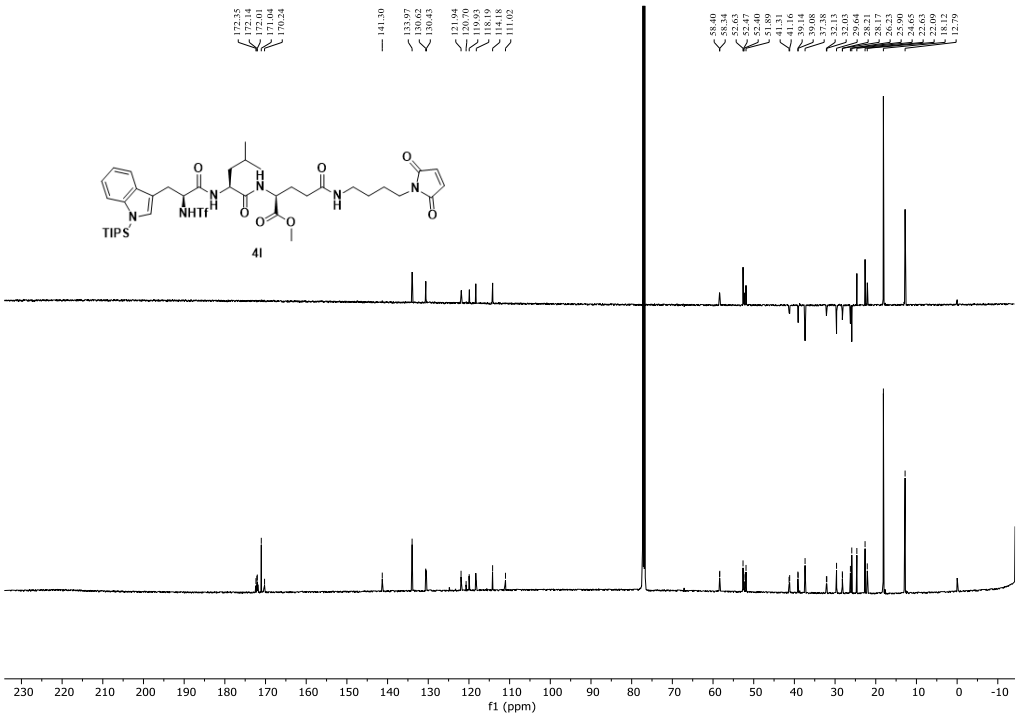


Methyl N^5*-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-*N^2*-(*N^a*-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4l**)*

^{1}H NMR of **4l** (600 MHz, $CDCl_3$)

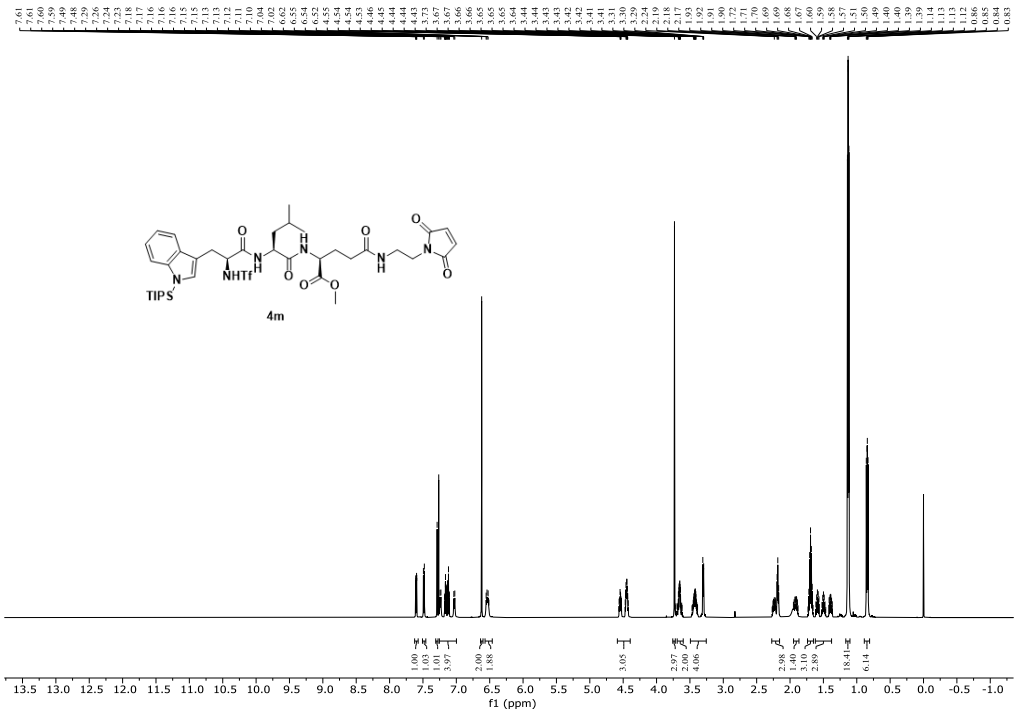


^{13}C{^{1}H} NMR of **4l** (126 MHz, $CDCl_3$)

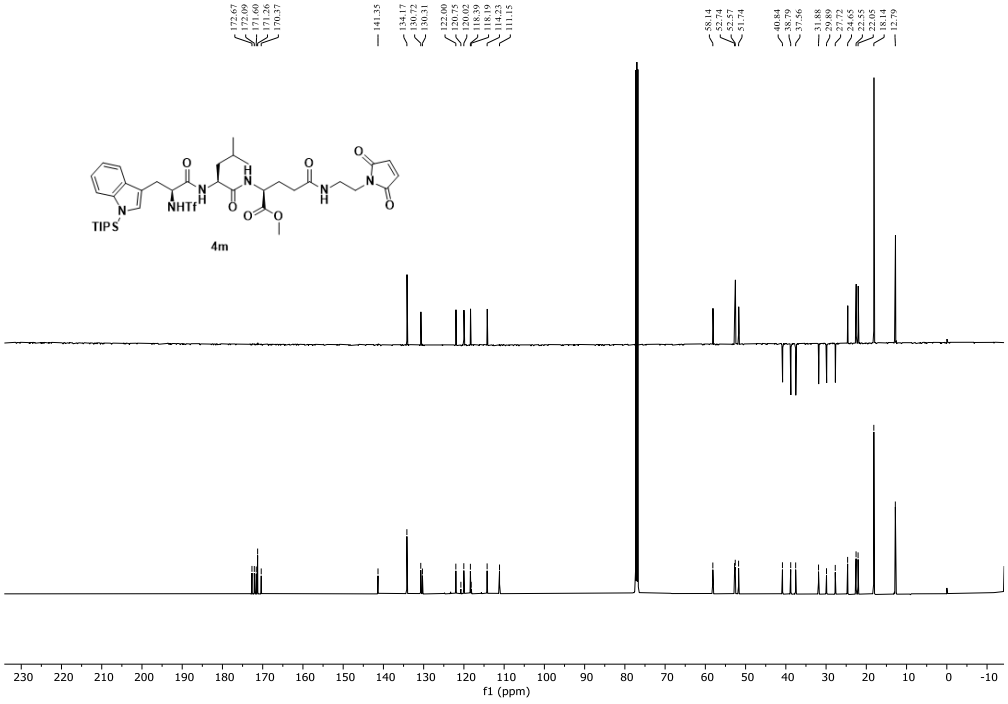


Methyl N^5*-(2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)ethyl)-*N^2*-(*N^a*-((trifluoromethyl)sulfonyl)-1-(triisopropylsilyl)-L-tryptophyl-L-leucyl)-L-glutaminate (**4m**)*

^{1}H NMR of **4m** (600 MHz, $CDCl_3$)

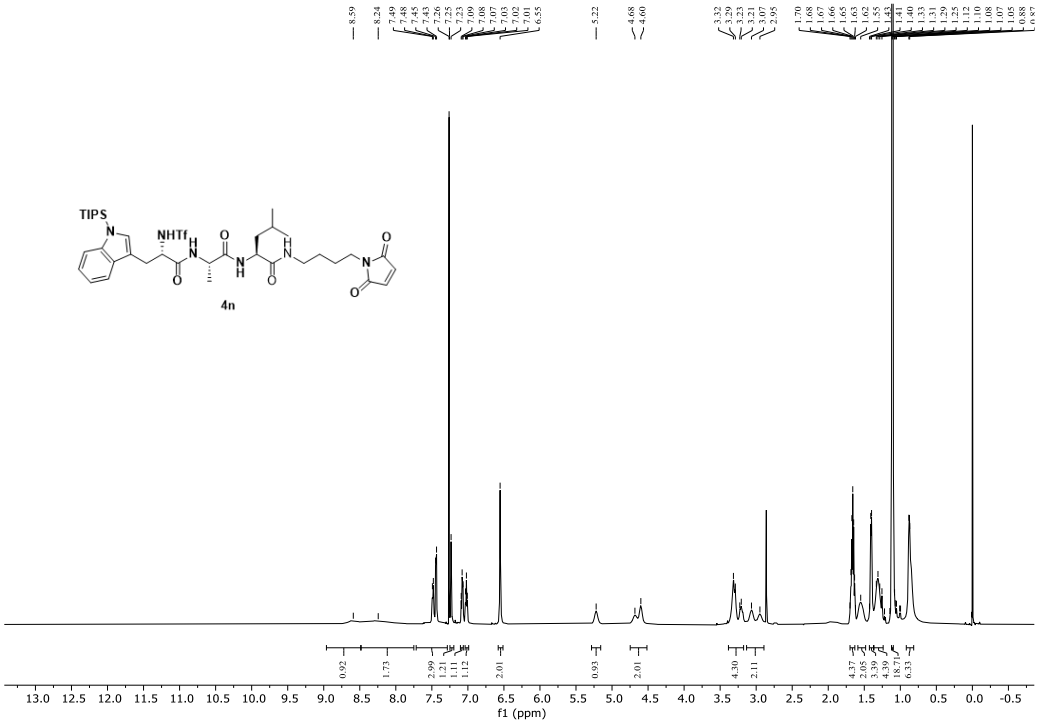


^{13}C{^{1}H} NMR of **4m** (126 MHz, $CDCl_3$)

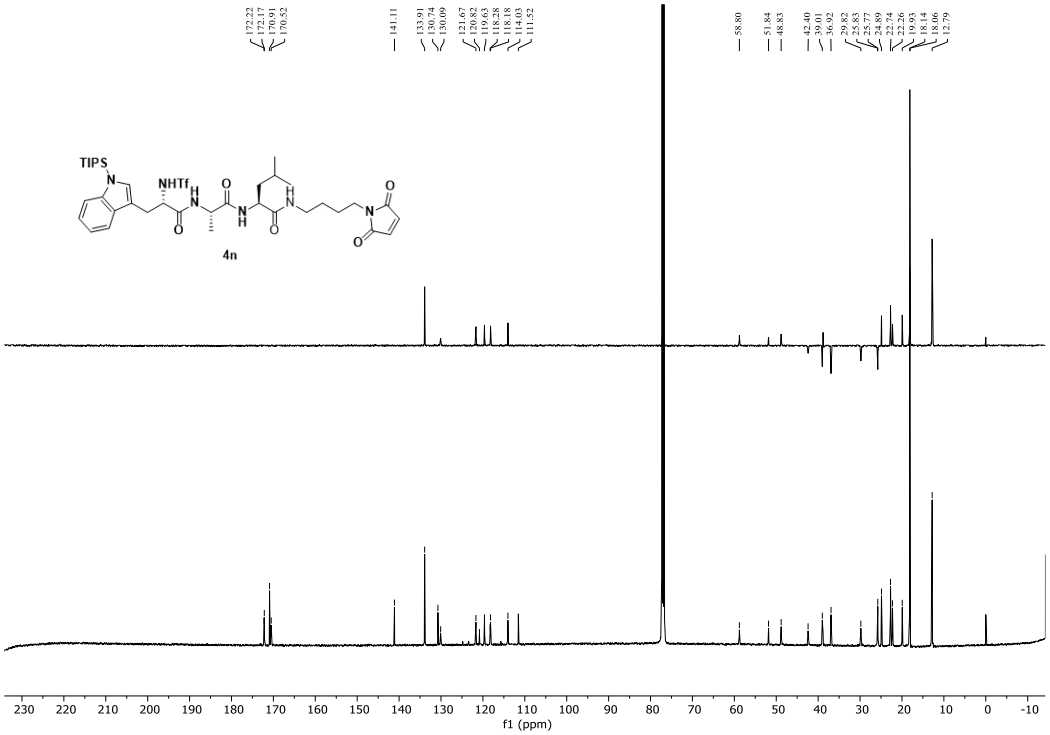


*(S)-N-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)butyl)-4-methyl-2-((S)-2-((S)-2-((trifluoromethyl)sulfonamido)-3-(1-(triisopropylsilyl)-1H-indol-3-yl)propanamido)propanamido)pentanamide (**4n**)*

^{1}H NMR of **4** (600 MHz, $CDCl_3$)

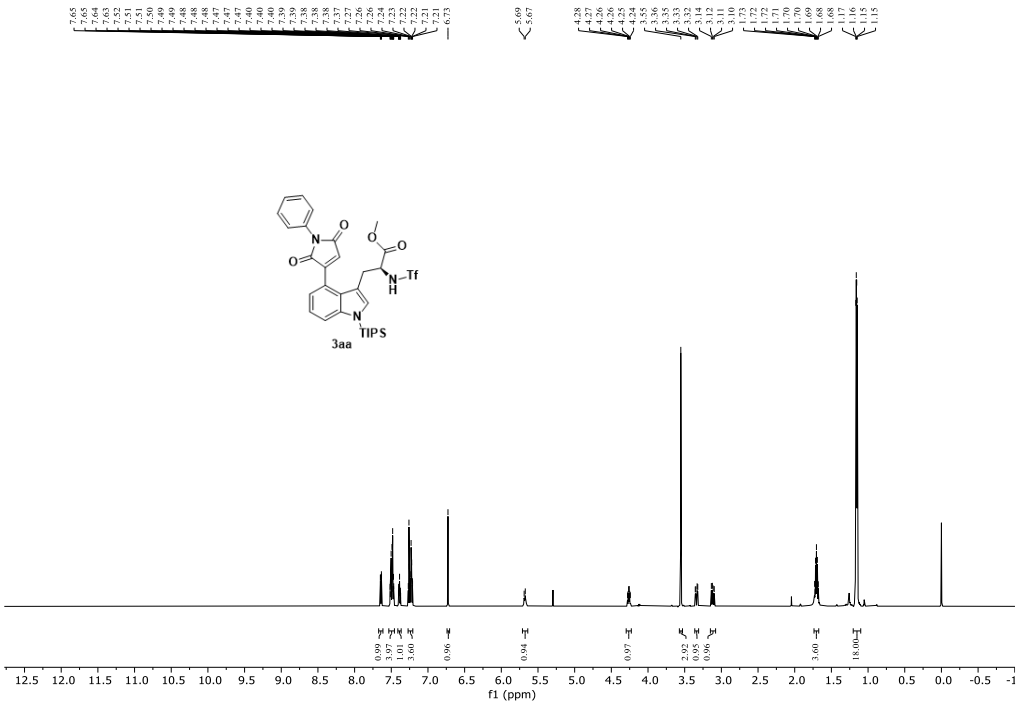


^{13}C{^{1}H} NMR of **4** (126 MHz, $CDCl_3$)

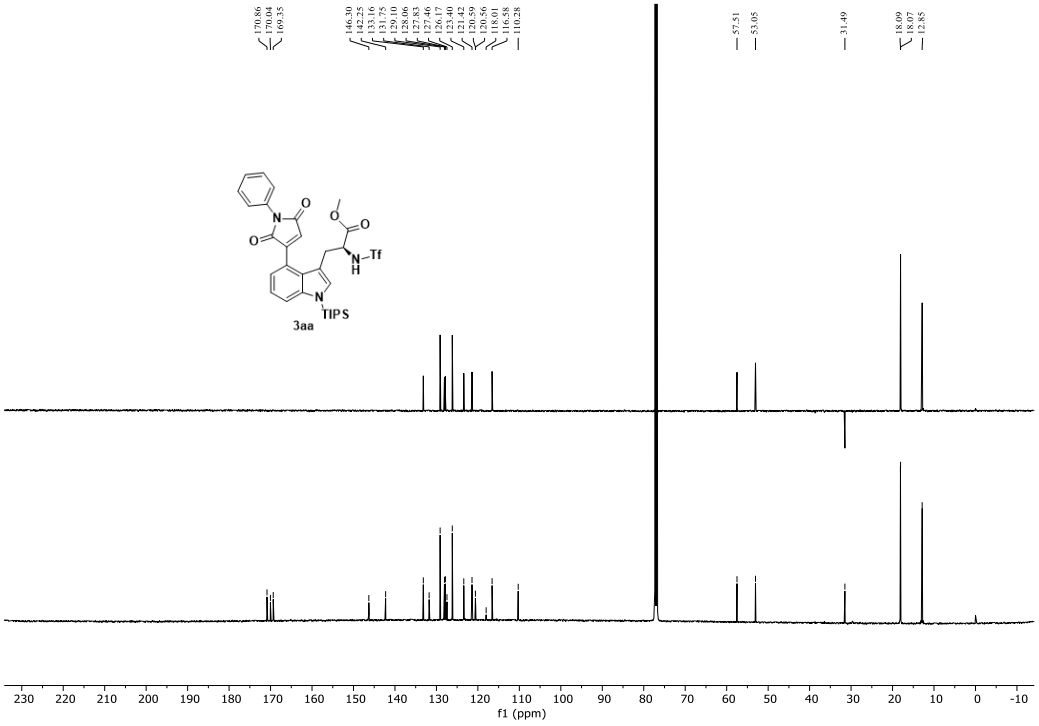


*Methyl (S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3aa**)*

^{1}H NMR of **3aa** (600 MHz, $CDCl_3$)

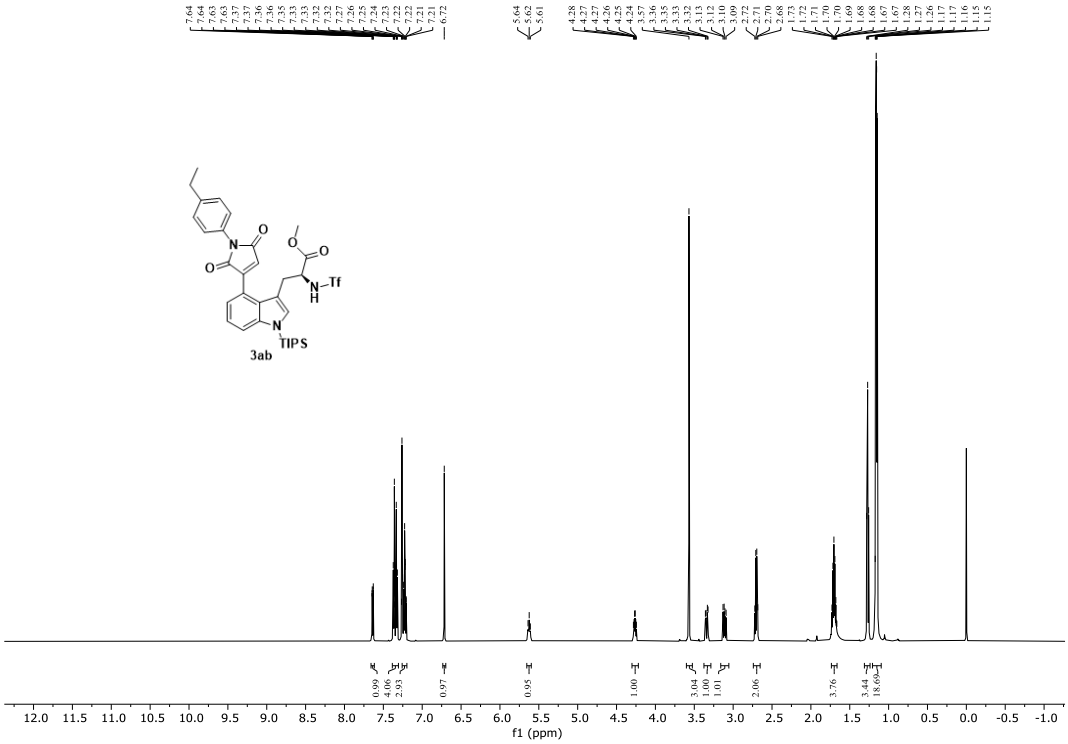


^{13}C{^{1}H} NMR of **3aa** (126 MHz, $CDCl_3$)

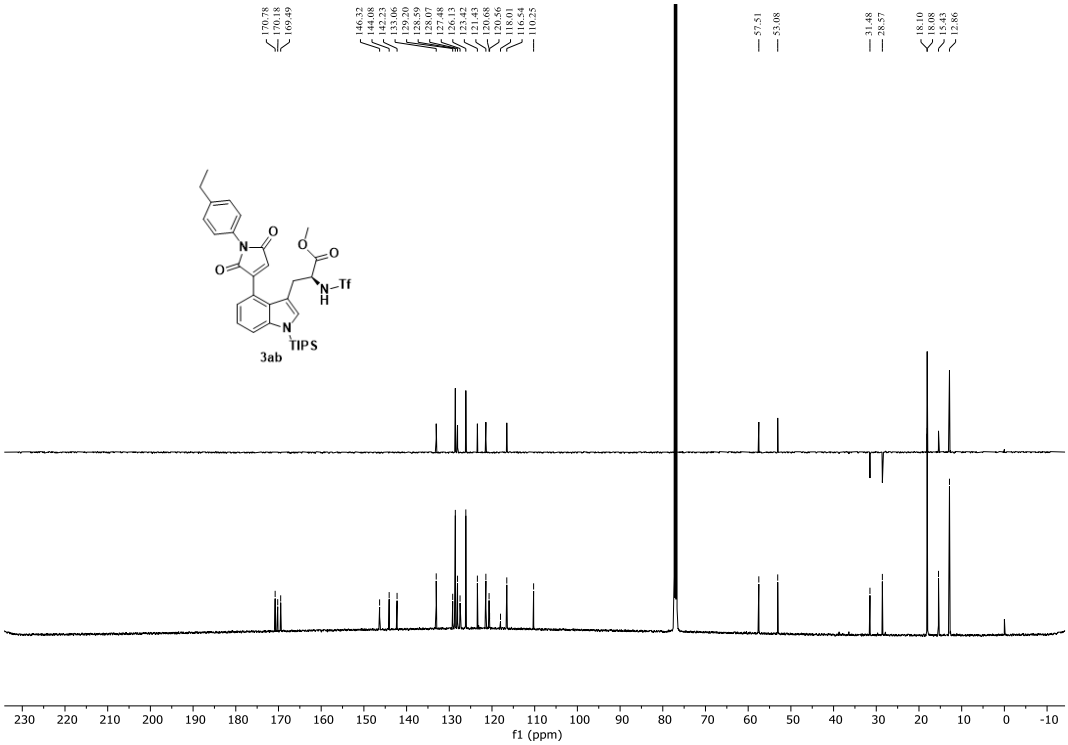


*Methyl (S)-3-(4-(1-(4-ethylphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ab**)*

^{1}H NMR of **3ab** (600 MHz, $CDCl_3$)

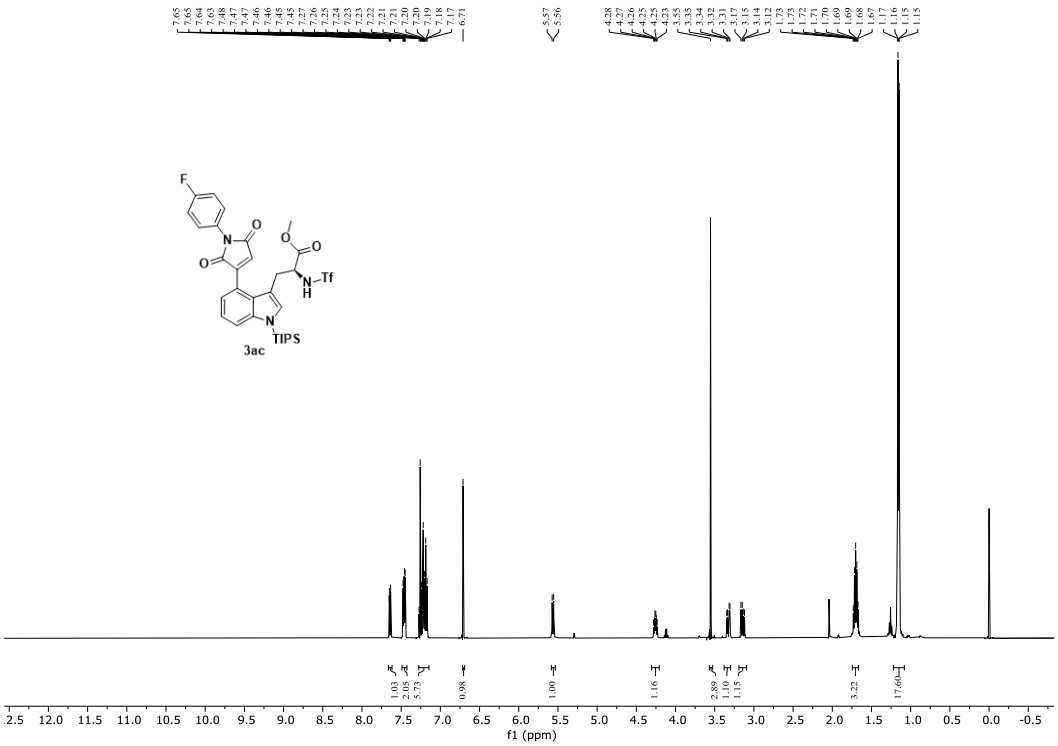


^{13}C{^{1}H} NMR of **3ab** (126 MHz, $CDCl_3$)

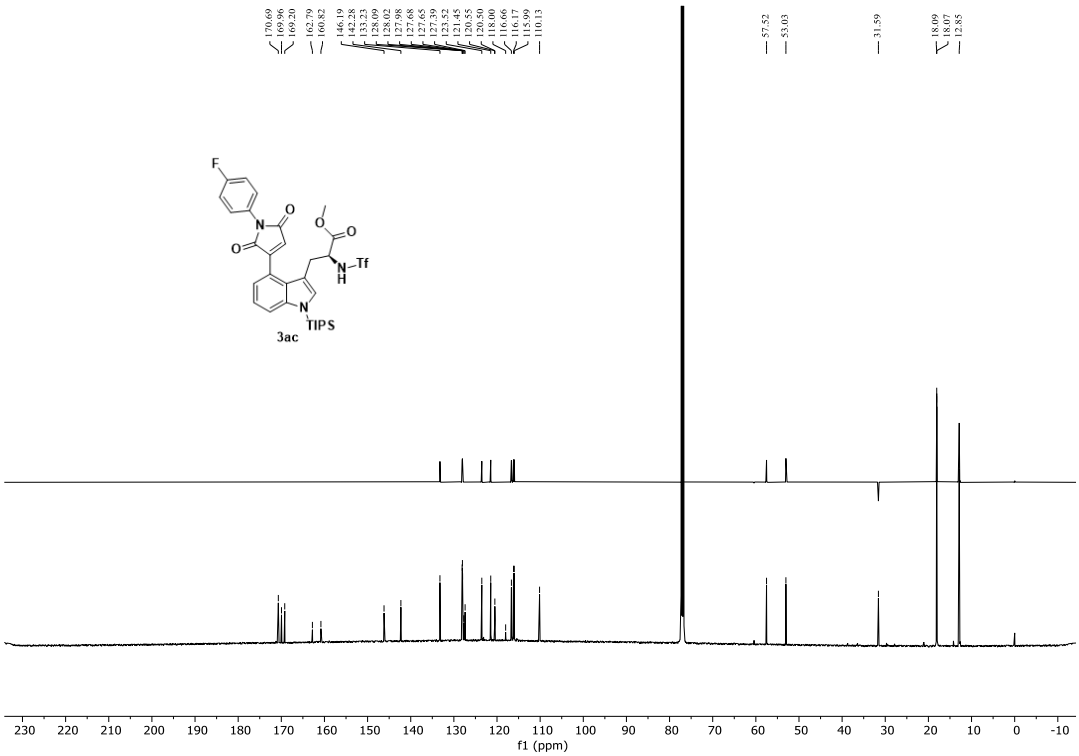


*Methyl (S)-3-(4-(1-(4-fluorophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ac**)*

^{1}H NMR of **3ac** (500 MHz, $CDCl_3$)

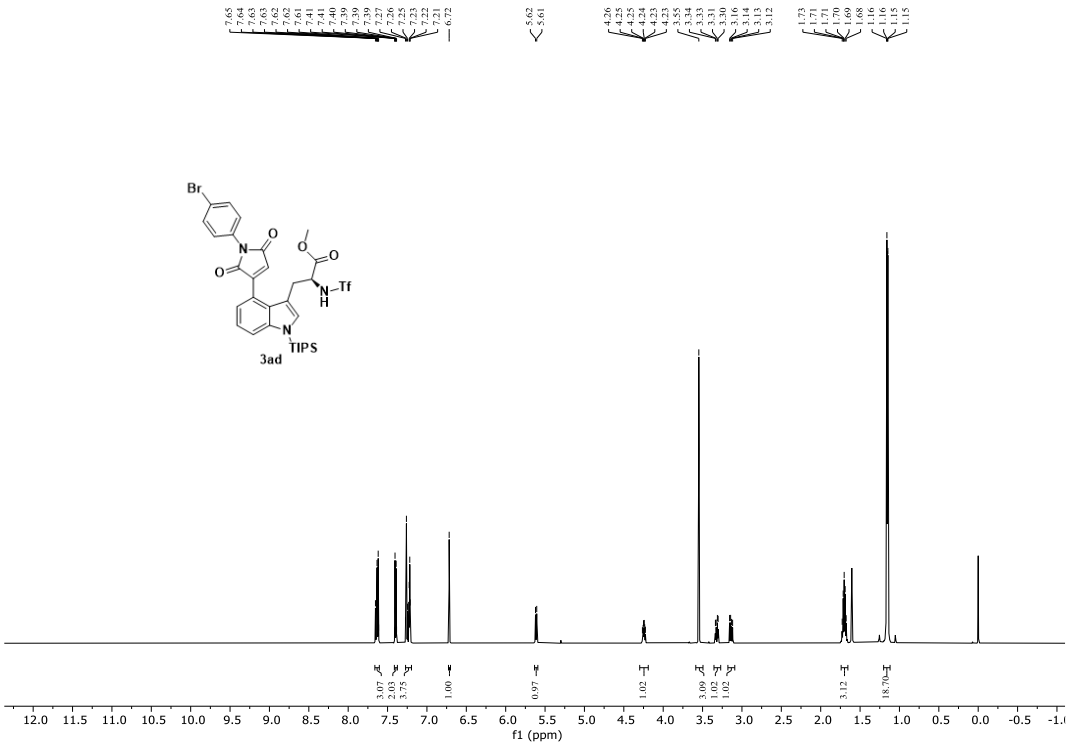


^{13}C{^{1}H} NMR of **3ac** (126 MHz, $CDCl_3$)

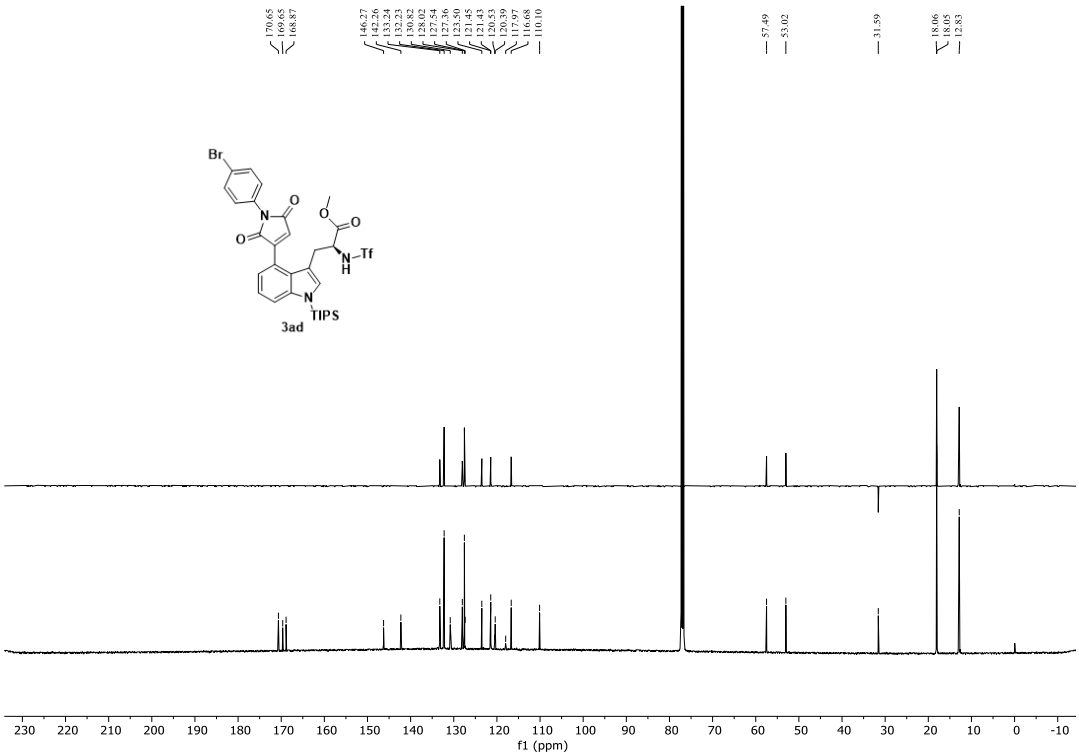


*Methyl (S)-3-(4-(1-(4-bromophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ad**)*

^{1}H NMR of **3ad** (600 MHz, $CDCl_3$)

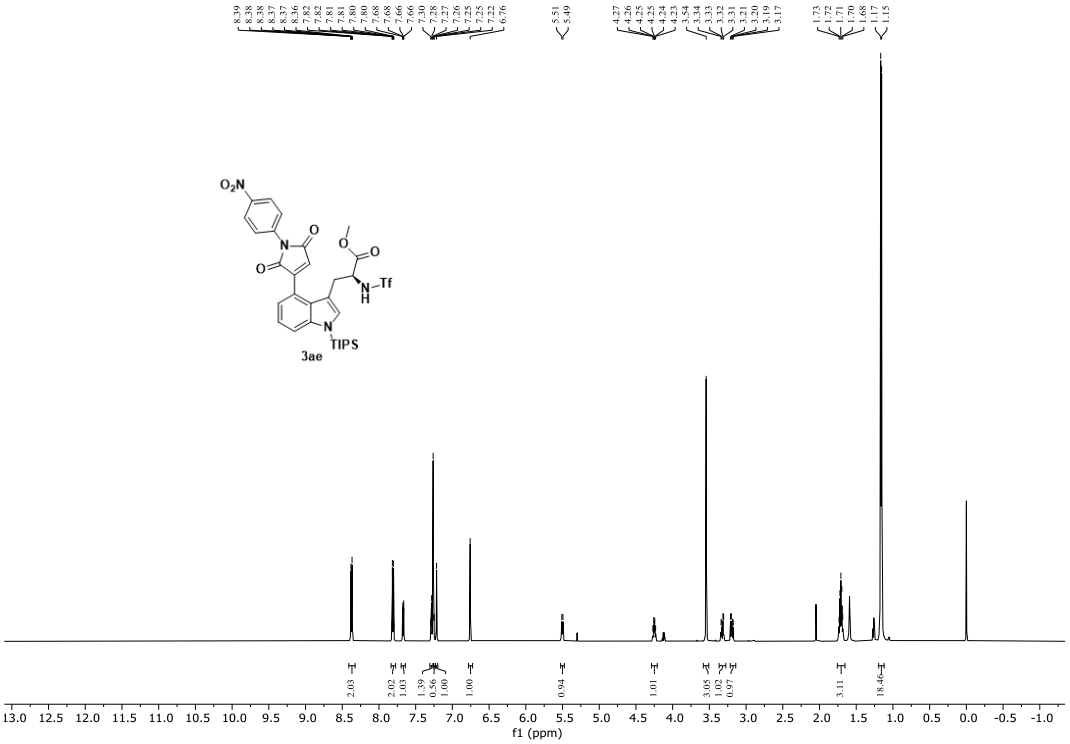


^{13}C{^{1}H} NMR of **3ad** (126 MHz, $CDCl_3$)

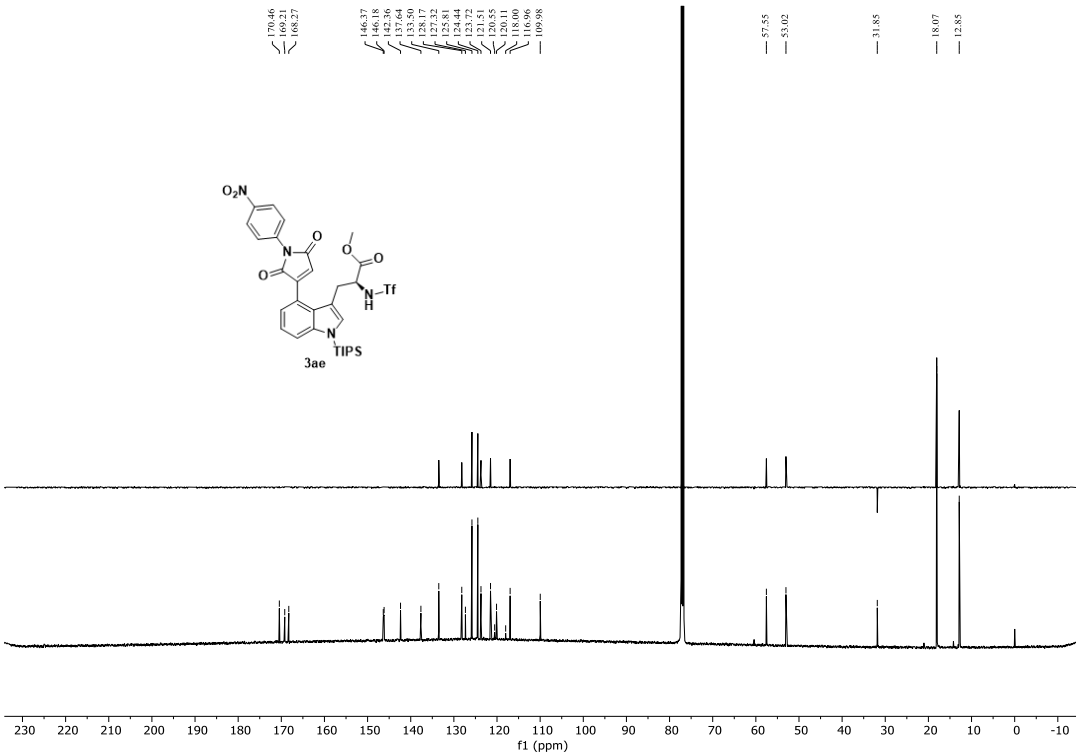


*Methyl (S)-3-(4-(1-(4-nitrophenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ae**)*

^{1}H NMR of **3ae** (600 MHz, $CDCl_3$)

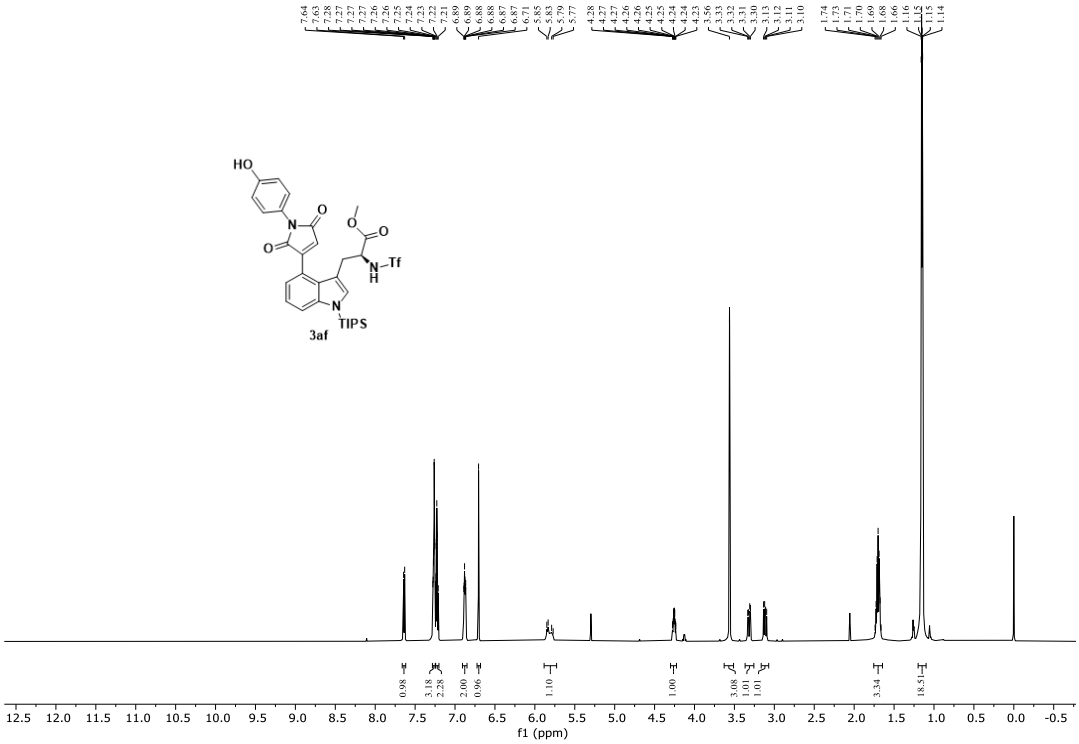


^{13}C{^{1}H} NMR of **3ae** (126 MHz, $CDCl_3$)

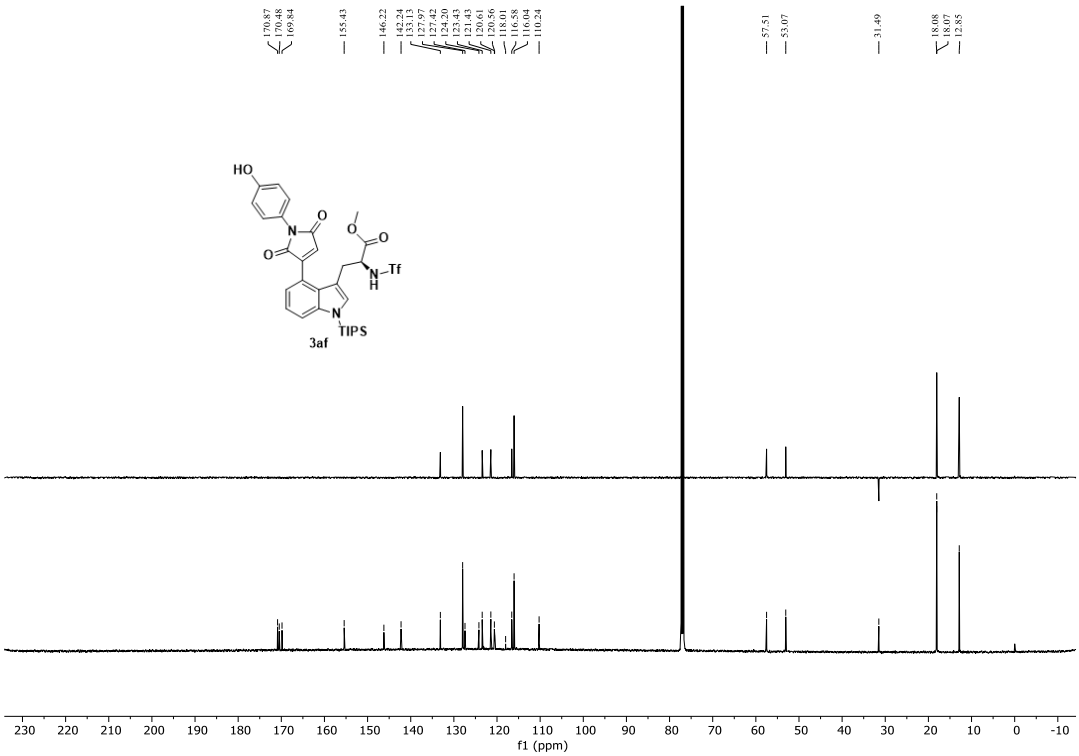


*Methyl (S)-3-(4-(1-(4-hydroxyphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3af**)*

^{1}H NMR of **3af** (600 MHz, $CDCl_3$)

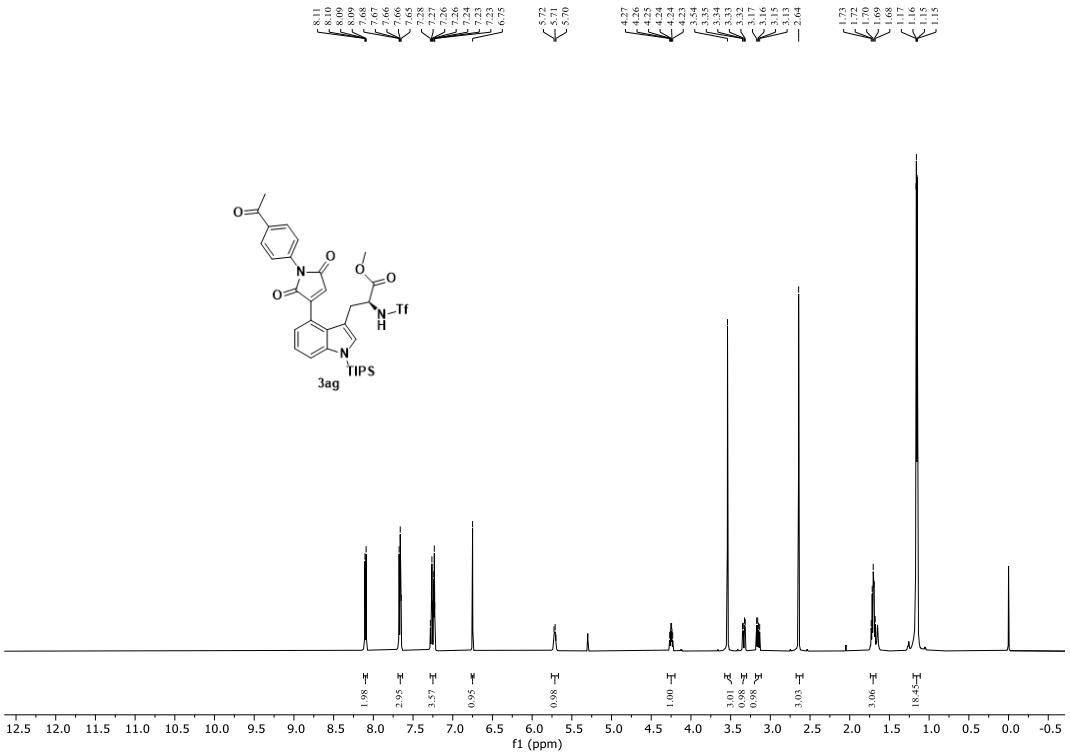


^{13}C{^{1}H} NMR of **3af** (126 MHz, $CDCl_3$)

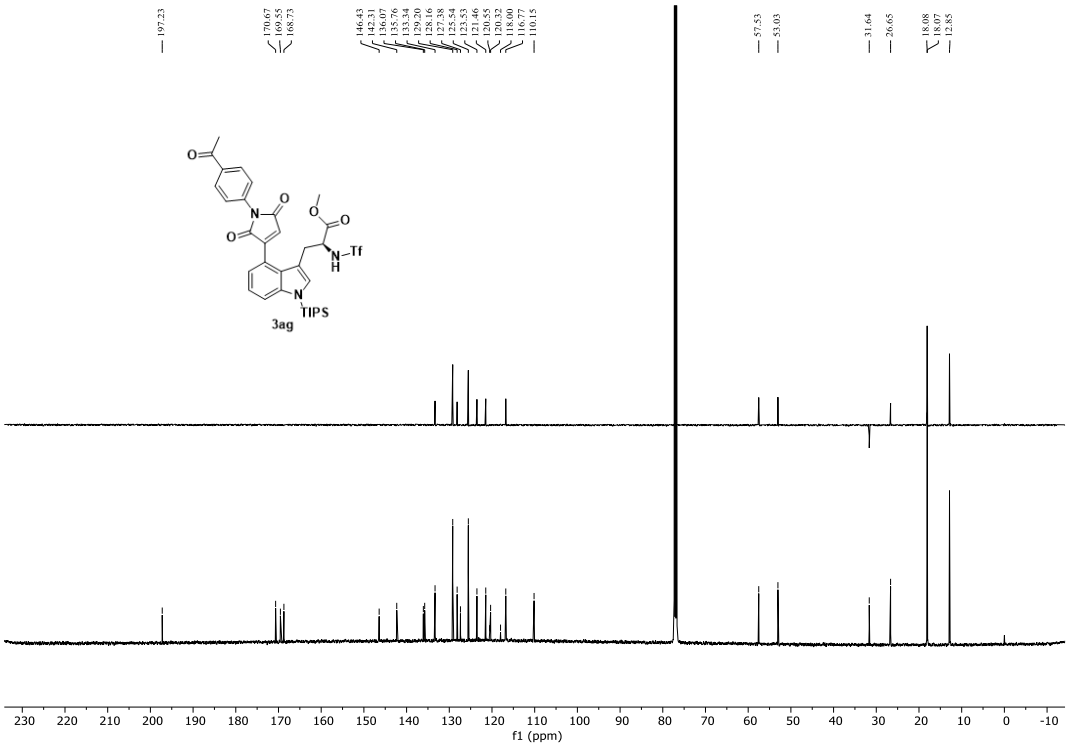


*Methyl (S)-3-(4-(1-(4-acetylphenyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ag**)*

^{1}H NMR of **3ag** (600 MHz, $CDCl_3$)

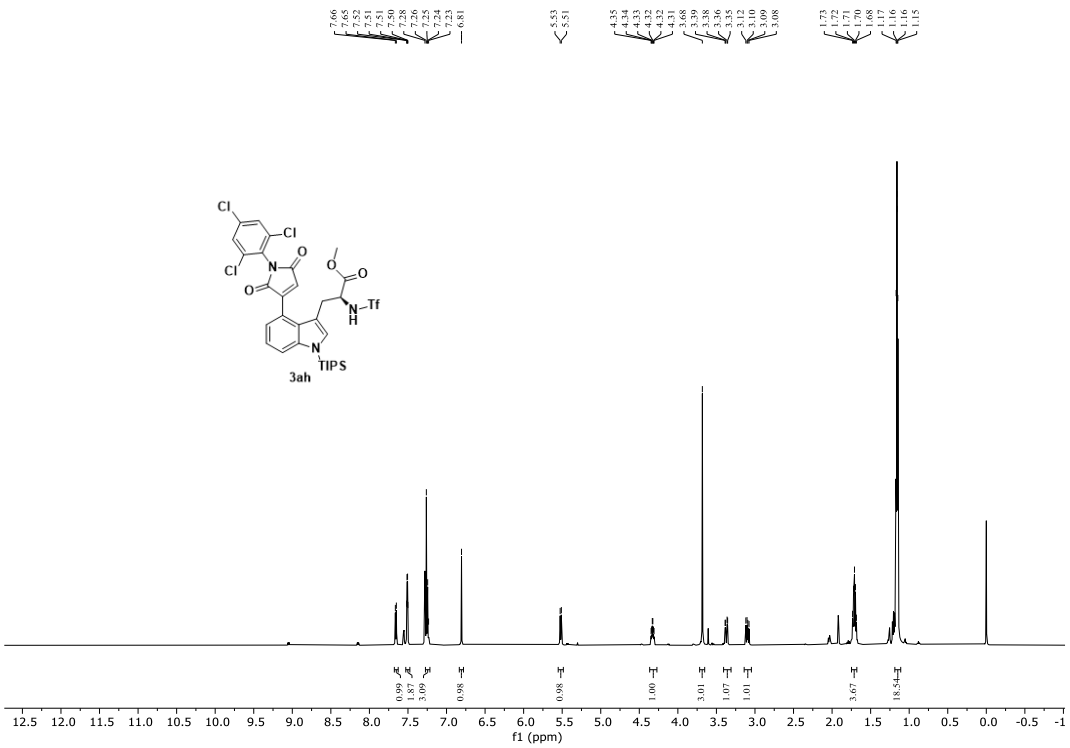


^{13}C{^{1}H} NMR of **3ag** (126 MHz, $CDCl_3$)

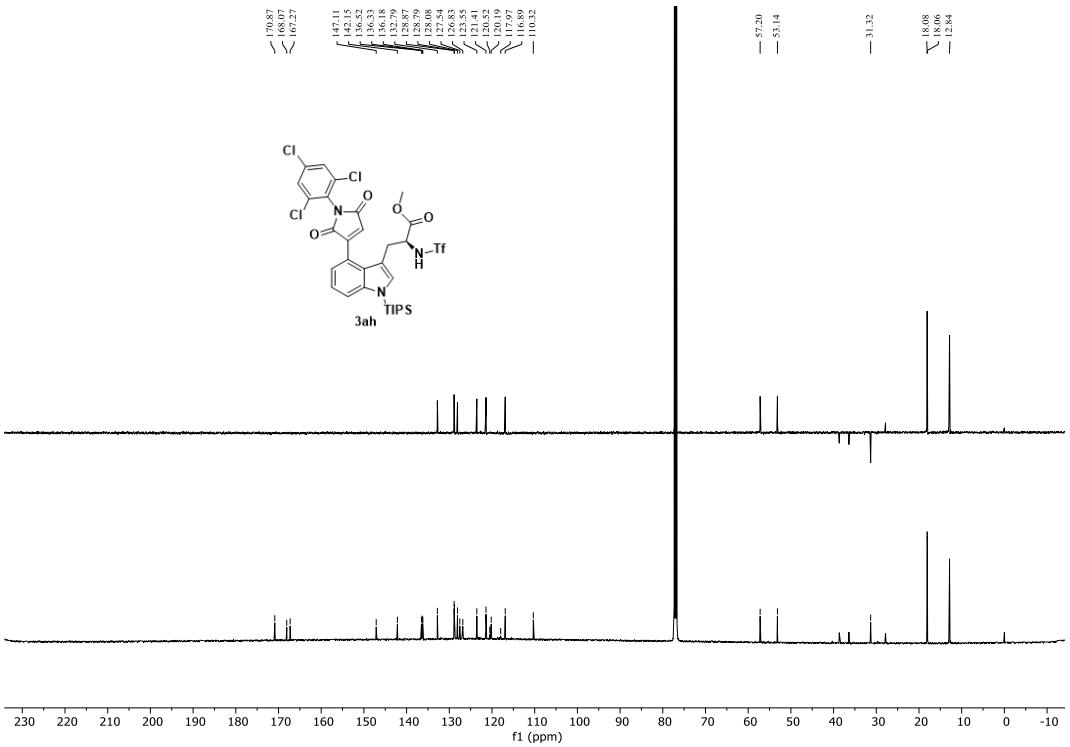


*Methyl (S)-3-(4-(2,5-dioxo-1-(2,4,6-trichlorophenyl)-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ah**)*

^{1}H NMR of **3ah** (600 MHz, $CDCl_3$)

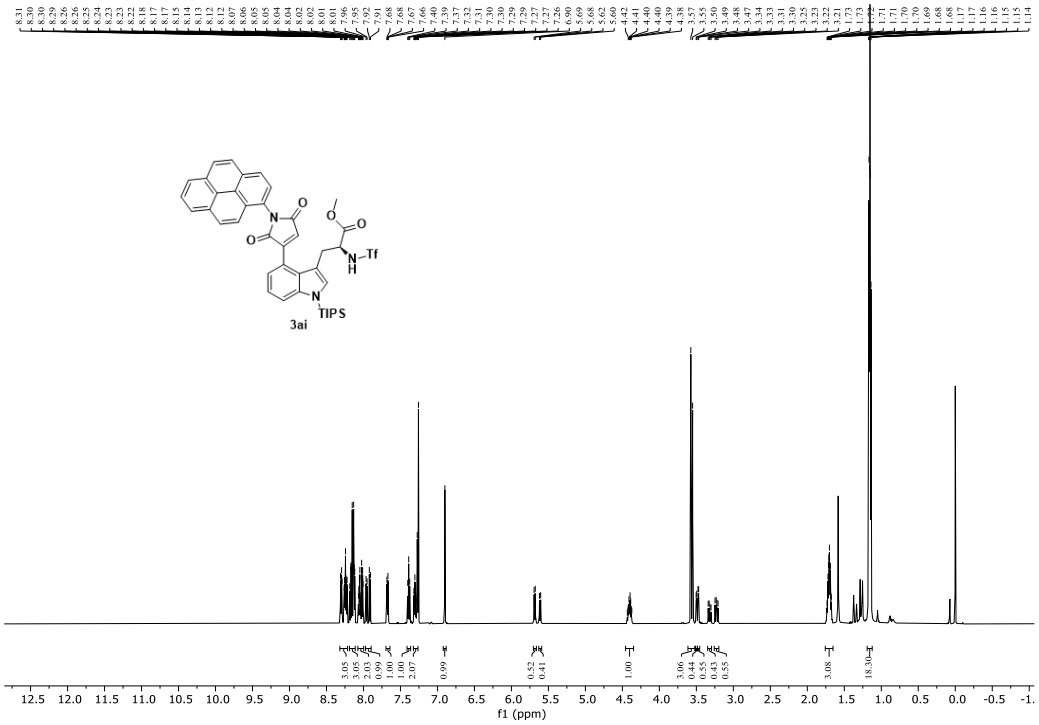


^{13}C{^{1}H} NMR of **3ah** (126 MHz, $CDCl_3$)

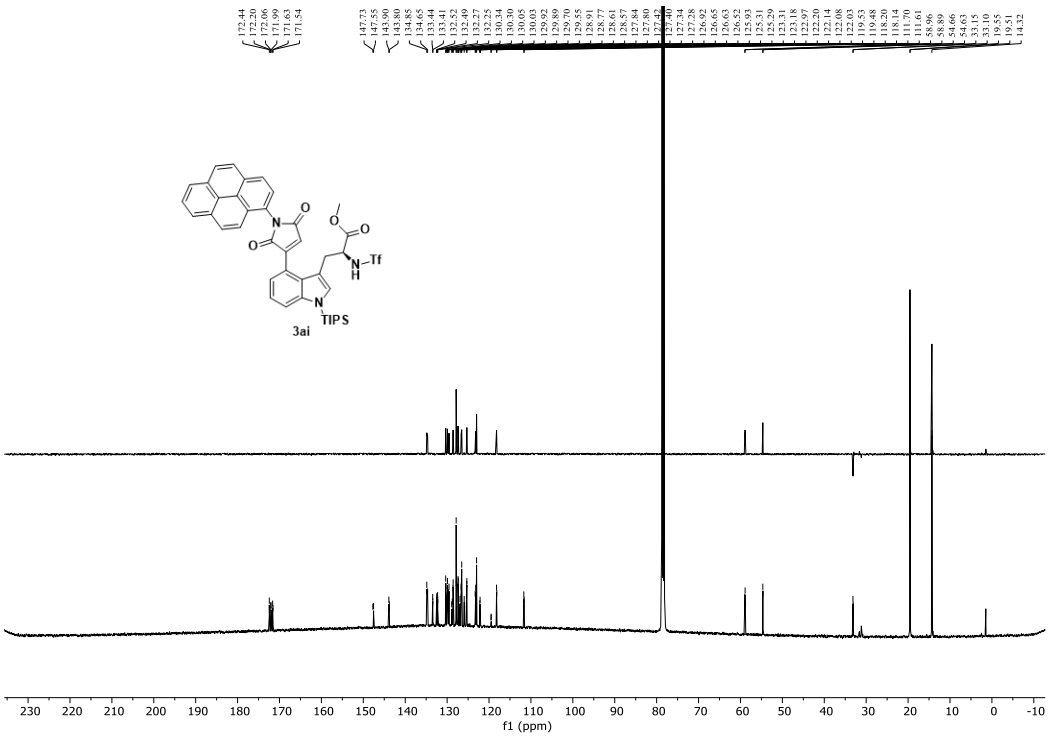


*Methyl (S)-3-(4-(2,5-dioxo-1-(pyren-1-yl)-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ai**)*

^{1}H NMR of **3ai** (600 MHz, $CDCl_3$)

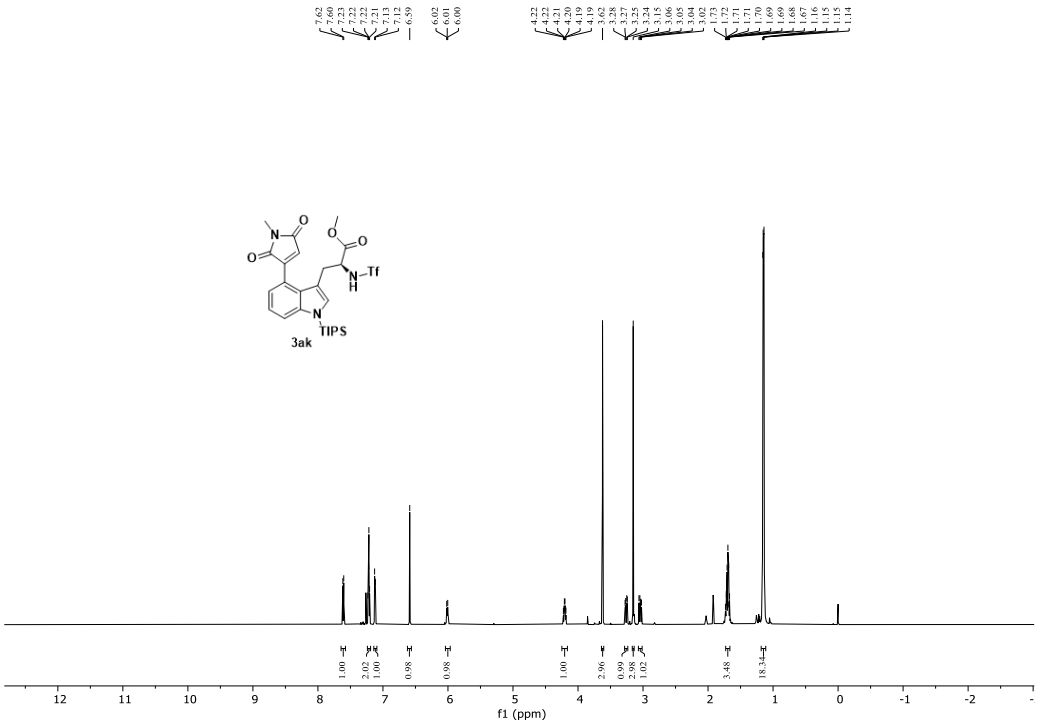


^{13}C{^{1}H} NMR of **3ai** (126 MHz, $CDCl_3$)

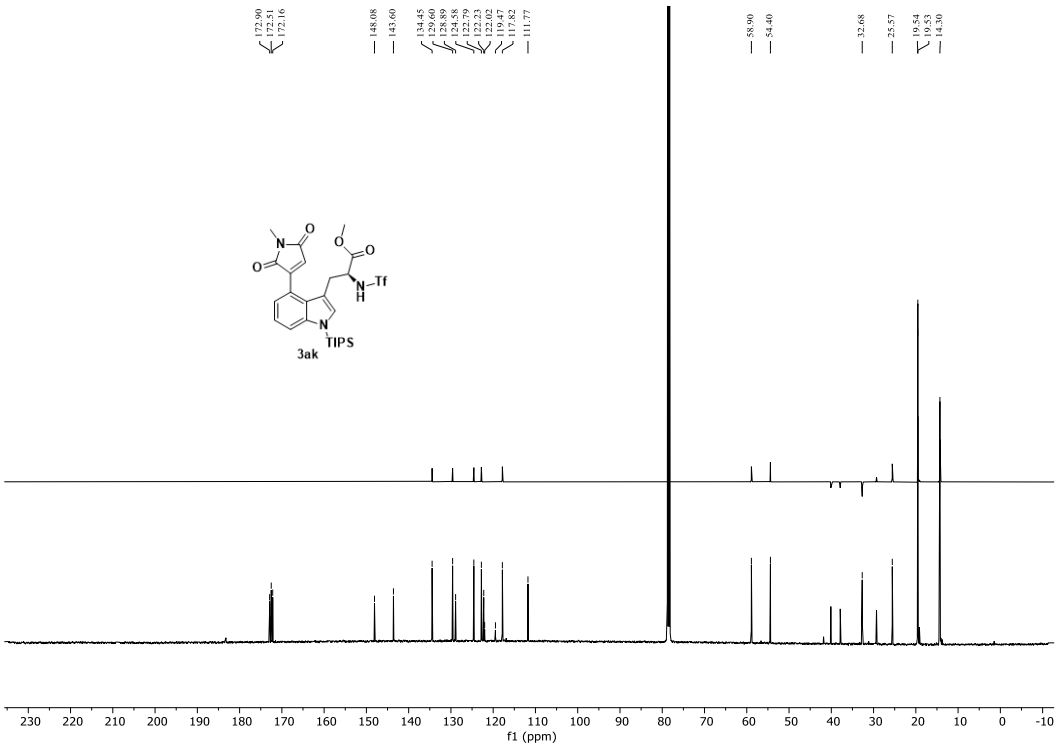


*Methyl (S)-3-(4-(1-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ak**)*

^{1}H NMR of **3ak** (600 MHz, $CDCl_3$)

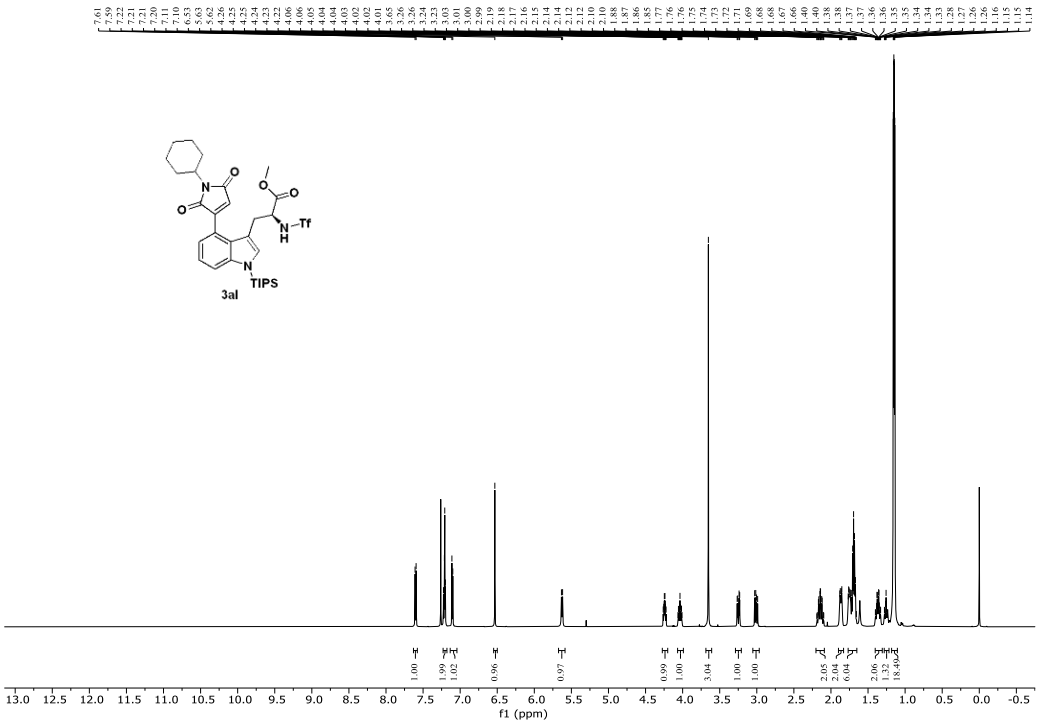


^{13}C{^{1}H} NMR of **3ak** (126 MHz, $CDCl_3$)

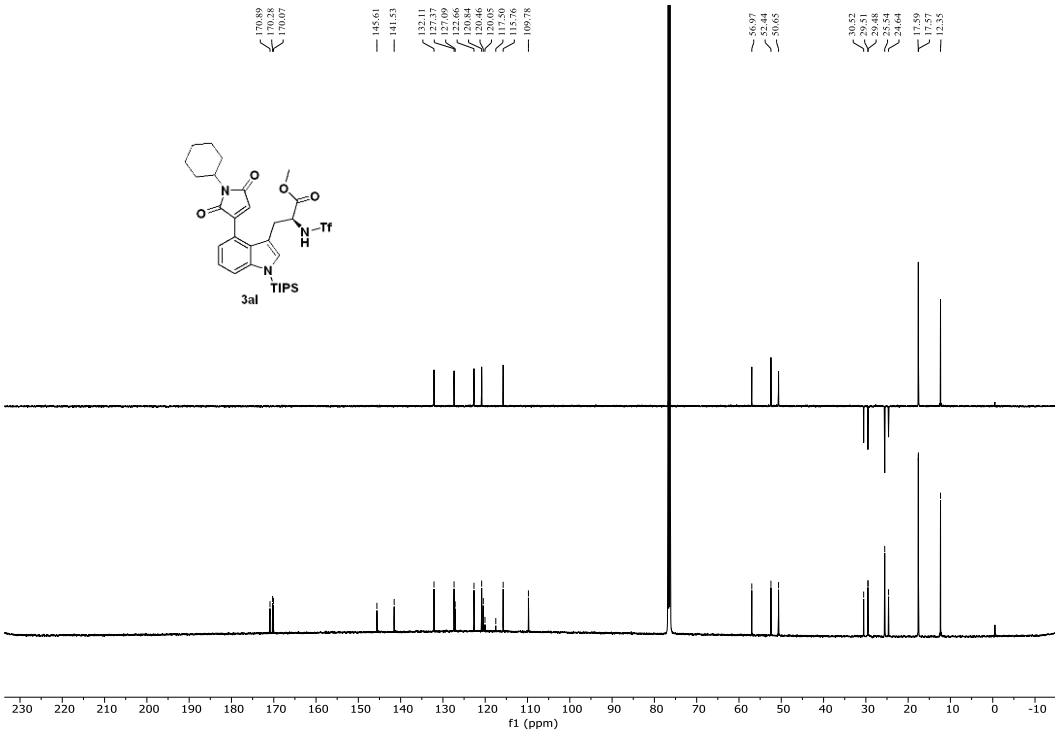


*Methyl (S)-3-(4-(1-cyclohexyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3al**)*

^{1}H NMR of **3al** (600 MHz, $CDCl_3$)

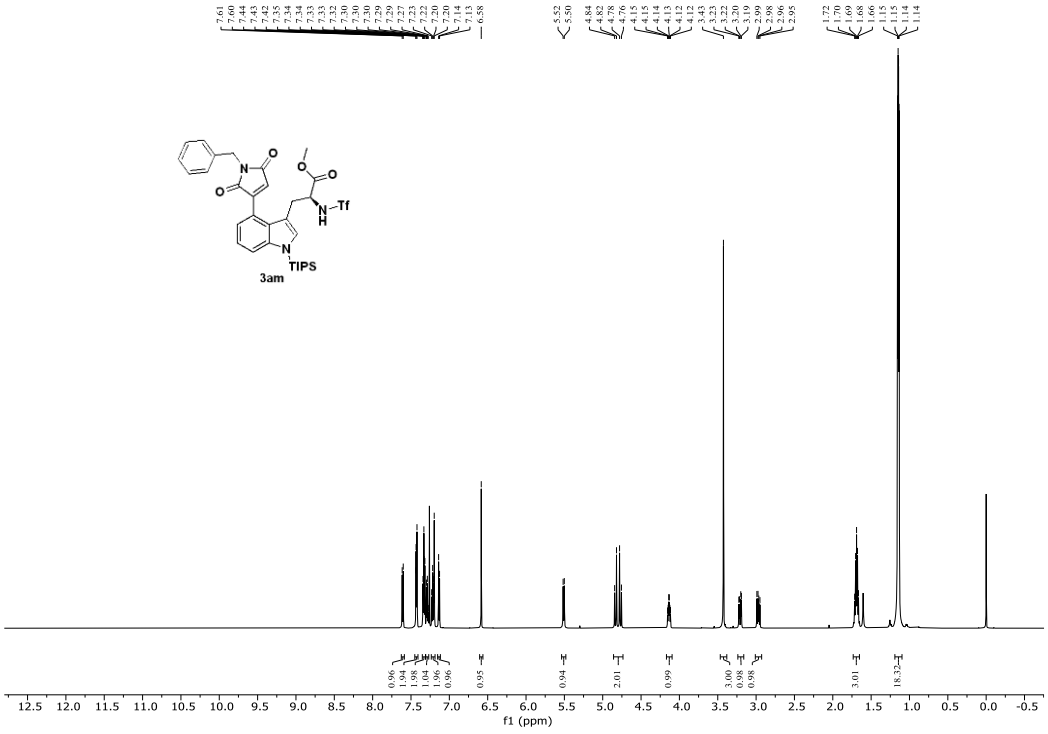


^{13}C{^{1}H} NMR of **3al** (126 MHz, $CDCl_3$)

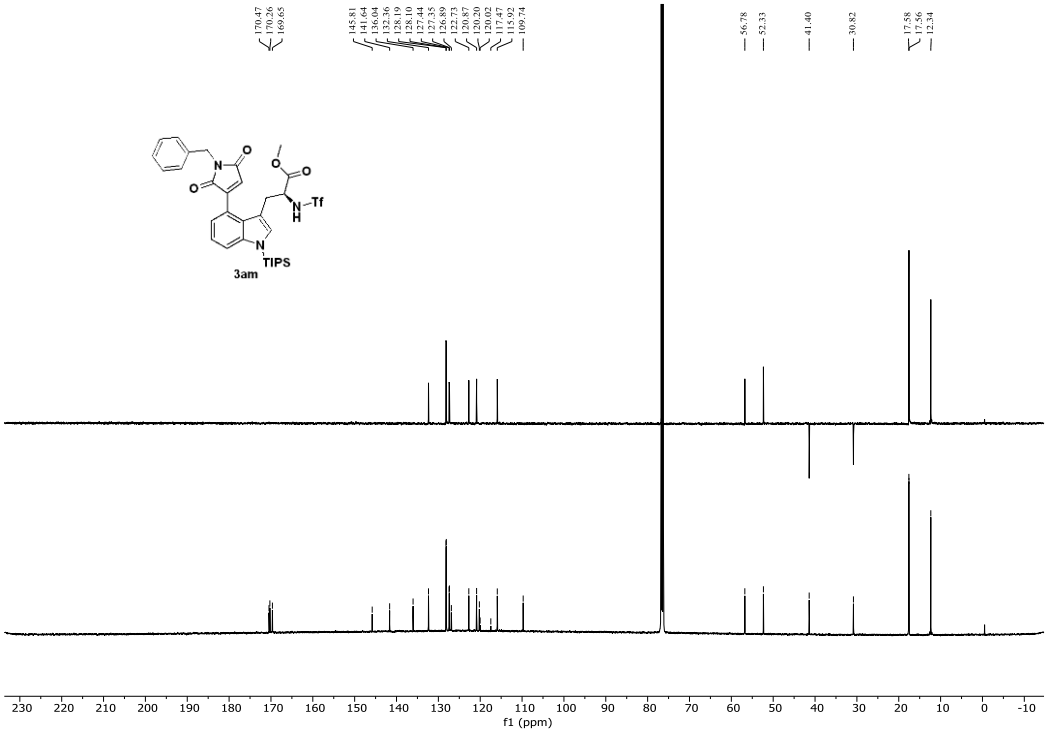


*Methyl (S)-3-(4-(1-benzyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3am**)*

^{1}H NMR of **3am** (600 MHz, $CDCl_3$)

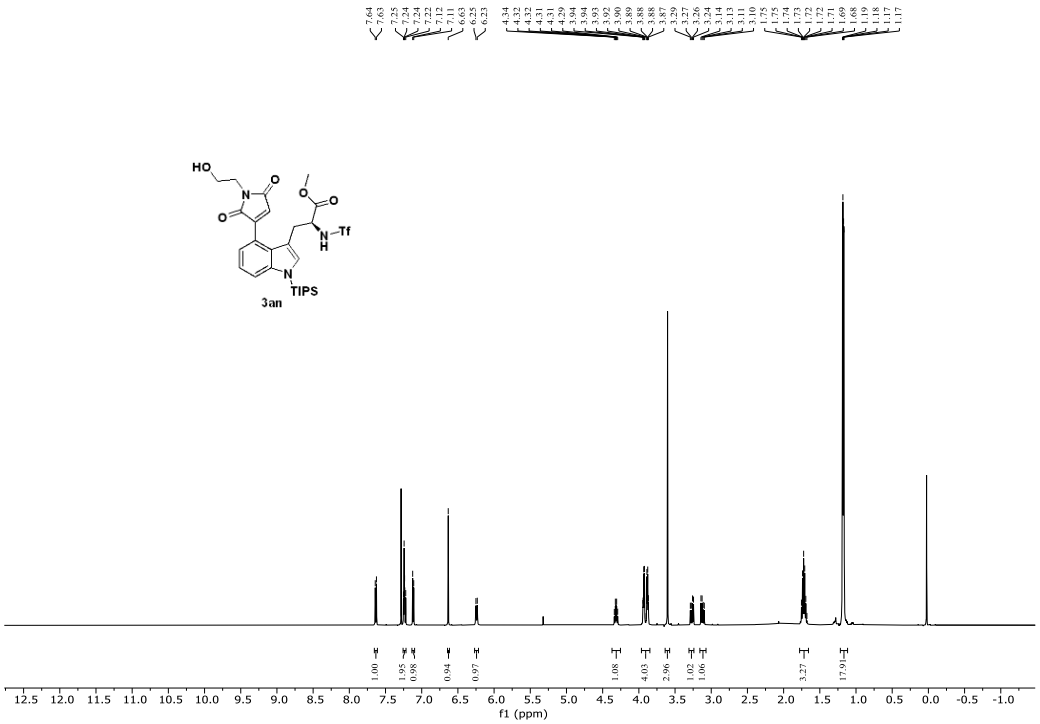


^{13}C{^{1}H} NMR of **3am** (126 MHz, $CDCl_3$)

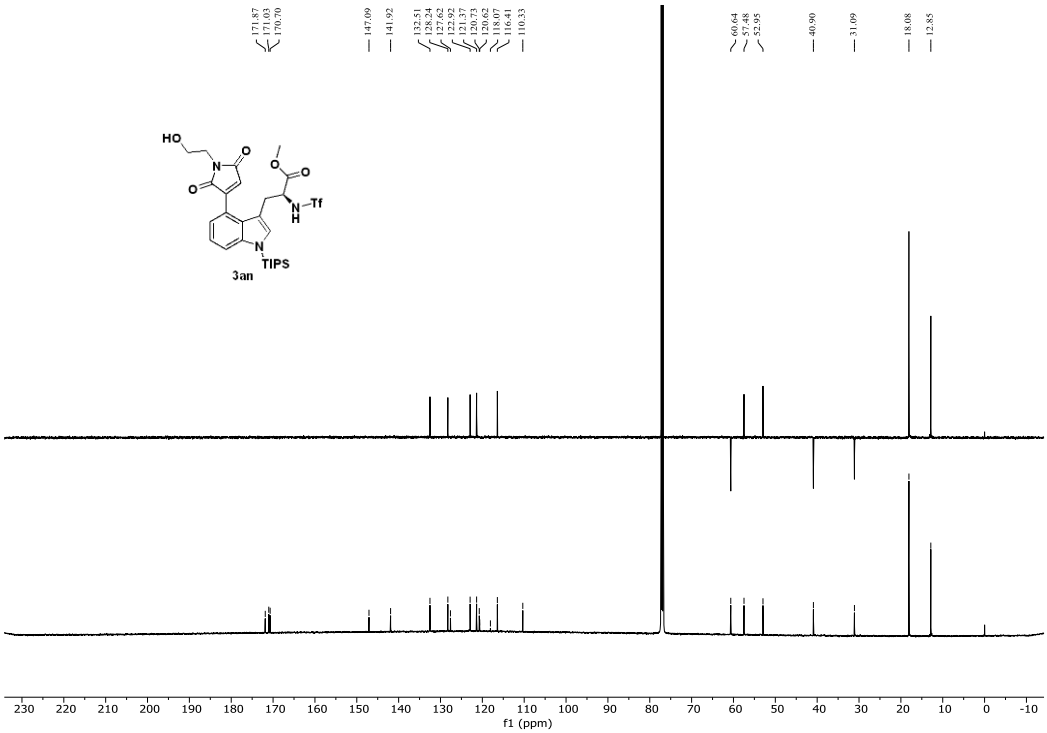


*Methyl (S)-3-(4-(1-(2-hydroxyethyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3an**)*

^{1}H NMR of **3an** (500 MHz, $CDCl_3$)

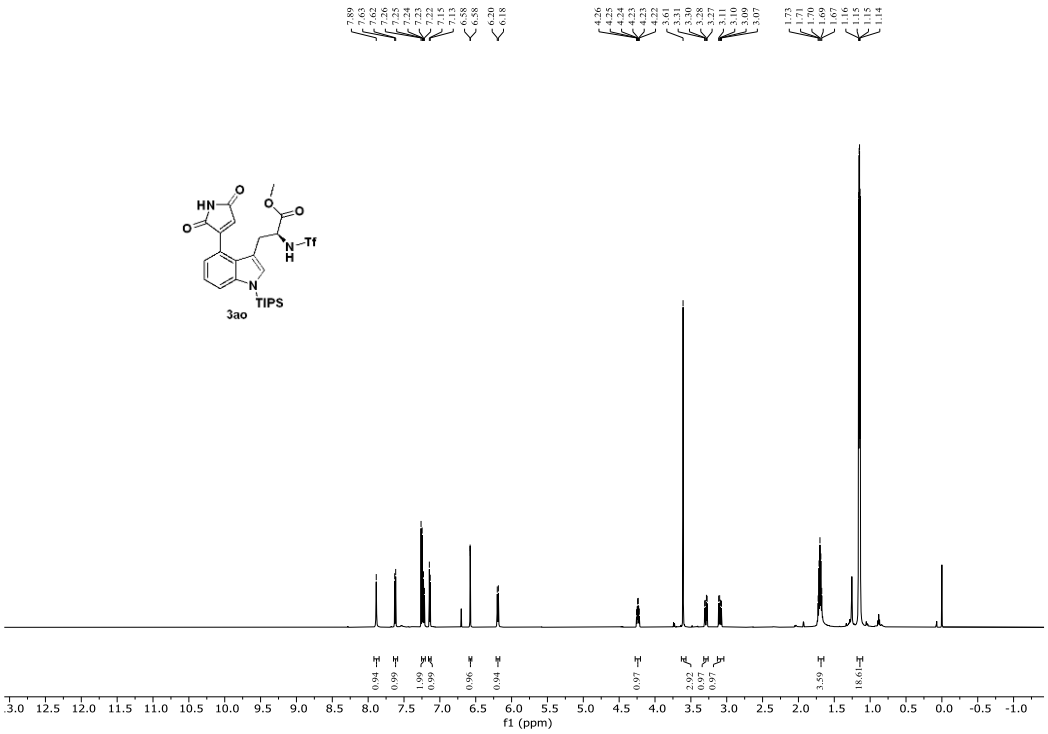


^{13}C{^{1}H} NMR of **3an** (126 MHz, $CDCl_3$)

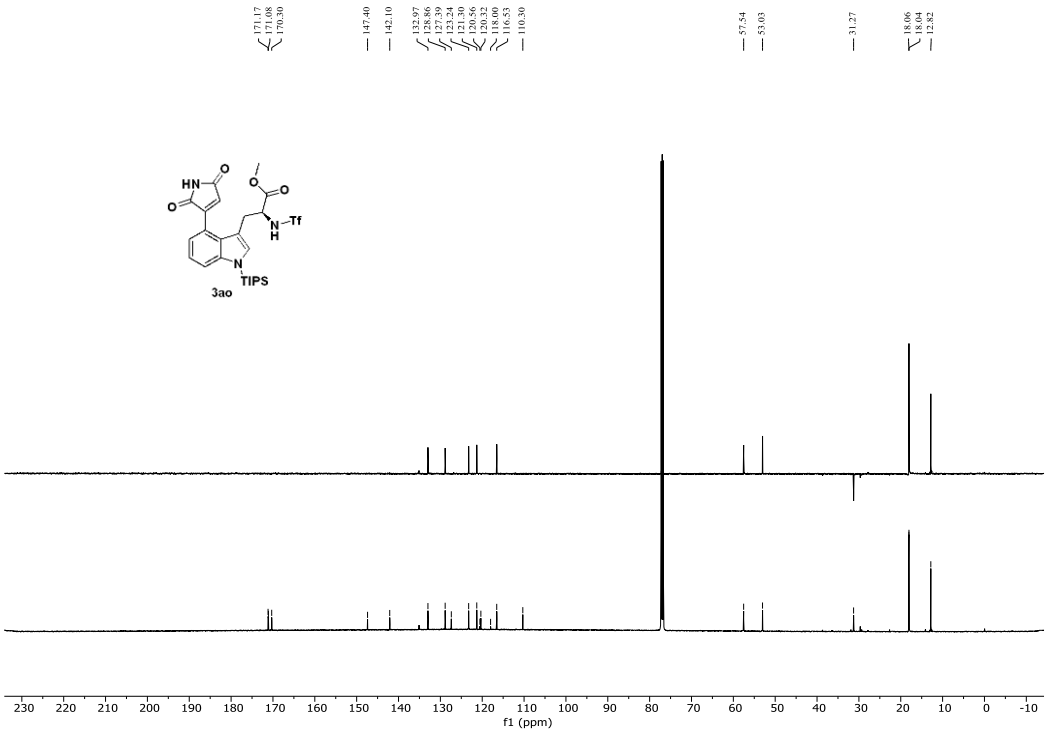


*Methyl (S)-3-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ao**)*

^{1}H NMR of **3ao** (600 MHz, $CDCl_3$)

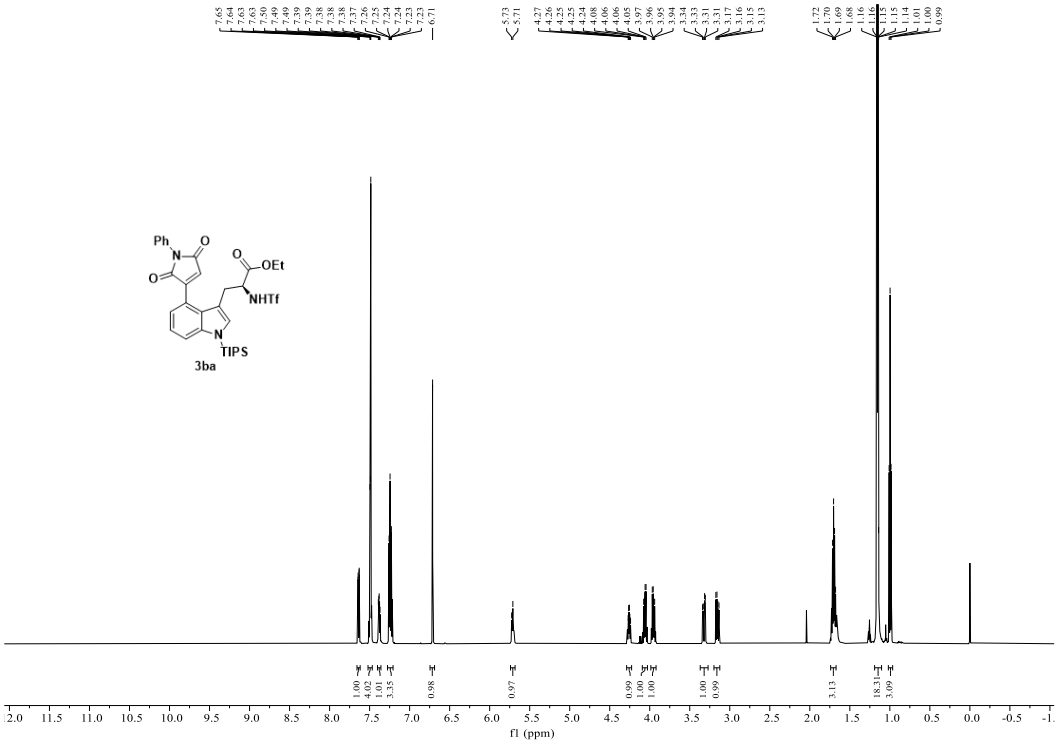


^{13}C{^{1}H} NMR of **3ao** (126 MHz, $CDCl_3$)

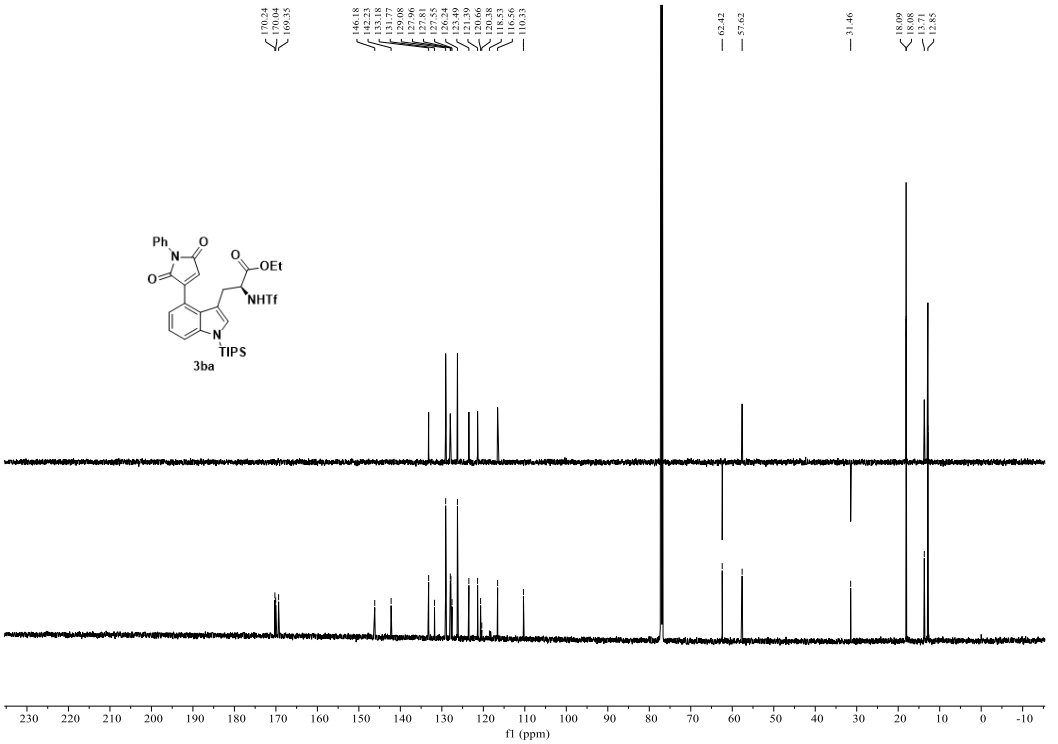


*Ethyl (S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate(**3ba**)*

^{1}H NMR of **3ba** (600 MHz, $CDCl_3$)

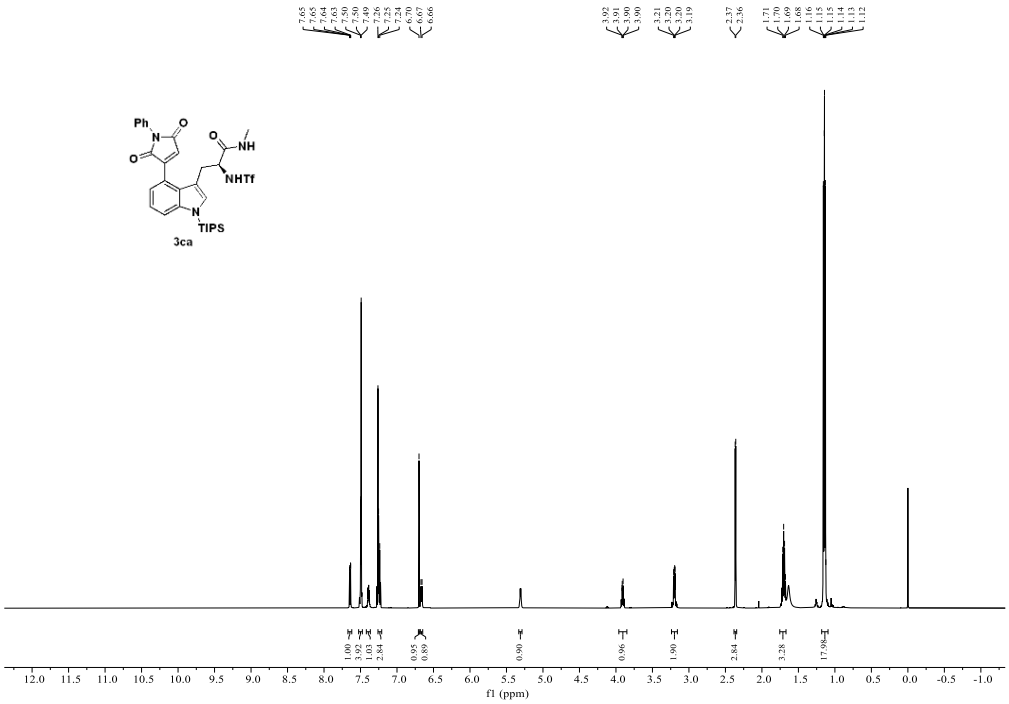


^{13}C{^{1}H} NMR of **3ba** (151 MHz, $CDCl_3$)

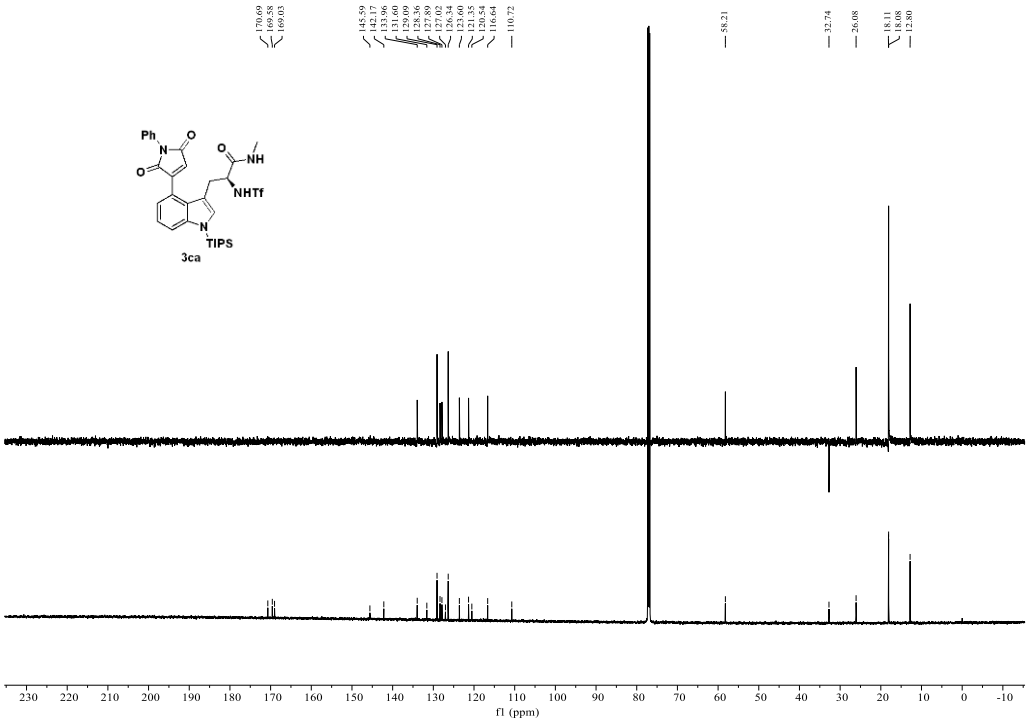


*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-methyl-2-((trifluoromethyl)sulfonamido)propenamide(**3ca**)*

^{1}H NMR of **3ca** (600 MHz, $CDCl_3$)

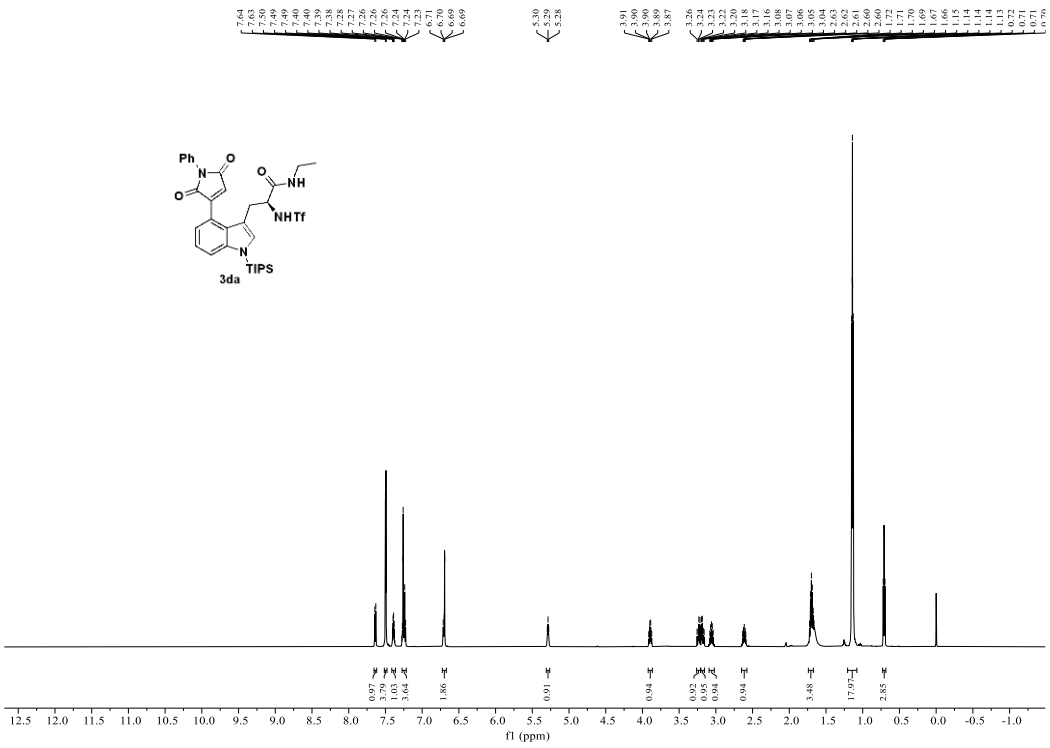


^{13}C{^{1}H} NMR of **3ca** (151 MHz, $CDCl_3$)

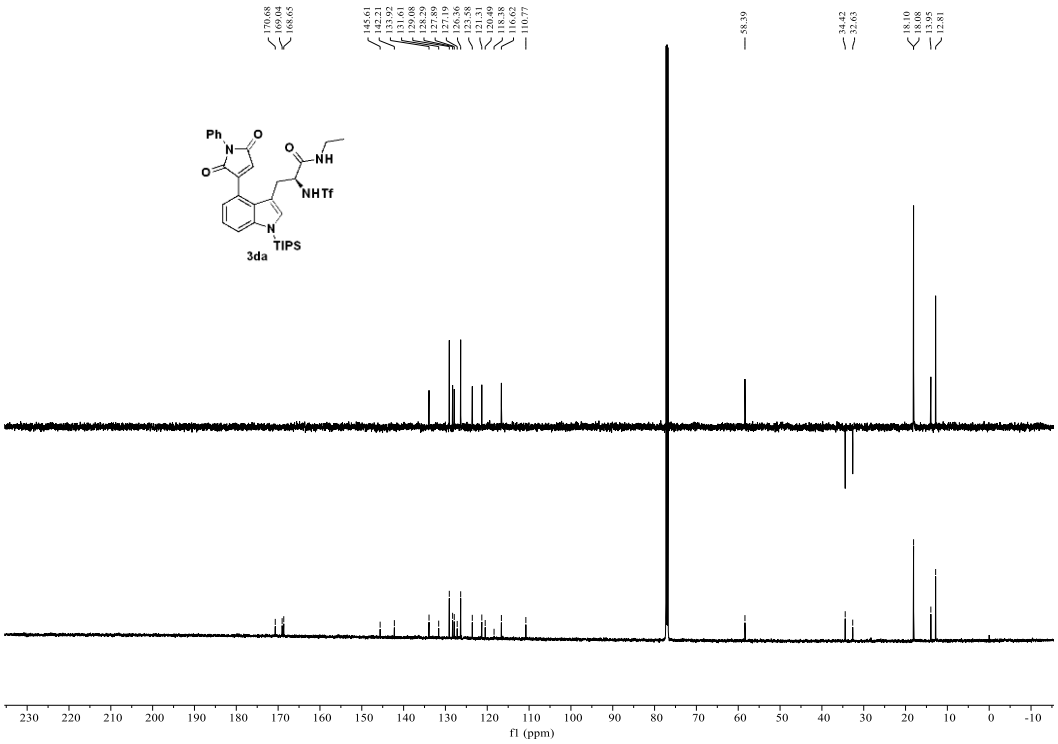


*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-ethyl-2-((trifluoromethyl)sulfonamido)propenamide(**3da**)*

^{1}H NMR of **3da** (600 MHz, $CDCl_3$)

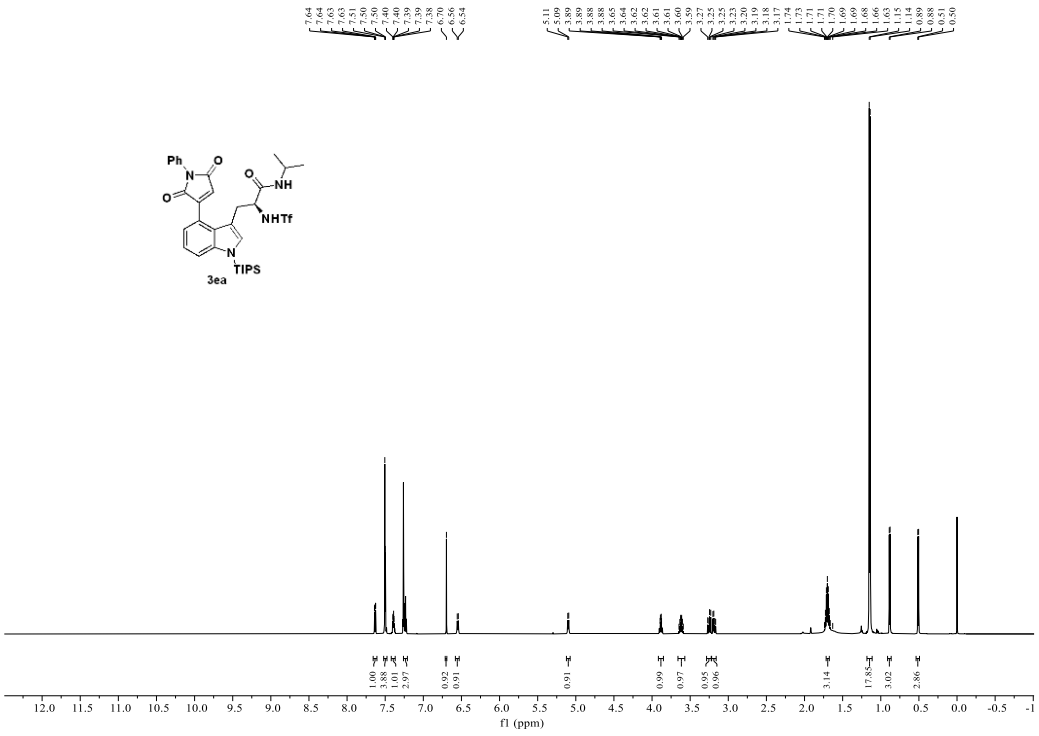


^{13}C{^{1}H} NMR of **3da** (151 MHz, $CDCl_3$)

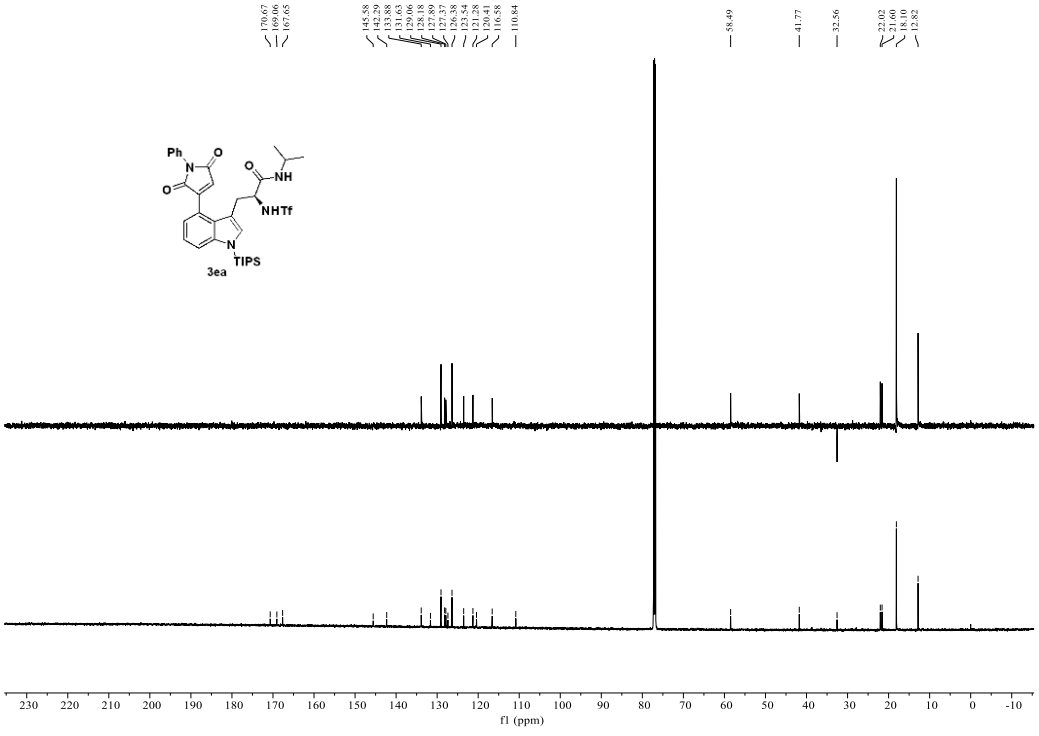


*(S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-N-isopropyl-2-((trifluoromethyl)sulfonamido)propenamide(**3ea**)*

^{1}H NMR of **3ea** (600 MHz, $CDCl_3$)

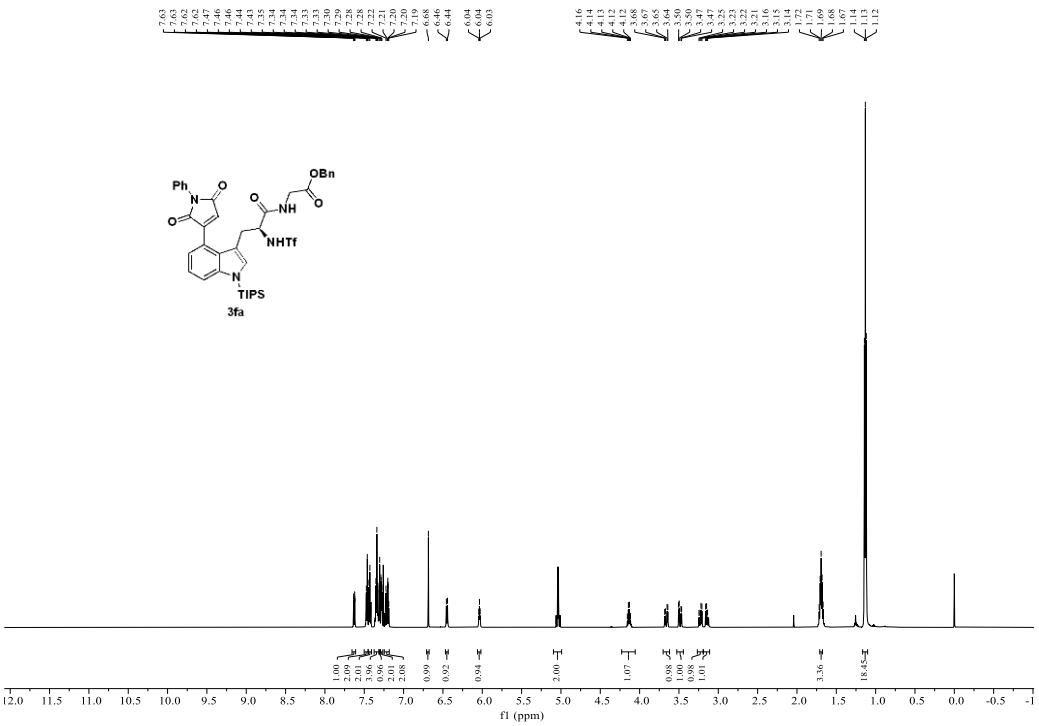


^{13}C{^{1}H} NMR of **3ea** (151 MHz, $CDCl_3$)

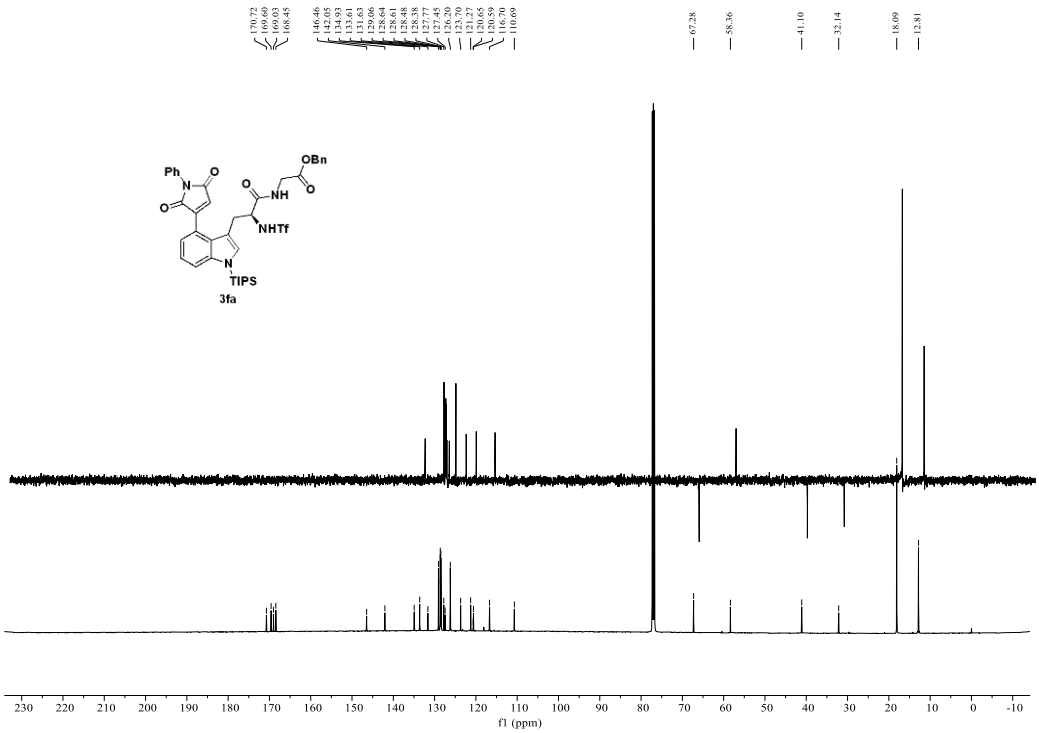


*Benzyl (S)-(3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)glycinate(**3fa**)*

^{1}H NMR of **3fa** (600 MHz, $CDCl_3$)

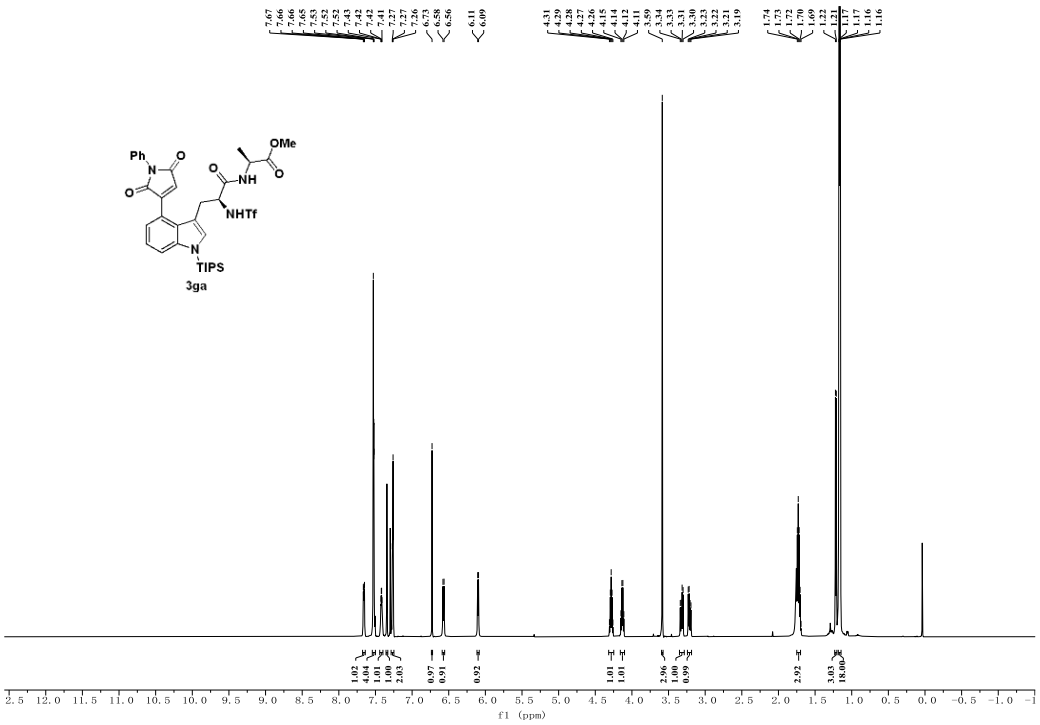


^{13}C{^{1}H} NMR of **3fa** (126 MHz, $CDCl_3$)

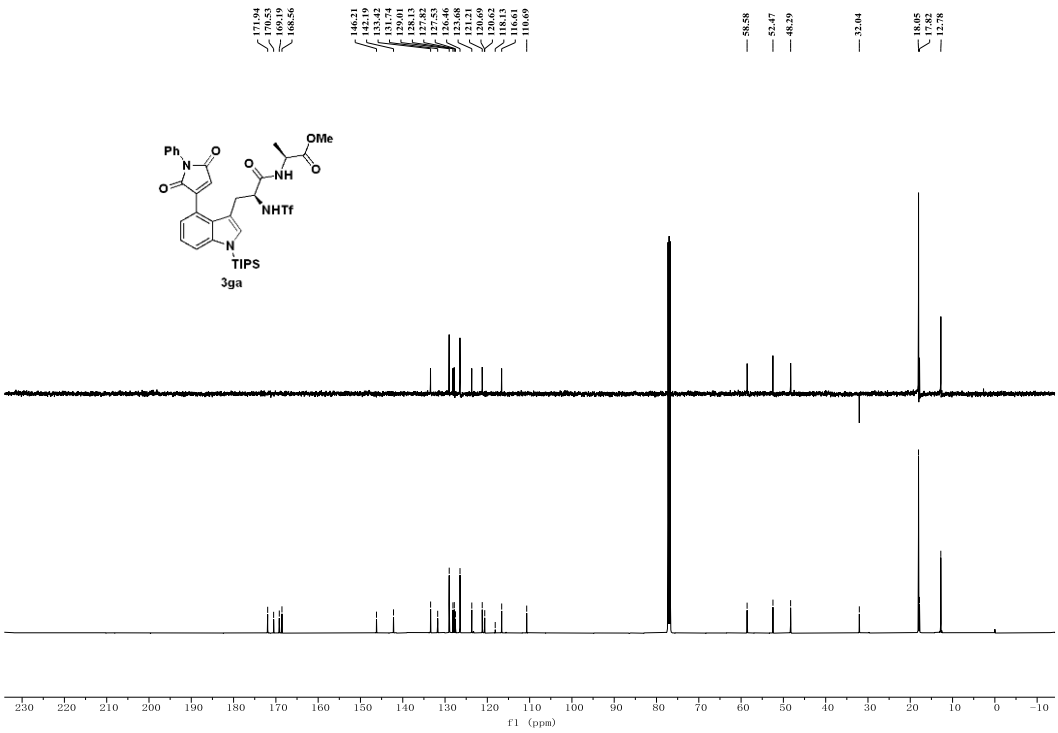


*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-alaninate (**3ga**)*

^{1}H NMR of **3ga** (600 MHz, $CDCl_3$)

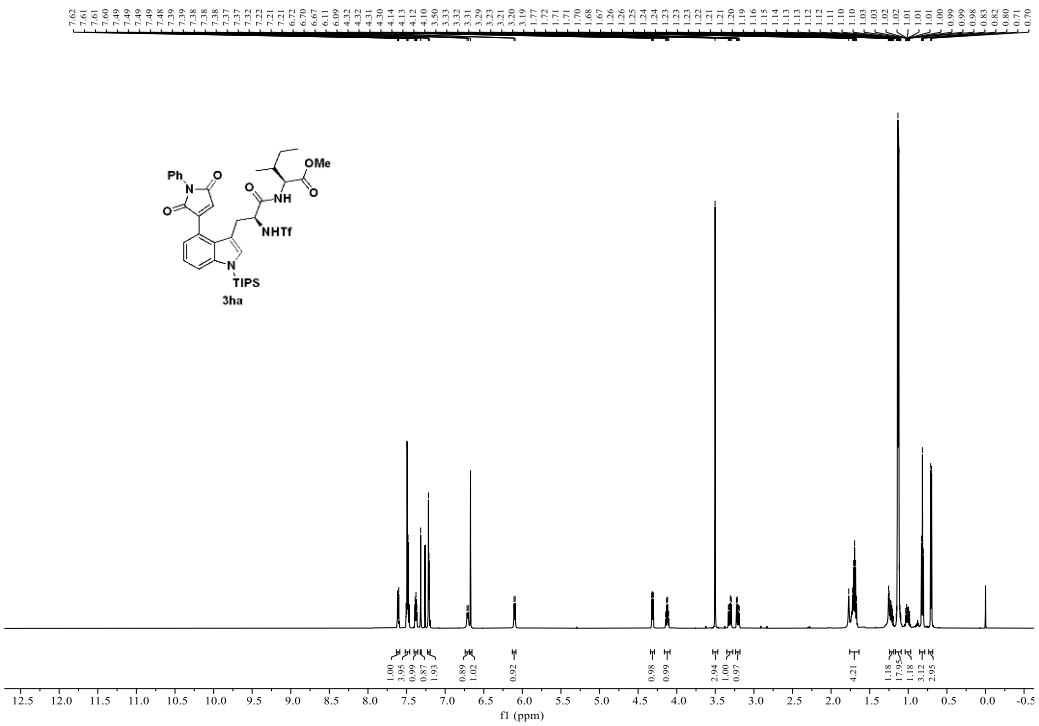


^{13}C{^{1}H} NMR of **3ga** (126 MHz, $CDCl_3$)

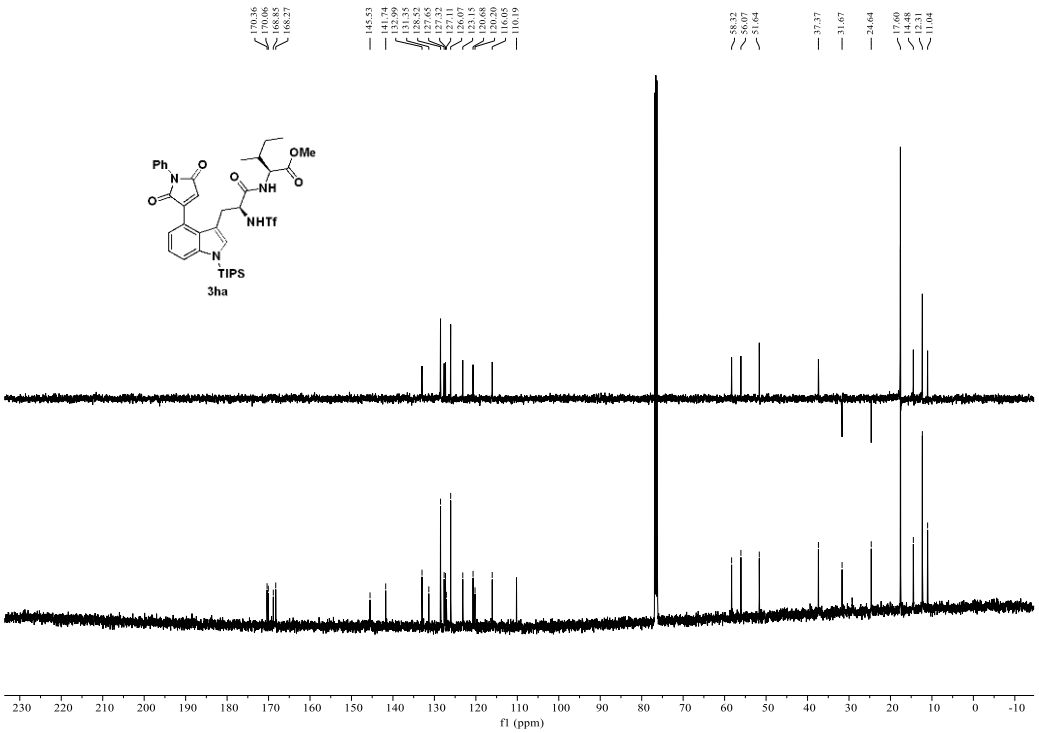


*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-alloisoleucinate(**3ha**)*

^{1}H NMR of **3ha** (600 MHz, $CDCl_3$)

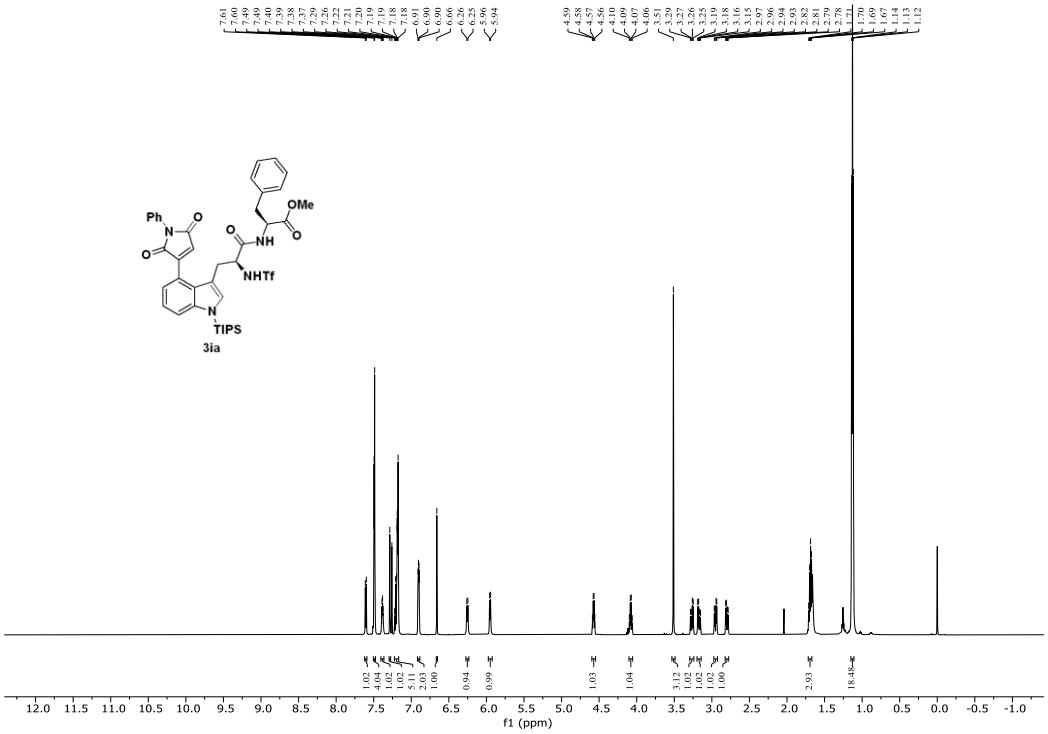


^{13}C{^{1}H} NMR of **3ha** (126 MHz, $CDCl_3$)

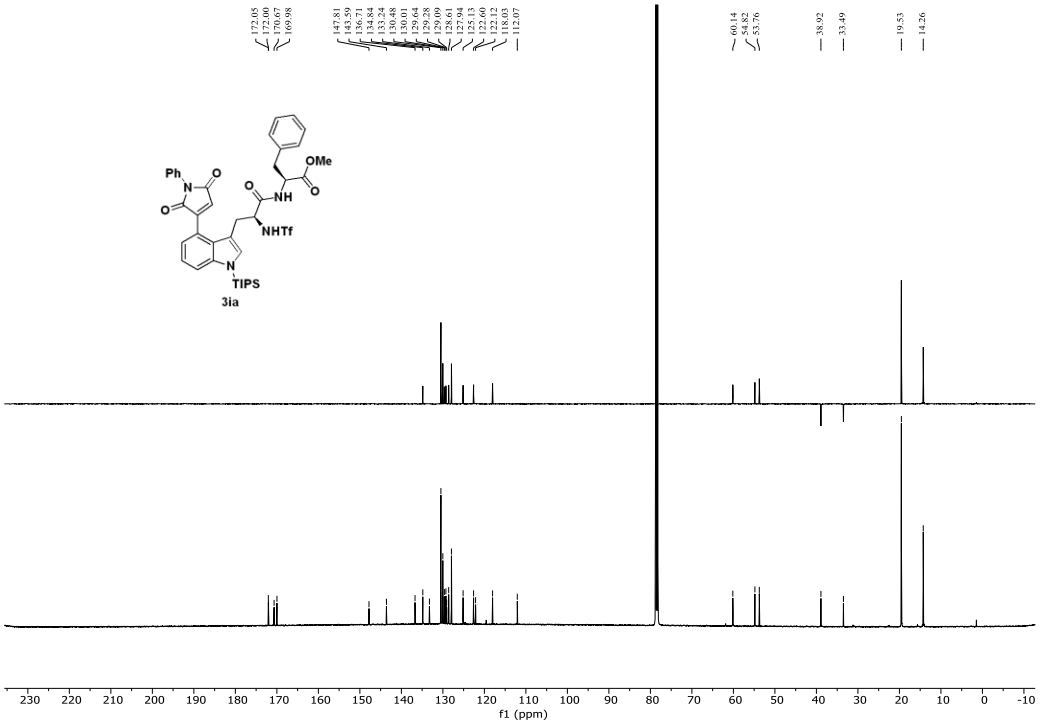


*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-phenylalaninate (**3ia**)*

^{1}H NMR of **3ia** (600 MHz, $CDCl_3$)

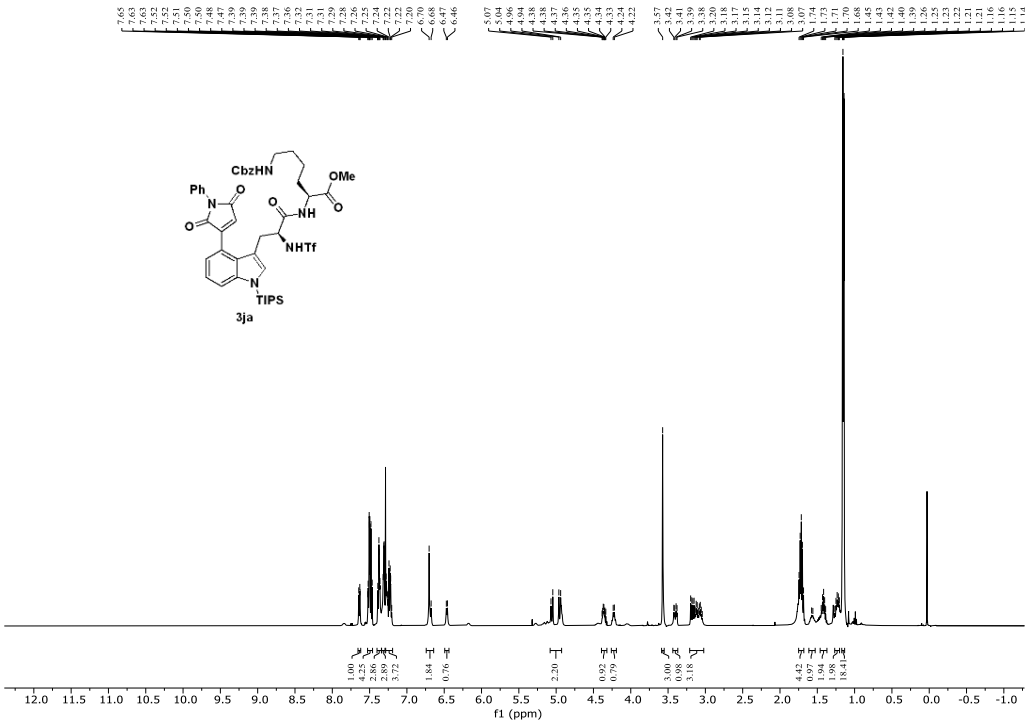


^{13}C{^{1}H} NMR of **3ia** (126 MHz, $CDCl_3$)

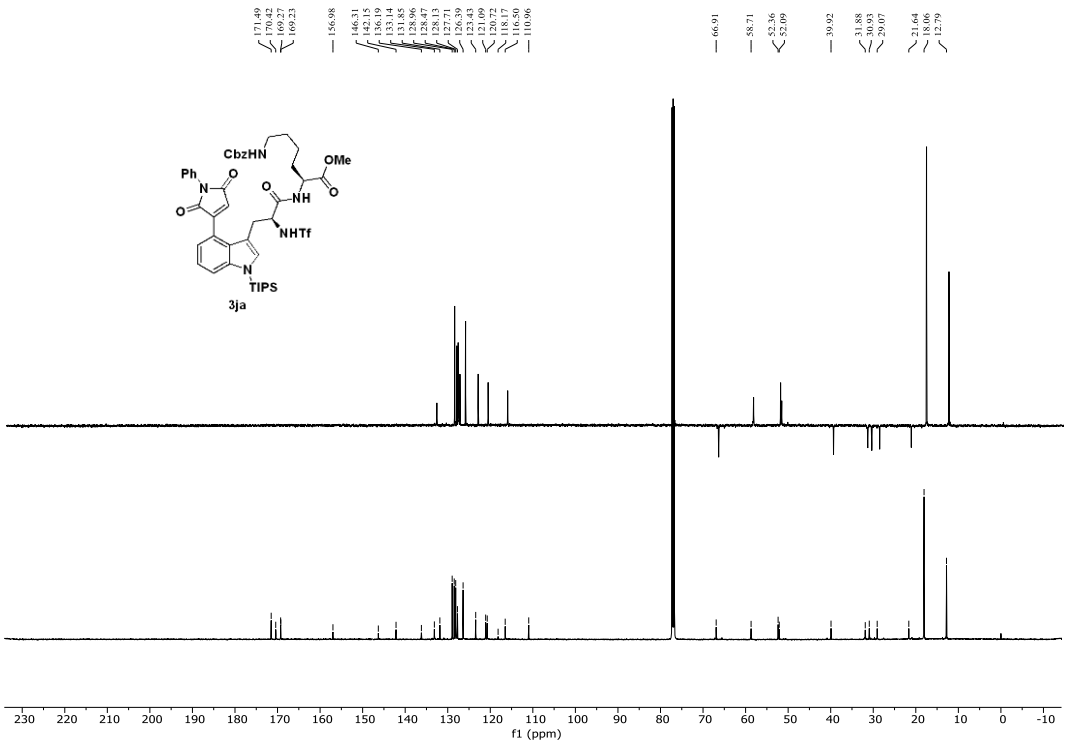


*Methyl N^6-((benzyloxy)carbonyl)-N^2-((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-lysinate (**3ja**)*

^{1}H NMR of **3ja** (500 MHz, $CDCl_3$)

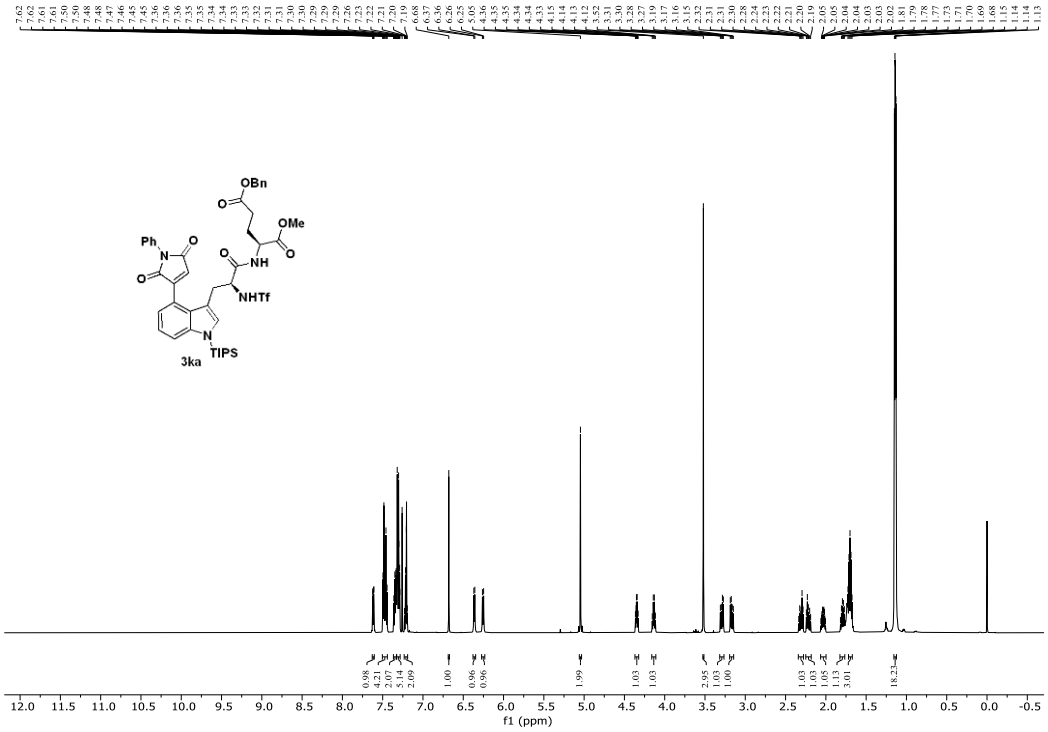


^{13}C{^{1}H} NMR of **3ja** (126 MHz, $CDCl_3$)

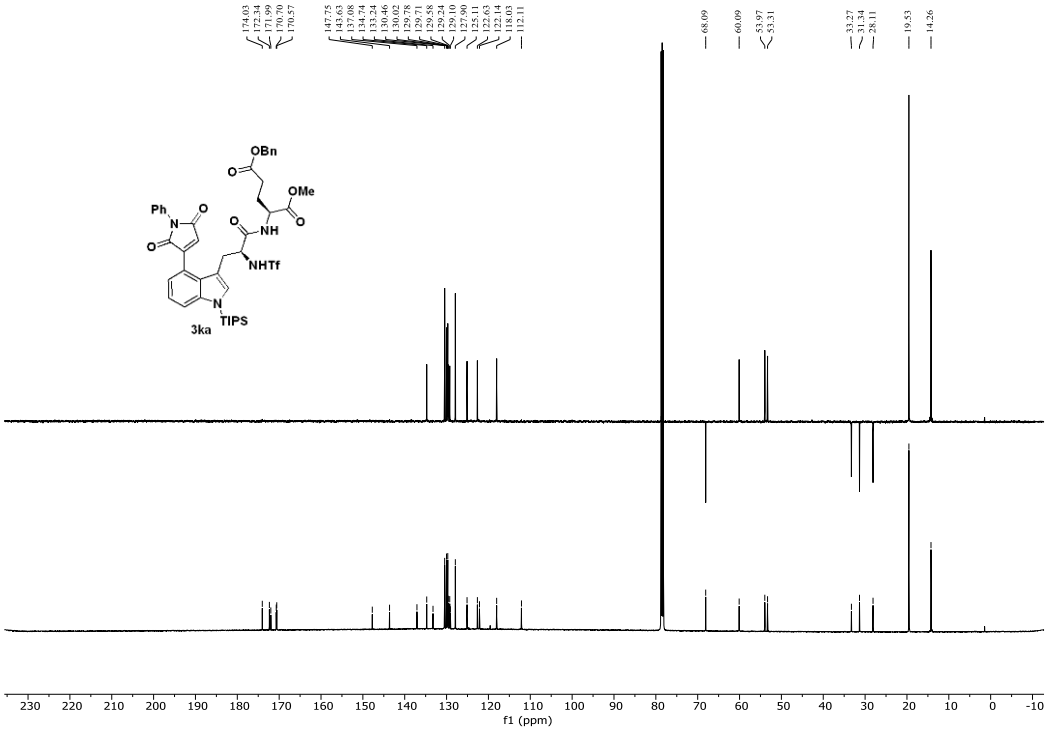


*5-Benzyl 1-methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-glutamate (**3ka**)*

^{1}H NMR of **3ka** (600 MHz, $CDCl_3$)

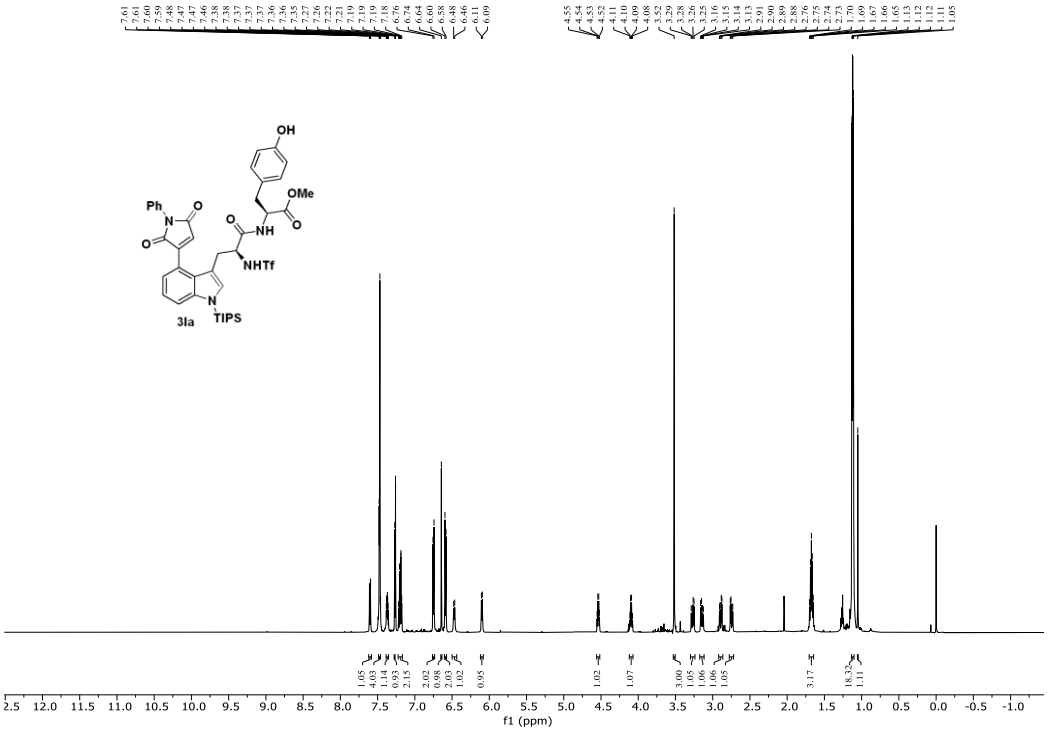


^{13}C{^{1}H} NMR of **3ka** (126 MHz, $CDCl_3$)

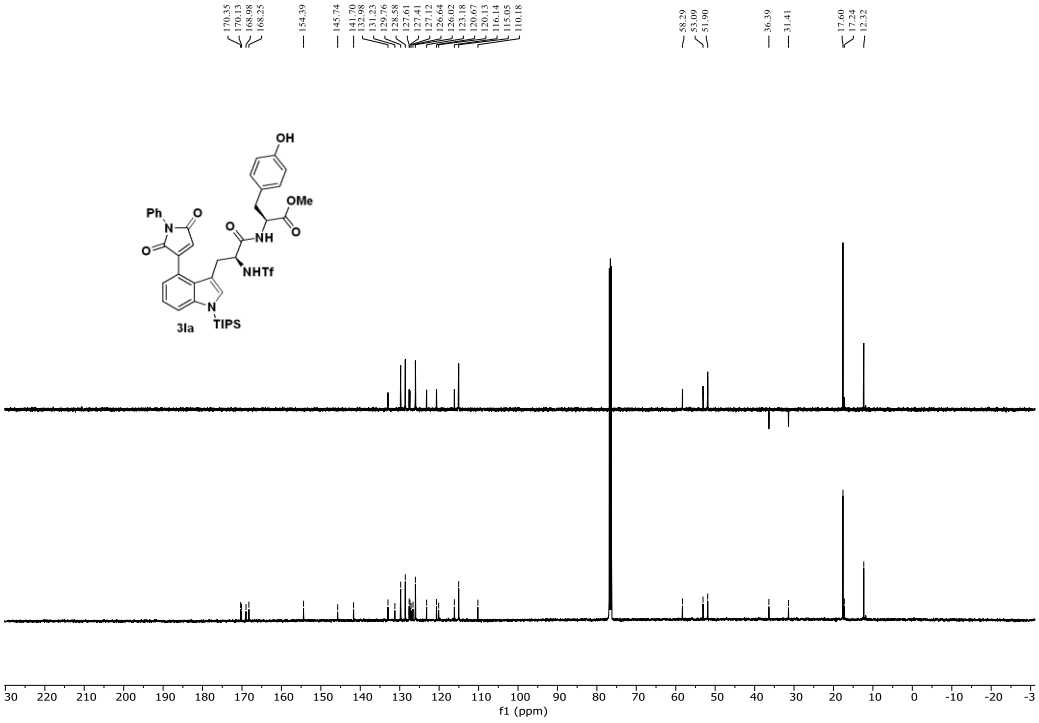


*Methyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-tyrosinate (**3la**)*

^{1}H NMR of **3la** (600 MHz, $CDCl_3$)

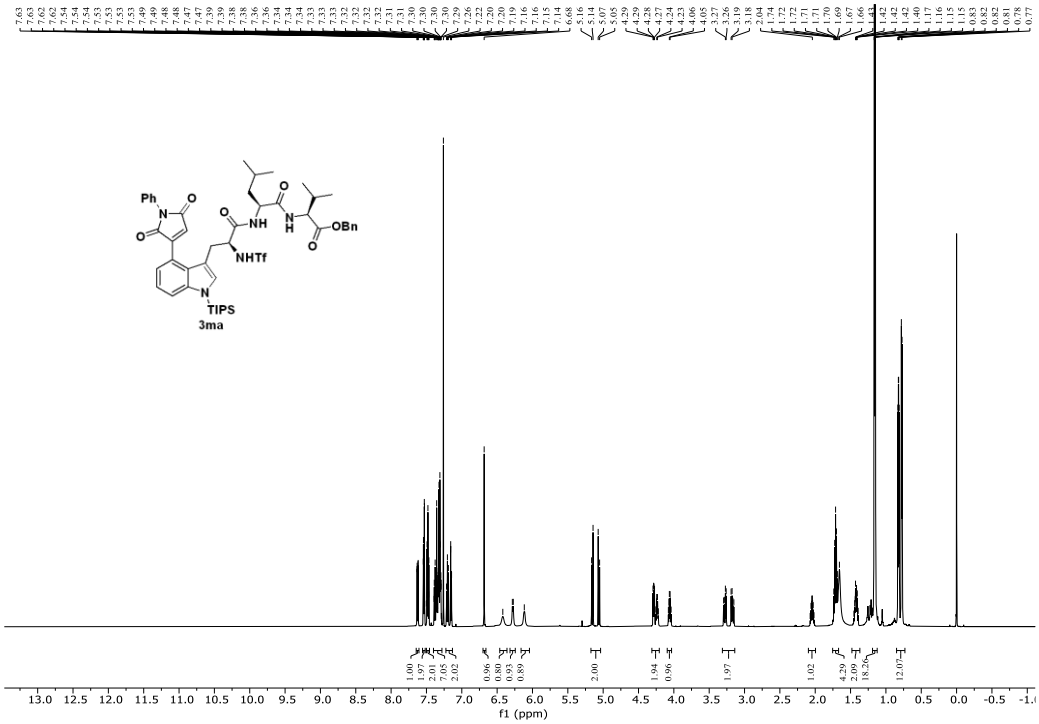


^{13}C{^{1}H} NMR of **3la** (126 MHz, $CDCl_3$)

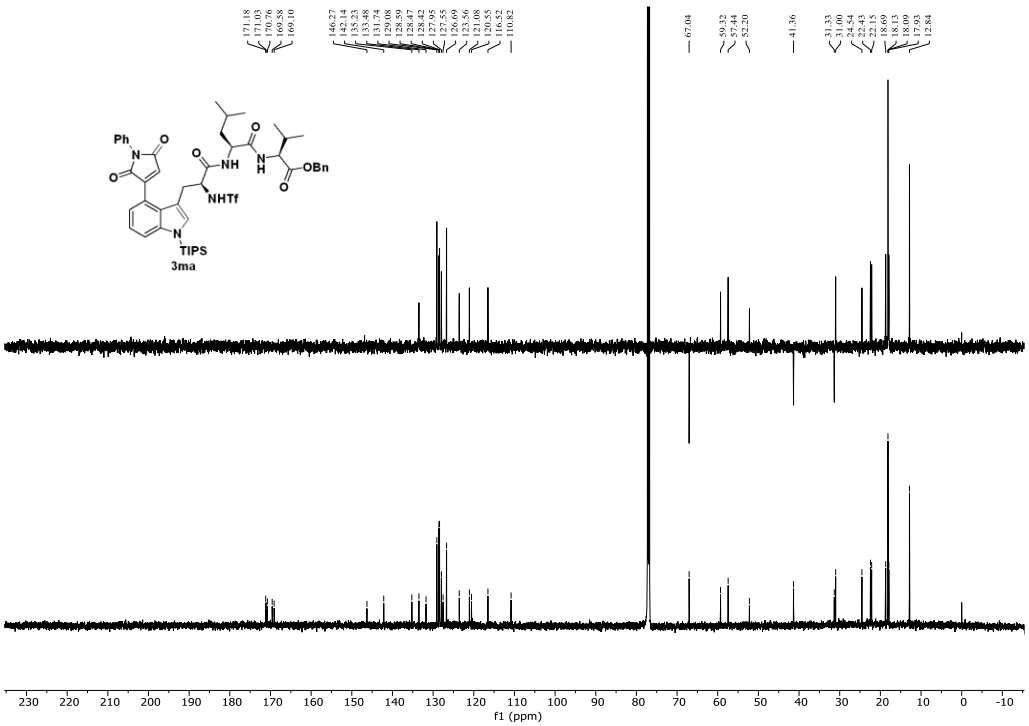


*Benzyl ((S)-3-(4-(2,5-dioxo-1-phenyl-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoyl)-L-leucyl-L-valinate (**3ma**)*

^{1}H NMR of **3ma** (600 MHz, $CDCl_3$)

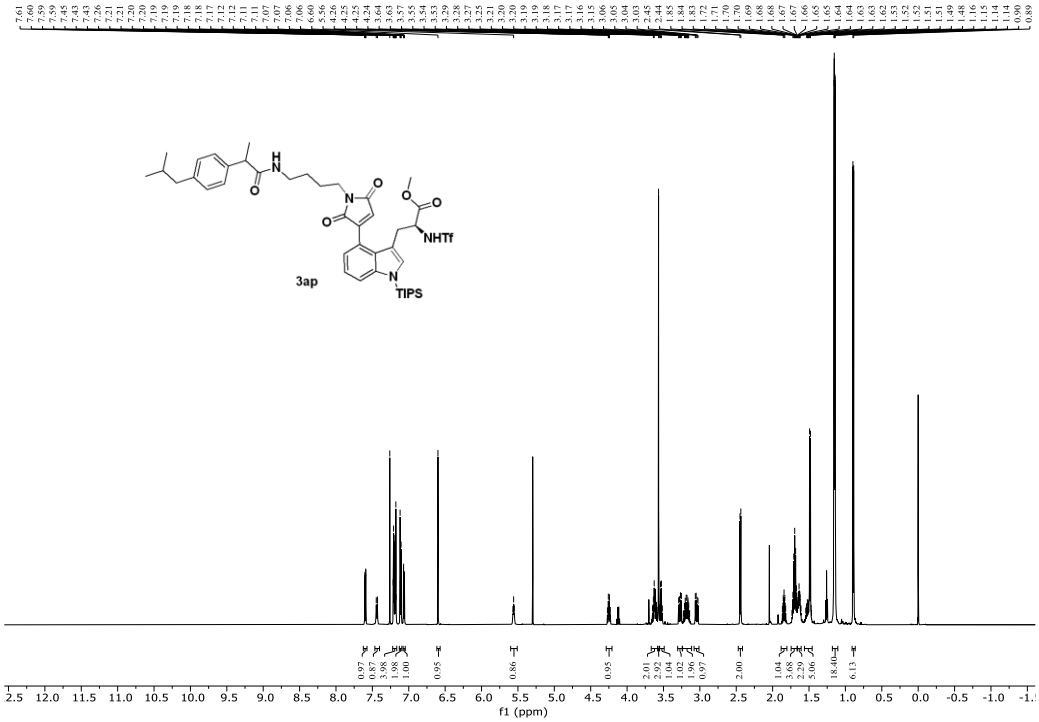


^{13}C{^{1}H} NMR of **3ma** (151 MHz, $CDCl_3$)

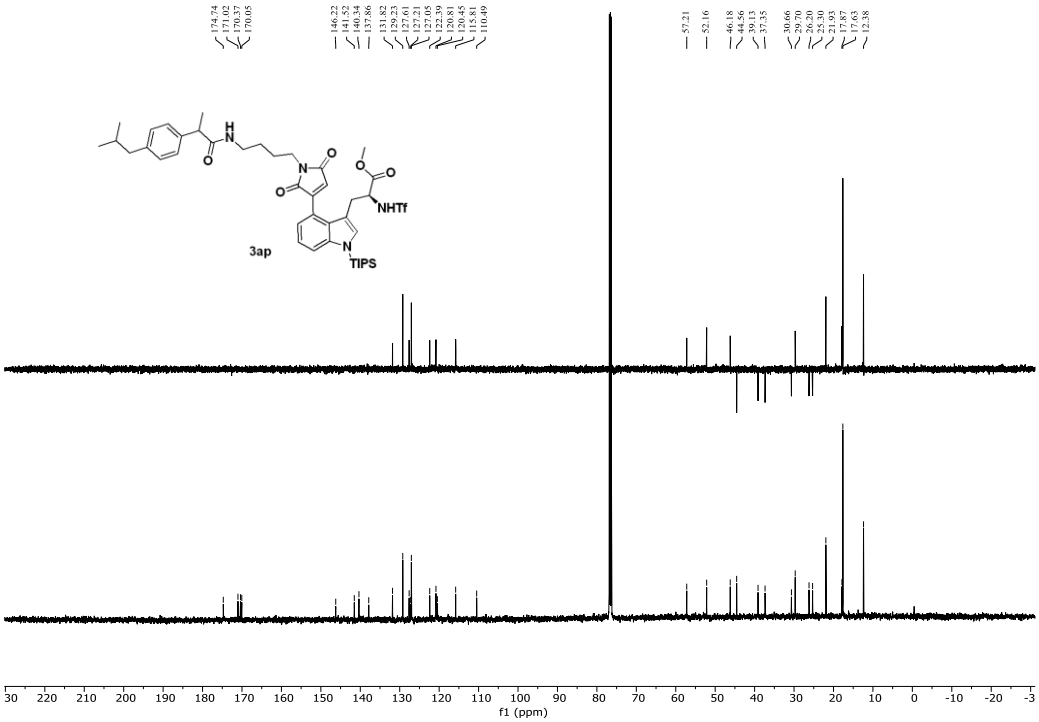


*Methyl (2S)-3-(4-(1-(4-(2-(4-isobutylphenyl)propanamido)butyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ap**)*

^{1}H NMR of **3ap** (600 MHz, $CDCl_3$)

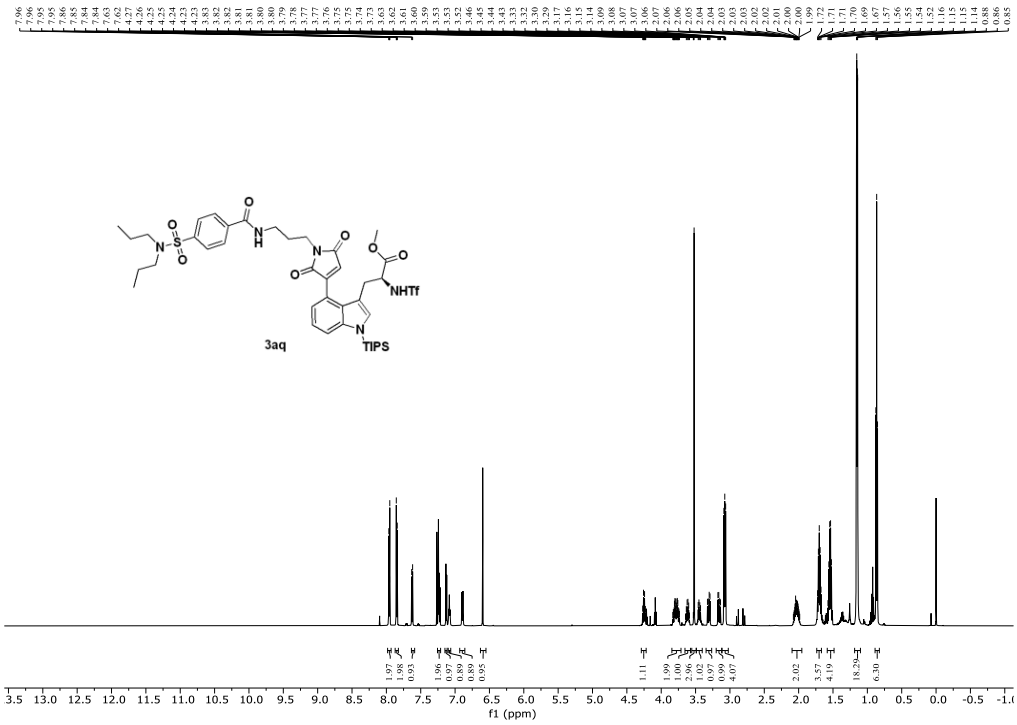


^{13}C{^{1}H} NMR of **3ap** (126 MHz, $CDCl_3$)

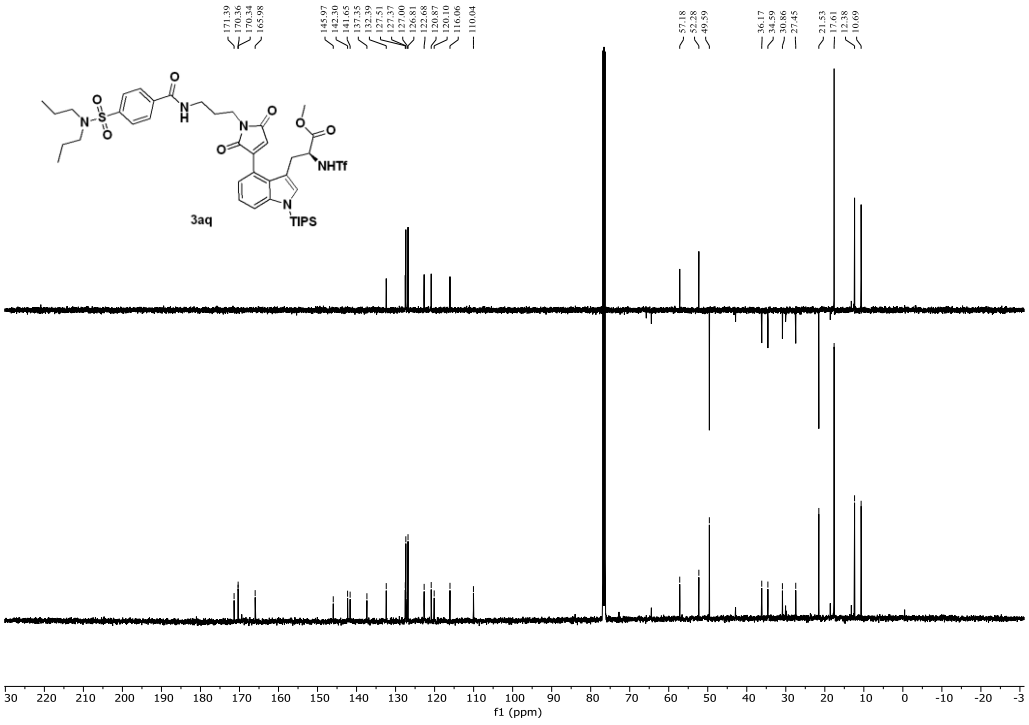


*Methyl (S)-3-(4-(1-(3-(4-(N,N-dipropylsulfamoyl)benzamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3aq**)*

^{1}H NMR of **3aq** (600 MHz, $CDCl_3$)

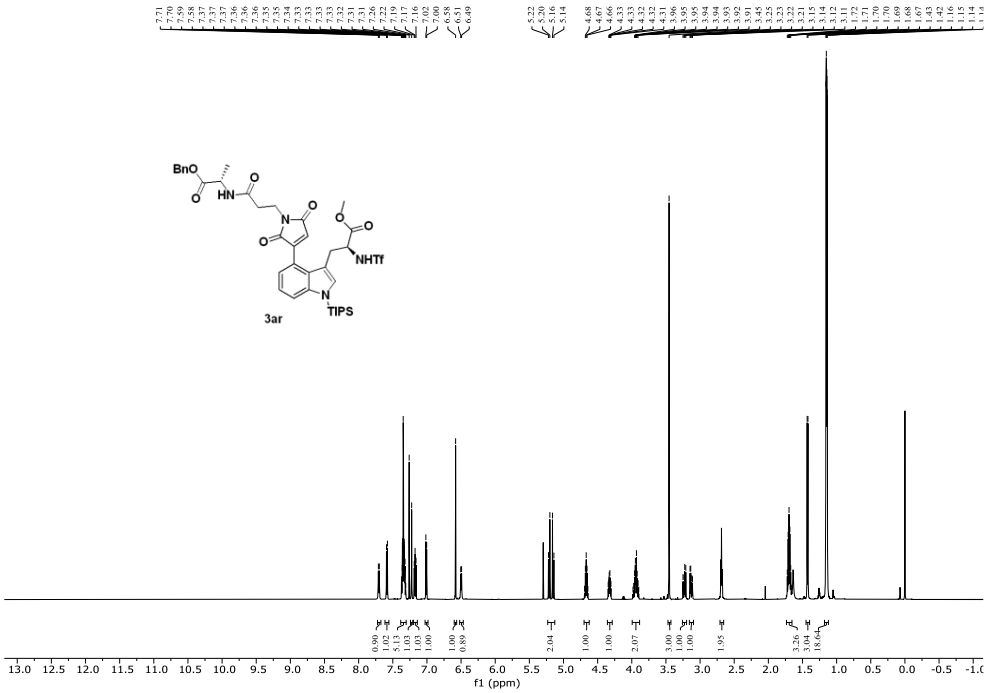


^{13}C{^{1}H} NMR of **3aq** (126 MHz, $CDCl_3$)

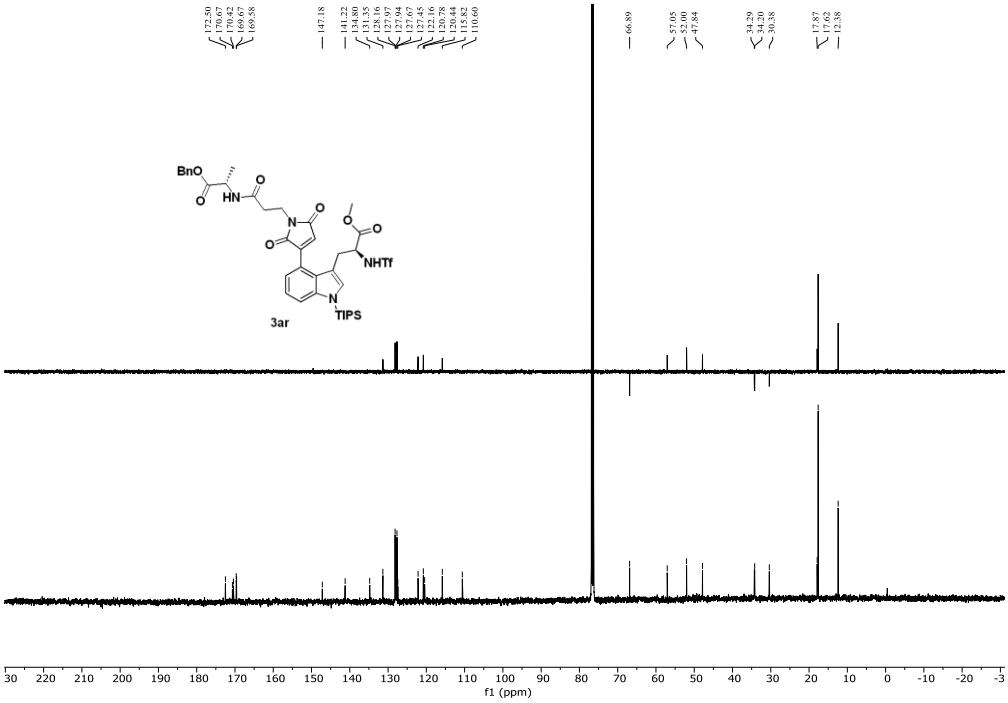


*Methyl (S)-3-(4-(1-(3-(((S)-1-(benzyloxy)-1-oxopropan-2-yl)amino)-3-oxopropyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3ar**)*

^{1}H NMR of **3ar** (600 MHz, $CDCl_3$)

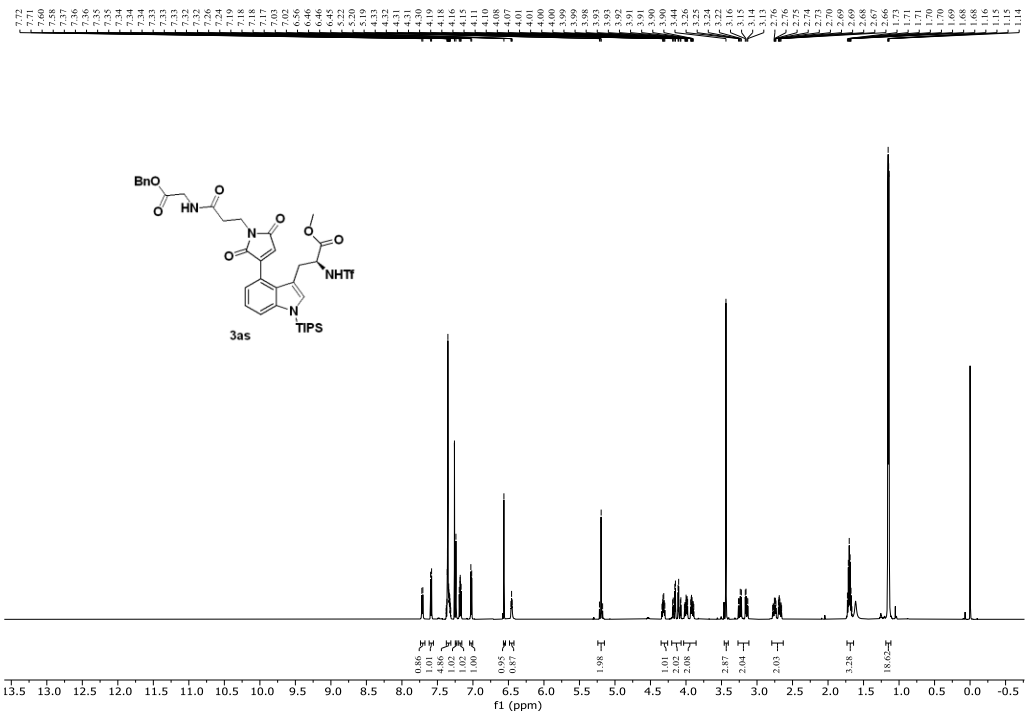


^{13}C{^{1}H} NMR of **3ar** (126 MHz, $CDCl_3$)

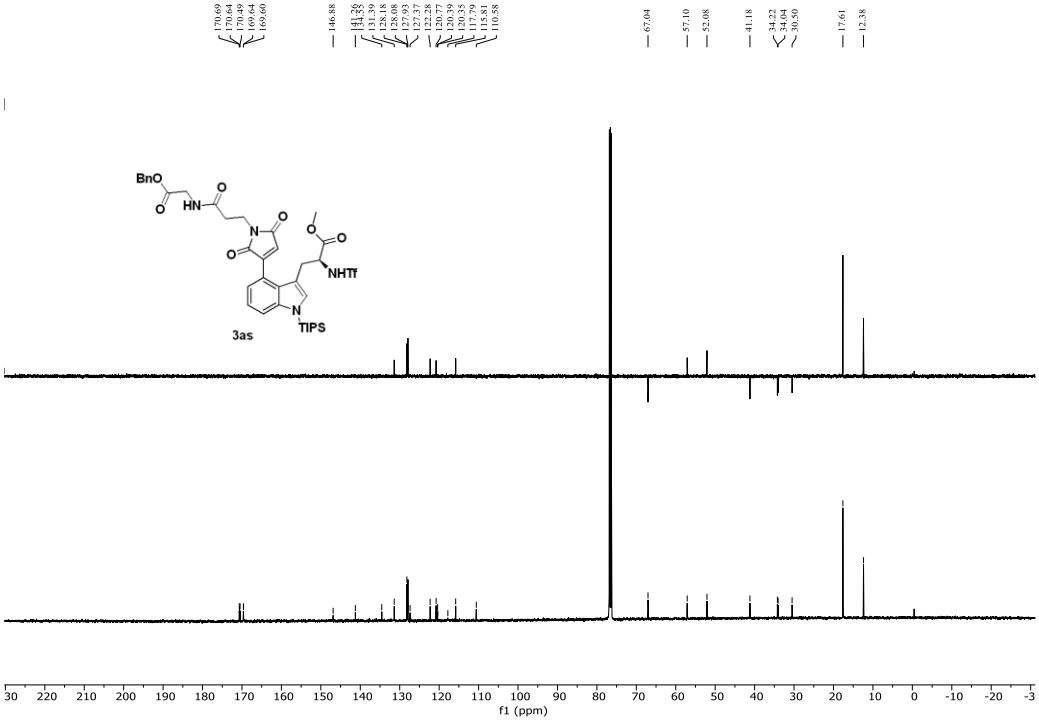


*Methyl (S)-3-(4-(1-(3-((2-(benzyloxy)-2-oxoethyl)amino)-3-oxopropyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3as**)*

^{1}H NMR of **3as** (600 MHz, $CDCl_3$)

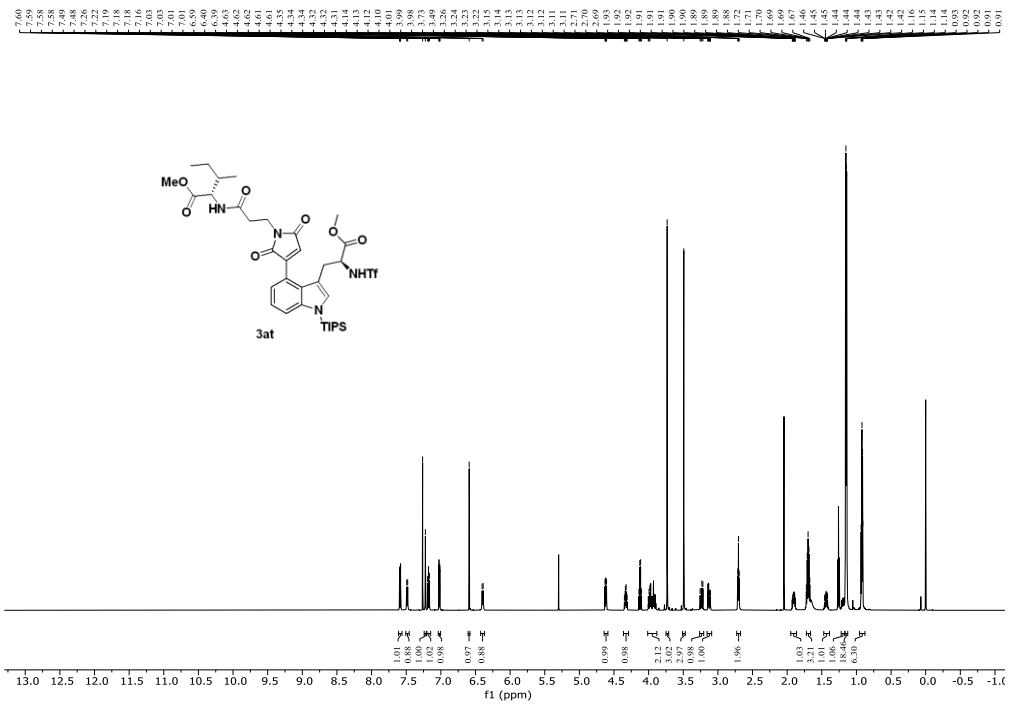


^{13}C{^{1}H} NMR of **3as** (126 MHz, $CDCl_3$)

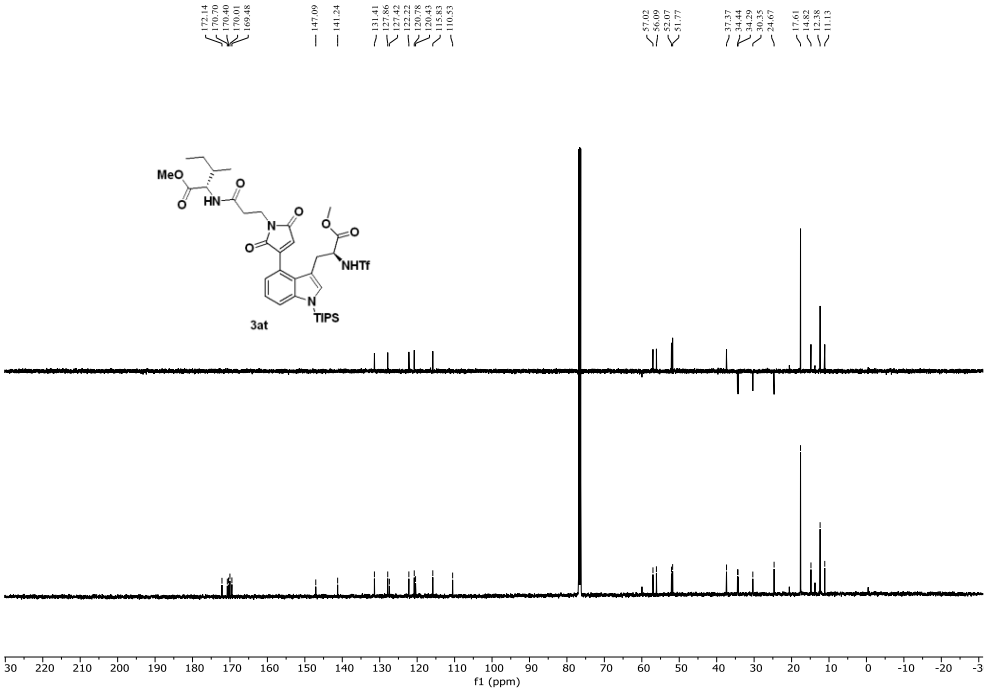


*Methyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucinate (**3at**)*

^{1}H NMR of **3at** (600 MHz, $CDCl_3$)

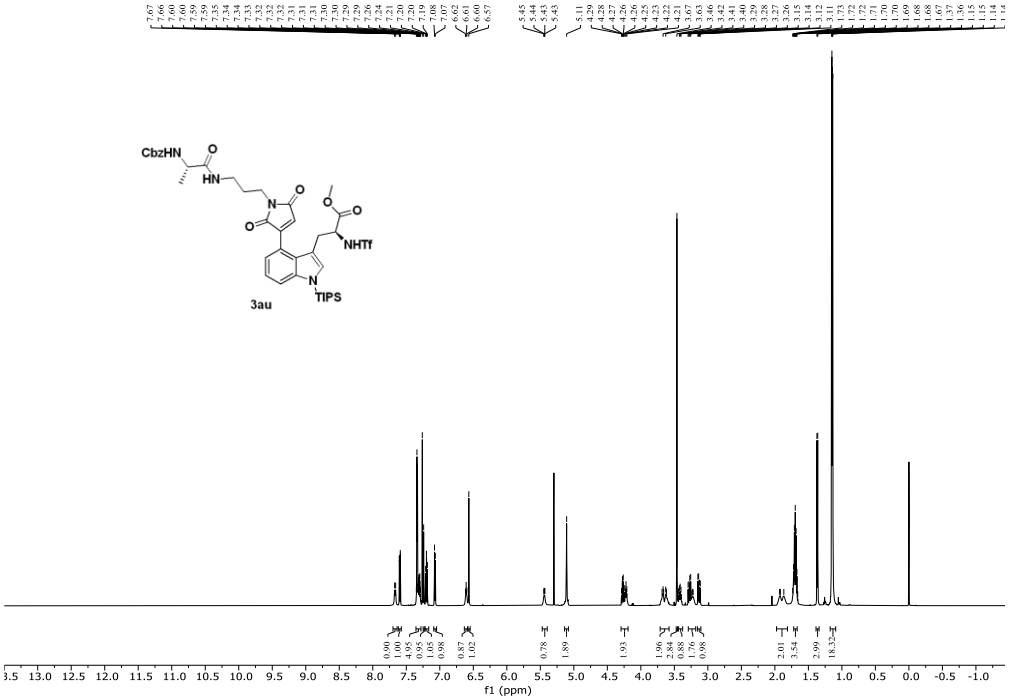


^{13}C{^{1}H} NMR of **3at** (126 MHz, $CDCl_3$)

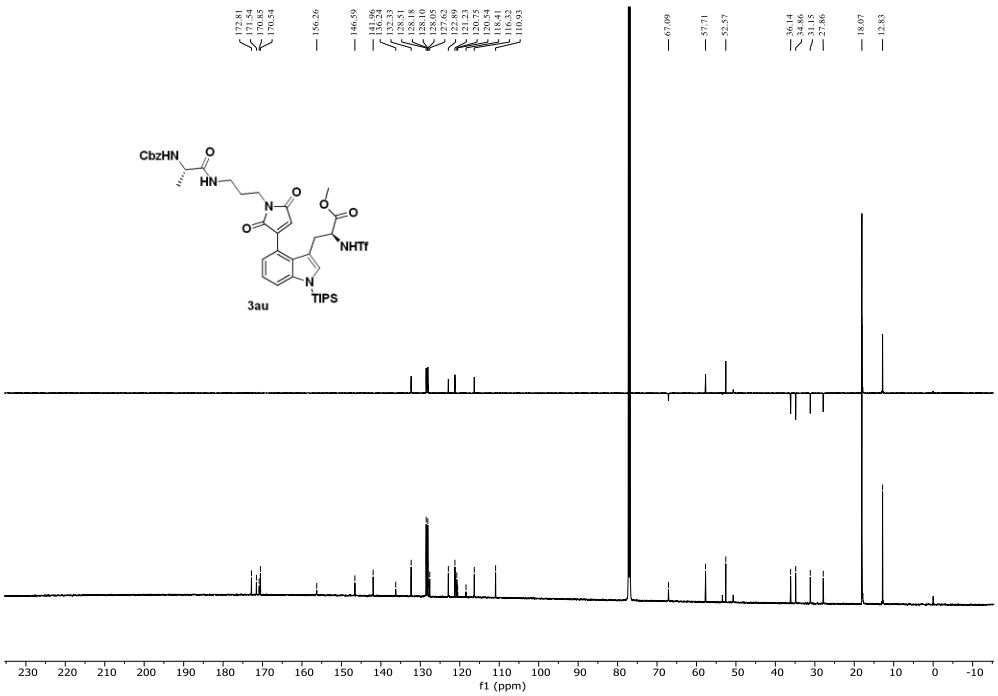


*Methyl (S)-3-(4-(1-(3-((S)-2-(((benzyloxy)carbonyl)amino)propanamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3au**)*

^{1}H NMR of **3au** (600 MHz, $CDCl_3$)

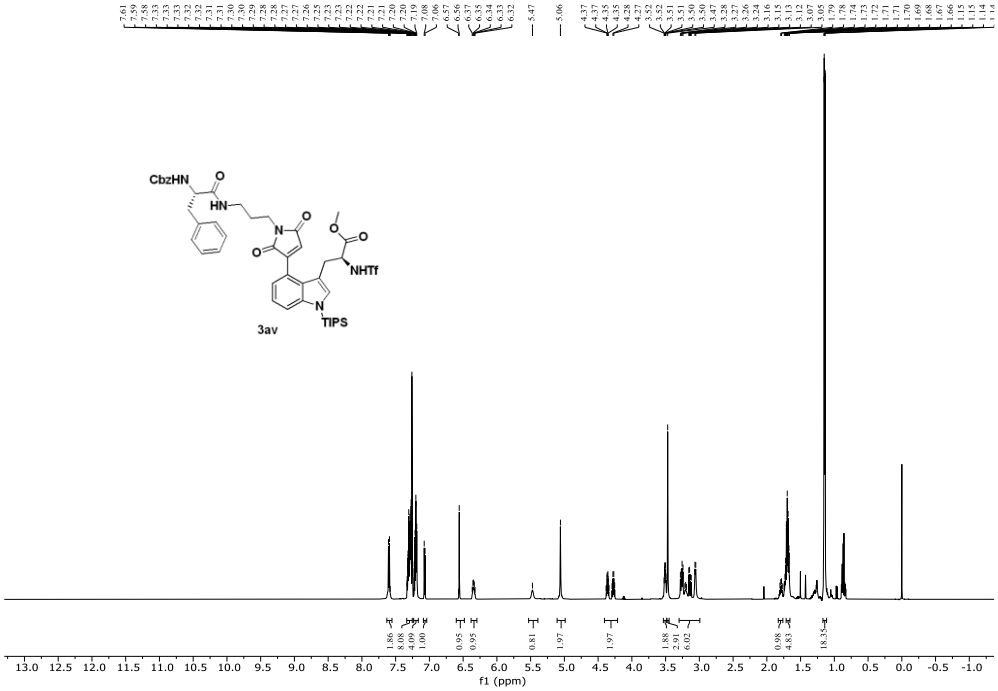


^{13}C{^{1}H} NMR of **3au** (126 MHz, $CDCl_3$)

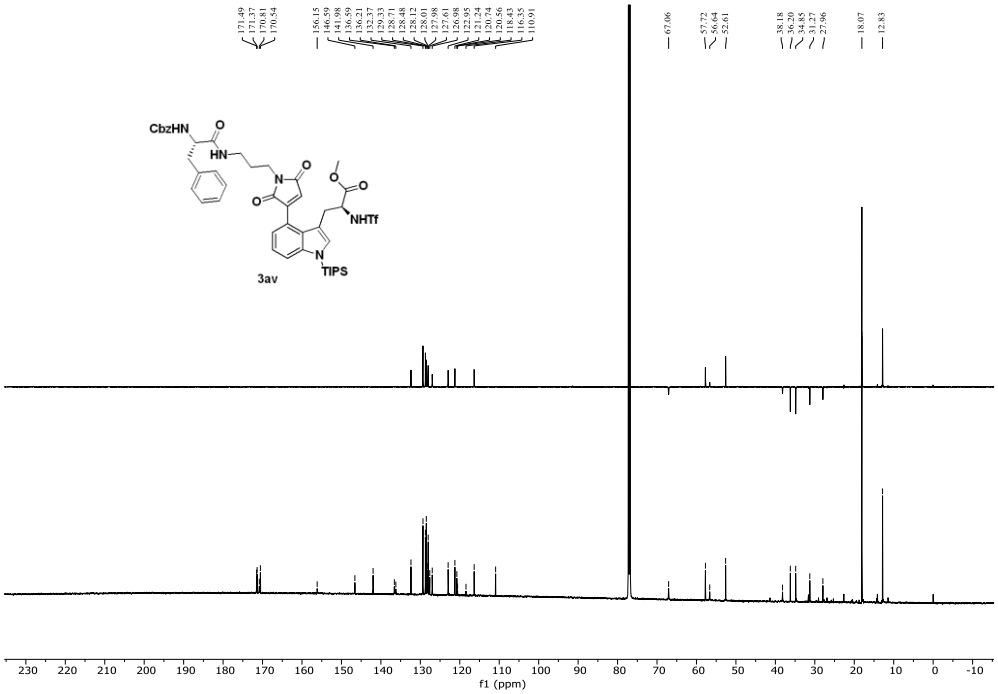


*Methyl (S)-3-(4-(1-(3-((S)-2-(((benzyloxy)carbonyl)amino)-3-phenylpropanamido)propyl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)-1-(triisopropylsilyl)-1H-indol-3-yl)-2-((trifluoromethyl)sulfonamido)propanoate (**3av**)*

^{1}H NMR of **3av** (600 MHz, $CDCl_3$)

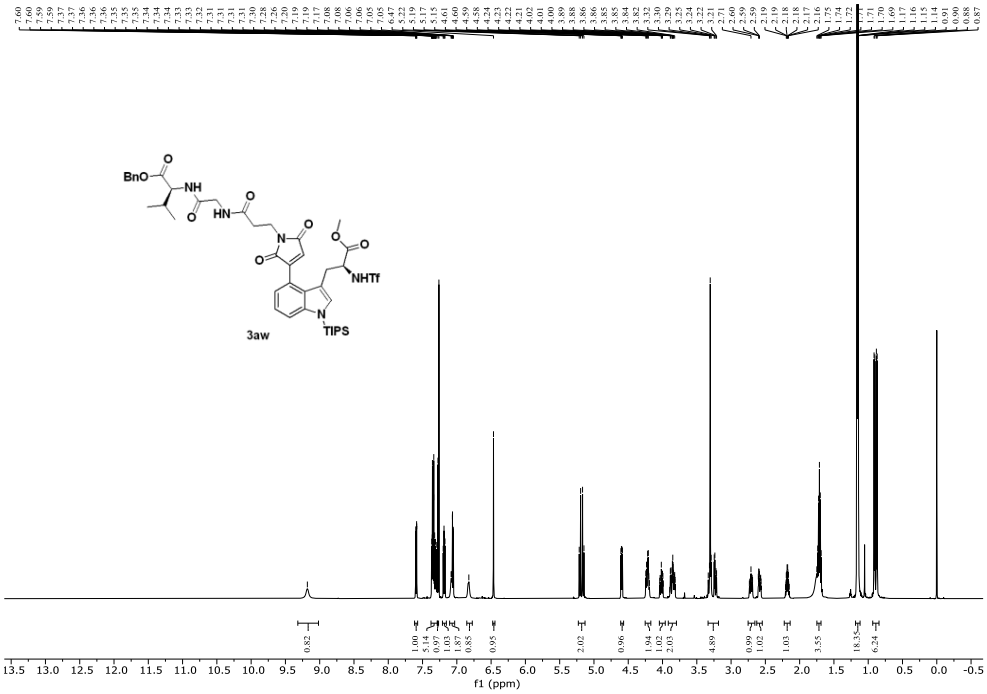


^{13}C{^{1}H} NMR of **3av** (126 MHz, $CDCl_3$)

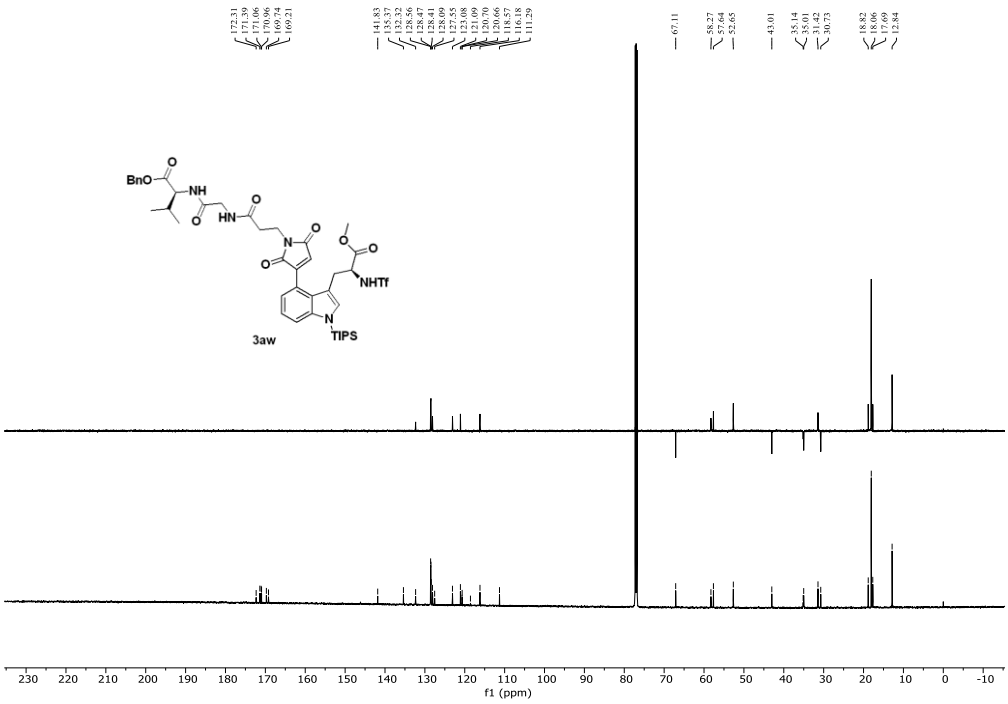


*Benzyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)glycyl-L-valinate (**3aw**)*

^{1}H NMR of **3aw** (600 MHz, $CDCl_3$)

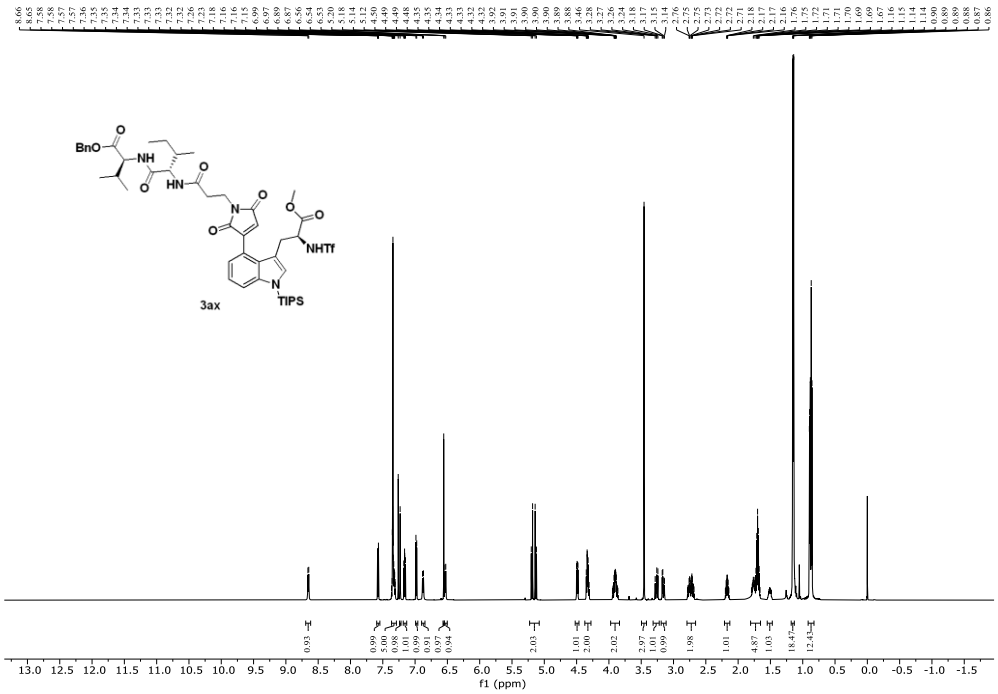


^{13}C{^{1}H} NMR of **3aw** (126 MHz, $CDCl_3$)

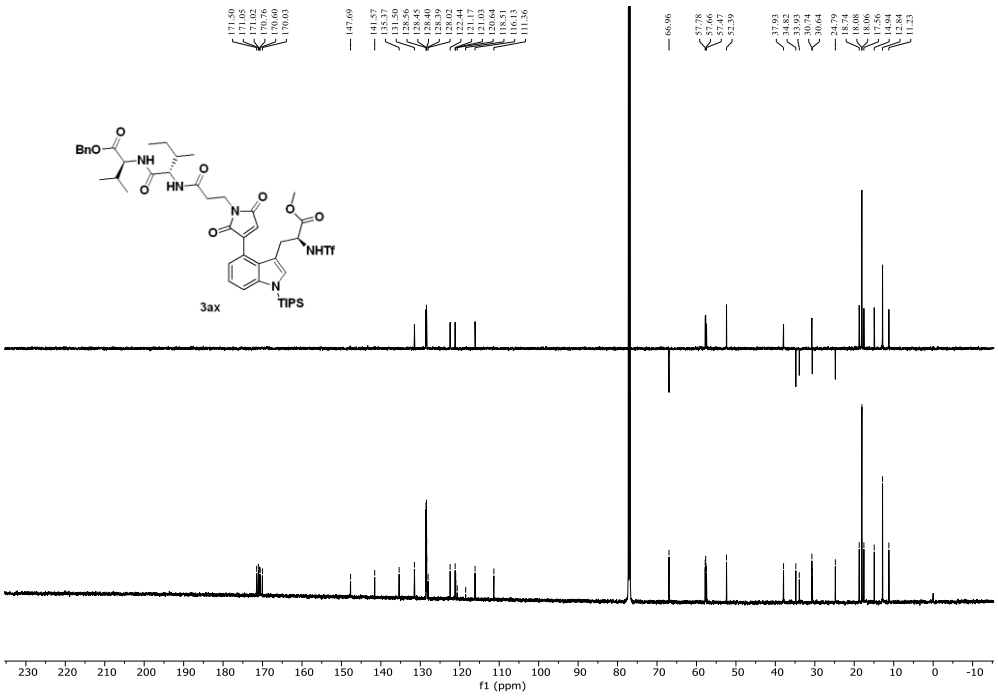


*Benzyl (3-(3-(3-((S)-3-methoxy-3-oxo-2-((trifluoromethyl)sulfonamido)propyl)-1-(triisopropylsilyl)-1H-indol-4-yl)-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoyl)-L-alloisoleucyl-L-valinate (**3ax**)*

^{1}H NMR of **3ax** (600 MHz, $CDCl_3$)

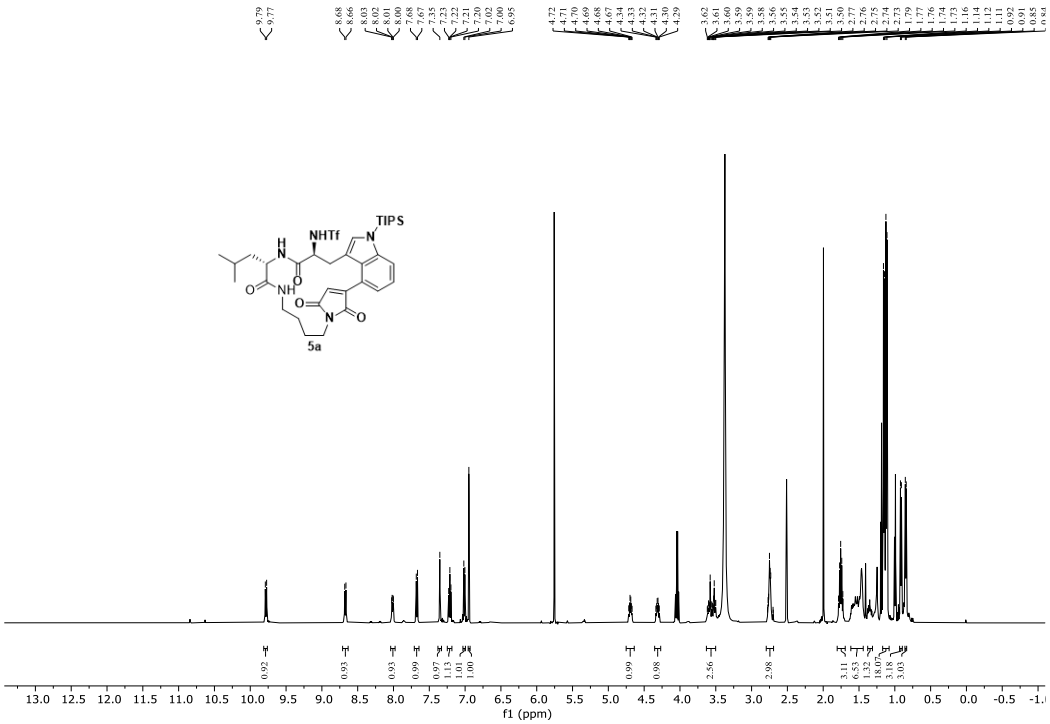


^{13}C{^{1}H} NMR of **3ay** (126 MHz, $CDCl_3$)

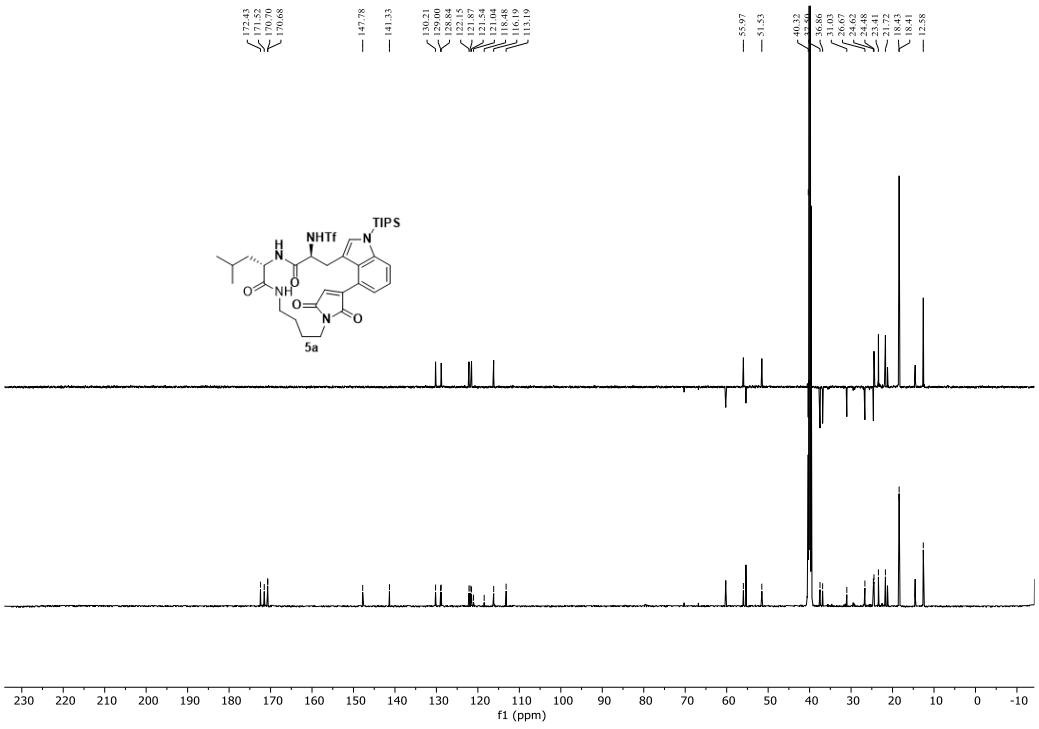


*1,1,1-Trifluoro-N-((9S,12S)-9-isobutyl-2²,2⁵,8,11-tetraoxo-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-7,10-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclotridecaphane-12-yl)methanesulfonamide (**5a**)*

^{1}H NMR of **5a** (500 MHz, DMSO-*d6*)

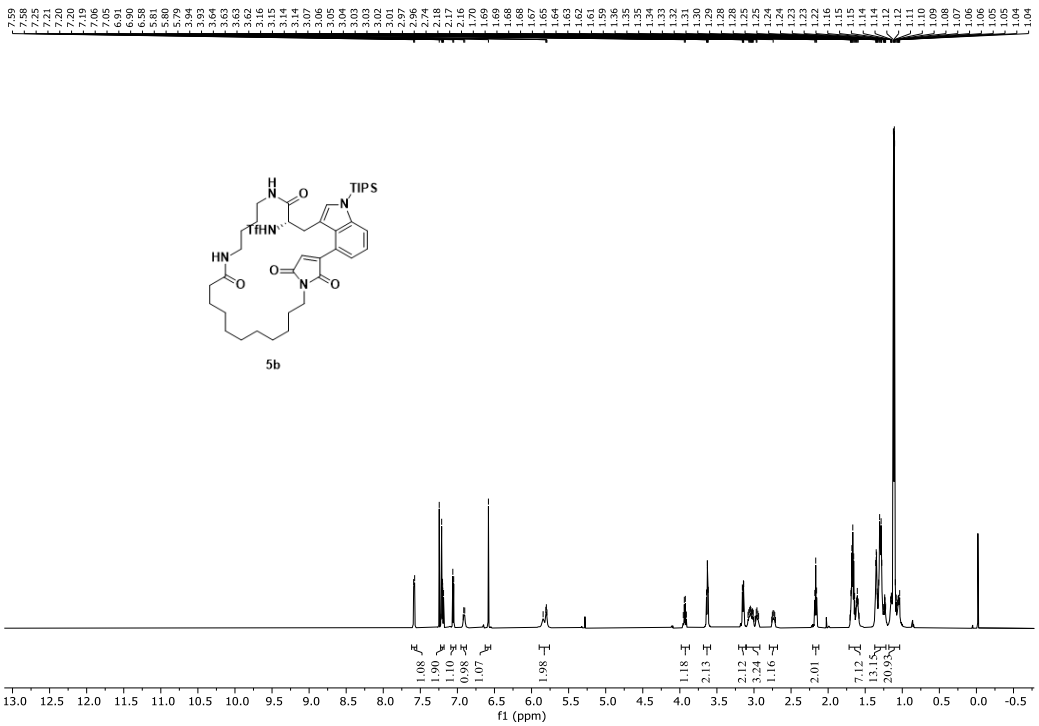


^{13}C{^{1}H} NMR of **5a** (126 MHz, DMSO-*d6*)

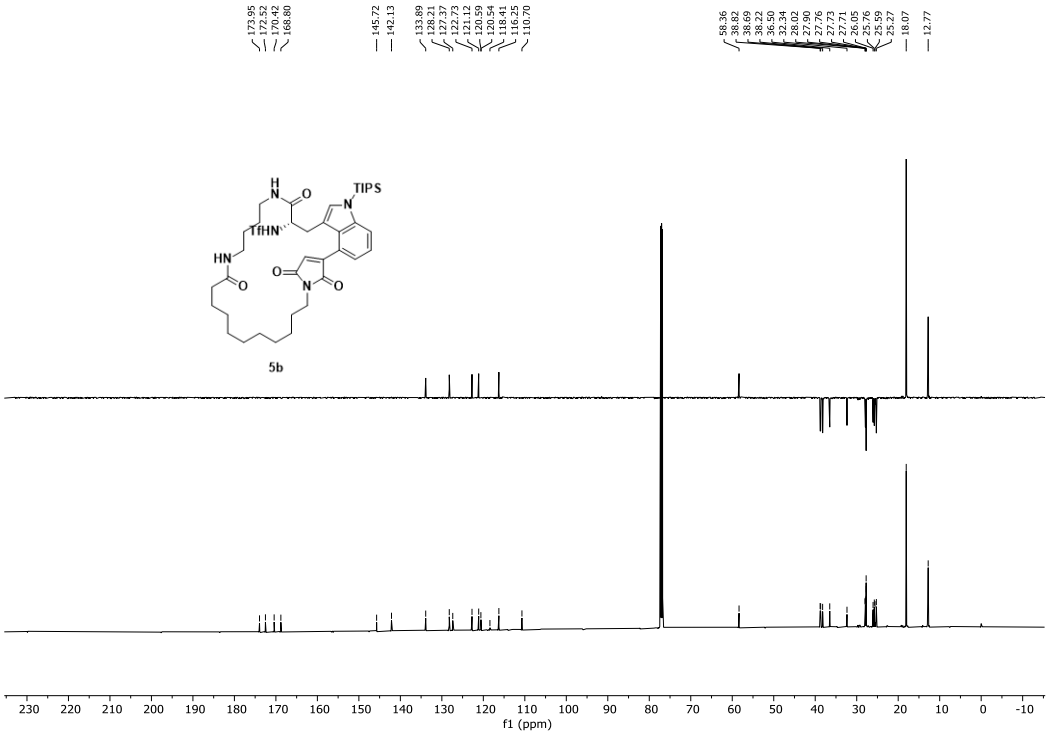


*1,1,1-Trifluoro-N-((21S)-2²,2⁵,13,20-tetraoxo-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-14,19-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclodocosaphane-21-yl)methanesulfonamide (**5b**)*

^{1}H NMR of **5b** (600 MHz, $CDCl_3$)

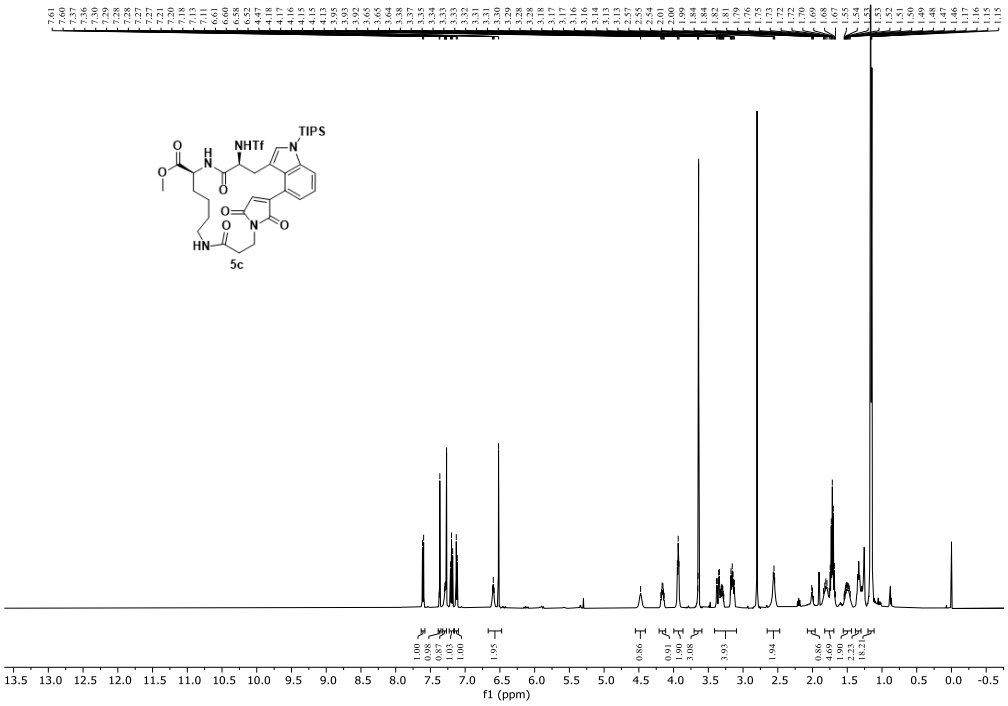


^{13}C{^{1}H} NMR of **5b** (151 MHz, $CDCl_3$)

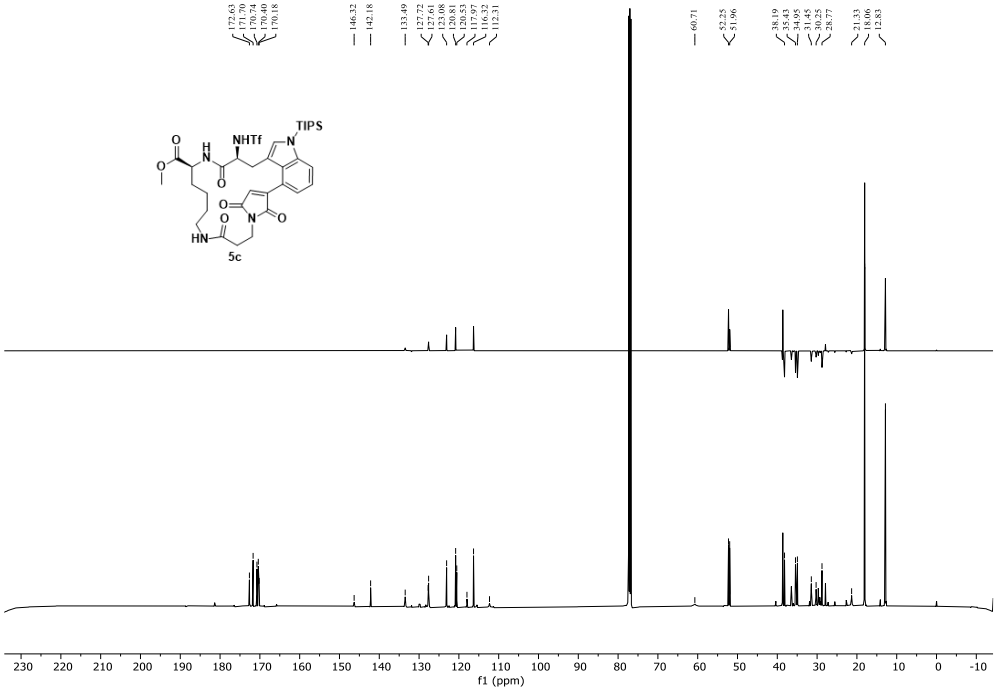


*Methyl (11S,14S)-2²,2⁵,5,13-tetraoxo-14-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-6,12-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclopentadecaphane-11-carboxylate (**5c**)*

^{1}H NMR of **5c** (500 MHz, $CDCl_3$)

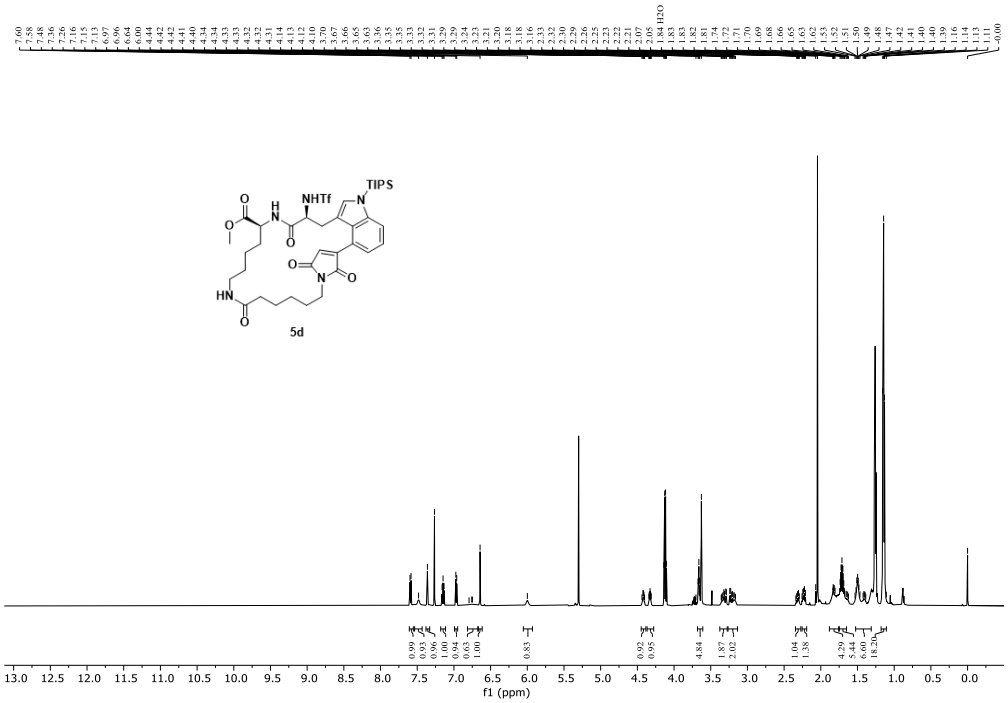


^{13}C{^{1}H} NMR of **5c** (126 MHz, $CDCl_3$)

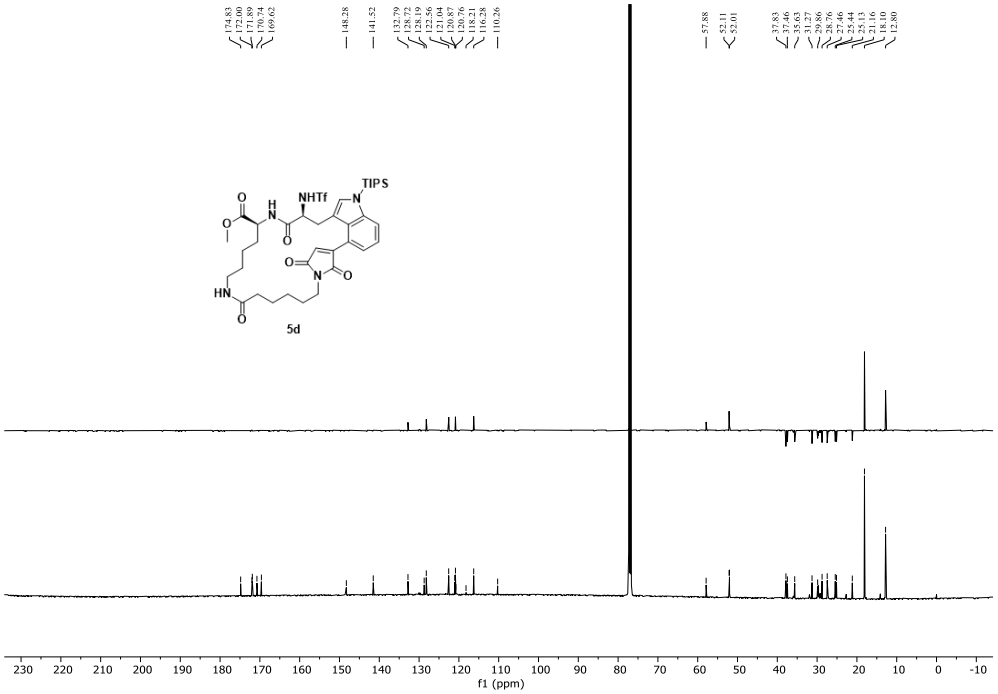


*Methyl (14S,17S)-2²,2⁵,8,16-tetraoxo-17-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-9,15-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-14-carboxylate (**5d**)*

^{1}H NMR of **5d** (600 MHz, $CDCl_3$)

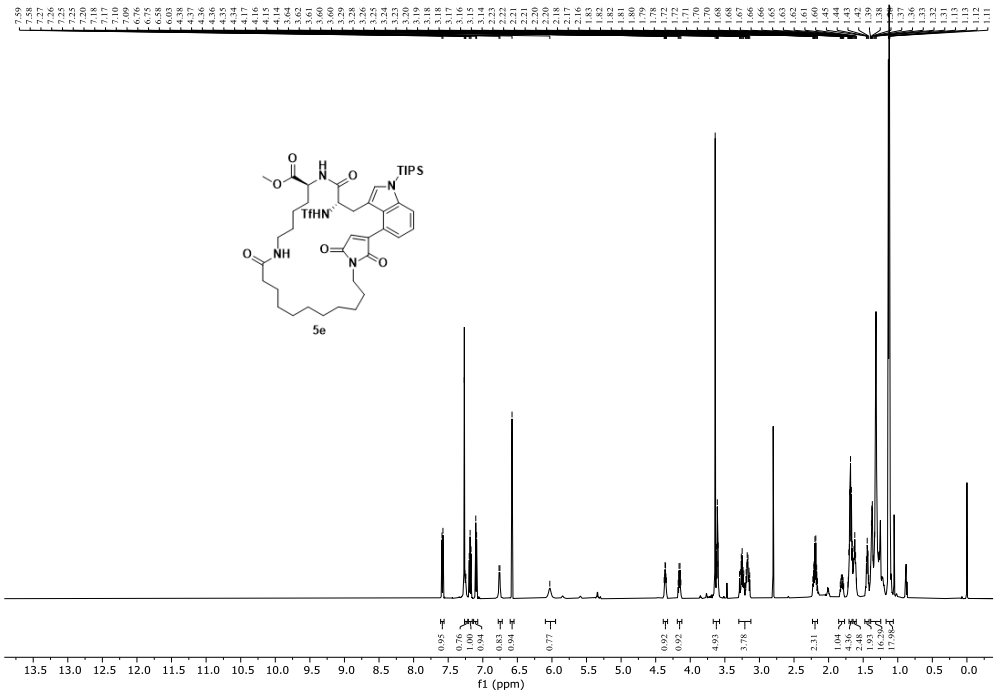


^{13}C{^{1}H} NMR of **5d** (126 MHz, $CDCl_3$)

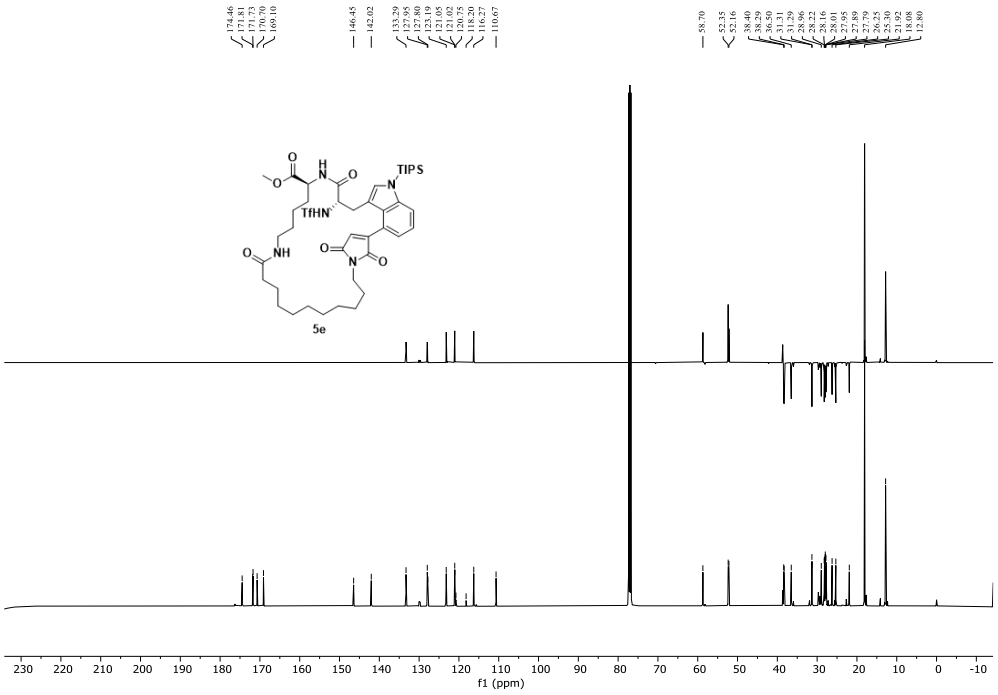


*Methyl (19S,22S)-2²,2⁵,13,21-tetraoxo-22-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-14,20-diaza-1(4,3)-indola-2(3,1)-pyrrolacyclotricosaphane-19-carboxylate (**5e**)*

^{1}H NMR of **5e** (600 MHz, $CDCl_3$)

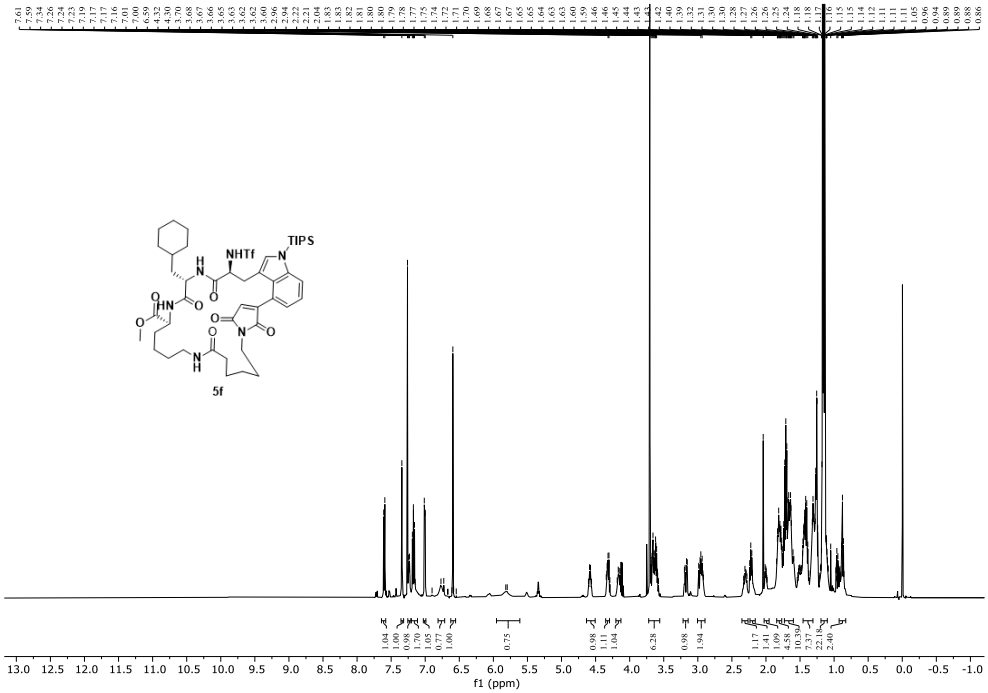


^{13}C{^{1}H} NMR of **5e** (126 MHz, $CDCl_3$)

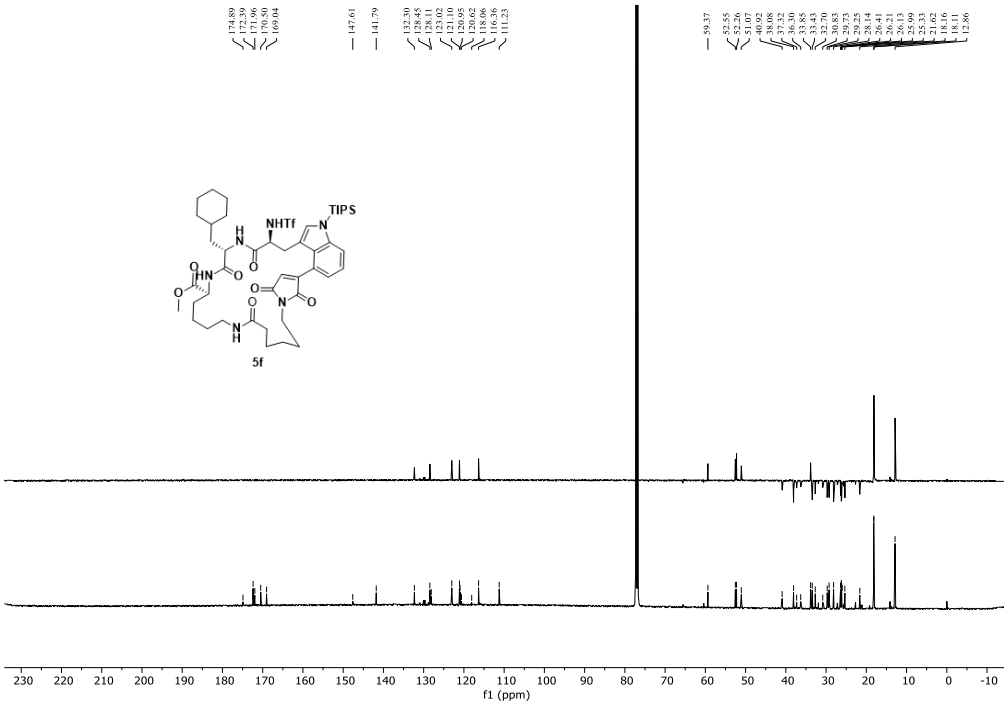


*Methyl (14S,17S,20S)-17-(cyclohexylmethyl)-2²,2⁵,8,16,19-pentaoxo-20-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-9,15,18-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohenicosaphane-14-carboxylate (**5f**)*

^{1}H NMR of **5f** (600 MHz, $CDCl_3$)

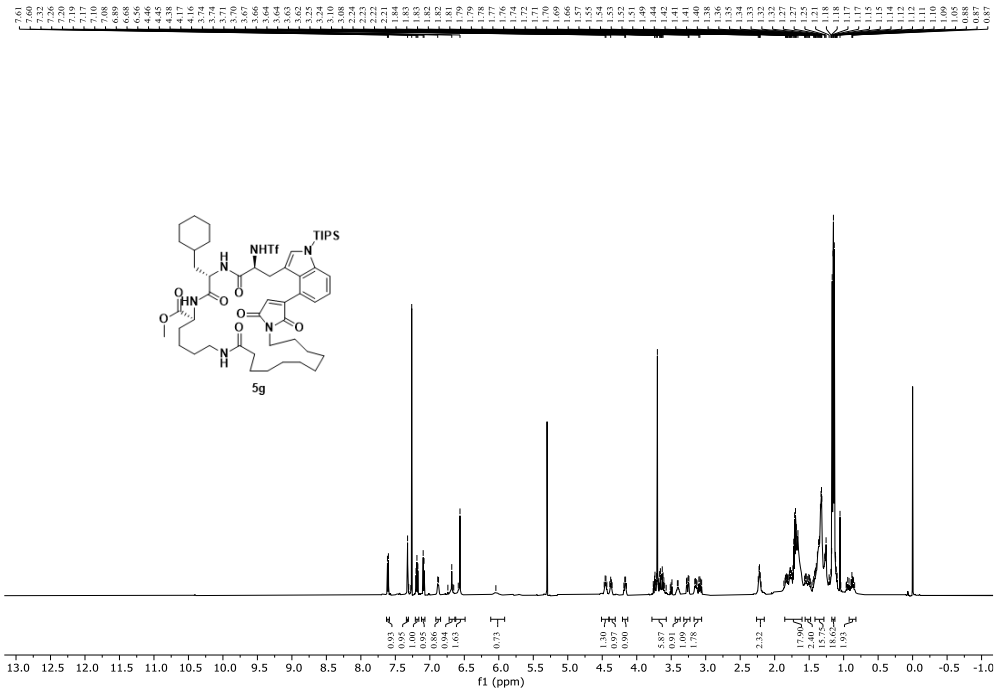


^{13}C{^{1}H} NMR of **5f** (126 MHz, $CDCl_3$)

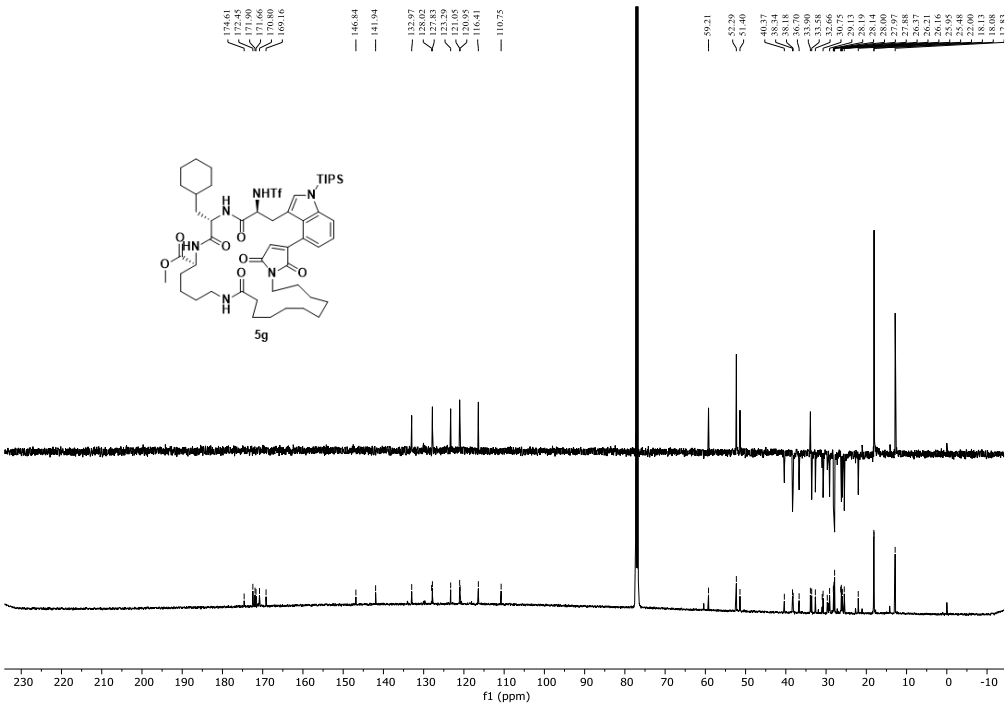


*Methyl (19S,22S,25S)-22-(cyclohexylmethyl)-2²,2⁵,13,21,24-pentaoxo-25-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-14,20,23-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexacosaphane-19-carboxylate (**5g**)*

^{1}H NMR of **5g** (600 MHz, $CDCl_3$)

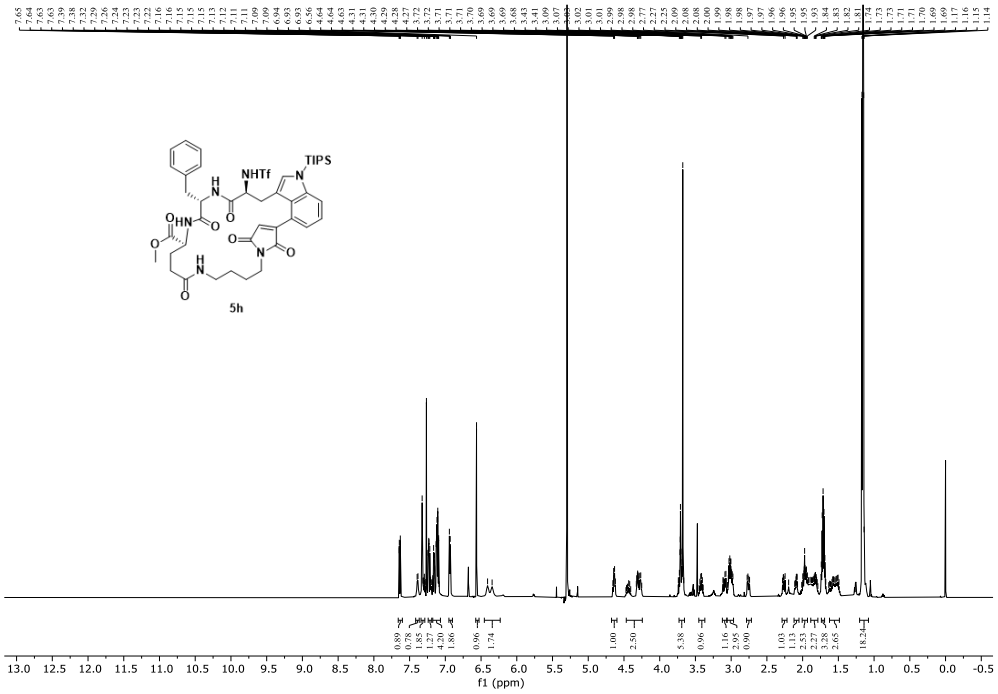


^{13}C{^{1}H} NMR of **5g** (126 MHz, $CDCl_3$)

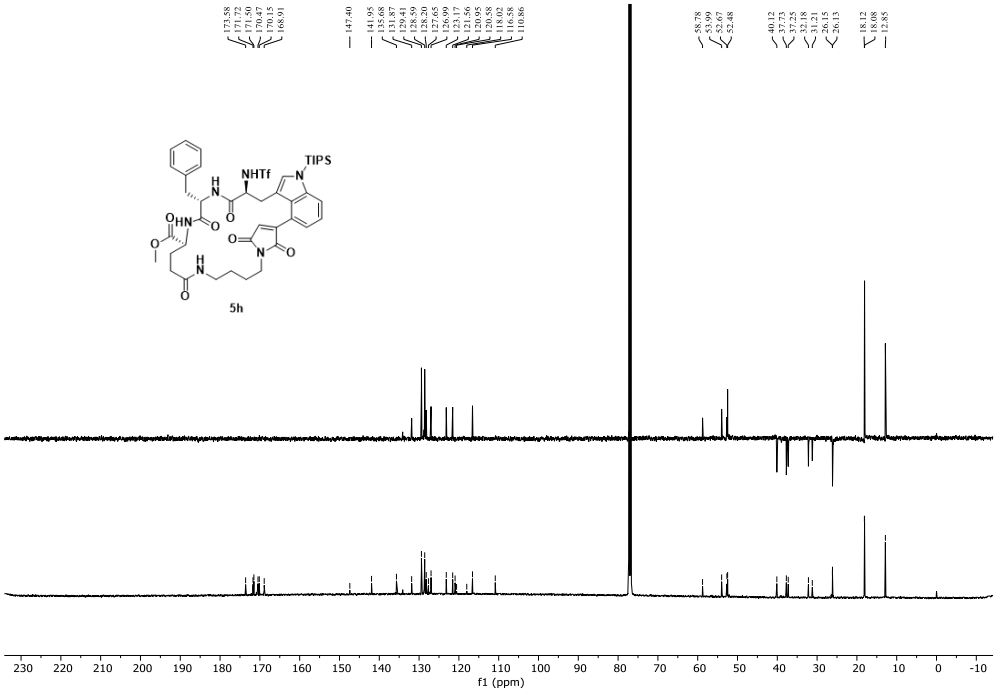


*Methyl (11S,14S,17S)-14-benzyl-2^2,2^5,8,13,16-pentaoxo-17-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,12,15-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-11-carboxylate (**5h**)*

^{1}H NMR of **5h** (600 MHz, $CDCl_3$)

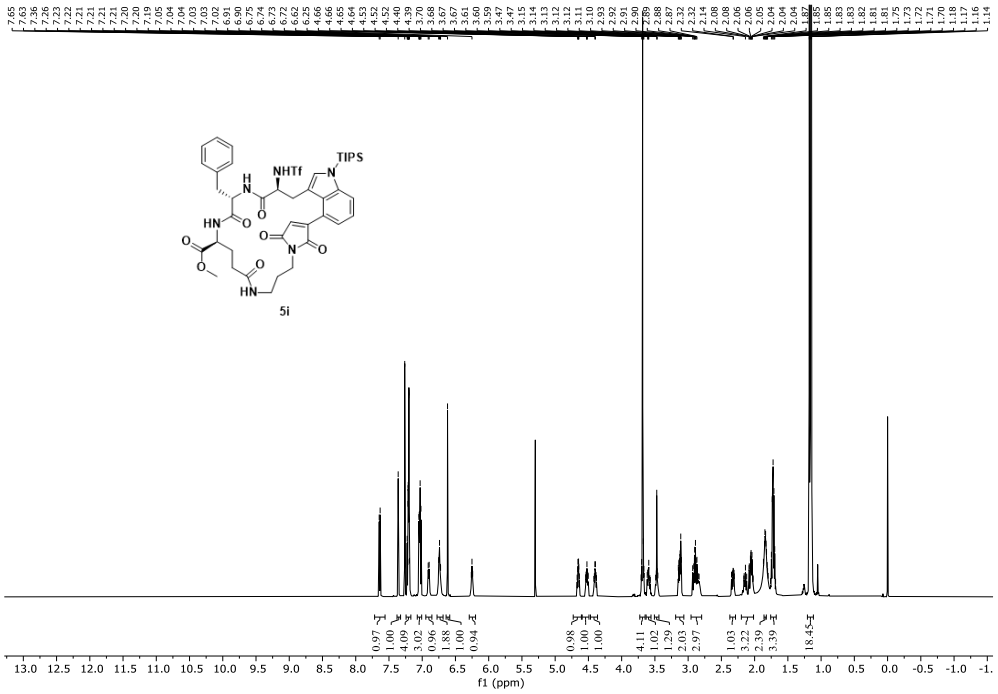


^{13}C{^{1}H} NMR of **5h** (126 MHz, $CDCl_3$)

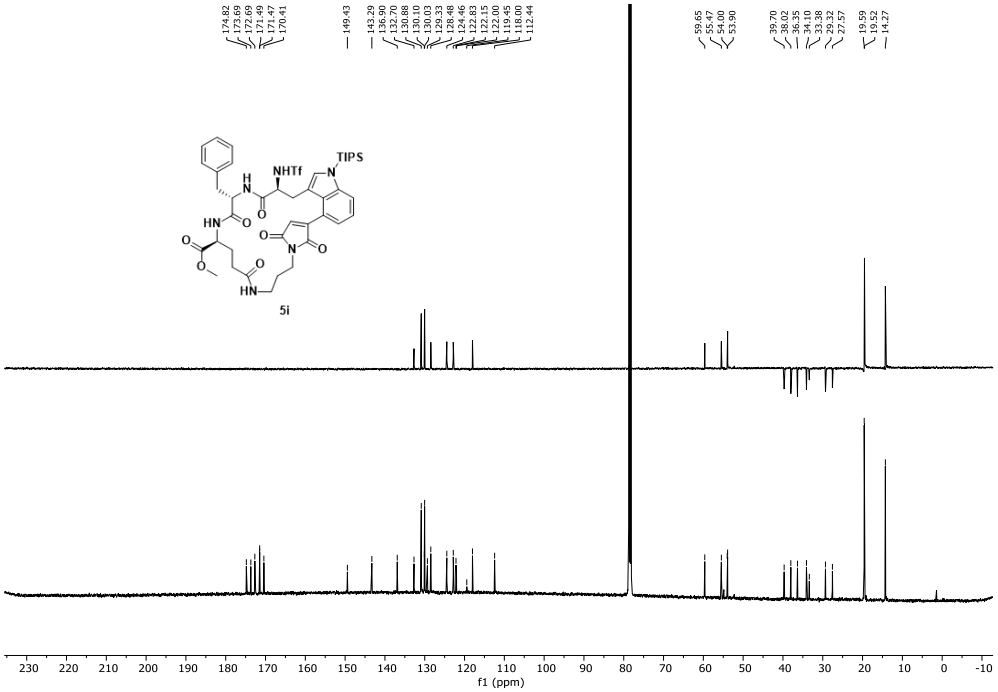


*Methyl (10S,13S,16S)-13-benzyl-2^2,2^5,7,12,15-pentaoxo-16-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-6,11,14-triaza-1(4,3)-indola-2(3,1)-pyrrolacycloheptadecaphane-10-carboxylate (**5i**)*

^{1}H NMR of **5i** (600 MHz, $CDCl_3$)

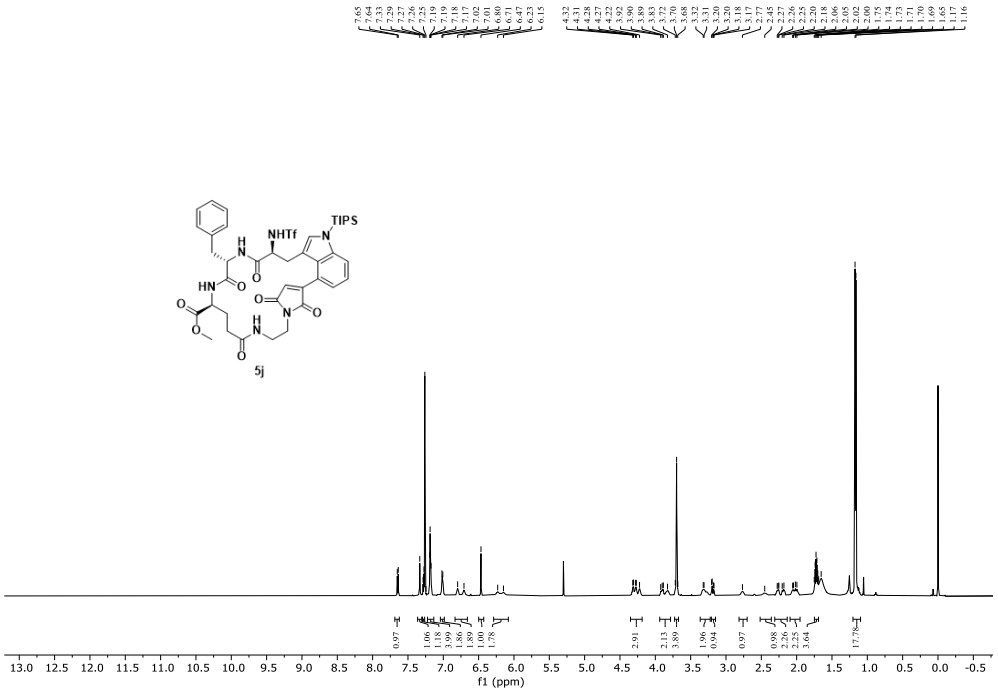


^{13}C{^{1}H} NMR of **5i** (126 MHz, $CDCl_3$)

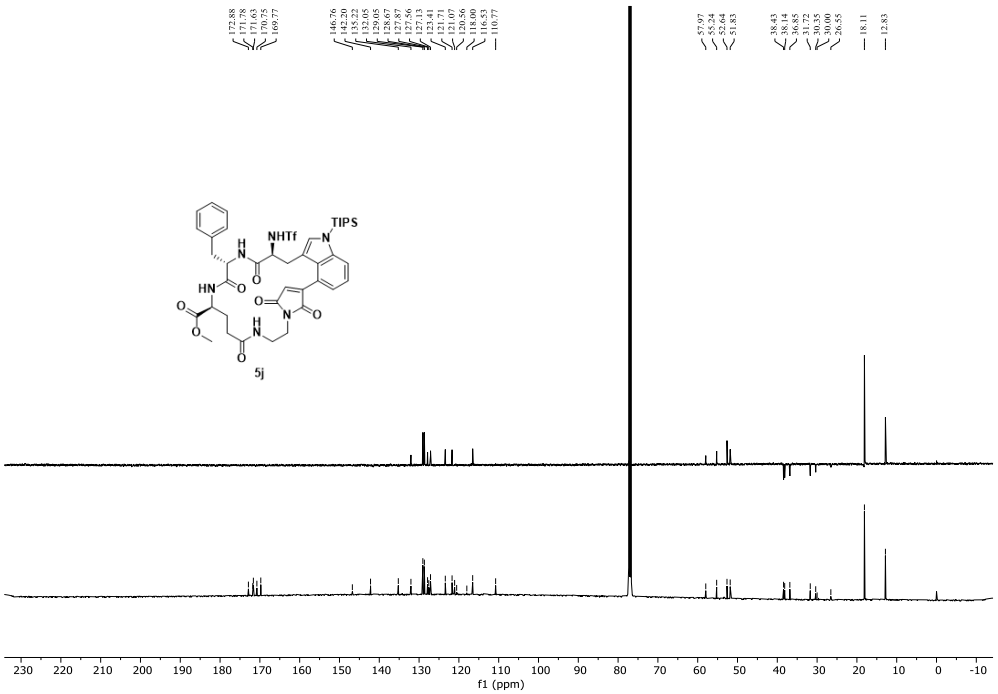


*Methyl (9S,12S,15S)-12-benzyl-2^2,2^5,6,11,14-pentaoxo-15-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-5,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-9-carboxylate (**5j**)*

^{1}H NMR of **5j** (600 MHz, $CDCl_3$)

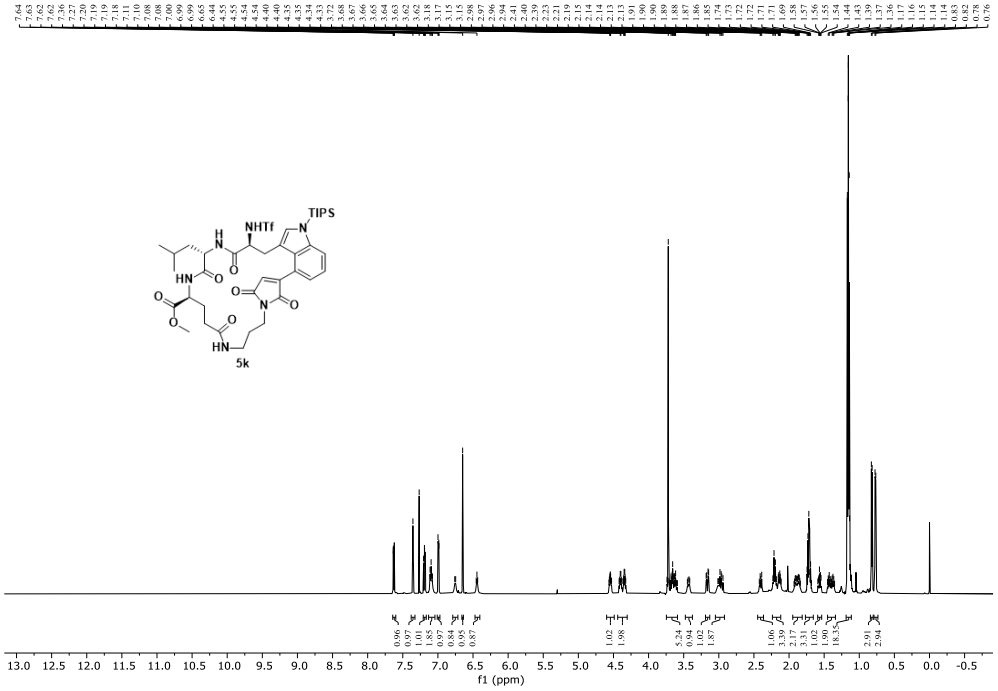


^{13}C{^{1}H} NMR of **5j** (126 MHz, $CDCl_3$)

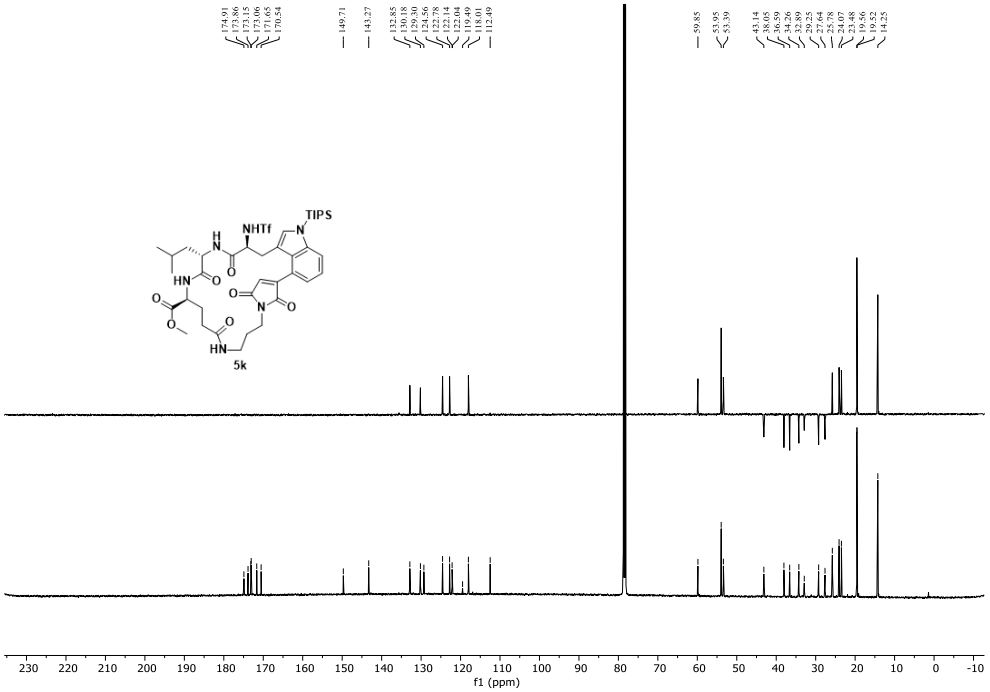


*Methyl (10S,13S,16S)-13-isobutyl-2²,2⁵,7,12,15-pentaoxo-16-((trifluoromethyl)sulfonamido)-1¹-(triisopropylsilyl)-2²,2⁵-dihydro-1¹H,2¹H-6,11,14-triaza-1(4,3)-indola-2(3,1)-pyrrolacycloheptadecaphane-10-carboxylate (**5k**)*

^{1}H NMR of **5k** (600 MHz, $CDCl_3$)

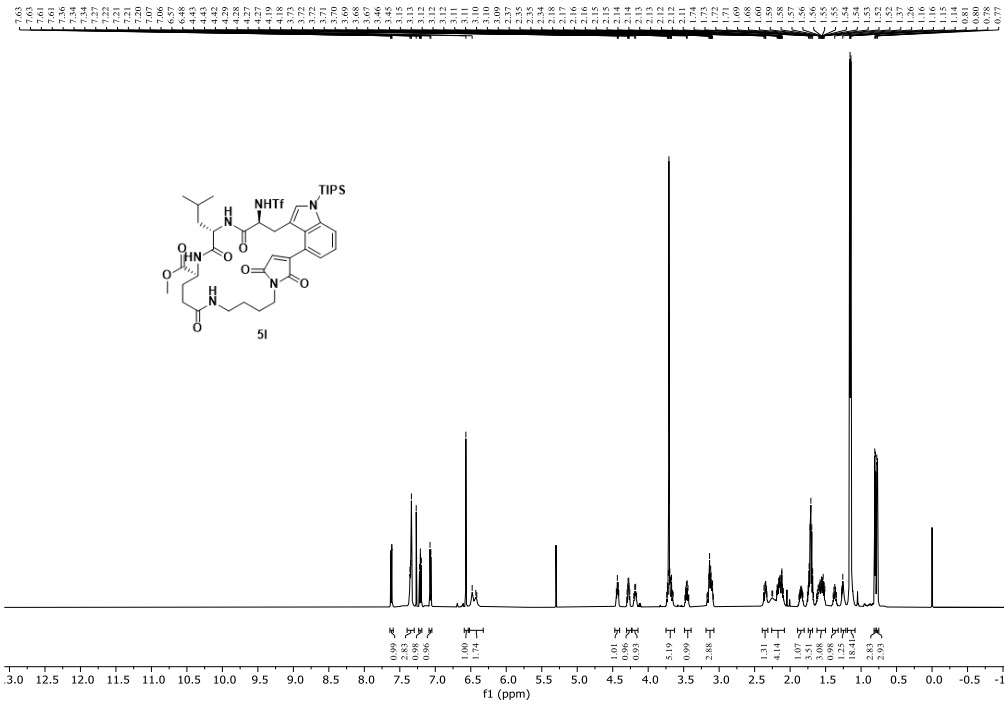


^{13}C{^{1}H} NMR of **5k** (126 MHz, $CDCl_3$)

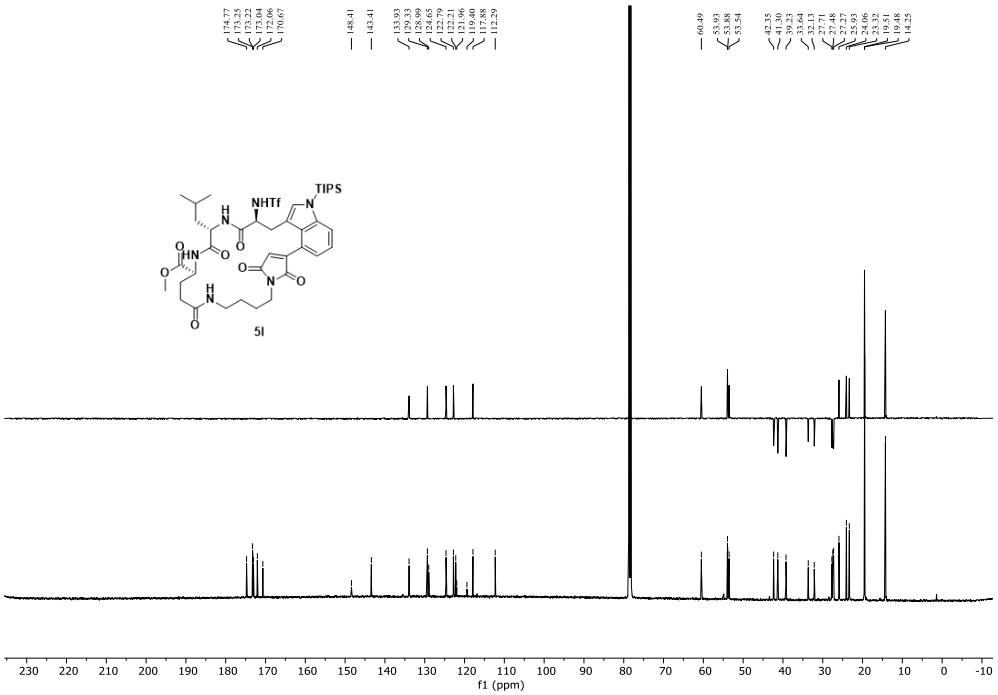


*Methyl (11S,14S,17S)-14-isobutyl-2^2,2^5,8,13,16-pentaoxo-17-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,12,15-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclooctadecaphane-11-carboxylate (**5l**)*

^{1}H NMR of **5l** (600 MHz, $CDCl_3$)

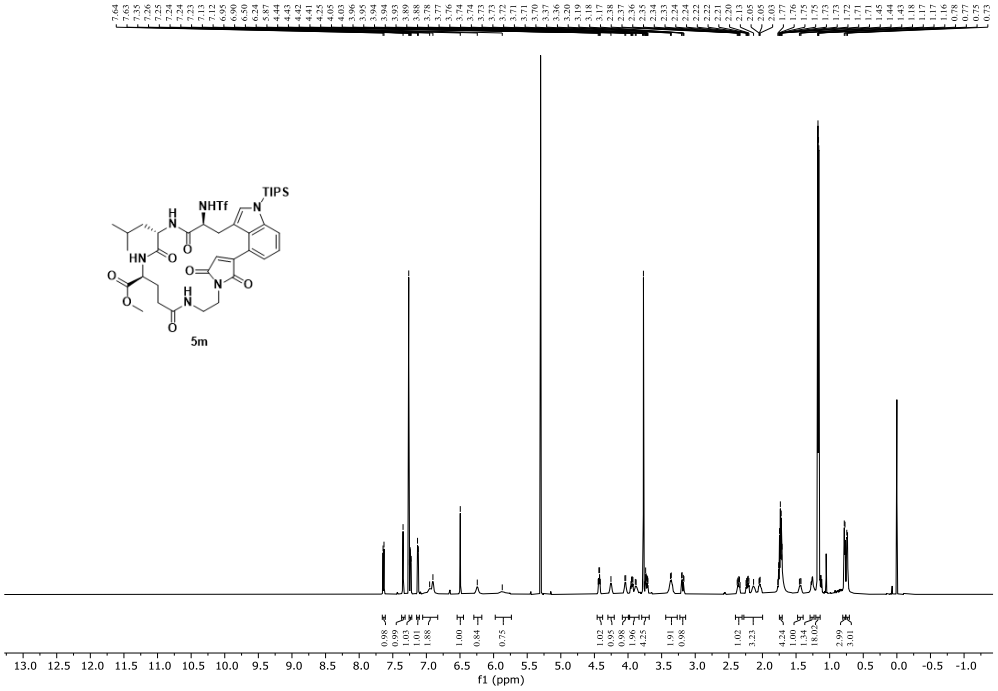


^{13}C{^{1}H} NMR of **5l** (126 MHz, $CDCl_3$)

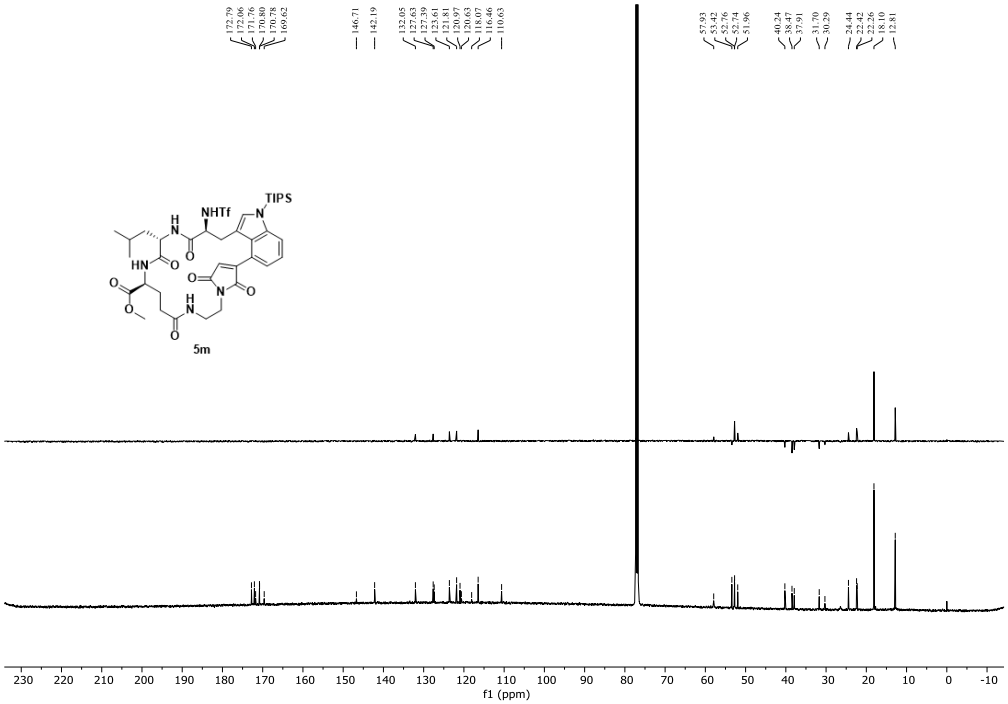


*Methyl (9S,12S,15S)-12-isobutyl-2^2,2^5,6,11,14-pentaoxo-15-((trifluoromethyl)sulfonamido)-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-5,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-9-carboxylate (**5m**)*

^{1}H NMR of **5m** (600 MHz, $CDCl_3$)

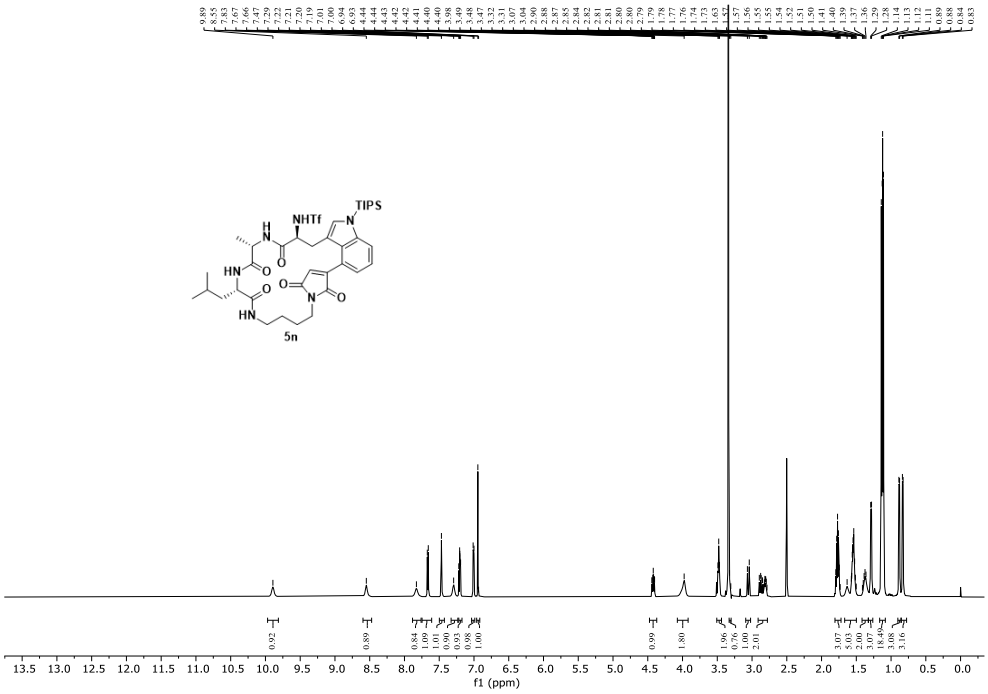


^{13}C{^{1}H} NMR of **5m** (126 MHz, $CDCl_3$)



*1,1,1-trifluoro-N-((9S,12S,15S)-9-isobutyl-12-methyl-2^2,2^5,8,11,14-pentaoxo-1^1-(triisopropylsilyl)-2^2,2^5-dihydro-1^{1}H,2^{1}H-7,10,13-triaza-1(4,3)-indola-2(3,1)-pyrrolacyclohexadecaphane-15-yl)methanesulfonamide (**5n**)*

^{1}H NMR of **5n** (600 MHz, $CDCl_3$)



^{13}C{^{1}H} NMR of **5n** (126 MHz, $CDCl_3$)