Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Total Synthesis of Apratoxin A and B using Matteson´s Homologation Approach

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Supporting Information

Experimental Section

General remarks: All air- or moisture-sensitive reactions were carried out in oven-dried glassware (75 °C) under an atmosphere of nitrogen. Dried solvents were distilled before use: THF was distilled from sodium/benzophenone, diisopropylamine was dried with CaH_2 before distillation. Anhydrous dichloromethane (DCM), DMSO and toluene were purchased from Acros Organics and stored under nitrogen. Petroleum ether (40-60 °C) and ethyl acetate were distilled prior to use. Zinc chloride was fused in vacuo (0.1 mbar) prior to use. The products were purified by flash chromatography on silica gel columns (Macherey-Nagel 60, 0.063-0.2 mm or 0.04-0.063 mm). For reversed-phase flash chromatography, a Büchi Reveleris® Prep Chromatography System and Büchi FlashPure Select C18 (30 µm spherical) columns were used. Preparative HPLC was performed on a Büchi Reveleris® Prep Chromatography System using a Phenomenex Luna® C18(2) 100 Å column (250 x 21.1 mm, 5 µm). Analytical TLC was performed on pre-coated silica gel plates (Macherey-Nagel, Polygram® SIL G/UV_{254}). Visualization was accomplished with UV-light, $KMnO_4$ solution or cerium(IV)/ammonium molybdate solution. Melting points were determined with a MEL-TEMP II apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with Bruker AV 400 Ultra Shield [400 MHz (^1H) and 100 MHz (^{13}C)] or Bruker AV 500 [500 MHz (^1H) and 125 MHz (^{13}C)] spectrometers in $CDCl_3$, DMSO-d_6, methanol-d_4 or CD_2Cl_2. Chemical shifts are reported in ppm (δ) with respect to TMS, and $CHCl_3$, DMSO-d_5, methanol-d_3 or $CHDCl_2$ was used as the internal standard. Selected signals for the minor diastereomers are extracted from the spectra of the diastereomeric mixture. Diastereomeric ratios were determined by HPLC [column: Phenomenex Luna® C18(2) 100 Å (50 x 4.6 mm, 3 µm)]. Optical rotations were measured with a PerkinElmer 241 or PerkinElmer 341 polarimeter at the sodium D line (589 nm), $[\alpha]_D^{20}$ values are given in 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded with a Finnigan MAT 95 spectrometer (CI) or a Bruker Daltonics maXis 4G hr-ToF spectrometer (ESI).

General procedure for Matteson homologations with dichloromethyllithium (GP 1).

LDA solution: *n*-butyllithium (1.6 M in hexanes, 1.25 eq.) was added dropwise to a solution of diisopropylamine (1.35 eq.) in anhydrous THF (0.2 ml/mmol) at –40 °C. The mixture was allowed to warm to room temperature and stirred for 20 min.

Homologation: The freshly prepared LDA solution was slowly added to a solution of the boronic ester (1.0 eq.) and anhydrous dichloromethane (3.0 eq.) in anhydrous THF (1.4 ml/mmol) at –40 °C. After stirring at this temperature for 10 min, a solution of zinc chloride (2.0–3.0 eq.) in anhydrous THF (0.6 ml/mmol $ZnCl_2$) was added and the mixture was stirred for 2 h at room temperature.

GP1a: Reaction with Grignard reagents or alkoxides as nucleophile: The mixture was cooled to 0 °C and the nucleophile solution was slowly added. After stirring for 1–3 d at room temperature, saturated NH_4Cl was added. The biphasic mixture was stirred for 5 min, then the layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography.

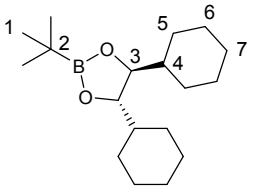
GP1b: Reaction with $LiBHEt_3$ as nucleophile: Saturated NH_4Cl was added to the mixture of the homologation step. After stirring for 5 min, the layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was directly used in the next step without further purification. $LiBHEt_3$ (1.0 M in THF, 1.1 eq.) was added dropwise to a solution of the crude α-chloroboronic ester in anhydrous THF (2.5 ml/mmol) at 0 °C. The mixture was warmed to

room temperature and stirred until NMR control indicated full conversion (16–19 h). After quenching with saturated NH_4Cl solution, the layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude product was purified by flash chromatography.

(4*S*,5*S*)-2-(*tert*-Butyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (2)

Diisopropyl *tert*-butylboronate **1**[1] and (*S*,*S*)-DICHED[2] were prepared according to literature procedures.

To a solution of 5.64 g (30.3 mmol, 1.2 eq.) diisopropyl *tert*-butylboronate **1** in 125 ml pentane were added 5.72 g (25.3 mmol, 1.0 eq.) (*S*,*S*)-DICHED at room temperature. After stirring for 18 h, the resulting clear solution was concentrated in vacuo and the residue was filtered through a short plug of silica (pentane, diethyl ether 98.5:1.5). **1** was obtained in 85 % yield (6.28 g, 21.5 mmol) as a colorless solid, R_f = 0.70 (pentane, diethyl ether 95:5); m.p. 72–73 °C (from pentane, diethyl ether); $[\alpha]_D^{20}$ = –49.2 (c = 1.0, $CHCl_3$).

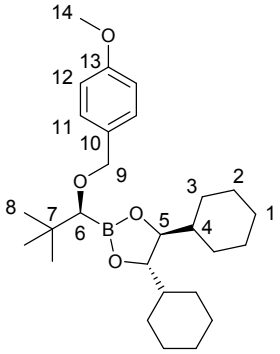


^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.85–1.00 (m, 11 H, 1-H, 6-H), 1.06 (m, 2 H, 5-H), 1.10–1.28 (m, 6 H, 5-H', 6-H'), 1.32 (m, 2 H, 4-H), 1.58 (m, 2 H, 5-H''), 1.68 (m, 2 H, 7-H), 1.70–1.84 (m, 6 H, 5-H''', 6-H'', 7-H'), 3.84 (m, 2 H, 3-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 26.0 (t, C-6), 26.0 (t, C-5), 26.5 (t, C-7), 27.3 (t, C-6'), 27.3 (q, C-1), 28.1 (t, C-5'), 43.1 (d, C-4), 83.1 (d, C-3).
The signal of C-2 could not be detected.
HRMS (CI) calcd for $C_{18}H_{34}BO_2$ $[M+H]^+$: 293.2646, found: 293.2633.

(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(*S*)-1-[(4-methoxybenzyl)oxy]-2,2-dimethylpropyl}-1,3,2-dioxaborolane (3)

According to GP1a, 6.70 g (22.9 mmol) **2** were treated with 4.42 ml (ρ = 1.32 g/ml, 68.8 mmol) dichloromethane, 17.9 ml (1.6 M in hexane, 28.7 mmol) *n*-butyllithium, 4.41 ml (ρ = 0.71 g/ml, 30.9 mmol) diisopropylamine and 6.25 g (45.8 mmol) zinc chloride. The nucleophile solution was prepared by adding 9.27 ml (ρ = 1.11 g/ml, 74.5 mmol, 3.25 eq.) 4-methoxybenzyl alcohol to a suspension of 2.75 g (60 % in mineral oil, 68.8 mmol, 3.0 eq.) sodium hydride in 14 ml anhydrous THF / 42 ml anhydrous DMSO and stirring at room temperature for 7 h. After addition of the nucleophile to the α-chloro boronic ester solution, the mixture was stirred for 3 d at room temperature, worked up and purified by flash chromatography (petroleum ether, ethyl acetate 97:3) to give **3** in 91 % yield (9.27 g, 21.0 mmol) as a colorless oil, R_f = 0.31 (petroleum ether, ethyl acetate 95:5); $[\alpha]_D^{20}$ = –12.2 (c = 1.0, $CHCl_3$).

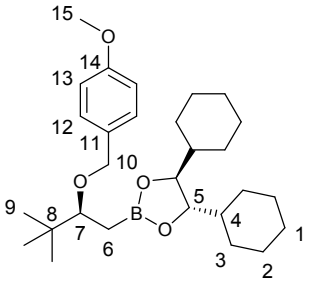
[1] H. C. Brown, M. Srebnik and T. E. Cole, *Organometallics* 1986, **5**, 11, 2300–2303.
[2] W. C. Hiscox and D. S. Matteson, *J. Org. Chem.* 1996, **61**, 8315–8316.



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.96 (s, 9 H, 8-H), 0.98–1.11 (m, 4 H, 2-H, 3-H), 1.12–1.35 (m, 8 H, 1-H, 2-H', 3-H‘, 4-H), 1.60 (m, 2 H, 3-H''), 1.68 (m, 2 H, 1-H'), 1.72–1.85 (m, 6 H, 2-H'', 3-H''‘), 2.89 (s, 1 H, 6-H), 3.80 (s, 3 H, 14-H), 3.87 (m, 2 H, 5-H), 4.35 (d, $^2J_{9a,9b}$ = 11.7 Hz, 1 H, 9-H_a), 4.54 (d, $^2J_{9b,9a}$ = 11.6 Hz, 1 H, 9-H_b), 6.85 (d, $^3J_{12,11}$ = 8.6 Hz, 2 H, 12-H), 7.27 (d, $^3J_{11,12}$ = 8.6 Hz, 2 H, 11-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 25.9 (t, C-2), 26.0 (t, C-3), 26.4 (t, C-1), 27.3 (q, C-8), 27.7 (t, C-2‘), 28.6 (t, C-3‘), 34.1 (s, C-7), 43.1 (d, C-4), 55.2 (q, C-14), 73.1 (t, C-9), 83.7 (d, C-5), 113.5 (d, C-12), 129.4 (d, C-11), 131.6 (s, C-10), 158.9 (s, C-13).
The signal of C-6 could not be detected.
HRMS (CI) calcd for $C_{27}H_{43}BO_4$ $[M]^+$: 442.3249, found: 442.3255.

(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(*S*)-2-[(4-methoxybenzyl)oxy]-3,3-dimethylbutyl}-1,3,2-dioxaborolane (4)

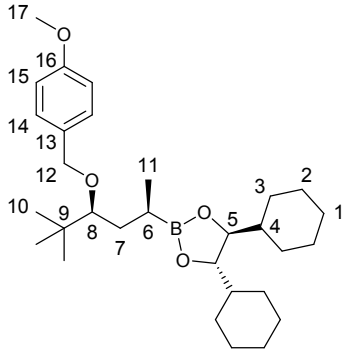
According to GP1b, 244 mg (551 µmol) **3** were treated with 106 µl (ρ = 1.32 g/ml, 1.65 mmol) dichloromethane, 431 µl (1.6 M in hexane, 689 µmol) *n*-butyllithium, 106 µl (ρ = 0.71 g/ml, 744 µmol) diisopropylamine, 225 mg (1.65 mmol) zinc chloride and 607 µl (1.0 M in THF, 607 µmol) $LiBHEt_3$. After stirring for 16 h at room temperature, the mixture was worked up and purified by flash chromatography (petroleum ether, ethyl acetate 97:3) to give **4** in 69 % yield (174 mg, 381 µmol) as a colorless solid, R_f = 0.27 (petroleum ether, ethyl acetate 95:5); m.p. 49–51 °C (from petroleum ether, ethyl acetate); $[\alpha]_D^{20}$ = –43.8 (c = 1.0, $CHCl_3$).



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.90 (s, 9 H, 9-H), 1.02 (m, 2 H, 2-H), 1.04–1.13 (m, 4 H, 3-H, 6-H), 1.13–1.24 (m, 6 H, 1-H, 2-H', 3-H‘), 1.29 (m, 2 H, 4-H), 1.58 (m, 2 H, 3-H''), 1.66 (m, 2 H, 1-H'), 1.70–1.78 (m, 4 H, 2-H'', 3-H''‘), 1.81 (m, 2 H, 2-H‘‘‘), 3.35 (dd, $^3J_{7,6a}$ = 6.8 Hz, $^3J_{7,6b}$ = 5.9 Hz, 1 H, 7-H), 3.80 (s, 3 H, 15-H), 3.83 (m, 2 H, 5-H), 4.41 (d, $^2J_{10a,10b}$ = 11.1 Hz, 1 H, 10-H_a), 4.66 (d, $^2J_{10b,10a}$ = 11.1 Hz, 1 H, 10-H_b), 6.85 (d, $^3J_{13,12}$ = 8.7 Hz, 2 H, 13-H), 7.27 (d, $^3J_{12,13}$ = 8.1 Hz, 2 H, 12-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 25.9 (t, C-2), 26.0 (t, C-3), 26.1 (q, C-9), 26.4 (t, C-1), 27.7 (t, C-2‘), 28.6 (t, C-3‘), 36.3 (s, C-8), 43.0 (d, C-4), 55.3 (q, C-15), 72.1 (t, C-10), 83.6 (d, C-5), 84.5 (d, C-7), 113.5 (d, C-13), 128.6 (d, C-12), 131.9 (s, C-11), 158.7 (s, C-14).
The signal of C-6 could not be detected.
HRMS (CI) calcd for $C_{28}H_{45}BO_4$ $[M]^+$: 456.3405, found: 456.3403.

(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(2*R*,4*S*)-4-[(4-methoxybenzyl)oxy]-5,5-dimethylhexan-2-yl}-1,3,2-dioxaborolane (5)

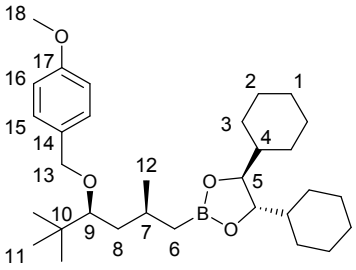
According to GP1a, 5.58 g (12.2 mmol) **4** were treated with 3.11 ml (ρ = 1.32 g/ml, 36.7 mmol) dichloromethane, 9.55 ml (1.6 M in hexane, 15.3 mmol) *n*-butyllithium, 2.35 ml (ρ = 0.71 g/ml, 16.5 mmol) diisopropylamine and 5.00 g (36.7 mmol) zinc chloride. To the α-chloro boronic ester solution were added 10.2 ml (3.0 M in THF, 30.6 mmol, 2.5 eq.) methylmagnesium iodide at 0 °C and the mixture was stirred for 15 h at room temperature, worked up and purified by flash chromatography (petroleum ether, ethyl acetate 97:3) to give **5** in 82 % yield (4.86 g, 10.0 mmol) as a colorless oil, R_f = 0.33 (petroleum ether, ethyl acetate 95:5); $[\alpha]_D^{20}$ = –70.7 (c =1.0, $CHCl_3$).



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.94 (s, 9 H, 10-H), 1.00–1.08 (m, $^3J_{11,6}$ = 7.3 Hz, 5 H, 2-H, 11-H), 1.08–1.27 (m, 8 H, 1-H, 2-H‘, 3-H), 1.33 (m, 2 H, 4-H), 1.38–1.50 (m, 2 H, 6-H, 7-H_a), 1.57–1.73 (m, 5 H, 1-H‘, 3-H', 7-H_b), 1.74–1.90 (m, 6 H, 2-H'', 3-H''), 3.11 (dd, $^3J_{8,7a}$ = 10.1 Hz, $^3J_{8,7b}$ = 2.1 Hz, 1 H, 8-H), 3.80 (s, 3 H, 17-H), 3.87 (m, 2 H, 5-H), 4.48 (d, $^2J_{12a,12b}$ = 10.3 Hz, 1 H, 12-H_a), 4.57 (d, $^2J_{12b,12a}$ = 10.4 Hz, 1 H, 12-H_b), 6.86 (d, $^3J_{15,14}$ = 8.7 Hz, 2 H, 15-H), 7.30 (d, $^3J_{14,15}$ = 8.6 Hz, 2 H, 14-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.1 (bs, C-6), 17.6 (q, C-11), 25.9 (t, C-2), 26.0 (t, C-3), 26.5 (t, C-1), 26.6 (q, C-10), 27.5 (t, C-2‘), 28.5 (t, C-3‘), 35.9 (t, C-7), 36.2 (s, C-9), 43.2 (d, C-4), 55.3 (q, C-17), 75.1 (t, C-12), 83.2 (d, C-5), 88.1 (d, C-8), 113.7 (d, C-15), 129.2 (d, C-14), 131.7 (s, C-13), 159.0 (s, C-16).
HRMS (CI) calcd for $C_{30}H_{49}BO_4$ $[M]^+$: 484.3718, found: 484.3719.

(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(2*S*,4*S*)-4-[(4-methoxybenzyl)oxy]-2,5,5-trimethylhexyl}-1,3,2-dioxaborolane (6)

According to GP1b, 4.83 g (9.97 mmol) **5** were treated with 2.54 ml (ρ = 1.32 g/ml, 29.9 mmol) dichloromethane, 7.79 ml (1.6 M in hexane, 12.5 mmol) *n*-butyllithium, 1.92 ml (ρ = 0.71 g/ml, 13.5 mmol) diisopropylamine, 4.08 g (29.9 mmol) zinc chloride and 11.0 ml (1.0 M in THF, 11.0 mmol) $LiBHEt_3$. After stirring for 19 h at room temperature, the mixture was worked up and purified by flash chromatography (petroleum ether, ethyl acetate 97:3) to give **6** in 86 % yield (4.25 g, 8.52 mmol) as a colorless oil, R_f = 0.30 (petroleum ether, ethyl acetate 95:5); $[\alpha]_D^{20}$ = –55.2 (c = 1.0, $CHCl_3$).



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.68 (dd, $^2J_{6a,6b}$ = 15.4 Hz, $^3J_{6a,7}$ = 8.9 Hz, 1 H, 6-H_a), 0.93 (s, 9 H, 10-H), 1.00 (d, $^3J_{12,7}$ = 6.7 Hz, 3 H, 12-H), 1.03–1.14 (m, 3 H, 2-H, 6-H_b), 1.09–1.37 (m, 10 H, 1-H, 2-H‘, 3-H, 4-H), 1.37–1.47 (m, 2 H, 8-H), 1.60 (m, 2 H, 3-H‘), 1.68 (m, 2 H, 1-H‘), 1.71–1.86 (m, 6 H, 2-H‘‘, 3-H‘‘), 1.97 (m, 1 H, 7-H), 3.11 (dd, $^3J_{9,8a}$ = 8.6 Hz, $^3J_{9,8b}$ = 3.1 Hz, 1 H, 9-H), 3.80 (s, 3 H, 18-H), 3.84 (m, 2 H, 5-H), 4.50 (d, $^2J_{13a,13b}$ = 10.3 Hz, 1 H, 13-H_a), 4.57 (d, $^2J_{13b,13a}$ = 10.5 Hz, 1 H, 13-H_b), 6.86 (d, $^3J_{16,15}$ = 8.7 Hz, 2 H, 16-H), 7.31 (d, $^3J_{15,16}$ = 8.7 Hz, 2 H, 15-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 23.9 (q, C-12), 25.9 (t, C-2), 26.0 (t, C-3), 26.5 (t, C-1), 26.5 (q, C-11), 26.8 (d, C-7), 27.5 (t, C-2‘), 28.5 (t, C-3‘), 36.1 (s, C-10), 41.1 (t, C-8), 43.1 (d, C-4), 55.3 (q, C-18), 74.4 (t, C-13), 83.3 (d, C-5), 85.7 (d, C-9), 113.6 (d, C-16), 129.2 (d, C-15), 131.7 (s, C-14), 158.9 (s, C-17).
The signal of C-6 could not be detected.
HRMS (CI) calcd for $C_{31}H_{51}BO_4$ $[M]^+$: 498.3875, found: 498.3866.

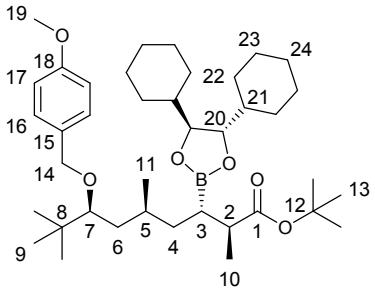
tert-Butyl (2*S*,3*S*,5*S*,7*S*)-3-[(4*S*,5*S*)-4,5-dicyclohexyl-1,3,2-dioxaborolan-2-yl]-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethylnonanoate (7)

LDA solution: 5.27 ml (1.6 M in hexanes, 8.42 mmol, 1.25 eq.) *n*-butyllithium were added dropwise to a solution of 1.30 ml (ρ = 0.71 g/ml, 9.10 mmol, 1.35 eq.) diisopropylamine in 1.7 ml anhydrous THF at –40 °C. The mixture was allowed to warm to room temperature and stirred for 20 min.

Homologation: The freshly prepared LDA solution was slowly added to a solution of 3.36 g (6.74 mmol, 1.0 eq.) boronic ester **6** and 1.41 ml (ρ = 2.49 g/ml, 20.2 mmol, 3.0 eq.) dibromomethane in 11.8 ml anhydrous THF at –78 °C. After stirring at this temperature for 60 min, a solution of 2.76 g (20.2 mmol, 3.0 eq.) zinc chloride in 12.1 ml anhydrous THF was added dropwise and the mixture was allowed to warm to –55 °C over 2 h. The cold solution was poured into a mixture of pentane and saturated NH_4Cl solution, the layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to yield the crude α-bromoboronic ester which was directly used in the next step.

Enolate alkylation: 5.27 ml (1.6 M in hexanes, 8.42 mmol, 1.25 eq.) *n*-butyllithium were added dropwise to a solution of 1.30 ml (ρ = 0.71 g/ml, 9.10 mmol, 1.35 eq.) diisopropylamine in 22 ml anhydrous THF at –40 °C. The mixture was allowed to warm to room temperature and stirred for 20 min followed by the addition of 1.27 ml (ρ = 0.865 g/ml, 8.42 mmol, 1.25 eq.) *tert*-butyl propionate at –78 °C. After stirring the enolate solution at this temperature for 30 min, a solution of the crude α-bromoboronic ester in 20 ml THF was added dropwise and the mixture was allowed to slowly warm to room temperature.

After stirring for 17 h, the reaction was quenched by the addition of saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted twice with pentane. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 96:4) gave **7** in 87 % yield (3.77 g, 5.88 mmol) as a colorless oil, R_f = 0.33 (petroleum ether, ethyl acetate 95:5); $[\alpha]_D^{20}$ = –34.0 (c =1.0, $CHCl_3$).

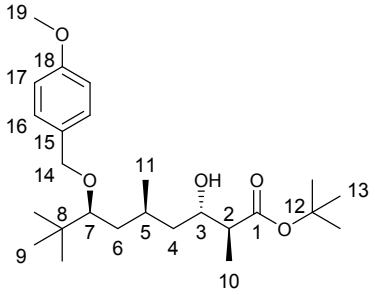


^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.91 (s, 9 H, 9-H), 0.93–1.23 (m, 17 H, 4-H_a, 10-H, 11-H, 22-H, 23-H, 24-H), 1.23–1.40 (m, 5 H, 3-H, 6-H, 21-H), 1.44 (s, 9 H, 13-H), 1.56 (m, 2 H, 22-H‘), 1.63 (m, 2 H, 24-H‘), 1.67–1.86 (m, 8 H, 4-H_b, 5-H, 22-H‘‘, 23-H‘), 2.53 (dq, $^3J_{2,10}$ = 7.2 Hz, $^3J_{2,3}$ = 4.6 Hz, 1 H, 2-H), 3.07 (dd, $^3J_{7,6b}$ = 7.1 Hz, $^3J_{7,6a}$ = 3.3 Hz, 1 H, 7-H), 3.74–3.86 (m, 5 H, 19-H, 20-H), 6.85 (d, $^3J_{17,16}$ = 8.7 Hz, 2 H, 17-H), 7.28 (d, $^3J_{16,17}$ = 8.6 Hz, 2 H, 16-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 16.0 (q, C-10), 20.7 (q, C-11), 25.9 (t, C-23), 26.0 (t, C-22), 26.4 (q, C-9), 26.5 (t, C-24), 27.9 (t, C-23‘), 28.1 (q, C-13), 28.5 (t, C-22‘), 30.3 (d, C-5), 35.9 (t, C-4), 36.1 (s, C-8), 40.6 (t, C-6), 42.8 (d, C-2), 42.9 (d, C-21), 55.3 (q, C-19), 73.4 (t, C-14), 79.7 (s, C-12), 83.4 (d, C-20), 86.0 (d, C-7), 113.6 (d, C-17), 128.9 (d, C-16), 131.9 (s, C-15), 158.8 (s, C-18), 176.2 (s, C-1).
The signal of C-3 could not be detected.
HRMS (CI) calcd for $C_{39}H_{66}BO_6$ $[M+H]^+$: 641.4947, found: 641.4959.

tert-Butyl (2*S*,3*S*,5*S*,7*S*)-3-hydroxy-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethylnonanoate (8)

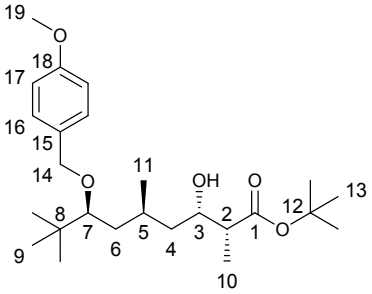
To a solution of 3.86 g (6.02 mmol, 1.0 eq.) boronic ester **7** in 12 ml THF were added 2.80 ml (33 % in water, 30.1 mmol, 5.0 eq.) hydrogen peroxide followed by a solution of 1.21 g (30.1 mmol, 5.0 eq.) sodium hydroxide in 12 ml water at 0 °C. After stirring for 1.5 at room temperature, brine was added and the mixture was extracted three times with diethyl ether. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 9:1, 85:15) gave **8** (d.r. *anti*:*syn* = 90:10 according to ^{1}H-NMR) in 70 % yield (1.79 g, 4.23 mmol) as a colorless oil, R_f = 0.38 (petroleum ether, ethyl acetate 8:2); [α]$_D^{20}$ = –35.9 (c =1.0, $CHCl_3$).

major diastereomer (anti diastereomer):



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 9 H, 9-H), 0.97 (d, $^3J_{11,5}$ = 6.6 Hz, 3 H, 11-H), 1.08 (ddd, $^2J_{4a,4b}$ = 13.4 Hz, $^3J_{4a,5}$ = 11.0 Hz, $^3J_{4a,3}$ = 2.0 Hz, 1 H, 4-H_a), 1.19 (d, $^3J_{10,2}$ = 7.1 Hz, 3 H, 10-H), 1.34 (ddd, $^2J_{6a,6b}$ = 13.9 Hz, $^3J_{6a,5}$ = 9.7 Hz, $^3J_{6a,7}$ = 2.2 Hz, 1 H, 6-H_a), 1.41–1.55 (m, 10 H, 6-H_b, 13-H), 1.64 (ddd, $^2J_{4b,4a}$ = 13.6 Hz, $^3J_{4b,3}$ = 11.0 Hz, $^3J_{4b,5}$ = 2.4 Hz, 1 H, 4-H_b), 2.04 (m, 1 H, 5-H), 2.38 (dq, $^3J_{2,3} \approx {}^3J_{2,10}$ = 6.9 Hz, 1 H, 2-H), 2.63 (bs, 1 H, OH), 3.08 (dd, $^3J_{7,6b}$ = 9.0 Hz, $^3J_{7,6a}$ = 2.2 Hz, 1 H, 7-H), 3.75 (ddd, $^3J_{3,4b}$ = 10.8 Hz, $^3J_{3,2}$ = 6.4 Hz, $^3J_{3,4a}$ = 2.0 Hz, 1 H, 3-H), 3.79 (s, 3 H, 19-H), 4.50 (d, $^2J_{14a,14b}$ = 10.4 Hz, 1 H, 14-H_a), 4.63 (d,

$^2J_{14b,14a}$ = 10.5 Hz, 1 H, 14-H_b), 6.86 (d, $^3J_{17,16}$ = 8.7 Hz, 2 H, 17-H), 7.30 (d, $^3J_{16,17}$ = 8.6 Hz, 2 H, 16-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 14.3 (q, C-10), 20.9 (q, C-11), 26.3 (d, C-5), 26.5 (q, C-9), 28.1 (q, C-13), 36.1 (s, C-8), 39.8 (t, C-6), 41.3 (t, C-4), 46.8 (d, C-2), 55.2 (q, C-19), 71.2 (d, C-3), 74.3 (t, C-14), 81.0 (s, C-12), 85.3 (d, C-7), 113.7 (d, C-17), 129.2 (d, C-16), 131.6 (s, C-15), 158.9 (s, C-18), 175.6 (s, C-1).
minor diastereomer (syn diastereomer, selected signals):

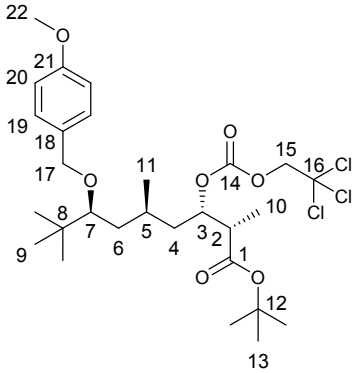


^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.05 (dd, $^3J_{7,6b}$ = 8.4 Hz, $^3J_{7,6a}$ = 3.2 Hz, 1 H, 7-H), 3.92 (ddd, $^3J_{3,4b}$ = 10.4 Hz, $^3J_{3,2}$ = 3.9 Hz, $^3J_{3,4a}$ = 1.9 Hz, 1 H, 3-H), 3.79 (s, 3 H, 19-H), 4.48 (d, $^2J_{14a,14b}$ = 10.5 Hz, 1 H, 14-H_a), 4.57 (d, $^2J_{14b,14a}$ = 11.1 Hz, 1 H, 14-H_b).
HRMS (CI) calcd for $C_{25}H_{43}O_5$ $[M+H]^+$: 423.3105, found: 423.3119.

tert-Butyl (2*S*,3*S*,5*S*,7*S*)-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoate (9)

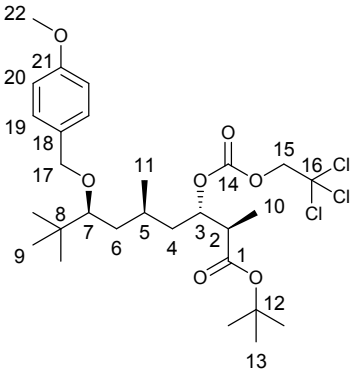
To a solution of 1.79 g (4.23 mmol, 1.0 eq.) alcohol **8**, 2.05 ml (ρ = 0.978 g/ml, 25.4 mmol, 6.0 eq.) pyridine and 5 mg (42 µmol, 1 mol-%) DMAP in 42 ml anhydrous DCM were added 1.75 ml (ρ = 1.539 g/ml, 12.7 mmol, 3.0 eq.) Troc-Cl at 0 °C. The mixture was warmed to room temperature and stirred for 5 h. Diethyl ether was added and the organic layer was washed twice with 0.25 M HCl, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 95:5, 9:1) gave the title compound (d.r. *anti*:*syn* = 90:10 according to ^{1}H-NMR) in 93 % yield (2.36 g, 3.95 mmol) as a colorless oil, R_f = 0.31 (petroleum ether, ethyl acetate 9:1); $[\alpha]_D^{20}$ = –19.6 (c =1.0, $CHCl_3$).

major diastereomer (anti diastereomer):



^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.92 (s, 9 H, 9-H), 1.04 (d, $^3J_{11,5}$ = 6.5 Hz, 3 H, 11-H), 1.09–1.24 (m, $^3J_{10,2}$ = 7.1 Hz, 4 H, 4-H_a, 10-H), 1.34 (ddd, $^2J_{6a,6b}$ = 14.1 Hz, $^3J_{6a,5}$ = 9.5 Hz, $^3J_{6a,7}$ = 2.0 Hz, 1 H, 6-H_a), 1.40–1.56 (m, 10 H, 6-H_b, 13-H), 1.80 (m, 1 H, 5-H), 1.95 (ddd, $^2J_{4b,4a}$ = 13.6 Hz, $^3J_{4b,3}$ = 11.1 Hz, $^3J_{4b,5}$ = 1.6 Hz, 1 H, 4-H_b), 2.81 (dq, $^3J_{2,3} \approx {}^3J_{2,10}$ = 7.0 Hz, 1 H, 2-H), 3.06 (dd, $^3J_{7,6b}$ = 9.3 Hz, $^3J_{7,6a}$ = 2.2 Hz, 1 H, 6-H_a), 3.79 (s, 3 H, 22-H), 4.46 (d, $^2J_{15a,15b}$ = 11.9 Hz, 1 H, 15-H_a), 4.50 (d, $^2J_{17a,17b}$ = 10.6 Hz, 1 H, 17-H_a), 4.58 (d, $^2J_{17b,17a}$ = 10.6 Hz, 1 H, 17-H_b), 4.74 (d, $^2J_{15b,15a}$ = 11.9 Hz, 1 H, 15-H_b), 5.21 (ddd, $^3J_{3,4b}$ = 10.9 Hz,

$^3J_{3,2}$ = 6.5 Hz, $^3J_{3,4a}$ = 1.3 Hz, 1 H, 3-H), 6.85 (d, $^3J_{20,19}$ = 8.7 Hz, 2 H, 20-H), 7.27 (d, $^3J_{19,20}$ = 8.8 Hz, 2 H, 20-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.1 (q, C-10), 20.9 (q, C-11), 26.2 (d, C-5), 26.5 (q, C-9), 28.0 (q, C-13), 36.1 (s, C-8), 37.2 (t, C-4), 39.8 (t, C-6), 44.6 (d, C-2), 55.3 (q, C-22), 74.4 (t, C-17), 76.6 (t, C-15), 78.4 (d, C-3), 81.1 (s, C-12), 85.1 (d, C-7), 94.4 (s, C-16), 113.7 (d, C-20), 128.8 (d, C-19), 131.4 (s, C-18), 153.8 (s, C-14), 158.9 (s, C-21), 172.1 (s, C-1).
minor diastereomer (syn diastereomer, selected signals):

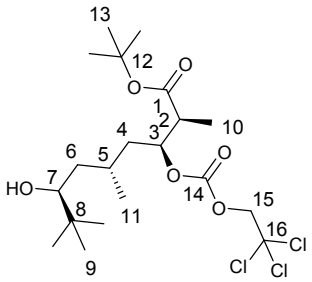


^{1}H-NMR (400 MHz, $CDCl_3$): δ = 2.65 (dq, $^3J_{2,3} \approx {}^3J_{2,10}$ = 7.0 Hz, 1 H, 2-H), 3.11 (dd, $^3J_{7,6b}$ = 9.3 Hz, $^3J_{7,6a}$ = 2.7 Hz, 1 H, 6-H$_a$), 3.79 (s, 3 H, 22-H), 4.45 (d, $^2J_{15a,15b}$ = 11.9 Hz, 1 H, 15-H$_a$), 5.14 (ddd, $^3J_{3,4b}$ = 10.7 Hz, $^3J_{3,2}$ = 7.2 Hz, $^3J_{3,4a}$ = 1.9 Hz, 1 H, 3-H), 6.85 (d, $^3J_{20,19}$ = 8.7 Hz, 2 H, 20-H), 7.27 (d, $^3J_{19,20}$ = 8.8 Hz, 2 H, 20-H).
HRMS (CI) calcd for $C_{28}H_{43}O_7Cl_3$ $[M]^+$: 596.2069, found: 596.2080.

tert-Butyl (2*S*,3*S*,5*R*,7*S*)-7-hydroxy-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoate (10)

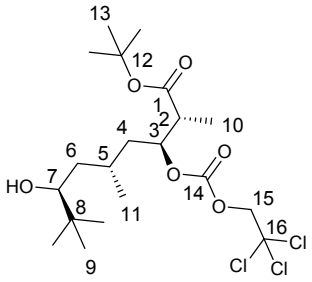
To a solution of 2.32 g (3.88 mmol, 1.0 eq.) PMB ether **9** in 23 ml DCM and 2.6 ml water were added 1.06 g (4.66 mmol, 1.2 eq.) DDQ at 0 °C. After stirring at this temperature for 1 h, the mixture was filtered. The filtrate was washed twice with saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 85:15) gave the title compound (d.r. *anti*:*syn* = 90:10 according to ^{1}H-NMR) in 92 % yield (1.77 g, 3.56 mmol) as a colorless oil, R_f = 0.40 (petroleum ether, ethyl acetate 8:2); $[\alpha]_D^{20}$ = –27.1 (c =1.0, $CHCl_3$).

major diastereomer (anti diastereomer):



^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.87 (s, 9 H, 9-H), 1.02 (d, $^3J_{11,5}$ = 6.6 Hz, 3 H, 11-H), 1.15 (d, $^3J_{10,2}$ = 7.3 Hz, 3 H, 10-H), 1.18 (m, 1 H, 4-H$_a$), 1.30 (m, 2 H, 6-H), 1.37–1.59 (m, 10 H, 13-H, OH), 1.76 (m, 1 H, 5-H), 1.83 (ddd, $^2J_{4b,4a}$ = 14.0 Hz, $^3J_{4b,3}$ = 11.0 Hz, $^3J_{4b,5}$ = 2.4 Hz, 1 H, 4-H$_b$), 2.77 (dq, $^3J_{2,3} \approx {}^3J_{2,10}$ = 7.0 Hz, 1 H, 2-H), 3.25 (dd, $^3J_{7,6b}$ = 9.8 Hz, $^3J_{7,6a}$ = 1.9 Hz, 1 H, 7-H), 4.74 (d, $^2J_{15a,15b}$ = 12.0 Hz, 1 H, 15-H$_a$), 4.77 (d, $^2J_{15b,15a}$ = 12.0 Hz, 1 H, 15-H$_b$), 5.16 (ddd, $^3J_{3,4b}$ = 10.4 Hz, $^3J_{3,2}$ = 6.9 Hz, $^3J_{3,4a}$ = 1.6 Hz, 1 H, 3-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.1 (q, C-10), 20.8 (q, C-11), 25.6 (q, C-9), 26.2 (d, C-5), 28.0 (q, C-13), 34.9 (s, C-8), 36.7 (t, C-4), 39.4 (t, C-6), 44.5 (d, C-2), 76.7 (t, C-15), 77.0 (d, C-7), 78.6 (d, C-3), 81.0 (s, C-12), 94.5 (s, C-16), 153.7 (s, C-14), 172.2 (s, C-1).
minor diastereomer (syn diastereomer, selected signals):

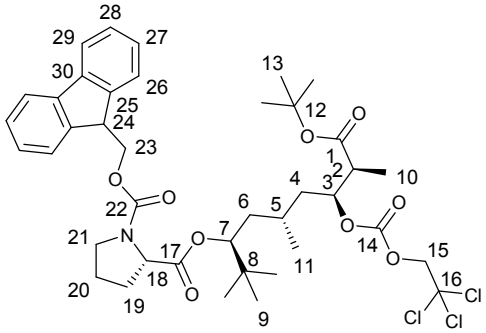


^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.60 (dq, $^{3}J_{2,3} \approx {}^{3}J_{2,10}$ = 7.1 Hz, 1 H, 2-H), 5.11 (ddd, $^{3}J_{3,4b}$ = 9.8 Hz, $^{3}J_{3,2}$ = 7.3 Hz, $^{3}J_{3,4a}$ = 2.5 Hz, 1 H, 3-H).
HRMS (CI) calcd for $C_{20}H_{36}O_6Cl_3$ $[M+H]^+$: 477.1572, found: 477.1570.

N-[(9*H*-Fluoren-9-yl)methyl] 2-({3*S*,5*S*,7*S*,8*S*}-9-{*tert*-butoxy}-2,2,5,8-tetramethyl-9-oxo-7-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonan-3-yl) (*S*)-pyrrolidine-1,2-dicarboxylate (11)

(*S*)-Fmoc-Pro-Cl was prepared as described previously.[3]

To a solution of 50 mg (104 µmol, 1.0 eq.) alcohol **10** in 1 ml anhydrous toluene were added 91 µl (522 µmol, 5.0 eq.) DIPEA, 26 mg (209 µmol, 2.0 eq.) DMAP and 93 mg (261 µmol, 2.5 eq.) (*S*)-Fmoc-Pro-Cl at 0 °C. After stirring the resulting white suspension for 1.5 h at room temperature, ethyl acetate was added and the mixture was washed with 1 M HCl, saturated $NaHCO_3$ solution and brine. The organic layer was dried over Na_2SO_4, concentrated in vacuo and purified by flash chromatography (petroleum ether, ethyl acetate 85:15) to give the title compound in 95 % yield (79 mg, 100 µmol) as a colorless foam, R_f = 0.31 (petroleum ether, ethyl acetate 8:2); $[\alpha]_D^{20}$ = –58.3 (c =1.0, $CHCl_3$).



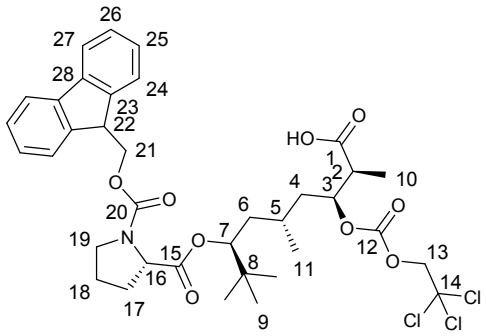
^{1}H-NMR (500 MHz, DMSO-d_6, 100 °C): δ = 0.80–0.91 (m, 12 H, 9-H, 11-H), 1.06 (d, $^{3}J_{10,2}$ = 7.2 Hz, 3 H, 10-H), 1.27 (m, 1 H, 4-H_a), 1.37–1.44 (m, 10 H, 6-H_a, 13-H), 1.46–1.57 (m, 2 H, 5-H, 6-H_b), 1.81 (ddd, $^{2}J_{4b,4a}$ = 14.4 Hz, $^{3}J_{4b,3}$ = 9.9 Hz, $^{3}J_{4b,5}$ = 2.7 Hz, 1 H, 4-H_b), 1.85–1.99 (m, 3 H, 19-H_a, 20-H), 2.25 (m, 1 H, 19-H_b), 2.70 (m, 1 H, 2-H), 3.42 (t, $^{3}J_{21,20}$ = 6.8 Hz, 2 H, 21-H), 4.12–4.48 (m, 4 H, 18-H, 23-H, 24-H), 4.68 (dd, $^{3}J_{7,6a}$ = 9.4 Hz, $^{3}J_{7,6b}$ = 1.9 Hz, 1 H, 7-H), 4.84 (m, 2 H, 15-H), 4.98 (m, 1 H, 3-H), 7.33 (m, 2 H, 27-H), 7.41 (ddd, $^{3}J_{28,27} \approx {}^{3}J_{28,29}$ = 7.5 Hz, $^{4}J_{28,26}$ = 0.9 Hz, 2 H, 28-H), 7.63 (m, 2 H, 26-H), 7.86 (d, $^{3}J_{29,28}$ = 7.5 Hz, 2 H, 29-H).
^{13}C-NMR (125 MHz, DMSO-d_6, 100 °C): δ = 11.8 (q, C-10), 19.5 (q, C-11), 22.9 (bs, C-20), 25.0 (q, C-9), 25.7 (d, C-5), 27.2 (q, C-13), 29.2 (bs, C-19), 33.9 (s, C-8), 36.5 (t, C-4), 37.3

[3] L. A. Carpino, B. J. Cohen, K. E. Stephens Jr., S. Y. Sadat-Aalaee, J. H. Tien, and D. C. Langridge, *J. Org. Chem.* 1986, **51**, 19, 3732–373.

(t, C-6), 43.7 (d, C-2), 45.8 (bs, C-21), 46.5 (d, C-24), 58.9 (d, C-18), 66.3 (t, C-23), 75.9 (t, C-15), 77.9 (d, C-8), 78.7 (d, C-3), 79.9 (s, C-12), 94.5 (s, C-16), 119.5 (d, C-29), 124.4 (d, C-26), 126.5 (d, C-27), 127.1 (d, C-28), 140.3 (s, C-30), 143.4 (s, C-25), 152.4 (s, C-14), 153.4 (bs, C-22), 170.9 (s, C-1), 171.3 (s, C-17).
HRMS (ESI) calcd for $C_{40}H_{53}NO_9Cl_3$ $[M+H]^+$: 796.2780, found: 796.2778.

(2*S*,3*S*,5*S*,7*S*)-7-[({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}-L-prolyl)oxy]-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoic acid (12)

24 ml Trifluoroacetic acid were added to a solution of 2.41 g (3.02 mmol, 1.0 eq.) *tert*-butyl ester **11** in 24 ml DCM at room temperature. After stirring at this temperature for 24 h, the mixture was concentrated in vacuo. The residue was azeotropically dried with toluene and DCM twice to yield crude acid **12** as a yellow foam in 100 % yield (2.24 g, 3.02 mmol), $[\alpha]_D^{20}$ = –63 (c = 1.0, $CHCl_3$). **12** was used in the next step without further purification.



^{1}H-NMR (500 MHz, DMSO-d_6, 100 °C): δ = 0.82–0.97 (m, 12 H, 9-H, 11-H), 1.12 (d, $^3J_{10,2}$ = 7.2 Hz, 3 H, 10-H), 1.23–1.48 (m, 2 H, 4-H_a, 6-H_a), 1.48–1.63 (m, 2 H, 5-H, 6-H_b), 1.83 (ddd, $^2J_{4b,4a}$ = 14.4 Hz, $^3J_{4b,3}$ = 10.0 Hz, $^3J_{4b,5}$ = 2.5 Hz, 1 H, 4-H_b), 1.87–2.02 (m, 3 H, 17-H_a, 18-H), 2.27 (m, 1 H, 17-H_b), 2.78 (dq, $^3J_{2,3} \approx {}^3J_{2,10}$ = 7.0 Hz, 1 H, 2-H), 3.44 (t, $^3J_{19,18}$ = 6.8 Hz, 2 H, 19-H), 4.14–4.49 (m, 4 H, 16-H, 21-H, 22-H), 4.71 (dd, $^3J_{7,6a}$ = 9.1 Hz, $^3J_{7,6b}$ = 1.6 Hz, 1 H, 7-H), 4.85 (d, $^2J_{13a,13b}$ = 12.2 Hz, 1 H, 13-H_a), 4.89 (d, $^2J_{13b,13a}$ = 12.2 Hz, 1 H, 13-H_b), 5.06 (ddd, $^3J_{3,4b}$ = 8.8 Hz, $^3J_{3,2}$ = 7.2 Hz, $^3J_{3,4a}$ = 1.9 Hz, 1 H, 3-H), 7.35 (m, 2 H, 25-H), 7.43 (ddd, $^3J_{26,25} \approx {}^3J_{26,27}$ = 7.5 Hz, $^4J_{26,24}$ = 0.9 Hz, 2 H, 26-H), 7.65 (m, 2 H, 24-H), 7.88 (d, $^3J_{27,26}$ = 7.5 Hz, 2 H, 27-H).
^{13}C-NMR (125 MHz, DMSO-d_6, 100 °C): δ = 11.5 (q, C-10), 19.4 (q, C-11), 23.0 (bs, C-18), 25.0 (q, C-9), 25.8 (d, C-5), 29.2 (bs, C-17), 33.9 (s, C-8), 36.1 (t, C-4), 37.2 (t, C-6), 42.5 (d, C-2), 45.8 (bs, C-19), 46.5 (d, C-22), 58.8 (d, C-16), 66.3 (t, C-21), 75.9 (t, C-13), 77.8 (d, C-3), 78.7 (d, C-7), 94.6 (s, C-14), 119.4 (d, C-27), 124.4 (d, C-24), 126.5 (d, C-25), 127.1 (d, C-26), 140.3 (s, C-28), 143.4 (s, C-23), 152.5 (s, C-12), 153.3 (bs, C-20), 171.3 (s, C-15), 173.0 (s, C-1).
HRMS (ESI) calcd for $C_{36}H_{45}NO_9Cl_3$ $[M+H]^+$: 740.2154, found: 740.2130.

1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-9-{[(*S*,*E*)-5-(allyloxy)-4-methyl-5-oxo-1-(tritylthio)pent-3-en-2-yl]amino}-2,2,5,8-tetramethyl-9-oxo-7-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonan-3-yl)] (*S*)-pyrrolidine-1,2-dicarboxylate (14)

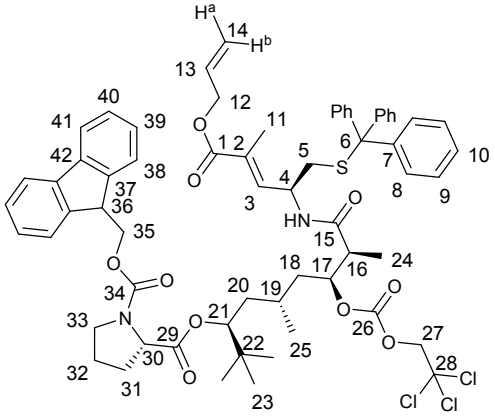
Allyl (*S*,*E*)-4-[(*tert*-Butoxycarbonyl)amino]-2-methyl-5-(tritylthio)pent-2-enoate **13** was prepared as described previously.[4]

Boc deprotection: To a solution of 1.15 g (2.11 mmol, 1.3 eq.) Boc protected amino acid **13** in 10.9 ml anhydrous DCM were added 1.47 ml (ρ = 0.92 g/ml, 12.6 mmol, 7.8 eq.) 2,6-lutidine

[4] T. Doi, Y. Numajiri, A. Munakata and T. Takahashi, *Org Lett.* 2006, **8**, 3, 531–534.

and 1.14 ml (ρ = 1.23 g/ml, 6.32 mmol, 3.9 eq) TMSOTf at room temperature. After stirring the yellow solution for 3 h, methanol and water were added and the mixture was extracted three times with $CHCl_3$. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to yield the crude deprotected amine which was used in the next step without further purification.

Peptide coupling: The residue was dissolved in 4.3 ml DCM and a solution of 1.20 g (1.62 mmol, 1.0 eq.) crude carboxylic acid **12** in 9.6 ml DCM was added followed by 566 µl (ρ = 0.74 g/ml, 3.24 mmol, 2.0 eq.) DIPEA and 800 mg (2.11 mmol, 1.3 eq.) HATU. After stirring at room temperature for 17 h, the mixture was diluted with EtOAc, washed with 1 M $KHSO_4$ solution, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 3:1) gave the title compound in 90 % yield (1.71 g, 1.47 mmol) as a colorless foam, R_f = 0.47 (petroleum ether, ethyl acetate 7:3); $[\alpha]_D^{20}$ = –35.4 (c = 1.0, $CHCl_3$). NMR spectra of **14** were in accordance with previously published data.[4]



major rotamer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.85 (s, 9 H, 23-H), 0.92 (d, $^3J_{25,19}$ = 6.6 Hz, 3 H, 25-H), 1.10 (d, $^3J_{24,16}$ = 6.9 Hz, 3 H, 24-H), 1.31 (m, 1 H, 20-H_a), 1.40–1.54 (m, 2 H, 18-H_a, 20-H_b), 1.62 (m, 1 H, 19-H), 1.73 (s, 3 H, 11-H), 1.87 (m, 1 H, 18-H_b), 1.95 (m, 2 H, 32-H), 2.07–2.56 (m, 5 H, 5-H, 16-H, 31-H), 3.44–3.71 (m, 2 H, 33-H), 4.16–4.32 (m, 2 H, 35-H_a, 36-H), 4.39 (m, 1 H, 35-H_b), 4.47–4.69 (m, 5 H, 4-H, 12-H, 27-H_a, 30-H), 4.70–4.88 (m, 2 H, 27-H_b, 21-H), 4.98 (m, 1 H, 17-H), 5.17 (d, $^3J_{14a,13}$ = 10.4 Hz, 1 H, 14-H_a), 5.25 (d, $^3J_{14b,13}$ = 18.6 Hz, 1 H, 14-H_b), 5.45 (d, $^3J_{NH,4}$ = 7.6 Hz, 1 H, NH), 5.85 (ddt, $^3J_{13,14b}$ = 16.9 Hz, $^3J_{13,14a}$ = 11.1 Hz, $^3J_{13,12}$ = 5.7 Hz, 1 H, 13-H), 6.39 (d, $^3J_{3,4}$ = 8.2 Hz, 1 H, 3-H), 7.15–7.44 (m, 19 H, 8-H, 9-H, 10-H, 39-H, 40-H), 7.59 (m, 2 H, 38-H), 7.76 (m, 2 H, 41-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.9 (q, C-11), 13.5 (q, C-24), 19.8 (q, C-25), 24.2 (t, C-32), 25.8 (q, C-23), 26.0 (d, C-19), 30.0 (t, C-31), 35.0 (s, C-22), 35.9 (t, C-5), 36.7 (t, C-18), 37.3 (t, C-20), 44.6 (d, C-16), 46.3 (t, C-33), 47.2 (d, C-36), 47.2 (d, C-4), 59.7 (d, C-30), 65.4 (t, C-12), 67.0 (s, C-6), 67.4 (t, C-35), 76.5 (t, C-27), 78.6 (d, C-21), 79.0 (d, C-17), 94.8 (s, C-28), 118.1 (t, C-14), 119.9 (d, C-41), 125.1 (d, C-38), 126.8 (d, C-10), 127.1 (d, C-40), 127.7 (d, C-39), 128.0 (d, C-8), 129.5 (d, C-9), 130.0 (s, C-2), 132.2 (d, C-13), 139.5 (d, C-3), 141.2 (s, C-42), 143.8 (s, C-37), 144.4 (s, C-7), 153.8 (s, C-26), 154.7 (s, C-34), 167.1 (s, C-1), 171.8 (s, C-15), 172.1 (s, C-29).

minor rotamer (selected signals):

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.73 (d, $^3J_{25,19}$ = 6.6 Hz, 3 H, 25-H), 0.87 (s, 9 H, 23-H), 1.07 (d, $^3J_{24,16}$ = 6.9 Hz, 3 H, 24-H), 5.32 (d, $^3J_{14b,13}$ = 17.3 Hz, 1 H, 14-H_b), 5.94 (ddt, $^3J_{13,14b}$ = 16.4 Hz, $^3J_{13,14a}$ = 10.7 Hz, $^3J_{13,12}$ = 6.0 Hz, 1 H, 13-H), 6.36 (d, $^3J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 7.70 (d, $^3J_{38,39}$ = 7.3 Hz, 2 H, 38-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 12.8 (q, C-24), 20.3 (q, C-25), 23.4 (t, C-32), 25.8 (q, C-23), 31.2 (t, C-31), 34.7 (s, C-22), 45.2 (d, C-16), 59.4 (d, C-30), 65.5 (t, C-12), 67.1 (s, C-6), 67.8 (t, C-35), 76.5 (t, C-27), 78.3 (d, C-21), 79.1 (d, C-17), 94.7 (s, C-28), 118.2 (t,

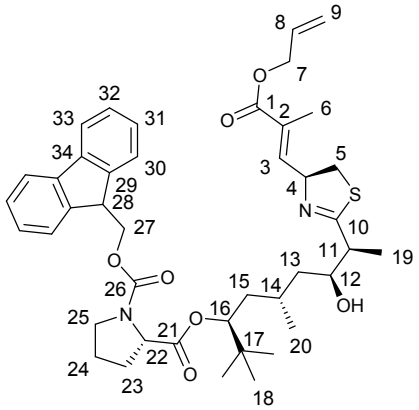
C-14), 125.1 (d, C-38), 126.9 (d, C-10), 127.0 (d, C-40), 127.7 (d, C-39), 128.0 (d, C-8), 130.2 (s, C-2), 139.3 (d, C-3), 141.1 (s, C-42), 144.0 (s, C-37), 144.3 (s, C-7), 153.7 (s, C-26), 154.4 (s, C-34), 167.1 (s, C-1), 171.7 (s, C-15), 172.5 (s, C-29).
HRMS (ESI) calcd for $C_{64}H_{72}N_2O_{10}SCl_3$ $[M+H]^+$: 1165.3968, found: 1165.3970.

1-[(9*H*-Fluoren-9-yl)methyl] 2-({3*S*,5*S*,7*S*,8*S*}-8-{(*S*)-4-[(*E*)-3-(allyloxy)-2-methyl-3-oxoprop-1-en-1-yl]-4,5-dihydrothiazol-2-yl}-7-hydroxy-2,2,5-trimethylnonan-3-yl) (*S*)-pyrrolidine-1,2-dicarboxylate (15)

15 was prepared according to a slightly modified literature procedure.[4]

Thiazoline formation: 157 µl (ρ = 1.67 g/ml, 927 µmol, 3.0 eq.) trifluoromethanesulfonic anhydride were added dropwise to a solution of 516 mg (1.85 mmol, 6.0 eq.) triphenylphosphine oxide in 7.2 ml anhydrous DCM at 0 °C. After stirring at this temperature for 10 min, 360 mg (309 µmol, 1.0 eq.) **14** were added and stirring at 0 °C was continued for another 30 min. Saturated $NaHCO_3$ solution was added to the cold mixture and the layers were separated. The aqueous layer was extracted three times with EtOAc, the combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was used in the next step without further purification.

Troc deprotection: A solution of the crude *O*-Troc protected thiazoline in 14.4 ml THF was treated with 3.60 ml (1.0 M in water, 3.60 mmol, 11.7 eq.) ammonium acetate solution and 202 mg (3.09 mmol, 10.0 eq.) zinc dust at room temperature. The suspension was vigorously stirred over 24 h. EtOAc and brine were added and the layers were separated. The aqueous layer was extracted twice with EtOAc, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by reversed-phase flash chromatography (H_2O/MeCN 9:1 → MeCN) gave the title compound in 75 % yield (170 mg, 233 µmol) as a colorless, amorphous solid, R_f = 0.33 (petroleum ether, ethyl acetate 7:3); $[\alpha]_D^{20}$ = –70.4 (c = 1.0, $CHCl_3$). NMR spectra of **15** were in accordance with previously published data.[4]



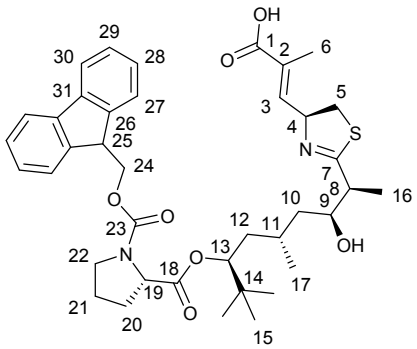
major rotamer:
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.88 (s, 9 H, 18-H), 0.96 (d, $^3J_{20,14}$ = 6.3 Hz, 3 H, 20-H), 1.00 (m, 1 H, 13-H_a), 1.21 (d, $^3J_{19,11}$ = 6.6 Hz, 3 H, 19-H), 1.26–1.77 (m, 4 H, 13-H_b, 15-H, OH), 1.85 (m, 1 H, 14-H), 1.90–2.09 (m, 6 H, 6-H, 23-H_a, 24-H), 2.25 (m, 1 H, 23-H_b), 2.71 (m, 1 H, 11-H), 2.97 (m, 1 H, 5-H_a), 3.30 (dd, $^2J_{5b,5a} \approx {}^3J_{5b,4}$ = 9.8 Hz, 1 H, 5-H_b), 3.52 (m, 1 H, 25-H_a), 3.63 (m, 1 H, 25-H_b), 3.79 (m, 1 H, 12-H), 4.27 (t, $^3J_{28,27}$ = 6.8 Hz, 1 H, 28-H), 4.33–4.54 (m, 3 H, 22-H, 27-H), 4.59 (d, $^3J_{7,8}$ = 5.0 Hz, 2 H, 7-H), 4.90 (d, $^3J_{16,15a}$ = 11.3 Hz, 1 H, 16-H), 5.10–5.39 (m, 3 H, 4-H, 9-H), 5.92 (m, 1 H, 8-H), 6.81 (d, $^3J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 7.30 (dd, $^3J_{31,30} \approx {}^3J_{31,30}$ = 7.3 Hz, 2 H, 31-H), 7.39 (dd, $^3J_{32,31} \approx {}^3J_{32,33}$ = 7.3 Hz, 2 H, 32-H), 7.63 (m, 2 H, 30-H), 7.75 (d, $^3J_{33,32}$ = 7.3 Hz, 2 H, 33-H).
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 13.1 (q, C-6), 16.1 (q, C-19), 20.3 (q, C-20), 24.5 (t, C-24), 24.8 (d, C-14), 26.0 (q, C-18), 29.9 (t, C-23), 34.7 (s, C-17), 37.5 (t, C-5), 37.6 (t, C-15), 38.9

(t, C-13), 45.8 (d, C-11), 46.4 (t, C-25), 47.1 (d, C-28), 59.5 (d, C-22), 65.4 (t, C-7), 67.7 (t, C-27), 71.3 (d, C-11), 74.0 (bs, C-4), 78.2 (d, C-16), 118.1 (t, C-9), 119.9 (d, C-33), 125.2 (d, C-30), 126.9 (d, C-31), 127.6 (d, C-32), 129.2 (s, C-2), 132.2 (d, C-8), 140.1 (bs, C-3), 141.2 (s, C-34), 143.9 (s, C-29), 154.8 (s, C-20), 167.2 (s, C-1), 172.4 (s, C-21, C-10).
minor rotamer (selected signals):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.79 (d, $^3J_{20,14}$ = 6.6 Hz, 3 H, 20-H), 1.25 (d, $^3J_{19,11}$ = 6.9 Hz, 3 H, 19-H), 2.65 (m, 1 H, 11-H), 3.43 (dd, $^2J_{5b,5a} \approx {}^3J_{5b,4}$ = 9.8 Hz, 1 H, 5-H_b), 3.68 (m, 1 H, 12-H), 4.21 (m, 1 H, 28-H), 4.64 (m, 2 H, 7-H), 4.82 (d, $^3J_{16,15a}$ = 10.7 Hz, 1 H, 16-H), 6.77 (d, $^3J_{3,4}$ = 10.1 Hz, 1 H, 3-H).
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 15.5 (q, C-19), 20.5 (q, C-20), 25.9 (q, C-18), 31.1 (t, C-23), 34.5 (s, C-17), 37.8 (t, C-15), 40.0 (t, C-13), 47.1 (d, C-28), 65.5 (t, C-7), 67.7 (t, C-27), 79.3 (d, C-16), 118.2 (t, C-9), 125.2 (d, C-30), 127.0 (d, C-31), 127.6 (d, C-32), 141.3 (s, C-34), 144.1 (s, C-29), 154.2 (s, C-20), 172.8 (s, C-21, C-10).
HRMS (ESI) calcd for $C_{42}H_{55}N_2O_7S$ $[M+H]^+$: 731.3724, found: 731.3747.

(*E*)-3-((*S*)-2-{(2*S*,3*S*,5*S*,7*S*)-7-[({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}-L-prolyl)oxy]-3-hydroxy-5,8,8-trimethylnonan-2-yl}-4,5-dihydrothiazol-4-yl)-2-methylacrylic acid (16)

16 was prepared according to a slightly modified literature procedure.[4]

20 mg (17 µmol, 10 mol-%) $Pd(PPh_3)_4$ were added to a solution of 126 mg (173 µmol. 1.0 eq.) allyl ester **15** and 47 µl (ρ = 0.989 g/ml, 433 µmol, 2.5 eq.) *N*-methylaniline in 10.7 ml anyhdrous THF at room temperature. After stirring for 40 min, the solvent was removed in vacuo and the residue was purified by flash chromatography (DCM, MeOH 95:5) to give **16** in 94 % yield (122 mg, 162 µmol) as a pale yellow foam, R_f = 0.29 (DCM, MeOH 95:5); $[\alpha]_D^{20}$ = –89 (c = 1.0, $CHCl_3$). NMR spectra of **16** were in accordance with previously published data.[4]



major rotamer:
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.87 (s, 9 H, 15-H), 0.92–1.06 (m, $^3J_{17,11}$ = 6.4 Hz, 4 H, 10-H_a, 17-H), 1.21 (d, $^3J_{16,8}$ = 7.0 Hz, 3 H, 16-H), 1.30 (m, 1 H, 12-H_a), 1.57–1.76 (m, 2 H, 10-H_b, 12-H_b), 1.84 (m, 1 H, 11-H), 1.93 (m, 3 H, 6-H), 1.97–2.10 (m, 3 H, 20-H_a, 21-H), 2.23 (m, 1 H, 20-H_b), 2.74 (m, 1 H, 8-H), 2.95 (m, 1 H, 5-H_a), 3.30 (dd, $^2J_{5b,5a}$ = 10.7 Hz, $^3J_{5b,4}$ = 8.9 Hz, 1 H, 5-H_b), 3.40–3.88 (m, 3 H, 9-H, 22-H), 4.16–4.56 (m, 4 H, 19-H, 24-H, 25-H), 4.90 (dd, $^3J_{13,12a}$ = 11.7 Hz, $^3J_{13,12b}$ = 1.7 Hz, 1 H, 13-H), 5.21 (m, 1 H, 4-H), 6.87 (dq, $^3J_{3,4}$ = 9.0 Hz, $^4J_{3,6}$ = 1.1 Hz, 1 H, 3-H), 7.29 (dd, $^3J_{28,27} \approx {}^3J_{28,29}$ = 7.5 Hz, 2 H, 28-H), 7.38 (dd, $^3J_{29,28} \approx {}^3J_{29,30}$ = 7.1 Hz, 2 H, 29-H), 7.62 (m, 2 H, 27-H), 7.74 (d, $^3J_{30,29}$ = 7.5 Hz, 2 H, 30-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.8 (q, C-6), 15.6 (q, C-16), 20.2 (q, C-17), 24.4 (t, C-21), 24.8 (d, C-11), 25.9 (q, C-15), 29.8 (t, C-20), 34.6 (s, C-14), 37.4 (t, C-5), 37.5 (t, C-12), 38.9 (t, C-10), 45.8 (d, C-8), 46.4 (t, C-22), 47.1 (d, C-25), 59.5 (d, C-19), 67.7 (t, C-27), 71.3 (d, C-9), 73.5 (bs, C-4), 78.3 (d, C-13), 119.8 (d, C-30), 125.2 (d, C-27), 127.0 (d, C-28), 127.6 (d, C-29), 129.2 (bs, C-2), 141.2 (s, C-34), 143.9 (s, C-26), 144.1 (s, C-26'), 154.9 (s, C-26), 171.7 (s, C-1), 172.4 (s, C-7, C-18).

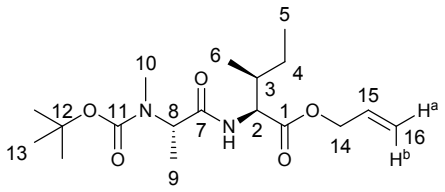
minor rotamer (selected signals):
^{1}H-NMR (400 MHz, $CDCl_3$): δ = 0.79 (d, $^3J_{17,11}$ = 6.6 Hz, 3 H, 17-H), 0.89 (s, 9 H, 15-H), 1.24 (d, $^3J_{16,8}$ = 7.1 Hz, 3 H, 16-H), 1.93 (m, 3 H, 6-H), 2.68 (m, 1 H, 8-H), 3.36 (dd, $^2J_{5b,5a}$ = 10.9 Hz, $^3J_{5b,4}$ = 8.7 Hz, 1 H, 5-H_b), 4.82 (d, $^3J_{13,12a}$ = 10.3 Hz, 1 H, 13-H), 6.84 (d, $^3J_{3,4}$ = 8.9 Hz, 1 H, 3-H), 7.56 (d, $^3J_{27,28}$ = 7.5 Hz, 2 H, 27-H).
^{13}C-NMR (100 MHz, $CDCl_3$): δ = 12.7 (q, C-6), 14.3 (q, C-16), 20.3 (q, C-17), 25.0 (d, C-11), 34.4 (s, C-14), 37.2 (t, C-5), 37.4 (t, C-12), 39.3 (t, C-10), 46.4 (t, C-22), 47.1 (d, C-25), 70.7 (d, C-9), 78.4 (d, C-13), 125.2 (d, C-27), 126.9 (d, C-28), 127.5 (d, C-29), 141.1 (s, C-34), 143.8 (s, C-26), 144.1 (s, C-26'), 155.0 (s, C-26), 171.8 (s, C-1), 172.8 (s, C-7, C-18).
HRMS (CI) calcd for $C_{39}H_{49}N_2O_6S$ $[M+H-H_2O]^+$: 673.3306, found: 673.3328.

Allyl *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-alanyl-L-isoleucinate (18b)

L-Boc-Ile-OAllyl **17b** was prepared as described previously.[5]

Boc deprotection: To a solution of 7.23 ml (ρ = 0.792 ml, 179 mmol, 12.1 eq.) methanol in 25 ml EtOAc were added 12.1 ml (170 mmol, 11.5 eq.) acetyl chloride at 0 °C. After stirring at this temperature for 20 min, the resulting HCl solution was added dropwise to a solution of 4.81 g (17.7 mmol, 1.2 eq.) **17b** in 5 ml DCM at 0 °C. Stirring at 0 °C was continued for 30 min, then the solvent was removed in a stream of nitrogen and the residual amine hydrochloride salt was dried in vacuo.

Peptide coupling: To a solution of the amine hydrochloride and 3.00 g (14.8 mmol, 1.0 eq.) L-Boc-*N*-Me-Ala-OH in 74 ml DCM were added 6.45 ml (ρ = 0.74 g/ml, 36.9 mmol, 2.5 eq.) DIPEA and 7.86 g (20.7 mmol, 1.4 eq.) HATU at room temperature. After stirring for 16 h, the solvent was removed in vacuo and the residue was suspended in EtOAc, washed with 1 M $KHSO_4$ solution, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 3:1) gave the title compound in 100 % yield (5.28 g, 14.8 mmol) as a pale yellow oil, R_f = 0.58 (petroleum ether, ethyl acetate 7:3); $[\alpha]_D^{20}$ = –68 (c = 1.0, $CHCl_3$).



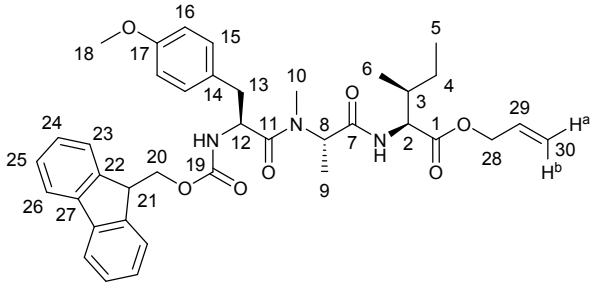
^{1}H-NMR (500 MHz, DMSO-d_6, 100 °C): δ = 0.83–0.93 (m, 6 H, 5-H, 6-H), 1.22 (m, 1 H, 4-H_a), 1.28 (d, $^3J_{9,8}$ = 7.3 Hz, 3 H, 9-H), 1.41–1.49 (m, 10 H, 4-H_b, 13-H), 1.87 (m, 1 H, 3-H), 2.78 (s, 3 H, 10-H), 4.31 (dd, $^3J_{2,3}$ = 8.2 Hz, $^3J_{2,NH}$ = 6.3 Hz, 1 H, 2-H), 4.54–4.65 (m, 3 H, 8-H, 14-H), 5.23 (ddt, $^3J_{16a,15}$ = 10.6 Hz, $^4J_{16a,14} \approx {}^2J_{16a,16b}$ = 1.1 Hz, 1 H, 16-H_a), 5.34 (ddt, $^3J_{16b,15}$ = 17.3 Hz, $^4J_{16b,14} \approx {}^2J_{16b,16a}$ = 1.6 Hz, 1 H, 16-H_b), 5.92 (ddt, $^3J_{15,16b}$ = 17.3 Hz, $^3J_{15,16a}$ = 10.7 Hz, $^3J_{15,14}$ = 5.4 Hz, 1 H, 15-H), 7.38 (d, $^3J_{NH,2}$ = 6.3 Hz, 1 H, NH).
^{13}C-NMR (125 MHz, DMSO-d_6, 100 °C): δ = 10.3 (q, C-5), 14.1 (q, C-6), 14.8 (q, C-9), 24.3 (t, C-4), 27.6 (q, C-13), 29.5 (q, C-10), 36.0 (d, C-3), 53.2 (d, C-8), 55.9 (d, C-2), 64.2 (t, C-14), 78.6 (s, C-12), 117.4 (t, C-16), 131.8 (d, C-15), 154.7 (s, C-11), 170.3 (s, C-1), 171.1 (s, C-7).
HRMS (CI) calcd for $C_{18}H_{33}N_2O_5$ $[M+H]^+$: 357.2384, found: 357.2397.

[5] J. Hur, J. Jang, J. Sim, W. S. Son, H.-C. Ahn, T. S. Kim, Y.-H. Shin, C. Lim, S. Lee, H. An, S.-H. Kim, D.-C. Oh, E.-K. Jo, J. Jang, J. Lee and Y.-G. Suh, *Angew. Chem. Int. Ed.* 2018, **57**, 12, 3069–3073, *Angew. Chem.* 2018, **130**, 12, 3123–3127.

Allyl *N*-[(*S*)-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-(4-methoxyphenyl)propanoyl]-*N*-methyl-L-alanyl-L-isoleucinate (19b)

Boc deprotection: To a solution of 3.38 ml (ρ = 0.792 ml, 83 mmol, 11.1 eq.) methanol in 12 ml EtOAc were added 5.67 ml (80.0 mmol, 10.6 eq.) acetyl chloride at 0 °C. After stirring at this temperature for 20 min, the resulting HCl solution was added dropwise to a solution of 2.95 g (8.27 mmol, 1.1 eq.) **18b** in 2.5 ml DCM at 0 °C. Stirring at 0 °C was continued for 30 min, then the solvent was removed in a stream of nitrogen and the residual amine hydrochloride salt was dried in vacuo.

Peptide coupling: To a solution of the amine hydrochloride and 3.14 g (7.52 mmol, 1.0 eq.) L-Fmoc-Tyr(Me)-OH in 37.5 ml DCM were added 3.94 ml (ρ = 0.74 g/ml, 22.6 mmol, 3.0 eq.) DIPEA and 4.29 g (11.3 mmol, 1.5 eq.) HATU at room temperature. After stirring for 19 h, the mixture was diluted with EtOAc, washed with 1 M $KHSO_4$ solution, saturated $NaHCO_3$ solution and brine, dried over Na_2SO_4 and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether, ethyl acetate 6:4) gave the title compound in 89 % yield (4.37 g, 6.66 mmol) as a colorless foam, R_f = 0.39 (petroleum ether, ethyl acetate 6:4); $[\alpha]_D^{20}$ = –46 (c = 1.0, $CHCl_3$).



^{1}H-NMR (500 MHz, DMSO-d_6, 100 °C): δ = 0.71–0.90 (m, 6 H, 5-H, 6-H), 1.01–1.34 (m, 4 H, 4-H_a, 9-H), 1.40 (m, 1 H, 4-H_b), 1.82 (dtq, $^3J_{3,2} \approx {}^3J_{3,4} \approx {}^3J_{3,6}$ = 6.6 Hz, 1 H, 3-H), 2.54–2.97 (m, 5 H, 10-H, 13-H), 3.71 (s, 3 H, 18-H), 4.13–4.33 (m, 4 H, 2-H, 20-H, 21-H), 4.51–5.07 (m, 4 H, 8-H, 12-H, 2-NH, 12-NH), 5.21 (d, $^3J_{30a,29}$ = 9.4 Hz, 1 H, 30-H_a), 5.31 (d, $^3J_{30b,29}$ = 17.3 Hz, 1 H, 30-H_b), 5.90 (m, 1 H, 29-H), 6.81 (d, $^3J_{16,15}$ = 8.2 Hz, 2 H, 16-H), 7.15 (d, $^3J_{15,16}$ = 6.9 Hz, 2 H, 15-H), 7.32 (m, 2 H, 24-H), 7.41 (dd, $^3J_{25,24} \approx {}^3J_{25,26}$ = 7.4 Hz, 2 H, 25-H), 7.64 (d, $^3J_{23,24}$ = 7.2 Hz, 2 H, 23-H), 7.85 (d, $^3J_{26,25}$ = 7.5 Hz, 2 H. 26-H).
^{13}C-NMR (125 MHz, DMSO-d_6, 100 °C): δ = 11.3 (q, C-5), 14.6 (q, C-9), 15.8 (q, C-6), 25.4 (t, C-4), 36.8 (d, C-3), 37.2 (bs, C-10, C-13), 47.4 (d, C-21), 53.2 (bs, C-8, C-12), 55.6 (q, C-18), 57.1 (d, C-2), 65.2 (t, C-28), 66.4 (t, C-20), 114.4 (d, C-16), 118.4 (t, C-30), 120.4 (d, C-26), 125.5 (d, C-23), 127.4 (d, C-24), 128.0 (d, C-25), 129.8 (s, C-14), 130.7 (d, C-15), 132.9 (d, C-29), 141.3 (s, C-27), 144.3 (s, C-22), 158.7 (s, C-19), 171.2 (s, C-1/7), 171.3 (s, C-1/7), 172.2 (s, C-11).
HRMS (CI) calcd for $C_{38}H_{46}N_3O_7$ $[M+H]^+$: 656.3330, found: 656.3321.

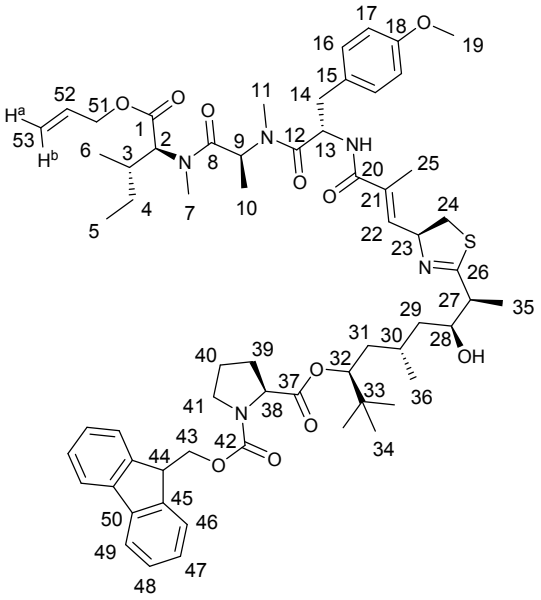
1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-8-({*S*}-4-{[5*S*,8*S*,11*S*,*E*]-11-[(*S*)-*sec*-butyl]-5-[4-methoxybenzyl]-2,7,8,10-tetramethyl-3,6,9,12-tetraoxo-13-oxa-4,7,10-triazahexadeca-1,15-dien-1-yl}-4,5-dihydrothiazol-2-yl)-7-hydroxy-2,2,5-trimethylnonan-3-yl] (*S*)-pyrrolidine-1,2-dicarboxylate (20a)

Allyl *N*-[(*S*)-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-(4-methoxyphenyl)-propanoyl]-*N*-methyl-L-alanyl-*N*-Methyl-L-isoleucinate (**19a**) was prepared as described previously.[4]

20a was prepared according to a slightly modified literature procedure.[4]

Fmoc deprotection: 161 mg (240 µmol, 1.5 eq.) **19a** were dissolved in 8.7 ml anhydrous MeCN and 3.2 ml diethylamine were added at room temperature. After stirring at room temperature for 20 min, excess amine and solvent were removed in vacuo. The residue was azeotropically dried with toluene and DCM twice and dried in vacuo.

Peptide coupling: To a solution of the crude free amine in 2.3 ml DCM were added 111 mg (160 µmol, 1.0 eq.) acid **16** dissolved in 6.6 ml DCM, 84 µl (ρ = 0.74 g/ml, 481 µmol, 3.0 eq.) DIPEA and 91 mg (240 µmol, 1.5 eq.) HATU at room temperature. After stirring at room temperature for 14 h, the solvent was removed in vacuo. Purification of the residue by flash chromatography (toluene, acetone 83:17) gave the title compound in 95 % yield (171 mg, 153 µmol) as a colorless foam, R_f = 0.10 (toluene, acetone 83:17); $[\alpha]_D^{20}$ = –89 (c = 1.0, $CHCl_3$). NMR spectra of **20a** were in accordance with previously published data.[4]



major rotamer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.76–1.02 (m, 23 H, 4-H_a, 5-H, 6-H, 29-H_a, 34-H, 35-H, 36-H), 1.16–1.40 (m, 5 H, 4-H_b, 10-H, 31-H_a), 1.58–1.78 (m, 2 H, 29-H_b, 31-H_b), 1.83 (m, 1 H, 30-H), 1.87–2.10 (m, 7 H, 3-H, 25-H, 39-H_a, 40-H), 2.21 (m, 1 H, 39-H_b), 2.65 (m, 1 H, 27-H), 2.72 (s, 3 H, 7-H), 2.81–2.93 (m, 2 H, 14-H_a, 24-H_a), 2.95 (s, 3 H, 11-H), 3.03 (m, 1 H, 14-H_b), 3.22–3.44 (m, 1 H, 24-H_b), 3.51 (m, 1 H, 41-H_a), 3.63 (m, 1 H, 41-H_b), 3.71–3.83 (m, 4 H, 19-H, 28-H), 4.13–4.53 (m, 4 H, 38-H, 43-H, 44-H), 4.58 (d, $^3J_{51,52}$ = 4.7 Hz, 2 H, 51-H), 4.89 (d, $^3J_{32,31b}$ = 10.4 Hz, 1 H, 32-H), 4.93 (d, $^3J_{2,3}$ = 9.8 Hz, 1 H, 2-H), 5.11 (m, 1 H, 23-H), 5.18 (m, 1 H, 13-H), 5.22 (d, $^3J_{53a,52}$ = 10.4 Hz, 1 H, 53-H_a), 5.29 (d, $^3J_{53b,52}$ = 17.0 Hz, 1 H, 53-H_b), 5.39 (q, $^3J_{9,10}$ = 6.9 Hz, 1 H, 9-H), 5.87 (ddt, $^3J_{52,53b}$ = 16.7 Hz, $^3J_{52,53a}$ = 11.0 Hz, $^3J_{52,51}$ = 5.6 Hz, 1 H, 52-H), 6.28 (m, 1 H, 22-H), 6.47 (bs, 1 H, NH), 6.77 (m, 2 H, 17-H), 7.07 (m, 2 H, 16-H), 7.29 (dd, $^3J_{46,45} \approx {}^3J_{46,47}$ = 7.3 Hz, 2 H, 46-H), 7.38 (dd, $^3J_{47,46} \approx {}^3J_{47,48}$ = 7.3 Hz, 2 H, 47-H), 7.63 (m, 2 H, 46-H), 7.74 (d, $^3J_{49,48}$ = 7.3 Hz, 2 H, 49-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 10.5 (q, C-35), 13.4 (q, C-25), 14.3 (q, C-10), 15.7 (q, C-6), 20.3 (q, C-5), 20.4 (q, C-36), 24.4 (t, C-40), 24.9 (d, C-30), 25.0 (t, C-4), 25.9 (q, C-34), 29.8 (t, C-39), 30.5 (q, C-11), 30.9 (q, C-7), 33.2 (d, C-3), 34.7 (s, C-33), 37.5 (t, C-31), 37.6 (t, C-14, t, C-24), 38.8 (t, C-29), 45.8 (d, C-27), 46.4 (t, C-41), 47.1 (d, C-44), 49.5 (d, C-9), 50.4 (d, C-13), 55.1 (q, C-19), 59.5 (d, C-38), 60.4 (d, C-2), 65.3 (t, C-51), 67.7 (t, C-43), 71.4 (d, C-28), 78.3 (d, C-32), 113.8 (d, C-17), 118.6 (t, C-53), 119.9 (d, C-49), 125.2 (d, C-46), 127.0 (d, C-47), 127.6 (d, C-48), 127.9 (s, C-15), 130.4 (d, C-16), 131.6 (d, C-52), 141.3 (s, C-50), 143.9 (s, C-45), 154.8 (s, C-42), 158.5 (s, C-18), 168.0 (s, C-20), 170.6 (s, C-1), 171.3 (s, C-12), 171.8 (s, C-8), 172.4 (s, C-37).

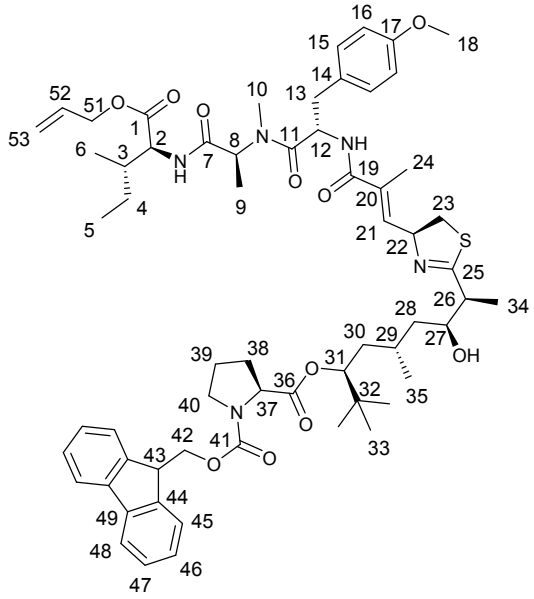
The signals of C-21, C-22 and C-26 could not be detected.

minor rotamer (selected signals):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 4.81 (d, $^3J_{32,31b}$ = 10.7 Hz, 1 H, 32-H).
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 30.5 (q, C-11), 30.9 (q, C-7), 34.6 (s, C-33), 46.4 (t, C-41), 47.1 (d, C-44), 78.4 (d, C-32), 125.2 (d, C-46), 141.2 (s, C-50), 144.1 (s, C-45), 155.0 (s, C-42), 171.4 (s, C-12), 172.4 (s, C-37).
HRMS (ESI) calcd for $C_{63}H_{86}N_5O_{11}S$ $[M+H]^+$: 1120.6039, found: 1120.6040.

1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-8-({*S*}-4-{[5*S*,8*S*,11*S*,*E*]-11-[(*S*)-*sec*-butyl]-5-[4-methoxybenzyl]-2,7,8-trimethyl-3,6,9,12-tetraoxo-13-oxa-4,7,10-triazahexadeca-1,15-dien-1-yl}-4,5-dihydrothiazol-2-yl)-7-hydroxy-2,2,5-trimethylnonan-3-yl] (*S*)-pyrrolidine-1,2-dicarboxylate (20b)

Fmoc deprotection: 69 mg (105 µmol, 1.5 eq.) **19b** were dissolved in 3.8 ml anhydrous MeCN and 1.4 ml diethylamine were added at room temperature. After stirring at room temperature for 20 min, excess amine and solvent were removed in vacuo. The residue was azeotropically dried with toluene and DCM twice and dried in vacuo.

Peptide coupling: To a solution of the crude free amine in 1.0 ml DCM were added 56 mg (70.0 µmol, 1.0 eq.) acid **16** dissolved in 2.9 ml DCM, 37 µl (ρ = 0.74 g/ml, 209 µmol, 3.0 eq.) DIPEA and 40 mg (105 µmol, 1.5 eq.) HATU at room temperature. After stirring at room temperature for 20 h, the solvent was removed in vacuo. Purification of the residue by flash chromatography (toluene, acetone 83:17) gave the title compound in 83 % yield (64 mg, 58 µmol) as a colorless foam, R_f = 0.13 (toluene, acetone 83:17); $[\alpha]_D^{20}$ = –94 (c = 0.33, $CHCl_3$).



major rotamer:
^{1}H-NMR (500 MHz, CD_3OD): δ = 0.15–1.01 (m, 20 H, 4-H_a, 5-H, 9-H, 28-H_a, 33-H, 35-H), 1.05–1.40 (m, 8 H, 4-H_b, 6-H, 30-H_a, 34-H), 1.47–1.70 (m, 2 H, 28-H_b, 30-H_b), 1.77–1.98 (m, 8 H, 3-H, 24-H, 29-H, 38-H_a, 39-H), 2.19 (m, 1 H, 38-H_b), 2.43 (s, 3 H, 10-H), 2.57 (m, 1 H, 26-H), 2.78–2.97 (m, 3 H, 13-H, 23-H_a), 3.27–3.52 (m, 3 H, 23-H_b, 40-H), 3.61–3.67 (m, 4 H, 18-H, 27-H), 4.07–4.77 (m, 9 H, 2-H, 8-H, 12-H, 37-H, 42-H, 43-H, 51-H), 4.83 (m, 1 H, 31-H), 5.04–5.28 (m, 3 H, 22-H, 53-H), 5.84 (m, 1 H, 52-H), 6.33 (dq, $^3J_{21,22}$ = 8.7 Hz, $^4J_{21,24}$ = 1.4 Hz, 1 H, 21-H), 6.66–7.07 (m, 4 H, 15-H, 16-H), 7.21 (m, 2 H, 46-H), 7.30 (m, 2 H, 47-H), 7.55 (m, 2 H, 45-H), 7.73 (m, 2 H, 48-H).

^{13}C-NMR (125 MHz, CD_3OD): δ = 11.9 (q, C-5), 13.7 (q, C-24), 13.8 (q, C-9), 16.2 (q, C-34), 16.3 (q, C-6), 20.6 (q, C-35), 25.7 (t, C-39), 26.3 (t, C-4), 26.5 (d, C-29), 26.6 (q, C-33), 29.5 (q, C-10), 31.1 (t, C-38), 35.9 (s, C-32), 37.7 (d, C-3), 38.3 (t, C-13), 38.4 (t, C-23), 39.0 (t, C-30), 40.3 (t, C-28), 47.1 (d, C-26), 47.9 (t, C-40), 48.5 (d, C-43), 53.3 (d, C-12), 55.9 (q, C-18), 57.0 (d, C-8), 59.2 (d, C-2), 61.1 (d, C-37), 66.7 (t, C-51), 69.2 (t, C-42), 73.0 (d, C-27), 75.4 (d, C-22), 79.8 (d, C-31), 115.3 (d, C-16), 118.9 (t, C-53), 121.1 (d, C-48), 126.4 (t, C-45), 126.9 (s, C-20), 128.4 (d, C-46), 129.0 (d, C-47), 129.1 (s, C-14), 131.7 (d, C-15), 133.5 (d, C-52), 137.0 (d, C-21), 142.8 (s, C-49), 145.0 (s, C-44), 156.7 (s, C-41), 171.7 (s, C-19), 172.7 (s, C-7), 173.0 (s, C-1), 174.4 (s, C-36), 174.7 (s, C-36), 178.5 (s, C-25).
minor rotamer 1 (selected signals):
^{1}H-NMR (500 MHz, CD_3OD): δ = 2.50 (s, 3 H, 10-H), 6.19 (dq, $^{3}J_{21,22}$ = 9.0 Hz, $^{4}J_{21,24}$ = 1.4 Hz, 1 H, 21-H).
minor rotamer 2 (selected signals):
^{1}H-NMR (500 MHz, CD_3OD): δ = 2.48 (s, 3 H, 10-H), 6.29 (dq, $^{3}J_{21,22}$ = 8.7 Hz, $^{4}J_{21,24}$ = 1.4 Hz, 1 H, 21-H).
HRMS (ESI) calcd for $C_{62}H_{84}N_5O_{11}S$ $[M+H]^+$: 1106.5883, found: 1106.5890.

Apratoxin A (21a) and 34-*epi*-Apratoxin A (*epi*-21a)

21a was prepared according to a slightly modified literature procedure.[4]

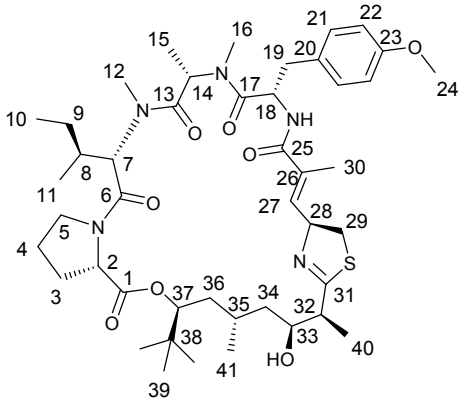
Allyl deprotection: 15 mg (13 µmol, 10 mol-%) $Pd(PPh_3)_4$ were added to a solution of 144 mg (129 µmol. 1.0 eq.) allyl ester **20a** and 34.8 µl (ρ = 0.989 g/ml, 321 µmol, 2.5 eq.) *N*-methylaniline in 9.2 ml anyhdrous THF at room temperature. After stirring for 20 min, the solvent was removed in vacuo and the residue was purified by flash chromatography (DCM, MeOH 96:4, 9:1) to give the free acid as a pale yellow solid, R_f = 0.23 (DCM, MeOH 96:4).

Fmoc deprotection: The *N*-Fmoc protected acid was dissolved in 9.2 ml anhydrous MeCN and 4.6 ml diethylamine were added at room temperature. After stirring at room temperature for 30 min, excess amine and solvent were removed in vacuo. The residue was azeotropically dried with toluene and DCM twice and dried in vacuo.

Cyclization: To a solution of the deprotected linear precursor in 130 ml anhydrous DCM were added 202 µl (ρ = 0.74 g/ml, 1.16 mmol, 9.0 eq.) DIPEA and 147 mg (386 µmol, 3.0 eq.) HATU at room temperature. After stirring for 14 h, the solvent was removed in vacuo. Purification of the residue by flash chromatography (DCM, *i*-PrOH 97:3, 94:6) gave a diastereomeric mixture of **21a** and ***epi*-21a** (d.r. = 70:30 according to HPLC) which was separated by preparative HPLC (*Phenomenex Luna® C18(2)*, H_2O, MeCN 6:4 → MeCN) to give **21a** in 34 % yield (36.7 mg, 44 µmol) as a colorless, amorphous solid, R_f = 0.33 (DCM, *i*-PrOH 94:6); $[\alpha]_D^{20}$ = –187.0 (c = 1.33, MeOH) and ***epi*-21a** in 15 % yield (15.9 mg, 19 µmol) as a colorless, amorphous solid, R_f = 0.33 (DCM, *i*-PrOH 94:6); $[\alpha]_D^{20}$ = –248 (c = 0.115, MeOH). NMR spectra of **21a** and ***epi*-21a** were in accordance with previously published data.[4,6]

[6] H. Luesch, W. Y. Yoshida, R. E. Moore, V. J. Paul and T. H. Corbett, *J. Am. Chem. Soc.* 2001, **123**, 5418–5423.

*Apratoxin A (**21a**):*

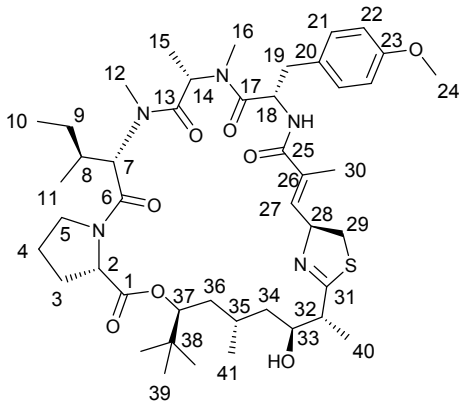


^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.87 (s, 9 H, 39-H), 0.91 (t, $^3J_{10,9}$ = 7.3 Hz, 3 H, 10-H), 0.95 (d, $^3J_{11,8}$ = 6.8 Hz, 3 H, 11-H), 0.97–1.01 (m, $^3J_{41,35}$ = 6.6 Hz, 4 H, 9-H_a, 41-H), 1.03–1.14 (m, $^3J_{40,32}$ = 6.9 Hz, 4 H, 34-H_a, 40-H), 1.21 (d, $^3J_{15,14}$ = 6.6 Hz, 3 H, 15-H), 1.23–1.35 (m, 2 H, 9-H_b, 36-H_a), 1.57 (ddd, $^2J_{34b,34a}$ = 13.2 Hz, $^3J_{34b,33}$ = 11.7 Hz, $^3J_{34b,35}$ = 4.1 Hz, 1 H, 34-H_b), 1.79 (ddd, $^2J_{36b,36a}$ = 14.2 Hz, $^3J_{36b,37}$ = 12.6 Hz, $^3J_{36b,35}$ = 3.5 Hz, 1 H, 36-H_b), 1.84–1.94 (m, 2 H, 3-H_a, 4-H_a), 1.96 (d, $^4J_{30,27}$ = 1.3 Hz, 3 H, 30-H), 2.06 (m, 1 H, 4-H_b), 2.16 (m, 1 H, 35-H), 2.19–2.30 (sh, 2 H, 3-H_b, 8-H), 2.63 (dq, $^3J_{32,33}$ = 10.0 Hz, $^3J_{32,40}$ = 7.0 Hz, 1 H, 32-H), 2.71 (s, 3 H, 12-H), 2.80 (s, 3 H, 16-H), 2.86 (dd, $^2J_{19a,19b}$ = 12.5 Hz, $^3J_{19a,18}$ = 4.6 Hz, 1 H, 19-H_a), 3.11 (dd, $^2J_{19b,19a}$ = 12.3 Hz, $^3J_{19b,18}$ = 11.3 Hz, 1 H, 19-H_b), 3.14 (dd, $^2J_{29a,29b}$ = 11.0 Hz, $^3J_{29a,28}$ = 3.8 Hz, 1 H, 29-H_a), 3.28 (q, $^3J_{14,15}$ = 6.3 Hz, 1 H, 14-H), 3.46 (dd, $^2J_{29b,29a}$ = 10.9 Hz, $^3J_{29b,28}$ = 8.7 Hz, 1 H, 29-H_b), 3.55 (dddd, $^3J_{33,32} \approx {}^3J_{33,34b} \approx {}^3J_{33,OH}$ = 10.7 Hz, $^3J_{33,34a}$ = 3.3 Hz, 1 H, 33-H), 3.66 (m, 1 H, 5-H_a), 3.78 (s, 3 H, 24-H), 4.18 (t, $^3J_{2,3}$ = 7.9 Hz, 1 H, 2-H), 4.24 (ddd, $^2J_{5b,5a}$ = 10.4 Hz, $^3J_{5b,4a}$ = 6.9 Hz, $^3J_{5b,4b}$ = 3.5 Hz, 1 H, 5-H_b), 4.70 (d, $^3J_{OH,33}$ = 10.7 Hz, 1 H, OH), 4.97 (dd, $^3J_{37,36b}$ = 12.5 Hz, $^3J_{37,36a}$ = 2.0 Hz, 1 H, 37-H), 5.04 (ddd, $^3J_{18,19b}$ = 10.9 Hz, $^3J_{18,NH}$ = 9.6 Hz, $^3J_{18,19a}$ = 4.7 Hz, 1 H, 18-H), 5.20 (d, $^3J_{7,8}$ = 11.7 Hz, 1 H, 7-H), 5.25 (ddd, $^3J_{28,27}$ = 9.7 Hz, $^3J_{28,29b}$ = 8.9 Hz, $^3J_{28,29a}$ = 4.2 Hz, 1 H, 28-H), 5.99 (d, $^3J_{NH,18}$ = 9.4 Hz, 1 H, NH), 6.35 (dq, $^3J_{27,28}$ = 9.8 Hz, $^4J_{27,30}$ = 1.3 Hz, 1 H, 27-H), 6.80 (d, $^3J_{22,21}$ = 8.5 Hz, 2 H, 22-H, 7.15 (d, $^3J_{21,22}$ = 8.5 Hz, 2 H, 21-H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 9.0 (q, C-10), 13.4 (q, C-30), 13.9 (q, C-15), 14.0 (q, C-11), 16.6 (q, C-40), 19.8 (q, C-41), 24.3 (d, C-35), 24.6 (t, C-9), 25.6 (t, C-4), 26.0 (q, C-39), 29.3 (t, C-3), 30.5 (q, C-12), 31.7 (d, C-8), 34.9 (s, C-38), 36.7 (q, C-16), 37.2 (t, C-19), 37.6 (t, C-29), 37.6 (t, C-36), 38.1 (t, C-34), 47.6 (t, C-5), 49.1 (d, C-32), 55.3 (q, C-24), 56.6 (t, C-4), 59.7 (d, C-2), 71.6 (d, C-33), 72.5 (d, C-28), 77.3 (d, C-37), 113.8 (d, C-22), 128.2 (s, C-20), 130.5 (s, C-26), 130.6 (d, C-21), 136.3 (d, C-27), 158.6 (s, C-23), 169.5 (s, C-25), 170.0 (s, C-13), 170.4 (s, C-17), 170.7 (s, C-6), 172.6 (s, C-1), 177.5 (s, C-31).

HRMS (ESI) calcd for $C_{45}H_{70}N_5O_8S$ $[M+H]^+$: 840.4940, found: 840.4936.

*34-epi-Apratoxin A (epi-**21a**):*



major rotamer:
^{1}H-NMR (500 MHz, CD_2Cl_2): δ = 0.62 (d, $^3J_{15,14}$ = 6.6 Hz, 3 H, 15-H), 0.75 (m, 1 H, 34-H_a), 0.82 (t, $^3J_{10,9}$ = 7.4 Hz, 3 H, 10-H), 0.87 (s, 9 H, 39-H), 0.93 (m, 1 H, 9-H_a), 0.99 (d, $^3J_{41,35}$ = 6.9 Hz, 3 H, 41-H), 1.05 (d, $^3J_{11,8}$ = 6.6 Hz, 3 H, 11-H), 1.11 (d, $^3J_{40,32}$ = 6.6 Hz, 3 H, 40-H), 1.20–1.35 (m, 2 H, 9-H_b. 36-H_a, OH), 1.67–1.85 (m, 2 H, 34-H_b, 36-H_b), 1.86–2.09 (m, $^4J_{30,27}$ = 1.3 Hz, 8 H, 3-H_a, 4-H, 8-H, 30-H, 35-H), 2.27 (m, 1 H, 3-H_b), 2,53 (m, 1 H, 32-H), 2.57 (s, 3 H, 12-H), 2.68 (s, 3 H, 16-H), 2.90 (dd, $^2J_{19a,19b}$ = 12.9 Hz, $^3J_{19a,18}$ = 5.0 Hz, 1 H, 19-H_a), 3.04–3.19 (m, 2 H, 19-H_b, 29-H_a), 3.44 (dd, $^2J_{29b,29a}$ = 10.7 Hz, $^3J_{29b,28}$ = 8.2 Hz, 1 H, 29-H_b), 3.59 (m, 1 H, 5-H_a), 3.75 (s, 3 H, 24-H), 3.98–4.15 (m, 2 H, 5-H_b, 33-H), 4.37 (dd, $^3J_{2,3a}$ = 8.4 Hz, $^3J_{2,3b}$ = 5.8 Hz, 1 H, 2-H), 4.77 (q, $^3J_{14,15}$ = 6.5 Hz, 1 H, 14-H), 4.84 (d, $^3J_{7,8}$ = 11.3 Hz, 1 H, 7-H), 4.90 (dd, $^3J_{37,36b}$ = 12.5 Hz, $^3J_{37,36a}$ = 3.3 Hz, 1 H, 37-H), 5.33–5.38 (m, 2 H, 18-H, 28-H), 6.25 (dq, $^3J_{27,28}$ = 10.2 Hz, $^4J_{27,30}$ = 1.4 Hz, 1 H, 27-H), 6.30 (d, $^3J_{NH,18}$ = 9.5 Hz, 1 H, NH), 6.81 (d, $^3J_{22,21}$ = 8.5 Hz, 2 H, 22-H), 7.15 (d, $^3J_{21,22}$ = 8.5 Hz, 2 H, 21-H).
^{13}C-NMR (125 MHz, CD_2Cl_2): δ = 9.6 (q, C-40), 9.9 (q, C-10), 12.9 (q, C-30), 13.9 (q, C-11), 15.7 (q, C-15), 20.4 (q, C-41), 25.4 (q, C-4), 25.4 (q, C-35), 25.8 (t, C-9), 26.2 (t, C-39), 28.9 (q, C-12), 29.6 (t, C-3), 29.8 (q, C-16), 34.1 (d, C-8), 35.3 (s, C-38), 37.4 (t, C-36), 38.2 (t, C-29), 39.4 (t, C-34), 39.6 (t, C-19), 45.9 (d, C-32), 48.0 (t, C-5), 50.2 (d, C-18), 54.2 (d, C-14), 55.5 (q, C-24), 58.1 (d, C-7), 59.4 (d, C-2), 70.3 (d, C-33), 73.2 (d, C-28), 77.7 (d, C-37), 114.2 (d, C-22), 128.7 (s, C-26), 129.1 (s, C-20), 130.8 (d, C-21), 137.8 (d, C-27), 159.0 (s, C-23), 167.8 (s, C-25), 170.1 (s, C-6), 170.6 (s, C-13), 170.9 (s, C-1), 172.3 (s, C-17), 176.3 (s, C-31).
minor rotamer (selected signals):
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.87 (s, 9 H, 39-H), 0.91 (d, $^3J_{15,14}$ = 6.6 Hz, 3 H, 15-H), 1.08 (d, $^3J_{40,32}$ = 6.9 Hz, 3 H, 39-H), 1.13 (d, $^3J_{11,8}$ = 6.6 Hz, 3 H, 11-H), 2.67 (s, 3 H, 16-H), 2.85 (dd, $^2J_{19a,19b}$ = 12.9 Hz, $^3J_{19a,18}$ = 5.7 Hz, 1 H, 19-H_a), 2.88 (s, 3 H, 12-H), 3.28 (bs, 1 H, OH), 3.50 (dd, $^2J_{29b,29a}$ = 10.9 Hz, $^3J_{29b,28}$ = 8.7 Hz, 1 H, 29-H_b), 3.76 (s, 3 H, 24-H), 4.11 (m, 1 H, 2-H), 5.02 (ddd, $^3J_{18,NH} \approx {}^3J_{18,19b}$ = 9.7 Hz, $^3J_{18,19a}$ = 5.5 Hz, 1 H, 18-H), 5.13 (d, $^3J_{7,8}$ = 8.8 Hz, 1 H, 7-H), 5.98 (d, $^3J_{NH,18}$ = 8.8 Hz, 1 H, NH), 6.18 (dq, $^3J_{27,28}$ = 9.6 Hz, $^4J_{27,30}$ = 1.4 Hz, 1 H, 27-H), 6.81 (d, $^3J_{22,21}$ = 8.8 Hz, 2 H, 22-H), 7.14 (d, $^3J_{21,22}$ = 8.5 Hz, 2 H, 21-H).
HRMS (ESI) calcd for $C_{45}H_{70}N_5O_8S$ $[M+H]^+$: 840.4940, found: 840.4939.
HPLC (*Phenomenex Luna® C18(2)*, H_2O + 0.1 % HCOOH, MeCN 35:65, 1.25 ml/min, 40 °C): t_R(**21a**) = 4.01 min, t_R(***epi*-21a**) = 4.69 min.

Apratoxin B (21b) and 34-*epi*-Apratoxin B (*epi*-21b)

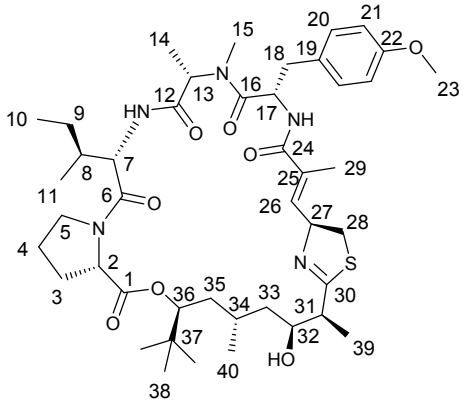
Allyl deprotection: 6 mg (5.2 µmol, 10 mol-%) $Pd(PPh_3)_4$ were added to a solution of 57 mg (52 µmol. 1.0 eq.) allyl ester **20b** and 14.0 µl (ρ = 0.989 g/ml, 129 µmol, 2.5 eq.) *N*-methylaniline in 3.7 ml anyhdrous THF at room temperature. After stirring for 20 min, the solvent was removed in vacuo and the residue was purified by flash chromatography (DCM, MeOH 96:4, 9:1) to give the free acid as a pale yellow solid, R_f = 0.21 (DCM, MeOH 96:4).

Fmoc deprotection: The *N*-Fmoc protected acid was dissolved in 3.7 ml anhydrous MeCN and 1.86 ml diethylamine were added at room temperature. After stirring at room temperature for 30 min, excess amine and solvent were removed in vacuo. The residue was azeotropically dried with toluene and DCM twice and dried in vacuo.

Cyclization: To a solution of the deprotected linear precursor in 52 ml anhydrous DCM were added 81 µl (ρ = 0.74 g/ml, 464 µmol, 9.0 eq.) DIPEA and 59 mg (155 µmol, 3.0 eq.) HATU at room temperature. After stirring for 15 h, the solvent was removed in vacuo. Purification of the residue by flash chromatography (DCM, *i*-PrOH 97:3, 94:6) gave a diastereomeric mixture of **21b** and ***epi*-21b** (d.r. = 73:27 according to HPLC) which was separated by preparative HPLC (*Phenomenex Luna® C18(2)*, H_2O, MeCN 35:65) to give **21b** in 36 % yield

(15.3 mg, 18.7 µmol) as a colorless, amorphous solid, R_f = 0.41 (DCM, *i*-PrOH 94:6); $[\alpha]_D^{20}$ = –165 (c = 0.2, MeOH) and ***epi*-21b** in 13 % yield (5.7 mg, 6.9 µmol) as a colorless, amorphous solid, R_f = 0.41 (DCM, *i*-PrOH 94:6); $[\alpha]_D^{20}$ = –150 (c = 0.2, MeOH). NMR spectra of **21b** were in accordance with previously published data.[7]

*Apratoxin B (**21b**):*



major rotamer:

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.65 (d, $^3J_{14,13}$ = 6.9 Hz, 3 H, 14-H), 0.71 (t, $^3J_{10,9}$ = 7.3 Hz, 3 H, 10-H), 0.82 (m, 1 H, 9-H_a), 0.88 (s, 9 H, 38-H), 0.95 (d, $^3J_{11,8}$ = 6.6 Hz, 3 H, 11-H), 0.97 (d, $^3J_{40,34}$ = 6.6 Hz, 3 H, 40-H), 1.03–1.16 (m, $^3J_{39,31}$ = 6.9 Hz, 5 H, 9-H_b, 33-H_a, 39-H), 1.25 (m, 1 H, 35-H_a), 1.55 (ddd, $^2J_{33b,33a}$ = 14.2 Hz, $^3J_{33b,31}$ = 10.4 Hz, $^3J_{33b,34}$ = 3.8 Hz, 1 H, 33-H_b), 1.73 (ddd, $^2J_{35b,35a}$ = 13.6 Hz, $^3J_{35b,36}$ = 12.6 Hz, $^3J_{35b,34}$ = 2.8 Hz, 1 H, 35-H_b), 1.86–2.05 (m, 8 H, 3-H_a, 4-H, 8-H, 29-H, 34-H), 2.23 (m, 1 H, 3-H_b), 2.65 (s, 3 H, 15-H), 2.68 (dq, $^3J_{31,32}$ = 9.8 Hz, $^3J_{31,39}$ = 6.9 Hz, 1 H, 31-H), 2.88 (dd, $^2J_{18a,18b}$ = 12.8 Hz, $^3J_{18a,17}$ = 4.9 Hz, 1 H, 18-H_a), 3.08 (d, $^2J_{28a,28b}$ = 10.4 Hz, 1 H, 28-H_a), 3.23 (dd, $^2J_{18b,18a}$ = 12.3 Hz, $^3J_{18b,17}$ = 11.0 Hz, 1 H, 18-H_b), 3.37 (dd, $^2J_{28b,28a}$ = 10.4 Hz, $^3J_{28b,27}$ = 8.2 Hz, 1 H, 28-H_b), 3.53 (m, 1 H, 32-H), 3.60 (d, $^3J_{OH,32}$ = 10.7 Hz, 1 H, OH), 3.68 (m, 1 H, 5-H_a), 3.77 (s, 3 H, 23-H), 4.17 (dd, $^3J_{7,8}$ = 10.7 Hz, $^3J_{7,NH}$ = 8.8 Hz, 1 H, 7-H), 4.19 (m, 1 H, 5-H_b), 4.46 (dd, $^3J_{2,3a}$ = 8.8 Hz, $^3J_{2,3b}$ = 4.7 Hz, 1 H, 2-H), 4.88–4.98 (m, 2 H, 13-H, 36-H), 5.21–5.32 (m, 2 H, 17-H, 27-H), 6.48 (d, $^3J_{NH,17}$ = 8.8 Hz, 1 H, 17-NH), 6.80 (d, $^3J_{21,20}$ = 8.5 Hz, 2 H, 21-H), 6.94 (d, $^3J_{26,27}$ = 9.1 Hz, 1 H, 26-H), 7.07 (d, $^3J_{20,21}$ = 8.5 Hz, 2 H, 21-H), 7.92 (d, $^3J_{NH,7}$ = 8.2 Hz, 1 H, 7-NH).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 9.4 (q, C-10), 12.2 (q, C-29), 14.1 (q, C-14), 14.2 (q, C-11), 16.4 (q, C-39), 20.1 (q, C-40), 24.2 (d, C-34), 24.7 (t, C-9), 24.8 (t, C-4), 26.0 (q, C-38), 28.3 (q, C-15), 29.1 t, C-3), 34.7 (s, C-37), 35.0 (d, C-8), 37.5 (t, C-35), 37.6 (t, C-18), 38.0 (t, C-28), 39.1 (t, C-33), 47.4 (t, C-5), 48.5 (d, C-31), 50.3 (d, C-17), 54.9 (d, C-7), 54.9 (d, C-13), 55.3 (q, C-23), 59.0 (d, C-2), 72.2 (d, C-32), 72.3 (d, C-27), 77.5 (d, C-36), 114.1 (d, C-21), 126.2 (s, C-25), 128.2 (s, C-19), 130.1 (d, C-20), 144.8 (d, C-26), 158.6 (s, C-22), 167.2 (s, C-24), 169.2 (s, C-12), 170.9 (s, C-6), 171.4 (s, C-16), 171.9 (s, C-1), 178.5 (s, C-30).

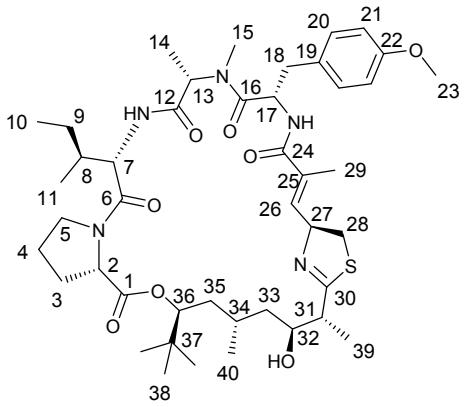
minor rotamer (selected signals):

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.82 (t, $^3J_{10,9}$ = 7.4 Hz, 3 H, 10-H), 0.86 (s, 9 H, 38-H), 1.08 (d, $^3J_{39,31}$ = 6.9 Hz, 3 H, 39-H), 1.27 (d, $^3J_{40,34}$ = 6.9 Hz, 3 H, 40-H), 2.84 (s, 3 H, 15-H), 2.91 (dd, $^2J_{18a,18b}$ = 12.9 Hz, $^3J_{18a,17}$ = 5.4 Hz, 1 H, 18-H_a), 3.28 (m, 1 H, 18-H_b), 3.40 (dd, $^2J_{28b,28a}$ = 10.7 Hz, $^3J_{28b,27}$ = 7.9 Hz, 1 H, 28-H_b), 3.78 (s, 3 H, 23-H), 4.33 (dd, $^3J_{7,NH}$ = 8.4 Hz, $^3J_{7,8}$ = 5.8 Hz, 1 H, 7-H), 4.61 (dd, $^3J_{2,3a}$ = 11.0 Hz, $^3J_{2,3b}$ = 9.5 Hz, 1 H, 2-H), 6.22 (d, $^3J_{NH,17}$ = 6.9 Hz, 1 H, 17-NH), 6.62 (d, $^3J_{26,27}$ = 10.1 Hz, 1 H, 26-H), 6.81 (d, $^3J_{21,20}$ = 8.2 Hz, 2 H, 21-H), 7.10 (d, $^3J_{NH,7}$ = 10.1 Hz, 1 H, 7-NH), 7.14 (d, $^3J_{20,21}$ = 8.5 Hz, 2 H, 20-H).

HRMS (ESI) calcd for $C_{44}H_{68}N_5O_8S$ $[M+H]^+$: 826.4783, found: 826.4784.

[7] H. Luesch, W. Y. Yoshida, R. E. Moore and V. J. Paul, *Bioorg. Med. Chem.*, 2002, **10**, 1973–1978.

*34-epi-Apratoxin B (epi-**21b**):*



^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.56 (d, $^3J_{14,13}$ = 6.9 Hz, 3 H, 14-H), 0.71 (t, $^3J_{10,9}$ = 7.3 Hz, 3 H, 10-H), 0.76–0.85 (m, 2 H, 9-H_a, 33-H_a), 0.88 (s, 9 H, 38-H), 0.98 (d, $^3J_{40,34}$ = 6.3 Hz, 3 H, 40-H), 0.98 (d, $^3J_{11,8}$ = 6.6 Hz, 3 H, 11-H), 1.14–1.31 (m, $^3J_{39,31}$ = 6.9 Hz, 5 H, 9-H_b, 35-H_a, 39-H), 1.66 (ddd, $^2J_{53b,35a}$ = 14.5 Hz, $^3J_{35b,36}$ = 12.0 Hz, $^3J_{35b,34}$ = 2.5 Hz, 1 H, 35-H_b), 1.80–2.04 (m, 9 H, 3-H_a, 4-H, 8-H, 29-H, 33-H_b, 34-H), 2.23 (m, 1 H, 3-H_b), 2.59 (dq, $^3J_{31,39}$ = 6.6 Hz, $^3J_{31,32}$ = 1.6 Hz, 1 H, 31-H), 2.63 (s, 3 H, 15-H), 2.88 (dd, $^2J_{18a,18b}$ = 12.3 Hz, $^3J_{18a,17}$ = 5.0 Hz, 1 H, 18-H_a), 3.06 (d, $^2J_{28a,28b}$ = 10.4 Hz, 1 H, 28-H_a), 3.19 (dd, $^2J_{18b,18a}$ = 12.1 Hz, $^3J_{18b,17}$ = 10.9 Hz, 1 H, 18-H_b), 3.43 (dd, $^2J_{28b,28a}$ = 10.7 Hz, $^3J_{28b,27}$ = 7.9 Hz, 1 H, 28-H_b), 3.46 (d, $^3J_{OH,\ 32}$ = 6.0 Hz, 1 H, OH), 3.68 (dt, $^2J_{5a,5b}$ = 9.7 Hz, $^3J_{5a,4}$ = 6.7 Hz, 1 H, 5-H_a), 3.77 (s, 3 H, 23-H), 4.04–4.13 (m, 2 H, 5-H_b, 32-H), 4.22 (dd, $^3J_{7,8}$ = 10.6 Hz, $^3J_{7,NH}$ = 8.4 Hz, 1 H, 7-H), 4.47 (dd, $^3J_{2,3a}$ = 8.4 Hz, $^3J_{2,3b}$ = 4.3 Hz, 1 H, 2-H), 4.88 (q, $^3J_{13,14}$ = 6.8 Hz, 1 H, 13-H), 4.98 (dd, $^3J_{36,35b}$ = 12.1 Hz, $^3J_{36,35a}$ = 1.4 Hz, 1 H. 36-H), 5.12 (m, 1 H, 17-H), 5.36 (dd, $^3J_{27,26} \approx {}^3J_{27,28b}$ = 8.2 Hz, 1 H, 27-H), 6.40 (d, $^3J_{NH,17}$ = 7.9 Hz, 1 H, 17-NH), 6.81 (d, $^3J_{21,20}$ = 8.8 Hz, 2 H, 21-H), 6.89 (d, $^3J_{26,27}$ = 8.5 Hz, 1 H, 26-H), 7.06 (d, $^3J_{20,21}$ = 8.5 Hz, 2 H, 20-H), 8.33 (d, $^3J_{NH,7}$ = 8.2 Hz, 1 H, 7-NH).

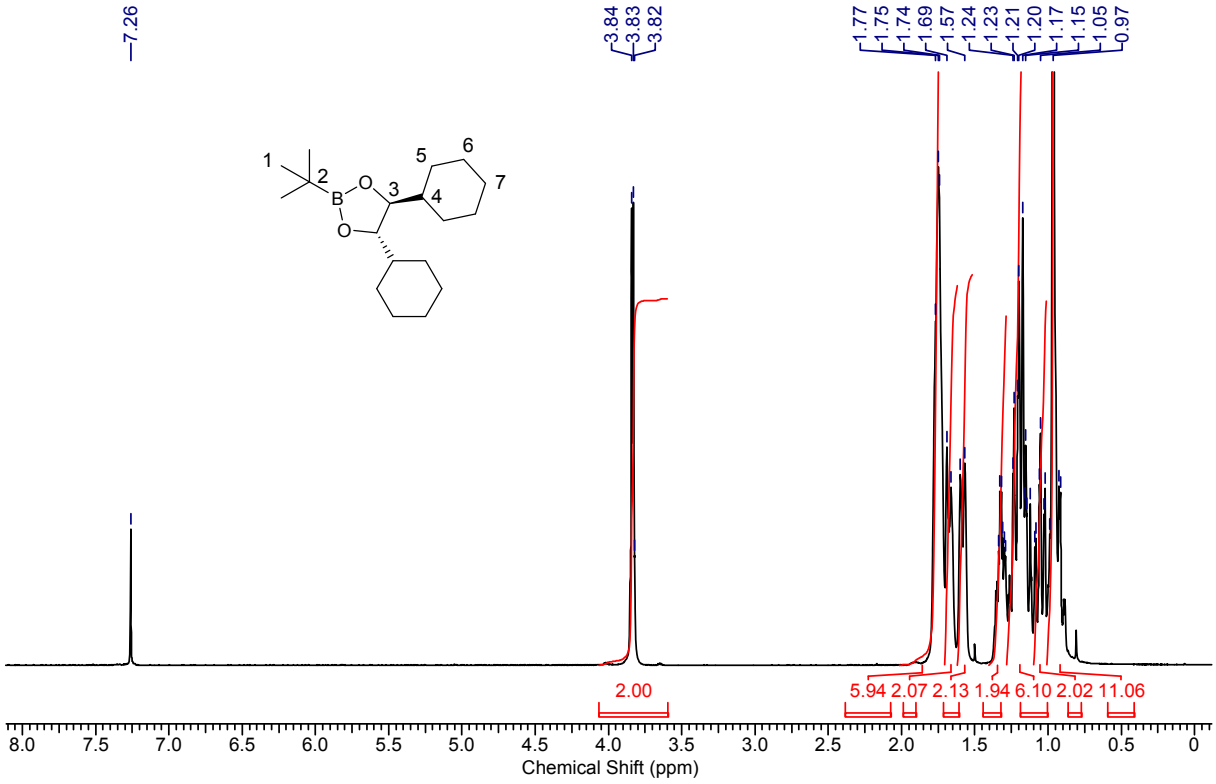
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 9.7 (q, C-39), 9.8 (q, C-10), 12.3 (q, C-29), 13.6 (q, C-14), 14.6 (q, C-11), 21.0 (q, C-40), 24.7 (t, C-9), 24.9 (t, C-4), 24.9 (d, C-34), 26.0 (q, C-38), 28.4 (q, C-15), 29.1 (t, C-3), 34.6 (s, C-37), 35.5 (d, C-8), 37.4 (t, C-35), 37.9 (t, C-18), 39.1 (t, C-28), 39.9 (t, C-33), 45.4 (d, C-31), 47.3 (t, C-5), 50.8 (d, C-17), 55.0 (d, C-7), 55.1 (d, C-13), 55.3 (q, C-23), 59.1 (d, C-2), 69.3 (d, C-32), 73.0 (d, C-27), 77.6 (d, C-36), 114.2 (d, C-21), 126.4 (s, C-25), 128.1 (s, C-19), 130.2 (d, C-20), 144.8 (d, C-26), 158.8 (s, C-22), 167.1 (s, C-24), 169.3 (s, C-12), 171.4 (s, C-6), 171.4 (s, C-16), 171.6 (s, C-1), 177.0 (s, C-30).

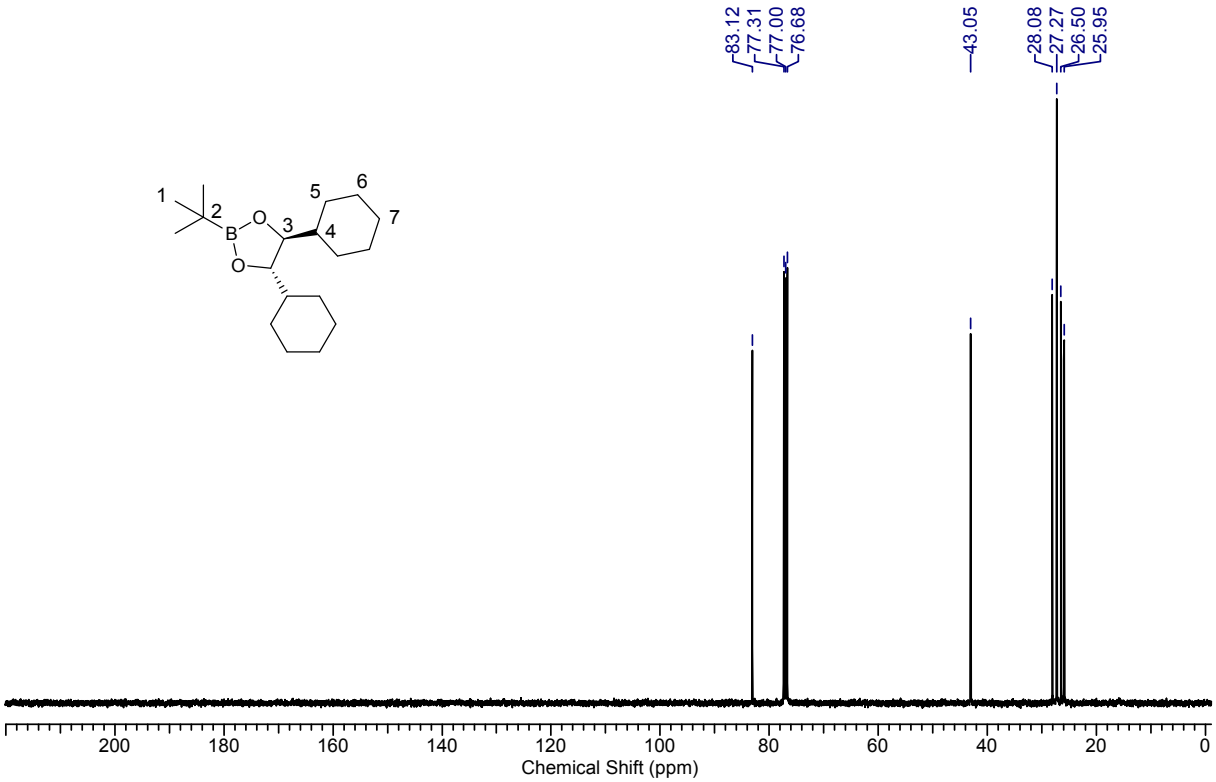
HRMS (ESI) calcd for $C_{44}H_{68}N_5O_8S$ $[M+H]^+$: 826.4783, found: 826.4783.

HPLC (*Phenomenex Luna® C18(2)*, H_2O + 0.1 % HCOOH, MeCN 35:65, 1.25 ml/min, 40 °C): t_R(**21b**) = 4.52 min, t_R(***epi*-21b**) = 4.03 min.

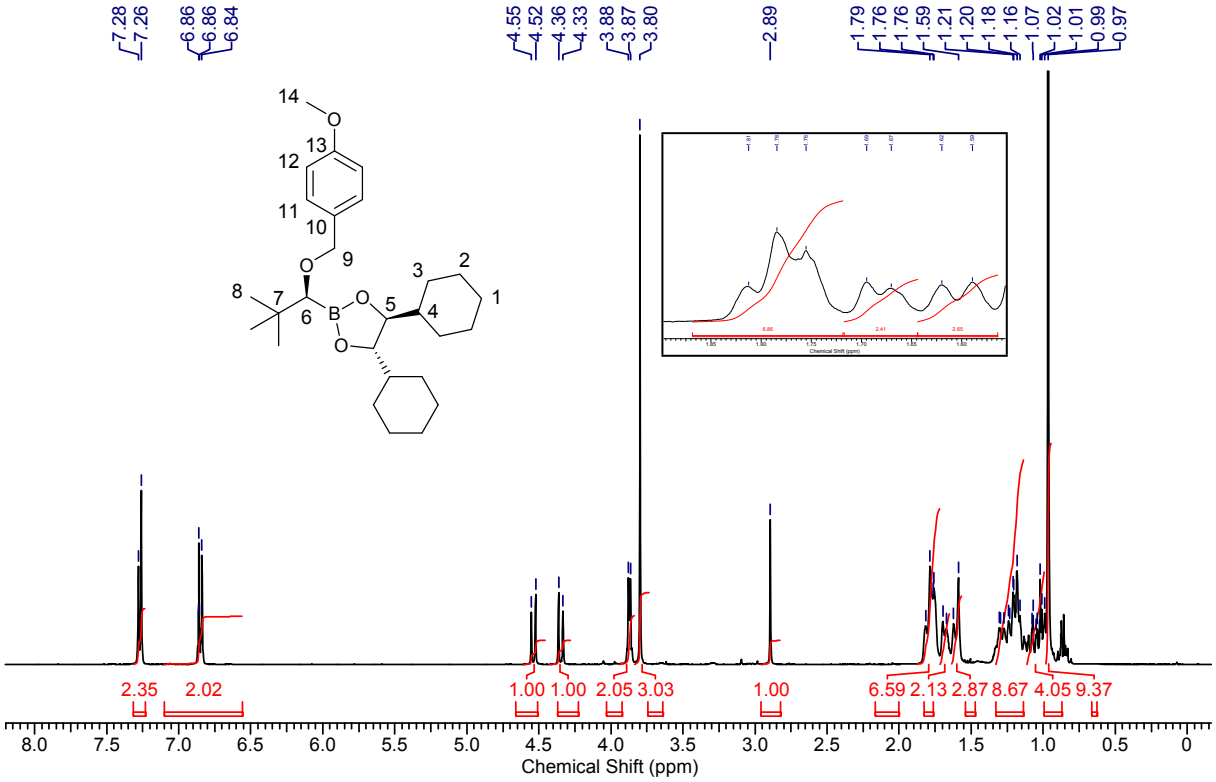
Copies of the NMR spectra and HPLC chromatograms

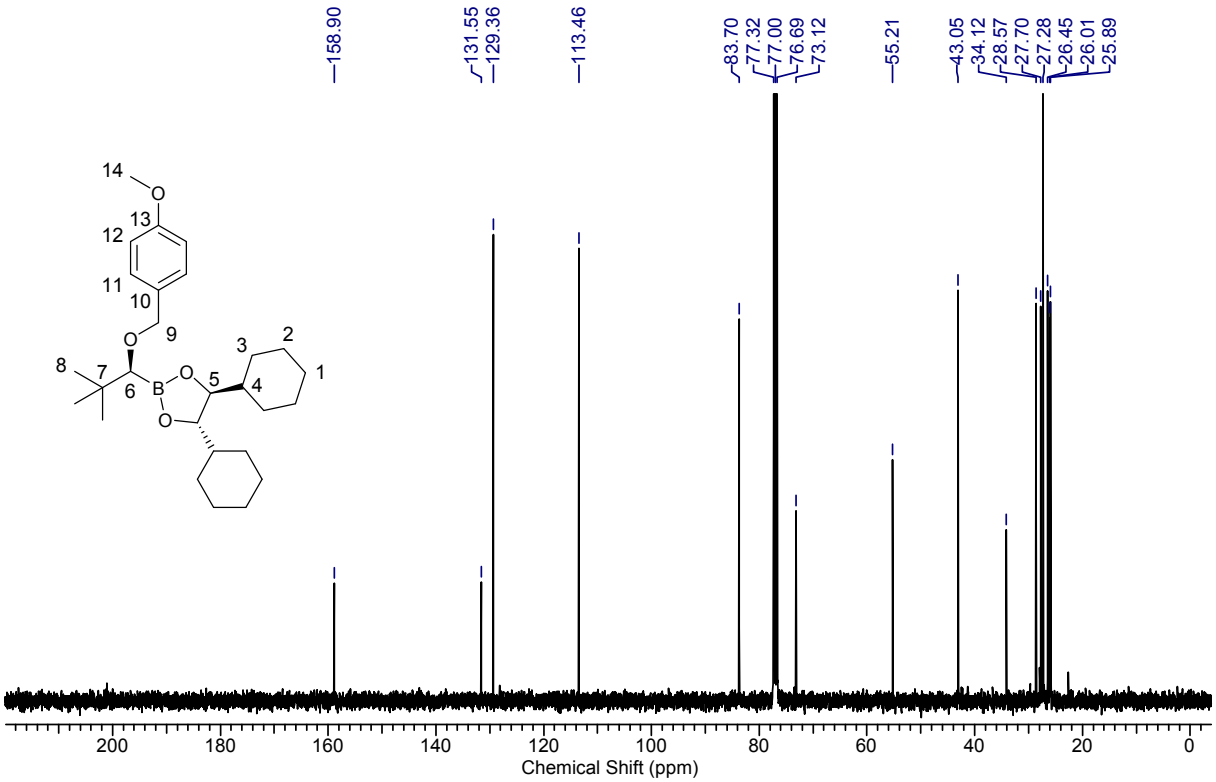
(4*S*,5*S*)-2-(*tert*-Butyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (2)



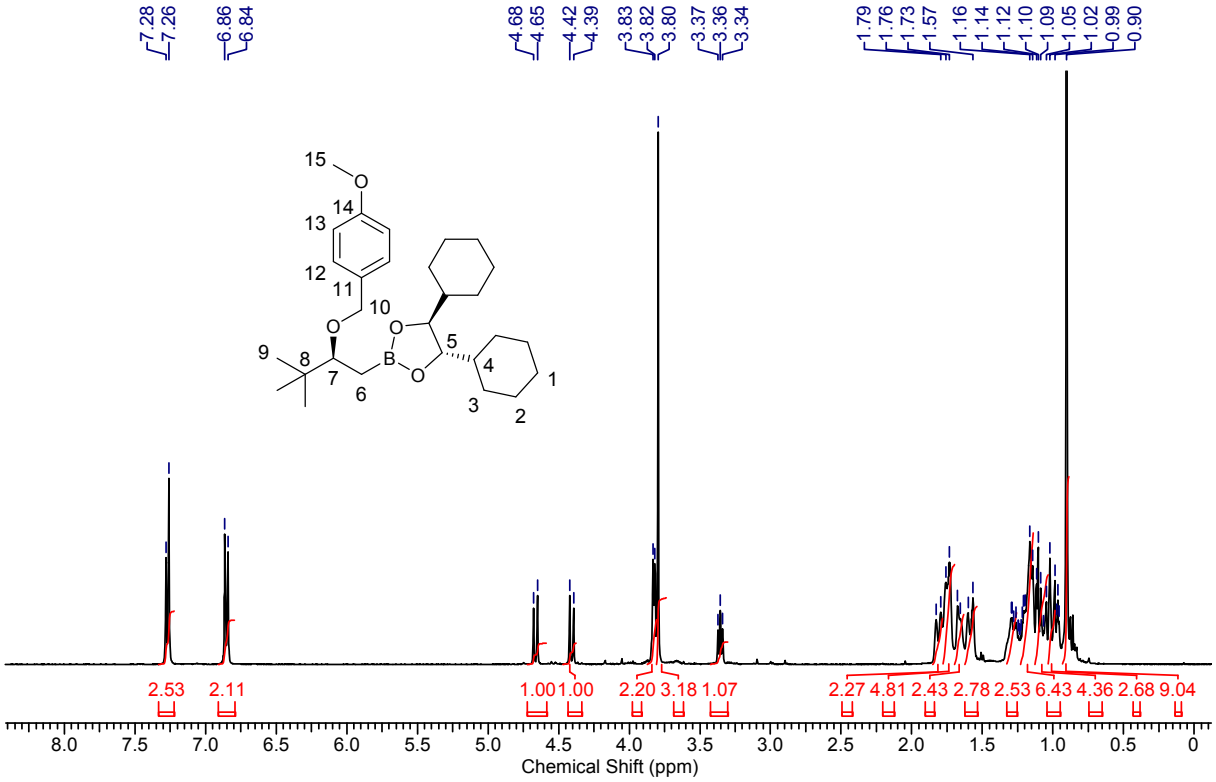


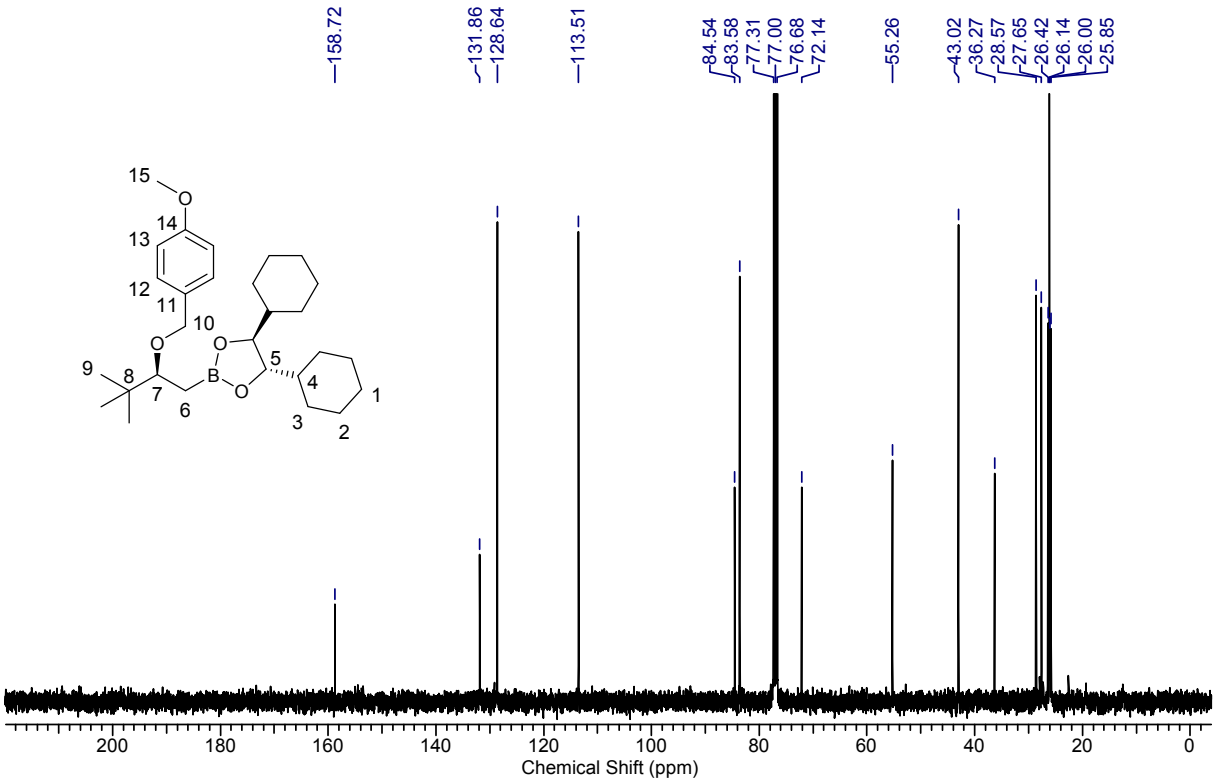
(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(*S*)-1-[(4-methoxybenzyl)oxy]-2,2-dimethylpropyl}-1,3,2-dioxaborolane (3)



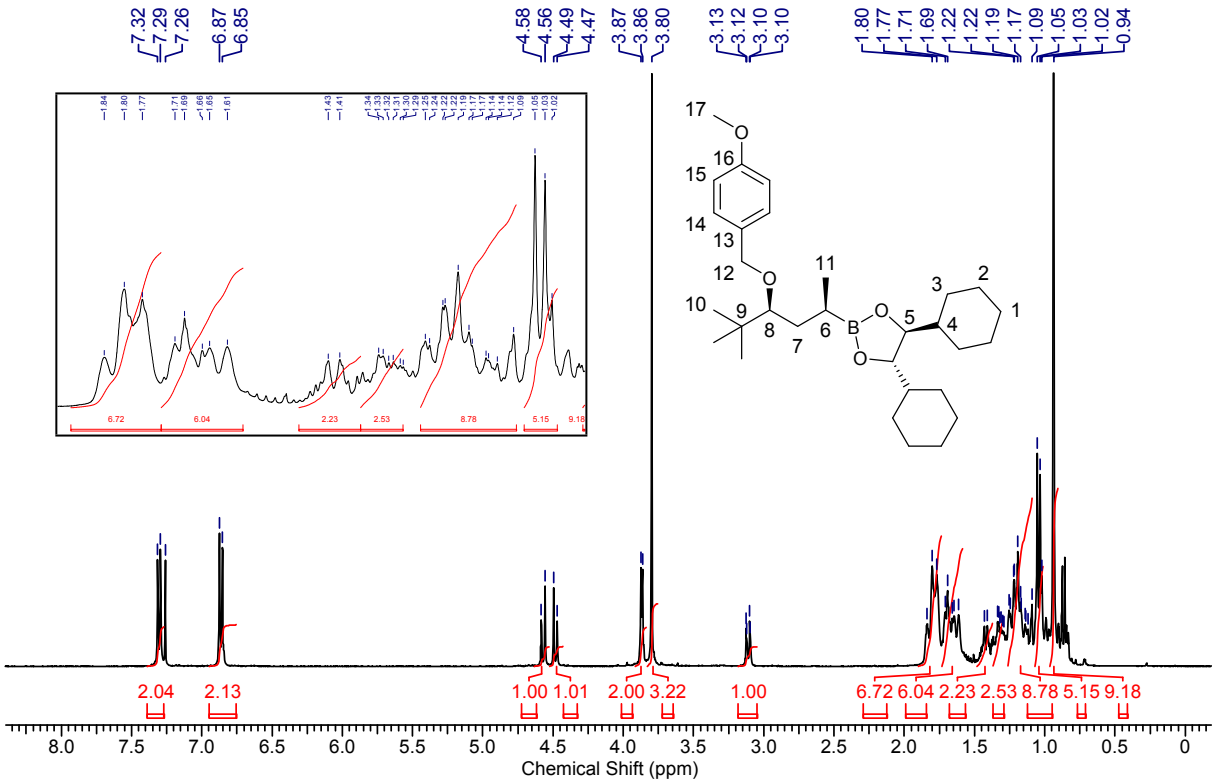


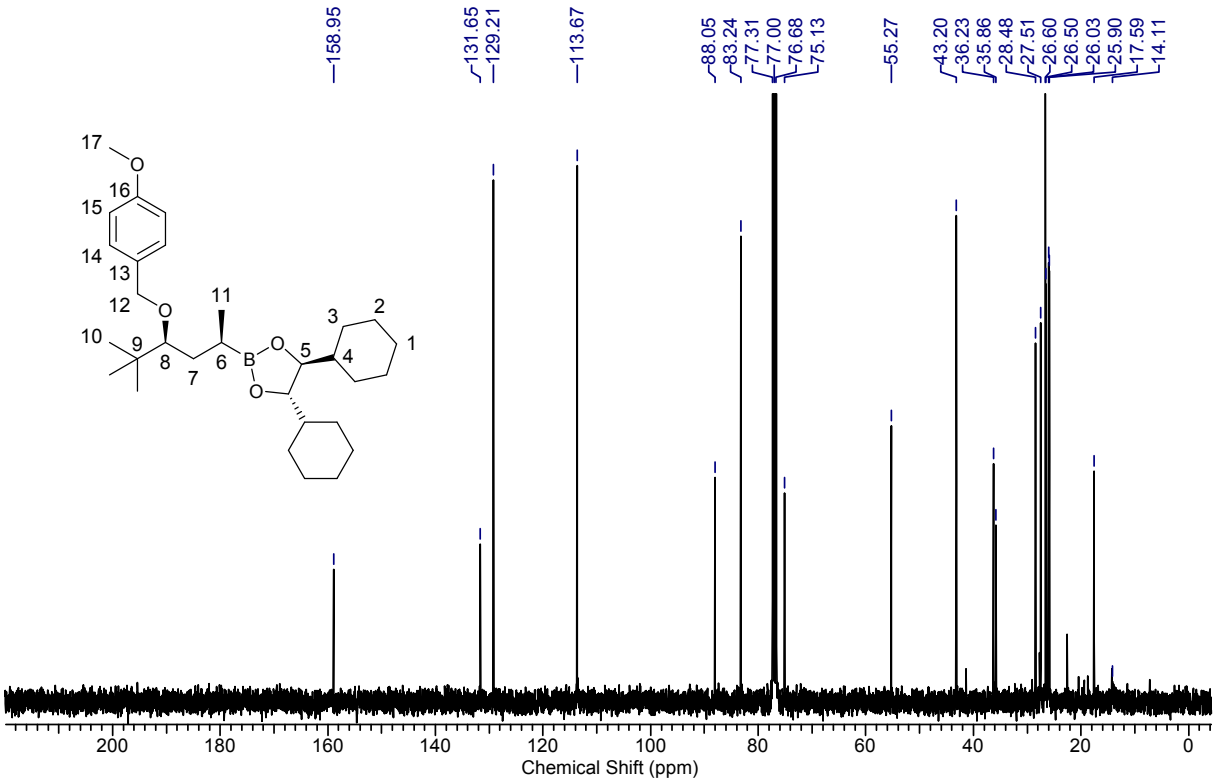
(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(*S*)-2-[(4-methoxybenzyl)oxy]-3,3-dimethylbutyl}-1,3,2-dioxaborolane (4)



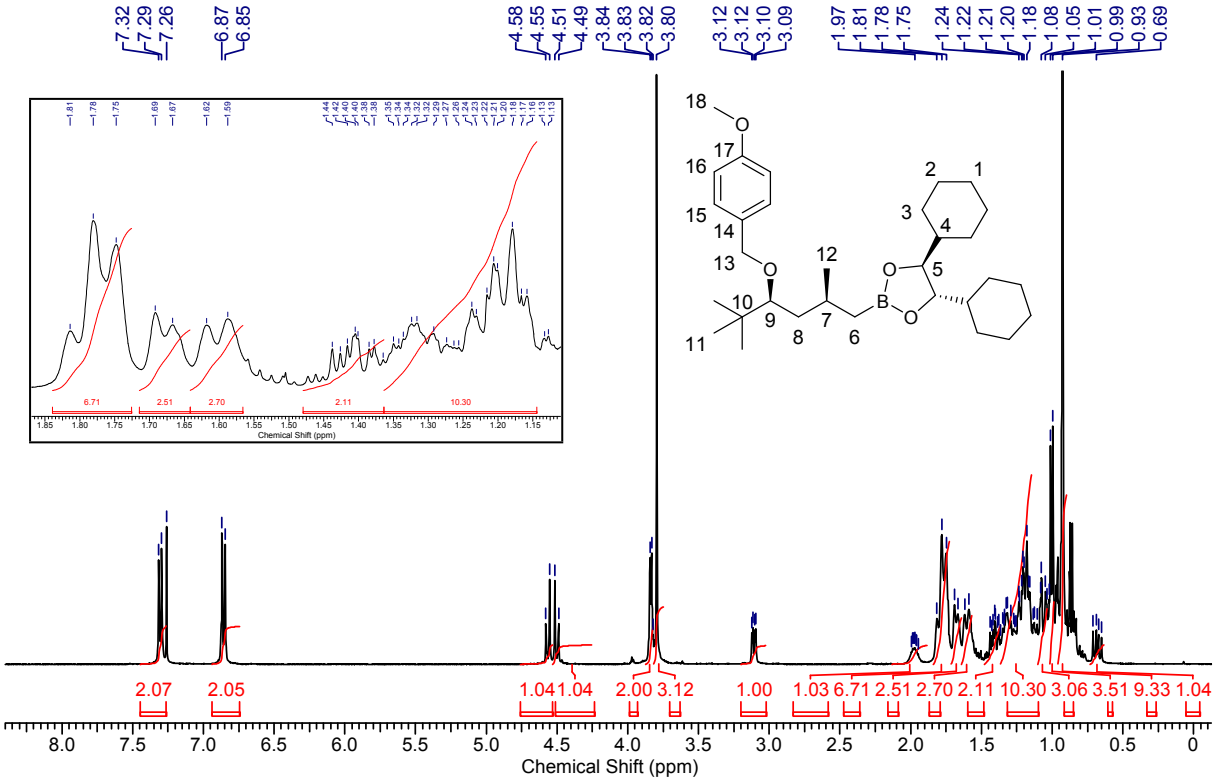


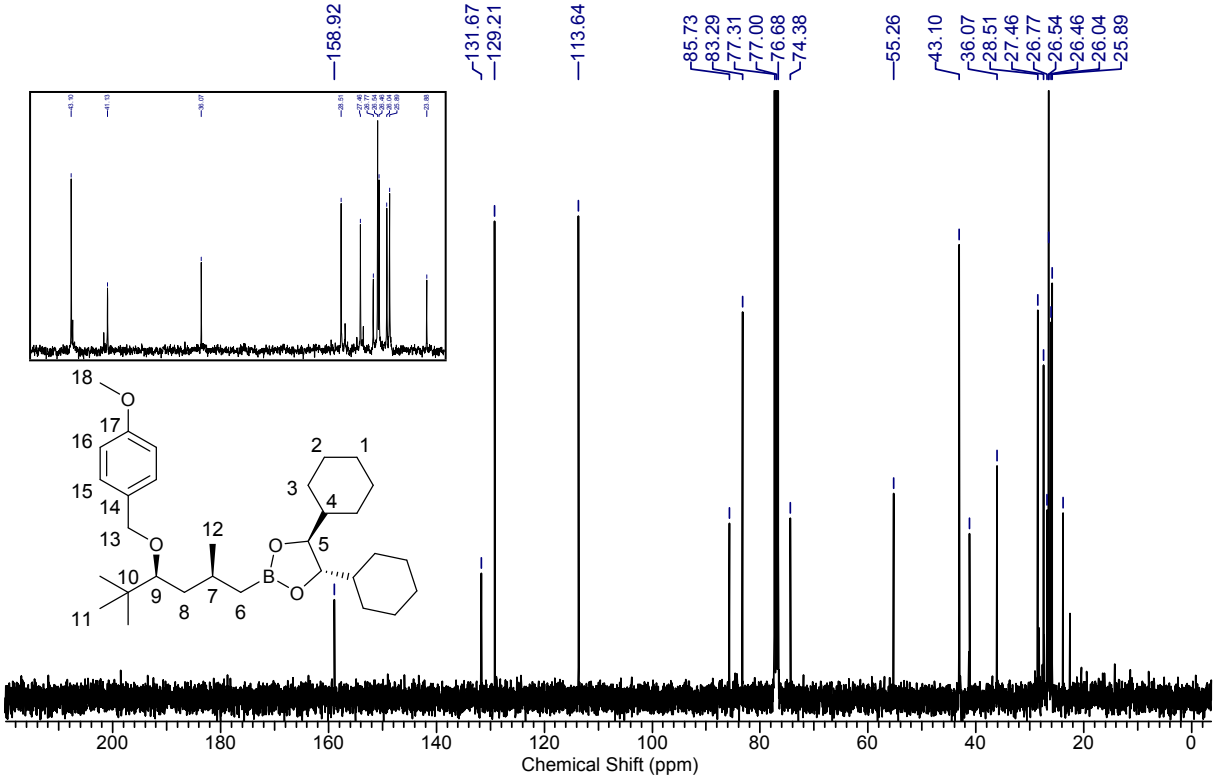
(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(2*R*,4*S*)-4-[(4-methoxybenzyl)oxy]-5,5-dimethylhexan-2-yl}-1,3,2-dioxaborolane (5)



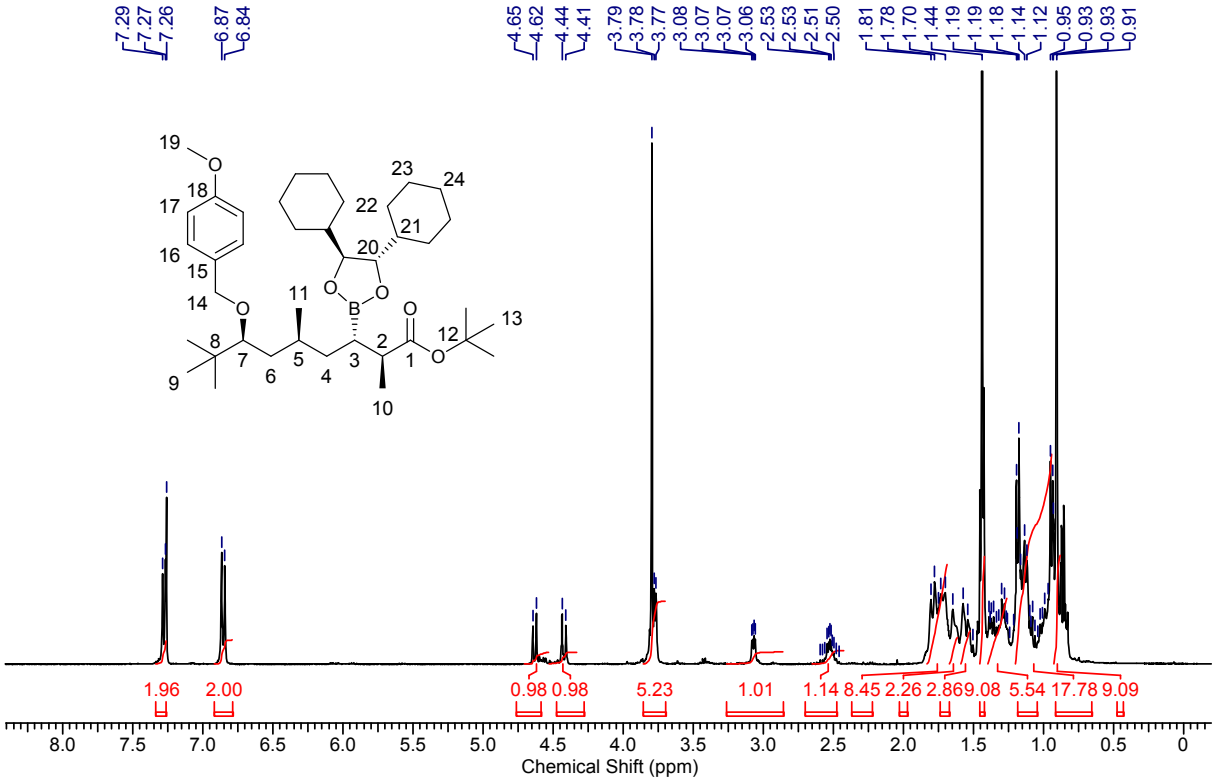


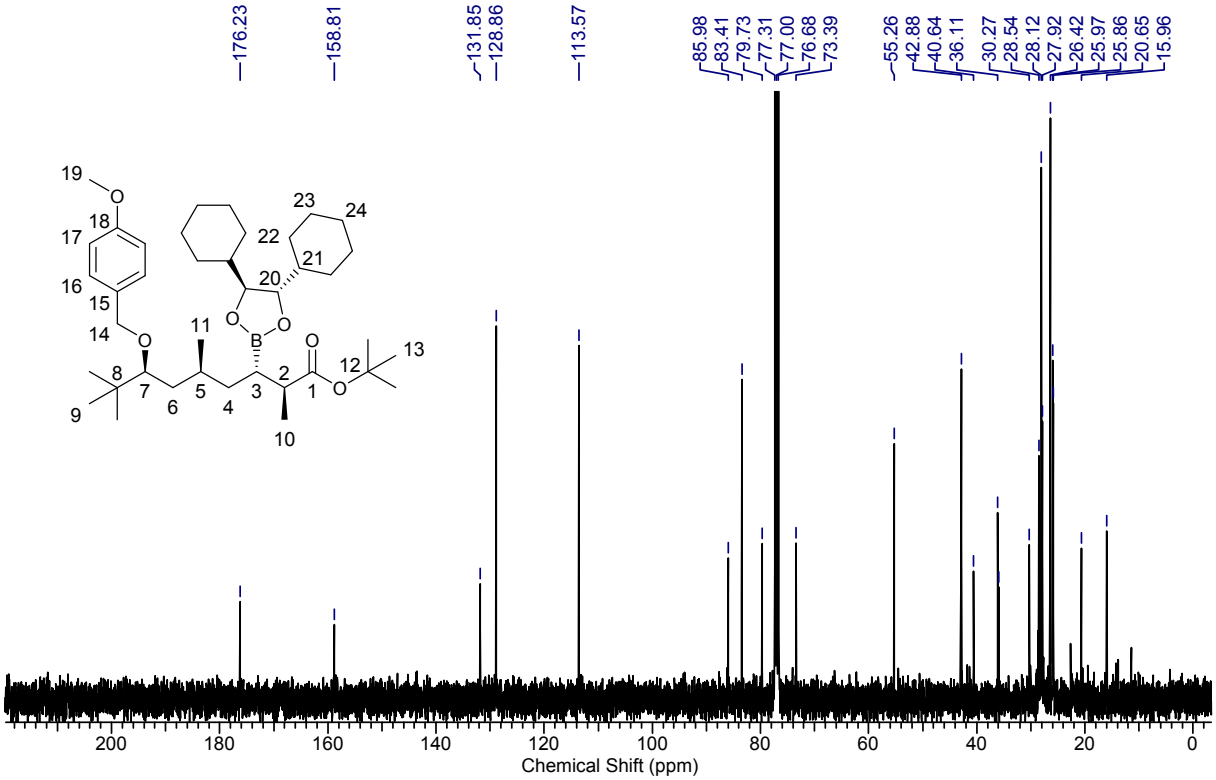
(4*S*,5*S*)-4,5-Dicyclohexyl-2-{(2*S*,4*S*)-4-[(4-methoxybenzyl)oxy]-2,5,5-trimethylhexyl}-1,3,2-dioxaborolane (6)



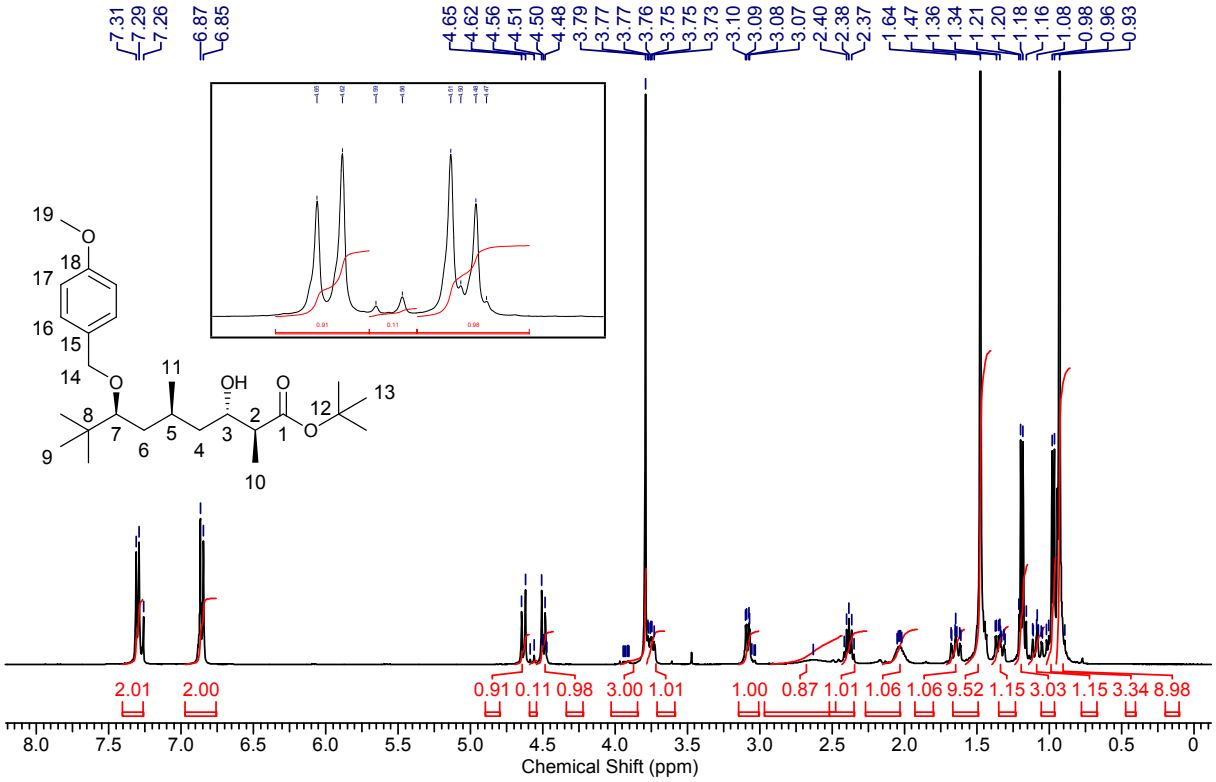


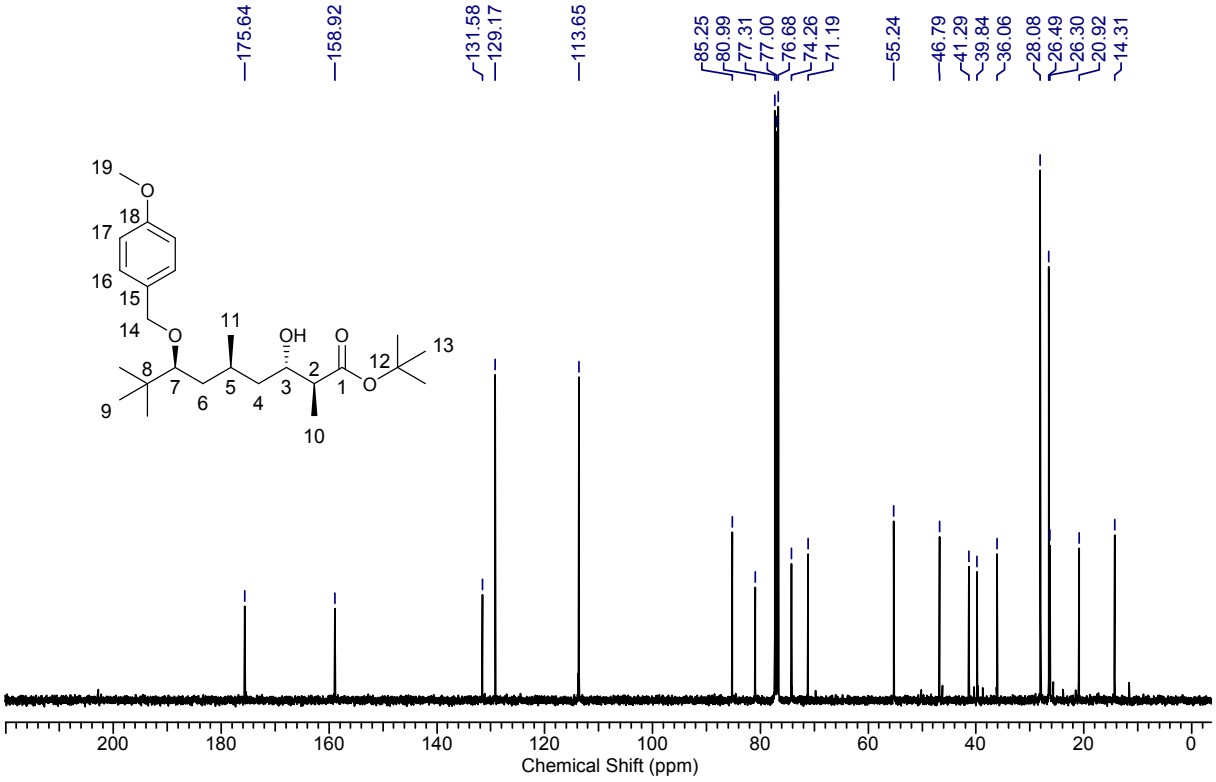
tert-Butyl (2*S*,3*S*,5*S*,7*S*)-3-[(4*S*,5*S*)-4,5-dicyclohexyl-1,3,2-dioxaborolan-2-yl]-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethylnonanoate (7)



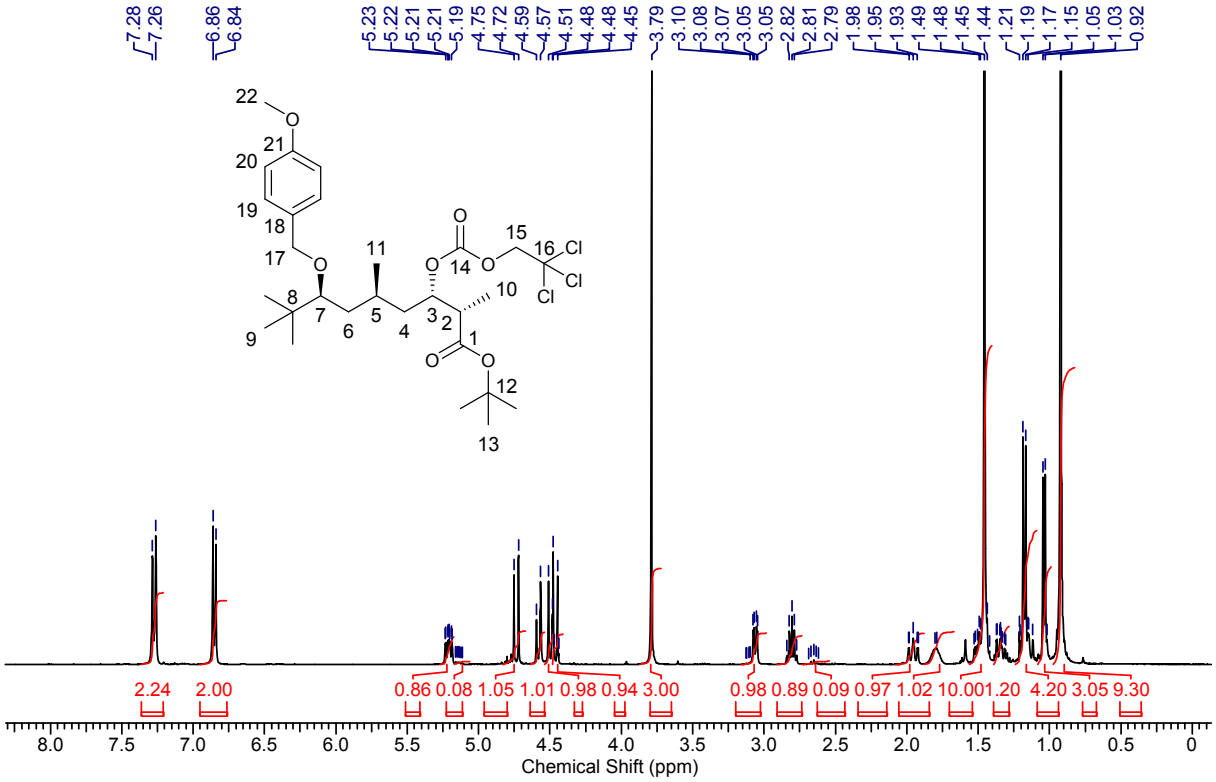


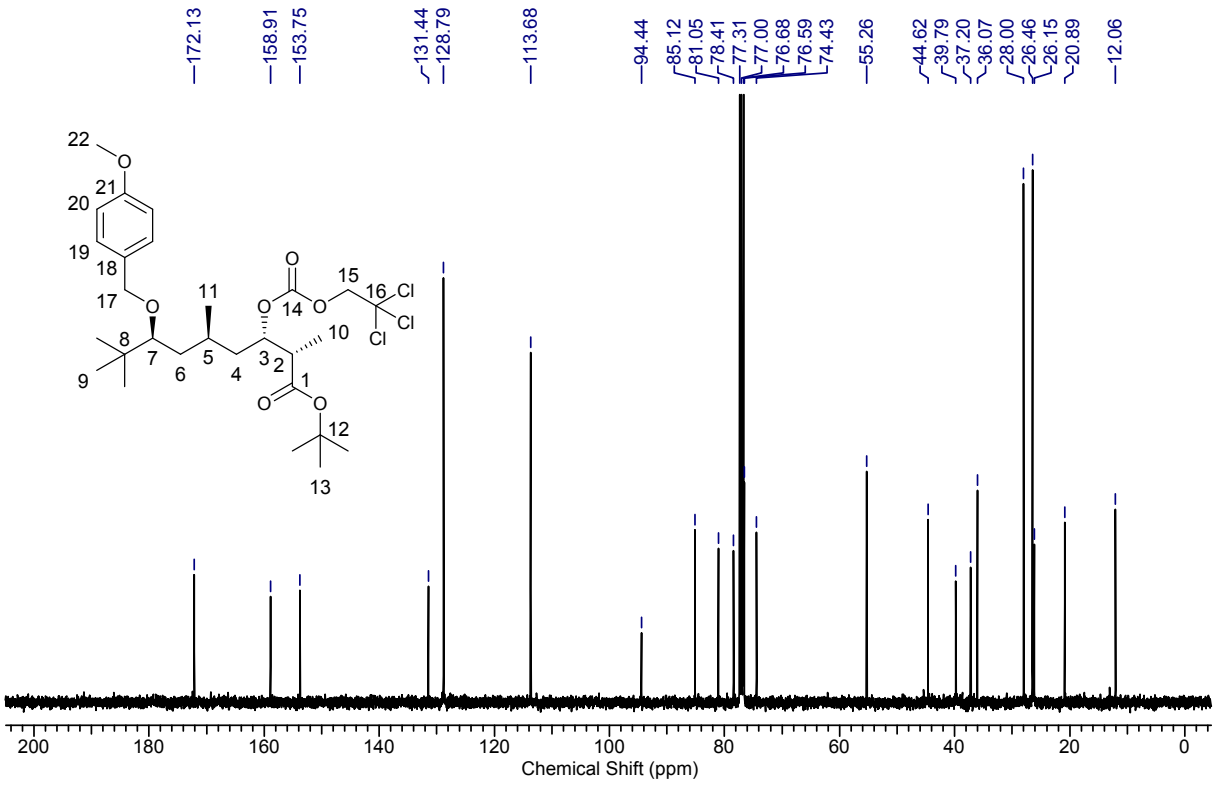
tert-Butyl (2*S*,3*S*, 5*S*,7*S*)-3-hydroxy-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethylnonanoate (8)



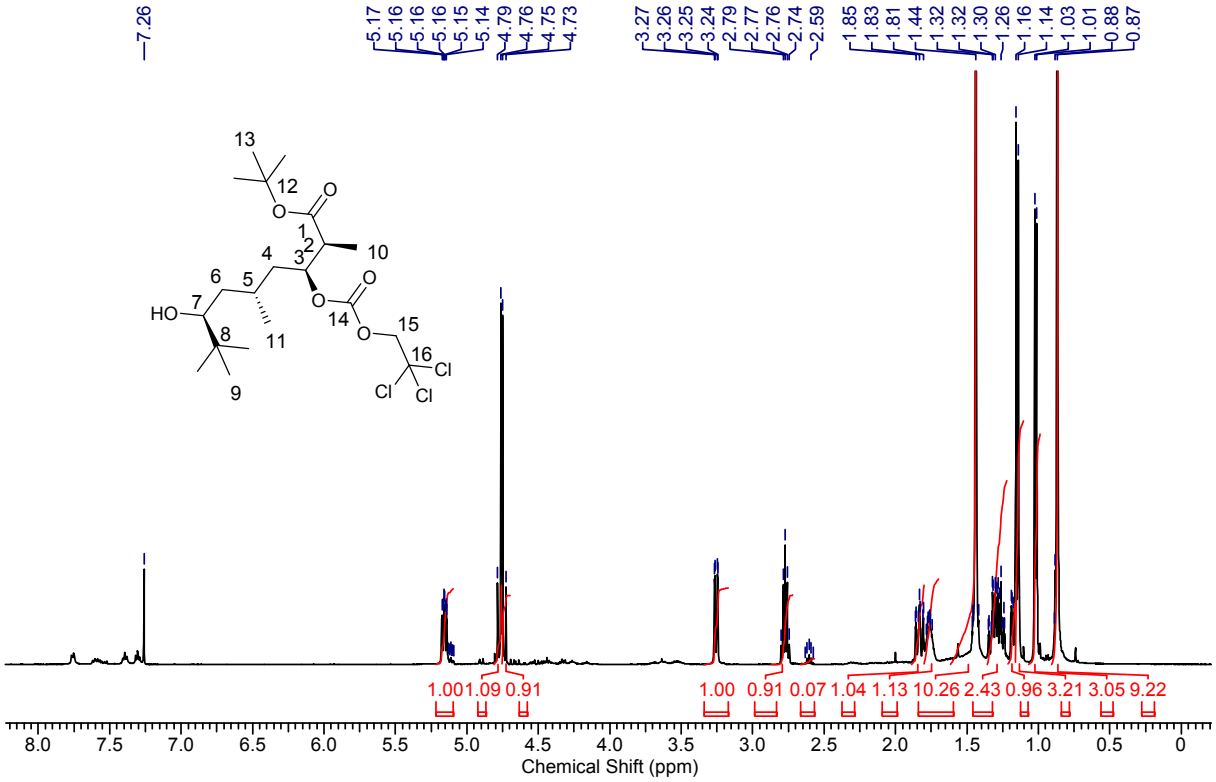


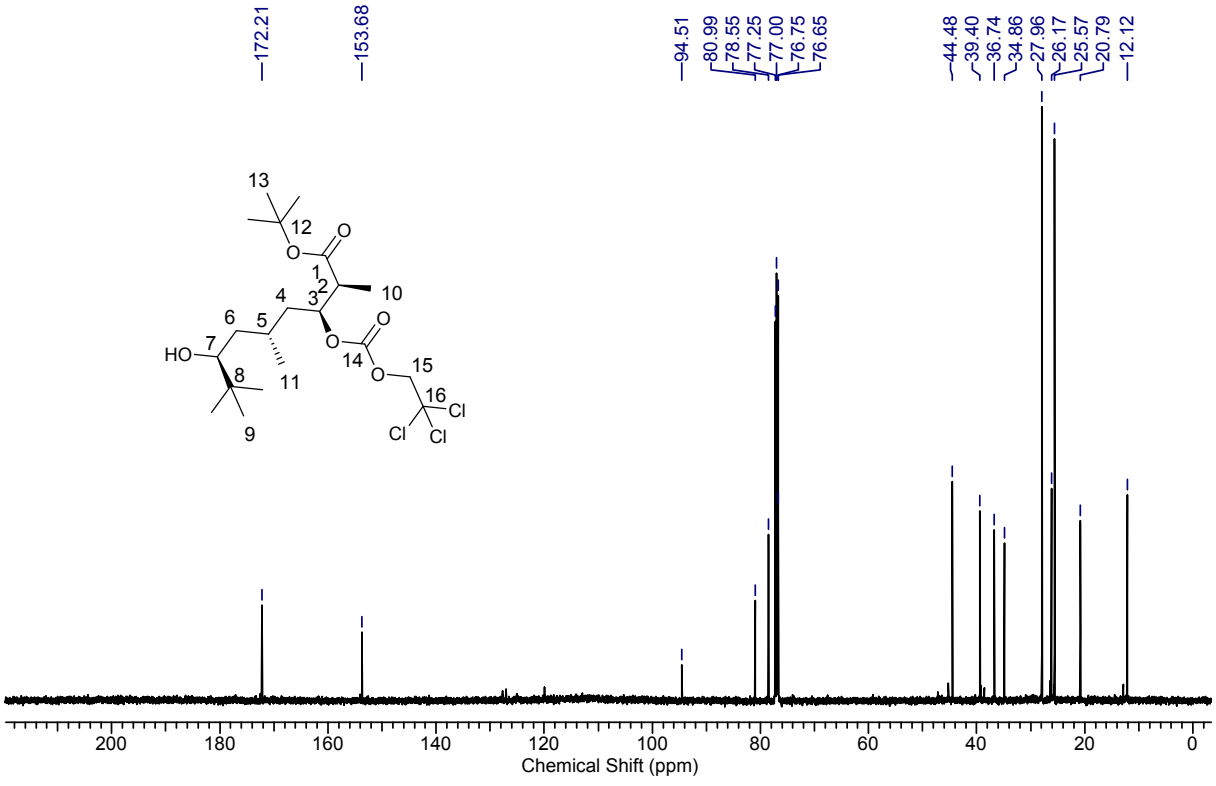
tert-Butyl (2*S*,3*S*,5*S*,7*S*)-7-[(4-methoxybenzyl)oxy]-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoate (9)



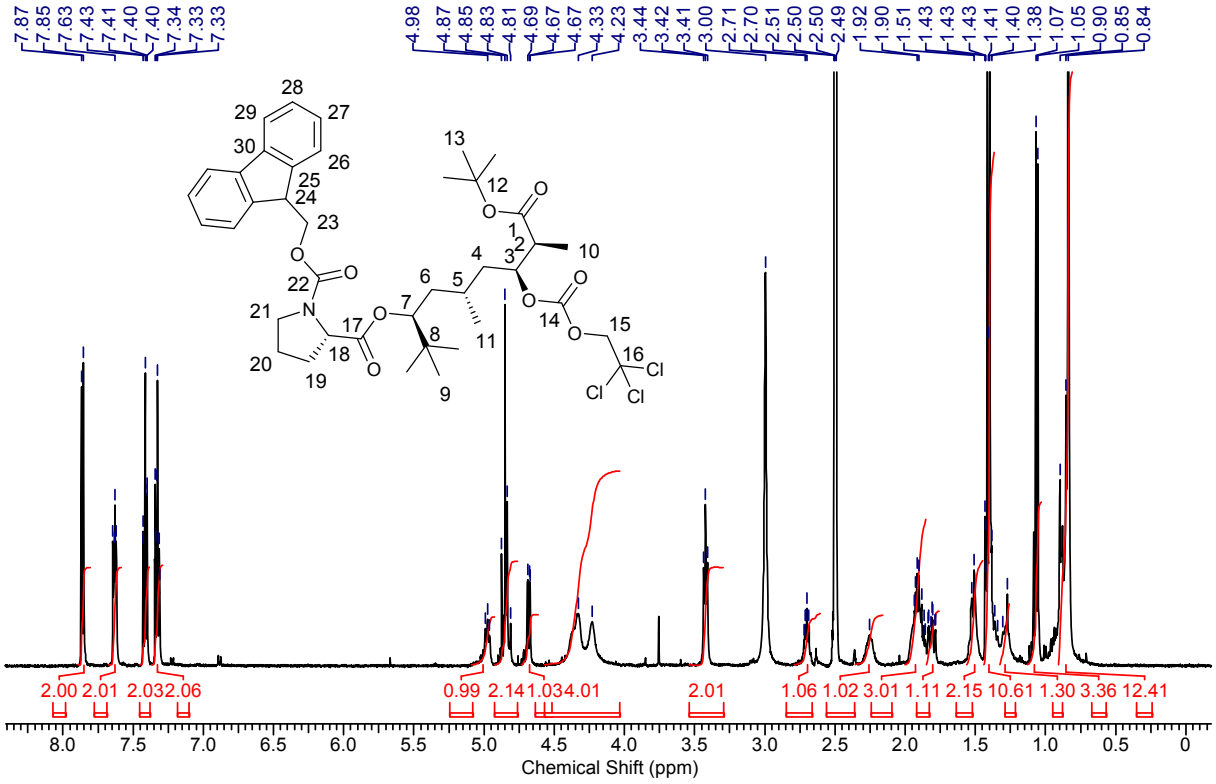


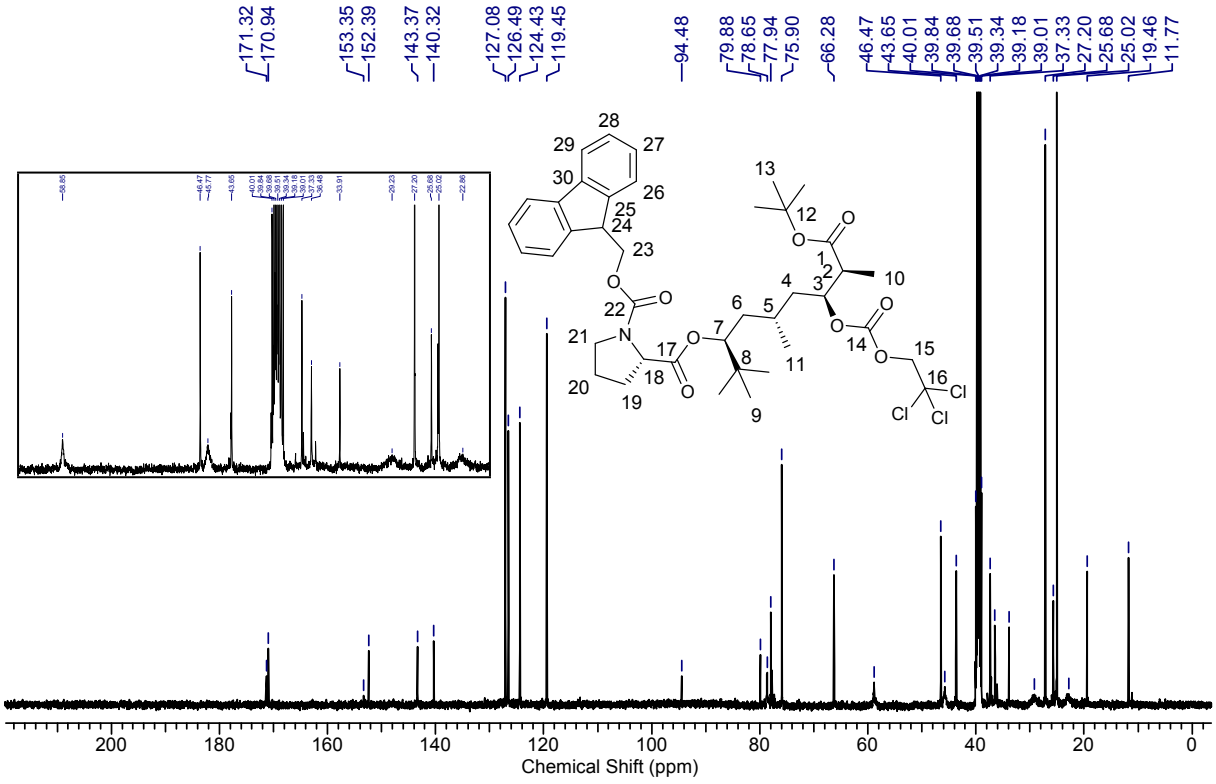
***tert*-Butyl (2*S*,3*S*,5*R*,7*S*)-7-hydroxy-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoate (10)**



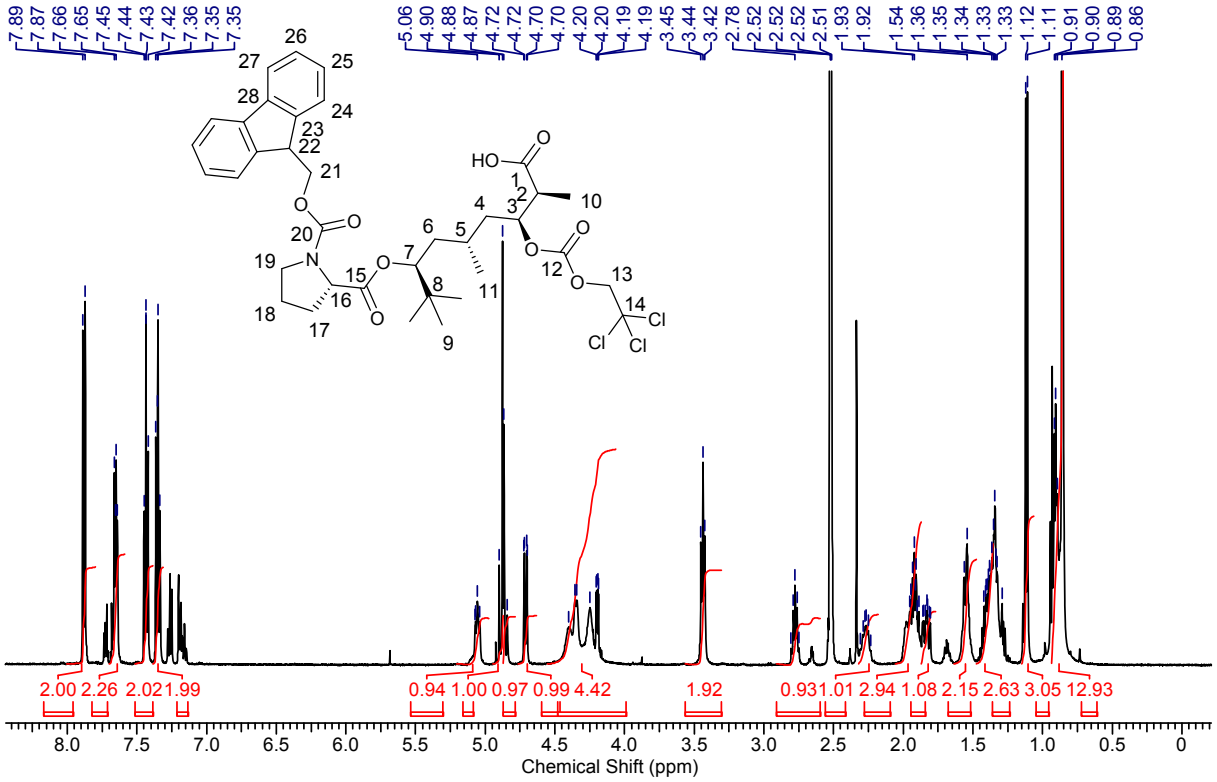


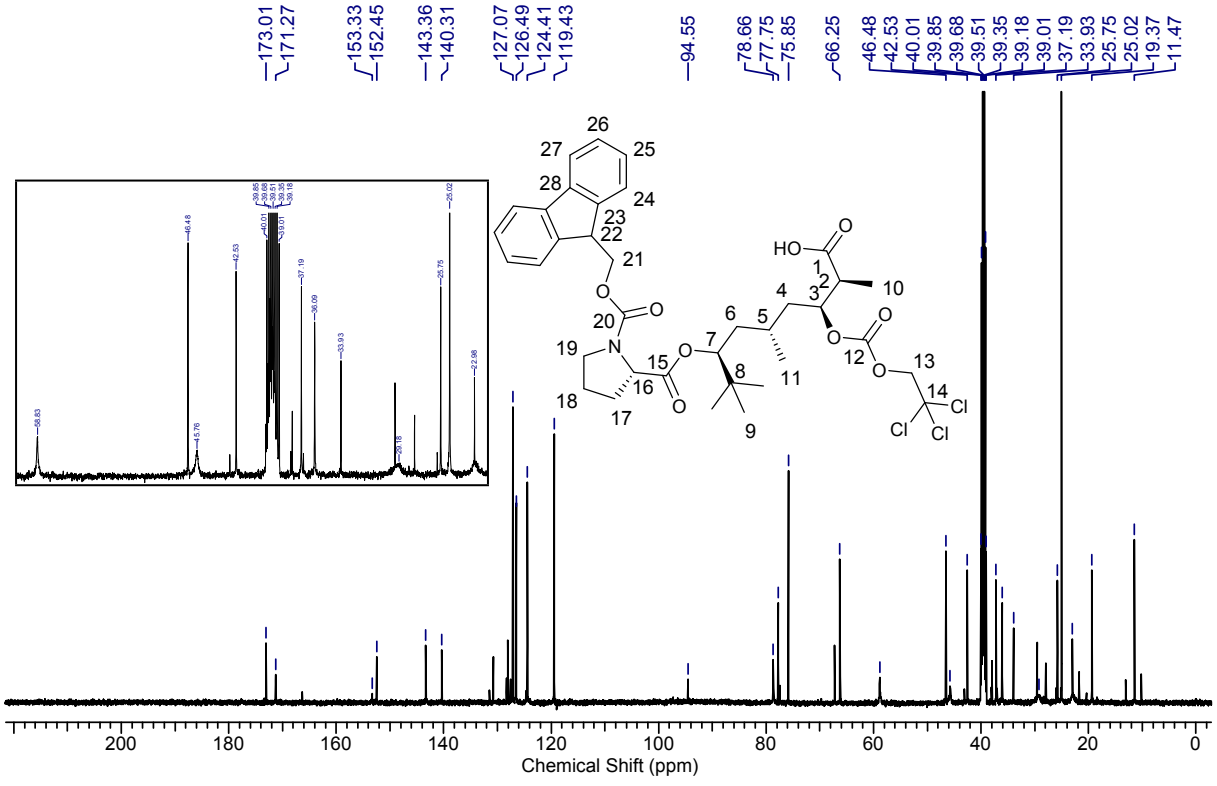
***N*-[(9*H*-Fluoren-9-yl)methyl] 2-({3*S*,5*S*,7*S*,8*S*}-9-{*tert*-butoxy}-2,2,5,8-tetramethyl-9-oxo-7-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonan-3-yl) (*S*)-pyrrolidine-1,2-dicarboxylate (11)**



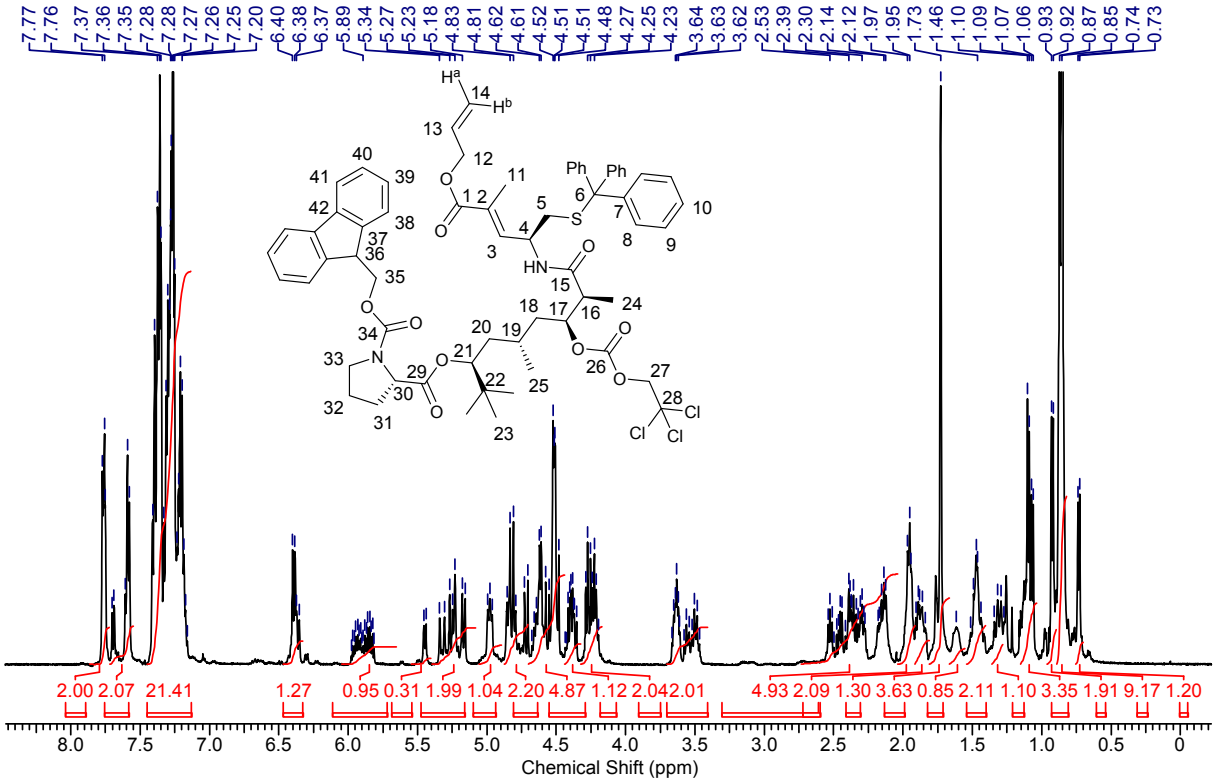


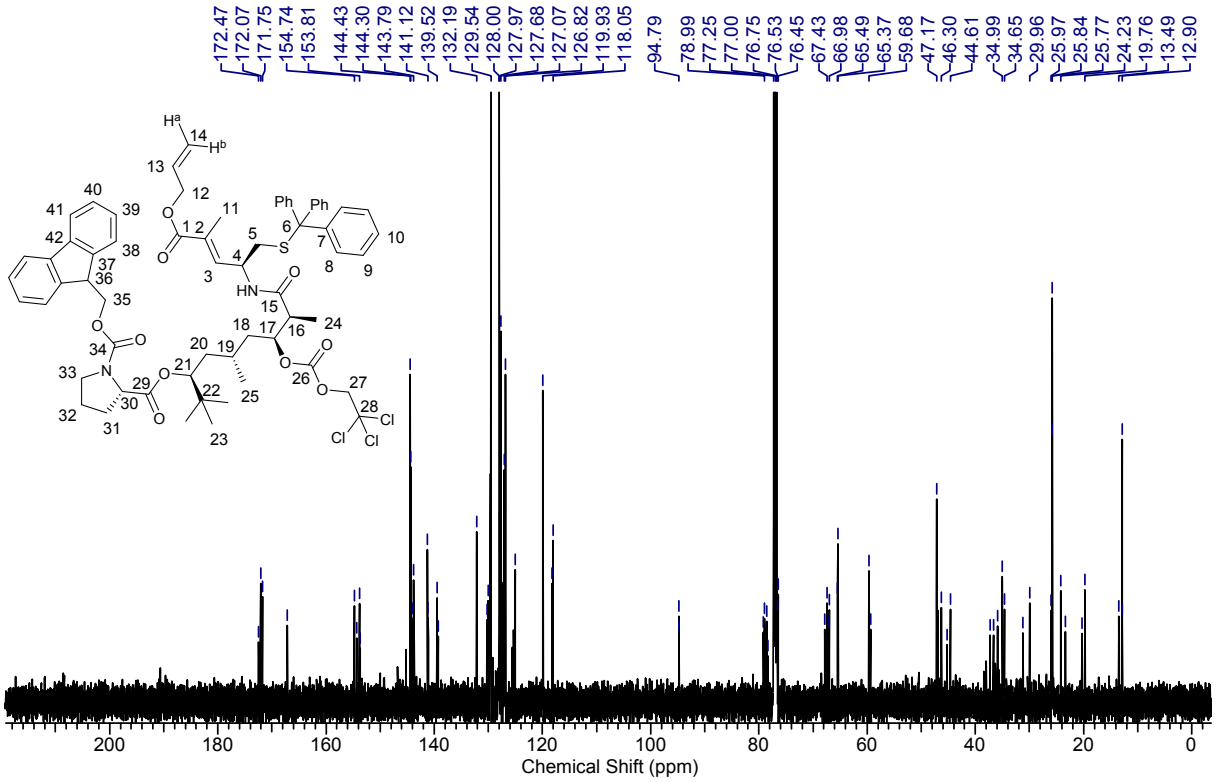
(2*S*,3*S*,5*S*,7*S*)-7-[({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}-L-prolyl)oxy]-2,5,8,8-tetramethyl-3-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonanoic acid (12, crude product)

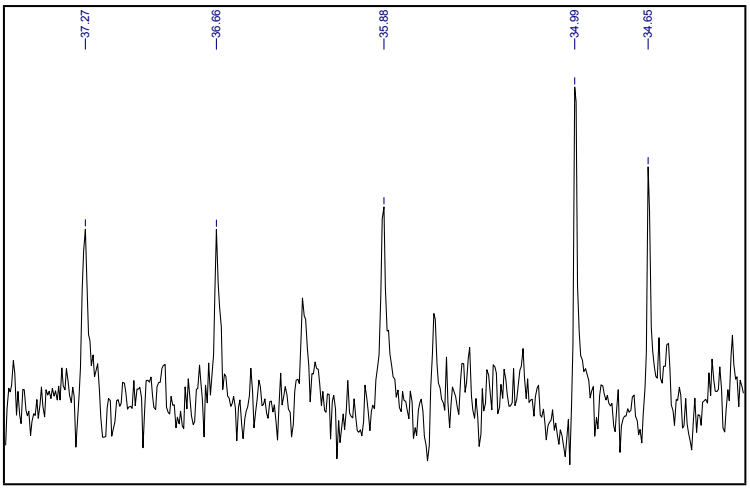


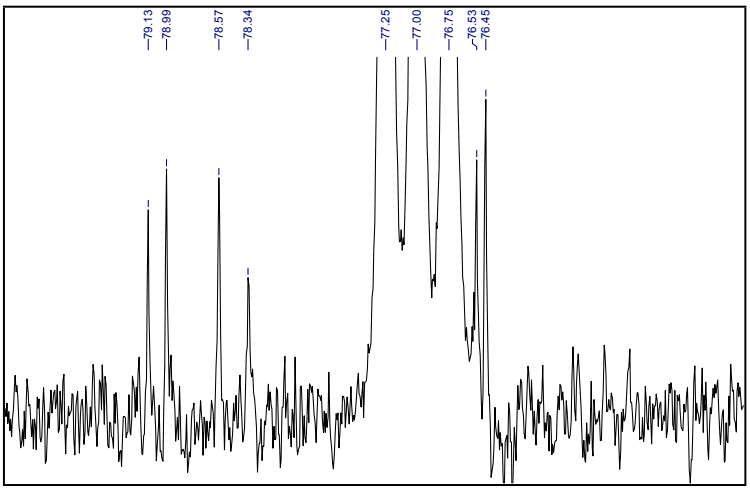


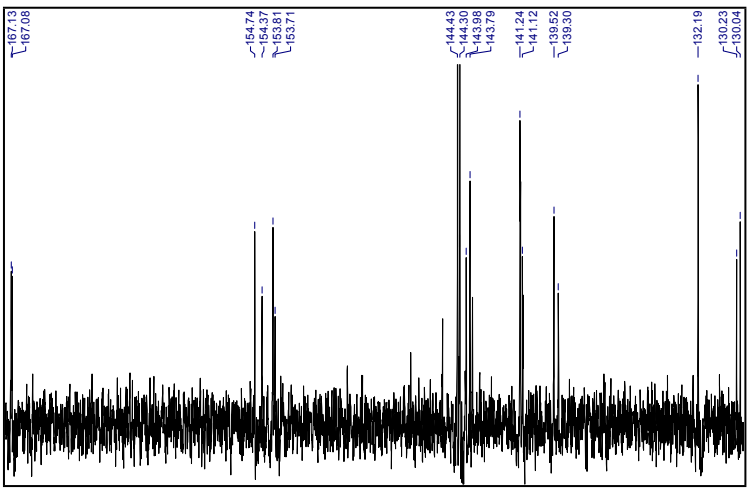
1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-9-{[(*S*,*E*)-5-(allyloxy)-4-methyl-5-oxo-1-(tritylthio)pent-3-en-2-yl]amino}-2,2,5,8-tetramethyl-9-oxo-7-{[(2,2,2-trichloroethoxy)carbonyl]oxy}nonan-3-yl)] (*S*)-pyrrolidine-1,2-dicarboxylate (14)



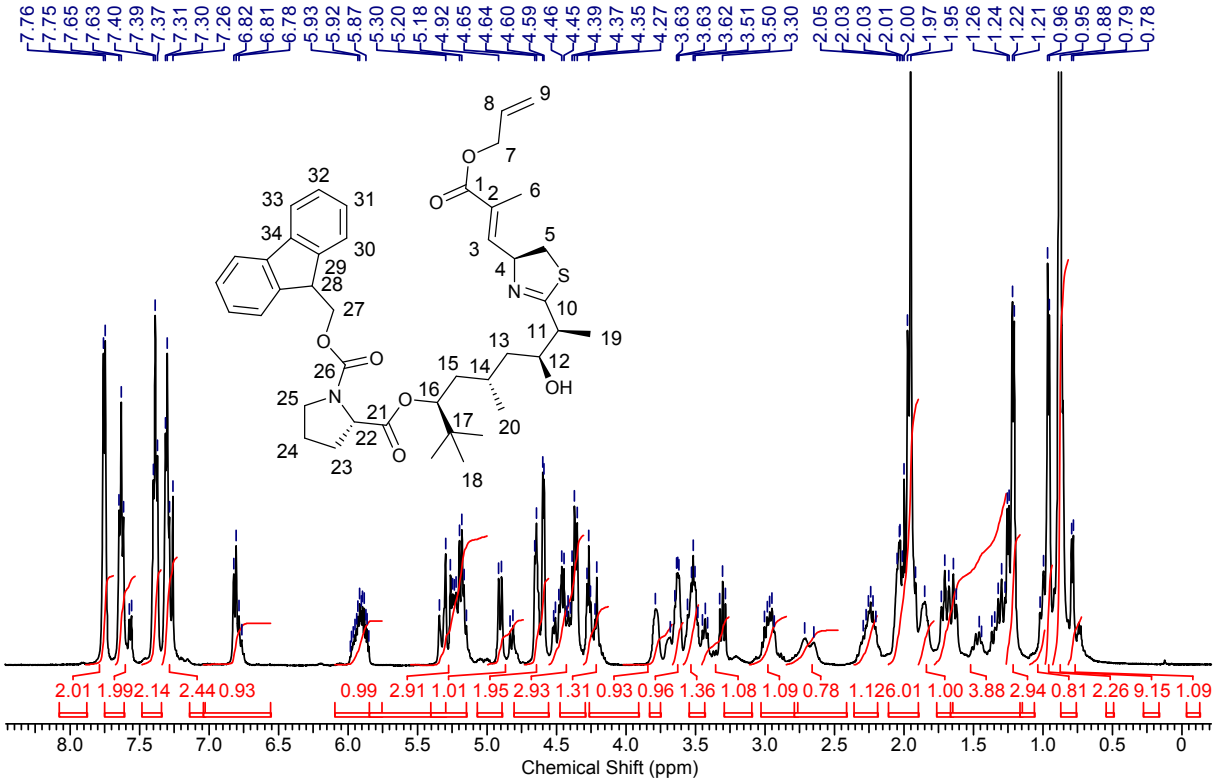


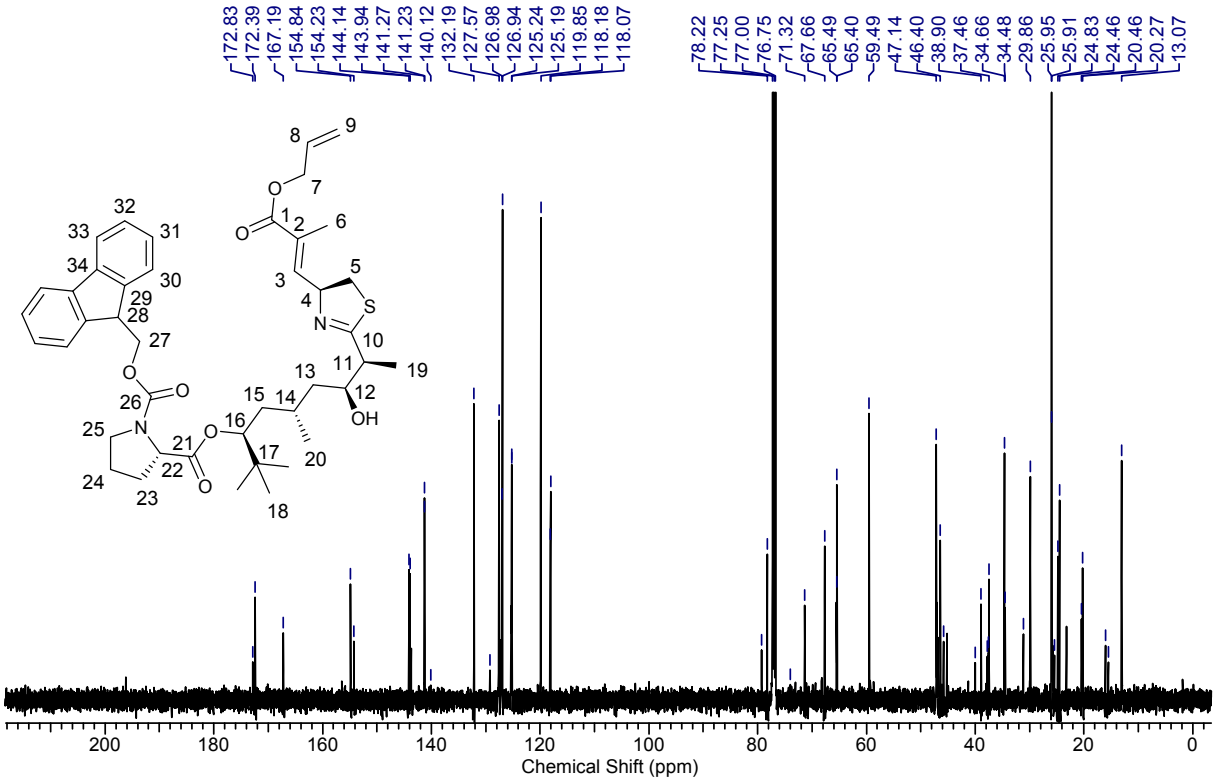

37.27
36.66
35.88
34.99
34.65


79.13
78.99
78.57
78.34
77.25
77.00
76.75
76.53
76.45

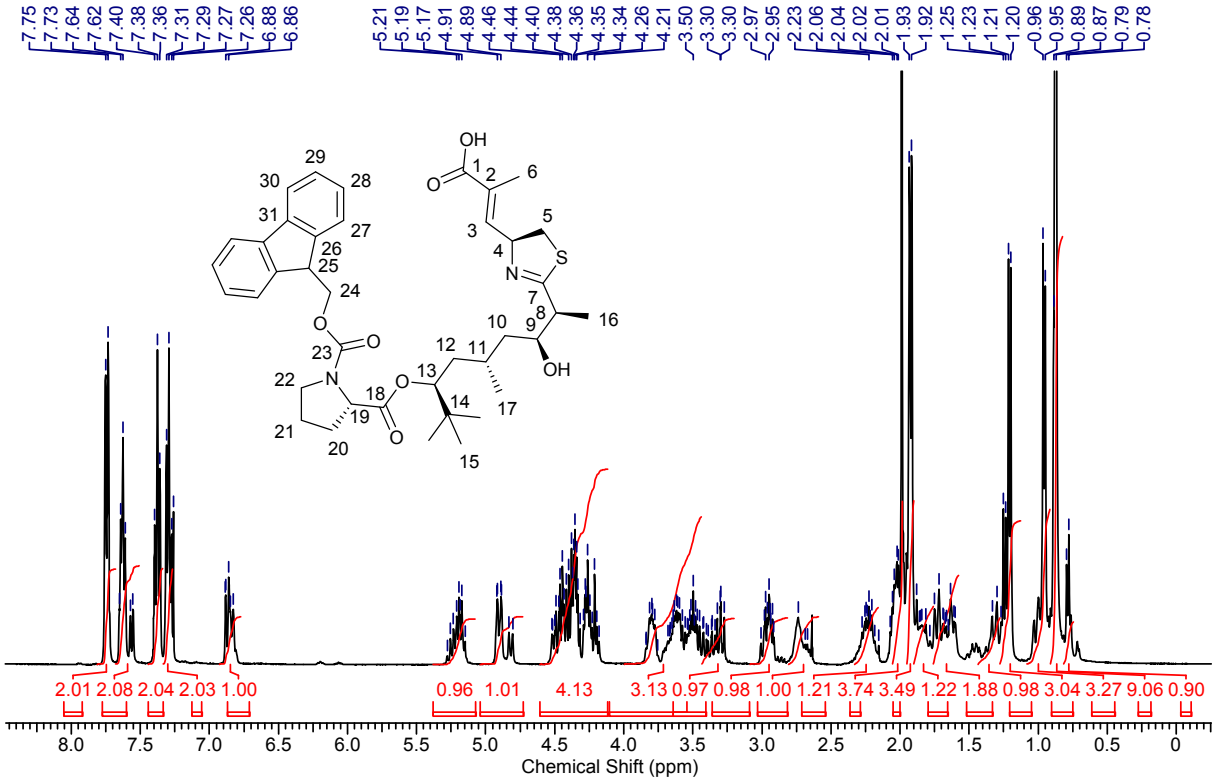

167.13
167.08
154.74
154.37
153.61
153.71
144.43
144.30
143.98
143.79
141.24
141.12
139.52
139.30
132.19
130.23
130.04

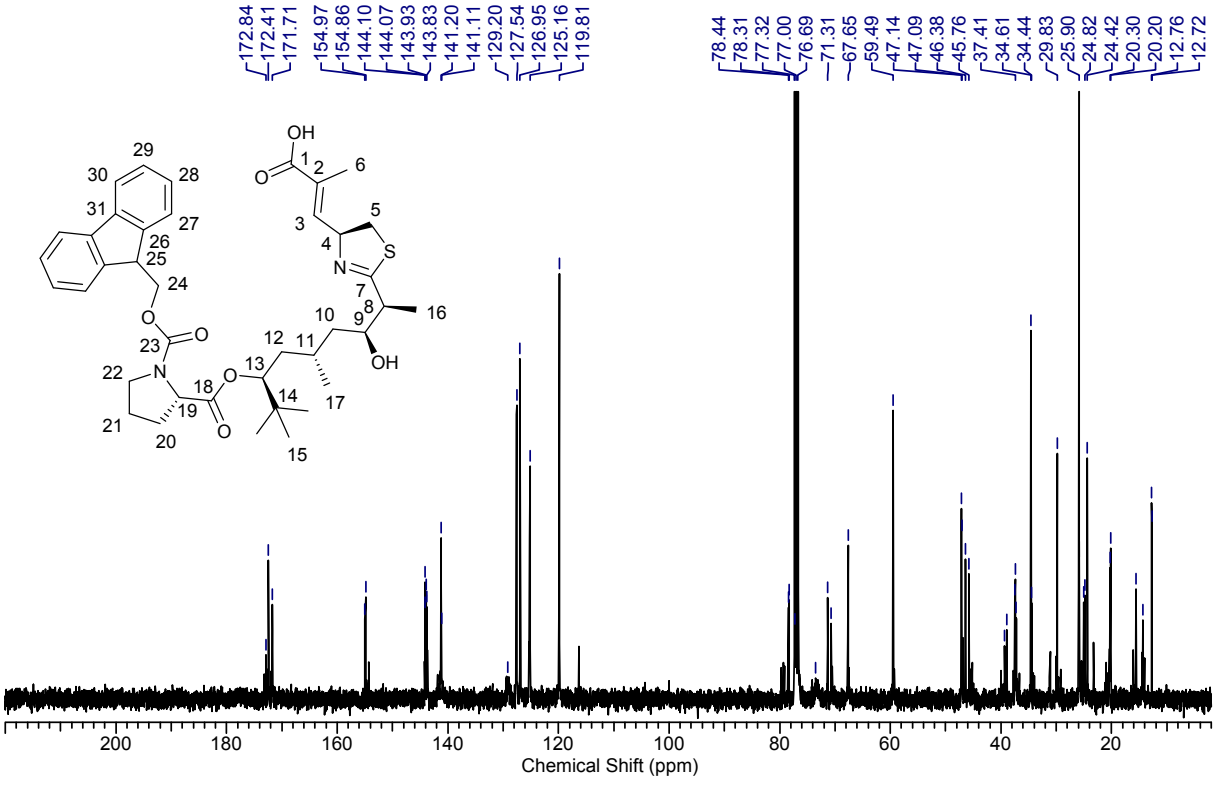
1-[(9*H*-Fluoren-9-yl)methyl] 2-({3*S*,5*S*,7*S*,8*S*}-8-{(*S*)-4-[(*E*)-3-(allyloxy)-2-methyl-3-oxoprop-1-en-1-yl]-4,5-dihydrothiazol-2-yl}-7-hydroxy-2,2,5-trimethylnonan-3-yl) (*S*)-pyrrolidine-1,2-dicarboxylate (15)



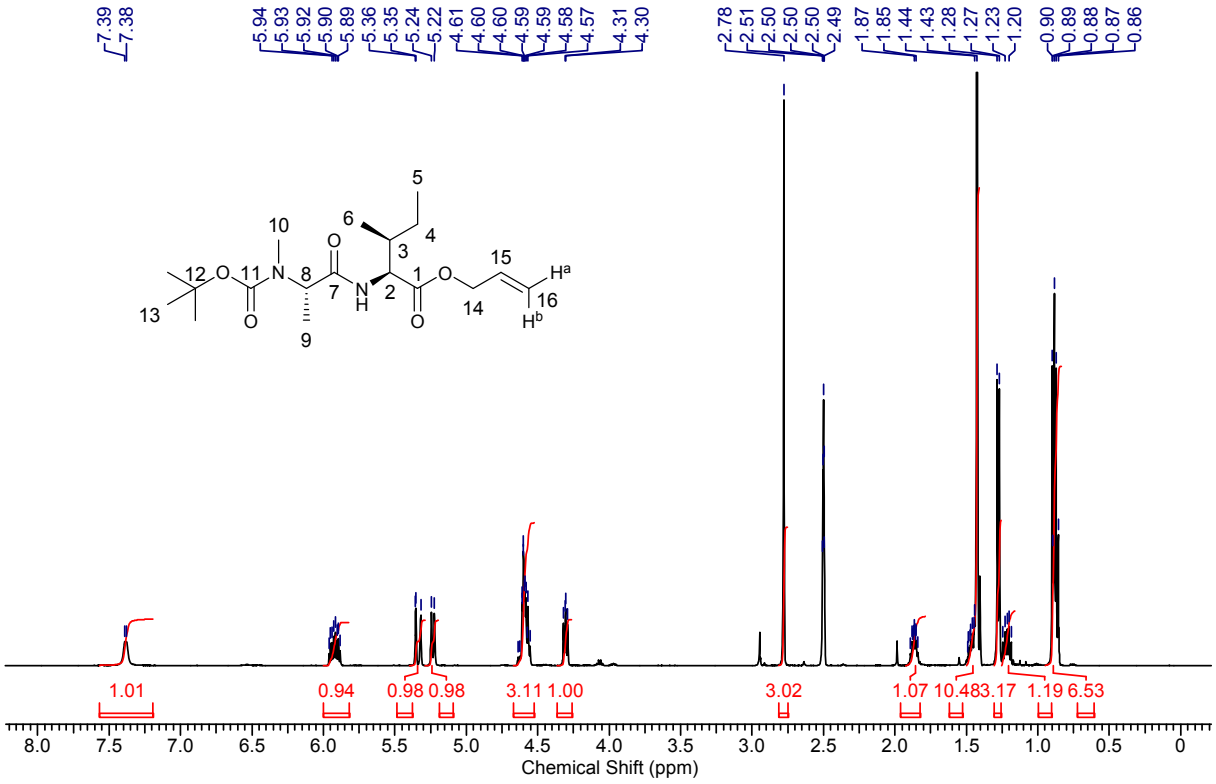


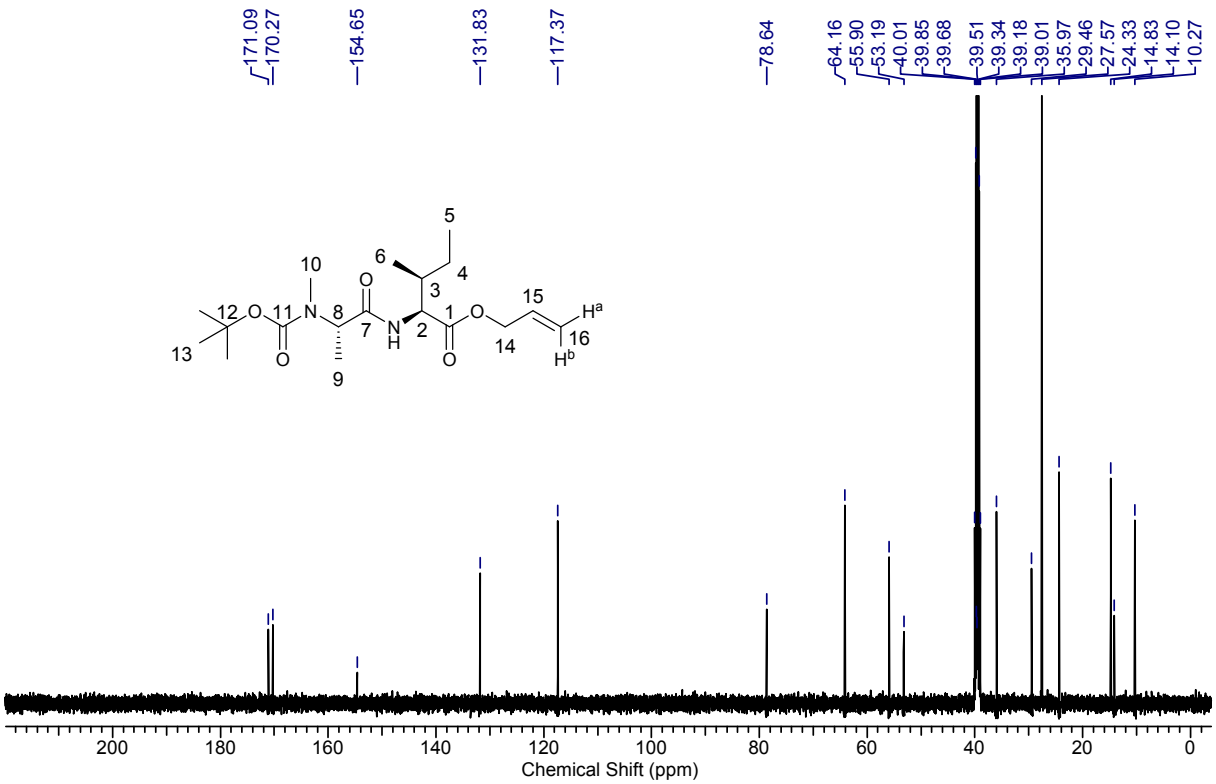
(*E*)-3-((*S*)-2-{(2*S*,3*S*,5*S*,7*S*)-7-[({[(9*H*-Fluoren-9-yl)methoxy]carbonyl}-L-prolyl)oxy]-3-hydroxy-5,8,8-trimethylnonan-2-yl}-4,5-dihydrothiazol-4-yl)-2-methylacrylic acid (16)



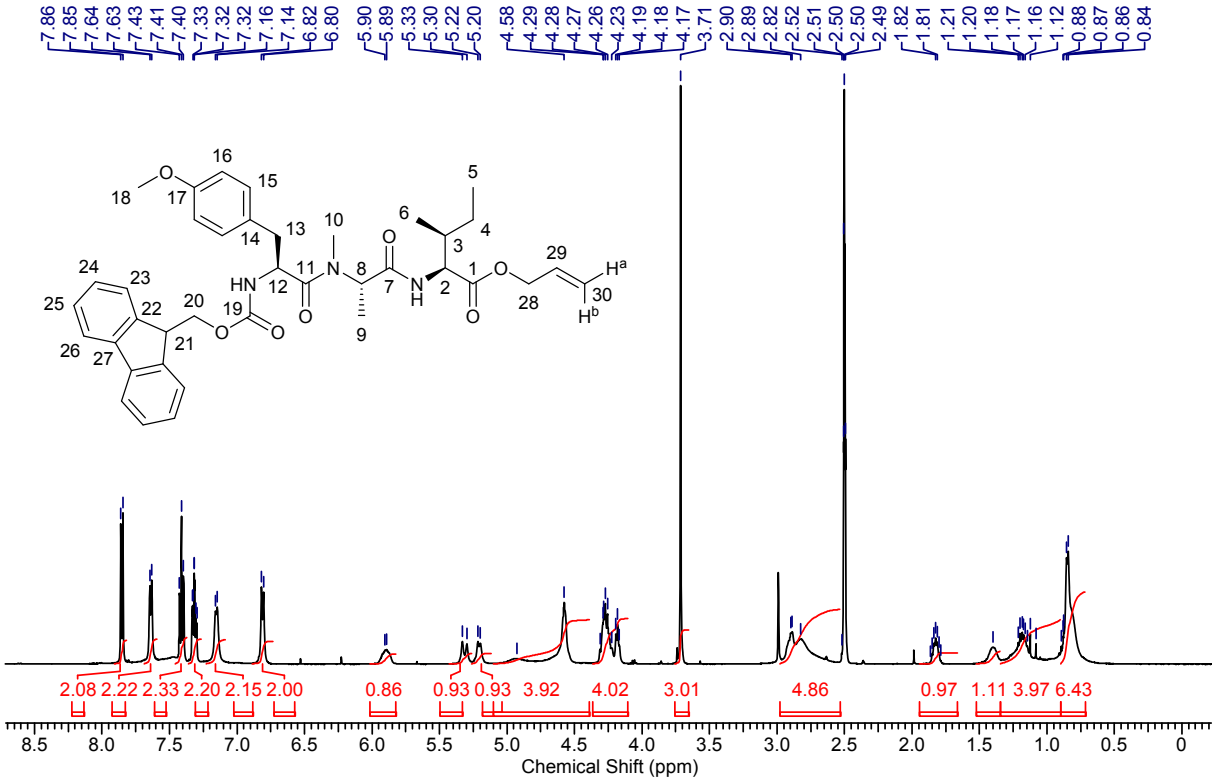


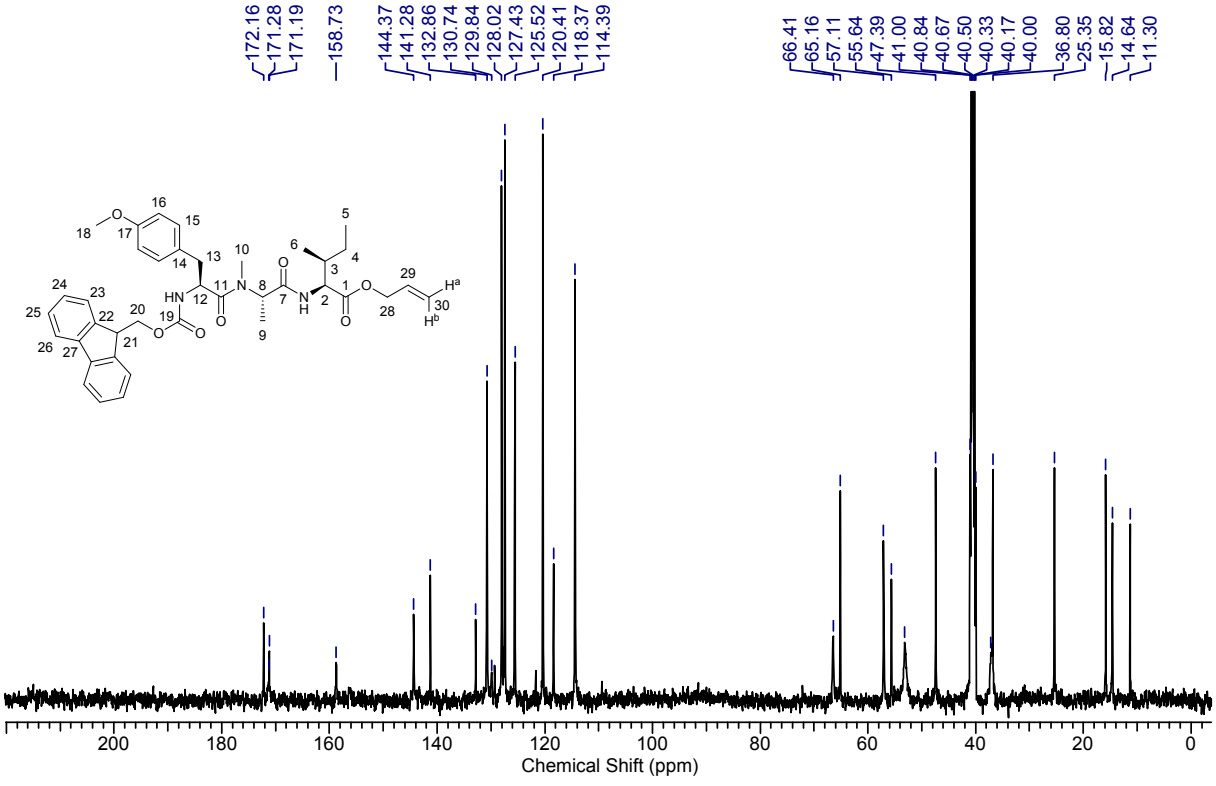
Allyl *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-alanyl-L-isoleucinate (18b)



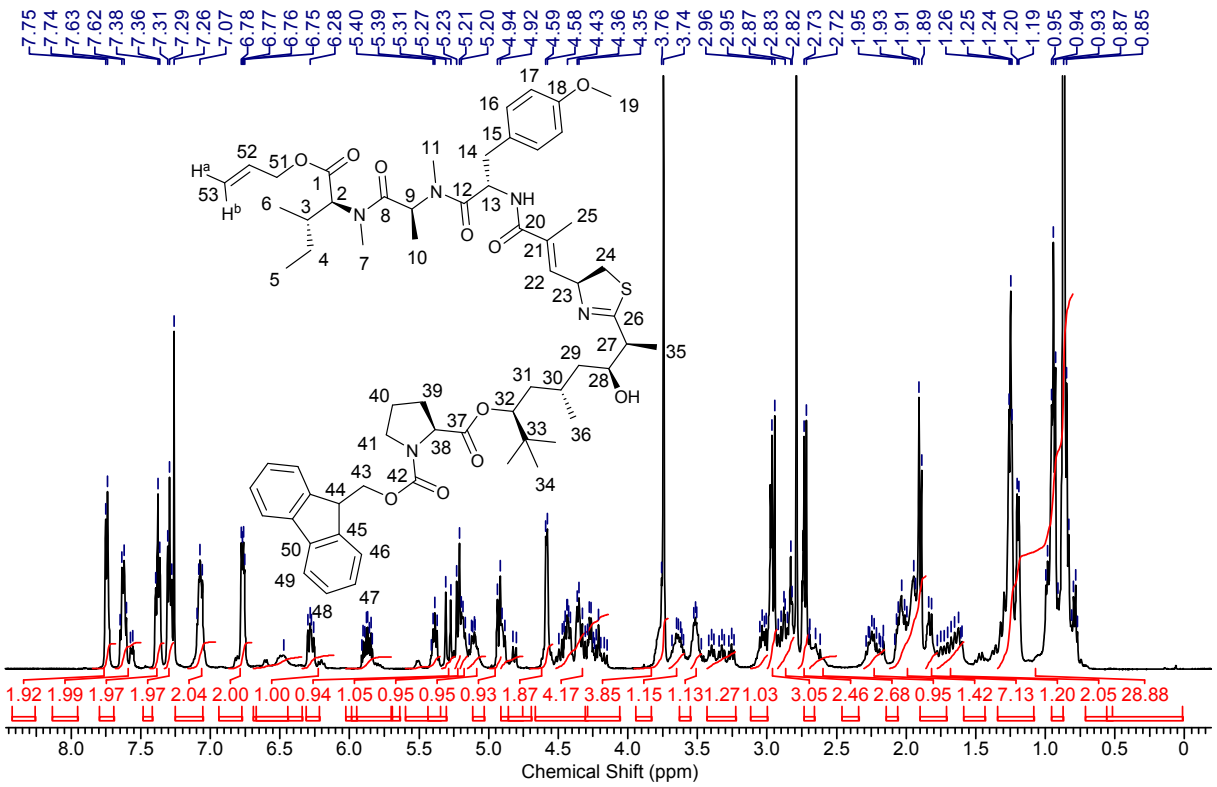


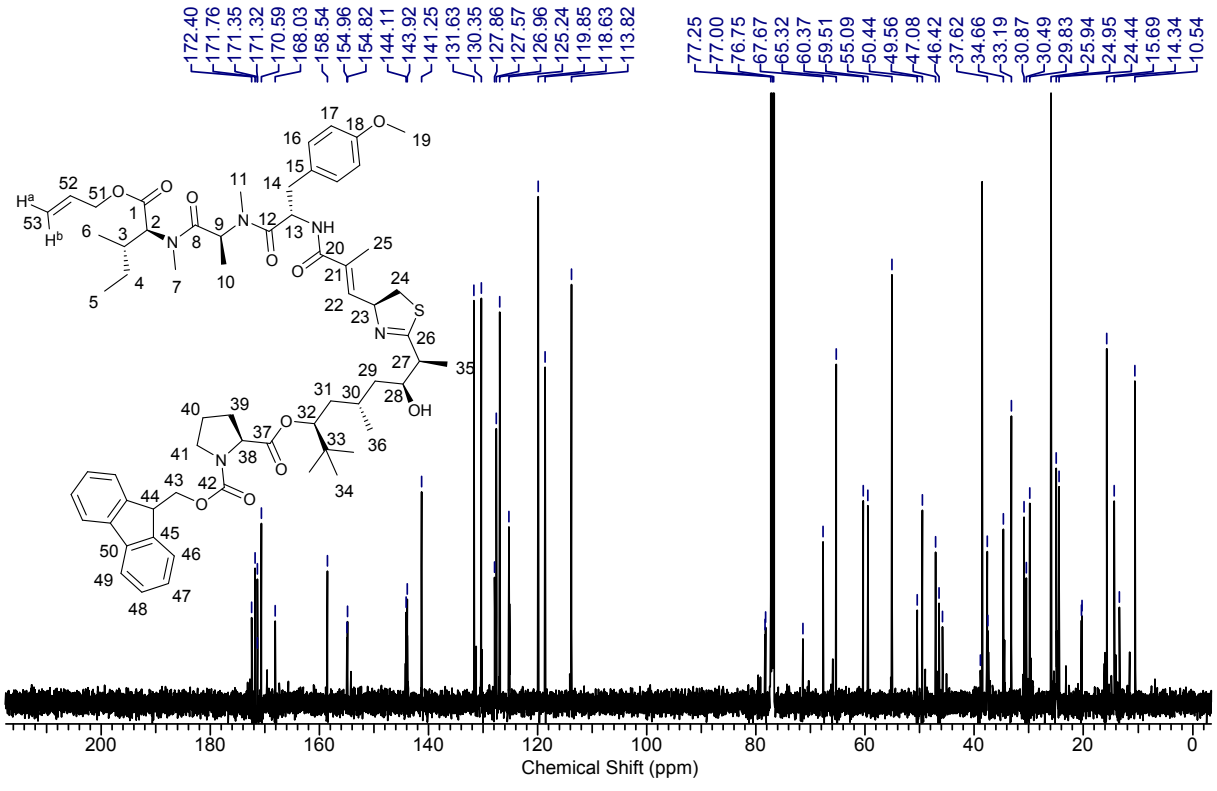
Allyl *N*-[(*S*)-2-({[(9*H*-fluoren-9-yl)methoxy]carbonyl}amino)-3-(4-methoxyphenyl)propanoyl]-*N*-methyl-L-alanyl-L-isoleucinate (19b)



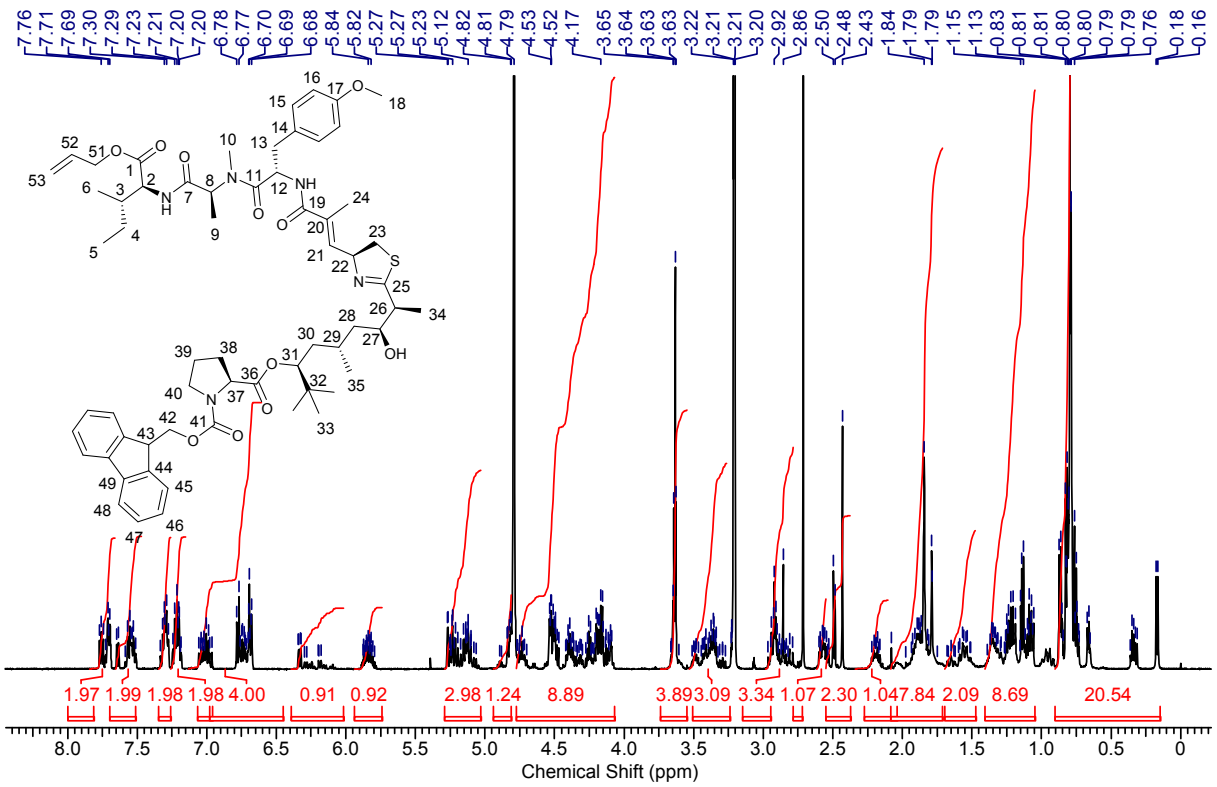


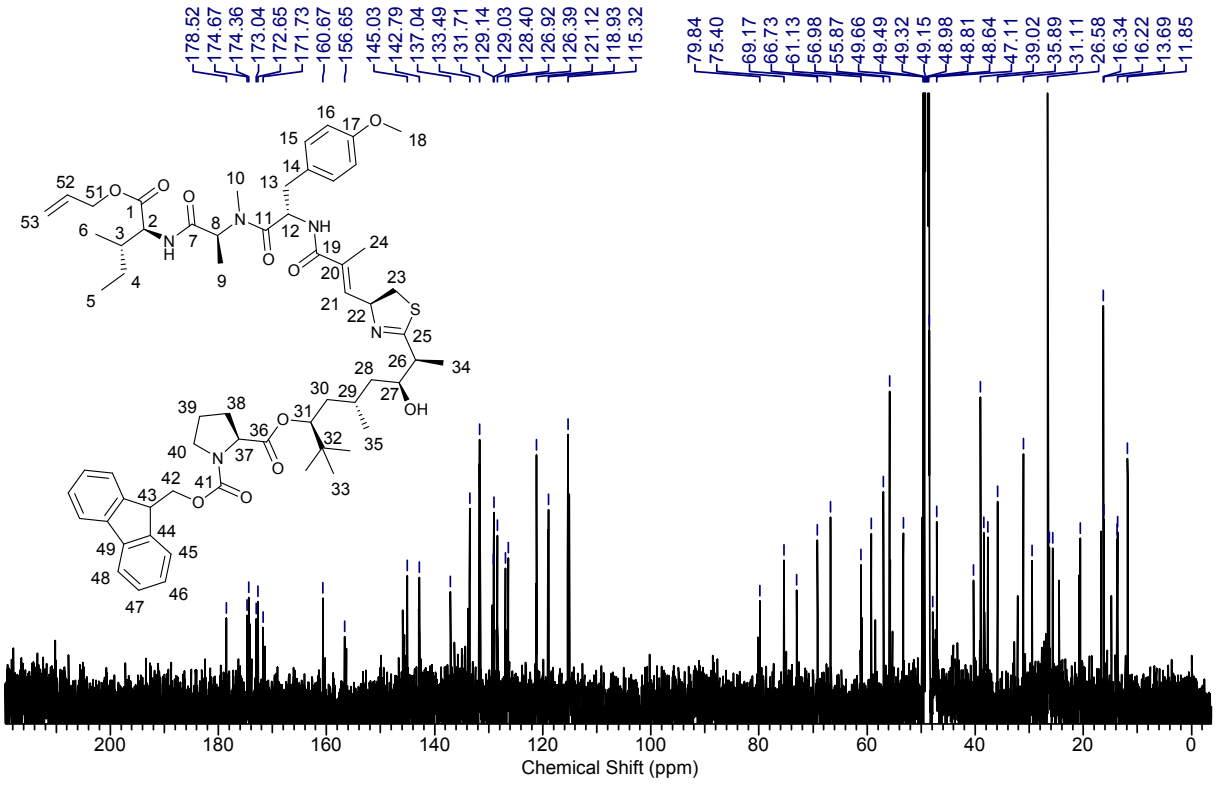
1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-8-({*S*}-4-{[5*S*,8*S*,11*S*,*E*]-11-[(*S*)-*sec*-butyl]-5-[4-methoxybenzyl]-2,7,8,10-tetramethyl-3,6,9,12-tetraoxo-13-oxa-4,7,10-triazahexadeca-1,15-dien-1-yl}-4,5-dihydrothiazol-2-yl)-7-hydroxy-2,2,5-trimethylnonan-3-yl] (*S*)-pyrrolidine-1,2-dicarboxylate (20a)



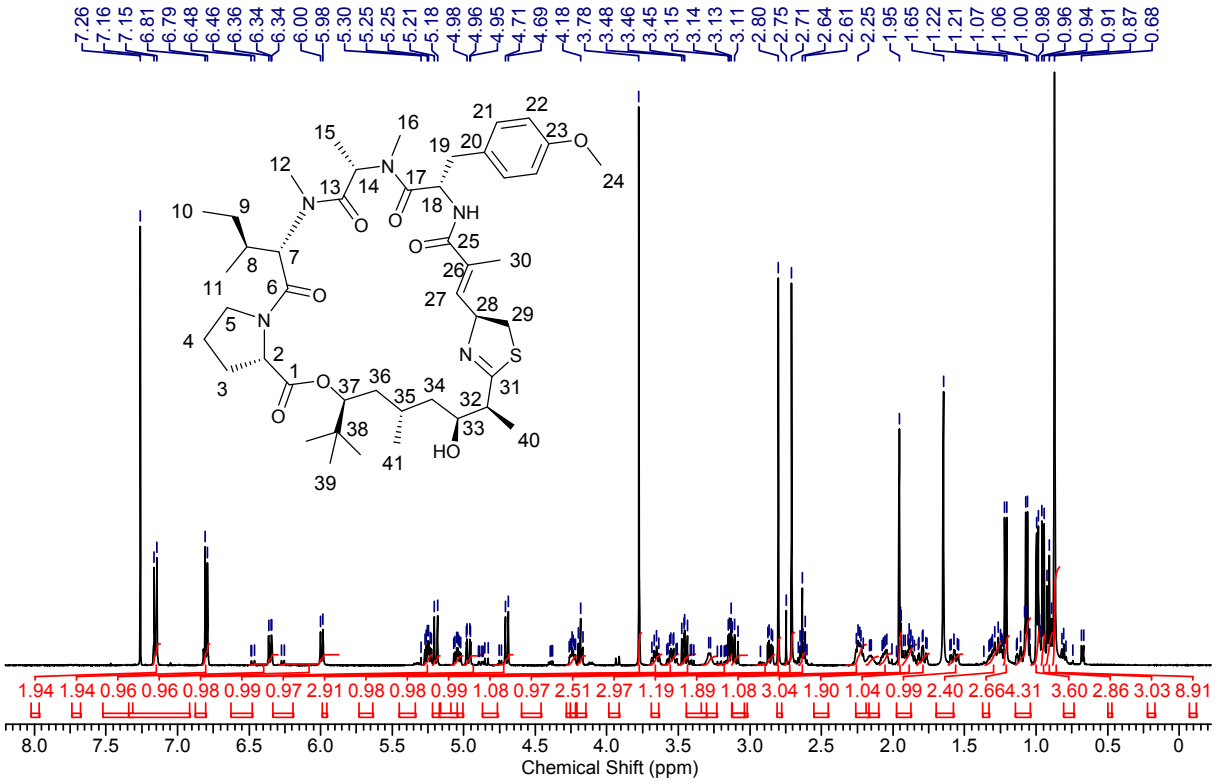


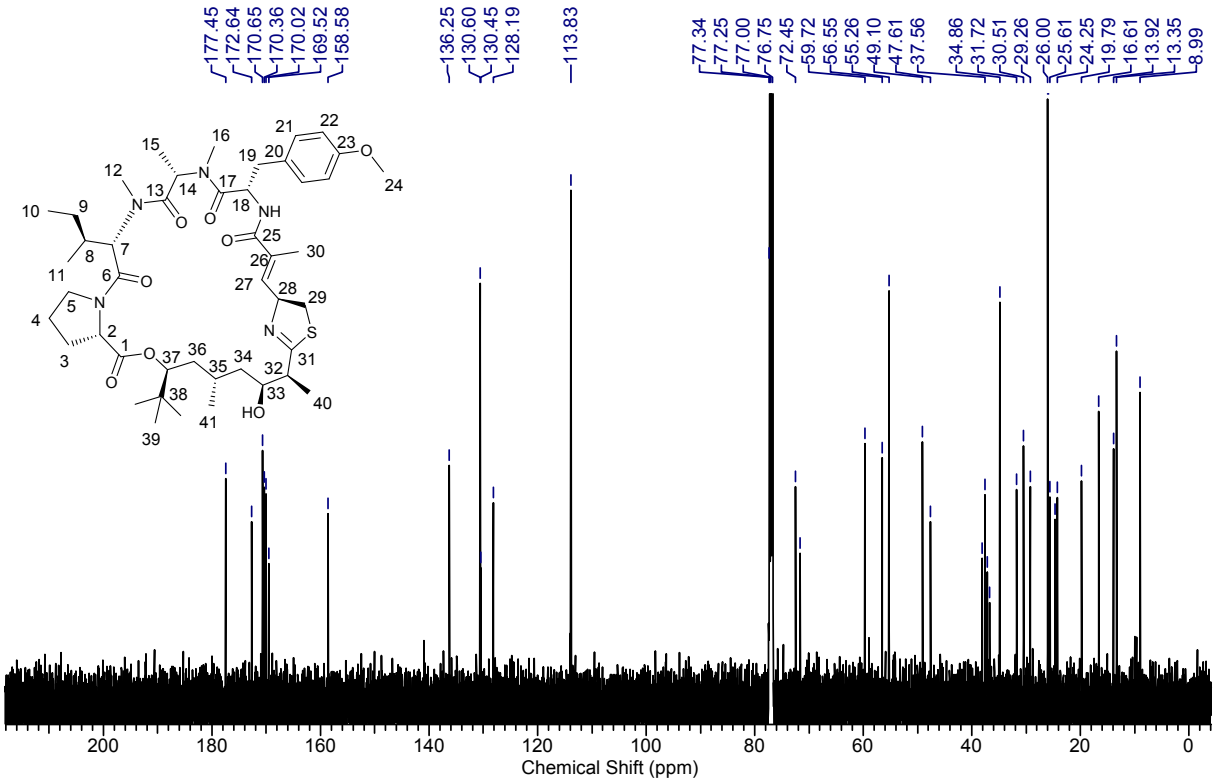
1-[(9*H*-Fluoren-9-yl)methyl] 2-[(3*S*,5*S*,7*S*,8*S*)-8-({*S*}-4-{[5*S*,8*S*,11*S*,*E*]-11-[(*S*)-*sec*-butyl]-5-[4-methoxybenzyl]-2,7,8-trimethyl-3,6,9,12-tetraoxo-13-oxa-4,7,10-triazahexadeca-1,15-dien-1-yl}-4,5-dihydrothiazol-2-yl)-7-hydroxy-2,2,5-trimethylnonan-3-yl] (*S*)-pyrrolidine-1,2-dicarboxylate (20b)



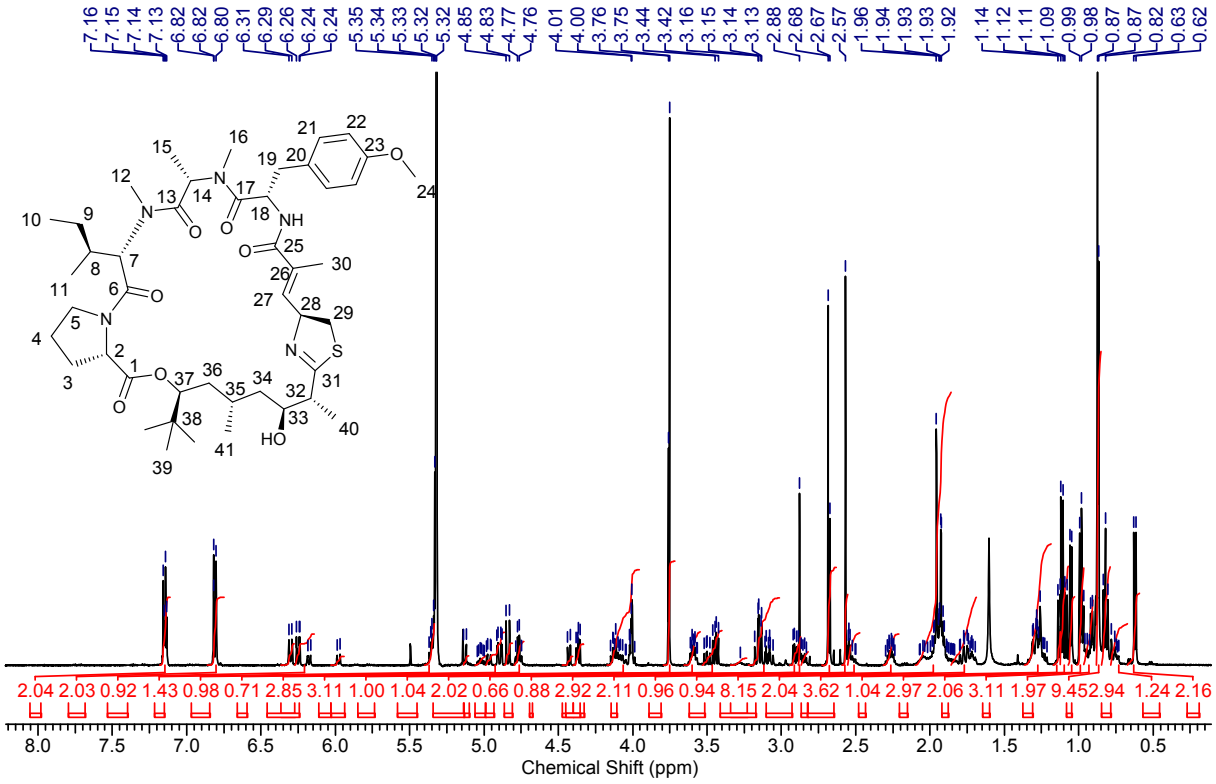


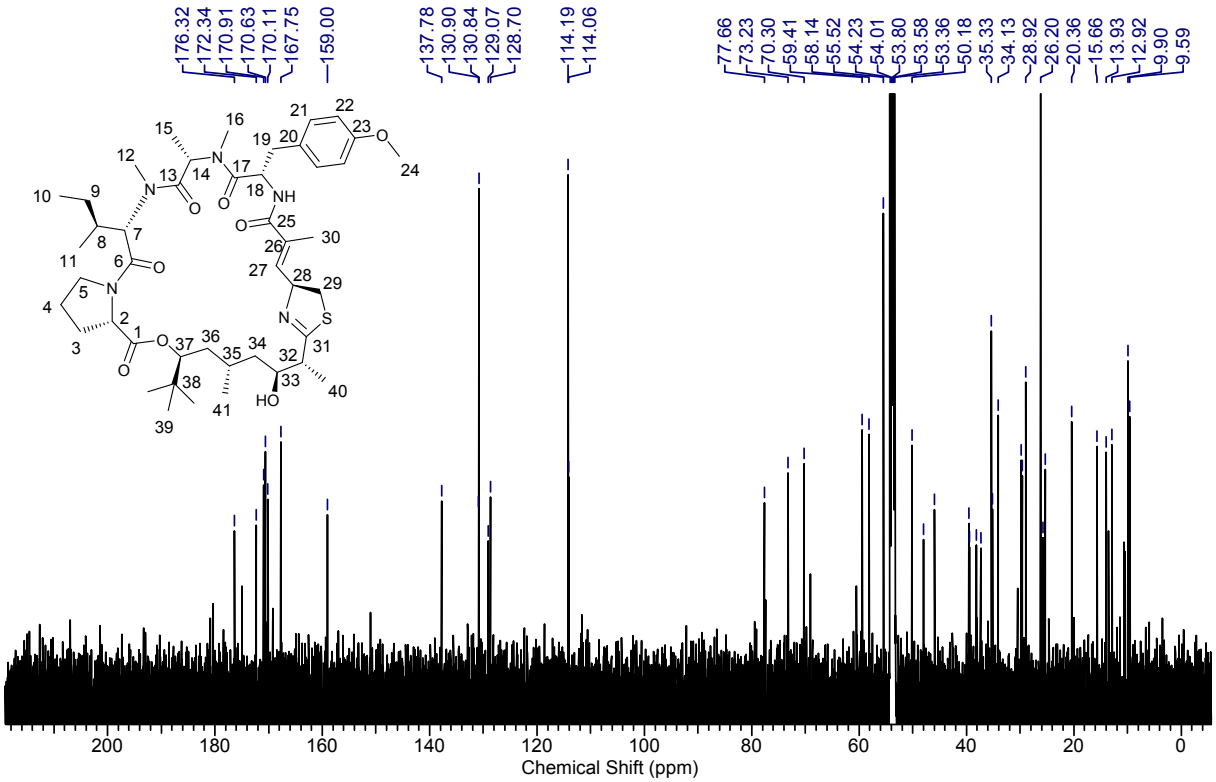
Apratoxin A (21a)





34-*epi*-Apratoxin A (*epi*-21a)

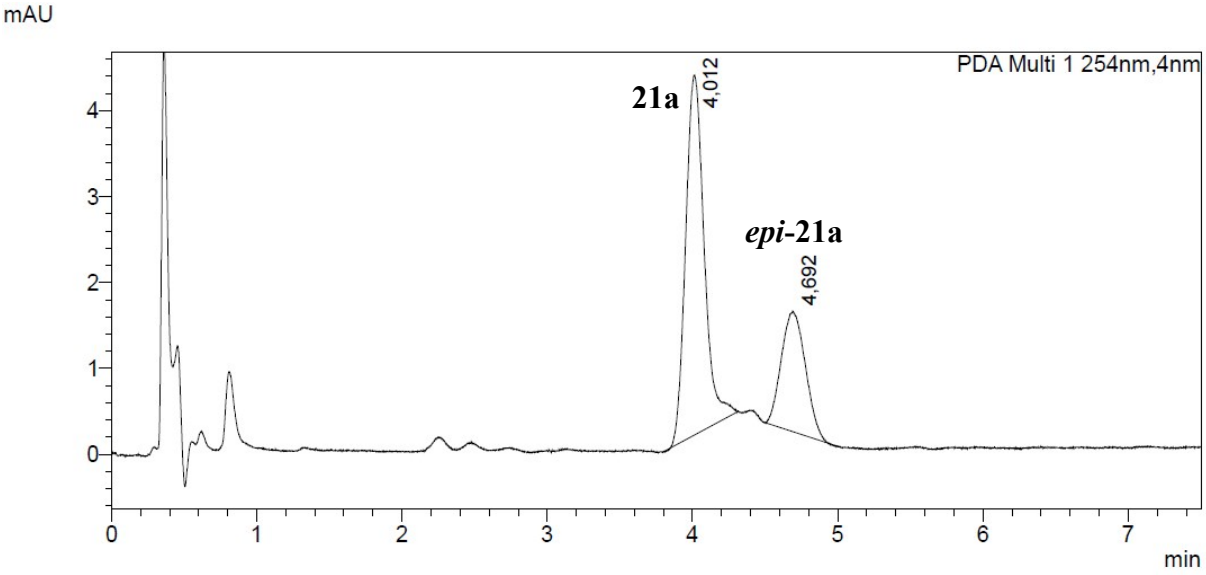




HPLC (21a and *epi*-21a)

Column: Phenomenex Luna® C18(2) 100 Å (50 x 4.6 mm, 3 μm)

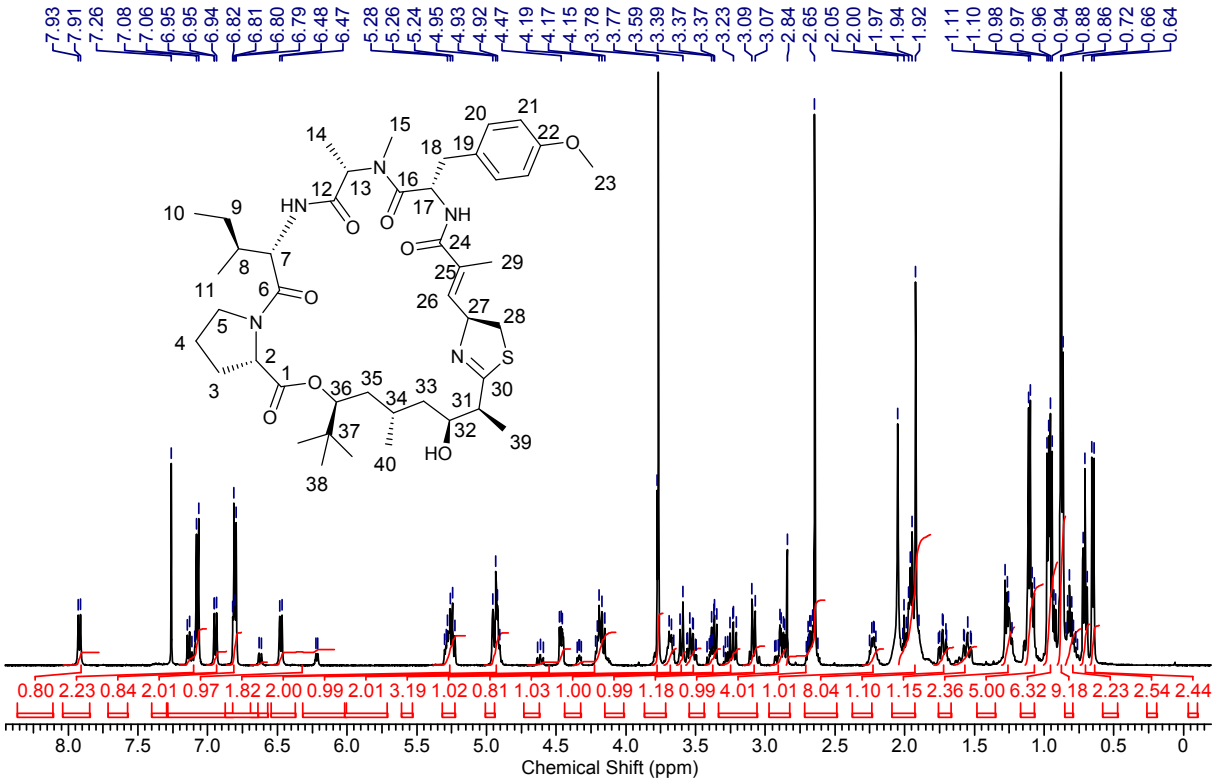
Eluent: H_2O + 0.1 % HCOOH, MeCN 35:65, 1.25 ml/min, 40 °C

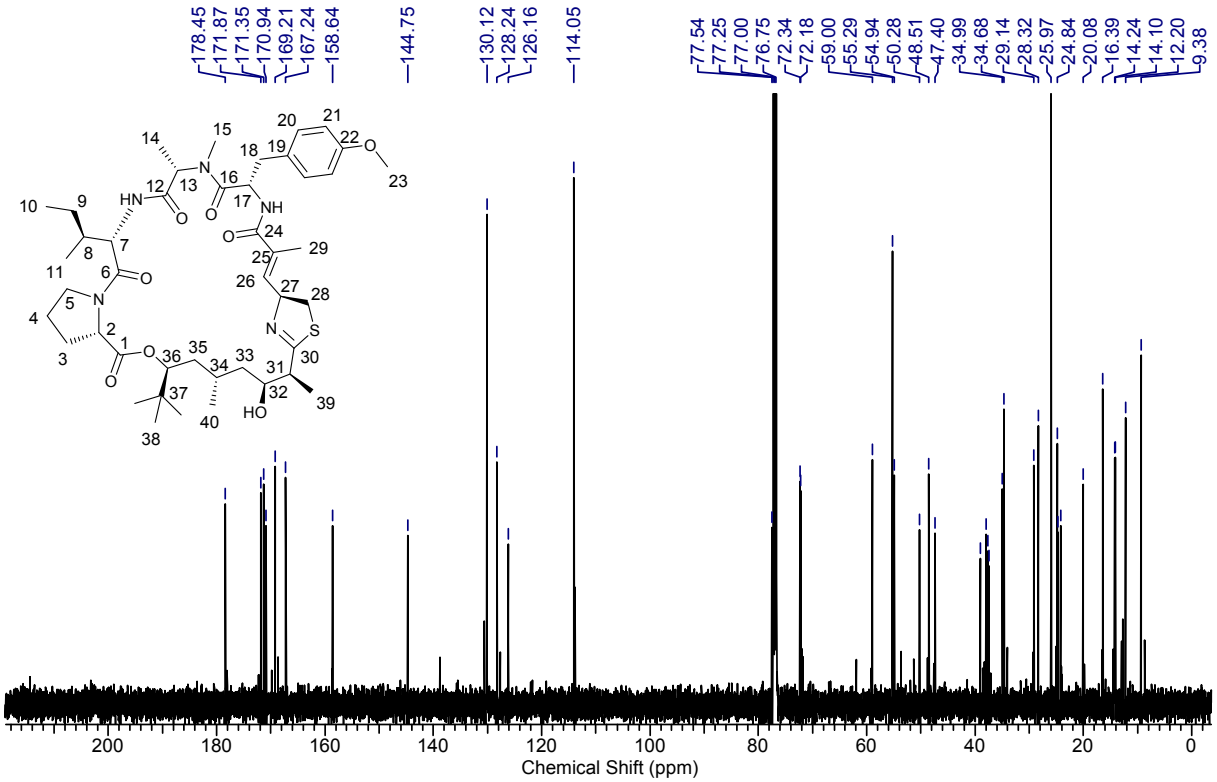


PDA Ch1 254nm

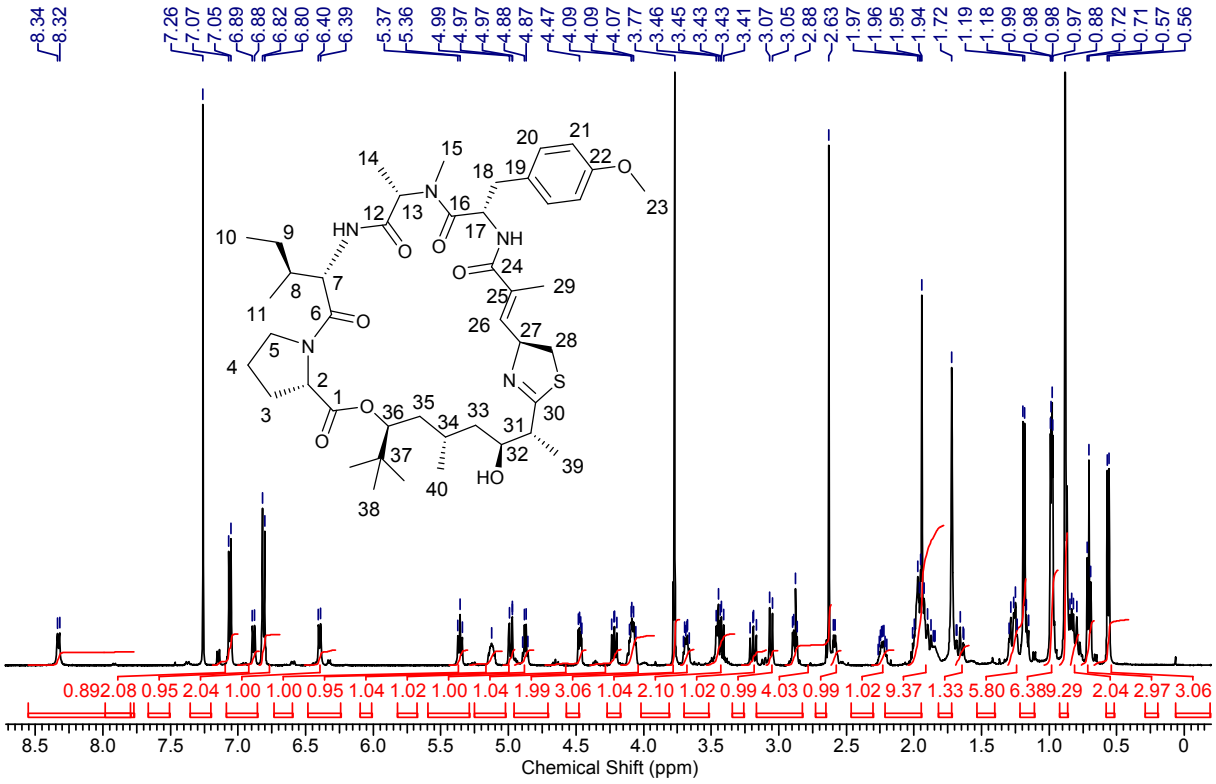
Peak#	Ret. Time	Area%
1	4.012	69.726
2	4.692	30.274
Total		100.000

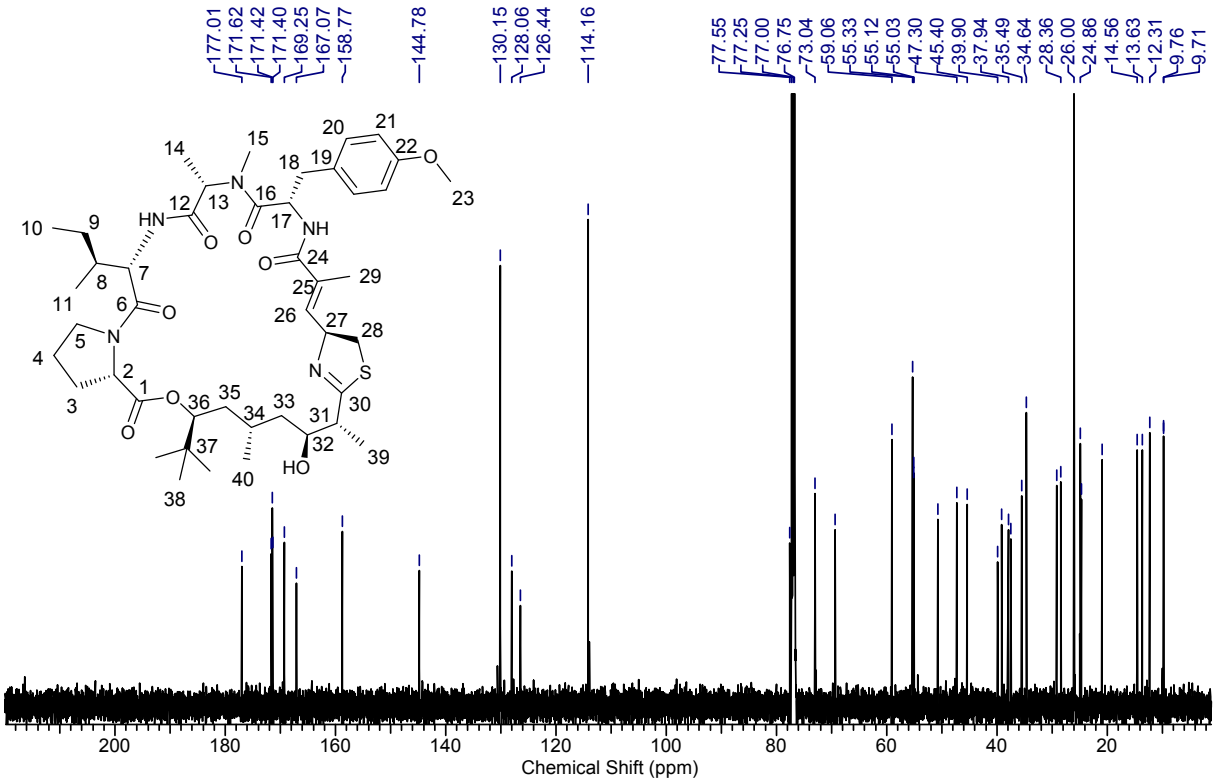
Apratoxin B (21b)





34-*epi*-Apratoxin B (*epi*-21b)

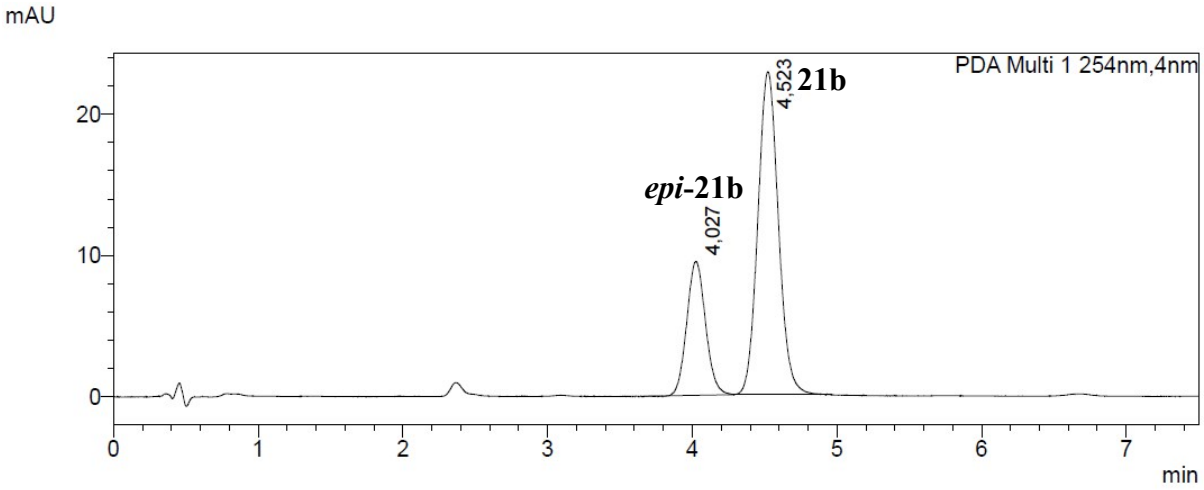




HPLC (21b and *epi*-21b)

Column: Phenomenex Luna® C18(2) 100 Å (50 x 4.6 mm, 3 µm)

Eluent: H_2O + 0.1 % HCOOH, MeCN 35:65, 1.25 ml/min, 40 °C



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	4.027	27.467
2	4.523	72.533
Total		100.000