Concise Total Synthesis of (+)-Gliocladins B and C

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Supporting Material

General Procedures. All reactions were performed in oven-dried or flame-dried round-bottom flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Cannulae or gas-tight syringes with stainless steel needles were used to transfer air- or moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by sparging with argon for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using granular silica gel (60-Å pore size, 40–63 μm, 4–6% H_2O content, Zeochem).[1] Analytical thin layer chromatography (TLC) was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to short wave ultraviolet light (254 nm) and an aqueous solution of ceric ammonium molybdate (CAM) followed by heating on a hot plate (~ 250 ºC). Organic solutions were concentrated at 29–30 °C on rotary evaporators capable of achieving a minimum pressure of ~2 torr. The benzenesulfonyl photodeprotection was accomplished by irradiation in a Rayonet RMR-200 photochemical reactor (Southern New England Ultraviolet Company, Branford, CT, USA) equipped with 16 lamps (RPR-3500, 24 W, λ_{max} = 350 nm, bandwidth ~ 20 nm).

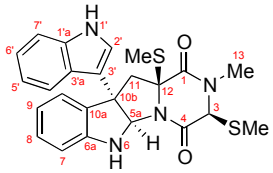
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile, tetrahydrofuran, methanol, pyridine, toluene, and triethylamine were purchased from J.T. Baker (Cycletainer™) and were purified by the method of Grubbs *et al*. under positive argon pressure.[2] Nitromethane and nitroethane (from Sigma–Aldrich) were purified by fractional distillation over calcium hydride and were stored over Linde 3 Å molecular sieves in Schlenk flasks sealed with septa and teflon tape under argon atmosphere.[3] L-Sarcosine methyl ester and *N*-Boc-L-tryptophan were purchased from Chem-Impex; 1,4-dimethoxynaphthalene, hafnium (IV) trifluoromethanesulfonate hydrate, and iodomethane were purchased from Alfa Aesar; 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride was purchased from Oakwood Products, Inc.; *N*-hydroxybenzotriazole was purchased from Aroz Technologies, LLC; and triphenylmethanesulfenyl chloride was purchased from TCI America, Inc. 2,6-Di-*tert*-butyl-4-methylpyridine (DTBMP) was purchased from OChem Incorporation. All other solvents and chemicals were purchased from Sigma–Aldrich. Silver tetrafluoroborate (≥99.99% trace metals basis) and hydrogen sulfide (≥99.5%) were purchased from Sigma–Aldrich. 1,4-Dimethoxynaphthalene was purified by crystallization from absolute ethanol.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with a Bruker AVANCE-600 NMR spectrometer (with a Magnex Scientific superconducting actively-shielded magnet), are reported in parts per million on the δ scale, and are referenced from the residual protium in the NMR solvent ($CDCl_3$: δ 7.26 ($CHCl_3$), DMSO-d_6: δ 2.50 (DMSO-d_5), acetone-d_6: δ 2.05 (acetone-d_5), acetonitrile-d_3: δ 2.13 (acetonitrile-d_2)).[4] Data are reported as follows: chemical shift [multiplicity (br = broad, s = singlet, d = doublet, t = triplet, sp = septet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded with a Bruker AVANCE-600 NMR Spectrometer (with a Magnex Scientific superconducting actively-shielded magnet) or a Bruker AVANCE-400 NMR Spectrometer (with a Magnex Scientific superconducting magnet), are reported in parts per million on the δ scale, and are referenced from the carbon resonances of the solvent ($CDCl_3$: δ 77.23, DMSO-d_6: δ 39.52, acetone-

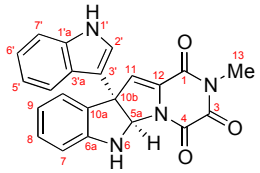
[1] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[3] Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*, 5th ed.; Butterworth–Heinemann: London, 2003.
[4] Fulmer, G. R.; Miller, A. J. M.; Sherden, N. H.; Gottlieb, H. E.; Nudelman, A.; Stoltz, B. M.; Bercaw, J. E.; Goldberg, K. I. *Organometallics* **2010**, *29*, 2176.

d_6: δ 29.84, acetonitrile-d_3: δ 118.26). Data are reported as follows: chemical shift (multiplicity, coupling constant(s) in Hertz, assignment). Fluorine-19 nuclear magnetic resonance (^{19}F NMR) spectra were recorded with a Bruker AVANCE-400 NMR Spectrometer (with a SpectroSpin superconducting magnet), are reported in parts per million on the δ scale, and are referenced from the fluorine resonance of neat trichlorofluoromethane ($CFCl_3$: δ 0). Data are reported as follows: chemical shift (assignment). Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). Optical rotations were measured on a Jasco-1010 polarimeter with a sodium lamp and are reported as follows: $[\alpha]_{\lambda}^{T\,^{\circ}C}$ (c = g/100 mL, solvent). We are grateful to Dr. Li Li and Deborah Bass for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics APEXIV 4.7 Tesla FT-ICR-MS using an electrospray (ESI) ionization source.

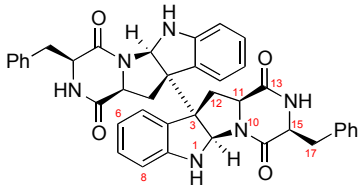
Positional Numbering System. At least three numbering systems for dimeric diketopiperazine alkaloids exist in the literature.[5] In assigning the ^{1}H and ^{13}C NMR data of all intermediates en route to our total syntheses of (+)-gliocladin B (**1**), and (+)-gliocladin C (**4**), we wished to employ a uniform numbering scheme. For ease of direct comparison, particularly between early intermediates, non-thiolated diketopiperazines, and advanced compounds, the numbering system used by Barrow for (+)-WIN-64821 (using positional numbers 1–21) is optimal and used throughout this report. In key instances, the products are accompanied by the numbering system as shown below.



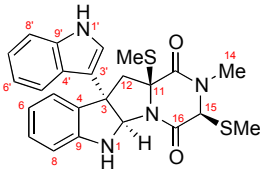
(+)-Gliocladin B (**1**)
Usami's isolation report



(+)-Gliocladin C (**4**)
Usami's isolation report
Overman's reports



(+)-WIN-64821
Barrow's numbering for the simpler diketopiperazine framework



(+)-**1**
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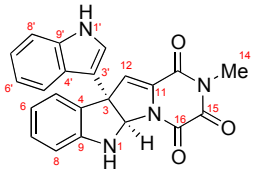

(+)-**4**
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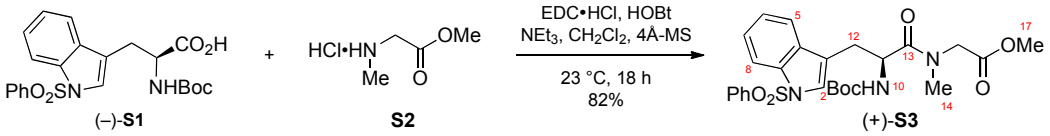
[5] (a) Von Hauser, D.; Weber, H. P.; Sigg, H. P. *Helv. Chim. Acta* **1970**, *53*, 1061. (b) Barrow, C. J.; Cai, P.; Snyder, J. K.; Sedlock, D. M.; Sun, H. H.; Cooper, R. *J. Org. Chem.* **1993**, *58*, 6016. (c) Springer, J. P.; Büchi, G.; Kobbe, B.; Demain, A. L.; Clardy, J. *Tetrahedron Lett.* **1977**, *28*, 2403.



(*S*)-Methyl 2-(2-((*tert*-butoxycarbonyl)amino)-*N*-methyl-3-(1-(phenylsulfonyl)-1*H*-indol-3-yl)propanamido)acetate (+)-S3:

A round-bottom flask was charged sequentially with L-sarcosine methyl ester (**S2**, 7.75 g, 55.5 mmol, 1.40 equiv), *N*'-sulfonylated *N*-Boc-L-tryptophan (–)-**S1**[6] (17.3 g, 38.9 mmol, 1 equiv, >99% ee), *N*-hydroxybenzotriazole (6.30 g, 46.6 mmol, 1.20 equiv), and powdered 4 Å molecular sieves (15.0 g). Anhydrous dichloromethane (300 mL) was introduced into the flask via cannula, and the resulting solution was cooled to 0 °C in an ice–water bath. After 5 min, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrogen chloride (EDC•HCl, 14.9 g, 77.7 mmol, 2.00 equiv) was added as a solid in one portion to the reaction mixture, and the flask was sealed under an argon atmosphere. Triethylamine (22.0 mL, 157 mmol, 4.00 equiv) was subsequently added dropwise via syringe. The ice–water bath was removed, and the reaction mixture was allowed to warm to 23 °C. After 18 h, aqueous hydrogen chloride solution (1 N, 200 mL) was added, and the aqueous layer was extracted with ethyl acetate (2 × 250 mL). The combined organic layers were washed with saturated aqueous sodium bicarbonate solution (2 × 100 mL), water (2 × 100 mL), and saturated aqueous sodium chloride solution (75 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting orange foam was purified by flash column chromatography on silica gel (eluent: gradient, 20 → 60% ethyl acetate in hexanes) to provide dipeptide (+)-**S3** (17 g, 82%) as a white foam. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC, 4:1 mixture of atropisomers, * denotes minor atropisomer): δ 7.96 (d, J = 8.3, 2H, C_8**H**, C_8**H***), 7.85 (d, J = 7.8, 4H, SO_2Ph-*o*-**H**, SO_2Ph-*o*-**H***), 7.57 (d, J = 7.8, 1H, C_5**H**), 7.54 (d, J = 7.8, 1H, C_5**H***), 7.50 (app-dd, J = 7.2, 7.8, 2H, SO_2Ph-*p*-**H**, SO_2Ph-*p*-**H***), 7.49 (s, 1H, C_2**H**), 7.42 (s, 1H, C_2**H***), 7.41 (app-t, J = 7.8, 4H, SO_2Ph-*m*-**H**, SO_2Ph-*m*-**H***), 7.30 (app-dd, J = 7.2, 8.4, 2H, C_7**H**, C_7**H***), 7.24 (app-dd, J = 7.2, 7.8, 1H, C_6**H**), 7.23 (app-dd, J = 7.2, 7.8, 1H, C_6**H***), 5.40 (d, J = 8.4, 1H, N_{Boc}**H**), 5.30 (d, J = 8.8, 1H, N_{Boc}**H***), 4.95 (app-dt, J = 6.2, 7.6, 1H, C_{11}**H**), 4.72 (app-dt, J = 7.1, 8.1, 1H, C_{11}**H***), 4.01 (d, J = 17.1, 1H, C_{15}**H**$_a$), 3.93 (d, J = 17.1, 1H, C_{15}**H**$_b$), 3.89 (d, J = 18.4, 1H, C_{15}**H**$_a$*), 3.81 (d, J = 18.4, 1H, C_{15}**H**$_b$*), 3.72 (s, 3H, C_{14}**H**$_3$), 3.59 (s, 3H, C_{14}**H**$_3$*), 3.15 (dd, J = 7.5, 14.5, 2H, C_{12}**H**$_a$, C_{12}**H**$_a$*), 3.05 (dd, J = 5.5, 14.5, 1H, C_{12}**H**$_b$), 3.00 (dd, J = 6.2, 14.5, 1H, C_{12}**H**$_b$*), 2.86 (s, 3H, OC**H**$_3$*), 2.77 (s, 3H, OC**H**$_3$), 1.40 (s, 9H, (OC(C**H**$_3$)$_3$), 1.39 (s, 9H, (OC(C**H**$_3$*)$_3$).

[6] Prepared from commercially available *N*-Boc-L-tryptophan in one step: Movassaghi, M.; Schmidt, M. A.; Ashenhurst, J. A. *Angew. Chem. Int. Ed.* **2008**, *47*, 1485.

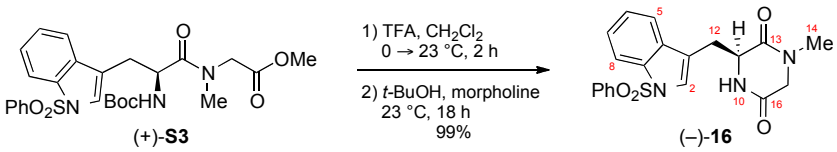
^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC, 4:1 mixture of atropisomers, * denotes minor atropisomer): δ 172.2 (**C**$_{13}$), 172.1 (**C***$_{13}$), 169.4 (**C**$_{16}$), 169.1 (**C***$_{16}$), 155.2 (**C**$_{carbamate}$), 155.2 (**C***$_{carbamate}$), 138.5 (SO_2Ph-*ipso*-**C**), 138.5 (SO_2Ph-*ipso*-**C***), 135.2 (**C***$_9$), 135.2 (**C**$_9$), 133.9 (SO_2Ph-*p*-**C**), 133.9 (SO_2Ph-*p*-**C***), 131.2 (**C**$_4$), 131.0 (**C***$_4$), 129.4 (SO_2Ph-*m*-**C***), 129.4 (SO_2Ph-*m*-**C**), 126.9 (SO_2Ph-*o*-**C**), 126.9 (SO_2Ph-*o*-**C***), 125.0 (**C**$_7$), 125.0 (**C**$_2$), 125.0 (**C***$_2$), 124.7 (**C***$_7$), 123.5 (**C**$_6$), 123.5 (**C***$_6$), 119.7 (**C**$_5$), 119.7 (**C***$_5$), 117.9 (**C***$_3$), 117.6 (**C**$_3$), 113.8 (**C**$_8$), 113.8 (**C***$_8$), 80.2 (O**C***$(CH_3)_3$), 80.0 (O**C**$(CH_3)_3$), 52.6 (O**C***H_3), 52.5 (O**C**H_3), 51.1 (**C***$_{11}$), 50.3 (**C**$_{11}$), 50.0 (**C***$_{15}$), 49.7 (**C**$_{15}$), 36.5 (**C**$_{14}$), 35.3 (**C***$_{14}$), 29.1 (**C***$_{12}$), 29.0 (**C**$_{12}$), 28.5 (OC(**C***$H_3)_3$), 28.5 (OC(**C**$H_3)_3$).

FTIR (thin film) cm^{-1}: 3310 (br-m), 2977 (m), 1749 (s), 1707 (s), 1651 (s), 1448 (m), 1367 (s), 1176 (s), 1122 (m), 749 (m).

HRMS (ESI) (*m*/*z*): calc'd for $C_{26}H_{31}N_3NaO_7S$ $[M+Na]^+$: 552.1775, found: 552.1793.

$[\alpha]_D^{25}$: +22.0 (*c* = 0.23, $CHCl_3$).

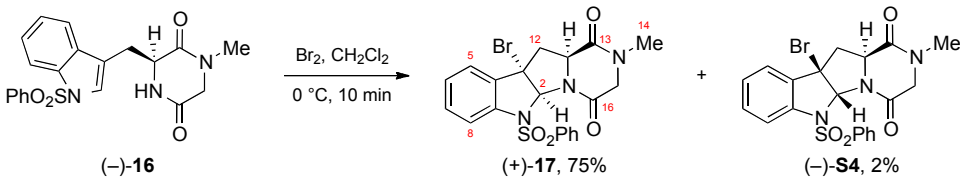
TLC (50% ethyl acetate in hexanes), R*f*: 0.25 (UV, CAM).



(*S*)-1-Methyl-3-((1-(phenylsulfonyl)-1*H*-indol-3-yl)methyl)piperazine-2,5-dione (–)-16:

Trifluoroacetic acid (50 mL) was added via syringe to a solution of the dipeptide (+)-**S3** (16.0 g, 30.2 mmol, 1 equiv) in dichloromethane (250 mL) at 0 °C. The ice–water bath was then removed, and the reaction mixture was allowed to warm to 23 °C. After 2 h, the brown solution was concentrated under reduced pressure to afford a brown residue, which was then dissolved in *tert*-butanol (230 mL). The reaction mixture was stirred vigorously as morpholine (85 mL) was introduced via cannula and the resulting mixture was sealed under an argon atmosphere. After 18 h, the yellow solution was concentrated under reduced pressure, and the resulting orange oil was taken up in a mixture of diethyl ether (150 mL) and ethyl acetate (50 mL). The organic solution was stirred vigorously as aqueous hydrogen chloride solution (1 N, 150 mL) was introduced at 23 °C. The formation of a white precipitate was observed. After 1 h, the resulting suspension was collected by filtration, washed sequentially with diethyl ether (3 × 80 mL) and deionized water (4 × 80 mL), and dried for 12 h at 50 °C under reduced pressure to provide diketopiperazine (–)-**16** (11.9 g, 99.1%) as a white solid. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, DMSO-d_6, 20 °C):	δ 8.35 (d, J = 1.3, 1H, N_1**H**), 7.91 (d, J = 7.7, 2H, SO_2Ph-*o*-**H**), 7.87 (d, J = 8.3, 1H, C_8**H**), 7.68 (t, J = 7.5, 1H, SO_2Ph-*p*-**H**), 7.58 (app-t, J = 7.9, 2H, SO_2Ph-*m*-**H**), 7.55–7.52 (m, 1H, C_5**H**), 7.53 (s, 1H, C_2**H**), 7.33 (app-t, J = 7.8, 1H, C_7**H**), 7.25 (app-dd, J = 7.4, 7.6, 1H, C_6**H**), 4.23–4.18 (m, 1H, C_{11}**H**), 3.54 (d, J = 17.4, 1H, C_{15}**H**$_a$), 3.33 (s, 3H, C_{14}**H**$_3$), 3.23 (dd, J = 4.3, 14.5, 1H, C_{12}**H**$_a$), 3.01 (dd, J = 4.9, 14.5, 1H, C_{12}**H**$_b$), 2.83 (d, J = 17.4, 1H, C_{15}**H**$_b$).
^{13}C NMR (150 MHz, DMSO-d_6, 20 °C):	δ 165.5 (**C**$_{13}$), 164.8 (**C**$_{16}$), 137.0 (SO_2Ph-*ipso*-**C**), 134.6 (SO_2Ph-*p*-**C**), 134.1 (**C**$_9$), 130.5 (**C**$_4$), 129.9 (SO_2Ph-*m*-**C**), 126.6 (SO_2Ph-*o*-**C**), 125.5 (**C**$_2$), 124.9 (**C**$_7$), 123.2 (**C**$_6$), 120.2 (**C**$_5$), 117.1 (**C**$_3$), 112.9 (**C**$_8$), 54.4 (**C**$_{11}$), 50.6 (**C**$_{15}$), 32.9 (**C**$_{14}$), 28.9 (**C**$_{12}$).
FTIR (thin film) cm^{-1}:	1662 (s), 1637 (s), 1445 (m), 1374 (m), 1326 (m), 1176 (s), 1121 (m), 978 (w), 751 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{20}H_{19}N_3NaO_4S$ $[M+Na]^+$: 420.0988, found: 420.0981.
$[\alpha]_D^{24}$:	–4.0 (c = 0.14, DMSO).
m.p.:	230 °C (dec).
TLC (5% methanol in dichloromethane), R*f*:	0.26 (UV, CAM).



(–)-**16** (+)-**17**, 75% (–)-**S4**, 2%

Monomeric Tetracyclic Diketopiperazine Bromide (+)-17:

A solution of bromine (1 M, 5.85 mL, 5.85 mmol, 4.80 equiv) in anhydrous dichloromethane was slowly poured into a solution of diketopiperazine (–)-**16** (0.486 g, 1.22 mmol, 1 equiv) in anhydrous dichloromethane (25 mL) at 0 °C. Upon completion of the reaction (*ca* 10 min) as monitored by TLC, a saturated aqueous sodium thiosulfate solution (40 mL) was added to the resulting dark red solution. Once the red color dissipated, the mixture was diluted with ethyl acetate (120 mL). The organic layer was washed with saturated aqueous sodium bicarbonate solution (2 × 40 mL), water (2 × 40 mL), and saturated aqueous sodium chloride solution (25 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting orange foam was purified by flash column chromatography on silica gel (eluent: gradient, 10 → 30% acetone in dichloromethane) to afford the diastereomerically pure *endo*-(2*S*,3*S*)-tetracyclic *N*-methyl diketopiperazine bromide (+)-**17** (437 mg, 75.0%)[7] as a white foam as the major product. The complete balance of the product mixture was the minor *exo*-(2*R*,3*R*)-diastereomer (–)-**S4**[8] (~97:3 *dr*) and the 2-bromoindole diketopiperazine. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 °C): δ 7.95 (app-dd, *J* = 1.1, 8.6, 2H, SO_2Ph-*o*-**H**), 7.54–7.49 (m, 1H, SO_2Ph-*p*-**H**), 7.54–7.49 (m, 1H, C_8**H**), 7.41 (app-dd, *J* = 7.5, 8.2, 2H, SO_2Ph-*m*-**H**), 7.34 (app-dd, *J* = 0.6, 7.7, 1H, C_5**H**), 7.28 (app-dt, *J* = 1.2, 7.8, 1H, C_7**H**), 7.12 (app-dt, *J* = 0.9, 7.6, 1H, C_6**H**), 6.27 (s, 1H, C_2**H**), 4.44 (app-dd, *J* = 7.7, 8.1, 1H, C_{11}**H**), 4.16 (d, *J* = 17.5, 1H, C_{15}**H**$_a$), 3.83 (d, *J* = 17.5, 1H, C_{15}**H**$_b$), 3.31 (dd, *J* = 6.8, 14.5, 1H, C_{12}**H**$_a$), 3.07 (dd, *J* = 9.0, 14.5, 1H, C_{12}**H**$_b$), 2.87 (s, 3H, C_{14}**H**$_3$).

^{13}C NMR (150 MHz, $CDCl_3$, 20 °C): δ 166.1 (**C**$_{13}$), 165.0 (**C**$_{16}$), 138.9 (**C**$_9$), 138.0 (SO_2Ph-*ipso*-**C**), 134.0 (**C**$_4$), 133.9 (SO_2Ph-*p*-**C**), 130.9 (**C**$_7$), 129.1 (SO_2Ph-*m*-**C**), 128.5 (SO_2Ph-*o*-

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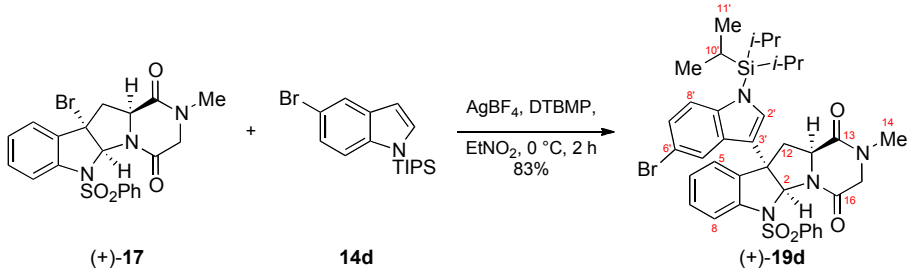
[7] *endo*-(2*S*,3*S*)-Tetracyclic *N*-methyl diketopiperazine bromide (+)-**17** can be also obtained in 69% yield (7.6g-scale) along with (–)-**S4** (31% yield) by treatment of an acetonitrile solution of diketopiperazine (–)-**16** with a solution of bromine in acetonitrile at *ca* 10 °C. The diastereomeric bromides were separated by flash column chromatography on silica gel (eluent: gradient, 2 → 10% isopropanol in hexanes and 50% dichloromethane).

[8] *exo*-Tetracyclic bromide (–)-**S4** was isolated by flash column chromatography on silica gel. ^{1}H NMR (600 MHz, $CDCl_3$, 20 °C): δ 7.87 (d, *J* = 7.8, 2H, SO_2Ph-*o*-**H**), 7.63 (d, *J* = 8.2, 1H, C_8**H**), 7.53 (app-dd, *J* = 7.4, 7.5, 1H, SO_2Ph-*p*-**H**), 7.42 (app-dd, *J* = 7.7, 7.9, 2H, SO_2Ph-*m*-**H**), 7.36 (t, *J* = 7.7, 1H, C_7**H**), 7.34 (d, *J* = 7.2, 1H, C_5**H**), 7.20 (app-dd, *J* = 7.5, 7.6, 1H, C_6**H**), 6.55 (s, 1H, C_2**H**), 4.20 (d, *J* = 17.1, 1H, C_{15}**H**$_a$), 3.88 (d, *J* = 17.1, 1H, C_{15}**H**$_b$), 3.84 (dd, *J* = 5.2, 11.7, 1H, C_{11}**H**), 3.24 (dd, *J* = 5.2, 12.9, 1H, C_{12}**H**$_a$), 2.95 (s, 3H, C_{14}**H**$_3$), 2.78 (app-dd, *J* = 12.1, 12.4, 1H, C_{12}**H**$_b$). ^{13}C NMR (150 MHz, $CDCl_3$, 20 °C): δ 164.0 (**C**$_{13}$), 161.3 (**C**$_{16}$), 141.3 (**C**$_9$), 137.8 (SO_2Ph-*ipso*-**C**), 134.0 (SO_2Ph-*p*-**C**), 132.8 (**C**$_4$), 131.4 (**C**$_7$), 129.3 (SO_2Ph-*m*-**C**), 128.1 (SO_2Ph-*o*-**C**), 126.7 (**C**$_6$), 124.9 (**C**$_5$), 117.9 (**C**$_8$), 85.5 (**C**$_2$), 58.5 (**C**$_{11}$), 58.2 (**C**$_3$), 53.2 (**C**$_{15}$), 47.7 (**C**$_{12}$), 33.8 (**C**$_{14}$). FTIR (thin film) cm^{-1}: 3067 (w), 2930 (w), 1691 (s), 1669 (s), 1446 (m), 1429 (m), 1367 (m), 1342 (m), 1171 (m), 1090 (w), 1036 (w), 758 (w), 727 (m). HRMS (ESI) (*m*/*z*): calc'd for $C_{20}H_{18}BrN_3NaO_4S$ $[M+Na]^+$: 498.0094, found: 498.0109. $[\alpha]_D^{25}$: –184.0 (*c* = 0.25, $CHCl_3$). TLC (20% acetone in dichloromethane), R*f*: 0.31 (UV, CAM).

	C), 126.1 ($\mathbf{C}_6$), 125.1 ($\mathbf{C}_5$), 117.1 ($\mathbf{C}_8$), 87.1 ($\mathbf{C}_2$), 61.2 ($\mathbf{C}_3$), 58.0 ($\mathbf{C}_{11}$), 54.3 ($\mathbf{C}_{15}$), 41.4 ($\mathbf{C}_{12}$), 33.8 ($\mathbf{C}_{14}$).
FTIR (thin film) cm^{-1}:	3015 (w), 1679 (s), 1463 (w), 1448 (w), 1399 (m), 1365 (m), 1169 (m), 1090 (m), 753 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{20}H_{18}BrN_3NaO_4S$ $[M+Na]^+$: 498.0094, found: 498.0082.
$[\alpha]_D^{25}$:	+115.5 (*c* = 0.12, $CHCl_3$).
TLC (20% acetone in dichloromethane), R*f*:	0.26 (UV, CAM).



(+)-**17** **14d** (+)-**19d**

C3-(5-Bromo-1-TIPS-indol-3-yl)-pyrrolidinoindoline (+)-19d:

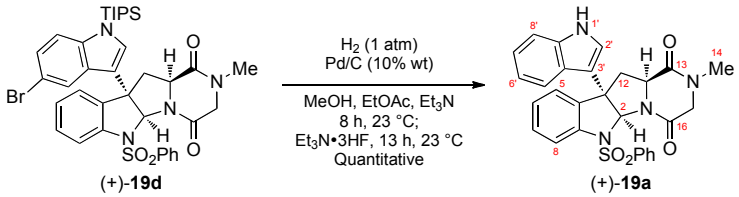
A round-bottom flask was charged with *endo*-tetracyclic bromide (+)-**17** (5.00 g, 10.5 mmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 2.59 g, 12.6 mmol, 1.20 equiv), and 5-bromo-1-triisopropylsilyl-1*H*-indole[9] **14d** (14.8 g, 42.0 mmol, 4.00 equiv), and the mixture was dried azeotropically (concentration of a benzene solution, 2 × 30 mL) under reduced pressure and placed under an argon atmosphere. Anhydrous nitroethane (120 mL) was introduced via syringe, and the mixture was cooled to 0 °C in an ice–water bath. A solution of silver (I) tetrafluoroborate (6.30 g, 32.4 mmol, 3.09 equiv) in anhydrous nitroethane (40 mL) at 0 °C was introduced via cannula to the solution containing the tetracyclic bromide (+)-**17** over 20 min. After 5 min, a white precipitate was observed in the clear yellow reaction solution. The reaction flask was covered in aluminum foil, and the suspension was maintained at 0 °C. After 2 h, saturated aqueous sodium chloride solution (25 mL) was introduced, and the resulting biphasic mixture was vigorously stirred for 30 min at 0 °C. The reaction mixture was diluted with ethyl acetate (150 mL), was filtered through a Celite pad, and the solid was washed with ethyl acetate (3 × 50 mL). The combined filtrates were washed with 5% aqueous citric acid solution (2 × 100 mL), water (3 × 100 mL), and saturated aqueous sodium chloride solution (75 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting orange residue was purified by flash column chromatography (eluent: gradient, 2 → 10% acetone in dichloromethane) to afford the indole adduct (+)-**19d** (6.56 g, 83.6%) as a white foam. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC):

δ 8.04 (app-d, J = 7.4, 2H, SO_2Ph-*o*-**H**), 7.77 (d, J = 8.3, 1H, C_8**H**), 7.56 (app-t, J = 7.5, 1H, SO_2Ph-*p*-**H**), 7.42 (app-dd, J = 7.8, 8.0, 2H, SO_2Ph-*m*-**H**), 7.30 (d, J = 8.9, 1H, $C_{8'}$**H**), 7.29 (app-dt, J = 1.1, 7.9, 1H, C_7**H**), 7.15 (dd, J = 1.8, 8.8, 1H, $C_{7'}$**H**), 6.98 (app-t, J = 7.5, 1H, C_6**H**), 6.94 (s, 1H, $C_{2'}$**H**), 6.84 (d, J = 7.4, 1H, C_5**H**), 6.55 (d, J = 1.3, 1H, $C_{5'}$**H**), 6.28 (s, 1H, C_2**H**), 4.47 (dd, J = 8.0, 9.5, 1H, C_{11}**H**), 4.07 (d, J = 17.8, 1H, C_{15}**H**$_a$), 3.94 (d, J = 17.8, 1H, C_{15}**H**$_b$), 3.03 (dd, J = 7.6, 13.8, 1H, C_{12}**H**$_a$), 3.00 (s, 3H, C_{14}**H**$_3$), 2.86 (dd, J = 10.0, 13.9, 1H, C_{12}**H**$_b$), 1.59 (app-sp, J = 7.5, 3H, $C_{10'}$**H**), 1.08 (app-d, J = 8.5, 18H, $C_{11'}$**H**).

[9] 5-Bromo-1-triisopropylsilyl-1*H*-indole **14d** was prepared in quantitative yield by silylation of commercially available 5-bromoindole using triisopropylsilyl chloride and sodium hydride in THF. For preparation and characterization, see: Brown, D. A.; Mishra, M.; Zhang, S.; Biswas, S.; Parrington, I.; Antonio, T.; Reith, M. E. A.; Dutta, A. K. *Bioorg. Med. Chem.* **2009**, *17*, 3923.

^{13}C NMR (100 MHz, $CDCl_3$, 20 ºC):	δ 167.7 (**C**$_{13}$), 166.8 (**C**$_{16}$), 141.3 (**C**$_{9'}$), 139.7 (**C**$_9$), 137.1 (SO_2Ph-*ipso*-**C**), 134.2 (SO_2Ph-*p*-**C**), 134.0 (**C**$_4$), 130.9 (**C**$_{2'}$), 130.3 (**C**$_{4'}$), 129.6 (**C**$_7$), 129.3 (SO_2Ph-*m*-**C**), 127.9 (SO_2Ph-*o*-**C**), 125.4 (**C**$_{7'}$), 124.6 (**C**$_6$), 124.0 (**C**$_5$), 121.9 (**C**$_{5'}$), 116.0 (**C**$_{8'}$), 115.7 (**C**$_8$), 115.1 (**C**$_{3'}$), 113.5 (**C**$_{6'}$), 82.7 (**C**$_2$), 59.5 (**C**$_{11}$), 55.4 (**C**$_3$), 54.6 (**C**$_{15}$), 37.6 (**C**$_{12}$), 33.8 (**C**$_{14}$), 18.2 (**C**$_{11'}$), 12.9 (**C**$_{10'}$).
FTIR (thin film) cm^{-1}:	2949 (m), 2869 (m), 1681 (s), 1447 (m), 1396 (m), 1366 (m), 1178 (s), 1092 (w), 987 (w), 732 (m), 690 (w).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{37}H_{44}BrN_4O_4SSi$ $[M+H]^+$: 747.2030, found: 747.2025.
$[\alpha]_D^{24}$:	+93.6 (*c* = 0.26, $CHCl_3$).
TLC (10% acetone in dichloromethane), R*f*:	0.67 (UV, CAM).



Deprotected C3-(indol-3-yl)-pyrrolidinoindoline (+)-19a:

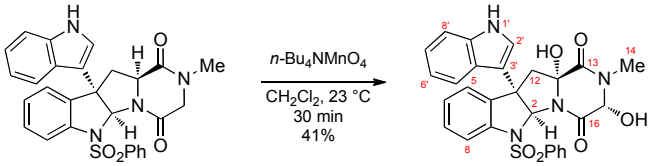
A mixture of anhydrous methanol and ethyl acetate (3:2 v/v, 160 mL) was introduced into a round-bottom flask charged with the indole adduct (+)-**19d** (6.56 g, 8.77 mmol, 1 equiv) and palladium on activated charcoal (10 % w/w, 0.50 g, 0.47 mmol, 0.05 equiv). The flask was purged by three cycles of vacuum and dihydrogen and sealed under an atmosphere of hydrogen gas (15 psi). Triethylamine (1.50 mL, 10.7 mmol, 1.22 equiv) was introduced to the flask via syringe and the resulting suspension was vigorously stirred at 23 °C. Upon completion of the reaction (*ca* 8 h) as monitored by TLC and MS, the flask was purged by three cycles of vacuum and argon and sealed under argon atmosphere. Neat triethylamine trihydrofluoride[10] (3.00 mL, 18.4 mmol, 2.15 equiv) was introduced to the flask via syringe and the resulting suspension was stirred at 23 °C. After 13 h, the reaction mixture was filtered through a pad of Celite. The solids were washed with ethyl acetate (3 × 50 mL). The combined filtrates were concentrated under reduced pressure. The resulting pale yellow solid was diluted in ethyl acetate (400 mL) and washed sequentially with an aqueous hydrogen chloride solution (1 N, 2 × 100 mL), water (2 × 100 mL), and saturated aqueous sodium chloride solution (50 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (eluent: 15% acetone in dichloromethane) to afford the indole adduct (+)-**19a** (4.59 g, 99.9%) as a white solid. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.03 (br-s, 1H, $N_{1'}$**H**), 7.75 (d, *J* = 8.2, 1H, C_8**H**), 7.50 (d, *J* = 7.6, 2H, SO_2Ph-*o*-**H**), 7.38 (t, *J* = 7.5, 1H, SO_2Ph-*p*-**H**), 7.35 (d, *J* = 8.2, 1H, $C_{8'}$**H**), 7.30 (dt, *J* = 1.1, 7.8, 1H, C_7**H**), 7.19 (app-t, *J* = 7.6, 1H, $C_{7'}$**H**), 7.10 (app-t, *J* = 7.9, 2H, SO_2Ph-*m*-**H**), 7.09–7.06 (m, 1H, C_5**H**), 7.06 (app-t, *J* = 7.4, 1H, C_6**H**), 6.93 (app-t, *J* = 7.4, 1H, $C_{6'}$**H**), 6.89 (d, *J* = 7.9, 1H, $C_{5'}$**H**), 6.37 (s, 1H, C_2**H**), 6.16 (d, *J* = 2.3, 1H, $C_{2'}$**H**), 4.56 (app-t, *J* = 8.1, 1H, C_{11}**H**), 4.13 (d, *J* = 17.5, 1H, C_{15}**H**$_a$), 3.85 (d, *J* = 17.5, 1H, C_{15}**H**$_b$), 3.09 (dd, *J* = 8.9, 14.1, 1H, C_{12}**H**$_a$), 3.03 (dd, *J* = 7.2, 14.1, 1H, C_{12}**H**$_b$), 2.90 (s, 3H, C_{14}**H**$_3$).

^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC): δ 167.5 (**C**$_{13}$), 165.9 (**C**$_{16}$), 139.6 (**C**$_9$), 137.6 (SO_2Ph-*ipso*-**C**), 137.4 (**C**$_{9'}$), 135.9 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 129.3 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 127.6 (SO_2Ph-*o*-**C**), 125.2 (**C**$_6$), 124.8 (**C**$_5$), 124.6 (**C**$_{4'}$), 123.6 (**C**$_{2'}$), 122.9 (**C**$_{7'}$), 120.3 (**C**$_{6'}$), 119.0 (**C**$_{5'}$), 117.1 (**C**$_8$), 115.0 (**C**$_{3'}$), 112.0 (**C**$_{8'}$), 83.8 (**C**$_2$), 58.8 (**C**$_{11}$), 55.4 (**C**$_3$), 54.6 (**C**$_{15}$), 36.1 (**C**$_{12}$), 33.8 (**C**$_{14}$).

[10] McClinton, M. A. *Aldrichimica Acta* **1995**, *28*, 31.

FTIR (thin film) cm^{-1}:	3384 (br-m), 3013 (w), 2925 (w), 1681 (s), 1457 (m), 1399 (m), 1355 (m), 1169 (m), 1091 (w), 751 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{28}H_{24}N_4NaO_4S$ $[M+Na]^+$: 535.1410, found: 535.1413.
$[\alpha]_D^{23}$:	+70.0 (*c* = 0.15, $CHCl_3$).
TLC (25% acetone in dichloromethane), R*f*:	0.41 (UV, CAM).



(+)-**19a** (–)-**20**

Hexacyclic diol (–)-20:

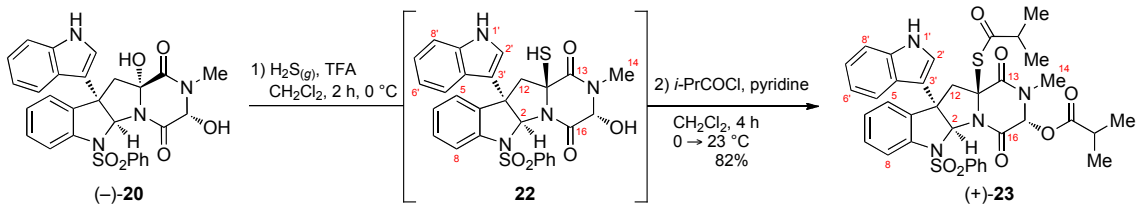
Freshly prepared tetra-*n*-butylammonium permanganate[11,12,13] (767 mg, 2.12 mmol, 3.79 equiv) was added as a solid to a solution of the indole adduct (+)**-19a** (287 mg, 0.56 mmol, 1 equiv) in dichloromethane (20 mL) at 23 °C. After 30 min, the dark purple solution was diluted with saturated aqueous sodium sulfite solution (20 mL) and then with ethyl acetate (160 mL). The resulting mixture was washed sequentially with saturated aqueous sodium bicarbonate solution (50 mL), water (2 × 50 mL), and saturated aqueous sodium chloride solution (30 mL). The aqueous layer was extracted with ethyl acetate (2 × 100 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting yellow residue was purified by flash column chromatography (eluent: gradient, 10 → 25% acetone in dichloromethane) to afford the diol (–)**-20** (127 mg, 41.6%) as a white solid.[14] Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, acetone-d_6, 20 ºC): δ 9.85 (br-s, 1H, $N_{1'}$**H**), 8.01 (d, J = 8.2, 1H, $C_{5'}$**H**), 7.56 (d, J = 8.1, 1H, C_8**H**), 7.49 (d, J = 8.1, 1H, $C_{8'}$**H**), 7.41 (d, J = 7.5, 1H, C_5**H**), 7.35 (app-t, J = 7.5, 1H, SO_2Ph-*p*-**H**), 7.35 (app-t, J = 7.5, 1H, C_7**H**), 7.24 (app-t, J = 7.6, 1H, $C_{7'}$**H**), 7.20 (app-t, J = 7.5, 1H, C_6**H**), 7.17 (app-t, J = 7.5, 1H, $C_{6'}$**H**), 7.04 (d, J = 7.5, 2H, SO_2Ph-*o*-**H**), 6.98 (app-t, J = 7.8, 2H, SO_2Ph-*m*-**H**), 6.80 (d, J = 6.2, 1H, C_{15}O**H**), 6.66 (s, 1H, C_2**H**), 6.22 (s, 1H, C_{11}O**H**), 5.65 (d, J = 2.5, 1H, $C_{2'}$**H**), 5.15 (d, J = 6.0, 1H, C_{15}**H**), 3.64 (d, J = 15.1, 1H, C_{12}**H**$_a$), 3.01 (d, J = 15.1, 1H, C_{12}**H**$_b$), 2.95 (s, 3H, C_{14}**H**$_3$).

^{13}C NMR (150 MHz, acetone-d_6, 20 ºC): δ 168.1 (**C**$_{13}$), 165.7 (**C**$_{16}$), 140.4 (**C**$_9$), 139.3 (SO_2Ph-*ipso*-**C**), 138.8 (**C**$_4$), 138.6 (**C**$_{9'}$), 133.7 (SO_2Ph-*p*-**C**), 129.8 (**C**$_7$), 128.9 (SO_2Ph-*m*-**C**), 127.5 (SO_2Ph-*o*-**C**), 126.3 (**C**$_5$), 126.2 (**C**$_6$), 125.7 (**C**$_{2'}$), 125.2 (**C**$_{4'}$), 122.9 (**C**$_{7'}$), 120.4 (**C**$_{6'}$), 119.6 (**C**$_{5'}$), 118.2 (**C**$_8$), 115.7 (**C**$_{3'}$), 113.0 (**C**$_{8'}$), 88.6 (**C**$_{11}$), 85.3 (**C**$_2$), 83.9 (**C**$_{15}$), 55.3 (**C**$_3$), 45.1 (**C**$_{12}$), 31.8 (**C**$_{14}$).

[11] Sala, T.; Sargent, M. V. *J. Chem. Soc., Chem. Commun.* **1978**, 253.
[12] Tetra-*n*-butylammonium permanganate was prepared according to a literature procedure (Karaman, H.; Barton, R. J.; Robertson, B. E.; Lee, D. G. *J. Org. Chem.* **1984**, *49*, 4509) and dried under reduced pressure at room temperature.
[13] (a) Gardner, K. A.; Mayer, J. M. *Science* **1995**, *269*, 1849. (b) Strassner, T.; Houk, K. N. *J. Am. Chem. Soc.* **2000**, *122*, 7821. (c) Shi, S.; Wang, Y.; Xu, A.; Wang, H.; Zhu, D.; Roy, S. B.; Jackson, T. A.; Busch, D. H.; Yin, G. *Angew. Chem. Int. Ed.* **2011**, *50*, 7321.
[14] Analytically pure samples of polar diol **20** could be obtained by trituration with minimal amount of chloroform.

FTIR (thin film) cm^{-1}:	3392 (br-m), 1700 (s), 1460 (w), 1400 (w), 1360 (m), 1169 (m), 1091 (w), 750 (w).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{28}H_{24}N_4NaO_6S$ $[M+Na]^+$: 567.1309, found: 567.1315.
$[\alpha]_D^{24}$:	–71.4 (*c* = 0.114, acetone).
m.p.:	212 °C.
TLC (20% acetone in dichloromethane), R*f*:	0.24 (UV, CAM).



(–)-**20** **22** (+)-**23**

Hexacyclic thioisobutyrate (+)-23:

A slow stream of hydrogen sulfide gas was introduced into a solution of diol (–)-**20** (507 mg, 931 μmol, 1 equiv) in anhydrous dichloromethane (117 mL) at 0 °C, providing a saturated hydrogen sulfide solution. After 40 min, trifluoroacetic acid (13 mL) was added via syringe, and the slow introduction of hydrogen sulfide into the mixture was maintained for another 10 min. The reaction mixture was left under an atmosphere of hydrogen sulfide for an additional 2 h at 0 °C. The resulting mixture was concentrated under reduced pressure to afford the hexacyclic aminothiol **22** that was used in the next step without further purification.[15]

The orange residue was dissolved in anhydrous dichloromethane (30 mL) and cooled to 0 °C in an ice–water bath. Anhydrous pyridine (1.60 mL, 19.8 mmol, 21.3 equiv) was added to the solution of the hydroxythiol **22** followed by addition of isobutyryl chloride (975 μL, 9.31 mmol, 10.0 equiv). After 10 min, the ice–water bath was removed, and the yellow solution was allowed to warm to 23 °C. After 4 h, methanol (1 mL) was added to the solution. After 5 min, the reaction mixture was diluted with ethyl acetate (200 mL). The resulting mixture was sequentially washed with aqueous hydrogen chloride solution (1 N, 2 × 80 mL), water (2 × 80 mL), and saturated aqueous sodium chloride solution (50 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The orange residue was purified by flash column chromatography on silica gel (eluent: gradient, 20 → 50% ethyl acetate in hexanes) to afford the thioisobutyrate (+)-**23** (534 mg, 81.8%) as a colorless foam. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.21 (br-s, 1H, $N_{1'}$**H**), 7.69 (d, *J* = 8.2, 1H, C_8**H**), 7.52 (d, *J* = 8.1, 2H, SO_2Ph-*o*-**H**), 7.36 (app-dd, *J* = 7.5, 7.9, 1H, C_7**H**), 7.27 (d, *J* = 7.9, 1H, $C_{8'}$**H**), 7.27–7.24 (m, 1H, SO_2Ph-*p*-**H**), 7.19 (d, *J* = 7.4, 1H, C_5**H**), 7.19–7.15 (m, 1H, $C_{5'}$**H**), 7.15 (app-t, *J* = 7.4, 1H, C_6**H**), 7.11 (app-dd, *J* = 7.5, 7.8, 1H, $C_{7'}$**H**), 6.99 (app-t, *J* = 7.6, 2H, SO_2Ph-*m*-**H**), 6.86 (app-t, *J* = 7.5, 1H, $C_{6'}$**H**), 6.76 (s, 1H, C_2**H**), 6.50–6.00 (br-s, 1H, C_{15}**H**),[16] 6.34 (s, 1H, $C_{2'}$**H**), 3.52

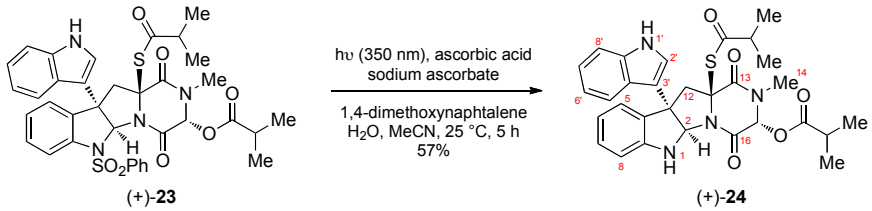
[15] ^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 7.86 (d, *J* = 8.1, 1H, C_8**H**), 7.82 (br-s, 1H, $N_{1'}$**H**), 7.43 (d, *J* = 7.7, 2H, SO_2Ph-*o*-**H**), 7.42 (t, *J* = 8.0, 1H, C_7**H**), 7.34 (app-t, *J* = 7.4, 1H, SO_2Ph-*p*-**H**), 7.31 (d, *J* = 8.1, 1H, $C_{8'}$**H**), 7.24–7.19 (m, 1H, $C_{5'}$**H**), 7.24–7.19 (m, 1H, C_6**H**), 7.18 (app-dd, *J* = 7.8, 8.0, 1H, $C_{7'}$**H**), 7.02 (app-t, *J* = 7.8, 2H, SO_2Ph-*m*-**H**), 6.94 (app-dd, *J* = 7.4, 7.7, 1H, $C_{6'}$**H**), 6.77 (d, *J* = 8.1, 1H, C_5**H**), 6.62 (s, 1H, C_2**H**), 6.22 (d, *J* = 2.5, 1H, $C_{2'}$**H**), 5.44 (br-s, 1H, C_{15}**H**), 5.30 (br-s, 1H, C_{15}O**H**), 3.80 (d, *J* = 14.8, 1H, C_{12}**H**$_a$), 3.12 (s, 3H, C_{14}**H**$_3$), 3.01 (d, *J* = 14.8, 1H, C_{12}**H**$_b$), 2.21 (s, 1H, C_{11}S**H**).

[16] Atropisomerism-induced peak broadening prevented complete NMR spectroscopic characterization of this center. The ^{1}H chemical shift of C_{15}H is present between 6.5 and 6.0 ppm, as a broad singlet and its ^{13}C chemical shift is at 80.7 ppm, as a broad and weak signal. Reliable heteronuclear HSQC correlation data was not obtained for this center. However, assignment is based on integration and homonuclear and heteronuclear data and is supported by key gHMBC signals (^{1}H, ^{13}C) in ppm: (2.97, 80.7), and key NOESY signals (^{1}H, ^{1}H) in ppm: (1.27, 6.86), (1.27, 6.76), (1.27, 6.34).

	(br-d, J = 13.8, 1H, $C_{12}\mathbf{H}_a$),[17] 2.97 (s, 3H, $C_{14}\mathbf{H}_3$), 2.83 (d, J = 14.3, 1H, $C_{12}\mathbf{H}_b$), 2.73(app-sp, J = 7.0, 1H, $C\mathbf{H}_{isobutyrate}$), 2.37 (app-sp, J = 6.9, 1H, $C\mathbf{H}_{thioisobutyrate}$), 1.28 (d, J = 6.8, 3H, $C\mathbf{H}_{3isobutyrate}$), 1.27 (d, J = 6.0, 3H, $C\mathbf{H}_{3isobutyrate}$), 0.96 (d, J = 7.0, 3H, $C\mathbf{H}_{3thioisobutyrate}$), 0.95 (d, J = 7.1, 3H, $C\mathbf{H}_{3thioisobutyrate}$).
^{13}C NMR (100 MHz, $CDCl_3$, 20 ºC):	δ 203.2 ($\mathbf{C}$=$O_{thioisobutyrate}$), 175.7 ($\mathbf{C}$=$O_{isobutyrate}$), 164.9 ($\mathbf{C}_{13}$), 160.7 ($\mathbf{C}_{16}$), 142.9 ($\mathbf{C}_9$), 137.9 (SO_2Ph-*ipso*-$\mathbf{C}$), 137.3 ($\mathbf{C}_{9'}$), 136.4 ($\mathbf{C}_4$), 133.2 (SO_2Ph-*p*-$\mathbf{C}$), 129.4 ($\mathbf{C}_7$), 128.7 (SO_2Ph-*m*-$\mathbf{C}$), 127.3 (SO_2Ph-*o*-$\mathbf{C}$), 125.5 ($\mathbf{C}_6$), 125.3 ($\mathbf{C}_5$), 124.3 ($\mathbf{C}_{4'}$), 123.6 ($\mathbf{C}_{2'}$), 122.5 ($\mathbf{C}_{7'}$), 120.2 ($\mathbf{C}_{6'}$), 119.4 ($\mathbf{C}_{5'}$), 117.5 ($\mathbf{C}_8$), 115.8 ($\mathbf{C}_{3'}$), 111.7 ($\mathbf{C}_{8'}$), 84.9 ($\mathbf{C}_2$), 80.7 ($\mathbf{C}_{15}$), 74.1 (C_{11}),[18] 54.0 ($\mathbf{C}_3$), 49.4 ($\mathbf{C}_{12}$), 43.3 ($\mathbf{C}H_{thioisobutyrate}$), 34.0 ($\mathbf{C}H_{isobutyrate}$), 31.3 ($\mathbf{C}_{14}$), 19.4 ($\mathbf{C}H_{3thioisobutyrate}$), 19.1 ($\mathbf{C}H_{3isobutyrate}$), 18.7 ($\mathbf{C}H_{3isobutyrate}$), 18.6 ($\mathbf{C}H_{3thioisobutyrate}$).
FTIR (thin film) cm^{-1}:	3398 (m), 2975 (w), 1747 (m), 1700 (s), 1461 (m), 1391 (m), 1172 (m), 961 (w), 751 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{36}H_{36}N_4NaO_7S_2$ $[M+Na]^+$: 723.1918, found 723.1935.
$[\alpha]_D^{25}$:	+186.2 (c = 0.067, $CHCl_3$).
TLC (50% ethyl acetate in hexanes), R*f*:	0.33 (UV, CAM).

[17] Atropisomerism induced peak broadening was observed for this center. Our assignment of this resonance is supported by key gCOSY signal (^{1}H, ^{1}H) in ppm: (3.52, 2.83), key HSQC signals (^{1}H, ^{13}C) in ppm: (3.52, 49.4), (2.83, 49.4), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (6.76, 49.4), (2.83, 136.4), (2.83, 84.9), (2.83, 74.2), (2.83, 54.0).

[18] Our assignment of this resonance is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (0.96/0.95, 7.69), (0.96/0.95, 7.52), (0.96/0.95, 7.36), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (6.76, 74.2), (2.83, 74.2), (2.73, 74.2).



(+)-**23** (+)-**24**

Hexacyclic aminothioisobutyrate (+)-24:

A 500-mL Pyrex tube-shaped flask (8 cm diameter) was sequentially charged with hexacyclic thioisobutyrate (+)-**23** (524 mg, 748 μmol, 1 equiv), L-ascorbic acid (1.32 g, 7.49 mmol, 10.0 equiv), sodium L-ascorbate (1.48 g, 7.49 mmol, 10.0 equiv), and 1,4-dimethoxynaphthalene (8.46 g, 45.0 mmol, 60.1 equiv), and the mixture was placed under an argon atmosphere.[19] A solution of water in acetonitrile (20% v/v, 125 mL) that was purged with argon for 15 min at 23 °C was transferred to the flask via cannula. The flask was then placed in a 150-mL Pyrex beaker containing a 2 wt% indole solution in acetonitrile (5 mm path length). The system was vigorously stirred under an argon atmosphere and irradiated with a Rayonet photoreactor equipped with 16 lamps emitting at 350 nm at 25 °C. After 5 h, the lamps were turned off, and the reaction mixture was diluted with ethyl acetate (200 mL) and diethyl ether (100 mL). The resulting solution was sequentially washed with saturated aqueous sodium bicarbonate solution (100 mL), water (2 × 80 mL), and saturated aqueous sodium chloride solution (50 mL). The aqueous layer was extracted with ethyl acetate (2 × 80 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 20 → 50% ethyl acetate in hexanes) to afford the aminothioisobutyrate (+)-**24** (240 mg, 57.2%) as a colorless oil. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC):

δ 8.24 (br-s, 1H, $N_{1'}$**H**), 7.65 (br-s, 1H, $C_{5'}$**H**),[20] 7.32 (d, J = 8.2, 1H, $C_{8'}$**H**), 7.17 (app-t, J = 6.5, 1H, $C_{7'}$**H**), 7.16 (d, J = 7.5, 1H, C_5**H**), 7.12 (app-dt, J = 0.7, 7.6, 1H, C_7**H**), 7.04 (app-t, J = 7.6, 1H, $C_{6'}$**H**), 6.89 (d, J = 1.9, 1H, $C_{2'}$**H**), 6.80 (app-t, J = 7.4, 1H, C_6**H**), 6.59 (d, J = 7.8, 1H, C_8**H**), 6.60–6.20 (br-s, 1H, C_{15}**H**),[21] 6.13 (s, 1H, C_2**H**), 4.91 (br-s, 1H, N_1**H**), 3.56 (br-d, J = 14.1, 1H, C_{12}**H**$_a$),[22] 3.04 (d, J = 14.1, 1H, C_{12}**H**$_b$), 2.98 (s, 3H, C_{14}**H**$_3$), 2.70 (app-sp, J = 7.0, 1H, C**H**$_{isobutyrate}$), 2.39 (app-sp, J = 6.9, 1H, C**H**$_{thioisobutyrate}$), 1.26 (d, J = 7.0, 3H, C**H**$_{3isobutyrate}$), 1.25 (d, J = 6.9, 3H, C**H**$_{3isobutyrate}$), 0.97

[19] Hamada, T.; Nishida, A.; Yonemitsu, O. *J. Am. Chem. Soc.* **1986**, *108*, 140.

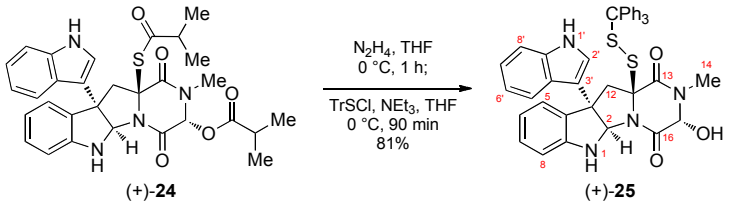
[20] Signal broadening in the ^{1}H and ^{13}C NMR spectra for C_{15}H is attributed to the more difficult rotation around the C3'$_{sp2}$–C3$_{sp3}$ bond. This is consistent with observed key NOESY signals (^{1}H, ^{1}H) in ppm: (1.26/1.25, 7.04), (1.26/1.25, 6.89), (1.26/1.25, 6.13).

[21] Atropisomerism induced peak broadening prevented complete NMR spectroscopic characterization of this center. The ^{1}H chemical shift of C_{15}H is present between 6.6 and 6.2 ppm, as a broad singlet and its ^{13}C chemical shift is at 80.5 ppm, as a broad and weak signal. Reliable heteronuclear HSQC correlation data was not obtained for this center. However, assignment is based on integration and homonuclear and heteronuclear data and is supported by key gHMBC signals (^{1}H, ^{13}C) in ppm: (2.98, 80.5), and key NOESY signals (^{1}H, ^{1}H) in ppm: (7.65, 6.13), (7.65, 3.56).

[22] Atropisomerism induced peak broadening was observed at this center. Our assignment of this resonance is supported by key gCOSY signal (^{1}H, ^{1}H) in ppm: (3.56, 3.04), key HSQC signals (^{1}H, ^{13}C) in ppm: (3.56, 49.2), (3.04, 49.2), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (6.13, 49.2), (3.56, 165.2), (3.56, 132.2), (3.04, 132.2), (3.56, 118.2), (3.04, 83.3), (3.56, 73.5), (3.04, 73.5), (3.56, 54.4), (3.04, 54.4).

	(d, J = 6.9, 3H, C**H**$_{3thioisobutyrate}$), 0.95 (d, J = 7.0, 3H, C**H**$_{3thioisobutyrate}$).
^{13}C NMR (100 MHz, $CDCl_3$, 20 ºC):	δ 204.6 (**C**=O$_{thioisobutyrate}$), 175.8 (**C**=O$_{isobutyrate}$), 165.2 (**C**$_{13}$), 162.1 (**C**$_{16}$), 149.4 (**C**$_{9}$), 137.4 (**C**$_{9'}$), 132.2 (**C**$_{4}$), 129.1 (**C**$_{7}$), 125.1 (**C**$_{4'}$), 124.8 (**C**$_{5}$), 122.6 (**C**$_{7'}$), 122.4 (**C**$_{2'}$), 120.1 (**C**$_{6'}$), 120.0 (**C**$_{5'}$), 119.6 (**C**$_{6}$), 118.2 (**C**$_{3'}$), 111.7 (**C**$_{8'}$), 109.3 (**C**$_{8}$), 83.3 (**C**$_{2}$), 80.5 (**C**$_{15}$), 73.5 (**C**$_{11}$),[23] 54.4 (**C**$_{3}$), 49.2 (**C**$_{12}$), 43.4 (**C**H$_{thioisobutyrate}$), 34.1 (**C**H$_{isobutyrate}$), 31.4 (**C**$_{14}$), 19.5 (**C**H$_{3thioisobutyrate}$), 19.0 (**C**H$_{3isobutyrate}$), 18.8 (**C**H$_{3isobutyrate}$), 18.6 (**C**H$_{3thioisobutyrate}$).
FTIR (thin film) cm^{-1}:	3372 (br-m), 2973 (w), 1750 (m), 1689 (s), 1460 (m), 1425 (m), 1400 (m), 1068 (m), 743 (m).
HRMS (ESI) (m/z):	calc'd for $C_{30}H_{32}N_4NaO_5S$ $[M+Na]^+$: 583.1986, found: 583.1993.
$[\alpha]_D^{24}$:	+93.6 (c = 0.15, $CHCl_3$).
TLC (50% ethyl acetate in hexanes), Rf:	0.58 (UV, CAM).

[23] Our assignment of this resonance is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (0.97/0.95, 7.12), (0.97/0.95, 6.80), (0.97/0.95, 4.91), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (6.13, 73.46), (3.56, 73.46), (3.04, 73.46).



(+)-**24** (+)-**25**

Hexacyclic triphenylmethanedisulfide (+)-25:

Anhydrous hydrazine (150 μL, 4.77 mmol, 11.1 equiv) was added via syringe to a solution of aminothioisobutyrate (+)-**24** (240 mg, 428 μmol, 1 equiv) in anhydrous tetrahydrofuran (50 mL) at 0 °C. After 1 h, the reaction mixture was diluted sequentially with saturated aqueous ammonium chloride solution (20 mL) and ethyl acetate (120 mL). The organic layer was sequentially washed with saturated aqueous ammonium chloride solution (50 mL), water (2 × 50 mL), and saturated aqueous sodium chloride solution (30 mL). The aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to afford the hexacyclic aminothiol that was used in the next step without further purification.[24]

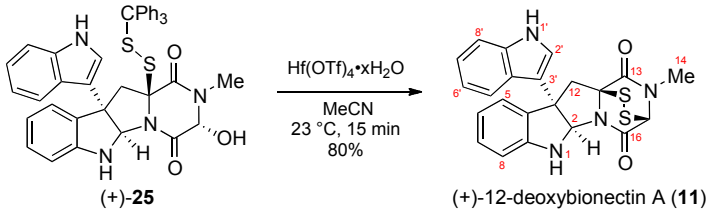
Triethylamine (600 μL, 4.27 mmol, 10.0 equiv) and solid triphenylmethanesulfenyl chloride (665 mg, 2.14 mmol, 5.00 equiv) were sequentially added to a solution of aminothiol in anhydrous tetrahydrofuran (60 mL) at 0 ºC under an argon atmosphere. After 90 min, the solution was partitioned between saturated aqueous ammonium chloride (50 mL) and ethyl acetate (130 mL). The aqueous layer was extracted with diethyl ether (2 × 50 mL), and the combined organic layers were washed sequentially with water (2 × 50 mL) and saturated aqueous sodium chloride solution (30 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 10 → 30% ethyl acetate in dichloromethane) to afford triphenylmethanedisulfide (+)-**25** (242 mg, 81.4 %)[25] as a white solid. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, CD_3CN, 20 ºC): δ 9.16 (br-s, 1H, $N_{1'}$**H**), 7.37 (d, J = 7.4, 1H, $C_{8'}$**H**), 7.36 (d, J = 7.6, 1H, $C_{5'}$**H**), 7.34–7.30 (m, 6H, C(Ph-*o*-**H**)$_3$), 7.34–7.30 (m, 3H, C(Ph-*p*-**H**)$_3$), 7.18–7.15 (m, 6H, C(Ph-*m*-**H**)$_3$), 7.15–7.11 (m, 1H, C_7**H**), 7.10 (app-dt, J = 0.8, 7.6, 1H, $C_{7'}$**H**), 6.97 (d, J = 2.7, 1H, $C_{2'}$**H**), 6.96 (app-t, J = 8.0, 1H, $C_{6'}$**H**), 6.68 (d, J = 7.9, 1H, C_8**H**), 6.64–6.60 (m, 1H, C_5**H**), 6.64–6.60 (m, 1H, C_6**H**), 5.75 (d, J = 1.0, 1H, C_2**H**), 5.60 (br-s, 1H, N_1**H**), 5.11 (s, 1H, C_{15}**H**), 4.59 (br-s, 1H, C_{15}O**H**), 3.32 (d, J = 14.5, 1H, C_{12}**H**$_a$), 2.89 (s, 3H, C_{14}**H**$_3$), 2.70 (d, J = 14.5, 1H, C_{12}**H**$_b$).

[24] This hexacyclic aminothiol can be purified by flash column chromatography on silica gel (eluent: gradient, 1 → 3% methanol in dichloromethane). ^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.16 (br-s, 1H, $N_{1'}$**H**), 7.40 (d, J = 8.1, 1H, $C_{5'}$**H**), 7.31 (d, J = 8.2, 1H, $C_{8'}$**H**), 7.23 (d, J = 7.4, 1H, C_5**H**), 7.19 (app-dt, J = 1.0, 7.7, 1H, C_7**H**), 7.17 (app-t, J = 7.4, 1H, $C_{7'}$**H**), 7.02 (app-t, J = 7.6, 1H, $C_{6'}$**H**), 6.89 (d, J = 2.6, 1H, $C_{2'}$**H**), 6.85 (app-t, J = 7.0, 1H, C_6**H**), 6.77 (d, J = 7.8, 1H, C_8**H**), 5.92 (s, 1H, C_2**H**), 5.36 (s, 1H, C_{15}**H**), 5.20 (br-s, 1H, N_1**H**), 3.76 (d, J = 14.3, 1H, C_{12}**H**$_a$), 3.75 (br-s, 1H, C_{15}O**H**), 3.30 (d, J = 14.3, 1H, C_{12}**H**$_b$), 3.09 (s, 3H, C_{14}**H**$_3$), 2.57 (br-s, 1H, C_{11}S**H**). ^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC): δ 166.6 (**C**$_{13}$), 166.6 (**C**$_{16}$), 148.2 (**C**$_9$), 137.4 (**C**$_{9'}$), 131.8 (**C**$_4$), 129.4 (**C**$_7$), 125.0 (**C**$_{4'}$), 125.0 (**C**$_5$), 122.7 (**C**$_{7'}$), 122.2 (**C**$_{2'}$), 120.4 (**C**$_6$), 120.2 (**C**$_{6'}$), 119.7 (**C**$_{5'}$), 117.3 (**C**$_{3'}$), 111.8 (**C**$_{8'}$), 110.4 (**C**$_8$), 82.5 (**C**$_2$), 77.2 (**C**$_{15}$), 69.0 (**C**$_{11}$), 54.2 (**C**$_3$), 50.9 (**C**$_{12}$), 29.3 (**C**$_{14}$). TLC (5% methanol in dichloromethane), R*f*: 0.27 (UV, CAM).

[25] This sequence can also been combined as a sequential single-flask two-step process to afford (+)-**25** in 74% yield.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC):	δ 8.00 (br-s, 1H, $N_{1'}$**H**), 7.31 (d, *J* = 7.8, 1H, $C_{5'}$**H**), 7.30 (d, *J* = 7.8, 1H, $C_{8'}$**H**), 7.29–7.26 (m, 6H, C(Ph-*o*-**H**)$_3$), 7.29–7.26 (m, 3H, C(Ph-*p*-**H**)$_3$), 7.20–7.17 (m, 6H, C(Ph-*m*-**H**)$_3$), 7.16 (app-t, *J* = 7.7, 1H, C_7**H**), 7.15 (app-t, *J* = 8.1, 1H, $C_{7'}$**H**), 7.02 (app-t, *J* = 7.5, 1H, $C_{6'}$**H**), 6.83 (d, *J* = 2.5, 1H, $C_{2'}$**H**), 6.74–6.68 (m, 1H, C_5**H**), 6.74–6.68 (m, 1H, C_6**H**), 6.74–6.68 (m, 1H, C_8**H**), 5.82 (s, 1H, C_2**H**), 5.24 (d, *J* = 3.6, 1H, C_{15}**H**), 4.99 (br-s, 1H, N_1**H**), 4.07 (d, *J* = 3.6, 1H, C_{15}O**H**), 3.43 (d, *J* = 14.7, 1H, C_{12}**H**$_a$), 3.00 (s, 3H, C_{14}**H**$_3$), 2.57 (d, *J* = 14.7, 1H, C_{12}**H**$_b$).
^{13}C NMR (150 MHz, CD_3CN, 20 ºC):	δ 166.9 (**C**$_{13}$), 164.1 (**C**$_{16}$), 149.2 (**C**$_9$), 145.0 (C(Ph-*ipso*-**C**)$_3$), 138.1 (**C**$_{9'}$), 133.3 (**C**$_4$), 131.2 (C(Ph-*m*-**C**)$_3$), 129.4 (**C**$_7$), 128.8 (C(Ph-*o*-**C**)$_3$), 128.4 (C(Ph-*p*-**C**)$_3$), 125.8 (**C**$_{4'}$), 125.4 (**C**$_5$), 122.8 (**C**$_{7'}$), 122.7 (**C**$_{2'}$), 120.3 (**C**$_6$), 120.3 (**C**$_{5'}$), 120.1 (**C**$_{6'}$), 118.6 (**C**$_{3'}$), 112.7 (**C**$_{8'}$), 110.6 (**C**$_8$), 83.1 (**C**$_2$), 78.4 (**C**Ph$_3$), 78.4 (**C**$_{15}$), 73.1 (**C**$_{11}$), 54.3 (**C**$_3$), 49.4 (**C**$_{12}$), 29.1 (**C**$_{14}$).
^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC):	δ 167.3 (**C**$_{16}$), 163.7 (**C**$_{13}$), 147.6 (**C**$_9$), 143.9 (C(Ph-*ipso*-**C**)$_3$), 137.3 (**C**$_{9'}$), 131.6 (**C**$_4$), 130.8 (C(Ph-*m*-**C**)$_3$), 129.5 (**C**$_7$), 127.9 (C(Ph-*o*-**C**)$_3$), 127.5 (C(Ph-*p*-**C**)$_3$), 125.2 (**C**$_5$), 125.1(**C**$_{4'}$), 122.6 (**C**$_{7'}$), 122.0 (**C**$_{2'}$), 120.2 (**C**$_{6'}$), 120.0 (**C**$_{5'}$), 119.9 (**C**$_6$), 117.5 (**C**$_{3'}$), 111.6 (**C**$_{8'}$), 110.1 (**C**$_8$), 82.6 (**C**$_2$), 77.6 (**C**Ph$_3$), 72.9 (**C**$_{15}$), 69.7 (**C**$_{11}$), 54.0 (**C**$_3$), 48.0 (**C**$_{12}$), 29.4 (**C**$_{14}$).
FTIR (thin film) cm^{-1}:	3345 (br-m), 3056 (w), 2926 (w), 1674 (s), 1483 (m), 1459 (m), 1442 (m), 1388 (m), 745 (s), 700 (s).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{41}H_{35}N_4O_3S_2$ $[M+H]^+$: 695.2145, found: 695.2147.
$[\alpha]_D^{24}$:	+165.2 (*c* = 0.12, $CHCl_3$).
TLC (5% methanol in dichloromethane), R*f*:	0.44 (UV, CAM).

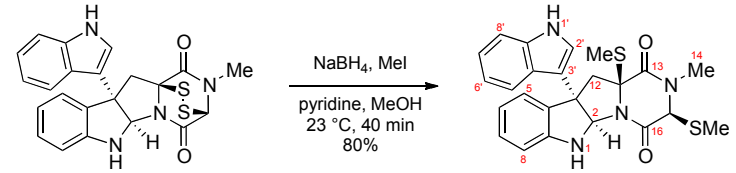


(+)-12-Deoxybionectin A (11):[26]

Hafnium (IV) trifluoromethanesulfonate hydrate (800.0 mg) was added as a solid to a colorless solution of hexacyclic triphenylmethanedisulfide (+)-**25** (100.0 mg, 143.9 μmol, 1 equiv) in anhydrous acetonitrile (40 mL) at 23 °C. A bright yellow coloration was observed immediately after the addition. The suspension was stirred at 23 °C under an argon atmosphere. After 15 min, the reaction mixture was partitioned between saturated aqueous sodium bicarbonate (60 mL) and ethyl acetate (100 mL). The aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed sequentially with water (3 × 50 mL) and saturated aqueous sodium chloride solution (30 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 1 → 6% acetone in dichloromethane) to afford (+)-12-deoxybionectin A (**11**) (50.2 mg, 80.3 %) as a colorless oil. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC):	δ 8.07 (br-s, 1H, $N_{1'}$**H**), 7.48 (d, *J* = 8.0, 1H, $C_{5'}$**H**), 7.37 (d, *J* = 8.2, 1H, $C_{8'}$**H**), 7.25 (d, *J* = 8.3, 1H, C_5**H**), 7.20 (app-dt, *J* = 0.7, 7.7, 1H, C_7**H**), 7.20 (app-dt, *J* = 0.7, 7.7, 1H, $C_{7'}$**H**), 7.09 (app-t, *J* = 7.6, 1H, $C_{6'}$**H**), 6.95 (d, *J* = 2.5, 1H, $C_{2'}$**H**), 6.88 (app-t, *J* = 7.4, 1H, C_6**H**), 6.76 (d, *J* = 7.9, 1H, C_8**H**), 5.95 (s, 1H, C_2**H**), 5.60–5.10 (br-s, 1H, N_1**H**), 5.21 (s, 1H, C_{15}**H**), 4.10 (d, *J* = 15.4, 1H, C_{12}**H**$_a$), 3.15 (s, 3H, C_{14}**H**$_3$), 2.95 (d, *J* = 15.4, 1H, C_{12}**H**$_b$).
^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC):	δ 165.8 (**C**$_{13}$), 162.2 (**C**$_{16}$), 148.2 (**C**$_9$), 137.5 (**C**$_{9'}$), 132.0 (**C**$_4$), 129.4 (**C**$_7$), 125.1 (**C**$_{4'}$), 124.3 (**C**$_5$), 122.9 (**C**$_{7'}$), 122.9 (**C**$_{2'}$), 120.4 (**C**$_{6'}$), 120.1 (**C**$_6$), 119.6 (**C**$_{5'}$), 116.7 (**C**$_{3'}$), 111.9 (**C**$_{8'}$), 110.4 (**C**$_8$), 83.0 (**C**$_2$), 74.8 (**C**$_{11}$), 68.4 (**C**$_{15}$), 56.1 (**C**$_3$), 43.6 (**C**$_{12}$), 32.2 (**C**$_{14}$).
FTIR (thin film) cm^{-1}:	3358 (br-w), 3006 (w), 2926 (w), 1684 (m), 1609 (w), 1460 (w), 1383 (w), 1232 (s), 748 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{22}H_{19}N_4O_2S_2$ $[M+H]^+$: 435.0944, found: 435.0943.
$[\alpha]_D^{24}$:	+387.3 (*c* = 0.10, $CHCl_3$).
TLC (10% acetone in dichloromethane), R*f*:	0.54 (UV, CAM).

[26] Zheng, C.-J.; Kim, C.-J.; Bae, K. S.; Kim, Y.-H.; Kim, W.-G. *J. Nat. Prod.* **2006**, *69*, 1816.



(+)-12-deoxybionectin A (**11**) (+)-gliocladin B (**1**)

(+)-Gliocladin B (1):

Sodium borohydride (20.1 mg, 531 μmol, 11.0 equiv) was added as a solid to a solution of disulfide (+)-**11** (20.9 mg, 48.1 μmol, 1 equiv) and iodomethane (1 mL) in anhydrous pyridine (1.5 mL) and anhydrous methanol (2.5 mL) at 23 °C under an argon atmosphere.[27] After 40 min, the yellow reaction mixture was partitioned between aqueous hydrogen chloride solution (1 N, 25 mL) and ethyl acetate (80 mL). The aqueous layer was extracted with ethyl acetate (2 × 30 mL), and the combined organic layers were washed sequentially with water (2 × 30 mL) and saturated aqueous sodium chloride solution (30 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 5 → 30% ethyl acetate in dichloromethane) to afford (+)-gliocladin B (**1**) (17.9 mg, 80.1%) as a colorless oil. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a saturated solution of (+)-gliocladin B (**1**) in chloroform at 23 °C. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data. The relative stereochemistry of (+)-gliocladin B (**1**) was secured by X-Ray diffraction of a single crystal (page S39, *vide infra*).[28]

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.11 (br-s, 1H, $N_{1'}$**H**), 7.43 (d, *J* = 8.0, 1H, $C_{5'}$**H**), 7.33 (d, *J* = 8.2, 1H, $C_{8'}$**H**), 7.16 (app-dt, *J* = 0.8, 7.7, 1H, $C_{7'}$**H**), 7.16 (d, *J* = 7.4, 1H, C_5**H**), 7.14 (app-dt, *J* = 1.0, 7.6, 1H, C_7**H**), 7.03 (app-dt, *J* = 0.8, 7.6, 1H, $C_{6'}$**H**), 6.95 (d, *J* = 2.5, 1H, C_2**H**), 6.75 (app-dt, *J* = 0.8, 7.4, 1H, C_6**H**), 6.69 (d, *J* = 7.8, 1H, C_8**H**), 6.06 (s, 1H, C_2**H**), 5.11 (br-s, 1H, N_1**H**), 4.61 (s, 1H, C_{15}**H**), 3.31 (d, *J* = 14.3, 1H, C_{12}**H**$_a$), 3.20 (d, *J* = 14.3, 1H, C_{12}**H**$_b$), 3.12 (s, 3H, C_{14}**H**$_3$), 2.46 (s, 3H, C_{15}SC**H**$_3$), 1.99 (s, 3H, C_{11}SC**H**$_3$).

^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC): δ 165.8 (**C**$_{13}$), 164.7 (**C**$_{16}$), 148.8 (**C**$_9$), 137.4 (**C**$_{9'}$), 132.7 (**C**$_4$), 128.9 (**C**$_7$), 125.2 (**C**$_{4'}$), 123.3 (**C**$_5$), 122.6 (**C**$_{7'}$), 121.9 (**C**$_{2'}$), 120.2 (**C**$_{6'}$), 119.8 (**C**$_{5'}$), 119.4 (**C**$_6$), 118.7 (**C**$_{3'}$), 111.7 (**C**$_{8'}$), 109.6 (**C**$_8$), 82.6 (**C**$_2$), 68.9 (**C**$_{11}$), 68.5 (**C**$_{15}$), 53.9 (**C**$_3$), 44.4 (**C**$_{12}$), 32.4 (**C**$_{14}$), 18.4 (C_{15}S**C**H$_3$), 15.5 (C_{11}S**C**H$_3$).

FTIR (thin film) cm^{-1}: 3345 (br-m), 2921 (w), 1665 (s), 1484 (w), 1420 (m), 1395 (m), 1238 (w), 1068 (w), 746 (m).

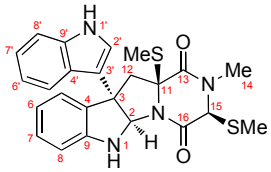
[27] (a) Cook, K. M.; Hilton, S. T.; Mecinović, J.; Motherwell, W. B.; Figg, W. D.; Schofield, C. J. *J. Biol. Chem.* **2009**, *284*, 26831. (b) Poisel, H.; Schmidt, U. *Chem. Ber.* **1971**, *104*, 1714.

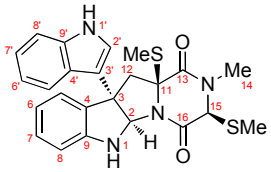
[28] Slow evaporation at room temperature of a solution of synthetic (+)-gliocladin B (**1**) in chloroform (300 μL) provided crystals suitable for X-Ray diffraction. For a thermal ellipsoid representation of (+)-**1**, please see page S39.

HRMS (ESI) (*m*/*z*):	calc'd for $C_{24}H_{24}N_4NaO_2S_2$ $[M+Na]^+$: 487.1233, found: 487.1218.
$[\alpha]_D^{24}$:	+200.4 (*c* = 0.062, $CHCl_3$).[29]
TLC (10% ethyl acetate in dichloromethane), R*f*:	0.22 (UV, CAM).

[29] Literature value: $[\alpha]_D^{16}$ = +200.0 (*c* = 0.06, $CHCl_3$), Usami, Y.; Yamaguchi, J.; Numata, A. *Heterocycles* **2004**, *63*, 1123.

Table S1. Comparison of our ^{1}H NMR data for (+)-gliocladin B (1) with literature data:





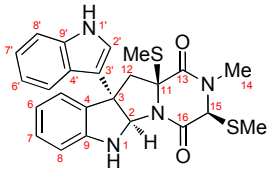
Assignment	**Usami's Report**[30] (+)-Gliocladin B (**1**) ^{1}H NMR,[31] 500 MHz, $CDCl_3$, 27 °C	**This Work** (+)-Gliocladin B (**1**) ^{1}H NMR, 600 MHz, $CDCl_3$, 20 °C
N1	5.10 (br-s, 1H)	5.11 (br-s, 1H)
C2	6.07 (s, 1H)	6.06 (s, 1H)
C3	—	—
C4	—	—
C5	7.17 (d, *J* = 7.8, 1H)	7.16 (app-d, *J* = 7.4, 1H)
C6	6.75 (t, *J* = 7.8, 1H)	6.75 (app-dt, *J* = 0.8, 7.4, 1H)
C7	7.14 (t, *J* = 7.8, 1H)	7.14 (app-dt, *J* = 1.0, 7.6, 1H)
C8	6.70 (d, *J* = 7.8, 1H)	6.69 (d, *J* = 7.8, 1H)
C9	—	—
N10	—	—
C11	—	—
C11-*S*Me	1.99 (s, 3H)	1.99 (s, 3H)
C12	3.33 (d, *J* = 14.3, 1H) 3.21 (d, *J* = 14.3, 1H)	3.31 (d, *J* = 14.3, 1H) 3.20 (d, *J* = 14.3, 1H)
C13	—	—
C14	3.12 (s, 3H)	3.12 (s, 3H)
C15	4.62 (s, 1H)	4.61 (s, 1H)
C15-*S*Me	2.46 (s, 3H)	2.46 (s, 3H)
C16	—	—
N1'	8.02 (br-s, 1H)	8.11 (br-s, 1H)
C2'	6.99 (d, *J* = 2.5, 1H)	6.95 (d, *J* = 2.5, 1H)
C3'	—	—
C4'	—	—
C5'	7.43 (d, *J* = 8.0, 1H)	7.43 (d, *J* = 8.0, 1H)
C6'	7.04 (br-t, *J* = 8.0, 1H)	7.03 (app-dt, *J* = 0.8, 7.6, 1H)
C7'	7.04 (ddd, *J* = 0.9, 8.0, 8.2, 1H)	7.16 (app-dt, *J* = 0.8, 7.7, 1H)[32]
C8'	7.34 (dd, *J* = 8.2, 1H)	7.33 (d, *J* = 8.2 , 1H)
C9'	—	—

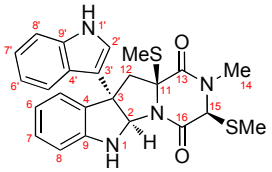
[30] Usami, Y.; Yamaguchi, J.; Numata, A. *Heterocycles* **2004**, *63*, 1123.

[31] NMR spectra were recorded at 27 °C on a Varian UNITY-500 spectrometer, operating at 125 MHz for ^{13}C in $CDCl_3$ with tetramethylsilane as internal reference.

[32] Our assignment of this resonance is supported by key gCOSY signals (^{1}H, ^{1}H) in ppm: (7.40, 6.90), (6.90, 7.23), (7.23, 6.72), key HSQC signals (^{1}H, ^{13}C) in ppm: (7.40, 125.4), (7.23, 130.7), (6.90, 120.6), (6.72, 110.9), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (7.40, 60.0), (6.90, 127.6), (7.23, 149.3).

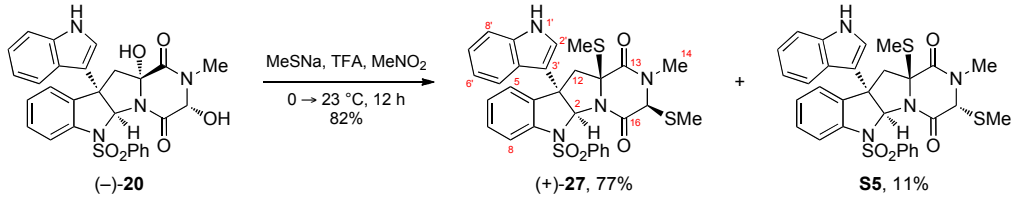
Table S2. Comparison of our ^{13}C NMR data for (+)-gliocladin B (1) with literature data:





Assignment	**Usami's Report**[30] (+)-Gliocladin B (**1**) ^{13}C NMR,[31] 125 MHz, $CDCl_3$, 27 °C	**This Work** (+)-Gliocladin B (**1**) ^{13}C NMR, 150 MHz, $CDCl_3$, 20 °C	**Chemical Shift Difference** $\Delta\delta = \delta$ (this work) $- \delta$ (ref. 30)
N1	—	—	—
C2	82.37	82.59	0.22
C3	53.72	53.93	0.21
C4	132.41	132.66	0.25
C5	123.08	123.30	0.22
C6	119.14	119.36	0.22
C7	128.64	128.85	0.21
C8	109.33	109.55	0.22
C9	148.58	148.81	0.23
N10	—	—	—
C11	68.64	68.85	0.21
C11-*S*Me	15.23	15.54	0.31
C12	44.1	44.41	0.31
C13	165.52	165.76	0.24
C14	32.17	32.37	0.20
C15	68.28	68.48	0.20
C15-*S*Me	18.23	18.44	0.21
C16	164.46	164.67	0.21
N1'	—	—	—
C2'	121.64	121.89	0.25
C3'	118.58	118.73	0.15
C4'	125.10	125.22	0.12
C5'	119.65	119.84	0.19
C6'	122.47	120.16[33]	–2.31
C7'	119.98	122.64[33]	2.66
C8'	111.47	111.73	0.26
C9'	137.19	137.42	0.23

[33] Our assignment of these resonances are supported by key gCOSY signals (^{1}H, ^{1}H) in ppm: (7.40, 6.90), (6.90, 7.23), (7.23, 6.72), key HSQC signals (^{1}H, ^{13}C) in ppm: (7.40, 125.4), (7.23, 130.7), (6.90, 120.6), (6.72, 110.9), and key gHMBC signals (^{1}H, ^{13}C) in ppm: (7.40, 60.0), (6.90, 127.6), (7.23, 149.3).



(–)-**20** (+)-**27**, 77% **S5**, 11%

Hexacyclic bis(methylthioether) (+)-27:

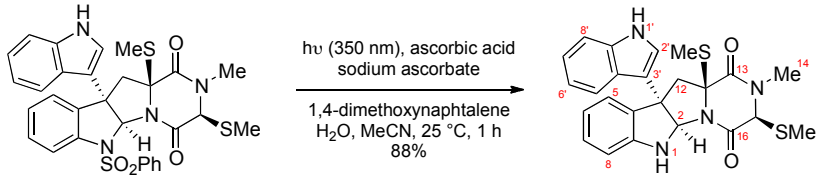
Trifluoroacetic acid (7 mL) was added via syringe to a vigorously stirred white suspension of diol (–)-**20** (53.0 mg, 97.4 μmol, 1 equiv) and sodium thiomethoxide (683 mg, 9.74 mmol, 100 equiv) in anhydrous nitromethane (7 mL) at 0 °C. After 10 min, the ice–water bath was removed, and the yellow solution was allowed to warm to 23 °C. After 12 h, the reaction mixture was diluted with ethyl acetate (120 mL) and slowly poured into saturated aqueous sodium bicarbonate solution (100 mL) at 23 °C. The organic layer was sequentially washed with water (3 × 50 mL) and saturated aqueous sodium chloride solution (50 mL). The combined aqueous layers were extracted with ethyl acetate (2 × 80 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 5 → 20% ethyl acetate in dichloromethane) to afford the bis(methylthioether) (+)-**27** (45.1 mg, 77.0%) as a yellow oil. {The minor (3*R*,5a*S*,10b*S*,11a*S*)-diastereomer **S5** was also isolated from this reaction (6.2 mg, 10.6%)}[34]. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and NOESY data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 °C): δ 8.23 (br-s, 1H, $N_{1'}$**H**), 7.68 (d, *J* = 8.1, 1H, C_8**H**), 7.65 (d, *J* = 7.7, 2H, SO_2Ph-*o*-**H**), 7.38–7.34 (m, 1H, SO_2Ph-*p*-**H**), 7.33 (app-dt, *J* = 1.1, 7.7, 1H, C_7**H**), 7.29 (d, *J* = 8.2, 1H, $C_{8'}$**H**), 7.21 (app-dd, *J* = 0.6, 7.5, 1H, C_5**H**), 7.12 (app-dd, *J* = 7.5, 8.2, 2H, SO_2Ph-*m*-**H**), 7.15–7.10 (m, 1H, $C_{7'}$**H**), 7.09 (app-dt, *J* = 0.6, 7.5, 1H, C_6**H**), 6.94–6.89 (m, 1H, $C_{5'}$**H**), 6.94–6.89 (m, 1H, $C_{6'}$**H**), 6.77 (s, 1H, C_2**H**), 6.42 (d, *J* = 2.6, 1H, $C_{2'}$**H**), 4.61 (s, 1H, C_{15}**H**), 3.29 (d, *J* = 14.7, 1H, C_{12}**H**$_a$), 3.10 (s, 3H, C_{14}**H**$_3$), 3.00 (d, *J* = 14.7, 1H, C_{12}**H**$_b$), 2.28 (s, 3H, C_{15}SC**H**$_3$), 1.94 (s, 3H, C_{11}SC**H**$_3$).

^{13}C NMR (100 MHz, $CDCl_3$, 20 °C): δ 165.2 (**C**$_{13}$), 162.7 (**C**$_{16}$), 142.1 (**C**$_9$), 138.7 (SO_2Ph-*ipso*-**C**), 137.4 (**C**$_{9'}$), 136.5 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 129.2 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 127.2 (SO_2Ph-*o*-**C**), 125.0 (**C**$_6$), 124.4 (**C**$_{4'}$), 123.7 (**C**$_5$), 123.3 (**C**$_{2'}$), 122.6 (**C**$_{7'}$), 120.3 (**C**$_{6'}$), 118.8

[34] The minor isomer **S5** can be isolated and characterized. ^{1}H NMR (600 MHz, $CDCl_3$, 20 °C): δ 8.29 (d, *J* = 7.8, 1H, C_5**H**), 7.65 (d, *J* = 8.0, 1H, C_8**H**), 7.53 (br-s, 1H, N_1**H**), 7.36 (d, *J* = 8.0, 1H, C_8**H**), 7.31 (app-dd, *J* = 7.1, 7.9, 1H, C_7**H**), 7.31 (app-dd, *J* = 7.1, 7.9, 1H, C_7**H**), 7.27 (app-t, *J* = 8.1, 1H, C_5**H**), 7.27 (app-t, *J* = 8.1, 1H, C_6**H**), 7.19 (app-t, *J* = 7.3, 1H, SO_2Ph-*p*-**H**), 7.14 (app-t, *J* = 7.5, 1H, C_6**H**), 7.07 (d, *J* = 7.7, 2H, SO_2Ph-*o*-**H**), 6.82 (app-t, *J* = 7.7, 2H, SO_2Ph-*m*-**H**), 6.72 (s, 1H, C_2**H**), 5.50 (d, *J* = 2.5, 1H, C_2**H**), 4.54 (s, 1H, C_{15}**H**), 3.63 (d, *J* = 15.1, 1H, C_{12}**H**$_a$), 3.34 (d, *J* = 15.1, 1H, C_{12}**H**$_b$), 2.95 (s, 3H, C_{14}**H**$_3$), 2.49 (s, 3H, C_{15}SC**H**$_3$), 2.22 (s, 3H, C_{11}SC**H**$_3$). ^{13}C NMR (100 MHz, $CDCl_3$, 20 °C): δ 165.1 (**C**$_{13}$), 164.9 (**C**$_{16}$), 139.2 (**C**$_9$), 138.6 (SO_2Ph-*ipso*-**C**), 137.25 (**C**$_{9'}$), 137.2 (**C**$_4$), 132.4 (SO_2Ph-*p*-**C**), 129.4 (**C**$_7$), 128.0 (SO_2Ph-*m*-**C**), 127.1 (SO_2Ph-*o*-**C**), 125.5 (**C**$_6$), 125.4 (**C**$_5$), 124.9 (**C**$_{2'}$), 124.2 (**C**$_{4'}$), 123.2 (**C**$_7$), 120.9 (**C**$_{6'}$), 119.4 (**C**$_{5'}$), 117.8 (**C**$_8$), 115.6 (**C**$_{3'}$), 111.7 (**C**$_{8'}$), 85.3 (**C**$_2$), 69.4 (**C**$_{15}$), 67.8 (**C**$_{11}$), 54.9 (**C**$_3$), 44.1 (**C**$_{12}$), 32.3 (**C**$_{14}$), 19.5 (C_{15}S**C**H$_3$), 14.7 (C_{11}S**C**H$_3$). FTIR (thin film) cm^{-1}: 3391 (br-m), 2921 (w), 1685 (s), 1459 (m), 1391 (m), 1361 (m), 1337 (m), 1252 (w), 1168 (m), 1091 (w), 737 (s). HRMS (ESI) (*m/z*): calc'd for $C_{30}H_{28}N_4O_4S_3Na$ [M+Na]$^+$: 627.1165, found 627.1158. TLC (eluent: 20% ethyl acetate in dichloromethane), R*f*: 0.44 (UV, CAM).

	(**C**$_{5'}$), 117.5 (**C**$_8$), 115.8 (**C**$_{3'}$), 112.0 (**C**$_{8'}$), 84.5 (**C**$_2$), 70.0 (**C**$_{11}$), 68.0 (**C**$_{15}$), 53.5 (**C**$_3$), 45.7 (**C**$_{12}$), 32.5 (**C**$_{14}$), 17.5 (C_{15}**S**$\mathbf{C}H_3$), 15.4 (C_{11}**S**$\mathbf{C}H_3$).
FTIR (thin film) cm^{-1}:	3392 (br-m), 3062 (w), 2921 (w), 1685 (s), 1459 (m), 1391 (m), 1266 (m), 1169 (m), 1092 (m), 1022 (m), 964 (w), 736 (s).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{30}H_{29}N_4O_4S_3$ $[M+H]^+$: 605.1345, found 605.1337.
$[\alpha]_D^{25}$:	+129.2 (*c* = 0.123, $CHCl_3$).
TLC (20% ethyl acetate in dichloromethane), R*f*:	0.36 (UV, CAM).

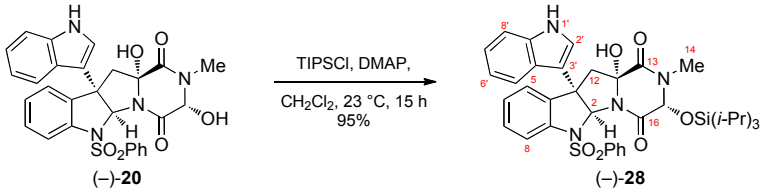


(+)-**27** (+)-gliocladin B (**1**)

(+)-Gliocladin B (1):

A 20 × 150 mm Pyrex tube was sequentially charged with bis(methylthioether) (+)-**27** (79.8 mg, 132 μmol, 1 equiv), L-ascorbic acid (232 mg, 1.32 mmol, 10.0 equiv), sodium L-ascorbate (271 mg, 1.38 mmol, 10.4 equiv), and 1,4-dimethoxynaphthalene (1.22 g, 6.48 mmol, 49.1 equiv), and the mixture was placed under an argon atmosphere. A solution of water in acetonitrile (20% v/v, 18 mL) that was purged with argon for 15 min at 23 °C was transferred to the flask via cannula. The system was vigorously stirred under an argon atmosphere and irradiated with a Rayonet photoreactor equipped with 16 lamps emitting at 350 nm at 25 °C. After 1 h, the lamps were turned off, and the reaction mixture was diluted with ethyl acetate (100 mL) and diethyl ether (50 mL). The resulting solution was sequentially washed with saturated aqueous sodium bicarbonate solution (50 mL), water (2 × 40 mL), and saturated aqueous sodium chloride solution (40 mL). The aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 5 → 30% ethyl acetate in dichloromethane) to afford (+)-gliocladin B (**1**) (53.9 mg, 87.9%) as a colorless oil.

Please see page S22 for the full characterization data for (+)-gliocladin B (**1**).



Hexacyclic *O*-TIPS protected monoalcohol (–)-28:

To a solution of diol (–)-**20** (90.1 mg, 166 μmol, 1 equiv) and 4-dimethylaminopyridine (DMAP, 404 mg, 3.31 mmol, 19.9 equiv) in anhydrous dichloromethane (5 mL) was added triisopropylsilyl chloride (TIPSCl, 360 μL, 1.68 mmol, 10.1 equiv) at 23 °C. After 6 h, another portion of TIPSCl (360 μL, 1.68 mmol, 10.1 equiv) was added. After 9 h, the reaction mixture was diluted with ethyl acetate (120 mL). The resulting mixture was sequentially washed with aqueous hydrogen chloride solution (1 N, 2 × 50 mL), water (2 × 50 mL), and saturated aqueous sodium chloride solution (30 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting yellow residue was purified by flash column chromatography (eluent: gradient, 20 → 50% ethyl acetate in hexanes) to afford the monoalcohol (–)-**28** (110.8 mg, 95.4%) as a white solid. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

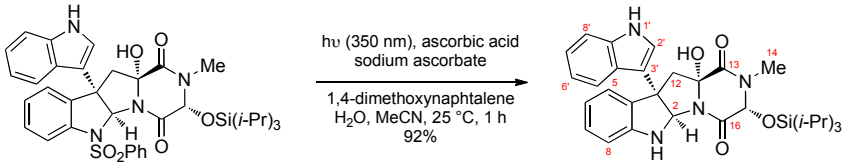
^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 7.98 (d, *J* = 7.8, 1H, $C_{5'}$**H**), 7.63 (d, *J* = 7.7, 1H, C_8**H**), 7.62 (br-s, 1H, $N_{1'}$**H**), 7.36 (d, *J* = 7.9, 1H, $C_{8'}$**H**), 7.31–7.23 (m, 1H, C_5**H**), 7.31–7.23 (m, 1H, C_7**H**), 7.31–7.23 (m, 1H, $C_{6'}$**H**), 7.31–7.23 (m, 1H, $C_{7'}$**H**), 7.23 (app-t, *J* = 7.4, 1H, SO_2Ph-*p*-**H**), 7.13 (app-dt, *J* = 0.8, 7.5, 1H, C_6**H**), 7.08 (app-dd, *J* = 1.0, 7.4, 2H, SO_2Ph-*o*-**H**), 6.87 (app-dd, *J* = 7.5, 8.3, 2H, SO_2Ph-*m*-**H**), 6.64 (s, 1H, C_2**H**), 5.58 (s, 1H, C_{11}O**H**), 5.46 (d, *J* = 2.5, 1H, $C_{2'}$**H**), 5.18 (s, 1H, C_{15}**H**), 3.65 (d, *J* = 15.3, 1H, C_{12}**H**$_a$), 3.10 (dd, *J* = 0.7, 15.3, 1H, C_{12}**H**$_b$), 2.96 (s, 3H, C_{14}**H**$_3$), 1.31 (app-sp, *J* = 7.5, 3H, SiC**H**$(CH_3)_2$), 1.18 (d, *J* = 7.5, 9H, SiCH(C**H**$_3)_2$), 1.15 (d, *J* = 7.5, 9H, SiCH(C**H**$_3)_2$).

^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC): δ 167.9 (**C**$_{13}$), 164.0 (**C**$_{16}$), 139.3 (**C**$_9$), 138.4 (SO_2Ph-*ipso*-**C**), 137.2 (**C**$_4$), 137.2 (**C**$_{9'}$), 132.5 (SO_2Ph-*p*-**C**), 129.2 (**C**$_7$), 128.1 (SO_2Ph-*m*-**C**), 127.2 (SO_2Ph-*o*-**C**), 125.7 (**C**$_6$), 125.5 (**C**$_5$), 124.3 (**C**$_{4'}$), 124.2 (**C**$_{2'}$), 123.1 (**C**$_{7'}$), 120.8 (**C**$_{6'}$), 119.5 (**C**$_{5'}$), 117.9 (**C**$_8$), 116.2 (**C**$_{3'}$), 111.7 (**C**$_{8'}$), 88.4 (**C**$_{11}$), 85.1 (**C**$_{15}$), 84.8 (**C**$_2$), 54.6 (**C**$_3$), 43.4 (**C**$_{12}$), 33.0 (**C**$_{14}$), 18.1 (SiCH(**C**$H_3)_2$), 12.4 (Si**C**H$(CH_3)_2$).

FTIR (thin film) cm^{-1}: 3398 (br-m), 2925 (s), 2867 (m), 1707 (s), 1461 (m), 1394 (w), 1361 (m), 1168 (m), 1027 (w), 746 (w), 668 (w).

HRMS (ESI) (*m*/*z*): calc'd for $C_{37}H_{45}N_4O_6SSi$ $[M+H]^+$: 701.2824, found: 701.2835.

$[\alpha]_D^{24}$:	–36.7 (c = 0.10, $CHCl_3$).
TLC (50% ethyl acetate in hexanes), Rf:	0.56 (UV, CAM).



(–)-**28** (+)-**29**

Hexacyclic *O*-TIPS protected aminoalcohol (+)-29:

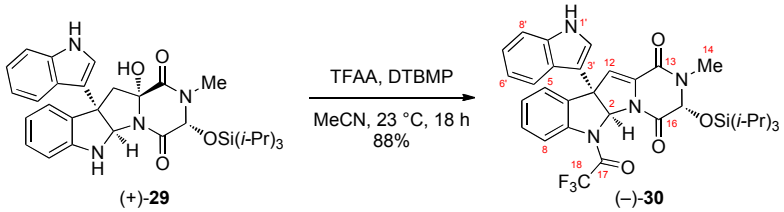
A 20 × 150 mm Pyrex tube was sequentially charged with hexacyclic silyl ether (–)-**28** (105 mg, 150 μmol, 1 equiv), L-ascorbic acid (265 mg, 1.50 mmol, 10.0 equiv), sodium L-ascorbate (300 g, 1.51 mmol, 10.0 equiv), and 1,4-dimethoxynaphthalene (1.35 g, 7.17 mmol, 47.8 equiv), and the mixture was placed under an argon atmosphere. A solution of water in acetonitrile (20% v/v, 22 mL) that was purged with argon for 15 min at 23 °C was transferred to the flask via cannula. The system was vigorously stirred under an argon atmosphere and irradiated with a Rayonet photoreactor equipped with 16 lamps emitting at 350 nm at 25 °C. After 1 h, the lamps were turned off, and the reaction mixture was diluted with ethyl acetate (80 mL) and diethyl ether (30 mL). The resulting solution was sequentially washed with saturated aqueous sodium bicarbonate solution (30 mL), water (2 × 30 mL), and saturated aqueous sodium chloride solution (20 mL). The aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent: gradient, 10 → 50% ethyl acetate in hexanes) to afford the aminoalcohol (+)-**29** (76.9 mg, 91.5%) as a colorless oil. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.04 (br-s, 1H, $N_{1'}$**H**), 7.42 (d, *J* = 8.0, 1H, $C_{5'}$**H**), 7.36 (d, *J* = 8.2, 1H, $C_{8'}$**H**), 7.17 (app-dt, *J* = 0.8, 7.6, 1H, $C_{7'}$**H**), 7.11 (app-dt, *J* = 1.1, 7.7, 1H, C_{7}**H**), 7.10 (d, *J* = 2.5, 1H, $C_{2'}$**H**), 7.06 (app-dd, *J* = 0.4, 7.3, 1H, C_{5}**H**), 7.02 (app-dt, *J* = 0.7, 7.6, 1H, $C_{6'}$**H**), 6.75 (app-dt, *J* = 0.7, 7.4, 1H, C_{6}**H**), 6.67 (d, *J* = 7.8, 1H, C_{8}**H**), 6.00 (s, 1H, C_{2}**H**), 5.13 (s, 1H, C_{15}**H**), 4.77 (s, 1H, C_{11}O**H**), 3.33 (d, *J* = 14.9, 1H, C_{12}**H**$_a$), 3.27 (dd, *J* = 1.2, 14.9, 1H, C_{12}**H**$_b$), 3.05 (s, 3H, C_{14}**H**$_3$), 1.20 (app-sp, *J* = 7.4, 3H, SiC**H**$(CH_3)_2$), 1.10 (d, *J* = 7.4, 9H, SiCH(C**H**$_3)_2$), 1.09 (d, *J* = 7.4, 9H, SiCH(C**H**$_3)_2$).

^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC): δ 168.4 (C_{13}), 165.6 (C_{16}), 147.2 (C_{9}), 137.4 ($C_{9'}$), 133.7 (C_{4}), 128.7 (C_{7}), 125.9 ($C_{4'}$), 124.7 (C_{5}), 123.5 ($C_{2'}$), 122.3 ($C_{7'}$), 120.1 ($C_{5'}$), 120.0 (C_{6}), 119.9 ($C_{6'}$), 117.8 ($C_{3'}$), 111.6 ($C_{8'}$), 109.8 (C_{8}), 88.3 (C_{11}), 84.8 (C_{15}), 84.2 (C_{2}), 54.5 (C_{3}), 46.7 (C_{12}), 33.1 (C_{14}), 18.0 (SiCH(**C**H$_3)_2$), 18.0 (SiCH(**C**H$_3)_2$), 12.4 (Si**C**H$(CH_3)_2$).

FTIR (thin film) cm^{-1}: 3406 (br-m), 2945 (m), 2868 (m), 1688 (s), 1485 (w), 1463 (m), 1399 (m), 1104 (w), 1020 (m), 742 (m).

HRMS (ESI) (*m*/*z*):	calc'd for $C_{31}H_{41}N_4O_4Si$ $[M+H]^+$: 561.2892, found: 561.2877.
$[\alpha]_D^{24}$:	+119.7 (*c* = 0.10, $CHCl_3$).
TLC (50% ethyl acetate in hexanes), R*f*:	0.76 (UV, CAM).



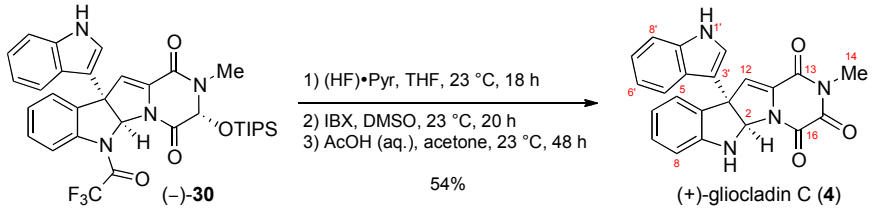
(+)-**29** (–)-**30**

Hexacyclic *O*-TIPS protected trifluoroacetamide (–)-30:

To a solution of aminoalcohol (+)-**29** (94.2 mg, 168 μmol, 1 equiv) and DTBMP (1.38 g, 6.72 mmol, 40.0 equiv) in anhydrous acetonitrile (15 mL) at 23 °C was added trifluoroacetic anhydride (TFAA, 470 μL, 3.38 mmol, 20.1 equiv). After 18 h, the reaction mixture was diluted with ethyl acetate (120 mL). The resulting mixture was sequentially washed with aqueous hydrogen chloride solution (1 N, 2 × 30 mL), water (2 × 40 mL), and saturated aqueous sodium chloride solution (25 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting yellow residue was purified by flash column chromatography (eluent: gradient, 10 → 50% ethyl acetate in hexanes) to afford the trifluoroacetamide (–)-**30** (94.3 mg, 87.9%) as a pale yellow oil. Structural assignments were made with additional information from gCOSY, HSQC, and gHMBC data.

^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC):	δ 8.21 (br-s, 1H, $N_{1'}$**H**), 8.19 (d, *J* = 8.2, 1H, C_8**H**), 7.41 (d, *J* = 8.3, 1H, $C_{8'}$**H**), 7.40 (app-dt, *J* = 1.5, 7.9, 1H, C_7**H**), 7.30 (app-dd, *J* = 1.1, 7.7, 1H, C_5**H**), 7.29–7.26 (m, 1H, $C_{5'}$**H**), 7.26 (app-dt, *J* = 0.8, 7.5, 1H, C_6**H**), 7.24 (app-dt, *J* = 0.7, 8.2, 1H, $C_{7'}$**H**), 7.06 (app-dt, *J* = 0.6, 7.6, 1H, $C_{6'}$**H**), 6.83 (d, *J* = 2.6, 1H, $C_{2'}$**H**), 6.82 (s, 1H, C_2**H**), 6.63 (s, 1H, C_{12}**H**), 5.26 (s, 1H, C_{15}**H**), 3.07 (s, 3H, C_{14}**H**$_3$), 1.26 (app-sp, *J* = 7.5, 3H, SiC**H**$(CH_3)_2$), 1.10 (d, *J* = 8.5, 9H, SiCH(C**H**$_3)_2$), 1.09 (d, *J* = 7.6, 9H, SiCH(C**H**$_3)_2$).
^{13}C NMR (150 MHz, $CDCl_3$, 20 ºC):	δ 161.7 (**C**$_{16}$), 157.5 (q, *J* = 39.6, **C**$_{17}$), 157.0 (**C**$_{13}$), 140.6 (**C**$_9$), 137.3 (**C**$_{9'}$), 134.1 (**C**$_4$), 132.8 (**C**$_{11}$), 129.6 (**C**$_7$), 127.1 (**C**$_6$), 125.4 (**C**$_{4'}$), 125.0 (**C**$_5$), 123.4 (**C**$_{2'}$), 123.3 (**C**$_{7'}$), 121.4 (**C**$_{12}$), 120.8 (**C**$_{6'}$), 119.2 (**C**$_{5'}$), 118.6 (**C**$_8$), 116.3 (q, *J* = 287.8, **C**$_{18}$), 114.1 (**C**$_{3'}$), 111.9 (**C**$_{8'}$), 83.5 (d, *J* = 5.2, **C**$_2$), 83.2 (**C**$_{15}$), 59.2 (**C**$_3$), 32.1 (**C**$_{14}$), 18.3 (SiCH(**C**$H_3)_2$), 18.2 (SiCH(**C**$H_3)_2$), 12.7 (Si**C**H$(CH_3)_2$).
^{19}F NMR (376.5 MHz, $CDCl_3$, 20 ºC):	δ –67.7.
FTIR (thin film) cm^{-1}:	3398 (br-w), 2946 (m), 2868 (m), 1710 (s), 1648 (m), 1460 (m), 1434 (m), 1401 (m), 1235 (m), 1191 (m), 1145 (m), 1107 (m), 1054 (m), 739 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{33}H_{37}F_3N_4NaO_4Si$ $[M+Na]^+$: 661.2428, found: 661.2445.

$[\alpha]_D^{24}$:	–43.4 (c = 0.09, $CHCl_3$).
TLC (50% ethyl acetate in hexanes), Rf:	0.65 (UV, CAM).



(+)-Gliocladin C (4):

To a solution of silyl ether (–)-**30** (53.0 mg, 83.0 μmol, 1 equiv) in anhydrous THF (5 mL) at 23 °C was added hydrogen fluoride–pyridine reagent[35] (550 μL, 21.2 mmol, 255 equiv). After 18 h, the reaction mixture was diluted with ethyl acetate (100 mL). The resulting mixture was sequentially washed with water (4 × 25 mL), saturated aqueous sodium bicarbonate solution (25 mL), and saturated aqueous sodium chloride solution (25 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure to afford the hexacyclic alcohol **31** that was used in the next step without further purification.[36]

To a solution of alcohol **31** in anhydrous DMSO (1 mL) at 23 °C was added 2-iodoxybenzoic acid[37] (IBX, 300 mg, 1.07 mmol, 12.9 equiv) as a solid. After 8 h, another portion of IBX (200 mg, 0.71 mmol, 8.6 equiv) was added as a solid. After 12 h, the reaction mixture was diluted with dichloromethane (10 mL). The diluted solution was passed through a short pad of silica gel and washed with a mixture of dichloromethane and ethyl acetate (9:1 v/v, 100 mL). The solvents were removed under reduced pressure to afford the triketopiperazine **32** that was used in the next step without further purification.[38]

To a solution of TFA-protected aniline **32** in a mixture of acetone and water (1:1 v/v, 18 mL) at 23 °C was added acetic acid (1 mL). After 48 h, the solvent was evaporated to dryness. The orange residual oil was taken up in ethyl acetate (100 mL). The organic solution was sequentially washed with water (5 × 20 mL) and saturated aqueous sodium chloride solution (20 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting yellow residue was purified by flash column chromatography on silica gel (eluent: gradient, 5 → 10% ethyl acetate in dichloromethane) to afford (+)-gliocladin C (+)-**1** (17.4 mg, 54.5%) as a yellow solid. Structural assignments were made with additional information from gCOSY, HSQC, gHMBC, and ROESY data.

^{1}H NMR (600 MHz, acetone-d_6, 20 ºC): δ 10.37 (br-s, 1H, $N_{1'}$**H**),7.43 (d, J = 8.2, 1H, $C_{8'}$**H**), 7.32 (d, J = 8.0, 1H, $C_{5'}$**H**), 7.23 (d, J = 2.6, 1H, $C_{2'}$**H**), 7.17 (d, J = 7.4, 1H, C_5**H**), 7.13 (app-dt, J = 1.1, 7.8, 1H, C_7**H**), 7.10 (app-dt, J = 0.6, 7.7, 1H, $C_{7'}$**H**), 6.96 (s, 1H, C_{12}**H**), 6.89 (app-dt, J = 0.6,

[35] Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872.

[36] ^{1}H NMR (600 MHz, $CDCl_3$, 20 ºC): δ 8.41 (br-s, 1H, $N_{1'}$**H**), 8.17 (d, J = 8.1, 1H, C_8**H**), 7.37 (d, J = 8.2, 1H, $C_{8'}$**H**), 7.42–7.37 (m, 1H, C_7**H**), 7.42–7.37 (m, 1H, C_6**H**), 7.25 (d, J = 8.3, 1H, C_5**H**), 7.19 (app-dd, J = 7.3, 8.0, 1H, $C_{7'}$**H**), 7.16 (d, J = 8.0, 1H, $C_{5'}$**H**), 7.01 (app-dd, J = 7.3, 7.8, 1H, $C_{6'}$**H**), 6.83 (d, J = 2.6, 1H, $C_{2'}$**H**), 6.82 (s, 1H, C_2**H**), 6.73 (s, 1H, C_{12}**H**), 5.20 (s, 1H, C_{15}**H**), 3.07 (s, 3H, C_{14}**H**$_3$). ^{1}H NMR (600 MHz, acetone-d_6, 20 ºC): δ 10.45 (br-s, 1H, $N_{1'}$**H**), 8.20 (d, J = 8.2, 1H, C_8**H**), 7.50 (app-dd, J = 0.8, 7.6, 1H, $C_{8'}$**H**), 7.47 (d, J = 8.2, 1H, $C_{5'}$**H**), 7.46 (app-dt, J = 1.3, 7.9, 1H, C_7**H**), 7.33 (app-dt, J = 7.3, 8.0, 1H, $C_{7'}$**H**), 7.23 (d, J = 8.1, 1H, C_5**H**), 7.15 (app-dt, J = 0.9, 7.6, 1H, $C_{6'}$**H**), 7.12 (d, J = 2.7, 1H, $C_{2'}$**H**), 6.97 (app-dt, J = 0.9, 7.6, 1H, C_6**H**), 6.89 (s, 1H, C_2**H**), 6.74 (s, 1H, C_{12}**H**), 5.24 (s, 1H, C_{15}**H**), 3.02 (s, 3H, C_{14}**H**$_3$). TLC (20% ethyl acetate in dichloromethane), R*f*: 0.13 (UV, CAM).

[37] Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, *64*, 4537.

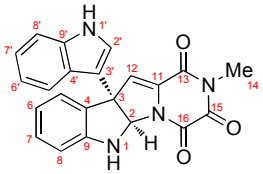
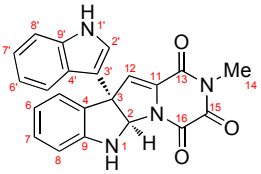
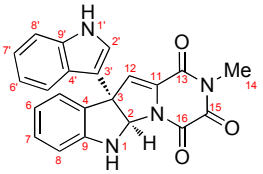
[38] ^{1}H NMR (600 MHz, acetone-d_6, 20 ºC): δ 10.55 (br-s, 1H, $N_{1'}$**H**), 8.20 (d, J = 8.2, 1H, C_8**H**), 7.62 (app-dd, J = 0.8, 7.6, 1H, $C_{8'}$**H**), 7.51 (app-dt, J = 1.3, 7.9, 1H, C_7**H**), 7.48 (d, J = 8.2, 1H, $C_{5'}$**H**), 7.43 (d, J = 8.1, 1H, C_5**H**), 7.39 (app-dt, J = 0.9, 7.5, 1H, $C_{7'}$**H**), 7.17 (app-dt, J = 0.9, 7.6, 1H, $C_{6'}$**H**), 7.15 (s, 1H, C_2**H**), 7.02 (d, J = 2.6, 1H, $C_{2'}$**H**), 6.99 (s, 1H, C_{12}**H**), 6.99 (app-dt, J = 0.8, 7.6, 1H, C_6**H**), 3.22 (s, 3H, C_{14}**H**$_3$). TLC (20% ethyl acetate in dichloromethane), R*f*: 0.68 (UV, CAM).

	7.5, 1H, $C_{6'}$**H**), 6.85 (d, J = 7.9, 1H, C_8**H**), 6.71 (app-dt, J = 0.6, 7.4, 1H, C_6**H**), 6.63 (br-s, 1H, N_1**H**), 6.23 (d, J = 2.5, 1H, C_2**H**), 3.25 (s, 3H, C_{14}**H**$_3$).
^{13}C NMR (150 MHz, acetone-d_6, 20 ºC):	δ 158.7 (**C**$_{15}$), 158.0 (**C**$_{13}$), 150.7 (**C**$_{16}$), 149.9 (**C**$_9$), 138.5 (**C**$_{9'}$), 133.1 (**C**$_{11}$), 131.1 (**C**$_4$), 129.7 (**C**$_7$), 127.0 (**C**$_{12}$), 126.3 (**C**$_{4'}$), 125.5 (**C**$_5$), 123.7 (**C**$_{2'}$), 122.8 (**C**$_{7'}$), 120.1 (**C**$_{5'}$), 120.1 (**C**$_{6'}$), 119.7 (**C**$_6$), 116.6 (**C**$_{3'}$), 112.6 (**C**$_{8'}$), 110.6 (**C**$_8$), 84.7 (**C**$_2$), 61.0 (**C**$_3$), 27.1 (**C**$_{14}$).
FTIR (thin film) cm^{-1}:	3394 (br-m), 1731 (w), 1679 (s), 1638 (m), 1607 (m), 1429 (m), 1315 (m), 742 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{22}H_{16}N_4O_3Na$ $[M+Na]^+$: 407.1115, found: 407.1127.
$[\alpha]_D^{25}$:	+125.8 (*c* = 0.08, MeOH).[39,40]
TLC (20% ethyl acetate in dichloromethane), R*f*:	0.52 (UV, CAM).

[39] Literature value: $[\alpha]_D^{16}$ = +115.3 (*c* = 0.6, MeOH), DeLorbe, J. E.; Jabri, S. Y.; Mennen, S. M.; Overman, L. E.; Zhang, F.-L. *J. Am. Chem. Soc.* **2011**, *133*, 6549.

[40] (a) Optical rotation measurement was conducted with crystalline (+)-gliocladin C (**4**). (b) As previously reported in ref. 39 the limited solubility of (+)-gliocladin C (**4**) in $CHCl_3$ (as well as CH_2Cl_2 or EtOAc) prevented an accurate measure of optical rotation. As a result, optical rotation was recorded in MeOH.

Table S3. Comparison of our ^{1}H NMR data for (+)-gliocladin C (4) with literature data:

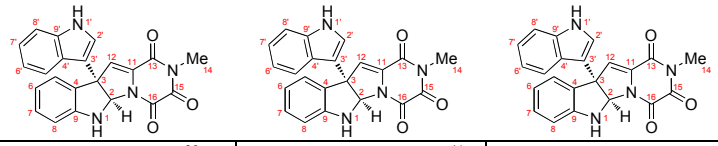




Assignment	**Usami's Report**[30] (+)-Gliocladin C (**4**) ^{1}H NMR,[31] 500 MHz, acetone-d_6, 27 °C	**Overman's Report**[41] (+)-Gliocladin C (**4**) ^{1}H NMR,[42] 600 MHz, acetone-d_6, 25 °C	**This Work** (+)-Gliocladin C (**4**) ^{1}H NMR, 600 MHz, acetone-d_6, 20 °C
N1	6.61 (br-d, J = 3.2, 1H)	6.61 (br-d, J = 1.9, 1H)	6.63 (br-s, 1H)
C2	6.24 (d, J = 3.2, 1H)	6.24 (d, J = 2.6, 1H)	6.23 (d, J = 2.5, 1H)
C3	—	—	—
C4	—	—	—
C5	7.18 (br-d, J = 7.3, 1H)	7.18 (br-d, J = 7.4, 1H)	7.17 (d, J = 7.4, 1H)
C6	6.72 (dddd, J = 1.1, 1.6, 7.3, 7.6, 1H)	6.72 (ddd, J = 1.0, 7.3, 7.4, 1H)	6.71 (app-dt, J = 0.6, 7.4, 1H)
C7	7.13 (br-dd, J = 7.6, 8.2, 1H)	7.13 (ddd, J = 1.1, 7.5, 8.7, 1H)	7.13 (app-dt, J = 1.1, 7.8, 1H)
C8	6.86 (br-d, J = 8.2, 1H)	6.86 (br-d, J = 7.9, 1H)	6.85 (d, J = 7.9, 1H)
C9	—	—	—
N10	—	—	—
C11	—	—	—
C12	6.96 (s, 1H)	6.96 (s, 1H)	6.96 (s, 1H)
C13	—	—	—
C14	3.25 (s, 3H)	3.26 (s, 3H)	3.25 (s, 3H)
C15	—	—	—
C16	—	—	—
N1'	10.3 (br-d, J = 1.6, 1H)	10.33 (br-s, 1H)	10.37 (br-s, 1H)
C2'	7.23 (d, J = 1.6, 1H)	7.23 (d, J = 2.6, 1H)	7.23 (d, J = 2.6, 1H)
C3'	—	—	—
C4'	—	—	—
C5'	7.33 (br-d, J = 8.2, 1H)	7.33 (dd, J = 0.7, 8.2, 1H)	7.32 (d, J = 8.0, 1H)
C6'	6.90 (ddd, J = 0.9, 7.1, 8.0, 1H)	6.90 (ddd, J = 0.8, 7.1, 8.0, 1H)	6.89 (app-dt, J = 0.6, 7.5, 1H)
C7'	7.10 (ddd, J = 1.1, 7.1, 8.2, 1H)	7.11 (ddd, J = 1.0, 7.1, 8.1, 1H)	7.10 (app-dt, J = 0.6, 7.7, 1H)
C8'	7.43 (br-d, J = 8.2, 1H)	7.43 (br-d, J = 8.2, 1H)	7.43 (d, J = 8.2, 1H)
C9'	—	—	—

[41] (a) Overman, L. E.; Shin, Y. *Org. Lett.* **2007**, *9*, 339. (b) DeLorbe, J. E.; Jabri, S. Y.; Mennen, S. M.; Overman, L. E.; Zhang, F.-L. *J. Am. Chem. Soc.* **2011**, *133*, 6549.

[42] NMR spectra were recorded at 25 °C on a Bruker Avance spectrometer, operating at 600 MHz.

Table S4. Comparison of our ^{13}C NMR data for (+)-gliocladin C (4) with literature data:



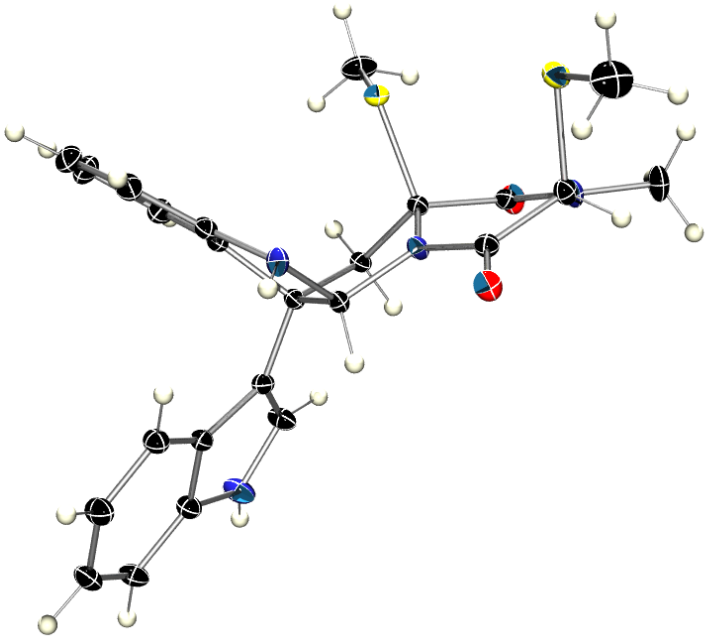
Assignment	Usami's Report[30] (+)-Gliocladin C (**4**) ^{13}C NMR,[31] 125 MHz, acetone-d_6, 27 °C	Overman's Report[41] (+)-Gliocladin C (**4**) ^{13}C NMR,[43] 125 MHz, acetone-d_6, 25 °C	This Work (+)-Gliocladin C (**4**) ^{13}C NMR, 150 MHz, acetone-d_6, 20 °C	Chemical Shift Difference Δδ = δ (this work) – δ (ref. 30)	Chemical Shift Difference Δδ = δ (this work) – δ (ref. 41a)
N1	—	—	—	—	—
C2	84.72	84.69	84.72	0.00	0.03
C3	61.00	60.97	60.99	-0.01	0.02
C4	131.12	131.11	131.10	-0.02	-0.01
C5	125.47	125.47	125.47	0.00	0.00
C6	119.66	119.65	119.66	0.00	0.01
C7	129.68	129.68	129.69	0.01	0.01
C8	110.59	110.58	110.60	0.01	0.02
C9	149.94	149.93	149.93	-0.01	0.00
N10	—	—	—	—	—
C11	133.08	133.08	133.06	-0.02	–0.02
C12	126.97	126.94	127.04	0.07	0.10
C13	158.62	158.62	158.03[44]	–0.59	–0.59
C14	27.10	27.09	27.10	0.00	0.01
C15	158.01	158.01	158.66[44]	0.65	0.65
C16	150.71	150.70	150.73	0.02	0.03
N1'	—	—	—	—	—
C2'	123.71	123.70	123.72	0.01	0.02
C3'	122.75	116.66[45]	116.63	–6.12	–0.03
C4'	123.55	126.29[46]	126.28	2.73	–0.01
C5'	119.71	120.11[46]	120.10	0.39	–0.01
C6'	119.71	120.13[46]	120.13	0.42	0.00
C7'	120.12	122.76[46]	122.75	2.63	–0.01
C8'	112.64	112.63	112.65	0.01	0.02
C9'	138.49	138.47	138.47	–0.02	0.00

[43] NMR spectra were recorded at 25 °C on a Bruker Avance spectrometer, operating at 125 MHz.
[44] Our assignment of these resonances are supported by key gHMBC signals (^{1}H, ^{13}C) in ppm: (6.96, 158.0), (3.25, 158.7).
[45] The small signal for the quaternary carbon C3' at 116.7 ppm, which is seen in the ^{13}C NMR spectrum of natural (+)-gliocladin C (**4**), was not reported in ref. 30. See ref. 41a for details.
[46] Assignments reported in ref. 41 (confirmed by HMQC and HMBC) for signals at 122.7 and 120.11/120.13 ppm should be changed to C7' and C5'/C6'.

Crystal structure of (+)-gliocladin B (1).

Structural parameters for (+)-gliocladin B (**1**) are freely available from the Cambridge Crystallographic Data Center under CCDC 866659.

View 1:



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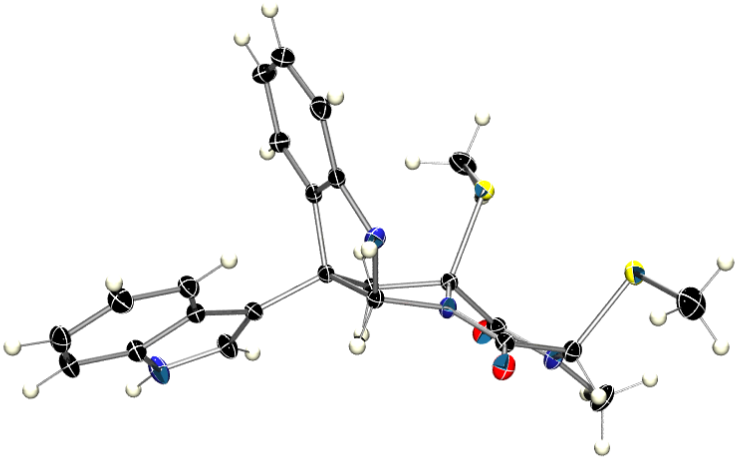


Table S5. Crystal data and structure refinement for (+)-gliocladin B (**1**).

Identification code	x8_11110	
Empirical formula	$C_{24}H_{24}N_4O_2S_2$	
Formula weight	464.59	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 8.5206(13) Å	α = 90°.
	b = 13.968(2) Å	β = 90°.
	c = 18.439(3) Å	γ = 90°.
Volume	2194.5(6) $Å^3$	
Z	4	
Density (calculated)	1.406 Mg/m^3	
Absorption coefficient	0.273 mm^{-1}	
F(000)	976	
Crystal size	0.25 × 0.15 × 0.15 mm^3	
Theta range for data collection	1.83 to 29.80°.	
Index ranges	-11<=h<=11, -19<=k<=19, -25<=l<=25	
Reflections collected	28691	
Independent reflections	6251 [R(int) = 0.0349]	
Completeness to theta = 29.80°	100.0 %	
Absorption correction	None	
Max. and min. transmission	0.9602 and 0.9349	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6251 / 2 / 298	
Goodness-of-fit on F^2	1.059	
Final R indices [I>2sigma(I)]	R1 = 0.0320, wR2 = 0.0770	
R indices (all data)	R1 = 0.0356, wR2 = 0.0791	
Absolute structure parameter	0.00(5)	
Largest diff. peak and hole	0.317 and -0.208 e.$Å^{-3}$	

Table S6. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for (+)-gliocladin B (**1**). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	8847(1)	2806(1)	1341(1)	15(1)
S(2)	11188(1)	4233(1)	264(1)	19(1)
O(1)	12292(1)	1680(1)	1728(1)	19(1)
O(2)	11757(1)	5430(1)	1855(1)	18(1)
N(1)	8498(2)	4864(1)	2626(1)	15(1)
C(2)	9889(2)	4306(1)	2787(1)	12(1)
C(3)	9333(2)	3346(1)	3151(1)	12(1)
C(4)	7564(2)	3401(1)	3019(1)	13(1)
C(5)	6417(2)	2731(1)	3166(1)	17(1)
C(6)	4839(2)	3007(1)	3102(1)	22(1)
C(7)	4459(2)	3942(1)	2900(1)	22(1)
C(8)	5603(2)	4608(1)	2728(1)	18(1)
C(9)	7167(2)	4321(1)	2780(1)	14(1)
N(10)	10695(2)	3978(1)	2122(1)	13(1)
C(11)	10510(2)	2960(1)	1980(1)	12(1)
C(12)	10202(2)	2547(1)	2737(1)	12(1)
C(13)	11966(2)	2530(1)	1628(1)	14(1)
N(14)	12838(2)	3118(1)	1209(1)	16(1)
C(15)	12427(2)	4115(1)	1082(1)	15(1)
C(16)	11597(2)	4577(1)	1720(1)	14(1)
C(17)	14215(2)	2744(1)	824(1)	23(1)
C(18)	11765(2)	5400(1)	-55(1)	32(1)
C(19)	8485(2)	1536(1)	1390(1)	23(1)
N(1')	10366(2)	2765(1)	5065(1)	21(1)
C(2')	10414(2)	2586(1)	4330(1)	18(1)
C(3')	9632(2)	3296(1)	3960(1)	13(1)
C(4')	9060(2)	3957(1)	4503(1)	14(1)
C(5')	8225(2)	4830(1)	4475(1)	17(1)
C(6')	7906(2)	5306(1)	5115(1)	21(1)
C(7')	8377(2)	4932(1)	5793(1)	21(1)
C(8')	9209(2)	4087(1)	5836(1)	20(1)
C(9')	9544(2)	3603(1)	5187(1)	16(1)

Table S7. Bond lengths [Å] and angles [°] for (+)-gliocladin B (**1**).

S(1)-C(19)	1.8026(16)
S(1)-C(11)	1.8553(15)
S(2)-C(18)	1.8019(19)
S(2)-C(15)	1.8481(16)
O(1)-C(13)	1.2332(19)
O(2)-C(16)	1.2255(18)
N(1)-C(9)	1.3932(19)
N(1)-C(2)	1.4488(18)
C(2)-N(10)	1.4771(18)
C(2)-C(3)	1.573(2)
C(3)-C(3')	1.515(2)
C(3)-C(4)	1.529(2)
C(3)-C(12)	1.5415(19)
C(4)-C(5)	1.380(2)
C(4)-C(9)	1.399(2)
C(5)-C(6)	1.403(2)
C(6)-C(7)	1.395(2)
C(7)-C(8)	1.385(2)
C(8)-C(9)	1.395(2)
N(10)-C(16)	1.3570(19)
N(10)-C(11)	1.4546(18)
C(11)-C(13)	1.524(2)
C(11)-C(12)	1.534(2)
C(13)-N(14)	1.3499(19)
N(14)-C(15)	1.4545(19)
N(14)-C(17)	1.4680(19)
C(15)-C(16)	1.516(2)
N(1')-C(2')	1.379(2)
N(1')-C(9')	1.383(2)
C(2')-C(3')	1.376(2)
C(3')-C(4')	1.448(2)
C(4')-C(5')	1.412(2)
C(4')-C(9')	1.417(2)
C(5')-C(6')	1.381(2)
C(6')-C(7')	1.412(2)
C(7')-C(8')	1.380(2)
C(8')-C(9')	1.404(2)
C(19)-S(1)-C(11)	102.32(7)
C(18)-S(2)-C(15)	101.00(8)
C(9)-N(1)-C(2)	109.34(12)
N(1)-C(2)-N(10)	112.14(12)
N(1)-C(2)-C(3)	107.41(11)
N(10)-C(2)-C(3)	103.29(11)
C(3')-C(3)-C(4)	108.98(12)
C(3')-C(3)-C(12)	111.89(12)
C(4)-C(3)-C(12)	115.53(12)
C(3')-C(3)-C(2)	114.15(12)
C(4)-C(3)-C(2)	100.74(11)
C(12)-C(3)-C(2)	105.15(11)
C(5)-C(4)-C(9)	120.89(13)
C(5)-C(4)-C(3)	129.28(13)
C(9)-C(4)-C(3)	109.51(12)
C(4)-C(5)-C(6)	118.37(14)
C(7)-C(6)-C(5)	120.15(15)
C(8)-C(7)-C(6)	121.75(15)
C(7)-C(8)-C(9)	117.61(15)
N(1)-C(9)-C(8)	127.34(14)
N(1)-C(9)-C(4)	111.57(13)
C(8)-C(9)-C(4)	121.08(14)
C(16)-N(10)-C(11)	124.37(12)
C(16)-N(10)-C(2)	121.77(12)
C(11)-N(10)-C(2)	113.74(11)
N(10)-C(11)-C(13)	112.02(12)
N(10)-C(11)-C(12)	102.83(11)
C(13)-C(11)-C(12)	112.28(12)
N(10)-C(11)-S(1)	108.11(10)
C(13)-C(11)-S(1)	107.77(10)
C(12)-C(11)-S(1)	113.78(10)
C(11)-C(12)-C(3)	105.09(11)
O(1)-C(13)-N(14)	123.23(14)
O(1)-C(13)-C(11)	119.94(13)
N(14)-C(13)-C(11)	116.83(13)
C(13)-N(14)-C(15)	122.84(12)
C(13)-N(14)-C(17)	119.95(13)
C(15)-N(14)-C(17)	117.10(13)
N(14)-C(15)-C(16)	113.24(12)
N(14)-C(15)-S(2)	110.77(10)
C(16)-C(15)-S(2)	109.16(10)
O(2)-C(16)-N(10)	123.40(14)
O(2)-C(16)-C(15)	121.36(13)
N(10)-C(16)-C(15)	115.24(12)
C(2')-N(1')-C(9')	109.18(13)
C(3')-C(2')-N(1')	110.04(13)
C(2')-C(3')-C(4')	106.26(13)
C(2')-C(3')-C(3)	127.10(13)
C(4')-C(3')-C(3)	126.53(13)
C(5')-C(4')-C(9')	118.75(13)
C(5')-C(4')-C(3')	134.05(14)
C(9')-C(4')-C(3')	107.16(13)
C(6')-C(5')-C(4')	118.90(14)
C(5')-C(6')-C(7')	121.44(15)
C(8')-C(7')-C(6')	120.96(14)
C(7')-C(8')-C(9')	117.82(14)
N(1')-C(9')-C(8')	130.52(14)
N(1')-C(9')-C(4')	107.36(13)
C(8')-C(9')-C(4')	122.10(14)

Symmetry transformations used to generate equivalent atoms.

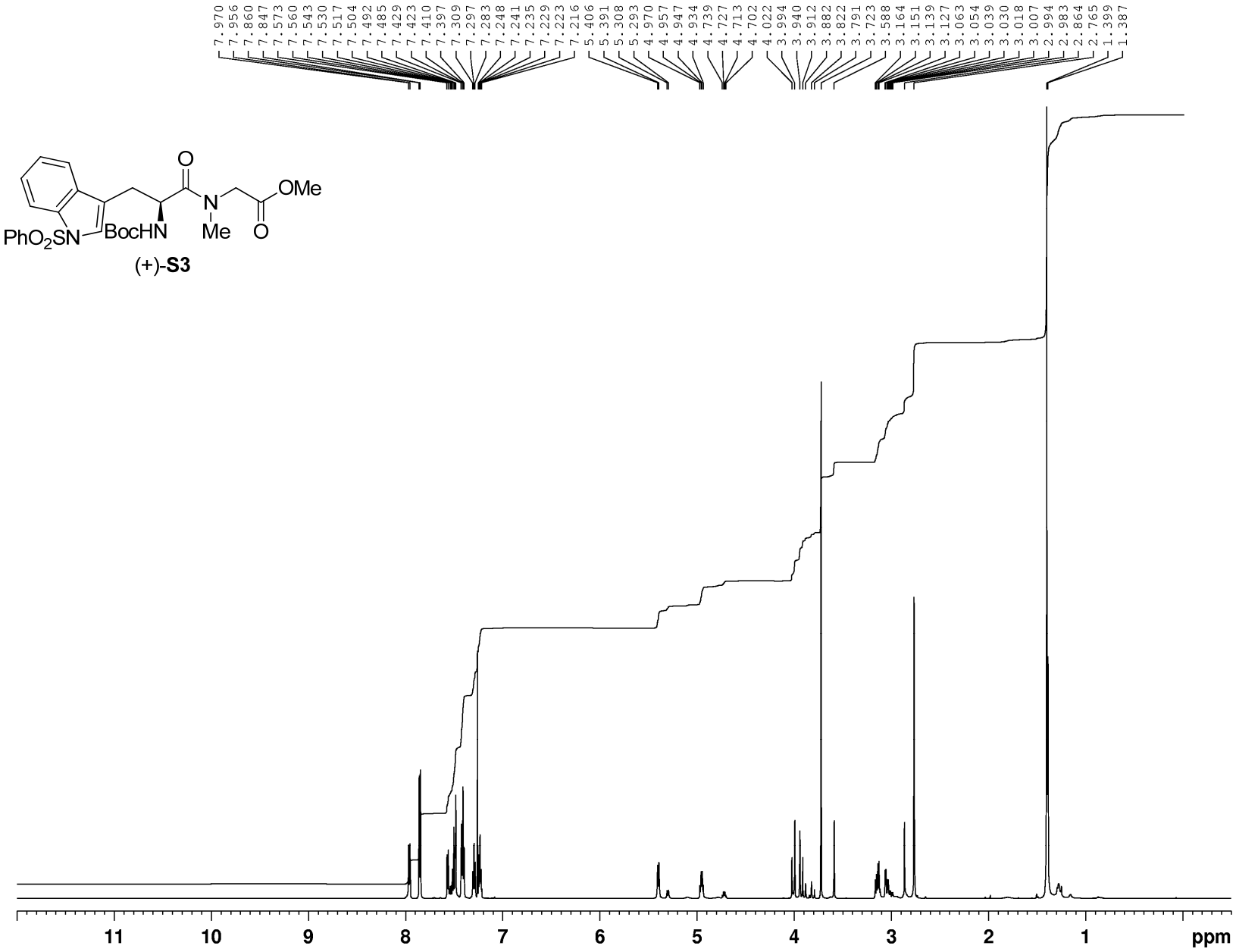
Table S8. Anisotropic displacement parameters ($Å^2 \times 10^3$) for (+)-gliocladin B (**1**). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

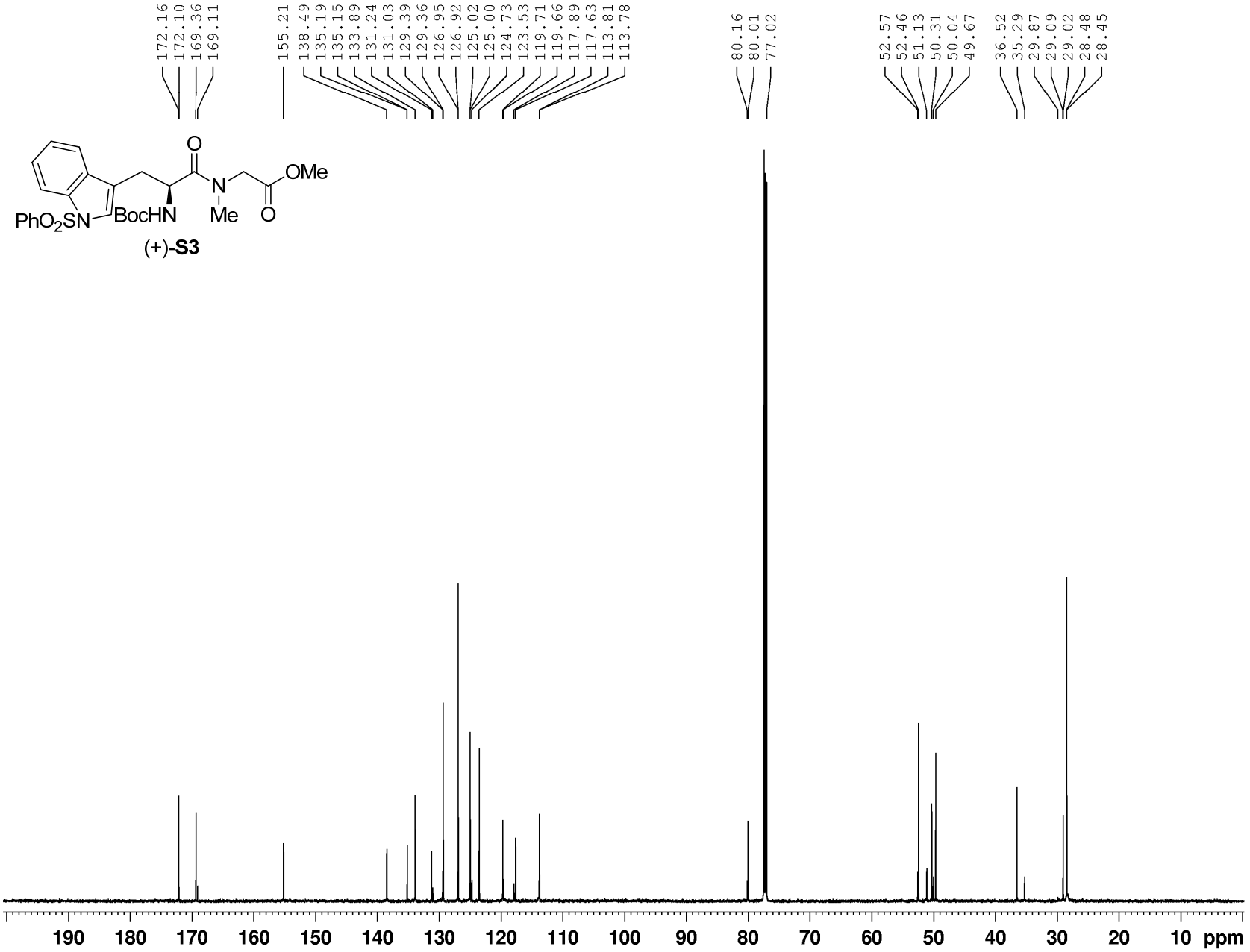
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	16(1)	15(1)	13(1)	0(1)	-2(1)	-1(1)
S(2)	22(1)	22(1)	14(1)	2(1)	0(1)	-3(1)
O(1)	20(1)	13(1)	22(1)	0(1)	4(1)	2(1)
O(2)	22(1)	12(1)	20(1)	0(1)	4(1)	-2(1)
N(1)	14(1)	14(1)	17(1)	1(1)	3(1)	2(1)
C(2)	13(1)	12(1)	11(1)	-1(1)	2(1)	0(1)
C(3)	12(1)	13(1)	10(1)	0(1)	0(1)	1(1)
C(4)	14(1)	16(1)	10(1)	0(1)	0(1)	1(1)
C(5)	16(1)	19(1)	16(1)	2(1)	0(1)	-1(1)
C(6)	14(1)	30(1)	23(1)	4(1)	0(1)	-4(1)
C(7)	14(1)	33(1)	18(1)	3(1)	-3(1)	4(1)
C(8)	19(1)	22(1)	15(1)	3(1)	-1(1)	6(1)
C(9)	15(1)	18(1)	10(1)	0(1)	0(1)	1(1)
N(10)	15(1)	11(1)	12(1)	-2(1)	2(1)	0(1)
C(11)	13(1)	12(1)	11(1)	-2(1)	0(1)	0(1)
C(12)	14(1)	13(1)	10(1)	0(1)	0(1)	1(1)
C(13)	14(1)	15(1)	13(1)	-3(1)	-1(1)	0(1)
N(14)	16(1)	14(1)	17(1)	-1(1)	5(1)	2(1)
C(15)	17(1)	14(1)	15(1)	0(1)	3(1)	-2(1)
C(16)	14(1)	15(1)	14(1)	1(1)	-1(1)	0(1)
C(17)	19(1)	21(1)	28(1)	-1(1)	11(1)	3(1)
C(18)	41(1)	24(1)	30(1)	11(1)	-4(1)	-6(1)
C(19)	29(1)	16(1)	25(1)	-1(1)	-8(1)	-6(1)
N(1')	31(1)	19(1)	13(1)	2(1)	-4(1)	7(1)
C(2')	24(1)	16(1)	13(1)	-2(1)	-2(1)	4(1)
C(3')	13(1)	14(1)	12(1)	0(1)	-1(1)	-1(1)
C(4')	14(1)	16(1)	12(1)	0(1)	0(1)	-1(1)
C(5')	18(1)	19(1)	14(1)	0(1)	-1(1)	3(1)
C(6')	21(1)	21(1)	20(1)	-4(1)	-2(1)	6(1)
C(7')	25(1)	24(1)	15(1)	-6(1)	1(1)	2(1)
C(8')	26(1)	23(1)	11(1)	0(1)	-3(1)	0(1)
C(9')	18(1)	17(1)	14(1)	0(1)	-1(1)	1(1)

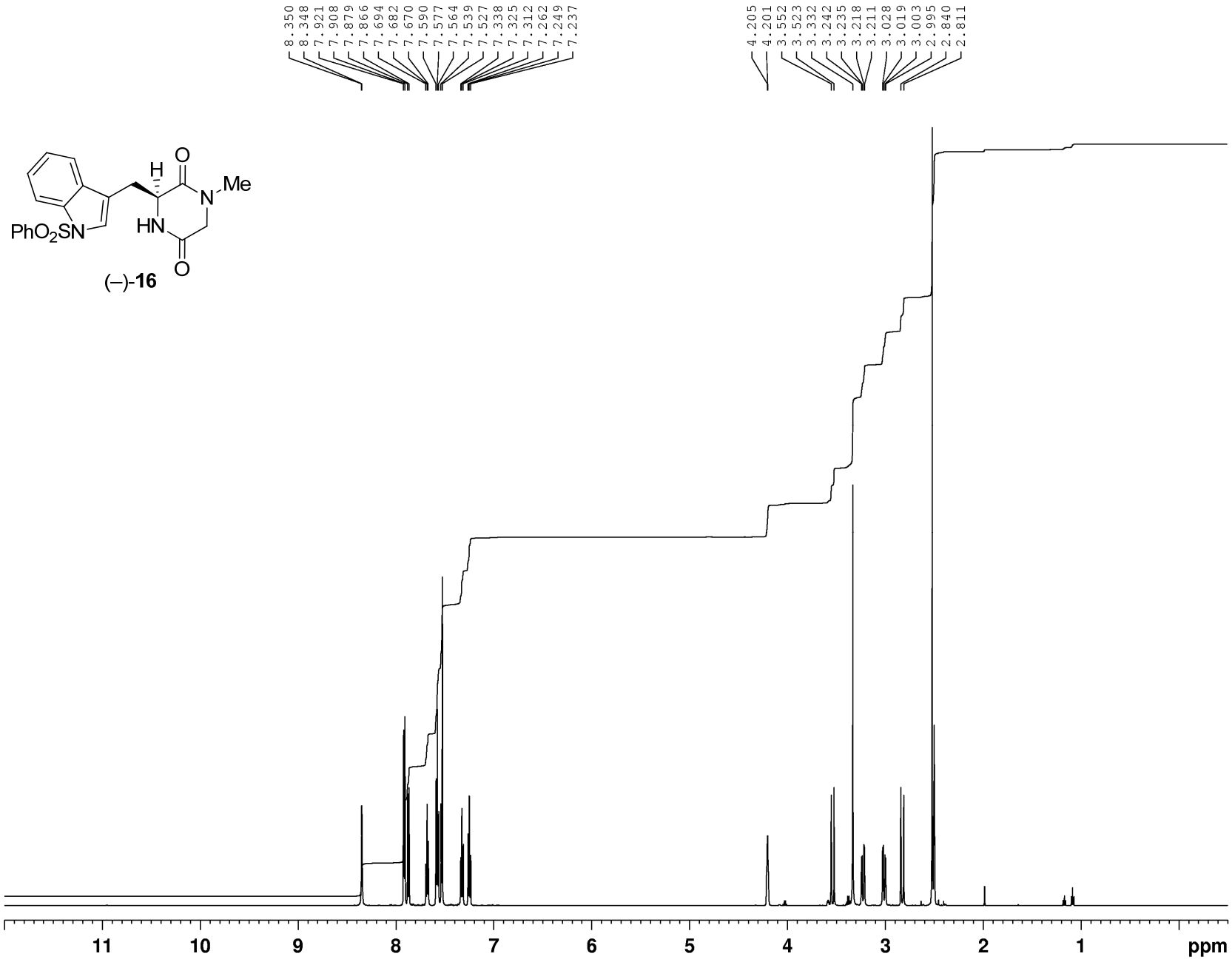
Table S9. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (+)-gliocladin B (**1**).

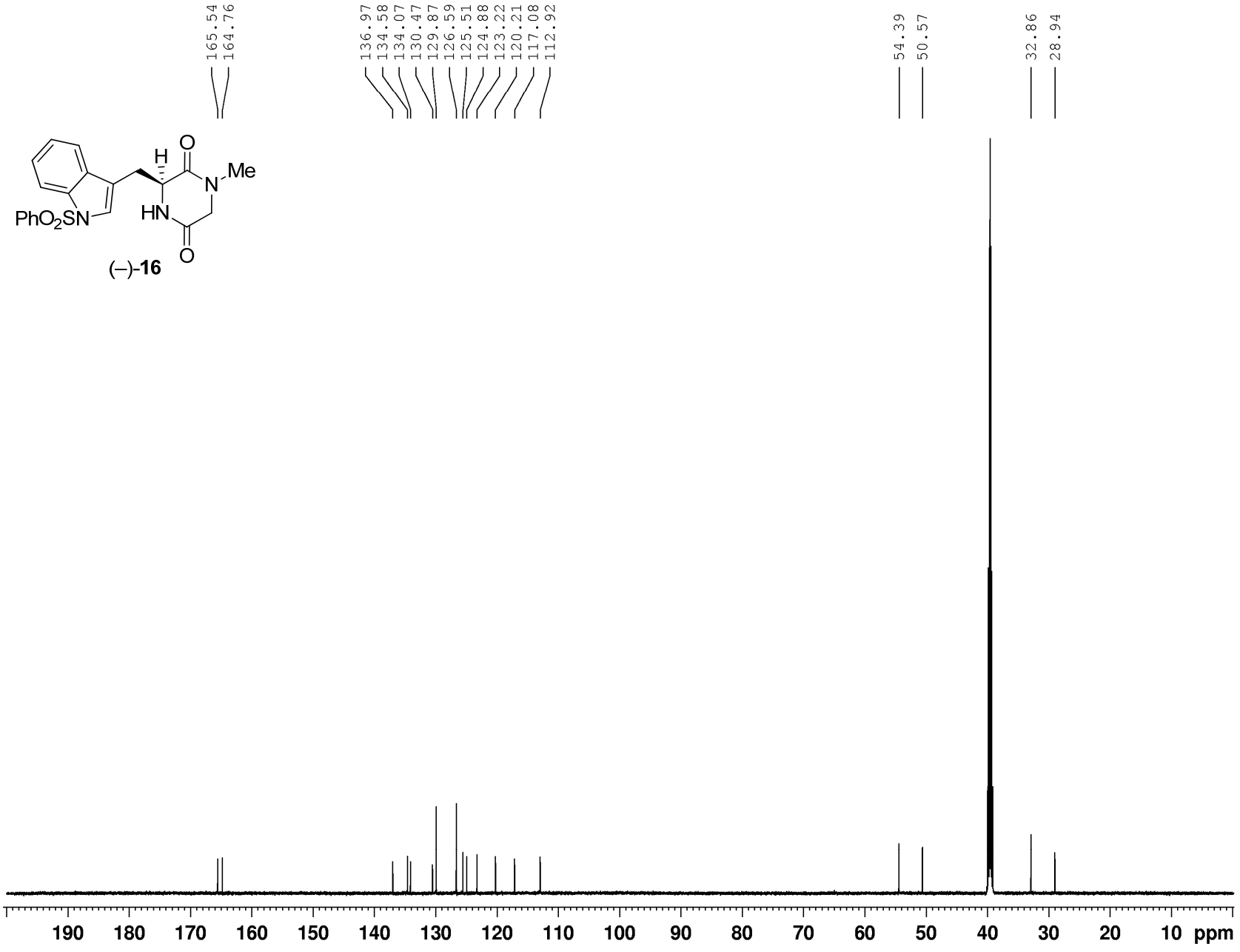
	x	y	z	U(eq)
H(1N)	8490(20)	5478(11)	2734(10)	18
H(2)	10620	4667	3111	15
H(5)	6688	2098	3307	21
H(6)	4029	2557	3196	27
H(7)	3386	4126	2881	26
H(8)	5333	5238	2580	22
H(12A)	11201	2384	2982	15
H(12B)	9546	1963	2706	15
H(15)	13421	4477	994	18
H(17A)	14296	2052	906	34
H(17B)	15164	3060	1006	34
H(17C)	14105	2869	304	34
H(18A)	11641	5868	337	48
H(18B)	11103	5585	-466	48
H(18C)	12866	5383	-209	48
H(19A)	9455	1188	1281	34
H(19B)	7676	1361	1037	34
H(19C)	8126	1369	1879	34
H(1'N)	10720(20)	2393(13)	5390(10)	25
H(2')	10915	2052	4111	21
H(5')	7888	5086	4024	20
H(6')	7357	5898	5099	25
H(7')	8117	5267	6225	25
H(8')	9545	3840	6291	24

Copies of ^{1}H, ^{13}C and ^{19}F NMR.

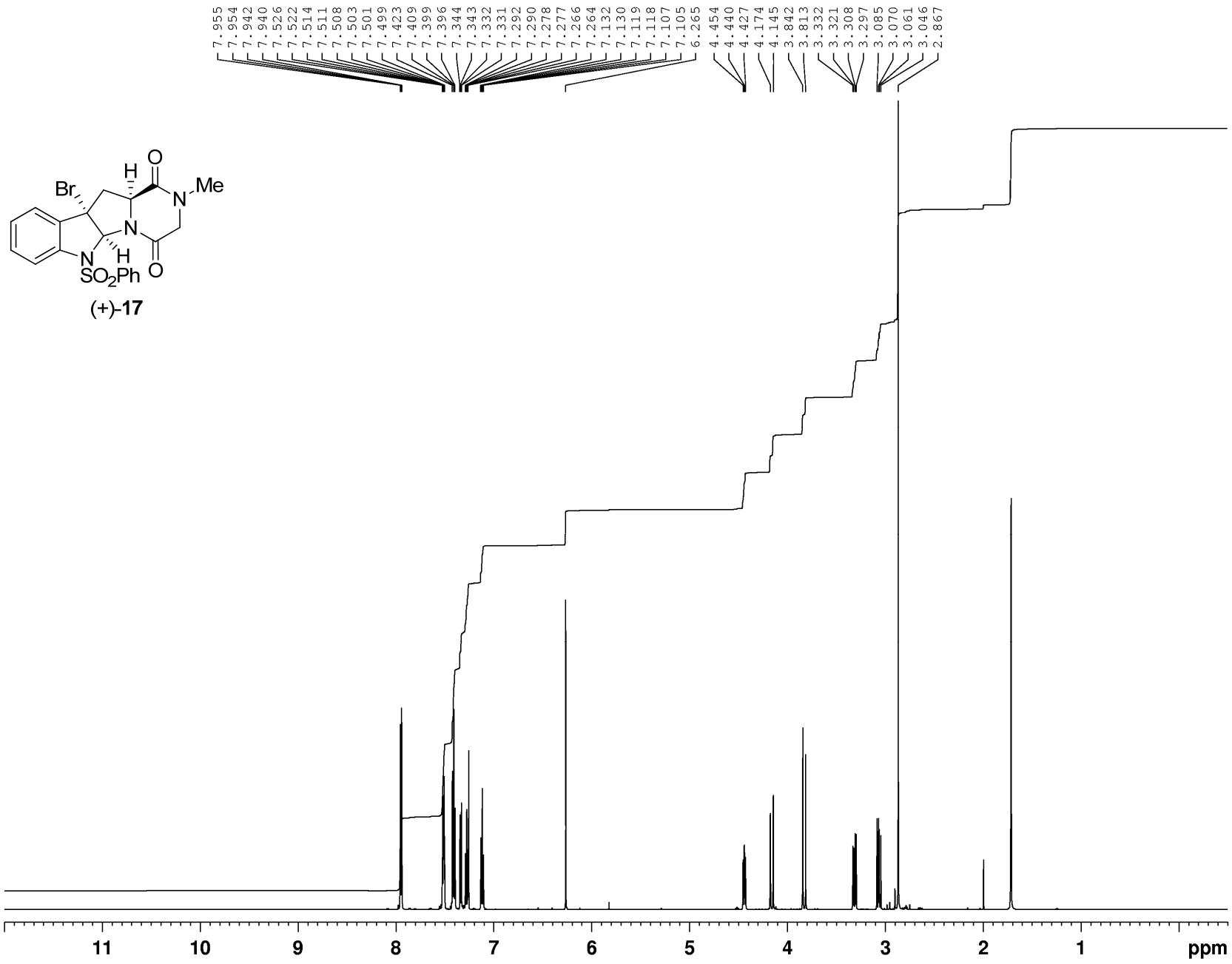


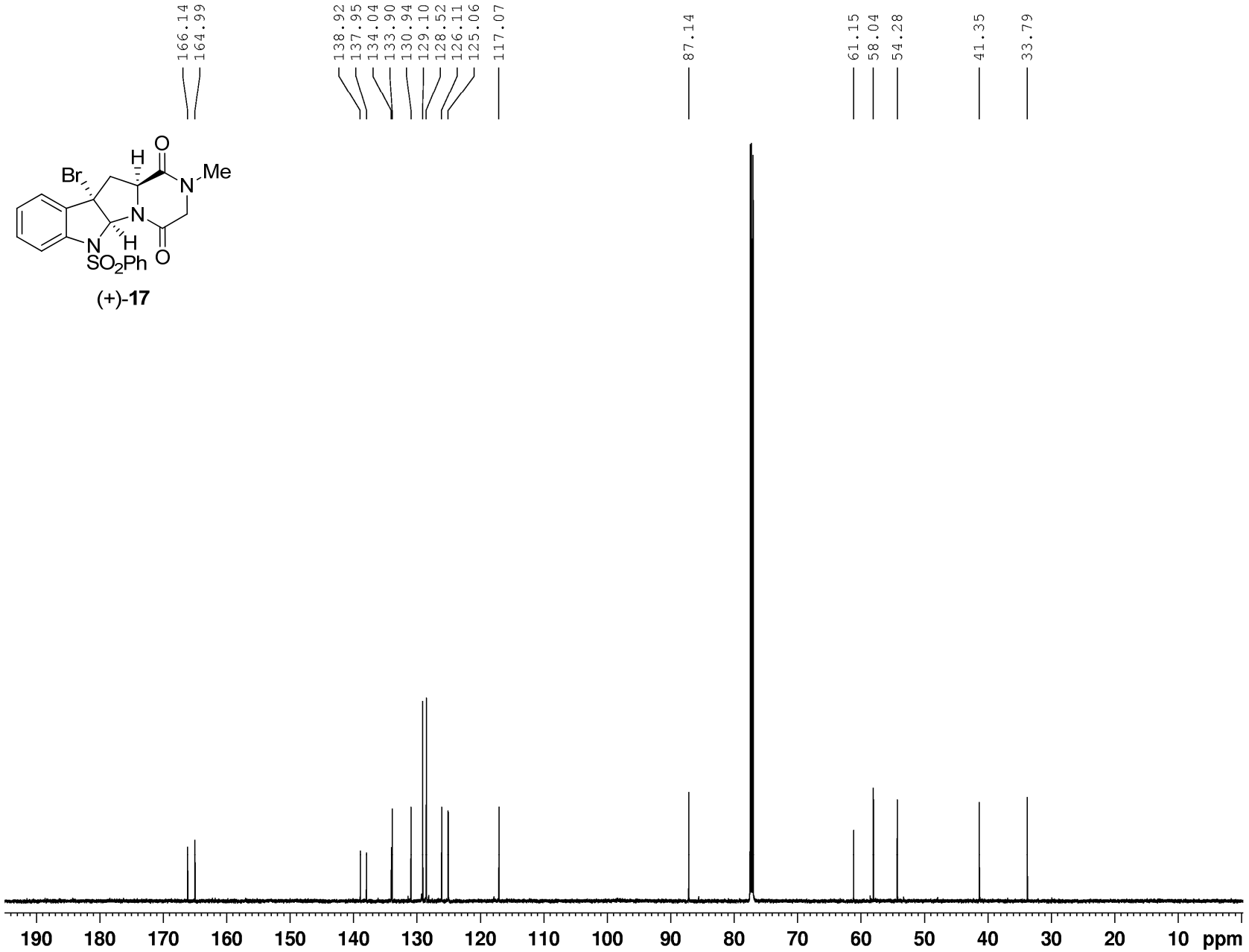




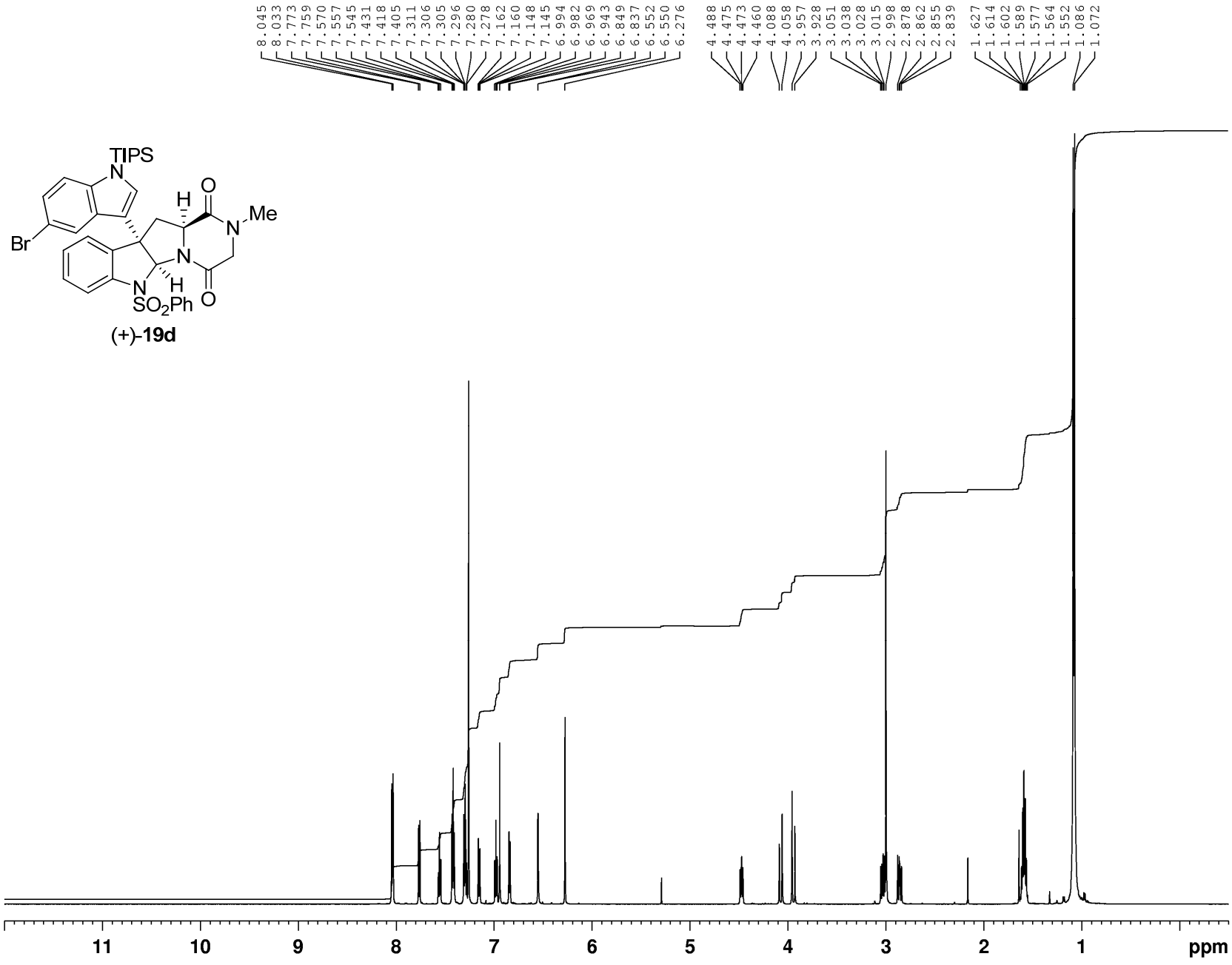


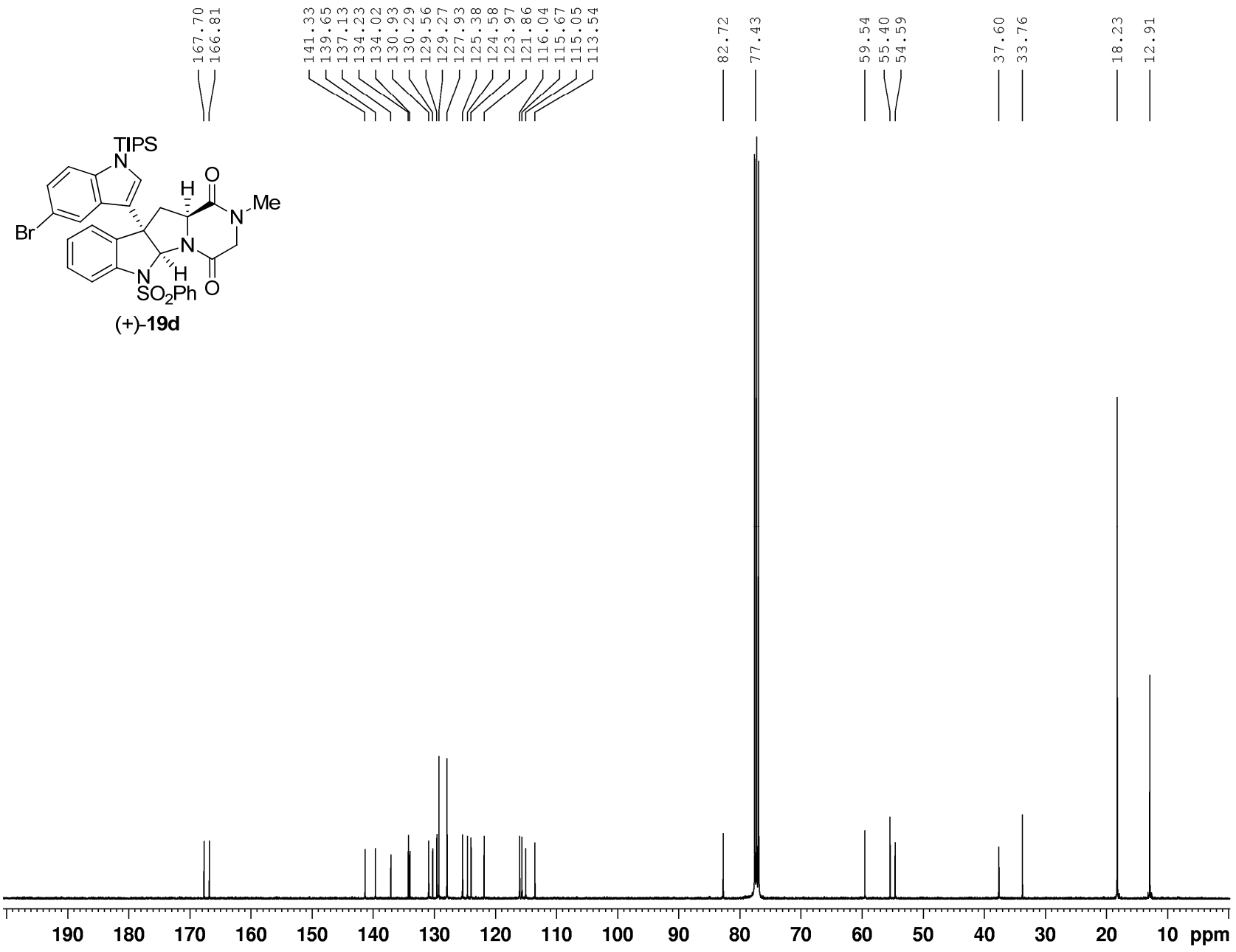
(–)-**16**

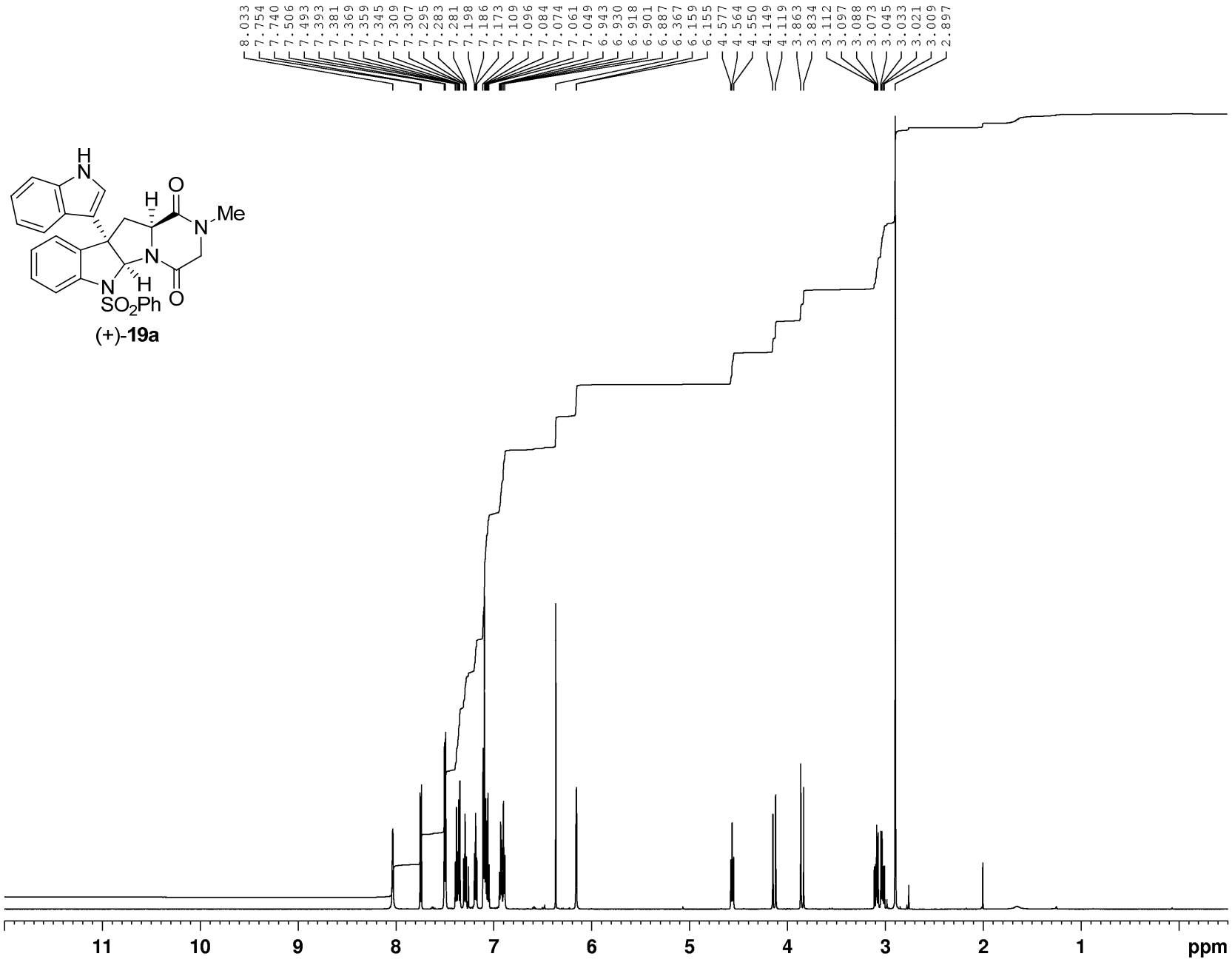


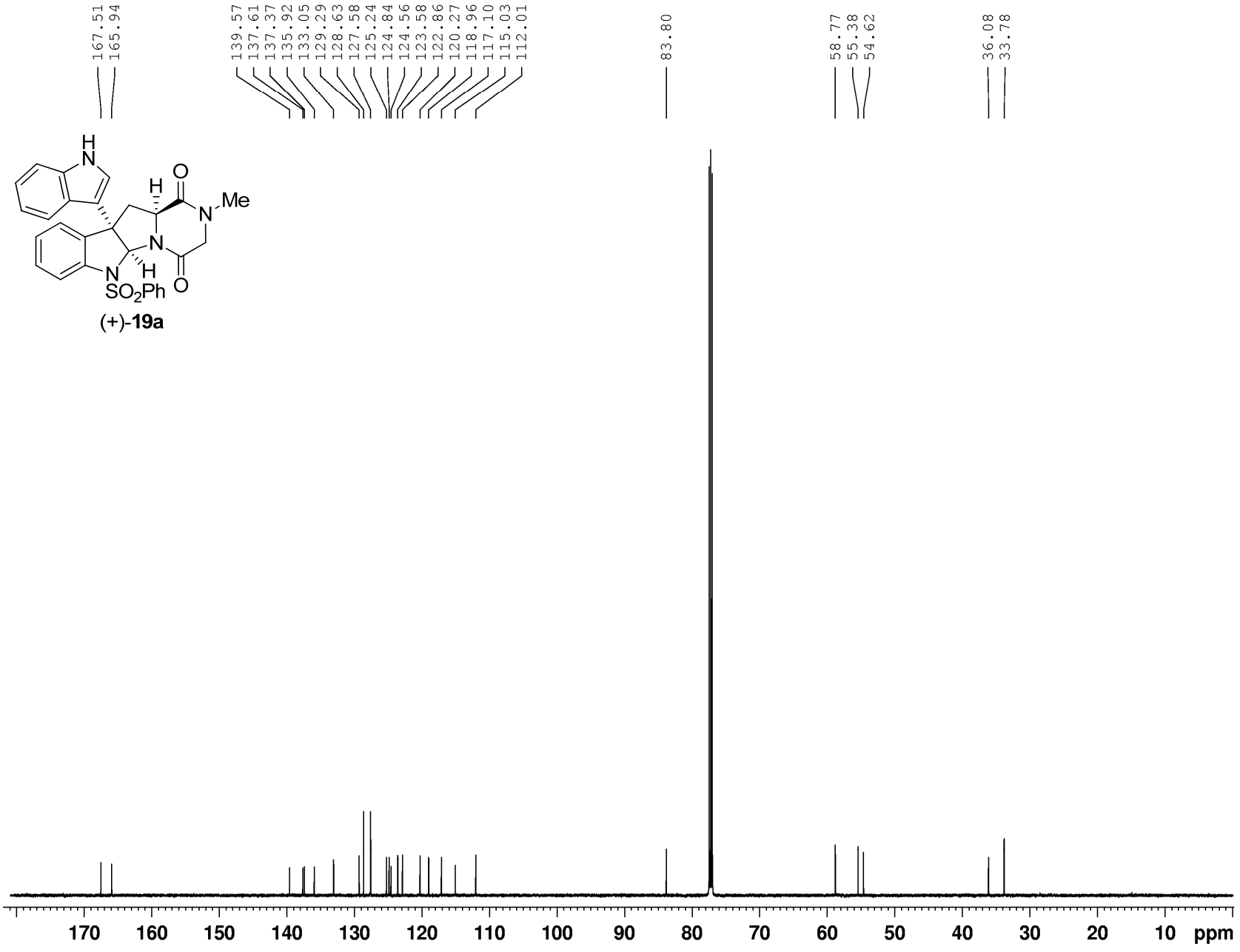


(+)-**17**

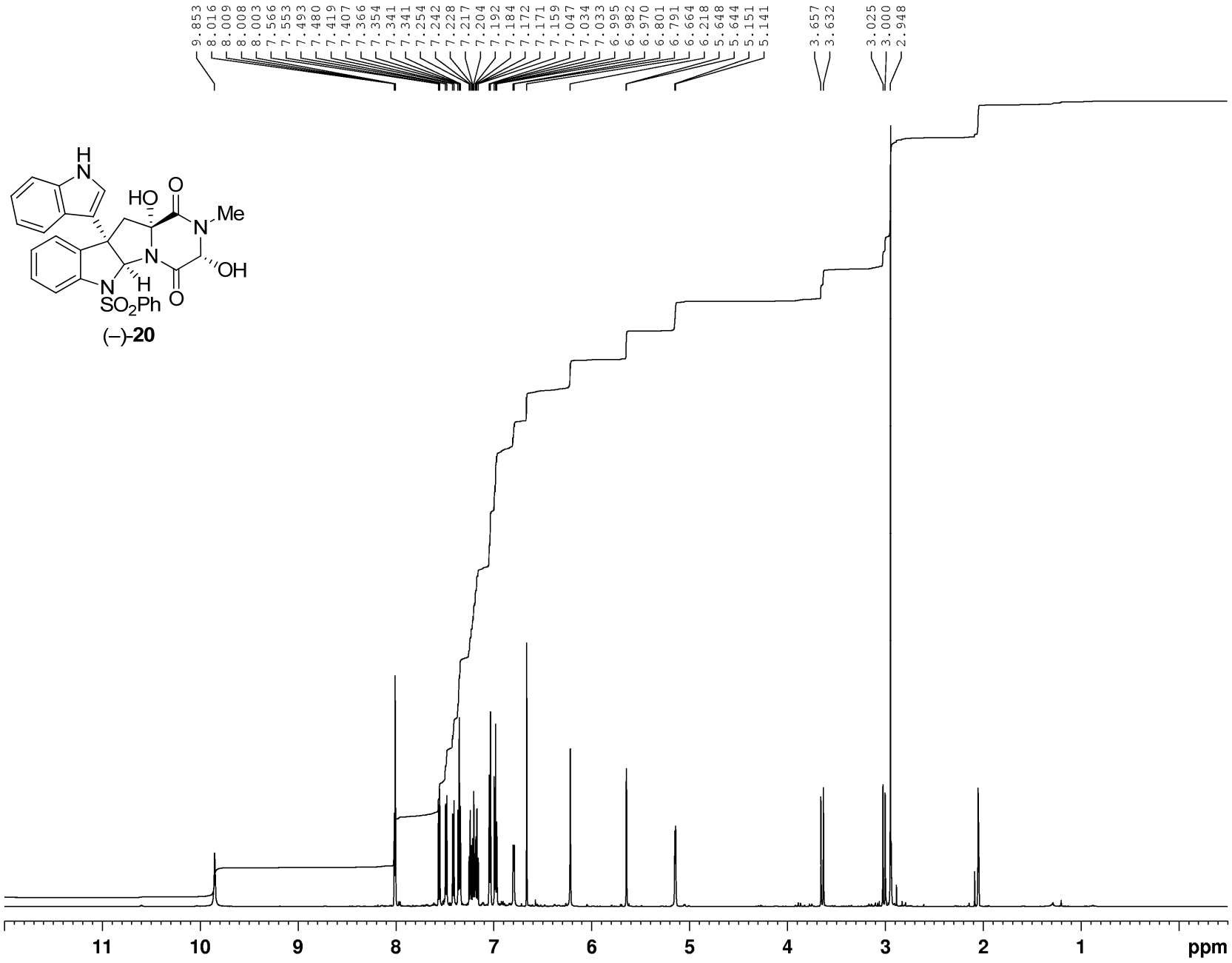


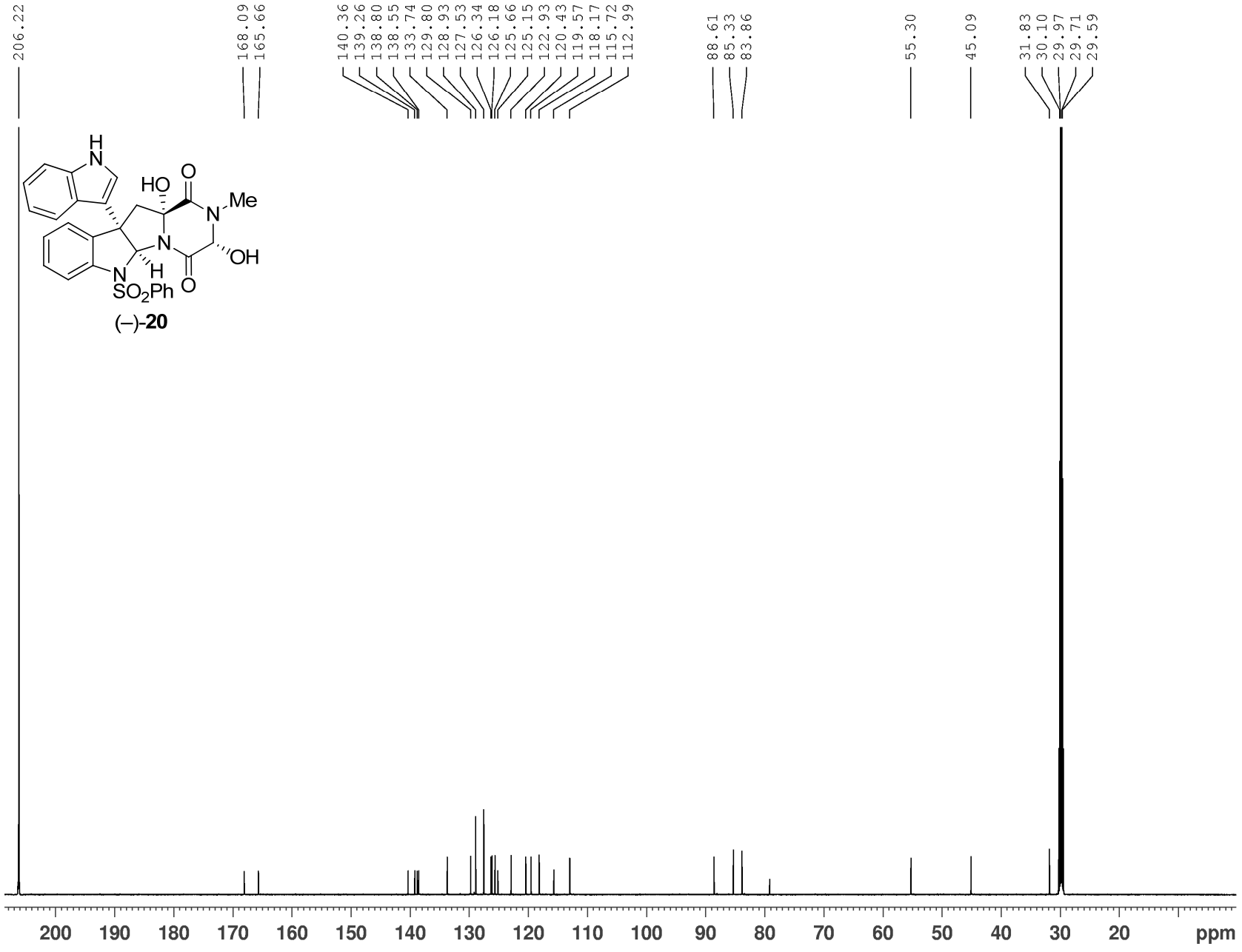


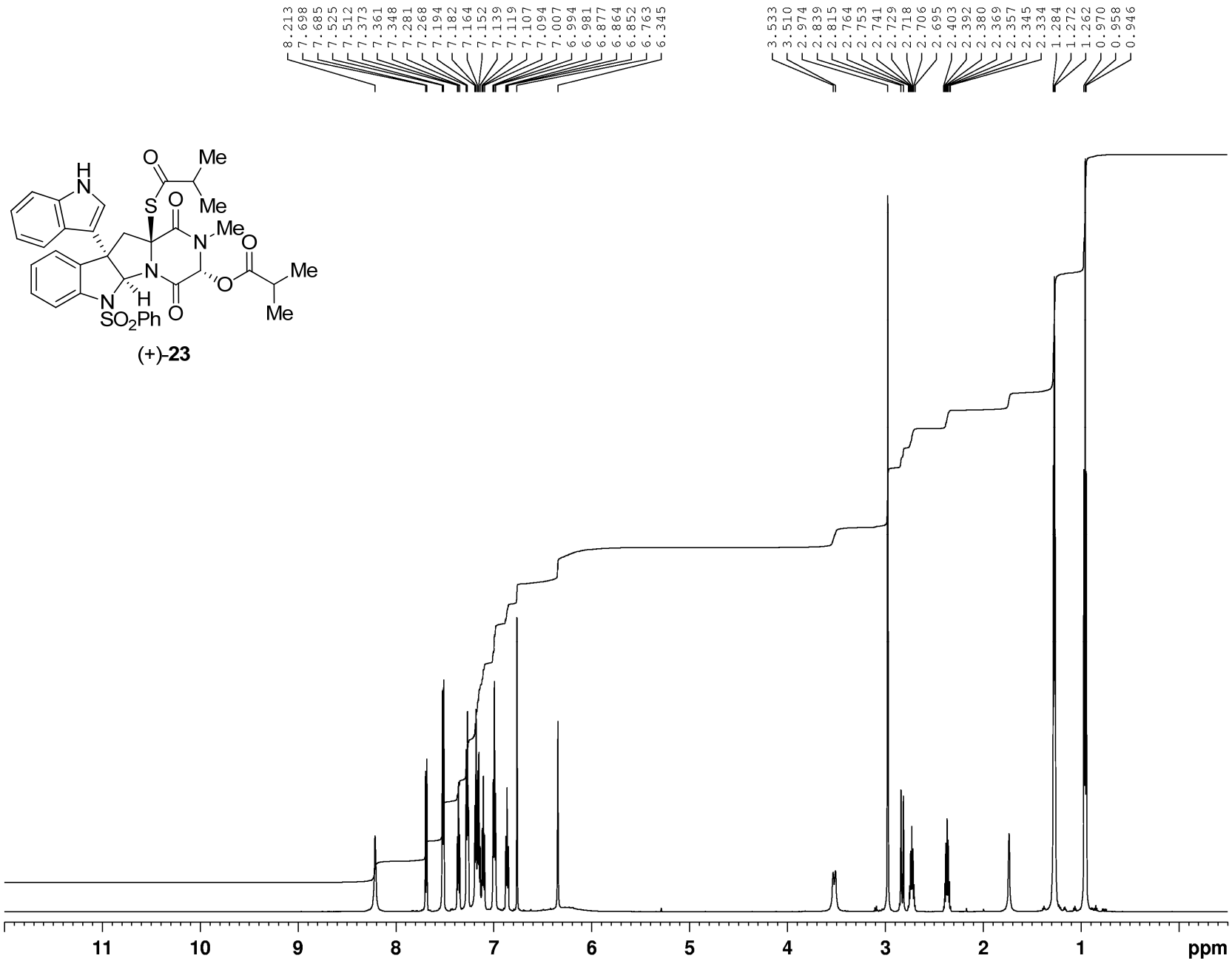


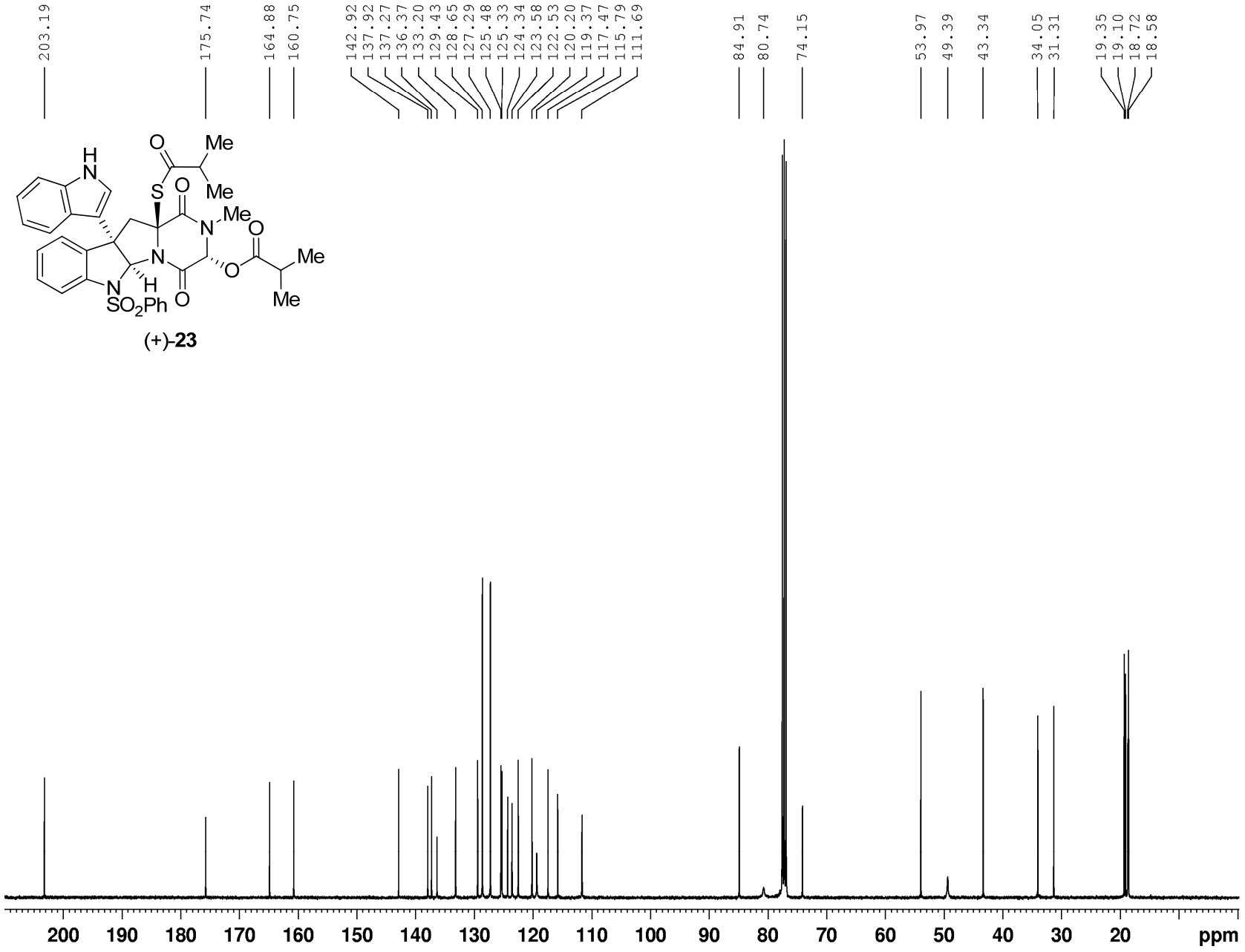


(+)-**19a**

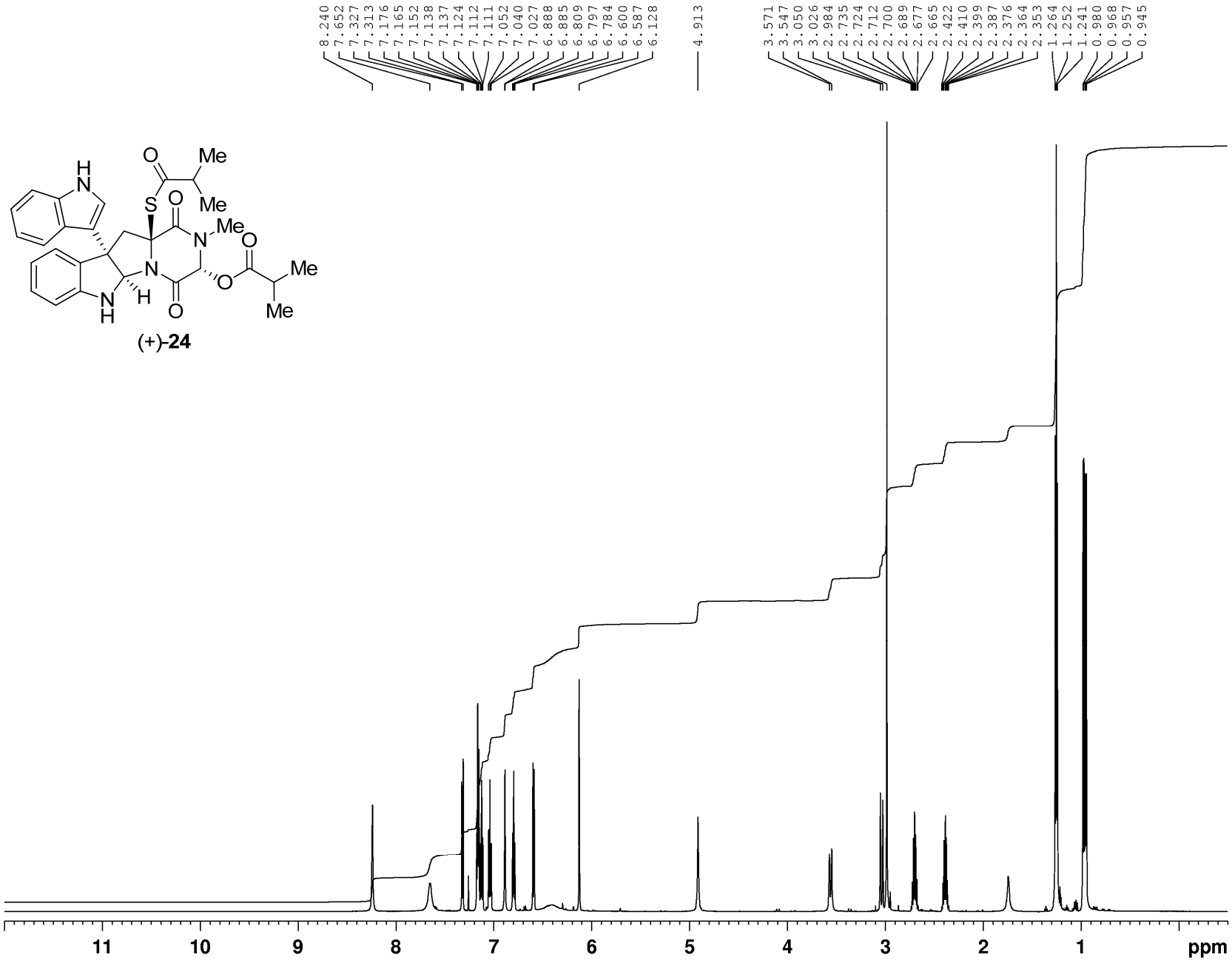




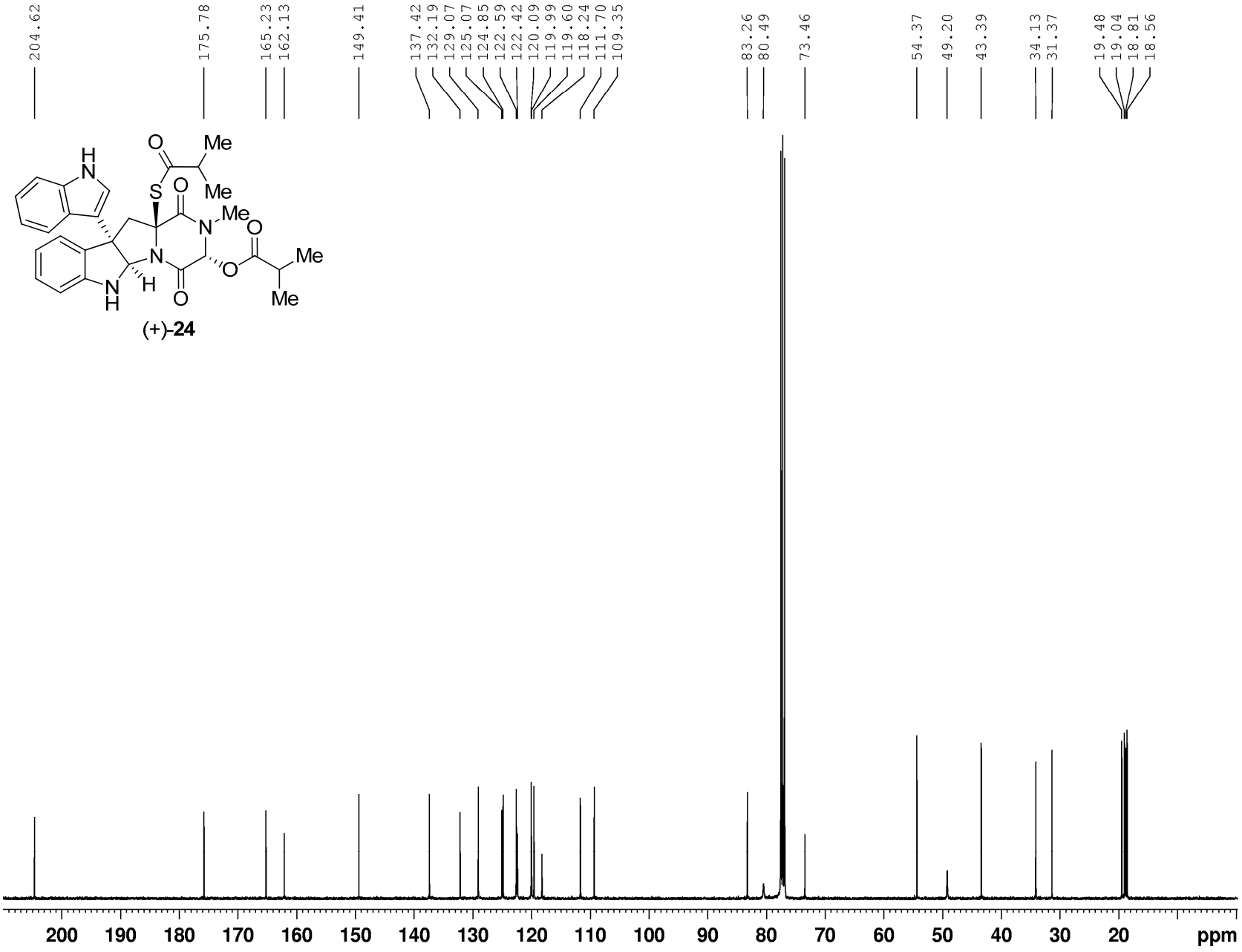


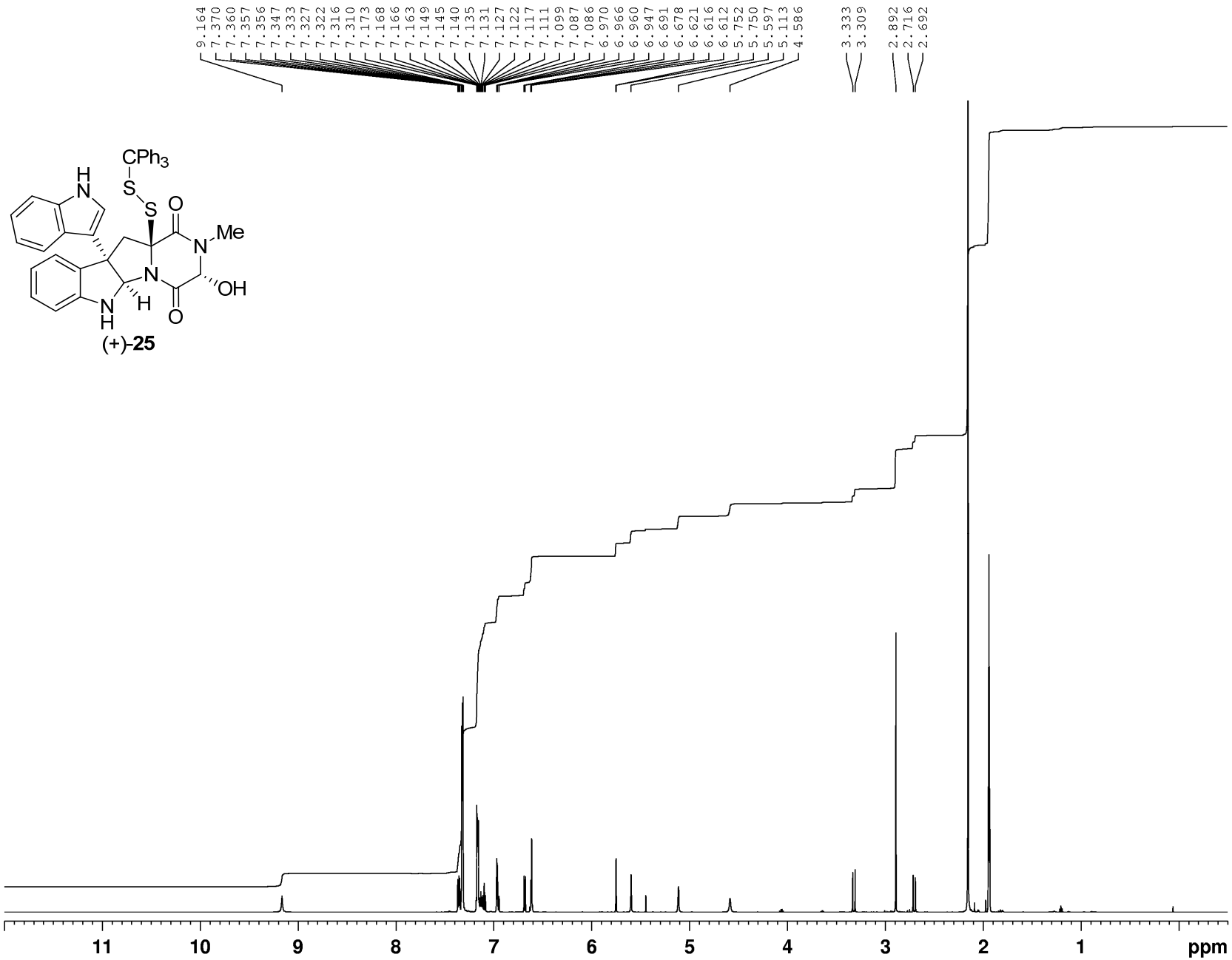


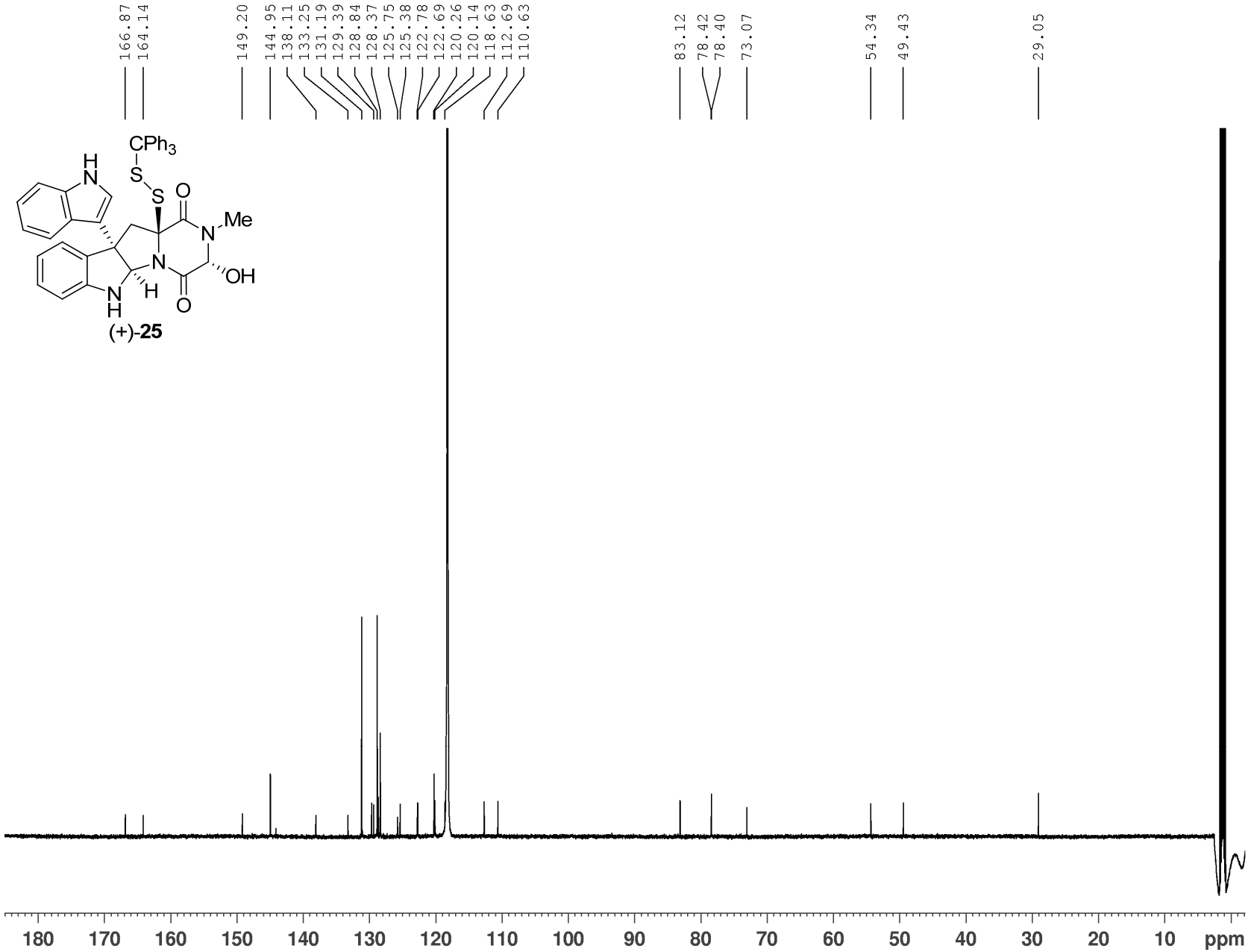
(+)-**23**

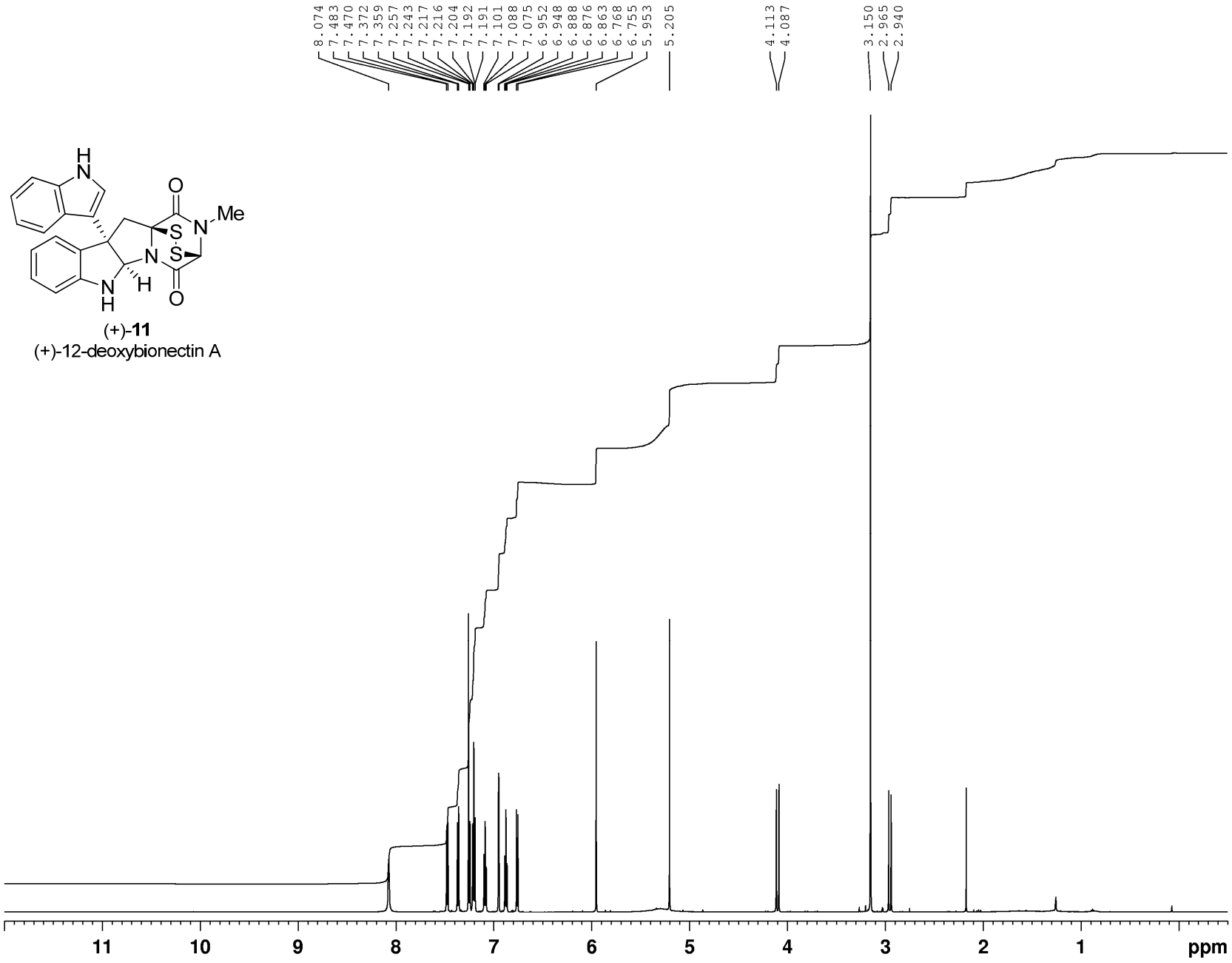


(+)-**24**









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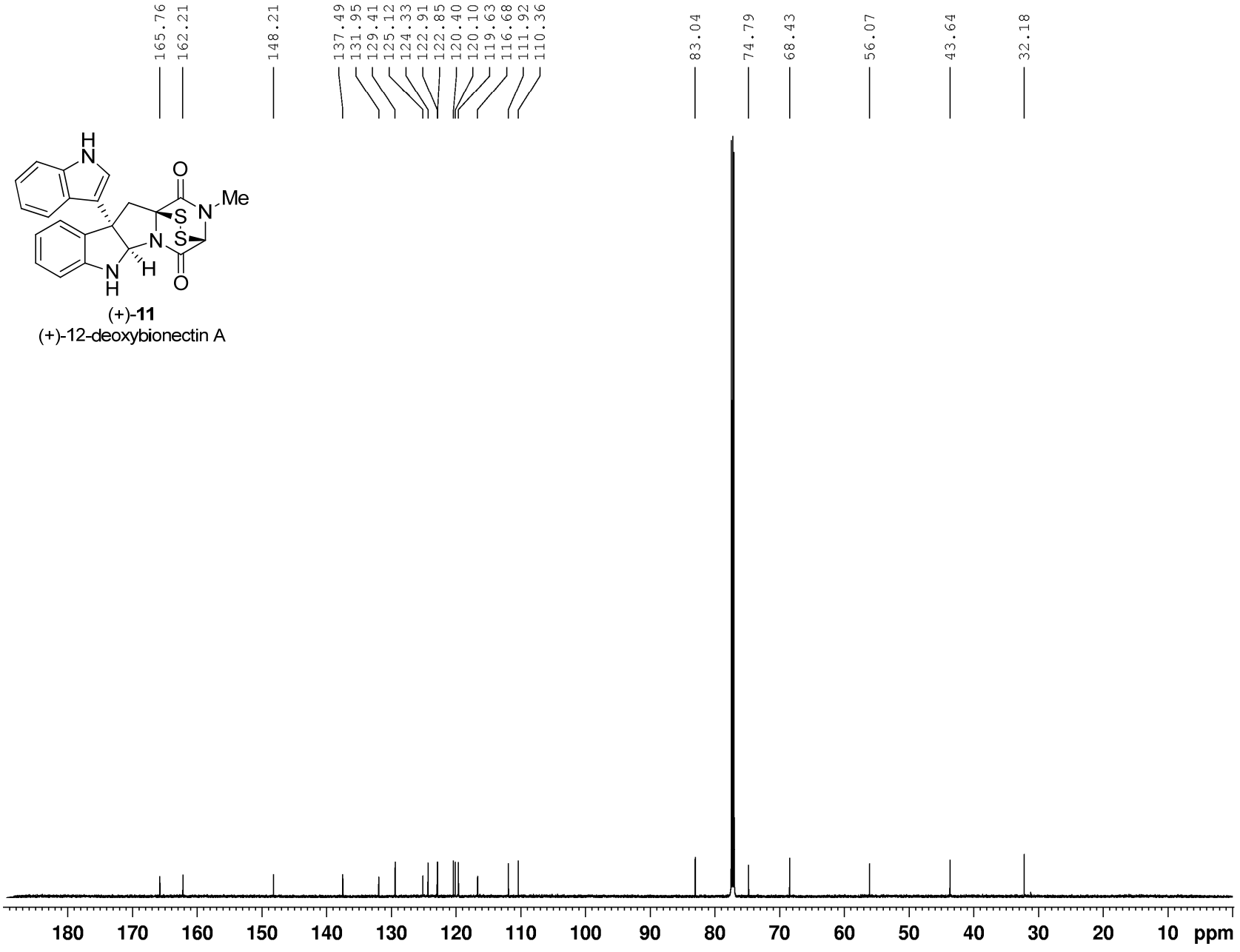

(+)-**11**
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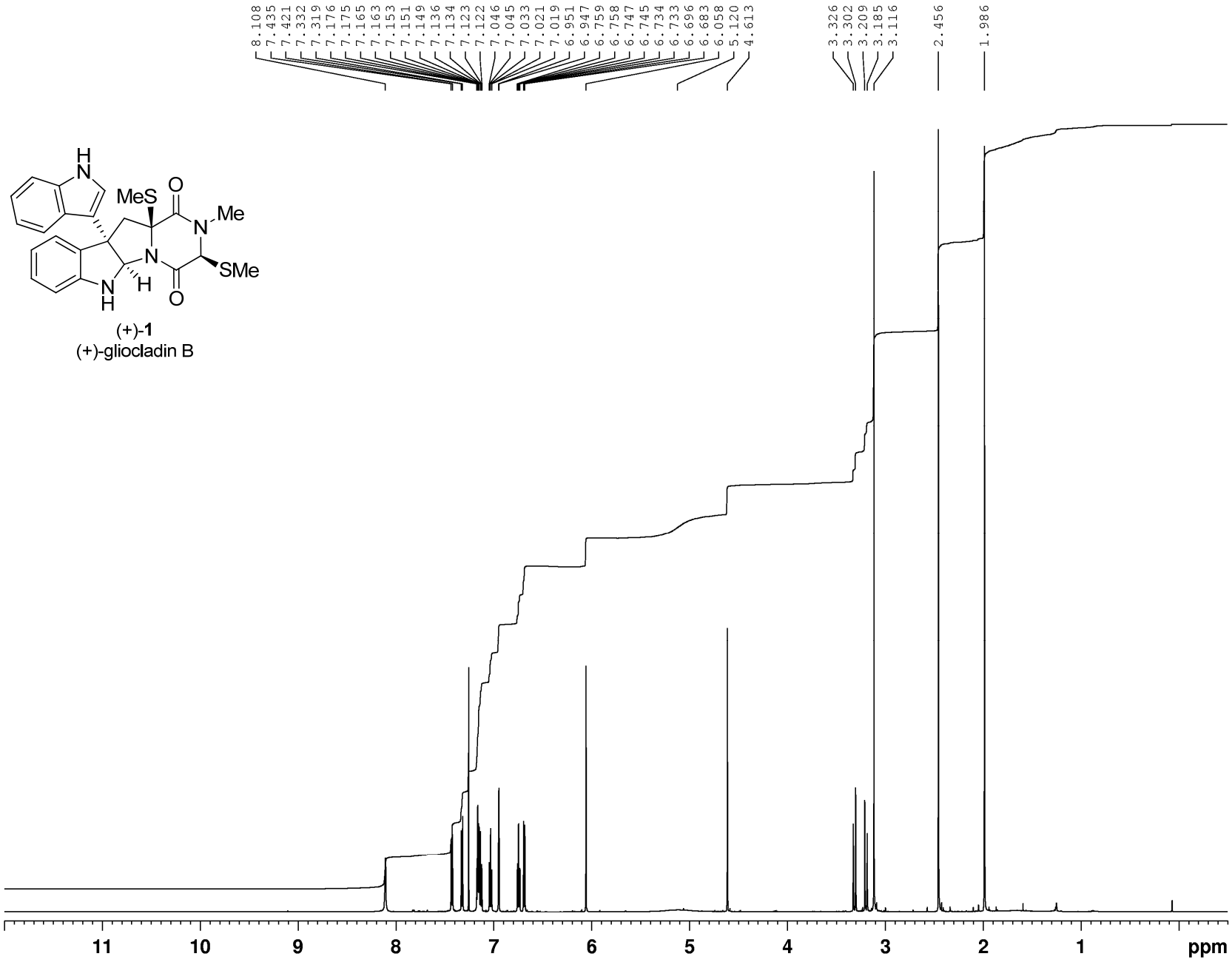
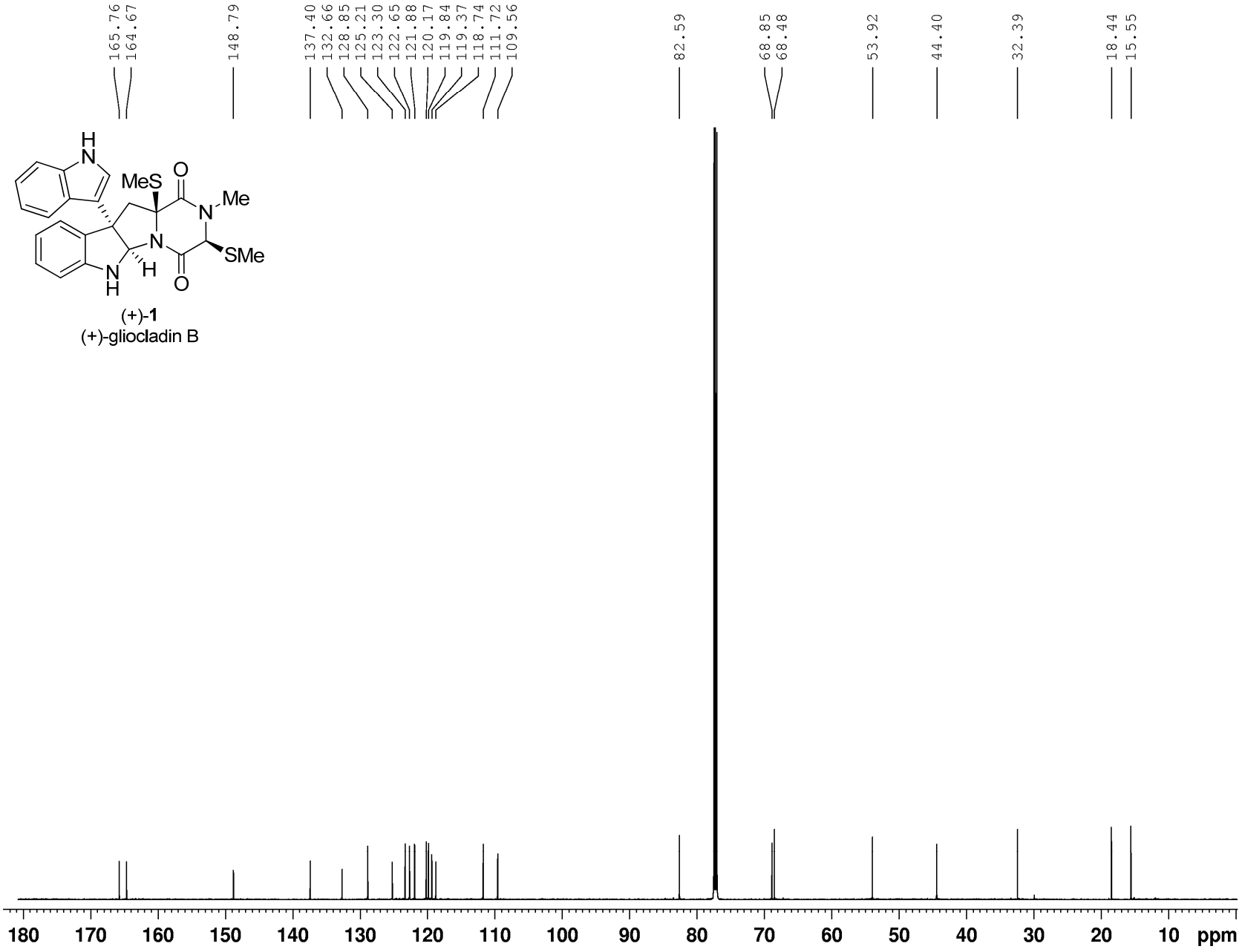
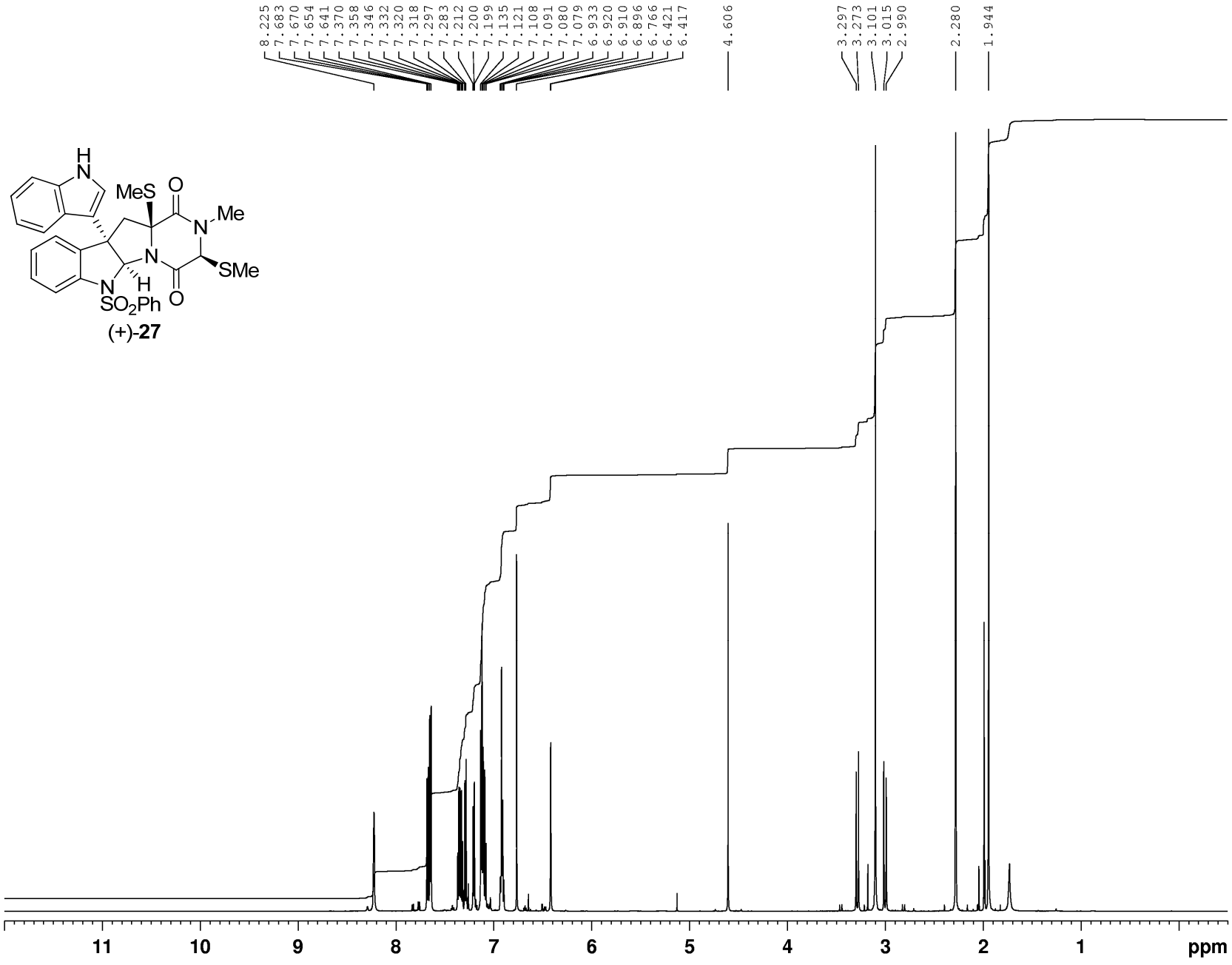
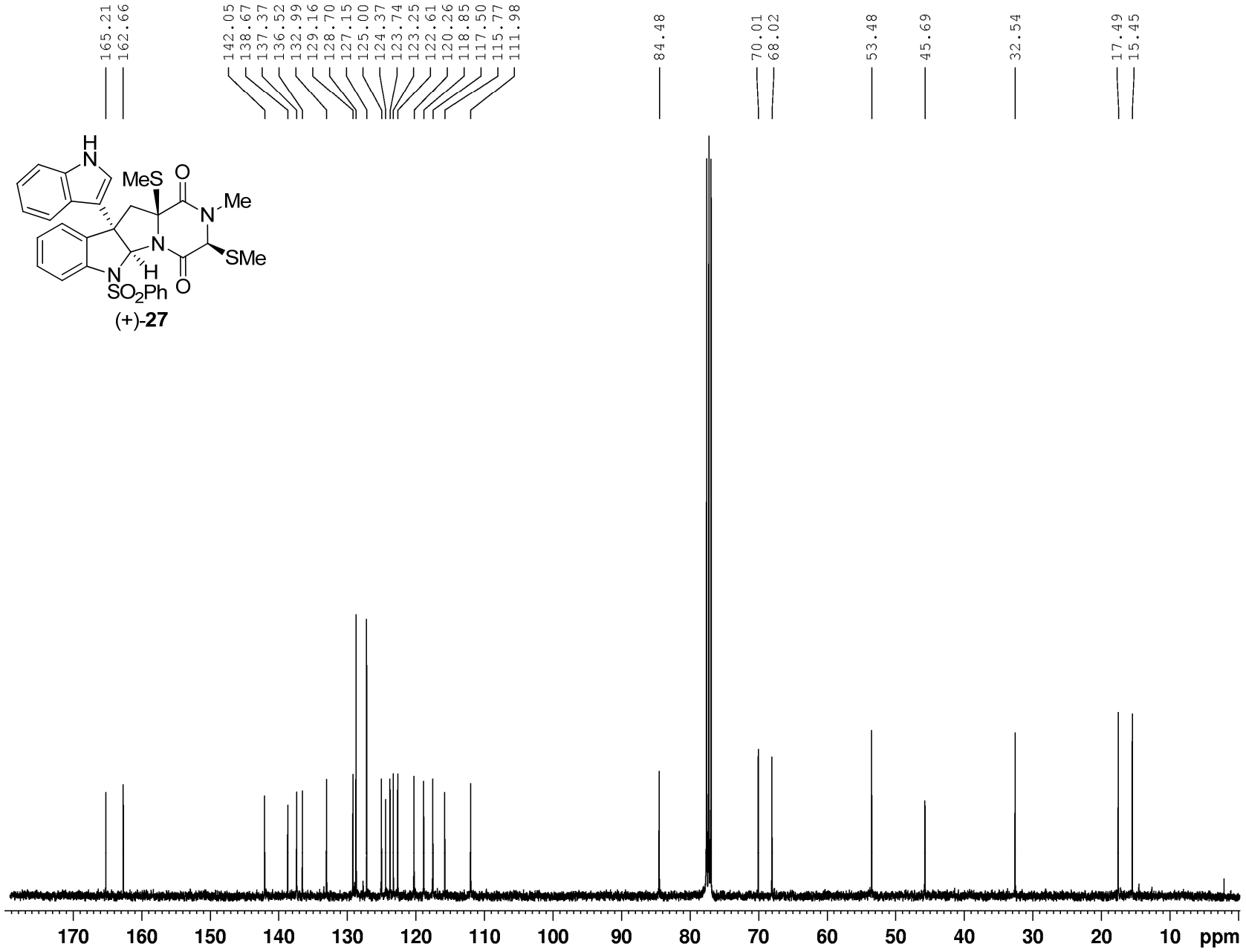
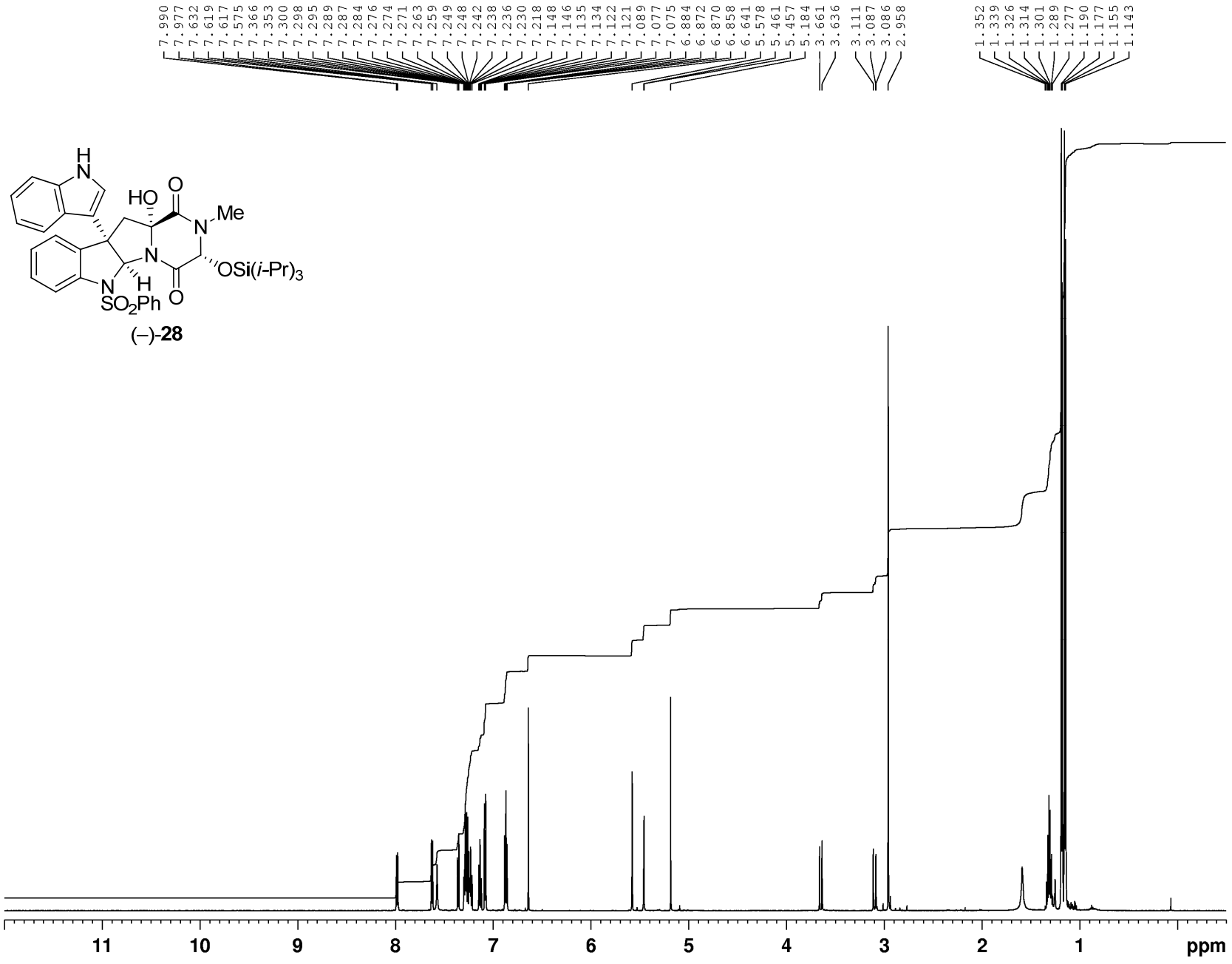


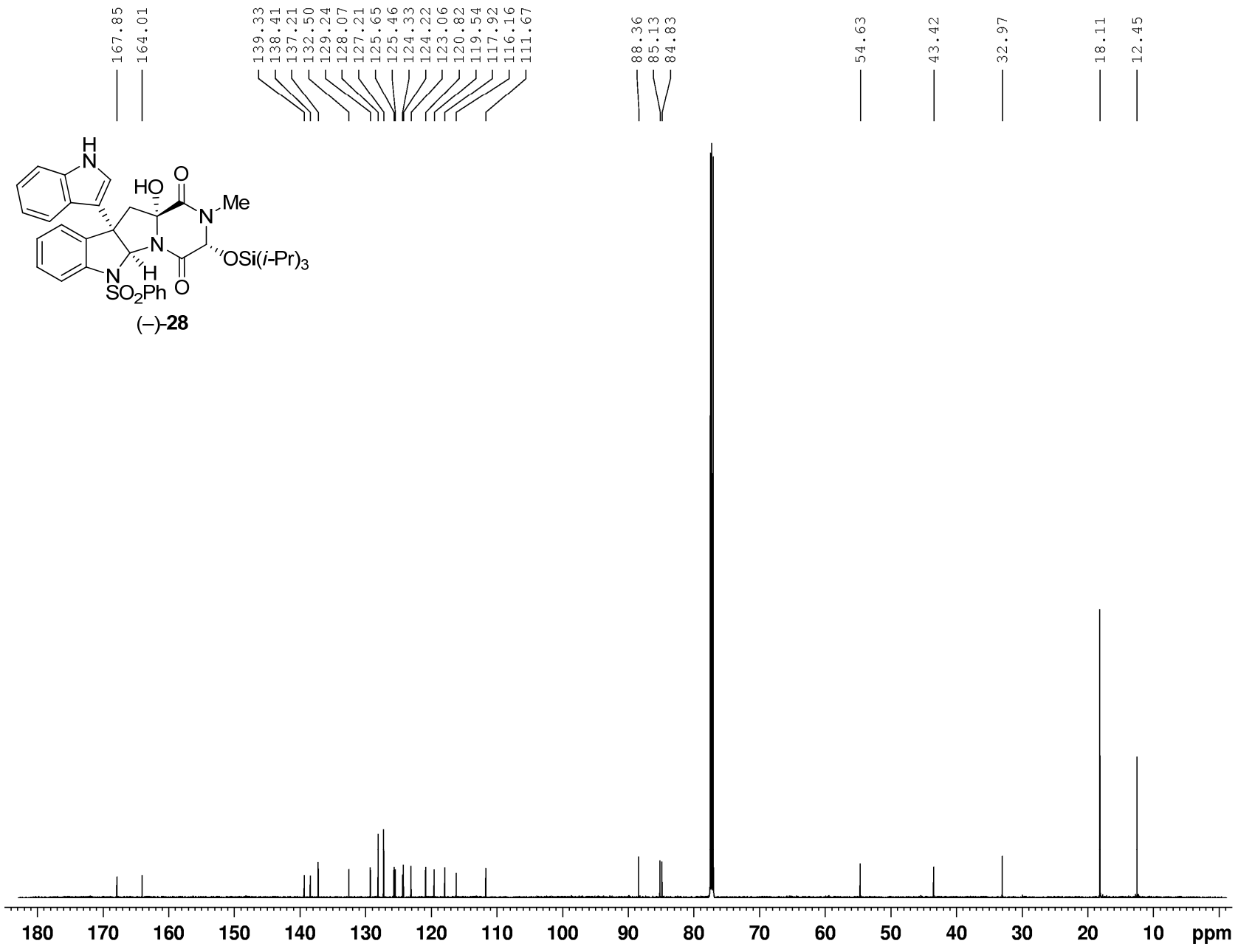


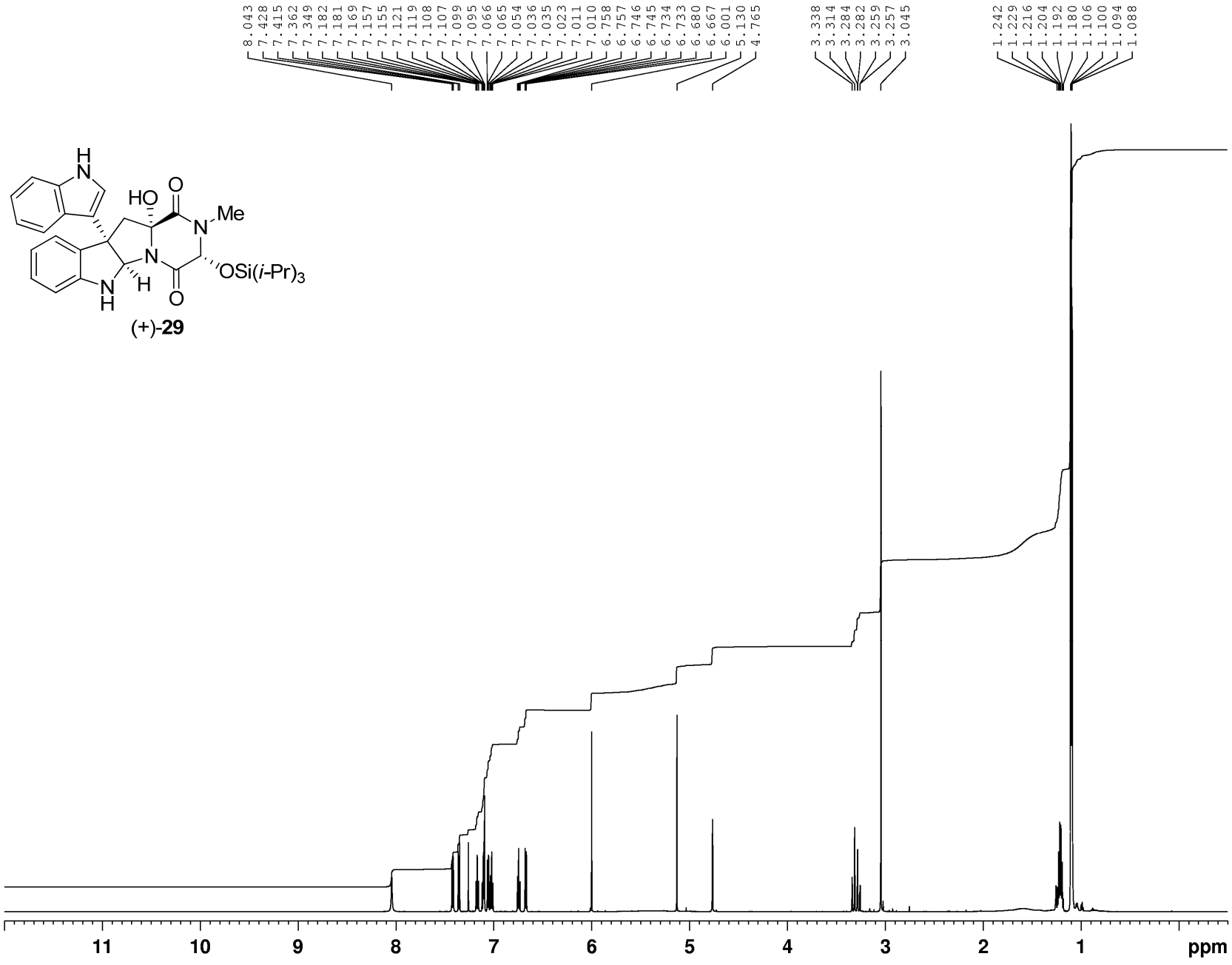
(+)-**1**
(+)-gliocladin B

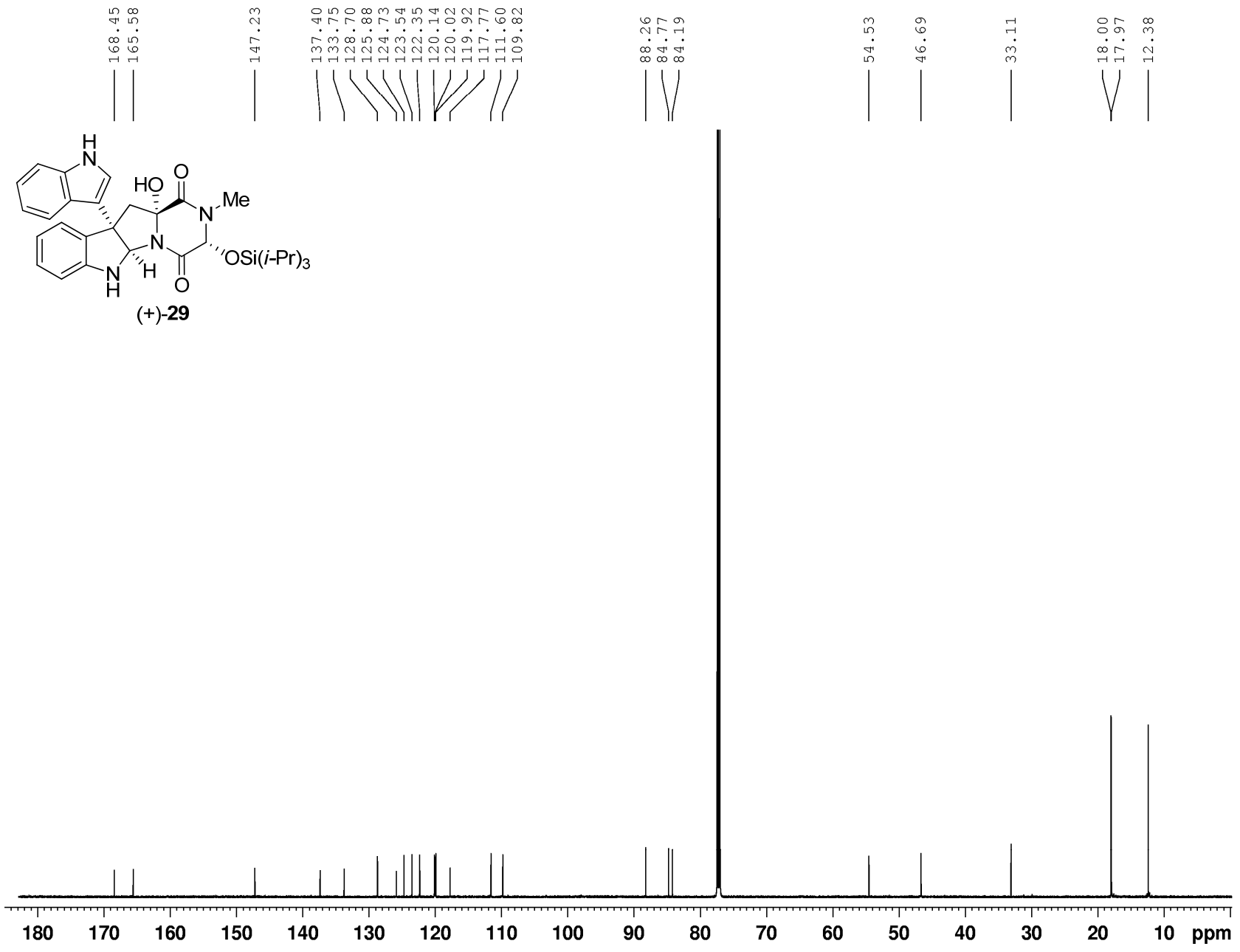


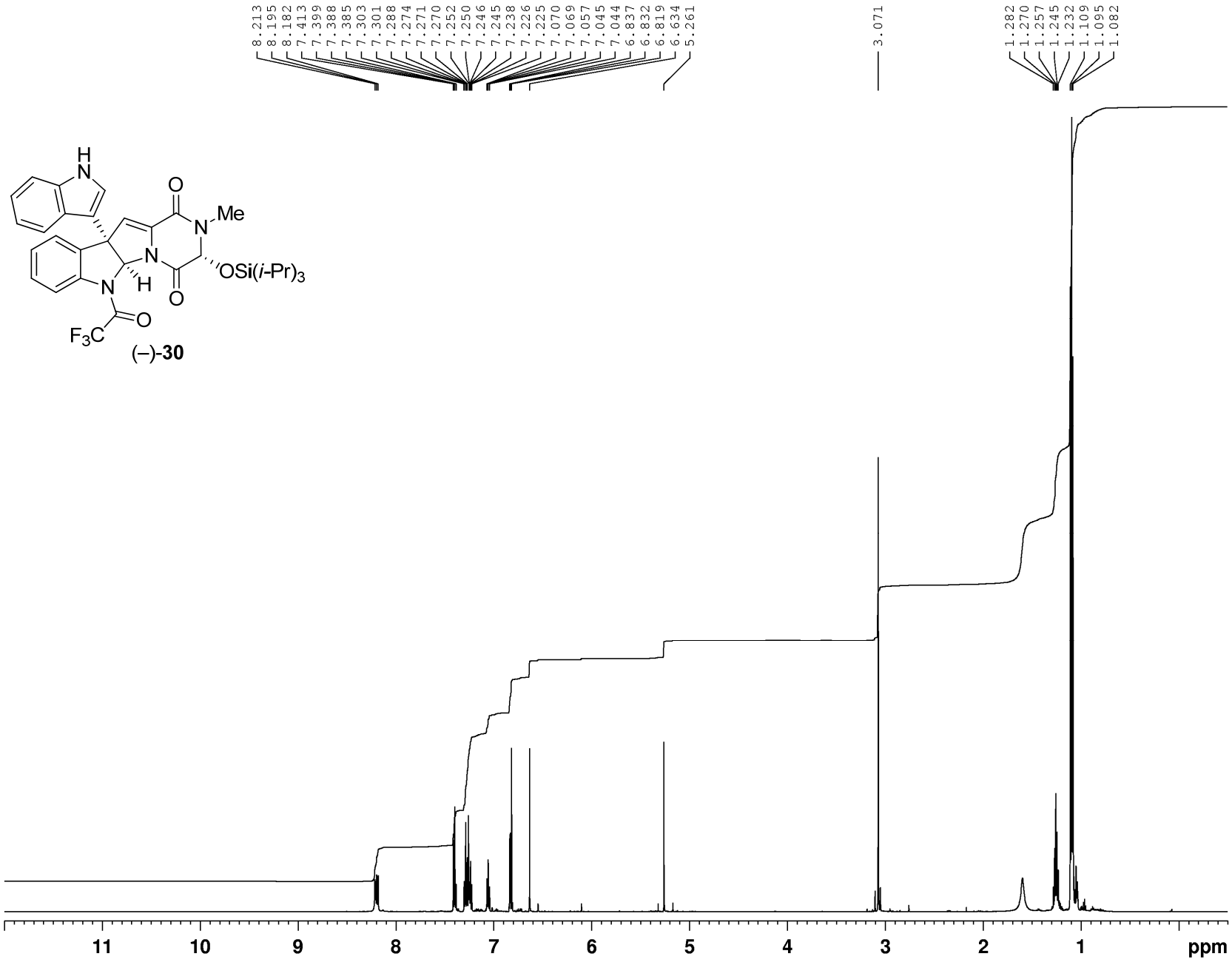


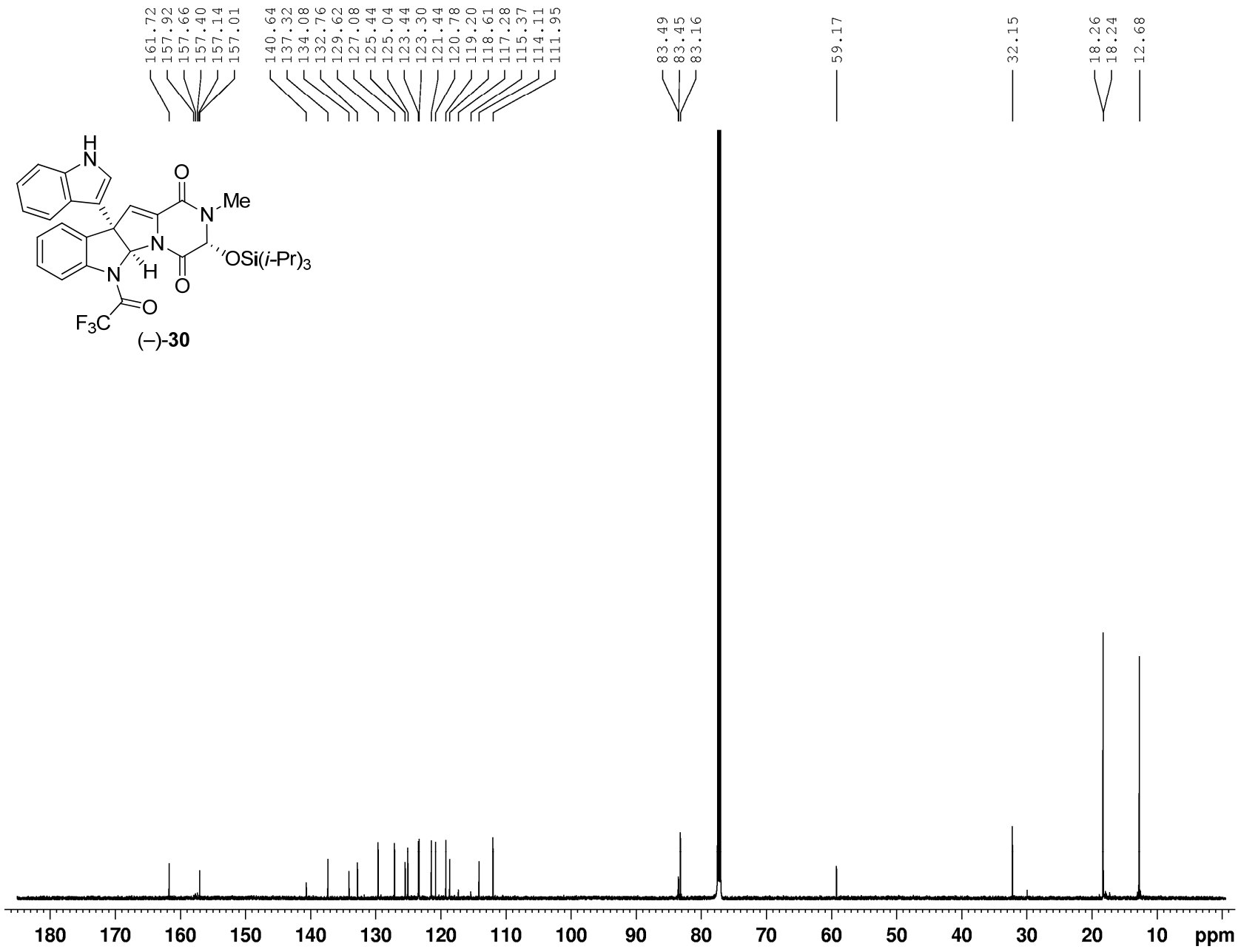


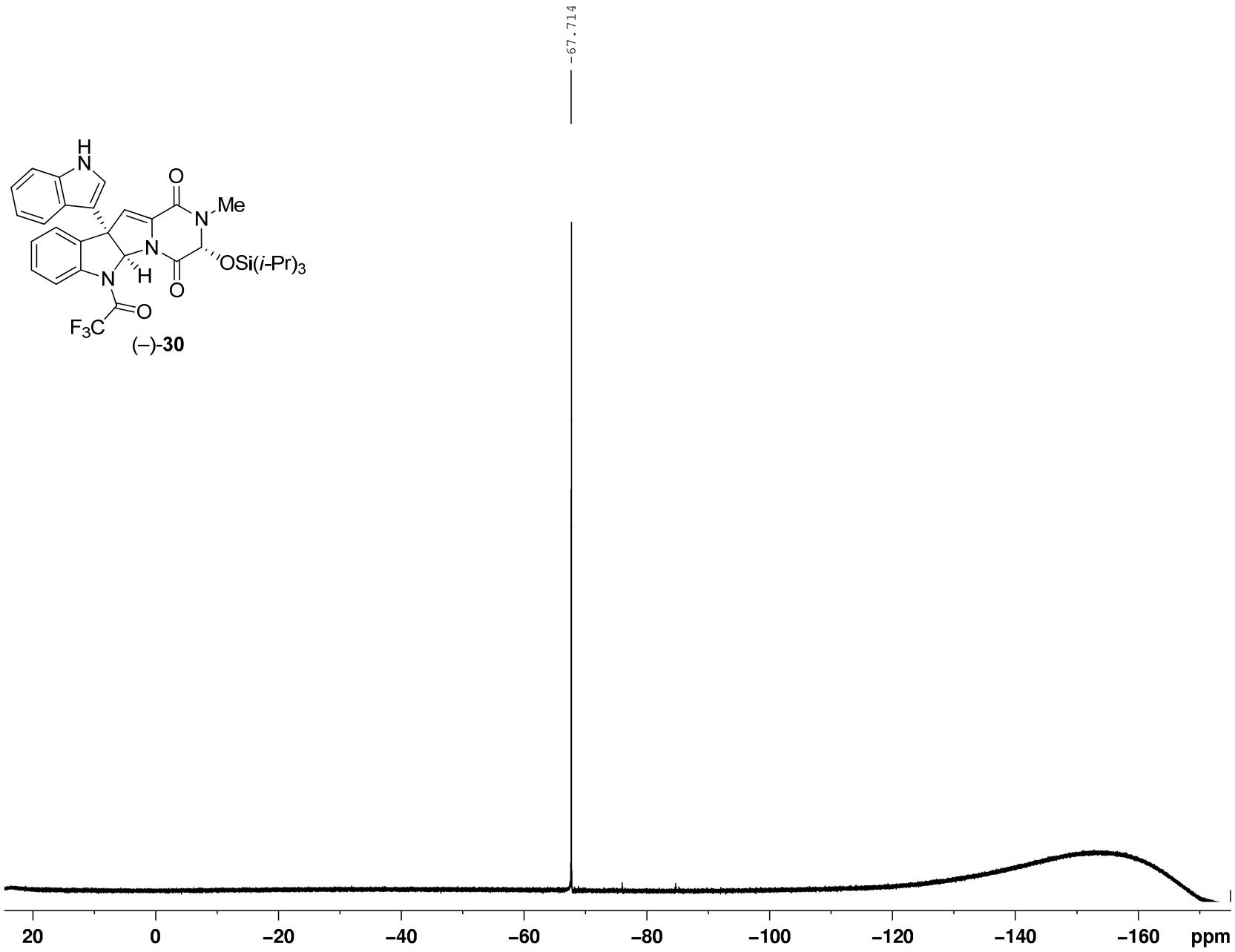












(–)-**30**