Synthesis of Potent Cytotoxic Epidithiodiketopiperazines Designed for Derivatization

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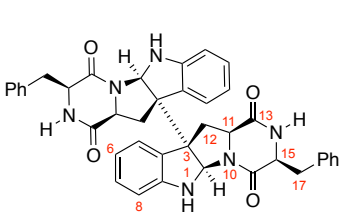
Supporting Information

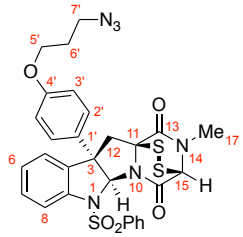
Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile, toluene, diethyl ether, tetrahydrofuran, *N*,*N*-dimethylformamide, and methanol were purified by the method of Grubbs under positive argon pressure.[1] Benzene, *N,N*-diisopropylethylamine, and 1,2-dichloroethane were dried by distillation over calcium hydride under an inert nitrogen atmosphere. Acetone 1,3-dimethyl-3,4,5,6-tetrahydro-2-pyrimidinone was dried by distillation over calcium hydride under an inert nitrogen atmosphere. 2,6-Di-*tert*-butyl-4-methylpyridine was purified by flash column chromatography on silica gel (eluent: hexanes).

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. Safe and Convenient Procedure for Solvent Purification. *Organometallics* **1996**, *15*, 1518−1520.

Figure S1: Positional Numbering System. At least three numbering systems exist for dimeric diketopiperazine alkaloids exist in the literature.[2] In assigning the ^{1}H and ^{13}C NMR data for all intermediates en route to our syntheses of monomeric ETPs (+)-**9a**, (+)-**9b**, (+)-**9c**, and (+)-**9d**, we 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 1-17) is optimal and used throughout this report. For each compound, per *Journal of Organic Chemistry* requirement, we have also provided the systematic names following the International Union of Pure and Applied Chemistry (IUPAC) convention, which has a different positional numbering system.



(+)-WIN-64821
Barrow's numbering for
dimeric diketopiperazines



(+)-**9a**
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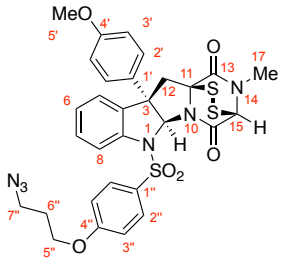

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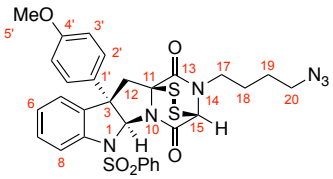

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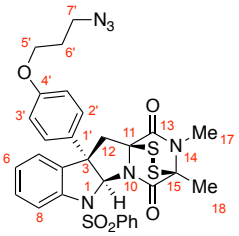

(+)-**9d**
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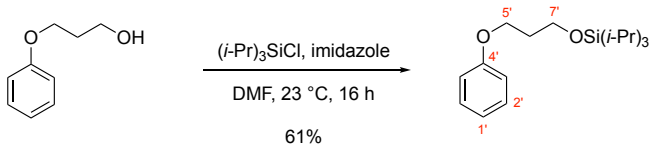
2. a) Yates, P.; MacLachlan, F. N.; Rae, I. D.; Rosenberger, M.; Szabo, A. G.; Willis, C. R.; Cava, M. P.; Behforouz, M.; Lakshmikantham, M. V.; Zeiger, W. Haplophytine. Novel Type of Indole Alkaloid. *J. Am. Chem. Soc.* **1973**, *95*, 7842−7850; b) J. E. Saxton, *The Alkaloids,* ed. G. A. Cordell, Academic Press: San Diego, **1998**, vol. 51.

Cell Culture Information. Cells were grown in media supplemented with fetal bovine serum (FBS) and antibiotics (100 μg/mL penicillin and 100 U/mL streptomycin). Specifically, experiments were performed using the following cell lines and media compositions: HeLa (cervical adenocarcimona) and A549 (lung carcinoma) were grown in RPMI-1640 + 10% FBS; HCT 116 (colorectal carcinoma) was grown in DMEM + 10% FBS; MCF7 (breast adenocarcinoma) and DU 145 (prostate carcinoma) were grown in EMEM + 10% FBS. Cells were incubated at 37 °C in a 5% CO_2, 95% humidity atmosphere.

Cell Viability Assays. Cells were plated at 250 cells/well into duplicate assay plates in 50 μL media into 384-well white, opaque, tissue-culture treated plates and allowed to adhere overnight at 37 °C/5% CO_2. Compounds were solubilized in DMSO as 1000× stocks and 100 nL was pin-transferred to cells. Compounds were tested in 10-pt, 2-fold dilution with concentrations tested between 1 nM – 20 μM for most compounds, except where indicated. DMSO (32 wells of 384-wells) was used as vehicle control. After 72 hours of incubation at 37 °C/5% CO_2, 10 μL Cell Titer-Glo was added to each well and plates were incubated at room temperature for 10 minutes before the luminescence was read on a plate reader. Cell Titer-Glo measures ATP levels of cells as a surrogate for cell viability. All compound-treated wells were normalized to the DMSO control averages and expressed as a % of DMSO viability. IC_{50} values were determined from the dose curves using Spotfire.



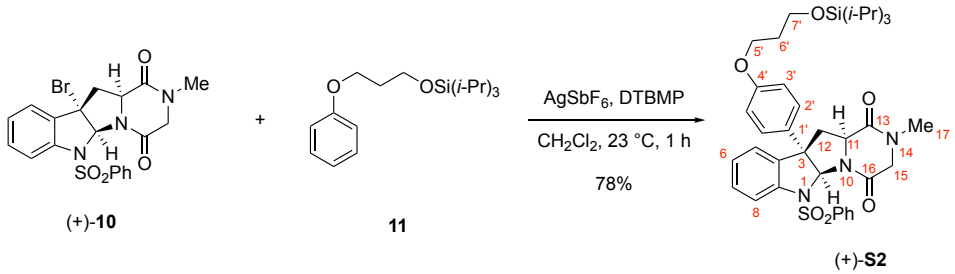
S1 **11**

Triisopropyl(3-phenoxypropoxy)silane (11):

Triisopropylsilyl chloride (5.84 mL, 27.3 mmol, 1.00 equiv) was added via syringe to a solution of 3-phenoxypropan-1-ol[3] (**S1**, 4.16 g, 27.3 mmol, 1 equiv) and imidazole (2.42 g, 62.3 mmol, 2.30 equiv) in *N*,*N*-dimethylformamide (45 mL) at 23 °C. After 18 h, the reaction mixture was diluted with ethyl acetate (300 mL) and was slowly poured into saturated aqueous sodium bicarbonate solution (100 mL). The organic layer was washed sequentially with a saturated aqueous sodium bicarbonate solution (2 × 50 mL), with water (3 × 50 mL), and with a saturated aqueous sodium chloride solution (40 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 on silica gel (eluent: 0→10% ethyl acetate in hexanes) to afford triisopropyl(3-phenoxypropoxy)silane (**11**, 4.90 g, 61.4%) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$, 25 °C):	δ 7.26 (app-t, *J* = 7.9 Hz, 2H, $C_{2'}$**H**), 6.92–6.89 (m, 3H, $C_{1'}$**H**, $C_{3'}$**H**), 4.08 (t, *J* = 6.3 Hz, 2H, $C_{5'}$**H**), 3.87 (t, *J* = 6.0 Hz, 2H, $C_{7'}$**H**), 1.99 (p, *J* = 6.1 Hz, 2H, $C_{6'}$**H**), 1.10–1.03 (m, 21H, Si**C**H$(CH_3)_2$, SiCH(C**H**$_3)_2$).
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C):	δ 159.3 (**C**$_{4'}$), 129.6 (**C**$_{2'}$), 120.7 (**C**$_{1'}$), 114.7 (**C**$_{3'}$) 64.7 (**C**$_{5'}$), 60.1 (**C**$_{7'}$), 32.9 (**C**$_{6'}$), 18.2 (Si**C**H$(CH_3)_2$), 12.2 (SiCH(**C**H$_3)_2$).
FTIR (thin film) cm^{-1}:	2941 (s), 2865 (s), 1497 (s), 1244 (s), 1103 (s), 881 (s), 751 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{18}H_{33}O_2Si$ $[M+H]^+$: 309.2244, found: 309.2266.
TLC (10% ethyl acetate in hexanes), R*f*:	0.39 (UV, CAM).

3. Muthyala, M. K.; Choudary, S.; Pandey, K.; Shelke, G. M.; Jha, M.; Kumar, A. Synthesis of Ionic-Liquid-Supported Diaryliodonium Salts. *Eur. J. Org. Chem.* **2014**, 2365−2370.



(+)-(5a*S*,10b*S*,11a*S*)-2-Methyl-6-(phenylsulfonyl)-10b-(4-(3-((triisopropylsilyl)oxy)propoxy) phenyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (S2); C3-adduct (+)-S2:

endo-Tetracyclic bromide (+)-**10**[4] (1.67 g, 3.50 mmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 1.81 g, 8.80 mmol, 2.51 equiv), and triisopropyl(3-phenoxypropoxy)silane (**11**, 2.16 g, 6.99 mmol, 2.00 equiv) were azeotropically dried by concentration from anhydrous benzene (30 mL) under reduced pressure. Dichloromethane (35 mL) was added via syringe, and silver hexafluoroantimonate (2.40 g, 6.99 mmol, 2.00 equiv) was added as a solid in one portion to the solution at 23 °C. After 1 h, the reaction mixture was diluted with dichloromethane (100 mL) and was filtered through a pad of diatomaceous earth. The filter cake was washed with dichloromethane (3 × 50 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→20% acetone in dichloromethane) to afford C3-adduct (+)-**S2** (1.93 g, 78.4%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

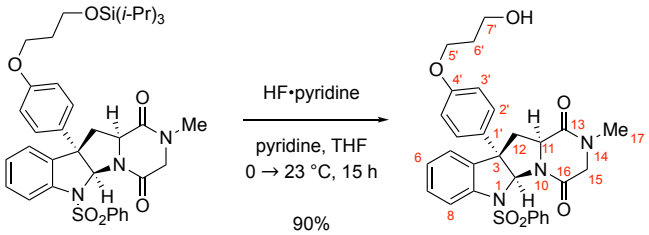
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.58 (d, J = 8.1 Hz, 1H, C_8**H**), 7.46 (app-d, J = 8.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.30 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.28–7.24 (m, 1H, C_7**H**), 7.10 (m, 4H, SO_2Ph-*o*-**H**, C_5**H**, C_6**H**), 6.68–6.61 (m, 4H, $C_{2'}$**H**, $C_{3'}$**H**), 6.13 (s, 1H, C_2**H**), 4.39 (app-t, J = 8.3 Hz, 1H, C_{11}**H**), 4.10 (d, J = 17.4 Hz, 1H, C_{15}**H**$_a$), 4.04 (t, J = 6.3 Hz, 2H, $C_{5'}$**H**), 3.86 (t, J = 6.1 Hz, 2H, $C_{7'}$**H**), 3.82 (d, J = 17.4 Hz, 1H, C_{15}**H**$_b$), 3.06 (dd, J = 7.0, 14.1 Hz, 1H, C_{12}**H**$_a$), 2.89–2.83 (m, 4H, C_{12}**H**$_b$, C_{17}**H**), 1.98 (p, J = 6.1 Hz, 2H, $C_{6'}$**H**),), 1.11–1.03 (m, 21H, SiC**H**$(CH_3)_2$, SiCH$(CH_3)_2$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.1 (**C**$_{13}$), 165.2 (**C**$_{16}$), 158.4 (**C**$_{4'}$), 139.9 (**C**$_9$) 138.2 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 132.5 (**C**$_{1'}$), 129.2 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$), 128.0 (SO_2Ph-*o*-**C**), 126.0 (**C**$_6$), 125.4 (**C**$_5$), 117.2 (**C**$_8$), 115.0 (**C**$_{3'}$), 87.2 (**C**$_2$), 64.9 (**C**$_{5'}$), 59.8 (**C**$_{7'}$), 59.4 (**C**$_3$), 58.6 (**C**$_{11}$), 54.5 (**C**$_{15}$), 39.1 (**C**$_{12}$), 33.7 (**C**$_{17}$), 32.7 (**C**$_{6'}$), 18.2 (Si**C**H$(CH_3)_2$), 12.1 (SiCH(**C**$H_3)_2$).

4. Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803.

FTIR (thin film) cm^{-1}:	3065 (m), 2943 (s), 2868 (s), 1684 (s), 1610 (m), 1512 (m), 1253 (m), 1171 (m), 883 (m), 686 (w).
HRMS (DART) (*m/z*):	calc'd for $C_{38}H_{50}N_3O_6SSi$ $[M+H]^+$: 704.3184, found: 704.3195.
$[\alpha]_D^{23}$:	+19 (*c* = 0.24, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.63 (UV, CAM).



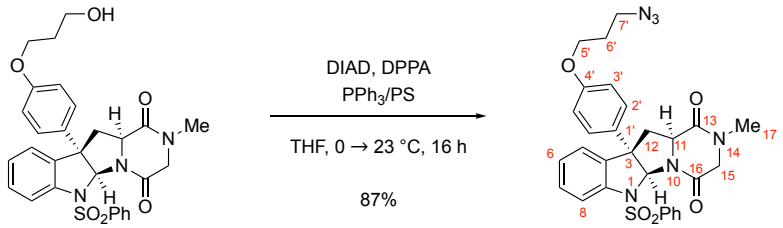
(+)-(5a*S*,10b*S*,11a*S*)-10b-(4-(3-Hydroxypropoxy)phenyl)-2-methyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (12); alcohol (+)-S12:

A freshly prepared solution of hydrogen fluoride–pyridine (70% HF, 9 mL), pyridine (18 mL), and tetrahydrofuran (72 mL) at 0 °C was poured into a solution of C3-adduct (+)-**S2** (1.89 g, 2.69 mmol, 1 equiv) in tetrahydrofuran (90 mL) at 0 °C contained in a 1–L polypropylene vessel. After 5 min, the ice−water bath was removed and the solution was allowed to stir and warm to 23 °C. After 20 h, the reaction mixture was cooled to 0 °C and was diluted with a saturated aqueous sodium bicarbonate solution (500 mL) in portions (50 mL) over 15 min. The resulting mixture was extracted with ethyl acetate (300 mL), the layers were separated, and the aqueous layer was extracted with ethyl acetate (2 × 75 mL). The combined organic extracts were washed sequentially with a saturated aqueous copper(II) sulfate solution (3 × 100 mL), with a saturated aqueous ammonium chloride solution (3 × 100 mL), and with a 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 residue was purified by flash column chromatography on silica gel (eluent: 0→60% acetone in dichloromethane) to afford alcohol (+)-**12** (1.33 g, 90.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.57 (d, J = 8.1 Hz, 1H, C_8**H**), 7.45 (app-d, J = 9.7 Hz, 2H, SO_2Ph-*o*-**H**), 7.33 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.28–7.23 (m, 1H, C_7**H**), 7.12–7.08 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 6.65 (app-d, J = 9.0 Hz, 2H, $C_{2'}$**H**) 6.60 (app-d, J = 9.0 Hz, 2H, $C_{3'}$**H**), 6.13 (s, 1H, C_2**H**), 4.41 (app-t, J = 8.3 Hz, 1H, C_{11}**H**), 4.10 (d, J = 17.3 Hz, 1H, C_{15}**H**$_a$), 4.05 (t, J = 6.0 Hz, 2H, $C_{5'}$**H**), 3.84 (t, J = 6.0 Hz, 2H, $C_{7'}$**H**), 3.81 (d, J = 17.7 Hz, 1H, C_{15}**H**$_b$), 3.06 (dd, J = 7.0, 14.1 Hz, 1H, C_{12}**H**$_a$), 2.88–2.82 (m, 4H, C_{12}**H**$_b$, C_{17}**H**), 2.02 (p, J = 5.9 Hz, 2H, $C_{6'}$**H**), 1.88 (br-s, 1H, O**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.1 (**C**$_{13}$), 165.3 (**C**$_{16}$), 158.1 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 135.9 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 132.9 (**C**$_{1'}$), 129.3 (**C**$_7$), 128.8 (SO_2Ph-*m*-**C**), 128.2 (**C**$_{2'}$), 127.6 (SO_2Ph-*o*-**C**), 126.0 (**C**$_6$), 125.5 (**C**$_5$), 117.2 (**C**$_8$), 115.0 (**C**$_{3'}$), 87.2 (**C**$_2$), 65.8 (**C**$_{5'}$),

	60.2 (**C**$_{7'}$), 59.4 (**C**$_3$), 58.6 (**C**$_{11}$), 54.4 (**C**$_{15}$), 39.0 (**C**$_{12}$), 33.7 (**C**$_{17}$), 32.1 (**C**$_{6'}$).
FTIR (thin film) cm^{-1}:	2954 (w), 1700 (s), 1684 (s), 1507 (m), 1362 (m), 1169 (m), 832 (w), 668 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{29}H_{30}N_3O_6S$ $[M+H]^+$: 548.1850, found: 548.1872.
$[\alpha]_D^{23}$:	+26 (*c* = 0.12, $CHCl_3$).
TLC (30% acetone in dichloromethane), R*f*:	0.21 (UV, CAM).



(+)-**12** (+)-**13**

(+)-(5a*S*,10b*S*,11a*S*)-10b-(4-(3-Azidopropoxy)phenyl)-2-methyl-6-(phenylsulfonyl)-2,3,6,10b, 11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (13); azide (+)-13:

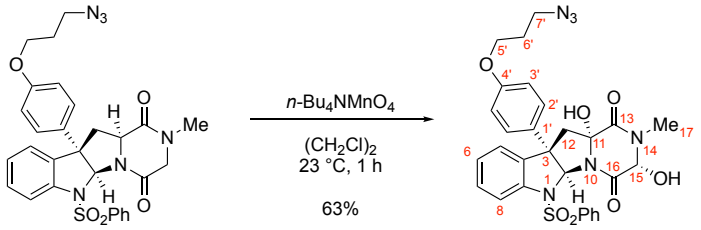
Diisopropyl azodicarboxylate (DIAD, 256 μL, 1.28 mmol, 1.50 equiv) and diphenylphosphoryl azide (DPPA, 276 μL, 1.28 mmol, 1.50 equiv) were added dropwise via syringe to a suspension of alcohol (+)-**12** (466 mg, 851 μmol, 1 equiv) and resin–bound triphenylphosphine (1.31 mmol/g on 100-200 mesh polystyrene cross–linked with 1% divinylbenzene, 973 mg, 1.28 mmol, 1.50 equiv) in tetrahydrofuran (20 mL) at 0 °C. After 5 min, the ice−water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 16 h, the reaction mixture was filtered through a 1 cm pad of diatomaceous earth in a 60-mL medium-porosity fritted-glass funnel. The filter cake was washed with dichloromethane (100 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 30% acetone in dichloromethane) to afford azide (+)-**13** (425 mg, 87.2%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.58 (d, J = 8.1 Hz, 1H, C_8**H**), 7.49 (app-d, J = 8.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.34 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.28–7.23 (m, 1H, C_7**H**), 7.14–7.09 (m, 4H, SO_2Ph-*o*-**H**, C_5**H**, C_6**H**), 6.68 (app-d, J = 9.0 Hz, 2H, $C_{2'}$**H**) 6.62 (app-d, J = 9.0 Hz, 2H, $C_{3'}$**H**), 6.13 (s, 1H, C_2**H**), 4.39 (app-t, J = 8.2 Hz, 1H, C_{11}**H**), 4.10 (d, J = 17.4 Hz, 1H, C_{15}**H**$_a$), 3.99 (t, J = 5.9 Hz, 2H, $C_{5'}$**H**), 3.82 (d, J = 17.4 Hz, 1H, C_{15}**H**$_b$), 3.51 (t, J = 6.5 Hz, 2H, $C_{7'}$**H**), 3.06 (dd, J = 7.1, 14.2 Hz, 1H, C_{12}**H**$_a$), 2.89–2.83 (m, 4H, C_{12}**H**$_b$, C_{17}**H**), 2.04 (p, J = 6.2 Hz, 2H, $C_{6'}$**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.1 (**C**$_{13}$), 165.3 (**C**$_{16}$), 157.9 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 133.0 (**C**$_{1'}$), 129.3 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.2 (**C**$_{2'}$), 127.7 (SO_2Ph-*o*-**C**), 126.0 (**C**$_6$), 125.4 (**C**$_5$), 117.2 (**C**$_8$), 115.0 (**C**$_{3'}$), 87.1 (**C**$_2$), 64.7 (**C**$_{5'}$), 59.4 (**C**$_3$), 58.6 (**C**$_{11}$), 54.4 (**C**$_{15}$), 48.3 (**C**$_{7'}$), 39.0 (**C**$_{12}$), 33.7 (**C**$_{17}$), 28.9 (**C**$_{6'}$).

FTIR (thin film) cm^{-1}:	2929 (w), 2099 (s), 1700 (s), 1684 (s), 1512 (m), 1362 (m), 1252 (m), 1169 (m), 1091 (w), 832 (w), 668 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{29}H_{29}N_6O_5S$ $[M+H]^+$: 573.1915, found: 573.1921.
$[\alpha]_D^{23}$:	+21.8 (*c* = 0.22, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.55 (UV, CAM).



(+)-**13** (−)-**14**

(−)-(3*R*,5a*S*,10b*S*,11a*R*)-10b-(4-(3-Azidopropoxy)phenyl)-3,11a-dihydroxy-2-methyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (14); diol (−)-14:

Tetra-*n*-butylammonium permanganate[5] (807 mg, 2.23 mmol, 5.05 equiv) was added as a solid to a solution of azide (+)-**13** (253 mg, 442 μmol, 1 equiv) in 1,2-dichloroethane (16 mL) at 23 °C. After 1 h, the reaction mixture was diluted with a saturated aqueous sodium sulfite solution (50 mL) and with ethyl acetate−hexanes (9:1, 200 mL). The resulting mixture was washed with a saturated aqueous sodium bicarbonate solution (50 mL), the layers were separated, and the organic layer was washed sequentially with a saturated aqueous sodium bicarbonate solution (50 mL), with deionized water (50 mL), and with a saturated aqueous sodium chloride solution (25 mL). The combined aqueous layers were extracted with ethyl acetate−hexanes (9:1, 2 × 50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→40% acetone in dichloromethane) to afford diol (−)-**14** (169 mg, 63.2%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

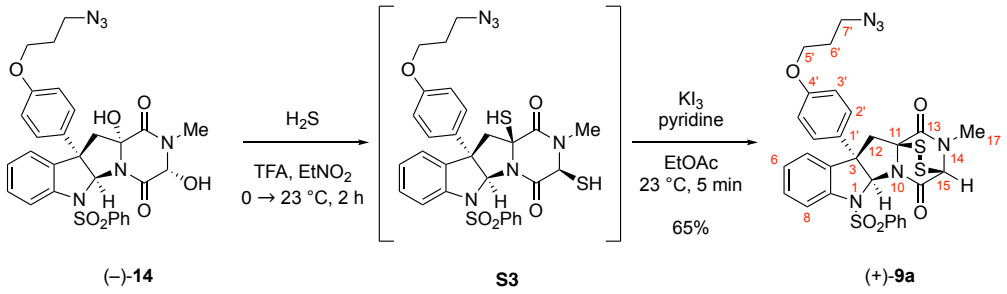
^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 7.43 (app-t, J = 7.4 Hz, 1H, SO_2Ph-*p*-**H**), 7.39–7.32 (m, 4H, SO_2Ph-*o*-**H**, C_7**H**, C_8**H**), 7.26–7.19 (m, 3H, $C_{11}O$**H**, C_5**H**, C_6**H**), 7.13 (app-t, J = 7.5 Hz, 2H, SO_2Ph-*m*-**H**), 7.01 (d, J = 7.2 Hz, 1H, $C_{15}O$**H**), 6.75 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.66 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.21 (s, 1H, C_2**H**), 5.00 (d, J = 6.8 Hz, 1H, C_{15}**H**), 4.02 (t, J = 6.0 Hz, 2H, $C_{5'}$**H**), 3.54 (t, J = 6.7 Hz, 2H, $C_{7'}$**H**), 3.19 (d, J = 14.9 Hz, 1H, C_{12}**H**$_a$), 2.77 (s, 3H, C_{17}**H**), 2.66 (d, J = 14.9 Hz, 1H, C_{12}**H**$_b$), 1.99 (p, J = 6.3 Hz, 2H, $C_{6'}$**H**).

^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 25 °C): δ 166.6 (**C**$_{13}$), 165.8 (**C**$_{16}$), 157.1 (**C**$_{4'}$), 139.3 (**C**$_9$), 138.0 (SO_2Ph-*ipso*-**C**), 137.7 (**C**$_4$), 133.6 (**C**$_{1'}$), 133.2 (SO_2Ph-*p*-**C**), 128.9 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 126.7 (SO_2Ph-*o*-**C**), 126.6 (**C**$_6$), 125.7 (**C**$_5$), 117.0 (**C**$_8$), 114.5 (**C**$_{3'}$), 87.3 (**C**$_2$), 86.0 (**C**$_{11}$), 80.9 (**C**$_{15}$), 64.6 (**C**$_{5'}$), 57.4 (**C**$_3$), 49.7 (**C**$_{12}$), 47.7 (**C**$_{7'}$), 30.5 (**C**$_{17}$), 28.1 (**C**$_{6'}$).

5. Karaman, H.; Barton, R. J.; Robertson, B. E.; Lee, D. G. Preparation and Properties of Quaternary Ammonium and Phosphonium Permanganates. *J. Org. Chem.* **1984**, *49*, 4509−4516.

FTIR (thin film) cm^{-1}:	2095 (m), 1844 (m), 1734 (m), 1700 (s), 1685 (s), 1653 (s), 1559 (s), 1540 (m), 1507 (m), 1457 (m), 1055 (w), 668 (m).
$[\alpha]_D^{23}$:	–6 (*c* = 0.16, DMSO).
HRMS (DART) (*m/z*):	calc'd for $C_{29}H_{29}N_6O_7S$ $[M+H]^+$: 605.1813, found: 605.1814.

TLC (30% acetone in dichloromethane), R*f*: 0.40 (UV, CAM).



(–)-**14** **S3** (+)-**9a**

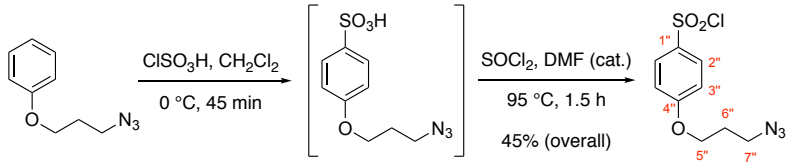
(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-(3-Azidopropoxy)phenyl)-2-methyl-6-(phenylsulfonyl)-2,3,5a, 6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (9a); epidithiodiketopiperazine azide (+)-9a:

A solution of diol (−)-**14** (190 mg, 314 μmol, 1 equiv) in anhydrous nitroethane (13 mL) at 0 °C was sparged with hydrogen sulfide gas for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture, providing a saturated hydrogen sulfide solution. Trifluoroacetic acid (TFA, 9.8 mL) was added via syringe over 20 seconds, and the sparging with hydrogen sulfide gas was maintained for another 20 min. The ice−water bath was removed and the solution was allowed to stir and warm to 23 °C under an atmosphere of hydrogen sulfide. After 2 h, the reaction mixture was diluted with ethyl acetate (125 mL), was slowly poured into a stirring saturated aqueous sodium bicarbonate solution (50 mL), and the organic layer was washed with a saturated aqueous sodium chloride solution (35 mL). A stock solution of potassium triiodide in pyridine[6] was added dropwise into the organic layer containing crude bisthiol **S3** until a persistent yellow color was observed. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 M, 2 × 35 mL), was washed with a saturated aqueous sodium chloride solution (35 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10→20% ethyl acetate in dichloromethane) to afford epidithiodiketopiperazine azide (+)-**9a** (129 mg, 65.4%) as a beige solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.[7]

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.59 (d, *J* = 8.0 Hz, 1H, C_8**H**), 7.40–7.34 (m, 3H, C_7**H**, SO_2Ph-*o*-**H**), 7.29 (app-t, *J* = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.25–7.21 (m, 2H, C_5**H**, C_6**H**), 7.03 (t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.75 (app-d, *J* = 8.9 Hz, 2H, $C_{2'}$**H**), 6.61 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.38 (s, 1H, C_2**H**), 5.24 (s, 1H, C_{15}**H**), 3.99 (t, *J* =

6. Prepared from potassium iodide (200 mg, 1.20 mmol) and iodine (305 mg, 1.20 mmol) in pyridine (5 mL).
7. The relative stereochemistry of the epidisulfide (+)-**9a** was confirmed by key NOESY cross–peaks on the corresponding bis(methylthioether). Our assignment is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (3.12, 7.10–7.04), (3.12, 1.88), (2.97, 6.88). This derivative was prepared in one step using our chemistry developed to access (+)-gliocladin B (Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803). The corresponding bis(methylthioether) of epidisulfide (+)-**9a** was characterized as follows: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.86 (d, *J* = 8.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.51 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.47 (t, *J* = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.35 (t, *J* = 8.1 Hz, 2H, SO_2Ph-*m*-**H**), 7.27 (ddd, *J* = 2.4, 6.4, 8.6 Hz, 1H, C_7**H**), 7.10–7.04 (m, 2H, C_5**H**, C_6**H**), 6.88 (d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.67 (d, *J* = 8.8 Hz, 2H, $C_{3'}$**H**), 6.63 (s, 1H, C_2**H**), 4.46 (s, 1H, C_{15}**H**), 3.96 (t, *J* = 6.0 Hz, 2H, $C_{5'}$**H**), 3.47 (t, *J* = 6.6 Hz, 2H, $C_{7'}$**H**), 3.12 (d, *J* = 14.3 Hz, 1H, C_{12}**H**$_a$), 3.03 (s, 3H, C_{17}**H**), 2.97 (d, *J* = 14.3 Hz, 1H, C_{12}**H**$_b$), 2.17 (s, 3H, C_{15}SC**H**$_3$), 2.00 (p, *J* = 6.2 Hz, 2H, $C_{6'}$**H**), 1.88 (s, 3H, C_{11}SC**H**$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.1 (**C**$_{13}$), 162.3 (**C**$_{16}$), 158.0 (**C**$_{4'}$), 142.4 (**C**$_9$), 140.2 (SO_2Ph-*ipso*-**C**), 136.7 (**C**$_4$), 134.6 (**C**$_{1'}$), 132.9 (SO_2Ph-*p*-**C**), 129.1 (**C**$_7$), 129.1 (SO_2Ph-*m*-**C**), 127.1 (**C**$_{2'}$), 127.0 (SO_2Ph-*o*-**C**), 124.9 (**C**$_6$), 123.8 (**C**$_5$), 117.0 (**C**$_8$), 115.0 (**C**$_{3'}$), 85.7 (**C**$_2$), 69.8 (**C**$_{11}$), 67.6 (**C**$_{15}$), 64.7 (**C**$_{5'}$), 57.0(**C**$_3$), 48.3 (**C**$_{7'}$), 45.7 (**C**$_{12}$), 32.5 (**C**$_{17}$), 28.9 (**C**$_{6'}$), 17.1 (C_{15}S**C**H$_3$), 15.5 (C_{11}S**C**H$_3$). HRMS (ESI) (*m*/*z*): calc'd for $C_{31}H_{32}N_6NaO_5S_3$ $[M+Na]^+$: 687.1489, found 687.1501.

	6.0 Hz, 2H, $C_{5'}\mathbf{H}$), 3.62 (d, J = 15.5 Hz, 1H, $C_{12}\mathbf{H}_a$), 3.51 (t, J = 6.5 Hz, 2H, $C_{7'}\mathbf{H}$), 3.11 (s, 3H, $C_{17}\mathbf{H}$), 2.84 (d, J = 15.5 Hz, 1H, $C_{12}\mathbf{H}_b$), 2.03 (p, J = 6.1 Hz, 2H, $C_{6'}\mathbf{H}$).
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C):	δ 165.2 ($\mathbf{C}_{13}$), 160.2 ($\mathbf{C}_{16}$), 158.1 ($\mathbf{C}_{4'}$), 141.3 ($\mathbf{C}_9$), 138.5 (SO_2Ph-*ipso*-**C**), 135.9 ($\mathbf{C}_4$), 133.1 (SO_2Ph-*p*-**C**), 131.6 ($\mathbf{C}_{1'}$), 129.9 ($\mathbf{C}_7$), 128.7 (SO_2Ph-*m*-**C**), 128.1 ($\mathbf{C}_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.2 ($\mathbf{C}_6$), 125.7 ($\mathbf{C}_5$), 119.0 ($\mathbf{C}_8$), 115.1 ($\mathbf{C}_{3'}$), 87.7 ($\mathbf{C}_2$), 74.6 ($\mathbf{C}_{11}$), 68.5 ($\mathbf{C}_{15}$), 64.7 ($\mathbf{C}_{5'}$), 59.6 ($\mathbf{C}_3$), 48.3 ($\mathbf{C}_{7'}$), 45.5 ($\mathbf{C}_{12}$), 32.2 ($\mathbf{C}_{17}$), 28.9 ($\mathbf{C}_{6'}$).
FTIR (thin film) cm^{-1}:	2926 (w), 2098 (m), 1717 (s), 1700 (s), 1685 (s), 1559 (m), 1507 (m), 1473 (w), 972 (w), 668 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{29}H_{30}N_7O_5S_3$ $[M+NH_4]^+$: 652.1465, found: 652.1454.
$[\alpha]_D^{23}$:	+236 (*c* = 0.10, $CHCl_3$).
TLC (20% ethyl acetate in CH_2Cl_2), R*f*:	0.32 (UV, CAM, $AgNO_3$).



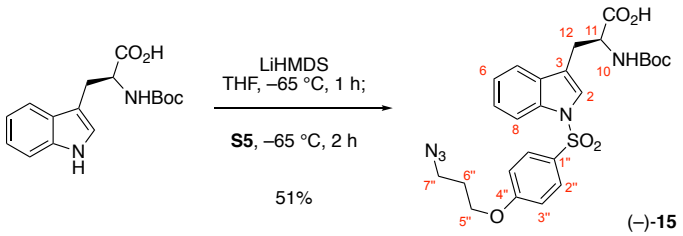
S4 **S5**

4-(3-Azidopropoxy)benzenesulfonyl chloride (S5):

Chlorosulfonic acid (5.20 mL, 77.9 mmol, 1.00 equiv) was added via syringe to a solution of (3-azidopropoxy)benzene[8] (**S4**, 13.8 g, 77.9 mmol, 1 equiv) in dichloromethane (165 mL) at 0 °C. After 45 min, the reaction mixture was concentrated under reduced pressure, and the resulting colorless residue was dissolved in thionyl chloride (100 mL). *N*,*N*-Dimethylformamide (250 µL, 3.2 mmol, 0.041 equiv) was added via syringe, and the reaction mixture was heated to reflux in an oil bath at 95 °C. After 1.5 h, the brown solution was concentrated under reduced pressure. The resulting residue was dissolved in dichloromethane (600 mL) and was washed with an aqueous sodium hydroxide solution (1.25 M, 2 × 100 mL) and with a saturated aqueous sodium chloride solution (150 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 on silica gel (eluent: 25% ethyl acetate in hexanes) to afford 4-(3-azidopropoxy)benzenesulfonyl chloride (**S5**, 9.58 g, 44.6%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$, 25 °C):	δ 7.95 (d, *J* = 9.0 Hz, 2H, $C_{2''}$**H**), 7.03 (d, *J* = 9.0 Hz, 2H, $C_{3''}$**H**), 4.14 (t, *J* = 5.9 Hz, 2H, $C_{5''}$**H**), 3.52 (t, *J* = 6.5 Hz, 2H, $C_{7''}$**H**), 2.08 (p, *J* = 6.2 Hz, 2H, $C_{6''}$**H**).
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C):	δ 164.1 (**C**$_{4''}$), 136.5 (**C**$_{1''}$), 129.8 (**C**$_{2''}$), 115.3 (**C**$_{3''}$) 65.6 (**C**$_{5''}$), 48.1 (**C**$_{7''}$), 28.6 (**C**$_{6''}$).
FTIR (thin film) cm^{-1}:	3101 (w), 2948 (m), 2098 (s), 1594 (s), 1374 (m), 1085 (m), 833 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_9H_{10}ClN_3NaO_3S$ $[M+Na]^+$: 298.0024, found: 298.0040.
TLC (25% ethyl acetate in hexanes), R*f*:	0.44 (UV, CAM).

8. Maury, J.; Feray, L.; Bertrand, M. P.; Kapat, A.; Renaud, P. Unexpected Conversion of Alkyl Azides to Alkyl Iodides and of Aryl Azides to *N*-*tert*-butyl Anilines. *Tetrahedron*, **2012**, *68*, 9606−9611.



(−)-1-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-*N*^{a}-(*tert*-butoxycarbonyl) -*L*-tryptophan (15); *N*-sulfonylated tryptophan (−)-15:

N-Boc-L-tryptophan (2.76 g, 9.07 mmol, 2.00 equiv) was azeotropically dried by concentration from anhydrous benzene (3 × 15 mL) under reduced pressure. The resulting residue was dissolved in tetrahydrofuran (20 mL) and cooled to −65 °C. A solution of lithium hexamethyldisilazide (LHMDS, 4.55 g, 47.2 mmol, 6.00 equiv) in tetrahydrofuran (20 mL) was added via cannula over 5 min. After 1 h, 4-(3-azidopropoxy)benzenesulfonyl chloride (**S5**, 1.25 g, 4.53 mmol, 1 equiv) was added via syringe in one portion and the reaction mixture was stirred for an additional 2 h at −65 °C. Excess base was quenched at this temperature by addition of a solution of acetic acid in ethyl acetate (1:1 v/v, 5 mL), then the ice−water bath was removed and the resulting mixture was allowed to stir and warm to room temperature. The mixture was then diluted with an aqueous hydrogen chloride solution (1 M, 100 mL) and was extracted with ethyl acetate (3 × 100 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated. The resulting residue was purified by flash column chromatography on silica gel (eluent: 5% acetic acid, 45% hexanes, 50% dichloromethane)[9] to afford *N*-sulfonylated tryptophan (−)-**15** (1.22 g, 50.8%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

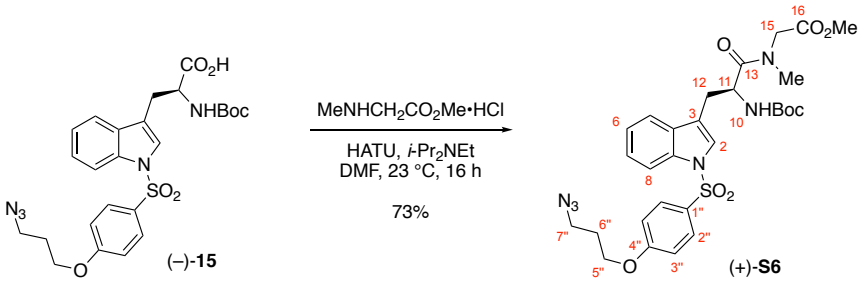
^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 12.7 (br-s, 1H, CO_2**H**), 7.88 (d, J = 8.2 Hz, 1H, C_8**H**), 7.84 (app-d, J = 9.0 Hz, 2H, $C_{2''}$**H**), 7.60–7.58 (m, 2H, C_2**H**, C_5**H**), 7.35 (t, J = 7.7 Hz, 1H, C_7**H**), 7.26 (t, J = 7.3 Hz, 1H, C_6**H**), 7.17 (d, J = 8.2 Hz, 1H, N-**H**), 7.05 (app-d, J = 9.0 Hz, 2H, $C_{3''}$**H**), 4.21–4.16 (m, 1H, C_{11}**H**), 4.05 (t, J = 6.0 Hz, 2H, $C_{5''}$**H**), 3.44 (t, J = 6.7 Hz, 2H, $C_{7''}$**H**), 3.11 (dd, J = 4.3, 14.8 Hz, 1H, C_{12}**H**$_a$), 2.95 (dd, J = 10.1, 14.8 Hz, 1H, C_{12}**H**$_b$), 1.93 (p, J = 6.4 Hz, 2H, $C_{6''}$**H**), 1.32 (s, 9H, C(C**H**$_3$)$_3$).

^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 25 °C): δ 173.3 (**C**$_{13}$), 162.7 (**C**$_{4''}$), 155.4 (**C**O_2*t*-Bu), 134.3 (**C**$_9$), 130.5 (**C**$_4$), 129.0 (**C**$_{2''}$), 128.5 (**C**$_{1''}$), 124.7 (**C**$_7$), 124.5 (**C**$_2$), 123.2 (**C**$_6$), 119.6(**C**$_5$), 118.7 (**C**$_3$), 115.3 (**C**$_{3''}$), 113.1 (**C**$_8$), 78.1 (**C**(CH$_3$)$_3$), 65.4 (**C**$_{5''}$), 53.3 (**C**$_{11}$), 47.5 (**C**$_{7''}$), 28.1 (C(**C**H$_3$)$_3$), 27.8 (**C**$_{6''}$), 26.2 (**C**$_{12}$).

9. To remove residual acetic acid, pooled fractions containing *N*-sulfonylated tryptophan (−)-**15** were concentrated under reduced pressure to approximately 10% of the volume, then diluted with benzene (100 mL) and concentrated. This process was repeated two more times.

FTIR (thin film) cm^{-1}:	2931 (w), 2100 (s), 1717 (s), 1653 (m), 1595 (m), 1497 (m), 1368 (s), 1261 (s), 1167 (s), 834 (m), 746 (w), 667 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{25}H_{33}N_6O_7S$ $[M+NH_4]^+$: 561.2126, found: 561.2131.
$[\alpha]_D^{23}$:	–18 (*c* = 0.14, DMSO).

TLC (5% AcOH, 5% CH_3OH, 40% hexanes, 50% CH_2Cl_2), R*f*: 0.47 (UV, CAM).



(+)-Methyl *N*-(1-((4-(3-azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-*N*^{a}-(*tert*-butoxycarbonyl)-*L*-tryptophyl)-*N*-methylglycinate (S6); dipeptide (+)-S6:

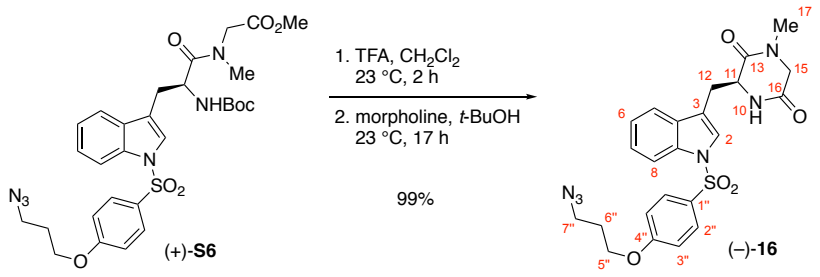
N,*N*-Diisopropylethylamine (3.00 mL, 17.0 mmol, 6.00 equiv) was added via syringe to a solution of carboxylic acid (−)-**15** (1.50 g, 2.83 mmol, 1 equiv), sarcosine methyl ester hydrochloride (791 mg, 5.66 mmol, 2.00 equiv), and *N*-[(Dimethylamino)-1*H*-1,2,3-triazolo-[4,5-*b*]pyridin-1-ylmethylene]-*N*-methyl-methanaminium hexafluorophosphate *N*-oxide (HATU, 2.59 g, 6.80 mmol, 2.40 equiv) in *N*,*N*-dimethylformamide (25 mL) at 23 °C. After 16 h, the reaction mixture was diluted with ethyl acetate (150 mL) and was washed with a saturated aqueous sodium bicarbonate solution (50 mL) and with a saturated aqueous sodium chloride solution (50 mL). The combined aqueous layers were extracted with ethyl acetate (2 × 50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 60% ethyl acetate in hexanes) to afford dipeptide (+)-**S6** (1.30 g, 73.3%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Based on the ^{1}H NMR analysis at 25 °C in $CDCl_3$, the product exists as a 5:1 mixture of conformers.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C):

Major conformer: δ 7.92 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.77 (app-d, *J* = 8.9 Hz, 2H, $C_{2''}$**H**), 7.54 (d, *J* = 7.7 Hz, 1H, C_5**H**), 7.44 (s, 1H, C_2**H**), 7.27 (app-t, *J* = 7.3 Hz, 1H, C_7**H**), 7.23–7.18 (m, 1H, C_6**H**), 6.83 (d, *J* = 9.0 Hz, 2H, $C_{3''}$**H**), 5.38 (d, *J* = 8.4 Hz, 1H, N_{10}**H**), 4.93 (dd, *J* = 6.2, 13.8 Hz, 1H, C_{11}**H**), 4.00 (d, *J* = 17.2 Hz, 1H, C_{15}**H**$_a$), 3.99 (t, *J* = 5.9 Hz, 2H, $C_{5''}$**H**), 3.92 (d, *J* = 17.2 Hz, 1H, C_{15}**H**$_b$), 3.71 (s, 3H, $N_{14}C$**H**$_3$), 3.43 (t, *J* = 6.5 Hz, 2H, $C_{7''}$**H**), 3.15–3.08 (m, 1H, C_{12}**H**$_a$), 3.05–2.95 (m, 1H, C_{12}**H**$_b$), 2.77 (s, 3H, C_{14}**H**), 1.98 (p, *J* = 6.2 Hz, 2H, $C_{6''}$**H**), 1.38 (s, 9H, C(C**H**$_3$)$_3$).

Minor conformer: δ 7.92 (d, *J* = 8.1 Hz, 2H, C_8**H**), 7.77 (app-d, *J* = 8.9 Hz, 2H, $C_{2''}$**H**), 7.51 (d, *J* = 7.8 Hz, 1H, C_5**H**), 7.39 (s, 1H, C_2**H**), 7.27 (app-t, *J* = 7.3 Hz, 1H, C_7**H**), 7.23–7.18 (m, 1H, C_6**H**), 6.83 (d, *J* = 9.0 Hz, 2H, $C_{3''}$**H**), 5.28 (d, *J* = 8.8 Hz, 1H, N_{10}**H**), 4.69 (dd, *J* = 6.9, 15.1 Hz, 1H, C_{11}**H**), 3.99 (t, *J* = 5.9 Hz, 2H, $C_{5''}$**H**), 3.87 (d, *J* = 18.4 Hz, 1H, C_{15}**H**$_a$), 3.79 (d, *J* = 18.3 Hz, 1H, C_{15}**H**$_b$), 3.59 (s,

	3H, $N_{14}C\mathbf{H}_3$), 3.43 (t, *J* = 6.5 Hz, 2H, $C_{7''}\mathbf{H}$), 3.15–3.08 (m, 1H, $C_{12}\mathbf{H}_a$), 3.05–2.95 (m, 1H, $C_{12}\mathbf{H}_b$), 2.85 (s, 3H, $C_{14}\mathbf{H}$), 1.98 (p, *J* = 6.2 Hz, 2H, $C_{6''}\mathbf{H}$), 1.37 (s, 9H, $C(C\mathbf{H}_3)_3$).
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C):	*Major conformer:* δ 172.2 ($\mathbf{C}_{13}$), 169.4 ($\mathbf{C}_{16}$), 162.9 ($\mathbf{C}_{4''}$), 155.2 ($N_{10}\mathbf{C}O_2t$-Bu), 135.1 ($\mathbf{C}_9$), 131.2 ($\mathbf{C}_4$), 130.2 ($\mathbf{C}_{1''}$), 129.3 ($\mathbf{C}_{2''}$), 125.0 ($\mathbf{C}_2$), 124.9 ($\mathbf{C}_7$), 123.3 ($\mathbf{C}_6$), 119.6 ($\mathbf{C}_5$), 117.3 ($\mathbf{C}_3$), 114.9 ($\mathbf{C}_{3''}$), 113.8 ($\mathbf{C}_8$), 80.0 ($\mathbf{C}(CH_3)_3$), 65.1 ($\mathbf{C}_{15}$), 52.4 ($N_{14}\mathbf{C}H_3$), 50.3 ($\mathbf{C}_{11}$), 49.7 ($\mathbf{C}_{5''}$), 48.0 ($\mathbf{C}_{7''}$), 36.5 ($\mathbf{C}_{14}$), 29.0 ($\mathbf{C}_{12}$), 28.6 ($\mathbf{C}_{6''}$), 28.4 ($C(\mathbf{C}H_3)_3$). *Minor conformer:* δ 172.1 ($\mathbf{C}_{13}$), 169.1 ($\mathbf{C}_{16}$), 162.9 ($\mathbf{C}_{4''}$), 155.2 ($N_{10}\mathbf{C}O_2t$-Bu), 135.1 ($\mathbf{C}_9$), 131.0 ($\mathbf{C}_4$), 130.2 ($\mathbf{C}_{1''}$), 129.2 ($\mathbf{C}_{2''}$), 125.0 ($\mathbf{C}_2$), 124.8 ($\mathbf{C}_7$), 123.3 ($\mathbf{C}_6$), 119.6 ($\mathbf{C}_5$), 117.6 ($\mathbf{C}_3$), 114.9 ($\mathbf{C}_{3''}$), 113.8 ($\mathbf{C}_8$), 80.1 ($\mathbf{C}(CH_3)_3$), 65.1 ($\mathbf{C}_{15}$), 52.6 ($N_{14}\mathbf{C}H_3$), 51.1 ($\mathbf{C}_{5''}$), 50.1 ($\mathbf{C}_{11}$), 48.0 ($\mathbf{C}_{7''}$), 36.5 35.3 ($\mathbf{C}_{14}$), 29.1 ($\mathbf{C}_{12}$), 28.6 ($\mathbf{C}_{6''}$), 28.4 ($C(\mathbf{C}H_3)_3$).
FTIR (thin film) cm^{-1}:	3318 (w), 2933 (w), 2100 (s), 1750 (s), 1700 (s), 1653 (s), 1594 (m), 1497 (w), 1365 (s), 1260 (s), 1168 (s), 977 (w), 834 (m), 668 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{29}H_{36}N_6NaO_8S$ $[M+Na]^+$: 651.2208, found: 651.2212.
$[\alpha]_D^{23}$:	+31 (*c* = 0.12, $CHCl_3$).
TLC (60% ethyl acetate in hexanes), R*f*:	0.56 (UV, CAM).



(−)-(*S*)-3-((1-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-1*H*-indol-3-yl)-methyl)-1-methylpiperazine-2,5-dione (16); diketopiperazine (−)-16:

Trifluoroacetic acid (TFA, 3.5 mL) was added via syringe to a solution of dipeptide (+)-**S6** (951 mg, 1.51 mmol, 1 equiv) in dichloromethane (17.5 mL) at 23 °C. After 2 h, the reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in *t*-butanol (15 mL). The reaction mixture was stirred vigorously at 23 °C as morpholine (5.6 mL) was added via syringe. After 17 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate (200 mL) and was washed with an aqueous hydrogen chloride solution (1 M, 3 × 50 mL) and with a 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 on silica gel (eluent: 75% acetone in dichloromethane) to afford diketopiperazine (−)-**16** (741 mg, 98.8%) as a colorless oil. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.90 (d, J = 8.3 Hz, 1H, C_8**H**), 7.78 (app-d, J = 8.9 Hz, 2H, $C_{2''}$**H**), 7.55–7.45 (m, 3H, C_2**H**, C_5**H**, N_{10}**H**), 7.27 (app-t, J = 6.7 Hz, 1H, C_7**H**), 7.19 (app-t, J = 7.6 Hz, 1H, C_6**H**), 6.85 (app-d, J = 9.0 Hz, 2H, $C_{3''}$**H**), 4.28 (br-s, 1H, C_{11}**H**), 3.98 (t, J = 5.9 Hz, 2H, $C_{5''}$**H**), 3.48–3.40 (m, 1H, C_{15}**H**$_a$), 3.42 (t, J = 6.5 Hz, 2H, $C_{7''}$**H**), 3.29 (dd, J = 5.6, 14.6 Hz, 1H, C_{12}**H**$_a$), 3.19 (dd, J = 3.4, 14.4 Hz, 1H, C_{12}**H**$_b$), 2.93 (d, J = 17.3 Hz, 1H, C_{15}**H**$_b$), 2.59 (s, 3H, C_{17}**H**), 1.97 (p, J = 6.1 Hz, 2H, $C_{6''}$**H**).

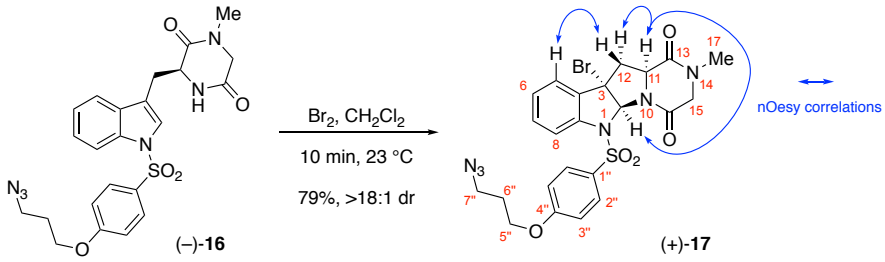
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.3 (**C**$_{13}$), 165.7 (**C**$_{16}$), 163.1 (**C**$_{4''}$), 135.0 (**C**$_9$), 130.3 (**C**$_4$), 129.7 (**C**$_{1''}$), 129.4 (**C**$_{2''}$), 126.0 (**C**$_2$), 125.2 (**C**$_7$), 123.5 (**C**$_6$), 120.0 (**C**$_5$), 116.1 (**C**$_3$), 115.2 (**C**$_{3''}$), 113.6 (**C**$_8$), 65.2 (**C**$_{5''}$), 55.2 (**C**$_{11}$), 51.1 (**C**$_{15}$), 48.0 (**C**$_{7''}$), 33.8 (**C**$_{17}$), 30.6 (**C**$_{12}$), 28.6 (**C**$_{6''}$).

FTIR (thin film) cm^{-1}: 3235 (w), 3103 (w), 2934 (w), 2100 (s), 1685 (s), 1653 (s), 1594 (m), 1364 (m), 1263 (s), 1167 (s), 1122 (m), 1096 (m), 978 (m), 835 (m), 694 (m).

HRMS (DART) (*m/z*): calc'd for $C_{23}H_{25}N_6O_5S$ $[M+H]^+$: 497.1602, found: 497.1616.

$[\alpha]_D^{23}$: –71 (c = 0.11, $CHCl_3$).

TLC (50% acetone in dichloromethane), R*f*: 0.43 (UV, CAM).



(+)-(5a*S*,10b*S*,11a*S*)-6-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-10b-bromo-2-methyl-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (17); *endo*-tetracyclic bromide (+)-17:

A solution of bromine (1.0 M, 6.1 mL, 6.1 mmol, 5.0 equiv) in dichloromethane was slowly poured into a solution of diketopiperazine (−)-**16** (606 mg, 1.22 mmol, 1 equiv) in dichloromethane (25 mL) at 23 °C. After 10 min, the solution was diluted with a saturated aqueous sodium thiosulfate solution (40 mL) and was extracted with ethyl acetate (120 mL). The organic layer was washed with a saturated aqueous sodium bicarbonate solution (2 × 40 mL), was washed with a saturated aqueous sodium chloride solution (25 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting solid was suspended in diethyl ether (120 mL), was collected by filtration, and was washed with diethyl ether (3 × 50 mL) to afford *endo*-tetracyclic bromide (+)-**17** and its minor *exo*-diastereomer (556 mg, 79.2%, >18:1 dr) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and gNOESY experiments.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 7.84 (app-d, J = 9.0 Hz, 2H, $C_{2''}$**H**), 7.48 (d, J = 7.5 Hz, 1H, C_5**H**), 7.35–7.28 (m, 2H, C_7**H**, C_8**H**), 7.16 (app-t, J = 7.0 Hz, 1H, C_6**H**), 7.04 (app-d, J = 9.0 Hz, 2H, $C_{3''}$**H**), 6.27 (s, 1H, C_2**H**), 4.61 (dd, J = 5.6, 9.7 Hz, 1H, C_{11}**H**), 4.19 (d, J = 17.1 Hz, 1H, C_{15}**H**$_a$), 4.07 (t, J = 6.1 Hz, 2H, $C_{5''}$**H**), 3.77 (d, J = 17.2 Hz, 1H, C_{15}**H**$_b$), 3.47 (t, J = 6.1 Hz, 2H, $C_{7''}$**H**), 3.28 (dd, J = 5.6, 14.2 Hz, 1H, C_{12}**H**$_\beta$), 3.01 (dd, J = 10.0, 14.2 Hz, 1H, C_{12}**H**$_\alpha$), 2.70 (s, 3H, C_{17}**H**), 1.94 (p, J = 6.4 Hz, 2H, $C_{6''}$**H**).

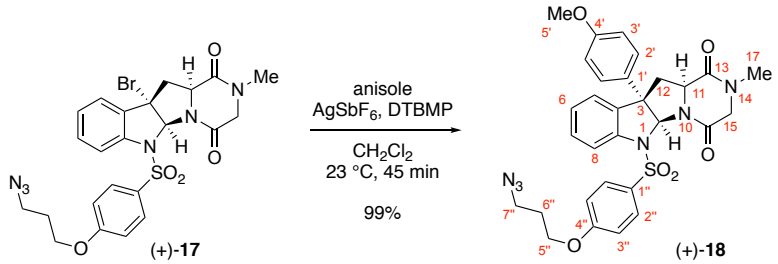
^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 25 °C): δ 166.3 (**C**$_{13}$), 165.0 (**C**$_{16}$), 162.4 (**C**$_{4''}$), 138.5 (**C**$_9$), 135.1 (**C**$_4$), 130.6 (**C**$_7$), 130.4 (**C**$_{2''}$), 129.6 (**C**$_{1''}$), 125.9 (**C**$_6$), 125.2 (**C**$_5$), 116.5 (**C**$_8$), 114.6 (**C**$_{3''}$), 86.1 (**C**$_2$), 65.3 (**C**$_{5''}$), 61.5 (**C**$_3$), 56.8 (**C**$_{11}$), 53.3 (**C**$_{15}$), 47.5 (**C**$_{7''}$), 38.6 (**C**$_{12}$), 32.7 (**C**$_{17}$), 27.9 (**C**$_{6''}$).

FTIR (thin film) cm^{-1}: 2097 (s), 1685 (s), 1653 (m), 1594 (m), 1497 (m), 1259 (m), 1073 (m), 668 (m).

HRMS (DART) (*m/z*): calc'd for $C_{23}H_{24}BrN_6O_5S$ $[M+H]^+$: 575.0707, found: 575.0713.

$[\alpha]_D^{23}$: +92 (*c* = 0.26, DMSO).

TLC (50% acetone in dichloromethane), R*f*: 0.65 (UV, CAM).



(+)-(5a*S*,10b*S*,11a*S*)-6-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-10b-(4-methoxyphenyl)-2-methyl-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (18); anisole adduct (+)-18:

Silver hexafluoroantimonate (708 mg, 8.58 mmol, 2.00 equiv) was added as a solid in one portion to a solution of bromide (+)-**17** (590 mg, 1.03 mmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 463 mg, 2.26 mmol, 2.20 equiv), and anisole (2.0 mL, 18 mmol, 17 equiv) in dichloromethane (8.0 mL) at 23 °C. After 45 min, the suspension was diluted with dichloromethane (50 mL) and was filtered through a pad of diatomaceous earth. The filter cake was washed with dichloromethane (3 × 50 mL) and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10→30% acetone in dichloromethane) to afford anisole adduct (+)-**18** (613 mg, 98.7%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.57 (d, J = 8.0 Hz, 1H, C_8**H**), 7.32 (app-d, J = 9.0 Hz, 2H, $C_{2''}$**H**), 7.28–7.24 (m, 1H, C_7**H**), 7.14–7.09 (m, 2H, C_5**H**, C_6**H**), 6.64 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.57 (app-d, J = 9.0 Hz, 2H, $C_{3'}$**H**), 6.49 (app-d, J = 9.0 Hz, 2H, $C_{3''}$**H**), 6.10 (s, 1H, C_2**H**), 4.42 (dd, J = 6.9, 8.9 Hz, 1H, C_{11}**H**), 4.09 (d, J = 17.4 Hz, 1H, C_{15}**H**$_a$), 3.95 (t, J = 6.2 Hz, 2H, $C_{5''}$**H**), 3.79 (d, J = 17.5 Hz, 1H, C_{15}**H**$_b$), 3.74 (s, 3H, $C_{5'}$**H**), 3.46 (t, J = 6.6 Hz, 2H, $C_{7''}$**H**), 3.07 (dd, J = 6.7, 14.1 Hz, 1H, C_{12}**H**$_a$), 2.86–2.77 (m, 1H, C_{12}**H**$_b$), 2.83 (s, 3H, C_{17}**H**), 1.99 (p, J = 6.2 Hz, 2H, $C_{6''}$**H**).

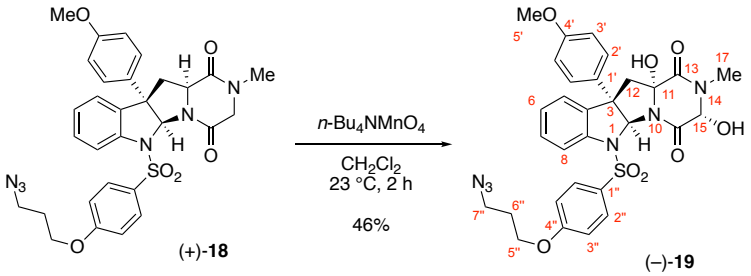
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.1 (**C**$_{13}$), 165.4 (**C**$_{16}$), 162.2 (**C**$_{4''}$), 158.6 (**C**$_{4'}$), 140.1 (**C**$_9$), 136.0 (**C**$_4$), 133.1 (**C**$_{1'}$), 130.0 (**C**$_{1''}$), 129.6 (**C**$_{2''}$), 129.2 (**C**$_7$), 128.1 (**C**$_{2'}$), 126.2 (**C**$_5$), 125.5 (**C**$_6$), 117.5 (**C**$_8$), 114.3 (**C**$_{3''}$), 114.2 (**C**$_{3'}$), 87.2 (**C**$_2$), 64.9 (**C**$_{5''}$), 59.4 (**C**$_3$), 58.4 (**C**$_{11}$), 55.4 (**C**$_{5'}$), 54.4 (**C**$_{15}$), 48.1 (**C**$_{7''}$), 39.2 (**C**$_{12}$), 33.6 (**C**$_{17}$), 28.6 (**C**$_{6''}$).

FTIR (thin film) cm^{-1}: 2936 (w), 2100 (s), 1684 (s), 1654 (m), 1457 (m), 1261 (s), 1159 (s), 830 (m), 667 (s).

HRMS (DART) (*m/z*): calc'd for $C_{30}H_{31}N_6O_6S$ $[M+H]^+$: 603.2020, found: 603.2012.

$[\alpha]_D^{23}$: +23 (*c* = 0.24, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.48 (UV, CAM).



(−)-(3*R*,5a*S*,10b*S*,11a*R*)-6-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-3,11a-dihydroxy-10b-(4-methoxyphenyl)-2-methyl-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (19); diol (−)-19:

Tetra-*n*-butylammonium permanganate[5] (900 mg, 2.49 mmol, 5.00 equiv) was added as a solid in one portion to a solution of anisole adduct (+)-**18** (300 mg, 486 μmol, 1 equiv) in dichloromethane (20 mL) at 23 °C. After 2 h, the dark purple reaction mixture was diluted with a saturated aqueous sodium sulfite solution (30 mL) and with ethyl acetate (125 mL). The resulting mixture was washed with a saturated aqueous sodium bicarbonate solution (40 mL), the layers were separated, and the organic layer was washed with a saturated aqueous sodium chloride solution (40 mL). The combined aqueous layers were extracted with ethyl acetate (2 × 50 mL) and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10→25% acetone in dichloromethane) to afford diol (−)-**19** (146 mg, 46.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.57 (d, J = 8.0 Hz, 1H, C_8**H**), 7.32–7.27 (m, 1H, C_7**H**), 7.19–7.15 (m, 4H, $C_{2''}$**H**, C_5**H**, C_6**H**), 6.78 (app-d, J = 8.7 Hz, 2H, $C_{2'}$**H**), 6.56 (app-d, J = 8.7 Hz, 2H, $C_{3'}$**H**), 6.41 (app-d, J = 8.8 Hz, 2H, $C_{3''}$**H**), 6.33 (s, 1H, C_2**H**), 6.07 (br-s, 1H, C_{15}O**H**), 5.48 (br-s, 1H, C_{11}O**H**), 5.19 (d, J = 5.7 Hz, 1H, C_{15}**H**), 3.96–3.92 (m, 2H, $C_{5''}$**H**), 3.75 (s, 3H, $C_{5'}$**H**), 3.48 (t, J = 6.5 Hz, 2H, $C_{7''}$**H**), 3.44 (m, 1H, C_{12}**H**$_a$), 3.00 (s, 3H, C_{17}**H**), 2.87 (d, J = 15.1 Hz, 1H, C_{12}**H**$_b$), 2.01 (p, J = 6.1 Hz, 2H, $C_{6''}$**H**).

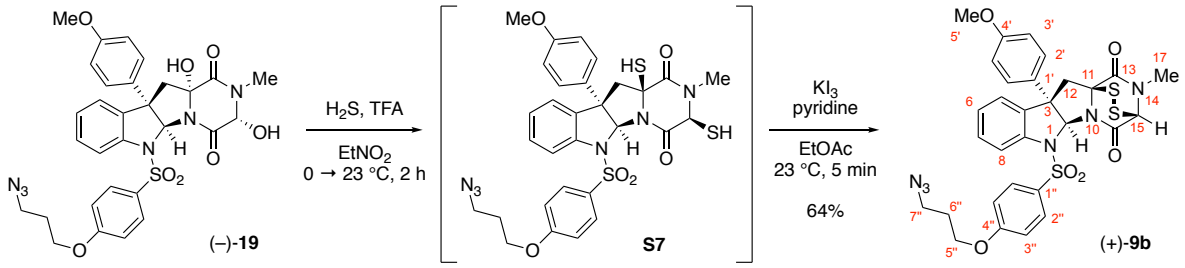
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C): δ 167.5 (**C**$_{13}$), 166.3 (**C**$_{16}$), 162.3 (**C**$_{4''}$), 158.5 (**C**$_{4'}$), 140.0 (**C**$_9$), 137.2 (**C**$_4$), 133.9 (**C**$_{1'}$), 129.8 (**C**$_{1''}$), 129.5 (**C**$_{2''}$), 129.3 (**C**$_7$), 128.7 (**C**$_{2'}$), 126.7 (**C**$_5$), 126.2 (**C**$_6$), 118.0 (**C**$_8$), 114.2 (**C**$_{3''}$), 114.1 (**C**$_{3'}$), 88.4 (**C**$_{11}$), 87.9 (**C**$_2$), 83.2 (**C**$_{15}$), 64.9 (**C**$_{5''}$), 58.7 (**C**$_3$), 55.4 (**C**$_{5'}$), 49.0 (**C**$_{12}$), 48.1 (**C**$_{7''}$), 32.4 (**C**$_{17}$), 28.7 (**C**$_{6''}$).

FTIR (thin film) cm^{-1}: 3385 (m), 2936 (w), 2099 (s), 1700 (s), 1685 (s), 1595 (m), 1513 (m), 1362 (m), 1258 (s), 1163 (s), 832 (m), 667 (m).

HRMS (DART) (*m/z*): calc'd for $C_{30}H_{31}N_6O_8S$ $[M+H]^+$: 635.1919, found: 635.1906.

$[\alpha]_D^{23}$: –11 (*c* = 0.10, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.36 (UV, CAM).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-6-((4-(3-Azidopropoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-10b-(4-methoxyphenyl)-2-methyl-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5] pyrrolo[2,3-*b*]indole-1,4-dione (9b); epidithiodiketopiperazine azide (+)-9b:

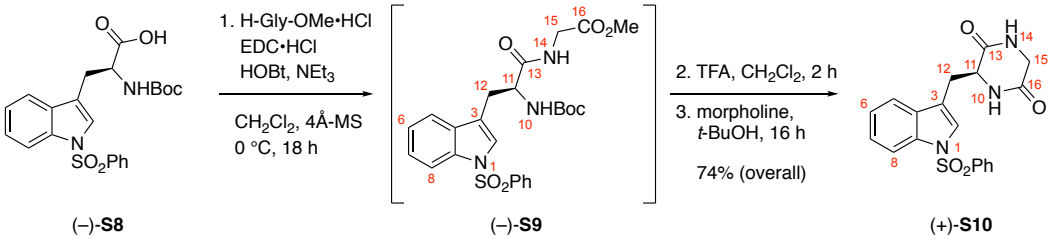
A solution of diol (−)-**19** (142 mg, 224 μmol, 1 equiv) in anhydrous nitroethane (9.5 mL) at 0 °C was sparged with hydrogen sulfide gas for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture, providing a saturated hydrogen sulfide solution. Trifluoroacetic acid (TFA, 7.1 mL) was added via syringe over 20 seconds, and the sparging with hydrogen sulfide was maintained for another 20 min. The ice–water bath was removed, and the solution was allowed to stir and warm to 23 °C under an atmosphere of hydrogen sulfide. After 2 h, the reaction mixture was diluted with ethyl acetate (110 mL) and was slowly poured into a saturated aqueous sodium bicarbonate solution (50 mL). The organic layer was washed with a saturated aqueous sodium chloride solution (30 mL). A stock solution of potassium triiodide in pyridine[6] was added dropwise into the organic layer containing crude bisthiol **S7** until a persistent yellow color was observed. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 M, 2 × 30 mL), was washed with a saturated aqueous sodium chloride solution (30 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→20% ethyl acetate in dichloromethane) to afford epidithiodiketopiperazine azide (+)-**9b** (93.9 mg, 64.2%) as a beige solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.[10]

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.64 (d, J = 8.0 Hz, 1H, C_8**H**), 7.39 (td, J = 1.6, 7.0 Hz, 1H, C_7**H**), 7.28–7.22 (m, 2H, C_6**H**, C_5**H**), 7.20 (app-d, J = 8.9 Hz, 2H, $C_{2''}$**H**), 6.73 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.61 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.40 (app-d, J = 8.9 Hz, 2H, $C_{3''}$**H**), 6.32 (s, 1H, C_2**H**), 5.25 (s, 1H, C_{15}**H**), 3.95–3.90 (m, 2H, $C_{5''}$**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.58 (d, J = 15.5 Hz, 1H, C_{12}**H**$_a$), 3.48 (t, J = 6.5 Hz, 2H, $C_{7''}$**H**), 3.10 (s, 3H,

10. The relative stereochemistry of epidisulfide (+)-**9b** has been confirmed by key NOESY cross–peaks on the corresponding bis(methylthioether). Our assignment is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (3.09–3.04, 7.10–7.06), (3.09–3.04, 1.86), (2.93, 6.82), (2.93, 6.55). This derivatized compound was prepared in one step using our methodology developed to access (+)-gliocladin B (Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803). The corresponding bis(methylthioether) of epidisulfide (+)-**9b** was characterized as follows: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.67 (d, J = 8.8 Hz, 2H, $C_{2''}$**H**), 7.56 (d, J = 8.1 Hz, 1H, C_8**H**), 7.29 (ddd, J = 3.0, 5.8, 8.4, 1H, C_7**H**), 7.10–7.06 (m, 2H, C_6**H**, C_5**H**), 6.82 (d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.70 (d, J = 8.9 Hz, 2H, $C_{3''}$**H**), 6.65 (d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.55 (s, 1H, C_2**H**), 4.51 (s, 1H, C_{15}**H**), 4.00 (t, J = 5.9 Hz, 2H, $C_{5''}$**H**), 3.73 (s, 3H, $C_{5'}$**H**), 3.49 (t, J = 6.5 Hz, 2H, $C_{7''}$**H**), 3.09–3.04 (m, 4H, C_{12}**H**$_a$, C_{17}**H**) 2.93 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.27 (s, 3H, C_{15}S**C**H$_3$), 2.03 (p, J = 6.2 Hz, 2H, $C_{6''}$**H**) 1.86 (s, 3H, C_{11}S**C**H$_3$). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.2 (**C**$_{13}$), 162.3 ($C_{4''}$**H** or **C**$_{16}$), 162.3 ($C_{4''}$**H** or **C**$_{16}$), 158.7 (**C**$_{4'}$), 142.6 (**C**$_9$), 136.6 (**C**$_4$), 134.2 (**C**$_{1'}$), 129.4 ($C_{1''}$**H**), 129.4 ($C_{2''}$**H**), 129.1 (**C**$_7$), 127.2 (**C**$_{2'}$), 125.0 (**C**$_6$), 124.1 (**C**$_5$), 117.6 (**C**$_8$), 114.5 (**C**$_{3'}$ or **C**$_{3''}$), 114.3 (**C**$_{3'}$ or **C**$_{3''}$), 86.2(**C**$_2$), 69.9 (**C**$_{11}$), 67.8 (**C**$_{15}$), 65.0 ($C_{5''}$**H**), 57.1 (**C**$_3$), 55.5 (**C**$_{5'}$), 48.2 ($C_{7''}$**H**), 46.4 (**C**$_{12}$), 32.5 (**C**$_{17}$), 28.7 ($C_{6''}$**H**), 17.2 (C_{15}S**C**H$_3$), 15.5 (C_{11}S**C**H$_3$). HRMS (ESI) (*m*/*z*): calc'd for $C_{32}H_{34}N_6NaO_6S_3$ [M+Na]$^+$: 717.1594, found 717.1588.

	C_{17}**H**), 2.82 (d, *J* = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.00 (p, *J* = 6.2 Hz, 2H, $C_{6''}$**H**).
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C):	δ 165.1 (**C**$_{13}$), 162.1(**C**$_{4''}$), 160.0 (**C**$_{16}$), 158.6 (**C**$_{4'}$), 141.5 (**C**$_9$), 135.8 (**C**$_4$), 131.3 (**C**$_{1'}$), 129.9 (**C**$_{1''}$), 129.7 (**C**$_7$), 129.2 (**C**$_{2''}$), 127.9 (**C**$_{2'}$), 126.1 (**C**$_5$), 125.6 (**C**$_6$), 119.3 (**C**$_8$), 114.3 (**C**$_{3'}$), 114.0 (**C**$_{3''}$), 87.7 (**C**$_2$), 74.5 (**C**$_{11}$), 68.3 (**C**$_{15}$), 64.7 (**C**$_{5''}$), 59.4 (**C**$_3$), 55.4 (**C**$_{5'}$), 48.0 (**C**$_{7''}$), 45.8 (**C**$_{12}$), 32.0 (**C**$_{17}$), 28.5 (**C**$_{6''}$).
FTIR (thin film) cm^{-1}:	2930 (w), 2098 (s), 1718 (s), 1700 (s), 1685 (s), 1653 (m), 1559 (m), 1507 (m), 1457 (m), 1362 (m), 1259 (s), 1162 (s), 831 (m), 667 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{30}H_{32}N_7O_6S_3$ $[M+NH_4]^+$: 682.1571, found: 682.1559.
$[\alpha]_D^{23}$:	+222 (*c* = 0.08, $CHCl_3$).

TLC (20% ethyl acetate in dichloromethane), R*f*: 0.35 (UV, CAM, $AgNO_3$).



(−)-**S8** (−)-**S9** (+)-**S10**

(+)-(*S*)-3-((1-(Phenylsulfonyl)-1*H*-indol-3-yl)methyl)piperazine-2,5-dione (S10); diketopiperazine (+)-S10:

Triethylamine (47.0 mL, 337 mmol, 7.00 equiv) was added via cannula to a solution of L-tryptophan derivative (−)-**S8**[11] (21.4 g, 48.1 mmol, 1 equiv), glycine methyl ester hydrochloride (7.86 g, 62.6 mmol, 1.30 equiv), 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrogen chloride (EDC•HCl, 21.2 g, 111 mmol, 2.30 equiv), *N*-hydroxybenzotriazole (HOBt, 9.76 g, 72.2 mmol, 1.20 equiv), and powdered 4 Å molecular sieves (25.0 g) in dichloromethane (500 mL) at 0 °C. The ice−water bath was removed and the solution was allowed to stir and warm to 23 °C. After 18 h, the reaction mixture was washed with an aqueous hydrogen chloride solution (1 M, 150 mL), the layers were separated, and the organic layer was washed sequentially with a saturated aqueous sodium bicarbonate solution (150 mL) and with a saturated aqueous sodium chloride solution (100 mL). The organic layer was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure to afford dipeptide (−)-**S9** as an orange foam that was used in the next step without further purification. [12]

Trifluoroacetic acid (TFA, 73 mL) was added to a solution of crude dipeptide (−)-**S9** (22.8 g) in dichloromethane (365 mL) at 23 °C. After 2 h, the reaction mixture was concentrated under reduced pressure, and the resulting residue was dissolved in *tert*-butanol (335 mL) and stirred vigorously at 23 °C as morpholine (125 mL) was added via cannula. After 16 h, the reaction mixture was concentrated under reduced pressure, and the resulting orange oil was dissolved in diethyl ether (225 mL) and ethyl acetate (75 mL). The resulting solution was stirred vigorously and was diluted with an aqueous hydrogen chloride solution (1 M, 225 mL), resulting in the formation of a white precipitate. After 1 h, the solids were collected by filtration and were washed sequentially with diethyl ether (3 × 100 mL) and with deionized water (4 × 100 mL), and were dried under reduced pressure at 50 °C for 12 h to afford diketopiperazine (+)-**S10** (13.6 g, 73.7% overall) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 8.26 (d, J = 2.1 Hz, 1H, N**H**), 7.92 (s, 1H, N**H**), 7.92–7.89 (m, 2H, SO_2Ph-*o*-**H**), 7.85 (d, J = 8.2 Hz, 1H, C_8**H**), 7.68 (app-t, J = 7.4 Hz, 1H, SO_2Ph-*p*-**H**),

11. Movassaghi, M.; Schmidt, M. A.; Ashenhurst, J. A. Concise Total Synthesis of (+)-WIN 64821 and (−)-Ditryptophenaline. *Angew. Chemie. Int. Ed.* **2008**, *47*, 1485−1487.
12. An analytical sample of amide (−)-**S9** was obtained by flash column chromatography on silica gel (eluent: 50% ethyl acetate in hexanes). The amide (−)-**S9** was characterized as follows: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.93 (d, J = 8.3 Hz, 1H, C_8**H**), 7.82 (d, J = 7.6 Hz, 2H, SO_2Ph-*o*-**H**), 7.52–7.46 (m, 2H, C_5**H**, SO_2Ph-*p*-**H**), 7.44 (s, 1H, C_2**H**), 7.38 (t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 7.27 (t, J = 7.6 Hz, 1H, C_7**H**), 7.19 (J = 7.6 Hz, 1H, C_6**H**), 6.62 (br-s, 1H, N**H**), 5.20 (d, J = 8.2 Hz, 1H, N**H**$CO_2C(CH_3)_3$), 4.47 (br-s, 1H, C_{11}**H**), 3.97–3.84 (m, 2H, C_{15}**H**), 3.67 (s, 3H, O**C**H_3), 3.21–3.04 (m, 2H, C_{12}**H**), 1.36 (s, 9H, OCCH_3). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 171.6 (**C**$_{13}$), 170.0 (**C**$_{16}$), 155.6 (NH**C**$O_2C(CH_3)_3$), 138.3 (SO_2Ph-*ipso*-**C**), 135.3 (**C**$_9$), 133.9 (SO_2Ph-*p*-**C**), 130.9 (**C**$_4$), 129.4 (SO_2Ph-*m*-**C**), 126.9 (SO_2Ph-*o*-**C**), 125.1 (**C**$_2$), 124.7 (**C**$_7$), 123.5 (**C**$_6$), 119.7 (**C**$_5$), 118.0 (**C**$_3$), 113.8 (**C**$_8$), 80.6 (O**C**$(CH_3)_3$), 54.3 (**C**$_{11}$), 52.5 (O**C**H_3), 41.3 (**C**$_{15}$), 28.4 (OC(**C**$H_3)_3$), 28.0 (**C**$_{12}$). FTIR (thin film) cm^{-1}: 3309 (m), 2977 (w), 1748 (m), 1662 (s), 1520 (s), 1447 (m), 1365 (s), 1278 (s), 746 (m). HRMS (ESI) (*m/z*): calc'd for $C_{25}H_{29}N_3NaO_7S$ $[M+Na]^+$: 538.1618, found 538.1624. $[\alpha]_D^{23}$: –5.0 (*c* = 0.20, $CHCl_3$). TLC (100% ethyl acetate), R*f*: 0.74 (UV, CAM).

7.63 (d, J = 7.6 Hz, 1H, C_5**H**), 7.59–7.56 (m, 3H, C_2**H**, SO_2Ph-*m*-**H**), 7.32 (app-t, J = 7.7 Hz, 1H, C_7**H**), 7.24 (app-t, J = 7.5 Hz, 1H, C_6**H**), 4.18–4.12 (m, 1H, C_{11}**H**), 3.42 (dd, J = 1.9, 17.6 Hz, 1H, C_{15}**H**$_a$), 3.21 (dd, J = 4.6, 14.7 Hz, 1H, C_{12}**H**$_a$), 3.01 (dd, J = 4.7, 14.4 Hz, 1H, C_{12}**H**$_b$), 2.86 (app-d, J = 16.5 Hz, 1H, C_{15}**H**$_b$).

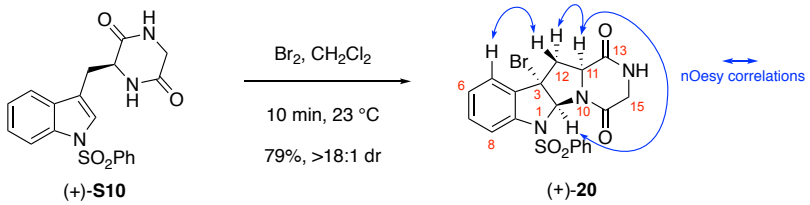
$^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6, 25 °C): δ 167.2 (**C**$_{13}$), 165.4 (**C**$_{16}$), 136.9 (SO_2Ph-*ipso*-**C**), 134.6 (SO_2Ph-*p*-**C**), 134.0 (**C**$_9$), 130.8 (**C**$_4$), 129.8 (SO_2Ph-*m*-**C**), 126.6 (SO_2Ph-*o*-**C**), 125.4 (**C**$_2$), 124.8 (**C**$_7$), 123.3 (**C**$_6$), 120.3 (**C**$_5$), 117.4 (**C**$_3$), 112.9 (**C**$_8$), 54.3 (**C**$_{11}$), 43.9 (**C**$_{15}$), 28.0 (**C**$_{12}$).

FTIR (thin film) cm^{-1}: 3048 (m), 1664 (s), 1457 (m), 1364 (m), 1326 (m), 1274 (m), 1169 (s), 1118 (s), 976 (w), 826 (w).

HRMS (DART) (*m/z*): calc'd for $C_{19}H_{18}N_3O_4S$ $[M+H]^+$: 384.1013, found: 384.1014.

$[\alpha]_D^{23}$: +13 (*c* = 0.20, DMSO).

TLC (30% acetone in dichloromethane), R*f*: 0.11 (UV, CAM).



(+)-(5a*S*,10b*S*,11a*S*)-10b-Bromo-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (20); *endo*-tetracyclic bromide (+)-20:

A solution of bromine (1.0 M, 26 mL, 26 mmol, 5.0 equiv) in dichloromethane was slowly poured into a solution of diketopiperazine (+)-**S10** (2.00 g, 5.22 mmol, 1 equiv) in dichloromethane (105 mL) at 23 °C. After 10 min, the reaction mixture was diluted with a saturated aqueous sodium thiosulfate solution (65 mL) and was extracted with ethyl acetate (350 mL). The organic layer was washed with a saturated aqueous sodium bicarbonate solution (2 × 80 mL) and with a saturated aqueous sodium chloride solution (80 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting solid was suspended in diethyl ether (200 mL), was collected by filtration, and was washed with diethyl ether (3 × 50 mL) to afford a mixture of the *endo*-tetracyclic bromide (+)-**20** and its minor *exo*-diastereomer (1.91 g, 79.2%, >18:1 dr) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, gHMBC, and gNOESY experiments.

^{1}H NMR (400 MHz, DMSO-d_6, 25 °C): δ 8.01 (app-d, J = 4.8 Hz, 1H, N_{14}**H**), 7.91 (app-d, J = 8.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.65–7.61 (app-t, J = 7.4 Hz, 1H, SO_2Ph-*p*-**H**), 7.55–7.51 (m, 2H, SO_2Ph-*m*-**H**), 7.47 (d, J = 7.6 Hz, 1H, C_5**H**), 7.34–7.32 (m, 2H, C_7**H**, C_8**H**), 7.17–7.13 (m, 1H, C_6**H**), 6.28 (s, 1H, C_2**H**), 4.54 (dd, J = 4.2, 10.0 Hz, 1H, C_{11}**H**), 3.98 (d, J = 17.1 Hz, 1H, C_{15}**H**$_a$), 3.48 (dd, J = 5.0, 17.1 Hz, 1H C_{15}**H**$_b$), 3.38–3.33 (m, 1H, C_{12}**H**$_\beta$), 2.97 (dd, J = 10.2, 14.0 Hz, 1H, C_{12}**H**$_\alpha$).

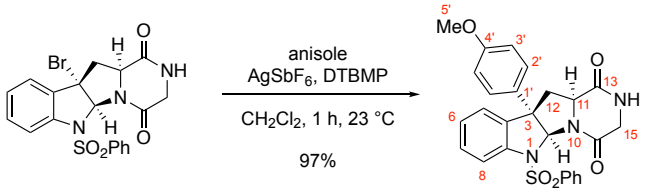
^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, 25 °C): δ 168.0 (**C**$_{13}$), 165.9 (**C**$_{16}$), 138.3 (**C**$_9$), 138.0 (SO_2Ph-*ipso*-**C**), 134.7 (**C**$_4$), 134.0 (SO_2Ph-*p*-**C**), 130.71 (**C**$_7$), 129.1 (SO_2Ph-*m*-**C**), 128.0 (SO_2Ph-*o*-**C**), 125.9 (**C**$_6$), 125.4 (**C**$_5$), 116.5 (**C**$_8$), 86.0 (**C**$_2$), 61.6 (**C**$_3$), 57.1 (**C**$_{11}$), 46.3 (**C**$_{15}$), 37.2 (**C**$_{12}$).

FTIR (thin film) cm^{-1}: 1684 (s), 1653 (s), 1559 (m), 1540 (m), 1473 (m), 1457 (m), 1165 (s), 1090 (m), 971 (w), 948 (w), 731 (m), 683 (w), 667 (m).

HRMS (DART) (*m/z*) calc'd for $C_{19}H_{17}BrN_3O_4S$ $[M+H]^+$: 462.0118, found: 462.0154.

$[\alpha]_D^{23}$: +143 (c = 0.29, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.37 (UV, CAM).



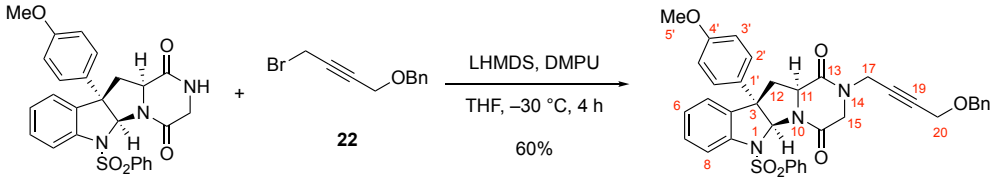
(+)-(5a*S*,10b*S*,11a*S*)-10b-(4-Methoxyphenyl)-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (21); anisole adduct (+)-21:

Silver hexafluoroantimonate (2.95 g, 8.58 mmol, 2.00 equiv) was added as a solid in one portion to a solution of *endo*-tetracyclic bromide (+)-**20** (2.00 g, 4.29 mmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 1.94 g, 9.44 mmol, 2.20 equiv), and anisole (22 mL) in dichloromethane (22 mL) at 23 °C. After 1 h, the reaction mixture was diluted with dichloromethane (50 mL) and was filtered through a pad of diatomaceous earth. The filter cake was washed with dichloromethane (3 × 50 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→70% acetone in dichloromethane) to afford anisole adduct (+)-**21** (2.03 g, 96.6%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C):	δ 7.56 (d, *J* = 8.0 Hz, 1H, C_8**H**), 7.41 (app-d, *J* = 8.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.31–7.26 (m, 2H, C_7**H**, SO_2Ph-*p*-**H**), 7.14-7.10 (m, 2H, C_5**H**, C_6**H**), 7.06 (app-t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**) 6.67 (app-d, *J* = 8.9 Hz, 2H, $C_{2'}$**H**), 6.59 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.50 (d, *J* = 4.5 Hz, 1H, N_{14}**H**), 6.16 (s, 1H, C_2**H**), 4.42 (dd, *J* = 5.6, 9.4 Hz, 1H, C_{11}**H**), 3.95 (d, *J* = 17.3 Hz, 1H, C_{15}**H**$_a$), 3.88–3.82 (m, 1H, C_{15}**H**$_b$), 3.75 (s, 3H, $C_{5'}$**H**), 3.10 (dd, *J* = 5.6, 14.1 Hz, 1H, C_{12}**H**$_a$), 2.79 (dd, *J* = 9.4, 14.1 Hz, 1H, C_{12}**H**$_b$).
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C):	δ 169.6 (**C**$_{13}$), 166.1 (**C**$_{16}$), 158.8 (**C**$_{4'}$), 139.8 (SO_2Ph-*ipso*-**C**), 138.2 (**C**$_9$), 135.2 (**C**$_4$), 132.9 (SO_2Ph-*p*-**C**), 132.4 (**C**$_{1'}$), 129.5 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.3 (**C**$_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.3 (**C**$_6$), 125.3 (**C**$_5$), 117.3 (**C**$_8$), 114.5 (**C**$_{3'}$), 87.3 (**C**$_2$), 59.5 (**C**$_3$), 58.4 (**C**$_{11}$), 55.5 (**C**$_{5'}$), 47.5 (**C**$_{15}$), 37.8 (**C**$_{12}$).
FTIR (thin film) cm^{-1}:	3254 (m), 3064 (w), 2929 (w), 1700 (s), 1654 (m), 1610 (m), 1514 (s), 1458 (m), 1362 (m), 1254 (s), 1170 (s), 1090 (m), 1033 (m), 975 (m), 833 (m), 687(m).
HRMS (DART) (*m/z*):	calc'd for $C_{26}H_{24}N_3O_5S$ $[M+H]^+$: 490.1431, found: 490.1453.

$[\alpha]_D^{23}$: +56 (*c* = 0.14, $CHCl_3$).

TLC (50% acetone in dichloromethane), R*f*: 0.30 (UV, CAM).



(+)-(5a*S*,10b*S*,11a*S*)-2-(4-(Benzyloxy)but-2-yn-1-yl)-10b-(4-methoxyphenyl)-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (23); alkyne (+)-23:

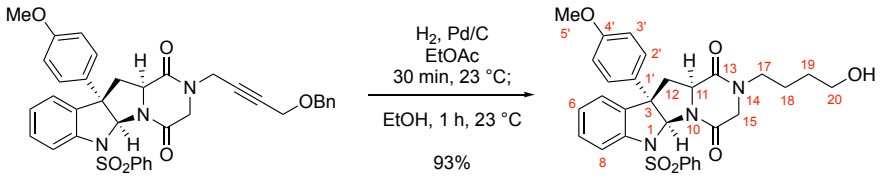
Anisole adduct (+)-**21** (1.94 g, 3.96 mmol, 1 equiv) was azeotropically dried by concentration from anhydrous benzene (3 × 50 mL) under reduced pressure. Tetrahydrofuran (70 mL) and anhydrous 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU, 25 mL) were introduced sequentially via cannula, and the solution was cooled to –78 °C. A solution of lithium bis(trimethylsilyl)amide (LHMDS, 861 mg, 5.15 mmol, 1.30 equiv) in tetrahydrofuran (28 mL) was then added via cannula, and the reaction mixture was warmed to –30 °C. After 20 min, a solution of bromide **22**[13] (2.37 g, 9.90 mmol, 2.50 equiv, azeotropically dried by concentration from anhydrous benzene (3 × 10 mL) under reduced pressure) in tetrahydrofuran (2.0 mL) was added via syringe. After 4 h, the reaction mixture was diluted with a saturated aqueous ammonium chloride solution (75 mL) and with ethyl acetate (350 mL). The organic layer was washed with a saturated aqueous ammonium chloride solution (3 × 100 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 5→10% acetone in dichloromethane) to afford alkyne (+)-**23** (1.53 g, 59.6%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.57 (d, J = 8.0 Hz, 1H, C_8**H**), 7.45 (app-d, J = 7.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.33–7.29 (m, 5H, OCH_2**Ph**), 7.28–7.27 (m, 2H, C_7**H**, SO_2Ph-*p*-**H**), 7.11–7.07 (m, 4H, C_5**H**, C_6**H**, SO_2Ph-*m*-**H**), 6.67 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.60 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.52 (s, 2H, OC**H**$_2$Ph), 4.43 (dd, J = 6.8, 8.8 Hz, 1H, C_{11}**H**), 4.36 (dt, J = 1.7, 17.4 Hz, 1H, C_{15}**H**$_a$), 4.13 (d, J = 17.2 Hz, 1H, C_{17}**H**$_a$), 4.13 (app-t, J = 1.8 Hz, 2H, C_{20}**H**) 3.98 (d, J = 17.3 Hz, 1H, C_{17}**H**$_b$), 3.93 (dt, J = 1.8, 17.4 Hz, 1H, C_{15}**H**$_b$), 3.74 (s, 3H, $C_{5'}$**H**), 3.07 (dd, J = 6.7, 14.2 Hz, 1H, C_{12}**H**$_a$), 2.85 (dd, J = 9.1, 14.1 Hz, 1H, C_{12}**H**$_b$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 166.7 (**C**$_{13}$), 165.3 (**C**$_{16}$), 158.8 (**C**$_{4'}$), 139.8 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 137.4 (OCH_2Ph-*ipso*-**C**), 135.6 (**C**$_4$), 132.9 (SO_2Ph-*p*-**C**), 132.5 (**C**$_{1'}$), 129.2

13. Kern, N.; Blanc, A.; Weibel, J.-M.; Pale, P. Gold(I)-Catalyzed Rearrangements of Aryl Alkynylaziridines to spiro[isochroman-4,2′-pyrrolines]. *Chem Commun.,* **2011**, *47*, 6665−6667.

	(**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.6 (OCH_2Ph-*m*-**C**), 128.2 (OCH_2Ph-*o*-**C**), 128.1 (**C**$_{2'}$), 128.0 (OCH_2Ph-*p*-**C**), 127.6 (SO_2Ph-*o*-**C**), 126.0 (**C**$_6$), 125.4 (**C**$_5$), 117.2 (**C**$_8$), 114.4 (**C**$_{3'}$), 87.1 (**C**$_2$), 81.2 (**C**$_{19}$), 79.6 (**C**$_{18}$), 72.0 (O**C**H_2Ph), 59.4 (**C**$_3$), 58.6 (**C**$_{11}$), 57.5 (**C**$_{20}$), 55.4 (**C**$_{5'}$), 51.7 (**C**$_{17}$), 38.7 (**C**$_{12}$), 35.3 (**C**$_{15}$).
FTIR (thin film) cm^{-1}:	3063 (w), 2932 (w), 1685 (s), 1609 (m), 1513 (m), 1409 (m), 1254 (m), 1171 (s), 1090 (m), 977 (w), 832 (m), 737 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{37}H_{34}N_3O_6S$ $[M+H]^+$: 648.2163, found: 648.2180.
$[\alpha]_D^{23}$:	+46 (*c* = 0.14, $CHCl_3$).
TLC (10% acetone in dichloromethane), R*f*:	0.65 (UV, CAM).



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

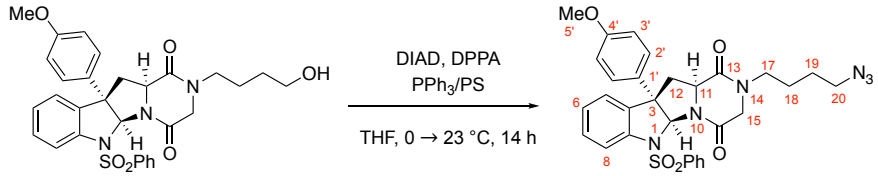
(+)-(5a*S*,10b*S*,11a*S*)-2-(4-Hydroxybutyl)-10b-(4-methoxyphenyl)-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (24); alcohol (+)-24:

A suspension of alkyne (+)-**23** (787 mg, 1.21 mmol, 1 equiv) and palladium on activated charcoal (5% w/w, 185 mg, 84.7 μmol, 0.0700 equiv) in ethyl acetate (45 mL) at 23 °C was sparged with hydrogen gas for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture, and was then allowed to stir under an atmosphere of hydrogen gas. After 30 min, ethanol (100 mL) was added via cannula to the reaction mixture, the reaction mixture was sparged with hydrogen gas for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture, and the reaction mixture was allowed to stir under an atmosphere of hydrogen gas. After 1 h, the reaction mixture was filtered through a pad of diatomaceous earth, the filter cake was washed with ethyl acetate (3 × 50 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 90% acetone in dichloromethane) to afford alcohol (+)-**24** (634 mg, 93.2%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.52 (d, J = 7.5 Hz, 1H, C_8**H**), 7.36 (app-d, J = 7.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.29–7.21 (m, 2H, C_7**H**, SO_2Ph-*p*-**H**), 7.14 (app-d, J = 7.5 Hz, 1H, C_5**H**) 7.08 (app-t, J = 7.4 Hz, 1H, C_6**H**), 7.02 (app-t, J = 8.1 Hz, 2H, SO_2Ph-*m*-**H**), 6.65 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.55 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.14 (s, 1H, C_2**H**), 4.44 (dd, J = 5.1, 9.1 Hz, 1H, C_{11}**H**), 4.09 (d, J = 17.1 Hz, 1H, C_{15}**H**$_a$), 3.79 (d, J = 17.1 Hz, 1H, C_{15}**H**$_b$), 3.71 (s, 3H, $C_{5'}$**H**), 3.47 (t, J = 6.2 Hz, 2H, C_{20}**H**), 3.41–3.34 (m, 1H, C_{17}**H**$_a$), 3.19–3.10 (m, 2H, C_{17}**H**$_b$, C_{12}**H**$_a$), 2.79 (dd, J = 9.4, 14.1 Hz, 1H, C_{12}**H**$_b$), 2.50 (br-s, 1H, O**H**), 1.41 (app-p, J = 7.2 Hz, 2H, C_{19}**H**), 1.22–1.14 (m, 2H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.4 (**C**$_{13}$), 165.8 (**C**$_{16}$), 158.7 (**C**$_{4'}$), 139.7 (**C**$_9$), 138.1 (SO_2Ph-*ipso*-**C**), 135.1 (**C**$_4$), 132.8 (SO_2Ph-*p*-**C**), 132.2 (**C**$_{1'}$), 129.2 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.2 (**C**$_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.4 (**C**$_6$), 125.2 (**C**$_5$), 116.9 (**C**$_8$), 114.3 (**C**$_{3'}$), 87.2 (**C**$_2$), 62.1 (**C**$_{20}$), 59.7 (**C**$_3$), 58.8 (**C**$_{11}$), 55.4 (**C**$_{5'}$), 52.4 (**C**$_{15}$), 45.8 (**C**$_{17}$), 37.8 (**C**$_{12}$), 29.0 (**C**$_{18}$), 23.7 (**C**$_{19}$).

FTIR (thin film) cm^{-1}:	3440 (w), 2936 (w), 1675 (s), 1653 (m), 1559 (m), 1514 (m), 1419 (m), 1362 (s), 1255 (s), 1169 (s), 1090 (w), 981 (w), 734 (m), 686 (m), 668 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{30}H_{32}N_3O_6S$ $[M+H]^+$: 562.2006, found: 562.1997.
$[\alpha]_D^{23}$:	+40 (*c* = 0.17, $CHCl_3$).
TLC (30% acetone in dichloromethane), R*f*:	0.13 (UV, CAM).



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

(+)-(5a*S*,10b*S*,11a*S*)-2-(4-Azidobutyl)-10b-(4-methoxyphenyl)-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (25); azide (+)-25:

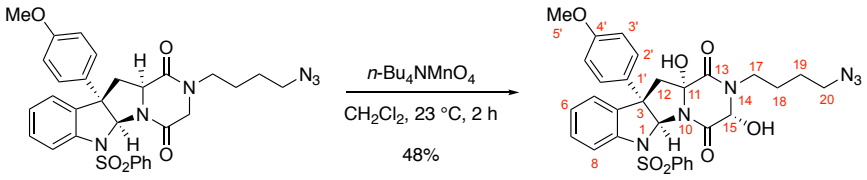
Diisopropyl azodicarboxylate (DIAD, 526 µL, 2.67 mmol, 1.50 equiv) and diphenylphosphoryl azide (DPPA, 575 µL, 2.67 mmol, 1.50 equiv) were added dropwise via syringe to a suspension of alcohol (+)-**24** (1.00 g, 1.78 mmol, 1 equiv) and resin-bound triphenylphosphine (1.31 mmol/g on 100-200 mesh polystyrene cross-linked with 1% divinylbenzene, 1.90 g, 2.49 mmol, 1.40 equiv) in tetrahydrofuran (43 mL) at 0 °C. After 5 min, the ice−water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 14 h, the reaction mixture was filtered through a 1 cm pad of diatomaceous earth in a 60-mL medium-porosity fritted-glass funnel. The filter cake was washed with dichloromethane (100 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10→15% acetone in dichloromethane) to afford azide (+)-**25** (697 mg, 66.7%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.56 (d, J = 7.5 Hz, 1H, C_8**H**), 7.41 (app-d, J = 7.9 Hz, 2H, SO_2Ph-*o*-**H**), 7.32–7.24 (m, 2H, C_7**H**, SO_2Ph-*p*-**H**), 7.15 (d, J = 7.5 Hz, 1H, C_5**H**) 7.12–7.04 (m, 3H, C_6**H**, SO_2Ph-*m*-**H**), 6.68 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.59 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.39 (dd, J = 5.2, 9.2 Hz, 1H, C_{11}**H**), 4.07 (d, J = 17.0 Hz, 1H, C_{15}**H**$_a$), 3.76 (d, J = 16.9 Hz, 1H, C_{15}**H**$_b$), 3.75 (s, 3H, $C_{5'}$**H**), 3.39 (dt, J = 7.2, 14.0 Hz, 1H, C_{17}**H**$_a$) 3.22–3.06 (m, 4H, C_{17}**H**$_b$, C_{20}**H**, C_{12}**H**$_a$), 2.82 (dd, J = 9.4, 14.1 Hz, 1H, C_{12}**H**$_b$), 1.47–1.37 (m, 2H, C_{18}**H**), 1.26–1.20 (m, 2H, C_{19}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.3 (**C**$_{13}$), 165.4 (**C**$_{16}$), 158.8 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.1 (**C**$_4$), 132.9 (SO_2Ph-*p*-**C**), 132.2 (**C**$_{1'}$), 129.3 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.2 (**C**$_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.4 (**C**$_6$), 125.2 (**C**$_5$), 117.0 (**C**$_8$), 114.4 (**C**$_{3'}$), 87.2 (**C**$_2$), 59.8 (**C**$_3$), 58.9 (**C**$_{11}$), 55.5 (**C**$_{5'}$), 52.5 (**C**$_{15}$), 51.0 (**C**$_{20}$), 45.5 (**C**$_{17}$), 37.9 (**C**$_{12}$), 25.7 (**C**$_{19}$), 24.5 (**C**$_{18}$).

FTIR (thin film) cm^{-1}:	3063 (w), 2932 (m), 2098 (s), 1700 (s), 1684 (s), 1514 (m), 1458 (m), 1362 (m), 1255 (m), 1169 (m), 1091 (m), 756 (s), 668 (s).
HRMS (DART) (*m/z*):	calc'd for $C_{30}H_{31}N_6O_5S$ $[M+H]^+$: 587.2071, found: 587.2073.
$[\alpha]_D^{23}$:	+32 (*c* = 0.17, $CHCl_3$).

TLC (10% acetone in dichloromethane), R*f*: 0.43 (UV, CAM).



(+)-**25** (+)-**26**

(+)-(3*R*,5a*S*,10b*S*,11a*R*)-2-(4-Azidobutyl)-3,11a-dihydroxy-10b-(4-methoxyphenyl)-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (26); diol (+)-26:

Tetra-*n*-butylammonium permanganate[5] (2.13 g, 5.90 mmol, 5.00 equiv) was added as a solid to a solution of azide (+)-**25** (692 mg, 1.18 mmol, 1 equiv) in dichloromethane (43 mL) at 23 °C. After 2 h, the reaction mixture was diluted with a saturated aqueous sodium sulfite solution (50 mL) and with ethyl acetate (150 mL). The resulting mixture was washed with a saturated aqueous sodium bicarbonate solution (50 mL), the layers were separated, and the organic layer was washed with a saturated aqueous sodium chloride solution (50 mL). The combined aqueous layers were extracted with ethyl acetate (2 × 50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 20% acetone in dichloromethane) to afford diol (+)-**26** (340 mg, 47.6%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.53 (d, *J* = 8.0 Hz, 1H, C_8**H**), 7.30–7.14 (m, 6H, C_5**H**, C_6**H**, C_7**H**, SO_2Ph-*o*-**H**, SO_2Ph-*p*-**H**), 6.99 (app-t, *J* = 7.6 Hz, 2H, SO_2Ph-*m*-**H**), 6.77 (app-d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.54 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.43 (s, 1H, C_2**H**), 6.06 (d, *J* = 6.4 Hz, 1H, C_{15}O**H**), 5.67 (s, 1H, C_{11}O**H**), 5.23 (d, *J* = 6.4 Hz, 1H, C_{15}**H**), 3.74 (s, 3H, $C_{5'}$**H**), 3.57 (d, *J* = 15.1 Hz, 1H, C_{12}**H**$_a$), 3.44–3.39 (m, 2H, C_{17}**H**) 3.18 (t, *J* = 6.8 Hz, 2H, C_{20}**H**), 2.87 (d, *J* = 15.0 Hz, 1H, C_{12}**H**$_b$), 1.66–1.48 (m, 2H, C_{18}**H**), 1.40–1.28 (m, 2H, C_{19}**H**).

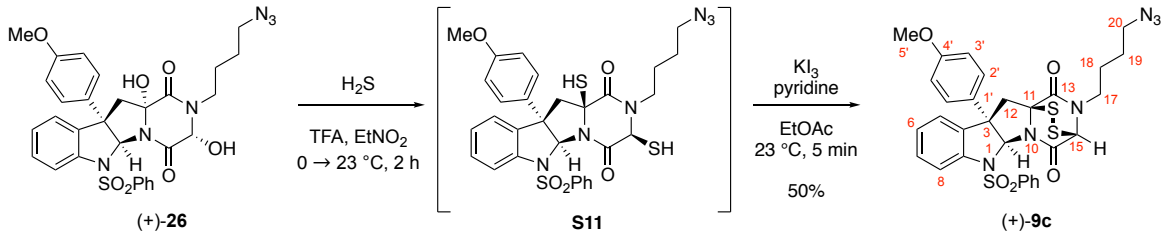
^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.3 (**C**$_{13}$), 166.4 (**C**$_{16}$), 158.7 (**C**$_{4'}$), 139.5 (**C**$_9$), 138.0 (SO_2Ph-*ipso*-**C**), 136.3 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 133.0 (**C**$_{1'}$), 129.3 (**C**$_7$), 128.7 (**C**$_{2'}$), 128.7 (SO_2Ph-*m*-**C**), 127.4 (SO_2Ph-*o*-**C**), 126.9 (**C**$_6$), 125.9 (**C**$_5$), 117.3 (**C**$_8$), 114.3 (**C**$_{3'}$), 88.3 (**C**$_{11}$), 88.3 (**C**$_2$), 82.0 (**C**$_{15}$), 58.9 (**C**$_3$), 55.5 (**C**$_{5'}$), 51.1 (**C**$_{20}$), 47.8 (**C**$_{12}$), 44.9 (**C**$_{17}$), 26.0 (**C**$_{19}$), 25.5 (**C**$_{18}$).

FTIR (thin film) cm^{-1}: 2936 (w), 2097 (s), 1700 (s), 1684 (s), 1513 (m), 1474 (m), 1458 (m), 1362 (m), 1254 (s), 1169 (s), 1091 (w), 832 (m), 668 (m).

HRMS (DART) (*m/z*): calc'd for $C_{30}H_{31}N_6O_7S$ $[M+H]^+$: 619.1969, found: 619.1991.

$[\alpha]_D^{23}$: +26 (*c* = 0.20, $CHCl_3$).

TLC (30% acetone in dichloromethane), R*f*: 0.55 (UV, CAM).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-2-(4-Azidobutyl)-10b-(4-methoxyphenyl)-6-(phenylsulfonyl)-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (9c); epidithiodiketopiperazine azide (+)-9c:

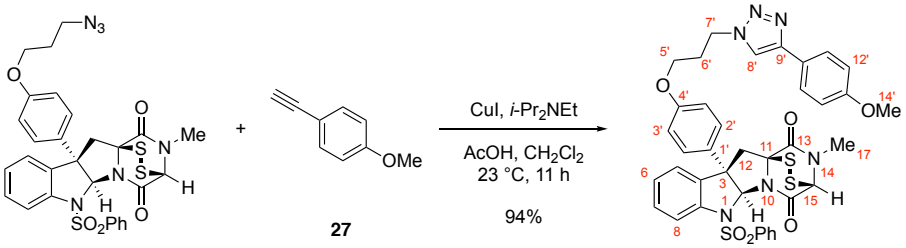
A solution of diol (+)-**26** (259 mg, 419 μmol, 1 equiv) in anhydrous nitroethane (18 mL) at 0 °C was sparged with hydrogen sulfide gas for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture, providing a saturated hydrogen sulfide solution. Trifluoroacetic acid (TFA, 13.5 mL) was added via syringe over 20 seconds, and the sparging with hydrogen sulfide gas was maintained for another 20 min. The ice−water bath was removed, and the solution was allowed to stir and warm to 23 °C under an atmosphere of hydrogen sulfide. After 2 h, the reaction mixture was diluted with ethyl acetate (150 mL) and was slowly poured into a saturated aqueous sodium bicarbonate solution (70 mL). The organic layer was washed with a saturated aqueous sodium chloride solution (40 mL). A stock solution of potassium triiodide in pyridine[6] was added dropwise into the organic layer containing crude bisthiol **S11** until a persistent yellow color was observed. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 M, 2 × 40 mL), was washed with a saturated aqueous sodium chloride solution (40 mL), was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 10→15% ethyl acetate in dichloromethane) to afford epidithiodiketopiperazine azide (+)-**9c** (136 mg, 50.0%) as a beige solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.[14]

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.61 (d, *J* = 8.0 Hz, 1H, C_8**H**), 7.40–7.37 (m, 1H, C_7**H**), 7.35 (app-d, *J* = 5.5 Hz, 2H, SO_2Ph-*o*-**H**), 7.30–7.21 (m, 3H, C_5**H**, C_6**H**, SO_2Ph-*p*-**H**, 7.02 (app-t, *J* = 8.0 Hz, 2H, SO_2Ph-*m*-**H**), 6.75 (app-d, *J* = 6.7 Hz, 2H, $C_{2'}$**H**), 6.61 (app-d, *J* = 6.8 Hz, 2H, $C_{3'}$**H**), 6.39 (s, 1H, C_2**H**), 5.32 (s, 1H, C_{15}**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.63 (d, *J* = 15.5 Hz, 1H, C_{12}**H**$_a$), 3.56 (t, *J* = 6.9 Hz, 2H, C_{17}**H**), 3.30 (t, *J* = 6.6 Hz, 2H,

14. The relative stereochemistry of the epidisulfide (+)-**9c** was confirmed by key NOESY cross–peaks on the corresponding bis(methylthioether). Our assignment is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (3.12, 7.09–7.04), (3.12, 1.88), (2.96, 6.88). This derivatized compound was prepared in one step using our methodology developed to access (+)-gliocladin B (Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803). The corresponding bis(methylthioether) of epidisulfide (+)-**9c** was characterized as follows: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.86 (d, *J* = 8.0 Hz, 2H, SO_2Ph-*o*-**H**), 7.52 (d, *J* = 8.2 Hz, 1H, C_8**H**), 7.47 (t, *J* = 7.4 Hz, 1H, SO_2Ph-*p*-**H**,) 7.35 (t, *J* = 8.0 Hz, 2H, SO_2Ph-*m*-**H**), 7.27 (ddd, *J* = 2.2, 6.5, 8.6 Hz, 1H, C_7**H**), 7.09–7.04 (m, 2H, C_5**H**, C_6**H**), 6.88 (d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.68 (d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.63 (s, 1H, C_2**H**), 4.49 (s, 1H, C_{15}**H**), 3.73 (s, 3H, $C_{5'}$**H**), 3.66–3.58 (m, 1H, C_{17}**H**$_a$), 3.34–3.28 (m, 1H, C_{17}**H**$_b$), 3.30 (t, *J* = 6.7 Hz, 2H, C_{20}**H**), 3.12 (d, *J* = 14.3 Hz, 1H, C_{12}**H**$_a$), 2.96 (*J* = 14.3 Hz, 1H, C_{12}**H**$_b$), 2.16 (s, 3H, C_{15}SC**H**$_3$), 1.88 (s, 3H, C_{11}SC**H**$_3$), 1.75–1.68 (m, 2H, C_{18}**H**), 1.63–1.55 (m, 2H, C_{19}**H**). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.3 (**C**$_{13}$), 162.3 (**C**$_{16}$), 158.9 (**C**$_{4'}$), 142.2 (**C**$_9$), 140.2 (SO_2Ph-*ipso*-**C**), 136.8 (**C**$_4$), 134.3 (**C**$_{1'}$), 132.9 (SO_2Ph-*p*-**C**), 129.2 (**C**$_7$, SO_2Ph-*m*-**C**), 127.0 (**C**$_{2'}$, SO_2Ph-*o*-**C**), 124.9 (**C**$_6$), 123.8 (**C**$_5$), 117.0 (**C**$_8$), 114.5 (**C**$_{3'}$), 85.7 (**C**$_2$), 69.8 (**C**$_{11}$), 65.7 (**C**$_{15}$), 57.0 (**C**$_3$), 55.5 (**C**$_{5'}$), 51.1 (**C**$_{20}$), 45.7 (**C**$_{12}$), 44.9 (**C**$_{17}$), 26.3 (**C**$_{19}$), 24.9 (**C**$_{18}$), 17.1 (C_{15}S**C**H$_3$), 15.4 (C_{11}S**C**H$_3$). HRMS (ESI) (*m*/*z*): calc'd for $C_{32}H_{34}N_6NaO_5S_3$ $[M+Na]^+$: 701.1645, found 701.1649.

	C_{20}**H**), 2.84 (d, *J* = 15.5 Hz, 1H, C_{12}**H**$_b$), 1.85–1.67 (m, 2H, C_{18}**H**), 1.65–1.58 (m, 2H, C_{19}**H**).
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C):	δ 165.0 (**C**$_{13}$), 160.3 (**C**$_{16}$), 159.0 (**C**$_{4'}$), 141.3 (**C**$_9$), 138.5 (SO_2Ph-*ipso*-**C**), 135.9 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 131.3 (**C**$_{1'}$), 129.9 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.2 (**C**$_6$), 125.7 (**C**$_5$), 119.0 (**C**$_8$), 114.6 (**C**$_{3'}$), 87.7 (**C**$_2$), 74.9 (**C**$_{11}$), 66.6 (**C**$_{15}$), 59.6 (**C**$_3$), 55.5 (**C**$_{5'}$), 51.1 (**C**$_{20}$), 45.5 (**C**$_{12}$), 45.4 (**C**$_{17}$), 26.2 (**C**$_{19}$), 25.3 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	3063 (w), 2932 (s), 2098 (s), 1717 (s), 1700 (s), 1685 (s), 1609 (m), 1514 (s), 1458 (m), 1363 (m), 1256 (s), 1171 (s), 1090 (m), 972 (m), 737 (m).
HRMS (DART) (*m/z*):	calc'd for $C_{30}H_{32}N_7O_5S_3$ $[M+NH_4]^+$: 666.1622, found: 666.1630.
$[\alpha]_D^{23}$:	+245 (*c* = 0.22, $CHCl_3$).

TLC (20% ethyl acetate in dichloromethane), R*f*: 0.61 (UV, CAM, $AgNO_3$).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-(3-(4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)propoxy)phenyl)-2-methyl-6-(phenylsulfonyl)-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino [1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (28a); triazole (+)-28a:

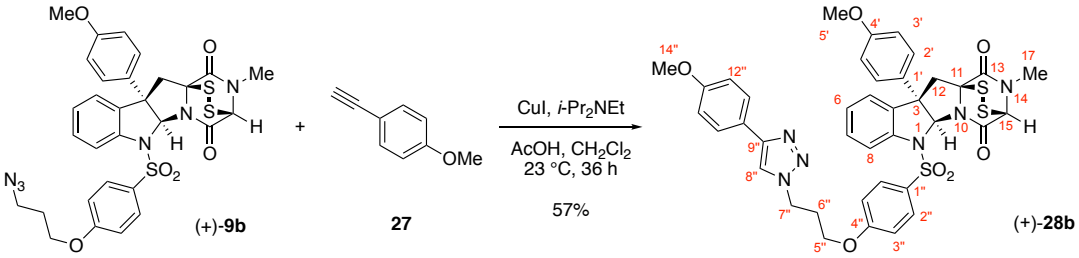
Copper (I) iodide (45.7 mg, 0.240 mmol, 1.50 equiv) was added as a solid to a solution of epidithiodiketopiperazine azide (+)-**9a** (102 mg, 0.160 mmol, 1 equiv), 4-ethynylanisole **27** (104 µL, 0.800 mmol, 5.00 equiv), acetic acid (28 µL, 0.48 mmol, 3.0 equiv), and *N,N*-diisopropylethylamine (84 µL, 0.48 mmol, 3.0 equiv) in dichloromethane (1.6 mL) at 23 °C. After 11 h, the reaction mixture was directly purified by flash column chromatography on silica gel (eluent: 20% ethyl acetate in dichloromethane→100% ethyl acetate) to afford triazole (+)-**28a** (116 mg, 94.3%) as a yellow solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.70 (app-d, J = 8.8 Hz, 2H, $C_{11'}$**H**), 7.68 (s, 1H, $C_{8'}$**H**), 7.57 (d, J = 8.0 Hz, 1H, C_8**H**), 7.39–7.35 (m, 3H, C_7**H**, SO_2Ph-*o*-**H**), 7.30–7.19 (m, 3H, C_5**H**, C_6**H**, SO_2Ph-*p*-**H**), 7.03 (t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.92 (app-d, J = 8.8 Hz, 2H, $C_{12'}$**H**), 6.76 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.60 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.38 (s, 1H, C_2**H**), 5.21 (s, 1H, C_{15}**H**), 4.61 (t, J = 6.7 Hz, 2H, $C_{7'}$**H**), 3.94–3.91 (m, 2H, $C_{5'}$**H**), 3.81 (s, 3H, $C_{14'}$**H**), 3.62 (d, J = 15.5 Hz, 1H, C_{12}**H**$_a$), 3.10 (s, 3H, C_{17}**H**), 2.83 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.42 (p, J = 6.3 Hz, 2H, $C_{6'}$**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.1 (**C**$_{13}$), 160.1 (**C**$_{16}$), 159.7 (**C**$_{14'}$), 157.8 (**C**$_{4'}$), 147.8 (**C**$_{9'}$), 141.3 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 131.7 (**C**$_{1'}$), 129.8 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 127.2 (SO_2Ph-*o*-**C**), 127.1 (**C**$_{11'}$), 126.2 (**C**$_6$), 125.6 (**C**$_5$), 123.3 (**C**$_{10'}$), 119.3 (**C**$_{8'}$), 118.9 (**C**$_8$), 115.0 (**C**$_{3'}$), 114.4 (**C**$_{12'}$), 87.6 (**C**$_2$), 74.5 (**C**$_{11}$), 68.4 (**C**$_{15}$), 64.3 (**C**$_{5'}$), 59.5 (**C**$_3$), 55.4 (**C**$_{14'}$), 47.1 (**C**$_{7'}$), 45.4 (**C**$_{12}$), 32.1 (**C**$_{17}$), 30.0 (**C**$_{6'}$).

FTIR (thin film) cm^{-1}: 3058 (m), 2958 (w), 1700 (s), 1646 (s), 1559 (m), 1512 (s), 1458 (m), 1250 (w), 1171 (s), 1032 (w), 836 (m).

HRMS (ESI) (*m/z*):	calc'd for $C_{38}H_{35}N_6O_6S_3$ $[M+H]^+$: 767.1775, found: 767.1796.
$[\alpha]_D^{23}$:	+315 (*c* = 0.10, $CHCl_3$).
TLC (100% ethyl acetate), R*f*:	0.38 (UV, CAM, $AgNO_3$).



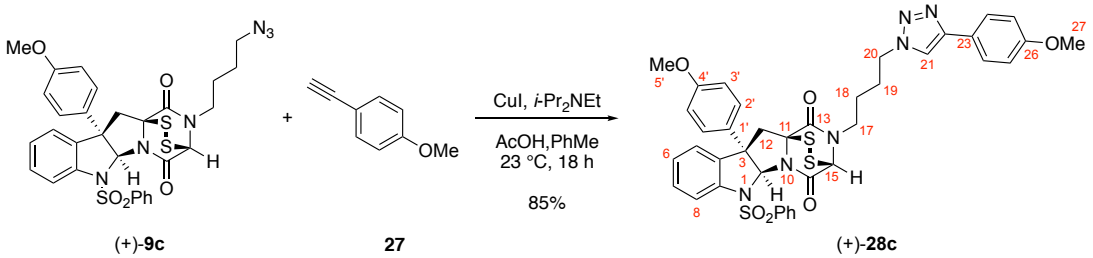
(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-Methoxyphenyl)-6-((4-(3-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)propoxy)phenyl)-(methyl)-(l^1-oxidaneyl)sulfinyl)-2-methyl-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (28b); triazole (+)-28b:

A suspension of copper(I) iodide (3.05 mg, 15.4 μmol, 0.500 equiv), acetic acid (1.77 μL, 30.8 μmol, 1.00 equiv), and *N*,*N*-diisopropylethylamine (5.40 μL, 30.8 μmol, 1.00 equiv) in dichloromethane (0.50 mL) was added via syringe to a solution of epidithiodiketopiperazine (+)-**9b** (20.5 mg, 30.8 μmol, 1 equiv) and 4-ethynylanisole (**27**, 20.8 μL, 0.160 mmol, 5.00 equiv) in dichloromethane (0.50 mL) at 23 °C. After 36 h, the reaction mixture was directly purified by flash column chromatography on silica gel (eluent: 20% ethyl acetate in dichloromethane→100% ethyl acetate) to afford triazole (+)-**28b** (14.2 mg, 56.8%) as a yellow solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.70–7.68 (m, 3H, $C_{8''}$**H**, $C_{11''}$**H**), 7.61, (d, *J* = 8.0 Hz, 1H, C_8**H**), 7.38 (app-t, *J* = 7.7 Hz, 1H, C_7**H**), 7.28–7.23 (m, 2H, C_6**H**, C_5**H**), 7.19 (app-d, *J* = 8.9 Hz, 2H, $C_{2''}$**H**), 6.91 (app-d, *J* = 8.4 Hz, 2H, $C_{12''}$**H**), 6.72 (app-d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.59 (app-d, *J* = 8.6 Hz, 2H, $C_{3'}$**H**), 6.38 (app-d, *J* = 8.8 Hz, 2H, $C_{3''}$**H**), 6.31 (s, 1H, C_2**H**), 5.22 (s, 1H, C_{15}**H**), 4.57 (t, *J* = 6.6 Hz, 2H, $C_{7''}$**H**), 3.92–3.88 (m, 2H, $C_{5''}$**H**), 3.81 (s, 3H, $C_{14''}$**H**), 3.73 (s, 3H, $C_{5'}$**H**), 3.57 (d, *J* = 15.6 Hz, 1H, C_{12}**H**$_a$), 3.09 (s, 3H, C_{17}**H**), 2.81 (d, *J* = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.40 (p, *J* = 6.2 Hz, 2H, $C_{6''}$**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.2 (**C**$_{13}$), 162.0 (**C**$_{4''}$), 160.2 (**C**$_{16}$), 159.8 (**C**$_{13''}$), 158.8 (**C**$_{4'}$), 147.9 (**C**$_{9''}$), 141.6 (**C**$_9$), 135.9 (**C**$_4$), 131.5 (**C**$_{1'}$), 130.3 (**C**$_{1''}$), 129.9 (**C**$_7$), 129.4 (**C**$_{2''}$), 128.1 (**C**$_{2'}$), 127.2 (**C**$_{11''}$), 126.3 (**C**$_5$), 125.8 (**C**$_6$), 123.3 (**C**$_{10''}$), 119.5 (**C**$_{8''}$), 119.4 (**C**$_8$), 114.5 (**C**$_{3'}$), 114.5 (**C**$_{12''}$), 114.2 (**C**$_{3''}$), 87.9 (**C**$_2$), 74.6 (**C**$_{11}$), 68.5 (**C**$_{15}$), 64.6 (**C**$_{5''}$), 59.6 (**C**$_3$), 55.6 (**C**$_{5'}$), 55.5 (**C**$_{14''}$), 47.1 (**C**$_{7''}$), 45.9 (**C**$_{12}$), 32.2 (**C**$_{17}$), 30.0 (**C**$_{16'}$).

FTIR (thin film) cm^{-1}:	2924 (w), 1717 (s), 1700 (s), 1685 (s), 1653 (m), 1559 (s), 1457 (m), 1362 (m), 1259 (s), 1162 (s), 1031 (m), 668 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{39}H_{37}N_6O_7S_3$ $[M+H]^+$: 797.1880, found: 797.1880.
$[\alpha]_D^{23}$:	+150 (*c* = 0.11, $CHCl_3$).
TLC (100% ethyl acetate), R*f*:	0.38 (UV, CAM, $AgNO_3$).



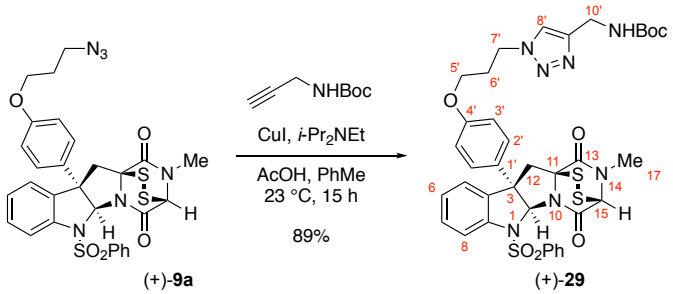
(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-Methoxyphenyl)-2-(4-(4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)butyl)-6-(phenylsulfonyl)-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5] pyrrolo[2,3-*b*]indole-1,4-dione (28c); triazole (+)-28c:

A suspension of copper(I) iodide (5.5 mg, 29 μmol, 0.51 equiv), acetic acid (3.3 μL, 57 μmol, 1.0 equiv) and *N*,*N*-diisopropylethylamine (9.9 μL, 57 μmol, 1.0 equiv) in toluene (0.50 mL) was added via syringe to a solution of epidithiodiketopiperazine (+)-**9c** (37.0 mg, 57.0 μmol, 1 equiv) and 4-ethynylanisole **27** (38 μL, 290 μmol, 5.1 equiv) in toluene (0.30 mL) at 23 °C. After 18 h, the reaction mixture was diluted with dichloromethane (1.6 mL) and was purified by flash column chromatography on silica gel (eluent: 20% ethyl acetate in dichloromethane→100% ethyl acetate) to afford triazole (+)-**28c** (37.6 mg, 84.5%) as a yellow solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.71 (app-d, J = 8.8 Hz, 2H, C_{24}**H**), 7.69 (s, 1H, C_{21}**H**), 7.60 (d, J = 8.0 Hz, 1H, C_8**H**), 7.38 (td, J = 1.8, 8.6 Hz, 1H, C_7**H**), 7.32 (app-d, J = 7.9 Hz, 2H, SO_2Ph-*o*-**H**), 7.29–7.21 (m, 3H, C_5**H**, C_6**H**, SO_2Ph-*p*-**H**), 7.01 (app-t, J = 7.6 Hz, 2H, SO_2Ph-*m*-**H**), 6.91 (app-d, J = 8.8 Hz, 2H, C_{25}**H**), 6.75 (app-d, J = 6.8 Hz, 2H, $C_{2'}$**H**), 6.61 (app-d, J = 6.9 Hz, 2H, $C_{3'}$**H**), 6.39 (s, 1H, C_2**H**), 5.37 (s, 1H, C_{15}**H**), 4.40 (t, J = 6.9 Hz, 2H, C_{20}**H**), 3.81 (s, 3H, C_{27}**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.66–3.51 (m, 2H, C_{17}**H**), 3.63 (d, J = 15.4 Hz, 1H, C_{12}**H**$_a$), 2.83 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 1.97 (p, J = 7.3 Hz, 2H, C_{19}**H**), 1.84–1.67 (m, 2H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 164.9 (**C**$_{13}$), 160.2 (**C**$_{16}$), 159.6 (**C**$_{26}$), 158.8 (**C**$_{4'}$), 147.7 (**C**$_{22}$), 141.1 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 135.7 (**C**$_4$), 132.9 (SO_2Ph-*p*-**C**), 131.0 (**C**$_{1'}$), 129.7 (**C**$_7$), 128.5 (SO_2Ph-*m*-**C**), 127.9 (**C**$_{2'}$), 127.1 (SO_2Ph-*o*-**C**), 127.1 (**C**$_{24}$), 126.1 (**C**$_6$), 125.6 (**C**$_5$), 123.4 (**C**$_{23}$), 119.0 (**C**$_{21}$), 118.8 (**C**$_8$), 114.4 (**C**$_{3'}$), 114.2 (**C**$_{25}$), 87.7 (**C**$_2$), 74.7 (**C**$_{11}$), 66.3 (**C**$_{15}$), 59.4 (**C**$_3$), 55.4 (**C**$_{5'}$), 55.3 (**C**$_{27}$), 49.6 (**C**$_{20}$), 45.3 (**C**$_{12}$), 44.9 (**C**$_{17}$), 27.3 (**C**$_{19}$), 24.9 (**C**$_{18}$).

FTIR (thin film) cm^{-1}:	2926 (m), 1717 (s), 1700 (s), 1685 (s), 1653 (m), 1559 (m), 1457 (m), 1362 (m), 1252 (s), 1172 (m), 1032 (m), 737 (m), 668 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{39}H_{37}N_6O_6S_3$ $[M+H]^+$: 781.1931, found: 781.1947.
$[\alpha]_D^{23}$:	+484 (*c* = 0.06, $CHCl_3$).
TLC (100% ethyl acetate), R*f*:	0.41 (UV, CAM, $AgNO_3$).



(+)-*tert*-Butyl ((1-(3-(4-((3*S*,5a*S*,10b*S*,11a*S*)-2-methyl-1,4-dioxo-6-(phenylsulfonyl)-1,2,3,4,5a,6-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indol-10b(11*H*)-yl)phenoxy)propyl)-1*H*-1,2,3-triazol-4-yl)methyl)carbamate (29); triazole (+)-29:

A suspension of copper(I) iodide (24.8 mg, 128 μmol. 0.750 equiv), acetic acid (15 μL, 260 μmol, 1.5 equiv), and DIPEA (45 μL, 260 μmol, 1.5 equiv) in toluene (1.5 mL) was introduced via syringe to a solution of epidithiodiketopiperazine (+)-**9a** (108 mg, 170 μmol, 1 equiv) and *N*-Boc-propargylamine (132 mg, 850 μmol, 5.00 equiv) in toluene (0.3 mL) at 23 °C. After 15 h, the reaction mixture was diluted with dichloromethane (3 mL) and was directly purified by flash column chromatography on silica gel (eluent: 0.8%→2.5% methanol in dichloromethane) to afford triazole (+)-**29** (119 mg, 88.8%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.68–7.50 (m, 2H, C_8**H**, $C_{8'}$**H**), 7.40–7.16 (m, 6H, C_7**H**, SO_2Ph-*o*-**H**, SO_2Ph-*p*-**H**, C_5**H**, C_6**H**), 7.00 (app-t, *J* = 7.1 Hz, 2H, SO_2Ph-*m*-**H**), 6.73 (app-d, *J* = 7.8 Hz, 2H, $C_{2'}$**H**), 6.56 (app-d, *J* = 6.8 Hz, 2H, $C_{3'}$**H**), 6.37 (s, 1H, C_2**H**), 5.31 (br-s, 2H, C_{15}**H**, N**H**), 4.54 (br-s, 2H, $C_{7'}$**H**), 4.36 (br-s, 2H, $C_{10'}$**H**), 3.89 (br-s, 2H, $C_{5'}$**H**), 3.60 (d, *J* = 15.4 Hz, 1H, C_{12}**H**$_a$), 3.09 (s, 3H, C_{17}**H**), 2.84 (d, *J* = 15.4 Hz, 1H, C_{12}**H**$_b$), 2.34 (br-s, 2H, $C_{6'}$**H**), 1.38 (s, 9H, C(C**H**$_3$)$_3$).

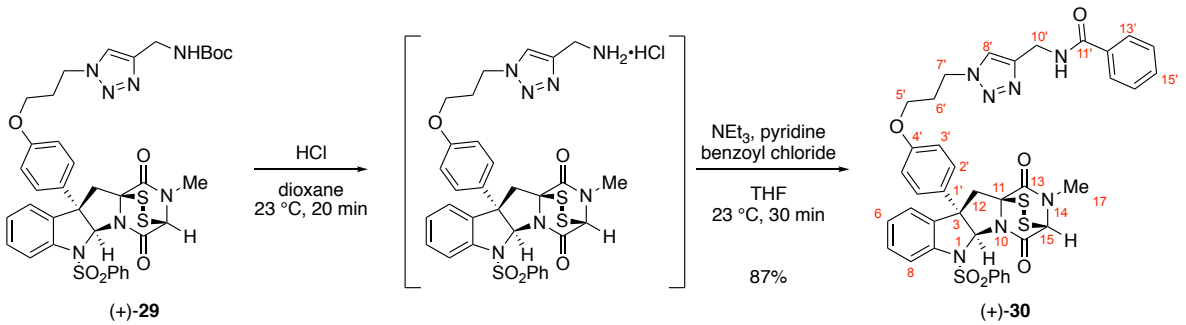
^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C): δ 165.1 (**C**$_{13}$), 160.2 (**C**$_{16}$), 157.7 (**C**$_{4'}$), 156.0 (N**C**O$_2$C(CH$_3$)$_3$), 145.8 (**C**$_{9'}$), 141.2 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.2 (SO_2Ph-*p*-**C**), 131.7 (**C**$_{1'}$), 129.9 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$), 127.2 (SO_2Ph-*o*-**C**), 126.2 (**C**$_6$), 125.7 (**C**$_5$), 122.7 (**C**$_{8'}$), 118.9 (**C**$_8$), 115.0 (**C**$_{3'}$), 87.7 (**C**$_2$), 79.8 (**C**(CH$_3$)$_3$), 74.6 (**C**$_{11}$), 68.3 (**C**$_{15}$), 64.3 (**C**$_{5'}$), 59.5 (**C**$_3$), 47.2 (**C**$_{7'}$), 45.4 (**C**$_{12}$), 36.1 (**C**$_{10'}$), 32.1 (**C**$_{17}$), 30.0 (**C**$_{6'}$), 28.5 (C(**C**H$_3$)$_3$).

FTIR (thin film) cm^{-1}: 3391 (w), 2977 (w), 1695 (s), 1512 (m), 1363 (m), 1251 (m), 1168 (s).

HRMS (ESI) (*m/z*): calc'd for $C_{37}H_{39}N_7NaO_7S_3$ $[M+Na]^+$: 812.1965, found: 812.1969.

$[\alpha]_D^{23}$: +185 (*c* = 0.20, $CHCl_3$).

TLC (5% methanol in dichloromethane), R*f*: 0.44 (UV, CAM, $AgNO_3$).



(+)-*N*-((1-(3-(4-((3*S*,5a*S*,10b*S*,11a*S*)-2-Methyl-1,4-dioxo-6-(phenylsulfonyl)-1,2,3,4,5a,6-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indol-10b(11*H*)-yl)phenoxy)propyl)-1*H*-1,2,3-triazol-4-yl)methyl)benzamide (30); benzamide (+)-30:

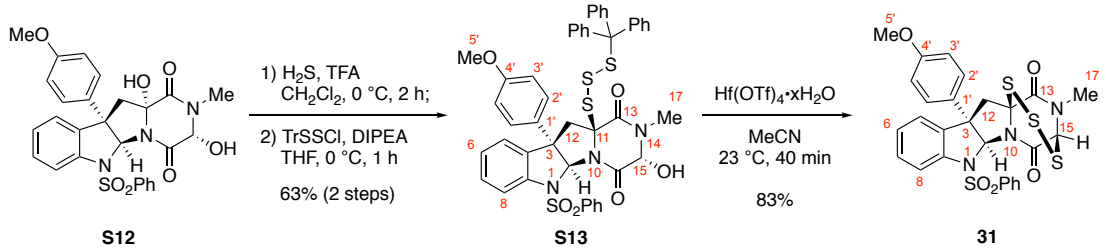
A solution of hydrogen chloride in 1,4-dioxane (4.0 M, 1.0 mL) was added via syringe to a solution of triazole (+)-**29** (15.0 mg, 19.0 μmol, 1 equiv) in 1,4-dioxane (0.5 mL) at 23 °C. After 20 min, the reaction mixture was concentrated under reduced pressure, and the resulting yellow solid was dissolved in pyridine (240 μL). A solution of benzoyl chloride (48 mM, 0.60 mL, 29 μmol, 1.5 equiv) in tetrahydrofuran was added via syringe, followed by the addition of triethylamine (40 μL, 290 μmol, 15 equiv) via syringe. After 30 min, the reaction mixture was diluted with ethyl acetate (30 mL) and was slowly poured into an aqueous hydrogen chloride solution (1 M, 5 mL). The organic layer was washed sequentially with an aqueous hydrogen chloride solution (1 M, 5 mL), with a saturated aqueous sodium bicarbonate solution (5 mL), and with a saturated aqueous sodium chloride solution (5 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 on silica gel (eluent: 1→2% methanol in dichloromethane) to afford benzamide (+)-**30** (13.1 mg, 86.8%) as a beige solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.77 (app-d, J = 7.3 Hz, 2H, $C_{13'}$**H**), 7.71 (br-s, 1H, $C_{8'}$**H**), 7.57 (d, J = 8.0 Hz, 1H, C_8**H**), 7.46 (app-t, J = 7.4 Hz, 1H, $C_{15'}$**H**), 7.40–7.32 (m, 5H, SO_2Ph-*o*-**H**, $C_{14'}$**H**, C_7**H**), 7.28–7.20 (m, 3H, SO_2Ph-*o*-**H**, C_5**H**, C_6**H**), 7.16 (br-s, 1H, N**H**), 7.01 (app-t, J = 7.8 Hz, 2H, SO_2Ph-*m*-**H**), 6.71 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.56 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.36 (s, 1H, C_2**H**), 5.27 (s, 1H, C_{15}**H**), 4.68 (br-s, 2H, $C_{10'}$**H**), 4.55 (t, J = 6.3 Hz, 2H, $C_{7'}$**H**), 3.95–3.84 (m, 2H, $C_{5'}$**H**), 3.60 (d, J = 15.5 Hz, 1H, C_{12}**H**$_a$), 3.10 (s, 3H, C_{17}**H**), 2.83 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.37 (p, J = 5.9 Hz, 2H, $C_{6'}$**H**).

^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C): δ 167.6 ($C_{11'}$), 165.2 (C_{13}), 160.2 (C_{16}), 157.8 ($C_{4'}$), 145.0 ($C_{9'}$), 141.3 (C_9), 138.4 (SO_2Ph-*ipso*-**C**), 135.9 (C_4), 134.0 ($C_{12'}$), 133.2 (SO_2Ph-*p*-**C**), 131.9 ($C_{15'}$), 131.8 ($C_{1'}$), 129.9 (C_7), 128.8 ($C_{14'}$), 128.7

	(SO_2Ph-*m*-**C**), 128.1 ($\mathbf{C}_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 127.2 ($\mathbf{C}_{13'}$), 126.3 ($\mathbf{C}_6$), 125.7 ($\mathbf{C}_5$), 123.3 ($\mathbf{C}_{8'}$), 119.0 ($\mathbf{C}_8$), 115.1 ($\mathbf{C}_{3'}$), 87.7 ($\mathbf{C}_2$), 74.6 ($\mathbf{C}_{11}$), 68.5 ($\mathbf{C}_{15}$), 64.3 ($\mathbf{C}_{5'}$), 59.5 ($\mathbf{C}_3$), 47.4 ($\mathbf{C}_{7'}$), 45.5 ($\mathbf{C}_{12}$), 35.5 ($\mathbf{C}_{10'}$), 32.2 ($\mathbf{C}_{17}$), 30.0 ($\mathbf{C}_{6'}$).
FTIR (thin film) cm^{-1}:	3345 (w), 3001 (w), 1695 (s), 1512 (m), 1461 (m), 1169 (m), 755 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{39}H_{36}N_7O_6S_3$ $[M+H]^+$: 794.1884, found: 794.1890.
$[\alpha]_D^{23}$:	+175 (*c* = 0.11, $CHCl_3$).

TLC (10% methanol in dichloromethane), R*f*: 0.52 (UV, CAM, $AgNO_3$).



S12 **S13** **31**

(4*S*,6a*S*,11b*S*,12a*S*)-11b-(4-Methoxyphenyl)-14-methyl-7-(phenylsulfonyl)-6a,7,11b,12-tetrahydro-4,12a-(epiminomethano)[1,2,3,5]trithiazepino[5',4':1,5]pyrrolo[2,3-*b*]indole-5,13-(4*H*)-dione (31); epitrithiodiketopiperazine 31:

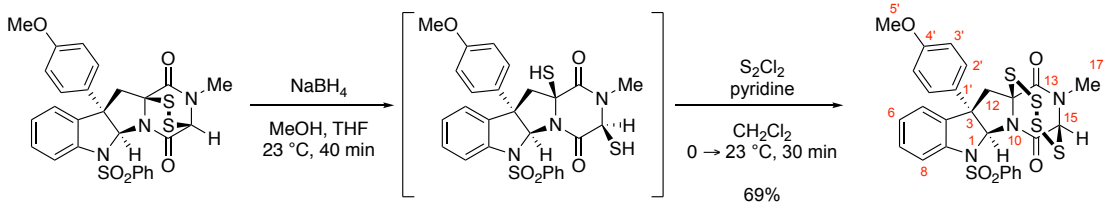
This compound was prepared in three steps starting from diol **S12**[15] using the methodology developed to access corresponding C3-(indol-3'-yl) epitrithiodiketopiperazine. First, the corresponding C11-thiohemiaminal was prepared from diol **S12** (57.2 mg, 107 µmol) and was purified by flash column chromatography on silica gel (eluent: 10→80% acetone in dichloromethane) to afford the C11-thiohemiaminal (49.2 mg, 83.5%)[16] as a white foam. Next, the C11-triphenylmethanetrisulfide **S13** was prepared from C11-thiohemiaminal (26.4 mg, 47.9 µmol) and was purified by flash column chromatography on silica gel (eluent: 0→30% ethyl acetate in dichloromethane) to afford C11-triphenylmethanetrisulfide **S13** (31.2 mg, 76.0%)[17] as a white solid. Finally, epitrithiodiketopiperazine **31** was prepared from the C11-triphenylmethanetrisulfide **S13** (29.5 mg, 34.4 µmol) and was purified by flash column chromatography on silica gel (eluent: 5→15% ethyl acetate in dichloromethane) to afford epitrithiodiketopiperazine **31** (17.0 mg, 82.7%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Based on ^{1}H NMR analysis at 25 °C degrees in $CDCl_3$, epitrithiodiketopiperazine **31** exists as a 2.6:1 mixture of conformers.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): *Major conformer:* δ 7.65 (app-d, *J* = 7.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.57 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.44–7.37 (m, 2H, C_7**H**, SO_2Ph-*p*-**H**), 7.23 (app-t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 7.21–7.09 (m, 2H, C_5**H**, C_6**H**), 6.86 (app-d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.69 (app-d, *J* = 8.8 Hz, 2H, $C_{3'}$**H**), 4.84 (s, 1H, C_{15}**H**), 3.77 (s,

15. For the preparation of diol **S12** and its conversion to the corresponding ETP (+)-**8**, see Boyer, N.; Morrison, K.C.; Kim, J.; Hergenrother, P. J.; Movassaghi, M. Synthesis and Anticancer Activity of Epipolythiodiketopiperazine Alkaloids. *Chem. Sci.*, **2013**, *4*, 1646–1657.
16. The C11-hemithioaminal has been characterized by NMR: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.75 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.47 (d, *J* = 8.0 Hz, 2H, SO_2Ph-*o*-**H**), 7.42 (t, *J* = 8.3, C_7**H**), 7.35 (t, *J* = 7.4 Hz, SO_2Ph-*p*-**H**), 7.29–7.22 (m, 2H, C_5**H**, C_6**H**), 7.11 (t, *J* = 7.8 Hz, 2H, SO_2Ph-*m*-**H**), 6.69 (d, *J* = 8.6 Hz, 2H, $C_{2'}$**H**), 6.60 (d, *J* = 8.4 Hz, 2H, $C_{3'}$**H**), 6.44 (s, 1H, C_2**H**), 5.33 (d, *J* = 4.7 Hz, 1H, C_{15}**H**), 4.64 (d, *J* = 4.8 Hz, C_{15}O**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.39 (d, *J* = 14.6 Hz, 1H, C_{12}**H**$_a$), 3.11 (d, *J* = 14.7 Hz, 1H, C_{12}**H**$_b$), 3.08 (s, 3H, C_{17}**H**), 2.45 (s, 1H, C_{11}S**H**). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 25 °C): δ 166.0 (C_{13}), 165.3 (C_{16}), 158.7 ($C_{4'}$), 141.6 (C_9), 137.9 (SO_2Ph-*ipso*-**C**), 135.3 (C_4), 133.2 (SO_2Ph-*p*-**C**), 132.0 ($C_{1'}$), 129.7 (C_7), 128.7 (SO_2Ph-*m*-**C**), 127.6 ($C_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.2 (C_5), 126.1 (C_6), 118.5 (C_8), 114.4 ($C_{3'}$), 86.8 (C_2), 76.9 (C_{15}), 69.3 (C_{11}), 57.6 (C_3), 55.4 ($C_{5'}$), 53.45 (C_{12}), 29.0 (C_{17}). TLC (25% acetone in dichloromethane), R*f*: 0.23 (UV, CAM, $AgNO_3$).
17. The C11-triphenylmethanetrisulfide **S13** has been characterized by NMR: ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.59 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.48 (d, *J* = 7.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.35 (t, *J* = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.30–7.22 (m, 9H, Ph-*m*-**H**, Ph-*p*-**H**), 7.18–7.13 (m, 6H, Ph-*o*-**H**), 7.11 (t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 7.05 (d, *J* = 7.0 Hz, 1H, C_5**H**), 6.98 (t, *J* = 7.4 Hz, 1H, C_6**H**), 6.62 (d, *J* = 8.9 Hz, 2H, $C_{2'}$**H**), 6.56 (d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.44 (s, 1H, C_2**H**), 5.36 (d, *J* = 4.0 Hz, 1H, C_{15}**H**), 4.23 (d, *J* = 4.0 Hz, 1H, C_{15}O**H**), 3.75 (s, 3H, $C_{5'}$**H**), 3.21 (d, *J* = 15.1 Hz, 1H, C_{12}**H**$_a$), 3.11 (d, *J* = 15.1 Hz, 1H, C_{12}**H**$_b$), 3.02 (s, 3H, C_{17}**H**). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.7 (C_{16}), 163.7 (C_{13}), 158.7 ($C_{4'}$), 143.0 (C(Ph-*ipso*-**C**)$_3$), 141.5 (C_9), 138.1 (SO_2Ph-*ipso*-**C**), 135.4 (C_4), 133.2 (SO_2Ph-*p*-**C**), 132.6 ($C_{1'}$), 130.3 (C(Ph-*m*-**C**)$_3$), 129.5 (C_7), 128.8 (SO_2Ph-*m*-**C**), 128.1 (C(Ph-*o*-**C**)$_3$), 127.5 ($C_{2'}$), 127.5 (C(Ph-*p*-**C**)$_3$), 127.3 (SO_2Ph-*o*-**C**), 125.9 (C_5), 125.9 (C_6), 118.1 (C_8), 114.4 ($C_{3'}$), 87.0 (C_2), 77.0 (C_{15}), 75.9 (C_{11}), 73.6 (**C**(Ph)$_3$), 57.5 (C_3), 55.5 ($C_{5'}$), 49.2 (C_{12}), 29.6 (C_{17}). TLC (10% acetone in dichloromethane), R*f*: 0.38 (UV, CAM, $AgNO_3$, Ellman's Reagent).

	3H, $C_{5'}$**H**), 3.44 (d, *J* = 14.8 Hz, 1H, C_{12}**H**$_a$), 3.16 (s, 3H, C_{17}**H**), 3.08 (d, *J* = 14.8 Hz, 1H, C_{12}**H**$_b$). *Minor conformer:* δ 7.51 (m, 3H, C_8**H**, SO_2Ph-*o*-**H**), 7.34 (app-t, *J* = 7.4, 1H, SO_2Ph-*p*-**H**), 7.30 (app-t, *J* = 8.1 Hz, C_7**H**), 7.21–7.09 (m, 4H, SO_2Ph-*m*-**H**, C_5H, C_6**H**), 6.83 (app-d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.72 (s, 1H, C_2**H**), 6.66 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 5.18 (s, 1H, C_{15}**H**), 3.78 (s, 3H, $C_{5'}$**H**), 3.29 (d, *J* = 14.9 Hz, 1H, C_{12}**H**$_a$), 2.98 (s, 3H, C_{17}**H**), 2.98 (d, *J* = 14.9 Hz, 1H, C_{12}**H**$_b$).
$^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$, 25 °C):	*Major conformer:* δ 168.0 (**C**$_{13}$), 162.1 (**C**$_{16}$), 159.0 (**C**$_{5'}$), 142.9 (**C**$_9$), 139.5 (SO_2Ph-*ipso*-**C**), 135.0 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 131.5 (**C**$_{1'}$), 130.2 (**C**$_7$), 128.8 (SO_2Ph-*m*-**C**), 127.5 (**C**$_{2'}$), 127.1 (SO_2Ph-*o*-**C**), 125.8 (**C**$_5$/**C**$_6$), 125.7 (**C**$_5$/**C**$_6$), 118.7 (**C**$_8$), 114.5 (**C**$_{3'}$), 86.1 (**C**$_2$), 79.6 (**C**$_{11}$), 67.1 (**C**$_{15}$), 57.6 (**C**$_3$), 55.4 (**C**$_{5'}$), 50.7 (**C**$_{12}$), 32.5 (**C**$_{17}$). *Minor conformer:* δ 166.9 (**C**$_{13}$), 161.2 (**C**$_{16}$), 158.9 (**C**$_{5'}$), 141.5 (**C**$_9$), 138.9 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 131.4 (**C**$_{1'}$), 129.6 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 127.8 (**C**$_{2'}$/SO_2Ph-*o*-**C**), 127.5 (**C**$_{2'}$/SO_2Ph-*o*-**C**), 126.3 (**C**$_5$/**C**$_6$), 125.7 (**C**$_5$/**C**$_6$), 118.6 (**C**$_8$), 114.5 (**C**$_{3'}$), 88.0 (**C**$_2$), 75.0 (**C**$_{11}$), 71.1 (**C**$_{15}$), 57.8 (**C**$_3$), 55.4 (**C**$_{5'}$), 48.8 (**C**$_{12}$), 33.0 (**C**$_{17}$).
FTIR (thin film) cm^{-1}:	3063 (w), 2837 (w), 1686 (br-s), 1609 (w), 1513 (m), 1364 (m), 1254 (m), 1168 (s), 1090 (w), 1033 (m), 832 (w), 797 (w), 736 (m), 600 (m), 575 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{27}H_{24}N_3O_5S_4$ $[M+H]^+$: 598.0593, found: 598.0585.

TLC (20% ethyl acetate in dichloromethane), R*f*: 0.51 (UV, CAM, $AgNO_3$).



(5*S*,7a*S*,12b*S*,13a*S*)-12b-(4-Methoxyphenyl)-15-methyl-8-(phenylsulfonyl)-7a,8,12b,13-tetrahydro-5,13a-(epiminomethano)[1,2,3,4,6]tetrathiazocino[6',5':1,5]pyrrolo[2,3-*b*]indole-6,14 (5*H*)-dione (32); epitetrathiodiketopiperazine 32:

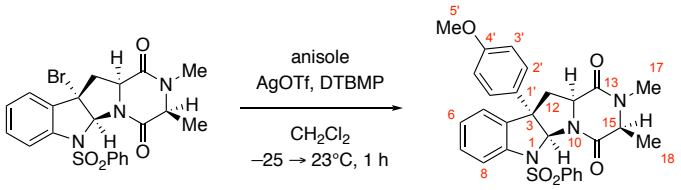
Sodium borohydride (2.4 mg, 63 μmol, 5.0 equiv) was added as a solid in one portion to a solution of epidithiodiketopiperazine (+)-**8**[15] (17.5 mg, 30.9 μmol, 1 equiv) in tetrahydrofuran (7.7 mL) and methanol (77 μL). After 40 min, the reaction mixture was diluted with dichloromethane (75 mL) and was washed with a saturated aqueous ammonium chloride solution (2 × 35 mL). The aqueous layer was extracted with dichloromethane (35 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the stirring reaction mixture. The reaction mixture was then concentrated under reduced pressure to approximately 15 mL and was cooled to 0 °C. Pyridine (25 μL, 0.31 mmol, 10 equiv) was added via syringe to the solution of bisthiol **S14**, followed by the dropwise addition of a solution of disulfur dichloride (0.50 M, 0.10 mL, 50 μmol, 1.6 equiv) in dichloromethane via syringe. The reaction mixture was removed from the ice−water bath and allowed to stir and warm to 23 °C. After 30 min, the reaction was diluted with dichloromethane (35 mL) and was washed sequentially with a saturated aqueous ammonium chloride solution (2 × 30 mL), with deionized water (30 mL), and with a saturated aqueous sodium chloride solution (30 mL). The combined aqueous layers were extracted with a single portion of dichloromethane (50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→10% ethyl acetate in dichloromethane) to afford the epitetrathiodiketopiperazine **32** (13.5 mg, 69.2%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ 7.94 (app-d, *J* = 7.8 Hz, 2H, SO_2Ph-*o*-**H**), 7.53 (td, *J* = 7.6, 1.3 Hz, 1H, SO_2Ph-*p*-**H**), 7.45 (d, *J* = 8.2 Hz, 1H, C_8**H**), 7.42 (app-t, *J* = 7.7 Hz, 2H, SO_2Ph-*m*-**H**), 7.29–7.23 (m, 1H, C_7**H**), 7.08 (app-t, *J* = 7.4 Hz, 1H, C_6**H**), 7.03 (d, *J* = 7.6 Hz, 1H, C_5**H**), 6.89 (app-d, *J* = 8.3 Hz, 2H, $C_{2'}$**H**), 6.83 (s, 1H, C_2**H**), 6.71 (app-d, *J* = 8.7 Hz, 1H, $C_{3'}$**H**), 5.12 (s, 1H, C_{15}**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.27 (d, *J* = 14.5 Hz, 1H, C_{12}**H**$_a$), 3.10 (d, *J* = 14.5 Hz, 1H, C_{12}**H**$_b$), 3.01 (s, 3H, C_{17}**H**).

^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$, 25 °C): δ 167.8 (**C**$_{13}$), 162.7 (**C**$_{16}$), 159.0 (**C**$_{4'}$), 141.7 (**C**$_9$), 139.2 (SO_2Ph-*ipso*-**C**), 136.6 (**C**$_4$), 133.5 (**C**$_{1'}$), 133.3 (SO_2Ph-*p*-**C**), 129.5 (**C**$_7$), 129.1 (SO_2Ph-*m*-

	C), 127.8 (SO_2Ph-*o*-**C**), 127.0 (**C**$_{2'}$), 125.5 (**C**$_6$), 124.8 (**C**$_5$), 116.6 (**C**$_8$), 114.6 (**C**$_{3'}$), 86.6 (**C**$_2$), 76.0 (**C**$_{11}$), 68.3 (**C**$_{15}$), 57.2 (**C**$_3$), 55.5 (**C**$_{5'}$), 49.7 (**C**$_{12}$), 32.3 (**C**$_{17}$).
FTIR (thin film) cm^{-1}:	3064 (w), 2836 (w), 1692 (s), 1674 (s), 1610 (w), 1513 (m), 1383 (m), 1254 (m), 1169 (s), 1090 (w), 1032 (m), 832 (w), 796 (w), 737 (m), 597 (m), 565 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{54}H_{46}N_6NaO_{10}S_{10}$ $[2M+Na]^+$: 1281.0375, found: 1281.0376.

TLC (20% ethyl acetate in dichloromethane), R*f*: 0.53 (UV, CAM, $AgNO_3$).



(+)-**36** (+)-**37**

(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-Methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (37); anisole adduct (+)-37:

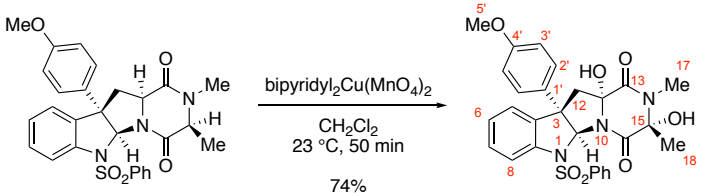
endo-Tetracyclic bromide[18] (+)-**36** (2.01 g, 4.10 mmol, 1 equiv) and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 2.11 g, 10.3 mmol, 2.51 equiv) were azeotropically dried by concentration from anhydrous benzene (2 x 10 mL) under reduced pressure. Dichloromethane (40 mL) and anisole (8.9 mL, 82 mmol, 20 equiv) were added sequentially, and the resulting colorless solution was cooled to –25 °C. Silver trifluoromethanesulfonate (AgOTf, 2.11 g, 8.21 mmol, 2.00 equiv) was added as a solid in one portion, the reaction mixture was stirred at –25 °C for 30 min, then the cold bath was removed and the resulting mixture was allowed to stir and warm to room temperature. After 30 min, the suspension was diluted with dichloromethane (200 mL) and was washed with a mixture of deionized water, saturated aqueous sodium thiosulfate solution, and saturated aqueous sodium bicarbonate solution (2:1:1, 2 × 300 mL). The aqueous layers were extracted with dichloromethane (2 × 100 mL), and the combined organic extracts were washed sequentially with deionized water (250 mL) and with a saturated aqueous sodium chloride solution (150 mL). The combined aqueous layers were extracted with dichloromethane (100 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting foam was purified by flash column chromatography on silica gel (eluent: 0→50% acetone in chloroform) to afford anisole adduct (+)-**37** (1.72 g, 81.2%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.61 (d, J = 8.1 Hz, 1H, C_8**H**), 7.45 (app-d, J = 8.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.32 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.30–7.26 (m, 1 H, C_7**H**) 7.14–7.11 (m, 2H, C_5**H**, C_6**H**), 7.09 (app-t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.67 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.61 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.39 (dd, J = 5.6, 9.0 Hz, 1H, C_{11}**H**), 4.04 (q, J = 7.0 Hz, 1H, C_{15}**H**), 3.77 (s, 3H, $C_{5'}$**H**), 3.14 (dd, J = 6.5, 14.1 Hz, 1H, C_{12}**H**$_a$), 2.87 (dd, J = 8.9, 14.0 Hz, 1H, C_{12}**H**$_b$), 2.85 (s, 3H, C_{17}**H**), 1.58 (d, J = 7.1 Hz, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 167.9 (**C**$_{16}$), 158.7 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.7 (**C**$_4$), 132.8 (SO_2Ph-*p*-**C**, **C**$_{1'}$), 129.2 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$),

18. Kim, J.; Ashenhurst, J. A.; Movassaghi, M. Total Synthesis of (+)-11,11′-Dideoxyverticillin A. *Science*, **2009**, *324*, 238-241.

	127.5 (SO_2Ph-*o*-**C**), 126.0 (**C**$_5$), 125.3 (**C**$_6$), 117.2 (**C**$_8$), 114.4 (**C**$_{3'}$), 87.3 (**C**$_2$), 59.3 (**C**$_3$), 58.8 (**C**$_{11}$), 57.1 (**C**$_{15}$), 55.4 (**C**$_{5'}$), 39.0 (**C**$_{12}$), 29.5 (**C**$_{17}$), 14.5 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	2994 (w), 1677 (s), 1513 (m), 1253 (m), 1169 (s), 1031 (w), 832 (w), 757 (w), 602 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{28}H_{28}N_3O_5S$ $[M+H]^+$: 518.1744, found: 518.1745.
$[\alpha]_D^{23}$:	+58 (*c* = 0.30, $CHCl_3$).
TLC (20% acetone in chloroform), R*f*:	0.26 (UV, CAM).



(+)-**37** **38**

(3*R*,5a*S*,10b*S*,11a*R*)-3,11a-Dihydroxy-10b-(4-methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (38); diol 38:

Bis(2,2'-bipyridyl)copper(II) permanganate[19] (1.61 g, 2.62 mmol, 2.70 equiv) was added as a solid to solution of anisole adduct (+)-**37** (502 mg, 0.970 mmol, 1 equiv) in dichloromethane (10 mL) at 23 °C. After 50 min, the reaction mixture was diluted with dichloromethane (100 mL) and was poured into an aqueous sodium bisulfite solution (1 M, 200 mL). The layers were separated, and the organic layer was washed sequentially with an aqueous sodium bisulfite solution (1 M, 75 mL), with a mixture of a saturated aqueous copper(II) sulfate solution and deionized water (1:1, 100 mL), with a saturated aqueous ammonium chloride solution (100 mL), and with a saturated aqueous sodium chloride solution (100 mL). The aqueous layers were separately extracted with dichloromethane (2 × 75 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting light blue foam was purified by flash column chromatography on silica gel (eluent: 0→30% acetone in dichloromethane) to afford diol **38** (393 mg, 74%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

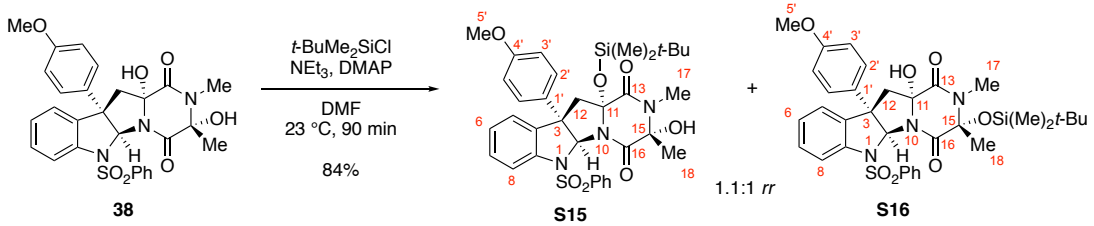
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.61 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.34–7.26 (m, 4H, C_7**H**, SO_2Ph-*p*-**H**, SO_2Ph-*o*-**H**), 7.22–7.15 (m, 2H, C_5**H**, C_6**H**), 7.02 (app-t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.78 (app-d, *J* = 8.9 Hz, 2H, $C_{2'}$**H**), 6.55 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.35, (s, 1H, C_2**H**), 5.62 (br-s, 1H, O**H**), 5.24 (br-s, 1H, O**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.38 (d, *J* = 15.1 Hz, 1H, C_{12}**H**$_a$), 2.99 (s, 3H, C_{17}**H**), 2.92 (d, *J* = 15.1 Hz, 1H, C_{12}**H**$_b$), 1.81 (s, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 168.2 (C_{13}), 166.8 (C_{16}), 158.4 ($C_{4'}$), 140.0 (C_9), 138.2 (SO_2Ph-*ipso*-**C**), 137.7 (C_4), 133.9 ($C_{1'}$), 132.9 (SO_2Ph-*p*-**C**), 129.1 (C_7), 128.6 (SO_2Ph-*m*-**C**/$C_{2'}$), 128.5 (SO_2Ph-*m*-**C**/$C_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.5 (C_5), 126.1 (C_6), 118.0 (C_8), 114.3 ($C_{3'}$), 88.7 (C_2), 87.4 (C_{11}), 85.7 (C_{15}), 58.1 (C_3), 55.4 ($C_{5'}$), 49.6 (C_{12}), 28.1 (C_{17}), 22.8 (C_{18}).

19. Firouzabadi, H.; Naderi, M.; Sardarian, A.; Vessal, B. The Facile Oxidation of Thiols to Disulfides with Bis(2,2′-Bipyridyl) Copper-(II) Permanganate. *Synth. Commun.* **1983**, *13*, 611−615.

FTIR (thin film) cm^{-1}:	3375 (br), 3067 (w), 1687 (m), 1512 (m), 1361 (m), 1252 (m), 1169 (s), 832 (w), 737 (w), 600 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{28}H_{28}N_3O_7S$ $[M+H]^+$: 550.1642, found: 550.1640.

TLC (20% acetone in dichloromethane), R*f*: 0.22 (UV, CAM).



38 S15 S16

(3*R*,5a*S*,10b*S*,11a*R*)-11a-((*tert*-Butyldimethylsilyl)oxy)-3-hydroxy-10b-(4-methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (S15) and (3*R*,5a*S*,10b*S*,11a*R*)-3-((*tert*-butyldimethylsilyl)oxy)-11a-hydroxy-10b-(4-methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (S16); silyl ethers S15 and S16:

Diol **38** (1.00 g, 1.82 mmol, 1 equiv) was azeotropically dried by concentration from anhydrous dichloromethane (2.5 mL) and anhydrous benzene (9.0 mL) under reduced pressure. The flask was charged with 4-(dimethylamino)pyridine (DMAP, 10.2 mg, 83.5 μmol, 0.0459 equiv), and the solids were dissolved in *N,N*-dimethylformamide (18 mL). Triethylamine (0.76 mL, 5.45 mmol, 3.00 equiv) was then added via syringe followed immediately by *tert*-butyldimethylsilyl chloride (352 mg, 2.34 mmol, 1.29 equiv) as a solid in one portion. After 90 min, the white suspension was diluted with ethyl acetate−hexanes (4:1, 125 mL) and was washed with a saturated aqueous ammonium chloride solution (100 mL). The aqueous layer was extracted with ethyl acetate−hexanes (4:1, 2 × 60 mL), and the combined organic extracts were washed sequentially with deionized water (3 × 100 mL) and with a saturated aqueous sodium chloride solution (100 mL). The combined aqueous layers were extracted with a single portion of ethyl acetate−hexanes (3:1, 100 mL), and the organic extract was washed sequentially with deionized water (3 × 50 mL) and with a saturated aqueous sodium chloride solution (50 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting white foam was purified by flash column chromatography on silica gel (eluent: 0→30% acetone in hexanes) to afford a mixture of regioisomeric silyl ethers **S15** and **S16** (1.01 g, 84%, 1.1:1) as a white foam. Analytical samples of regioisomeric silyl ethers **S15** and **S16** were obtained by flash column chromatography on silica gel (eluent: 0→10% diethyl ether in dichloromethane). Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

Silyl ether S15:

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.60 (d, J = 8.0 Hz, 1H, C_8**H**), 7.33−7.23 (m, 4H, C_7**H,** SO_2Ph-*p*-**H**, SO_2Ph-*o*-**H**), 7.20−7.15 (m, 2H, C_5**H**, C_6**H**), 6.99 (app-t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.71 (app-d, J =8.9 Hz, 2H, $C_{2'}$**H**), 6.56 (app-d, J =8.9 Hz, 2H, $C_{3'}$**H**), 6.42 (s, 1H, C_2**H**), 3.82 (s, 1H, C_{15}O**H**), 3.78 (s, 3H, $C_{5'}$**H**$_3$), 3.53 (d, J = 15.0 Hz, 1H, C_{12}**H**$_a$), 2.93 (s, 3H, C_{17}**H**), 2.78 (d, J = 15.1 Hz, 1H, C_{12}**H**$_b$), 1.65 (s, 3H, C_{18}**H**), 0.97 (s, 9H, SiC(C**H**$_3$)$_3$), 0.23 (s, 3H, SiC**H**$_3$), 0.09 (s, 3H, SiC**H**$_3$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.3 (**C**$_{16}$), 166.3 (**C**$_{13}$), 158.6 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.6 (SO_2Ph-*ipso*-**C**), 136.9 (**C**$_4$), 133.4 (**C**$_{1'}$),

132.7 (SO_2Ph-*p*-**C**), 129.2 (**C**$_7$), 128.5 (SO_2Ph-*m*-**C**), 128.3 (**C**$_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.4 (**C**$_5$), 125.9 (**C**$_6$), 118.0 (**C**$_8$), 114.3 (**C**$_{3'}$), 89.2 (**C**$_{11}$), 88.2 (**C**$_2$), 85.2 (**C**$_{15}$), 58.3 (**C**$_3$), 55.5 (**C**$_{5'}$), 50.7 (**C**$_{12}$), 27.9 (**C**$_{17}$), 25.8 (SiC(**C**H$_3$)$_3$) 24.2 (**C**$_{18}$), 18.4 (Si**C**(CH$_3$)$_3$), −3.3 (Si**C**H$_3$), −4.6 (Si**C**H$_3$).

FTIR (thin film) cm^{-1}: 3450 (br-w), 2956 (w), 2931 (w), 1677 (m), 1513 (m), 1254 (s), 1170 (s), 829 (m), 687 (w), 601 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{34}H_{42}N_3O_7SSi$ $[M+H]^+$: 664.2507, found: 665.2508.

TLC (40% acetone in hexanes), R*f*: 0.43 (UV, CAM).
TLC (7% diethyl ether in dichloromethane), R*f*: 0.26 (UV, CAM).

Silyl ether S16:

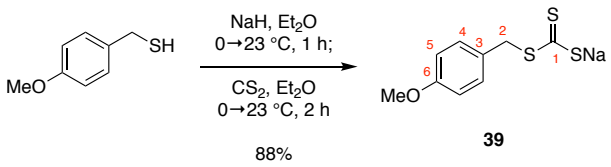
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.61 (d, *J* = 8.1 Hz, 1H, C$_8$**H**), 7.31−7.25 (m, 4H, C$_7$**H,** SO_2Ph-*p*-**H**, SO_2Ph-*o*-**H**), 7.17−7.14 (m, 2H, C$_5$**H**, C$_6$**H**), 7.00 (app-t, *J* = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.74 (app-d, *J* =8.8 Hz, 2H, C$_{2'}$**H**), 6.58 (app-d, *J* =8.9 Hz, 2H, C$_{3'}$**H**), 6.30 (s, 1H, C$_2$**H**), 4.84 (s, 1H, C$_{11}$O**H**), 3.78 (s, 3H, C$_{5'}$**H**$_3$), 3.37 (d, *J* = 15.1 Hz, 1H, C$_{12}$**H**$_a$), 2.97 (s, 3H, C$_{17}$**H**), 2.84 (d, *J* = 15.1 Hz, 1H, C$_{12}$**H**$_b$), 1.83 (s, 3H, C$_{18}$**H**), 0.92 (s, 9H, SiC(C**H**$_3$)$_3$), 0.33 (s, 3H, SiC**H**$_3$), 0.32 (s, 3H, SiC**H**$_3$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.9 (**C**$_{13}$), 164.8 (**C**$_{16}$), 158.4 (**C**$_{4'}$), 140.1 (**C**$_9$), 138.4 (SO_2Ph-*ipso*-**C**), 137.7 (**C**$_4$), 134.1 (**C**$_{1'}$), 132.8 (SO_2Ph-*p*-**C**), 129.0 (**C**$_7$), 128.5 (SO_2Ph-*m*-**C**, **C**$_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.4 (**C**$_5$), 125.9 (**C**$_6$), 117.9 (**C**$_8$), 114.2 (**C**$_{3'}$), 88.9 (**C**$_2$), 87.9 (**C**$_{15}$), 87.3 (**C**$_{11}$), 58.0 (**C**$_3$), 55.4 (**C**$_{5'}$), 49.2 (**C**$_{12}$), 28.1 (**C**$_{17}$), 25.7 (SiC(**C**H$_3$)$_3$), 23.5 (**C**$_{18}$), 18.2 (Si**C**(CH$_3$)$_3$), −2.3 (Si**C**H$_3$), −3.4 (Si**C**H$_3$).

FTIR (thin film) cm^{-1}: 3415 (br-w), 2930 (w), 2859 (w), 2102 (w), 1714 (w), 1513 (w), 1365 (m), 1253 (s), 1171 (s), 833 (m), 601 (w).

HRMS (ESI) (*m/z*): calc'd for $C_{34}H_{42}N_3O_7SSi$ $[M+H]^+$: 664.2507, found: 664.2499.

TLC (40% acetone in hexanes), R*f*: 0.43 (UV, CAM).
TLC (7% diethyl ether in dichloromethane), R*f*: 0.53 (UV, CAM).



Sodium 4-methoxybenzyl carbonotrithioate (39); monosodium trithiocarbonate 39:

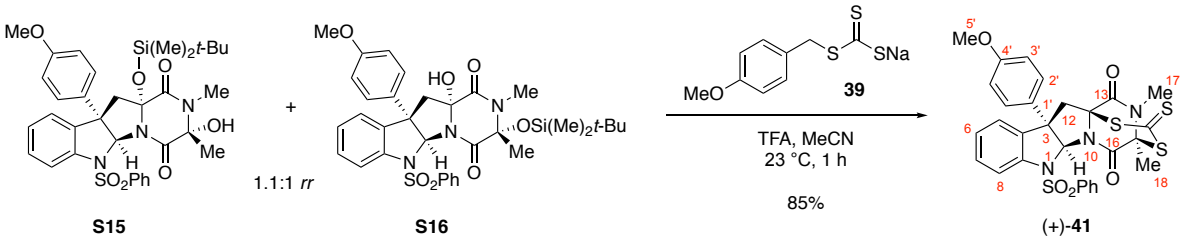
A suspension of sodium hydride (60% dispersion, 1.03 g, 25.8 mmol, 1 equiv) in diethyl ether (125 mL) at 0 °C was sparged with argon for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture. *p*-Methoxybenzyl thiol (4.5 mL, 33 mmol, 1.3 equiv) was added dropwise via syringe over 2 min, the solution was stirred for 5 min, then the ice−water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 1 h, the light-gray suspension was cooled to 0 °C, and carbon disulfide (2.0 mL, 33 mmol, 1.3 equiv) was added dropwise via syringe over 3.5 min. The ice−water bath was removed and the reaction mixture was allowed to stir and warm to 23 °C. After 2 h, a yellow precipitate was collected by filtration of the yellow suspension through a 350-mL medium-porosity fritted-glass funnel. The yellow precipitate was washed with hexanes (2 × 50 mL) and was dried under reduced pressure to afford monosodium trithiocarbonate **39** (5.76 g, 88.4%) as a yellow solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (600 MHz, DMSO-d_6, 25 °C): δ 7.20 (d, J = 8.6 Hz, 2H, C_4**H**), 6.81 (d, J = 8.6 Hz, 2H, C_5**H**), 4.29 (s, 2H, C_2**H**), 3.71 (s, 3H, OC**H**$_3$).

^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6, 25 °C): δ 239.0 (**C**$_1$), 157.8 (**C**$_6$), 130.9 (**C**$_3$), 129.8 (**C**$_4$), 113.5 (**C**$_5$), 55.0 (O**C**H$_3$), 44.6 (**C**$_2$).

FTIR (thin film) cm^{-1}: 1507 (w), 1248 (w), 1229 (w), 1177 (w), 1003 (s), 833 (m), 539 (m).

HRMS (DART-TOF) (*m/z*): calc'd for $C_9H_9OS_3$ [M−Na]$^-$: 228.9821, found: 228.9813.



(+)-(4*S*,6a*S*,11b*S*,12a*S*)-11b-(4-Methoxyphenyl)-4,14-dimethyl-7-(phenylsulfonyl)-2-thioxo-6a,7,11b,12-tetrahydro-4,12a-(epiminomethano)[1,3,5]dithiazepino[5',4':1,5]pyrrolo[2,3-*b*]indole-5,13(4*H*)-dione (41); dithiepanethione (+)-41:

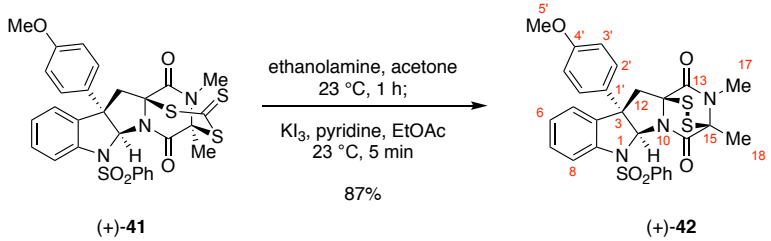
A mixture of regioisomeric silyl ethers **S15** and **S16** (1.1:1, 956 mg, 1.44 mmol, 1 equiv) was azeotropically dried by concentration from dichloromethane (5 mL) and anhydrous benzene (50 mL) under reduced pressure. The resulting white foam was dissolved in acetonitrile (100 mL) via cannula, and monosodium trithiocarbonate **39** (1.82 g, 7.21 mmol, 5.01 equiv) was added as a solid. Trifluoroacetic acid (TFA, 50 mL) was poured rapidly into the reaction mixture over 15 seconds, resulting in a homogeneous yellow solution. After 1 h, the dark orange solution was diluted with ethyl acetate−hexanes (9:1, 100 mL), was slowly poured into a saturated aqueous sodium bicarbonate solution (650 mL), and the biphasic mixture was stirred vigorously for 30 min. The aqueous layer was extracted with ethyl acetate−hexanes (9:1, 2 × 100 mL), and the combined organic extracts were washed sequentially with deionized water (200 mL) and with a saturated aqueous sodium chloride solution (150 mL). The combined aqueous layers were extracted with a single portion of ethyl acetate−hexanes (4:1, 100 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→7.5% diethyl ether in dichloromethane) to afford dithiepanethione (+)-**41** (766 mg, 85.0%) as a yellow foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.55 (d, J = 8.1 Hz, 1H, C_8**H**), 7.43 (app-d, J = 7.6 Hz, 2H, SO_2Ph-*o*-**H**), 7.30–7.21 (m, 2H, C_7H, SO_2Ph-p-**H**), 7.30–7.21 (m, 2H, C_5**H**, C_6**H**), 7.13 (app-t, 2H, J = 7.9 Hz, SO_2Ph-*m*-**H**), 6.87 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.68 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.59 (s, 1H, C_2**H**), 3.78 (s, 3H, $C_{5'}$**H**), 3.53 (d, J = 15.3 Hz, 1H, C_{12}**H**$_a$), 3.06 (s, 3H, C_{17}**H**), 3.05 (d, J = 15.2 Hz, 1H, C_{12}**H**$_b$), 1.92 (s, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): 215.7 (**C**S_3), 164.7 (**C**$_{13}$), 160.5 (**C**$_{16}$), 159.0 (**C**$_{4'}$), 141.5 (**C**$_9$), 138.9 (SO_2Ph-*ipso*-**C**), 134.9 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 131.4 (**C**$_{1'}$), 130.1 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 127.5 (**C**$_{2'}$), 126.8 (SO_2Ph-*o*-**C**), 126.4 (**C**$_6$), 125.5 (**C**$_5$), 118.7 (**C**$_8$), 114.6 (**C**$_{3'}$), 87.8 (**C**$_2$), 75.0 (**C**$_{11}$), 73.5 (**C**$_{15}$), 57.8 (**C**$_3$), 55.5 (**C**$_{5'}$), 48.7 (**C**$_{12}$), 28.4 (**C**$_{17}$), 19.8 (**C**$_{18}$).

FTIR (thin film) cm^{-1}:	3002 (w), 1713 (s), 1685 (s), 1476 (w), 1362 (s), 1169 (s), 1034 (m), 999 (m), 895 (w), 737 (m), 599 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{29}H_{26}N_3O_5S_4$ $[M+H]^+$: 624.0750, found: 624.0747.
$[\alpha]_D^{23}$:	+148 (*c* = 0.61, $CHCl_3$).

TLC (5% diethyl ether in dichloromethane), R*f*: 0.31 (UV, CAM, $AgNO_3$, DTNB).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-Methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (42); epidithiodiketopiperazine (+)-42:

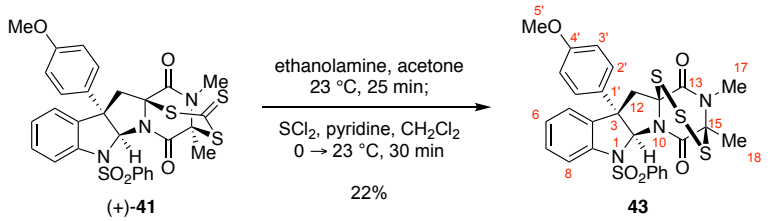
A yellow solution of dithiepanethione (+)-**41** (374 mg, 0.600 mmol, 1 equiv) in acetone (15 mL) at 23 °C was sparged with argon for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Ethanolamine (3.75 mL) was added via syringe over 30 seconds, resulting in a nearly colorless solution. After 1 h, the reaction mixture was diluted with ethyl acetate−hexanes (9:1, 100 mL) and was washed with an aqueous hydrogen chloride solution (1 M, 150 mL). The aqueous layer was extracted with ethyl acetate−hexanes (9:1, 2 × 50 mL), and the combined organic extracts were washed with a saturated aqueous sodium chloride solution (100 mL). A stock solution of potassium triiodide in pyridine[6] was added dropwise into the organic layer containing crude bisthiol until a persistent yellow color was observed. The resulting mixture was washed sequentially with an aqueous hydrogen chloride solution (1 M, 2 × 75 mL), with a mixture of deionized water and a saturated aqueous sodium thiosulfate solution (3:1, 100 mL), with deionized water (100 mL), and with a saturated aqueous sodium chloride solution (100 mL). The aqueous layers were separately extracted with a single portion of ethyl acetate−hexanes (9:1, 100 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 15% dichloromethane, 0→7.5% isopropanol in hexanes) to afford epidithiodiketopiperazine (+)-**42** (304 mg, 87.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.[20]

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.65 (d, J = 8.0 Hz, 1H, C_8**H**), 7.40 (app-t, d, J = 7.1, 1.5 Hz, 1H, C_7**H**), 7.34 (dd, J = 8.5, 1.2 Hz, 2H, SO_2Ph-*o*-**H**), 7.31–7.22 (m, 3H, SO_2Ph-*p*-**H**, $\mathbf{H}_5$, $\mathbf{H}_6$), 7.02 (app-t, J = 7.5 Hz, 2H, SO_2-*m*-**H**), 6.74 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.62 (app-d, J = 8.7 Hz, 2H, $C_{3'}$**H**), 6.42 (s, 1H, C_2**H**), 3.79 (s, 3H, $C_{5'}$**H**), 3.67 (d, J = 15.6 Hz, 1H, $C_{12}\mathbf{H}_a$), 3.05 (s, 3H,

20. The relative stereochemistry of epidisulfide (+)-**42** was confirmed by key NOESY cross–peaks on the corresponding bis(methylthioether). Our assignment is supported by key NOESY signals (^{1}H, ^{1}H) in ppm: (2.07, 3.18), (3.18, 7.11–7.03), (2.95, 6.70), (2.95, 6.76). This derivatized compound was prepared in one step using our methodology developed to access (+)-gliocladin B (Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803). The corresponding bis(methylthioether) of epidisulfide (+)-**42** was characterized as follows: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ δ 7.94 (d, J = 7.3 Hz, 2H, SO_2Ph-*o*-**H**), 7.61 (d, J = 8.2 Hz, 1H, C_8**H**), 7.52 (t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.40 (t, J = 7.8 Hz, 2H, SO_2Ph-*m*-**H**), 7.33–7.25 (m, 2H, C_7**H**), 7.11–7.03 (m, 2H, C_5**H**, C_6**H**), 6.76 (d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.70 (s, 1H, C_2**H**), 6.65 (d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 3.74 (s, 2H, $C_{5'}$**H**), 3.18 (d, J = 14.1 Hz, 1H, $C_{12}\mathbf{H}_a$), 3.07 (s, 3H, C_{17}**H**), 2.95 (d, J = 14.2 Hz, 1H, $C_{12}\mathbf{H}_b$), 2.07 (s, 3H, C_{11}S**C**$\mathbf{H}_3$), 1.91 (s, 3H, C_{15}S**C**$\mathbf{H}_3$), 1.84 (s, 3H, C_{18}**H**). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7 ($\mathbf{C}_{13}$), 163.3 ($\mathbf{C}_{16}$), 158.7 ($\mathbf{C}_{4'}$), 142.6 ($\mathbf{C}_9$), 139.7 (SO_2Ph-*ipso*-**C**), 136.7 ($\mathbf{C}_4$), 134.8 ($\mathbf{C}_{1'}$), 133.0 (SO_2Ph-*p*-**C**), 129.2 (SO_2Ph-*m*-**C**), 129.0 ($\mathbf{C}_7$), 127.1 (SO_2Ph-*o*-**C**), 126.9 ($\mathbf{C}_{2'}$), 124.7 ($\mathbf{C}_{5/6}$), 123.8 ($\mathbf{C}_{5/6}$), 116.7 ($\mathbf{C}_8$), 114.4 ($\mathbf{C}_{3'}$), 86.1 ($\mathbf{C}_2$), 70.0 ($\mathbf{C}_{11}$), 67.4 ($\mathbf{C}_{15}$), 56.7 ($\mathbf{C}_3$), 55.4 ($\mathbf{C}_{5'}$), 46.2 ($\mathbf{C}_{12}$), 29.3 ($\mathbf{C}_{17}$), 23.7 ($\mathbf{C}_{18}$), 15.8 (C_{15}S**C**H_3), 14.4 (C_{11}S**C**H_3). HRMS (ESI) (*m*/*z*): calc'd for $C_{30}H_{31}N_3NaO_5S_3$ [M+Na]$^+$: 632.1318, found 632.1315.

	C_{17}**H**), 2.88 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 1.97 (s, 3H, C_{18}**H**).
$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, 25 °C):	δ 165.8 (**C**$_{13}$), 161.4 (**C**$_{16}$), 158.8 (**C**$_{4'}$), 141.2 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 132.9 (SO_2Ph-*p*-**C**), 131.4 (**C**$_{1'}$), 129.7 (**C**$_7$), 128.5 (SO_2Ph-*m*-**C**), 127.9 (**C**$_{2'}$), 127.2 (SO_2Ph-*o*-**C**), 126.1 (**C**$_6$), 125.6 (**C**$_5$), 119.0 (**C**$_8$), 114.5 (**C**$_{3'}$), 88.0 (**C**$_2$), 73.9 (**C**$_{11}$), 73.5 (**C**$_{15}$), 59.1 (**C**$_3$), 55.5 (**C**$_{5'}$), 46.1 (**C**$_{12}$), 27.6 (**C**$_{17}$), 18.2 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	2951 (br), 2359 (w), 1679 (s), 1514 (s), 1457 (m), 1341 (s), 1249 (s), 1163 (s), 1028 (m), 905 (m), 730 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{28}H_{26}N_3O_5S_3$ $[M+H]^+$: 580.1029, found: 580.1032.
$[\alpha]_D^{23}$:	+293 (c = 0.57, $CHCl_3$).

TLC (15% dichloromethane and 15% isopropanol in hexanes), R*f*: 0.42 (UV, CAM, $AgNO_3$).



(4*S*,6a*S*,11b*S*,12a*S*)-11b-(4-Methoxyphenyl)-4,14-dimethyl-7-(phenylsulfonyl)-6a,7,11b,12-tetrahydro-4,12a-(epiminomethano)[1,2,3,5]trithiazepino[5',4':1,5]pyrrolo[2,3-*b*]indole-5,13(4*H*)-dione (43); epitrithiodiketopiperazine 43:

A yellow solution of dithiepanethione (+)-**41** (30.2 mg, 48.4 μmol, 1 equiv) in acetone (1.6 mL) at 23 °C was sparged with argon for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Ethanolamine (0.4 mL) was added via syringe over 30 seconds, resulting in a nearly colorless solution. After 25 min, the reaction mixture was diluted with dichloromethane (30 mL) and was washed with an aqueous hydrogen chloride solution (1 M, 2 × 30 mL). The combined aqueous layers were extracted with dichloromethane (30 mL), and the combined organic extracts were washed with a saturated aqueous sodium chloride solution (30 mL). The aqueous layer was extracted with dichloromethane (15 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the stirring reaction mixture. The reaction mixture was then concentrated under reduced pressure to approximately 25 mL and was cooled to 0 °C. Pyridine (25 μL, 310 μmol, 6.4 equiv) was added via syringe to the crude bisthiol solution, followed by the dropwise addition of a solution of monosulfur dichloride (0.39 M, 0.50 mL, 0.20 mmol, 4.1 equiv) in dichloromethane via syringe over 30 seconds. The reaction mixture was removed from the ice−water bath and allowed to stir and warm to 23 °C. After 30 min, the reaction mixture was washed sequentially with a saturated aqueous sodium bicarbonate solution (2 × 30 mL) and with a saturated aqueous ammonium chloride solution (2 x 40 mL). The aqueous layers were separately extracted with a single portion of dichloromethane (20 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue[21] was purified by flash column chromatography on silica gel (eluent: 0→20% ethyl acetate in dichloromethane) to afford epitrithiodiketopiperazine **43** (7.4 mg, 22%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments. Based on ^{1}H NMR analysis at 25 °C in $CDCl_3$, the product exists as a 3.5:1 mixture of conformers.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C):

Major conformer: δ 7.60 (m, 3H, SO_2Ph-*o*-**H**, C_8**H**), 7.48–7.36 (m, 2H, SO_2Ph-*p*-**H**, C_7**H**), 7.23–7.12 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 6.85 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.67 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.47 (s, 1H, C_2**H**), 3.77 (s, 3H, $C_{5'}$**H**), 3.41 (d, J = 14.7 Hz, 1H, C_{12}**H**$_a$), 3.18 (s, 3H, C_{17}**H**), 3.12 (d, J = 14.7 Hz, 1H, C_{12}**H**$_b$), 1.84 (s, 3H, C_{18}**H**).

21. As measured by crude ^{1}H NMR ($CDCl_3$) analysis, the ratio of tetrasulfide **44** : trisulfide **43** : disulfide (+)-**42** epithiodiketopiperazines was 1 : 2 : 1.2, respectively, before chromatography.

Minor conformer: δ 7.31 (m, 2H), 7.10–7.04 (m, 1H), 6.80 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.72 (s, 1H, C_2**H**), 6.64 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 3.78 (s, 3H, $C_{5'}$**H**), 3.28 (d, J = 14.9 Hz, 1H, C_{12}**H**$_a$), 3.03–2.95 (m, 4H, C_{17}**H**, C_{12}**H**$_b$), 1.93 (s, 3H, C_{18}**H**).

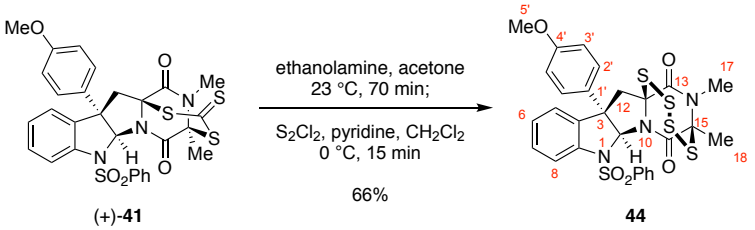
$^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$, 25 °C): *Major conformer:* δ 168.8 (**C**$_{13}$), 163.8 (**C**$_{16}$), 159.0 (**C**$_{4'}$), 143.2 (**C**$_9$), 139.6 (SO_2Ph-*ipso*-**C**), 135.0 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 131.7 (**C**$_{1'}$), 130.2 (**C**$_7$), 128.8 (SO_2Ph-*m*-**C**), 127.5 (**C**$_{2'}$), 127.1 (SO_2Ph-*o*-**C**), 125.8 (**C**$_5$), 125.8 (**C**$_6$), 118.9 (**C**$_8$), 114.6 (**C**$_{3'}$), 86.8 (**C**$_2$), 79.9 (**C**$_{11}$), 72.2 (**C**$_{15}$), 57.2 (**C**$_3$), 55.5 (**C**$_{5'}$), 51.7 (**C**$_{12}$), 28.5 (**C**$_{18}$), 21.8 (**C**$_{17}$).

Minor conformer: δ 167.2 (**C**$_{13}$), 141.6 (**C**$_9$), 138.7 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 129.6, 129.2, 128.6, 127.8, 127.6, 126.3, 125.5, 118.8 (**C**$_8$), 88.8 (**C**$_2$), 75.7 (**C**$_{5/6}$), 75.5 (**C**$_{5/6}$), 57.5 (**C**$_3$), 49.8 (**C**$_{12}$), 29.2 (**C**$_{17}$), 24.1 (**C**$_{18}$).

FTIR (thin film) cm^{-1}: 2936 (br-w), 1682 (s), 1513 (m), 1350 (s), 1167 (s), 1033 (m), 896 (w), 687 (w), 577 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{28}H_{26}N_3O_5S_4$ $[M+H]^+$: 612.0750, found: 612.0748.

TLC (10% ethyl acetate in dichloromethane), R*f*: 0.42 (UV, CAM).



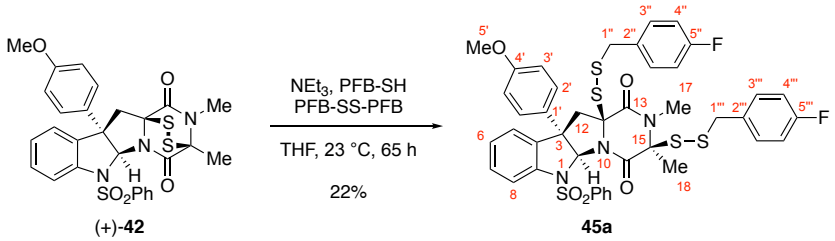
(5*S*,7a*S*,12b*S*,13a*S*)-12b-(4-Methoxyphenyl)-5,15-dimethyl-8-(phenylsulfonyl)-7a,8,12b,13-tetrahydro-5,13a-(epiminomethano)[1,2,3,4,6]tetrathiazocino[6',5':1,5]pyrrolo[2,3-*b*]indole-6,14(5*H*)-dione (44); epitetrathiodiketopiperazine 44:

A yellow solution of dithiepanethione (+)-**41** (40.3 mg, 64.6 μmol, 1 equiv) in acetone (2.0 mL) at 23 °C was sparged with argon for 10 min by discharge of a balloon equipped with a needle extending into the reaction mixture. Ethanolamine (0.4 mL) was added via syringe over 30 seconds, resulting in a nearly colorless solution. After 70 min, the reaction mixture was diluted with dichloromethane (30 mL) and was washed with an aqueous hydrogen chloride solution (1 M, 2 × 30 mL). The combined aqueous layers were extracted with dichloromethane (30 mL), and the combined organic extracts were washed with a saturated aqueous sodium chloride solution (30 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the stirring reaction mixture. The reaction mixture was then concentrated under reduced pressure to approximately 30 mL and was cooled to 0 °C. Pyridine (26 μL, 320 μmol, 5.0 equiv) was added via syringe to the stirring crude bisthiol solution, followed by the dropwise addition of a solution of disulfur dichloride (0.50 M, 0.50 mL, 250 μmol, 3.9 equiv) in dichloromethane via syringe over 30 seconds. After 15 min, the reaction mixture was washed with a saturated aqueous ammonium chloride solution (2 × 30 mL), and the combined aqueous layers were extracted with dichloromethane (25 mL). The combined organic extracts were washed with a saturated aqueous sodium chloride solution (45 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→20% ethyl acetate in dichloromethane) to afford epitetrathiodiketopiperazine **44** (27.6 mg, 66.3%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.96 (app-d, J = 7.2 Hz, 2H, SO_2Ph-*o*-**H**), 7.54 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.48 – 7.39 (m, 3H, C_8**H**, SO_2Ph-*m*-**H**), 7.27–7.20 (m, 1H, C_7**H**), 7.05 (app-t, J = 7.5, 1H, C_6**H**), 6.99 (d, J = 7.6, 1H, C_5**H**), 6.89 (s, 1H, C_2**H**), 6.84 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.70 (app-d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.27 (d, J = 14.4 Hz, 1H, C_{12}**H**$_a$), 3.10 (d, J = 14.4 Hz, 1H, C_{12}**H**$_b$), 3.05 (s, 3H, C_{17}**H**), 1.99 (s, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 164.8 (**C**$_{16}$), 158.9 (**C**$_{4'}$), 141.7 (**C**$_9$), 139.1 (SO_2Ph-*ipso*-**C**), 136.8 (**C**$_4$), 133.8 (**C**$_{1'}$), 133.4 (SO_2Ph-*p*-**C**), 129.4 (**C**$_7$), 129.2 (SO_2Ph-*m*-

	C), 127.8 (SO_2Ph-*o*-**C**), 126.9 (**C**$_{2'}$), 125.5 (**C**$_6$), 124.6 (**C**$_5$), 116.5 (**C**$_8$), 114.5 (**C**$_{3'}$), 87.1 (**C**$_2$), 76.1 (**C**$_{11}$), 74.4 (**C**$_{15}$), 56.9 (**C**$_3$), 55.5 (**C**$_{5'}$), 49.9 (**C**$_{12}$), 29.6 (**C**$_{17}$), 22.8 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	2930 (w), 1668 (s), 1610 (w), 1513 (m), 1354 (s), 1168 (s), 1032 (m), 899 (w), 738 (m), 565 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{28}H_{25}N_3NaO_5S_5$ $[M+Na]^+$: 666.0290, found: 666.0289.
TLC (5% ethyl acetate in hexanes), R*f*:	0.35 (UV, CAM).



(3*S*,5a*S*,10b*S*,11a*S*)-3,11a-Bis((4-fluorobenzyl)disulfaneyl)-10b-(4-methoxyphenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (45a); bis(*p*-fluorobenzyl)disulfide 45a:

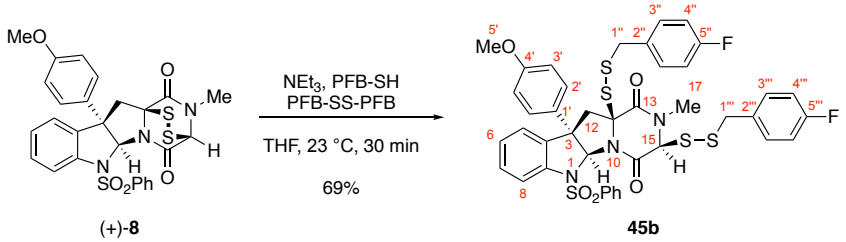
Triethylamine (70 µL, 0.50 mmol, 2.5 equiv) and (*p*-fluorophenyl)methanethiol (PFB-SH, 25 µL, 0.20 mmol, 1.0 equiv) were added via syringe to a solution of epidithiodiketopiperazine (+)-**42** (116 mg, 0.200 mmol, 1 equiv) and 1,2-bis(*p*-fluorobenzyl)disulfane (PFB-SS-PFB, 552 mg, 1.95 mmol, 9.75 equiv) in tetrahydrofuran (0.5 mL) at 23 °C. After 15 h, additional tetrahydrofuran (1.1 mL) was added via syringe to dissolve a white precipitate. After an additional 50 h, the reaction mixture was concentrated under reduced pressure and the resulting residue was purified by flash column chromatography on silica gel (eluent: 0→15% ethyl acetate in dichloromethane) to afford bisdisulfide **45a** (38.7 mg, 22.4%) as a white solid and recovered epidithiodiketopiperazine (+)-**42** (76.6 mg, 66.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): 7.67 (d, J = 8.1 Hz, 1H, C_8**H**), 7.48 (app-d, J = 7.6 Hz, 2H, SO_2Ph-*o*-**H**), 7.38–7.33 (m, 3H, $C_{3''/3'''}$**H**, C_7**H**), 7.30 (app-t, J = 7.7 Hz, 1H, SO_2Ph-*p*-**H**), 7.22–7.15 (m, 2H, C_5**H**, C_6**H**), 7.14–7.09 (m, 4H, $C_{3''/3'''}$**H**, SO_2Ph-*m*-**H**), 6.95 (app-t, J = 8.7 Hz, 2H, $C_{4''/4'''}$**H**), 6.90 (app-t, J = 8.6 Hz, $C_{4''/4'''}$**H**), 6.67 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.59 (s, 1H, C_2**H**), 6.58 (app-d, J = 9.1 Hz, 2H, $C_{3'}$**H**), 4.09 (d, J = 12.9 Hz, 1H, $C_{1''/1'''}$**H**), 3.99 (d, J = 12.9 Hz, 1H, $C_{1''/1'''}$**H**), 3.84 (d, J = 14.7 Hz, 1H, $C_{12}H_a$), 3.83 (s, 2H, $C_{1''/1'''}$**H**), 3.76 (s, 3H, $C_{5'}$**H**), 3.10 (s, 3H, C_{17}**H**), 2.99 (d, J = 14.8 Hz, 1H, $C_{12}H_b$), 2.09 (s, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 167.4 (C_{13}), 164.2 (C_{16}), 162.3 (d, J = 245.6 Hz, $C_{5''/5'''}$), 162.3 (d, J = 246.3 Hz, $C_{5''/5'''}$), 158.6 ($C_{4'}$), 142.2 (C_9), 137.9 (SO_2Ph-*ipso*-**C**), 135.5 (C_4), 133.2 ($C_{1'}$/SO_2Ph-*p*-**C**), 133.1 ($C_{1'}$/SO_2Ph-*p*-**C**), 132.9 (d, J = 3.2 Hz, $C_{2''/2'''}$), 132.4 (d, J = 3.3 Hz, $C_{2''/2'''}$), 131.7 (d, J = 8.2 Hz, $C_{3''/3'''}$), 131.3 (d, J = 8.2 Hz, $C_{3''/3'''}$), 129.4 (C_7), 128.7 (SO_2Ph-*m*-**C**), 127.5 ($C_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 125.9 ($C_{5/6}$), 125.7 ($C_{5/6}$), 118.5 (C_8), 115.5 (d, J = 21.5 Hz, $C_{4''/4'''}$), 115.4 (d, J = 21.5 Hz, $C_{4''/4'''}$), 114.3 ($C_{3'}$), 88.3 (C_2),

	73.7 (**C**$_{11}$), 71.1 (**C**$_{15}$), 57.1 (**C**$_{3}$), 55.5 (**C**$_{5'}$), 46.9 (**C**$_{12}$), 42.2 (**C**$_{1''/1'''}$), 41.7 (**C**$_{1''/1'''}$), 29.5 (**C**$_{17}$), 22.8 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	3485 (br), 2927 (br), 2106 (w), 1663 (m), 1600 (w), 1509 (s), 1362 (s), 833 (m), 687 (w), 599 (m).
HRMS (ESI) (*m/z*):	calc'd for $C_{42}H_{38}F_2N_3O_5S_5$ $[M+H]^+$: 862.1378, found: 862.1371.

TLC (5% ethyl acetate in dichloromethane), R*f*: 0.35 (UV, CAM, $AgNO_3$).



(+)-**8** **45b**

(3*S*,5a*S*,10b*S*,11a*S*)-3,11a-Bis((4-fluorobenzyl)disulfaneyl)-10b-(4-methoxyphenyl)-2-methyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (45b); bis(*p*-fluorobenzyl)disulfide 45b:

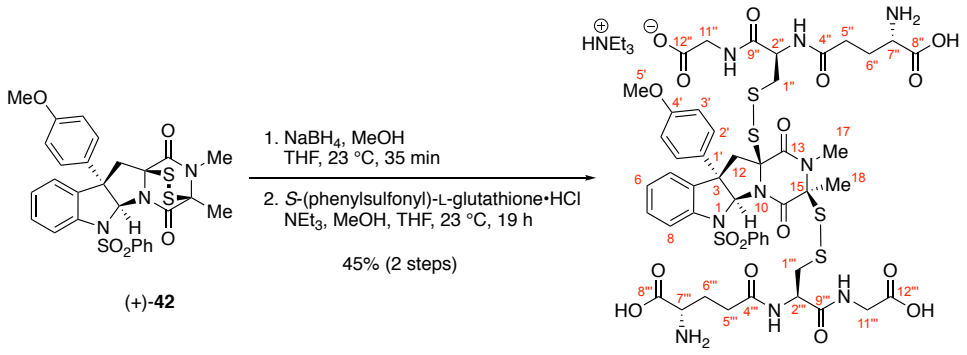
A solution of triethylamine (0.72 M, 54 µL, 39 µmol, 2.2 equiv) in tetrahydrofuran and a solution of (*p*-fluorophenyl)methanethiol (PFB-SH, 0.41 M, 22 µL, 9.0 µmol, 0.51 equiv) in tetrahydrofuran were added dropwise via syringe to a solution of epidithiodiketopiperazine (+)-**8** (10.0 mg, 17.7 µmol, 1 equiv) and 1,2-bis(*p*-fluorobenzyl)disulfane (PFB-SS-PFB, 15.2 mg, 54.0 mmol, 3.05 equiv) in tetrahydrofuran (0.9 mL). After 30 min, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 2→50% ethyl acetate in dichloromethane) to afford bisdisulfide **45b** (10.3 mg, 68.6%) as a white solid, epitrithiodiketopiperazine **31** (0.2 mg, 2%) as a white solid, and recovered epidithiodiketopiperazine (+)-**8** (1.7 mg, 17%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.64 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.59 (app-d, *J* = 7.4 Hz, 2H, SO_2Ph-*o*-**H**), 7.42–7.31 (m, 4H, $C_{3''/3'''}$**H**, SO_2Ph-*p*-**H**, C_7**H**), 7.19–7.13 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 7.08 (dd, *J* = 8.6, 5.4 Hz, 2H, $C_{3''/3'''}$**H**), 7.04 (d, *J* = 8.7 Hz, 2H, $C_{4''/4'''}$**H**), 6.91 (t, *J* = 8.7 Hz, 2H, $C_{4''/4'''}$**H**), 6.74 (app-d, *J* = 8.8 Hz, 2H, $C_{2'}$**H**), 6.63 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.59 (s, 1H, C_2**H**), 4.91 (s, 1H, C_{15}**H**), 4.21 (d, *J* = 12.8 Hz, 1H, $C_{1''/1'''}$**H**), 4.01 (d, *J* = 12.8 Hz, 1H, $C_{1''/1'''}$**H**), 3.83 (d, *J* = 12.3 Hz, 1H, $C_{1''/1'''}$**H**), 3.79 (d, *J* = 12.6 Hz, 1H, $C_{1''/1'''}$**H**), 3.77 (s, 3H, $C_{5'}$**H**), 3.55 (d, *J* = 14.8 Hz, 1H, C_{12}**H**$_a$), 3.12 (s, 3H, C_{17}**H**), 3.06 (d, *J* = 14.9 Hz, 1H, C_{12}**H**$_b$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 165.7 (**C**$_{13}$), 162.5 (**C**$_{16}$), 162.4 (d, *J* = 246 Hz, **C**$_{5''/5'''}$), 162.3 (d, *J* = 246 Hz, **C**$_{5''/5'''}$), 158.7 (**C**$_{5'}$), 142.1 (**C**$_9$), 138.5 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 133.1 (**C**$_{1'}$), 132.4 (d, *J* = 3.3 Hz, **C**$_{2''/2'''}$), 132.1 (d, *J* = 3.1 Hz, **C**$_{2''/2'''}$), 131.8 (d, *J* = 8.2 Hz, **C**$_{3''/3'''}$), 131.2 (d, *J* = 8.1 Hz, **C**$_{3''/3'''}$), 129.5 (**C**$_7$), 128.9 (SO_2Ph-*m*-**C**), 127.4 (**C**$_2$), 127.4 (SO_2Ph-*o*-**C**), 125.8 (**C**$_{5/6}$), 125.4 (**C**$_{5/6}$), 118.1 (**C**$_8$), 115.6 (d, *J* = 21.6 Hz, **C**$_{4''/4'''}$), 115.5 (d, *J* = 21.5 Hz, **C**$_{4''/4'''}$), 114.4 (**C**$_{3'}$), 87.4 (**C**$_2$), 77.7 (**C**$_{15}$), 73.9 (**C**$_{11}$),

	57.4 (**C**$_3$), 55.5 (**C**$_{5'}$), 47.1 (**C**$_{12}$), 42.5 (**C**$_{1''/1'''}$), 42.1 (**C**$_{1''/1'''}$), 32.6 (**C**$_{17}$).
FTIR (thin film) cm^{-1}:	2937 (w), 1695 (m), 1672 (m), 1509 (s), 1384 (m), 1222 (m), 1033 (w), 833 (w), 597 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{41}H_{36}F_2N_3O_5S_5$ $[M+H]^+$: 848.1221, found: 848.1223.

TLC (10% ethyl acetate in dichloromethane), R*f*: 0.53 (UV, CAM, $AgNO_3$).



Triethylammonium *S*-(((3*S*,5a*S*,10b*S*,11a*S*)-3-(((*R*)-2-((*S*)-4-amino-4-carboxybutanamido)-3-((carboxymethyl)amino)-3-oxopropyl)disulfaneyl)-10b-(4-methoxyphenyl)-2,3-dimethyl-1,4-dioxo-6-(phenylsulfonyl)-1,2,3,4,5a,6,10b,11-octahydro-11a*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indol-11a-yl)thio)-*N*-((*S*)-4-amino-4-carboxybutanoyl)-*L*-cysteinylglycinate (46); bis(L-glutathione)disulfide 46:

Sodium borohydride (4.9 mg, 0.13 mmol, 4.3 equiv) was added as a solid in one portion to a solution of epidithiodiketopiperazine (+)-**42** (17.3 mg, 29.8 μmol, 1 equiv) in tetrahydrofuran (4.0 mL) and methanol (30 μL). After 35 min, the reaction mixture was diluted with ethyl acetate–hexanes (9:1, 40 mL) and was washed sequentially with a saturated aqueous ammonium chloride solution (40 mL), with deionized water (30 mL), and with a saturated aqueous sodium chloride solution (20 mL). The aqueous layers were separately extracted with a single portion of ethyl acetate–hexanes (9:1, 25 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were sparged with argon for 15 min by discharge of a balloon equipped with a needle extending into the stirring reaction mixture. The reaction mixture was then concentrated under reduced pressure, and the resulting residue containing bisthiol was dissolved in tetrahydrofuran (0.25 mL) and added dropwise via syringe to a solution of *S*-(phenylsulfonyl)-L-glutathione hydrogen chloride[22] (72.9 mg, 163 μmol, 5.45 equiv) and triethylamine (45 μL, 320 μmol, 11 equiv) in tetrahydrofuran (1.1 mL) and methanol (1.1 mL). The transfer was quantitated with additional tetrahydrofuran (2 × 0.25 mL). After 19 h, the reaction mixture was diluted with methanol and adsorbed onto diatomaceous earth (0.4 g) by concentration under reduced pressure until a free-flowing powder was obtained. The diatomaceous earth-absorbed crude mixture was purified by flash column chromatography on C_{18}-reversed phase silica gel (eluent: 10→80% acetonitrile in water) to afford the bisdisulfide **46** (17.2 mg, 44.6%) as a white solid and recovered epidithiodiketopiperazine (+)-**42** (6.0 mg, 21%). Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, 5:1 D_2O:CD_3CN,[23] 25 °C): δ 7.45 (d, *J* = 8.2 Hz, 1H, C_8**H**), 7.42–7.34 (m, 3H, SO_2Ph-*p*-**H**, SO_2Ph-*o*-**H**), 7.32 (app-t, *J* = 7.7 Hz, 1H, C_7**H**), 7.26 (d, *J* = 7.6 Hz, 1H, C_5**H**), 7.16 (app-t, *J* = 7.5 Hz, 1H, C_6**H**), 7.10 (app-t, *J* = 7.8

22. Hart, T. Some Observations Concerning the S-nitroso and S-phenylsulfonyl Derivatives of L-Cysteine and Glutathione. *Tetrahedron Lett.* **1985**, *26*, 2013-2016.
23. Signal broadening was observed when D_2O alone was used as solvent.

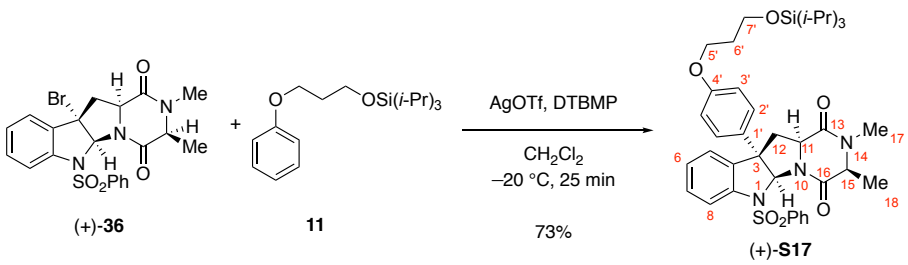
Hz, 2H, SO_2Ph-*m*-**H**), 6.70 (app-d, *J* = 8.4 Hz, 2H, $C_{2'}$**H**), 6.59 (app-d, *J* = 8.4 Hz, 2H, $C_{3'}$**H**), 6.40 (s, 1H, C_2**H**), 4.66 (dd, *J* = 8.6, 5.1 Hz, 1H, $C_{2''/2'''}$**H**), 4.42 (dd, *J* = 10.0, 4.0 Hz, 1H, $C_{2''/2'''}$**H**), 3.80–3.57 (m, 9H, $C_{5'}$**H**, $C_{7''}$**H**, $C_{7'''}$**H**, $C_{11''}$**H**, $C_{11'''}$**H**), 3.54 (d, *J* = 14.6 Hz, C_{12}**H**$_a$), 3.26–3.03 (m, 9H, $HN^+(CH_2CH_3)_3$, $C_{1''}$**H**$_a$, $C_{1'''}$**H**$_b$, $C_{1'''}$**H**$_a$), 3.03–2.93 (m, 4H, C_{17}**H**, C_{12}**H**$_b$), 2.65–2.54 (m, 1H, $C_{1'''}$**H**$_b$), 2.42 (app-t, *J* = 7.6 Hz, 2H, $C_{5''/5'''}$**H**), 2.34 (app-t, *J* = 7.7 Hz, 2H, $C_{5''/5'''}$**H**), 2.04 (app-q, *J* = 7.2 Hz, 2H, $C_{6''/6'''}$**H**), 1.98 (app-q, *J* = 7.5 Hz, 2H, $C_{6''/6'''}$**H**), 1.89 (s, 3H, C_{18}**H**), 1.17 (t, *J* = 7.3 Hz, 9H, $HN^+(CH_2CH_3)_3$).

$^{13}C\{^1H\}$ NMR (125 MHz, 5:1 D_2O:CD_3CN,[23] 25 °C): δ 174.5 (br, 2C, **C**$_{12''}$, **C**$_{12'''}$), 173.7 (**C**$_{4''/4'''}$), 173.6 (**C**$_{4''/4'''}$), 172.8 (br, 2C, **C**$_{8''}$, **C**$_{8'''}$), 170.5 (**C**$_{9''/9'''}$), 170.0 (**C**$_{9''/9'''}$), 166.6 (**C**$_{13}$), 163.9 (**C**$_{16}$), 157.0 (**C**$_{4'}$), 140.3 (**C**$_9$), 135.6 (SO_2Ph-*ipso*-**C**), 134.7 (**C**$_4$), 133.5 (SO_2Ph-*p*-**C**), 132.3 (**C**$_{1'}$), 128.8 (**C**$_7$), 128.4 (SO_2Ph-*m*-**C**), 126.7 (**C**$_{2'}$), 125.9 (SO_2Ph-*o*-**C**), 125.6 (**C**$_6$), 125.3 (**C**$_5$), 117.3 (**C**$_8$), 113.7 (**C**$_{3'}$), 87.1 (**C**$_2$), 73.1 (**C**$_{11}$), 71.5 (**C**$_{15}$), 56.1 (**C**$_3$), 54.6 (**C**$_{5'}$), 53.3 (**C**$_{7''/7'''}$), 53.2 (**C**$_{7''/7'''}$), 52.1 (**C**$_{2''/2'''}$), 51.7 (**C**$_{2''/2'''}$), 45.8 ($HN^+(CH_2CH_3)_3$), 44.4 (**C**$_{12}$), 42.3 (**C**$_{11''/11'''}$), 42.2 (**C**$_{11''/11'''}$), 40.4 (**C**$_{1''/1'''}$), 37.5 (**C**$_{1''/1'''}$), 30.8 (**C**$_{5''/5'''}$), 30.7 (**C**$_{5''/5'''}$), 29.2 (**C**$_{17}$), 25.5 (**C**$_{6''/6'''}$), 25.4 (**C**$_{6''/6'''}$), 20.8 (**C**$_{18}$), 7.4 ($HN^+(CH_2CH_3)_3$).

FTIR (thin film) cm^{-1}: 3273 (br), 1645 (s), 1513 (s), 1253 (m), 1167 (m), 1109 (w), 1028 (w), 832 (w), 686 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{48}H_{57}N_9NaO_{17}S_5$ $[M+Na]^+$: 1214.2368, found: 1214.2359.

TLC (30% acetonitrile in water, C_{18}-reversed phase), R*f*: 0.25 (UV, CAM, $AgNO_3$).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-2,3-Dimethyl-6-(phenylsulfonyl)-10b-(4-(3-((triisopropylsilyl)oxy) propoxy)phenyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (S17); C3-adduct (+)-S17:

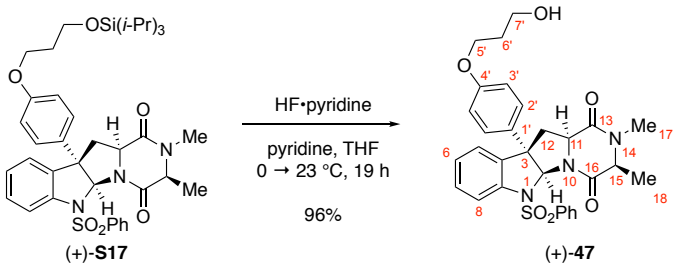
endo-Tetracyclic bromide[18] (+)-**36** (1.03 g, 2.09 mmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP, 1.11 g, 5.39 mmol, 2.58 equiv), and triisopropyl(3-phenoxypropoxy)silane (**11**, 1.35 g, 4.37 mmol, 2.09 equiv) were azeotropically dried by concentration from anhydrous benzene (5 mL) under reduced pressure. Dichloromethane (21 mL) was added via cannula, the resulting colorless solution was cooled to –20 °C, and silver trifluoromethanesulfonate (1.09 g, 4.22 mmol, 2.02 equiv) was added as a solid in one portion. After 25 min, the reaction mixture was filtered through a pad of diatomaceous earth, the filter cake was washed with dichloromethane (200 mL), and the filtrate was concentrated under reduced pressure. The resulting residue was dissolved in ethyl acetate (200 mL) and was washed sequentially with a mixture of saturated aqueous sodium chloride solution and deionized water (1:1, 2 × 50 mL) and with a 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 on silica gel (eluent: 0→20% acetone in dichloromethane) to afford C3-adduct (+)-**S17** (1.10 g, 73.2%) as a white foam. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.61 (d, J = 8.1 Hz, 1H, C_8**H**), 7.45 (app-d, J = 7.9 Hz, 2H, SO_2Ph-*o*-**H**), 7.35–7.23 (m, 2H, SO_2Ph-*p*-**H**, C_7**H**), 7.15–7.05 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 6.68–6.59 (m, 4H, $C_{2'}$**H**, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.39 (dd, J = 9.0, 6.6 Hz, 1H, C_{11}**H**), 4.10–3.99 (m, 3H, C_{15}**H**, $C_{5'}$**H**), 3.88 (t, J = 5.9 Hz, 2H, $C_{7'}$**H**), 3.13 (dd, J = 14.1, 6.6 Hz, 1H, C_{12}**H**$_a$), 2.87 (dd, J = 14.1, 19.2 Hz, 1H, C_{12}**H**$_b$), 2.86 (s, 3H, C_{17}**H**), 2.00 (p, J = 6.1 Hz, 2H, $C_{6'}$**H**), 1.58 (d, J = 7.0 Hz, 3H, C_{18}**H**), 1.15–0.99 (m, 21H, SiC**H**$(CH_3)_2$, SiCH$(C$**H**$_3)_2$).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 167.8 (**C**$_{16}$), 158.2 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 135.7 (**C**$_4$), 132.8 (SO_2Ph-*p*-**C**), 132.5 (**C**$_{1'}$), 129.1 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.0 (**C**$_5$), 125.2 (**C**$_6$), 117.2 (**C**$_8$), 114.9 (**C**$_{3'}$), 87.3 (**C**$_2$), 64.8 (**C**$_{5'}$), 59.8 (**C**$_{7'}$), 59.3 (**C**$_3$), 58.7 (**C**$_{11}$), 57.1 (**C**$_{15}$), 39.0

	(**C**$_{12}$), 32.6 (**C**$_{6'}$), 29.5 (**C**$_{17}$), 18.1 (SiCH(**C**H$_3$)$_2$), 14.5 (**C**$_{18}$), 12.0 (Si**C**H(CH$_3$)$_2$).
FTIR (thin film) cm^{-1}:	2944 (m), 2866 (m), 2359 (w), 1679 (s), 1509 (s), 1457 (s), 1381 (s), 1249 (s), 1168 (s), 1092 (s), 877 (m), 754 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{39}H_{52}N_3O_6SSi$ $[M+H]^+$: 718.3341, found: 718.3339.
$[\alpha]_D^{23}$:	+34 (*c* = 0.39, $CHCl_3$).

TLC (10% acetone in dichloromethane), R*f*: 0.45 (UV, CAM).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-(3-Hydroxypropoxy)phenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (47); alcohol (+)-47:

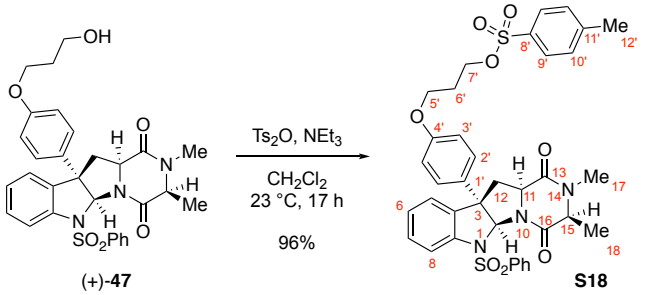
A freshly prepared stock solution of hydrogen fluoride–pyridine (70% HF, 4.8 mL), pyridine (9.6 mL), and tetrahydrofuran (38 mL) at 0 °C was poured into a solution of C3-adduct (+)-**S17** (1.03 g, 1.44 mmol, 1 equiv) in tetrahydrofuran (48 mL) at 0 °C contained in a 1–L polypropylene vessel. After 20 min, the ice–water bath was removed and the solution was allowed to stir and to warm to 23 °C. After 19 h, the reaction mixture was cooled to 0 °C and was diluted with a saturated aqueous sodium bicarbonate solution (350 mL) in portions (50 mL) over 15 min. The resulting mixture was extracted with ethyl acetate (2 × 100 mL), and the combined organic extracts were washed sequentially with a saturated aqueous copper(II) sulfate solution (4 × 50 mL) and with a saturated aqueous ammonium chloride solution (3 × 50 mL). The combined aqueous layers were extracted with a single portion of ethyl acetate (100 mL), and the organic extract was washed sequentially with a saturated aqueous copper(II) sulfate solution (2 × 25 mL) and with a saturated aqueous ammonium chloride solution (2 × 25 mL). The combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 20→50% acetone in dichloromethane) to afford alcohol (+)-**47** (775 mg, 96.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.60 (d, J = 8.1 Hz, 1H, C_8**H**), 7.44 (app-d, J = 7.6 Hz, 2H, SO_2Ph-*o*-**H**), 7.33 (app-t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.29–7.23 (m, 1H, C_7**H**), 7.16–7.05 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 6.64 (app-d, J = 8.9 Hz, 2H, $C_{2'}$**H**), 6.59 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.14 (s, 1H, C_2**H**), 4.39 (dd, J = 9.0, 6.5 Hz, 1H, C_{11}**H**), 4.11–4.00 (m, 3H, C_{15}**H**, $C_{5'}$**H**), 3.85 (t, J = 5.9 Hz, 2H, $C_{7'}$**H**), 3.12 (dd, J = 14.1, 6.5 Hz, 1H, C_{12}**H**$_a$), 2.91–2.80 (m, 4H, C_{12}**H**$_b$, C_{17}**H**), 2.15–1.99 (br-s, 1H, O**H**), 2.03 (p, J = 6.0 Hz, 2H, $C_{7'}$**H**), 1.56 (d, J = 7.0 Hz, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 167.8 (**C**$_{16}$), 157.9 (**C**$_{4'}$), 139.8 (**C**$_9$), 138.2 (SO_2Ph-*ipso*-**C**), 135.6 (**C**$_4$), 132.9 (**C**$_{1'}$/SO_2Ph-*p*-**C**), 132.8 (**C**$_{1'}$/SO_2Ph-*p*-**C**), 129.2 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 127.4 (SO_2Ph-*o*-**C**), 126.0 (**C**$_5$), 125.3 (**C**$_6$), 117.2 (**C**$_8$),

	114.9 (**C**$_{3'}$), 87.2 (**C**$_2$), 65.6 (**C**$_{5'}$), 60.1 (**C**$_{7'}$), 59.3 (**C**$_3$), 58.7 (**C**$_{11}$), 57.0 (**C**$_{15}$), 38.9 (**C**$_{12}$), 32.0 (**C**$_{6'}$), 29.5 (**C**$_{17}$), 14.4 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	3455 (br-w), 2951 (w), 2361 (w), 1672 (s), 1511 (m), 1386 (s), 1253 (s), 1170 (s), 1690 (s), 981 (m), 751 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{30}H_{32}N_3O_6S$ $[M+H]^+$: 562.2006, found: 562.2007.
$[\alpha]_D^{23}$:	+52 (*c* = 0.26, $CHCl_3$).

TLC (40% acetone in dichloromethane), R*f*: 0.35 (UV, CAM).



3-(4-((3*S*,5a*S*,10b*S*,11a*S*)-2,3-Dimethyl-1,4-dioxo-6-(phenylsulfonyl)-1,2,3,4,5a,6,11,11a-octahydro-10b*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indol-10b-yl)phenoxy)propyl 4-methylbenzenesulfonate (S18); tosylate S18:

Alcohol (+)-**47** (277 mg, 0.494 mmol, 1 equiv) was azeotropically dried by concentration from anhydrous benzene (3 mL) under reduced pressure. Dichloromethane (4.9 mL) was added via syringe, followed by the addition of triethylamine (0.35 mL, 2.5 mmol, 5.1 equiv) via syringe and *p*-toluenesulfonic anhydride (655 mg, 1.99 mmol, 4.03 equiv) as a solid in one portion. After 17 h, the reaction mixture was diluted with dichloromethane (75 mL) and was washed with a saturated aqueous sodium bicarbonate solution (25 mL). The aqueous layer was extracted with dichloromethane (50 mL), and the combined organic extracts were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→25% acetone in dichloromethane) to afford tosylate **S18** (339 mg, 95.8%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

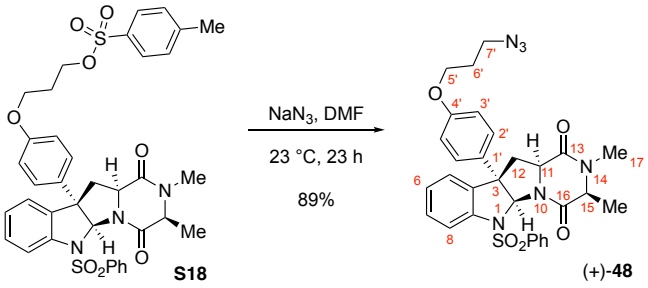
^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 7.77 (app-d, *J* = 8.3 Hz, 2H, $C_{9'}$**H**), 7.61 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.47 (app-d, *J* = 7.6 Hz, 1H, SO_2Ph-*o*-**H**), 7.34 (app-t, *J* = 7.4 Hz, 1H, SO_2Ph-*p*-**H**) 7.31–7.24 (m, 3H, C_7**H**, $C_{10'}$**H**), 7.15–7.06 (m, 3H, C_5**H**, C_6**H**, SO_2Ph-*m*-**H**), 6.66 (app-d, *J* = 8.7 Hz, 1H, $C_{2'}$**H**), 6.54 (app-d, *J* = 8.7 Hz, 1H, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.39 (app-t, *J* = 7.3 Hz, 1H, C_{11}**H**), 4.25 (t, *J* = 5.8 Hz, 1H, $C_{5'}$**H**), 4.04 (q, *J* = 7.0 Hz, 1H, C_{15}**H**), 3.95 (t, *J* = 5.9 Hz, 1H, $C_{7'}$**H**), 3.13 (dd, *J* = 14.1, 6.6 Hz, 1H, C_{12}**H**$_a$), 2.93–2.83 (m, 4H, C_{12}**H**$_b$, C_{17}**H**), 2.40 (s, 3H, $C_{12'}$**H**), 2.13 (p, *J* = 5.9 Hz, 2H, $C_{6'}$**H**), 1.58 (d, *J* = 7.0 Hz, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 167.9 (**C**$_{16}$), 157.7 (**C**$_{4'}$), 145.0 (**C**$_{11'}$), 139.9 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.6 (**C**$_4$), 133.1 (**C**$_{1'}$), 133.0 (**C**$_{8'}$), 133.0 (SO_2Ph-*p*-**C**), 130.0 (**C**$_{10'}$), 129.2 (**C**$_7$), 128.7 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$), 128.0 (**C**$_{9'}$), 127.5 (SO_2Ph-*o*-**C**), 126.0 (**C**$_5$), 125.3 (**C**$_6$), 117.2 (**C**$_8$), 114.9 (**C**$_{3'}$), 87.2 (**C**$_2$), 67.0 (**C**$_{5'}$), 63.4 (**C**$_{7'}$), 59.3 (**C**$_3$), 58.7 (**C**$_{11}$), 57.1 (**C**$_{15}$), 39.0 (**C**$_{12}$), 29.6 (**C**$_{17}$), 29.0 (**C**$_{6'}$), 21.8 (**C**$_{12'}$), 14.5 (**C**$_{18}$).

FTIR (thin film) cm^{-1}: 2918 (br-w), 2361 (m), 1672 (m), 1511 (m), 1357 (m), 1256 (m), 1173 (s), 1095 (m), 938 (w), 747 (s).

HRMS (ESI) (*m/z*): calc'd for $C_{37}H_{38}N_3O_8S_2$ $[M+H]^+$: 716.2095, found: 716.2092.

TLC (10% acetone in dichloromethane), R*f*: 0.30 (UV, CAM).



(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-(3-Azidopropoxy)phenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,6,10b,11,11a-hexahydro-4*H*-pyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4(5a*H*)-dione (48); azide (+)-48:

Sodium azide (145 mg, 2.24 mmol, 3.99 equiv) was added as a solid in one portion to a solution of tosylate **S18** (401 mg, 0.560 mmol, 1 equiv) in *N,N*-dimethylformamide (3.7 mL). After 23 h, the reaction mixture was diluted with ethyl acetate−hexanes (9:1, 150 mL) and was washed sequentially with a saturated aqueous sodium bicarbonate solution (2 × 50 mL), with deionized water (3 × 40 mL), and with a 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 residue was purified by flash column chromatography on silica gel (eluent: 0→20% acetone in dichloromethane) to afford azide (+)-**48** (292 mg, 89.0%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.62 (d, *J* = 8.1 Hz, 1H, C_8**H**), 7.48 (dd, *J* = 8.5, 1.2 Hz, 2H, SO_2Ph-*o*-**H**), 7.34 (tt, *J* = 7.4, 1.2 Hz, 1H, SO_2Ph-*p*-**H**), 7.31–7.25 (m, 1H, C_7**H**), 7.15–7.08 (m, 4H, SO_2Ph-*m*-**H**, C_5**H**, C_6**H**), 6.68 (app-d, *J* = 8.9 Hz, 2H, $C_{2'}$**H**), 6.62 (app-d, *J* = 8.9 Hz, 2H, $C_{3'}$**H**), 6.15 (s, 1H, C_2**H**), 4.38 (dd, *J* = 8.9, 6.7 Hz, 1H, C_{11}**H**), 4.04 (q, *J* = 7.1 Hz, 1H, C_{15}**H**), 4.00 (t, *J* = 5.9 Hz, 2H, $C_{5'}$**H**), 3.53 (t, *J* = 6.5 Hz, 2H, $C_{7'}$**H**), 3.13 (dd, *J* = 14.1, 6.7 Hz, 1H, C_{12}**H**$_a$), 2.88 (dd, *J* = 14.0, 9.0 Hz, 1H, C_{12}**H**$_b$), 2.86 (s, 3H, C_{17}**H**), 2.05 (p, *J* = 6.2 Hz, 2H, $C_{6'}$**H**), 1.58 (d, *J* = 7.1 Hz, 3H, C_{18}**H**).

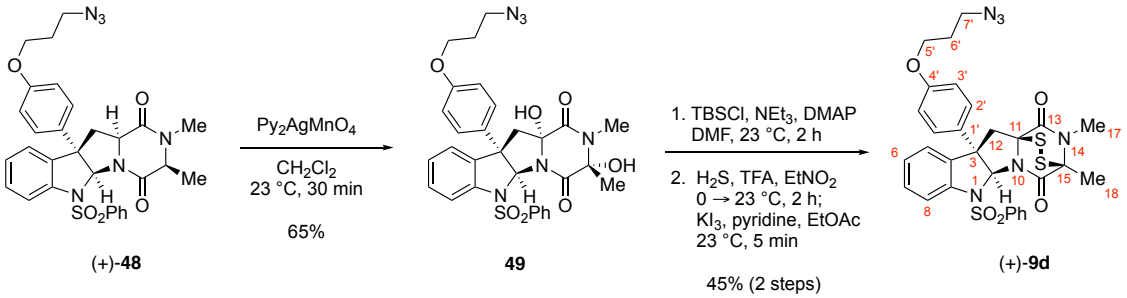
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 25 °C): δ 168.4 (**C**$_{13}$), 167.9 (**C**$_{16}$), 157.8 (**C**$_{4'}$), 139.9 (**C**$_9$), 138.3 (SO_2Ph-*ipso*-**C**), 135.6 (**C**$_4$), 133.0 (**C**$_{1'}$), 132.9 (SO_2Ph-*p*-**C**), 129.2 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.1 (**C**$_{2'}$), 127.5 (SO_2Ph-*o*-**C**), 126.0 (**C**$_5$), 125.3 (**C**$_6$), 117.2 (**C**$_8$), 114.9 (**C**$_{3'}$), 87.2 (**C**$_2$), 64.6 (**C**$_{5'}$), 58.8 (**C**$_{11}$), 57.1 (**C**$_{15}$), 48.3 (**C**$_{7'}$), 39.0 (**C**$_{12}$), 29.5 (**C**$_{17}$), 28.8 (**C**$_{6'}$), 14.5 (**C**$_{18}$).

FTIR (thin film) cm^{-1}: 2956 (br-w), 2096 (s), 1670 (s), 1611 (w), 1476 (m), 1360 (s), 1168 (s), 1090 (m), 971 (w), 829 (w), 758 (m).

HRMS (ESI) (*m/z*): calc'd for $C_{30}H_{31}N_6O_5S$ $[M+H]^+$: 587.2071, found: 587.2073.

$[\alpha]_D^{23}$: +46 (*c* = 0.25, $CHCl_3$).

TLC (10% acetone in dichloromethane), R*f*: 0.27 (UV, CAM).



(+)-**48** **49** (+)-**9d**

(+)-(3*S*,5a*S*,10b*S*,11a*S*)-10b-(4-(3-Azidopropoxy)phenyl)-2,3-dimethyl-6-(phenylsulfonyl)-2,3,5a,6,10b,11-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indole-1,4-dione (9d); epidithiodiketopiperazine azide (+)-9d:

Bis(pyridine)silver(I) permanganate (178 mg, 0.464 mmol, 3.03 equiv) was added as a solid to a solution of azide (+)-**48** (90 mg, 0.153 mmol, 1 equiv) in dichloromethane (3 mL). After 30 min, the reaction mixture was diluted with a saturated aqueous sodium bisulfite solution (10 mL) and was extracted with ethyl acetate−hexanes (9:1, 2 × 20 mL). The combined organic extracts were washed sequentially with deionized water (15 mL) and with a saturated aqueous ammonium chloride solution (3 × 30 mL). The combined aqueous layers were extracted with ethyl acetate−hexanes (4:1, 20 mL), and the organic extract was washed with a saturated aqueous ammonium chloride solution (2 × 20 mL). The combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 5→15% acetone in dichloromethane) to afford diol **49** (61.3 mg, 64.6%) as a white foam.[24]

Diol **49** (55.0 mg, 88.9 μmol, 1 equiv) was azeotropically dried by concentration from dichloromethane (0.5 mL) and anhydrous benzene (1.5 mL) under reduced pressure. The flask was charged with 4-dimethylaminopyridine (DMAP, 1.5 mg, 12 μmol, 0.14 equiv), and the solids were dissolved in *N,N*-dimethylformamide (0.9 mL). Triethylamine (40 μL, 290 μmol, 3.2 equiv) was then added via syringe followed by the dropwise addition of a solution of *t*-butyldimethylsilyl chloride (TBSCl, 2.05 M, 88 μL, 180 μmol, 2.0 equiv) in *N,N*-dimethylformamide. After 2 h, the reaction mixture was diluted with ethyl acetate−hexanes (4:1, 25 mL) and with a saturated aqueous ammonium chloride solution (15 mL). The aqueous layer was extracted with ethyl acetate−hexanes (4:1, 25 mL). The combined organic extracts were washed with deionized water (3 × 10 mL) and with a saturated aqueous sodium chloride solution (10 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 on silica gel (eluent: 0→30% acetone in hexanes) to afford a near equal mixture of regioisomeric silyl ethers (55.4 mg, 85.0%, 1.1:1 regioisomers) as a white foam.[25]

24. Diol **49** has been characterized by ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.62 (d, J = 8.1 Hz, 1H, C_8**H**), 7.36–7.27 (m, 4H), 7.22–7.14 (m, 2H), 7.02 (t, J = 7.8 Hz, 2H, SO_2Ph-*m*-**H**), 6.78 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.55 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.35 (s, 1H, C_2**H**), 5.65–5.40 (br-s, O**H**), 3.99 (t, J = 5.9 Hz, 2H, $C_{5'}$**H**), 3.54 (t, J = 6.5 Hz, 2H, $C_{7'}$**H**), 3.37 (d, J = 15.1 Hz, 1H, C_{12}**H**$_a$), 3.00 (s, 3H, C_{17}**H**), 2.92 (d, J = 15.2 Hz, 1H, C_{12}**H**$_b$), 2.10–2.01 (m, 2H, $C_{6'}$**H**), 1.82 (s, 3H, C_{18}**H**). TLC (20% acetone in dichloromethane), R*f*: 0.34 (UV, CAM).

25. The regioisomeric silyl ethers have been characterized by ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C, 1.1:1 mixture of regioisomers): δ 7.63–7.57 (m), 7.34–7.29 (m), 7.31–7.24 (m), 7.22–7.13 (m), 7.05–6.96 (m), 6.77–6.69 (m), 6.57 (t, J = 9.2 Hz), 6.42 (s), 6.30 (s), 4.01 (t, d, J = 5.9, 2.4 Hz), 3.85 (s), 3.57–3.52 (m), 3.51 (s), 3.37 (dd, J = 15.2, 1.5 Hz), 2.97 (s), 2.93 (s), 2.85 (d, J = 14.6 Hz), 2.78 (d, J = 15.1 Hz), 2.06 (p, J = 6.1 Hz), 1.83 (s), 1.65 (s), 0.97 (s), 0.92 (s, 3H), 0.33 (s), 0.32 (s), 0.24 (s), 0.23 (s). TLC (40% acetone in hexanes), R*f*: 0.51 and 0.58 (UV, CAM).

A solution of regioisomeric silyl ethers (16.5 mg, 22.5 μmol, 1 equiv) in anhydrous nitroethane (1.0 mL) at 0 °C was sparged with hydrogen sulfide gas for 20 min by discharge of a balloon equipped with a needle extending into the reaction mixture, providing a saturated hydrogen sulfide solution. Trifluoroacetic acid (TFA, 0.75 mL) was added via syringe over 20 seconds, and the sparging with hydrogen sulfide was maintained for another 20 min. The ice–water bath was removed, and the solution was allowed to stir and warm to 23 °C under an atmosphere of hydrogen sulfide. After 2 h, the reaction mixture was diluted with a saturated aqueous sodium bicarbonate solution (20 mL) and the resulting mixture was extracted with ethyl acetate (2 × 10 mL). A stock solution of potassium triiodide in pyridine[6] was added dropwise into the organic layer containing crude bisthiol until a persistent yellow color was observed. The resulting mixture was washed with an aqueous hydrogen chloride solution (1 M, 2 × 15 mL) and with a saturated aqueous sodium chloride solution (10 mL). The combined aqueous layers were extracted with ethyl acetate (10 mL), and the combined organic layers were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel (eluent: 0→10% ethyl acetate in dichloromethane) to afford the epidithiodiketopiperazine (+)-**9d** (7.8 mg, 53%) as a beige solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.[26]

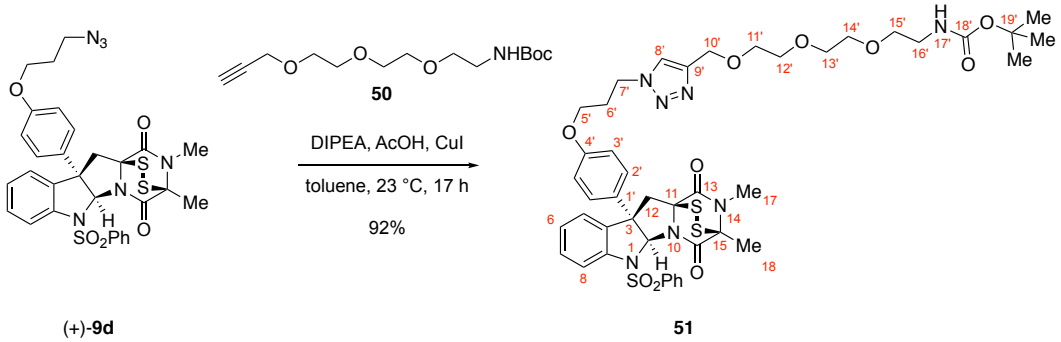
^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): 7.65 (d, J = 8.5 Hz, 1H, C_8**H**), 7.40 (app-t, J = 8.3 Hz, 1H, C_7**H**), 7.36 (app-d, J = 8.1 Hz, 2H, SO_2Ph-*o*-**H**), 7.33–7.22 (m, 3H, C_6**H**, C_5**H**, SO_2Ph-*p*-**H**), 7.04 (app-t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 6.75 (app-d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.62 (app-d, J = 8.9 Hz, 2H, $C_{3'}$**H**), 6.42 (s, 1H, C_2**H**), 4.01 (t, J = 5.9 Hz, 2H, $C_{5'}$**H**), 3.67 (d, J = 15.5 Hz, 1H, C_{12}**H**$_a$), 3.54 (t, J = 6.5 Hz, 2H, $C_{7'}$**H**), 3.05 (s, 3H, C_{17}**H**), 2.88 (d, J = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.07 (p, J = 6.2 Hz, 2H, $C_{6'}$**H**), 1.97 (s, 3H, C_{18}**H**).

^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, 25 °C): 165.8 (**C**$_{13}$), 161.4 (**C**$_{16}$), 158.0 (**C**$_{4'}$), 141.3 (**C**$_9$), 138.5 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.0 (SO_2Ph-*p*-**C**), 131.7 (**C**$_{1'}$), 129.8 (**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 127.3 (SO_2Ph-*o*-**C**), 126.1 (**C**$_6$), 125.6 (**C**$_5$), 119.0 (**C**$_8$), 115.1 (**C**$_{3'}$), 88.0 (**C**$_2$), 74.0 (**C**$_{11}$), 73.5 (**C**$_{15}$), 64.7 (**C**$_{5'}$), 59.2 (**C**$_3$), 48.3 (**C**$_{7'}$), 46.1 (**C**$_{12}$), 28.9 (**C**$_{17}$), 27.6 (**C**$_{6'}$), 18.3 (**C**$_{18}$).

26. The relative stereochemistry of the epidithiodiketopiperazine (+)-**9d** was confirmed by key NOE correlations on the corresponding bis(methylthioether). Our assignment is supported by key NOE signals (^{1}H, ^{1}H) in ppm: (7.34, 3.29), (3.29, 1.88), (6.94, 3.03). This derivatized compound was prepared in one step using our methodology developed to access (+)-gliocladin B (Boyer, N.; Movassaghi, M. Concise Total Synthesis of (+)-Gliocladins B and C. *Chem. Sci.* **2012**, *3*, 1798−1803). The corresponding bis(methylthioether) of epidithiodiketopiperazine (+)-**9d** was characterized as follows: ^{1}H NMR (500 MHz, acetone-d_6) δ 8.00 (d, J = 7.3 Hz, 2H, SO_2Ph-*o*-**H**), 7.69 (t, J = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.56 (t, J = 7.9 Hz, 2H, SO_2Ph-*m*-**H**), 7.52 (d, J = 8.1 Hz, 1H, C_8**H**), 7.34 (d, J = 7.6 Hz, 1H, C_5**H**), 7.30 (t, J = 7.8 Hz, 1H, C_7**H**), 7.10 (t, J = 7.9 Hz, 1H, C_6**H**), 6.94 (d, J = 8.8 Hz, 2H, $C_{2'}$**H**), 6.77 (d, J = 8.8 Hz, 2H, $C_{3'}$**H**), 6.75 (s, 1H, C_2**H**), 4.05 (t, J = 6.0 Hz, 2H, $C_{5'}$**H**), 3.54 (t, J = 6.7 Hz, 2H, $C_{7'}$**H**), 3.29 (d, J = 14.1 Hz, 1H, C_{12}**H**$_\beta$), 3.03 (d, J = 14.1 Hz, 1H, C_{12}**H**$_\alpha$), 2.99 (s, 3H, C_{17}**H**), 2.06–2.03 (m, 2H, $C_{6'}$**H**), 2.02 (s, 3H, C_{18}**H**), 1.88 (s, 3H, C_{11}S**CH**$_3$), 1.80 (s, 3H, C_{15}S**CH**$_3$).

FTIR (thin film) cm^{-1}:	2922 (w), 2097 (s), 1712 (s), 1686 (s), 1610 (w), 1512 (s), 1251 (s), 1169 (s), 1056 (m), 895 (w), 738 (m), 601 (s).
HRMS (ESI) (*m/z*):	calc'd for $C_{30}H_{29}N_6O_5S_3$ $[M+H]^+$: 649.1356, found: 649.1356.
$[\alpha]_D^{23}$:	+231 (*c* = 0.06, $CHCl_3$).

TLC (15% ethyl acetate in dichloromethane), R*f*: 0.38 (UV, CAM).



tert-Butyl (2-(2-(2-((1-(3-(4-((3*S*,5a*S*,10b*S*,11a*S*)-2,3-dimethyl-1,4-dioxo-6-(phenylsulfonyl)-1,2,3,4,5a,6-hexahydro-3,11a-epidithiopyrazino[1',2':1,5]pyrrolo[2,3-*b*]indol-10b(11*H*)-yl)phenoxy)propyl)-1*H*-1,2,3-triazol-4-yl)methoxy)ethoxy)ethoxy)ethyl)carbamate (51); triazole 51:

A solution of *N,N*-diisopropylethylamine (DIPEA, 2.7 µL, 16 µmol, 1.5 equiv) and acetic acid (AcOH, 0.90 µL, 16 µmol, 1.5 equiv) in toluene (0.2 mL) was added to a flask containing azide (+)-**9d** (6.8 mg, 11 µmol, 1 equiv) and alkyne[27] **50** (11.6 mg, 40.4 µmol, 3.67 equiv). Copper (I) iodide (0.9 mg, 5 µmol, 0.5 equiv) was added as a solid, and the suspension was sparged with argon for 2 min by discharge of balloon equipped with a needle extending into the reaction mixture. After 17 h, the reaction mixture was diluted with dichloromethane (0.5 mL) and was purified by flash chromatography on silica gel (eluent: 5→40% acetone in dichloromethane) to afford triazole **51** as a yellow solid. The mixture was further purified by flash column chromatography on silica gel (eluent: 0→4% methanol in dichloromethane) to afford triazole **51** (9.0 mg, 91.7%) as a white solid. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ 7.68–7.60 (m, 2H, C_8**H**, $C_{8'}$**H**), 7.40 (app-t, *J* = 7.6 Hz, 1H, C_7**H**), 7.36 (app-d, *J* = 7.9 Hz, 2H, SO_2Ph-*o*-**H**), 7.31 (app-t, *J* = 7.5 Hz, 1H, SO_2Ph-*p*-**H**), 7.29–7.22 (m, 2H, C_5**H**, C_6**H**), 7.05 (app-t, *J* = 7.7 Hz, 2H, SO_2Ph-*m*-**H**), 6.74 (app-d, *J* = 8.2 Hz, 2H, $C_{2'}$**H**), 6.59 (br-s, 2H, $C_{3'}$**H**), 6.42 (s, 1H, C_2**H**), 5.04 (br-s, 1H, $N_{17'}$**H**), 4.70 (s, 2H, $C_{10'}$**H**), 4.60 (t, *J* = 5.7 Hz, 2H, $C_{7'}$**H**), 3.97–3.88 (m, 2H, $C_{5'}$**H**), 3.73–3.57 (m, 9H, C_{12}**H**$_a$, $C_{11'}$**H**, $C_{12'}$**H**, $C_{13'}$**H**, $C_{14'}$**H**), 3.53 (t, *J* = 5.0 Hz, 2H, $C_{15'}$**H**), 3.30 (app-q, *J* = 5.5 Hz, 2H, $C_{16'}$**H**), 3.05 (s, 3H, C_{17}**H**), 2.88 (d, *J* = 15.5 Hz, 1H, C_{12}**H**$_b$), 2.40 (p, *J* = 6.4 Hz, 2H, $C_{6'}$**H**), 1.96 (s, 3H, C_{18}**H**), 1.43 (s, 9H, $C_{19'}$(C**H**$_3$)$_3$).

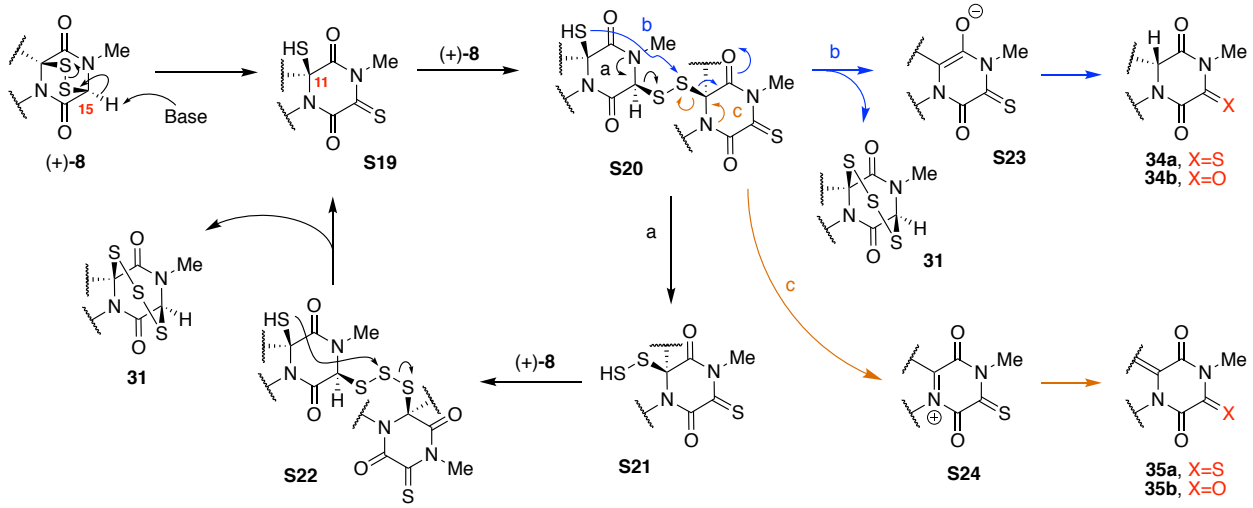
^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$, 25 °C): δ 165.8 (**C**$_{13}$), 161.4 (**C**$_{16}$), 157.7 (**C**$_{4'}$), 156.1 (**C**$_{18'}$), 145.5 (**C**$_{9'}$), 141.3 (**C**$_9$), 138.5 (SO_2Ph-*ipso*-**C**), 135.8 (**C**$_4$), 133.1 (SO_2Ph-*p*-**C**), 132.0 (**C**$_{1'}$), 129.8

27. Grimes, K. D.; Aldrich, C. C. A High-Throughput Screening Fluorescence Polarization Assay for Fatty Acid Adenylating Enzymes in *Mycobacterium Tuberculosis*. *Analytical Biochemistry*, **2011**, *417*, 264–273.

	(**C**$_7$), 128.6 (SO_2Ph-*m*-**C**), 128.0 (**C**$_{2'}$), 127.2 (SO_2Ph-*o*-**C**), 126.1 (**C**$_6$), 125.5 (**C**$_5$), 123.0 (**C**$_{8'}$), 119.0 (**C**$_8$), 115.0 (**C**$_{3'}$), 87.9 (**C**$_2$), 79.3 (**C**$_{19'}$), 73.9 (**C**$_{11}$), 73.5 (**C**$_{15}$), 70.7 (3C, **C**$_{12'}$, **C**$_{13'}$, **C**$_{14'}$), 70.4 (**C**$_{15'}$), 69.9 (**C**$_{11'}$), 64.8 (**C**$_{10'}$), 64.2 (**C**$_{5'}$), 59.1 (**C**$_3$), 47.1 (**C**$_{7'}$), 46.0 (**C**$_{12}$), 40.5 (**C**$_{16'}$), 30.0 (**C**$_{6'}$), 28.6 (C$_{19'}$(**C**H$_3$)$_3$), 27.7 (**C**$_{17}$), 18.2 (**C**$_{18}$).
FTIR (thin film) cm^{-1}:	3360 (br-m), 2921 (s), 2851 (m), 1659 (m), 1632 (m), 1468 (w), 1411 (w), 1024 (w), 801 (w).
HRMS (ESI) (*m/z*):	calc'd for $C_{44}H_{53}N_7NaO_{10}S_3$ $[M+Na]^+$: 958.2908, found: 958.2902.

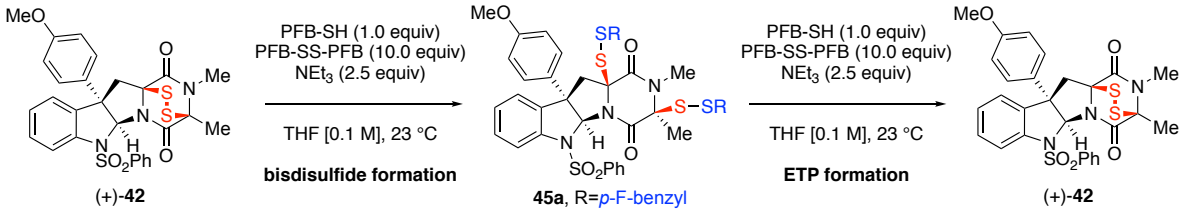
TLC (40% acetone in dichloromethane), R*f*: 0.39 (UV, CAM, $AgNO_3$).
TLC (5% methanol in dichloromethane), R*f*: 0.26 (UV, CAM, $AgNO_3$).

Scheme S1: Plausible Mechanism for Base-Catalyzed Decomposition of ETP (+)-8:



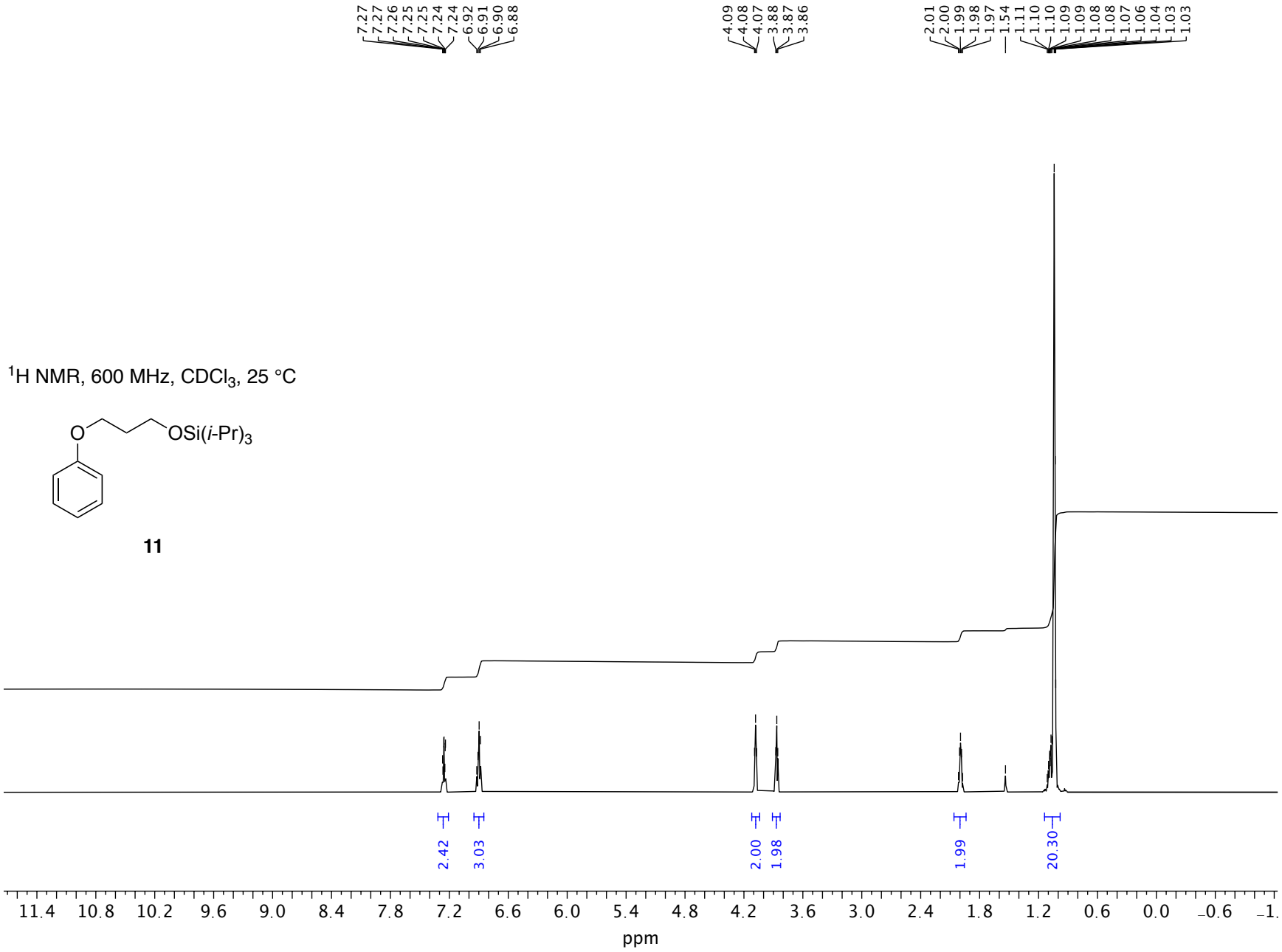
We anticipate the base promoted opening of C15-H epidisulfides such as ETP (+)-**8** leads to nucleophilic thiols capable of scrambling disulfanes in addition to allowing various decomposition pathways, including C15-ionization (path a), epipolysulfide formation with concomitant reductive desulfuration (path b), and C11-ionization followed by deprotonation (path c). This iterative generation of higher order polysulfides is characteristic of our unified hypothesis on the biogenesis of ETPs (see Supporting Information of reference 28).[28,29]

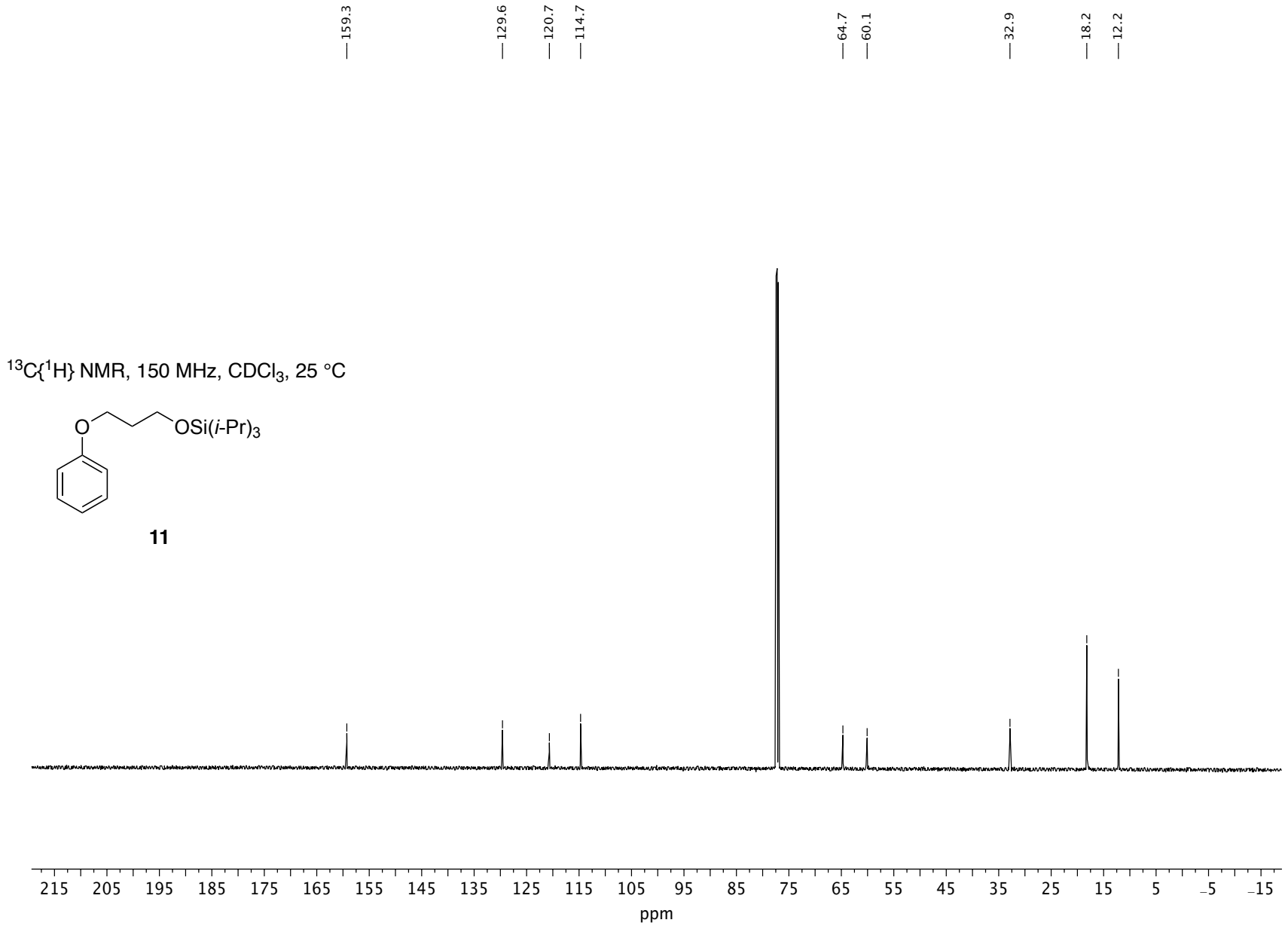
Scheme S2: Interconversion of ETP (+)-42 and Bisdisulfide 45a:

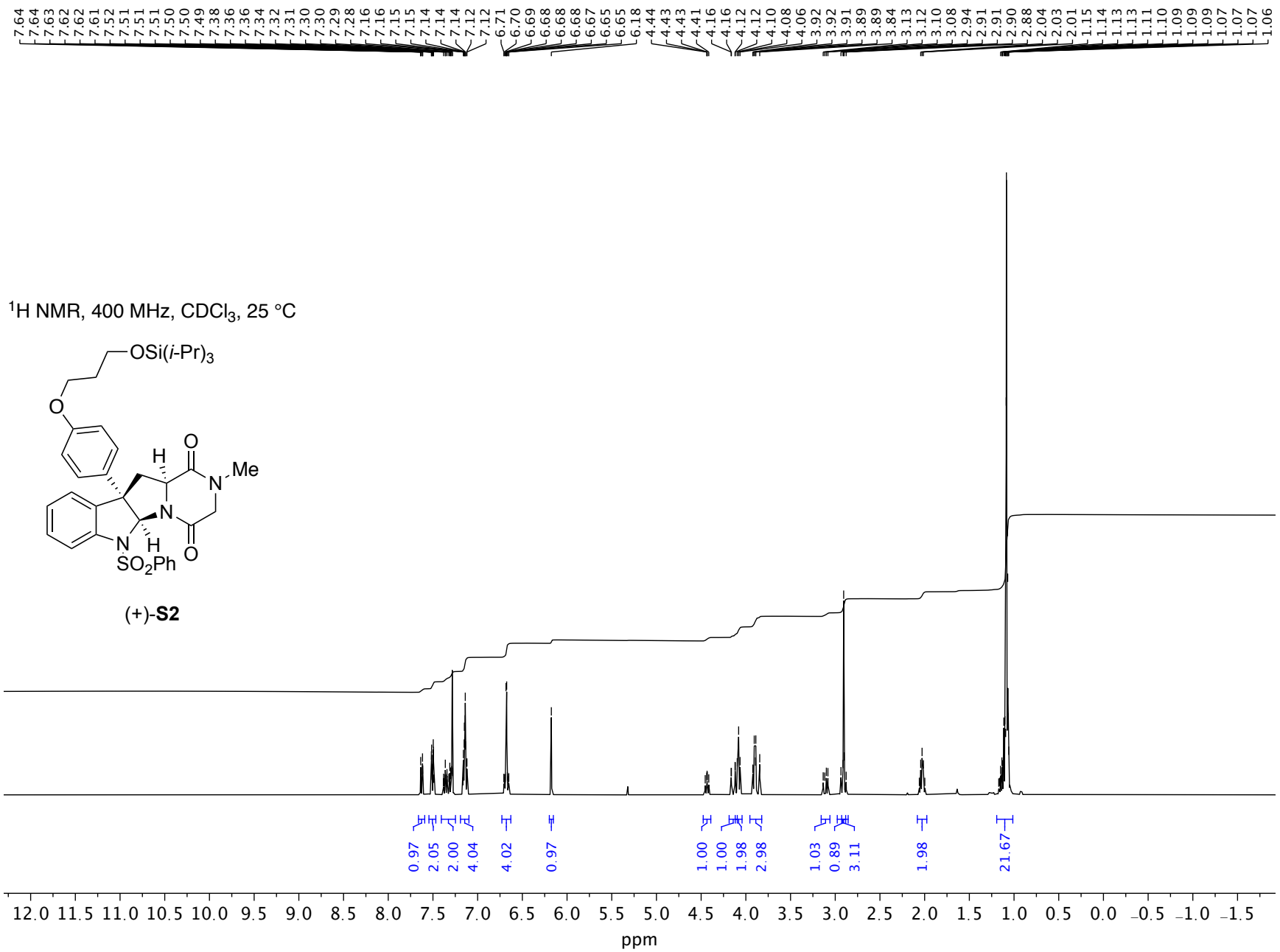


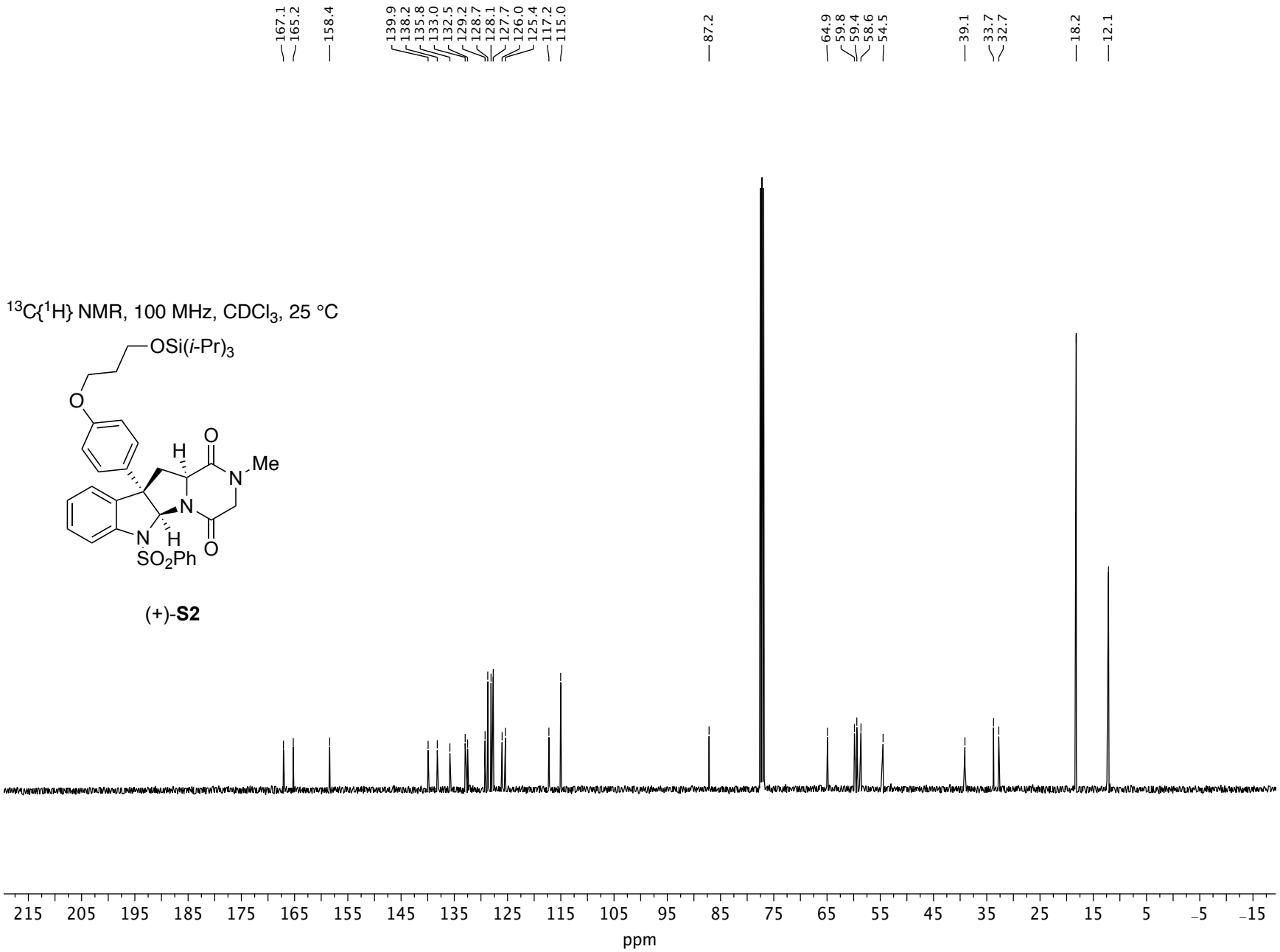
The equilibration of ETP (+)-**42** and bisdisulfide **45a** was investigated from both directions by exposure of either ETP (+)-**42** or bisdisulfide **45a** to identical reaction conditions. As shown on page S76, the isolated quantities of ETP (+)-**42** and bisdisulfide **45a** are consistent with an equilibrium ratio of 3:1 favoring ETP (+)-**42** under the reaction conditions examined. This ratio was also observed (^{1}H NMR monitoring) in the conversion of ETP (+)-**42** to bisdisulfide **45a** and the conversion of the latter back to ETP (+)-**42** as illustrated above in THF [0.1 M]. Each step was monitored periodically over 100 h, and the ratio of ETP (+)-**42** to bisdisulfide **45a** was determined by taking aliquots (30 μL) of the reaction mixture followed by dilution into $CDCl_3$ (600 μL) for analysis. In both directions, under the examined reaction conditions, the equilibrium favored ETP (+)-**42** to bisdisulfide **45a** within 35 h or less (>5:1, respectively), and the equilibrium slowly reached steady state within 80 h with a final ratio of ~3:1, respectively.

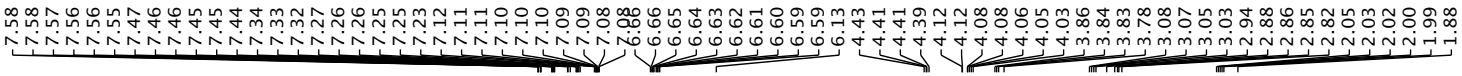
28. Kim, J.; Movassaghi, M. General Approach to Epipolythiodiketopiperazine Alkaloids: Total Synthesis of (+)-Chaetocins A and C and (+)-12,12'-Dideoxychetracin A. *J. Am. Chem. Soc.* **2010**, *132*, 14376–14378.
29. Kim, J.; Movassaghi, M. Biogenetically-Inspired Total Synthesis of Epidithiodiketopiperazines and Related Alkaloids. *Acc. Chem. Res.* **2015**, *48*, 1159−1171.


7.27
7.27
7.26
7.25
7.25
7.24
7.24
6.92
6.91
6.90
6.88
4.09
4.08
4.07
3.88
3.87
3.86
2.01
2.00
1.99
1.98
1.97
1.54
1.11
1.10
1.10
1.09
1.09
1.08
1.08
1.07
1.06
1.04
1.03
1.03
^{1}H NMR, 600 MHz, $CDCl_3$, 25 °C
O
OSi(*i*-Pr)$_3$
11
2.42
3.03
2.00
1.98
1.99
20.30
11.4 10.8 10.2 9.6 9.0 8.4 7.8 7.2 6.6 6.0 5.4 4.8 4.2 3.6 3.0 2.4 1.8 1.2 0.6 0.0 −0.6 −1.
ppm

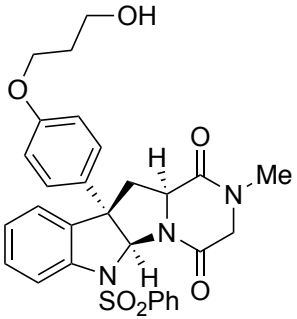

159.3
129.6
120.7
114.7
64.7
60.1
32.9
18.2
12.2
$^{13}C\{^{1}H\}$ NMR, 150 MHz, $CDCl_3$, 25 °C
O
OSi(*i*-Pr)$_3$
11
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.64 7.64 7.63 7.62 7.62 7.61 7.52 7.51 7.51 7.50 7.50 7.49 7.38 7.36 7.36 7.34 7.32 7.31 7.30 7.30 7.29 7.28 7.16 7.16 7.15 7.15 7.14 7.14 7.14 7.12 7.12 6.71 6.70 6.69 6.68 6.68 6.68 6.67 6.65 6.65 6.18 4.44 4.43 4.43 4.41 4.16 4.12 4.12 4.10 4.08 4.06 3.92 3.92 3.91 3.89 3.89 3.84 3.13 3.12 3.10 3.08 2.94 2.91 2.91 2.90 2.88 2.04 2.03 2.01 1.15 1.14 1.13 1.13 1.11 1.10 1.09 1.09 1.09 1.07 1.07 1.07 1.06
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
OSi(*i*-Pr)$_3$
O
H
O
N
Me
N
N
H
O
SO$_2$Ph
(+)-**S2**
0.97 2.05 2.00 4.04 4.02 0.97 1.00 1.00 1.98 2.98 1.03 0.89 3.11 1.98 21.67
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0 −1.5
ppm

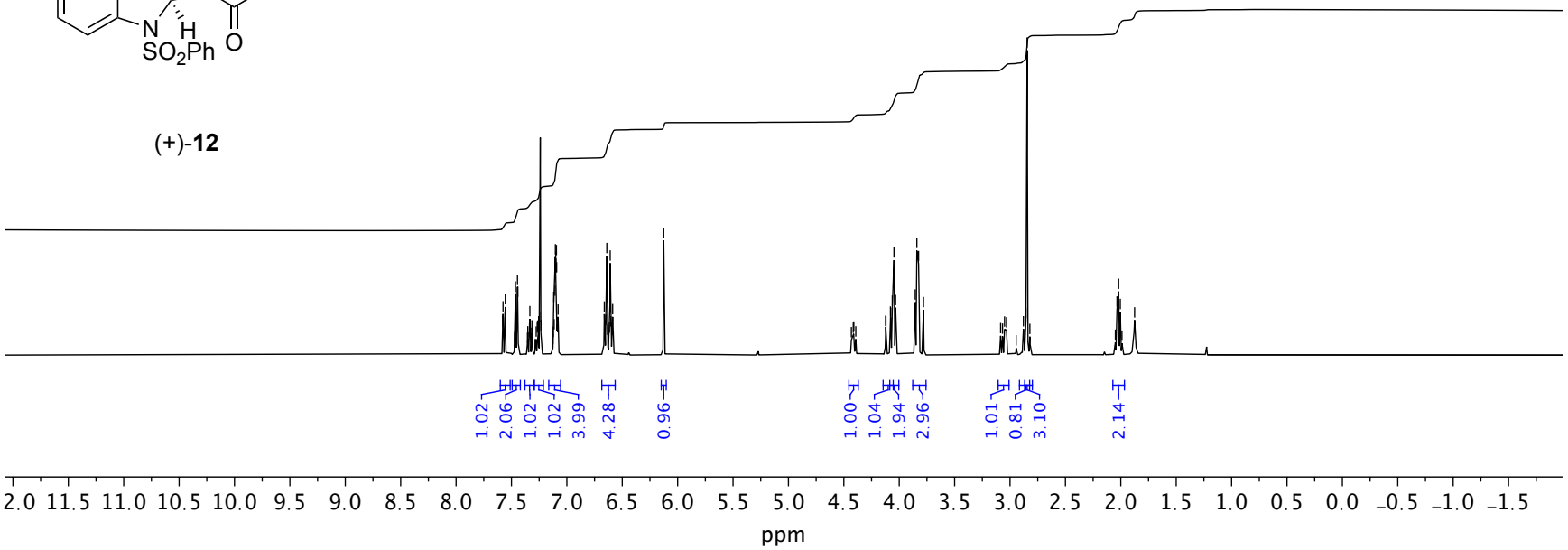

167.1
165.2
158.4
139.9
138.2
135.8
133.0
132.5
129.2
128.7
128.1
127.7
126.0
125.4
117.2
115.0
87.2
64.9
59.8
59.4
58.6
54.5
39.1
33.7
32.7
18.2
12.1
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
OSi(*i*-Pr)$_3$
O
H
O
N
Me
N
N
H
O
SO_2Ph
(+)-**S2**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm



^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

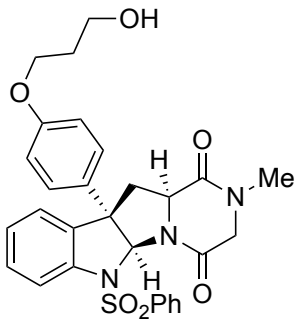


(+)-**12**

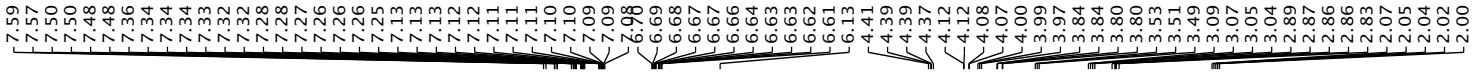


167.1
165.3
158.1
139.9
138.2
135.9
133.1
132.9
129.3
128.8
128.2
127.6
127.5
126.0
125.5
117.2
115.0
87.2
65.8
60.2
59.4
58.6
54.4
39.0
33.7
32.1

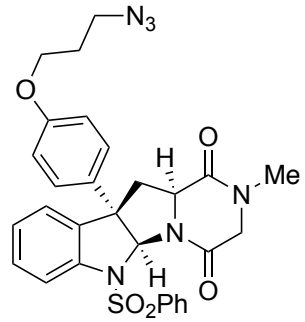
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C



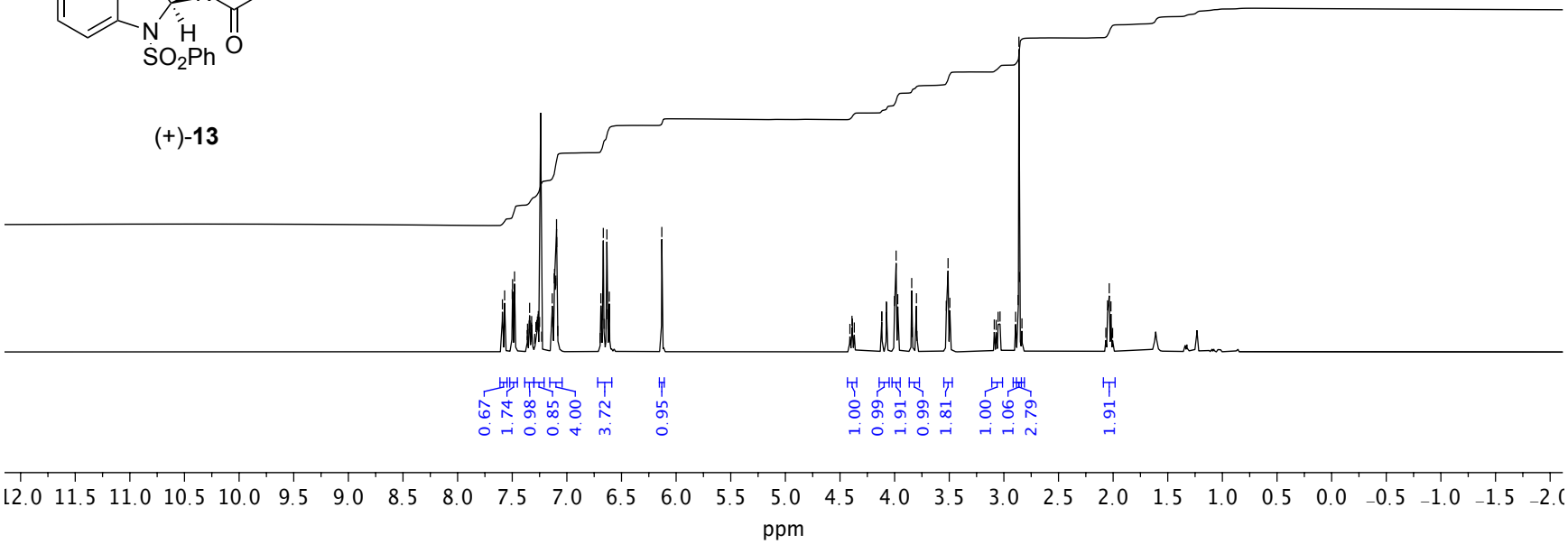
(+)-**12**

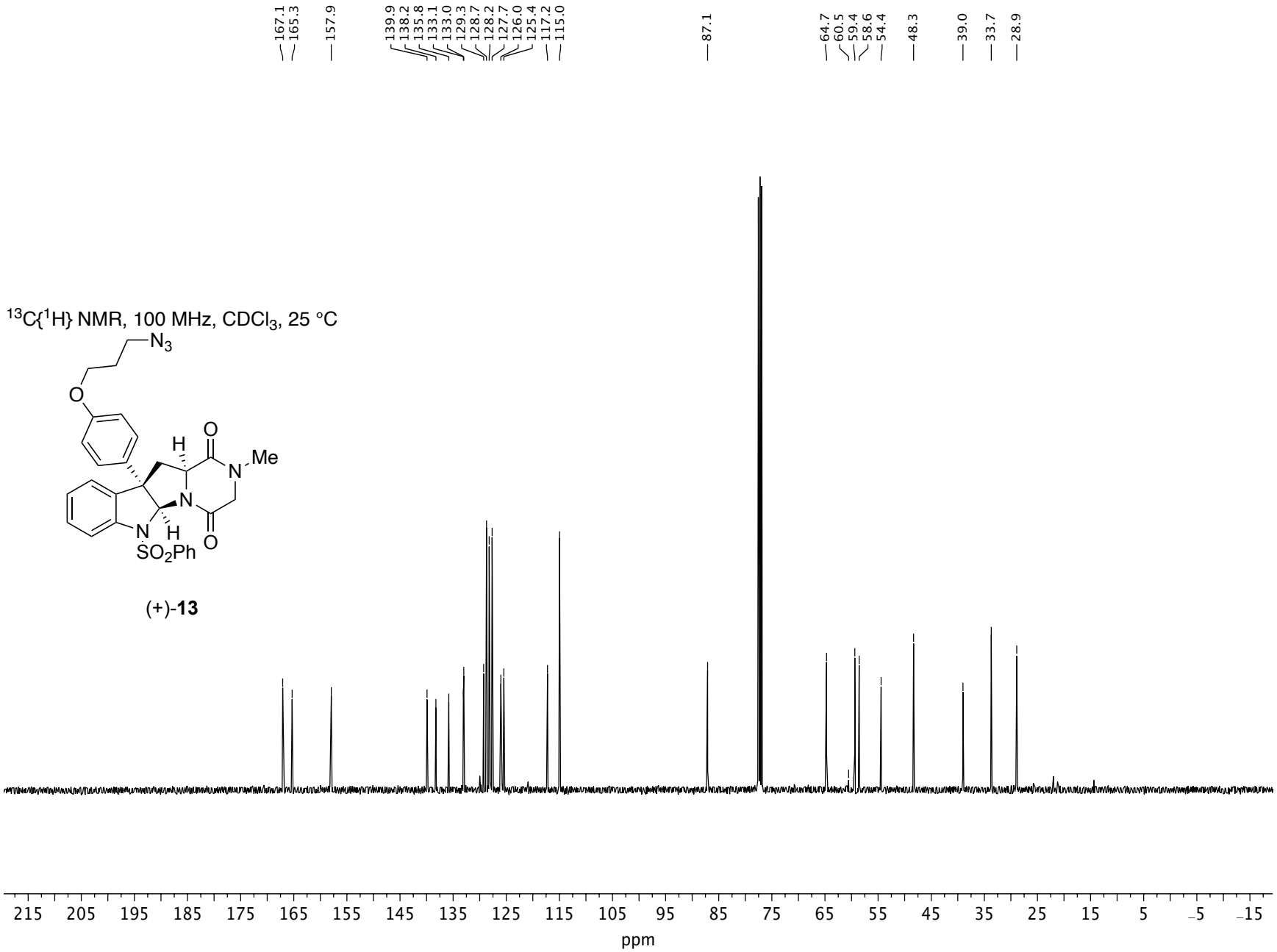


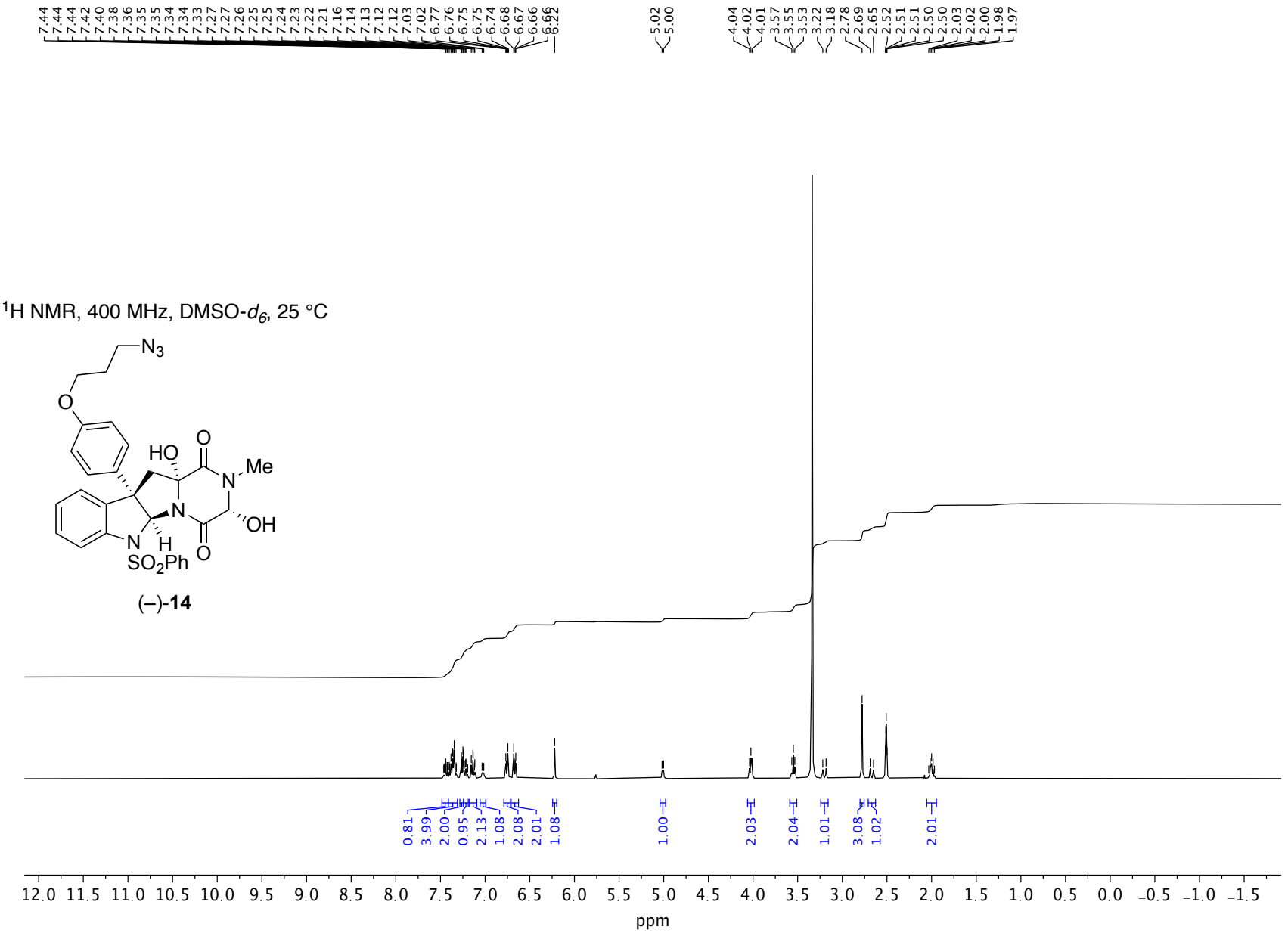
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

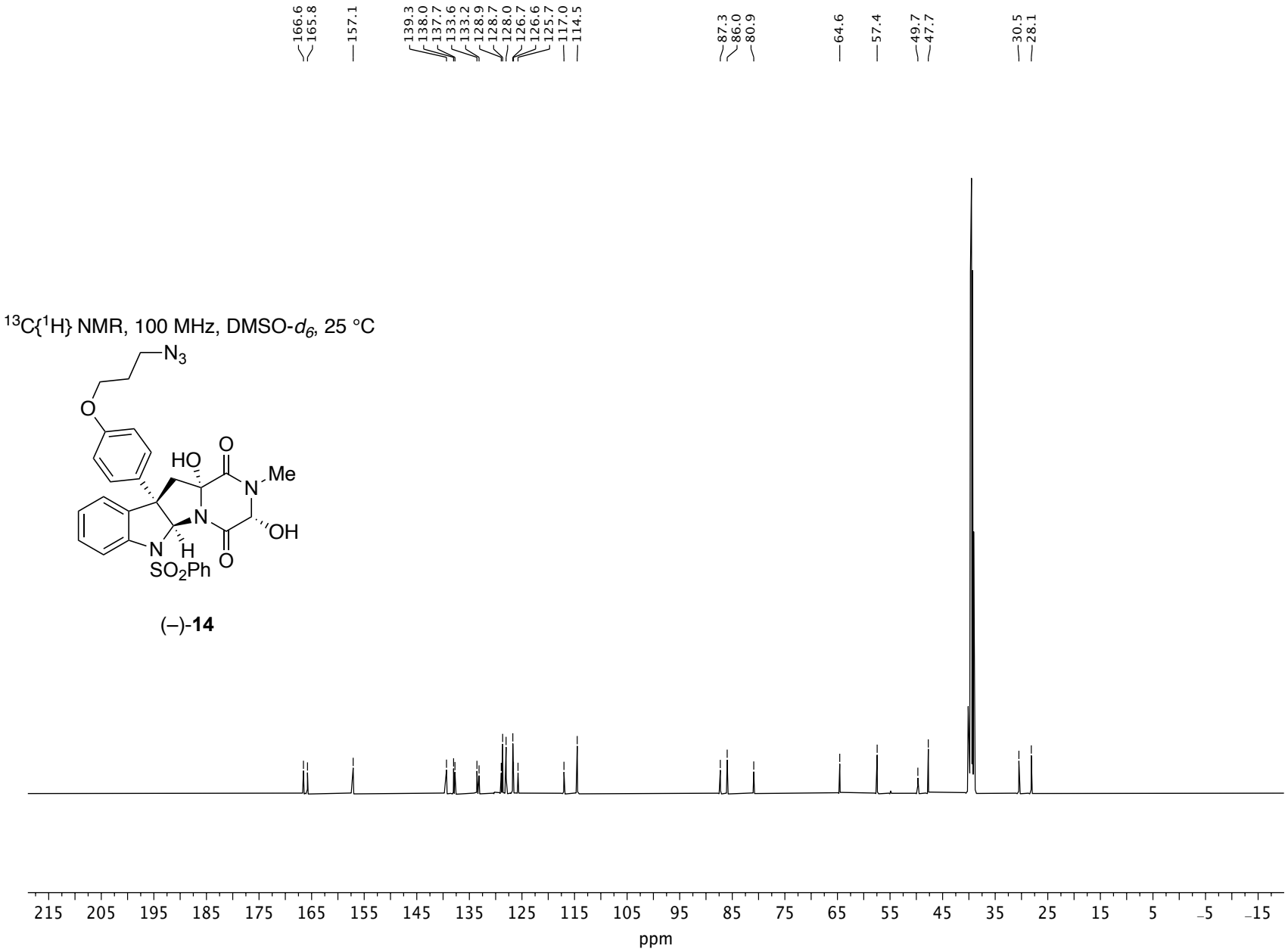


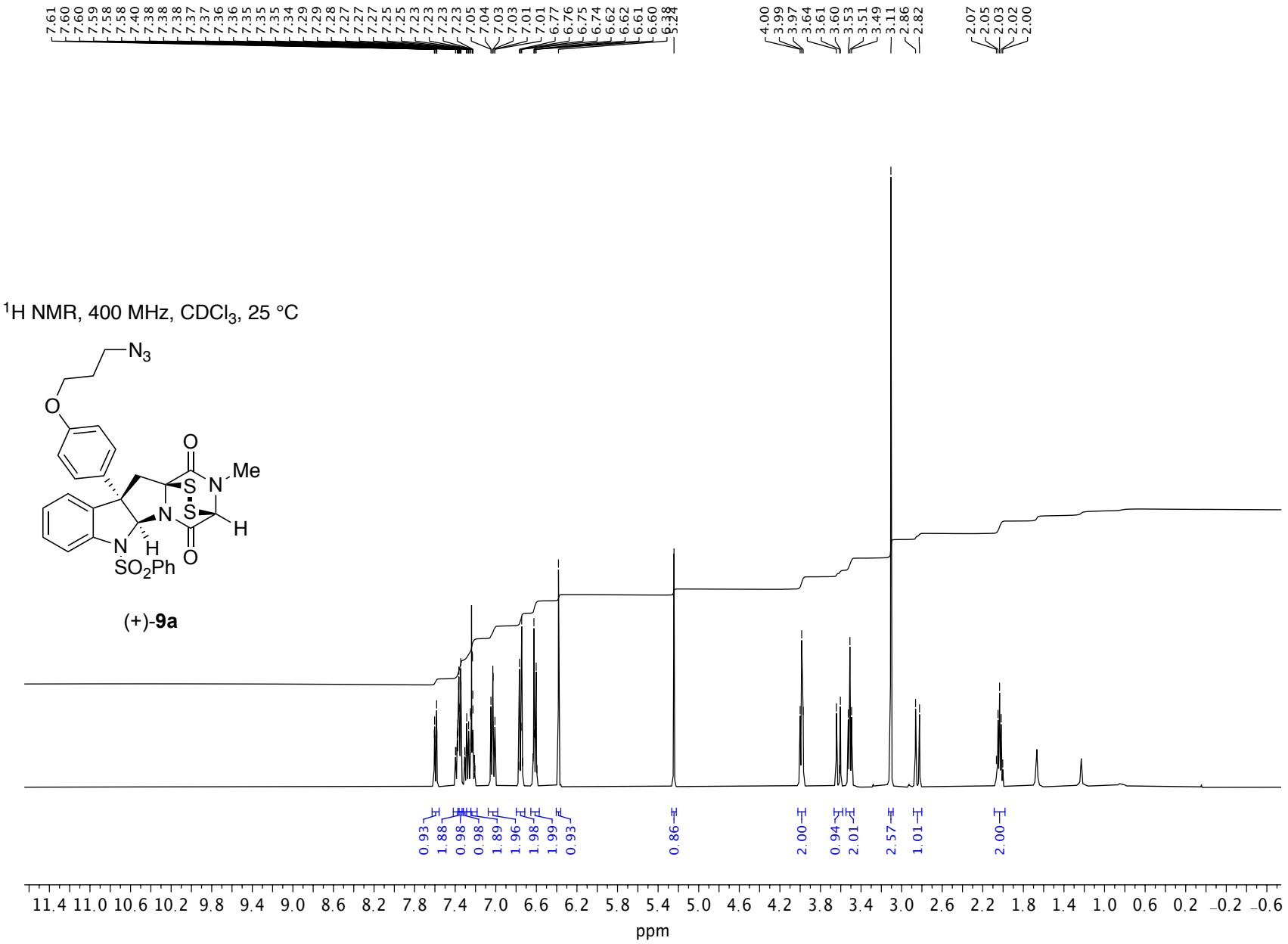
(+)-**13**



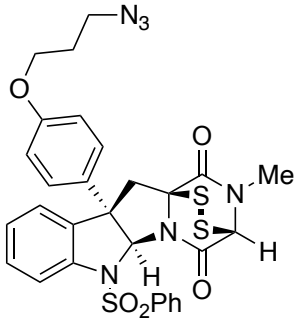

167.1
165.3
157.9
139.9
138.2
135.8
133.1
133.0
129.3
128.7
128.2
127.7
126.0
125.4
117.2
115.0
87.1
64.7
60.5
59.4
58.6
54.4
48.3
39.0
33.7
28.9
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
N3
O
H
O
N
Me
N
N
H
O
SO2Ph
(+)-13
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.44
7.44
7.44
7.42
7.40
7.38
7.36
7.35
7.35
7.34
7.34
7.33
7.27
7.27
7.26
7.25
7.25
7.24
7.23
7.22
7.21
7.16
7.14
7.13
7.12
7.12
7.03
7.02
6.77
6.76
6.75
6.75
6.74
6.68
6.67
6.66
6.66
6.22
5.02
5.00
4.04
4.02
4.01
3.57
3.55
3.53
3.22
3.18
2.78
2.69
2.65
2.52
2.51
2.51
2.50
2.50
2.03
2.02
2.00
1.98
1.97
1H NMR, 400 MHz, DMSO-d6, 25 °C
N3
O
HO
O
N
Me
N
OH
N
H
O
SO2Ph
(–)-14
0.81
3.99
2.00
0.95
2.13
1.08
2.08
2.01
1.08
1.00
2.03
2.04
1.01
3.08
1.02
2.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0 −1.5
ppm


166.6
165.8
157.1
139.3
138.0
137.7
133.6
133.2
128.9
128.7
128.0
126.7
126.6
125.7
117.0
114.5
87.3
86.0
80.9
64.6
57.4
49.7
47.7
30.5
28.1
$^{13}C\{^{1}H\}$ NMR, 100 MHz, DMSO-d_6, 25 °C
N_3
O
HO
O
N
Me
N
OH
N
H
O
SO_2Ph
(–)-**14**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 –5 –15
ppm

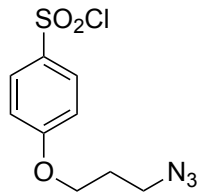

7.61 7.60 7.60 7.59 7.58 7.58 7.40 7.38 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.35 7.34 7.29 7.29 7.28 7.27 7.27 7.27 7.25 7.25 7.23 7.23 7.23 7.23 7.05 7.04 7.03 7.03 7.01 7.01 6.77 6.76 6.75 6.74 6.62 6.62 6.61 6.60 6.38 5.24
4.00 3.99 3.97 3.64 3.61 3.60 3.53 3.51 3.49 3.11 2.86 2.82
2.07 2.05 2.03 2.02 2.00
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
N3
O
O
S
N
Me
N
S
H
N
H
SO2Ph
O
(+)-9a
0.93 1.88 0.98 0.98 1.89 1.96 1.98 1.99 0.93
0.86
2.00
0.94 2.01
2.57
1.01
2.00
11.4 11.0 10.6 10.2 9.8 9.4 9.0 8.6 8.2 7.8 7.4 7.0 6.6 6.2 5.8 5.4 5.0 4.6 4.2 3.8 3.4 3.0 2.6 2.2 1.8 1.4 1.0 0.6 0.2 -0.2 -0.6
ppm

$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C



(+)-**9a**

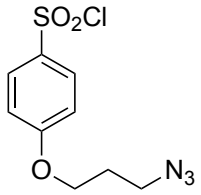
^{1}H NMR, 600 MHz, $CDCl_3$, 25 °C



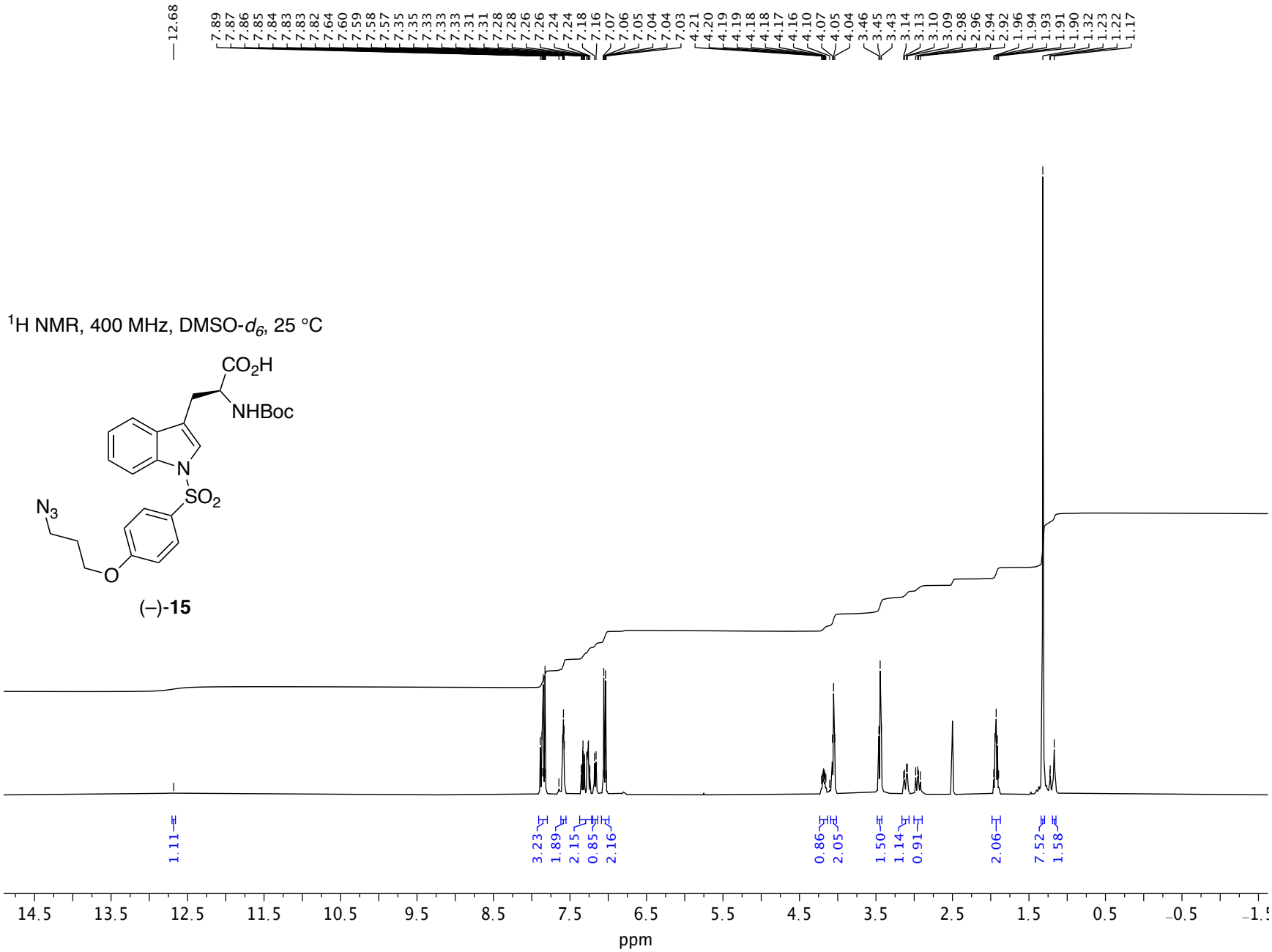
S5

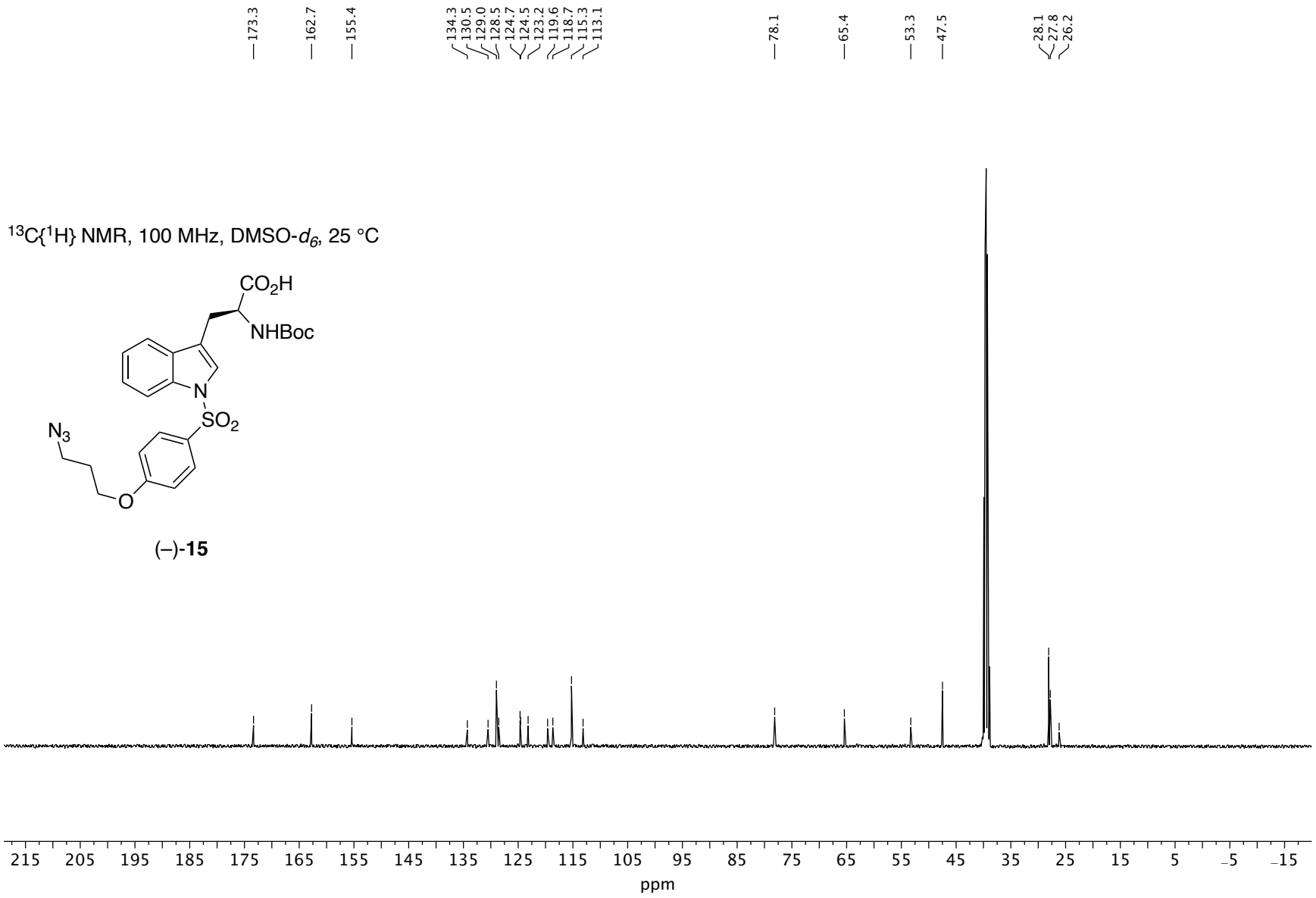
164.1
136.5
129.8
115.3
65.6
48.1
28.6

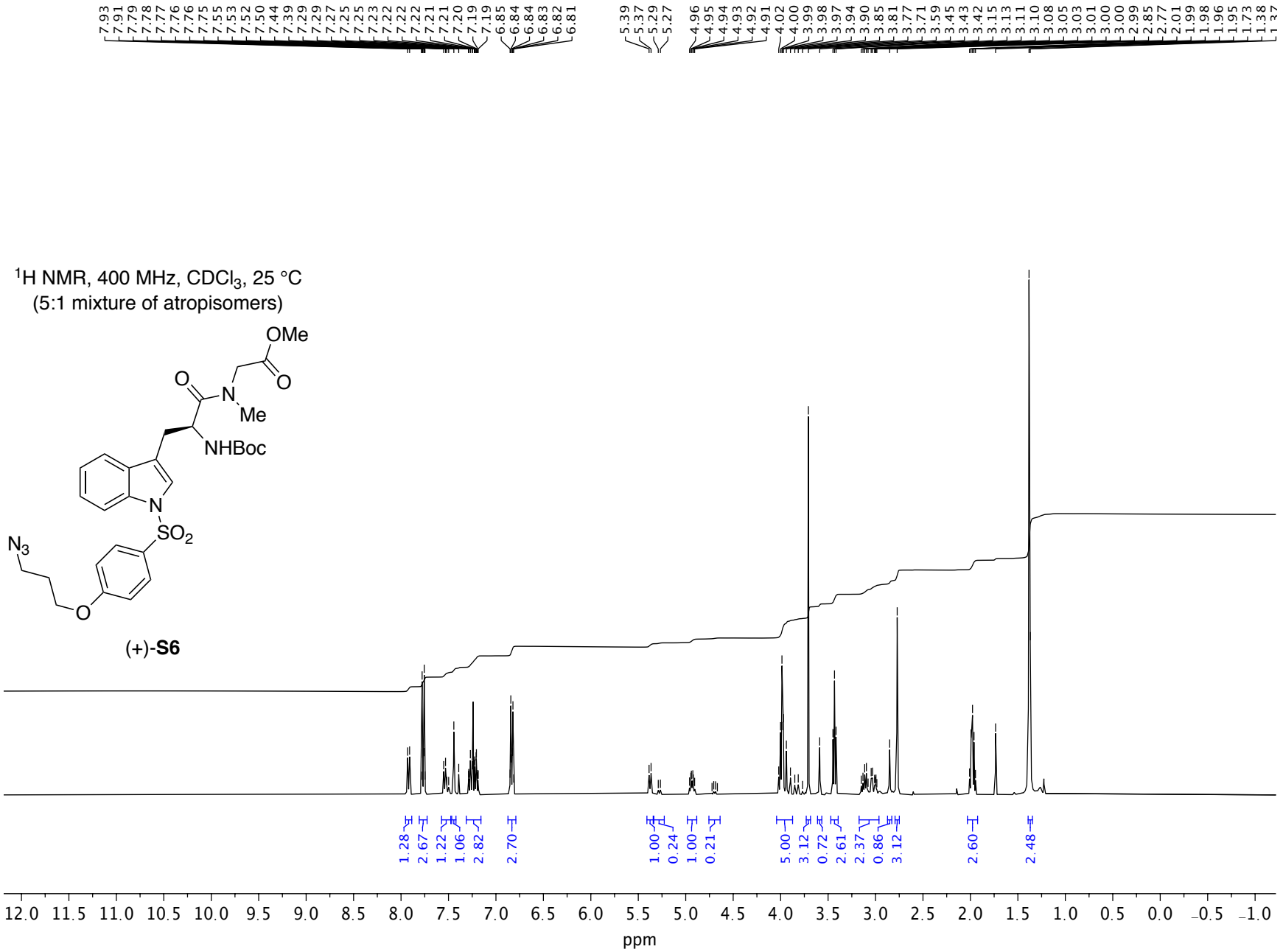
$^{13}C\{^{1}H\}$ NMR, 150 MHz, $CDCl_3$, 25 °C

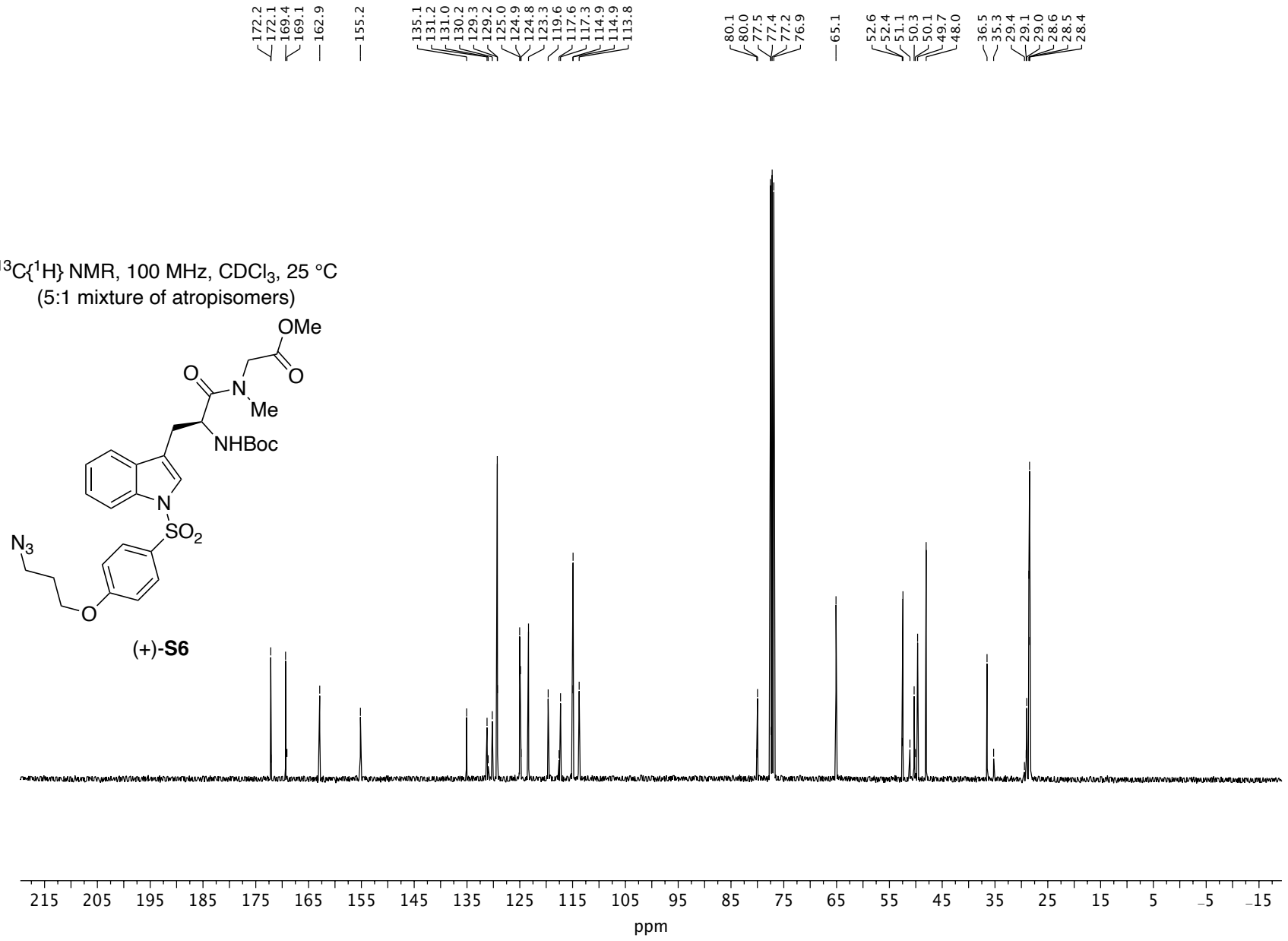


S5


12.68
7.89 7.87 7.86 7.85 7.84 7.83 7.83 7.82 7.64 7.60 7.59 7.58 7.57 7.35 7.33 7.33 7.33 7.31 7.31 7.28 7.28 7.26 7.26 7.24 7.24 7.18 7.16 7.07 7.06 7.05 7.04 7.04 7.03
4.21 4.20 4.19 4.19 4.18 4.18 4.17 4.16 4.10 4.07 4.05 4.04
3.46 3.45 3.43 3.14 3.13 3.10 3.09 2.98 2.96 2.94 2.92 1.96 1.94 1.93 1.91 1.90 1.32 1.23 1.22 1.17
1H NMR, 400 MHz, DMSO-d6, 25 °C
CO2H
NHBoc
N
SO2
N3
O
(–)-15
1.11
3.23 1.89 2.15 0.85 2.16
0.86 2.05
1.50 1.14 0.91
2.06
7.52 1.58
14.5 13.5 12.5 11.5 10.5 9.5 8.5 7.5 6.5 5.5 4.5 3.5 2.5 1.5 0.5 -0.5
ppm


173.3
162.7
155.4
134.3
130.5
129.0
128.5
124.7
124.5
123.2
119.6
118.7
115.3
113.1
78.1
65.4
53.3
47.5
28.1
27.8
26.2
$^{13}C\{^{1}H\}$ NMR, 100 MHz, DMSO-d_6, 25 °C
CO_2H
NHBoc
N
SO_2
N_3
O
(–)-**15**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 –5 –15
ppm


7.93 7.91 7.79 7.78 7.77 7.76 7.76 7.75 7.55 7.53 7.52 7.50 7.44 7.39 7.29 7.29 7.27 7.25 7.25 7.23 7.22 7.22 7.22 7.21 7.20 7.19 7.19 6.85 6.84 6.84 6.83 6.82 6.81
5.39 5.37 5.29 5.27
4.96 4.95 4.94 4.93 4.92 4.91 4.02 4.00 3.99 3.98 3.97 3.94 3.90 3.85 3.81 3.77 3.71 3.59 3.45 3.43 3.42 3.15 3.13 3.11 3.10 3.08 3.05 3.03 3.01 3.00 3.00 2.99 2.85 2.77 2.01 1.99 1.98 1.96 1.95 1.73 1.38
1H NMR, 400 MHz, CDCl3, 25 °C
(5:1 mixture of atropisomers)
OMe
O
O
N
Me
NHBoc
N
SO2
N3
O
(+)-S6
1.28 2.67 1.22 1.06 2.82 2.70 1.00 0.24 1.00 0.21 5.00 3.12 0.72 2.61 2.37 0.86 3.12 2.60 2.48
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

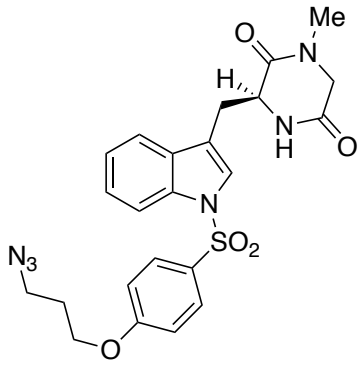

172.2
172.1
169.4
169.1
162.9
155.2
135.1
131.2
131.0
130.2
129.3
129.2
125.0
124.9
124.8
123.3
119.6
117.6
117.3
114.9
114.9
113.8
80.1
80.0
77.5
77.4
77.2
76.9
65.1
52.6
52.4
51.1
50.3
50.1
49.7
48.0
36.5
35.3
29.4
29.1
29.0
28.6
28.5
28.4
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
(5:1 mixture of atropisomers)
OMe
O
O
N
Me
NHBoc
N
SO_2
N_3
O
(+)-**S6**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

7.91 7.89 7.80 7.77 7.50 7.48 7.29 7.29 7.27 7.27 7.26 7.25 7.25 7.21 7.21 7.19 7.19 7.17 7.17 6.86 6.84

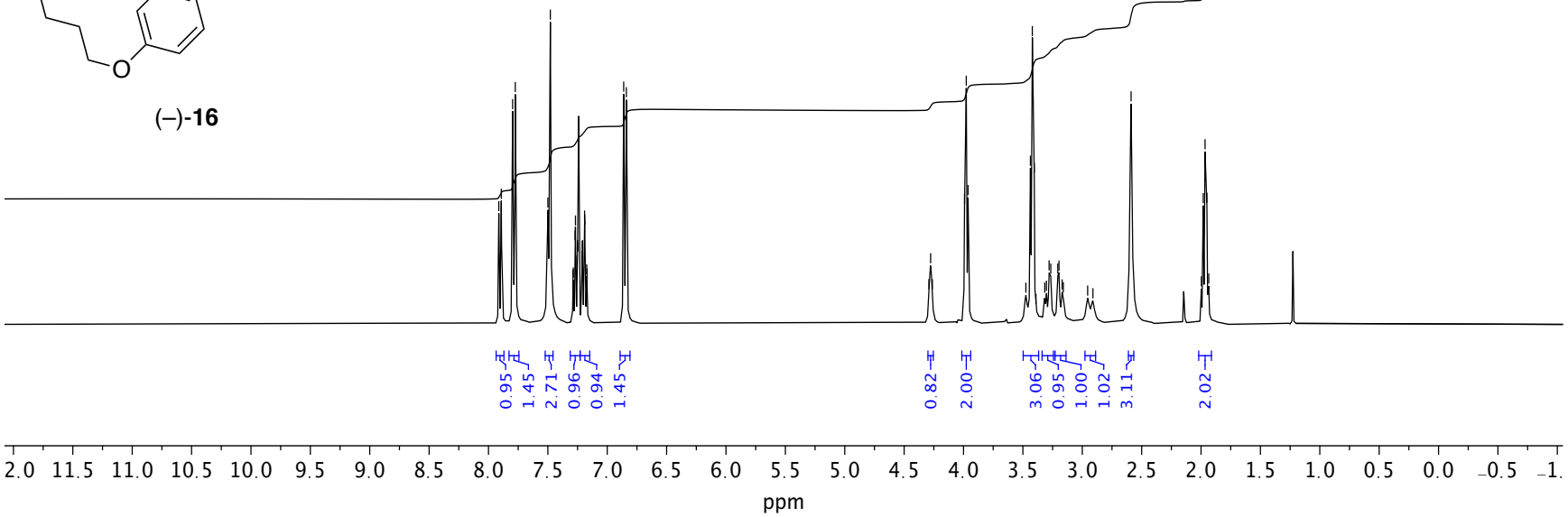
4.29 4.28 4.26 3.99 3.98 3.96 3.48 3.44 3.42 3.40 3.39 3.32 3.30 3.28 3.27 3.21 3.20 3.17 3.16 2.95 2.91 2.59

2.00 1.98 1.97 1.95 1.94

^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

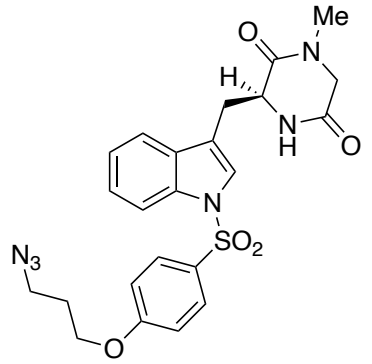


(–)-**16**

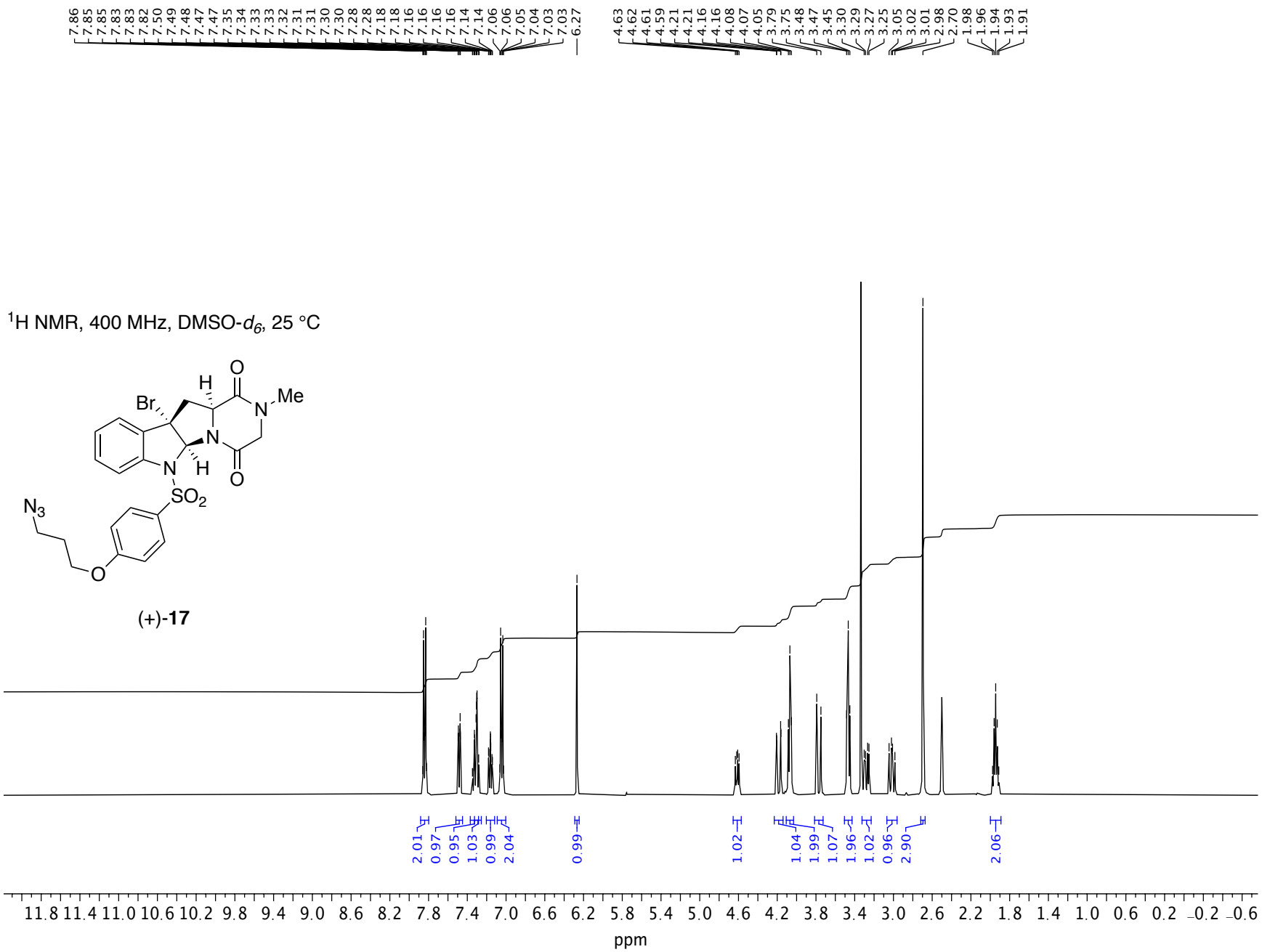


166.3
165.7
163.1
135.0
130.3
129.7
129.4
126.0
125.2
123.5
120.0
116.1
115.2
113.6
65.2
55.2
51.1
48.0
33.8
30.6
28.6

$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C

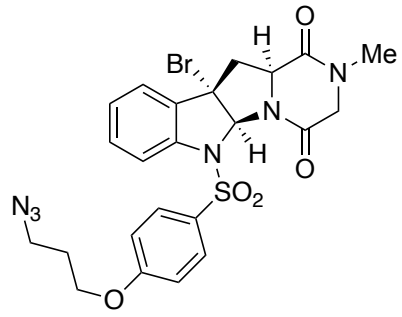


(–)-**16**

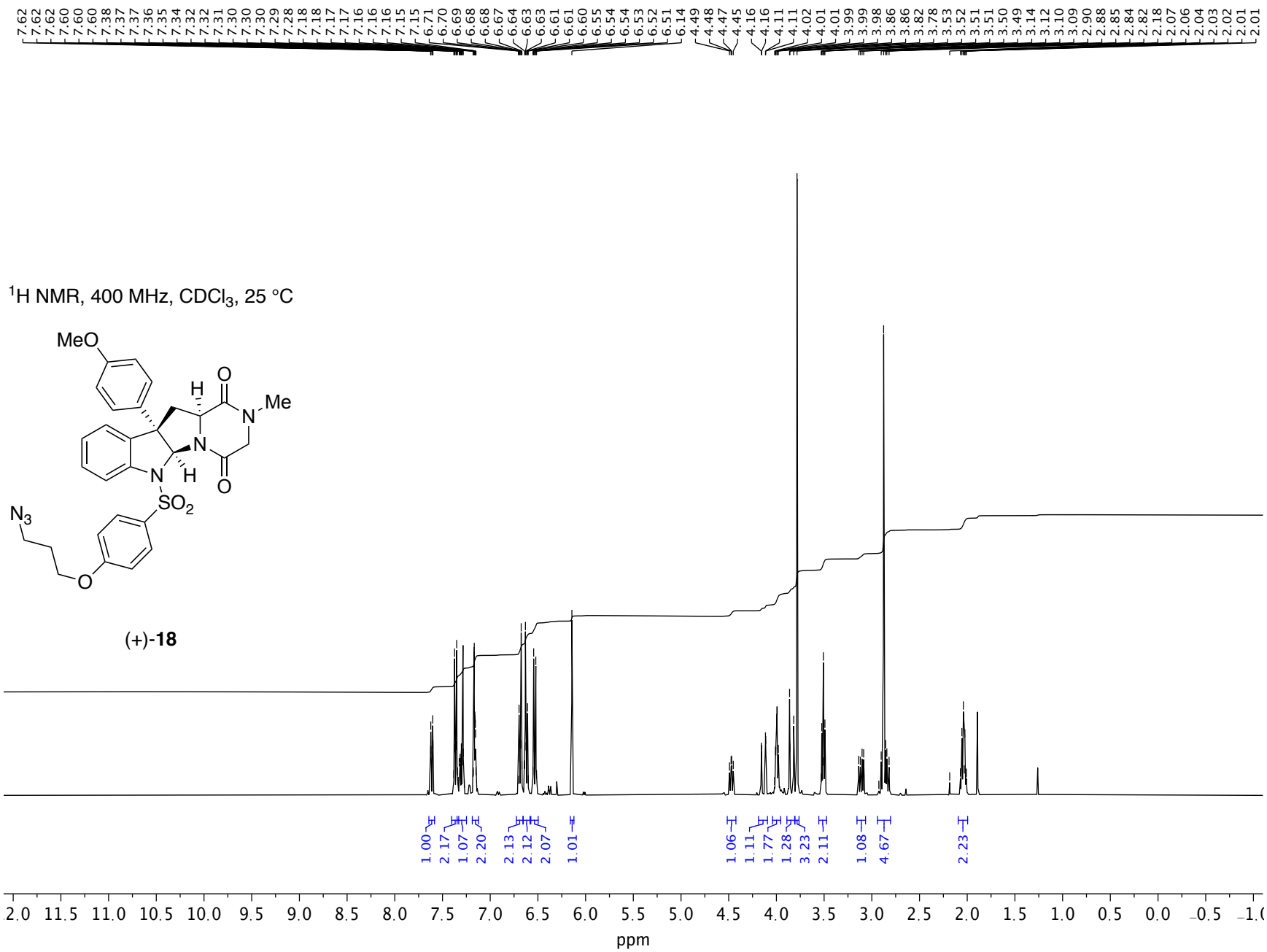

7.86 7.85 7.85 7.83 7.83 7.82 7.50 7.49 7.48 7.47 7.47 7.35 7.34 7.33 7.33 7.32 7.31 7.31 7.30 7.30 7.28 7.28 7.18 7.16 7.16 7.16 7.14 7.14 7.06 7.06 7.05 7.04 7.03 7.03 6.27
4.63 4.62 4.61 4.59 4.21 4.21 4.16 4.16 4.08 4.07 4.05 3.79 3.75 3.48 3.47 3.45 3.30 3.29 3.27 3.25 3.05 3.02 3.01 2.98 2.70 1.98 1.96 1.94 1.93 1.91
1H NMR, 400 MHz, DMSO-d6, 25 °C
Br
H
O
N
Me
N
N
H
O
N3
SO2
O
(+)-17
2.01 0.97 0.95 1.03 0.99 2.04 0.99 1.02 1.04 1.99 1.07 1.96 1.02 0.96 2.90 2.06
11.8 11.4 11.0 10.6 10.2 9.8 9.4 9.0 8.6 8.2 7.8 7.4 7.0 6.6 6.2 5.8 5.4 5.0 4.6 4.2 3.8 3.4 3.0 2.6 2.2 1.8 1.4 1.0 0.6 0.2 -0.2 -0.6
ppm

166.3
165.0
162.4
138.5
135.1
130.6
130.4
129.6
125.9
125.2
116.5
114.6
86.1
65.3
61.5
56.8
53.3
47.5
38.6
32.7
27.9

$^{13}C\{^{1}H\}$ NMR, 100 MHz, DMSO-d_6, 25 °C

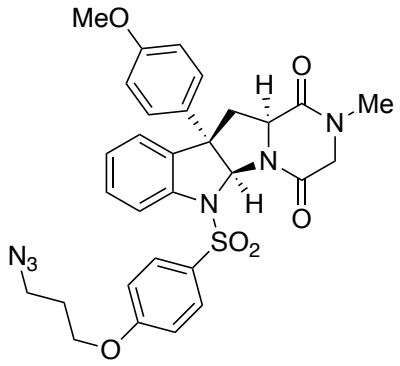


(+)-**17**

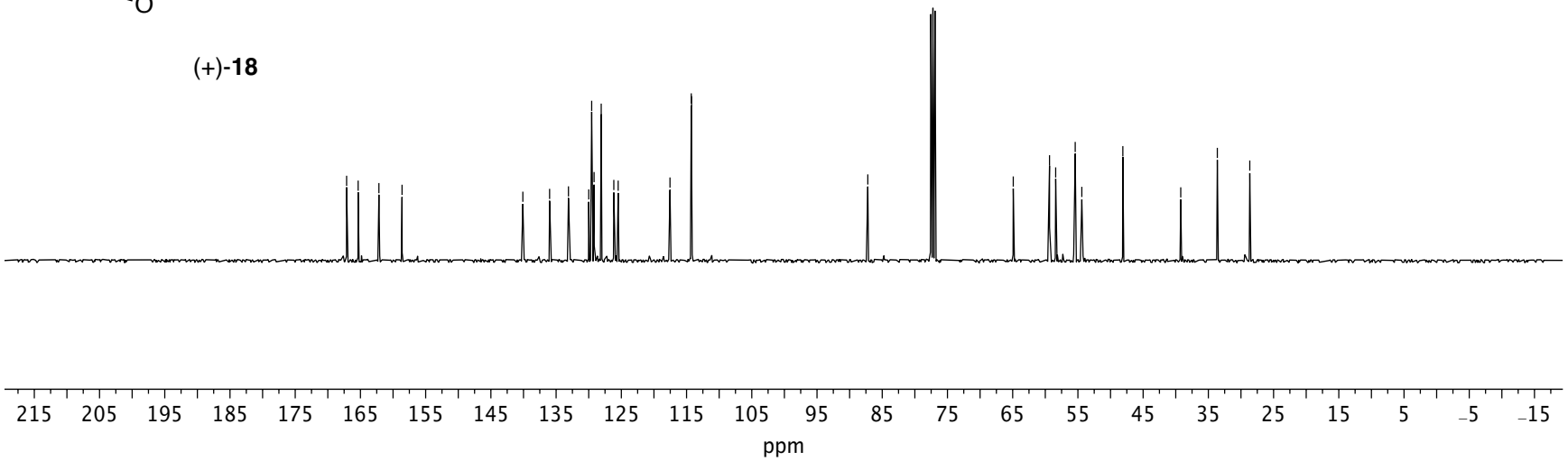

7.62 7.62 7.60 7.60 7.60 7.38 7.37 7.36 7.35 7.34 7.32 7.32 7.31 7.30 7.30 7.30 7.29 7.28 7.18 7.18 7.17 7.17 7.16 7.16 7.16 7.15 7.15 6.71 6.70 6.69 6.68 6.68 6.67 6.64 6.63 6.63 6.61 6.61 6.60 6.55 6.54 6.54 6.53 6.52 6.51 6.14 4.49 4.48 4.47 4.45 4.16 4.16 4.11 4.11 4.02 4.01 4.01 3.99 3.99 3.98 3.86 3.86 3.82 3.78 3.53 3.52 3.51 3.51 3.50 3.49 3.14 3.12 3.10 3.09 2.90 2.88 2.85 2.84 2.82 2.18 2.07 2.06 2.04 2.03 2.02 2.01 2.01
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
H
O
N
Me
N
N
H
O
N3
SO2
O
(+)-18
1.00 2.17 1.07 2.20 2.13 2.12 2.07 1.01 1.06 1.11 1.77 1.28 3.23 2.11 1.08 4.67 2.23
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm

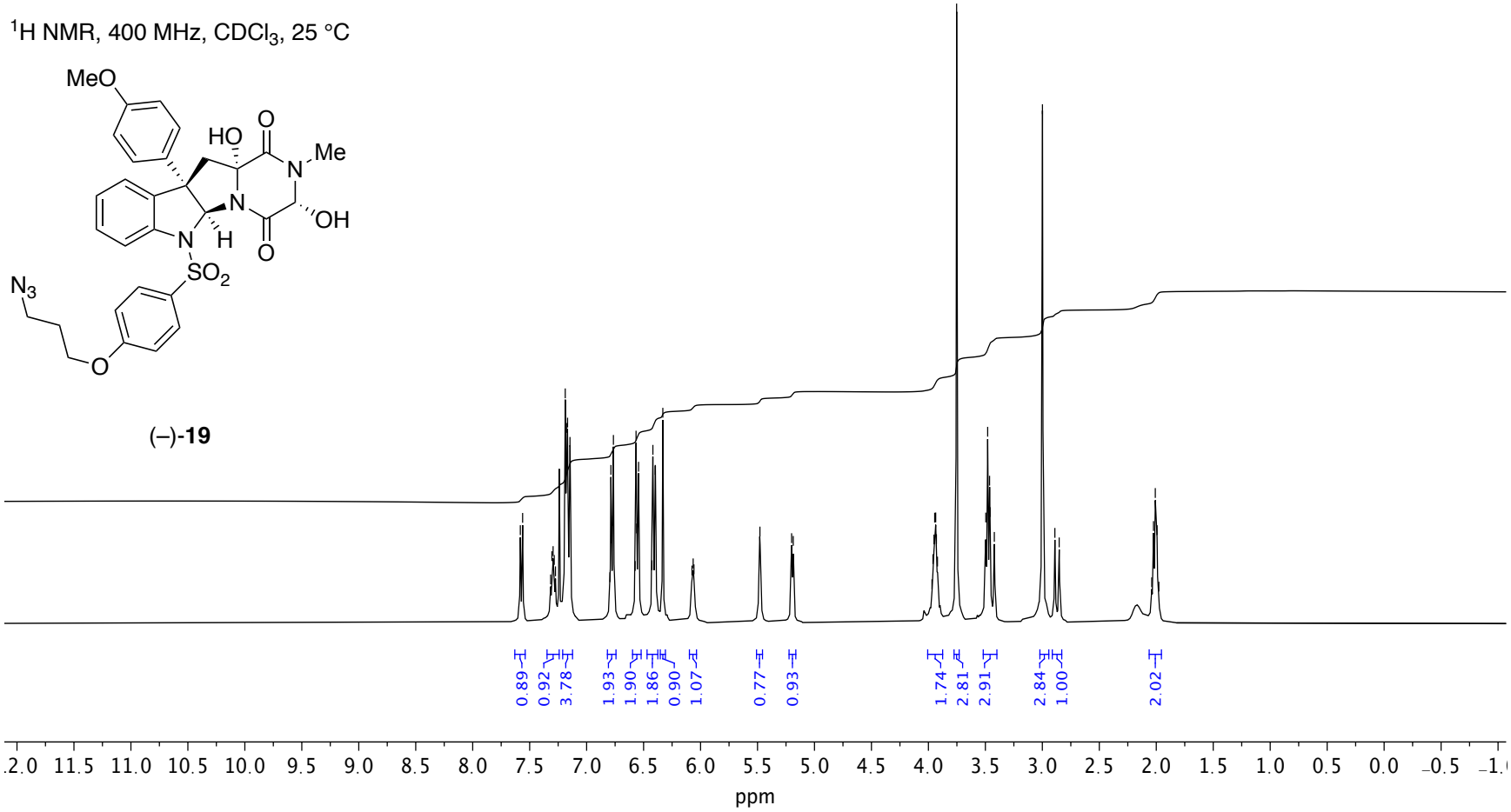
167.1
165.4
162.2
158.6
140.1
136.0
133.1
130.0
129.5
129.2
128.1
126.2
125.5
117.5
114.3
114.2
87.2
64.9
59.4
58.4
55.4
54.4
48.1
39.2
33.6
28.6

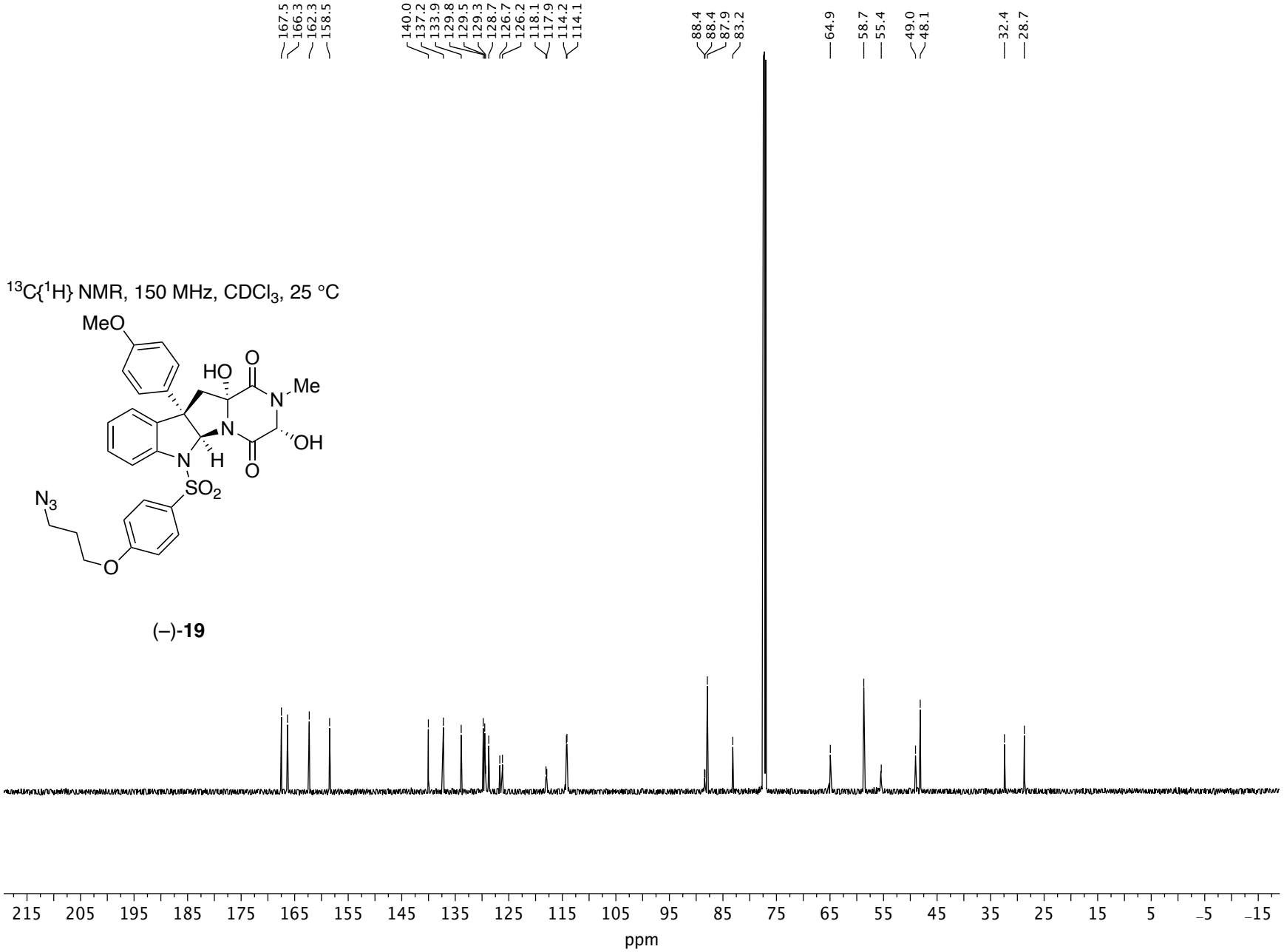
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C

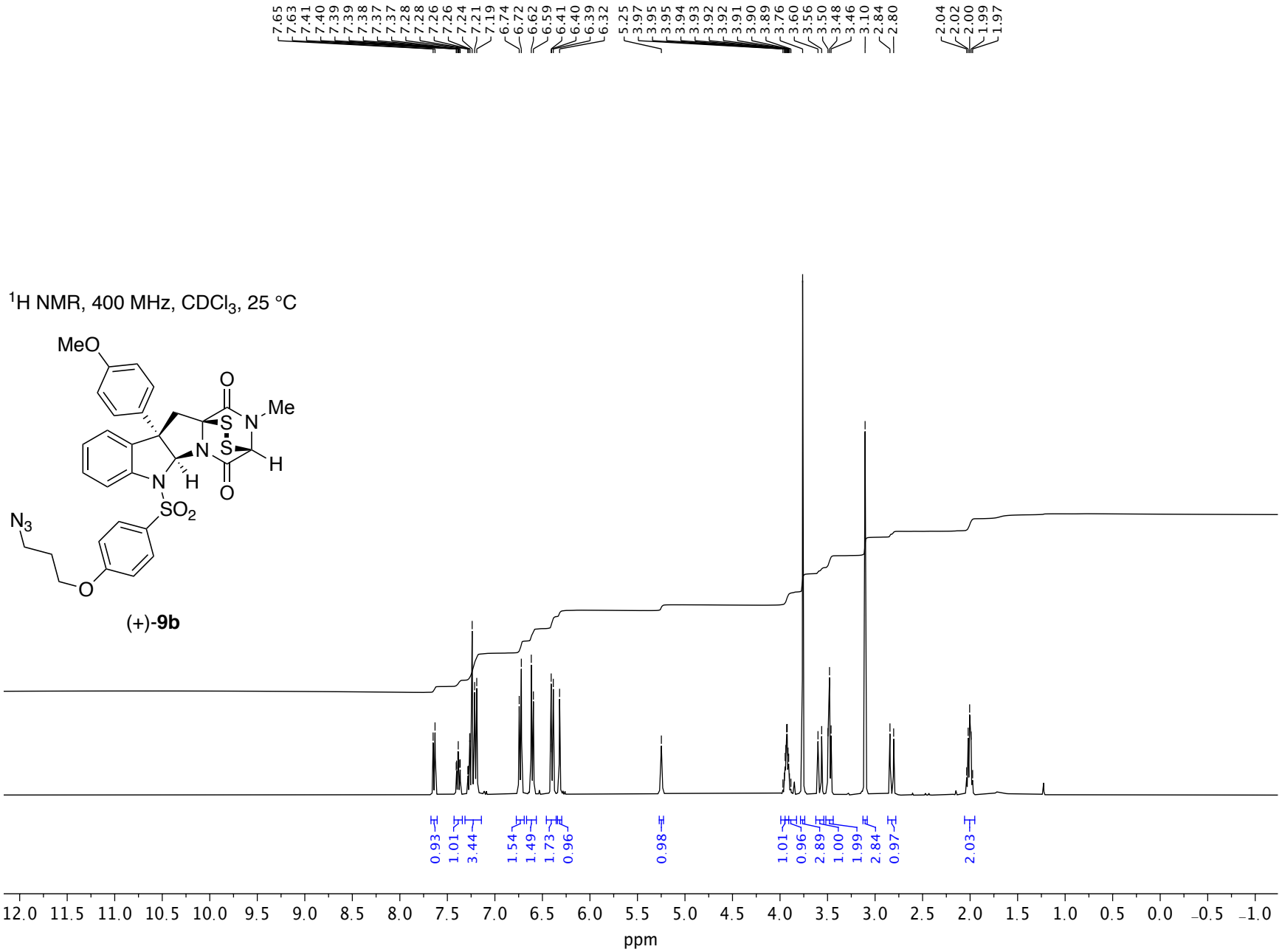


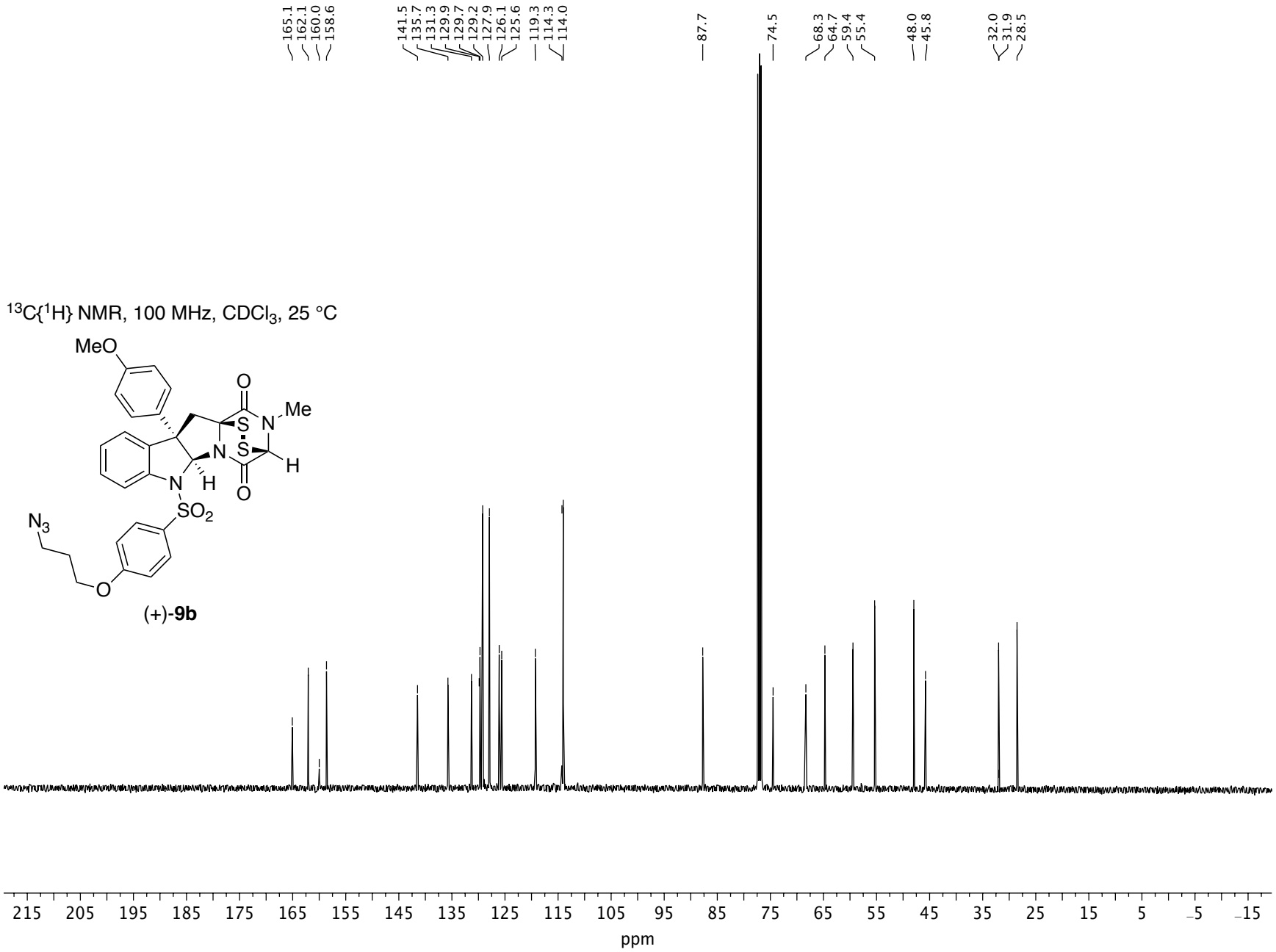
(+)-**18**

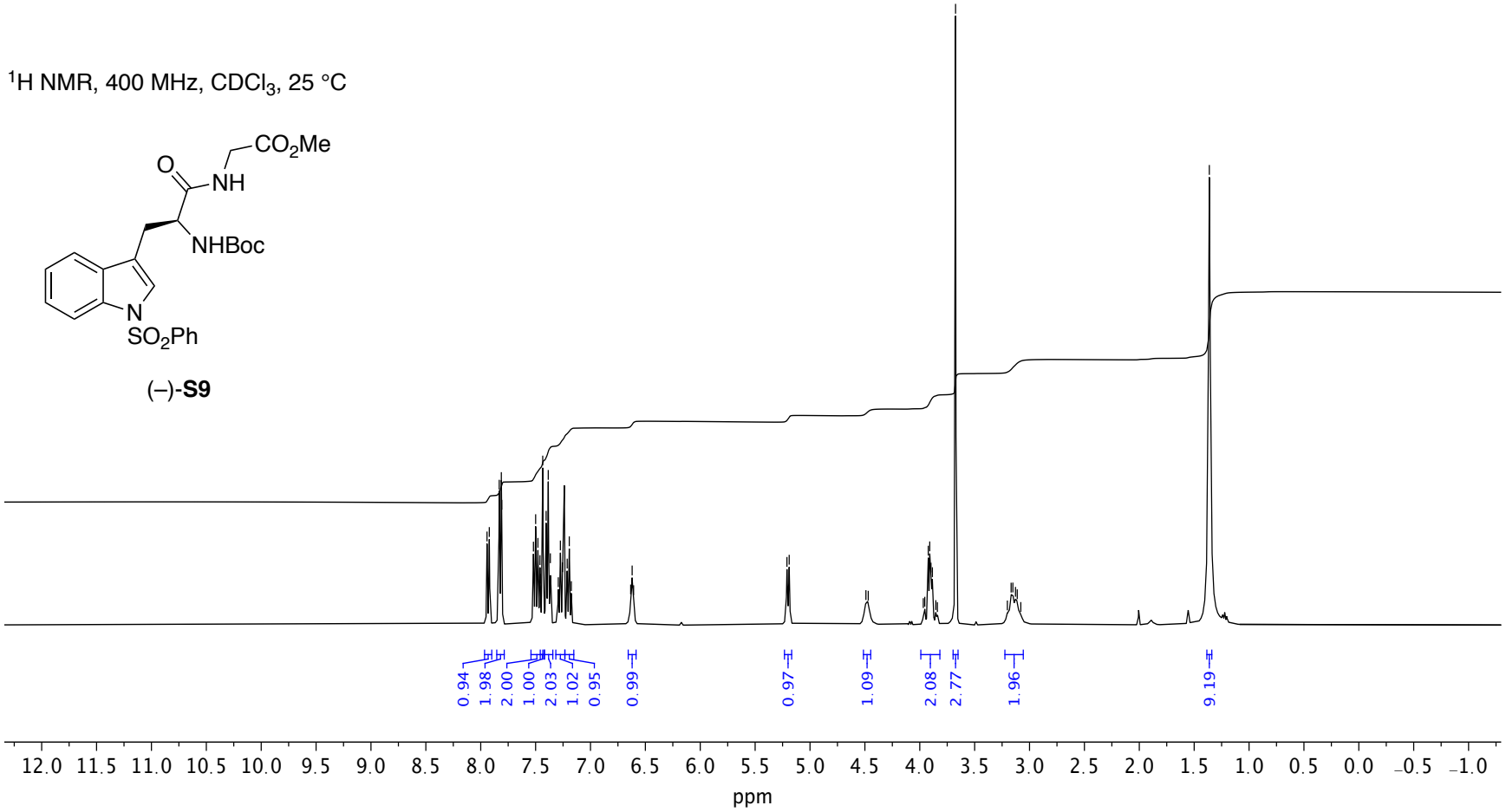


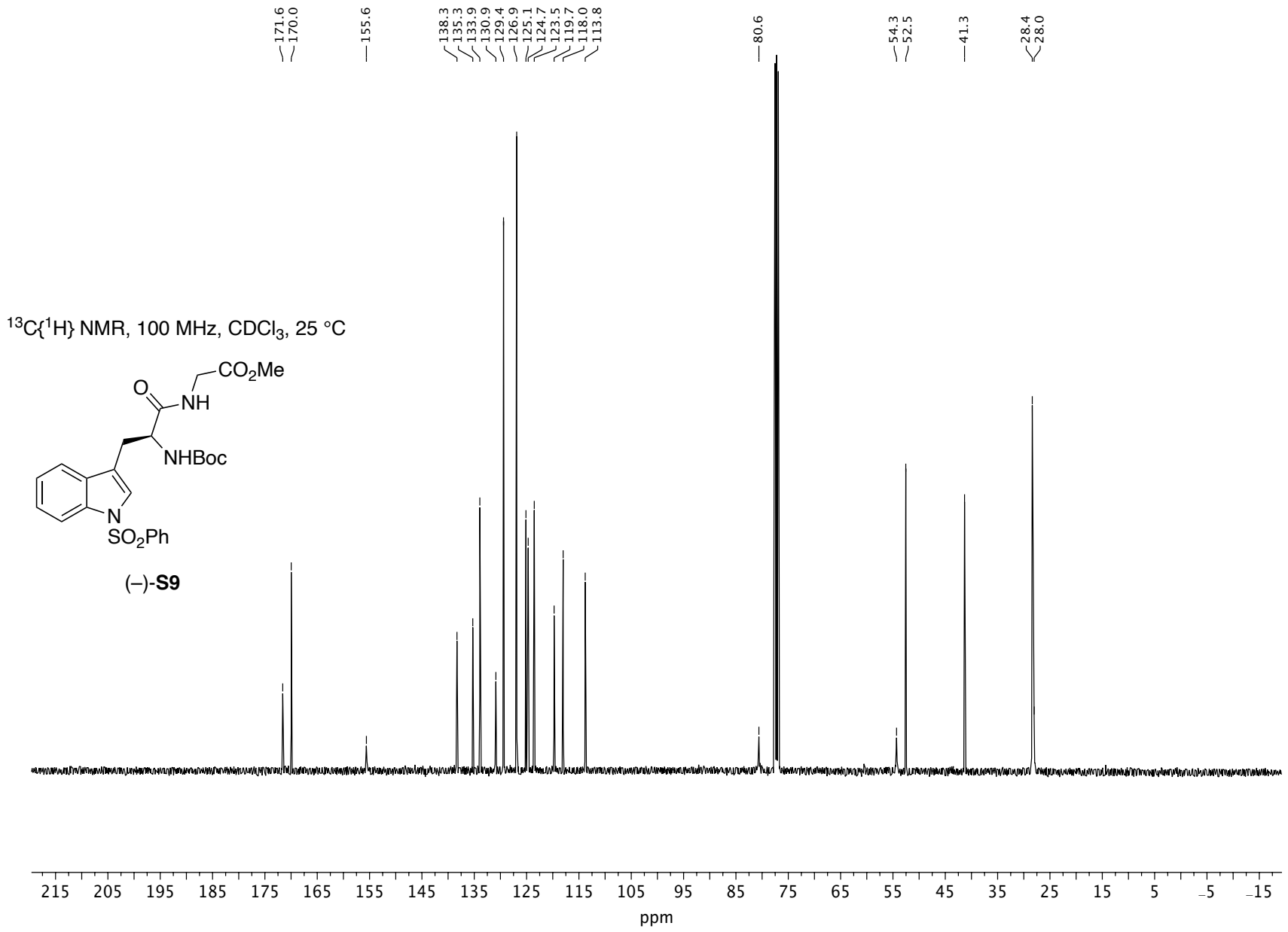

7.58
7.56
7.32
7.30
7.29
7.28
7.27
7.19
7.18
7.17
7.15
6.80
6.79
6.78
6.77
6.76
6.57
6.57
6.56
6.55
6.54
6.43
6.42
6.40
6.33
6.08
6.06
6.06
5.48
5.20
5.19
3.97
3.96
3.95
3.94
3.94
3.93
3.92
3.75
3.50
3.48
3.46
3.46
3.42
3.00
2.89
2.85
2.04
2.02
2.01
1.99
1.98
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
HO
O
N
Me
N
OH
N
H
O
SO2
N3
O
(–)-19
0.89
0.92
3.78
1.93
1.90
1.86
0.90
1.07
0.77
0.93
1.74
2.81
2.91
2.84
1.00
2.02
ppm

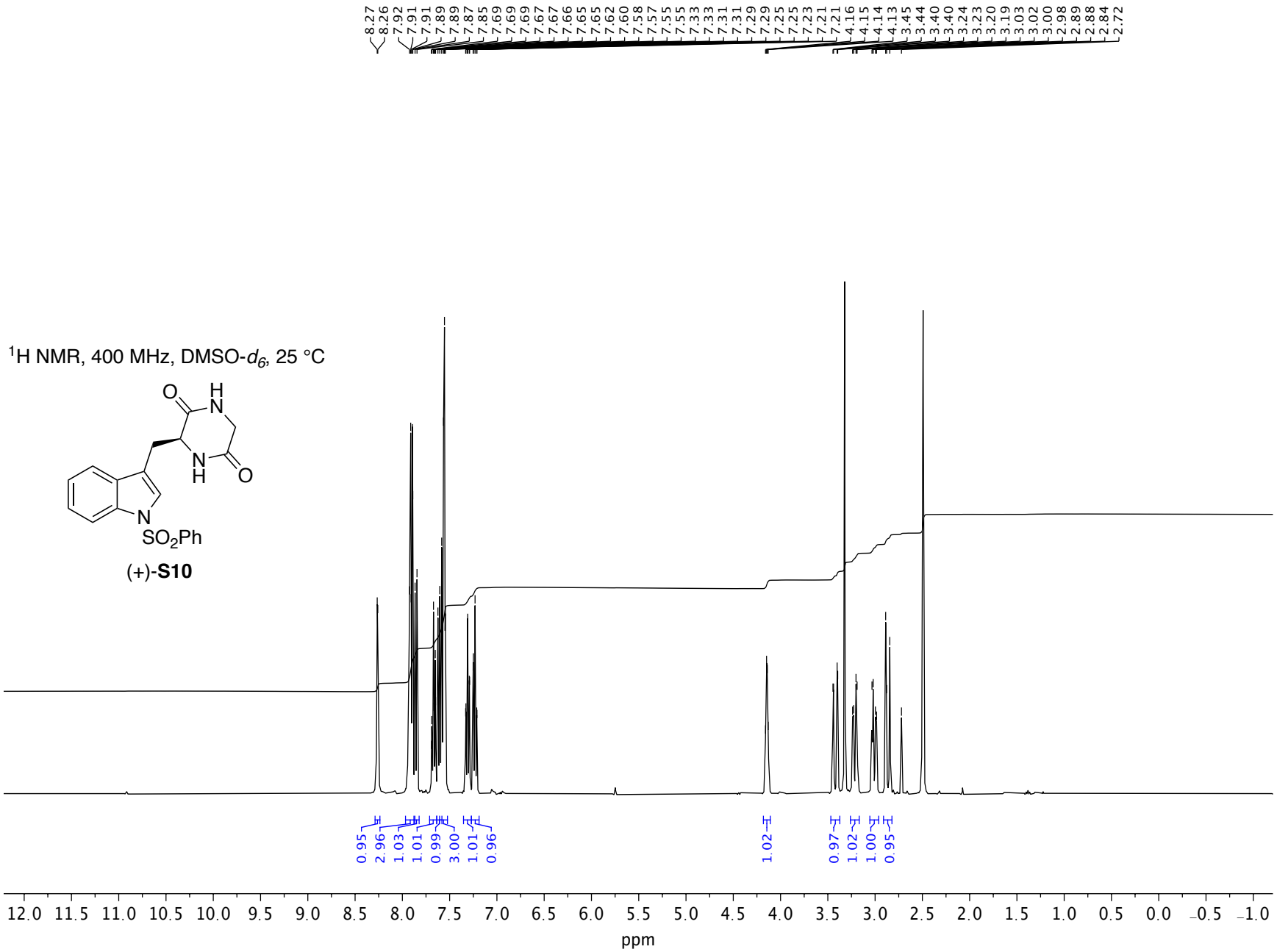

167.5
166.3
162.3
158.5
140.0
137.2
133.9
129.8
129.5
129.3
128.7
126.7
126.2
118.1
117.9
114.2
114.1
88.4
88.4
87.9
83.2
64.9
58.7
55.4
49.0
48.1
32.4
28.7
$^{13}C\{^{1}H\}$ NMR, 150 MHz, $CDCl_3$, 25 °C
MeO
HO
O
N
Me
N
OH
N
H
O
SO_2
N_3
O
(–)-**19**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 –5 –15
ppm

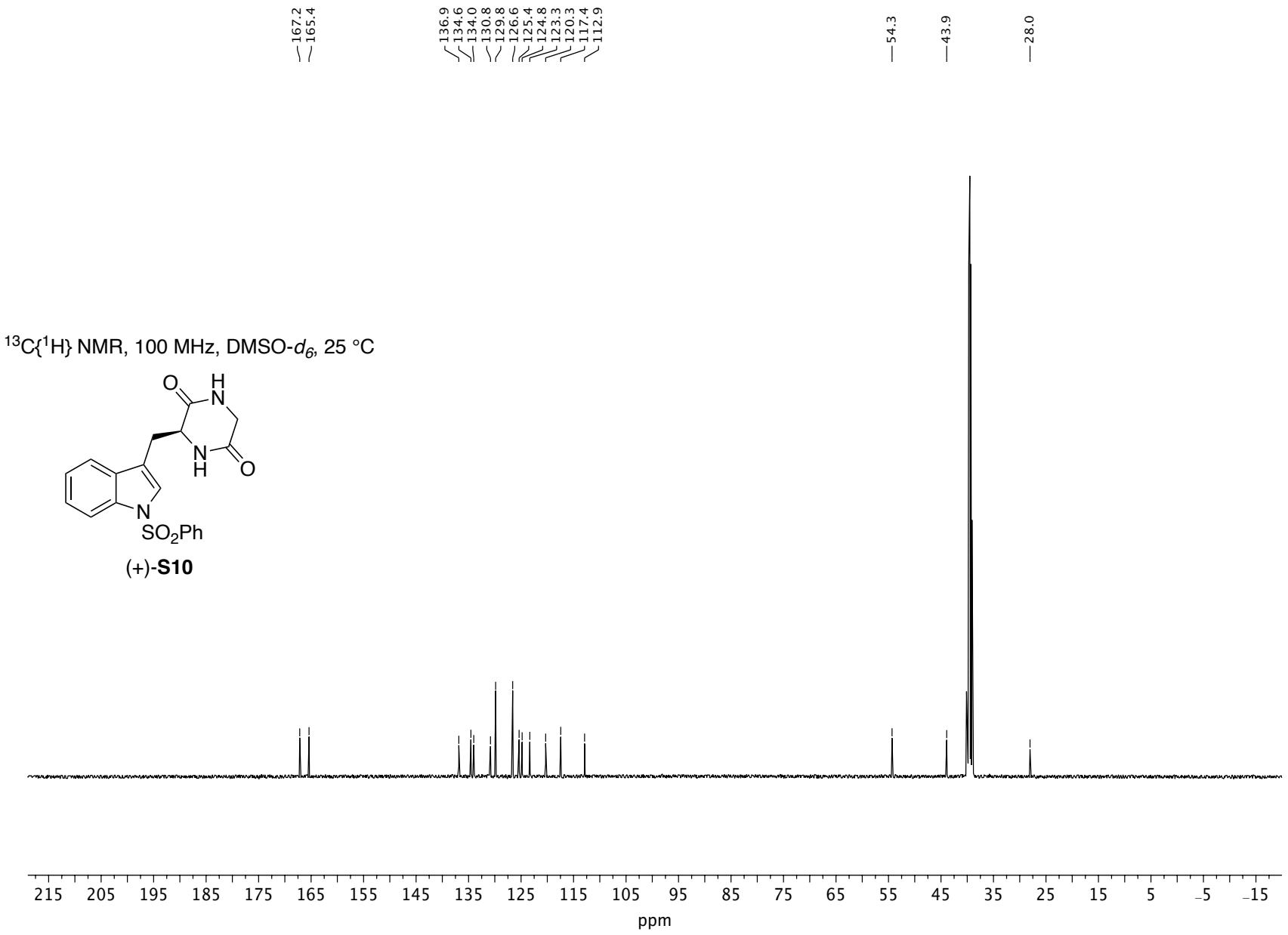

7.65
7.63
7.41
7.40
7.39
7.39
7.38
7.37
7.37
7.28
7.28
7.26
7.26
7.24
7.21
7.19
6.74
6.72
6.62
6.59
6.41
6.40
6.39
6.32
5.25
3.97
3.95
3.95
3.94
3.93
3.92
3.92
3.91
3.90
3.89
3.76
3.60
3.56
3.50
3.48
3.46
3.10
2.84
2.80
2.04
2.02
2.00
1.99
1.97
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
O
S
N
Me
N
S
H
N
H
O
SO2
N3
O
(+)-9b
0.93
1.01
3.44
1.54
1.49
1.73
0.96
0.98
1.01
0.96
2.89
1.00
1.99
2.84
0.97
2.03
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

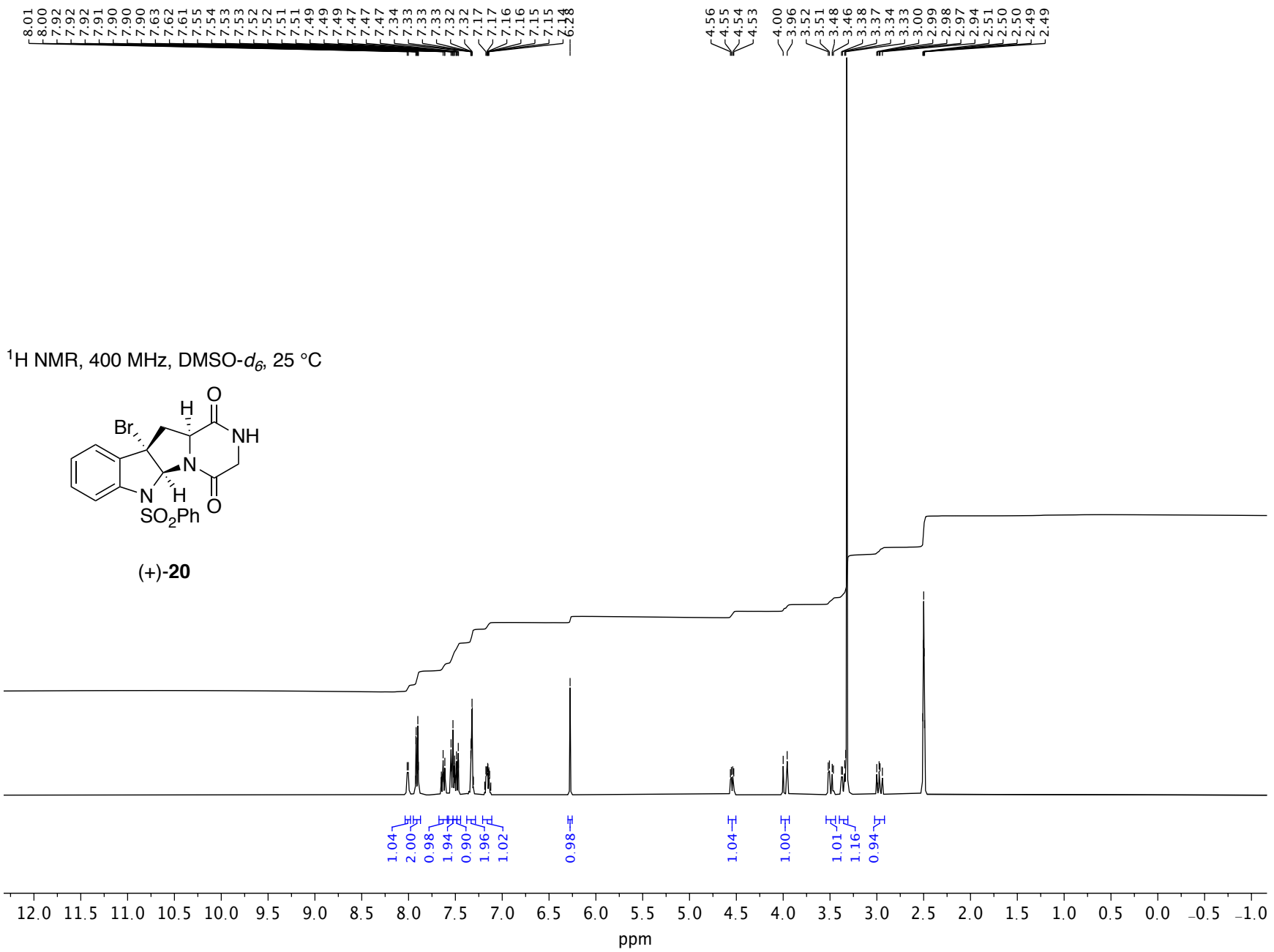

165.1
162.1
160.0
158.6
141.5
135.7
131.3
129.9
129.7
129.2
127.9
126.1
125.6
119.3
114.3
114.0
87.7
74.5
68.3
64.7
59.4
55.4
48.0
45.8
32.0
31.9
28.5
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
O
N
Me
S
N
S
H
O
N
H
SO_2
N_3
O
(+)-**9b**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

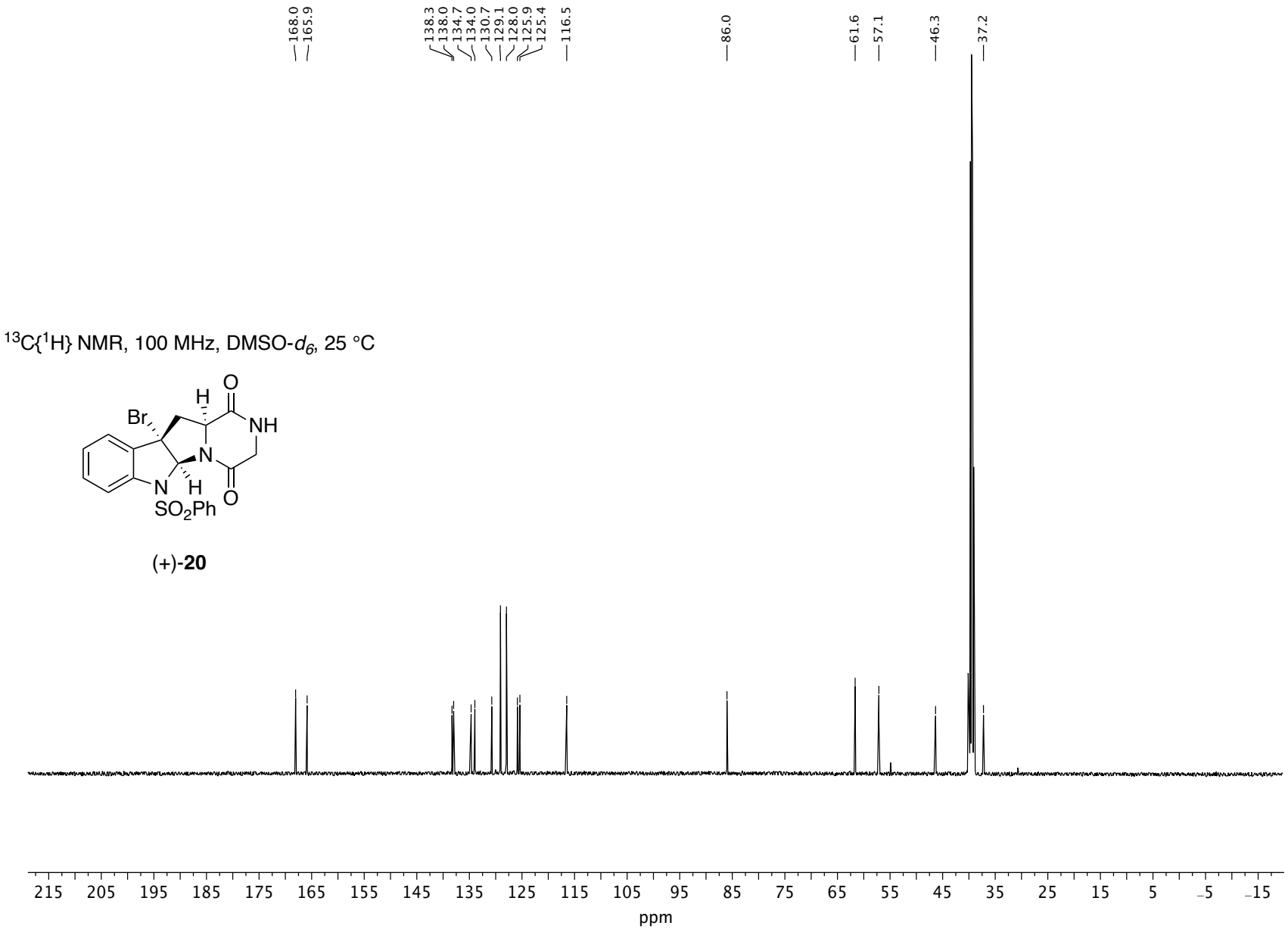

7.94
7.92
7.83
7.83
7.81
7.81
7.52
7.50
7.48
7.46
7.46
7.46
7.44
7.40
7.38
7.37
7.29
7.27
7.25
7.21
7.19
7.17
6.63
6.62
6.61
5.21
5.19
4.49
4.47
3.97
3.95
3.92
3.91
3.90
3.89
3.85
3.84
3.67
3.20
3.17
3.15
3.13
3.11
3.08
1.36
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
CO_2Me
O
NH
NHBoc
N
SO_2Ph
(–)-**S9**
0.94
1.98
2.00
1.00
2.03
1.02
0.95
0.99
0.97
1.09
2.08
2.77
1.96
9.19
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 –0.5 –1.0
ppm

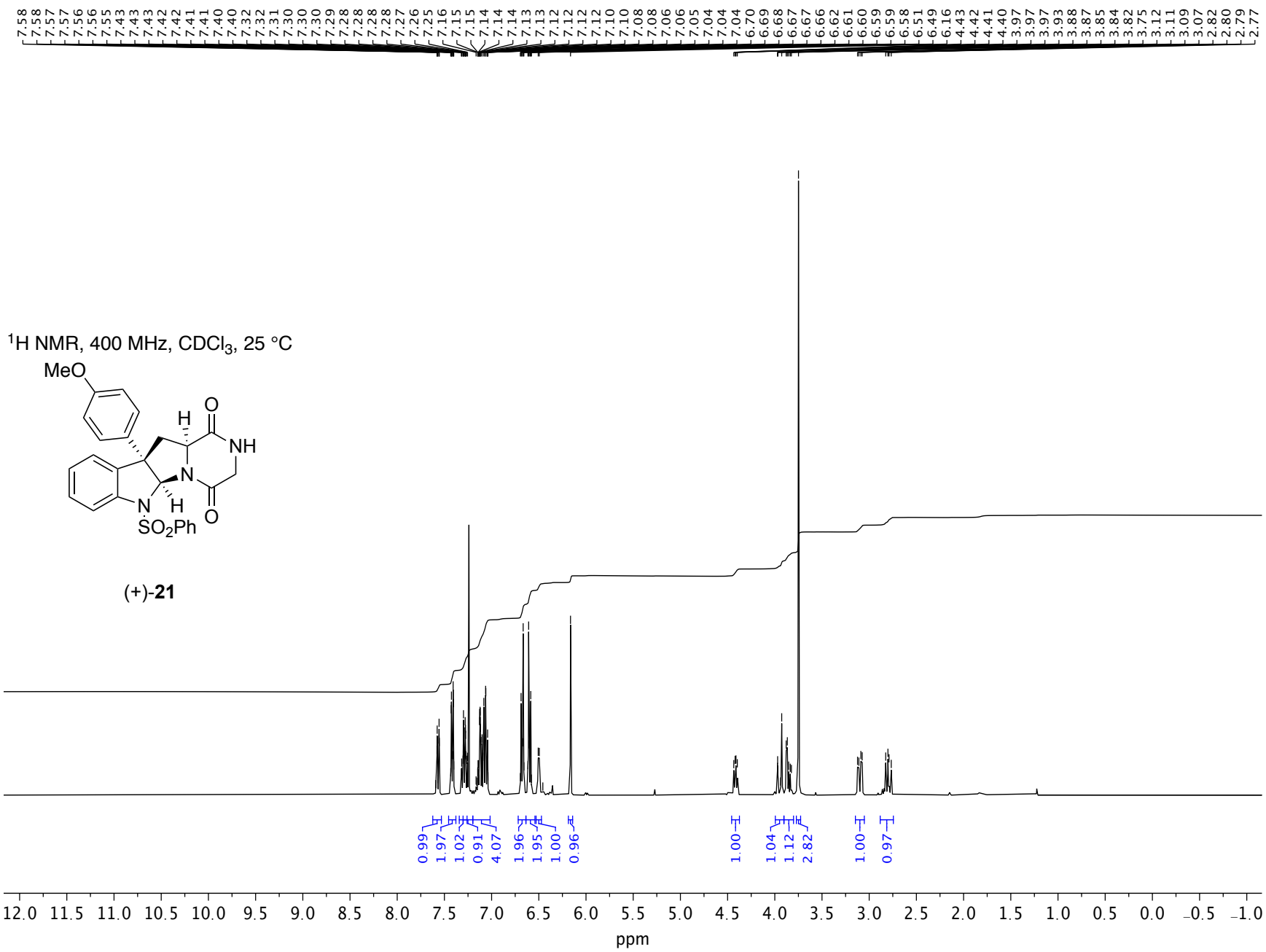

171.6
170.0
155.6
138.3
135.3
133.9
130.9
129.4
126.9
125.1
124.7
123.5
119.7
118.0
113.8
80.6
54.3
52.5
41.3
28.4
28.0
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
CO_2Me
O
NH
NHBoc
N
SO_2Ph
(–)-**S9**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 –5 –15
ppm

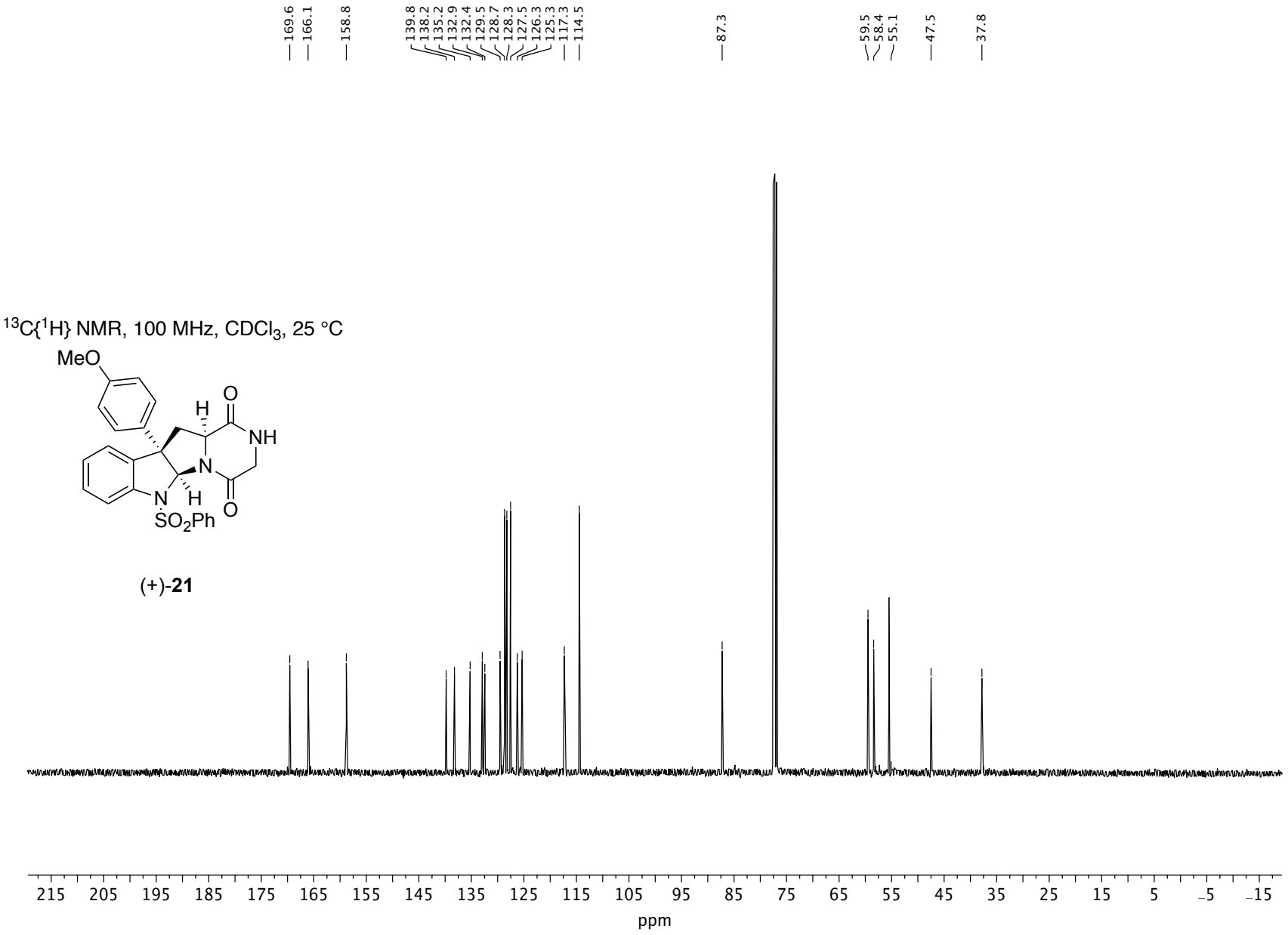

8.27
8.26
7.92
7.91
7.91
7.89
7.89
7.87
7.85
7.69
7.69
7.69
7.67
7.67
7.66
7.65
7.65
7.62
7.60
7.58
7.57
7.55
7.55
7.33
7.31
7.31
7.29
7.29
7.25
7.25
7.23
7.21
7.21
4.16
4.15
4.14
4.13
3.45
3.44
3.40
3.40
3.24
3.23
3.20
3.19
3.03
3.02
3.00
2.98
2.89
2.88
2.84
2.72
^{1}H NMR, 400 MHz, DMSO-d_6, 25 °C
O
H
N
N
H
O
N
SO_2Ph
(+)-**S10**
0.95
2.96
1.03
1.01
0.99
3.00
1.01
0.96
1.02
0.97
1.02
1.00
0.95
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm

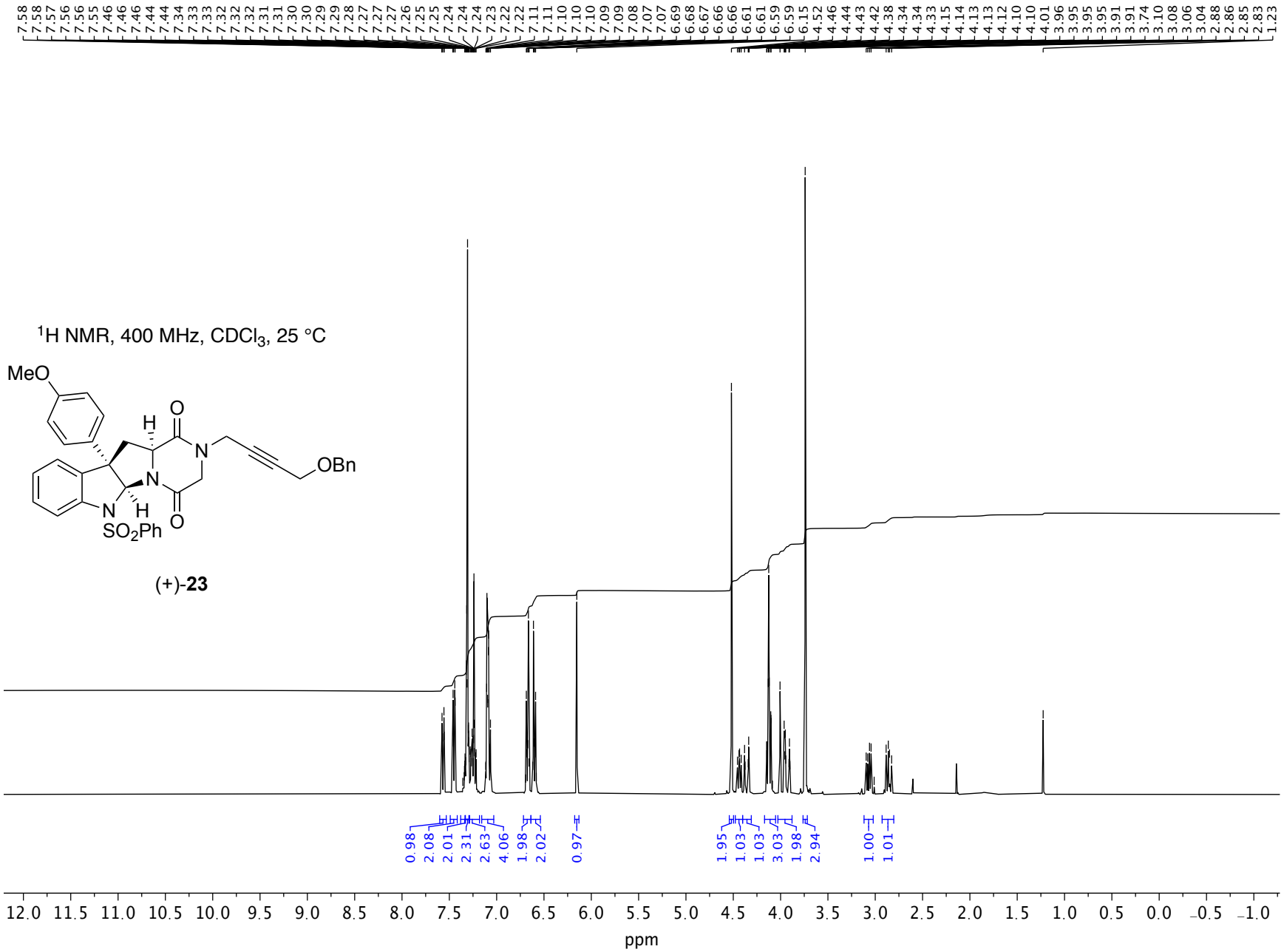

167.2
165.4
136.9
134.6
134.0
130.8
129.8
126.6
125.4
124.8
123.3
120.3
117.4
112.9
54.3
43.9
28.0
$^{13}C\{^{1}H\}$ NMR, 100 MHz, DMSO-d_6, 25 °C
O
H
N
N
H
O
N
SO_2Ph
(+)-**S10**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

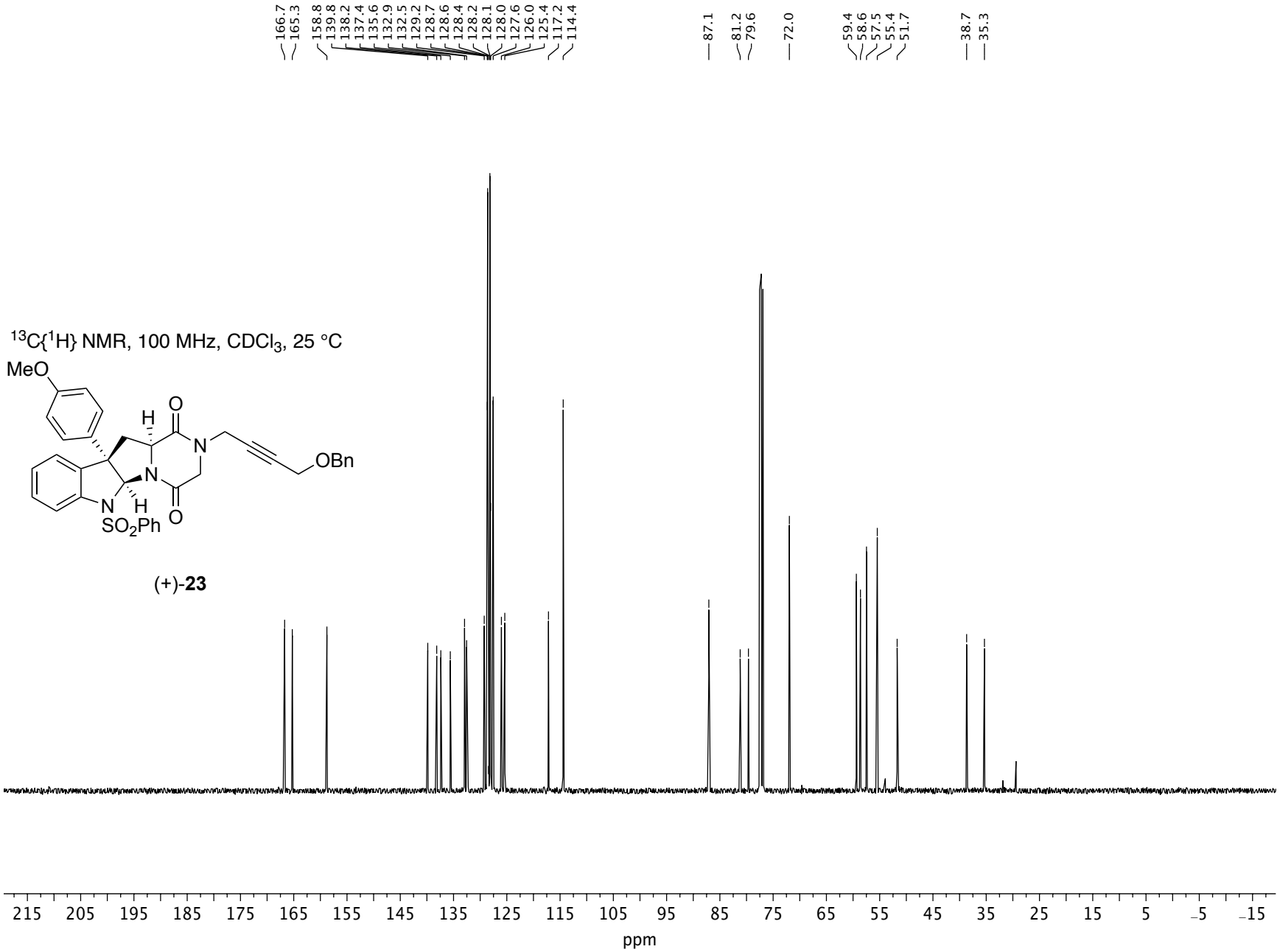

8.01
8.00
7.92
7.92
7.92
7.91
7.90
7.90
7.90
7.63
7.62
7.61
7.55
7.54
7.53
7.53
7.52
7.52
7.51
7.51
7.49
7.49
7.49
7.47
7.47
7.47
7.34
7.33
7.33
7.33
7.32
7.32
7.17
7.17
7.16
7.16
7.15
7.15
7.14
6.28
4.56
4.55
4.54
4.53
4.00
3.96
3.52
3.51
3.48
3.46
3.38
3.37
3.34
3.33
3.00
2.99
2.98
2.97
2.94
2.51
2.50
2.50
2.49
2.49
1H NMR, 400 MHz, DMSO-d6, 25 °C
Br
H
O
NH
N
N
H
O
SO2Ph
(+)-20
1.04
2.00
0.98
1.94
0.90
1.96
1.02
0.98
1.04
1.00
1.01
1.16
0.94
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

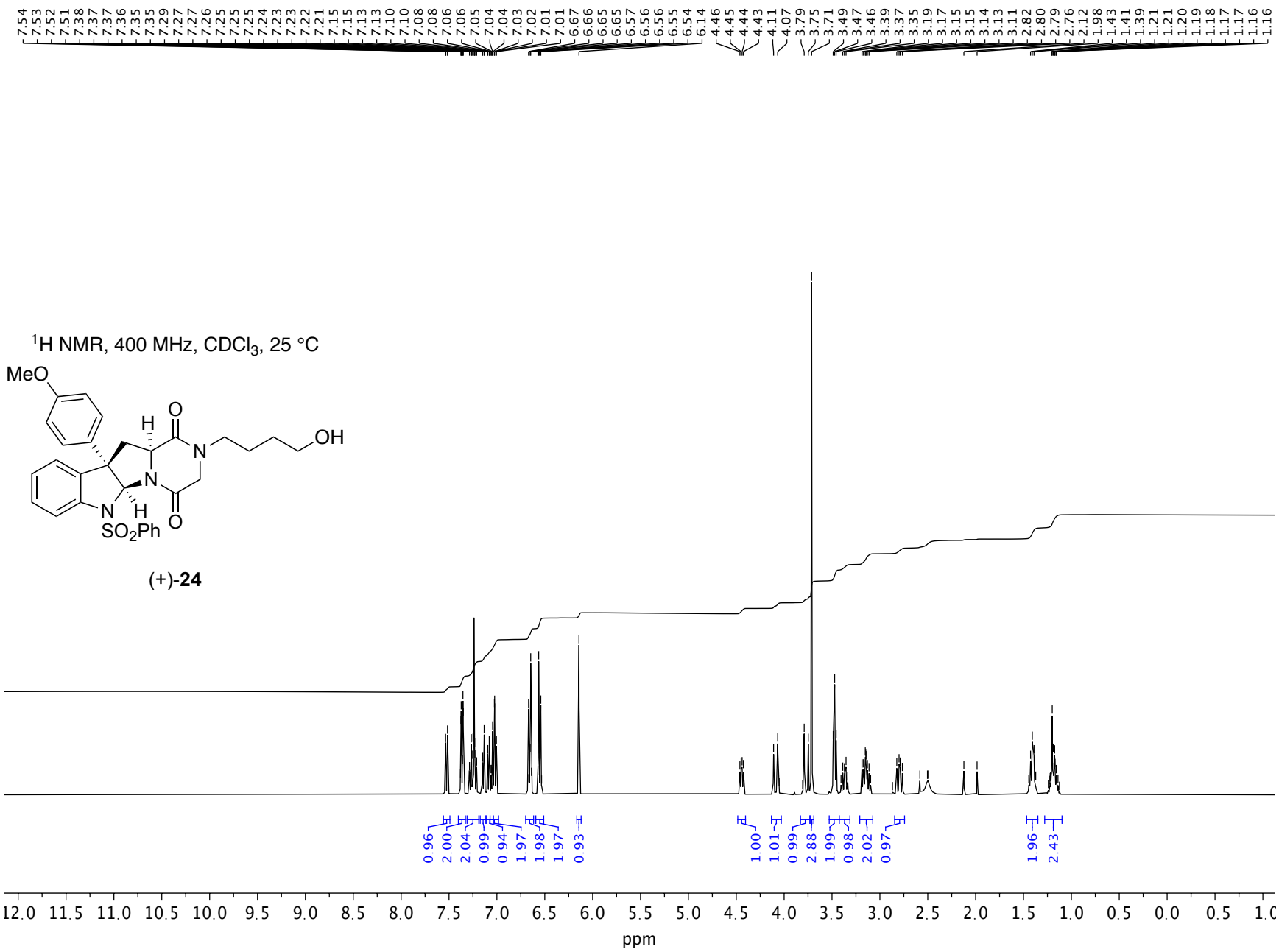

168.0
165.9
138.3
138.0
134.7
134.0
130.7
129.1
128.0
125.9
125.4
116.5
86.0
61.6
57.1
46.3
37.2
$^{13}C\{^{1}H\}$ NMR, 100 MHz, DMSO-d_6, 25 °C
Br
H
O
NH
N
N H
O
SO_2Ph
(+)-**20**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

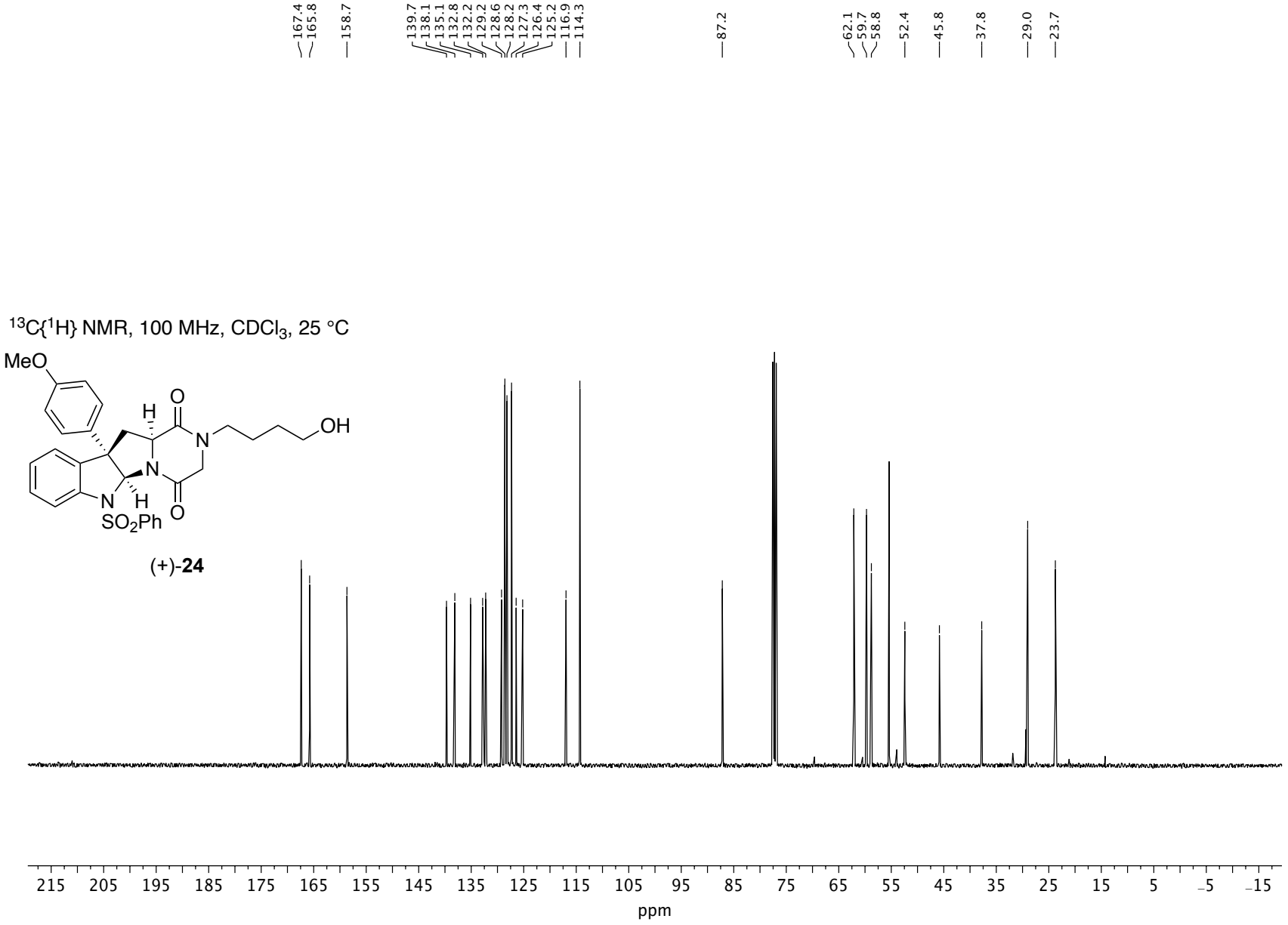

7.58 7.58 7.57 7.57 7.56 7.56 7.55 7.43 7.43 7.43 7.42 7.42 7.41 7.41 7.40 7.40 7.32 7.32 7.31 7.30 7.30 7.30 7.29 7.28 7.28 7.28 7.28 7.27 7.26 7.25 7.16 7.15 7.15 7.14 7.14 7.14 7.13 7.13 7.12 7.12 7.12 7.12 7.10 7.08 7.08 7.06 7.06 7.05 7.04 7.04 7.04 6.70 6.69 6.68 6.67 6.67 6.66 6.62 6.61 6.60 6.59 6.59 6.58 6.51 6.49 6.16 4.43 4.42 4.41 4.40 3.97 3.97 3.97 3.93 3.88 3.87 3.85 3.84 3.82 3.75 3.12 3.11 3.09 3.07 2.82 2.80 2.79 2.77
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
H
O
NH
N
N
H
O
SO_2Ph
(+)-**21**
0.99 1.97 1.02 0.91 4.07 1.96 1.95 1.00 0.96 1.00 1.04 1.12 2.82 1.00 0.97
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

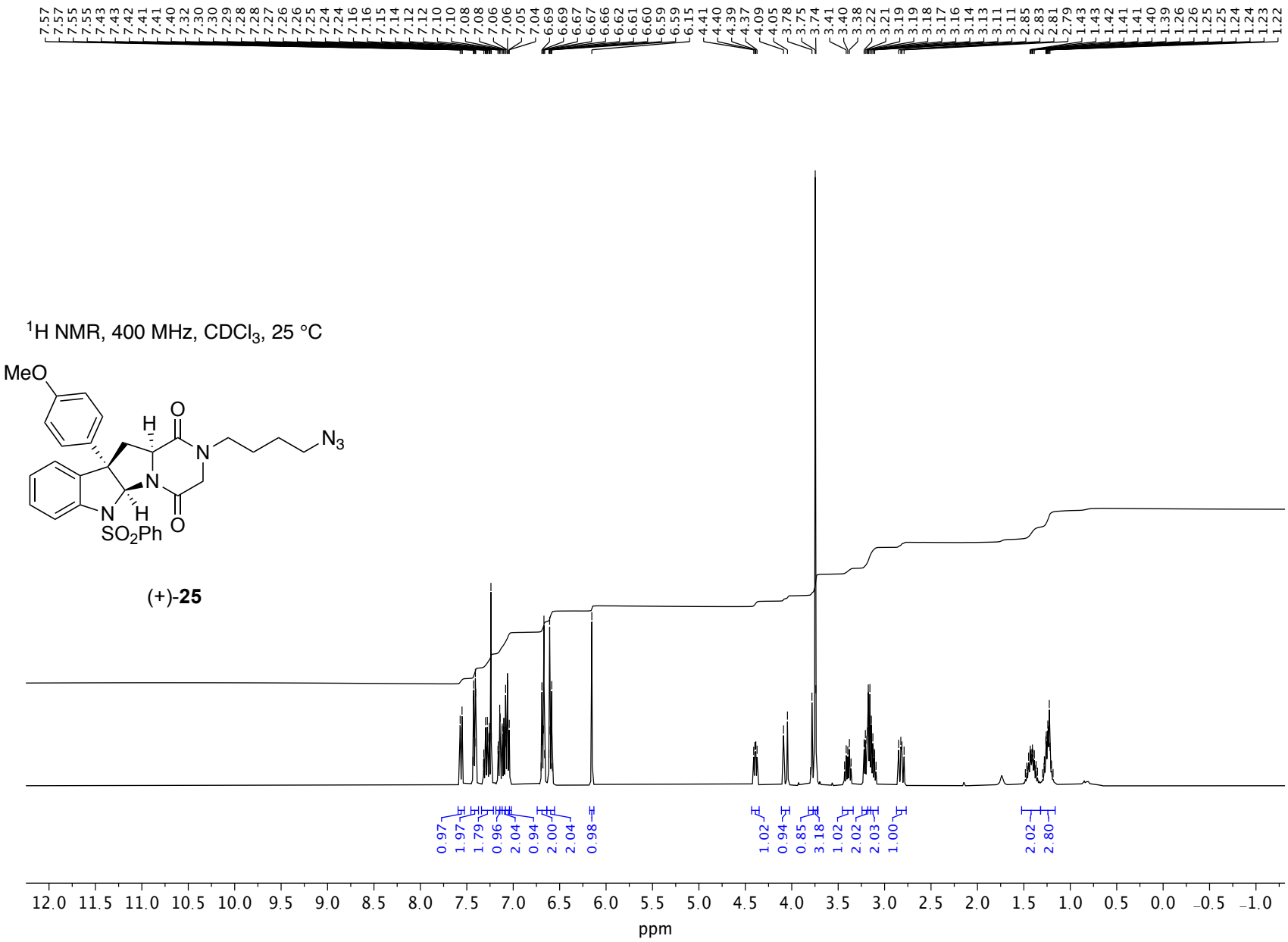

169.6
166.1
158.8
139.8
138.2
135.2
132.9
132.4
129.5
128.7
128.3
127.5
126.3
125.3
117.3
114.5
87.3
59.5
58.4
55.1
47.5
37.8
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
H
O
NH
N
N
H
O
SO_2Ph
(+)-**21**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

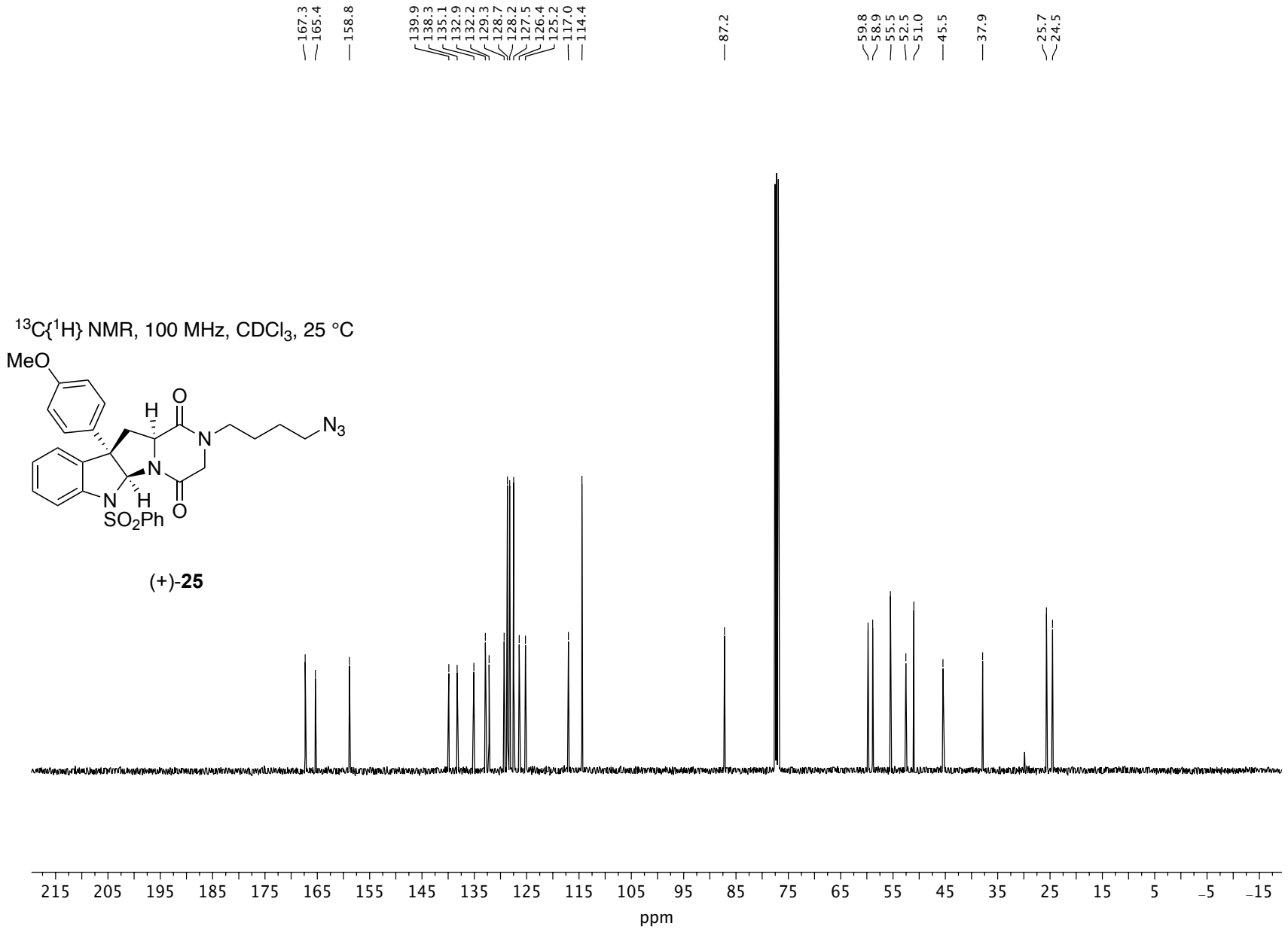

7.58 7.58 7.57 7.56 7.56 7.55 7.46 7.46 7.44 7.44 7.34 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.27 7.27 7.26 7.25 7.25 7.24 7.24 7.24 7.23 7.22 7.22 7.11 7.11 7.10 7.10 7.10 7.09 7.09 7.08 7.07 7.07 6.69 6.68 6.67 6.66 6.66 6.61 6.61 6.59 6.59 6.15 4.52 4.46 4.44 4.43 4.42 4.38 4.34 4.34 4.33 4.15 4.14 4.13 4.13 4.12 4.10 4.10 4.01 3.96 3.95 3.95 3.95 3.91 3.91 3.74 3.10 3.08 3.06 3.04 2.88 2.86 2.85 2.83 1.23
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
O
H
N
OBn
N
N
H
O
SO_2Ph
(+)-**23**
0.98 2.08 2.01 2.31 2.63 4.06 1.98 2.02 0.97 1.95 1.03 1.03 3.03 1.98 2.94 1.00 1.01
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

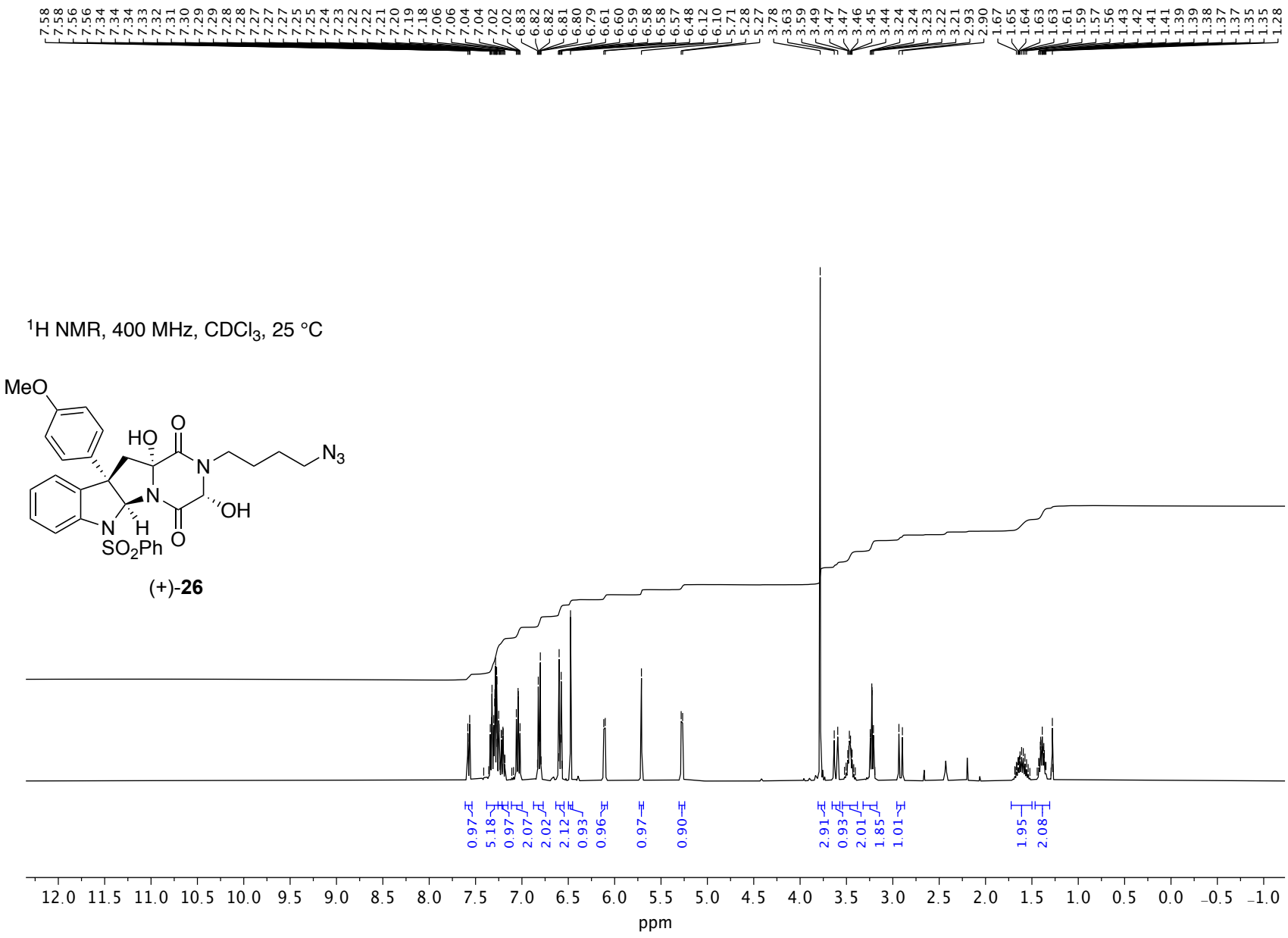

166.7
165.3
158.8
139.8
138.2
137.4
135.6
132.9
132.5
129.2
128.7
128.6
128.4
128.2
128.1
128.0
127.6
126.0
125.4
117.2
114.4
87.1
81.2
79.6
72.0
59.4
58.6
57.5
55.4
51.7
38.7
35.3
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
H
O
N
OBn
N
N
H
SO2Ph
O
(+)-23
215
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
−5
−15
ppm

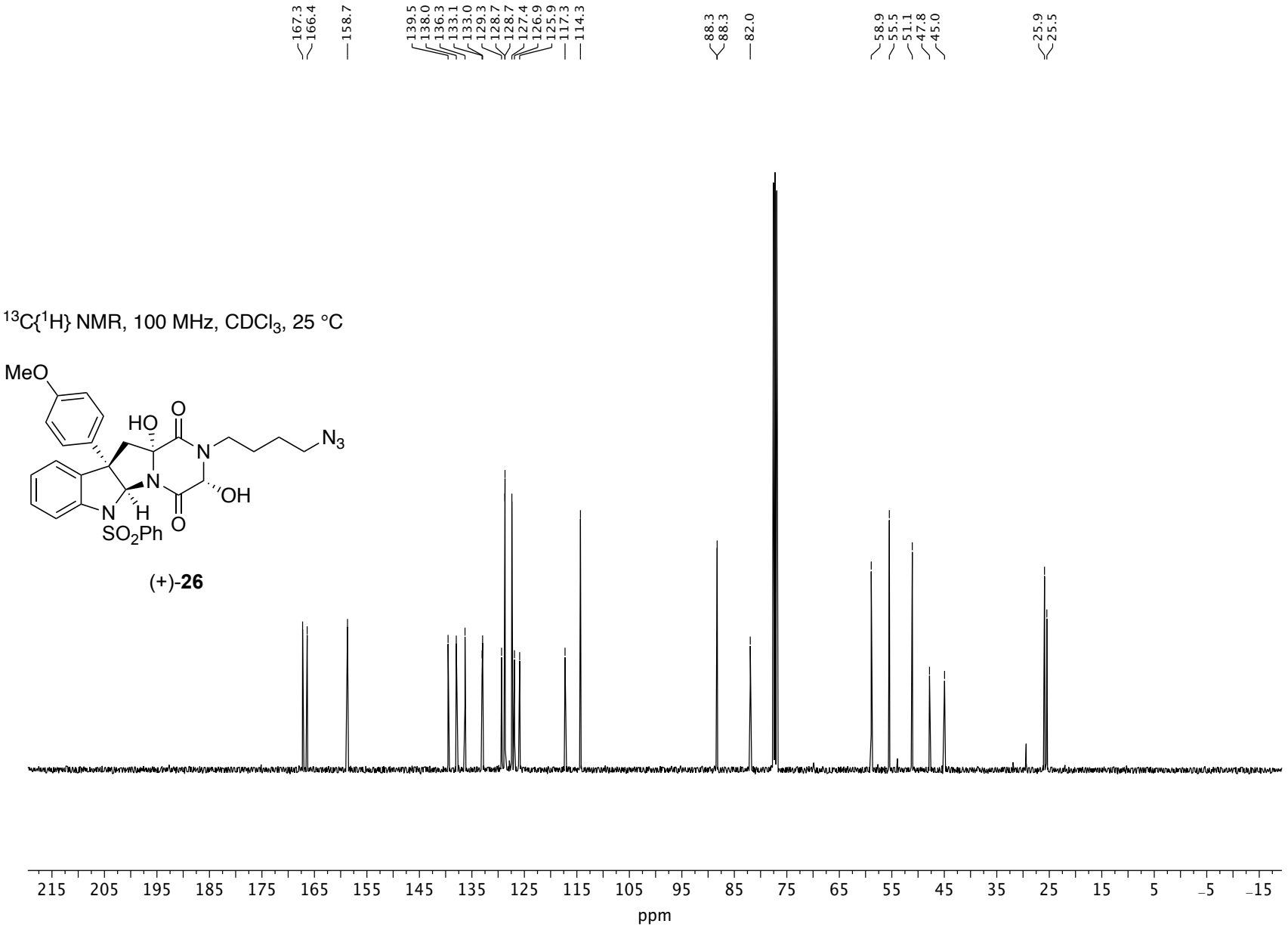

7.54 7.53 7.52 7.51 7.38 7.37 7.37 7.36 7.35 7.35 7.29 7.27 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.23 7.22 7.21 7.15 7.15 7.13 7.13 7.10 7.10 7.08 7.08 7.06 7.06 7.05 7.04 7.04 7.03 7.02 7.01 7.01 6.67 6.66 6.65 6.65 6.57 6.56 6.56 6.55 6.54 6.14 4.46 4.45 4.44 4.43 4.11 4.07 3.79 3.75 3.71 3.49 3.47 3.46 3.39 3.37 3.35 3.19 3.17 3.15 3.15 3.14 3.13 3.11 2.82 2.80 2.79 2.76 2.12 1.98 1.43 1.41 1.39 1.21 1.21 1.20 1.19 1.18 1.17 1.17 1.16 1.16
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
H
O
N
OH
N
N
H
O
SO_2Ph
(+)-**24**
0.96 2.00 2.04 0.99 0.94 1.97 1.98 1.97 0.93 1.00 1.01 0.99 2.88 1.99 0.98 2.02 0.97 1.96 2.43
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

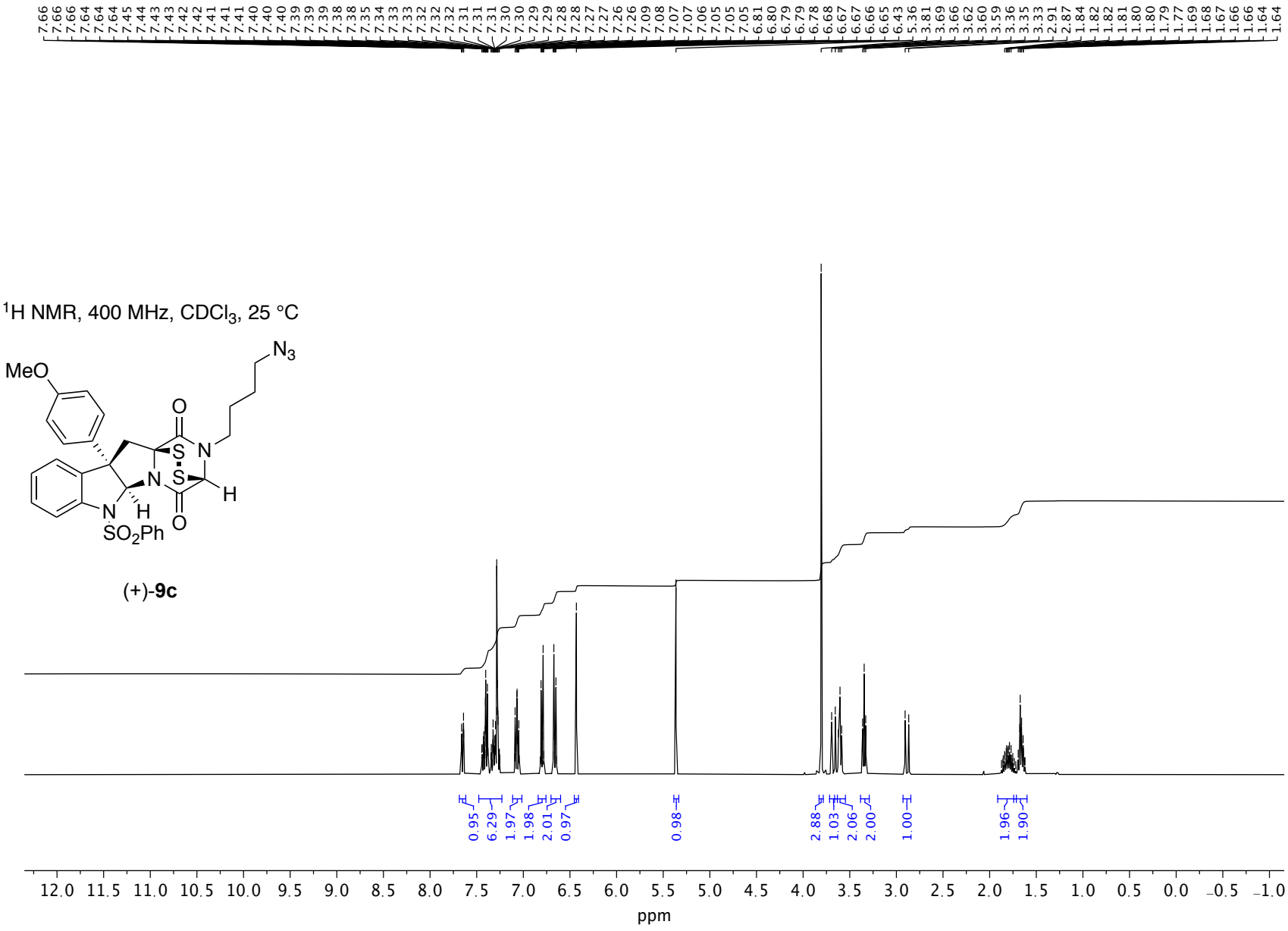

167.4
165.8
158.7
139.7
138.1
135.1
132.8
132.2
129.2
128.6
128.2
127.3
126.4
125.2
116.9
114.3
87.2
62.1
59.7
58.8
52.4
45.8
37.8
29.0
23.7
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
H
O
N
OH
N
N
H
O
SO_2Ph
(+)-**24**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

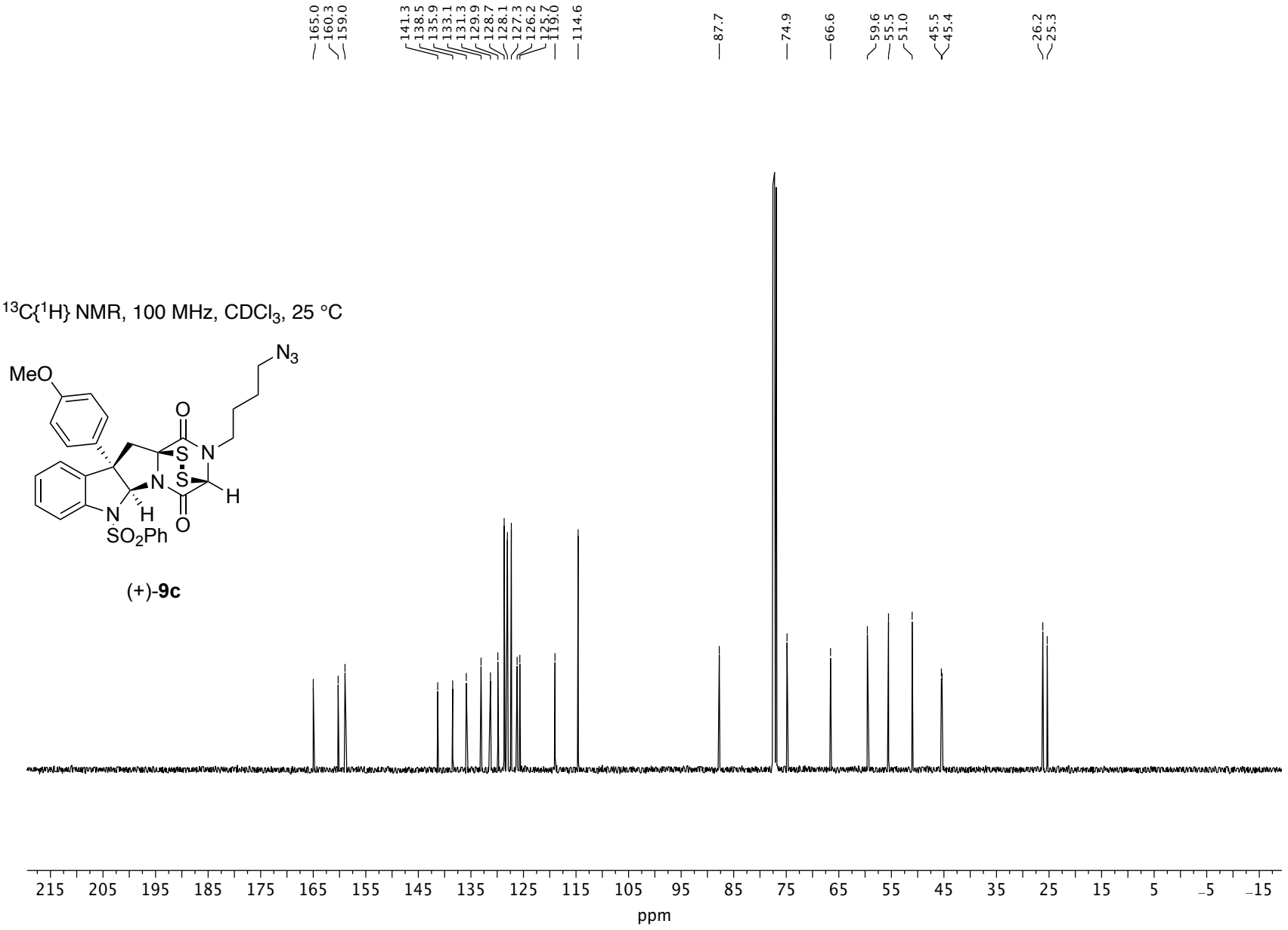

7.57 7.57 7.55 7.55 7.43 7.42 7.41 7.41 7.40 7.32 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.26 7.25 7.24 7.24 7.16 7.15 7.14 7.12 7.12 7.10 7.08 7.08 7.06 7.06 7.05 7.04 6.69 6.69 6.67 6.67 6.66 6.62 6.61 6.60 6.59 6.59 6.15 4.41 4.40 4.39 4.37 4.09 4.05 3.78 3.75 3.74 3.41 3.40 3.38 3.22 3.21 3.19 3.19 3.18 3.17 3.16 3.14 3.13 3.11 3.11 2.85 2.83 2.81 2.79 1.43 1.43 1.42 1.41 1.41 1.40 1.39 1.26 1.26 1.25 1.25 1.24 1.24 1.23 1.22
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
H
O
N
N_3
N
N
H
O
SO_2Ph
(+)-**25**
0.97 1.97 1.79 0.96 2.04 0.94 2.00 2.04 0.98
1.02 0.94 0.85 3.18 1.02 2.02 2.03 1.00
2.02 2.80
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

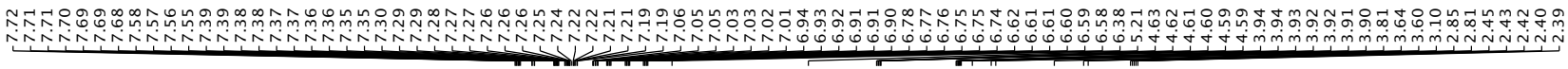

167.3
165.4
158.8
139.9
138.3
135.1
132.9
132.2
129.3
128.7
128.2
127.5
126.4
125.2
117.0
114.4
87.2
59.8
58.9
55.5
52.5
51.0
45.5
37.9
25.7
24.5
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
H
O
N
N3
N
N H
SO2Ph
O
(+)-25
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.58 7.58 7.56 7.56 7.34 7.34 7.33 7.32 7.31 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.27 7.25 7.25 7.24 7.23 7.22 7.22 7.21 7.20 7.19 7.18 7.06 7.06 7.04 7.04 7.02 7.02 6.83 6.82 6.82 6.81 6.80 6.79 6.61 6.60 6.59 6.58 6.58 6.57 6.48 6.12 6.10 5.71 5.28 5.27 3.78 3.63 3.59 3.49 3.47 3.47 3.46 3.45 3.44 3.24 3.24 3.23 3.22 3.21 2.93 2.90 1.67 1.65 1.64 1.63 1.63 1.61 1.59 1.57 1.56 1.43 1.42 1.41 1.41 1.39 1.39 1.38 1.37 1.37 1.35 1.35 1.28
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
HO
O
N
N_3
N
OH
N
H
O
SO_2Ph
(+)-**26**
0.97 5.18 0.97 2.07 2.02 2.12 0.93 0.96 0.97 0.90 2.91 0.93 2.01 1.85 1.01 1.95 2.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
ppm

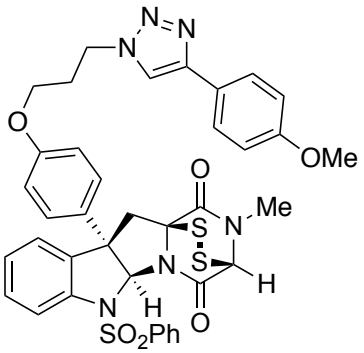

167.3
166.4
158.7
139.5
138.0
136.3
133.1
133.0
129.3
128.7
128.7
127.4
126.9
125.9
117.3
114.3
88.3
88.3
82.0
58.9
55.5
51.1
47.8
45.0
25.9
25.5
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
HO
O
N
N_3
N
OH
N
H
O
SO_2Ph
(+)-**26**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.66 7.66 7.66 7.64 7.64 7.45 7.44 7.43 7.43 7.42 7.42 7.41 7.41 7.41 7.40 7.40 7.40 7.39 7.39 7.39 7.38 7.38 7.35 7.34 7.33 7.33 7.32 7.32 7.32 7.31 7.31 7.31 7.30 7.30 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.26 7.26 7.09 7.08 7.07 7.07 7.06 7.05 7.05 7.05 6.81 6.80 6.79 6.79 6.78 6.68 6.67 6.67 6.66 6.65 6.43 5.36 3.81 3.69 3.66 3.62 3.60 3.59 3.36 3.35 3.33 2.91 2.87 1.84 1.82 1.82 1.81 1.80 1.80 1.79 1.77 1.69 1.68 1.67 1.66 1.66 1.64 1.64
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
N_3
O
S
N
N
S
H
N
H
O
SO_2Ph
(+)-**9c**
0.95
6.29
1.97
1.98
2.01
0.97
0.98
2.88
1.03
2.06
2.00
1.00
1.96
1.90
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

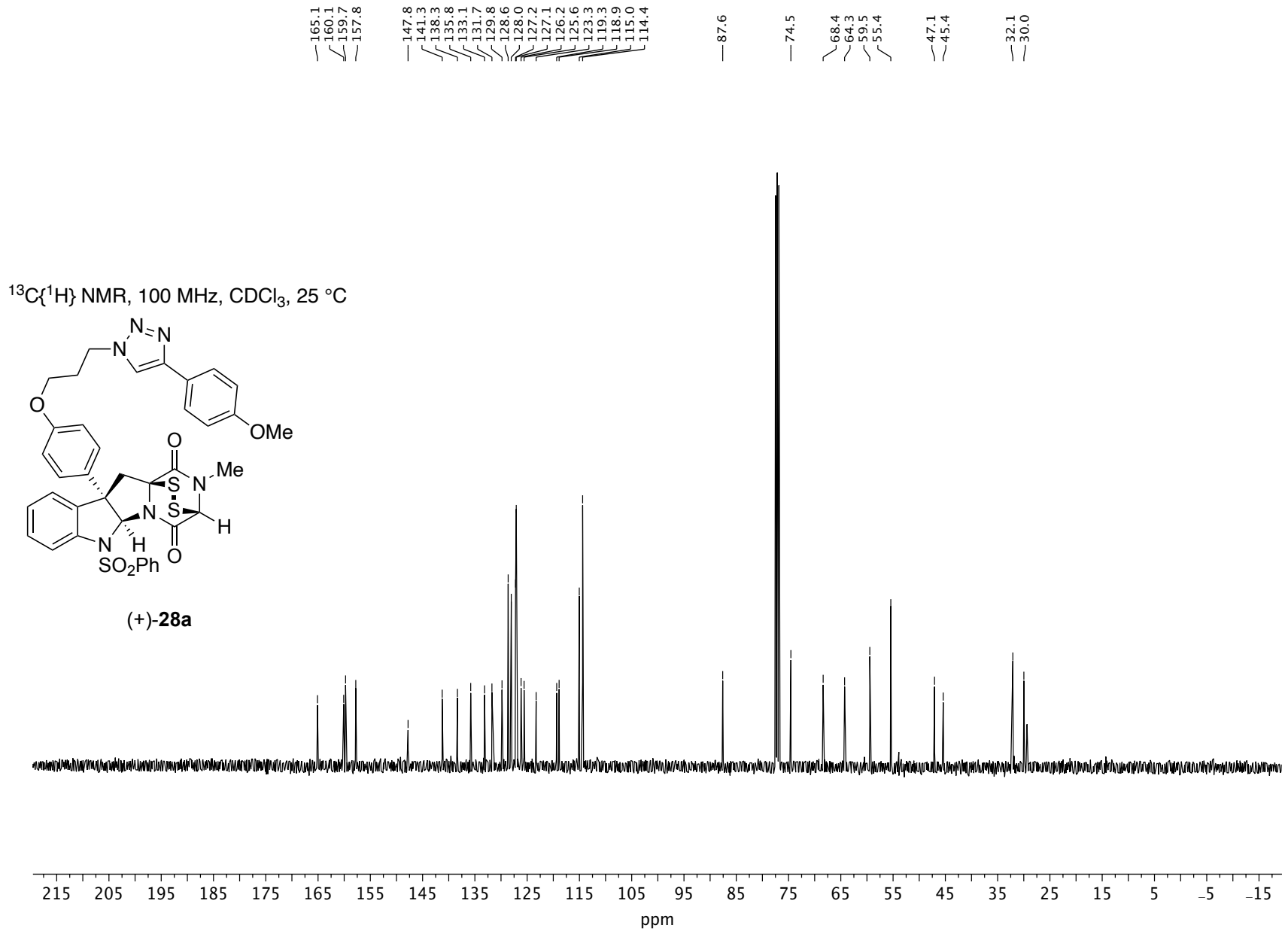

165.0
160.3
159.0
141.3
138.5
135.9
133.1
131.3
129.9
128.7
128.1
127.3
126.2
114.6
87.7
74.9
66.6
59.6
55.5
51.0
45.5
45.4
26.2
25.3
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
N_3
O
S
N
N
S
H
N
H
O
SO_2Ph
(+)-**9c**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 –5 –15
ppm



^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



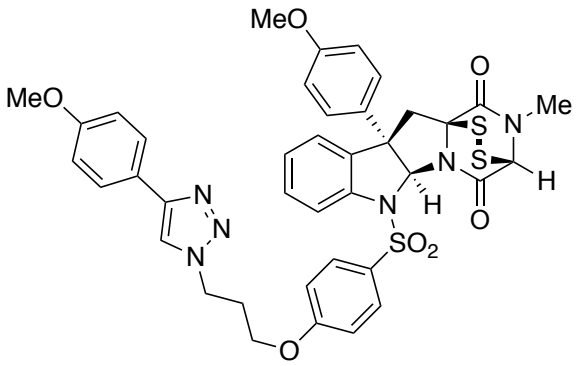
(+)-**28a**


165.1
160.1
159.7
157.8
147.8
141.3
138.3
135.8
133.1
131.7
129.8
128.6
128.0
127.2
127.1
126.2
125.6
123.3
119.3
118.9
115.0
114.4
87.6
74.5
68.4
64.3
59.5
55.4
47.1
45.4
32.1
30.0
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
OMe
Me
H
SO2Ph
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

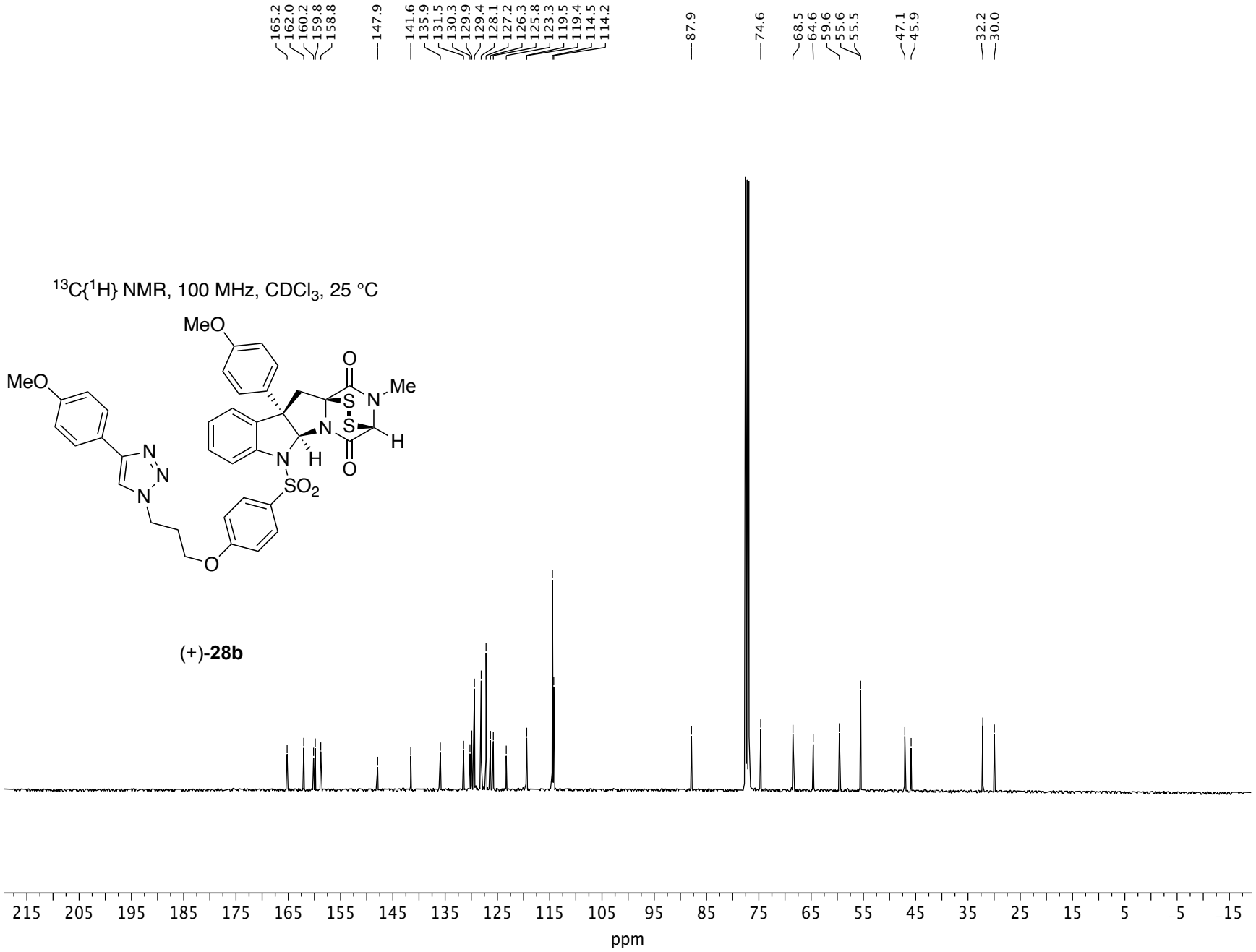
(+)-**28a**

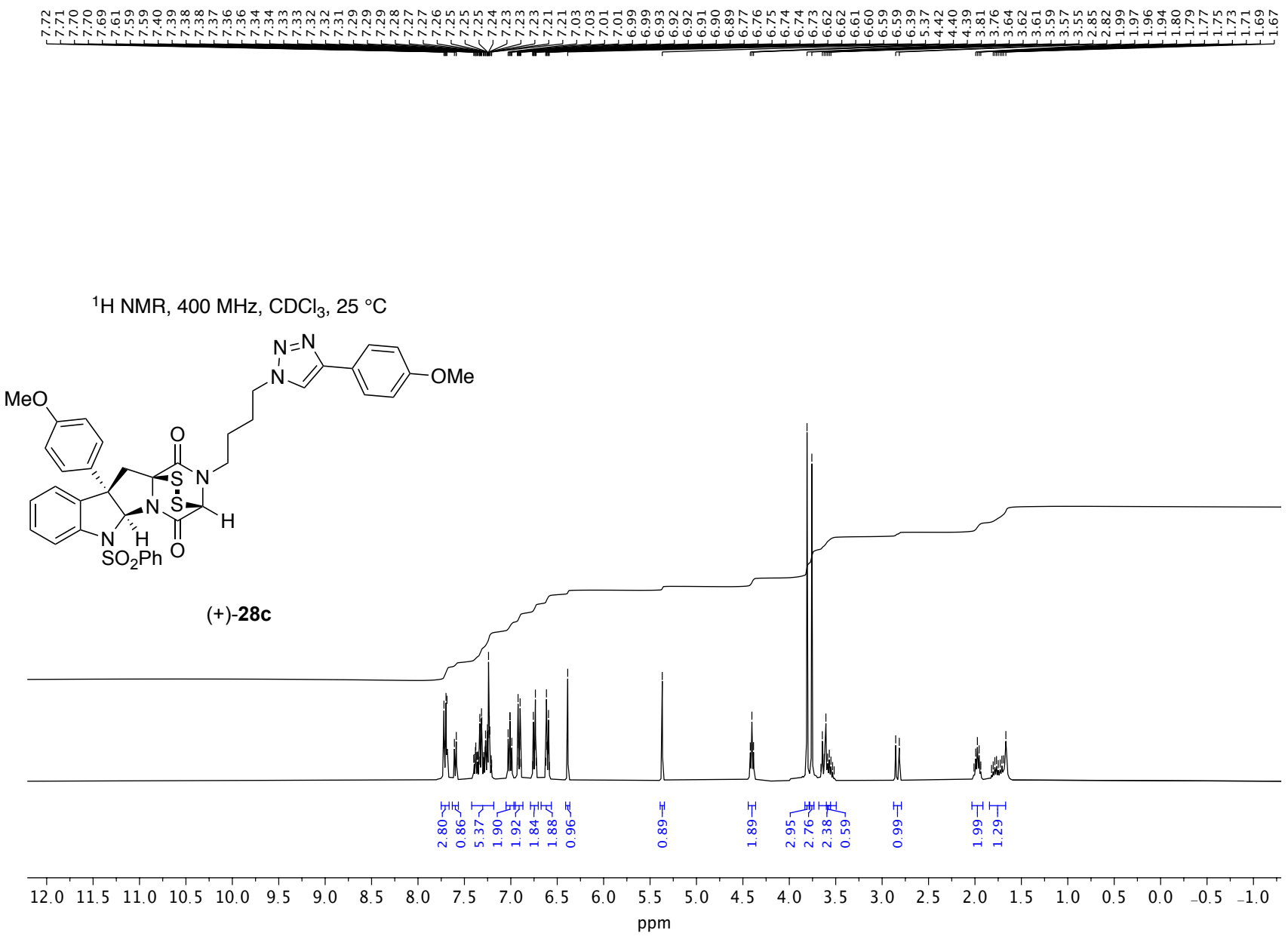
7.70 7.69 7.62 7.60 7.40 7.39 7.38 7.38 7.36 7.36 7.28 7.28 7.26 7.26 7.24 7.24 7.23 7.23 7.21 7.20 7.20 7.19 7.18 7.17 6.92 6.90 6.73 6.73 6.71 6.71 6.70 6.61 6.60 6.60 6.58 6.58 6.39 6.37 6.37 6.36 6.31 5.22 4.58 4.57 4.55 3.91 3.89 3.89 3.88 3.82 3.81 3.73 3.59 3.55 3.09 2.83 2.79 2.43 2.42 2.40 2.39 2.37

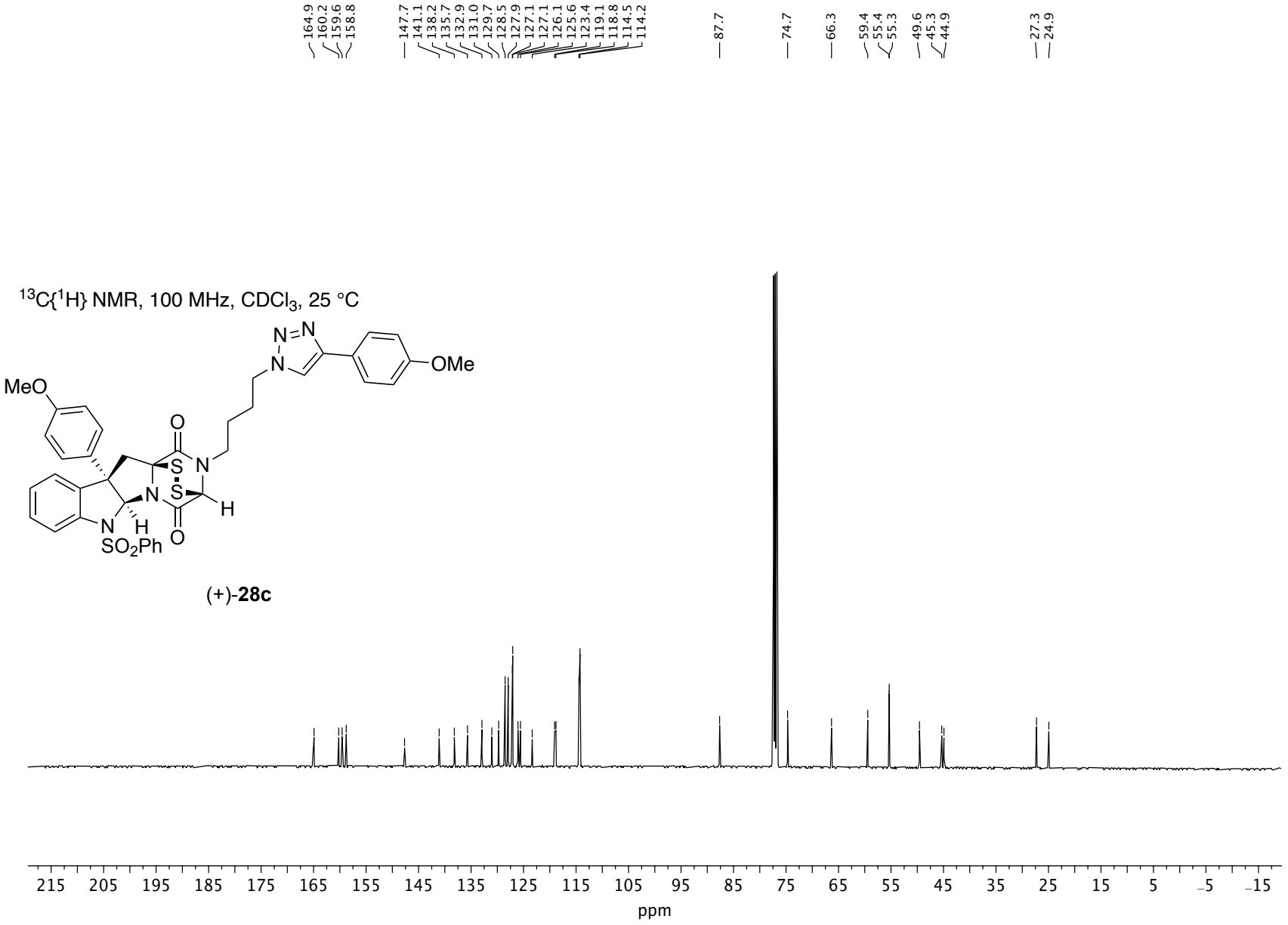
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

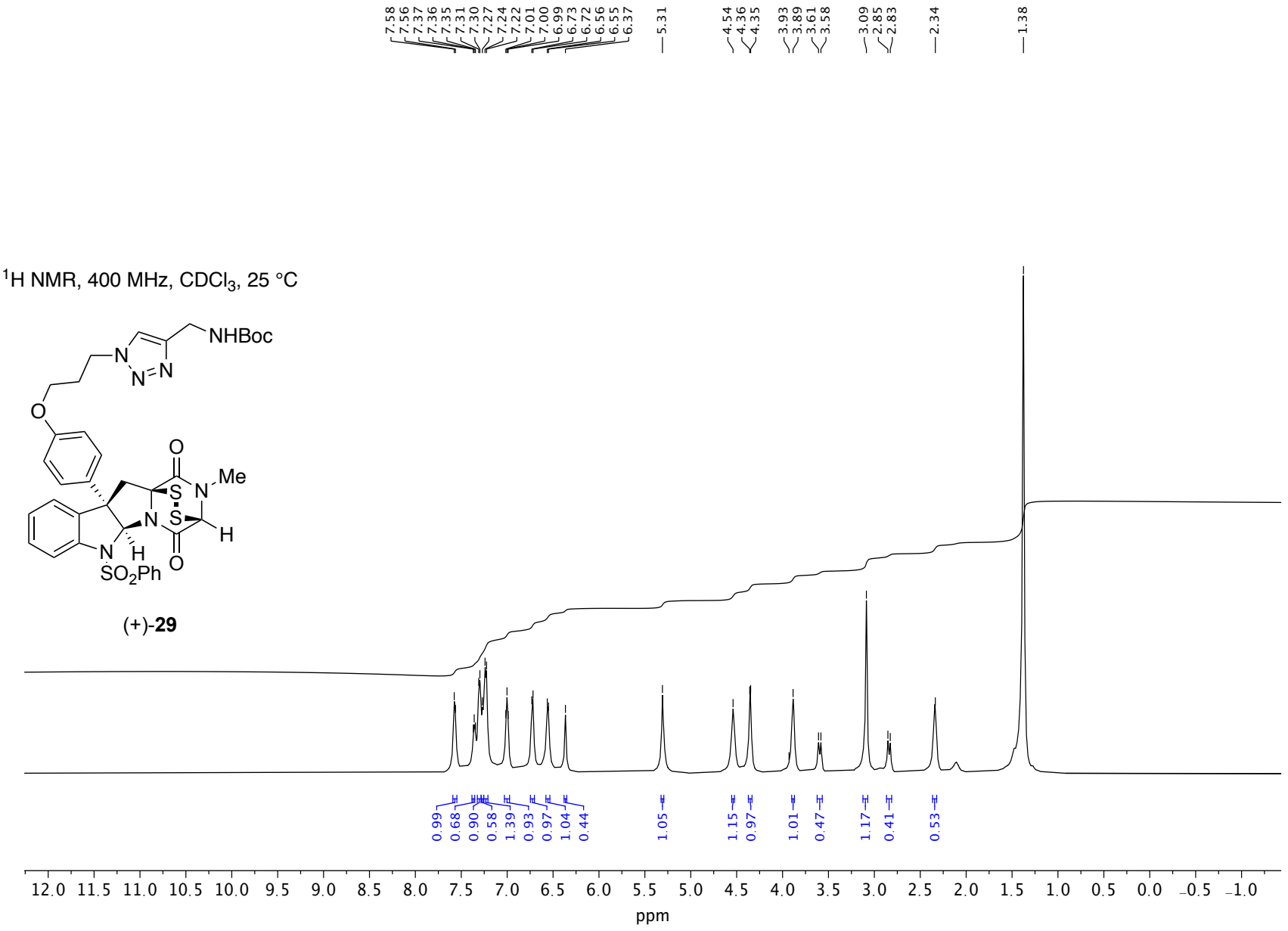


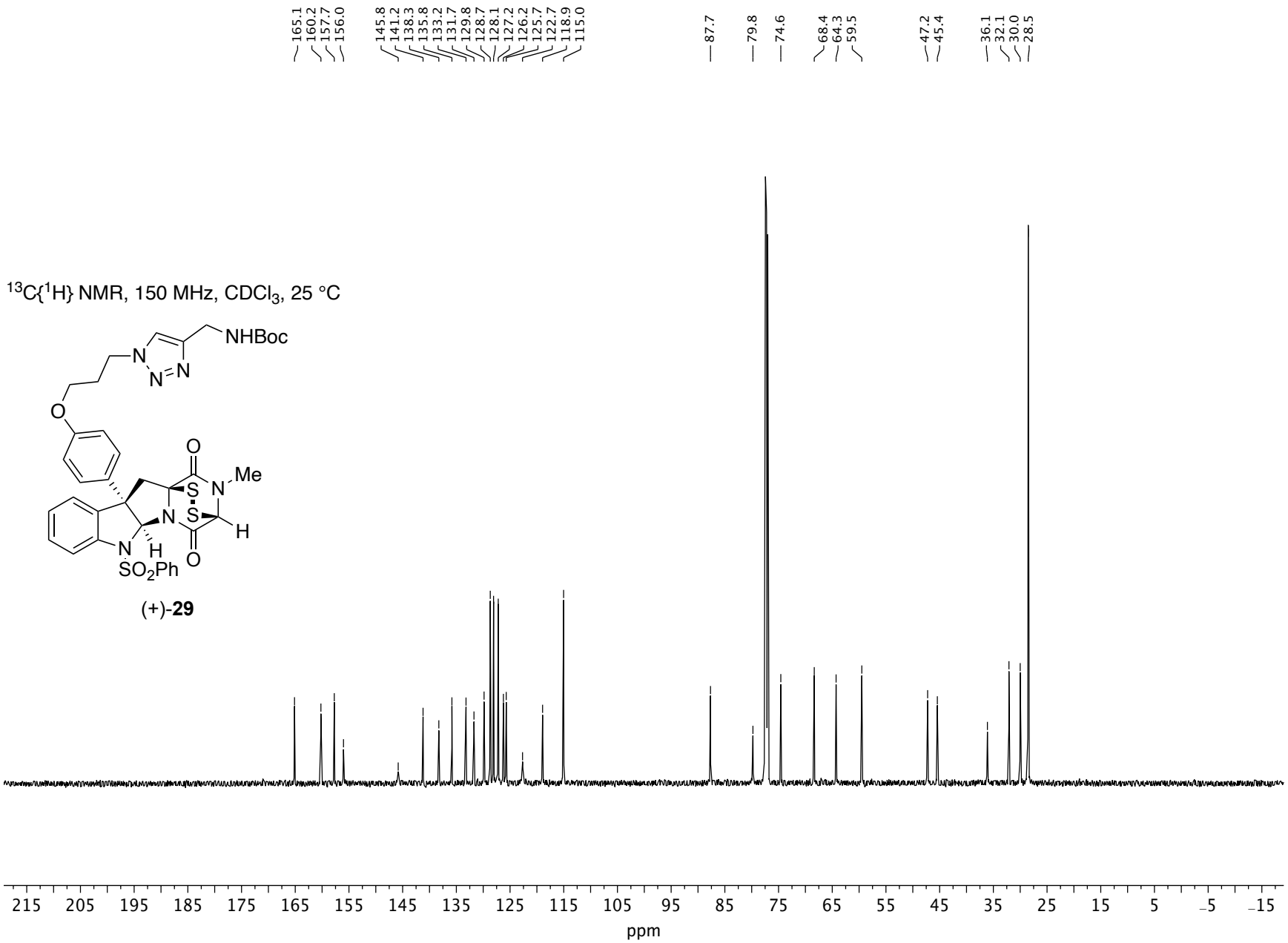
(+)-**28b**

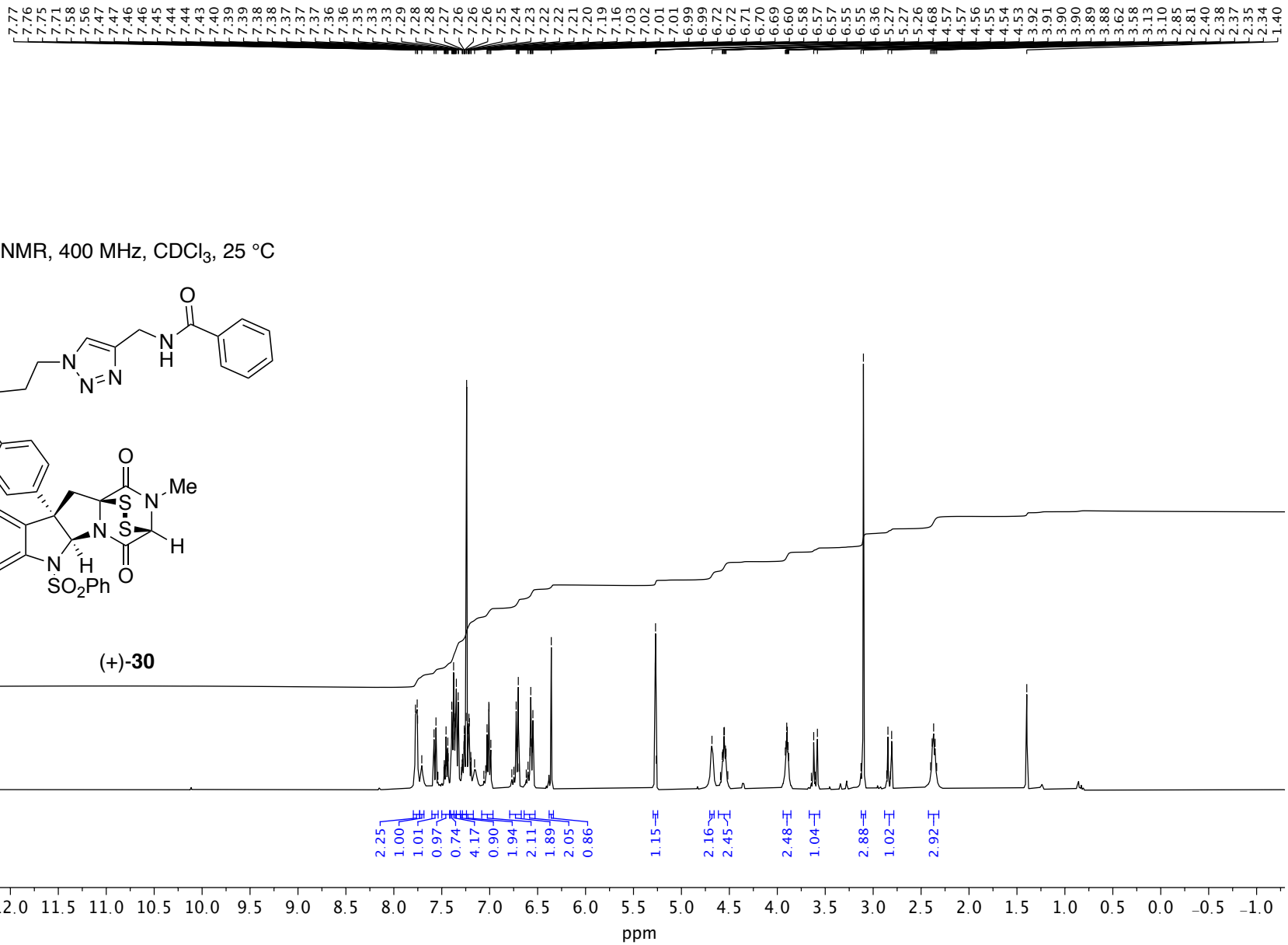

165.2
162.0
160.2
159.8
158.8
147.9
141.6
135.9
131.5
130.3
129.9
129.4
128.1
127.2
126.3
125.8
123.3
119.5
119.4
114.5
114.2
87.9
74.6
68.5
64.6
59.6
55.6
55.5
47.1
45.9
32.2
30.0
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
MeO
O
S
N
Me
N
S
H
N
H
O
N
N
N
SO_2
O
(+)-**28b**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

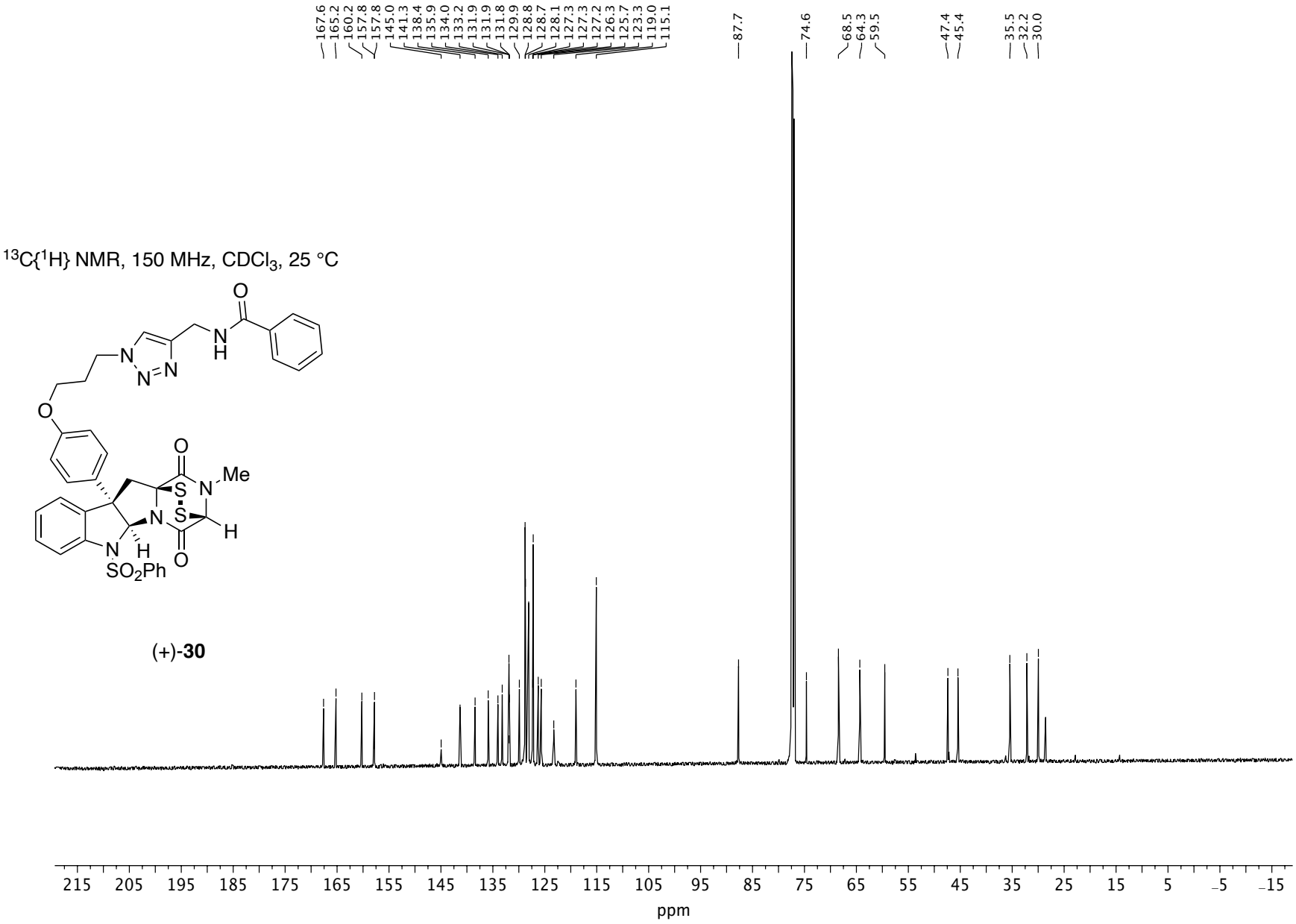

7.72 7.71 7.70 7.70 7.69 7.61 7.59 7.59 7.40 7.39 7.38 7.38 7.37 7.36 7.36 7.34 7.34 7.33 7.33 7.32 7.31 7.29 7.29 7.29 7.28 7.27 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.23 7.23 7.21 7.21 7.03 7.03 7.01 7.01 6.99 6.99 6.93 6.92 6.92 6.91 6.90 6.89 6.77 6.76 6.75 6.74 6.74 6.73 6.62 6.62 6.61 6.60 6.59 6.59 6.39 5.37 4.42 4.40 4.39 3.81 3.76 3.64 3.62 3.61 3.59 3.57 3.55 2.85 2.82 1.99 1.97 1.96 1.94 1.80 1.79 1.77 1.75 1.73 1.71 1.69 1.67
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
OMe
N=N
N
O
S
N
N
S
H
N
H
O
SO_2Ph
(+)-**28c**
2.80 0.86 5.37 1.90 1.92 1.84 1.88 0.96 0.89 1.89 2.95 2.76 2.38 0.59 0.99 1.99 1.29
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

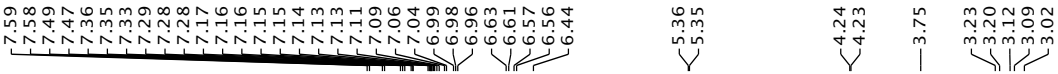

164.9
160.2
159.6
158.8
147.7
141.1
138.2
135.7
132.9
131.0
129.7
128.5
127.9
127.1
127.1
126.1
125.6
123.4
119.1
118.8
114.5
114.2
87.7
74.7
66.3
59.4
55.4
55.3
49.6
45.3
44.9
27.3
24.9
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
OMe
SO_2Ph
(+)-**28c**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.58
7.56
7.37
7.36
7.35
7.31
7.30
7.27
7.24
7.22
7.01
7.00
6.99
6.73
6.72
6.56
6.55
6.37
5.31
4.54
4.36
4.35
3.93
3.89
3.61
3.58
3.09
2.85
2.83
2.34
1.38
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
NHBoc
Me
H
SO_2Ph
(+)-29
0.99
0.68
0.90
0.58
1.39
0.93
0.97
1.04
0.44
1.05
1.15
0.97
1.01
0.47
1.17
0.41
0.53
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

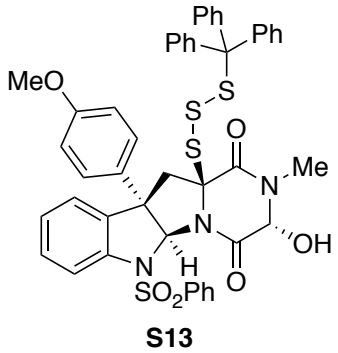

165.1
160.2
157.7
156.0
145.8
141.2
138.3
135.8
133.2
131.7
129.8
128.7
128.1
127.2
126.2
125.7
122.7
118.9
115.0
87.7
79.8
74.6
68.4
64.3
59.5
47.2
45.4
36.1
32.1
30.0
28.5
$^{13}C\{^{1}H\}$ NMR, 150 MHz, $CDCl_3$, 25 °C
NHBoc
Me
H
SO_2Ph
(+)-**29**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm


7.77 7.76 7.75 7.71 7.58 7.56 7.47 7.47 7.46 7.46 7.45 7.44 7.44 7.43 7.40 7.39 7.39 7.38 7.38 7.37 7.37 7.37 7.36 7.36 7.35 7.33 7.33 7.29 7.28 7.28 7.27 7.26 7.26 7.26 7.25 7.24 7.23 7.22 7.22 7.21 7.20 7.19 7.16 7.03 7.02 7.01 7.01 6.99 6.99 6.72 6.72 6.71 6.70 6.69 6.60 6.58 6.57 6.57 6.55 6.55 6.36 5.27 5.27 5.26 4.68 4.57 4.57 4.56 4.55 4.54 4.53 3.92 3.91 3.90 3.90 3.89 3.88 3.62 3.58 3.13 3.10 2.85 2.81 2.40 2.38 2.37 2.35 2.34 1.40
1H NMR, 400 MHz, CDCl3, 25 °C
(+)-30
2.25 1.00 1.01 0.97 0.74 4.17 0.90 1.94 2.11 1.89 2.05 0.86 1.15 2.16 2.45 2.48 1.04 2.88 1.02 2.92
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm


167.6
165.2
160.2
157.8
157.8
145.0
141.3
138.4
135.9
134.0
133.2
131.9
131.9
131.8
129.9
128.8
128.7
128.1
127.3
127.3
127.2
126.3
125.7
123.3
119.0
115.1
87.7
74.6
68.5
64.3
59.5
47.4
45.4
35.5
32.2
30.0
13C{1H} NMR, 150 MHz, CDCl3, 25 °C
O
N
H
N
N=N
O
O
N
Me
S
N
S
H
N
H
SO2Ph
O
(+)-30
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

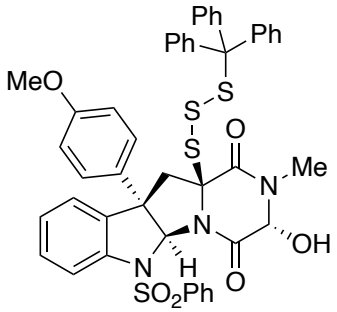


^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C

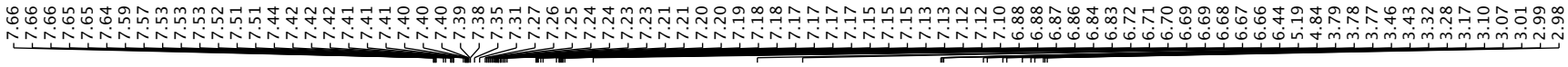


S13

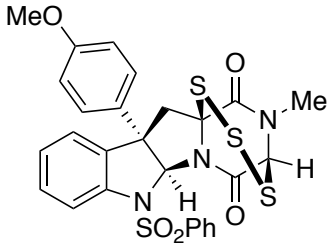
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C



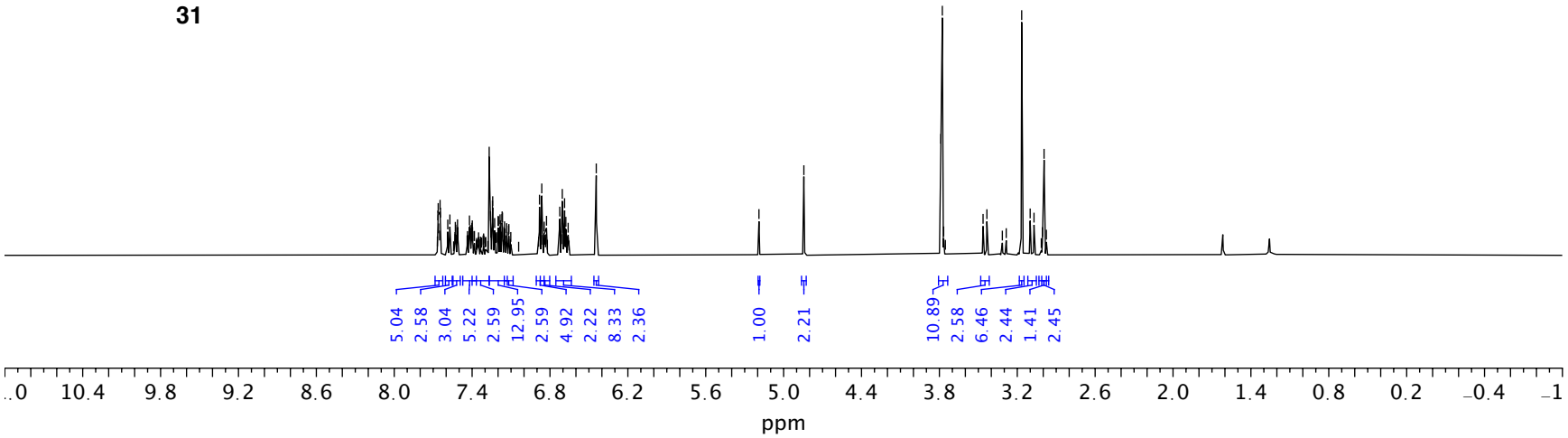
S13

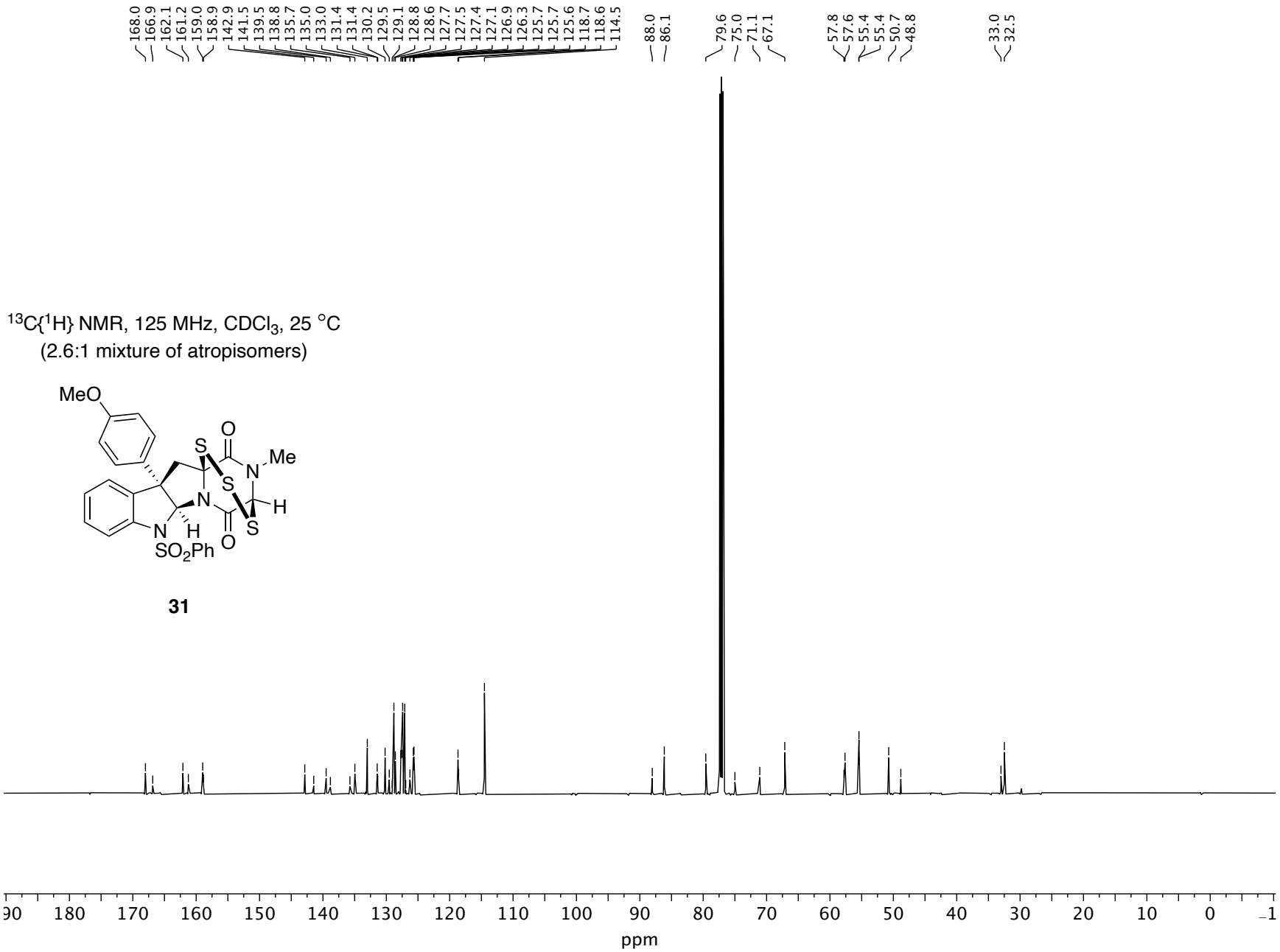


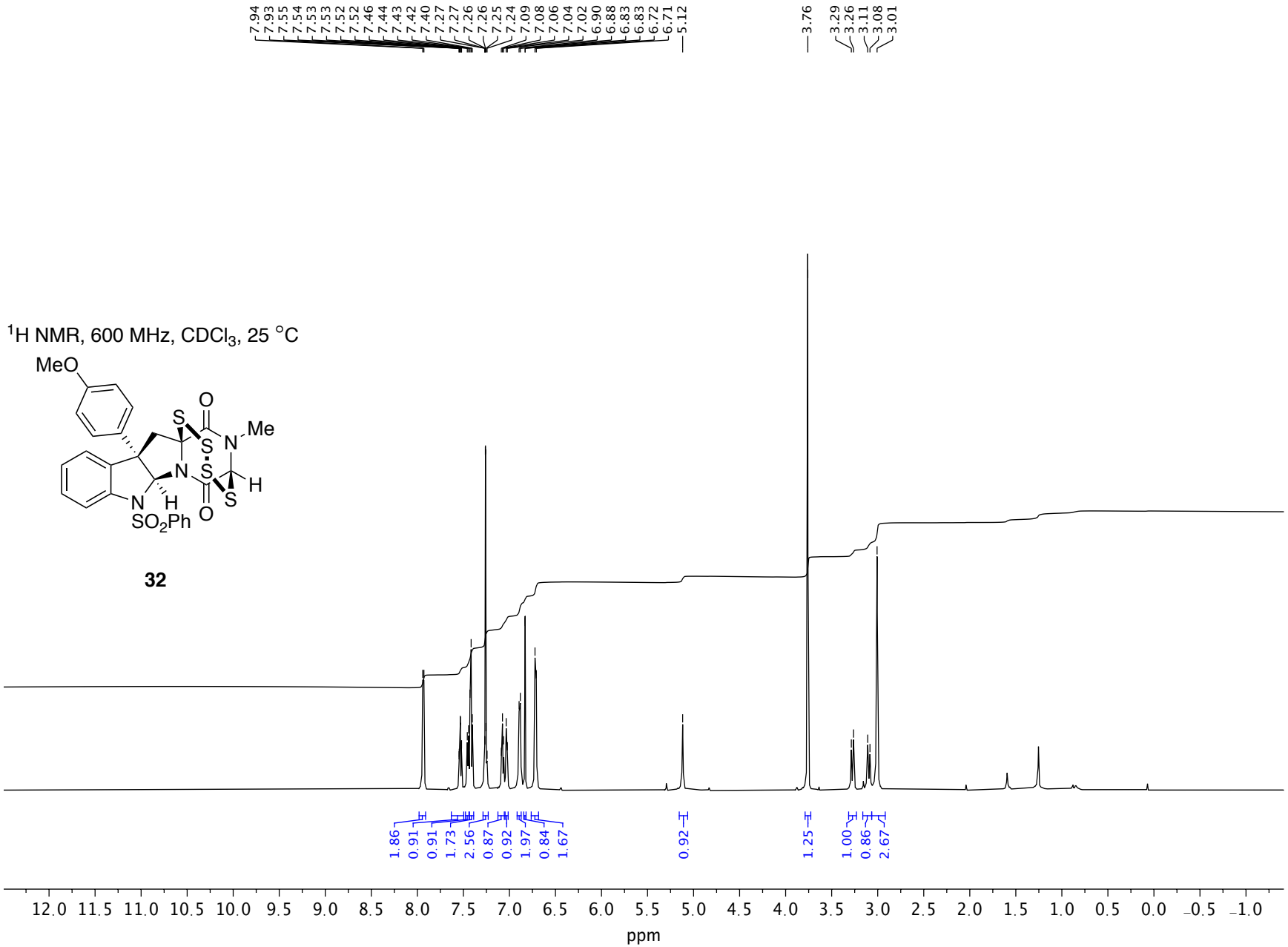
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C
(2.6:1 mixture of atropisomers)

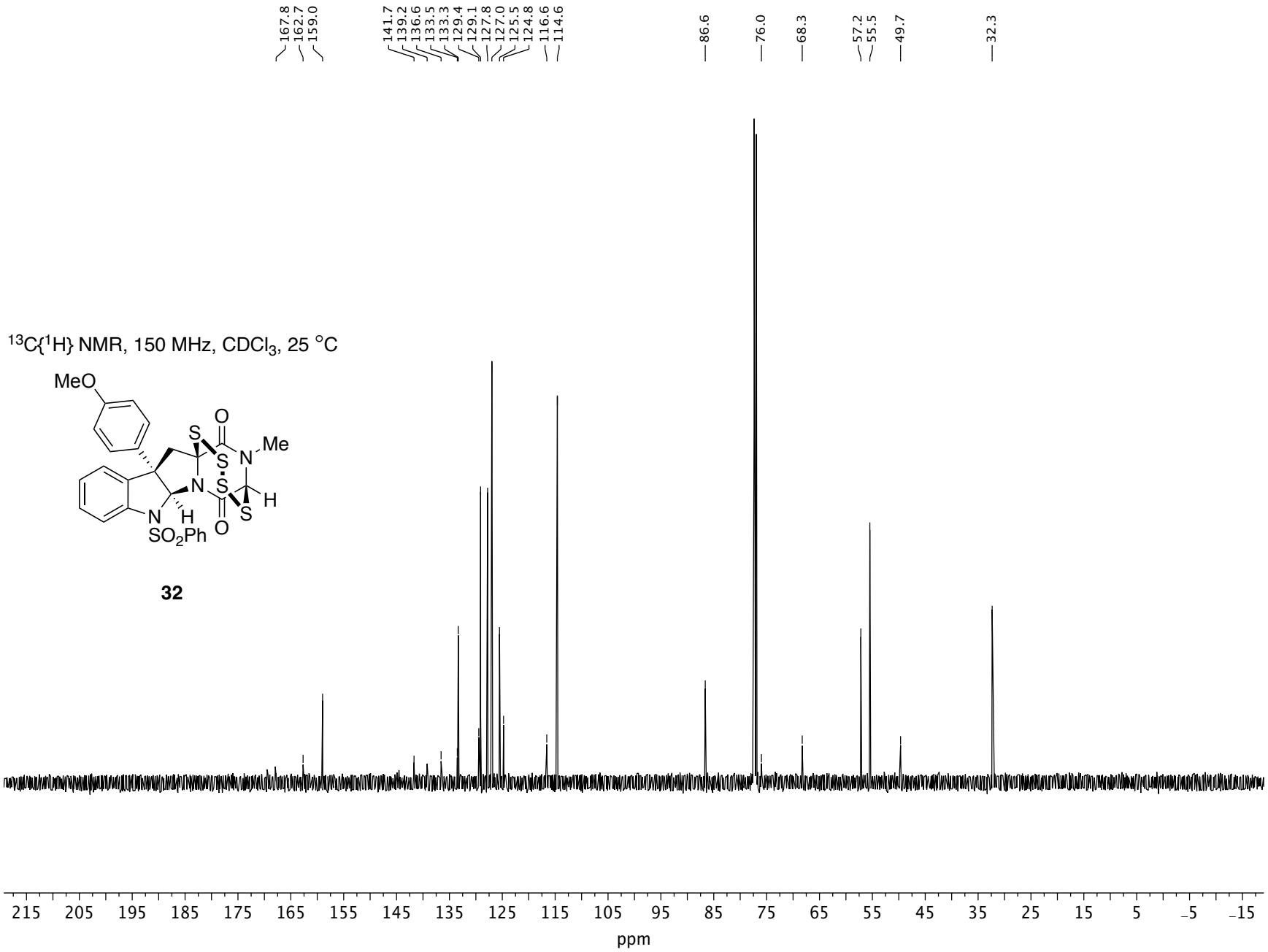


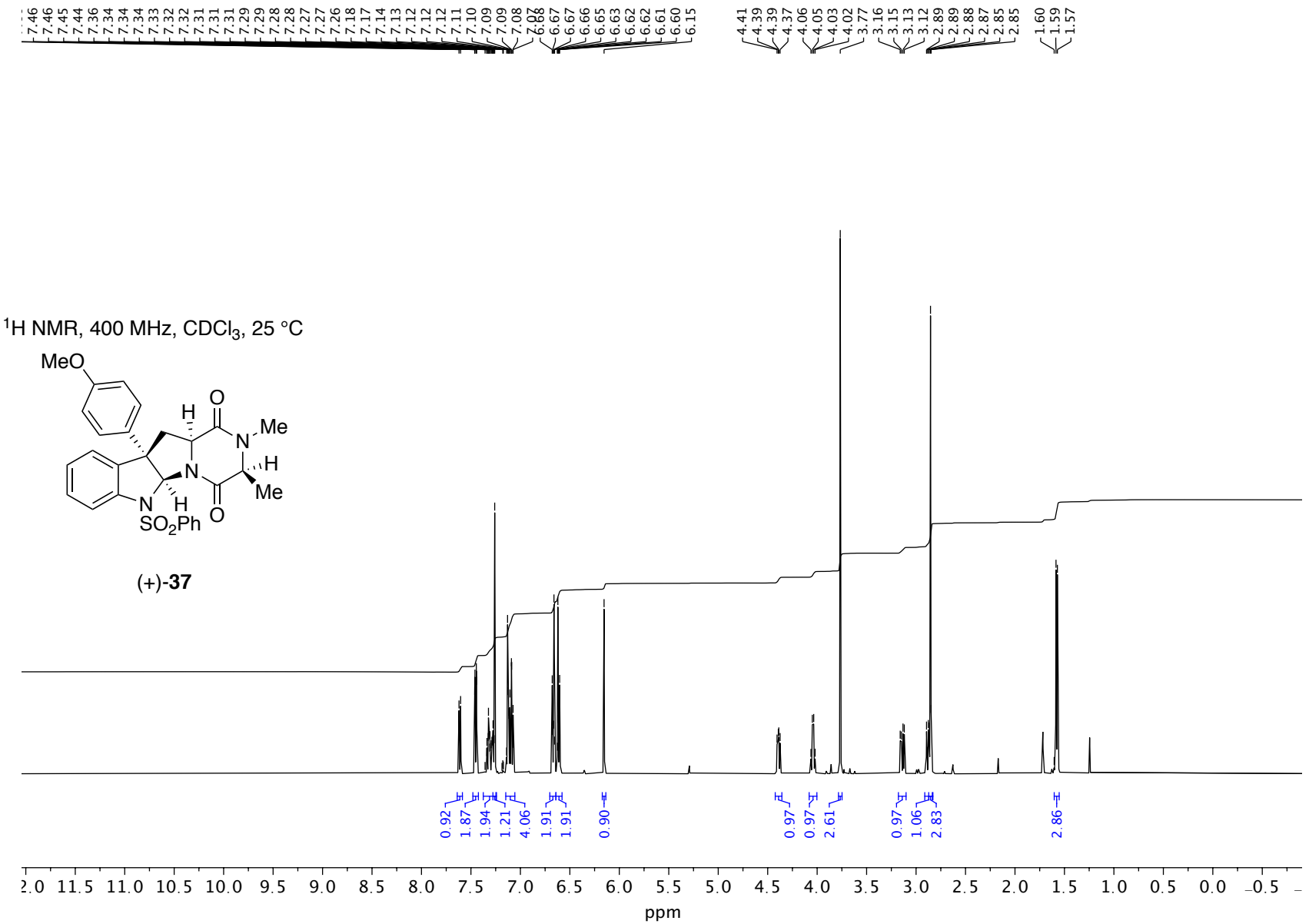
31

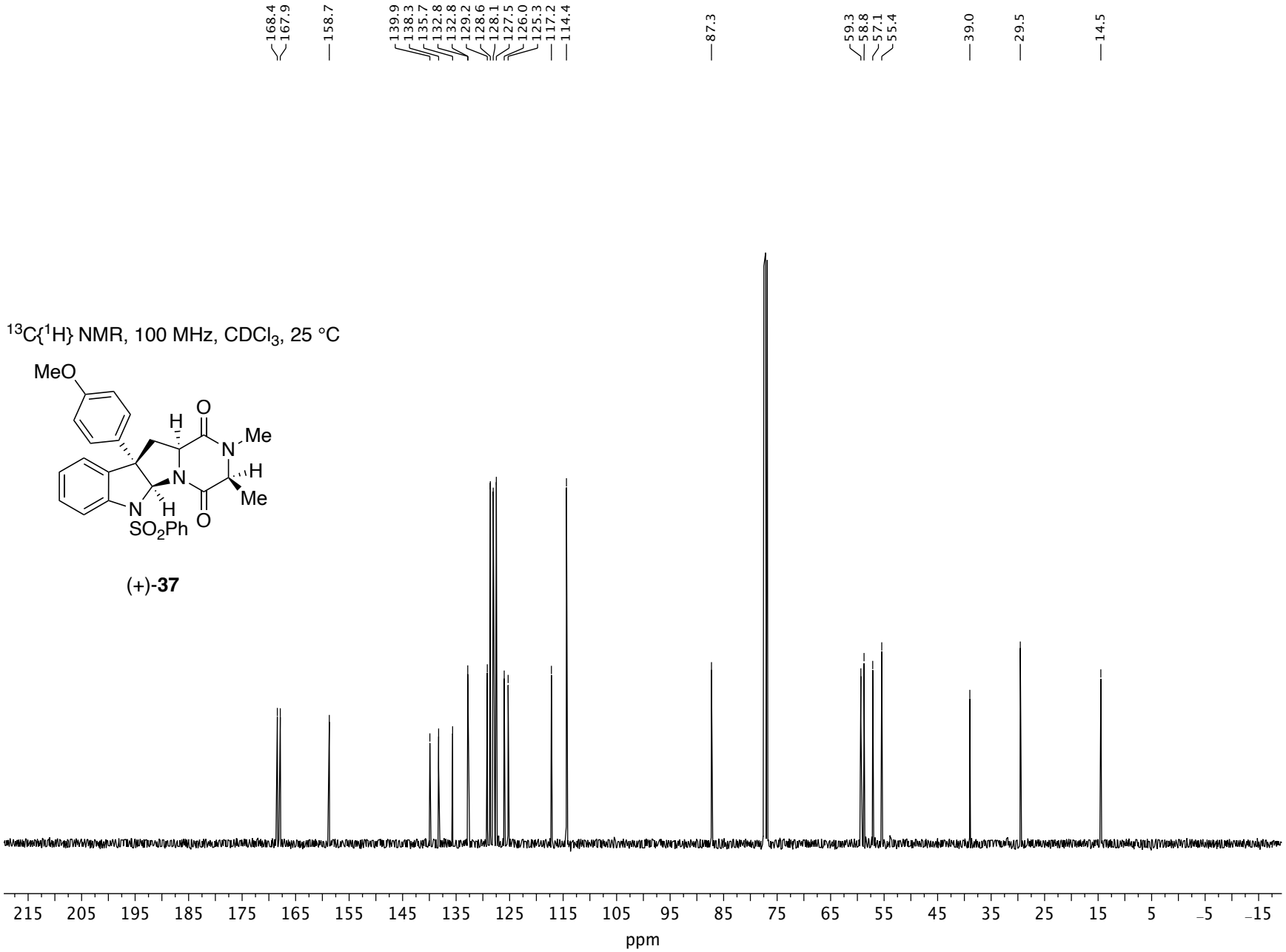


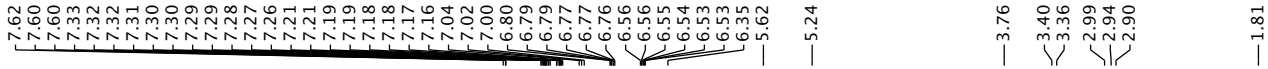

168.0
166.9
162.1
161.2
159.0
158.9
142.9
141.5
139.5
138.8
135.7
135.0
133.0
131.4
131.4
130.2
129.5
129.1
128.8
128.6
127.7
127.5
127.4
127.1
126.9
126.3
125.7
125.7
125.6
118.7
118.6
114.5
88.0
86.1
79.6
75.0
71.1
67.1
57.8
57.6
55.4
55.4
50.7
48.8
33.0
32.5
$^{13}C\{^{1}H\}$ NMR, 125 MHz, $CDCl_3$, 25 °C
(2.6:1 mixture of atropisomers)
MeO
O
S
N
Me
S
N
H
N
H
S
O
SO_2Ph
31
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
ppm


7.94
7.93
7.55
7.54
7.53
7.53
7.52
7.52
7.46
7.44
7.43
7.42
7.40
7.27
7.27
7.26
7.26
7.25
7.24
7.09
7.08
7.06
7.04
7.02
6.90
6.88
6.83
6.83
6.72
6.71
5.12
3.76
3.29
3.26
3.11
3.08
3.01
1H NMR, 600 MHz, CDCl3, 25 °C
MeO
O
S
N
Me
S
S
N
S
H
N
H
O
S
SO2Ph
32
1.86
0.91
0.91
1.73
2.56
0.87
0.92
1.97
0.84
1.67
0.92
1.25
1.00
0.86
2.67
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

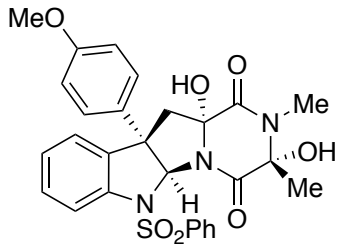

167.8
162.7
159.0
141.7
139.2
136.6
133.5
133.3
129.4
129.1
127.8
127.0
125.5
124.8
116.6
114.6
86.6
76.0
68.3
57.2
55.5
49.7
32.3
13C{1H} NMR, 150 MHz, CDCl3, 25 °C
MeO
O
S
N
Me
S
N
S
H
S
N
H
O
SO2Ph
32
215
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
−5
−15
ppm


7.46 7.46 7.45 7.44 7.36 7.34 7.34 7.33 7.32 7.32 7.31 7.31 7.29 7.29 7.28 7.28 7.27 7.27 7.26 7.18 7.17 7.14 7.13 7.12 7.12 7.12 7.11 7.10 7.09 7.09 7.08 7.07 6.88 6.67 6.67 6.66 6.65 6.63 6.62 6.62 6.61 6.60 6.15
4.41 4.39 4.39 4.37 4.06 4.05 4.03 4.02 3.77 3.16 3.15 3.13 3.12 2.89 2.89 2.88 2.87 2.85 2.85 1.60 1.59 1.57
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
H
O
N
Me
N
H
Me
N
H
O
SO2Ph
(+)-37
0.92 1.87 1.94 1.21 4.06 1.91 1.91 0.90 0.97 0.97 2.61 0.97 1.06 2.83 2.86
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm


168.4
167.9
158.7
139.9
138.3
135.7
132.8
132.8
129.2
128.6
128.1
127.5
126.0
125.3
117.2
114.4
87.3
59.3
58.8
57.1
55.4
39.0
29.5
14.5
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
O
H
N
Me
N
H
Me
N
H
O
SO_2Ph
(+)-**37**
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

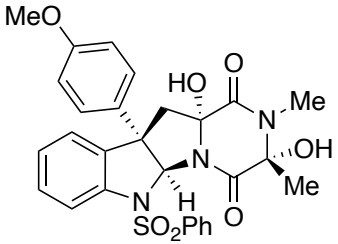


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



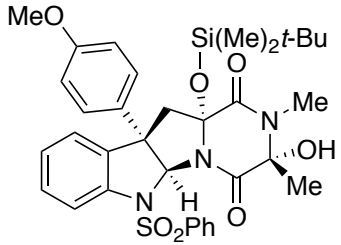
38

$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C



38

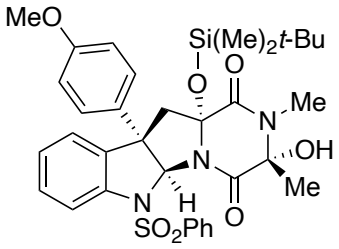
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



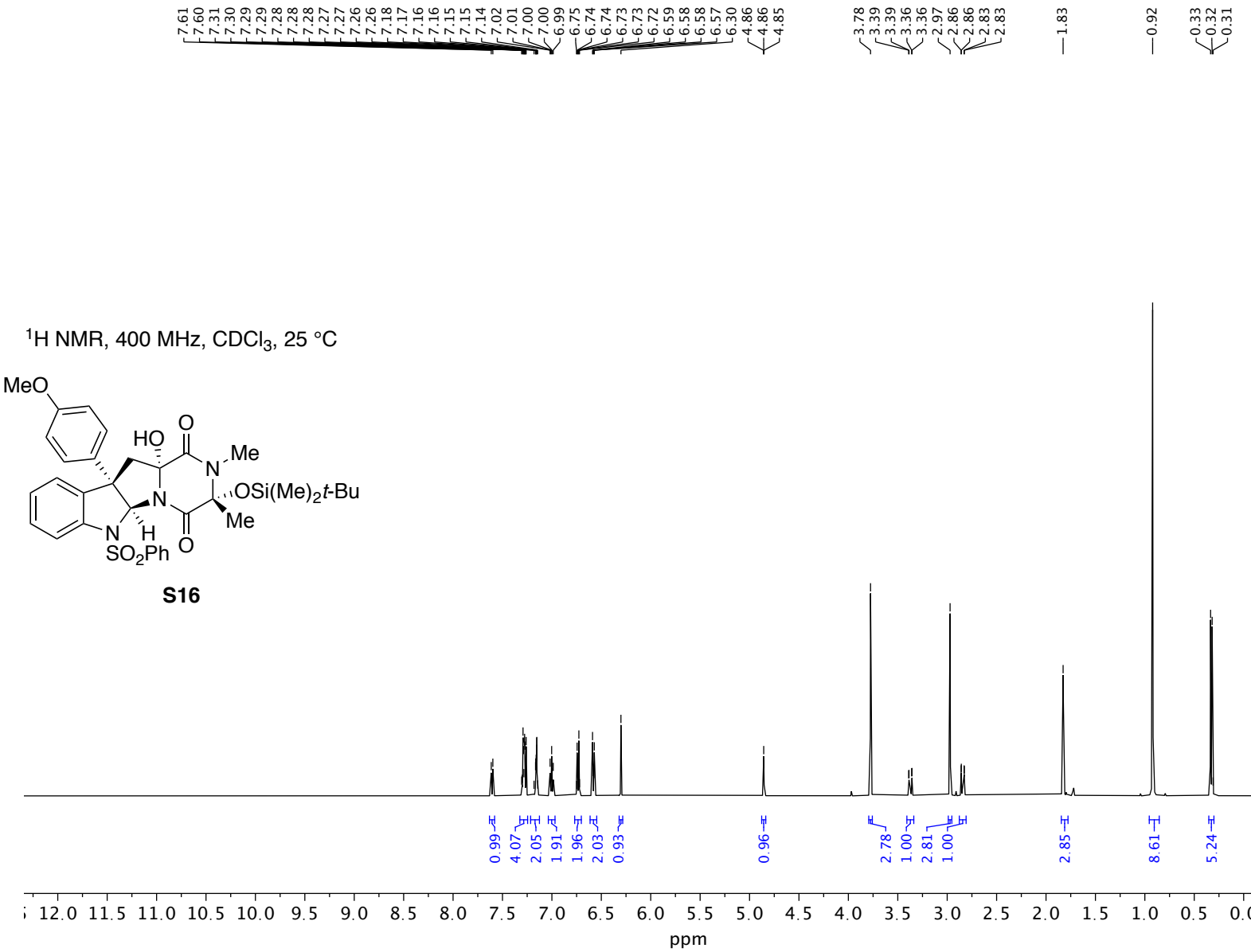
S15

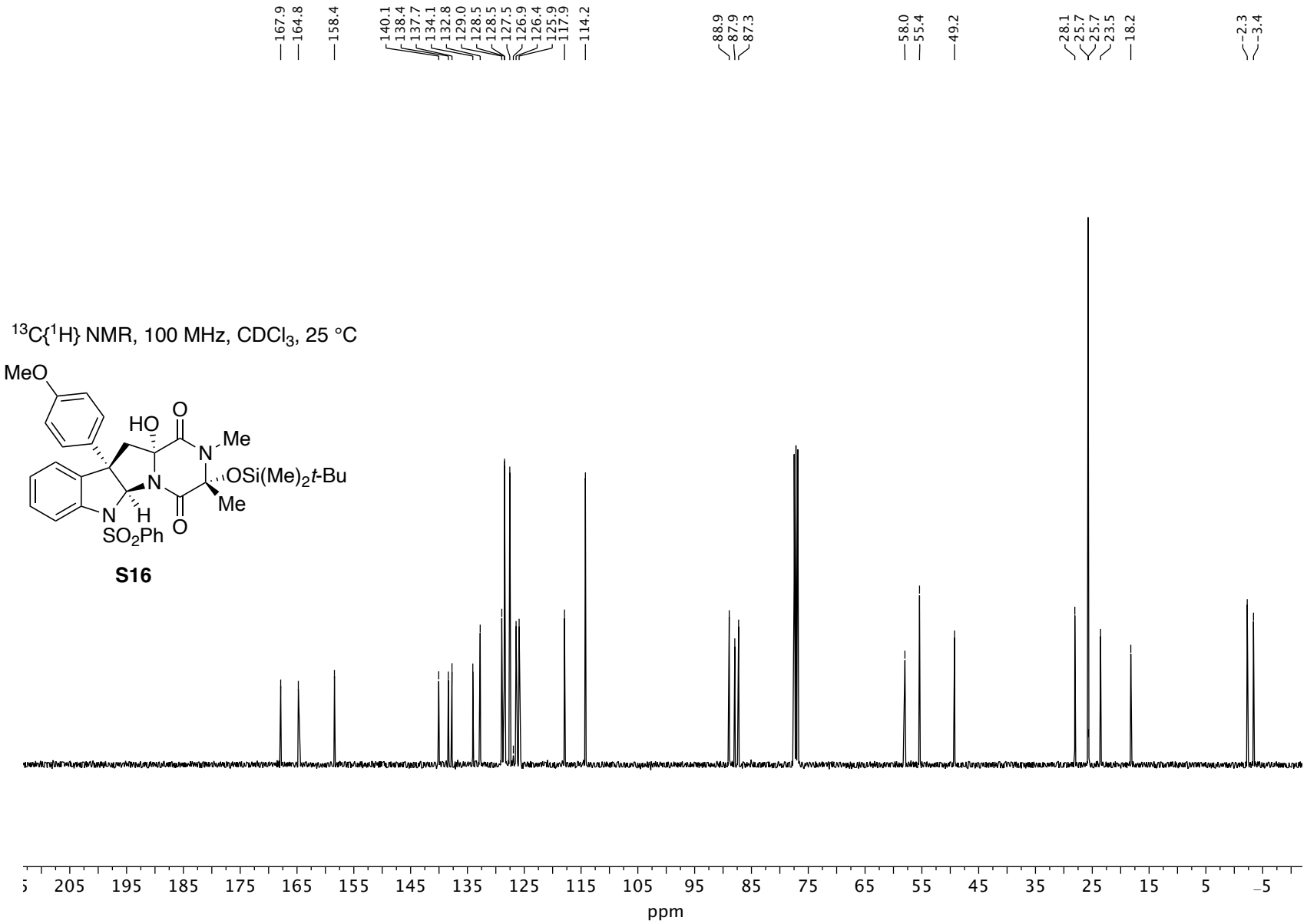
167.3
166.3
158.6
139.9
138.6
136.9
133.4
132.7
129.2
128.5
128.2
127.3
126.4
125.9
118.0
114.3
89.2
88.2
85.2
58.3
55.5
50.7
27.9
25.8
24.2
18.4
-3.3
-4.6

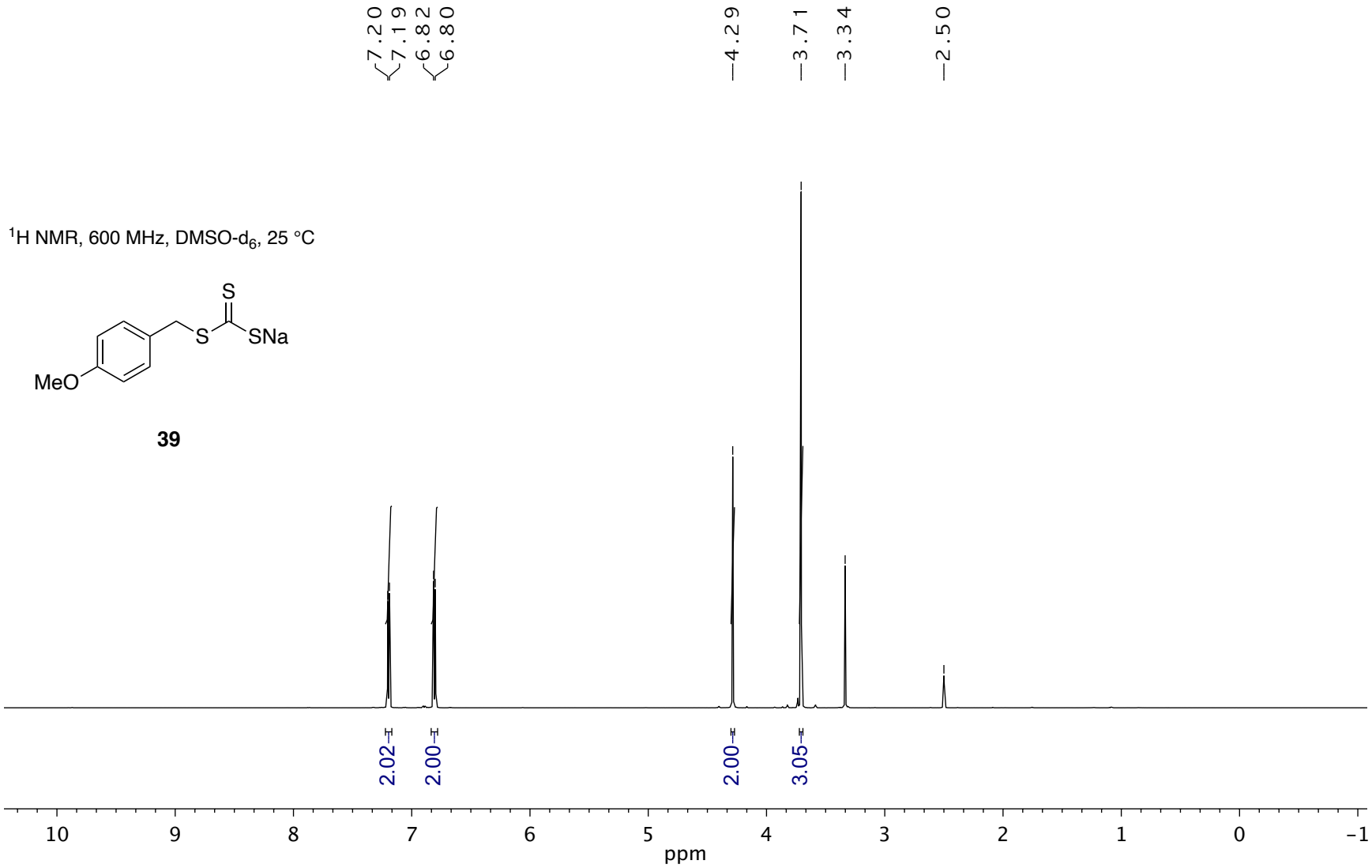
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C

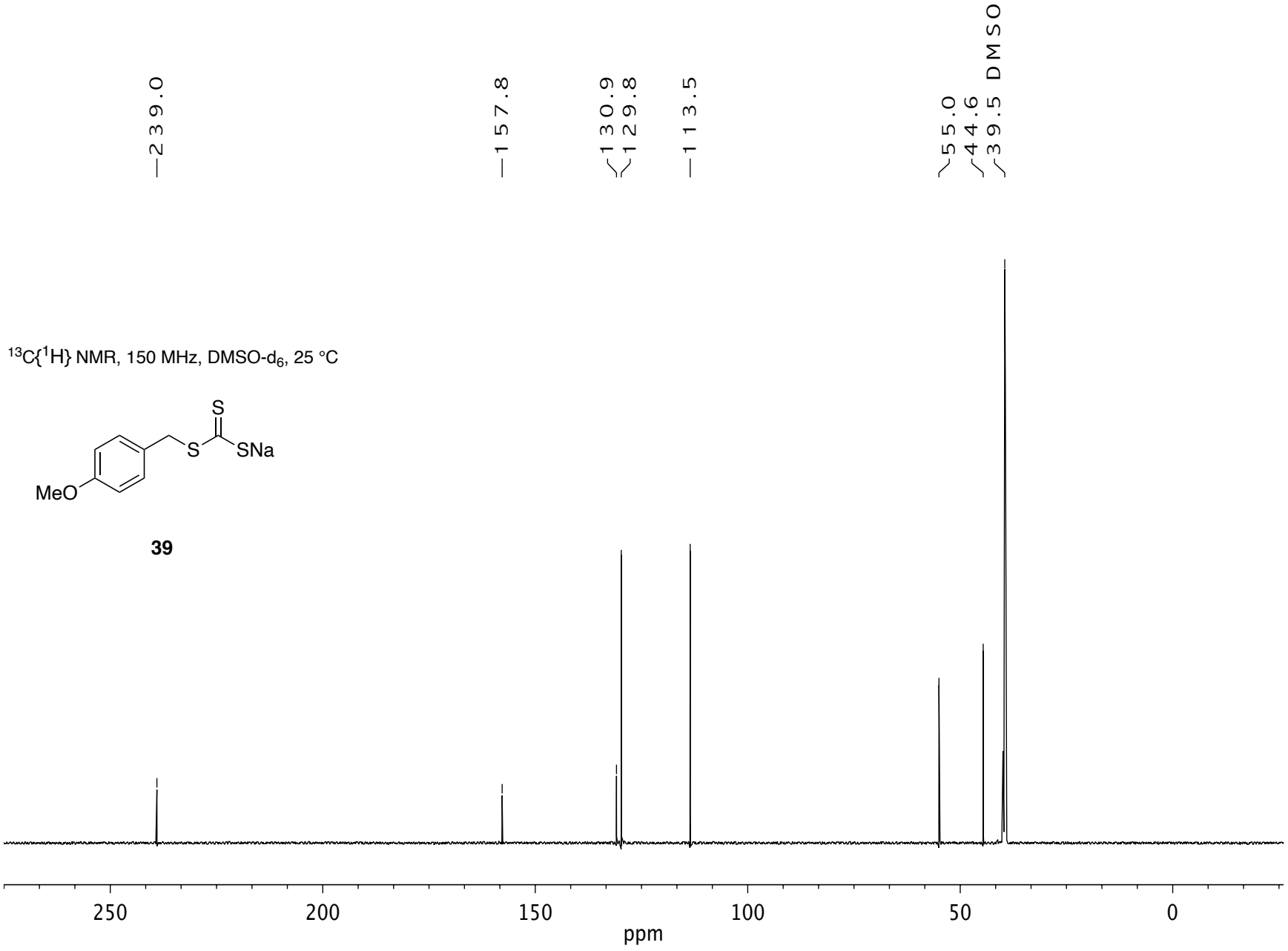


S15

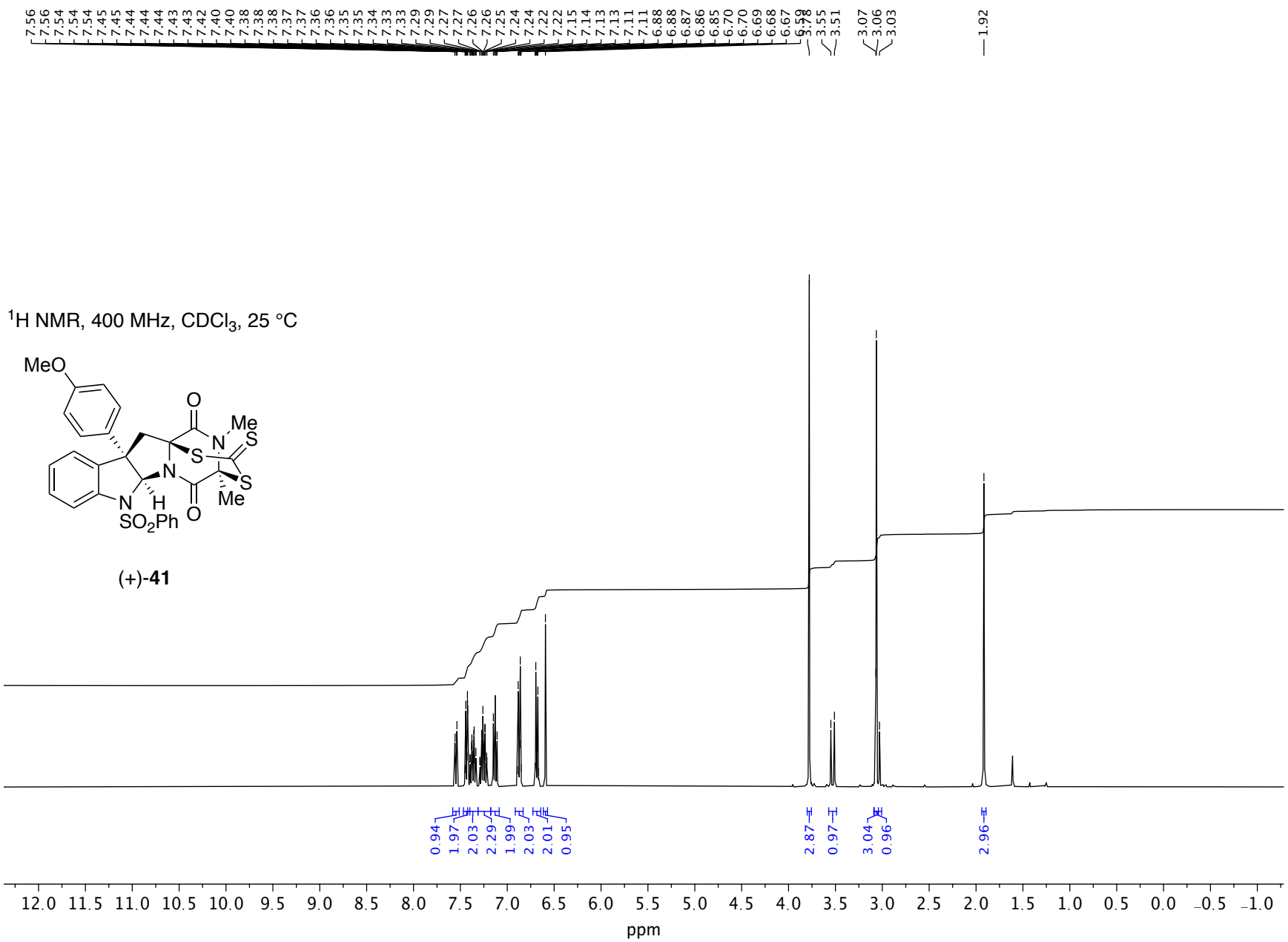

7.61 7.60 7.31 7.30 7.29 7.29 7.28 7.28 7.28 7.27 7.27 7.26 7.26 7.18 7.17 7.16 7.16 7.15 7.15 7.14 7.02 7.01 7.00 7.00 6.99 6.75 6.74 6.74 6.73 6.73 6.72 6.59 6.58 6.58 6.57 6.30 4.86 4.86 4.85
3.78 3.39 3.39 3.36 3.36 2.97 2.86 2.86 2.83 2.83
1.83
0.92
0.33 0.32 0.31
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
HO
O
N
Me
OSi(Me)2t-Bu
Me
N
H
SO2Ph
O
S16
0.99 4.07 2.05 1.91 1.96 2.03 0.93 0.96 2.78 1.00 2.81 1.00 2.85 8.61 5.24
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
ppm

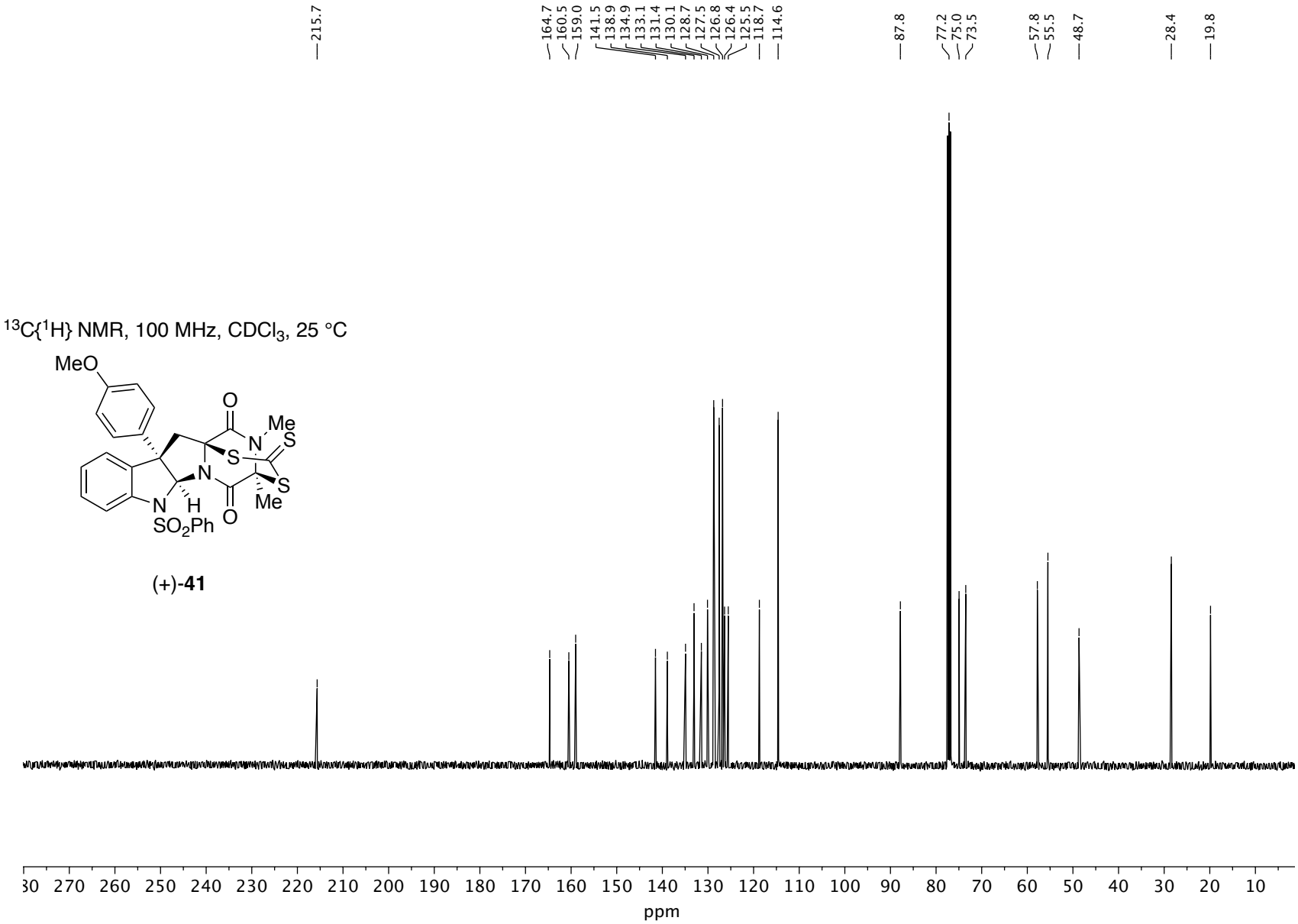

167.9
164.8
158.4
140.1
138.4
137.7
134.1
132.8
129.0
128.5
128.5
127.5
126.9
126.4
125.9
117.9
114.2
88.9
87.9
87.3
58.0
55.4
49.2
28.1
25.7
25.7
23.5
18.2
-2.3
-3.4
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
HO
O
N
Me
OSi(Me)2t-Bu
Me
N
H
SO2Ph
O
S16
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
-5
ppm

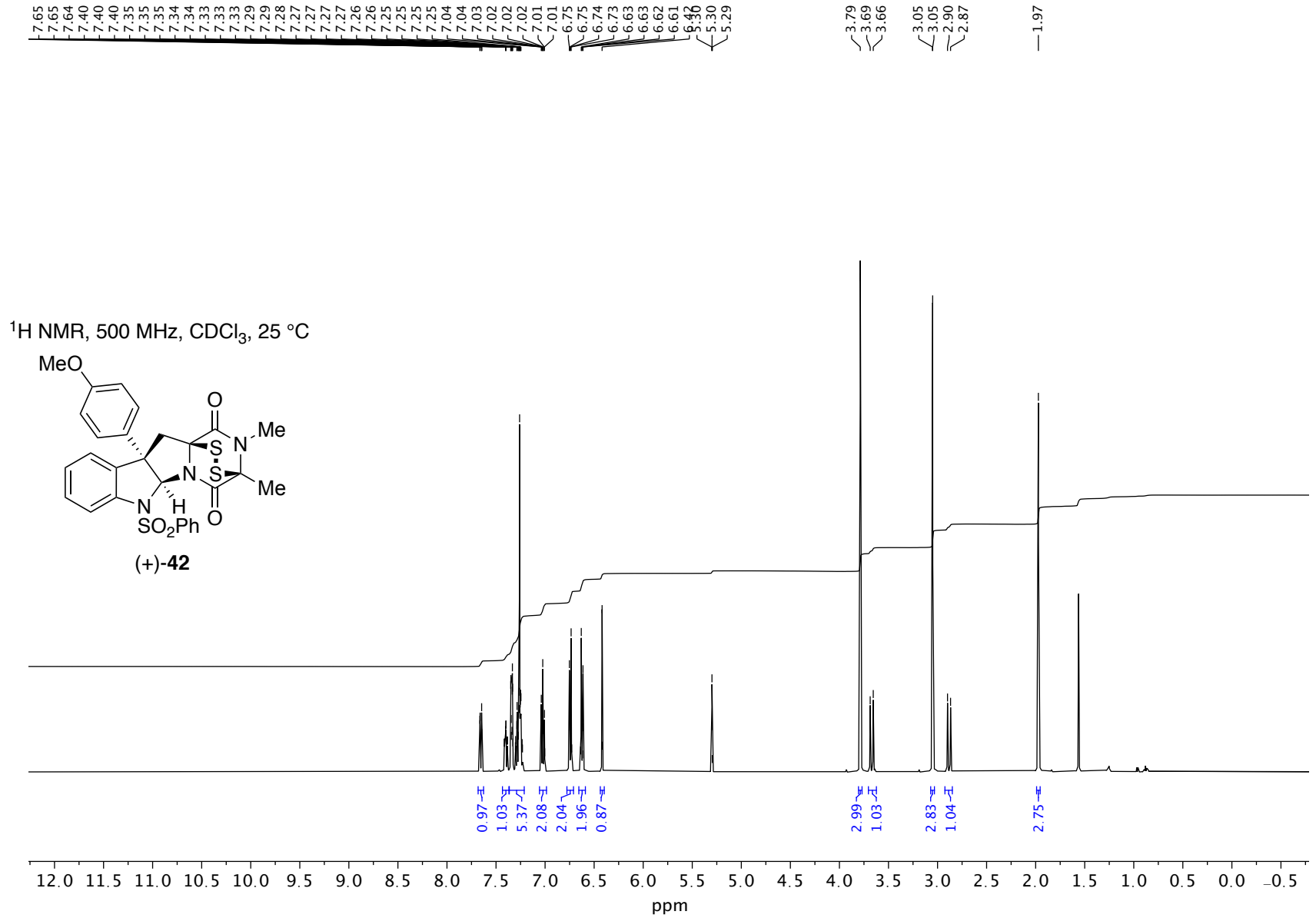

7.20
7.19
6.82
6.80
4.29
3.71
3.34
2.50
^{1}H NMR, 600 MHz, DMSO-d$_6$, 25 °C
S
S
SNa
MeO
39
2.02
2.00
2.00
3.05
10
9
8
7
6
5
4
3
2
1
0
-1
ppm

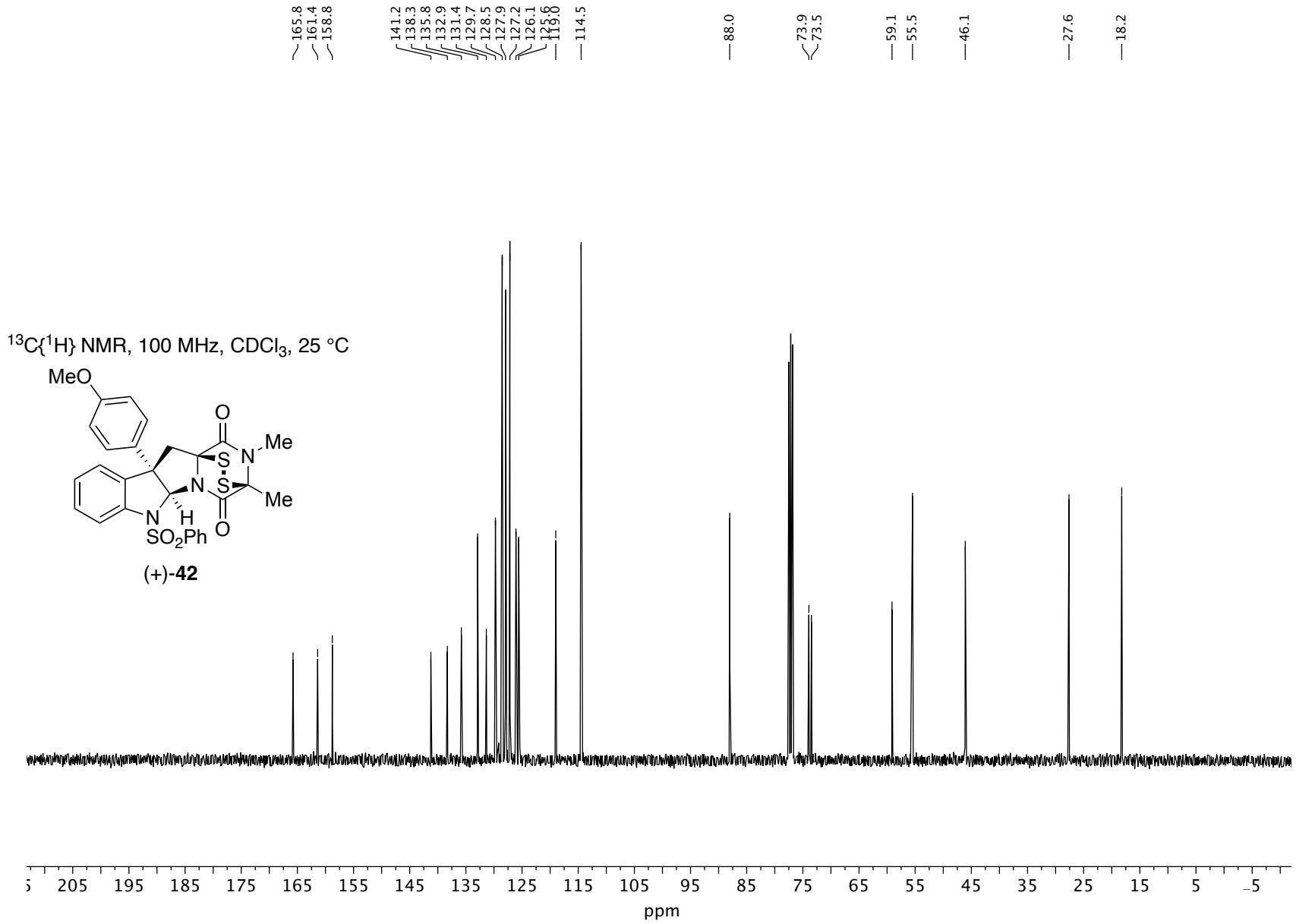

239.0
157.8
130.9
129.8
113.5
55.0
44.6
39.5 DMSO
13C{1H} NMR, 150 MHz, DMSO-d6, 25 °C
S
S
SNa
MeO
250
200
150
100
50
0
ppm

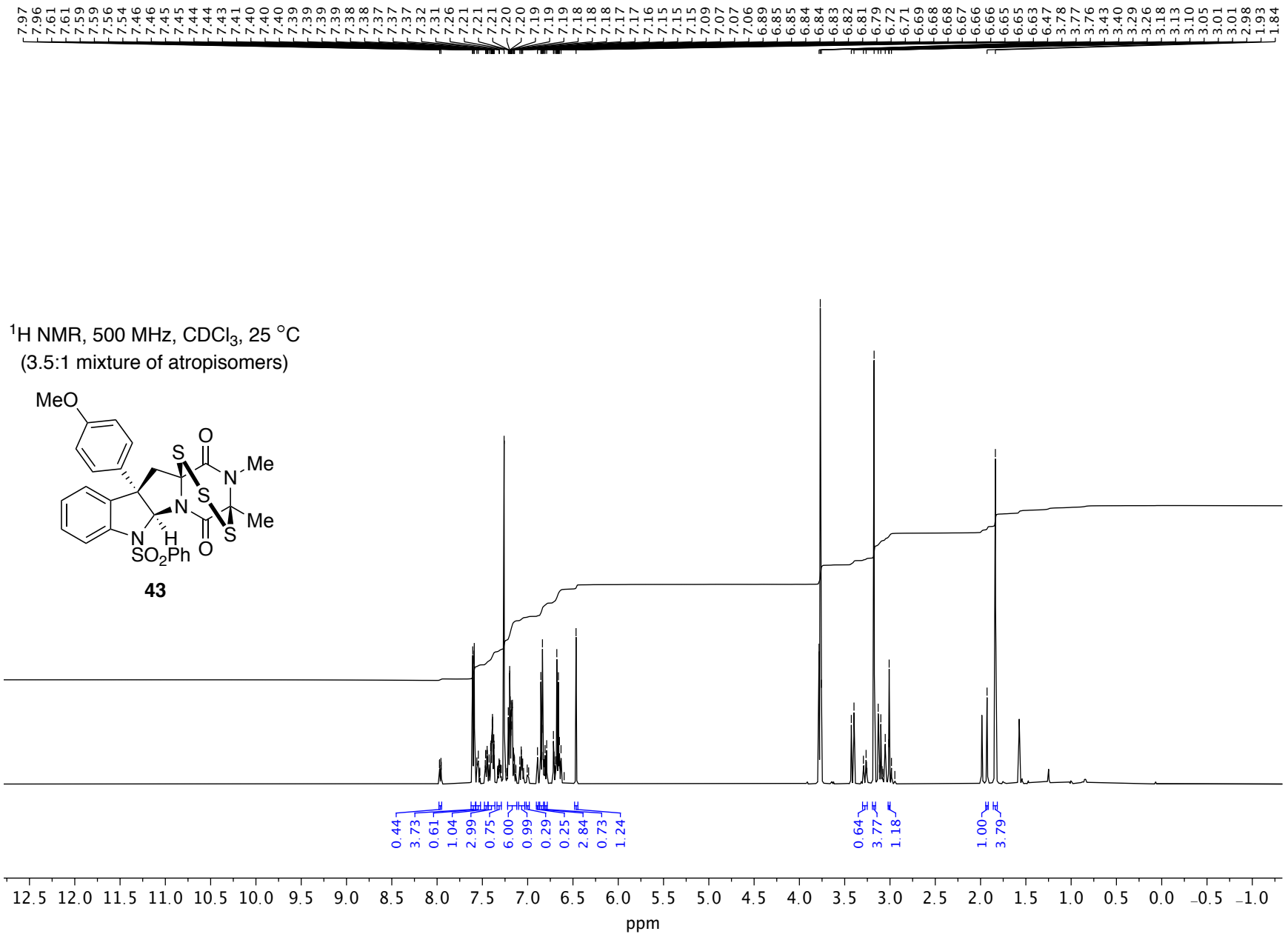
39


7.56 7.56 7.54 7.54 7.54 7.45 7.45 7.44 7.44 7.44 7.43 7.43 7.42 7.40 7.40 7.38 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.34 7.33 7.33 7.29 7.29 7.27 7.27 7.26 7.26 7.25 7.24 7.24 7.22 7.22 7.15 7.14 7.13 7.13 7.11 7.11 6.88 6.88 6.87 6.86 6.85 6.70 6.70 6.69 6.68 6.67 6.59 3.78 3.55 3.51 3.07 3.06 3.03 1.92
1H NMR, 400 MHz, CDCl3, 25 °C
MeO
O
Me
N
S
S
N
S
N H
O
Me
SO2Ph
O
(+)-41
0.94 1.97 2.03 2.29 1.99 2.03 2.01 0.95 2.87 0.97 3.04 0.96 2.96
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm


215.7
164.7
160.5
159.0
141.5
138.9
134.9
133.1
131.4
130.1
128.7
127.5
126.8
126.4
125.5
118.7
114.6
87.8
77.2
75.0
73.5
57.8
55.5
48.7
28.4
19.8
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
O
N
Me
S
S
N
S
Me
N
H
O
SO2Ph
(+)-41
ppm

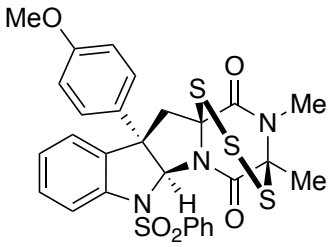

7.65 7.65 7.64 7.40 7.40 7.40 7.35 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.29 7.29 7.28 7.27 7.27 7.27 7.27 7.26 7.26 7.25 7.25 7.25 7.25 7.04 7.04 7.03 7.02 7.02 7.02 7.01 7.01 6.75 6.75 6.74 6.73 6.63 6.63 6.62 6.61 6.42 6.40 5.30 5.29
3.79 3.69 3.66
3.05 3.05 2.90 2.87
1.97
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C
MeO
O
N
Me
S
N
S
Me
N
H
O
SO_2Ph
(+)-**42**
0.97 1.03 5.37 2.08 2.04 1.96 0.87
2.99 1.03 2.83 1.04 2.75
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
ppm


165.8
161.4
158.8
141.2
138.3
135.8
132.9
131.4
129.7
128.5
127.9
127.2
126.1
125.6
119.0
114.5
88.0
73.9
73.5
59.1
55.5
46.1
27.6
18.2
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
O
N
Me
S
N
S
Me
N
H
O
SO2Ph
(+)-42
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
−5
ppm


7.97 7.96 7.61 7.61 7.59 7.59 7.56 7.54 7.46 7.46 7.45 7.45 7.44 7.44 7.43 7.41 7.40 7.40 7.40 7.39 7.39 7.39 7.38 7.38 7.37 7.37 7.37 7.32 7.31 7.26 7.21 7.21 7.21 7.20 7.20 7.19 7.19 7.19 7.18 7.18 7.18 7.17 7.17 7.16 7.15 7.15 7.15 7.09 7.07 7.07 7.06 6.89 6.85 6.85 6.84 6.84 6.83 6.82 6.81 6.79 6.72 6.71 6.69 6.68 6.68 6.67 6.66 6.66 6.65 6.65 6.63 6.47 3.78 3.77 3.76 3.43 3.40 3.29 3.26 3.18 3.13 3.10 3.05 3.01 3.01 2.98 1.93 1.84
1H NMR, 500 MHz, CDCl3, 25 °C
(3.5:1 mixture of atropisomers)
MeO
O
S
N
Me
S
N
Me
N
H
S
SO2Ph
O
43
0.44 3.73 0.61 1.04 2.99 0.75 6.00 0.99 0.29 0.25 2.84 0.73 1.24
0.64 3.77 1.18
1.00 3.79
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
ppm

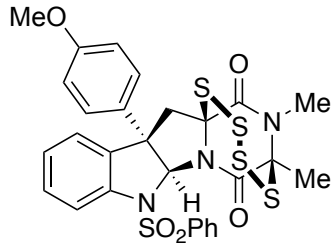
168.8
167.2
163.8
159.0
143.2
141.6
139.6
135.0
133.3
133.0
132.9
131.7
130.2
129.6
129.2
128.8
128.6
127.8
127.8
127.6
127.5
127.1
126.9
126.3
125.8
125.8
125.8
125.5
118.9
118.8
114.6
114.6
88.7
87.1
86.8
79.9
77.4
77.4
77.2
77.2
77.0
76.9
75.7
75.5
72.2
56.9
55.5
55.5
51.7
49.8
29.2
28.5
24.1
21.8

$^{13}C\{^{1}H\}$ NMR, 150 MHz, $CDCl_3$, 25 °C
(3.5:1 mixture of atropisomers)



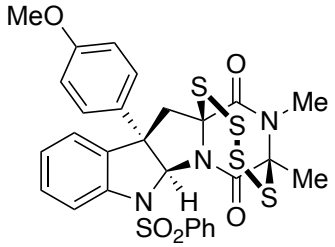
43

^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C



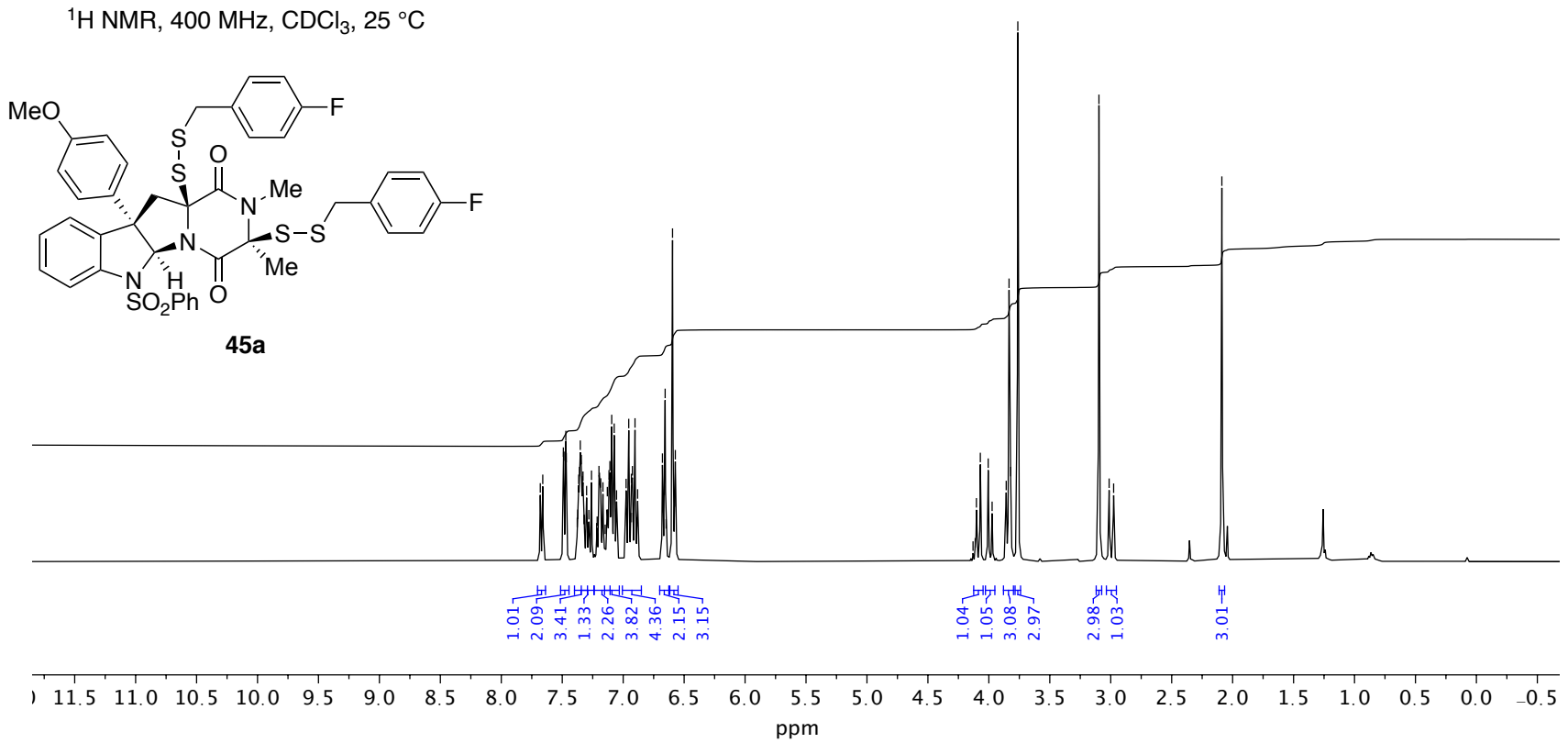
44

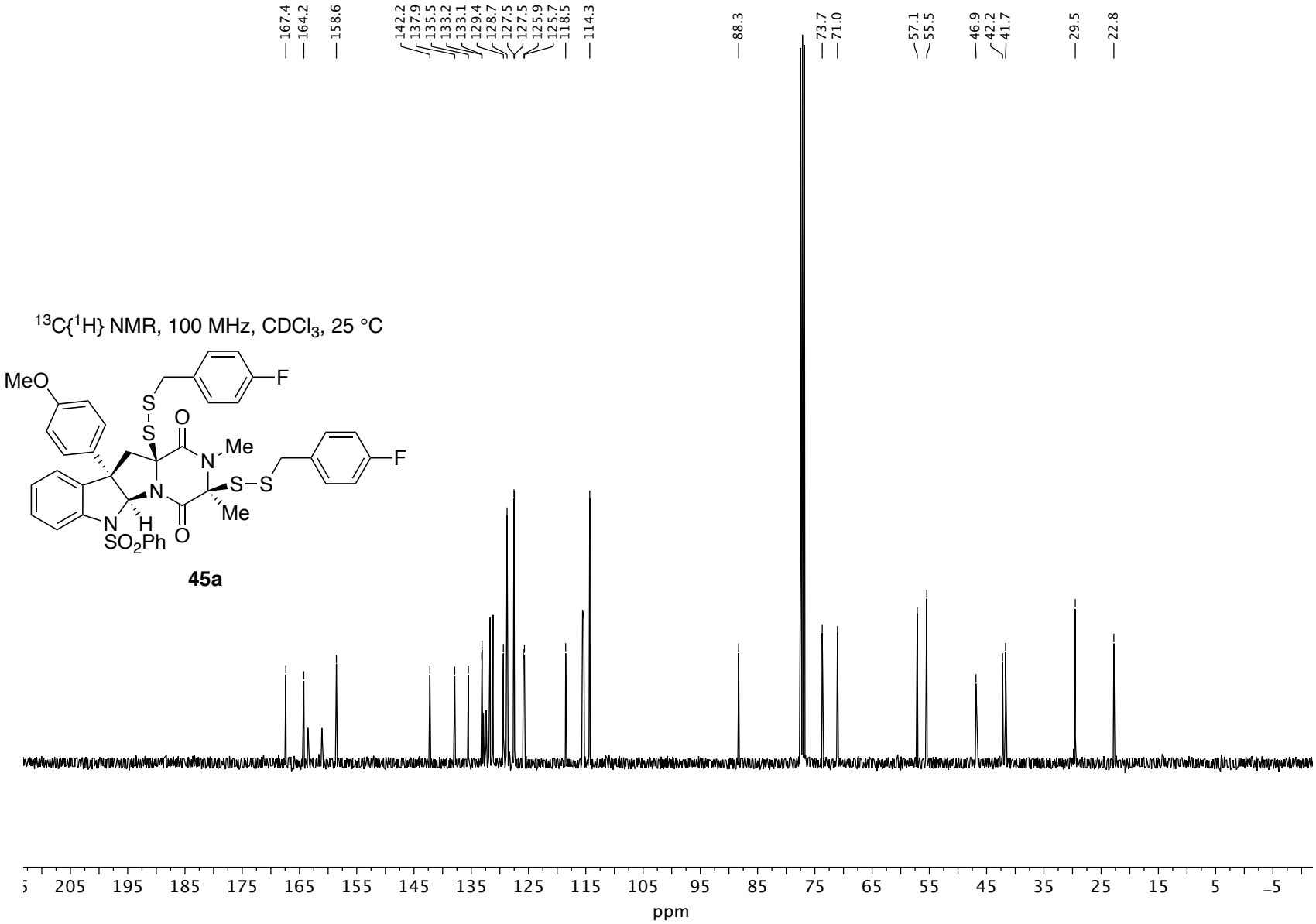
$^{13}C\{^{1}H\}$ NMR, 125 MHz, $CDCl_3$, 25 °C



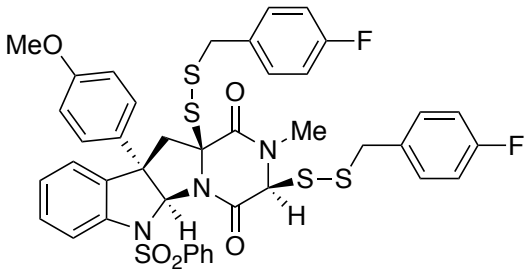
44


7.49
7.49
7.47
7.47
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.33
7.32
7.32
7.30
7.28
7.26
7.22
7.21
7.20
7.19
7.18
7.17
7.13
7.13
7.12
7.11
7.09
7.07
7.05
6.98
6.97
6.95
6.94
6.93
6.92
6.92
6.90
6.89
6.88
6.68
6.67
6.66
6.66
6.65
6.59
6.58
4.13
4.11
4.10
4.07
4.01
3.97
3.86
3.83
3.82
3.76
3.10
3.01
2.98
2.09

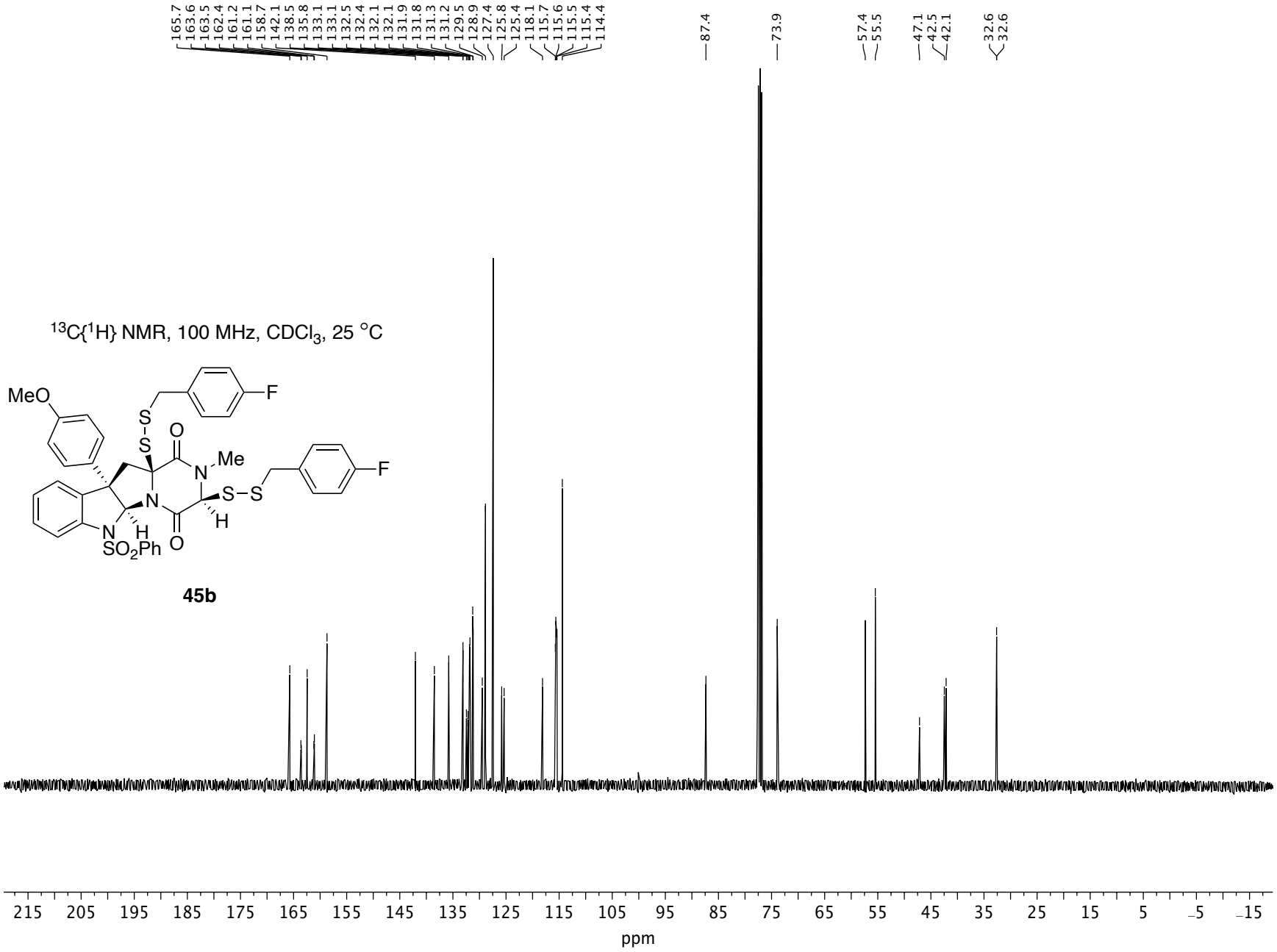

^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C
MeO
F
S
S
O
N
Me
F
S–S
N
Me
N
H
SO_2Ph
O
45a
1.01
2.09
3.41
1.33
2.26
3.82
4.36
2.15
3.15
1.04
1.05
3.08
2.97
2.98
1.03
3.01
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 –0.5
ppm

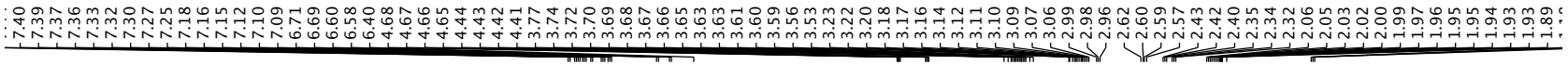

167.4
164.2
158.6
142.2
137.9
135.5
133.2
133.1
129.4
128.7
127.5
127.5
125.9
125.7
118.5
114.3
88.3
73.7
71.0
57.1
55.5
46.9
42.2
41.7
29.5
22.8
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
MeO
F
S
S
O
N
Me
F
N
S–S
Me
N
H
O
SO2Ph
45a
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
–5
ppm

^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C

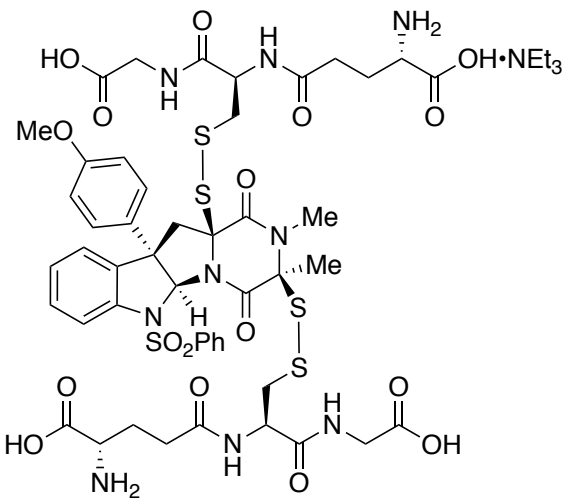


45b

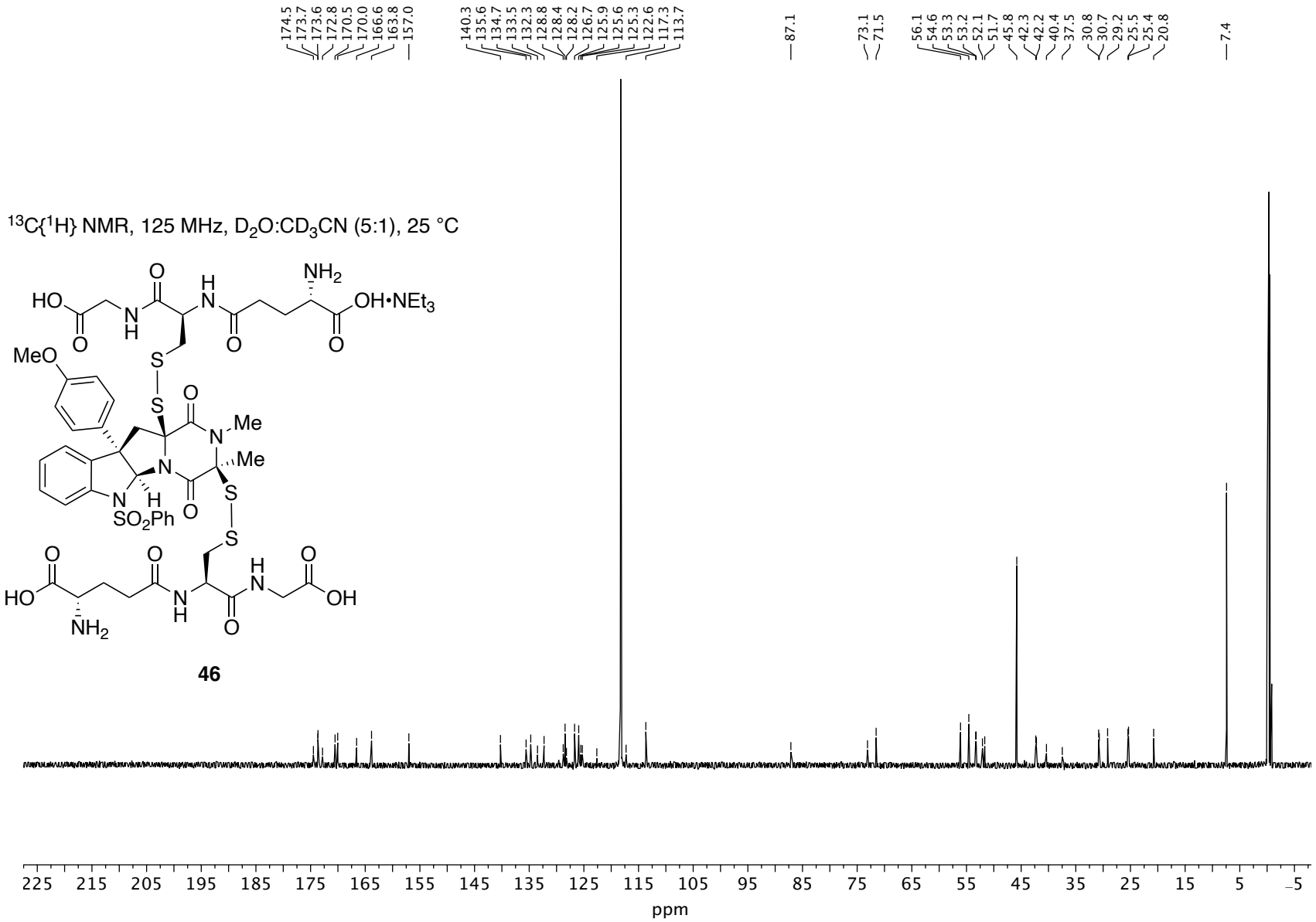

165.7
163.6
163.5
162.4
161.2
161.1
158.7
142.1
138.5
135.8
133.1
133.1
132.5
132.4
132.1
132.1
131.9
131.8
131.3
131.2
129.5
128.9
127.4
125.8
125.4
118.1
115.7
115.6
115.5
115.4
114.4
87.4
73.9
57.4
55.5
47.1
42.5
42.1
32.6
32.6
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
MeO
F
S
S
O
N
Me
F
N
S–S
H
N
H
SO_2Ph
O
45b
215
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
–5
–15
ppm



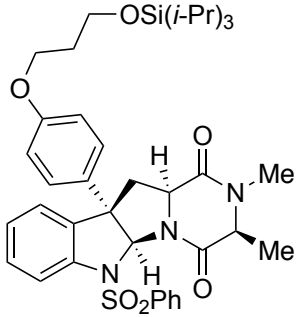
^{1}H NMR, 500 MHz, D_2O:CD_3CN (5:1), 25 °C



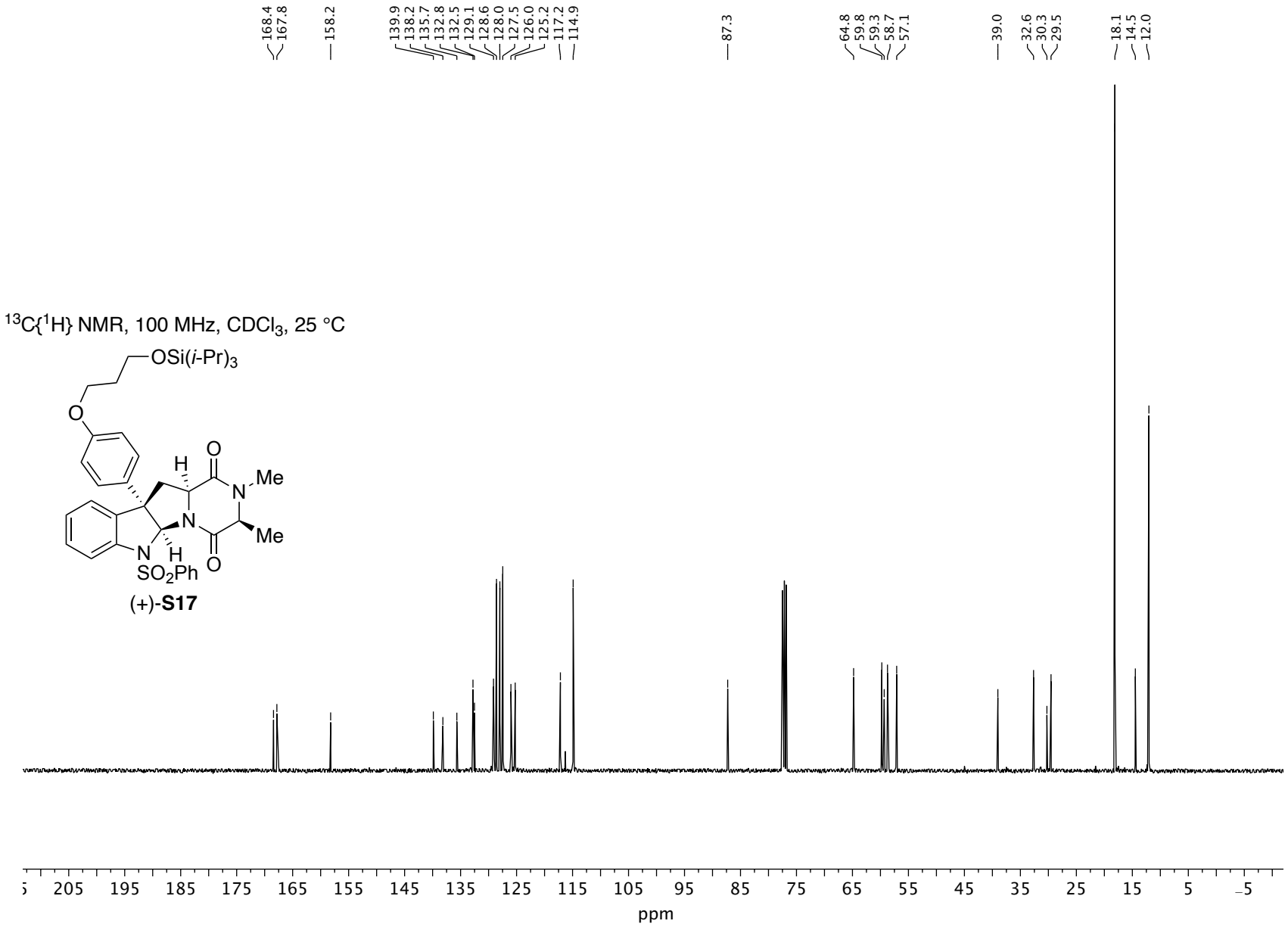
46


174.5
173.7
173.6
172.8
170.5
170.0
166.6
163.8
157.0
140.3
135.6
134.7
133.5
132.3
128.8
128.4
128.2
126.7
125.9
125.6
125.3
122.6
117.3
113.7
87.1
73.1
71.5
56.1
54.6
53.3
53.2
52.1
51.7
45.8
42.3
42.2
40.4
37.5
30.8
30.7
29.2
25.5
25.4
20.8
7.4
13C{1H} NMR, 125 MHz, D2O:CD3CN (5:1), 25 °C
HO
OH•NEt3
NH2
MeO
Me
Me
SO2Ph
OH
NH2
46
225 215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5
ppm

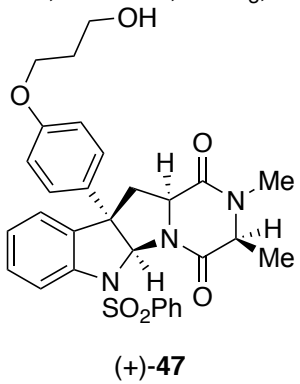
^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



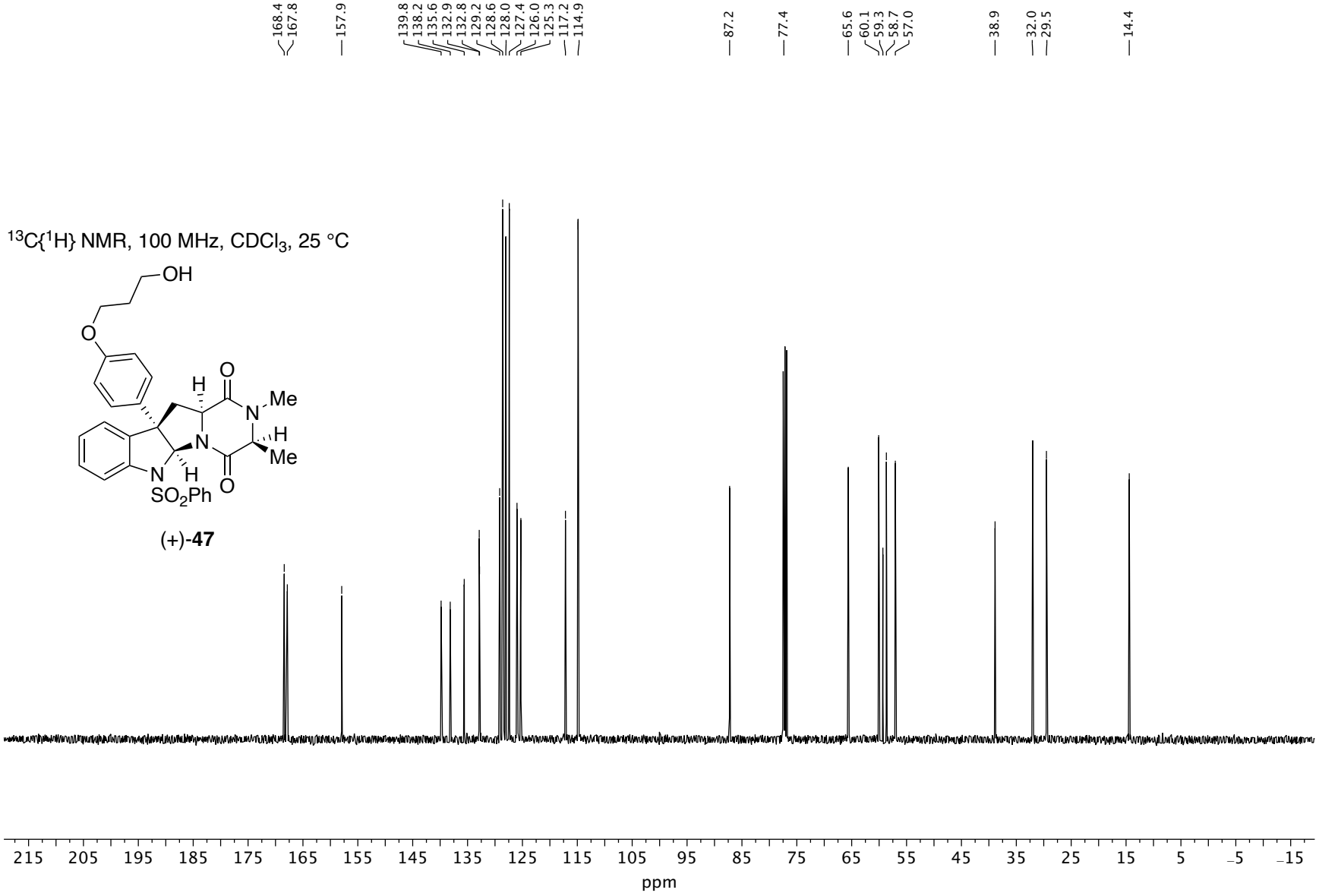
(+)-**S17**

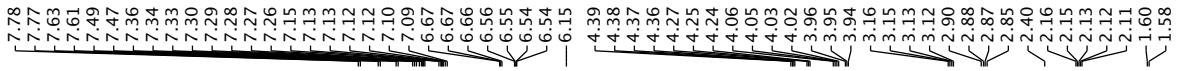

168.4
167.8
158.2
139.9
138.2
135.7
132.8
132.5
129.1
128.6
128.0
127.5
126.0
125.2
117.2
114.9
87.3
64.8
59.8
59.3
58.7
57.1
39.0
32.6
30.3
29.5
18.1
14.5
12.0
$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C
OSi(*i*-Pr)$_3$
O
H
O
N
Me
N
Me
N
H
O
SO_2Ph
(+)-**S17**
205
195
185
175
165
155
145
135
125
115
105
95
85
75
65
55
45
35
25
15
5
−5
ppm

^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C

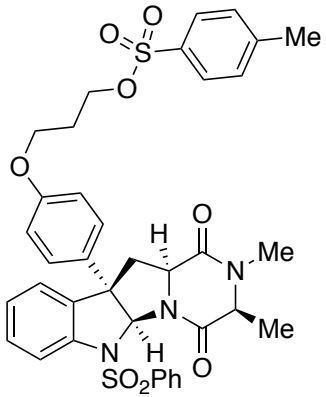


(+)-**47**

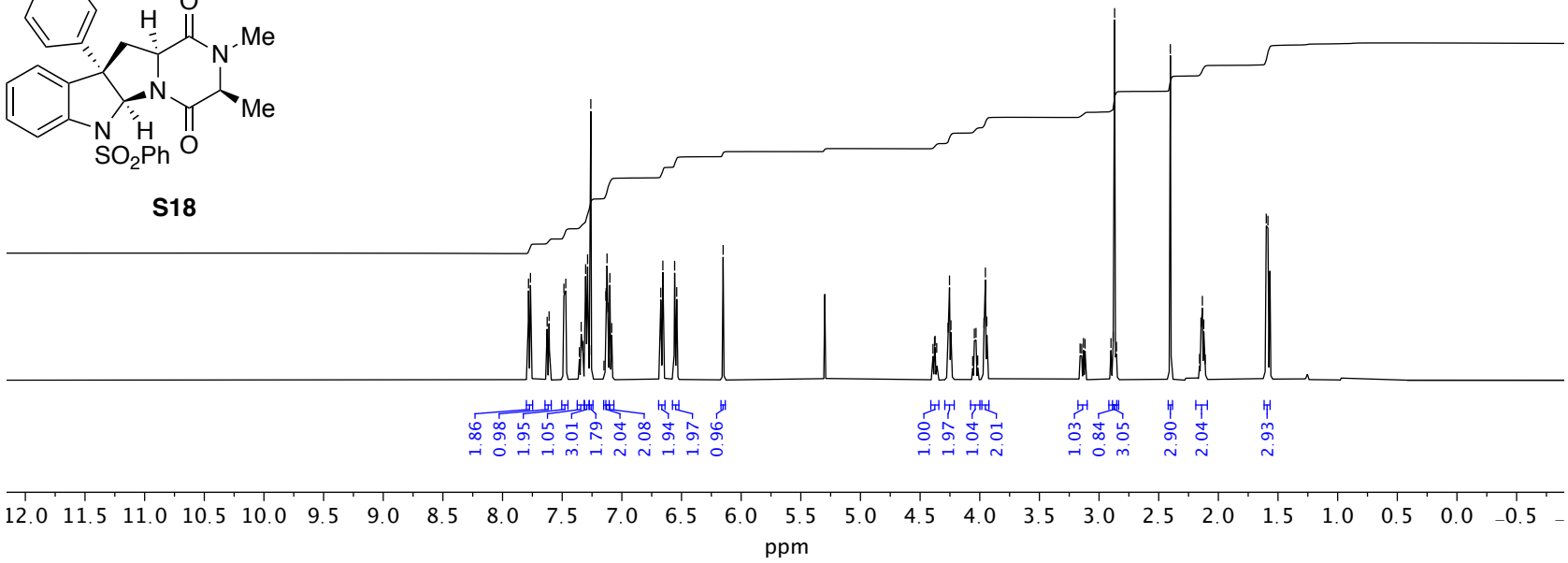

168.4
167.8
157.9
139.8
138.2
135.6
132.9
132.8
129.2
128.6
128.0
127.4
126.0
125.3
117.2
114.9
87.2
77.4
65.6
60.1
59.3
58.7
57.0
38.9
32.0
29.5
14.4
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
OH
O
H
O
N
Me
N
H
Me
N
H
O
SO2Ph
(+)-47
215 205 195 185 175 165 155 145 135 125 115 105 95 85 75 65 55 45 35 25 15 5 −5 −15
ppm

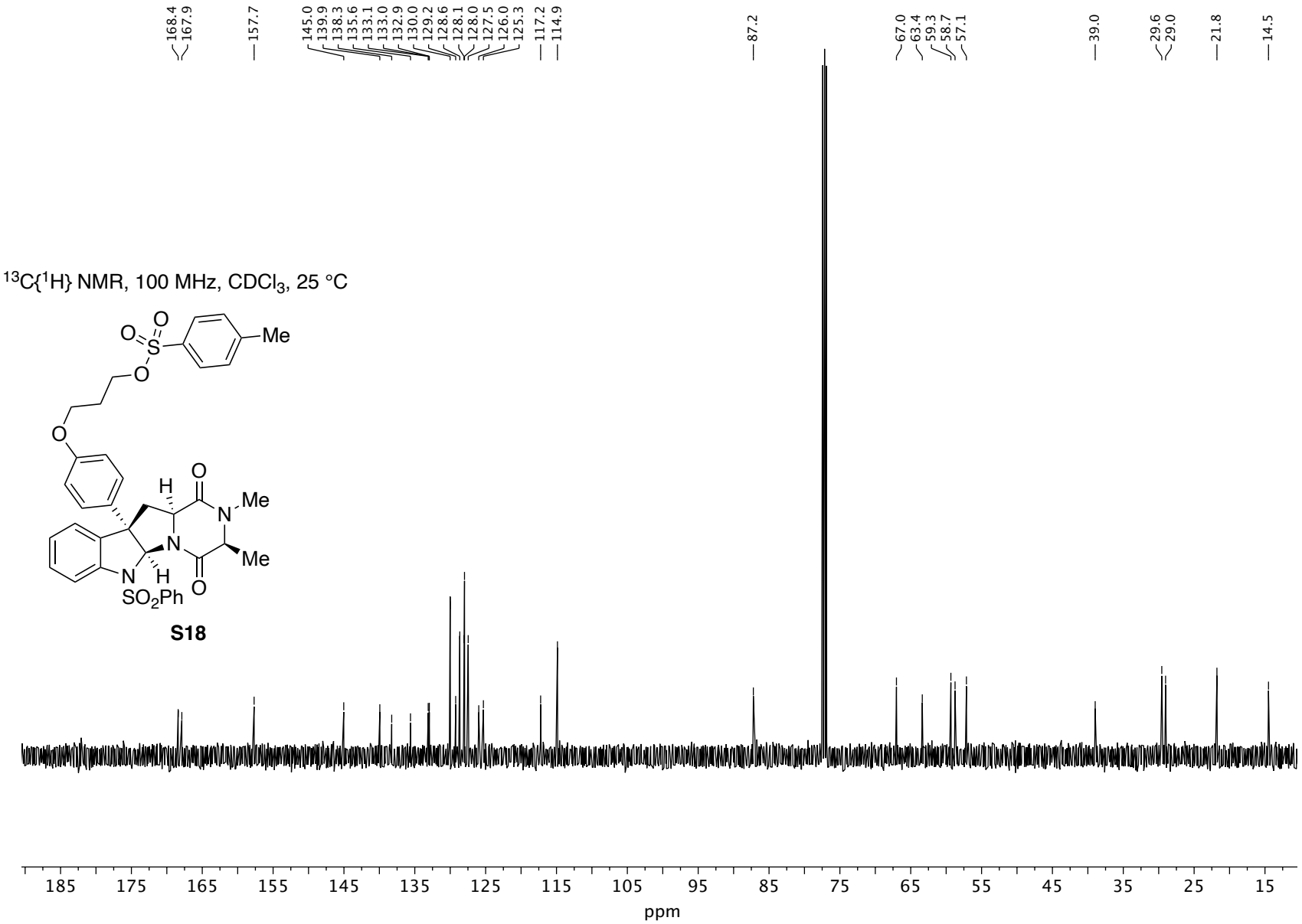


^{1}H NMR, 400 MHz, $CDCl_3$, 25 °C



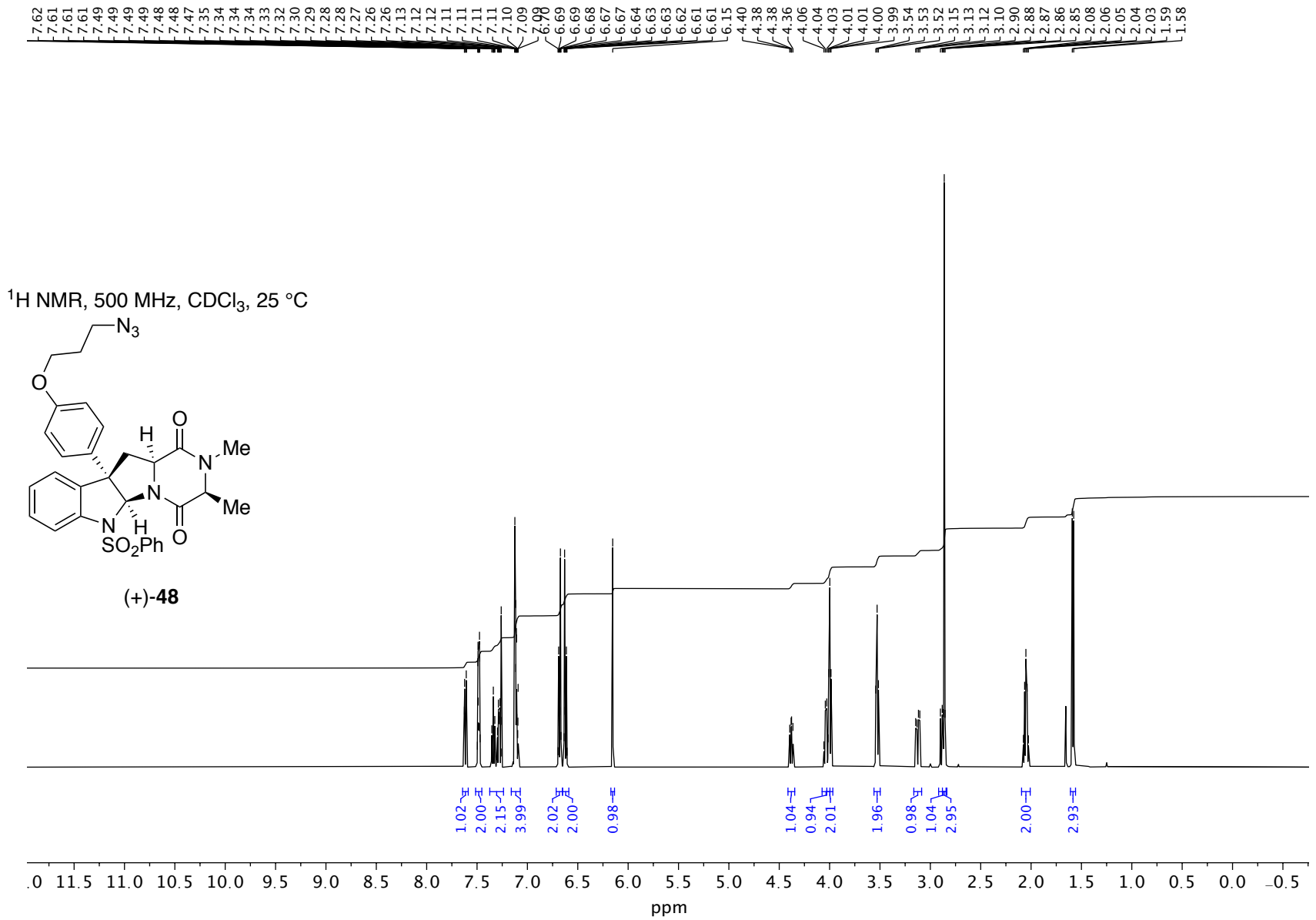
S18

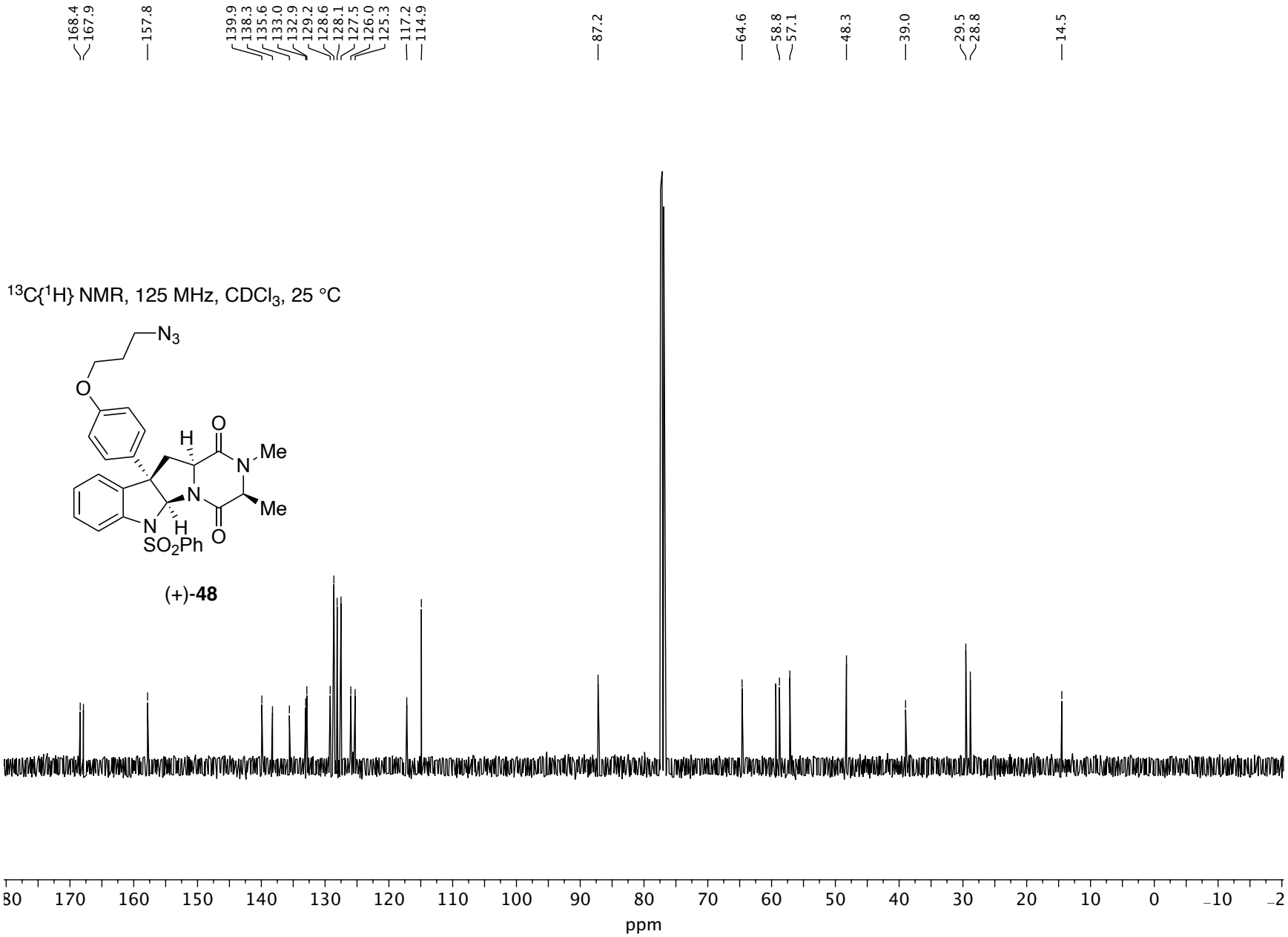


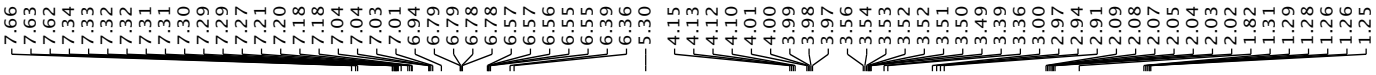


$^{13}C\{^{1}H\}$ NMR, 100 MHz, $CDCl_3$, 25 °C

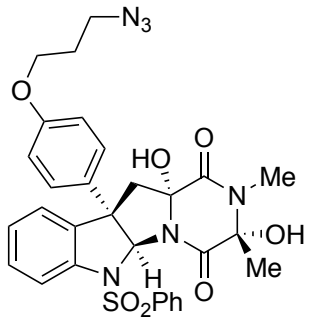
S18


7.62 7.61 7.61 7.61 7.49 7.49 7.49 7.49 7.48 7.48 7.47 7.35 7.34 7.34 7.34 7.33 7.32 7.30 7.29 7.28 7.28 7.27 7.26 7.26 7.13 7.12 7.12 7.11 7.11 7.11 7.11 7.10 7.09 7.00 6.69 6.69 6.68 6.67 6.67 6.64 6.63 6.63 6.62 6.61 6.61 6.15 4.40 4.38 4.38 4.36 4.06 4.04 4.03 4.01 4.01 4.00 3.99 3.54 3.53 3.52 3.15 3.13 3.12 3.10 2.90 2.88 2.87 2.86 2.85 2.08 2.06 2.05 2.04 2.03 1.59 1.58
1H NMR, 500 MHz, CDCl3, 25 °C
N3
O
H
O
N
Me
N
Me
N H
SO2Ph
O
(+)-48
1.02 2.00 2.15 3.99 2.02 2.00 0.98 1.04 0.94 2.01 1.96 0.98 1.04 2.95 2.00 2.93
.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
ppm

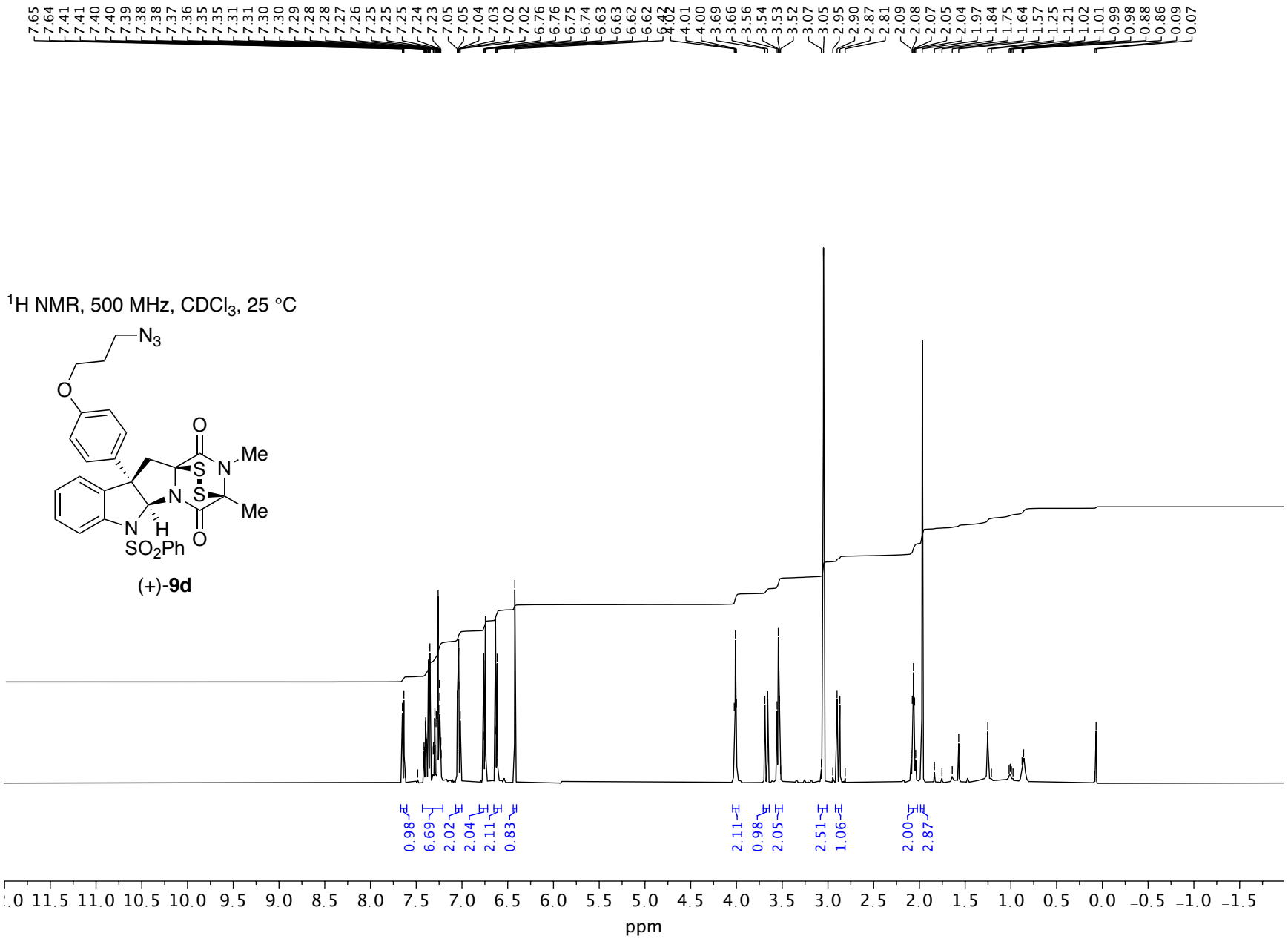

168.4
167.9
157.8
139.9
138.3
135.6
133.0
132.9
129.2
128.6
128.1
127.5
126.0
125.3
117.2
114.9
87.2
64.6
58.8
57.1
48.3
39.0
29.5
28.8
14.5
$^{13}C\{^{1}H\}$ NMR, 125 MHz, $CDCl_3$, 25 °C
N_3
O
H
O
N
Me
N
Me
N
H
SO_2Ph
O
(+)-**48**
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−2
ppm

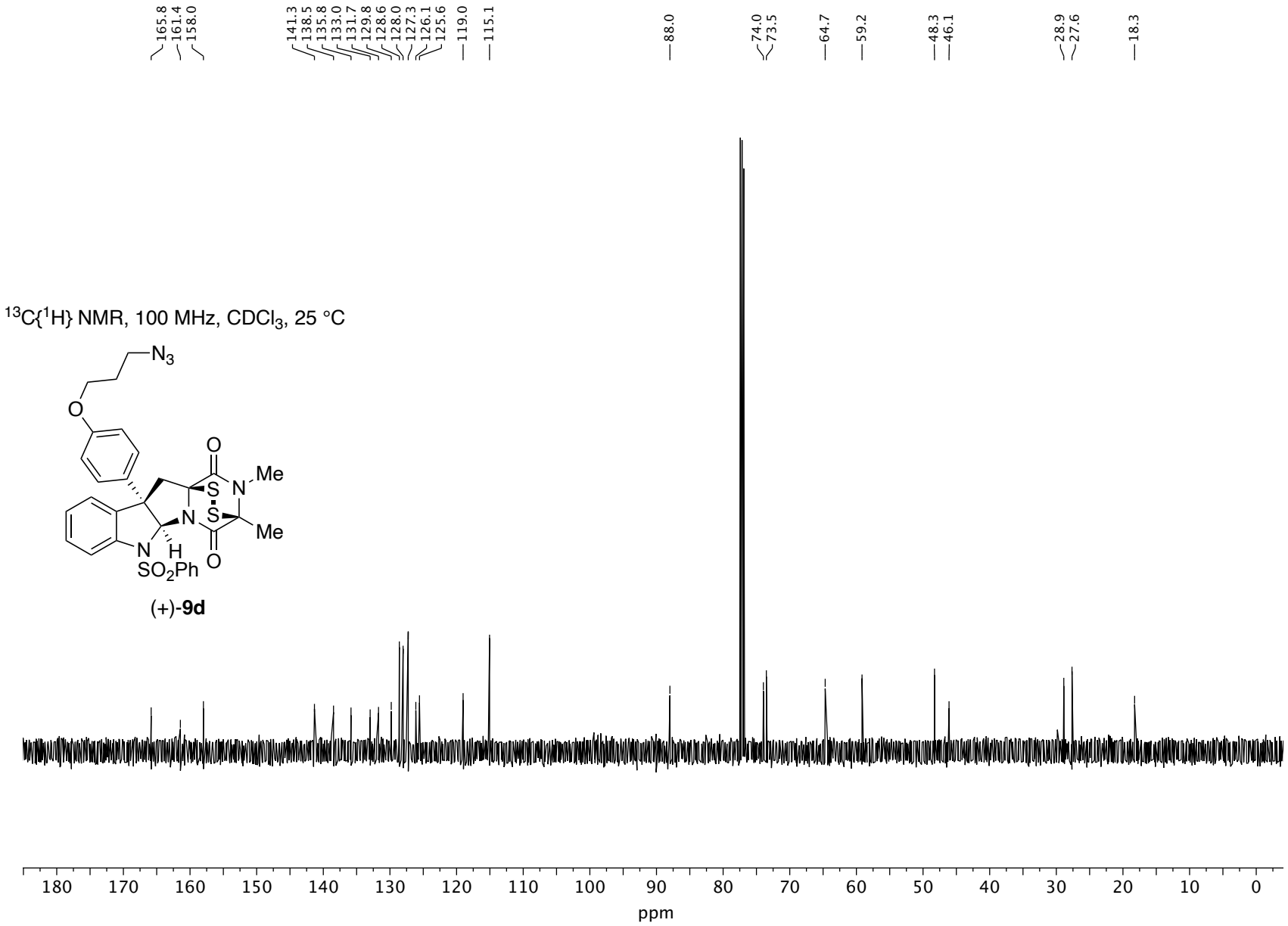


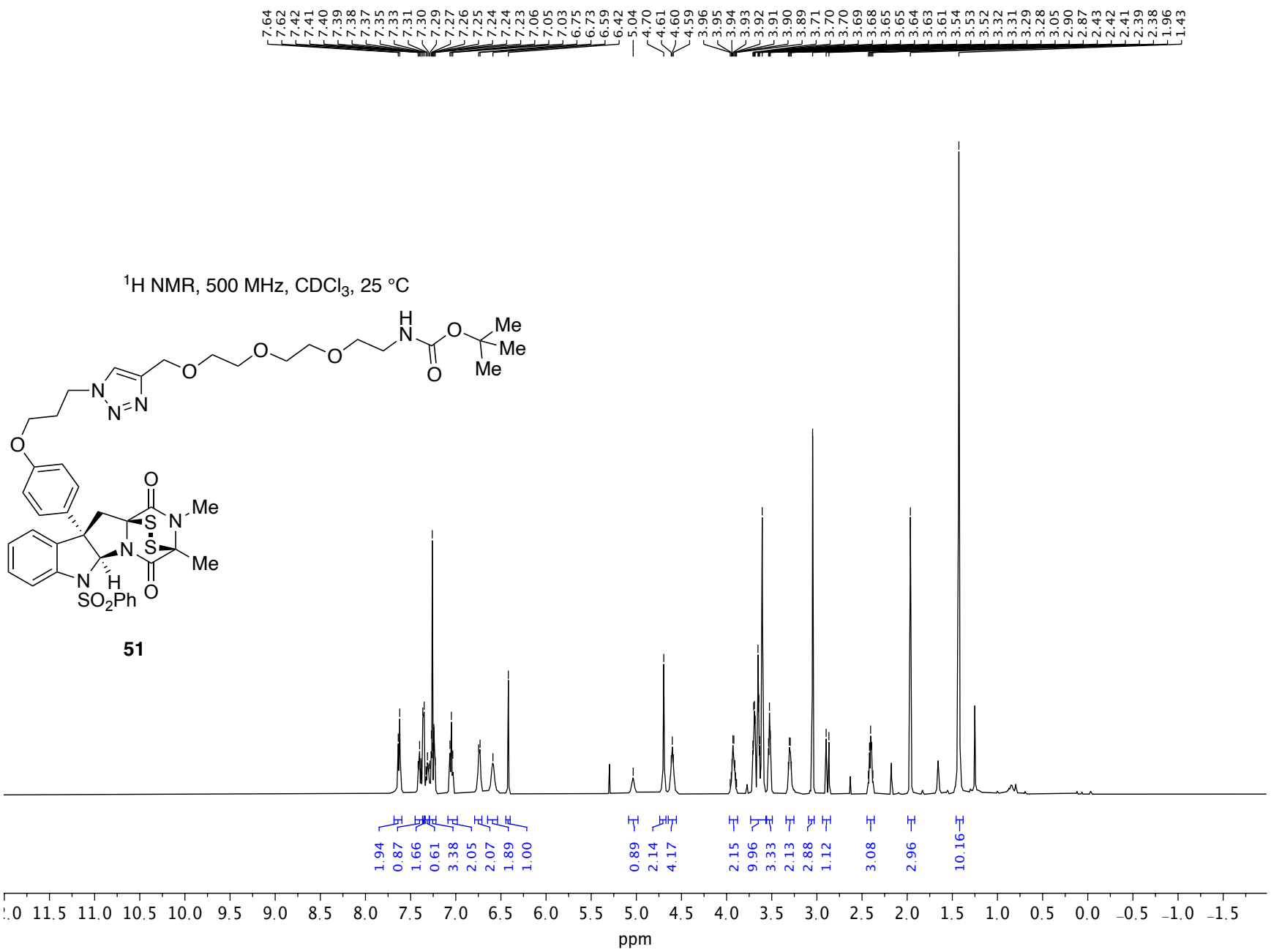
^{1}H NMR, 500 MHz, $CDCl_3$, 25 °C

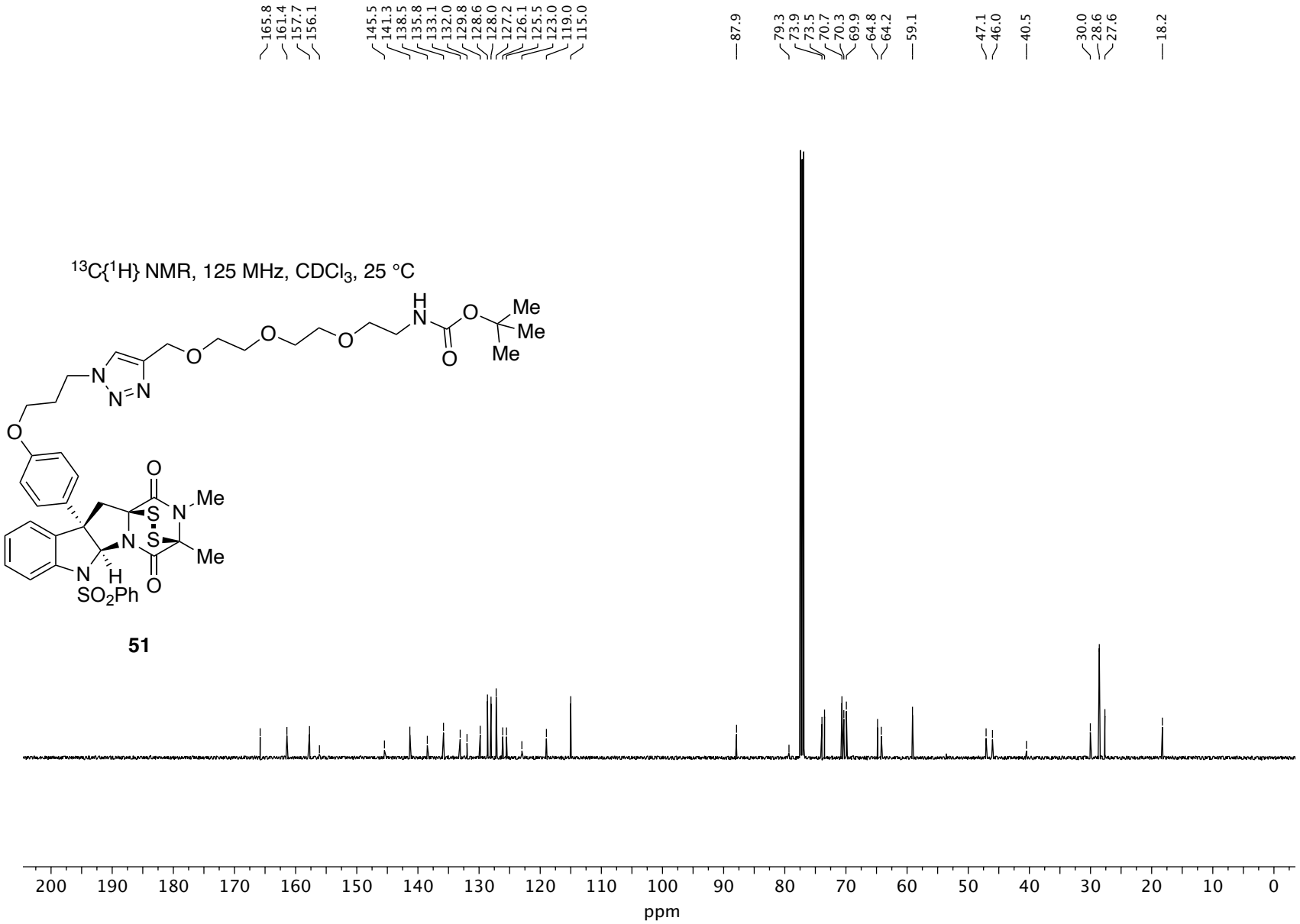


49


7.65 7.64 7.41 7.41 7.40 7.40 7.39 7.38 7.38 7.37 7.36 7.35 7.35 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.25 7.25 7.25 7.24 7.23 7.05 7.05 7.04 7.03 7.02 7.02 6.76 6.76 6.75 6.74 6.63 6.63 6.62 6.62 6.42 4.02 4.01 4.00 3.69 3.66 3.56 3.54 3.53 3.52 3.07 3.05 2.95 2.90 2.87 2.81 2.09 2.08 2.07 2.05 2.04 1.97 1.84 1.75 1.64 1.57 1.25 1.21 1.02 1.01 0.99 0.98 0.88 0.86 0.09 0.07
1H NMR, 500 MHz, CDCl3, 25 °C
N3
O
O
S
N
Me
N
S
Me
N
H
SO2Ph
O
(+)-9d
0.98 6.69 2.02 2.04 2.11 0.83 2.11 0.98 2.05 2.51 1.06 2.00 2.87
ppm


165.8
161.4
158.0
141.3
138.5
135.8
133.0
131.7
129.8
128.6
128.0
127.3
126.1
125.6
119.0
115.1
88.0
74.0
73.5
64.7
59.2
48.3
46.1
28.9
27.6
18.3
13C{1H} NMR, 100 MHz, CDCl3, 25 °C
N3
O
O
Me
S
N
N
S
Me
N
H
SO2Ph
O
(+)-9d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.64 7.62 7.42 7.41 7.40 7.39 7.38 7.37 7.35 7.33 7.31 7.30 7.29 7.27 7.26 7.25 7.24 7.24 7.23 7.06 7.05 7.03 6.75 6.73 6.59 6.42 5.04 4.70 4.61 4.60 4.59 3.96 3.95 3.94 3.93 3.92 3.91 3.90 3.89 3.71 3.70 3.70 3.69 3.68 3.65 3.65 3.64 3.63 3.61 3.54 3.53 3.52 3.32 3.31 3.29 3.28 3.05 2.90 2.87 2.43 2.42 2.41 2.39 2.38 1.96 1.43
1H NMR, 500 MHz, CDCl3, 25 °C
Me
Me
Me
Me
Me
SO2Ph
51
1.94 0.87 1.66 0.61 3.38 2.05 2.07 1.89 1.00 0.89 2.14 4.17 2.15 9.96 3.33 2.13 2.88 1.12 3.08 2.96 10.16
ppm


165.8
161.4
157.7
156.1
145.5
141.3
138.5
135.8
133.1
132.0
129.8
128.6
128.0
127.2
126.1
125.5
123.0
119.0
115.0
87.9
79.3
73.9
73.5
70.7
70.3
69.9
64.8
64.2
59.1
47.1
46.0
40.5
30.0
28.6
27.6
18.2
13C{1H} NMR, 125 MHz, CDCl3, 25 °C
51
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm