Concise Total Synthesis of (+)-Asperazine A and (+)-Pestalazine B

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Supporting Information

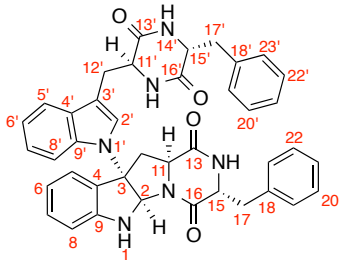
General Procedures. Unless otherwise stated, all reactions were performed under an argon atmosphere, either in oven-dried or flame-dried round bottom flasks, or modified Schlenk (Kjeldahl shape) flasks. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Where necessary (so noted), solutions were deoxygenated by argon purging for a minimum of 10 min. Flash column chromatography was performed as described by Still et al. using silica gel (60 Å pore size, 40–63 μm, 4–6% H_2O content).[1] Analytical thin–layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or an aqueous solution of ceric ammonium molybdate (CAM) followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on rotary evaporators at ~2 torr (house vacuum) at 25–35 °C, then at ~0.5 torr (vacuum pump) unless otherwise indicated.

Materials. Commercial reagents and solvents were used as received with the following exceptions: dichloromethane, acetonitrile, tetrahydrofuran, methanol, *N*,*N*-dimethylformamide and triethylamine were purchased from J. T. Baker (Cycletainer TM) and were purified by the method of Grubbs et al. under positive argon pressure.[2] Nitroethane was distilled over calcium hydride and stored neat; prior to use, it was dried over 4 Å molecular sieves for 2 hours. All amino acid derivatives, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, *N*-hydroxybenzotriazole, and *tert*-butyl-dimethylsilyl trifluoromethanesulfonate were purchased from Chem-Impex International; 2,6-di-*tert*-butyl-4-methylpyridine was purchased from Matrix Scientific. All other solvents and chemicals were purchased from either Sigma–Aldrich, Strem Chemicals, or Alfa Aesar–Johnson Matthey.

Instrumentation. Nuclear magnetic resonance (^{1}H and ^{13}C NMR) spectra were recorded with Varian inverse probe INOVA-500, Varian INOVA-500, and Bruker AVANCE III 400 spectrometers, and are reported in parts per million on the δ scale. ^{1}H NMR are referenced from the residual protium in the NMR solvent[3] (Acetone-d_6: δ 2.05 (Acetone-d_5), DMSO-d_6: δ 2.50 (DMSO-d_5). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet), coupling constant(s) in Hertz (Hz), integration, assignment]. ^{13}C NMR are referenced from the carbon resonances of the solvent (Acetone-d_6: δ 29.92, DMSO-d_6: δ 39.52). Data are reported as follows: chemical shift (assignment). Infrared data (IR) were obtained with a Perkin-Elmer 2000 FTIR, and are reported as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). Optical rotations were measured on a Jasco-1010 polarimeter. We are grateful to Dr. Li Li for obtaining the mass spectrometric data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics APEXIV 4.7 Tesla FTICR-MS using an electrospray (ESI) ionization source.

[1] Still, W. C.; Kahn M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[3] Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.

Positional Numbering System. At least three numbering systems for dimeric diketopiperazine alkaloids exist in the literature.[4] In assigning the ^{1}H NMR and ^{13}C NMR data of all intermediates en route to our total syntheses of (+)-asperazine A (**1**) and (+)-pestalazine B (**2**), we wished to employ a uniform numbering scheme. For ease of direct comparison, particularly between early intermediates, and advanced compounds, the numbering system used by Barrow for (+)-WIN-64821 (using positional numbers 1–21)[4b] is optimal and used throughout this report. In all instances, the products are accompanied by the numbering system as shown below.



(+)-asperazine A (**1**)
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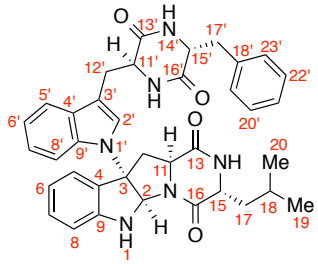

(+)-pestalazine B (**2**)
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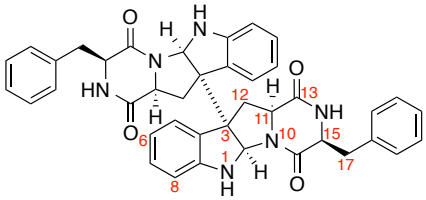
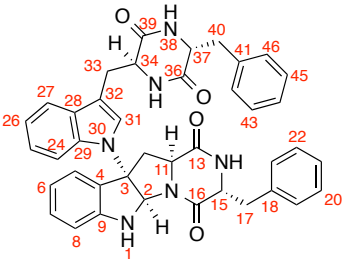
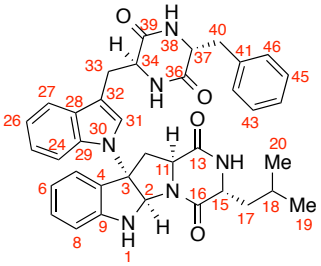


(+)-WIN-64821
Barrow's numbering for the simpler diketopiperazine framework

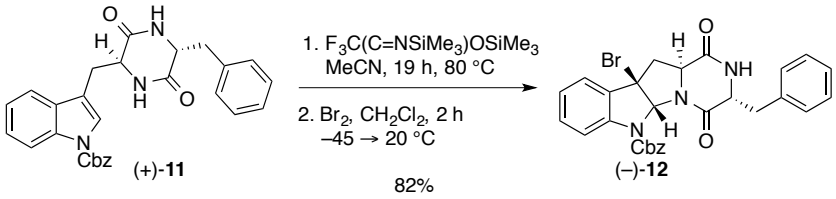


(+)-asperazine A (**1**)
Lou's isolation report



(+)-pestalazine B (**2**)
De Lera's synthesis

[4] (a) Barrow, C. J.; Cai, P.; Snyder, J. K.; Sedlock, D. M.; Sun, H. H.; Cooper, R. *J. Org. Chem.* **1993**, *58*, 6016. (b) Li, X.-B.; Li, Y.-L.; Zhou, J.-C.; Yuan, H.-Q.; Wang, X.-N.; Lou, H.-X. *J. Asian Nat. Prod. Res.* **2015**, *17*, 182. (c) Perez-Balado, C.; De Lera, A. R. *Org. Biomol. Chem.* **2010**, *8*, 5179.



D-Phenylalanine tetracyclic bromide (–)-12:

A flame-dried 100 mL round-bottomed flask equipped with a stir bar was charged with diketopiperazine (+)-**11** (1.13 g, 2.42 mmol, 1 equiv),[5] was dried azeotropically by concentration from anhydrous toluene (3 × 10 mL), was capped with a rubber septum and secured with copper wire. After additional drying under vacuum (1–2 Torr) for 2 h, anhydrous acetonitrile (15 mL) and *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (2.18 g, 8.46 mmol, 3.50 equiv) were added sequentially, and the reaction mixture was heated to 80 °C. After 19 h at 80 °C, volatiles were removed by concentration, taking care to avoid contact with air, and then drying under vacuum (1–2 Torr) for 2 days. The resulting orange oily semi-solid was too unstable to characterize, and it was used in the next step with no further purification.

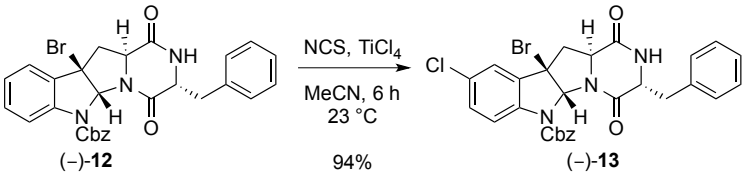
The crude semi-solid was dissolved in anhydrous dichloromethane (15 mL), was cooled to −45 °C, and bromine (130 μL, 2.54 mmol, 1.05 equiv) was added dropwise. The resulting light orange solution was allowed to warm to −20 °C over 2 h, at which point a saturated aqueous solution of sodium thiosulfate (30 mL) was added and the biphasic mixture was allowed to warm to 23 °C. The organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The organic layers were combined, were washed with a saturated aqueous solution of sodium chloride (150 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting light orange foamy solid was purified by flash column chromatography on silica gel (eluent: 8→15→25% acetone in dichloromethane) to afford exo-tetracyclic bromide (–)-**12** as a light yellow solid (1.08 g, 81.7%).

^{1}H NMR (400 MHz, Acetone-d_6, 20 ºC): δ 7.89 (d, J = 8.1 Hz, 1H, C_8**H**), 7.64 (app-d, J = 6.7 Hz, 2H, Ph_{Cbz}-*o*-C**H**), 7.51–7.45 (m, 2H, C_5**H**, C_7**H**), 7.41 (app-tt, J = 6.5, 1.1 Hz, 2H, Ph_{Cbz}-*m*-C**H**), 7.38–7.32 (m, 1H, Ph_{Cbz}-*p*-C**H**), 7.20 (td, J = 7.6, 1.0 Hz, 1H, C_6**H**), 6.95 (dd, J = 4.1, 3.3 Hz, 2H, C_{19}**H**, C_{23}**H**), 6.91–6.81 (m, 3H, $C_{20\text{-}22}$**H**), 6.50 (s, 1H, C_2**H**), 5.45 (d, J = 12.3 Hz, 1H, $Ph_{Cbz}C\mathbf{H_a}$), 5.35 (d, J = 12.2 Hz, 1H, $Ph_{Cbz}C\mathbf{H_b}$), 4.26 (app-q, J = 4.3 Hz, 1H, C_{15}**H**), 3.12 (dd, J = 13.5, 3.9 Hz, 1H, $C_{17}\mathbf{H_a}$), 3.01 (dd, J = 12.5, 5.4, 1H, $C_{12}\mathbf{H_a}$), 2.92 (dd, J = 13.5, 4.9 Hz, 1H, $C_{17}\mathbf{H_b}$), 2.72 (dd, J = 12.5, 11.6 Hz, 1H, $C_{12}\mathbf{H_a}$), 2.11 (dd, J = 11.8, 5.5 Hz, 1H, C_{11}**H**).

^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC): δ 167.1 (**C_{13}**), 165.7 (**C_{16}**), 153.6 (**C**=O_{Cbz}), 142.8 (**C_9**), 137.3 (Ph_{Cbz}-*ipso*-**C**), 135.9 (**C_{18}**), 132.7 (**C_4**), 131.8 (**C_7**), 130.9 (**C_{19}**, **C_{23}**), 129.3 (Ph_{Cbz}-*m*-**C**),

[5] For optimal synthesis of diketopiperazine (+)-**11**, see Supporting Information in: Loach, R. P.; Fenton, O. S.; Movassaghi, M. *J. Am. Chem.* **2016**, *138*, 1057.

	129.3 (Ph_{Cbz}-*o*-**C**), 129.0 (Ph_{Cbz}-*p*-**C**), 129.0 (**C_{20}**, **C_{22}**), 127.5 (**C_{21}**), 125.6 (**C_6**), 124.9 (**C_5**), 117.7 (**C_8**), 84.4 (**C_2**), 68.8 (Ph_{Cbz}**C**H_2), 60.3 (**C_3**), 59.0 (**C_{15}**), 58.5 (**C_{11}**), 44.4 (**C_{12}**), 41.1 (**C_{17}**).
FTIR (thin film) cm^{-1}	3270 (br-m), 3061 (w), 3031 (w), 1720 (s), 1684 (s), 1422 (m), 1270 (m), 1154 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{28}H_{25}BrN_3O_4$, $[M+H]^+$: 546.1023, found: 546.1029.
$[\alpha]_D^{23}$:	–102 (*c* = 0.19, $CHCl_3$).
TLC (20% acetone in dichloromethane), R*f*:	0.30 (UV, CAM).



6-Chloro-D-phenylalanine tetracyclic bromide (–)-13:

To a solution of tetracyclic bromide (–)-**12** (994 mg, 1.82 mmol, 1 equiv) in anhydrous acetonitrile (10.0 mL) at 23 °C was added *N*-chlorosuccinimide (NCS, 729 mg, 5.46 mmol, 3.00 equiv) in one portion. Titanium tetrachloride (1 M in dichloromethane, 5.46 mL, 5.46 mmol, 3.00 equiv) was added slowly dropwise via syringe, and the bright orange reaction mixture was stirred at 23 ºC. After 6 h, the reaction mixture was quenched by slow addition of a saturated aqueous solution of sodium bicarbonate (50 mL). The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 50 mL). The combined organic layers were then washed with a saturated aqueous solution of sodium thiosulfate (100 mL), were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure. The resulting dark orange residue was purified by flash column chromatography on silica gel (eluent: 18% acetone in dichloromethane) to furnish 6-chloro-tetracyclic bromide (–)-**13** as a pale yellow solid (990 mg, 93.6%).

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.88 (d, J = 8.7 Hz, 1H, C_8**H**), 7.66–7.62 (m, 2H, Ph_{Cbz}-*o*-C**H**), 7.57 (d, J = 2.2 Hz, 1H, C_5**H**), 7.52 (dd, J = 8.6, 2.2 Hz, 1H, C_7**H**), 7.45 (s, 1H, N_{14}**H**), 7.41 (dd, J = 8.2, 6.6 Hz, 2H, Ph_{Cbz}-*m*-C**H**), 7.39–7.33 (m, 1H, Ph_{Cbz}-*p*-C**H**), 7.00–6.93 (m, 2H, C_{19}**H**, **C_{23}**H), 6.92 (app-td, J = 5.9, 2.9 Hz, 3H, $C_{20\text{-}23}$**H**), 6.49 (s, 1H, C_2**H**), 5.44 (d, J = 12.2 Hz, 1H, $Ph_{Cbz}C$**H_a**), 5.35 (d, J = 12.2 Hz, 1H, $Ph_{Cbz}C$**H_b**), 4.26 (q, J = 4.2 Hz, 1H, C_{15}**H**), 3.10 (app-ddd, J = 18.4, 13.1, 4.7 Hz, 2H, C_{17}**H_a**, C_{12}**H_a**), 2.93 (dd, J = 13.5, 4.9 Hz, 1H, C_{17}**H_b**), 2.73 (t, J = 12.2 Hz, 1H, C_{12}**H_b**), 2.17 (dd, J = 11.8, 5.3 Hz, 1H, C_{11}**H**).

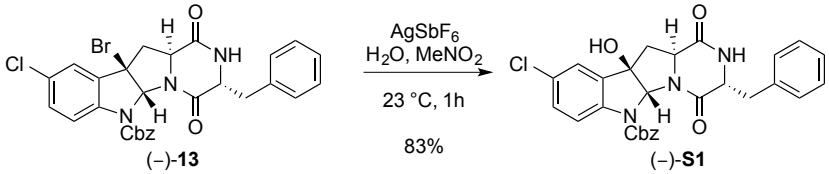
^{13}C NMR (100 MHz, Acetone-d_6, 20 ºC): δ 166.9 (**C_{13}**), 165.7 (**C_{16}**), 153.4 (**C**=O_{Cbz}), 141.6 (**C_9**), 137.2 (Ph_{Cbz}-*ipso*-**C**), 136.0 (**C_{18}**), 134.8 (**C_4**), 131.8 (**C_7**), 130.9 (**C_{19}**, **C_{23}**), 130.0 (**C_6**), 129.3 (Ph_{Cbz}-*m*-**C**H, Ph_{Cbz}-*o*-**C**H), 129.1 (**C_{20}**, **C_{22}**, Ph_{Cbz}-*p*-**C**H), 127.5 (**C_{21}**), 125.0 (**C_5**), 119.0 (**C_8**), 84.6 (**C_2**), 69.0 (Ph_{Cbz}**CH_2**), 59.2 (**C_3**), 59.0 (**C_{15}**), 58.5 (**C_{11}**), 43.9 (**C_{12}**), 41.1(**C_{17}**).

FTIR (thin film) cm^{-1}: 3232 (br-m), 3067 (w), 3030 (w), 1717 (s), 1682 (s), 1475 (s), 1419 (m), 1307 (m), 1253 (m), 1156 (m).

HRMS (ESI) (*m*/*z*): calc'd for $C_{28}H_{24}BrClN_3O_4$, $[M+H]^+$: 582.0625, found: 582.0639.

$[\alpha]_D^{23}$: –56 (*c* = 0.24, $CHCl_3$).

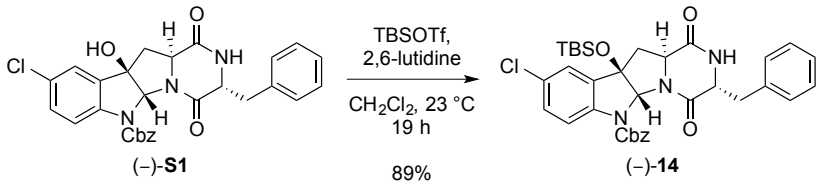
TLC (15% acetone in dichloromethane), R*f*: 0.29 (UV, CAM).



6-Chloro-D-phenylalanine tetracyclic alcohol (–)-S1:

Nitromethane (16.0 mL) and deionized water (290 μL, 16.1 mmol, 10.0 equiv) were sequentially added to a round-bottom flask charged with tetracyclic bromide (–)-**13** (935 mg, 1.61 mmol, 1 equiv) at 23 °C. The flask was opened to air and a solution of silver(I) hexafluoroantimonate (830 mg, 2.41 mmol, 1.50 equiv) in nitromethane (6.00 mL) was added by glass pipette over 1 min. The reaction flask was closed and the reaction mixture was stirred at 23 °C. After 1 h, a saturated aqueous solution of sodium chloride (50 mL) and dichloromethane (50 mL) were added sequentially, the organic layer was separated, and the aqueous layer was extracted with dichloromethane (3 × 50 mL). The organic layers were combined, were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to give a brown residue. This residue was purified by flash column chromatography on silica gel (eluent: 25→50% acetone in dichloromethane) to furnish chloro-tetracyclic alcohol (–)-**S1** as a white powder (689 mg, 82.6%).

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC):	δ 7.87 (d, J = 8.6 Hz, 1H, C_8**H**), 7.64 (d, J = 7.5 Hz, 2H, Ph_{Cbz}-*o*-C**H**), 7.46–7.27 (m, 6H, Ph_{Cbz}-*m*-C**H**, Ph_{Cbz}-*p*-C**H**, C_5**H**, C_7**H**, N_{14}**H**), 6.95 (m, 5H, C_{19-23}**H**), 6.14 (s, 1H, C_2**H**), 5.43 (s, 1H, C_3O**H**), 5.41 (d, J = 12.5 Hz, 1H, $Ph_{Cbz}C$**H$_a$**), 5.30 (d, J = 12.3 Hz, 1H, $Ph_{Cbz}C$**H$_b$**), 4.26 (q, J = 4.2 Hz, 1H, C_{15}**H**), 3.11 (dd, J = 13.5, 4.1 Hz, 1H, C_{17}**H$_a$**), 2.93 (dd, J = 13.5, 4.8 Hz, 1H, C_{17}**H$_b$**), 2.53 (dd, J = 13.2, 8.1 Hz, 1H, C_{12}**H$_a$**), 2.34–2.20 (m, 2H, C_{12}**H$_b$**, C_{11}**H**).
^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC):	δ 167.6 (**C_{13}**), 165.6 (**C_{16}**), 153.9 (**C**=O_{Cbz}), 143.0 (**C_9**), 137.4 (Ph_{Cbz}-*ipso*-**C**), 136.0 (**C_{18}**), 135.4 (**C_4**), 131.1 (**C_{19}**, **C_{23}**), 130.9 (**C_7**), 129.5 (**C_{20}**, **C_{22}**), 129.3 (Ph_{Cbz}-*o*-**C**H), 129.2 (**C_6**), 129.0 (Ph_{Cbz}-*p*-**C**H, Ph_{Cbz}-*m*-**C**H), 127.5 (**C_{21}**), 124.9 (**C_5**), 118.3 (**C_8**), 83.6 (**C_3**), 81.8 (**C_2**), 68.5 (Ph_{Cbz}**C**H_2), 58.8 (**C_{11}**), 58.2 (**C_{15}**), 41.8 (**C_{12}**), 41.3 (**C_{17}**).
FTIR (thin film) cm^{-1}	3253 (br-s), 3062 (w), 2923 (w), 1724 (s), 1669 (s), 1476 (s), 1441 (m), 1308 (s), 1256 (m), 1104 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{28}H_{25}ClN_3O_5$, $[M+H]^+$: 518.1477, found: 518.1472.
$[\alpha]_D^{23}$:	–44 (c = 0.24, $CHCl_3$).
TLC (25% acetone in dichloromethane), R*f*:	0.17 (UV, CAM).



D-Phenylalanine tetracyclic *tert*-butyldimethylsilyl ether (–)-14:

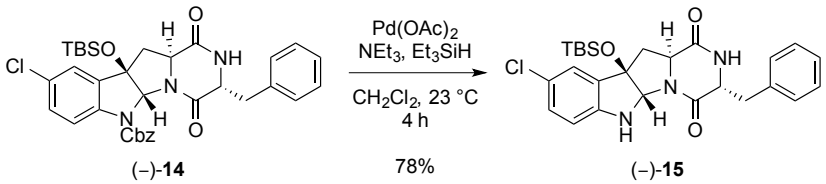
A sample of 2,6-lutidine (930 µL, 8.29 mmol, 7.97 equiv) was added via syringe to a a white slurry of tetracyclic alcohol (–)-**S1** (537 mg, 1.04 mmol, 1 equiv) in anhydrous dichloromethane (10.0 mL) at 23 °C. After 5 min, the slurry became a light yellow solution, whereupon *tert*-butyldimethylsilyl trifluoromethanesulfonate (953 µL, 4.15 mmol, 3.99 equiv) was added via syringe slowly dropwise over 3 min. After 19 h, a saturated aqueous solution of sodium bicarbonate (30 mL) was added to the reaction mixture and the organic layer was separated. The aqueous layer was extracted with dichloromethane (3 × 50 mL), the organic layers were combined, and were washed with a saturated aqueous solution of sodium chloride (100 mL). The organic phase was dried over anhydrous sodium sulfate, was filtered, and was concentrated under reduced pressure to give a yellow oil. This oil was dried azeotropically by concentration from toluene (3 × 20 mL) and the resulting waxy yellow solid was purified by flash column chromatography on silica gel (eluent: 15% acetone in dichloromethane) to give a yellow oil. This oil was placed under vacuum (1–2 Torr) overnight, delivering tetracyclic silyl ether (–)-**14** as a tan foamy solid (584 mg, 89.2%).

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.91 (d, J = 8.7 Hz, 1H, C_8**H**), 7.61 (d, J = 7.5 Hz, 2H, Ph_{Cbz}-*o*-C**H**), 7.51 (dd, J = 8.6, 2.2 Hz, 1H, C_7**H**), 7.45 (d, J = 2.1 Hz, 1H, C_5**H**), 7.42 (br-s, 1H, N_{14}**H**), 7.40 (app-t, J = 7.4 Hz, 2H, Ph_{Cbz}-*m*-C**H**), 7.34 (app- t, J = 7.4 Hz, 1H, Ph_{Cbz}-*p*-C**H**), 6.95 (m, 5H, $C_{19\text{-}23}$**H**), 6.12 (s, 1H, C_2**H**), 5.47 (d, J = 12.3 Hz, 1H, $Ph_{Cbz}C$**H$_a$**), 5.31 (d, J = 12.2 Hz, 1H, $Ph_{Cbz}C$**H$_b$**), 4.25 (q, J = 4.2 Hz, 1H, C_{15}**H**), 3.12 (dd, J = 13.5, 4.0 Hz, 1H, C_{17}**H**), 2.93 (dd, J = 13.2, 4.6 Hz, 1H, C_{17}**H**), 2.61 (dd, J = 12.1, 5.2 Hz, 1H, C_{12}**H$_a$**), 2.28 (t, J = 12.1 Hz,1H, C_{12}**H$_a$**), 2.18 (dd, J = 12.3, 5.2 Hz, 1H, C_{11}**H**), 0.77 (s, 9H, SiC(C**H$_3$**)$_3$), –0.26 (s, 3H, SiC**H$_{3a}$**), –0.27 (s, 3H, SiC**H$_{3b}$**).

^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC): δ 167.5 (**C$_{13}$**), 165.9 (**C$_{16}$**), 153.7 (**C**=O_{Cbz}), 143.1 (**C$_9$**), 137.4 (Ph_{Cbz}-*ipso*-**C**), 136.0 (**C$_{18}$**), 134.4 (**C$_4$**), 131.4 (**C$_7$**), 131.0 (**C$_{19}$**, **C$_{23}$**), 129.4 (**C$_{20}$**, **C$_{22}$**), 129.3 (**C$_6$**, Ph_{Cbz}-*o*-**C**H), 129.1 (Ph_{Cbz}-*m*-**C**H), 129.0 (Ph_{Cbz}-*p*-**C**H), 127.5 (**C$_{21}$**), 125.5 (**C$_5$**), 118.7 (**C$_8$**), 85.3 (**C$_3$**), 81.4 (**C$_2$**), 68.6 ($Ph_{Cbz}C$**H$_2$**), 58.8 (**C$_{15}$**), 57.9 (**C$_{11}$**), 42.4 (**C$_{12}$**), 41.2 (**C$_{17}$**), 25.8 (SiC(**C**H$_3$)$_3$), 18.5 (Si**C**(CH$_3$)$_3$), –3.4 (Si**C$_a$**H$_3$), –3.7 (Si**C$_b$**H$_3$).

FTIR (thin film) cm^{-1} 3227 (br-m), 3063 (w), 2857 (w), 1717 (m), 1682 (s), 1473 (s), 1420 (m), 1252 (s), 1146 (m), 1095 (m).

HRMS (ESI) (*m*/*z*):	calc'd for $C_{34}H_{39}ClN_3O_5Si$, $[M+H]^+$: 632.2342, found: 632.2344.
$[\alpha]_D^{23}$:	–36 (*c* = 0.71, $CHCl_3$).
TLC (15% acetone in dichloromethane), R*f*:	0.40 (UV, CAM).

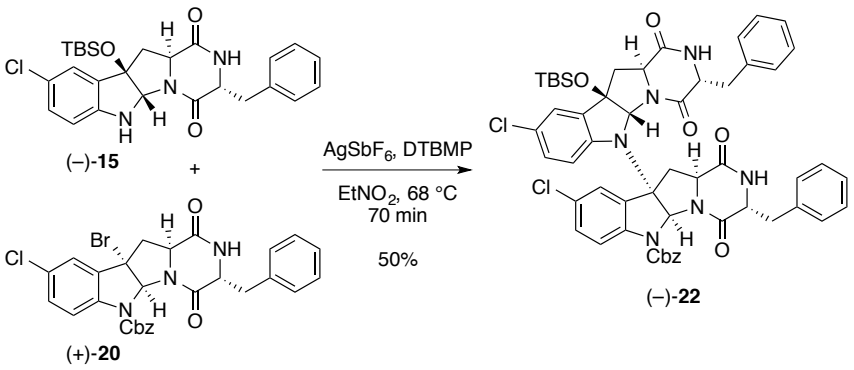


(–)-**14** (–)-**15**

D-Phenylalanine tetracyclic indoline (–)-15:

Tetracyclic ether (–)-**14** (580 mg, 917 μmol, 1 equiv) was dissolved in anhydrous dichloromethane (4.50 mL) at 23 °C. In a separate flame-dried, pear-shaped flask, triethylamine (32.0 μL, 229 μmol, 25.0 mol%) and triethylsilane (220 μL, 1.38 mmol, 1.50 equiv) were added sequentially to palladium(II) acetate (14.4 mg, 64.2 μmol, 7.0 mol%) in anhydrous dichloromethane (1.00 mL). The orange solution instantly turned black, and this was cannulated rapidly into the main reaction mixture and stirred at 23 °C. After 4 h, the reaction mixture was concentrated under reduced pressure to give a black residue. The residue was purified by flash column chromatography on silica gel (eluent: 30→50% acetone in dichloromethane) to afford tetracyclic indoline (–)-**15** as a white powder (356 mg, 78.0%).

^{1}H NMR (500 MHz, DMSO-d_6, 20 ºC):	δ 8.22 (s, 1H, N_{14}**H**), 7.18 (app-dd, J = 9.1, 1.8 Hz, 2H, C_5**H**, C_7**H**), 7.13–7.04 (m, 3H, N_1**H**, C_{19}**H**, C_{23}**H**), 6.97–6.89 (m, 3H, $C_{20\text{-}22}$**H**), 6.69 (d, J = 9.0 Hz, 1H, C_8**H**), 5.08 (s, 1H, C_2**H**), 4.12 (q, J = 4.0 Hz, 1H, C_{15}**H**), 3.07 (dd, J = 13.4, 3.6 Hz, 1H, C_{17}**H$_a$**), 2.80 (dd, J = 13.4, 5.1 Hz, 1H, C_{17}**H$_b$**), 2.48 (dd, J = 12.3, 5.4 Hz, 1H, C_{12}**H$_a$**), 2.02 (t, J = 12.0 Hz, 1H, C_{12}**H$_b$**), 1.95 (dd, J = 12.3, 5.0 Hz, 1H, C_{11}**H**), 0.77 (s, 9H, SiC(C**H$_3$**)$_3$), –0.15 (s, 3H, SiC**H$_{3a}$**), –0.28 (s, 3H, SiC**H$_{3b}$**).
^{13}C NMR (125 MHz, DMSO-d_6, 20 ºC):	δ 167.1 (**C$_{13}$**), 165.1 (**C$_{16}$**), 150.0 (**C$_9$**), 134.8 (**C$_{18}$**), 130.2 (**C$_{19}$**, **C$_{23}$**), 130.0 (**C$_5$**), 129.2 (**C$_4$**), 128.0 (**C$_{20}$**, **C$_{22}$**), 126.4 (**C$_{21}$**), 124.4 (**C$_7$**), 120.6 (**C$_6$**), 110.5 (**C$_8$**), 86.1 (**C$_3$**), 79.5 (**C$_2$**), 56.7 (**C$_{15}$**), 56.2 (**C$_{11}$**), 42.1 (**C$_{12}$**), 39.6 (**C$_{17}$**), 25.4 (SiC(**C**H$_3$)$_3$), 17.5 (Si**C**(CH$_3$)$_3$), –3.7 (Si**C$_a$**H$_3$), –4.0 (Si**C$_b$**H$_3$).
FTIR (thin film) cm^{-1}	3289 (br-m), 3236 (br-m), 2854 (w), 1682 (s), 1641 (m), 1452 (m), 1252 (w), 1176 (w), 1106 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{26}H_{33}ClN_3O_3Si$, $[M+H]^+$: 498.1974, found: 498.1972.
$[\alpha]_D^{23}$:	–249 (*c* = 0.11, MeOH).
TLC (30% acetone in dichloromethane), R*f*:	0.65 (UV, CAM).



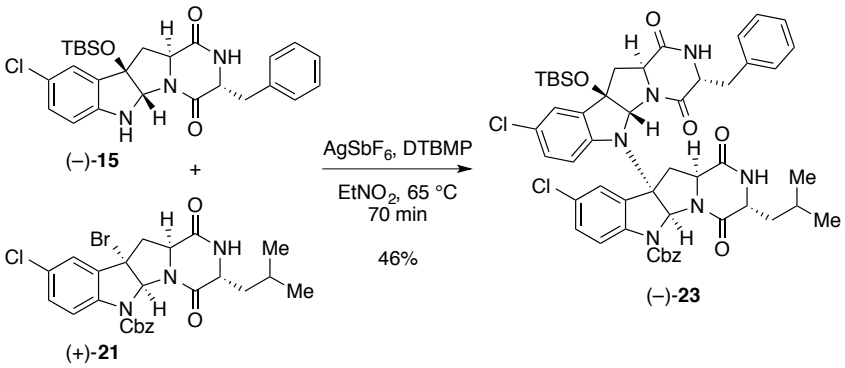
Bis-D-phenylalanine dimer (–)-22:

Two 50–mL flame-dried Schlenk (Kjeldahl shape) flasks were equipped with a magnetic stir bar. The first flask was charged with tetracyclic indoline (–)-**15** (196 mg, 394 μmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (162 mg, 788 μmol, 2.00 equiv), and tetracyclic bromide (+)-**20** (298 mg, 512 μmol, 1.30 equiv).[6] The second flask was also charged with tetracyclic indoline (–)-**15** (136 mg, 272 μmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (112 mg, 272 μmol, 2.00 equiv), and tetracyclic bromide (+)-**20** (206 mg, 354 μmol, 1.30 equiv). The mixture of solids in each flask was crushed with the end of a glass rod into a fine powder, anhydrous acetonitrile (10 mL, 10 mL, respectively) was added and the mixture was stirred and sonicated to give a milky solution. Benzene (10 mL, 10 mL, respectively) was introduced into each reaction flask and the contents were dried azeotropically by concentration under reduced pressure. This addition of acetonitrile (10 mL), sonication for 3 min, followed by addition of benzene (10 mL), and concentration under reduced pressure was repeated two more times for each reaction flask. The resulting finely-powdered off-white contents were dried by concentration from freshly-distilled benzene (3 × 10 mL) under reduced pressure, and the respective mixtures in the two reaction flasks were placed under vacuum (1–2 Torr) for 14 hours. Each flask was then placed under an argon atmosphere, nitroethane (19.5 mL, 12.5 mL, respectively) was added to each flask, and the resulting reaction mixtures were warmed to 68 °C and stirred vigorously to completely dissolve the contents. In two pear-shaped 10 mL flasks, separate suspensions of silver(I) hexafluoroantimonate (271 mg, 788 μmol, 2.00 equiv) in nitroethane (3.10 mL) and silver(I) hexafluoroantimonate (187 mg, 544 μmol, 2.00 equiv) in nitroethane (2.00 mL) were prepared under argon atmosphere. These suspensions were warmed to 68 °C. The two suspensions were transferred rapidly (<10 seconds) and in one portion via cannulae to the respective reactions vessels containing the indoline (–)-**15**. The resulting light yellow reaction mixtures were stirred vigorously at 68 °C and resulted in dark brown mixtures. After 70 min, the dark purple–brown reaction mixtures were cooled to 23 °C independently. Each reaction mixture was diluted with a saturated aqueous solution of sodium chloride (20 mL, 20 mL, respectively) and dichloromethane (10 mL, 10 mL, respectively) were added sequentially to each mixture separately and the organic phases were separated. In each case the aqueous phase was extracted with dichloromethane (3 × 50 mL), and the combined organic layers for each batch were washed with a saturated solution of sodium chloride (150 mL), were dried over anhydrous sodium sulfate, were filtered over celite, and were concentrated under reduced pressure to give the corresponding two batches of crude product as light yellow solids. The two batches of solid crude material were combined and purified together by flash column chromatography on silica gel (eluent: 8→12→18→25% acetone in dichloromethane), including a

[6] For optimal synthesis of endocyclic bromide (+)-**20**, see: Loach, R. P.; Fenton, O. S.; Movassaghi, M. *J. Am. Chem.* **2016**, *138*, 1057.

second chromatographic purification of a mixed fraction of product (–)-**22** and indoline (–)-**15** on silica gel (eluent: 25% acetone in dichloromethane), to yield dimer (–)-**22** as a tan powder (331 mg, 49.9%).

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC):	δ 7.82 (d, J = 8.7 Hz, 2H, C_8**H**), 7.47–7.28 (m, 10H, C_5**H**, C_7**H**, Ph_{Cbz}**H**$_5$, $C_{20\text{-}22}$**H**), 7.24 (d, J = 7.6 Hz, 2H, C_{19}**H**, C_{23}**H**), 7.22 (d, J = 2.2 Hz, 1H, C_5'**H**), 7.18 (d, J = 8.3 Hz, 1H, C_7'**H**), 6.94 (d, J = 7.4 Hz, 2H, C_{19}'**H**, C_{23}'**H**), 6.88 (t, J = 7.4 Hz, 1H, C_{21}'**H**), 6.79 (t, J = 7.5 Hz, 2H, C_{20}'**H**, C_{22}'**H**), 6.61 (s, 1H, C_2**H**), 6.13 (d, J = 8.5 Hz, 1H, C_8'**H**), 5.30 (d, J = 12.3 Hz, 1H, Ph_{Cbz}**H**$_a$), 5.27 (d, J = 12.3 Hz, 1H, Ph_{Cbz}**H**$_b$), 5.21 (s, 1H, C_2'**H**), 4.26 (q, J = 3.4 Hz, 1H, C_{15}**H**), 4.10 (q, J = 5.1 Hz, 1H, C_{15}'**H**), 3.82 (t, J = 8.6 Hz, 1H, C_{11}**H**), 3.21 (dd, J = 13.5, 6.5 Hz, 1H, C_{17}'**H**$_a$), 3.17 (t, J = 8.3 Hz, 1H, C_{12}**H**$_a$), 3.04 (t, J = 4.0 Hz, 1H, C_{17}**H**$_a$), 3.01 (t, J = 4.0 Hz, 1H, C_{17}**H**$_b$), 2.99–2.95 (m, 1H, C_{12}**H**$_b$), 2.87 (dd, J = 13.6, 5.0 Hz, 1H, C_{17}'**H**$_b$), 2.52 (dd, J = 11.9, 5.5 Hz, 1H, C_{12}'**H**$_a$), 2.17 (t, J = 12.0 Hz, 1H, C_{12}'**H**$_b$), 1.99 (dd, J = 12.3, 5.8 Hz, 1H, C_{11}'**H**), 0.70 (s, 9H, SiC(C**H**$_3$)$_3$), 0.06 (s, 3H, SiC**H**$_{3a}$), –0.29 (s, 3H, SiC**H**$_{3b}$).
^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC):	δ 168.4 (**C**$_{13}$), 168.0 (**C**$_{13}'$), 167.6 (**C**$_{16}$), 167.2 (**C**$_{16}'$), 153.3 (**C**=O_{Cbz}), 147.2 (**C**$_9'$), 141.7 (**C**$_9$), 137.4 (Ph_{Cbz}-*ipso*-**C**), 137.1 (**C**$_{18}$), 136.1 (**C**$_{18}'$), 135.4 (**C**$_4$), 134.3 (**C**$_4'$), 130.9 (**C**$_7$, **C**$_{19}$, **C**$_{23}$), 130.4 (**C**$_{19}'$, **C**$_{23}'$), 129.7 (**C**$_7'$), 129.4 (**C**$_6'$), 129.3 (**C**$_{20}$, **C**$_{22}$), 129.0 (Ph_{Cbz}-*o*-**C**H, Ph_{Cbz}-*m*-**C**H), 128.9 (**C**$_6$, Ph_{Cbz}-*p*-**C**H), 128.0 (**C**$_{21}$, **C**$_{20}'$, **C**$_{22}'$), 127.4 (**C**$_{21}'$), 125.4 (**C**$_5$), 125.2 (**C**$_5'$), 118.0 (**C**$_8$), 115.3 (**C**$_8'$), 85.8 (**C**$_2'$), 84.3 (**C**$_3'$), 80.2 (**C**$_2$), 72.3 (**C**$_3$), 68.5 (Ph_{Cbz}**C**H_2), 59.8 (**C**$_{15}'$), 59.0 (**C**$_{15}$), 58.8 (**C**$_{11}'$), 55.9 (**C**$_{11}$), 40.9 (**C**$_{17}'$), 40.3 (**C**$_{17}$), 38.8 (**C**$_{12}'$), 36.5 (**C**$_{12}$), 26.1 (SiC(**C**H_3)$_3$), 18.5 (Si**C**$(CH_3)_3$), –2.7(Si**C**$_a$$H_3$), –3.0(Si**C**$_b$$H_3$).
FTIR (thin film) cm^{-1}	3225 (br-w), 3062 (w), 2857 (w), 1675 (br-s), 1476 (m), 1437 (m), 1319 (m), 1265 (m), 1101 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{54}H_{55}Cl_2N_6O_7Si$, $[M+H]^+$: 997.3273, found: 997.3258.
$[\alpha]_D^{23}$:	–4 (c = 0.13, $CHCl_3$).
TLC (18% acetone in dichloromethane), R*f*:	0.22 (UV, CAM).



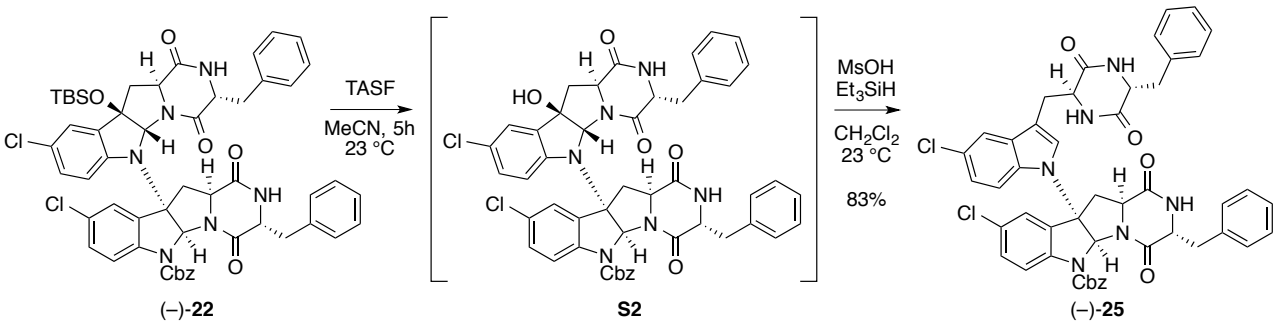
D-Phenylalanine D-leucine dimer (–)-23:

A 25 mL flame-dried Schlenk (Kjeldahl shape) flask equipped with a magnetic stir bar was charged with tetracyclic indoline (–)-**15** (38.5 mg, 79.0 μmol, 1 equiv), 2,6-di-*tert*-butyl-4-methylpyridine (32.5 mg, 158 μmol, 2.00 equiv) and tetracyclic bromide (+)-**21** (56.2 mg, 103 μmol, 1.30 equiv).[7] The mixture of solids was crushed with the end of a glass rod into a fine powder, anhydrous acetonitrile (5 mL) was added and the mixture was stirred and sonicated to give a milky solution. Benzene (5 mL) was added and the contents were dried azeotropically. This addition of acetonitrile (5 mL), sonication, addition of benzene (5 mL) and azeotropic drying was repeated twice more. The resulting finely-powdered off-white contents were dried azeotropically with freshly-distilled benzene (3 × 5 mL), and this mixture was placed under vacuum (1–2 Torr) overnight. The flask was then placed under an argon atmosphere, nitroethane (3.6 mL) was added, and the reaction mixture was heated to 65 °C and stirred vigorously to completely dissolve the contents. In a pear-shaped 10 mL flask, a separate solution/suspension of silver(I) hexafluoroantimonate (54.3 mg, 158 μmol, 2.00 equiv) in nitroethane (1.30 mL) was prepared under an argon atmosphere, was heated to 65 °C, and then cannulated rapidly into the reaction mixture (also at 65 °C) in one portion using a short cannula (<10 sec). The light yellow reaction mixture was stirred vigorously at 65 °C, rapidly turning dark brown. After 70 min, the dark purple/brown reaction mixture was cooled to 23 °C, a saturated aqueous solution of sodium chloride (10 mL) and dichloromethane (10 mL) were added sequentially to the reaction mixture and the organic phase was separated. The aqueous phase was extracted with dichloromethane (3 × 10 mL), and the combined organic layers were washed with a saturated solution of sodium chloride (50 mL), were dried over anhydrous sodium sulfate, were filtered over celite, and were concentrated under reduced pressure to give a light yellow solid. This crude material was purified by flash column chromatography on silica gel (eluent: 8→12→18→25% acetone in dichloromethane), including a second chromatographic purification of a mixed fraction of product (–)-**23** and indoline (–)-**15** on silica gel (eluent: 20% acetone in dichloromethane), to yield dimer (–)-**23** as a tan powder (33.7 mg, 45.7%).

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.81 (d, J = 8.6 Hz, 1H, C_8**H**), 7.77 (d, J = 2.3 Hz, 1H, C_5**H**), 7.41–7.26 (m, 7H, C_7**H**, Ph_{Cbz}**H**, N_{14}′**H**), 7.21 (d, J = 2.3 Hz, 1H, C_5′**H**), 7.10–7.05 (m, 2H, C_7′**H**, N_{14}**H**), 6.95 (d, J = 7.5 Hz, 2H, C_{19}′**H**, C_{23}′**H**), 6.86 (dd, J = 8.1, 5.9 Hz, 1H, C_{21}′**H**), 6.79 (t, J = 7.4 Hz, 2H, C_{20}′**H**, C_{22}′**H**), 6.73 (s, 1H, C_2**H**), 6.38 (d, J = 8.6 Hz, 1H, C_8′**H**), 5.36 (s, 1H, C_2′**H**), 5.25 (app-q,

[7] For optimal synthesis of endocyclic bromide (+)-**21**, see: Loach, R. P.; Fenton, O. S.; Movassaghi, M. *J. Am. Chem.* **2016**, *138*, 1057.

	J = 12.4 Hz, 2H, $Ph_{Cbz}C\mathbf{H_2}$), 4.90 (dd, *J* = 10.1, 4.7 Hz, 1H, $C_{11}\mathbf{H}$), 4.23 (t, *J* = 4.2 Hz, 1H, $C_{15}'\mathbf{H}$), 3.76 (dt, *J* = 9.6, 5.0 Hz, 1H, $C_{15}\mathbf{H}$), 3.57 (dd, *J* = 14.1, 10.4 Hz, 1H, $C_{12}\mathbf{H_a}$), 3.48 (dd, *J* = 14.1, 4.7 Hz, 1H, $C_{12}\mathbf{H_b}$), 2.98 (dd, *J* = 13.5, 3.7 Hz, 1H, $C_{17}'\mathbf{H_a}$), 2.83 (app-d, *J* = 5.0 Hz, 1H, $C_{17}'\mathbf{H_b}$), 2.53 (dd, *J* = 11.9, 5.6 Hz, 1H, $C_{12}'\mathbf{H_a}$), 2.18 (app-t, *J* = 12.0 Hz, 1H, $C_{12}'\mathbf{H_b}$), 2.00 (dd, *J* = 12.2, 5.7 Hz, 1H, $C_{11}'\mathbf{H}$), 1.78 (app-ddd, *J* = 19.0, 10.0, 5.7 Hz, 2H, $C_{17}\mathbf{H_a}$, $C_{18}\mathbf{H}$), 1.61 (ddd, *J* = 13.8, 8.5, 5.5 Hz, 1H, $C_{17}\mathbf{H_b}$), 0.99 (d, *J* = 6.3 Hz, 3H, $C_{19}\mathbf{H}$), 0.95 (d, *J* = 6.4 Hz, 3H, $C_{20}\mathbf{H}$), 0.77 (s, 9H, $SiC(C\mathbf{H_3})_3$), 0.11 (s, 3H, $SiC\mathbf{H_{3a}}$), –0.25 (s, 3H, $SiC\mathbf{H_{3b}}$).
^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC):	δ 168.8 ($\mathbf{C_{13}}$, $\mathbf{C_{16}}$), 168.0 ($\mathbf{C_{13}}'$), 167.4 ($\mathbf{C_{16}}'$), 153.5 ($\mathbf{C}{=}O_{Cbz}$), 147.5 ($\mathbf{C_9}'$), 141.8 ($\mathbf{C_9}$), 137.1 (Ph_{Cbz}-*ipso*-**C**), 136.0 ($\mathbf{C_{18}}'$), 134.8 ($\mathbf{C_4}$), 134.0 ($\mathbf{C_4}'$), 130.9 ($\mathbf{C_{19}}'$, $\mathbf{C_{23}}'$, $\mathbf{C_7}$), 130.5 ($\mathbf{C_5}'$), 129.2 (Ph_{Cbz}-*o*-**C**), 129.0 (Ph_{Cbz}-*m*-**C**, Ph_{Cbz}-*p*-**C**, $\mathbf{C_6}$), 128.9 ($\mathbf{C_{20}}'$, $\mathbf{C_{22}}'$), 128.8 ($\mathbf{C_5}$), 127.3 ($\mathbf{C_{21}}'$), 125.2 ($\mathbf{C_6}'$), 125.0 ($\mathbf{C_7}'$), 118.2 ($\mathbf{C_8}$), 115.2 ($\mathbf{C_8}'$), 85.8 ($\mathbf{C_2}'$), 84.2 ($\mathbf{C_3}'$), 80.8 ($\mathbf{C_2}$), 72.8 ($\mathbf{C_3}$), 68.4 ($Ph_{Cbz}\mathbf{C}H_2$), 58.9 ($\mathbf{C_{11}}'$, $\mathbf{C_{15}}'$), 57.1 ($\mathbf{C_{15}}$), 56.5 ($\mathbf{C_{11}}$), 41.9 ($\mathbf{C_{17}}$), 41.0 ($\mathbf{C_{17}}'$), 38.9 ($\mathbf{C_{12}}'$), 34.7 ($\mathbf{C_{12}}$), 26.1 ($SiC(\mathbf{C}H_3)_3$), 25.3 ($\mathbf{C_{18}}$), 23.4 ($\mathbf{C_{19}}$), 21.9 ($\mathbf{C_{20}}$), 18.5 ($Si\mathbf{C}(CH_3)_3$), –2.7 ($Si\mathbf{C_a}H_3$), –3.00 ($Si\mathbf{C_b}H_3$).
FTIR (thin film) cm^{-1}	3279 (br-m), 2859 (w), 1685 (br-s), 1616 (m), 1473 (m), 1303 (m), 1249 (m), 1092 (m).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{51}H_{57}Cl_2N_6O_7Si$, $[M+H]^+$: 963.3430, found: 963.3449.
$[\alpha]_D^{23}$:	–26 (*c* = 0.17, $CHCl_3$).
TLC (18% acetone in dichloromethane), R*f*:	0.26 (UV, CAM).



(–)-**22** **S2** (–)-**25**

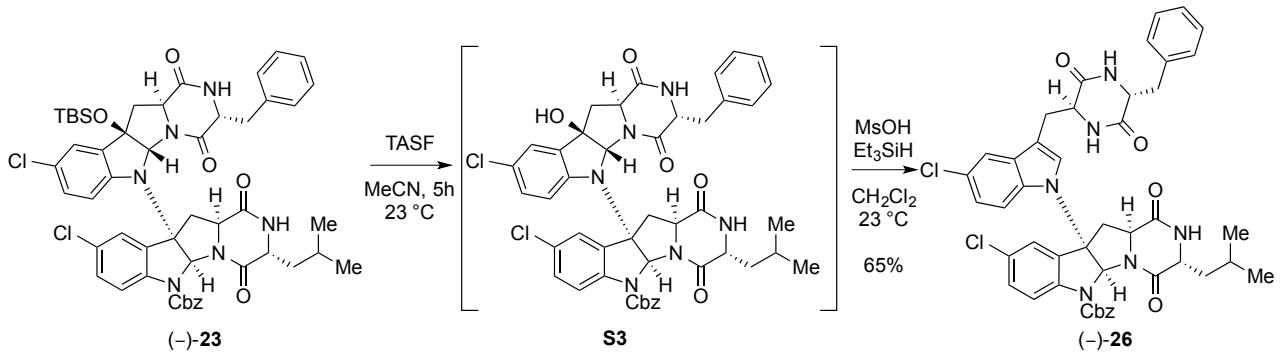
Bis-D-Phenylalanine-indole dimer (–)-25:

To a solution of tris(dimethylamino)sulfonium difluorotrimethylsilicate (9.6 mg, 35 μmol, 5.00 equiv) in acetonitrile (300 μL) was added dimer (–)-**22** (7.0 mg, 7.0 μmol, 1 equiv) as a solid. The reaction mixture was stirred under an argon atmosphere at 23 °C. After 5 hr, a saturated aqueous solution of sodium bicarbonate (10 mL) and dichloromethane (20 mL) were added sequentially, and the organic phase was separated. The aqueous phase was extracted with dichloromethane (3 × 20 mL), the organic layers were combined, were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to give a brown residue.

Crude dimeric diketopiperazine **S2** was dissolved in dichloromethane (500 μL) and to the solution was added triethylsilane (87.9 μL, 550 μmol, 50.0 equiv) and methanesulfonic acid (17.9 μL, 275 μmol, 25.0 equiv). After 18 hr, a saturated aqueous solution of sodium bicarbonate (10 mL) and dichloromethane (10 mL) were added sequentially. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 10 mL). The organic fractions were combined, were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to give a yellow oil. The residue was purified by flash column chromatography on silica gel (eluent: 20→30% acetone in dichloromethane) to furnish indole dimer (–)-**25** (5.0 mg, 5.8 μmol, 82.7%) as a white solid.

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.82 (d, J = 8.7 Hz, 1H, C_8**H**), 7.64 (d, J = 2.1 Hz, 1H, C_5**H**), 7.55 (d, J = 2.0 Hz, 1H, C_5'**H**), 7.52 (s, 1H, N_{14}'**H**), 7.50 (d, J = 7.1 Hz, 2H, Ph_{Cbz}-*o*-C**H**), 7.45 (dd, J = 8.7, 2.1 Hz, 2H, C_7**H**, C_{21}**H**), 7.38 (app-t, J = 7.2 Hz, 2H, Ph_{Cbz}-*m*-C**H**), 7.36–7.32 (m, 3H, C_{20}**H**, C_{22}**H**, Ph_{Cbz}-*p*-C**H**), 7.26–7.21 (m, 4H, C_{19}**H**, C_{23}**H**, C_{20}'**H**, C_{22}'**H**), 7.19 (dd, J = 8.8, 2.0 Hz, 1H, C_7'**H**), 7.15–7.07 (m, 3H, C_{19}'**H**, C_{21}'**H**, C_{23}'**H**), 7.08 (d, J = 9.0 Hz, 1H, C_8'**H**), 6.87 (s, 1H, N_{10}'**H**), 6.81 (s, 1H, N_{14}**H**), 6.71 (s, 1H, C_2'**H**), 6.33 (s, 1H, C_2**H**), 5.36 (d, J = 12.1 Hz, 1H, Ph_{Cbz}**H$_a$**), 5.29 (d, J = 12.1 Hz, 1H, Ph_{Cbz}**H$_b$**), 4.16 (dt, J = 5.7, 4.2 Hz, 1H, C_{15}**H**), 3.54 (dd, J = 9.8, 7.6 Hz, 1H, C_{11}**H**), 3.50 (dt, J = 4.8, 3.0 Hz, 1H, C_{11}'**H**), 3.32–3.28 (m, 1H, C_{15}'**H**), 3.25 (dd, J = 13.5, 6.1 Hz, 1H, C_{17}**H$_a$**), 3.14 (dd, J = 13.6, 8.7 Hz, 1H, C_{12}**H$_a$**), 3.09 (dd, J = 9.5, 4.5 Hz, 1H, C_{12}**H$_b$**), 3.07–3.05 (m, 1H, C_{12}'**H$_a$**),

	3.03 (dd, J = 4.9, 2.2 Hz, 1H, $C_{17}\mathbf{H_b}$), 3.01–2.97 (m, 1H, $C_{17}'\mathbf{H_a}$), 2.96 (d, J = 4.4 Hz, 1H, $C_{12}'\mathbf{H_b}$), 2.87 (dd, J = 13.8, 4.7 Hz, 1H, $C_{17}'\mathbf{H_b}$).
^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC):	δ 168.5 (**C_{13}'**), 168.0 (**C_{16}'**, **C_{16}**), 167.5 (**C_{13}**), 153.3 (**C**=O_{Cbz}), 140.9 (**C_9**), 137.3 (**C_{18}**), 137.1 (**C_{18}'**, Ph_{Cbz}-*ipso*-**C**) 134.5 (**C_4**), 133.7 (**C_9'**), 132.5 (**C_4'**), 131.9 (**C_7**), 131.0 (**C_{19}'**, **C_{23}'**, **C_{19}**, **C_{23}**), 129.7 (Ph_{Cbz}-*o*-**C**H), 129.6 (**C_6**), 129.4 (**C_{20}**, **C_{22}**, Ph_{Cbz}-*m*-**C**H), 129.3 (**C_2'**), 129.2 (**C_{20}'**, **C_{22}'**), 129.1 (Ph_{Cbz}-*p*-**C**H), 128.2 (**C_{21}**), 127.8 (**C_{21}'**), 127.0 (**C_5**), 126.6 (**C_6'**), 123.0 (**C_7'**), 120.6 (**C_5'**), 119.0 (**C_8**), 113.2 (**C_8'**), 110.4 (**C_3'**), 81.2 (**C_2**), 71.0 (**C_3**), 69.0 (Ph_{Cbz}**C**H_2), 59.8 (**C_{15}**), 56.4 (**C_{15}'**), 56.1 (**C_{11}**), 55.7 (**C_{11}'**), 40.6 (**C_{17}**), 39.6 (**C_{17}'**), 35.7 (**C_{12}**), 29.5 (**C_{12}'**).
FTIR (thin film) cm^{-1}	3211 (br-m), 2923 (m), 1726 (m), 1679 (s), 1454 (m), 1319 (m), 1180 (w), 739 (w), 702 (m).
HRMS (ESI) (*m*/*z*):	calc'd for, $C_{48}H_{40}Cl_2N_6NaO_6$ $[M+Na]^+$: 889.2279, found: 889.2274.
$[\alpha]_D^{23}$:	–32 (*c* = 0.17, $CHCl_3$).
TLC (20% acetone in dichloromethane), R*f*:	0.33 (UV, CAM).



(–)-**23** **S3** (–)-**26**

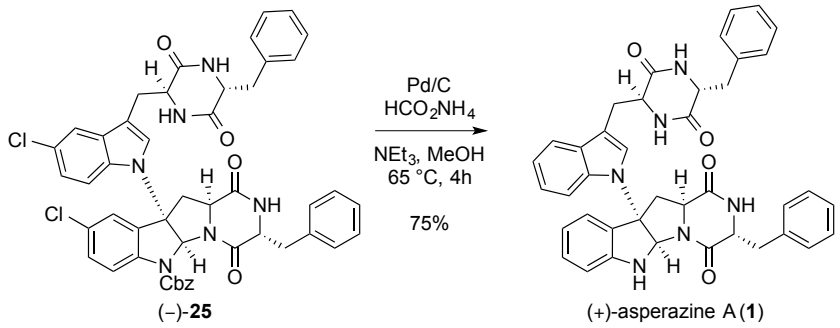
D-Phenylalanine-D-leucine indole dimer (–)-26:

To a solution of tris(dimethylamino)sulfonium difluorotrimethylsilicate (21.5 mg, 77.8 μmol, 5.00 equiv) in acetonitrile (300 μL) was added dimer (–)-**23** (15.0 mg, 15.6 μmol, 1 equiv) as a solid. The reaction mixture was stirred under an argon atmosphere at 23 °C. After 5 hr, a saturated aqueous solution of sodium bicarbonate (10 mL) and dichloromethane (20 mL) were added sequentially, and the organic phase was separated. The aqueous phase was extracted with dichloromethane (3 × 20 mL), the organic layers were combined, were dried over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to give a brown residue.

Crude dimeric diketopiperazine **S3** was dissolved in dichloromethane (1.00 mL) and to the solution was added triethylsilane (125 μL, 780 μmol, 50.0 equiv) and methanesulfonic acid (25.3 μL, 390 μmol, 25.0 equiv). After 18 hr, a saturated aqueous solution of sodium bicarbonate (10 mL) and dichloromethane (10 mL) were added sequentially. The organic layer was separated and the aqueous layer was extracted with dichloromethane (2 × 10 mL). The organic fractions were combined, were dired over anhydrous sodium sulfate, were filtered, and were concentrated under reduced pressure to give a yellow oil. The residue was purified by flash column chromatography on silica gel (eluent: 25 →40% acetone in dichloromethane) to furnish indole dimer (–)-**26** (8.5 mg, 10.2 μmol, 65.4%) as a white solid.

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.80 (d, J = 8.6 Hz, 1H, C_8**H**), 7.70 (d, J = 2.3 Hz, 1H, C_5**H**), 7.63 (d, J = 8.9 Hz, 1H, C_8'**H**), 7.55 (d, J = 2.1 Hz, 1H, C_5'**H**), 7.51 (d, J = 4.8 Hz, 1H, Ph_{Cbz}-*p*-C**H**), 7.46 (dd, J = 8.7, 2.2 Hz, 1H, C_7**H**), 7.43 (dd, J = 6.6, 3.1 Hz, 2H, Ph_{Cbz}-*o*-C**H**), 7.34–7.29 (m, 2H, Ph_{Cbz}-*m*-C**H**), 7.25–7.19 (m, 3H, $C_{20\text{-}22}'$**H**), 7.16–7.06 (m, 3H, C_7'**H**, C_{19}'**H**, C_{23}'**H**), 6.83 (s, 2H, C_2'**H**, N_{10}'**H**), 6.71 (s, 1H, N_{14}**H**), 6.67 (s, 1H, C_2**H**), 5.30 (s, 2H, Ph_{Cbz}**H$_2$**), 5.06 (dd, J = 10.1, 5.4 Hz, 1H, C_{11}**H**), 3.79 (app-ddt, J = 12.0, 4.3, 3.6 Hz, 1H, C_{15}**H**), 3.55 (dd, J = 14.5, 5.5 Hz, 1H, C_{12}**H$_a$**), 3.52–3.44 (m, 2H, C_{11}'**H**, C_{12}**H$_b$**), 3.29 (t, J = 5.2 Hz, 1H, C_{15}'**H**), 3.08 (dd, J = 14.8, 4.9 Hz, 1H, C_{12}'**H$_a$**), 2.99 (app-tt, J = 9.3, 4.9 Hz, 2H, C_{12}'**H$_b$**, C_{17}'**H$_a$**), 2.87 (app-d, J = 4.6 Hz, 1H, C_{17}'**H$_b$**), 1.79 (ddd, J = 14.9, 11.1, 5.6 Hz, 2H, C_{17}**H$_a$**, C_{18}**H**), 1.62 (tt, J = 8.2, 4.3 Hz, 1H, C_{17}**H$_b$**), 0.99 (d, J = 6.3 Hz, 3H, C_{19}**H$_3$**), 0.93 (d, J = 6.3 Hz, 3H C_{20}**H$_3$**).

^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC):	δ 168.5 (**C$_{16}$**), 168.4 (**C$_{13}$**, **C$_{13}$′**), 168.0 (**C$_{16}$′**), 153.4 (**C**=O$_{Cbz}$), 140.9 (**C$_9$**), 137.1 (Ph$_{Cbz}$-*ipso*-**C**), 137.0 (**C$_{18}$′**), 134.3 (**C$_4$**), 134.1 (**C$_9$′**), 132.4 (**C$_4$′**), 131.9 (**C$_7$**), 131.0 (**C$_{19}$′**, **C$_{23}$′**), 129.5 (**C$_6$**), 129.3 (Ph$_{Cbz}$-*o*-**C**H), 129.2 (Ph$_{Cbz}$-*m*-**C**H), 129.1 (**C$_{20}$′**, **C$_{22}$′**, **C$_2$′**), 129.0 (Ph$_{Cbz}$-*p*-**C**H), 127.7 (**C$_{21}$′**), 127.0 (**C$_5$**), 126.6 (**C$_6$′**), 123.1 (**C$_7$′**), 120.4 (**C$_5$′**), 119.1 (**C$_8$**), 113.9 (**C$_8$′**), 110.4 (**C$_3$′**), 81.6 (**C$_2$**), 71.6 (**C$_3$**), 68.8 (Ph$_{Cbz}$**C**H$_2$), 57.0 (**C$_{15}$**), 56.7 (**C$_{11}$**), 56.4 (**C$_{15}$′**), 55.7 (**C$_{11}$′**), 42.3 (**C$_{17}$**), 39.6 (**C$_{17}$′**), 34.3 (**C$_{12}$**), 29.4 (**C$_{12}$′**), 25.2 (**C$_{18}$**), 23.3 (**C$_{19}$**), 21.8 (**C$_{20}$**).
FTIR (thin film) cm^{-1}	3304 (br-w), 3059 (w), 2923 (w), 1710 (s), 1684 (m), 1419 (m), 1360 (s), 1221 (s), 1091 (w).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{45}H_{43}Cl_2N_6O_6$, $[M+H]^+$: 833.2616, found: 833.2600.
$[\alpha]_D^{23}$:	–16 (*c* = 0.16, $CHCl_3$).
TLC (25% acetone in dichloromethane), R*f*:	0.39 (UV, CAM).



(+)-Asperazine A (1):

To a solution of dimer (–)-**25** (9.7 mg, 11.2 μmol, 1 equiv) in degassed methanol (300 μL) and triethylamine (15.6 μL, 112 μmol, 10.0 equiv) was added 10% palladium on carbon (17.9 mg, 16.8 μmol, 1.50 equiv) and ammonium formate (35.3 mg, 560 μmol, 50.0 equiv) sequentially. The reaction mixture was heated to 65 °C. After 4 h, the black suspension was cooled to 23 °C and was concentrated under reduced pressure affording a black residue. The residue was purified by flash column chromotagraphy on silica gel (eluent: 45→60% acetone in dichloromethane) to provide (+)-asperazine A (**1**) as a white solid (5.6 mg, 8.4 μmol, 75.2%).

^{1}H NMR (400 MHz, DMSO-d_6, 20 ºC): δ 8.36 (d, J = 4.2 Hz, 1H, N_{14}**H**), 8.00 (s, 1H, N_{10}′**H**), 7.96 (s, 1H, N_{14}′**H**), 7.52 (d, J = 7.8 Hz, 1H, C_5′**H**), 7.32 (d, J = 4.0 Hz, 1H, N_1**H**), 7.27–7.16 (m, 5H, $C_{20\text{-}22}$**H**, C_2′**H**, C_{21}′**H**), 7.15–7.04 (m, 7H, C_7**H**, C_{19}**H**, C_{23}**H**, $C_{19\text{-}20}$′**H**, $C_{22\text{-}23}$′**H**), 6.99 (t, J = 7.5 Hz, 1H, C_6′**H**), 6.92 (t, J = 7.6 Hz, 1H, C_7′**H**), 6.72 (d, J = 7.7 Hz, 1H, C_5**H**), 6.58 (t, J = 7.4 Hz, 1H, C_6**H**), 6.53 (d, J = 8.2 Hz, 1H, C_8′**H**), 5.73 (d, J = 3.9 Hz, 1H, C_2**H**), 4.10 (q, J = 5.0 Hz, 1H, C_{15}**H**), 3.61 (t, J = 5.4 Hz, 1H, C_{11}′**H**), 3.42 (dd, J = 11.9, 5.7 Hz, 1H, C_{11}**H**), 3.30–3.25 (m, 2H, C_{12}**H**$_\mathbf{a}$, C_{15}′**H**), 3.24 (dd, J = 15.0, 5.5 Hz, 1H, C_{12}′**H**$_\mathbf{a}$), 3.08 (dd, J = 13.3, 6.4 Hz, 1H, C_{17}**H**$_\mathbf{a}$), 3.02 (app-s, 1H, C_{17}′**H**$_\mathbf{a}$), 2.98 (dd, J = 15.0, 4.5 Hz, 1H, C_{12}′**H**$_\mathbf{b}$), 2.89 (dd, J = 13.5, 4.6 Hz, 1H, C_{17}**H**$_\mathbf{b}$), 2.71 (dd, J = 13.6, 4.8 Hz, 1H, C_{17}′**H**$_\mathbf{b}$), 2.06 (t, J = 13.1 Hz, 1H, C_{12}**H**$_\mathbf{b}$).

^{13}C NMR (125 MHz, DMSO-d_6, 20 ºC): δ 167.9 (**C**$_{13}$′), 167.7 (**C**$_{13}$), 167.6 (**C**$_{16}$′), 166.8 (**C**$_{16}$), 148.0 (**C**$_9$), 136.0 (**C**$_{18}$, **C**$_{18}$′), 134.6 (**C**$_9$′), 130.1 (**C**$_{19}$′, **C**$_{23}$′), 129.7 (**C**$_7$), 129.6 (**C**$_{19}$, **C**$_{23}$), 129.5 (**C**$_4$′), 128.4 (**C**$_4$), 128.3 (**C**$_{20}$′, **C**$_{22}$′), 127.9 (**C**$_{20}$, **C**$_{22}$), 126.9 (**C**$_{21}$), 126.5 (**C**$_{21}$′), 125.5 (**C**$_2$′), 122.2 (**C**$_5$), 121.3 (**C**$_7$′), 119.4 (**C**$_6$′), 119.3 (**C**$_5$′), 118.4 (**C**$_6$), 111.4 (**C**$_8$′), 110.1 (**C**$_8$), 108.3 (**C**$_3$′), 81.8 (**C**$_2$), 72.7 (**C**$_3$), 58.1 (**C**$_{15}$), 55.4 (**C**$_{11}$), 54.5 (**C**$_{11}$′), 54.4 (**C**$_{15}$′), 40.2 (**C**$_{12}$), 39.3 (**C**$_{17}$), 37.1 (**C**$_{17}$′), 29.1 (**C**$_{12}$′).

FTIR (thin film) cm^{-1}	3349 (br-w), 3246 (br-m), 2924 (w), 1674 (s), 1611 (w), 1436 (m), 1316 (m), 1176 (w), 1093 (w).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{40}H_{37}N_6O_4$, $[M+H]^+$: 665.2871, found: 665.2858.
$[\alpha]_D^{23}$:	+135 (*c* = 0.11, MeOH).
TLC (60% acetone in dichloromethane), R*f*:	0.32 (UV, CAM).

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

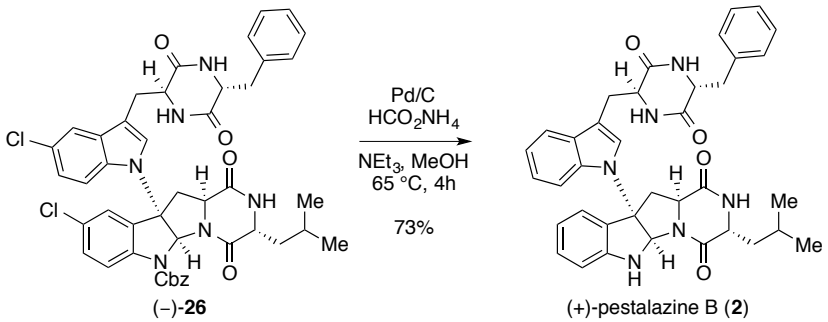
	Lou's report[8] (−)-Asperazine A (**1**) ^{1}H NMR, 600 MHz DMSO-d_6	**This work** (+)-Asperazine A (**1**) ^{1}H NMR, 500 MHz DMSO-d_6, 20 °C
N1	7.35 (s)	7.32 (d, J = 4.0 Hz)
C2	5.72 (s)	5.73 (d, J = 3.9 Hz)
C5	6.71 (d, J = 7.2 Hz)	6.72 (app-d, J = 7.7 Hz)
C6	6.58 (t, J = 7.2 Hz)	6.58 (t, J = 7.4 Hz)
C7	7.08	7.15–7.04 (m)
C8	6.71 (d, J = 7.2 Hz)	6.72 (app-d, J = 7.7 Hz)
C11	3.43–3.37 (m)	3.42(dd, J = 11.9, 5.7 Hz)
C12	3.29 2.05 (t, J = 13.2 Hz)	3.30-3.25[9] 2.06 (t, J = 13.1 Hz)
N14	8.39 (s)	8.36 (d, J = 4.2 Hz)
C15	4.15–4.09 (m)	4.10 (q, J = 5.0 Hz)
C17	3.06 2.88 (d, J = 13.2 Hz)	3.08 (dd, J = 13.3, 6.4 Hz) 2.89 (dd, J = 13.6, 4.8 Hz)
C19, C23	7.08	7.15–7.04 (m)
C20, C22	7.21 (t, J = 7.0 Hz)	7.27–7.16 (m)
C21	7.19 (t, J = 7.0 Hz)	7.27–7.16 (m)
C2′	7.17 (s)	7.27–7.16 (m)
C5′	7.52 (d, J = 7.8 Hz)	7.52 (d, J = 7.8 Hz)
C6′	6.98 (t, J = 7.8 Hz)	6.99 (t, J = 7.5 Hz)
C7′	6.92 (t, J = 7.8 Hz)	6.92 (t, J = 7.6 Hz)
C8′	6.52 (d, J = 7.8 Hz)	6.53 (d, J = 8.2 Hz)
N10′	8.03 (s)	8.00 (s)
C11′	3.62–3.59 (m)	3.61 (t, J = 5.4 Hz)
C12′	3.25 3.00	3.24 (dd, J = 15.0, 5.5 Hz) 2.98 (dd, J = 15.0, 4.5 Hz)
N14′	7.99 (s)	7.96 (s)
C15′	3.30–3.26 (m)	3.30–3.25[9]
C17′	3.04 2.70 (d, J = 13.2 Hz)	3.02 (app-s) 2.71 (dd, J = 13.6, 4.8 Hz)
C19′, C23′	7.12	7.15–7.04 (m)
C20′, C22′	7.08	7.15–7.04 (m)
C21′	7.19 (t, J = 7.0 Hz)	7.27–7.16 (m)

[8] Li, X.-B.; Li, Y.-L.; Zhou, J.-C.; Yuan, H.-Q.; Wang, X.-N.; Lou, H.-X. *J. Asian. Nat. Prod. Res.* **2015**, *17*, 182.
[9] This resonance overlaps with that of water in DMSO-d_6; the exact position of resonance was determined by HSQC data.

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

	Lou´s report[8] (−)-Asperazine A (**1**) ^{13}C NMR, 150 MHz DMSO-d_6	**This work** (+)-Asperazine A (**1**) ^{13}C NMR, 125 MHz DMSO-d_6, 20 °C	**Δδ**[10] (ppm)
C2	81.8	81.8	0
C3	72.7	72.7	0
C4	128.4	128.4	0
C5	122.2	122.2	0
C6	118.4	118.4	0
C7	129.5	129.7	+0.2
C8	110.1	110.1	0
C9	148.0	148.0	0
C11	55.0	55.4	+0.4
C12	40.1	40.2	+0.1
C13	167.7	167.7	0
C15	58.1	58.1	0
C16	166.8	166.8	0
C17	39.0	39.3	+0.3
C18	136.1	136.0	–0.1
C19, C23	129.7	129.6	–0.1
C20, C22	127.9	127.9	0
C21	126.9	126.9	0
C2′	125.6	125.5	–0.1
C3′	108.3	108.3	0
C4′	129.8	129.5	–0.3
C5′	119.4	119.3	–0.1
C6′	119.5	119.4	–0.1
C7′	121.3	121.3	0
C8′	111.5	111.4	–0.1
C9′	134.7	134.6	–0.1
C11′	54.5	54.5	0
C12′	29.1	29.1	0
C13′	167.9	167.9	0
C15′	54.4	54.4	0
C16′	167.6	167.6	0
C17′	37.0	37.1	+0.1
C18′	136.1	136.0	–0.1
C19′, C23′	130.2	130.1	–0.1
C20′, C22′	128.3	128.3	0
C21′	126.6	126.5	–0.1

[10] Chemical Shift Difference Δδ = δ (this work, solvent ref: δ 39.50) – δ (Lou's report, solvent ref: not available)



(+)-Pestalazine B (2):

To a solution of dimer (–)-**26** (6.0 mg, 7.2 μmol, 1 equiv) in degassed methanol (250 μL) and triethylamine (10.0 μL, 72.0 μmol, 10.0 equiv) was added 10% palladium on carbon (11.5 mg, 10.8 μmol, 1.50 equiv) and ammonium formate (22.7 mg, 360 μmol, 50.0 equiv) sequentially. The reaction mixture was heated to 65 °C. After 4 h, the black suspension was cooled to 23 °C and was concentrated under reduced pressure affording a black residue. The residue was purified by flash column chromotagraphy on silica gel (eluent: 45→60% acetone in dichloromethane) to provide (+)-pestalazine B (**2**) as a white solid (3.3 mg, 5.2 μmol, 72.7%). Due to poor solubility in acetone NMR spectra are also provided in DMSO-d_6.

^{1}H NMR (500 MHz, Acetone-d_6, 20 ºC): δ 7.69 (d, J = 4.6 Hz, 1H, N_{14}**H**), 7.67 (s, 1H, C_2'**H**), 7.51 (d, J = 7.7 Hz, 1H, C_5'**H**), 7.20 (app-dd, J = 5.1, 1.9 Hz, 3H, $C_{20\text{-}22}'$**H**), 7.18 (dd, J = 7.7, 6.3 Hz, 1H, C_7**H**), 7.10 (dd, J = 6.8, 2.8 Hz, 2H, C_{19}'**H**, C_{23}'**H**), 7.00–6.96 (m, 2H, N_{10}'**H**, C_6'**H**), 6.95 (d, J = 6.7 Hz, 1H, C_7'**H**), 6.92 (d, J = 6.8 Hz, 1H, C_5**H**), 6.85 (d, J = 8.0 Hz, 1H, C_8**H**), 6.81 (s, 1H, N_{14}'**H**), 6.78 (d, J = 8.2 Hz, 1H, C_8'**H**), 6.64 (t, J = 7.4 Hz, 1H, C_6**H**), 6.60 (d, J = 3.8 Hz, 1H, N_1**H**), 6.05 (d, J = 3.5 Hz, 1H, C_2**H**), 4.85 (dd, J = 11.7, 6.0 Hz, 1H, C_{11}**H**), 3.91 (dt, J = 9.7, 5.0 Hz, 1H, C_{15}**H**), 3.73–3.64 (m, 2H, C_{11}'**H**, C_{12}**H$_a$**), 3.51 (t, J = 5.1 Hz, 1H, C_{15}'**H**), 3.22 (d, J = 5.2 Hz, 2H, C_{12}'**H$_2$**), 3.06 (dd, J = 13.9, 5.5 Hz, 1H, C_{17}'**H$_a$**), 2.98 (dd, J = 13.9, 4.6 Hz, 1H, C_{17}'**H$_b$**), 2.46 (dd, J = 14.8, 11.7 Hz, 1H, C_{12}**H$_b$**), 1.87–1.69 (m, 2H, C_{18}**H**, C_{17}**H$_a$**), 1.53 (ddd, J = 13.7, 8.5, 5.3 Hz, 1H, C_{17}**H$_b$**), 0.95 (d, J = 6.5 Hz, 3H, C_{19}**H**), 0.90 (d, J = 6.5 Hz, 3H, C_{20}**H**).

^{13}C NMR (125 MHz, Acetone-d_6, 20 ºC): δ 169.0 (**C$_{13}$**, **C$_{16}'$**), 168.6 (**C$_{16}$**), 168.5 (**C$_{13}'$**), 149.0 (**C$_9$**), 137.1 (**C$_{18}'$**), 136.7 (**C$_9'$**), 130.9 (**C$_{19}'$**, **C$_{23}'$**), 130.8 (**C$_4'$**), 130.3 (**C$_7$**), 129.9 (**C$_4$**), 129.2 (**C$_{20}'$**, **C$_{22}'$**), 127.7 (**C$_{21}'$**), 126.6 (**C$_2'$**), 123.6 (**C$_5$**), 122.5 (**C$_7'$**), 120.6 (**C$_6'$**), 120.4 (**C$_5'$**), 119.8 (**C$_6$**), 113.0 (**C$_8'$**), 111.0 (**C$_8$**), 110.0 (**C$_3'$**), 83.6 (**C$_2$**), 74.5 (**C$_3$**),

	57.4 (**C_{11}**), 56.9 (**C_{15}**), 56.3 (**C_{15}'**), 55.9 (**C_{11}'**), 43.0 (**C_{17}**), 41.4 (**C_{12}**), 39.3 (**C_{17}'**), 30.1 (**C_{12}'**), 25.3 (**C_{18}**), 23.3 (**C_{19}**), 21.8 (**C_{20}**).
FTIR (thin film) cm^{-1}	3350 (br-w), 3254 (br-m), 2956 (w), 2926 (w), 1671 (s), 1612 (w), 1431 (m), 1315 (m), 1215 (w), 1090 (w).
HRMS (ESI) (*m*/*z*):	calc'd for $C_{37}H_{39}N_6O_4$, $[M+H]^+$: 631.3027, found: 631.3036.
$[\alpha]_D^{23}$:	+191 (c = 0.10, MeOH).
TLC (50% acetone in dichloromethane), R*f*:	0.46 (UV, CAM).

Table S3. Comparison of our ^{1}H NMR data for (+)-Pestalazine B (2) with literature:

	Che´s report[11] (+)-Pestalazine B (**2**) ^{1}H NMR, 600 MHz acetone-d_6	**de Lera´s report**[12] (+)-Pestalazine B (**2**) ^{1}H NMR, 600 MHz acetone-d_6	**This work** (+)-Pestalazine B (**2**) ^{1}H NMR, 400 MHz acetone-d_6, 20 °C
N1	6.83 (d, J = 3.0 Hz)	6.65 (d, J = 3.0 Hz)	6.60 (d, J = 3.8 Hz)
C2	6.03 (d, J = 3.0 Hz)	6.05 (d, J = 3.3 Hz)	6.05 (d, J = 3.5 Hz)
C5	6.90 (d, J = 7.2 Hz)	6.93 (m)[13]	6.92 (d, J = 6.8 Hz)
C6	6.62 (d, J = 7.2 Hz)	6.64 (t, J = 7.2 Hz)	6.64 (t, J = 7.4 Hz)
C7	7.14 (m)	7.17 (m)[14]	7.18 (dd, J = 7.7, 6.3 Hz)
C8	6.83 (d, J = 7.8 Hz)	6.85 (d, J = 7.8 Hz)	6.85 (d, J = 8.0 Hz)
C11	4.82 (dd, J = 12, 6.0 Hz)	4.84 (dd, J = 11.7, 6.0 Hz)	4.85 (dd, J = 11.7, 6.0 Hz)
C12	3.68 (dd, J = 14.0, 6.0 Hz) 2.42 (dd, J = 14.0, 12.0 Hz)	3.69 (dd, J = 14.8, 6.0 Hz) 2.41 (dd, J = 14.8, 11.7 Hz)	3.68 (m) 2.46 (dd, J = 14.8, 11.7 Hz)
N14	7.32 (br-s)	6.98 (m)[13]	7.69 (d, J = 4.6 Hz)
C15	3.85 (m)	3.89 (dt, J = 9.6, 4.8 Hz)	3.91 (dt, J = 9.7, 5.0 Hz)
C17	1.73(m) 1.50 (m)	1.75 (m) 1.52 (ddd, J = 13.6, 8.5, 5.3 Hz)	1.77 (m) 1.53 (ddd, J = 13.7, 8.5, 5.3 Hz)
C18	1.80 (m)	1.80 (m)	1.77 (m)
C19	0.95 (d, J = 6.6 Hz)	0.95 (d, J = 6.5 Hz)	0.95(d, J = 6.5 Hz)
C20	0.90 (d, J = 6.0 Hz)	0.90 (d, J = 6.5 Hz)	0.90 (d, J = 6.5 Hz)
C2′	7.64 (s)	7.66 (s)	7.67 (s)
C5′	7.53 (d, J = 7.8 Hz)	7.52 (d, J = 7.8 Hz)	7.51 (d, J = 7.7 Hz)
C6′	6.98 (t, J = 7.8 Hz)	7.0–6.9 (m)[13]	6.98 (m)
C7′	6.95 (t, J = 7.8 Hz)	7.0–6.9 (m)[13]	6.95 (app-d, J = 6.7 Hz)
C8′	6.75 (d, J = 7.8 Hz)	6.78 (d, J = 8.2 Hz)	6.78 (app-d, J = 8.2 Hz)
N10′	7.38 (br. s)	7.2–7.1 (m)[14]	6.98 (m)
C11′	3.62 (dd, J = 5.2, 4.8 Hz)	3.7–3.6 (m)	3.69 (m)
C12′	3.21 (dd, J = 14.0, 5.4 Hz) 3.15 (dd, J = 14.0, 4.8 Hz)	3.21 (app. d, J = 3.2 Hz) 3.21 (app. d, J = 3.2 Hz)	3.22 (app-d, J = 5.2 Hz) 3.22 (app-d, J = 5.2 Hz)
N14′	8.05 (d, J = 3.5 Hz)	7.81 (d, J = 4.3 Hz)	6.81 (s)
C15′	3.47 (br-t, J = 4.8 Hz)	3.50 (br-t, J = 4.7 Hz)	3.51 (br-t, J = 5.1 Hz)
C17′	3.06 (dd, J = 14.5, 4.8 Hz) 2.88 (m)	3.06 (dd, J = 13.9, 5.4 Hz) 2.96 (dd, J = 13.9, 4.6 Hz)	3.06 (dd, J = 13.9, 5.5 Hz) 2.98 (dd, J = 13.9, 4.6 Hz)
C19′, C23′	7.14 (m)	7.12 (m) [14]	7.10 (app-dd, J = 6.8, 2.8 Hz)
C20′, C22′	7.20 (m)	7.20 (m) [14]	7.20 (app-dd, J = 5.1, 1.9 Hz)
C21′	7.20 (m)	7.20 (m) [14]	7.20 (app-dd, J = 5.1, 1.9 Hz)

[11] Ding, G.; Jiang, L.; Guo, L.; Chen, X.; Zhang, H.; Che, Y. *J. Nat. Prod.* **2008**, *71*, 1861.
[12] Pérez-Balado, C.; de Lera, Á. R. *Bioorg. Med. Chem.* **2010**, *8*, 5179.
[13] This resonance was reported as a multiplet at 7.0–6.9 (4H) in the cited report.
[14] This resonance was reported as a multiplet at 7.2–7.1 (7H) in the cited report.

Table S4. Comparison of our ^{13}C NMR data for (+)-Pestalazine B (2) with literature:

	Che´s report[11] (+)-Pestalazine B (**2**) ^{13}C NMR, 150 MHz acetone-d_6	**de Lera´s report**[12] (+)-Pestalazine B (**2**) ^{13}C NMR, 150 MHz acetone-d_6	**This work** (+)-Pestalazine B (**2**) ^{13}C NMR,125 MHz acetone-d_6, 20 °C	**Δδ**[15] (ppm)	**Δδ**[16] (ppm)
C2	83.4	83.5	83.6	+0.2	+0.1
C3	74.2	74.4	74.5	+0.3	+0.1
C4	129.8	129.9	129.9	+0.1	0
C5	123.3	123.6	123.6	+0.3	0
C6	119.4	119.7	119.8	+0.4	+0.1
C7	130.5	130.8	130.3	–0.2	–0.5
C8	110.9	111.0	111.0	+0.1	0
C9	148.9	148.9	149.0	+0.1	+0.1
C11	57.2	57.3	57.4	+0.2	+0.1
C12	41.2	41.3	41.4	+0.2	+0.1
C13	168.8	169.0	169.0	+0.2	0
C15	56.7	56.9	56.9	+0.2	0
C16	168.4	168.6	168.6	+0.2	0
C17	42.8	42.9	43.0	+0.2	+0.1
C18	24.9	25.1	25.3	+0.4	+0.2
C19	23.2	23.3	23.3	+0.1	0
C20	21.7	21.8	21.8	+0.1	0
C2′	126.4	126.6	126.6	+0.2	0
C3′	109.9	110.0	110.0	+0.1	0
C4′	130.8	130.8	130.8	0	0
C5′	120.3	120.4	120.4	+0.1	0
C6′	120.3	120.5	120.6	+0.3	+0.1
C7′	122.2	122.4	122.5	+0.3	+0.1
C8′	112.8	112.8	113.0	+0.2	+0.2
C9′	136.3	136.6	136.7	+0.4	+0.1
C11′	55.8	55.8	55.9	+0.1	+0.1
C12′	30.2	30.3	30.1	–0.1	–0.2
C13′	168.6	168.6	168.5	–0.1	–0.1
C15′	56.1	56.3	56.3	+0.2	0
C16′	168.9	169.0	169.0	+0.1	0
C17′	38.9	39.1	39.3	+0.4	+0.2
C18′	137.1	137.1	137.1	0	0
C19′, C23′	130.9	131.0	130.9	0	–0.1
C20′, C22′	130.9	129.1	129.2	–1.7[17]	+0.1
C21′	127.4	127.7	127.7	+0.3	0

[15] Chemical Shift Difference Δδ = δ (this work, solvent ref: δ 29.92) – δ (Che's report, solvent ref: 29.8)
[16] Chemical Shift Difference Δδ = δ (this work, solvent ref: δ 29.92) – δ (de Lera, solvent ref δ 29.92)
[17] Our assignment for this resonance is consistent with the value reported in reference 12.

Calculated Structures of Tetracyclic Indolines 18-19:

The conformation distribution and equilibrium geometries (gas phase) in the ground state of the tetracyclic indolines were optimized with Merck Molecular Force Field (MMFF)[18] followed by density functional theory at B3LYP level with 6-31G(d) as basis set (Spartan ′14, Version 1.1.1, by Wavefunction, Inc.).[19] The 3D representations of the molecular structures were generated from CYLview[20] and the highest occupied molecular orbital (HOMO) are shown.

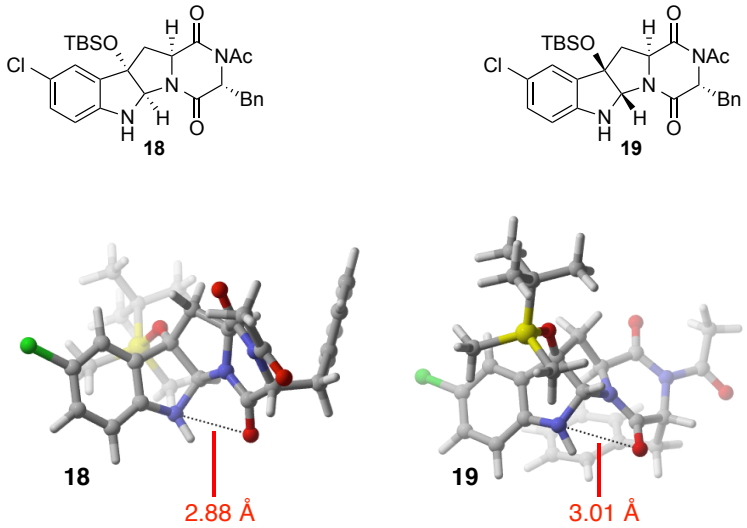


Figure S1. Calculated Structures of Indolines **18** and **19**. The distance between N1 and C16=O is displayed in red.

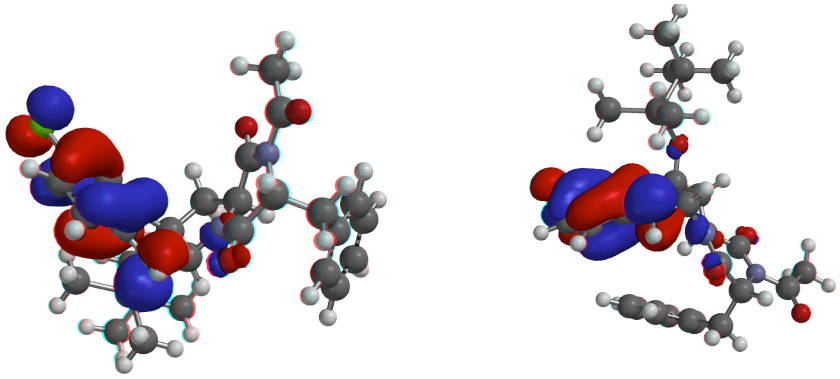
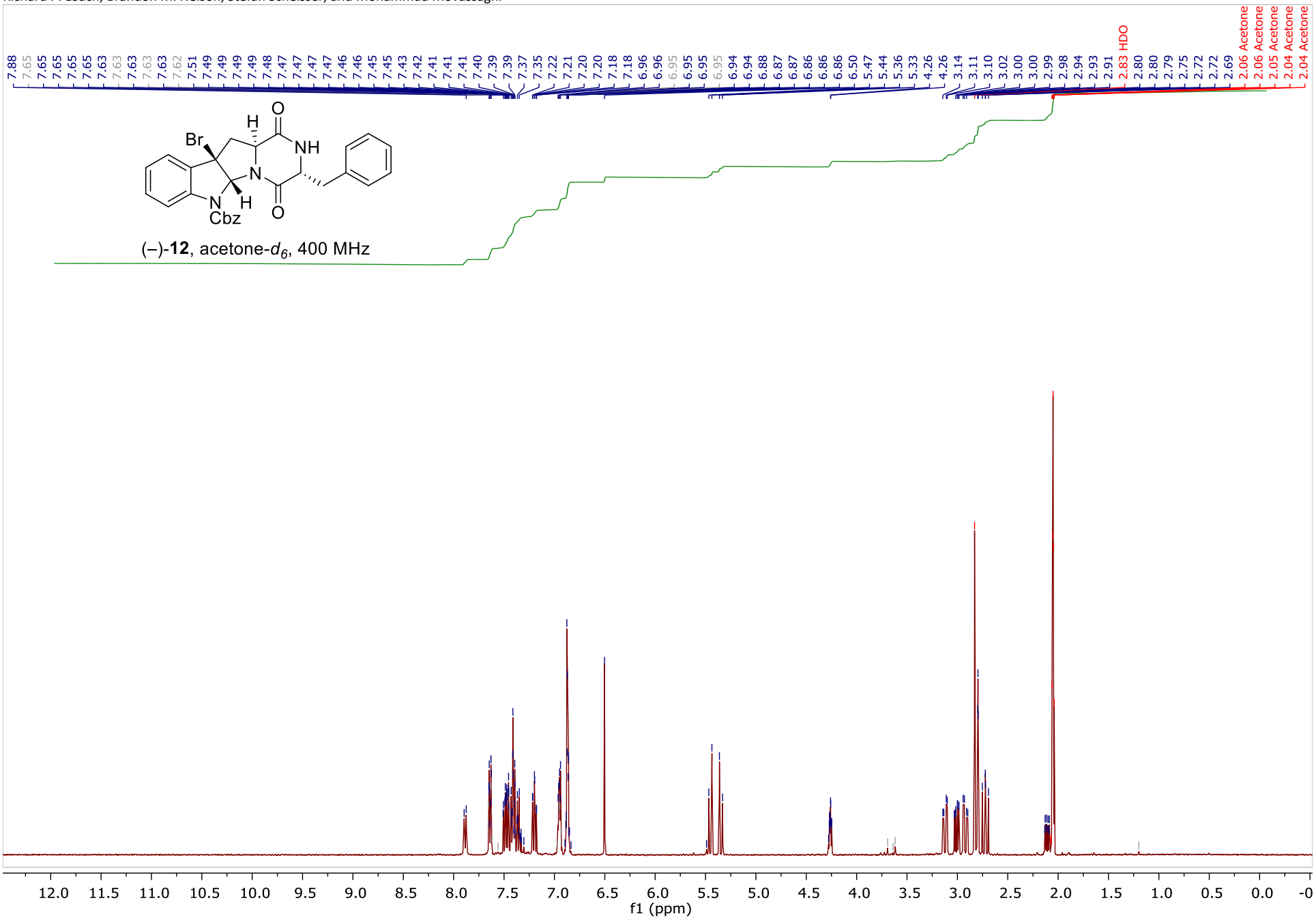


Figure S2. Calculated Structures of Indolines **18** and **19**. The highest occupied molecular orbital for each indoline is shown.

[18] Halgren, T. A. *J. Comput. Chem.* **1996**, *17*, 490.
[19] Spartan'14 Wavefunction, Inc. Irvine, CA. Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan have been documented in: Shao, Y.; Molnar, L. F.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; DiStasio Jr., R. A.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B.D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W. Z.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock III, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172.
[20] CYLview, 1.0b; Legault, C. Y., Université de Sherbrooke, 2009 (http://www.cylview.org).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Br
H
O
NH
N
N
H
Cbz
O
(–)-12, acetone-d6, 400 MHz
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
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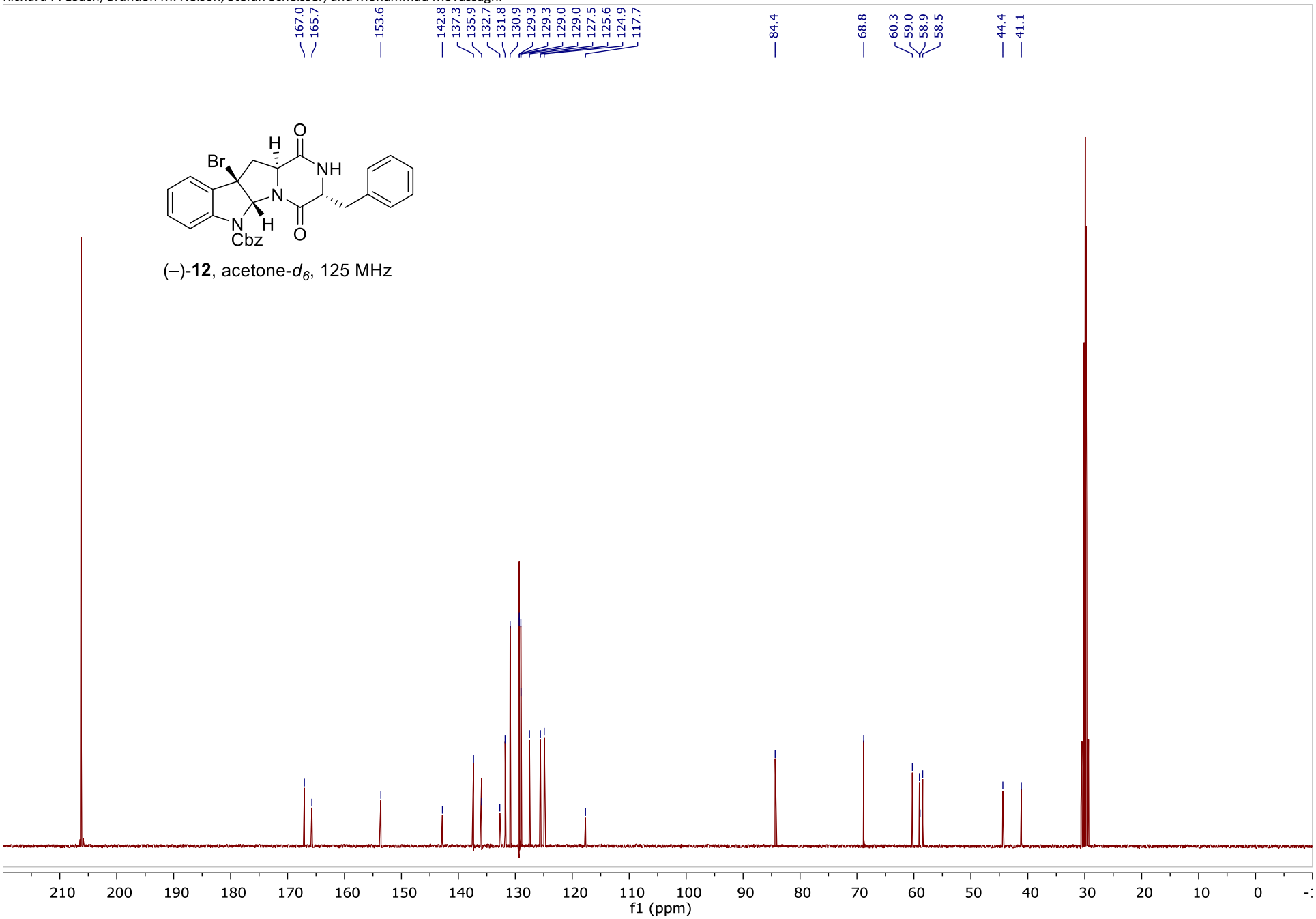
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165.7
153.6
142.8
137.3
135.9
132.7
131.8
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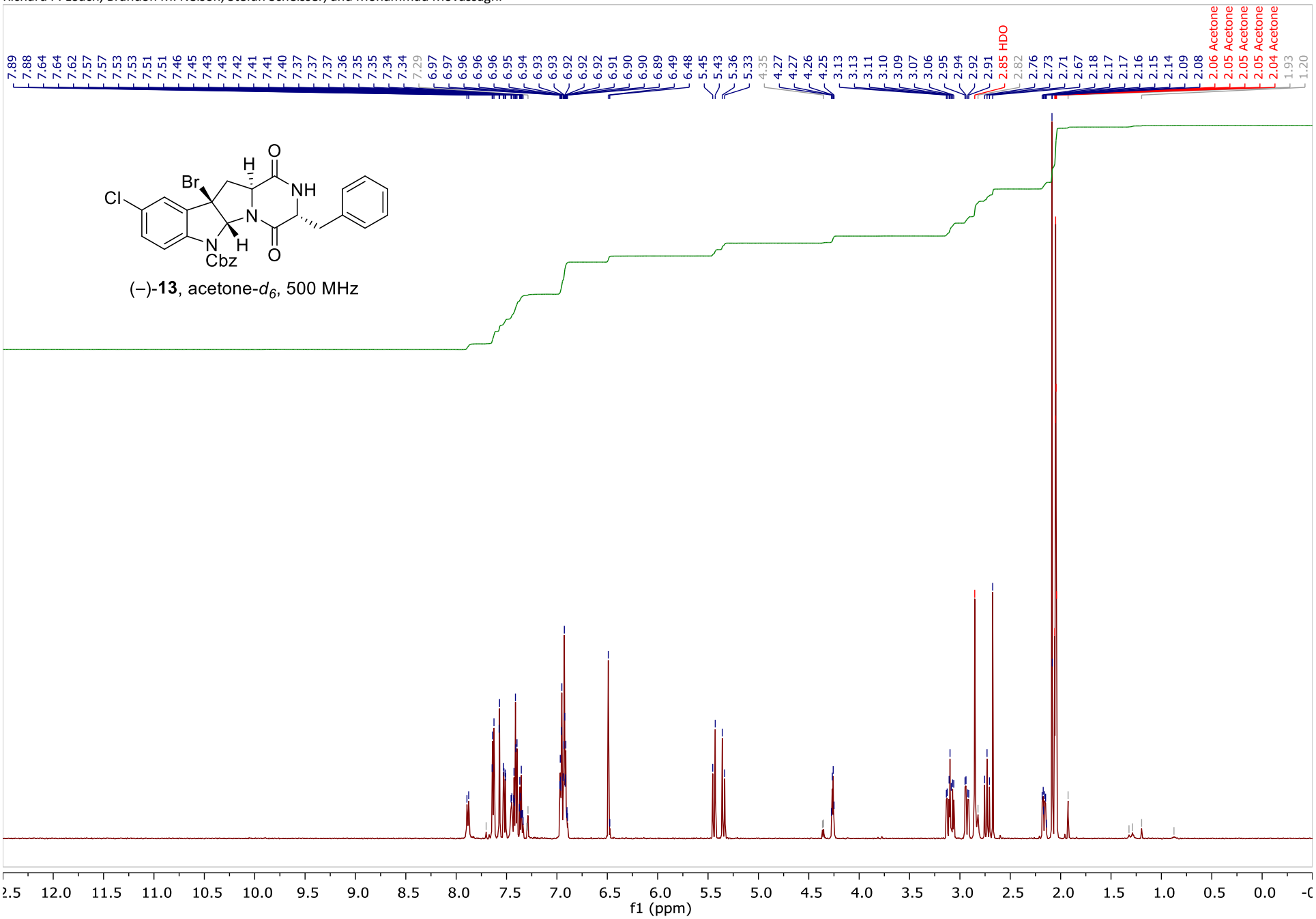
129.3
129.3
129.0
129.0
127.5
125.6
124.9
117.7
84.4
68.8
60.3
59.0
58.9
58.5
44.4
41.1
Br
H
O
NH
N
N
H
Cbz
O
(–)-12, acetone-d6, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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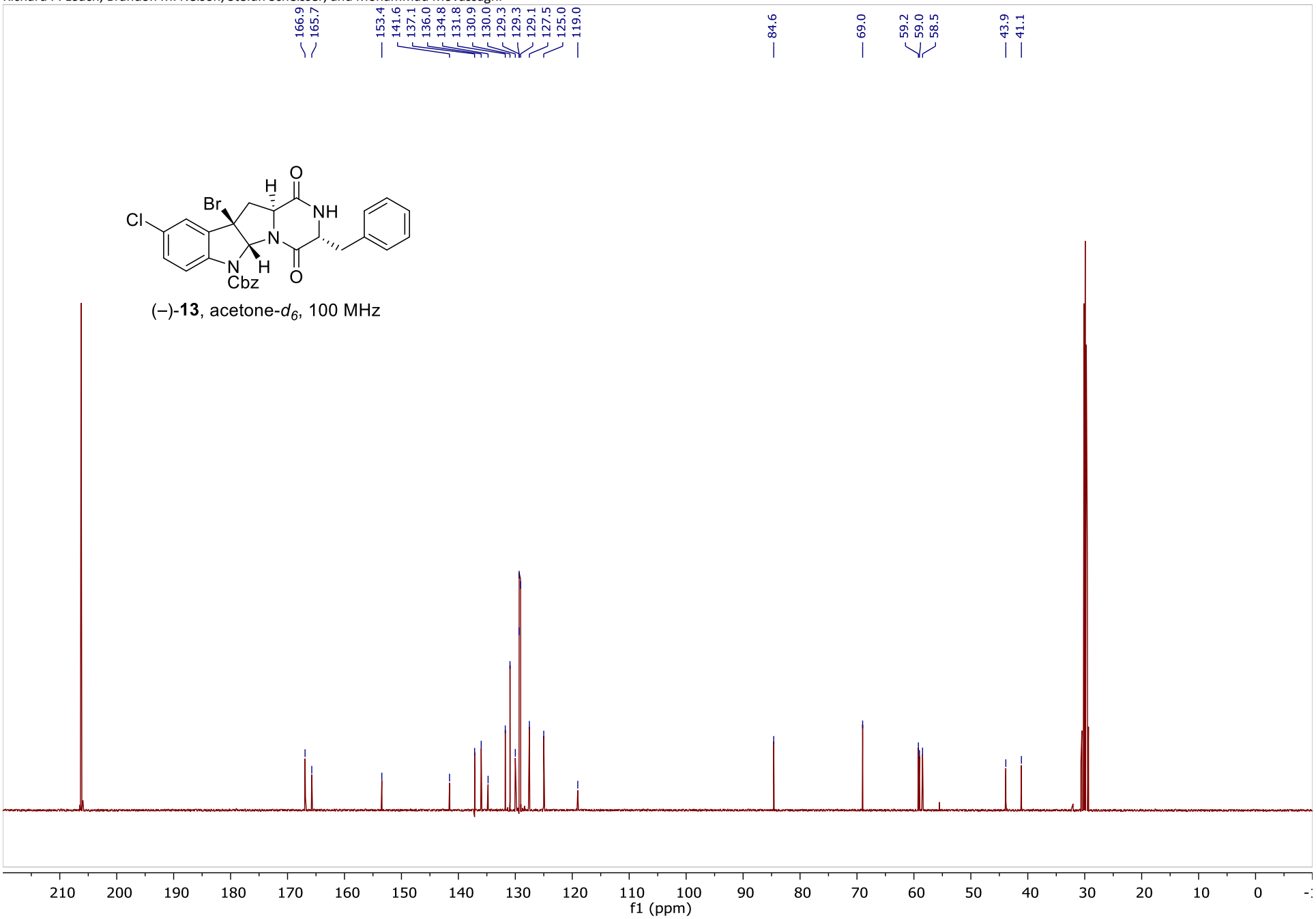
Cl
Br
H
O
NH
N
N
H
Cbz
O
(–)-13, acetone-d6, 500 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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129.3
129.3
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127.5
125.0
119.0
84.6
69.0
59.2
59.0
58.5
43.9
41.1
Cl
Br
H
O
NH
N
N
H
Cbz
O
(–)-13, acetone-d6, 100 MHz
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200
190
180
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50
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10
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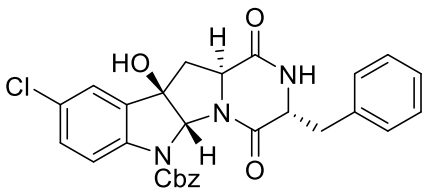
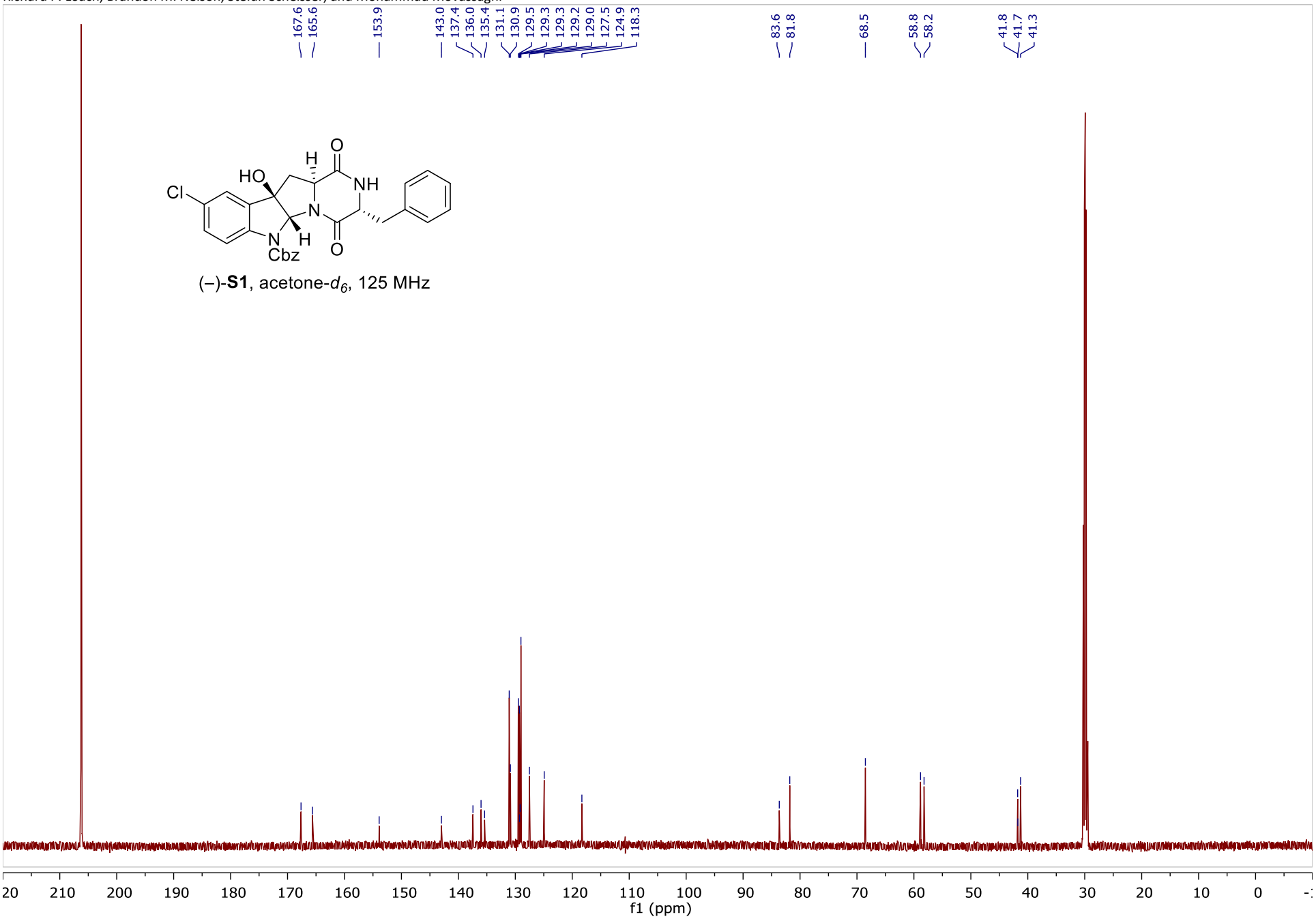
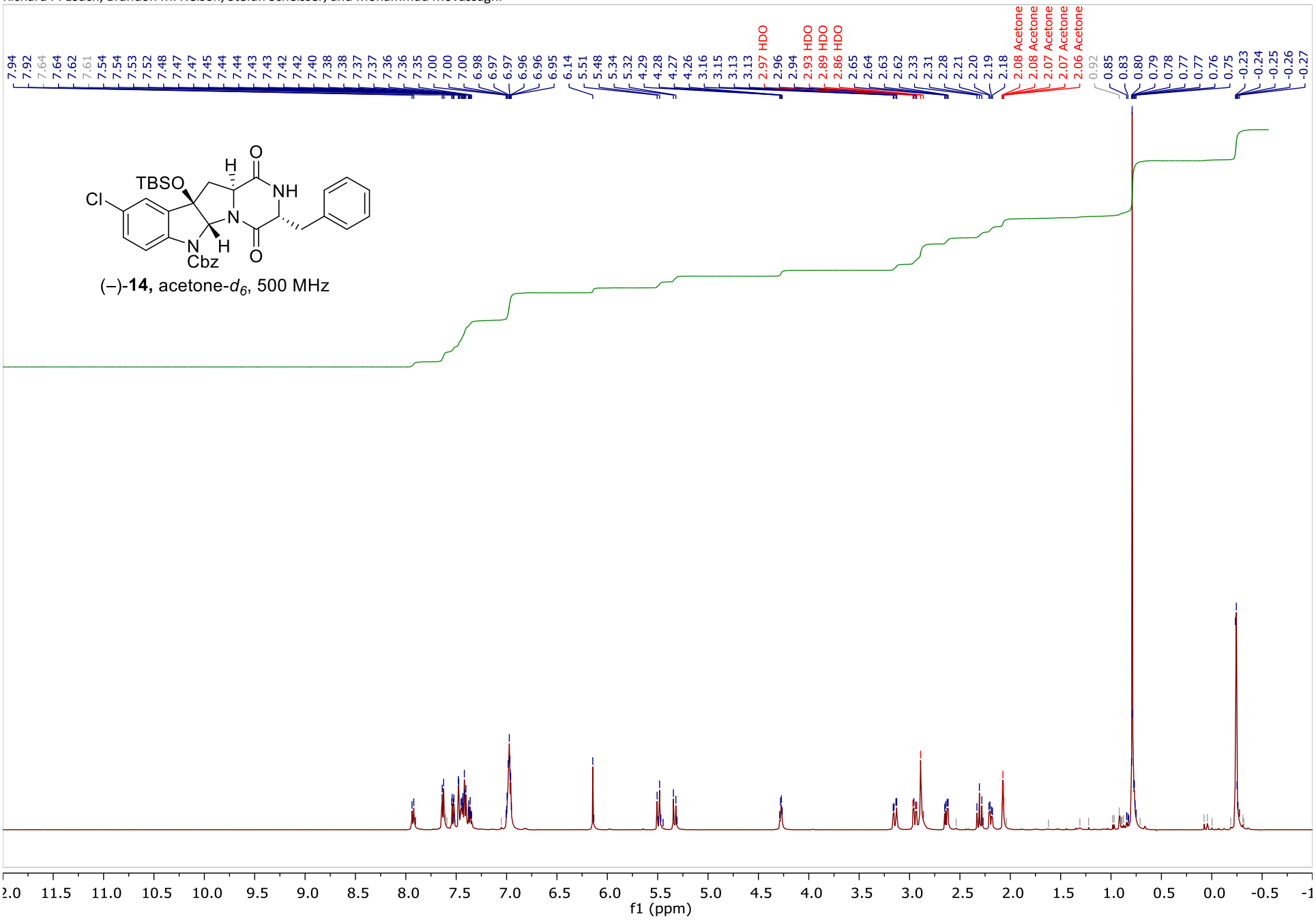
f1 (ppm)

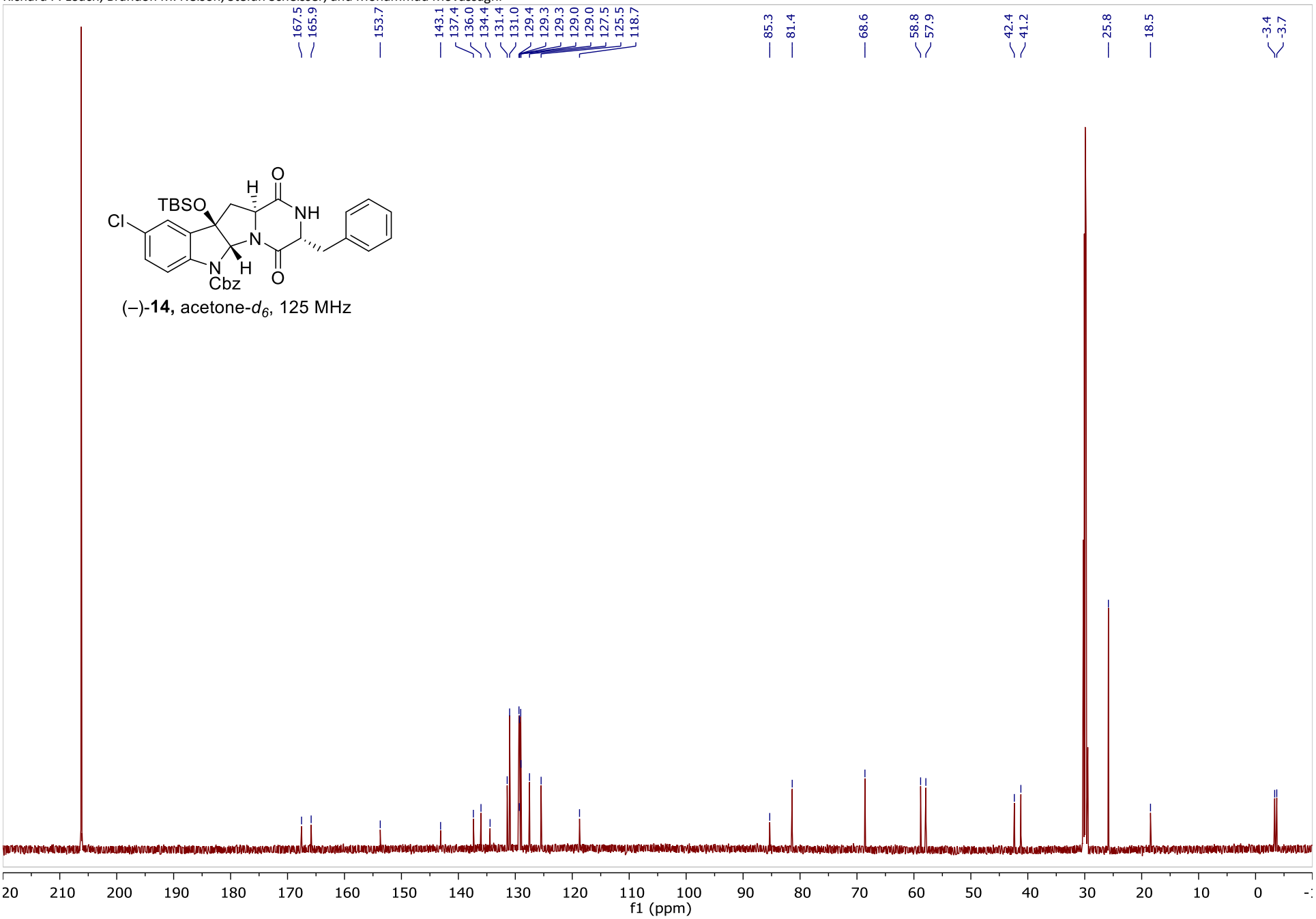


(–)-**S1**, acetone-d_6, 500 MHz

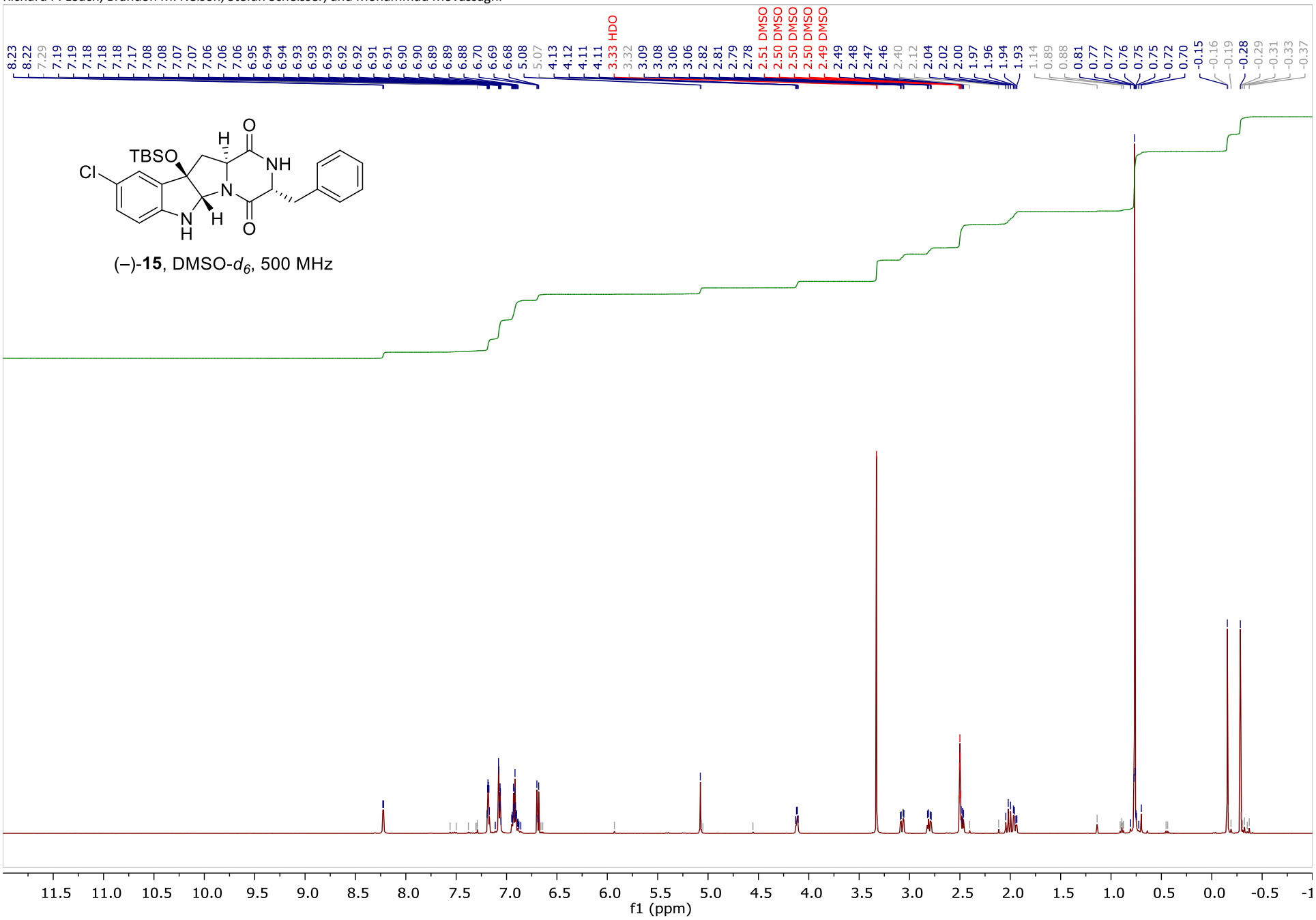


(–)-**S1**, acetone-d_6, 125 MHz


7.94 7.92 7.64 7.64 7.62 7.61 7.54 7.54 7.53 7.52 7.48 7.47 7.47 7.45 7.44 7.44 7.43 7.43 7.42 7.42 7.40 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.00 7.00 7.00 6.98 6.97 6.97 6.96 6.96 6.95 6.14 5.51 5.48 5.34 5.32 4.29 4.28 4.27 4.26 3.16 3.15 3.13 3.13 2.97 HDO 2.96 2.94 2.93 HDO 2.89 HDO 2.86 HDO 2.65 2.64 2.63 2.62 2.33 2.31 2.28 2.21 2.20 2.19 2.18 2.08 Acetone 2.08 Acetone 2.07 Acetone 2.07 Acetone 2.06 Acetone 0.92 0.85 0.83 0.80 0.79 0.78 0.77 0.77 0.76 0.75 -0.23 -0.24 -0.25 -0.26 -0.27
TBSO
Cl
H
O
NH
N
N
H
Cbz
O
(–)-14, acetone-d_6, 500 MHz
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
f1 (ppm)



(–)-**14,** acetone-d_6, 125 MHz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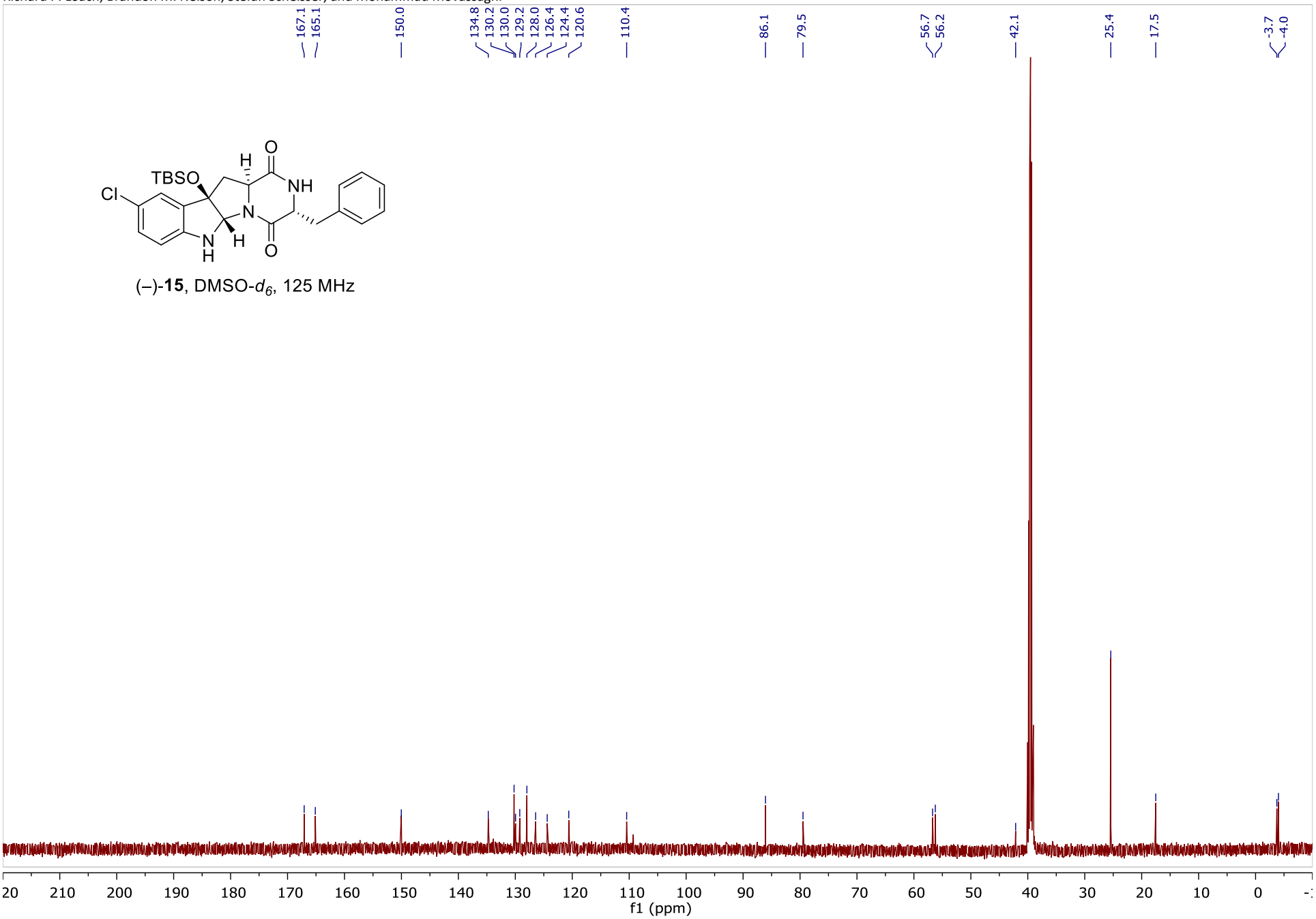
TBSO
Cl
H
O
NH
N
N
H
H
O
(–)-15, DMSO-d6, 500 MHz
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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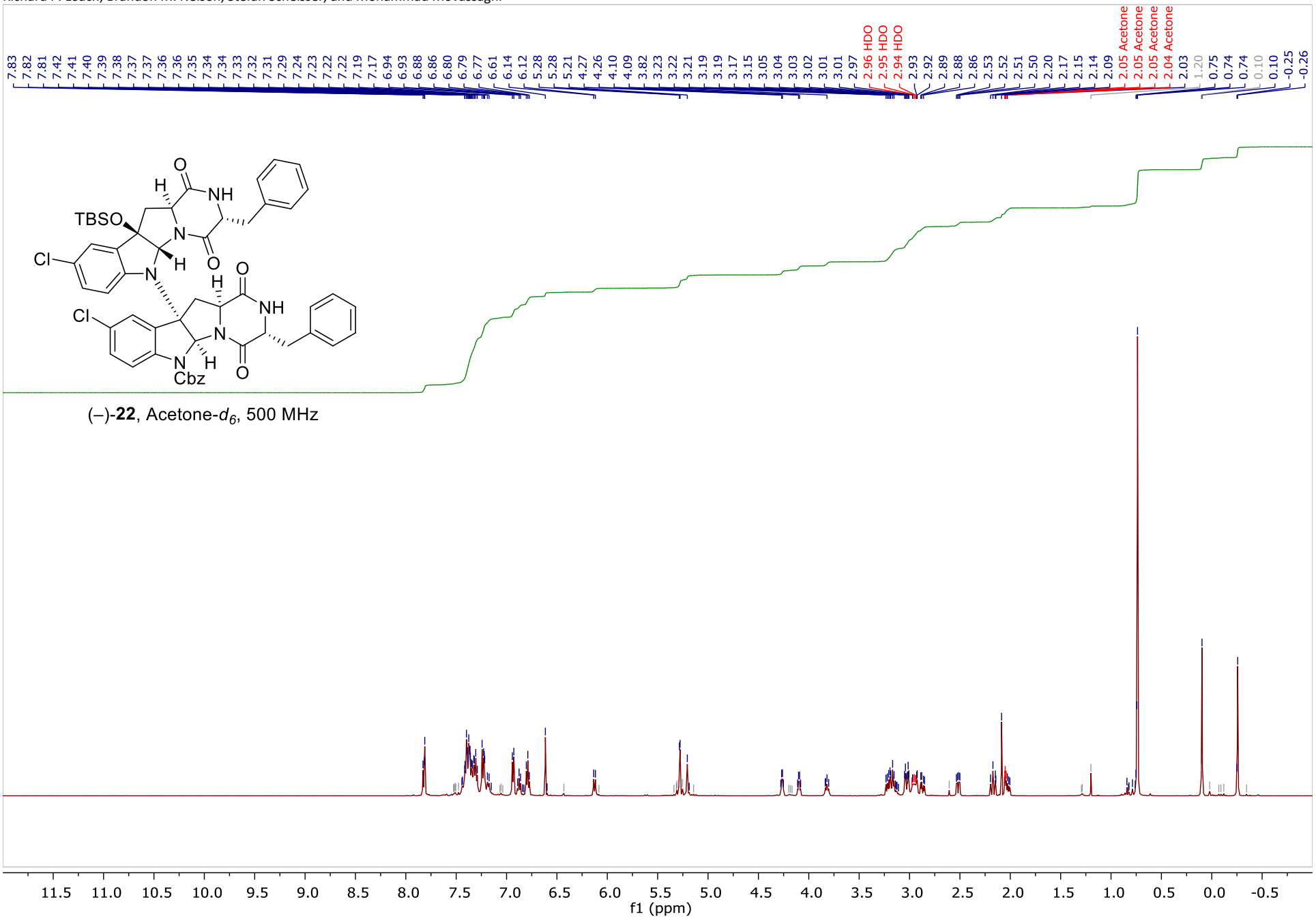
124.4
120.6
110.4
86.1
79.5
56.7
56.2
42.1
25.4
17.5
-3.7
-4.0
TBSO
Cl
H
O
NH
N
N
H
H
O
(–)-15, DMSO-d6, 125 MHz
f1 (ppm)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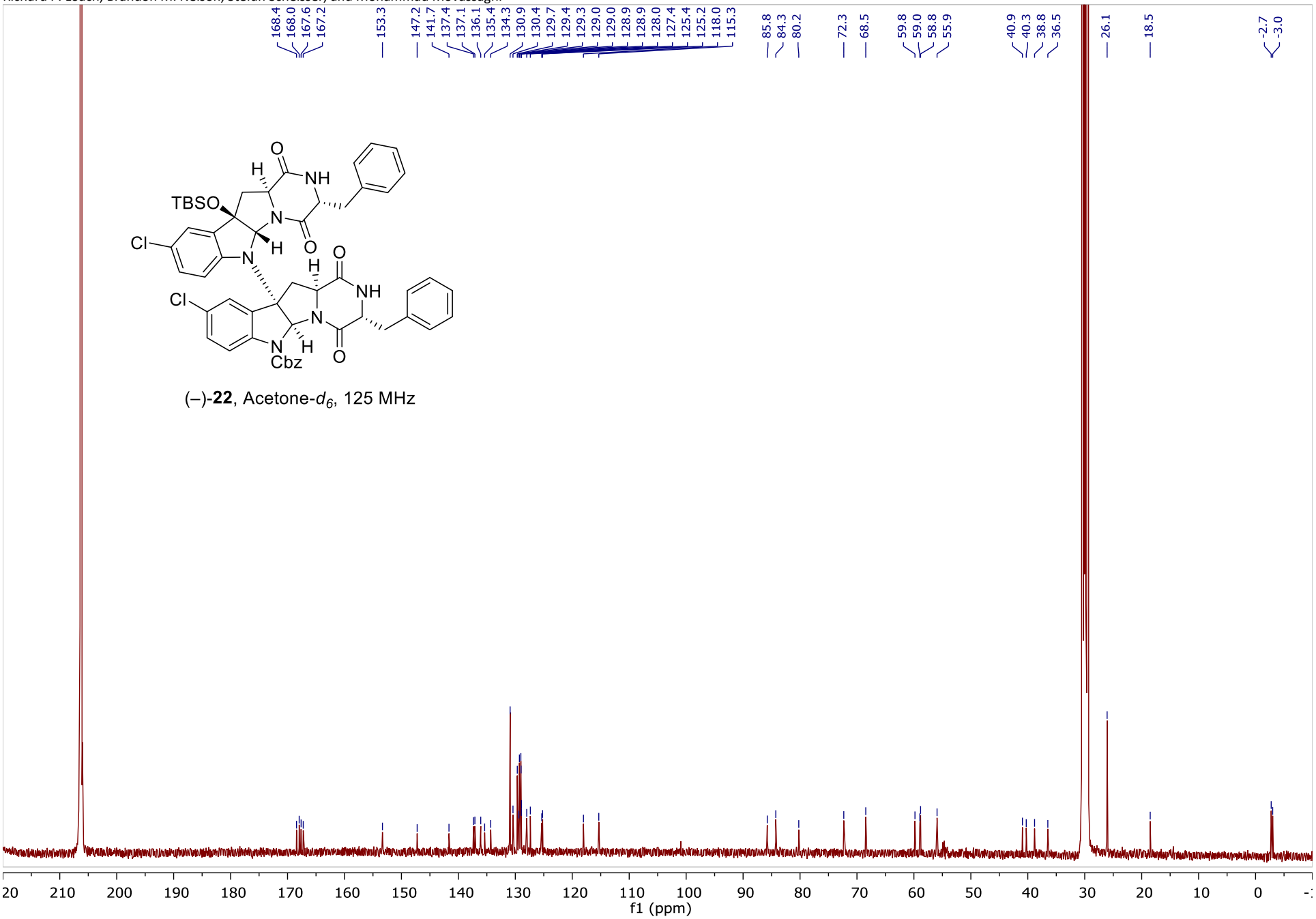
TBSO
Cl
Cl
NH
NH
Cbz
(–)-**22**, Acetone-d_6, 500 MHz
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.9
128.0
127.4
125.4
125.2
118.0
115.3
85.8
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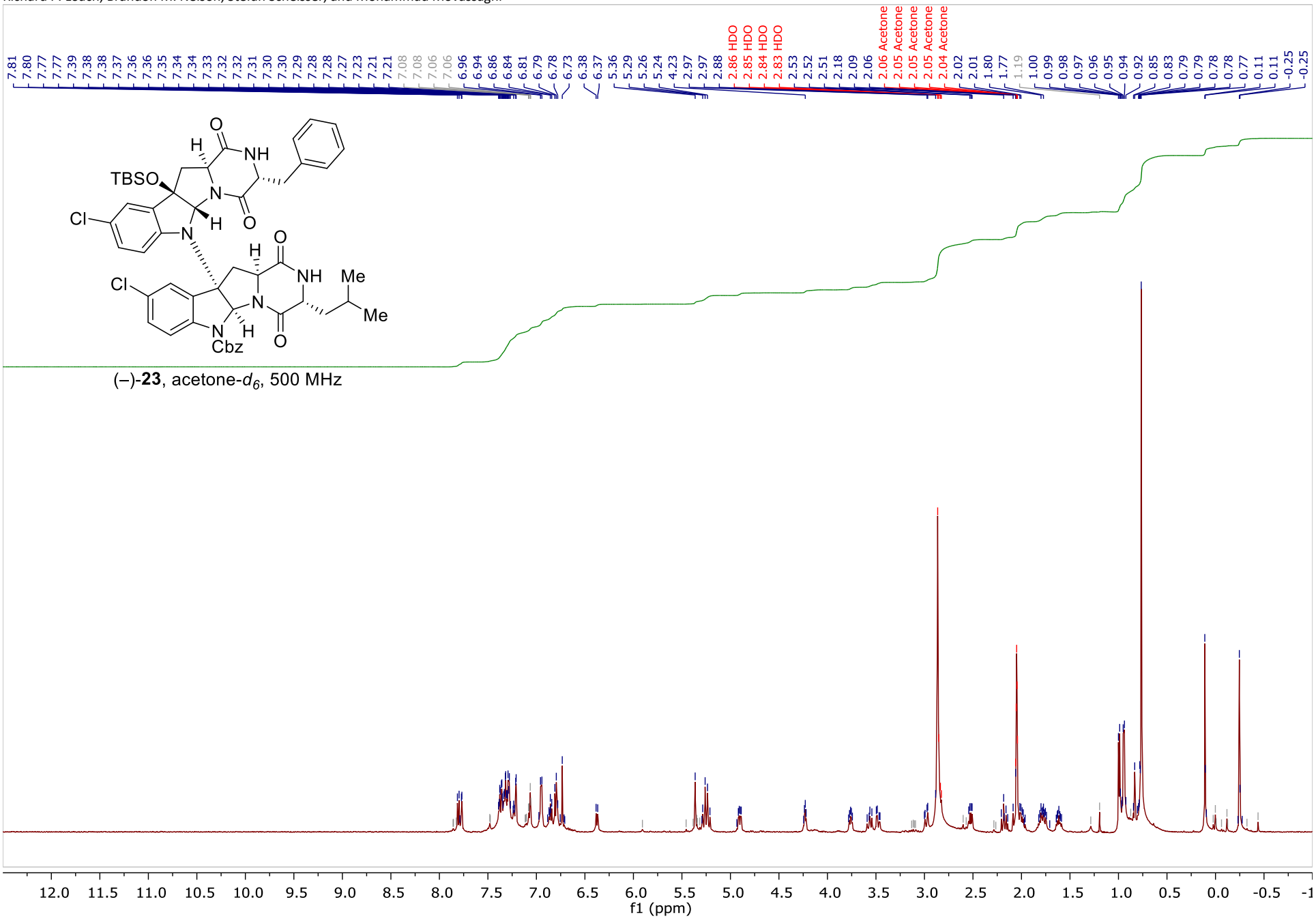
80.2
72.3
68.5
59.8
59.0
58.8
55.9
40.9
40.3
38.8
36.5
26.1
18.5
-2.7
-3.0
TBSO
Cl
Cl
NH
NH
N
N
N
H
H
H
O
O
O
O
O
Cbz
(–)-**22**, Acetone-d_6, 125 MHz
f1 (ppm)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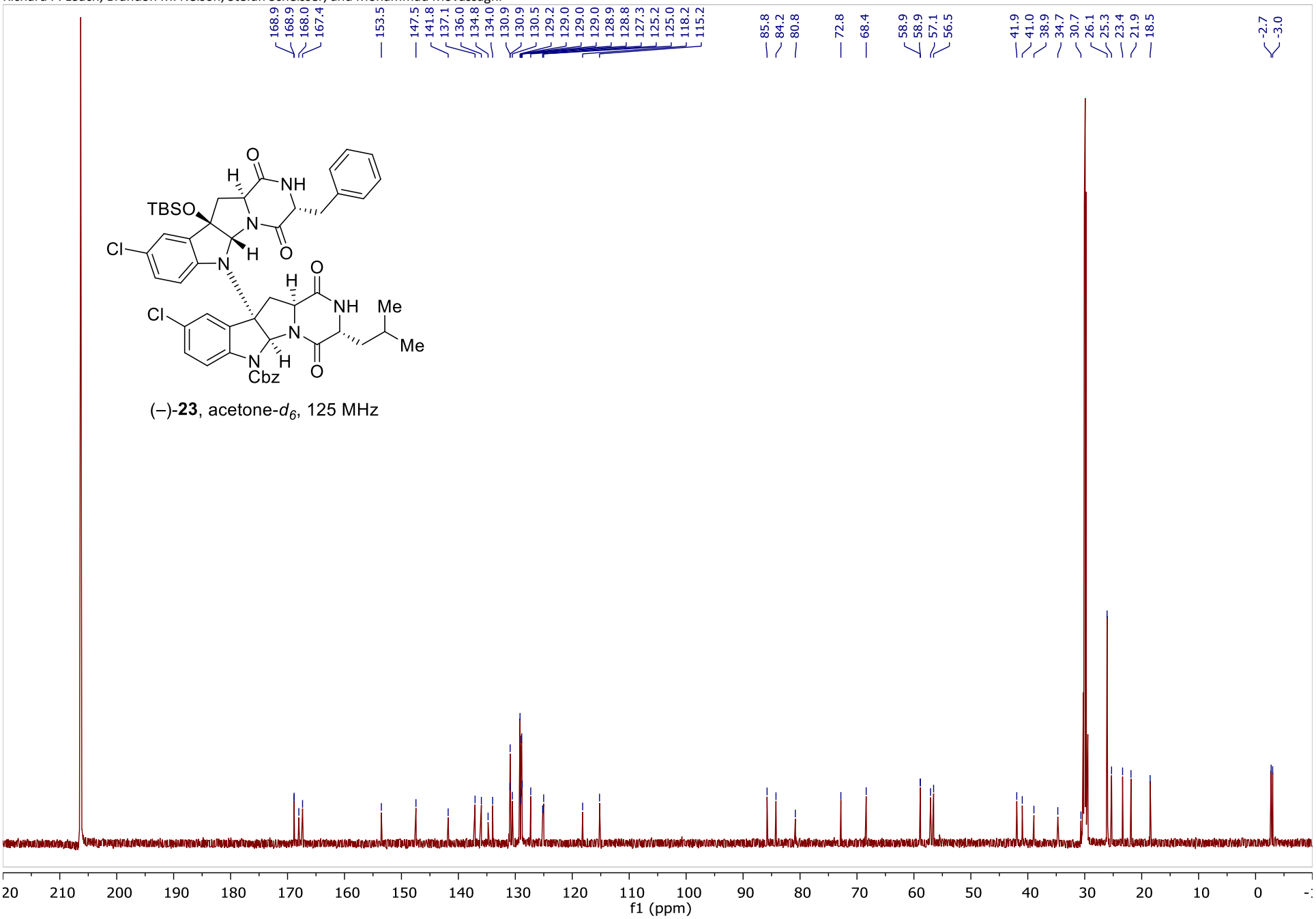
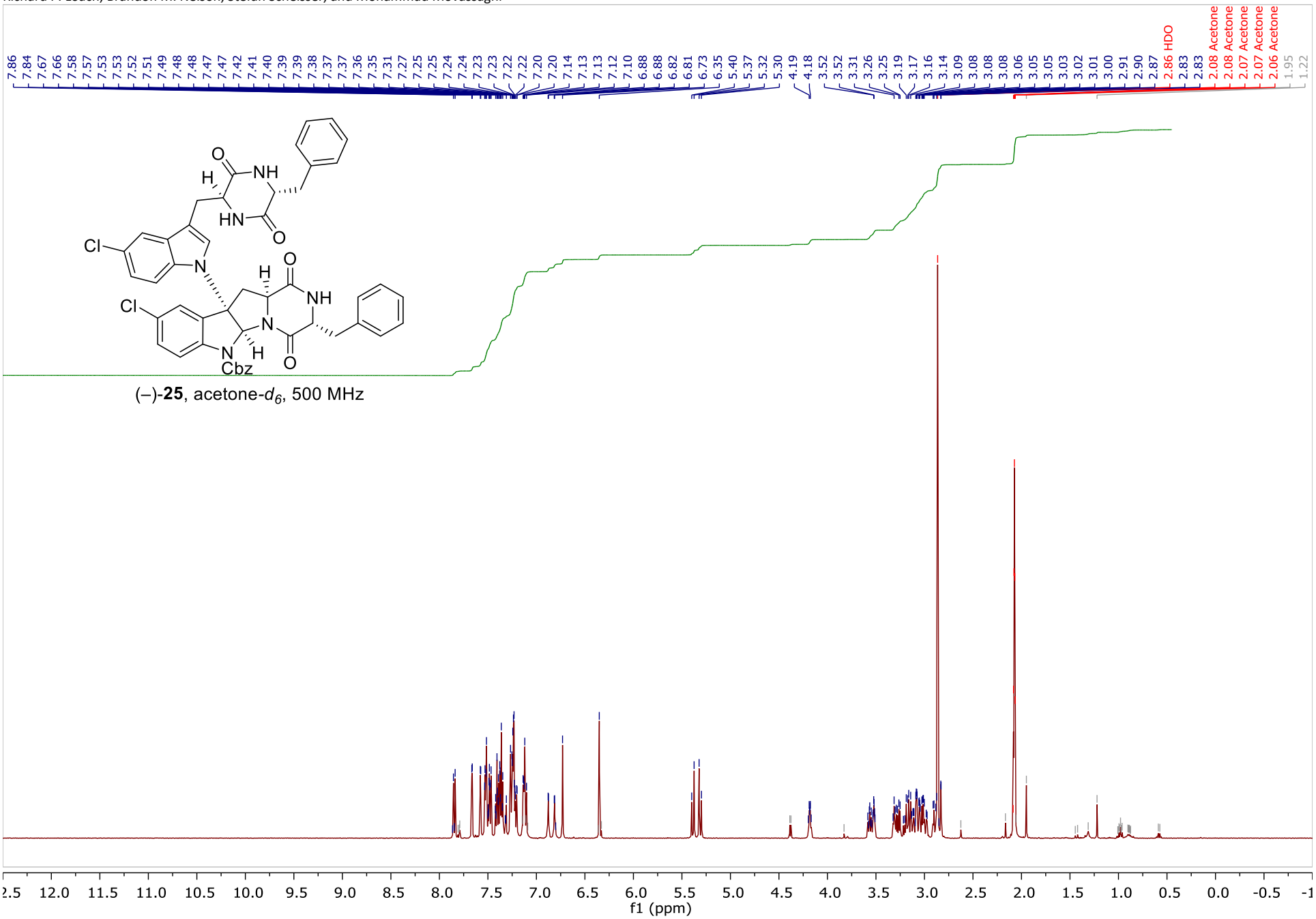
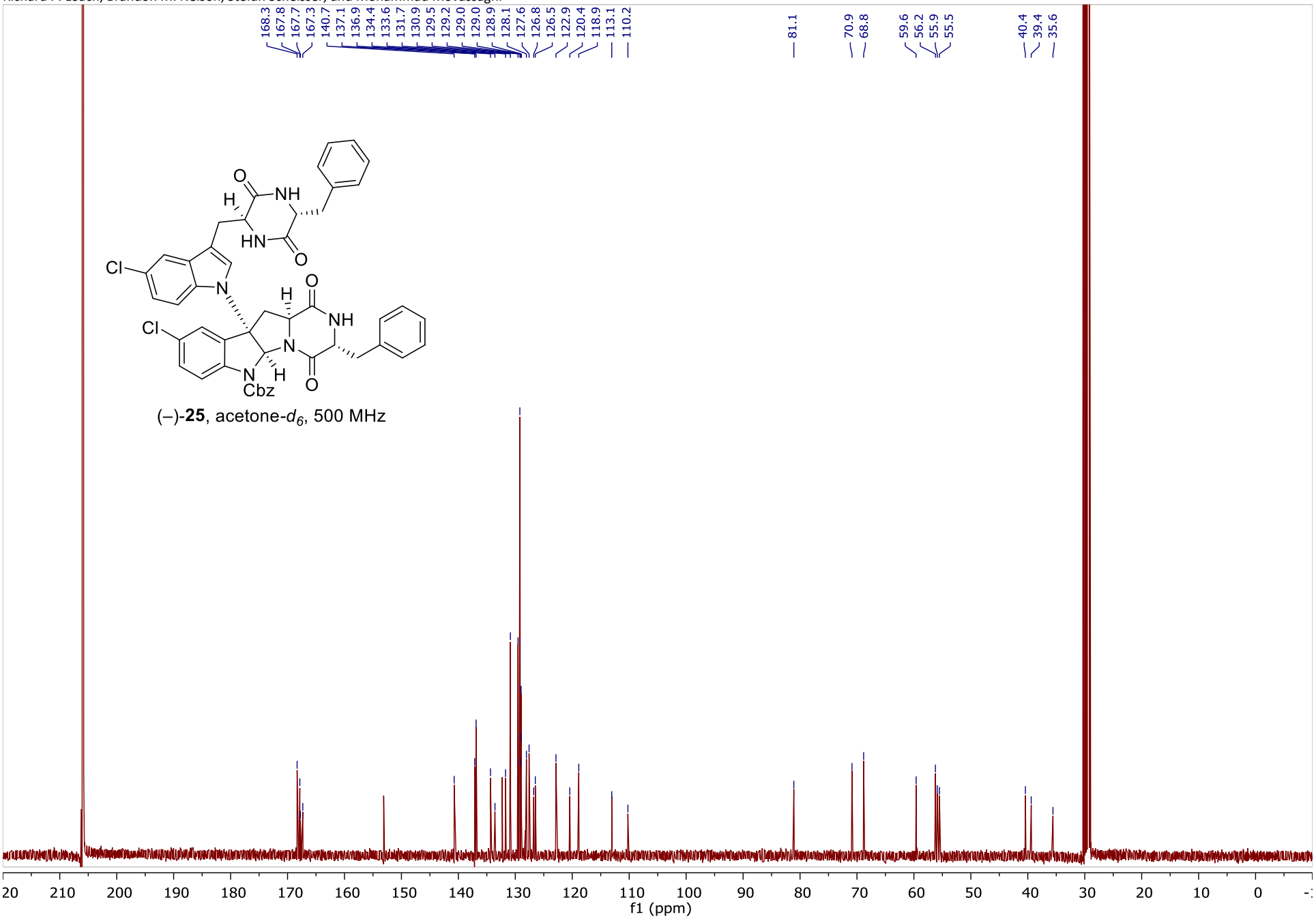
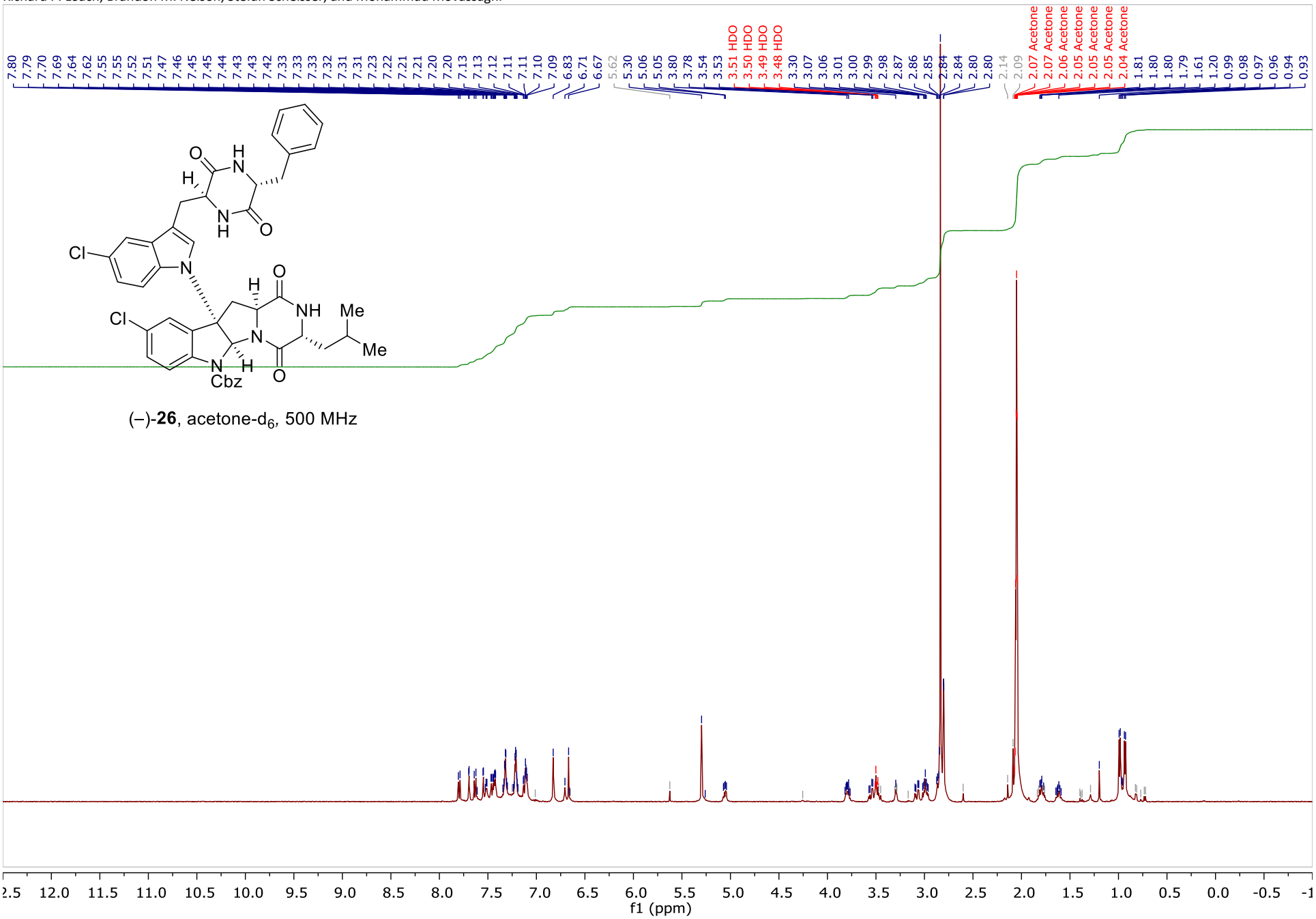
TBSO
Cl
Cl
NH
Me
Me
Cbz
(–)-23, acetone-d6, 500 MHz
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)



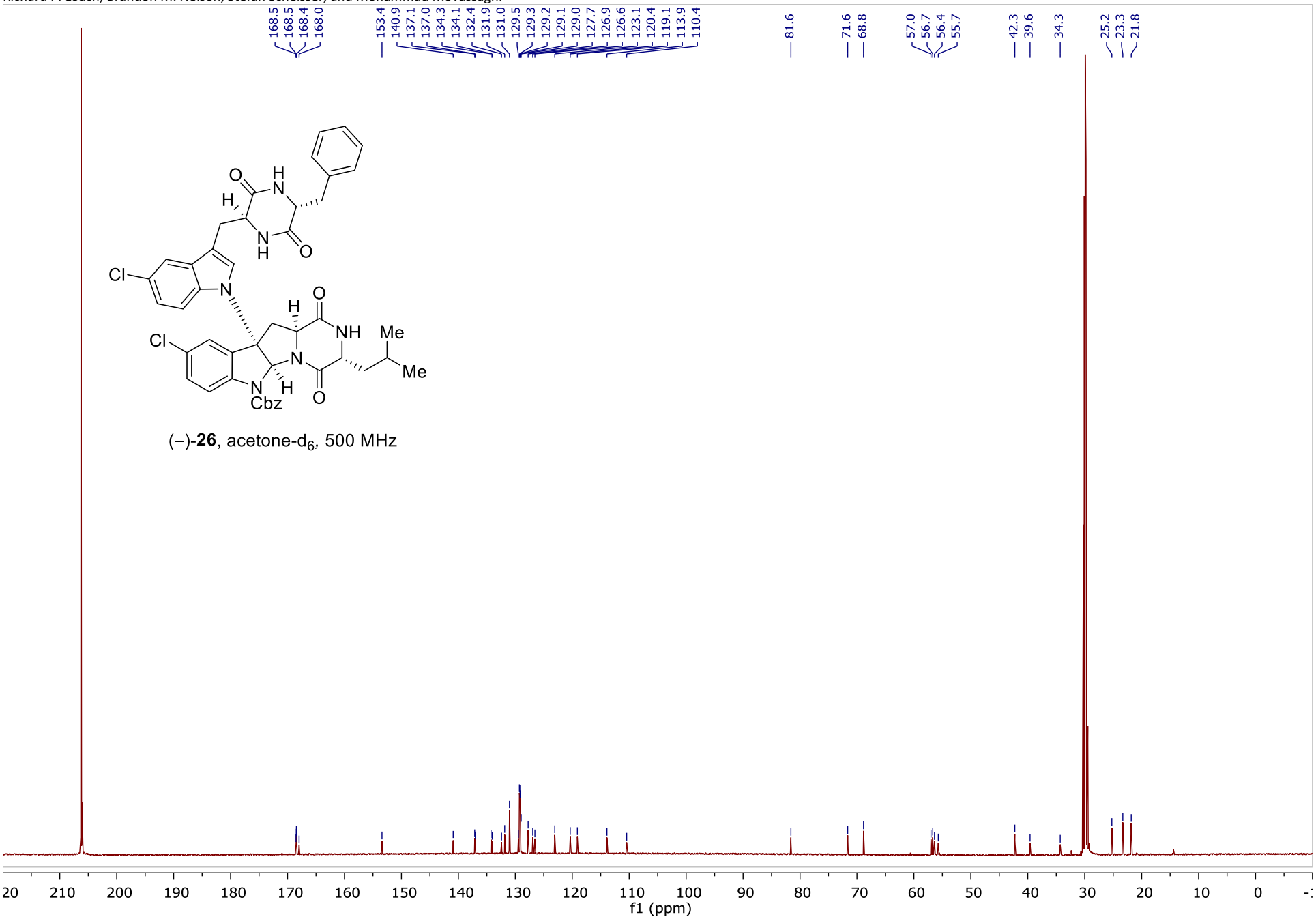
(–)-**23**, acetone-d_6, 125 MHz


7.86 7.84 7.67 7.66 7.58 7.57 7.53 7.53 7.52 7.51 7.49 7.48 7.48 7.47 7.47 7.42 7.41 7.40 7.39 7.39 7.38 7.37 7.37 7.36 7.35 7.31 7.27 7.25 7.25 7.24 7.24 7.23 7.22 7.22 7.20 7.20 7.14 7.13 7.13 7.12 7.10 6.88 6.88 6.82 6.81 6.73 6.35 5.40 5.37 5.32 5.30 4.19 4.18 3.52 3.52 3.31 3.26 3.25 3.19 3.17 3.16 3.14 3.09 3.08 3.08 3.08 3.06 3.05 3.03 3.02 3.01 3.00 2.91 2.90 2.87 2.86 HDO 2.83 2.83 2.08 Acetone 2.08 Acetone 2.07 Acetone 2.07 Acetone 2.06 Acetone 1.95 1.22
O
H
NH
HN
O
Cl
N
H
O
NH
Cl
N
N
H
Cbz
O
(–)-25, acetone-d6, 500 MHz
2.5 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
f1 (ppm)

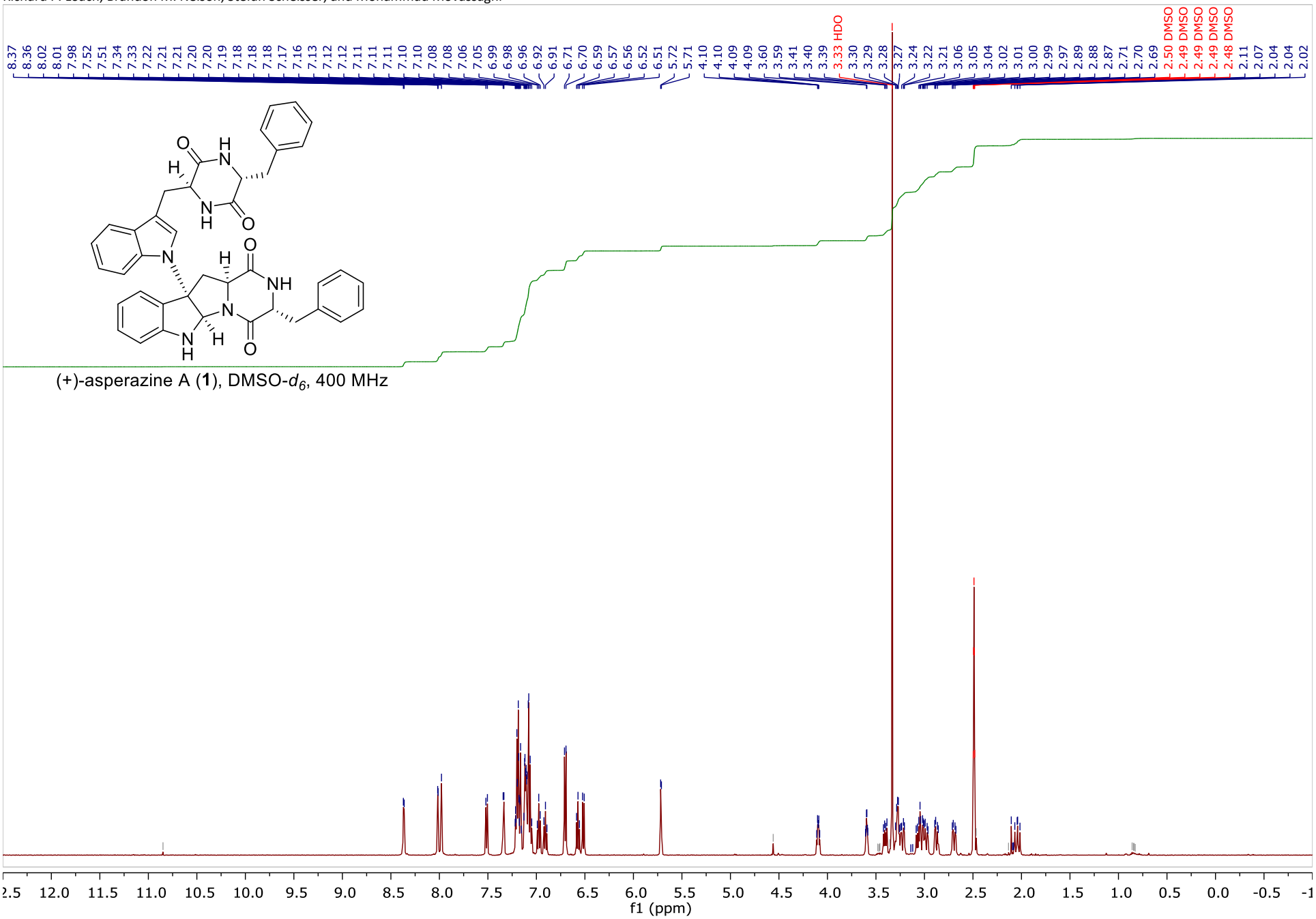

168.3
167.8
167.7
167.3
140.7
137.1
136.9
134.4
133.6
131.7
130.9
129.5
129.2
129.0
129.0
128.9
128.1
127.6
126.8
126.5
122.9
120.4
118.9
113.1
110.2
81.1
70.9
68.8
59.6
56.2
55.9
55.5
40.4
39.4
35.6
O
NH
H
HN
O
Cl
N
O
H
NH
Cl
N
N
H
O
Cbz
(–)-25, acetone-d6, 500 MHz
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

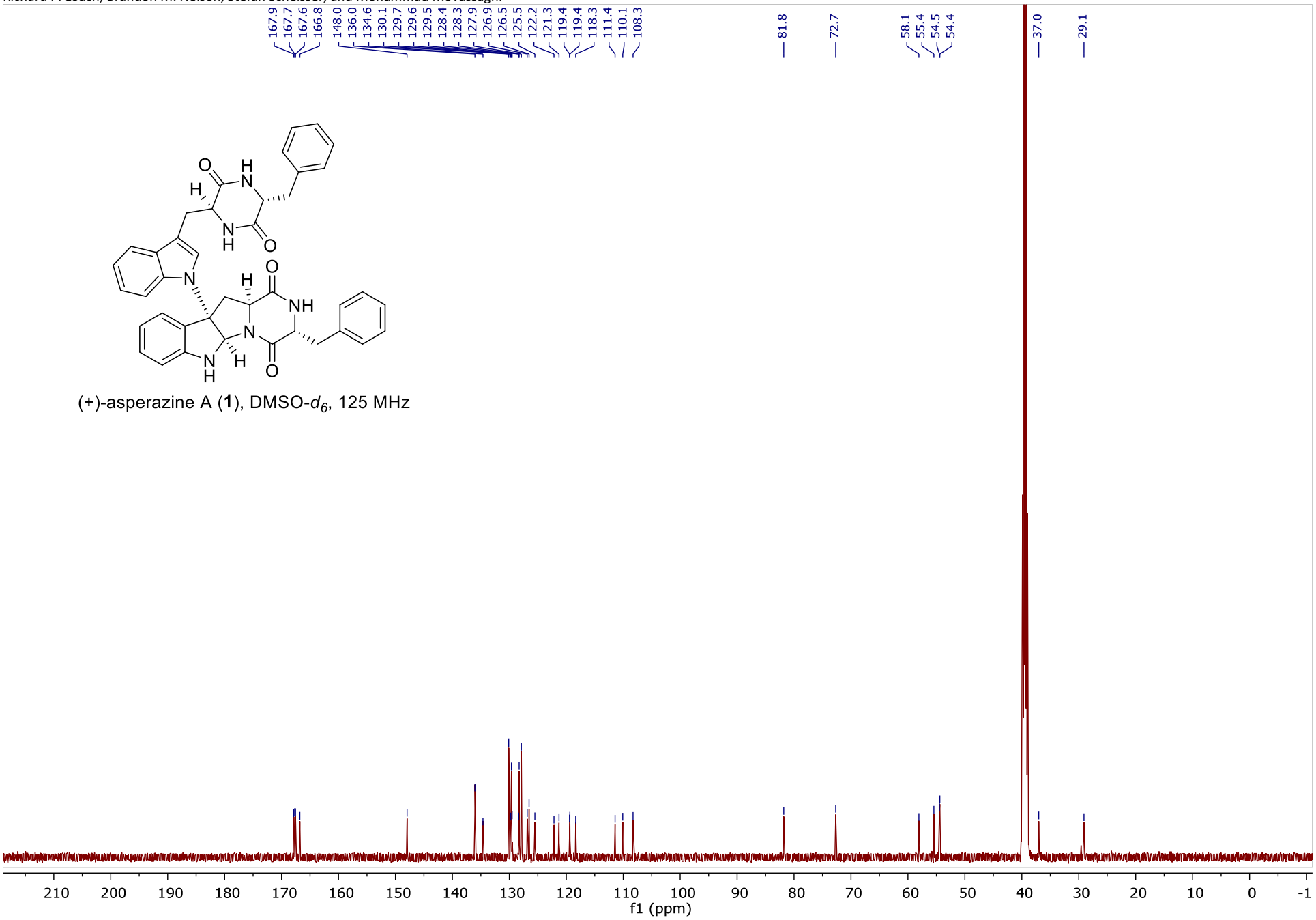


(–)-**26**, acetone-d_6, 500 MHz

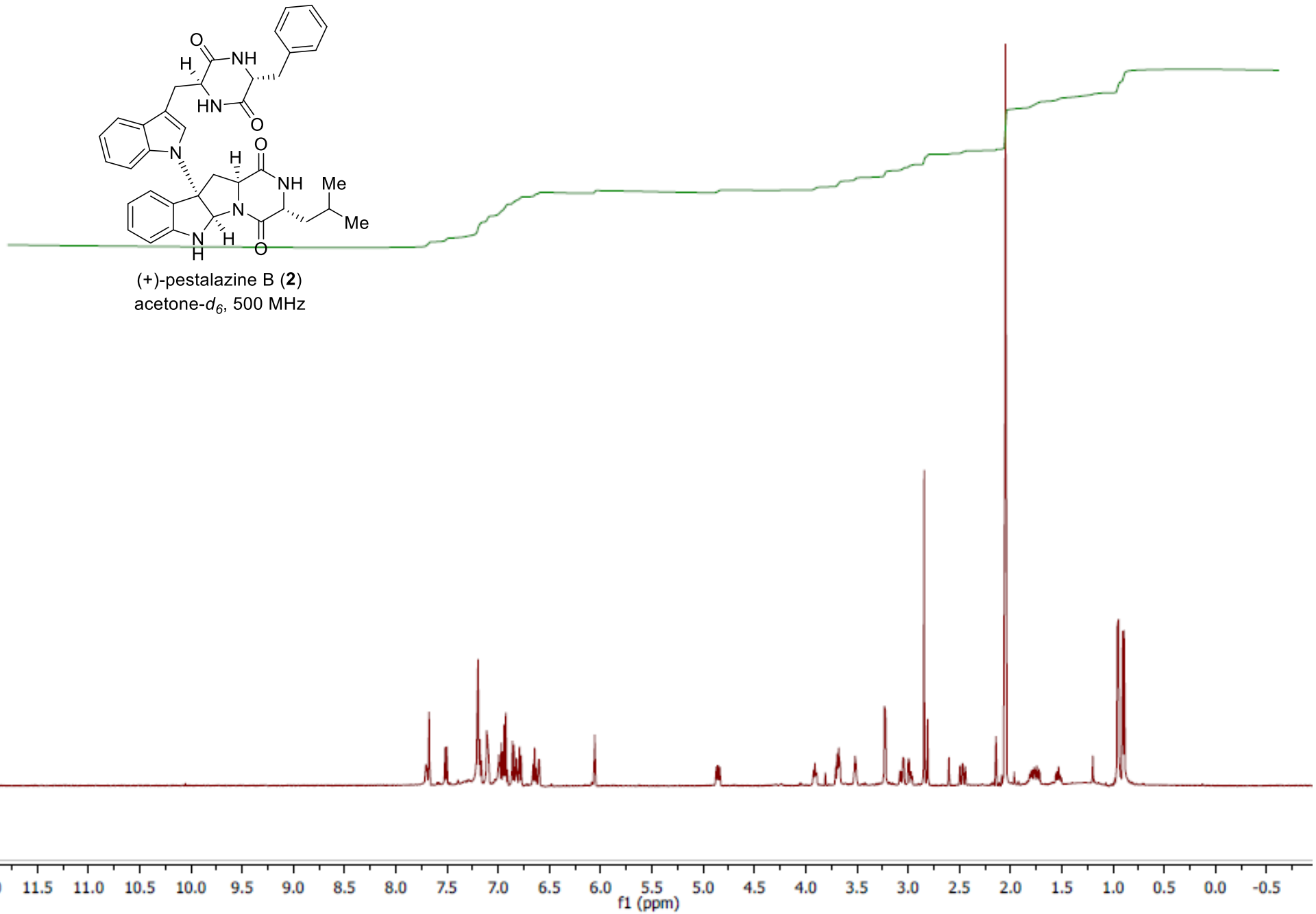


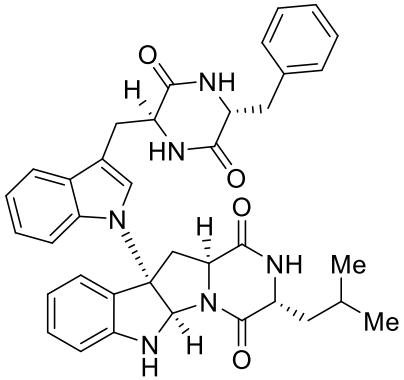
(–)-**26**, acetone-d_6, 500 MHz


8.37 8.36 8.02 8.01 7.98 7.52 7.51 7.34 7.33 7.22 7.21 7.21 7.20 7.20 7.19 7.18 7.18 7.18 7.17 7.16 7.13 7.12 7.12 7.11 7.11 7.11 7.10 7.10 7.08 7.08 7.06 7.05 6.99 6.98 6.96 6.92 6.91 6.71 6.70 6.59 6.57 6.56 6.52 6.51 5.72 5.71 4.10 4.10 4.09 4.09 3.60 3.59 3.41 3.40 3.39 3.33 HDO 3.30 3.29 3.28 3.27 3.24 3.22 3.21 3.06 3.05 3.04 3.02 3.01 3.00 2.99 2.97 2.89 2.88 2.87 2.71 2.70 2.69 2.50 DMSO 2.49 DMSO 2.49 DMSO 2.49 DMSO 2.48 DMSO 2.11 2.07 2.04 2.04 2.02
(+)-asperazine A (1), DMSO-d6, 400 MHz
f1 (ppm)

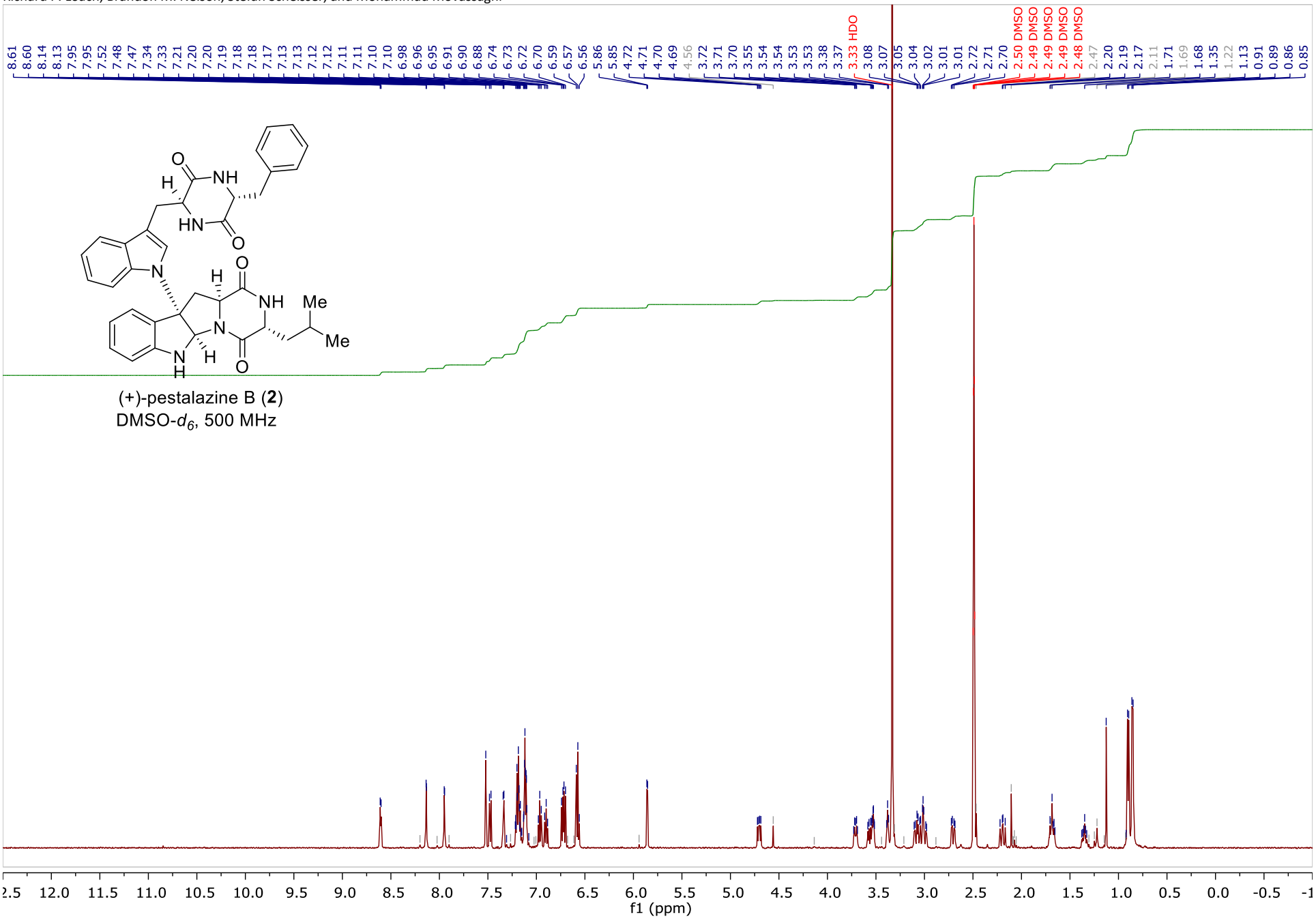


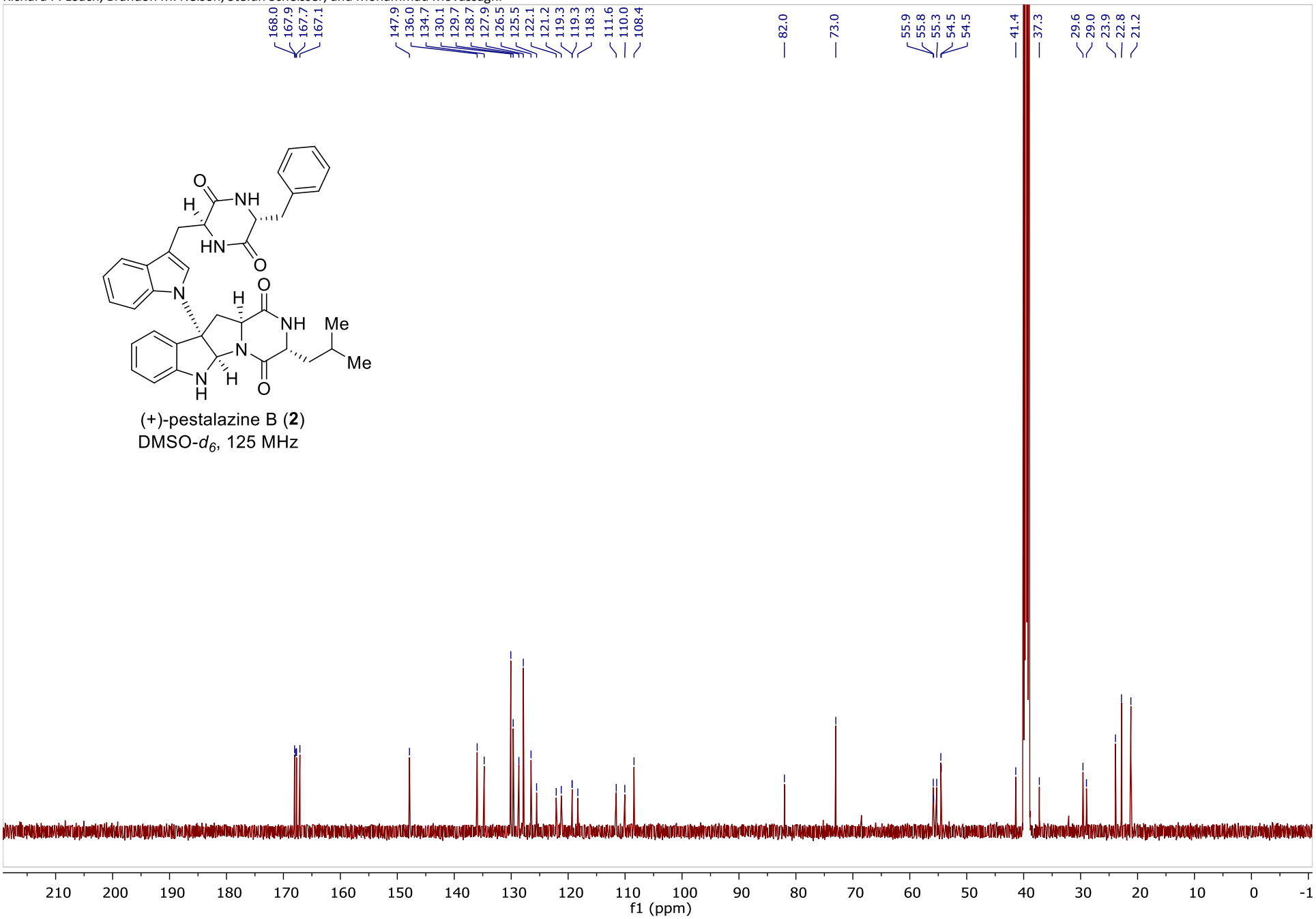
(+)-asperazine A (**1**), DMSO-d_6, 125 MHz


(+)-pestalazine B (2)
acetone-d6, 500 MHz
f1 (ppm)



(+)-pestalazine B (**2**)
acetone-d_6, 125 MHz


8.61 8.60 8.14 8.13 7.95 7.95 7.52 7.48 7.47 7.34 7.33 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.13 7.13 7.12 7.12 7.11 7.11 7.10 7.10 6.98 6.96 6.95 6.91 6.90 6.88 6.74 6.73 6.72 6.70 6.59 6.57 6.56 5.86 5.85 4.72 4.71 4.70 4.69 4.56 3.72 3.71 3.70 3.55 3.54 3.54 3.53 3.53 3.38 3.37 3.33 HDO 3.08 3.07 3.05 3.04 3.02 3.01 3.01 2.72 2.71 2.70 2.50 DMSO 2.49 DMSO 2.49 DMSO 2.49 DMSO 2.48 DMSO 2.47 2.20 2.19 2.17 2.11 1.71 1.69 1.68 1.35 1.22 1.13 0.91 0.89 0.86 0.85
O
H
NH
HN
O
N
H
O
NH
Me
Me
N
H
N
H
O
(+)-pestalazine B (2)
DMSO-d6, 500 MHz
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
f1 (ppm)


168.0
167.9
167.7
167.1
147.9
136.0
134.7
130.1
129.7
128.7
127.9
126.5
125.5
122.1
121.2
119.3
119.3
118.3
111.6
110.0
108.4
82.0
73.0
55.9
55.8
55.3
54.5
54.5
41.4
37.3
29.6
29.0
23.9
22.8
21.2
O
H
NH
HN
O
N
H
O
NH
Me
Me
N
N
H
H
O
(+)-pestalazine B (2)
DMSO-d6, 125 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)