Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Supporting information

Thiolation of Symmetrical and Unsymmetrical Diketopiperazines

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General

^{1}H NMR spectra were recorded on a *Bruker* Avance 300 (300 MHz), a *Bruker* AM 400 (400 MHz) or a *Bruker* Avance 600 (600 MHz) spectrometer as solutions. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to chloroform (7.26 ppm) as internal standards. All couplings constants are absolute values and *J* values are expressed in Hertz (Hz). The spectra were analyzed according to first order and the descriptions of signals include: s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet. Diastereotopic methylene protons were assigned with H_A and H_B, where H_A was used for the more downfield shifted proton. ^{13}C NMR spectra were recorded on a *Bruker* Avance 300 (75 MHz) or a *Bruker* AM 400 (100 MHz) spectrometer as solutions. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CDCl_3$ (77.0 ppm) as internal standards. The signal structure was analyzed by DEPT and is described as follows: + = primary or tertiary C-atom (positive signal), – = secondary C-atom (negative signal) and C_q = quaternary C-atom (no signal).

EI-MS (electron impact mass spectrometry) and FAB-MS (fast atom bombardment mass spectrometry) were performed by using a *Finnigan* MAT 90 (70 eV). The molecular fragments are quoted as the relation between mass and charge (*m/z*), the intensities as a percentaged value relative to the intensity of the base signal (100%). The abbreviation $[M]^+$ refers to the molecule ion. ESI-MS was performed by using an *Agilent* 6230 TOF LC/MS.

IR (infrared spectroscopy) data were recorded on FT-IR *Bruker* IFS 88 and are reported as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad).

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Elemental analysis was performed by using *Elementar* Vario Microcube. Descriptions were done at room temperature, and the following abbreviations were used: *calc.* (theoretical value), *found* (measured value). Information is given in mass percent.

Optical rotations were determined on a *Perkin Elmer* 241 polarimeter at 20 °C with a glass cuvette (l = 1 dm) and the D line of sodium. The values were calculated according to the following formula: $[\alpha]_D^{20} = \alpha/\beta \times d$ with D = sodium D line (λ = 589.3 nm); α = average of the obtained optical rotations; d = length of the cuvette (in dm, d = 1); β = concentration in g/ml. Information is given as, e.g. $[\alpha]_D^{20} = -64.8$ (c = 0.58, $CHCl_3$) with c = concentration in g/100 mL.

Reactions were monitored by silica gel coated aluminium plates (*Merck*, silica gel 60, F_{254}). Detection was performed by examination under UV light (254 nm) and by staining with molybdato phosphate (5% phosphor molybdic acid in ethanol) or ninhydrine solution (3% ninhydrine in ethanol). Solvents, reagents and chemicals were purchased from *Aldrich*, *Fluka*, *ABCR* and *Acros*. Tetrahydrofuran was distilled from sodium/potassium prior to use. Dichloromethane was distilled from calcium hydride. Toluene was distilled from sodium. All reactions involving moisture sensitive reactants were executed under argon atmosphere using oven dried glassware. All other solvents, reagents and chemicals were used as purchased unless stated otherwise.

Experimental

General Procedures:

General Procedure (GP 1): Synthesis of *mono*-(methylthio)diketopiperazines

To a solution of DKP **1{xy}** (1.00 equiv.) in dry THF was added NaHMDS (1.0 M in THF, 6.00 equiv.) at –78 °C. The mixture was allowed to stir for 1 h. Then, *S*-methyl methanesulfonothioate (**12**, 2.50 equiv.) in dry THF was added and the mixture was stirred for 2 h while it was allowed to warm up to room temperature. Saturated NH_4Cl solution was added, it was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Purification by column chromatography afforded the title compounds.

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General Procedure (GP 2): Synthesis of *bis*-(methylthio)diketopiperazines

To a solution of sulfur (8.00 equiv.) in dry THF was added NaHMDS (1.0 M in THF, 3.00 equiv.) at room temperature. Then, DKP **1{xy}** (1.00 equiv.) in dry THF and more NaHMDS (1.0 M in THF, 3.00 equiv.) were added and the mixture was stirred for 0.5 h at room temperature. Saturated NH_4Cl solution was added, it was extracted with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was dissolved in degassed THF/EtOH (1:1) and $NaBH_4$ (25.0 equiv.) was added. The mixture was stirred for 45 min at room temperature. Then, MeI (50.0 equiv.) was added and it was stirred overnight. Saturated NH_4Cl solution was added, it was extracted with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Purification by column chromatography afforded the title compounds.

General Procedure (GP 3): Synthesis of epithiodiketopiperazines

To a solution of sulfur (8.00 equiv.) in dry THF was added NaHMDS (1.0 M in THF, 3.00 equiv.) at room temperature. Then, DKP **1{xy}** (1.00 equiv.) in dry THF and more NaHMDS (1.0 M in THF, 3.00 equiv.) were added and the mixture was stirred for 0.5 h at room temperature. Saturated NH_4Cl solution was added, it was extracted with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was dissolved in degassed THF/EtOH (1:1) and $NaBH_4$ (25.0 equiv.) was added. The mixture was stirred for 45 min at room temperature. Then, the mixture was cooled to 0 °C, quenched by the addition of saturated NH_4Cl solution and extracted with EtOAc. The combined organic extracts were stirred with KI_3 solution for 10 min, $Na_2S_2O_3$ solution was added and it was extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. Purification by column chromatography afforded the title compounds.

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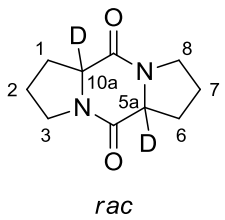
Syntheses:

(*rac*)-(5a,10a)-dideuterium-octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione

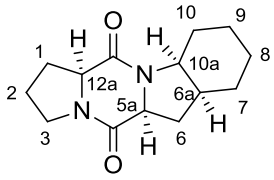


rac

To a solution of DKP **1{aa}** (20.0 mg, 103 µmol) in dry THF (3 mL) was added NaHMDS (1.0 M in THF, 6.00 equiv.) or a freshly prepared LDA solution (472 µL, 618 µmol, 6.00 equiv.) at –78 °C. The mixture was allowed to stir for 1 h. Then D_2O (0.6 mL) was added at 0 °C and the mixture was stirred for 2 h while it was allowed to warm up to room temperature. Saturated NH_4Cl solution was added, it was extracted with CH_2Cl_2, the combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The title compound was obtained as colorless thick oil.

***R*f** = 0.10 (EtOAc). – **^{1}H NMR** (250 MHz, DMSO-d_6): δ = 1.37–2.11 (m, 8H, 1-H_2, 2-H_2, 6-H_2, 7-H_2), 3.21–3.45 (m, 4H, 3-H_2, 8-H_2) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3374 (m), 1624 (m), 1408 (m), 1085 (w), 860 (w), 665 (w), 470 (w) – **MS** (EI): *m/z* (%): 196 (81) $[M]^+$, 140 (17), 72 (100), 44 (98). – **HRMS** ($C_{10}H_{12}D_2N_2O_2$): calc. 196.1181; found 196.1181.

(5a*S*,6a*S*,10a*S*,12a*S*)-dodecahydropyrrolo[1',2':4,5]pyrazino[1,2-a]indole-5,12-dione (**1{ab}**)



L-Proline (100 mg, 870 µmol) was suspended in toluene (3 mL). Triethylamine (482 µL, 3.47 mmol, 4.00 equiv.) and methyl dichlorophosphite (82.5 µL, 869 µmol) were added and the mixture was stirred at 35 °C overnight. Then, L-octahydroindole-2-carboxylic acid (162 mg, 955 µmol, 1.10 equiv.) and toluene (2 mL) were added. After irradiation under closed-vessel microwave conditions at 145 °C for 1 h, the solution was filtered, and the precipitate was washed with hot toluene (50 mL). The filtrate was evaporated under reduced pressure and the resulting crude product was purified by column chromatography (EtOAc). The title compound was obtained as colorless solid (54.0 mg, 25%).

***R*f** = 0.16 (EtOAc). – **mp**: 137 °C. – **$[\alpha]_D^{20}$** = –37.1 (c = 0.17, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.93–1.08 (m, 1H, CH_2), 1.10–1.39 (m, 2H, CH_2), 1.46–1.57 (m, 1H, CH_2), 1.58–2.09 (m, 6H, CH_2), 2.14–2.43 (m, 5H, CH_2, 6a-H), 3.46–3.60 (m, 2H, 3-H_2), 3.98 (dt, ^3J = 10.6, 12.1 Hz, 1H, 10a-H), 4.09 (t, ^3J = 8.0 Hz, 1H, 5a-H or 12a-H), 4.21 (t, ^3J = 8.4 Hz, 1H, 5a-H or 12a-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 20.8 (–, *C*H_2), 23.4 (–, *C*H_2), 23.6 (–, *C*H_2), 25.9 (–, *C*H_2), 27.4 (–, *C*H_2), 27.5 (–, *C*H_2), 28.6 (–, *C*H_2), 36.1 (+, C-6a), 45.1 (–, C-3), 56.5 (+, C-10a), 60.6 (+, C-5a, C-12a), 166.7 (C_q, *C*=O), 167.2 (C_q, *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3853 (vs), 3442 (vs), 2925 (vs), 1653 (s), 1445 (vs), 1261 (vs), 1158 (vs), 1077 (vs), 800 (vs), 663 (vs), 611 (vs) cm^{-1}. – **MS** (EI): *m/z* (%): 248 (95) $[M]^+$, 124 (42), 113

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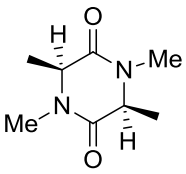
(22), 98 (21), 97 (38), 85 (65), 83 (17), 71 (33), 70 (100), 69 (44), 57 (94), 55 (35), 43 (31), 41 (23). – **HRMS** ($C_{17}H_{20}N_2O_3$): calc. 248.1525; found 248.1522.

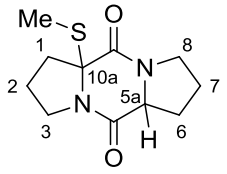
(3*R*,6*R*)-1,3,4,6-tetramethyl-3,6-bis(methylthio)piperazine-2,5-dione (**1{dd}**)



N-Methyl-L-Alanine (300 mg, 2.91 mmol) was suspended in toluene (8 mL). Triethylamine (1.64 mL, 11.6 mmol, 4.00 equiv.) and methyl dichlorophosphite (141 µl, 1.45 mmol, 0.50 equiv.) were added and the mixture was stirred at 35 °C overnight. After irradiation under closed-vessel microwave conditions at 145 °C for 1 h, the solution was filtered, and the precipitate was washed with hot toluene (50 mL). The filtrate was evaporated under reduced pressure and the resulting crude product was purified by column chromatography (CH_2Cl_2/MeOH 98:2). The title compound was obtained as colorless solid (83.7 mg, 34 %).

***R*$_f$** = 0.14 (CH_2Cl_2/MeOH 98:2). – **mp**: 96 °C. – **[α]$_D^{20}$** = +62.6 (c = 0.38, $CHCl_3$). – **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 1.49 (d, ^3J = 7.0 Hz, 6H, CHC*H*$_3$), 2.89 (s, 6H, NC*H*$_3$), 3.89 (q, ^3J = 7.0 Hz, 2H, C*H*) ppm. – **^{13}C NMR** (75 MHz, $CDCl_3$): δ = 19.0 (+, 2 × CH*C*H$_3$), 32.0 (+, 2 × N*C*H$_3$), 58.1 (+, 2 × *C*H), 166.8 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2984 (s), 2931 (s), 1650 (m), 1484 (m), 1450 (m), 1405 (m), 1369 (m), 1330 (m), 1298 (m), 1255 (m), 1172 (m), 1089 (m), 1063 (m), 1035 (m), 896 (s), 748 (m), 737 (m), 704 (m), 630 (s), 498 (m) cm^{-1}. – **MS** (EI): *m/z* (%): 170 (100) [M]$^+$, 127 (54), 85 (17), 58 (45), 42 (18). – **HRMS** ($C_{17}H_{20}N_2O_3$): calc. 170.1055; found 170.1057.

10a-(methylthio)octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione (**2{aa}**)



S-Me and α-H = *cis*

Prepared according to **GP 1**, starting from DKP **1{aa}** (50.0 mg, 257 µmol). Column chromatography (*c*Hex/EtOAc 1:5) afforded the title compound (10.3 mg, 17%, scalemic mixture) as yellow oil.

***R*$_f$** = 0.15 (*c*Hex/EtOAc 1:5). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.91–2.13 (m, 4H, 2-H$_A$, 6-H$_A$, 7-H$_2$), 2.16 (s, 3H, SC*H*$_3$), 2.26–2.45 (m, 4H, 1-H$_2$, 2-H$_B$, 6-H$_B$), 3.48–3.65 (m, 4H, 3-H$_2$, 8-H$_2$), 4.41–4.49 (m, 1H, H-5a) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 13.9 (+, S*C*H$_3$), 20.8 (–, C-2), 23.1 (–, C-7), 27.9 (–, C-6), 33.9 (–, C-1), 45.4 (–, C-3, C-8), 59.9 (+, C-5a), 59.9 (–, C-5a), 72.5 (C_q, C-10a), 164.3 (C_q, C=O), 167.2 (C_q, C=O) ppm. – **IR** (film): $\tilde{\nu}$ = 2956 (m), 2924 (m), 1664 (s), 1417 (s), 1340 (m), 1207 (m), 1158 (m), 1009 (w), 198 (w), 638 (w) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 241(1) [M+H]$^+$, 193 (8) [M$^+$–SCH$_3$], 165 (7), 133 (100). – **HRMS** ($C_{10}H_{13}N_2O_2^+$): calc. 193.0977; found 193.0979.

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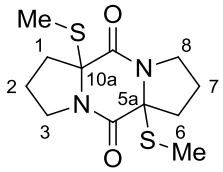
5a,10a-bis(methylthio)octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione (**3{aa}**)

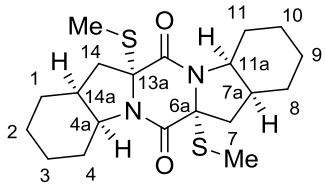


S-Me = *cis*

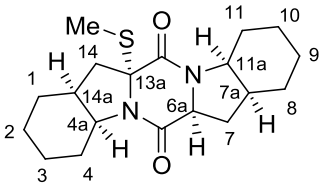
Prepared according to **GP 2**, starting from DKP **1{aa}** (200 mg, 1.03 mmol). Column chromatography (*c*Hex/EtOAc 1:5) afforded the title compound (153 mg, 52%, scalemic mixture) as colorless solid.

***R*$_f$** = 0.30 (*c*Hex/EtOAc 1:5). – **mp**: 126 °C. – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.88–2.06 (m, 4H, 1-H_A, 2-H_A, 6-H_A, 7-H_A), 2.10–2.19 (s, 6H, SCH_3), 2.18–2.31 (m, 2H, 2-H_B, 7-H_B), 2.35–2.47 (m, 2H, 1-H_B, 6-H_B), 3.45–3.71 (m, 4H, 3-H_2, 8-H_2) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.3 (+, 2 × S*C*H_3), 19.7 (–, C-2, C-7), 33.9 (–, C-1, C-6), 45.1 (–, C-3, C-8), 71.1 (C_q, C-5a, C-10a), 164.6 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3499 (m), 2922 (s), 1660 (s), 1415 (m), 1340 (m), 1200 (m), 1150 (w), 1018 (w), 672 (w) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 239 (100) [M^+–SCH_3], 211 (17), 192 (68) [M^+–2×SCH_3], 164 (19), 133 (63), 95 (44), 81 (30). – **HRMS** ($C_{11}H_{15}N_2O_2S^+$): calc. 239.0854; found 239.0853. – **elemental analysis** ($C_{12}H_{18}N_2O_2S_2$): calc. C 50.32, H 6.33, N 9.78, S 22.39; found C 50.49, H 6.46, N 9.63, S 21.45.

(4a*S*,6a*R*,7a*S*,11a*S*,13a*R*,14a*S*)-6a,13a-bis(methylthio)hexadecahydropyrazino[1,2-a:4,5-a']diindol-6,13-dione (**3{bb}**) + (4a*S*,6a*S*,7a*S*,11a*S*,13a*R*,14a*S*)-13a-(methylthio)hexadecahydropyrazino[1,2-a:4,5-a']diindol-6,13-dione **(2{bb})**



3{bb}



2{bb}

Prepared according to **GP 2**, starting from DKP **1{bb}** (50.0 mg, 165 µmol). Column chromatography (*c*Hex/EtOAc 7:1) afforded the title compounds (**3{bb}**: 19.7 mg, 30%; **2{bb}**: 28.5 mg, 50%) as colorless solid and colorless oil.

Alternative synthesis of **2{bb}**: Prepared according to **GP 1**, starting from DKP **1{bb}** (50.0 mg, 165 µmol). Column chromatography (*c*Hex/EtOAc 7:1) afforded the title compound (28.3 mg, 50%) as colorless oil.

3{bb}: ***R*$_f$** = 0.28 (*c*Hex/EtOAc 7:1). – **mp**: 153 °C. – **$[\alpha]_D^{20}$** = –3.7 (c = 0.46, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.79–0.90 (m, 2H, 4-H_A, 11-H_A), 2.27–2.36 (m, 4H, 2-H_A, 3-H_A, 9-H_A, 10-H_A), 1.51–1.67 (m, 4H, 2-H_B, 3-H_B, 9-H_B, 10-H_B), 1.67–1.80 (m, 4H, 1-H_2, 8-H_2), 2.14–2.19 (m, 2H, 7-H_A, 14-H_A), 2.20 (s, 6H, 2 × SCH_3), 2.27–2.35 (m, 2H, 7-H_B, 14-H_B), 2.56–2.68 (m, 2H, 4-H_B, 11-H_B), 2.87–3.04 (m, 2H, 7a-H, 14a-H), 4.01–4.12 (m, 2H, 4a-H, 11a-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 15.0 (+, S*C*H_3), 21.1 (–, C-2, C-9), 23.3 (–, C-3, C-10), 25.3 (–, C-1, C-8), 27.0 (–, C-4, C-11), 32.2 (+, C-7a, C-14a), 36.4 (–, C-7, C-14), 57.9 (+, C-4a, C-11a), 71.3 (C_q, C-6a, C-13a), 166.3 (C_q, 2 × *C*=O) ppm. – **IR**

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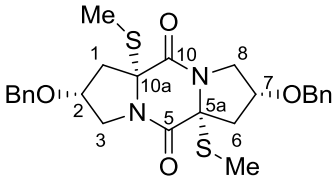
(film): $\tilde{\nu}$ = 3490 (w), 2924 (vs), 2855 (s), 1726 (m), 1666 (vs), 1390 (vs), 1346 (s), 1171 (m), 1067 (m), 726 (m) cm^{-1}. – **MS** (EI): *m/z* (%): 394 (2.5) $[M]^+$, 347 (58), 300 (100), 279 (42), 250 (31), 167 (42), 149 (90), 96 (79), 82 (98), 55 (85), 43 (50). – **HRMS** ($C_{20}H_{30}N_2O_2S_2$): calc. 394.1749; found 394.1752.

2{bb}: R_f = 0.11 (*c*Hex/EtOAc 7:1). – $[\alpha]_D^{20}$ = +5.7 (c = 0.43, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.82–1.03 (m, 2H, 4-H_A, 11-H_A), 1.08–1.84 (m, 12H, 1-H_2, 2-H_2, 3-H_2, 8-H_2, 9-H_2, 10-H_2), 2.00–2.12 (m, 2H, 7-H_A, 14-H_A), 2.13 (s, 3H, SCH_3), 2.99–2.31 (m, 1H, 7-H_B), 2.33–2.46 (m, 3H, 4-H_B, 7a-H, 11-H_B), 2.48–2.59 (m, 1H, 14-H_B), 2.77–2.89 (m, 1H, 14a-H), 3.95–4.05 (m, 2H, 4a-H, 11a-H), 4.67 (dd, ^3J = 7.2, 10.6 Hz, 1H, 6a-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.1 (+, S*C*H_3), 20.7, 21.0, 23.3, 23.4, 25.3, 25.8 (6 × –, C-1, C-2, C-3, C-8, C-9, C-10), 27.2, 27.3 (2 × –, C-4, C-11), 29.0 (–, C-7), 32.9 (+, C-14a), 35.3 (–, C-14), 35.9 (+, C-7a), 56.4, 57.0 (2 × +, C-4a, C-11a), 59.9 (+, C-6a), 72.6 (C_q, C-13a), 164.8 (C_q, *C*=O), 168.5 (C_q, *C*=O) ppm. – **IR** (film): $\tilde{\nu}$ = 2922 (w), 2854 (w), 1657 (m), 1396 (m), 1346 (w), 1168 (w), 820 (w), 728 (w), 710 (w) cm^{-1}. – **MS** (FAB, matrix: 3-NBA**)**: *m/z* (%): 349 (15) $[M+H]^+$, 301 (100), 273 (28), 167 (25), 149 (57). – **HRMS** ($C_{19}H_{28}N_2O_2S+H^+$): calc. 349.1944; found 349.1949.

(2*R*,5a*R*,7*R*,10a*R*)-2,7-Bis(benzyloxy)-5a,10a-bis(methylthio)octahydrodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10-dione (**3{cc}**)



Prepared according to **GP 2**, starting from DKP **1{cc}** (100 mg, 246 µmol). Column chromatography (*c*Hex/EtOAc 1:1) afforded the title compound (28.6 mg, 23%) as yellow oil.

R_f = 0.29 (*c*Hex/EtOAc 1:1). – $[\alpha]_D^{20}$ = –40.1 (c = 0.22, $CHCl_3$) – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.15 (s, 6H, SCH_3), 2.30 (dd, ^3J = 7.2 Hz, ^2J = 15.0 Hz, 2H, 1-H_A, 6-H_A), 2.63 (dd, ^3J = 1.6 Hz, ^2J = 15.0 Hz, 2H, 1-H_B, 6-H_B), 3.47 (dd, ^3J = 3.4 Hz, ^2J = 12.8 Hz, 2H, 3-H_A, 8-H_A), 4.02–4.08 (m, 2H, 2-H, 7-H), 4.12 (dd, ^3J = 7.2 Hz, ^2J = 12.8 Hz, 2H, 3-H_B, 8-H_B), 4.37–4.46 (m, 4H, 2 × OCH_2Ph), 7.10–7.23 (m, 10H, H_{Ph}) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 15.1 (+, 2 × S*C*H_3), 40.8 (–, C-1, C-6), 51.5 (–, C-3, C-8), 69.5 (q, *C*SCH_3), 71.5 (–, O*C*H_2Ph), 73.7 (+, C-2, C-7), 127.6 (+, C_{Ar}), 127.8 (+, C_{Ar}), 128.5 (+, C_{Ar}), 137.5 (C_q, C_{Ar}), 164.3 (C_q, 2 × *C*=O) ppm. – **IR** (film): $\tilde{\nu}$ = 3485 (w), 3031 (m), 2921 (s), 1667 (s), 1415 (s), 1362 (s) 1101 (s) 912 (m), 736 (s), 699 (s) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 451 (16) [M^+–SCH_3], 405 (19) [M+H^+–2×SCH_3], 297 (9), 189 (8), 91 (100). – **HRMS** ($C_{25}H_{27}N_2O_4S^+$): calc. 451.1692; found 451.1695.

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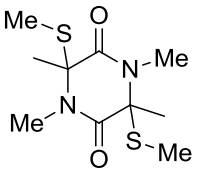
1,3,4,6-tetramethyl-3,6-bis(methylthio)piperazine-2,5-dione (**3{dd}**)

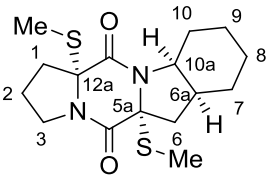


S-Me = *cis*

Prepared according to **GP 2**, starting from DKP **1{dd}** (34.2 mg, 201 µmol)**.** Column chromatography (*c*Hex/EtOAc 5:1) afforded the title compound (21.5 mg, 41%, scalemic mixture) as colorless solid.

***R*f** = 0.05 (*c*Hex/EtOAc 5:1). – **mp**: 59 °C. – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.84 (s, 6H, CC*H*$_3$), 2.21 (s, 6H, SC*H*$_3$), 3.13 (s, 6H, NC*H*$_3$) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.6 (+, 2 × S*C*H$_3$), 25.3 (+, 2 × C*C*H$_3$), 30.0 (+, 2 × N*C*H$_3$), 68.0 (C_q, 2 × *C*C=O), 165.7 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2990 (vs), 2923 (vs), 1646 (s), 1413 (s), 1365 (s), 1239 (s), 1226 (s), 1112 (s), 1073 (s), 967 (s), 908 (s), 768 (s), 715 (vs), 699 (s), 666 (s), 571 (s), 524 (s), 439 (s) cm^{-1}. – **MS** (EI): *m/z* (%): 262 (1) [M]$^+$, 215 (98), 178 (21), 168 (77), 141 (21), 140 (100). 139 (44), 56 (89). – **HRMS** ($C_{10}H_{18}N_2O_2S_2$): calc. 262.0809; found 262.0807.

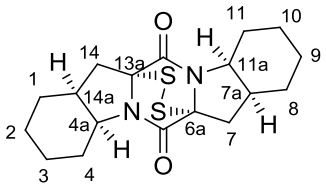
(5a*R*,6a*S*,10a*S*,12a*R*)-5a,12a-bis(methylthio)dodecahydropyrrolo[1',2':4,5]pyrazino[1,2-a]indole-5,12-dione (**3{ab}**)



Prepared according to **GP 2**, starting from DKP **1{ab}** (54.9 mg, 221 µmol). Column chromatography (*c*Hex/EtOAc 5:1) afforded the title compound (15.6 mg, 21%) as pink solid.

***R*f** = 0.13 (*c*Hex/EtOAc 5:1). – **mp**: 147 °C. – **$[\alpha]_D^{20}$** = –31.5 (c = 0.38, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 0.83–0.94 (m, 1H, C*H*$_2$), 4.04–4.12 (m, 2H, C*H*$_2$), 1.49–1.66 (m, 2H, C*H*$_2$), 1.68–1.80 (m, 2H, C*H*$_2$), 1.94–2.04 (m, 2H, C*H*$_2$), 2.11–2.17 (m, 1H, C*H*$_2$), 2.18 (s, 3H, SC*H*$_3$), 2.25 (s, 3H, SC*H*$_3$), 2.26–2.39 (m, 2H, C*H*$_2$), 2.48–2.59 (m, 2H, C*H*$_2$), 2.94–3.04 (m, 1H, 6a-H), 3.52–3.60 (m, 1H, 3-H$_A$), 3.70–3.79 (m, 1H, 3-H$_B$), 4.04–4.12 (m, 1H, 10a-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.6 (–, S*C*H$_3$), 14.9 (–, S*C*H$_3$), 19.8 (+, *C*H$_2$), 21.2 (+, *C*H$_2$), 23.2 (+, *C*H$_2$), 25.3 (+, *C*H$_2$), 27.0 (+, *C*H$_2$), 32.3 (–, C-6a), 34.8 (+, *C*H$_2$), 35.5 (+, *C*H$_2$), 45.2 (+, C-3), 57.7 (–, C-10a), 71.1, 71.4 (2 × C_q, C-5a, C-12a), 165.2 (C_q, C=O), 165.9 (C_q, C=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2924 (vw), 2349 (vw), 1659 (w), 1398 (vw), 1260 (vw), 1156 (vw), 1015 (vw), 967 (vw), 712 (vw), 613 (vw) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 341 (4) [M]$^+$, 293 (85) [M$^+$–SCH$_3$], 246 (100) [M$^+$–2×SCH$_3$], 165 (31), 95 (41). – **HRMS** ($C_{15}H_{21}N_2O_2S^+$): calc. 293.1324; found 293.1327.

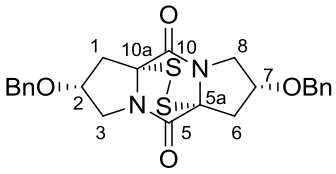
(4a*S*,6a*R*,7a*S*,11a*S*,13a*R*,14a*S*)-dodecahydro-6a,13a-epidithiopyrazineo[1,2-a:4,5-a']diindol-6,13(1H,7H)-dione (**4{bb}**)



Prepared according to **GP 3**, starting from DKP **1{bb}** (150 mg, 496 µmol). Column chromatography (*c*Hex/EtOAc 7:1) afforded the title compound (58.2 mg, 32%) as colorless solid.

***R*f** = 0.34 (*c*Hex/EtOAc 5:1). – **mp**: 172 °C. – **[α]D20** = –130.3 (c = 0.35, $CHCl_3$). –**^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.10–1.26 (m, 4H, 2-H_A, 3-H_A, 9-H_A, 10-H_A,), 1.30–1.42 (m, 2H, 4-H_A, 11-H_A), 1.52–1.65 (m, 4H, 2-H_B, 3-H_B, 9-H_B, 10-H_B), 1.68–1.81 (m, 4H, 1-H_2, 8-H_2), 2.02–2.10 (m, 2H, 7-H_A, 14-H_A), 2.10–2.19 (m, 2H, 4-H_B, 11-H_B), 2.80–2.94 (m, 2H, 7a-H, 14a-H), 2.95–3.05 (m, 2H, 7-H_B, 14-H_B), 4.10–4.22 (m, 2H, 4a-H, 11a-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 20.7 (–, C-3, C-10), 22.8 (–, C-2, C-9), 25.2 (–, C-1, C-8), 27.7 (–, C-4, C-11), 34.1 (–, C-7, C-14), 35.7 (+, C-7a, C-14a), 57.8 (+, C-4a, C-11a), 76.3 (C_q, C-6a, C-13a), 163.6 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2921 (w), 2854 (w), 1679 (m), 1377 (m), 1346 (w), 1179 (w), 716 (w), 621 (w) cm^{-1}. – **MS** (EI): *m/z* (%): 364 (0.21) $[M]^+$, 300 (100), 219 (67), 139 (6), 81 (22). – **HRMS** ($C_{18}H_{24}N_2O_2S_2$): calc. 364.1279; found 364.1278. – **Elemental analysis** ($C_{18}H_{24}N_2O_2S_2$): calc. C 59.31, H 6.64, N 7.68, S 17.59; found C 58.55, H 6.56, N 7.45, S 17.43.

(2*R*,5a*R*,7*R*,10a*R*)-2,7-Bis(benzyloxy)tetrahydro-5a,10a-epidithiodipyrrolo[1,2-a:1',2'-d]pyrazine-5,10(1H,6H)-dione (**4{cc}**)



Prepared according to **GP 3**, starting from DKP **1{cc}** (150 mg, 369 µmol). Column chromatography (*c*Hex/EtOAc 1:1) afforded the title compound (72.8 mg, 42%) as yellow solid.

***R*f** = 0.23 (*c*Hex/EtOAc 1:1). – **mp**: 105 °C. – **[α]D20** = –250.7 (c = 0.34, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.49 (dd, ^3J = 2.7 Hz, ^2J = 15.4 Hz, 2H, 1-H_A, 6-H_A), 3.21 (dd, ^3J = 6.0 Hz, ^2J = 15.4 Hz, 2H, 1-H_B, 6-H_B), 3.80 (dd, ^3J = 6.0 Hz, ^2J = 12.4 Hz, 2H, 3-H_A, 8-H_A), 3.90 (dd, ^3J = 2.7 Hz, ^2J = 12.4 Hz, 2H, 3-H_B, 8-H_B), 4.35 (tt, ^3J = 2.7 Hz, ^3J = 6.0 Hz, 2H, 2-H_2, 7-H_2), 4.56 (d, ^2J = 2.4 Hz, 4H, 2 × OCH_2Ph), 7.28–7.38 (m, 10H, H_{Ph}) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 37.8 (–, C-1, C-6), 51.0 (–, C-3, C-8), 71.6 (–, O*C*H_2Ph), 75.0 (C_q, C-5a, C-10a), 75.3 (+, C-2, C-7), 127.7 (+, C_{Ph}), 128.1 (+, C_{Ph}), 128.6 (+, C_{Ph}), 137.1 (C_q, 2 × C_{Ph}), 163.3 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3029 (vw), 2861 (vw), 1683 (m), 1379 (w), 1095 (w), 734 (w), 696 (w) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 469 (4) $[M]^+$, 421 (4), 405 (43), 224 (15), 154 (30), 136 (36), 197 (16), 91 (100). – **HRMS** ($C_{24}H_{24}N_2O_4S_2$+H^+): calc. 469.1256; found 469.1254.

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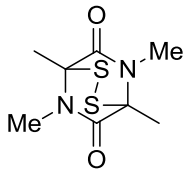
1,4,5,7-tetramethyl-2,3-dithia-5,7-diazabicyclo[2.2.2]octane-6,8-dione (**4{dd}**)

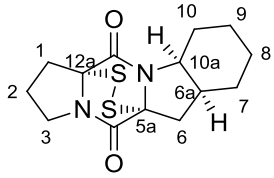


S-S = *cis*

Prepared according to **GP 3**, starting from DKP **1{dd}** (83.7 mg, 492 µmol). Column chromatography (*c*Hex/EtOAc 3:1) afforded the title compound (35.1 mg, 31%, scalemic mixture) as colorless solid.

***R*f** = 0.35 (*c*Hex/EtOAc 5:1). – **mp**: 135 °C. – **[α]D20** = –14.3 (c = 0.27, $CHCl_3$). – **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 2.01 (s, 6H, cCH_3), 3.08 (s, 6H, NCH_3) ppm. – **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 19.0 (+, 2 × CCH_3), 27.5 (+, 2 × NCH_3), 71.8 (C_q, 2 × *C*C=O), 166.0 (C_q, 2 × *C*=O) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2920 (m), 2852 (w), 1681 (w), 1613 (w), 1461 (w), 1415 (w), 1377 (w), 1072 (vw), 888 (vw), 634 (vw) cm^{-1}. – **MS** (ESI): *m/z*: 169 [M^+–SS+H^+]. – **HRMS** (ESI, $C_8H_{12}N_2O_2$+H^+): calc. 169.0977; found 169.0802.

(5a*R*,6a*S*,10a*S*,12a*R*)-octahydro-5a,12a-epidithiopyrrolo[1',2':4,5]pyrazino[1,2-a]indole-5,12(1*H*,6*H*)-dione (**4{ab}**)



Prepared according to **GP 3**, starting from DKP **1{ab}** (27.1 mg, 109 µmol). Column chromatography (*c*Hex/EtOAc 5:1) afforded the title compound (5.4 mg, 16%) as colorless oil.

***R*f** = 0.09 (*c*Hex/EtOAc 5:1). – **[α]D20** = –104.7 (c = 0.26, $CHCl_3$). – **^{1}H-NMR** (400 MHz, $CDCl_3$): δ = 1.14–1.25 (m, 3H, CH_2), 1.69–1.87 (m, 3H, CH_2), 2.07.–2.38 (m, 6H, CH_2), 2.85–3.10 (m, 3H, CH_2, 6a-H), 3.54–3.66 (m, 1H, 3-H_A), 3.81–3.90 (m, 1H, 3-H_B), 4.10–4.24 (m, 1H, 10a-H) ppm. – **^{13}C-NMR** (100 MHz, $CDCl_3$): δ = 20.8 (–, *C*H_2), 22.8 (–, *C*H_2), 23.5 (–, *C*H_2), 25.2 (–, *C*H_2), 27.8 (–, *C*H_2), 32.3 (–, *C*H_2), 34.0 (–, *C*H_2), 35.8 (+, C-6a), 45.9 (–, C-3), 57.9 (+, C-10a), 77.2 (C_q, C-5a, C-12a), 163.0, 163.9 (2 × C_q, C-5a, C-12a) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2923 (m), 2853 (w), 1687 (m), 1444 (w), 1376 (m), 1346 (w), 1311 (w), 1182 (w), 752 (w), 697 (w), 667 (w) cm^{-1}. – **MS** (ESI): *m/z*: 247 [M^+–SS+H^+]. – **HRMS** (ESI, $C_{14}H_{18}N_2O_2$+H^+): calc. 247.1447; found 247.1222.

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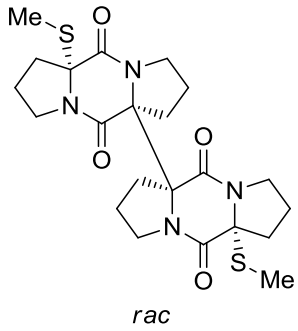
(*rac*)–10a,10'a-bis(methylthio)octahydro–1*H*,1'*H*-5a,5'a-bidipyrrolo[1,2-a:1',2'-d]pyrazine-5,5',10,10'(6H,6'H,10aH,10'aH)-tetraone (**14**)

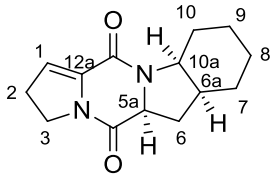


rac

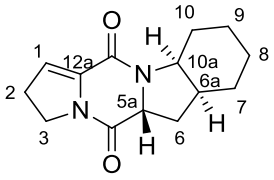
Prepared according to **GP 1** starting from DKP **1{aa}** (50.0 mg, 257 µmol), using LDA (6.00 equiv.) as a base instead of NaHMDS. Column chromatography (*c*Hex/EtOAc 1:5) afforded the title compound (44.0 mg, 71%) as yellow solid.

***R*f** = 0.20 (*c*Hex/EtOAc 1:5). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.90 (s, 6H, SCH_3), 1.96–2.25 (m, 10H, CH_2), 2.32–2.45 (m, 2H, CH_2), 2.93–3.01 (m, 4H, CH_2), 3.34–3.47 (m, 4H, CH_2), 3.73–3.81 (m, 4H, CH_2) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 12.9 (+, 2 × SCH_3), 19.0, 22.5 (–, 4 × NCH$_2$$CH_2$), 31.8, 31.9 (–, 4 × CCH_2), 44.8, 49.3 (–, 4 × NCH_2), 74.4, 75.9 (C_q, 2 × *C*S, *CC*), 163.9, 165.5 (C_q, 4 × *C*=O) ppm. – **IR** (drift): $\tilde{\nu}$ = 3378 (w), 2984 (w), 1650 (m), 1385 (m), 1240 (m), 1052 (m), 825 (w) cm^{-1}. – **MS** (EI): *m/z* (%): 478 (0.27) $[M]^+$, 192 (15), 169 (8), 84 (69), 66 (100). – **HRMS** (ESI, $C_{22}H_{30}N_4O_4S_2$+H^+): calc. 479.1787; found 479.1500.

(5a*S*,6a*S*,10a*S*)-2,3,5a,6,6a,7,8,9,10,10a-decahydropyrrolo[1',2':4,5]pyrazino[1,2-a]indole-5,12-dione (**16**) + (5a*R*,6a*S*,10a*S*)-2,3,5a,6,6a,7,8,9,10,10a-decahydropyrrolo[1',2':4,5]pyrazino[1,2-a]indole-5,12-dione (*epi*-**16**)



16



epi-**16**

Prepared according to **GP 1**, starting from DKP **1{ab}** (29.7 mg, 120 µmol). Column chromatography (*c*Hex/EtOAc 1:5) afforded the title compounds (25.8 mg, 87%) as yellow oil (mixture of diastereomers 2:1).

***R*f** = 0.14 (*c*Hex/EtOAc 1:5). – **[α]$_D^{20}$** = –36.2 (c = 0.15, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$)[a]: δ = 0.78–2.26 (m, 13H, 2-H_2, 6-H_2, 6a-H, 7-H_2, 8-H_2, 9-H_2, 10-H_2), 3.83–3.94, 4.03–4.16, 4.24–4.39, 4.42–4.50 (4 × m, 4H, 3-H_2, 5a-H, 10a-H), 6.10–6.15 (m, 1H, 1-H) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$)[b]: δ = 20.3, 21.1 (–, CH_2), 22.4, 23.2 (–, CH_2), 25.5, 26.0 (–, CH_2), 25.8, 27.3 (–, CH_2), 28.2, 28.5 (–, CH_2), 30.1, 31.1 (–, CH_2), 34.7, 35.8 (+, C-6a), 45.1, 45.3 (–, C-3), 56.5, 57.1 (+, C-10a), 58.3, 61.5 (+, C-5a), 118.2, 118.3 (+, C-1), 135.2, 136.1 (C_q, C-12a), 155.0, 156.0, 163.3, 163.4 (2 × C_q, *C*=O) ppm. – **IR** (film): $\tilde{\nu}$ = 3473 (m), 2927 (s), 2857 (m), 2241 (w), 1667 (s), 1433 (m), 1281 (m), 1186 (m), 915 (m), 730 (m) cm^{-1}. – **MS** (EI): *m/z* (%): 246 (7) $[M]^+$, 152 (9), 86 (74), 84 (100), 47 (27). – **HRMS** ($C_{14}H_{18}N_2O_2$): calc. 246.1368; found 246.1367.

[a] Integrals do not match due to the mixture of epimers.
[b] Every carbon atom has two signals in a 2:1 ratio.

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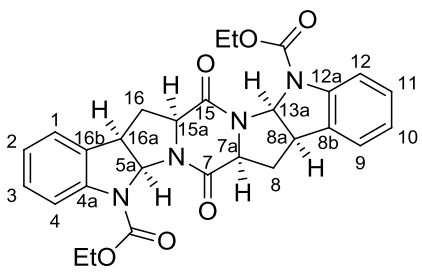
5a,8,8a,13,13a,15a,16,16a-octahydro-(5a*S*,7a*S*,8a*S*,13a*S*,15a*S*,16a*S*)-pyrazino[1",2":1,5;4",5":1',5']di-pyrrolo[2,3-*b*:2',3'-*b*']diindole-7,15(5*H*,7a*H*)-dione (**23**)



Amino acid **22** (220 mg, 796 µmol) was suspended in toluene (4 mL). Triethylamine (0.45 µL, 3.19 mmol, 4.00 equiv.), methyl dichlorophosphite (54 µL, 557 µmol, 0.70 equiv.) and 1,3-dimethylimidazolium dimethylphosphate (5 drops) were added and the mixture was stirred at 30 °C overnight. After irradiation under closed-vessel microwave conditions at 145 °C for 1 h, the solution was filtered, and the precipitate was washed with hot toluene (25 mL). The filtrate was evaporated under reduced pressure and the resulting crude product was purified by column chromatography (CH_2Cl_2/MeOH 98:2). The title compound was obtained as colorless solid (65.1 mg, 32%).

***R*$_f$** = 0.14 (CH_2Cl_2/MeOH 98:2). – **mp**: 215 °C. – **[α]$_D^{20}$** = –53.1 (c = 0.36, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.32 (t, ^3J = 7.1 Hz, 6H, CH_2CH_3), 2.46 (ddd, ^3J = 8.1, ^3J = 10.2, ^2J = 13.8 Hz, 2H, 8-H_A, 16-H_A), 3.07 (ddd, ^3J = 1.1, ^3J = 2.5, ^2J = 13.8 Hz, 2H, 8-H_B, 16-H_B), 3.80 (t, ^3J = 6.9 Hz, 2H, 8a-H, 16a-H), 4.13 (dd, ^3J = 2.5, ^3J = 10.2 Hz, 2H, 7a-H, 15a-H), 4.16–4.24, 4.29–4.37 (2 × m, 4H, CH_2CH_3), 6.08 (d, ^3J = 6.1 Hz, 2H, 5a-H, 13a-H), 6.95–6.99 (m, 2H, H_{Ar}), 7.08–7.14 (m, 6H, H_{Ar}) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 14.5 (+, CH_2CH_3), 26.4 (–, C-8, C-16), 44.6 (+, C-8a, C-16a), 60.0 (+, C-7a, C-15a), 61.9 (–, CH_2CH_3), 76.8 (+, C-5a, C-13a), 116.7, 123.3, 124.3, 128.4 (4 × +, C-1, C-2, C-3, C-4, C-9, C-10, C-11, C-12), 130.6, 139.8 (2 × C_q, C-4a, C-8b, C-12a, C-16b), 152.8 (C_q, 2 × CO_2Et), 165.9 (C_q, C-7, C-15) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2981 (vw), 1714 (w), 1606 (vw), 1483 (w), 1463 (vw), 1409 (w), 1374 (w), 1358 (vw), 1326 (w), 1263 (vw), 1225 (vw), 1176 (vw), 1143 (vw), 1098 (vw), 1051 (vw), 1022 (vw), 866 (vw), 741 (vw), 657 (vw), 555 (vw), 439 (vw) cm^{-1}. – **MS** (EI): *m/z* (%): 516 (100) $[M]^+$, 472 (1), 426 (1), 327 (2), 314 (8), 258 (4), 242 (21), 231 (21), 202 (72), 158 (28), 130 (54), 117 (15). – **HRMS** ($C_{28}H_{28}N_4O_6$): calc. 516.2009; found 516.2010.

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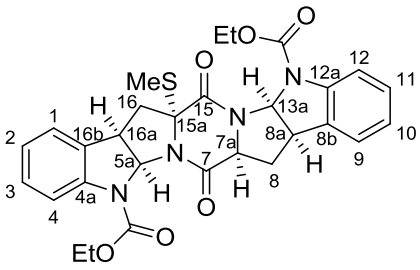
15a-(methylthio)-5a,8,8a,13,13a,15a,16,16a-octahydro-(5a*S*,7a*S*,8a*S*,13a*S*,15a*R*,16a*S*)-pyrazino-[1",2":1,5;4",5":1',5']dipyrrolo[2,3-*b*:2',3'-*b*']diindole-7,15(5*H*,7a*H*)-dione (**24**)



Prepared according to **GP 2**, starting from DKP **23** (37.4 mg, 72.4 µmol). Column chromatography (*c*Hex/EtOAc 1:1) afforded the title compound (9.5 mg, 23%) as an orange oil.

***R*$_f$** = 0.27 (*c*Hex/EtOAc 1:1). – **[α]$_D^{20}$** = –23.9 (c = 0.23, $CHCl_3$). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.33 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 1.34 (t, ^3J = 7.1 Hz, 3H, CH_2CH_3), 2.24 (s, 3H, SCH_3), 2.59–2.71 (m, 1H, 8-H_A), 2.75 (ddd, ^3J = 3.0, ^3J = 5.7, ^2J = 13.7 Hz, 1H, 8-H_B), 2.88 (dd, ^3J = 9.0, ^2J = 14.4 Hz, 1H, 16-H_A), 3.01 (dd, ^3J = 3.7, ^2J = 14.4 Hz, 1H, 16-H_B), 3.83–3.88 (m, 1H, 8a-H), 3.92–3.97 (m, 1H, 16a-H), 4.20–4.42 (m, 4H, 2 × CH_2CH_3), 4.66 (dd, ^3J = 5.7, ^3J = 9.9 Hz, 1H, 7a-H), 6.17 (d, ^3J = 6.6 Hz, 1H, 13a-H), 6.28 (d, ^3J = 6.9 Hz, 1H, 5a-H), 6.93–6.99 (m, 2H, H_{Ar}), 7.04–7.14 (m, 4H, H_{Ar}), 7.26–7.32 (m, 2H, H_{Ar}) ppm. – **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 13.5 (+, SCH_3), 14.5 (–, 2 × CH_2CH_3), 28.7 (–, C-8), 38.4 (–, C-16), 42.6 (+, C-16a), 43.5 (+, C-8a), 58.6 (+, C-7a), 62.1, 62.2 (2 × –, 2 × CH_2CH_3), 71.2 (C_q, C-15a), 77.4 (+, C-5a), 77.5 (+, C-13a), 116.3, 116.5, 123.5, 123.6, 124.0, 124.2 (6 × +, 6 × CH_{Ar}), 128.5 (+, 2 × CH_{Ar}), 131.9, 132.1, 140.3, 140.4 (4 × C_q, C-4a, C-8b, C-12a, C-16b), 153.1, 153.2 (2 × C_q, CO_2Et), 163.1, 166.9 (2 × C_q, C-7, C-15) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2923 (w), 1682 (m), 1605 (vw), 1482 (m), 1462 (w), 1406 (m), 1374 (m), 1356 (w), 1318 (m), 1298 (w), 1262 (m), 1222 (w), 1176 (w), 1142 (m), 1098 (w), 1053 (m), 1022 (w), 909 (vw), 870 (vw), 743 (m), 647 (w), 613 (vw), 557 (vw), 444 (vw) cm^{-1}. – **MS** (FAB, matrix: 3-NBA): *m/z* (%): 563 (6) $[M+H]^+$, 515 (13), 469 (3), 443 (1), 391 (2), 327 (4), 281 (7), 221 (11), 202 (47), 109 (82), 97 (88), 95 (100). – **HRMS** ($C_{29}H_{30}SN_4O_6+H^+$): calc. 563.1964; found 563.1963.

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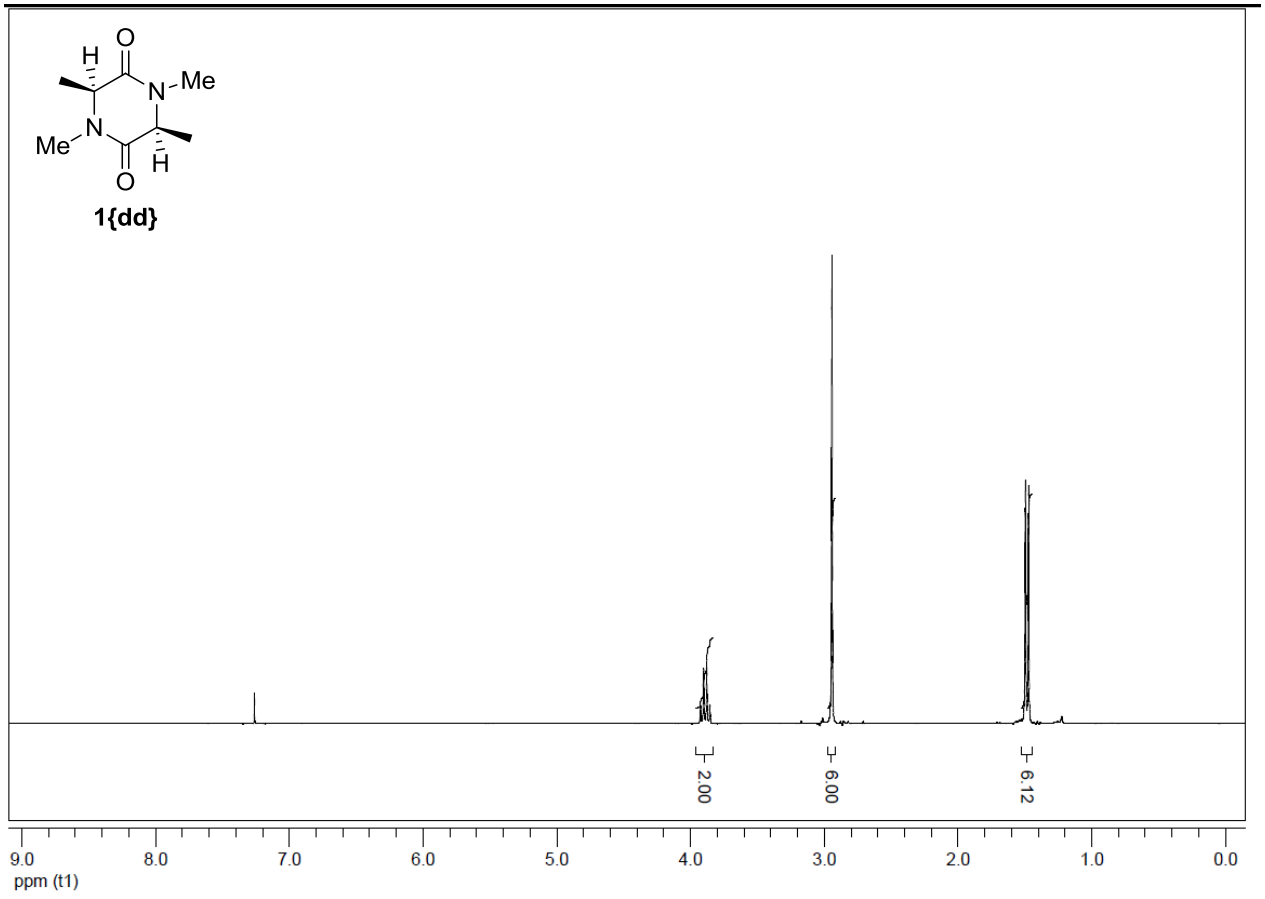
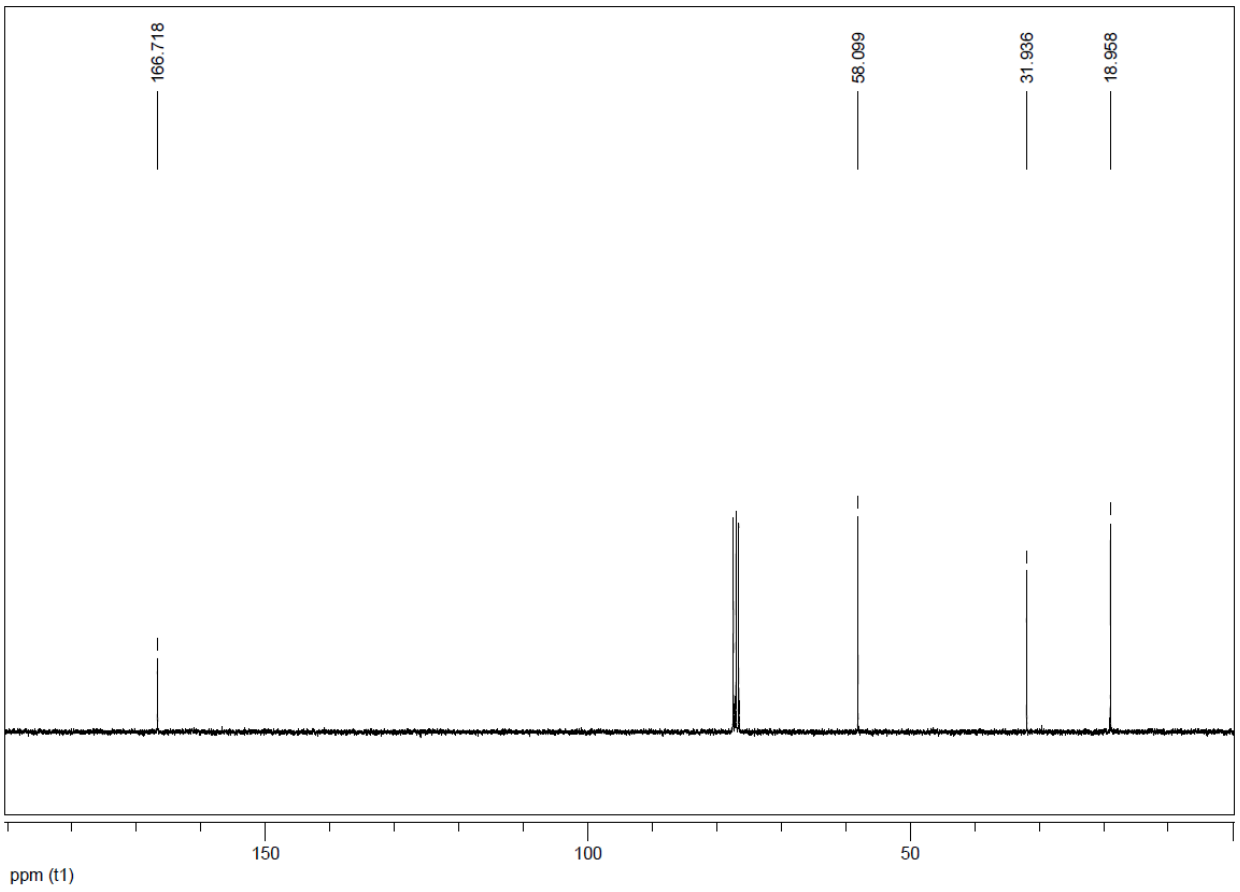
Spectral data





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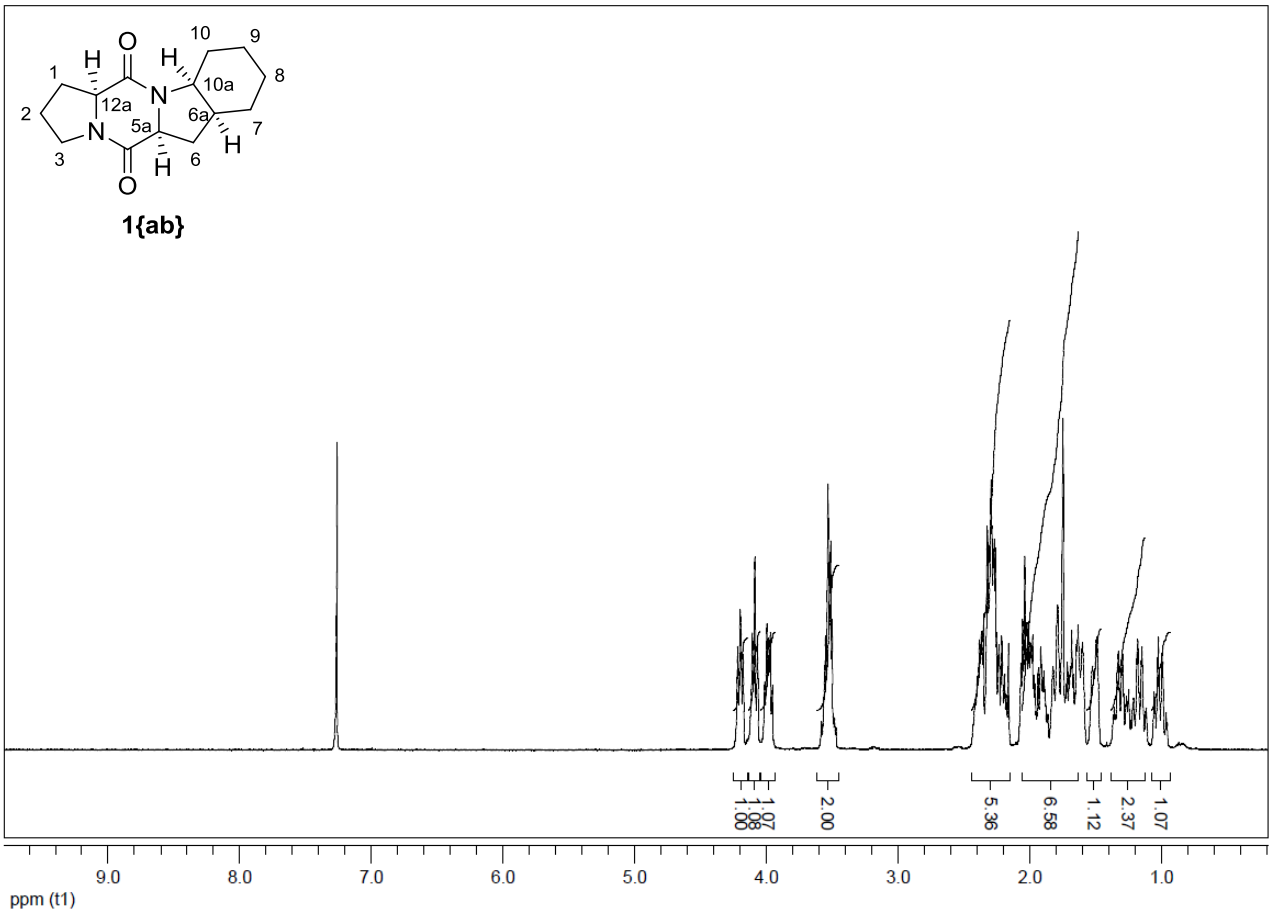

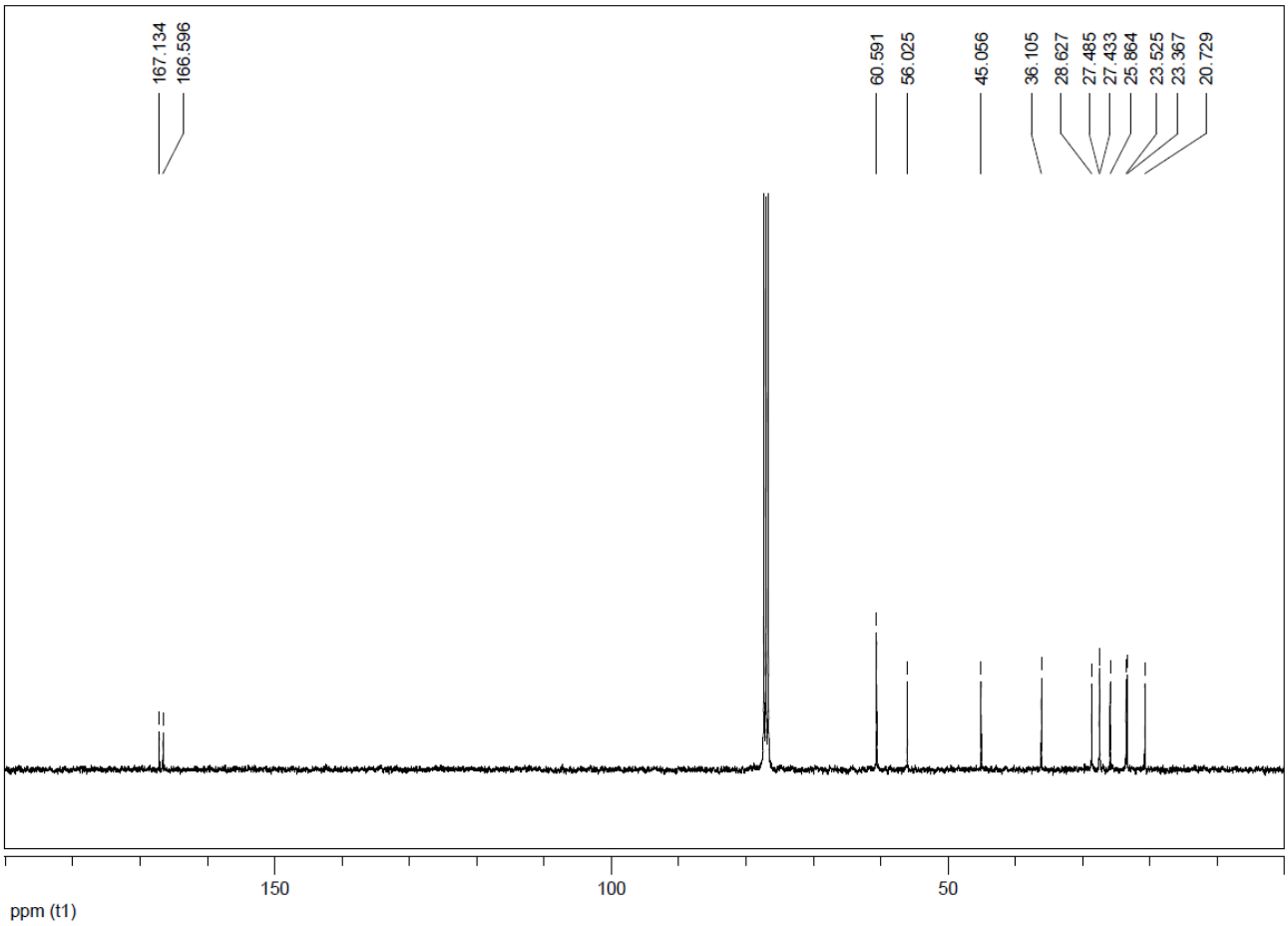

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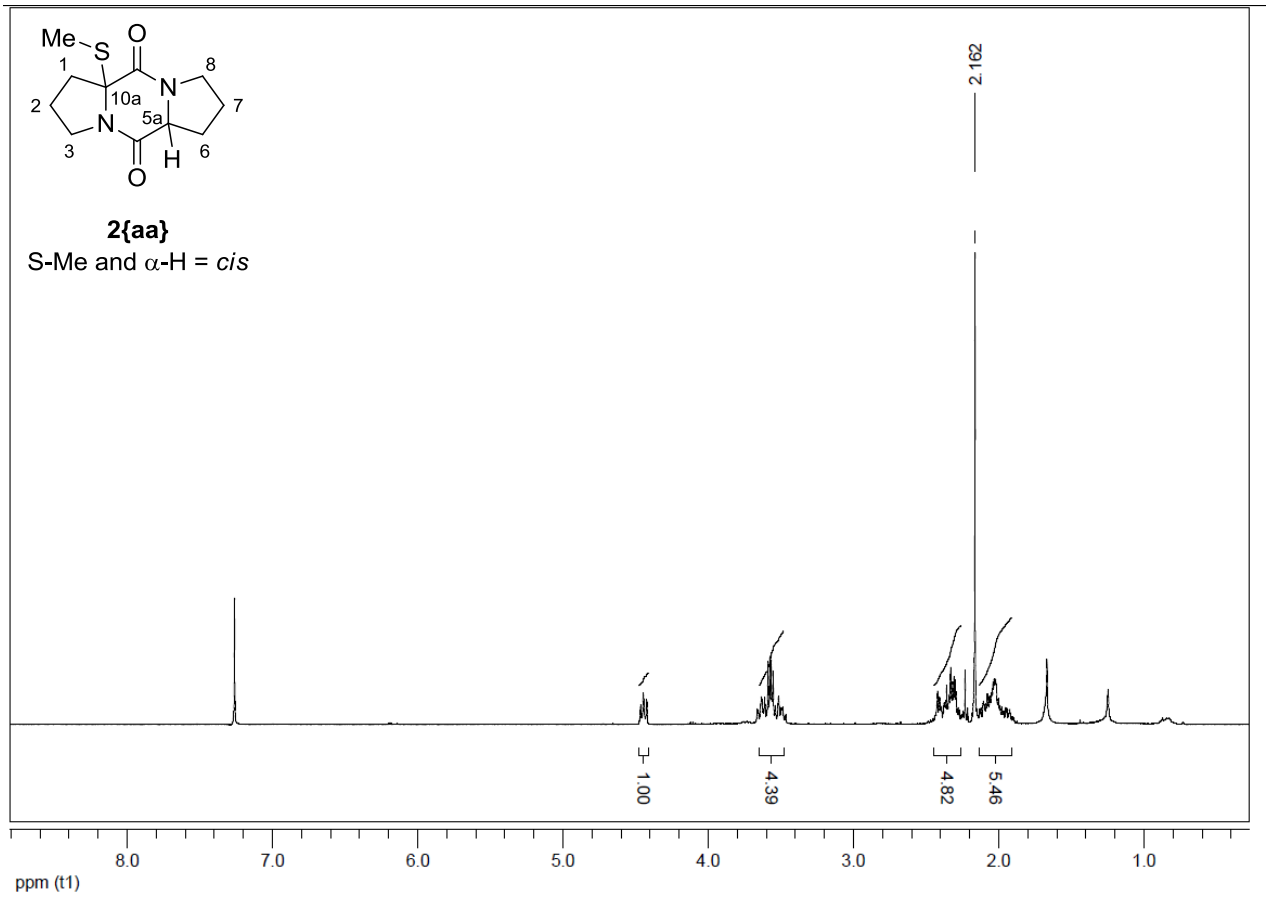
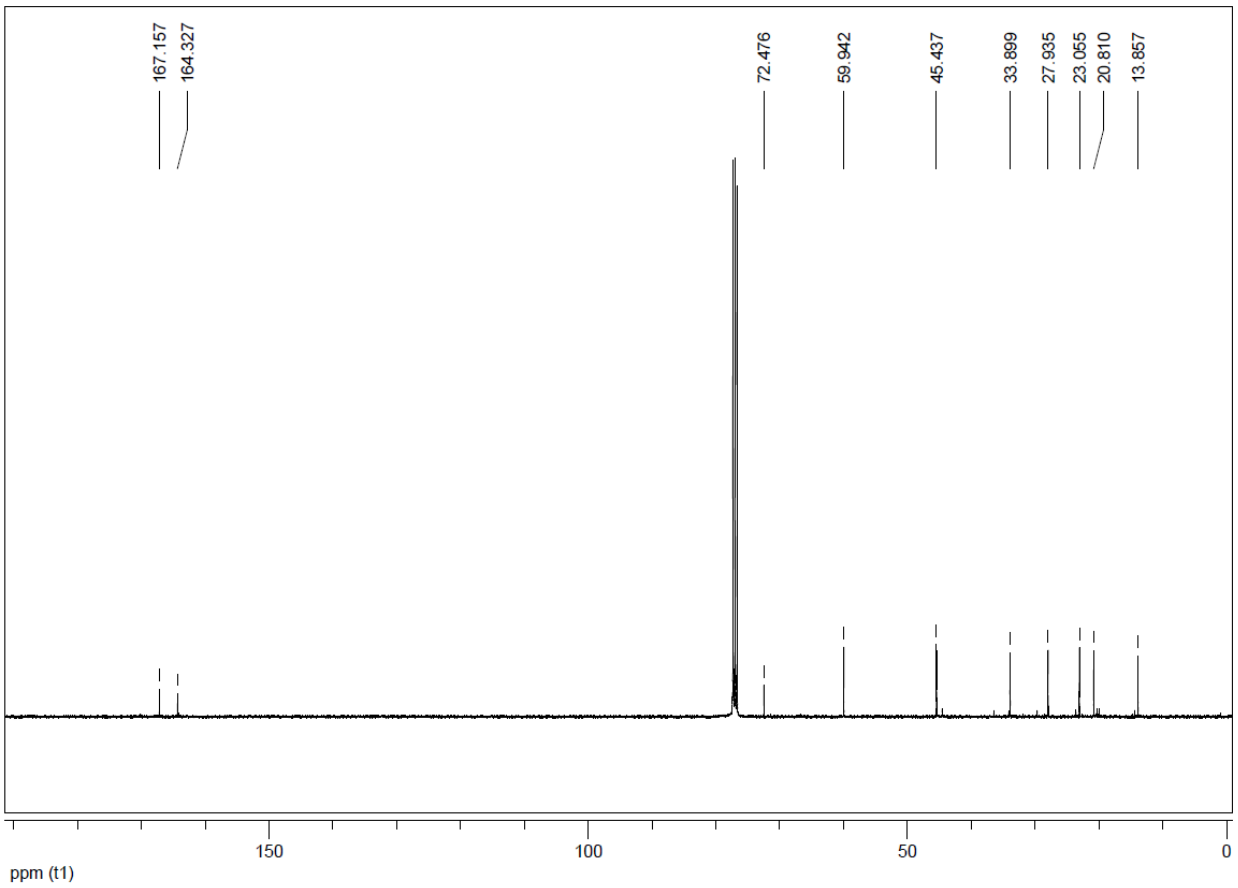


2{aa}

S-Me and α-H = *cis*



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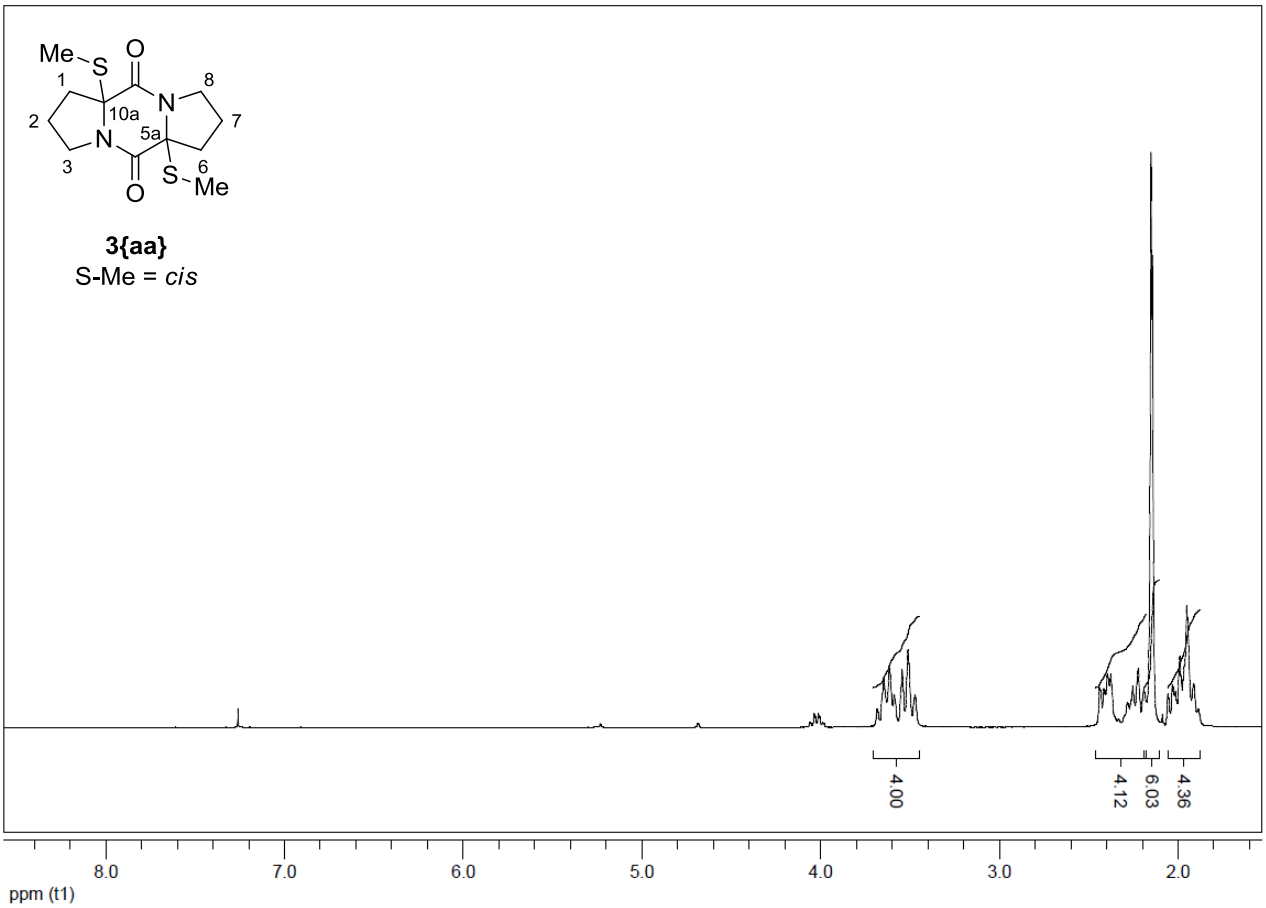
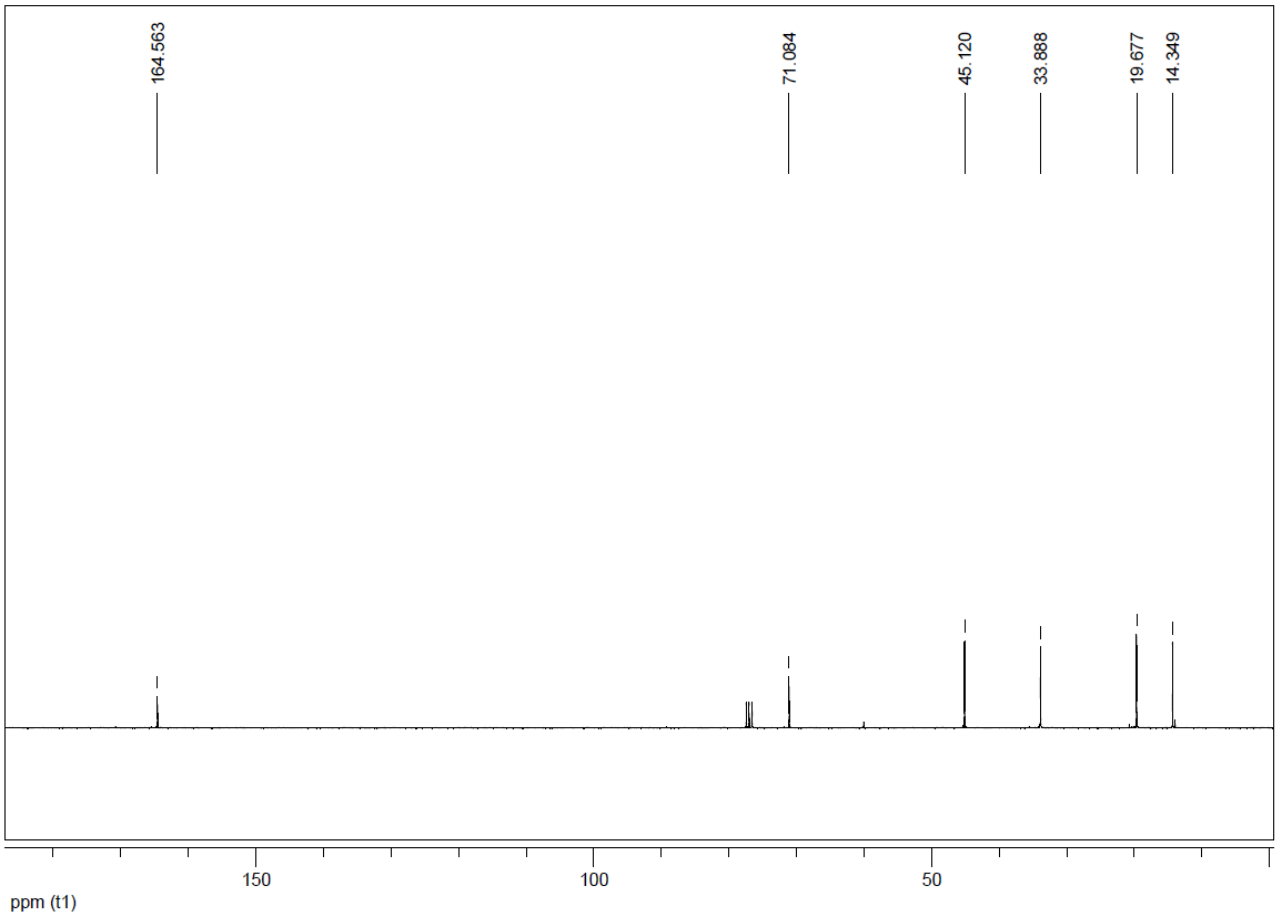


3{aa}
S-Me = *cis*



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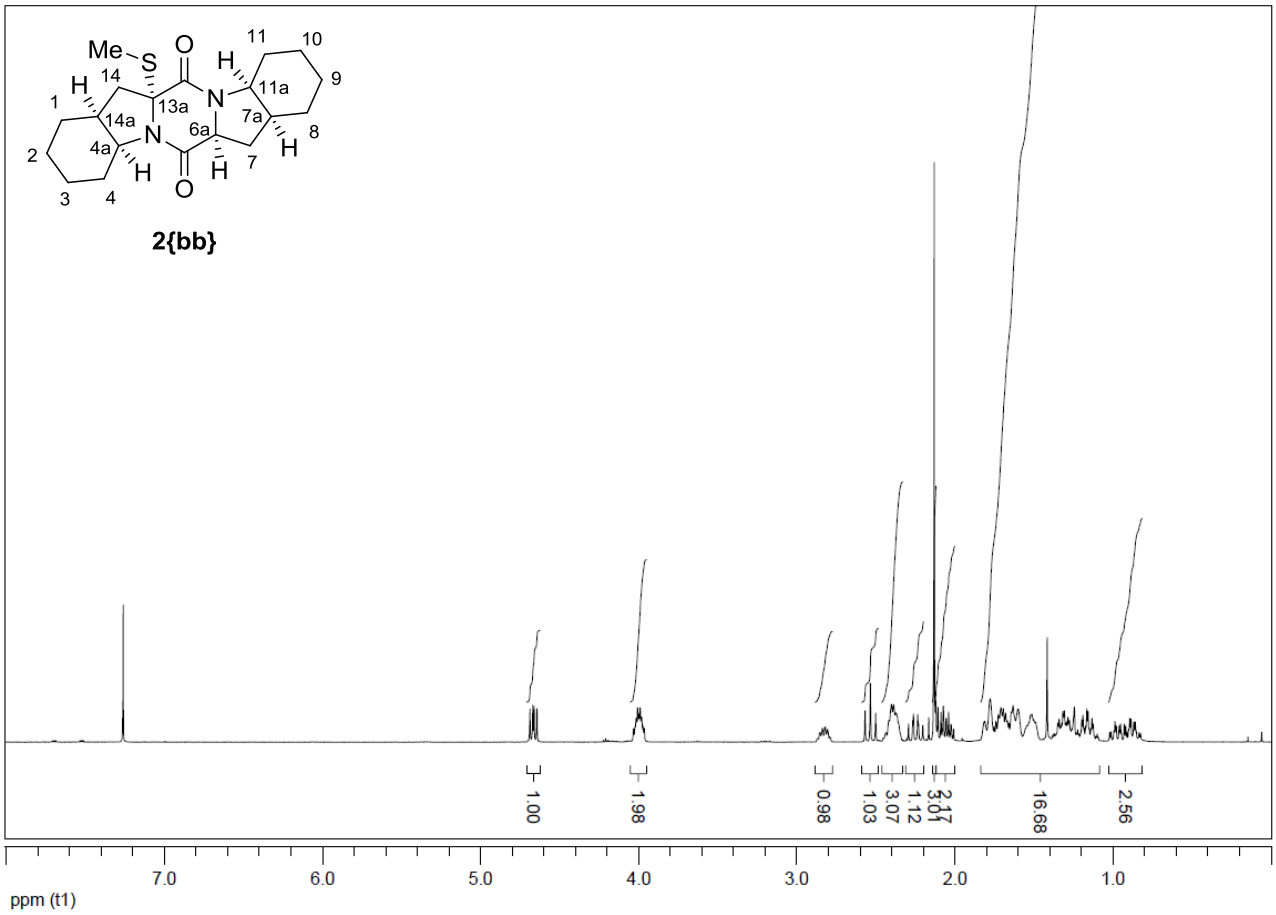
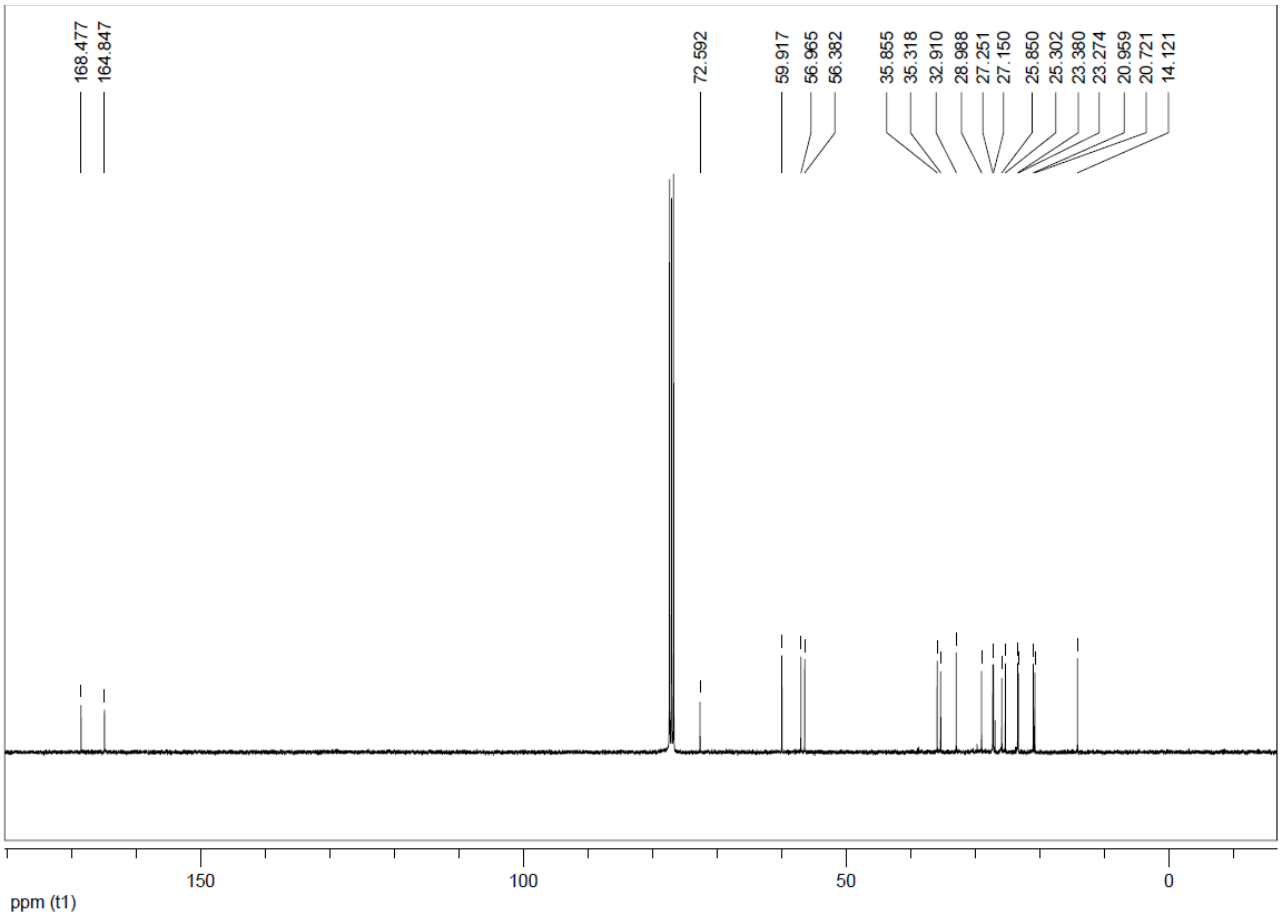
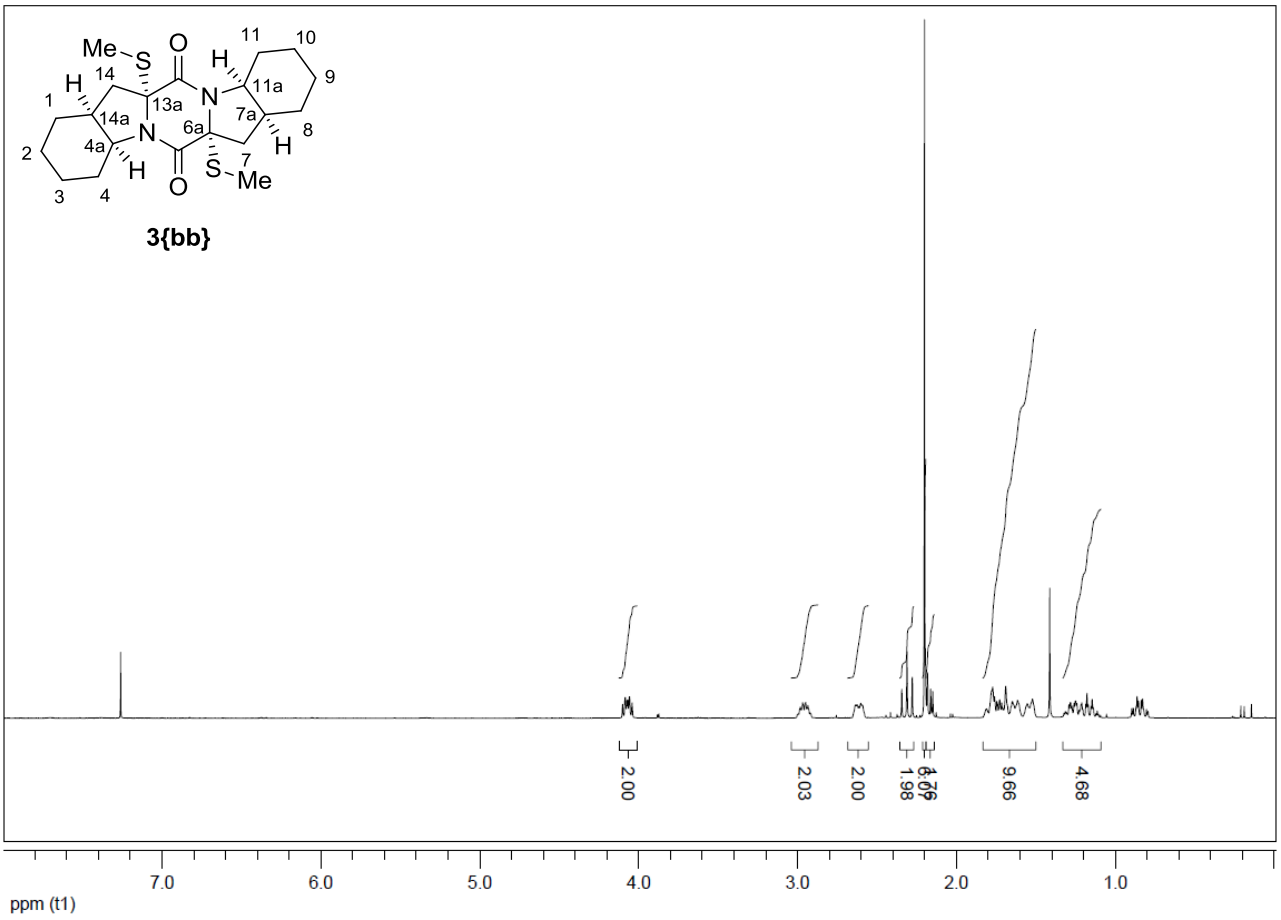
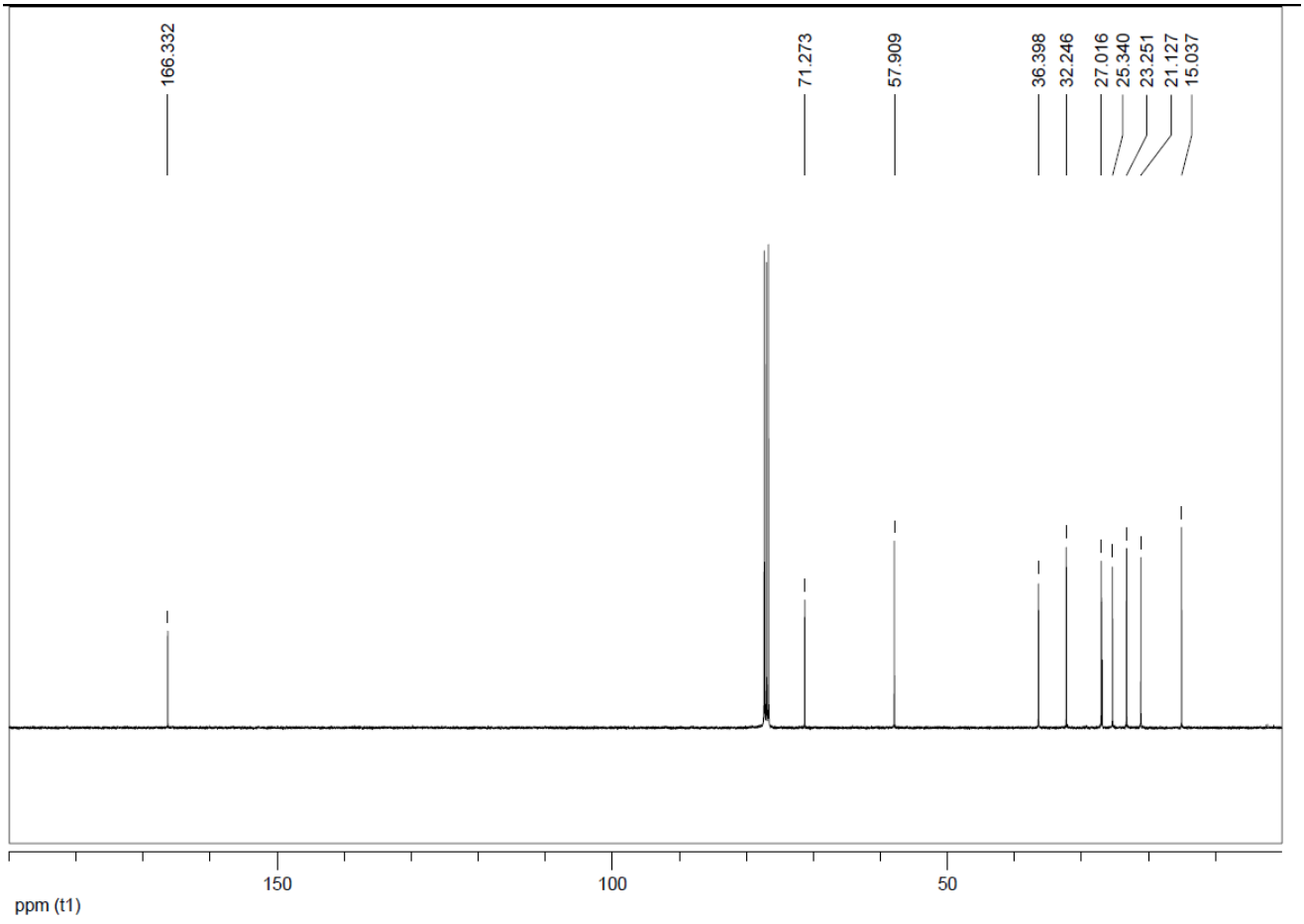


2{bb}




Me
S
O
H
11
10
9
1
H
14
13a
N
11a
14a
7a
8
2
4a
6a
H
H
7
S
Me
3
4
O
2.00
2.03
2.00
1.98
9.66
4.68
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

3{bb}


166.332
71.273
57.909
36.398
32.246
27.016
25.340
23.251
21.127
15.037
150
100
50
ppm (t1)

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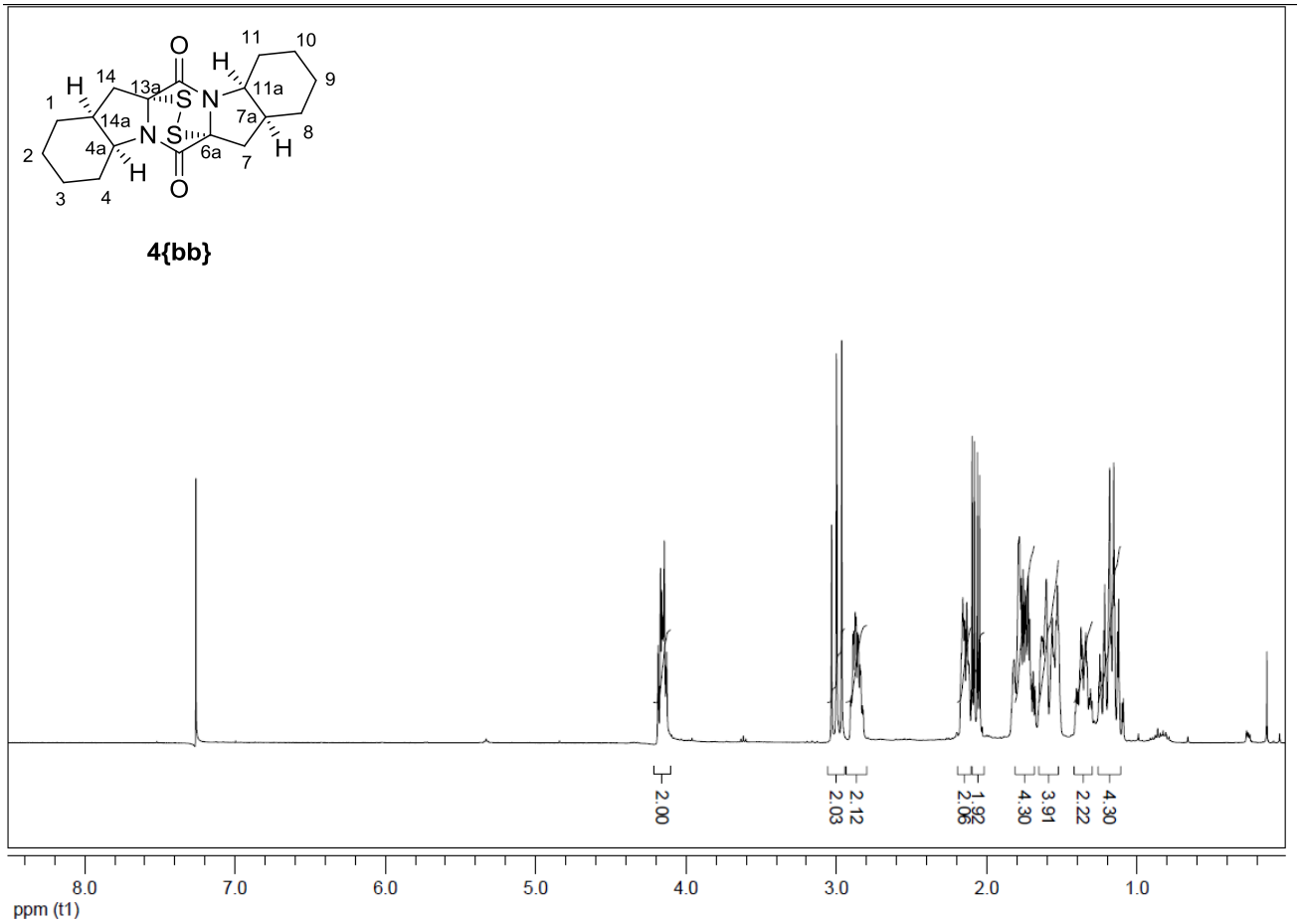
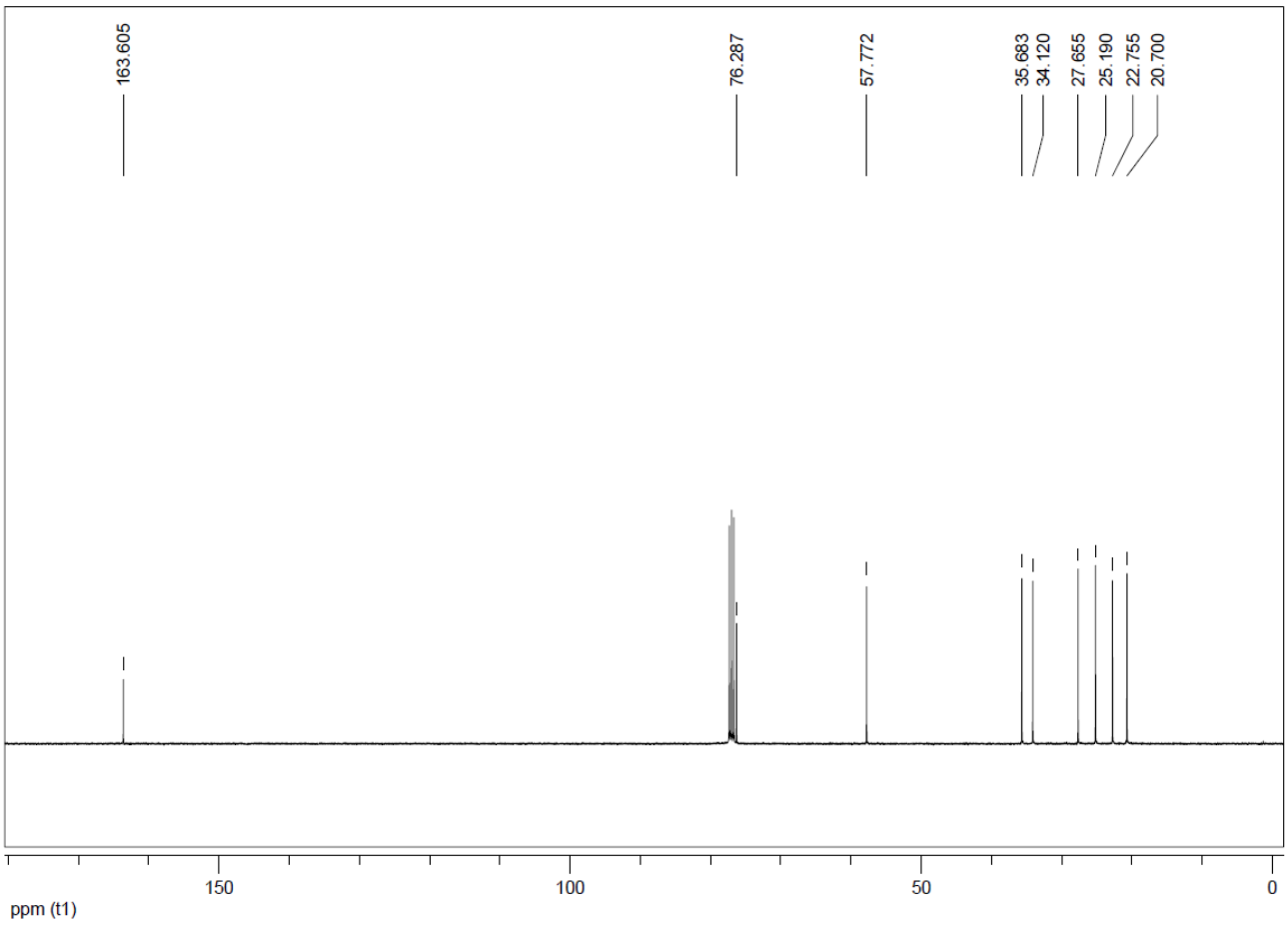


4{bb}



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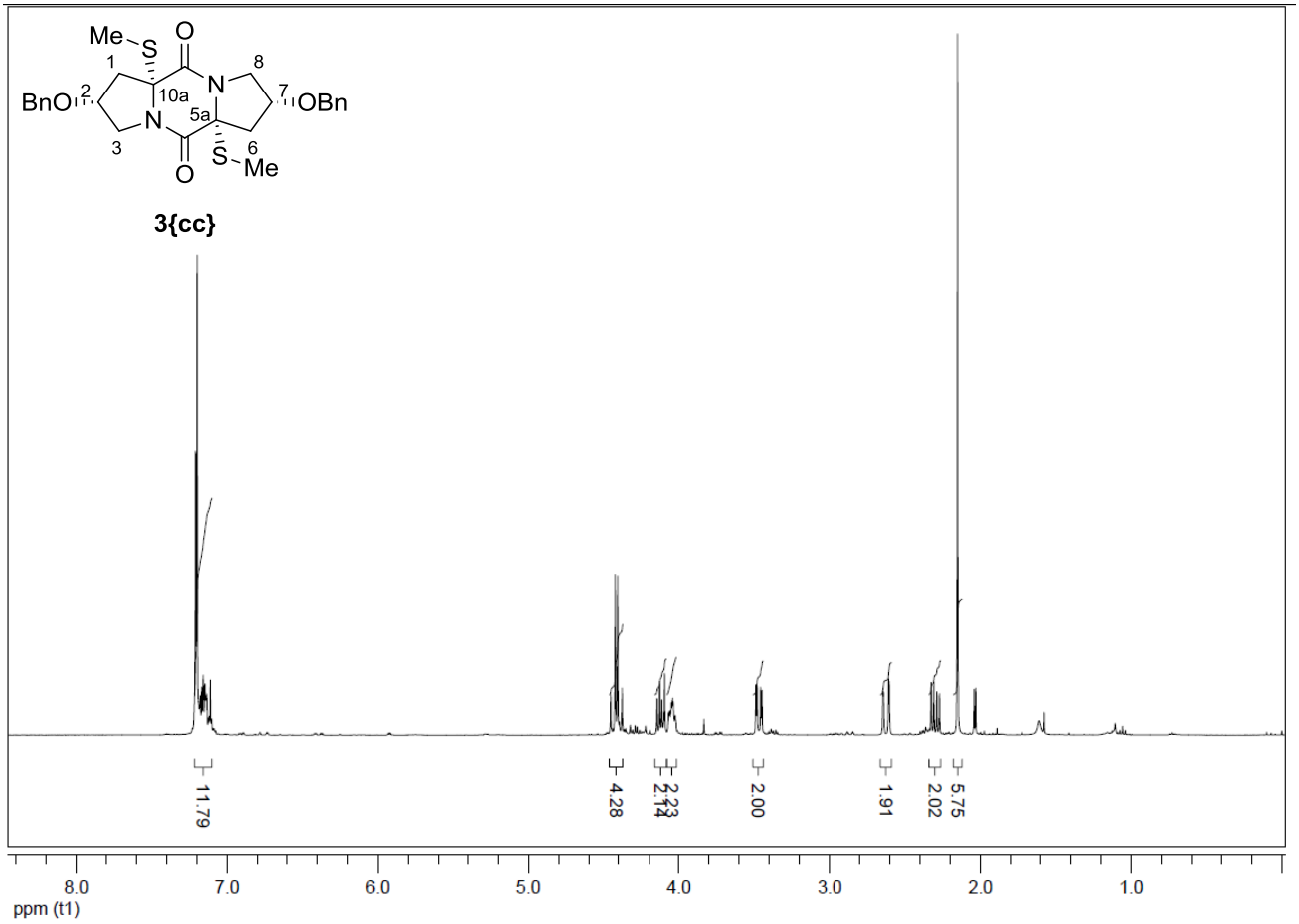

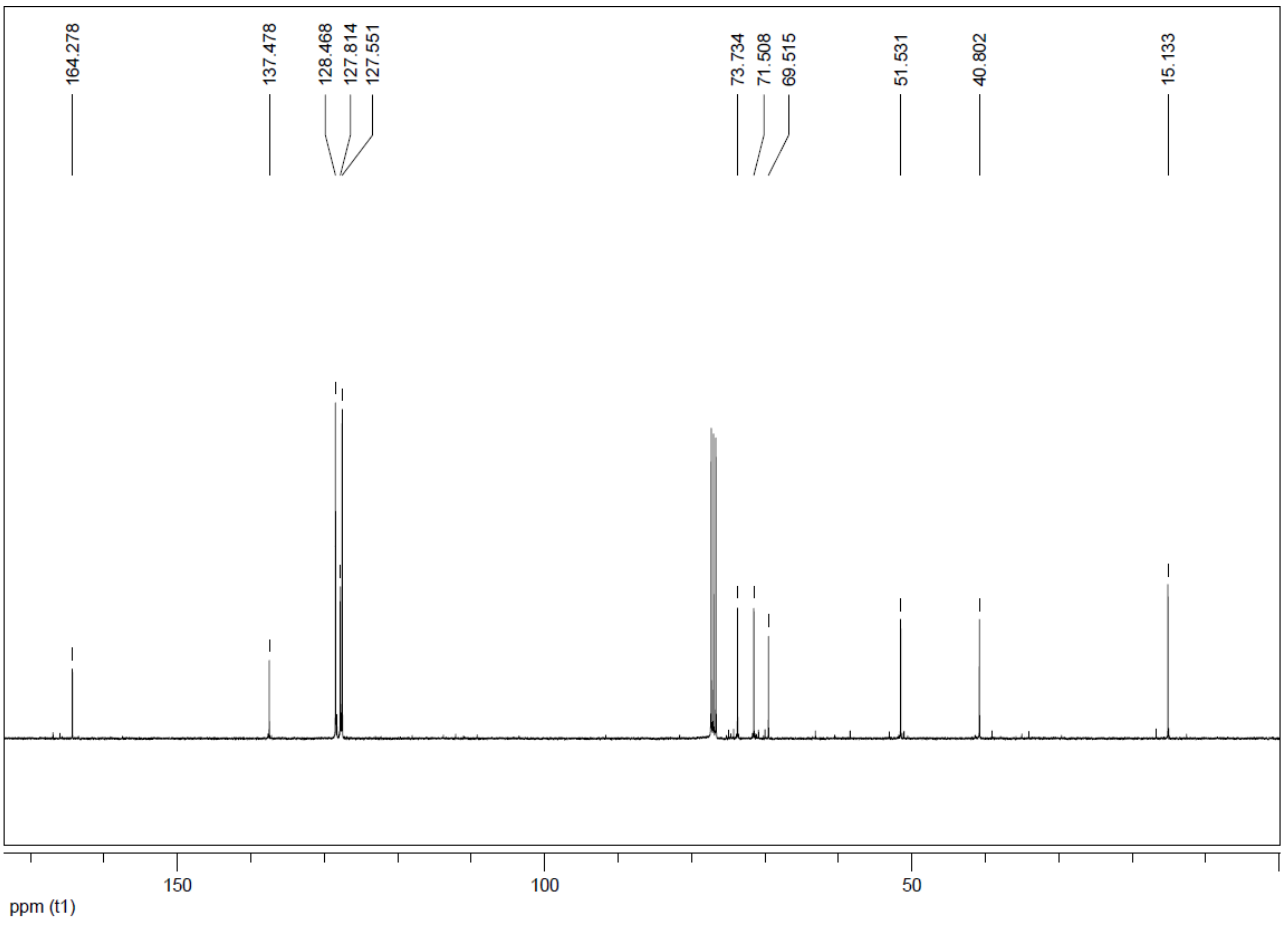

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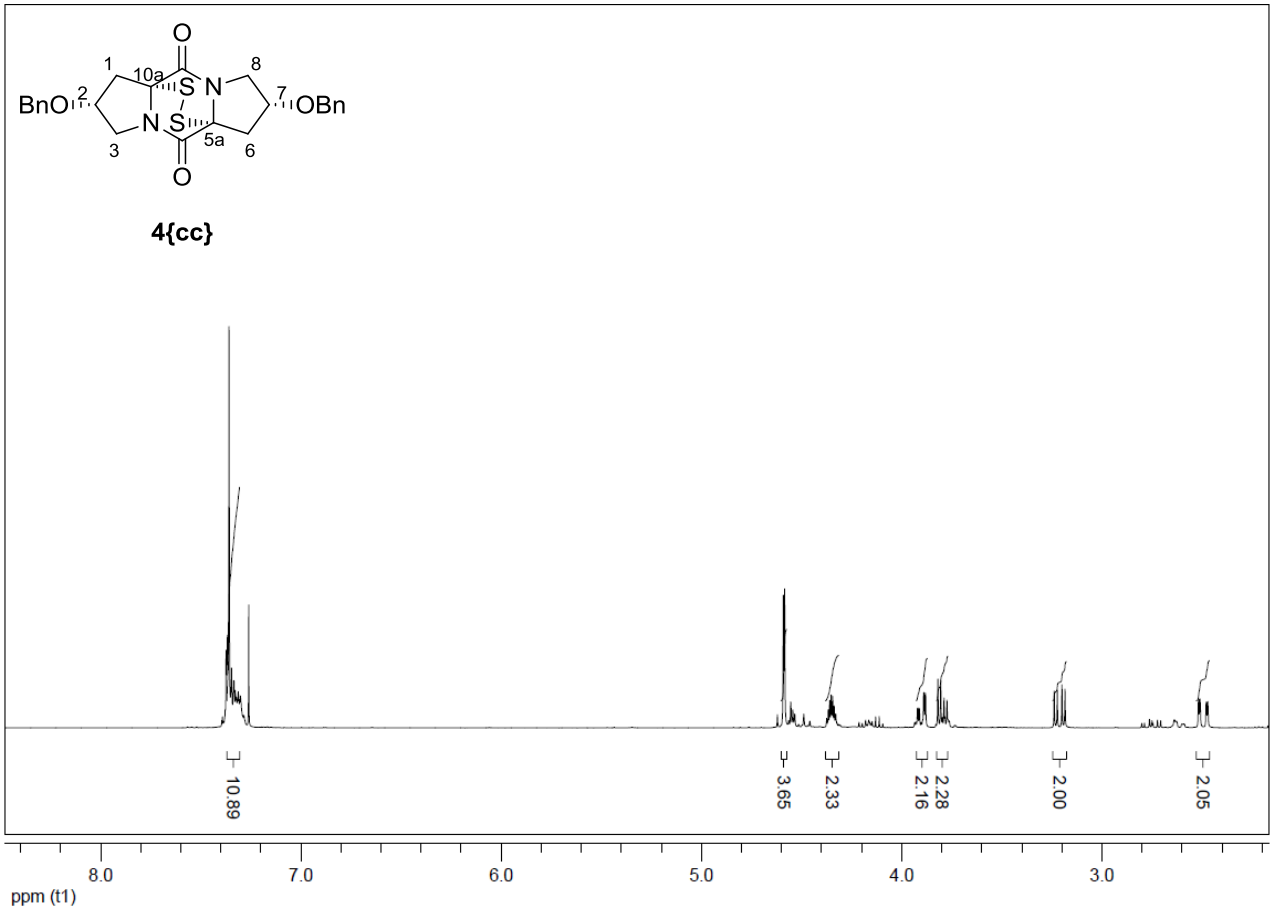
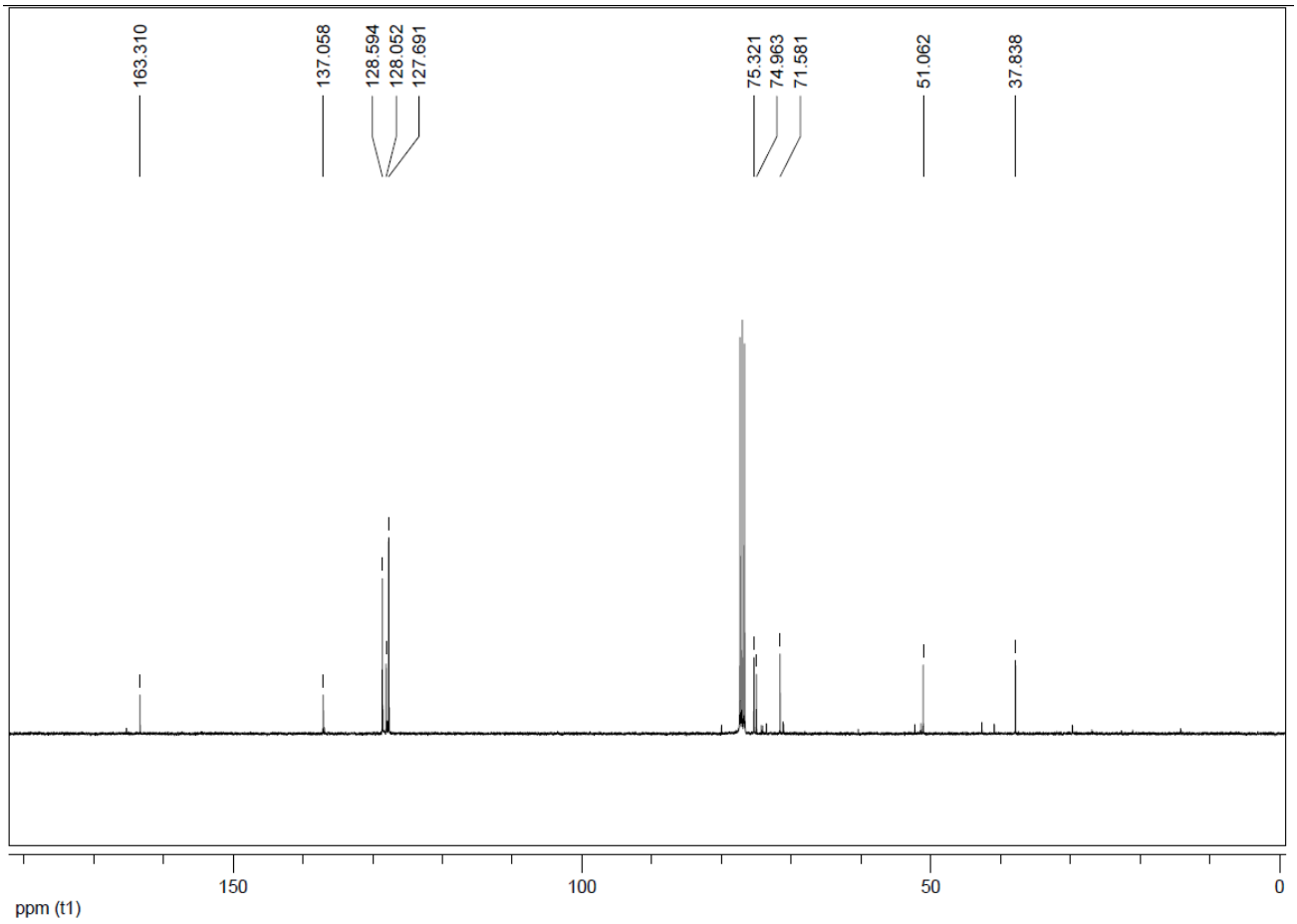
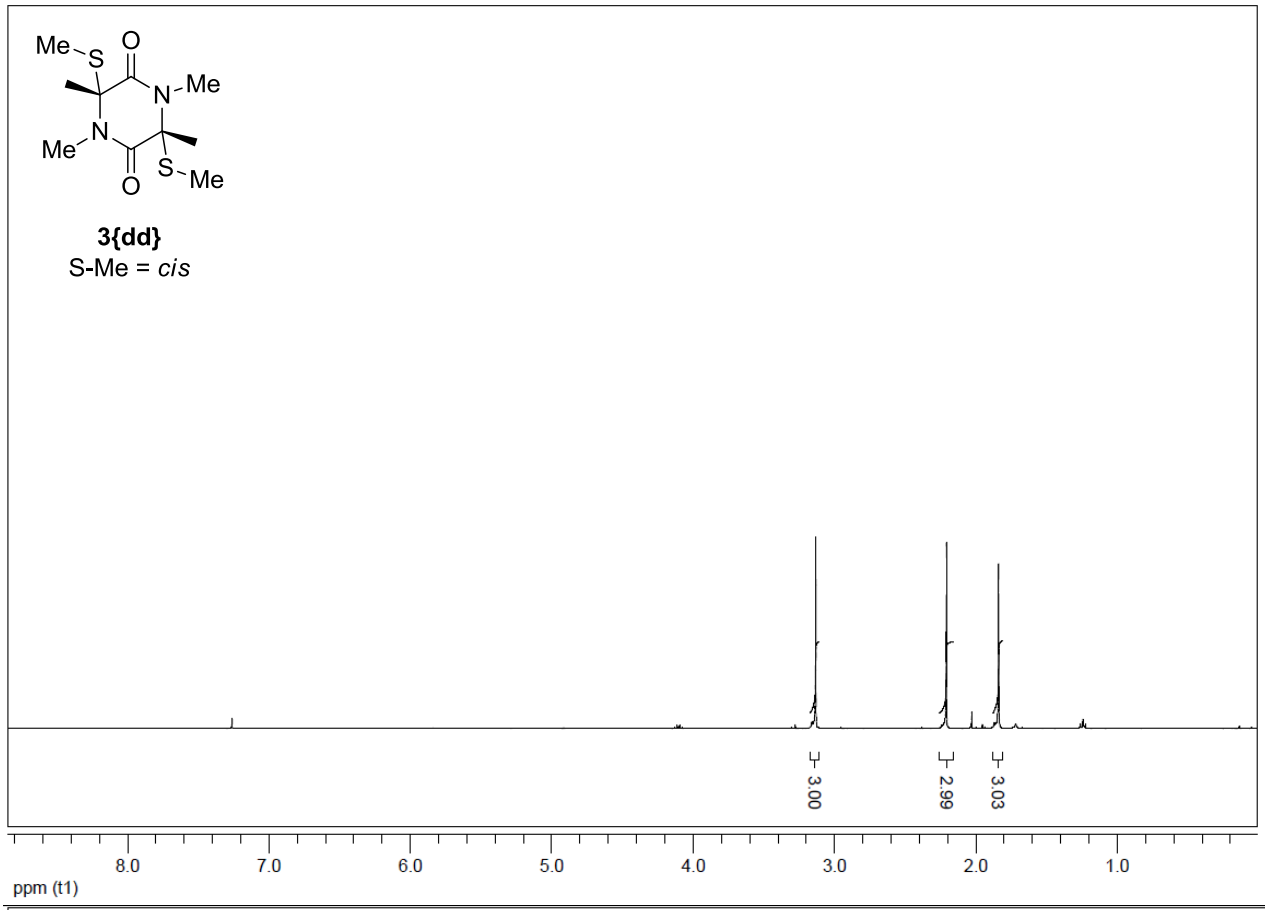
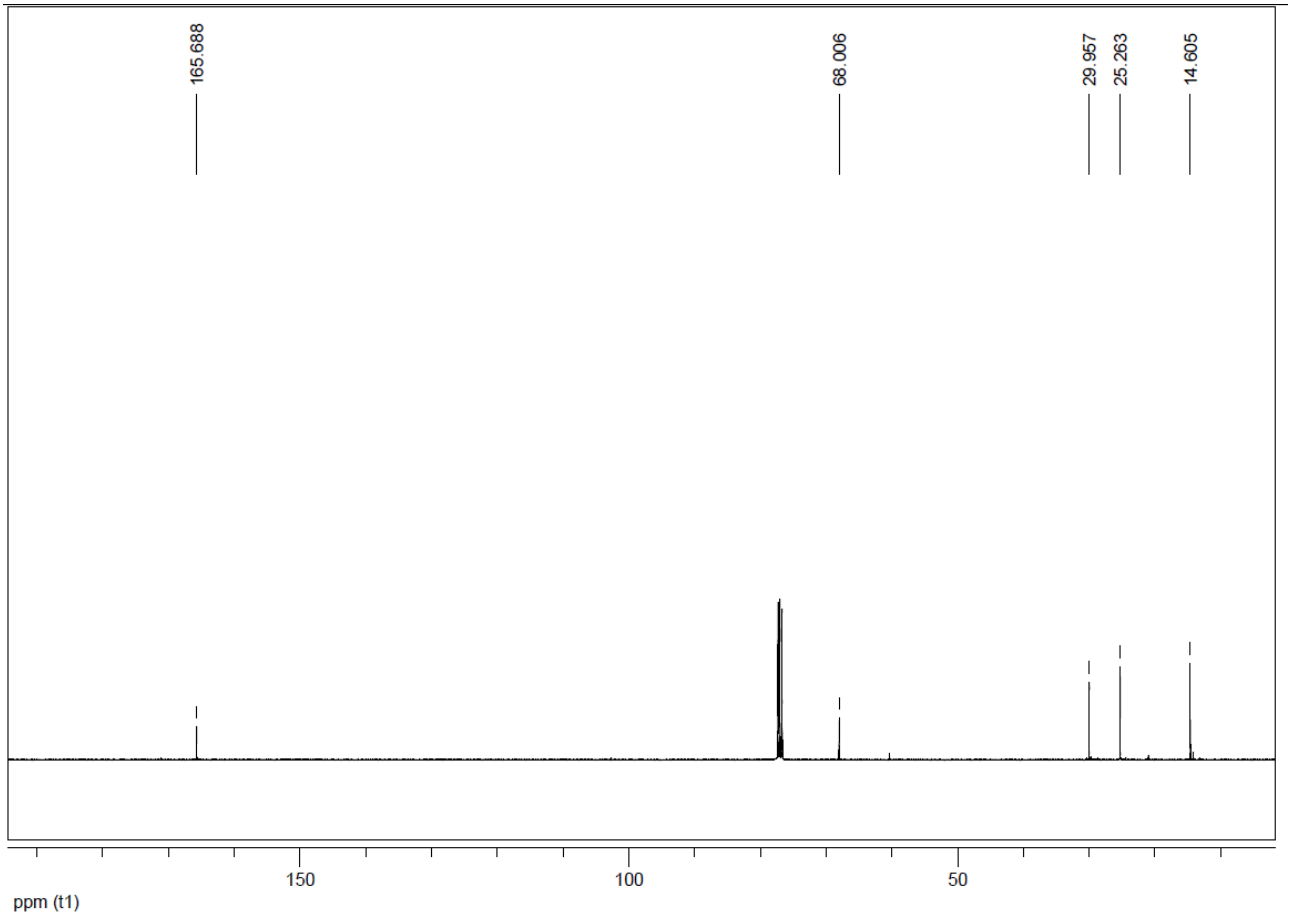


4{cc}




Me
S
O
N
Me
Me
N
S
Me
O
3.00
2.99
3.03
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

3{dd}
S-Me = *cis*


165.688
68.006
29.957
25.263
14.605
150
100
50
ppm (t1)

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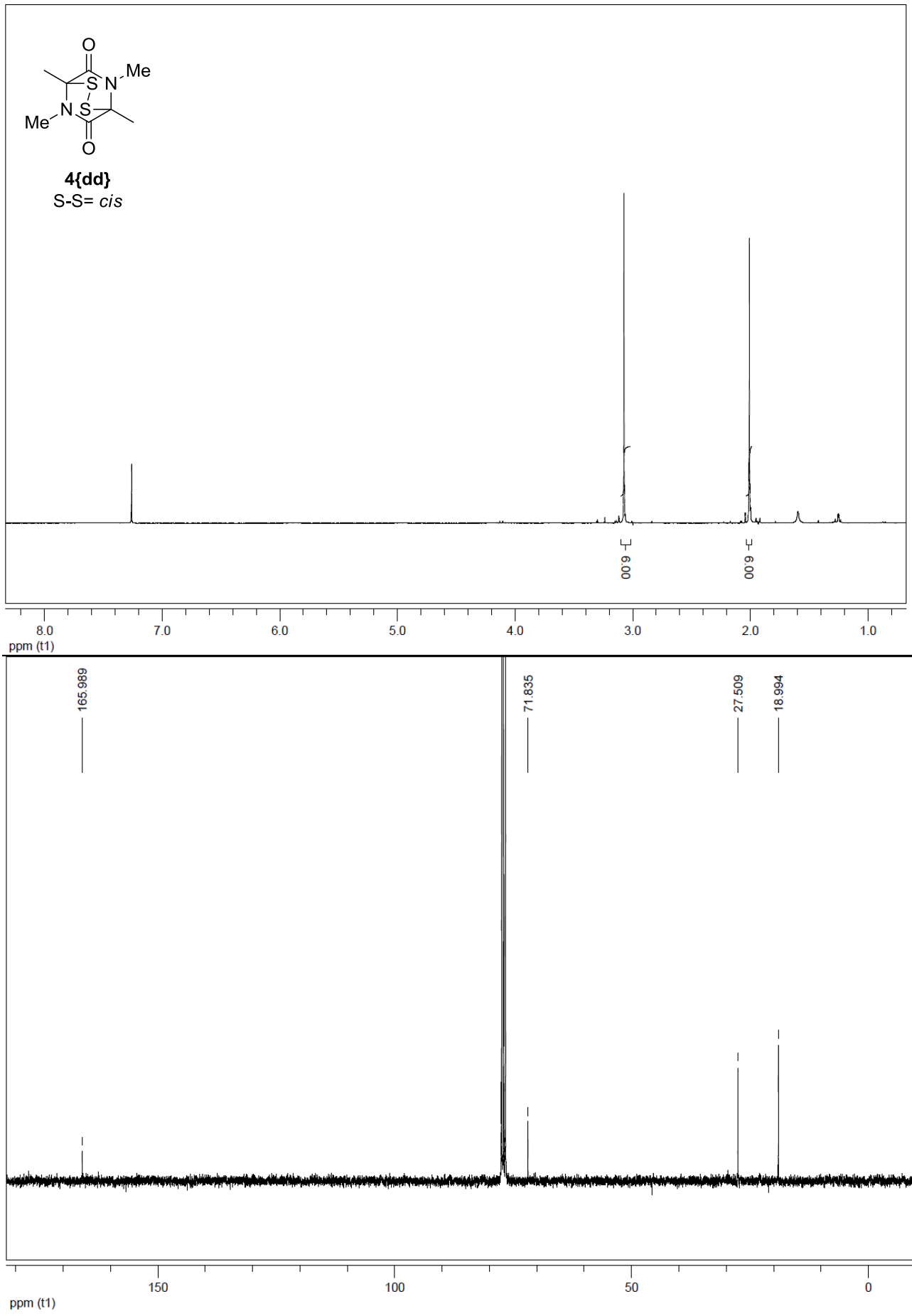
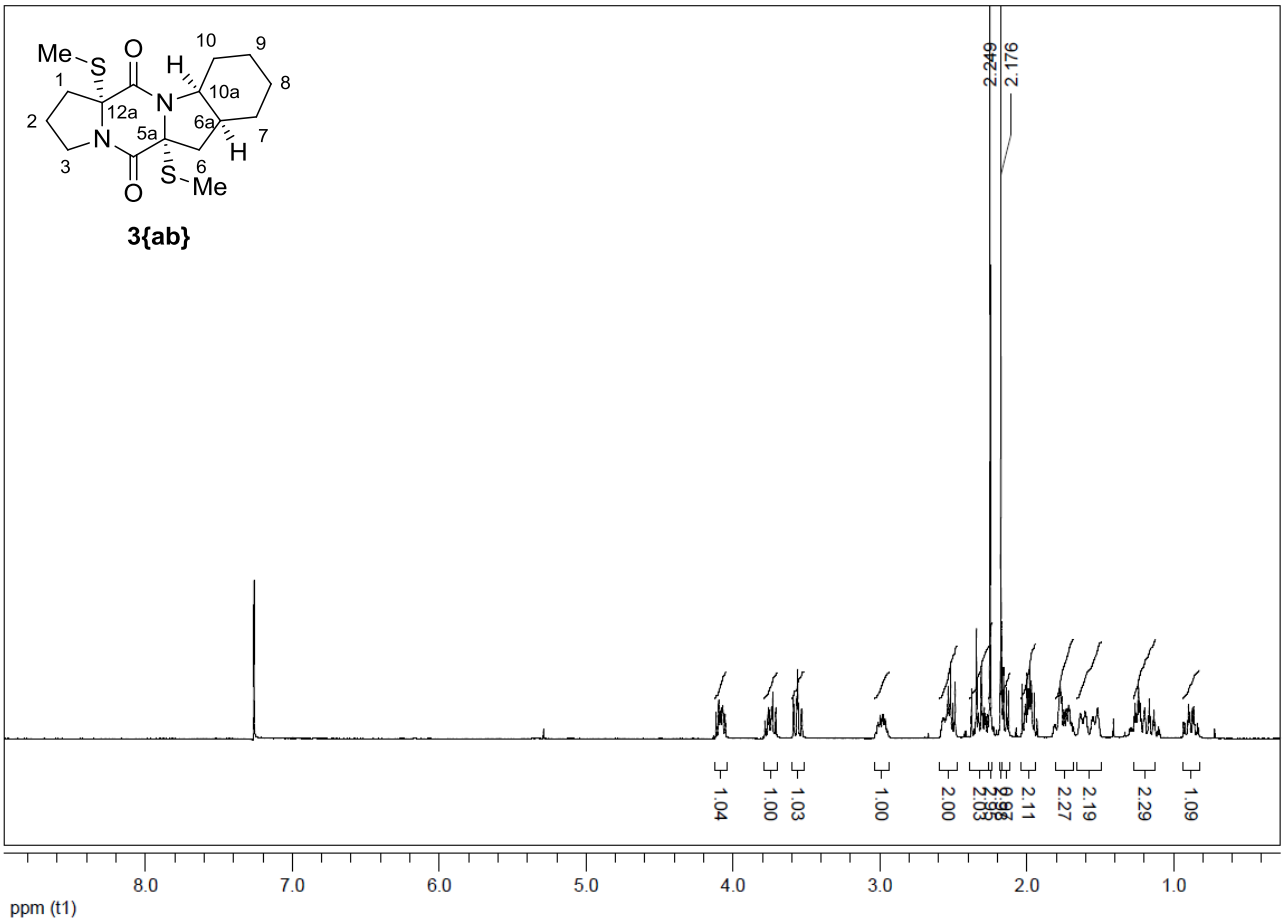
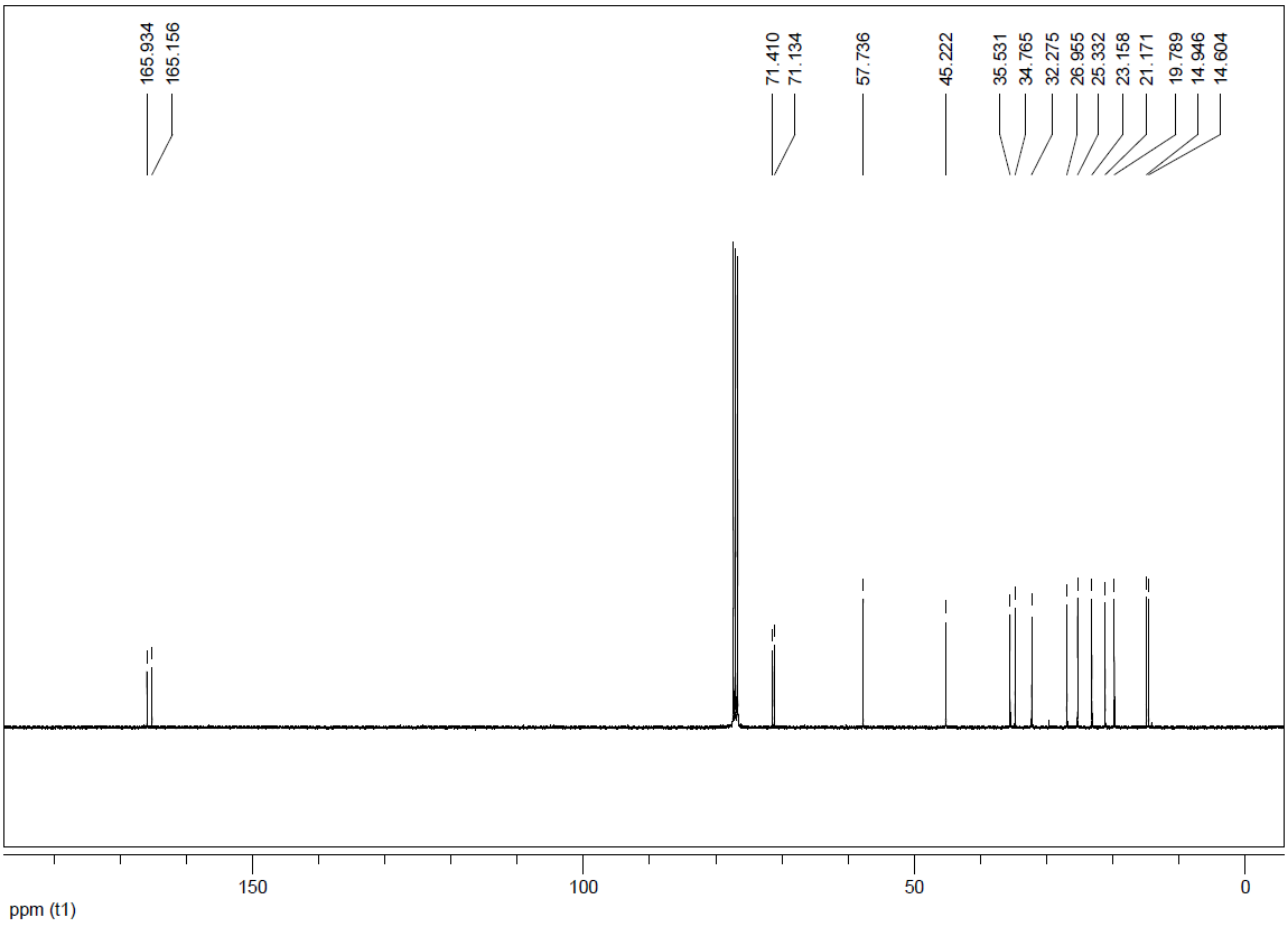



Me
S
1
2
3
O
N
12a
5a
10
H
9
8
10a
6a
7
H
S
6
Me
O
2.249
2.176
1.04
1.00
1.03
1.00
2.00
2.11
2.27
2.19
2.29
1.09
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

3{ab}


165.934
165.156
71.410
71.134
57.736
45.222
35.531
34.765
32.275
26.955
25.332
23.158
21.171
19.789
14.946
14.604
150
100
50
0
ppm (t1)

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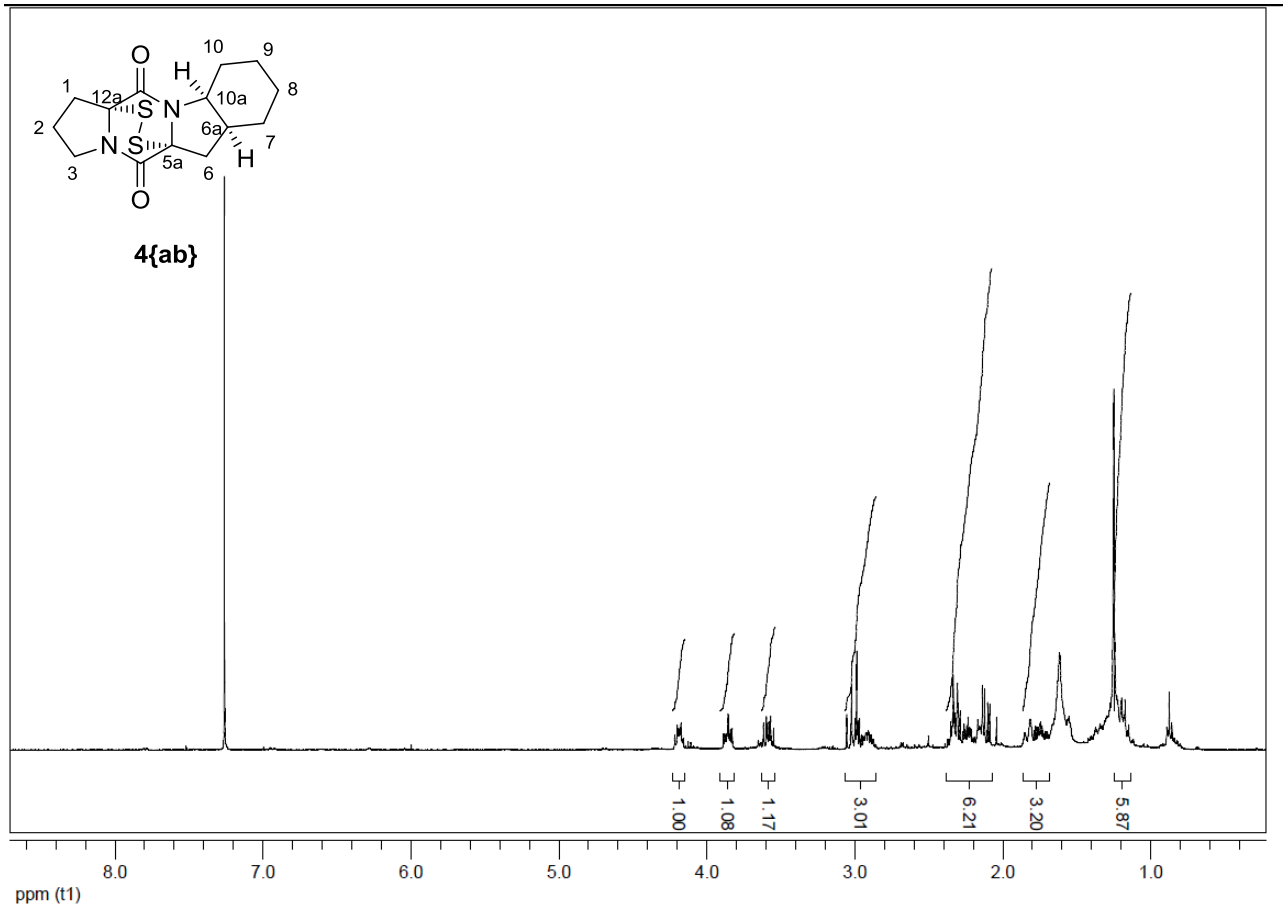

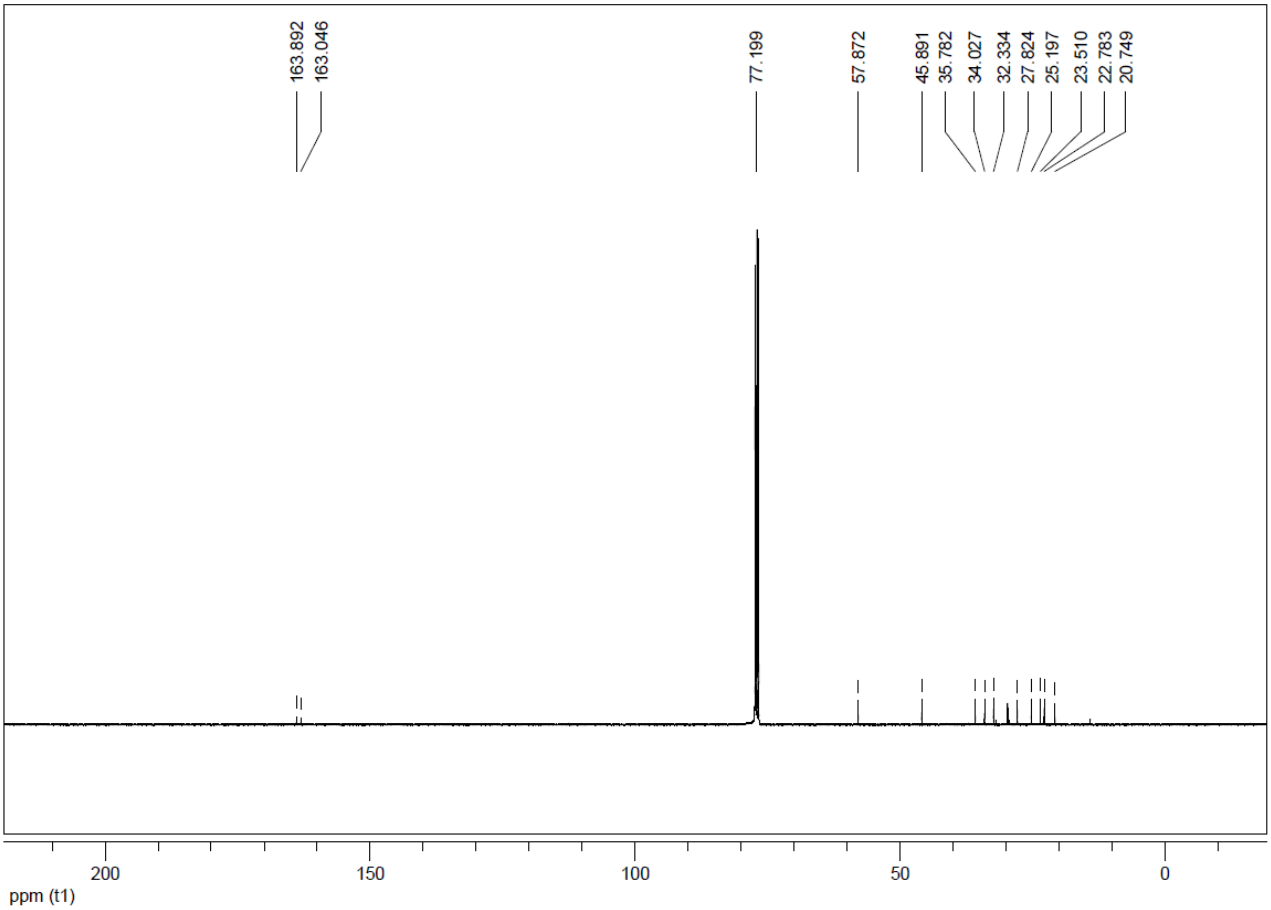

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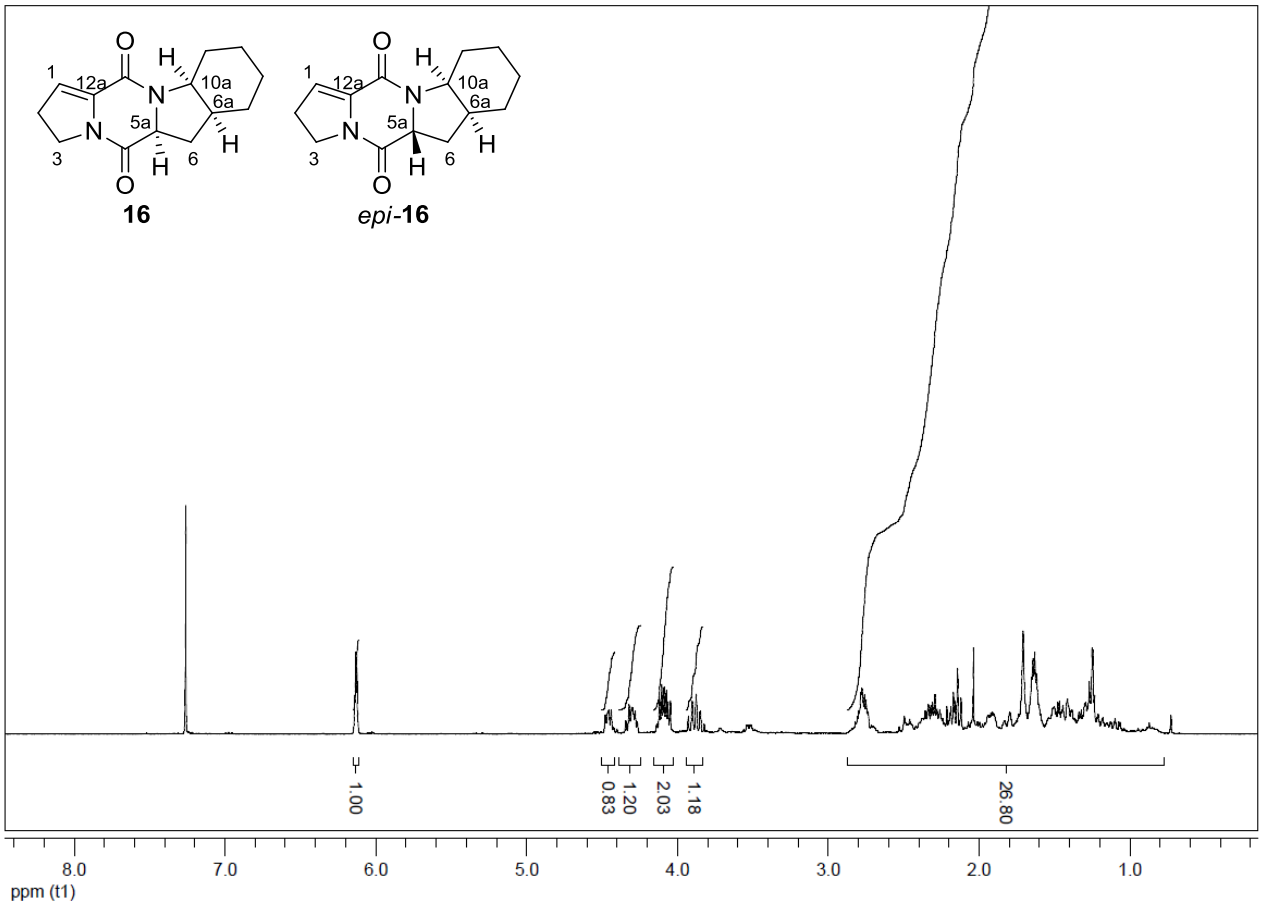

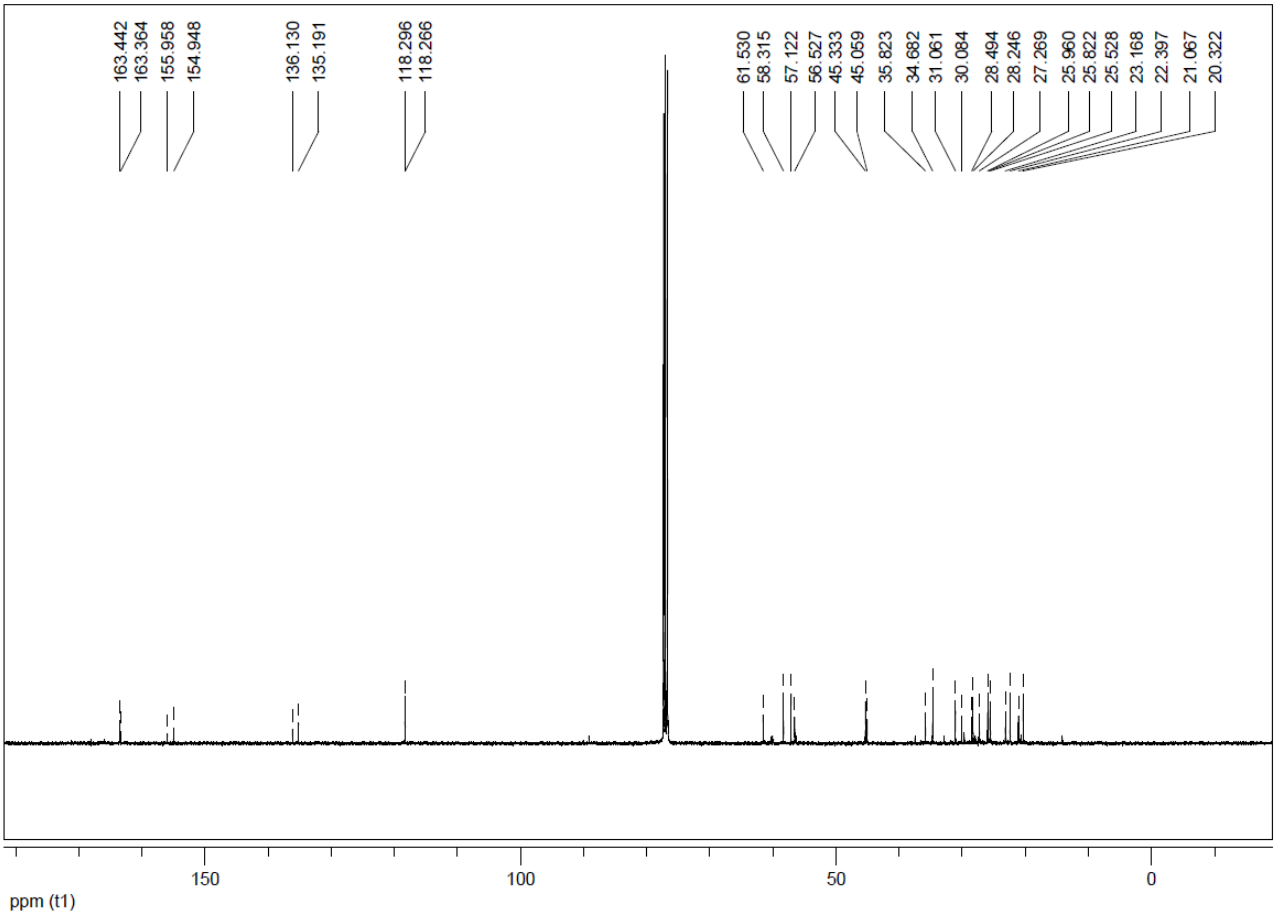

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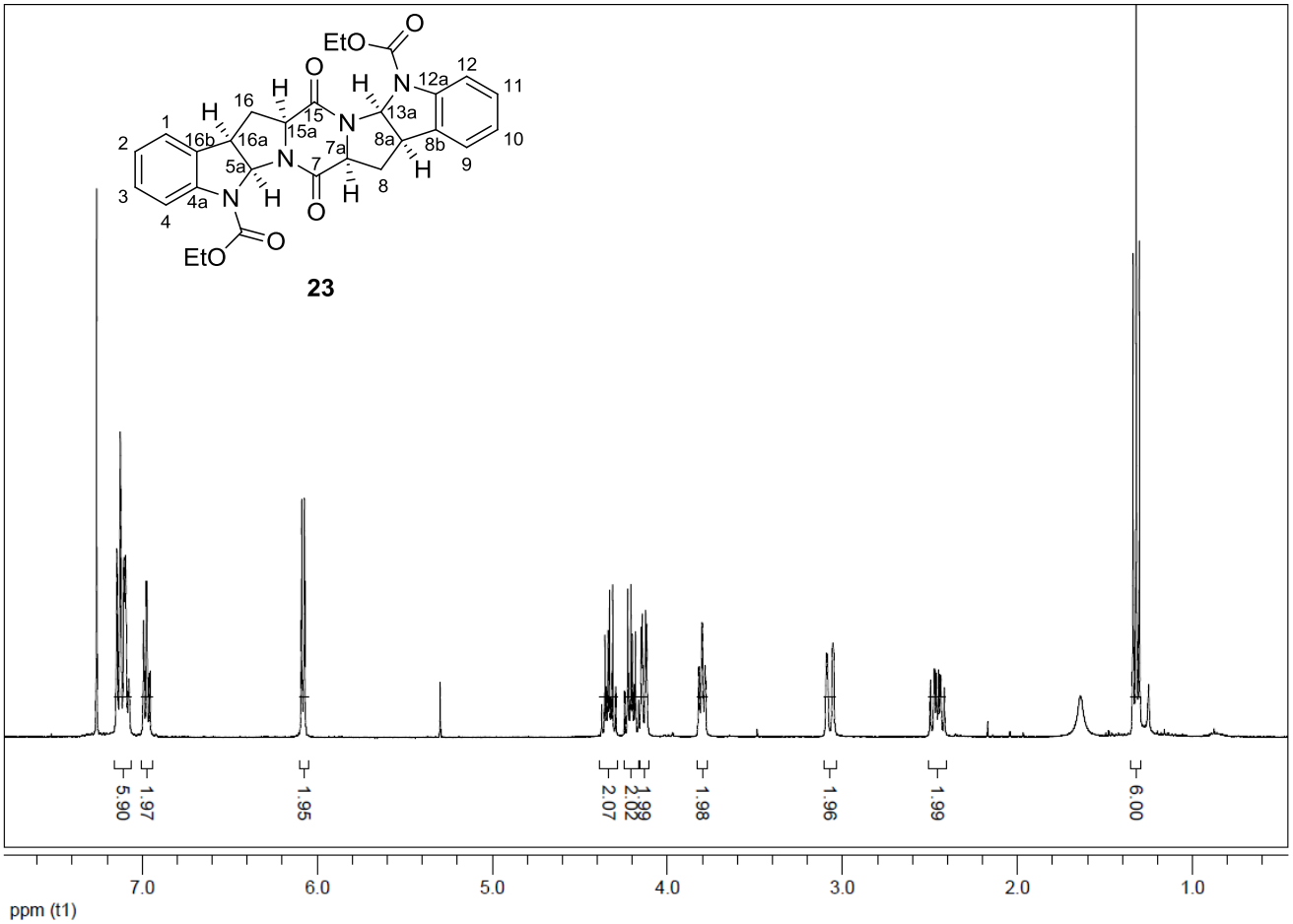

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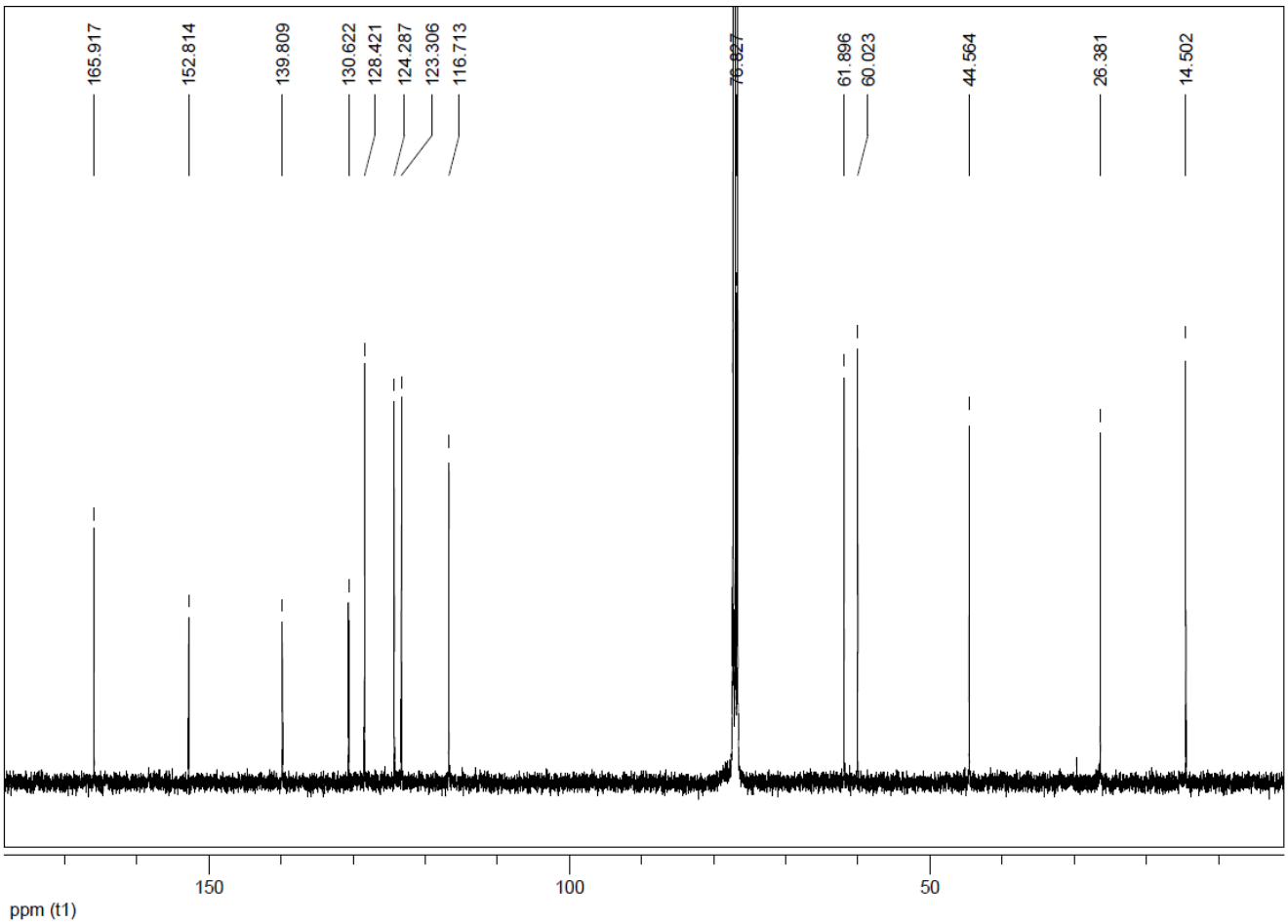

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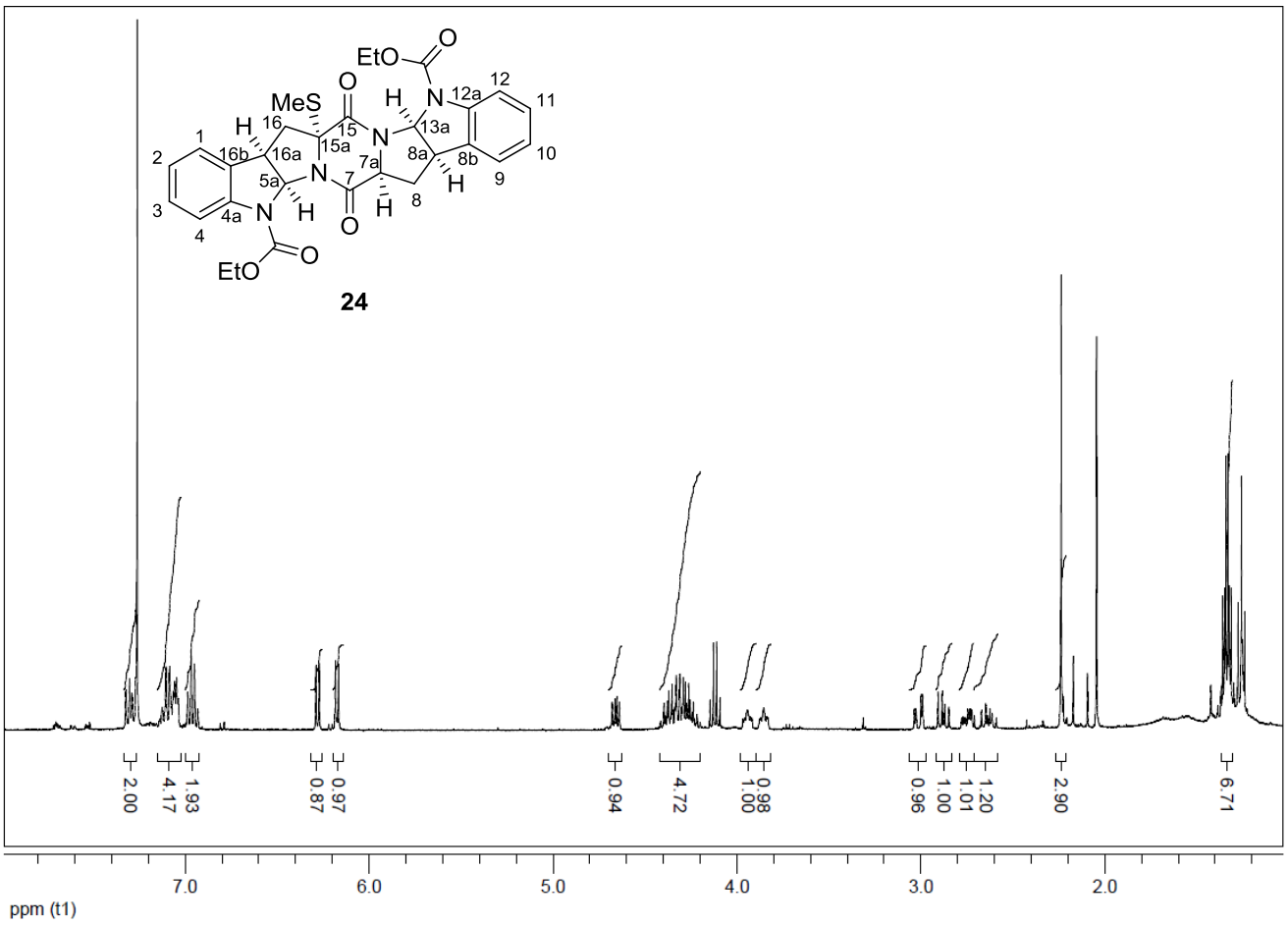

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