Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

for

Asymmetric Approach toward Chiral Multicyclic Spirooxindoles from Isothiocyanato Oxindoles and Unsaturated Pyrazolones by a Chiral Tertiary Amine Thiourea Catalyst

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Table of Contents:

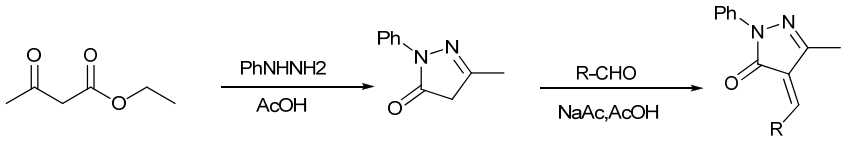
1.0 General Information

All commercially available reagents were used without further purification unless otherwise stated. Reactions were monitored by thin layer chromatography (TLC), column chromatography purifications were carried out using silica gel. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on 300 MHz spectrometer in $CDCl_3$ and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on 75 MHz spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. Data are presented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, m = multiplet) and coupling constant in Hertz (Hz). Infrared (IR) spectra were recorded on a FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter. HR-MS was measured with an APEX II 47e mass spectrometer. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiracel AD-H column or Chiracel IA column on Waters with a 2998 UV-detector and the dr values determined by 300 Hz ^{1}H NMR. MTBE (methyl *tert*-butyl ether) and other solvents (THF, Et_2O, dichloromethane and toluene) were freshly distilled from sodium before use.

Materials

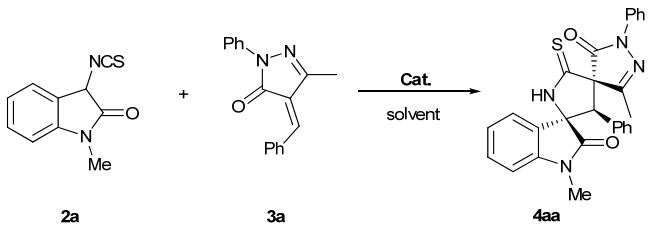
Thiourea catalysts **1a**, **1b, 1f** were synthesized according to the procedures.[1] Thiourea catalyst **1c** was synthesized according to the procedures.[2] Thiourea catalyst **1e** was synthesized according to the procedures.[1a,3] Thiourea catalyst **1d** was synthesized according to the procedures.[4] Cupreine **1g** was synthesized according to the procedures.[5] Isothiocyanato oxindoles **2a**-**2d** were synthesized by following the reported procedure in the literature.[6]

2.0 General Procedure for the Substrates



To the mixture of the ethyl 3-oxobutanoate (10 mmol, 1 equiv) and phenylhydrazine (10 mmol, 1 equiv) was added 2 mL glacial acetic acid. The resulting mixture was stirred at room temperature for 2-4 h. After the reaction was completed, diethyl ether (20mL) was added and then filtered, the residue was washed by diethyl ether to afford the purified pyrazolone. Then the above pyrazolone (5.5 mmol, 1.1 equiv) was slowly added to the mixture of the corresponding aldehyde (5 mmol, 1 equiv) and sodium acetate in glacial acetic acid. The mixture was refluxed for 15-30 min. After the reaction was completed, ethyl acetate (50 mL) was added. The precipitate was filtered and the filtrate was washed with water (three times). The combined organic layers were dried over Na_2SO_4 and then concentrated in vacuo. The product was obtained after purified by flash column chromatography on silica gel (petroleum ether /ethyl acetate 10:1) as red or yellow solid.

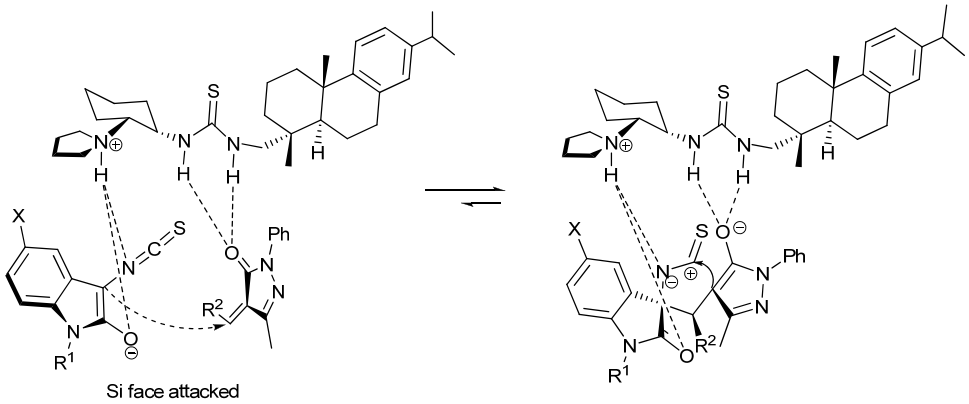
3.0 General Procedure for the Asymmetric Reaction of 2a to 3a



2a **3a** **4aa**

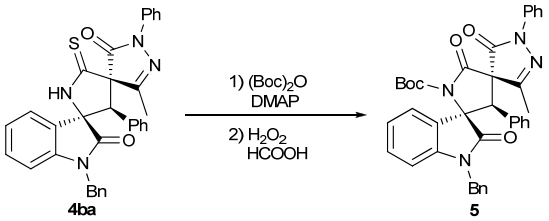
3-Isothiocyanato-1-methylindolin-2-one **2a** (0.1 mmol, 1 equiv) and catalyst **1a** (0.01 mmol, 10 mol%) were dissolved in 1 mL MTBE, (Z)-4-benzylidene-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **3a** (0.11 mmol, 1.1 equiv) was added to the mixture at 0 °C. The mixture was stirred at the same temperature until the reaction was completed monitored by TLC analysis. The crude product was purified by flash chromatography on silica gel (petroleum ether/ ethyl acetate 2:1). Compound **4aa** was obtained as a white solid.

4.0 Proposed Model for the Asymmetric Michael/Cyclization Sequence



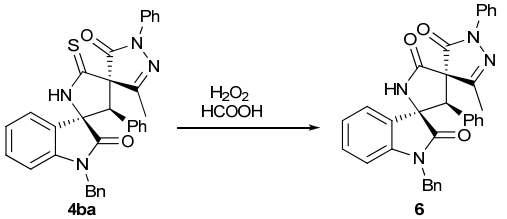
5.0 Elaboration of the Spirooxindole Products

Synthesis of compound 5



To a solution of $(Boc)_2O$ (65.4 mg, 0.3 mmol) and **4ba** (54.2 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) was added DMAP (0.6 mg, 0.005 mmol) at 0 °C. After stirring for 30 min, successively 30% aqueous H_2O_2 (0.42mL) and 98 % aqueous HCOOH (0.33 mL) was added. The resulting mixture was stirred for another 12 h, then quenched with 1 M aqueous K_2CO_3 and extracted with CH_2Cl_2 (three times). The combined organic layers were dried over Na_2SO_4. After evaporation of solvent, the product **5** was obtained after purified by flash column chromatography on silica gel (petroleum ether /ethyl acetate 5:1).

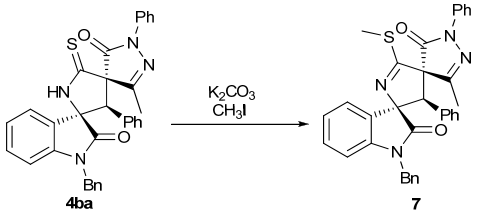
Synthesis of compound 6



To **4ba** (54.2 mg, 0. 1mmol) in CH_2Cl_2 (1 mL) was added successively 30% aqueous H_2O_2 (0.42

mL) and 98 % aqueous HCOOH (0.33 mL) at 0 °C . The resulting mixture was stirred for 4 h and then quenched with 1 M aqueous K_2CO_3 and extracted with CH_2Cl_2 (three times). The combined organic layers were dried over Na_2SO_4. After evaporation of solvent, the product **6** was obtained after purified by flash column chromatography on silica gel (petroleum ether /ethyl acetate 2:1).

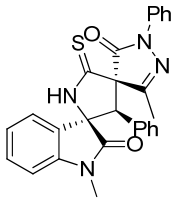
Synthesis of compound 7



To mixture of **4ba** (54.2 mg, 0.1 mmol) and anhydrous K_2CO_3 (15.3 mg, 0.11 mmol) in 2 mL acetone was added CH_3I (6.9 uL, 0.11 mmol) at 0 °C. The reaction was stirred overnight and then concentrated in vacuo. The residue mixture was purified by flash column chromatography on silica gel (petroleum ether /ethyl acetate 4:1) to give compound **7** as white solid.

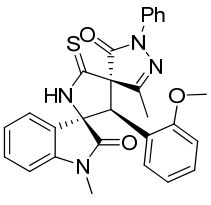
6.0 Characterization Data

Compound **4aa:**



The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 96% yield; mp = 143-145°C; $[\alpha]_D^{20}$= -16 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.69 (d, *J* = 7.3 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.20 – 7.08 (m, 5H), 6.91 (d, *J* = 6.9 Hz, 2H), 6.76 (d, *J* = 7.8 Hz, 1H), 4.90 (s, 1H), 3.10 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.82, 173.31, 171.36, 158.77, 143.11, 137.56, 131.37, 130.80, 128.96, 128.85, 128.60, 127.77, 126.23, 125.47, 124.48, 124.26, 119.16, 109.04, 77.50, 73.55, 61.28, 26.72, 17.04. IR (KBr): 3286, 2926, 2853, 1720, 1643, 1613, 1496, 1472, 1368, 1128, 739 cm^{-1}; HRMS calcd for $C_{27}H_{22}N_4NaO_2S$ $[M+Na]^+$: 489.1356, found: 489.1350.

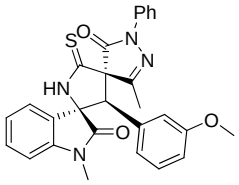
Compound **4ab:**



The ee value determination was carried out using chiral high-performance liquid chromatography

(HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 93% yield; mp = 144-145°C; $[\alpha]_D^{20}$ = +50 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 – 7.95 (m, 2H), 7.72 (d, *J* = 7.0 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.19 – 7.10 (m, 4H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.78 – 6.73 (m, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.22 (s, 1H), 3.33 (s, 3H), 3.30 (s, 3H), 2.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.26, 174.21, 172.63, 158.29, 157.34, 143.38, 138.17, 131.28, 129.36, 128.86, 126.81, 125.44, 125.06, 124.77, 124.04, 120.30, 120.10, 118.41, 110.25, 109.06, 76.79, 72.36, 54.91, 52.19, 26.98, 16.46. IR (KBr): 3232, 2962, 2933, 1724, 1613, 1495, 1470, 1369, 1254, 1124, 752 cm^{-1}; HRMS calcd for $C_{28}H_{24}N_4NaO_3S$ [M+ Na] $^+$: 519.1461, found: 519.1467.

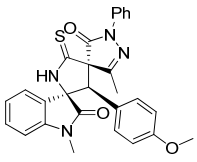
Compound **4ac:**



4ac

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 91% ee). White solid, 93% yield; mp = 129-131°C; $[\alpha]_D^{20}$ = -13 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.88 (d, *J* = 7.7 Hz, 2H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.40 – 7.35 (m, 3H), 7.18 (t, *J* = 7.5 Hz, 2H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 7.7 Hz, 1H), 6.68 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.48 (d, *J* = 8.1 Hz, 1H), 6.43 (d, *J* = 1.9 Hz, 1H), 4.89 (s, 1H), 3.54 (s, 3H), 3.12 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.73, 173.26, 171.37, 159.61, 158.83, 143.17, 137.57, 132.26, 131.40, 129.97, 128.86, 126.23, 125.48, 124.52, 124.26, 119.71, 119.14, 114.48, 112.86, 109.03, 77.39, 73.36, 61.00, 54.99, 26.73, 17.06. IR (KBr): 3236, 2960, 2933, 1725, 1611, 1495, 1472, 1371, 1269, 1161, 754, 737, 692 cm^{-1}; HRMS calcd for $C_{28}H_{24}N_4NaO_3S$ [M+ Na] $^+$: 519.1461, found: 519.1465.

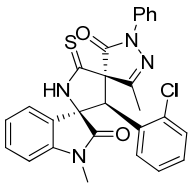
Compound **4ad:**



4ad

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 95% yield; mp = 153-154°C; $[\alpha]_D^{20}$ = -6 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.85 (d, *J* = 7.9 Hz, 2H), 7.69 (d, *J* = 7.3 Hz, 1H), 7.38 – 7.32 (m, 3H), 7.17 (t, *J* = 7.5 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 7.8 Hz, 1H), 6.61 (d, *J* = 8.8 Hz, 2H), 4.82 (s, 1H), 3.65 (s, 3H), 3.08 (s, 3H), 2.60 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.15, 173.44, 171.39, 159.55, 158.69, 143.11, 137.55, 131.26, 129.40, 128.82, 126.36, 125.41, 124.39, 124.20, 122.29, 119.09, 114.23, 108.96, 77.73, 73.74, 61.61, 55.12, 26.70, 17.04. IR (KBr): 3242, 2932, 1724, 1613, 1495, 1473, 1370, 1257, 755, 738 cm^{-1}; HRMS calcd for $C_{28}H_{24}N_4NaO_3S$ [M+ Na] $^+$: 519.1461, found: 519.1462.

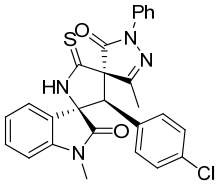
Compound **4ae:**



4ae

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 99% ee). White solid, 90% yield; mp = 134-135°C; $[\alpha]_D^{20}$ = +7 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.81 (dd, *J* = 7.4, 3.6 Hz, 3H), 7.68 (d, *J* = 7.3 Hz, 1H), 7.34 (t, *J* = 7.9 Hz, 3H), 7.19 – 7.10 (m, 5H), 6.71 (d, *J* = 7.7 Hz, 1H), 5.78 (s, 1H), 3.07 (s, 3H), 2.68 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.38, 173.66, 170.85, 157.49, 142.88, 137.50, 135.67, 131.31, 130.32, 130.05, 129.97, 128.78, 127.94, 126.87, 125.32, 125.28, 124.14, 119.05, 108.91, 77.21, 74.26, 56.20, 26.75, 16.94. IR (KBr): 3244, 2926, 1723, 1613, 1495, 1474, 1371, 1351, 1159, 752 cm^{-1}; HRMS calcd for $C_{27}H_{21}ClN_4NaO_2S$ [M+ Na] $^+$: 523.0966, found: 523.0965.

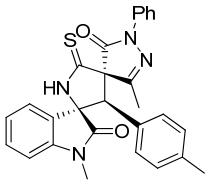
Compound **4af:**



4af

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 95% ee). White solid, 90% yield; mp = 155-157°C; $[\alpha]_D^{20}$ = -6 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 3H), 7.22 – 7.16 (m, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 7.7 Hz, 1H), 4.84 (s, 1H), 3.11 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.62, 173.11, 171.12, 158.35, 143.02, 137.41, 134.82, 131.55, 129.44, 129.20, 129.14, 128.89, 125.92, 125.59, 124.44, 124.40, 119.11, 109.15, 77.40, 73.50, 61.01, 26.79, 17.04. IR (KBr): 3235, 2959, 2930, 1725, 1613, 1496, 1474, 1371, 1096, 754, 738 cm^{-1}; HRMS calcd for $C_{27}H_{21}ClN_4NaO_2S$ [M+ Na] $^+$: 523.0966, found: 523.0965.

Compound **4ag:**

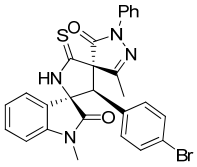


4ag

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 96% yield; mp = 143-144°C; $[\alpha]_D^{20}$ = -8 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.89 – 7.86 (m, 2H), 7.69 (d, *J* = 7.0 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.17 (t, *J* = 7.5 Hz, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.87 (s, 1H), 3.12

(s, 3H), 2.56 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.03, 173.41, 171.40, 158.75, 143.14, 138.47, 137.59, 131.30, 129.63, 128.82, 127.75, 127.56, 126.33, 125.40, 124.45, 124.21, 119.13, 108.99, 77.62, 73.53, 61.34, 26.71, 20.94, 17.03. IR (KBr): 3237, 2926, 1724, 1613, 1495, 1474, 1371, 1351, 754, 737 cm^{-1}; HRMS calcd for $C_{28}H_{24}N_4NaO_2S$ [M+ Na] $^+$: 503.1512, found: 503.1511.

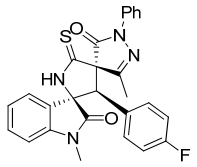
Compound **4ah:**



4ah

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 95% ee). White solid, 81% yield; mp = 132-133°C; $[\alpha]_D^{20}$ = -10 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 2H), 7.71 (d, *J* = 7.1 Hz, 1H), 7.42 – 7.36 (m, 3H), 7.27 (d, *J* = 3.4 Hz, 1H), 7.25 – 7.14 (m, 3H), 6.82 (dd, *J* = 10.4, 8.2 Hz, 3H), 4.84 (s, 1H), 3.13 (s, 3H), 2.59 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.59, 173.10, 171.10, 158.32, 143.02, 137.41, 132.16, 131.55, 129.71, 129.69, 128.88, 125.90, 125.59, 124.45, 124.41, 123.04, 119.11, 109.15, 77.33, 73.41, 61.03, 26.78, 17.04. IR (KBr): 3247, 2956, 2926, 1723, 1613, 1495, 1472, 1370, 1351, 1128, 754 cm^{-1}; HRMS calcd for $C_{27}H_{21}BrN_4NaO_2S$ [M+ Na] $^+$: 567.0461, found: 567.0464.

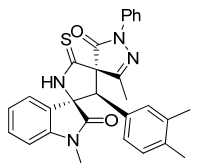
Compound **4ai:**



4ai

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 95% ee). White solid, 87% yield; mp = 141-143°C; $[\alpha]_D^{20}$ = -21 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.40 – 7.35 (m, 3H), 7.19 (dd, *J* = 13.7, 7.2 Hz, 2H), 6.97 – 6.92 (m, 2H), 6.80 (dd, *J* = 16.6, 8.1 Hz, 3H), 4.85 (s, 1H), 3.10 (s, 3H), 2.61 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.82, 173.17, 171.16, 164.31, 161.01, 158.39, 143.04, 137.44, 131.48, 130.06, 129.95, 128.87, 126.39, 126.34, 126.02, 125.55, 124.41, 124.36, 119.10, 116.14, 115.85, 109.06, 77.25, 73.65, 61.24, 26.71, 17.03. IR (KBr): 3228, 2960, 2927, 1721, 1612, 1496, 1474, 1369, 1236, 1160, 756, 738 cm^{-1}; HRMS calcd for $C_{27}H_{21}FN_4NaO_2S$ [M+ Na] $^+$: 507.1261, found: 507.1262.

Compound **4aj:**

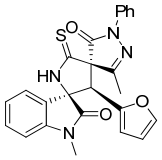


4aj

The ee value determination was carried out using chiral high-performance liquid chromatography

(HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 87% yield; mp = 131-133°C; $[\alpha]_D^{20}$ = -3 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.89 – 7.86 (m, 2H), 7.70 (d, *J* = 7.1 Hz, 1H), 7.40 – 7.15 (m, 3H), 7.18 (t, *J* = 7.7 Hz, 2H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.72 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.64 (s, 1H), 4.85 (s, 1H), 3.14 (s, 3H), 2.55 (s, 3H), 2.08 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.07, 173.50, 171.49, 158.83, 143.17, 137.60, 137.09, 131.26, 130.10, 129.31, 128.82, 127.96, 126.39, 125.41, 124.87, 124.48, 124.19, 119.20, 108.95, 77.67, 73.46, 61.20, 26.69, 19.74, 19.27, 17.04. IR (KBr): 3233, 3060, 2927, 1726, 1613, 1497, 1474, 1371, 1351, 1267, 737, 694 cm^{-1}; HRMS calcd for $C_{29}H_{26}N_4NaO_2S$ [M+ Na] $^+$: 517.1669, found: 517.1666.

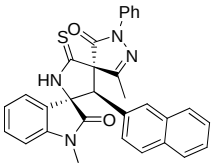
Compound **4ak:**



4ak

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 96% ee). White solid, 86% yield; mp = 112-113°C; $[\alpha]_D^{20}$ = -3 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 3H), 7.19 (q, *J* = 7.0 Hz, 3H), 6.85 (d, *J* = 7.9 Hz, 1H), 6.22 – 6.04 (m, 1H), 5.94 (t, *J* = 4.3 Hz, 1H), 4.91 (s, 1H), 3.19 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.30, 172.81, 171.10, 158.80, 144.75, 143.39, 143.00, 137.64, 131.46, 128.88, 126.04, 125.44, 124.57, 124.19, 119.09, 110.59, 108.94, 108.59, 75.72, 71.97, 54.17, 26.79, 16.46. IR (KBr): 3228, 2958, 2927, 1728, 1614, 1497, 1474, 1370, 1318, 1155, 738, 693 cm^{-1}; HRMS calcd for $C_{25}H_{20}N_4NaO_3S$ [M+ Na] $^+$: 479.1148, found: 479.1144.

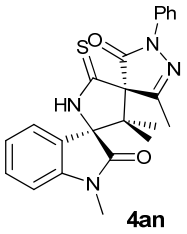
Compound **4al:**



4al

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 92% ee). White solid, 85% yield; mp = 148-149°C; $[\alpha]_D^{20}$ = -4 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.86 (d, *J* = 7.9 Hz, 2H), 7.77 (d, *J* = 7.3 Hz, 1H), 7.70 – 7.67 (m, 1H), 7.62 – 7.58 (m, 2H), 7.45 (s, 1H), 7.42 – 7.33 (m, 5H), 7.18 (dt, *J* = 11.6, 7.4 Hz, 2H), 7.07 (dd, *J* = 8.7, 1.8 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 5.08 (s, 1H), 3.11 (s, 3H), 2.62 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.94, 173.46, 171.39, 158.66, 143.15, 137.52, 132.97, 132.86, 131.42, 128.84, 128.81, 128.07, 127.68, 127.41, 126.72, 126.50, 126.23, 125.49, 125.19, 124.51, 124.31, 119.19, 109.06, 77.67, 73.56, 61.78, 26.73, 17.12. IR (KBr): 3235, 2957, 2925, 1724, 1612, 1496, 1474, 1370, 1317, 1156, 1130,753 cm^{-1}; HRMS calcd for $C_{31}H_{24}N_4NaO_2S$ [M+ Na] $^+$: 539.1512, found: 539.1515.

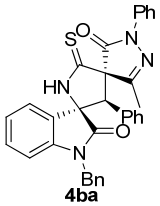
Compound **4an:**



4an

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 75: 25, 1.0 mL/min, 11% ee). White solid, 82% yield; mp =189-190°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.2 Hz, 2H), 7.87 (d, *J* = 7.7 Hz, 2H), 7.39 (q, *J* = 7.8 Hz, 3H), 7.17 (dt, *J* = 18.9, 7.5 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 3.19 (s, 3H), 2.46 (s, 3H), 1.42 (s, 3H), 1.17 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.52, 175.18, 170.24, 158.52, 143.49, 137.51, 130.73, 128.86, 128.25, 125.61, 125.40, 123.16, 119.25, 108.58, 79.78, 77.74, 49.60, 27.22, 27.08, 26.97, 18.40. IR (KBr): 3228, 2926, 1716, 1611, 1494, 1351, 1271, 756cm^{-1}; HRMS calcd for $C_{23}H_{22}N_4NaO_2S$ [M+ Na] $^{+}$: 441.1356, found: 441.1356.

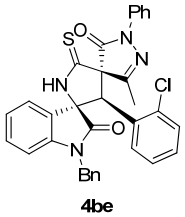
Compound **4ba:**



4ba

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 96% yield; mp = 145-146°C; $[\alpha]_D^{20}$ = -68 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.8 Hz, 2H), 7.73 (d, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.27 – 7.21 (m, 2H), 7.19 (dd, *J* = 7.1, 6.0 Hz, 5H), 7.13 – 7.07 (m, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 6.78 (d, *J* = 6.5 Hz, 2H), 6.58 (d, *J* = 7.5 Hz, 1H), 5.09 (d, *J* = 15.8 Hz, 1H), 4.95 (s, 1H), 4.48 (d, *J* = 15.8 Hz, 1H), 2.67 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.04, 173.22, 171.25, 158.68, 142.50, 137.59, 134.32, 131.33, 130.52, 129.11, 128.85, 128.76, 128.47, 127.72, 126.89, 126.21, 125.45, 124.60, 124.27, 119.11, 110.03, 73.86, 62.10, 44.38, 17.15. IR (KBr): 3282, 2924, 2854, 1721, 1645, 1613, 1493, 1469, 1362, 748 cm^{-1}; HRMS calcd for $C_{33}H_{26}N_4NaO_2S$ [M+ Na] $^{+}$: 565.1669, found: 565.1671.

Compound **4be:**

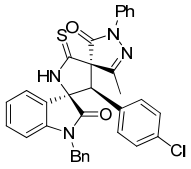


4be

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 91% ee). White solid, 72% yield; mp = 149-150°C; $[\alpha]_D^{20}$ = -50 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.87 – 7.82 (m, 2H), 7.69 (d, *J* = 7.2 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 3H), 7.27 – 7.23 (m, 1H), 7.20 –

7.07 (m, 9H), 6.72 (d, *J* = 7.1 Hz, 2H), 6.54 (d, *J* = 7.5 Hz, 1H), 5.88 (s, 1H), 5.11 (d, *J* = 15.9 Hz, 1H), 4.46 (d, *J* = 15.9 Hz, 1H), 2.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.38, 173.54, 170.78, 157.50, 142.26, 137.54, 135.80, 134.26, 131.32, 130.56, 130.35, 130.06, 128.82, 128.79, 127.97, 127.68, 127.17, 126.60, 125.57, 125.35, 125.32, 124.12, 119.04, 109.85, 77.37, 74.26, 56.50, 44.28, 17.00. IR (KBr): 3250, 2925, 1722, 1612, 1492, 1367, 1163, 750, 697 cm^{-1}; HRMS calcd for $C_{33}H_{25}ClN_4NaO_2S$ [M+ Na] $^+$: 599.1279, found: 599.1280.

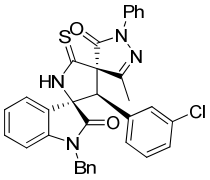
Compound **4bf:**



4bf

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 90% ee). White solid, 96% yield; mp = 138-139°C; [α] $_D^{20}$ = -60 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.85 (d, *J* = 7.9 Hz, 2H), 7.72 (d, *J* = 7.1 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 2H), 7.28 – 7.15 (m, 6H), 7.05 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 6.1 Hz, 2H), 6.61 (d, *J* = 7.6 Hz, 1H), 5.09 (d, *J* = 15.8 Hz, 1H), 4.87 (s, 1H), 4.45 (d, *J* = 15.8 Hz, 1H), 2.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.85, 172.98, 171.02, 158.31, 142.44, 137.44, 135.04, 134.21, 131.49, 130.08, 129.32, 128.87, 127.90, 126.82, 125.93, 125.58, 124.56, 124.39, 119.08, 110.05, 77.34, 73.86, 61.83, 44.37, 17.17. IR (KBr): 3257, 2925, 2855, 1723, 1612, 1494, 1470, 1366, 1157, 753, 735 cm^{-1}; HRMS calcd for $C_{33}H_{25}ClN_4NaO_2S$ [M+ Na] $^+$: 599.1279, found: 599.1286.

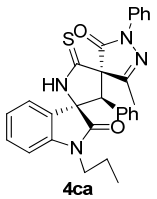
Compound **4bm:**



4bm

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 70: 30, 1.0 mL/min, 80% ee). White solid, 82% yield; mp = 126-128°C; [α] $_D^{20}$ = -45 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 2H), 7.74 (d, *J* = 6.9 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.20 (dd, *J* = 10.2, 4.4 Hz, 6H), 7.02 (dd, *J* = 10.3, 5.1 Hz, 2H), 6.87 (d, *J* = 6.6 Hz, 3H), 6.64 (d, *J* = 7.6 Hz, 1H), 5.09 (d, *J* = 15.8 Hz, 1H), 4.89 (s, 1H), 4.52 (d, *J* = 15.8 Hz, 1H), 2.69 (d, *J* = 3.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.67, 172.98, 170.96, 158.18, 142.48, 137.44, 134.90, 134.25, 132.46, 131.57, 130.35, 129.13, 128.92, 128.87, 128.62, 127.85, 126.83, 126.80, 125.82, 125.59, 124.53, 124.43, 119.15, 110.13, 77.22, 73.61, 61.48, 44.45, 17.09. IR (KBr): 3242, 2926, 1723, 1612, 1492, 1368, 1179, 754, 736, 694 cm^{-1}; HRMS calcd for $C_{33}H_{25}ClN_4NaO_2S$ [M+ Na] $^+$: 599.1279, found: 599.1280.

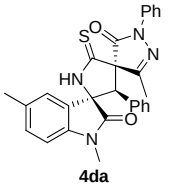
Compound **4ca:**



4ca

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 60: 40, 1.0 mL/min, 98% ee). White solid, 86% yield; mp = 103-105°C; $[\alpha]_D^{20}$ = -16 (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.90 – 7.87 (m, 2H), 7.71 (d, *J* = 6.9 Hz, 1H), 7.39 – 7.33 (m, 3H), 7.21 – 7.07 (m, 5H), 6.92 (d, *J* = 7.2 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.90 (s, 1H), 3.74 – 3.64 (m, 1H), 3.41 – 3.31 (m, 1H), 2.63 (s, 3H), 1.51 – 1.36 (m, 2H), 0.75 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.94, 173.00, 171.27, 158.75, 142.85, 137.59, 131.31, 130.64, 128.88, 128.83, 128.66, 128.10, 126.33, 125.42, 124.64, 124.02, 119.08, 109.18, 77.41, 73.66, 61.80, 42.26, 20.49, 17.10, 11.30. IR (KBr): 3239, 2964, 2930, 1721, 1612, 1496, 1468, 1367, 752cm^{-1}; HRMS calcd for $C_{29}H_{26}N_4NaO_2S$ $[M+ Na]^+$: 517.1693, found: 517.1677.

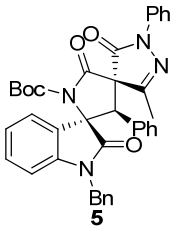
Compound **4da:**



4da

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 70: 30, 1.0 mL/min, >99% ee). White solid, 88% yield; mp = 140-142°C; $[\alpha]_D^{20}$ = -31 (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H), 7.91 (dd, *J* = 8.7, 1.0 Hz, 2H), 7.50 (s, 1H), 7.41 – 7.36 (m, 2H), 7.21 – 7.09 (m, 5H), 6.92 – 6.89 (m, 2H), 6.69 (d, *J* = 7.9 Hz, 1H), 4.91 (s, 1H), 3.11 (s, 3H), 2.54 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.78, 173.20, 171.43, 158.85, 140.70, 137.60, 134.25, 131.67, 130.93, 128.95, 128.85, 128.54, 127.68, 126.23, 125.46, 125.06, 119.11, 108.87, 73.54, 61.10, 26.74, 21.06, 17.01. IR (KBr): 3232, 2959, 2926, 1724, 1599, 1499, 1360, 1265, 1243, 1107, 736, 695 cm^{-1}; HRMS calcd for $C_{28}H_{24}N_4NaO_2S$ $[M+ Na]^+$: 503.1512, found: 503.1504.

Compound **5:**

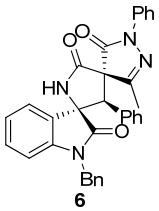


5

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel IA column (hexane: 2-propanol = 60: 40, 1.0 mL/min, 99% ee). White solid, 86% yield; mp = 99-101°C; $[\alpha]_D^{20}$ = -17 (c 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.66 – 7.63 (m, 1H), 7.37 – 7.32 (m, 2H), 7.28 – 7.16 (m, 5H), 7.13– 7.08 (m, 4H), 6.97 (d, *J*

= 7.5 Hz, 2H), 6.57 (d, *J* = 7.2 Hz, 2H), 6.50 – 6.47 (m, 1H), 5.17 (d, *J* = 16.0 Hz, 1H), 4.66 (s, 1H), 4.29 (d, *J* = 15.9 Hz, 1H), 2.82 (s, 3H), 1.18 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.83, 169.77, 165.65, 156.95, 147.27, 142.83, 137.37, 134.35, 130.29, 129.58, 129.35, 129.08, 129.05, 128.78, 128.69, 127.43, 126.59, 125.47, 123.76, 122.50, 118.94, 109.59, 85.16, 70.55, 70.24, 58.46, 44.30, 27.46, 17.68. IR (KBr): 3336, 2979, 2930, 1790, 1729, 1708, 1360, 1298, 1249, 1140, 750cm^{-1}; HRMS calcd for $C_{38}H_{34}N_4NaO_5$ [M+ Na] $^+$: 649.2421, found: 649.2438.

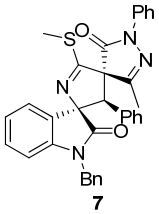
Compound **6:**



6

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 60: 40, 1.0 mL/min, 99% ee). White solid, 98% yield; mp = 130-132°C; $[\alpha]_D^{20}$ = +3 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.7 Hz, 2H), 7.75 – 7.72 (m, 1H), 7.36 (t, *J* = 8.0 Hz, 2H), 7.22 – 7.14(m, 7H), 7.12 – 7.07 (m, 2H), 6.93 (d, *J* = 7.6 Hz, 2H), 6.73 – 6.71 (m, 2H), 6.56 – 6.53 (m, 1H), 5.08 (d, *J* = 15.9 Hz, 1H), 4.85 (s, 1H), 4.45 (d, *J* = 15.9 Hz, 1H), 2.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.69, 170.66, 169.34, 157.74, 142.57, 137.60, 134.41, 131.06, 130.88, 129.02, 128.78, 128.63, 128.47, 127.58, 127.37, 126.78, 125.34, 124.23, 124.08, 118.86, 109.87, 69.37, 67.19, 60.39, 44.24, 17.63. IR (KBr): 3265, 2925, 2864, 1729, 1612, 1495, 1364, 1266, 748, 695cm^{-1}; HRMS calcd for $C_{33}H_{26}N_4NaO_3$ [M+ Na] $^+$: 549.1897, found: 549.1904.

Compound **7:**



7

The ee value determination was carried out using chiral high-performance liquid chromatography (HPLC) with Chiracel AD-H column (hexane: 2-propanol = 60: 40, 1.0 mL/min, 96% ee). White solid, 98% yield; mp = 188-189°C; $[\alpha]_D^{20}$ = +37 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.7 Hz, 2H), 7.60 (d, *J* = 6.6 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 2H), 7.26 – 7.13 (m, 7H), 7.07 (t, *J* = 7.5 Hz, 2H), 6.99 – 6.96 (m, 2H), 6.90 (d, *J* = 7.6 Hz, 2H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.19 (d, *J* = 15.8 Hz, 1H), 4.94 (s, 1H), 4.58 (d, *J* = 15.8 Hz, 1H), 2.60 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.95, 171.59, 171.09, 158.60, 142.73, 137.72, 134.98, 132.29, 130.19, 130.07, 128.98, 128.92, 128.77, 127.96, 127.94, 127.60, 127.14, 125.57, 124.36, 123.75, 118.94, 109.58, 84.85, 77.94, 63.68, 44.21, 17.36, 13.98. IR (KBr): 3389, 3061, 2928, 1718, 1571, 1498, 1358, 1176, 753cm^{-1}; HRMS calcd for $C_{34}H_{28}N_4NaO_2S$ [M+ Na] $^+$: 579.1825, found: 579.1838.

7.0 References

1 (a) X.-X. Jiang, Y.-F. Zhang, A. S. C. Chan and R. Wang, *Org. Lett* ., 2009, **11**, 153; (b) X.-X. Jiang, Y.-F. Zhang, X. Liu, G. Zhang, L.-H. Lai, L.-P. Wu, J.-N. Zhang and R. Wang, *J. Org. Chem.*, 2009, **74**, 5562.

2 T. Okino, Y. Hoashi and Y. Takemoto, *J. Am. Chem. Soc.*, 2003, **125**, 12672.

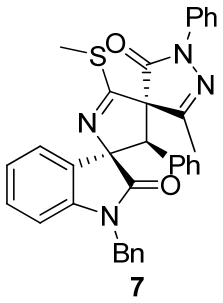
3 B. Henri, B. Juergen and N. Bernhard, *Tetrahedron: Asymmetry.*, 1995, 1699.

4 B. Vakulya, S. Varga, A. Csampai and T. Soos, *Org. Lett.*, 2005, **7**, 1967.

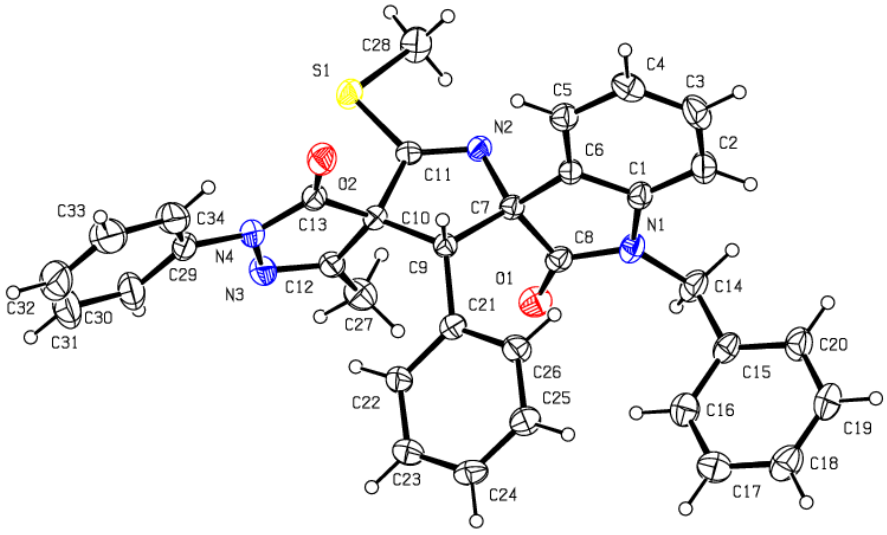
5 T. Furuya, A. E. Strom and T. Ritter, *J. Am. Chem. Soc.*, 2009, **131**, 1662.

6 W.-B. Chen, Z.-J. Wu, J. Hu, L.-F. Cun, X.-M. Zhang and W.-C. Yuan, *Org. Lett.*, 2011, **13**, 2472.

8.0 X-Ray Structure of 7 (CCDC: 909596)



7

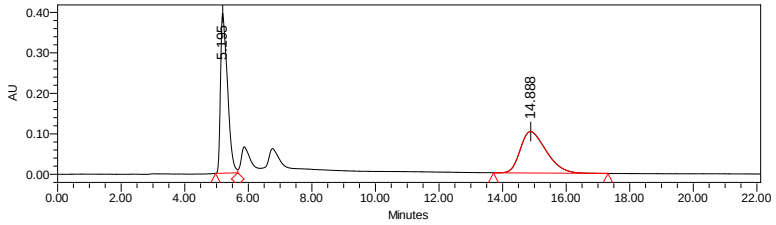


30% probability chosen for the ellipsoids in the ORTEP plot

Empirical formula	$C_{34}H_{28}N_4O_2S$
Formula weight	556.66
Temperature/K	293.04(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.0892(3)
b/Å	18.1126(16)
c/Å	19.1621(7)
α/°	90.00
β/°	90.00
γ/°	90.00
Volume/Å^3	2807.6(3)
Z	4
ρ_{calc}mg/mm^3	1.317
m/mm^{-1}	0.154
F(000)	1168.0
Crystal size/mm^3	0.2 × 0.08 × 0.06
2Θ range for data collection	6.2 to 51.36°
Index ranges	$-6 \le h \le 9$, $-22 \le k \le 11$, $-23 \le l \le 20$
Reflections collected	6101
Independent reflections	4415[R(int) = 0.0242]
Data/restraints/parameters	4415/0/372
Goodness-of-fit on F^2	1.094
Final R indexes [I>=2σ (I)]	R_1 = 0.0464, wR_2 = 0.0949
Final R indexes [all data]	R_1 = 0.0575, wR_2 = 0.1028
Largest diff. peak/hole / e Å^{-3}	0.14/-0.21
Flack parameter	0.02(10)

9.0 Copies of HPLC Spectra of Racemic and Chiral Products

4aa



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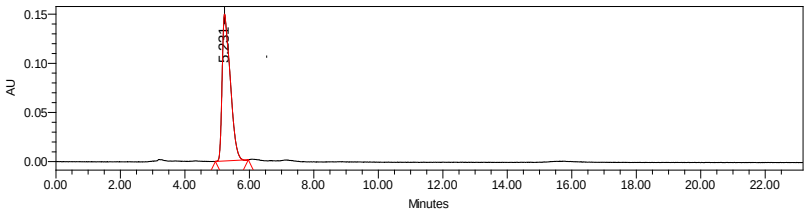

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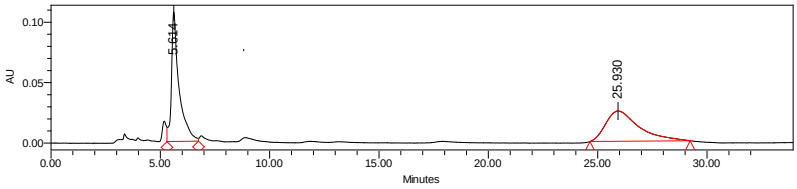
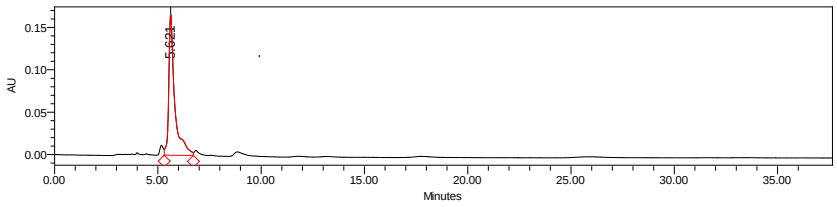
4ab



Entry	Retention Time	Area	% Area	Height	Int Type
1	5.614	2581845	49.39	107213	vV
2	25.930	2645683	50.61	25129	bb



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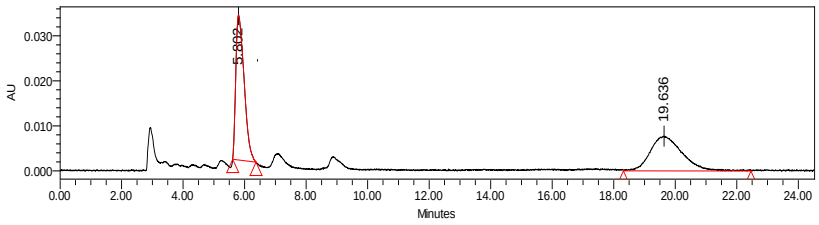
4ac



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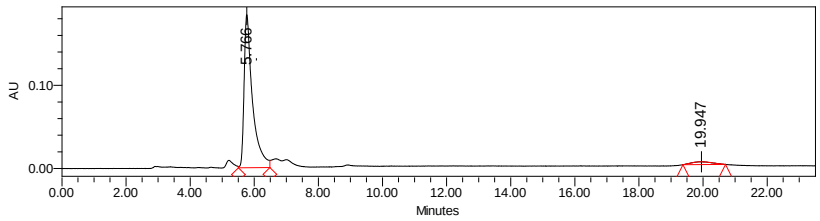

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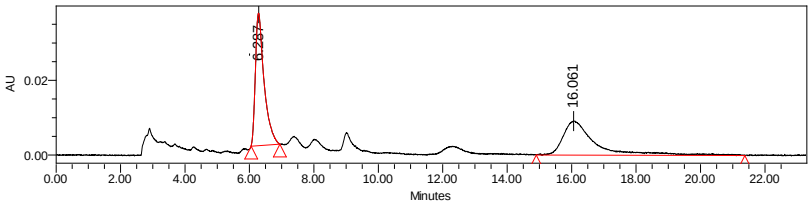
4ad



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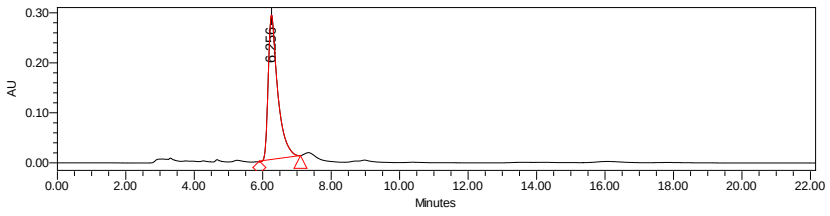

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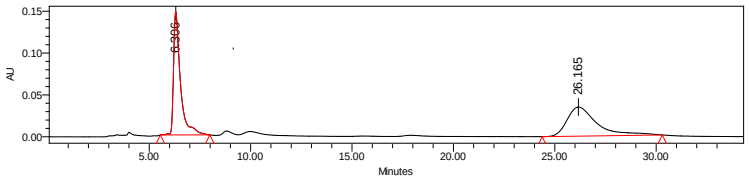
4ae



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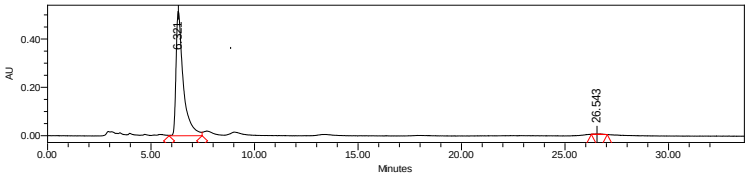
2	26.165	3563554	50.44	34869	bb



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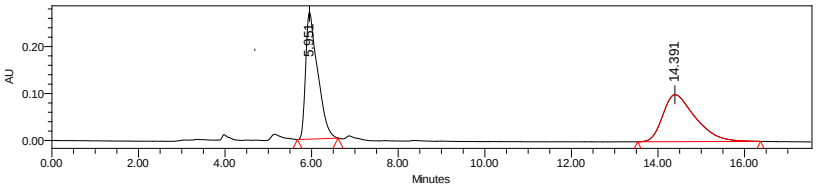
2	26.543	41860	0.33	1691	bb

4af



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1	5.951	5203534	50.02	269891	bb
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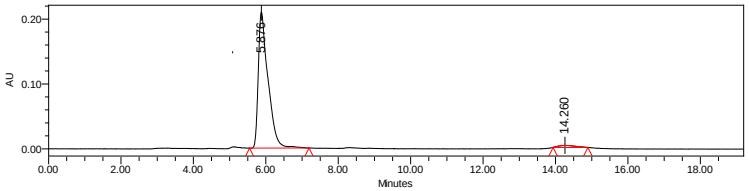

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1	5.876	3916169	97.51	209593	bb
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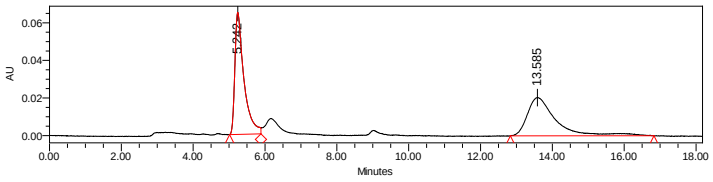
4ag



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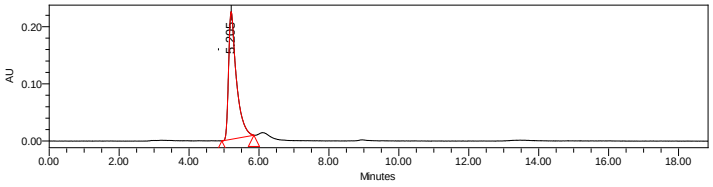

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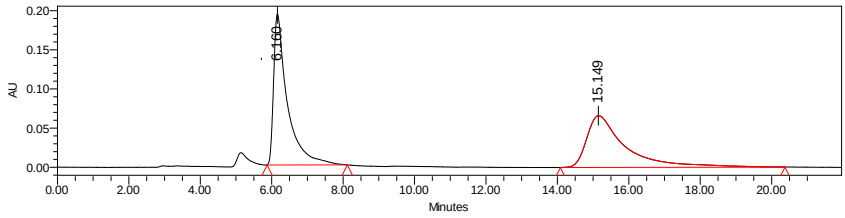
4ah



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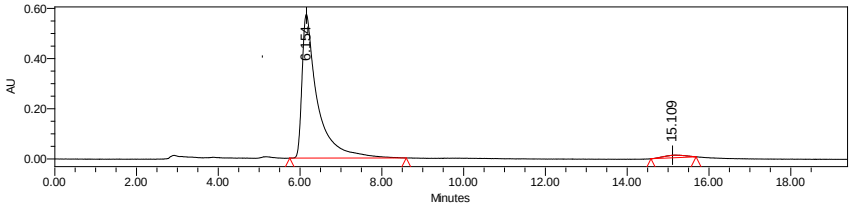

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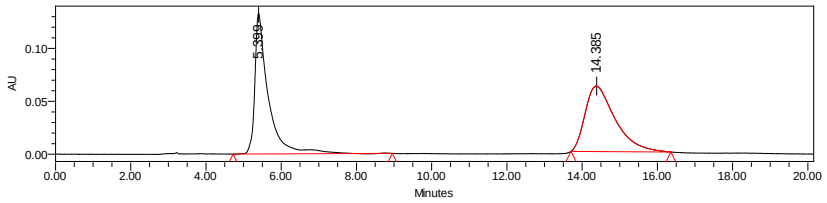
4ai



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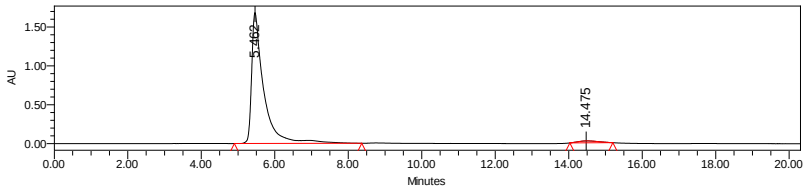
2	14.385	3432579	50.92	61998	bb



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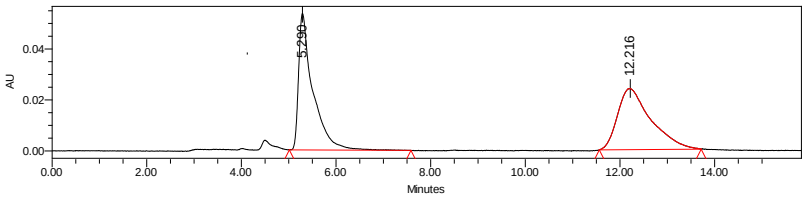
2	14.475	986864	2.50	25441	bb

4aj



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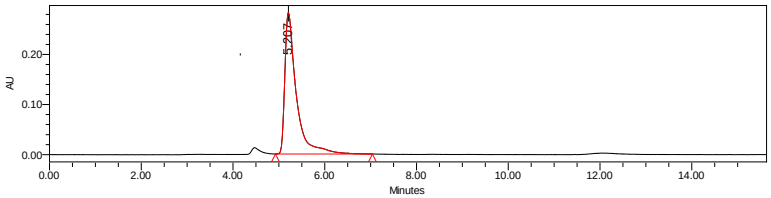

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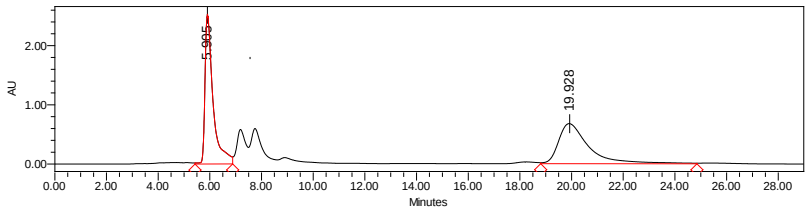
4ak



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1	5.905	54700365	49.52	2531550	VV
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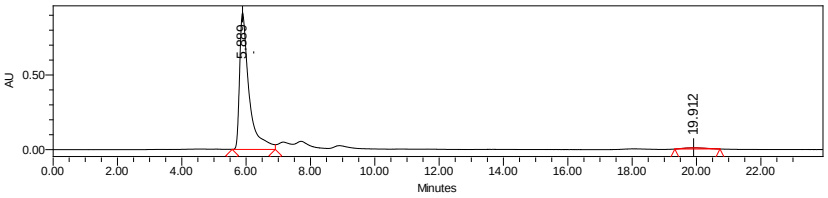

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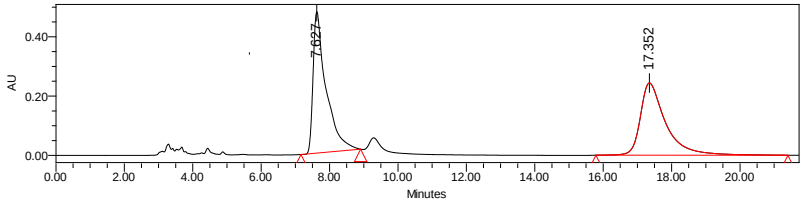
4al



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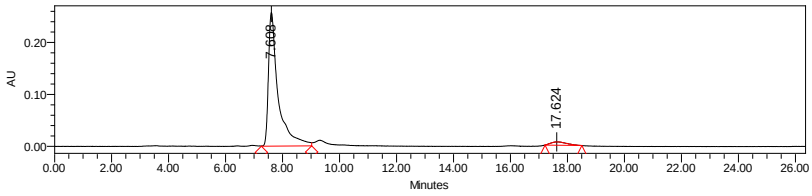
2	17.352	12533416	49.89	243895	bb



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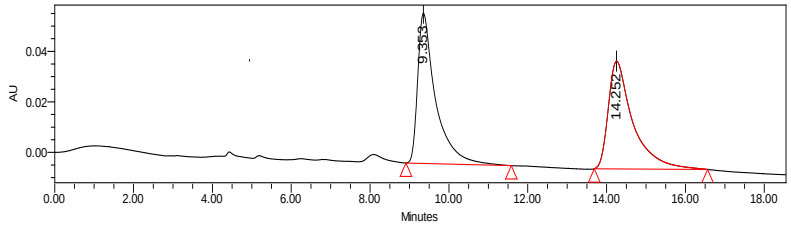

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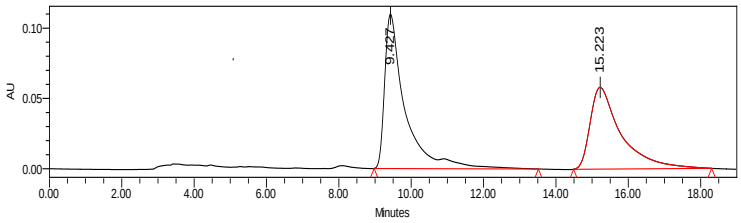

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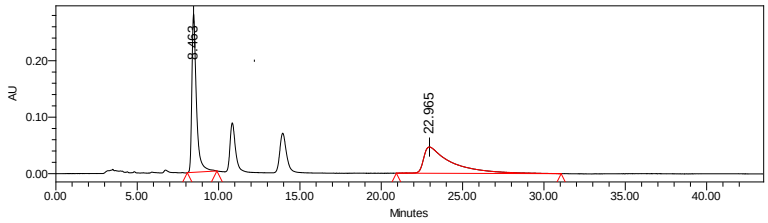
4ba



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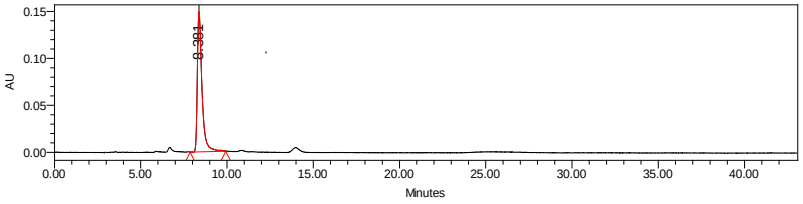

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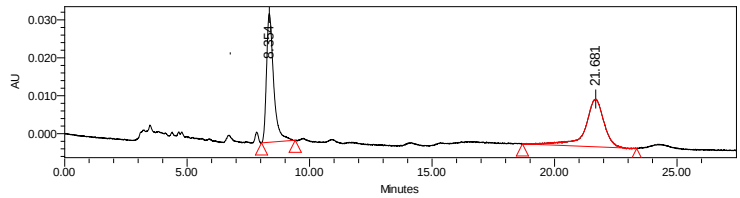

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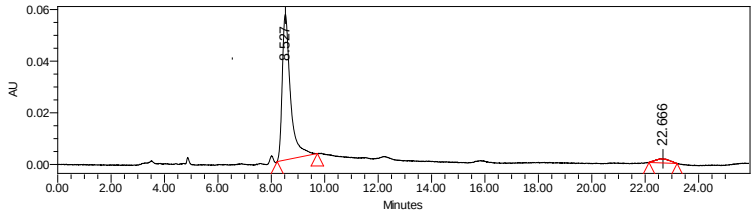

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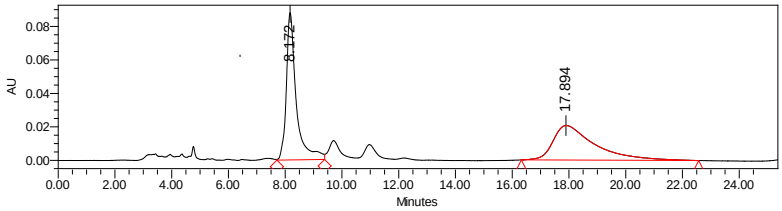

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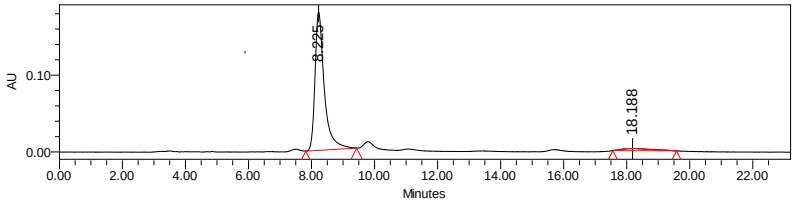

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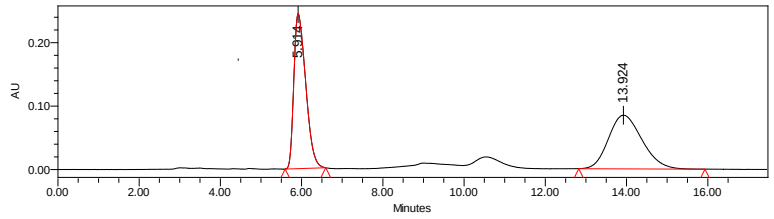

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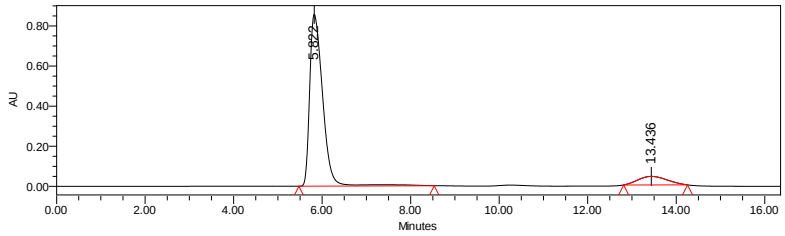
2	13.924	4837265	49.48	84523	Bb



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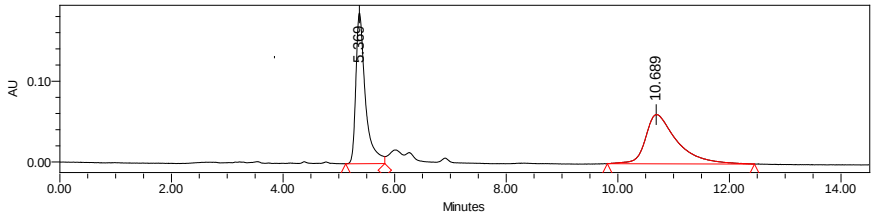
4ca



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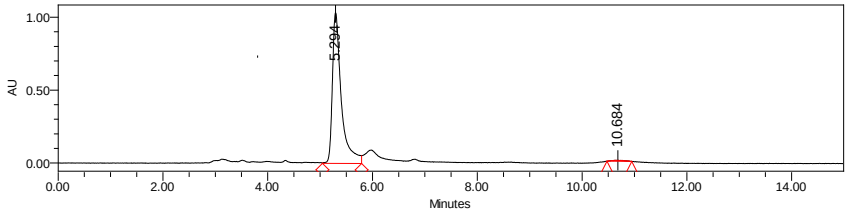

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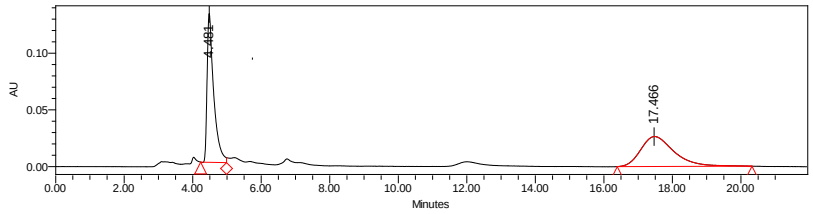
4da



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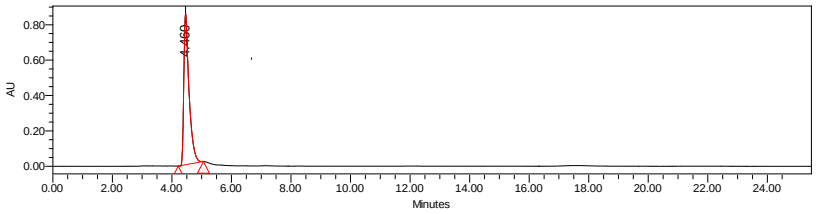
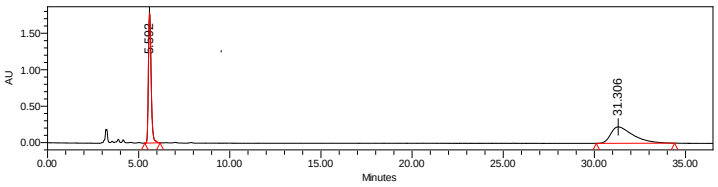
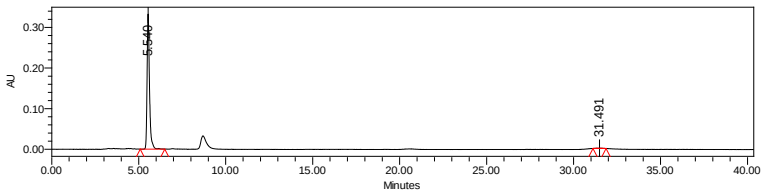


Entry	Retention Time	Area	% Area	Height	Int Type
1	4.460	10408309	100.00	853725	bb

5

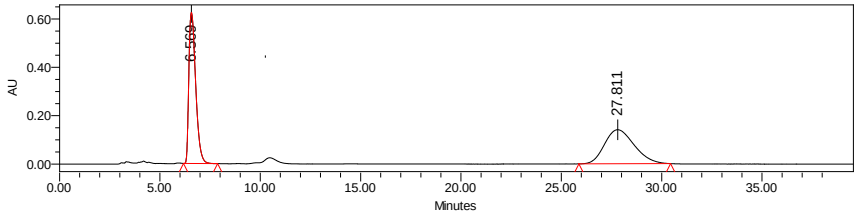


Entry	Retention Time	Area	% Area	Height	Int Type
1	5.592	18441484	49.11	1779989	bb
2	31.306	19113280	50.89	224890	bb

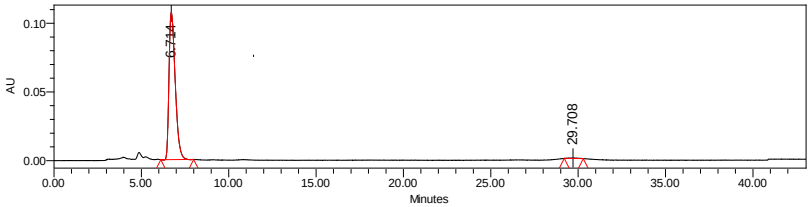


Entry	Retention Time	Area	% Area	Height	Int Type
1	5.540	3250198	99.51	332614	bb
2	31.491	15933	0.49	648	bb

6

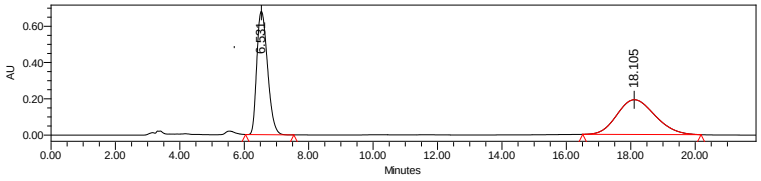


Entry	Retention Time	Area	% Area	Height	Int Type
1	6.569	14716811	50.37	624302	bb
2	27.811	14501673	49.63	140747	bb

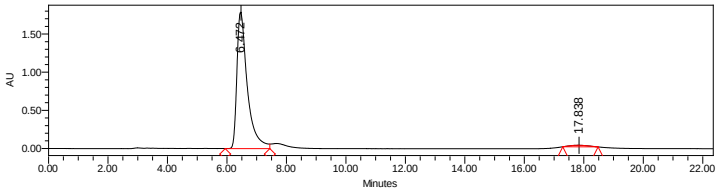


Entry	Retention Time	Area	% Area	Height	Int Type
1	6.714	2649096	99.50	107107	bb
2	29.708	13309	0.50	399	bb

7

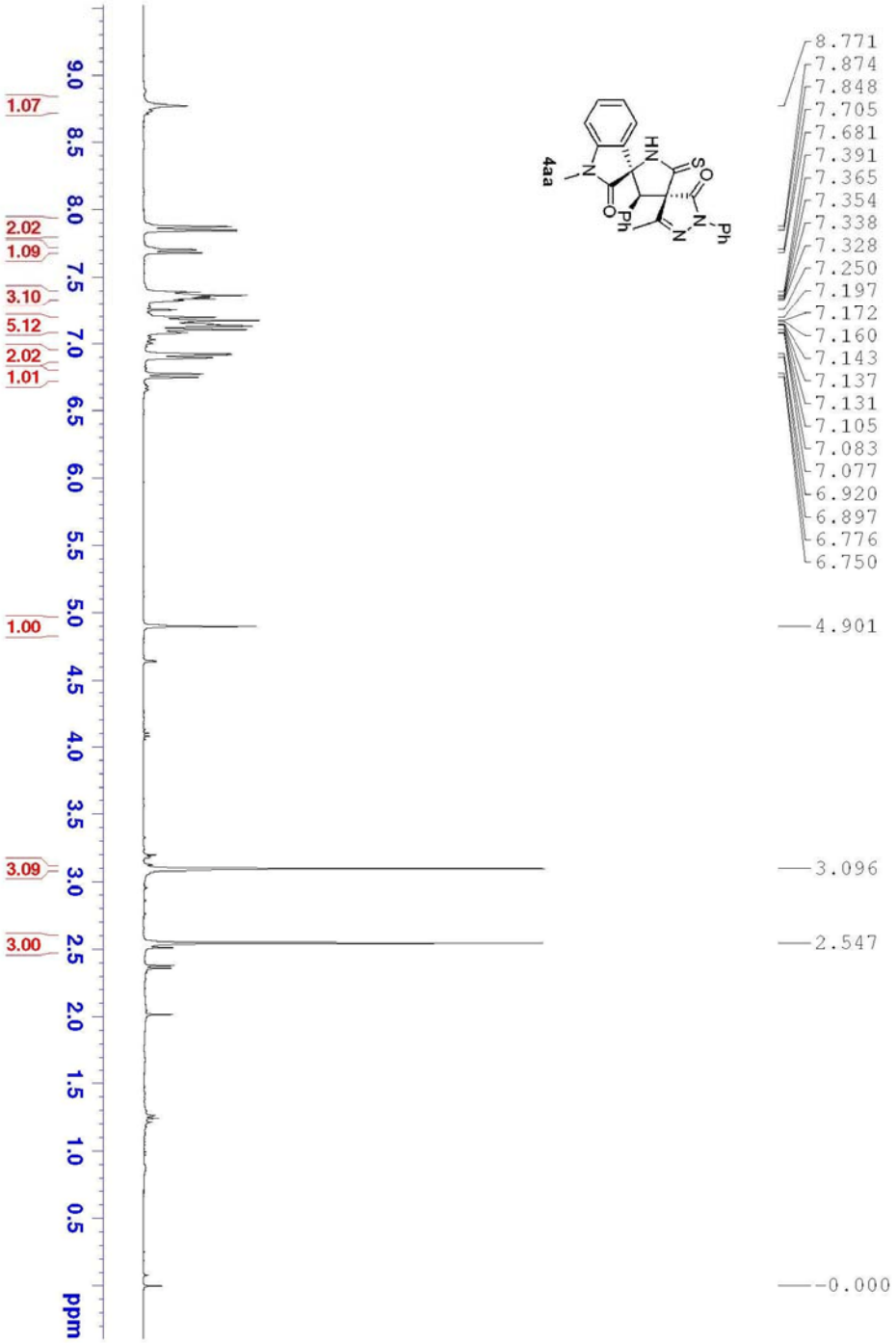


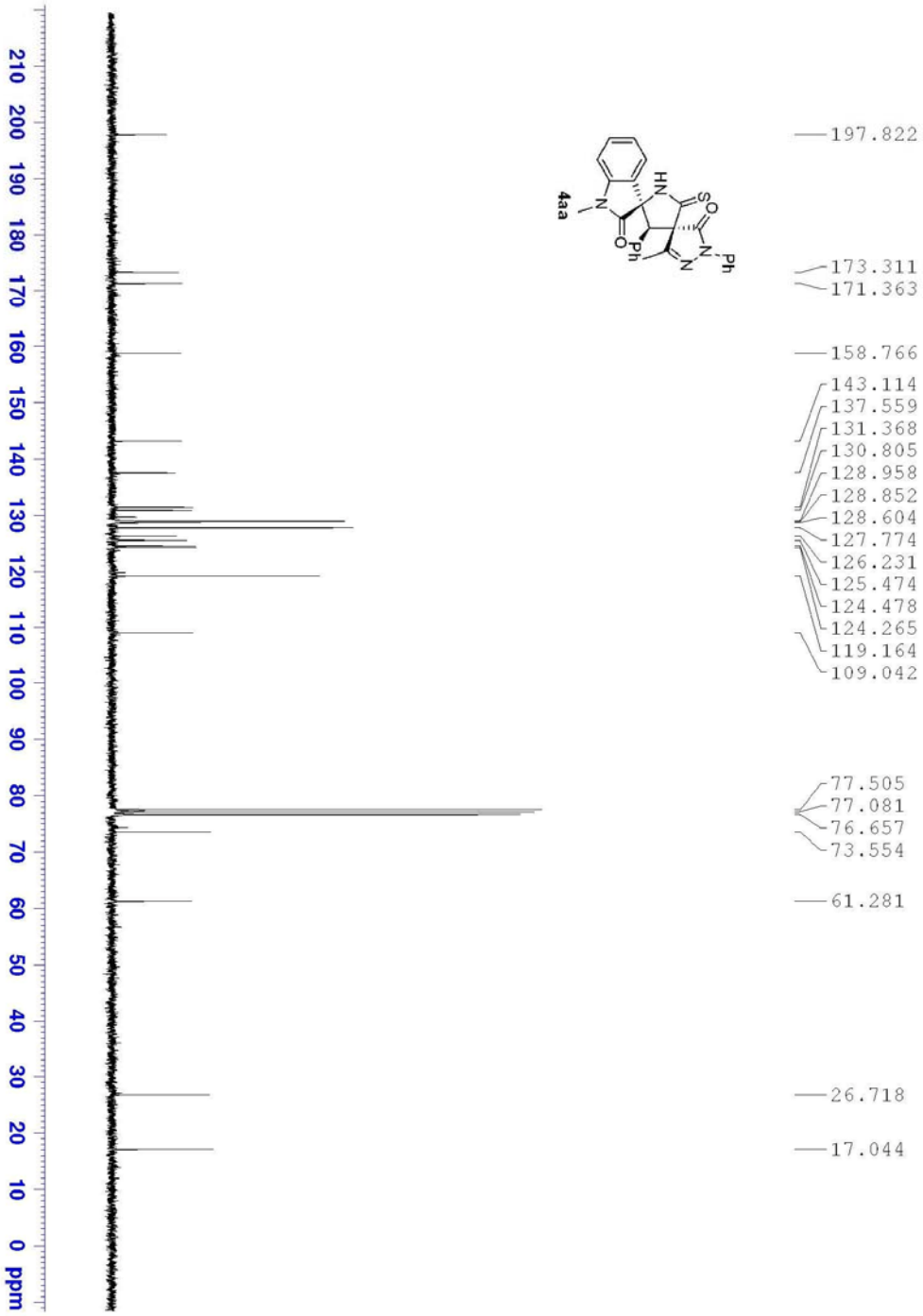
Entry	Retention Time	Area	% Area	Height	Int Type
1	6.531	15788456	50.03	679640	bb
2	18.105	15769095	49.97	191868	bb



Entry	Retention Time	Area	% Area	Height	Int Type
1	6.472	43570451	98.00	1789409	VV
2	17.838	890307	2.00	20350	bb

10.0 Copies of NMR Spectra of Products

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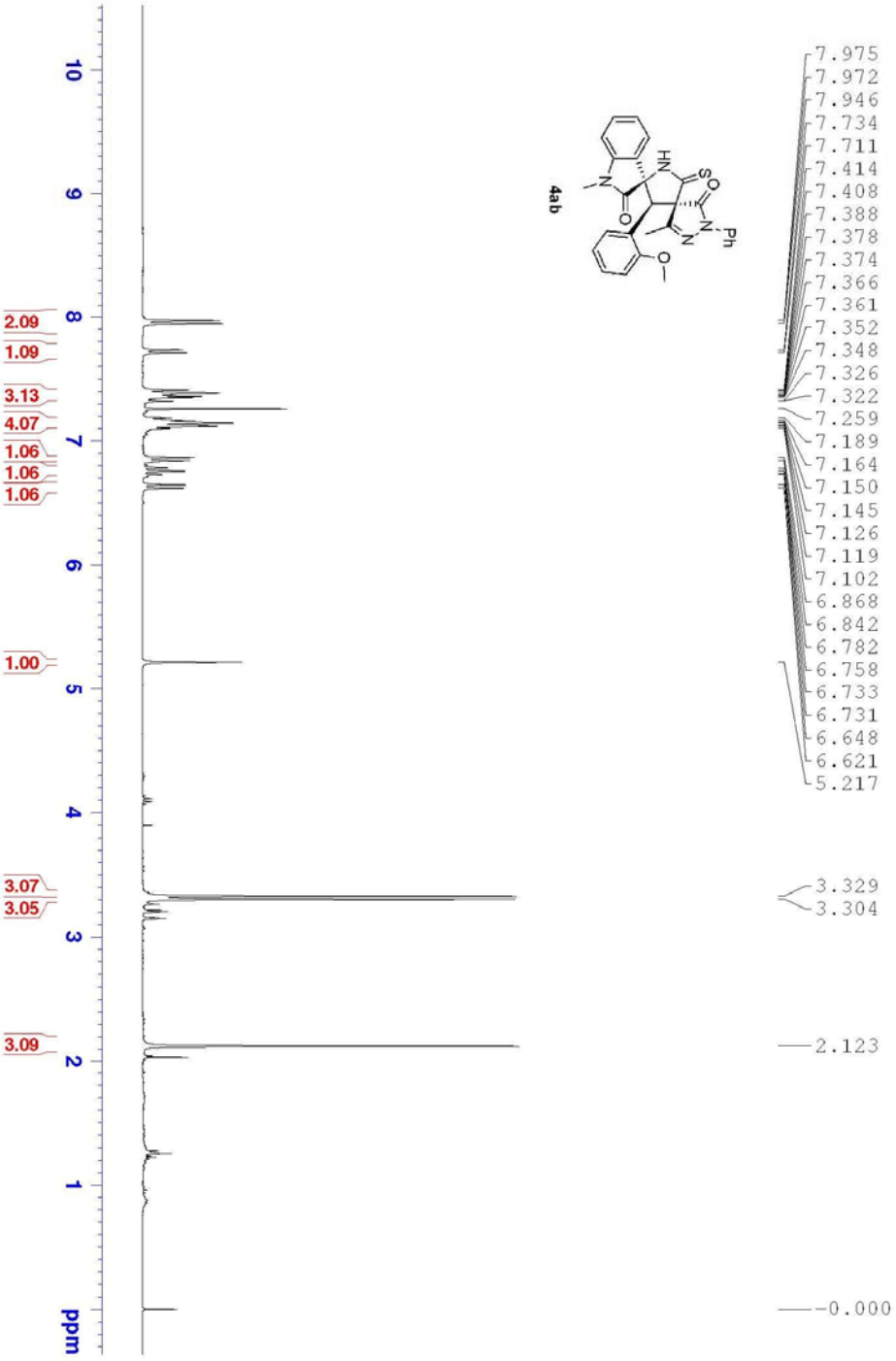
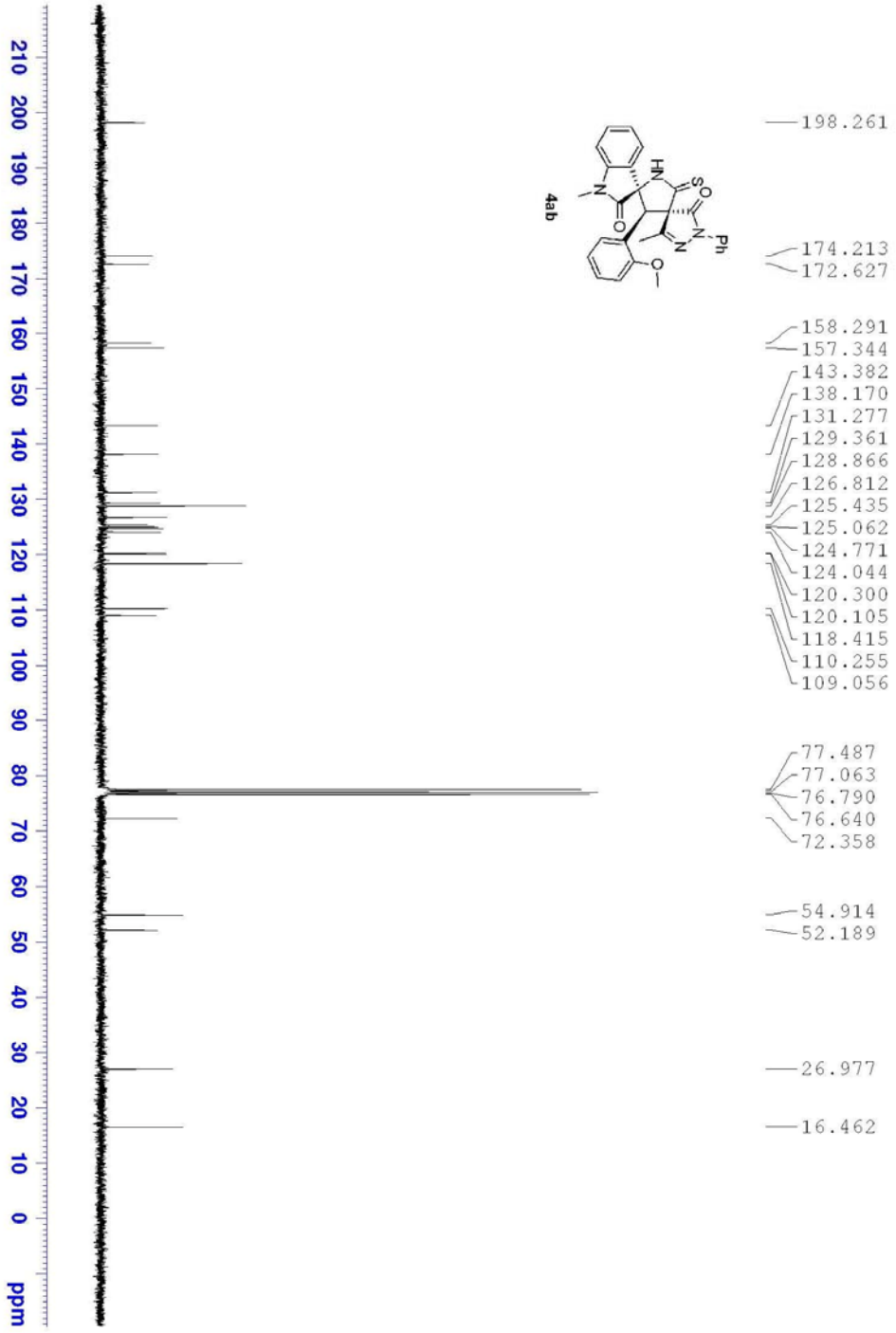
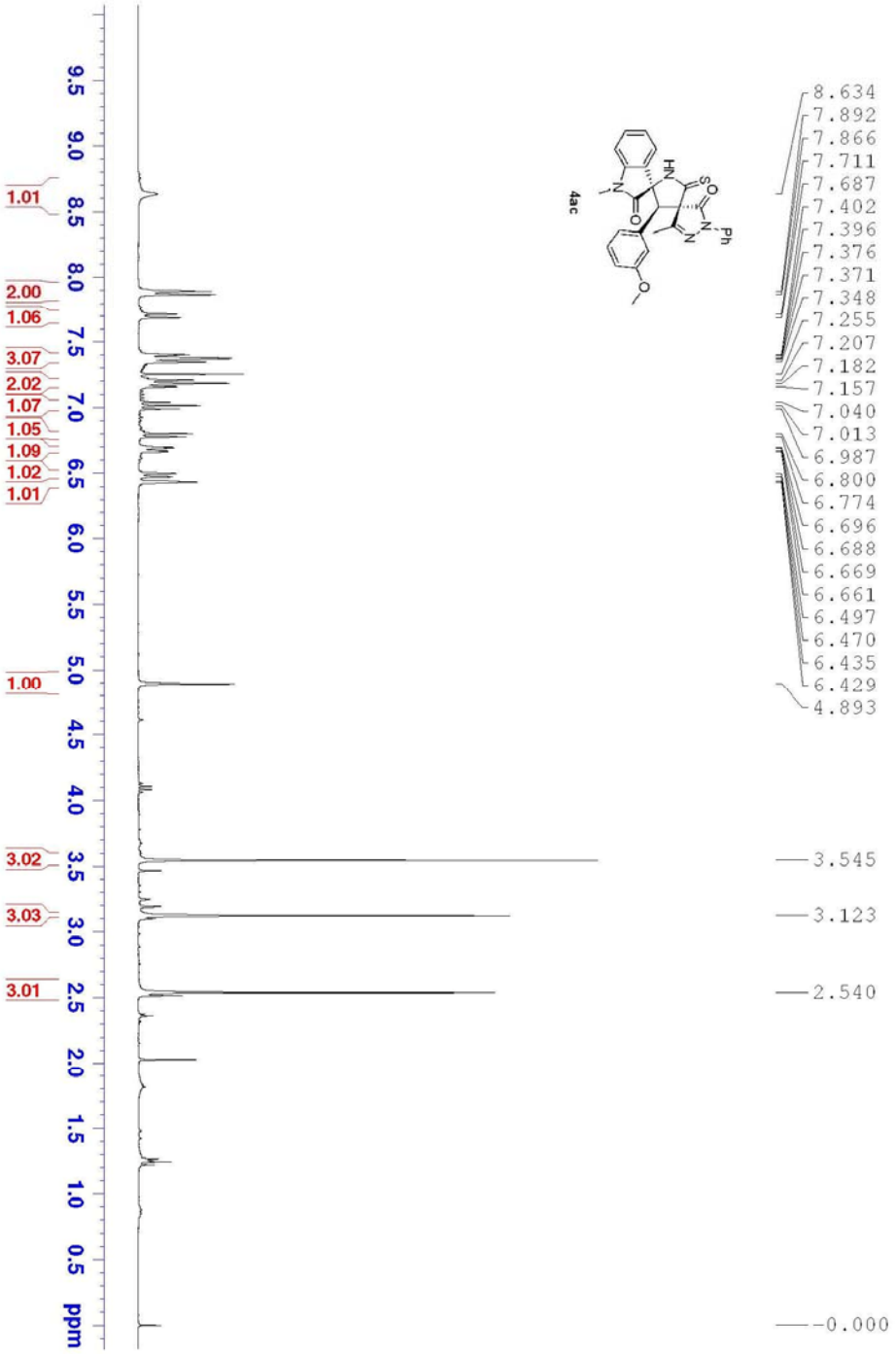
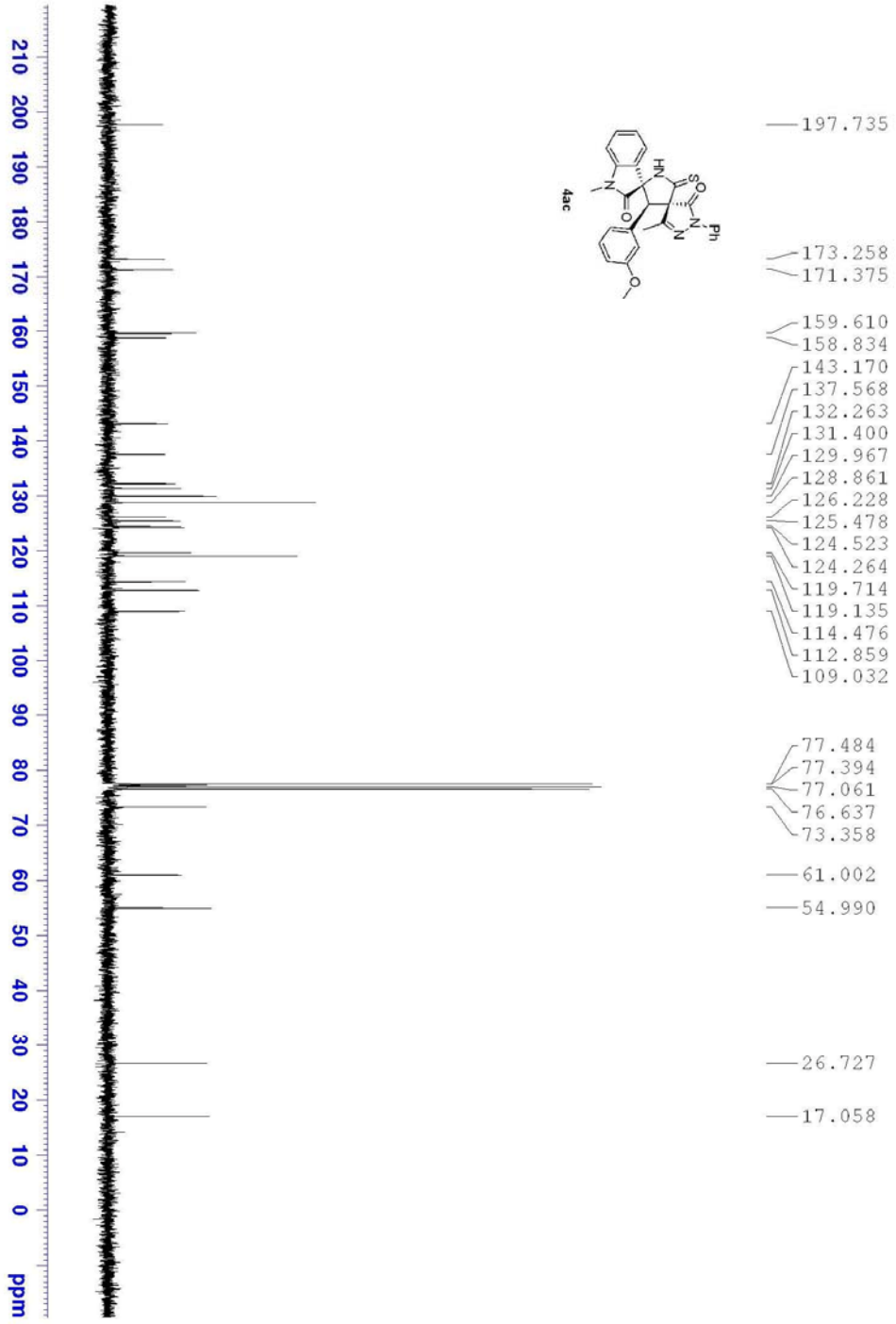
197.822
173.311
171.363
158.766
143.114
137.559
131.368
130.805
128.958
128.852
128.604
127.774
126.231
125.474
124.478
124.265
119.164
109.042
77.505
77.081
76.657
73.554
61.281
26.718
17.044
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4ab
Ph
7.975
7.972
7.946
7.734
7.711
7.414
7.408
7.388
7.378
7.374
7.366
7.361
7.352
7.348
7.326
7.322
7.259
7.189
7.164
7.150
7.145
7.126
7.119
7.102
6.868
6.842
6.782
6.758
6.733
6.731
6.648
6.621
5.217
3.329
3.304
2.123
0.000
2.09
1.09
3.13
4.07
1.06
1.06
1.06
1.00
3.07
3.05
3.09
ppm


4ab
198.261
174.213
172.627
158.291
157.344
143.382
138.170
131.277
129.361
128.866
126.812
125.435
125.062
124.771
124.044
120.300
120.105
118.415
110.255
109.056
77.487
77.063
76.790
76.640
72.358
54.914
52.189
26.977
16.462
ppm


4ac
8.634
7.892
7.866
7.711
7.687
7.402
7.396
7.376
7.371
7.348
7.255
7.207
7.182
7.157
7.040
7.013
6.987
6.800
6.774
6.696
6.688
6.669
6.661
6.497
6.470
6.435
6.429
4.893
3.545
3.123
2.540
0.000
1.01
2.00
1.06
3.07
2.02
1.07
1.05
1.09
1.02
1.01
1.00
3.02
3.03
3.01
ppm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173.258
171.375
159.610
158.834
143.170
137.568
132.263
131.400
129.967
128.861
126.228
125.478
124.523
124.264
119.714
119.135
114.476
112.859
109.032
77.484
77.394
77.061
76.637
73.358
61.002
54.990
26.727
17.058
4asc
HN
N
O
S
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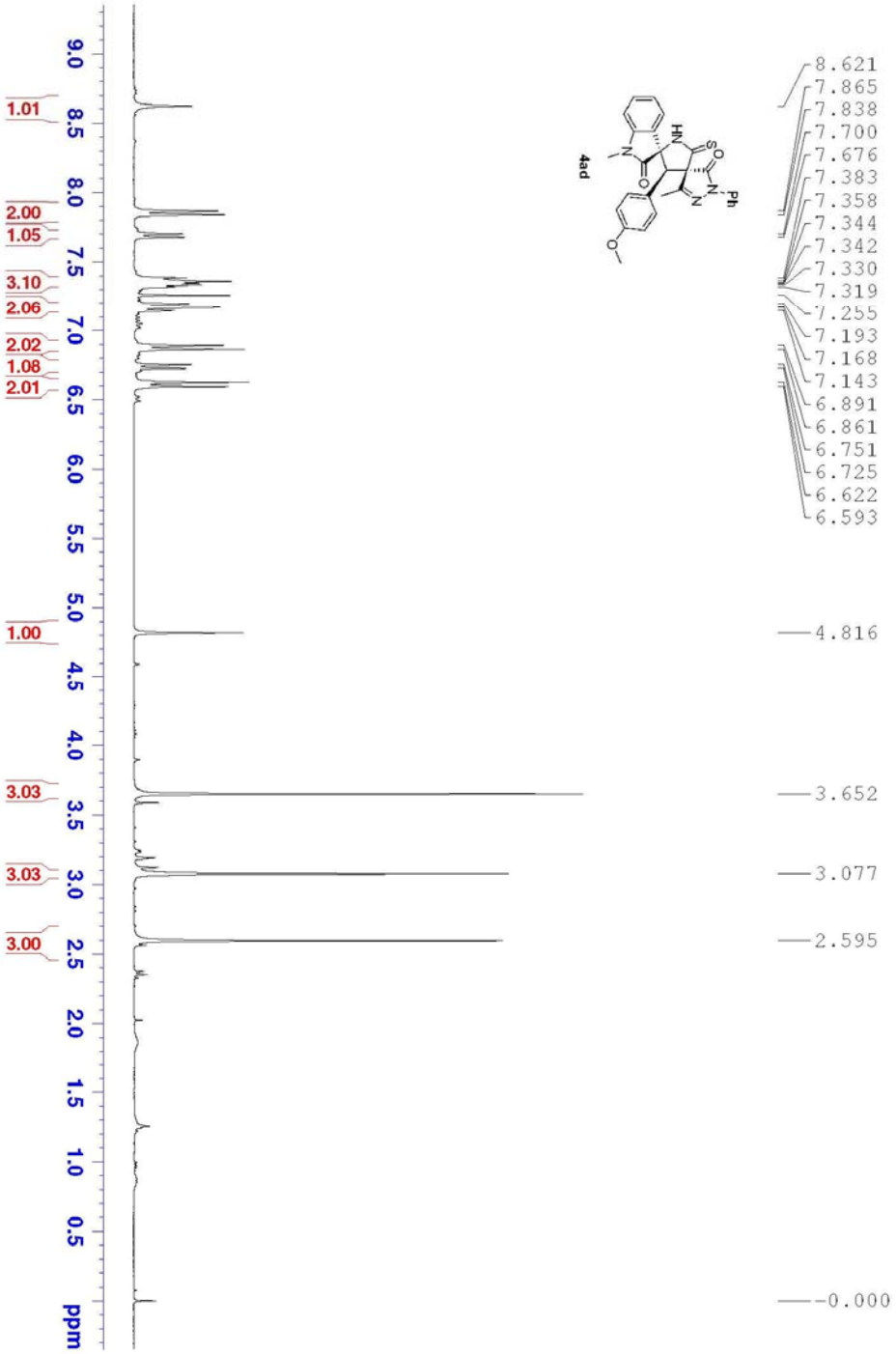
N
Ph
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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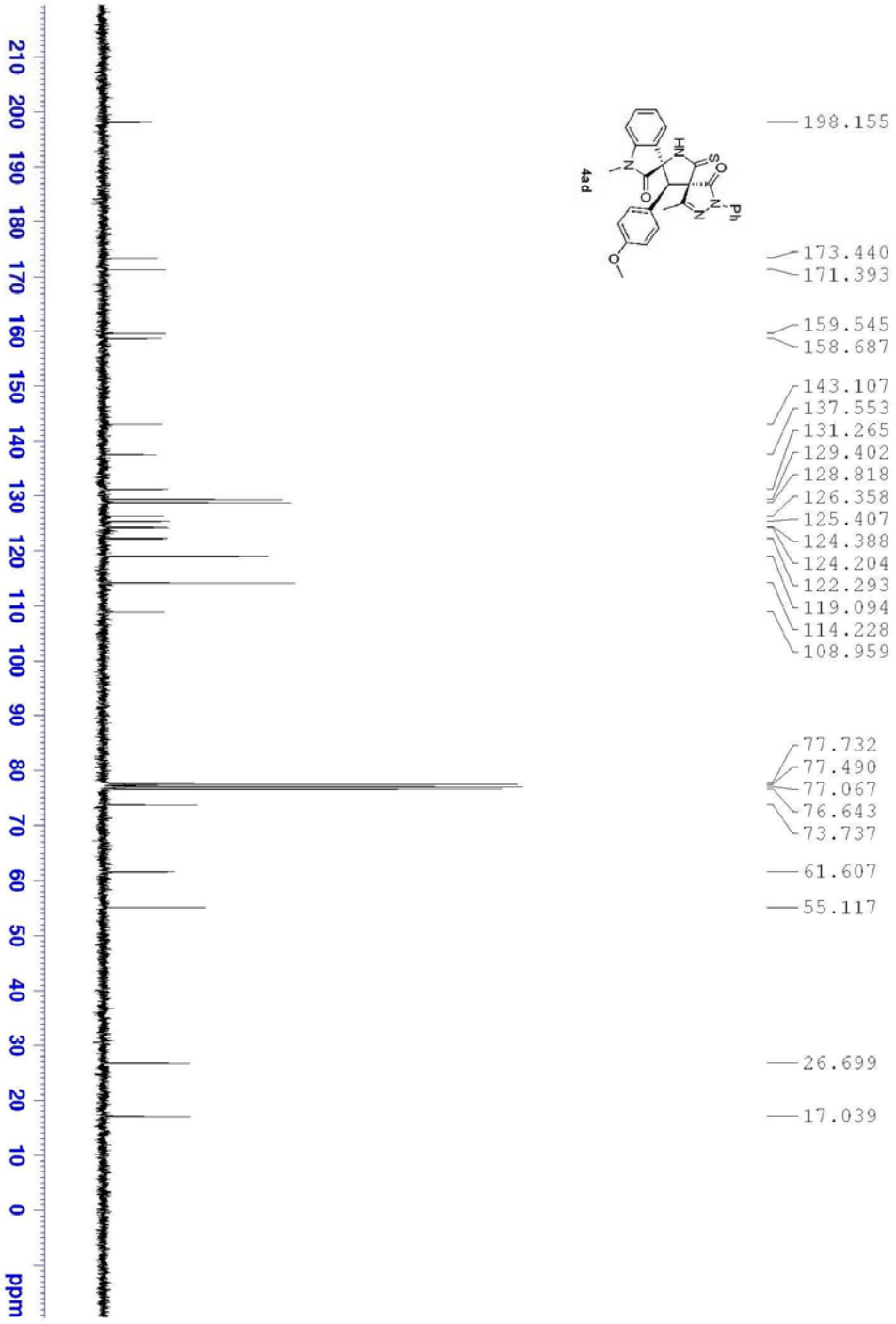
8.621
7.865
7.838
7.700
7.676
7.383
7.358
7.344
7.342
7.330
7.319
7.255
7.193
7.168
7.143
6.891
6.861
6.751
6.725
6.622
6.593
4.816
3.652
3.077
2.595
-0.000
1.01
2.00
1.05
3.10
2.06
2.02
1.08
2.01
1.00
3.03
3.03
3.00
ppm


4ad
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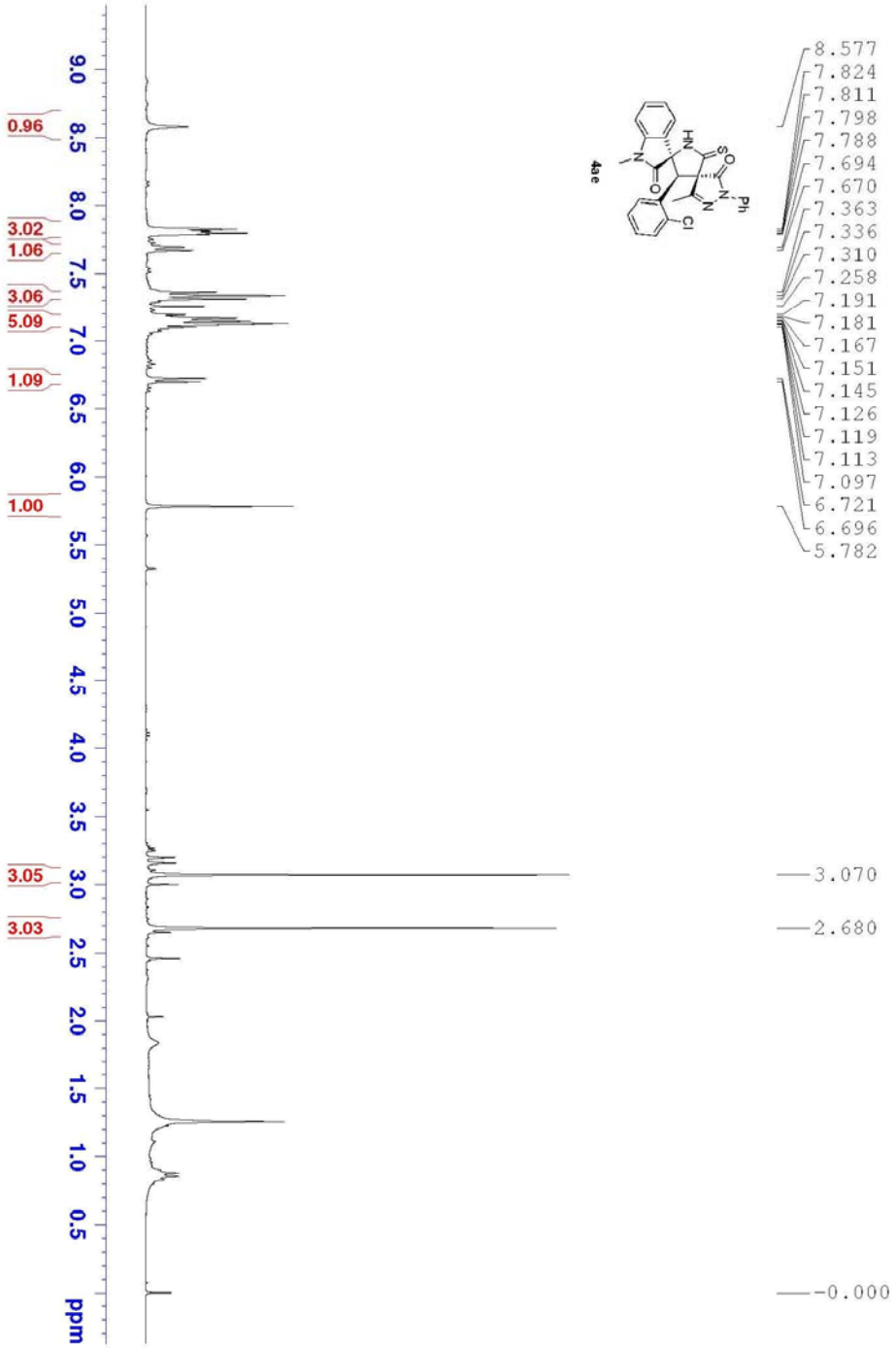
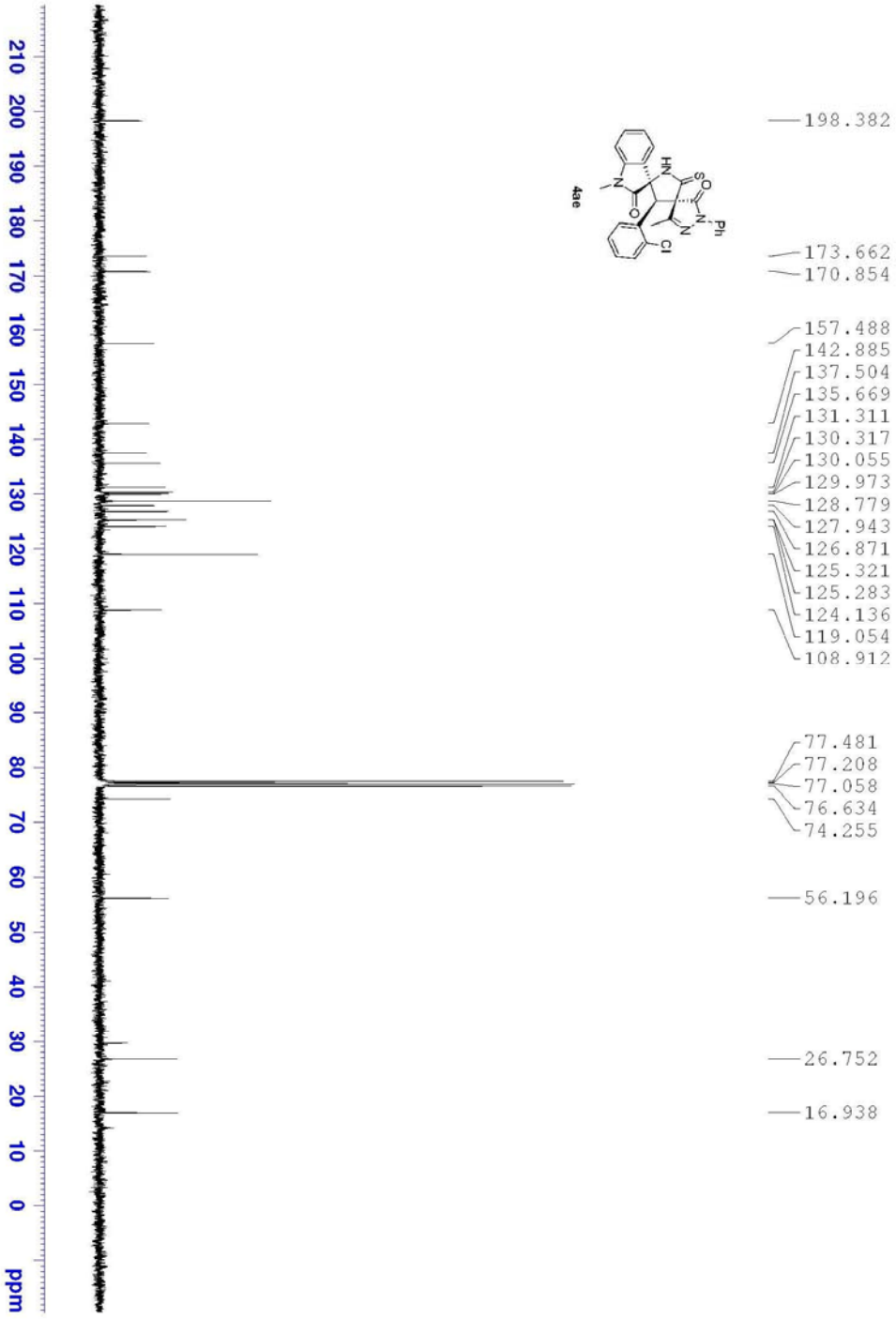
173.440
171.393
159.545
158.687
143.107
137.553
131.265
129.402
128.818
126.358
125.407
124.388
124.204
122.293
119.094
114.228
108.959
77.732
77.490
77.067
76.643
73.737
61.607
55.117
26.699
17.039
ppm


4ae
8.577
7.824
7.811
7.798
7.788
7.694
7.670
7.363
7.336
7.310
7.258
7.191
7.181
7.167
7.151
7.145
7.126
7.119
7.113
7.097
6.721
6.696
5.782
3.070
2.680
-0.000
0.96
3.02
1.06
3.06
5.09
1.09
1.00
3.05
3.03
ppm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135.669
131.311
130.317
130.055
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128.779
127.943
126.871
125.321
125.283
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74.255
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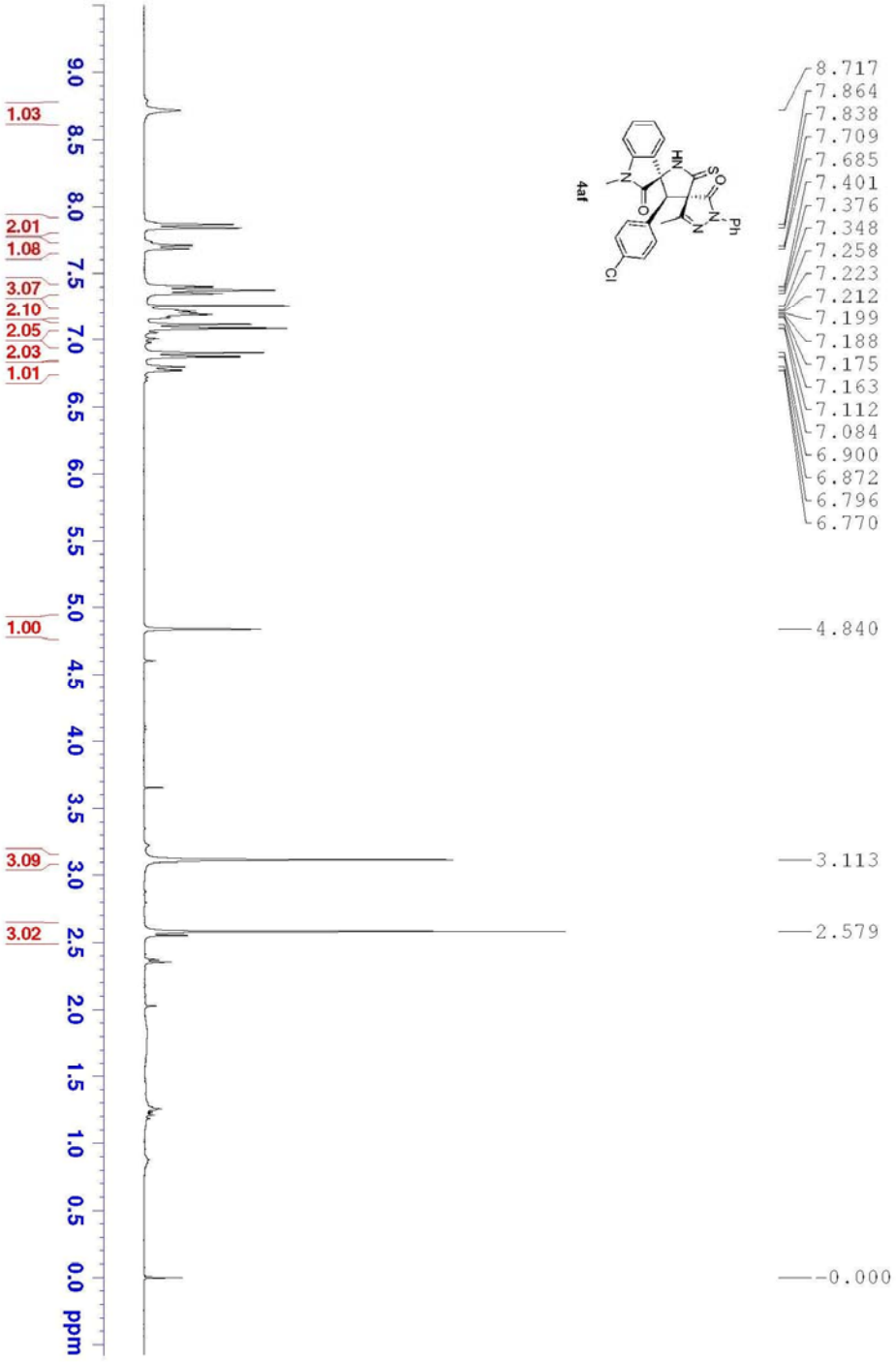
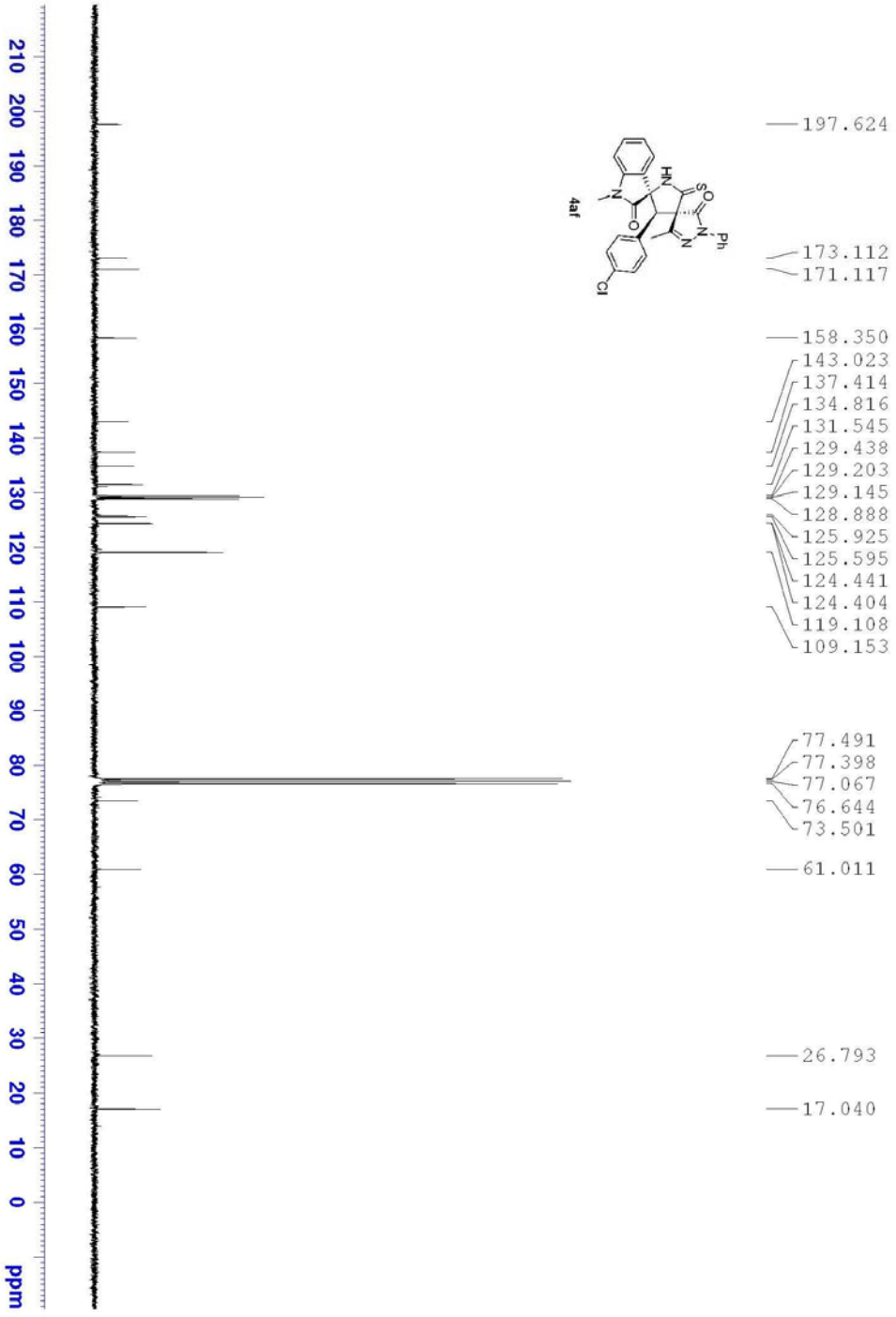
ppm


4af
8.717
7.864
7.838
7.709
7.685
7.401
7.376
7.348
7.258
7.223
7.212
7.199
7.188
7.175
7.163
7.112
7.084
6.900
6.872
6.796
6.770
4.840
3.113
2.579
0.000
1.03
2.01
1.08
3.07
2.10
2.05
2.03
1.01
1.00
3.09
3.02
ppm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131.545
129.438
129.203
129.145
128.888
125.925
125.595
124.441
124.404
119.108
109.153
77.491
77.398
77.067
76.644
73.501
61.011
26.793
17.040
4af
HN
N
O
S
O
N
Ph
Cl
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
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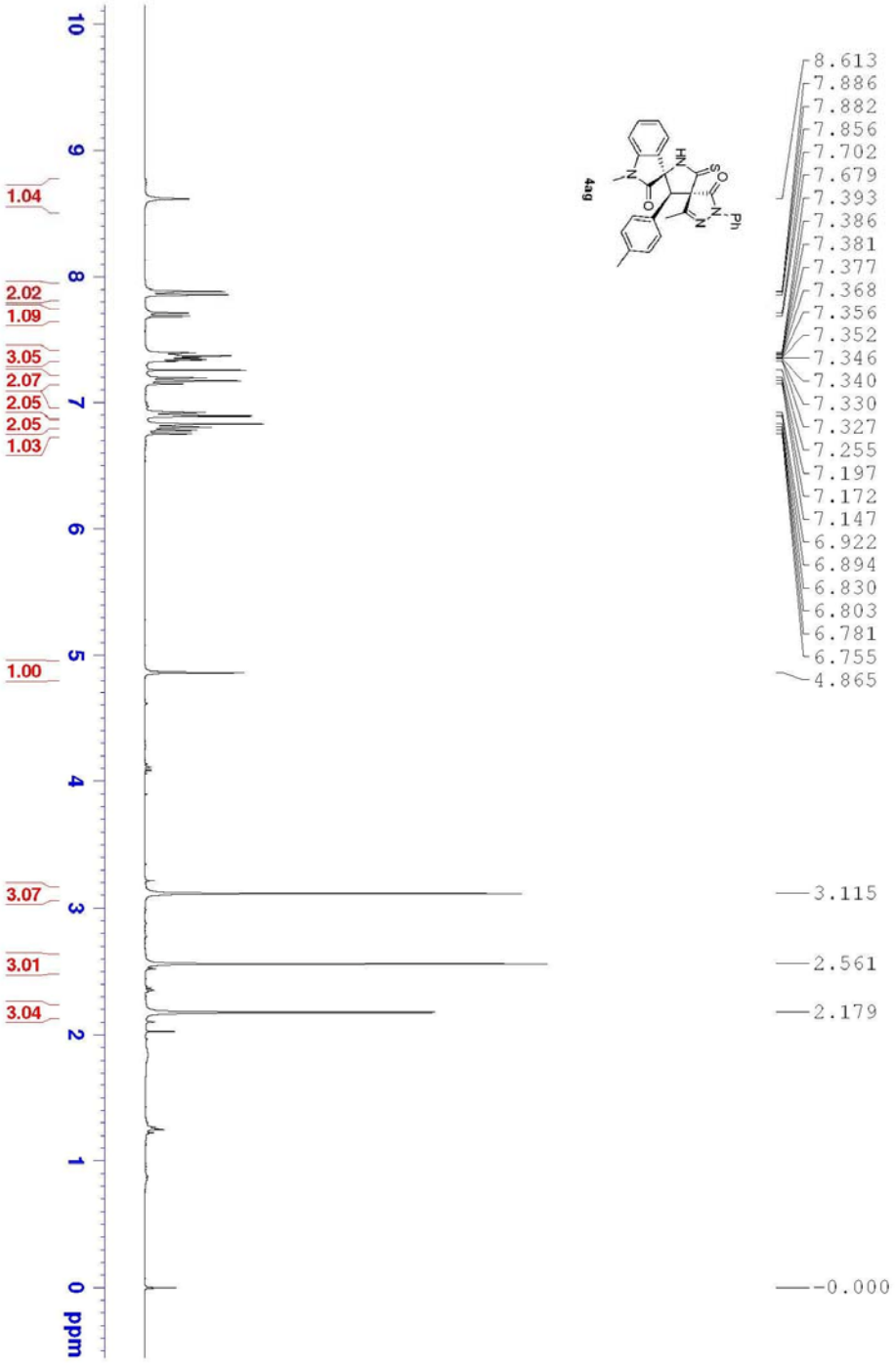
30
20
10
0
ppm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7.856
7.702
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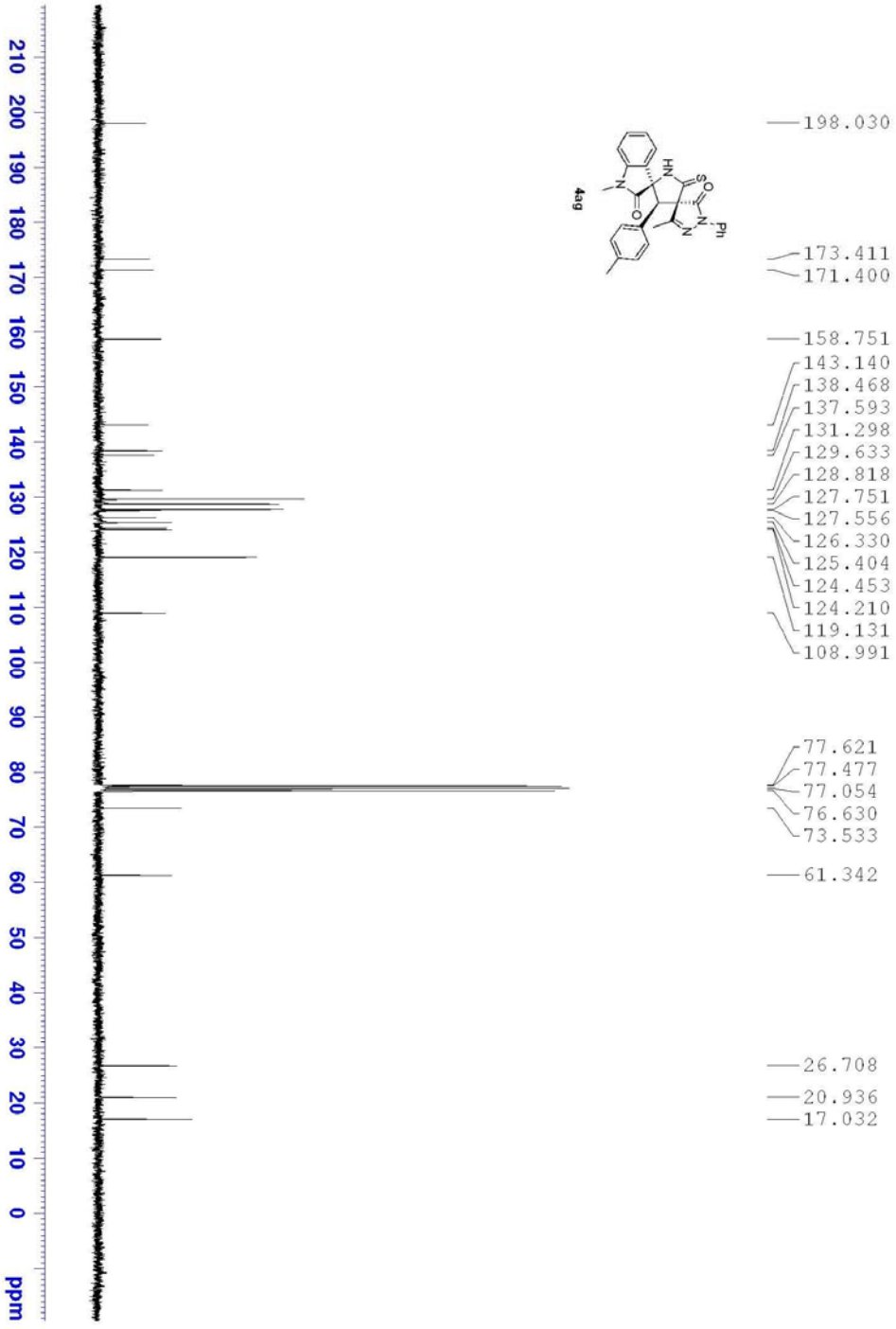
7.393
7.386
7.381
7.377
7.368
7.356
7.352
7.346
7.340
7.330
7.327
7.255
7.197
7.172
7.147
6.922
6.894
6.830
6.803
6.781
6.755
4.865
3.115
2.561
2.179
-0.000
1.04
2.02
1.09
3.05
2.07
2.05
2.05
1.03
1.00
3.07
3.01
3.04
ppm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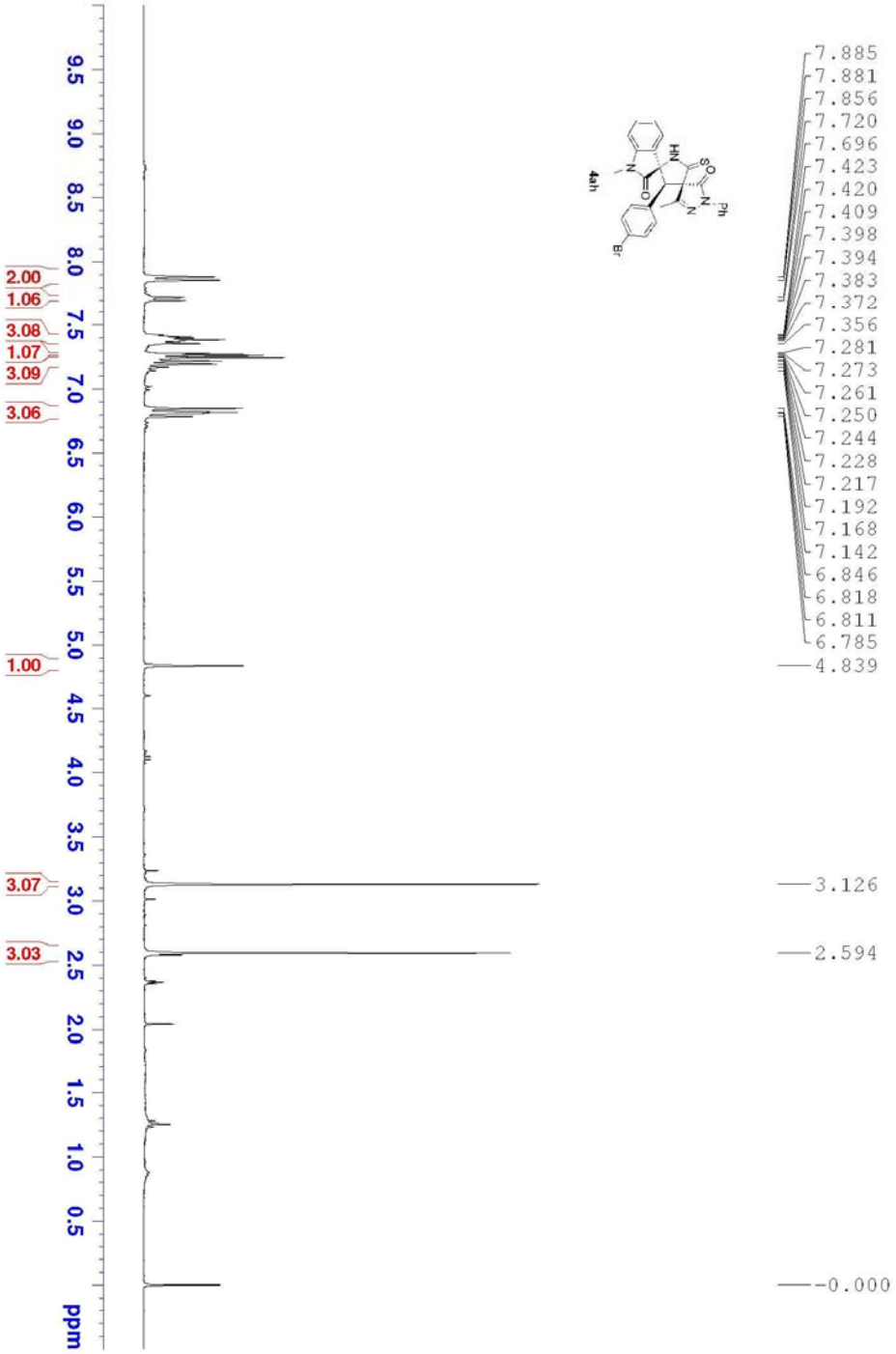
143.140
138.468
137.593
131.298
129.633
128.818
127.751
127.556
126.330
125.404
124.453
124.210
119.131
108.991
77.621
77.477
77.054
76.630
73.533
61.342
26.708
20.936
17.032
4ag
HN
O
S
N
N
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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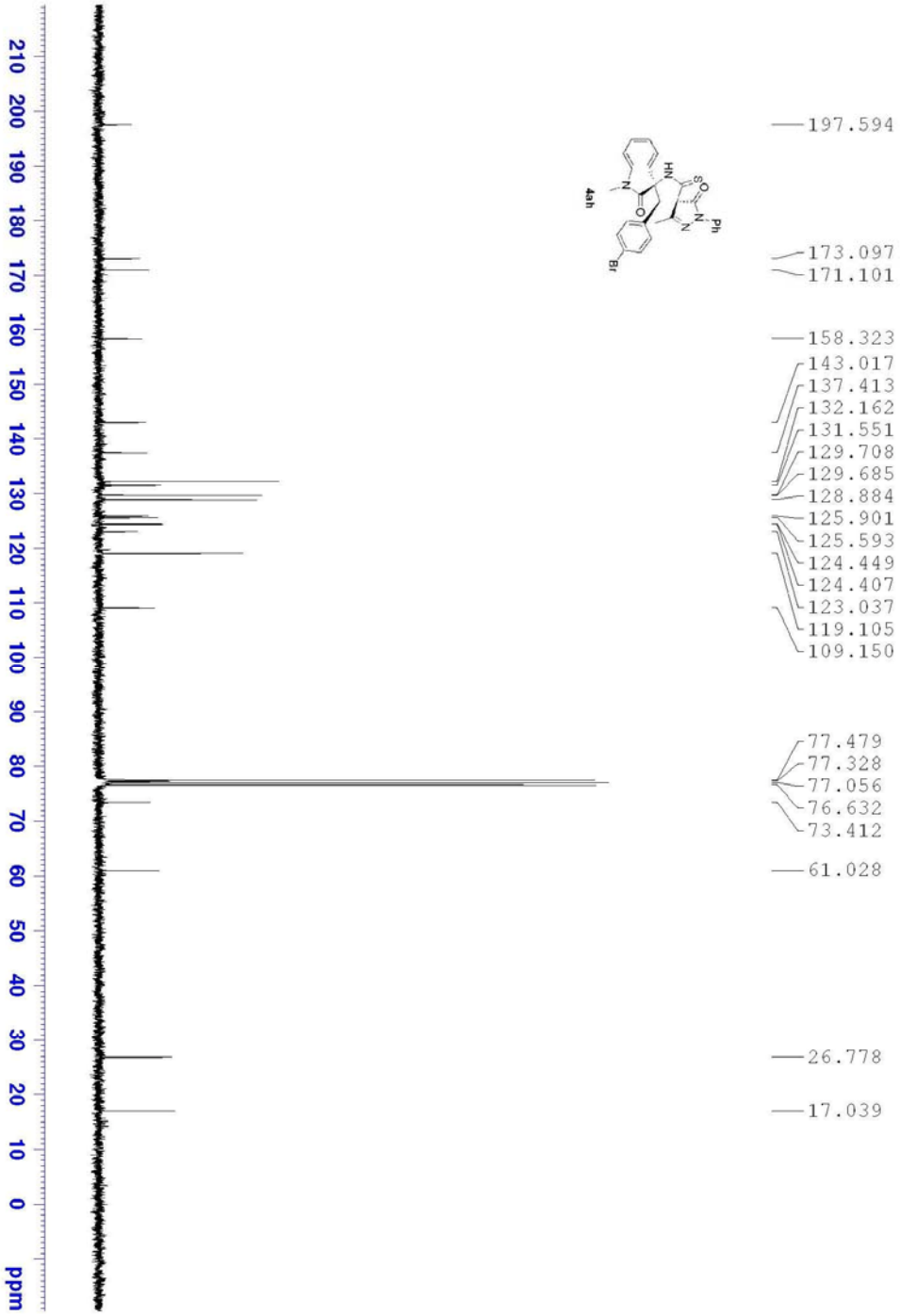
7.881
7.856
7.720
7.696
7.423
7.420
7.409
7.398
7.394
7.383
7.372
7.356
7.281
7.273
7.261
7.250
7.244
7.228
7.217
7.192
7.168
7.142
6.846
6.818
6.811
6.785
4.839
3.126
2.594
-0.000
2.00
1.06
3.08
1.07
3.09
3.06
1.00
3.07
3.03
ppm
4ah
HN
N
O
S
N
Ph
Br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158.323
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137.413
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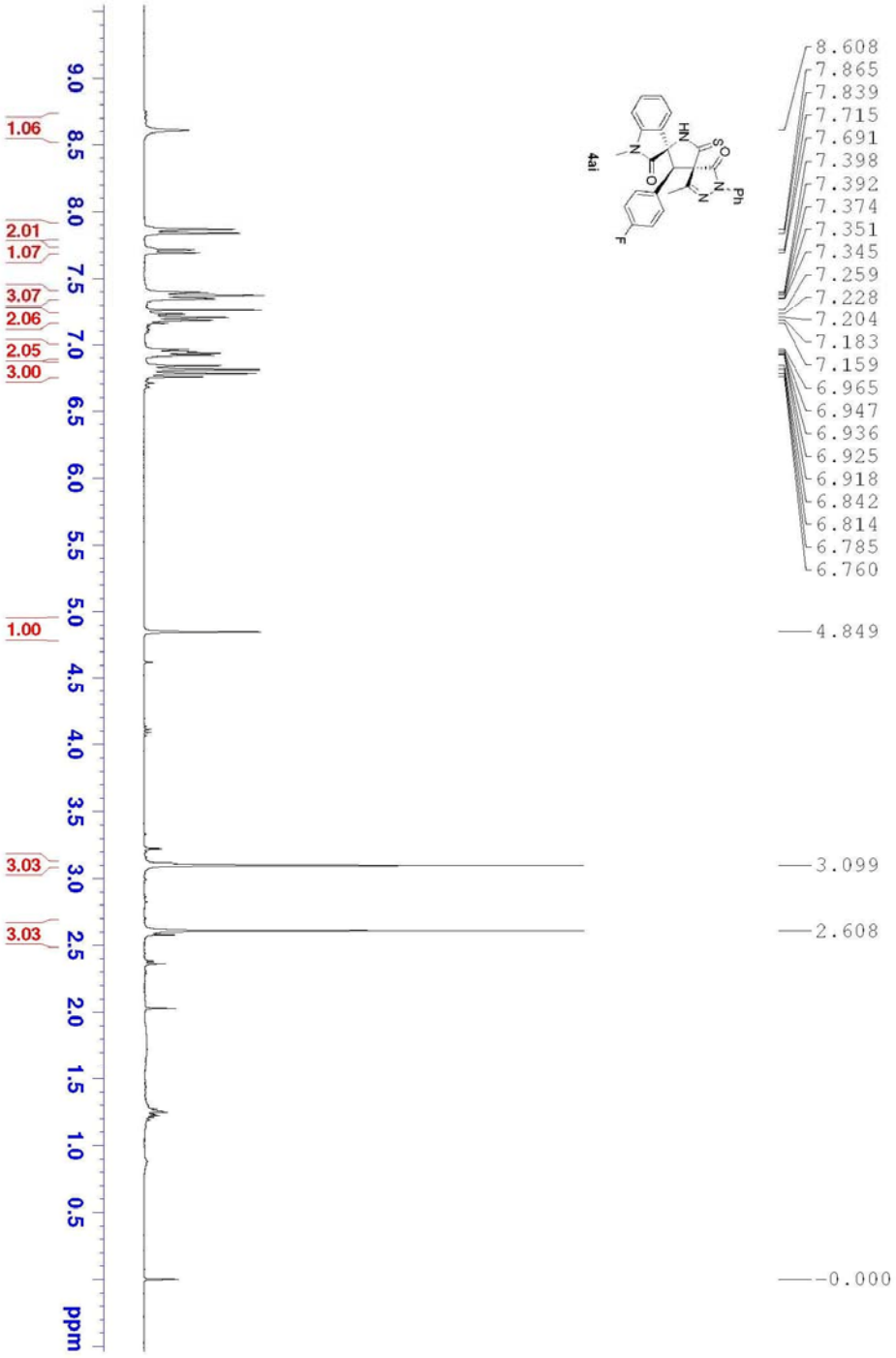
131.551
129.708
129.685
128.884
125.901
125.593
124.449
124.407
123.037
119.105
109.150
77.479
77.328
77.056
76.632
73.412
61.028
26.778
17.039
ppm
4ah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7.392
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7.345
7.259
7.228
7.204
7.183
7.159
6.965
6.947
6.936
6.925
6.918
6.842
6.814
6.785
6.760
4.849
3.099
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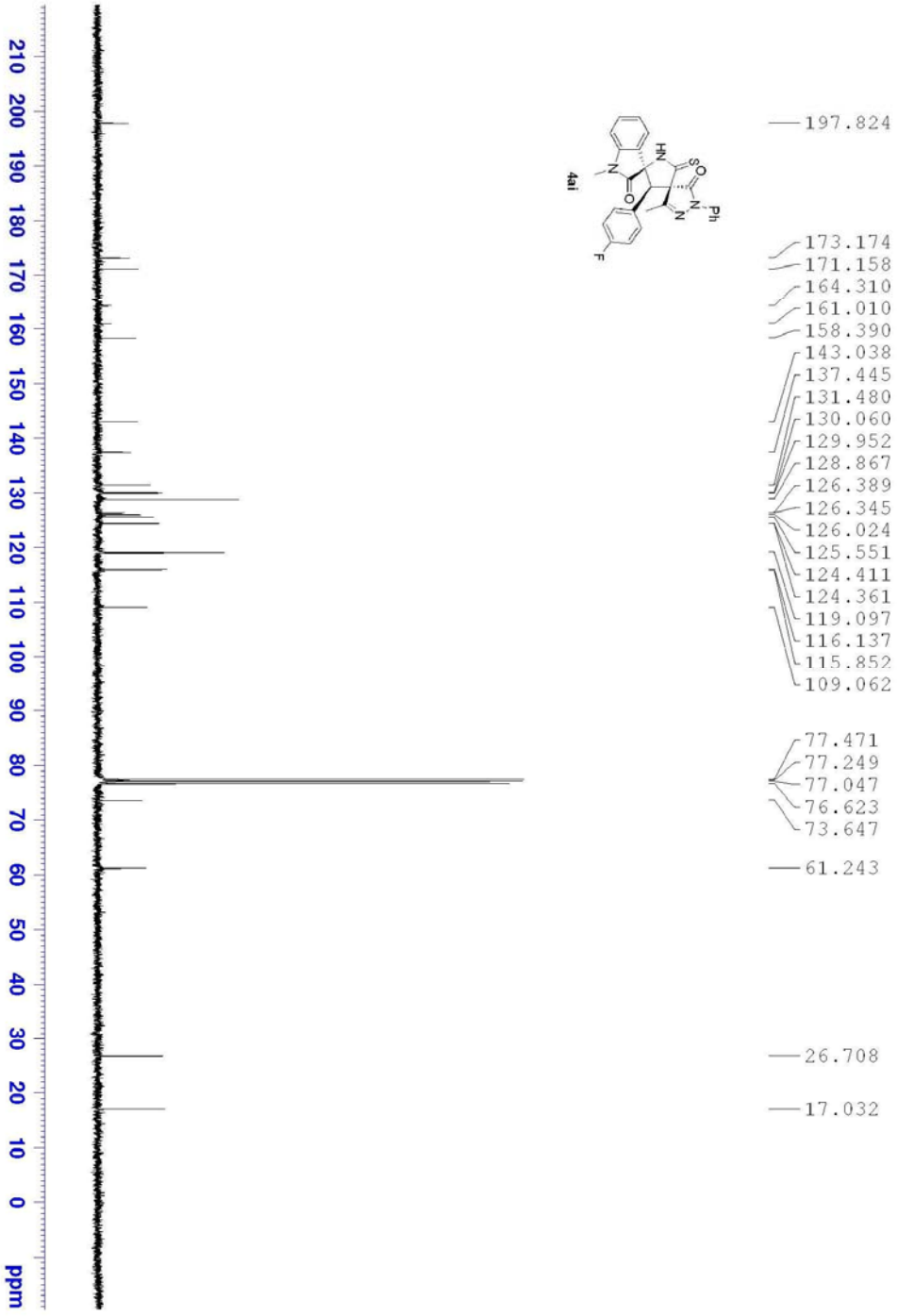
2.01
1.07
3.07
2.06
2.05
3.00
1.00
3.03
3.03
ppm


4al
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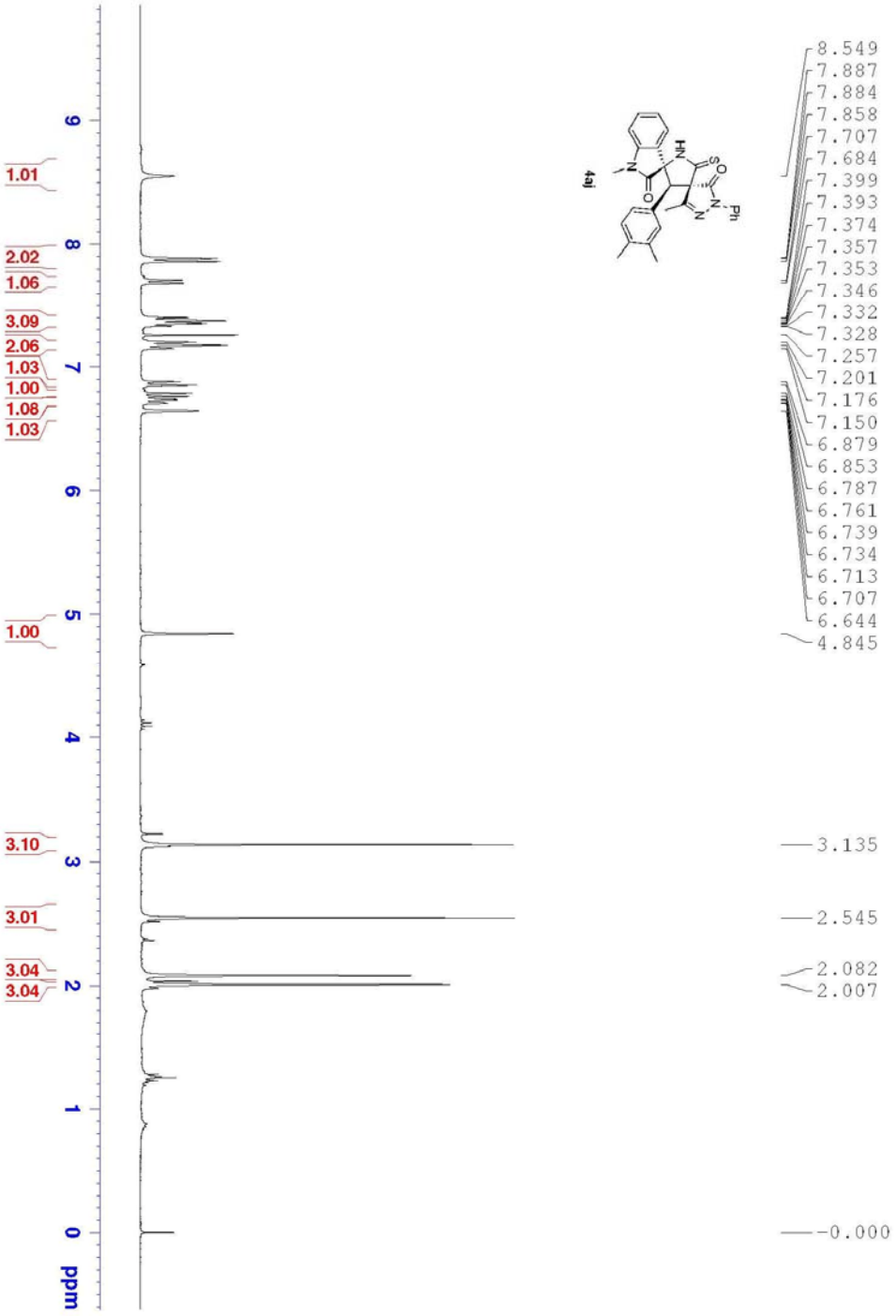
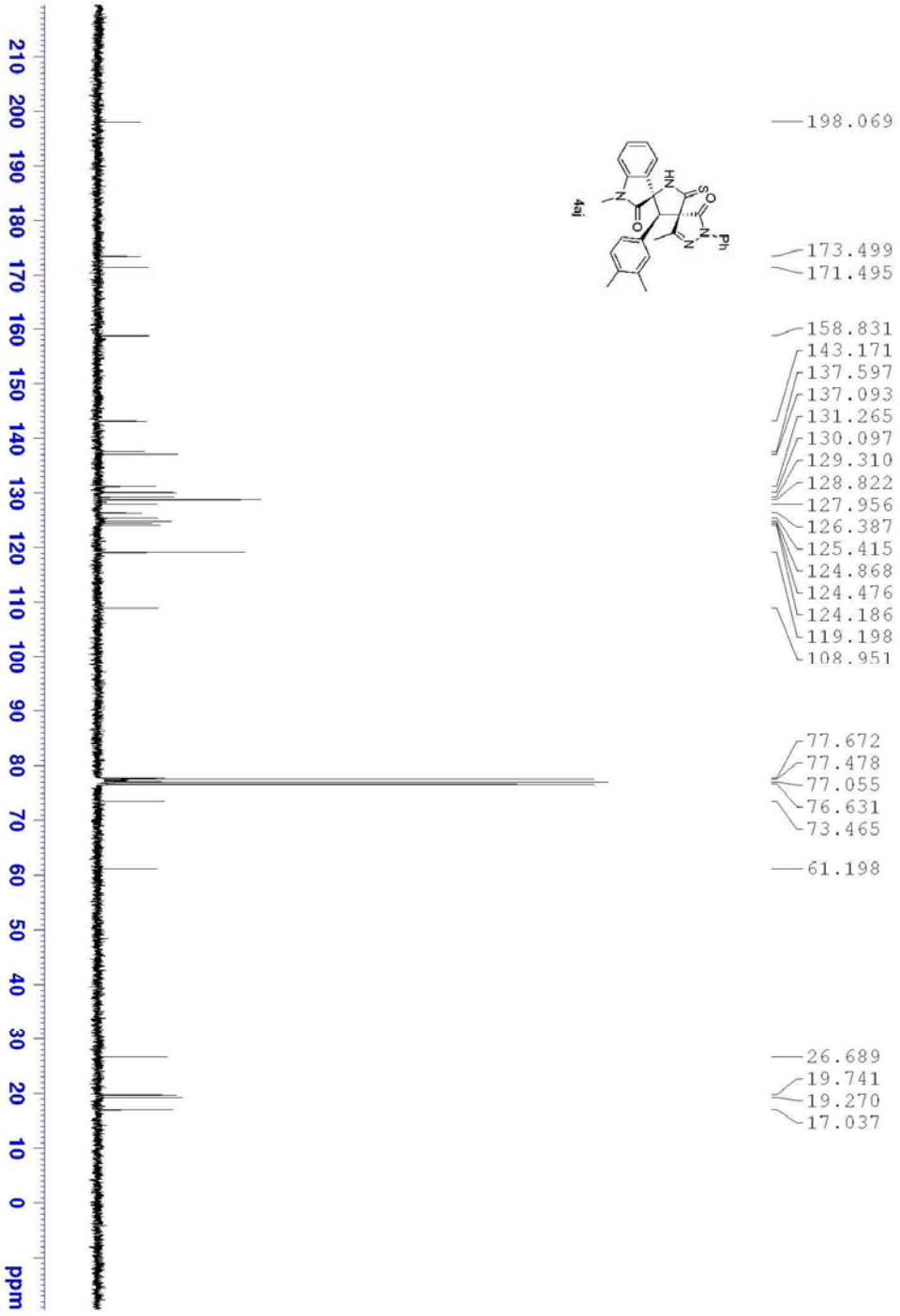
129.952
128.867
126.389
126.345
126.024
125.551
124.411
124.361
119.097
116.137
115.852
109.062
77.471
77.249
77.047
76.623
73.647
61.243
26.708
17.032
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

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137.093
131.265
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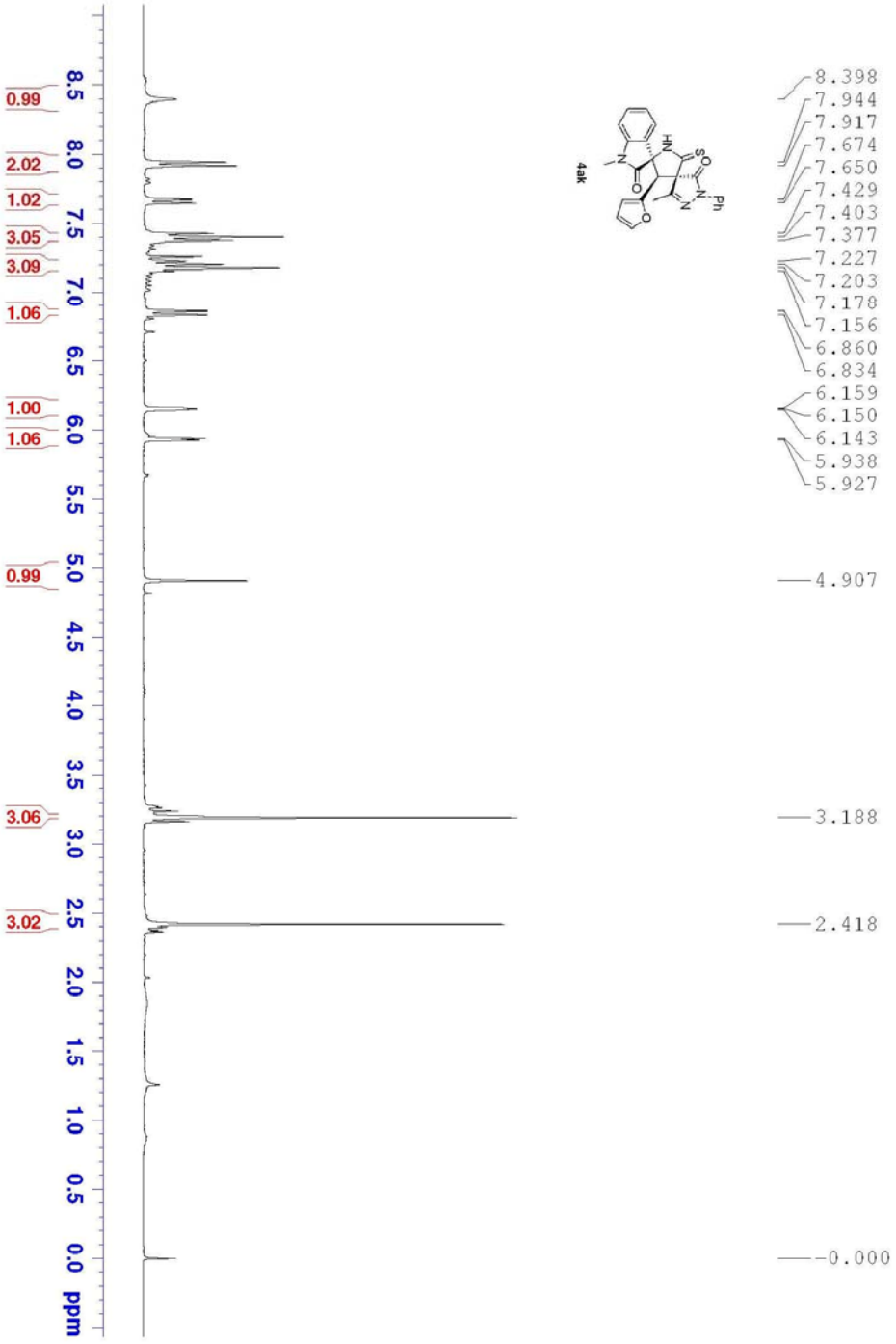
126.387
125.415
124.868
124.476
124.186
119.198
108.951
77.672
77.478
77.055
76.631
73.465
61.198
26.689
19.741
19.270
17.037
4aj
HN
O
N
O
N
N
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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2.02
1.02
3.05
3.09
1.06
1.00
1.06
0.99
3.06
3.02
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
ppm
4ak
8.398
7.944
7.917
7.674
7.650
7.429
7.403
7.377
7.227
7.203
7.178
7.156
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6.834
6.159
6.150
6.143
5.938
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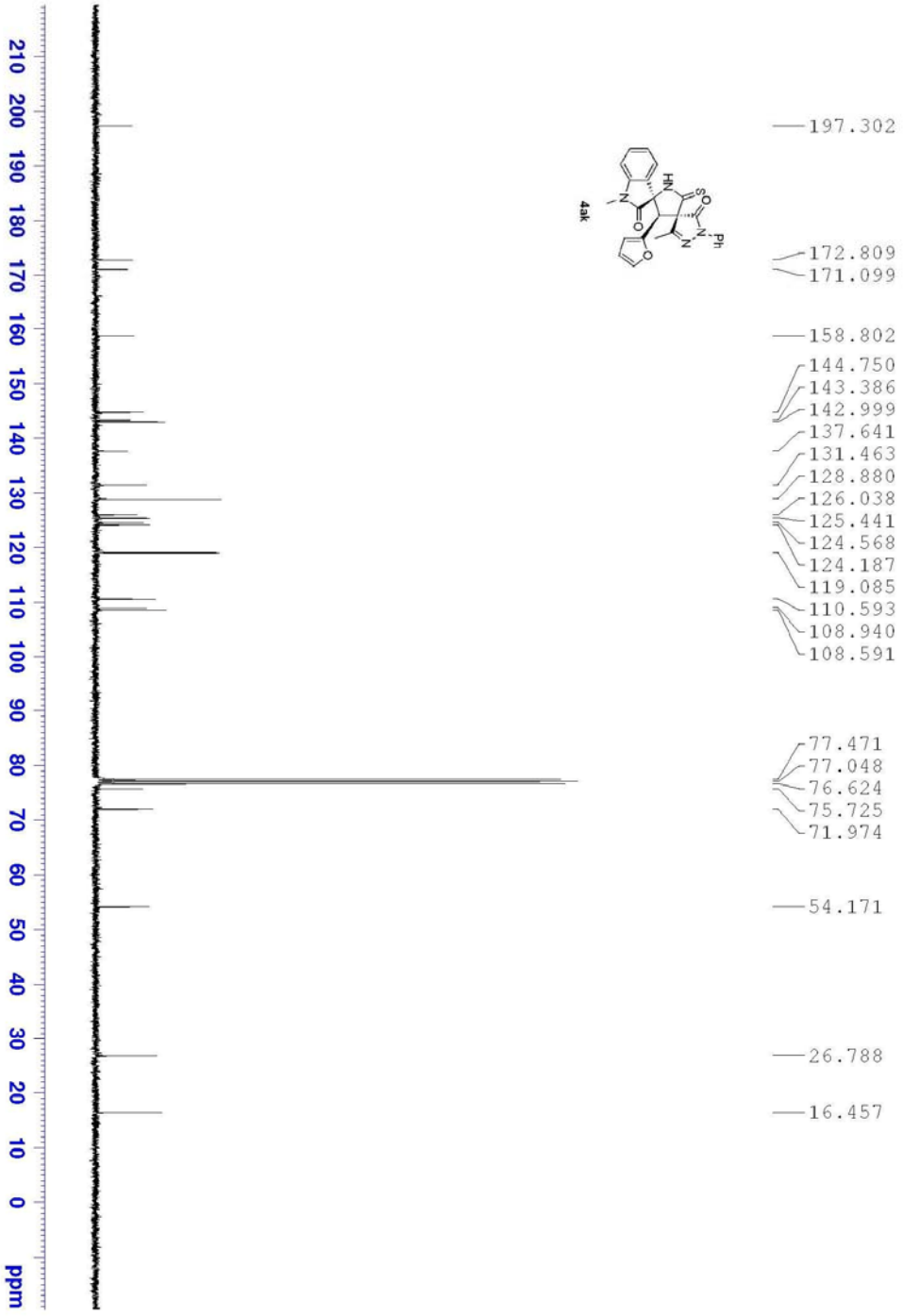
2.418
0.000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143.386
142.999
137.641
131.463
128.880
126.038
125.441
124.568
124.187
119.085
110.593
108.940
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77.048
76.624
75.725
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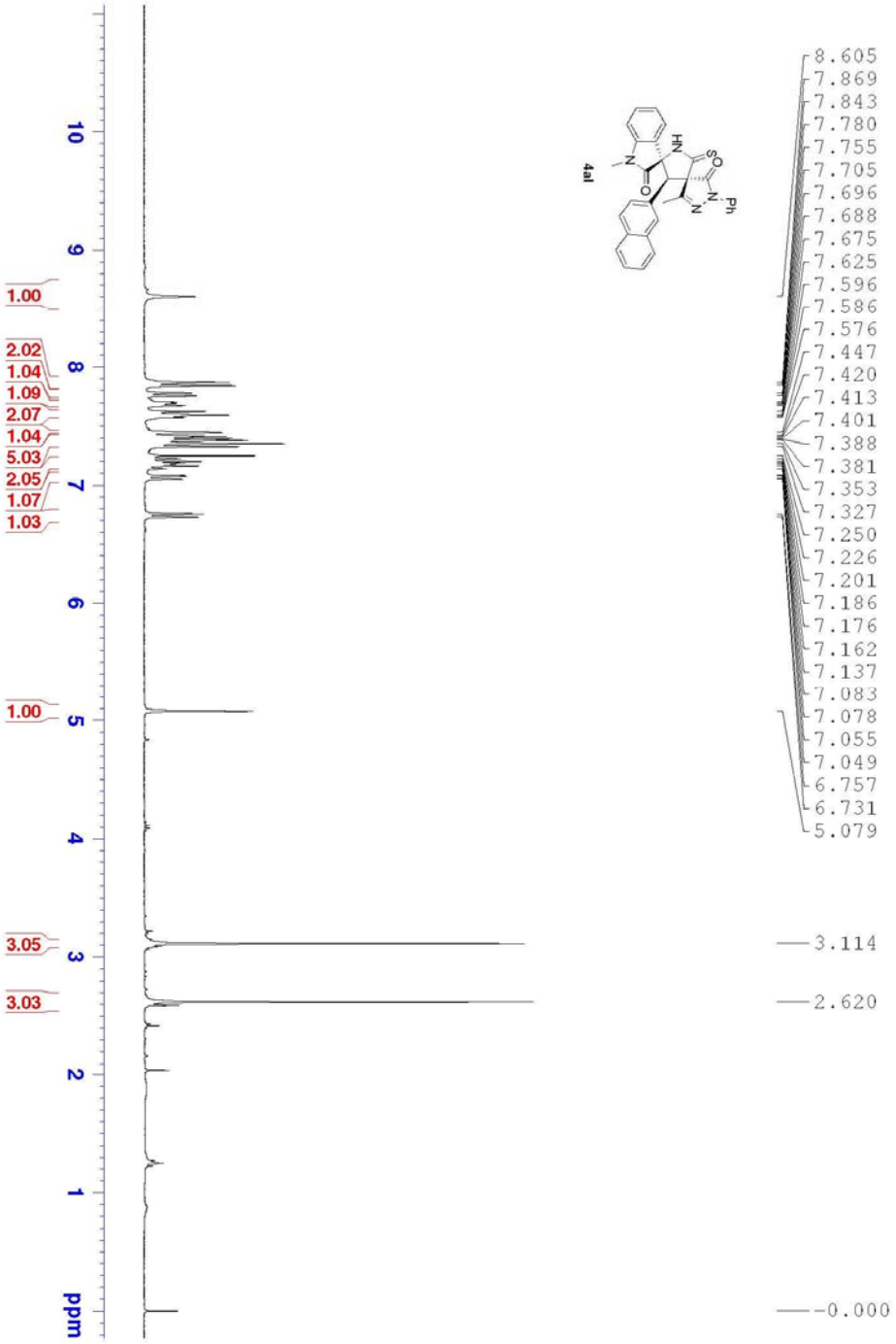
54.171
26.788
16.457
4ak
Ph
ppm


4al
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7.780
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7.696
7.688
7.675
7.625
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7.586
7.576
7.447
7.420
7.413
7.401
7.388
7.381
7.353
7.327
7.250
7.226
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7.186
7.176
7.162
7.137
7.083
7.078
7.055
7.049
6.757
6.731
5.079
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1.00
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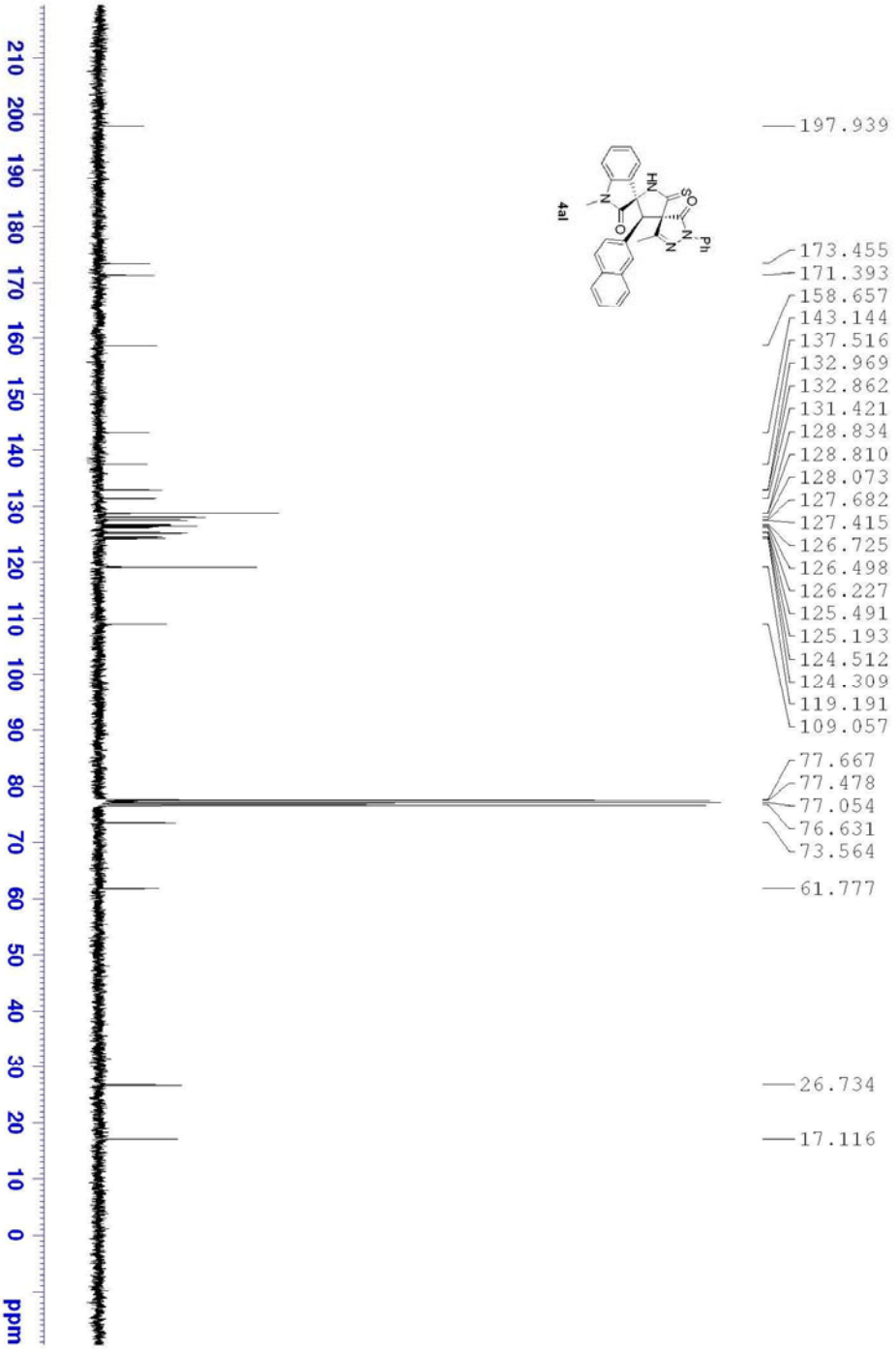
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127.415
126.725
126.498
126.227
125.491
125.193
124.512
124.309
119.191
109.057
77.667
77.478
77.054
76.631
73.564
61.777
26.734
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HN
N
O
SO
N
N
Ph
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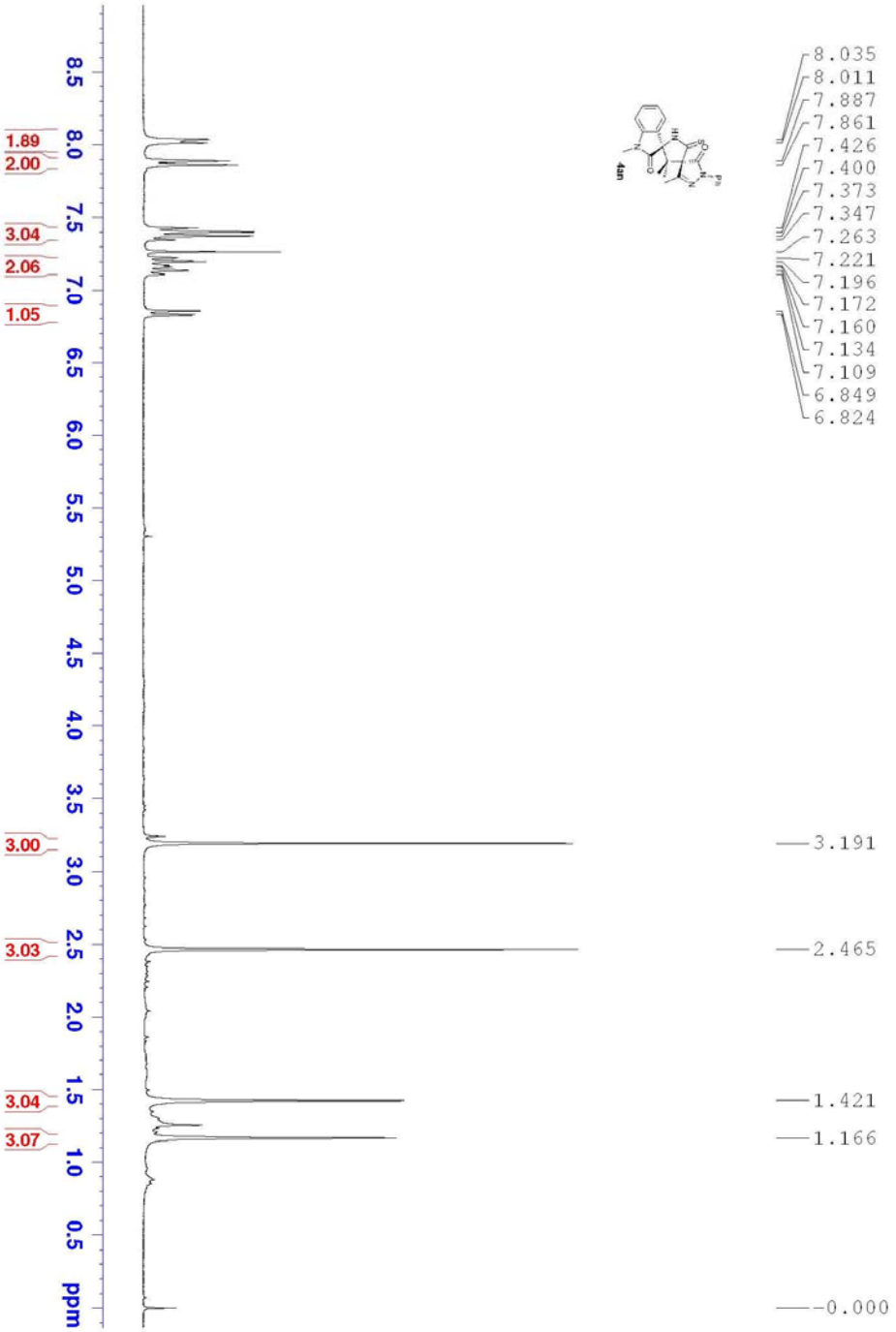
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7.160
7.134
7.109
6.849
6.824
3.191
2.465
1.421
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3.00
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3.04
3.07
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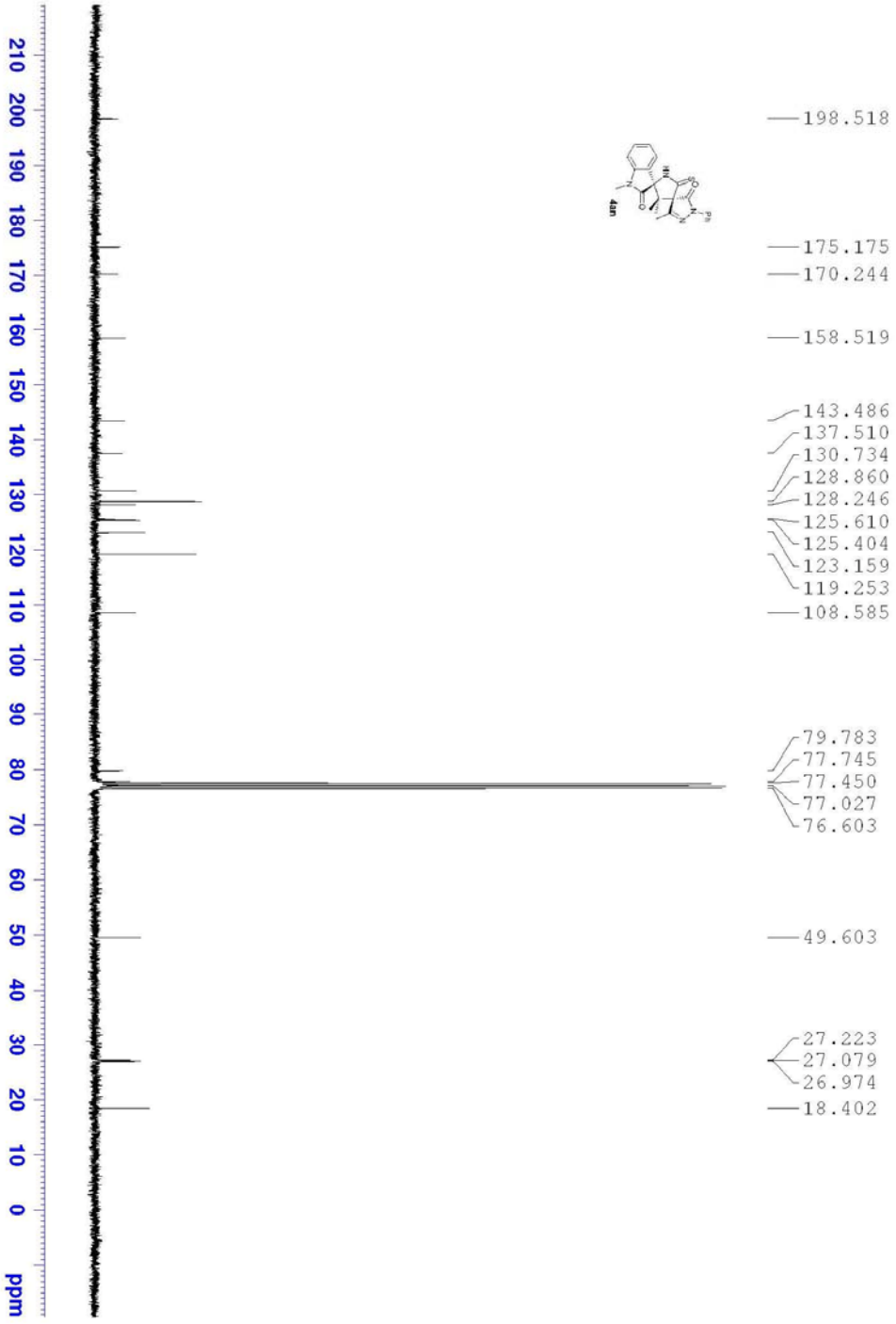
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123.159
119.253
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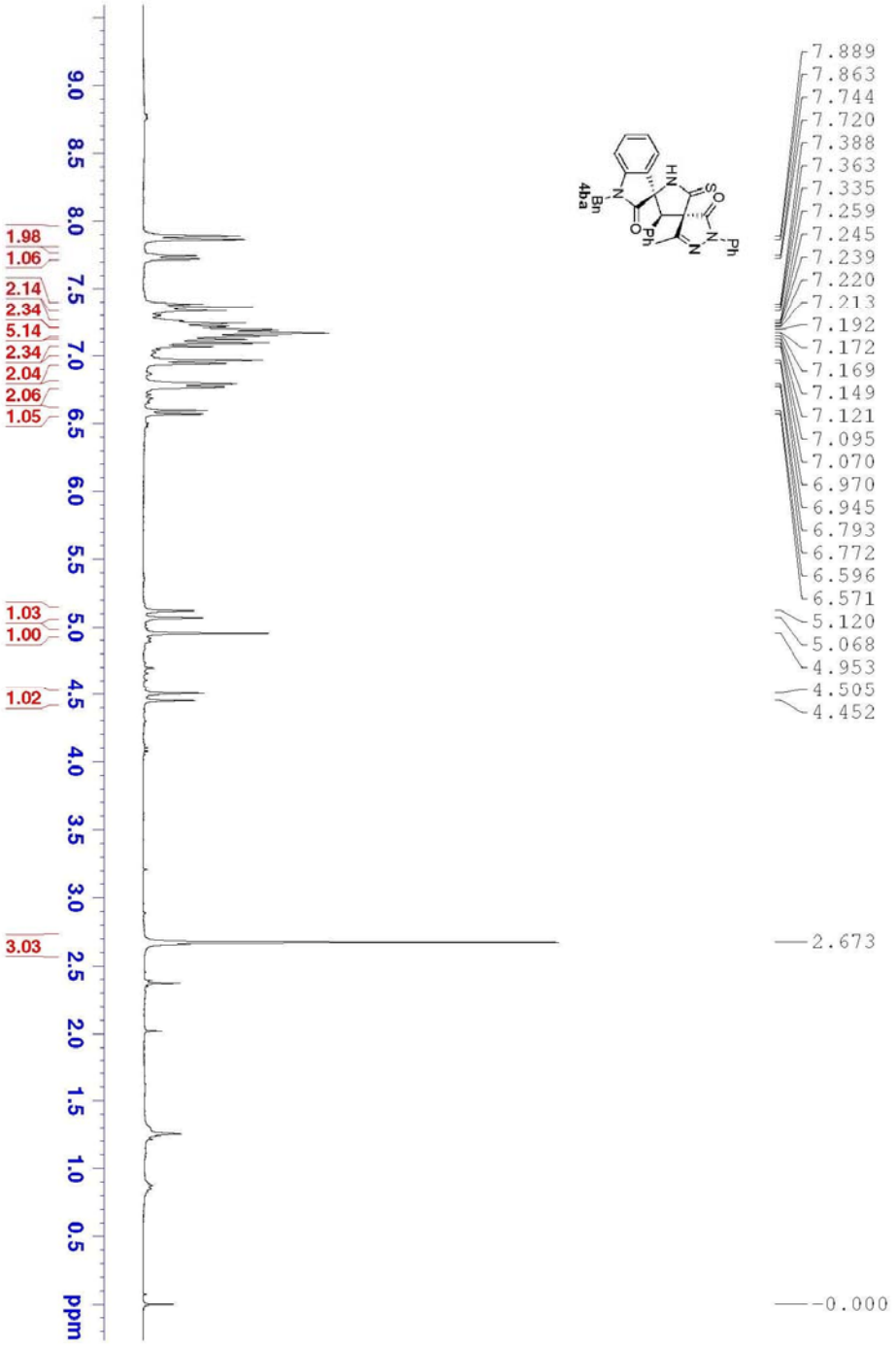
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Bn
Ph
Ph
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2.06
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1.00
1.02
3.03
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7.335
7.259
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7.213
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7.172
7.169
7.149
7.121
7.095
7.070
6.970
6.945
6.793
6.772
6.596
6.571
5.120
5.068
4.953
4.505
4.452
2.673
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9.0
8.5
8.0
7.5
7.0
6.5
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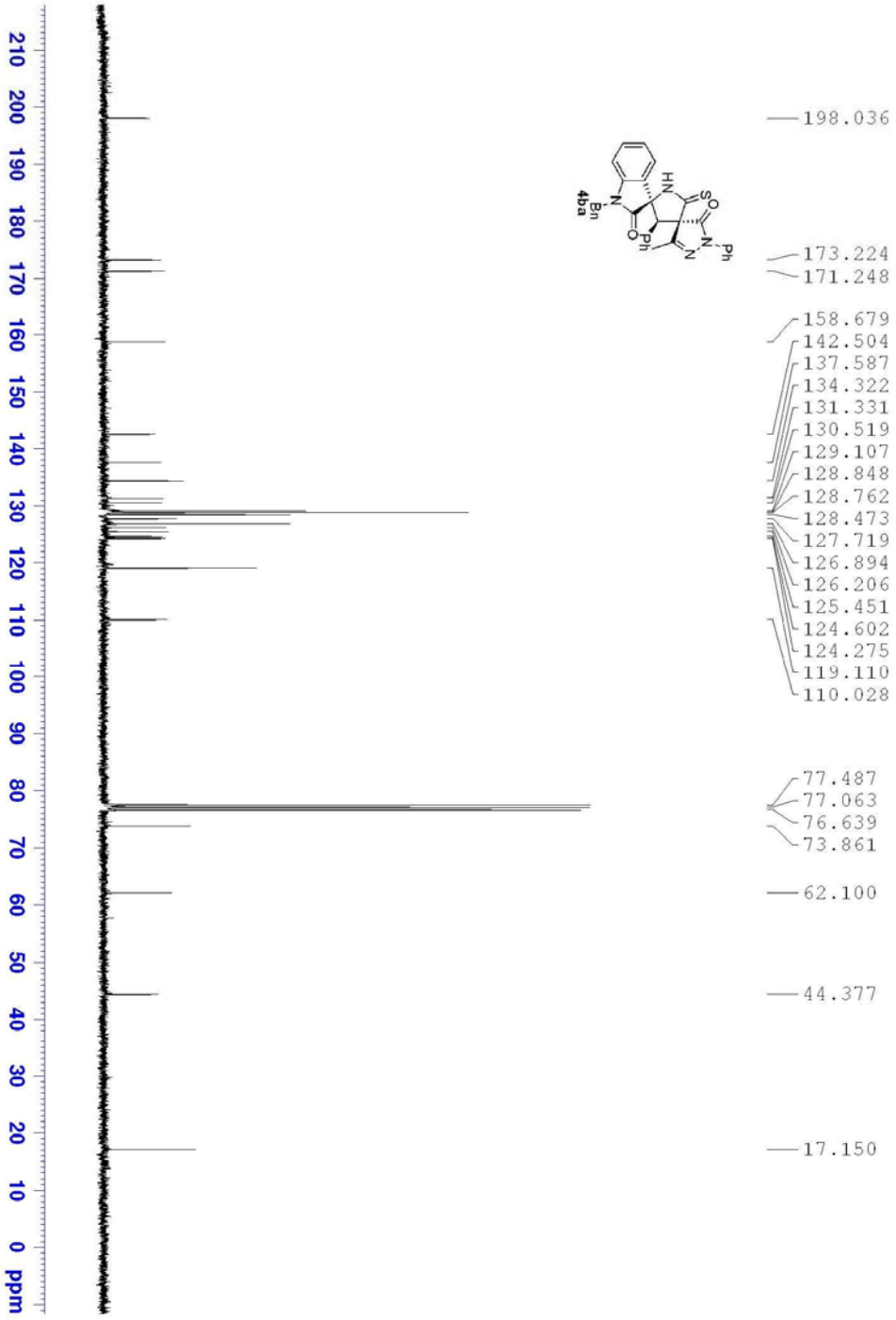
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110.028
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77.063
76.639
73.861
62.100
44.377
17.150
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Bn
Ph
Ph
HN
O
S
O
N
N
N
Ph
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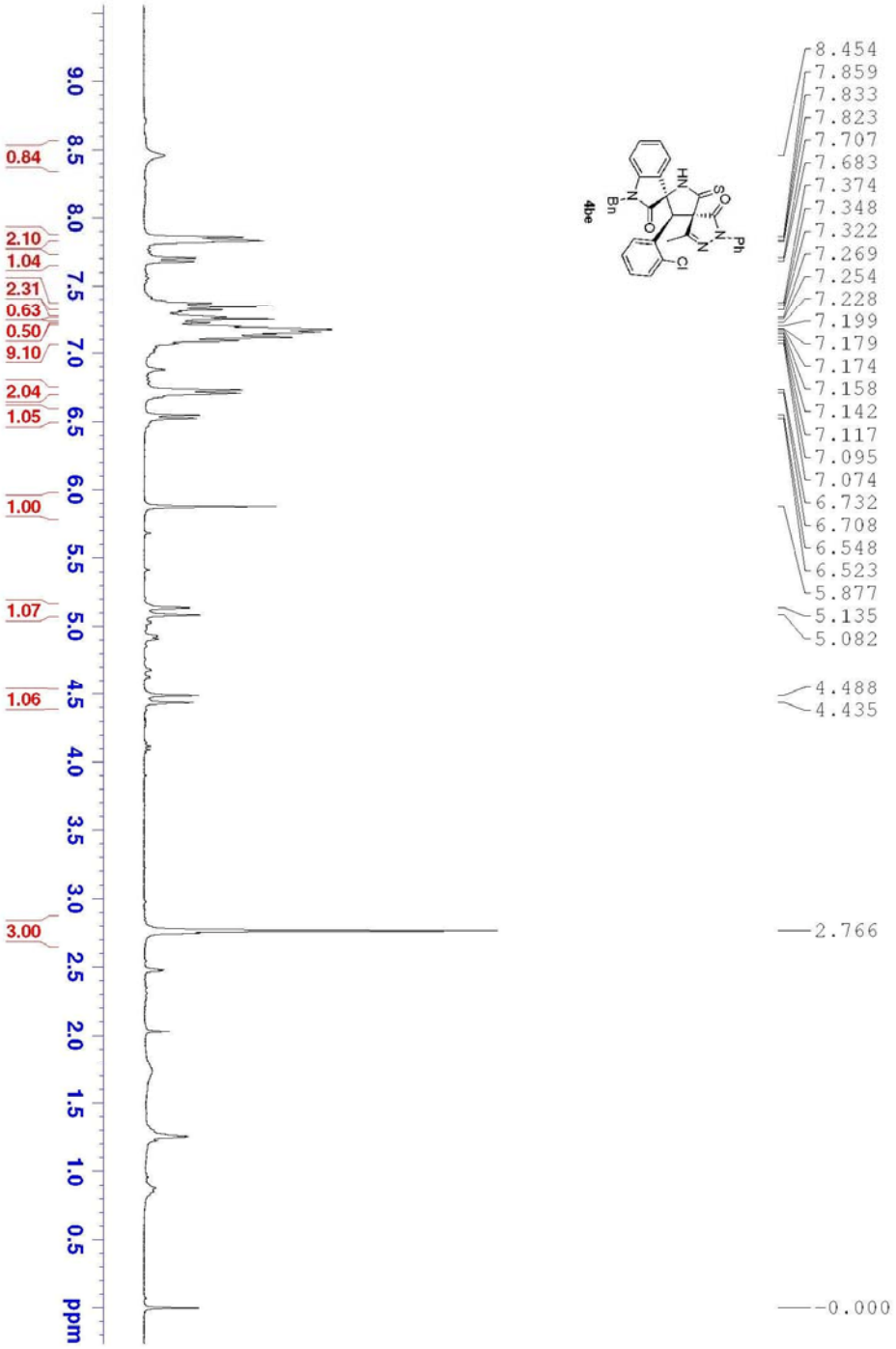
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7.199
7.179
7.174
7.158
7.142
7.117
7.095
7.074
6.732
6.708
6.548
6.523
5.877
5.135
5.082
4.488
4.435
2.766
-0.000
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2.10
1.04
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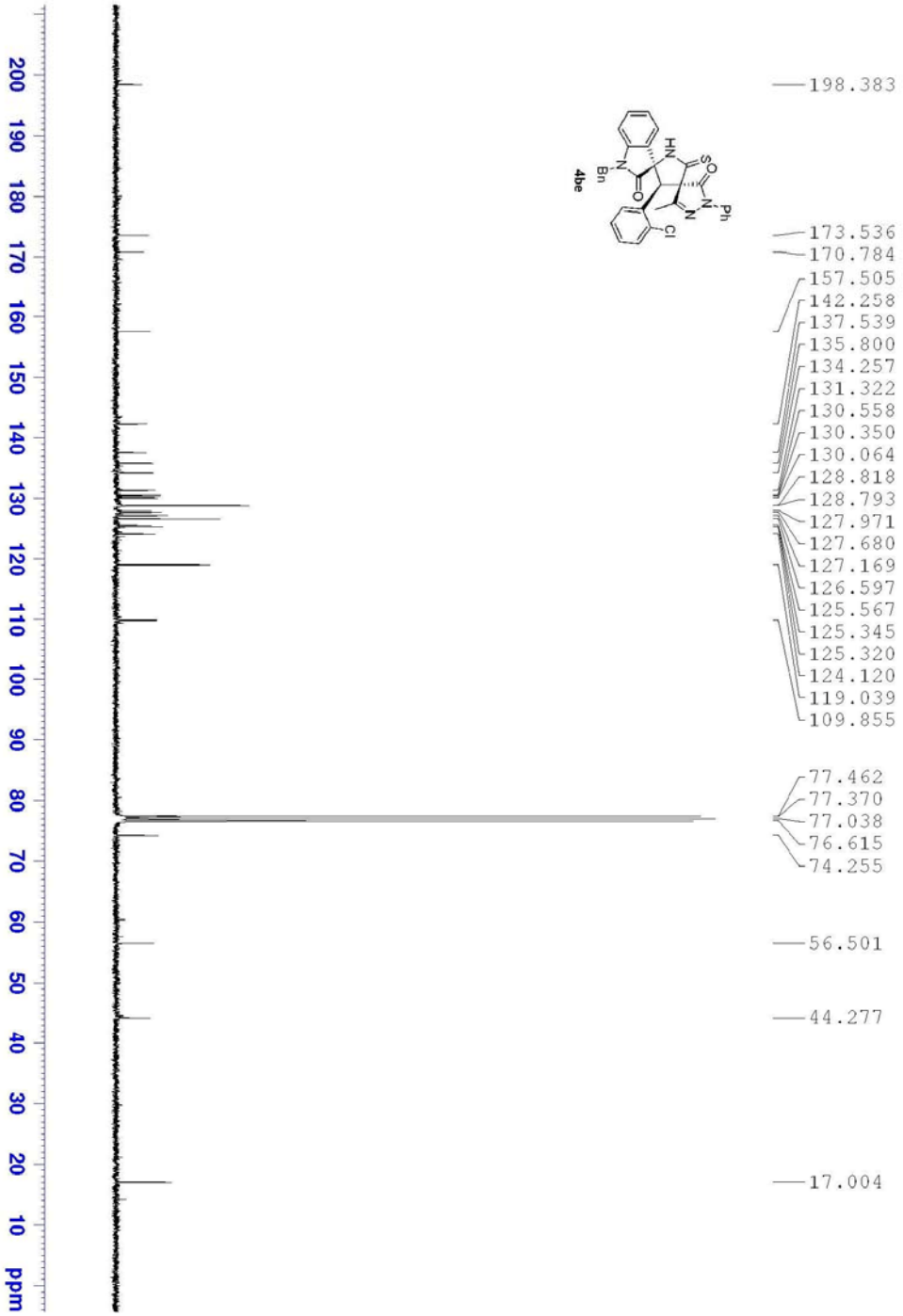
0.50
9.10
2.04
1.05
1.00
1.07
1.06
3.00
ppm
4be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128.793
127.971
127.680
127.169
126.597
125.567
125.345
125.320
124.120
119.039
109.855
77.462
77.370
77.038
76.615
74.255
56.501
44.277
17.004
4be
Bn
Ph
Cl
HN
O
S
N
200
190
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170
160
150
140
130
120
110
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70
60
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30
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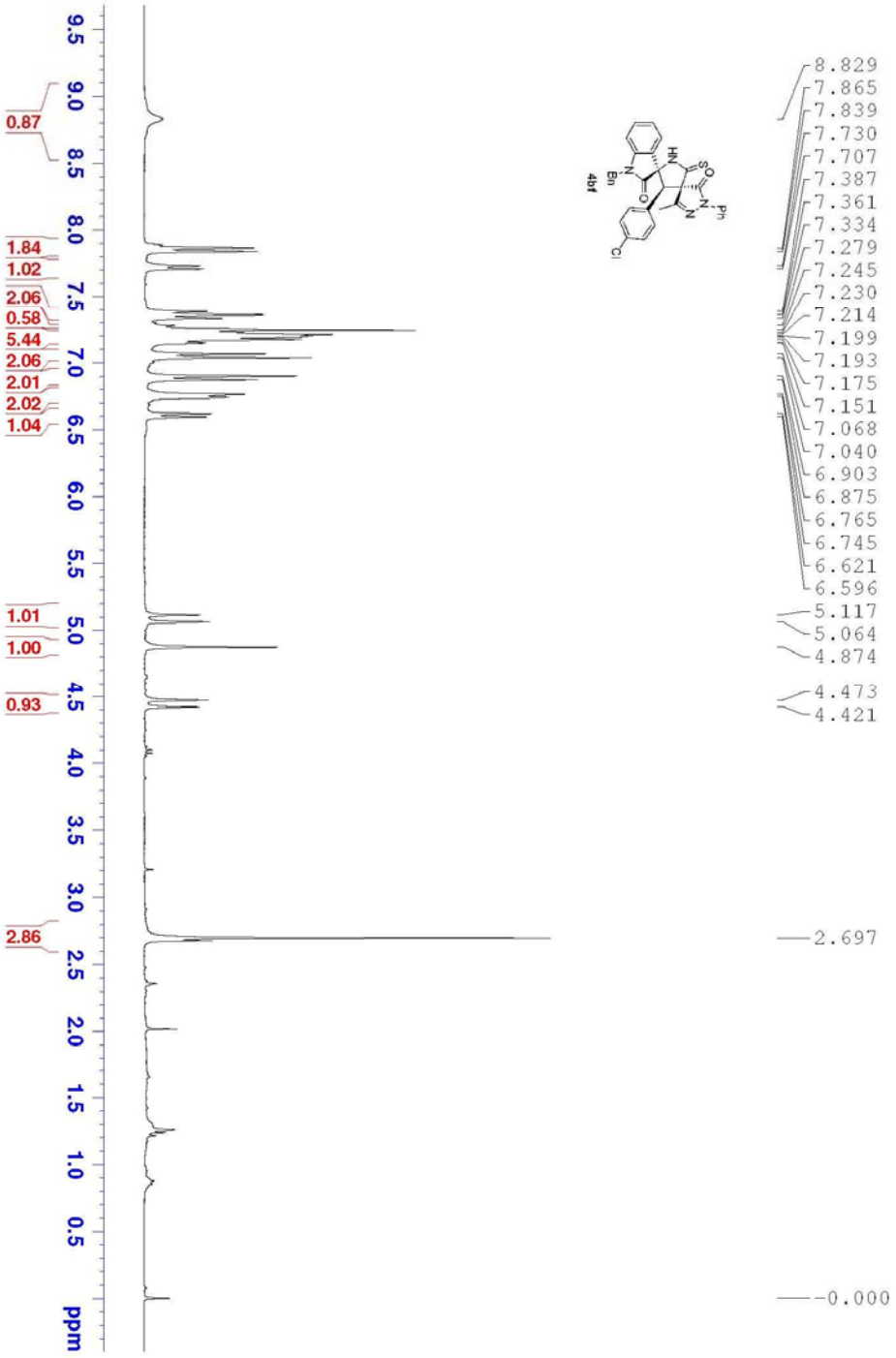
10
ppm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6.0
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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1.02
2.06
0.58
5.44
2.06
2.01
2.02
1.04
1.01
1.00
0.93
2.86
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7.865
7.839
7.730
7.707
7.387
7.361
7.334
7.279
7.245
7.230
7.214
7.199
7.193
7.175
7.151
7.068
7.040
6.903
6.875
6.765
6.745
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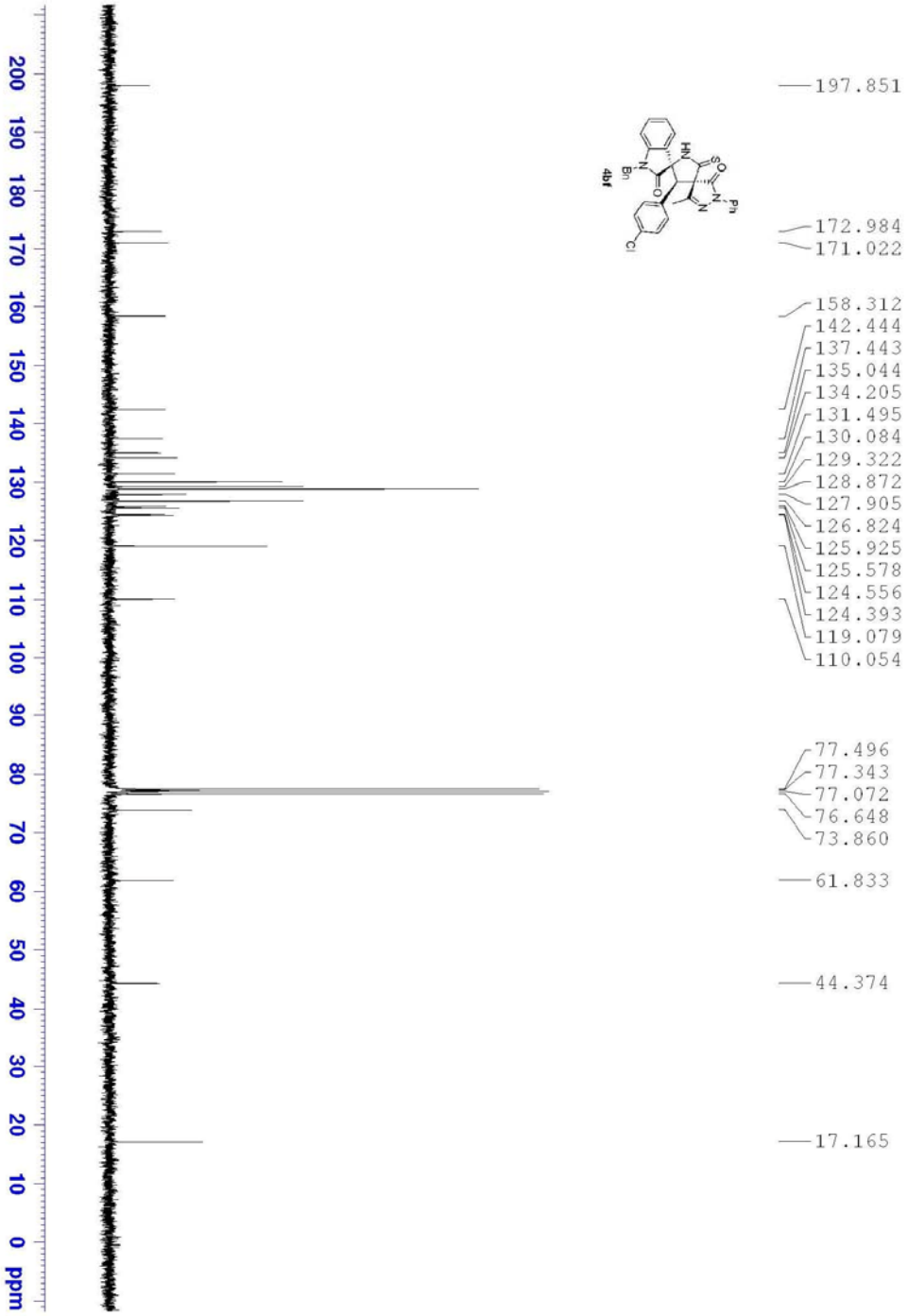
Bn
Ph
Cl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125.925
125.578
124.556
124.393
119.079
110.054
77.496
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73.860
61.833
44.374
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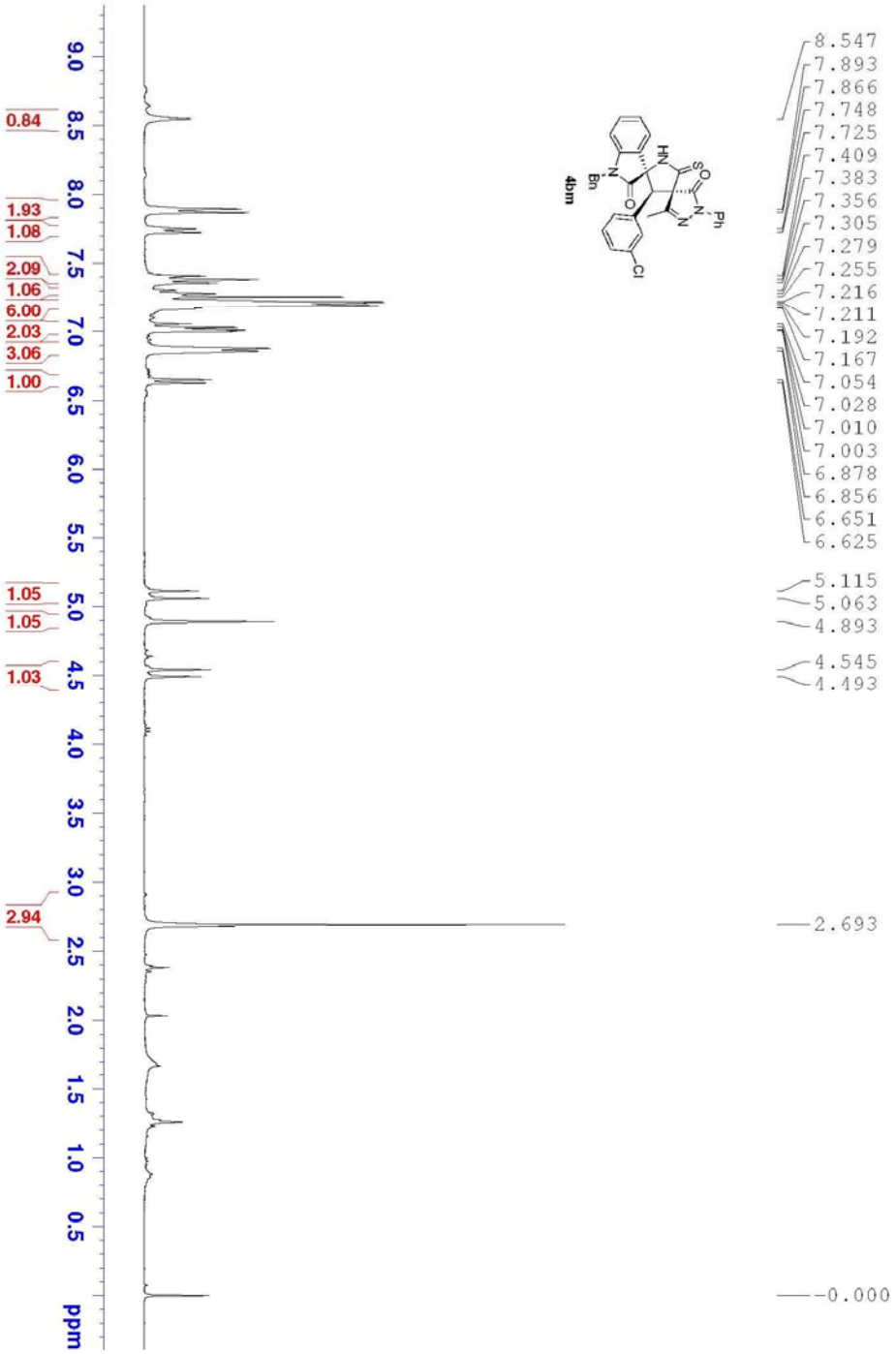
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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7.255
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7.211
7.192
7.167
7.054
7.028
7.010
7.003
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6.856
6.651
6.625
5.115
5.063
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4.545
4.493
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-0.000
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1.93
1.08
2.09
1.06
6.00
2.03
3.06
1.00
1.05
1.05
1.03
2.94
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8.5
8.0
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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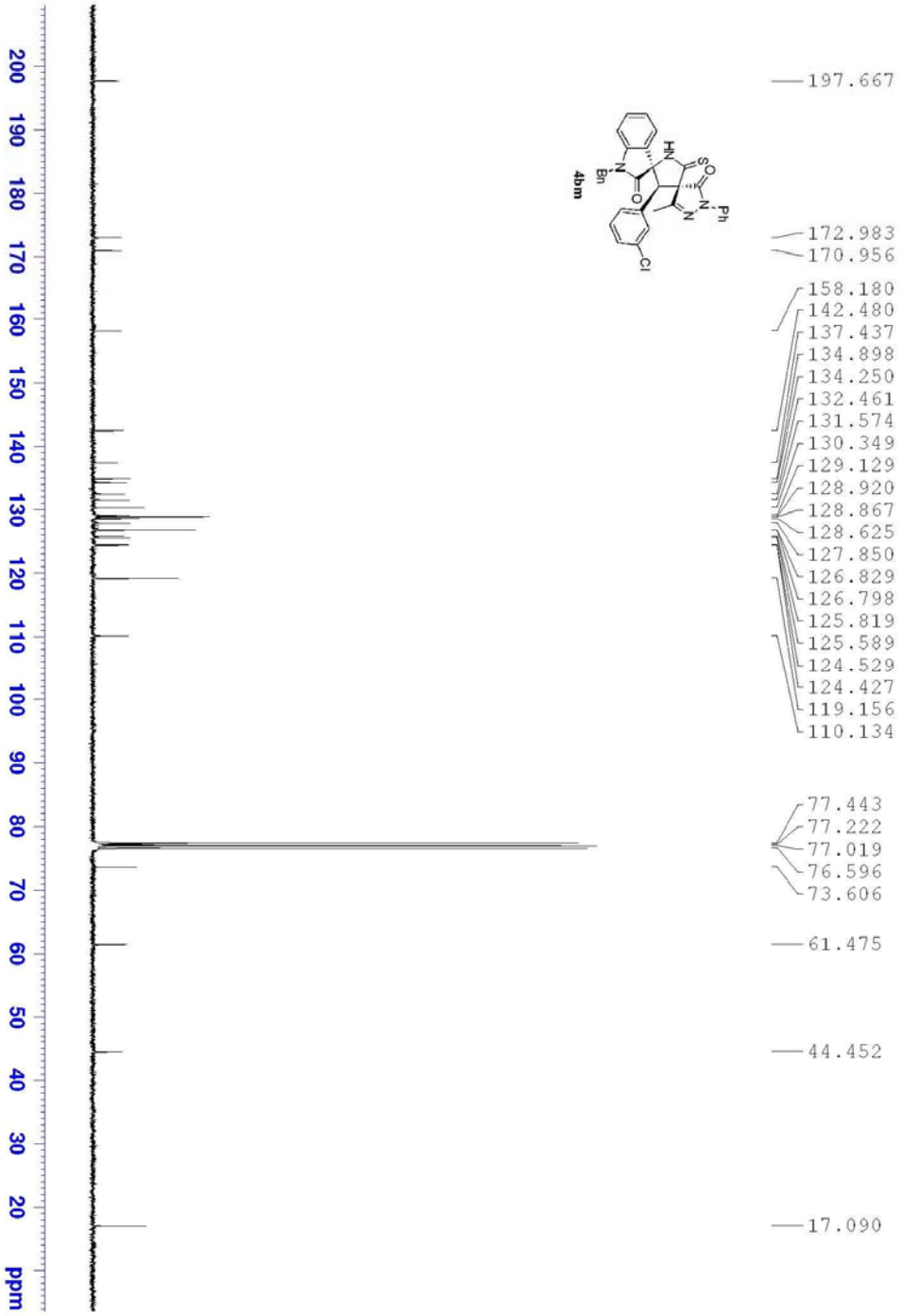
1.0
0.5
ppm
4bm
HN
N
Bn
O
O
S
N
Ph
N
Cl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128.920
128.867
128.625
127.850
126.829
126.798
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125.589
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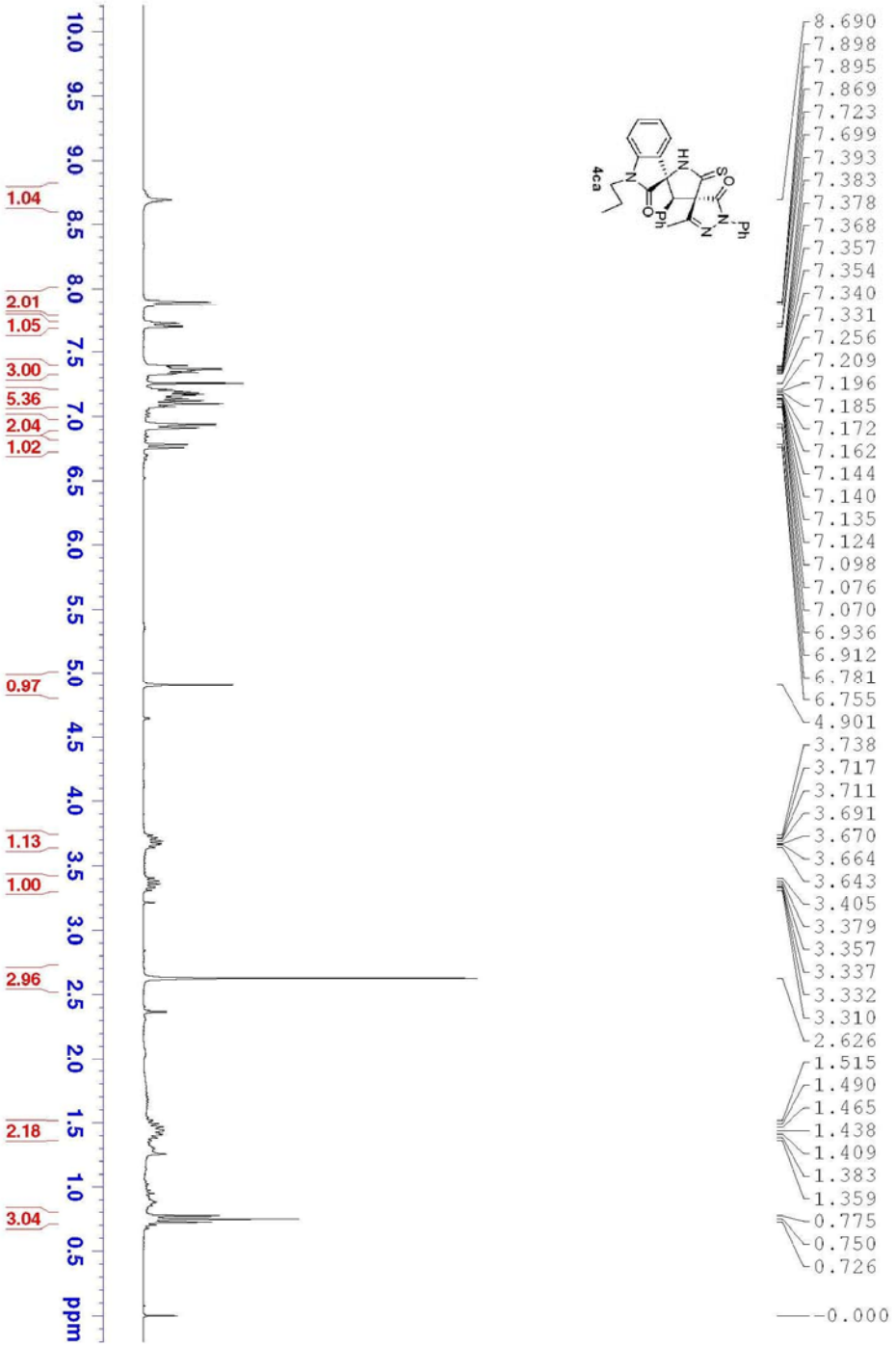
ppm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4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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2.01
1.05
3.00
5.36
2.04
1.02
0.97
1.13
1.00
2.96
2.18
3.04
4ca
HN
N
O
O
Ph
Ph
N
N
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7.354
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7.209
7.196
7.185
7.172
7.162
7.144
7.140
7.135
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7.076
7.070
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6.781
6.755
4.901
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3.717
3.711
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3.670
3.664
3.643
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3.379
3.357
3.337
3.332
3.310
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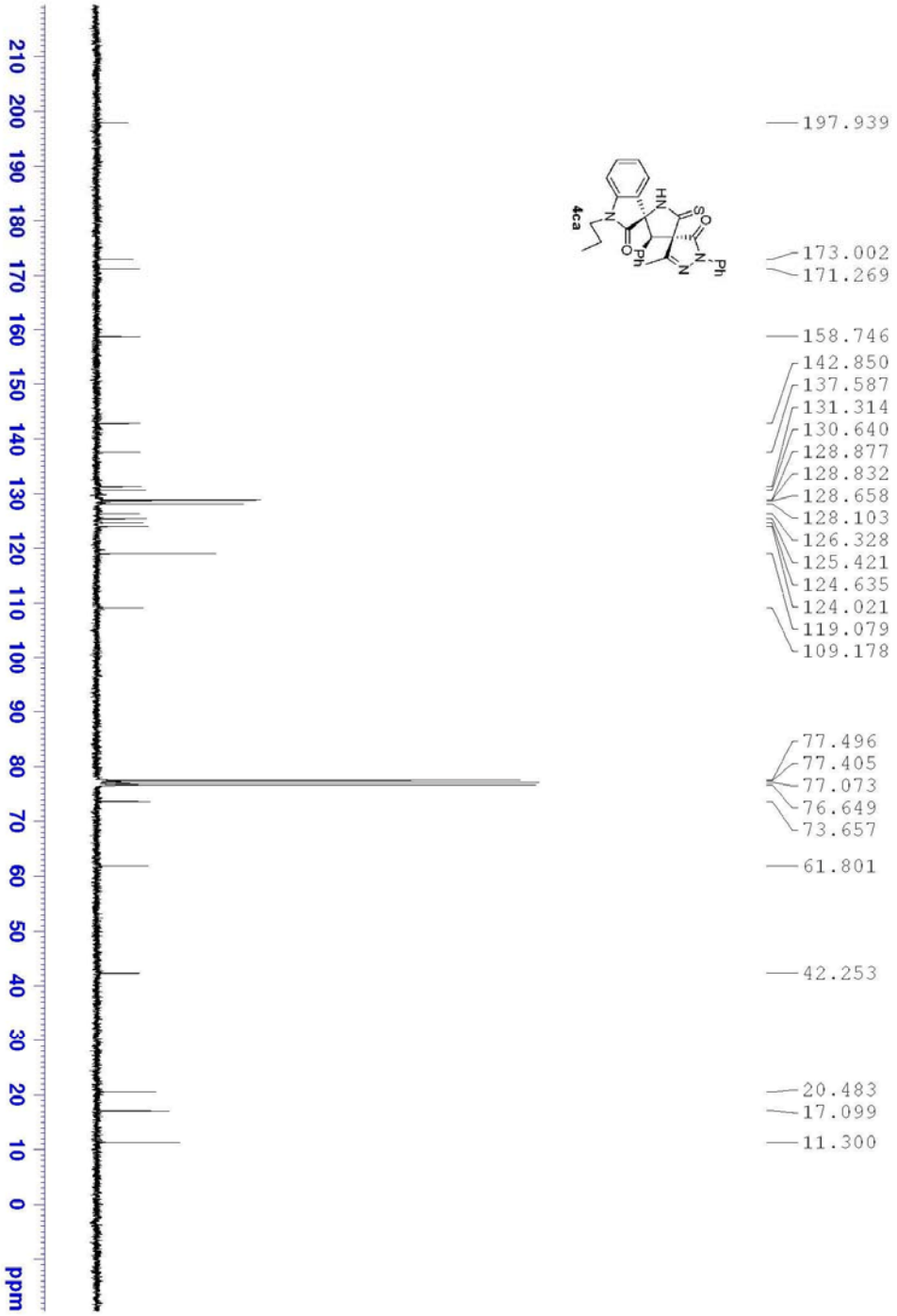
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125.421
124.635
124.021
119.079
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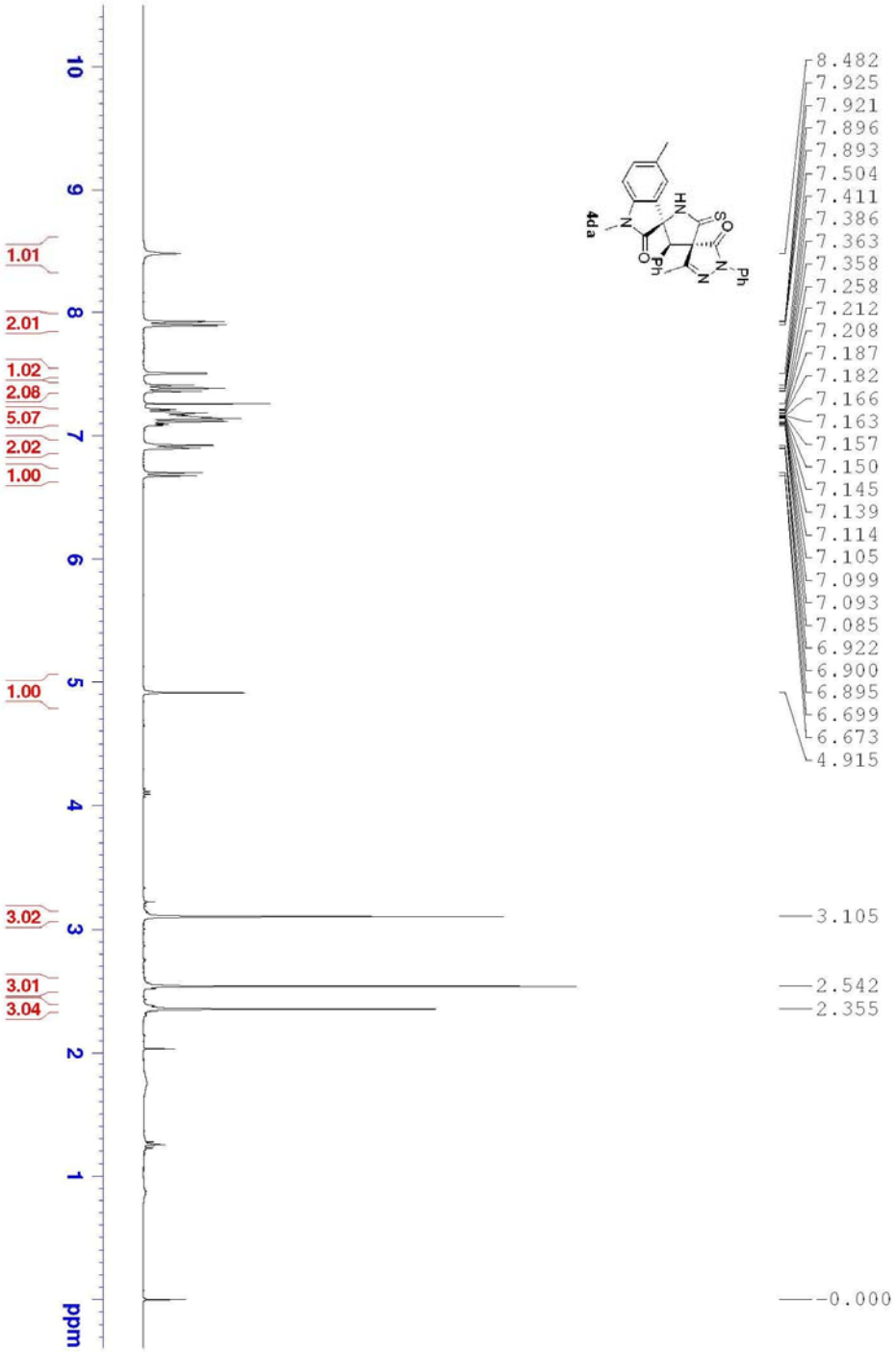
ppm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7.145
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7.085
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2.01
1.02
2.08
5.07
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3.02
3.01
3.04
ppm
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HN
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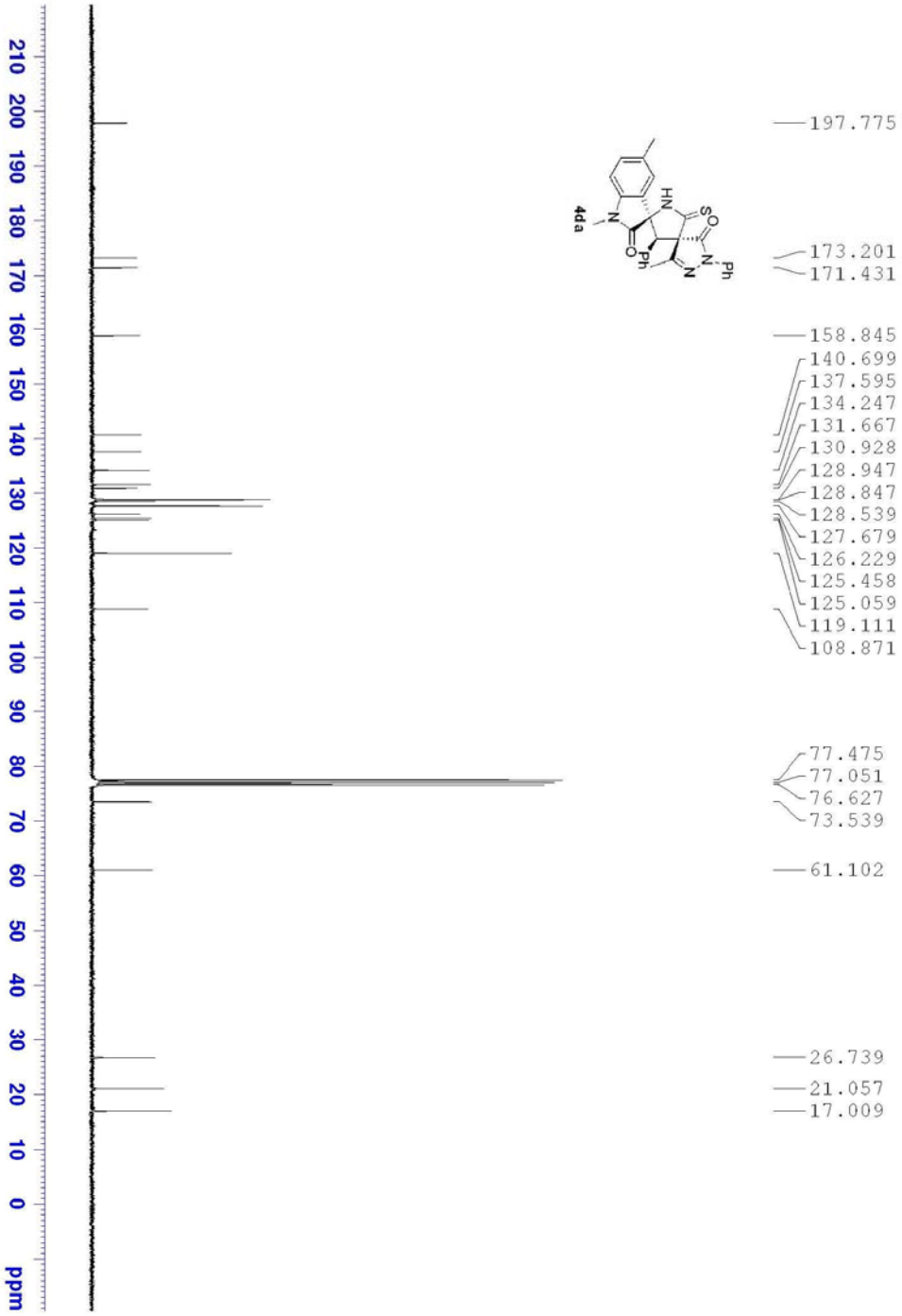
S
O
N
N
Ph
Ph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77.051
76.627
73.539
61.102
26.739
21.057
17.009
4da
HN
O
N
Ph
O
S
N
N
Ph
210
200
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60
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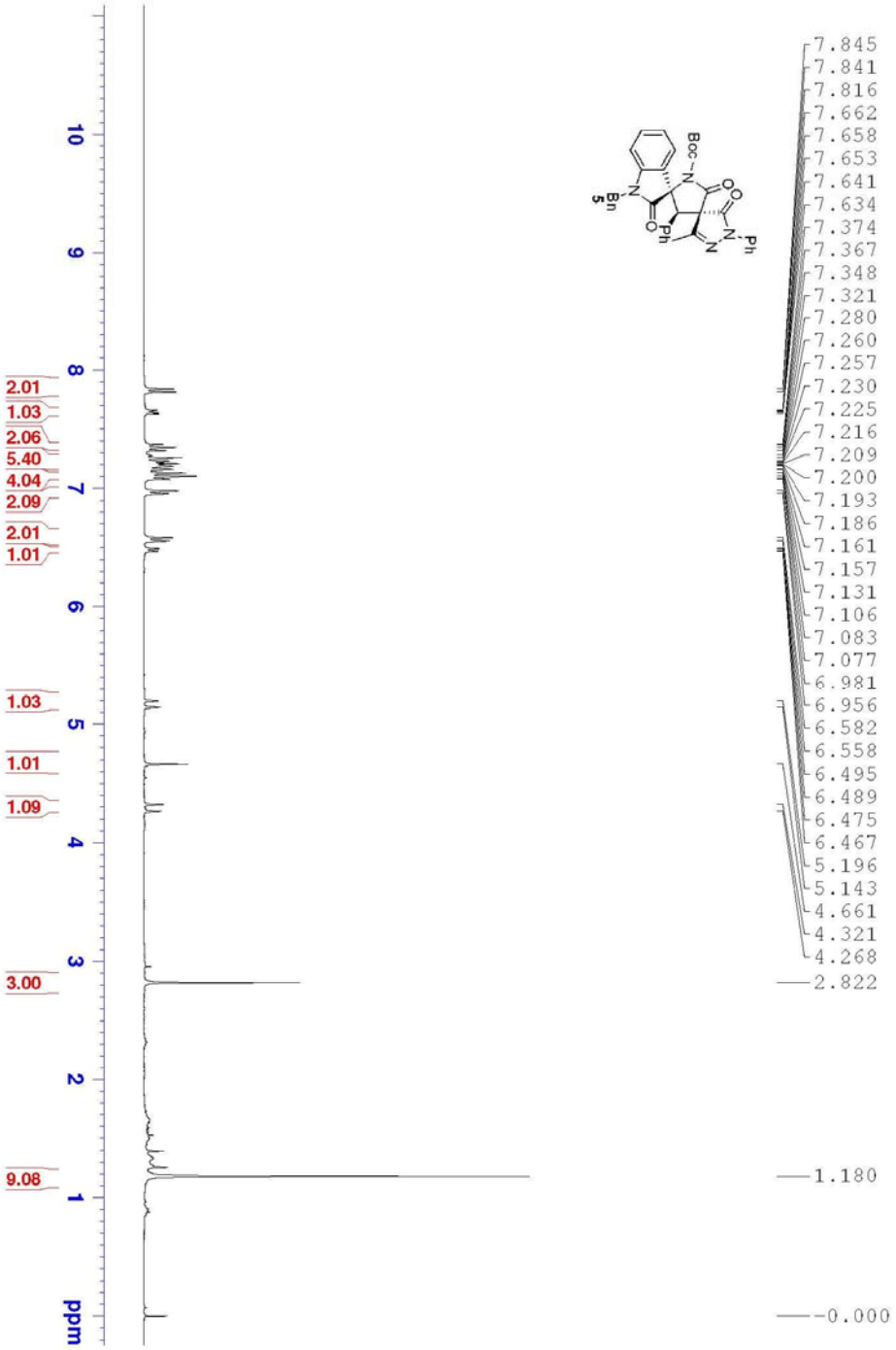
ppm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7.157
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7.077
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1.03
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1.09
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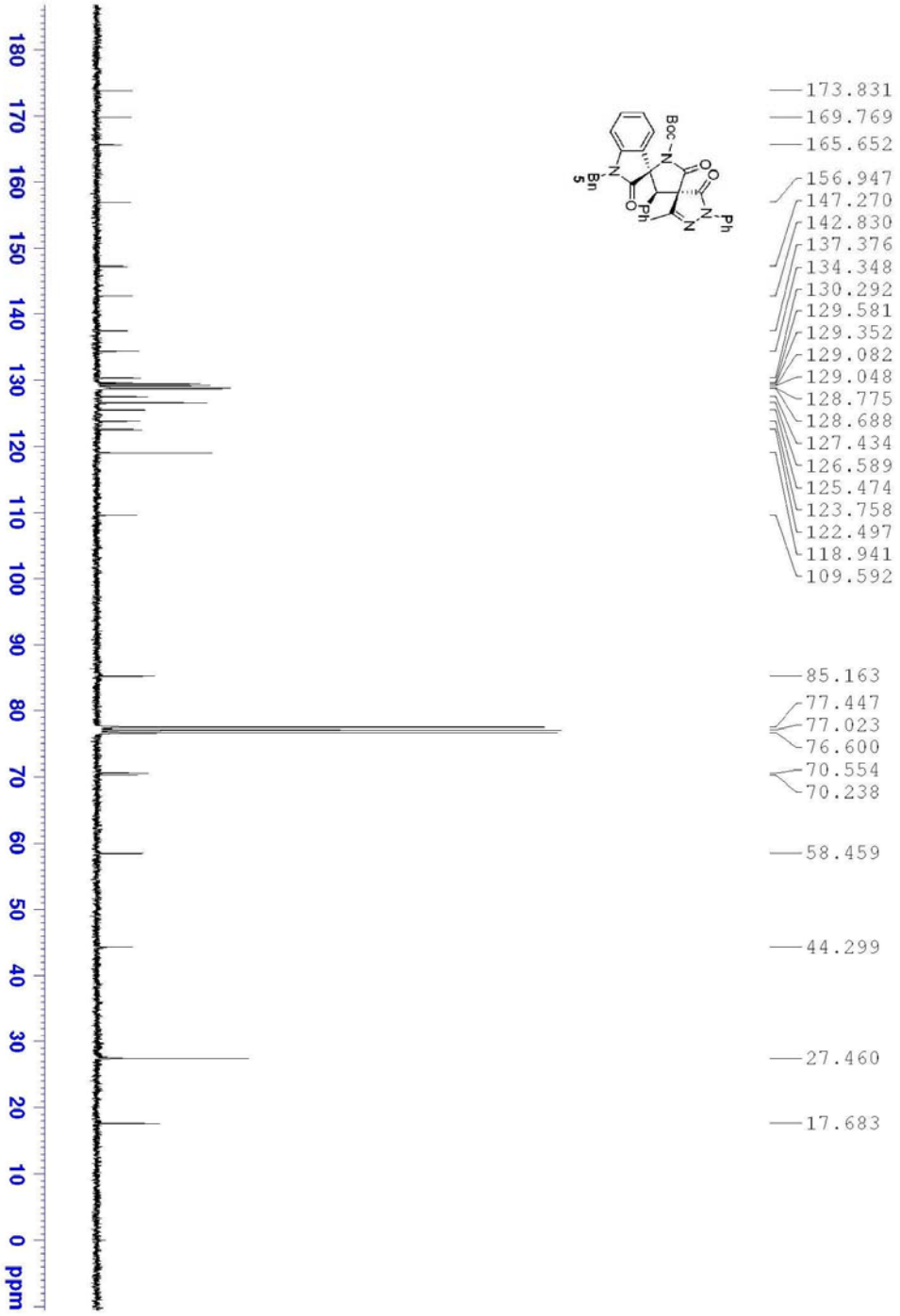
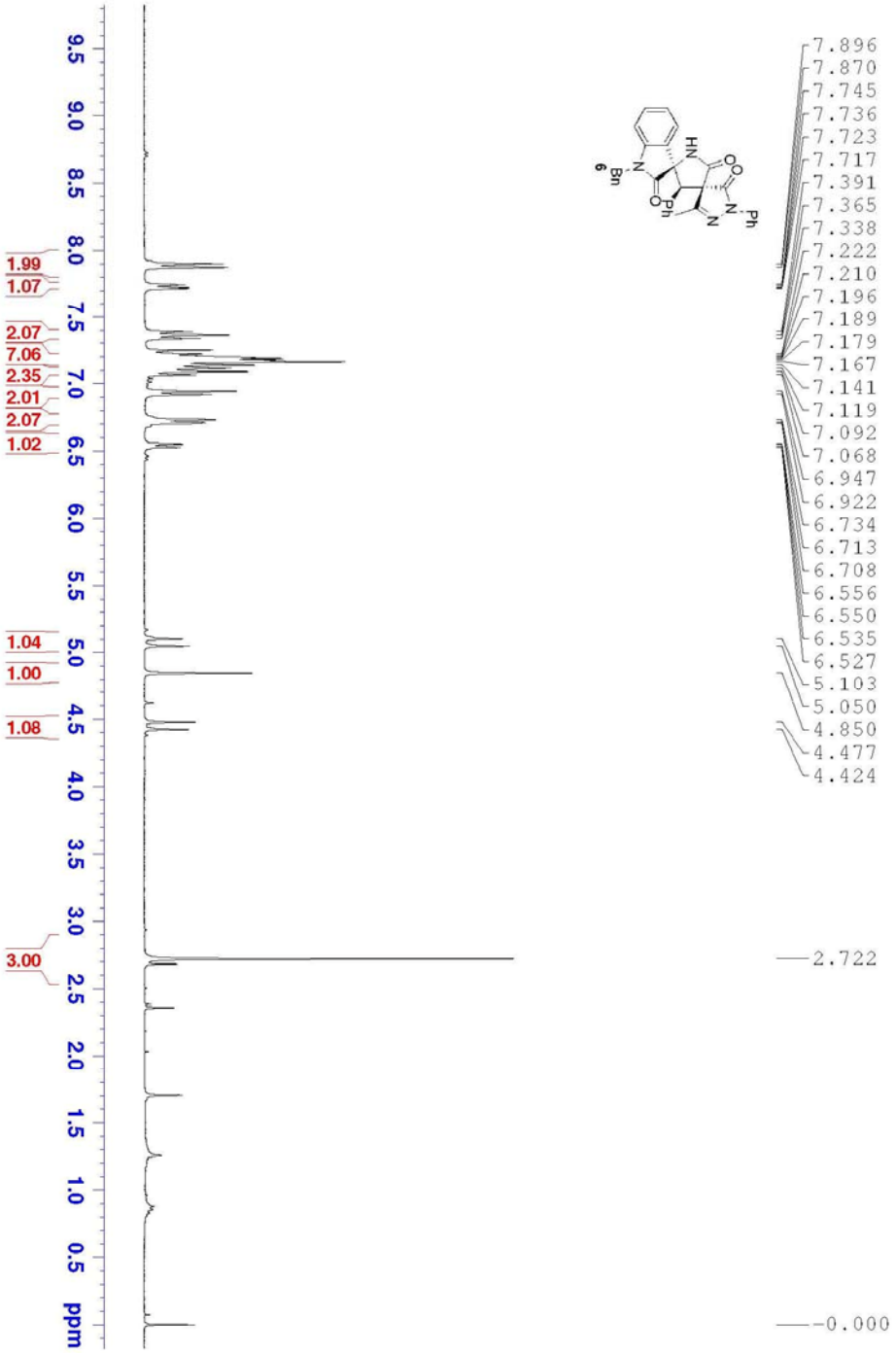
Boc
Bn
Ph
Ph
Ph

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2.0
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1.0
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ppm
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1.07
2.07
7.06
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2.01
2.07
1.02
1.04
1.00
1.08
3.00
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7.717
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7.196
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7.179
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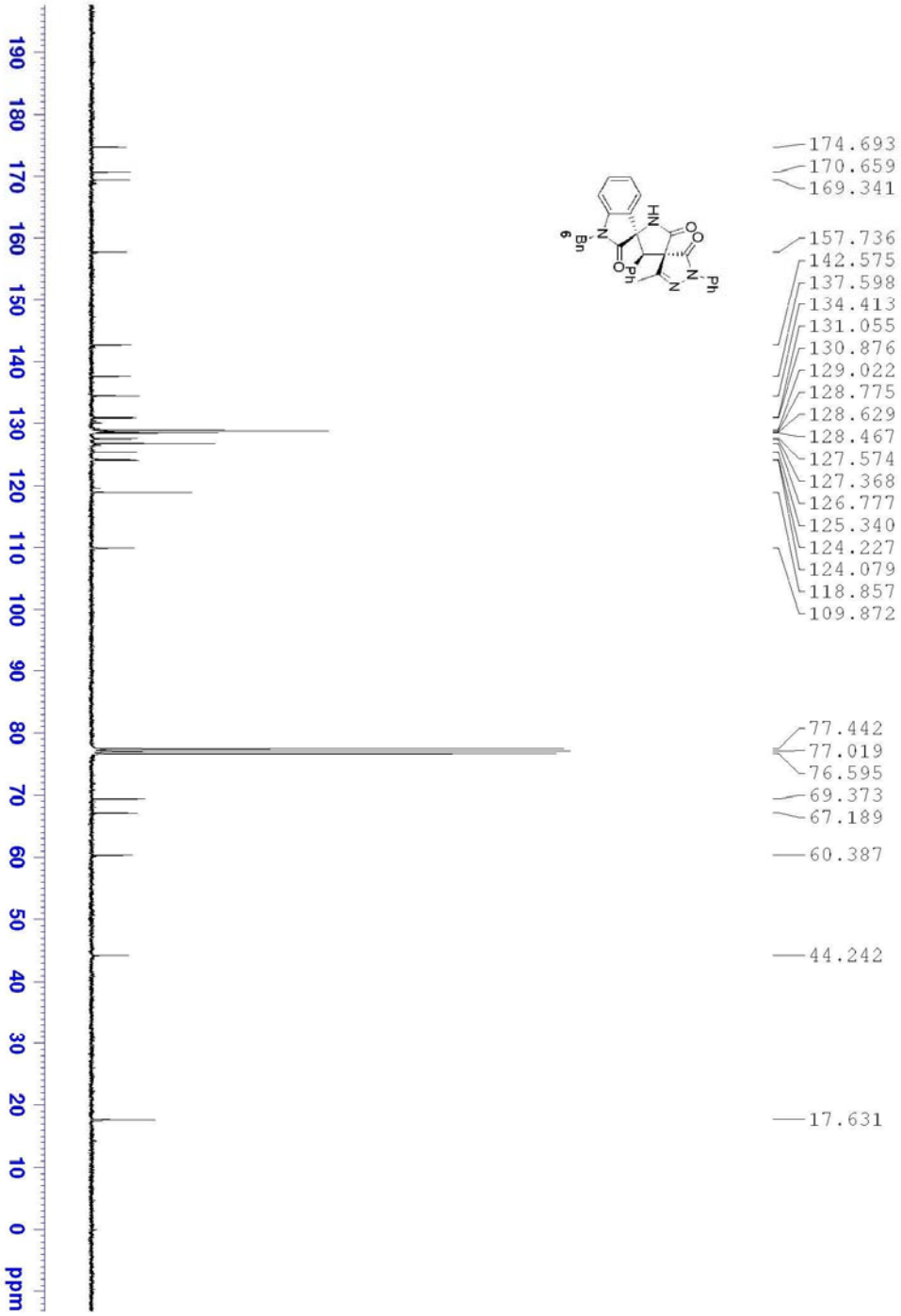
O
O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127.368
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125.340
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109.872
77.442
77.019
76.595
69.373
67.189
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44.242
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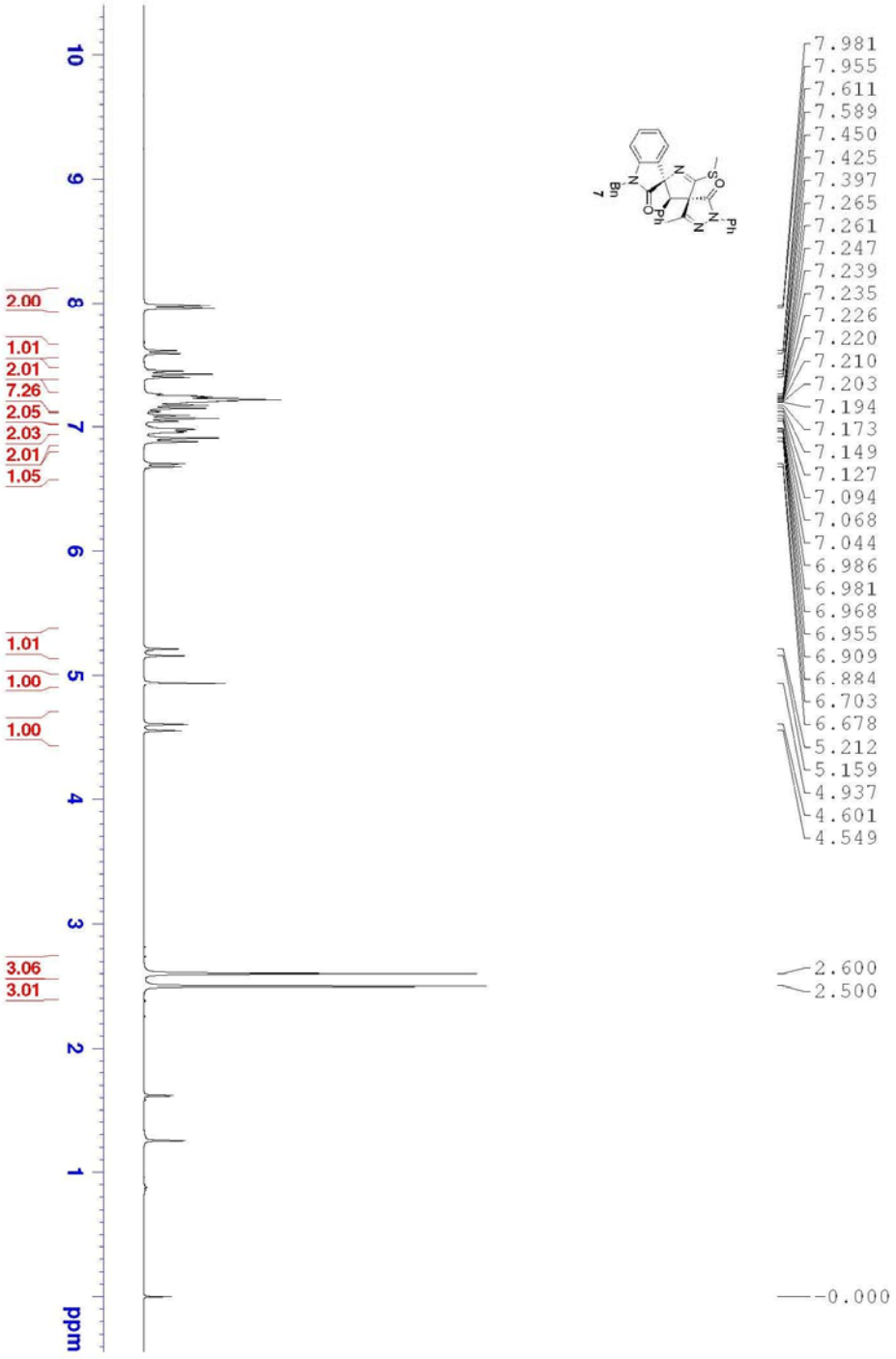
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7.210
7.203
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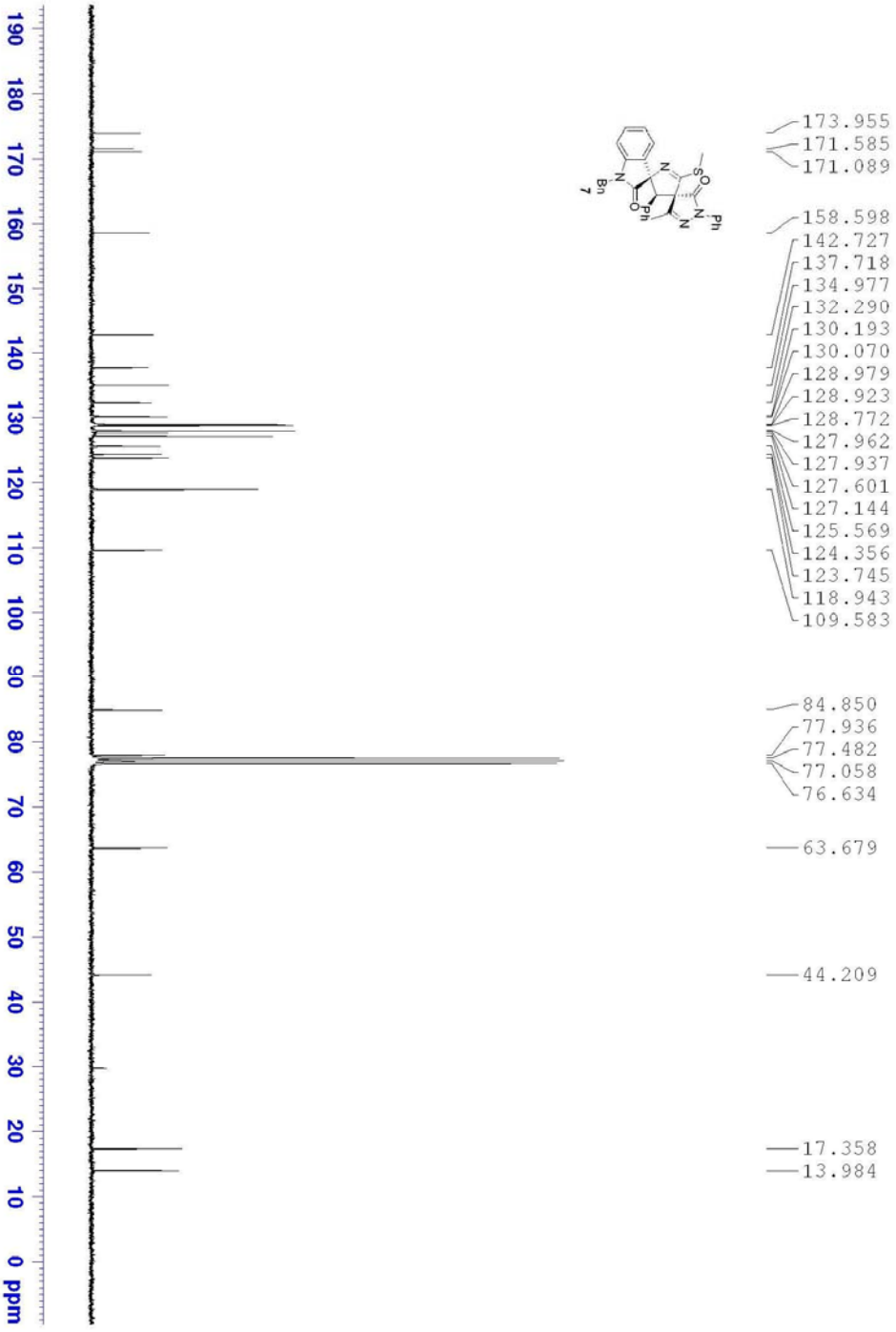
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150
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130
120
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60
50
40
30
20
10
0 ppm