Electronic Supplementary Material (ESI) for ChemComm.

Organocatalytic Cascade Michael/Michael Reaction for the Asymmetric Synthesis of Spirocyclic Oxindoles Containing Five Contiguous Stereocenters

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Supporting Information

Contents

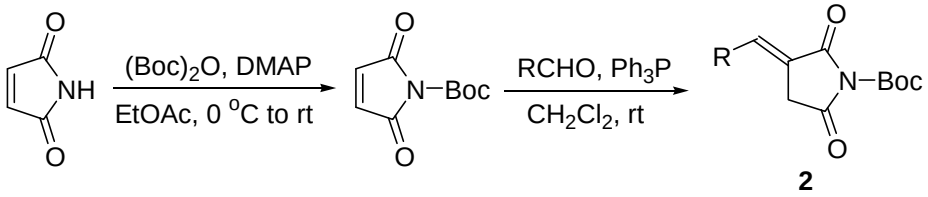
General information

General Methods: Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Column chromatography was performed with silica gel (200−300 mesh). Melting points were determined with an XT−4 melting-point apparatus and are uncorrected. ^{1}H NMR spectra were measured with a Bruker Avance 400 MHz spectrometer. Chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were measured at 100 MHz; chemical shifts were reported in ppm relative to TMS with the solvent resonance as internal standard. Infrared spectra were obtained with a Perkin Elmer Spectrum One spectrometer. High resolution mass spectra (Electron spray ionization) were measured with a Bruker APEX IV Fourier-Transform mass spectrometer or an Agilent 6520 Accurate-Mass-Q-TOF MS system equipped with an electrospray ionization (*ESI*) source. Optical rotations were measured with a WZZ−3 polarimeter. Enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1200 LC instrument with a Daicel Chiralpak IA, IB or AD-H column.

Materials

Chiral squaramide catalysts **I**, **II**, **IV**, **V**, **VIII** and **IX**,[1] **III**,[2] **VI** and **VII**,[3] and chiral thiourea catalyst **X** [4] were prepared according to the reported procedures.

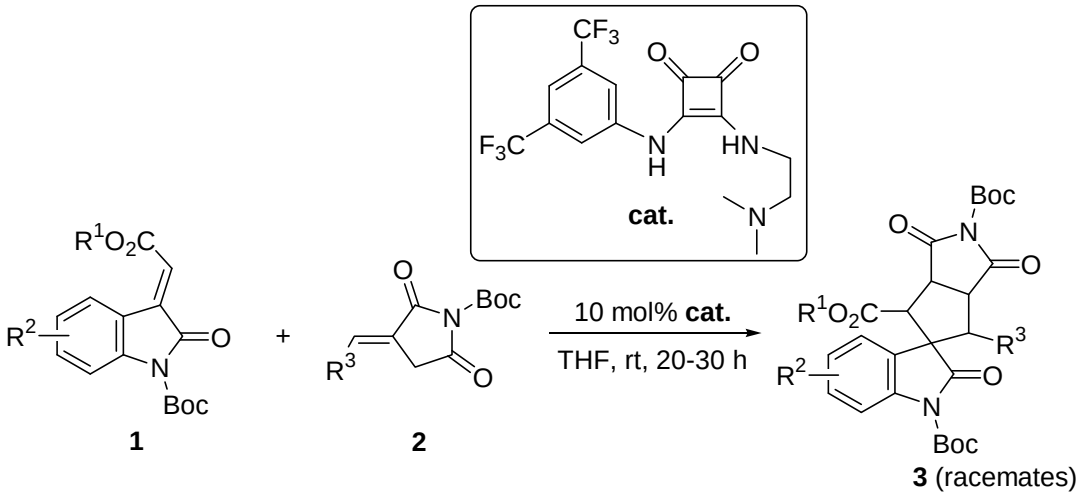
α-Alkylidene succinimides **2** were prepared following modification of literatures protocol.[5]



2

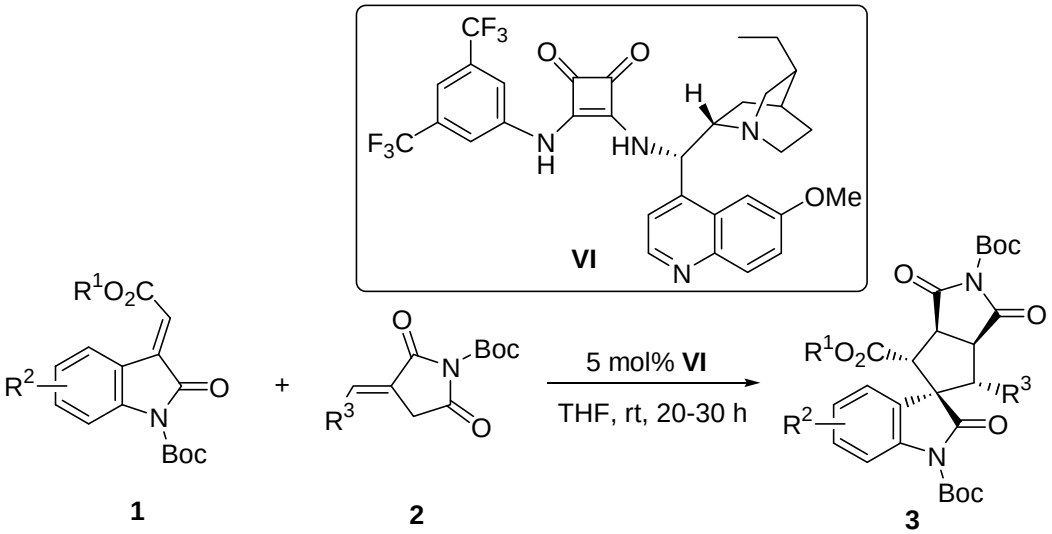
Maleimide (0.97 g, 10.0 mmol), 4-(dimethylamino)pyridine (122 mg, 1.0 mmol) and EtOAc (50 mL) were added in a dry 100 mL round-bottom flask, equipped with a stir bar. The reaction vessel was cooled to 0 °C on an ice bath. Di-*tert*-butyl dicarbonate (3.27 g, 15.0 mmol) was added dropwise at 0 °C over a period of 20 min into the stirred reaction mixture. After the addition was complete, the reaction mixture was allowed to stir at ambient temperature until TLC analysis indicated full conversion of starting material (about 20 h). The solvent was removed under reduced pressure and the mixture was purified by flash column chromatography (with CH_2Cl_2 as eluant) to yield the *N*-Boc protected maleimide. The *N*-Boc protected maleimide (394 mg, 2.0 mmol), triphenylphosphine (577 mg, 2.2 mmol) and corresponding aldehyde (2.4 mmol), were dissolved in anhydrous CH_2Cl_2 (5 mL) and stirred at room temperature for 24 h. The solvent was removed in vacuo and purification of the crude product by flash column chromatography yielded the α-alkylidene succinimides **2**.

General procedure for the synthesis of the racemates of 3

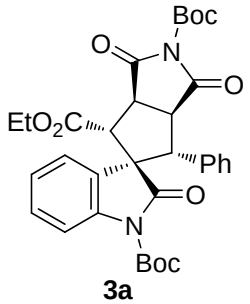


To a dried small bottle were added **2** (0.1 mmol), **cat.** (4.0 mg, 0.01 mmol) and 0.5 ml THF. The mixture was stirred at room temperature for 15 min, and **1** was then added. After stirring at room temperature for 20–30 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the racemates of **3**.

General procedure for organocatalytic enantioselective cascade Michael/Michael reaction

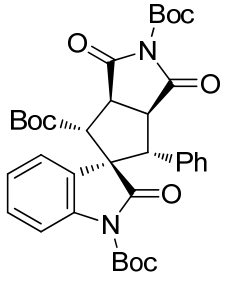


To a dried small bottle were added **2** (0.2 mmol) and catalyst **VI** (6.3 mg, 0.01 mmol, 5 mol %) in THF (1.0 mL). The mixture was stirred at room temperature for 15 min, and **1** (0.22 mmol) was then added. After stirring at room temperature for 20–30 h, the **2** was completely consumped as detected by TLC analysis (petroleum ether/EtOAc 4:1). After that, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the desired product **3**.



3a

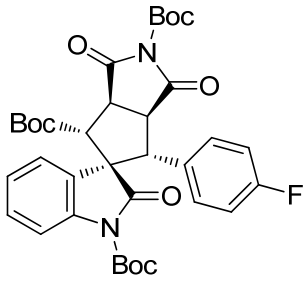
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-1',2-Di-*tert*-butyl 4-ethyl 1,2',3-trioxo-6-phenyl-3a,4,6,6a-etrahydro-1*H*-spiro[cyclopenta[c]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3a): The title compound **3a** was obtained according to the general procedure as a colorless solid (100.2 mg, 83% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 7.7 min, t_{major} = 20.0 min; minor diastereomer: t_R = 8.3, 11.1 min; 86:14 dr, 98% *ee*. M.p. 108–109 °C; $[\alpha]_D^{25}$ –79.3 (*c* 3.99, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.0 Hz, 1H, ArH), 7.21 (t, *J* = 7.6 Hz, 1H, ArH), 7.17–7.08 (m, 3H, ArH), 7.04 (t, *J* = 7.4 Hz, 2H, ArH), 6.93 (d, *J* = 7.6 Hz, 2H, ArH), 4.42 (dd, J_1 = 9.4 Hz, J_2 = 7.8 Hz, 1H, CH), 4.06 (t, *J* = 12.0 Hz, 1H, CH), 4.03 (d, *J* = 7.6 Hz, 1H, CH), 3.94 (d, *J* = 11.6 Hz, 1H, CH), 3.86–3.78 (m, 1H, CH_2), 3.74–3.66 (m, 1H, CH_2), 1.59 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.66 (t, *J* = 7.0 Hz, 1H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 172.9, 171.2, 168.4, 148.3, 145.9, 139.7, 132.2, 129.4, 128.2, 128.1, 127.6, 124.4, 124.1, 123.5, 115.1, 86.5, 84.6, 65.5, 61.5, 59.0, 53.6, 47.7, 45.8, 27.9, 27.7, 13.2 ppm; IR (KBr): $\tilde{\nu}$ 3061, 2982, 2935, 1768, 1730, 1607, 1481, 1466, 1395, 1371, 1348, 1310, 1286, 1256, 1150, 1102, 1032, 842, 757, 737, 700, 634 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{33}H_{40}N_3O_9$ $[M + NH_4]^+$ 622.27591, found 622.27658; calcd. for $C_{33}H_{36}N_2NaO_9$ $[M + Na]^+$ 627.23130, found 627.23228.



3b

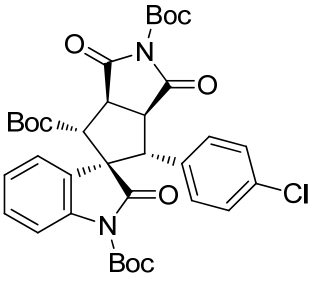
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3b): The title compound **3b** was obtained according to the general procedure as a colorless solid (115.0 mg, 91% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.6 min, t_{major} = 20.5 min; minor diastereomer: t_R = 8.0, 11.9 min; 93:7 dr, 93% *ee*. M.p. 116–117 °C; $[\alpha]_D^{25}$ –91.0 (*c* 4.04, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, *J* = 8.0 Hz, 1H, ArH), 7.24–7.20 (m, 1H,

ArH), 7.17 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H, ArH), 7.13 (d, J_1 = 6.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.10–7.02 (m, 3H, ArH), 6.93 (d, J = 6.8 Hz, 2H, ArH), 4.34 (dd, J_1 = 9.8 Hz, J_2 = 7.8 Hz, 1H, CH), 4.04 (dd, J_1 = 11.8 Hz, J_2 = 9.8 Hz, 1H, CH), 3.96–3.91 (m, 2H, 2CH), 1.58 (s, 18H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 173.0, 171.3, 167.2, 148.4, 146.0, 139.9, 132.4, 129.3, 128.11, 128.08, 127.7, 125.0, 124.1, 123.7, 115.0, 86.4, 84.5, 82.5, 65.4, 58.8, 54.6, 47.8, 45.6, 27.9, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2981, 2935, 1792, 1769, 1732, 1607, 1481, 1466, 1395, 1370, 1350, 1309, 1289, 1255, 1151, 1101, 842, 761, 737, 699, 633 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{44}N_3O_9$ $[M + NH_4]^+$ 650.30721, found 650.30659; calcd. for $C_{35}H_{40}N_2NaO_9$ $[M + Na]^+$ 655.26260, found 655.26259.



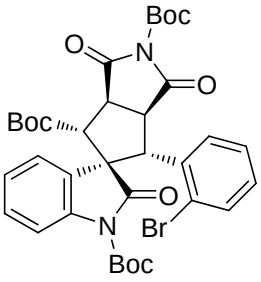
3c

(3a*S*,3'*R*,4*R*,6*R*,6a*S*)- Tri-*tert*-butyl 6-(4-fluorophenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro -1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3c): The title compound **3c** was obtained according to the general procedure as a colorless solid (110.4 mg, 85% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.6 min, t_{major} = 20.1 min; minor diastereomer: t_R = 9.3, 15.8 min; 94:6 dr, 88% *ee*. M.p. 118–119 °C; $[\alpha]_D^{25}$ –79.0 (*c* 1.76, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 8.0 Hz, 1H, ArH), 7.27–7.23 (m, 1H, ArH), 7.18–7.12 (m, 2H, ArH), 6.92 (d, J = 8.8 Hz, 1H, ArH), 6.91 (d, J = 8.8 Hz, 1H, ArH), 6.75 (t, J = 8.8 Hz, 2H, ArH), 4.34 (dd, J_1 = 9.4 Hz, J_2 = 7.8 Hz, 1H, CH), 3.98 (dd, J_1 = 12.0 Hz, J_2 = 9.6 Hz, 1H, CH), 3.93 (d, J = 8.0 Hz, 1H, CH), 3.89 (d, J = 12.0 Hz, 1H, CH), 1.59 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.9, 171.3, 167.1, 162.4 (d, $^1J_{C\text{-}F}$ = –245.9 Hz), 148.3, 145.9, 139.9, 129.5, 129.4 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 128.3 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 124.8, 124.2, 123.6, 115.14, 115.13 (d, $^2J_{C\text{-}F}$ = 21.4 Hz), 86.5, 84.7, 82.5, 65.3, 58.0, 54.5, 48.1, 45.5, 27.9, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3058, 2981, 2934, 1793, 1769, 1733, 1607, 1514, 1481, 1465, 1395, 1371, 1351, 1310, 1255, 1151, 1098, 842, 804, 759, 738, 631 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}FN_3O_9$ $[M + NH_4]^+$ 668.29778, found 668.29774; calcd. for $C_{35}H_{39}FN_2NaO_9$ $[M + Na]^+$ 673.25318, found 673.25288.



3d

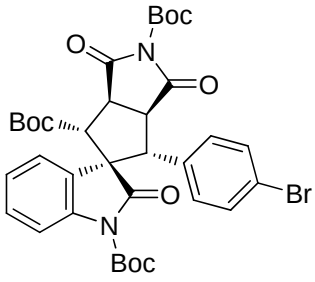
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 6-(4-chlorophenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3d): The title compound **3d** was obtained according to the general procedure as a colorless solid (115.8 mg, 87% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.7 min, t_{major} = 21.3 min; 90:10 dr, 92% *ee*. M.p. 109–110 °C; $[\alpha]_D^{25}$ –81.8 (*c* 1.48, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.4 Hz, 1H, ArH), 7.28–7.24 (m, 1H, ArH), 7.17–7.12 (m, 2H, ArH), 7.04 (d, *J* = 8.4 Hz, 2H, ArH), 6.88 (d, *J* = 8.4 Hz, 2H, ArH), 4.33 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 3.97 (dd, J_1 = 12.0 Hz, J_2 = 10.0 Hz, 1H, CH), 3.93 (d, *J* = 8.0 Hz, 1H, CH), 3.88 (d, *J* = 12.0 Hz, 1H, CH), 1.59 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 172.8, 171.2, 167.0, 148.3, 145.9, 139.9, 134.1, 131.1, 129.6, 129.1, 128.4, 124.6, 124.3, 123.6, 115.3, 86.6, 84.8, 82.6, 65.1, 58.0, 54.7, 48.0, 45.5, 28.0, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2981, 2933, 1792, 1769, 1734, 1608, 1495, 1481, 1465, 1395, 1371, 1351, 1310, 1256, 1151, 1098, 842, 762 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}ClN_3O_9$ $[M + NH_4]^+$ 684.26823, found 684.26752.



3e

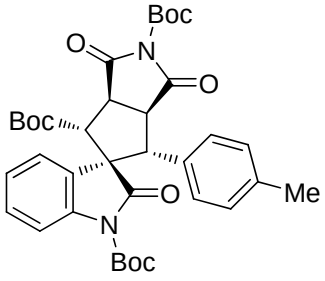
(3a*S*,3'*R*,4*S*,6*R*,6a*S*)-Tri-*tert*-butyl 4-(2-bromophenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,6(3*H*)-tricarboxylate (3e): The title compound **3e** was obtained according to the general procedure as a white solid (126.3 mg, 89% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 60:40, flow rate 0.5 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.2 min, t_{major} = 22.7 min; minor diastereomer: t_R = 19.9, 28.0 min; 96:4 dr, 87% *ee*. M.p. 141–142 °C; $[\alpha]_D^{25}$ –66.9 (*c* 1.65, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 1H, ArH), 7.45 (d, *J* = 8.0 Hz, 1H, ArH), 7.31 (t, *J* = 7.8 Hz, 1H, ArH), 7.25 (d, *J* = 7.6 Hz, 1H, ArH), 7.18 (t, *J* = 7.4 Hz, 1H, ArH), 6.95 (t, *J* = 7.6 Hz, 1H, ArH), 6.85 (t, *J* = 7.4 Hz, 1H, ArH), 6.64 (d, *J* = 8.0 Hz, 1H,

ArH), 4.68 (d, J = 11.6 Hz, 1H, CH), 4.33 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.04 (d, J = 8.0 Hz, 1H, CH), 3.78 (t, J = 10.4 Hz, 1H, CH), 1.58 (s, 9H, CH_3), 1.55 (s, 9H, CH_3), 0.95 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.9, 172.8, 171.0, 167.1, 148.7, 145.9, 140.3, 133.2, 129.6, 129.4, 128.9, 126.6, 125.7, 124.9, 124.1, 124.0, 115.3, 86.4, 84.4, 82.5, 64.2, 55.5, 54.8, 50.7, 45.6, 27.9, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2981, 2932, 1794, 1770, 1732, 1067, 1480, 1465, 1395, 1370, 1351, 1321, 1272, 1256, 1150, 1098, 1033, 842, 759 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{35}H_{43}BrN_3O_9$ $[M + NH_4]^+$ 728.21772, found 728.21894.



3f

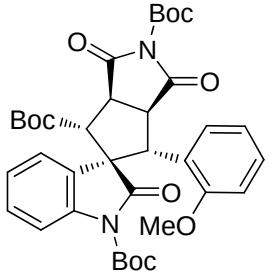
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 4-(4-bromophenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1H-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,6(3*H*)-tricarboxylate (3f): The title compound **3f** was obtained according to the general procedure as a colorless solid (117.8 mg, 83% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 60:40, flow rate 0.5 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 10.0 min, t_{major} = 29.5 min; minor diastereomer: t_R = 19.8, 34.4 min; 92:8 dr, 87% *ee*. M.p. 95–96 ^{o}C; $[\alpha]_D^{25}$ –73.4 (*c* 3.48, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, J = 8.4 Hz, 1H, ArH), 7.29–7.24 (m, 1H, ArH), 7.20–7.12 (m, 4H, ArH), 6.82 (d, J = 8.4 Hz, 2H, ArH), 4.33 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 3.97 (dd, J_1 = 12.0 Hz, J_2 = 10.0 Hz, 1H, CH), 3.93 (d, J = 8.0 Hz, 1H, CH), 3.87 (d, J = 12.0 Hz, 1H, CH), 1.59 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 172.8, 171.2, 167.0, 148.3, 145.9, 139.9, 131.6, 131.4, 129.6, 129.4, 124.6, 124.3, 123.6, 122.4, 115.3, 86.6, 84.8, 82.6, 65.1, 58.1, 54.8, 48.0, 45.5, 28.0, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2980, 2934, 1769, 1732, 1481, 1465, 1395, 1370, 1350, 1309, 1286, 1255, 1151, 1099, 1076, 1010, 842, 760, 737 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{35}H_{43}BrN_3O_9$ $[M + NH_4]^+$ 728.21772, found 728.21822.



3g

(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 1,2',3-trioxo-6-(*p*-tolyl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3g): The

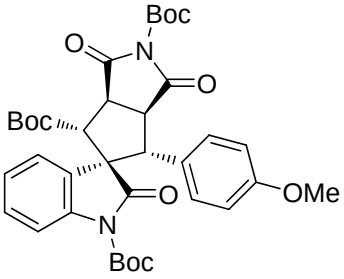
title compound **3g** was obtained according to the general procedure as a colorless solid (122.8 mg, 95% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.2 min, t_{major} = 18.2 min; minor diastereomer: t_R = 8.4, 11.5 min; 93:7 dr, 95% *ee*. M.p. 121–122 °C; $[\alpha]_D^{25}$ –89.4 (*c* 2.80, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 8.4 Hz, 1H, ArH), 7.25–7.21 (m, 1H, ArH), 7.17 (dd, J_1 = 1.0 Hz, J_2 = 7.4 Hz, 1H, ArH), 7.12 (dt, J_1 = 0.8 Hz, J_2 = 7.6 Hz, 1H, ArH), 6.85 (d, J = 8.4 Hz, 1H, ArH), 6.81 (d, J = 8.4 Hz, 1H, ArH), 4.32 (dd, J_1 = 9.8 Hz, J_2 = 7.8 Hz, 1H, CH), 4.01 (dd, J_1 = 12.0 Hz, J_2 = 9.6 Hz, 1H, CH), 3.93 (d, J = 8.0 Hz, 1H, CH), 3.89 (d, J = 12.0 Hz, 1H, CH), 2.16 (s, 3H, CH_3), 1.58 (s, 9H, CH_3), 1.57 (s, 9H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 173.1, 171.3, 167.2, 148.5, 146.0, 139.9, 137.7, 129.3, 129.2, 128.8, 127.5, 125.1, 124.1, 123.7, 115.0, 86.3, 84.4, 82.4, 65.3, 58.6, 54.7, 48.0, 45.5, 27.9, 27.7, 27.0, 20.9 ppm; IR (KBr): $\tilde{\nu}$ 2981, 2934, 1790, 1769, 1733, 1608, 1517, 1481, 1465, 1395, 1370, 1351, 1322, 1310, 1256, 1151, 1099, 1062, 1034, 1000, 842, 813, 759, 737, 701 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{36}H_{46}N_3O_9$ $[M + NH_4]^+$ 664.32286, found 664.32290; calcd. for $C_{36}H_{42}N_2NaO_9$ $[M + Na]^+$ 669.27825, found 669.27788.



3h

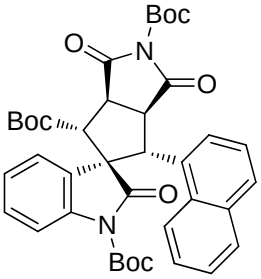
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 6-(2-methoxyphenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3h): The title compound **3h** was obtained according to the general procedure as a white solid (108.5 mg, 82% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 6.9 min, t_{major} = 22.1 min; minor diastereomer: t_R = 9.6, 26.2 min; 94:6 dr, 93% *ee*. M.p. 132–133 °C; $[\alpha]_D^{25}$ –96.6 (*c* 2.16, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, J = 8.4 Hz, 1H, ArH), 7.17–7.13 (m, 1H, ArH), 7.09–7.01 (m, 3H, ArH), 6.92 (d, J = 6.8 Hz, 1H, ArH), 6.64–6.60 (m, 2H, ArH), 4.42 (d, J = 11.2 Hz, 1H, CH), 4.32 (dd, J_1 = 9.8 Hz, J_2 = 7.8 Hz, 1H, CH), 4.22 (t, J = 10.6 Hz, 1H, CH), 4.04 (d, J = 7.6 Hz, 1H, CH), 3.66 (s, 3H, OCH_3), 1.59 (s, 9H, CH_3), 1.57 (s, 9H, CH_3), 0.93 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 173.2, 171.8, 167.4, 157.1, 148.9, 146.0, 139.9, 128.90, 128.86, 128.4, 125.8, 123.9, 123.6, 121.4, 119.8, 114.7, 110.0, 86.2, 84.0, 82.2, 64.4, 55.3, 54.7, 47.5, 45.4, 28.0, 27.7, 26.9 ppm; IR (KBr): $\tilde{\nu}$ 3058, 2980, 2935, 1794, 1770, 1729, 1607, 1496, 1481, 1465, 1395, 1370, 1353, 1304, 1254, 1152,

1099, 1060, 1028, 1005, 843, 788, 774, 753, 702, 635 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{36}H_{46}N_3O_{10}$ $[M + NH_4]^+$ 680.31777, found 680.31752.



3i

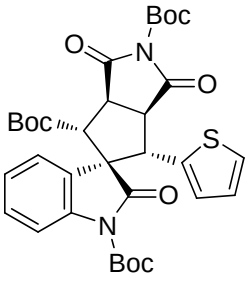
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 6-(4-methoxyphenyl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3i): The title compound **3i** was obtained according to the general procedure as a colorless solid (113.8 mg, 86% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.9 min, t_{major} = 21.1 min; minor diastereomer: t_R = 9.4, 13.5 min; 95:5 dr, 94% *ee*. M.p. 94–95 °C; $[\alpha]_D^{25}$ –89.3 (*c* 3.68, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, *J* = 8.4 Hz, 1H, ArH), 7.17 (t, *J* = 7.6 Hz, 1H, ArH), 7.13–7.04 (m, 2H, ArH), 6.78 (d, *J* = 8.0 Hz, 2H, ArH), 6.50 (d, *J* = 8.0 Hz, 2H, ArH), 4.27–4.23 (m, 1H, CH), 3.92 (t, *J* = 10.8 Hz, 1H, CH), 3.86 (d, *J* = 7.6 Hz, 1H, CH), 3.81 (d, *J* = 12.0 Hz, 1H, CH), 3.58 (s, 3H, OCH_3), 1.51 (s, 9H, CH_3), 1.50 (s, 9H, CH_3), 0.86 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 173.1, 171.4, 167.2, 159.0, 148.4, 145.9, 139.8, 129.3, 128.8, 125.0, 124.2, 124.1, 123.6, 115.0, 113.4, 86.3, 84.5, 82.3, 65.2, 58.2, 54.9, 54.5, 48.1, 45.4, 27.9, 27.6, 26.9 ppm; IR (KBr): $\tilde{\nu}$ 3057, 2981, 2935, 1792, 1769, 1731, 1611, 1516, 1481, 1465, 1395, 1371, 1352, 1310, 1257, 1152, 1099, 1075, 1063, 1034, 843, 788, 759, 739 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{36}H_{46}N_3O_{10}$ $[M + NH_4]^+$ 680.31777, found 680.31876.



3j

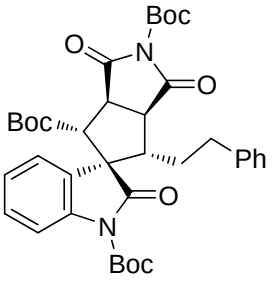
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 6-(naphthalen-1-yl)-1,2',3-trioxo-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3j): The title compound **3j** was obtained according to the general procedure as a white solid (122.7 mg, 90% yield). HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 50:50, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 9.1 min, t_{major} = 17.5 min; minor diastereomer: t_R = 20.9, 30.9 min; 95:5 dr, 90% *ee*. M.p. 130–131 °C; $[\alpha]_D^{25}$ –222.5 (*c* 2.69,

CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (d, J = 8.8 Hz, 1H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.57 (d, J = 7.6 Hz, 1H, ArH), 7.49 (t, J = 7.4 Hz, 2H, ArH), 7.41 (t, J = 7.4 Hz, 1H, ArH), 7.27 (dd, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1H, ArH), 7.20–7.12 (m, 2H, ArH), 7.06–7.00 (m, 2H, ArH), 4.89 (d, J = 11.6 Hz, 1H, CH), 4.43 (dd, J_1 = 9.6 Hz, J_2 = 8.0 Hz, 1H, CH), 4.19 (t, J = 10.8 Hz, 1H, CH), 4.15 (d, J = 8.0 Hz, 1H, CH), 1.56 (s, 9H, CH_3), 1.36 (s, 9H, CH_3), 0.93 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 173.1, 171.5, 167.3, 148.2, 146.0, 139.9, 133.5, 131.7, 129.2, 128.6, 128.53, 128.50, 126.4, 125.7, 125.5, 125.4, 124.0, 123.9, 122.9, 115.0, 86.4, 84.0, 82.5, 65.1, 54.9, 52.2, 49.8, 45.5, 27.7, 27.6, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3054, 2981, 2934, 1790, 1769, 1733, 1608, 1481, 1465, 1395, 1370, 1353, 1309, 1287, 1255, 1152, 1104, 1062, 842, 776, 758, 738, 702 632 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{39}H_{46}N_3O_9$ $[M + NH_4]^+$ 700.32286, found 700.32395.



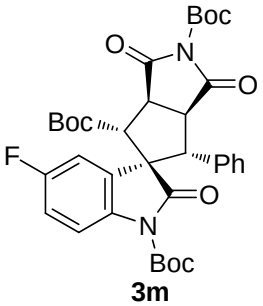
3k

(3a*S*,3'*S*,4*R*,6*S*,6a*R*)-Tri-*tert*-butyl 1,2',3-trioxo-6-(thiophen-2-yl)-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3k): The title compound **3k** was obtained according to the general procedure as a colorless solid (117.3 mg, 92% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 7.2 min, t_{major} = 22.5 min; minor diastereomer: t_R = 8.2, 11.1 min; 95:5 dr, 94% *ee*. M.p. 115–116 °C; $[\alpha]_D^{25}$ –70.1 (*c* 2.86, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.4 Hz, 1H, ArH), 7.33–7.28 (m, 1H, ArH), 7.18–7.13 (m, 2H, ArH), 7.00 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H, ArH), 6.78–6.73 (m, 2H, ArH), 4.31 (dd, J_1 = 10.0 Hz, J_2 = 8.0 Hz, 1H, CH), 4.22 (d, J = 12.0 Hz, 1H, CH), 3.90–3.82 (m, 2H, CH), 1.60 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.96 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 172.6, 170.8, 166.9, 148.5, 145.8, 140.3, 135.6, 129.7, 127.1, 126.3, 125.6, 124.8, 124.4, 123.9, 115.2, 86.5, 84.6, 82.5, 64.8, 54.7, 54.3, 50.6, 45.5, 27.9, 27.6, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3057, 2981, 2935, 1793, 1769, 1732, 1608, 1481, 1466, 1395, 1371, 1350, 1320, 1309, 1256, 1152, 1100, 842, 759, 738, 702 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{33}H_{42}N_3O_9S$ $[M + NH_4]^+$ 656.26363, found 656.26416.



3l

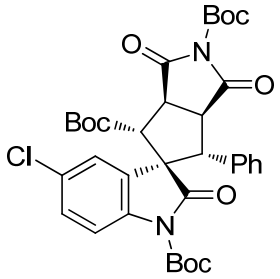
(3a*S*,3'*R*,4*R*,6*S*,6a*S*)-Tri-*tert*-butyl 1,2',3-trioxo-6-phenethyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3l): The title compound **3l** was obtained according to the general procedure as a colorless solid (83.2 mg, 63% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 6.4 min, t_{major} = 7.3 min; minor diastereomer: t_R = 4.4, 4.6, 12.8, 17.2 min; 86:14 dr, 96% *ee*. M.p. 84–85 °C; $[\alpha]_D^{25}$ –35.1 (*c* 2.10, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 8.0 Hz, 1H, ArH), 7.40 (t, *J* = 7.8 Hz, 1H, ArH), 7.20–7.15 (m, 3H, ArH), 7.11 (t, *J* = 7.0 Hz, 1H, ArH), 7.04 (d, *J* = 7.6 Hz, 1H, ArH), 6.89 (d, *J* = 7.6 Hz, 2H, ArH), 4.17 (t, *J* = 9.0 Hz, 1H, CH), 3.74 (d, *J* = 8.0 Hz, 1H, CH), 3.30 (t, *J* = 10.4 Hz, 1H, CH), 2.89–2.83 (m, 1H, CH), 2.63–2.55 (m, 1H, CH_2), 2.32–2.24 (m, 1H, CH_2), 1.88–1.79 (m, 1H, CH_2), 1.64 (s, 9H, CH_3), 1.60 (s, 9H, CH_3), 1.38–1.29 (m, 1H, CH_2), 0.98 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 172.7, 172.6, 166.9, 148.8, 146.0, 140.9, 140.2, 129.6, 128.3, 128.1, 125.9, 125.0, 124.6, 123.8, 115.4, 86.5, 84.8, 82.5, 63.1, 56.2, 53.0, 50.6, 45.9, 33.3, 32.6, 28.0, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3062, 2981, 2933, 1794, 1767, 1732, 1607, 1496, 1480, 1465, 1395, 1371, 1350, 1323, 1286, 1256, 1151, 1106, 1076, 843, 758, 738, 701, 633 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{48}N_3O_9$ $[M + NH_4]^+$ 678.33851, found 678.33953; calcd. for $C_{37}H_{44}N_2NaO_9$ $[M + Na]^+$ 683.29390, found 683.29477.



3m

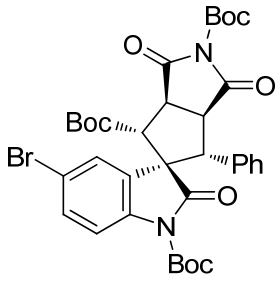
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-tert-butyl 5'-fluoro-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3m): The title compound **3m** was obtained according to the general procedure as a colorless solid (101.2 mg, 78% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 0.5 mL/min, detection at 254 nm): major diastereomer: t_{major} = 9.9 min, t_{minor} = 10.7 min; minor diastereomer: t_R = 17.2 min; 99:1 dr, 91% *ee*. M.p. 155–156 °C; $[\alpha]_D^{25}$ –75.1 (*c* 2.12,

CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, J_1 = 9.8 Hz, J_2 = 4.6 Hz, 1H, ArH), 7.14–7.06 (m, 3H, ArH), 6.98–6.90 (m, 4H, ArH), 4.32 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.04 (dd, J_1 = 12.0 Hz, J_2 = 10.0 Hz, 1H, CH), 3.96 (d, J = 7.6 Hz, 1H, CH), 3.95 (d, J = 12.0 Hz, 1H, CH), 1.58 (s, 18H, CH_3), 0.99 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 172.8, 171.1, 166.9, 159.3 (d, $^1J_{C\text{-}F}$ = –243.5 Hz), 148.4, 145.9, 135.9 (d, $^4J_{C\text{-}F}$ = 2.4 Hz), 132.1, 128.28, 128.25, 127.5, 126.7 (d, $^3J_{C\text{-}F}$ = 7.7 Hz), 116.3 (d, $^3J_{C\text{-}F}$ = 7.8 Hz), 115.7 (d, $^2J_{C\text{-}F}$ = 22.3 Hz), 111.4 (d, $^2J_{C\text{-}F}$ = 24.6 Hz), 86.5, 84.8, 82.7, 65.6 (d, $^4J_{C\text{-}F}$ = 1.6 Hz), 58.7, 54.5, 47.4, 45.4, 27.9, 27.7, 27.1 ppm; IR (KBr): $\tilde{\nu}$ 3064, 2981, 2934, 1769, 1733, 1607, 1483, 1457, 1395, 1371, 1345, 1306, 1253, 1150, 1106, 1078, 1059, 1009, 868, 841, 820, 763, 737, 700 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}FN_3O_9$ $[M + NH_4]^+$ 668.29778, found 668.29844.



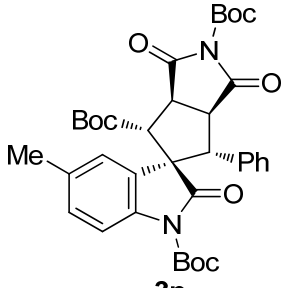
3n

(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 5'-chloro-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3n): The title compound **3n** was obtained according to the general procedure as a colorless solid (113.0 mg, 85% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 0.5 mL/min, detection at 254 nm): major diastereomer: t_{major} = 9.7 min, t_{minor} = 10.3 min; minor diastereomer: t_R = 10.9, 14.1 min; 90:10 dr, 86% *ee*. M.p. 119–120 °C; $[\alpha]_D^{25}$ –110.3 (*c* 2.34, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (d, J = 8.8 Hz, 1H, ArH), 7.20 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H, ArH), 7.14 (d, J = 2.0 Hz, 1H, ArH), 7.12–7.07 (m, 3H, ArH), 6.95 (dd, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 2H, ArH), 4.33 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.05 (dd, J_1 = 11.8 Hz, J_2 = 9.8 Hz, 1H, CH), 3.96 (d, J = 8.0 Hz, 1H, CH), 3.93 (d, J = 12.0 Hz, 1H, CH), 1.58 (s, 18H, CH_3), 0.99 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.8, 172.8, 171.0, 166.9, 148.2, 145.9, 138.4, 132.0, 129.6, 129.2, 128.30, 128.27, 127.5, 127.0, 123.7, 116.2, 86.5, 84.9, 82.7, 65.4, 58.8, 54.4, 47.5, 45.5, 27.9, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2979, 2934, 1770, 1735, 1587, 1476, 1456, 1395, 1371, 1336, 1306, 1272, 1254, 1150, 1114, 1076, 841, 778, 761, 735, 699 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}ClN_3O_9$ $[M + NH_4]^+$ 684.26823, found 684.26914.



3o

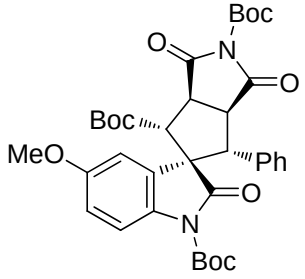
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-tert-butyl 5'-bromo-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3o): The title compound **3o** was obtained according to the general procedure as a colorless solid (120.6 mg, 85% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 0.5 mL/min, detection at 254 nm): major diastereomer: t_{major} = 9.8 min, t_{minor} = 10.4 min; minor diastereomer: t_R = 10.9, 14.6 min; 89:11 dr, 86% *ee*. M.p. 122–123 °C; $[\alpha]_D^{25}$ –121.1 (*c* 1.51, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 8.8 Hz, 1H, ArH), 7.35 (dd, J_1 = 8.6 Hz, J_2 = 1.8 Hz, 1H, ArH), 7.28 (d, J = 1.6 Hz, 1H, ArH), 7.12–7.07 (m, 3H, ArH), 6.95 (d, J = 8.0 Hz, 2H, ArH), 4.34 (dd, J_1 = 9.8 Hz, J_2 = 7.8 Hz, 1H, CH), 4.05 (dd, J_1 = 11.6 Hz, J_2 = 10.0 Hz, 1H, CH), 3.96 (d, J = 7.6 Hz, 1H, CH), 3.92 (d, J = 12.0 Hz, 1H, CH), 1.58 (s, 18H, CH_3), 0.99 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.8, 171.0, 166.9, 148.2, 145.9, 138.9, 132.2, 132.0, 128.31, 128.27, 127.5, 127.4, 126.5, 116.9, 116.6, 86.5, 85.0, 82.7, 65.3, 58.8, 54.4, 47.5, 45.5, 27.9, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 2980, 2934, 1770, 1733, 1473, 1457, 1395, 1371, 1335, 1306, 1274, 1255, 1150, 1114, 1073, 1004, 841, 762, 736, 699 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}BrN_3O_9$ $[M + NH_4]^+$ 728.21772, found 728.21888; calcd. for $C_{35}H_{39}BrN_2NaO_9$ $[M + Na]^+$ 733.17311, found 733.17412.



3p

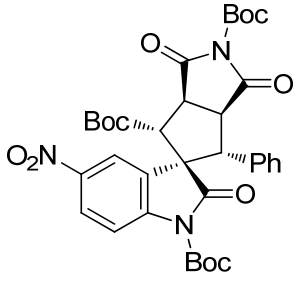
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-tert-butyl 5'-methyl-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3p): The title compound **3p** was obtained according to the general procedure as a colorless solid (113.5 mg, 88% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 4.5 min, t_{major} = 13.0 min; minor diastereomer: t_R = 6.5, 10.1 min; 91:9 dr, 90% *ee*. M.p. 112–113 °C; $[\alpha]_D^{25}$ –102.0 (*c* 1.51, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.4 Hz, 1H, ArH), 7.11–7.01 (m, 4H, ArH), 6.94 (t, J = 6.8 Hz, 3H, ArH), 4.34 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.04 (t, J =

10.8 Hz, 1H, CH), 3.94 (d, J = 7.6 Hz, 1H, CH), 3.90 (d, J = 12.0 Hz, 1H, CH), 2.33 (s, 3H, CH_3), 1.58 (s, 9H, CH_3), 1.57 (s, 9H, CH_3), 0.94 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 173.0, 171.3, 167.2, 148.5, 146.0, 137.5, 133.8, 132.4, 129.7, 128.1, 127.7, 125.0, 124.1, 114.8, 86.4, 84.3, 82.4, 65.4, 58.8, 54.5, 47.9, 45.6, 27.9, 27.7, 27.0, 21.1 ppm; IR (KBr): $\tilde{\nu}$ 3063, 2981, 2933, 1769, 1732, 1489, 1457, 1395, 1371, 1341, 1310, 1256, 1153, 1115, 1079, 1063, 841, 820, 763, 737, 700 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{36}H_{46}N_3O_9$ [M + NH_4]$^+$ 664.32286, found 664.32394.



3q

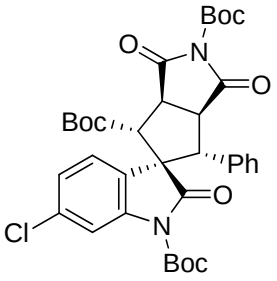
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 5'-methoxy-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3q): The title compound **3q** was obtained according to the general procedure as a colorless solid (115.1 mg, 87% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.9 min, t_{major} = 6.5 min; minor diastereomer: t_R = 7.2, 9.3 min; 92:8 dr, 92% *ee*. M.p. 110–111 ^{o}C; $[\alpha]_D^{25}$ –102.8 (*c* 1.76, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, J = 8.4 Hz, 1H, ArH), 7.12–7.05 (m, 3H, ArH), 6.96 (d, J = 7.2 Hz, 2H, ArH), 6.75–6.72 (m, 2H, ArH), 4.32 (t, J = 8.6 Hz, 1H, CH), 4.03 (t, J = 10.8 Hz, 1H, CH), 3.94 (d, J = 8.0 Hz, 1H, CH), 3.92 (d, J = 12.8 Hz, 1H, CH), 3.78 (s, 3H, OCH_3), 1.57 (s, 18H, CH_3), 0.97 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 172.9, 171.3, 167.1, 156.5, 148.5, 145.9, 133.3, 132.4, 128.1, 127.7, 126.3, 115.8, 113.2, 111.0, 86.4, 84.3, 82.4, 65.6, 58.8, 55.9, 54.6, 47.7, 45.6, 28.0, 27.7, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3064, 2981, 2936, 1768, 1729, 1487, 1457, 1395, 1371, 1308, 1269, 1253, 1152, 1116, 1079, 1060, 1040, 840, 763, 737, 699 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{36}H_{46}N_3O_{10}$ [M + NH_4]$^+$ 680.31777, found 680.31853; for $C_{36}H_{42}N_2NaO_{10}$ [M + Na]$^+$ 685.27317, found 685.27406.



3r

(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 5'-nitro-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1

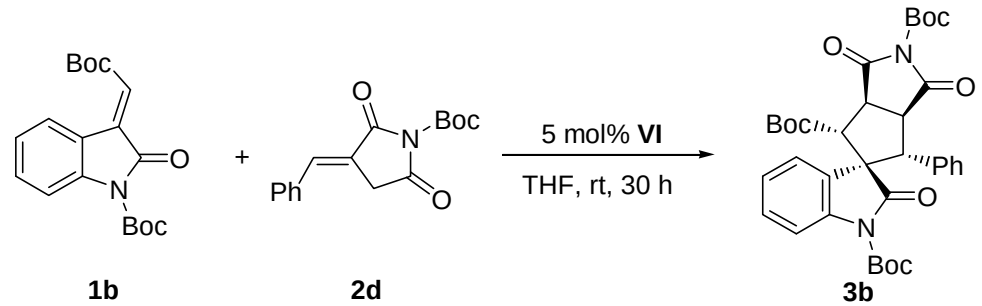
***H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3r):** The title compound **3r** was obtained according to the general procedure as a colorless solid (98.6 mg, 73% yield). HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 85:15, flow rate 0.8 mL/min, detection at 254 nm): major diastereomer: t_{major} = 12.0 min, t_{minor} = 14.8 min; minor diastereomer: t_R = 17.5, 27.6 min; 97:3 dr, 84% *ee*. M.p. 127–128 °C; $[\alpha]_D^{25}$ –120.0 (*c* 1.76, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (dd, J_1 = 9.0 Hz, J_2 = 2.2 Hz, 1H, ArH), 8.04 (d, J = 2.4 Hz, 1H, ArH), 7.80 (d, J = 9.2 Hz, 1H, ArH), 7.14–7.06 (m, 3H, ArH), 6.97–6.95 (m, 2H, ArH), 4.46 (dd, J_1 = 9.8 Hz, J_2 = 7.8 Hz, 1H, CH), 4.21 (dd, J_1 = 11.6 Hz, J_2 = 10.0 Hz, 1H, CH), 4.02 (d, J = 11.6 Hz, 1H, CH), 4.01 (d, J = 7.6 Hz, 1H, CH), 1.61 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.98 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 172.6, 170.8, 166.6, 147.9, 145.8, 145.0, 143.9, 131.7, 128.52, 128.47, 127.4, 126.6, 125.6, 118.9, 115.0, 86.6, 85.9, 83.0, 65.3, 58.7, 54.5, 47.2, 45.4, 27.9, 27.7, 27.1 ppm; IR (KBr): $\tilde{\nu}$ 3062, 2981, 2934, 1804, 1772, 1739, 1529, 1476, 1457, 1371, 1345, 1307, 1280, 1256, 1150, 1119, 1101, 865, 842, 762, 736, 700 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}N_4O_{11}$ $[M + NH_4]^+$ 695.29228, found 695.29289.



3s

(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-Tri-*tert*-butyl 6'-chloro-1,2',3-trioxo-6-phenyl-3a,4,6,6a-tetrahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-1',2,4(3*H*)-tricarboxylate (3s): The title compound **3s** was obtained according to the general procedure as a colorless solid (102.3 mg, 77% yield). HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_{minor} = 5.9 min, t_{major} = 7.0 min; >99:1 dr, 94% *ee*. M.p. 129–130 °C; $[\alpha]_D^{25}$ –99.3 (*c* 2.45, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (s, 1H, ArH), 7.15–7.07 (m, 5H, ArH), 6.94 (d, J = 7.2 Hz, 2H, ArH), 4.32 (dd, J_1 = 9.6 Hz, J_2 = 7.6 Hz, 1H, CH), 4.04 (dd, J_1 = 11.8 Hz, J_2 = 9.8 Hz, 1H, CH), 3.94 (d, J = 7.8 Hz, 1H, CH), 3.93 (d, J = 13.2 Hz, 1H, CH), 1.59 (s, 9H, CH_3), 1.58 (s, 9H, CH_3), 0.98 (s, 9H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 172.9, 171.2, 167.0, 148.1, 145.8, 140.7, 135.1, 132.0, 128.32, 128.27, 127.5, 124.5, 124.1, 123.4, 115.7, 86.5, 85.1, 82.7, 65.1, 58.6, 54.6, 47.5, 45.3, 27.8, 27.6, 27.0 ppm; IR (KBr): $\tilde{\nu}$ 3065, 2981, 2936, 1800, 1770, 1733, 1607, 1586, 1480, 1457, 1425, 1395, 1371, 1350, 1312, 1281, 1254, 1150, 1109, 1083, 1057, 843, 762, 737, 699, 639 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{35}H_{43}ClN_3O_9$ $[M + NH_4]^+$ 684.2682, found 684.2678.

Gram-scale asymmetric cascade Michael/Michael reaction of α-alkylidene succinimide 2d to 1b.



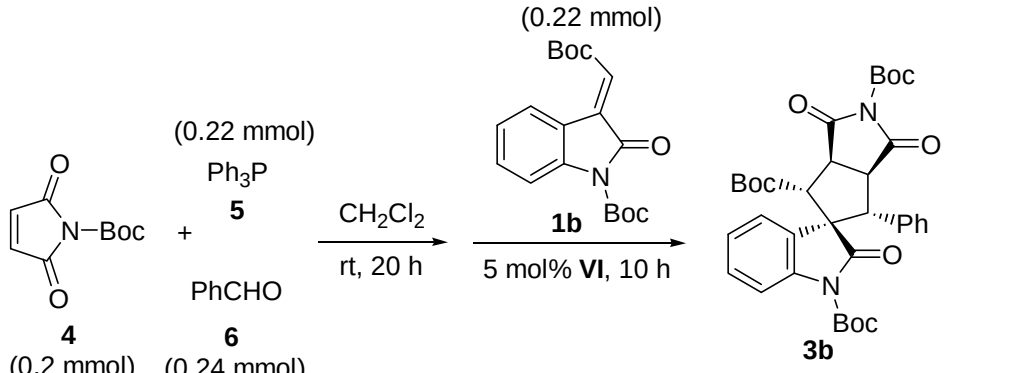
1b
4.4 mmol

2d
4.0 mmol

3b
2.14 g, 85% yield
92:8 dr, 91% ee

To a dried 50 mL bottle were added **2d** (4.0 mmol, 0.574 g) and catalyst **VI** (126.5 mg, 0.2 mmol, 5 mol %) in THF (20.0 mL). The mixture was stirred at room temperature for 30 min, and **1b** (1.52 g, 4.4 mmol) was then added. After stirring at room temperature for 30 h, the **2d** was completely consumped as detected by TLC analysis (petroleum ether/EtOAc 4:1). Product **3b** was obtained by silica gel column chromatography (petroleum ether/EtOAc 5:1), as a colorless solid (2.14 g, 85% yield) with 92:8 dr and 91% ee.

One-pot four-component reaction for the synthsis of 3b.



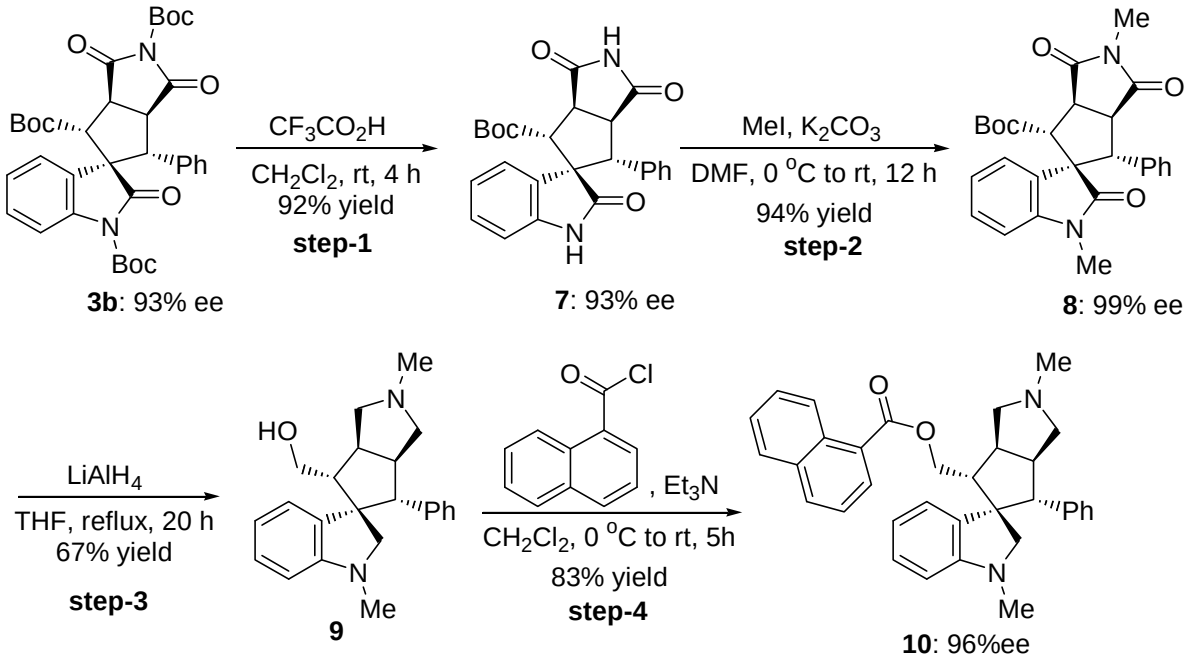
4
(0.2 mmol)

(0.24 mmol)

54% yield, 89:11 dr, 96% ee

The *N*-Boc prodected maleimide (0.2 mmol, 39.4 mg), triphenylphosphine (57.7 mg, 0.22 mmol) and benzaldehyde (25.4 mg, 2.4 mmol), were dissolved in anhydrous CH_2Cl_2 (1.0 mL) and stirred at room temperature for 20 h. After that, catalyst **VI** (6.3 mg, 0.01 mmol, 5 mol %) and **1b** (76.0 mg, 0.22 mmol) were added. After stirring at room temperature for 10 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/EtOAc 5:1) to afford the desired product **3b** as a colorless solid (68.3 mg, 54% yield) with 89:11 dr and 96% ee.

Synthetic transformation of Michael/Michael adduct 3b.

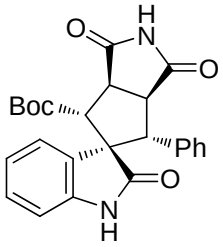


Step-1: The major diastereomer of **3b** (1.26 g, 2.0 mmol) was dissolved in CH_2Cl_2 (30 mL) at room temperature. TFA was added dropwise and the reaction mixture was stirred at room temperature for another 4 h. After that, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/EtOAc 1:1) to afford the desired product **7** as a white solid (0.795 g, 92% yield).

Step-2: To a solution of product **7** (0.52 g, 1.2 mmol) in DMF (10 mL) was added K_2CO_3 (1.0 g, 7.2 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 min. Then 0.3 mL MeI (0.68 g, 4.8 mmol) was added dropwise over a period of 10 min into the stirred reaction mixture. After the addition of the MeI was complete, the reaction mixture was allowed to stir at room temperature. The mixture was stirred for 12 h and was then quenched with 100 water, the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic phases were dried over anhydrous Na_2SO_4. The solvent was removed in vacuo and the residue was purified by silica gel flash column chromatography (petroleum ether/ethyl acetate = 2:1) to afford **8** as a white solid (0.52 g, 94% yield).

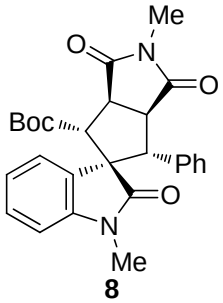
Step-3: Compound **8** (92.0 mg, 0.2 mmol) was dissolved in dry THF (4 mL) at 0 °C under a argon atmosphere. Lithium aluminium hydride (60.7 mg, 1.6 mmol) was added in portions. Cooling was removed and the mixture was heated at reflux for 20 h protected from air. The mixture was cooled to 0 °C and quenched with EtOAc. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 10:1) to afford the product **9** as a pale yellow soild (46.6 mg, 67% yield).

Step-4: To a stirred solution of product **9** (52.2 mg, 0.15 mmol) in CH_2Cl_2 (3 mL) was added Et_3N (51 mg, 0.5 mmol) at 0 °C. Then naphthoyl chlorid (95 mg, 0.5 mmol) in 2 mL CH_2Cl_2 was added dropwise into the stirred reaction mixture. The reaction mixture was allowed to stir at room temperature for another 5 h, the product **9** was completely consumped as detected by TLC analysis. After that, the reaction mixture was concentrated and directly purified by silica gel column chromatography (CH_2Cl_2/MeOH = 30:1) to afford the desired product **10** as a pale yellow soild (62.5 mg, 83% yield).



7

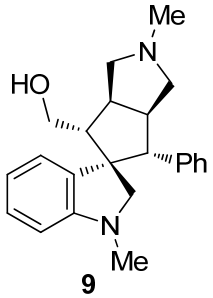
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-*tert*-Butyl 1,2',3-trioxo-6-phenyl-2,3,3a,4,6,6a-hexahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indoline]-4-carboxylate (7): HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): t_{minor} = 6.9 min, t_{major} = 9.6 min; 93% *ee*. M.p. 171–173 °C; $[\alpha]_D^{25}$ –127.2 (*c* 2.48, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.28 (s, 1H, NH), 8.79 (s, 1H, NH), 7.21 (d, *J* = 7.2 Hz, 1H, ArH), 7.15–6.99 (m, 5H, ArH), 6.95 (d, *J* = 7.6 Hz, 2H, ArH), 6.66 (d, *J* = 7.6 Hz, 1H, ArH), 4.39 (t, *J* = 8.6 Hz, 1H, CH), 4.03 (t, *J* = 10.6 Hz, 1H, CH), 3.89–3.85 (m, 2H, CH), 0.98 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4, 178.1, 176.7, 167.9, 141.0, 133.0, 129.3, 128.1, 128.05, 127.97, 126.5, 124.6, 122.5, 110.3, 82.5, 66.1, 58.0, 53.5, 49.5, 46.9, 27.2 ppm; IR (KBr): $\tilde{\nu}$ 3239, 3063, 2978, 1776, 1718, 1619, 1486, 1472, 1456, 1369, 1340, 1293, 1248, 1183, 1155, 836, 746, 698, 679 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{28}N_3O_5$ $[M + NH_4]^+$ 450.20235, found 450.20285; calcd. for $C_{25}H_{24}N_2NaO_5$ $[M + Na]^+$ 455.15774, found 455.15834.



8

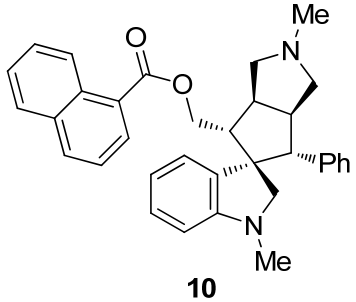
(3a*S*,3'*R*,4*R*,6*R*,6a*S*)-*tert*-Butyl 1',2-dimethyl-1,2',3-trioxo-6-phenyl-2,3,3a,4,6,6a-hexahydro-1*H*-spiro[cyclopenta[c]pyrrole-5,3'-indoline]-4-carboxylate (8): HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 15.8 min; >99% *ee*. M.p. 237–239 °C; $[\alpha]_D^{25}$ –135.5 (*c* 3.40, CH_2Cl_2); ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.21–7.16 (m, 2H, ArH), 7.07–7.00 (m, 4H, ArH), 6.92 (d, J = 7.2 Hz, 2H, ArH), 6.57 (d, J = 8.0 Hz, 1H, ArH), 4.33 (t, J = 8.6 Hz, 1H, CH), 4.03 (dd, J_1 = 9.6 Hz, J_2 = 11.6 Hz, 1H, CH), 3.83 (d, J = 8.0 Hz, 1H, CH), 3.76 (d, J = 11.6 Hz, 1H, CH), 3.02 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 0.92 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.2, 176.0, 175.5, 167.8, 143.6, 133.1, 129.0, 127.7, 127.64, 127.60, 126.1, 124.1, 122.2, 107.9, 81.6, 65.3, 57.8, 53.1, 47.7, 45.7, 27.1, 26.1, 25.0 ppm; IR (KBr): $\tilde{\nu}$ 3059, 2978, 2935, 1779, 1706, 1612, 1496, 1471, 1455, 1434, 1378, 1352, 1294, 1262, 1155, 1137, 1099, 1021, 960, 843, 809, 755, 735, 699 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{27}H_{29}N_2O_5$ $[M + H]^+$ 461.20710, found 461.20760.



9

((3a*S*,3'*R*,4*R*,6*R*,6a*S*)-1',2-Dimethyl-4-phenyl-2,3,3a,4,6,6a-hexahydro-1*H*-spiro[cyclopenta[*c*]pyrrole-5,3'-indolin]-6-yl)methanol (9): The enantiomers of title compound **9** can not be seprated by chiral HPLC analysis. M.p. 61–62 °C; $[\alpha]_D^{25}$ –183.4 (*c* 1.53, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 7.2 Hz, 1H, ArH), 7.21–7.08 (m, 6H, ArH), 6.83 (t, J = 7.6 Hz, 1H, ArH), 6.51 (d, J = 7.6 Hz, 1H, ArH), 4.19 (br s, 1H, OH), 3.42 (dd, J_1 = 11.8 Hz, J_2 = 1.8 Hz, 1H, CH), 3.34 (d, J = 9.2 Hz, 1H, CH), 3.29–3.21 (m, 2H, CH_2), 2.99 (d, J = 8.8 Hz, 1H, CH), 2.91 (d, J = 11.6 Hz, 1H, CH), 2.88–2.82 (m, 1H, CH_2), 2.80 (d, J = 11.6 Hz, 1H, CH_2), 2.57 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 2.41–2.36 (m, 2H, CH_2), 2.28–2.25 (m, 1H, CH_2), 2.18 (dd, J_1 = 9.2 Hz, J_2 = 6.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.6, 139.3, 130.2, 130.1, 128.1, 127.9, 126.6, 125.9, 119.2, 109.8, 64.1, 63.8, 61.5, 61.1, 60.9, 60.7, 59.0, 48.2, 43.1, 41.8, 36.2 ppm; IR (KBr): $\tilde{\nu}$ 3358, 3030, 2941, 2850, 2783, 1602, 1492, 1454, 1424, 1384, 1350, 1303, 1259, 1206, 1156, 1139, 1104, 1044, 1027, 979, 744, 701 cm^{-1}; HRMS (ESI): m/z calcd. for $C_{23}H_{29}N_2O$ $[M + H]^+$ 349.2274, found 349.2279.



10

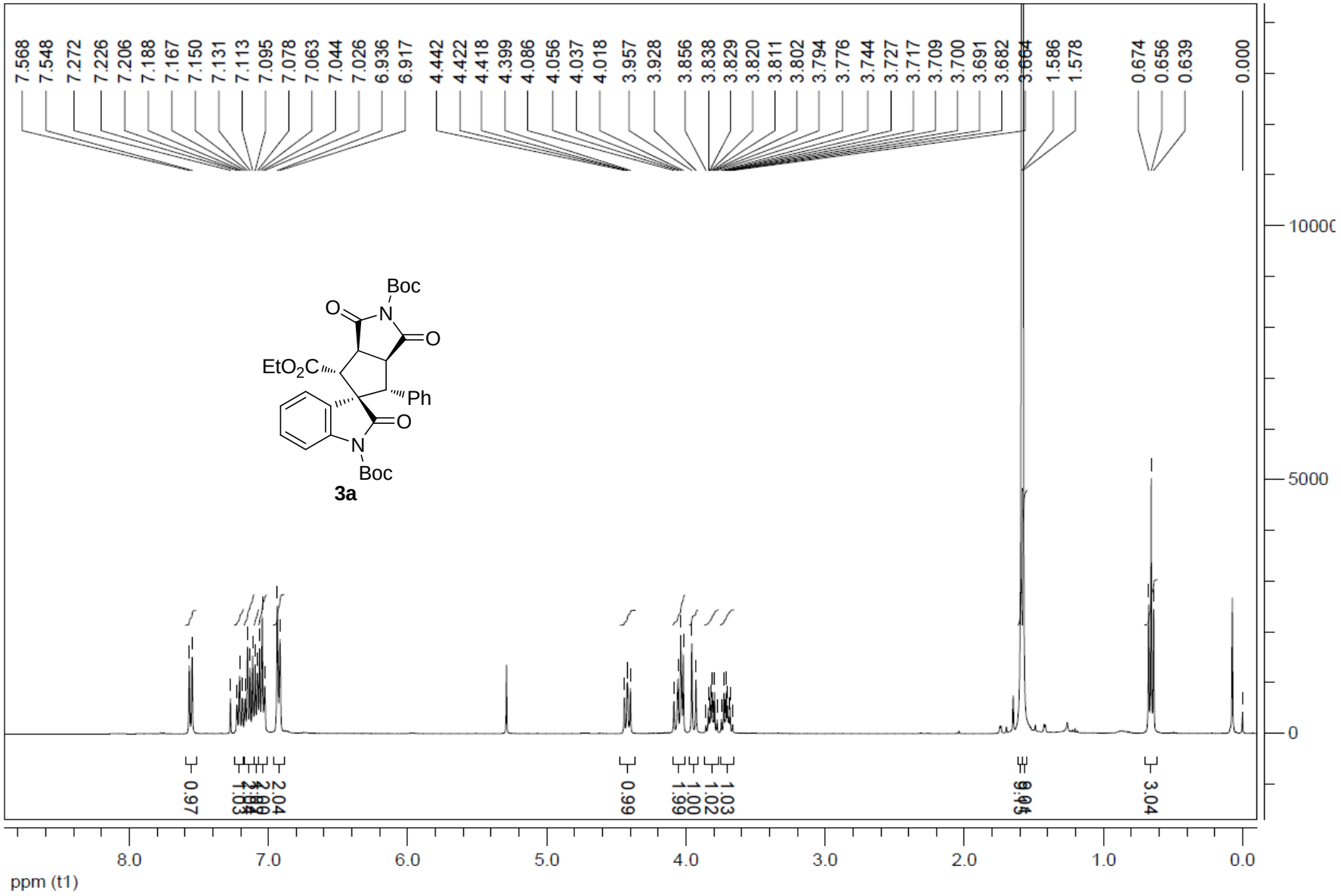
((3a*S*,3'*R*,4*R*,6*R*,6a*S*)-1',2-Dimethyl-4-phenyl-2,3,3a,4,6,6a-hexahydro-1*H*-spiro[cyclopen

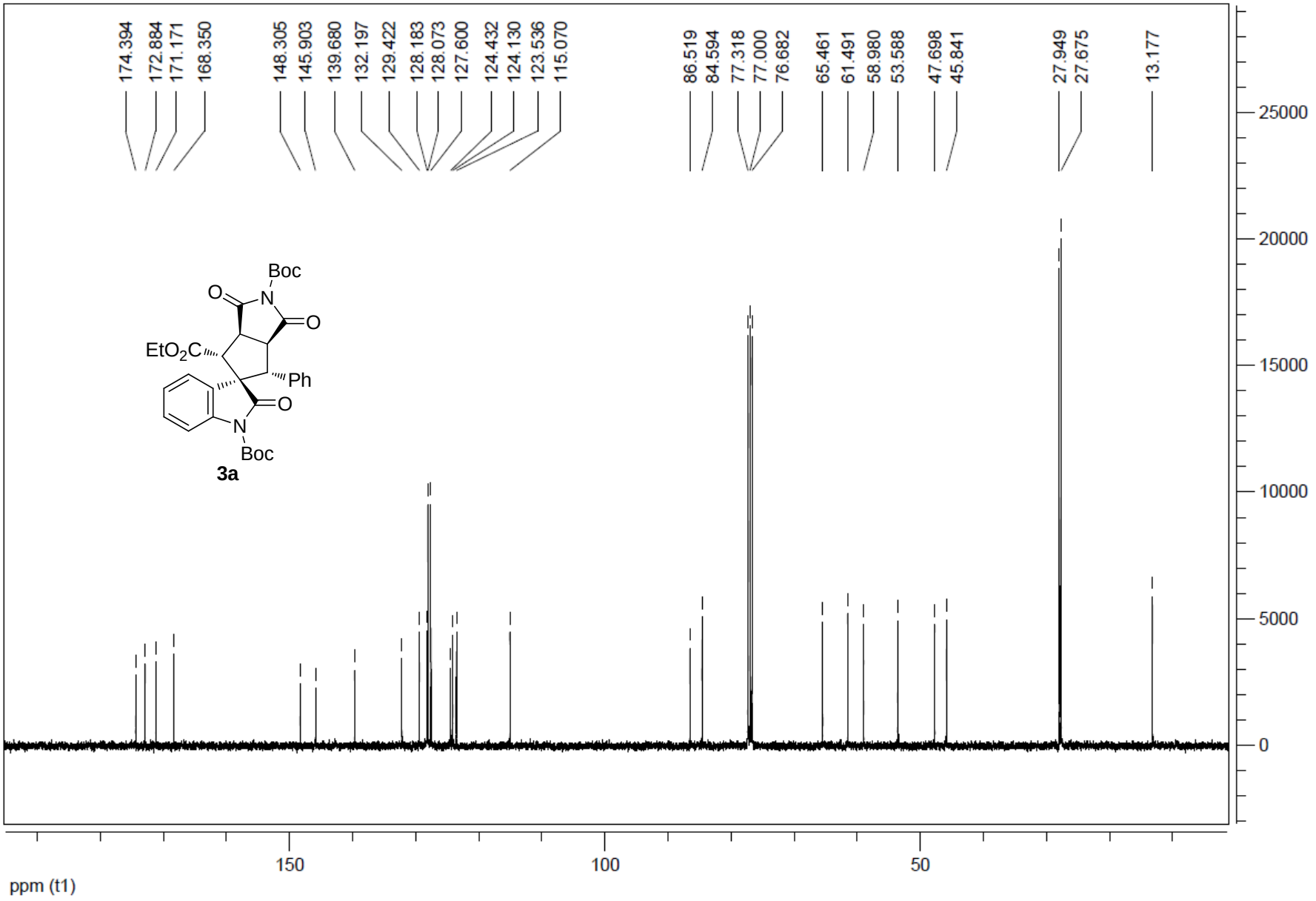
ta[*c*]pyrrole-5,3'-indolin]-6-yl)methyl 1-naphthoate (10): HPLC (Daicel Chiralpak AD-H, *n*-hexane/2-propanol = 95:5, flow rate 1.0 mL/min, detection at 254 nm): t_{major} = 8.4 min, t_{minor} = 10.3 min; 96% *ee*. M.p. 57–58 ^{o}C; $[\alpha]_D^{25}$ –10.0 (*c* 2.03, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.87 (d, *J* = 8.8 Hz, 1H, ArH), 8.10 (d, *J* = 6.8 Hz, 1H, ArH), 7.99 (d, *J* = 8.0 Hz, 1H, ArH), 7.86 (d, *J* = 8.0 Hz, 1H, ArH), 7.58 (t, *J* = 7.8 Hz, 1H, ArH), 7.52 (d, *J* = 7.6 Hz, 1H, ArH), 7.48 (t, *J* = 7.8 Hz, 1H, ArH), 7.28 (d, *J* = 7.6 Hz, 1H, ArH), 7.07–7.02 (m, 4H, ArH), 6.96–6.94 (m, 2H, ArH), 6.67 (t, *J* = 7.4 Hz, 1H, ArH), 6.18 (t, *J* = 8.0 Hz, 1H, ArH), 4.53 (dd, J_1 = 11.2 Hz, J_2 = 5.6 Hz, 1H, CH), 4.27 (dd, J_1 = 11.2 Hz, J_2 = 8.8 Hz, 1H, CH), 3.47 (d, *J* = 9.2 Hz, 1H, CH), 3.35 (d, *J* = 9.6 Hz, 1H, CH), 3.18–3.14 (m, 2H, CH_2), 3.07 (d, *J* = 9.6 Hz, 1H, CH_2), 3.01–2.95 (m, 1H, CH_2), 2.76 (d, *J* = 9.6 Hz, 1H, CH_2), 2.65–2.59 (m, 1H, CH_2), 2.40 (s, 3H, CH_3), 2.38 (s, 4H, CH_2 + CH_3), 2.19–2.15 (m, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 154.3, 139.0, 133.8, 133.2, 131.3, 129.9, 129.3, 128.4, 128.1, 127.6, 127.5, 127.3, 126.6, 126.2, 125.8, 125.4, 124.4, 116.5, 107.2, 66.7, 63.5, 62.4, 62.2, 60.5, 60.2, 54.4, 48.7, 46.3, 41.7, 35.0 ppm; IR (KBr): $\tilde{\nu}$ 3050, 2943, 2899, 2780, 1712, 1603, 1509, 1492, 1454, 1349, 1277, 1243, 1196, 1135, 1033, 1010, 783, 738, 701 cm^{-1}; HRMS (ESI): *m*/*z* calcd. for $C_{34}H_{35}N_2O_2$ $[M + H]^+$ 503.2693, found 503.2694.

References

1. (a) W. Yang and D.-M. Du, *Org. Lett.*, 2010, **12**, 5450; (b) W. Yang and D.-M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241.
2. B.-L. Zhao and D.-M. Du, *RSC Adv.*, 2014,**4**, 27346.
3. H. Y. Bae, S. Some, J. H. Lee, J.-Y. Kim, M. J. Song, S. Lee, Y. J. Zhang and C. E. Song, *Adv. Synth. Catal.*, 2011, **353**, 3196.
4. B. Vakulya, S. Varga, A. Csampai and T. Soós, *Org. Lett.*, 2005, **7**, 1967.
5. (a) W.-L. Yang, Y.-Z. Liu, S. Luo, X. Yu, J. S. Fossey and W.-P. Deng, *Chem. Commun.*, 2015, **51**, 9212; (b) Y. Liu and W. Zhang, *Angew. Chem. Int. Ed.*, 2013, **52**, 2203.

Copies of ^{1}H and ^{13}C NMR spectra of new compounds

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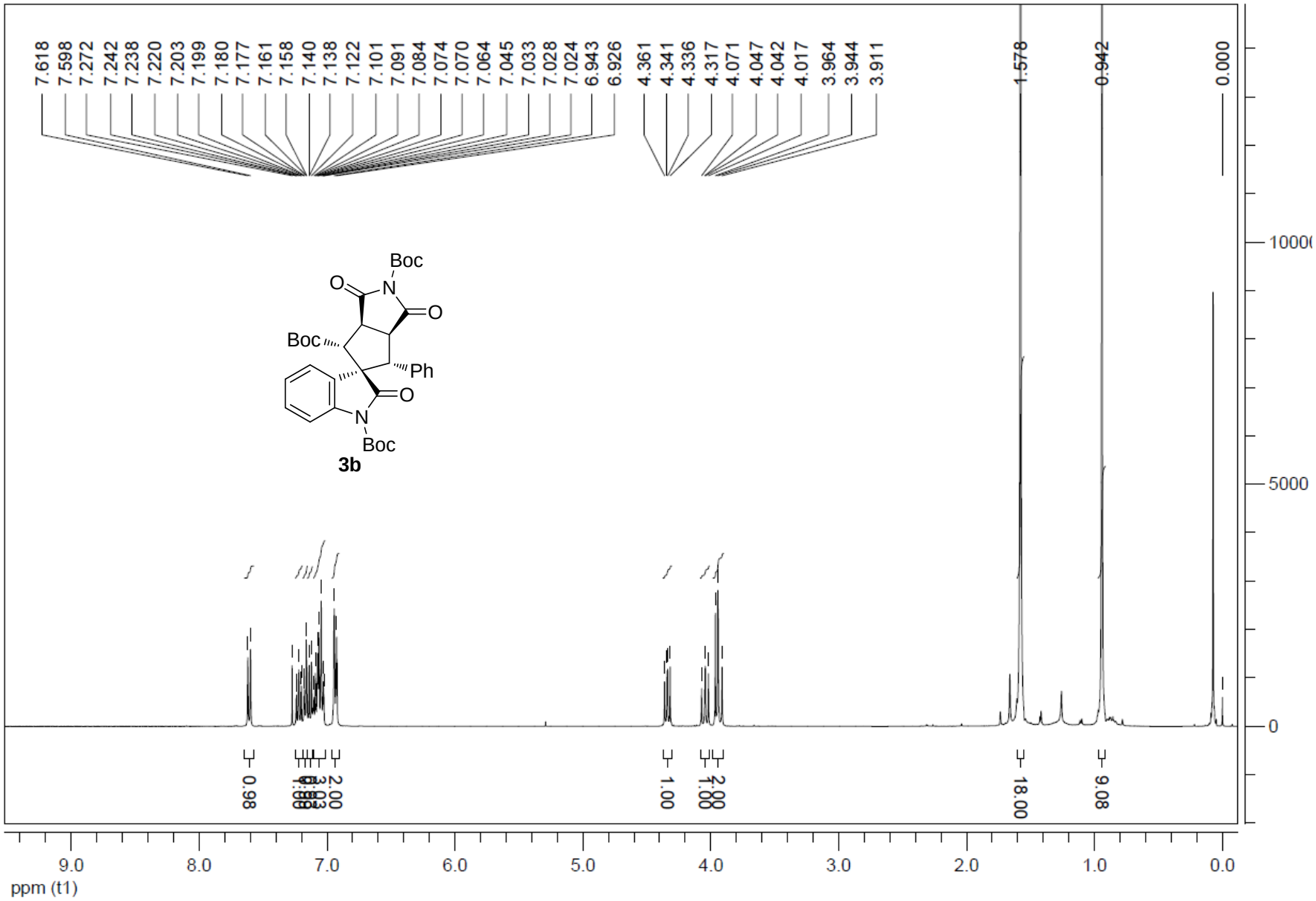
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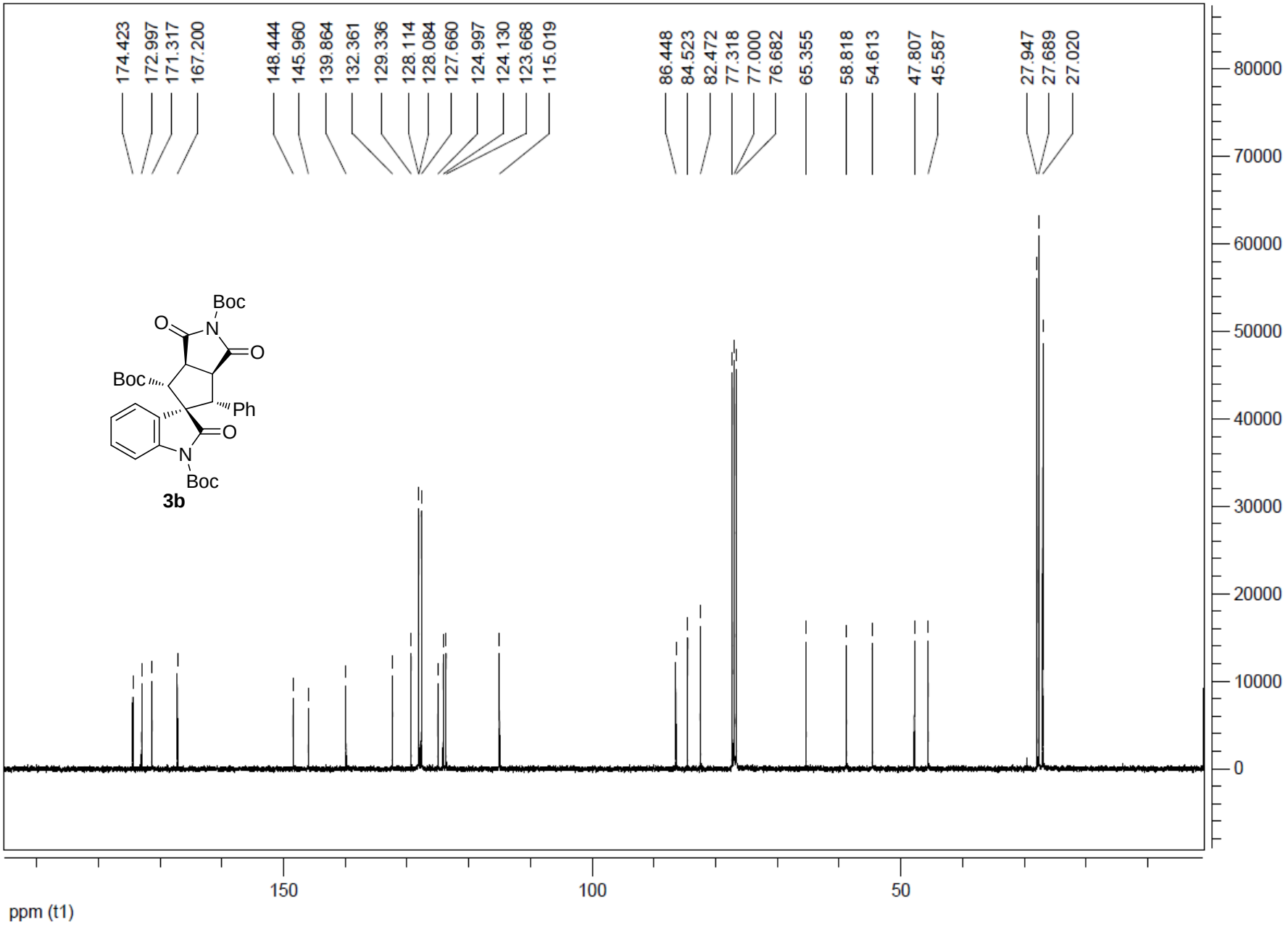
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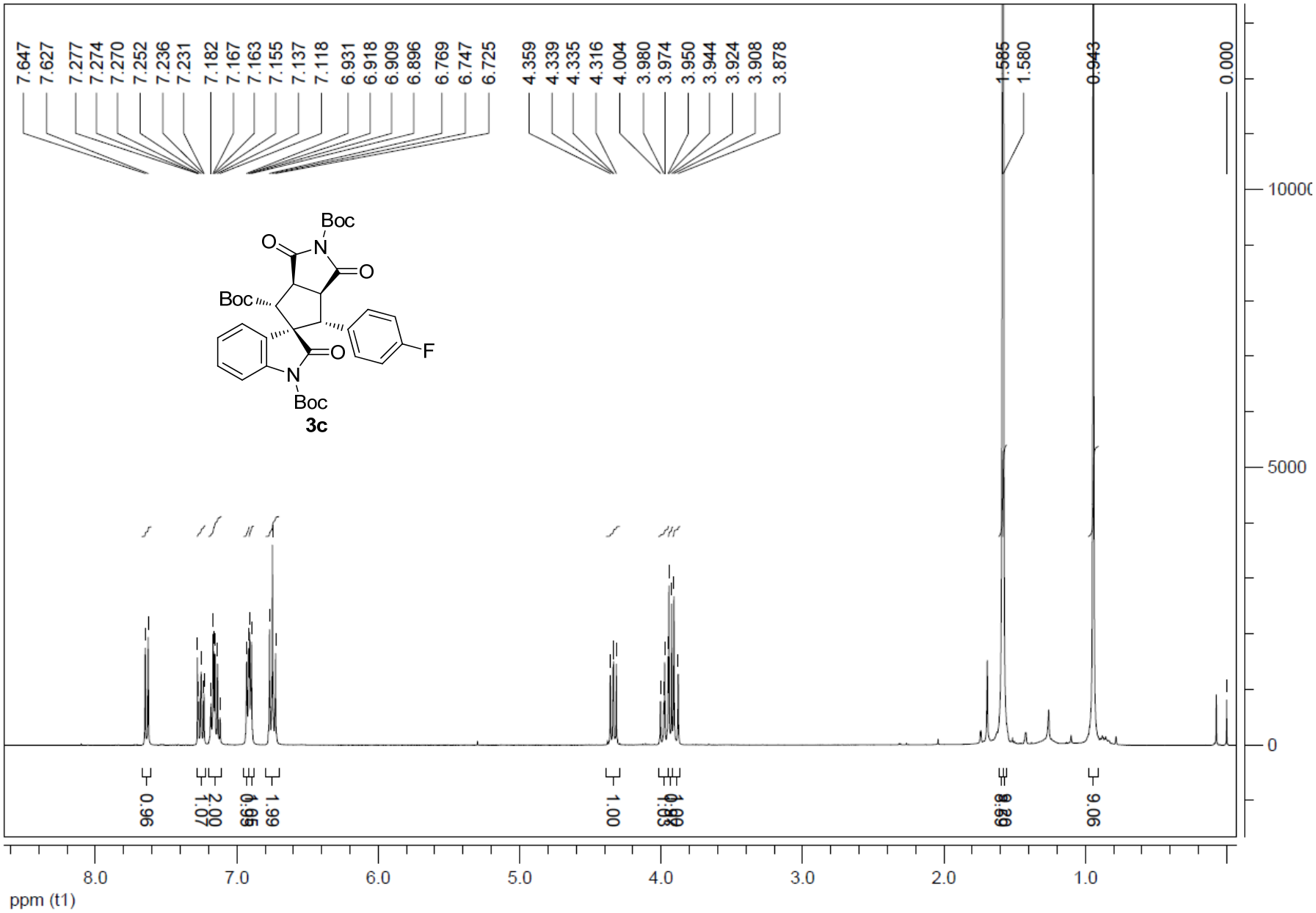
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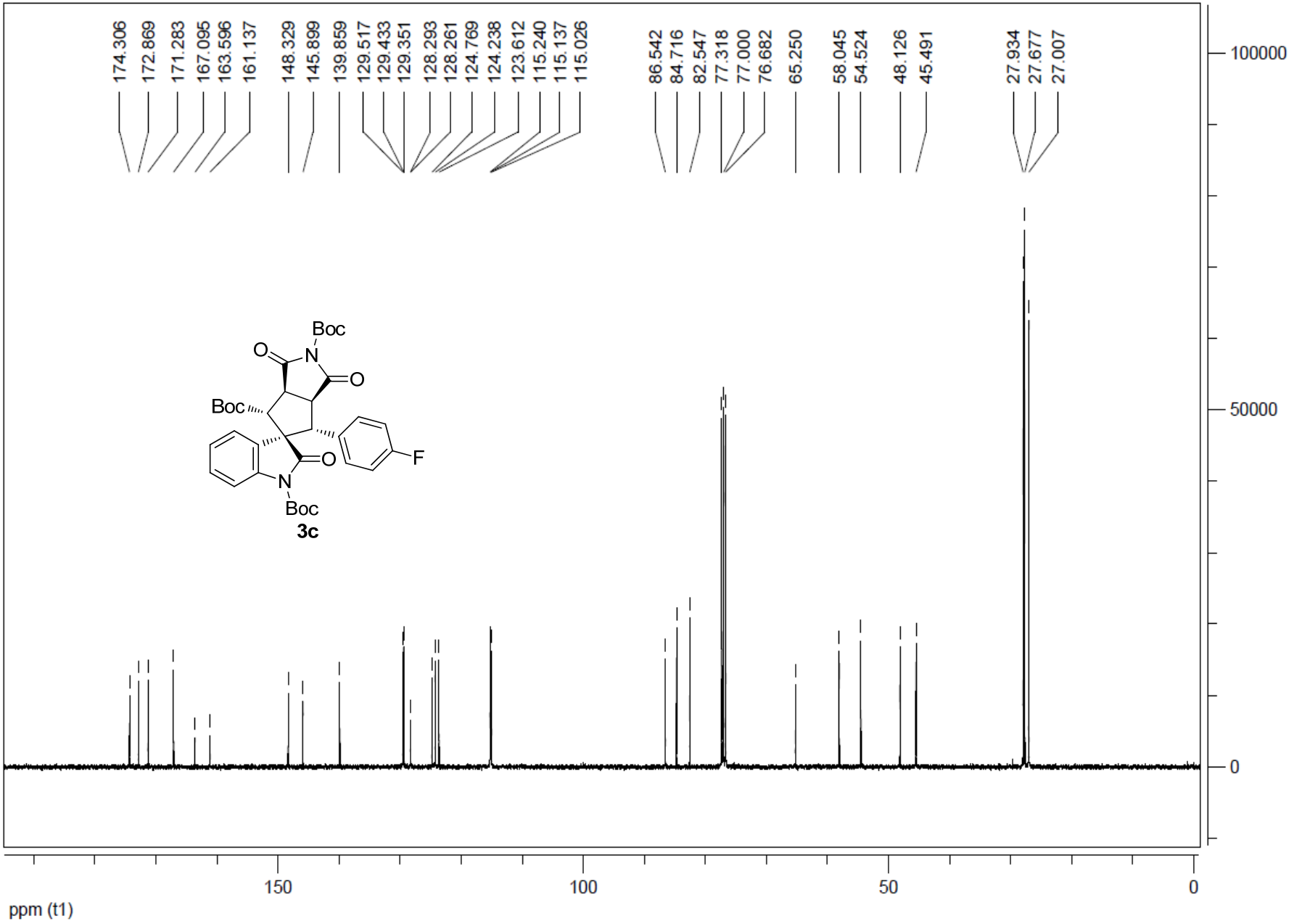
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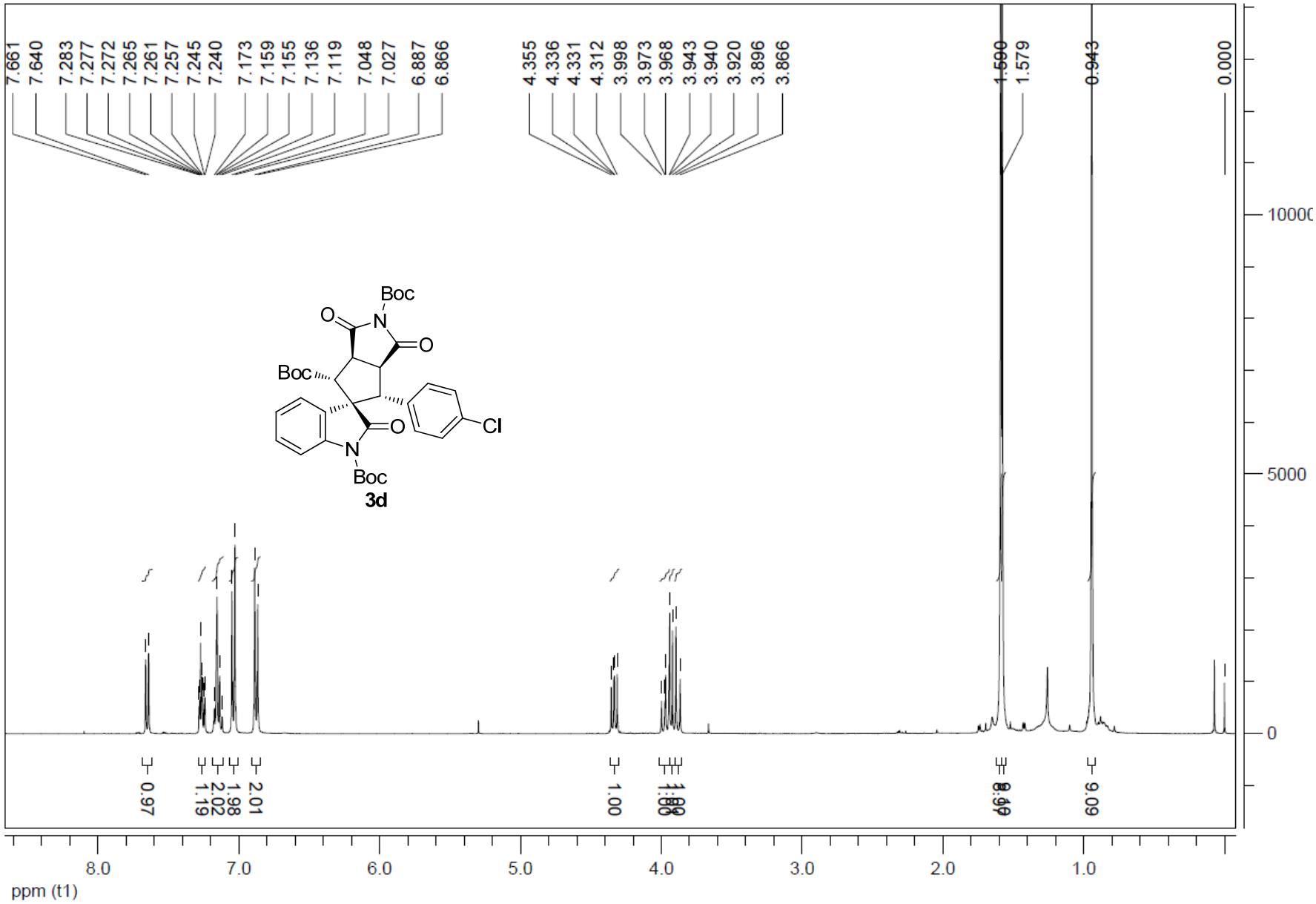
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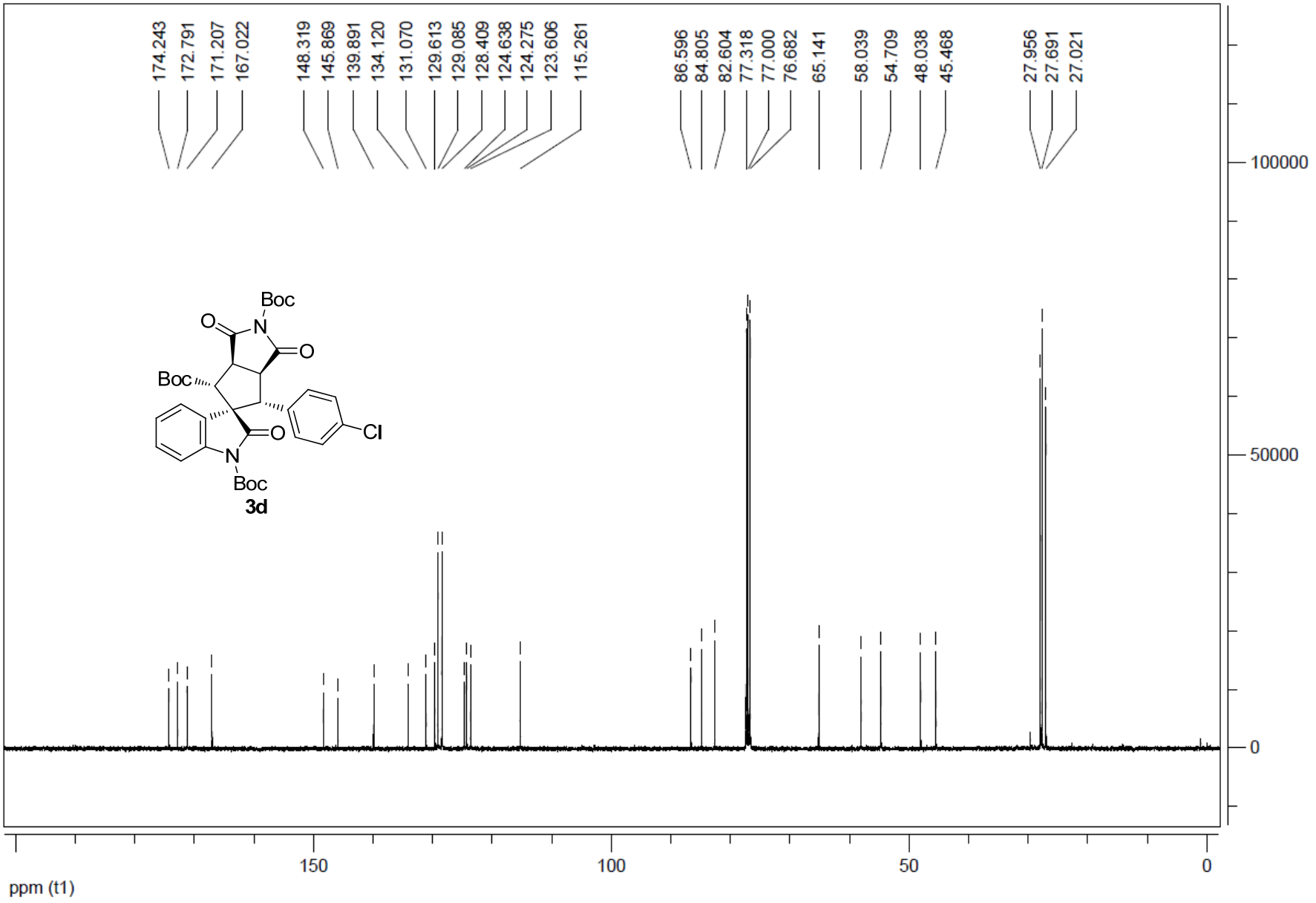
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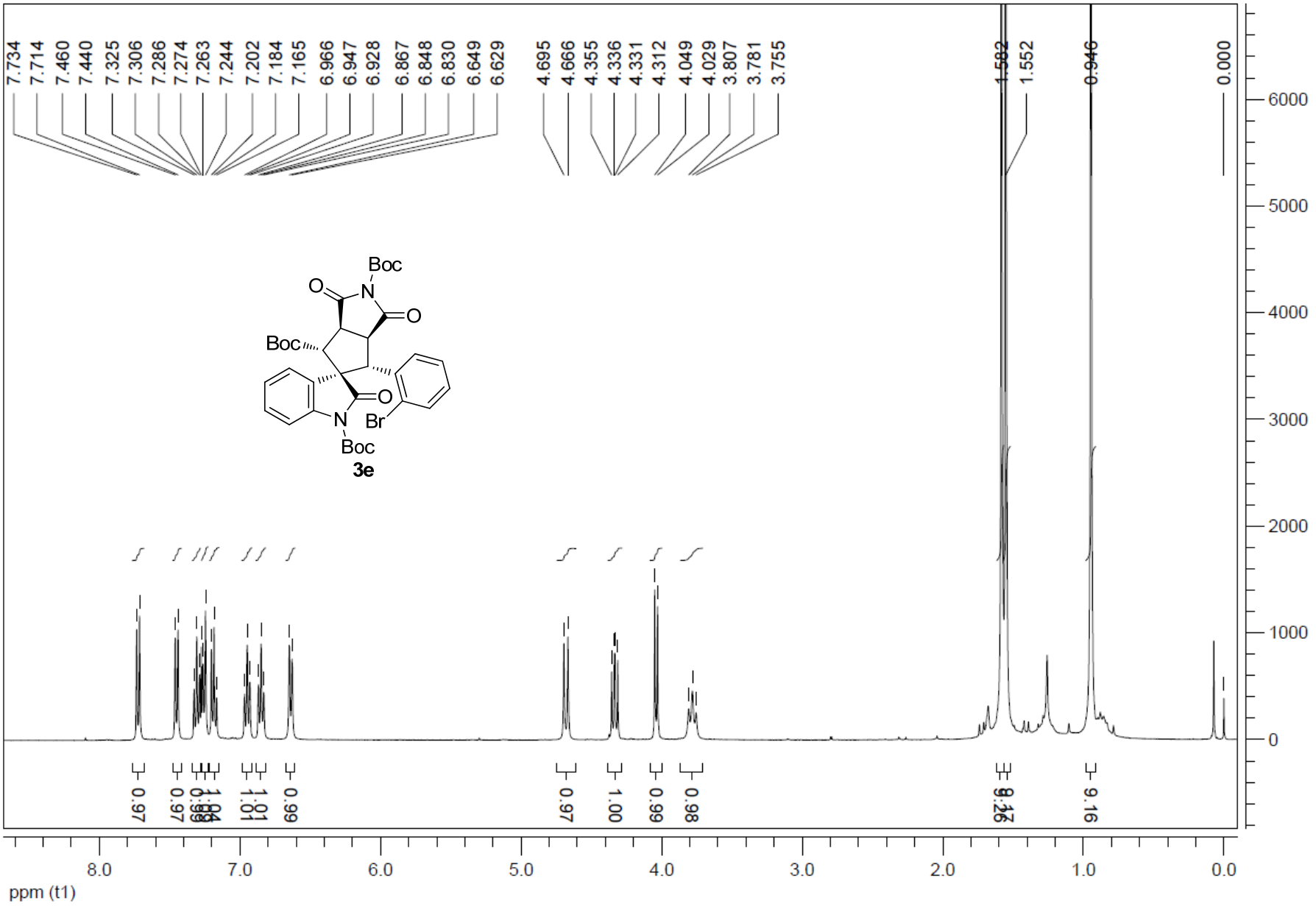
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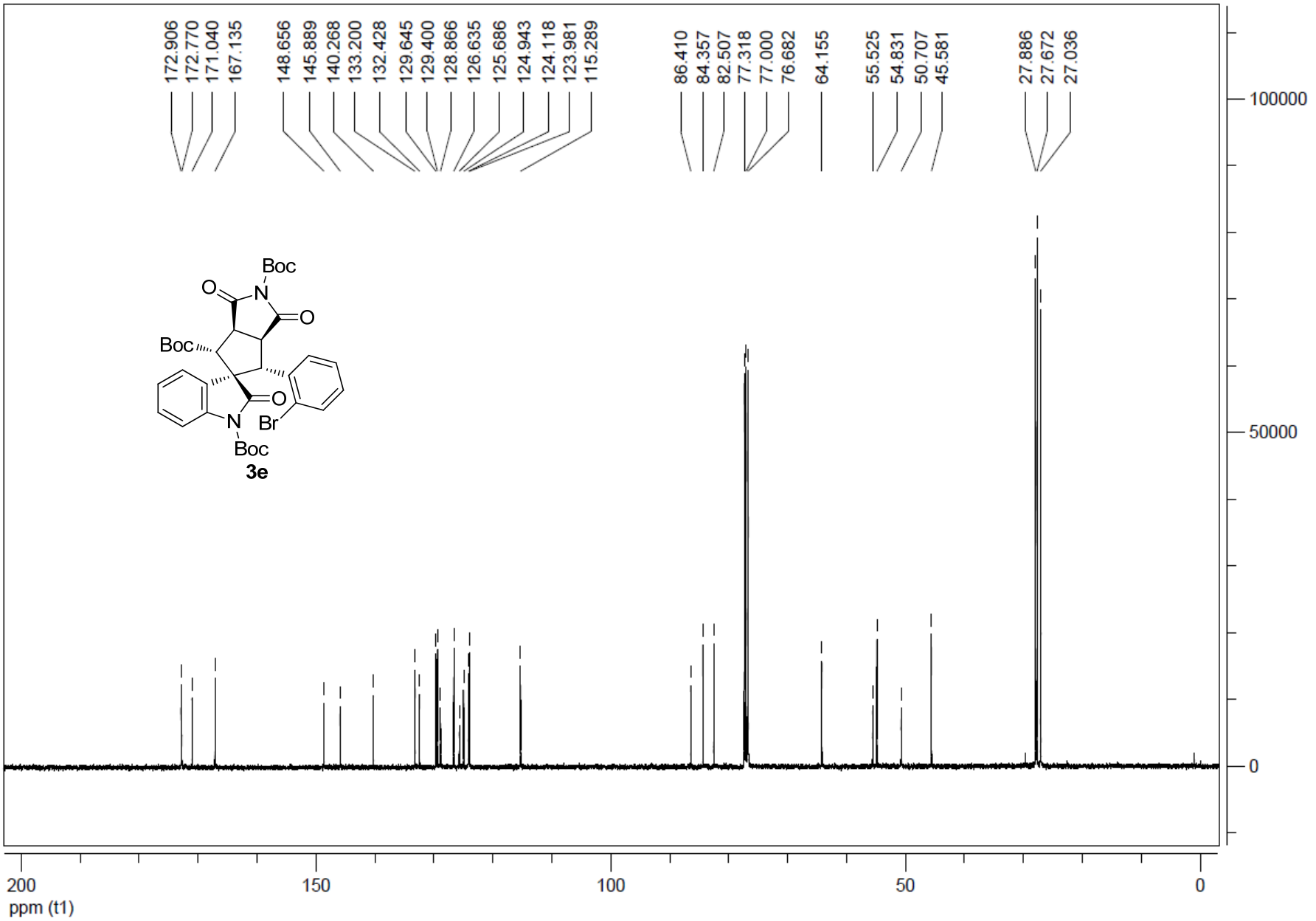
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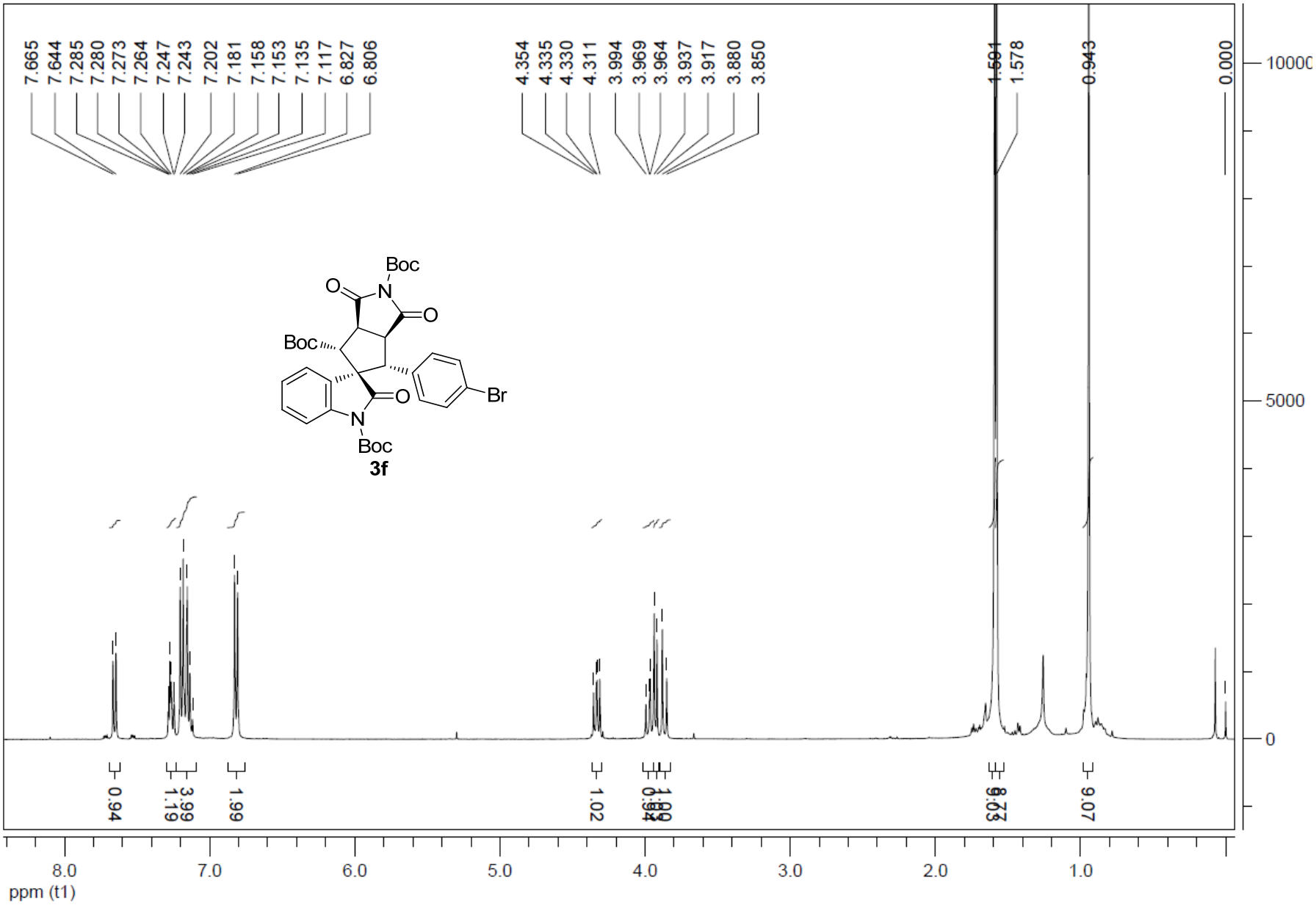
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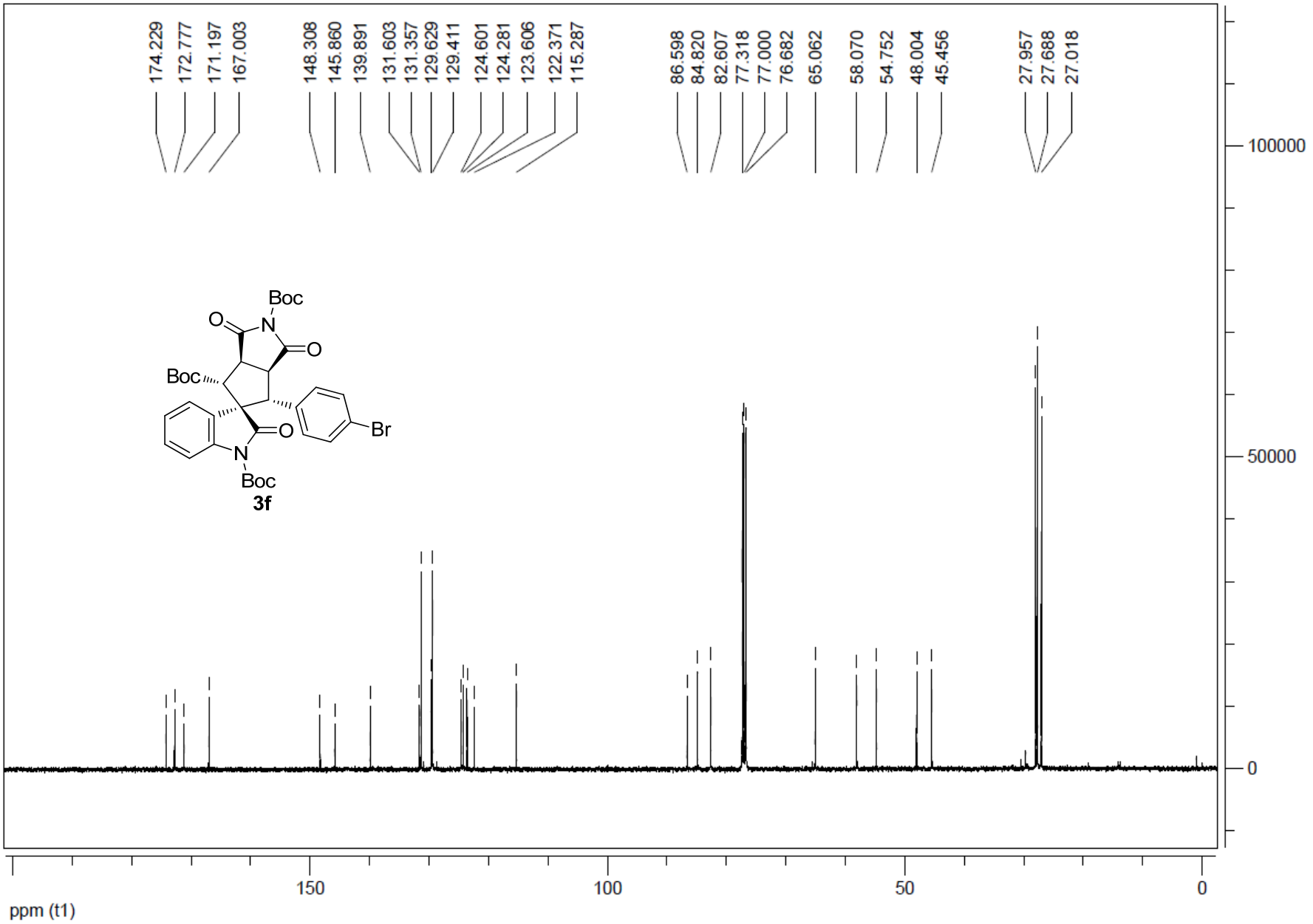
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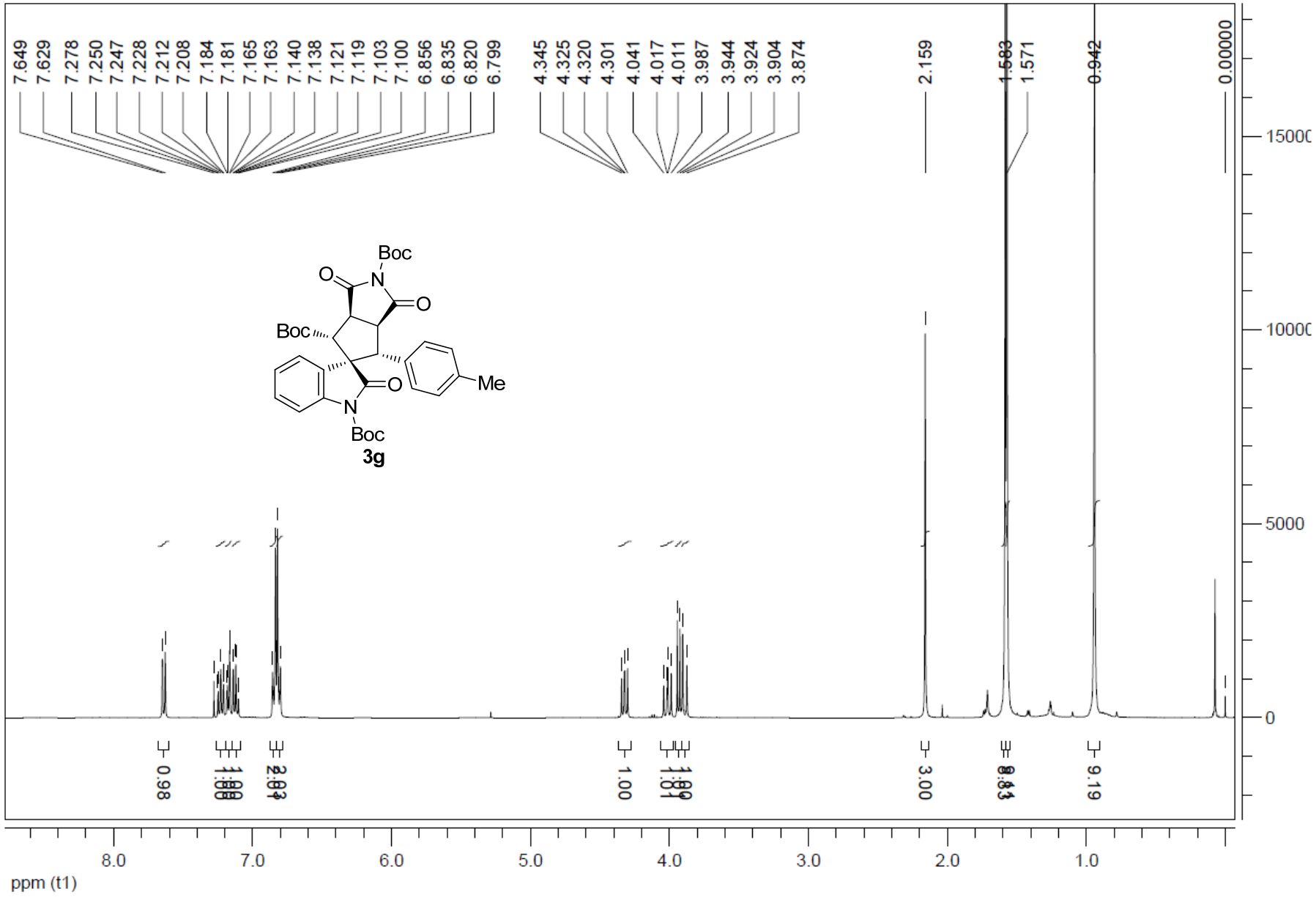
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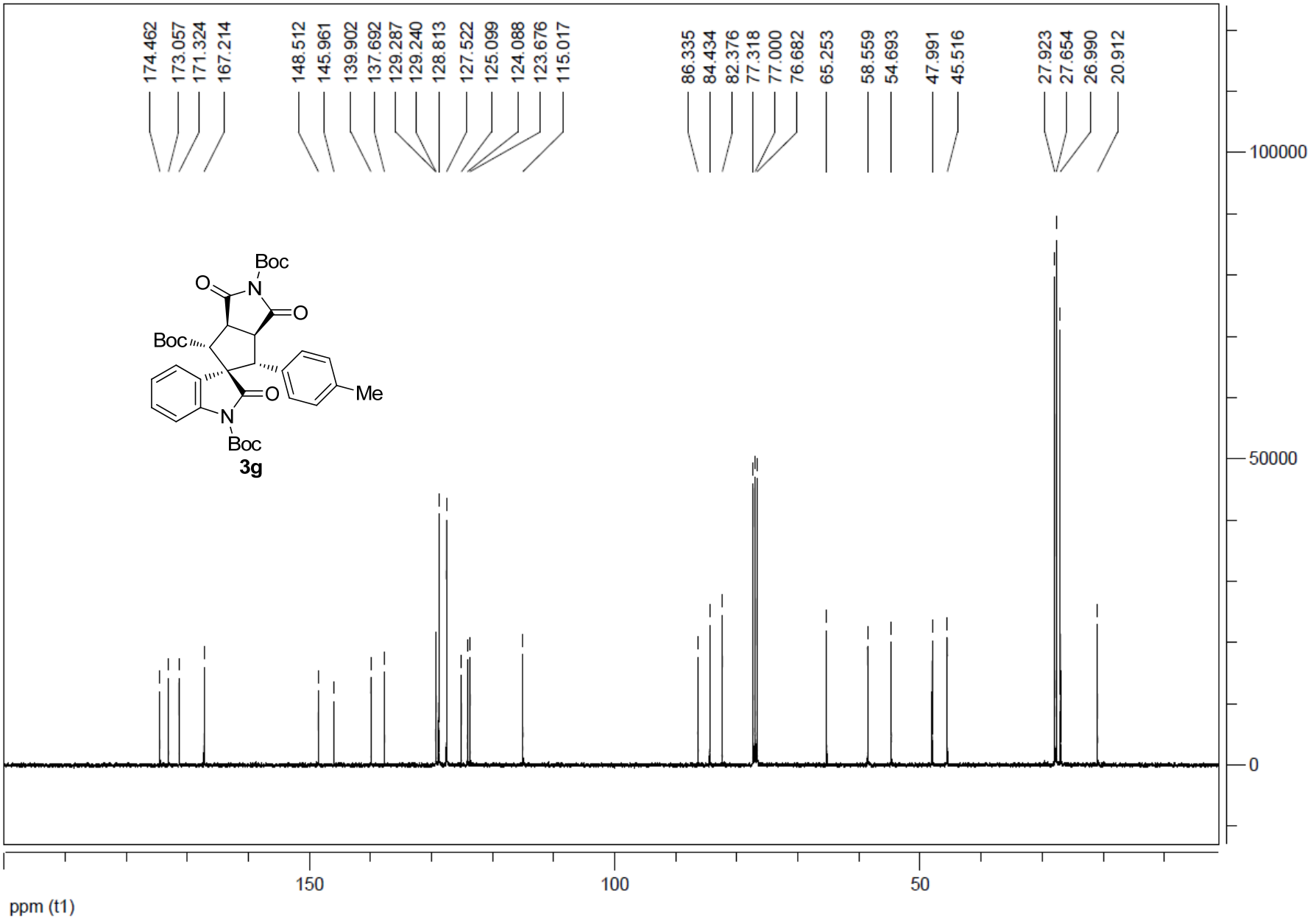
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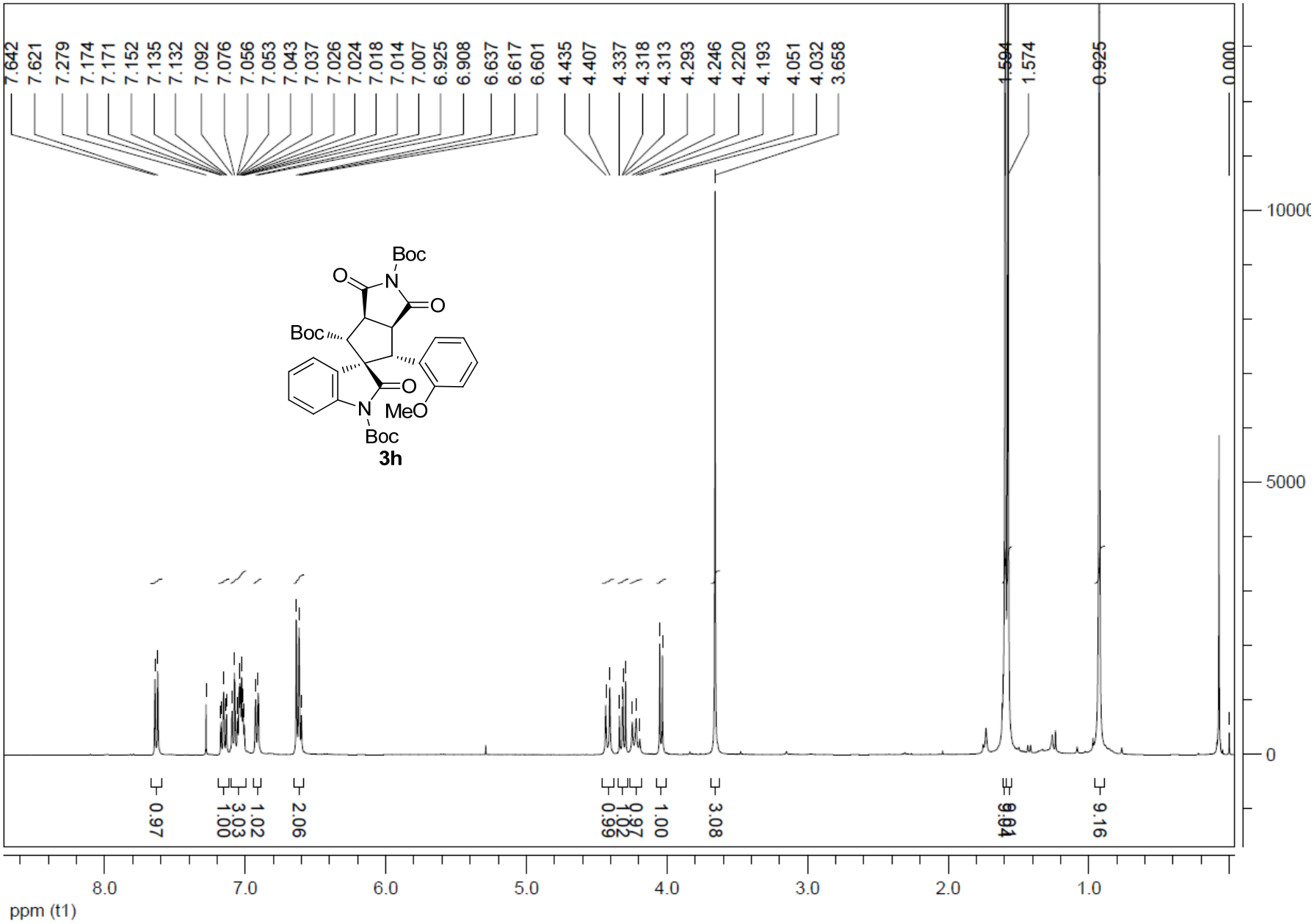
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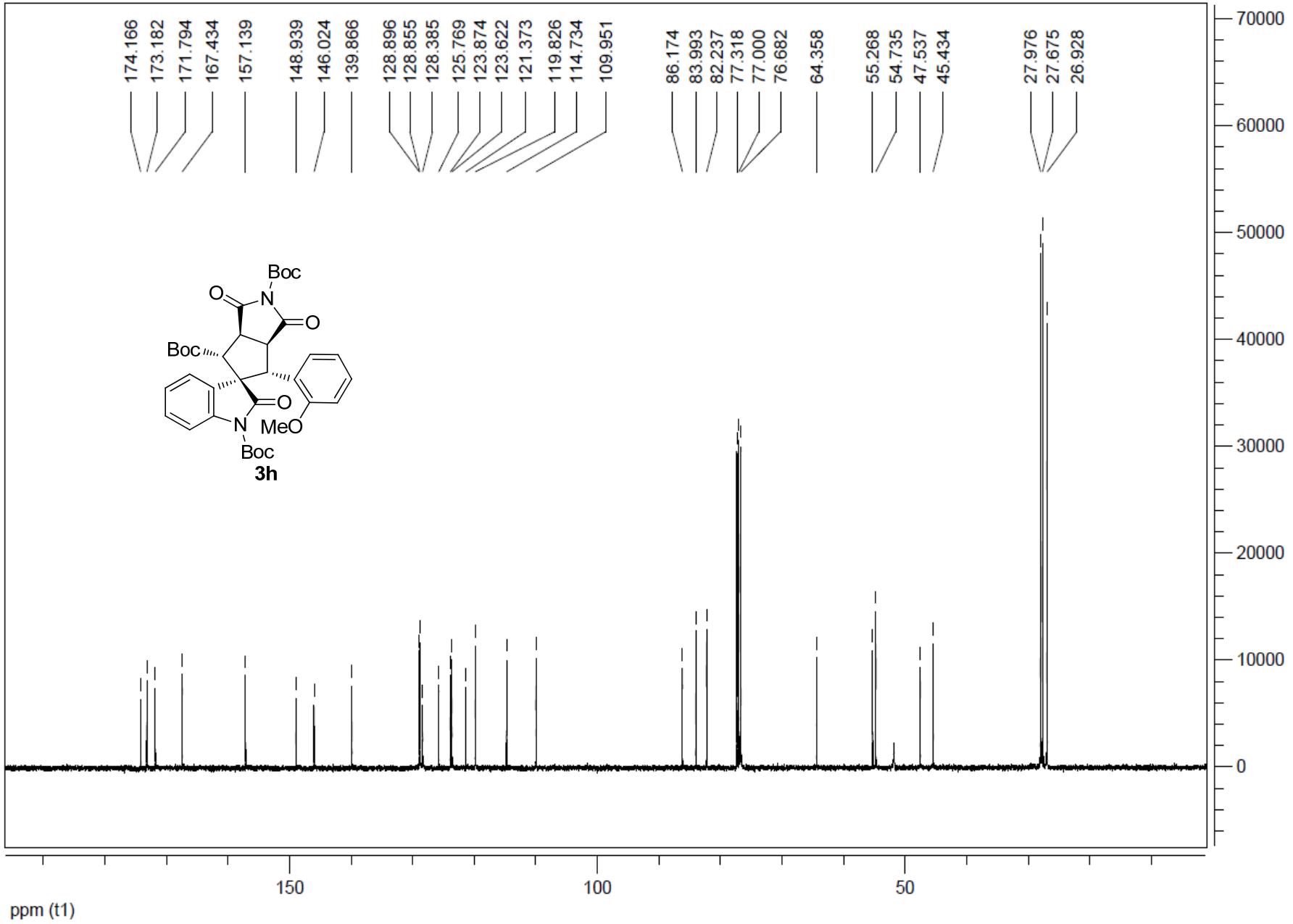
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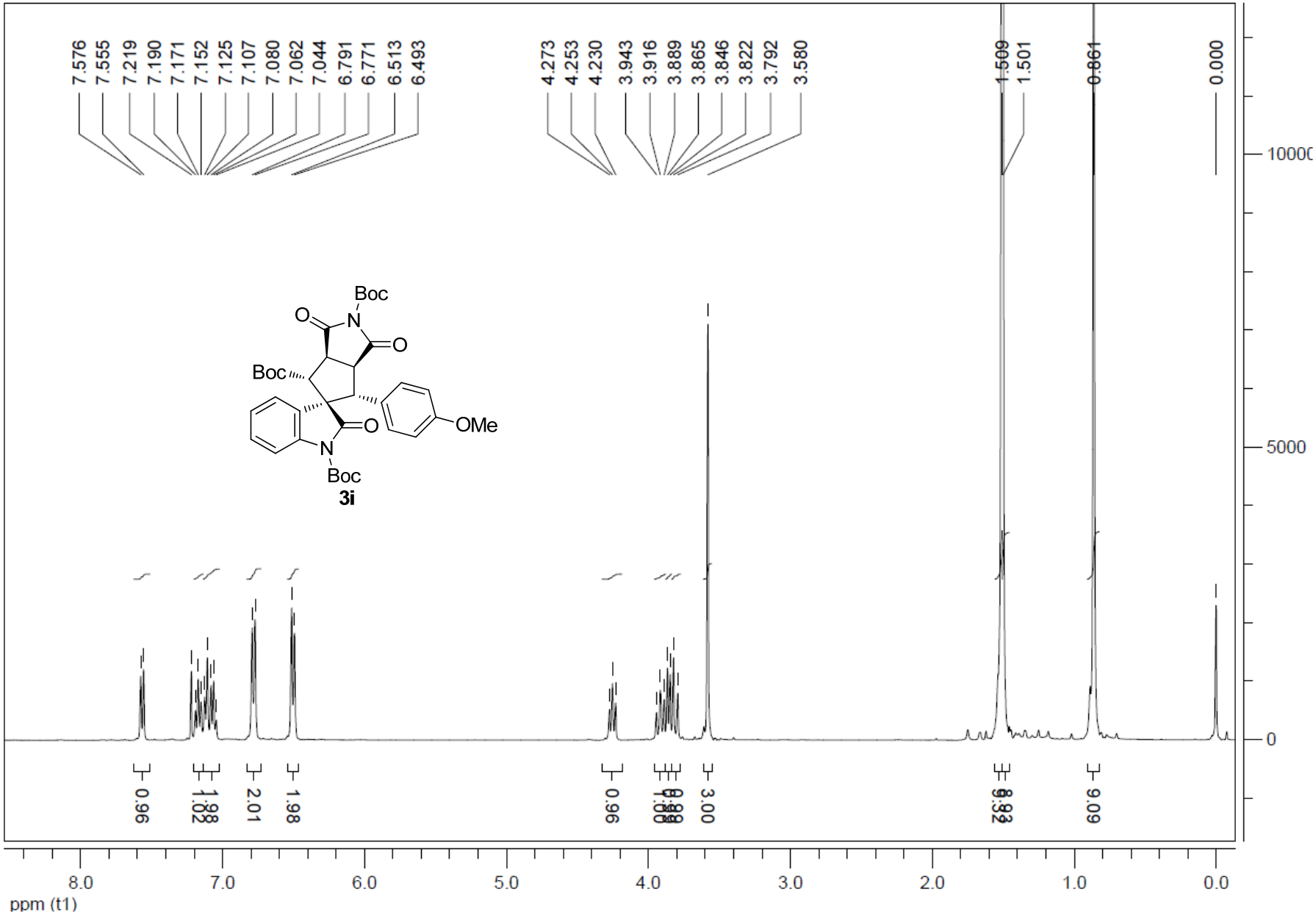
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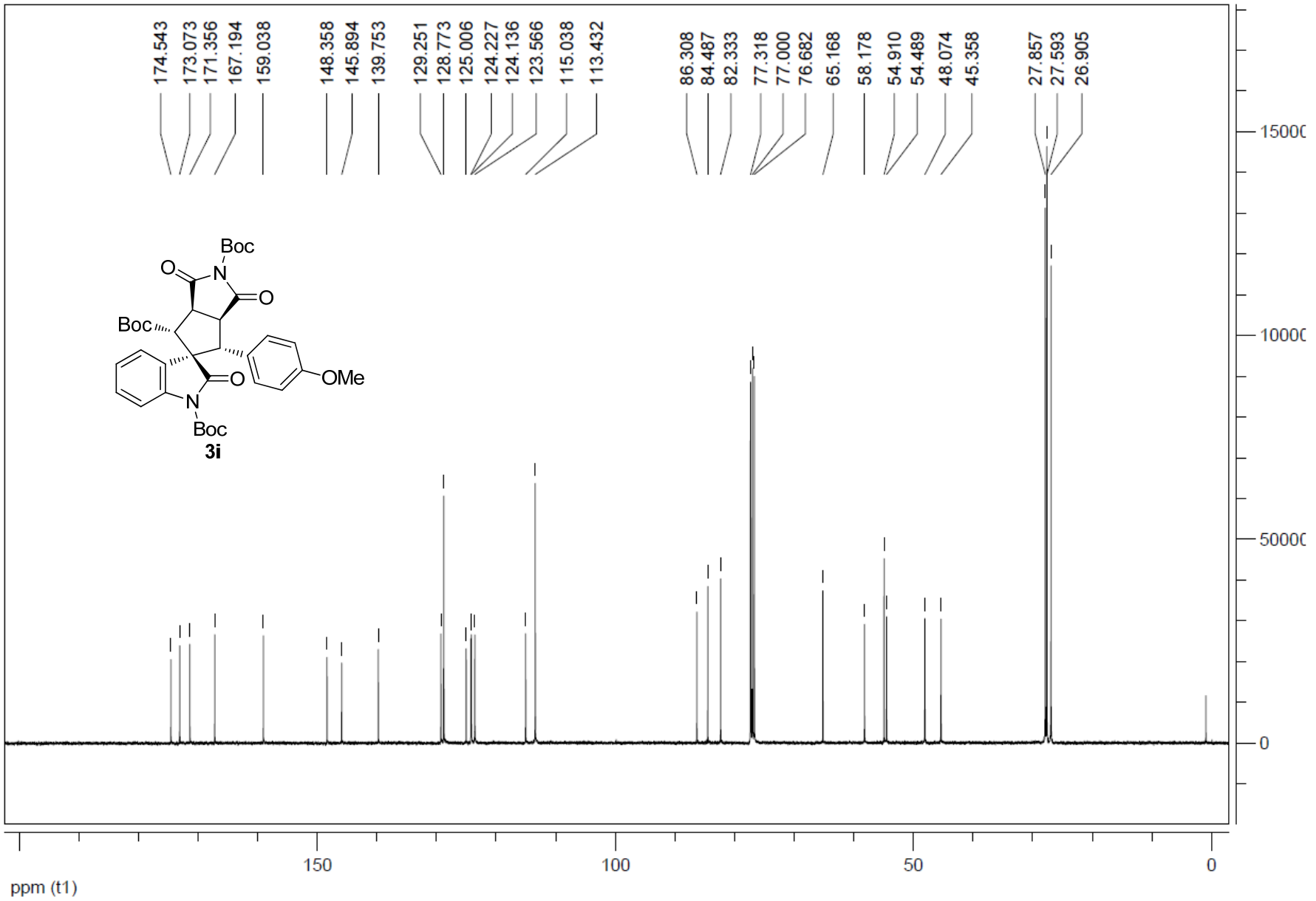
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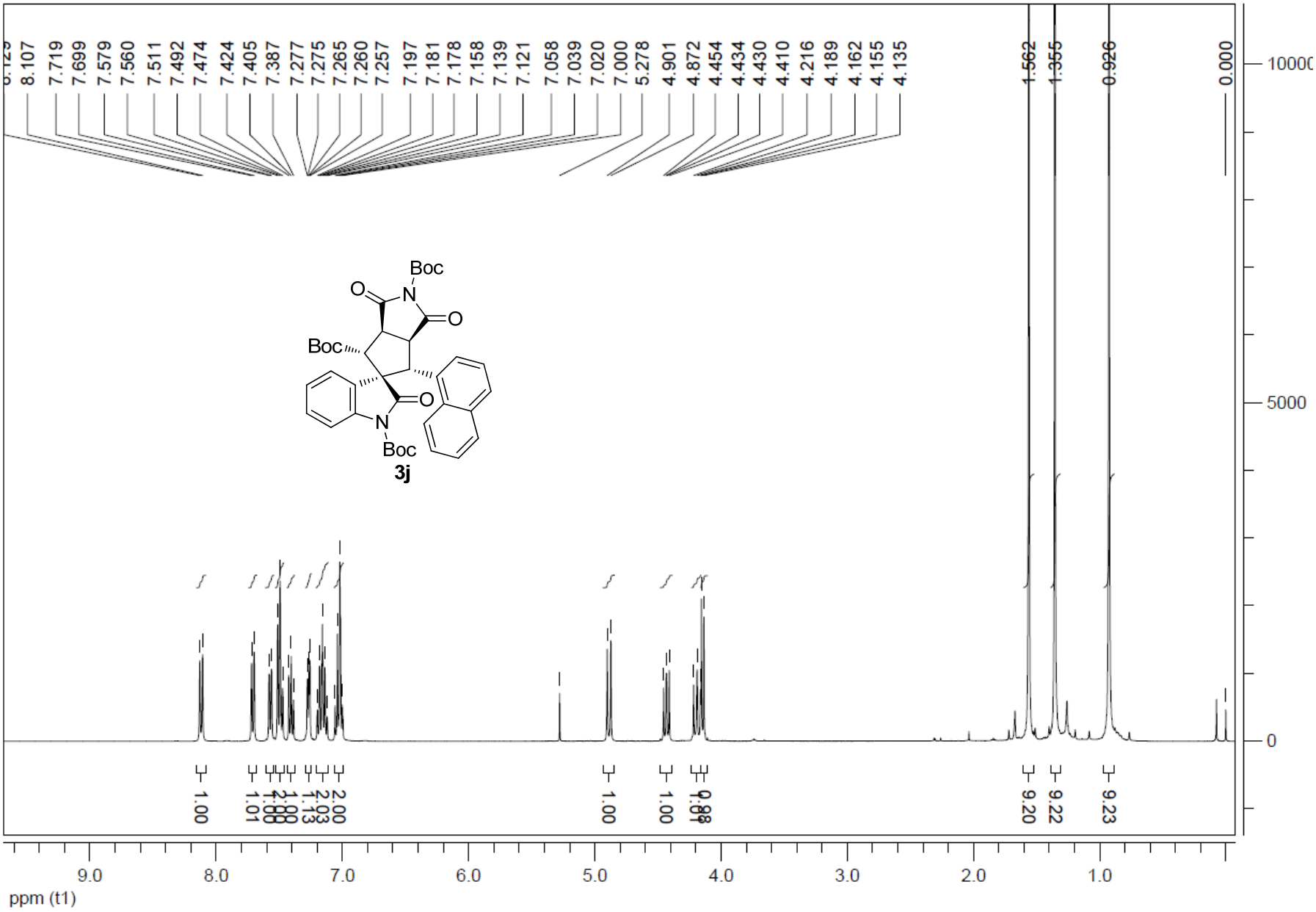
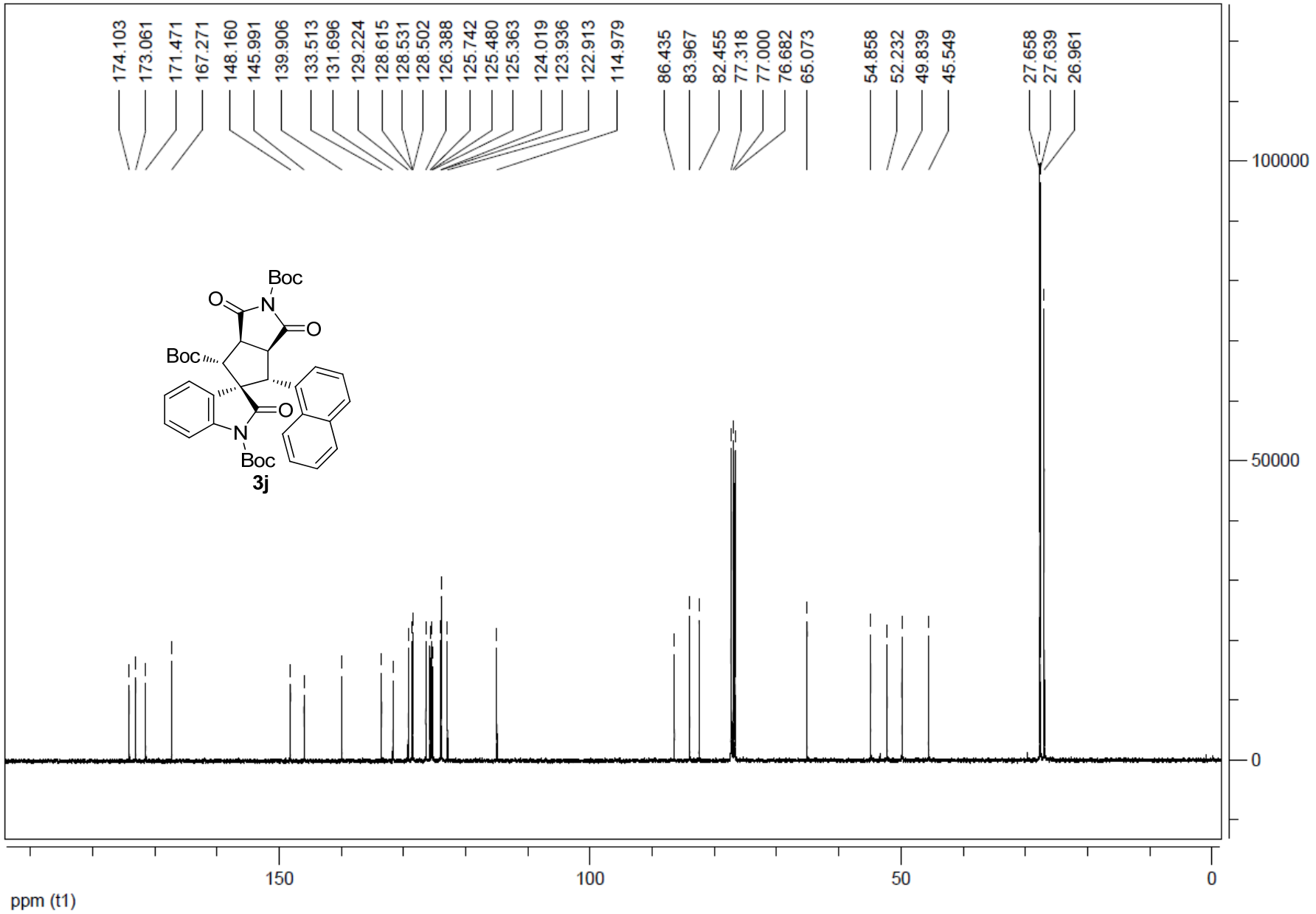
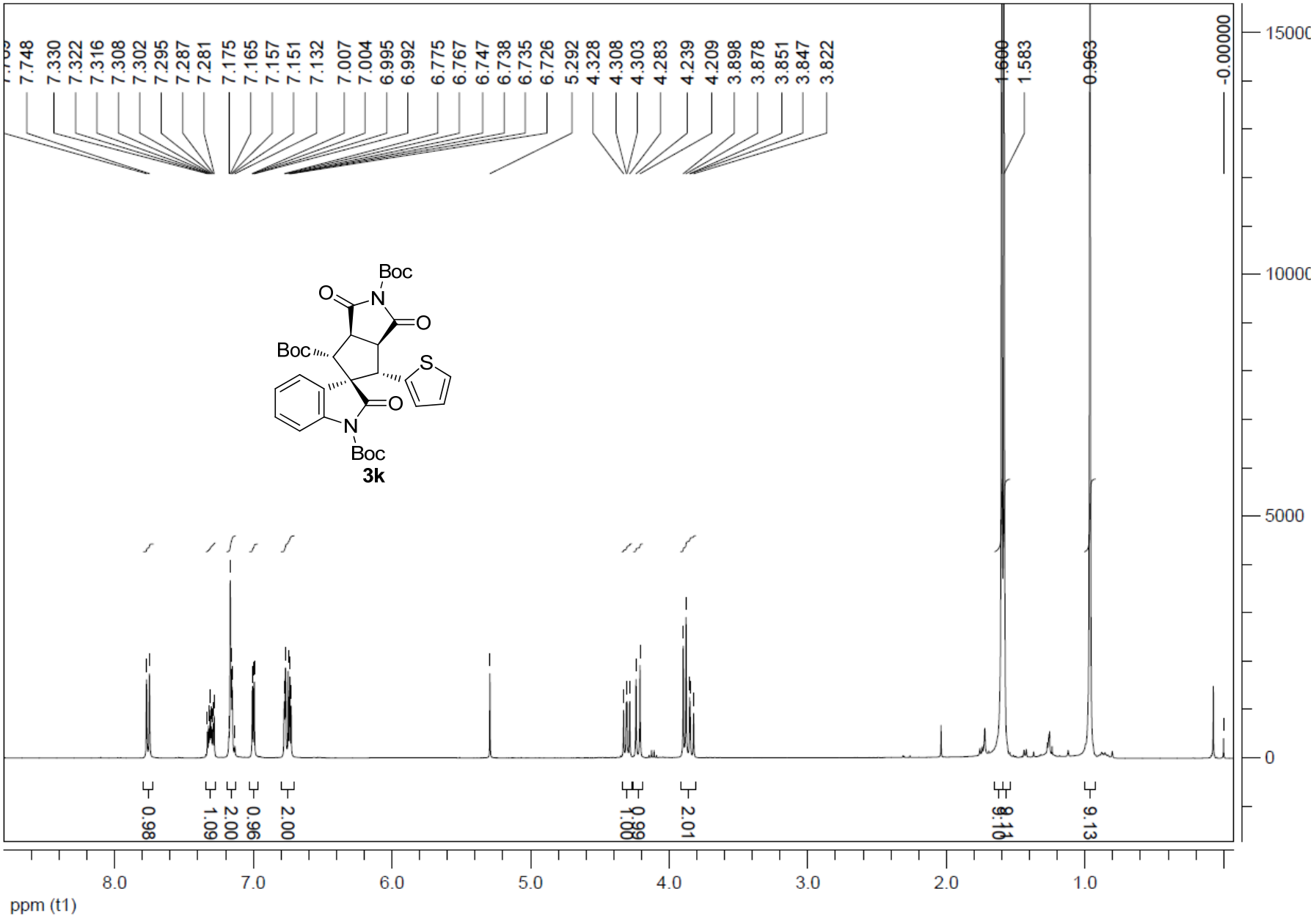
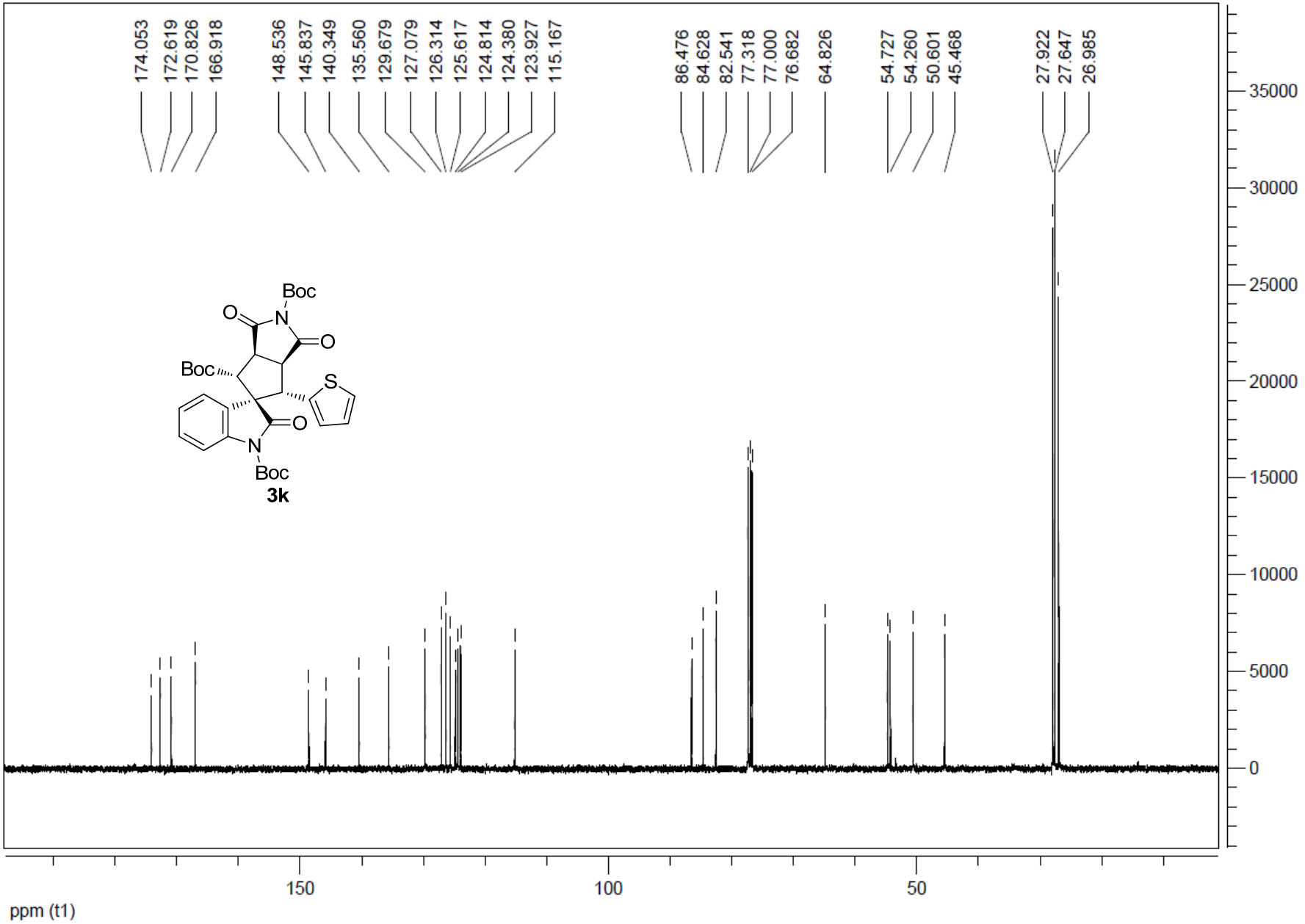
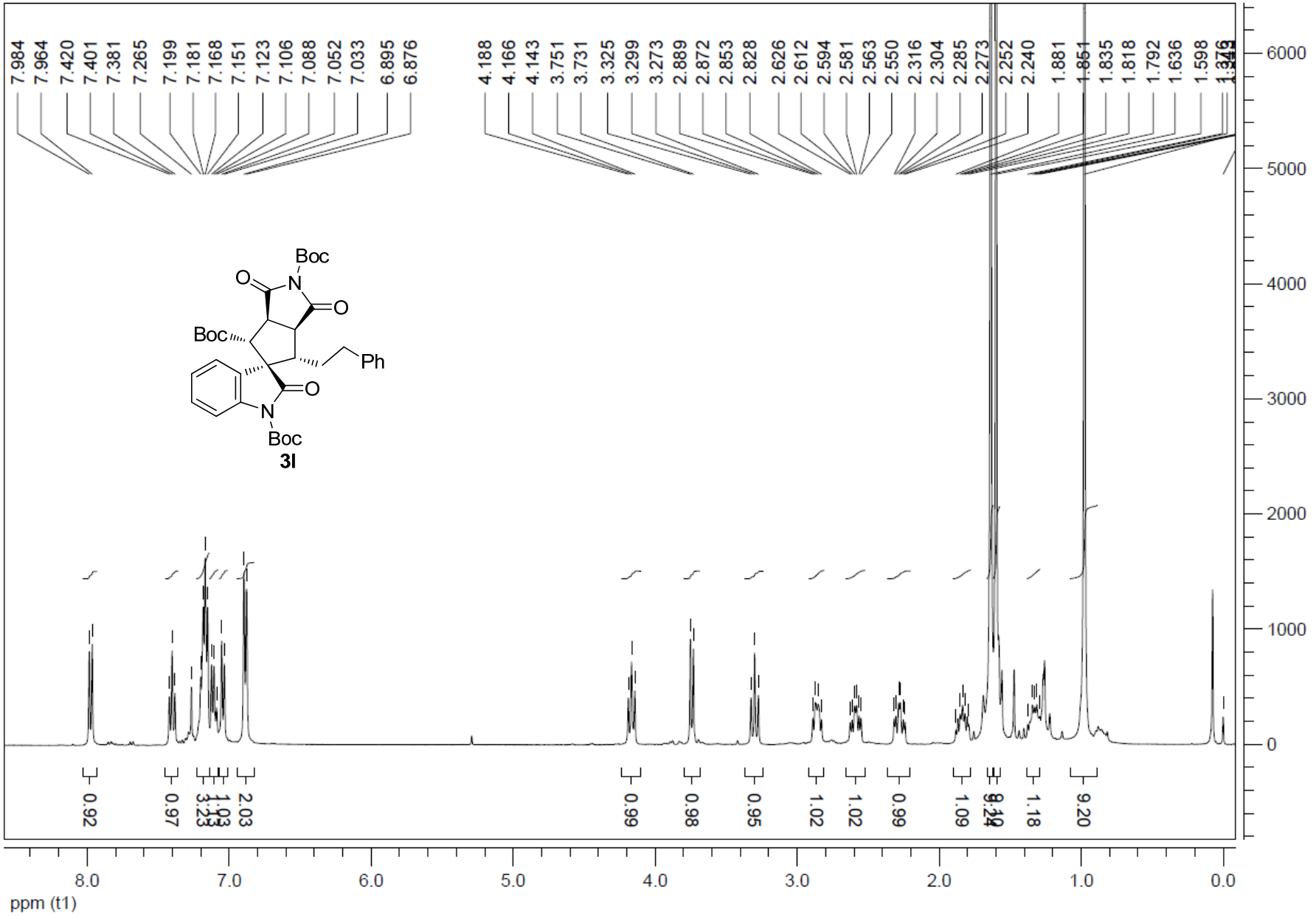
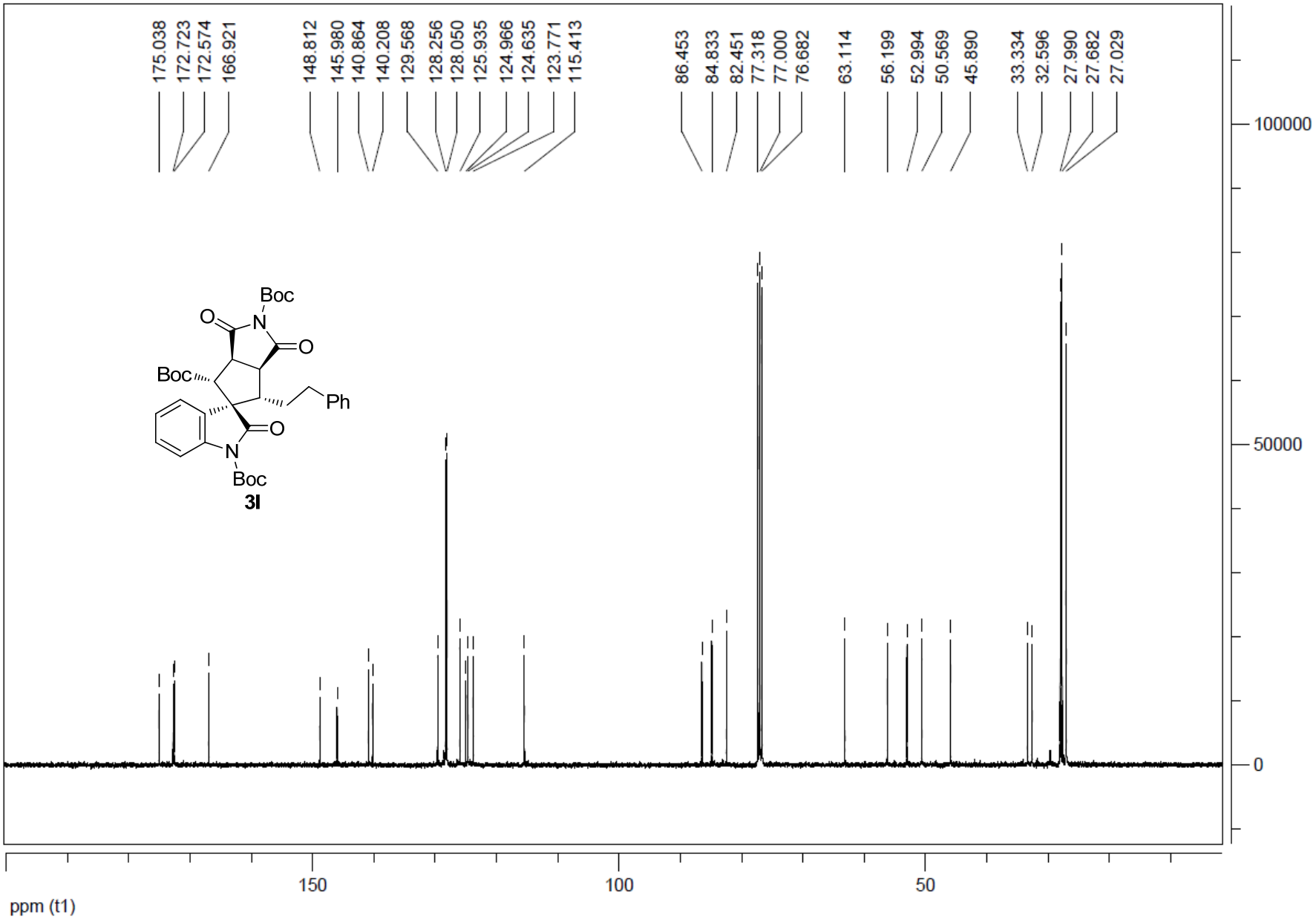

8.107
7.719
7.699
7.579
7.560
7.511
7.492
7.474
7.424
7.405
7.387
7.277
7.275
7.265
7.260
7.257
7.197
7.181
7.178
7.158
7.139
7.121
7.058
7.039
7.020
7.000
5.278
4.901
4.872
4.454
4.434
4.430
4.410
4.216
4.189
4.162
4.155
4.135
1.562
1.355
0.926
0.000
Boc
Boc
Boc
3j
10000
5000
0
1.00
1.01
1.00
1.00
1.13
2.03
2.00
1.00
1.00
9.20
9.22
9.23
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

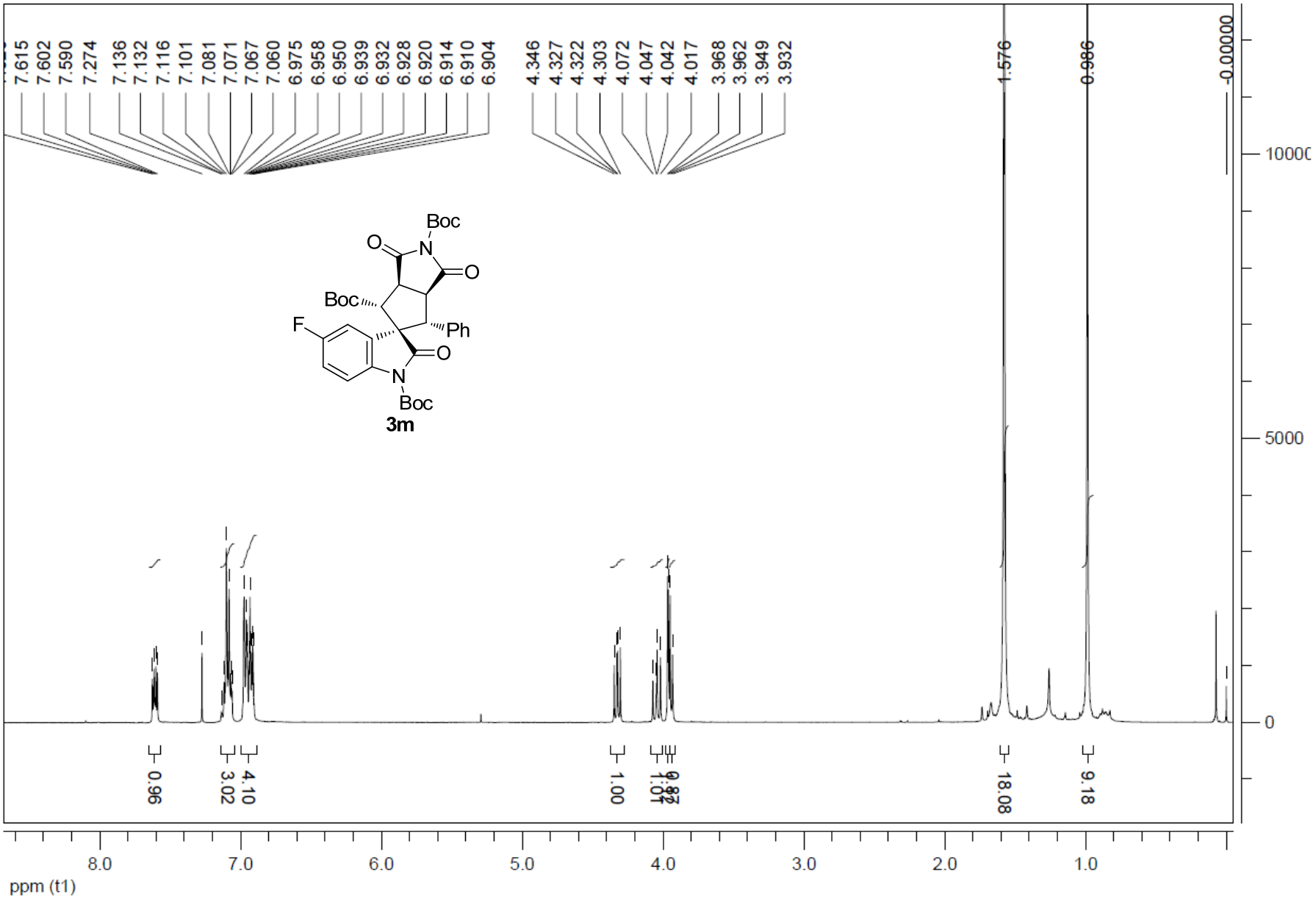

174.103
173.061
171.471
167.271
148.160
145.991
139.906
133.513
131.696
129.224
128.615
128.531
128.502
126.388
125.742
125.480
125.363
124.019
123.936
122.913
114.979
86.435
83.967
82.455
77.318
77.000
76.682
65.073
54.858
52.232
49.839
45.549
27.658
27.639
26.961
Boc
O
N
O
Boc
O
N
Boc
3j
100000
50000
0
150
100
50
0
ppm (t1)

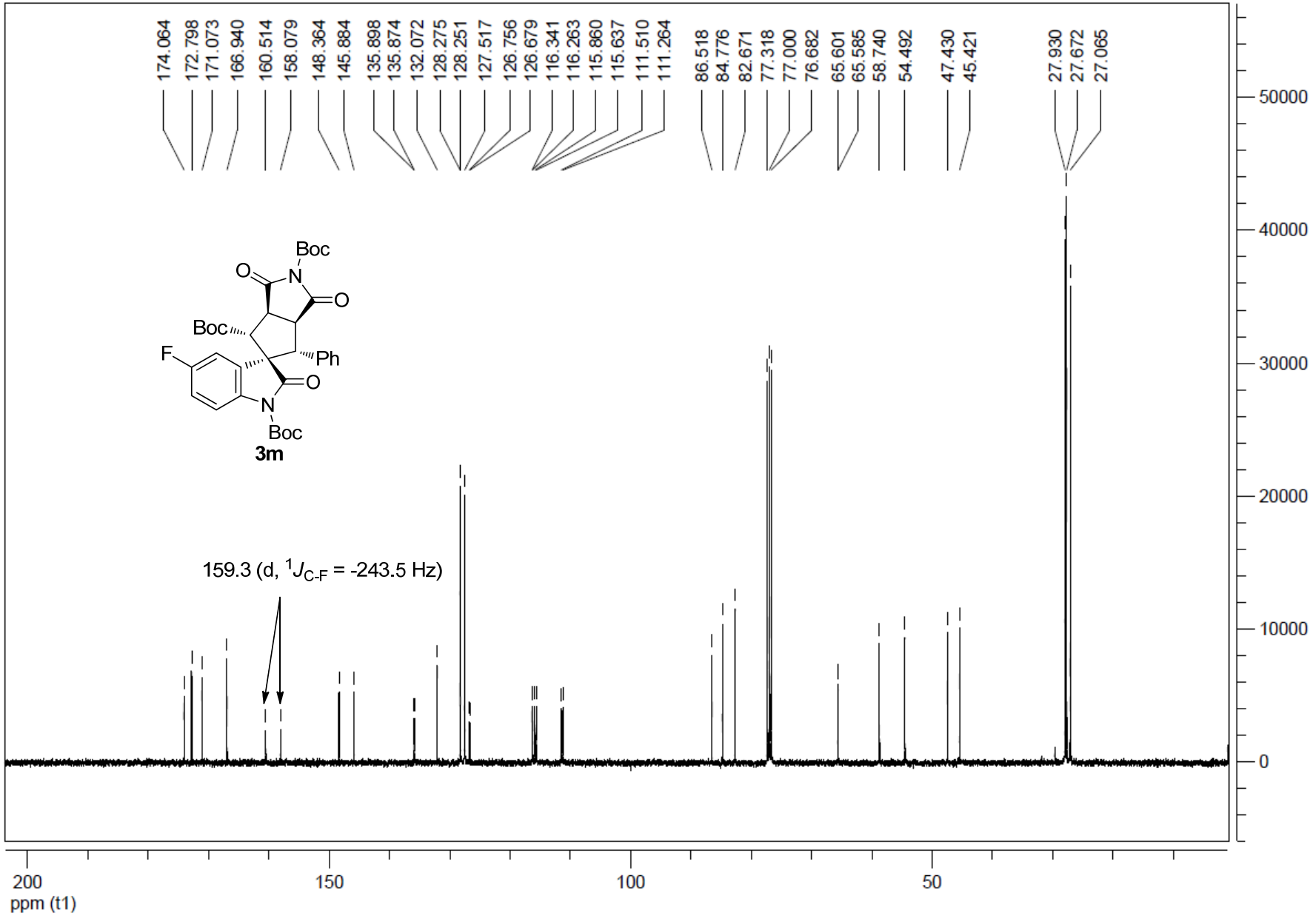

7.748
7.330
7.322
7.316
7.308
7.302
7.295
7.287
7.281
7.175
7.165
7.157
7.151
7.132
7.007
7.004
6.995
6.992
6.775
6.767
6.747
6.738
6.735
6.726
5.292
4.328
4.308
4.303
4.283
4.239
4.209
3.898
3.878
3.851
3.847
3.822
1.600
1.583
0.963
-0.00000
Boc
Boc
Boc
3k
0.98
1.09
2.00
0.96
2.00
1.00
0.98
2.01
9.10
9.13
ppm (t1)

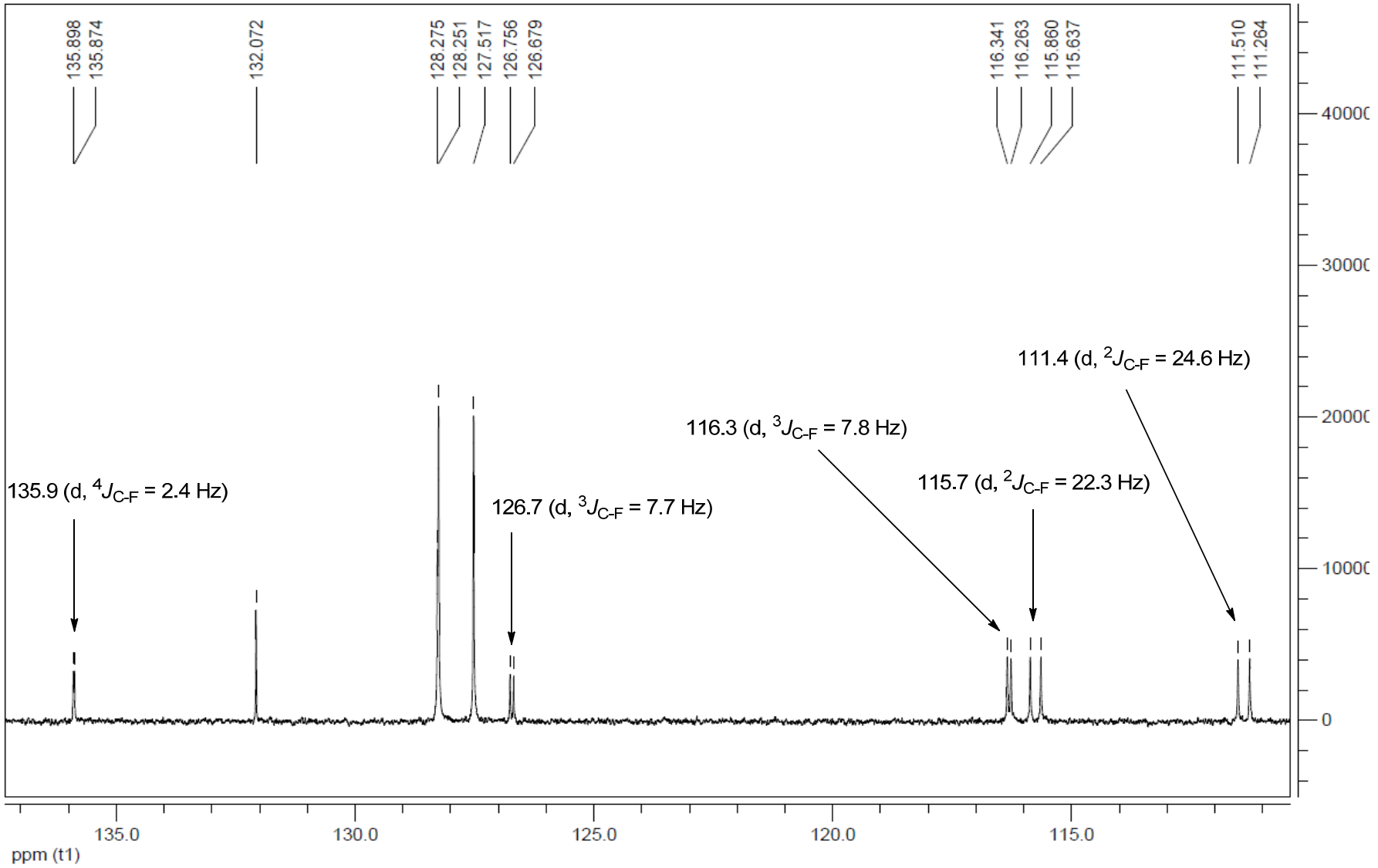

174.053
172.619
170.826
166.918
148.536
145.837
140.349
135.560
129.679
127.079
126.314
125.617
124.814
124.380
123.927
115.167
86.476
84.628
82.541
77.318
77.000
76.682
64.826
54.727
54.260
50.601
45.468
27.922
27.647
26.985
Boc
O
N
O
Boc
S
O
N
Boc
3k
35000
30000
25000
20000
15000
10000
5000
0
150
100
50
ppm (t1)


7.984
7.964
7.420
7.401
7.381
7.265
7.199
7.181
7.168
7.151
7.123
7.106
7.088
7.052
7.033
6.895
6.876
4.188
4.166
4.143
3.751
3.731
3.325
3.299
3.273
2.889
2.872
2.853
2.828
2.626
2.612
2.594
2.581
2.563
2.550
2.316
2.304
2.285
2.273
2.252
2.240
1.881
1.851
1.835
1.818
1.792
1.636
1.598
Boc
Boc
Ph
Boc
3l
0.92
0.97
3.23
2.03
0.99
0.98
0.95
1.02
1.02
0.99
1.09
1.18
9.20
6000
5000
4000
3000
2000
1000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

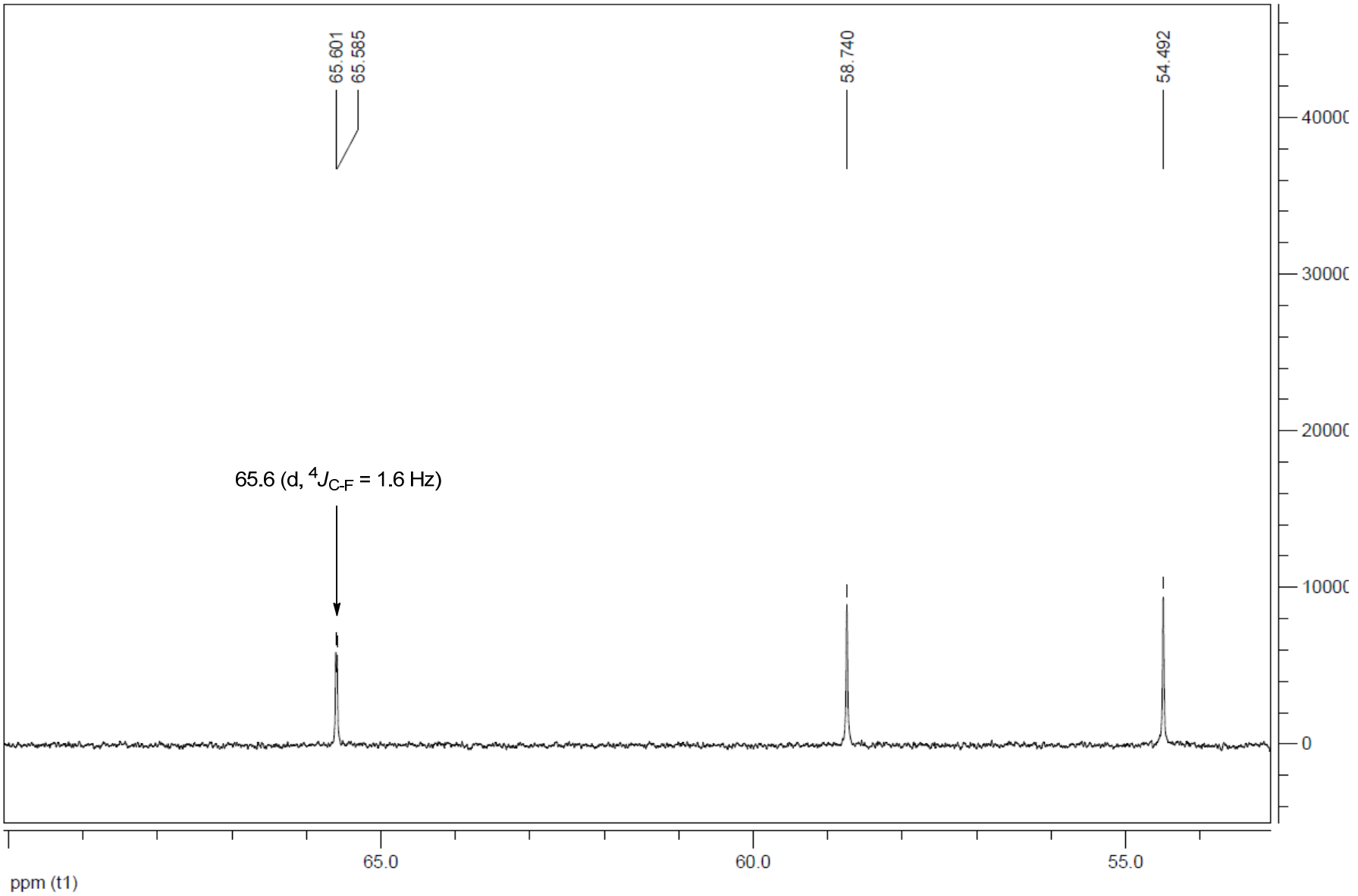

175.038
172.723
172.574
166.921
148.812
145.980
140.864
140.208
129.568
128.256
128.050
125.935
124.966
124.635
123.771
115.413
86.453
84.833
82.451
77.318
77.000
76.682
63.114
56.199
52.994
50.569
45.890
33.334
32.596
27.990
27.682
27.029
Boc
N
O
O
Boc
Ph
O
N
Boc
3l
100000
50000
0
150
100
50
ppm (t1)


7.615
7.602
7.590
7.274
7.136
7.132
7.116
7.101
7.081
7.071
7.067
7.060
6.975
6.958
6.950
6.939
6.932
6.928
6.920
6.914
6.910
6.904
4.346
4.327
4.322
4.303
4.072
4.047
4.042
4.017
3.968
3.962
3.949
3.932
1.576
0.986
-0.00000
Boc
O
N
O
Boc
F
Ph
O
N
Boc
3m
10000
5000
0
0.96
3.02
4.10
1.00
1.01
18.08
9.18
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

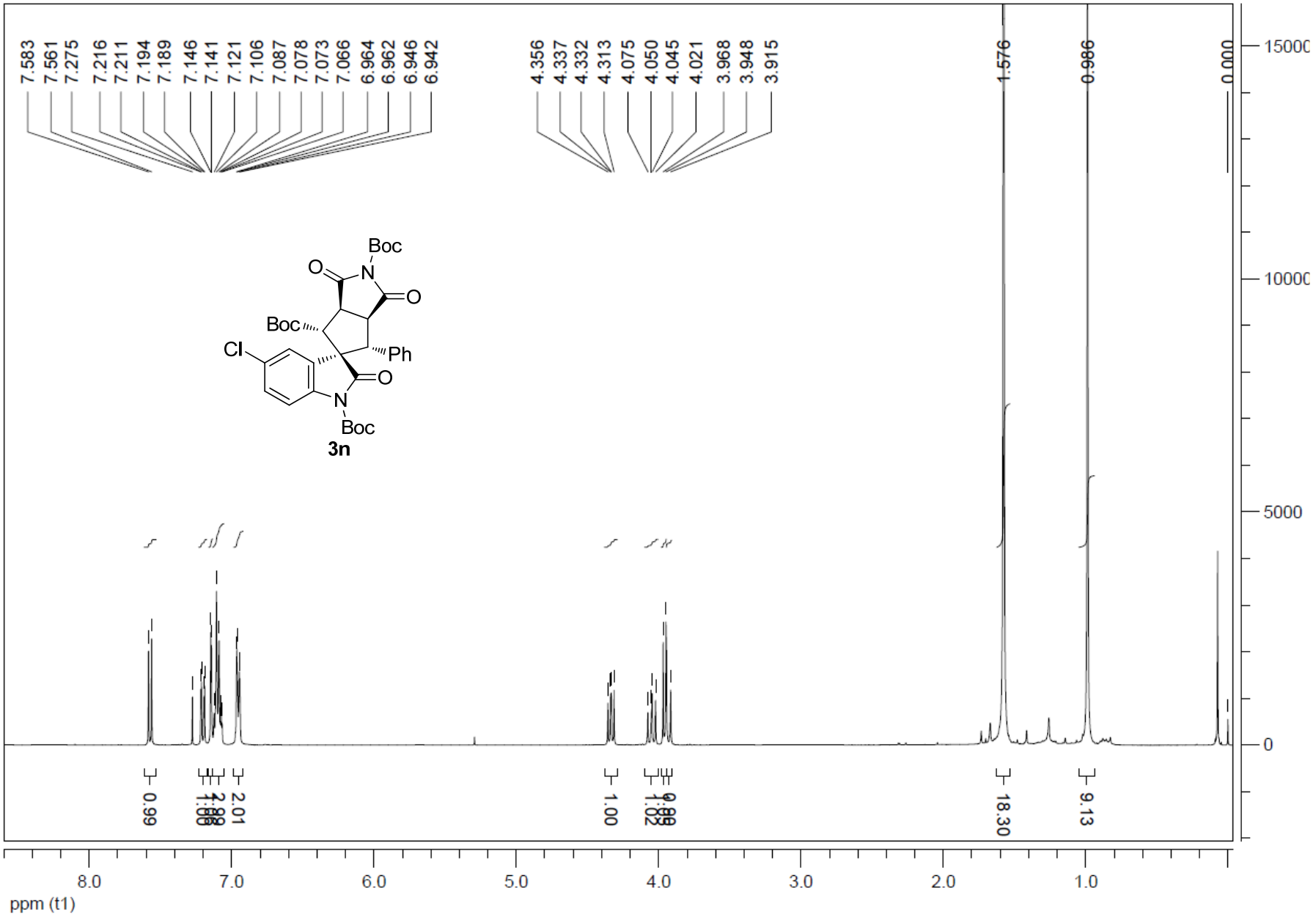

174.064
172.798
171.073
166.940
160.514
158.079
148.364
145.884
135.898
135.874
132.072
128.275
128.251
127.517
126.756
126.679
116.341
116.263
115.860
115.637
111.510
111.264
86.518
84.776
82.671
77.318
77.000
76.682
65.601
65.585
58.740
54.492
47.430
45.421
27.930
27.672
27.065
Boc
N
O
O
Boc
F
Ph
O
N
Boc
3m
159.3 (d, $^{1}J_{C-F}$ = -243.5 Hz)
50000
40000
30000
20000
10000
0
200
150
100
50
ppm (t1)

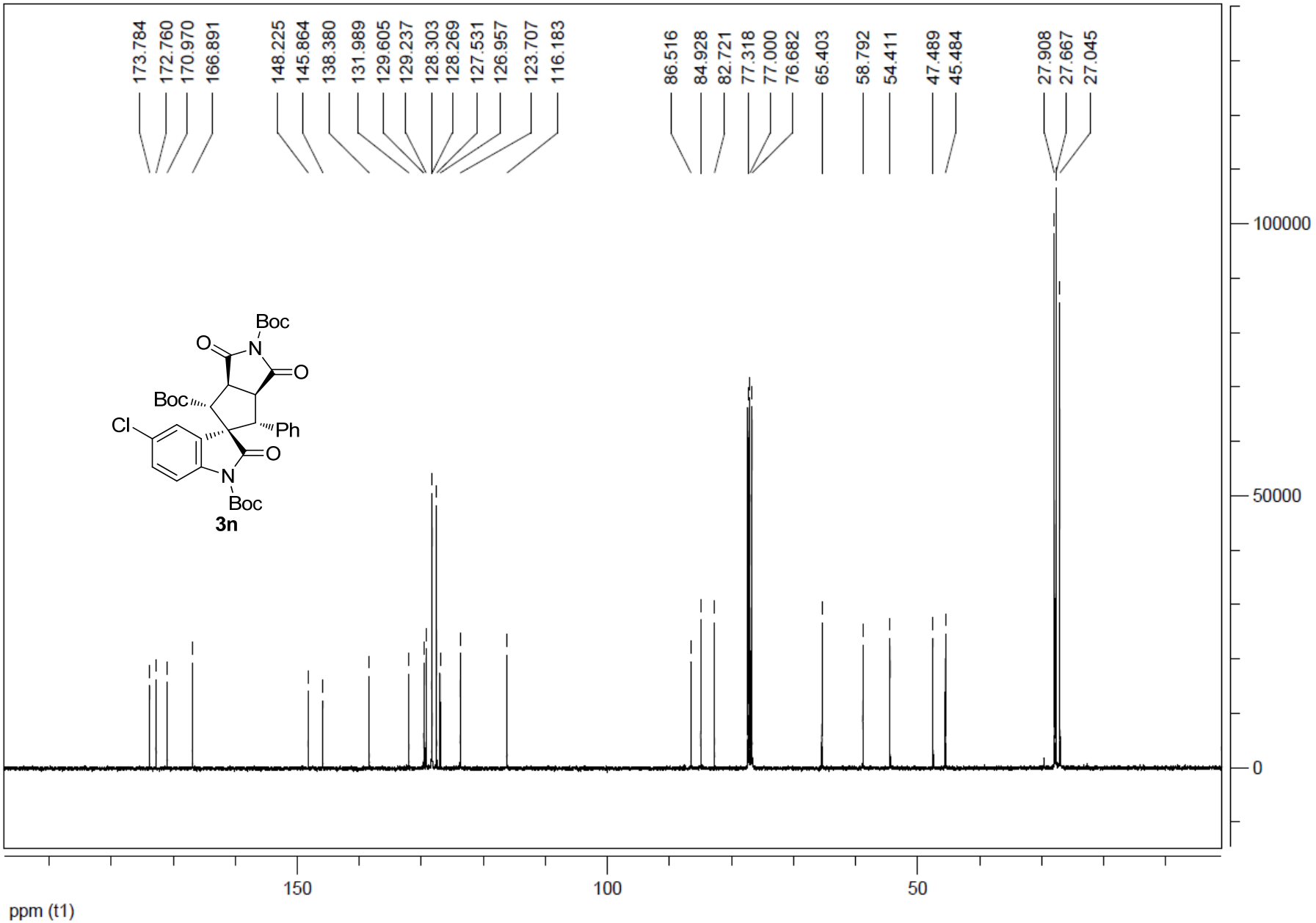


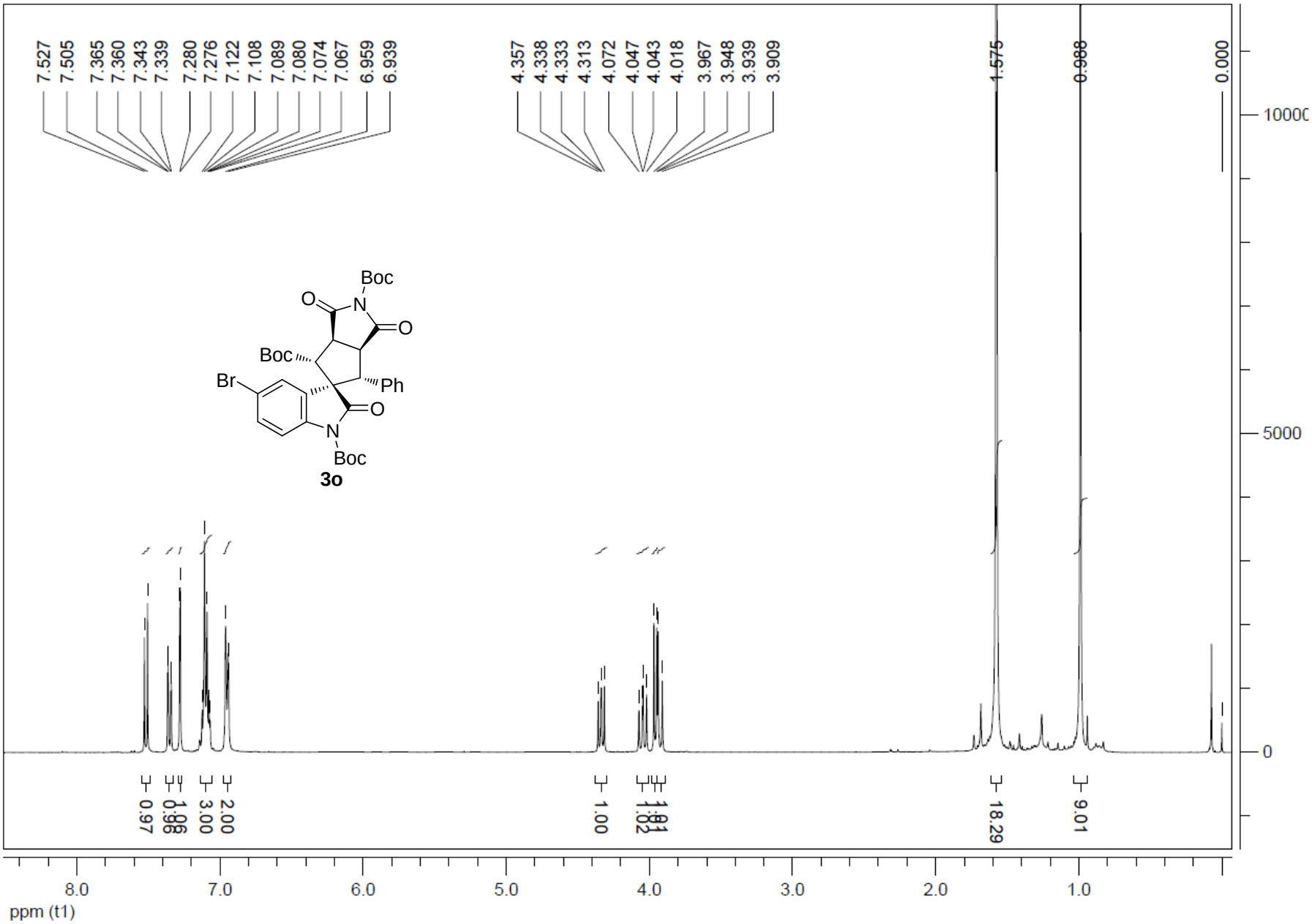
Partial enlargement of ^{13}C NMR of **3m** for clarify the C-F coupling.

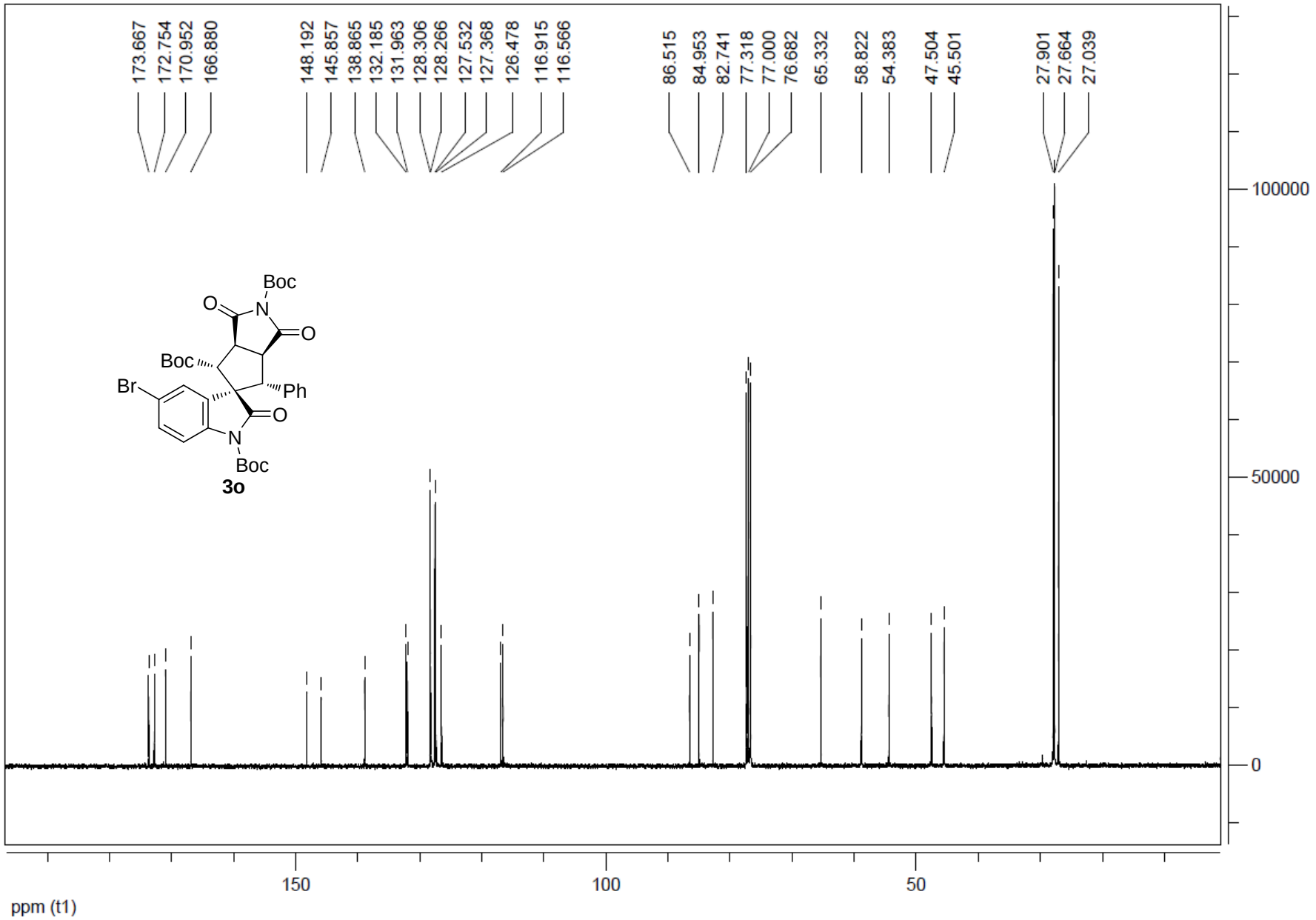


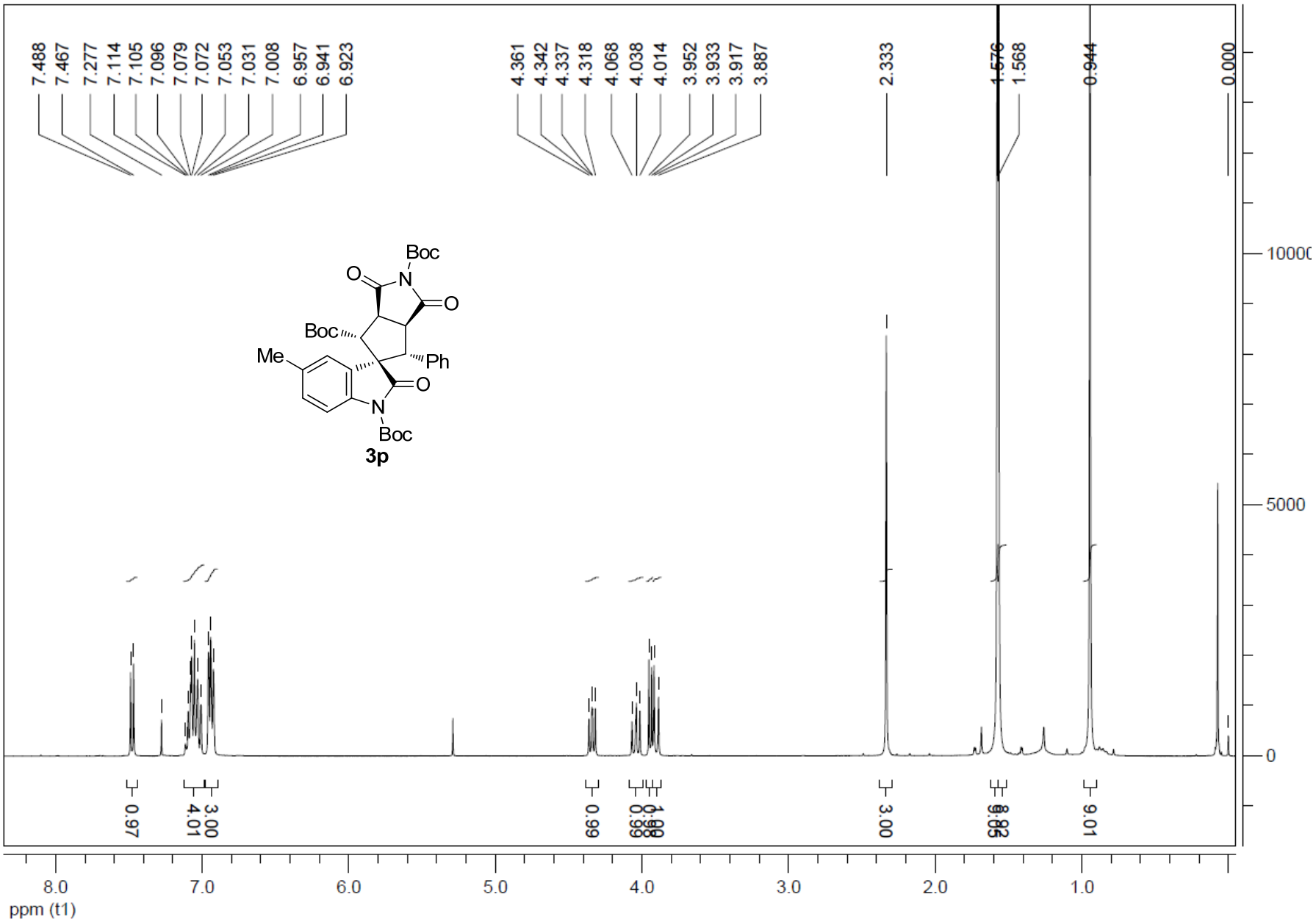
Partial enlargement of ^{13}C NMR of **3m** for clarify the C-F coupling.

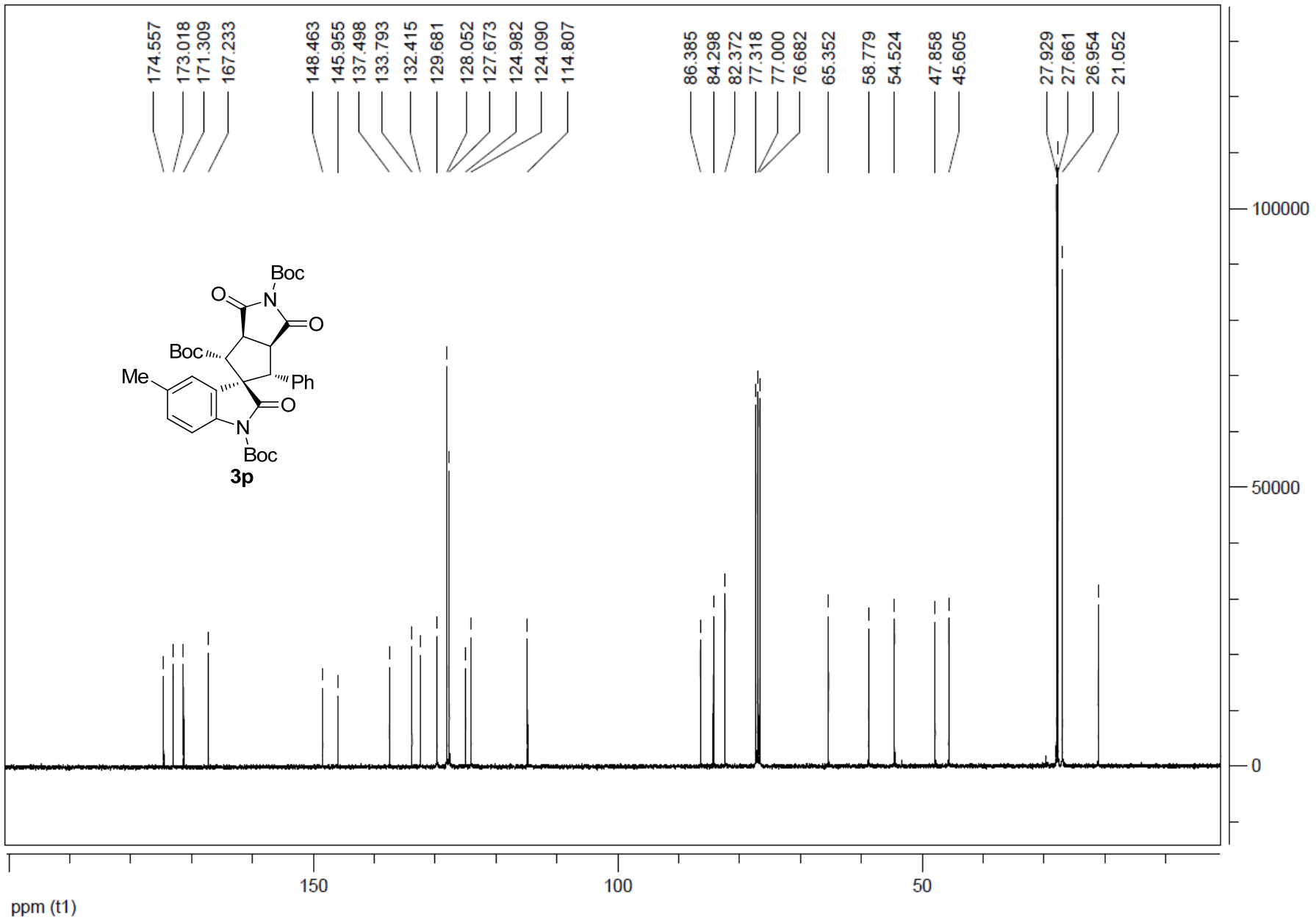

7.583
7.561
7.275
7.216
7.211
7.194
7.189
7.146
7.141
7.121
7.106
7.087
7.078
7.073
7.066
6.964
6.962
6.946
6.942
4.356
4.337
4.332
4.313
4.075
4.050
4.045
4.021
3.968
3.948
3.915
1.576
0.986
0.000
Boc
N
O
O
Boc
Cl
Ph
O
N
Boc
3n
0.99
2.01
1.00
18.30
9.13
15000
10000
5000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

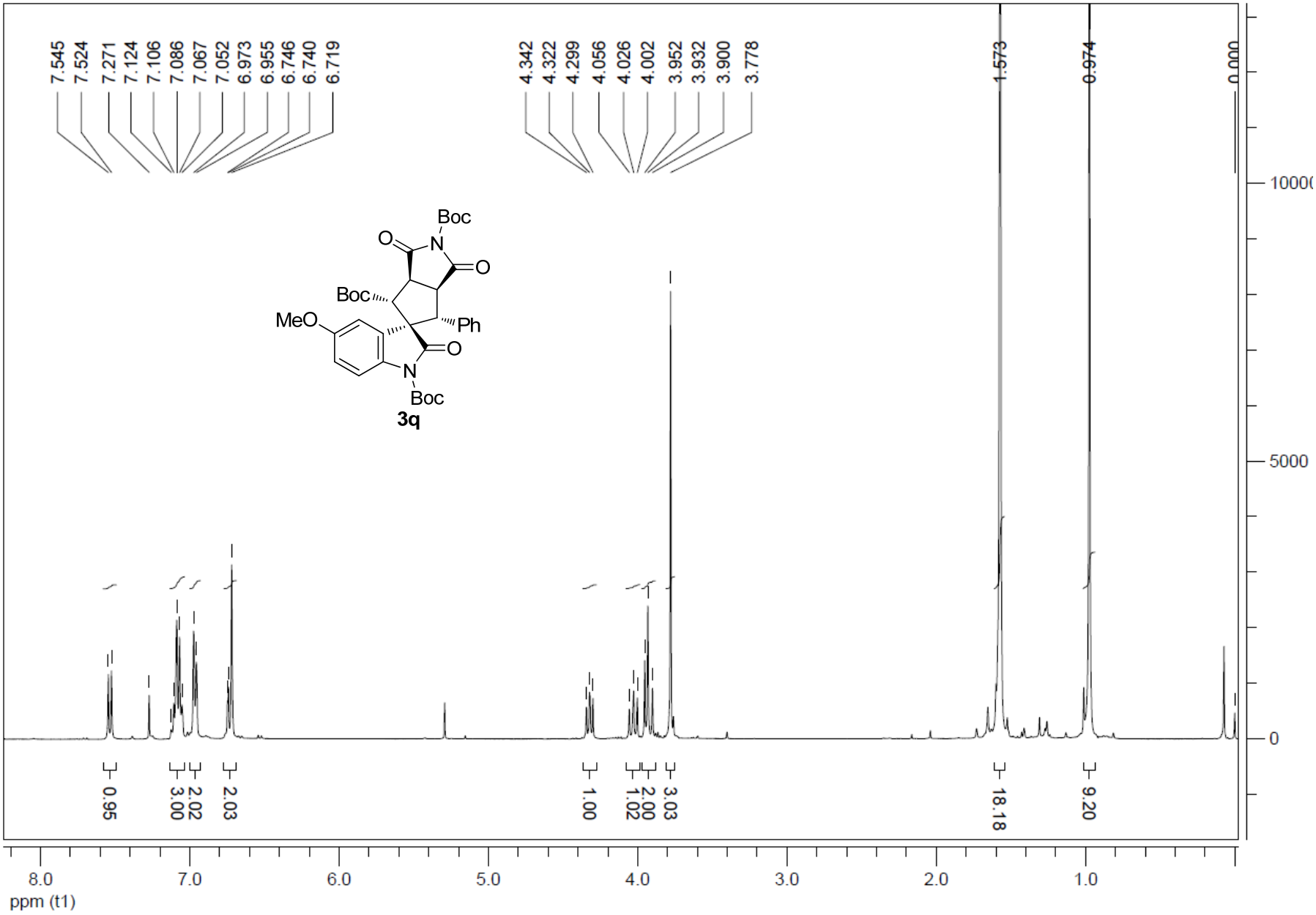

173.784
172.760
170.970
166.891
148.225
145.864
138.380
131.989
129.605
129.237
128.303
128.269
127.531
126.957
123.707
116.183
86.516
84.928
82.721
77.318
77.000
76.682
65.403
58.792
54.411
47.489
45.484
27.908
27.667
27.045
Boc
O
N
O
Boc
Cl
Ph
O
N
Boc
3n
100000
50000
0
150
100
50
ppm (t1)

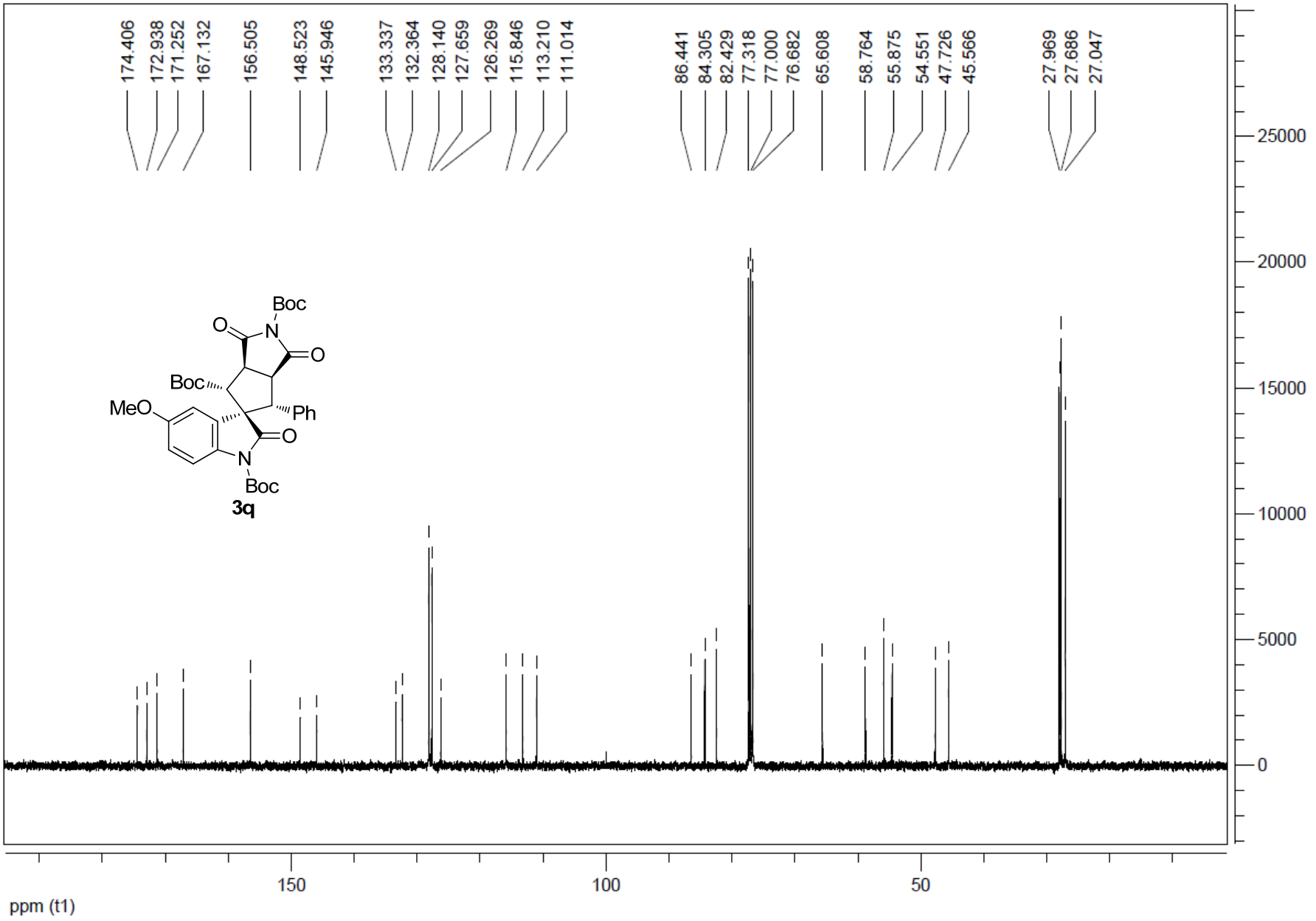

7.527
7.505
7.365
7.360
7.343
7.339
7.280
7.276
7.122
7.108
7.089
7.080
7.074
7.067
6.959
6.939
4.357
4.338
4.333
4.313
4.072
4.047
4.043
4.018
3.967
3.948
3.939
3.909
1.575
0.988
0.000
Boc
O
N
O
Boc
Br
Ph
O
N
Boc
3o
0.97
1.96
0.98
3.00
2.00
1.00
1.02
1.01
1.01
18.29
9.01
10000
5000
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

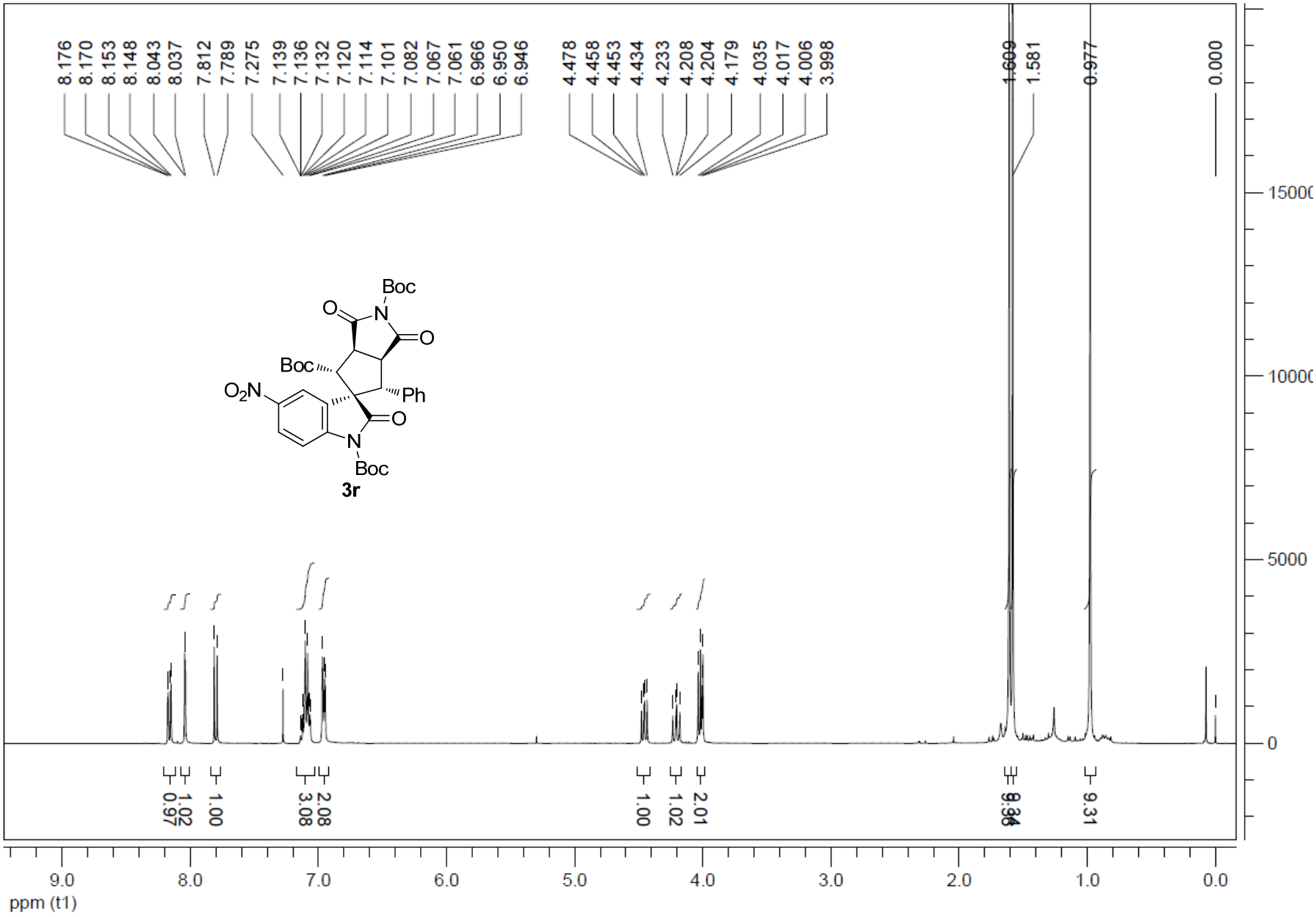

173.667
172.754
170.952
166.880
148.192
145.857
138.865
132.185
131.963
128.306
128.266
127.532
127.368
126.478
116.915
116.566
86.515
84.953
82.741
77.318
77.000
76.682
65.332
58.822
54.383
47.504
45.501
27.901
27.664
27.039
Boc
O
N
O
Boc
Br
Ph
O
N
Boc
3o
100000
50000
0
150
100
50
ppm (t1)

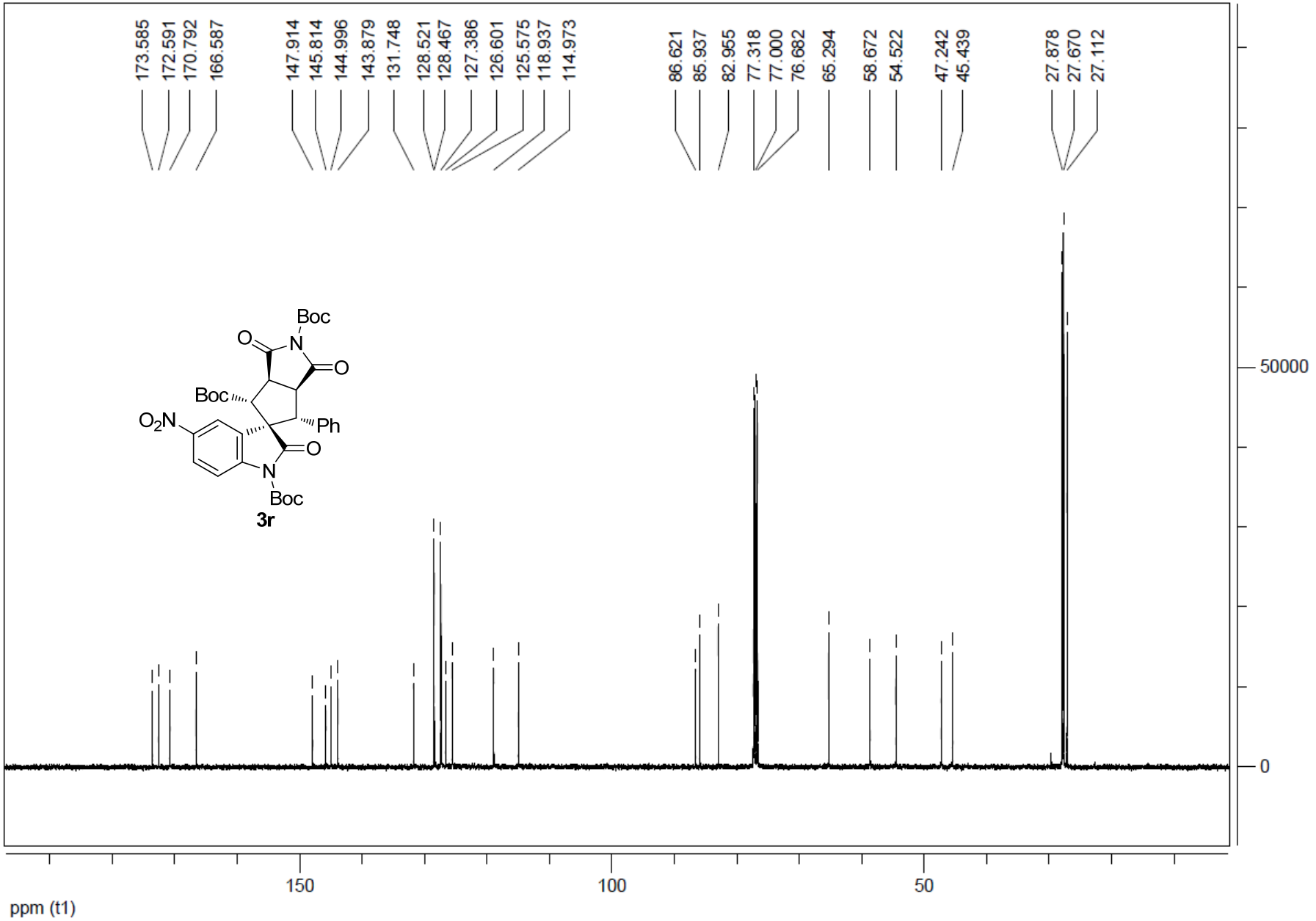

7.488
7.467
7.277
7.114
7.105
7.096
7.079
7.072
7.053
7.031
7.008
6.957
6.941
6.923
4.361
4.342
4.337
4.318
4.068
4.038
4.014
3.952
3.933
3.917
3.887
2.333
1.576
1.568
0.944
0.000
Boc
O
N
O
Boc
Me
Ph
O
N
Boc
3p
10000
5000
0
0.97
4.01
3.00
0.99
3.00
9.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

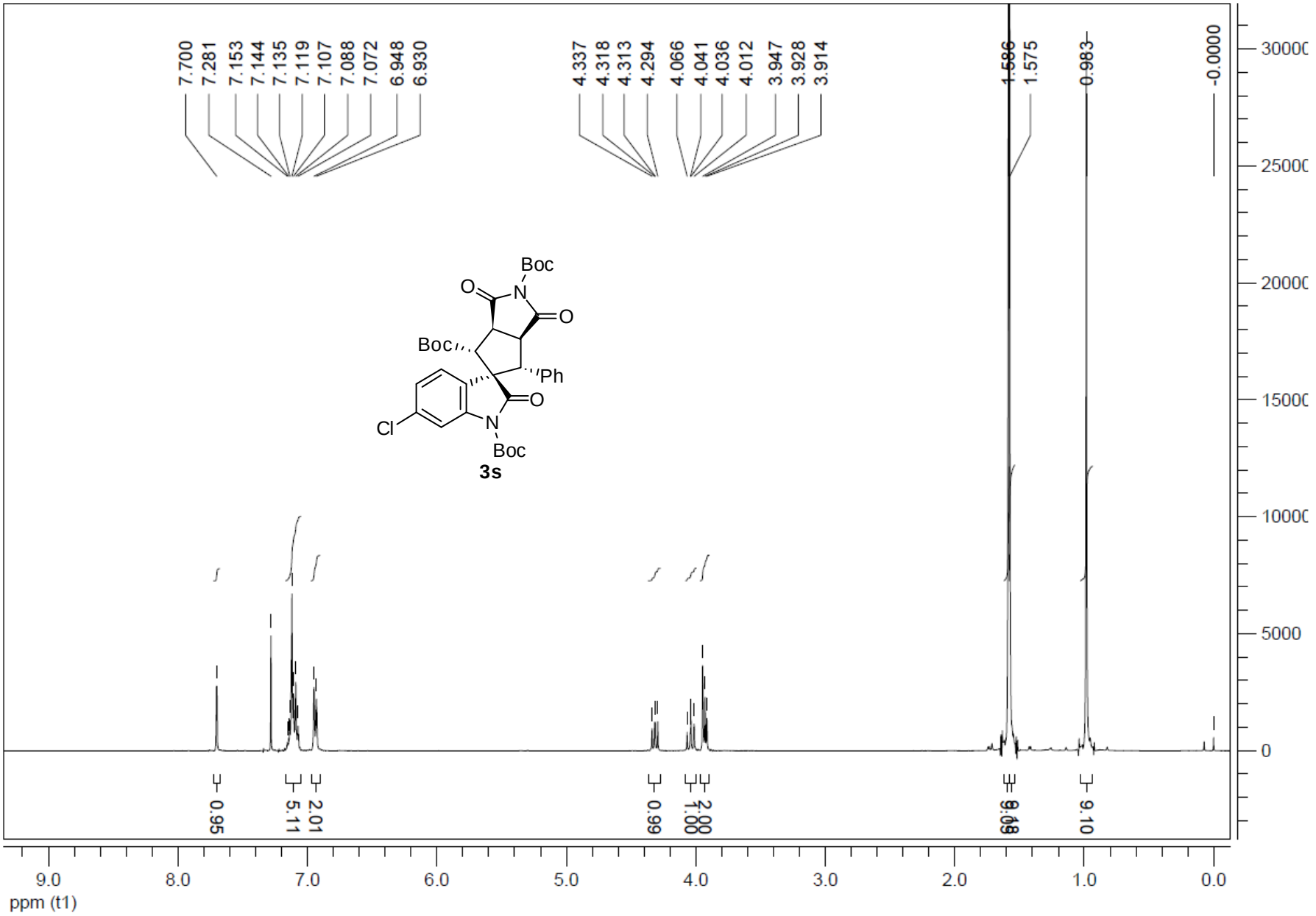

174.557
173.018
171.309
167.233
148.463
145.955
137.498
133.793
132.415
129.681
128.052
127.673
124.982
124.090
114.807
86.385
84.298
82.372
77.318
77.000
76.682
65.352
58.779
54.524
47.858
45.605
27.929
27.661
26.954
21.052
Boc
O
N
O
Boc
Me
Ph
O
N
Boc
3p
100000
50000
0
150
100
50
ppm (t1)

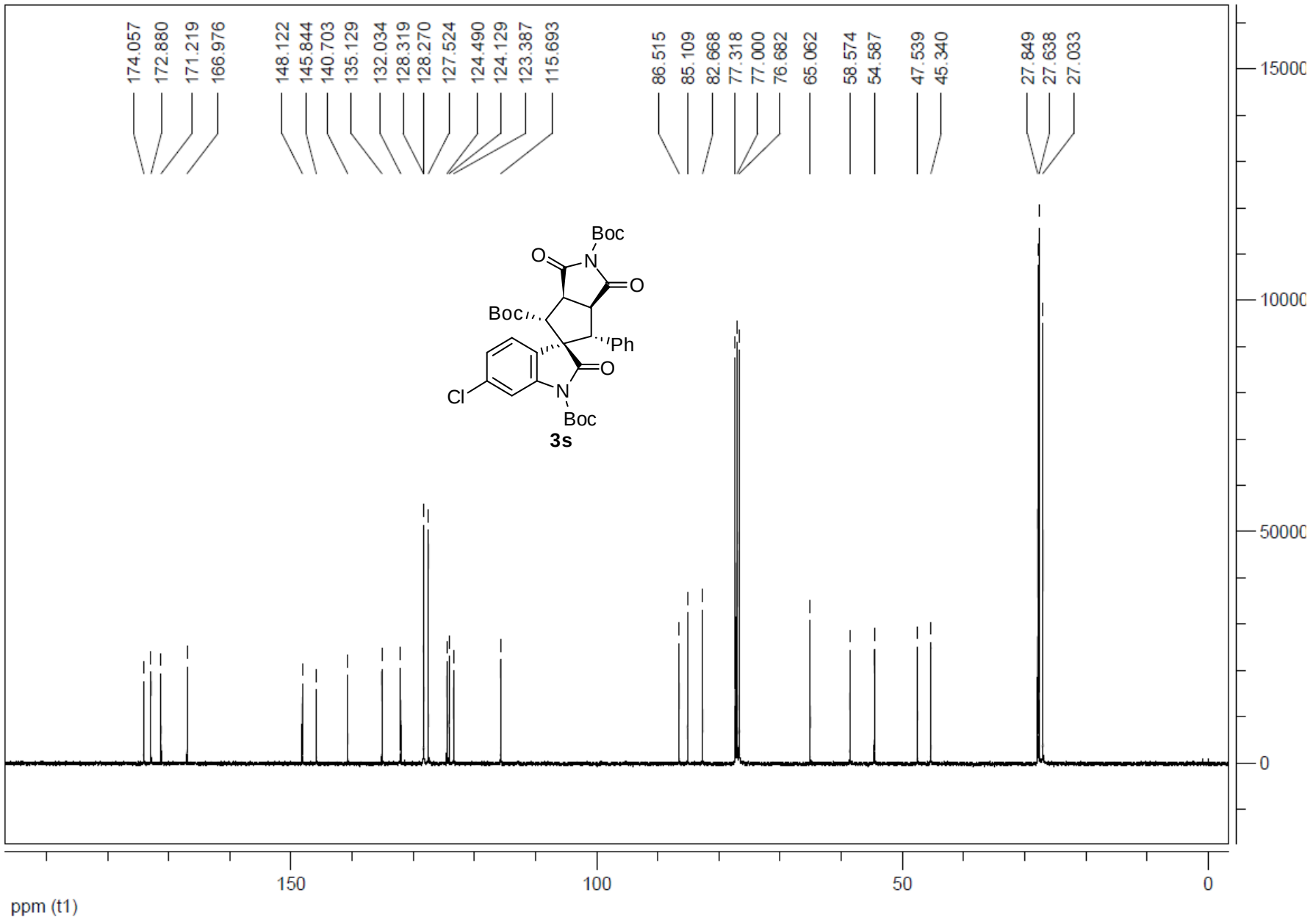

7.545
7.524
7.271
7.124
7.106
7.086
7.067
7.052
6.973
6.955
6.746
6.740
6.719
4.342
4.322
4.299
4.056
4.026
4.002
3.952
3.932
3.900
3.778
1.573
0.974
0.000
Boc
N
O
O
Boc
MeO
Ph
O
N
Boc
3q
10000
5000
0
0.95
3.00
2.02
2.03
1.00
1.02
2.00
3.03
18.18
9.20
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


174.406
172.938
171.252
167.132
156.505
148.523
145.946
133.337
132.364
128.140
127.659
126.269
115.846
113.210
111.014
86.441
84.305
82.429
77.318
77.000
76.682
65.608
58.764
55.875
54.551
47.726
45.566
27.969
27.686
27.047
Boc
O
N
O
Boc
MeO
Ph
O
N
Boc
3q
25000
20000
15000
10000
5000
0
150
100
50
ppm (t1)


8.176
8.170
8.153
8.148
8.043
8.037
7.812
7.789
7.275
7.139
7.136
7.132
7.120
7.114
7.101
7.082
7.067
7.061
6.966
6.950
6.946
4.478
4.458
4.453
4.434
4.233
4.208
4.204
4.179
4.035
4.017
4.006
3.998
1.609
1.581
0.977
0.000
Boc
O
N
O
Boc
O2N
Ph
O
N
Boc
3r
0.97
1.02
1.00
3.08
2.08
1.00
1.02
2.01
9.36
9.31
15000
10000
5000
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


173.585
172.591
170.792
166.587
147.914
145.814
144.996
143.879
131.748
128.521
128.467
127.386
126.601
125.575
118.937
114.973
86.621
85.937
82.955
77.318
77.000
76.682
65.294
58.672
54.522
47.242
45.439
27.878
27.670
27.112
Boc
O
N
O
Boc
Ph
O_2N
O
N
Boc
3r
50000
0
150
100
50
ppm (t1)


7.700
7.281
7.153
7.144
7.135
7.119
7.107
7.088
7.072
6.948
6.930
4.337
4.318
4.313
4.294
4.066
4.041
4.036
4.012
3.947
3.928
3.914
1.586
1.575
0.983
-0.0000
Boc
O
N
O
Boc
Ph
O
Cl
N
Boc
3s
0.95
5.11
2.01
0.99
1.00
2.00
9.10
ppm (t1)


174.057
172.880
171.219
166.976
148.122
145.844
140.703
135.129
132.034
128.319
128.270
127.524
124.490
124.129
123.387
115.693
86.515
85.109
82.668
77.318
77.000
76.682
65.062
58.574
54.587
47.539
45.340
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O
Boc
Ph
O
Cl
N
Boc
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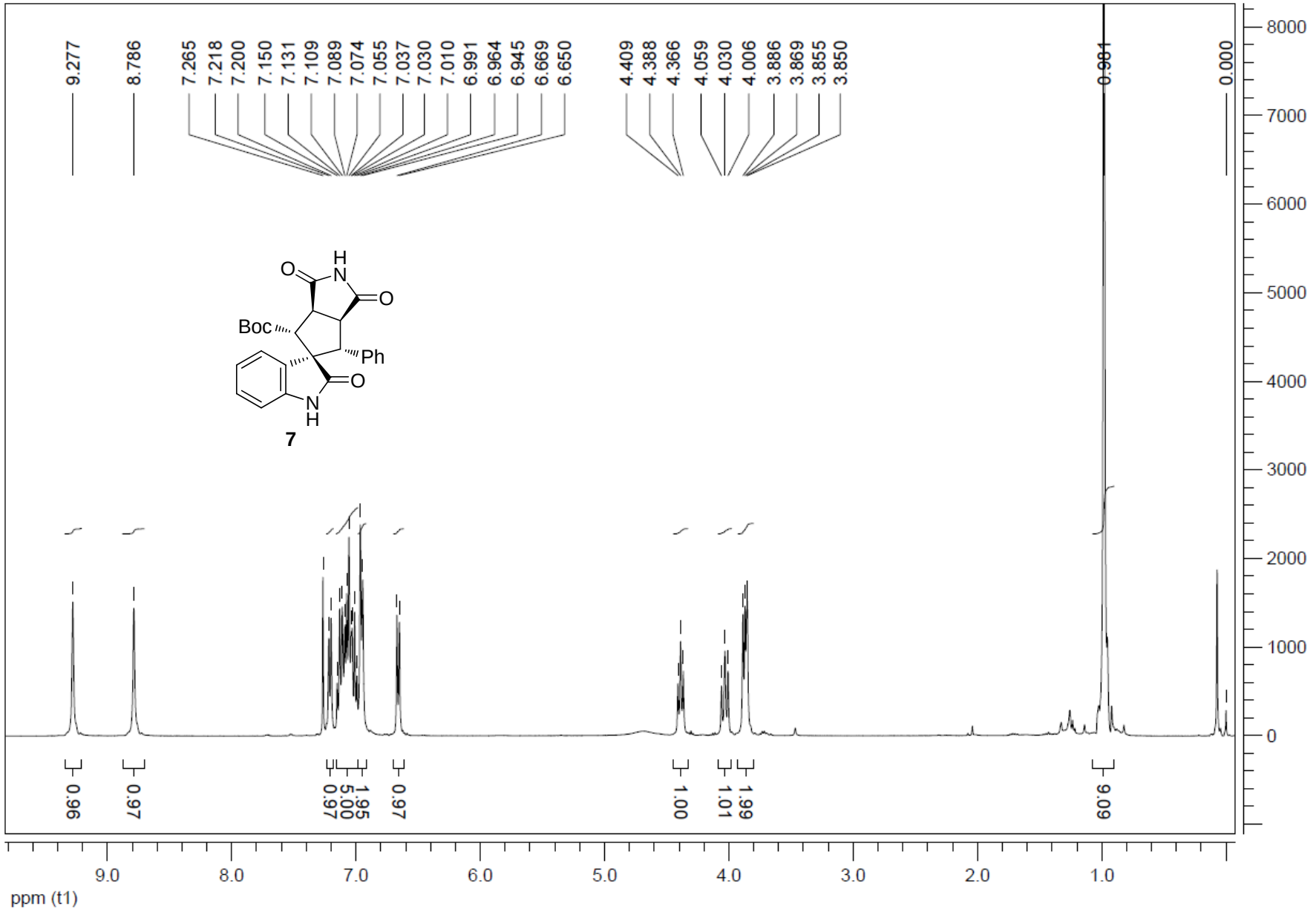
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7.030
7.010
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6.964
6.945
6.669
6.650
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4.366
4.059
4.030
4.006
3.886
3.869
3.855
3.850
0.981
0.000
Boc
Ph
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0.97
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0.97
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1.01
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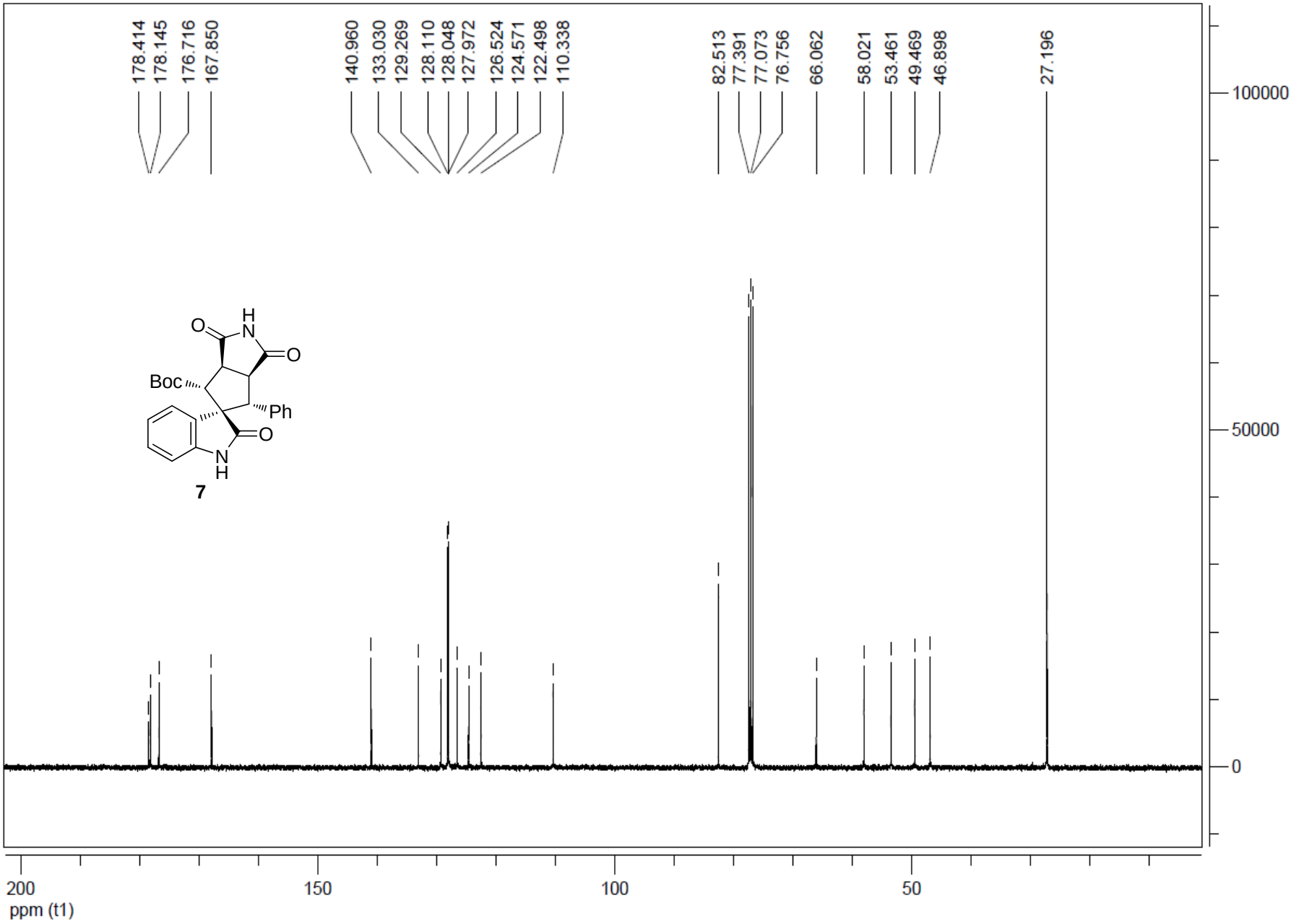
ppm (t1)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77.391
77.073
76.756
66.062
58.021
53.461
49.469
46.898
27.196
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50000
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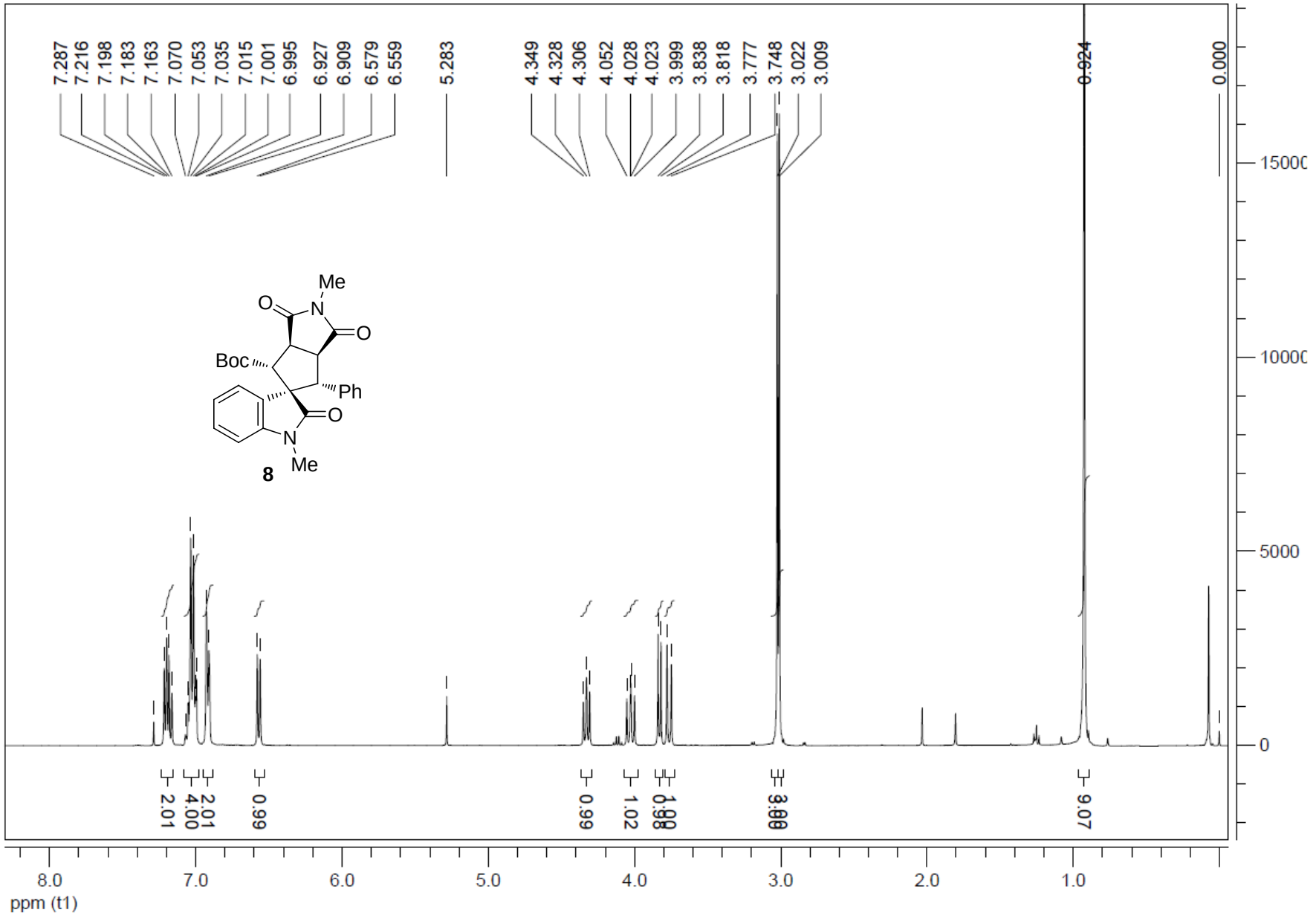
200
150
100
50
ppm (t1)
Boc
Ph
O
H
N
O
O
N
H
7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6.579
6.559
5.283
4.349
4.328
4.306
4.052
4.028
4.023
3.999
3.838
3.818
3.777
3.748
3.022
3.009
0.924
0.000
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O
N
O
Boc
Ph
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N
Me
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10000
5000
0
2.01
4.00
2.01
0.99
0.99
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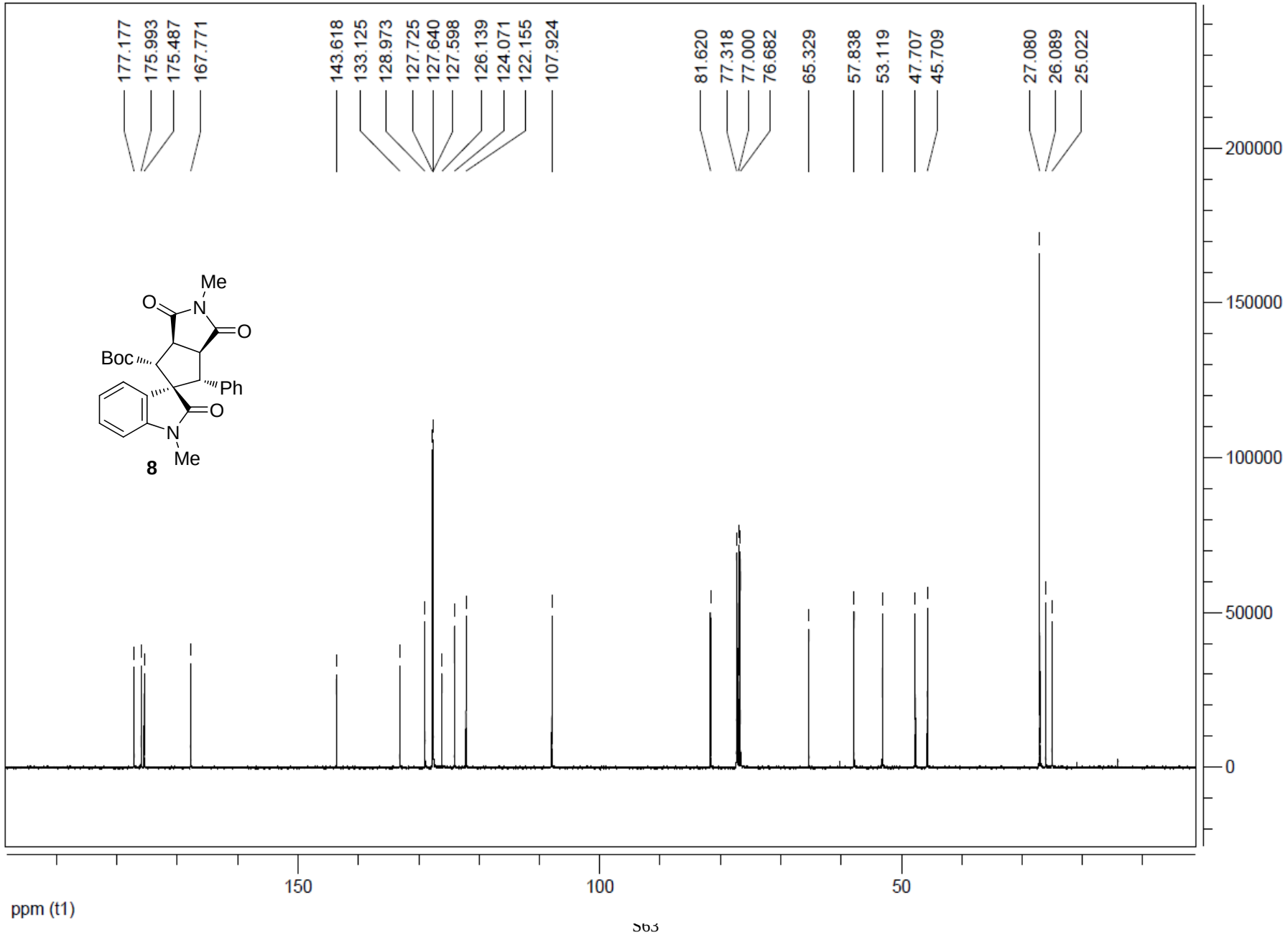
ppm (t1)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122.155
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77.318
77.000
76.682
65.329
57.838
53.119
47.707
45.709
27.080
26.089
25.022
Me
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O
Boc
Ph
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N
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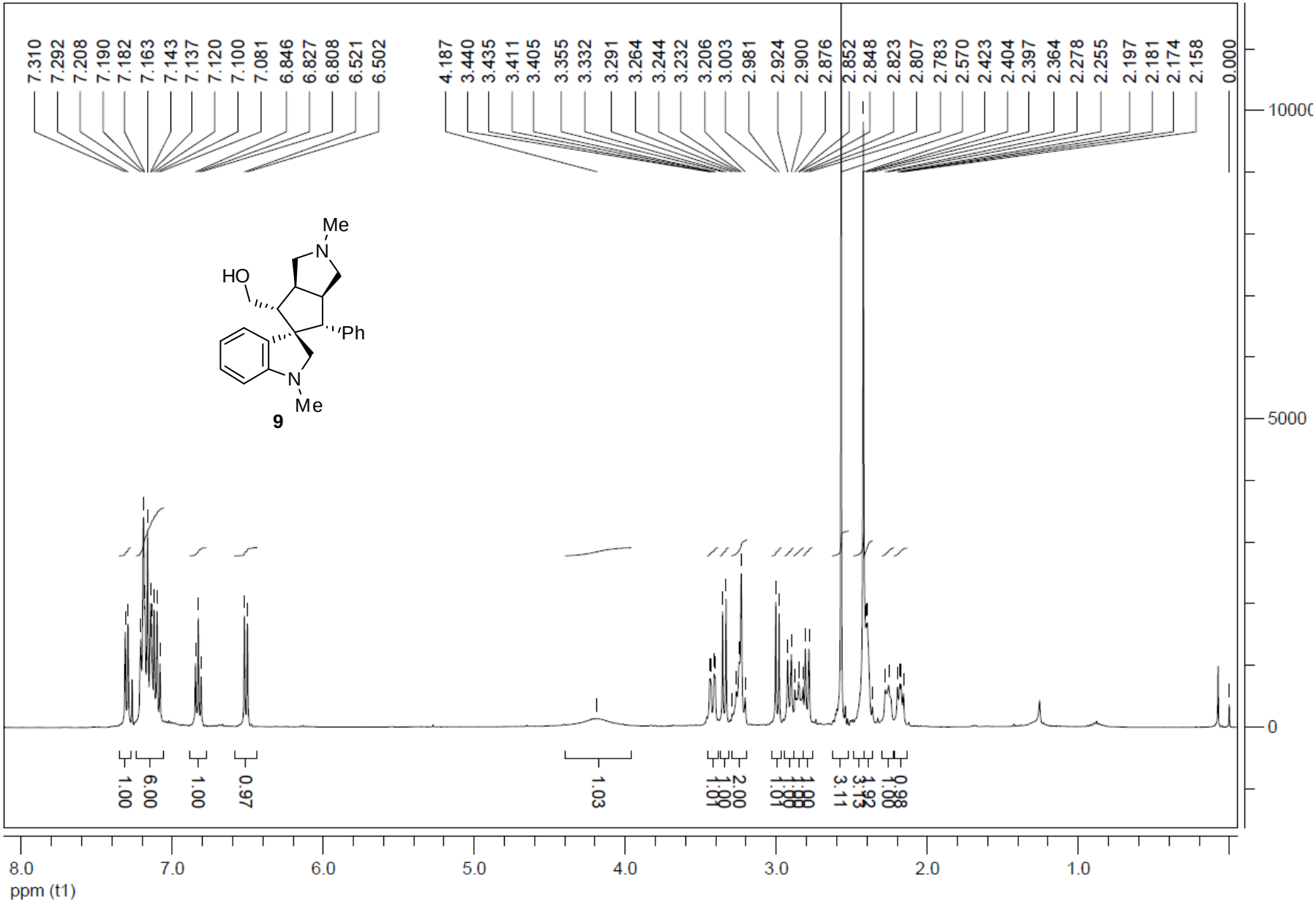
100
50
ppm (t1)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6.521
6.502
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3.435
3.411
3.405
3.355
3.332
3.291
3.264
3.244
3.232
3.206
3.003
2.981
2.924
2.900
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2.852
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2.823
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2.783
2.570
2.423
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2.397
2.364
2.278
2.255
2.197
2.181
2.174
2.158
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N
HO
Ph
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Me
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10000
5000
0
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6.00
1.00
0.97
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1.00
1.01
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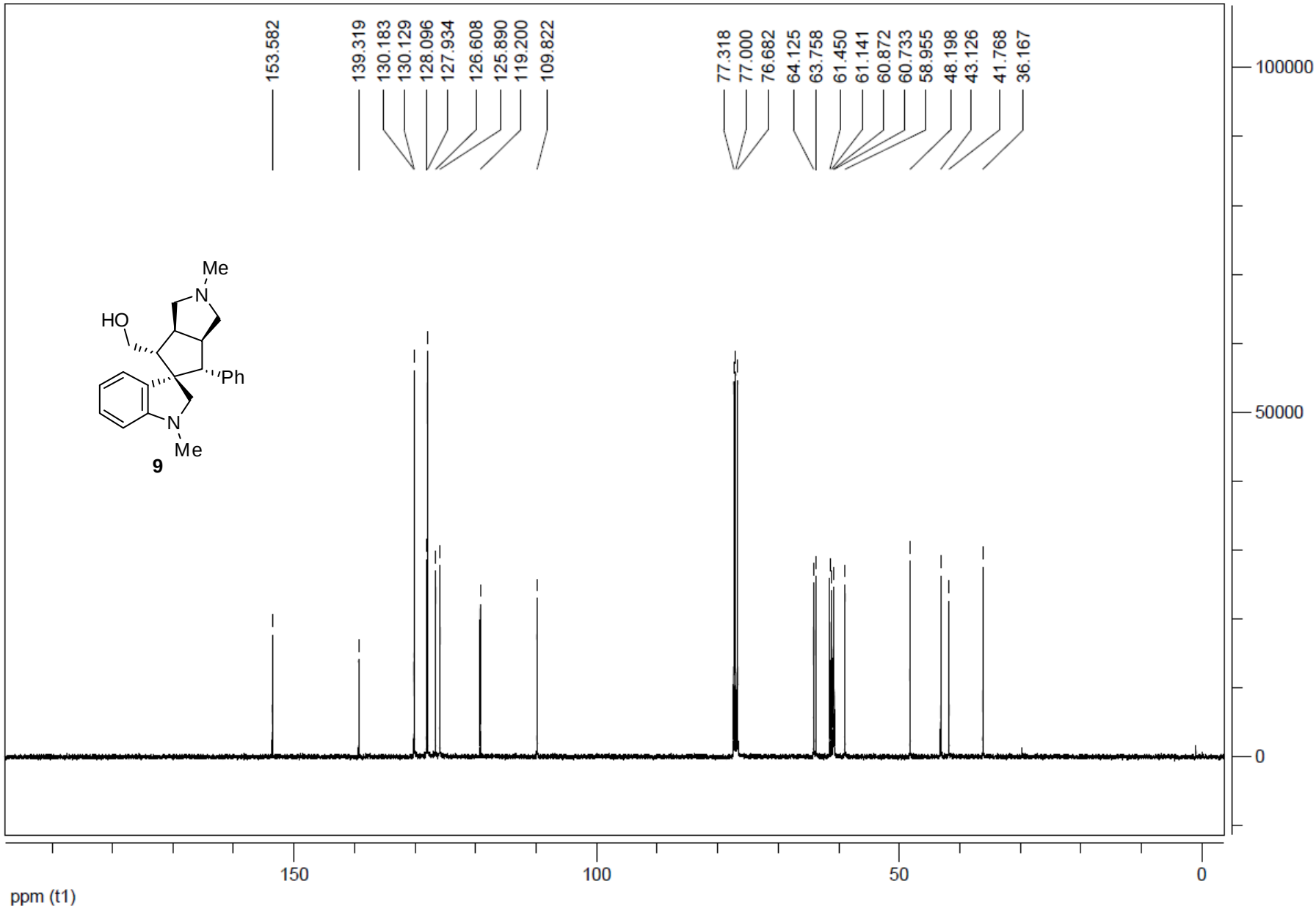
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63.758
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61.141
60.872
60.733
58.955
48.198
43.126
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HO
Ph
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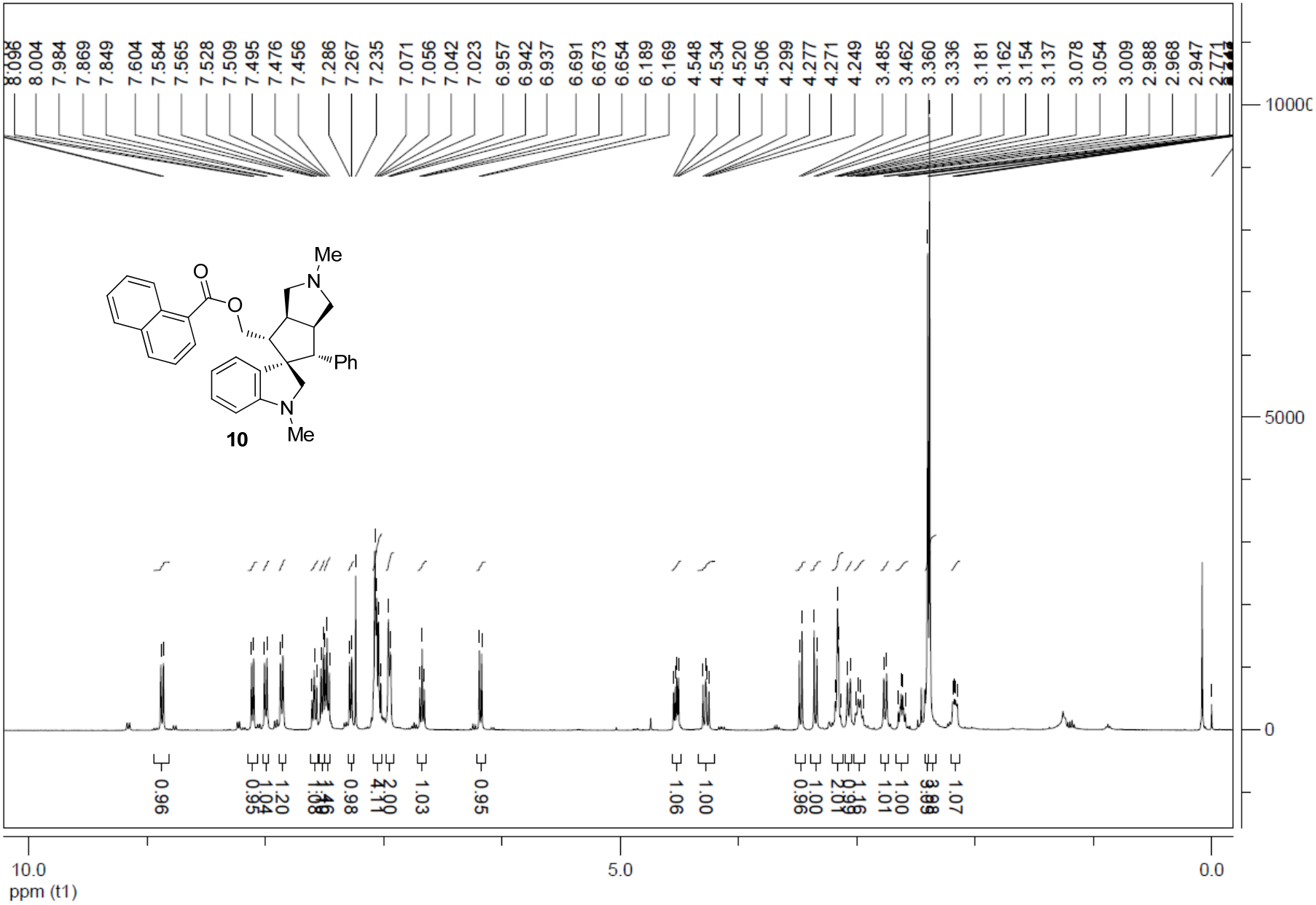
ppm (t1)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6.691
6.673
6.654
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4.506
4.299
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4.271
4.249
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Ph
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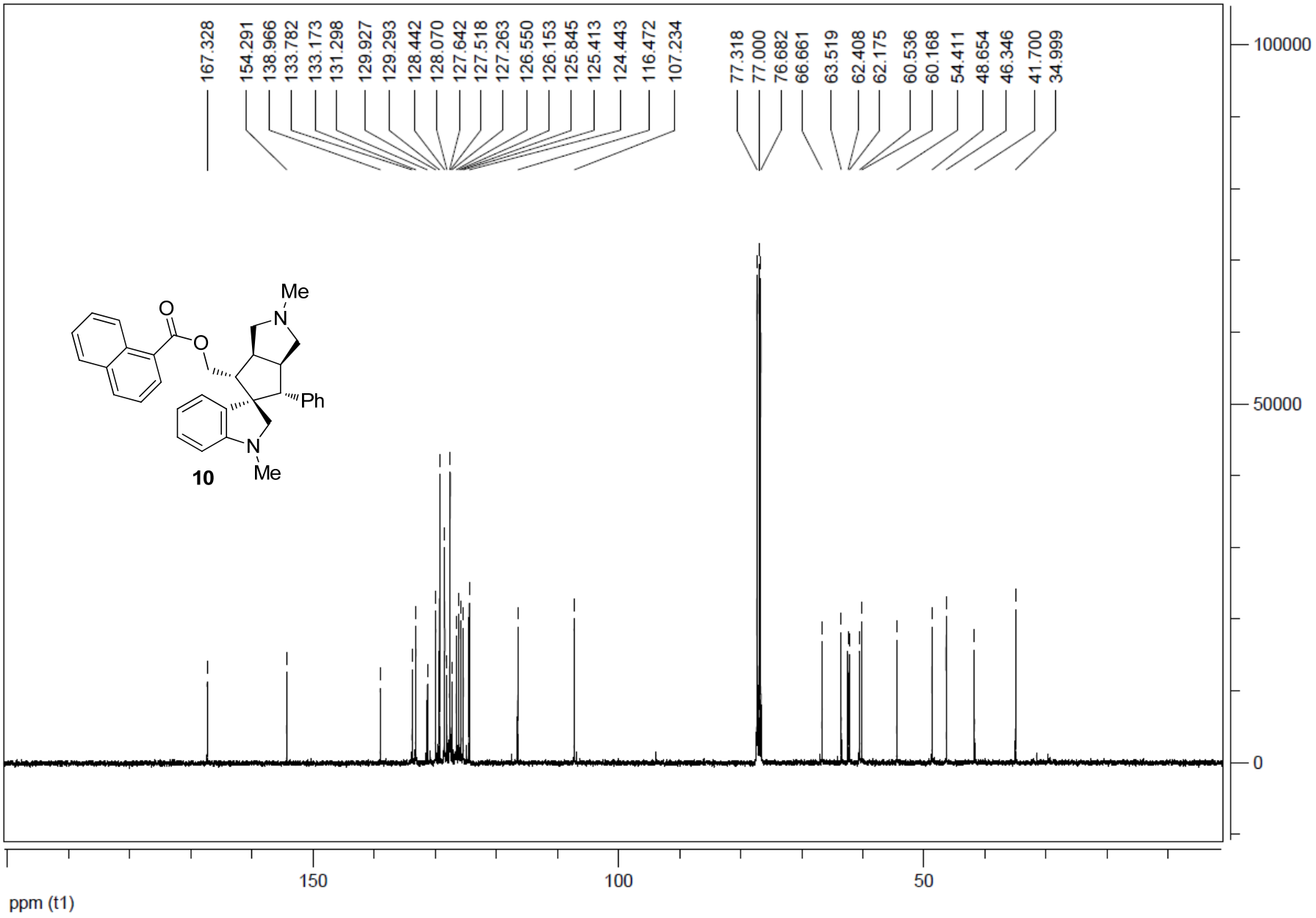
ppm (t1)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62.175
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60.168
54.411
48.654
46.346
41.700
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150
100
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ppm (t1)
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O
Ph
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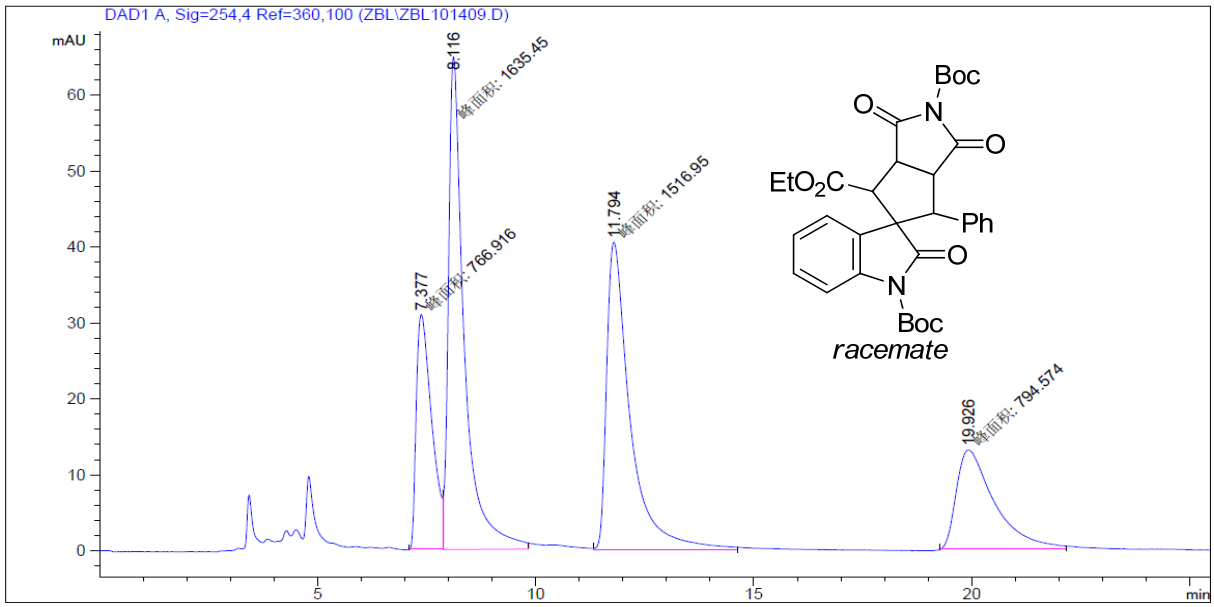
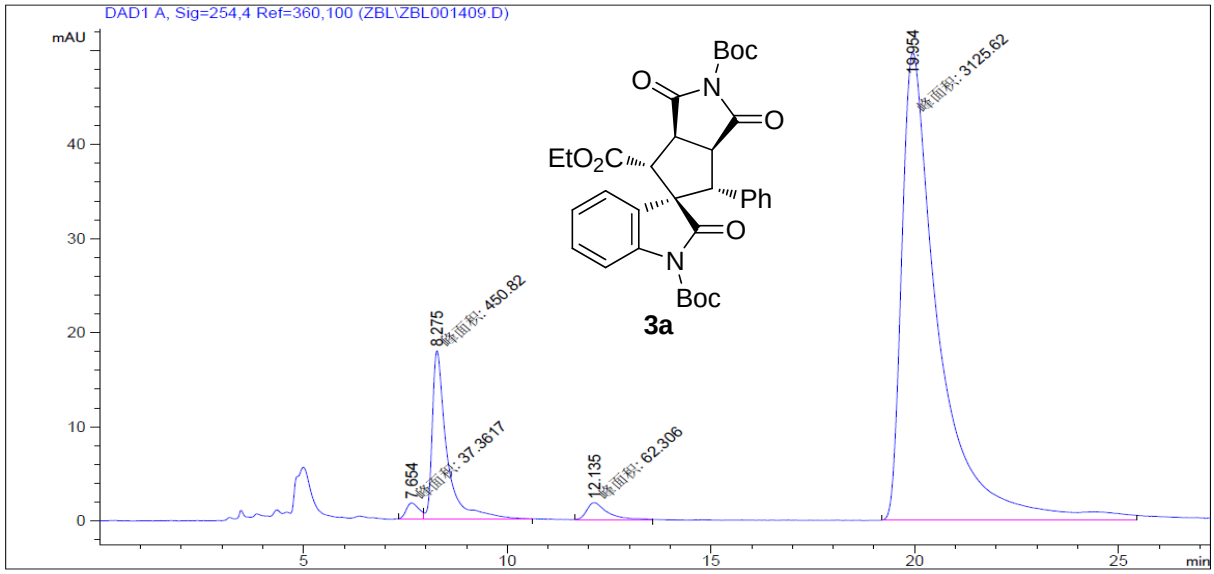
Me
10

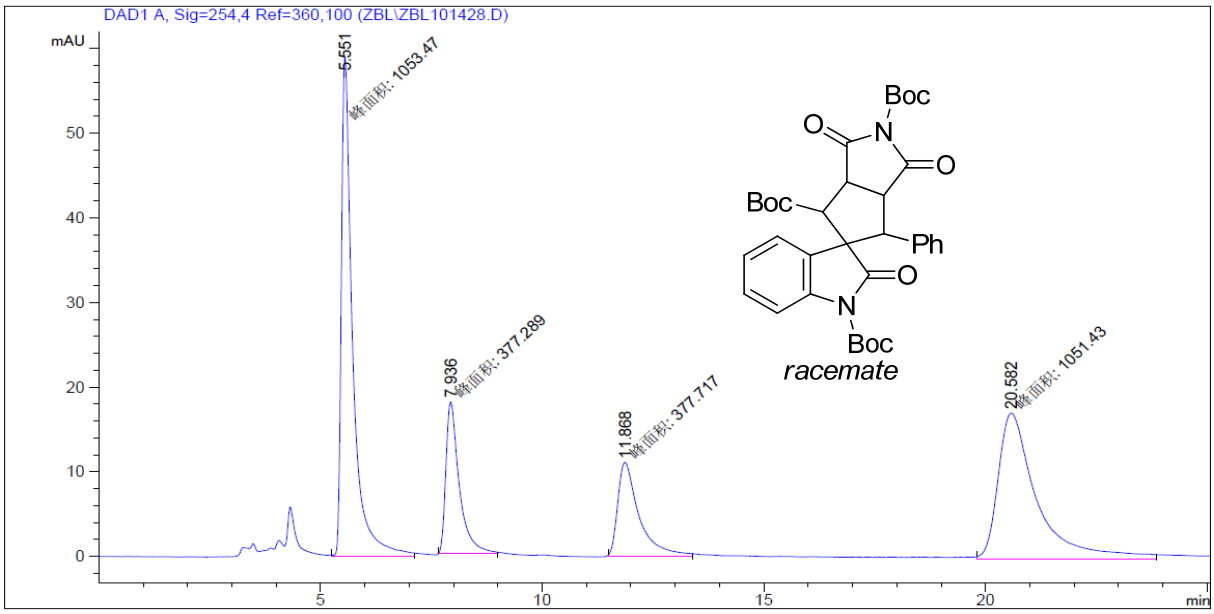
Copies of HPLC chromatograms



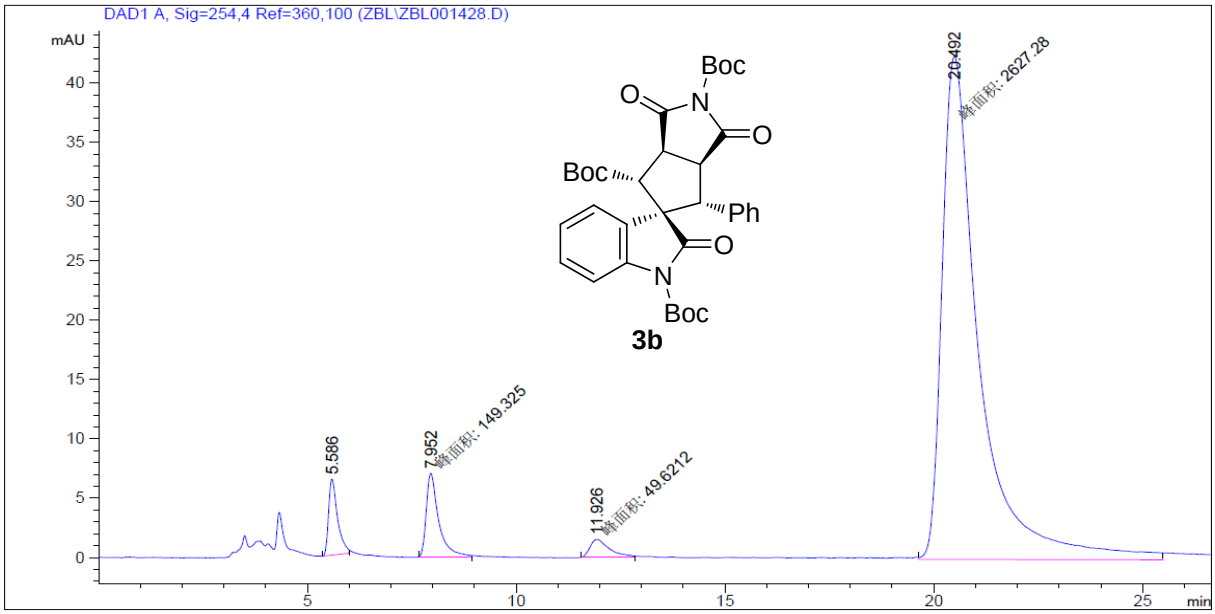
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.377	MM	0.4139	766.91589	30.87918	16.2693
2	8.116	MM	0.4200	1635.44983	64.89325	34.6943
3	11.794	MM	0.6249	1516.94800	40.45853	32.1804
4	19.926	MM	1.0157	794.57422	13.03854	16.8560



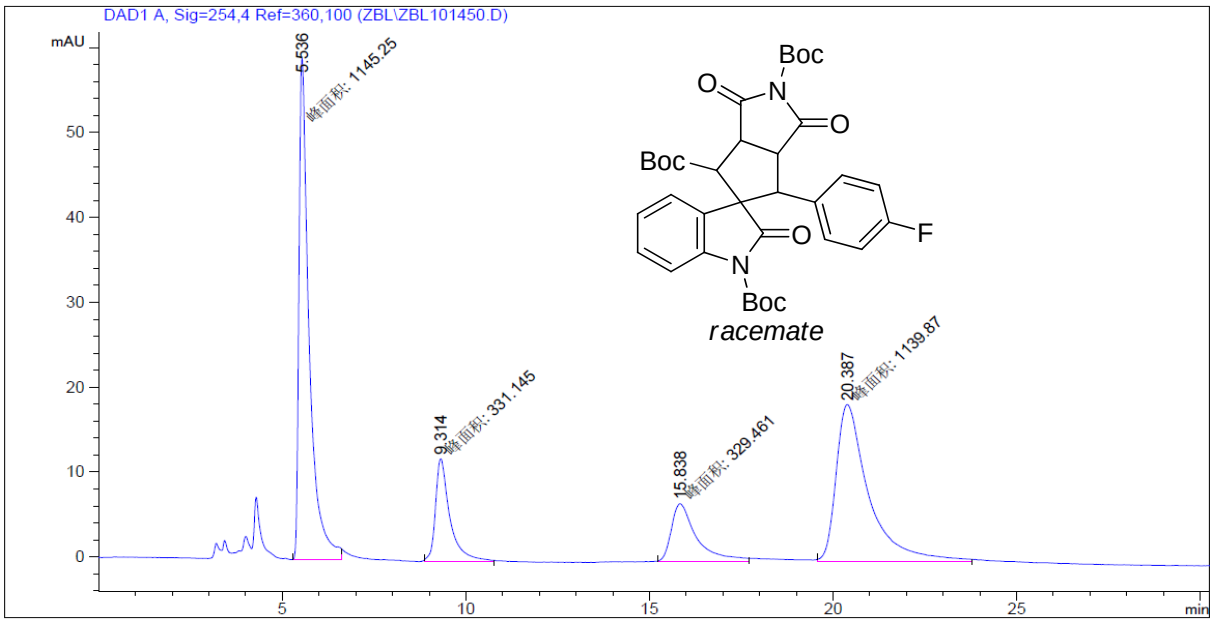
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.654	MM	0.3641	37.36168	1.71037	1.0163
2	8.275	MM	0.4199	450.82016	17.89532	12.2635
3	12.135	MM	0.5773	62.30605	1.79885	1.6949
4	19.954	MM	1.0489	3125.61743	49.66695	85.0252



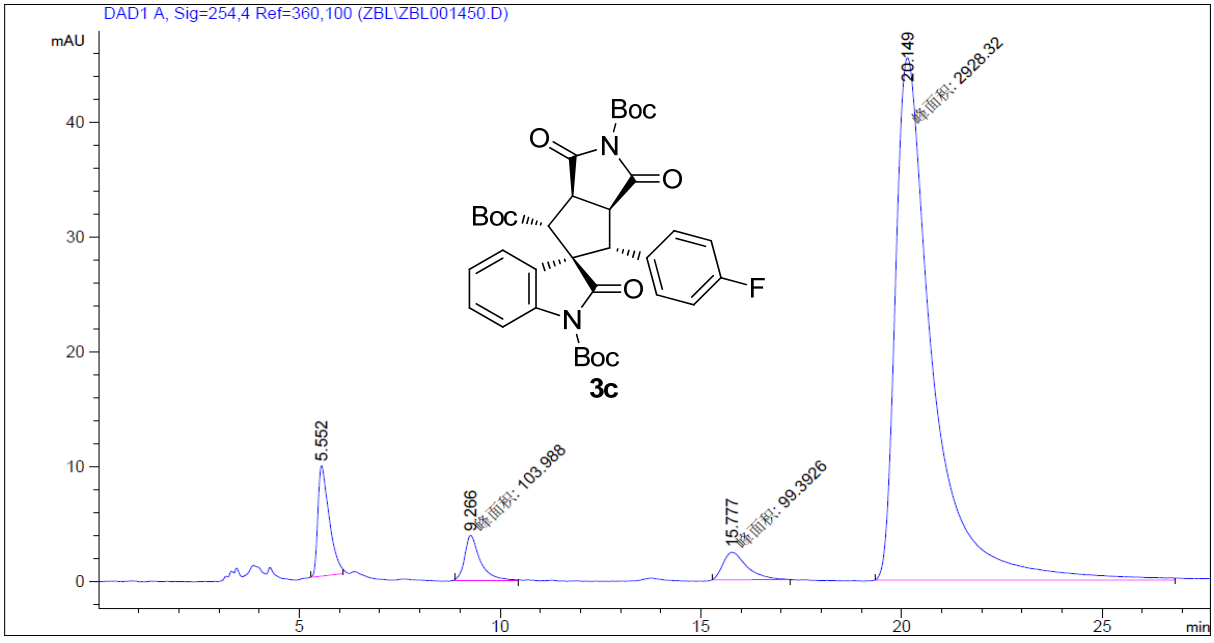
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.551	MM	0.2973	1053.47058	59.06449	36.8359
2	7.936	MM	0.3506	377.28867	17.93779	13.1924
3	11.868	MM	0.5644	377.71701	11.15329	13.2073
4	20.582	MM	0.0155	1051.42859	17.25550	36.7645



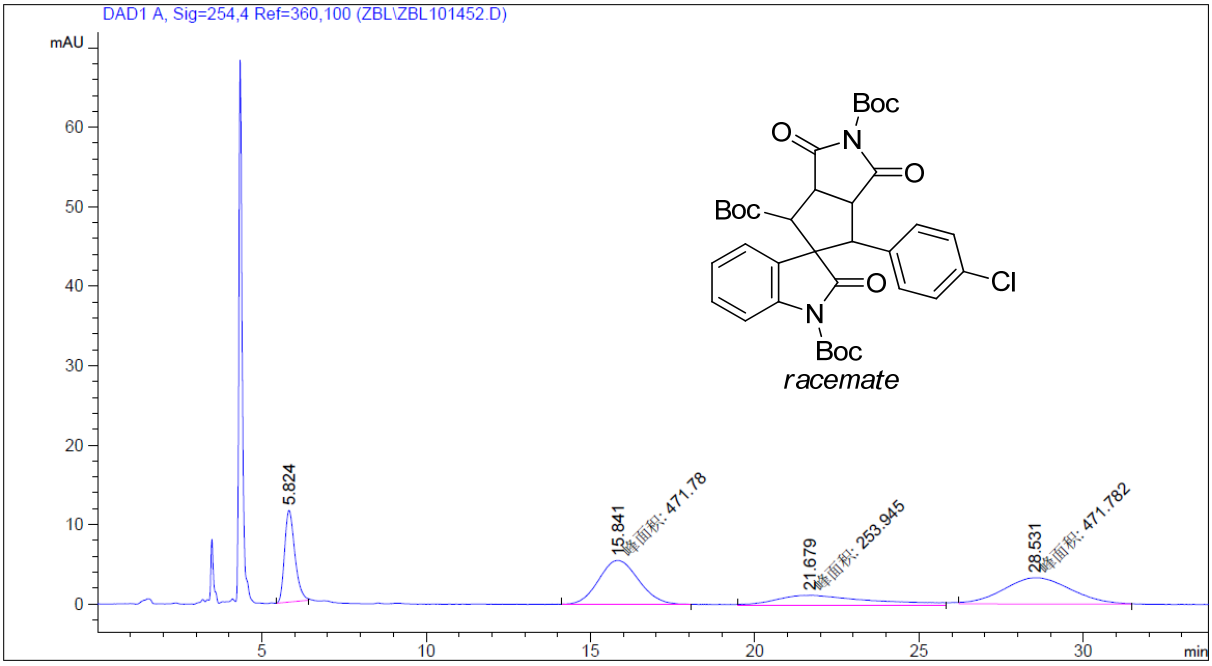
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.586	BB	0.2222	95.72656	6.41256	3.2761
2	7.952	MM	0.3511	149.32504	7.08863	5.1104
3	11.926	MM	0.5463	49.62119	1.51395	1.6982
4	20.492	MM	1.0331	2627.28394	42.38701	89.9152



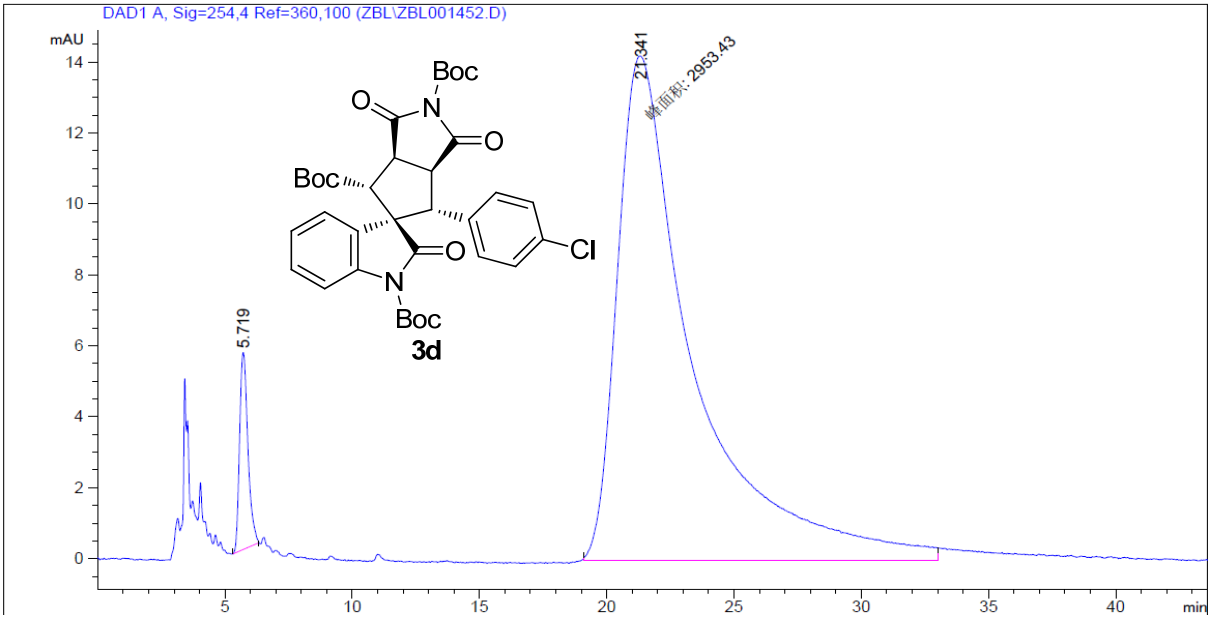
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.536	MM	0.3232	1145.25208	59.05415	38.8784
2	9.314	MM	0.4570	331.14490	12.07667	11.2415
3	15.838	MM	0.8040	329.46085	6.82925	11.1844
4	20.387	MM	1.0284	1139.86877	18.47273	38.6957



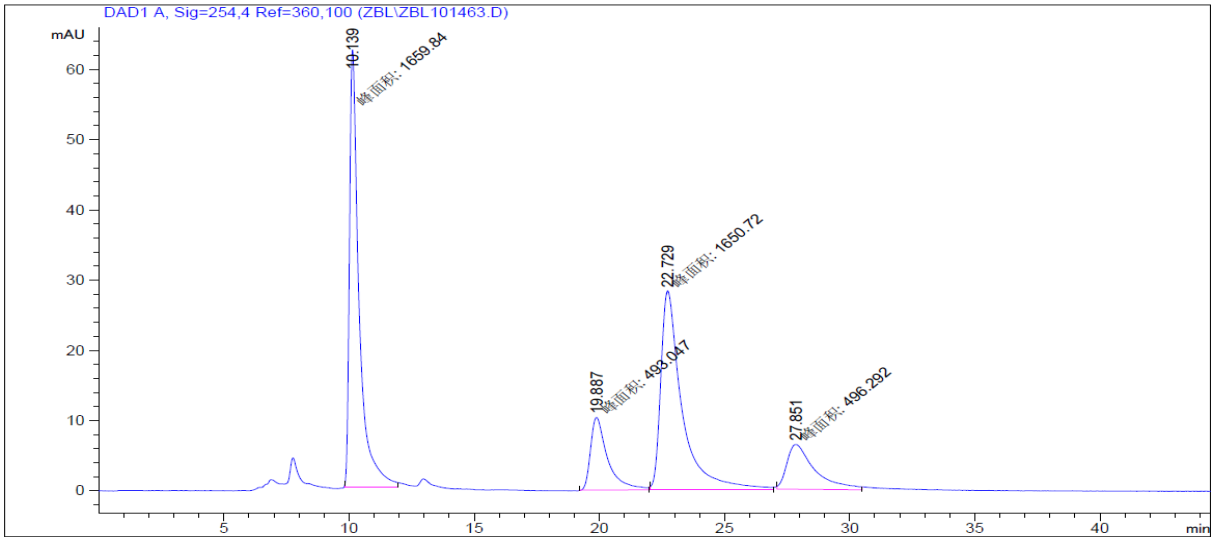
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.552	BB	0.2789	188.65700	9.61398	5.6818
2	9.266	MM	0.4430	103.98769	3.91202	3.1318
3	15.777	MM	0.6881	99.39258	2.40753	2.9934
4	20.149	MM	1.0737	2928.32349	45.45622	88.1929



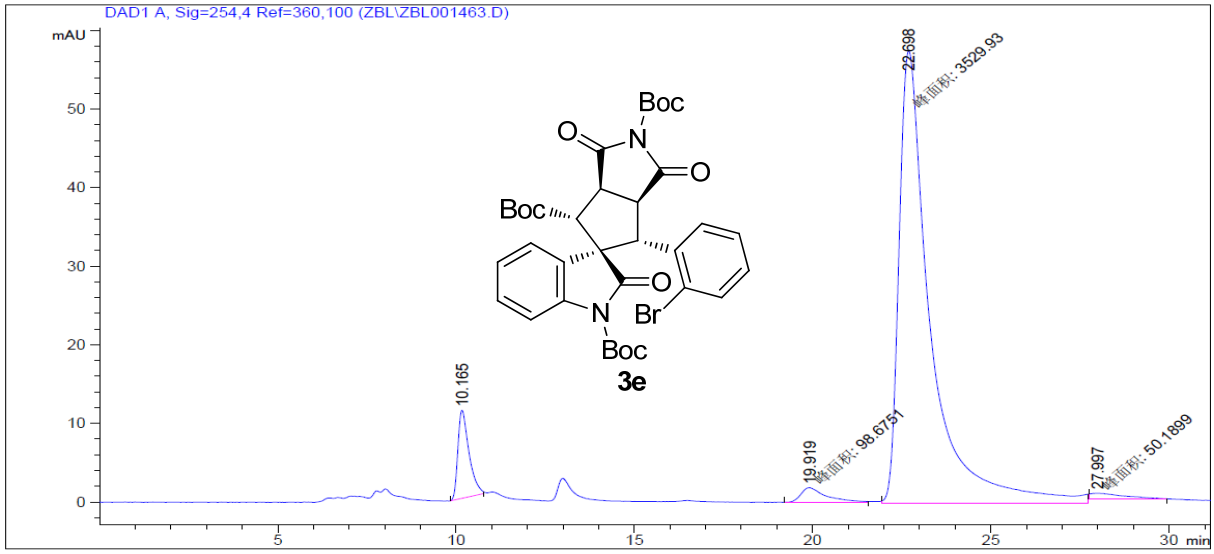
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.824	BB	0.3343	251.50803	11.53759	17.3572
2	15.841	MM	1.4157	471.77975	5.55432	32.5586
3	21.679	MM	3.3159	253.94531	1.27640	17.5254
4	28.531	MM	2.3806	471.78229	3.30303	32.5588



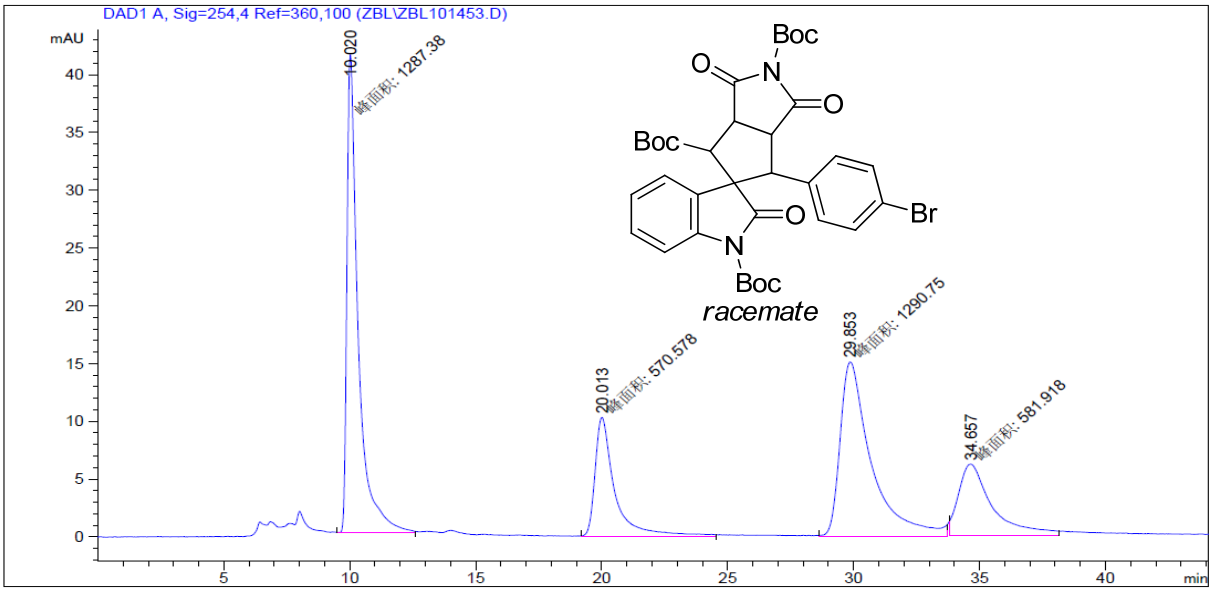
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.719	BB	0.3490	126.22916	5.55799	4.0988
2	21.341	MM	3.4613	2953.42529	14.22135	95.9012



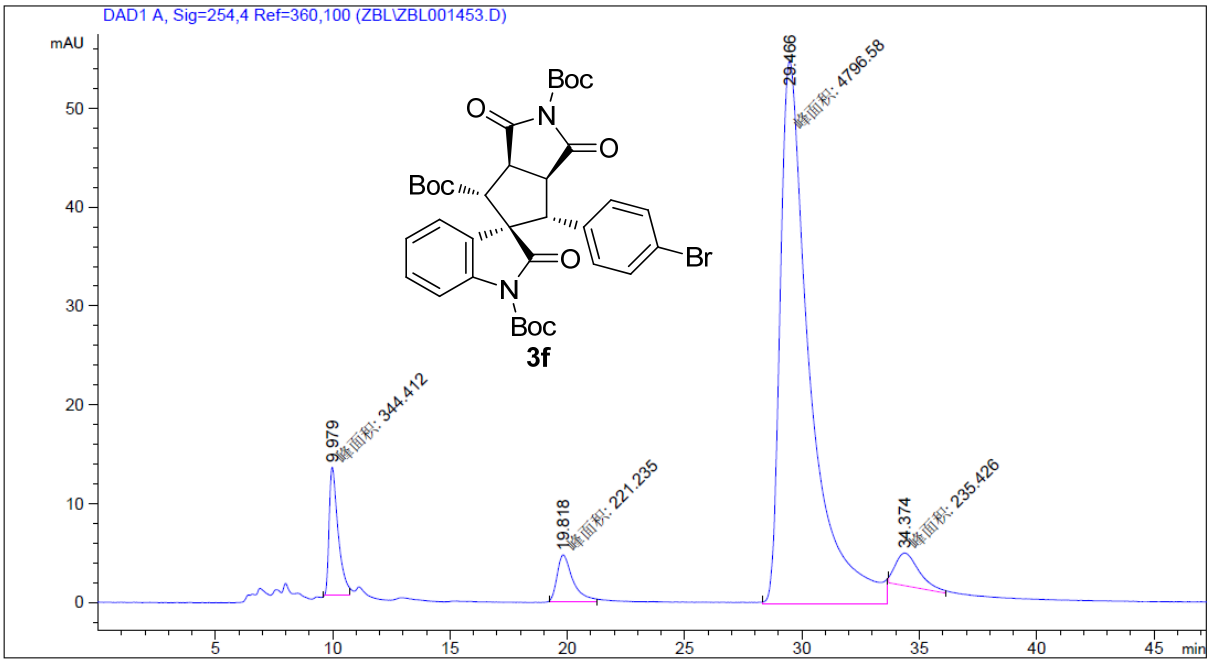
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.139	MM	0.4446	1659.83850	62.22473	38.6018
2	19.887	MM	0.7936	493.04739	10.35415	11.4665
3	22.729	MM	0.9737	1650.72266	28.25415	38.3898
4	27.851	MM	1.2970	496.29221	6.37763	11.5419



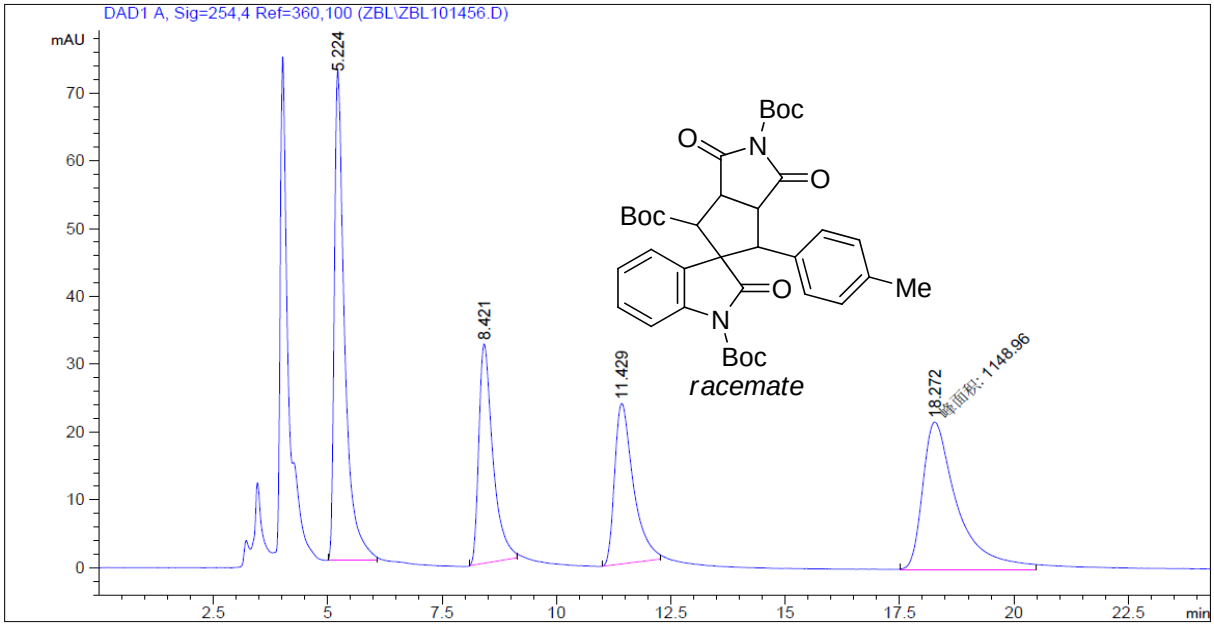
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.165	BB	0.3244	242.54337	11.20967	6.1852
2	19.919	MM	0.8660	98.67513	1.89910	2.5164
3	22.698	MM	1.0212	3529.93115	57.60817	90.0185
4	27.997	MM	1.1358	50.18986	7.36506e-1	1.2799



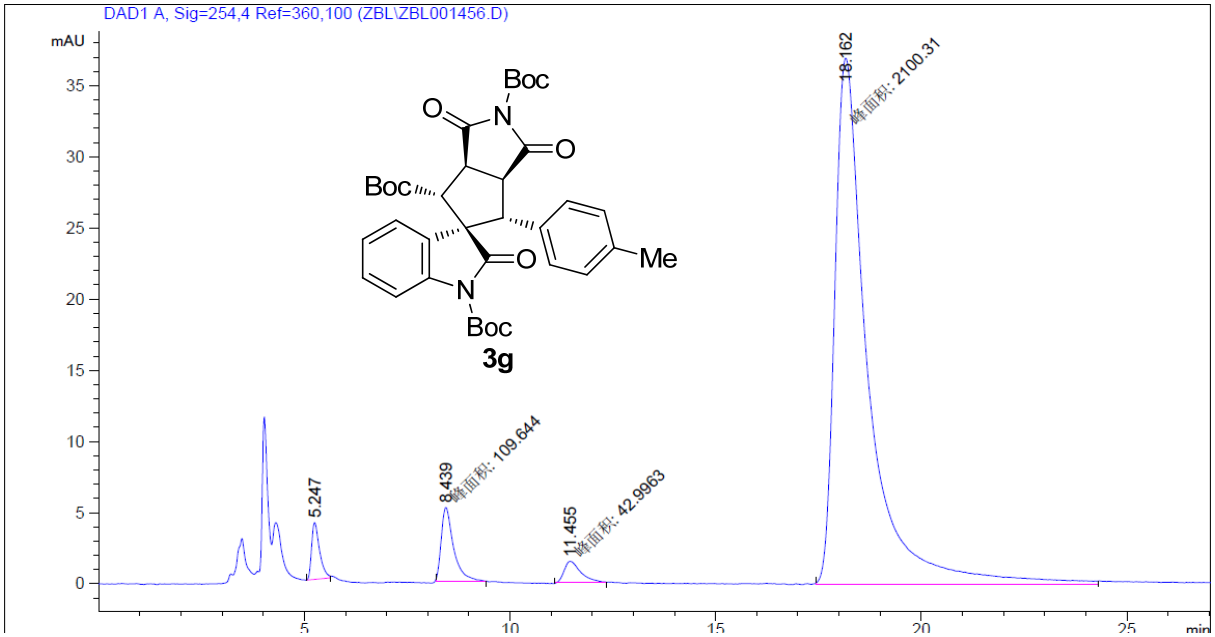
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.020	MM	0.5184	1287.37842	41.38658	34.5084
2	20.013	MM	0.9226	570.57776	10.30688	15.2944
3	29.853	MM	1.4282	1290.75110	15.06303	34.5988
4	34.657	MM	1.5630	581.91779	6.20505	15.5984



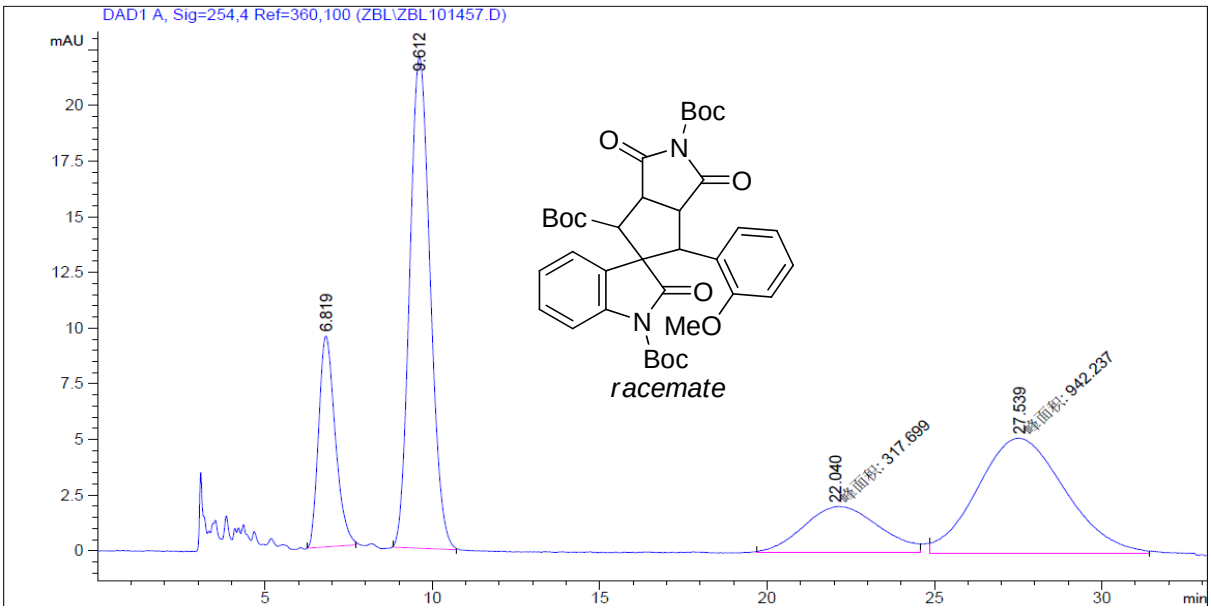
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.979	MM	0.4438	344.41232	12.93533	6.1528
2	19.818	MM	0.7798	221.23482	4.72848	3.9523
3	29.466	MM	1.4567	4796.58496	54.87965	85.6891
4	34.374	MM	1.1841	235.42647	3.31366	4.2058



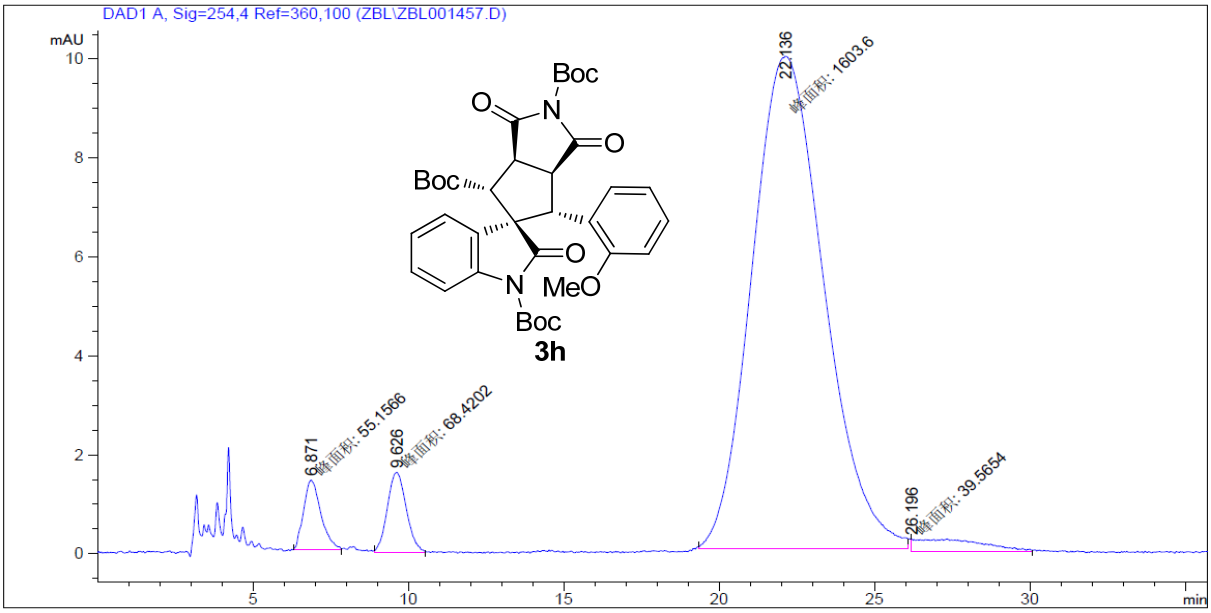
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.224	BB	0.2299	1139.65234	72.28301	31.2002
2	8.421	BB	0.3173	691.21082	32.34324	18.9233
3	11.429	BB	0.4239	672.88629	23.65207	18.4216
4	18.272	MM	0.8797	1148.95532	21.76790	31.4549



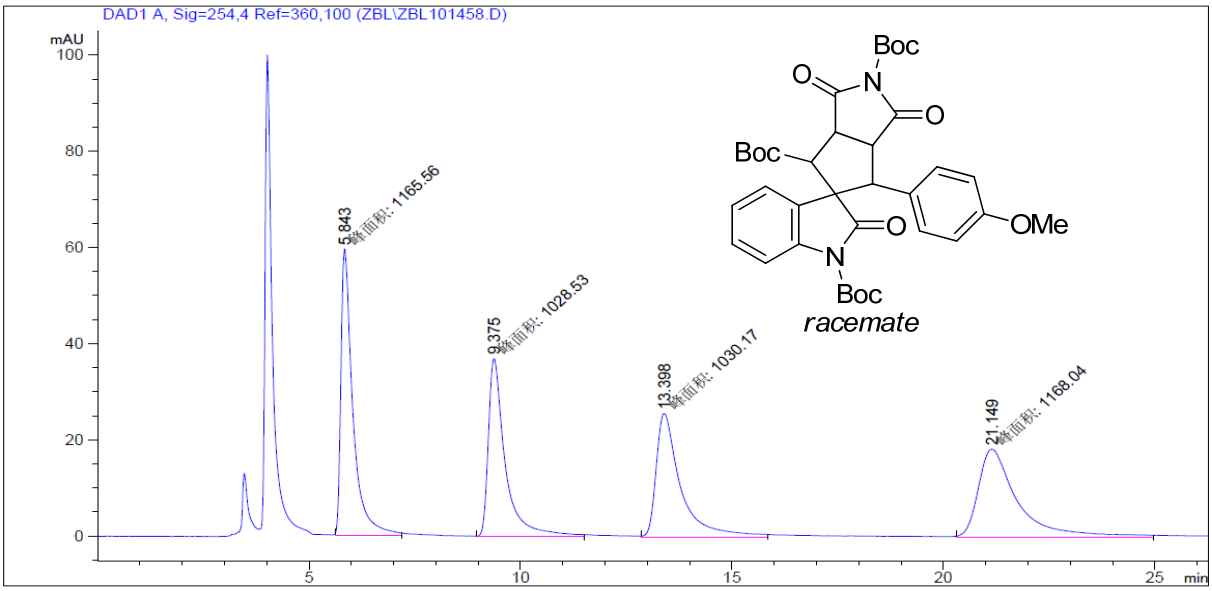
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.247	BB	0.1989	53.74623	3.99673	2.3300
2	8.439	MM	0.3515	109.64433	5.19937	4.7533
3	11.455	MM	0.4775	42.99629	1.50076	1.8640
4	18.162	MM	0.9458	2100.30908	37.01126	91.0527



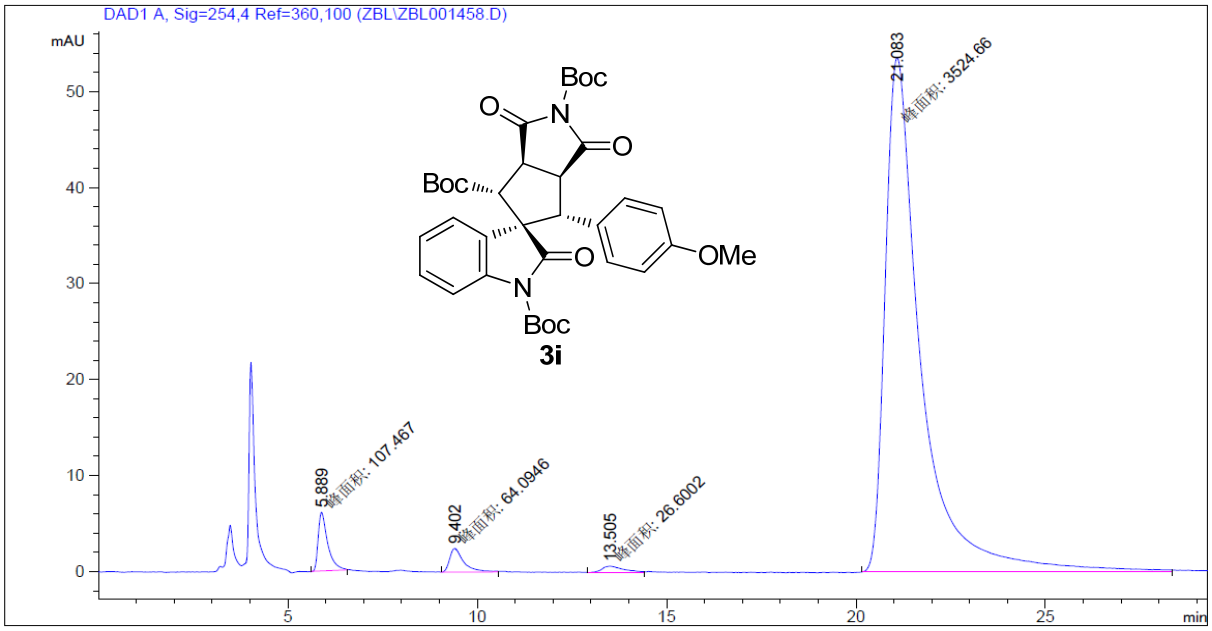
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.819	BB	0.5108	325.16452	9.46507	12.8930
2	9.612	BB	0.6597	936.91516	22.04947	37.1495
3	22.040	MM	2.5848	317.69852	2.04853	12.5970
4	27.539	MM	3.0306	942.23749	5.18177	37.3605



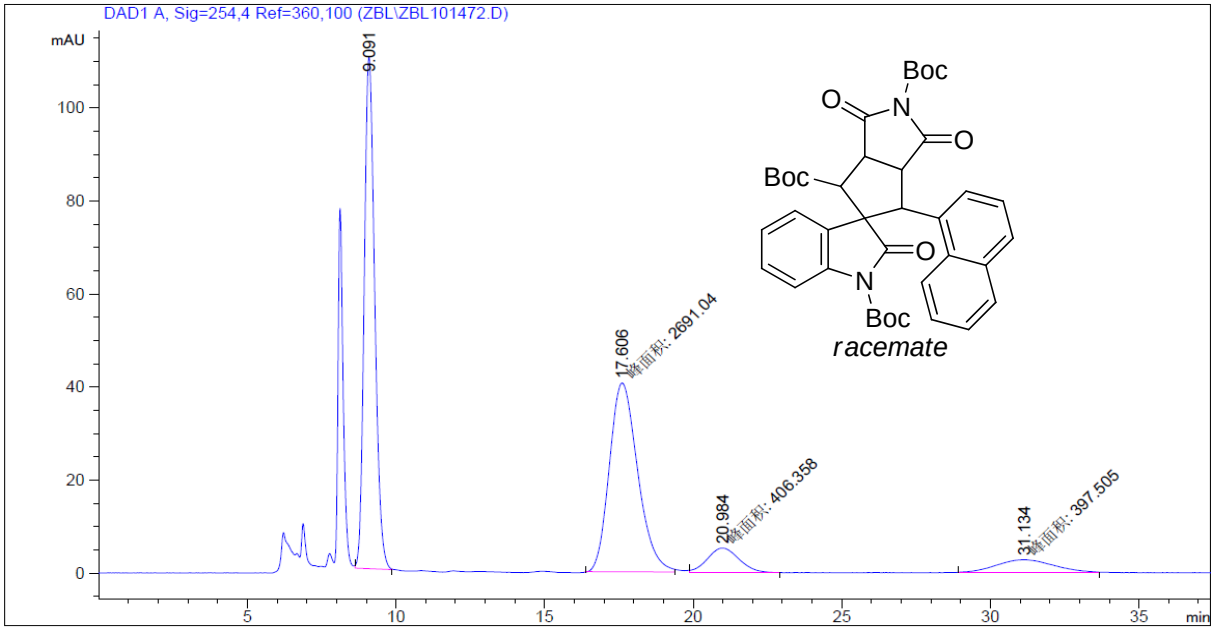
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.871	MM	0.6489	55.15655	1.41673	3.1219
2	9.626	MM	0.7043	68.42015	1.61902	3.8727
3	22.136	MM	2.6839	1603.59570	9.95803	90.7659
4	26.196	MM	1.8027	39.56542	2.58008e-1	2.2395



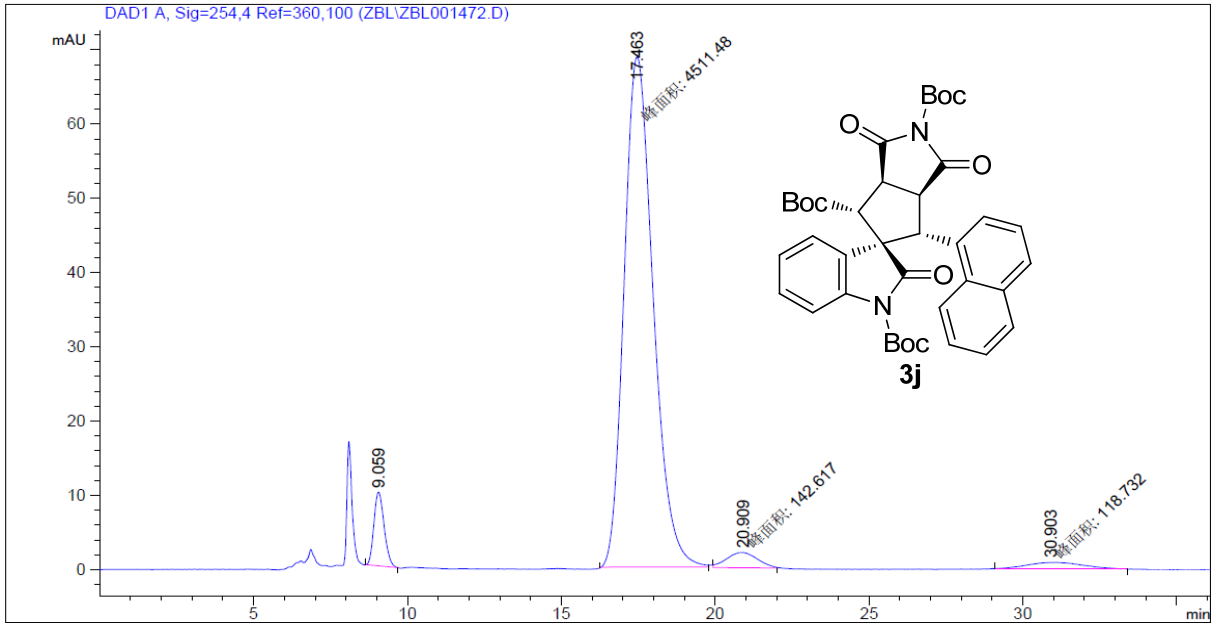
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.843	MM	0.3264	1165.55969	59.51390	26.5365
2	9.375	MM	0.4640	1028.53064	36.94677	23.4167
3	13.398	MM	0.6693	1030.16748	25.65305	23.4540
4	21.149	MM	1.0681	1168.03882	18.22679	26.5929



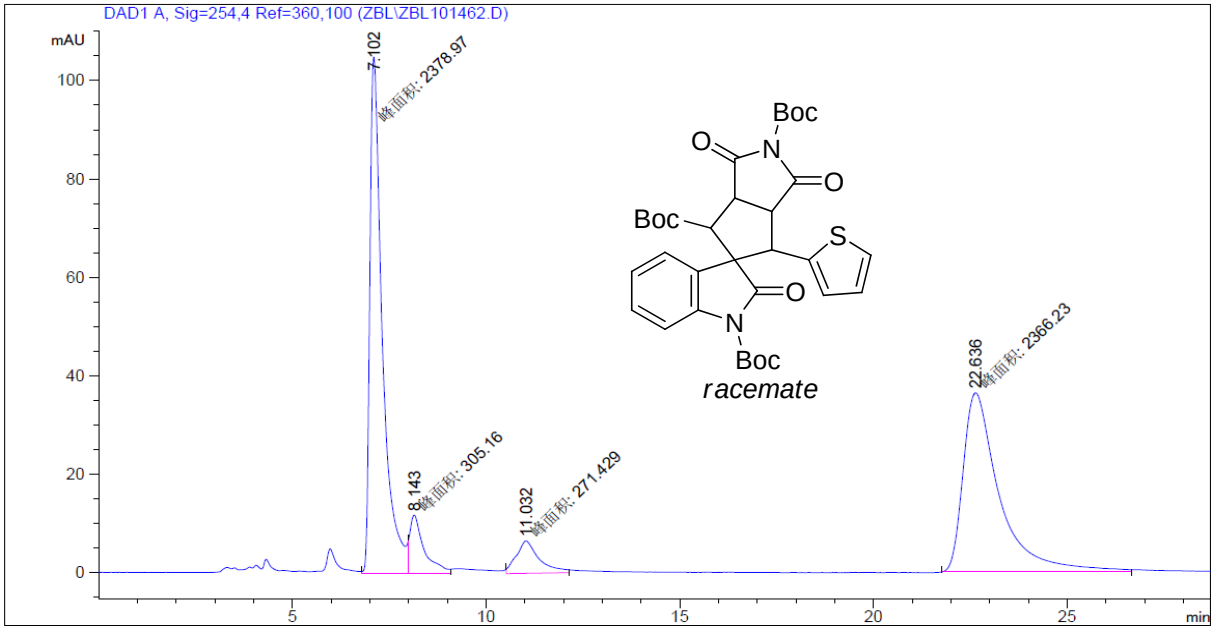
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.889	MM	0.2930	107.46729	6.11226	2.8867
2	9.402	MM	0.4303	64.09457	2.48274	1.7217
3	13.505	MM	0.6635	26.60025	6.68142e-1	0.7145
4	21.083	MM	1.0971	3524.65845	53.54668	94.6771



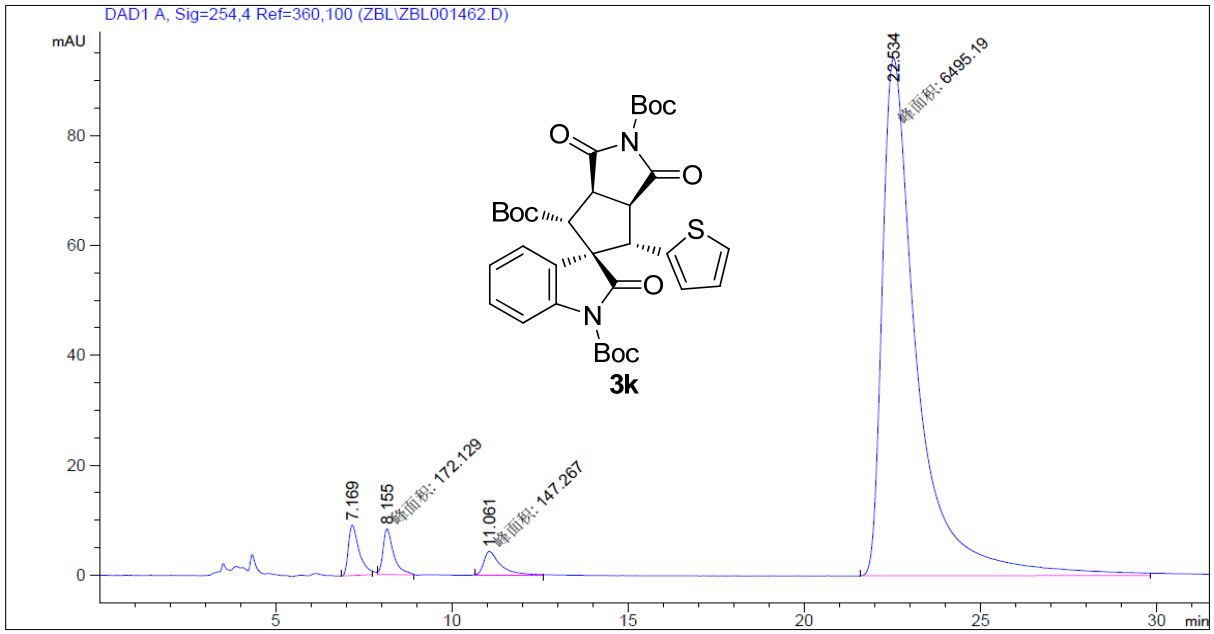
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.091	BB	0.3821	2697.24243	109.98201	43.5591
2	17.606	MM	1.1045	2691.04175	40.60697	43.4589
3	20.984	MM	1.2608	406.35751	5.37148	6.5625
4	31.134	MM	2.3298	397.50500	2.84365	6.4195



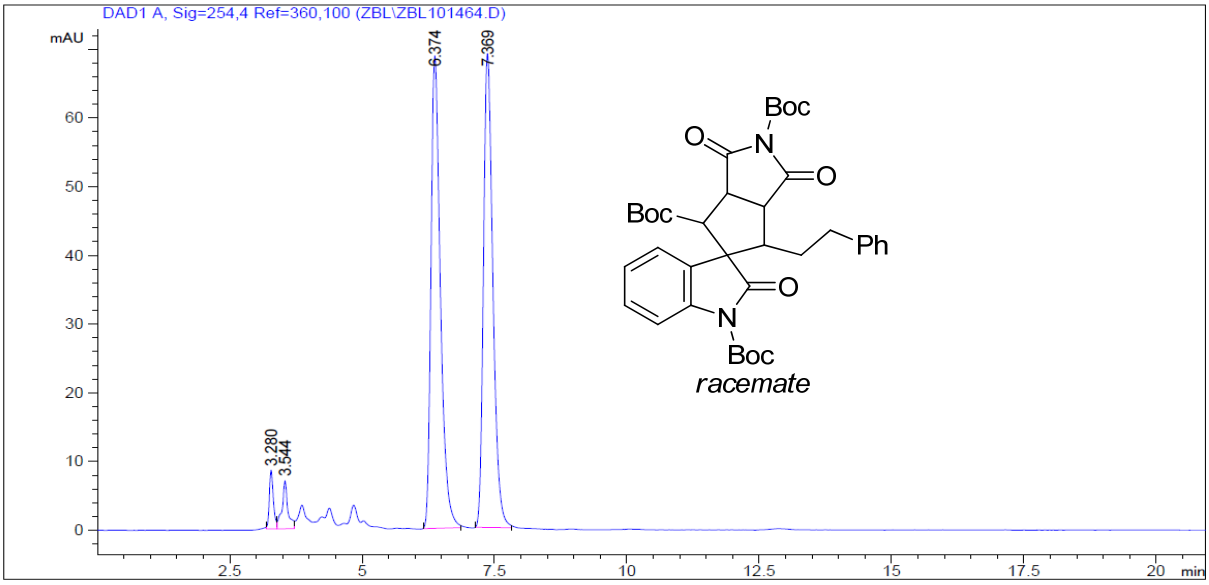
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.059	BB	0.3516	229.16571	9.91719	4.5815
2	17.463	MM	1.0938	4511.48437	68.74028	90.1936
3	20.909	MM	1.1549	142.61716	2.05807	2.8512
4	30.903	MM	2.1654	118.73232	9.13872e-1	2.3737



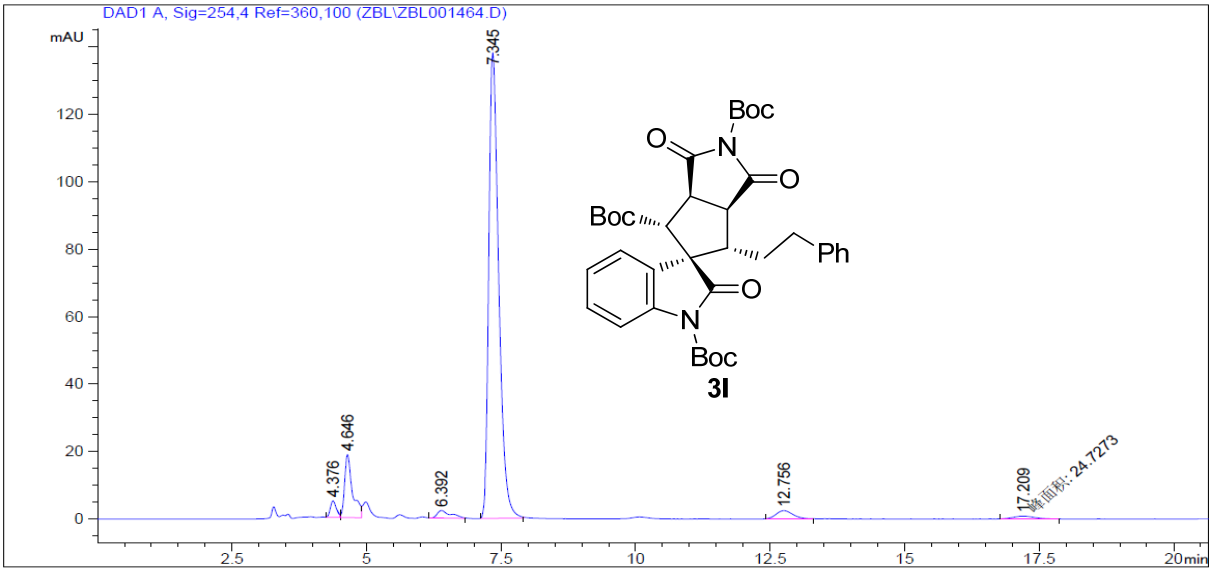
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.102	MM	0.3774	2378.97168	105.05898	44.7024
2	8.143	MM	0.4273	305.16031	11.90240	5.7342
3	11.032	MM	0.6897	271.42880	6.55893	5.1003
4	22.636	MM	1.0844	2366.23437	36.36885	44.4631



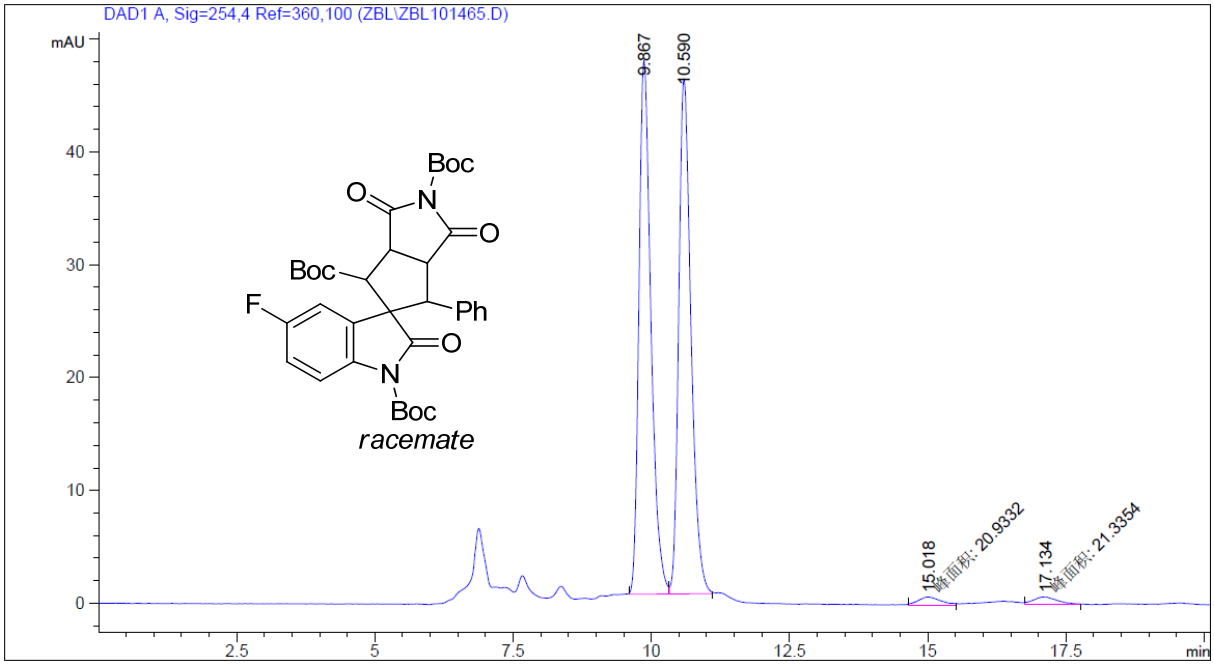
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.169	BB	0.3117	194.34605	9.15334	2.7728
2	8.155	MM	0.3452	172.12914	8.31134	2.4559
3	11.061	MM	0.5665	147.26675	4.33229	2.1011
4	22.534	MM	1.1504	6495.19189	94.10136	92.6702



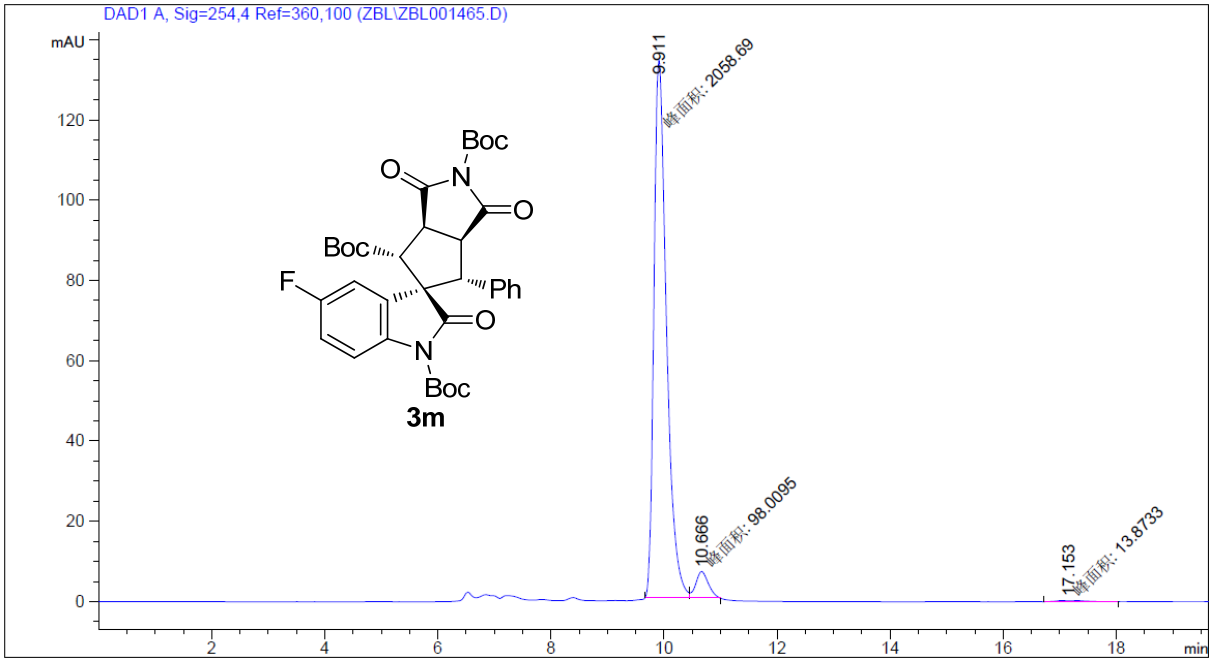
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.280	BV	0.0801	45.67750	8.58173	2.5327
2	3.544	VB	0.1081	54.07652	6.99914	2.9984
3	6.374	BB	0.1882	850.41113	68.82379	47.1531
4	7.369	BB	0.1902	853.34680	69.02339	47.3158



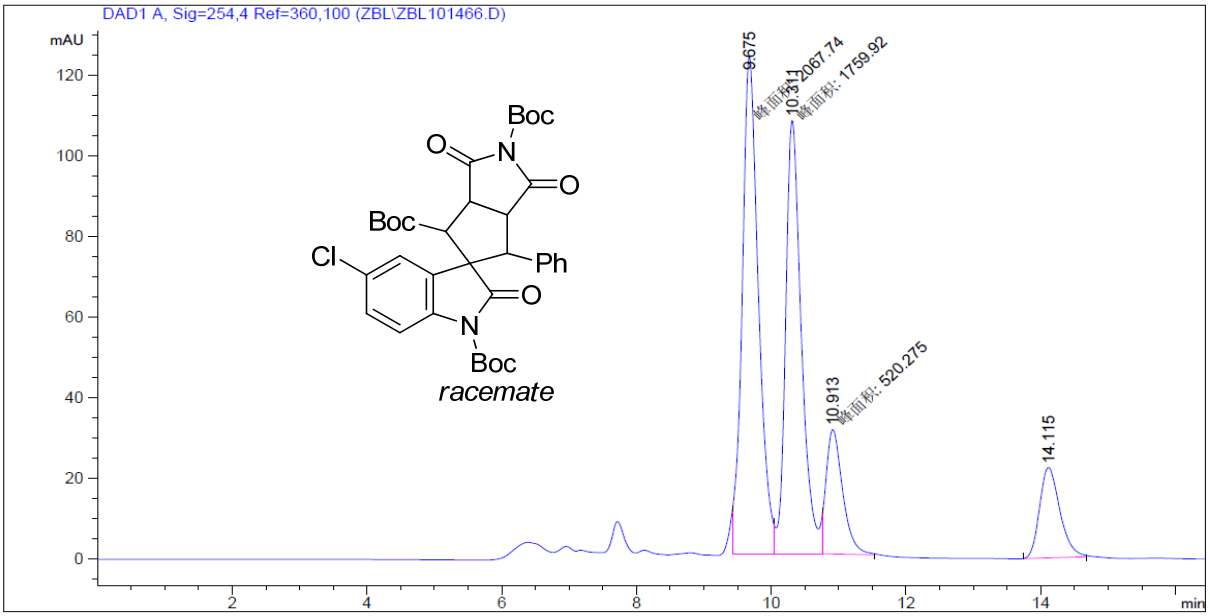
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.376	BV	0.1185	37.92332	4.89031	1.7879
2	4.646	VV	0.1496	191.44055	18.67562	9.0254
3	6.392	BB	0.2483	39.37080	2.24844	1.8561
4	7.345	BB	0.1959	1774.58765	138.07240	83.6622
5	12.756	BB	0.3353	53.08363	2.44516	2.5026
6	17.209	MM	0.4835	24.72729	8.52379e-1	1.1658



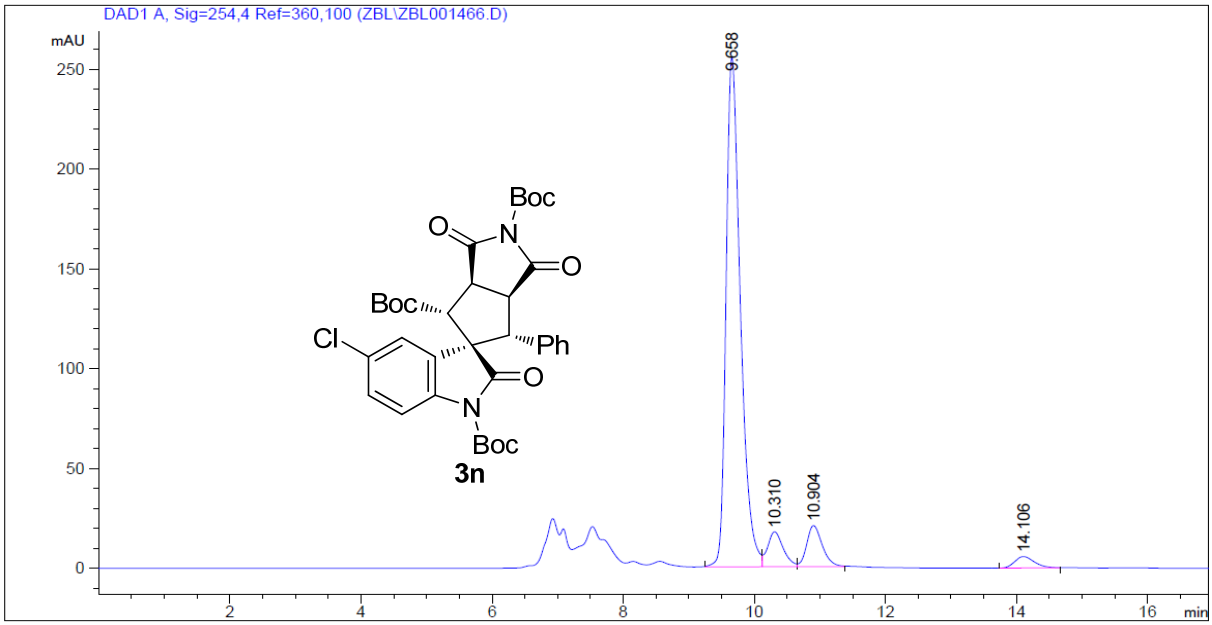
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.867	BV	0.2302	714.49634	47.30681	48.9321
2	10.590	VB	0.2358	703.41534	45.64487	48.1732
3	15.018	MM	0.4767	20.93322	7.31814e-1	1.4336
4	17.134	MM	0.5180	21.33540	6.86443e-1	1.4611



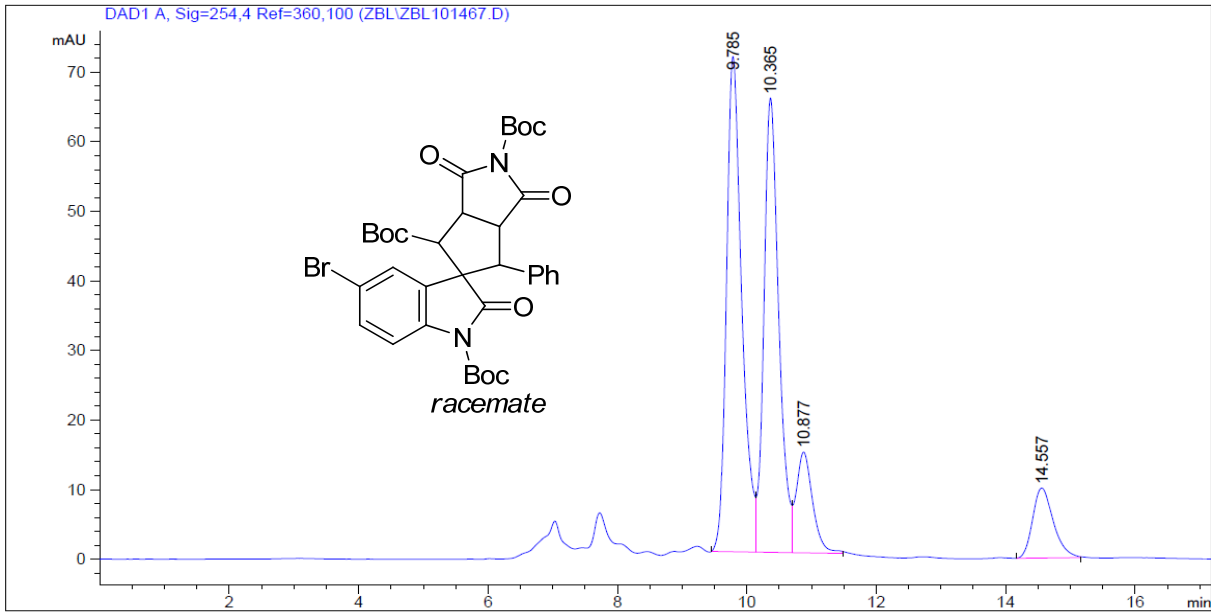
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.911	MM	0.2561	2058.69360	134.00322	94.8455
2	10.666	MM	0.2520	98.00949	6.48258	4.5154
3	17.153	MM	0.5984	13.87329	3.86376e-1	0.6392



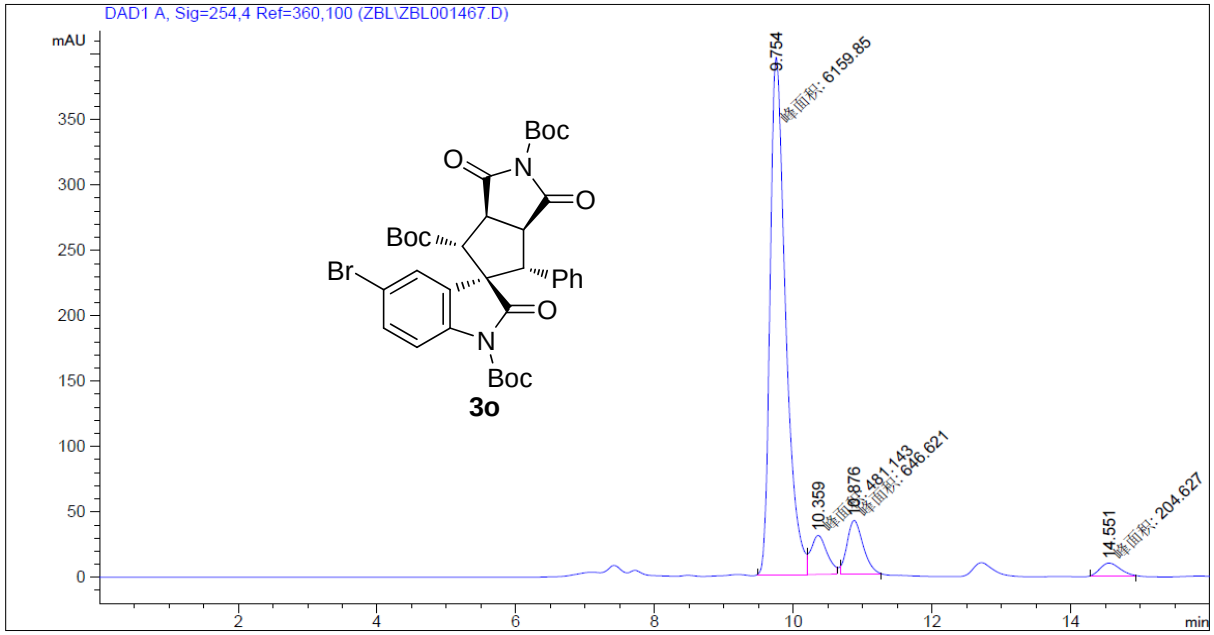
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.675	MM	0.2796	2067.74463	123.26939	42.9287
2	10.311	MM	0.2730	1759.92322	107.43500	36.5380
3	10.913	MM	0.2812	520.27484	30.83566	10.8015
4	14.115	BB	0.3202	468.75577	22.39483	9.7319



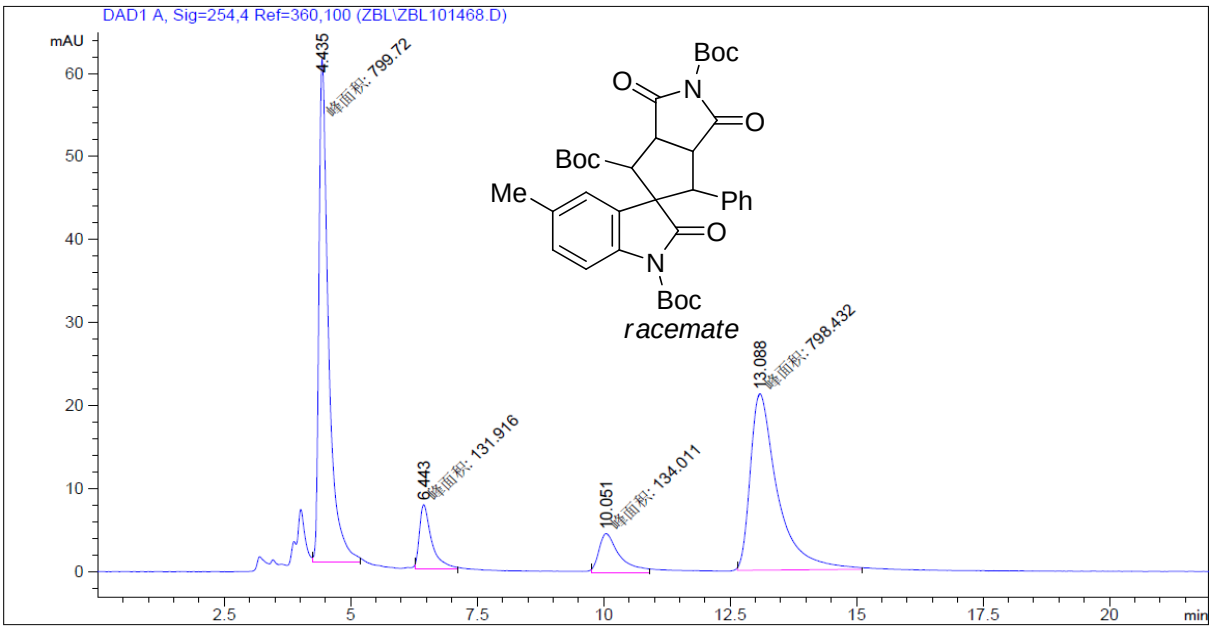
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.658	BV	0.2312	3877.17700	255.28909	83.7973
2	10.310	VV	0.2475	290.80801	17.53687	6.2852
3	10.904	VB	0.2528	339.93564	20.57145	7.3470
4	14.106	BB	0.3241	118.93306	5.73049	2.5705



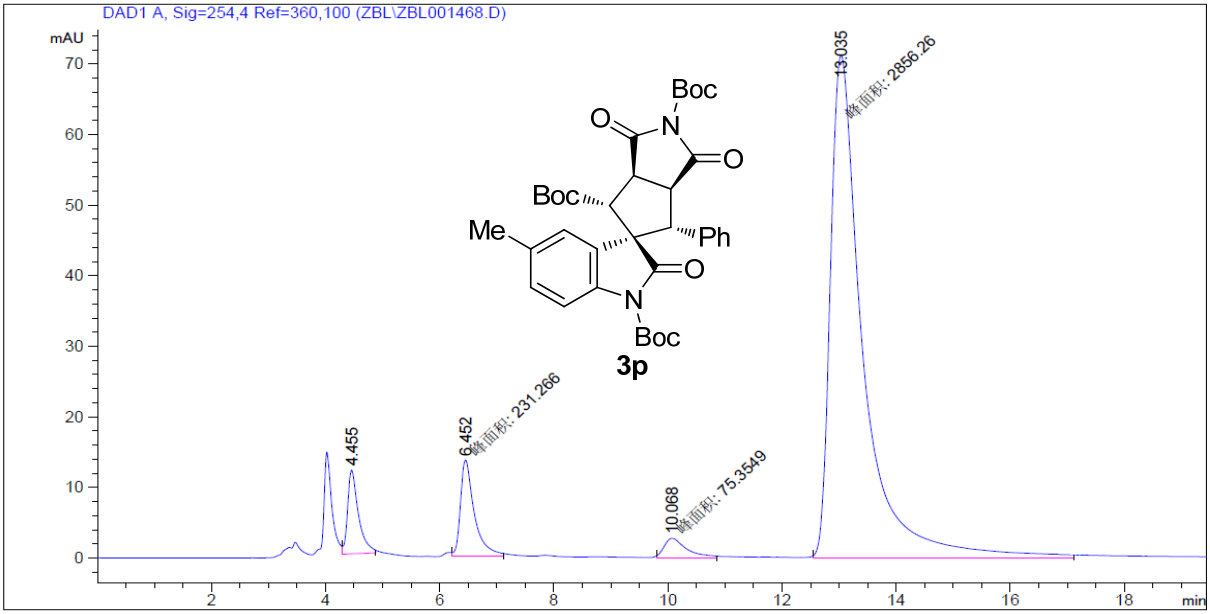
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.785	BV	0.2481	1172.30151	71.19570	43.4137
2	10.365	VV	0.2413	1048.65723	65.32318	38.8348
3	10.877	VB	0.2600	255.60672	14.47951	9.4659
4	14.557	BB	0.3414	223.73715	10.06292	8.2856



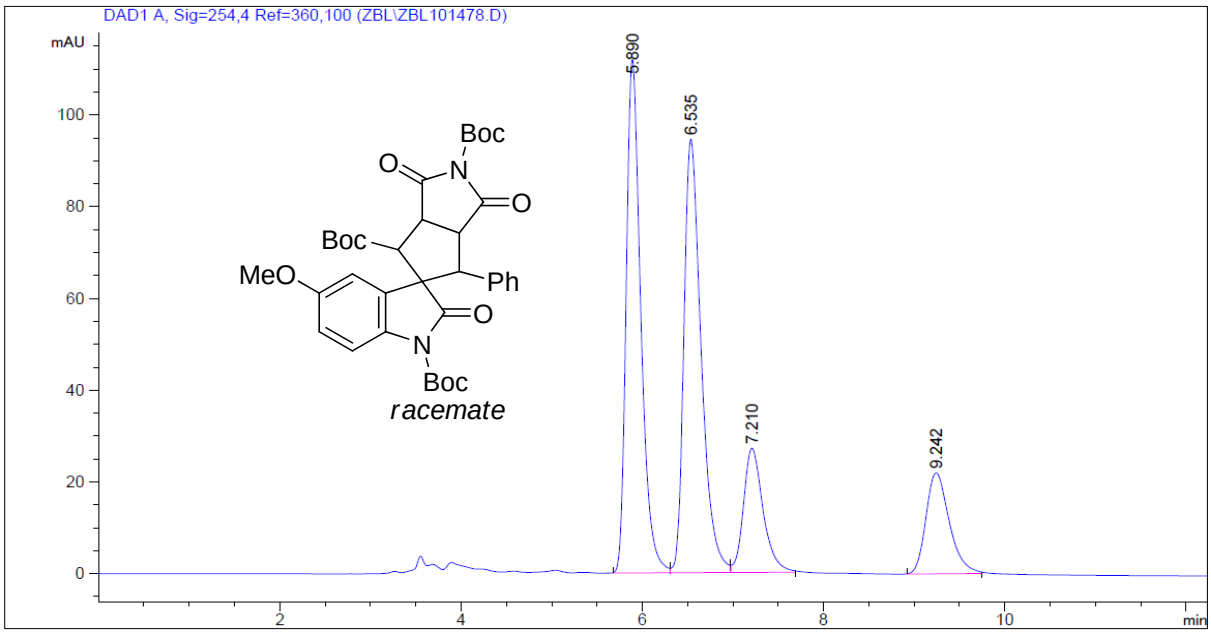
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.754	MM	0.2594	6159.84766	395.77359	82.2164
2	10.359	MM	0.2691	481.14322	29.80350	6.4219
3	10.876	MM	0.2643	646.62097	40.78099	8.6305
4	14.551	MM	0.3368	204.62714	10.12600	2.7312



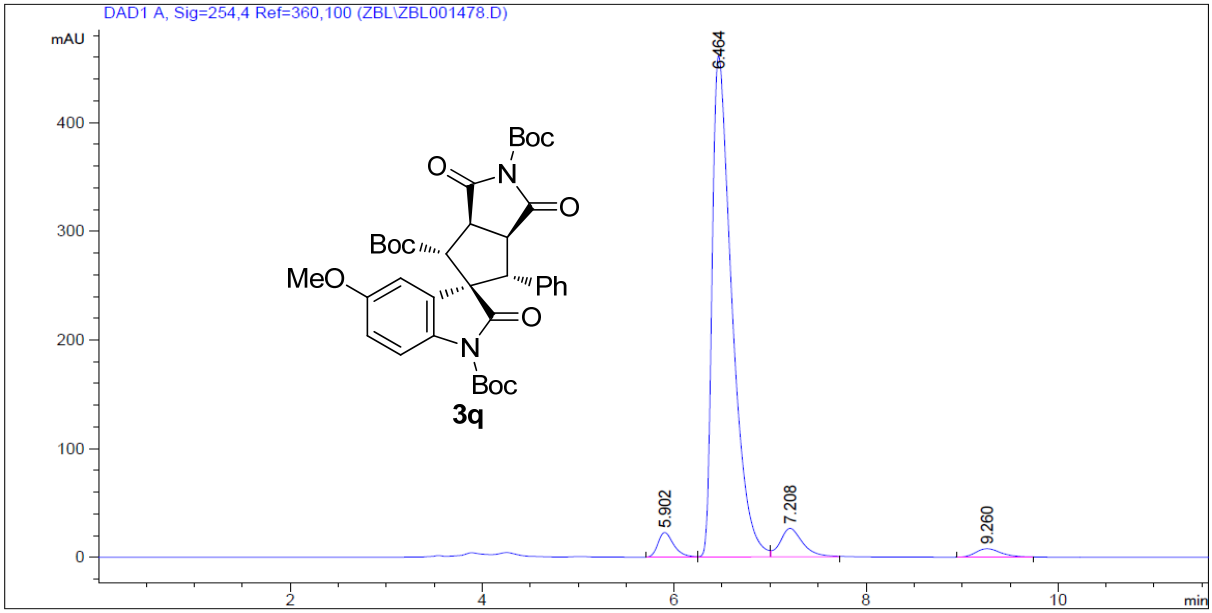
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.435	MM	0.2198	799.71960	60.64570	42.9016
2	6.443	MM	0.2818	131.91553	7.80332	7.0767
3	10.051	MM	0.4760	134.01088	4.69260	7.1891
4	13.088	MM	0.6257	798.43152	21.26863	42.8325



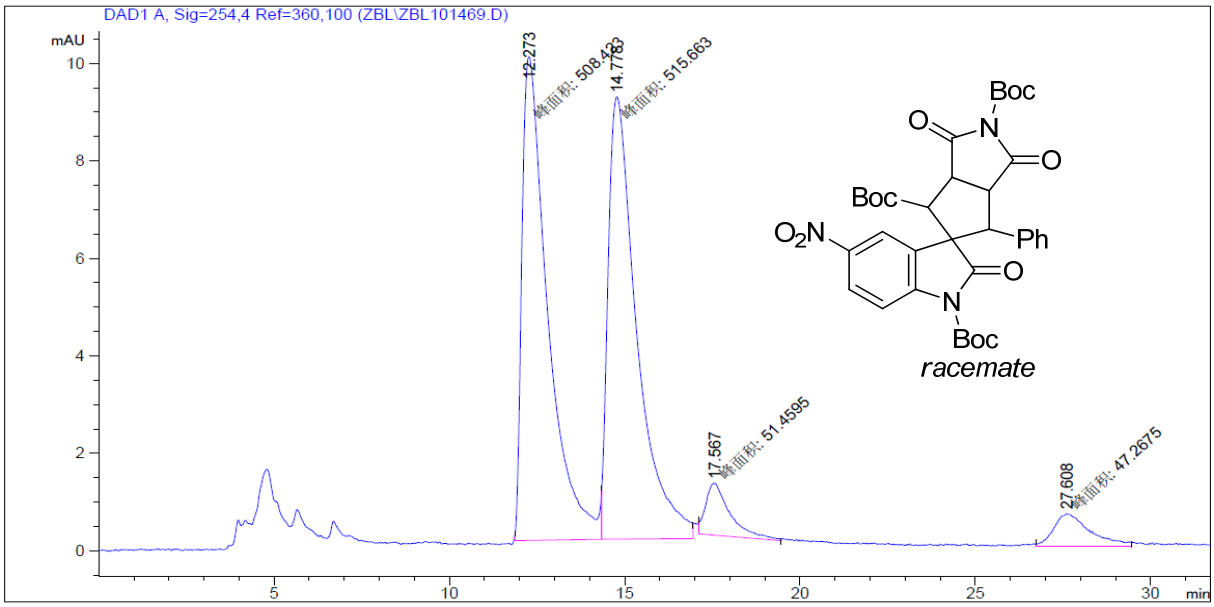
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.455	VB	0.1948	157.47096	11.86721	4.7426
2	6.452	MM	0.2823	231.26558	13.65276	6.9651
3	10.068	MM	0.4574	75.35486	2.74583	2.2695
4	13.035	MM	0.6674	2856.26392	71.32452	86.0228



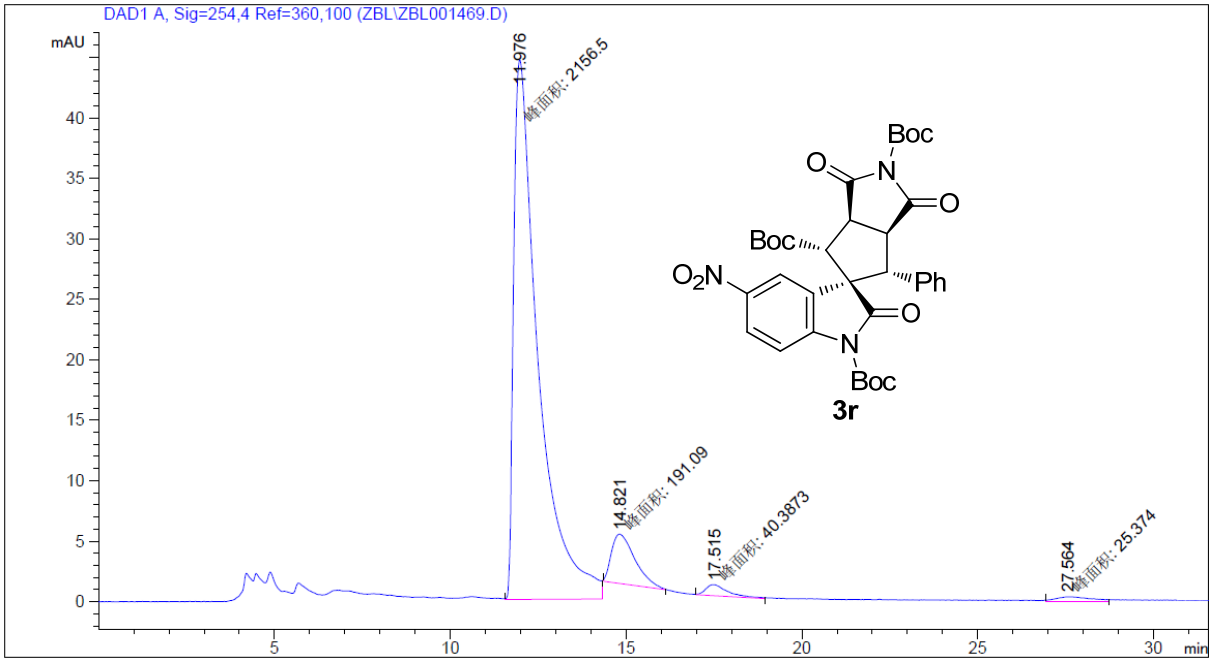
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.890	BV	0.1703	1251.50586	112.06731	37.8496
2	6.535	VV	0.2026	1253.02258	94.53667	37.8955
3	7.210	VB	0.2276	407.69135	27.08568	12.3299
4	9.242	BB	0.2728	394.30139	22.03621	11.9250



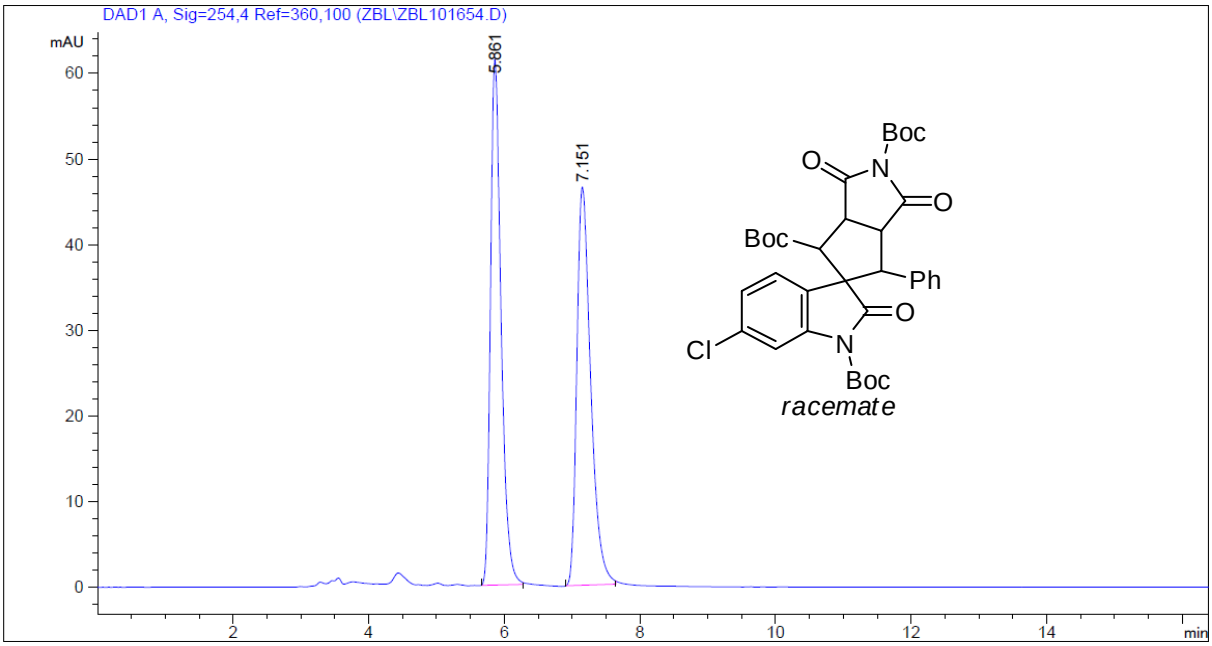
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.902	BV	0.1731	259.55368	22.74313	3.4906
2	6.464	VV	0.2149	6603.91992	461.68042	88.8139
3	7.208	VB	0.2422	427.74597	26.23552	5.7526
4	9.260	BB	0.2813	144.46646	7.82749	1.9429



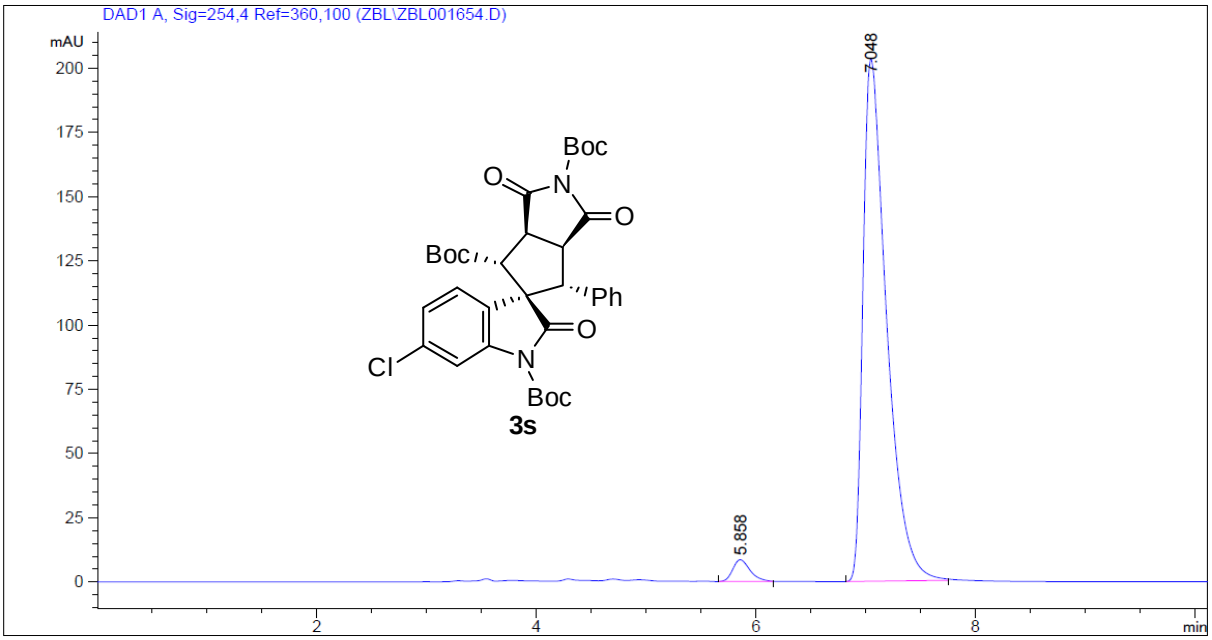
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.273	MM	0.8540	508.42258	9.92223	45.2812
2	14.778	MM	0.9469	515.66272	9.07678	45.9260
3	17.567	MM	0.8031	51.45955	1.06792	4.5831
4	27.608	MM	1.1846	47.26754	6.65029e-1	4.2097



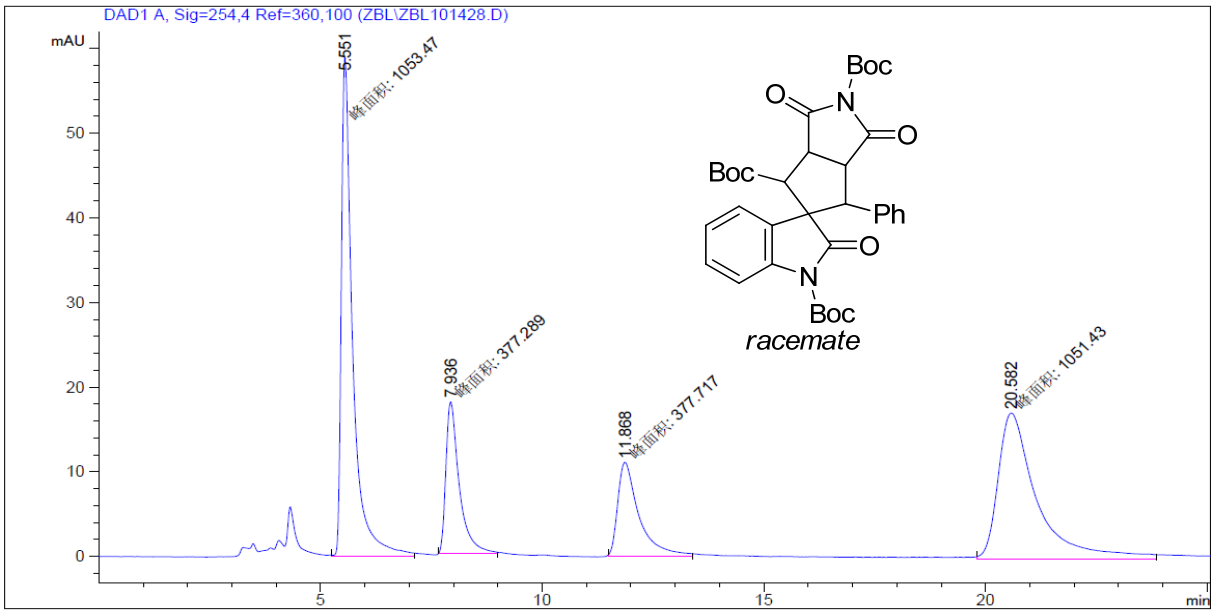
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.976	MM	0.8058	2156.50220	44.60376	89.3571
2	14.821	MM	0.7797	191.09036	4.08478	7.9180
3	17.515	MM	0.7393	40.38726	9.10454e-1	1.6735
4	27.564	MM	1.1521	25.37398	3.67081e-1	1.0514



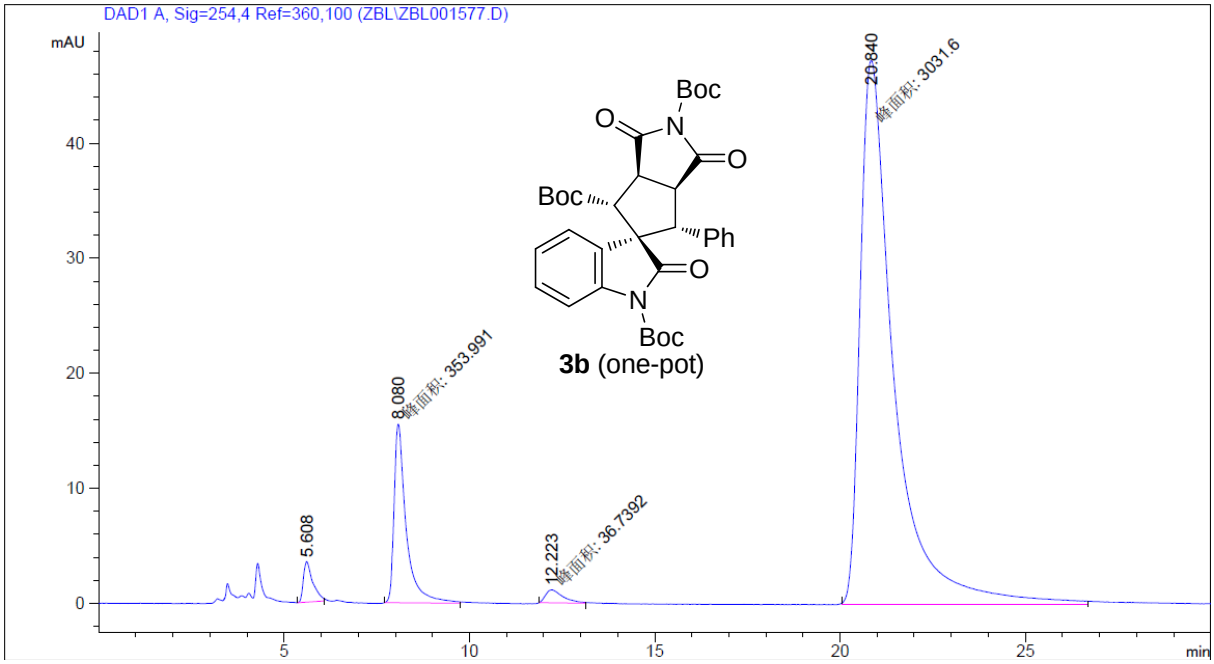
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.861	BB	0.1663	665.45734	61.47102	50.1889
2	7.151	BB	0.2156	660.44757	46.53242	49.8111



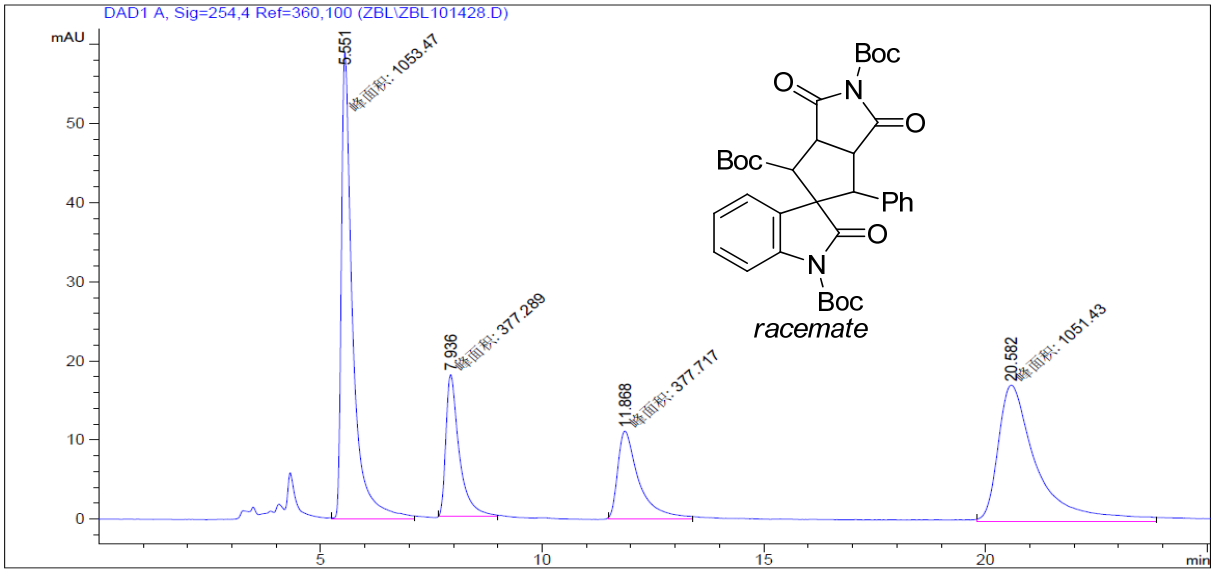
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.858	BB	0.1680	92.90256	8.46785	2.9710
2	7.048	BB	0.2239	3034.02783	203.52028	97.0290



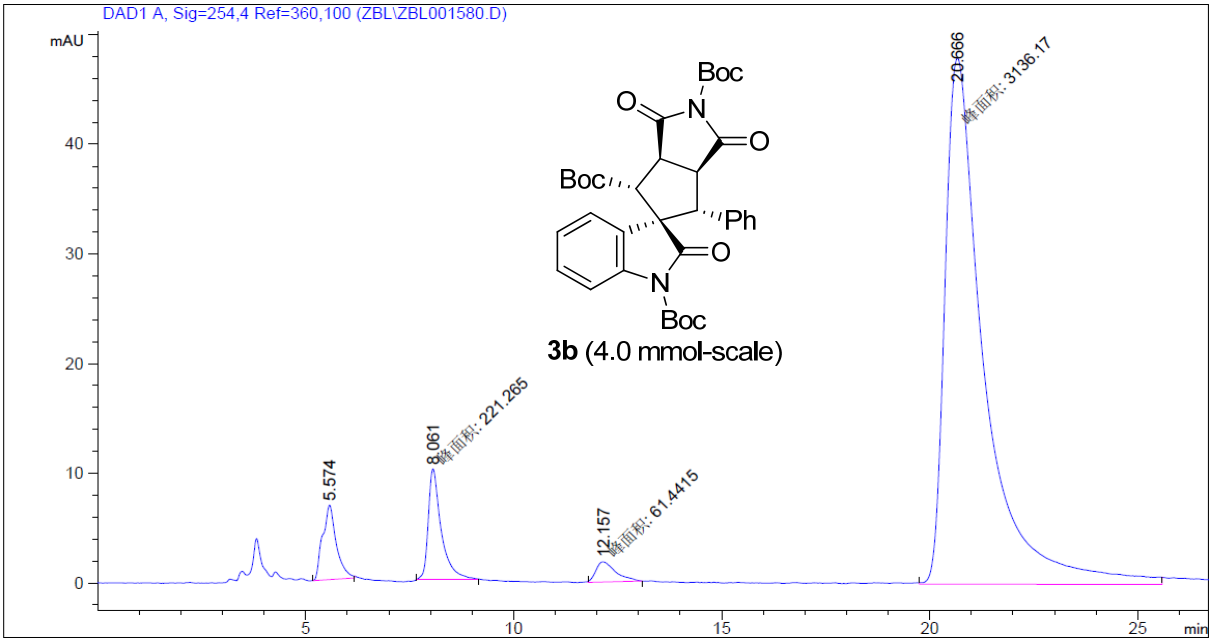
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.551	MM	0.2973	1053.47058	59.06449	36.8359
2	7.936	MM	0.3506	377.28867	17.93779	13.1924
3	11.868	MM	0.5644	377.71701	11.15329	13.2073
4	20.582	MM	1.0155	1051.42859	17.25550	36.7645



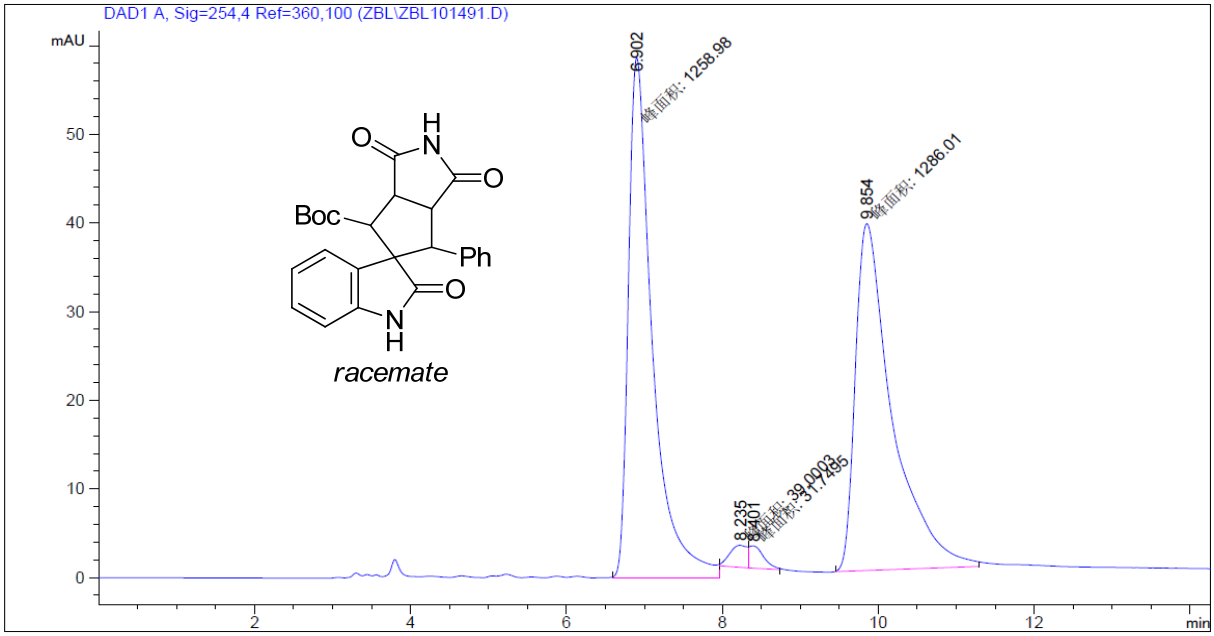
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.608	BB	0.2529	62.01617	3.53054	1.7799
2	8.080	MM	0.3798	353.99088	15.53530	10.1595
3	12.223	MM	0.5468	36.73915	1.11986	1.0544
4	20.840	MM	1.0669	3031.59839	47.35625	87.0063



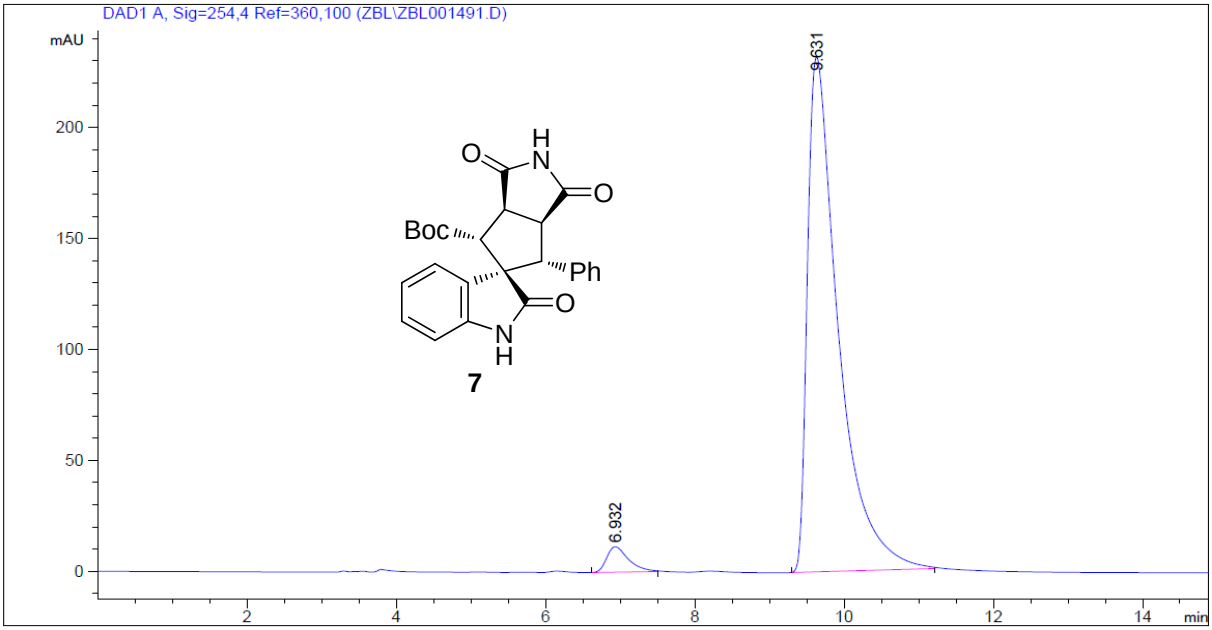
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.551	MM	0.2973	1053.47058	59.06449	36.8359
2	7.936	MM	0.3506	377.28867	17.93779	13.1924
3	11.868	MM	0.5644	377.71701	11.15329	13.2073
4	20.582	MM	1.0155	1051.42859	17.25550	36.7645



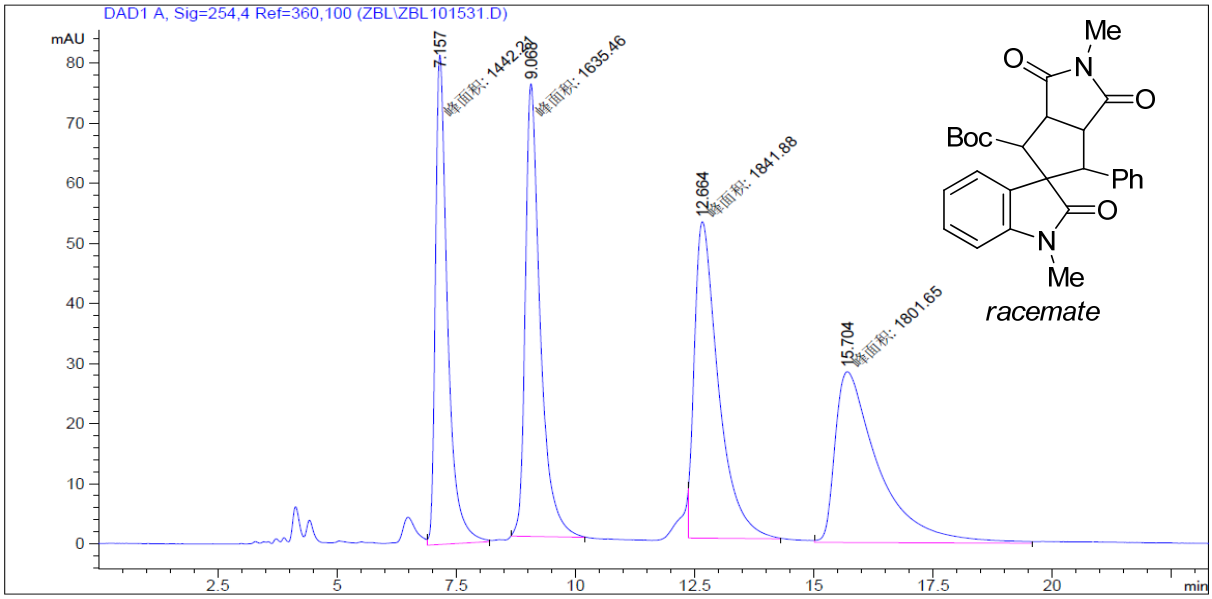
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.574	BB	0.3088	155.21782	6.78781	4.3429
2	8.061	MM	0.3651	221.26540	10.09987	6.1908
3	12.157	MM	0.5543	61.44147	1.84747	1.7191
4	20.666	MM	1.0895	3136.16724	47.97551	87.7472



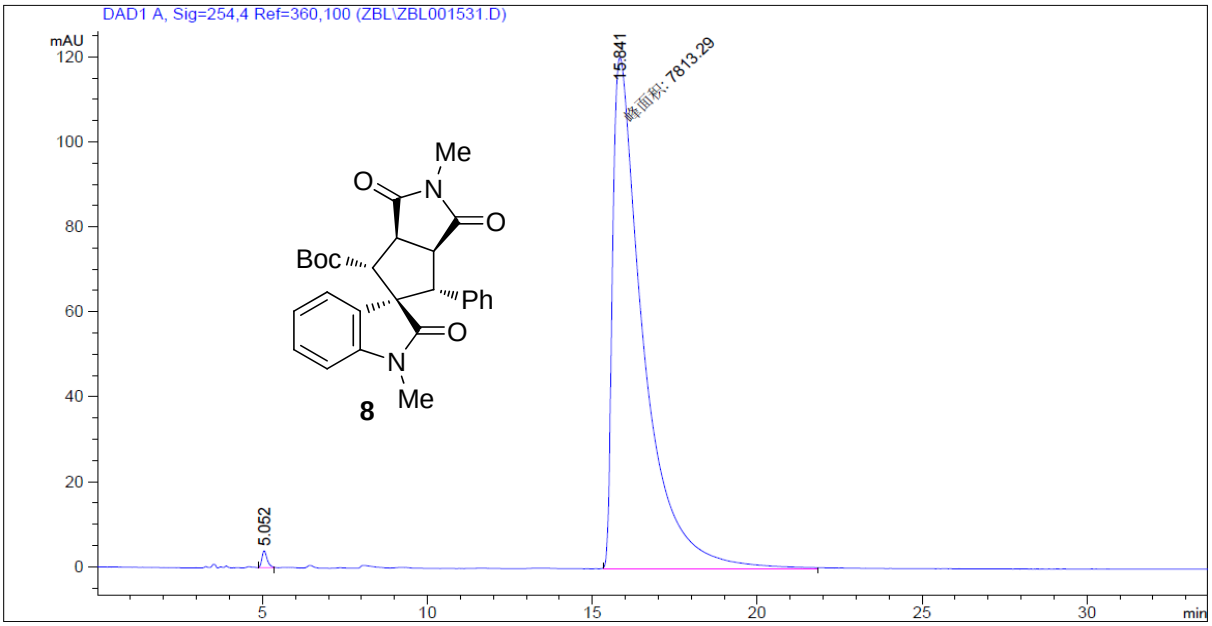
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.902	MM	0.3574	1258.97803	58.71751	48.1308
2	8.235	MM	0.2618	39.00031	2.48305	1.4910
3	8.401	MM	0.2106	31.74947	2.51251	1.2138
4	9.854	MM	0.5479	1286.01355	39.11625	49.1644



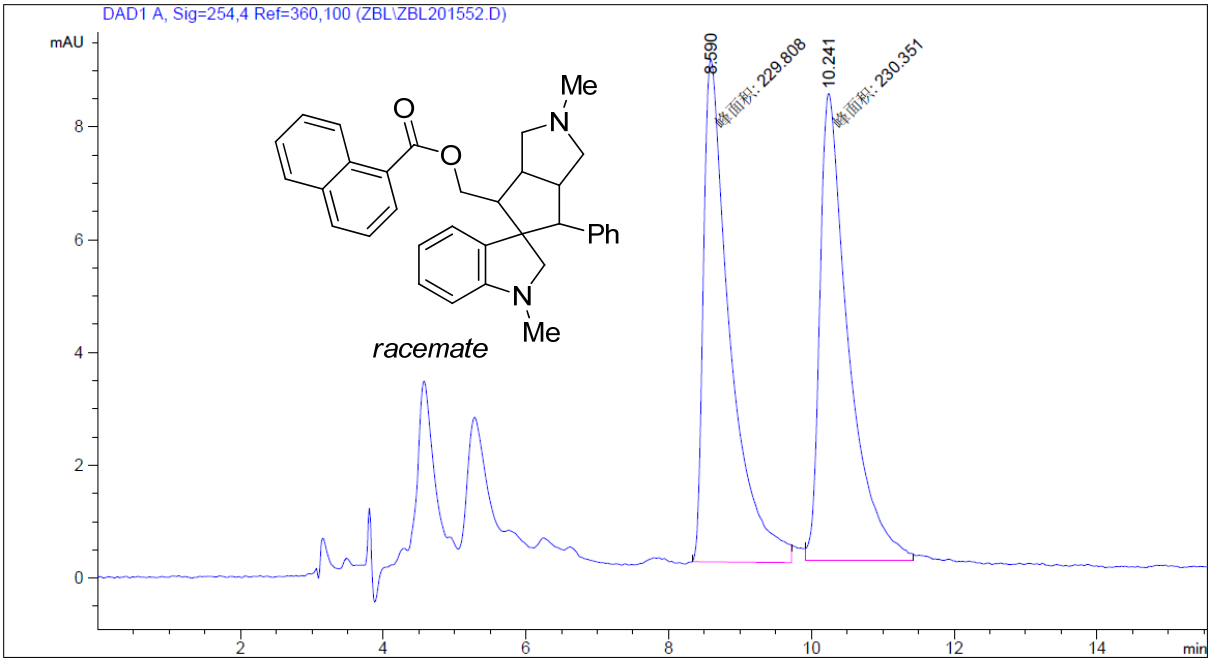
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.932	BB	0.3034	233.59752	11.47968	3.3738
2	9.631	BB	0.4203	6690.28223	232.12482	96.6262



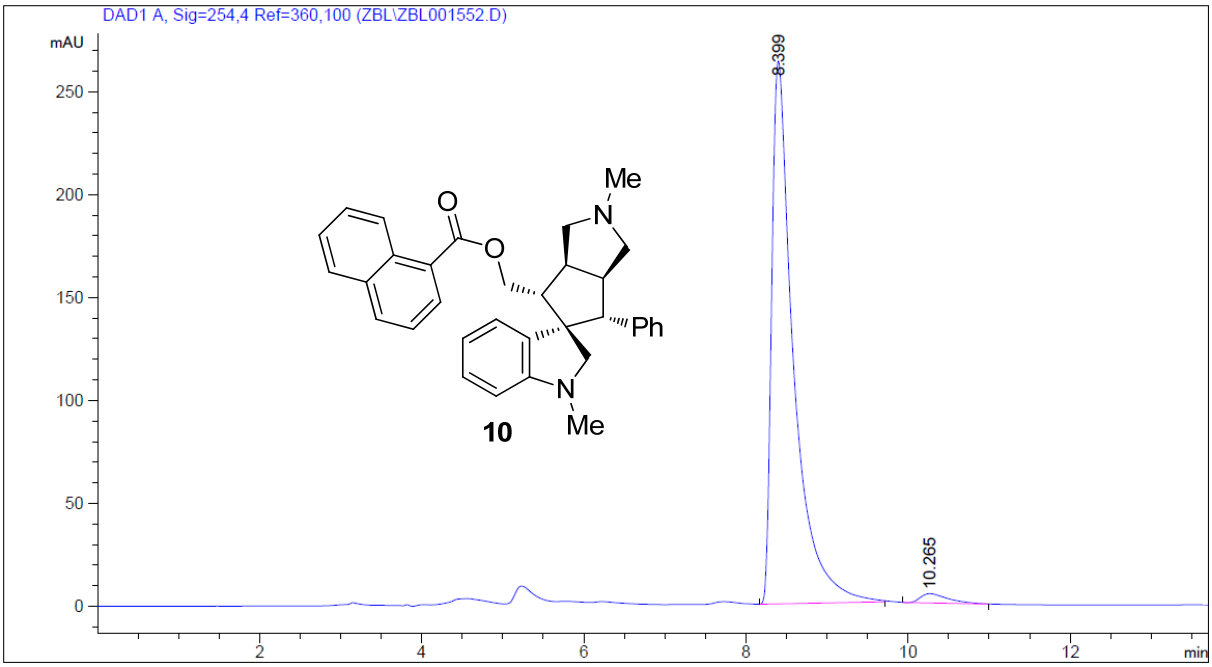
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.157	MM	0.2949	1442.21118	81.51088	21.4576
2	9.068	MM	0.3617	1635.46191	75.35751	24.3329
3	12.664	MM	0.5827	1841.87891	52.68142	27.4040
4	15.704	MM	1.0561	1801.65479	28.43256	26.8055



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.052	BB	0.1704	44.32750	3.96720	0.5641
2	15.841	MM	1.0809	7813.28809	120.47459	99.4359



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.590	MM	0.4300	229.80838	8.90787	49.9410
2	10.241	MM	0.4639	230.35092	8.27609	50.0590



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.399	BB	0.2709	4949.63135	263.84717	97.8904
2	10.265	BB	0.3470	106.66554	4.52505	2.1096