Bifunctional squaramide-catalysed enantioselective vinylogous Michael addition/cyclization cascade reaction of 4-unsaturated isoxazol-5-ones and α,α-dicyanoalkenes

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Supporting Information

Contents

1. General information

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 Ascend 400 MHz spectrometer, chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as an internal standard. ^{13}C NMR spectra were measured at 100 MHz with a 400 MHz spectrometer, chemical shifts are reported in ppm relative to tetramethylsilane and referenced to solvent peak ($CDCl_3$, δ C = 77.00). High resolution mass spectra (Electron spray ionization) were measured with an Agilent 6520 Accurate-Mass Q-TOF MS system equipped with an electrospray ionization (ESI) source. Optical rotations were measured with a Krüss P8000 polarimeter at the indicated concentration with the units of g/100 mL. Enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1200 LC instrument with a Daicel Chiralpak IA or IC column.

2. Materials

The various unsaturated isoxazolones **1** were prepared according to the reported literature procedure.[1] The α,α-dicyanoalkylidenes **2** were prepared according to the literature.[2] Chiral squaramide catalysts and chiral thiourea catalyst were prepared according to the reported procedures.[3]

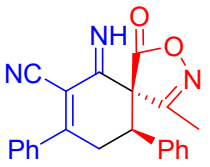
3. General procedure for the synthesis of the racemates of 3

To a dried small bottle were added **1** (0.10 mmol), Et_3N (1.1 mg, 0.01 mmol) and $CHCl_3$ (1.0 mL). The mixture was stirred at room temperature for 5 min, and **2** (0.12 mmol) was then added. After no **1** was monitored by TLC anymore, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/ethyl acetate 5:1 v/v) to afford the racemates of **3**.

4. General procedure for the synthesis of chiral compounds 3

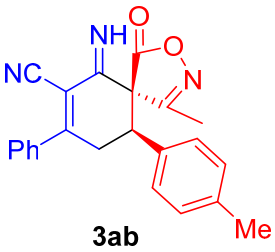
To a dried small bottle were added **1** (0.10 mmol), chiral organocatalyst **C6** (0.6 mg, 0.001 mmol, 1 mol%) and $CHCl_3$ (1.0 mL). The mixture was stirred at room temperature for 5 min,

and **2** (0.12 mmol) was then added. After no **1** was monitored by TLC anymore, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/ethyl acetate 5:1 v/v) to afford the desired products **3**.



3aa

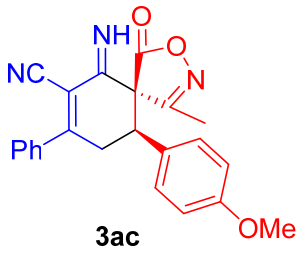
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-8,10-diphenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3aa). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3aa** as a white solid (25.6 mg, 72% yield), m. p. 83–85 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 11.4 min (minor enantiomer), t_R = 18.0 min (major enantiomer); 90% *ee*. $[\alpha]_D^{25}$ = –79.3 (*c* = 1.75, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H, NH), 7.61–7.59 (m, 2H, ArH), 7.54–7.46 (m, 3H, ArH), 7.37–7.35 (m, 3H, ArH), 7.25–7.23 (m, 2H, ArH), 3.88 (dd, J_1 = 19.6 Hz, J_2 = 11.6 Hz, 1H, CH_2), 3.65 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.04 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.09 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.2, 165.6, 162.1, 136.5, 135.7, 131.5, 129.6, 129.2, 129.0, 127.4, 127.1, 114.1, 108.0, 61.2, 44.0, 34.3, 12.7 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{18}N_3O_2$ $[M + H]^+$ 356.1394, found 356.1386.



3ab

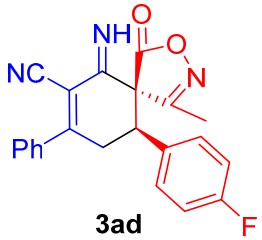
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-8-phenyl-10-(*p*-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ab). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ab** as a white solid (27.7 mg, 75% yield), m. p. 145–147 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.1 min (minor enantiomer), t_R = 13.8 min (major enantiomer); 87% *ee*. $[\alpha]_D^{25}$ = –143.6 (*c* = 0.50, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.40 (s, 1H, NH), 7.60

(dd, J = 7.6, 1.6 Hz, 2H, ArH), 7.54–7.48 (m, 3H, ArH), 7.18–7.14 (m, 4H, ArH), 3.87 (dd, J_1 = 19.8 Hz, J_2 = 11.8 Hz, 1H, CH_2), 3.60 (dd, J_1 = 11.8 Hz, J_2 = 4.2 Hz, 1H, CH), 3.02 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.33 (s, 3H, CH_3), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.2, 165.7, 162.2, 139.2, 136.6, 132.6, 131.5, 130.2, 129.0, 127.4, 127.0, 114.1, 108.0, 61.4, 43.7, 34.4, 21.0, 12.7 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1550, found 370.1539.



3ac

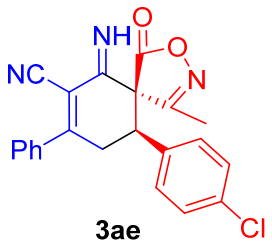
(5*S*,10*R*)-6-Imino-10-(4-methoxyphenyl)-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5] deca-3,7-diene-7-carbonitrile (3ac). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ac** as a white solid (22.3 mg, 78% yield), m. p. 83–85 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 11.2 min (minor enantiomer), t_R = 16.8 min (major enantiomer); 91% *ee*. $[\alpha]_D^{25}$ = –61.0 (*c* = 0.50, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.43 (s, 1H, NH), 7.62–7.59 (m, 2H, ArH), 7.53–7.47 (m, 3H, ArH), 7.18–7.15 (m, 2H, ArH), 6.89–6.86 (m, 2H, ArH), 3.85 (dd, J_1 = 19.6 Hz, J_2 = 11.6 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 3.59 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.01 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.11 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 166.2, 165.7, 162.2, 160.0, 136.6, 131.5, 129.0, 128.3, 127.5, 127.4, 114.9, 114.1, 108.1, 61.5, 55.3, 43.4, 34.6, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1499, found 386.1486.



3ad

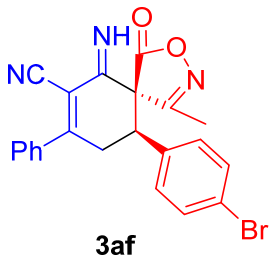
(5*S*,10*R*)-10-(4-Fluorophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ad). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as

eluent to obtain **3ad** as a white solid (22.4 mg, 60% yield), m. p. 143–145 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 12.2 min (minor enantiomer), t_R = 20.3 min (major enantiomer); 77% *ee*. $[\alpha]_D^{25} = -54.0$ (*c* = 0.30, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.44 (s, 1H, NH), 7.60 (dd, *J* = 7.8, 1.8 Hz, 2H, ArH), 7.54–7.48 (m, 3H, ArH), 7.26–7.22 (m, 2H, ArH), 7.07 (t, *J* = 8.6 Hz, 2H, ArH), 3.85 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.64 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.03 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.11 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 166.0, 165.3, 162.9 (d, $^1J_{C-F}$ = 247.8 Hz), 161.9, 136.4, 131.6, 131.5 (d, $^4J_{C-F}$ = 3.4 Hz), 129.1, 129.0 (d, $^3J_{C-F}$ = 8.2 Hz), 127.4, 116.7 (d, $^2J_{C-F}$ = 21.6 Hz), 114.0, 108.1, 61.3, 43.3, 34.4, 12.7 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –111.6 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}FN_3O_2$ $[M + H]^+$ 374.1299, found 374.1293.



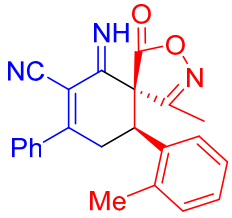
3ae

(5*S*,10*R*)-10-(4-Chlorophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ae). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ae** as a white solid (29.2 mg, 75% yield), m. p. 120–122 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 12.6 min (minor enantiomer), t_R = 22.5 min (major enantiomer); 77% *ee*. $[\alpha]_D^{25} = -58.0$ (*c* = 0.25, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H, NH), 7.60 (dd, *J* = 8.0, 1.6 Hz, 2H, ArH), 7.54–7.48 (m, 3H, ArH), 7.36 (d, *J* = 8.4 Hz, 2H, ArH), 7.19 (d, *J* = 8.8 Hz, 2H, ArH), 3.85 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.62 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.02 (dd, J_1 = 19.4 Hz, J_2 = 4.2 Hz, 1H, CH_2), 2.11 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 165.9, 161.8, 136.4, 135.3, 134.1, 131.7, 129.9, 129.1, 128.5, 127.4, 114.0, 108.1, 61.1, 43.4, 34.2, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}ClN_3O_2$ $[M + H]^+$ 390.1004, found 390.1007.



3af

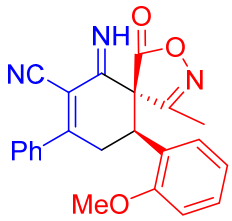
(5*S*,10*R*)-10-(4-Bromophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3af). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3af** as a white solid (32.5 mg, 75% yield), m. p. 140–142 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 13.1 min (minor enantiomer), t_R = 23.4 min (major enantiomer); 89% *ee*. $[\alpha]_D^{25}$ = –63.4 (*c* = 0.65, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H, NH), 7.60 (dd, *J* = 7.8, 1.8 Hz, 2H, ArH), 7.54–7.48 (m, 5H, ArH), 7.14–7.12 (m, 2H, ArH), 3.84 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.61 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.02 (dd, J_1 = 19.2 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 165.9, 165.1, 161.8, 136.4, 134.7, 132.8, 131.7, 129.1, 128.8, 127.4, 123.4, 114.0, 108.1, 61.1, 43.5, 34.1, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}{}^{79}BrN_3O_2$ $[M + H]^+$ 434.0499, found 434.0494; calcd. for $C_{22}H_{17}{}^{81}BrN_3O_2$ $[M + H]^+$ 436.0478, found 436.0475.



3ag

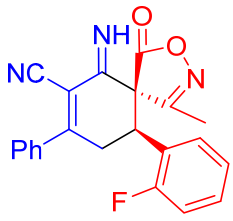
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-8-phenyl-10-(o-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ag). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ag** as a white solid (25.5 mg, 69% yield), m. p. 91–93 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 14.4 min (minor enantiomer), t_R = 27.9 min (major enantiomer); 85% *ee*. $[\alpha]_D^{25}$ = –31.5 (*c* = 1.05, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.37 (s, 1H, NH), 7.60 (dd,

J = 8.0, 1.6 Hz, 2H, ArH), 7.55–7.47 (m, 3H, ArH), 7.22 (s, 4H, ArH), 3.87 (dd, J = 11.6 Hz, J_2 = 4.4 Hz, 1H, CH), 3.69 (dd, J_1 = 19.8 Hz, J_2 = 11.8 Hz, 1H, CH_2), 2.95 (dd, J_1 = 20.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.41 (s, 3H, CH_3), 1.96 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 166.1, 165.9, 162.8, 136.4, 134.7, 131.6, 129.1, 128.7, 127.8, 127.4, 125.0, 114.2, 107.8, 60.3, 39.1, 35.2, 19.7, 12.5 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1550, found 370.1545.



3ah

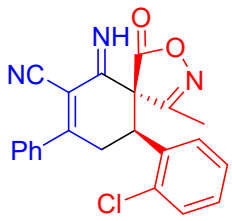
(5*S*,10*R*)-6-Imino-10-(2-methoxyphenyl)-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5] deca-3,7-diene-7-carbonitrile (3ah). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ah** as a white solid (34.6 mg, 90% yield), m. p. 84–86 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 10.7 min (minor enantiomer), t_R = 20.1 min (major enantiomer); 89% *ee*. ^1H NMR (400 MHz, $CDCl_3$): δ 10.36 (s, 1H, NH), 7.62–7.60 (m, 2H, ArH), 7.54–7.46 (m, 3H, ArH), 7.33–7.25 (m, 2H, ArH), 6.96 (t, J = 7.6 Hz, 1H, ArH), 6.91 (d, J = 8.0 Hz, 1H, ArH), 4.36 (s, 1H, CH), 3.83 (s, 4H, OCH_3 + CH_2), 2.93 (dd, J = 19.8, 4.2 Hz, 1H, CH_2), 2.06 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.0, 166.7, 166.5, 162.9, 156.2, 136.7, 131.4, 129.0, 127.5, 124.1, 121.6, 114.3, 111.0, 108.0, 60.8, 55.0, 34.1, 12.3 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1499, found 386.1492.



3ai

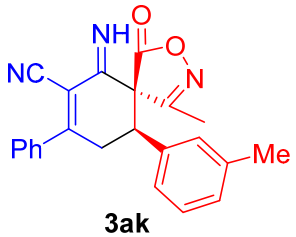
(5*S*,10*R*)-10-(2-Fluorophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]de ca-3,7-diene-7-carbonitrile (3ai). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as

eluent to obtain **3ai** as a white solid (23.5 mg, 63% yield), m. p. 82–84 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 13.0 min (minor enantiomer), t_R = 22.2 min (major enantiomer); 56% *ee*. $[\alpha]_D^{25} = -33.6$ (*c* = 0.50, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H, NH), 7.62–7.60 (m, 2H, ArH), 7.54–7.48 (m, 3H, ArH), 7.38–7.32 (m, 2H, ArH), 7.19 (t, J = 7.6 Hz, 1H, ArH), 7.12 (t, J = 9.4 Hz, 1H, ArH), 4.20 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.85 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 2.99 (dd, J_1 = 19.4 Hz, J_2 = 4.6 Hz, 1H, CH_2), 2.13 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 166.4, 165.4, 162.0, 159.7 (d, $^1J_{C-F}$ = 244.3 Hz), 136.5, 131.6, 130.7 (d, $^3J_{C-F}$ = 8.7 Hz), 129.1, 127.52 (d, $^4J_{C-F}$ = 2.4 Hz), 127.46, 125.7 (d, $^3J_{C-F}$ = 3.6 Hz), 122.9 (d, $^2J_{C-F}$ = 13.5 Hz), 116.2 (d, $^2J_{C-F}$ = 23.0 Hz), 114.0, 108.2, 60.9, 34.5 (d, $^3J_{C-F}$ = 4.5 Hz), 33.7, 12.1 (d, $^4J_{C-F}$ = 4.8 Hz) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –114.3 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}FN_3O_2$ $[M + H]^+$ 374.1299, found 374.1294.



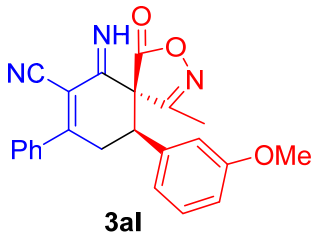
3aj

(5*S*,10*R*)-10-(2-Chlorophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3aj). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3aj** as a white solid (22.2 mg, 57% yield), m. p. 83–88 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 13.5 min (minor enantiomer), t_R = 24.7 min (major enantiomer); 51% *ee*. $[\alpha]_D^{25} = -31.4$ (*c* = 0.70, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.44 (s, 1H, NH), 7.61 (dd, J = 7.8, 1.8 Hz, 2H, ArH), 7.55–7.44 (m, 4H, ArH), 7.37–7.28 (m, 3H, ArH), 4.42 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH), 3.66 (dd, J_1 = 19.8 Hz, J_2 = 11.8 Hz, 1H, CH_2), 3.02 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.09 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 166.4, 165.4, 162.3, 136.3, 133.8, 133.1, 131.6, 130.6, 130.2, 129.1, 128.6, 127.5, 127.0, 114.0, 108.0, 60.4, 38.8, 34.4, 12.5 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}ClN_3O_2$ $[M + H]^+$ 390.1004, found 390.1018.



3ak

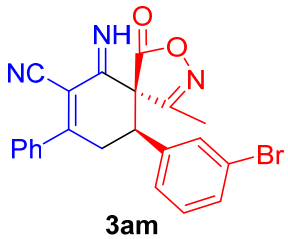
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-8-phenyl-10-(*m*-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ak). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ak** as a white solid (21.4 mg, 58% yield), m. p. 82–84 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 13.4 min (minor enantiomer), t_R = 22.5 min (major enantiomer); 85% *ee*. $[\alpha]_D^{25}$ = –25.7 (*c* = 0.90, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H, NH), 7.61 (dd, J_1 = 7.8 Hz, J_2 = 1.8 Hz, 2H, ArH), 7.53–7.47 (m, 3H, ArH), 7.27–7.23 (m, 1H, ArH), 7.16 (d, *J* = 7.6 Hz, 1H, ArH), 7.16 (d, *J* = 6.8 Hz, 2H, ArH), 3.88 (dd, J_1 = 19.8 Hz, 11.8 Hz, 1H, CH_2), 3.59 (dd, J_1 = 12.0 Hz, 4.4 Hz, J_2 = 1H, CH), 3.03 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.33 (s, 3H, CH_3), 2.1 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.2, 165.7, 162.2, 139.5, 136.6, 135.7, 131.5, 130.0, 129.4, 129.0, 127.7, 127.4, 124.3, 114.1, 108.0, 61.2, 44.1, 34.5, 21.4, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1550, found 370.1556.



3al

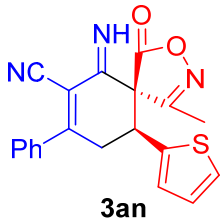
(5*S*,10*R*)-6-Imino-10-(3-methoxyphenyl)-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3al). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3al** as a white solid (26.9 mg, 70% yield), m. p. 81–83 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.4 min (minor enantiomer), t_R = 14.7 min (major enantiomer); 82% *ee*. $[\alpha]_D^{25}$ = –64.6 (*c* = 0.70, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.41 (s, 1H, NH), 7.61–7.59 (m, 2H, ArH), 7.55–7.48 (m, 3H, ArH), 7.29 (t, *J* = 8.0 Hz, 1H, ArH), 6.88 (dd, J_1 = 8.2 Hz, J_2 = 2.2 Hz, 1H, ArH), 6.82 (d, *J* = 7.6 Hz, 1H, ArH), 6.77 (s, 1H, ArH),

3.87 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.79 (s, 3H, OCH_3), 3.60 (dd, J_1 = 11.8 Hz, J_2 = 4.2 Hz, 1H, CH), 3.04 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.11 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 166.1, 165.6, 162.1, 137.2, 136.5, 131.6, 130.7, 129.1, 127.5, 119.3, 114.3, 114.1, 113.1, 108.1, 61.2, 55.3, 44.1, 34.4, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1499, found 386.1500.



3am

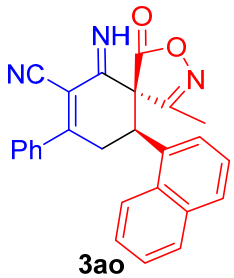
(5*S*,10*R*)-10-(3-Bromophenyl)-6-imino-4-methyl-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3am). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3am** as a white solid (23.5 mg, 54% yield), m. p. 71–73 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 11.0 min (minor enantiomer), t_R = 17.1 min (major enantiomer); 62% *ee*. $[\alpha]_D^{25}$ = –27.8 (*c* = 0.40, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H, NH), 7.61–7.59 (m, 2H, ArH), 7.54–7.48 (m, 4H, ArH), 7.39 (s, 1H, ArH), 7.28–7.24 (t, *J* = 8.0 Hz, 1H, ArH), 7.20 (d, *J* = 8.0 Hz, 1H, ArH), 3.86 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH), 3.59 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.03 (dd, J_1 = 19.4 Hz, J_2 = 4.2 Hz, 1H, CH_2), 2.12 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 165.9, 165.1, 161.8, 138.0, 136.4, 132.5, 131.7, 131.3, 130.6, 129.1, 127.4, 125.5, 123.5, 113.9, 108.1, 61.0, 43.6, 34.2, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}{}^{79}BrN_3O_2$ $[M + H]^+$ 434.0499, found 434.0515; calcd. for $C_{22}H_{17}{}^{81}BrN_3O_2$ $[M + H]^+$ 436.0478, found 436.0497.



3an

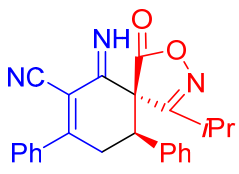
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-8-phenyl-10-(thiophen-2-yl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3an). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3an** as a pale yellow solid (27.1 mg, 75% yield), m. p. 83–85 °C. HPLC

(Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 18.4 min (minor enantiomer), t_R = 28.2 min (major enantiomer); 92% *ee*. $[\alpha]_D^{25}$ = –60.0 (*c* = 0.35, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.47 (s, 1H, NH), 7.62–7.60 (m, 2H, ArH), 7.54–7.49 (m, 3H, ArH), 7.27–7.26 (m, 1H, =CH), 7.03–7.00 (m, 2H, =CH), 3.99–3.88 (m, 2H, CH+CH_2), 3.16 (dd, J_1 = 16.6 Hz, J_2 = 1.4 Hz, 1H, CH_2), 2.18 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 165.9, 164.8, 161.6, 137.5, 136.4, 131.7, 129.1, 127.8, 127.5, 125.9, 125.6, 114.0, 108.2, 61.8, 38.6, 35.3, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{20}H_{16}N_3O_2S$ $[M + H]^+$ 362.0958, found 362.0955.



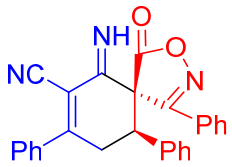
3ao

(5*S*,10*R*)-6-Imino-4-methyl-10-(naphthalen-1-yl)-1-oxo-8-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ao). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ao** as a white solid (31.6 mg, 78% yield), m. p. 105–107 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 14.7 min (minor enantiomer), t_R = 30.2 min (major enantiomer); 88% *ee*. $[\alpha]_D^{25}$ = –50.8 (*c* = 0.85, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H, NH), 8.08 (d, *J* = 8.4 Hz, 1H, ArH), 7.93 (d, *J* = 7.6 Hz, 1H, ArH),7.86 (d, *J* = 7.2 Hz, 1H, ArH), 7.63–7.46 (m, 9H, ArH), 4.65 (dd, J_1 = 11.6 Hz, J_2 = 4.4 Hz, 1H, CH), 3.88 (dd, J_1 = 20.0 Hz, J_2 = 11.6 Hz, 1H, CH_2), 3.15 (dd, J_1 = 19.8 Hz, J_2 = 4.2 Hz, 1H, CH_2), 1.86 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.1, 166.3, 166.0, 162.8, 136.4, 134.3, 132.1, 131.6, 130.5, 129.9, 129.5, 129.1, 127.5, 127.2, 126.2, 125.9, 123.8, 121.0, 114.2, 107.9, 60.9, 37.3, 35.5, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{20}N_3O_2$ $[M + H]^+$ 406.1550, found 406.1549.



3ap

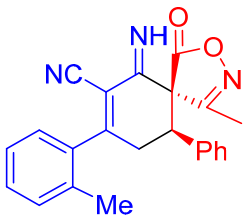
(5*S*,10*R*)-6-Imino-4-isopropyl-1-oxo-8,10-diphenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ap). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ap** as a white solid (17.3 mg, 45% yield), m. p. 83–85 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/isopropanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 6.7 min (major enantiomer), t_R = 7.9 min (minor enantiomer); 96% *ee*. $[\alpha]_D^{25}$ = –45.6 (*c* = 0.85, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.49 (s, 1H, NH), 7.61 (dd, J_1 = 7.6 Hz, J_2 = 1.6 Hz, 2H, ArH), 7.54–7.47 (m, 3H, ArH), 7.39–7.34 (m, 3H, ArH), 7.27–7.24 (m, 2H, ArH), 3.88 (dd, J_1 = 19.2 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.72 (dd, J_1 = 11.8 Hz, J_2 = 4.2 Hz, 1H, CH), 3.00 (dd, *J* = 19.2 Hz, J_2 = 4.0 Hz, 1H, CH_2), 2.69–2.59 (m, 1H, CH), 1.30 (d, *J* = 6.8 Hz, 3H, CH_3), 1.01 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.4, 172.9, 165.3, 162.6, 136.54, 136.49, 131.6, 129.5, 129.0, 127.5, 127.4, 114.2, 108.1, 61.8, 44.0, 35.4, 28.7, 22.1, 19.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{24}H_{22}N_3O_2$ $[M + H]^+$ 384.1707, found 384.1697.



3aq

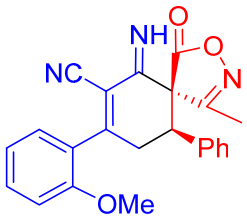
(5*S*,10*R*)-6-Imino-1-oxo-4,8,10-triphenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3aq). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3aq** as a white solid (54.4 mg, 57% yield), m. p. 77–79 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 18.9 min (minor enantiomer), t_R = 22.4 min (major enantiomer); 90% *ee*. $[\alpha]_D^{25}$ = –15.1 (*c* = 0.80, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.61 (s, 1H, NH), 7.67 (dd, J_1 = 7.6 Hz, J_2 = 2.0 Hz, 2H, ArH), 7.58–7.50 (m, 6H, ArH), 7.46 (t, *J* = 7.6 Hz, 2H, ArH), 7.29–7.26 (m, 1H, ArH), 7.19 (t, *J* = 7.4 Hz, 2H, ArH), 6.84 (d, *J* = 7.2 Hz, 2H, ArH), 4.03 (dd, J_1 = 18.8 Hz, J_2 = 12.0 Hz, 1H, CH), 3.92 (dd, J_1 = 12.2 Hz, J_2 = 3.8 Hz, 1H, CH_2), 3.05 (dd, J_1 = 19.0 Hz, J_2 = 3.8 Hz, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.9, 166.3, 165.4, 162.9, 136.7, 135.1, 132.7, 131.8, 131.7, 131.3, 129.6, 129.1, 129.0, 127.8,

127.6, 126.9, 114.2, 108.2, 61.7, 44.2, 33.7 ppm. HRMS (ESI): *m/z* calcd. for $C_{27}H_{20}N_3O_2$ [M + H]$^+$ 418.1550, found 418.1545.



3ba

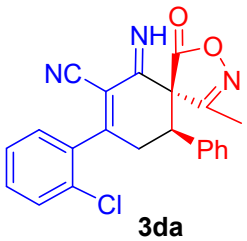
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-10-phenyl-8-(*o*-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ba). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ba** as a white solid (23.3 mg, 63% yield), m. p. 99–101 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.4 min (minor enantiomer), t_R = 14.1 min (major enantiomer); 76% *ee*. $[\alpha]_D^{25}$ = –31.8 (*c* = 0.60, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.35 (s, 1H, NH), 7.36–7.22 (m, 9H, ArH), 3.77 (dd, J_1 = 19.0 Hz, J_2 = 11.8 Hz, 1H, CH_2), 3.65 (d, J = 10.4 Hz, 1H, CH), 2.87 (dd, J_1 = 20.0 Hz, J_2 = 4.0 Hz, 1H, CH_2), 2.47 (s, 3H, CH_3), 2.12 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 166.1, 161.9, 136.8, 135.6, 131.1, 130.0, 129.6, 129.3, 127.1, 126.4, 113.1, 110.8, 61.2, 44.2, 35.9, 19.3, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_2$ [M + H]$^+$ 370.1550, found 370.1540.



3ca

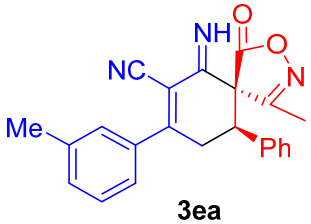
(5*S*,10*R*)-6-Imino-8-(2-methoxyphenyl)-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ca). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ca** as a white solid (21.6 mg, 56% yield), m. p. 83–85 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.3 min (minor enantiomer), t_R = 12.7 min (major enantiomer); 86% *ee*. $[\alpha]_D^{25}$ = –61.0 (*c* = 0.50, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.33 (s, 1H,

NH), 7.47–7.43 (m, 1H, ArH), 7.37–7.34 (m, 4H, ArH), 7.26–7.23 (m, 2H, ArH), 7.07 (t, J = 7.4 Hz, 1H, ArH), 6.99 (d, J = 8.4 Hz, 1H, ArH), 3.87 (s, 3H, OCH_3), 3.77 (dd, J_1 = 19.2 Hz, J_2 = 12.0 Hz, 1H, CH), 3.64 (dd, J_1 = 12.0 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.12 (dd, J_1 = 19.6 Hz, J_2 = 4.0 Hz, 1H, CH_2), 2.12 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.2, 166.0, 162.2, 156.0, 136.0, 132.3, 129.5, 129.1, 128.9, 127.2, 125.9, 121.0, 113.7, 111.5, 110.0, 61.5, 55.7, 44.2, 33.8, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_3$ $[M + H]^+$ 386.1499, found 386.1495.



3da

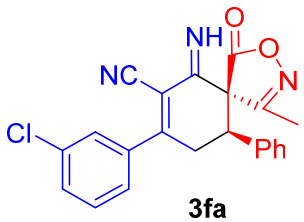
(5*S*,10*R*)-8-(2-Chlorophenyl)-6-imino-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3da). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3da** as a white solid (31.6 mg, 81% yield), m. p. 91–93 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 11.4 min (minor enantiomer), t_R = 16.9 min (major enantiomer); 91% *ee*. $[\alpha]_D^{25}$ = –36.1 (*c* = 0.75, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H, NH), 7.51–7.49 (m, 1H, ArH), 7.46–7.42 (m, 3H, ArH), 7.36–7.35 (m, 3H, ArH), 7.26–7.23 (m, 2H, ArH), 3.67–3.64 (m, 2H, CH+CH_2), 3.05 (s, 1H, CH_2), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 166.0, 161.6, 136.0, 135.5, 131.5, 130.9, 130.3, 129.6, 129.3, 128.6, 127.6, 127.2, 112.6, 111.4, 61.3, 44.2, 34.4, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}ClN_3O_2$ $[M + H]^+$ 390.1004, found 390.0997.



3ea

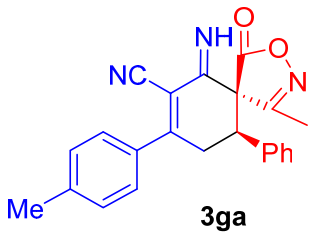
(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-10-phenyl-8-(*m*-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ea). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ea** as a white solid (22.9 mg, 62% yield), m. p. 78–80 °C. HPLC (Daicel

Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 12.8 min (minor enantiomer), t_R = 20.2 min (major enantiomer); 77% *ee*. $[\alpha]_D^{25} = -35.3$ (*c* = 0.60, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.40 (s, 1H, NH), 7.42–7.32 (m, 7H, ArH), 7.26–7.24 (m, 2H, ArH), 3.87 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH), 3.62 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.04 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.41 (s, 3H, CH_3), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.1, 165.9, 162.2, 139.0, 136.5, 135.8, 132.3, 129.6, 129.2, 128.9, 127.9, 127.2, 124.6, 114.1, 107.9, 61.3, 44.1, 35.9, 21.3, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1550, found 370.1540.



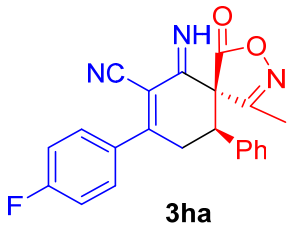
3fa

(5*S*,10*R*)-8-(3-Chlorophenyl)-6-imino-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3fa). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3fa** as a white solid (35.0 mg, 90% yield), m. p. 86–88 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 10.9 min (minor enantiomer), t_R = 17.2 min (major enantiomer); 86% *ee*. $[\alpha]_D^{25} = -83.7$ (*c* = 0.65, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.48 (s, 1H, NH), 7.55–7.49 (m, 3H, ArH), 7.45 (t, *J* = 7.8 Hz, 1H, ArH), 7.38–7.36 (m, 3H, ArH), 7.26–7.23 (m, 2H, ArH), 3.86 (dd, J_1 = 19.8 Hz, J_2 = 11.8 Hz, 1H, CH), 3.63 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.99 (dd, J_1 = 20.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.6, 166.0, 163.8, 161.8, 138.2, 135.4, 135.2, 131.4, 130.5, 129.7, 129.4, 127.3, 127.1, 125.6, 113.6, 108.9, 61.2, 44.1, 34.5, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}ClN_3O_2$ $[M + H]^+$ 390.1004, found 390.0989.



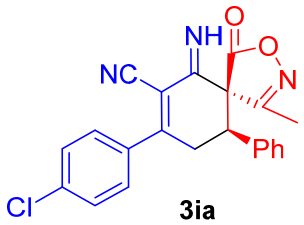
3ga

(5*S*,10*R*)-6-Imino-4-methyl-1-oxo-10-phenyl-8-(*p*-tolyl)-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ga). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ga** as a white solid (22.5 mg, 61% yield), m. p. 144–146 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.8 min (minor enantiomer), t_R = 14.7 min (major enantiomer); 85% *ee*. $[\alpha]_D^{25}$ = –8.4 (*c* = 0.50, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.36 (s, 1H, NH), 7.52 (d, *J* = 8.4 Hz, 2H, ArH), 7.37–7.35 (m, 3H, ArH), 7.30 (d, *J* = 8.0 Hz, 2H, ArH), 7.26–7.23 (m, 2H, ArH), 3.86 (dd, J_1 = 19.4 Hz, J_2 = 11.8 Hz, 1H, CH_2), 3.62 (dd, J_1 = 11.8 Hz, J_2 = 4.2 Hz, 1H, CH), 3.04 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.41 (s, 3H, CH_3), 2.09 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.2, 165.5, 162.3, 142.4, 135.8, 133.6, 129.7, 129.6, 129.2, 127.5, 127.2, 114.4, 107.3, 61.3, 44.1, 34.1, 21.5, 12.7 ppm. HRMS (ESI): *m/z* calcd. For $C_{23}H_{20}N_3O_2$ $[M + H]^+$ 370.1550, found 370.1542.



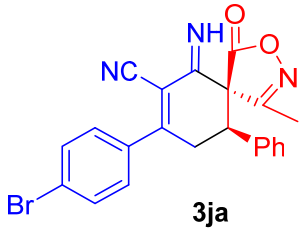
3ha

(5*S*,10*R*)-8-(4-Fluorophenyl)-6-imino-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ha). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ha** as a white solid (26.5 mg, 71% yield), m. p. 82–84 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 9.0 min (minor enantiomer), t_R = 12.3 min (major enantiomer); 88% *ee*. $[\alpha]_D^{25}$ = –51.1 (*c* = 0.90, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.40 (s, 1H, NH), 7.65–7.62 (m, 2H, ArH), 7.38–7.37 (m, 3H, ArH), 7.26–7.18 (m, 4H, ArH), 3.87 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH), 3.63 (dd, J_1 = 11.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.01 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.0, 164.5 (d, $^1J_{C-F}$ = 252.5 Hz), 164.2, 162.0, 135.6, 132.5 (d, $^4J_{C-F}$ = 3.2 Hz), 129.8 (d, $^3J_{C-F}$ = 8.8 Hz), 129.7, 129.3, 127.2, 116.4 (d, $^2J_{C-F}$ = 21.9 Hz), 114.0, 108.1, 61.2, 44.1, 34.4, 12.8 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –106.9 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}FN_3O_2$ $[M + H]^+$ 374.1299, found 374.1297.



3ia

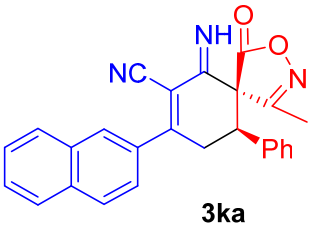
(5*S*,10*R*)-8-(4-Chlorophenyl)-6-imino-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ia). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ia** as a white solid (26.5 mg, 68% yield), m. p. 70–72 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/isopropanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 12.6 min (minor enantiomer), t_R = 20.2 min (major enantiomer); 88% *ee*. $[\alpha]_D^{25}$ = –78.0 (*c* = 0.60, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H, NH), 7.57–7.54 (m, 2H, ArH), 7.50–7.47 (m, 2H, ArH), 7.38–7.37 (m, 3H, ArH), 7.26–7.23 (m, 2H, ArH), 3.87 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH), 3.63 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.00 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.10 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.0, 164.1, 161.9, 135.5, 135.3, 132.4, 129.7, 129.4, 129.0, 127.1, 126.3, 113.8, 108.4, 61.2, 44.1, 34.2, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}ClN_3O_2$ $[M + H]^+$ 390.1004, found 390.0993.



3ja

(5*S*,10*R*)-8-(4-Bromophenyl)-6-imino-4-methyl-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ja). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ja**as a white solid (31.7 mg, 73% yield), m. p. 178–180 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 85:15, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 15.3 min (minor enantiomer), t_R = 24.9 min (major enantiomer); 77% *ee*. $[\alpha]_D^{25}$ = –65.8 (*c* = 0.55, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.46 (s, 1H, NH), 7.65 (d, *J* = 8.4 Hz, 2H, ArH), 7.48 (d, *J* = 8.4 Hz, 2H, ArH), 7.38–7.37 (m, 3H, ArH), 7.26–7.23 (m, 2H, ArH), 3.87 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH), 3.62 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.99 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.10 (s, 3H,

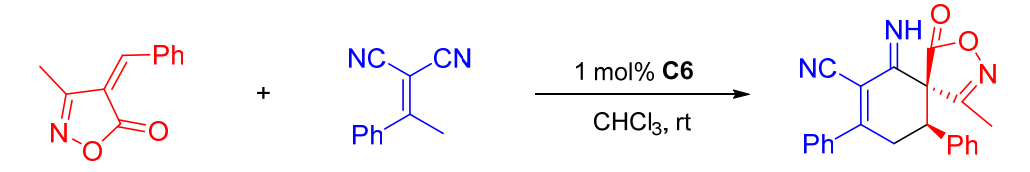
CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.7, 166.0, 164.0, 161.9, 137.9, 135.5, 134.8, 129.7, 129.44, 129.37, 128.9, 127.2, 113.9, 108.4, 61.2, 44.1, 34.3, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}{}^{79}BrN_3O_2$ $[M + H]^+$ 434.0499, found 434.0483; calcd. for $C_{22}H_{17}{}^{81}BrN_3O_2$ $[M + H]^+$ 436.0478, found 436.0465.



3ka

(5*S*,10*R*)-6-Imino-4-methyl-8-(naphthalen-2-yl)-1-oxo-10-phenyl-2-oxa-3-azaspiro[4.5]deca-3,7-diene-7-carbonitrile (3ka). Employing the general procedure and purified by silica gel (200-300 mesh) column chromatography using petroleum ether/ethyl acetate (5:1 v/v) as eluent to obtain **3ka** as a white solid (29.6 mg, 73% yield), m. p. 85–87 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 10.6 min (minor enantiomer), t_R = 17.1 min (major enantiomer); 76% *ee*. $[\alpha]_D^{25} = -52.0$ (*c* = 1.00, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 10.45 (s, 1H, NH), 8.14 (d, J = 1.2 Hz, 1H, ArH), 7.95 (d, J = 8.4 Hz, 1H, ArH), 7.93–7.87 (m, 2H, ArH), 7.65 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H, ArH), 7.62–7.55 (m, 2H, ArH), 7.41–7.37 (m, 3H, ArH), 7.29–7.26 (m, 2H, ArH), 3.98 (dd, J_1 = 19.6 Hz, J_2 = 12.0 Hz, 1H, CH_2), 3.69 (dd, J_1 = 12.0 Hz, J_2 = 4.4 Hz, 1H, CH_2), 3.17 (dd, J_1 = 19.6 Hz, J_2 = 4.4 Hz, 1H, CH_2), 2.12 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 166.2, 165.5, 162.2, 135.7, 134.4, 133.8, 132.6, 129.6, 129.3, 129.0, 128.8, 128.22, 128.16, 127.8, 127.3, 127.2, 123.8, 114.3, 108.2, 61.3, 44.2, 34.4, 12.8 ppm. HRMS (ESI): *m/z* calcd. for $C_{26}H_{20}N_3O_2$ $[M + H]^+$ 406.1550, found 406.1540.

5. Scale-up synthesis of 3a



1a
3 mmol, 561.6 mg

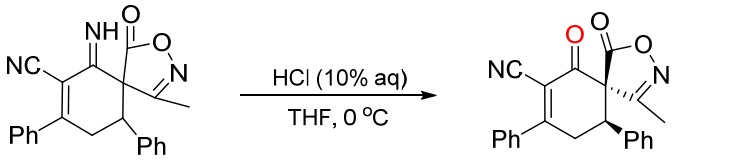
2a
3.6 mmol, 605.5 mg

3aa
458.5 mg, 43% yield
>20:1 dr, 81% ee

4-benzylidene-3-methylisoxazol-5(4*H*)-one **1a** (561.6 mg, 3 mmol), 2-(1-phenylethylidene)

malononitrile **2a** (605.5 mg, 3.6 mmol) and catalyst **C6** (18 mg, 1 mol%) were dissolved in chloroform (20 mL) at room temperature. After stirring at room temperature for 3 weeks, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/ethyl acetate 5:1 v/v) to afford the desired product **3aa** as a white solid (458.5 mg, 43% yield) with >20:1 dr and 81% ee.

6. Procedure and the characterization data of compound 4



3aa
>20:1 dr, 81% ee

4
85% yield, >20:1 dr, 89% ee

Add dilute hydrochloric acid (0.5 ml, 10% aq.) dropwise to the stirred solution of chiral product **3aa** (35.5 mg, 0.1 mmol) in tetrahydrofuran solution (0.5 mL) in an ice-water bath. After the solution was stirred for 10 min, saturated sodium bicarbonate (0.5 ml) was added to quench the reaction, then the mixture was extracted with dichloromethane (3 × 1 mL). The organic phase was dried with anhydrous Na_2SO_4 and the solvent was removed under vacuum. The crude product was purified by flash column chromatography on silica gel (CH_2Cl_2 as the eluent) to afford the pure product **4** as a white soild (30.3 mg, 85% yield), m. p. 101–103 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/ethyl acetate = 87:13, flow rate 1.0 mL/min, detection at 254 nm): major diastereomer: t_R = 18.7 min (major enantiomer), t_R = 23.3 min (minor enantiomer); 89% *ee*. $[\alpha]_D^{25} = -57.6$ (*c* = 0.50, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 7.2 Hz, 2H, ArH), 7.58 (t, J = 7.2 Hz, 1H, ArH), 7.52 (t, J = 7.4 Hz, 2H, ArH), 7.38–7.36 (m, 3H, ArH), 7.26–7.23 (m, 2H, ArH), 4.04 (dd, J_1 = 19.8 Hz, J_2 = 11.8 Hz, 1H, CH), 3.91 (dd, J_1 = 11.6 Hz, J_2 = 4.0 Hz, 1H, CH_2), 3.20 (dd, J_1 = 19.6 Hz, J_2 = 4.0 Hz, 1H, CH_2), 2.07 (s, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 182.7, 175.4, 172.1, 164.8, 135.6, 135.0, 132.6, 129.7, 129.5, 129.2, 127.6, 127.0, 113.5, 110.0, 65.2, 44.5, 34.6, 12.7 ppm. HRMS (ESI): *m/z* calcd. for $C_{22}H_{17}N_2O_3$ $[M + H]^+$ 357.1234, found 357.1230.

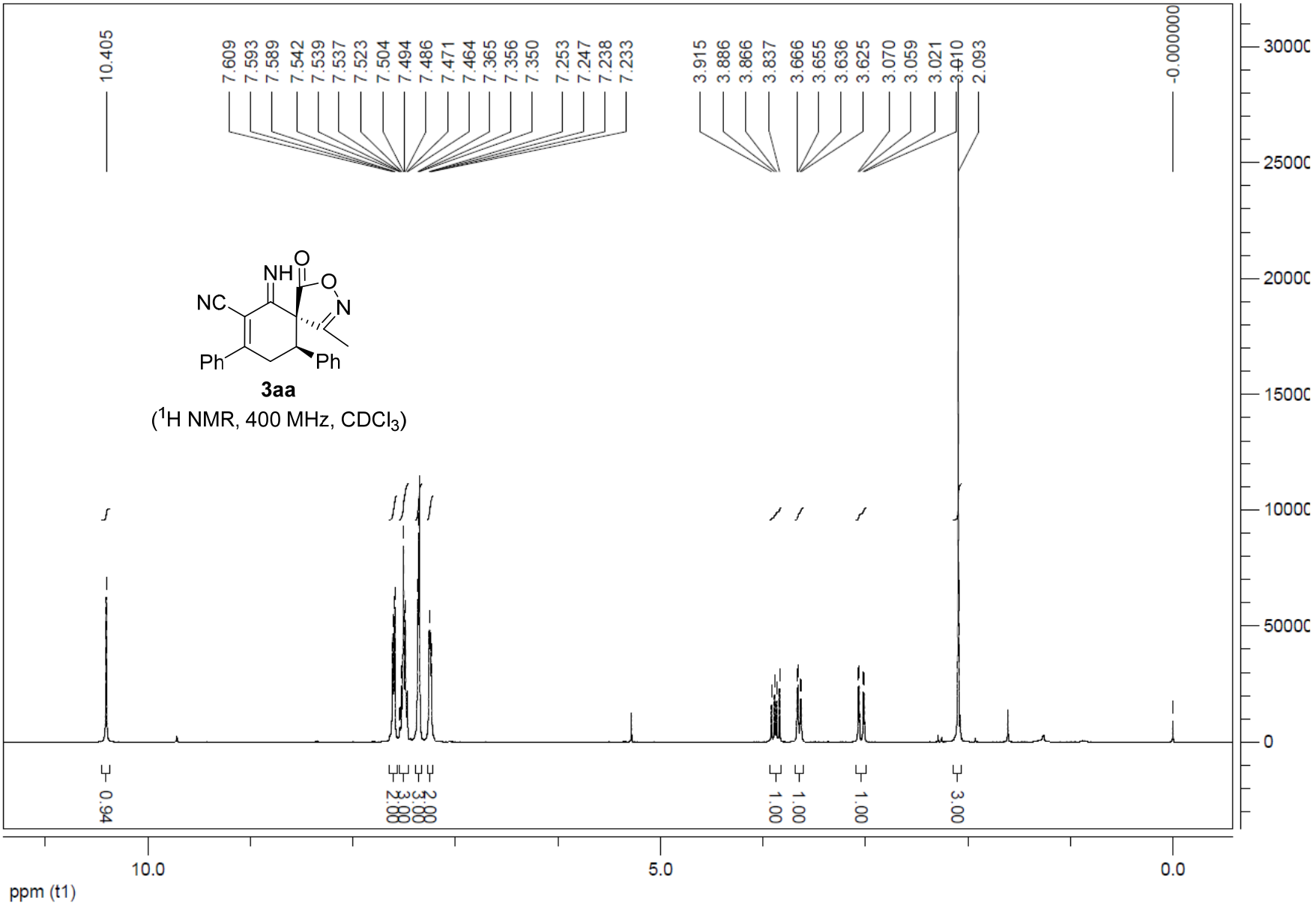
7. Reference

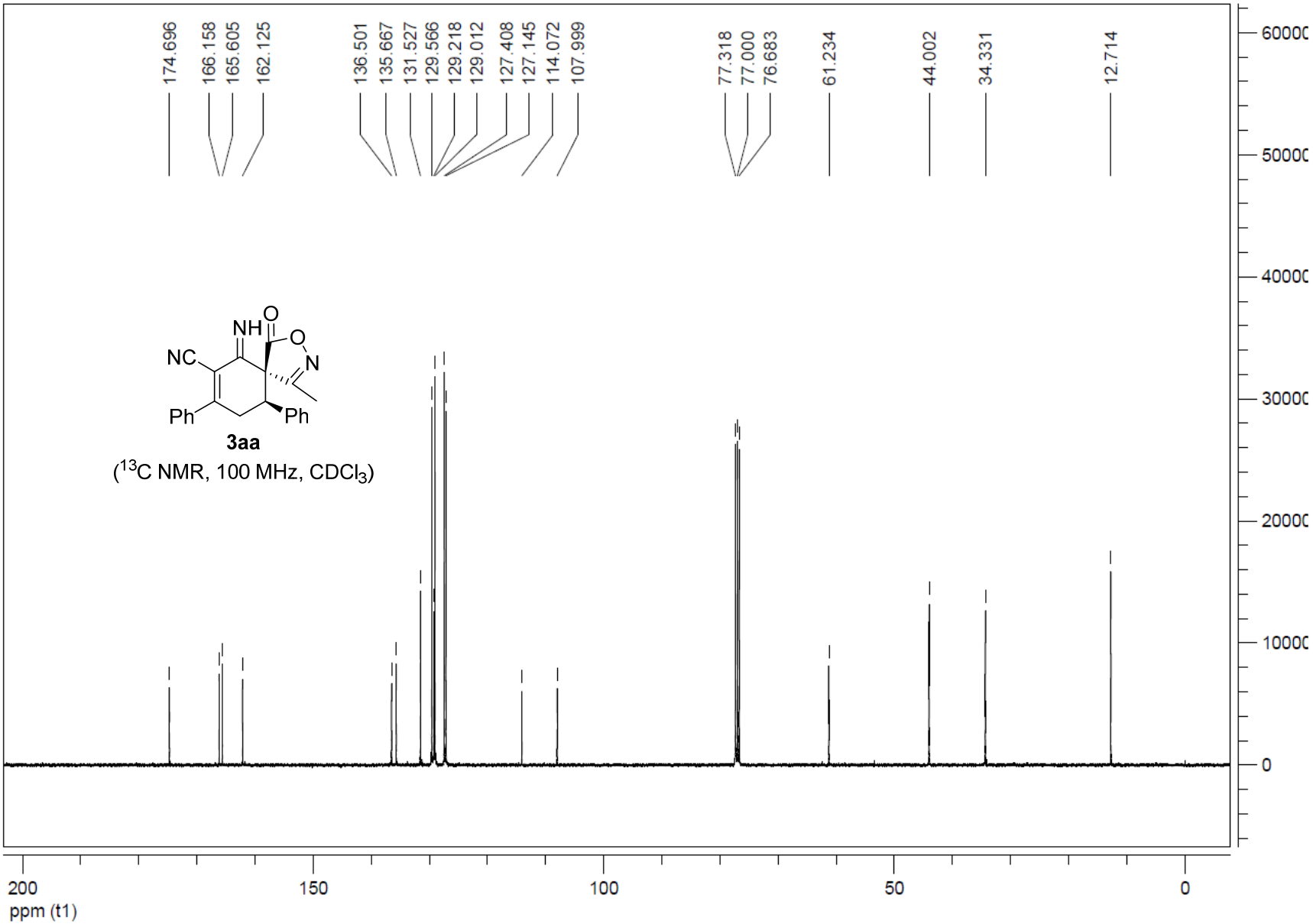
[1] (a) R. H. Vekariya, K. D. Patel, H. D. Patel, *Res. Chem. Intermed*. **2016**, *42*, 7559–7579. (b) A. B. Rikani, D. Setamdideh, *Orient. J. Chem.* **2016**, *32*, 1433-1437. (c) R. Laroum, A. Debache, *Synth. Commun*. **2018**, *48*, 1876–1882.

[2] (a) I. Liepuoniute, P. Commins, D. P. Karothu, S. Schramm, H. Hara and P. Naumov, *Chem. Eur. J.*, 2019, **25**, 373–378. (b) H. C. Wu, C. Wang, Y. H. Chen and Y. K. Liu, *Chem. Commun.*, 2021, **57**, 1762–1765.

[3] (a) Y. Zhu, J. P. Malerich and V. H. Rawal, *Angew. Chem. Int. Ed.*, 2010, **49**, 153–156; *Angew. Chem.* **2010**, 122, 157–160. (b) W. Yang and D. M. Du, *Org. Lett.*, 2010, **12**, 5450–5453. (c) W. Yang and D. M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241–1246. (d) B. Vakulya, S. Varga, A. Csampai and T. Soós, *Org. Lett.*, 2005, **7**, 1967–1969.

8. Copies of ^{1}H, ^{13}C and ^{19}F NMR spectra of new compounds

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162.125
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129.566
129.218
129.012
127.408
127.145
114.072
107.999
77.318
77.000
76.683
61.234
44.002
34.331
12.714
NC
NH
O
O
N
Ph
Ph
3aa
(13C NMR, 100 MHz, CDCl3)
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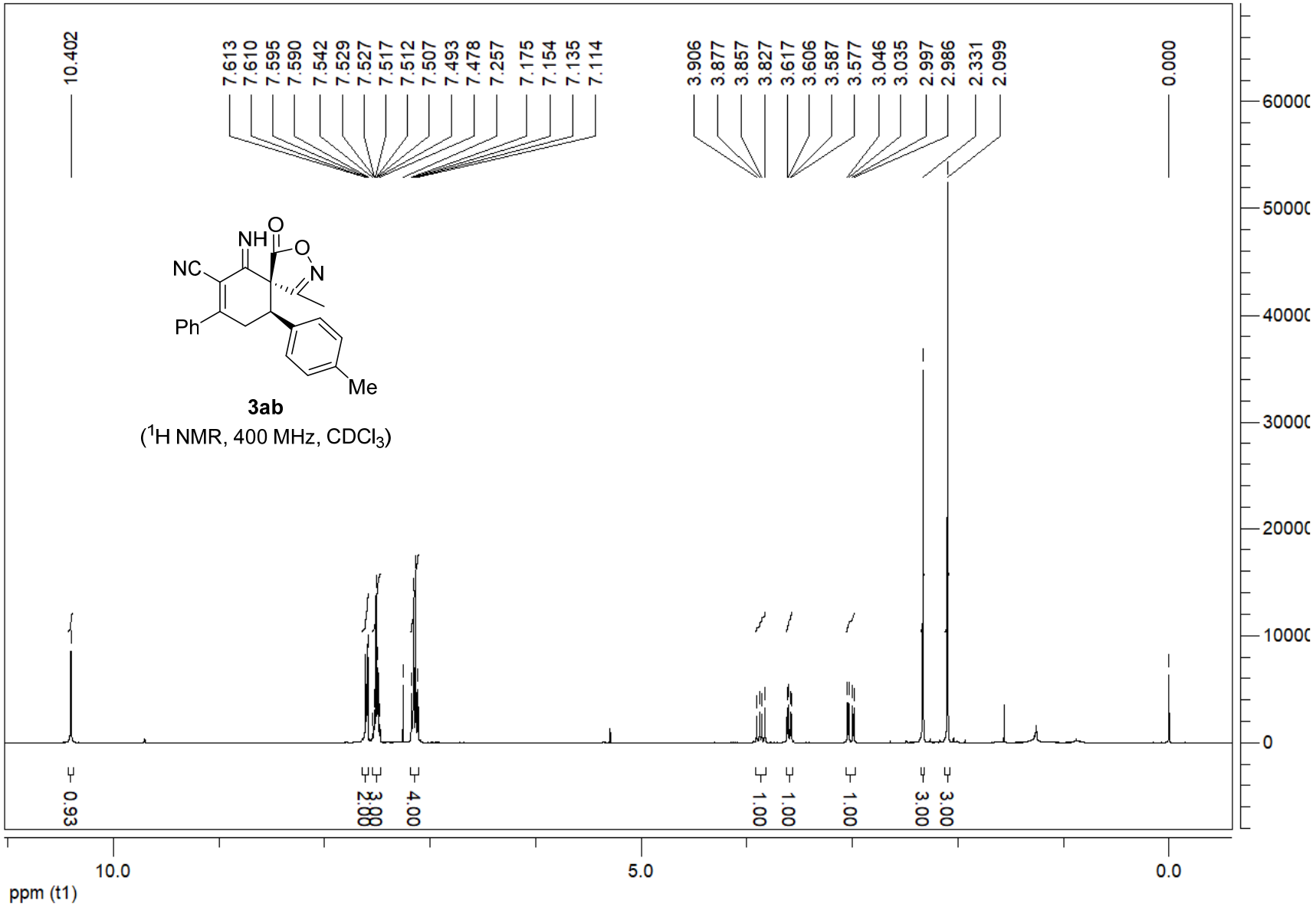
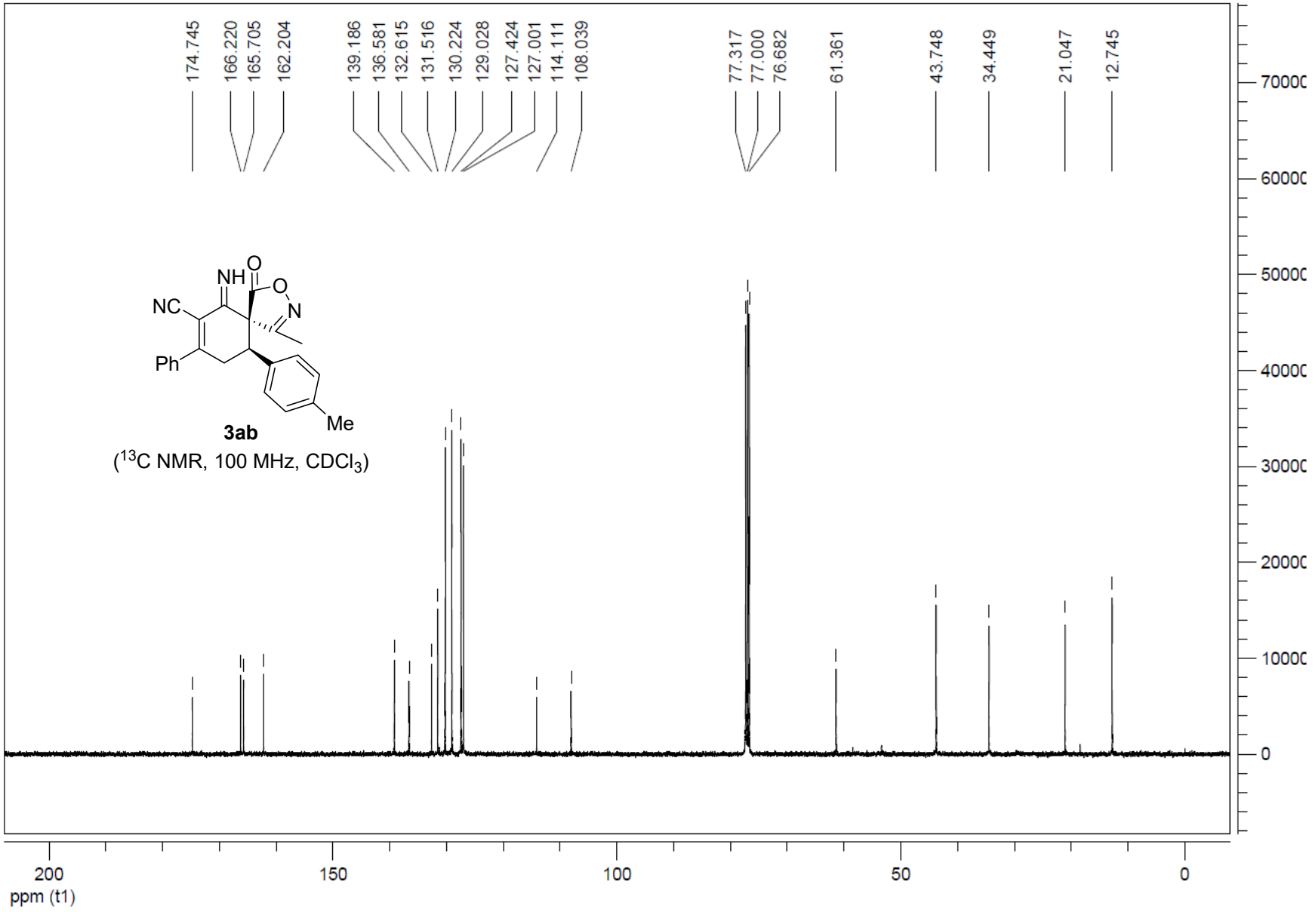
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)



3ab

(^{1}H NMR, 400 MHz, $CDCl_3$)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162.204
139.186
136.581
132.615
131.516
130.224
129.028
127.424
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114.111
108.039
77.317
77.000
76.682
61.361
43.748
34.449
21.047
12.745
NH
O
O
N
NC
Ph
Me
3ab
(^{13}C NMR, 100 MHz, $CDCl_3$)
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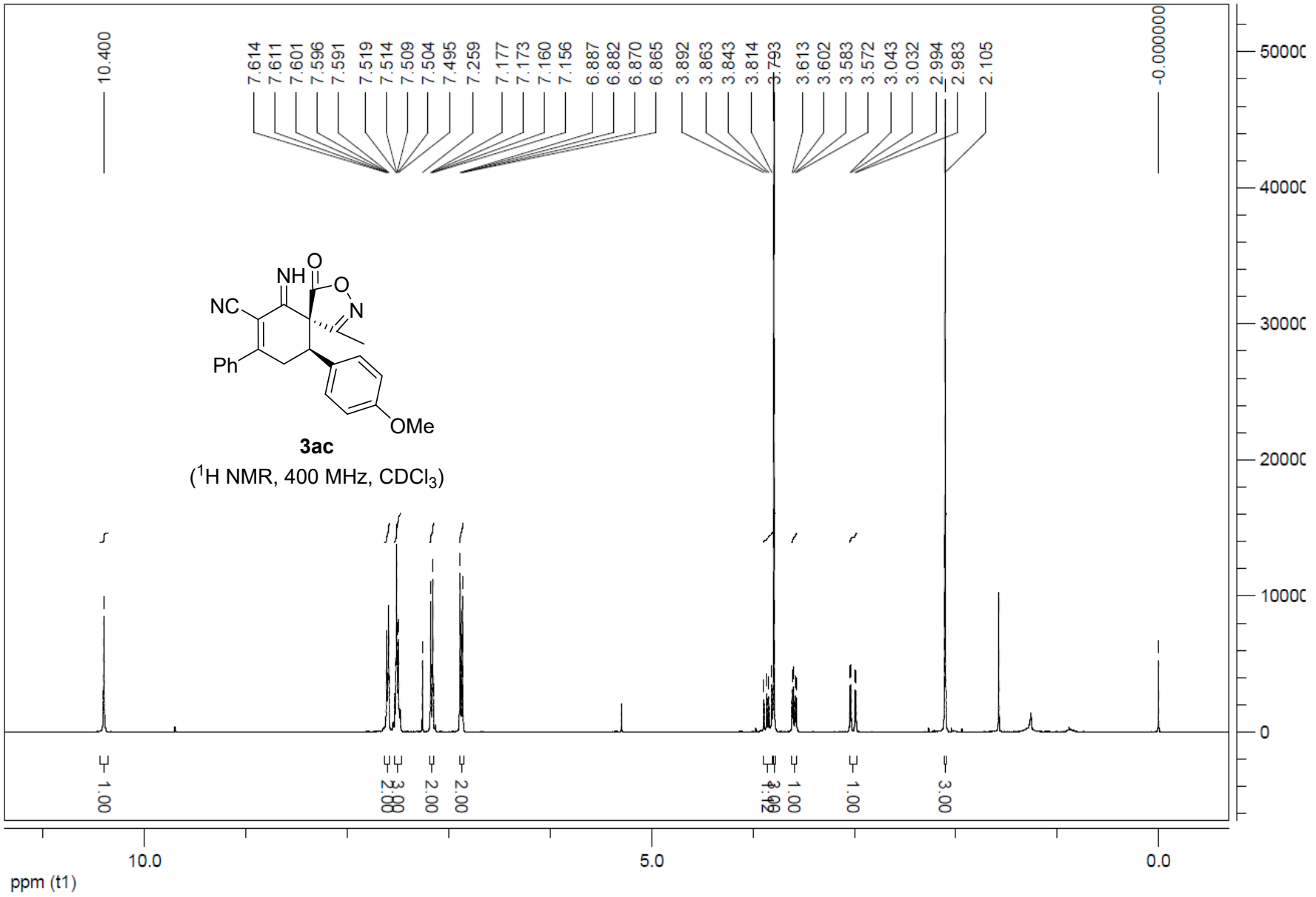
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)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7.611
7.601
7.596
7.591
7.519
7.514
7.509
7.504
7.495
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3.843
3.814
3.793
3.613
3.602
3.583
3.572
3.043
3.032
2.994
2.983
2.105
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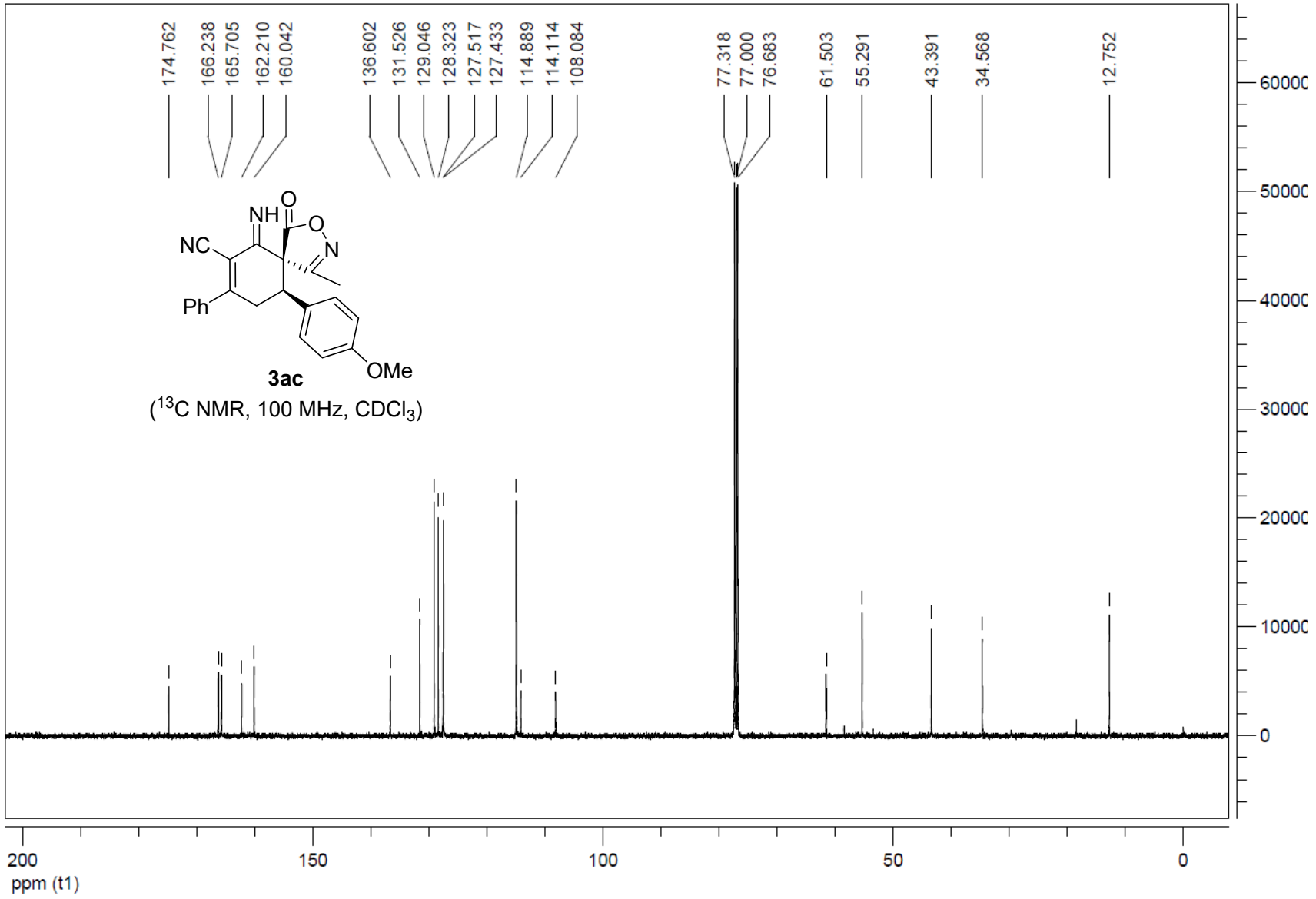
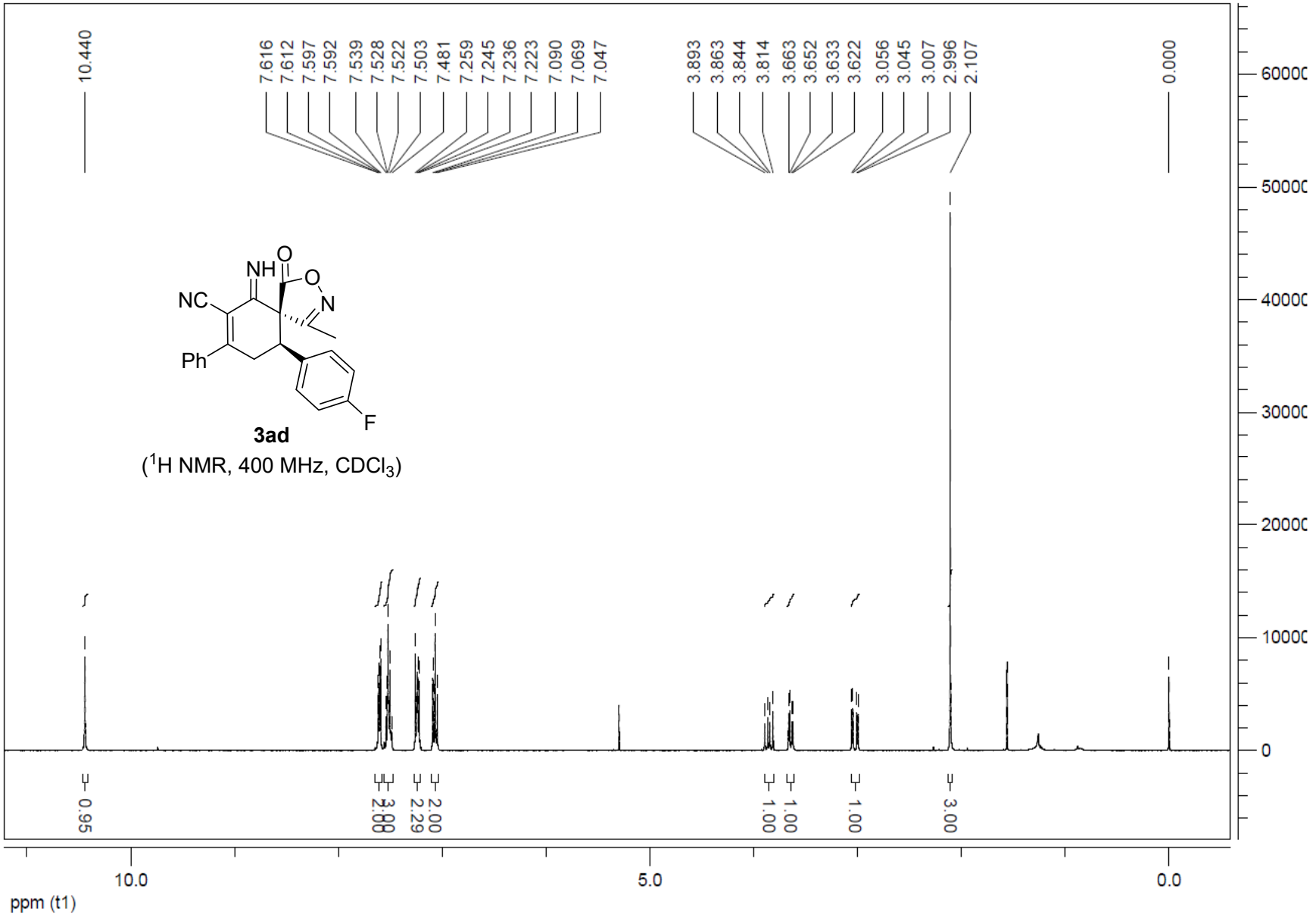
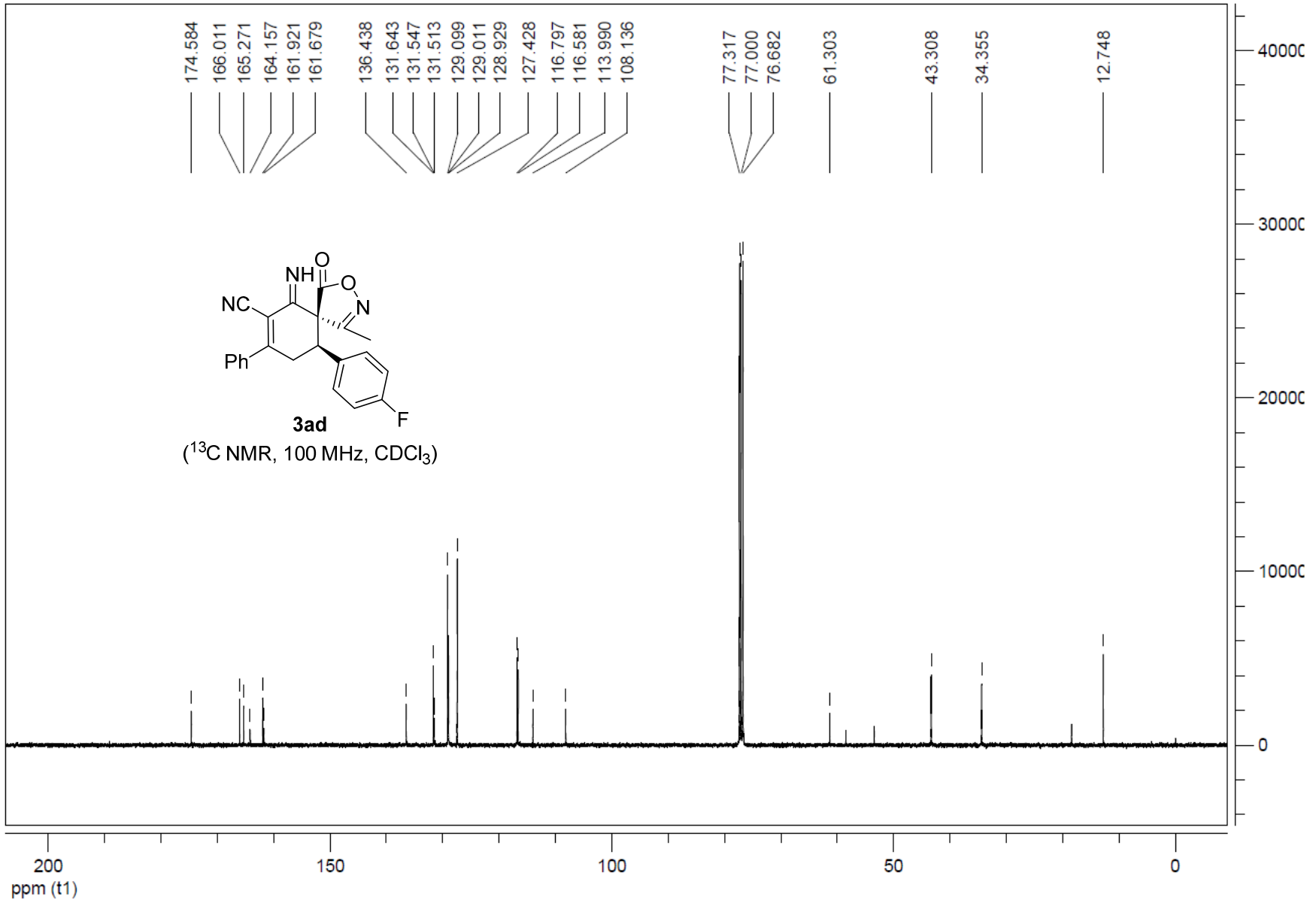
NC
NH
O
O
N
Ph
OMe
3ac
(^{1}H NMR, 400 MHz, $CDCl_3$)
1.00
2.00
3.00
2.00
2.00
1.00
1.00
3.00
10.0
5.0
0.0
ppm (t1)

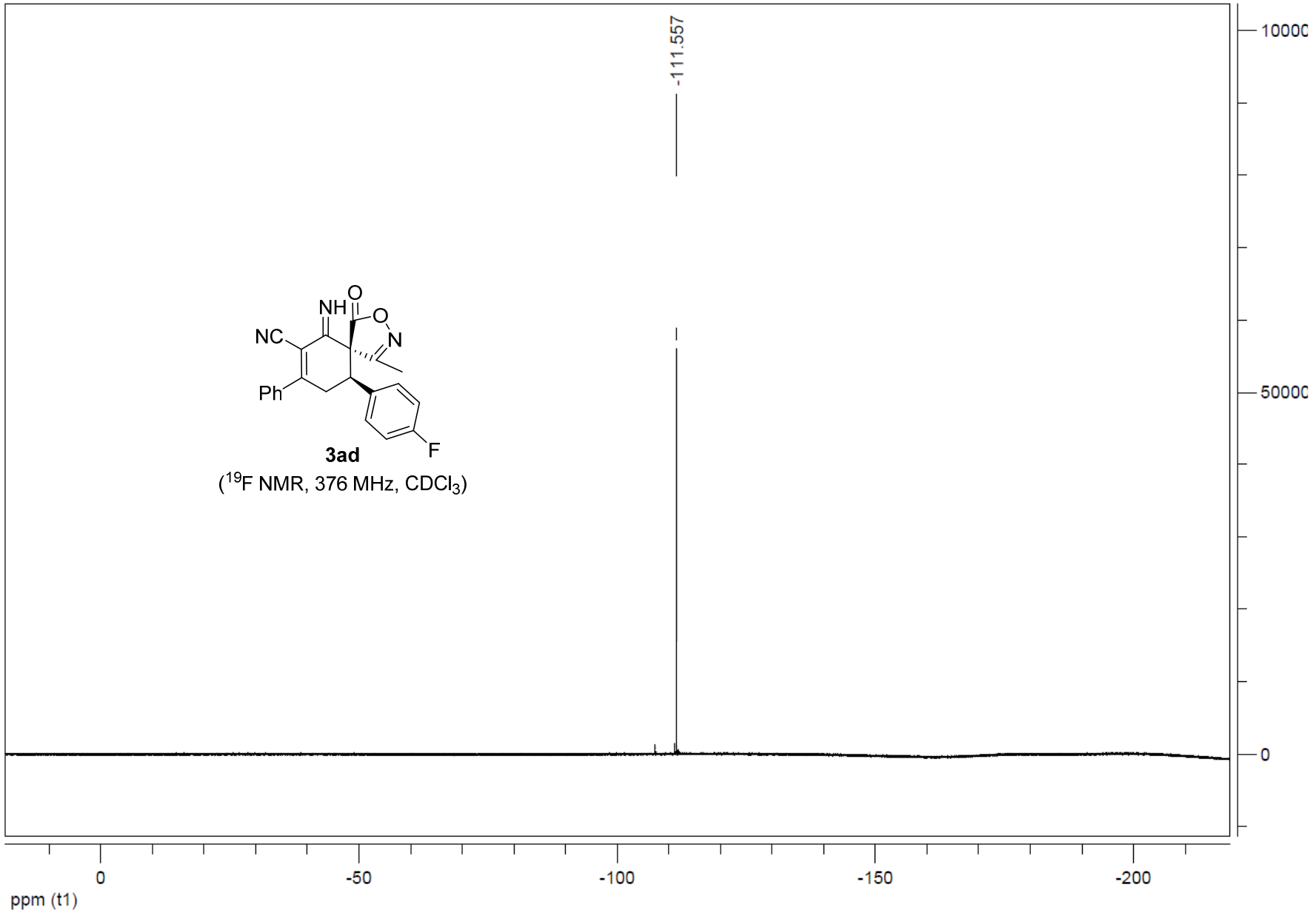

174.762
166.238
165.705
162.210
160.042
136.602
131.526
129.046
128.323
127.517
127.433
114.889
114.114
108.084
77.318
77.000
76.683
61.503
55.291
43.391
34.568
12.752
NC
NH
O
O
N
Ph
OMe
3ac
(^{13}C NMR, 100 MHz, $CDCl_3$)
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

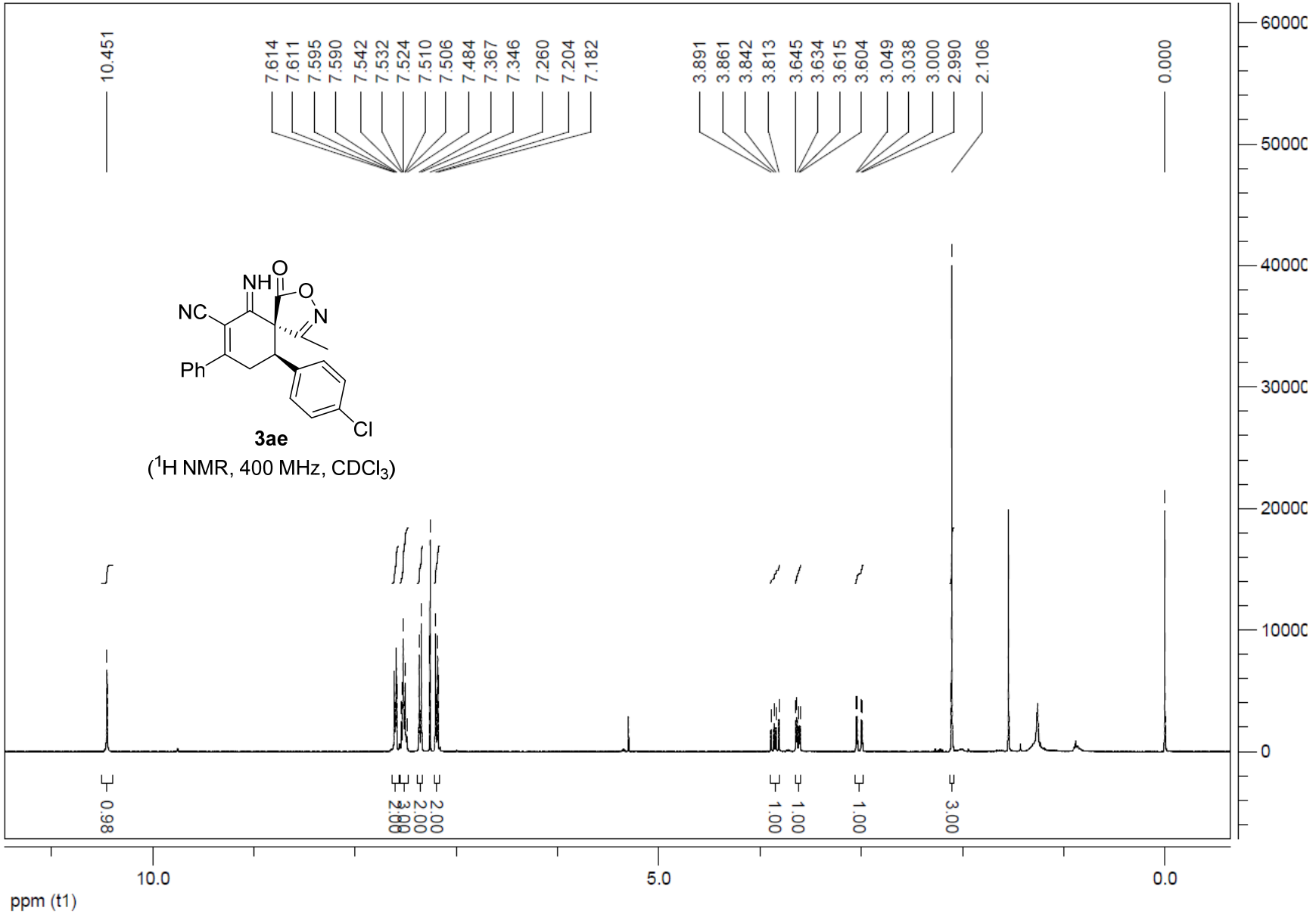


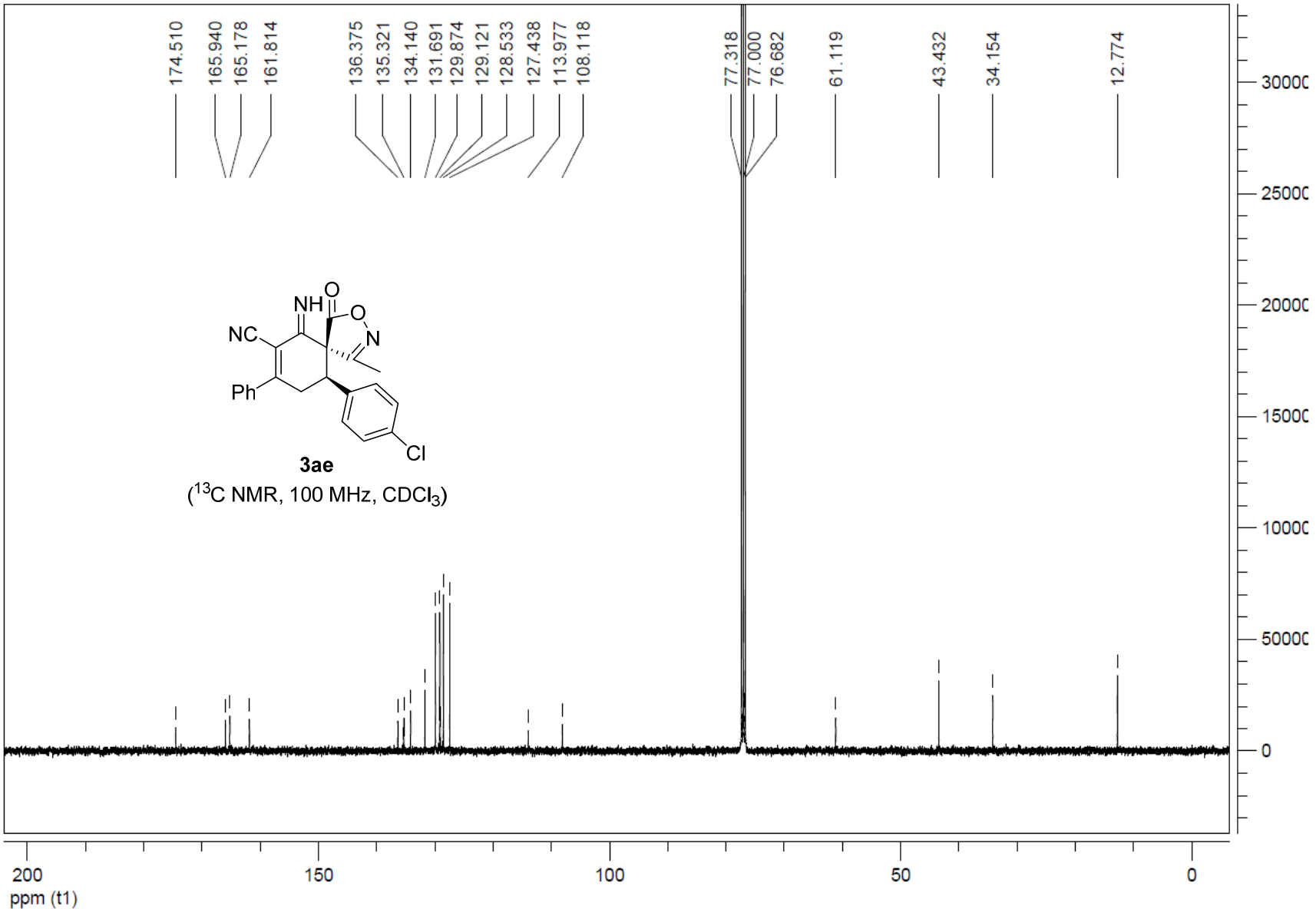
3ad

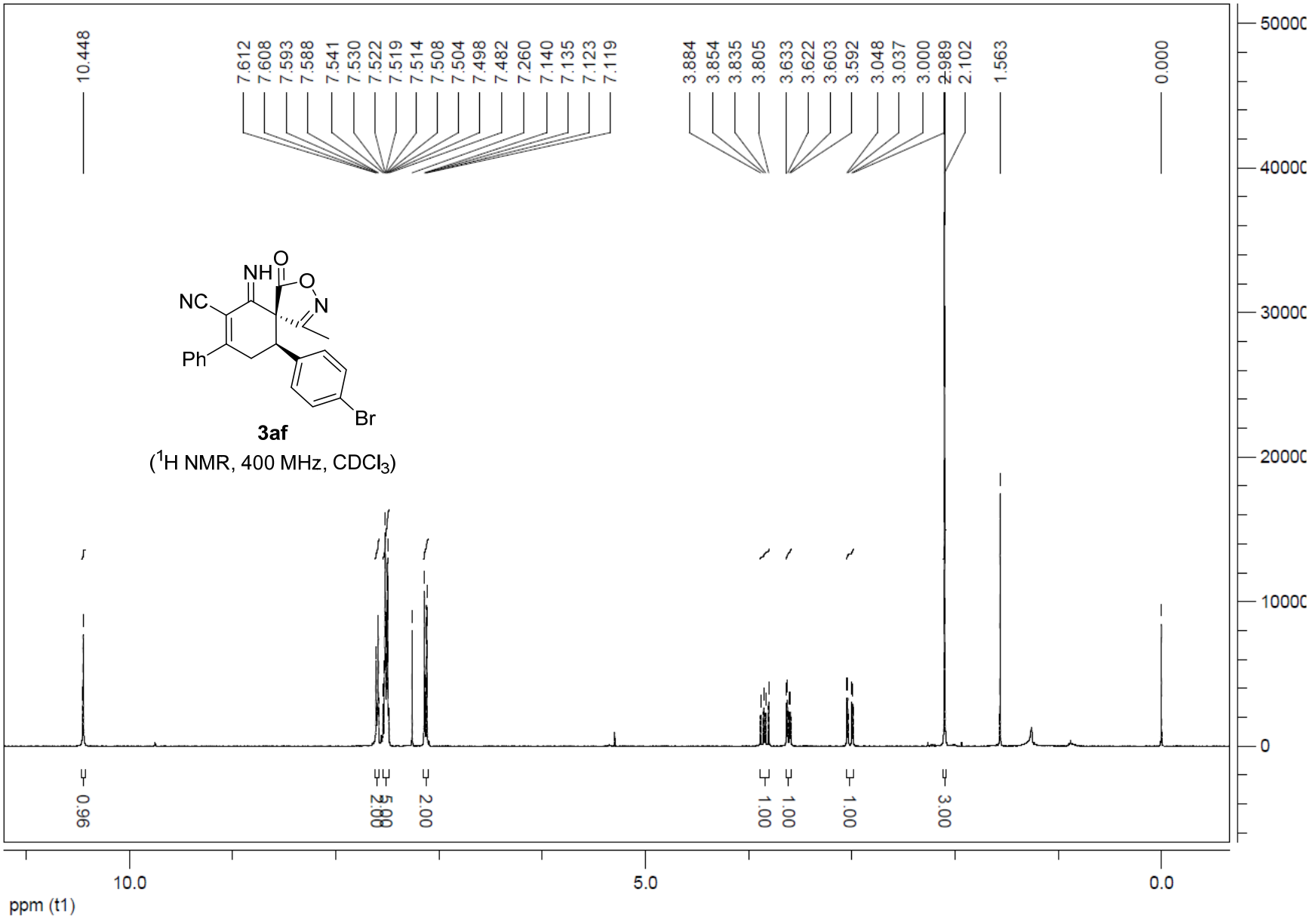
(^{1}H NMR, 400 MHz, $CDCl_3$)


174.584
166.011
165.271
164.157
161.921
161.679
136.438
131.643
131.547
131.513
129.099
129.011
128.929
127.428
116.797
116.581
113.990
108.136
77.317
77.000
76.682
61.303
43.308
34.355
12.748
NH
O
O
N
NC
Ph
F
3ad
(13C NMR, 100 MHz, CDCl3)
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


-111.557
10000
50000
0
NC
NH
O
O
N
Ph
F
3ad
(19F NMR, 376 MHz, CDCl3)
0
-50
-100
-150
-200
ppm (t1)

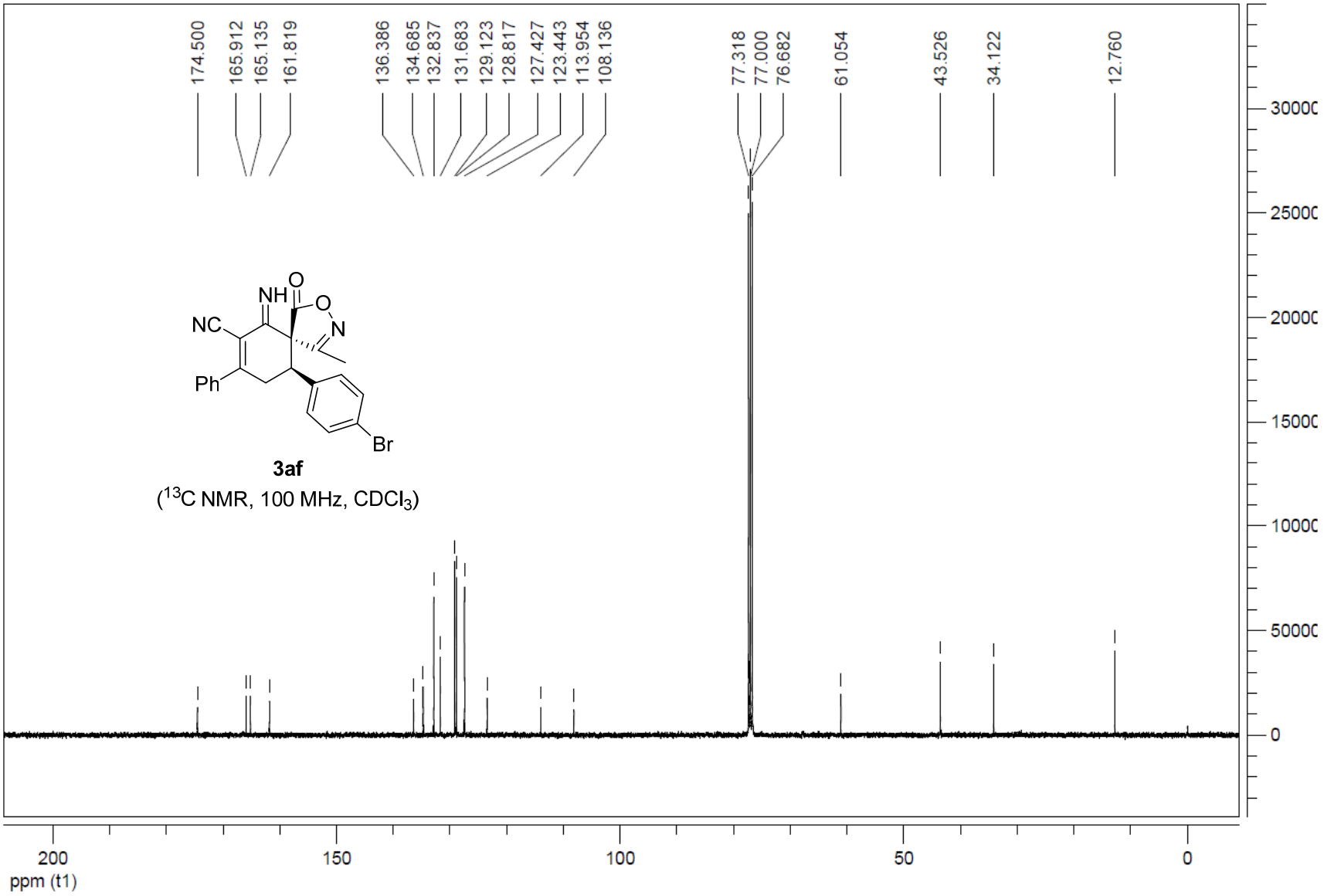

10.451
7.614
7.611
7.595
7.590
7.542
7.532
7.524
7.510
7.506
7.484
7.367
7.346
7.260
7.204
7.182
3.891
3.861
3.842
3.813
3.645
3.634
3.615
3.604
3.049
3.038
3.000
2.990
2.106
0.000
NC
NH
O
O
N
Ph
Cl
3ae
(1H NMR, 400 MHz, CDCl3)
60000
50000
40000
30000
20000
10000
0
0.98
2.00
3.00
2.00
2.00
1.00
1.00
1.00
3.00
10.0
5.0
0.0
ppm (t1)


174.510
165.940
165.178
161.814
136.375
135.321
134.140
131.691
129.874
129.121
128.533
127.438
113.977
108.118
77.318
77.000
76.682
61.119
43.432
34.154
12.774
NH
O
O
N
NC
Ph
Cl
3ae
(13C NMR, 100 MHz, CDCl3)
30000
25000
20000
15000
10000
5000
0
200
150
100
50
0
ppm (t1)



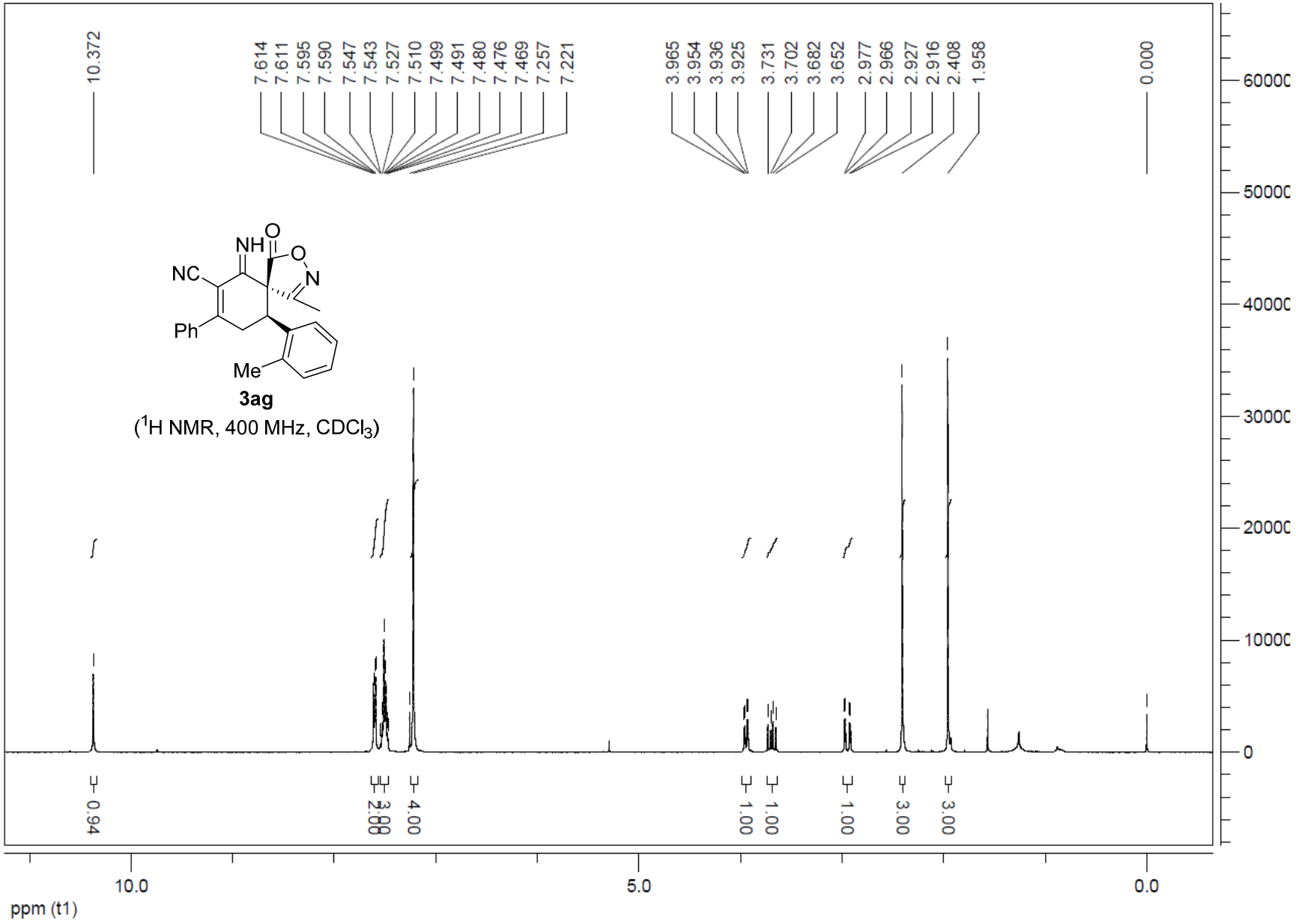
3af

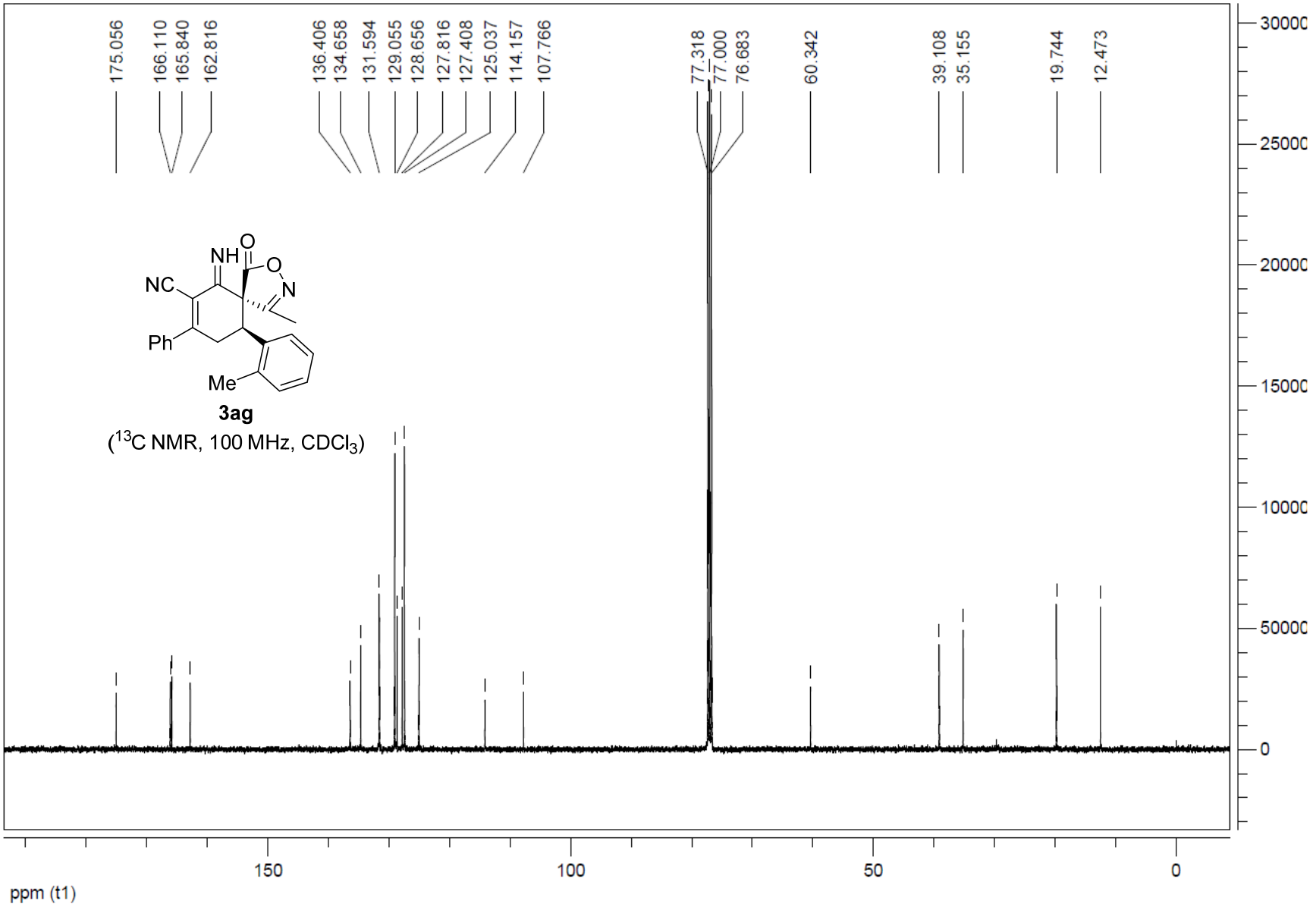
(^{1}H NMR, 400 MHz, $CDCl_3$)

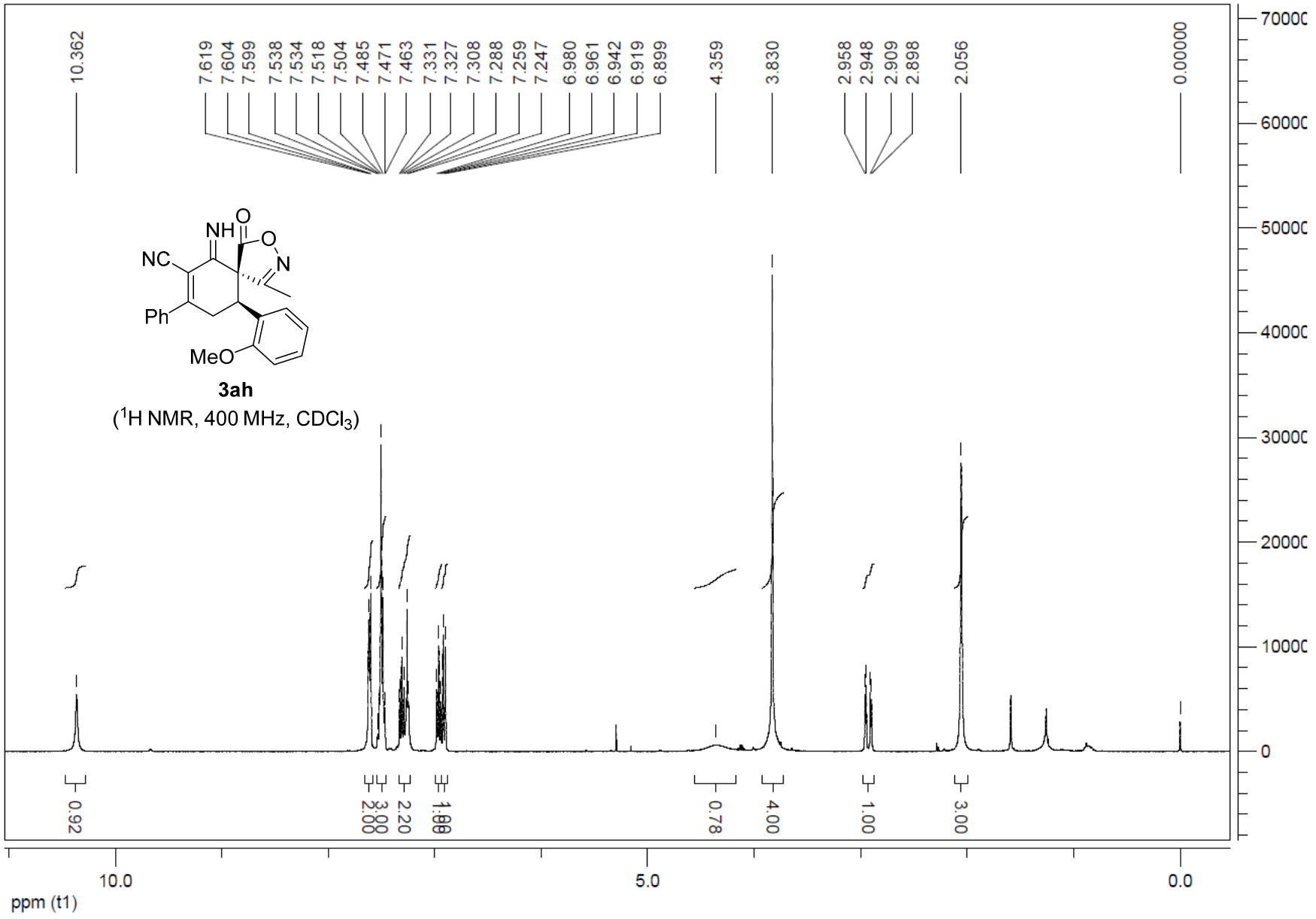


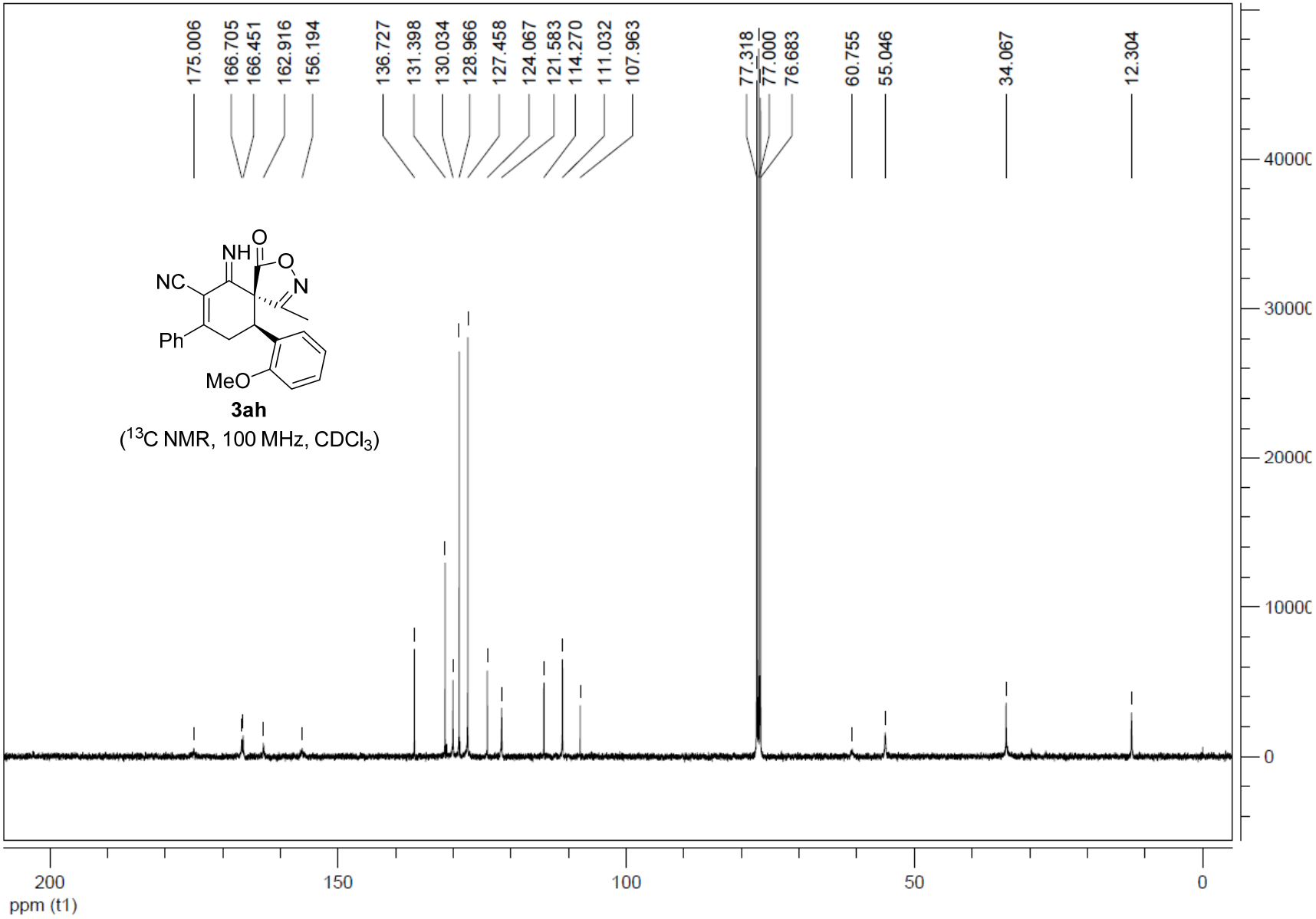
3af

(^{13}C NMR, 100 MHz, $CDCl_3$)


10.372
7.614
7.611
7.595
7.590
7.547
7.543
7.527
7.510
7.499
7.491
7.480
7.476
7.469
7.257
7.221
3.965
3.954
3.936
3.925
3.731
3.702
3.682
3.652
2.977
2.966
2.927
2.916
2.408
1.958
0.000
NC
NH
O
O
N
Ph
Me
3ag
(1H NMR, 400 MHz, CDCl3)
0.94
2.00
3.00
4.00
1.00
1.00
1.00
3.00
3.00
60000
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

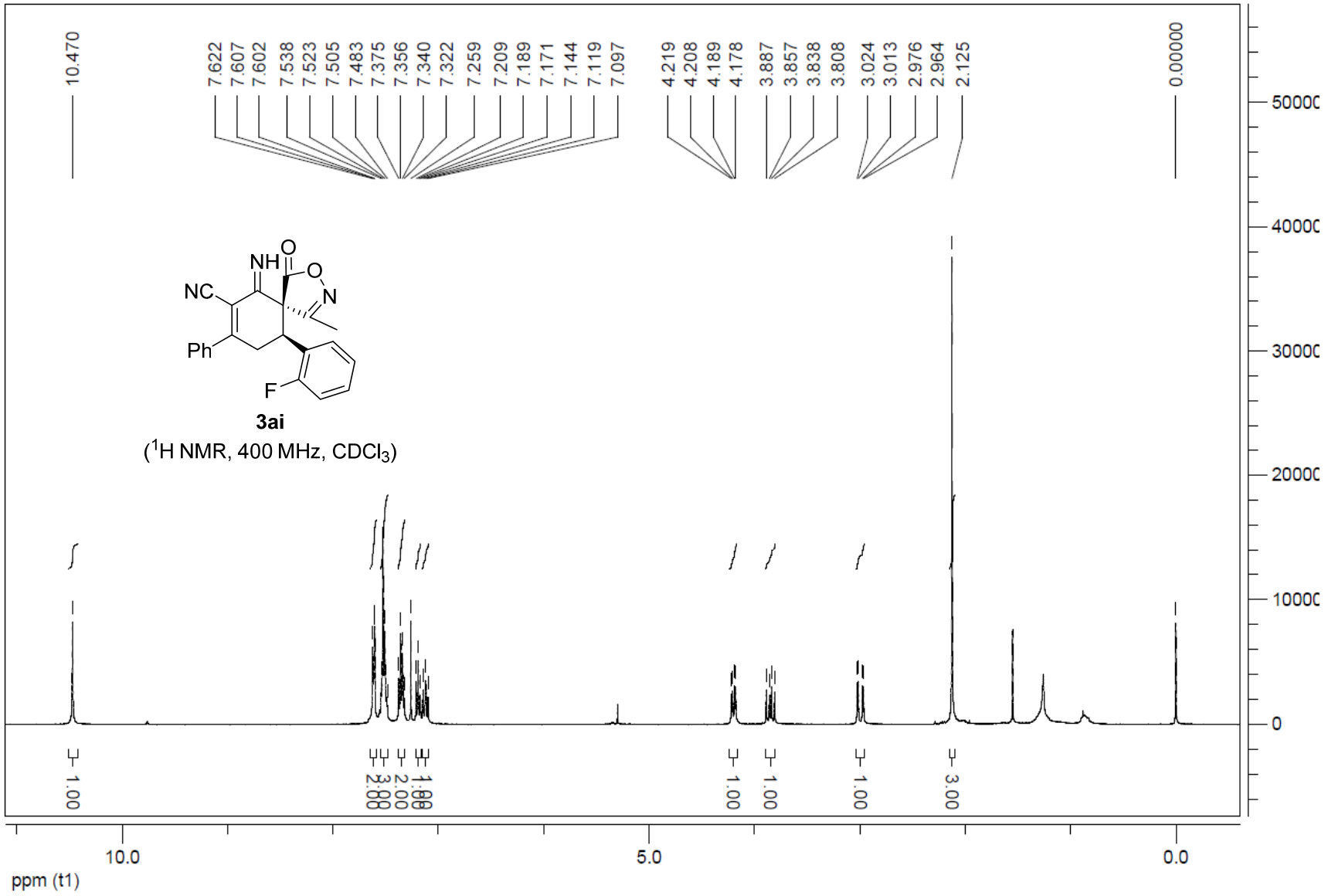

175.056
166.110
165.840
162.816
136.406
134.658
131.594
129.055
128.656
127.816
127.408
125.037
114.157
107.766
77.318
77.000
76.683
60.342
39.108
35.155
19.744
12.473
NC
NH
O
O
N
Ph
Me
3ag
(^{13}C NMR, 100 MHz, $CDCl_3$)
30000
25000
20000
15000
10000
5000
0
150
100
50
0
ppm (t1)

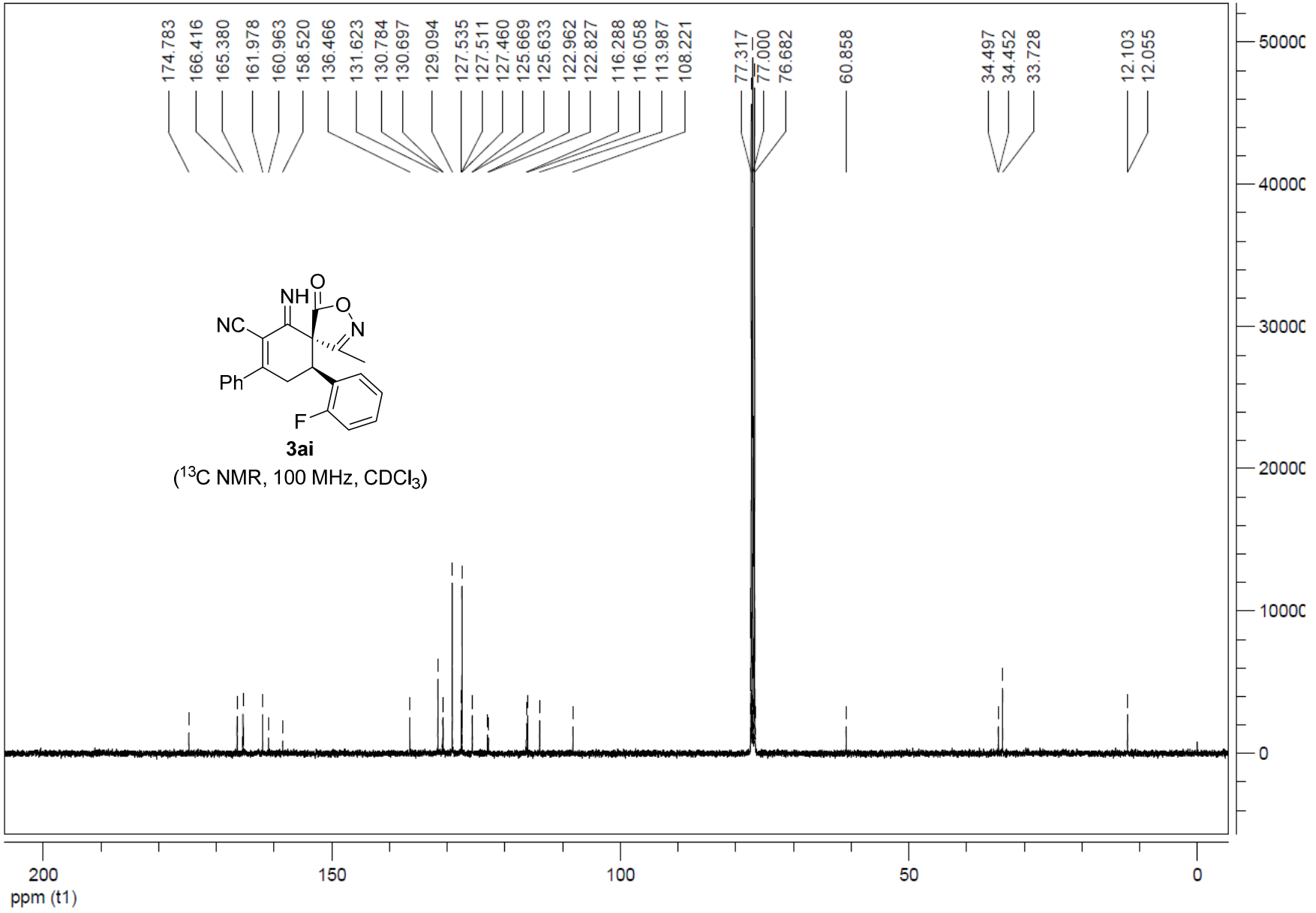

10.362
7.619
7.604
7.599
7.538
7.534
7.518
7.504
7.485
7.471
7.463
7.331
7.327
7.308
7.288
7.259
7.247
6.980
6.961
6.942
6.919
6.899
4.359
3.830
2.958
2.948
2.909
2.898
2.056
0.00000
NC
NH
O
O
N
Ph
MeO
3ah
(1H NMR, 400 MHz, CDCl3)
0.92
3.00
2.00
2.20
1.00
0.78
4.00
1.00
3.00
70000
60000
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)



3ah

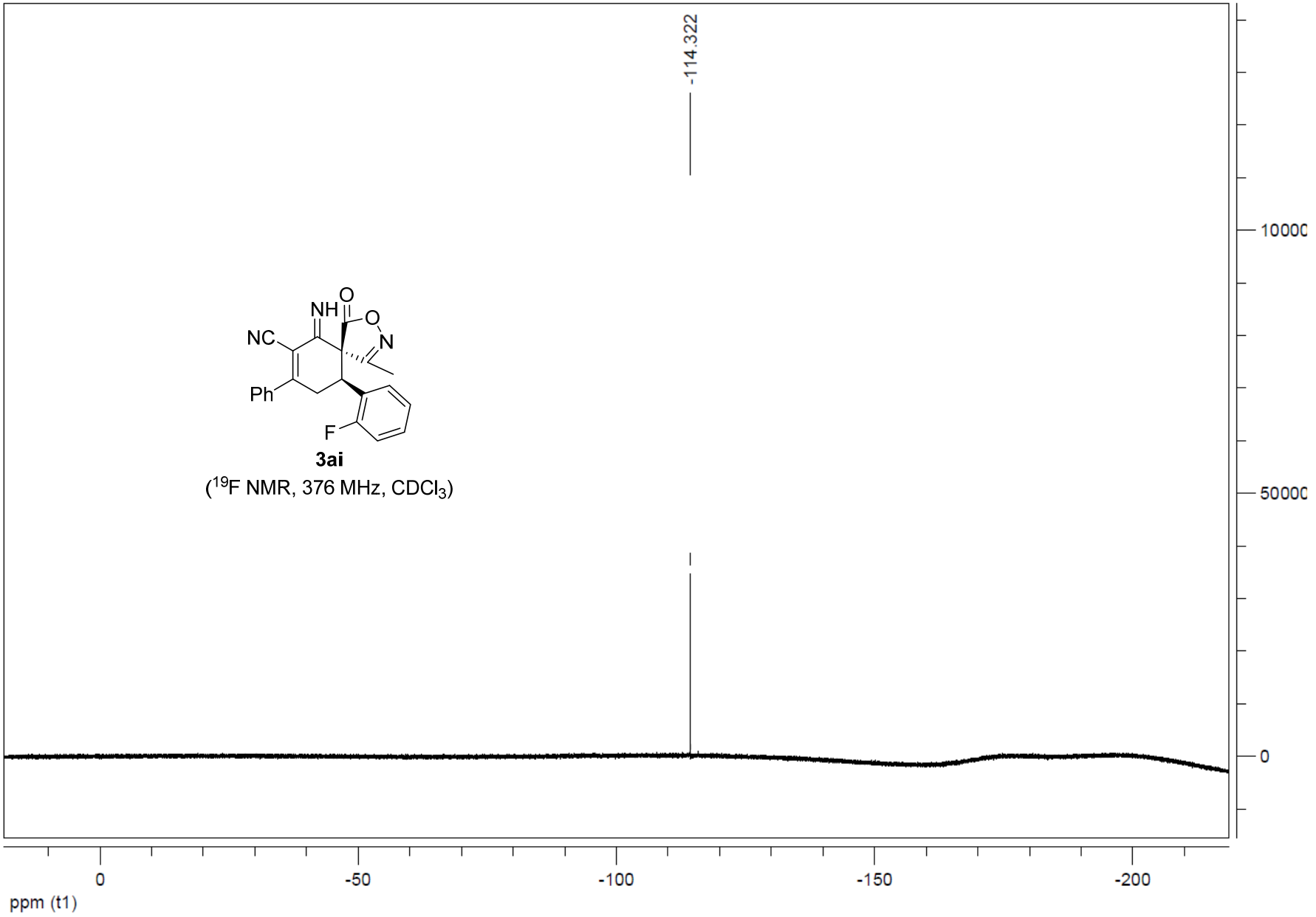
(^{13}C NMR, 100 MHz, $CDCl_3$)


10.470
7.622
7.607
7.602
7.538
7.523
7.505
7.483
7.375
7.356
7.340
7.322
7.259
7.209
7.189
7.171
7.144
7.119
7.097
4.219
4.208
4.189
4.178
3.887
3.857
3.838
3.808
3.024
3.013
2.976
2.964
2.125
0.00000
NC
NH
O
O
N
Ph
F
3ai
(1H NMR, 400 MHz, CDCl3)
1.00
2.00
3.00
1.00
1.00
1.00
3.00
10.0
5.0
0.0
ppm (t1)



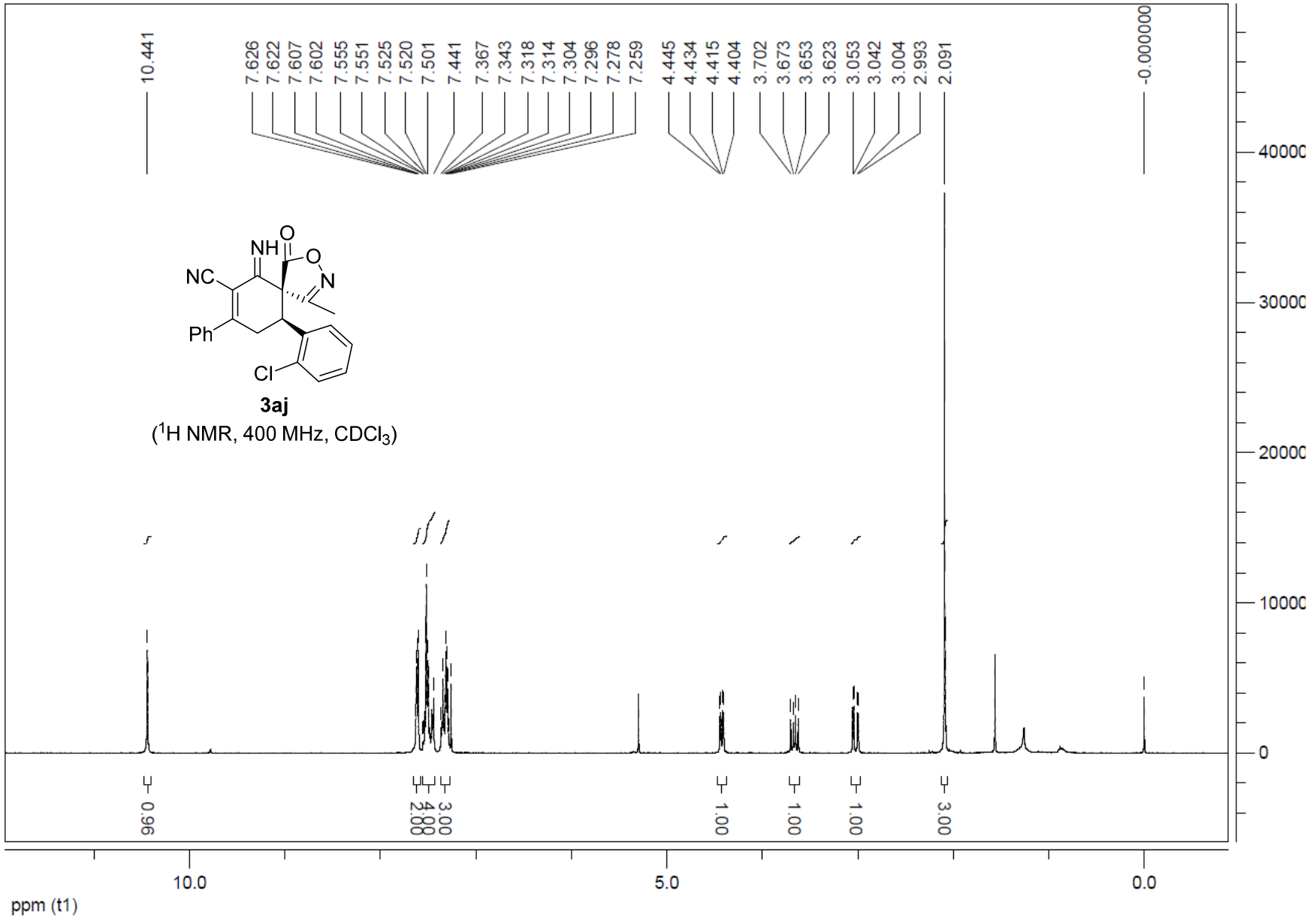
3ai

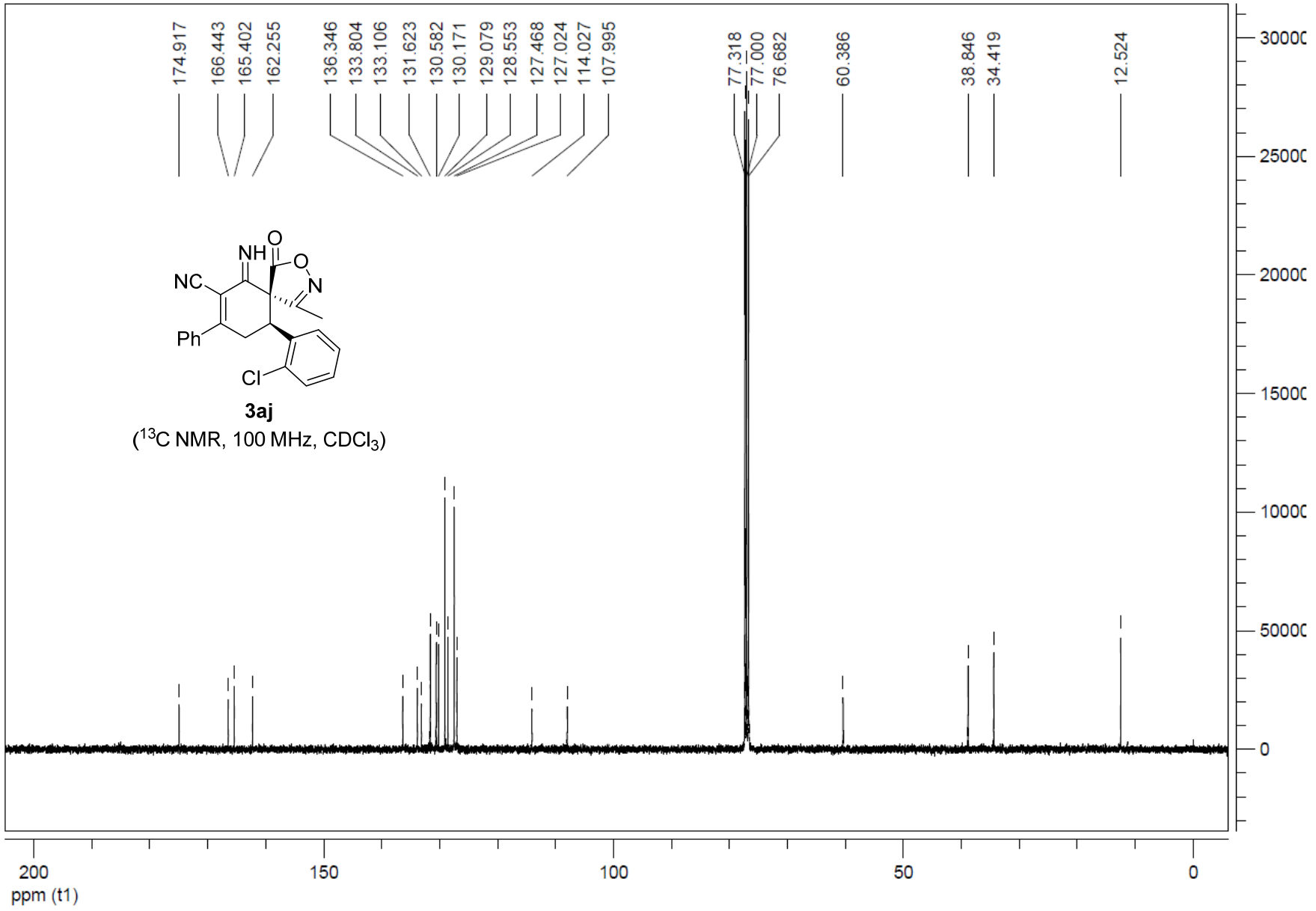
(^{13}C NMR, 100 MHz, $CDCl_3$)

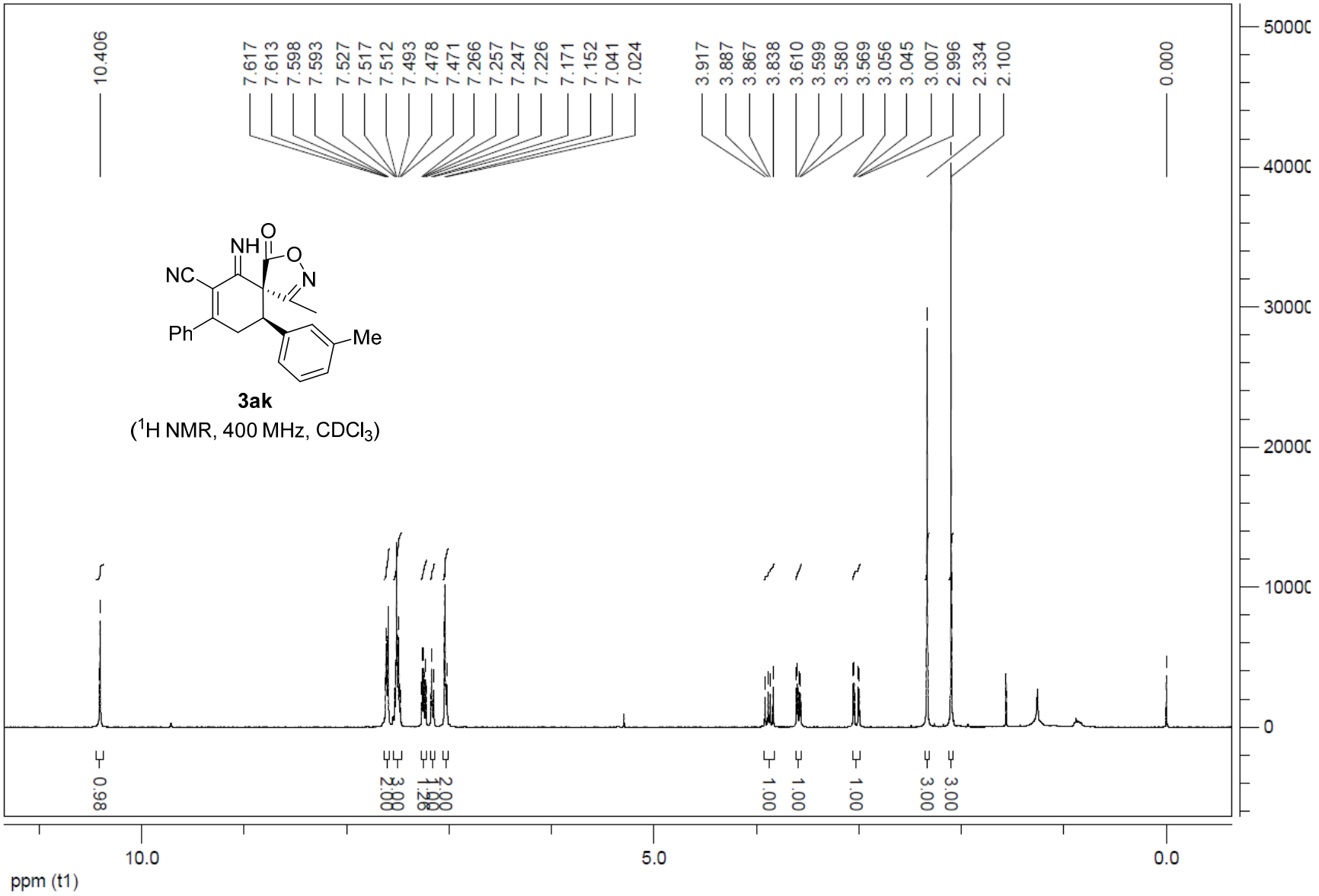


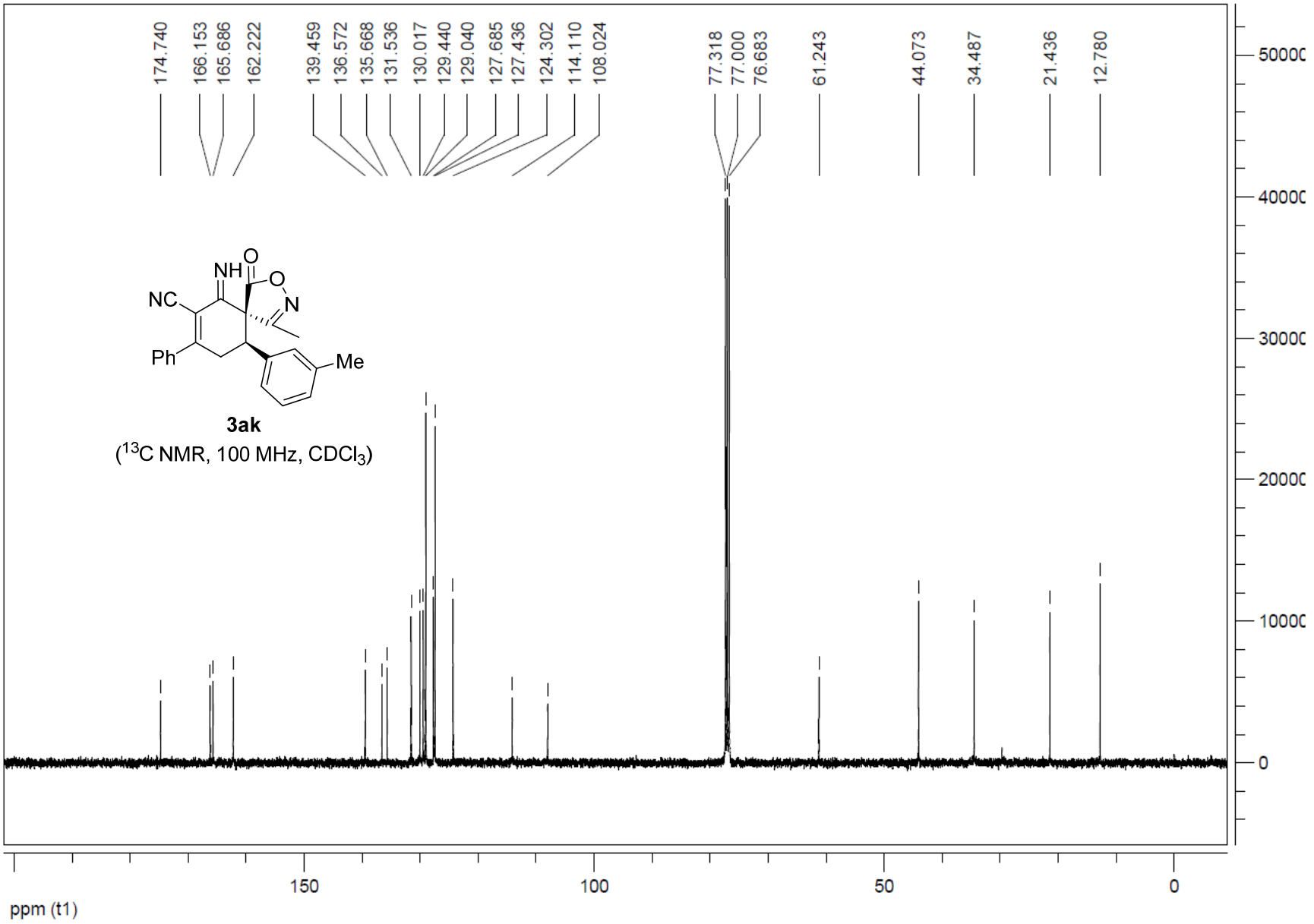
3ai

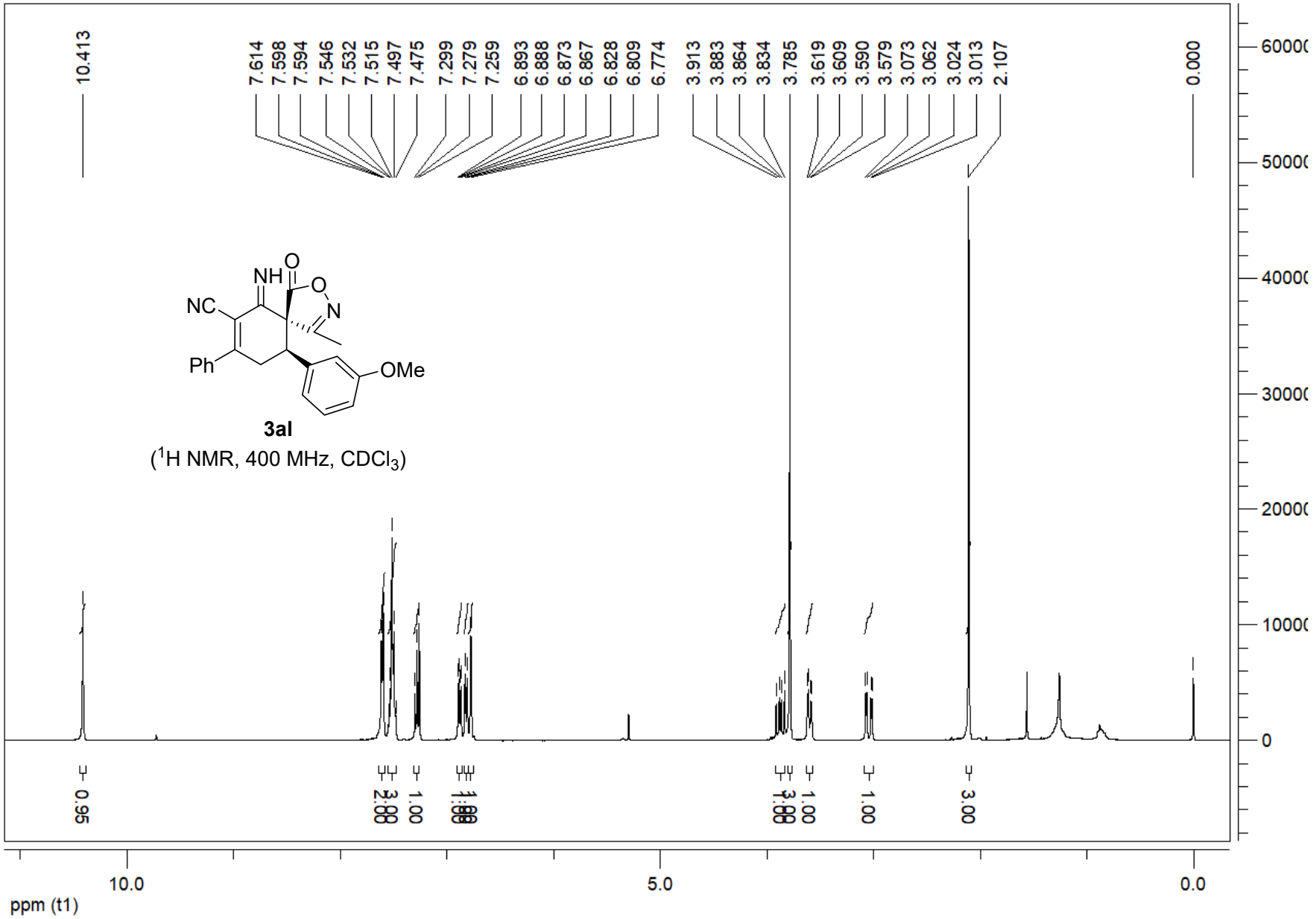
(^{19}F NMR, 376 MHz, $CDCl_3$)

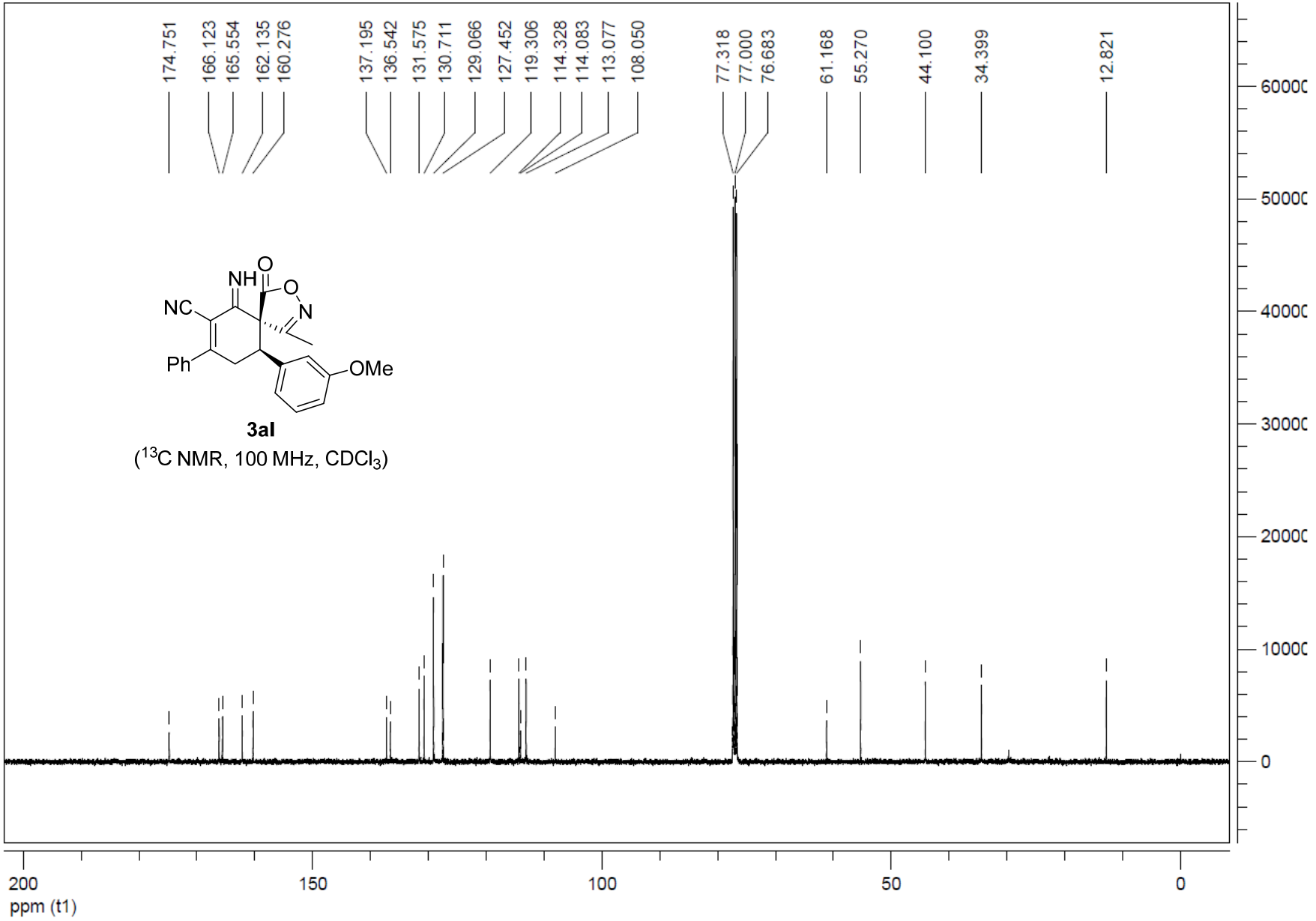

10.441
7.626
7.622
7.607
7.602
7.555
7.551
7.525
7.520
7.501
7.441
7.367
7.343
7.318
7.314
7.304
7.296
7.278
7.259
4.445
4.434
4.415
4.404
3.702
3.673
3.653
3.623
3.053
3.042
3.004
2.993
2.091
-0.000000
NC
NH
O
O
N
Ph
Cl
3aj
(1H NMR, 400 MHz, CDCl3)
0.96
2.00
4.00
3.00
1.00
1.00
1.00
3.00
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

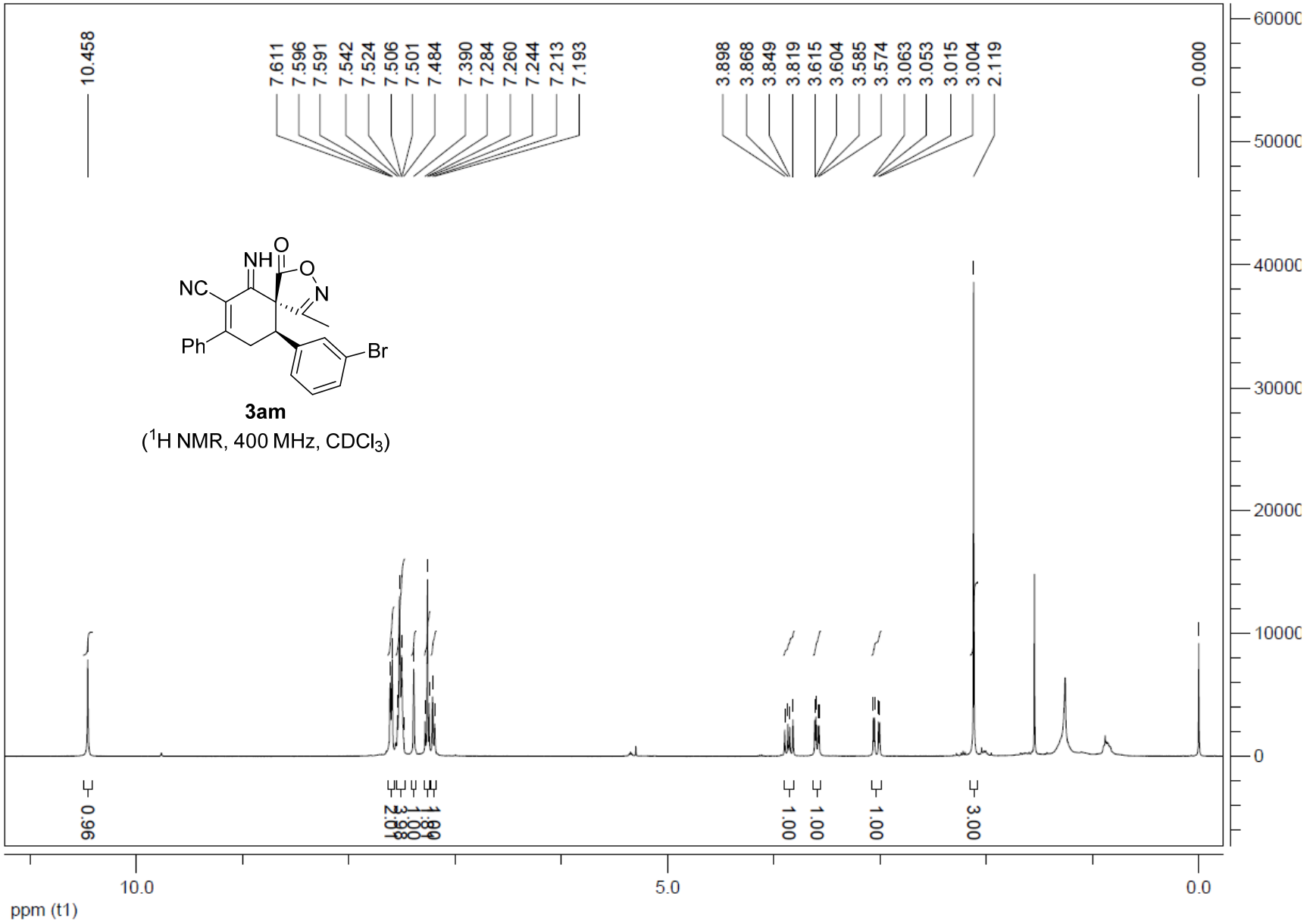

174.917
166.443
165.402
162.255
136.346
133.804
133.106
131.623
130.582
130.171
129.079
128.553
127.468
127.024
114.027
107.995
77.318
77.000
76.682
60.386
38.846
34.419
12.524
NH
O
O
N
NC
Ph
Cl
3aj
(^{13}C NMR, 100 MHz, $CDCl_3$)
30000
25000
20000
15000
10000
50000
0
200
150
100
50
0
ppm (t1)

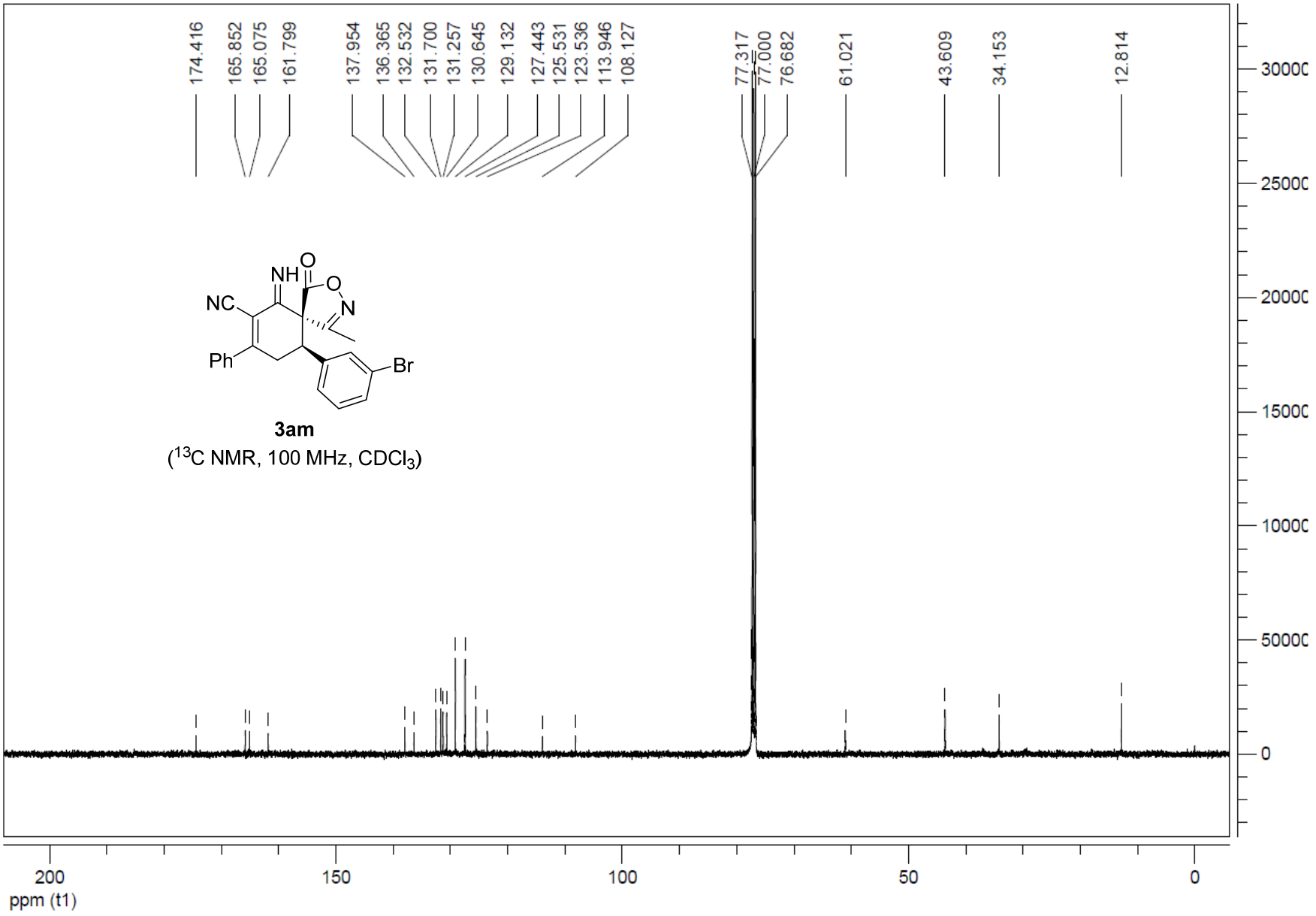

10.406
7.617
7.613
7.598
7.593
7.527
7.517
7.512
7.493
7.478
7.471
7.266
7.257
7.247
7.226
7.171
7.152
7.041
7.024
3.917
3.887
3.867
3.838
3.610
3.599
3.580
3.569
3.056
3.045
3.007
2.996
2.334
2.100
0.000
NC
NH
O
O
N
Ph
Me
3ak
(1H NMR, 400 MHz, CDCl3)
0.98
3.88
1.98
2.00
1.00
1.00
1.00
3.00
3.00
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)


174.740
166.153
165.686
162.222
139.459
136.572
135.668
131.536
130.017
129.440
129.040
127.685
127.436
124.302
114.110
108.024
77.318
77.000
76.683
61.243
44.073
34.487
21.436
12.780
NH
O
O
N
NC
Ph
Me
3ak
(^{13}C NMR, 100 MHz, $CDCl_3$)
50000
40000
30000
20000
10000
0
150
100
50
0
ppm (t1)


10.413
7.614
7.598
7.594
7.546
7.532
7.515
7.497
7.475
7.299
7.279
7.259
6.893
6.888
6.873
6.867
6.828
6.809
6.774
3.913
3.883
3.864
3.834
3.785
3.619
3.609
3.590
3.579
3.073
3.062
3.024
3.013
2.107
0.000
NH
O
O
N
NC
Ph
OMe
3al
(1H NMR, 400 MHz, CDCl3)
0.95
2.88
1.00
1.00
1.00
1.00
1.00
3.00
10.0
5.0
0.0
ppm (t1)

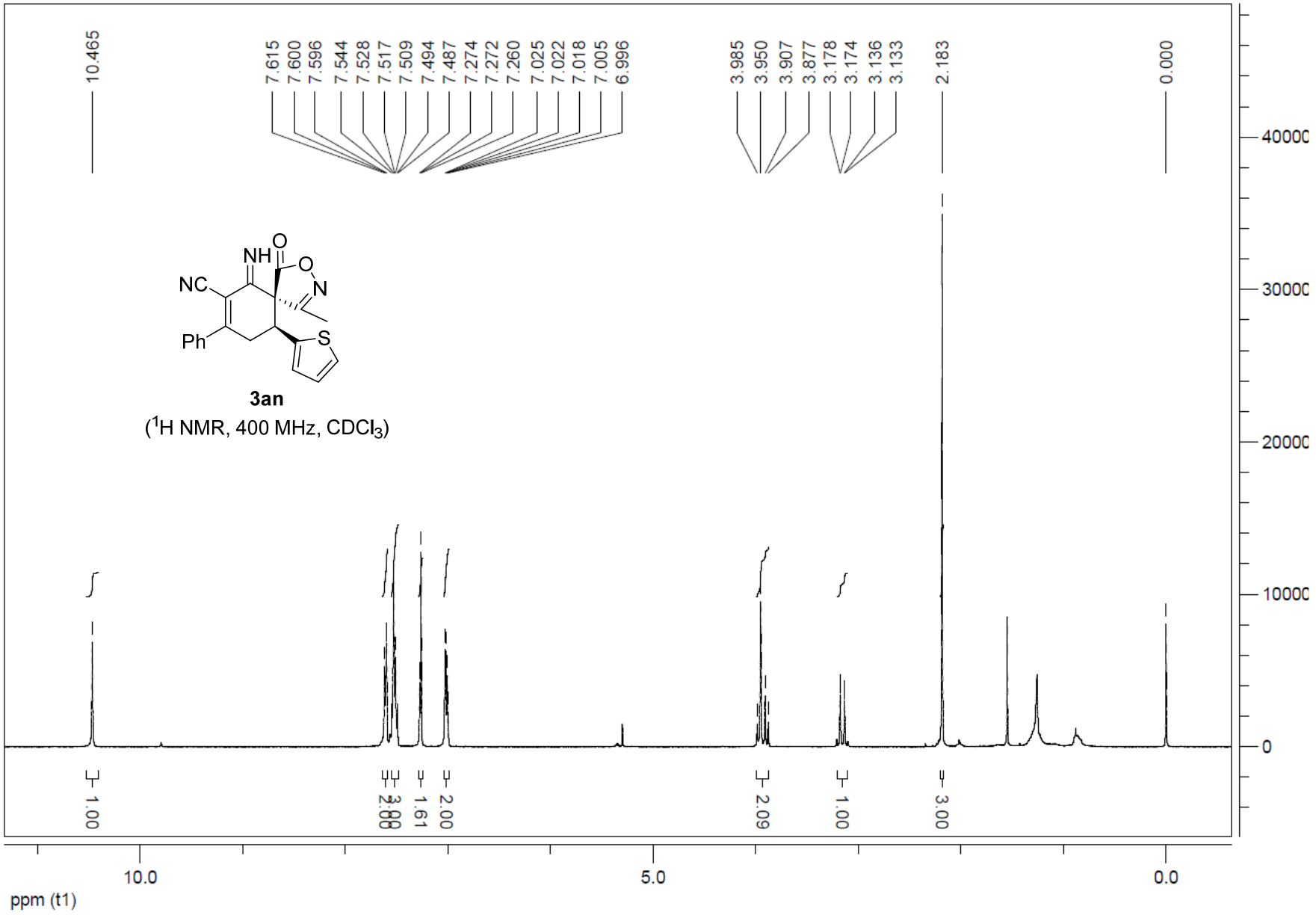

174.751
166.123
165.554
162.135
160.276
137.195
136.542
131.575
130.711
129.066
127.452
119.306
114.328
114.083
113.077
108.050
77.318
77.000
76.683
61.168
55.270
44.100
34.399
12.821
NC
NH
O
O
N
Ph
OMe
3aI
(^{13}C NMR, 100 MHz, $CDCl_3$)
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

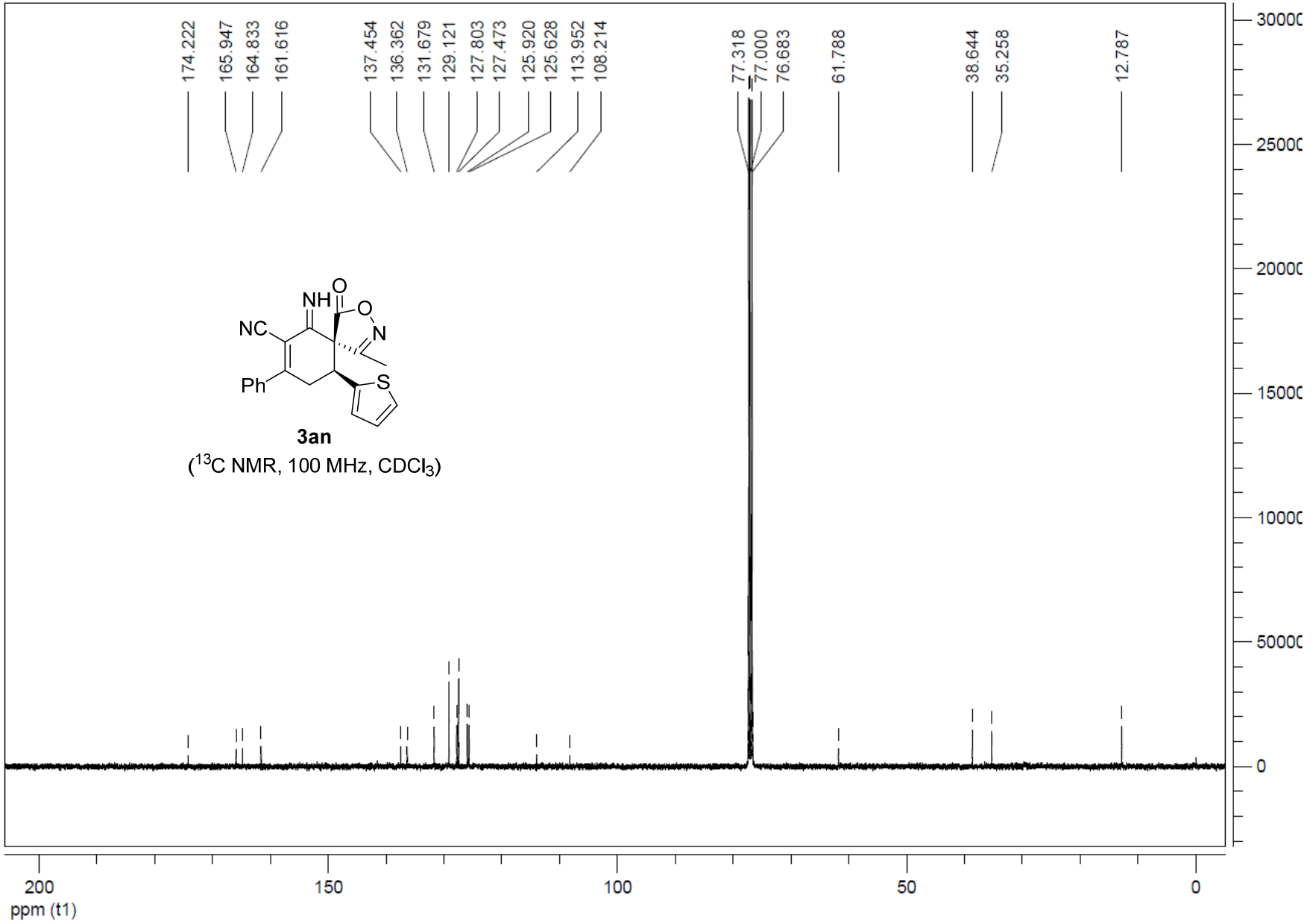

10.458
7.611
7.596
7.591
7.542
7.524
7.506
7.501
7.484
7.390
7.284
7.260
7.244
7.213
7.193
3.898
3.868
3.849
3.819
3.615
3.604
3.585
3.574
3.063
3.053
3.015
3.004
2.119
0.000
NC
NH
O
O
N
Ph
Br
3am
(1H NMR, 400 MHz, CDCl3)
0.96
2.01
3.88
1.89
1.00
1.00
1.00
3.00
60000
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

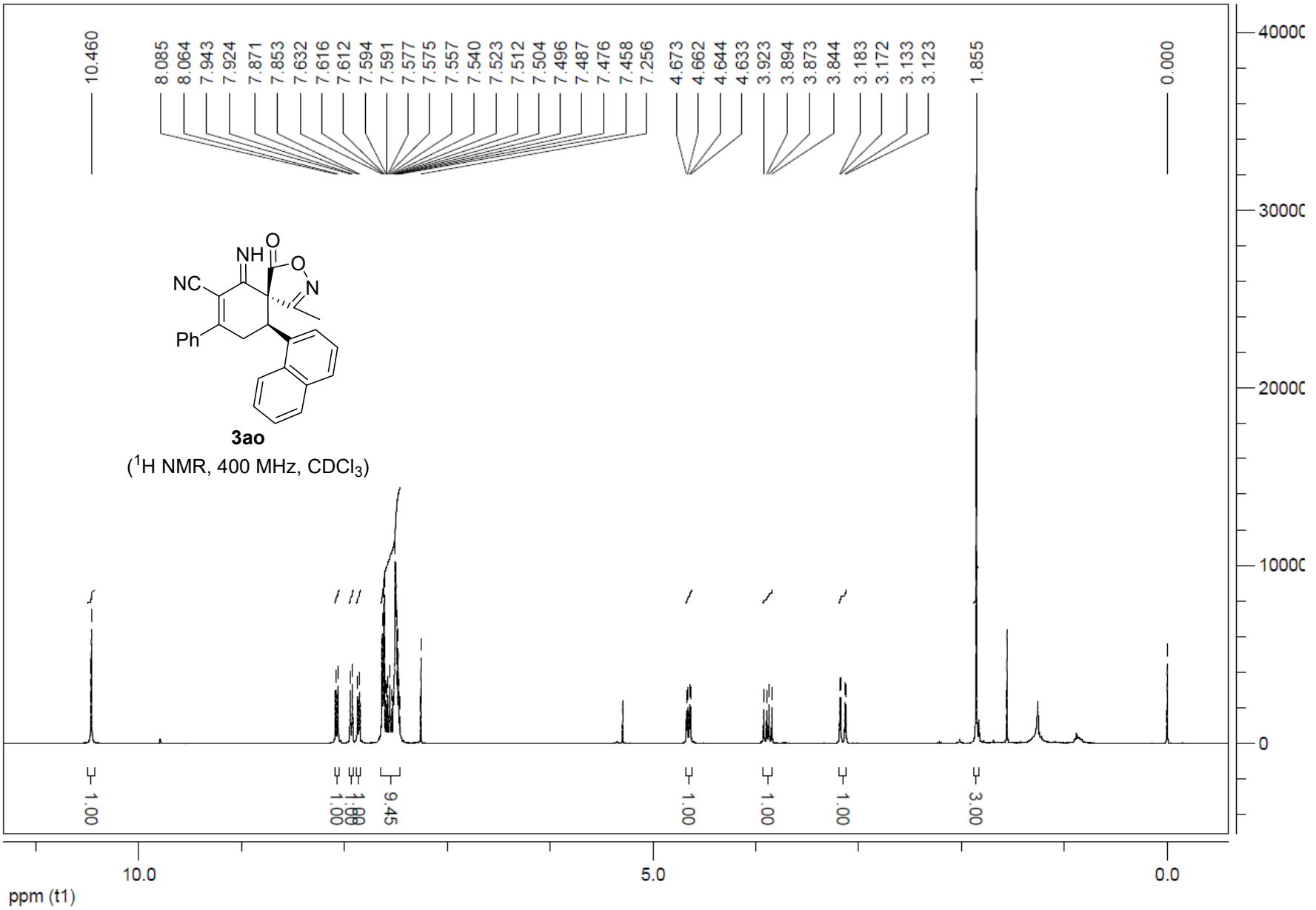


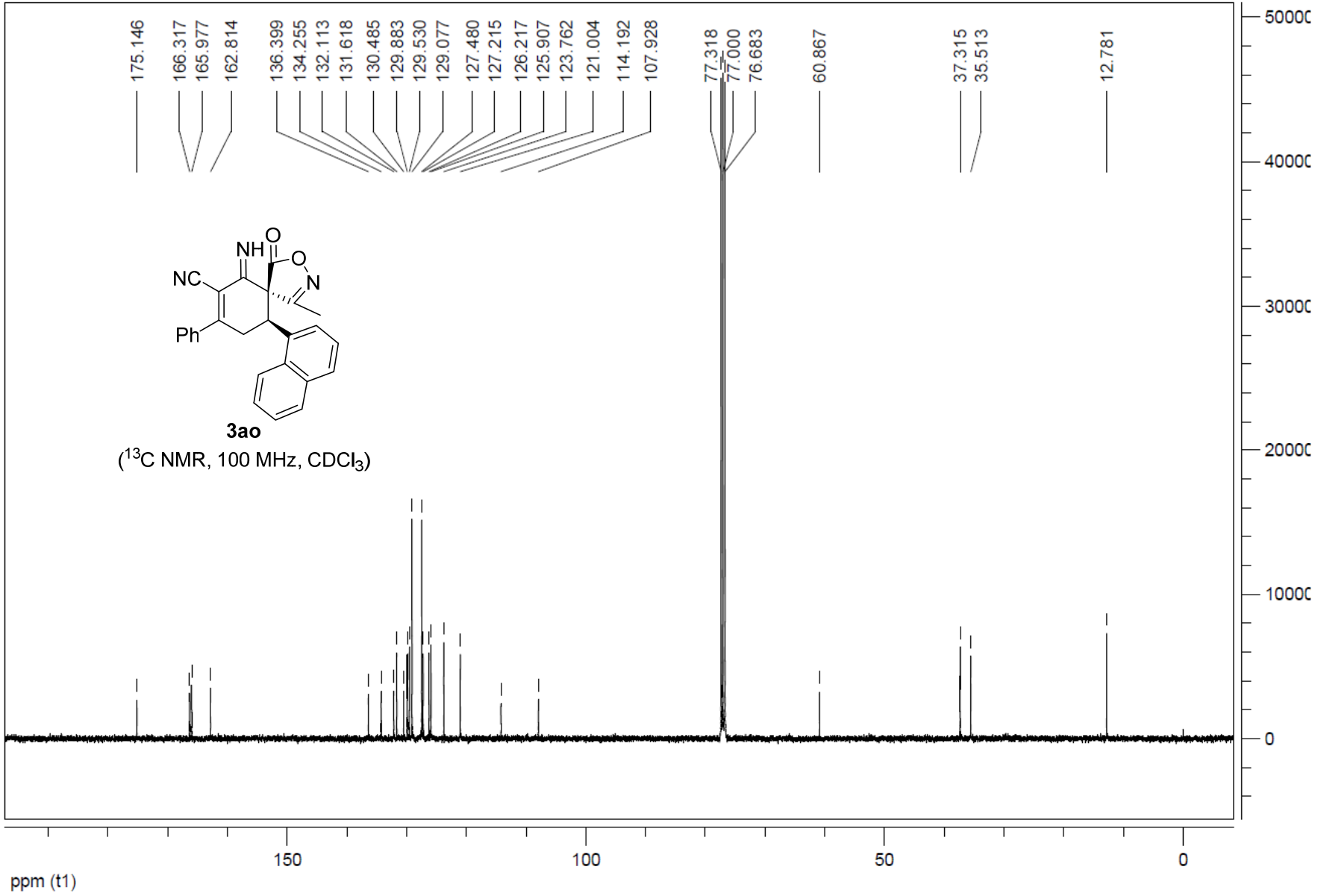
3am

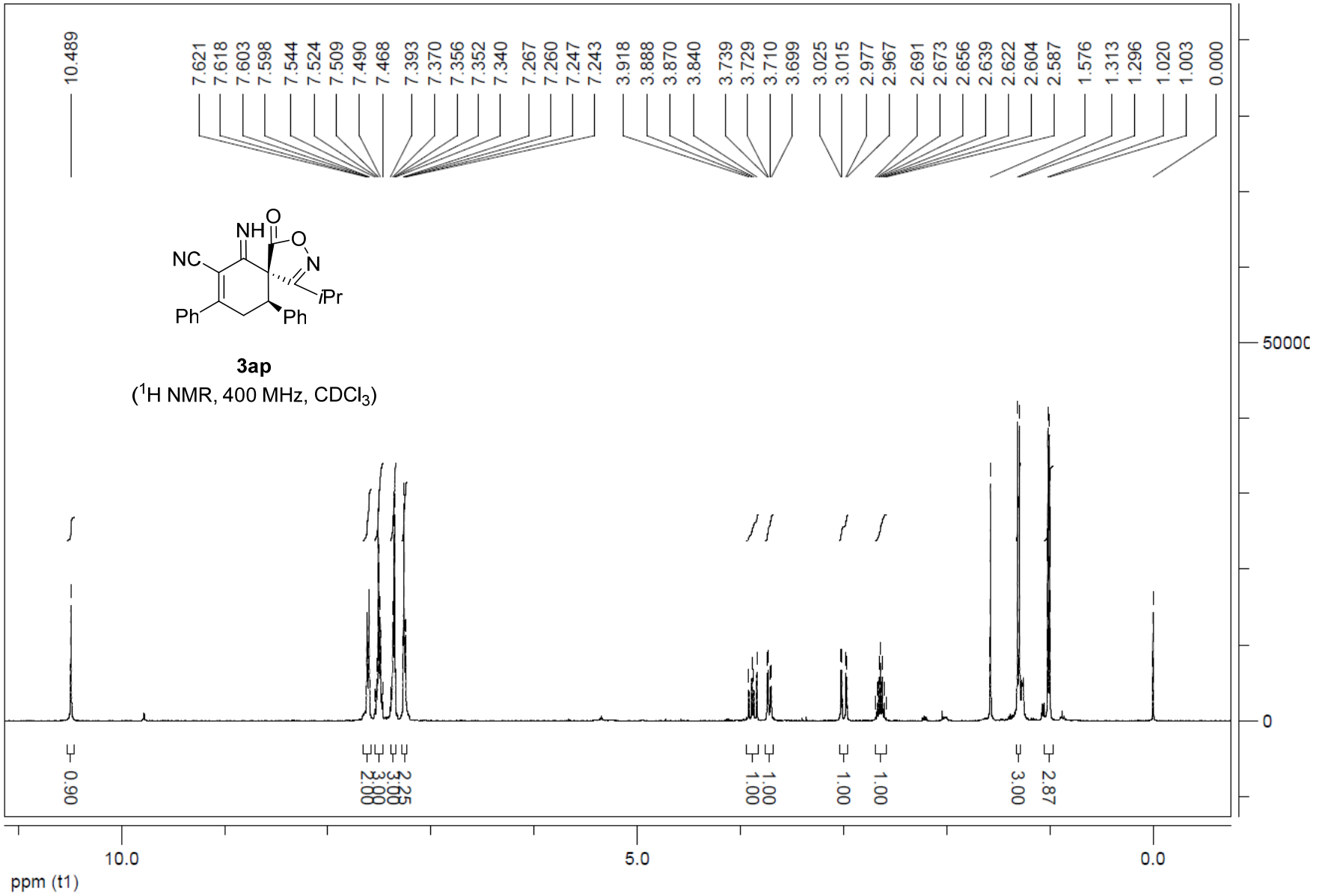
(^{13}C NMR, 100 MHz, $CDCl_3$)

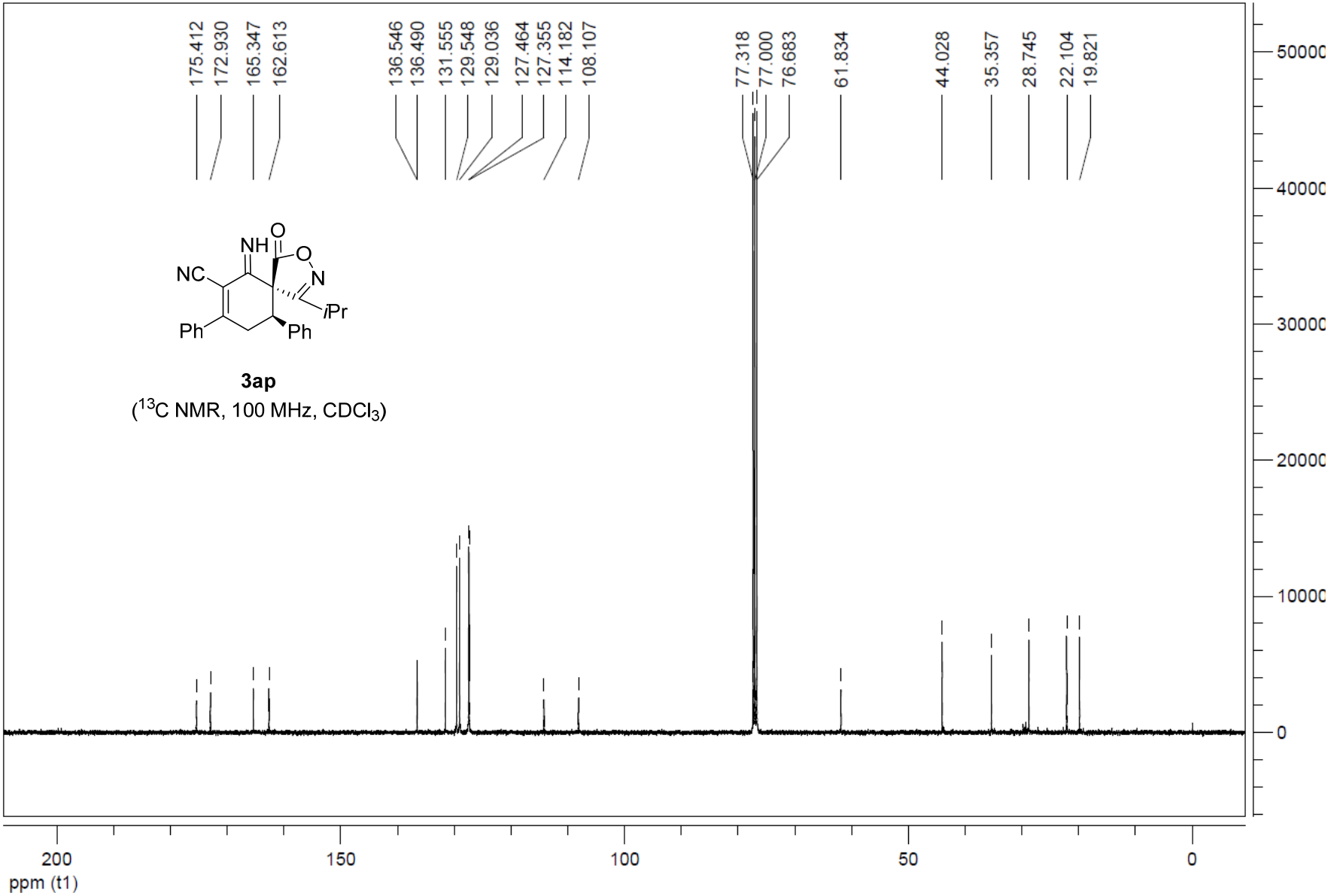

10.465
7.615
7.600
7.596
7.544
7.528
7.517
7.509
7.494
7.487
7.274
7.272
7.260
7.025
7.022
7.018
7.005
6.996
3.985
3.950
3.907
3.877
3.178
3.174
3.136
3.133
2.183
0.000
NC
NH
O
O
N
Ph
S
3an
(1H NMR, 400 MHz, CDCl3)
1.00
2.08
3.00
1.91
2.00
2.09
1.00
3.00
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)


174.222
165.947
164.833
161.616
137.454
136.362
131.679
129.121
127.803
127.473
125.920
125.628
113.952
108.214
77.318
77.000
76.683
61.788
38.644
35.258
12.787
NH
O
O
N
NC
Ph
S
3an
(13C NMR, 100 MHz, CDCl3)
30000
25000
20000
15000
10000
50000
0
200
150
100
50
0
ppm (t1)


10.460
8.085
8.064
7.943
7.924
7.871
7.853
7.632
7.616
7.612
7.594
7.591
7.577
7.575
7.557
7.540
7.523
7.512
7.504
7.496
7.487
7.476
7.458
7.256
4.673
4.662
4.644
4.633
3.923
3.894
3.873
3.844
3.183
3.172
3.133
3.123
1.855
0.000
NH
O
O
N
NC
Ph
3ao
(1H NMR, 400 MHz, CDCl3)
1.00
1.00
9.45
1.00
1.00
1.00
3.00
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

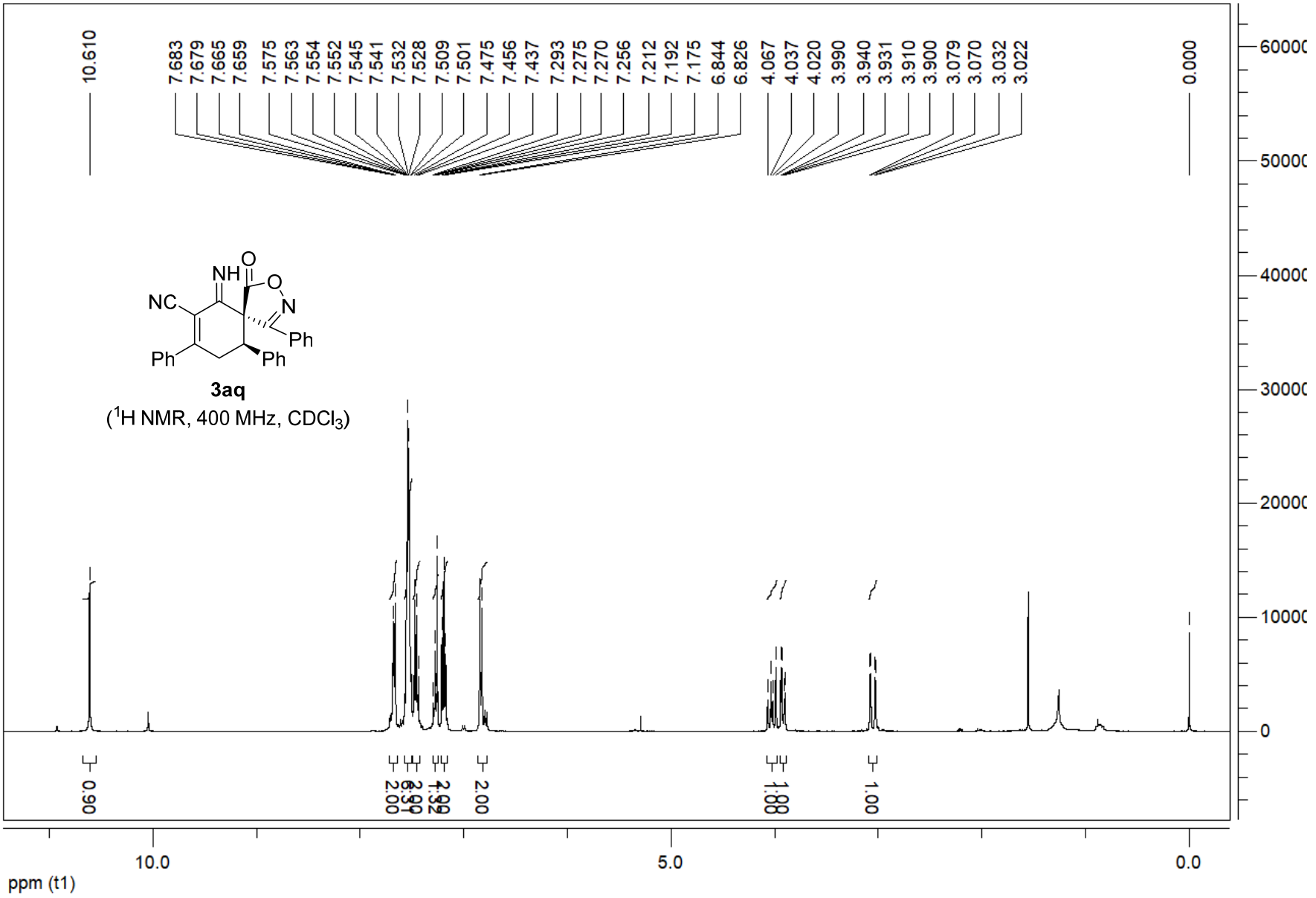

175.146
166.317
165.977
162.814
136.399
134.255
132.113
131.618
130.485
129.883
129.530
129.077
127.480
127.215
126.217
125.907
123.762
121.004
114.192
107.928
77.318
77.000
76.683
60.867
37.315
35.513
12.781
NC
NH
O
O
N
Ph
3ao
(^{13}C NMR, 100 MHz, $CDCl_3$)
50000
40000
30000
20000
10000
0
150
100
50
0
ppm (t1)

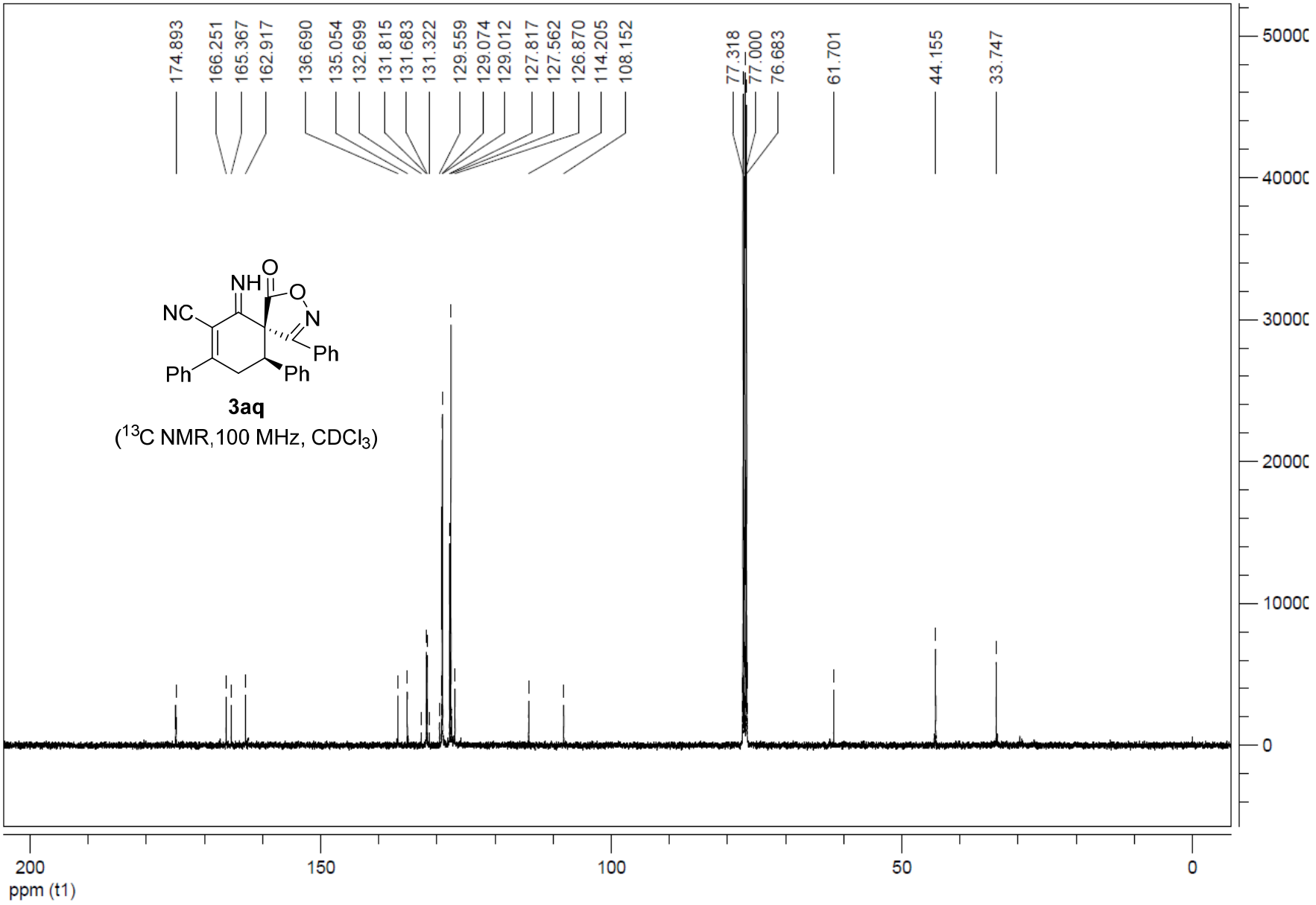

10.489
7.621
7.618
7.603
7.598
7.544
7.524
7.509
7.490
7.468
7.393
7.370
7.356
7.352
7.340
7.267
7.260
7.247
7.243
3.918
3.888
3.870
3.840
3.739
3.729
3.710
3.699
3.025
3.015
2.977
2.967
2.691
2.673
2.656
2.639
2.622
2.604
2.587
1.576
1.313
1.296
1.020
1.003
0.000
NC
NH
O
O
N
iPr
Ph
Ph
3ap
(1H NMR, 400 MHz, CDCl3)
50000
0
0.90
2.00
3.00
3.05
2.25
1.00
1.00
1.00
1.00
3.00
2.87
10.0
5.0
0.0
ppm (t1)

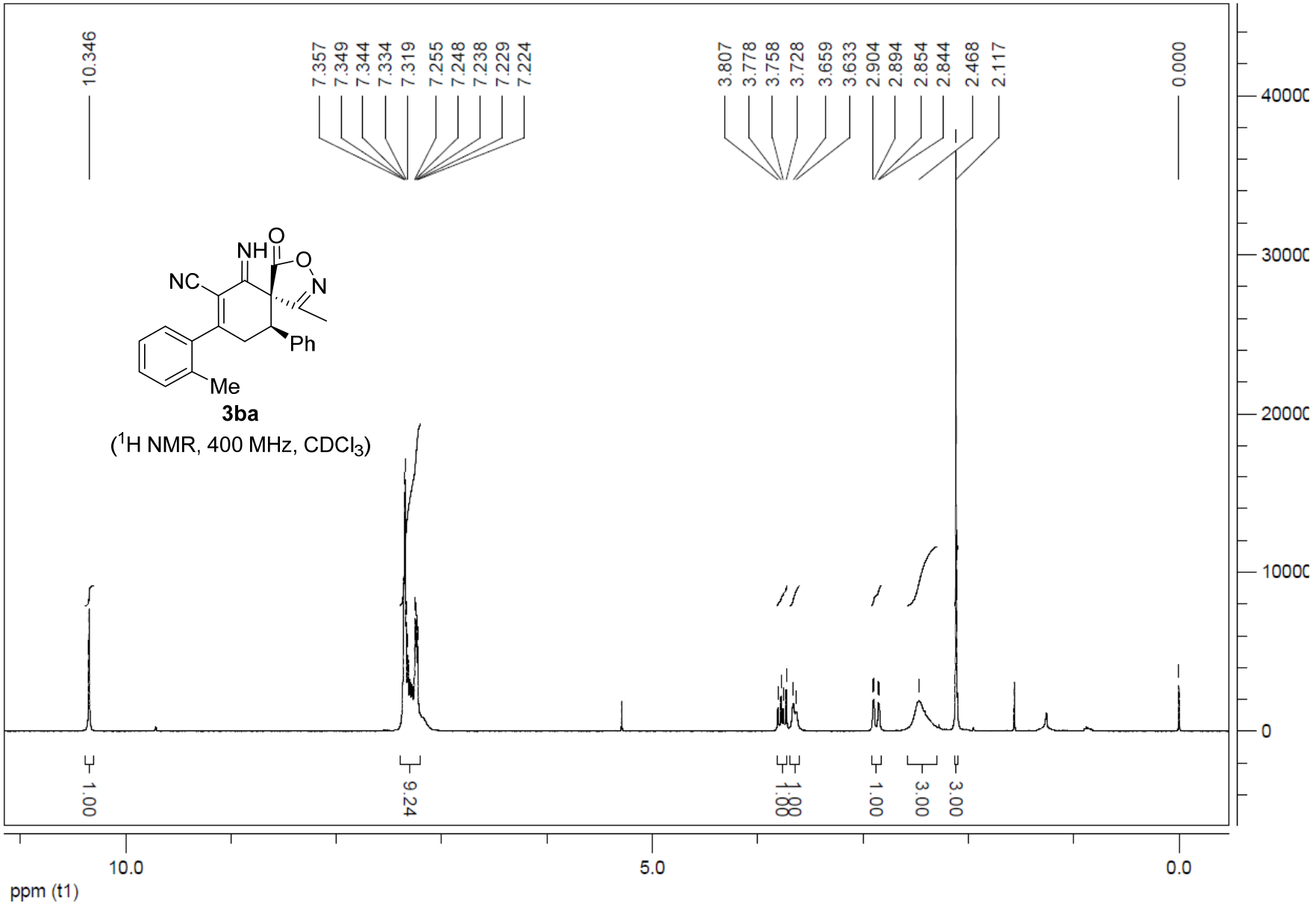


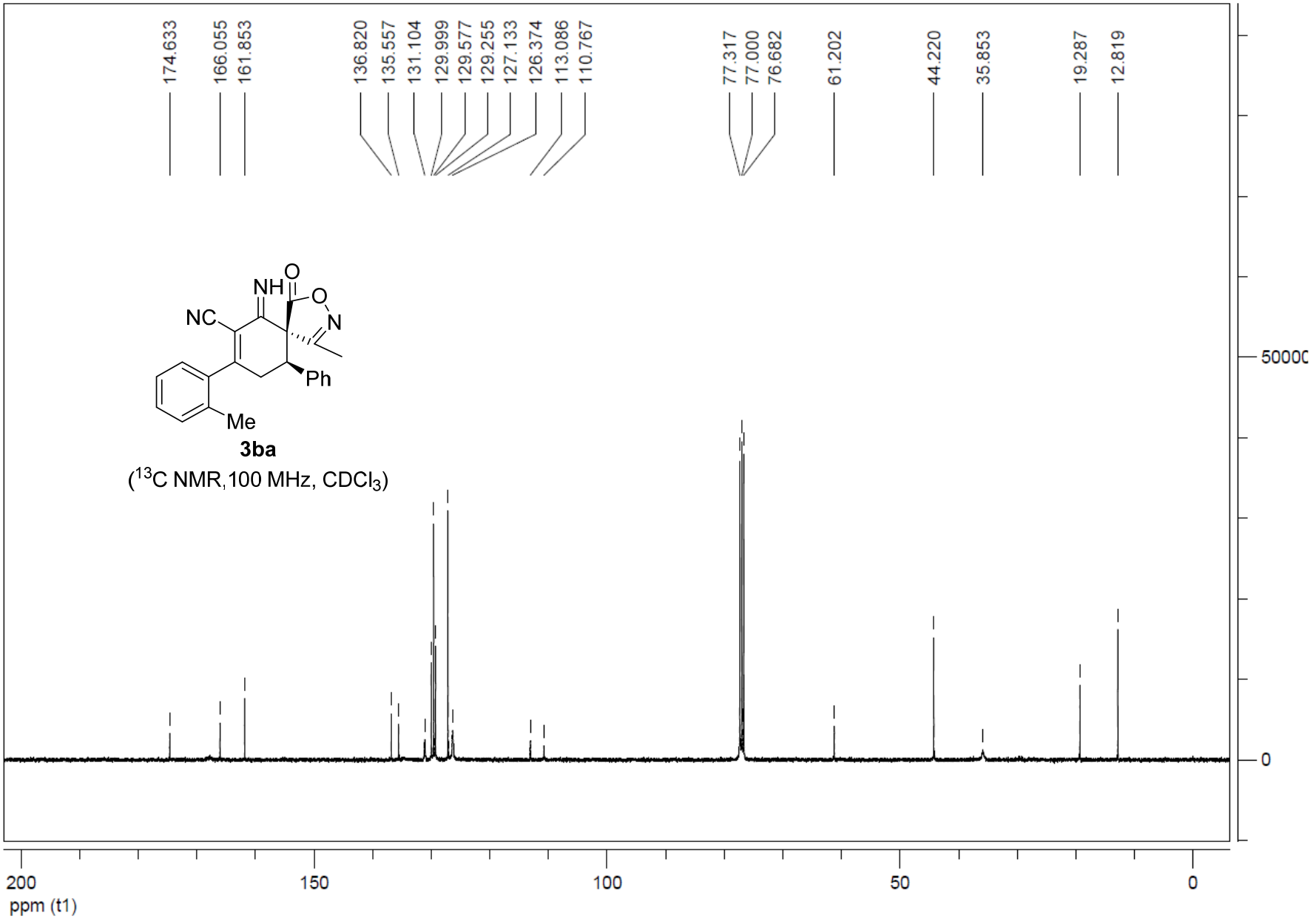
3ap

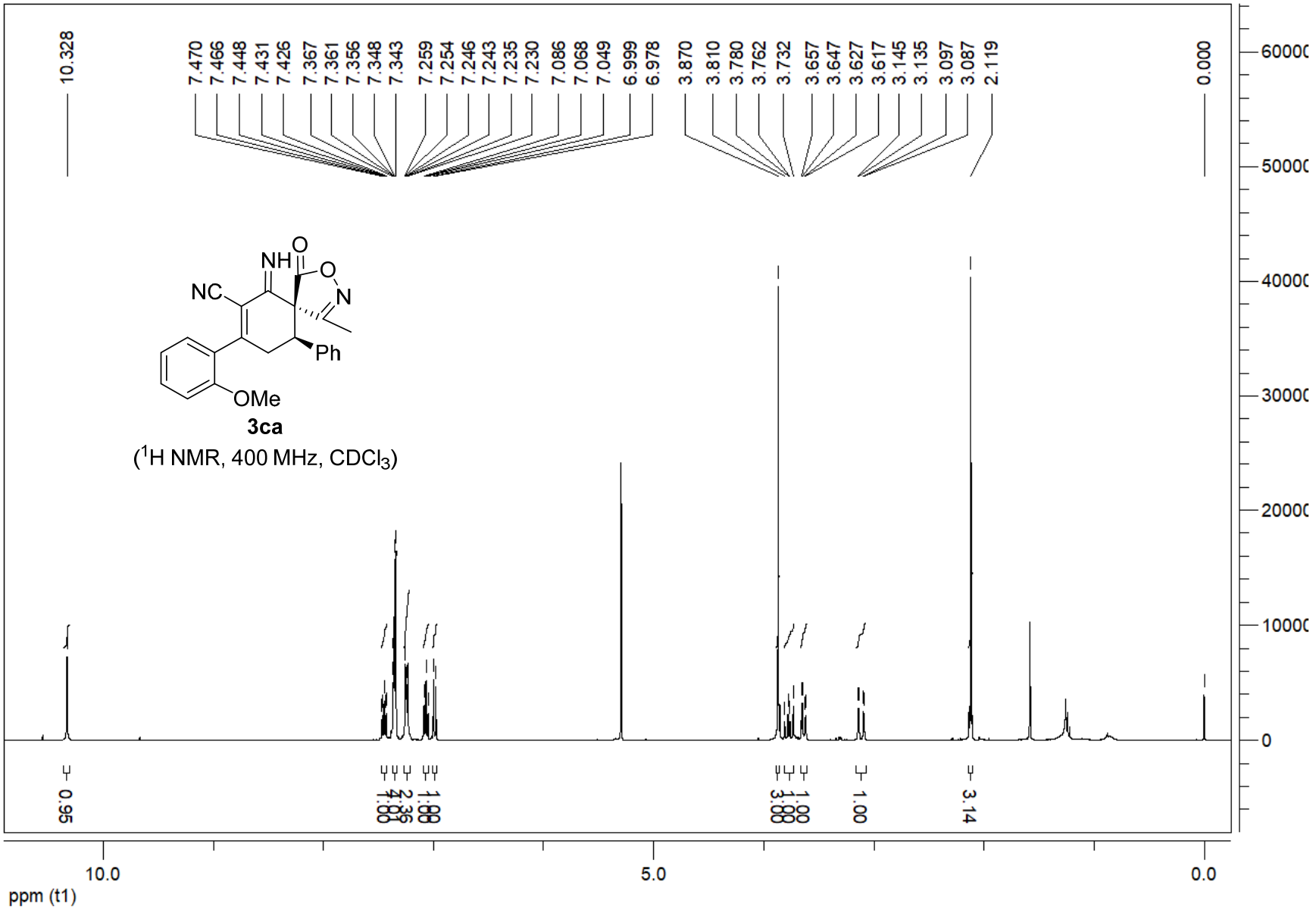
(^{13}C NMR, 100 MHz, $CDCl_3$)

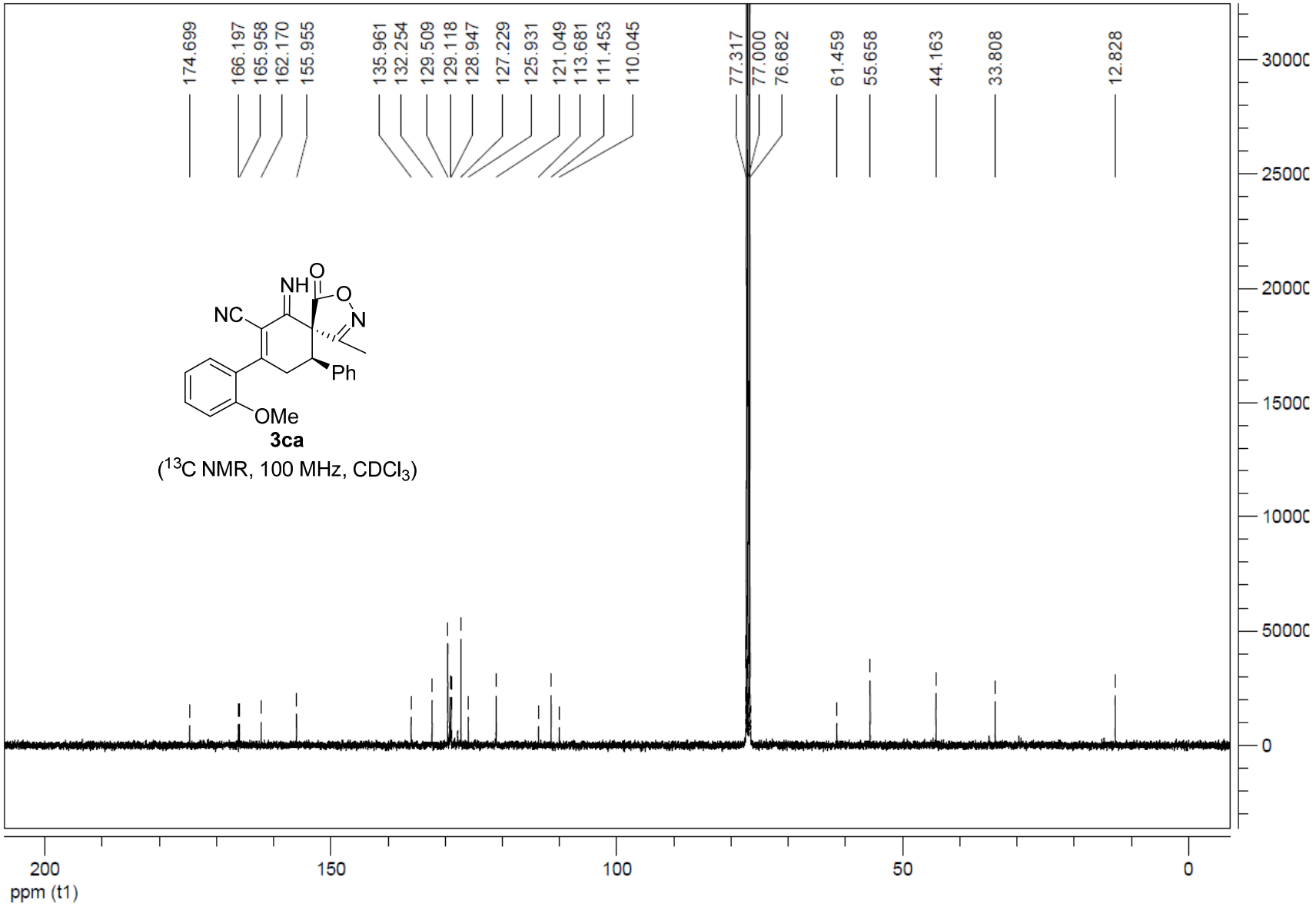

10.610
7.683
7.679
7.665
7.659
7.575
7.563
7.554
7.552
7.545
7.541
7.532
7.528
7.509
7.501
7.475
7.456
7.437
7.293
7.275
7.270
7.256
7.212
7.192
7.175
6.844
6.826
4.067
4.037
4.020
3.990
3.940
3.931
3.910
3.900
3.079
3.070
3.032
3.022
0.000
NC
NH
O
O
N
Ph
Ph
Ph
3aq
(1H NMR, 400 MHz, CDCl3)
0.90
2.00
2.00
2.00
2.00
1.88
1.00
10.0
5.0
0.0
ppm (t1)

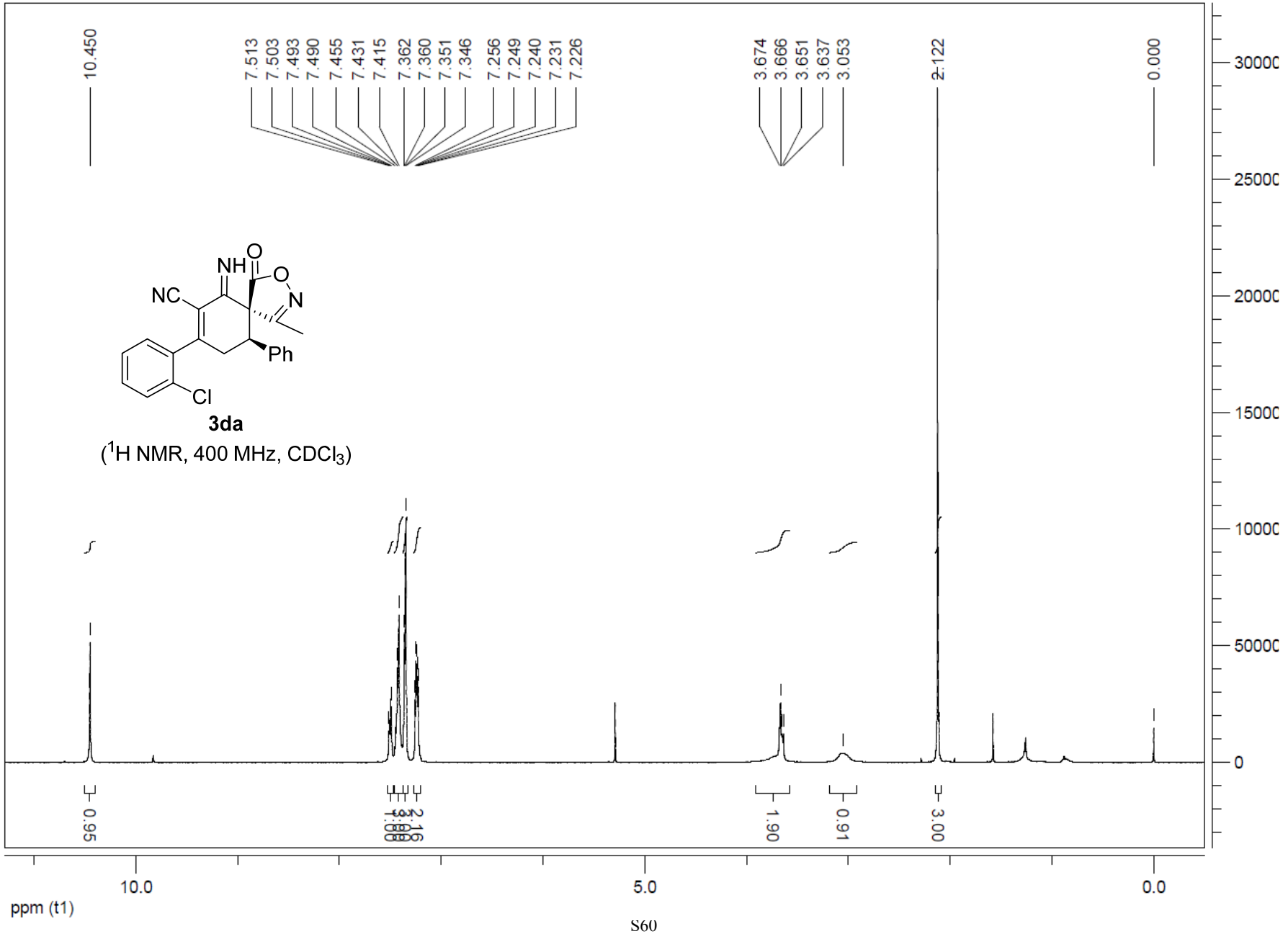

174.893
166.251
165.367
162.917
136.690
135.054
132.699
131.815
131.683
131.322
129.559
129.074
129.012
127.817
127.562
126.870
114.205
108.152
77.318
77.000
76.683
61.701
44.155
33.747
NC
NH
O
O
N
Ph
Ph
Ph
3aq
(^{13}C NMR,100 MHz, $CDCl_3$)
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

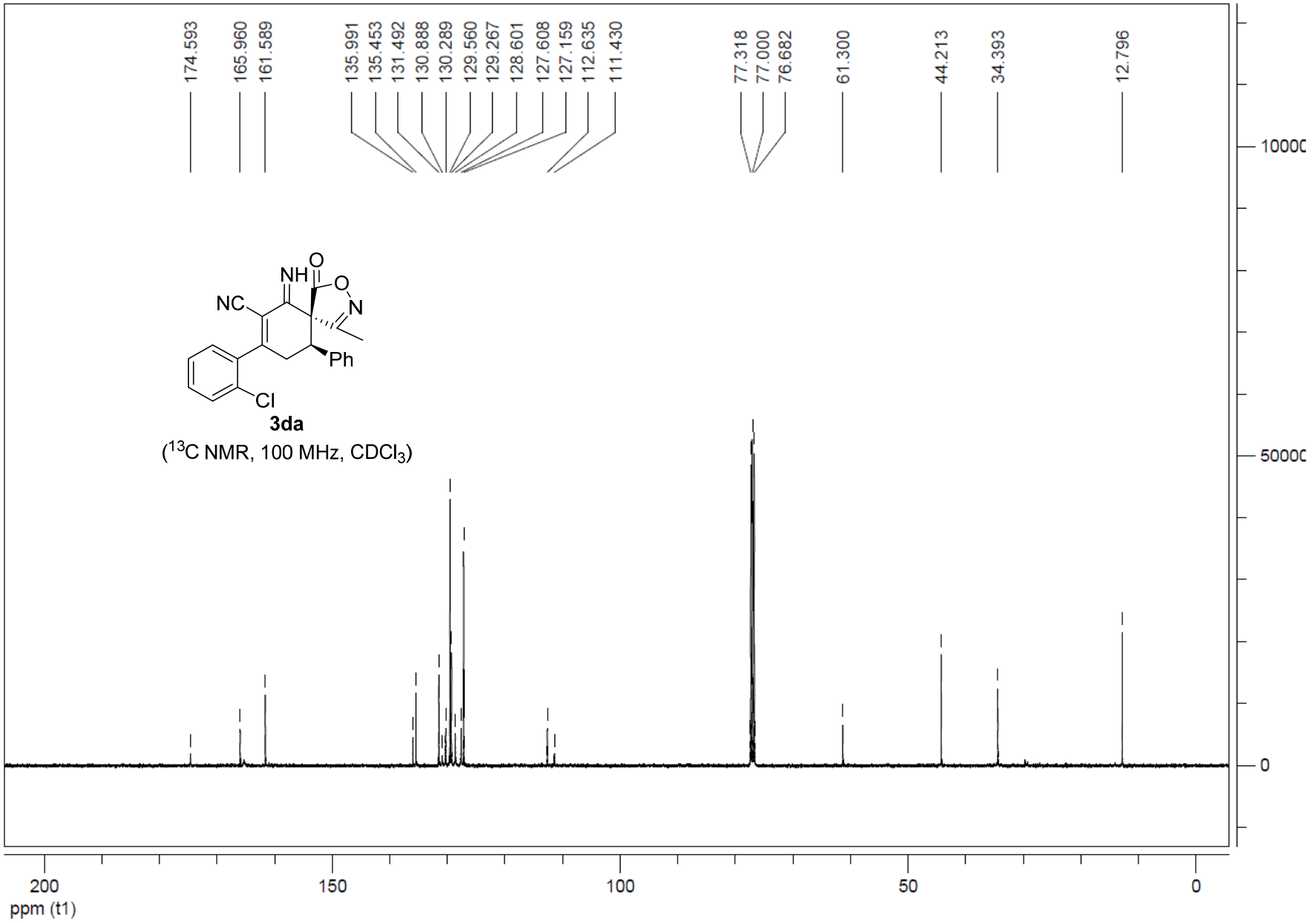

10.346
7.357
7.349
7.344
7.334
7.319
7.255
7.248
7.238
7.229
7.224
3.807
3.778
3.758
3.728
3.659
3.633
2.904
2.894
2.854
2.844
2.468
2.117
0.000
NH
O
O
N
NC
Ph
Me
3ba
(1H NMR, 400 MHz, CDCl3)
1.00
9.24
1.08
1.00
3.00
3.00
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)


174.633
166.055
161.853
136.820
135.557
131.104
129.999
129.577
129.255
127.133
126.374
113.086
110.767
77.317
77.000
76.682
61.202
44.220
35.853
19.287
12.819
NH
O
O
N
NC
Ph
Me
3ba
(^{13}C NMR, 100 MHz, $CDCl_3$)
50000
0
200
150
100
50
0
ppm (t1)


10.328
7.470
7.466
7.448
7.431
7.426
7.367
7.361
7.356
7.348
7.343
7.259
7.254
7.246
7.243
7.235
7.230
7.086
7.068
7.049
6.999
6.978
3.870
3.810
3.780
3.762
3.732
3.657
3.647
3.627
3.617
3.145
3.135
3.097
3.087
2.119
0.000
NC
NH
O
O
N
Ph
OMe
3ca
(1H NMR, 400 MHz, CDCl3)
0.95
1.83
2.36
1.88
3.88
1.00
1.00
3.14
60000
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

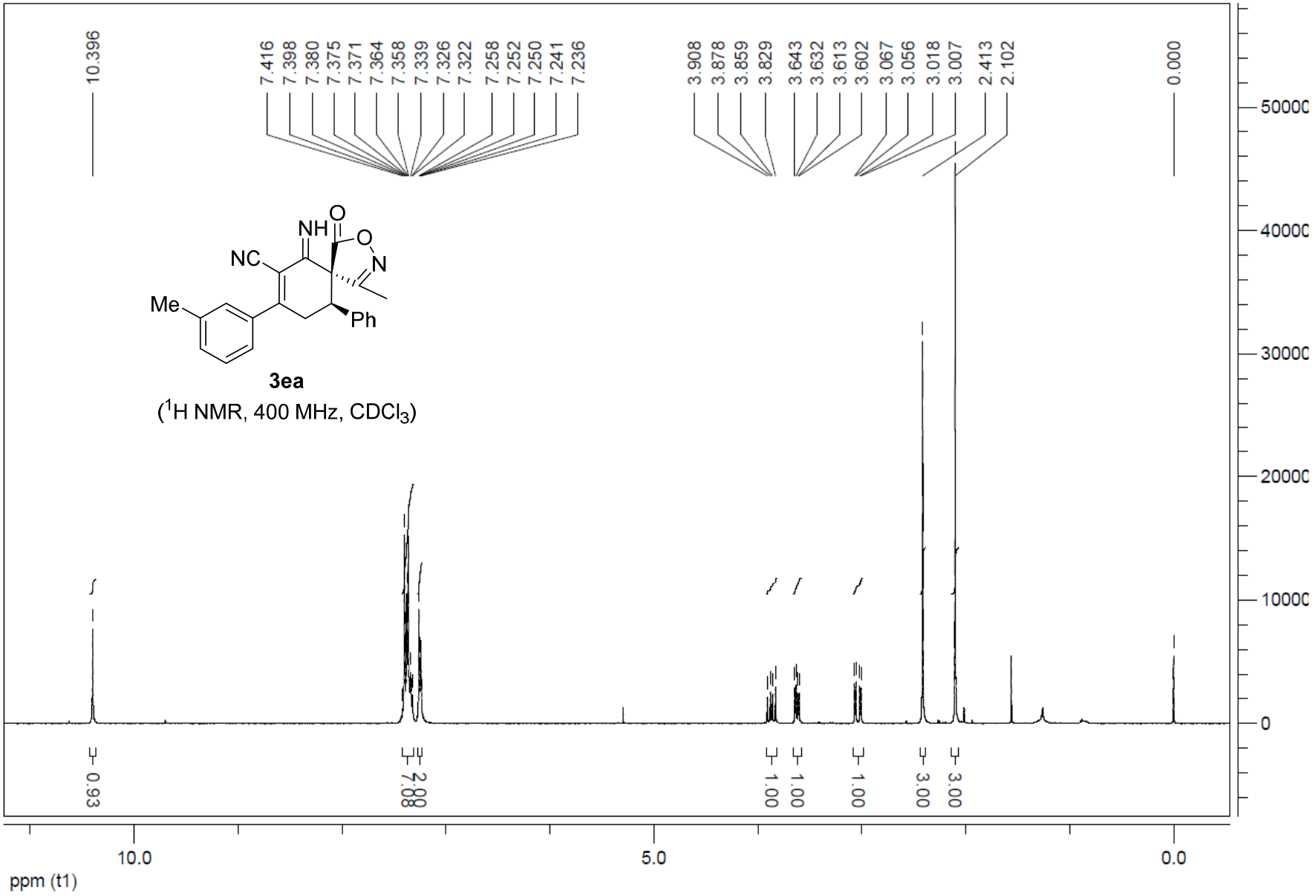

174.699
166.197
165.958
162.170
155.955
135.961
132.254
129.509
129.118
128.947
127.229
125.931
121.049
113.681
111.453
110.045
77.317
77.000
76.682
61.459
55.658
44.163
33.808
12.828
NC
NH
O
O
N
Ph
OMe
3ca
(^{13}C NMR, 100 MHz, $CDCl_3$)
200
150
100
50
0
ppm (t1)

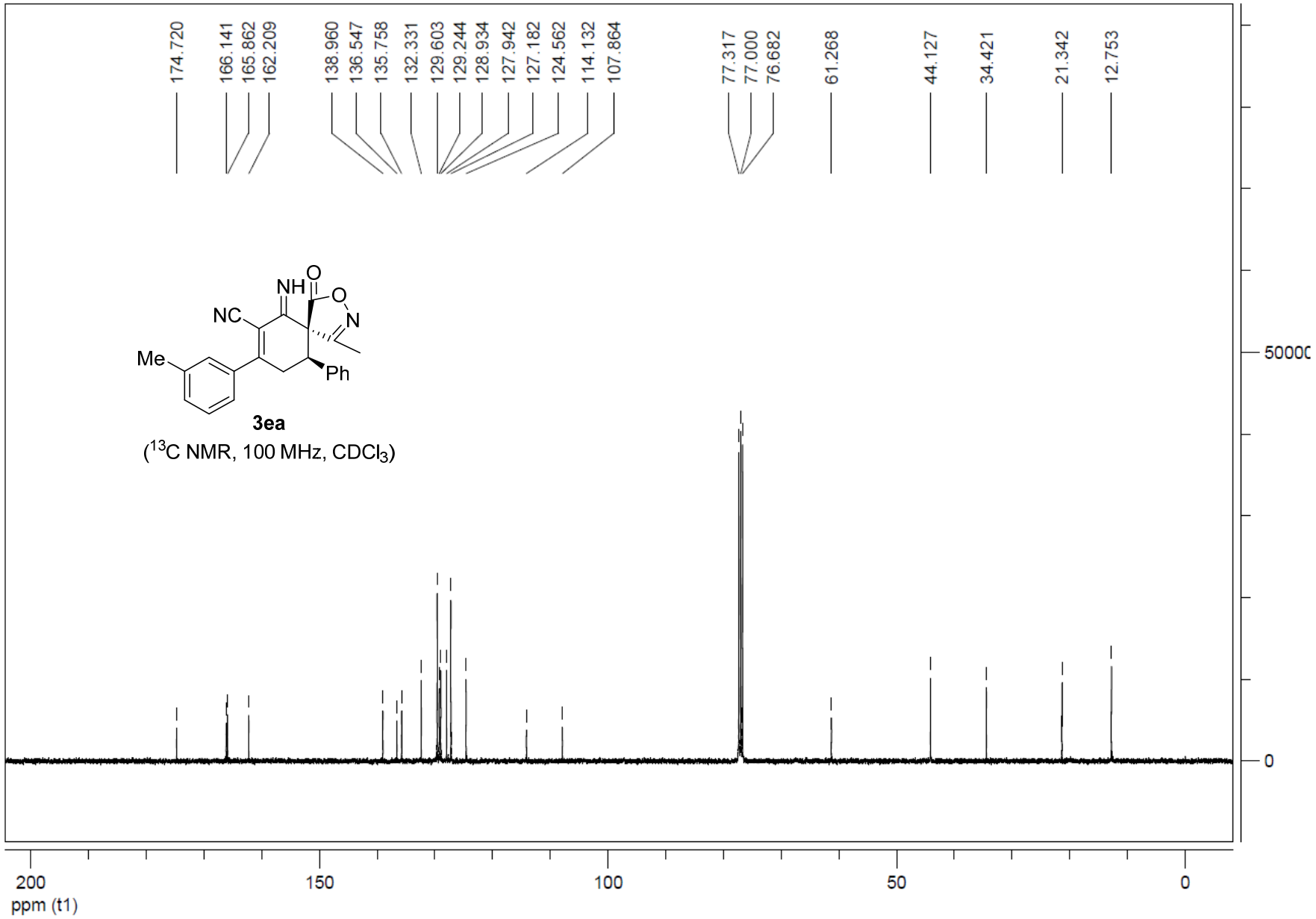

10.450
7.513
7.503
7.493
7.490
7.455
7.431
7.415
7.362
7.360
7.351
7.346
7.256
7.249
7.240
7.231
7.226
3.674
3.666
3.651
3.637
3.053
2.122
0.000
NC
NH
O
O
N
Ph
Cl
3da
(1H NMR, 400 MHz, CDCl3)
0.95
2.16
1.90
0.91
3.00
30000
25000
20000
15000
10000
5000
0
10.0
5.0
0.0
ppm (t1)



3da

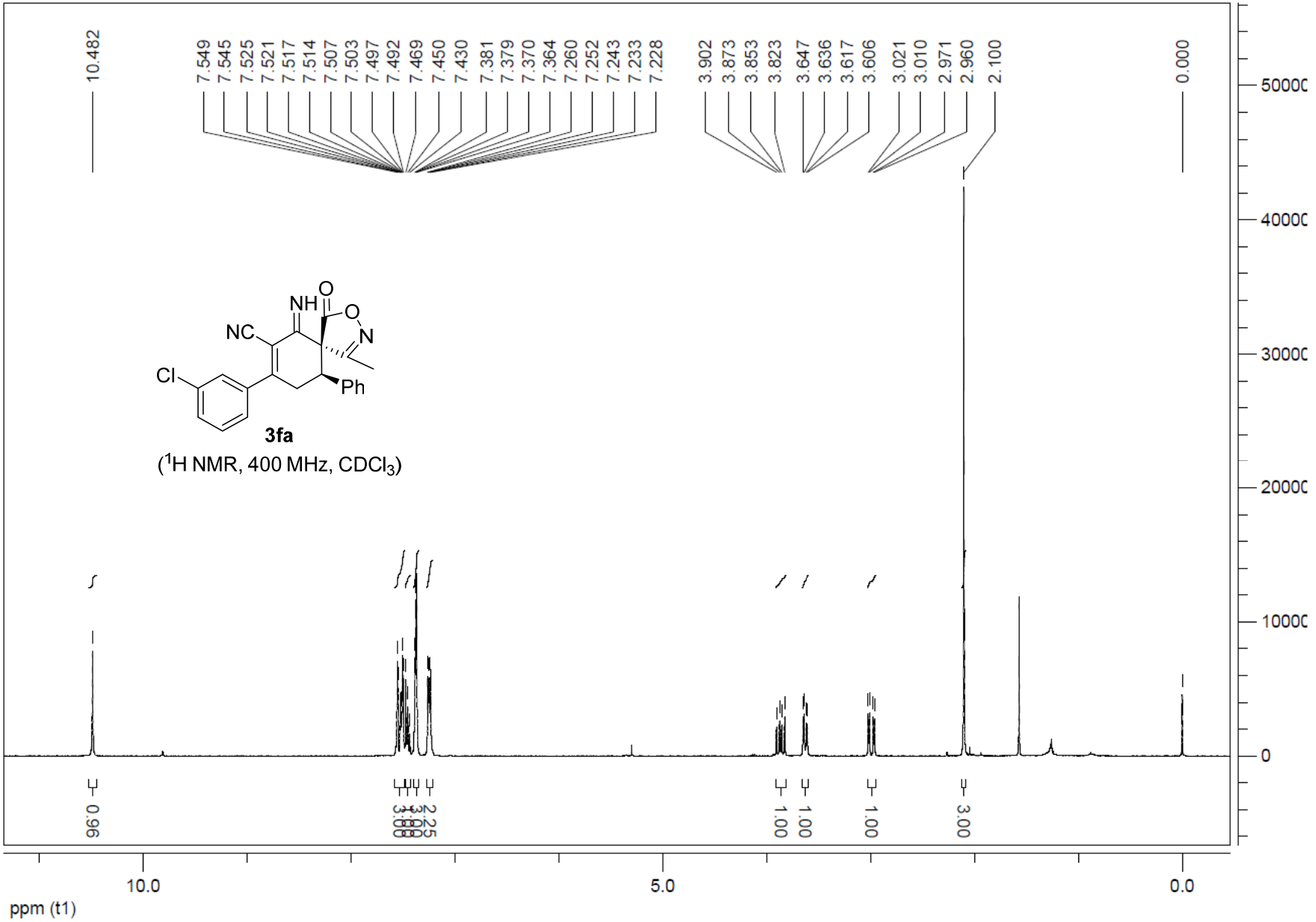
(^{13}C NMR, 100 MHz, $CDCl_3$)

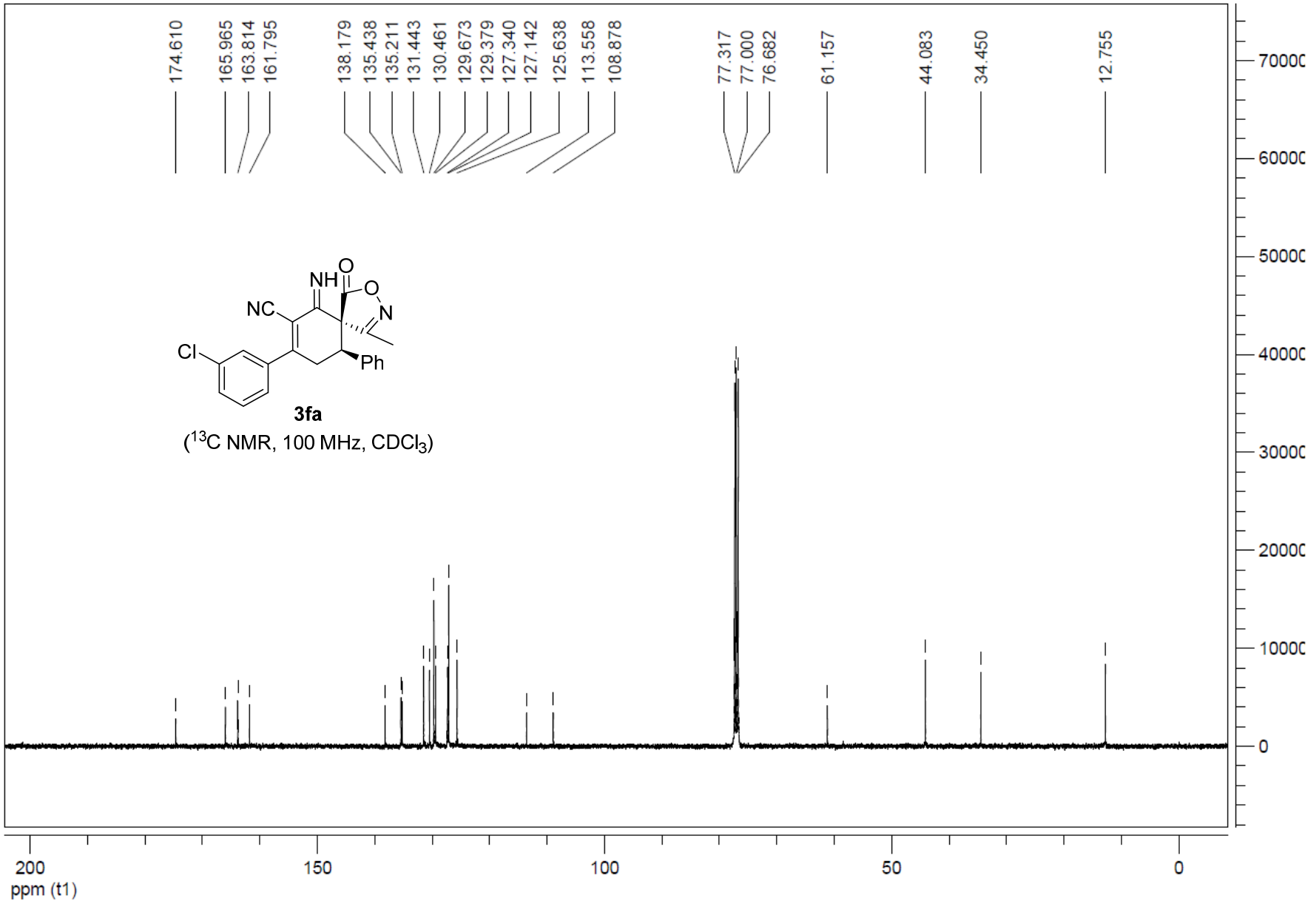

10.396
7.416
7.398
7.380
7.375
7.371
7.364
7.358
7.339
7.326
7.322
7.258
7.252
7.250
7.241
7.236
3.908
3.878
3.859
3.829
3.643
3.632
3.613
3.602
3.067
3.056
3.018
3.007
2.413
2.102
0.000
NC
NH
O
O
N
Me
Ph
3ea
(1H NMR, 400 MHz, CDCl3)
0.93
2.08
1.00
1.00
1.00
3.00
3.00
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

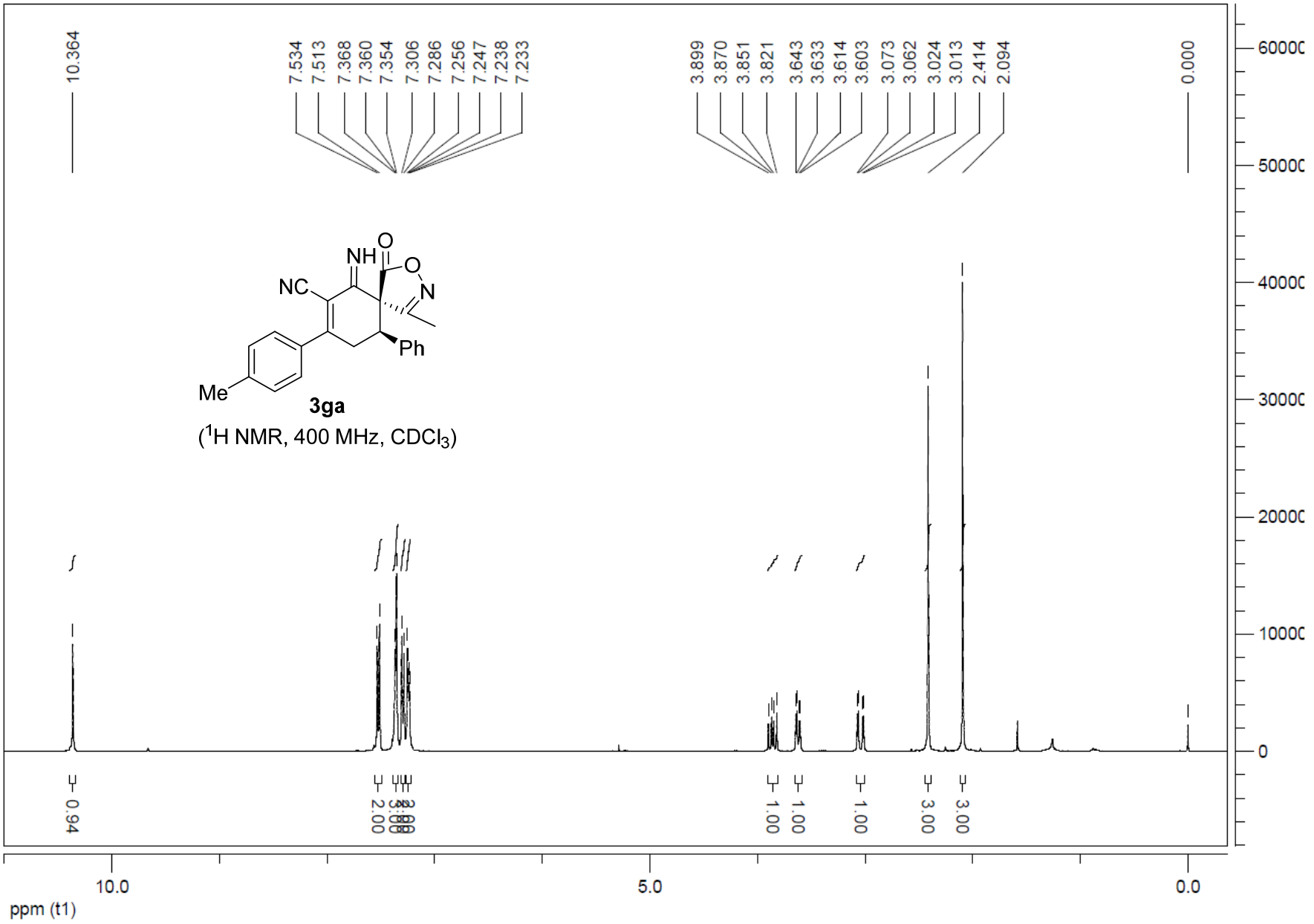


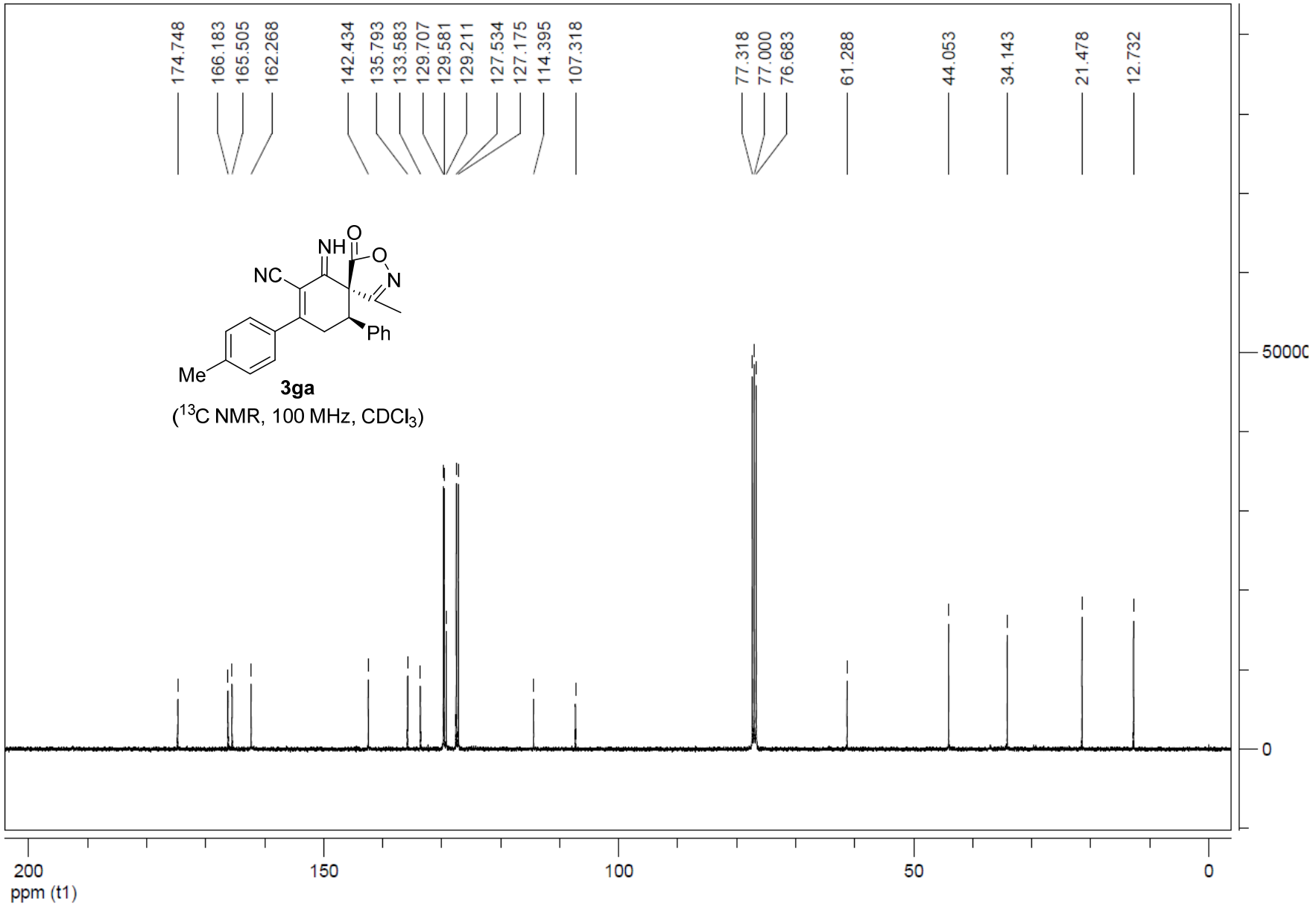
3ea

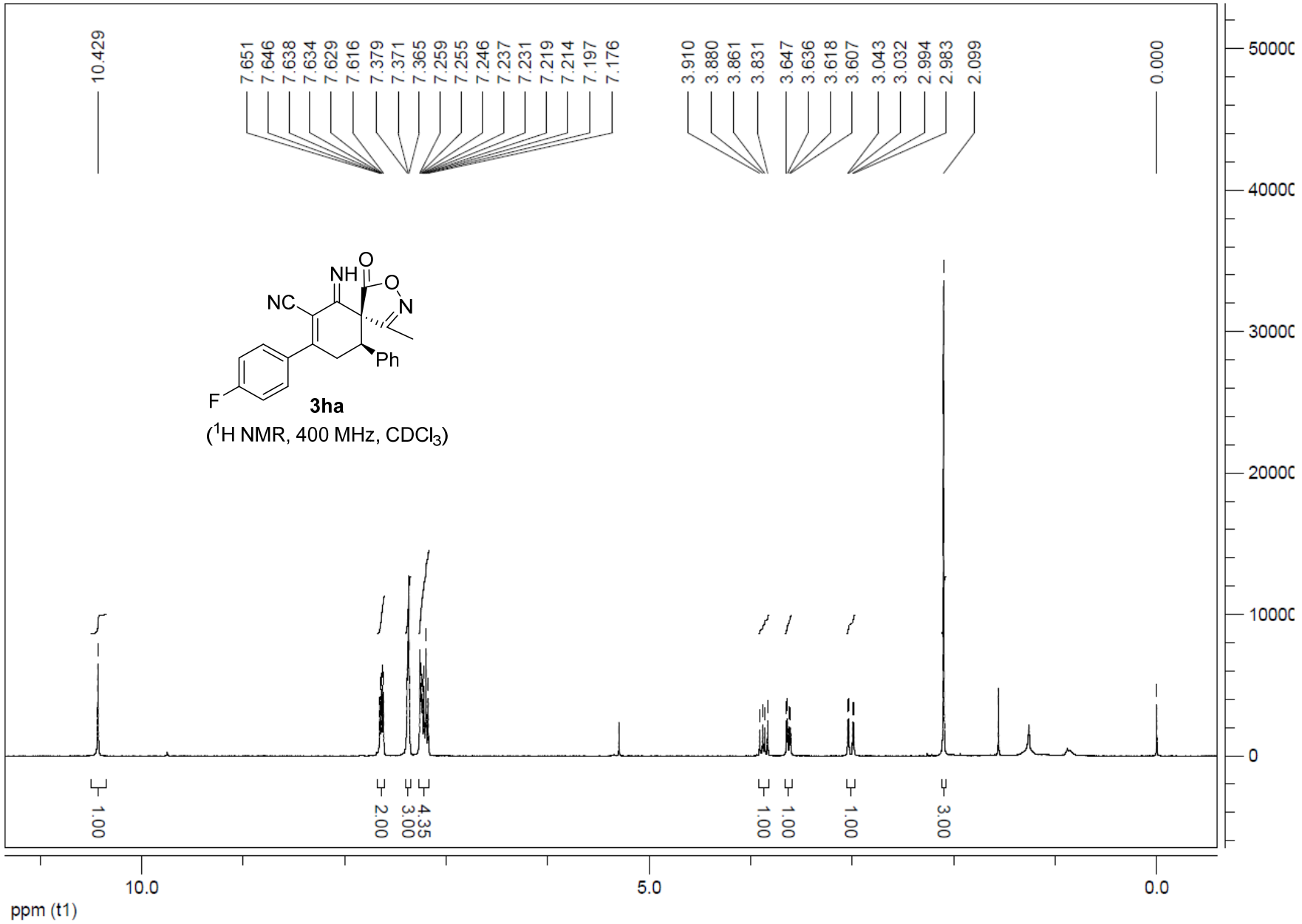
(^{13}C NMR, 100 MHz, $CDCl_3$)

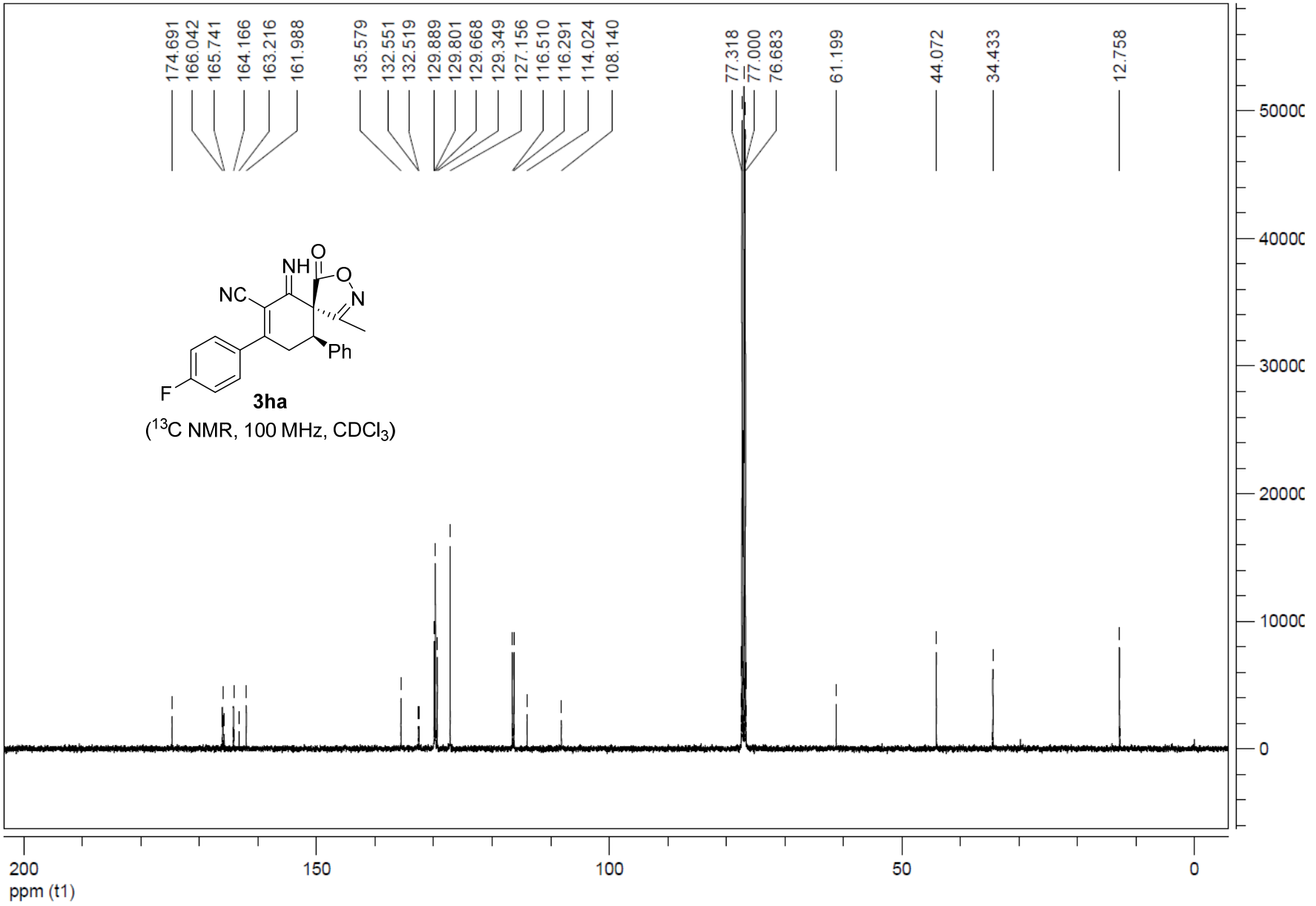

10.482
7.549
7.545
7.525
7.521
7.517
7.514
7.507
7.503
7.497
7.492
7.469
7.450
7.430
7.381
7.379
7.370
7.364
7.260
7.252
7.243
7.233
7.228
3.902
3.873
3.853
3.823
3.647
3.636
3.617
3.606
3.021
3.010
2.971
2.960
2.100
0.000
NH
O
O
N
NC
Cl
Ph
3fa
(1H NMR, 400 MHz, CDCl3)
0.96
2.25
1.00
1.00
1.00
3.00
5000
4000
3000
2000
1000
0
10.0
5.0
0.0
ppm (t1)

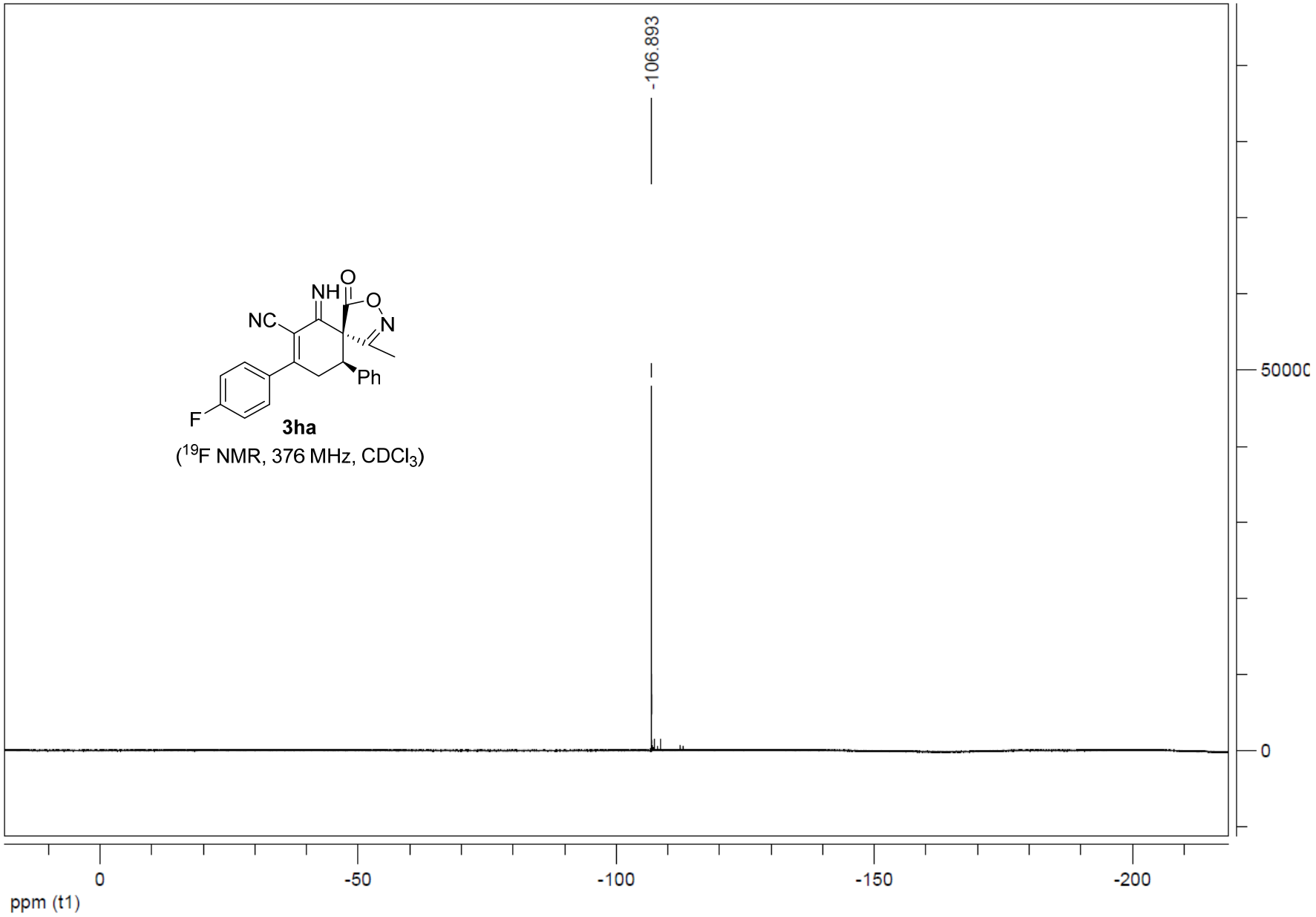

174.610
165.965
163.814
161.795
138.179
135.438
135.211
131.443
130.461
129.673
129.379
127.340
127.142
125.638
113.558
108.878
77.317
77.000
76.682
61.157
44.083
34.450
12.755
NH
O
O
N
NC
Cl
Ph
3fa
(13C NMR, 100 MHz, CDCl3)
70000
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)


10.364
7.534
7.513
7.368
7.360
7.354
7.306
7.286
7.256
7.247
7.238
7.233
3.899
3.870
3.851
3.821
3.643
3.633
3.614
3.603
3.073
3.062
3.024
3.013
2.414
2.094
0.000
NC
NH
O
O
N
Ph
Me
3ga
(1H NMR, 400 MHz, CDCl3)
0.94
2.00
1.00
1.00
1.00
3.00
3.00
10.0
5.0
0.0
ppm (t1)


174.748
166.183
165.505
162.268
142.434
135.793
133.583
129.707
129.581
129.211
127.534
127.175
114.395
107.318
77.318
77.000
76.683
61.288
44.053
34.143
21.478
12.732
NH
O
O
N
NC
Ph
Me
3ga
(13C NMR, 100 MHz, CDCl3)
50000
0
200
150
100
50
0
ppm (t1)

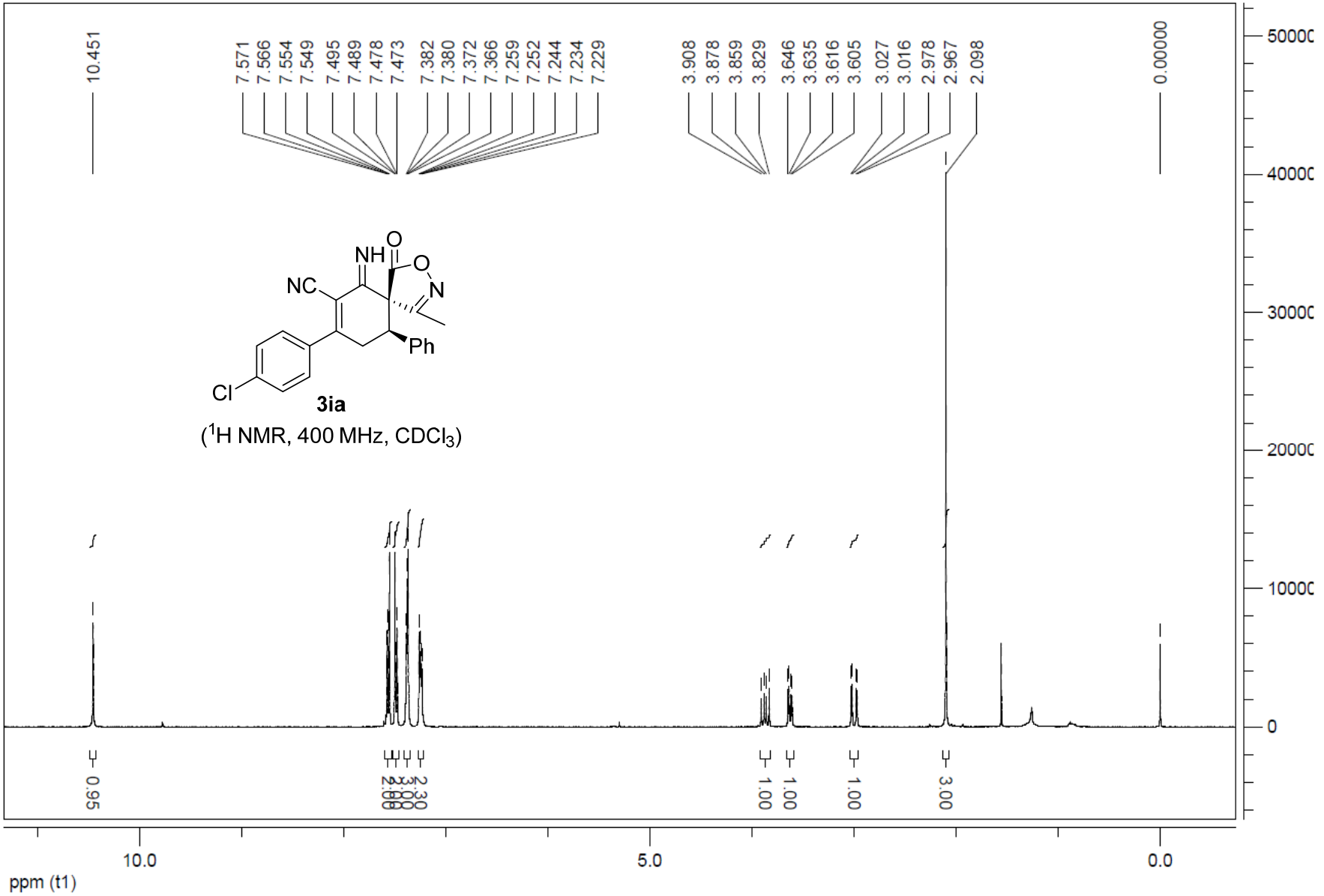

10.429
7.651
7.646
7.638
7.634
7.629
7.616
7.379
7.371
7.365
7.259
7.255
7.246
7.237
7.231
7.219
7.214
7.197
7.176
3.910
3.880
3.861
3.831
3.647
3.636
3.618
3.607
3.043
3.032
2.994
2.983
2.099
0.000
NC
NH
O
O
N
Ph
F
3ha
(1H NMR, 400 MHz, CDCl3)
1.00
2.00
3.00
4.35
1.00
1.00
1.00
3.00
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

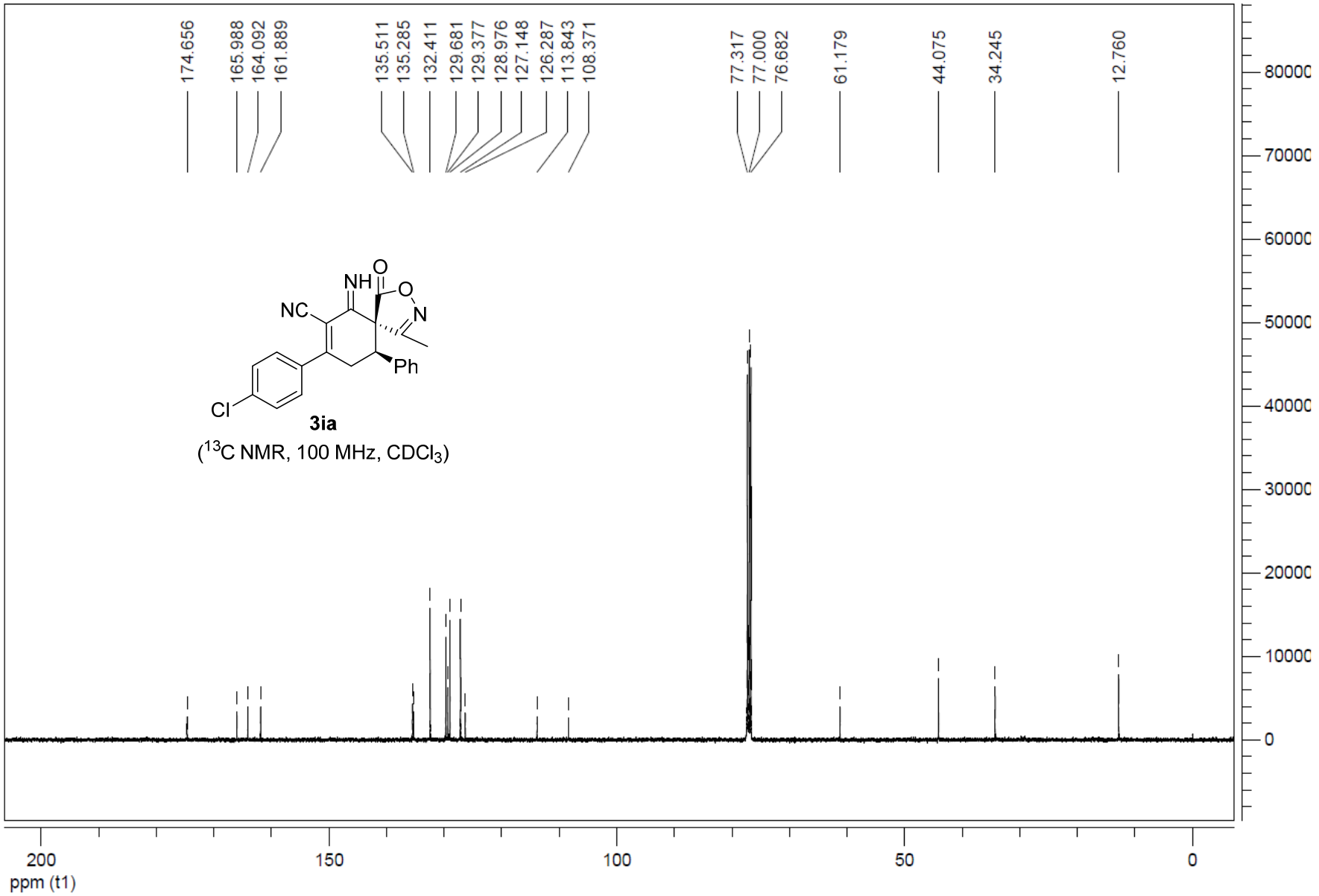

174.691
166.042
165.741
164.166
163.216
161.988
135.579
132.551
132.519
129.889
129.801
129.668
129.349
127.156
116.510
116.291
114.024
108.140
77.318
77.000
76.683
61.199
44.072
34.433
12.758
NC
NH
O
O
N
Ph
F
3ha
(13C NMR, 100 MHz, CDCl3)
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

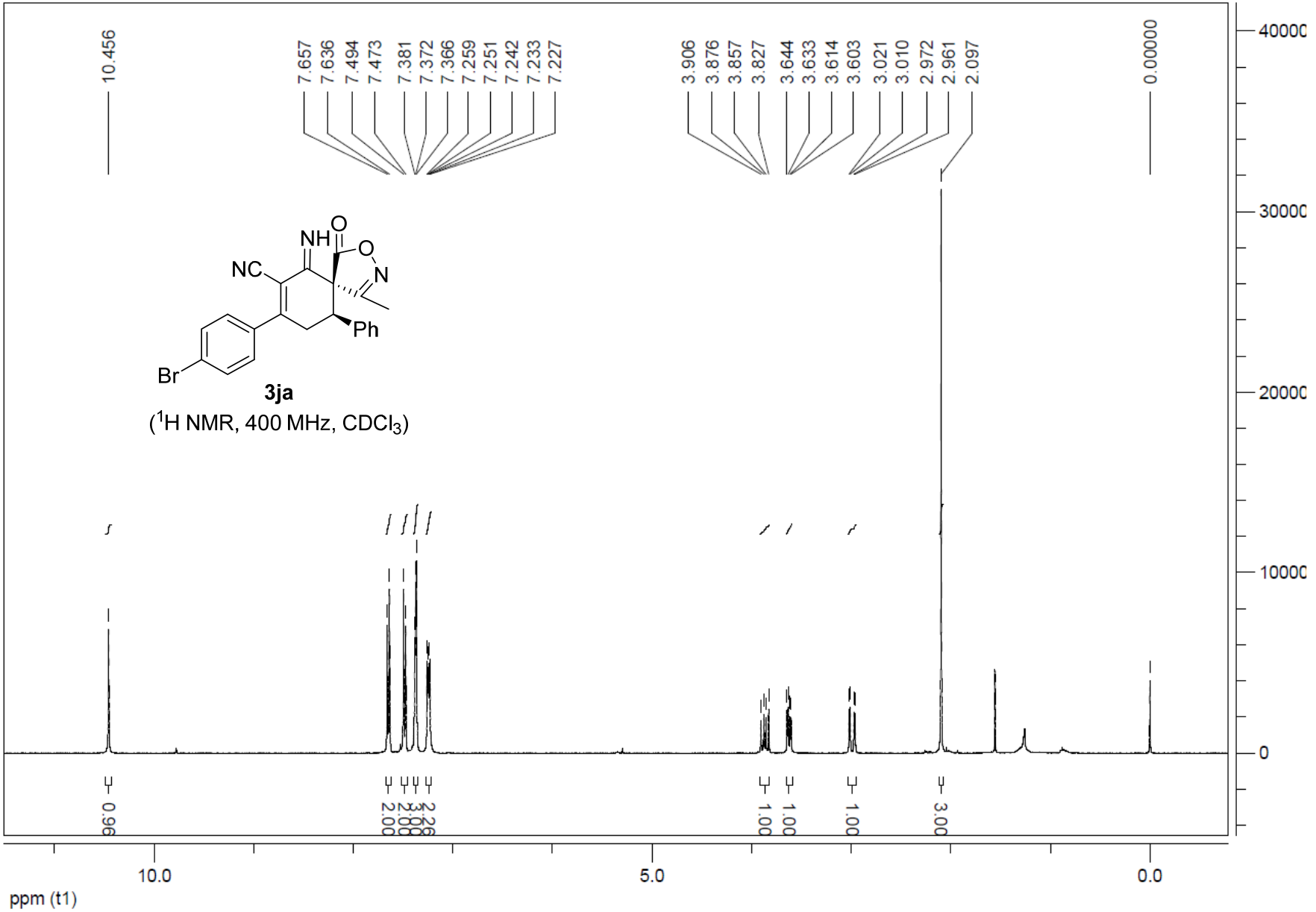


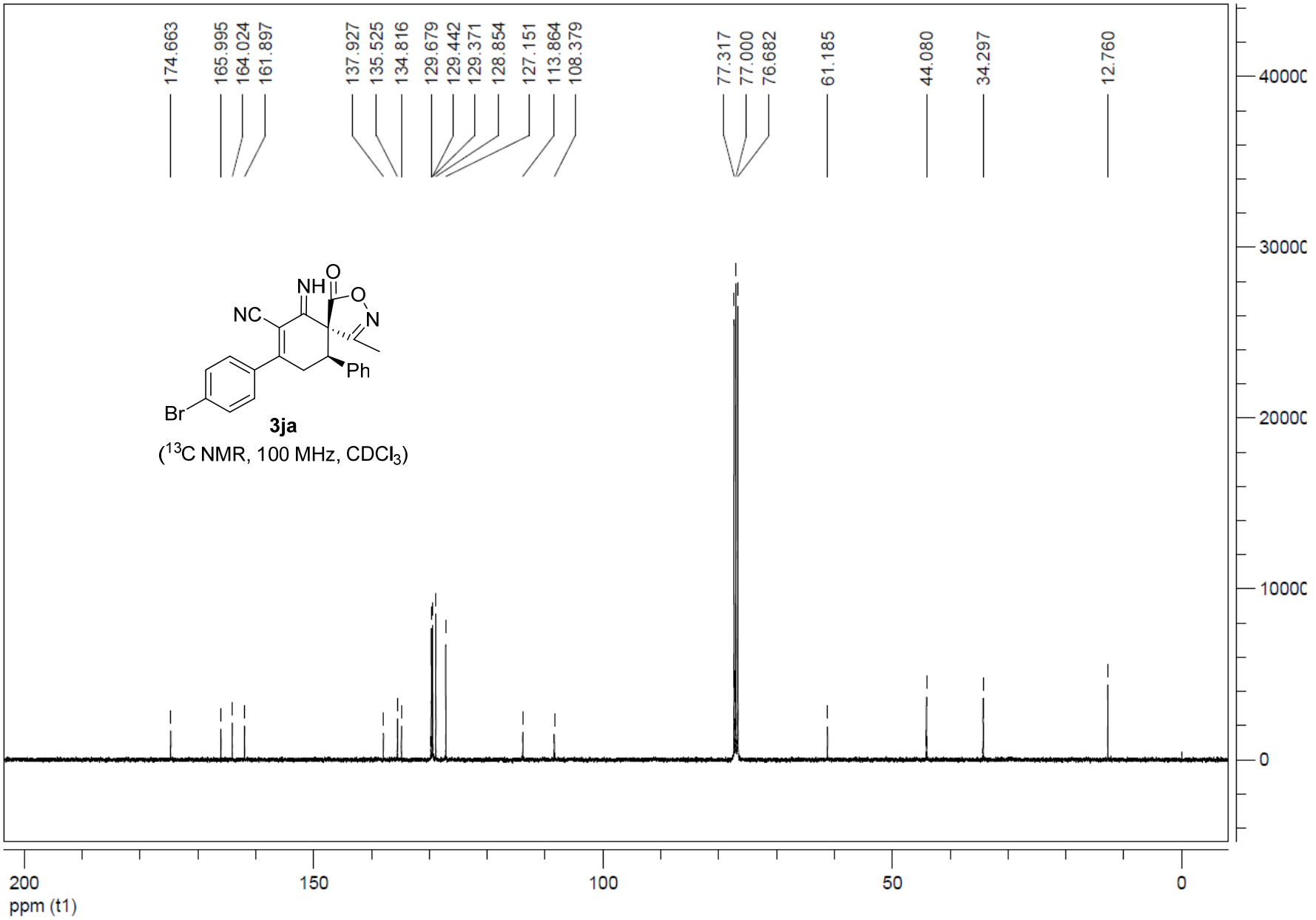
3ha

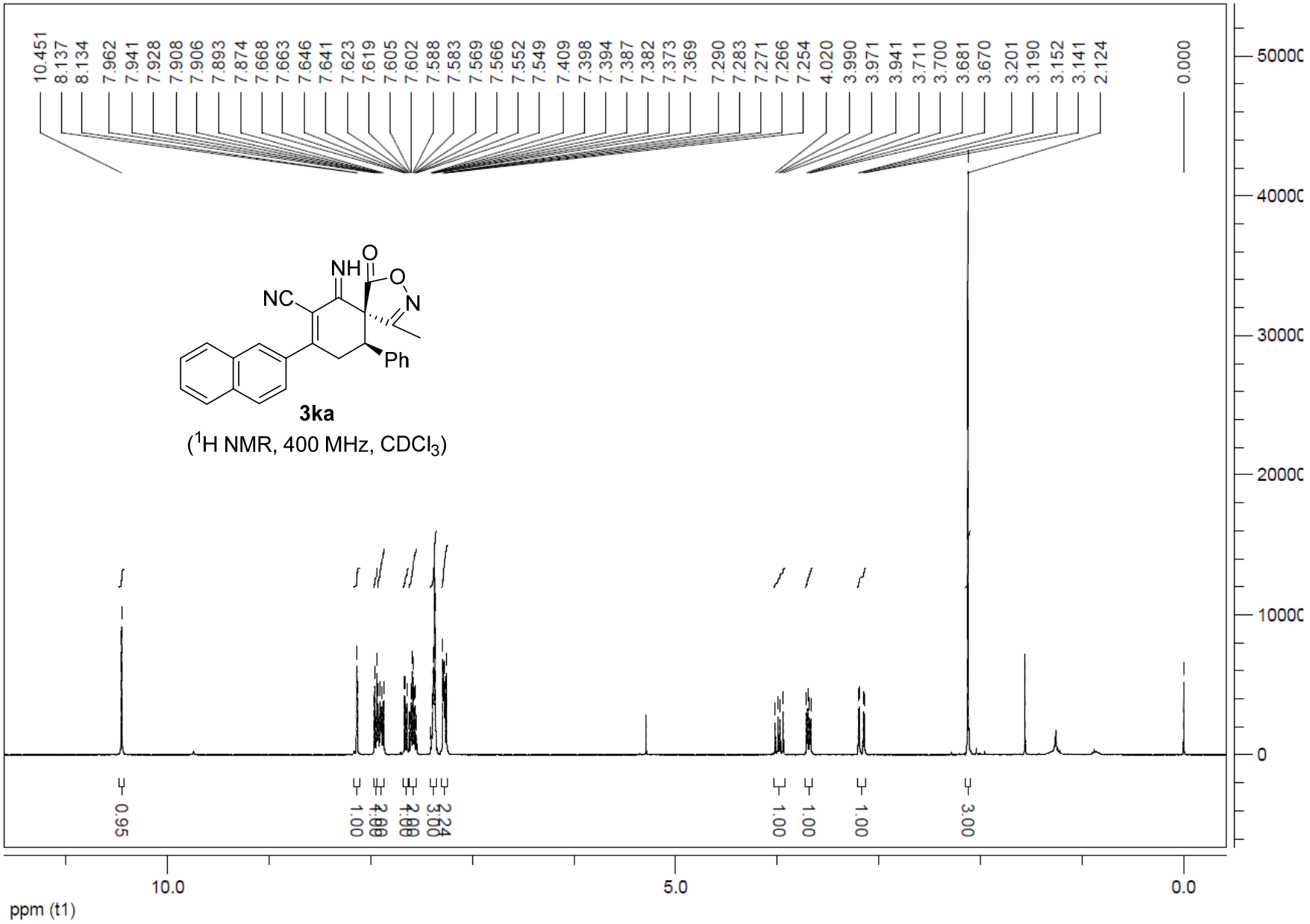
(^{19}F NMR, 376 MHz, $CDCl_3$)


10.451
7.571
7.566
7.554
7.549
7.495
7.489
7.478
7.473
7.382
7.380
7.372
7.366
7.259
7.252
7.244
7.234
7.229
3.908
3.878
3.859
3.829
3.646
3.635
3.616
3.605
3.027
3.016
2.978
2.967
2.098
0.00000
NH
O
O
N
NC
Ph
Cl
3ia
(1H NMR, 400 MHz, CDCl3)
0.95
2.30
1.00
1.00
1.00
3.00
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)


174.656
165.988
164.092
161.889
135.511
135.285
132.411
129.681
129.377
128.976
127.148
126.287
113.843
108.371
77.317
77.000
76.682
61.179
44.075
34.245
12.760
NH
O
O
N
NC
Ph
Cl
3ia
(^{13}C NMR, 100 MHz, $CDCl_3$)
80000
70000
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

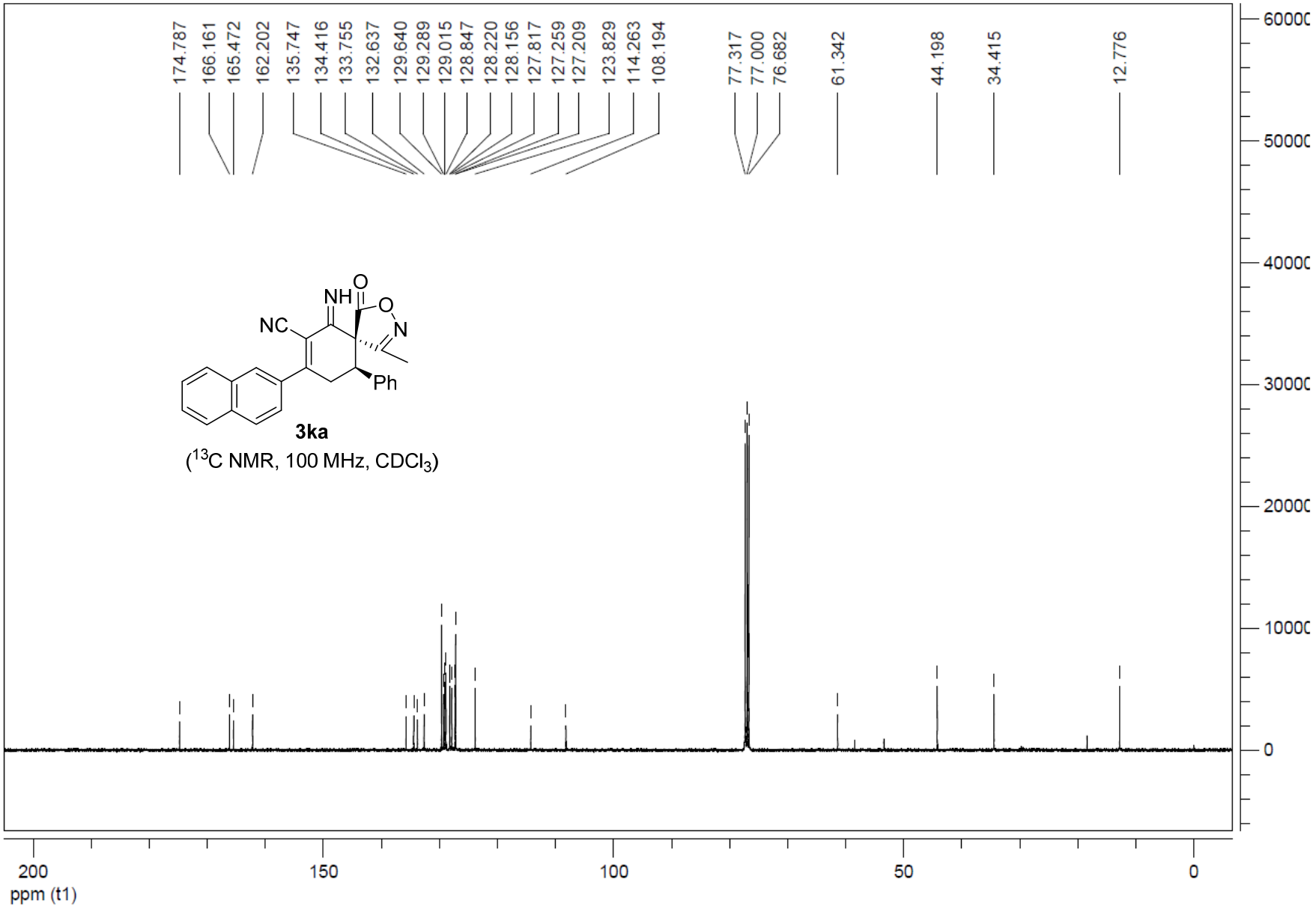

10.456
7.657
7.636
7.494
7.473
7.381
7.372
7.366
7.259
7.251
7.242
7.233
7.227
3.906
3.876
3.857
3.827
3.644
3.633
3.614
3.603
3.021
3.010
2.972
2.961
2.097
0.00000
NC
NH
O
O
N
Ph
Br
3ja
(1H NMR, 400 MHz, CDCl3)
0.96
2.00
3.00
2.26
1.00
1.00
1.00
3.00
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)

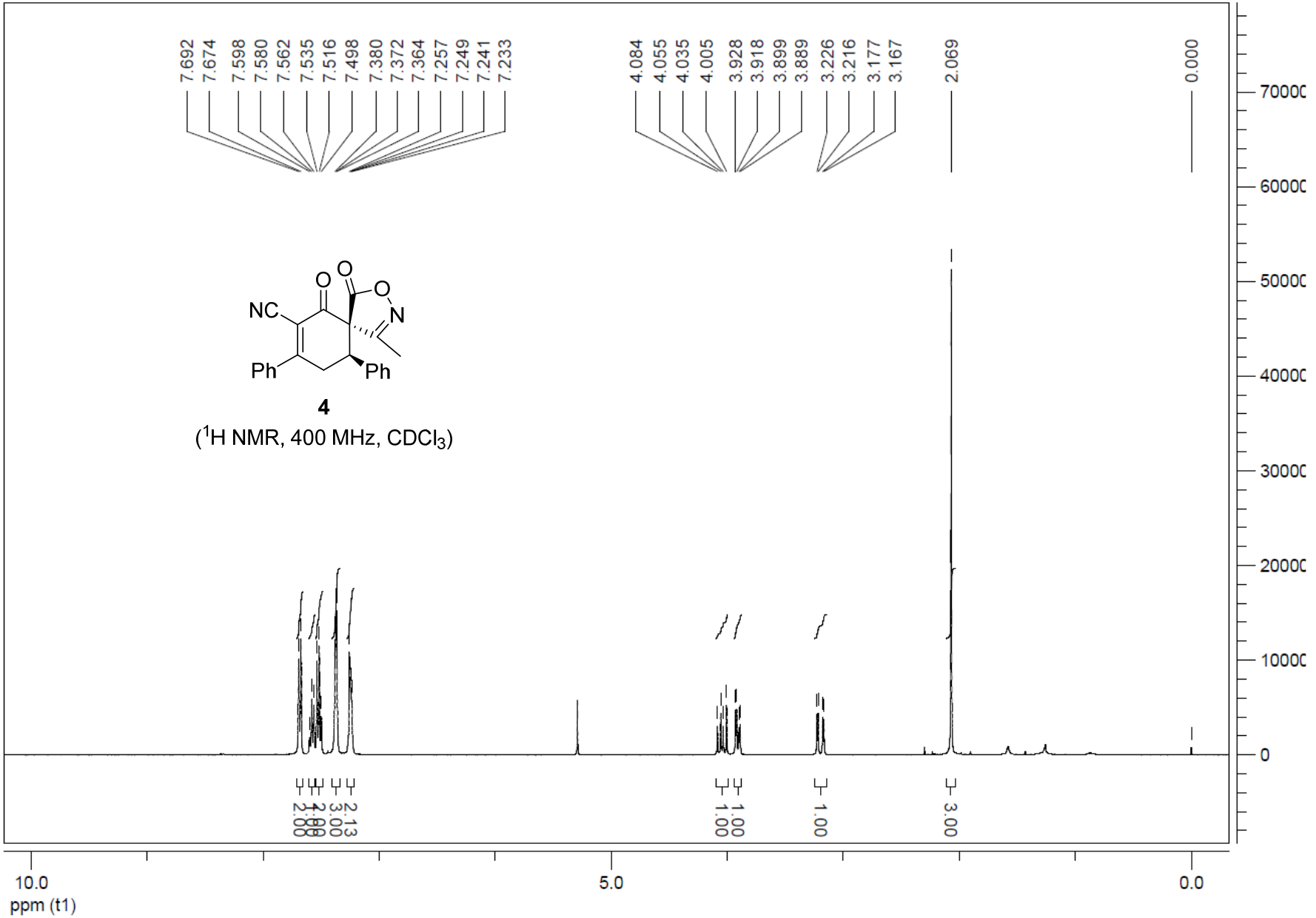

174.663
165.995
164.024
161.897
137.927
135.525
134.816
129.679
129.442
129.371
128.854
127.151
113.864
108.379
77.317
77.000
76.682
61.185
44.080
34.297
12.760
NH
O
O
N
NC
Ph
Br
3ja
(13C NMR, 100 MHz, CDCl3)
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

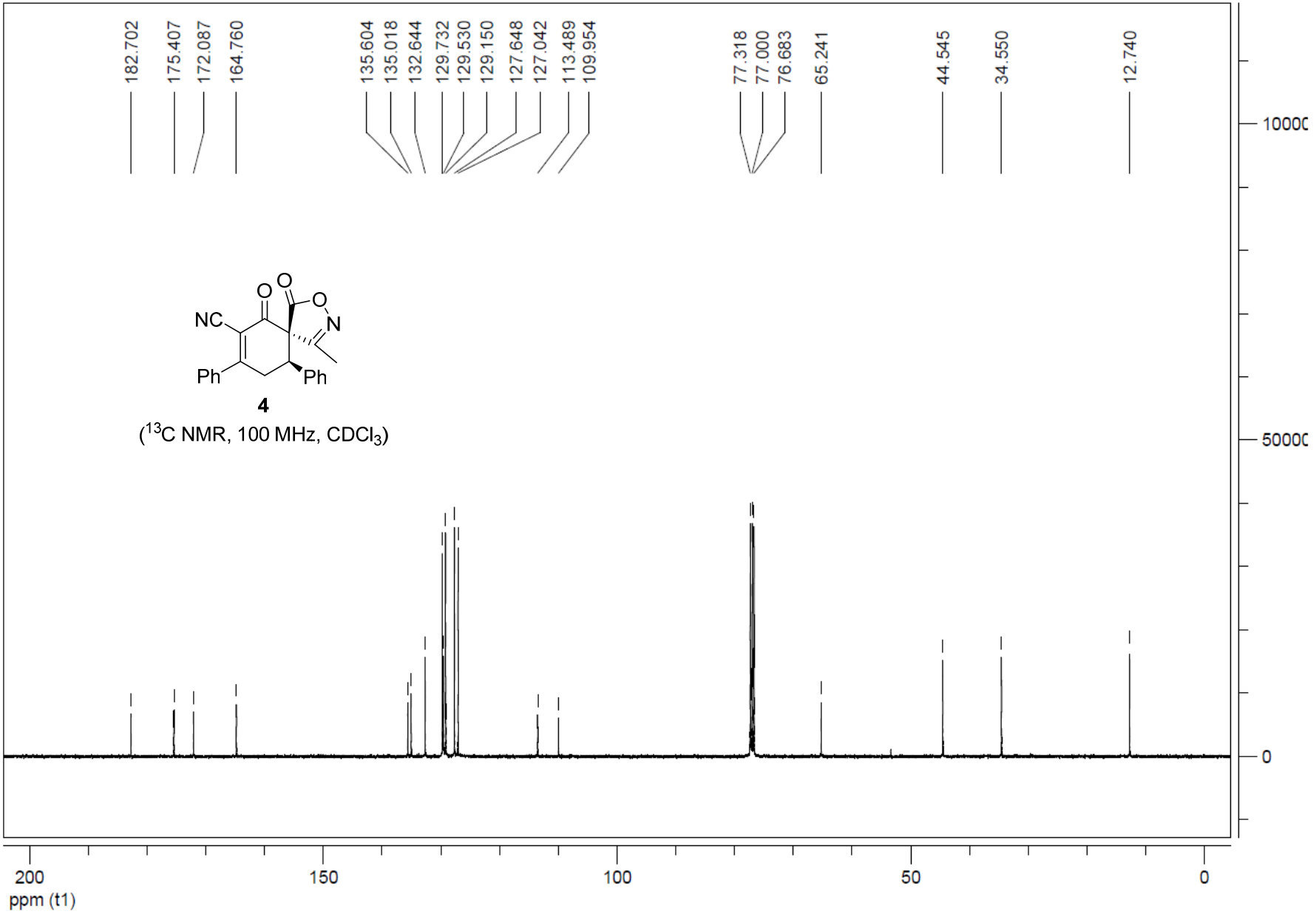


3ka

(^{1}H NMR, 400 MHz, $CDCl_3$)


174.787
166.161
165.472
162.202
135.747
134.416
133.755
132.637
129.640
129.289
129.015
128.847
128.220
128.156
127.817
127.259
127.209
123.829
114.263
108.194
77.317
77.000
76.682
61.342
44.198
34.415
12.776
NC
NH
O
O
N
Ph
3ka
(13C NMR, 100 MHz, CDCl3)
60000
50000
40000
30000
20000
10000
0
200
150
100
50
0
ppm (t1)

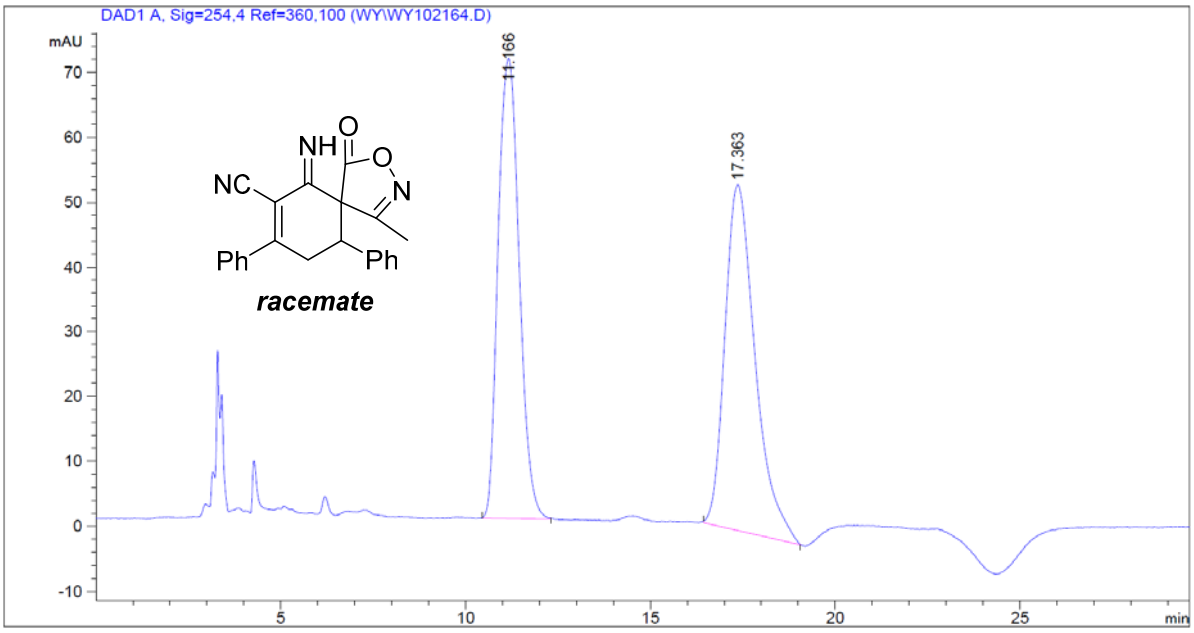

7.692
7.674
7.598
7.580
7.562
7.535
7.516
7.498
7.380
7.372
7.364
7.257
7.249
7.241
7.233
4.084
4.055
4.035
4.005
3.928
3.918
3.899
3.889
3.226
3.216
3.177
3.167
2.069
0.000
O
O
O
N
NC
Ph
Ph
4
(1H NMR, 400 MHz, CDCl3)
2.00
2.00
2.00
3.00
2.13
1.00
1.00
1.00
3.00
70000
60000
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)



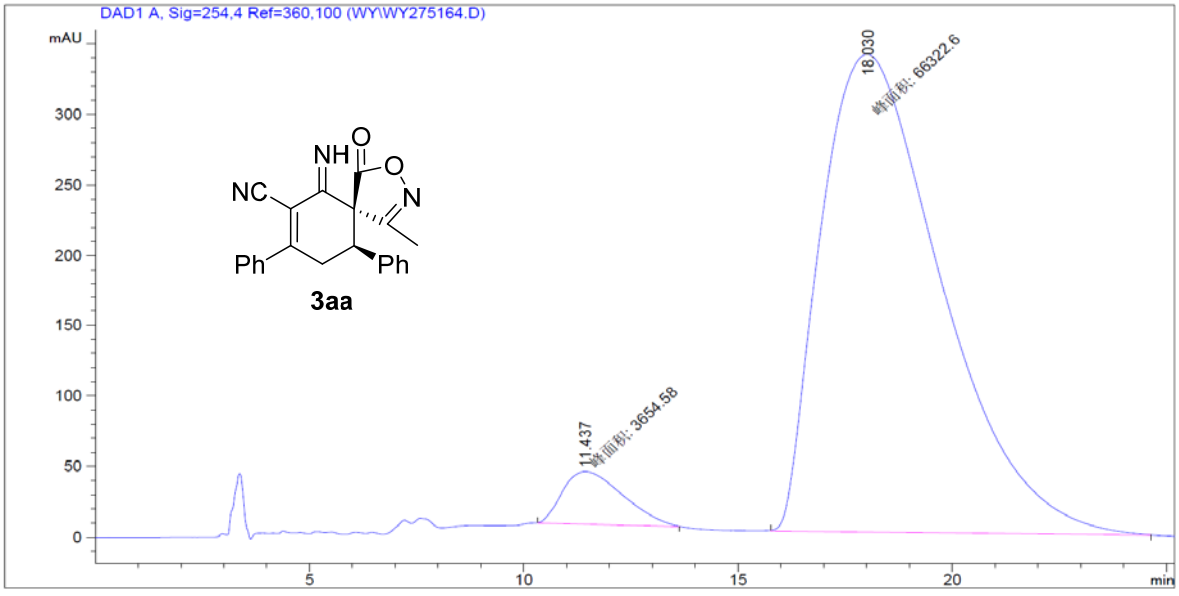
4

(^{13}C NMR, 100 MHz, $CDCl_3$)

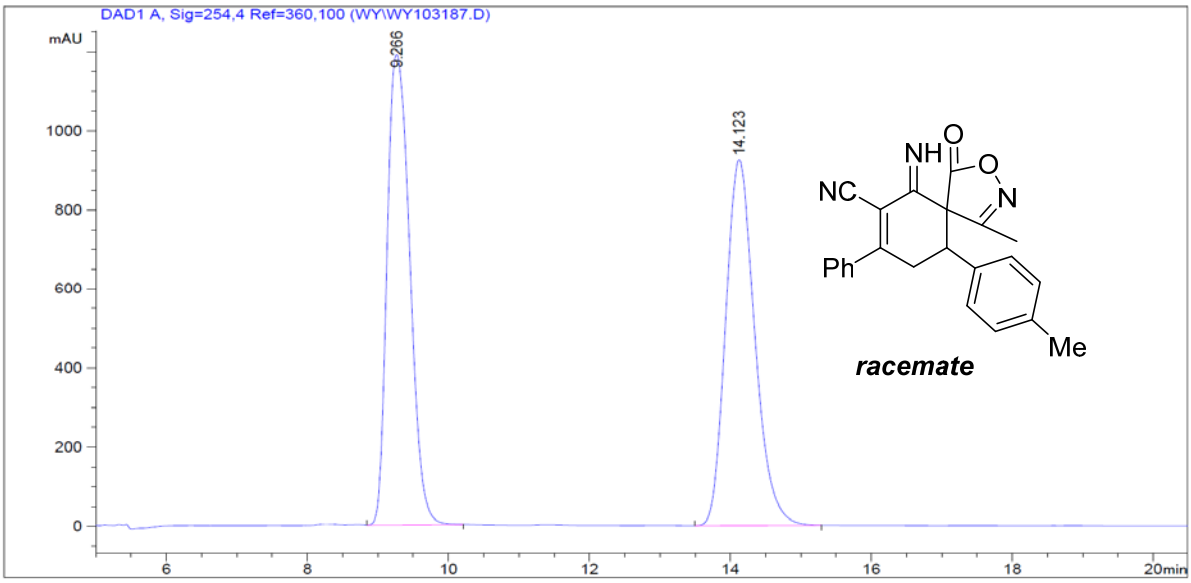
9. Copies of HPLC chromatograms



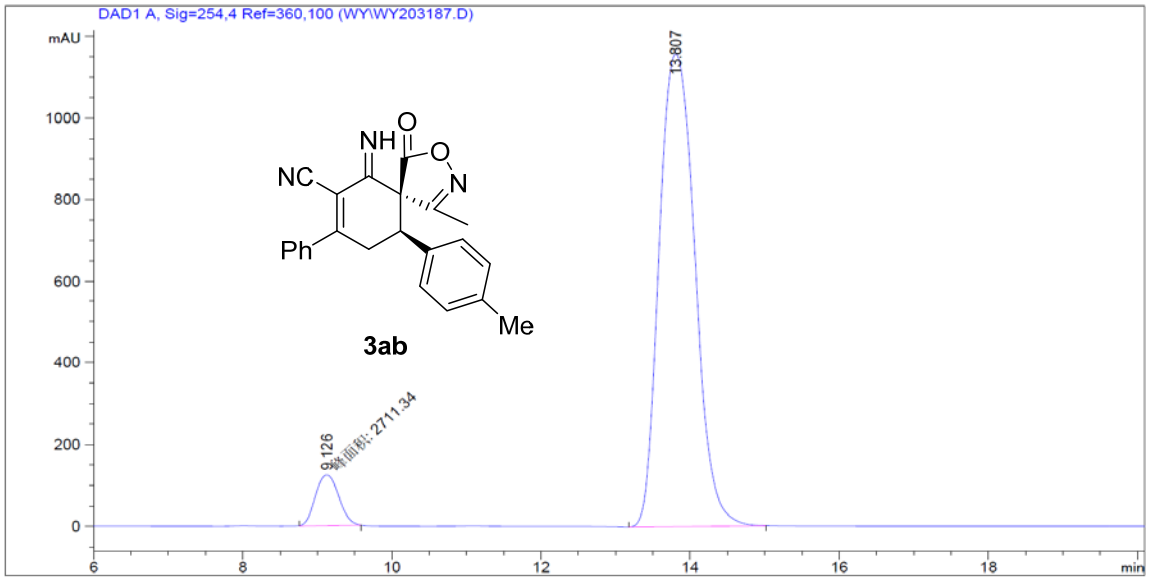
Peak #	RetTime Type [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.166 BB	0.6332	2815.93115	70.93016	48.1703
2	17.363 BB	0.8205	3029.85059	53.35348	51.8297



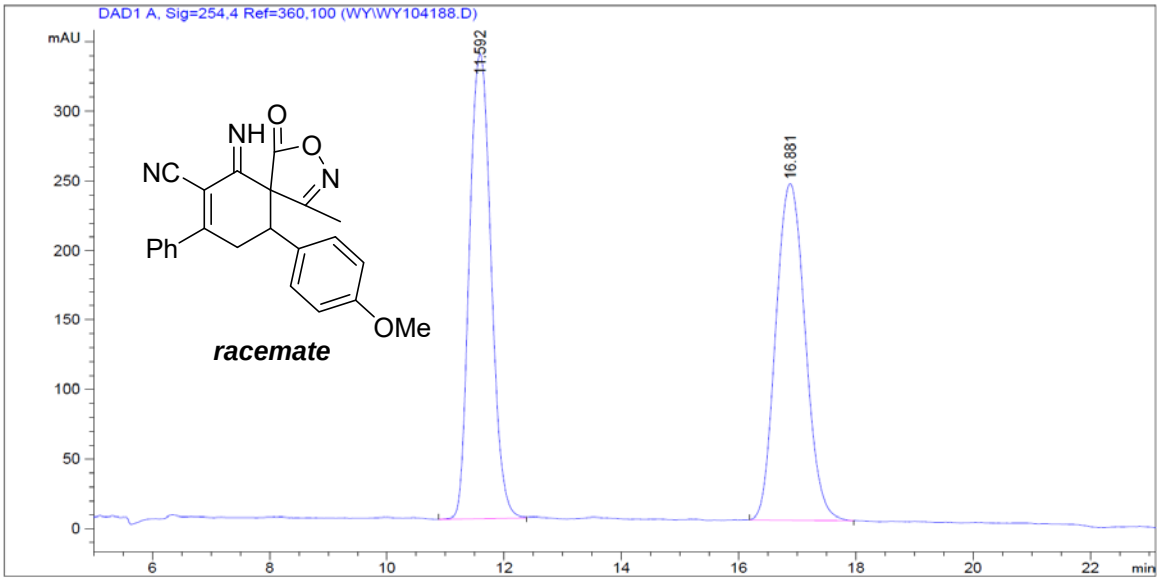
Peak #	RetTime Type [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.437 MM	1.6337	3654.58179	37.28378	5.2225
2	18.030 MM	3.2602	6.63226e4	339.05377	94.7775



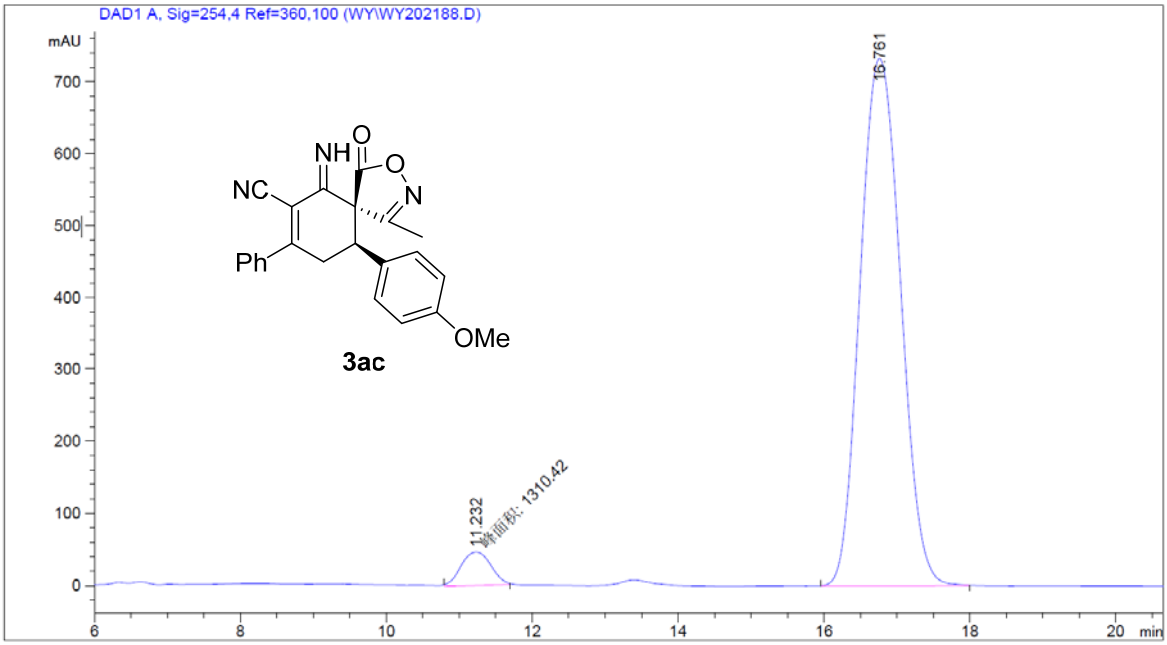
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.266	VB	0.3606	2.65624e4	1189.11438	50.0378
2	14.123	BB	0.4426	2.65223e4	924.82520	49.9622



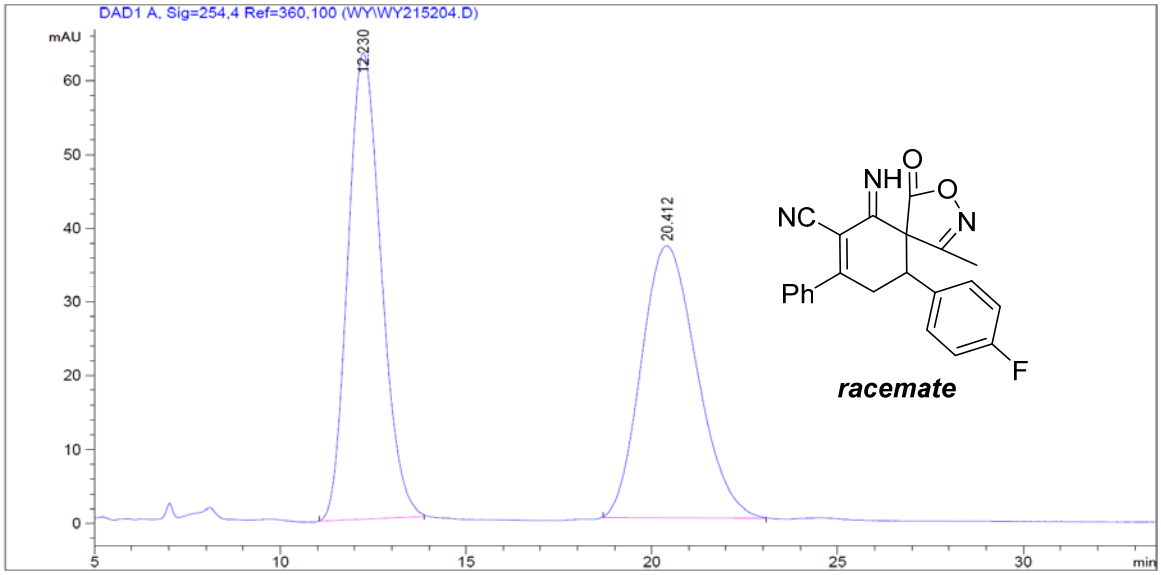
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.126	MM	0.3621	2711.34058	124.80051	6.5793
2	13.807	BB	0.5462	3.84990e4	1157.08606	93.4207



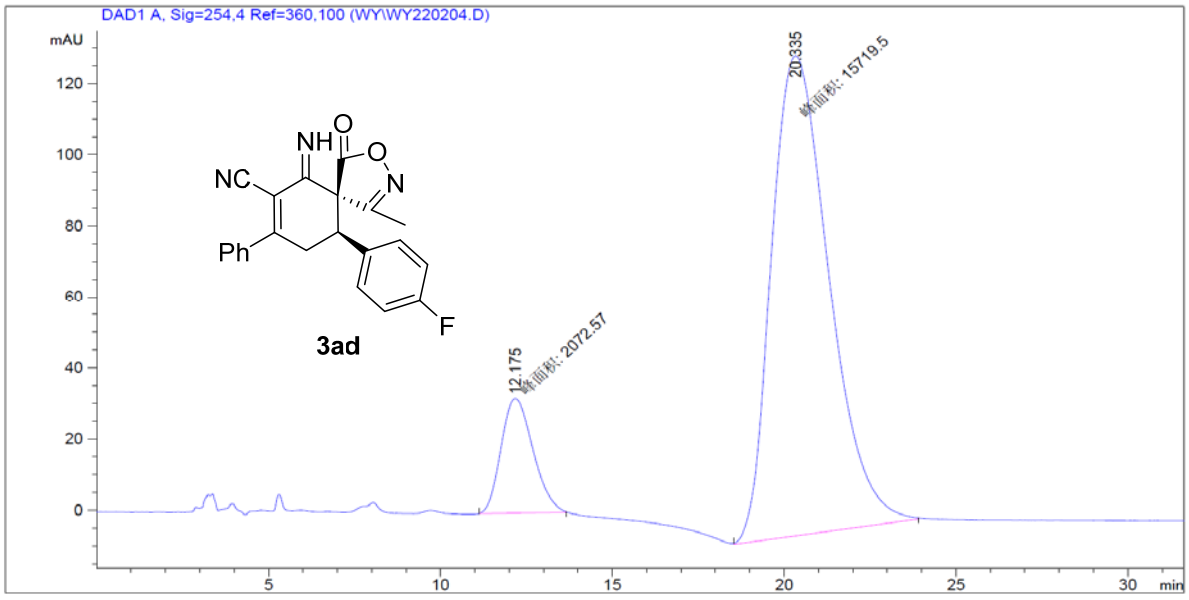
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.592	BB	0.4095	8573.58496	334.01581	50.4193
2	16.881	BB	0.5566	8430.98828	241.92810	49.5807



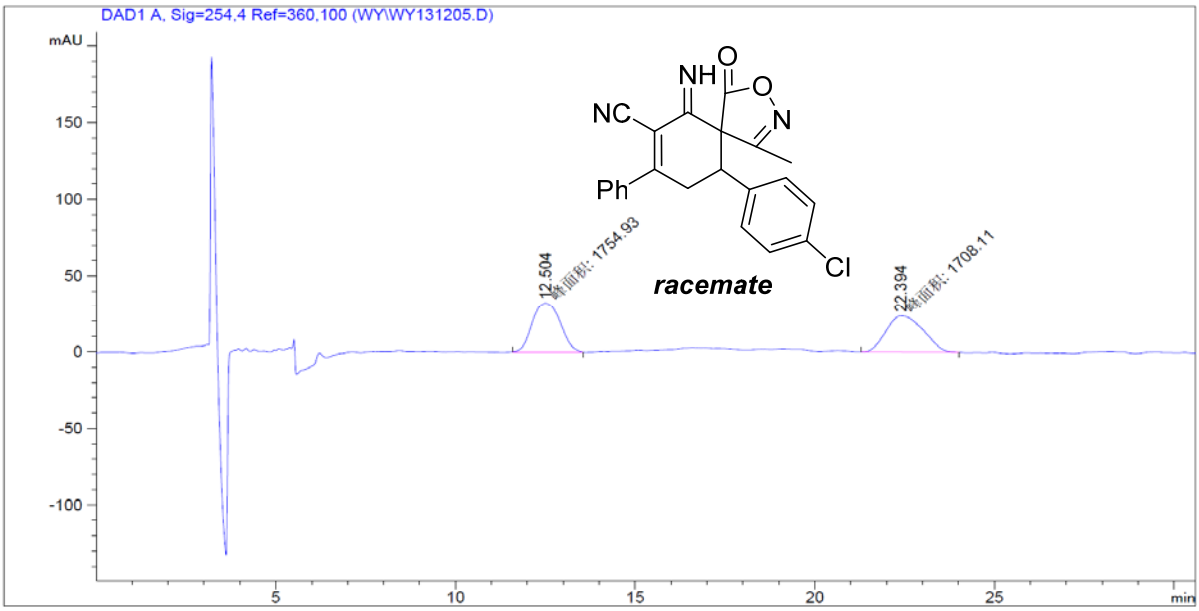
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.232	MM	0.4715	1310.42053	46.32589	4.4421
2	16.761	BB	0.6150	2.81898e4	732.53064	95.5579



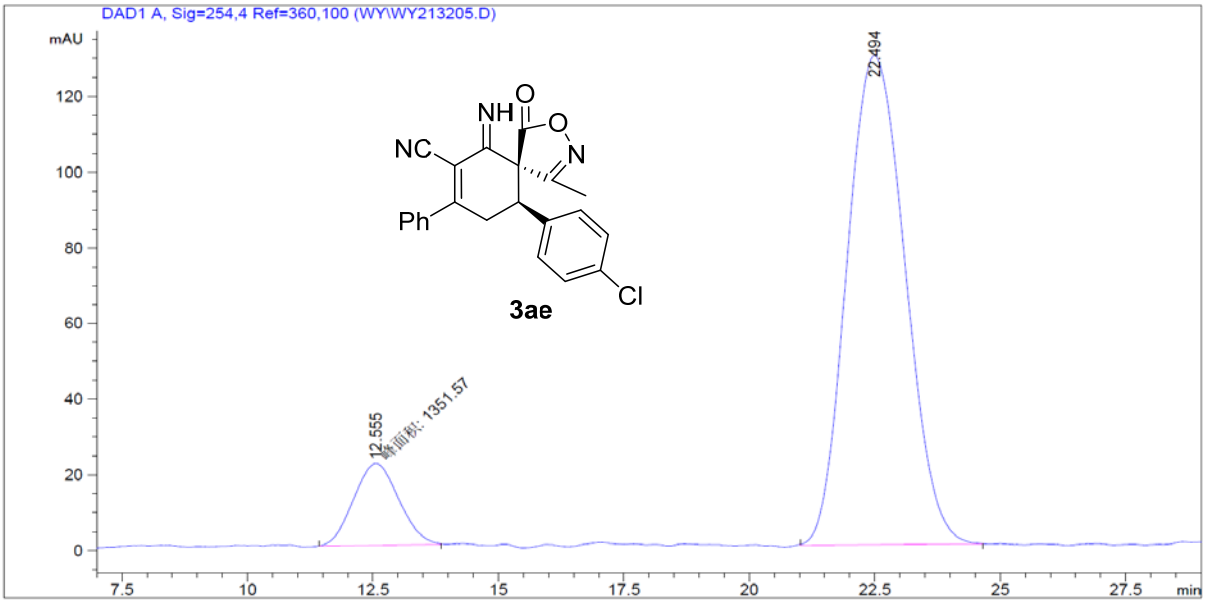
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.230	BB	0.9450	3939.16333	63.21283	50.7009
2	20.412	BB	1.2288	3830.25317	36.90601	49.2991



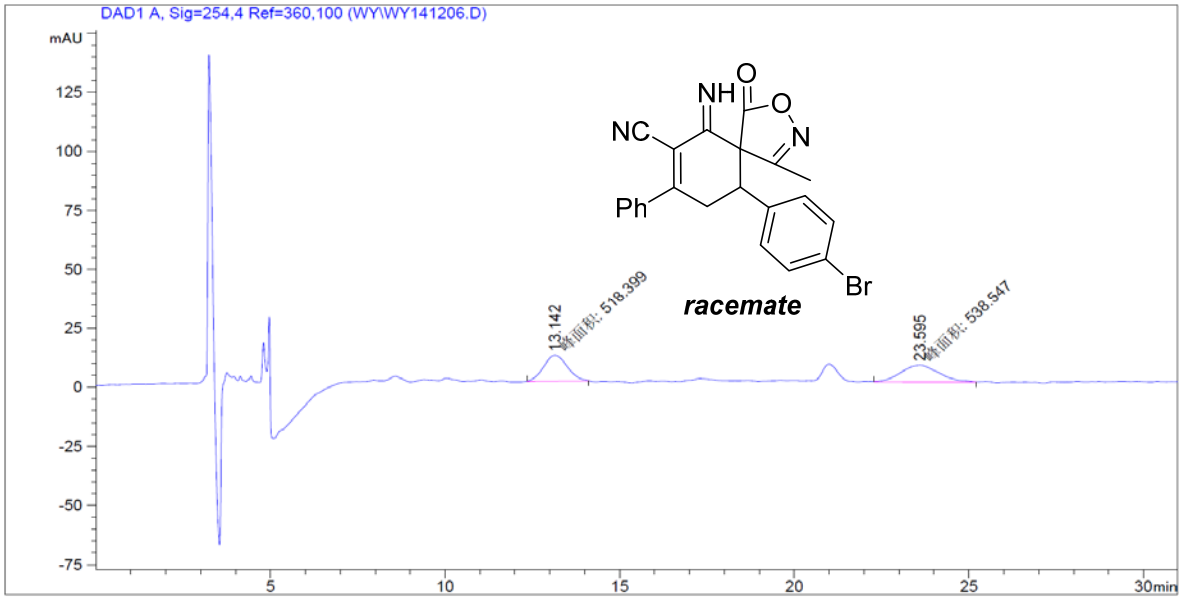
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.175	MM	1.0750	2072.56763	32.13149	11.6488
2	20.335	MM	1.9425	1.57195e4	134.87367	88.3512



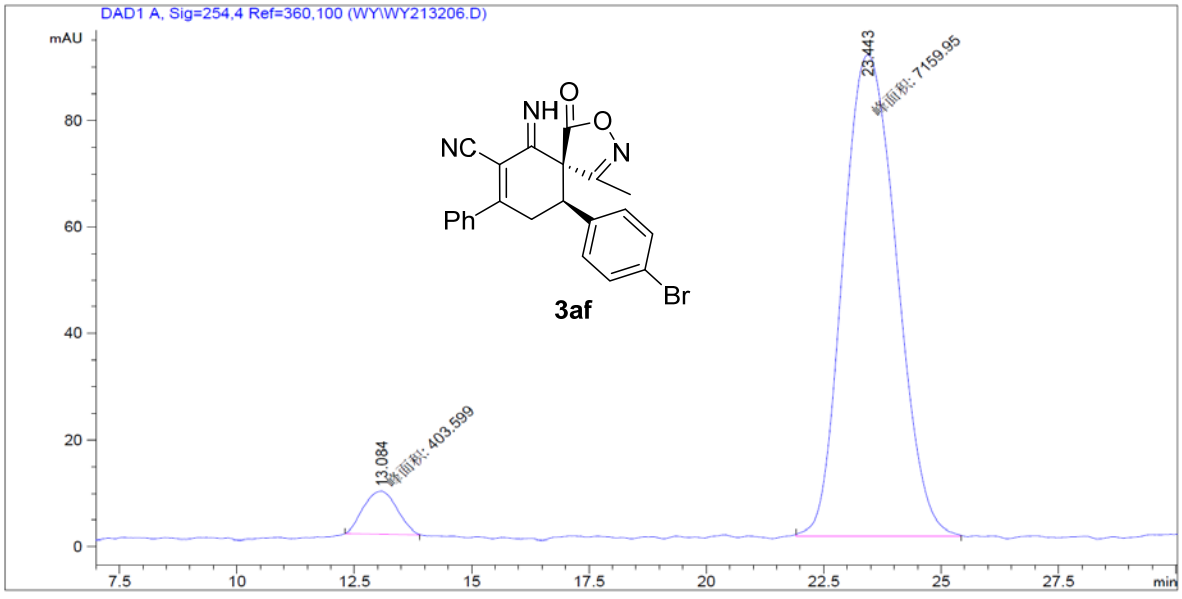
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.504	MM	0.9041	1754.93445	32.35089	50.6760
2	22.394	MM	1.1973	1708.11206	23.77815	49.3240



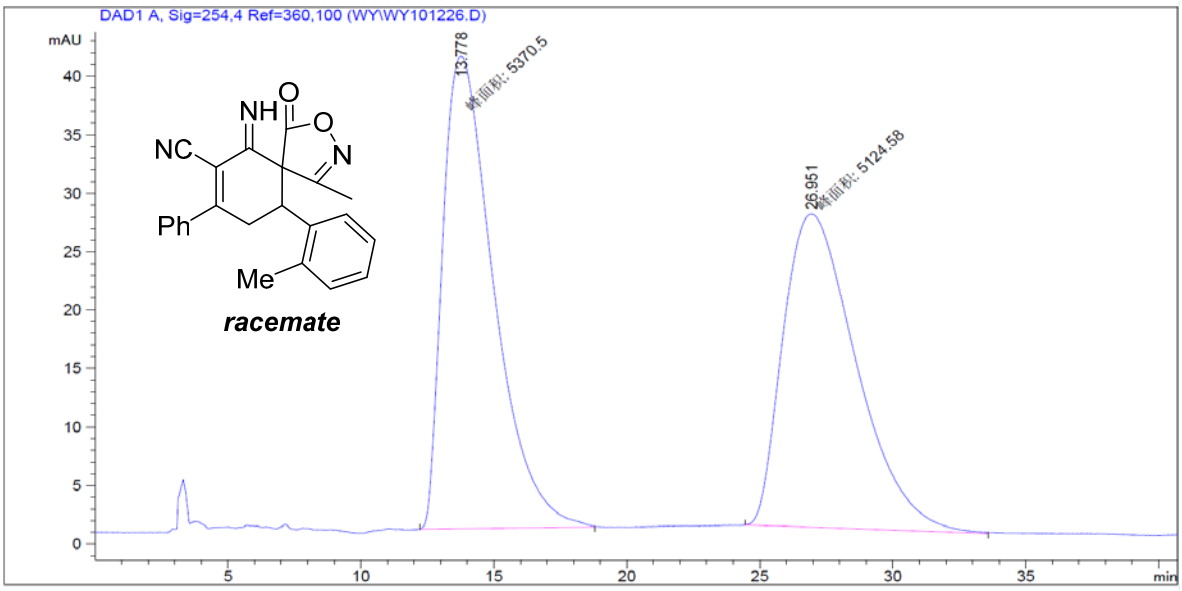
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.555	MM	1.0419	1351.57410	21.62125	11.5087
2	22.494	BB	1.2618	1.03923e4	129.28760	88.4913



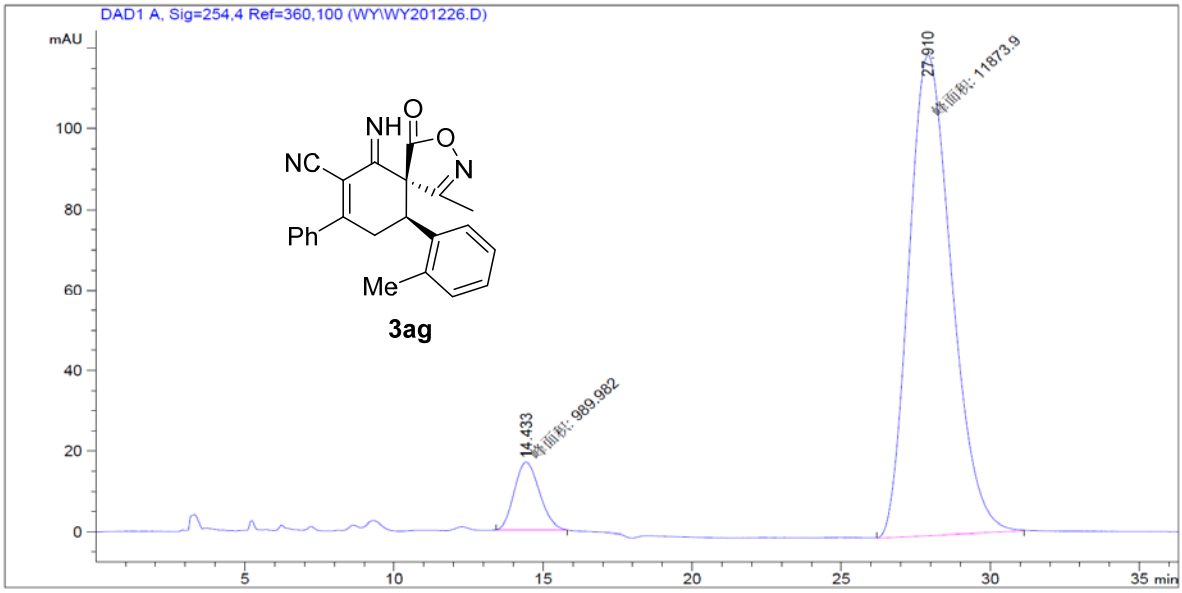
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.142	MM	0.7848	518.39899	11.00887	49.0469
2	23.595	MM	1.2519	538.54657	7.16989	50.9531



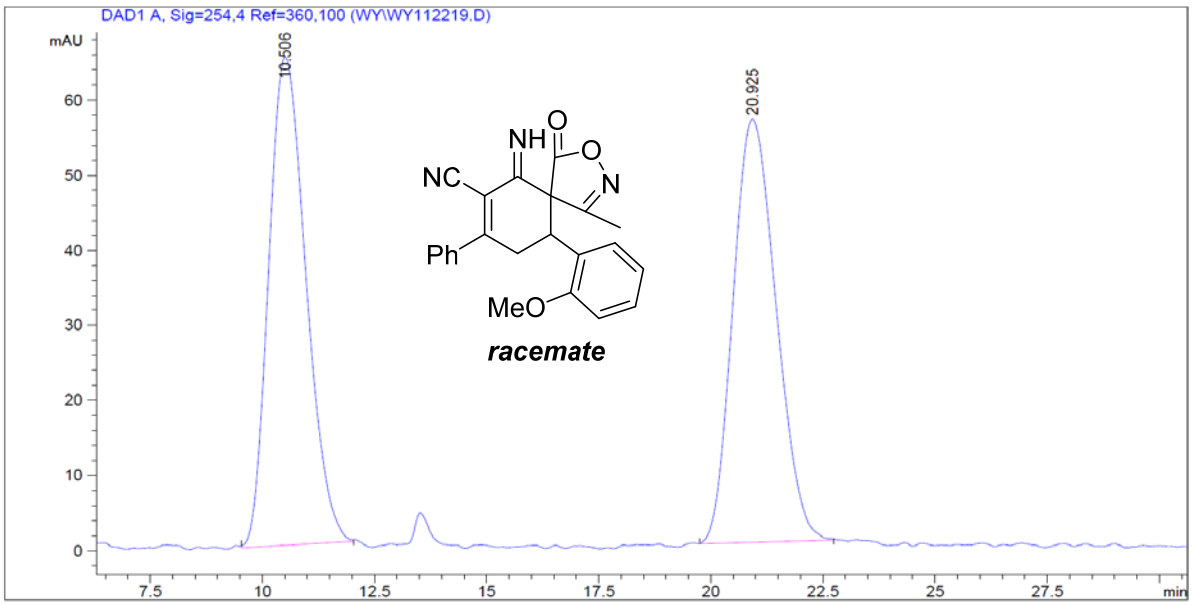
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.084	MM	0.8282	403.59927	8.12233	5.3361
2	23.443	MM	1.3210	7159.95312	90.33161	94.6639



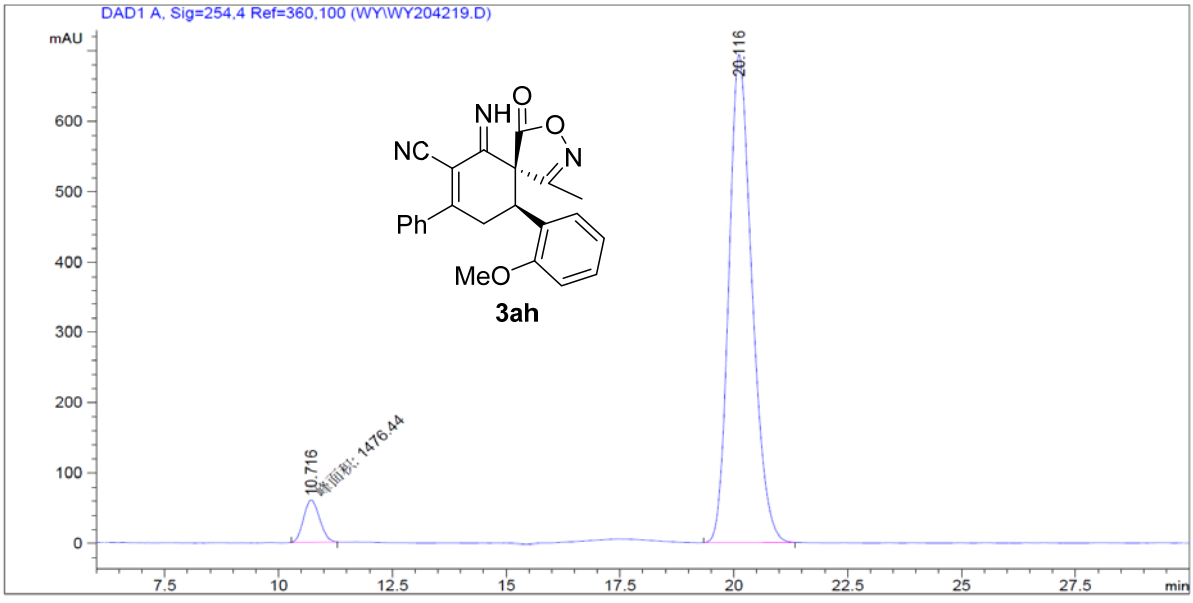
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.778	MM	2.2141	5370.49854	40.42559	51.1716
2	26.951	MM	3.1849	5124.57813	26.81724	48.8284



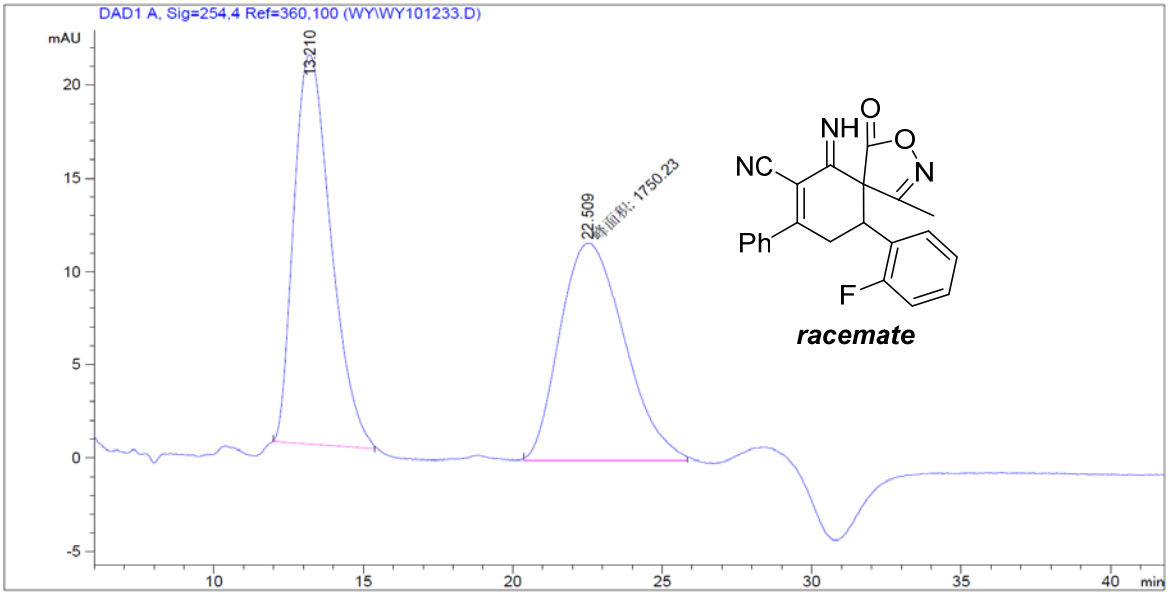
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.433	MM	0.9841	989.98224	16.76697	7.6959
2	27.910	MM	1.6618	1.18739e4	119.08746	92.3041



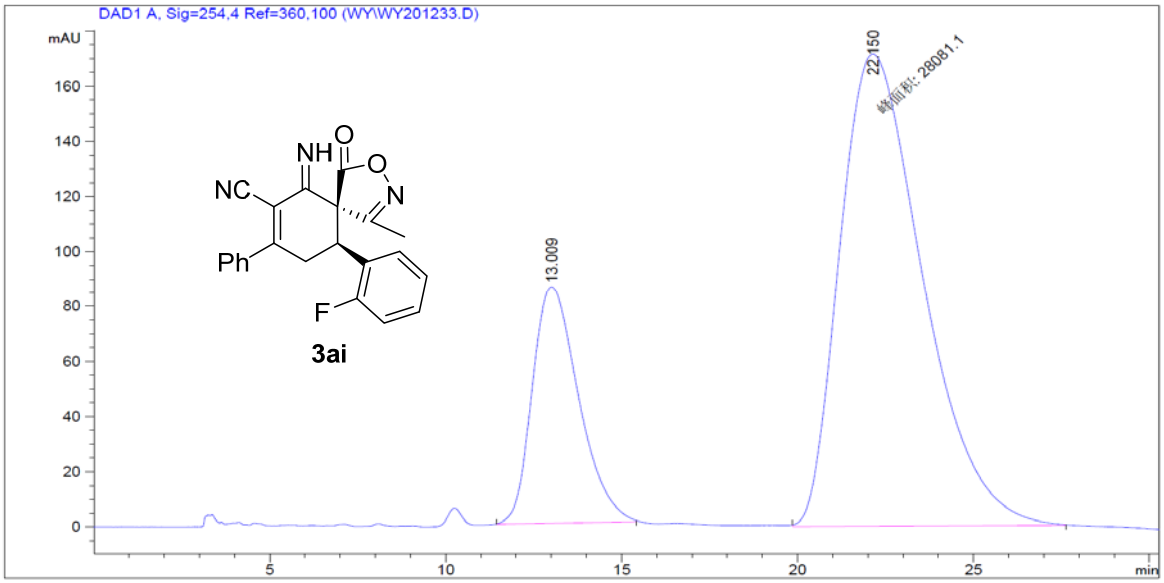
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.506	BB	0.8436	3750.07642	64.95065	49.9202
2	20.925	BB	0.9255	3762.06934	56.30492	50.0798



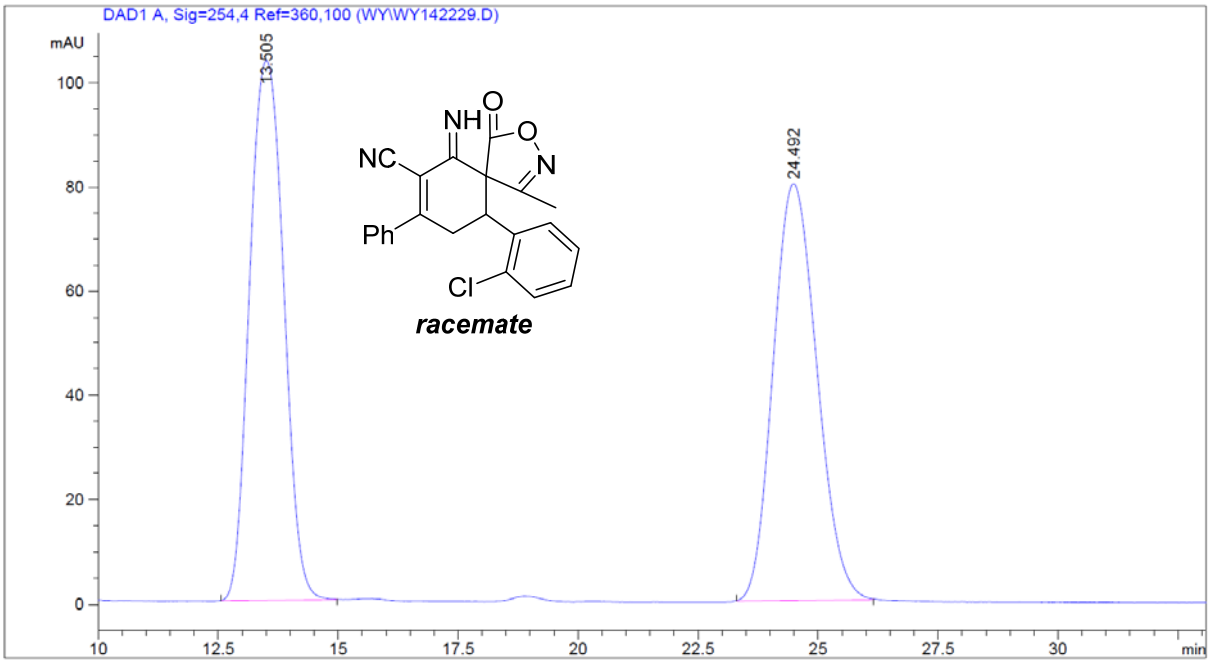
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.716	MM	0.4106	1476.44458	59.92375	5.6845
2	20.116	BB	0.5341	2.44967e4	693.51447	94.3155



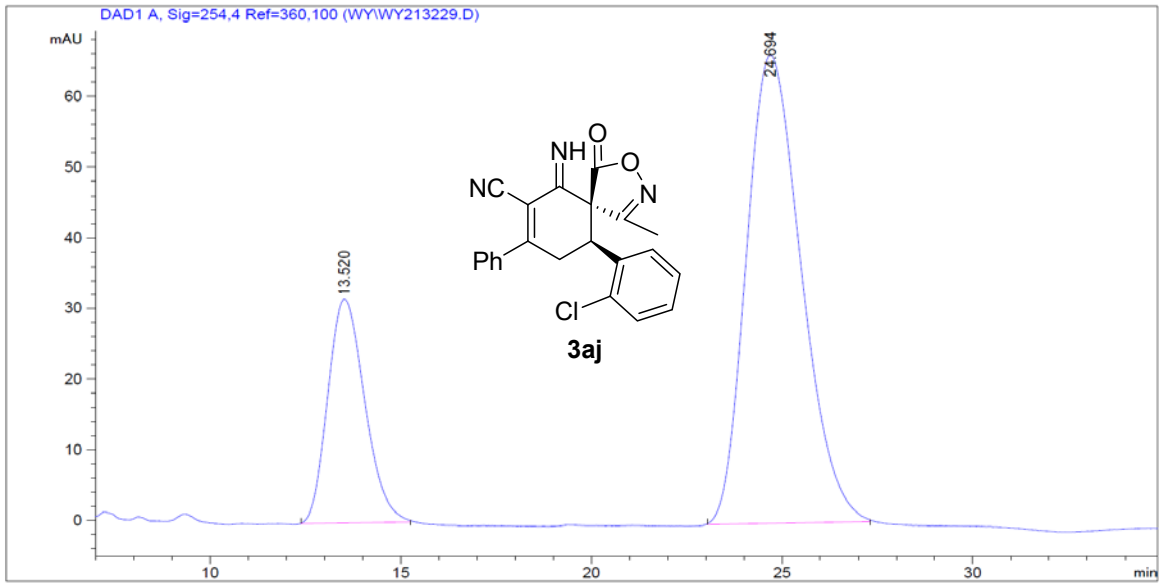
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.210	BB	1.0215	1803.43787	20.88284	50.7486
2	22.509	MM	2.5023	1750.23059	11.65732	49.2514



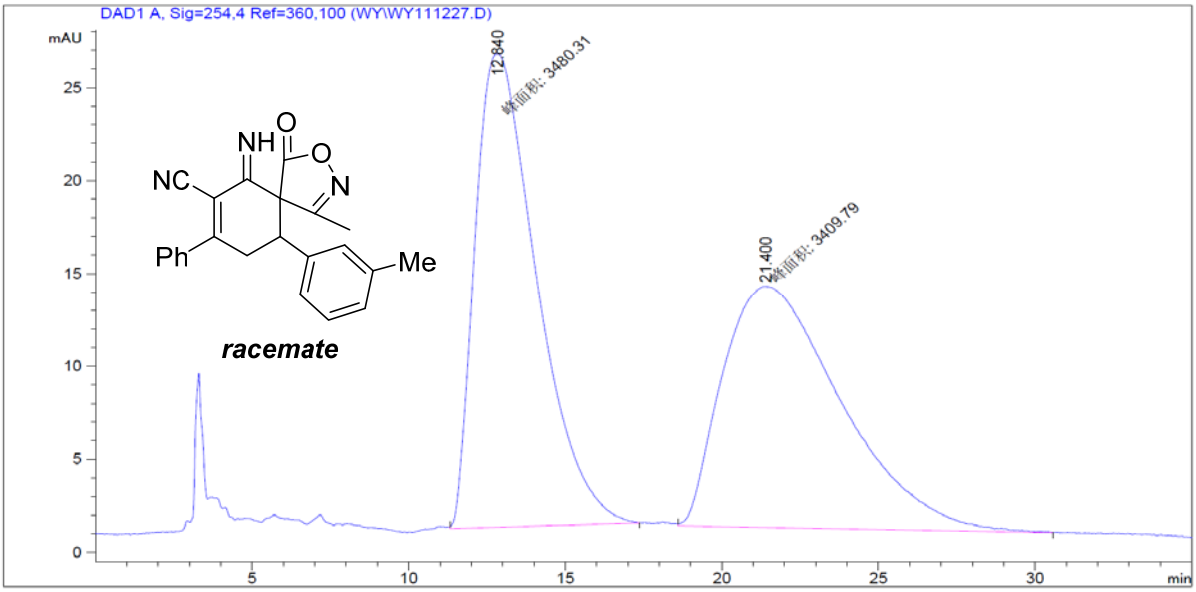
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.009	BB	1.3432	7849.12109	85.96470	21.8454
2	22.150	MM	2.7302	2.80811e4	171.42064	78.1546



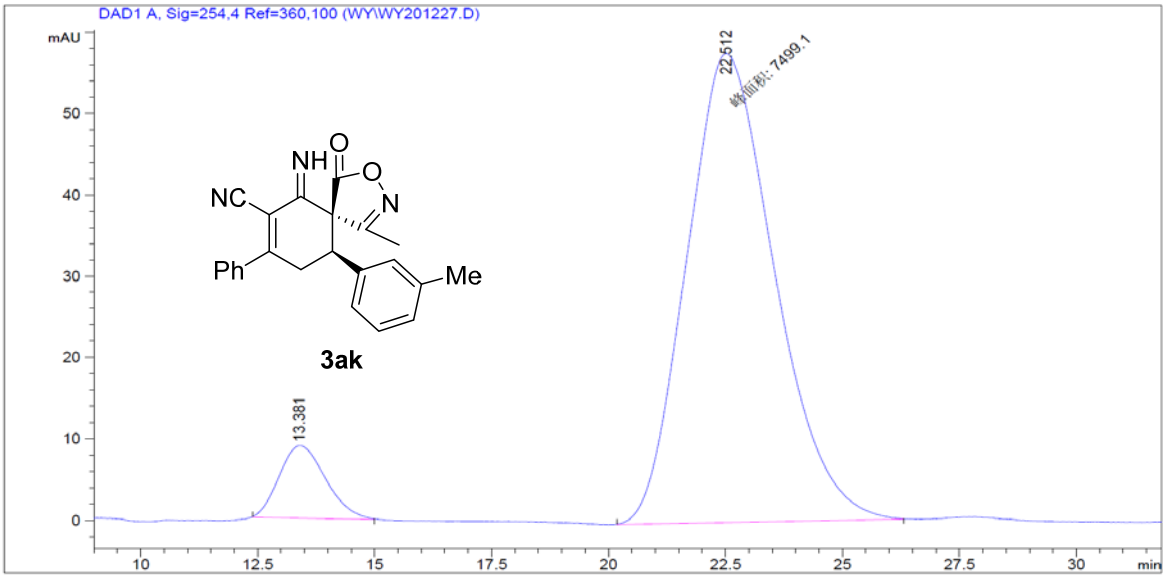
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.505	BB	0.7978	5110.86914	103.55353	50.2741
2	24.492	BB	0.9858	5055.13623	79.93973	49.7259



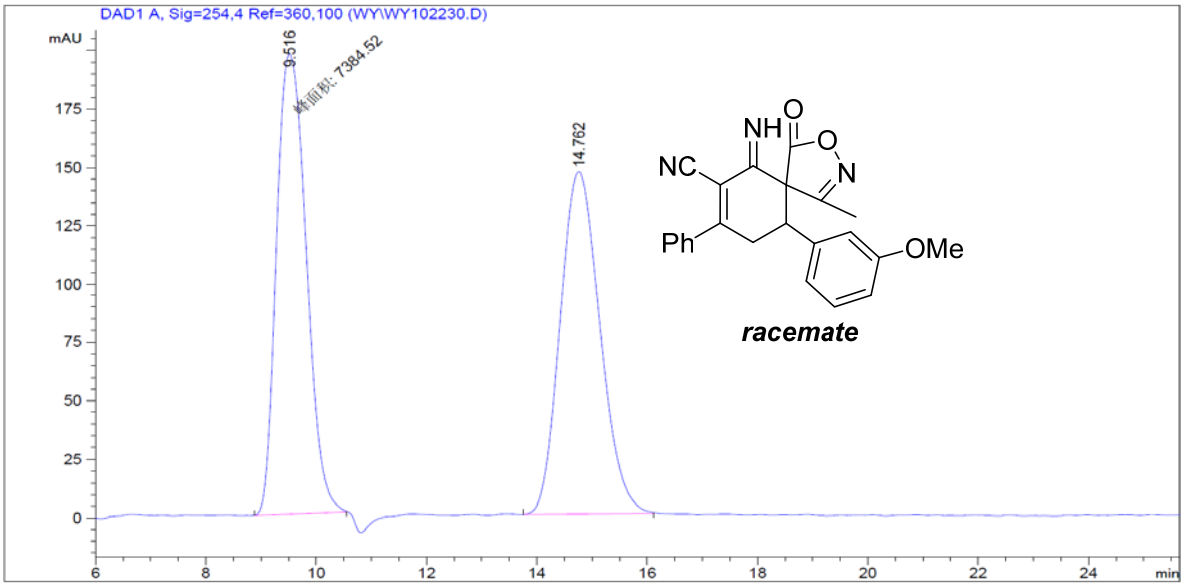
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.520	BB	0.9909	2137.66016	31.69368	24.3750
2	24.694	BB	1.3859	6632.23584	66.25448	75.6250



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.840	MM	2.2804	3480.31372	25.43592	50.5118
2	21.400	MM	4.3786	3409.78735	12.97886	49.4882



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.381	BB	0.8169	610.55951	8.87215	7.5288
2	22.512	MM	2.1703	7499.09521	57.59002	92.4712



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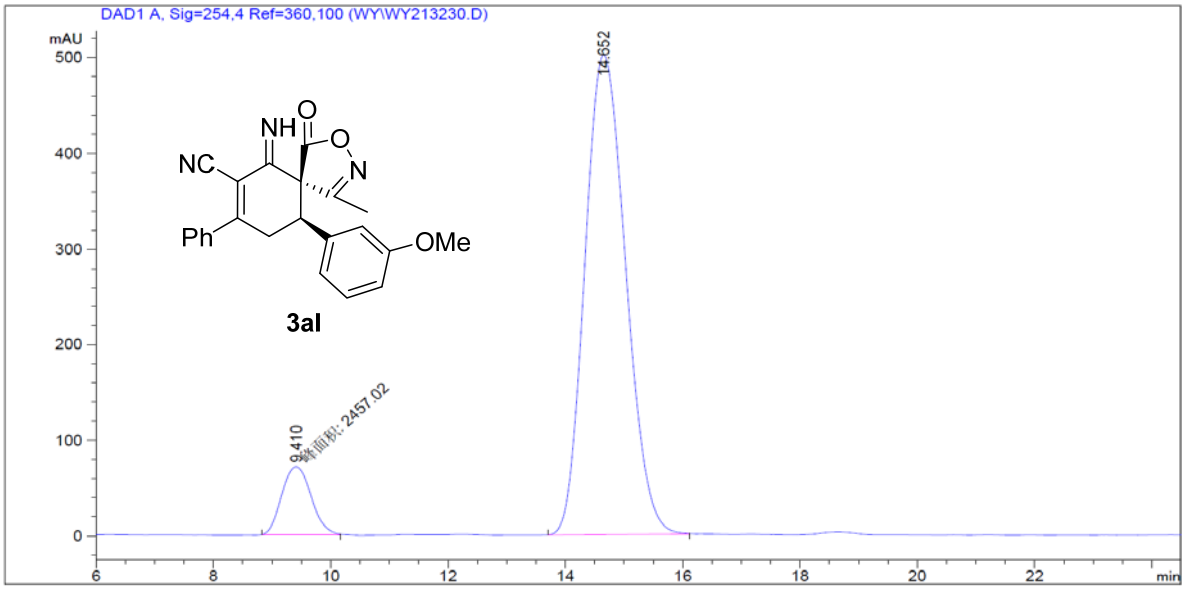
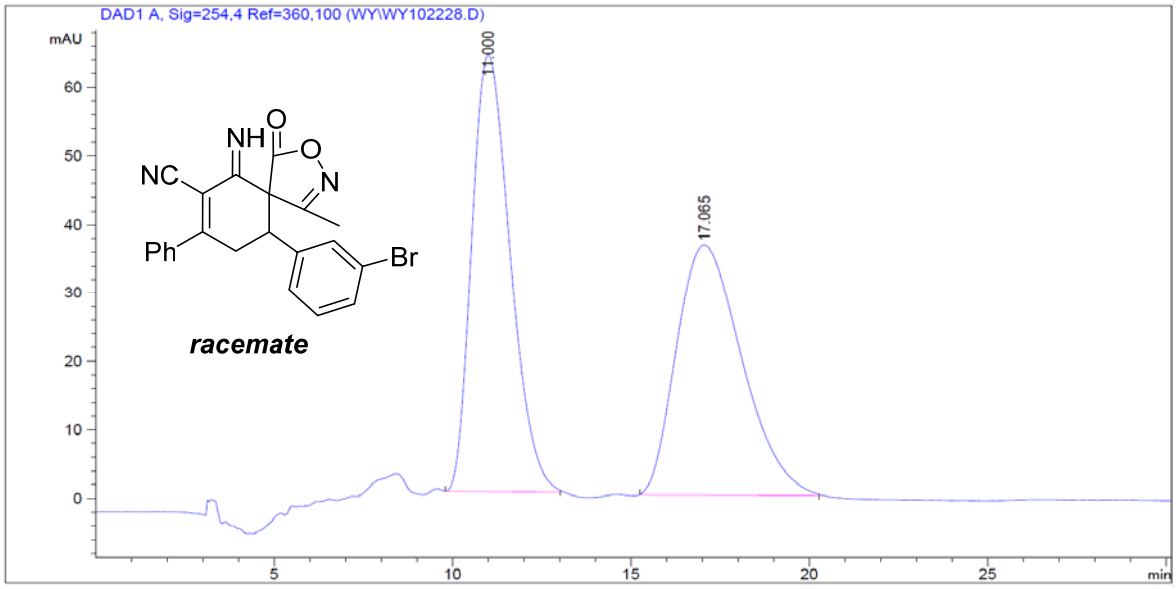
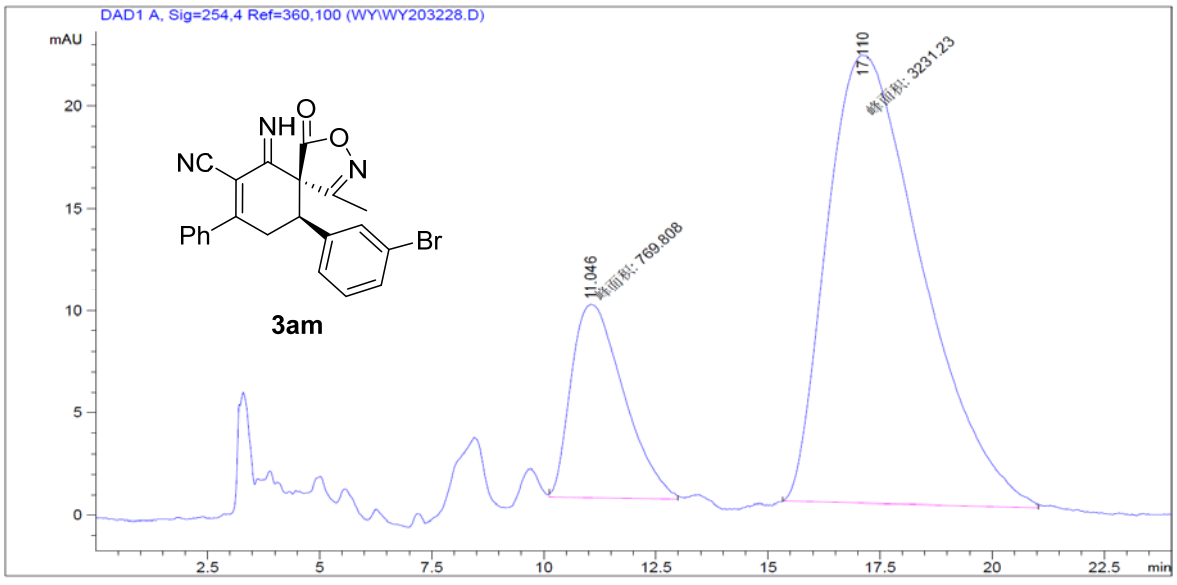
1	9.516	MM	0.6254	7384.52002	196.78851	50.1426
2	14.762	BB	0.7661	7342.51074	146.65277	49.8574



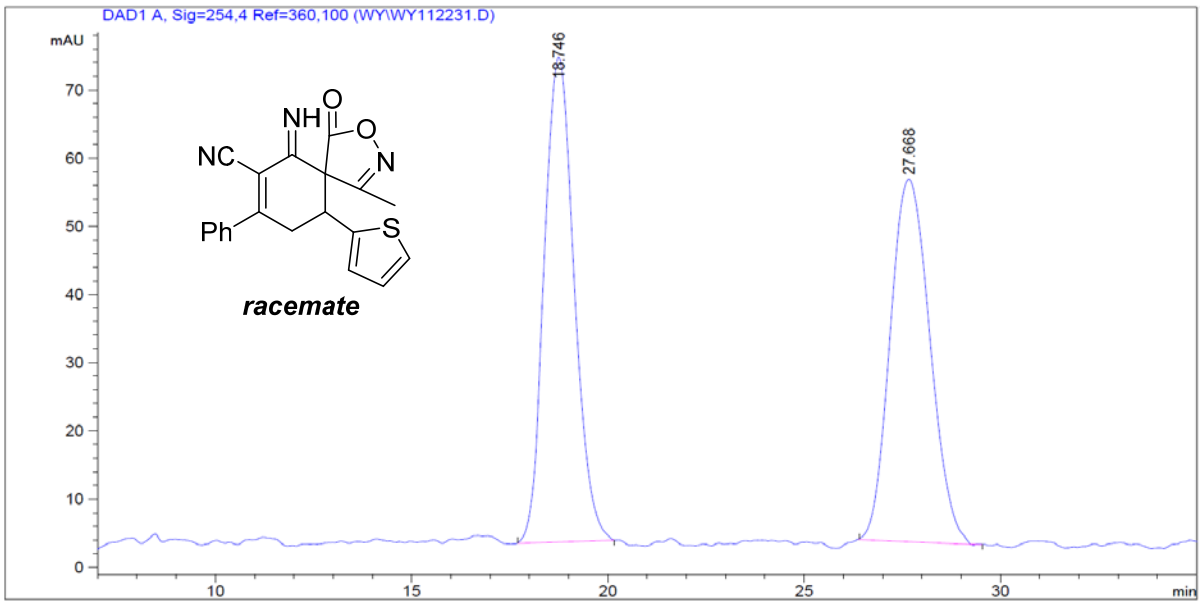
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.410	MM	0.5775	2457.01978	70.90916	9.2064
2	14.652	BB	0.7635	2.42313e4	501.66245	90.7936



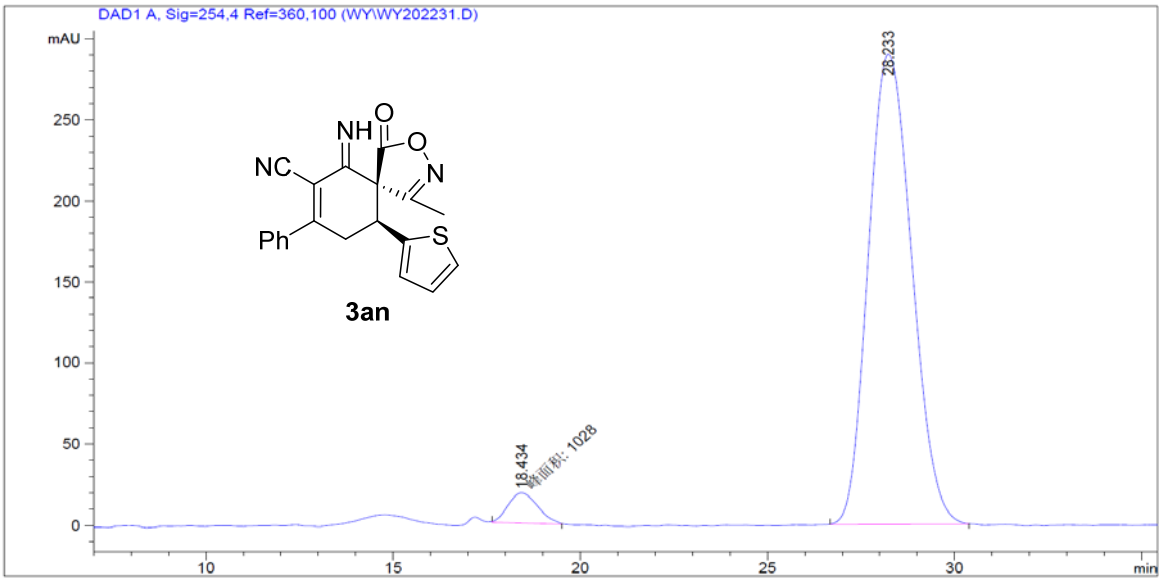
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.000	BB	1.1120	4775.97949	63.75285	50.6707
2	17.065	BB	1.4995	4649.54980	36.51720	49.3293



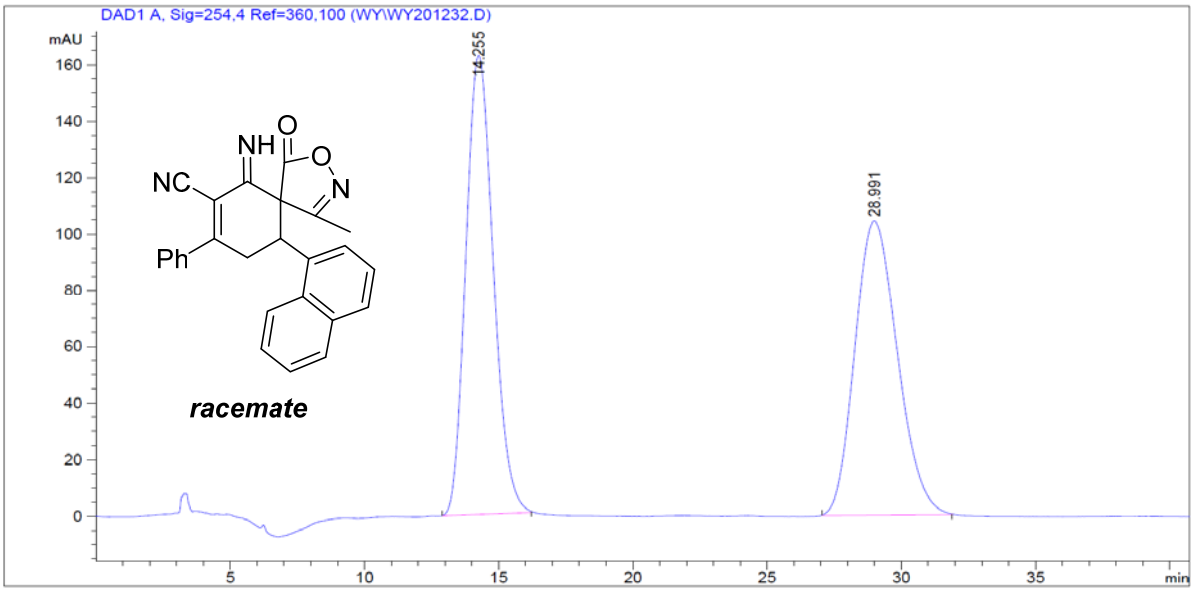
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.046	MM	1.3560	769.80768	9.46145	19.2402
2	17.110	MM	2.4629	3231.22607	21.86613	80.7598



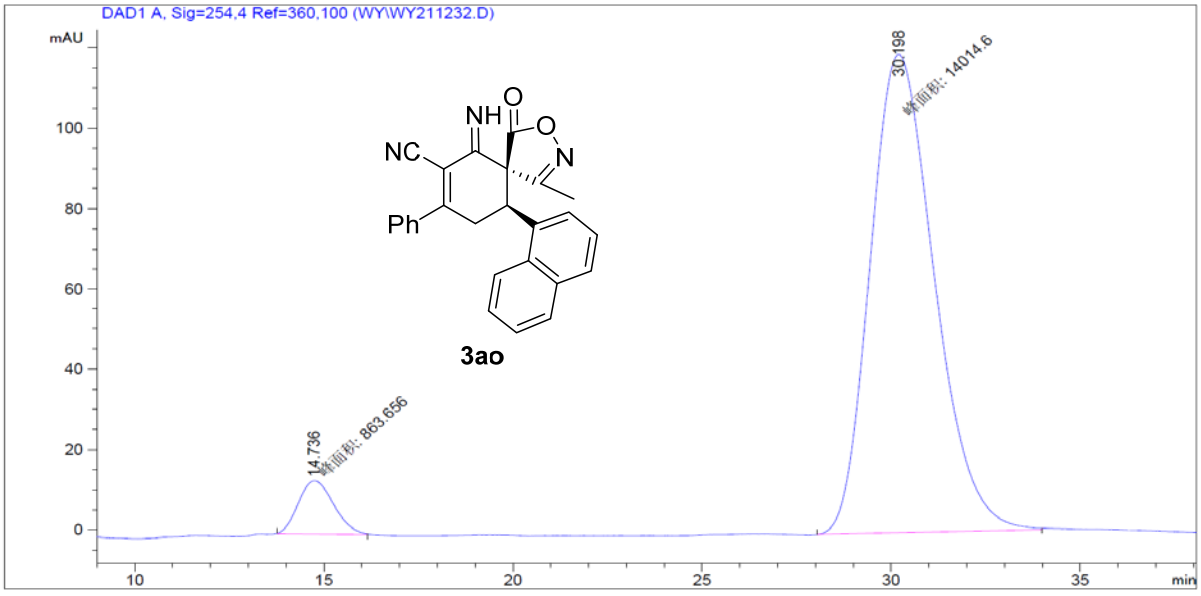
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.746	BB	0.8311	3774.50073	71.12998	50.2210
2	27.668	BB	0.9306	3741.28711	53.18829	49.7790



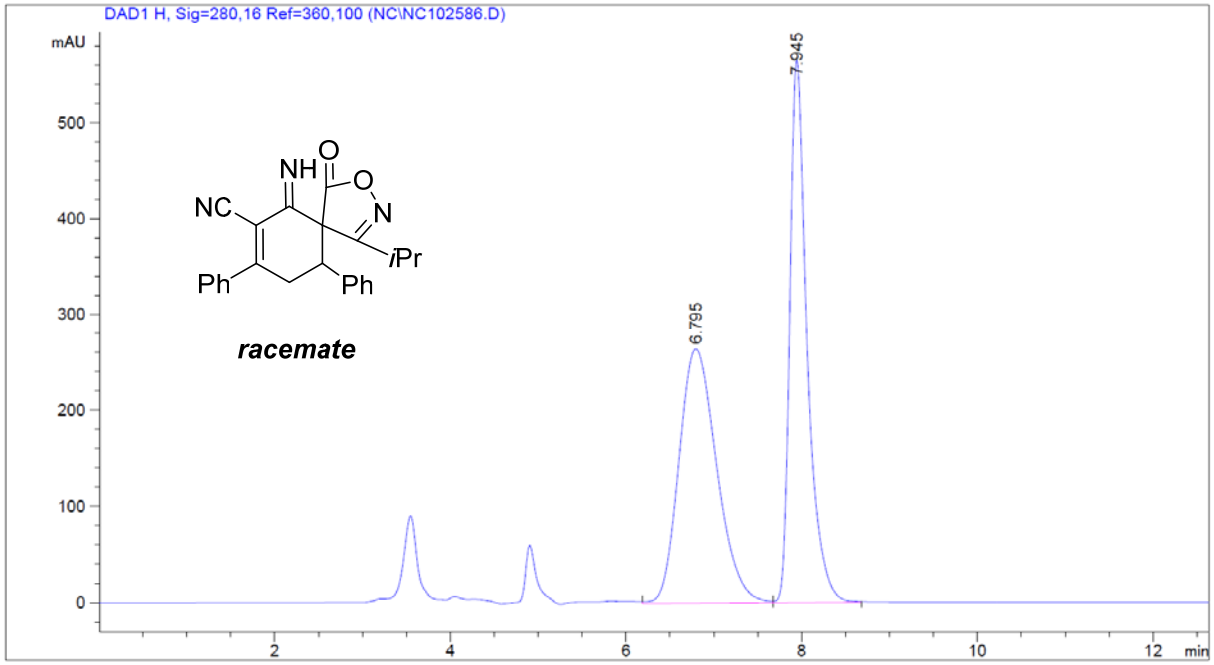
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.434	MM	0.9180	1028.00427	18.66287	4.2124
2	28.233	BB	1.2591	2.33764e4	289.78394	95.7876



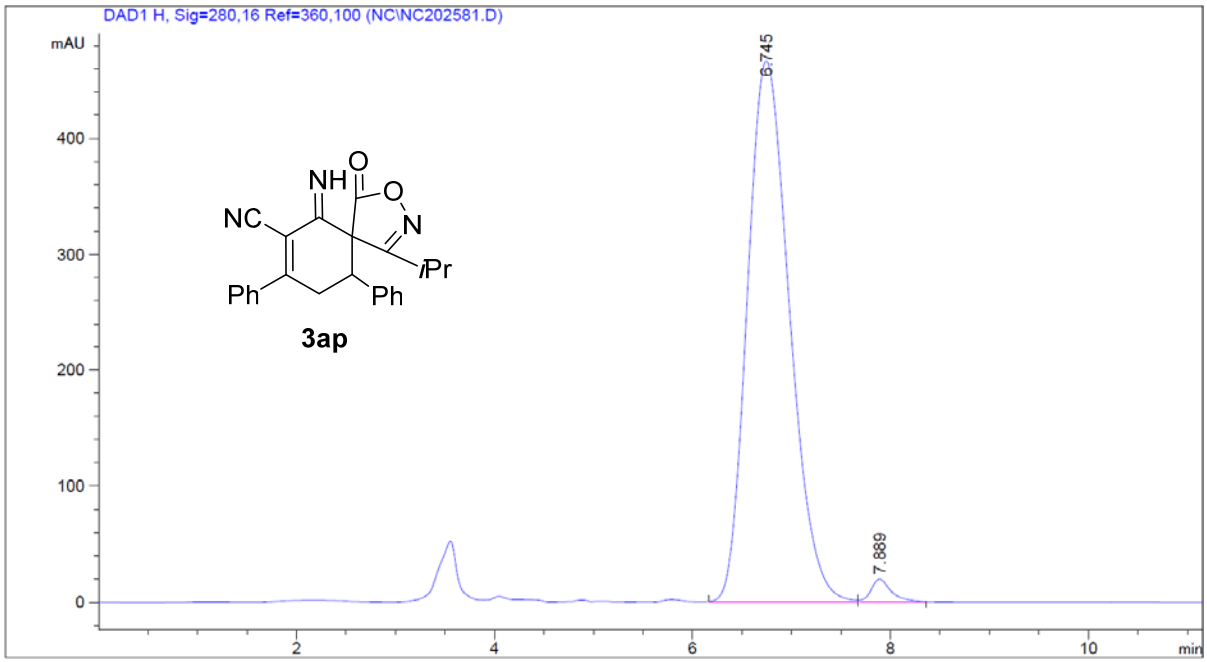
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.255	BB	1.1000	1.15731e4	162.66670	50.1812
2	28.991	BB	1.5501	1.14895e4	104.22237	49.8188



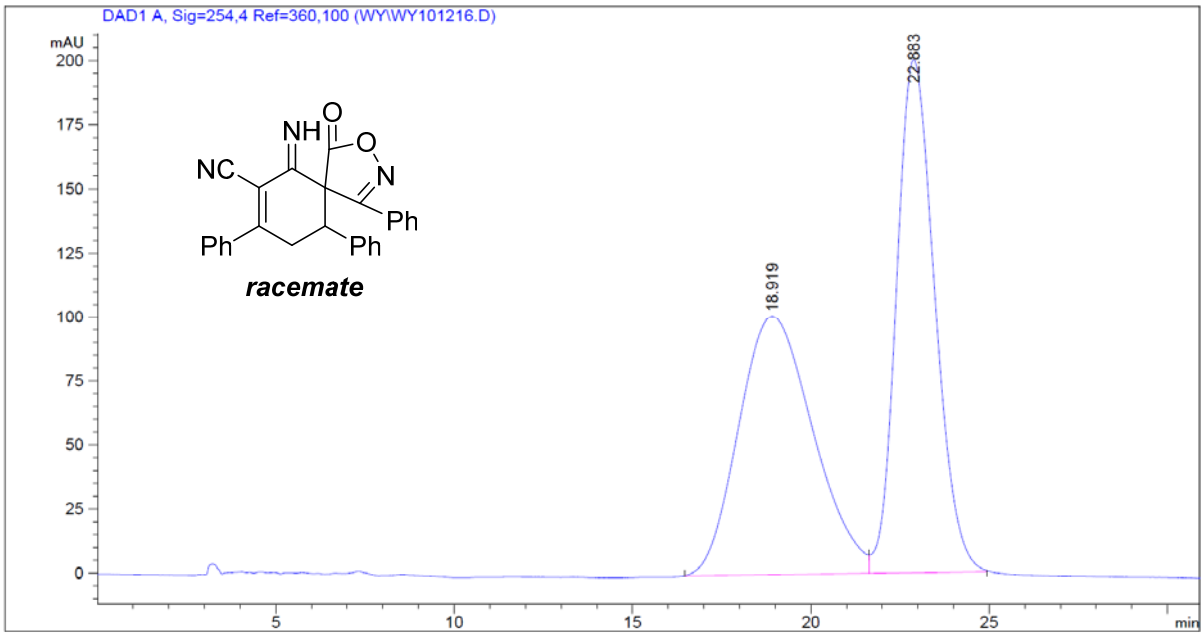
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.736	MM	1.0820	863.65570	13.30365	5.8048
2	30.198	MM	1.9633	1.40146e4	118.97267	94.1952



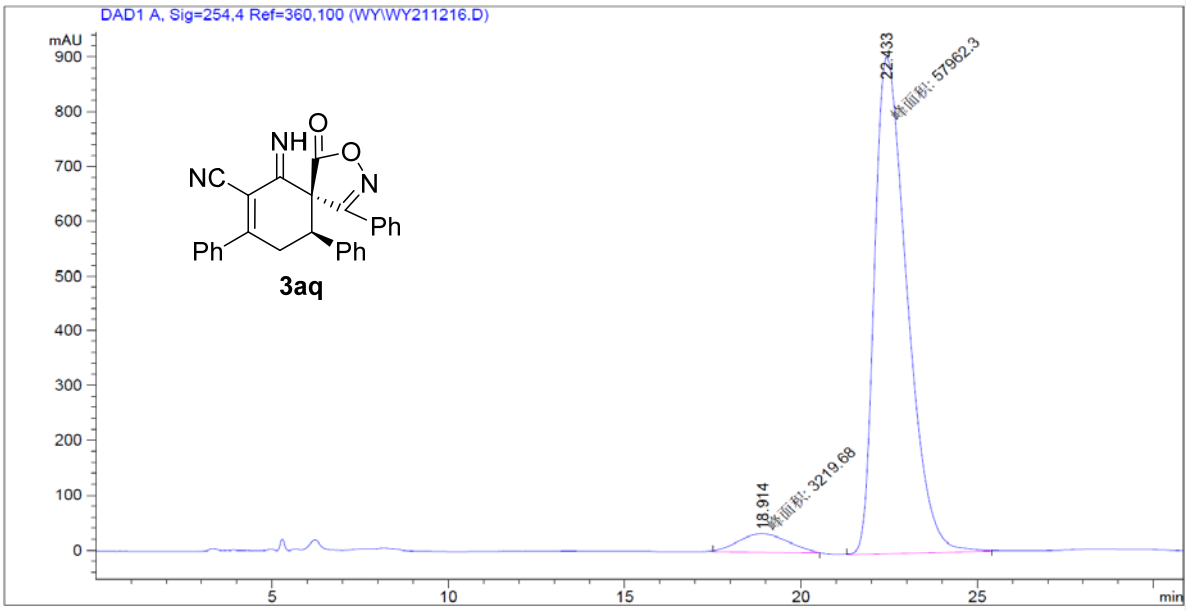
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.795	VV	0.4643	7891.34326	264.29288	50.5531
2	7.945	VB	0.2032	7718.66064	565.65802	49.4469



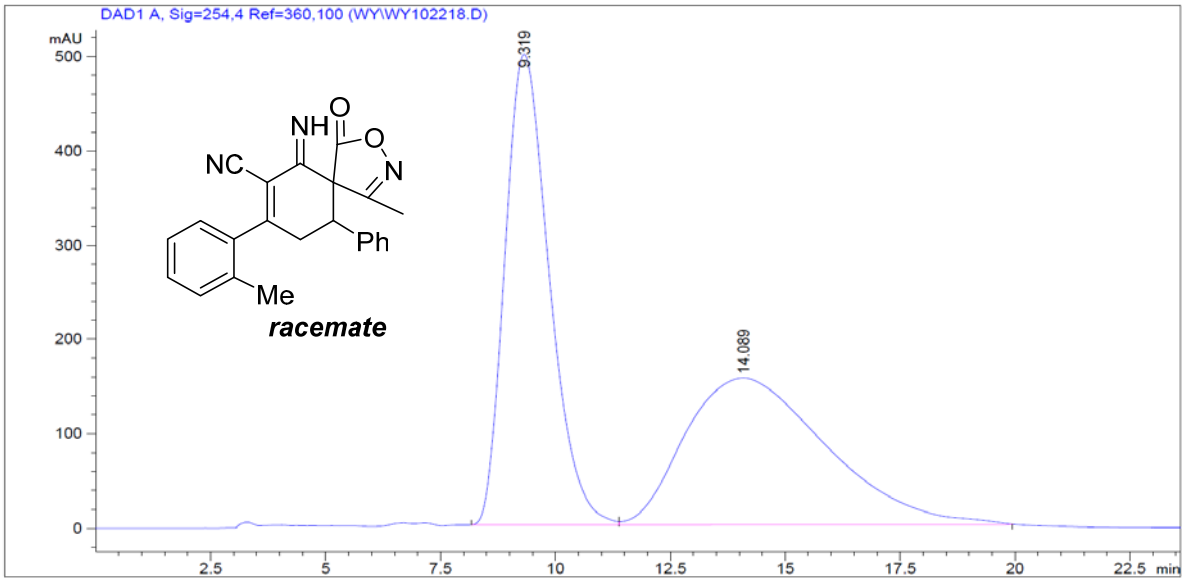
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.745	BV	0.4602	1.37561e4	466.21072	98.0234
2	7.889	VB	0.2098	277.38058	19.51855	1.9766



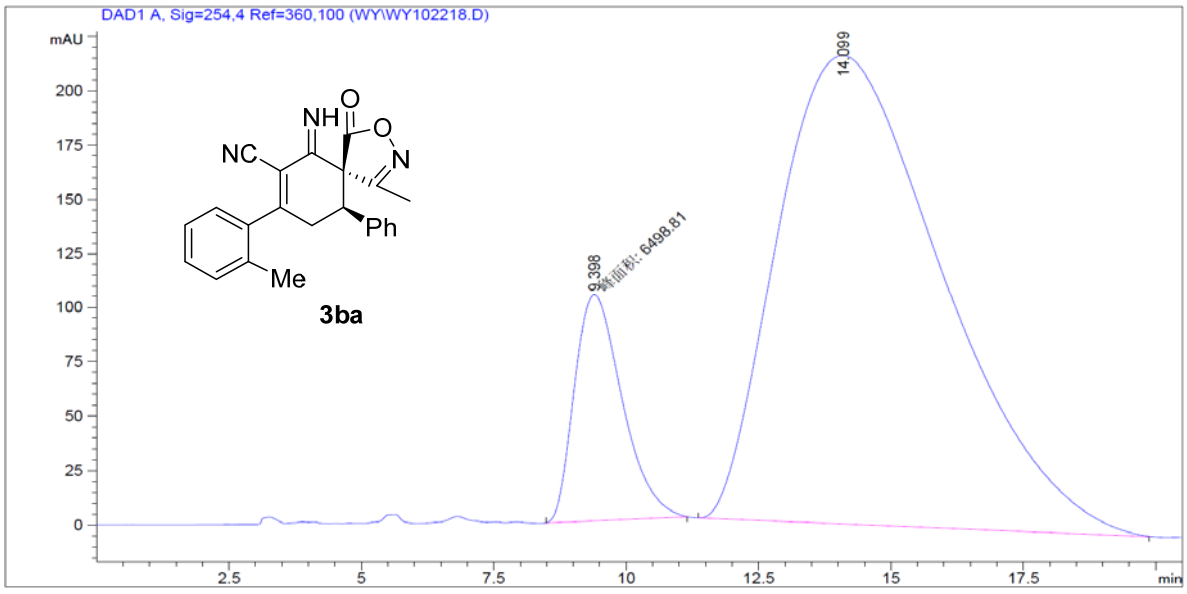
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.919	BV	1.8017	1.46104e4	100.99961	49.4417
2	22.883	VB	1.1486	1.49404e4	200.20671	50.5583



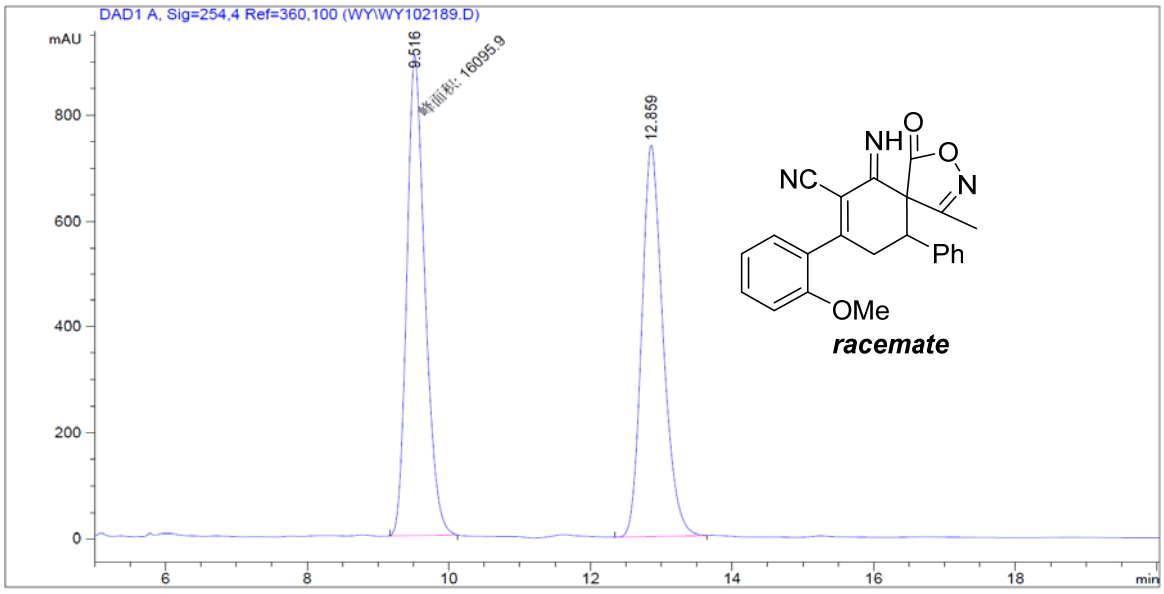
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.914	MM	1.6132	3219.68408	33.26468	5.2625
2	22.433	MM	1.0665	5.79623e4	905.77771	94.7375



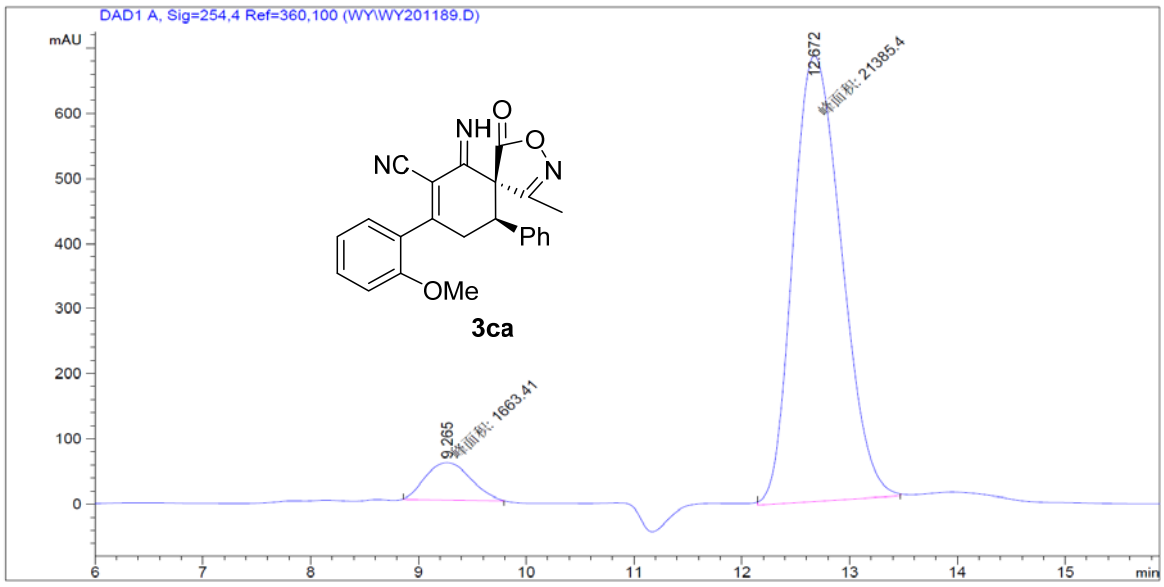
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.319	BB	1.0173	3.34830e4	498.70706	50.2189
2	14.089	BB	2.5474	3.31910e4	155.42696	49.7811



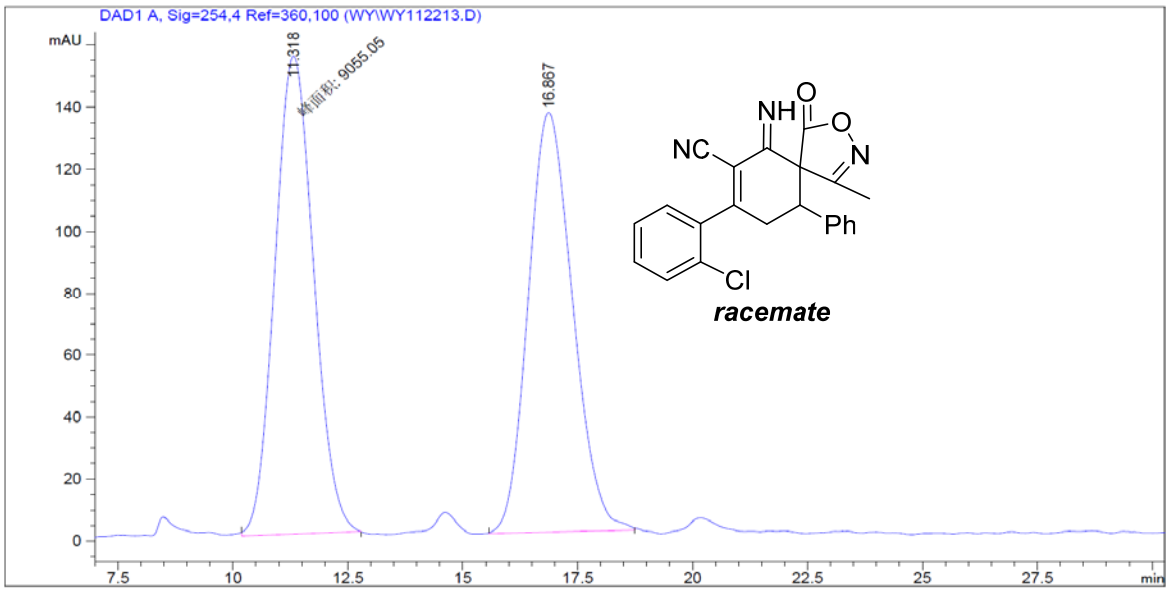
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.398	MM	1.0443	6498.81201	103.71588	12.2216
2	14.099	BB	2.5428	4.66760e4	215.50917	87.7784



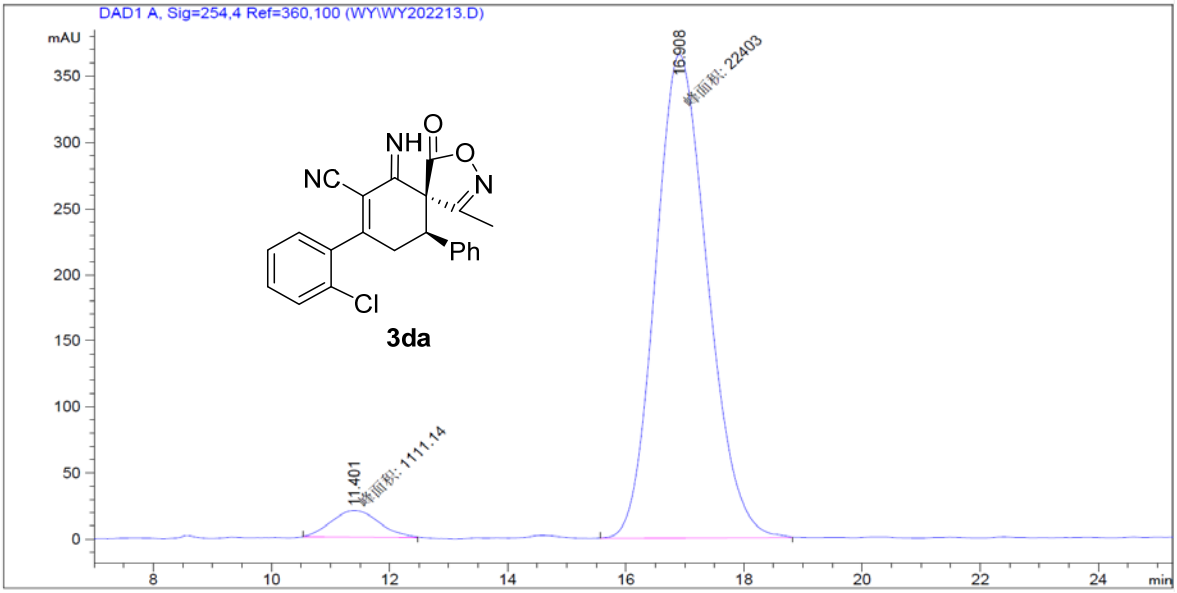
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.516	MM	0.2957	1.60959e4	907.08929	51.0601
2	12.859	VB	0.3133	1.54276e4	739.77148	48.9399



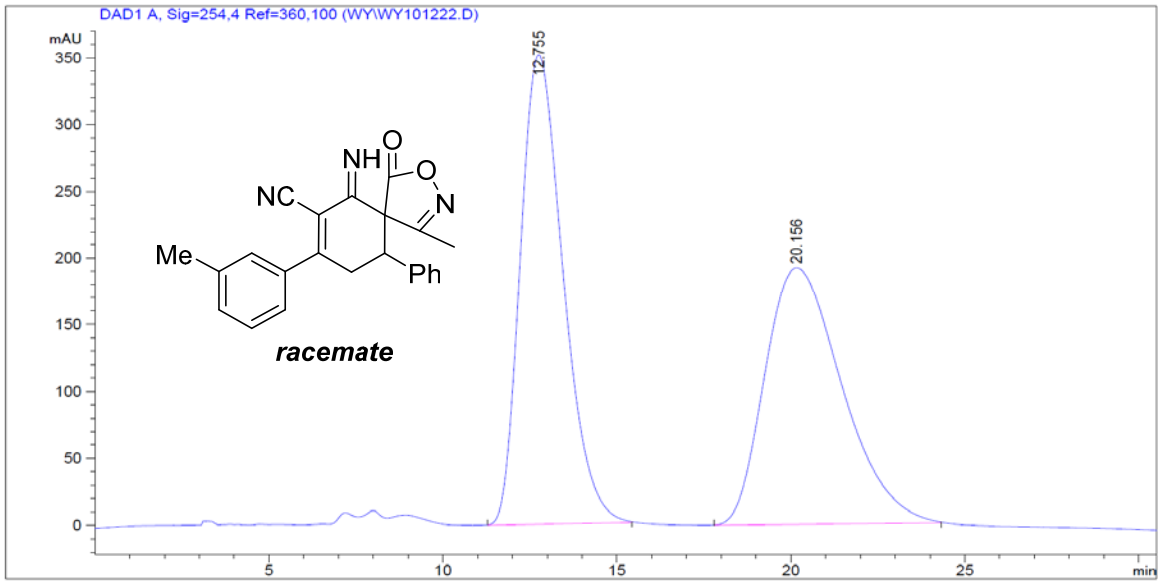
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.265	MM	0.4856	1663.40613	57.09542	7.2169
2	12.672	MM	0.5210	2.13854e4	684.07593	92.7831



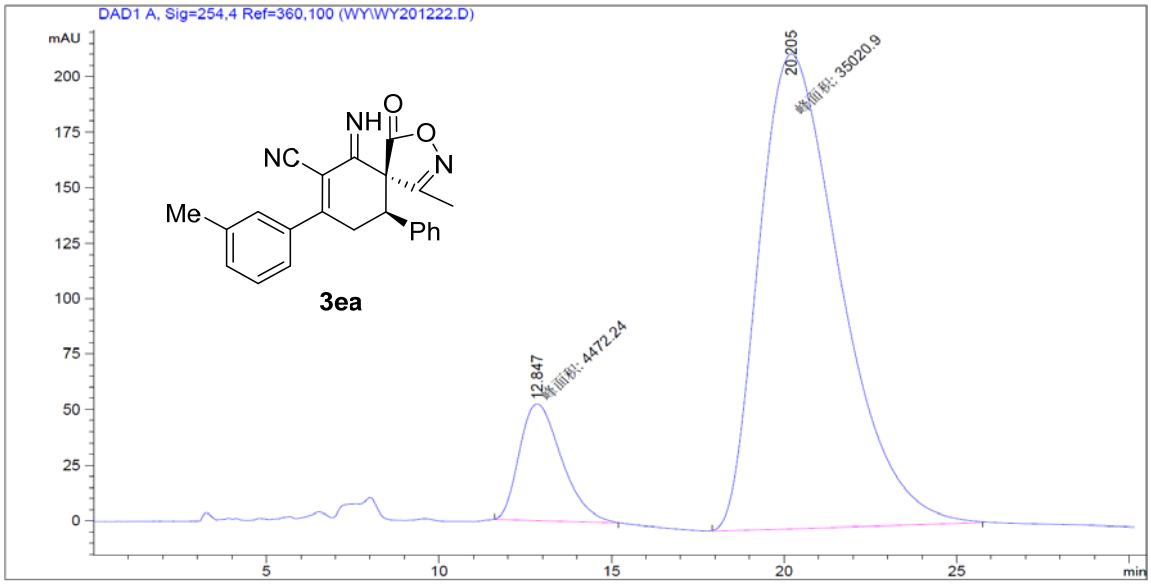
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.318	MM	0.9791	9055.05469	154.13698	49.9045
2	16.867	BB	1.0117	9089.70020	135.31770	50.0955



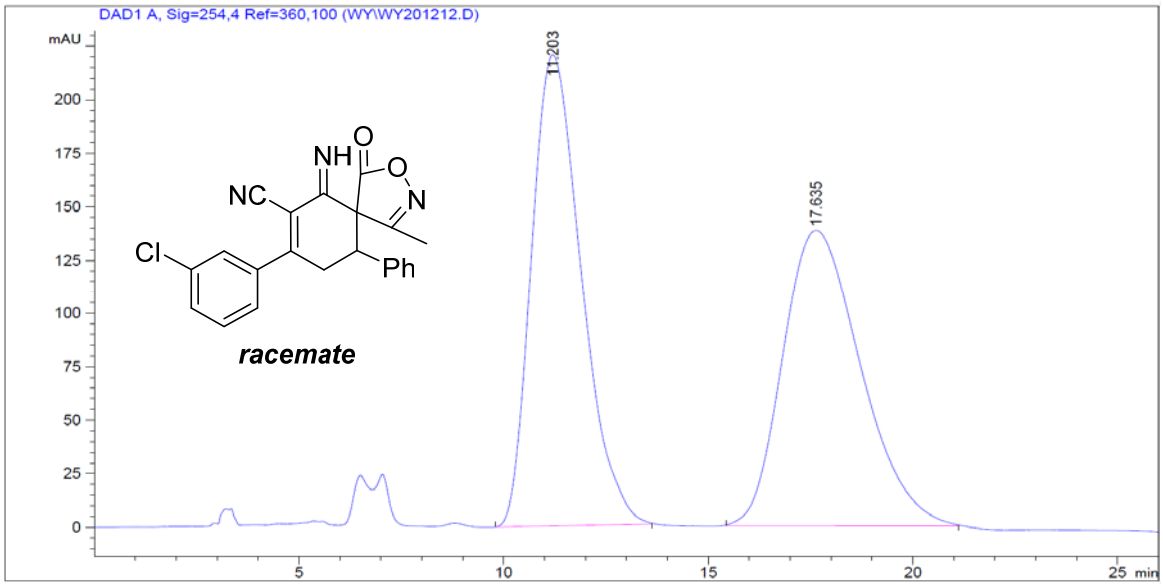
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.401	MM	0.9304	1111.13928	19.90432	4.7254
2	16.908	MM	1.0211	2.24030e4	365.65015	95.2746



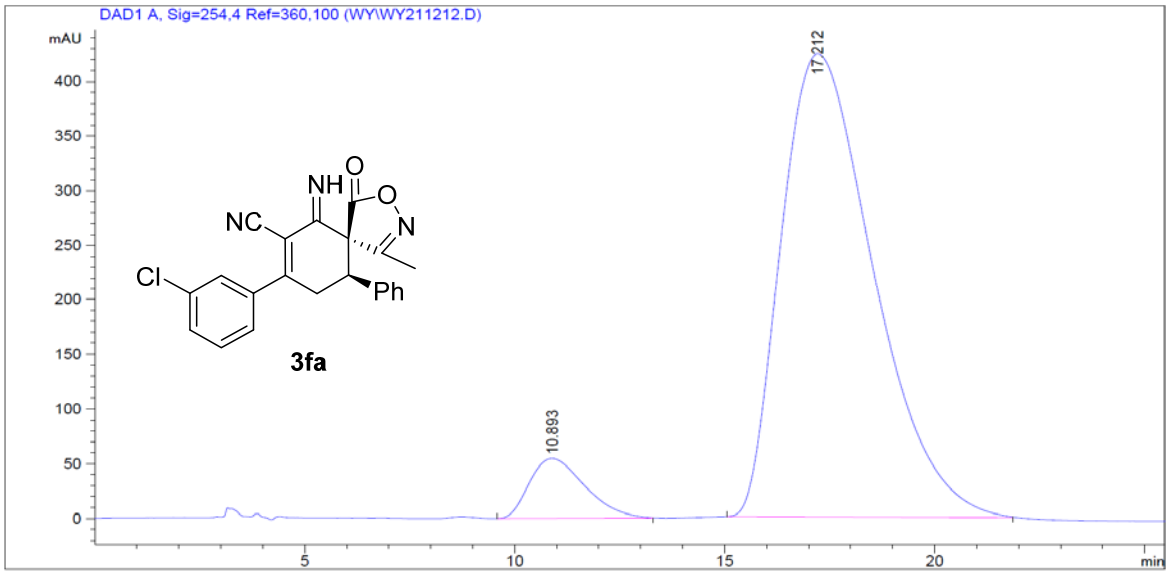
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.755	BB	1.2919	2.99996e4	351.42188	50.4309
2	20.156	BB	2.0869	2.94870e4	192.09537	49.5691



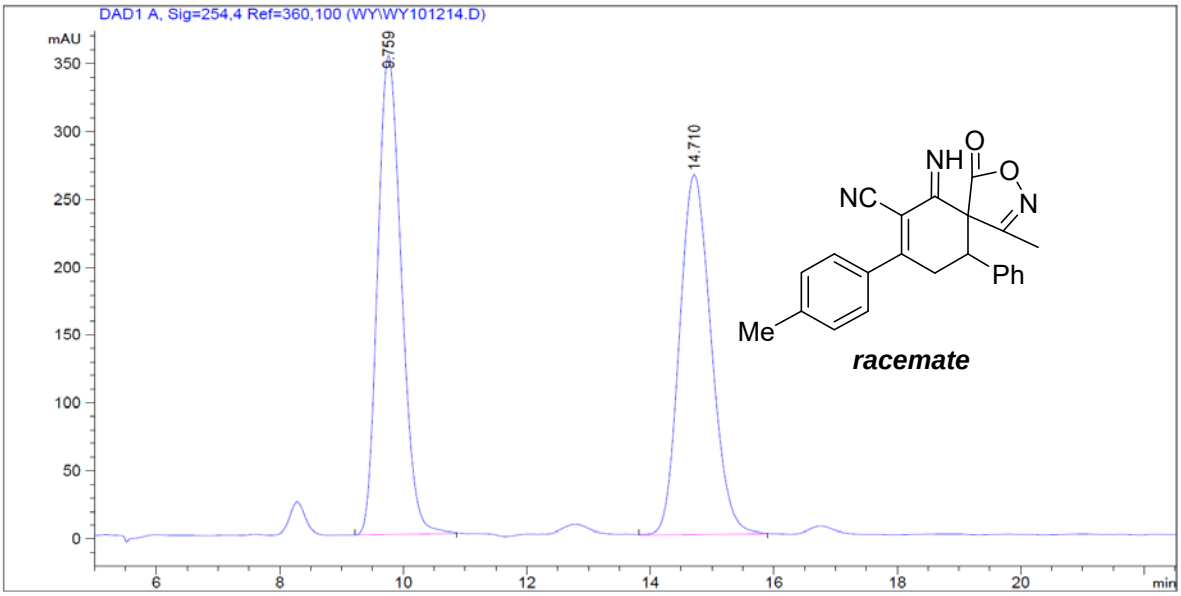
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.847	MM	1.4223	4472.24072	52.40461	11.3241
2	20.205	MM	2.7326	3.50209e4	213.59589	88.6759



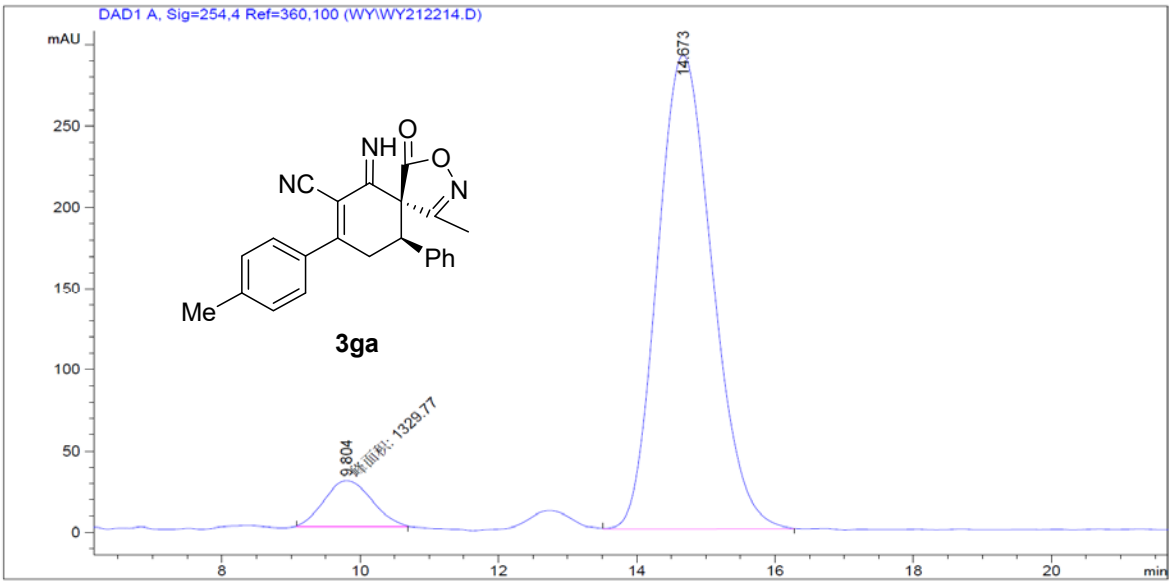
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.203	BB	1.2844	1.86342e4	220.38632	50.5049
2	17.635	BB	1.8294	1.82616e4	138.40280	49.4951



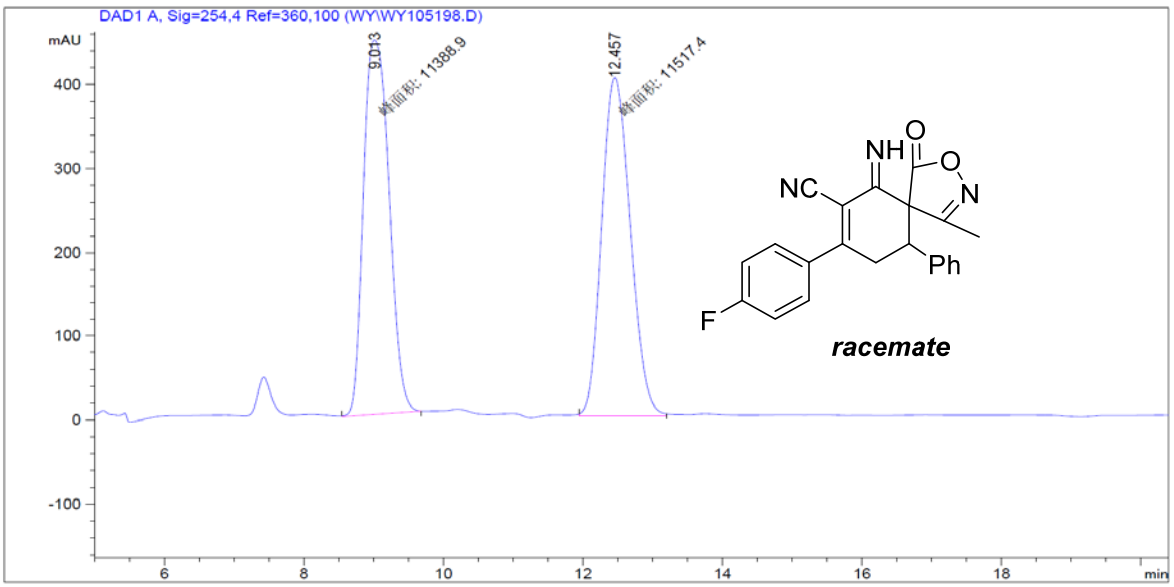
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.893	BB	1.0793	4998.43652	54.64012	7.1775
2	17.212	BB	2.2198	6.46414e4	423.72876	92.8225



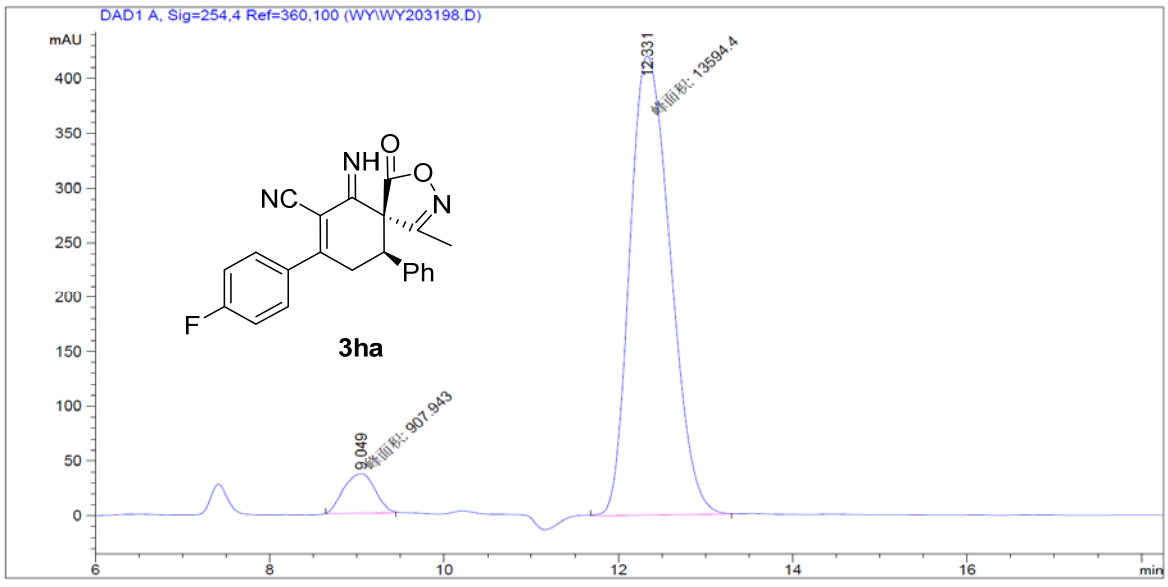
Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	9.759	BB	0.4177	9421.15332	352.65833	49.9802
2	14.710	VB	0.5570	9428.61230	265.06186	50.0198



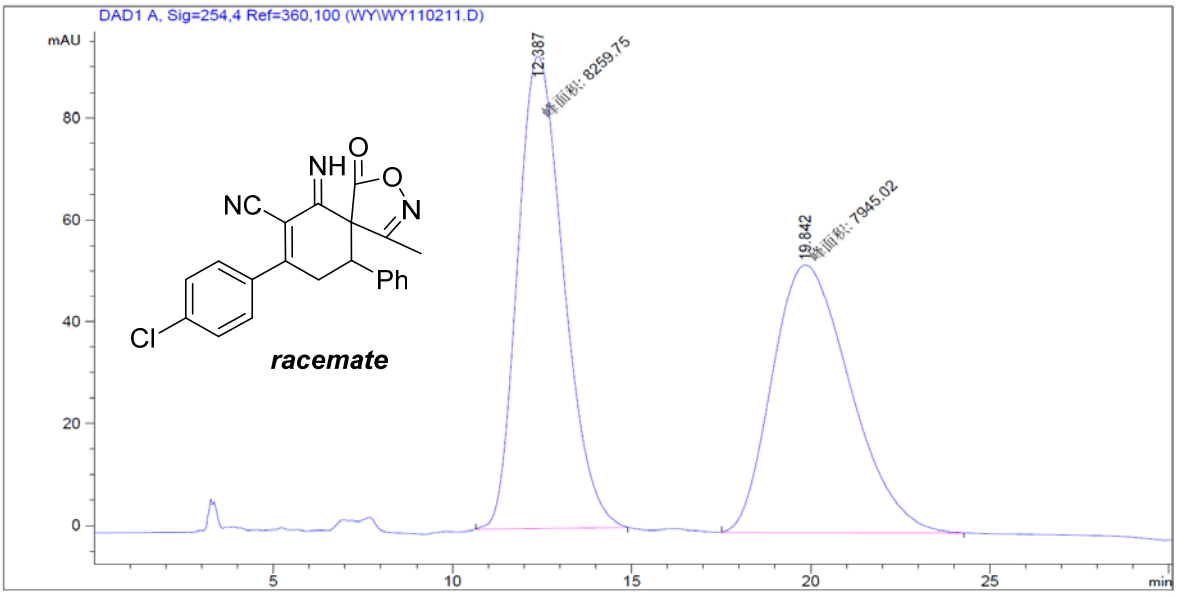
Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	9.804	MM	0.7878	1329.77454	28.13284	7.6476
2	14.673	VB	0.8443	1.60584e4	291.67145	92.3524



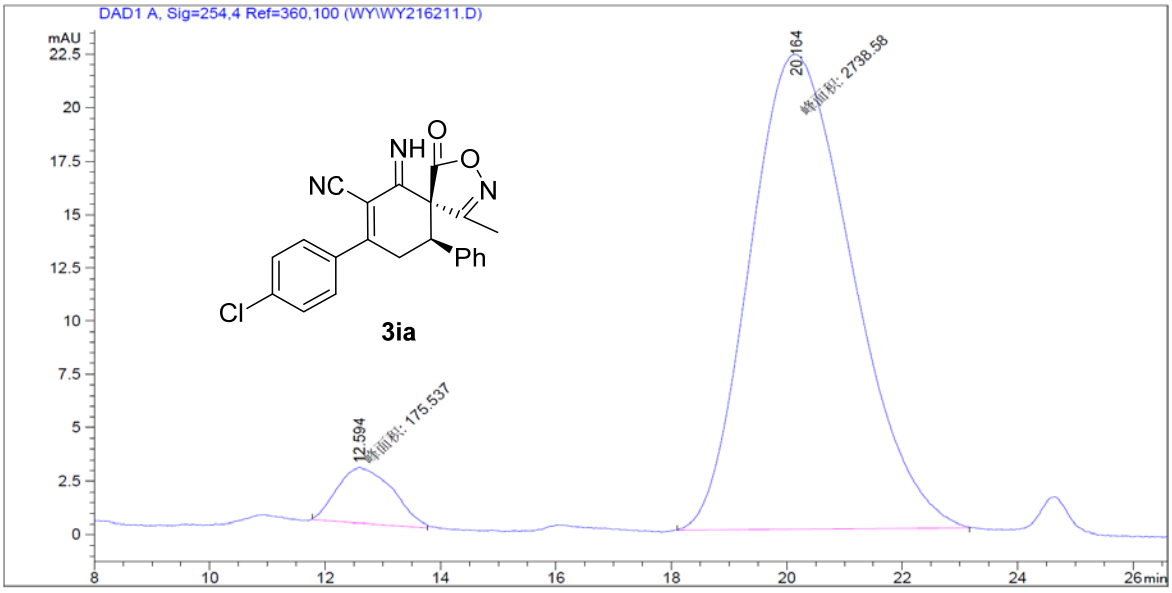
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.013	MM	0.4252	1.13889e4	446.38321	49.7196
2	12.457	MM	0.4756	1.15174e4	403.59198	50.2804



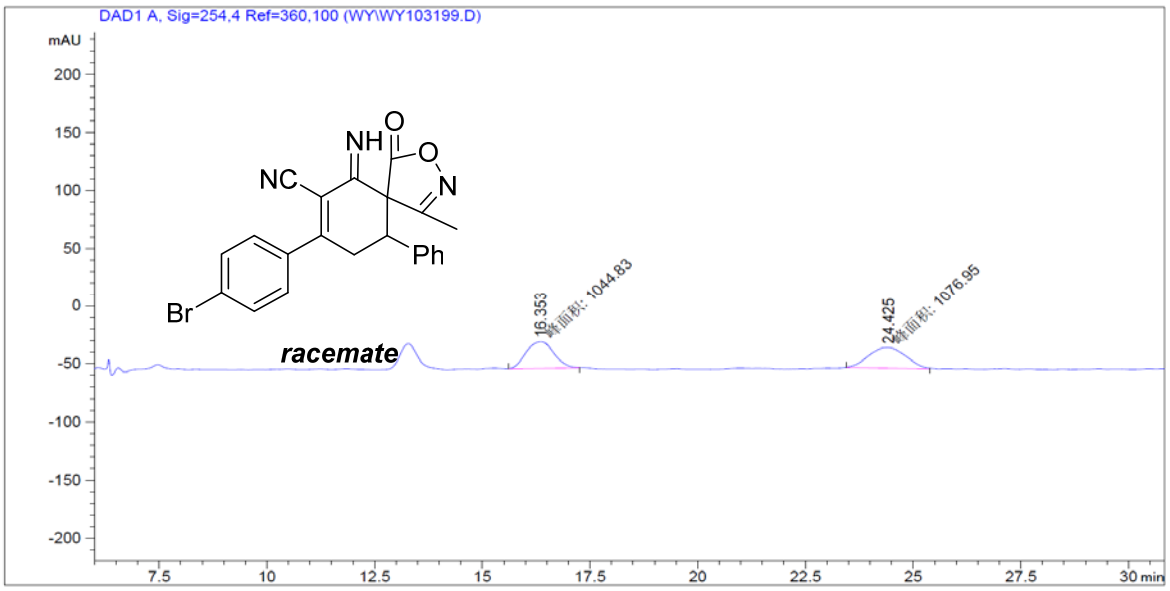
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.049	MM	0.4189	907.94324	36.12468	6.2606
2	12.331	MM	0.5386	1.35944e4	420.64349	93.7394



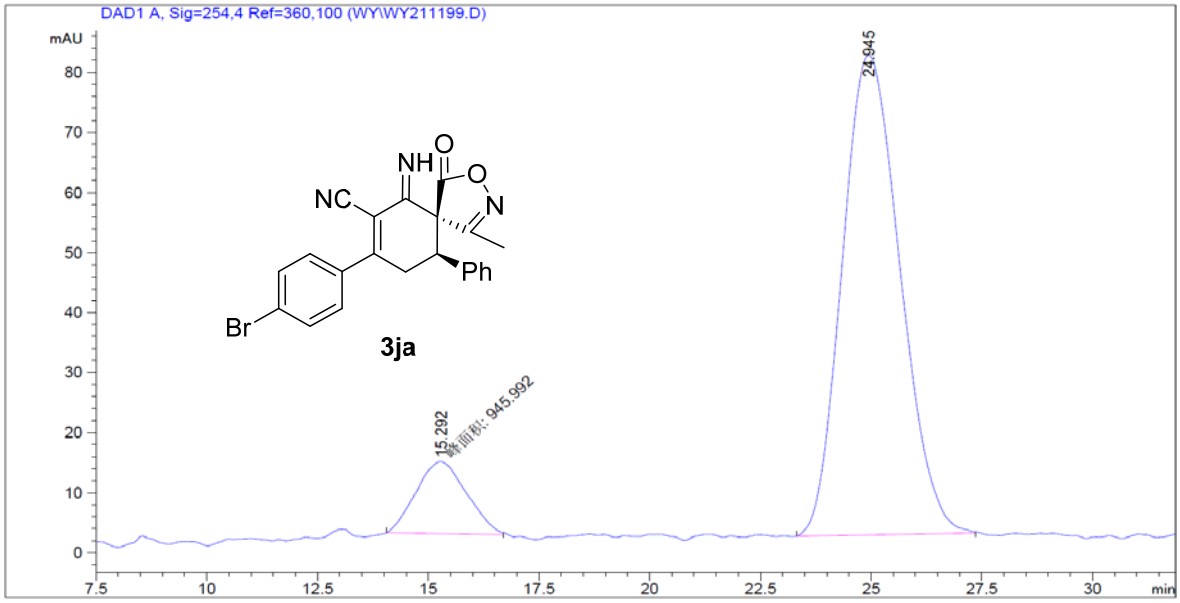
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.387	MM	1.4854	8259.75293	92.67703	50.9711
2	19.842	MM	2.5199	7945.02393	52.54873	49.0289



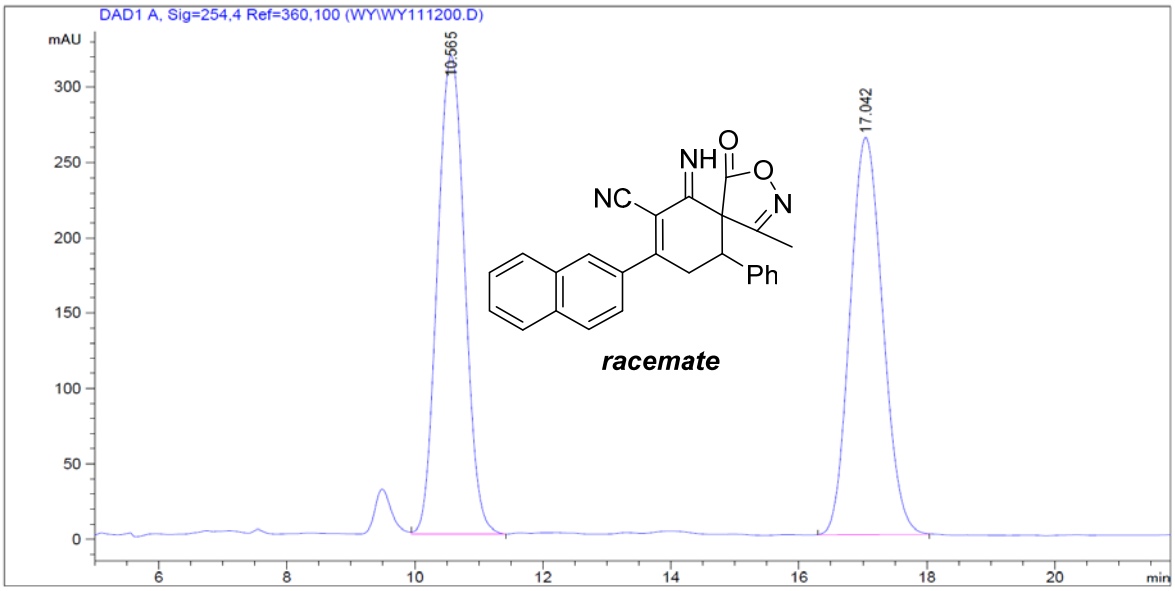
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.594	MM	1.1232	175.53683	2.60469	6.0237
2	20.164	MM	2.0514	2738.57568	22.25016	93.9763



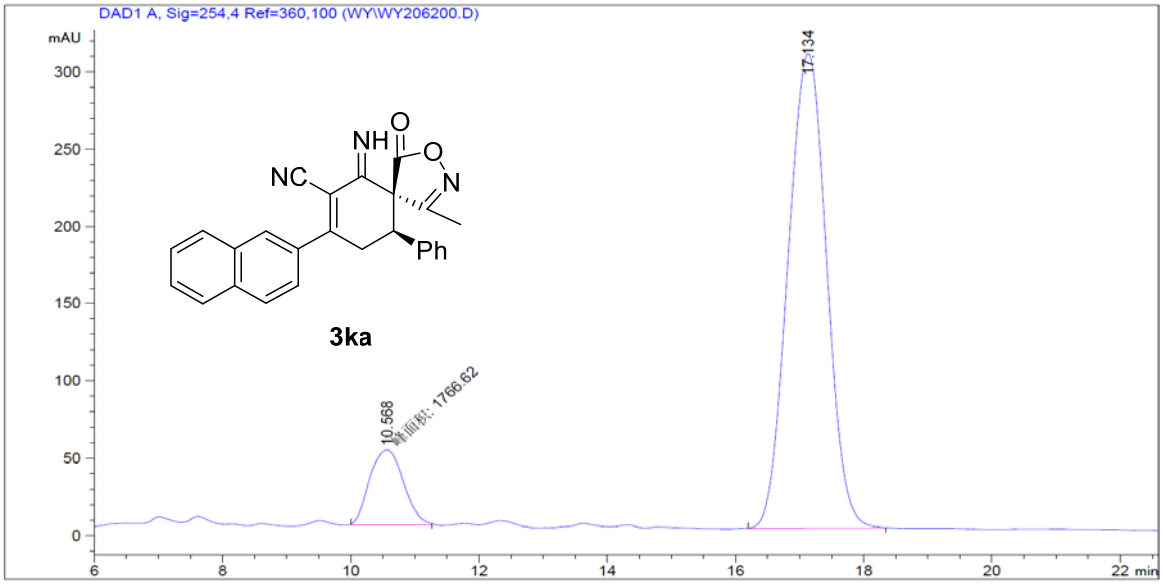
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.353	MM	0.7497	1044.83289	23.22872	49.2431
2	24.425	MM	0.9986	1076.95081	17.97524	50.7569



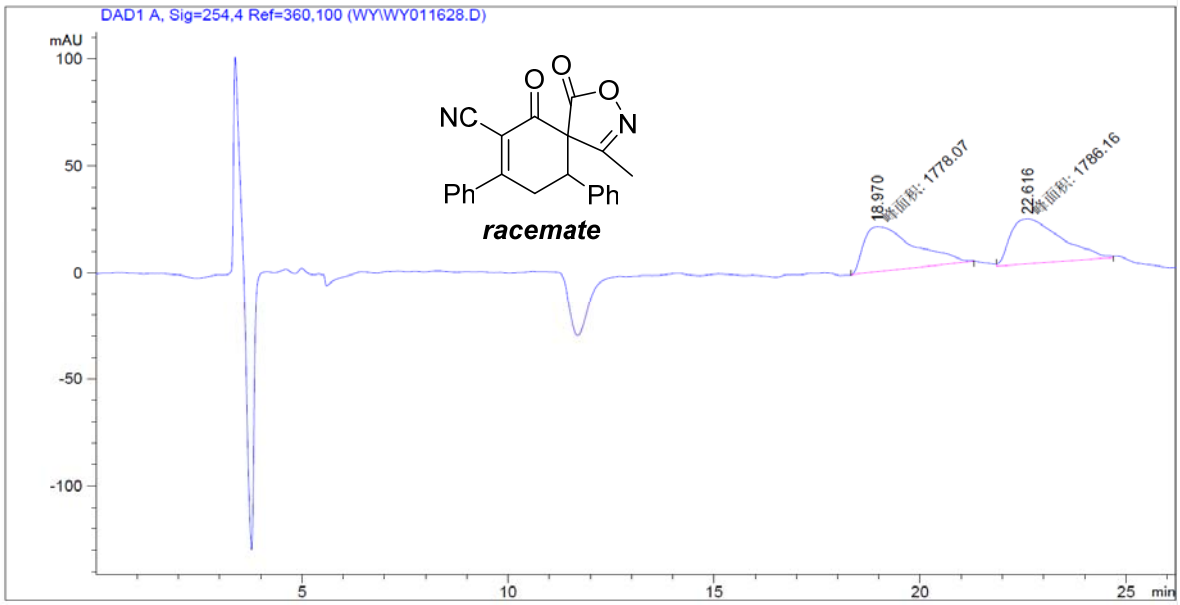
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.292	MM	1.3147	945.99176	11.99271	11.5384
2	24.945	BB	1.2056	7252.65576	79.85174	88.4616



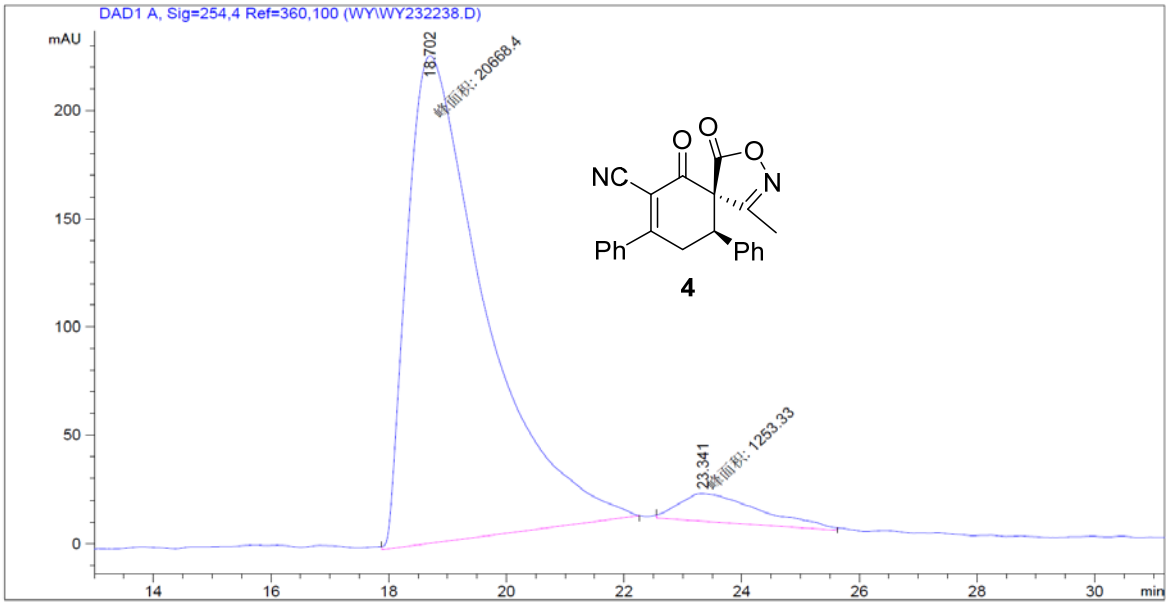
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.565	VB	0.4657	9404.36328	317.41415	50.1117
2	17.042	BB	0.5602	9362.45508	263.68091	49.8883



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.568	MM	0.6090	1766.62292	48.34830	12.1084
2	17.134	BB	0.6671	1.28234e4	307.13055	87.8916



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.970	MM	1.4019	1778.06836	21.13936	49.8865
2	22.616	MM	1.4093	1786.15564	21.12369	50.1135



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.702	MM	1.5309	2.06684e4	225.01427	94.2827
2	23.341	MM	1.6473	1253.33350	12.68086	5.7173