Asymmetric Synthesis of Isoxazole and Trifluoromethyl-Containing 3,2'-Pyrrolidinyl Dispirooxindoles via Squaramide-Catalysed [3 + 2] Cycloaddition Reactions

Tong-Hao Li and Da-Ming Du*

School of Chemistry and Chemical Engineering, Beijing Institute of Technology, No.5 Zhongguancun South Street, Beijing 100081, People's Republic of China

E-mail: dudm@bit.edu.cn

Supporting Information

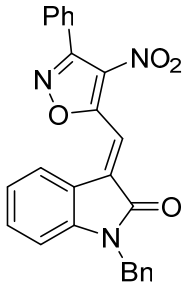
Contents

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 Bruker Ascend 400 MHz spectrometer, chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as internal standard. ^{13}C NMR spectra were measured at 100 MHz with 400 MHz spectrometer, chemical shifts are reported in ppm relative to tetramethylsilane and referenced to solvent peak ($CDCl_3$, δ C = 77.00 ppm; acetone-d6, δ C = 30.83 ppm). ^{19}F NMR spectra were measured at 376 MHz. 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. Optical rotations were measured with a 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

1a–**1l** were prepared according to literature reported by Fan and co-workers.[1] **1m** was prepared following a slightly modified procedure.[2] **2a**–**2m** were prepared according to the literature.[3] The chiral organocatalysts were prepared by following the reported procedures.[4]



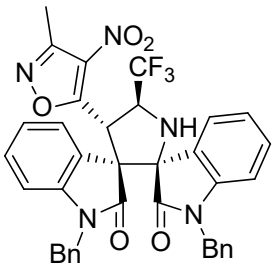
1m

1-Benzyl-3-((4-nitro-3-phenylisoxazol-5-yl)methylene)indolin-2-one (1m). Red solid, m.p. 195–197 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, J = 8.0 Hz, 1H, ArH), 8.16 (s, 1H, =CH), 7.70–7.67 (m, 2H, ArH), 7.59–7.52 (m, 3H, ArH), 7.35–7.29 (m, 6H, ArH), 7.09 (td, J_1 = 7.8

Hz, J_2 = 0.8 Hz, 1H, ArH), 6.77 (d, J = 8.0 Hz, 1H, ArH), 5.00 (s, 2H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.3, 165.4, 158.5, 145.8, 135.9, 135.2, 133.5, 131.1, 129.3, 128.9, 128.7, 127.9, 127.4, 127.3, 125.3, 123.1, 119.7, 112.4, 109.7, 44.1 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{25}H_{18}N_3O_4$ $[M + H]^+$ 424.1292, found 424.1285.

3. Procedure for the synthesis of compounds 3

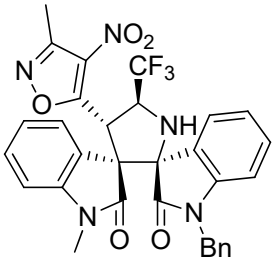
To a dried small bottle were added **1** (0.10 mmol), **2** (0.12 mmol), chiral organocatalyst **C2** (2.8 mg, 0.005 mmol, 5 mol%) and DCE (1.0 mL). The mixture was stirred at –10 °C for 12–48 h. After completion of the reaction, the residue was purified by flash column chromatography on silica gel to afford the pure products **3** as solid. Racemates were prepared following a similar procedure with achiral catalyst (5 mol%).



3aa

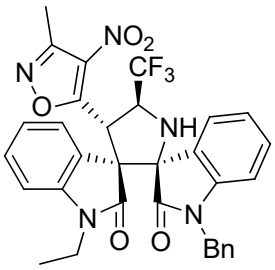
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Bibenzyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3aa). From **1a** (36.1 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 67.3 mg (99% yield) compound **3aa** as a white solid, m.p. 131–133 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.5 min (minor), t_R = 24.2 min (major); 93% *ee*. $[\alpha]_D^{25}$ = +13.0 (c = 3.13, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.14–6.92 (m, 11H, ArH), 6.86 (d, J = 4.8 Hz, 2H, ArH), 6.82–6.78 (m, 3H, ArH), 6.50 (d, J = 7.6 Hz, 1H, ArH), 6.44 (d, J = 7.6 Hz, 1H, ArH), 6.12 (d, J = 9.6 Hz, 1H, NH), 5.36–5.28 (m, 1H, CH), 5.23 (d, J = 15.6 Hz, 1H, CH_2), 5.09 (d, J = 16.0 Hz, 1H, CH_2), 4.44 (d, J = 15.6 Hz, 1H, CH_2), 4.42 (d, J = 16.0 Hz, 1H, CH_2), 3.55 (d, J = 9.6 Hz, 1H, CH), 2.42 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 172.7, 167.5, 155.9, 143.5, 143.3, 134.7, 134.6, 131.0, 130.3, 129.9, 128.47, 128.45, 127.3, 127.2, 126.9, 126.7,

126.0, 125.1, 124.8 (q, $^{1}J_{C–F}$ = 278.9 Hz), 124.7, 122.8, 122.1, 121.8, 109.75, 109.70, 73.7, 65.1, 62.3 (q, $^{2}J_{C–F}$ = 31.8 Hz), 44.1, 44.0, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{29}F_3N_5O_5$ $[M + H]^+$ 680.2115, found 680.2113.



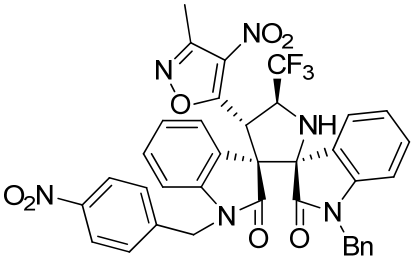
3ba

(3*R*,3'*R*,4'*S*,5'*S*)-1-Benzyl-1''-methyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ba). From **1b** (28.5 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 56.3 mg (93% yield) compound **3ba** as a white solid, m.p. 131–133 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 12.3 min (minor), t_R = 26.8 min (major); 90% *ee*. $[\alpha]_D^{25}$ = +33.4 (*c* = 2.28, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 7.2 Hz, 1H, ArH), 7.21–7.14 (m, 4H, ArH), 7.10 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 6.93 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H, ArH), 6.87–6.84 (m, 2H, ArH), 6.68 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 6.64 (d, *J* = 7.6 Hz, 1H, ArH), 6.44 (d, *J* = 7.6 Hz, 1H, ArH), 6.35 (d, *J* = 7.2 Hz, 1H, ArH), 5.68 (d, *J* = 9.2 Hz, 1H, NH), 5.34–5.31 (m, 1H, CH), 5.17 (d, *J* = 16.0 Hz, 1H, CH_2), 4.37 (d, *J* = 16.0 Hz, 1H, CH_2), 3.74 (d, *J* = 11.2 Hz, 1H, CH), 3.07 (s, 3H, CH_3), 2.43 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 172.6, 168.3, 156.1, 144.3, 143.0, 134.8, 130.8, 130.2, 129.8, 128.6, 127.3, 126.7, 125.9, 125.5, 125.0, 124.6 (q, $^{1}J_{C–F}$ = 278.7 Hz), 122.33, 122.29, 121.5, 109.6, 108.5, 74.3, 65.2, 62.4 (q, $^{2}J_{C–F}$ = 31.4 Hz), 45.1, 43.9, 26.6, 11.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.4 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{31}H_{25}F_3N_5O_5$ $[M + H]^+$ 604.1802, found 604.1795.



3ca

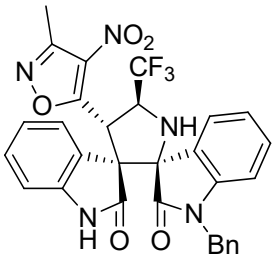
(3*R*,3'*R*,4'*S*,5'*S*)-1-Benzyl-1''-ethyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ca). From **1c** (29.9 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 53.8 mg (87% yield) compound **3ca** as a white solid, m.p. 120–122 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.9 min (minor), t_R = 23.7 min (major); 96% *ee*. $[\alpha]_D^{25}$ = +45.9 (*c* = 2.14, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.6 Hz, 1H, ArH), 7.21–7.13 (m, 4H, ArH), 7.09 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H, ArH), 6.93 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H, ArH), 6.84–6.82 (m, 2H, ArH), 6.69–6.65 (m, 2H, ArH), 6.42 (d, *J* = 7.6 Hz, 1H, ArH), 6.33 (d, *J* = 7.2 Hz, 1H, ArH), 5.67 (d, *J* = 9.6 Hz, 1H, NH), 5.40–5.30 (m, 1H, CH), 5.19 (d, *J* = 16.0 Hz, 1H, CH_2), 4.34 (d, *J* = 16.0 Hz, 1H, CH_2), 3.76–3.68 (m, 2H, CH_2 + CH), 3.59–3.50 (m, 1H, CH_2), 2.44 (s, 3H, CH_3), 0.95 (t, *J* = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.5, 168.4, 156.1, 143.5, 143.1, 134.9, 130.7, 130.2, 129.7, 128.6, 127.3, 126.6, 125.9, 125.7, 124.9, 124.6 (q, $^1J_{C–F}$ = 278.7 Hz), 122.5, 122.3, 121.3, 109.6, 108.6, 74.5, 65.2, 62.5 (q, $^2J_{C–F}$ = 31.4 Hz), 44.9, 43.9, 35.0, 11.8, 11.3 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{32}H_{27}F_3N_5O_5$ $[M + H]^+$ 618.1959, found 618.1943.



3da

(3*R*,3'*R*,4'*S*,5'*S*)-1-Benzyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-1''-(4-nitrobenzyl)-5'-(triflu oromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3da). From **1d**

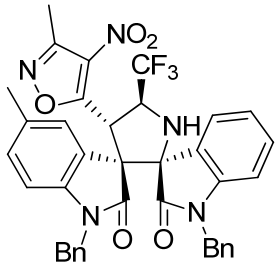
(40.6 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 30.6 mg (42% yield) compound **3da** as a light yellow solid, m.p. 149–151 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 14.6 min (minor), t_R = 32.4 min (major); 87% *ee*. $[\alpha]_D^{25}$ = +23.8 (*c* = 1.28, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.8 Hz, 1H, ArH), 7.27 (d, *J* = 8.8 Hz, 1H, ArH), 7.19-7.13 (m, 2H, ArH), 7.00–6.90 (m, 6H, ArH), 6.81 (t, *J* = 7.6 Hz, 1H, ArH), 6.72 (d, *J* = 7.6 Hz, 2H, ArH), 6.61 (d, *J* = 7.6 Hz, 1H, ArH), 6.49 (d, *J* = 8.0 Hz, 1H, ArH), 6.44 (d, *J* = 7.6 Hz, 1H, ArH), 5.90 (d, *J* = 9.6 Hz, 1H, NH), 5.42–5.34 (m, 1H, CH), 5.29 (d, *J* = 16.4 Hz, 2H, CH_2), 4.43 (d, *J* = 16.4 Hz, 1H, CH_2), 4.33 (d, *J* = 16.4 Hz, 1H, CH_2), 3.67 (d, *J* = 10.4 Hz, 1H, CH), 2.45 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.9, 167.9, 156.1, 147.1, 143.4, 143.0, 142.1, 134.4, 131.0, 130.5, 130.0, 128.5, 127.6, 127.2, 126.4, 126.1, 125.3, 125.1, 124.6 (q, $^1J_{C-F}$ = 278.9 Hz), 123.7, 122.6, 122.5, 122.2, 109.7, 109.2, 74.3, 65.2, 62.6 (q, $^2J_{C-F}$ = 31.6 Hz), 44.8, 43.9, 43.6, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.4 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}F_3N_6O_7$ $[M + H]^+$ 725.1966, found 725.1951.



3ea

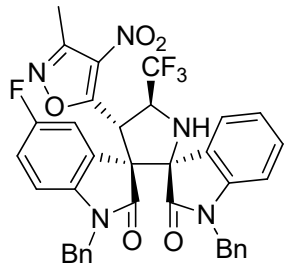
(3*R*,3'*R*,4'*S*,5'*S*)-1-Benzyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ea). From **1e** (27.1 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:2) as eluent to obtain 48.5 mg (82% yield) compound **3ea** as a light yellow solid, m.p. 165–167 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 6.9 min (minor), t_R = 9.1 min (major); 53% *ee*. $[\alpha]_D^{25}$ = +13.7 (*c* = 0.99, CH_2Cl_2). ^1H NMR (400 MHz, acetone-d6): δ 9.45 (s, 1H, NH), 8.08 (d, *J* = 7.6 Hz, 1H, ArH), 7.45 (d, *J* = 7.2 Hz, 2H, ArH), 7.31–7.18 (m, 5H, ArH), 7.06 (td, J_1 = 7.8 Hz, J_2 = 1.2 Hz, 1H, ArH), 6.85 (d, *J* = 8.0 Hz, 1H,

ArH), 6.72–6.93 (m, 2H, NH + ArH), 6.63–6.59 (m, 2H, ArH), 5.42–5.31 (m, 1H, CH), 5.13 (d, J = 16.0 Hz, 1H, CH_2), 4.66–4.61 (m, 2H, CH_2 + CH), 2.39 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, acetone-d6): δ 176.8, 173.4, 168.4, 157.7, 146.1, 143.7, 138.2, 133.1, 132.0, 131.8, 130.3, 129.5, 129.3, 129.1, 127.7 (q, $^1J_{C–F}$ = 278.7 Hz), 127.5, 126.5, 125.3, 123.3, 123.0, 111.9, 110.8, 74.2, 67.7, 63.2 (q, $^2J_{C–F}$ = 31.8 Hz), 45.3, 44.3, 12.3 ppm. ^{19}F NMR (376 MHz, acetone-d6): δ −73.0 ppm. HRMS (ESI): m/z calcd. for $C_{30}H_{23}F_3N_5O_5$ $[M + H]^+$ 590.1646, found 590.1638.



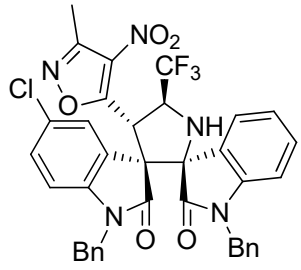
3fa

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5''-methyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3fa). From **1f** (37.5 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 49.2 mg (71% yield) compound **3fa** as a white solid, m.p. 119–121 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 7.7 min (minor), t_R = 15.6 min (major); 94% *ee*. $[\alpha]_D^{25}$ = +3.1 (c = 1.81, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.11–7.02 (m, 6H, ArH), 6.98–6.91 (m, 5H, ArH), 6.80 (td, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H, ArH), 6.74 (t, J = 7.0 Hz, 3H, ArH), 6.44 (d, J = 7.6 Hz, 1H, ArH), 6.37 (d, J = 8.0 Hz, 1H, ArH), 6.17 (d, J = 9.6 Hz, 1H, NH), 5.34–5.26 (m, 1H, CH), 5.22 (d, J = 16.0 Hz, 1H, CH_2), 5.04 (d, J = 15.6 Hz, 1H, CH_2), 4.43 (d, J = 16.0 Hz, 1H, CH_2), 4.41 (d, J = 16.0 Hz, 1H, CH_2), 3.48 (d, J = 9.2 Hz, 1H, CH), 2.42 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 172.4, 167.5, 155.9, 143.6, 140.9, 134.7, 131.3, 131.0, 130.23, 130.17, 128.5, 127.23, 127.21, 127.0, 126.8, 126.7, 125.2, 124.8 (q, $^1J_{C–F}$ = 278.9 Hz), 124.7, 123.0, 122.0, 109.7, 109.4, 73.5, 65.2, 62.3 (q, $^2J_{C–F}$ = 31.6 Hz), 44.2, 44.0, 43.8, 21.1, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.3 ppm. HRMS (ESI): m/z calcd. for $C_{38}H_{31}F_3N_5O_5$ $[M + H]^+$ 694.2272, found 694.2263.



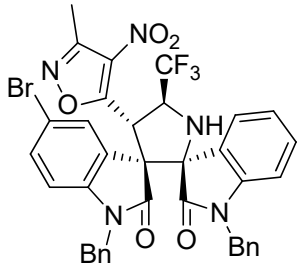
3ga

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5''-fluoro-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoro methyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ga). From **1g** (30.0 mg, 0.08 mmol) and **2a** (30.0 mg, 0.10 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 54.4 mg (97% yield) compound **3ga** as a white solid, m.p. 131–133 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.1 min (minor), t_R = 15.3 min (major); 91% *ee*. $[\alpha]_D^{25}$ = +12.2 (*c* = 1.73, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16–6.96 (m, 10H, ArH), 6.87–6.81 (m, 2H, ArH), 6.78 (d, *J* = 7.6 Hz, 2H, ArH), 6.65 (dd, J_1 = 8.2 Hz, J_2 = 1.8 Hz, 1H, ArH), 6.49 (d, *J* = 7.6 Hz, 1H, ArH), 6.41 (dd, J_1 = 8.6 Hz, J_2 = 4.2 Hz, 1H, ArH), 6.14 (d, *J* = 9.6 Hz, 1H, NH), 5.29–5.21 (m, 1H, CH), 5.21 (d, *J* = 16.0 Hz, 1H, CH_2), 5.06 (d, *J* = 16.0 Hz, 1H, CH_2), 4.44 (d, *J* = 16.0 Hz, 1H, CH_2), 4.43 (d, *J* = 16.0 Hz, 1H, CH_2), 3.52 (d, *J* = 9.2 Hz, 1H, CH), 2.45 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 172.4, 167.1, 158.0 (d, $^1J_{C–F}$ = 240.3 Hz), 156.0, 143.5, 139.32, 139.30, 134.6, 134.3, 131.1, 130.5, 128.6, 128.5, 127.4 (d, $^3J_{C–F}$ = 8.7 Hz), 127.0, 126.7, 125.0, 124.7 (q, $^1J_{C–F}$ = 279.1 Hz), 124.5, 124.4, 122.3, 116.3 (d, $^2J_{C–F}$ = 23.2 Hz), 114.1 (d, $^2J_{C–F}$ = 25.8 Hz), 110.3 (d, $^3J_{C–F}$ = 8.0 Hz), 109.9, 73.6, 65.2, 62.2 (q, $^2J_{C–F}$ = 31.7 Hz), 44.22, 44.20, 43.8, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.2, –119.5 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}F_4N_5O_5$ $[M + H]^+$ 698.2021, found 698.1998.



3ha

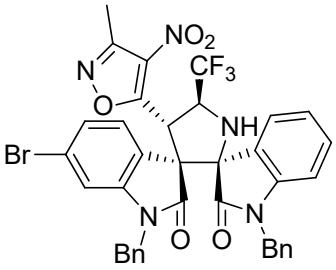
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5''-chloro-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoro methyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ha). From **1h** (39.6 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 67.0 mg (94% yield) compound **3ha** as a white solid, m.p. 126–128 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.2 min (minor), t_R = 25.0 min (major); 93% *ee*. $[\alpha]_D^{25}$ = –1.3 (*c* = 0.71, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.16–7.04 (m, 7H, ArH), 7.01–6.97 (m, 4H, ArH), 6.89–6.84 (m, 2H, ArH), 6.77 (d, *J* = 7.2 Hz, 2H, ArH), 6.50 (d, *J* = 8.0 Hz, 1H, ArH), 6.40 (d, *J* = 8.4 Hz, 1H, ArH), 6.13 (d, *J* = 9.6 Hz, 1H, NH), 5.29–5.21 (m, 1H, CH), 5.20 (d, *J* = 16.0 Hz, 1H, CH_2), 5.04 (d, *J* = 16.0 Hz, 1H, CH_2), 4.46 (d, *J* = 16.0 Hz, 1H, CH_2), 4.44 (d, *J* = 15.6 Hz, 1H, CH_2), 3.48 (d, *J* = 9.2 Hz, 1H, CH), 2.46 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 172.3, 167.2, 156.1, 143.5, 141.9, 134.7, 134.2, 131.1, 130.6, 129.8, 128.64, 128.55, 127.5, 127.4, 127.3, 127.0, 126.7, 126.4, 125.1, 124.70, 124.66 (q, $^1J_{C–F}$ = 279.1 Hz), 124.5, 122.4, 110.6, 109.9, 73.6, 65.1, 62.3 (q, $^2J_{C–F}$ = 31.8 Hz), 44.27, 44.26, 43.9, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}ClF_3N_5O_5$ $[M + H]^+$ 714.1726, found 714.1728.



3ia

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5''-bromo-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoro methyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ia). From **1i** (44.0 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 53.1 mg (70% yield) compound **3ia** as a white solid, m.p. 129–131 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.5 min (minor), t_R = 25.4 min (major); 91% *ee*. $[\alpha]_D^{25}$ = –3.1 (*c* = 0.84, CH_2Cl_2). ^{1}H NMR

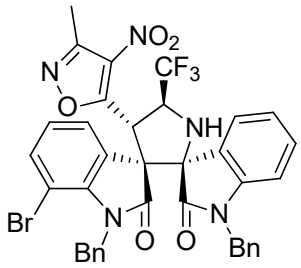
(400 MHz, $CDCl_3$): δ 7.23 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H, ArH), 7.16–7.03 (m, 6H, ArH), 7.01–6.96 (m, 4H, ArH), 6.92–6.87 (m, 2H, ArH), 6.78 (d, J = 7.2 Hz, 2H, ArH), 6.50 (d, J = 8.0 Hz, 1H, ArH), 6.35 (d, J = 8.4 Hz, 1H, ArH), 6.09 (d, J = 10.0 Hz, 1H, NH), 5.30–5.21 (m, 1H, CH), 5.19 (d, J = 15.6 Hz, 1H, CH_2), 5.03 (d, J = 15.6 Hz, 1H, CH_2), 4.45 (d, J = 16.0 Hz, 1H, CH_2), 4.43 (d, J = 15.6 Hz, 1H, CH_2), 3.50 (d, J = 9.2 Hz, 1H, CH), 2.46 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 172.3, 167.2, 156.1, 143.5, 142.4, 134.6, 134.2, 132.6, 131.1, 130.6, 129.1, 128.64, 128.55, 127.5, 127.4, 127.0, 126.8, 125.1, 125.0, 124.64 (q, $^1J_{C–F}$ = 279.7 Hz), 124.57, 122.4, 114.4, 111.1, 110.0, 73.7, 65.1, 62.3 (q, $^2J_{C–F}$ = 31.8 Hz), 44.3, 44.0, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}{}^{79}BrF_3N_5O_5$ $[M + H]^+$ 758.1221, found 758.1247; calcd. for $C_{37}H_{28}{}^{81}BrF_3N_5O_5$ $[M + H]^+$ 760.1200, found 760.1221.



3ja

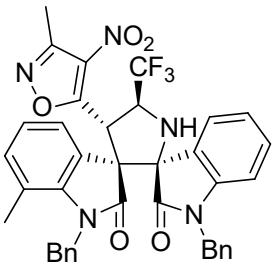
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-6''-bromo-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ja). From **1j** (44.0 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1/3) as eluent to obtain 75.6 mg (99% yield) compound **3ia** as a white solid, m.p. 137−139 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 7.9 min (minor), t_R = 17.2 min (major); 90% *ee*. $[\alpha]_D^{25}$ = +20.1 (*c* = 3.13, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J = 6.4 Hz, 1H, ArH), 7.15–6.99 (m, 7H, ArH), 6.92–6.84 (m, 6H, ArH), 6.64 (d, J = 1.6 Hz, 1H, ArH), 6.51–6.46 (m, 2H, ArH), 5.94 (d, J = 9.2 Hz, 1H, NH), 5.34–5.25 (m, 1H, CH), 5.20 (d, J = 15.6 Hz, 1H, CH_2), 5.04 (d, J = 16.0 Hz, 1H, CH_2), 4.43 (d, J = 16.0 Hz, 1H, CH_2), 4.39 (d, J = 16.4 Hz, 1H, CH_2), 3.63 (d, J = 10.0 Hz, 1H, CH), 2.45 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 172.9, 167.6, 156.1, 144.8, 143.3, 134.4, 134.1, 131.0, 130.5, 128.6, 128.5, 127.5, 127.4, 126.9, 126.8, 126.7, 125.1,

125.0, 124.58 (q, $^{1}J_{C–F}$ = 279.0 Hz), 124.57, 123.8, 122.4, 121.6, 113.1, 109.9, 74.0, 64.9, 62.5 (q, $^{2}J_{C–F}$ = 31.7 Hz), 44.4, 44.3, 44.1, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}{}^{79}BrF_3N_5O_5$ $[M + H]^+$ 758.1221, found 758.1214; calcd. for $C_{37}H_{28}{}^{81}BrF_3N_5O_5$ $[M + H]^+$ 760.1200, found 760.1199.



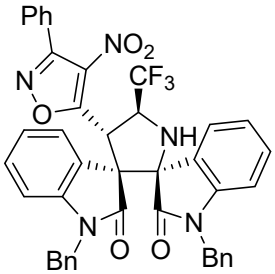
3ka

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-7''-bromo-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ka). From **1k** (44.0 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 69.9 mg (92% yield) compound **3ka** as a white solid, m.p. 136–138 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 7.8 min (minor), t_R = 19.7 min (major); 88% *ee*. $[\alpha]_D^{25}$ = –11.8 (*c* = 3.08, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, J_1 = 8.2 Hz, J_2 = 0.6 Hz, 1H, ArH), 7.25 (d, *J* = 7.2 Hz, 1H, ArH), 7.13 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.10–7.02 (m, 6H, ArH), 6.99–6.89 (m, 4H, ArH), 6.80 (t, *J* = 7.8 Hz, 1H, ArH), 6.55 (d, *J* = 7.2 Hz, 2H, ArH), 6.47 (d, *J* = 7.6 Hz, 1H, ArH), 6.34 (d, *J* = 10.0 Hz, 1H, NH), 5.32–5.13 (m, 4H, CH + CH_2), 4.43 (d, *J* = 16.0 Hz, 1H, CH_2), 3.39 (d, *J* = 8.0 Hz, 1H, CH), 2.45 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 172.5, 166.6, 156.0, 143.8, 140.7, 136.4, 136.2, 134.7, 131.2, 130.6, 128.5, 128.3, 127.3, 127.0, 126.7, 126.4, 125.6, 125.4, 125.3, 124.8 (q, $^{1}J_{C–F}$ = 279.3 Hz), 123.7, 123.1, 122.2, 109.9, 103.0, 73.4, 64.3, 62.1 (q, $^{2}J_{C–F}$ = 31.9 Hz), 45.0, 44.3, 43.5, 11.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.1 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}{}^{79}BrF_3N_5O_5$ $[M + H]^+$ 758.1221, found 758.1212; calcd. for $C_{37}H_{28}{}^{81}BrF_3N_5O_5$ $[M + H]^+$ 760.1200, found 760.1203.



3la

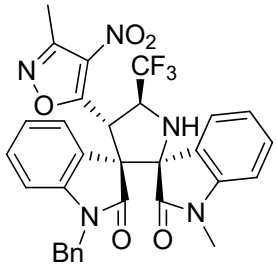
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-7''-methyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3la). From **1l** (37.5 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 50.2 mg (72% yield) compound **3la** as a white solid, m.p. 137−139 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 10.1 min (minor), t_R = 26.6 min (major); 90% *ee*. $[\alpha]_D^{25}$ = –6.1 (*c* = 2.27, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.08–6.89 (m, 12H, ArH), 6.79 (t, *J* = 7.4 Hz, 1H, ArH), 6.50–6.45 (m, 3H, ArH), 6.32 (d, *J* = 10.0 Hz, 1H, NH), 5.31–5.25 (m, 3H, CH + CH_2), 4.76 (d, *J* = 17.2 Hz, 1H, CH_2), 4.41 (d, *J* = 16.0 Hz, 1H, CH_2), 3.41 (d, *J* = 8.4 Hz, 1H, CH), 2.45 (s, 3H, CH_3), 2.02 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.3, 172.9, 167.2, 155.9, 143.9, 141.4, 136.6, 134.8, 134.1, 131.1, 130.4, 128.6, 128.4, 127.2, 126.9, 126.8, 125.4, 124.89 (q, $^1J_{C–F}$ = 279.2 Hz), 124.86, 124.3, 124.2, 123.8, 122.1, 122.0, 120.4, 109.7, 73.5, 64.4, 62.2 (q, $^2J_{C–F}$ = 31.9 Hz), 45.4, 44.2, 43.7, 18.7, 11.5 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.1 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{38}H_{31}F_3N_5O_5$ $[M + H]^+$ 694.2272, found 694.2257.



3ma

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-4'-(4-nitro-3-phenylisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ma). From **1m** (42.3 mg, 0.10 mmol) and **2a** (38.2 mg, 0.12 mmol), purified by silica gel (200-300

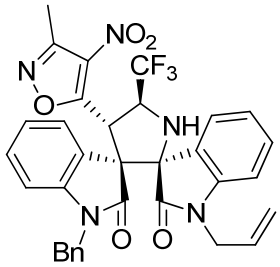
mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 73.5 mg (99% yield) compound **3ma** as a white solid, m.p. 109–111 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 15.7 min (major), t_R = 19.9 min (minor); 92% *ee*. $[\alpha]_D^{25}$ = +18.7 (*c* = 3.68, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.42 (m, 5H, ArH), 7.15–7.00 (m, 7H, ArH), 6.97–6.78 (m, 9H, ArH), 6.51 (d, *J* = 8.0 Hz, 1H, ArH), 6.45 (d, *J* = 7.6 Hz, 1H, ArH), 6.10 (d, *J* = 10.0 Hz, 1H, NH), 5.44–5.34 (m, 1H, CH), 5.22 (d, *J* = 15.6 Hz, 1H, CH_2), 5.11 (d, *J* = 16.0 Hz, 1H, CH_2), 4.44 (d, *J* = 15.6 Hz, 1H, CH_2), 4.42 (d, *J* = 16.0 Hz, 1H, CH_2), 3.60 (d, *J* = 9.2 Hz, 1H, CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.6, 172.8, 168.0, 157.9, 143.51, 143.46, 134.7, 134.6, 131.0, 130.5, 130.3, 130.0, 129.0, 128.51, 128.48, 127.3, 126.9, 126.7, 126.0, 125.1, 124.9, 124.82, 124.81 (q, $^1J_{C–F}$ = 278.9 Hz), 122.9, 122.2, 121.8, 109.8, 109.7, 73.7, 65.3, 62.2 (q, $^2J_{C–F}$ = 31.7 Hz), 44.3, 44.1 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{42}H_{30}F_3N_5O_5Na$ $[M + Na]^+$ 764.2091, found 764.2098.



3ab

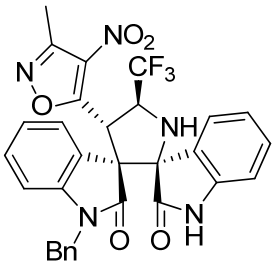
(3*R*,3'*R*,4'*S*,5'*S*)-1''-Benzyl-1-methyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ab). From **1a** (36.1 mg, 0.10 mmol) and **2b** (29.1 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:2) as eluent to obtain 59.7 mg (99% yield) compound **3ab** as a white solid, m.p. 128–130 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.0 min (minor), t_R = 18.4 min (major); 89% *ee*. $[\alpha]_D^{25}$ = +4.1 (*c* = 2.77, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (d, *J* = 7.6 Hz, 1H, ArH), 7.24 (t, *J* = 7.6 Hz, 1H, ArH), 7.17–7.08 (m, 4H, ArH), 7.03 (t, *J* = 7.6 Hz, 1H, ArH), 6.87 (d, *J* = 7.6 Hz, 1H, ArH), 6.76–6.70 (m, 3H, ArH), 6.66 (d, *J* = 7.6 Hz, 1H, ArH), 6.47 (d, *J* = 8.0 Hz, 1H, ArH), 6.36 (d, *J* = 10.0 Hz, 1H, NH), 5.29–5.15 (m, 1H, CH), 4.94 (d, *J* = 15.6 Hz, 1H, CH_2), 4.41 (d, *J* = 15.6 Hz, 1H, CH_2),

3.30 (d, J = 8.0 Hz, 1H, CH), 3.11 (s, 3H, CH_3), 2.39 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 171.3, 166.9, 155.7, 144.4, 142.7, 134.8, 131.0, 130.4, 130.1, 128.6, 127.3, 126.7, 126.3, 125.2, 124.9 (q, $^1J_{C–F}$ = 279.2 Hz), 123.9, 123.3, 122.0, 121.9, 109.6, 108.2, 72.8, 64.9, 61.9 (q, $^2J_{C–F}$ = 31.9 Hz), 43.8, 42.9, 26.4, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.3 ppm. HRMS (ESI): m/z calcd. for $C_{31}H_{25}F_3N_5O_5$ $[M + H]^+$ 604.1802, found 604.1799.



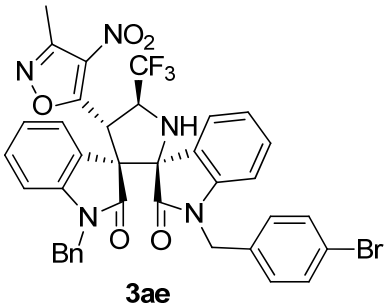
3ac

(3*R*,3'*R*,4'*S*,5'*S*)-1-Allyl-1''-benzyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl) dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ac). From **1a** (36.1 mg, 0.10 mmol) and **2c** (32.2 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 62.3 mg (99% yield) compound **3ac** as a white solid, m.p. 117–119 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.4 min (minor), t_R = 35.8 min (major); 88% *ee*. $[\alpha]_D^{25}$ = +7.0 (c = 2.79, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.20 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.16–7.09 (m, 4H, ArH), 7.05–7.01 (m, 2H, ArH), 6.92 (t, J = 7.4 Hz, 1H, ArH), 6.81–6.77 (m, 3H, ArH), 6.65 (d, J = 8.0 Hz, 1H, ArH), 6.47 (d, J = 7.6 Hz, 1H, ArH), 6.19 (d, J = 9.6 Hz, 1H, NH), 5.66–5.56 (m, 1H, =CH), 5.32–5.22 (m, 1H, CH), 5.03 (d, J = 16.0 Hz, 1H, CH_2), 4.93 (d, J = 10.4 Hz, 1H, =CH_2), 4.81 (d, J = 17.6 Hz, 1H, =CH_2), 4.56–4.51 (m, 1H, CH_2), 4.41 (d, J = 16.0 Hz, 1H, CH_2), 3.96 (dd, J_1 = 16.4 Hz, J_2 = 5.6 Hz, 1H, CH_2), 3.42 (d, J = 8.8 Hz, 1H, CH), 2.40 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 172.1, 167.3, 155.8, 143.6, 143.1, 134.8, 131.0, 130.9, 130.3, 130.0, 128.6, 127.3, 126.7, 126.1, 125.1, 124.8 (q, $^1J_{C–F}$ = 279.1 Hz), 124.4, 123.0, 122.0, 121.8, 117.4, 109.6, 109.4, 73.3, 65.1, 62.2 (q, $^2J_{C–F}$ = 31.8 Hz), 44.0, 43.5, 42.6, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.3 ppm. HRMS (ESI): m/z calcd. for $C_{33}H_{27}F_3N_5O_5$ $[M + H]^+$ 630.1959, found 630.1963.



3ad

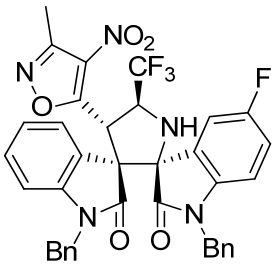
(3*R*,3'*R*,4'*S*,5'*S*)-1''-Benzyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro [indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ad). From **1a** (36.1 mg, 0.10 mmol) and **2d** (27.4 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:2) as eluent to obtain 48.5 mg (82% yield) compound **3ad** as a white solid, m.p. 159–161 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 13.9 min (minor), t_R = 44.6 min (major); 66% *ee*. $[\alpha]_D^{25}$ = +11.1 (*c* = 1.08, CH_2Cl_2). ^{1}H NMR (400 MHz, acetone-d6): δ 9.35 (s, 1H, NH), 8.18–8.14 (m, 1H, ArH), 7.25–7.18 (m, 3H, ArH), 7.14–7.05 (m, 3H, ArH), 6.87 (d, *J* = 7.6 Hz, 1H, ArH), 6.75 (d, *J* = 10.8 Hz, 1H, NH), 6.69 (d, *J* = 7.6 Hz, 1H, ArH), 6.62 (d, *J* = 7.2 Hz, 2H, ArH), 6.59–6.53 (m, 2H, ArH), 5.40–5.29 (m, 1H, CH), 4.82 (d, *J* = 16.0 Hz, 1H, CH_2), 4.59 (d, *J* = 9.2 Hz, 1H, CH), 4.46 (d, *J* = 16.4 Hz, 1H, CH_2), 2.37 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, acetone-d6): δ 177.9, 171.9, 168.4, 157.6, 145.3, 144.6, 137.3, 133.1, 132.2, 131.7, 130.4, 129.2, 128.9, 128.1, 127.8, 127.7 (q, $^1J_{C–F}$ = 278.7 Hz), 126.1, 125.3, 123.7, 122.5, 111.4, 111.4, 74.5, 67.4, 63.4 (q, $^2J_{C–F}$ = 31.8 Hz), 44.6, 43.7, 12.4 ppm. ^{19}F NMR (376 MHz, acetone-d6): δ −72.9 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{30}H_{23}F_3N_5O_5$ $[M + H]^+$ 590.1646, found 590.1634.



3ae

(3*R*,3'*R*,4'*S*,5'*S*)-1''-Benzyl-1-(4-bromobenzyl)-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifl uoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ae). From **1a** (36.1 mg, 0.10 mmol) and **2e** (47.8 mg, 0.12 mmol), purified by silica gel (200-300

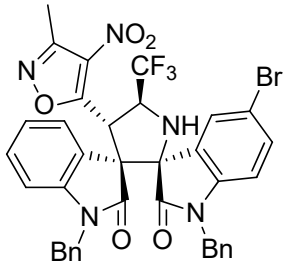
mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 73.0 mg (96% yield) compound **3ae** as a white solid, m.p. 125–127 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.4 min (minor), t_R = 25.4 min (major); 92% *ee*. $[\alpha]_D^{25}$ = –4.7 (*c* = 3.16, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18–7.02 (m, 7H, ArH), 6.97–6.91 (m, 3H, ArH), 6.82–6.78 (m, 3H, ArH), 6.69 (d, *J* = 7.6 Hz, 2H, ArH), 6.52 (d, *J* = 8.0 Hz, 1H, ArH), 6.39 (d, *J* = 7.6 Hz, 1H, ArH), 6.22 (d, *J* = 10.0 Hz, 1H, NH), 5.35–5.27 (m, 1H, CH), 5.23 (d, *J* = 16.0 Hz, 1H, CH_2), 5.09 (d, *J* = 16.0 Hz, 1H, CH_2), 4.41 (d, *J* = 16.0 Hz, 1H, CH_2), 4.29 (d, *J* = 16.0 Hz, 1H, CH_2), 3.50 (d, *J* = 9.2 Hz, 1H, CH), 2.42 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 172.2, 167.3, 155.9, 143.3, 143.2, 134.4, 133.7, 131.5, 131.0, 130.4, 130.1, 128.7, 128.5, 127.3, 126.4, 126.1, 125.3, 124.8 (q, $^1J_{C–F}$ = 279.0 Hz), 124.5, 122.9, 122.3, 122.0, 121.2, 109.7, 109.5, 73.5, 65.0, 62.2 (q, $^2J_{C–F}$ = 31.8 Hz), 43.9, 43.7, 43.6, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.4 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}{}^{79}BrF_3N_5O_5$ $[M + H]^+$ 758.1220, found 758.1204; calcd. for $C_{37}H_{28}{}^{81}BrF_3N_5O_5$ $[M + H]^+$ 760.1200, found 760.1189.



3af

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5-fluoro-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3af). From **1a** (36.1 mg, 0.10 mmol) and **2f** (40.4 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1/3) as eluent to obtain 66.1 mg (95% yield) compound **3af** as a white solid, m.p. 128–130 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.0 min (minor), t_R = 20.3 min (major); 88% *ee*. $[\alpha]_D^{25}$ = +5.4 (*c* = 2.71, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.12–6.95 (m, 10H, ArH), 6.81–6.76 (m, 4H, ArH), 6.54 (d, *J* = 8.0 Hz, 1H, ArH), 6.37 (dd, J_1 = 8.4 Hz, J_2 = 4.4 Hz, 1H,

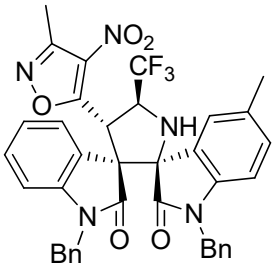
ArH), 6.26 (d, J = 8.0 Hz, 1H, NH), 5.29–5.20 (m, 2H, CH + CH_2), 5.02 (d, J = 15.6 Hz, 1H, CH_2), 4.44 (t, J = 15.6 Hz, 2H, CH_2), 3.44 (d, J = 8.4 Hz, 1H, CH), 2.41 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.9, 171.9, 167.0, 158.2 (d, $^1J_{C–F}$ = 240.2 Hz), 155.9, 143.1, 139.6, 134.5 (d, $^3J_{C–F}$ = 8.6 Hz), 131.1, 130.3, 128.6, 128.5, 127.4 (d, $^4J_{C–F}$ = 3.0 Hz), 127.1, 126.7, 126.1, 126.0, 125.9, 124.7 (q, $^1J_{C–F}$ = 279.2 Hz), 122.7, 122.1, 116.6 (d, $^2J_{C–F}$ = 23.0 Hz), 113.6 (d, $^2J_{C–F}$ = 26.1 Hz), 110.2 (d, $^3J_{C–F}$ = 7.8 Hz), 110.0, 73.4, 64.9, 62.1 (q, $^2J_{C–F}$ = 31.8 Hz), 44.4, 44.0, 43.4, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3, –119.5 ppm. HRMS (ESI): m/z calcd. for $C_{37}H_{28}F_4N_5O_5$ $[M + H]^+$ 698.2021, found 698.2023.



3ag

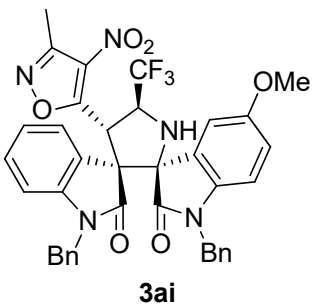
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5-bromo-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ag). From **1a** (36.1 mg, 0.10 mmol) and **2g** (47.8 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 75.0 mg (99% yield) compound **3ag** as a white solid, m.p. 119–121 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.1 min (minor), t_R = 21.5 min (major); 89% *ee*. $[\alpha]_D^{25}$ = +58.0 (c = 3.64, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22–7.16 (m, 3H, ArH), 7.11–6.96 (m, 10H, ArH), 6.72 (d, J = 7.2 Hz, 2H, ArH), 6.55 (d, J = 8.0 Hz, 1H, ArH), 6.32–6.30 (m, 2H, ArH + NH), 5.28–5.19 (m, 1H, CH), 5.18 (d, J = 16.0 Hz, 1H, CH_2), 4.99 (d, J = 16.0 Hz, 1H, CH_2), 4.47 (d, J = 15.6 Hz, 1H, CH_2), 4.45 (d, J = 15.6 Hz, 1H, CH_2), 3.39 (d, J = 8.4 Hz, 1H, CH), 2.41 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.7, 171.5, 166.8, 155.9, 143.0, 142.6, 134.5, 134.3, 133.0, 131.1, 130.3, 128.62, 128.56, 128.5, 127.5, 127.4, 127.1, 126.6, 126.2, 124.7 (q, $^1J_{C–F}$ = 279.2 Hz), 122.8, 122.2, 114.5, 111.0, 110.0, 73.1, 64.9, 62.1 (q, $^2J_{C–F}$ = 31.9 Hz), 44.3, 44.0, 43.1, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): m/z calcd. for

$C_{37}H_{27}{}^{79}BrF_3N_5O_5Na$ $[M + Na]^+$ 780.1040, found 780.1043; calcd. for $C_{37}H_{27}{}^{81}BrF_3N_5O_5Na$ $[M + Na]^+$ 782.1020, found 782.1031.



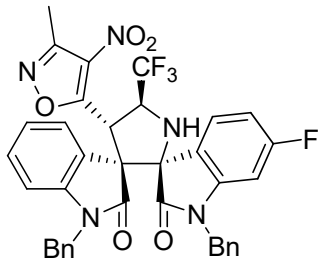
3ah

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5-methyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoro methyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ah). From **1a** (36.1 mg, 0.10 mmol) and **2h** (39.9 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 68.7 mg (99% yield) compound **3ah** as a white solid, m.p. 123–125 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.8 min (minor), t_R = 24.4 min (major); 90% *ee*. $[\alpha]_D^{25}$ = +39.7 (*c* = 3.24, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14–6.95 (m, 7H, ArH), 6.91–6.86 (m, 6H, ArH), 6.78 (d, *J* = 7.6 Hz, 2H, ArH), 6.49 (d, *J* = 7.6 Hz, 1H, ArH), 6.31 (d, *J* = 8.0 Hz, 1H, ArH), 6.13 (d, *J* = 9.6 Hz, 1H, NH), 5.36–5.27 (m, 1H, CH), 5.19 (d, *J* = 16.0 Hz, 1H, CH_2), 5.09 (d, *J* = 16.0 Hz, 1H, CH_2), 4.44 (d, *J* = 16.0 Hz, 1H, CH_2), 4.40 (d, *J* = 16.0 Hz, 1H, CH_2), 3.55 (d, *J* = 9.6 Hz, 1H, CH), 2.42 (s, 3H, CH_3), 2.11 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 172.8, 167.6, 156.0, 143.4, 141.0, 134.8, 134.6, 131.7, 131.0, 130.4, 129.8, 128.5, 128.4, 127.3, 127.2, 126.9, 126.7, 126.02, 126.01, 124.8 (q, $^1J_{C–F}$ = 279.0 Hz), 124.7, 122.9, 121.7, 109.8, 109.4, 73.9, 65.2, 62.4 (q, $^2J_{C–F}$ = 31.7 Hz), 44.08, 44.06, 44.0, 20.9, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{38}H_{31}F_3N_5O_5$ $[M + H]^+$ 694.2272, found 694.2274.



3ai

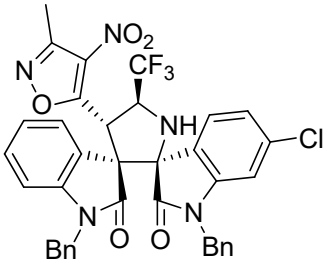
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5-methoxy-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ai). From **1a** (36.1 mg, 0.10 mmol) and **2i** (41.8 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 66.7 mg (94% yield) compound **3ai** as a white solid, m.p. 123–125 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 11.2 min (minor), t_R = 27.8 min (major); 89% *ee*. $[\alpha]_D^{25}$ = +37.0 (*c* = 2.83, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (td, J_1 = 7.7 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.07–6.93 (m, 10H, ArH), 6.76 (d, *J* = 7.6 Hz, 2H, ArH), 6.68 (d, *J* = 2.0 Hz, 1H, ArH), 6.63 (dd, J_1 = 8.4 Hz, J_2 = 2.4 Hz, 1H, ArH), 6.50 (d, *J* = 7.6 Hz, 1H, ArH), 6.33 (d, *J* = 8.4 Hz, 1H, ArH), 6.21 (d, *J* = 9.6 Hz, 1H, NH), 5.34–5.26 (m, 1H, CH), 5.20 (d, *J* = 16.0 Hz, 1H, CH_2), 5.09 (d, *J* = 16.0 Hz, 1H, CH_2), 4.44 (d, *J* = 16.0 Hz, 1H, CH_2), 4.39 (d, *J* = 16.0 Hz, 1H, CH_2), 3.53 (s, 3H, CH_3), 3.52 (d, *J* = 9.2 Hz, 1H, CH), 2.42 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 172.4, 167.4, 156.0, 155.3, 143.4, 136.8, 134.8, 134.5, 131.0, 130.0, 128.5, 128.4, 127.3, 127.2, 126.9, 126.6, 126.1, 125.5, 124.8 (q, $^1J_{C–F}$ = 279.1 Hz), 123.0, 121.8, 115.9, 111.8, 110.2, 109.9, 73.8, 65.0, 62.3 (q, $^2J_{C–F}$ = 31.7 Hz), 55.8, 44.2, 44.0, 43.7, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{38}H_{31}F_3N_5O_6$ $[M + H]^+$ 710.2221, found 710.2231.



3aj

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-6-fluoro-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3aj). From **1a** (36.1 mg, 0.10 mmol) and **2j** (40.4 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 69.1 mg (99% yield) compound **3aj** as a white solid, m.p. 121–123 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R =

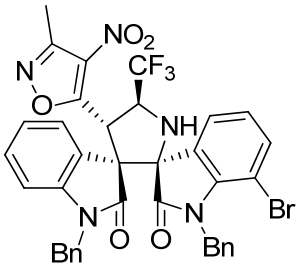
7.5 min (minor), t_R = 18.5 min (major); 93% *ee*. $[\alpha]_D^{25}$ = +3.0 (*c* = 3.29, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.22–7.16 (m, 2H, ArH), 7.11–6.95 (m, 9H, ArH), 6.84 (dd, J_1 = 8.4 Hz, J_2 = 5.2 Hz, 1H, ArH), 6.69 (d, *J* = 7.6 Hz, 2H, ArH), 6.52 (d, *J* = 8.0 Hz, 1H, ArH), 6.38 (td, J_1 = 8.9 Hz, J_2 = 2.0 Hz, 1H, ArH), 6.33 (d, *J* = 9.6 Hz, 1H, NH), 6.18 (dd, J_1 = 8.8 Hz, J_2 = 2.0 Hz, 1H, ArH), 5.28–5.21 (m, 1H, CH), 5.19 (d, *J* = 15.6 Hz, 1H, CH_2), 5.04 (d, *J* = 15.6 Hz, 1H, CH_2), 4.42 (d, *J* = 15.6 Hz, 2H, CH_2), 3.41 (d, *J* = 8.4 Hz, 1H, CH), 2.41 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 171.6, 166.9, 163.9 (d, $^1J_{C–F}$ = 247.7 Hz), 155.9, 145.5 (d, $^3J_{C–F}$ = 11.7 Hz), 143.0, 134.5, 134.3, 131.1, 130.2, 128.6, 128.5, 127.5, 127.4, 127.1, 126.6 (d, $^3J_{C–F}$ = 9.9 Hz), 126.5, 126.2, 124.8 (q, $^1J_{C–F}$ = 279.3 Hz), 123.1, 122.1, 119.5 (d, $^4J_{C–F}$ = 2.9 Hz), 109.9, 108.2 (d, $^2J_{C–F}$ = 22.3 Hz), 98.4 (d, $^2J_{C–F}$ = 27.5 Hz), 72.9, 64.9, 62.0 (q, $^2J_{C–F}$ = 32.0 Hz), 44.4, 43.9, 43.1, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3, –108.0 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}F_4N_5O_5$ $[M + H]^+$ 698.2022, found 698.2003.



3ak

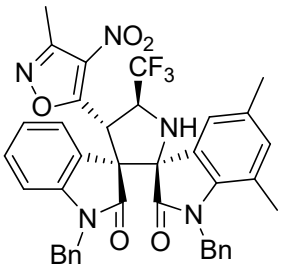
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-6-chloro-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3ak). From **1a** (36.1 mg, 0.10 mmol) and **2k** (42.3 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 63.7 mg (89% yield) compound **3ak** as a white solid, m.p. 127–129 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 7.5 min (minor), t_R = 18.0 min (major); 92% *ee*. $[\alpha]_D^{25}$ = +6.1 (*c* = 2.81, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.24–7.16 (m, 2H, ArH), 7.12–6.96 (m, 9H, ArH), 6.78 (d, *J* = 8.0 Hz, 1H, ArH), 6.69–6.66 (m, 3H, ArH), 6.52 (d, *J* = 7.6 Hz, 1H, ArH), 6.44 (d, *J* = 2.0 Hz, 1H, ArH), 6.34 (d, *J* = 10.0 Hz, 1H, NH), 5.29–5.20 (m, 1H, CH), 5.19 (d, *J* = 15.6 Hz, 1H, CH_2), 5.05 (d, *J* = 16.0 Hz, 1H, CH_2), 4.43 (d, *J* = 16.0 Hz, 1H, CH_2), 4.41 (d, *J* = 16.0 Hz, 1H, CH_2), 3.37 (d, *J* = 8.0 Hz, 1H, CH), 2.41 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ

174.3, 171.4, 166.8, 155.9, 145.0, 143.0, 136.3, 134.4, 134.3, 131.1, 130.3, 128.6, 128.5, 127.5, 127.4, 127.1, 126.5, 126.24, 126.17, 124.8 (q, $^{1}J_{C–F}$ = 279.3 Hz), 123.0, 122.4, 122.2, 121.9, 110.1, 109.9, 72.9, 64.9, 62.1 (q, $^{2}J_{C–F}$ = 32.0 Hz), 44.4, 43.9, 43.0, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.3 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}ClF_3N_5O_5$ [M + H]$^+$ 714.1726, found 714.1733.



3al

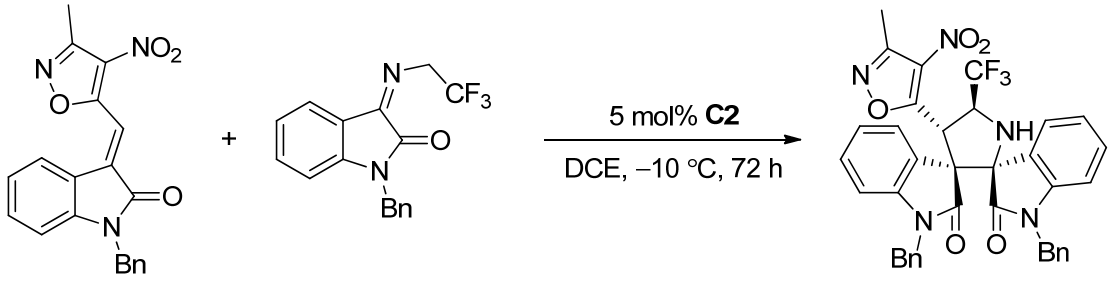
(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-7-bromo-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3al). From **1a** (36.1 mg, 0.10 mmol) and **2l** (47.8 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 70.8 mg (93% yield) compound **3al** as a white solid, m.p. 200–202 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.0 min (minor), t_R = 16.0 min (major); 90% *ee*. $[\alpha]_D^{25}$ = –36.9 (*c* = 3.25, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (dd, J_1 = 8.2 Hz, J_2 = 0.6 Hz, 1H, ArH), 7.18–7.13 (m, 2H, ArH), 7.11–7.04 (m, 6H, ArH), 6.91–6.83 (m, 6H, ArH), 6.70 (t, *J* = 7.8 Hz, 1H, ArH), 6.52 (d, *J* = 7.6 Hz, 1H, ArH), 6.08 (d, *J* = 9.6 Hz, 1H, NH), 5.36–5.24 (m, 3H, CH + CH_2), 4.97 (d, *J* = 15.6 Hz, 1H, CH_2), 4.46 (d, *J* = 15.6 Hz, 1H, CH_2), 3.55 (d, *J* = 9.2 Hz, 1H, CH), 2.41 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.5, 172.5, 167.3, 156.0, 143.3, 141.1, 136.8, 136.4, 134.6, 131.0, 130.2, 128.6, 128.3, 128.1, 127.4, 126.71, 126.66, 126.1, 125.9, 124.7 (q, $^{1}J_{C–F}$ = 279.1 Hz), 124.4, 123.3, 122.4, 121.9, 109.9, 102.7, 73.0, 65.2, 62.2 (q, $^{2}J_{C–F}$ = 31.6 Hz), 45.0, 44.2, 44.0, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{37}H_{28}BrF_3N_5O_5$ [M + H]$^+$ 758.1220, found 758.1253; calcd. for $C_{37}H_{28}{}^{81}BrF_3N_5O_5$ [M + H]$^+$ 760.1200, found 760.1216.



3am

(3*R*,3'*R*,4'*S*,5'*S*)-1,1''-Dibenzyl-5,7-dimethyl-4'-(3-methyl-4-nitroisoxazol-5-yl)-5'-(trifluoromethyl)dispiro[indoline-3,2'-pyrrolidine-3',3''-indoline]-2,2''-dione (3am). From **1a** (36.1 mg, 0.10 mmol) and **2m** (41.6 mg, 0.12 mmol), purified by silica gel (200-300 mesh) column chromatography using ethyl acetate/petroleum ether (1:3) as eluent to obtain 66.1 mg (97% yield) compound **3am** as a white solid, m.p. 219–221 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 11.3 min (minor), t_R = 23.9 min (major); 92% *ee*. $[\alpha]_D^{25}$ = +22.3 (*c* = 2.61, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (td, J_1 = 7.8 Hz, J_2 = 0.8 Hz, 1H, ArH), 7.08–6.96 (m, 7H, ArH), 6.86–6.81 (m, 3H, ArH), 6.73 (s, 1H, ArH), 6.69 (d, *J* = 7.2 Hz, 3H, ArH), 6.51 (d, *J* = 8.0 Hz, 1H, ArH), 5.98 (d, *J* = 9.2 Hz, 1H, NH), 5.41–5.31 (m, 1H, CH), 5.24 (d, *J* = 17.2 Hz, 1H, CH_2), 5.12 (d, *J* = 15.6 Hz, 1H, CH_2), 4.86 (d, *J* = 17.2 Hz, 1H, CH_2), 4.44 (d, *J* = 16.0 Hz, 1H, CH_2), 3.64 (d, *J* = 10.0 Hz, 1H, CH), 2.43 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 1.97 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 173.6, 168.0, 156.0, 143.7, 138.9, 136.9, 134.8, 134.7, 131.7, 130.9, 129.8, 128.5, 128.4, 127.3, 126.8, 126.7, 126.0, 125.9, 125.2, 124.8 (q, $^1J_{C–F}$ = 279.0 Hz), 124.0, 122.7, 121.6, 119.9, 109.8, 73.6, 65.4, 62.5 (q, $^2J_{C–F}$ = 31.6 Hz), 45.2, 44.7, 44.2, 20.7, 18.5, 11.4 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ –72.2 ppm. HRMS (ESI): *m*/*z* calcd. for $C_{39}H_{33}F_3N_5O_5$ $[M + H]^+$ 708.2428, found 708.2425.

4. Gram-scale synthesis of 3aa



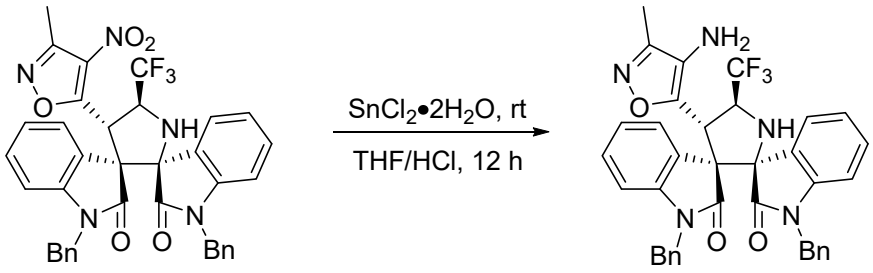
1a 1.5 mmol, 542.0 mg

2a 1.8 mmol, 572.9 mg

3aa 1.48 mmol, 1.0075 g, >20:1 *dr*, 93% *ee*

3-methyl-4-nitro-5-isatylidenyl-isoxazole **1a** (542.0 mg, 1.5 mmol), *N*-2,2,2-trifluoroethyl-isatin ketimine **2a** (572.9 mg, 1.8 mmol) and catalyst **C2** (42.2 mg, 5 mol%) were dissolved in dry DCE (15 mL) at –10 °C. After stirring at this temperature for 72 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/ethyl acetate, 3:1) to afford the desired product **3aa** as a white solid (1.0075 g, 99% yield) with >20:1 *dr* and 93% *ee*.

5. Procedure and the characterization data of compounds 4



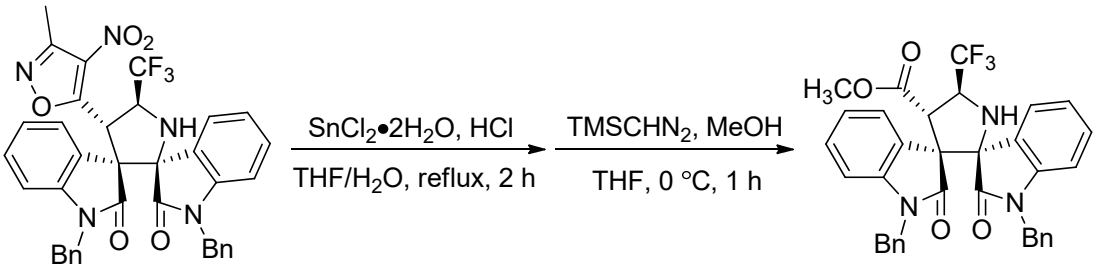
3aa, >20:1 *dr*, 93% *ee*

4, 40% yield, >20:1 *dr*, 93% *ee*

$SnCl_2$•$2H_2O$ (225.7 mg, 1.0 mmol) was added to the solution of compound **3aa** (135.9 mg, 0.20 mmol) in THF (4 mL) at room temperature. Then HCl (conc.) (0.25 mL) was added to it dropwise and the reaction mixture was stirred for 12 h. After that, the reaction mixture was added NaOH (1 N) solution until the pH value is 13 and extracted with ethyl acetate (3 × 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate, 2:1) to afford the desired product **4** as a white solid (52.0 mg, 40% yield). m.p. 194–196 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 85:15, flow rate 1.0 mL/min, detection at 254 nm): t_R = 29.2 min (minor), t_R = 36.0 min (major); 93% *ee*. $[\alpha]_D^{25}$ = –33.8 (*c* = 2.49, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.2 Hz, 1H, ArH), 7.28–7.26 (m, 2H,

ArH), 7.20–7.11 (m, 2H, ArH), 7.09–7.02 (m, 5H, ArH), 6.92 (t, J = 7.6 Hz, 2H, ArH), 6.56–6.50 (m, 2H, ArH), 6.45 (d, J = 7.6 Hz, 3H, ArH), 6.37 (d, J = 7.6 Hz, 1H, ArH), 5.79 (d, J = 10.4 Hz, 1H, NH), 5.29 (d, J = 15.6 Hz, 1H, CH_2), 5.26–5.19 (m, 1H, CH), 5.00 (d, J = 16.4 Hz, 1H, CH_2), 4.42 (d, J = 15.6 Hz, 2H, CH_2), 3.03–2.73 (m, 3H, CH + NH_2), 2.04 (s, 3H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 172.7, 154.4, 146.7, 143.9, 142.6, 135.2, 134.4, 130.1, 129.7, 128.5, 127.5, 127.3, 127.1, 126.5, 125.9, 125.4 (q, $^1J_{C–F}$ = 279.3 Hz), 125.1, 125.0, 124.0, 123.6, 122.4, 121.8, 109.7, 109.2, 72.1, 64.4, 60.2 (q, $^2J_{C–F}$ = 31.8 Hz), 44.3, 43.6, 41.1, 9.2 ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ −72.6 ppm. HRMS (ESI): m/z calcd. for $C_{37}H_{31}F_3N_5O_3$ $[M + H]^+$ 650.2374, found 650.2357.

6. Procedure and the characterization data of compound 5



3aa, >20:1 *dr*, 93% *ee*

5, 43% yield
>20:1 *dr*, 93% *ee*

The mixture of compound **3aa** (135.9 mg, 0.2 mmol), $SnCl_2·2H_2O$ (135.4 mg, 0.6 mmol), THF (5.0 mL), water (5.0 mL), and HCl (conc.) (0.5 mL) was heated at reflux for 2 h and then cooled to room temperature. THF was evaporated in vacuo, and the water layer was extracted with ethyl acetate (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. After evaporation of solvent, the resulted residue was dissolved in dry THF (2 mL) at 0 °C, then $TMSCHN_2$ (0.4 mL) and MeOH (80 μL) were added to the reaction mixture slowly. After stirring at this temperature for 1 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography (petroleum ether/ethyl acetate, 3:1) to afford the desired product **5** as a white solid (53.2 mg, 43% yield). m.p. 244–246 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 10.3 min (minor), t_R = 34.9 min (major); 93% *ee*. $[\alpha]_D^{25}$ = –103.9 (c = 0.64, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 7.2 Hz, 1H, ArH), 7.33–7.31 (m, 2H, ArH), 7.21 (t, J = 7.6 Hz, 1H, ArH), 7.15–7.04 (m, 6H, ArH), 6.97 (t, J =

7.6 Hz, 2H, ArH), 6.61 (d, J = 7.2 Hz, 2H, ArH), 6.55–6.50 (m, 3H, ArH), 6.40 (d, J = 7.6 Hz, 1H, ArH), 5.23 (d, J = 15.6 Hz, 1H, CH_2), 5.15 (d, J = 9.6 Hz, 1H, NH), 5.08–4.98 (m, 2H, CH_2 + CH), 4.48 (d, J = 16.0 Hz, 1H, CH_2), 4.45 (d, J = 15.6 Hz, 1H, CH_2), 3.24 (s, 3H, CH_3), 2.86 (d, J = 6.4 Hz, 1H, CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.4, 171.4, 168.5, 143.9, 142.9, 135.4, 134.8, 130.2, 129.9, 128.53, 128.48, 127.7, 127.4, 127.2, 126.4, 125.44, 125.40 (q, $^1J_{C–F}$ = 279.5 Hz), 125.0, 123.4, 122.2, 121.7, 109.5, 109.2, 72.4, 63.0, 60.7 (q, $^2J_{C–F}$ = 32.3 Hz), 52.2, 49.7, 44.3, 43.6 ppm. HRMS (ESI): m/z calcd. for $C_{35}H_{28}F_3N_3O_4Na$ $[M + Na]^+$ 634.1924, found 634.1928.

7. Reference

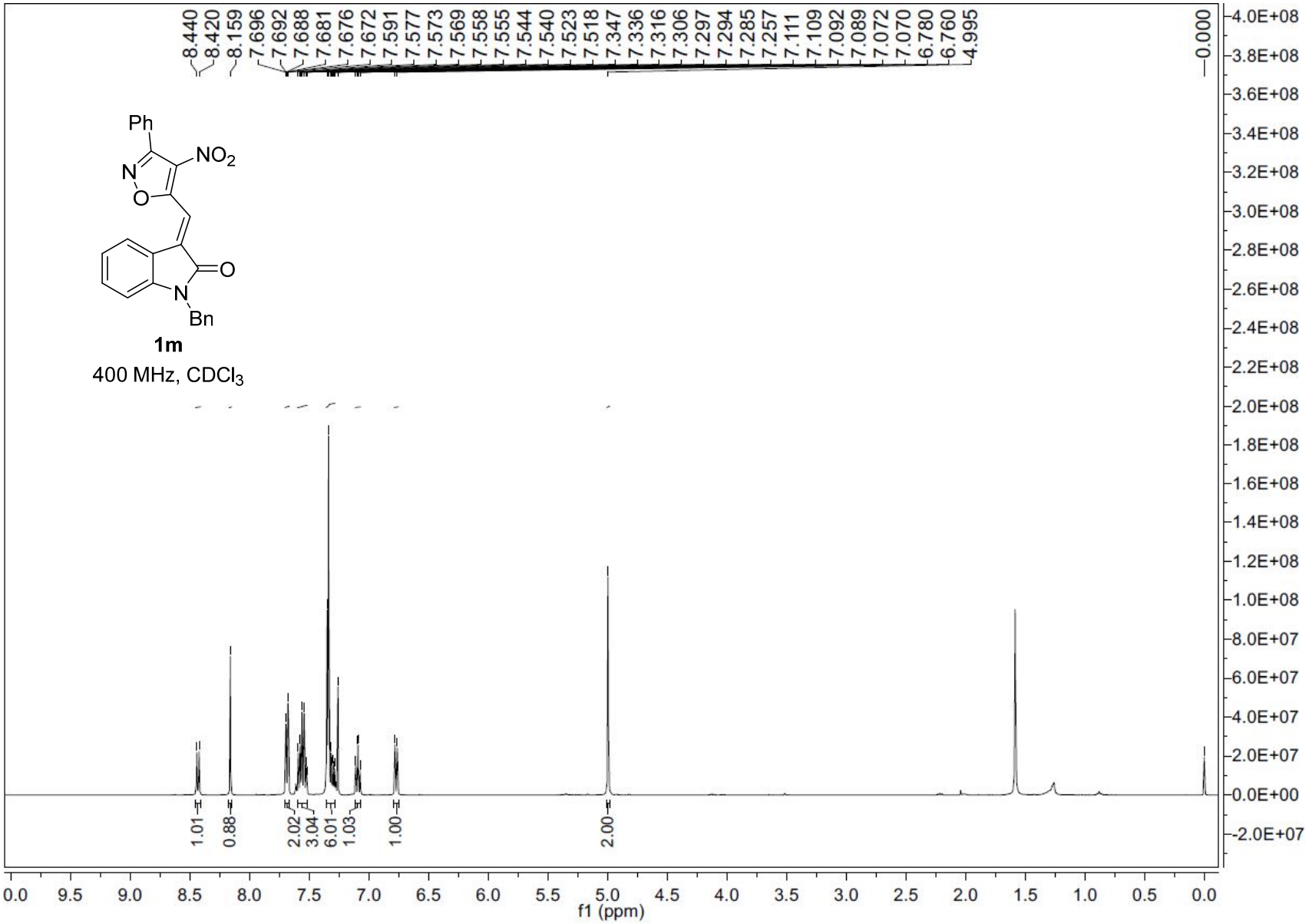
[1] Y. Zhang, B. W. Wei, H. Lin, L. Zhang, J. X. Liu, H. Q. Luo and X. L. Fan, *Green Chem.*, 2015, **17**, 3266–3270.

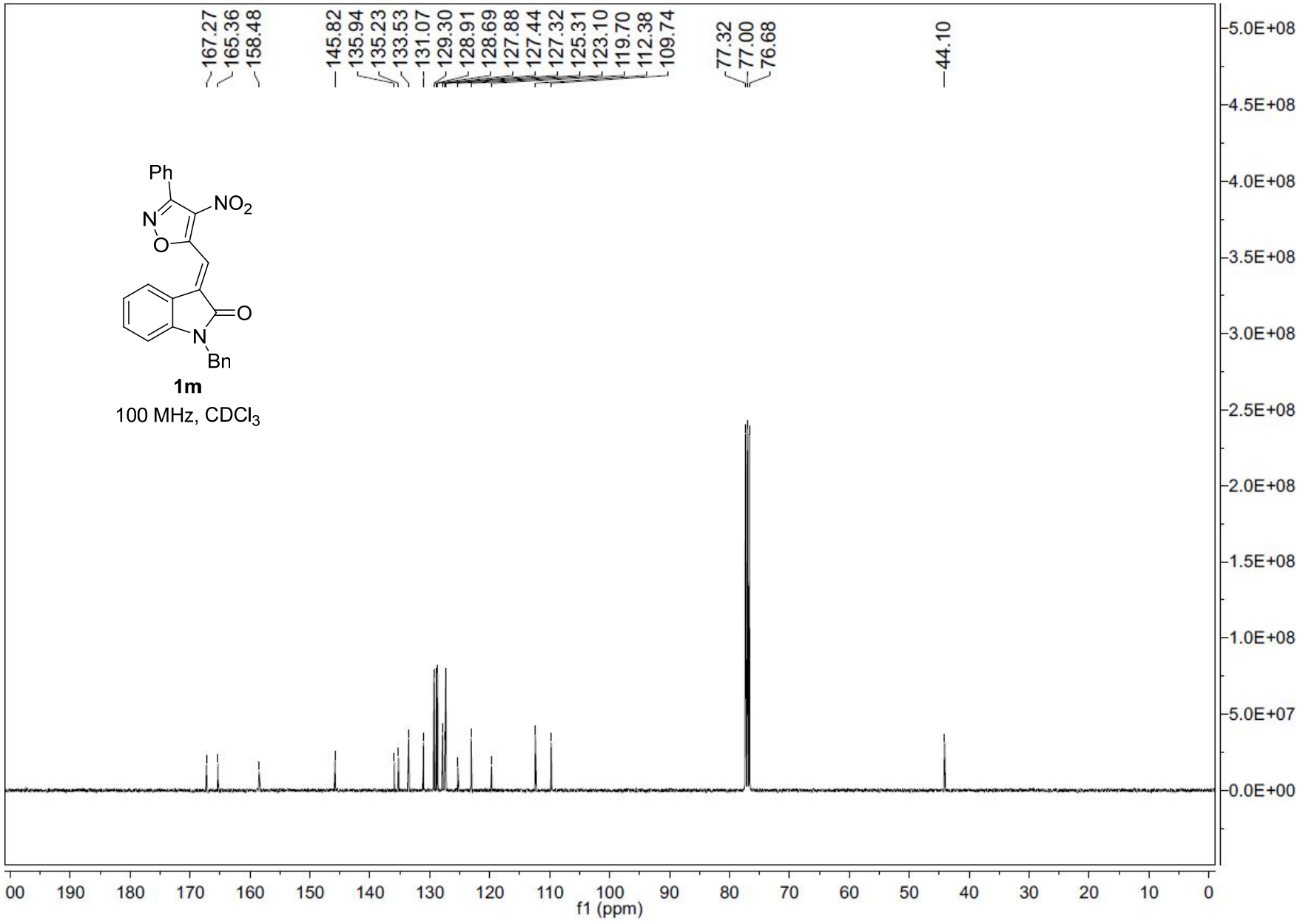
[2] (a) D. A. Vasilenko, K. S. Sadovnikov, K. N. Sedenkova, A. V. Kurova, Y. K. Grishin, T. S. Kuznetsova, V. B. Rybakov, Y. A. Volkova and E. B. Averina, *Synthesis*, 2020, **52**, 1398–1406. (b) Y. Zhang, B. W. Wei, H. Lin, L. Zhang, J. X. Liu, H. Q. Luo and X. L. Fan, *Green Chem.*, 2015, **17**, 3266–3270.

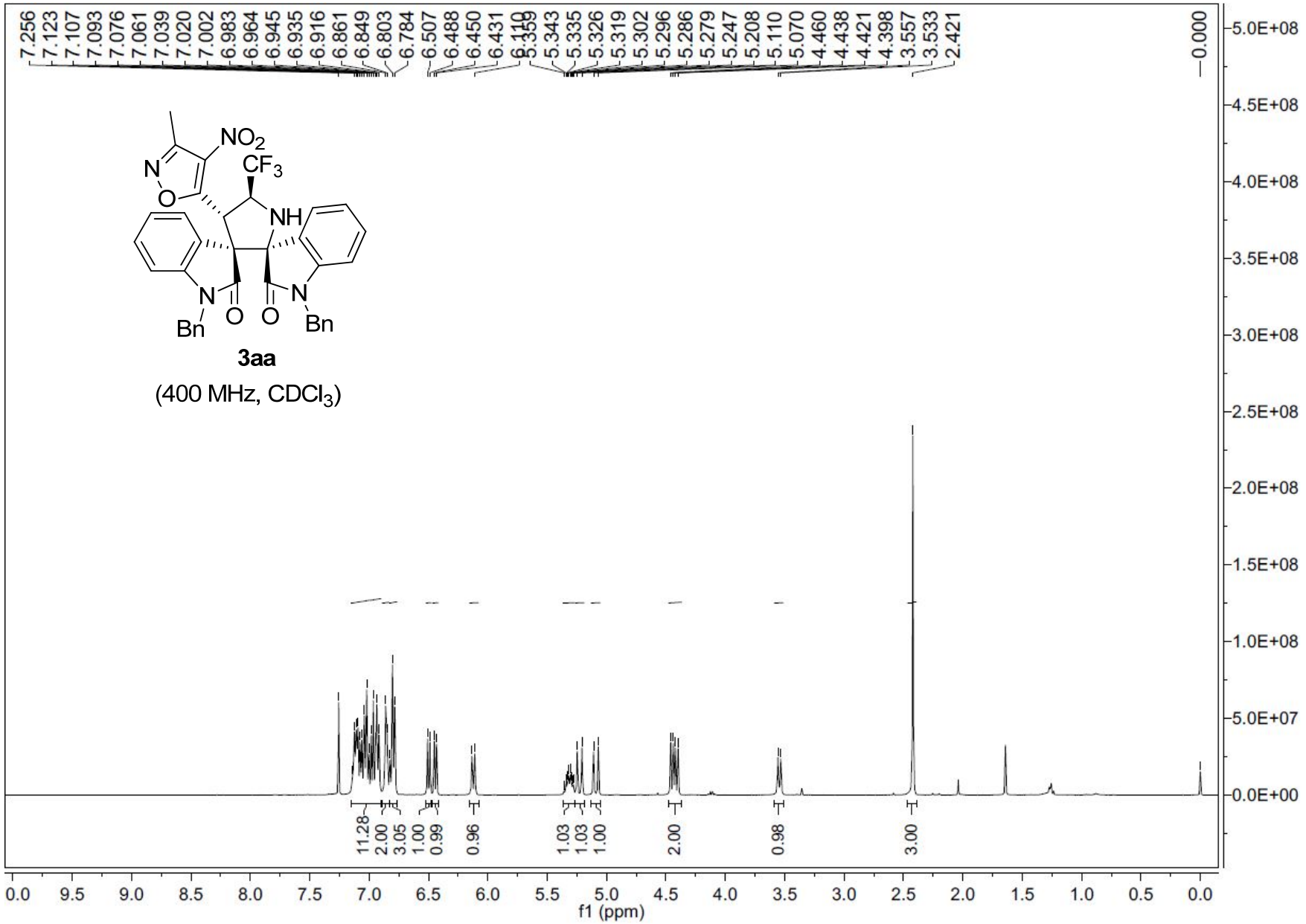
[3] M. Ma, Y. Zhu, Q. Sun, X. Li, J. Su, L. Zhao, Y. Zhao, S. Qiu, W. Yan, K. Wang and R. Wang, *Chem. Commun.*, 2015, **51**, 8789–8792.

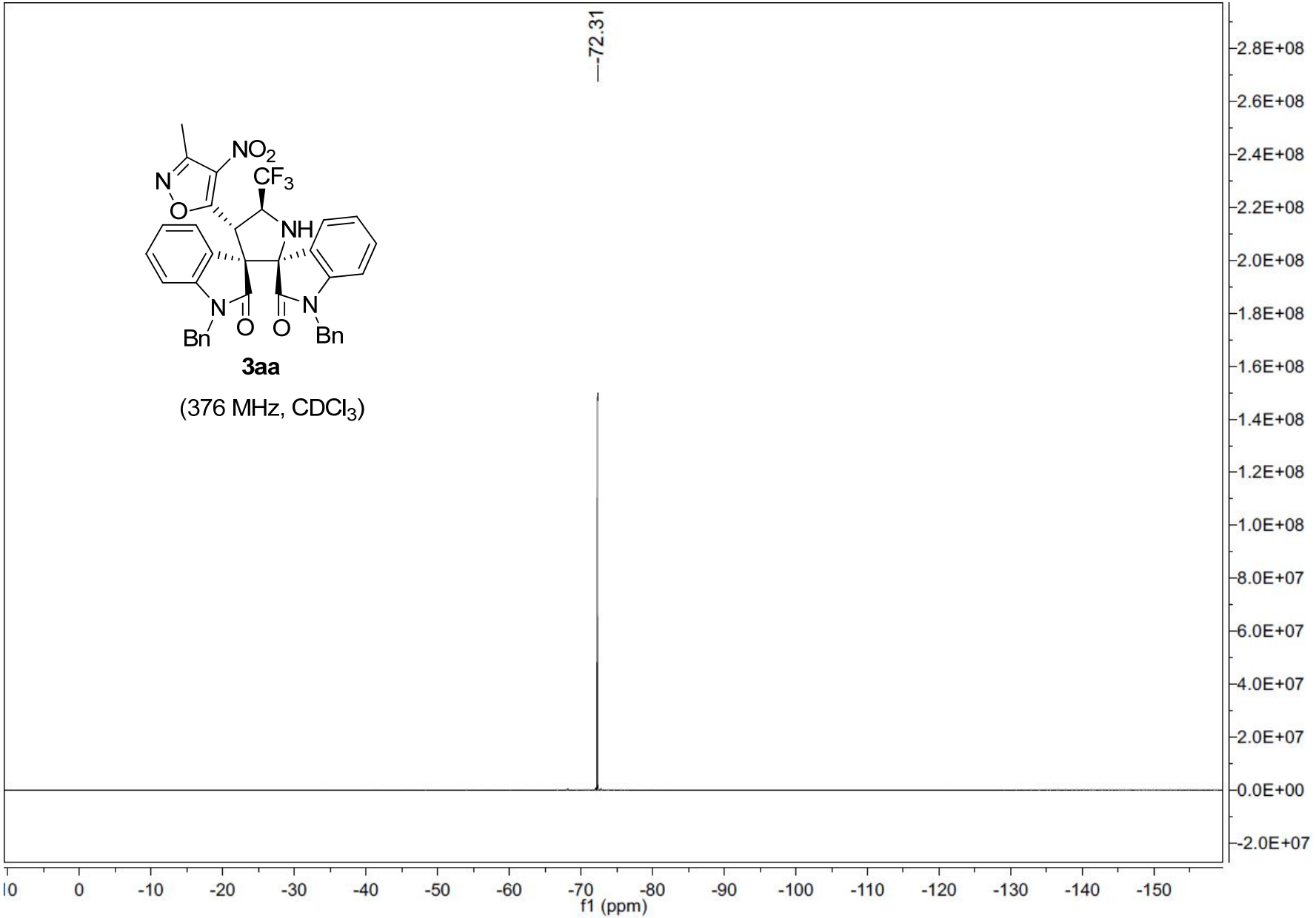
[4] (a) Y. Zhu, J. P. Malerich and V. H. Rawal, *Angew. Chem. Int. Ed.*, 2010, **49**, 153–156; *Angew. Chem.* **2010**, 122, 157–160. (b) W. Yang and D. M. Du, *Org. Lett.*, 2010, **12**, 5450–5453. (c) W. Yang and D. M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241–1246. (d) B. Vakulya, S. Varga, A.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

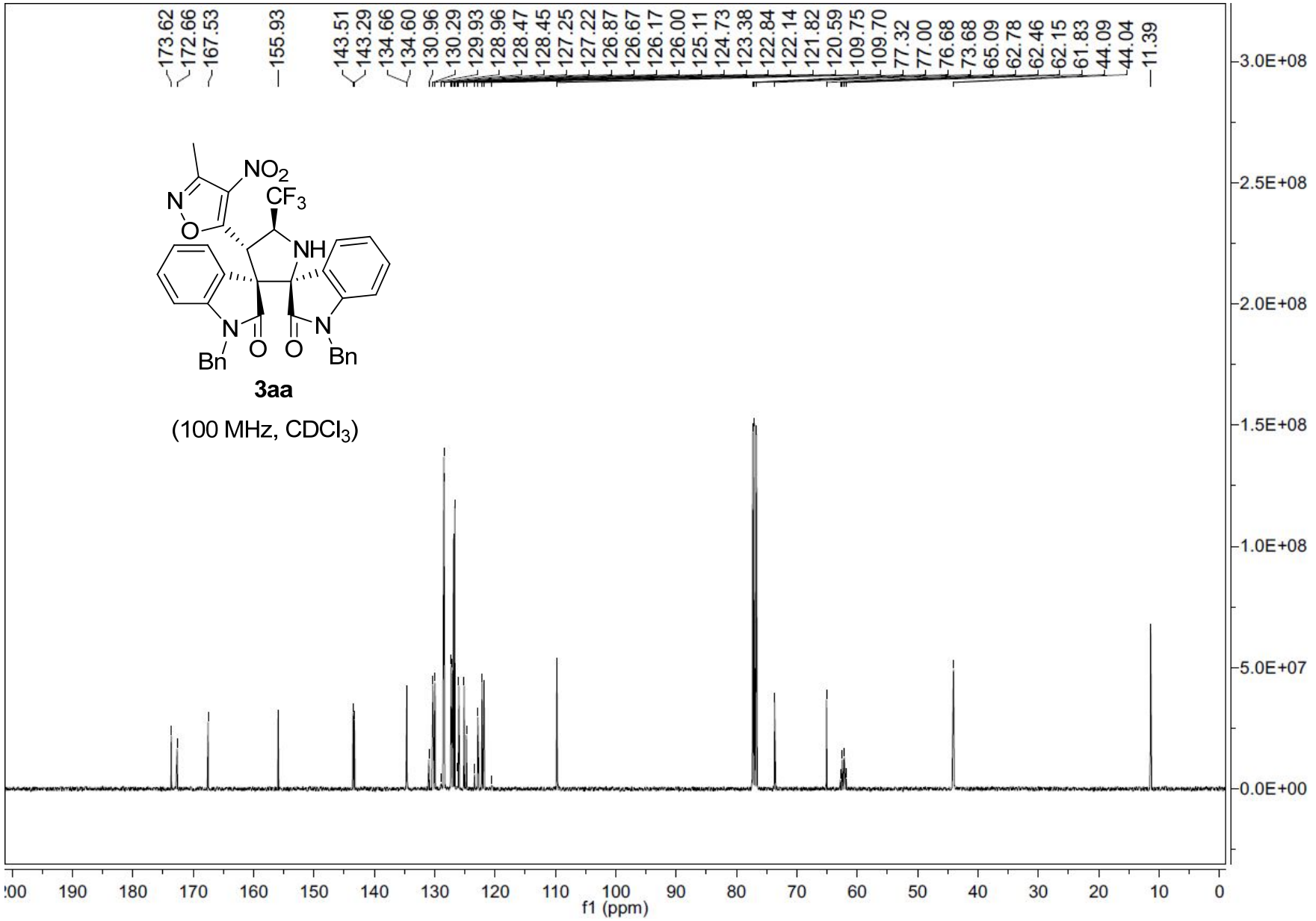
8. Copies of ^{1}H, ^{19}F and ^{13}C NMR spectra of new compounds

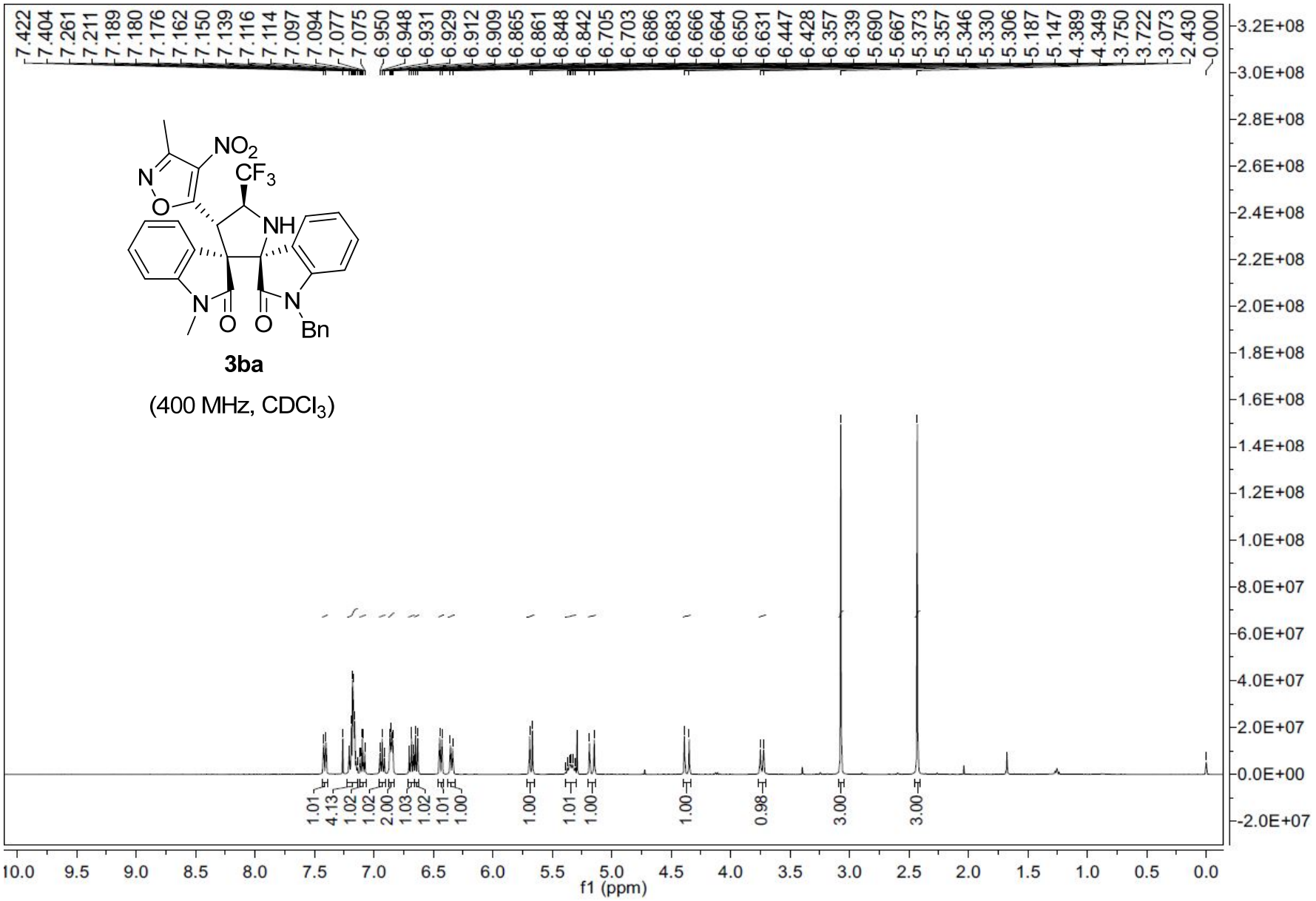


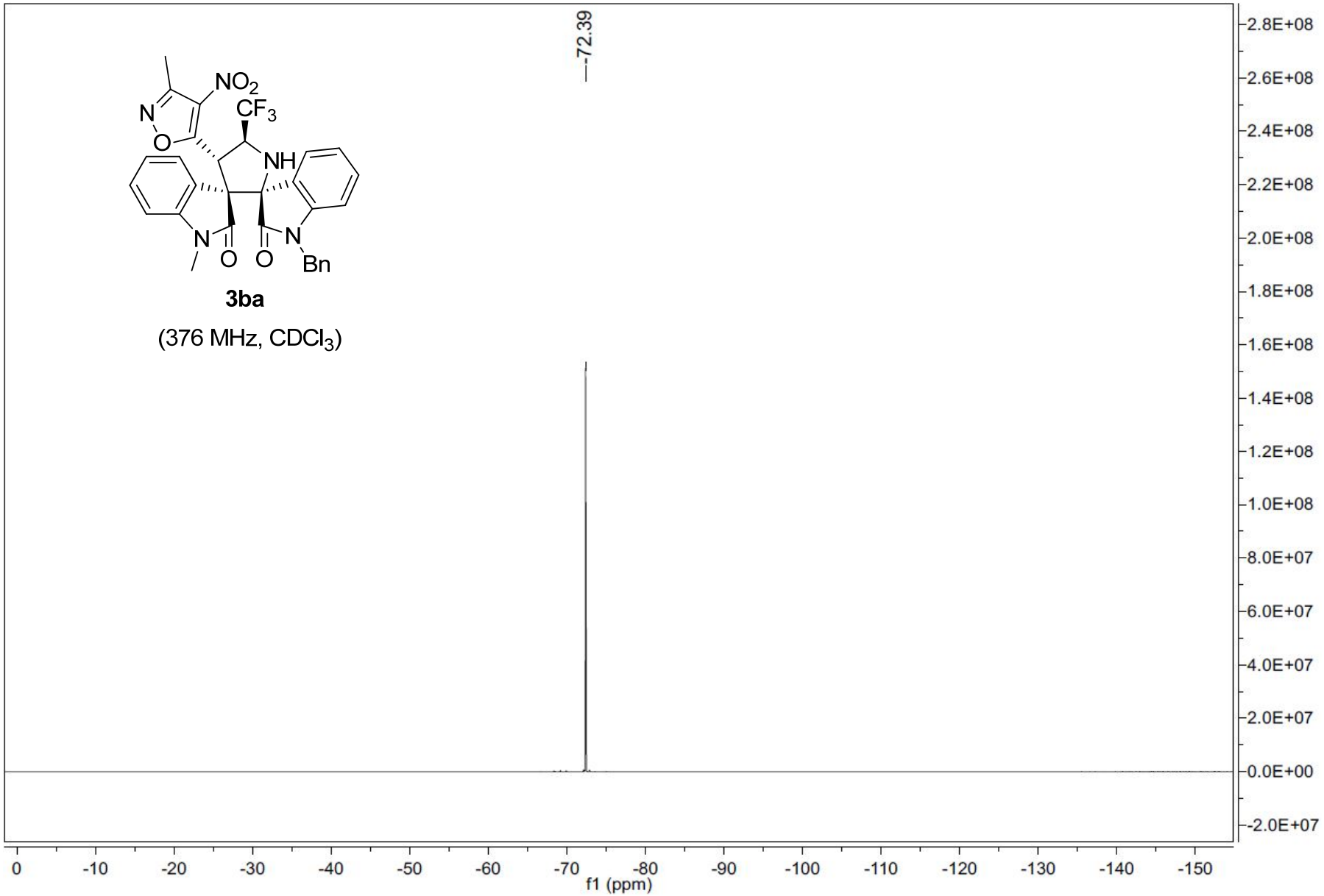

167.27
165.36
158.48
145.82
135.94
135.23
133.53
131.07
129.30
128.91
128.69
127.88
127.44
127.32
125.31
123.10
119.70
112.38
109.74
77.32
77.00
76.68
44.10
Ph
NO2
N
O
O
N
Bn
1m
100 MHz, CDCl3
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

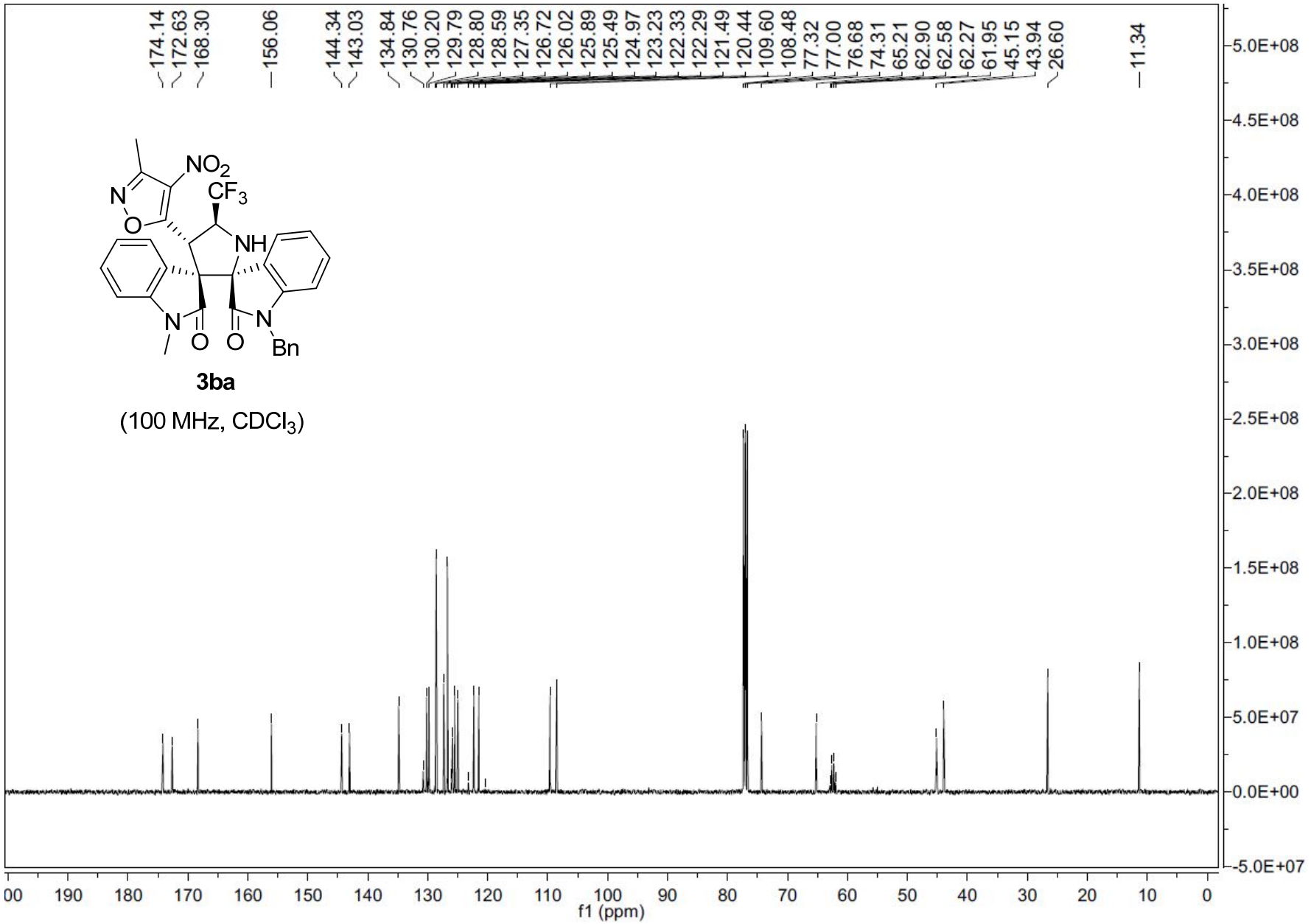

7.256
7.123
7.107
7.093
7.076
7.061
7.039
7.020
7.002
6.983
6.964
6.945
6.935
6.916
6.861
6.849
6.803
6.784
6.507
6.488
6.450
6.431
6.359
5.343
5.335
5.326
5.319
5.302
5.296
5.286
5.279
5.247
5.208
5.110
5.070
4.460
4.438
4.421
4.398
3.557
3.533
2.421
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3aa
(400 MHz, CDCl3)
11.28
2.00
3.05
1.00
0.99
0.96
1.03
1.03
1.00
2.00
0.98
3.00
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

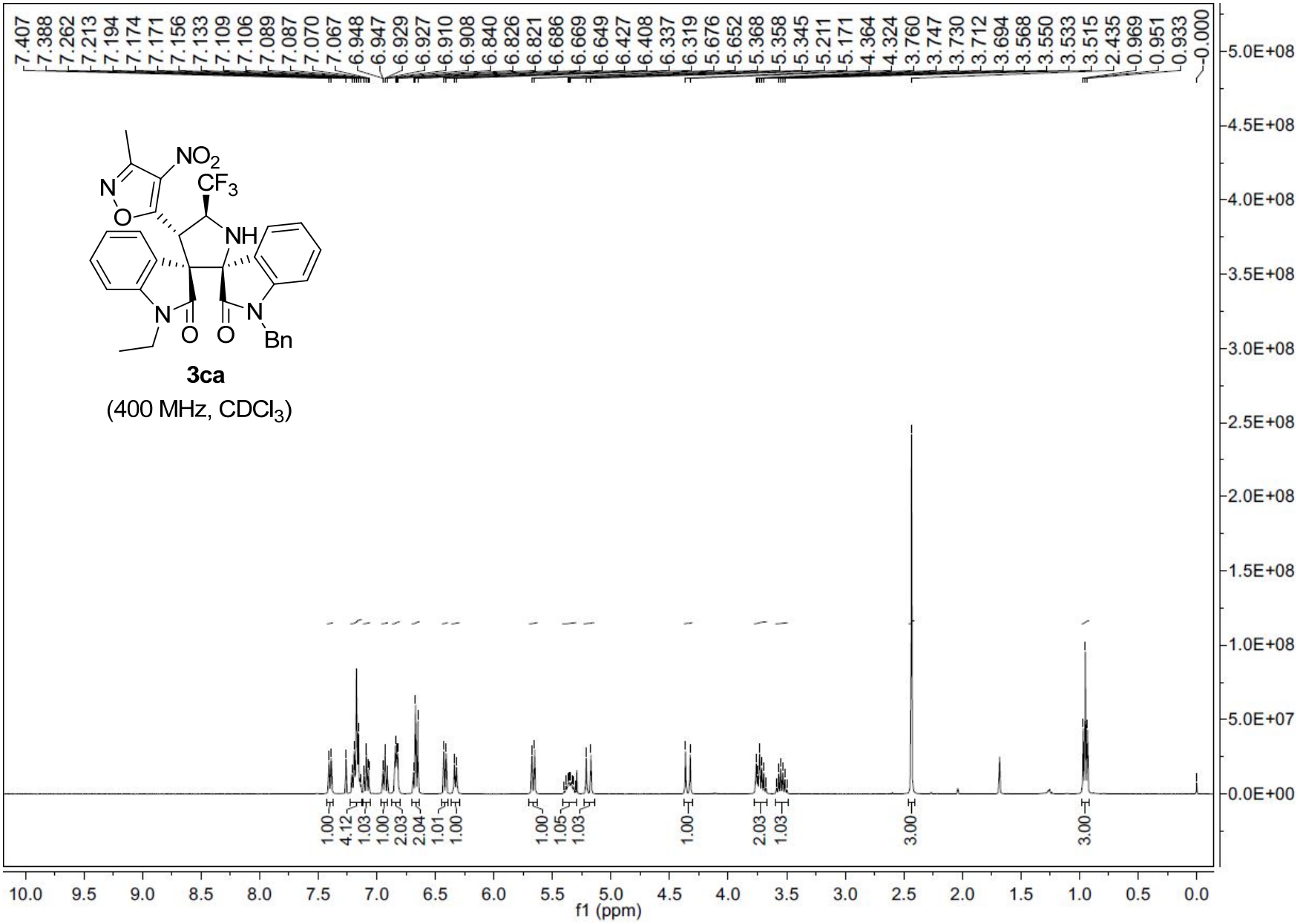

-72.31
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3aa
(376 MHz, CDCl3)
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

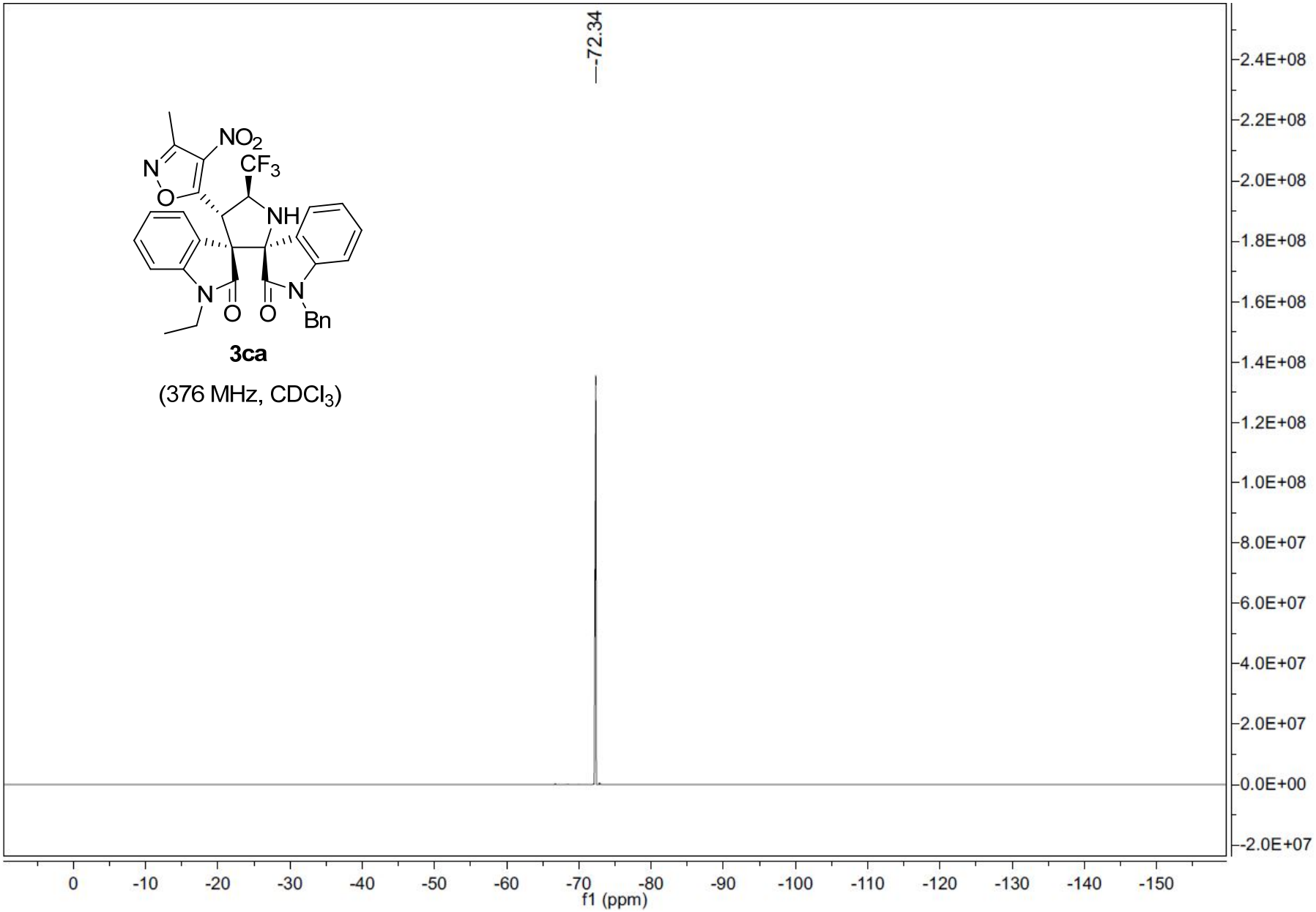

173.62
172.66
167.53
155.93
143.51
143.29
134.66
134.60
130.96
130.29
129.93
128.96
128.47
128.45
127.25
127.22
126.87
126.67
126.17
126.00
125.11
124.73
123.38
122.84
122.14
121.82
120.59
109.75
109.70
77.32
77.00
76.68
73.68
65.09
62.78
62.46
62.15
61.83
44.09
44.04
11.39
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3aa
(100 MHz, CDCl3)
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

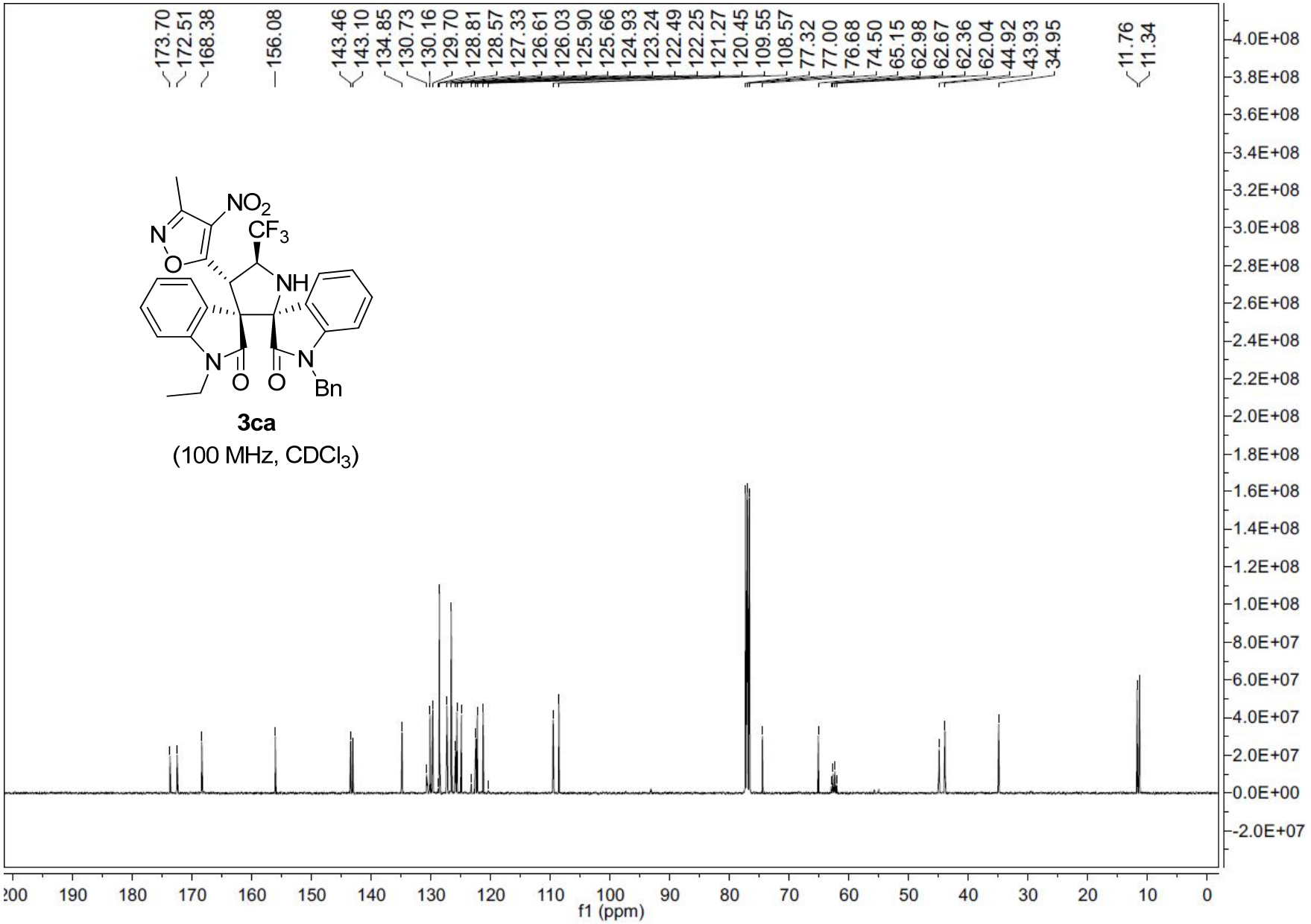

7.422
7.404
7.261
7.211
7.189
7.180
7.176
7.162
7.150
7.139
7.116
7.114
7.097
7.094
7.077
7.075
6.950
6.948
6.931
6.929
6.912
6.909
6.865
6.861
6.848
6.842
6.705
6.703
6.686
6.683
6.666
6.664
6.650
6.631
6.447
6.428
6.357
6.339
5.690
5.667
5.373
5.357
5.346
5.330
5.306
5.187
5.147
4.389
4.349
3.750
3.722
3.073
2.430
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ba
(400 MHz, CDCl3)
1.01
4.13
1.02
1.02
2.00
1.03
1.02
1.01
1.00
1.00
1.01
1.00
1.00
0.98
3.00
3.00
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-72.39
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ba
(376 MHz, CDCl3)
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)


174.14
172.63
168.30
156.06
144.34
143.03
134.84
130.76
130.20
129.79
128.80
128.59
127.35
126.72
126.02
125.89
125.49
124.97
123.23
122.33
122.29
121.49
120.44
109.60
108.48
77.32
77.00
76.68
74.31
65.21
62.90
62.58
62.27
61.95
45.15
43.94
26.60
11.34
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ba
(100 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

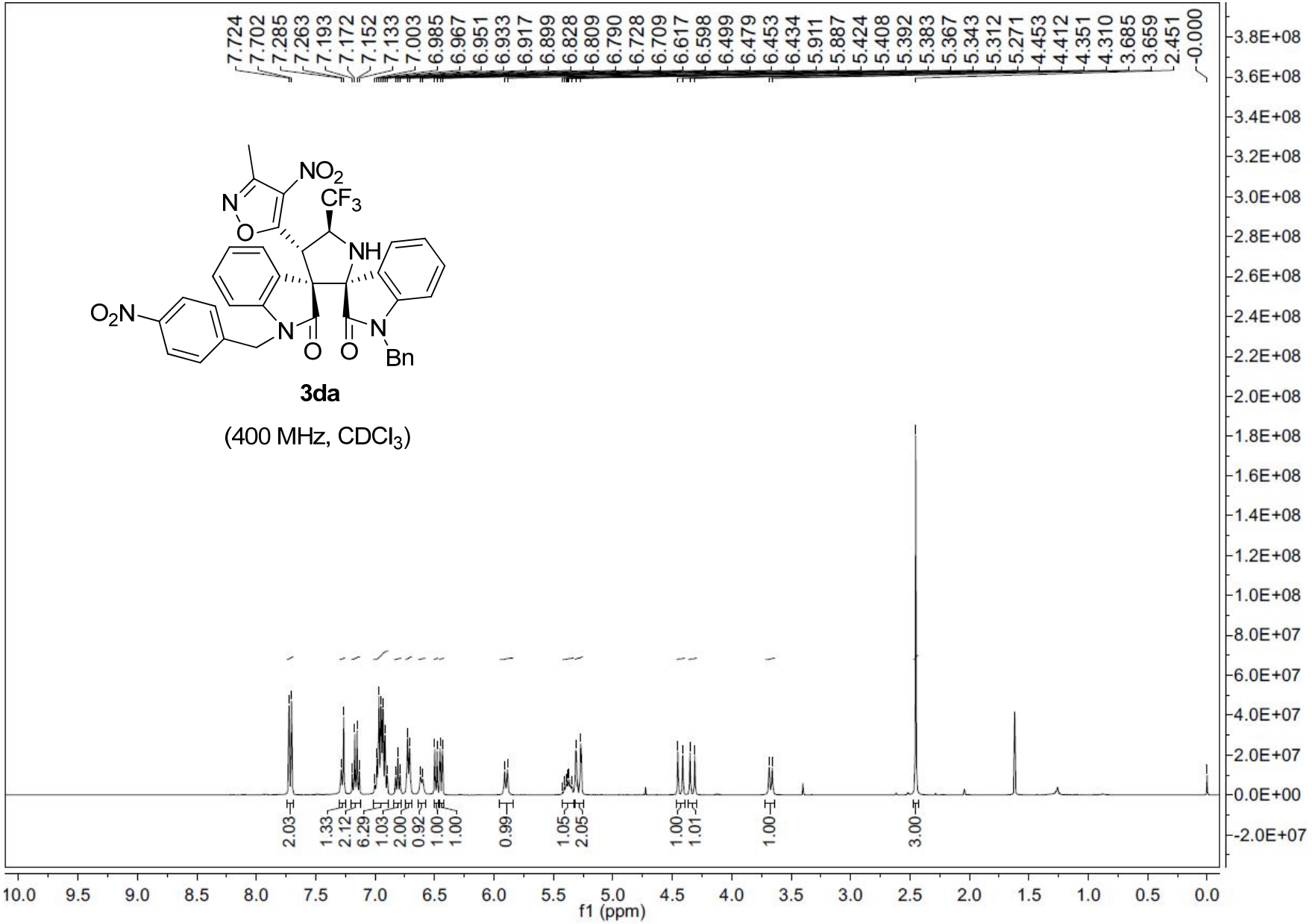

7.407
7.388
7.262
7.213
7.194
7.174
7.171
7.156
7.133
7.109
7.106
7.089
7.087
7.070
7.067
6.948
6.947
6.929
6.927
6.910
6.908
6.840
6.826
6.821
6.686
6.669
6.649
6.427
6.408
6.337
6.319
5.676
5.652
5.368
5.358
5.345
5.211
5.171
4.364
4.324
3.760
3.747
3.730
3.712
3.694
3.568
3.550
3.533
3.515
2.435
0.969
0.951
0.933
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ca
(400 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
1.00
4.12
1.03
1.00
2.03
2.04
1.01
1.00
1.00
1.05
1.03
1.00
2.03
1.03
3.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

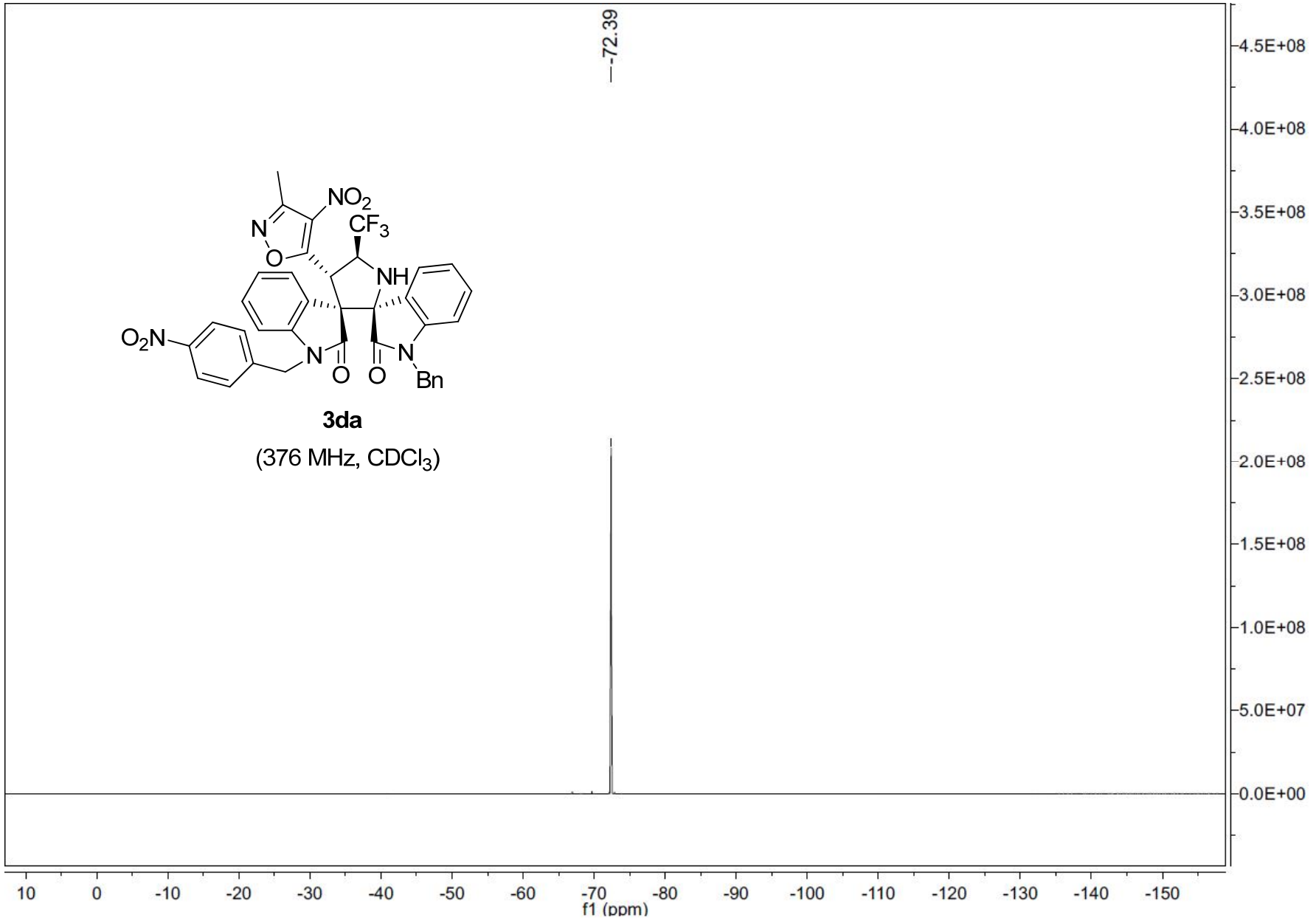

-72.34
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ca
(376 MHz, CDCl3)
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)



3ca

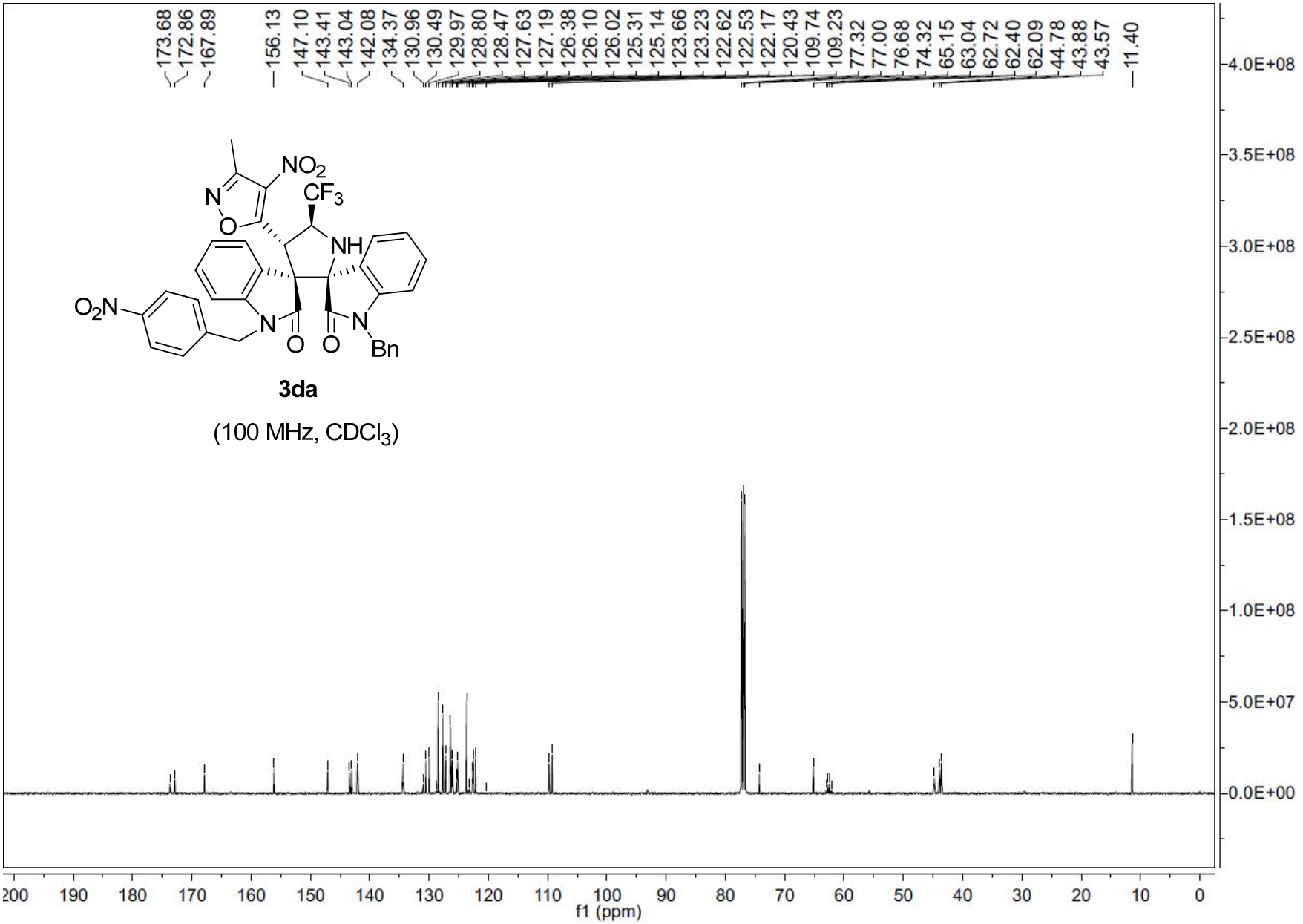
(100 MHz, $CDCl_3$)


7.724
7.702
7.285
7.263
7.193
7.172
7.152
7.133
7.003
6.985
6.967
6.951
6.933
6.917
6.899
6.828
6.809
6.790
6.728
6.709
6.617
6.598
6.499
6.479
6.453
6.434
5.911
5.887
5.424
5.408
5.392
5.383
5.367
5.343
5.312
5.271
4.453
4.412
4.351
4.310
3.685
3.659
2.451
-0.000
NO2
CF3
N
O
NH
O2N
N
O
O
N
Bn
3da
(400 MHz, CDCl3)
2.03
1.33
2.12
6.29
1.03
2.00
0.92
1.00
1.00
0.99
1.05
2.05
1.00
1.01
1.00
3.00
f1 (ppm)



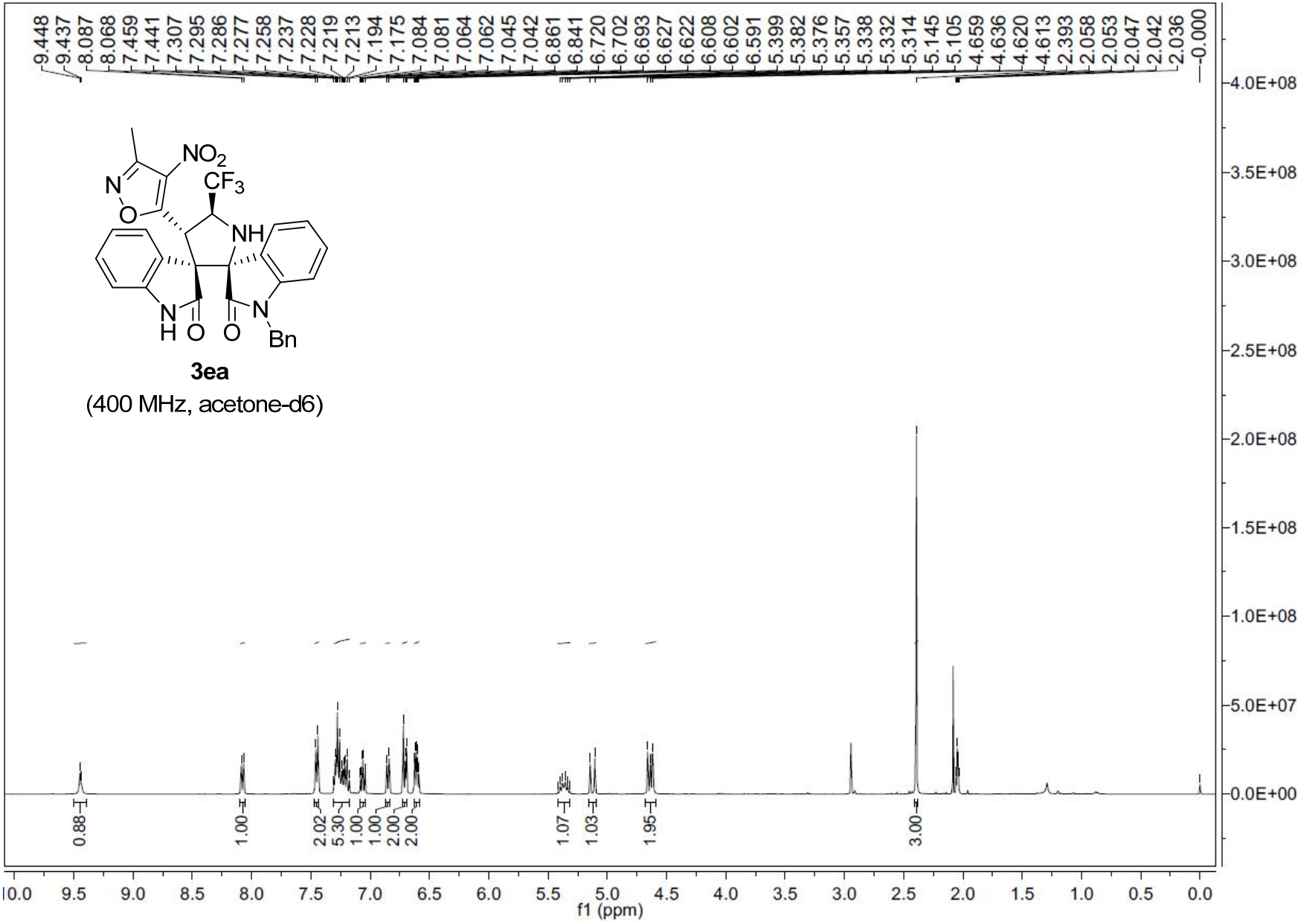
3da

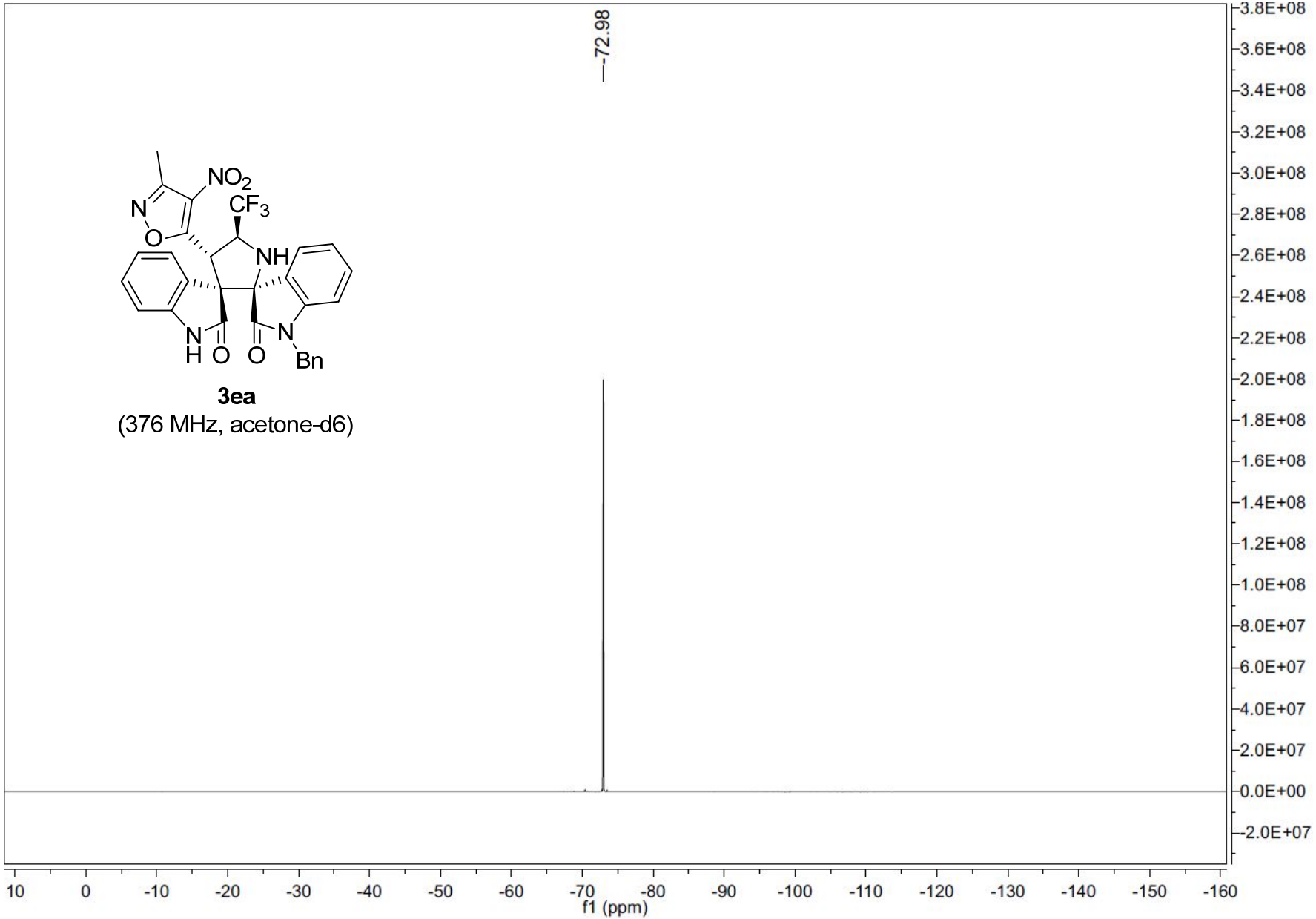
(376 MHz, $CDCl_3$)



3da

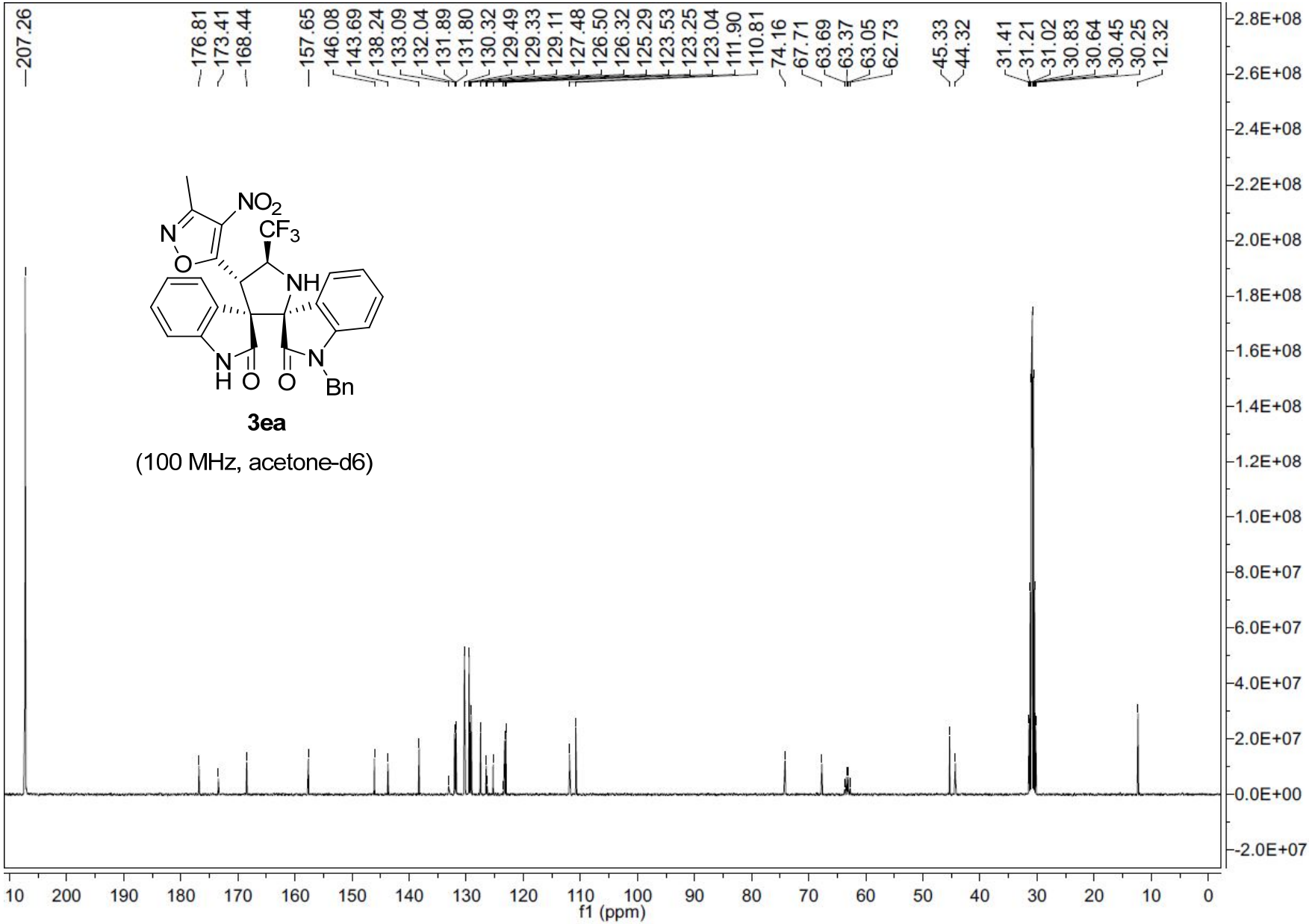
(100 MHz, $CDCl_3$)

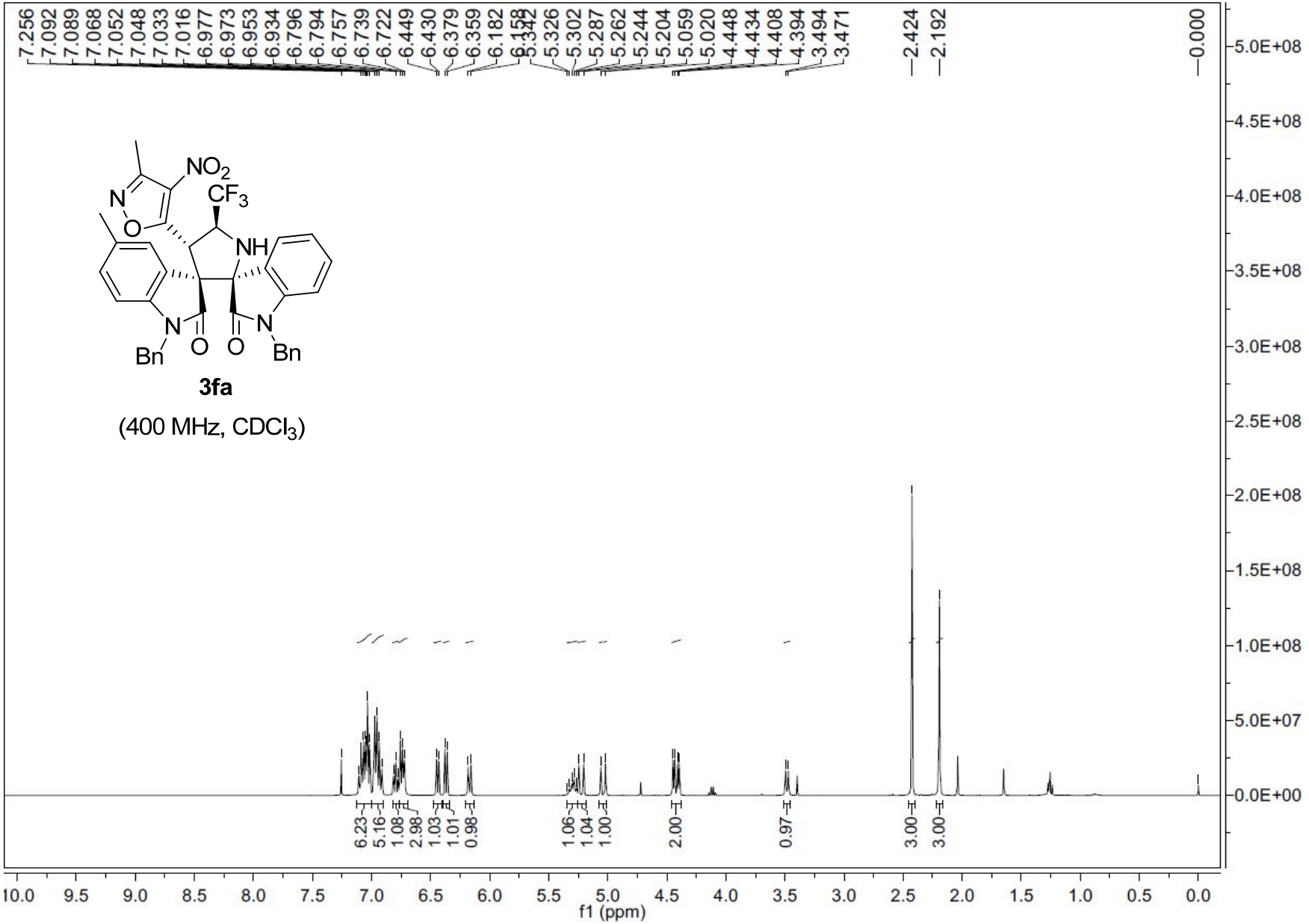

9.448
9.437
8.087
8.068
7.459
7.441
7.307
7.295
7.286
7.277
7.258
7.237
7.228
7.219
7.213
7.194
7.175
7.084
7.081
7.064
7.062
7.045
7.042
6.861
6.841
6.720
6.702
6.693
6.627
6.622
6.608
6.602
6.591
5.399
5.382
5.376
5.357
5.338
5.332
5.314
5.145
5.105
4.659
4.636
4.620
4.613
2.393
2.058
2.053
2.047
2.042
2.036
0.000
NO2
CF3
N
O
NH
N
H O
O
N
Bn
3ea
(400 MHz, acetone-d6)
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
0.88
1.00
2.02
5.30
1.00
1.00
2.00
2.00
1.07
1.03
1.95
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

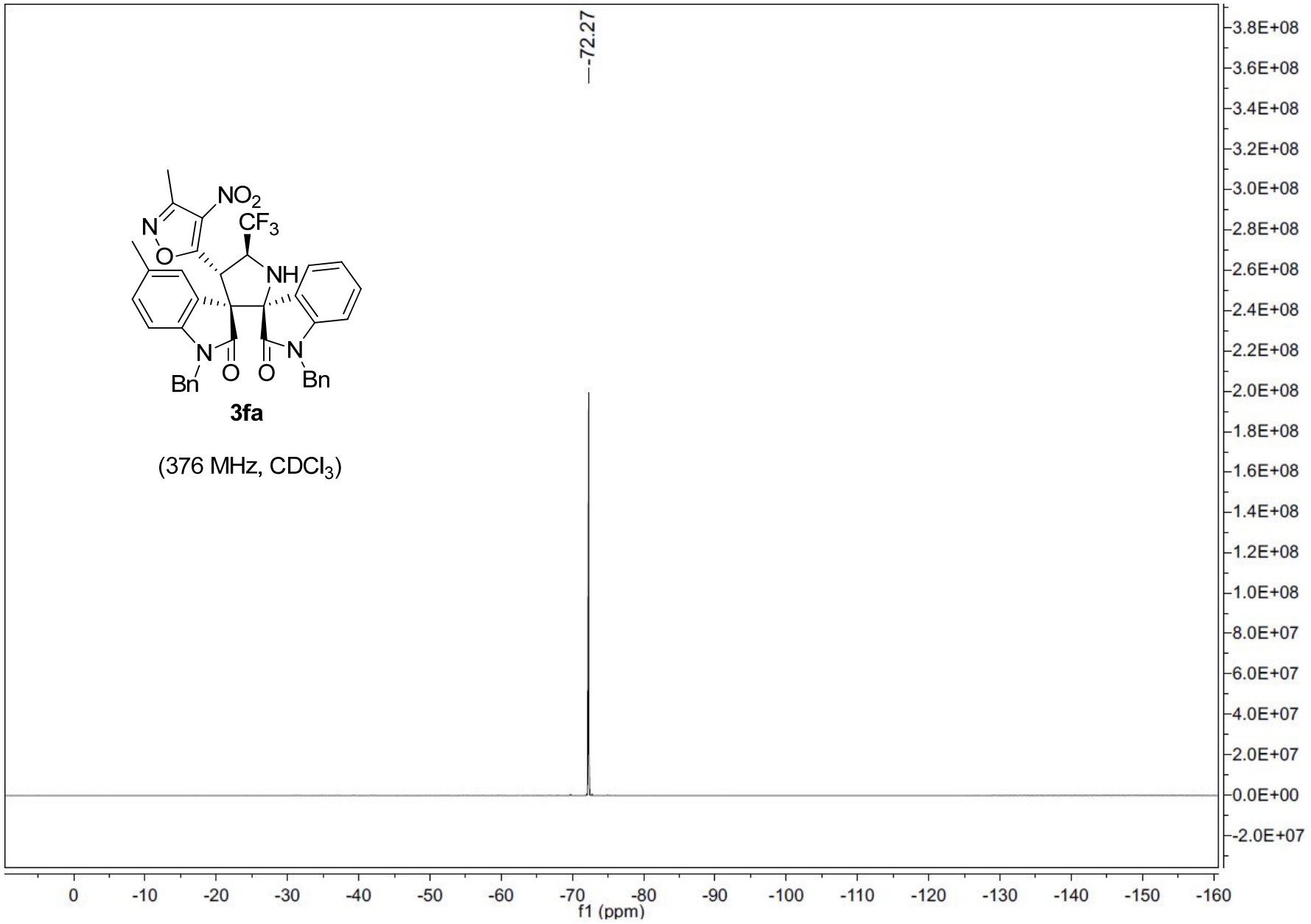


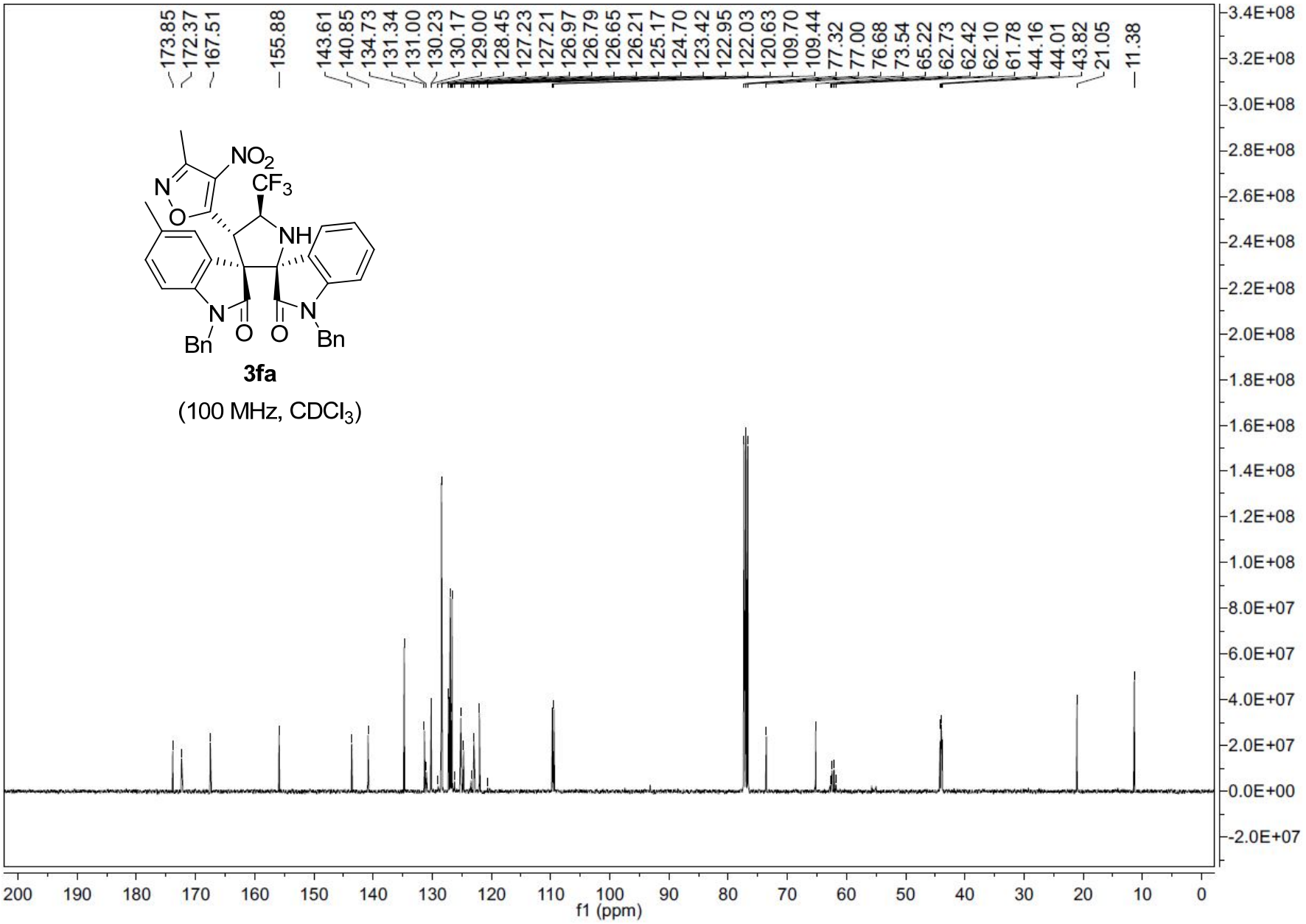
3ea

(376 MHz, acetone-d6)


207.26
176.81
173.41
168.44
157.65
146.08
143.69
138.24
133.09
132.04
131.89
131.80
130.32
129.49
129.33
129.11
127.48
126.50
126.32
125.29
123.53
123.25
123.04
111.90
110.81
74.16
67.71
63.69
63.37
63.05
62.73
45.33
44.32
31.41
31.21
31.02
30.83
30.64
30.45
30.25
12.32
NO2
CF3
N
O
NH
N
H
O
O
N
Bn
3ea
(100 MHz, acetone-d6)
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
f1 (ppm)

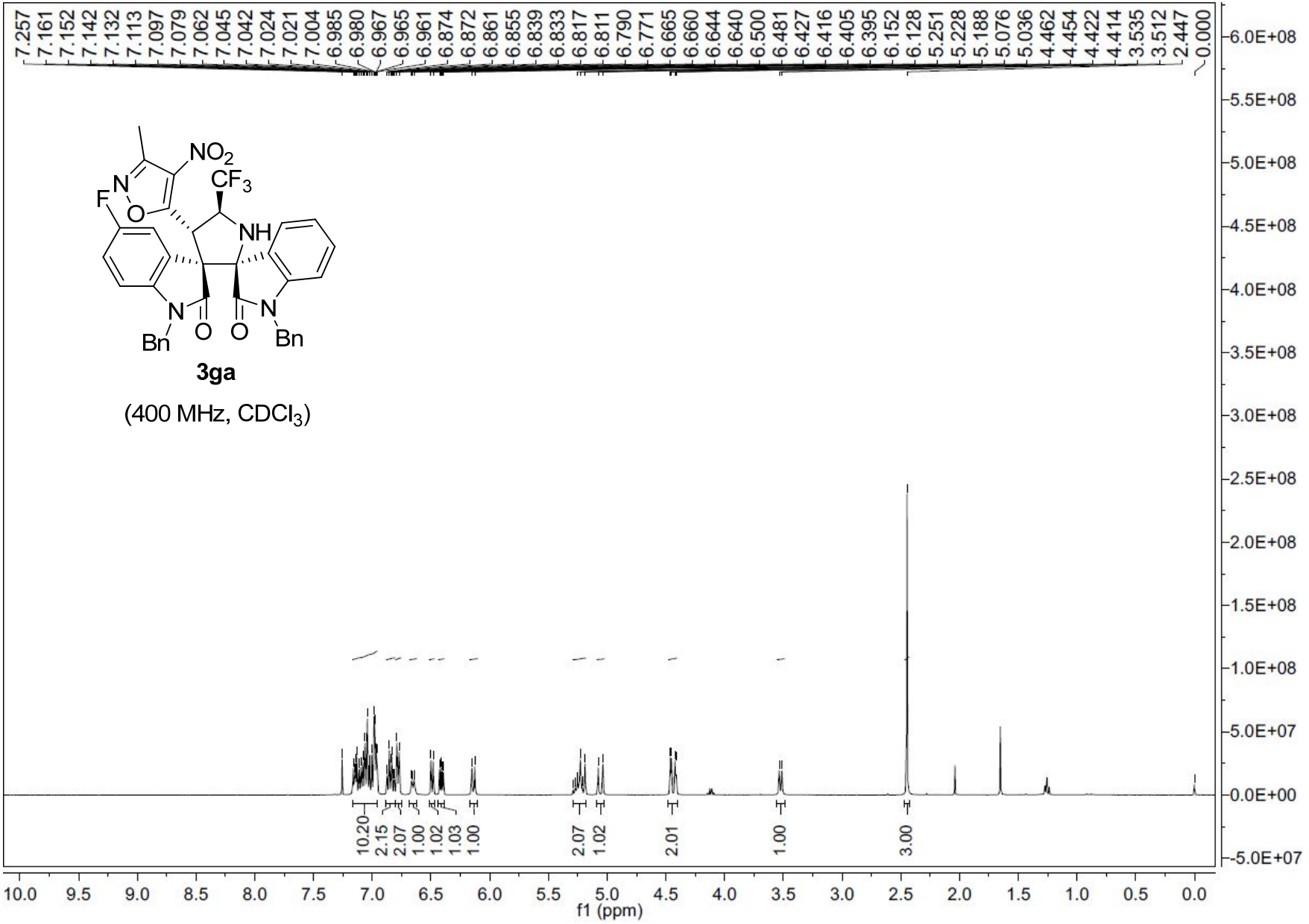

7.256
7.092
7.089
7.068
7.052
7.048
7.033
7.016
6.977
6.973
6.953
6.934
6.796
6.794
6.757
6.739
6.722
6.449
6.430
6.379
6.359
6.182
6.158
5.342
5.326
5.302
5.287
5.262
5.244
5.204
5.059
5.020
4.448
4.434
4.408
4.394
3.494
3.471
2.424
2.192
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3fa
(400 MHz, CDCl3)
6.23
5.16
1.08
2.98
1.03
1.01
0.98
1.06
1.04
1.00
2.00
0.97
3.00
3.00
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

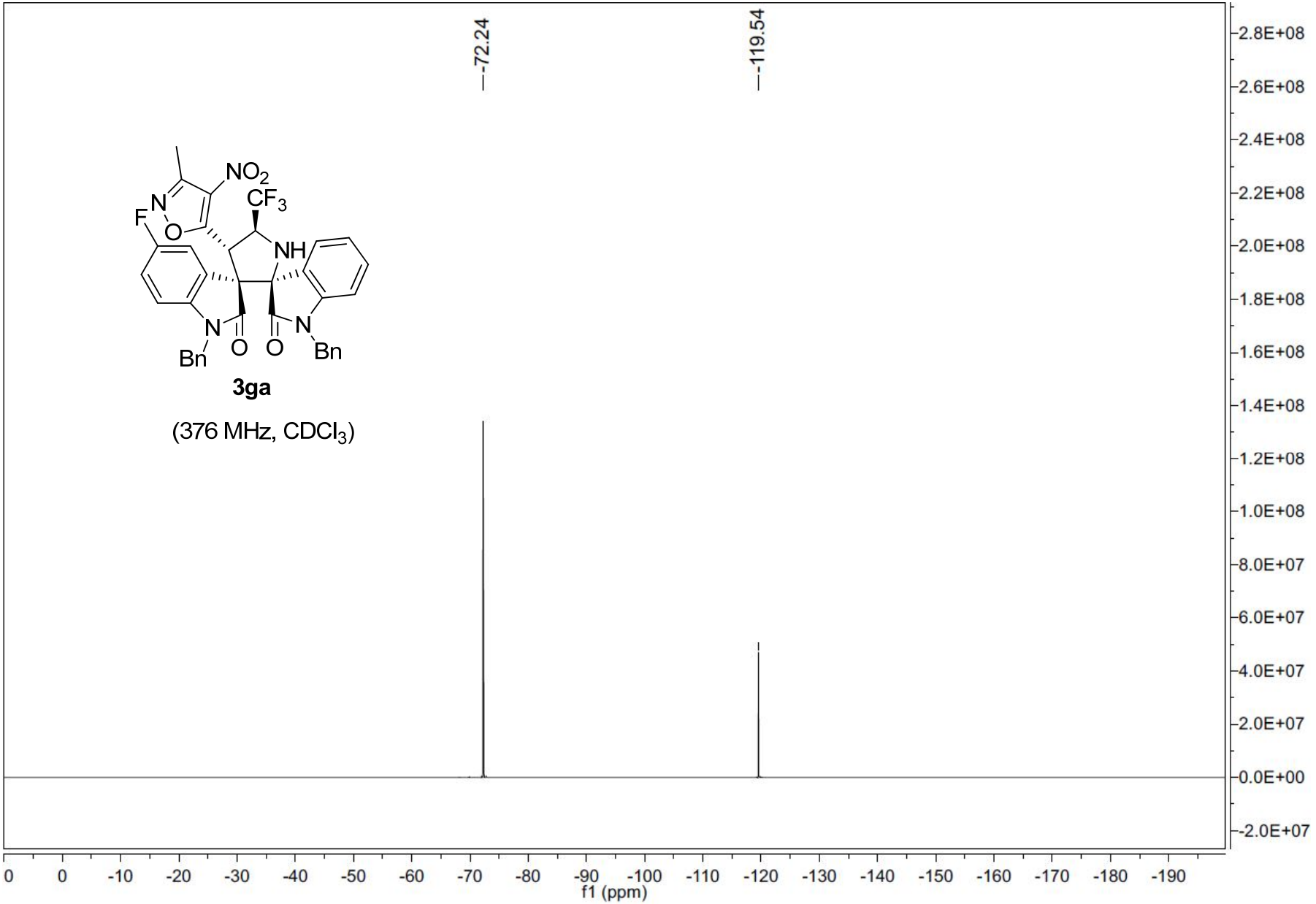

-72.27
NO2
CF3
N
O
NH
N
Bn
O
O
N
Bn
3fa
(376 MHz, CDCl3)
3.8E+08
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

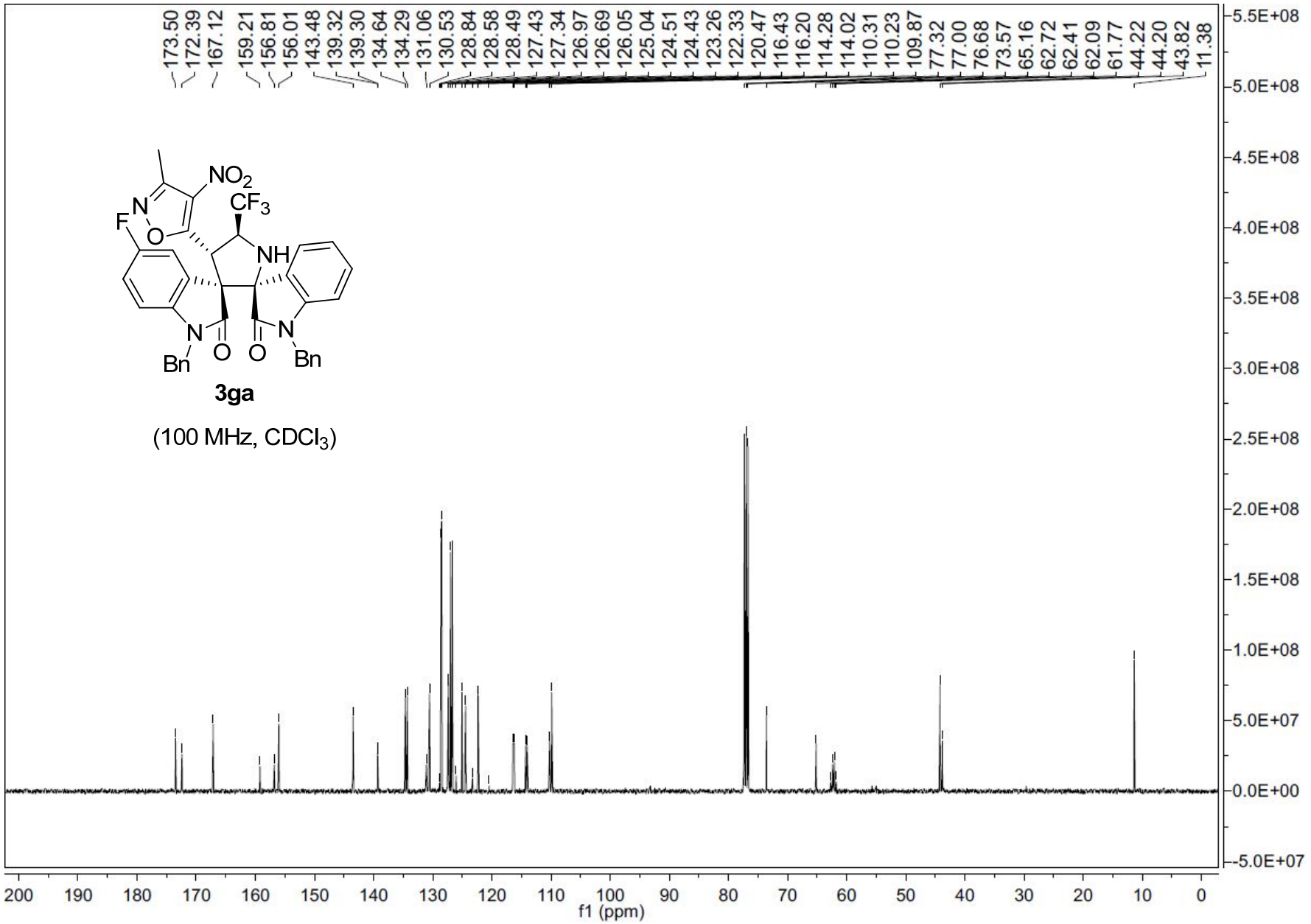


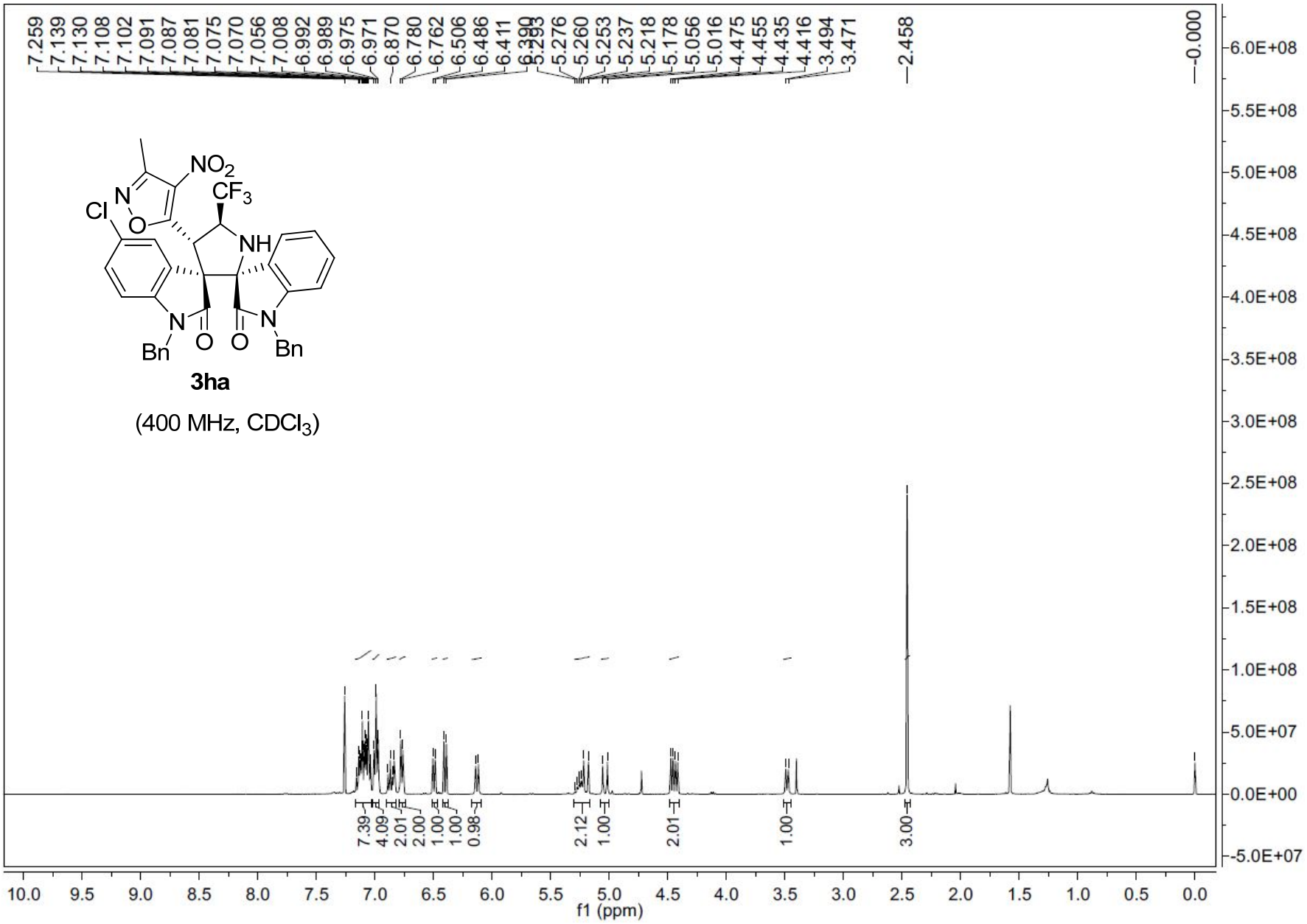
3fa

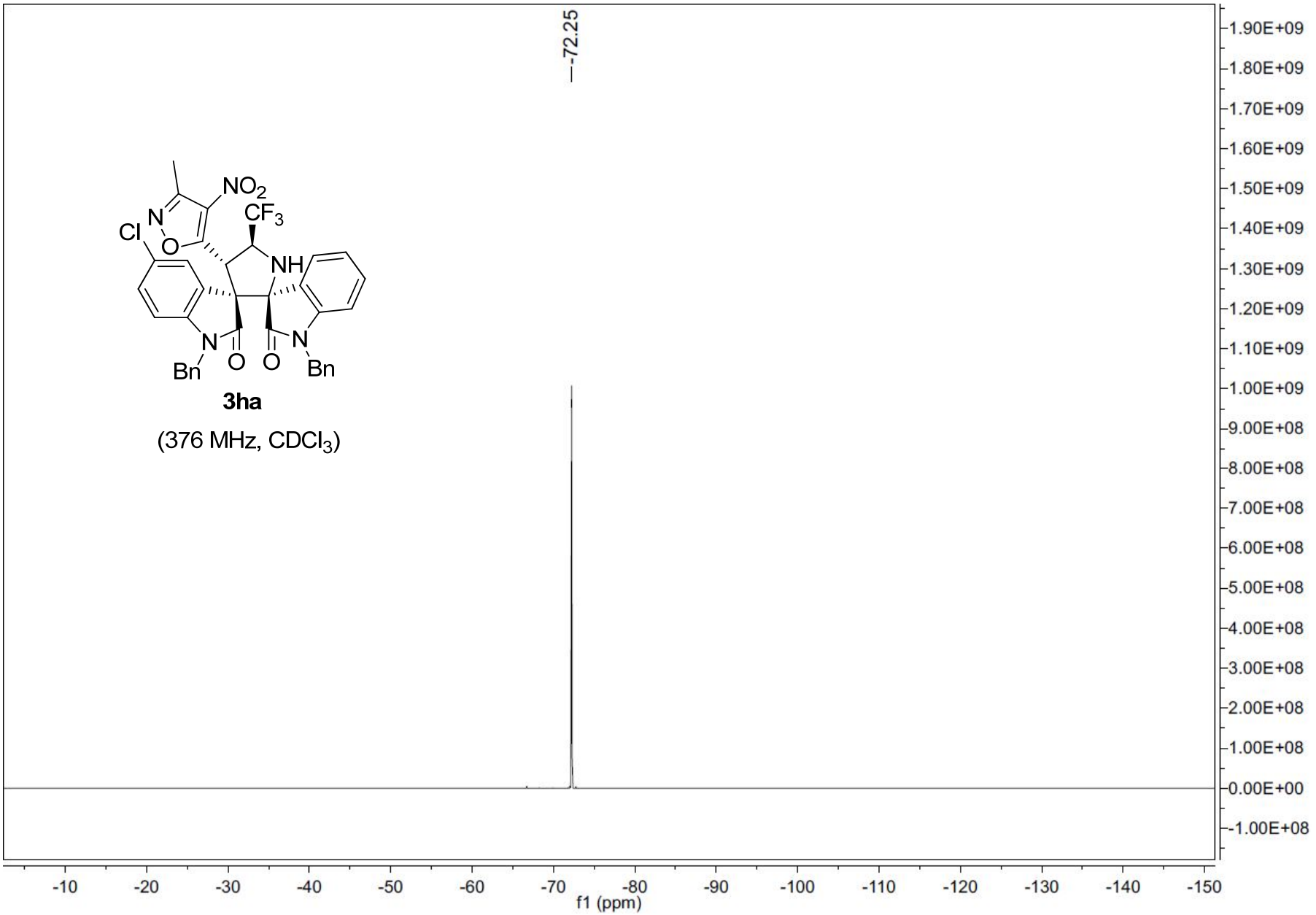
(100 MHz, $CDCl_3$)


7.257
7.161
7.152
7.142
7.132
7.113
7.097
7.079
7.062
7.045
7.042
7.024
7.021
7.004
6.985
6.980
6.967
6.965
6.961
6.874
6.872
6.861
6.855
6.839
6.833
6.817
6.811
6.790
6.771
6.665
6.660
6.644
6.640
6.500
6.481
6.427
6.416
6.405
6.395
6.152
6.128
5.251
5.228
5.188
5.076
5.036
4.462
4.454
4.422
4.414
3.535
3.512
2.447
0.000
NO2
CF3
F
N
O
NH
N
O
O
N
Bn
Bn
3ga
(400 MHz, CDCl3)
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
10.20
2.15
2.07
1.00
1.02
1.03
1.00
2.07
1.02
2.01
1.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


-72.24
-119.54
NO2
CF3
F
N
O
NH
N
Bn
O
O
N
Bn
3ga
(376 MHz, CDCl3)
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

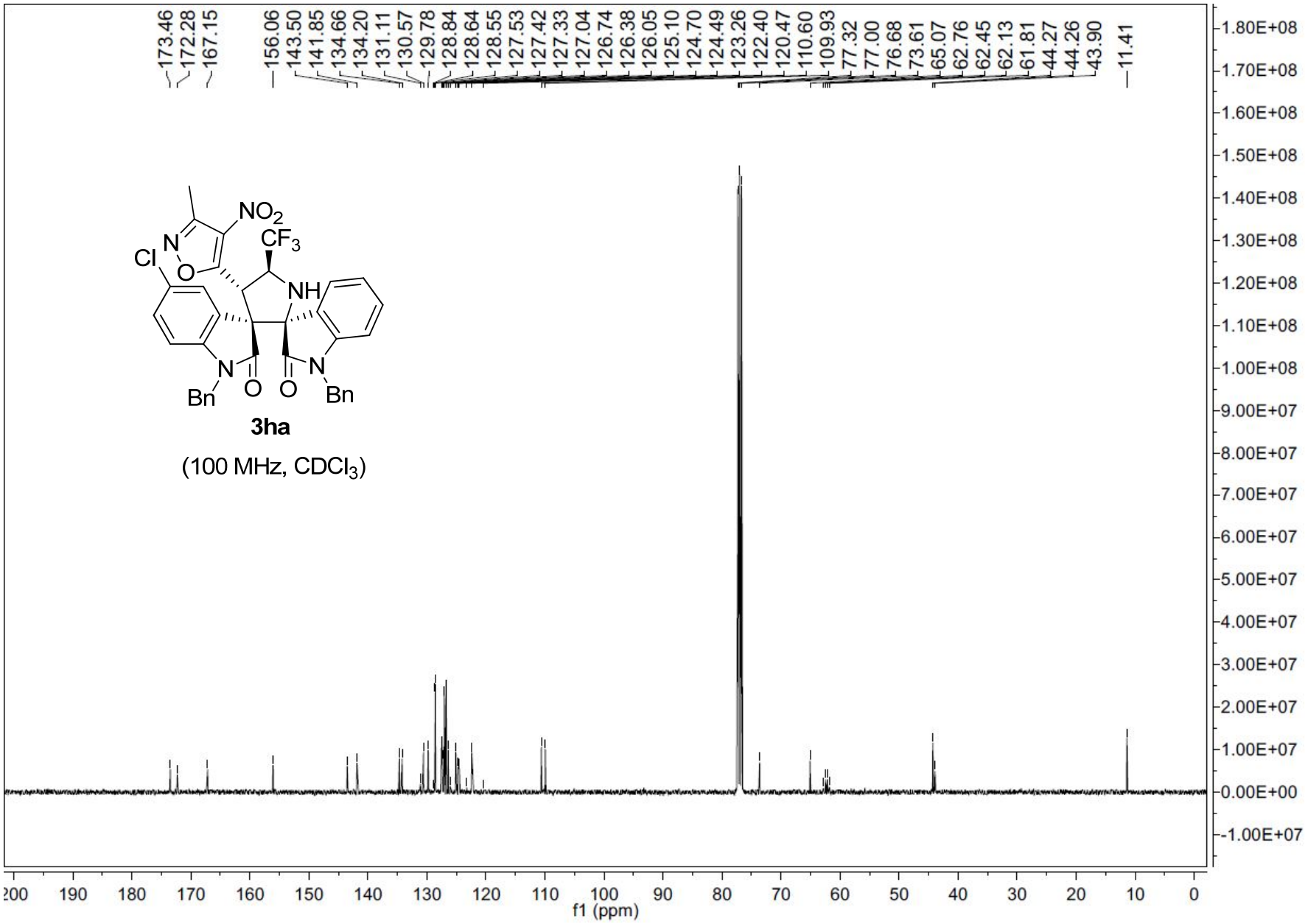

173.50
172.39
167.12
159.21
156.81
156.01
143.48
139.32
139.30
134.64
134.29
131.06
130.53
128.84
128.58
128.49
127.43
127.34
126.97
126.69
126.05
125.04
124.51
124.43
123.26
122.33
120.47
116.43
116.20
114.28
114.02
110.31
110.23
109.87
77.32
77.00
76.68
73.57
65.16
62.72
62.41
62.09
61.77
44.22
44.20
43.82
11.38
NO2
CF3
F
N
O
NH
N
O
O
N
Bn
Bn
3ga
(100 MHz, CDCl3)
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

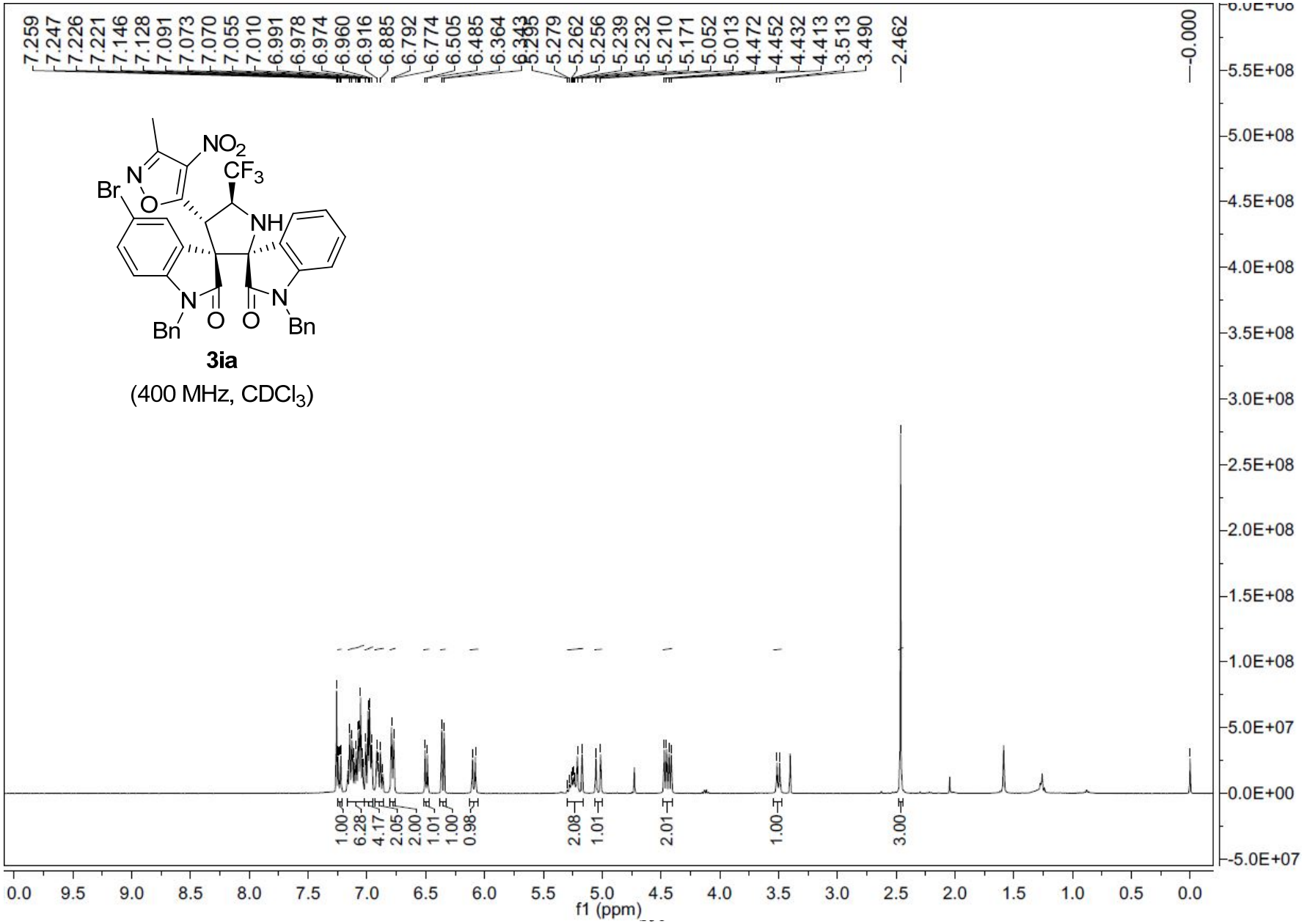

7.259
7.139
7.130
7.108
7.102
7.091
7.087
7.081
7.075
7.070
7.056
7.008
6.992
6.989
6.975
6.971
6.870
6.780
6.762
6.506
6.486
6.411
6.390
6.383
5.276
5.260
5.253
5.237
5.218
5.178
5.056
5.016
4.475
4.455
4.435
4.416
3.494
3.471
2.458
0.000
NO2
CF3
Cl
N
O
NH
N
O
O
N
Bn
Bn
3ha
(400 MHz, CDCl3)
7.39
4.09
2.01
2.00
1.00
1.00
0.98
2.12
1.00
2.01
1.00
3.00
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

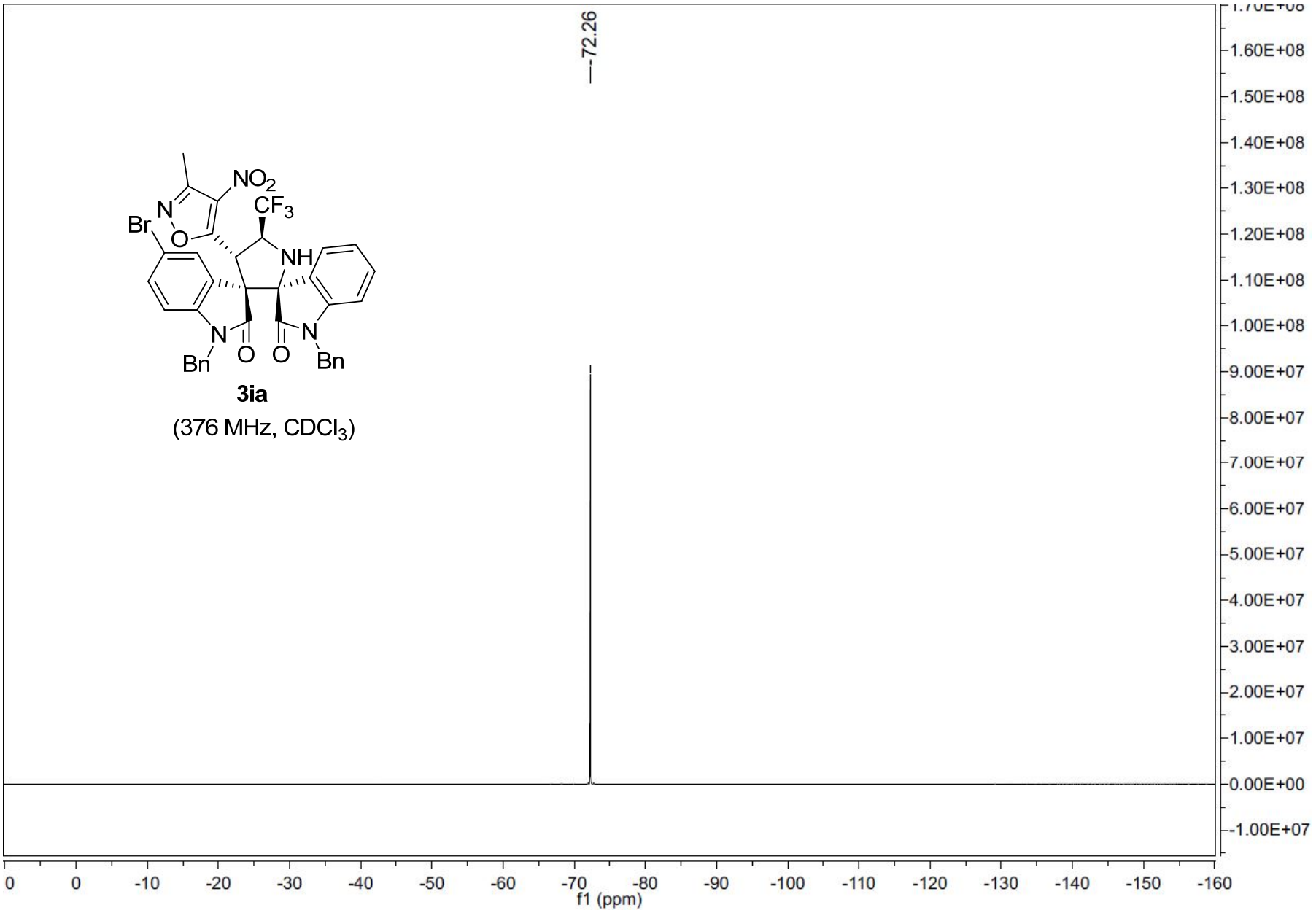


3ha

(376 MHz, $CDCl_3$)

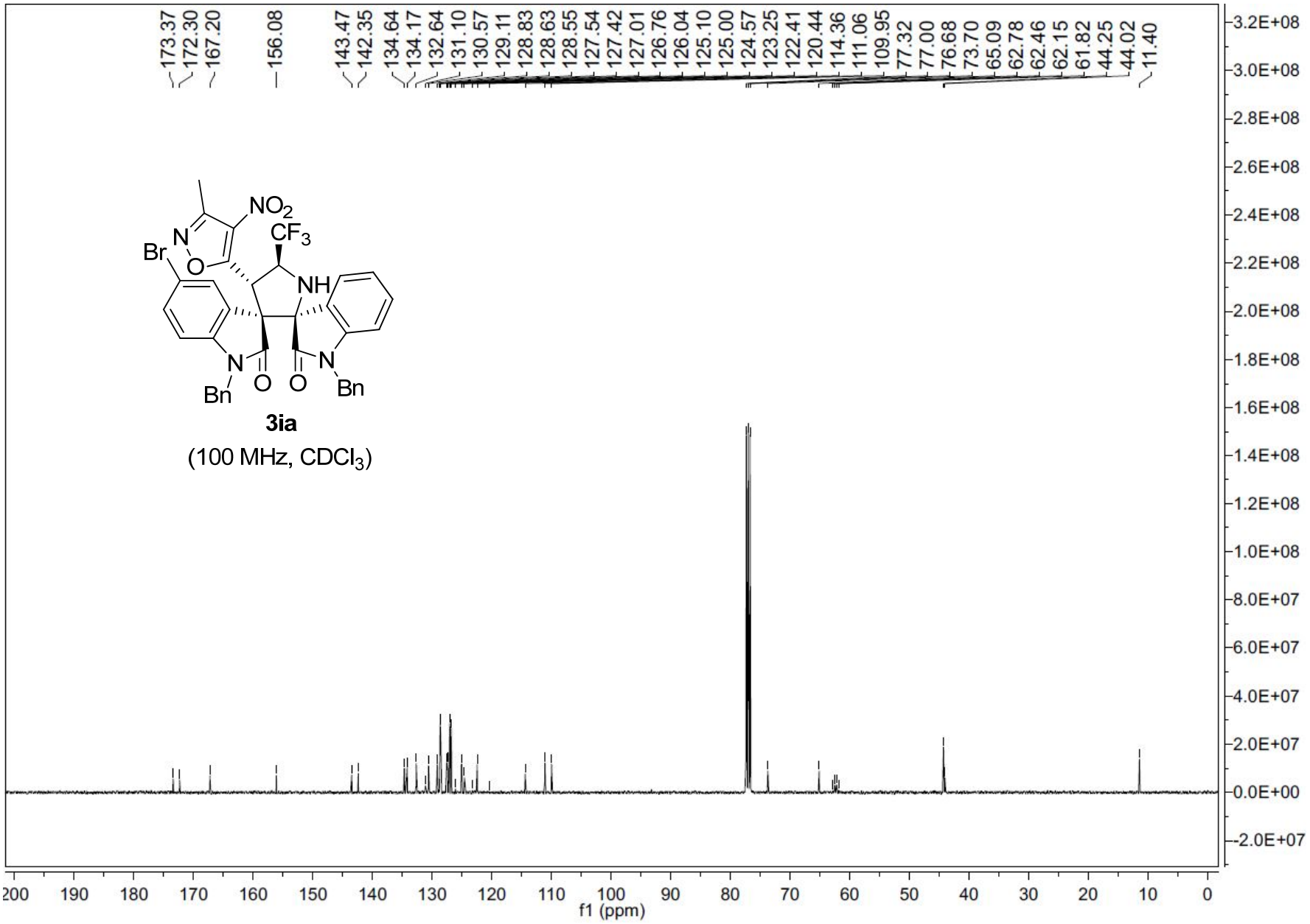

173.46
172.28
167.15
156.06
143.50
141.85
134.66
134.20
131.11
130.57
129.78
128.84
128.64
128.55
127.53
127.42
127.33
127.04
126.74
126.38
126.05
125.10
124.70
124.49
123.26
122.40
120.47
110.60
109.93
77.32
77.00
76.68
73.61
65.07
62.76
62.45
62.13
61.81
44.27
44.26
43.90
11.41
NO2
CF3
N
Cl
O
NH
N
O
O
N
Bn
Bn
3ha
(100 MHz, CDCl3)
1.80E+08
1.70E+08
1.60E+08
1.50E+08
1.40E+08
1.30E+08
1.20E+08
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

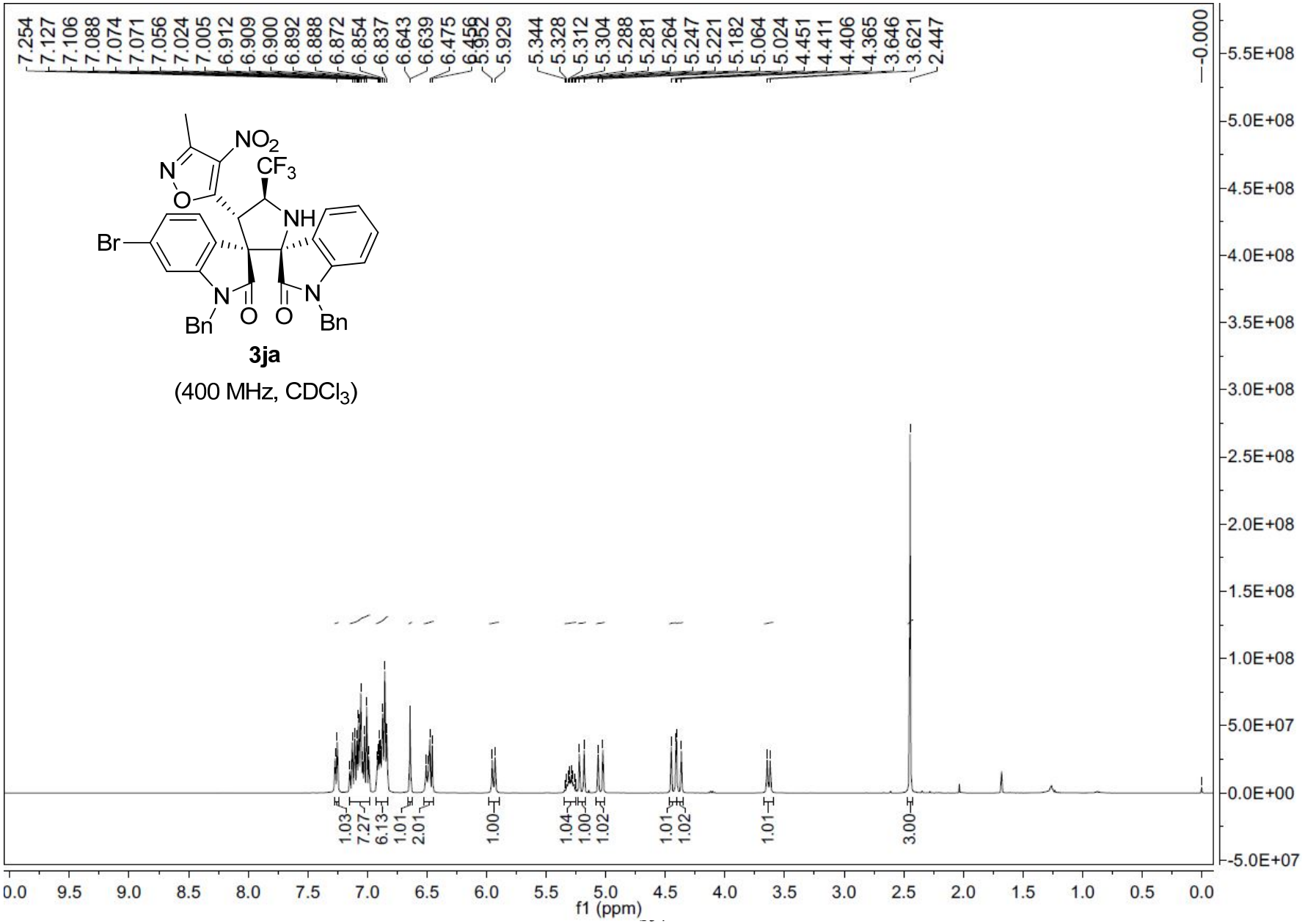

7.259
7.247
7.226
7.221
7.146
7.128
7.091
7.073
7.070
7.055
7.010
6.991
6.978
6.974
6.960
6.916
6.885
6.792
6.774
6.505
6.485
6.364
5.279
5.262
5.256
5.239
5.232
5.210
5.171
5.052
5.013
4.472
4.452
4.432
4.413
3.513
3.490
2.462
0.000
NO2
CF3
Br
N
O
NH
N
O
O
N
Bn
Bn
3ia
(400 MHz, CDCl3)
1.00
6.28
4.17
2.05
2.00
1.01
1.00
0.98
2.08
1.01
2.01
1.00
3.00
f1 (ppm)

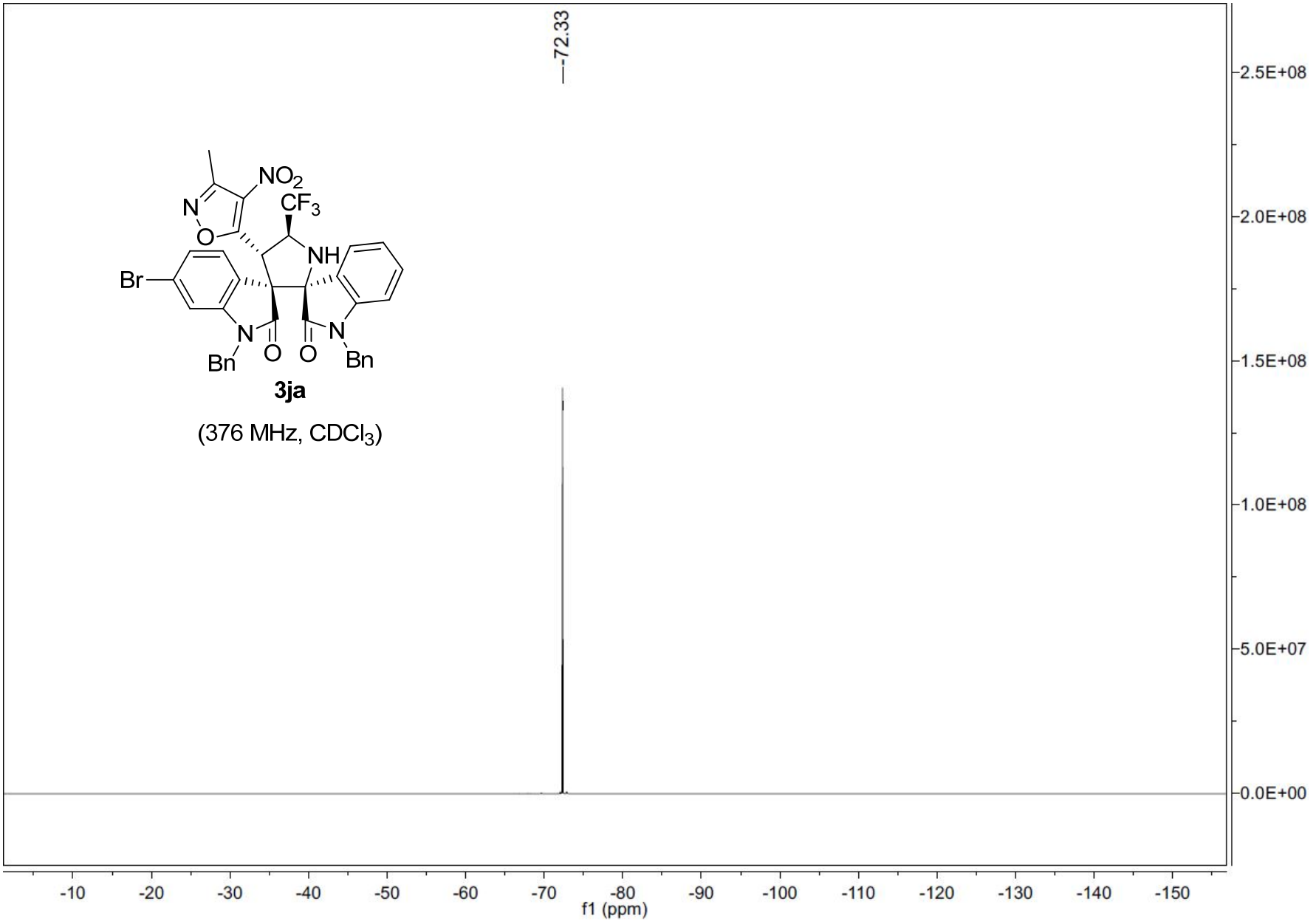


3ia

(376 MHz, $CDCl_3$)

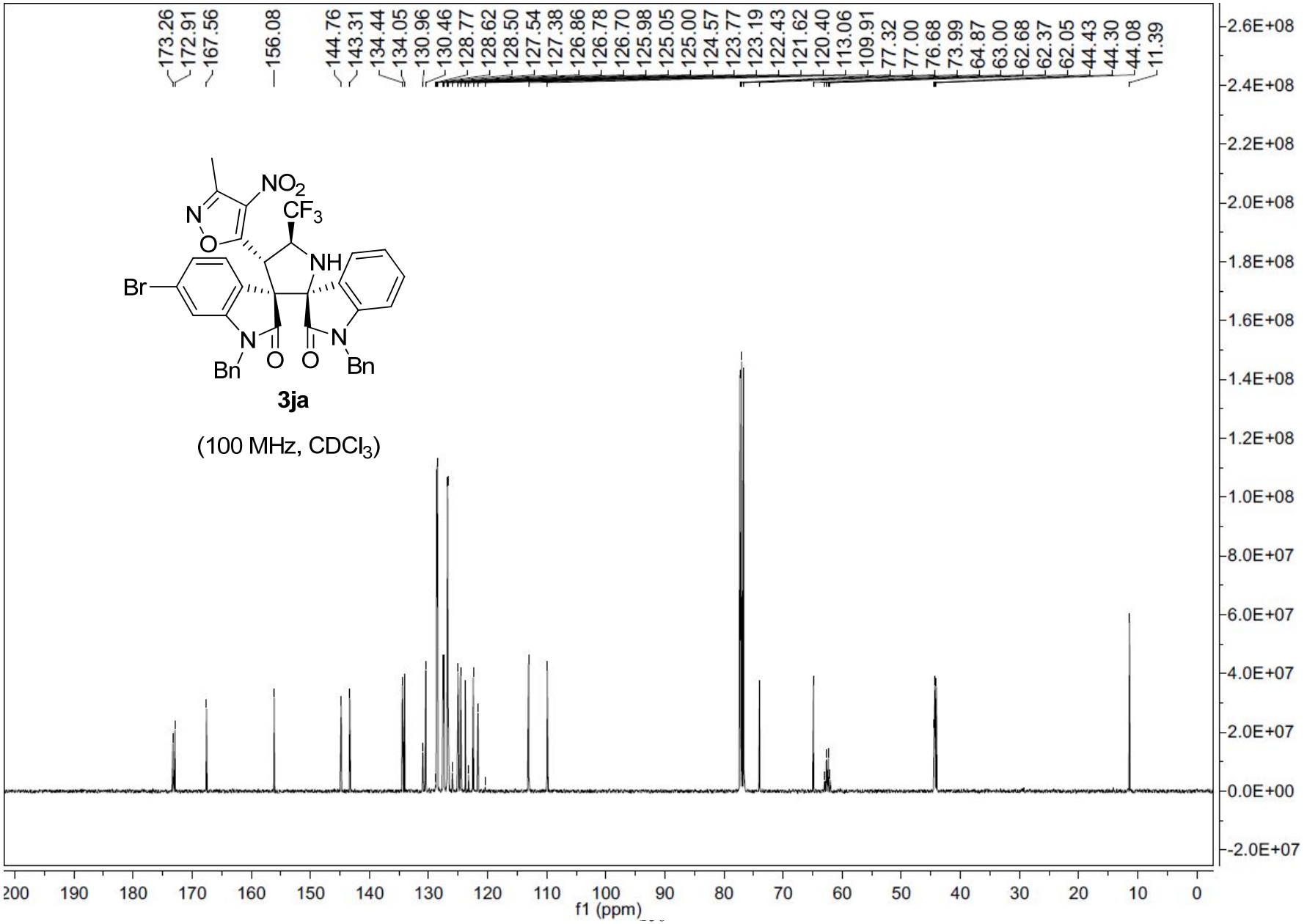

173.37
172.30
167.20
156.08
143.47
142.35
134.64
134.17
132.64
131.10
130.57
129.11
128.83
128.63
128.55
127.54
127.42
127.01
126.76
126.04
125.10
125.00
124.57
123.25
122.41
120.44
114.36
111.06
109.95
77.32
77.00
76.68
73.70
65.09
62.78
62.46
62.15
61.82
44.25
44.02
11.40
NO2
CF3
Br
N
O
NH
N
Bn
O
O
N
Bn
3ia
(100 MHz, CDCl3)
f1 (ppm)

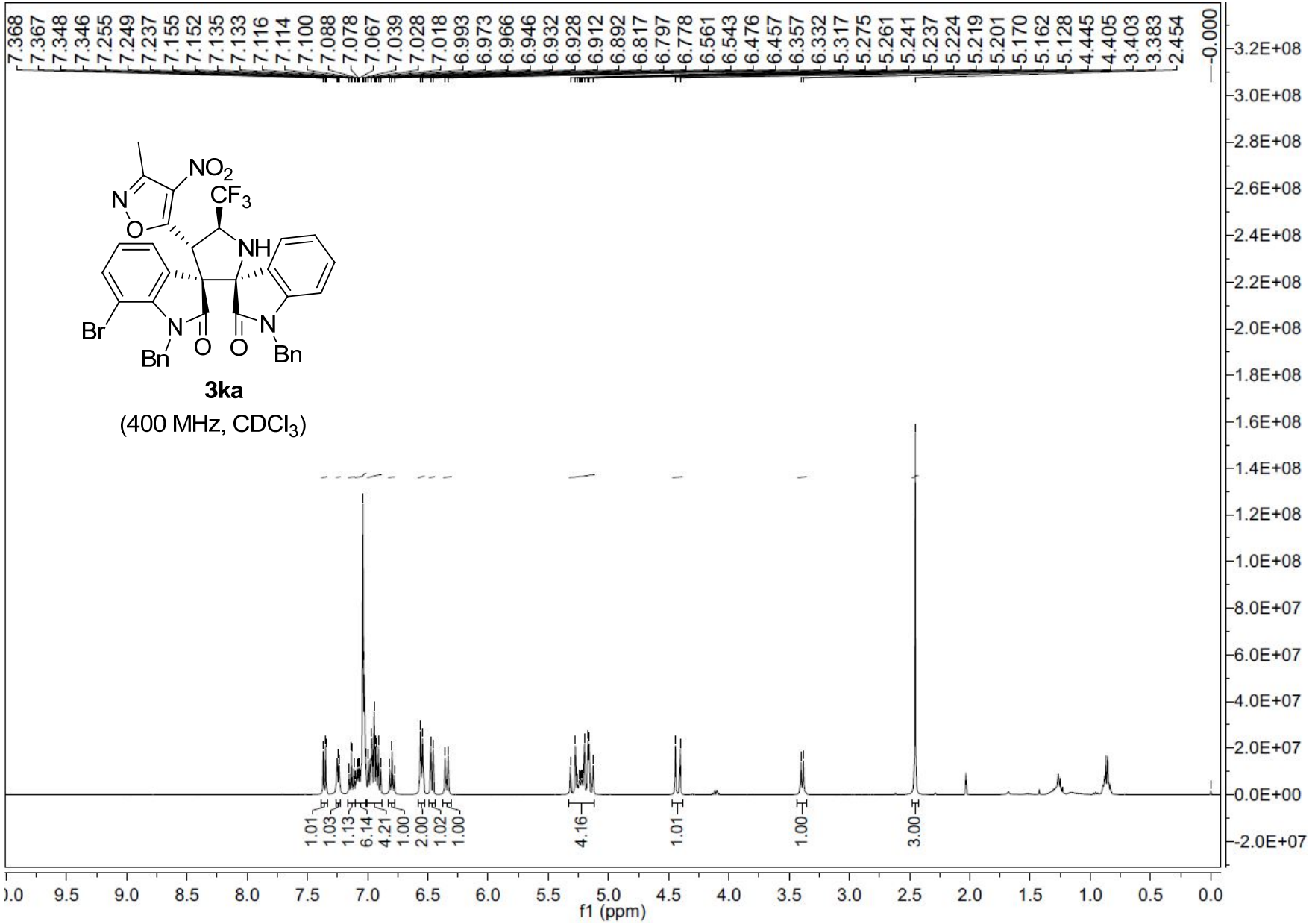

7.254
7.127
7.106
7.088
7.074
7.071
7.056
7.024
7.005
6.912
6.909
6.900
6.892
6.888
6.872
6.854
6.837
6.643
6.639
6.475
6.456
5.952
5.929
5.344
5.328
5.312
5.304
5.288
5.281
5.264
5.247
5.221
5.182
5.064
5.024
4.451
4.411
4.406
4.365
3.646
3.621
2.447
-0.000
NO2
CF3
N
O
NH
Br
N
O
O
N
Bn
Bn
3ja
(400 MHz, CDCl3)
1.03
7.27
6.13
1.01
2.01
1.00
1.04
1.00
1.02
1.01
1.02
1.01
3.00
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

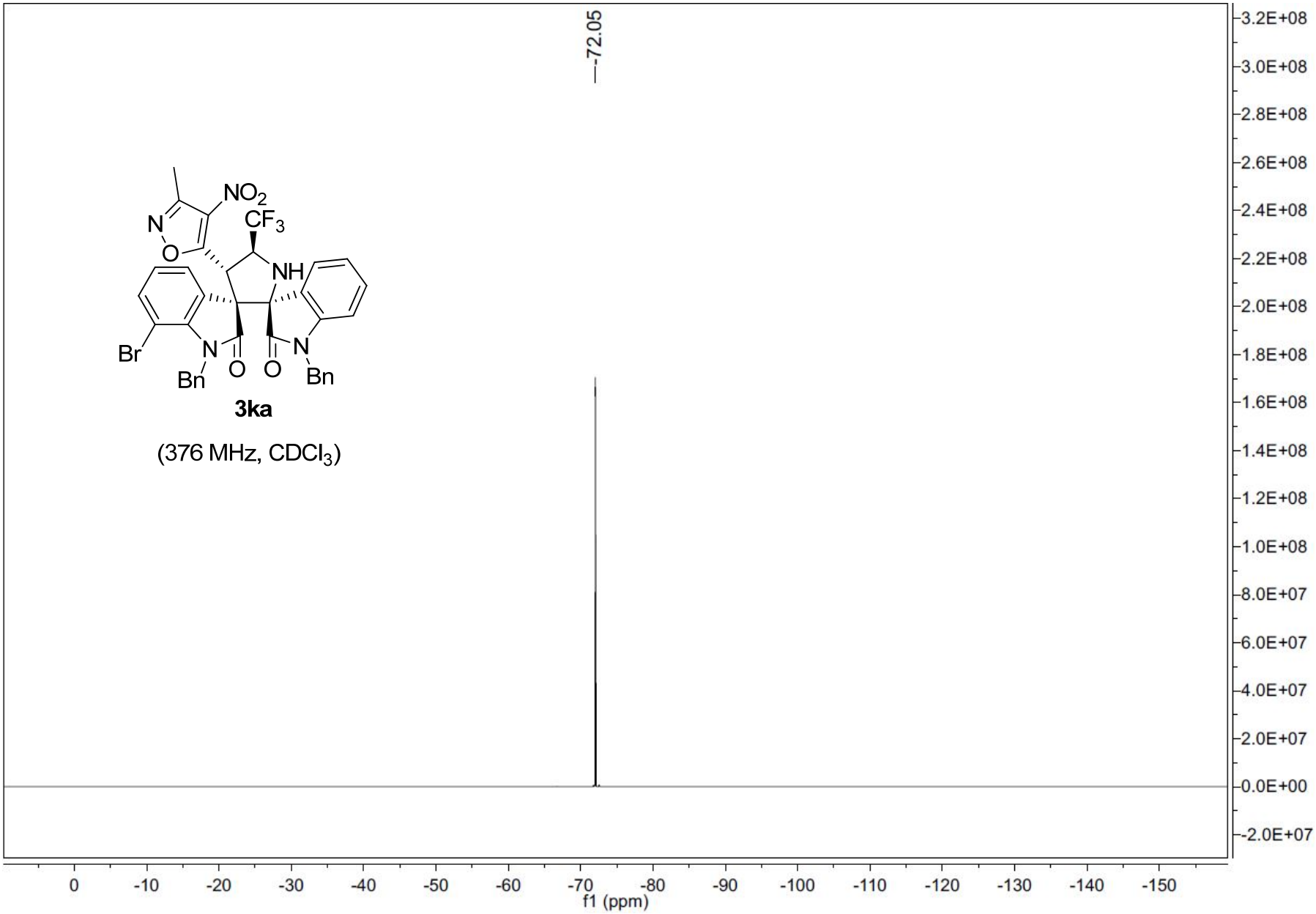


3ja

(376 MHz, $CDCl_3$)

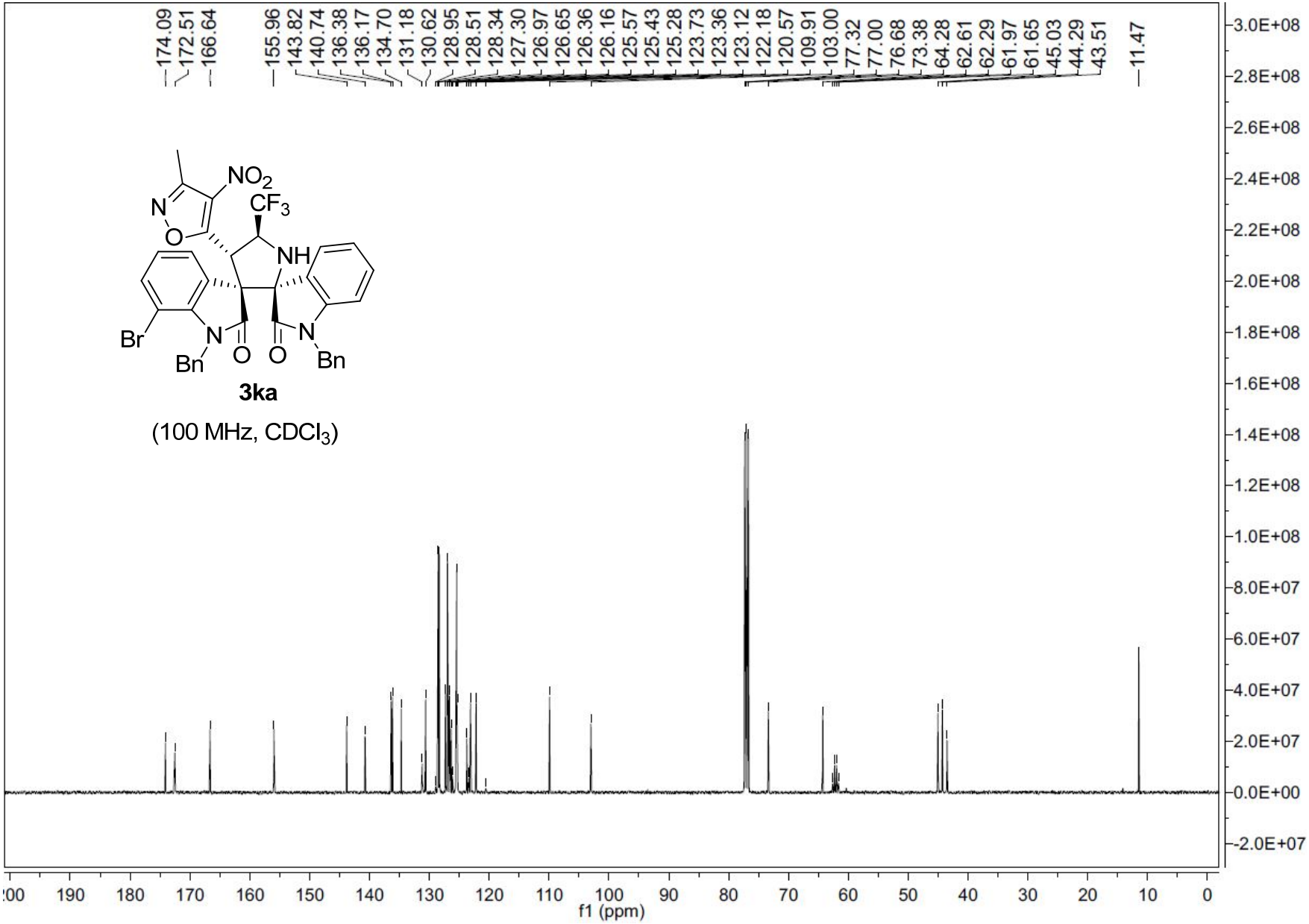

173.26
172.91
167.56
156.08
144.76
143.31
134.44
134.05
130.96
130.46
128.77
128.62
128.50
127.54
127.38
126.86
126.78
126.70
125.98
125.05
125.00
124.57
123.77
123.19
122.43
121.62
120.40
113.06
109.91
77.32
77.00
76.68
73.99
64.87
63.00
62.68
62.37
62.05
44.43
44.30
44.08
11.39
NO2
CF3
N
O
NH
Br
N
Bn
O
O
N
Bn
3ja
(100 MHz, CDCl3)
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

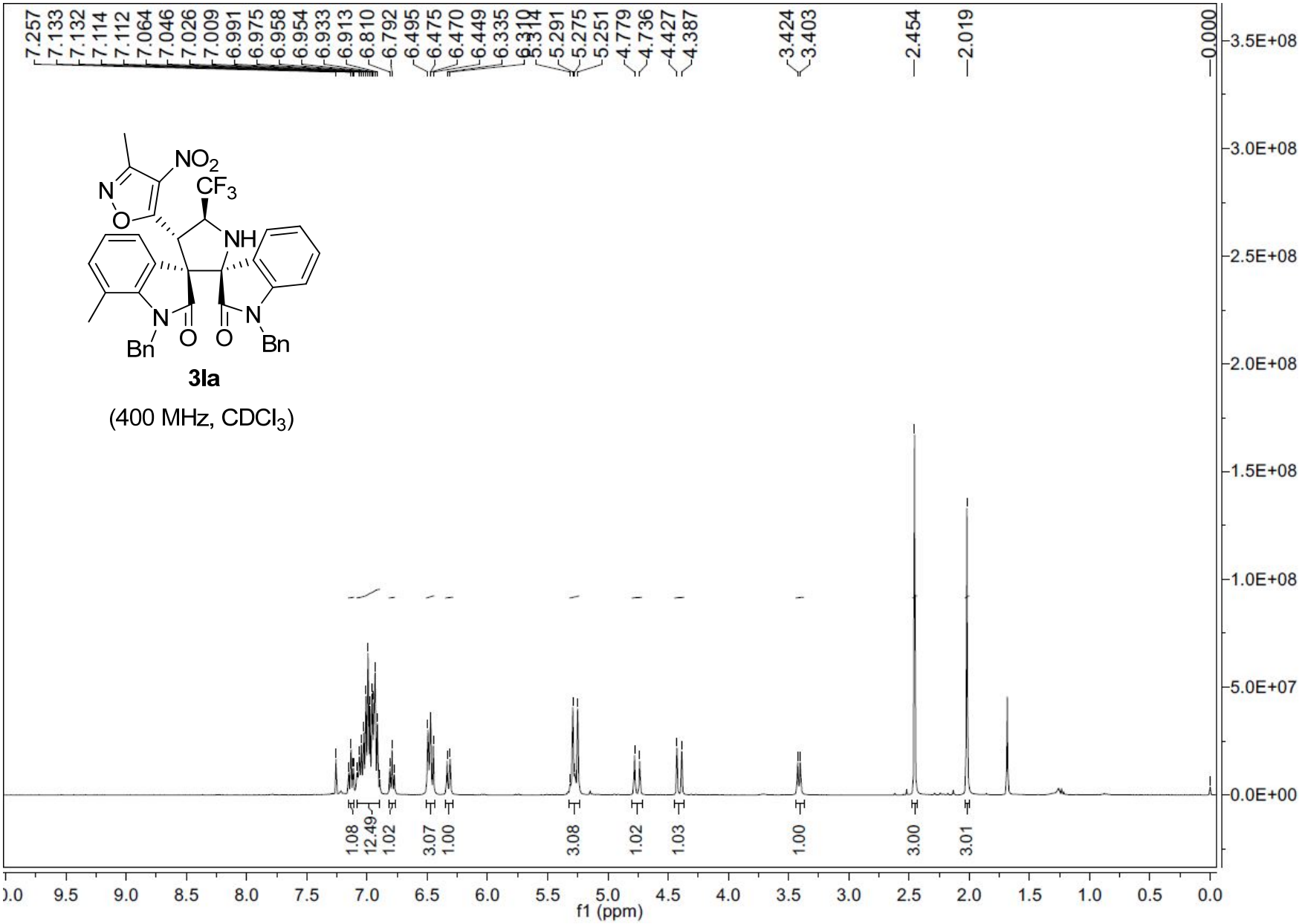

7.368
7.367
7.348
7.346
7.255
7.249
7.237
7.155
7.152
7.135
7.133
7.116
7.114
7.100
7.088
7.078
7.067
7.039
7.028
7.018
6.993
6.973
6.966
6.946
6.932
6.928
6.912
6.892
6.817
6.797
6.778
6.561
6.543
6.476
6.457
6.357
6.332
5.317
5.275
5.261
5.241
5.237
5.224
5.219
5.201
5.170
5.162
5.128
4.445
4.405
3.403
3.383
2.454
0.000
NO2
CF3
N
O
NH
Br
N
O
O
N
Bn
Bn
3ka
(400 MHz, CDCl3)
1.01
1.03
1.13
6.14
4.21
1.00
2.00
1.02
1.00
4.16
1.01
1.00
3.00
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

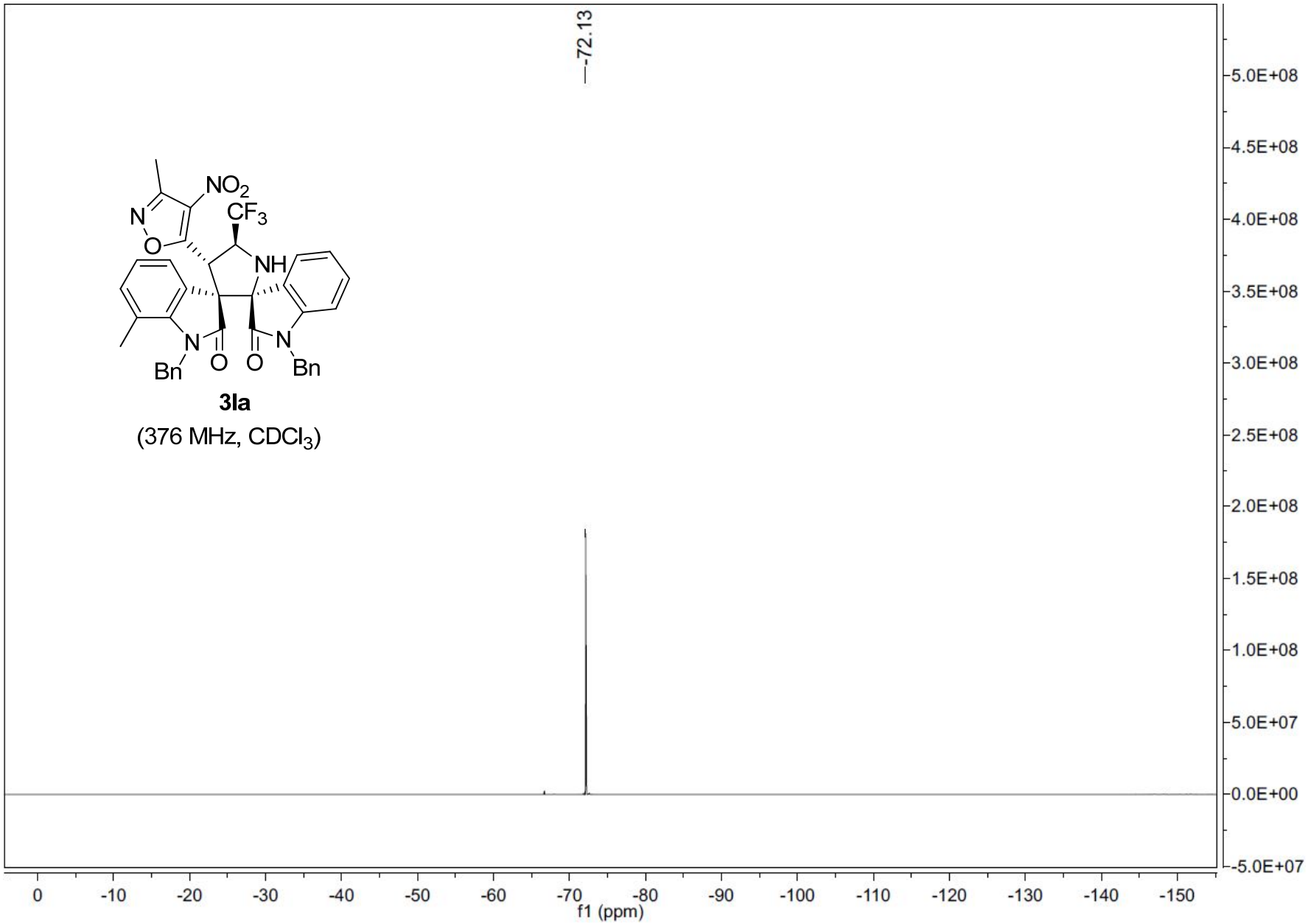


3ka

(376 MHz, $CDCl_3$)

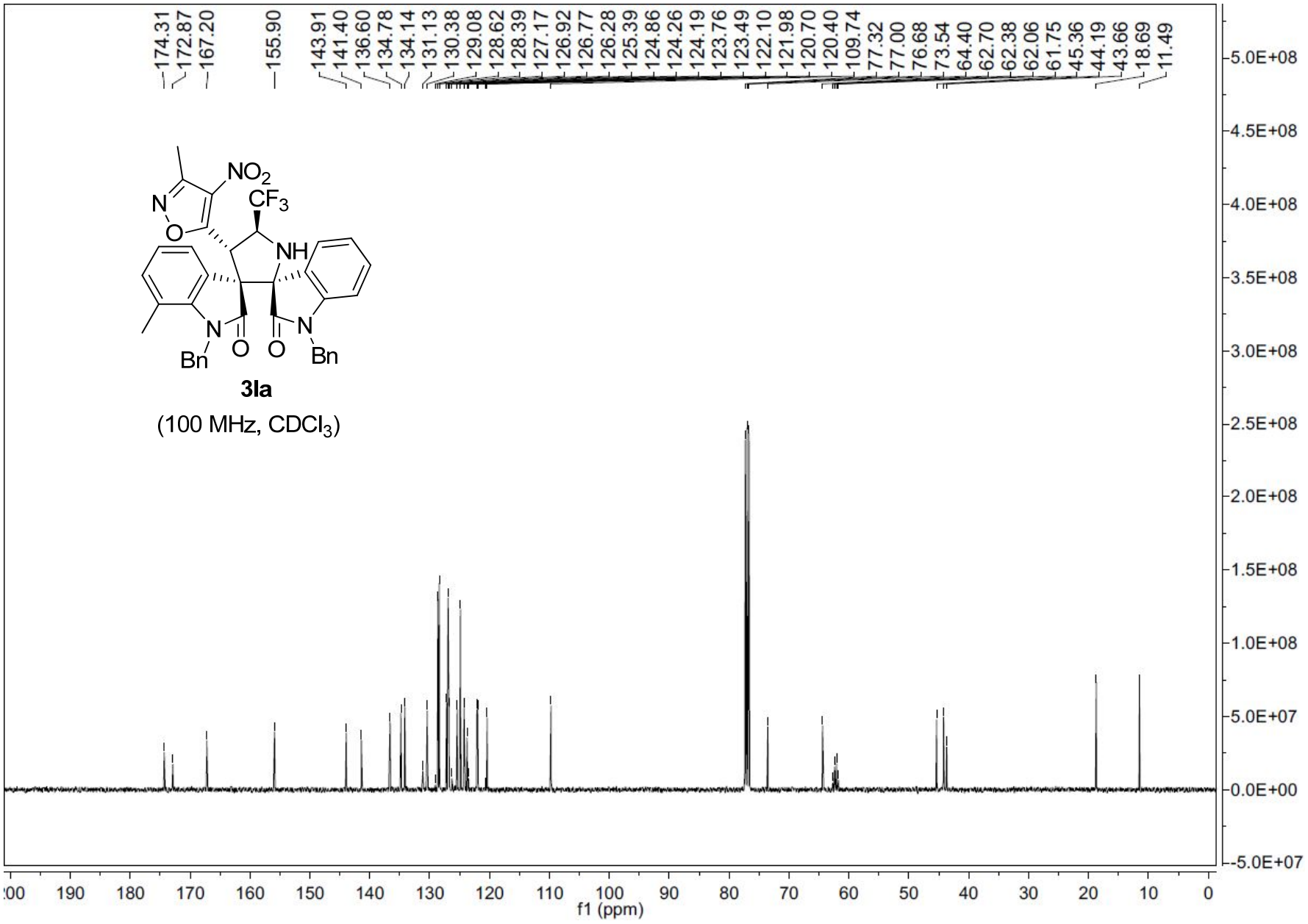

174.09
172.51
166.64
155.96
143.82
140.74
136.38
136.17
134.70
131.18
130.62
128.95
128.51
128.34
127.30
126.97
126.65
126.36
126.16
125.57
125.43
125.28
123.73
123.36
123.12
122.18
120.57
109.91
103.00
77.32
77.00
76.68
73.38
64.28
62.61
62.29
61.97
61.65
45.03
44.29
43.51
11.47
NO2
CF3
N
O
NH
Br
N
O
O
N
Bn
Bn
3ka
(100 MHz, CDCl3)
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

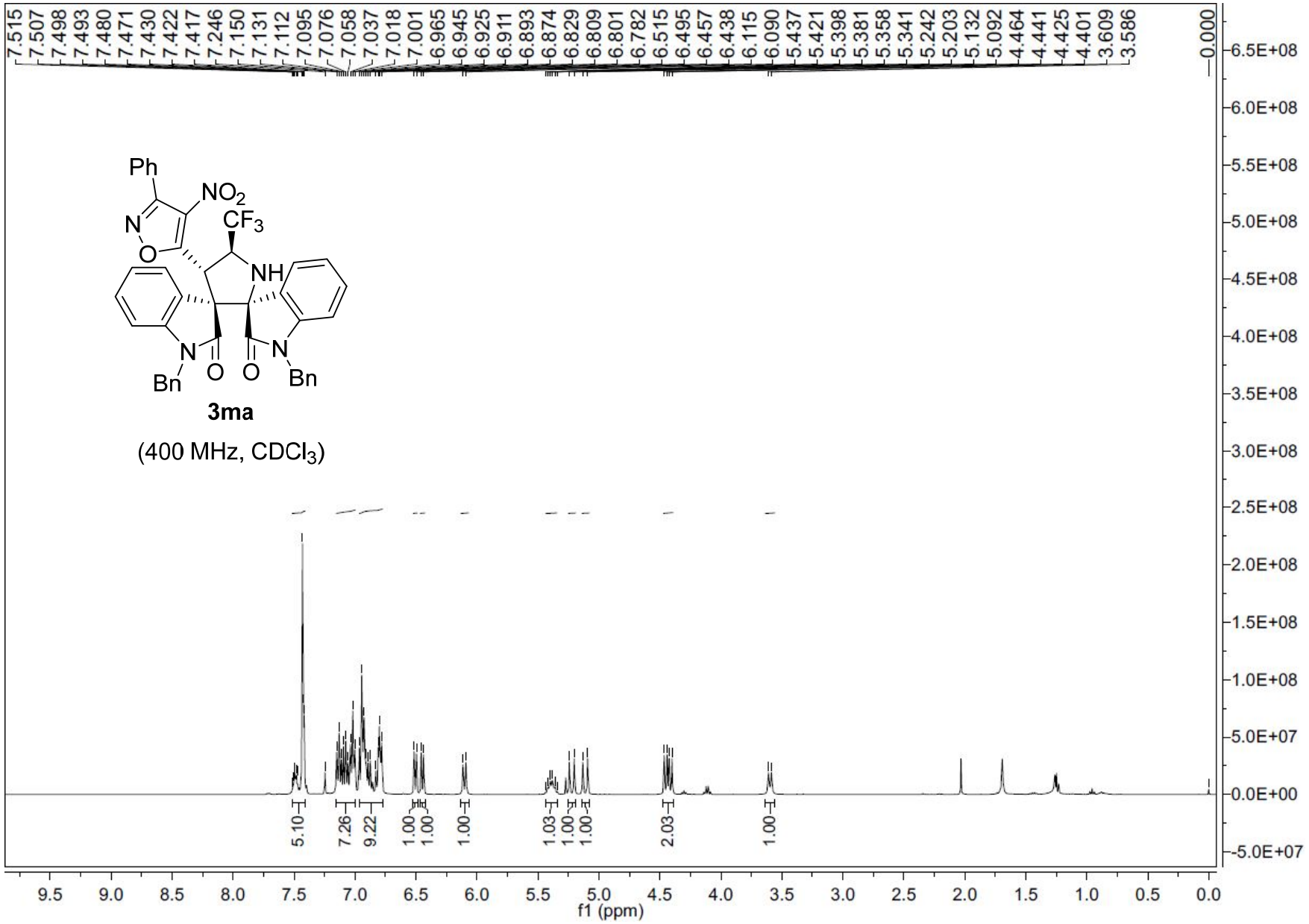

7.257
7.133
7.132
7.114
7.112
7.064
7.046
7.026
7.009
6.991
6.975
6.958
6.954
6.933
6.913
6.810
6.792
6.495
6.475
6.470
6.449
6.335
6.310
6.314
5.291
5.275
5.251
4.779
4.736
4.427
4.387
3.424
3.403
2.454
2.019
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3Ia
(400 MHz, CDCl3)
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
1.08
12.49
1.02
3.07
1.00
3.08
1.02
1.03
1.00
3.00
3.01
f1 (ppm)

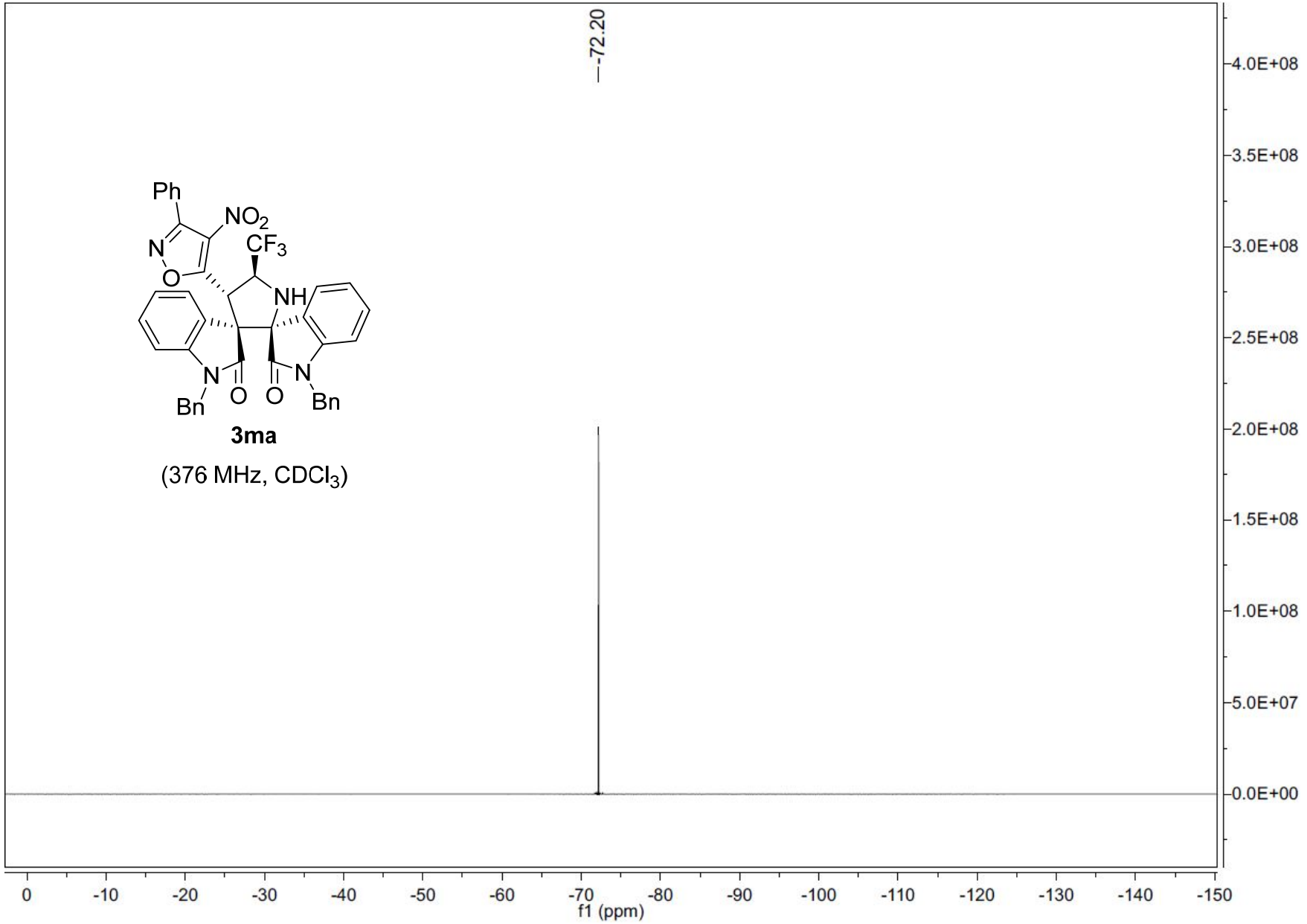


3la

(376 MHz, $CDCl_3$)

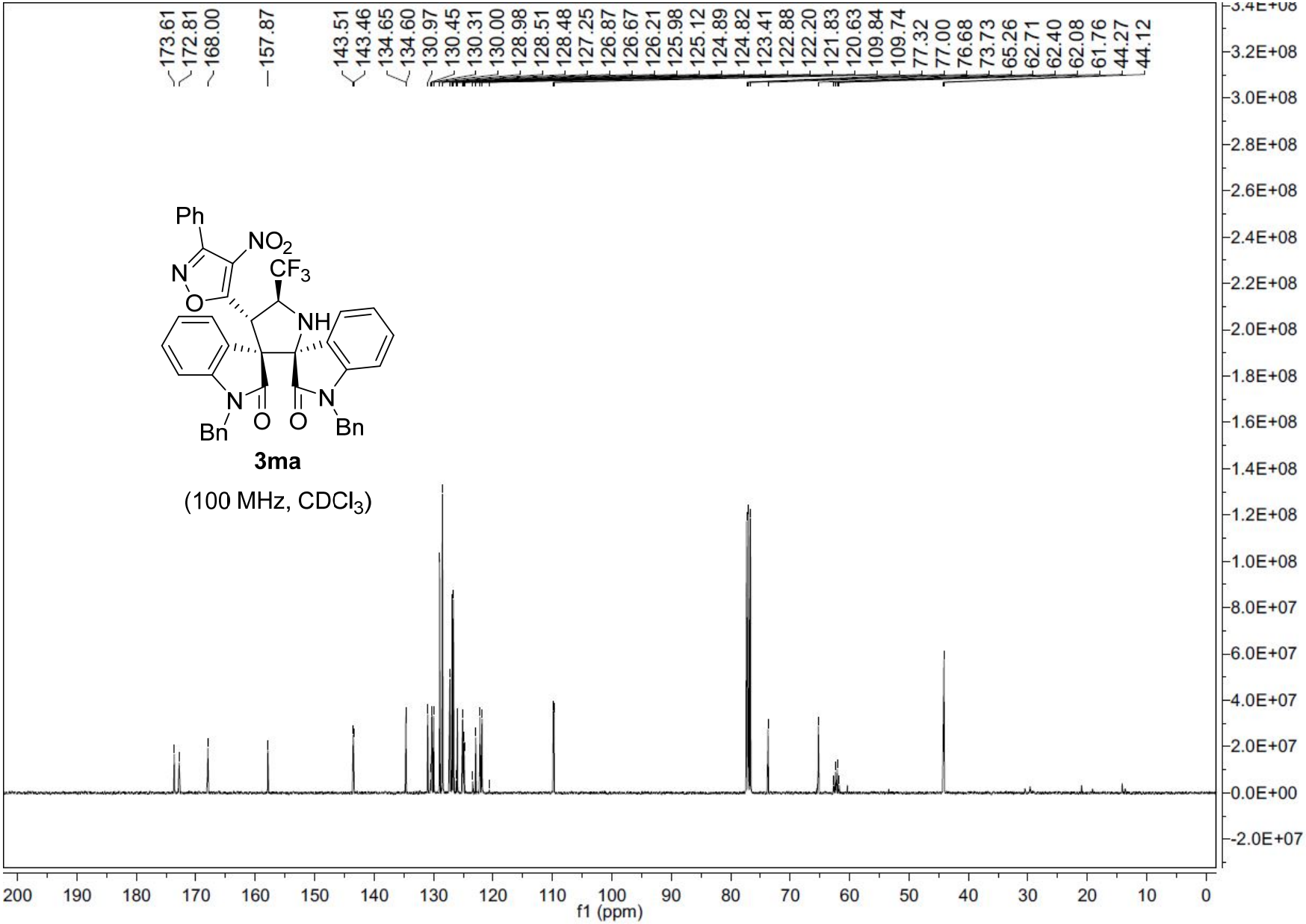

174.31
172.87
167.20
155.90
143.91
141.40
136.60
134.78
134.14
131.13
130.38
129.08
128.62
128.39
127.17
126.92
126.77
126.28
125.39
124.86
124.26
124.19
123.76
123.49
122.10
121.98
120.70
120.40
109.74
77.32
77.00
76.68
73.54
64.40
62.70
62.38
62.06
61.75
45.36
44.19
43.66
18.69
11.49
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3Ia
(100 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

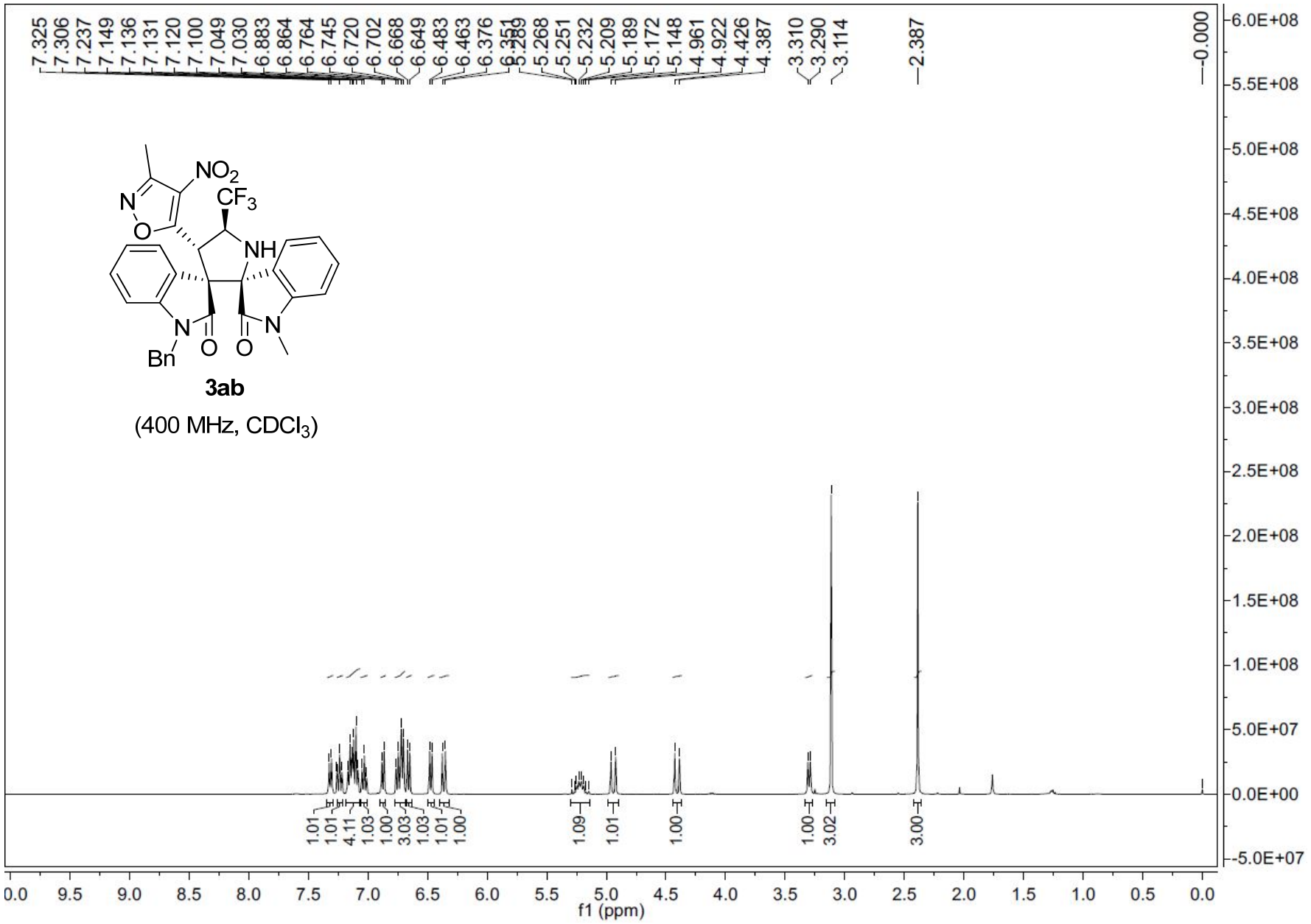

7.515
7.507
7.498
7.493
7.480
7.471
7.430
7.422
7.417
7.246
7.150
7.131
7.112
7.095
7.076
7.058
7.037
7.018
7.001
6.965
6.945
6.925
6.911
6.893
6.874
6.829
6.809
6.801
6.782
6.515
6.495
6.457
6.438
6.115
6.090
5.437
5.421
5.398
5.381
5.358
5.341
5.242
5.203
5.132
5.092
4.464
4.441
4.425
4.401
3.609
3.586
0.000
Ph
NO2
CF3
N
O
NH
N
Bn
O
O
N
Bn
3ma
(400 MHz, CDCl3)
5.10
7.26
9.22
1.00
1.00
1.00
1.03
1.00
1.00
2.03
1.00
6.5E+08
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



3ma

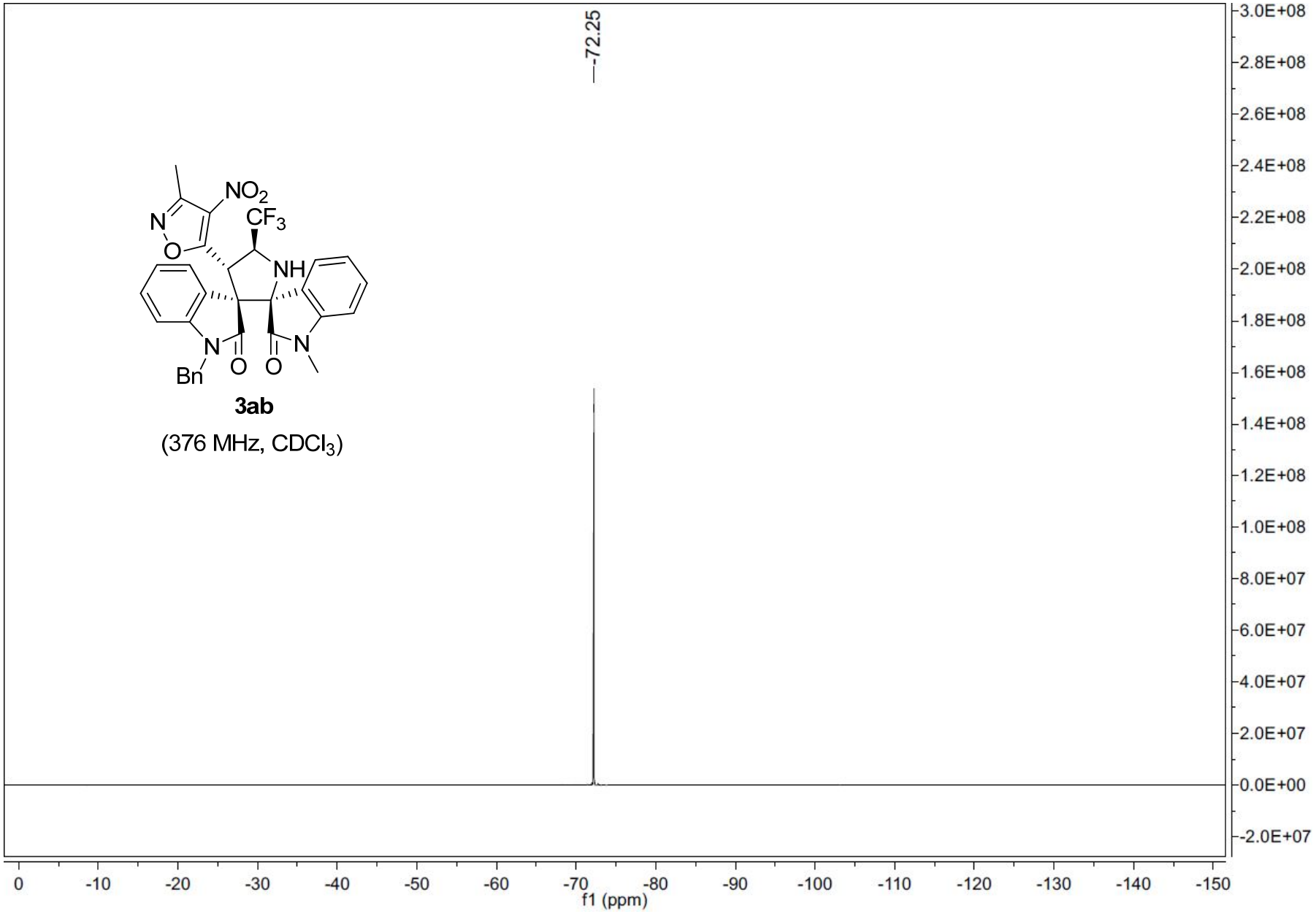
(376 MHz, $CDCl_3$)

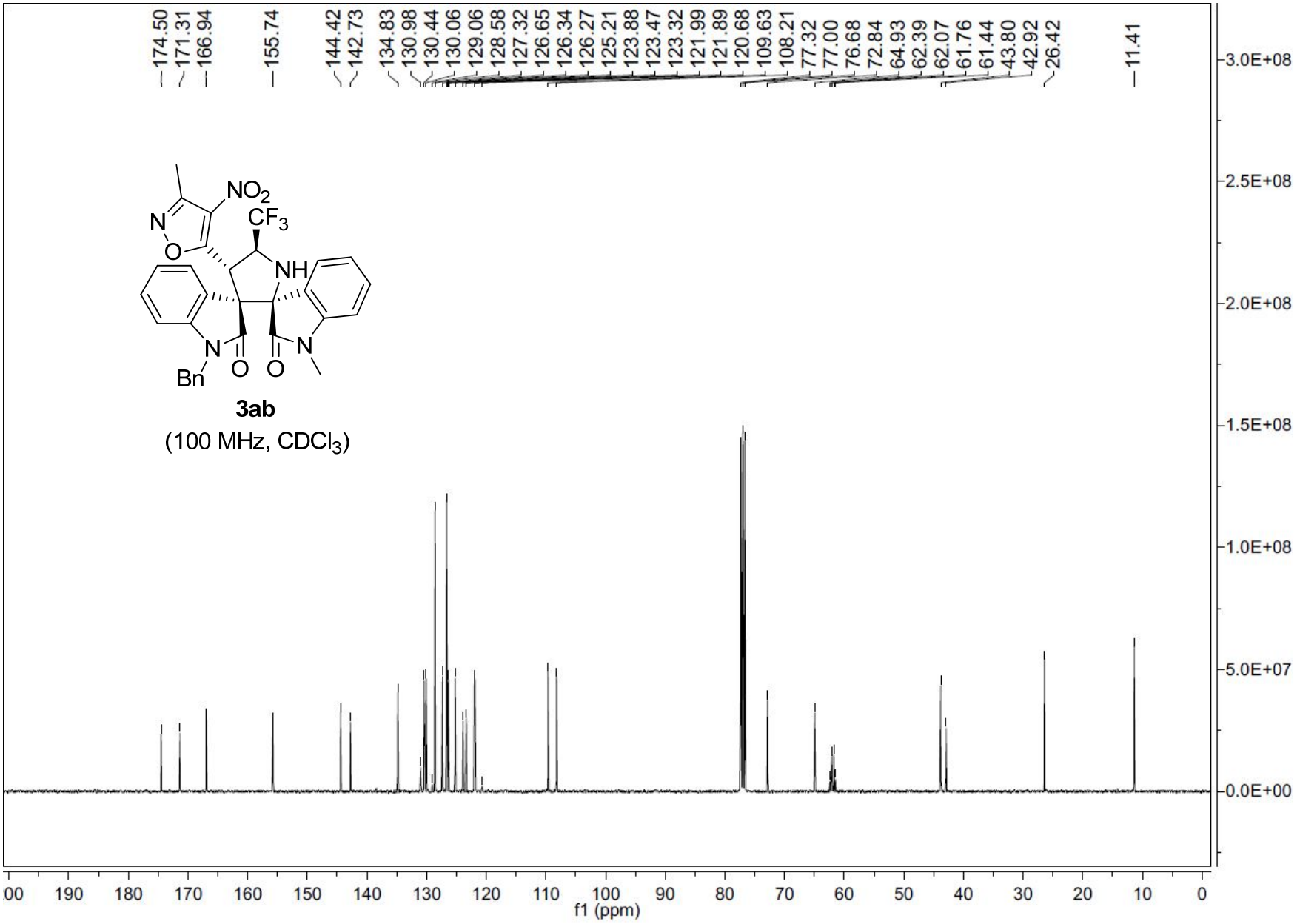

173.61
172.81
168.00
157.87
143.51
143.46
134.65
134.60
130.97
130.45
130.31
130.00
128.98
128.51
128.48
127.25
126.87
126.67
126.21
125.98
125.12
124.89
124.82
123.41
122.88
122.20
121.83
120.63
109.84
109.74
77.32
77.00
76.68
73.73
65.26
62.71
62.40
62.08
61.76
44.27
44.12
Ph
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3ma
(100 MHz, CDCl3)
f1 (ppm)



3ab

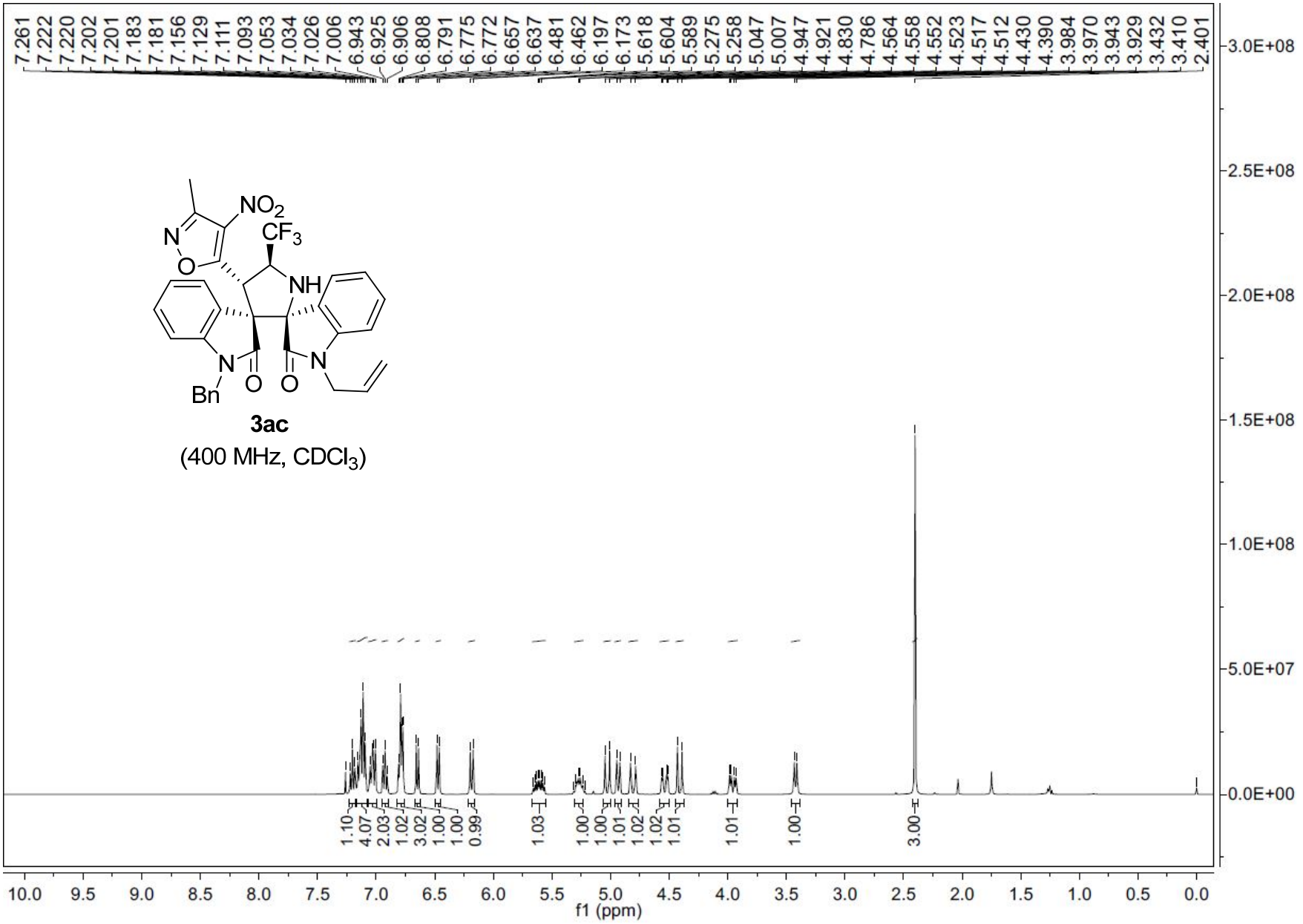
(400 MHz, $CDCl_3$)

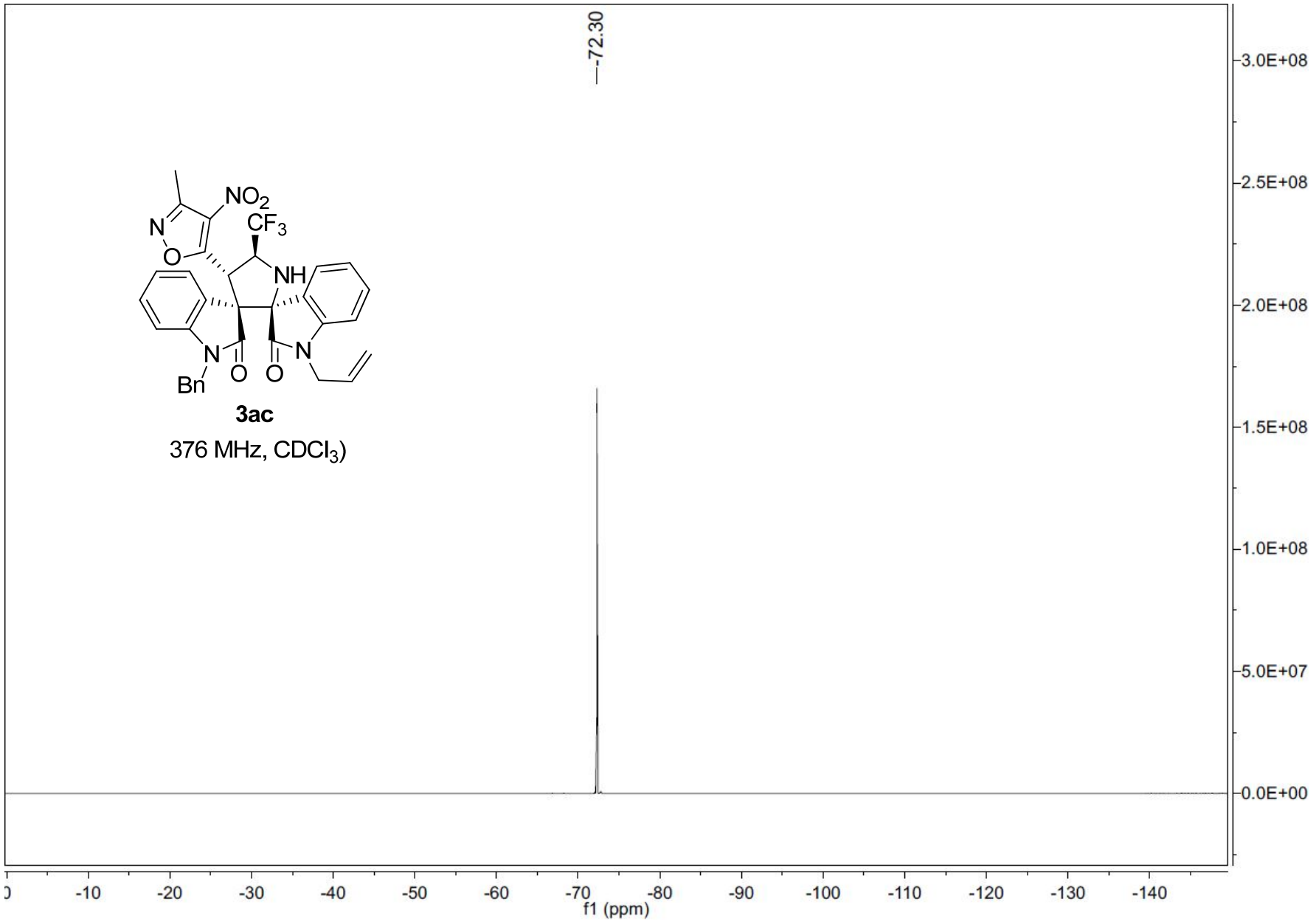

-72.25
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ab
(376 MHz, CDCl3)
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)



3ab

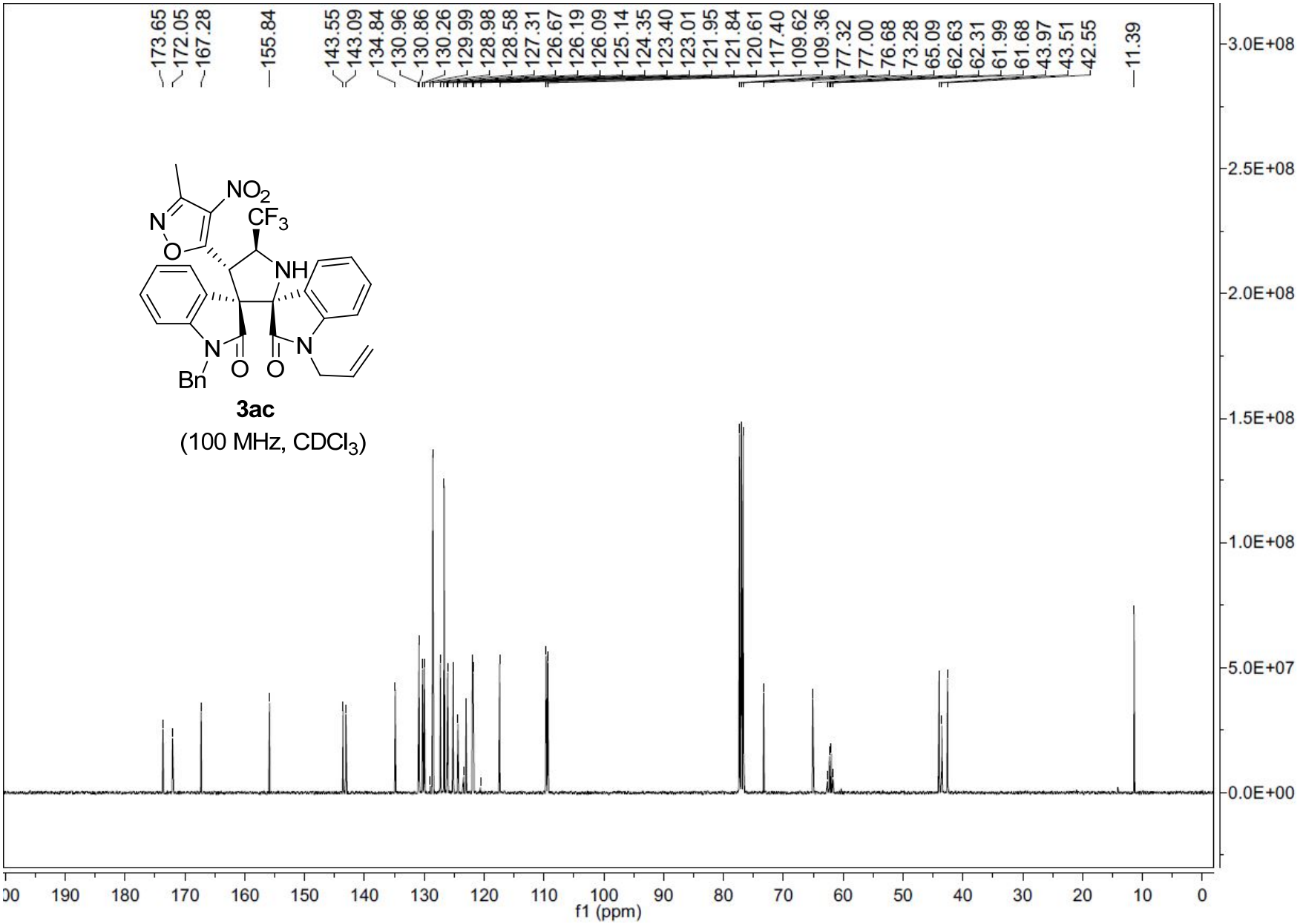
(100 MHz, $CDCl_3$)

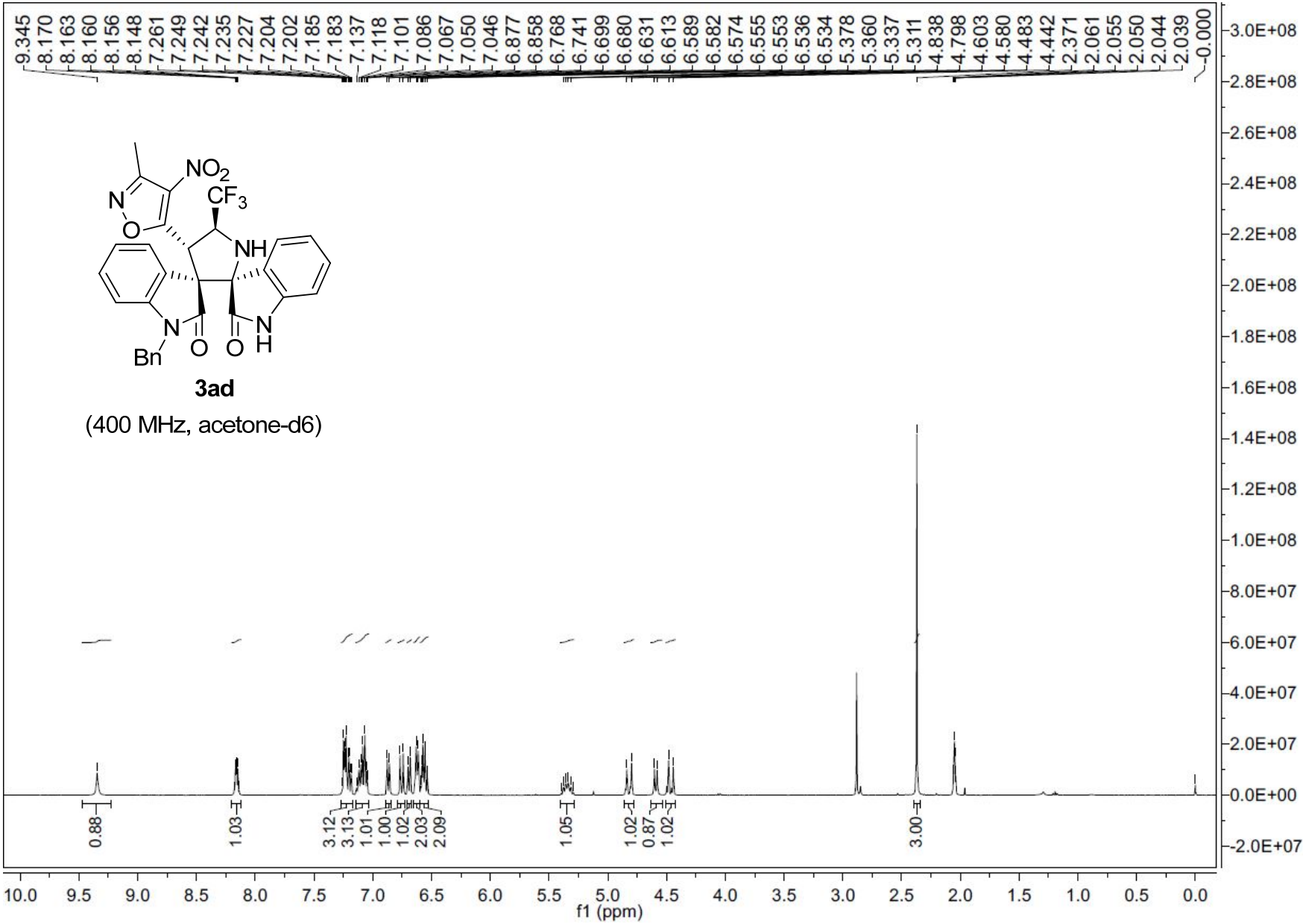

7.261
7.222
7.220
7.202
7.201
7.183
7.181
7.156
7.129
7.111
7.093
7.053
7.034
7.026
7.006
6.943
6.925
6.906
6.808
6.791
6.775
6.772
6.657
6.637
6.481
6.462
6.197
6.173
5.618
5.604
5.589
5.275
5.258
5.047
5.007
4.947
4.921
4.830
4.786
4.564
4.558
4.552
4.523
4.517
4.512
4.430
4.390
3.984
3.970
3.943
3.929
3.432
3.410
2.401
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ac
(400 MHz, CDCl3)
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
1.10
4.07
2.03
1.02
3.02
1.00
1.00
0.99
1.03
1.00
1.00
1.01
1.02
1.02
1.01
1.01
1.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

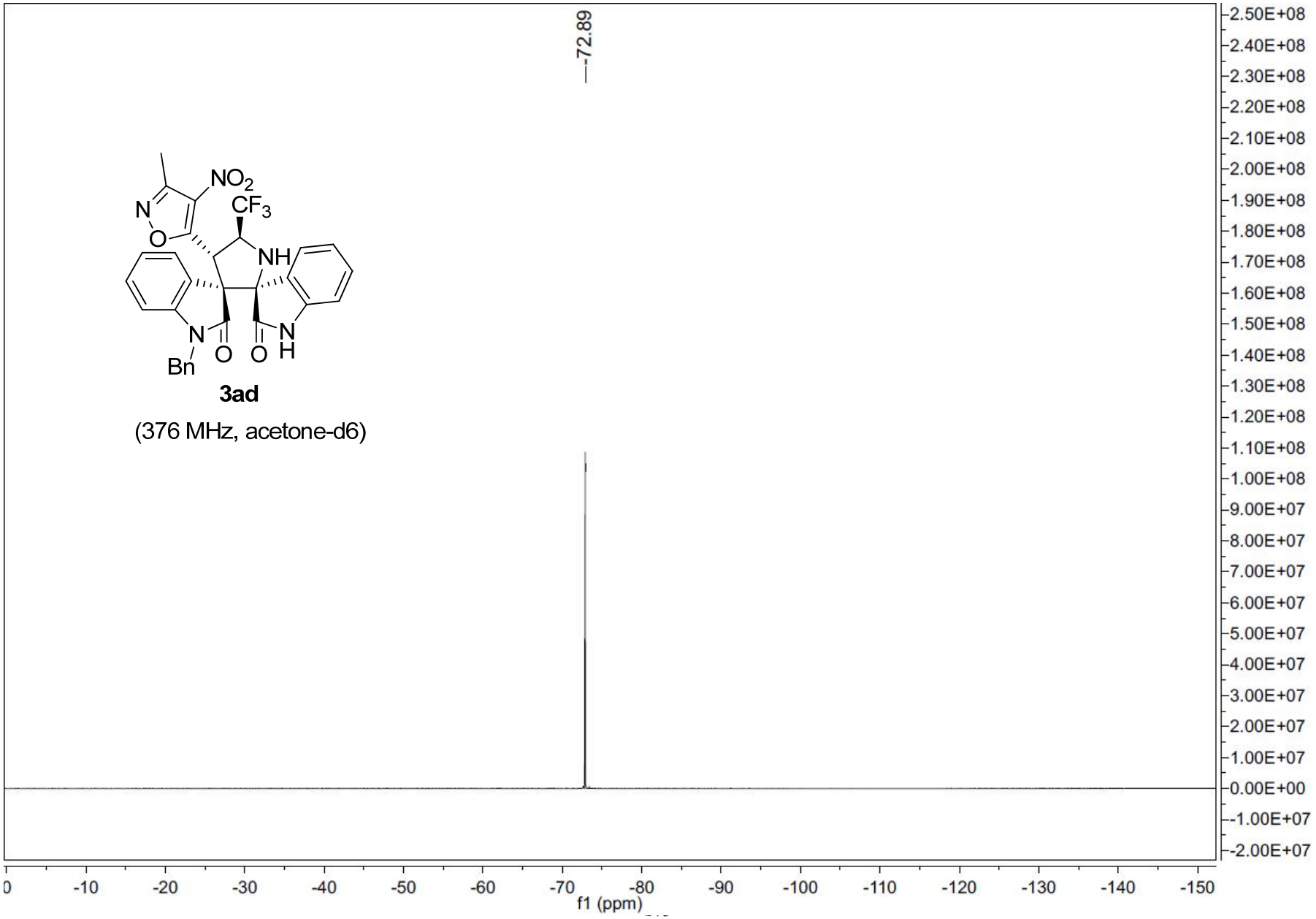


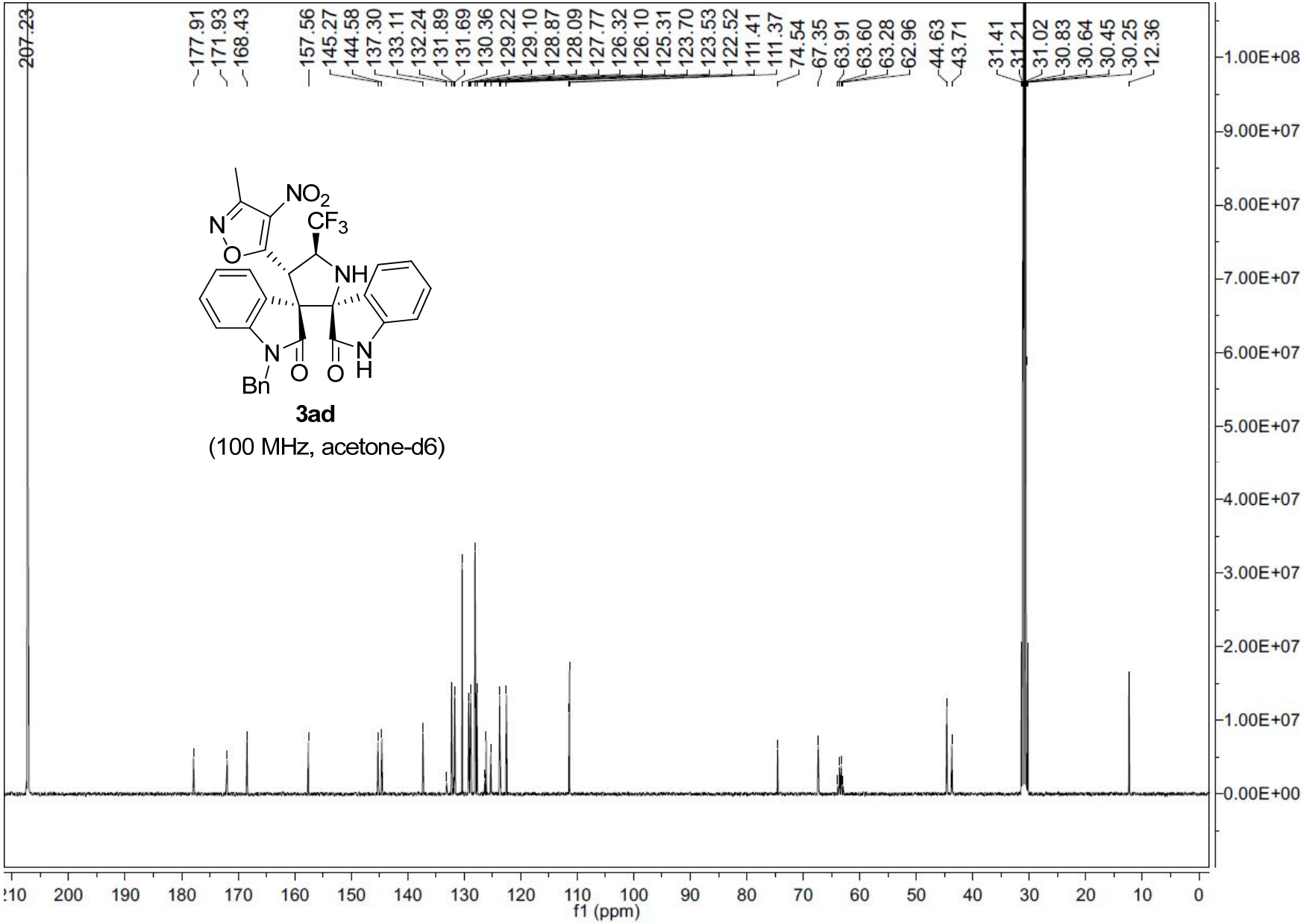
3ac

376 MHz, $CDCl_3$)


173.65
172.05
167.28
155.84
143.55
143.09
134.84
130.96
130.86
130.26
129.99
128.98
128.58
127.31
126.67
126.19
126.09
125.14
124.35
123.40
123.01
121.95
121.84
120.61
117.40
109.62
109.36
77.32
77.00
76.68
73.28
65.09
62.63
62.31
61.99
61.68
43.97
43.51
42.55
11.39
NO2
CF3
N
O
NH
N
O
O
N
Bn
3ac
(100 MHz, CDCl3)
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

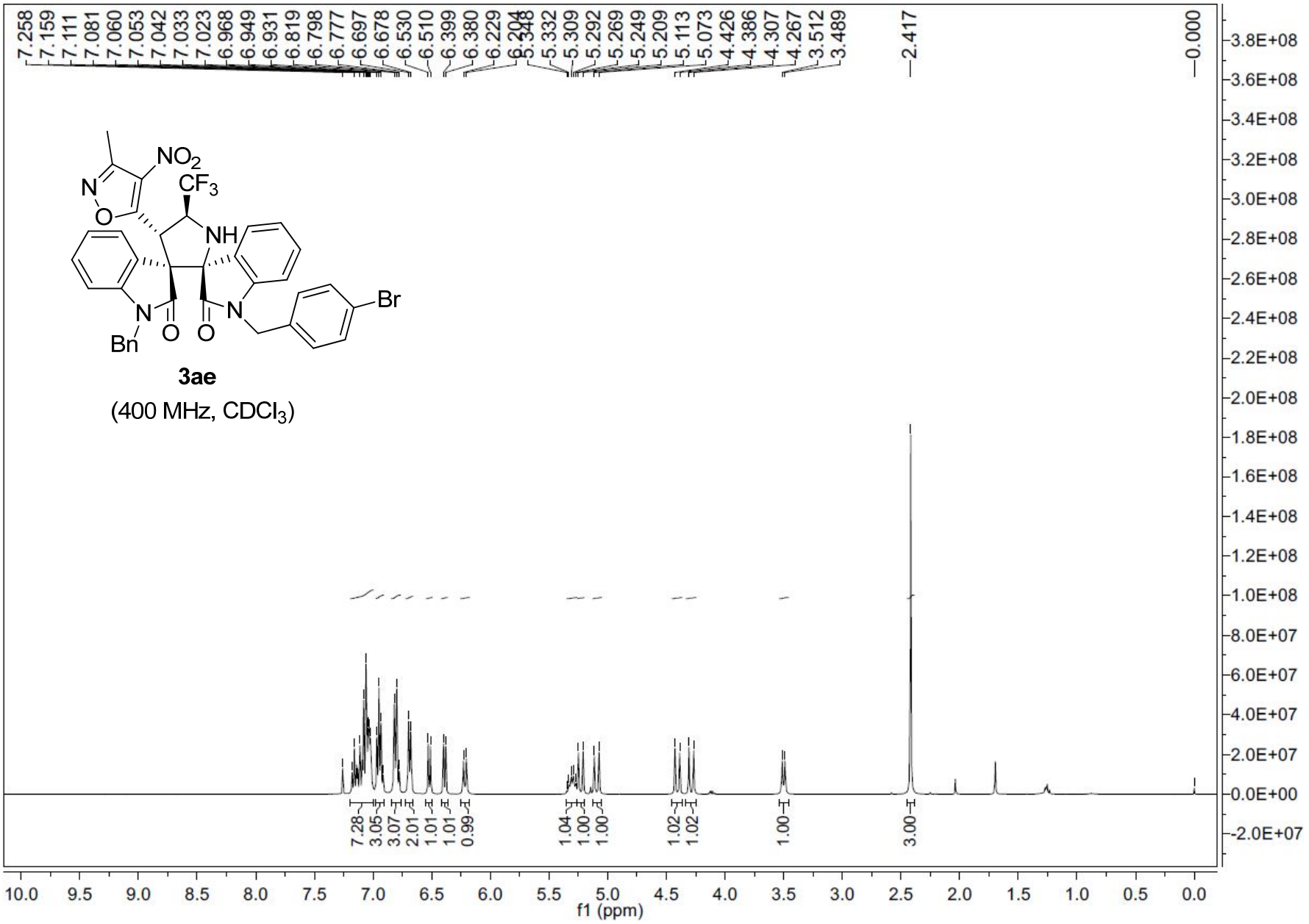

9.345
8.170
8.163
8.160
8.156
8.148
7.261
7.249
7.242
7.235
7.227
7.204
7.202
7.185
7.183
7.137
7.118
7.101
7.086
7.067
7.050
7.046
6.877
6.858
6.768
6.741
6.699
6.680
6.631
6.613
6.589
6.582
6.574
6.555
6.553
6.536
6.534
5.378
5.360
5.337
5.311
4.838
4.798
4.603
4.580
4.483
4.442
2.371
2.061
2.055
2.050
2.044
2.039
0.000
NO2
CF3
N
O
NH
N
Bn
O
O
N
H
3ad
(400 MHz, acetone-d6)
0.88
1.03
3.12
3.13
1.01
1.00
1.02
2.03
2.09
1.05
1.02
0.87
1.02
3.00
f1 (ppm)

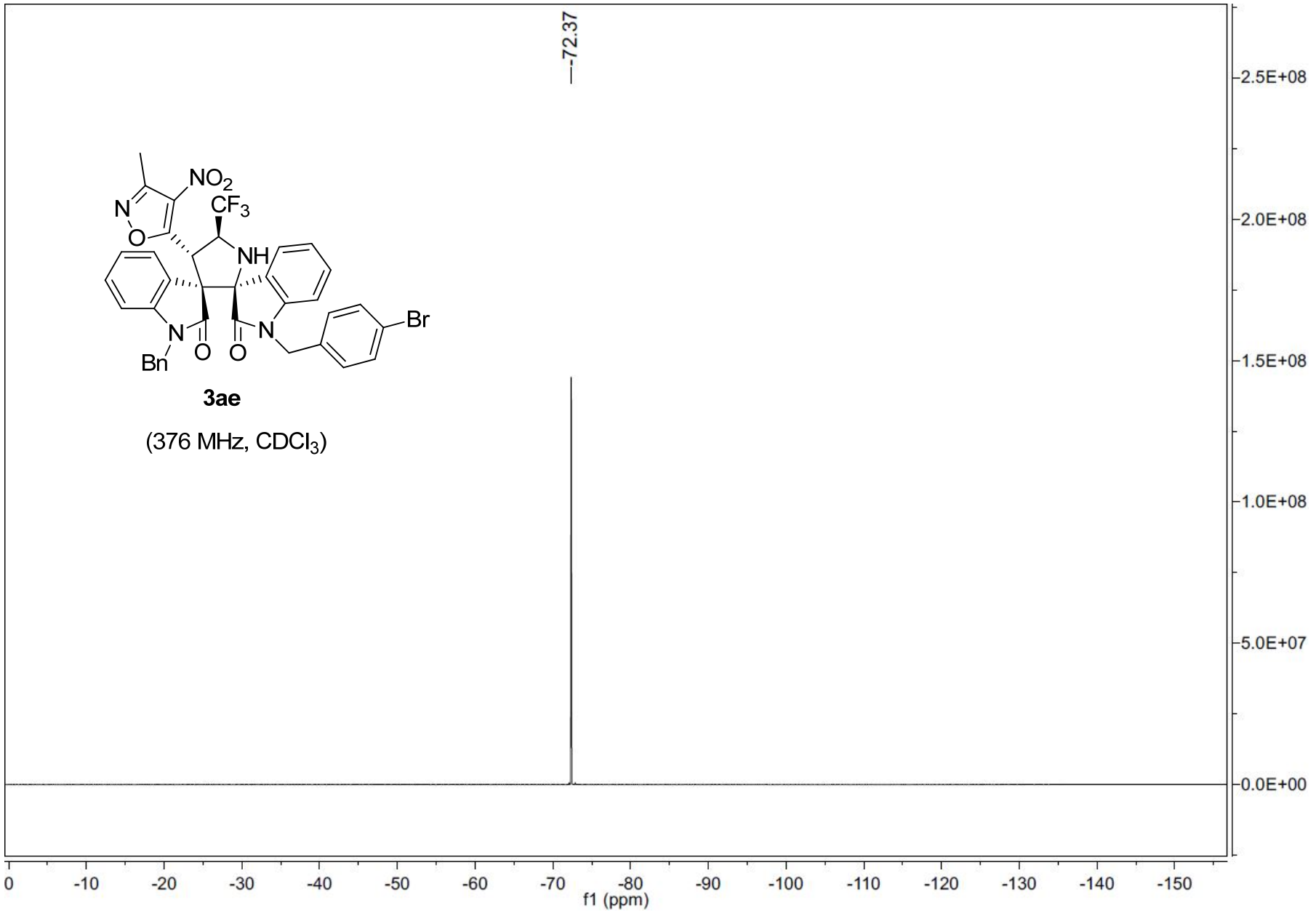

-72.89
NO2
CF3
N
O
NH
N
O
O
N
H
Bn
3ad
(376 MHz, acetone-d6)
2.50E+08
2.40E+08
2.30E+08
2.20E+08
2.10E+08
2.00E+08
1.90E+08
1.80E+08
1.70E+08
1.60E+08
1.50E+08
1.40E+08
1.30E+08
1.20E+08
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
-2.00E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)



3ad

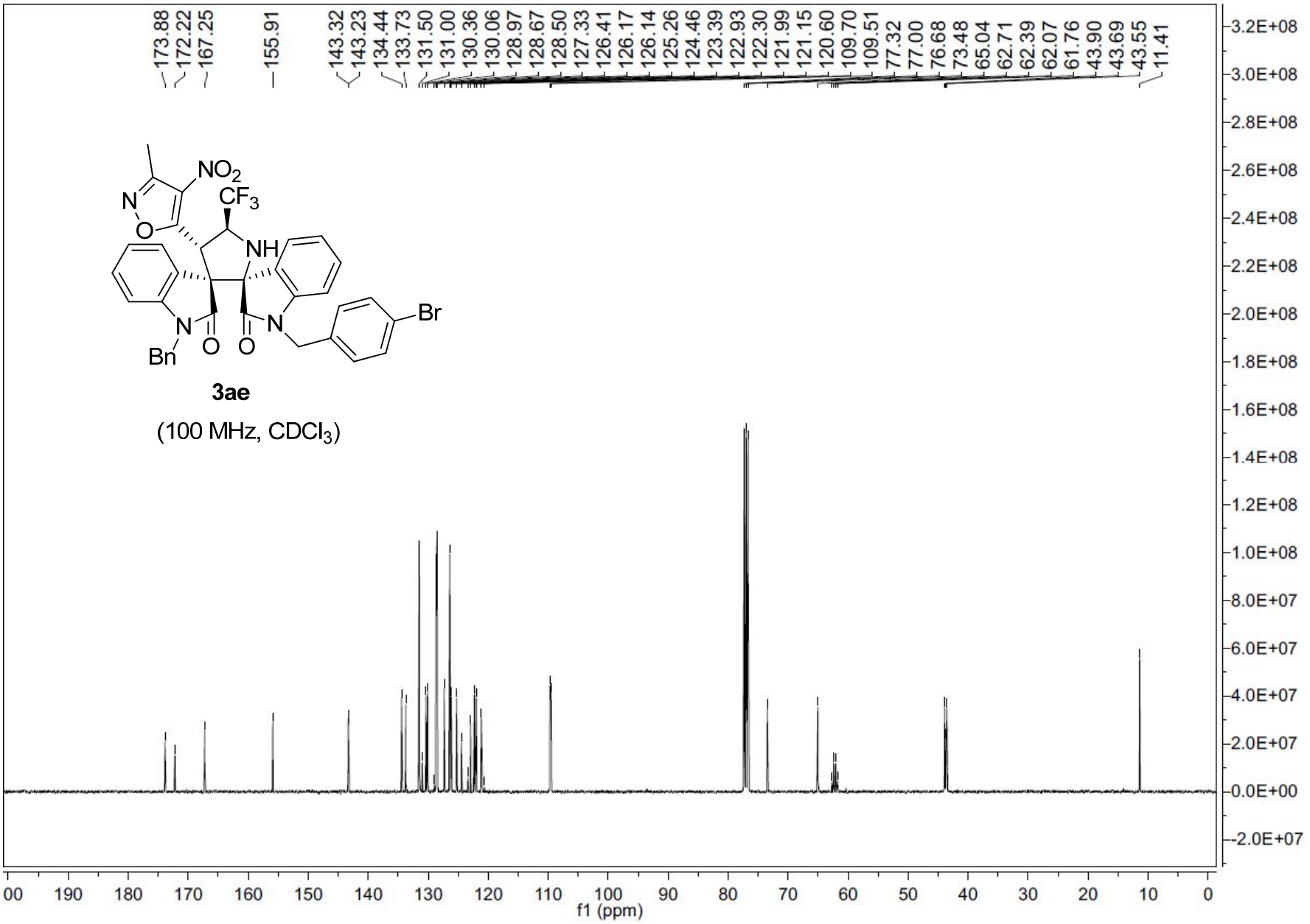
(100 MHz, acetone-d6)

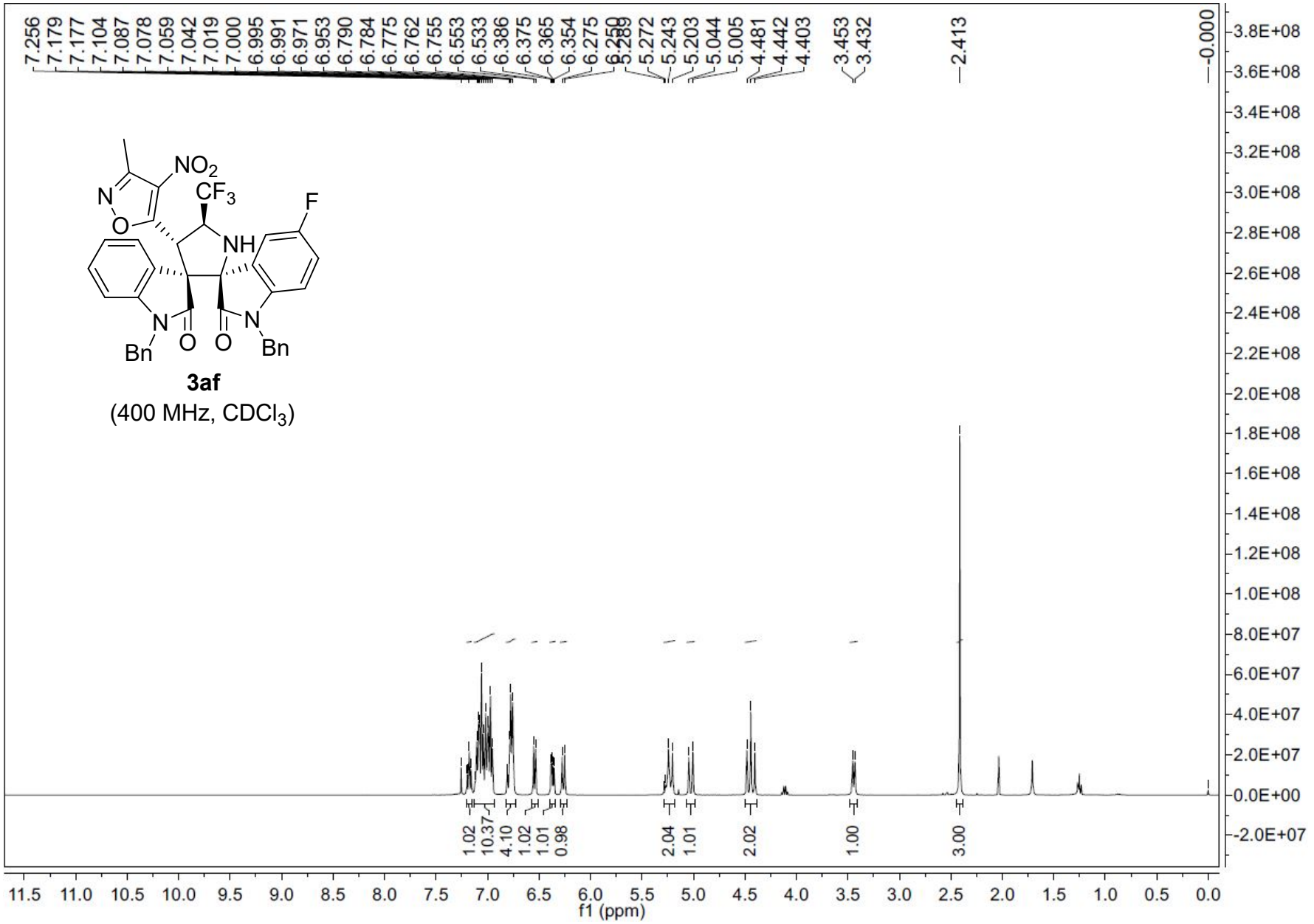

7.258
7.159
7.111
7.081
7.060
7.053
7.042
7.033
7.023
6.968
6.949
6.931
6.819
6.798
6.777
6.697
6.678
6.530
6.510
6.399
6.380
6.229
6.204
5.348
5.332
5.309
5.292
5.269
5.249
5.209
5.113
5.073
4.426
4.386
4.307
4.267
3.512
3.489
2.417
0.000
NO2
CF3
N
O
NH
N
O
O
N
Br
Bn
3ae
(400 MHz, CDCl3)
7.28
3.05
3.07
2.01
1.01
1.01
0.99
1.04
1.00
1.00
1.02
1.02
1.00
3.00
f1 (ppm)

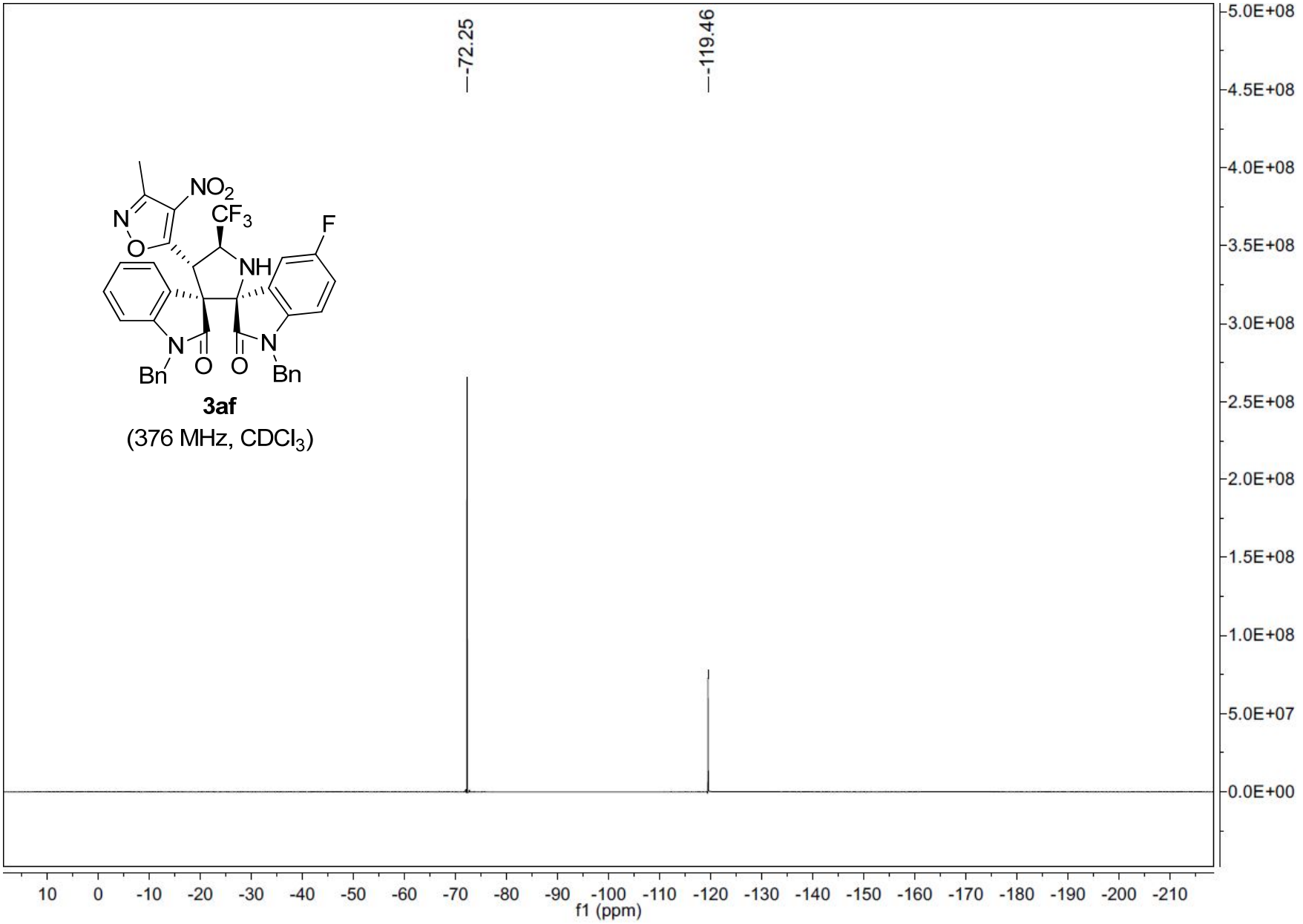


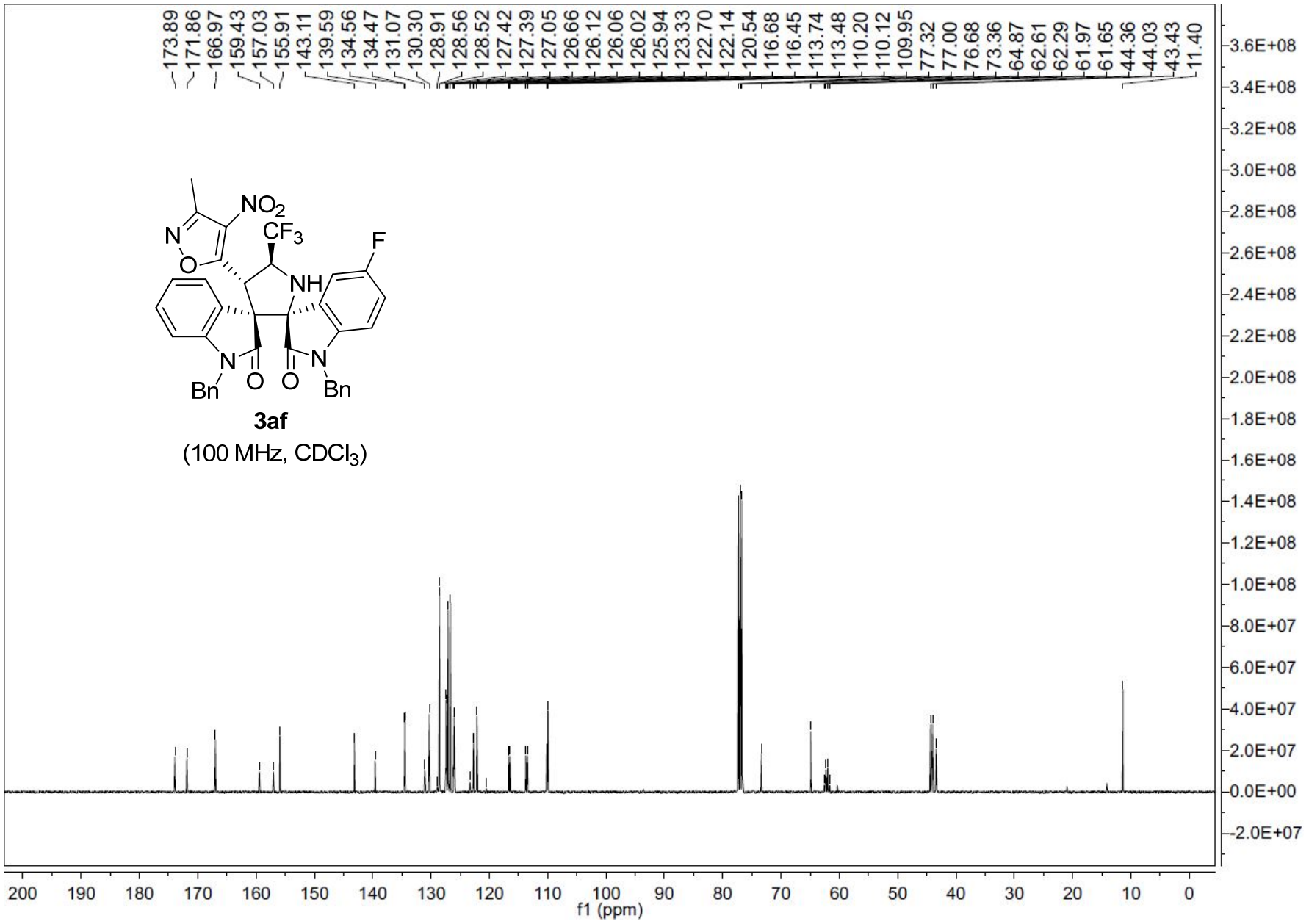
3ae

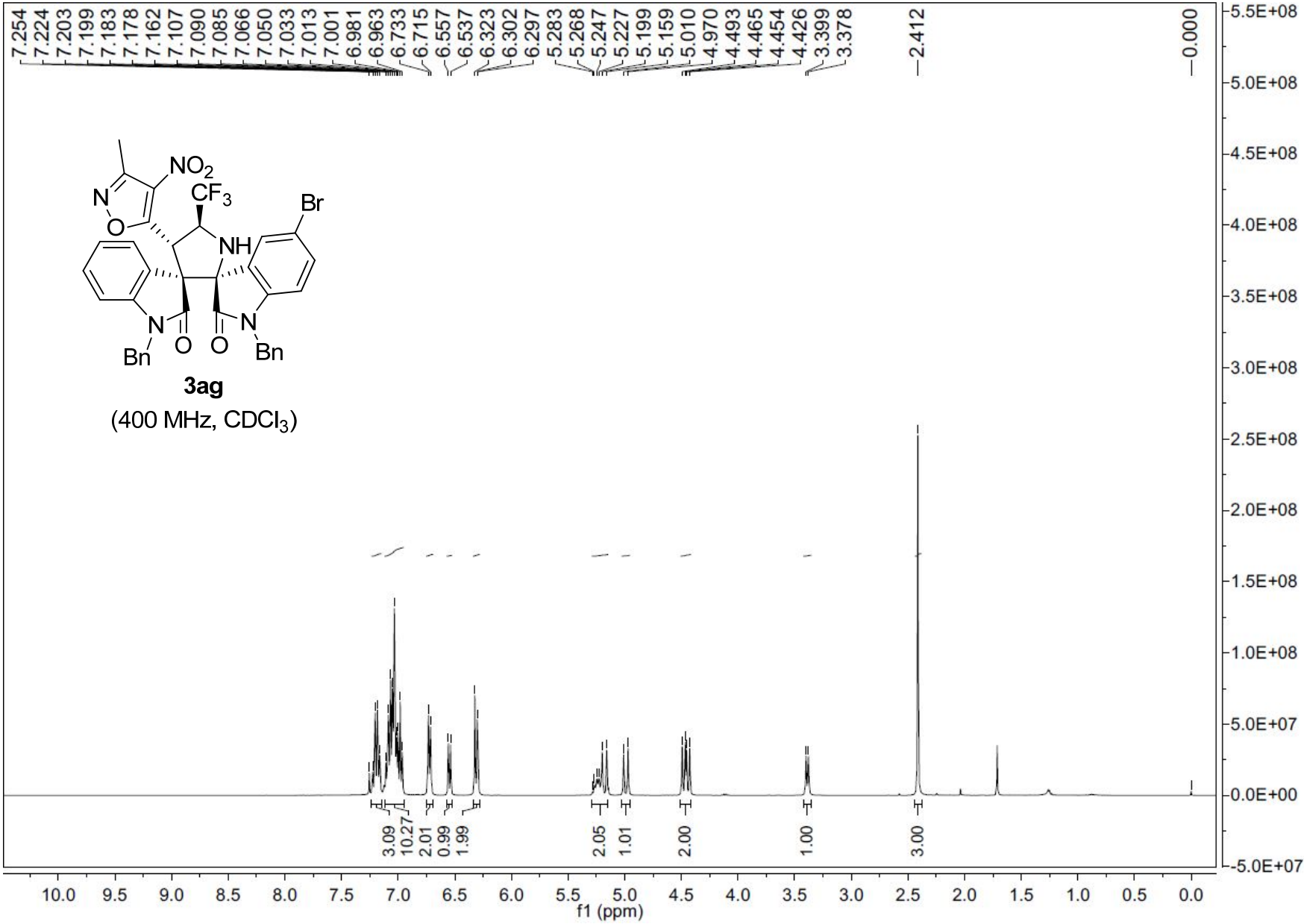
(376 MHz, $CDCl_3$)

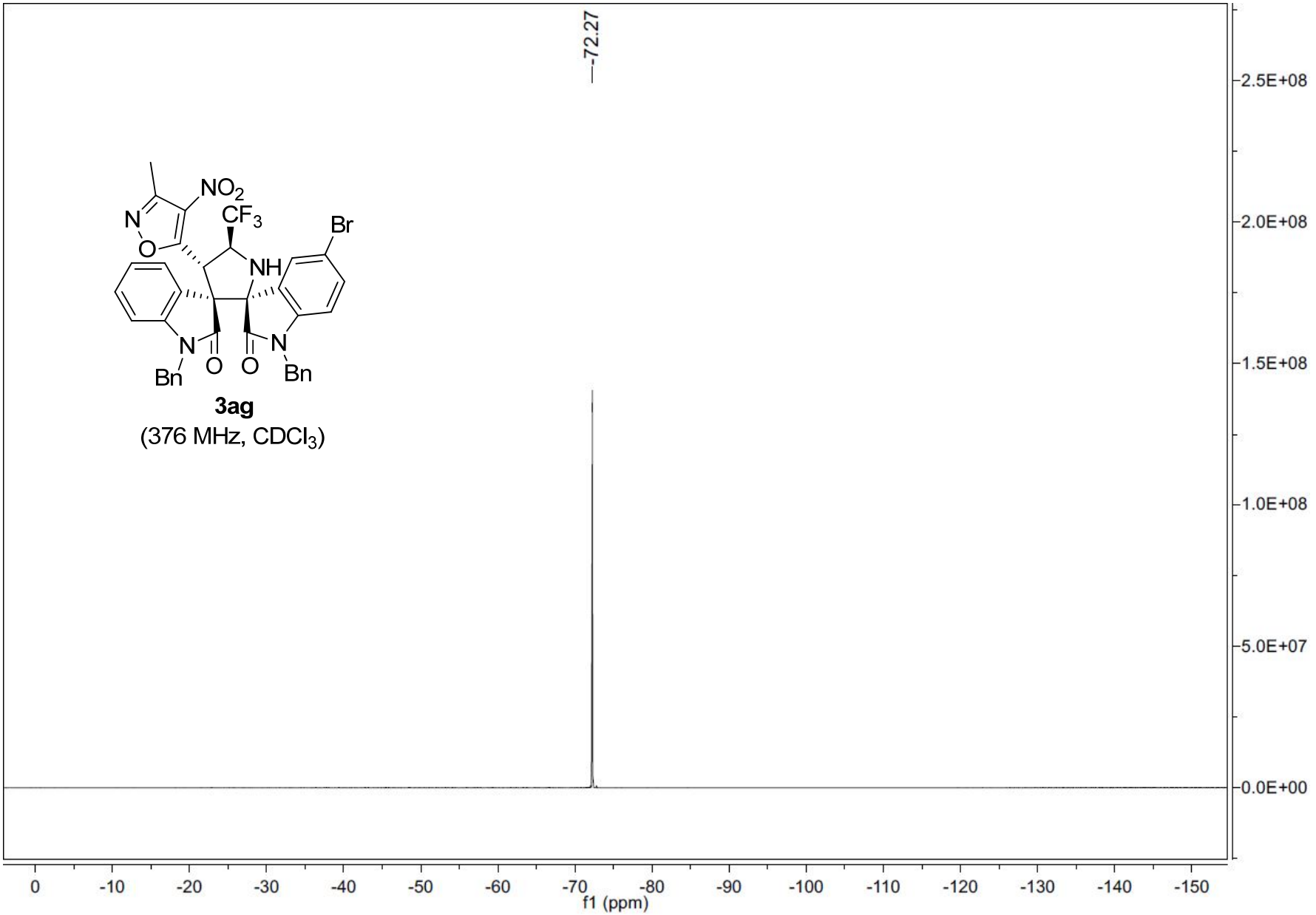

173.88
172.22
167.25
155.91
143.32
143.23
134.44
133.73
131.50
131.00
130.36
130.06
128.97
128.67
128.50
127.33
126.41
126.17
126.14
125.26
124.46
123.39
122.93
122.30
121.99
121.15
120.60
109.70
109.51
77.32
77.00
76.68
73.48
65.04
62.71
62.39
62.07
61.76
43.90
43.69
43.55
11.41
NO2
CF3
N
O
NH
N
O
O
N
Br
Bn
3ae
(100 MHz, CDCl3)
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.256
7.179
7.177
7.104
7.087
7.078
7.059
7.042
7.019
7.000
6.995
6.991
6.971
6.953
6.790
6.784
6.775
6.762
6.755
6.553
6.533
6.386
6.375
6.365
6.354
6.275
6.250
5.289
5.272
5.243
5.203
5.044
5.005
4.481
4.442
4.403
3.453
3.432
2.413
-0.000
NO2
CF3
F
N
O
NH
N
O
O
N
Bn
Bn
3af
(400 MHz, CDCl3)
1.02
10.37
4.10
1.02
1.01
0.98
2.04
1.01
2.02
1.00
3.00
f1 (ppm)


-72.25
-119.46
NO2
CF3
F
NH
N
O
N
O
O
N
Bn
Bn
3af
(376 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

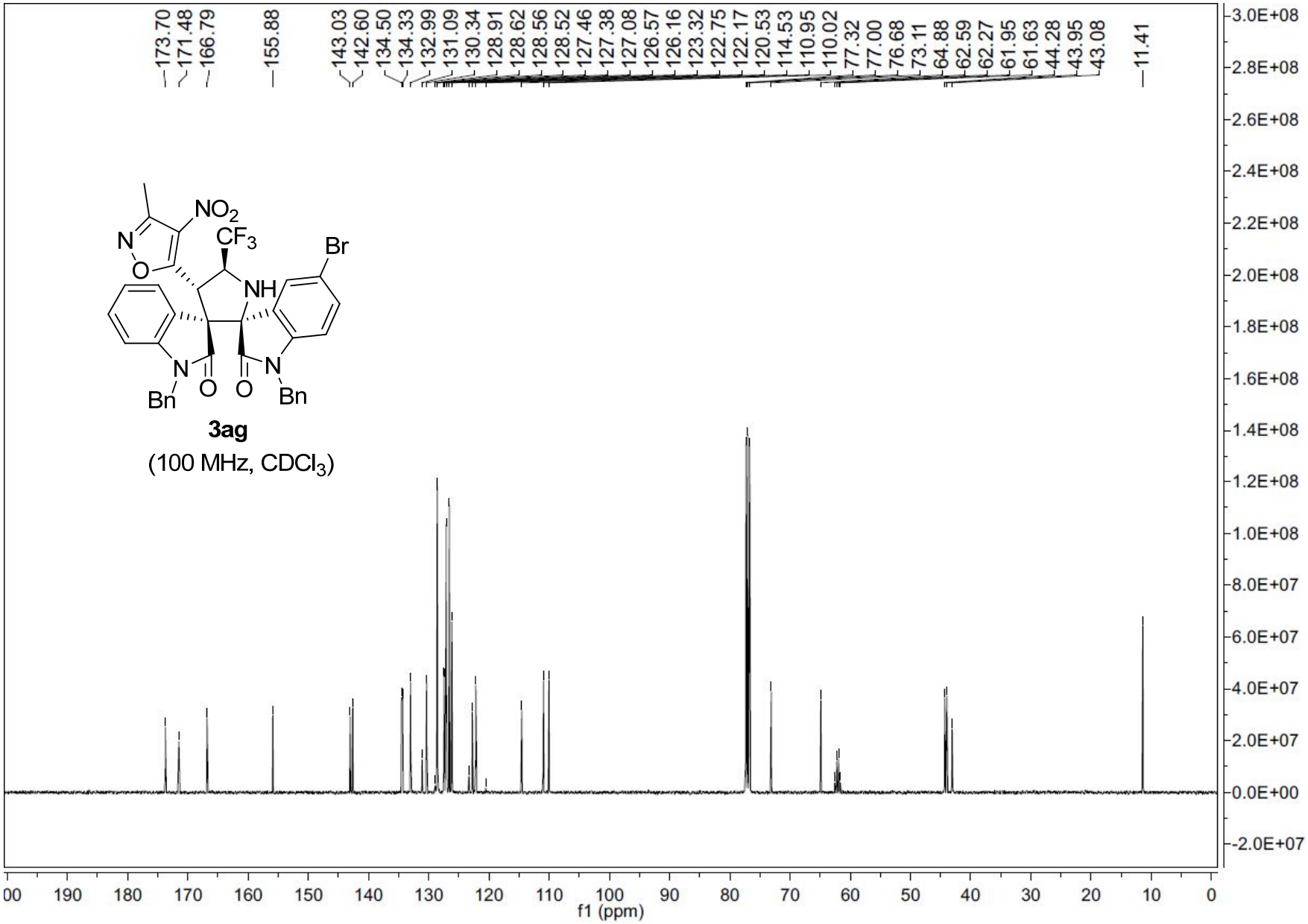

173.89
171.86
166.97
159.43
157.03
155.91
143.11
139.59
134.56
134.47
131.07
130.30
128.91
128.56
128.52
127.42
127.39
127.05
126.66
126.12
126.06
126.02
125.94
123.33
122.70
122.14
120.54
116.68
116.45
113.74
113.48
110.20
110.12
109.95
77.32
77.00
76.68
73.36
64.87
62.61
62.29
61.97
61.65
44.36
44.03
43.43
11.40
NO2
CF3
F
N
O
NH
N
O
O
N
Bn
Bn
3af
(100 MHz, CDCl3)
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

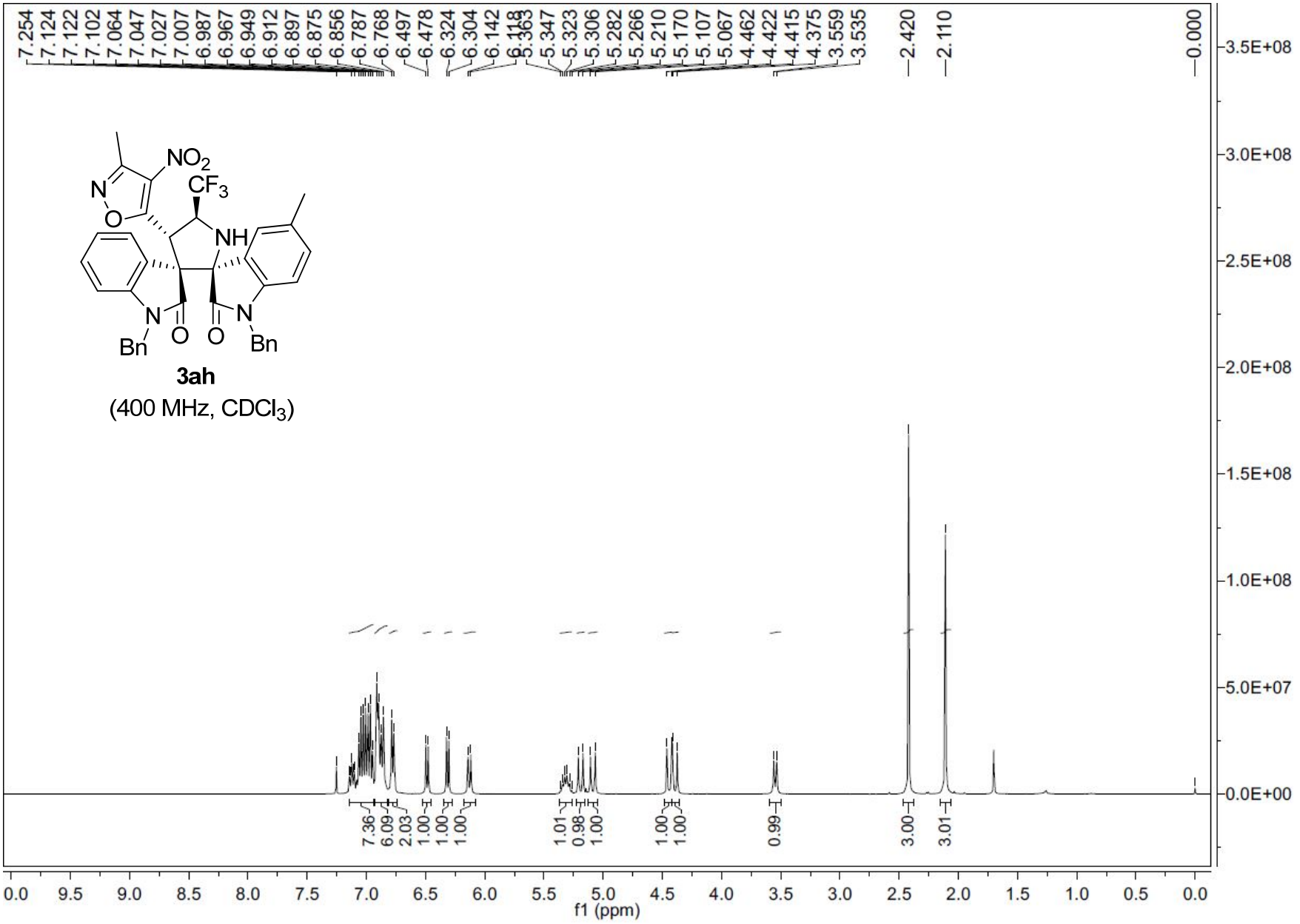

7.254
7.224
7.203
7.199
7.183
7.178
7.162
7.107
7.090
7.085
7.066
7.050
7.033
7.013
7.001
6.981
6.963
6.733
6.715
6.557
6.537
6.323
6.302
6.297
5.283
5.268
5.247
5.227
5.199
5.159
5.010
4.970
4.493
4.465
4.454
4.426
3.399
3.378
2.412
0.000
NO2
CF3
Br
N
O
NH
N
O
O
N
Bn
Bn
3ag
(400 MHz, CDCl3)
3.09
10.27
2.01
0.99
1.99
2.05
1.01
2.00
1.00
3.00
f1 (ppm)

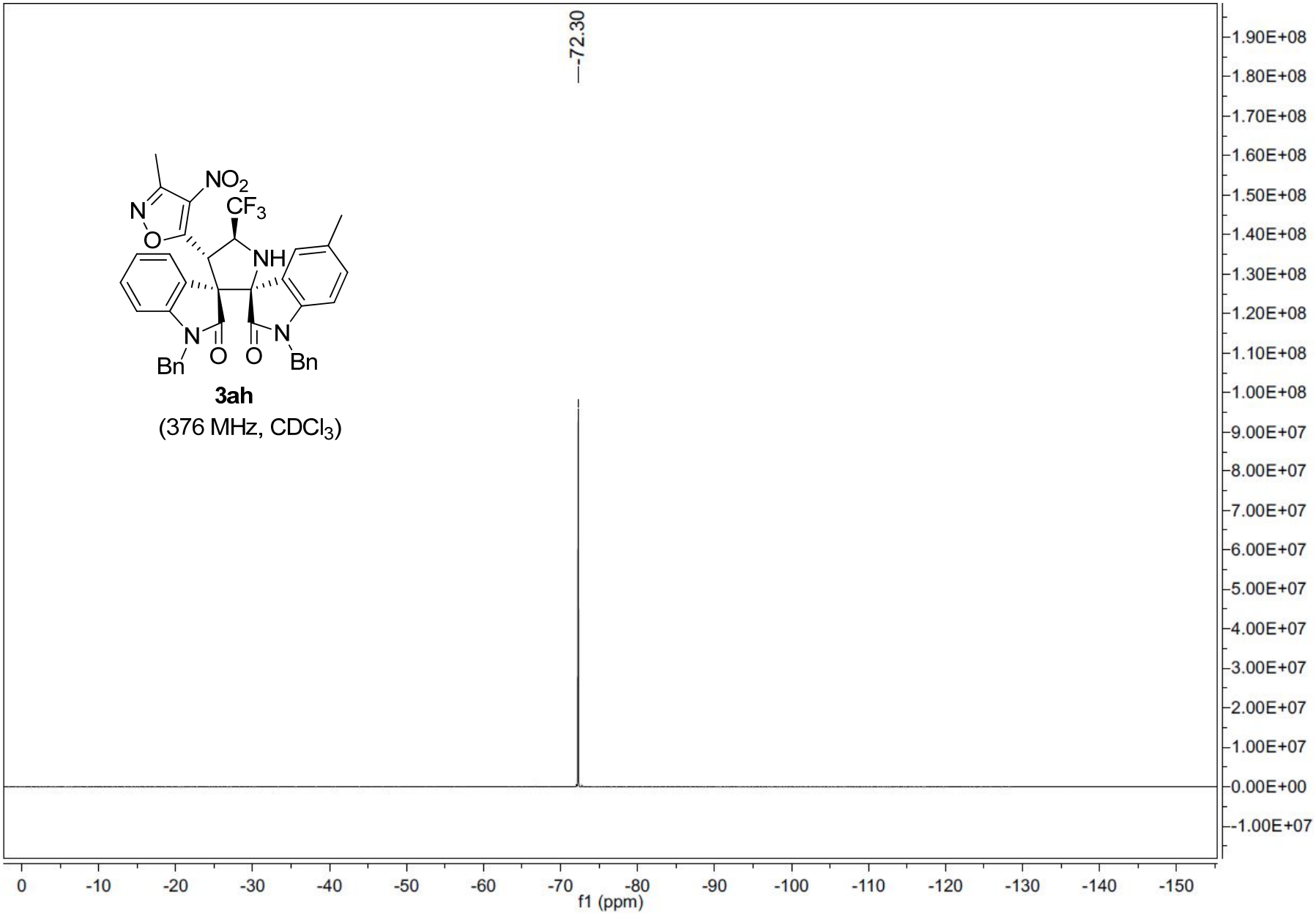


3ag

(376 MHz, $CDCl_3$)

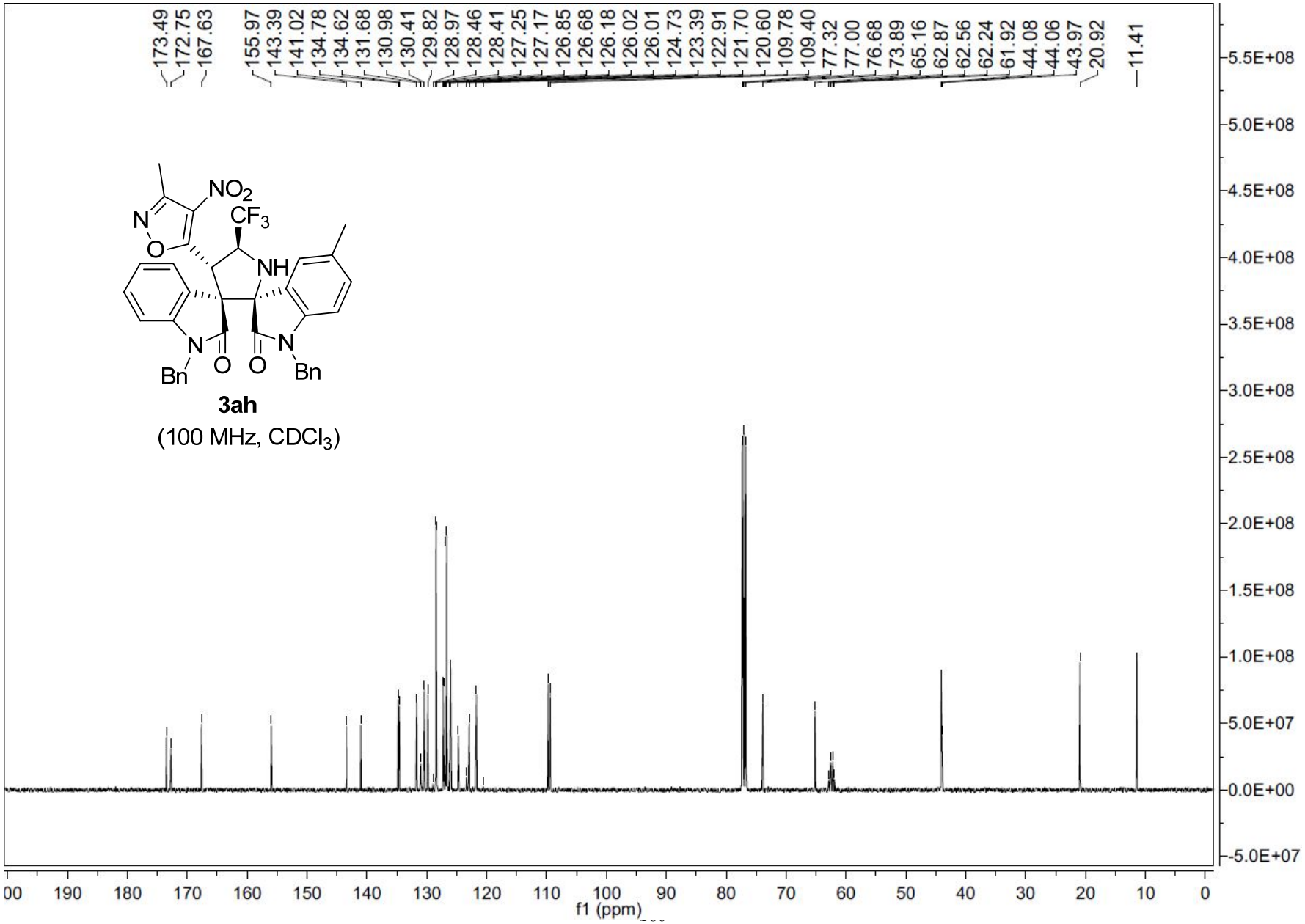

173.70
171.48
166.79
155.88
143.03
142.60
134.50
134.33
132.99
131.09
130.34
128.91
128.62
128.56
128.52
127.46
127.38
127.08
126.57
126.16
123.32
122.75
122.17
120.53
114.53
110.95
110.02
77.32
77.00
76.68
73.11
64.88
62.59
62.27
61.95
61.63
44.28
43.95
43.08
11.41
NO2
CF3
Br
NH
N
O
N
O
O
N
Bn
Bn
3ag
(100 MHz, CDCl3)
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

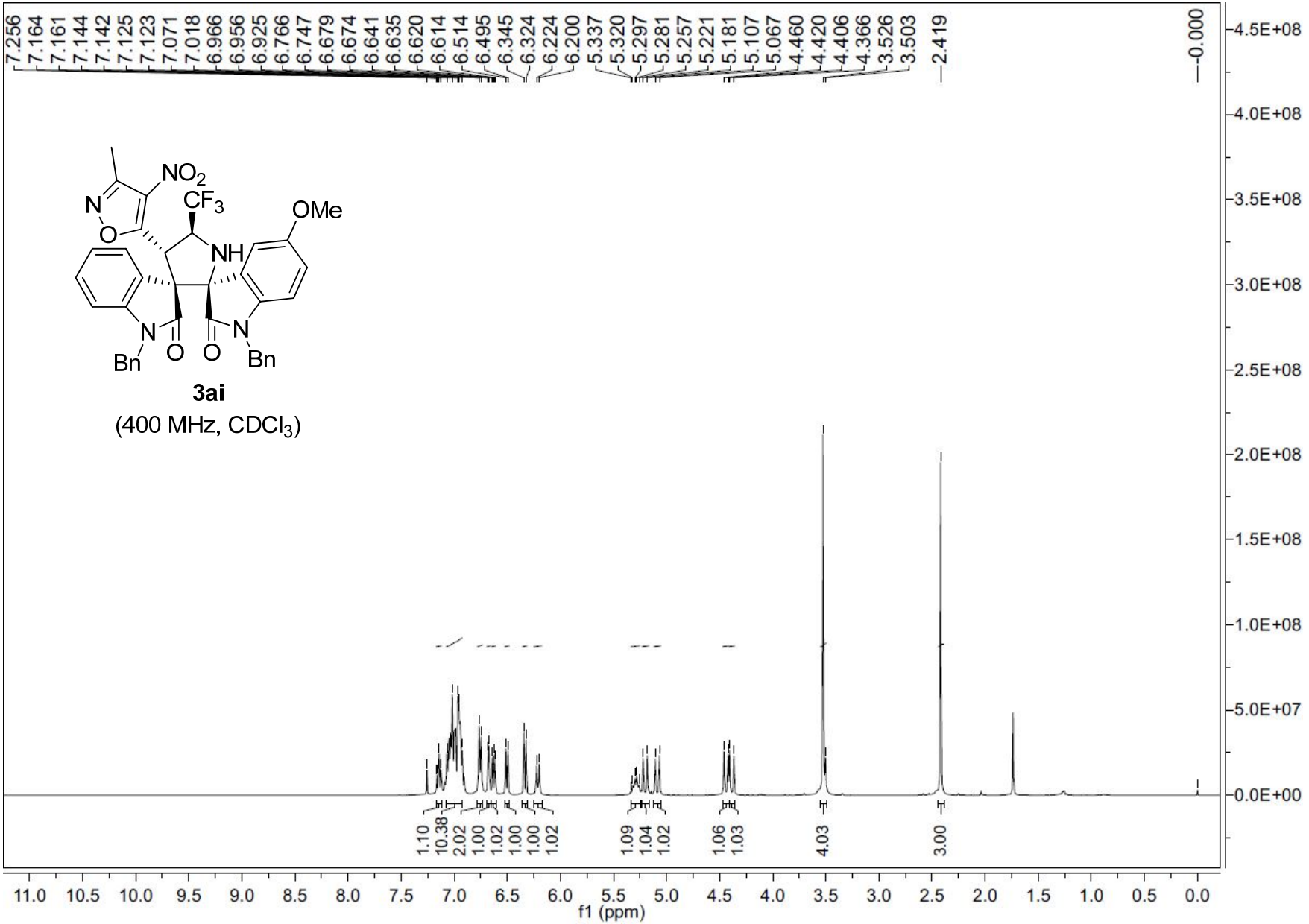

7.254
7.124
7.122
7.102
7.064
7.047
7.027
7.007
6.987
6.967
6.949
6.912
6.897
6.875
6.856
6.787
6.768
6.497
6.478
6.324
6.304
6.142
6.118
6.103
5.363
5.347
5.323
5.306
5.282
5.266
5.210
5.170
5.107
5.067
4.462
4.422
4.415
4.375
3.559
3.535
2.420
2.110
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3ah
(400 MHz, CDCl3)
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
7.36
6.09
2.03
1.00
1.00
1.00
1.01
0.98
1.00
1.00
1.00
0.99
3.00
3.01
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

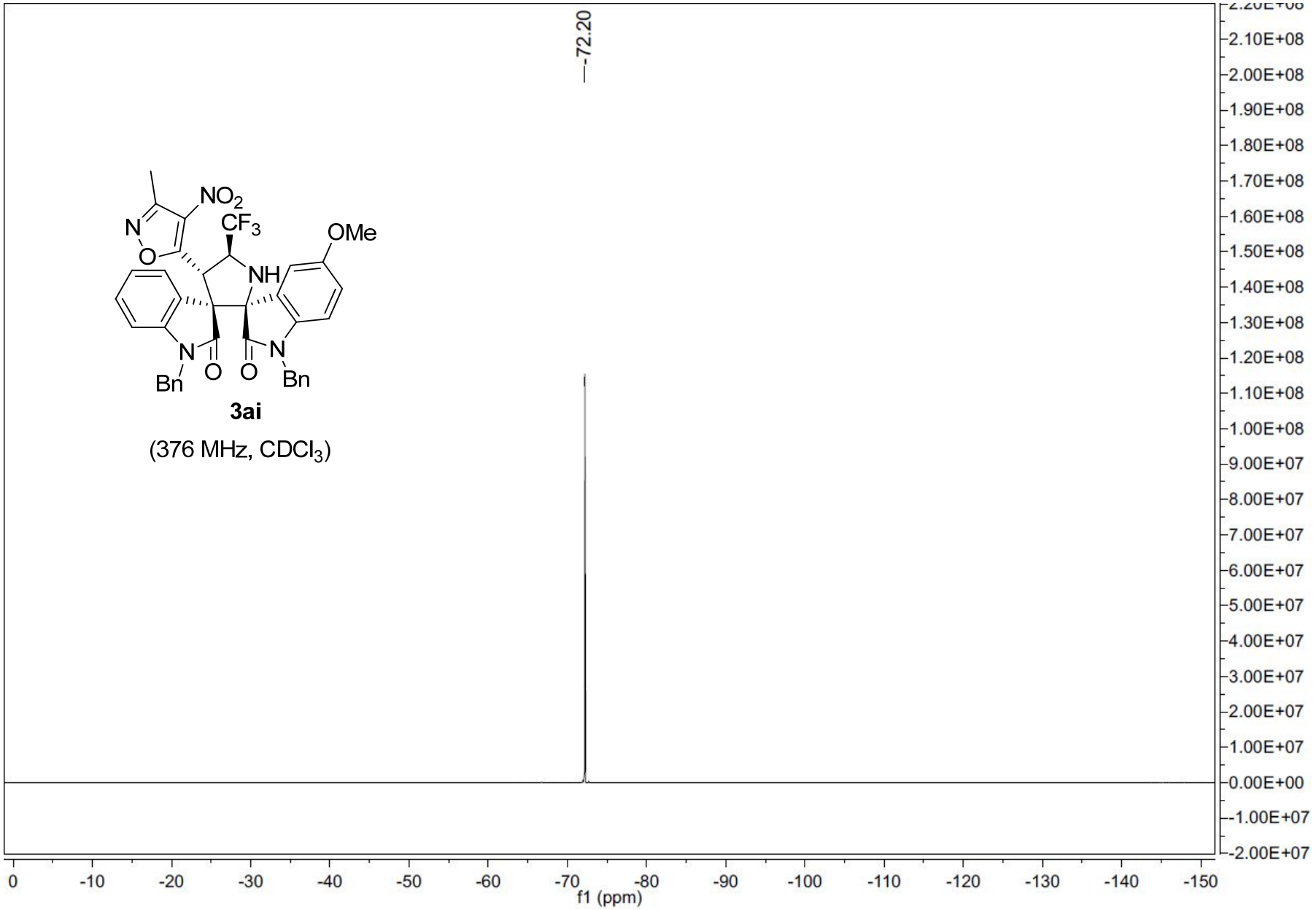


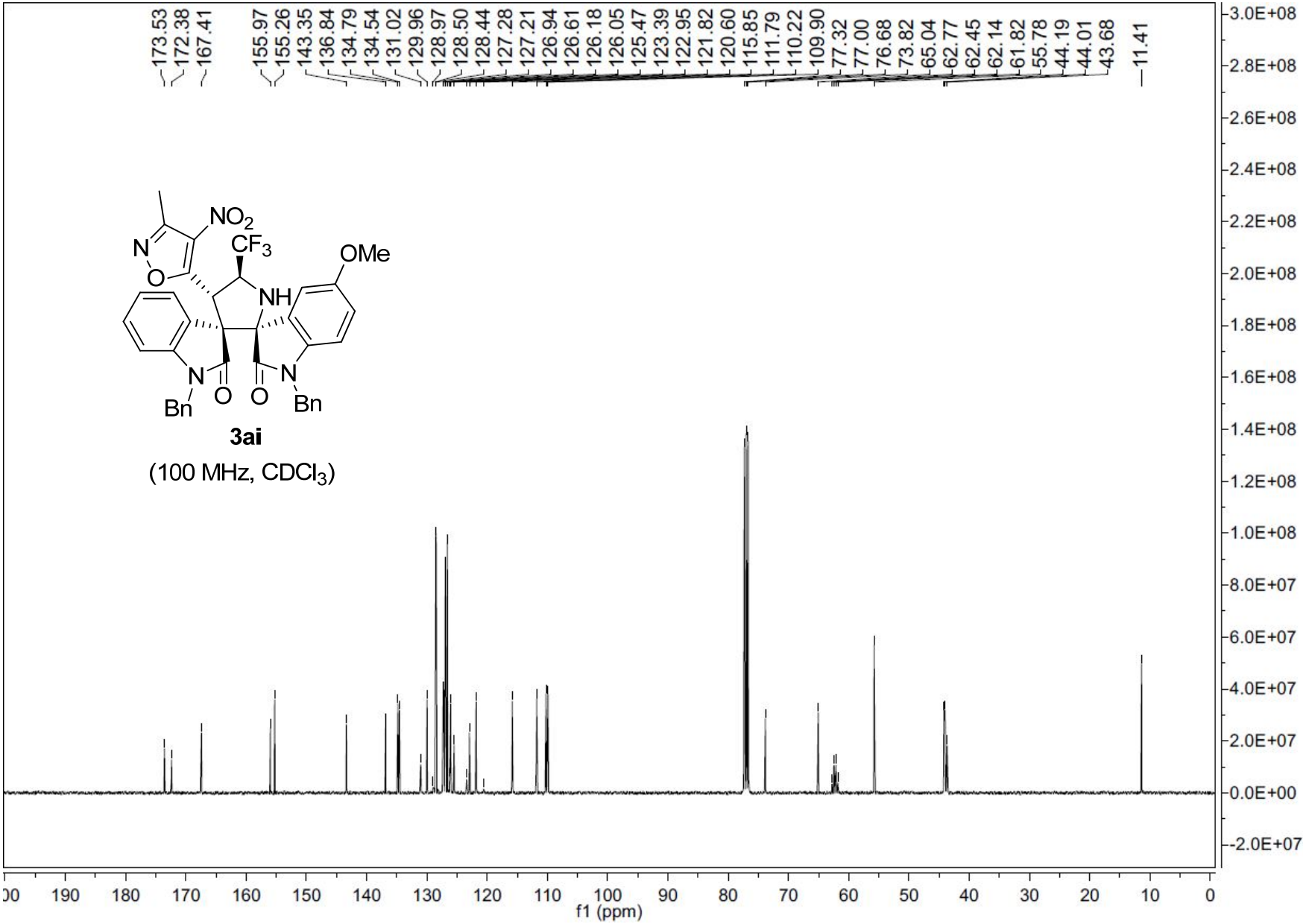
3ah

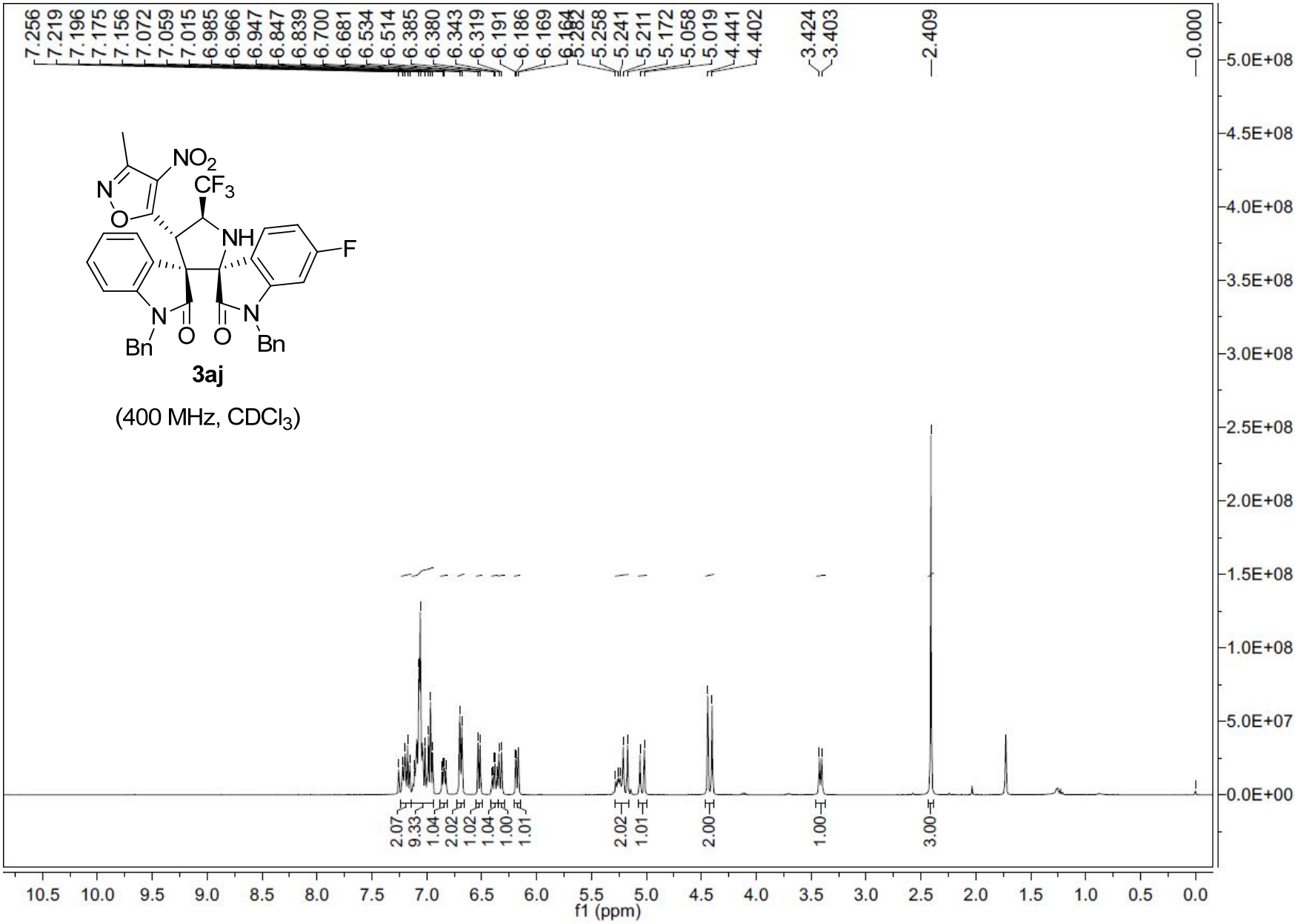
(376 MHz, $CDCl_3$)

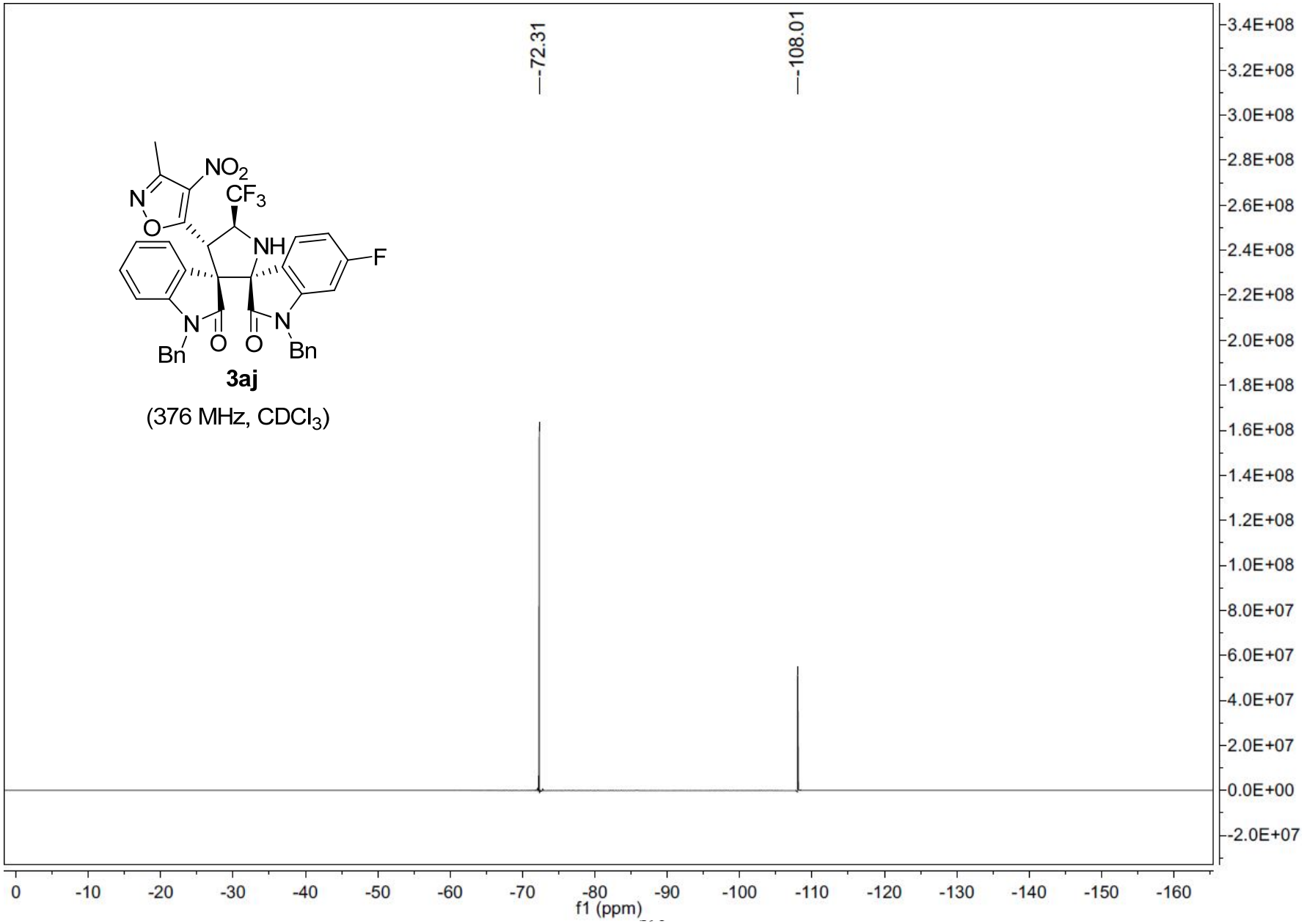

173.49
172.75
167.63
155.97
143.39
141.02
134.78
134.62
131.68
130.98
130.41
129.82
128.97
128.46
128.41
127.25
127.17
126.85
126.68
126.18
126.02
126.01
124.73
123.39
122.91
121.70
120.60
109.78
109.40
77.32
77.00
76.68
73.89
65.16
62.87
62.56
62.24
61.92
44.08
44.06
43.97
20.92
11.41
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3ah
(100 MHz, CDCl3)
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

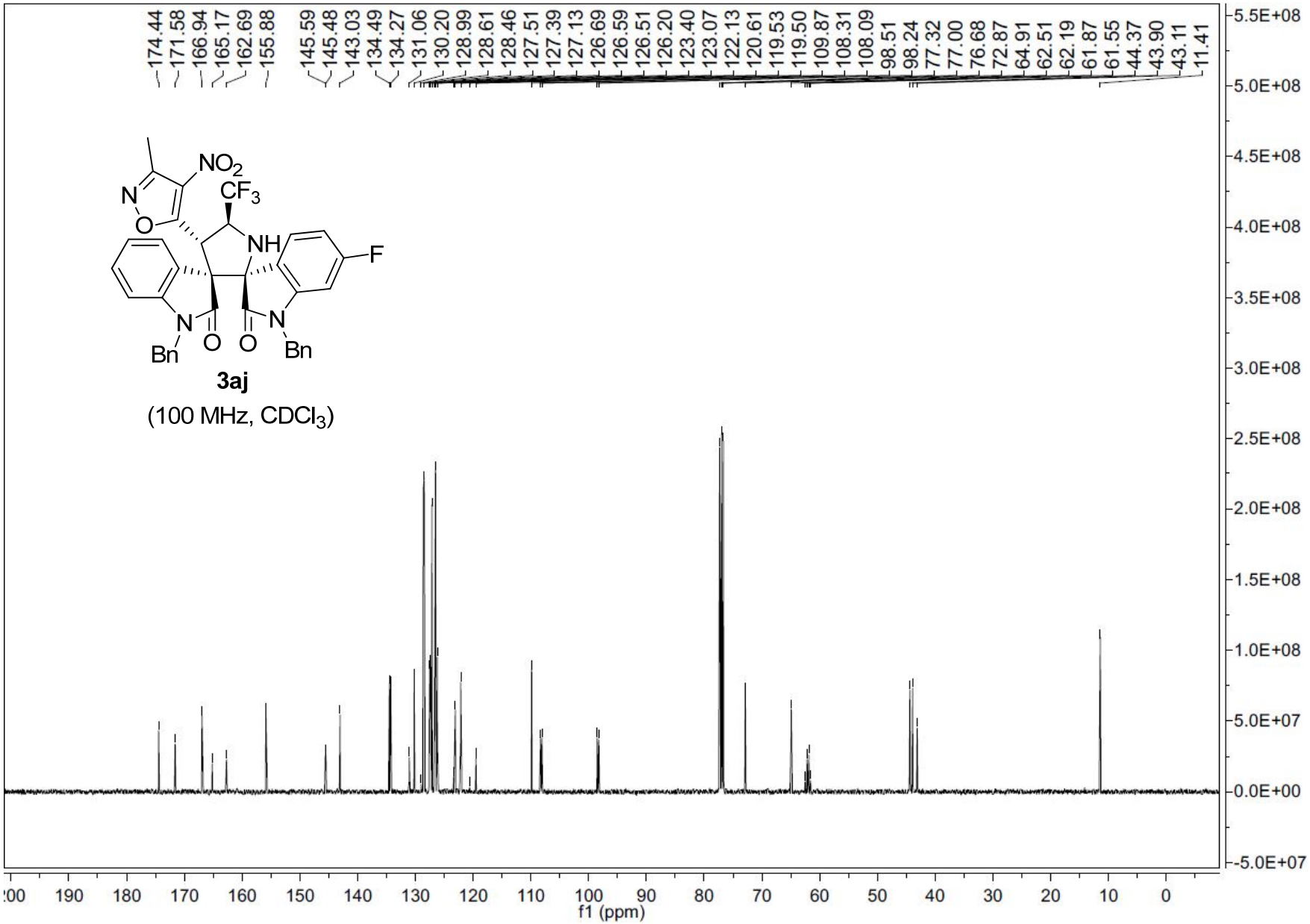

7.256
7.164
7.161
7.144
7.142
7.125
7.123
7.071
7.018
6.966
6.956
6.925
6.766
6.747
6.679
6.674
6.641
6.635
6.620
6.614
6.514
6.495
6.345
6.324
6.224
6.200
5.337
5.320
5.297
5.281
5.257
5.221
5.181
5.107
5.067
4.460
4.420
4.406
4.366
3.526
3.503
2.419
0.000
NO2
CF3
OMe
N
O
NH
N
O
O
N
Bn
Bn
3ai
(400 MHz, CDCl3)
1.10
10.38
2.02
1.00
1.02
1.00
1.00
1.02
1.09
1.04
1.02
1.06
1.03
4.03
3.00
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

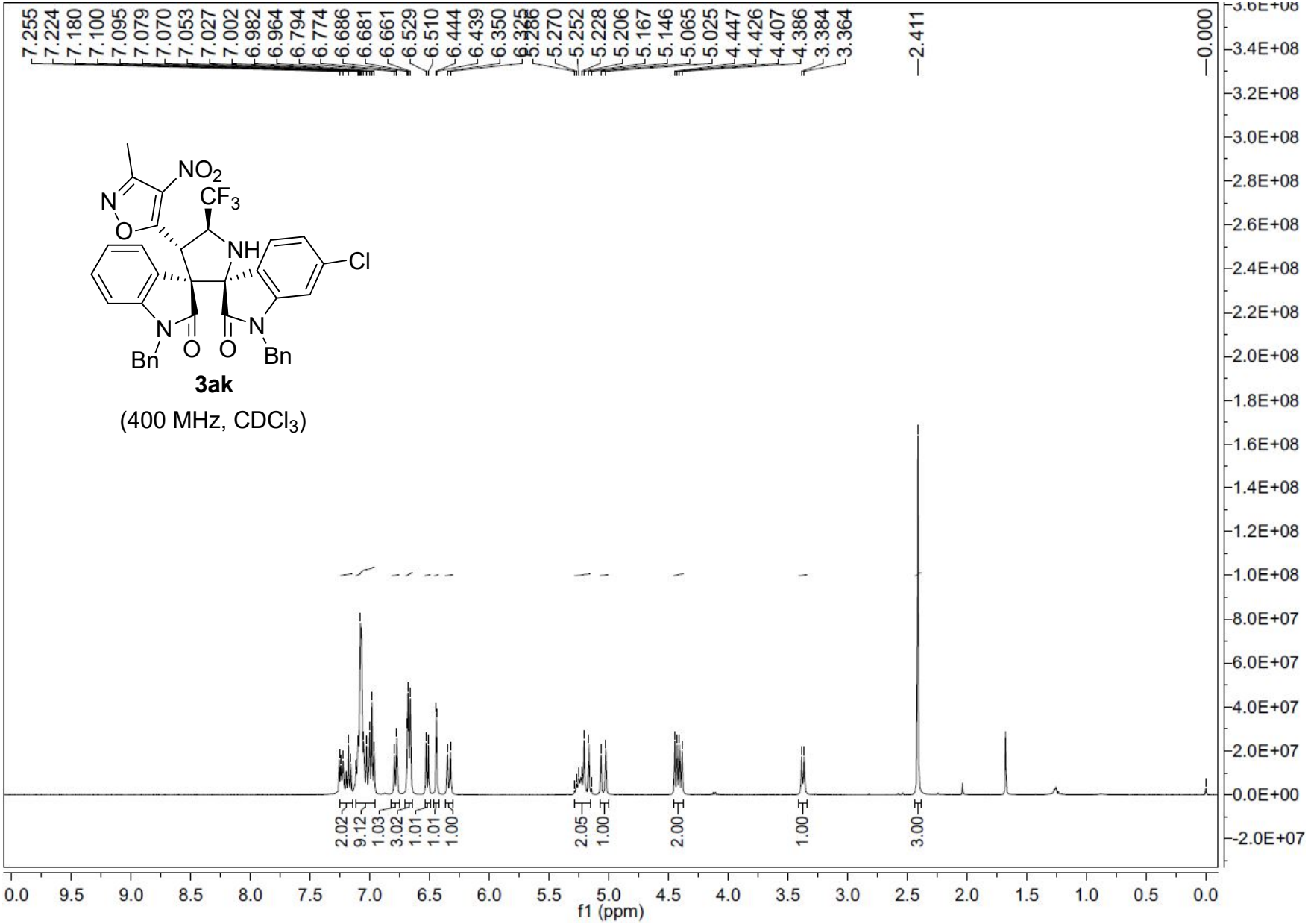

-72.20
NO2
CF3
OMe
N
O
NH
N
O
O
N
Bn
Bn
3ai
(376 MHz, CDCl3)
2.10E+08
2.00E+08
1.90E+08
1.80E+08
1.70E+08
1.60E+08
1.50E+08
1.40E+08
1.30E+08
1.20E+08
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
-2.00E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

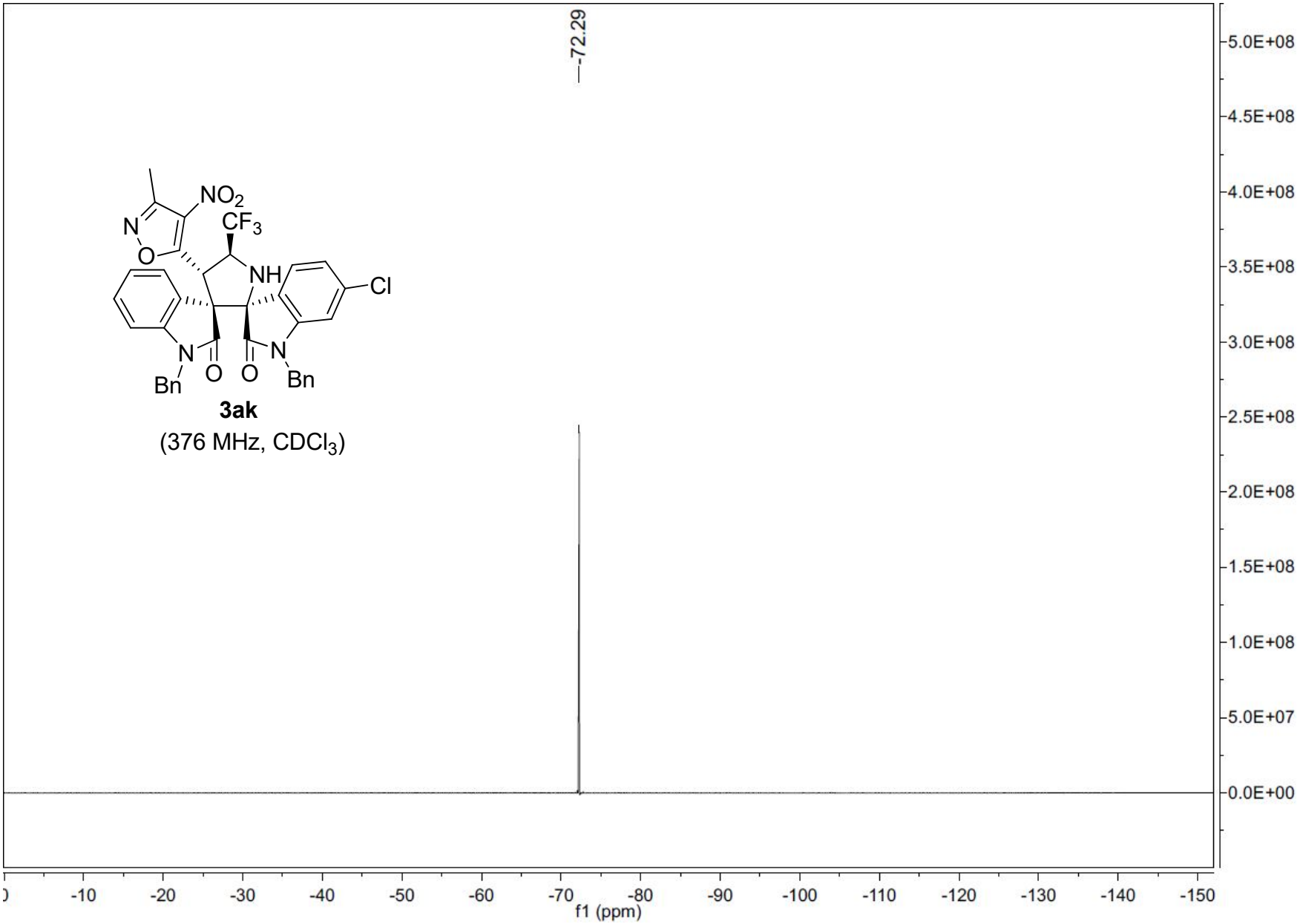

173.53
172.38
167.41
155.97
155.26
143.35
136.84
134.79
134.54
131.02
129.96
128.97
128.50
128.44
127.28
127.21
126.94
126.61
126.18
126.05
125.47
123.39
122.95
121.82
120.60
115.85
111.79
110.22
109.90
77.32
77.00
76.68
73.82
65.04
62.77
62.45
62.14
61.82
55.78
44.19
44.01
43.68
11.41
NO2
CF3
OMe
NH
N
O
N
Bn
O
O
N
Bn
3ai
(100 MHz, CDCl3)
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

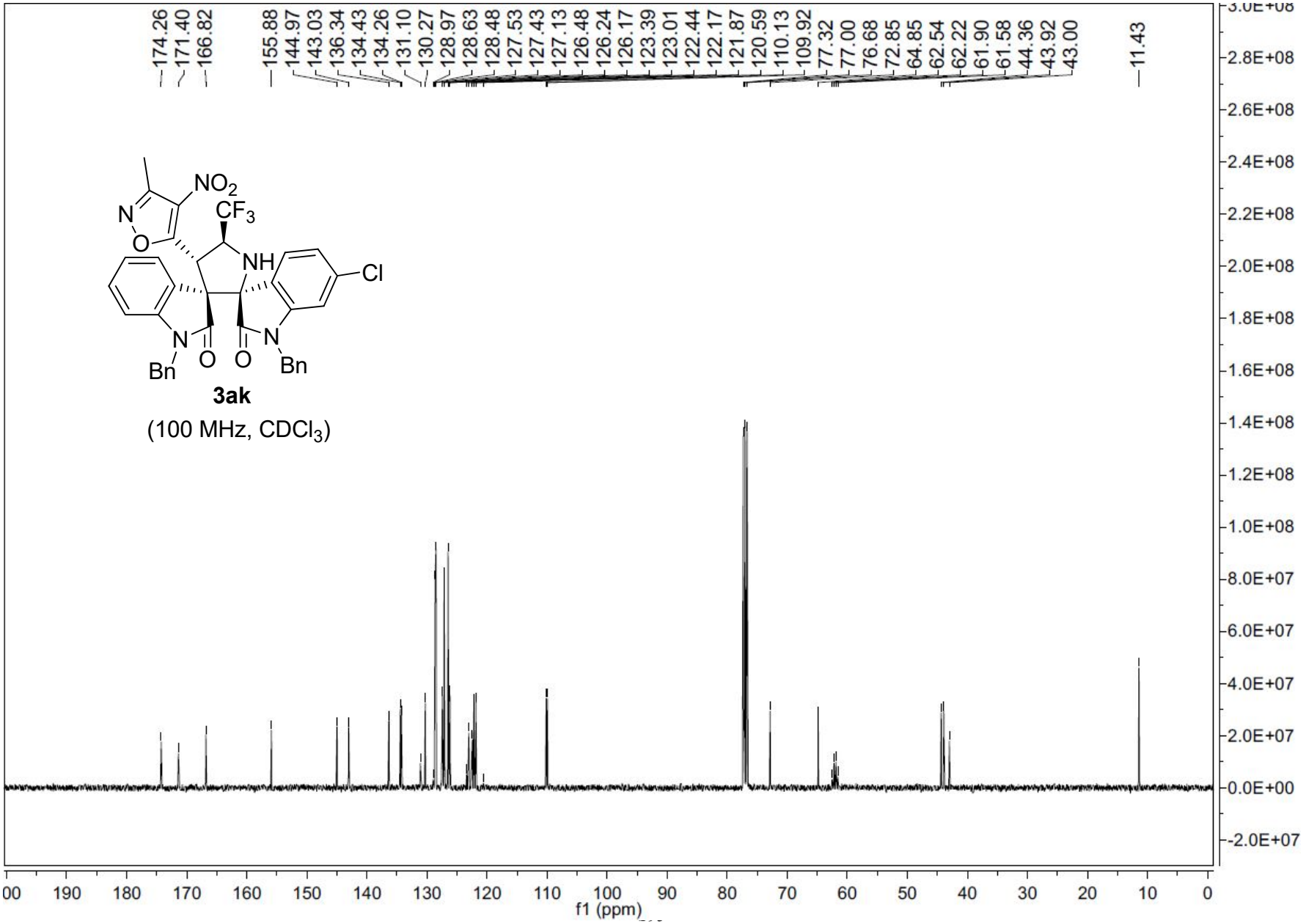

7.256
7.219
7.196
7.175
7.156
7.072
7.059
7.015
6.985
6.966
6.947
6.847
6.839
6.700
6.681
6.534
6.514
6.385
6.380
6.343
6.319
6.191
6.186
6.169
5.258
5.241
5.211
5.172
5.058
5.019
4.441
4.402
3.424
3.403
2.409
0.000
NO2
CF3
N
O
NH
F
N
O
O
N
Bn
Bn
3aj
(400 MHz, CDCl3)
2.07
9.33
1.04
2.02
1.02
1.04
1.00
1.01
2.02
1.01
2.00
1.00
3.00
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

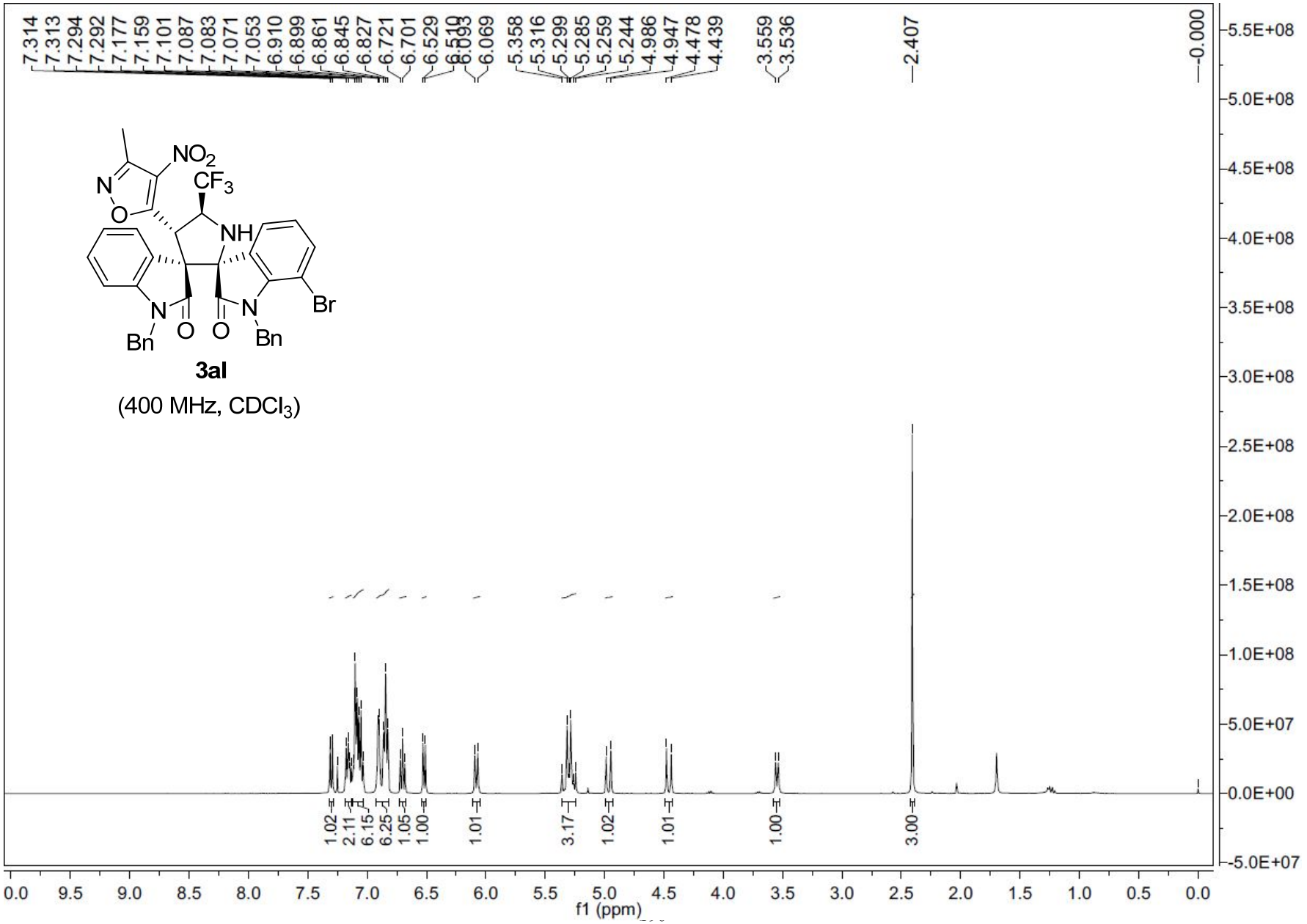

-72.31
-108.01
NO2
CF3
N
O
NH
F
N
O
O
N
Bn
Bn
3aj
(376 MHz, CDCl3)
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
f1 (ppm)

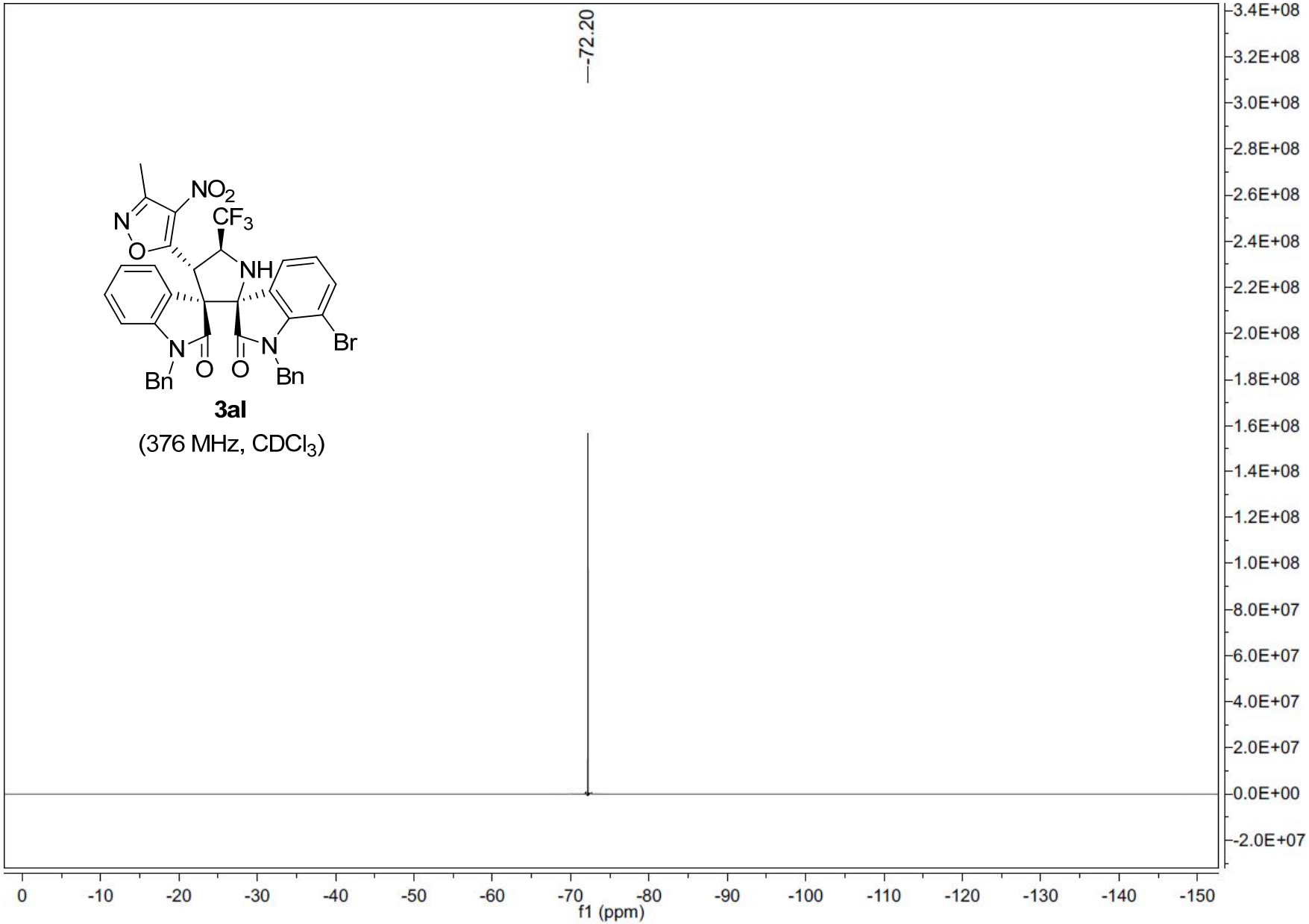

174.44
171.58
166.94
165.17
162.69
155.88
145.59
145.48
143.03
134.49
134.27
131.06
130.20
128.99
128.61
128.46
127.51
127.39
127.13
126.69
126.59
126.51
126.20
123.40
123.07
122.13
120.61
119.53
119.50
109.87
108.31
108.09
98.51
98.24
77.32
77.00
76.68
72.87
64.91
62.51
62.19
61.87
61.55
44.37
43.90
43.11
11.41
NO2
CF3
N
O
NH
F
N
O
O
N
Bn
Bn
3aj
(100 MHz, CDCl3)
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

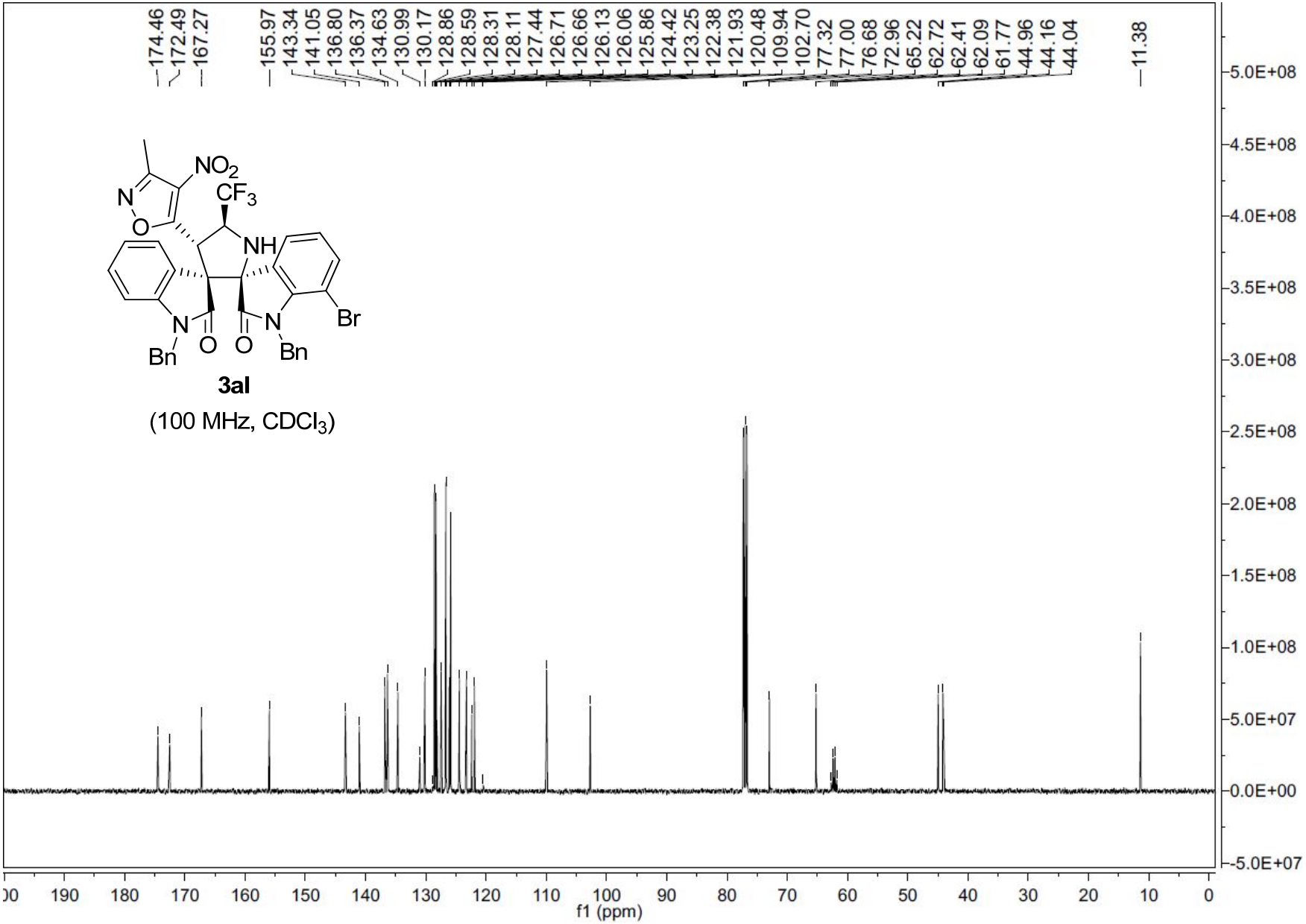

7.255
7.224
7.180
7.100
7.095
7.079
7.070
7.053
7.027
7.002
6.982
6.964
6.794
6.774
6.686
6.681
6.661
6.529
6.510
6.444
6.439
6.350
5.270
5.252
5.228
5.206
5.167
5.146
5.065
5.025
4.447
4.426
4.407
4.386
3.384
3.364
2.411
0.000
NO2
CF3
N
O
NH
Cl
N
O
O
N
Bn
Bn
3ak
(400 MHz, CDCl3)
2.02
9.12
1.03
3.02
1.01
1.01
1.00
2.05
1.00
2.00
1.00
3.00
f1 (ppm)

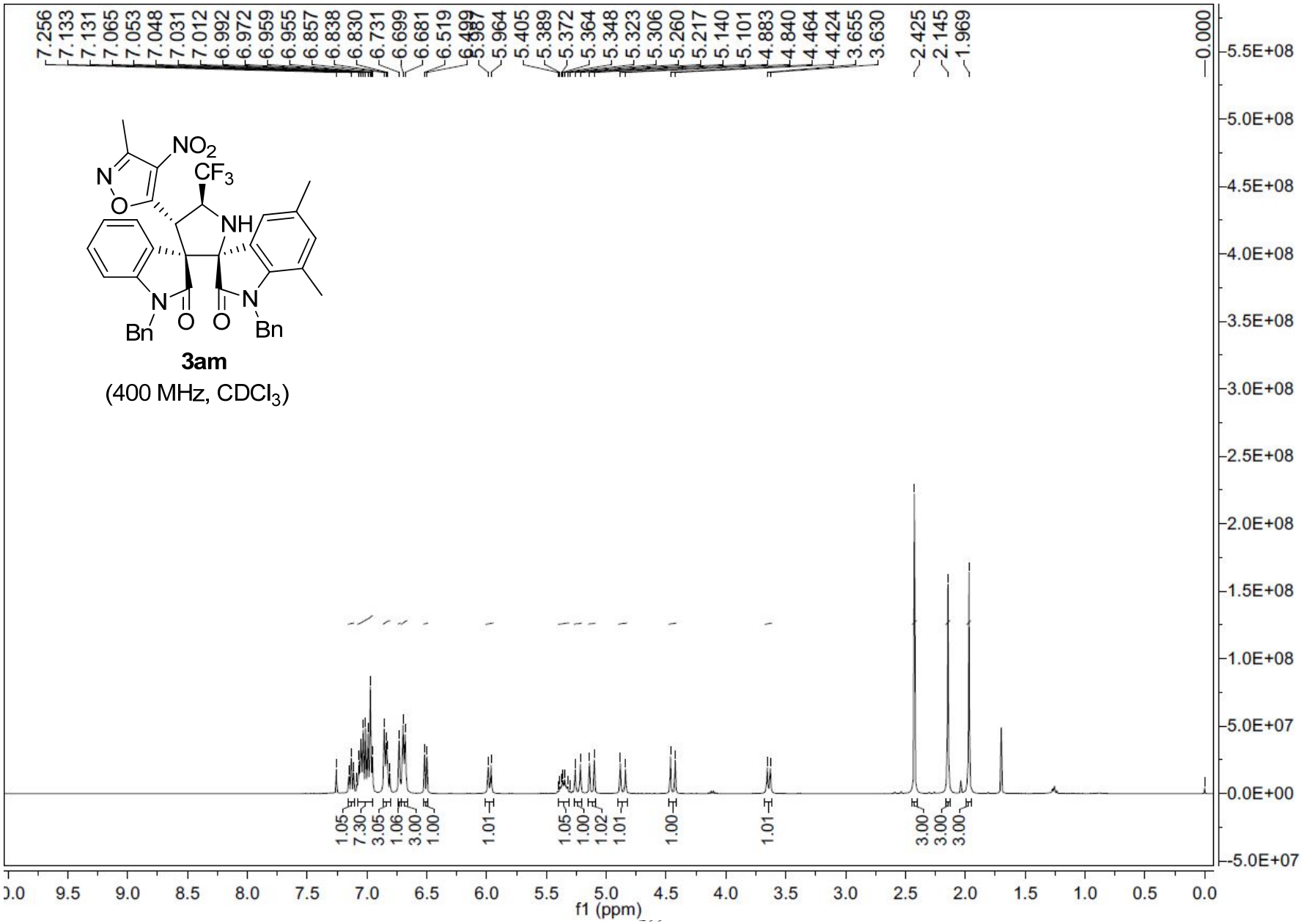

-72.29
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)
NO2
CF3
N
O
NH
Cl
N
O
O
N
Bn
Bn
3ak
(376 MHz, CDCl3)

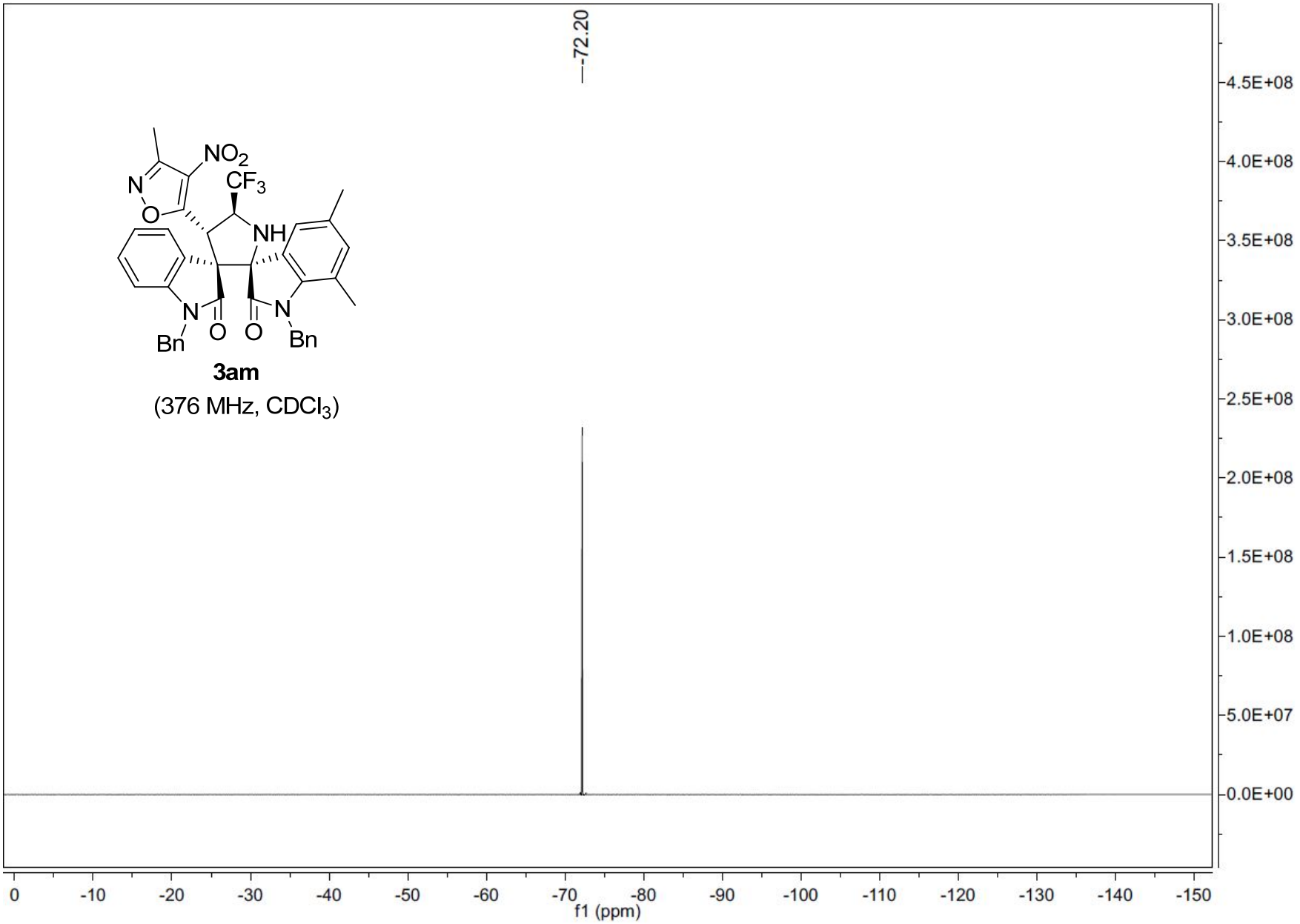

174.26
171.40
166.82
155.88
144.97
143.03
136.34
134.43
134.26
131.10
130.27
128.97
128.63
128.48
127.53
127.43
127.13
126.48
126.24
126.17
123.39
123.01
122.44
122.17
121.87
120.59
110.13
109.92
77.32
77.00
76.68
72.85
64.85
62.54
62.22
61.90
61.58
44.36
43.92
43.00
11.43
NO2
CF3
N
O
NH
Cl
N
Bn
O
O
N
Bn
3ak
(100 MHz, CDCl3)
f1 (ppm)


7.314
7.313
7.294
7.292
7.177
7.159
7.101
7.087
7.083
7.071
7.053
6.910
6.899
6.861
6.845
6.827
6.721
6.701
6.529
6.510
6.093
6.069
5.358
5.316
5.299
5.285
5.259
5.244
4.986
4.947
4.478
4.439
3.559
3.536
2.407
0.000
NO2
CF3
N
O
NH
N
O
O
N
Br
Bn
Bn
3aI
(400 MHz, CDCl3)
1.02
2.11
6.15
6.25
1.05
1.00
1.01
3.17
1.02
1.01
1.00
3.00
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-72.20
NO2
CF3
N
O
NH
N
Bn
O
O
N
Bn
Br
3aI
(376 MHz, CDCl3)
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

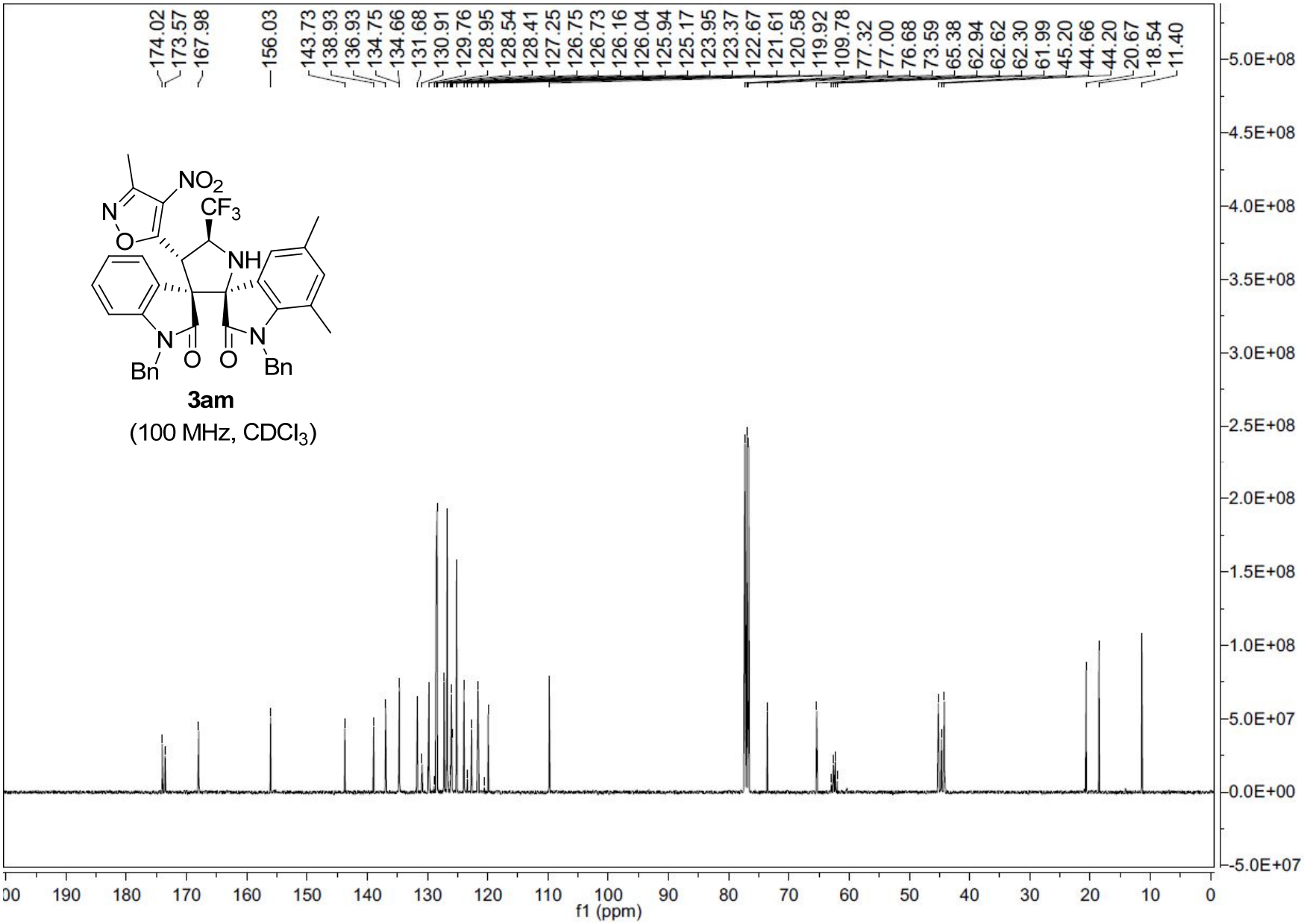

174.46
172.49
167.27
155.97
143.34
141.05
136.80
136.37
134.63
130.99
130.17
128.86
128.59
128.31
128.11
127.44
126.71
126.66
126.13
126.06
125.86
124.42
123.25
122.38
121.93
120.48
109.94
102.70
77.32
77.00
76.68
72.96
65.22
62.72
62.41
62.09
61.77
44.96
44.16
44.04
11.38
NO2
CF3
N
O
NH
N
O
O
N
Br
Bn
Bn
3al
(100 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

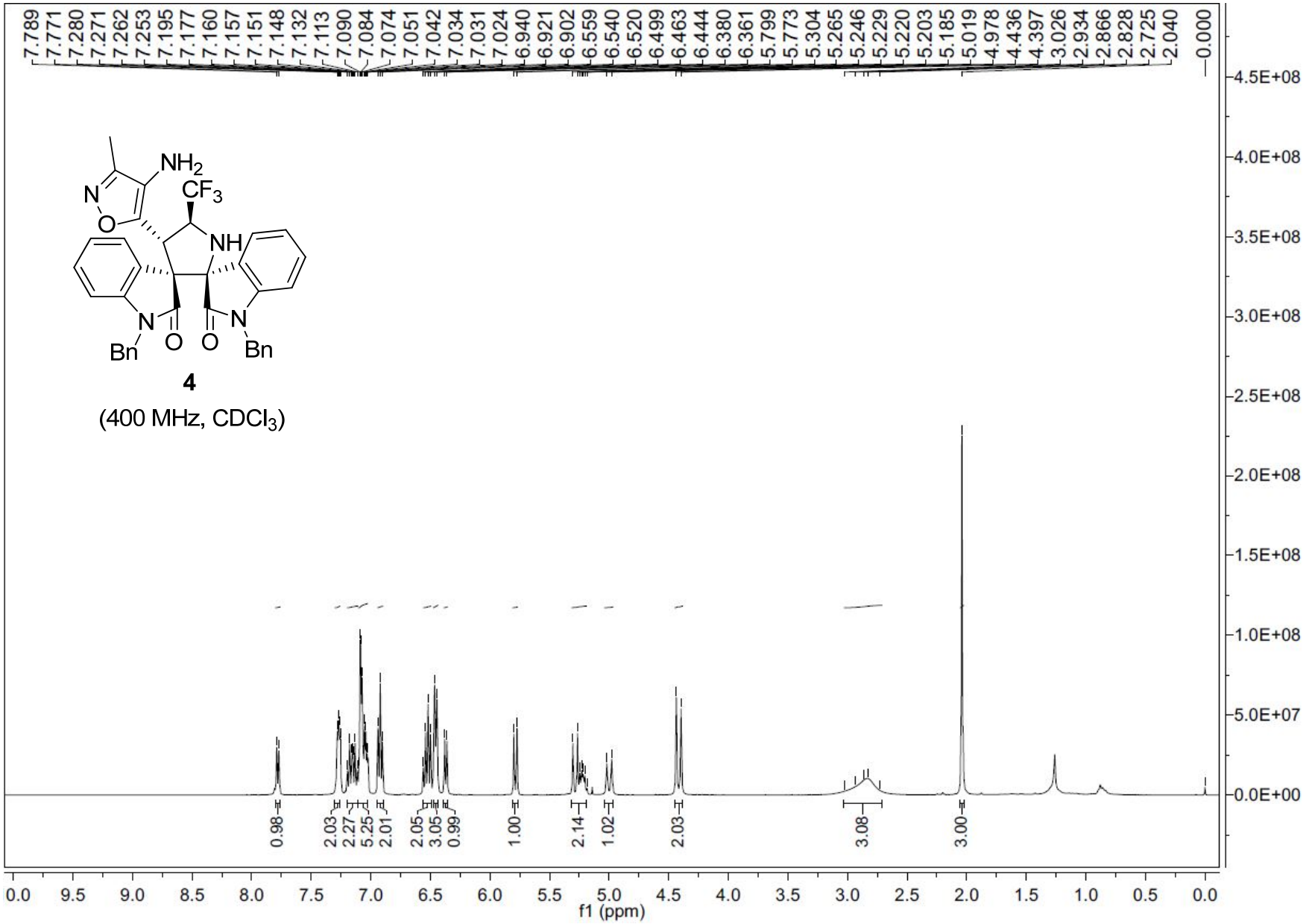

7.256
7.133
7.131
7.065
7.053
7.048
7.031
7.012
6.992
6.972
6.959
6.955
6.857
6.838
6.830
6.731
6.699
6.681
6.519
6.499
5.964
5.405
5.389
5.372
5.364
5.348
5.323
5.306
5.260
5.217
5.140
5.101
4.883
4.840
4.464
4.424
3.655
3.630
2.425
2.145
1.969
0.000
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3am
(400 MHz, CDCl3)
1.05
7.30
3.05
1.06
3.00
1.00
1.01
1.05
1.00
1.02
1.01
1.00
1.01
3.00
3.00
3.00
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
f1 (ppm)

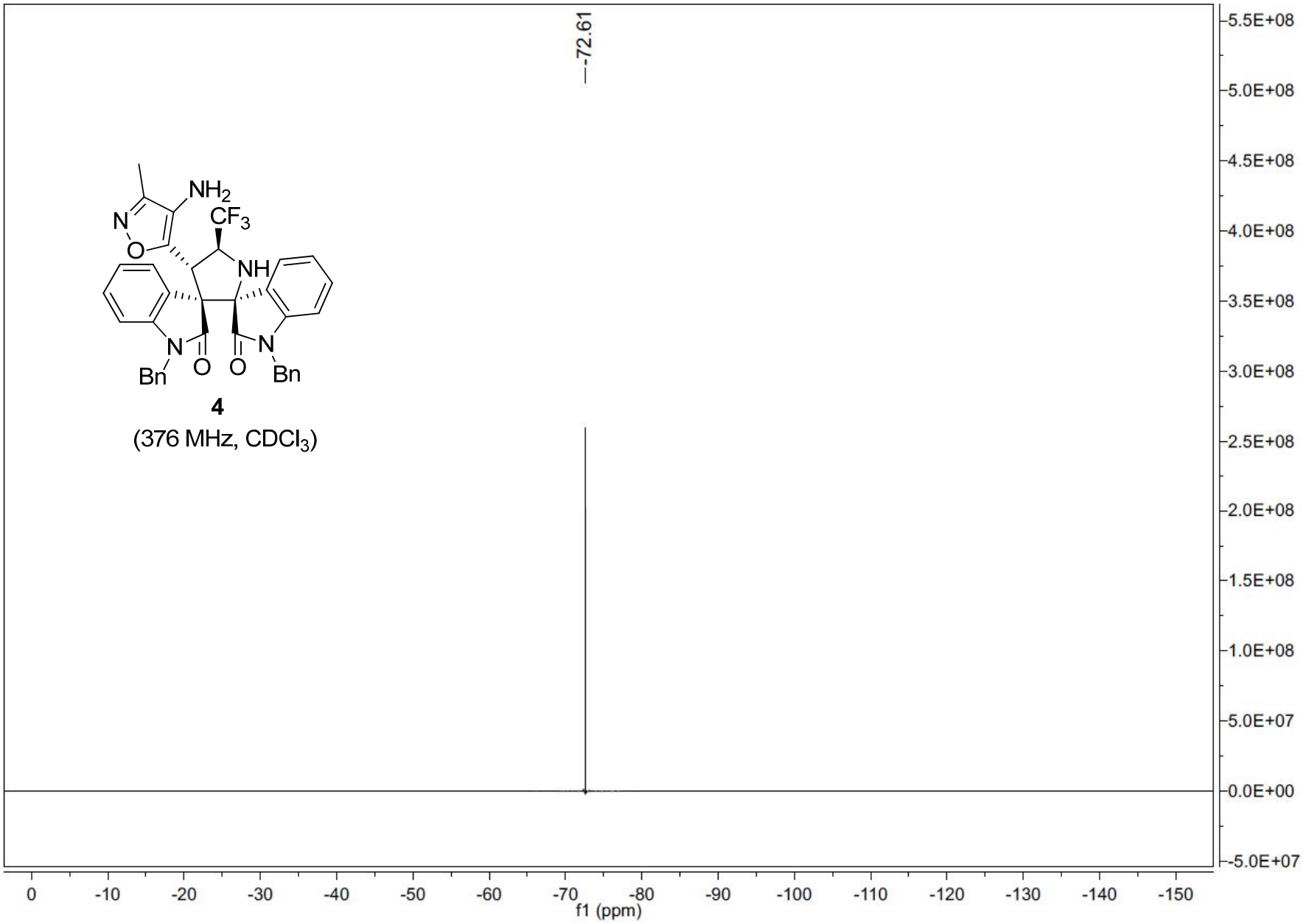


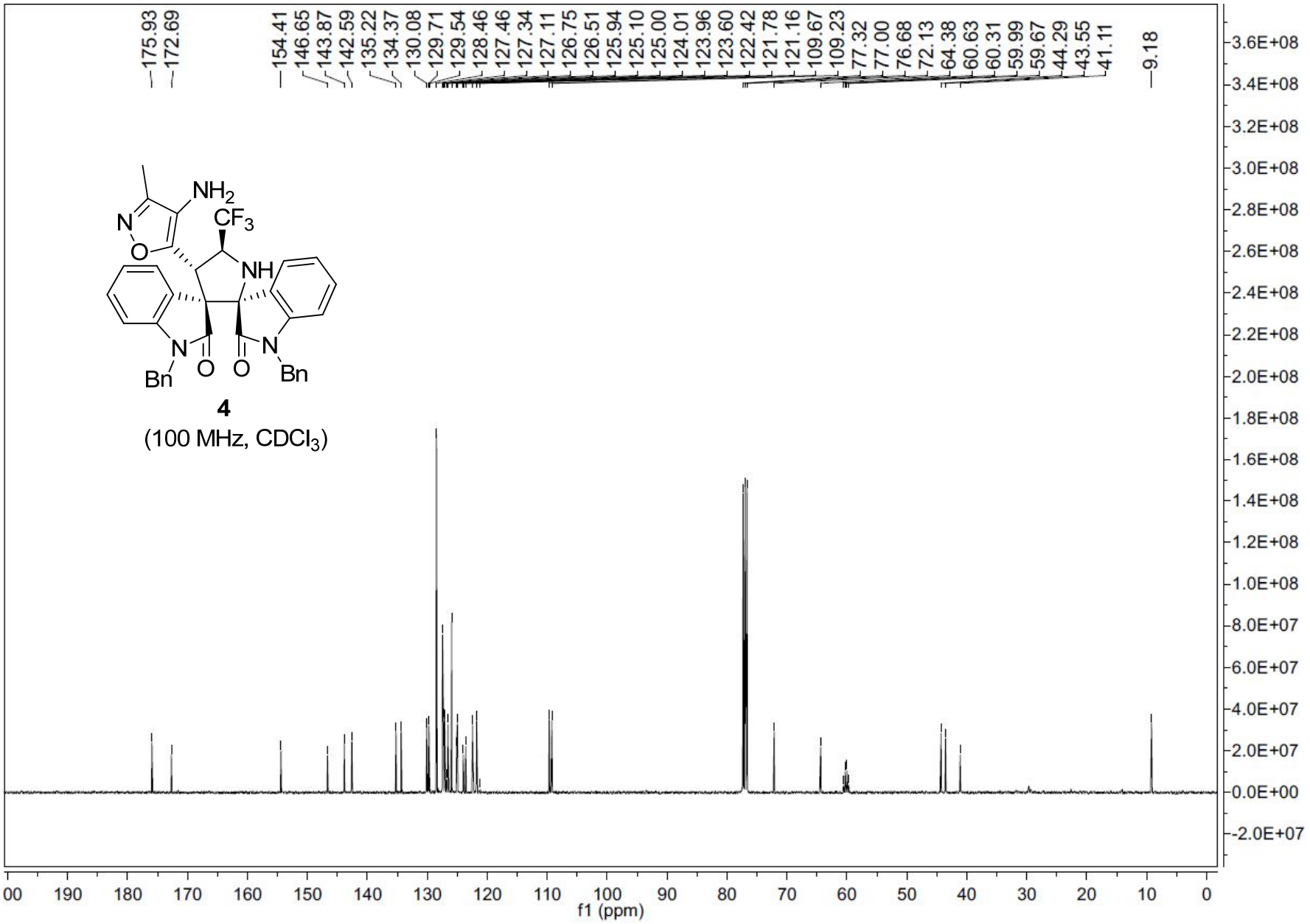
3am

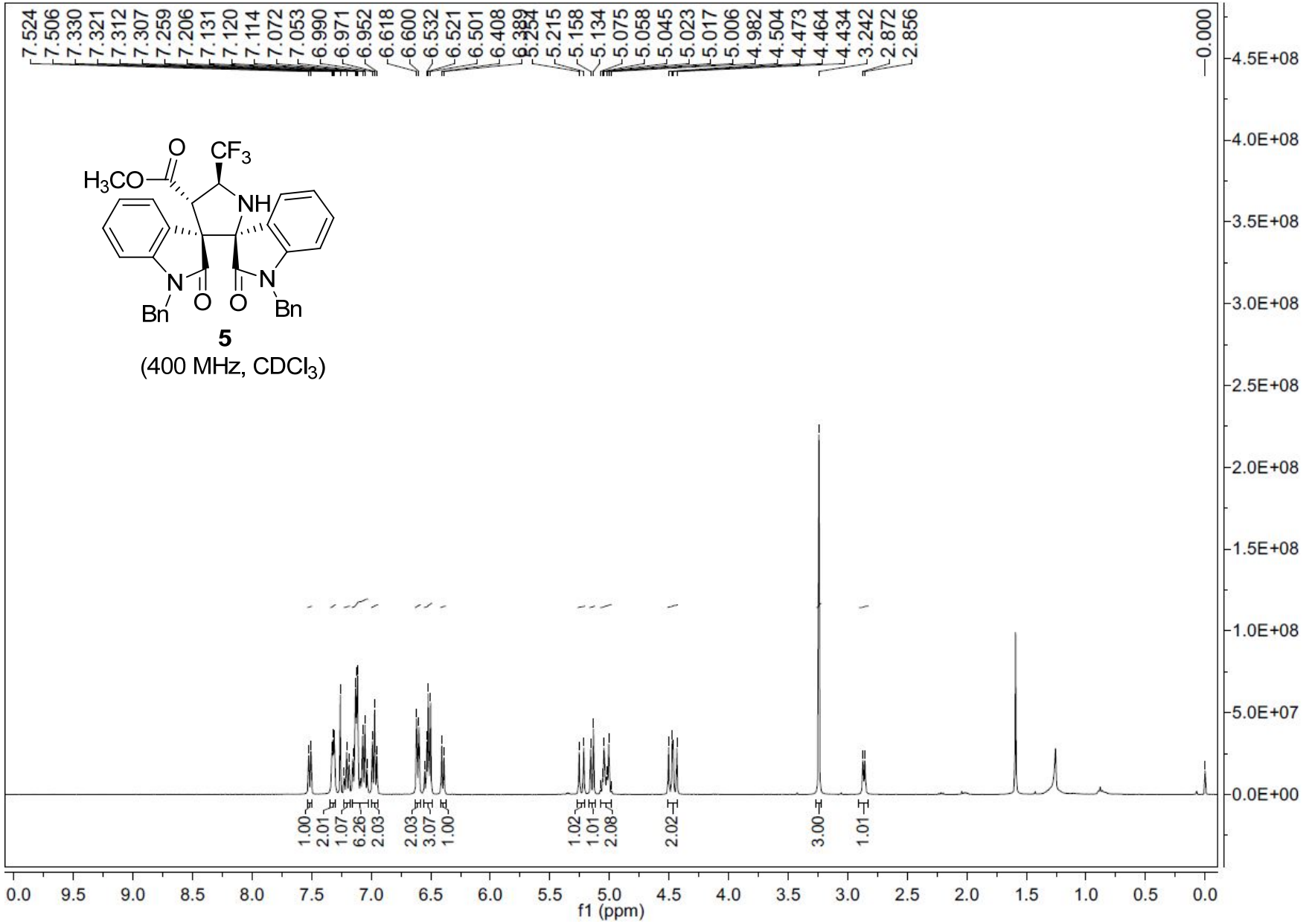
(376 MHz, $CDCl_3$)

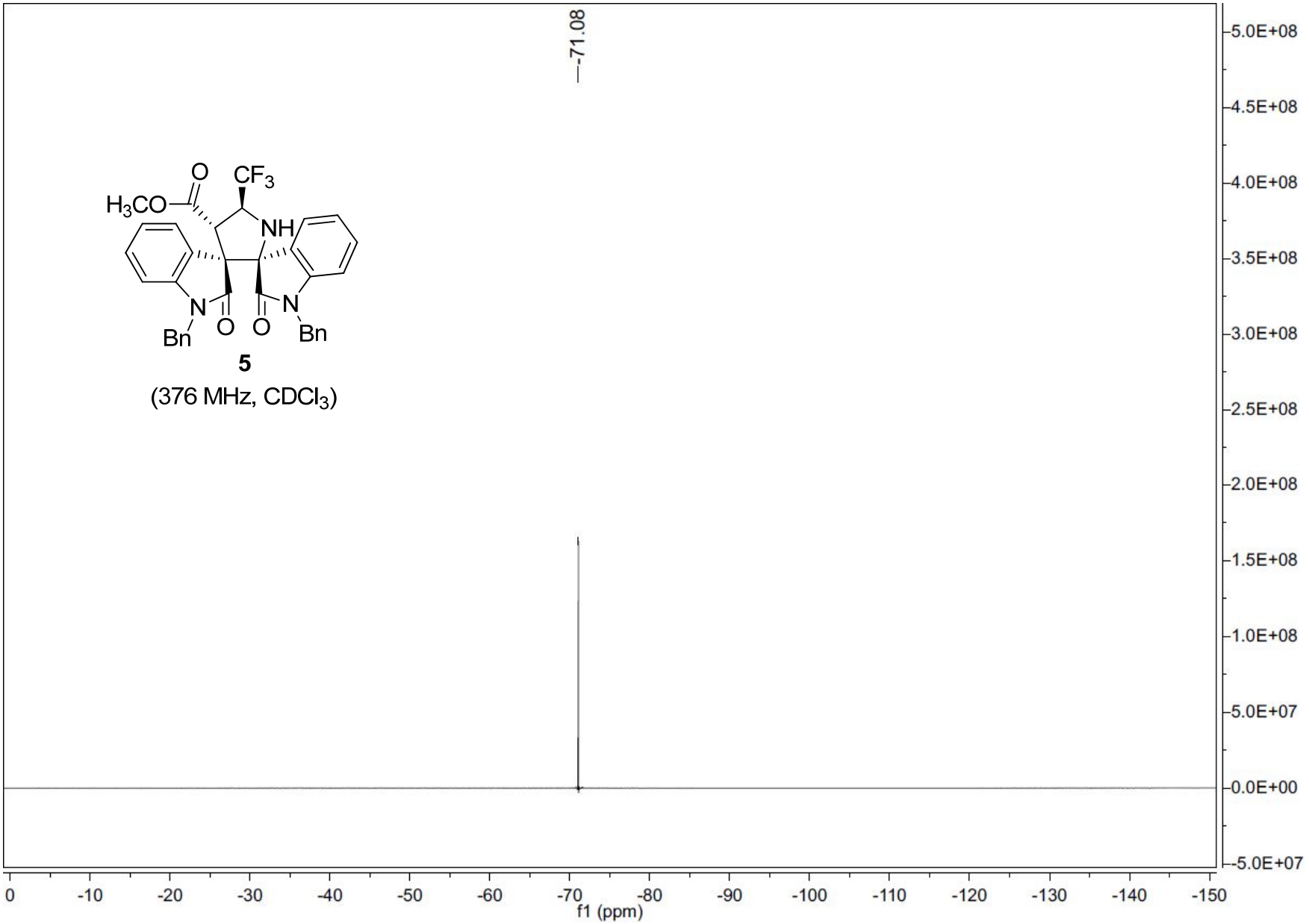

174.02
173.57
167.98
156.03
143.73
138.93
136.93
134.75
134.66
131.68
130.91
129.76
128.95
128.54
128.41
127.25
126.75
126.73
126.16
126.04
125.94
125.17
123.95
123.37
122.67
121.61
120.58
119.92
109.78
77.32
77.00
76.68
73.59
65.38
62.94
62.62
62.30
61.99
45.20
44.66
44.20
20.67
18.54
11.40
NO2
CF3
N
O
NH
N
O
O
N
Bn
Bn
3am
(100 MHz, CDCl3)
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.789
7.771
7.280
7.271
7.262
7.253
7.195
7.177
7.160
7.157
7.151
7.148
7.132
7.113
7.090
7.084
7.074
7.051
7.042
7.034
7.031
7.024
6.940
6.921
6.902
6.559
6.540
6.520
6.499
6.463
6.444
6.380
6.361
5.799
5.773
5.304
5.265
5.246
5.229
5.220
5.203
5.185
5.019
4.978
4.436
4.397
3.026
2.934
2.866
2.828
2.725
2.040
0.000
NH2
CF3
N
O
NH
N
O
O
N
Bn
Bn
4
(400 MHz, CDCl3)
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
0.98
2.03
2.27
5.25
2.01
2.05
3.05
0.99
1.00
2.14
1.02
2.03
3.08
3.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


-72.61
NH2
CF3
N
O
NH
N
Bn
O
O
N
Bn
4
(376 MHz, CDCl3)
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
f1 (ppm)

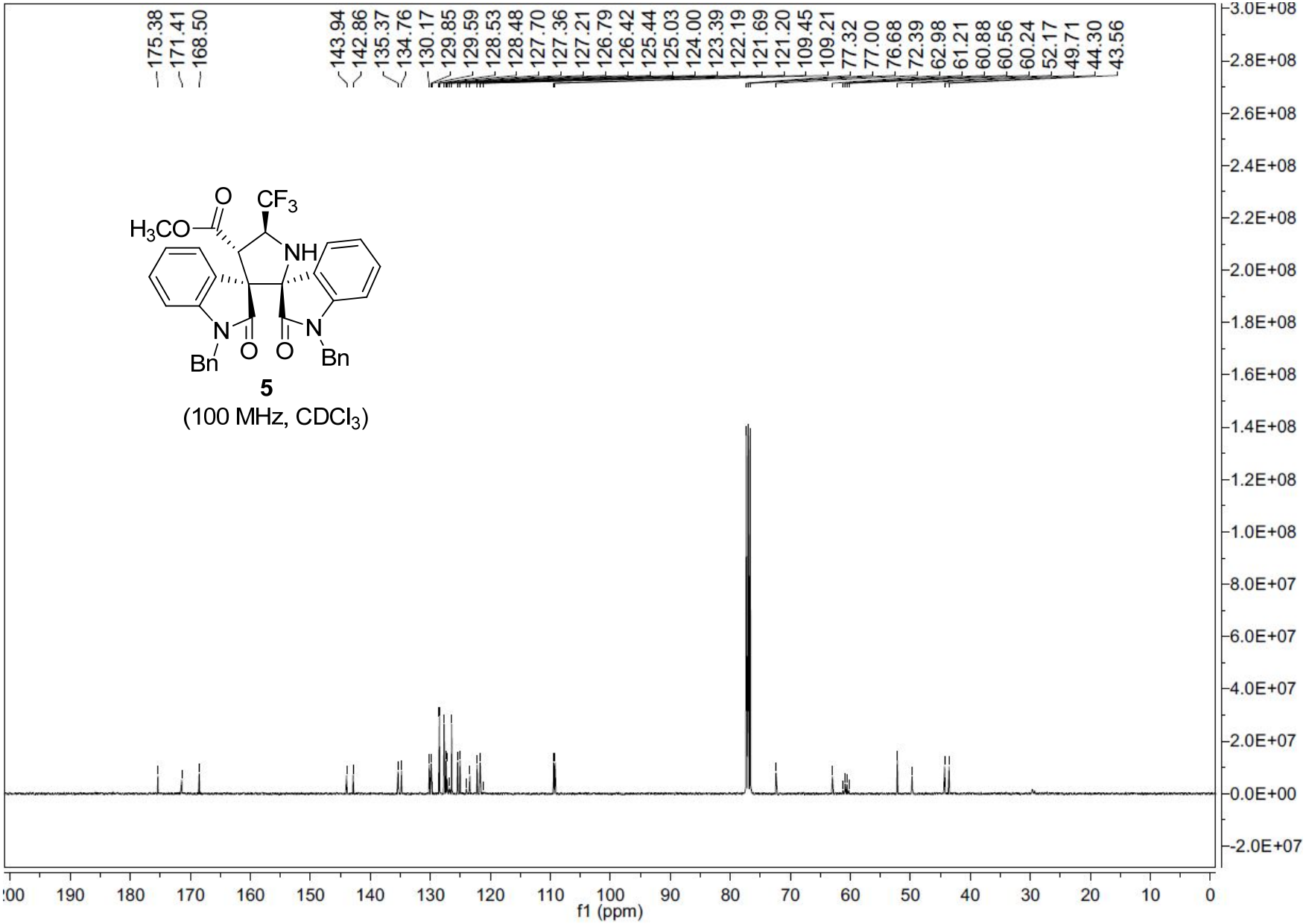

175.93
172.69
154.41
146.65
143.87
142.59
135.22
134.37
130.08
129.71
129.54
128.46
127.46
127.34
127.11
126.75
126.51
125.94
125.10
125.00
124.01
123.96
123.60
122.42
121.78
121.16
109.67
109.23
77.32
77.00
76.68
72.13
64.38
60.63
60.31
59.99
59.67
44.29
43.55
41.11
9.18
NH2
CF3
N
O
NH
N
Bn
O
O
N
Bn
4
(100 MHz, CDCl3)
3.6E+08
3.4E+08
3.2E+08
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.524
7.506
7.330
7.321
7.312
7.307
7.259
7.206
7.131
7.120
7.114
7.072
7.053
6.990
6.971
6.952
6.618
6.600
6.532
6.521
6.501
6.408
5.254
5.215
5.158
5.134
5.075
5.058
5.045
5.023
5.017
5.006
4.982
4.504
4.473
4.464
4.434
3.242
2.872
2.856
0.000
O
CF3
H3CO
NH
N
O
O
N
Bn
Bn
5
(400 MHz, CDCl3)
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
1.00
2.01
1.07
6.26
2.03
2.03
3.07
1.00
1.02
1.01
2.08
2.02
3.00
1.01
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

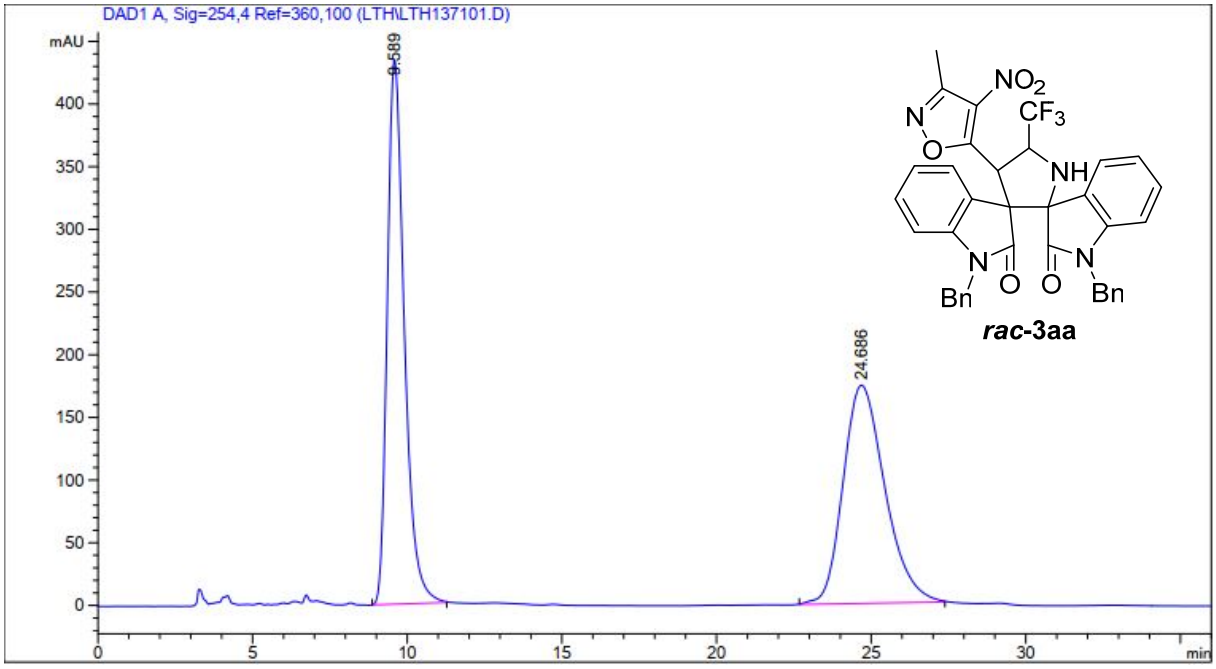


5

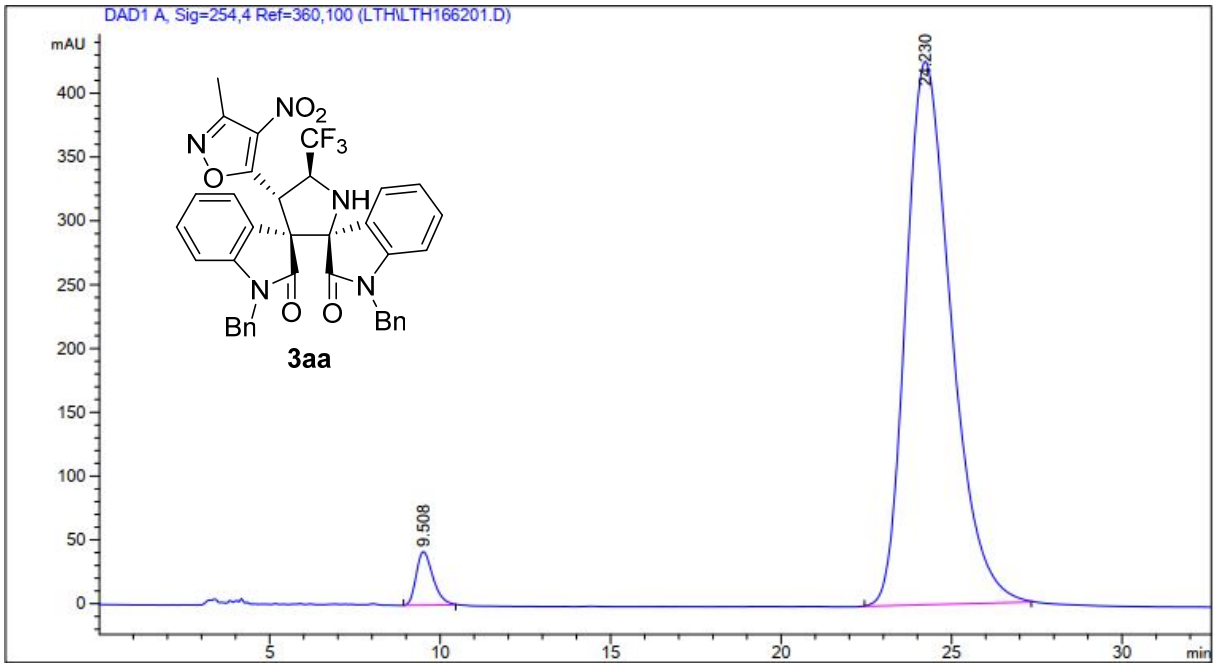
(376 MHz, $CDCl_3$)


175.38
171.41
168.50
143.94
142.86
135.37
134.76
130.17
129.85
129.59
128.53
128.48
127.70
127.36
127.21
126.79
126.42
125.44
125.03
124.00
123.39
122.19
121.69
121.20
109.45
109.21
77.32
77.00
76.68
72.39
62.98
61.21
60.88
60.56
60.24
52.17
49.71
44.30
43.56
O
CF3
H3CO
NH
N
O
O
N
Bn
Bn
5
(100 MHz, CDCl3)
3.0E+08
2.8E+08
2.6E+08
2.4E+08
2.2E+08
2.0E+08
1.8E+08
1.6E+08
1.4E+08
1.2E+08
1.0E+08
8.0E+07
6.0E+07
4.0E+07
2.0E+07
0.0E+00
-2.0E+07
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

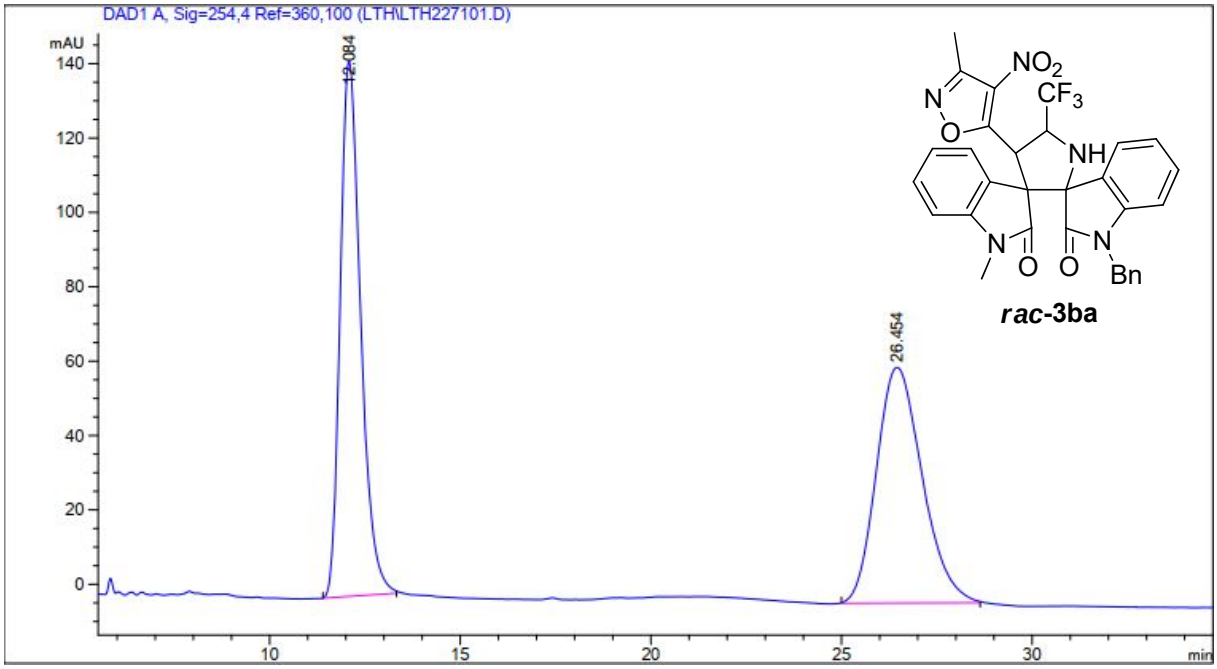
9. Copies of HPLC chromatograms



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.589	BB	0.5843	1.66173e4	434.36752	50.3552
2	24.686	BB	1.4180	1.63828e4	174.07886	49.6448

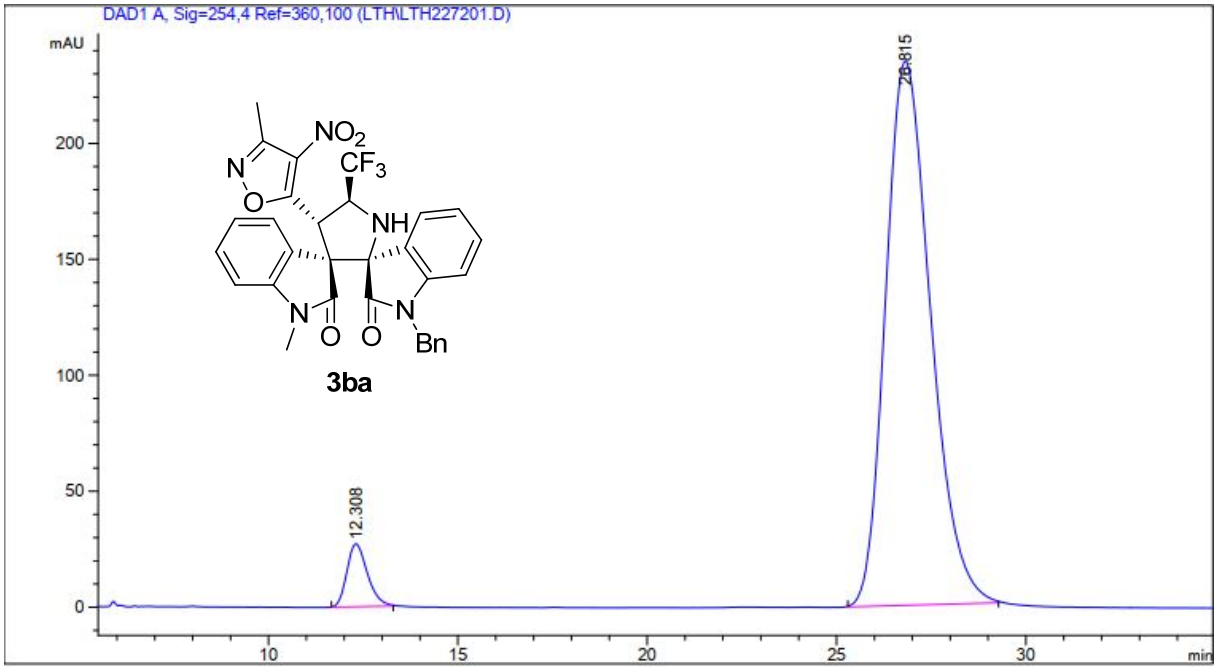


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.508	BB	0.5166	1433.89478	41.97222	3.5157
2	24.230	BB	1.3945	3.93513e4	425.66849	96.4843



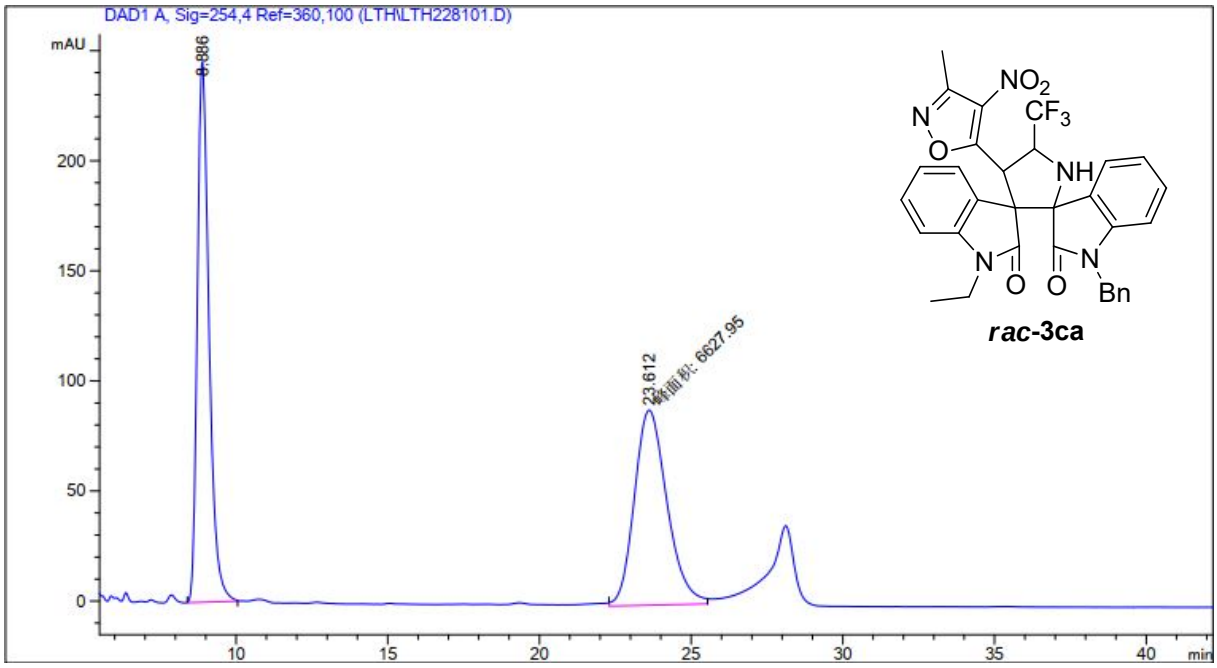
***rac*-3ba**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.084	BB	0.5733	5347.25928	143.96870	50.2972
2	26.454	BB	1.1891	5284.06641	63.35369	49.7028

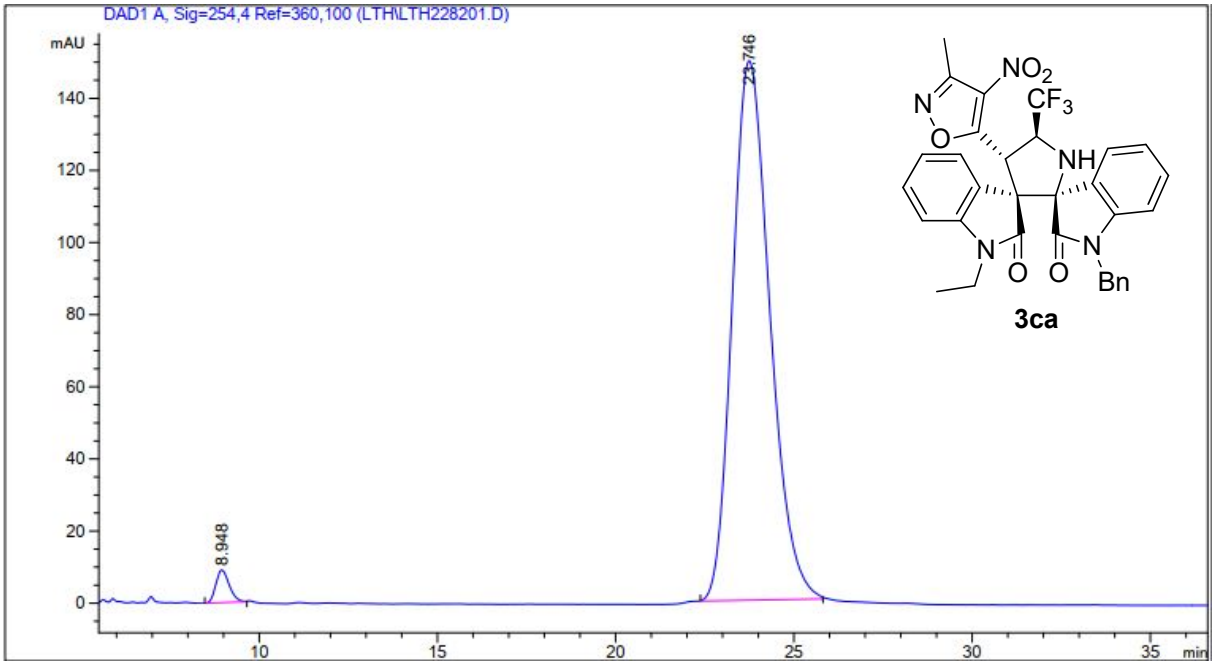


3ba

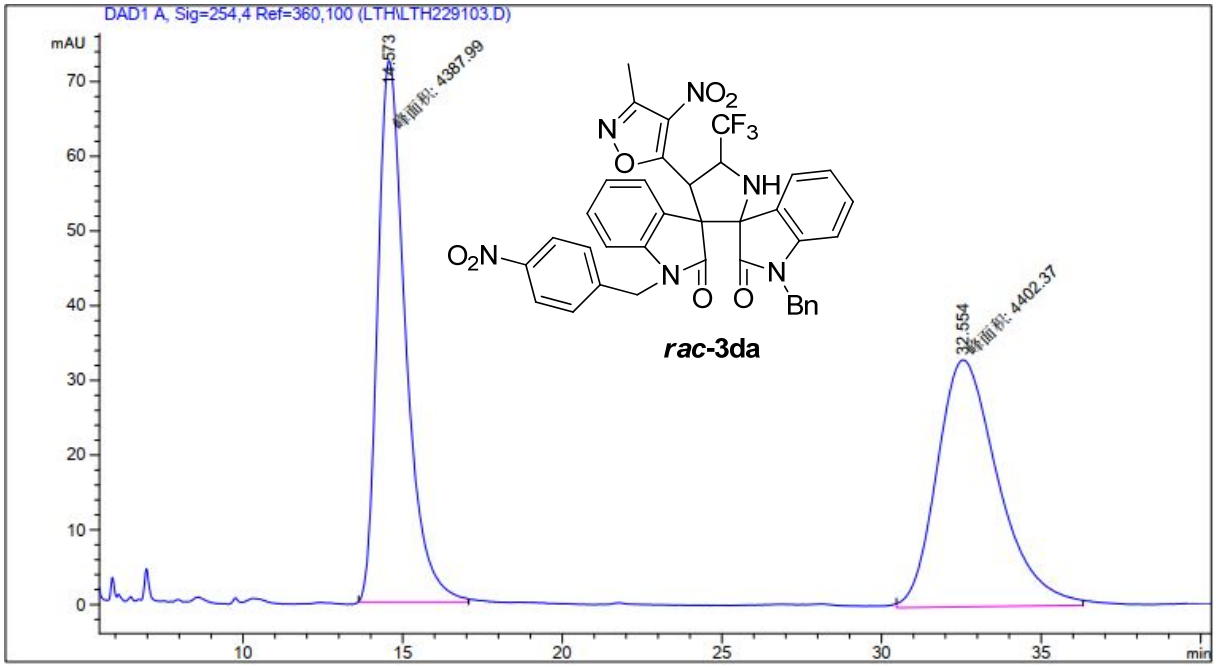
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.308	BB	0.5654	1020.02991	27.08209	4.9815
2	26.815	BB	1.2491	1.94563e4	234.72018	95.0185



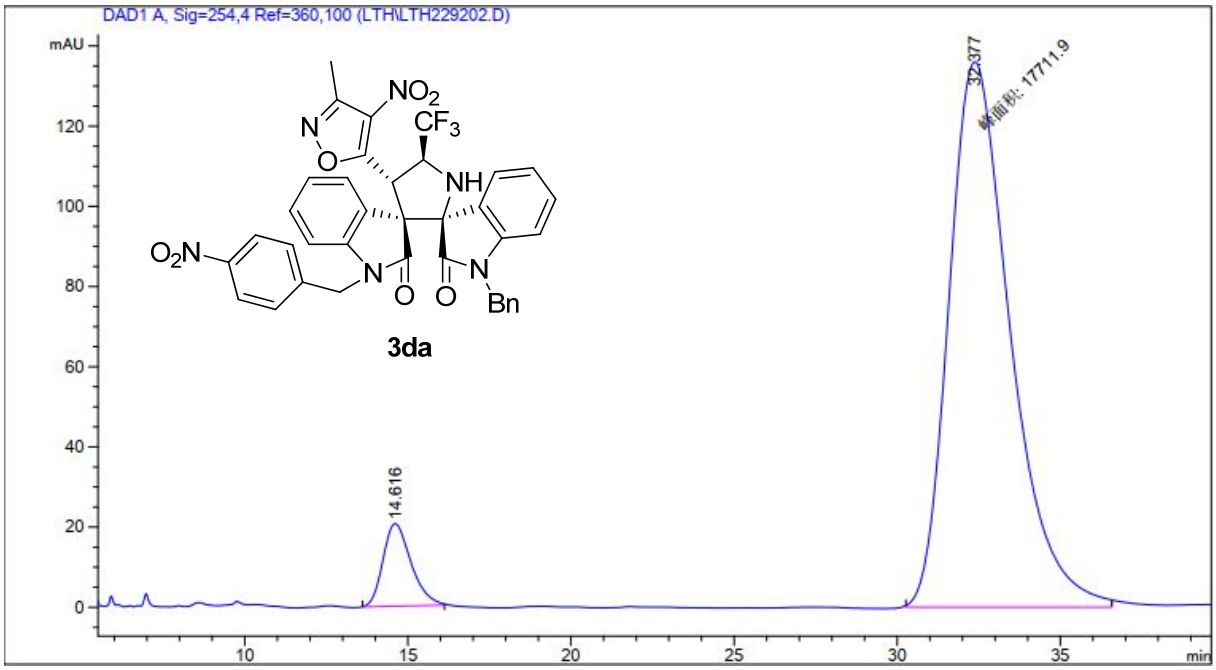
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.886	BB	0.4109	6581.51563	245.42955	49.8242
2	23.612	MM	1.2465	6627.94971	88.61771	50.1758



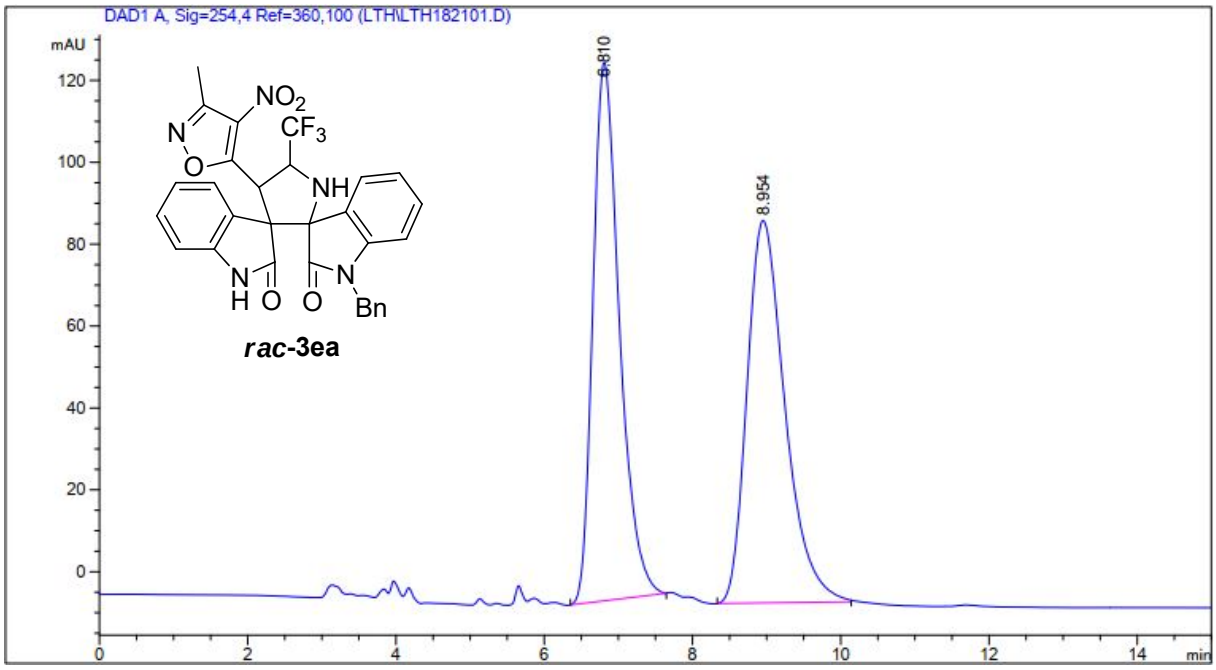
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.948	BB	0.3916	234.55772	9.01413	2.1038
2	23.746	BB	1.1174	1.09148e4	149.57164	97.8962



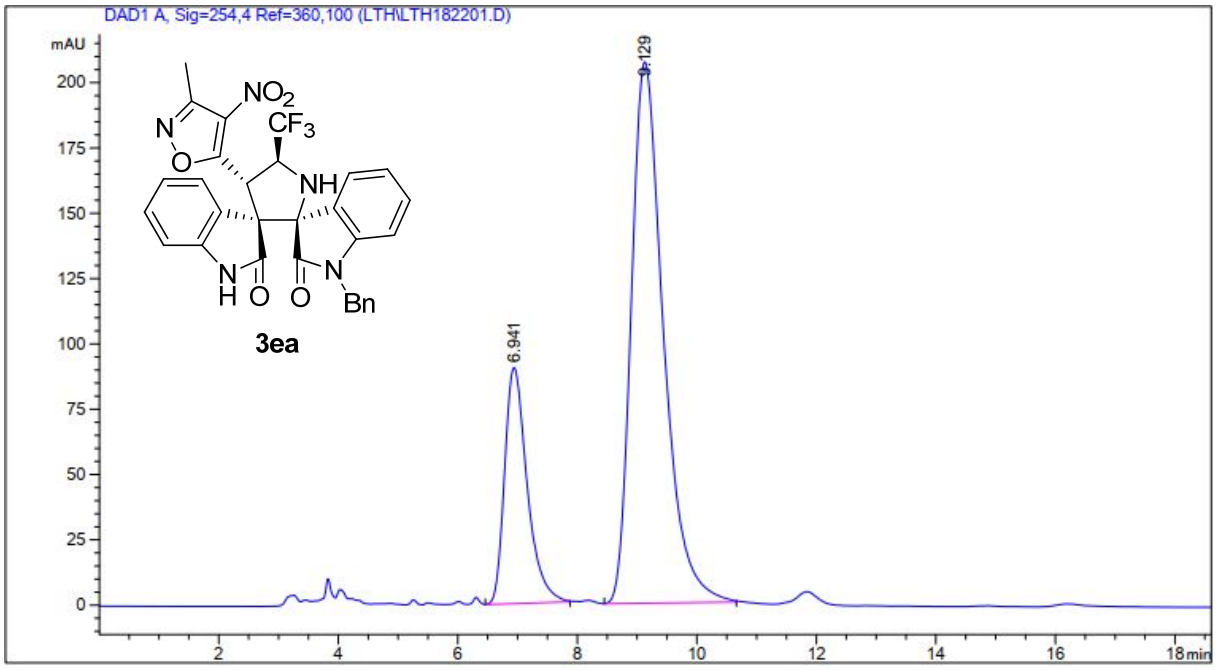
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.573	MM	1.0099	4387.99365	72.41456	49.9182
2	32.554	MM	2.2206	4402.37354	33.04235	50.0818



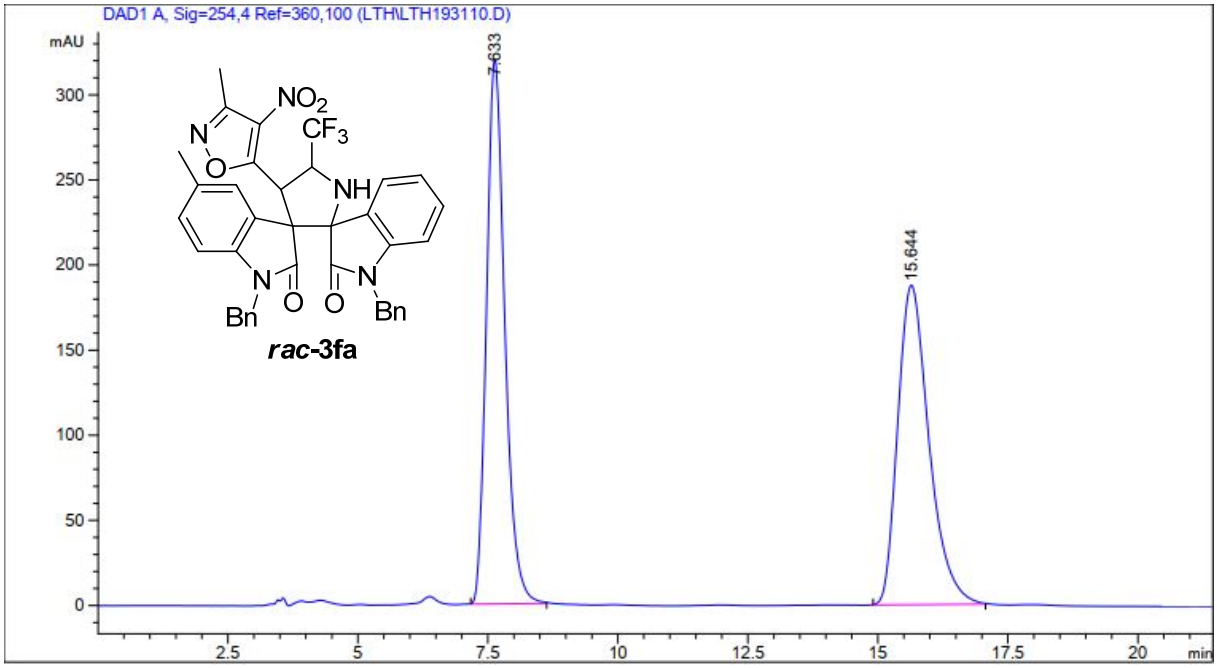
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.616	BB	0.7855	1230.20276	20.57676	6.4945
2	32.377	MM	2.1713	1.77119e4	135.95334	93.5055



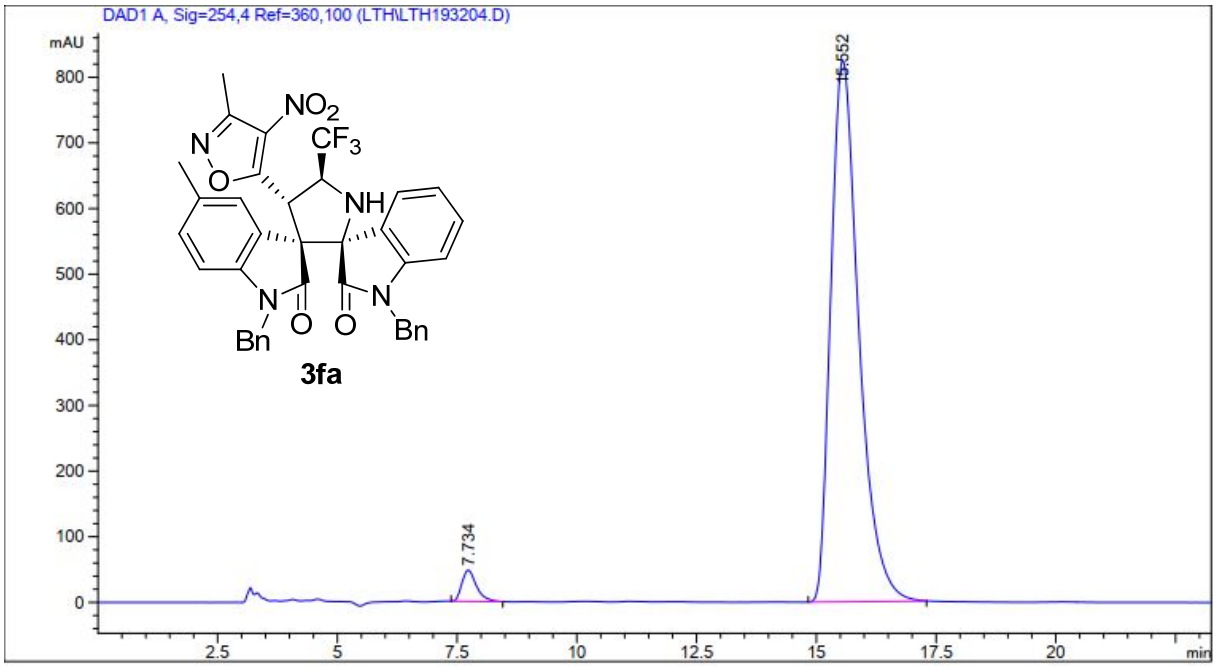
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.810	BB	0.3800	3268.35352	131.48869	49.6104
2	8.954	BB	0.5405	3319.68701	93.43784	50.3896



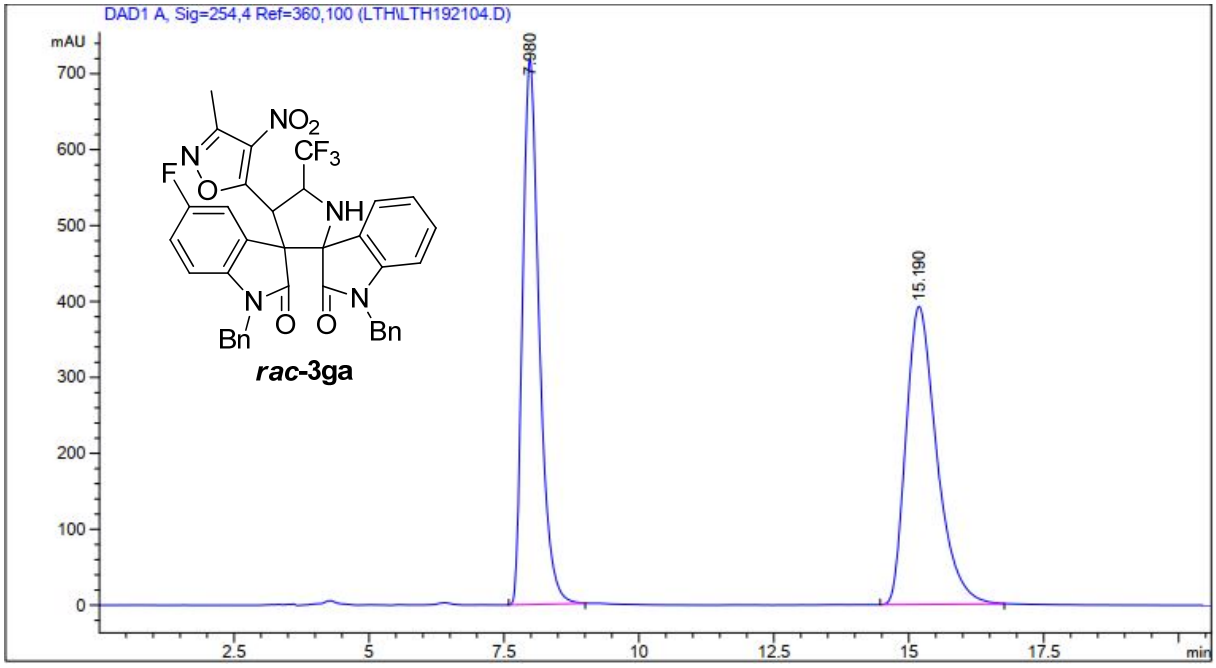
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.941	VB	0.4019	2368.17383	90.32169	23.4862
2	9.129	VB	0.5664	7715.07373	207.19849	76.5138



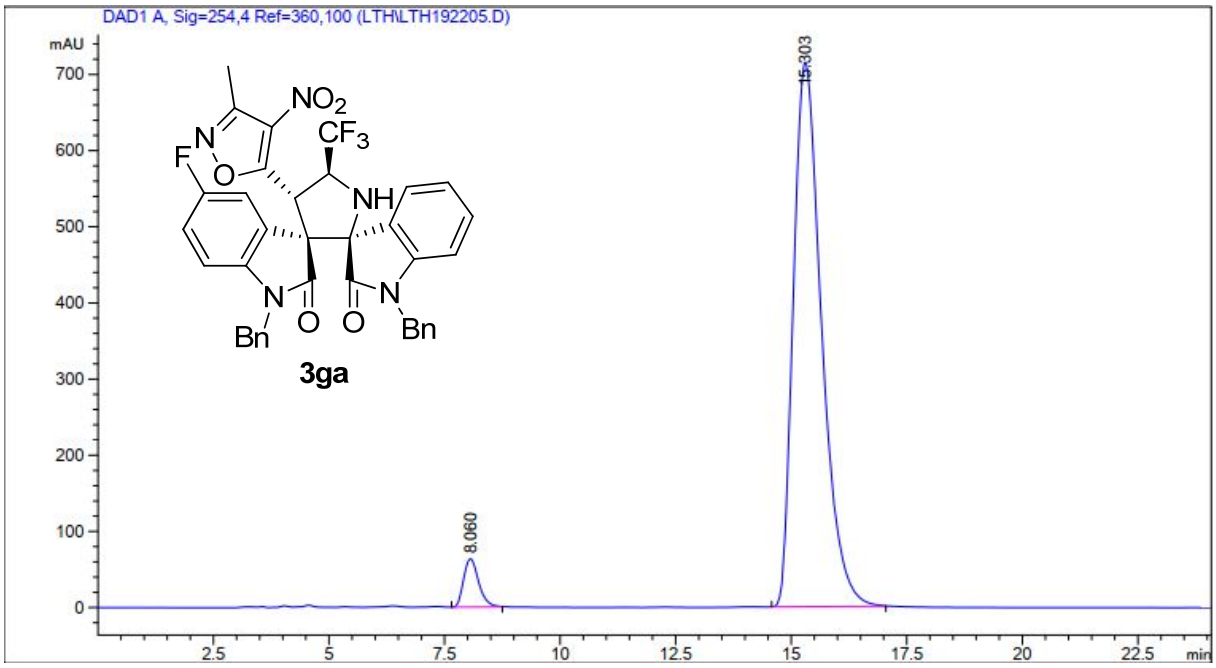
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.633	BB	0.3712	7815.68652	319.69849	49.9432
2	15.644	BB	0.6408	7833.46582	187.72234	50.0568



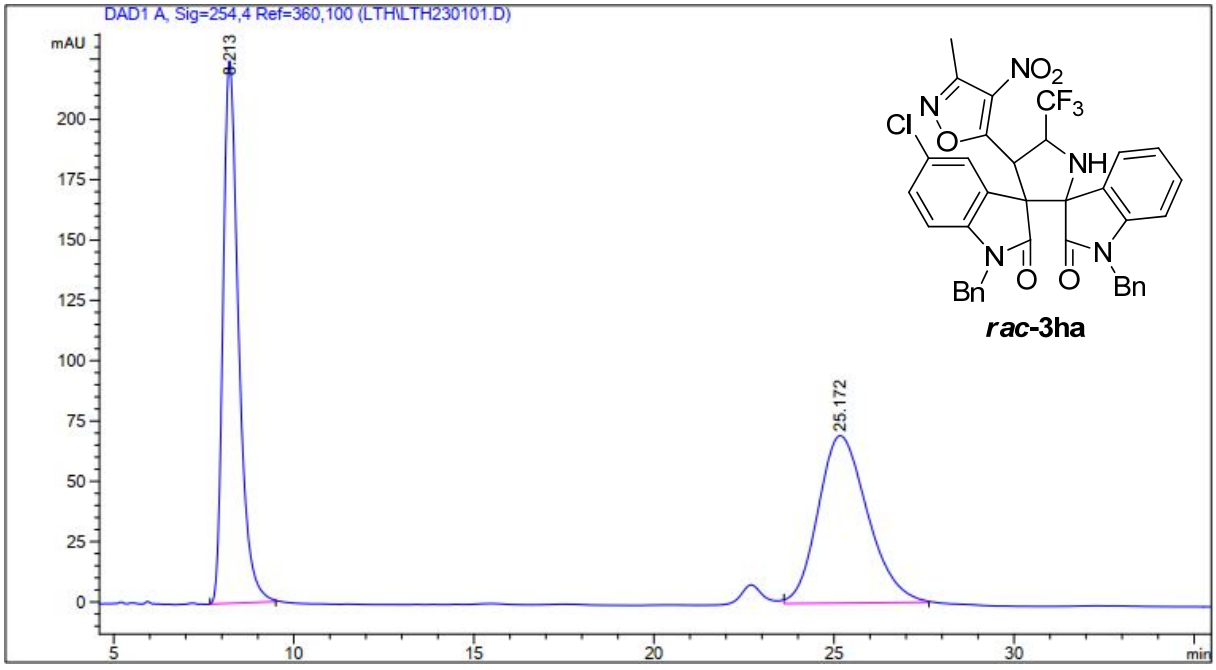
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.734	BB	0.3242	1007.16479	47.73445	2.9201
2	15.552	BB	0.6277	3.34832e4	824.64398	97.0799



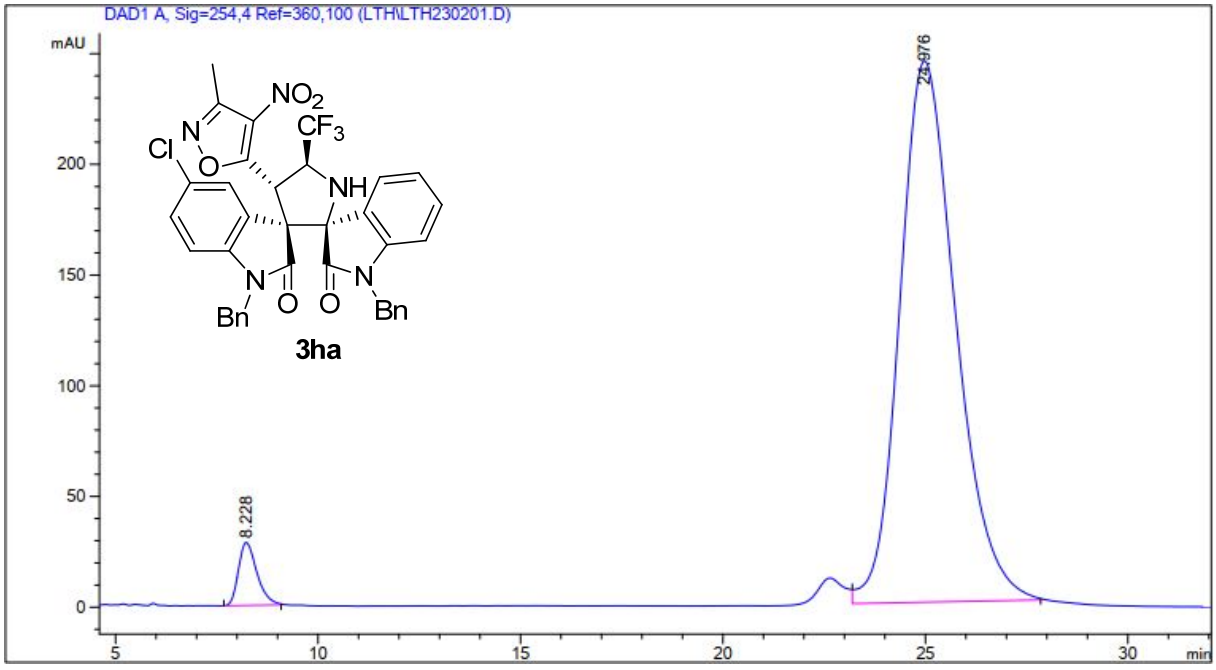
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.980	BB	0.3318	1.53725e4	717.85193	49.7356
2	15.190	BB	0.6098	1.55359e4	392.53250	50.2644



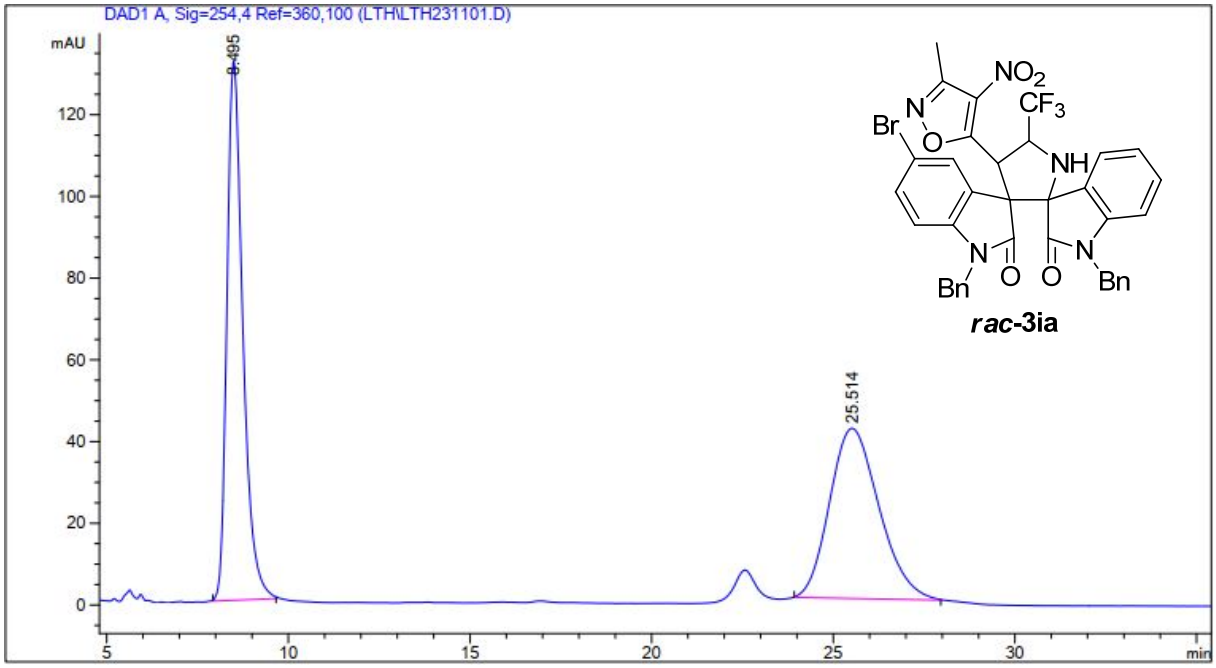
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.060	BB	0.3537	1432.09839	63.36412	4.5230
2	15.303	BB	0.6572	3.02306e4	715.09332	95.4770



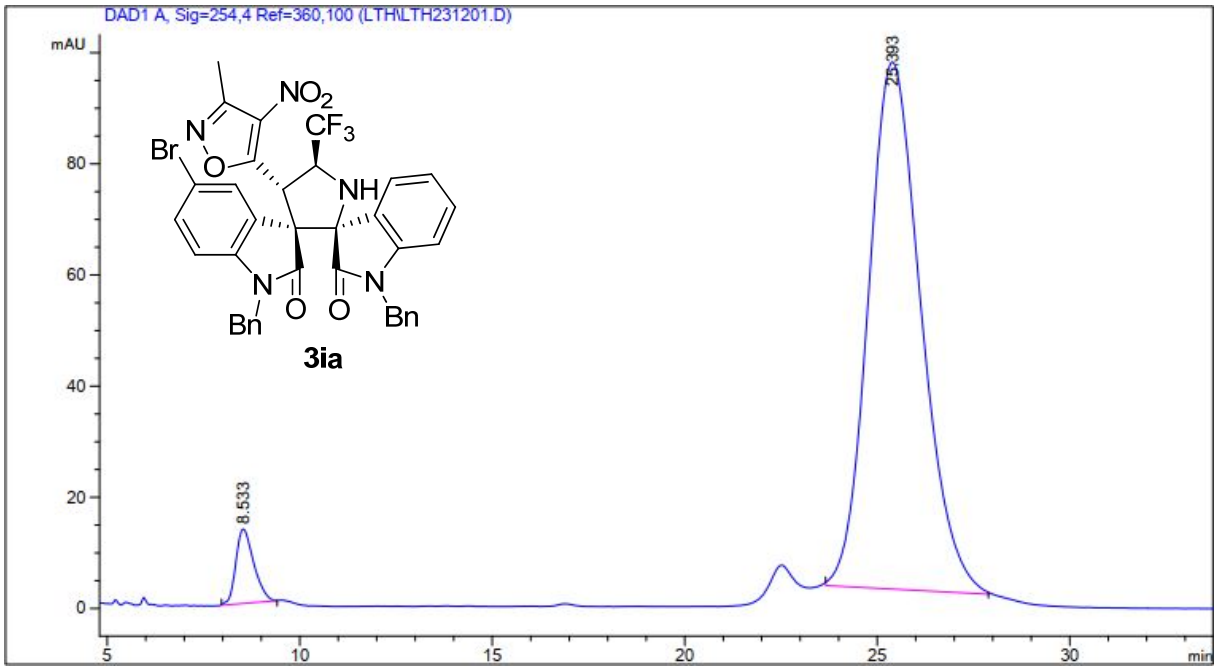
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.213	BB	0.4584	6751.65283	224.81125	50.4563
2	25.172	BB	1.2854	6629.52930	69.34307	49.5437



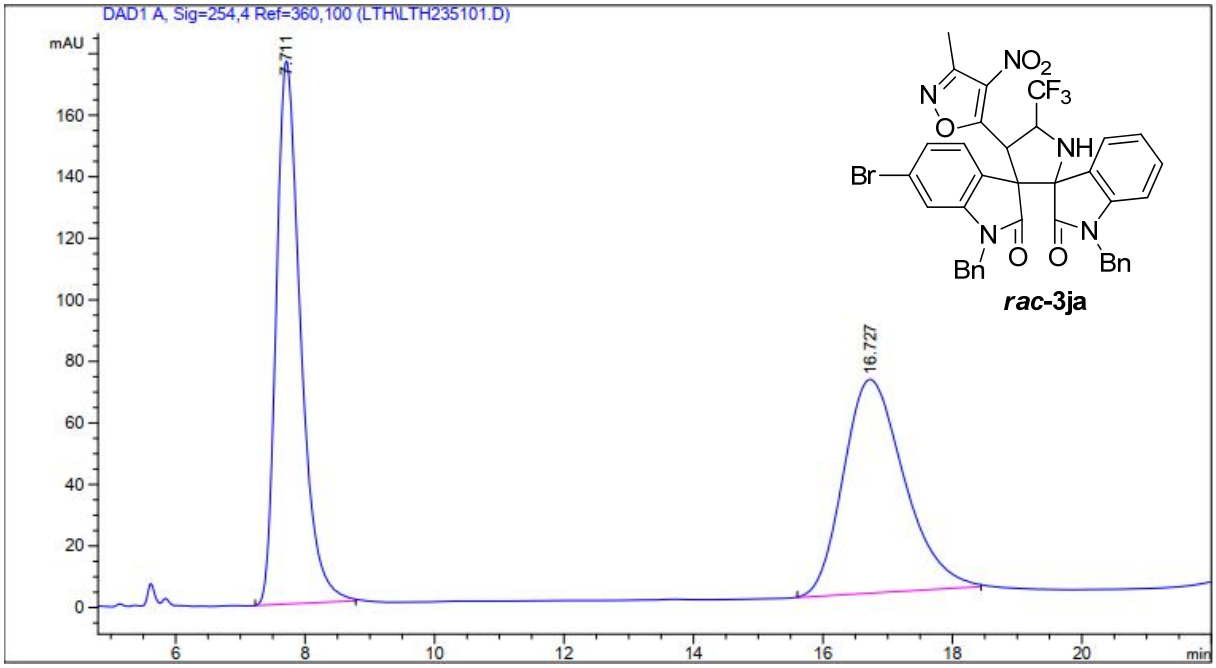
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.228	BB	0.4870	900.18024	28.45836	3.6899
2	24.976	VB	1.4092	2.34953e4	244.47247	96.3101



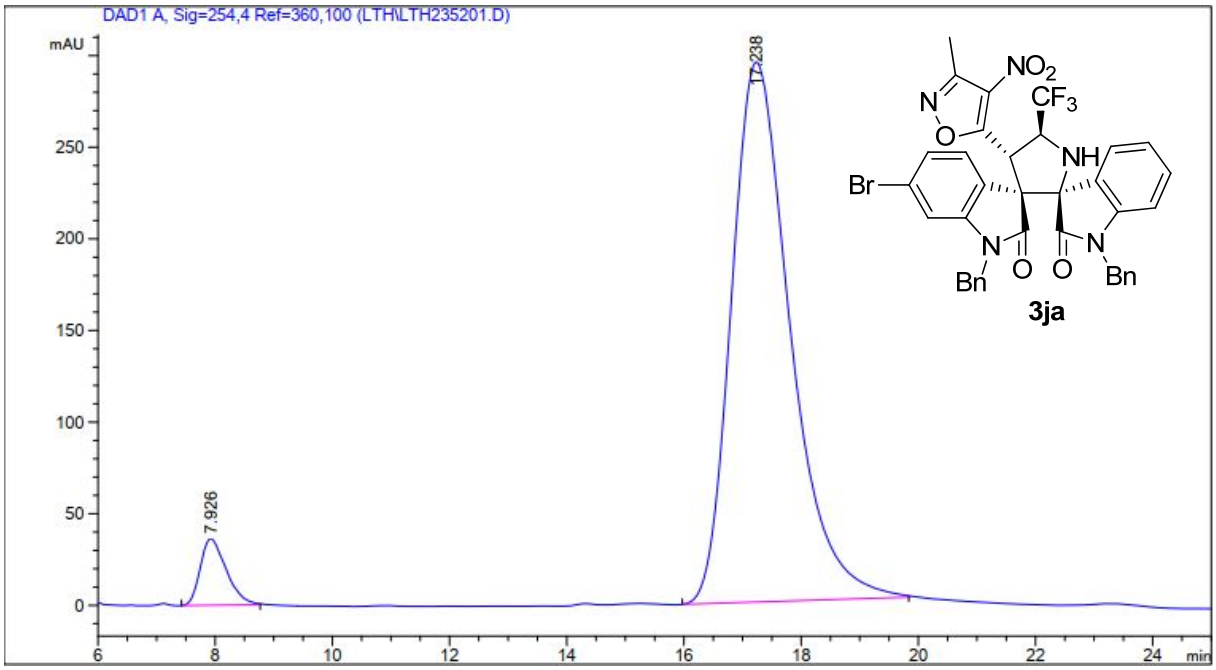
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.495	BB	0.4631	4019.28564	132.03746	50.4752
2	25.514	BB	1.1204	3943.61060	41.65766	49.5248



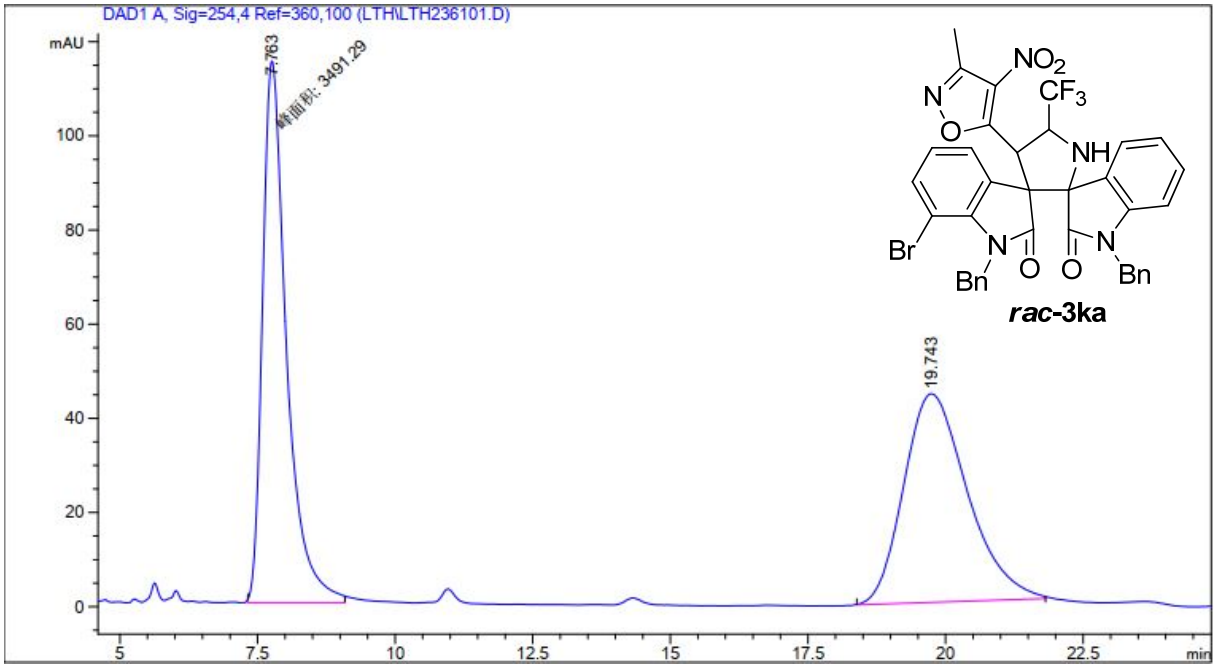
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.533	BB	0.4928	434.49976	13.38141	4.6077
2	25.393	BB	1.3607	8995.36230	94.82470	95.3923



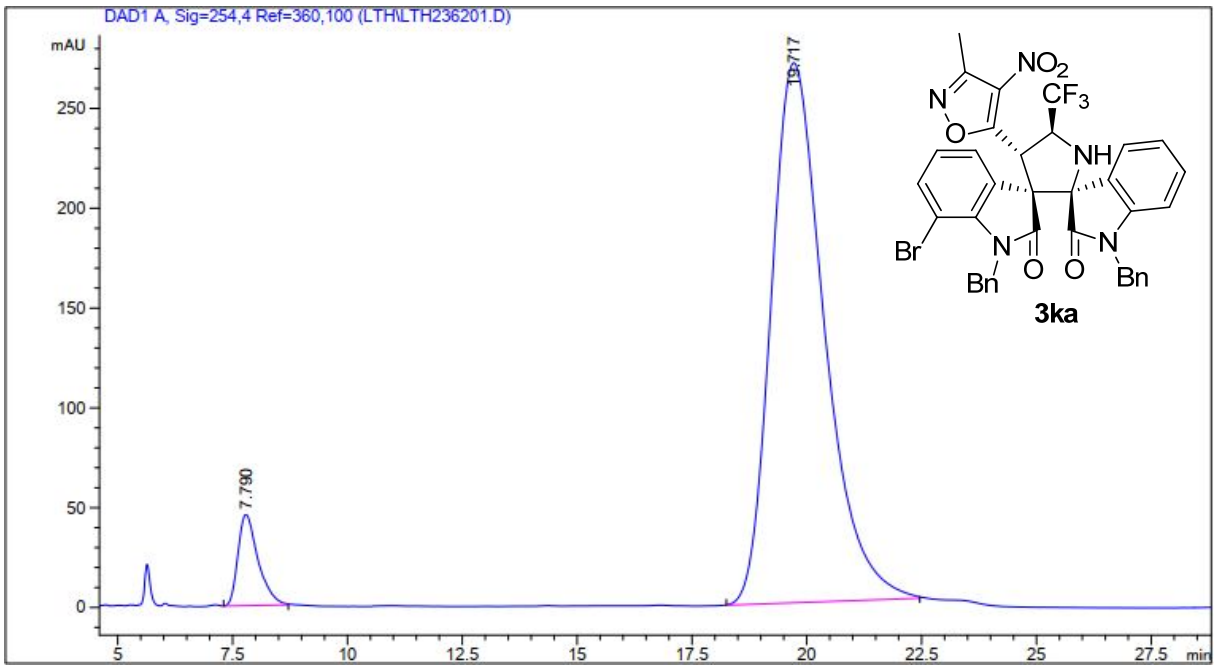
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.711	BB	0.3982	4603.08105	176.51608	50.3622
2	16.727	BB	0.9637	4536.86621	69.48831	49.6378



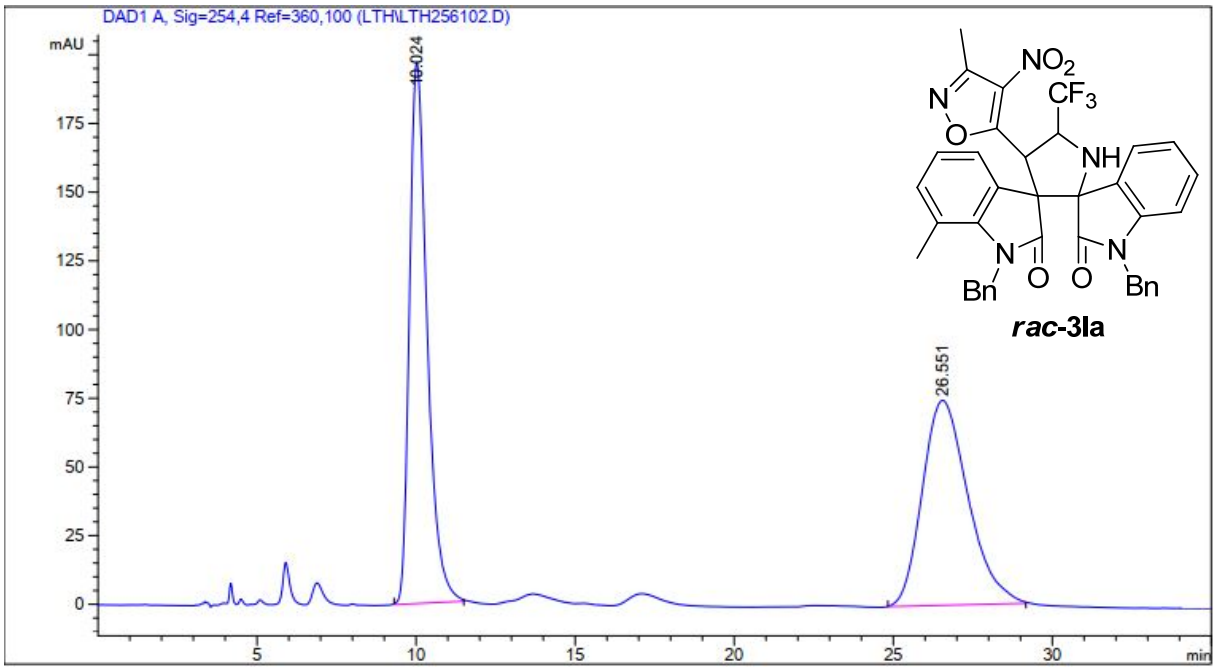
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.926	BB	0.4544	1118.56848	36.41131	5.1713
2	17.238	BB	1.0641	2.05118e4	294.68817	94.8287



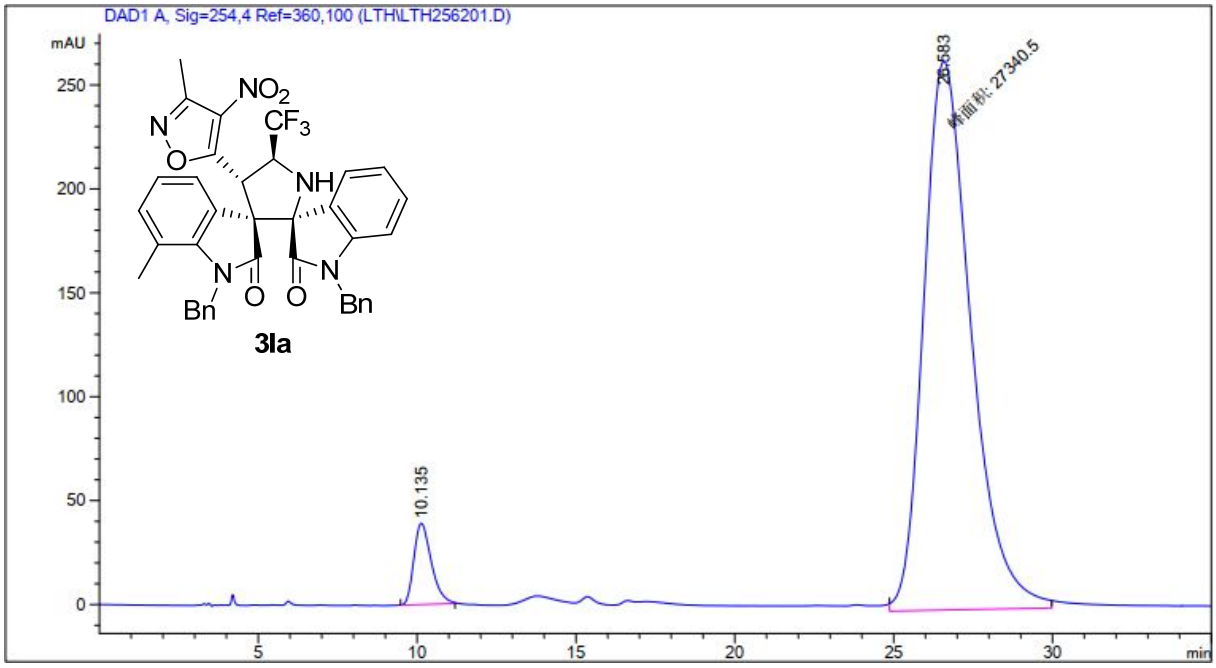
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.763	MM	0.5056	3491.28931	115.07774	49.4890
2	19.743	BB	1.1079	3563.39063	44.32479	50.5110



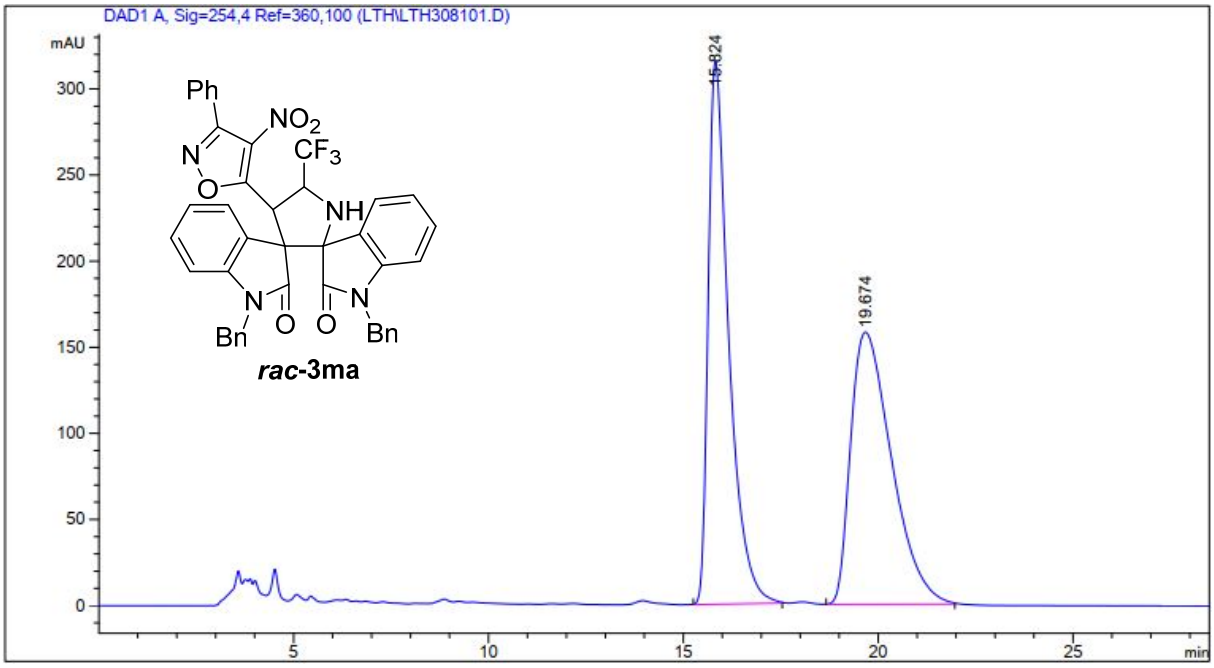
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.790	BB	0.4502	1387.71887	45.70973	5.9833
2	19.717	BB	1.2264	2.18054e4	270.52628	94.0167



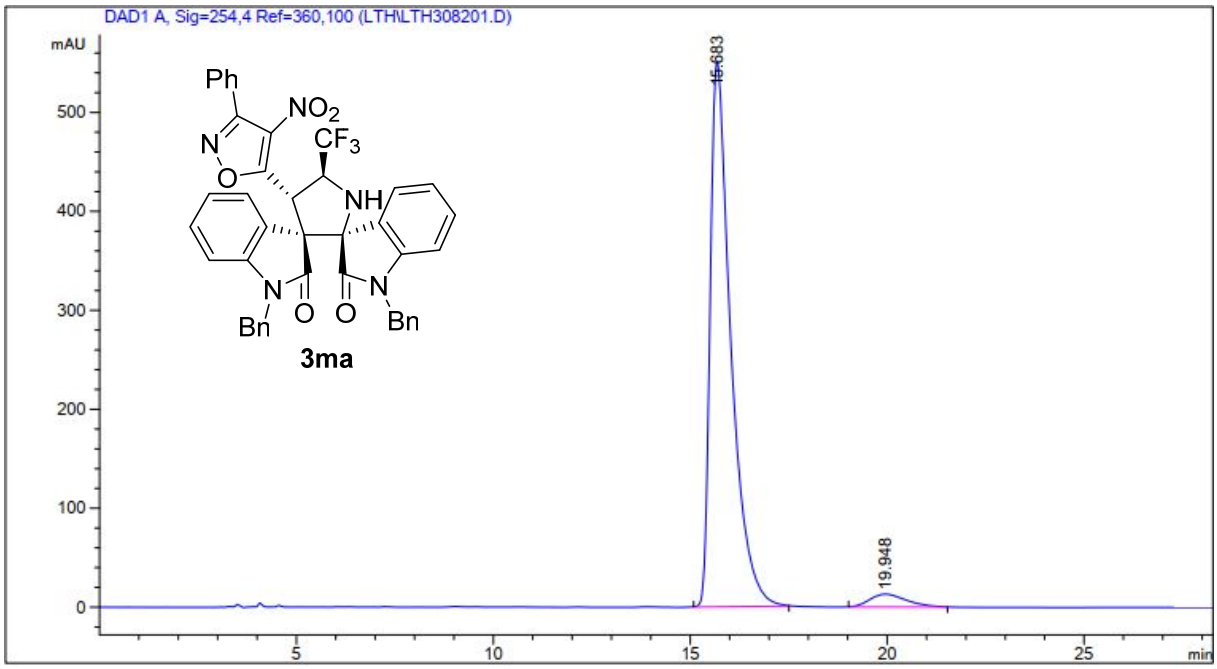
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.024	BB	0.5870	7582.71436	197.02251	50.4394
2	26.551	BB	1.3693	7450.61182	74.59399	49.5606



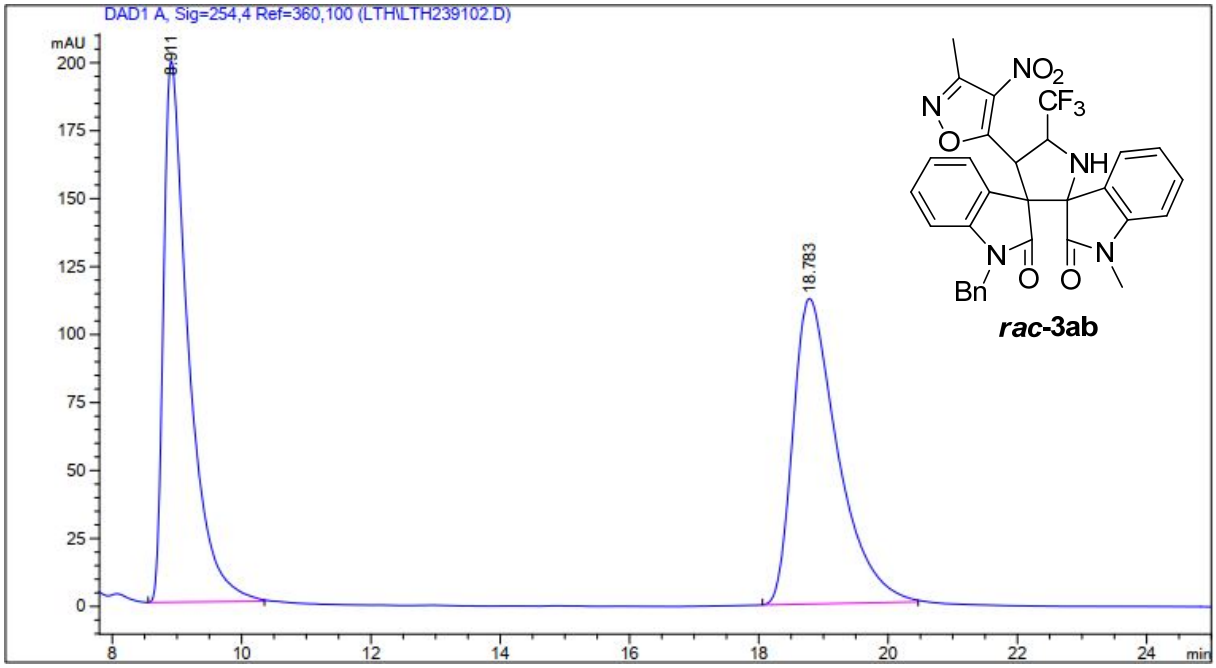
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.135	BB	0.5859	1493.53174	39.07468	5.1798
2	26.583	MM	1.7251	2.73405e4	264.13684	94.8202



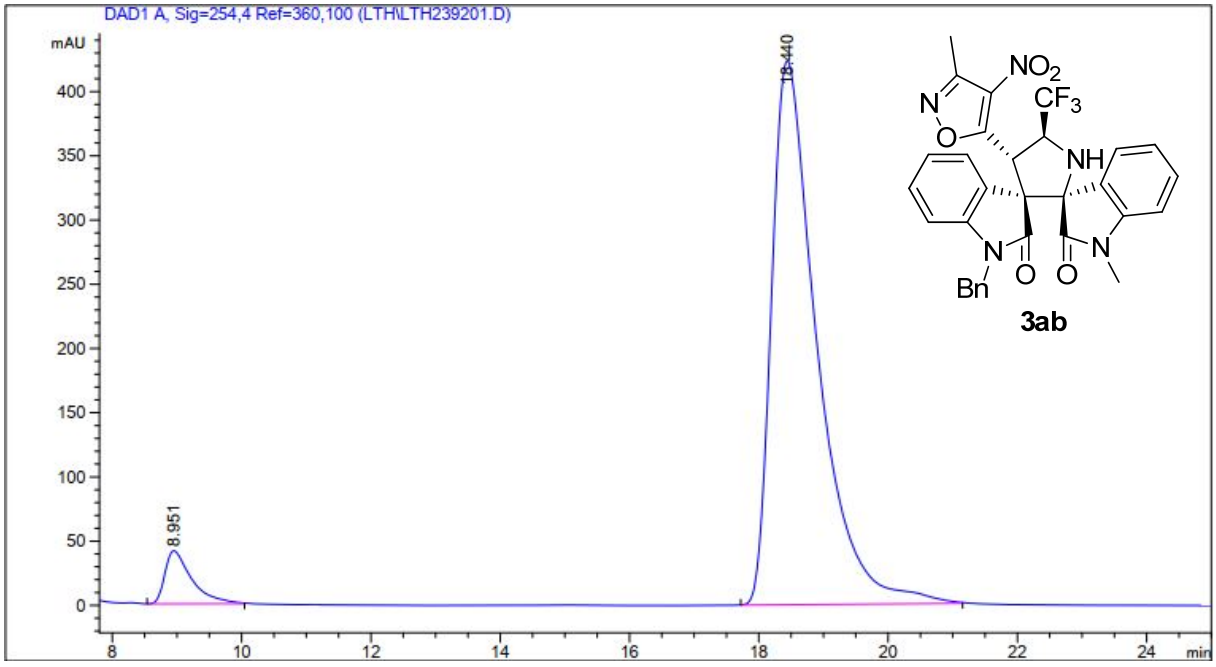
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.824	BB	0.5453	1.15450e4	315.20096	50.1051
2	19.674	BB	1.1074	1.14966e4	157.90695	49.8949



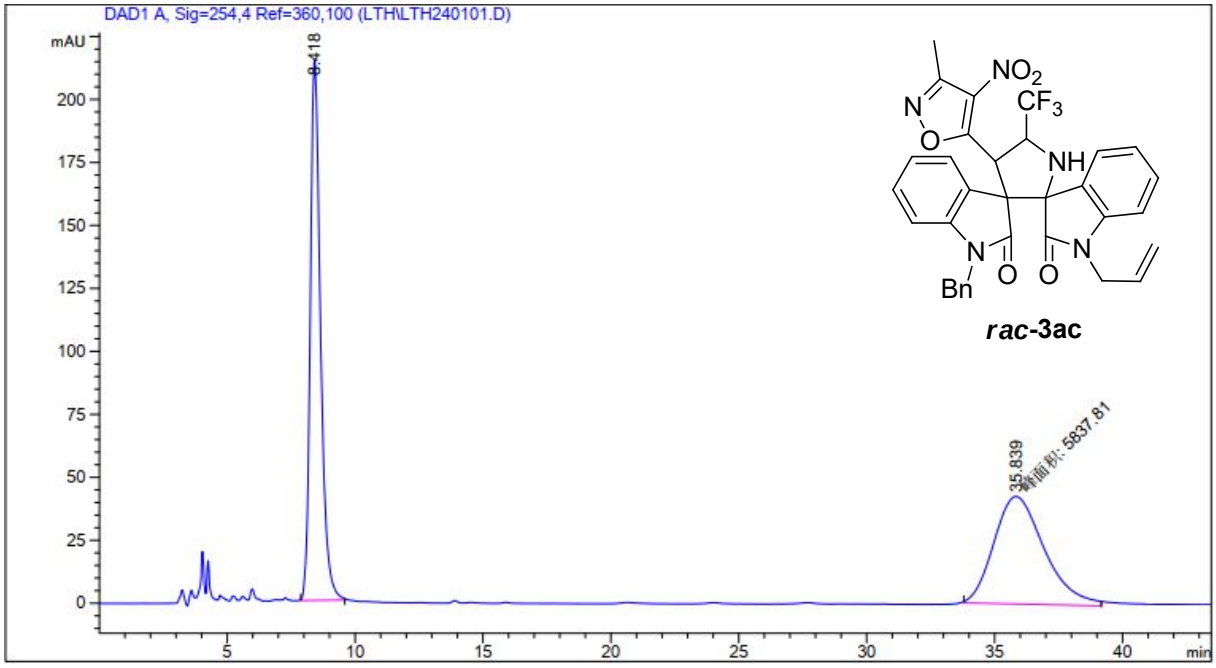
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.683	BB	0.5403	2.00193e4	550.43134	95.9902
2	19.948	BB	0.7598	836.26813	12.94356	4.0098



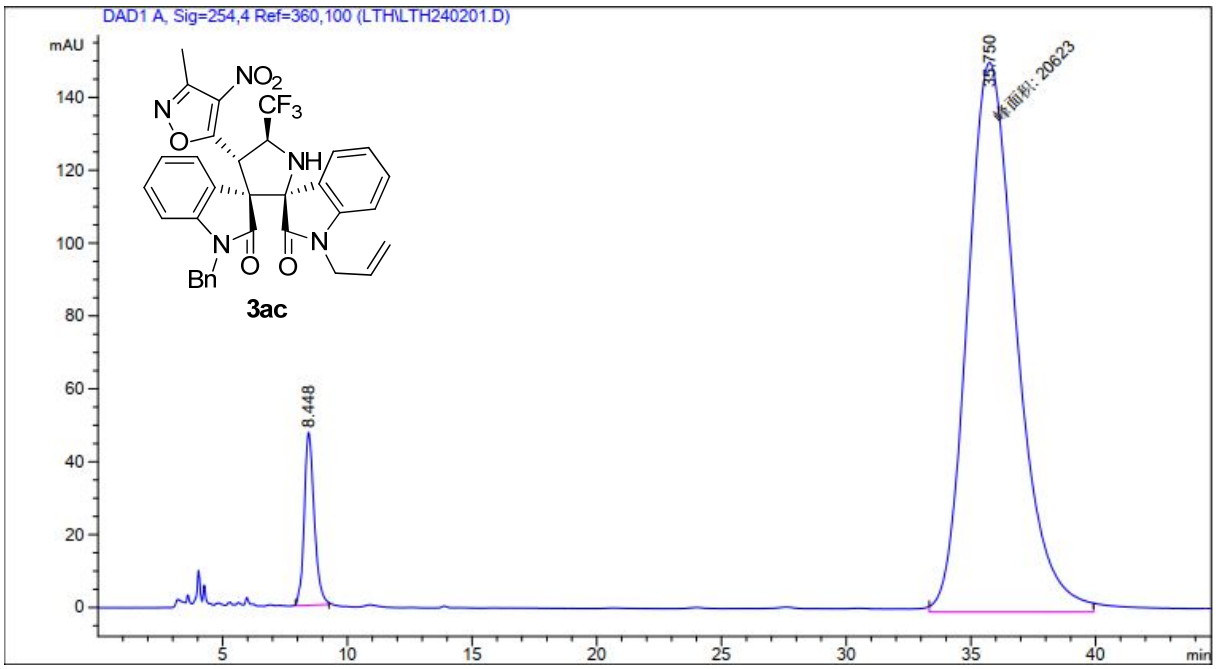
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.911	BB	0.3905	5332.89160	199.10149	49.6222
2	18.783	BB	0.7201	5414.09717	112.37960	50.3778



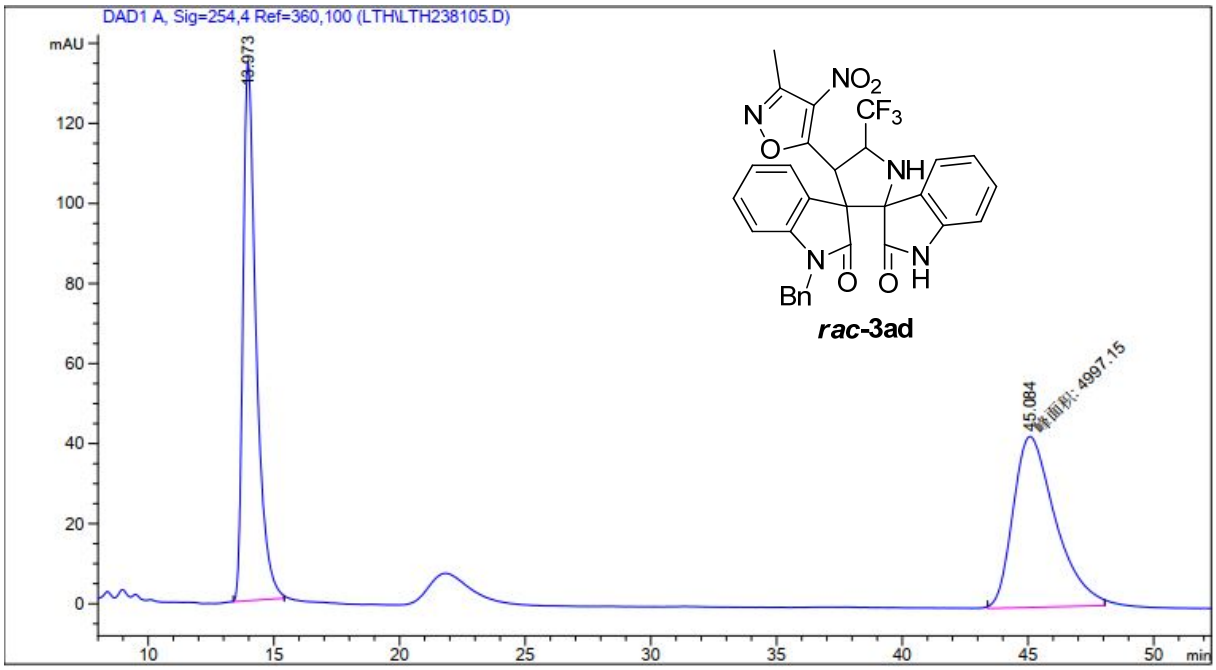
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.951	BB	0.4151	1186.28064	41.30219	5.4223
2	18.440	BB	0.7221	2.06914e4	423.46747	94.5777



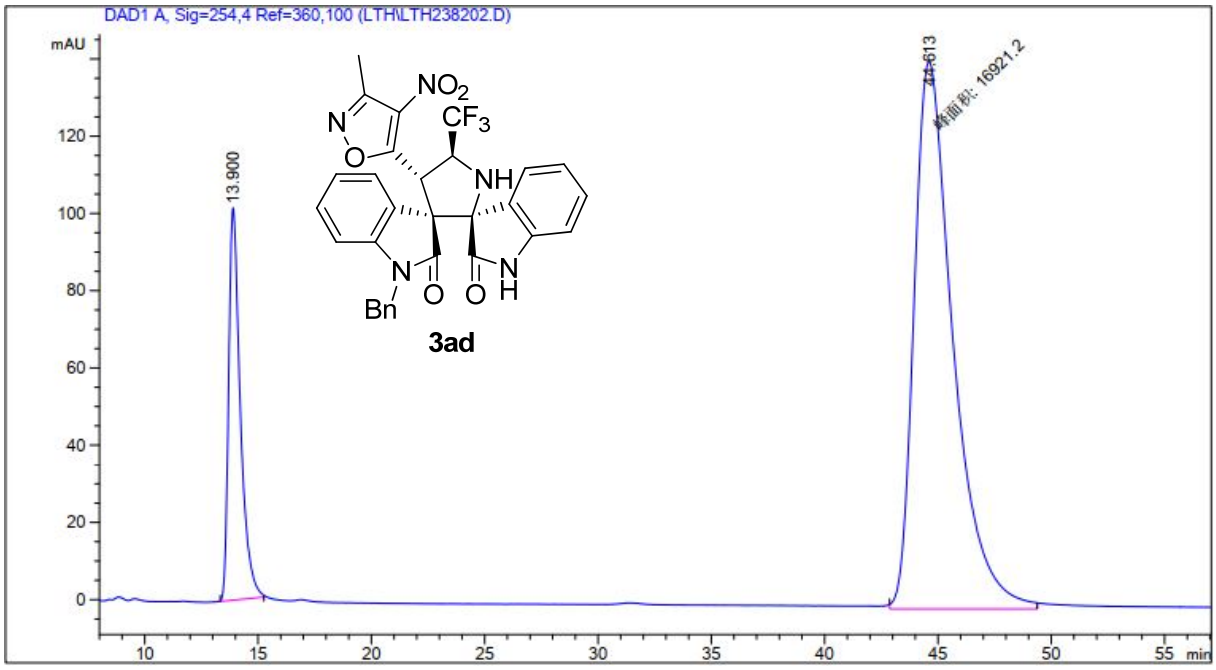
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.418	BB	0.4219	5955.31396	214.51907	50.4982
2	35.839	MM	2.2781	5837.81152	42.70917	49.5018



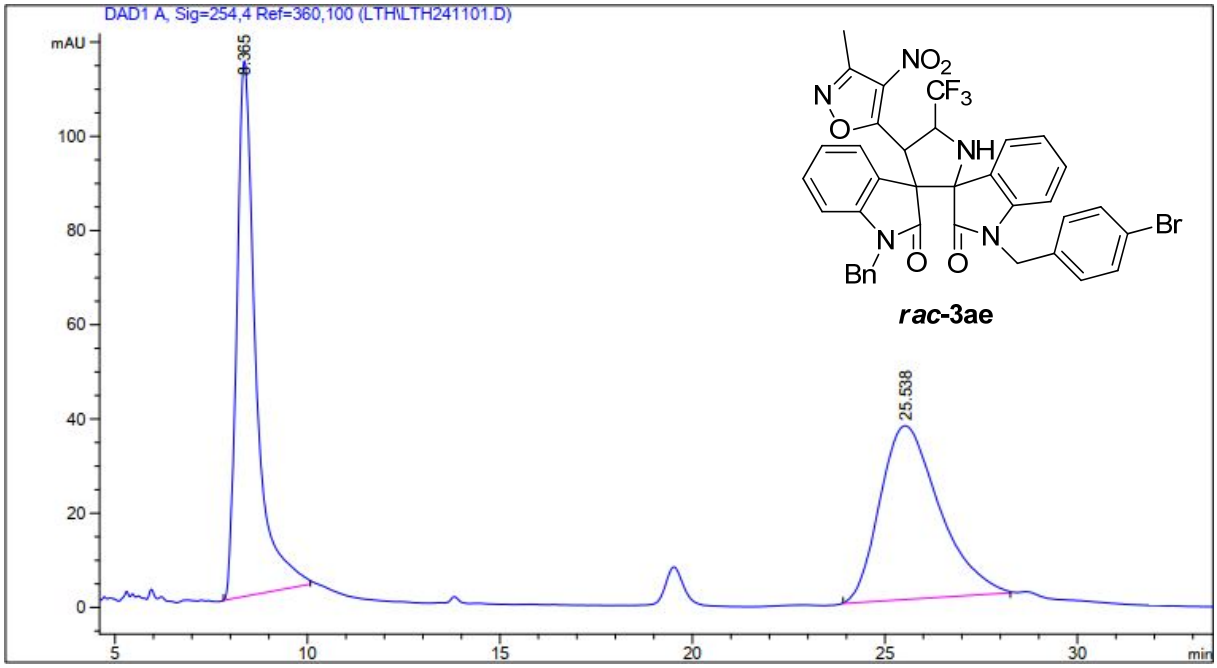
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.448	BB	0.4238	1323.88220	47.41007	6.0322
2	35.750	MM	2.2798	2.06230e4	150.76454	93.9678



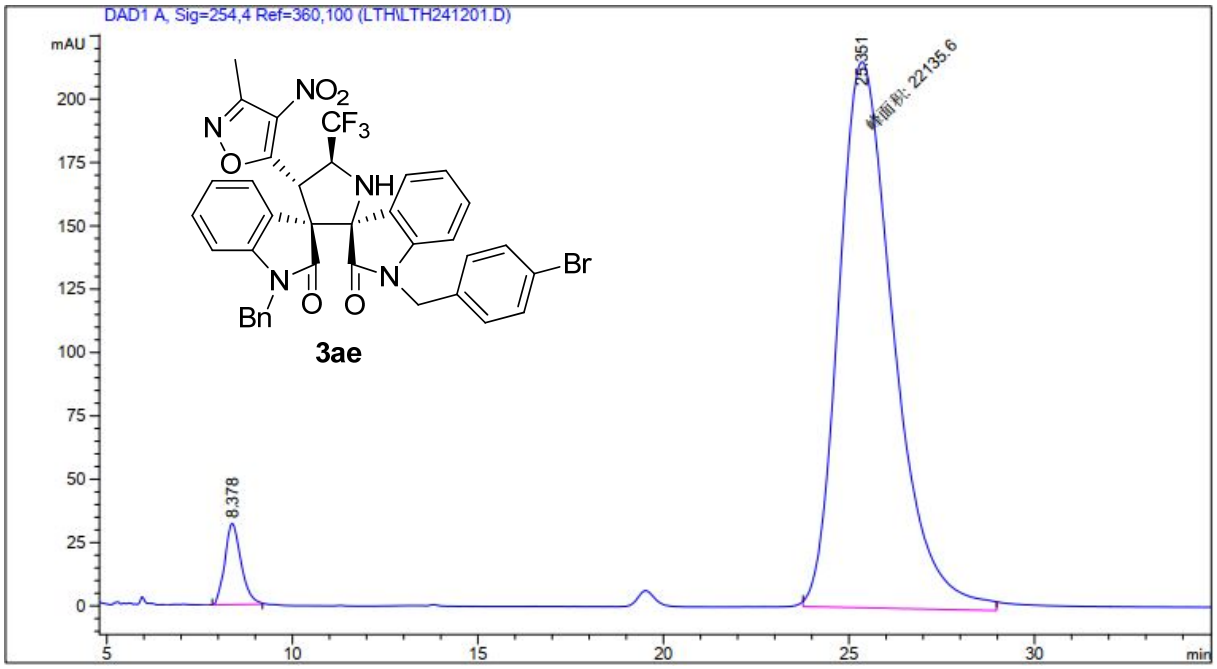
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.973	BB	0.5432	4902.18311	134.52068	49.5203
2	45.084	MM	1.9507	4997.15234	42.69475	50.4797



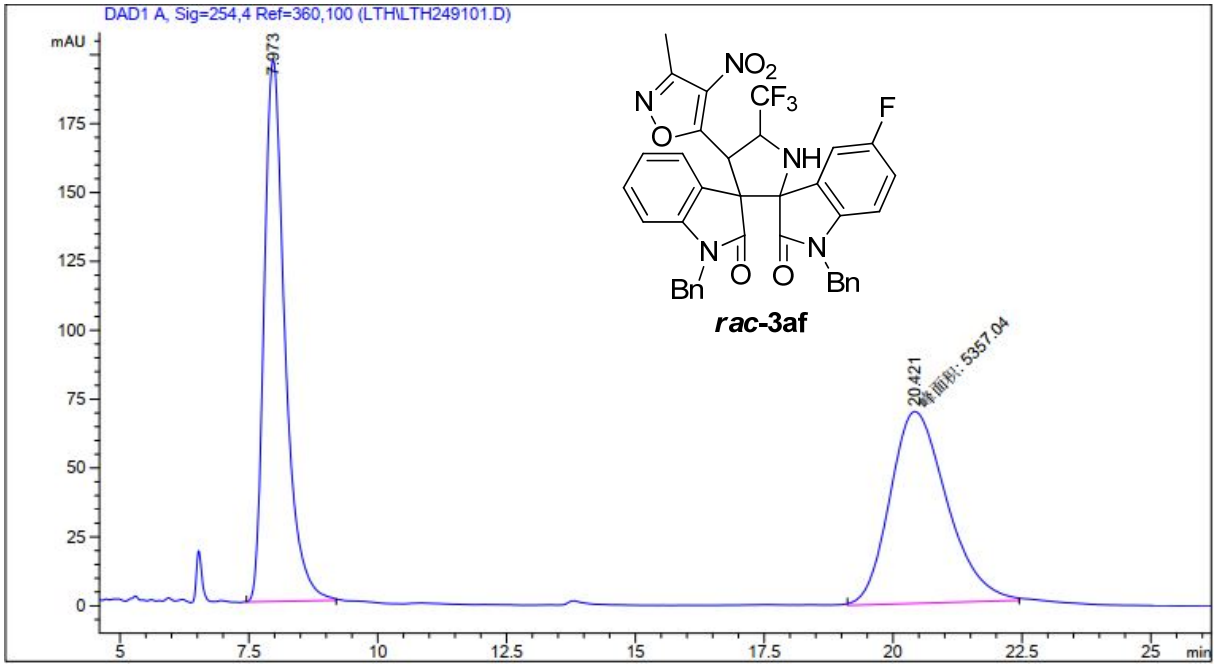
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.900	BB	0.5277	3618.98706	101.56035	17.6191
2	44.613	MM	1.9910	1.69212e4	141.64505	82.3809



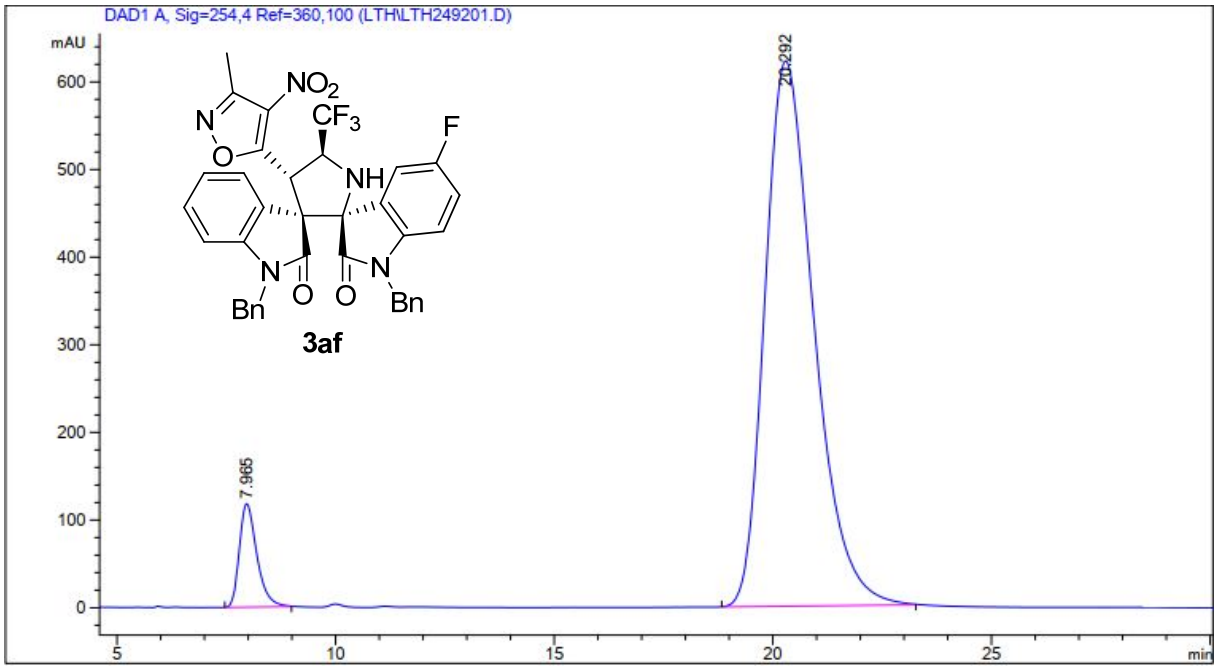
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.365	BB	0.5021	3898.86255	113.68356	49.5976
2	25.538	BB	1.3470	3962.12183	36.89146	50.4024



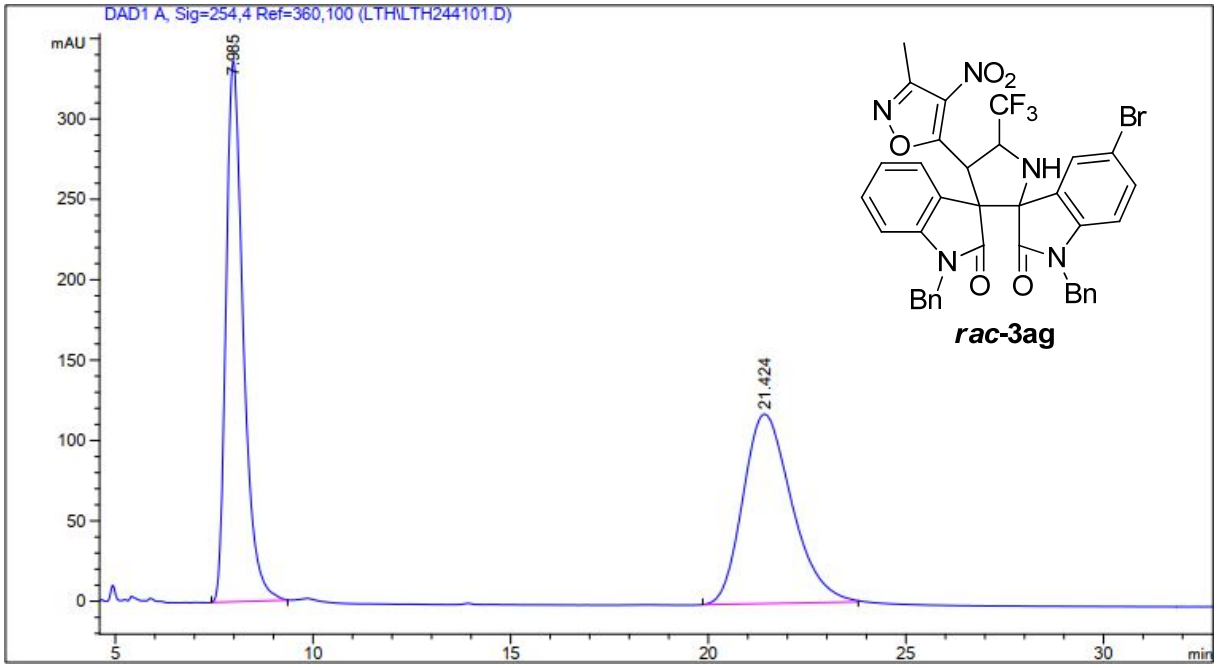
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.378	BB	0.4548	978.73865	32.00469	4.2343
2	25.351	MM	1.7125	2.21356e4	215.42778	95.7657



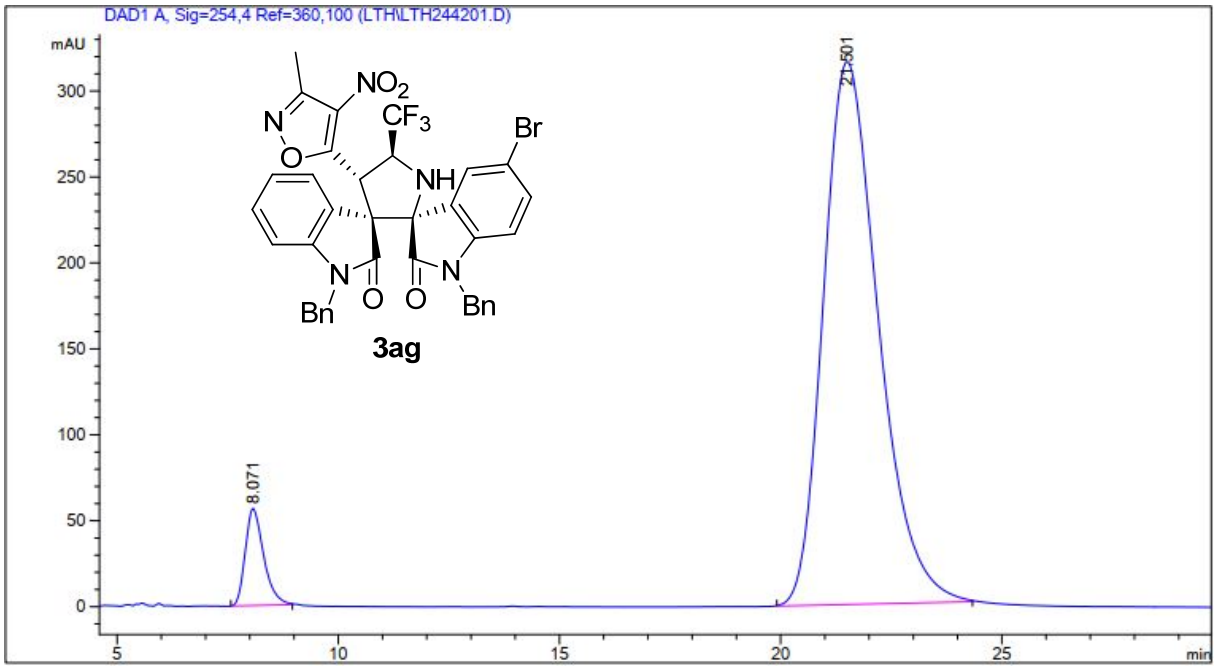
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.973	BB	0.4230	5509.69434	196.57663	50.7024
2	20.421	MM	1.2815	5357.04443	69.67210	49.2976



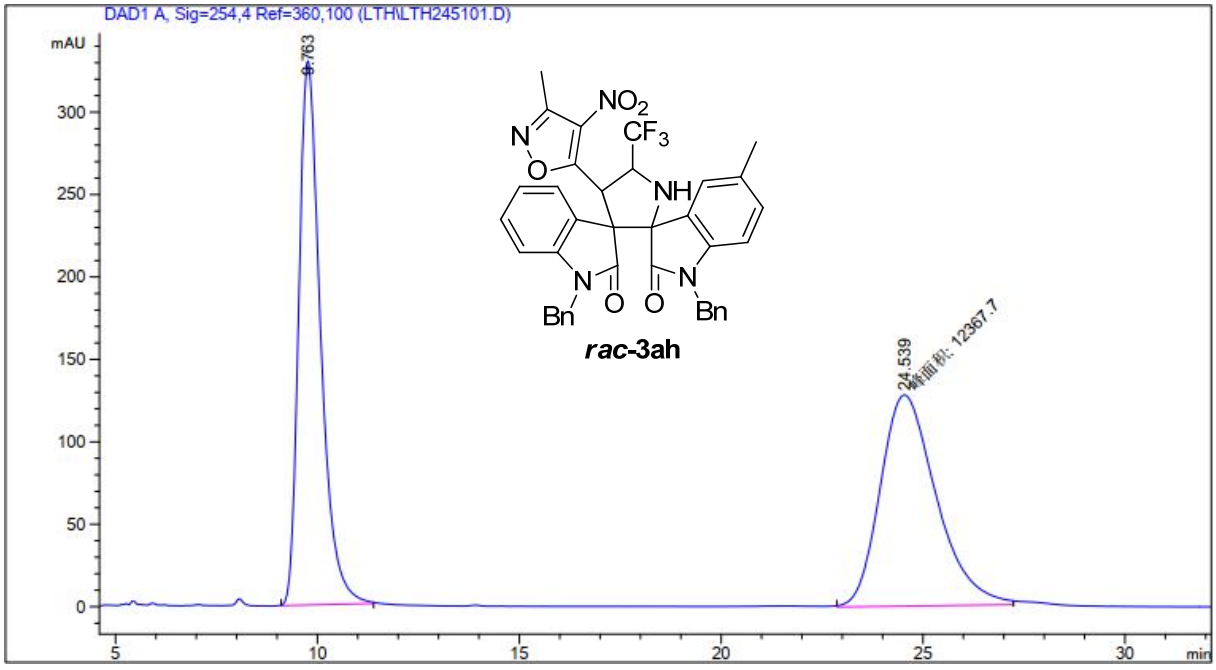
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.965	BB	0.4274	3287.87012	117.88233	6.3503
2	20.292	BB	1.1893	4.84875e4	622.14380	93.6497



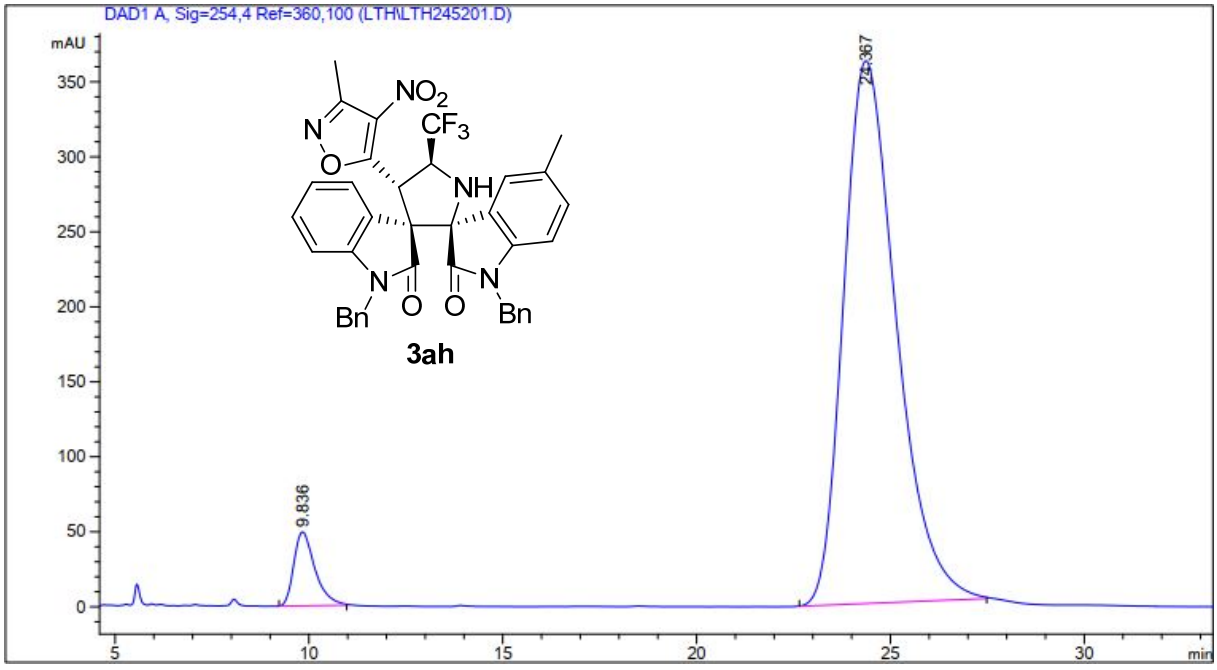
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.985	BB	0.4603	1.02159e4	336.43469	50.1867
2	21.424	BB	1.2999	1.01399e4	117.83678	49.8133



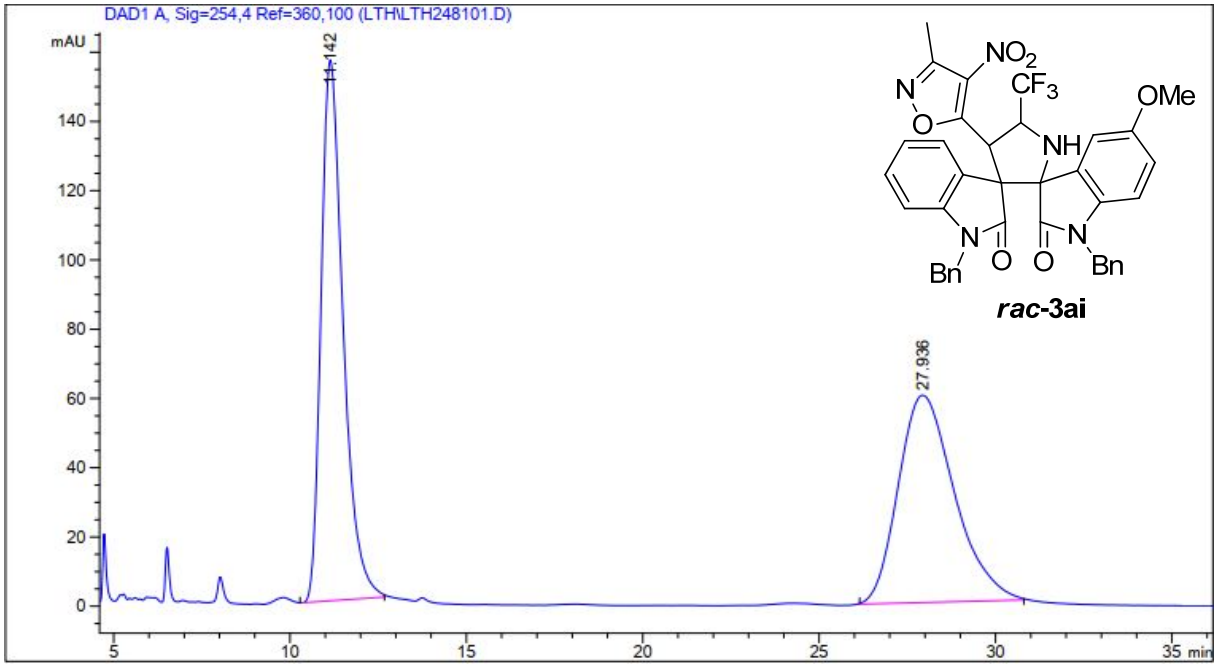
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.071	BB	0.4458	1634.27698	56.44934	5.6455
2	21.501	BB	1.2955	2.73140e4	315.65430	94.3545



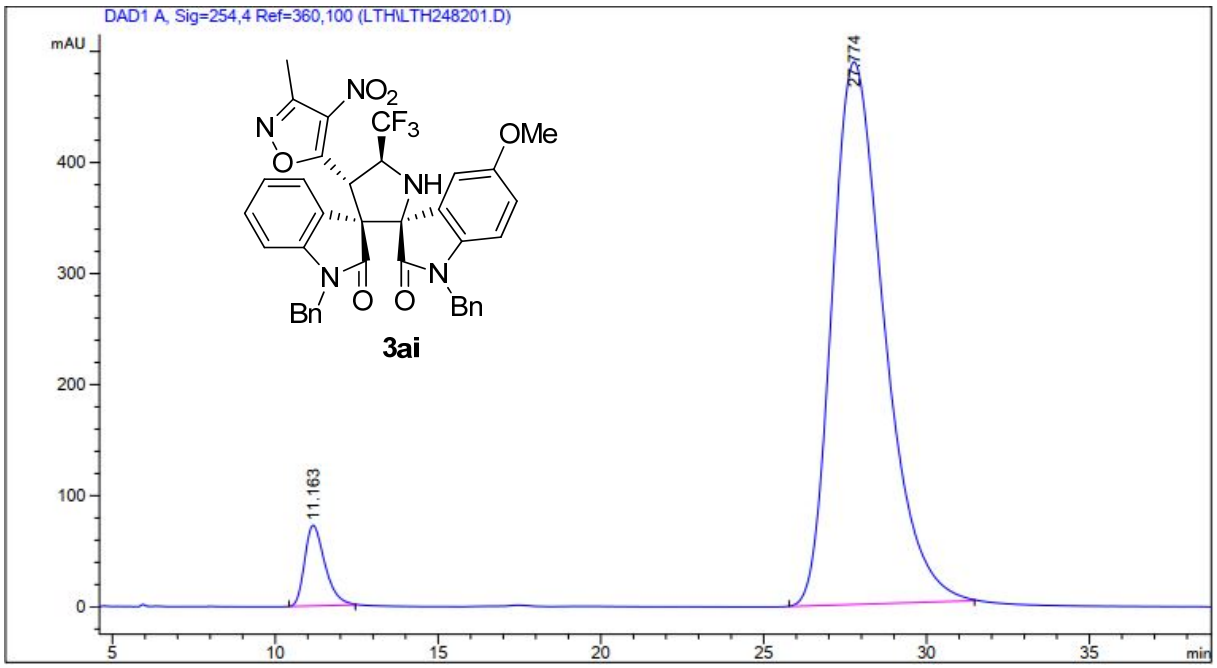
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.763	BB	0.5707	1.23556e4	330.12253	49.9757
2	24.539	MM	1.6085	1.23677e4	128.15193	50.0243



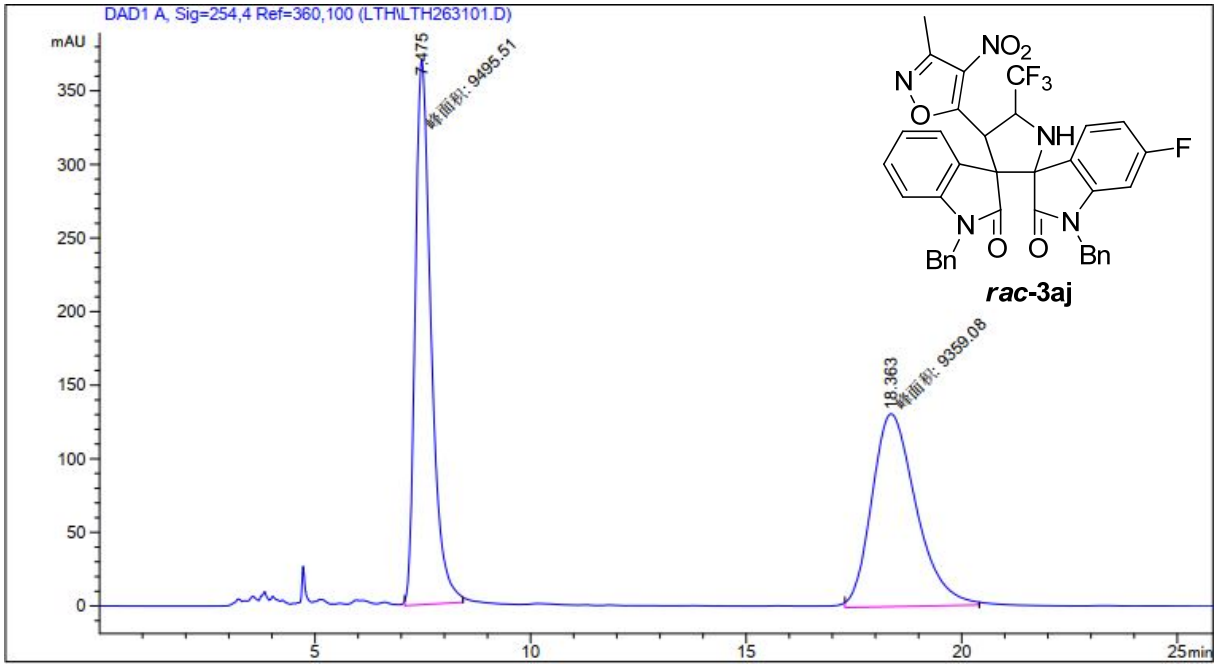
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.836	BB	0.5706	1859.12402	49.23327	5.1560
2	24.367	BB	1.4230	3.41980e4	361.70880	94.8440



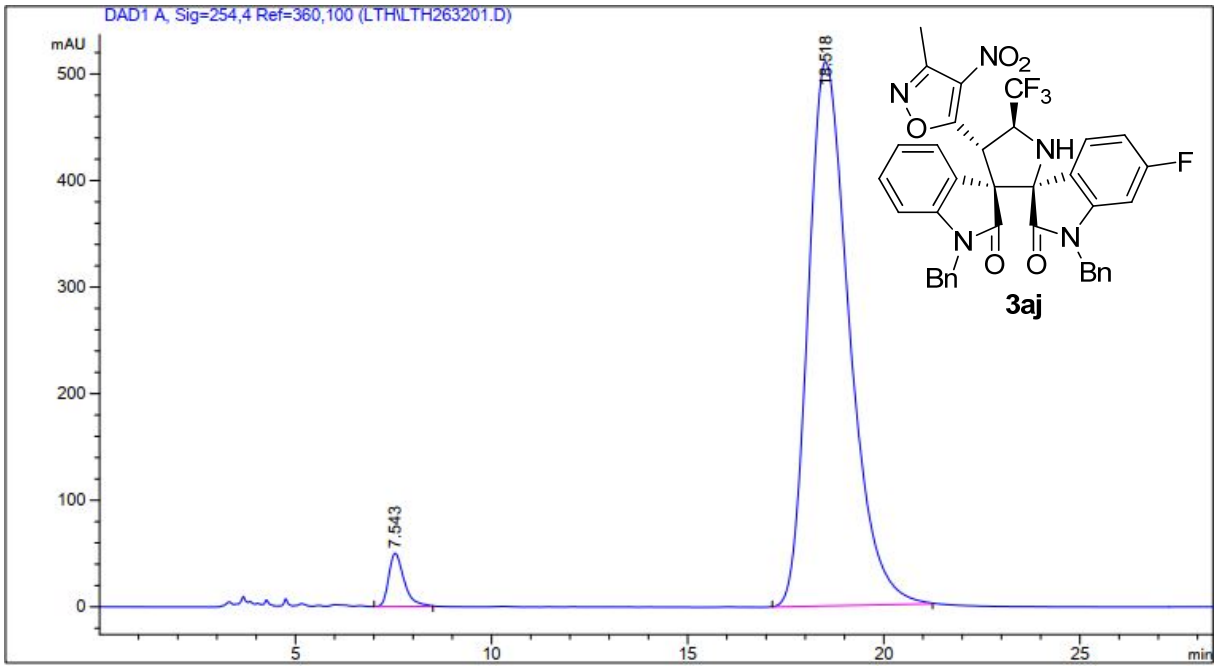
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.142	VB	0.6664	6780.08105	156.19193	50.5941
2	27.936	BB	1.5709	6620.86377	59.83882	49.4059



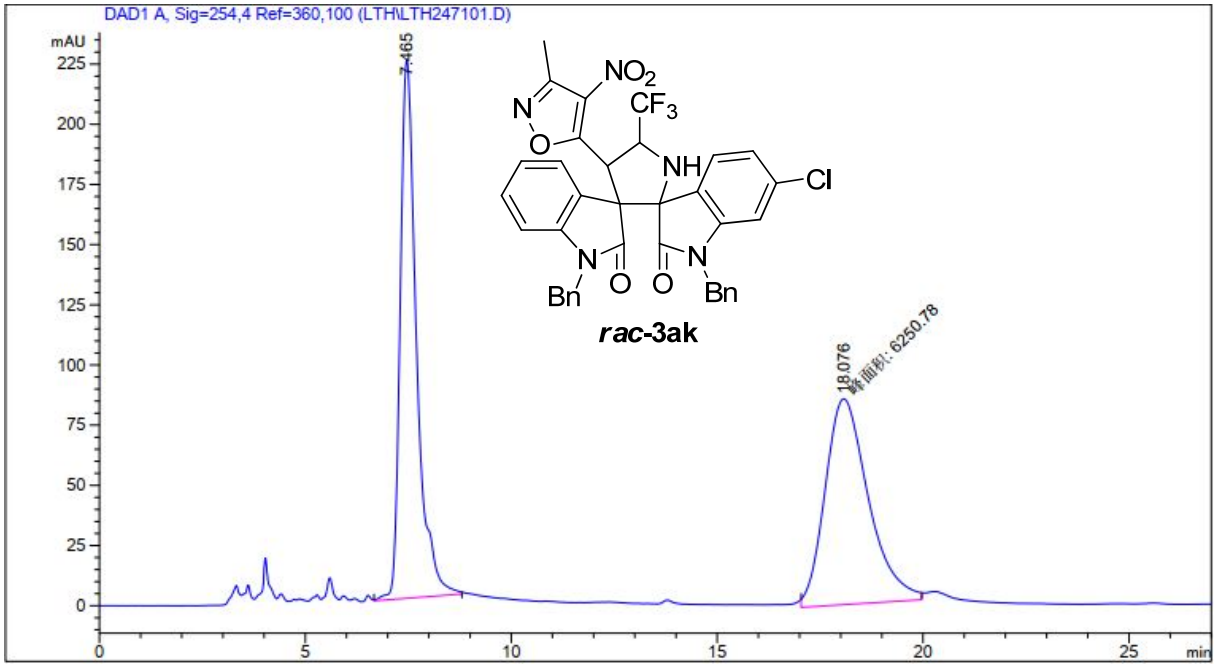
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.163	BB	0.6643	3152.43286	72.64636	5.4888
2	27.774	BB	1.6523	5.42815e4	488.53629	94.5112



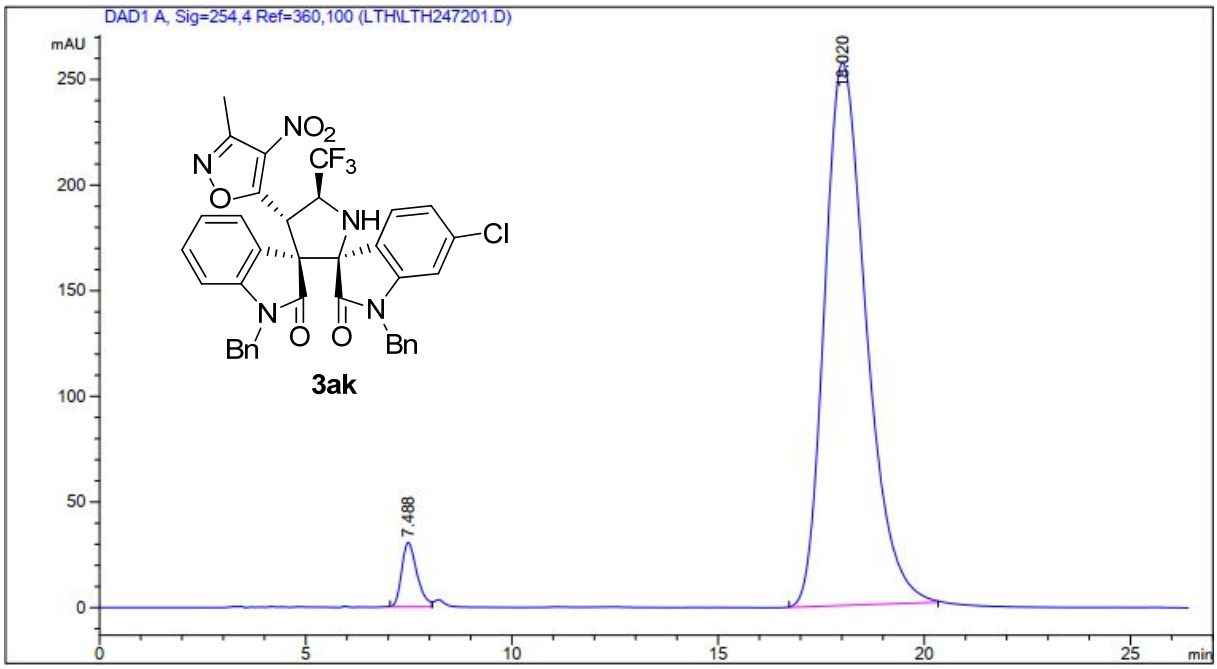
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.475	MM	0.4279	9495.51465	369.84464	50.3618
2	18.363	MM	1.1915	9359.08301	130.91785	49.6382



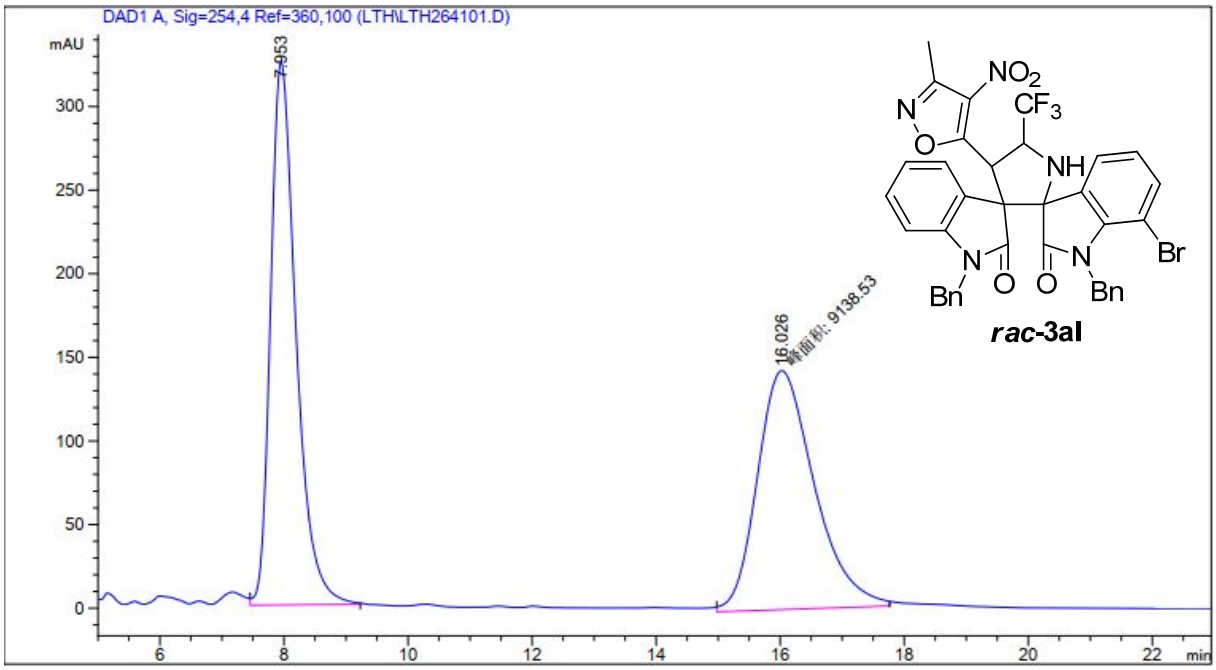
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.543	VB	0.4112	1357.62744	49.93183	3.5222
2	18.518	BB	1.1159	3.71868e4	510.47736	96.4778



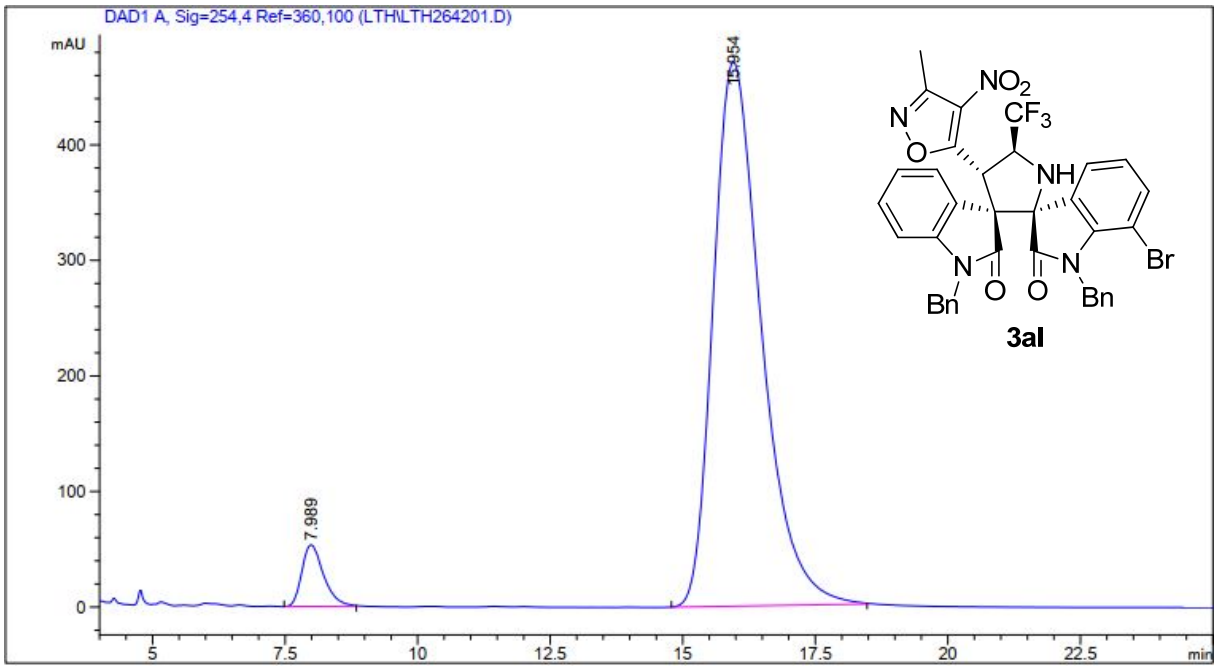
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.465	VB	0.4156	6164.95215	223.63997	49.6544
2	18.076	MM	1.2179	6250.78027	85.54081	50.3456



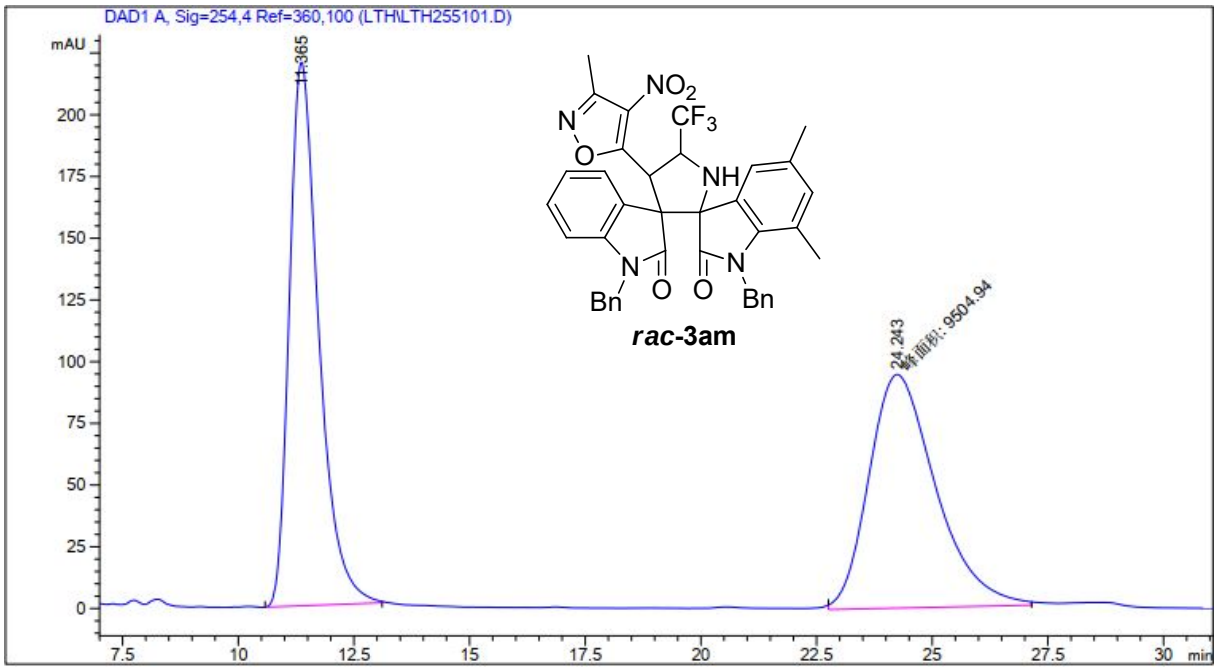
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.488	BV	0.3953	780.29120	30.41434	4.1445
2	18.020	BB	1.0831	1.80467e4	257.03793	95.8555



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.953	VB	0.4333	9272.63574	324.60013	50.3642
2	16.026	MM	1.0659	9138.53418	142.88840	49.6358

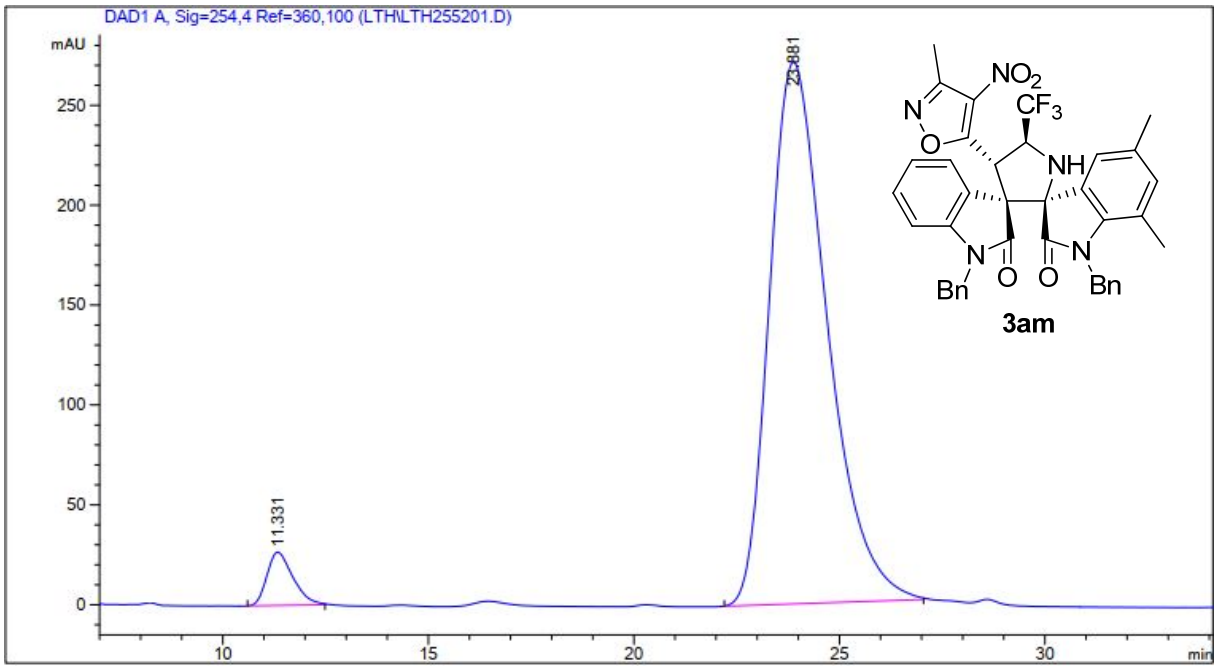


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.989	BB	0.4344	1519.02686	53.31531	4.8574
2	15.954	BB	0.9672	2.97536e4	470.84564	95.1426



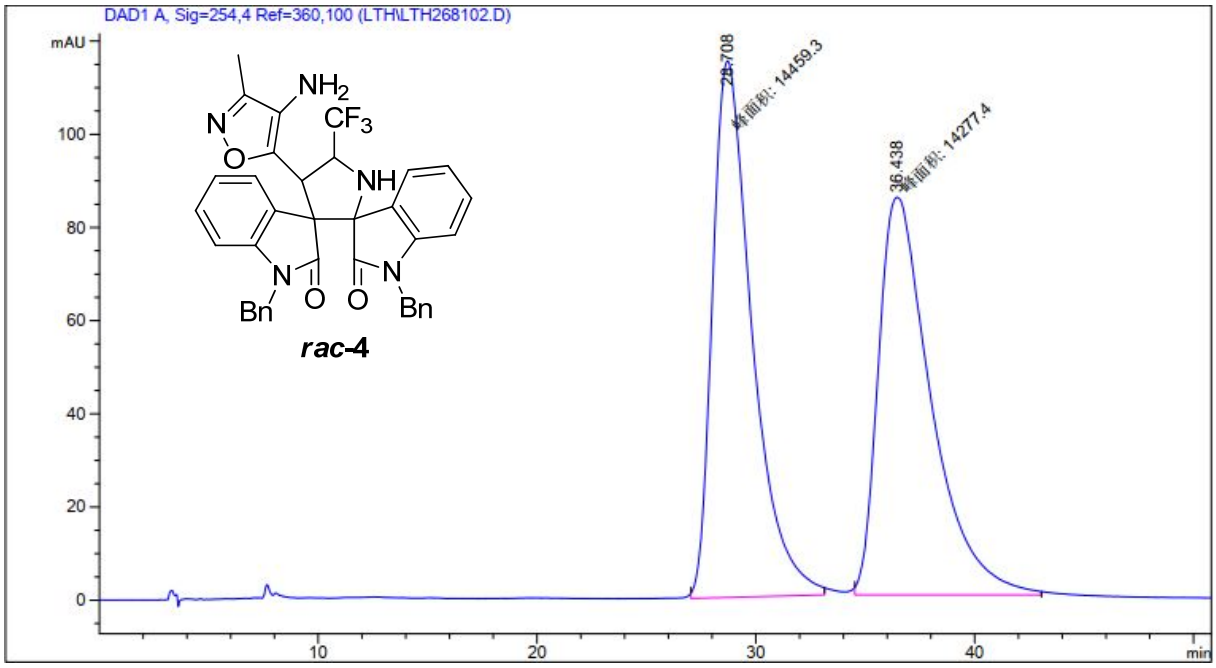
rac-3am

Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.365	BB	0.6726	9749.37012	220.17325	50.6347
2	24.243	MM	1.6744	9504.93750	94.60841	49.3653

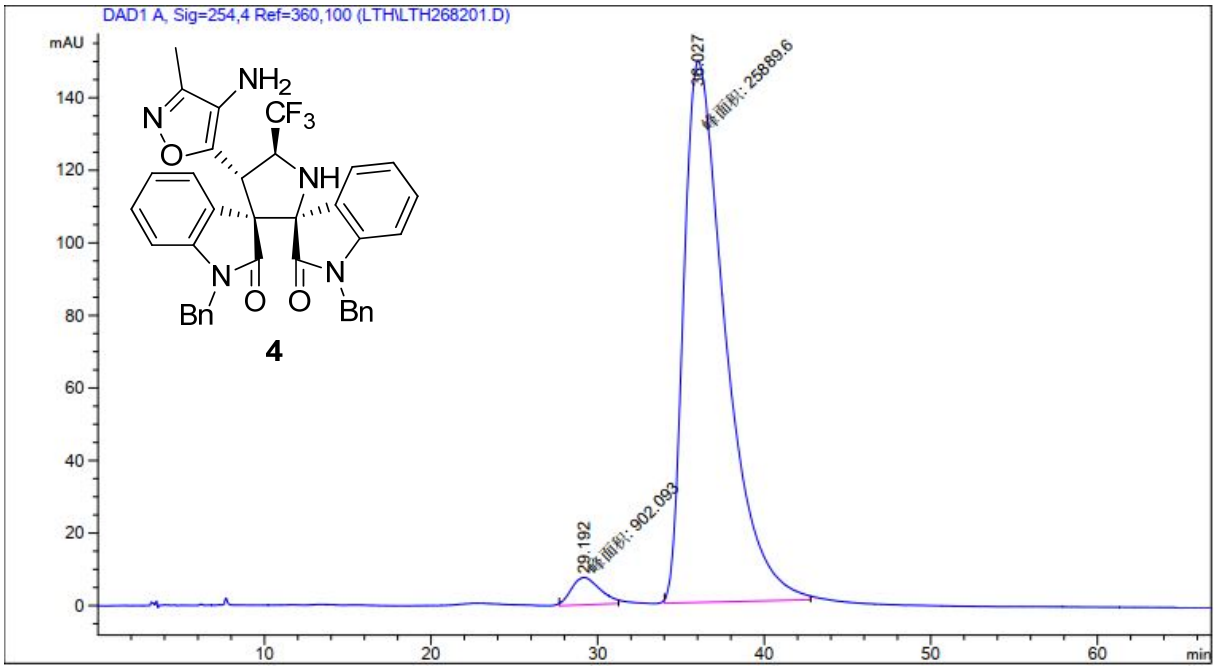


3am

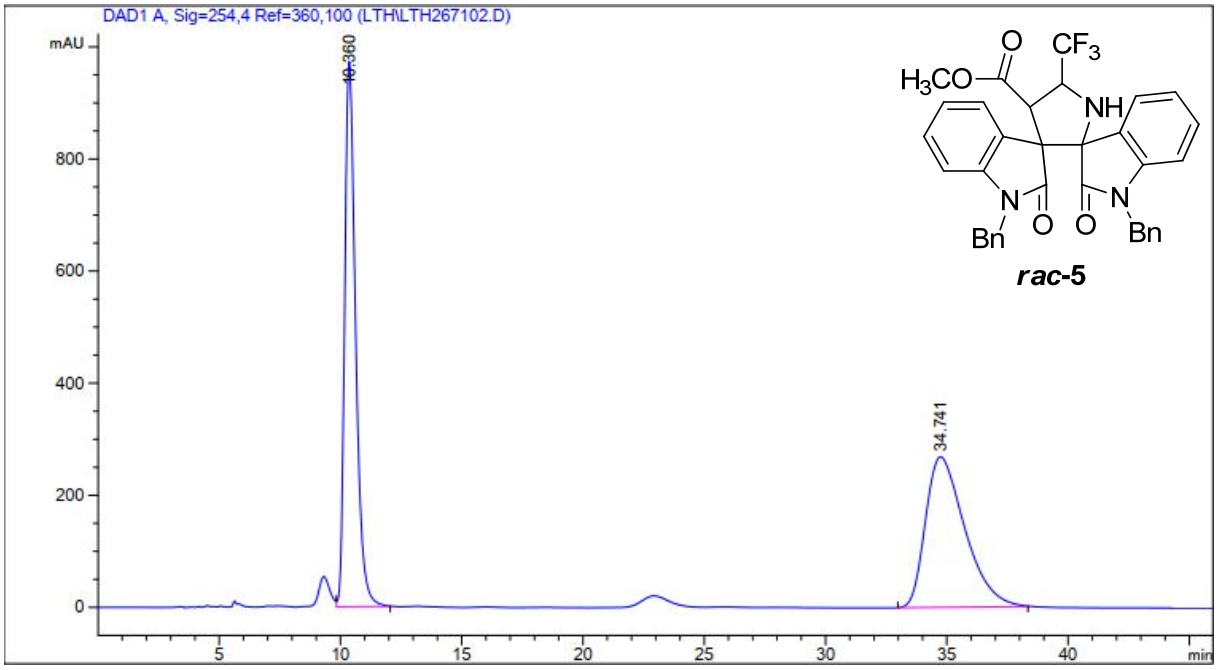
Peak	RetTime	Type	Width	Area	Height	Area
#	[min]		[min]	[mAU*s]	[mAU]	%
1	11.331	BB	0.6580	1171.24512	26.68610	4.2347
2	23.881	BB	1.4655	2.64870e4	271.18781	95.7653



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.708	MM	2.0927	1.44593e4	115.15593	50.3165
2	36.438	MM	2.7882	1.42774e4	85.34364	49.6835

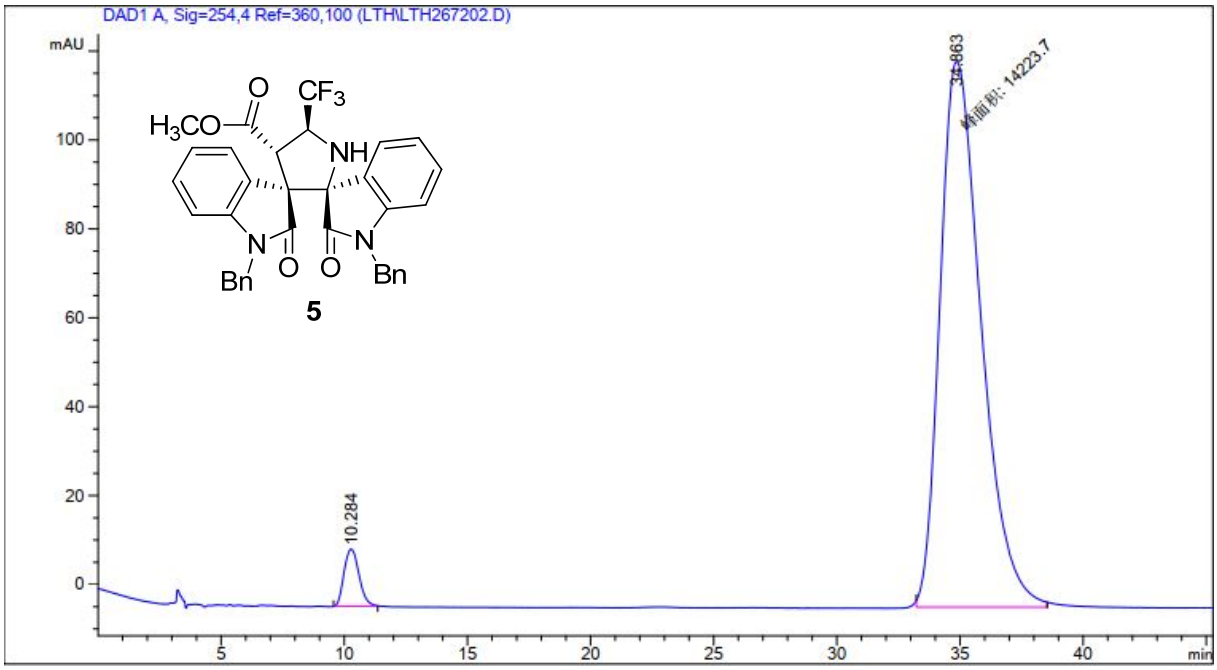


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.192	MM	1.9915	902.09283	7.54940	3.3671
2	36.027	MM	2.8913	2.58896e4	149.23619	96.6329



rac-**5**

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.360	VB	0.4805	3.04033e4	973.03302	50.1106
2	34.741	BB	1.6444	3.02691e4	268.67599	49.8894



5

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.284	BB	0.6136	544.16193	12.86062	3.6848
2	34.863	MM	1.9321	1.42237e4	122.69910	96.3152