Electronic Supplementary Material (ESI) for ChemComm.

Preparation of new chiral diene ligands and Their Use in the Rhodium Catalyzed Asymmetric Annulation of 2-Formylarylboronic acid with unactivated Alkynes

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Supporting Information

Contents

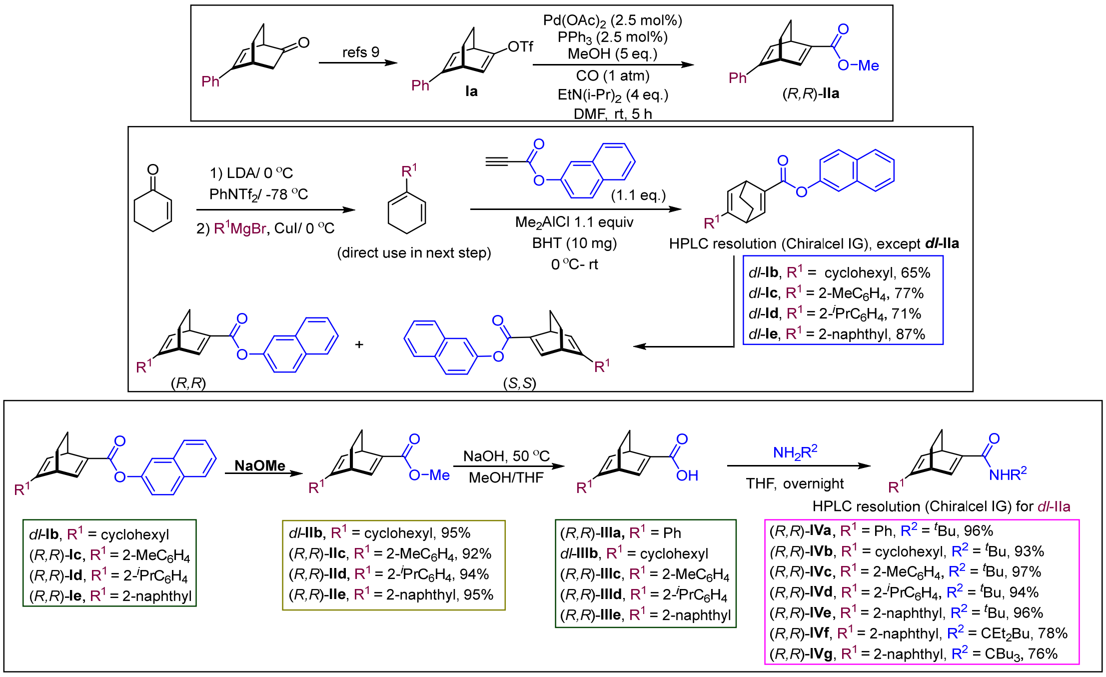
1. General information

All anaerobic manipulations were carried out with standard Schlenk techniques under nitrogen gas. Analytical thin-layer chromatography (TLC) was performed on silica gel, irradiation with UV light. For column chromatography, 200-300 mesh silica gel was used. NMR spectra were recorded on a BRUKER 600 MHz (or 400 Hz) spectrometer and ^{13}C NMR spectra were recorded in CDCl3 at 151 MHz (or 101 Hz). ^{1}H and ^{13}C NMR were referenced to CDCl3 at δ 7.26 and 77.00 respectively. The following abbreviations were used to explain the multiplicities; s (singlet), bs (broad singlet), d (doublet), t (triplet), m (multiplet); coupling constants (J) are in Hertz (Hz). Optical rotations were measured on an Anton Paar MCP 100 automatic polarimeter. HRMS spectra were obtained by BRUKER microTOF-Q III instrument with ESI source. Enantiomeric excesses (ee) were determined by HPLC analysis on SHIMADZU HPLC system with Daicel chiral columns. GPC (gel permeation chromatography) was performed using LaboACE LC-5060 recycling preparative HPLC.

2. Materials

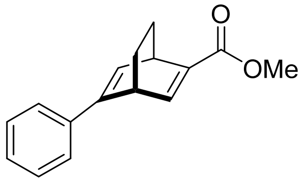
Unless otherwise noted, all the solvents and commercially available reagents were used as received for the reactions without further purification. The solvent and chemicals were purchased from Energy Chemical or J&K Scientific. Preparation of all these starting materials, **2c-2e**-[1-3] were synthesized according the reported references and they were assigned by comparison of their NMR spectra with the reported data. Chiral diene ligands, L5*-L13*[4-8] were prepared according to the reported procedures.

3. Preparation of new chiral diene ligands



Scheme S1

Ligand (*R,R*)-**IIa**: To a solution of (*1R,4R*)-5-phenylbicyclo[2.2.2]octa-2,5-dien-2-yl trifluoromethanesulfonate[9] (**Ia**, 1.32 g, 4 mmol), and $Pd(OAc)_2$ (22.4 mg, 0.10 mmol), and PPh3 (26.2 mg, 0.10 mmol) in DMF (10 mL) were added MeOH (0.50 mL, 12 mmol) and N-ethyldiisopropylamine (0.86 mL, 4.8 mmol). Further, the system was degassed with CO gas for 10 minnuts, and the mixture was stirred at room temperature for 5 h under CO atmosphere (1 atm). Then the reaction was quenched with saturated ammonium chloride aqueous solution and extracted with ether for three times, the combined organic layer was washed with 1 brine, dried over Na_2SO_4, filtered, and concentrated on a rotary evaporator. The crude product was purified by silica gel column chromatography using hexane/ethyl acetate (4/1) to afford the corresponding product (*R,R*)-**IIa** (1.10 g, 87% yield).

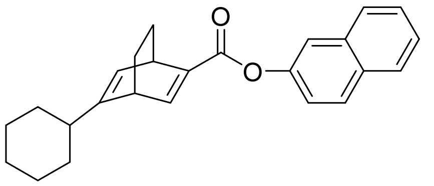


Ligand (*R,R*)-**IIa**, $[\alpha]^{25}_{D}$ = -38.5 (c 2.22, $CHCl_3$), ^1H NMR ($CDCl_3$, 400 MHz) δ 1.49-1.57 (m, 4H), 3.75 (s, 3H), 4.25-4.31 (m, 2H), 6.58 (dd, J = 1.9, 6.4Hz, 1H), 7.23-7.26 (m, 1H), 7.30-7.34 (m, 2H), 7.37-7.41 (m, 3H). ^{13}C NMR ($CDCl_3$, 151 MHz) δ 24.6, 25.2, 37.2, 40.5, 51.6, 124.9, 127.1, 128.6, 129.4, 137.7, 139.4, 145.2, 145.6, 165.3.HRMS (ESI) Calcd for $C_{16}H_{17}O_2$ $[M+H]^+$ 241.1223, found 241.1228.

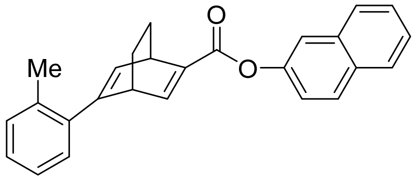
Ligand **I**: To a solution of LDA (22.0 mmol) in THF (25 ml), freshly prepared from diisopropylamine (2.89 mL, 22.0 mmol) and n-butyllithium (2.5 M in hexane, 8.8 mL, 22.0 mmol) at 0 °C under N_2 for 10 minutes. The resulting mixture was cooled to -78 °C. A solution of 2-cyclohexenone (1.92 g, 20.0 mmol) in THF (25 mL) was added dropwise, and stirred for another 30 minutes at -78 °C. Then A solution of Tf_2NPh (7.15 g, 20.0 mmol) dissolved in THF (30 mL) was slowly added for 10 minutes. After that, the reaction mixture was warmed to 0 °C and stirred at 0 °C until the reaction was judged complete according to TLC. The solvent was evaporated, quenched by saturated ammonium chloride aqueous solution, and extracted with ether for three times, the combined organic layer was dried over MgSO4, and concentrated under vacuum to give a colorless oil, which directly used in copper-catalyzed cross-coupling reaction.

CuI (20 mg, 0.1 mmol) was added to a solution of the above dienyl triflate in THF (10 mL) at 0 °C under nitrogen. Grignard reagent (30 mmol) was then added slowly by syringe for 20 minutes. The mixture was stirred for a further 30 minutes. Then the reaction was quenched with saturated ammonium chloride aqueous solution and extracted with ether for three times, the combined organic layer was dried over MgSO4, filtered, dried over Na_2SO_4, and concentrated under vacuum. Considering the stability of the substituted cyclohexadiene products, which was directly used for synthesis of **Ib**-**Ie** without further purification.

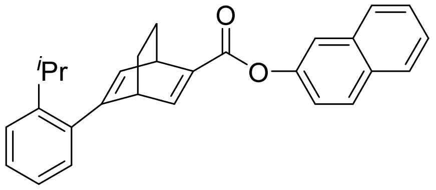
To a solution of the above crude substituted cyclohexadiene, 2-naphthyl propiolate (3.5 g, 17.87 mmol) in CH_2Cl_2 (60 mL) and BHT (10.0 mg) was slowly added Me_2AlCl (1.0 M in heptane, 20.0 mL, 20.0 mmol) at –78 °C, and the mixture was warmed to room temperature and stirred for 16 h. Then the solution was carefully poured into a vigorously stirred, ice-cooled aqueous solution of 1N HCl (70 mL). Then the resulting solution was extracted with CH_2Cl_2 (50 mL) for three times, the combined organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification of the residue by column chromatography on silica gel with hexane/EtOAc (20/1~5/1) gave corresponding ligands *dl*-**I**.



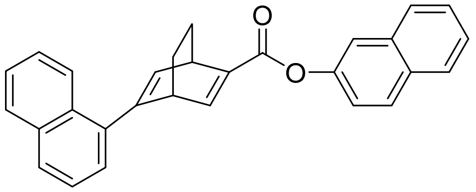
Ligand *dl*-**Ib**, (4.2 g, 65% yield), ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.09-1.25 (m, 3H), 1.26-1.39 (m, 2H), 1.39-1.48 (m, 4H), 1.71-1.84 (m, 5H), 2.03-2.09 (m, 1H), 3.75-3.77 (m, 1H), 4.27 (dd, J = 2.1, 6.3 Hz, 1H), 5.97 (d, J = 6.3 Hz, 1H), 7.29 (dd, J = 2.3, 8.6 Hz, 1H), 7.45-7.51 (m, 2H), 7.59-7.62 (m, 2H), 7.80-7.82 (m, 1H), 7.84-7.88 (m, 2H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 24.7, 25.6, 26.4, 31.4, 31.5, 36.7, 41.3, 42.0, 118.7, 121.5, 124.6, 125.5, 126.4, 127.6, 127.8, 129.3, 131.4, 133.9, 139.4, 148.2, 148.8, 151.6, 163.5. HRMS (ESI) Calcd for $C_{25}H_{27}O_2$ $[M+H]^+$ 59.2006, found 359.2006.



Ligand *dl*-**Ic**, (5.1 g, 77% yield). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.53-1.74 (m, 4H), 2.36 (s, 3H), 4.04-4.06 (m, 1H), 4.49-4.51 (m, 1H), 6.40 (dd, J = 1.8, 6.3 Hz, 1H), 7.16-7.18 (m, 1H), 7.21-7.26 (m, 3H), 7.36 (dd, J = 2.3, 8.8 Hz, 1H), 7.49-7.56 (m, 2H), 7.69 (d, J = 2.2 Hz, 1H), 7.81 (dd, J = 1.9, 6.4 Hz, 1H), 7.85-7.87 (m, 1H), 7.88-7.93 (m, 2H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 20.8, 24.5, 25.4, 37.1, 43.9, 118.7, 121.5, 125.7, 125.8, 126.6, 127.3, 127.7, 127.8, 128.4, 129.4, 130.5, 131.5, 131.5, 13.3.9, 135.6, 139.1, 139.3, 146.3, 147.9, 148.7, 163.5. HRMS (ESI) Calcd for $C_{26}H_{23}O_2$ $[M+H]^+$ 367.1703, found 367.1693. Resolution of *dl*-**Ic** was carried out by use of a chiral stationary phase column [Chiral IG (2.0 cm I.D. × 25 cm), hexane/CH_2Cl_2/ IPA= 89:10/1 to give both enantiomers (*S*,*S*)-**Ic** and (*R*,*R*)-**Ic**, quantitatively. t_1 = 86 min for (*S*,*S*)-**Ic**, t_2 = 97 min for (*R*,*R*)-**Ic**. $[\alpha]^{25}_D$ = +78.1 (c 0.93, CHCl$_3$) for (*R*,*R*)-**Ic**.



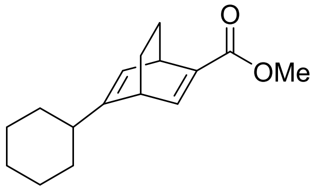
Ligand *dl*-**Id** (5.0 g, 71% yield). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.1 (d, J = 6.8 Hz, 3H), 1.31 (d, J = 6.8 Hz, 3H), 1.51-1.72 (m, 4H), 3.01-3.07 (m, 1H), 3.95 (dd, J = 1.8, 6.3 Hz, 1H), 4.46 (dd, J = 1.9, 6.1 Hz, 1H), 6.31 (dd, J = 1.5, 6.3 Hz, 1H),7.07 (d, J = 7.6 Hz, 1H), 7.16-7.20 (m, 1H), 7.29-7.36 (m, 3H), 7.47-7.53 (m, 2H), 7.67 (d, J = 1.6 Hz, 1H), 7.76-7.78 (m, 1H), 7.83-7.85 (m, 1H), 7.87-7.91 (m, 2H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 24.1, 24.4, 24.5, 25.3, 29.9, 37.1, 44.8, 118.7, 121.5, 125.5, 125.6, 125.6, 126.5, 127.7, 127.8, 127.8, 128.7, 129.3, 130.8, 131.4, 133.9, 138.6, 138.9, 146.2, 146.7, 147.7,148.7, 163.5. HRMS (ESI) Calcd for $C_{28}H_{27}O_2$ $[M+H]^+$ 395.2006, found 395.2015. Resolution of *dl*- **Id** was carried out by use of a chiral stationary phase column [Chiral IG (2.0 cm I.D. × 25 cm), hexane/CH_2Cl_2/ IPA= 89:10/1 to give both enantiomers (*S*,*S*)-**Id** and (*R*,*R*)-**Id**, quantitatively. t_1 = 41 min for (*S*,*S*)-**Id**, t_2 = 49 min for (*R*,*R*)-**Id**. $[\alpha]^{25}_D$ = +93.5 (c 0.92, CHCl$_3$) for (*R*,*R*)-**Id**.



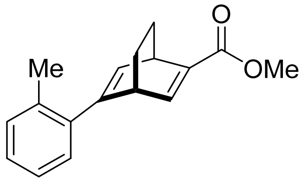
Ligand *dl*-**Ie** (6.2 g, 87% yield). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.57-1.82 (m, 4H), 4.16-4.19 (m, 1H), 4.57-4.59 (m, 1H), 6.60 (dd, J = 1.8, 6.3 Hz, 1H), 7.34 (dd, J = 1.1, 7.0 Hz, 1H), 7.39 (dd, J = 2.3, 8.8 Hz, 2H), 7.46-7.55 (m, 5H), 7.71 (d, J = 2.2 Hz, 1H), 7.82-7.95 (m, 7H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 24.8, 25.5, 37.4, 44.8, 118.8, 121.5, 125.2, 125.4, 125.7, 125.7, 125.9, 126.1, 126.6, 127.7, 127.8, 128.5, 129.4, 131.5, 131.5, 132.6, 133.9, 137.6, 139.3, 145.4, 147.8, 148.7, 163.5. HRMS (ESI) Calcd for $C_{29}H_{23}O_2$ $[M+H]^+$ 403.1693, found 403.1695. Resolution of *dl*-**Ie** was carried out by use of a chiral stationary phase column [Chiral IG (2.0 cm I.D.×25 cm), hexane/CH_2Cl_2/ IPA= 89:10/1 to give both enantiomers (*S*,*S*)-

Ie and (*R,R*)-**Ie**, quantitatively. t_1 = 41 min for (*S,S*)-**Ie**, t_2 = 53 min for (*R,R*)-**Ie**. ([α]^{25} $_D$ +125.7 (c 0.69, CHCl$_3$) for (*R,R*)-**Ie**.

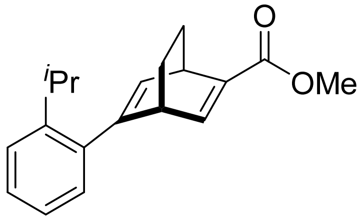
Ligand **II**: A solution of the corresponding (*R,R*)-**I** or *dl*-**Ic** (2.0 mmol) and NaOMe (216 mg, 4.0 mmol) in MeOH (8 mL) was stirred at room temperature for 24 h. The reaction mixture was concentrated under vacuum. Purification of the residue by column chromatography on silica gel with hexane/EtOAc (10/1) gave corresponding ligands **II**.



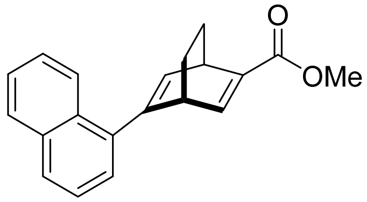
Compound *dl*-**IIb** (467.4 mg, 95% yield), ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.06-1.15 (m, 3H), 1.20-1.34 (m, 6H), 1.64-1.75 (m, 5H), 1.94-2.00 (m, 1H), 3.62-3.64 (m, 1H), 3.71 (s, 3H), 4.08 (dd, J = 1.8, 6.3Hz, 1H), 5.83-5.86 (m, 1H), 7.26 (dd, J = 2.1, 6.5Hz, 1H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 24.6, 25.4, 26.3, 31.3, 31.4, 36.5, 41.0, 41.9, 51.4, 124.4, 139.8, 145.9, 151.7, 165.5. HRMS (ESI) Calcd for $C_{16}H_{23}O_2$ [M+H]$^+$ 247.1693, found 247.1701.



Ligand (*R,R*)-**IIc** (467.3 mg, 92% yield), [α]$^{25}_D$ = +61.0 (c 1.10, CHCl$_3$). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.39-1.63 (m, 4H), 2.26 (s, 3H), 3.79 (s, 3H), 3.89-3.92 (m, 1H), 4.30-4.33 (m, 1H), 6.26-6.28 (m, 1H), 7.06-7.11 (m, 1H), 7.13-7.19 (m, 3H), 7.46 (dd, J = 1.87, 6.39 Hz, 1H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 20.6, 24.4, 25.2, 36.9, 43.6, 51.5, 125.7, 127.1, 128.2, 130.3, 131.3, 135.5, 139.4, 139.4, 145.6, 146.4, 165.4. HRMS (ESI) Calcd for $C_{17}H_{19}O_2$ [M+H]$^+$ 255.1380, found 255.1391.

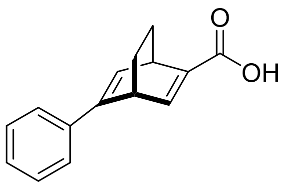


Ligand (*R,R*)-**IId** (530.2 mg, 94% yield), [α]$^{25}_D$ = +68.1 (c 1.62, CHCl$_3$), ^{1}H NMR (CDCl$_3$, 400 MHz) δ 1.12 (d, J = 6.8 Hz 3H), 1.25 (d, J = 6.9 Hz, 3H), 1.38-1.49 (m, 2H), 1.51-1.66 (m, 2H), 2.92-2.99 (m, 1H), 3.79 (s, 1H), 4.29-4.31 (m, 1H), 6.20-6.22 (m, 1H), 6.99-7.01 (m, 1H), 7.11-7.15 (m, 1H), 7.24-7.31 (m, 2H), 7.45-7.47 (m, 1H). ^{13}C NMR (CDCl$_3$, 101 MHz) δ 23.9, 24.3, 24.4, 25.1, 29.7, 36.9, 44.4, 51.5, 125.3, 125.4, 127.5, 128.6, 130.7, 138.7, 139.2, 145.4, 146.3, 146.6, 165.4. HRMS (ESI) Calcd for $C_{28}H_{27}O_2$ [M+H]$^+$ 283.1693, found 283.1694.

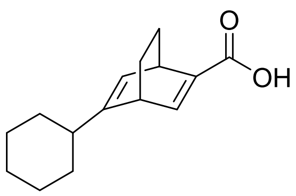


Ligand (*R,R*)-**IIe** (551.0 mg, 95% yield), [α]$^{25}_D$ = +78.8 (c 0.67, CHCl$_3$), ^{1}H NMR (CDCl3, 400 MHz) δ 1.45-1.55 (m, 2H), 1.62-1.71 (m, 2H), 3.82 (S, 3H), 4.02-4.06 (m, 1H), 4.39-4.41 (m, 1H), 6.47-6.49 (m, 1H), 7.25-7.27 (m, 1H), 7.41-7.51 (m, 3H), 7.58-7.60 (m, 1H), 7.77 (d, J = 8.2Hz, 1H), 7.82-7.87 (m, 2H). ^{13}C NMR (CDCl3, 101 MHz) δ 24.7, 25.3, 37.2, 44.4, 51.6, 125.1, 125.3, 125.7, 125.9, 127.6, 128.4, 131.5, 132.5, 133.8, 137.8, 139.7, 145.5, 145.5, 165.4. HRMS (ESI) Calcd for $C_{20}H_{19}O_2$ [M+H]$^+$ 291.1380, found 291.1379.

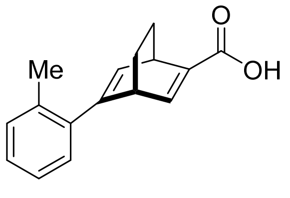
Ligand **III**: A solution of the corresponding (*R,R*)-**II** or *dl*-**IIc** (1.0 mmol) in MeOH (8 mL) and NaOH (160 mg, 4.0 mmol) was stirred at 60 °C for 8 h. Then 1N HCl (10 mL) was added in to the solution. The resulting solution was extracted with CH_2Cl_2 (10 mL) for three times, the combined organic layer was dried over $MgSO_4$, filtered, and concentrated under vacuum, which directly used in next step (quantitative yields for all cases).



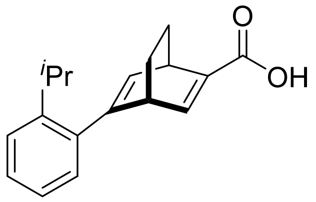
Ligand (*R,R*)-**IIIa**, $[\alpha]^{25}_{D}$ = -35.6 (c 0.62, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47-1.63 (m, 4H), 4.31-4.33 (m, 2H), 6.62 (dd, J = 1.9, 6.4Hz, 1H), 7.26-7.28 (m, 1H), 7.34-7.37 (m, 2H), 7.41-7.43 (m, 2H), 7.59 (dd, J = 1.9, 6.5Hz, 1H). ^{13}C NMR (CDCl3, 101 MHz) δ 24.5, 25.2, 36.9, 40.7, 124.9, 127.2, 128.6, 129.3, 138.9, 145.0, 148.4, 169.7. HRMS (ESI) Calcd for $C_{15}H_{15}O_2$ $[M+H]^+$ 227.1067, found 227.1069.



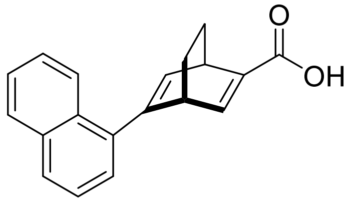
Compound *dl*-**IIIb**, ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88-1.19 (m, 3H), 1.22-1.37 (m, 6H), 1.65-1.74 (m, 5H), 1.96-2.01 (m, 1H), 3.67 (d, J = 6.4Hz, 1H), 4.07 (d, J = 6.2Hz, 1H), 5.87 (d, J = 6.3Hz, 1H), 7.42 (dd, J = 1.9, 6.5Hz, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 24.5, 25.4, 26.3, 31.3, 31.5, 36.2, 41.2, 41.9, 124.5, 139.4, 148.8, 151.4, 170.2. HRMS (ESI) Calcd for $C_{15}H_{21}O_2$ $[M+H]^+$ 233.1536, found 233.1544.



Ligand (*R,R*)-**IIIc**, $[\alpha]^{25}_{D}$ = +41.2 (c 1.65, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.41-1.66 (m, 4H), 2.26 (s, 3H), 3.94 (d, J = 6.1Hz, 3H), 4.31 (d, J = 6.1Hz, 1H), 6.29 (d, J = 6.3Hz, 1H), 7.08-7.09 (m, 1H), 7.14-7.20 (m, 3H), 7.64 (d, J = 6.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 20.6, 24.3, 25.2, 36.6, 43.8, 125.7, 127.1, 128.2, 130.4, 131.3, 135.5, 139.0, 139.3, 146.2, 148.6, 170.2. HRMS (ESI) Calcd for $C_{16}H_{17}O_2$ $[M+H]^+$ 241.1223, found 241.1223.



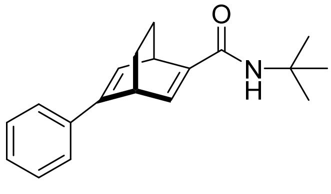
Ligand (*R,R*)-**IIId** $[\alpha]^{25}_{D}$ = +68.7 (c 1.54, $CHCl_3$), ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (d, J = 6.8 Hz 3H), 1.26 (d, J = 6.8 Hz, 3H), 1.40-1.50 (m, 2H), 1.53-1.65 (m, 2H), 2.91-2.98 (m, 1H), 3.86-3.88 (m, 1H), 4.29-4.31 (m, 1H), 6.22-6.24 (m, 1H), 7.01-7.02 (m, 1H), 7.12-7.16 (m, 1H), 7.25-7.32 (m, 2H), 7.62-7.65 (m, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 24.0, 24.3, 24.4, 25.1, 29.8, 36.7, 44.7, 125.4, 125.5, 127.6, 128.6, 130.7, 138.6, 138.9, 146.2, 146.7, 148.5, 170.3. HRMS (ESI) Calcd for $C_{18}H_{21}O_2$ $[M+H]^+$ 269.1536, found 269.1545.



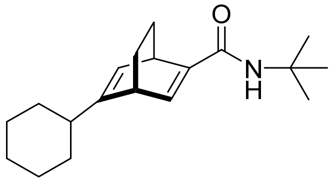
Ligand (*R,R*)-**IIIe**, $[\alpha]^{25}_{D}$ = +83.1 (c 0.68, $CHCl_3$), ^{1}H NMR (CDCl3, 400 MHz) δ 1.48-1.61 (m, 2H), 1.64-1.74 (m, 2H), 4.09 (dd, J = 1.9,6.3Hz, 1H), 4.41 (dd, J = 1.9,6.2Hz, 1H), 6.54 (dd, J = 1.7, 6.3Hz, 1H), 7.26-7.28 (m, 1H), 7.42-7.51 (m, 3H), 7.77-7.79 (m, 2H), 7.82-7.87 (m, 2H). ^{13}C NMR (CDCl3, 101 MHz) δ 24.6, 25.3, 36.9, 44.6, 125.1, 125.3, 125.6, 125.8, 126.0, 127.6, 128.4, 131.4, 132.4, 133.8, 137.6, 139.2, 145.2, 148.4, 170.1. HRMS (ESI) Calcd for $C_{19}H_{17}O_2$ $[M+H]^+$ 277.1223, found 277.1234.

Ligand **IV**: To a solution of the carboxylic acid **III** (0.5 mmol) and DMF (7.5 μL, 0.1 mmol) in CH_2Cl_2 (0.2 mL) was added dropwise oxalyl chloride (85 μL, 1.0 mmol) at 0 °C, and the mixture was warmed to room temperature and stirred for 3 h. The solvent was removed under vacuum, and the residue was dissolved in THF (1.0 mL). To a solution of the corresponding amine (1.2 mmol) in THF (0.8 mL) was added the solution of the acid chloride dropwise at

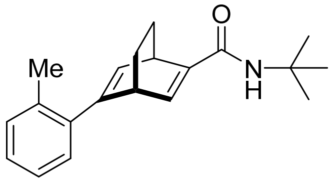
0 °C. The mixture was stirred at room temperature for 20 h. saturated aqueous Na_2CO_3 solution was added, and the mixture was extracted with diethyl ether for three times. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification of the residue by column chromatography on silica gel with hexane/EtOAc (10/1) gave corresponding ligands **IV**.



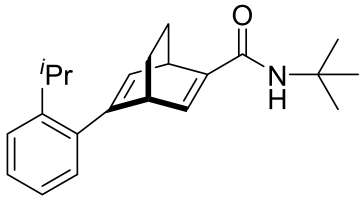
Ligand (*R*,*R*)-**IVa** (133.5 mg, 96% yield), $[\alpha]^{25}_{D}$ = -97.6 (c 0.05, $CHCl_2$), ^1H NMR ($CDCl_3$, 400 MHz) δ 1.41 (s, 9H), 1.50-1.50 (m, 4H), 4.21-4.26 (m, 2H), 5.57 (s, 1H), 6.61 (dd, J = 2.0, 6.4Hz, 1H), 6.84 (dd, J = 1.8, 6.4Hz, 1H), 7.23-7.27 (m, 1H), 7.32-7.36 (m, 2H), 7.40-7.42 (m, 2H). ^{13}C NMR (CDCl3, 101 MHz) δ 24.9, 25.4, 28.9, 37.5, 40.0, 51.1, 124.8, 127.0, 128.5, 129.5, 136.3, 137.7, 144.7, 145.6, 165.3. HRMS (ESI) Calcd for $C_{19}H_{21}NO$ $[M+H]^+$ 282.1852, found 282.1855.



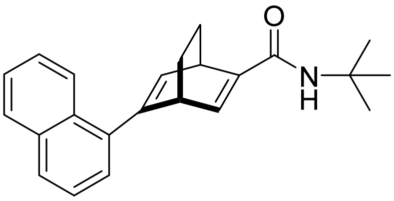
Compound *dl*-**IVb** (133.5 mg, 93% yield), ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87-1.17 (m, 3H), 1.20-1.32 (m, 6H), 1.35 (s, 9H), 1.64-1.77 (m, 5H), 1.93-1.99 (m, 1H), 3.55 (d, J = 4.6Hz, 1H), 3.96 (d, J = 4.0Hz, 1H), 5.51 (s, 1H), 5.83 (d, J = 6.2Hz, 1H), 6.71 (t, 1H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 24.9, 25.6, 26.3, 28.9, 31.2, 31.4, 36.8, 40.5, 41.9, 50.9, 124.3, 136.9, 144.8, 152.1, 165.3.HRMS (ESI) Calcd for $C_{19}H_{30}NO$ $[M+H]^+$ 288.2322, found 288.2333. Resolution of *dl*- **IVb** was carried out by use of a chiral stationary phase column [Chiral IG (2.0 cm I.D. × 25 cm), hexane/IPA= 98:2 to give both enantiomers (*S*,*S*)-**IVb** and (*R*,*R*)-**IVb**, quantitatively. t_1 = 34 min for (*R*,*R*)-**IVb**, t_2 = 42 min for (*S*,*S*) -**IVb**. $[\alpha]^{25}_{D}$ = +8.5 (c 0.85, $CHCl_3$) for (*R*,*R*)-**IVb**.



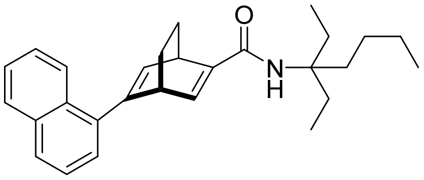
Ligand (*R*,*R*)-**IVc** (143.1 mg, 97% yield), $[\alpha]^{25}_{D}$ = +59.5 (c 0.77, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.41(s, 4H), 1.46-1.58 (m, 4H), 2.26 (s, 3H), 3.82-3.84 (m, 1H), 4.18-4.20 (m, 1H), 5.59 (s, 1H), 6.25 (dd, J = 1.7, 6.3Hz, 1H), 6.89 (dd, J = 1.9, 6.3Hz, 1H), 7.05-7.07 (m, 1H), 7.12-7.17 (m, 3H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 20.7, 24.6, 25.4, 28.9, 37.3, 43.1, 51.2, 125.6, 127.0, 128.2, 130.3, 131.5, 135.4, 136.6, 139.5, 144.4, 146.7, 165.2. HRMS (ESI) Calcd for $C_{20}H_{26}NO$ $[M+H]^+$ 296.2009, found 296.2022.



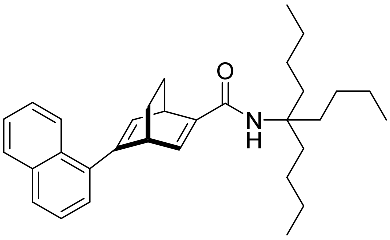
Ligand (*R*,*R*)-**IVd** (151.2 mg, 94% yield), $[\alpha]^{25}{}_{D}$ +60.9 (c 0.97, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.12 (d, J = 6.8 Hz 3H), 1.24 (d, J = 6.9 Hz, 3H), 1.42 (s, 1H), 1.46-1.61 (m, 3H), , 2.93-3.03 (m, 1H), 3.75-3.77 (m, 1H), 4.16-4.18 (m, 1H), 5.61 (s, 1H), 6.18-6.20 (m, 1H), 6.89-6.91 (m, 1H), 6.99-7.01 (m, 1H), 7.09-7.13 (m, 1H), 7.22-7.30 (m, 2H),. ^{13}C NMR ($CDCl_3$, 101 MHz) δ 24.1, 24.5, 24.6, 25.3, 28.2, 29.0, 29.7, 37.3, 44.1, 51.2, 125.4, 125.5, 127.4, 128.6, 130.8, 136.6, 138.8, 144.2, 146.6, 165.1. HRMS (ESI) Calcd for $C_{22}H_{30}NO$ $[M+H]^+$ 324.2322, found 324.2336.



Ligand (*R*,*R*)-**IVe** (158.9 mg, 96% yield), $[\alpha]^{25}_{D}$ = +79.1 (c 0.69, $CHCl_3$), ^1H NMR (CDCl3, 400 MHz) δ 1.44 (s, 9H), 1.55-1.65 (m, 4H), 3.98-4.00 (m, 1H), 4.27-4.29 (m, 1H), 5.67 (s, 1H), 6.47 (dd, J = 1.8, 6.3Hz, 1H), 7.02 (dd, J = 1.9, 6.3Hz, 1H), 7.25-7.27 (m, 1H), 7.40-7.48 (m, 3H), 7.76 (d, J = 8.2Hz, 1H), 7.84-7.88 (m, 2H). ^{13}C NMR (CDCl3, 101 MHz) δ 25.0, 25.5, 29.0, 37.6, 44.0, 51.2, 125.0, 125.3, 125.7, 125.8, 125.9, 127.4, 128.4, 131.4, 132.6, 133.9, 136.5, 137.9, 144.7, 145.8, 165.1. HRMS (ESI) Calcd for $C_{23}H_{26}NO$ $[M+H]^+$ 332.2009, found 332.2010.

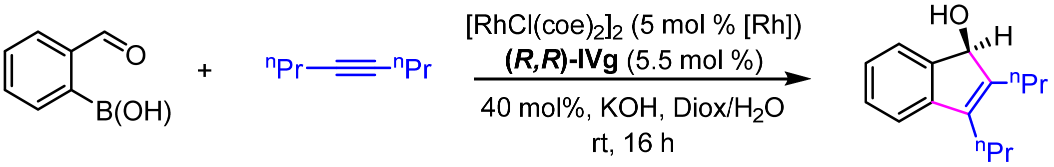


Ligand (*R*,*R*)-**IVf** (156.4 mg, 78% yield), $[\alpha]^{25}_{D}$ = +48.6 (c 0.84, $CHCl_3$), ^1H NMR (CDCl3, 400 MHz) δ 0.81-0.88 (m, 6H), 0.88-0.94 (m, 3H), 1.19-1.26 (m, 3H), 1.28-1.41 (m, 4H), 1.49-1.53 (m, 3H), 1.68-1.80 (m, 4H), 4.00 (dd, J = 1.9, 6.2Hz, 1H), 4.26 (dd, J = 2.0, 6.3Hz, 1H), 5.26 (s, 1H), 6.47 (dd, J = 1.8, 6.2Hz, 1H), 7.03 (dd, J = 1.8, 6.3Hz, 1H), 7.26-7.27 (m, 1H), 7.40-7.50 (m, 3H), 7.76 (d, J = 8.2Hz, 1H), 7.84-7.89 (m, 2H). ^{13}C NMR (CDCl3, 101 MHz) δ 7.7, 14.2, 23.1, 25.0, 25.4, 25.6, 27.2, 29.7, 34.0, 37.7, 44.0, 59.4, 125.0, 125.3, 125.7, 125.8, 125.9, 127.4, 128.4, 131.4, 132.5, 133.9, 136.3, 137.9, 144.8, 145.8, 164.9. HRMS (ESI) Calcd for $C_{28}H_{36}NO$ $[M+H]^+$ 402.2791, found 402.2804.



Ligand (*R,R*)-**IVg** (173.7 mg, 76% yield), $[\alpha]^{25}_{D}$ = +59.3 (c 1.00, $CHCl_3$), ^1H NMR ($CDCl_3$, 400 MHz) δ 0.93 (t, 9H), 1.17-1.25 (m, 6H), 1.30-1.37 (m, 6H), 1.50-1.53 (m, 2H), 1.63-1.75 (m, 8H), 3.99 (d, J = 4.6Hz, 1H), 4.25 (d, J = 4.6Hz, 1H), 5.23 (s, 1H), 6.47 (d, J = 5.0Hz, 1H), 7.01-7.03 (m, 1H), 7.27 (d, J = 6.8Hz, 1H), 7.40-7.48 (m, 3H), 7.76 (d, J = 8.2Hz, 1H), 7.84-7.89 (m, 2H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 14.2, 23.1, 25.0, 25.5, 25.6, 35.1, 37.7, 44.0, 58.9, 125.0, 125.3, 125.7, 125.8, 127.4, 128.4, 131.4, 132.6, 133.9, 136.2, 144.9, 145.8, 164.8. HRMS (ESI) Calcd for $C_{32}H_{44}NO$ $[M+H]^+$ 458.3417, found 458.3426.

4. A typical procedure for rhodium-catalyzed domino reaction of 2-formyl phenylboric acid (1a) with 4-octyne (2a)

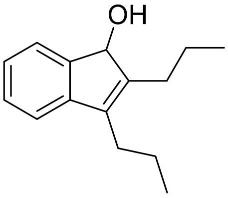


1a **2a** **3aa**

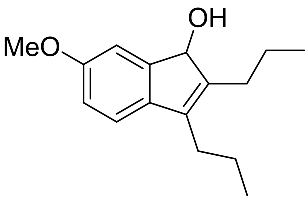
Scheme S2

$[RhCl(coe)_2]_2$ (2.7 mg, 0.0038 mmol, 5 mol% of Rh) and (R,R)-IVg * (3.8 mg, 0.0083 mmol) were placed in an oven dried 10 mL schlenk tube. The tube was evacuated and re-filled with nitrogen gas for 3 cycles. Anhydrous 1,4-dioxane (0.20 mL) was added, and the resulting mixture was stirred at room temperature for 10 min. To the mixture, 4-octyne (**2a**, 16.5 mg, 0.15 mmol, 1.0 equiv.), 2-formyl phenylboric acid (**1a**, 34.8 mg, 0.225 mmol, 1.5 equiv.), the freshly degassed H_2O (0.025 mL), 40 mol% KOH (0.060 mmol, 40.0 mol%) and 1,4-dioxane (0.30 mL) were added. The resulting mixture was stirred at rt for 16 h. The mixture was passed through a short pad of silica gel with ethyl acetate as eluent. The organic solution was concentrated under reduced pressure, and the residue was purified by flash chromatography on silica gel using 10/1 PE/EA as eluent to give the target compound **3aa** (29.6 mg, 91% yield). Subsequently, the ee value of the target product **3aa** was determined by HPLC.

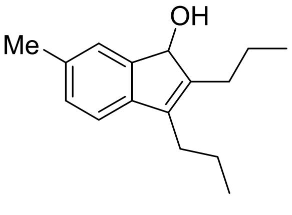
5. Characterization of products



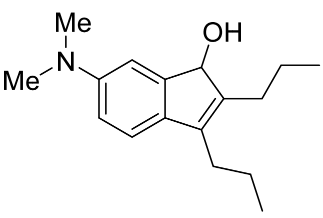
Compound **3aa** (29.6 mg, 91% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 90/10, flow 0.7 mL/min, 256 nm, t_{major} = 7.7 min, t_{minor} = 8.4 min. $[\alpha]^{25}_{D}$ +9.5 (c 0.80, $CHCl_3$) for **3aa** of 92% ee (S). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 0.7 mL/min, 256 nm, t_{major} = 10.2 min, t_{minor} = 7.4 min. $[\alpha]^{25}_{D}$ -5.8 (c 0.54, $CHCl_3$) for **3aa** of 90% ee (R). ^1H NMR ($CDCl_3$, 600 MHz) δ 0.98 (td, J = 2.76, 7.32 Hz, 6H), 1.50-1.65 (m, 4H), 2.38-2.44 (m, 4H), 4.97 (d, J = 9.47 Hz, 1H), 7.13-7.17 (m, 2H), 7.25-7.27 (m, 1H), 7.47 (d, J = 7.17 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 14.4, 21.8, 22.9, 27.3, 27.8, 118.7, 123.1, 124.9, 128.3, 137.9, 144.3, 145.0, 145.2. HRMS (ESI) Calcd for $C_{15}H_{20}O$ $[M+H]^+$ 217.1587, found 217.1584.



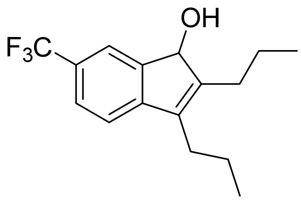
Compound **3ba** (28.0 mg, 76% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 256 nm, t_{major} = 9 min, t_{minor} = 8 min. $[\alpha]^{25}_{D}$ +20.2 (c 0.47, $CHCl_3$) for **3ba** of 89% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 0.97 (td, J = 2.19, 7.35 Hz, 6H), 1.49-164 (m, 4H), 2.34-2.41 (m, 4H), 3.82 (s, 3H), 4.94 (s, 1H), 6.78 (dd, J = 2.40, 8.14 Hz, 1H), 7.04 (d, J = 8.14 Hz 1H), 7.10 (d, J = 2.29 Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 14.3, 14.3, 21.8, 22.9, 27.4, 27.7, 55.6, 110.4, 112.9, 119.1, 137.0, 137.6, 143.0, 146.9, 158.1. HRMS (ESI) Calcd for $C_{16}H_{22}O_2$ $[M+H]^+$ 247.1693, found 247.1692.



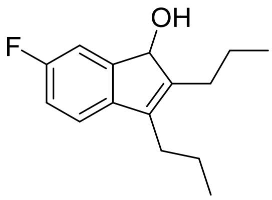
Compound **3ca** (28.0 mg, 81% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 98/2, flow 1 mL/min, 256 nm, t_{major} = 5 min, t_{minor} = 8 min. $[\alpha]^{25}_{D}$ +14.7 (c 0.47, $CHCl_3$) for **3ca** of 95% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 0.95-1.00 (m, 6H), 1.55-1,59 (m, 4H), 2.37-2.41 (m, 7H), 4.94 (s, 1H), 6.96 (d, J = 9.45 Hz, 2H), 7.35 (d, J = 7.26 Hz 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 14.3, 14.4, 21.7, 21.8, 22.9, 27.3, 27.8, 119.6, 122.8, 125.4, 137.8, 138.1, 142.2, 144.5, 145.5. HRMS (ESI) Calcd for $C_{16}H_{22}O$ $[M+H]^+$ 231.1743, found 231.1742.



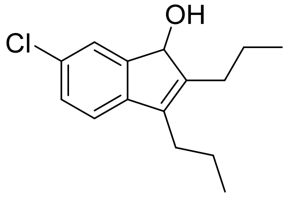
Compound **3da** (31.1 mg, 80% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 256 nm, t_{major} = 11 min, t_{minor} = 10 min. $[\alpha]^{25}_{D}$ +45.7 (c 0.47, $CHCl_3$) for **3da** of 84% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 0.97 (q, J = 6.57 Hz, 6H), 1.54-1.65 (m, 4H), 2.33-2.40 (m, 4H), 2.94 (s, 6H), 4.93 (s, 1H), 6.62 (dd, J = 2.23, 8.16 Hz, 1H), 7.01-7.03 (m, 2H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 14.3, 14.4, 21.9, 23.0, 27.4, 27.7, 41.3, 109.7, 111.9, 119.0, 133.6, 137.8, 141.3, 146.7, 149.3. HRMS (ESI) Calcd for $C_{17}H_{25}NO$ $[M+H]^+$ 260.2009, found 260.2007.



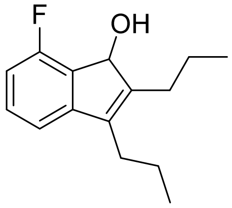
Compound **3ea** (34.1 mg, 80% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 5 min, t_{minor} = 7 min. $[\alpha]^{25}{}_{D}$ +1.8 (c 0.51, CHCl$_3$) for **3ea** of 96% ee (S). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.98 (t, J = 7.31 Hz, 6H), 1.52-1.67 (m, 4H), 2.42-2.44 (m, 4H), 5.01 (s, 1H), 7.22 (d, J = 7.80 Hz, 2H), 7.53 (d, J = 7.77 Hz, 1H), 7.69 (s, 1H); ^{13}C NMR (CDCl$_3$, 151 MHz) δ 14.3, 14.3, 21.7, 22.8, 27.2, 27.9, 118.6, 119.9, 125.8, 127.2, 137.5, 145.4, 147.7, 148.4. ^{19}F NMR (CDCl$_3$, 565MHz) δ -113.2. HRMS (ESI) Calcd for $C_{16}H_{19}F_3O$ $[M+H]^+$ 285.1461, found 285.1460.



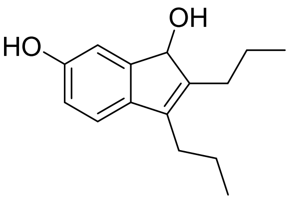
Compound **3fa** (25.6 mg, 73% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 90/10, flow 1 mL/min, 230 nm, t_{major} = 7 min, t_{minor} = 7 min. $[\alpha]^{25}{}_{D}$ +17.7 (c 0.47, CHCl$_3$) for **3fa** of 88% ee (S). ^{1}H NMR (CDCl$_3$, 400 MHz) δ 0.97 (t, Hz, 6H), 1.51-1.64 (m, 4H), 2.35-2.42 (m, 4H), 4.92 (s, 1H), 6.91-6.96 (m, 1H), 7.03-7.06 (m, 1H), 7.17 (d, J = 8.16 Hz, 1H); ^{13}C NMR (CDCl$_3$, 101 MHz) δ 14.3, 21.7, 22.8, 27.3, 27.8, 111.4 (d, J = 23.4 Hz), 114.4 (d, J = 22.5 Hz), 119.2 (d, J = 8.1 Hz), 137.2, 139.9, 144.8 (d, J = 4.0 Hz), 147.2 (d, J = 7.7 Hz), 161.56 (d, J = 243.9). ^{19}F NMR (CDCl$_3$, 565MHz) δ -121.9（m, 1F）.HRMS (ESI) Calcd for $C_{15}H_{19}FO$ $[M+H]^+$ 235.1493, found 235.1490.



Compound **3ga** (28.6 mg, 76% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 98/2, flow 1 mL/min, 256 nm, t_{major} = 7 min, t_{minor} = 5 min. $[\alpha]^{25}{}_{D}$ +10.3 (c 0.37, CHCl$_3$) for **3ga** of 99% ee (S). ^{1}H NMR (CDCl$_3$, 600 MHz) δ 0.97 (td, J = 2.45, 7.35 Hz, 6H), 1.49-1.57 (m, 4H), 2.37-2.40 (m, 4H), 4.95 (d, J = 9.62 Hz, 1H), 7.05 (d, J = 7.95 Hz, 1H), 7.23 (dd, J = 1.86, 7.94 Hz, 1H), 7.43 (d, J = 1.58 Hz, 1H); ^{13}C NMR (CDCl$_3$, 101 MHz) δ 14.3, 14.3, 21.7, 22.8, 27.2, 27.8, 119.5, 123.8, 128.2, 130.9, 137.4, 142.7, 145.6, 146.8. HRMS (ESI) Calcd for $C_{15}H_{19}FO$ $[M+H]^+$ 251.1197, found 251.1202

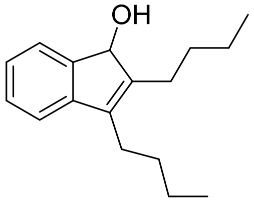


Compound **3ha** (25.0 mg, 71% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 10 min, t_{minor} = 8 min. $[\alpha]^{25}{}_{D}$ +4.0 (c 0.05, CHCl$_2$) for **3ha** of 99% ee (S). ^{1}H NMR (CDCl$_3$, 600 MHz) δ 1 (t, 6H), 1.50-1.69 (m, 4H), 2.39 (t, 2H), 2.51-2.52 (m, 2H), 5.00 (s, 1H), 6.94-6.97 (m, 1H), 7.10-7.14 (m, 1H), 7.27-7.28 (m, 1H); ^{13}C NMR (CDCl$_3$, 151 MHz) δ 14.3, 14.3, 21.8, 22.7, 27.4, 27.7, 74.8, 112.6 (d, J = 2.1 Hz), 114.9 (d, J = 323.3 Hz), 129.3, 130.6 (d, J = 7.1 Hz), 137.8, 146.7 (d, J = 323.3 Hz), 159.0 (d, J = 248.0 Hz).s ^{19}F NMR (CDCl$_3$, 565MHz) δ -121.9 (t, 1F). HRMS (ESI) Calcd for $C_{15}H_{19}FO$ $[M+H]^+$ 235.1493, found 235.1494.

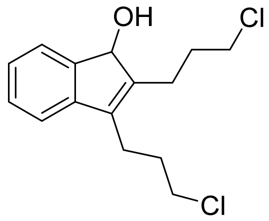


Compound **3ia** (24.5 mg, 70% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 12 min, t_{minor} = 13 min. $[\alpha]^{25}{}_{D}$ +9.7 (c 0.05, CHCl$_2$) for **3ia** of 86% ee (S). ^{1}H NMR (CDCl$_3$, 600 MHz) δ 0.94-0.97 (m, 6H), 1.40-1.63 (m, 4H), 2.32-2.38 (m, 4H), 4.90 (s, 1H), 6.70-6.72 (m, 1H), 6.96-6.97 (m, 1H), 7.01 (d, J=2.1Hz, 1H); ^{13}C NMR (CDCl$_3$, 151 MHz) δ 14.3, 14.3, 21.8, 22.9, 24.8, 27.4, 27.7, 111.8, 114.4, 119.3,

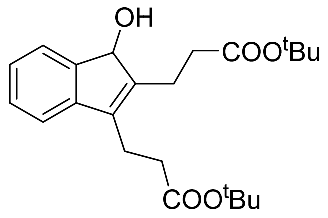
137.7, 142.7, 147.0, 154.0. HRMS (ESI) Calcd for $C_{15}H_{20}O_2$ [M+H]$^+$ 233.1536, found 233.1539.



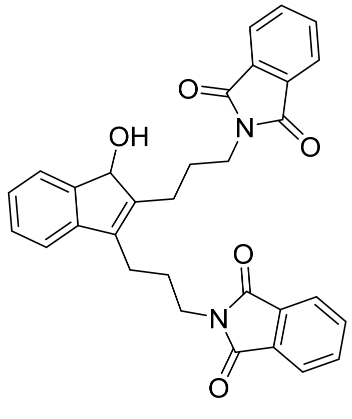
Compound **3ab** (31.1 mg, 85% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 6 min, t_{minor} = 7 min. $[\alpha]^{25}_{D}$ +5.07 (c 0.48, $CHCl_2$) for **3ab** of 86% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 0.94-0.96 (m, 6H), 1.37-1.44 (m, 4H), 1.45-1.62 (m, 4H), 2.40-2.46 (m, 4H), 4.97 (s, 1H), 7.13-7.16 (m, 2H), 7.25-7.28 (m, 1H), 7.47 (d, J = 7.1 Hz, 1H),; ^{13}C NMR ($CDCl_3$, 151 MHz) δ 14.0, 22.9, 25.0, 25.4, 30.8, 31.8, 118.7, 123.0, 124.9, 128.3, 137.9, 144.3, 145.0, 145.1. HRMS (ESI) Calcd for $C_{17}H_{24}O$ [M+H]$^+$ 245.1900, found 245.1903



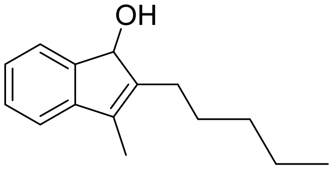
Compound **3ac** (36.3 mg, 85% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 11 min, t_{minor} = 12 min. $[\alpha]^{25}_{D}$ -0.4 (c 0.47, $CHCl_3$) for **3ac** of 77% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.98-2.14 (m, 4H), 2.58-2.67 (m, 4H), 2.57-3.62 (m, 7H), 4.97 (s, 1H), 7.17-7.20 (m, 2H), 7.28-7.31 (m, 1H), 7.48 (d, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 22.3, 23.0, 31.2, 32.1, 44.7, 44.7, 118.8, 123.3, 125.6, 128.6, 137.5, 143.3, 144.3, 144.8. HRMS (ESI) Calcd for $C_{15}H_{18}Cl_2O$ [M+H]$^+$ 285.0807, found 285.0801



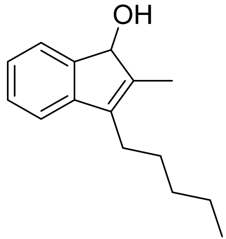
Compound **3ad** (42.3 mg, 81% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 7 min, t_{minor} = 6 min. $[\alpha]^{25}_{D}$ +2.9 (c 0.14, $CHCl_3$) for **3ad** of 71% ee (S). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.43 (s, 9H), 1.44 (s, 9H), 2.41-2.44 (m, 2H), 2.52-2.55 (m, 2H), 2.72-2.76 (m, 4H), 4.95 (s, 1H), 7.16-7.18 (m, 2H), 7.26-7.28 (m, 1H), 7.48 (d, J = 7.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 20.7, 21.0, 24.4, 24.9, 28.1, 28.1, 34.1, 34.8, 80.6, 80.9, 118.7, 123.2, 125.5, 128.3, 137.2, 143.0, 144.2, 144.8, 172.3, 173.2. HRMS (ESI) Calcd for $C_{23}H_{32}O_5$ [M+H]$^+$389.2323, found 389.2323。



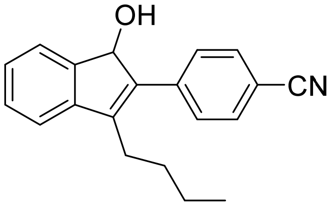
Compound **3ae** (47.9 mg, 63% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 95/5, flow 1 mL/min, 230 nm, t_{major} = 19 min, t_{minor} = 20 min. $[\alpha]^{25}_{D}$ +20.4 (c 0.05, $CHCl_3$) for **3ae** of 71% ee (R). ^1H NMR ($CDCl_3$, 600 MHz) δ 1.92-2.05 (m, 4H), 2.49-2.55 (m, 4H), 3.70-3.73 (m, 4H), 4.99 (d, J= 8.1Hz, 1H), 7.05-7.08 (m, 2H), 7.18 (t, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.66-7.70 (m, 4H), 7.76-7.79 (m, 2H), 7.80-7.82 (m, 2H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 22.8, 23.3, 27.0, 28.0, 37.9, 37.9, 118.7, 123.2, 123.2, 125.3, 128.3, 132.2, 133.8, 133.9, 137.3, 143.2, 144.3, 144.9, 168.3, 168.4. HRMS (ESI) Calcd for $C_{31}H_{26}N_2O_5$ [M+H]$^+$ 507.1914, found 507.1915.



Compound **3af** (20.7 mg, 64% yield). The ee was measured by HPLC (Daicel Chiralpak IC column), hexane/2-propanol = 95/5, flow 0.7 mL/min, 245 nm, t_{major} = 10 min, t_{minor} = 13 min. $[\alpha]^{25}$ D -4.0 (c 0.08, $CHCl_2$) for **3af** of 80% ee (S). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.9 (t, 3H), 1.34-1.35 (m, 4H), 1.48-1.54 (m, 1H), 1.58-1.64 (m, 1H), 1.99 (s, 3H), 2.42 (t, 2H), 4.97 (s, 1H), 7.13-7.17 (m, 2H), 7.27-7.30 (m, 1H), 7.46 (d, J=7.2Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 10.2, 14.1, 22.6, 25.5, 29.1, 31.9, 118.3, 122.9, 125.1, 128.4, 133.4, 144.7, 145.0, 145.1. HRMS (ESI) Calcd for $C_{15}H_{20}O$ $[M+H]^+$ 217.1587, found 217.1592.

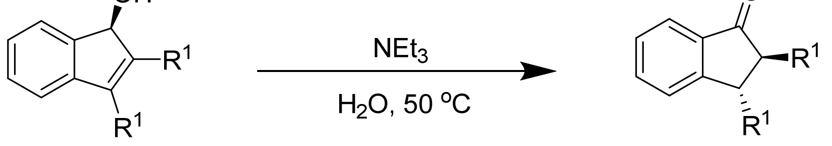


Compound **3af'**(7.1 mg, 22% yield). The ee was measured by HPLC (Daicel Chiralpak IC column), hexane/2-propanol = 95/5, flow 0.7 mL/min, 245 nm, t_{major} = 7 min, t_{minor} = 8 min. $[\alpha]^{25}$ D +13.3 (c 0.09, $CHCl_2$) for **3af'** of 85% ee (S). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.89 (t, 3H), 1.26-1.35 (m, 6H), 1.99 (s, 3H), 2.43 (t, 2H), 4.83 (d, J=6.5Hz, 1H), 7.13-7.15 (m, 2H), 7.26 (s, 1H), 7.46 (d, J=7.4Hz, 1H); ^{13}C NMR ($CDCl_3$, 151 MHz) δ 11.1, 14.1, 22.6, 25.1, 27.9, 31.9, 78.9, 118.5, 123.0, 124.9, 128.3. HRMS (ESI) Calcd for $C_{15}H_{20}O$ $[M+H]^+$ 217.1587, found 217.1590.



Compound **3ag** (30.8 mg, 71% yield). The ee was measured by HPLC (Daicel Chiralpak OD-H column), hexane/2-propanol = 90/10, flow 0.7 mL/min, 256 nm, t_{major} = 14 min, t_{minor} = 17 min. $[\alpha]^{25}$ D -110.6 (c 0.62, $CHCl_3$) for **3ag** of 77% ee (R). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.94 (t, 3H), 1.42-1.46 (m, 2H), 1.60-1.69 (m, 2H), 2.64-2.68 (m, 2H), 5.52 (s, 1H), 7.29-7.32 (m, 1H), 7.34-7.40 (m, 2H), 7.58-7.60 (m, 3H), 7.72 (d, J = 8.4Hz, 2H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 13.8, 23.0, 25.9, 30.7, 110.5, 120.3, 123.5, 126.9, 128.9, 129.3, 132.3, 140.1, 141.3, 143.1, 143.3, 144.6. HRMS (ESI) Calcd for $C_{20}H_{20}NO$ $[M+H]^+$ 290.1539, found 290.1540.

6. Transformations



R1 = ^{n}Pr, (*S*)-**3aa**, 92% ee, 0.10 mmol
R1 = ^{n}Bu, (*S*)-**3ab**, 86% ee, 0.10 mmol

R1 = ^{n}Pr, (*S,S*)-**4a** (95% 89% ee)
R1 = ^{n}Bu, (*S,S*)-**5a**,(62%, 84% ee)

To a Schlenk tube (10 mL) under an atmosphere of nitrogen was added (S)-**3aa** (21.6 mg, 0.1 mmol) in NEt_3 (30.4 mg, 0.3 mmol). The mixture was stirring 16 h at 50 °C. The mixture was washed with $NaHCO_3$ the organic layer was extracted with EA for 3 times, then dried over Na_2SO_4 and concentrated under vacuum to give the compound **4a**[10] in 95% yield. The ee was measured by HPLC (Daicel Chiralpak ODH column), hexane/2-propanol = 95/5, flow 0.7

mL/min, 245 nm, t_{major} = 7 min, t_{minor} = 8 min. $[\alpha]^{25}{}_{D}$ +2.4 (c 0.05, $CHCl_2$) for (S,S)-**4a** of 89% ee (R). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.92-0.97 (m, 6H), 1.40-1.46 (m, 2H), 1.55-1.59 (m, 2H), 1.73-1.79 (m, 2H), 2.35-2.37 (m, 1H), 3.04-3.07 (m, 1H), 7.34-7.36 (m, 1H), 7.46-7.47 (m, 1H), 7.57-7.59 (m, 1H), 7.71 (d, J=7.7Hz, 1H). HRMS (ESI) Calcd for $C_{15}H_{21}O$ $[M+H]^+$ 217.1592, found 290.1587.

To a Schlenk tube (10 mL) under an atmosphere of nitrogen was added **3ab** (24.4 mg, 0.1 mmol) in NEt_3 (40.5 mg, 0.4mmol). The mixture was stirring 16 h at 50 °C. The mixture was washed with $NaHCO_3$ the organic layer was extracted with EA for 3 times, then dried over Na_2SO_4 and concentrated under vacuum to give the compound **5a**[11] in 62% yield. The ee was measured by HPLC (Daicel Chiralpak IC column), hexane/2-propanol = 99.8/0.2, flow 0.5 mL/min, 245 nm, t_{major} = 33 min, t_{minor} = 50 min. $[\alpha]^{25}{}_{D}$ +5.2 (c 0.5, $CHCl_2$) for (S,S)-**5a** of 84% ee. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.90 (q, 6H), 1.28-1.39 (m, 10H), 1.75-1.85 (m, 2H), 2.34-2.37 (m, 1H), 3.05-3.07 (m, 1H), 7.36 (t, 1H), 7.48 (d, J=7.6Hz, 1H). 7.58-7.60 (m, 1H), 7.72 (d, J=7.6Hz, 1H). HRMS (ESI) Calcd for $C_{17}H_{25}O$ $[M+H]^+$ 245.1905, found 290.1901.

7. Reference

[1] Z. Ding and N. Yoshikai. *Org. Lett*., 2010, **12**, 4180-4183.

[2] T. von Hirschheydt, V. Wolfart, R. Gleite, H. Irngartinger, T. Oeser, F. Rominger and F. Eisenträger F, *J. Chem. Soc., Perkin Trans*., 2000, **2**, 175-183.

[3] S. U. Nitinkumar, J. Jayakumara and C.-H. Cheng, *Chem. Commun*. 2017, **53**, 2491-2494.

[4] Y. Otomaru, K. Okamoto, R. Shintani and T. Hayashi, *J. Org. Chem.,* 2005, **70**, 2503-2508.

[5] K. Okamoto, T. Hayashi and V. H. Rawal, *Chem. Commun.,* 2009, 4815-4817.

[6] R. Li, Z. Wen and N. Wu, *Org. Biomol. Chem.,* 2016, **14**, 11080-11084.

[7] T. Yasukawa, A. Suzuki, H. Miyamura, K. Nishino and S. Kobayashi, *J. Am. Chem. Soc.,* 2015, **137**, 6616-6623.

[8] F. Xue and Hayashi T, *Angew. Chem. Int. Ed.,* 2018, **57**, 10368-10372.

[9] S. Abele, R. Inauen, D. Spielvogel and C. Moessner, *J. Org. Chem.,* 2012, **77**, 4765−4773.

[10] A. Zhu, Y. Sun, J. Lai, Z Chen, X. Bu, Y.-N. Yue, M. Ma and F. Xue, J. *Org. Chem*., 2022, **87**, 7884-7894.

[11] J. Yang, A. Rérat, Y. J. Lim, C. Gosmini and N. Yoshikai, *Angew. Chem., Int. Ed*., 2017, **56**, 2449-2453.

8. Data for X-ray crystal structure of (*S*)-3aa

Crystals of (S)-**3aa** (92% ee) suitable for X-ray crystallographic analysis were obtained by recrystallization from hexane and ether. A suitable crystal of 3aa (recrystallized from n-Hexane at room temperature) was selected and mounted. The diffraction data were collected on a Bruker D8 venture microsource diffractometer using monochromatic Cu-Kα radiation (1.54178 Å) at 150 K. Date reduction, scaling and absorption corrections were performed using SAINT (Bruker, V8.40A, 2016). The structures were solved with the ShelXT (Sheldrick, 2015) structure solution program using the Intrinsic Phasing solution method and by using Olex2 (Dolmanov et al., 2009) as the graphical interface. The model was refined with version 2016/6 of ShelXT (Sheldrick, 2008) using Least Squares minimization. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre (CCDC 2262466).

Table 1. Crystal data and structure refinement for (*S*)-3aa

Bond precision: C-C = 0.0019 A Wavelength=1.54178

Cell: a=4.7593(1) b=16.2350(3) c=16.5153(4)
alpha=90 beta=90 gamma=90

Temperature: 150 K

	Calculated	Reported
Volume	1276.09(5)	1276.09(5)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C15 H20 O	C15 H20 O
Sum formula	C15 H20 O	C15 H20 O
Mr	216.31	216.31
Dx,g cm-3	1.126	1.126
Z	4	4
Mu (mm-1)	0.522	0.522
F000	472.0	816.0
F000’	473.23	
h,k,lmax	5,20,20	5,20,20
Nref	2602[1548]	2591
Tmin,Tmax	0.963, 0.974	0.676, 0.754
Tmin’	0.934	

Correction method= # Reported T Limits: Tmin=0.676 Tmax=0.754

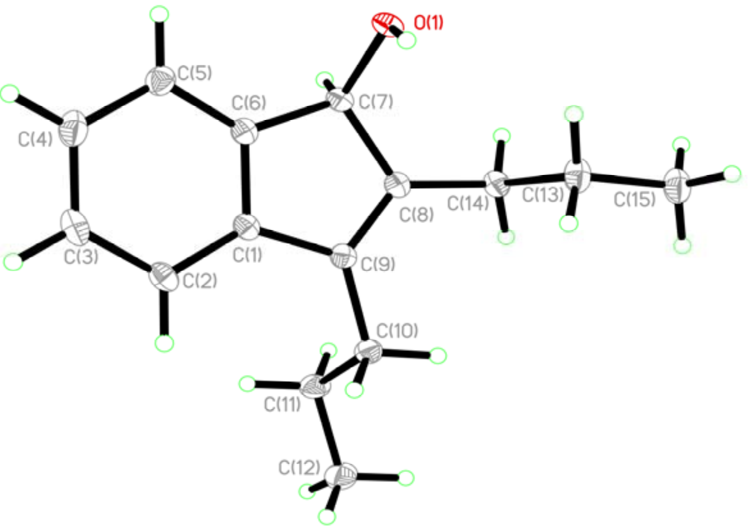
AbsCorr =REFDELF

Data completeness= 1.67/1.00 Theta(max)= 74.575

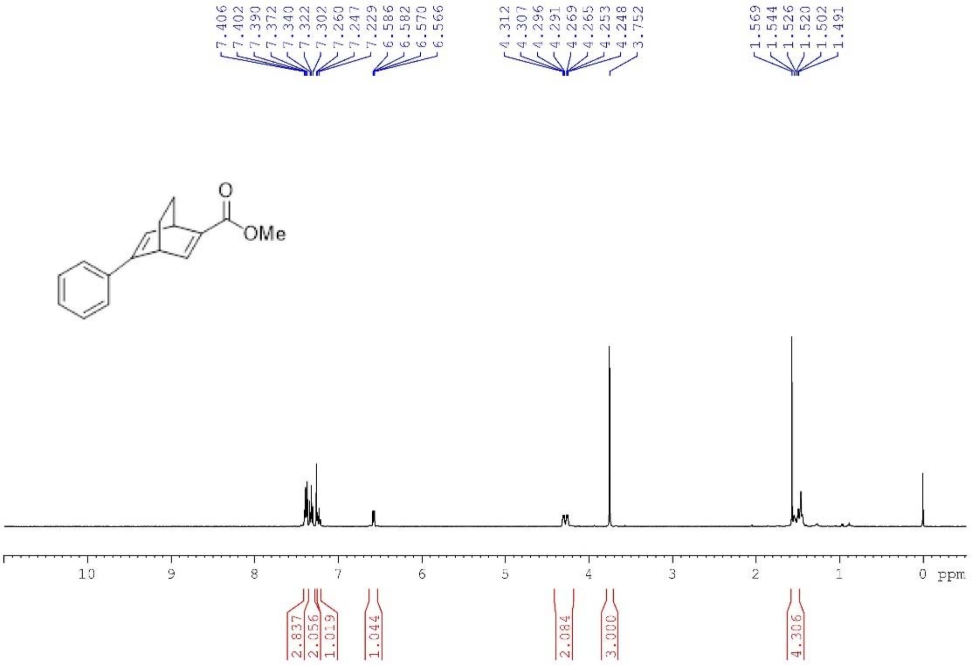
R(reflections)= 0.0271(2543) wR2(reflections)
= 0.0694(2591)

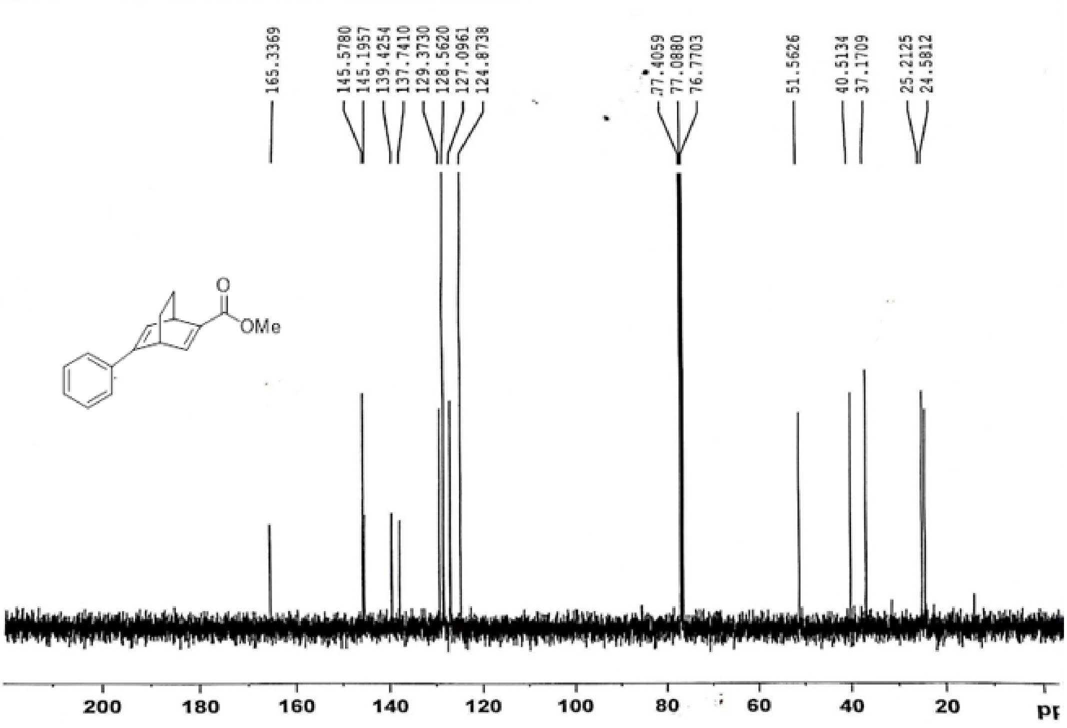
S = 1.038 Npar= 251

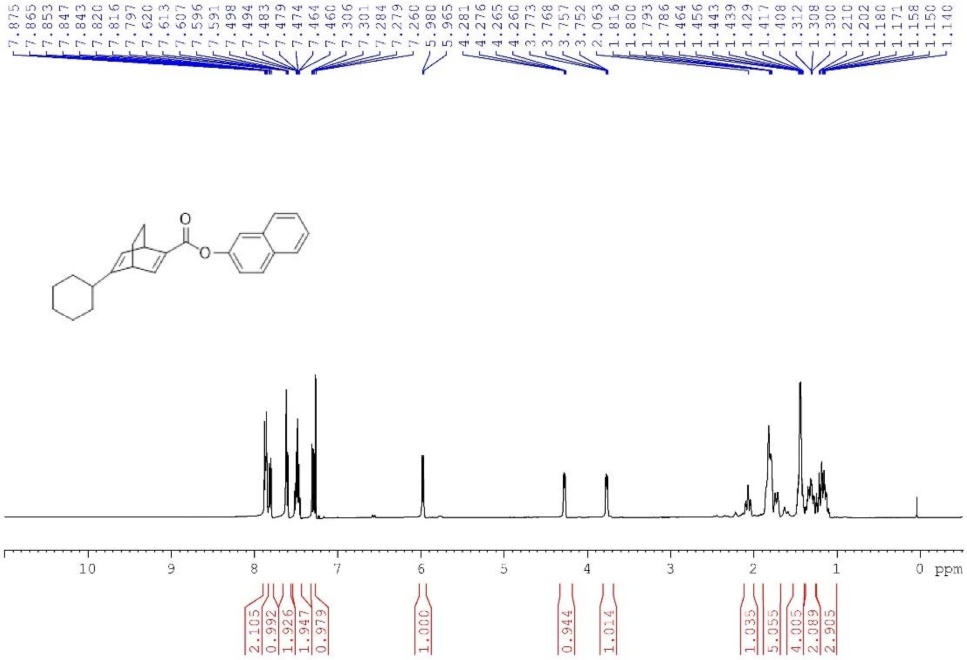
The ORTEP drawing of (*S*)-**3aa** with ellipsoid contour at 30% probability level is shown as follows:



9. NMR spectra



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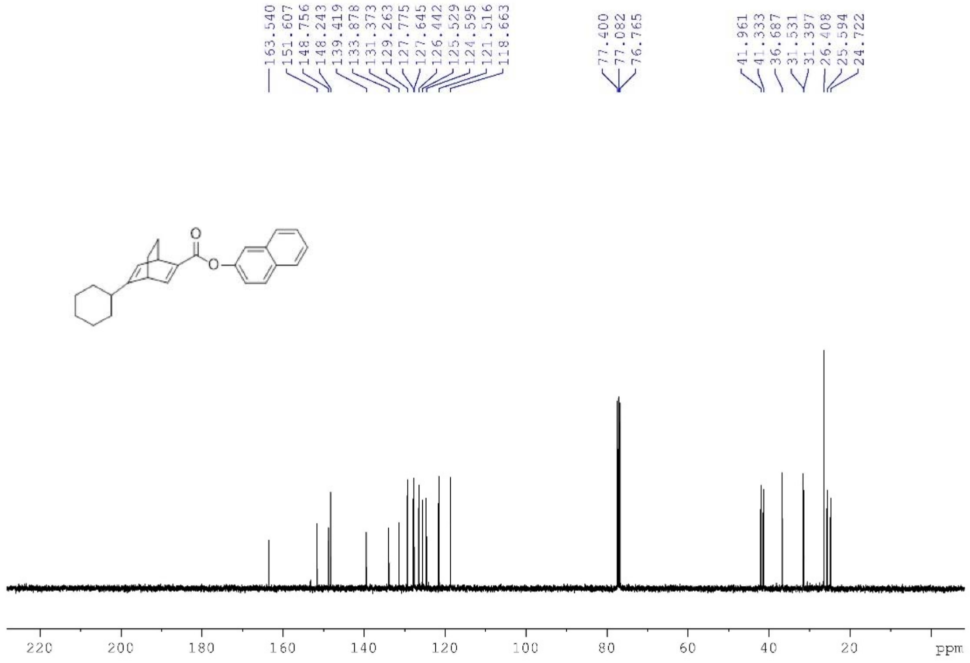
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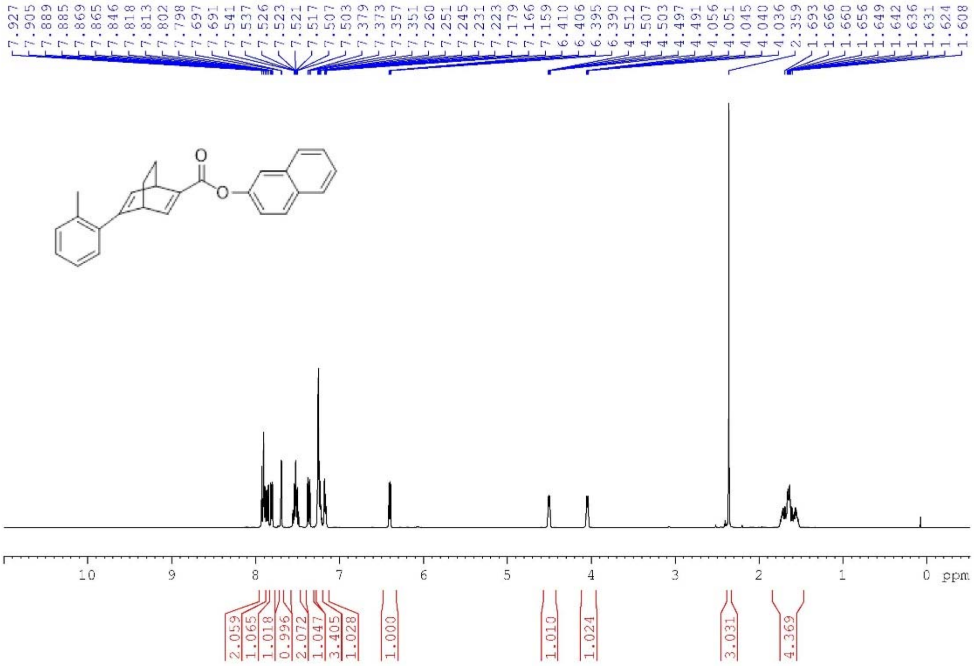
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1.608
O
O
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7
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3
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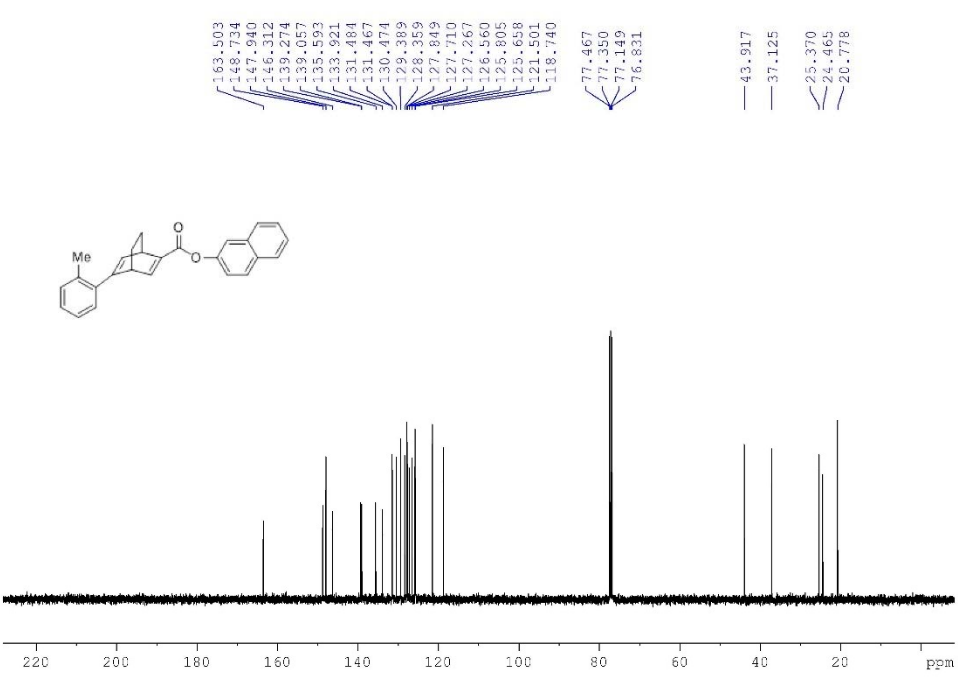
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127.267
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126.805
125.658
121.501
118.740
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77.149
76.831
43.917
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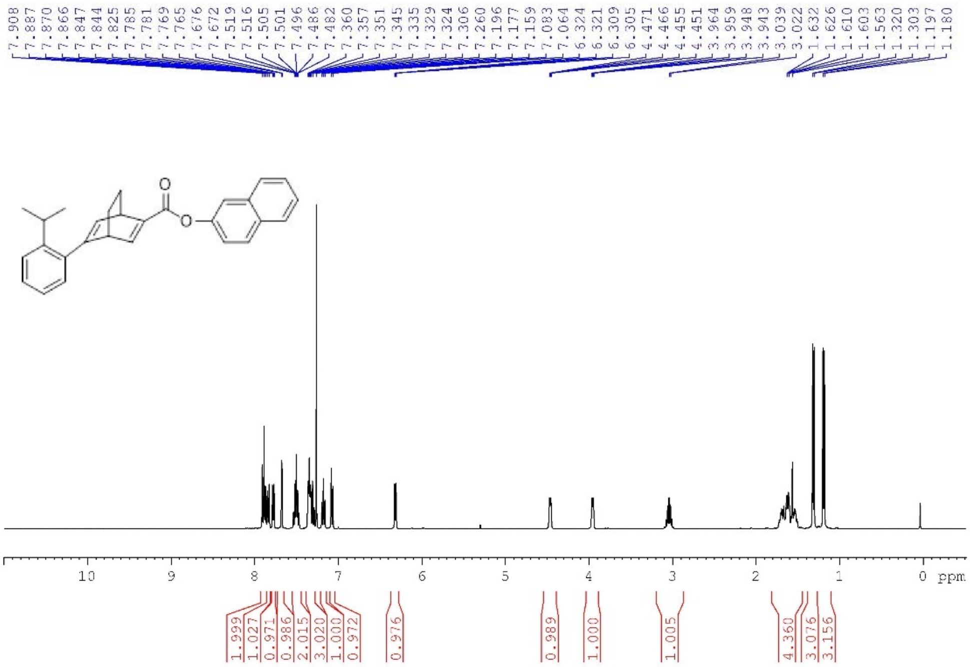
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6.309
6.305
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1.180
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O
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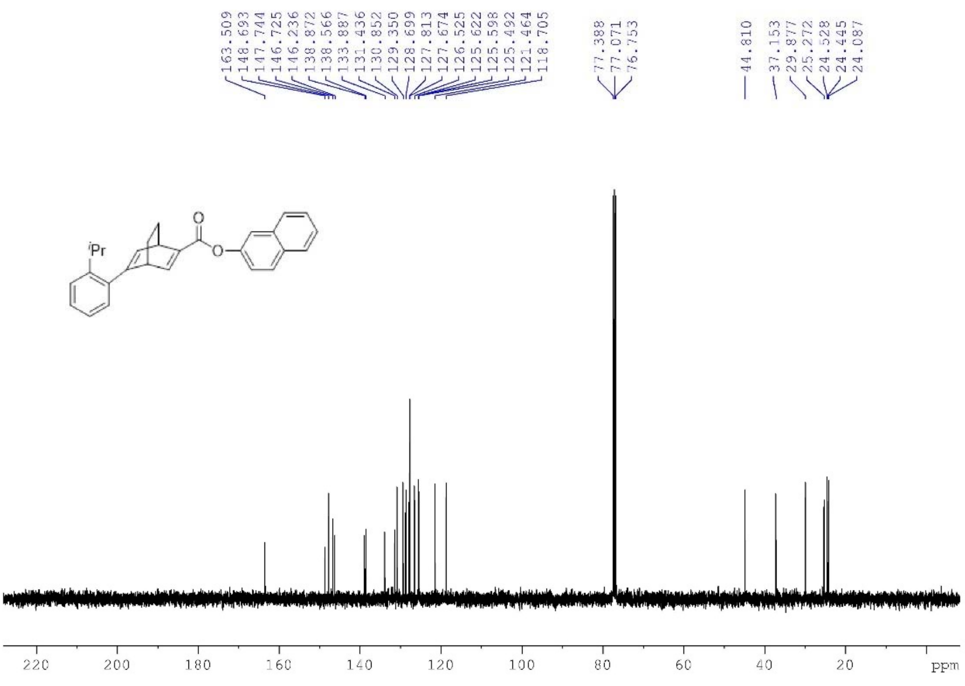
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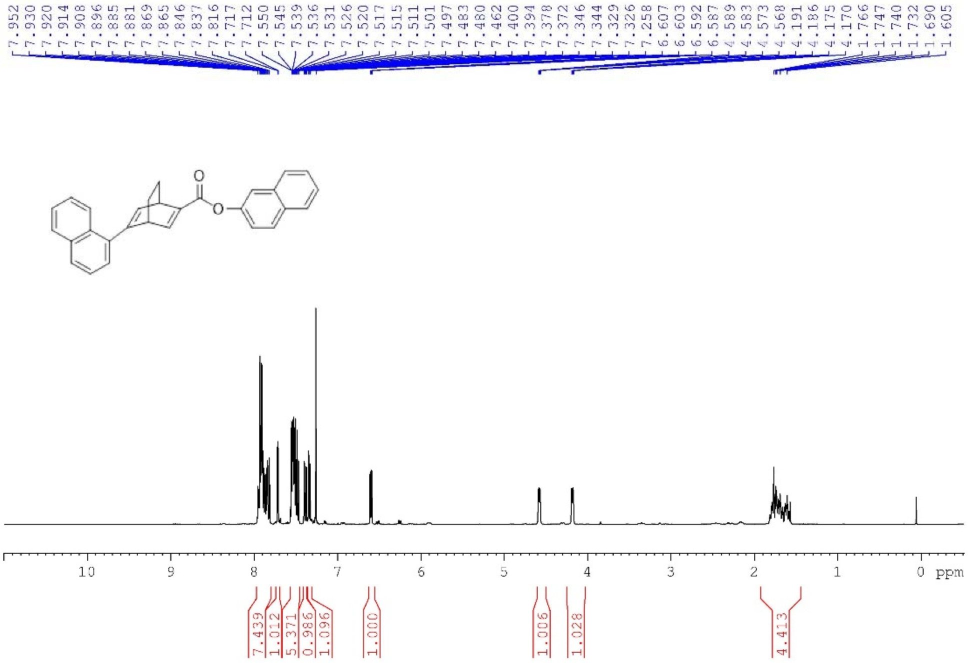
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7.536
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7.515
7.511
7.501
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7.344
7.329
7.326
7.258
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6.603
6.592
6.587
4.589
4.583
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4.175
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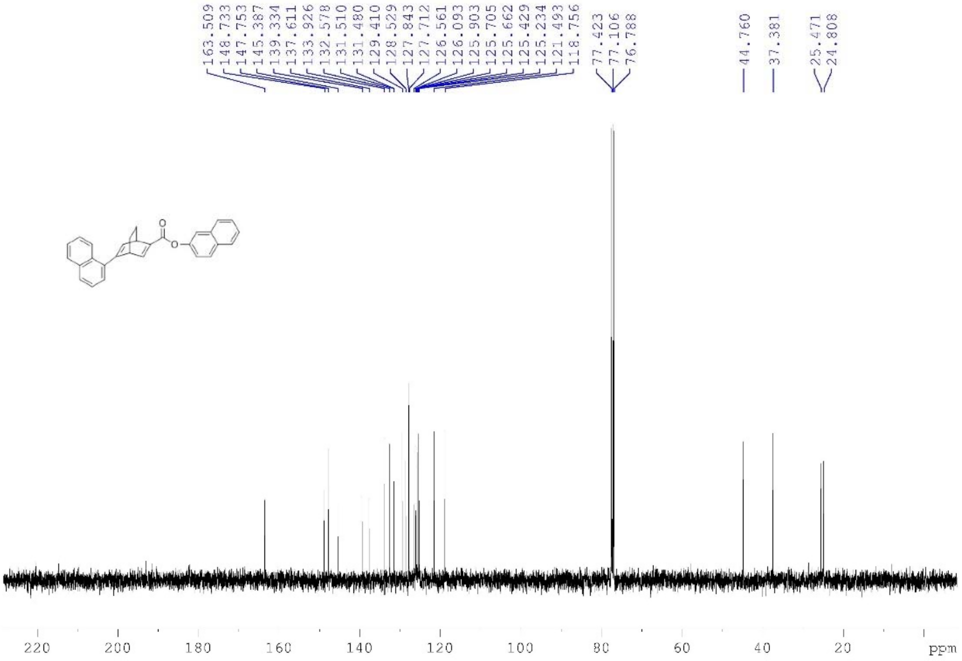
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76.788
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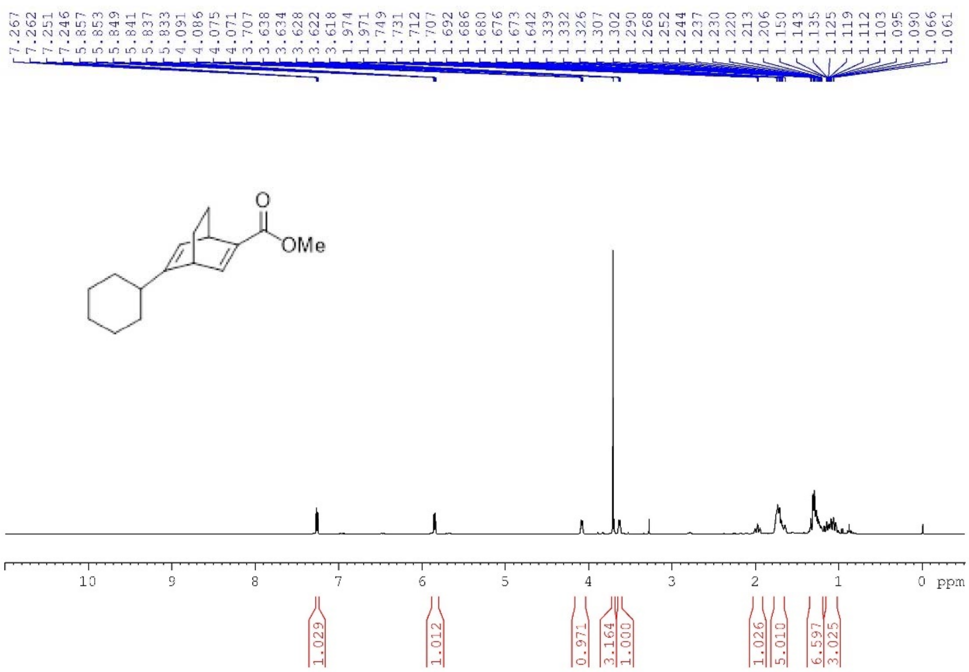
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4.071
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3.634
3.628
3.622
3.618
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1.971
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1.731
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1.676
1.673
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1.332
1.326
1.307
1.302
1.290
1.268
1.252
1.244
1.237
1.230
1.220
1.213
1.206
1.150
1.143
1.135
1.125
1.119
1.112
1.103
1.095
1.090
1.066
1.061
OMe
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9
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5
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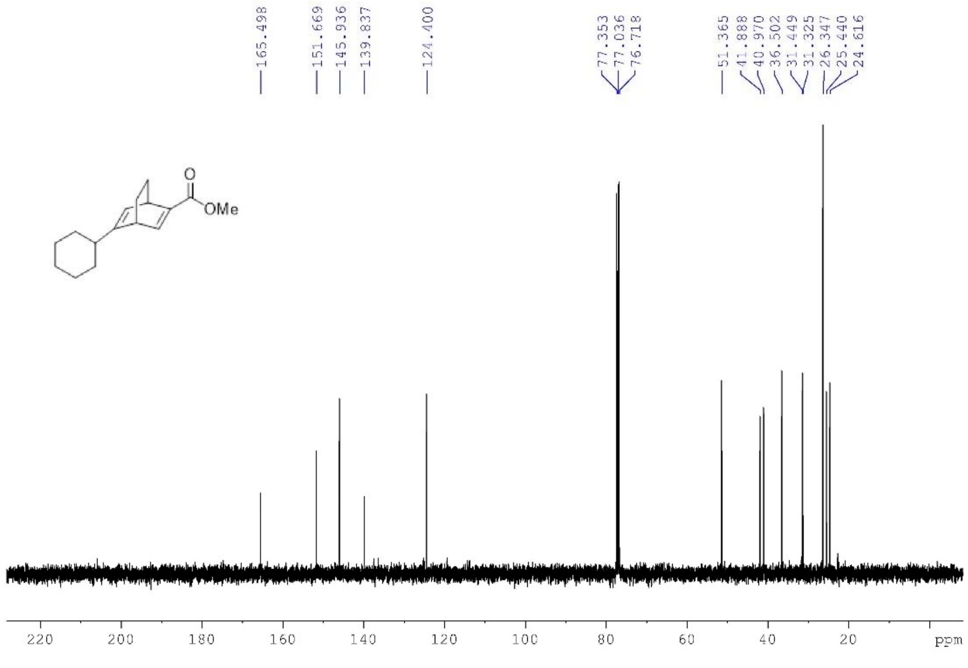
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24.616
OMe
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140
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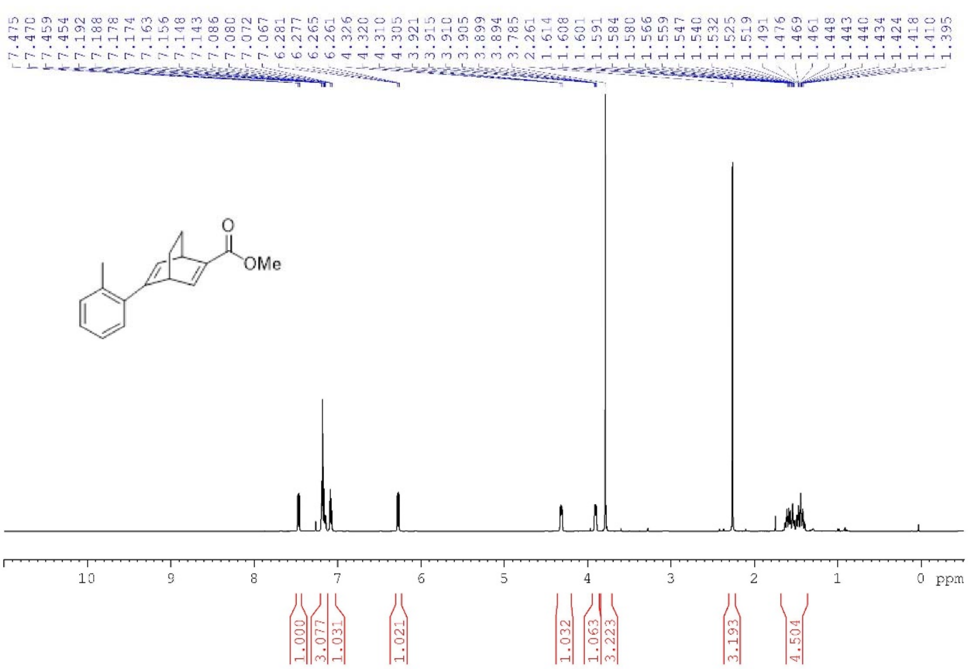
20
ppm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7.080
7.072
7.067
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6.265
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4.310
4.305
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3.915
3.910
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1.608
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1.559
1.547
1.540
1.532
1.525
1.519
1.491
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1.469
1.461
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1.443
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1.434
1.424
1.418
1.410
1.395
O
OMe
10
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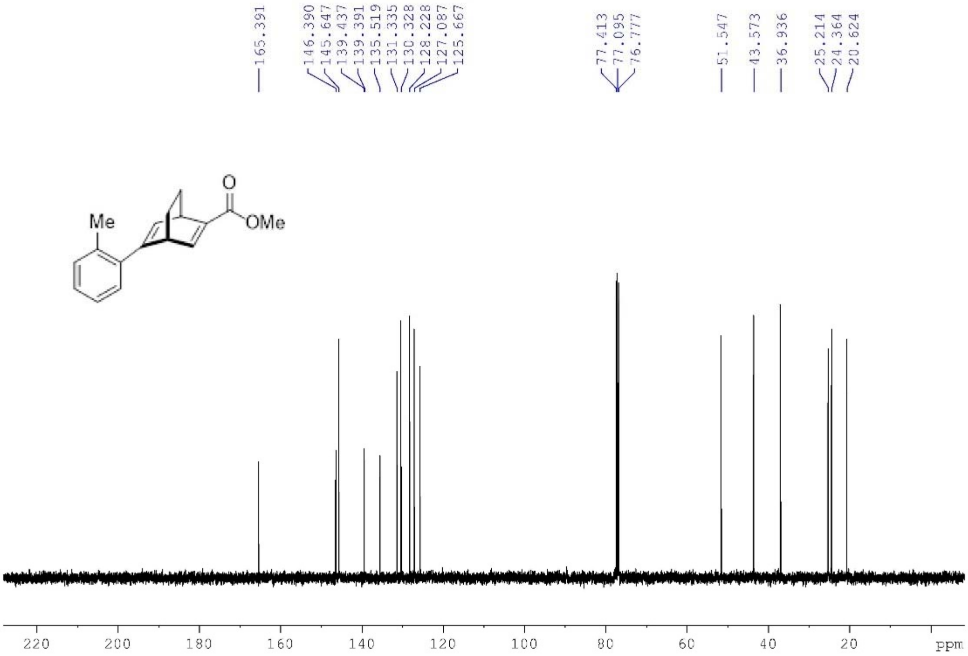
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76.777
51.547
43.573
36.936
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OMe
Me
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140
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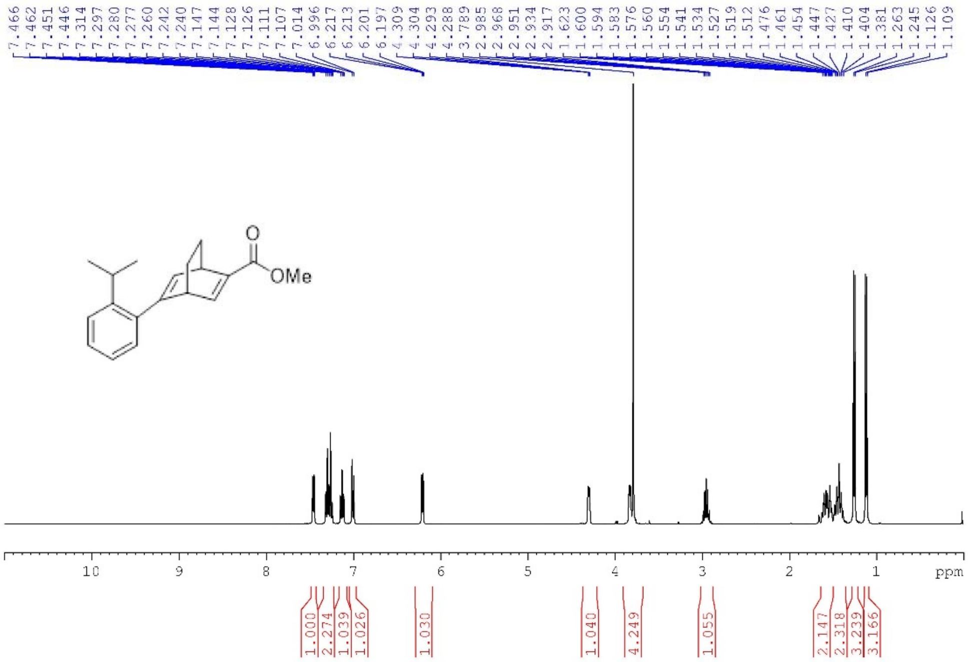
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7.128
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2.917
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1.534
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1.519
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OMe
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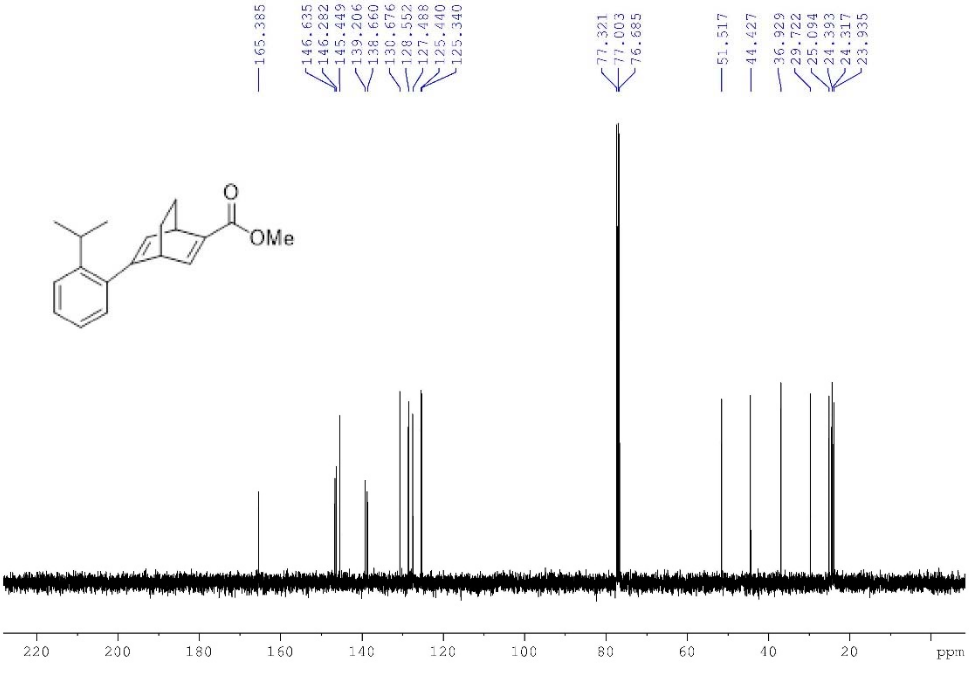
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44.427
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29.722
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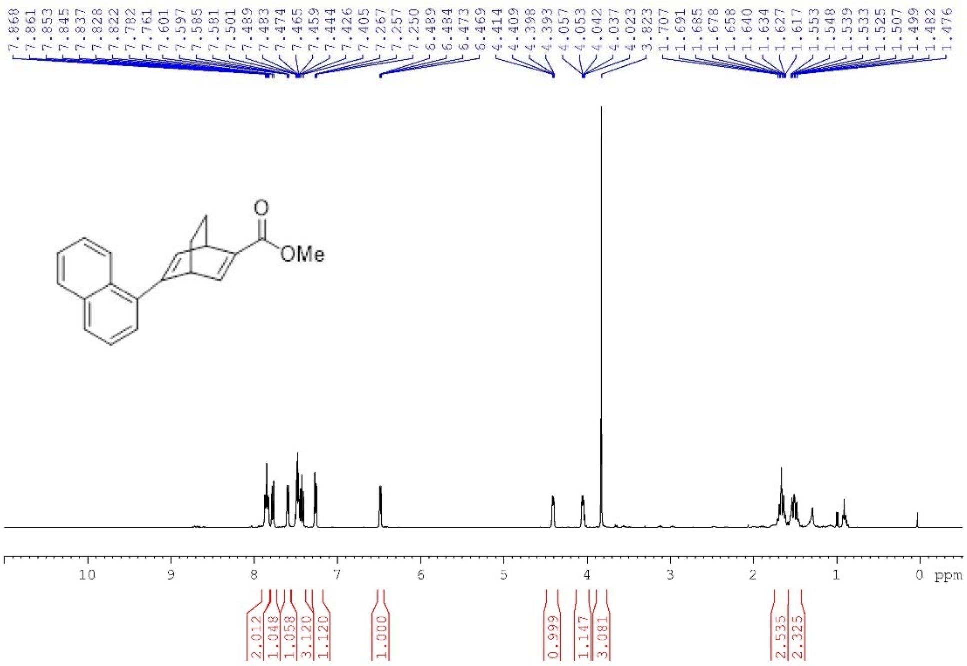
20
ppm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7.581
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1.507
1.499
1.482
1.476
O
OMe
10
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8
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6
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4
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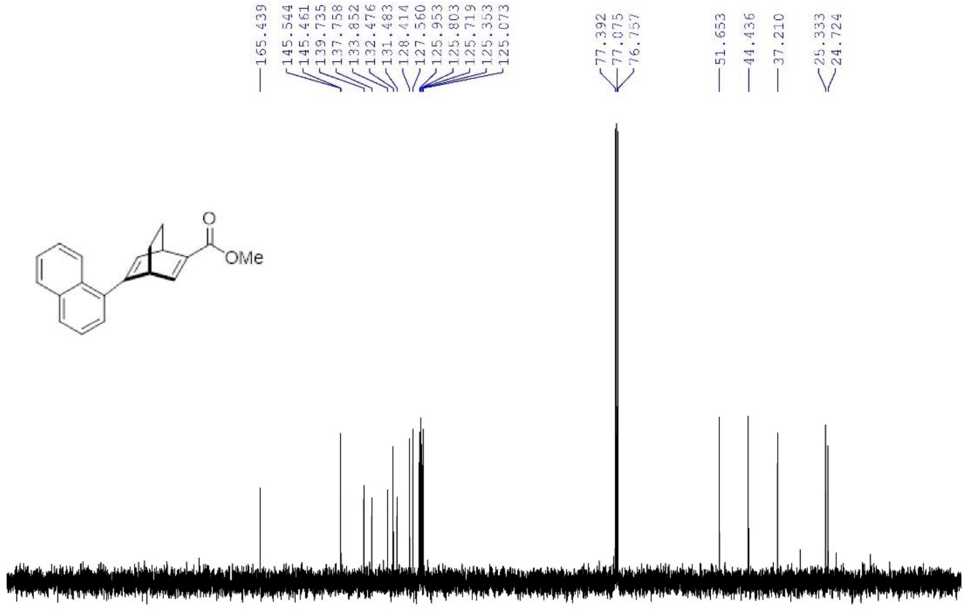
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125.353
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77.392
77.075
76.757
51.653
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60
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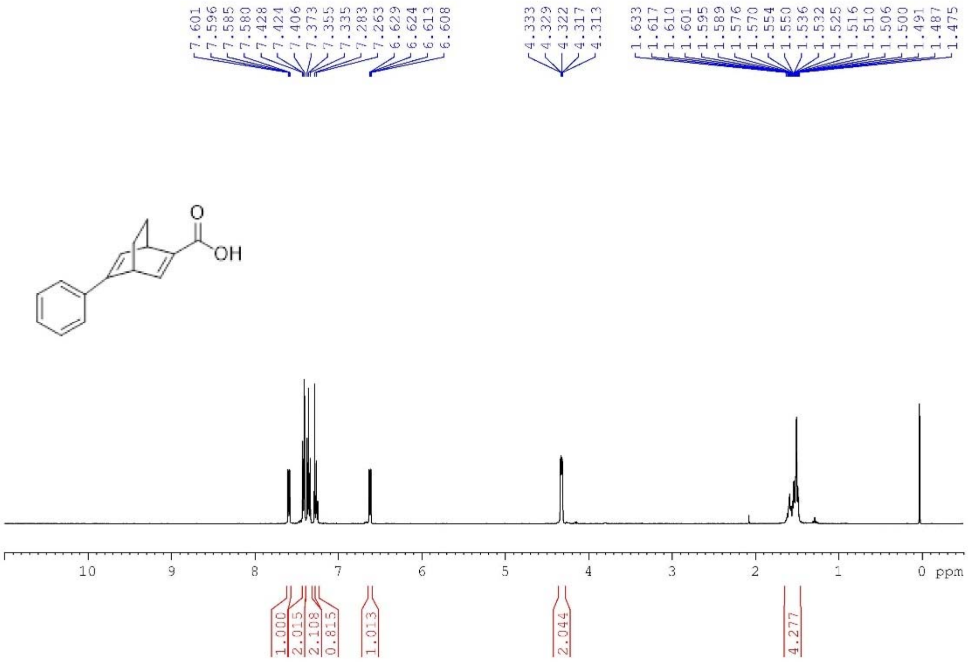
20
ppm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6.624
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6.608
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4.329
4.322
4.317
4.313
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1.617
1.610
1.601
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1.570
1.554
1.550
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1.506
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O
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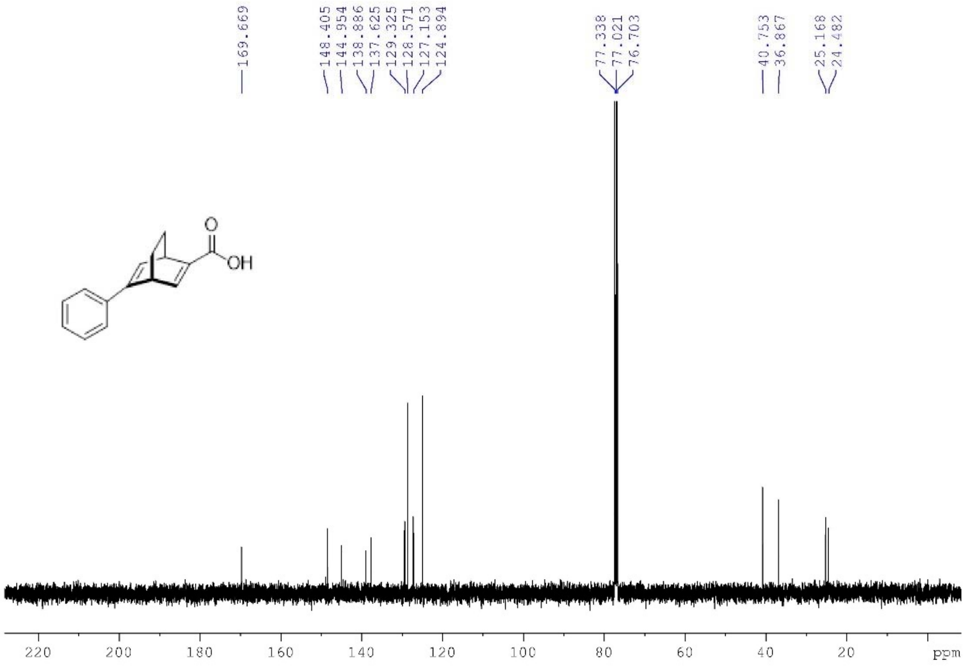
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20
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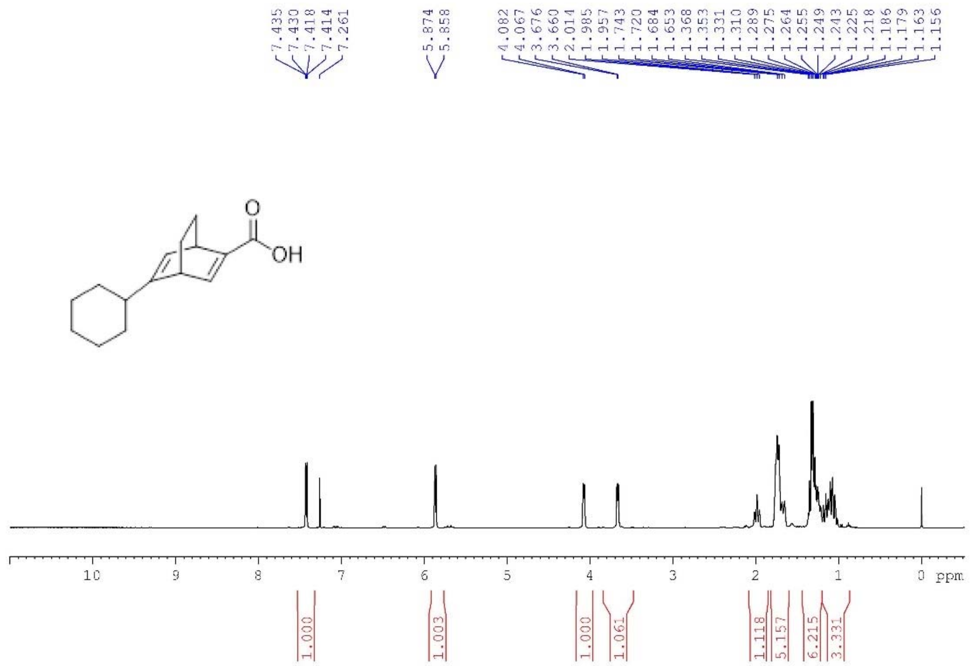

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1.957
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1.720
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1.275
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1.255
1.249
1.243
1.225
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1.179
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1.156
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OH
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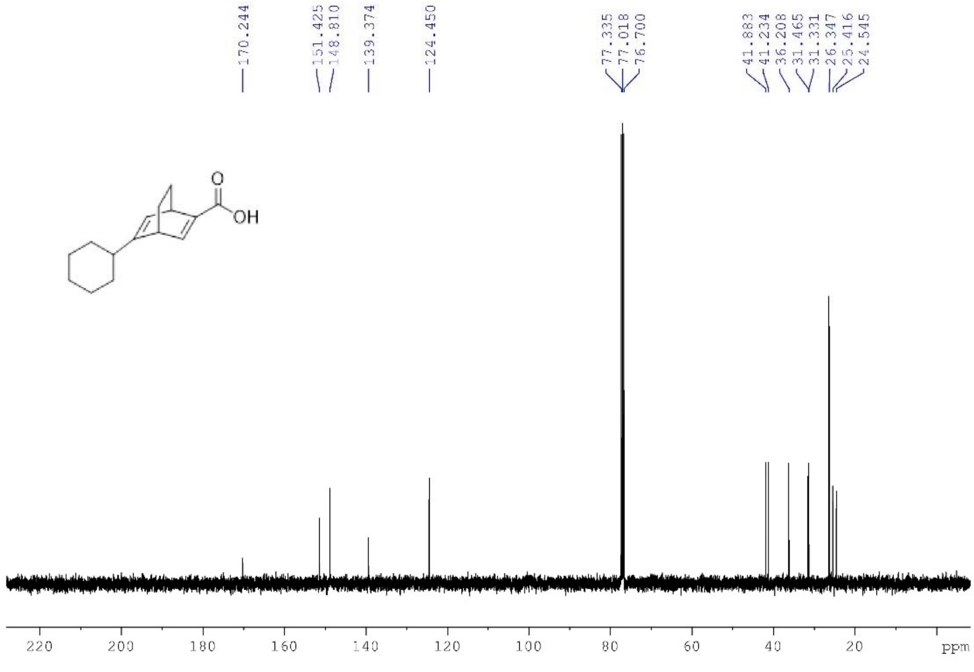

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20
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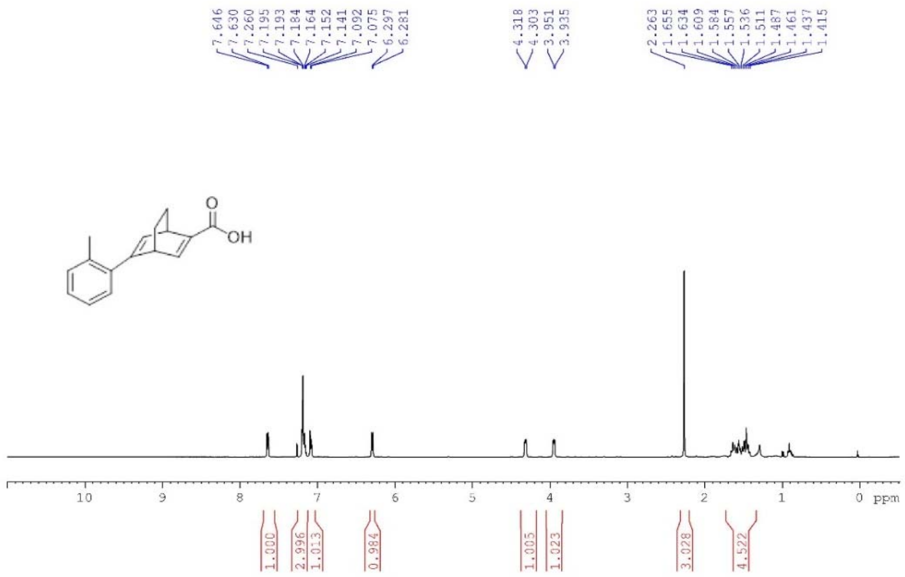
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O
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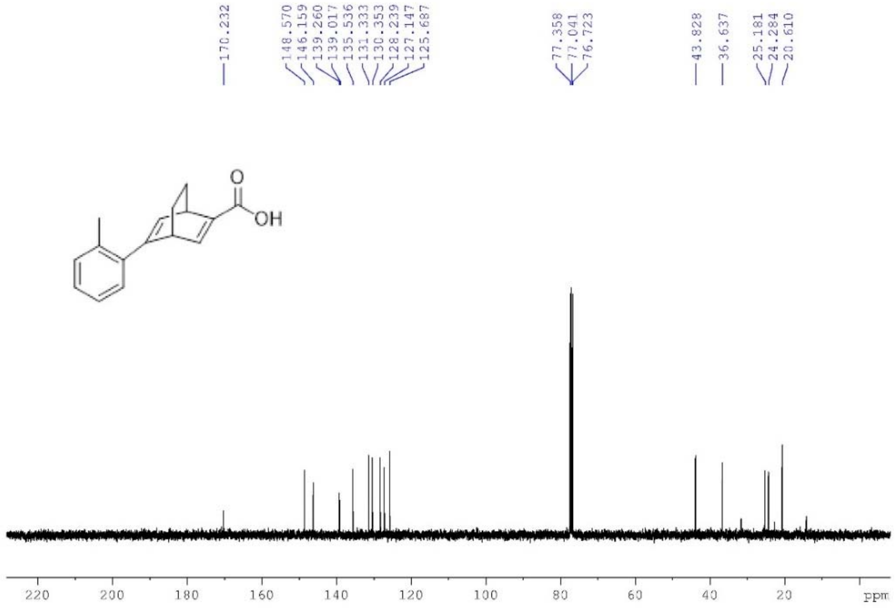
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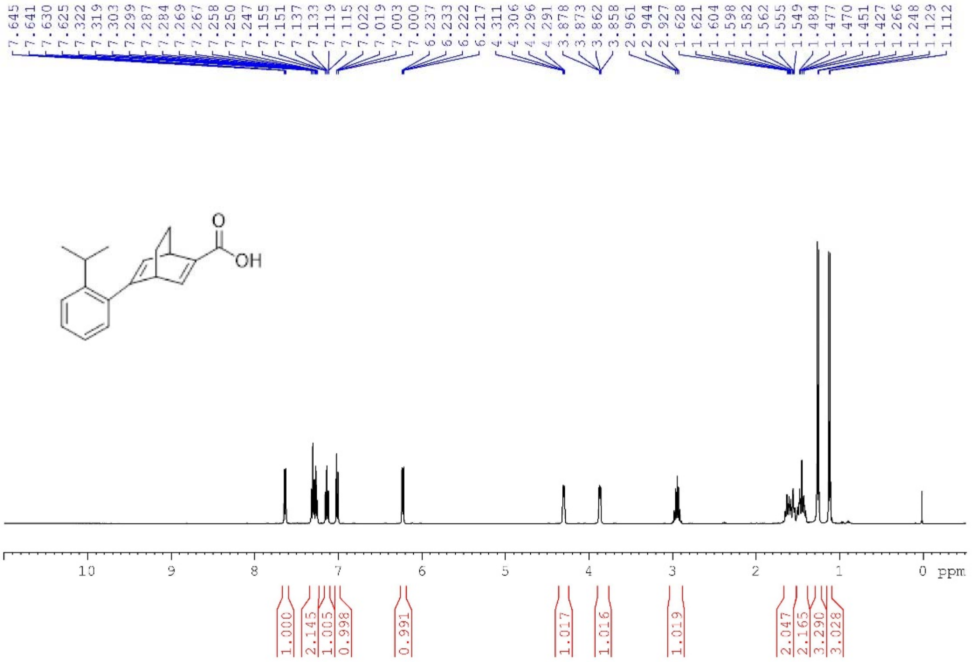
20
ppm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OH
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4
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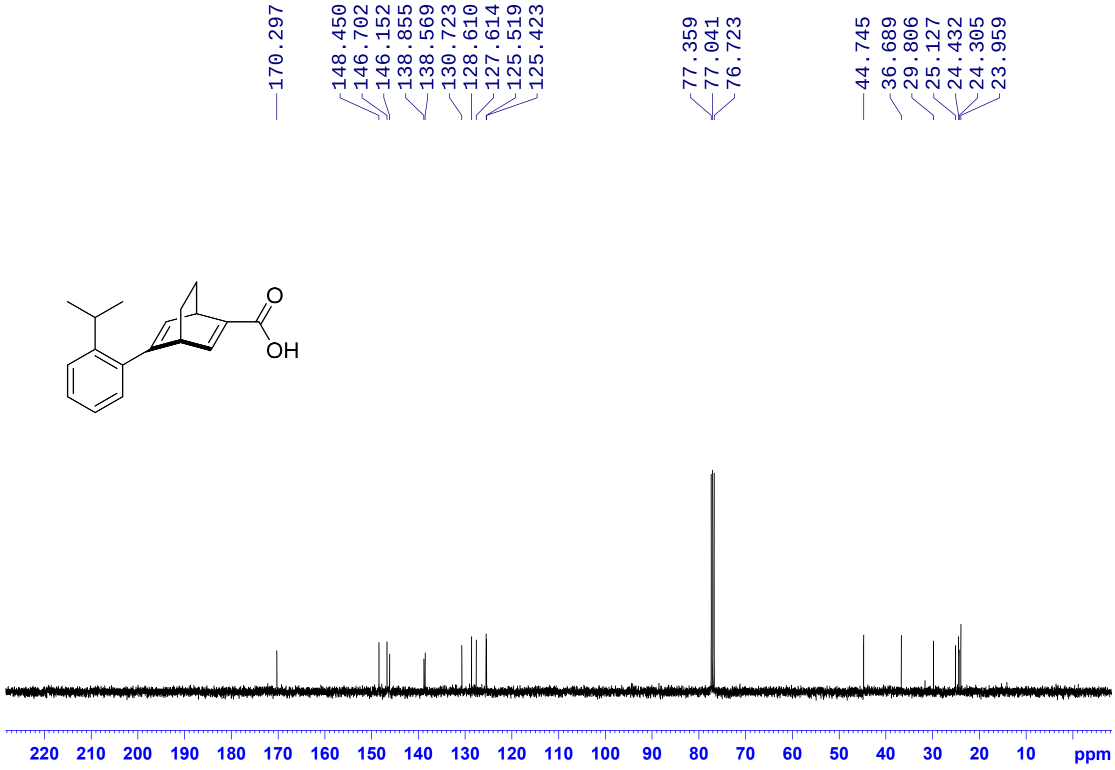
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77.041
76.723
44.745
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25.127
24.432
24.305
23.959
O
OH
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210
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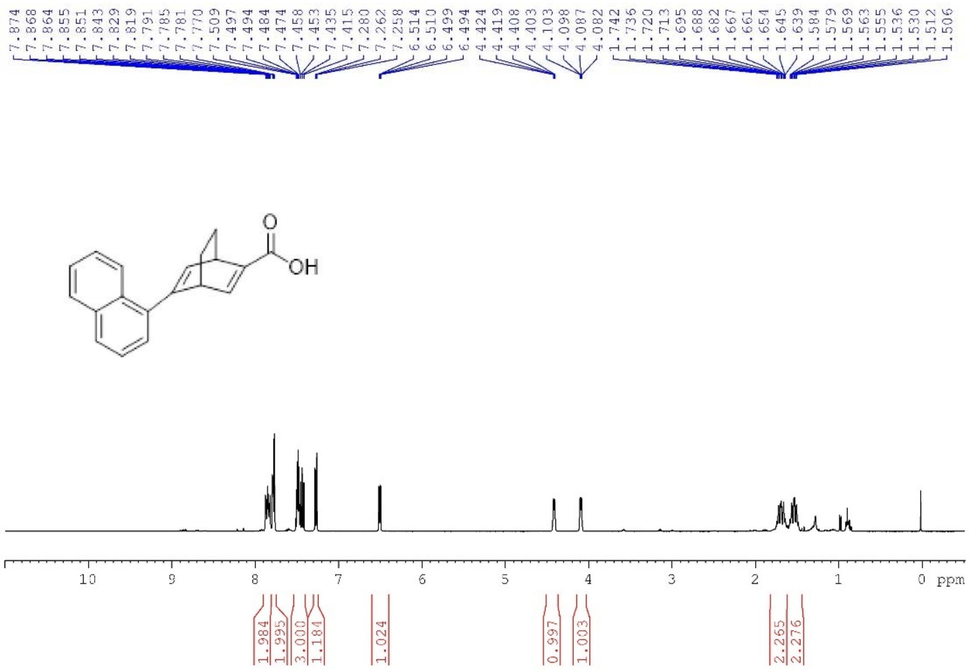
10
ppm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7.494
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7.474
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7.258
6.514
6.510
6.499
6.494
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4.419
4.408
4.403
4.103
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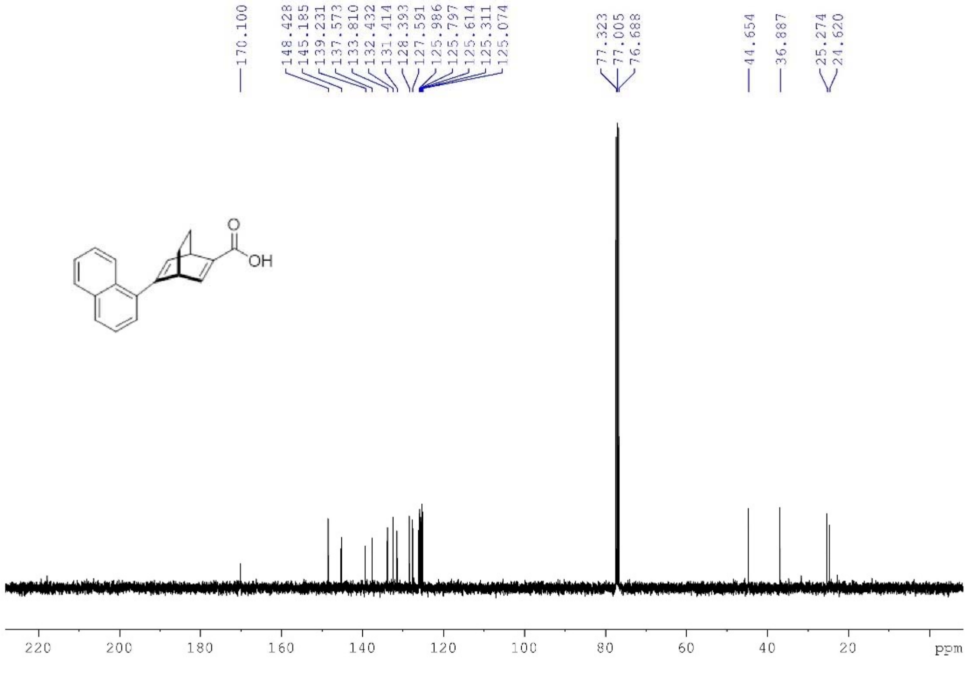
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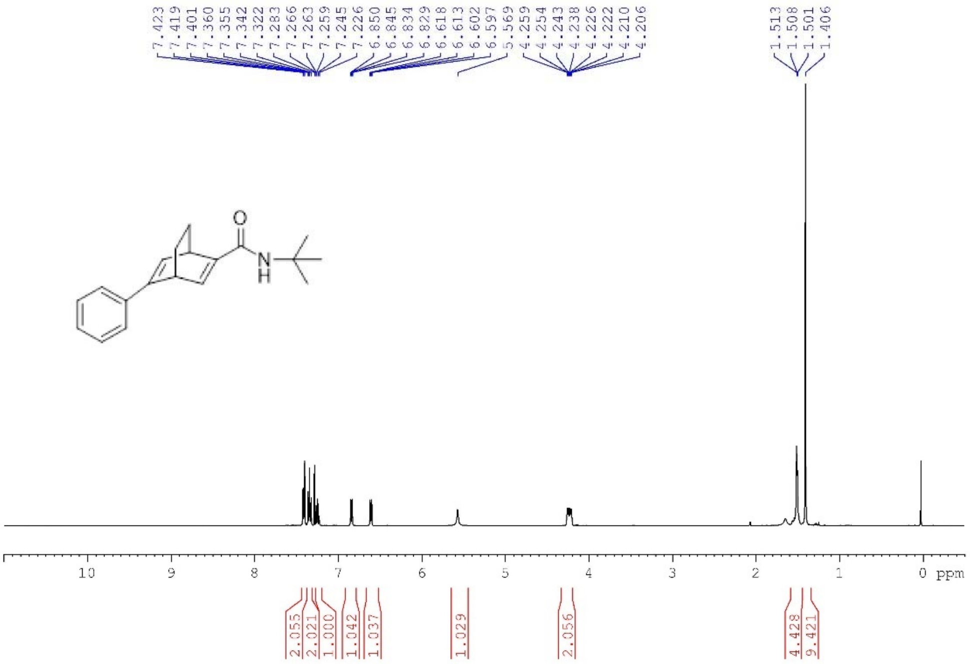
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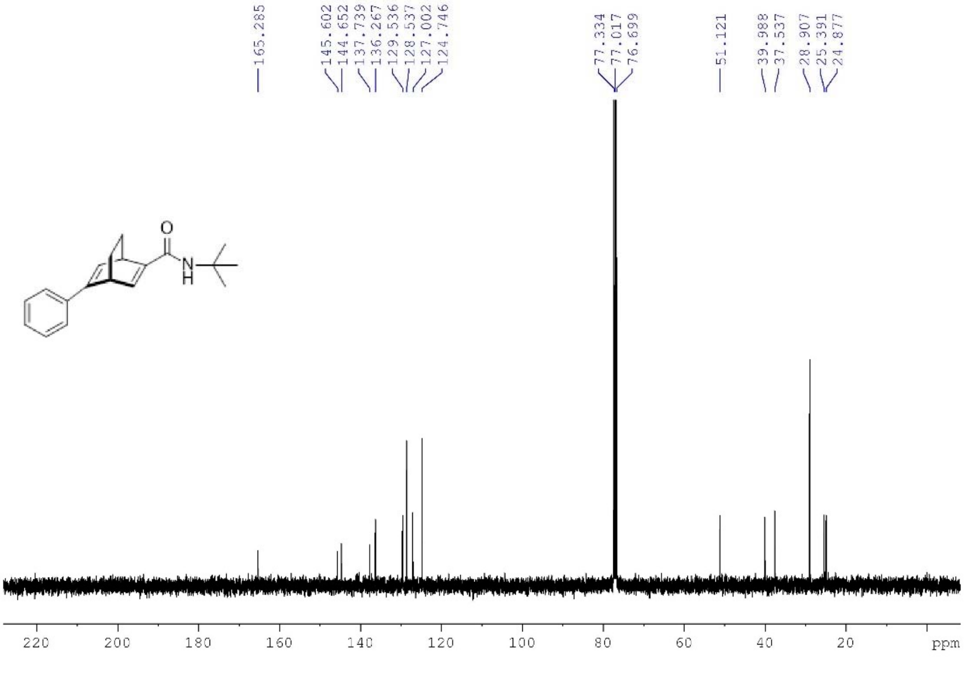
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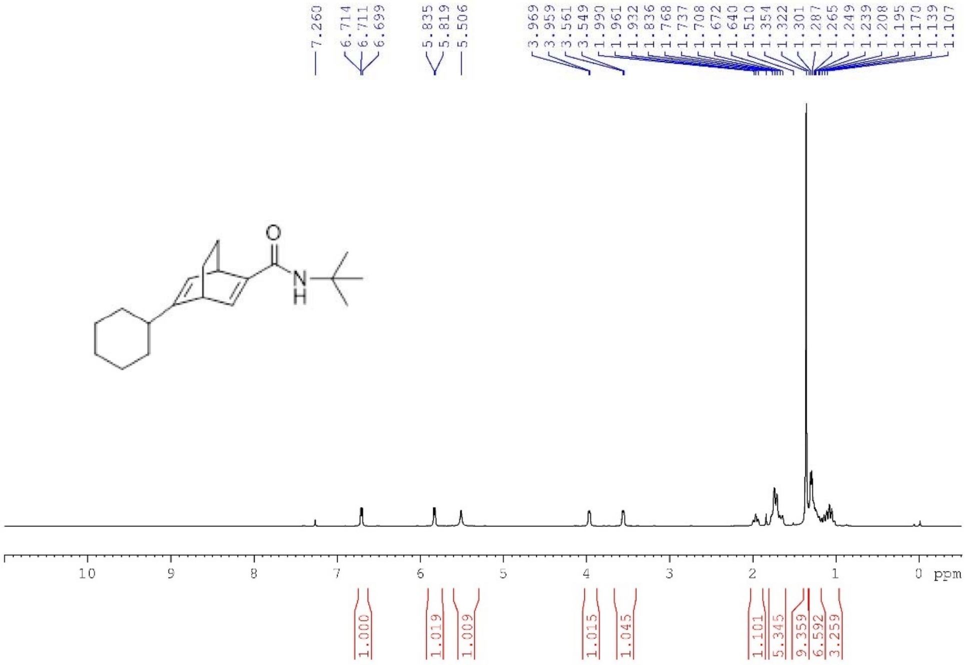
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1.932
1.836
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1.287
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1.208
1.195
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1.107
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H
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5
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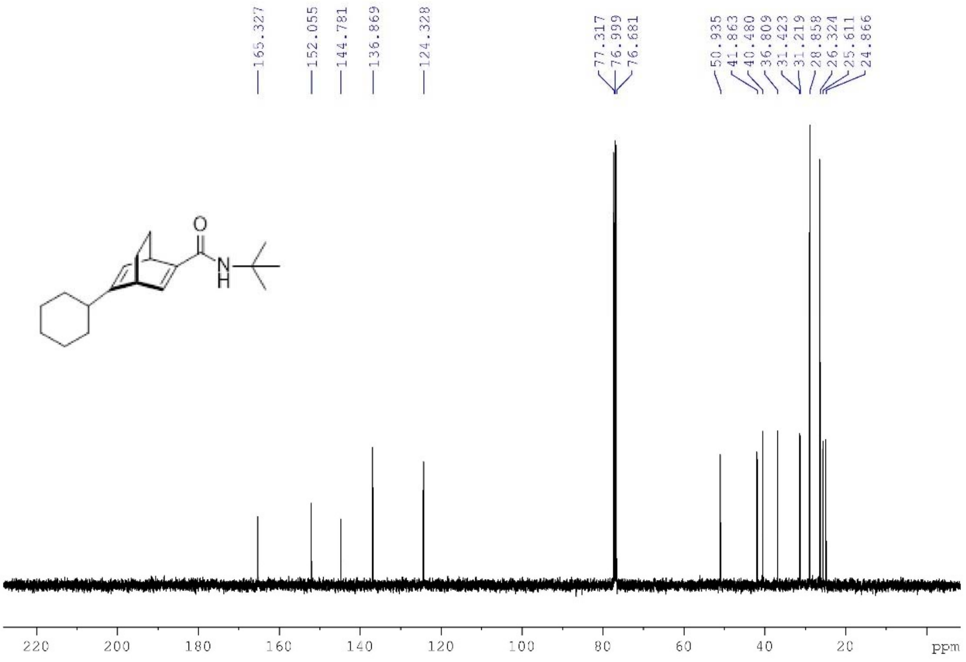
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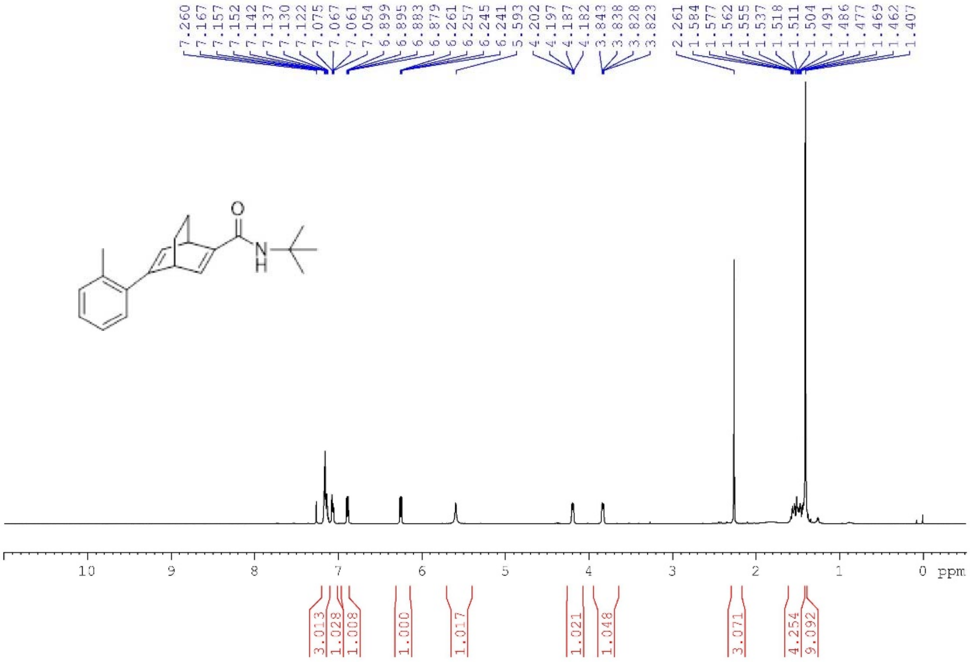
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6.245
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3.823
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1.537
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1.511
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1.477
1.469
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H
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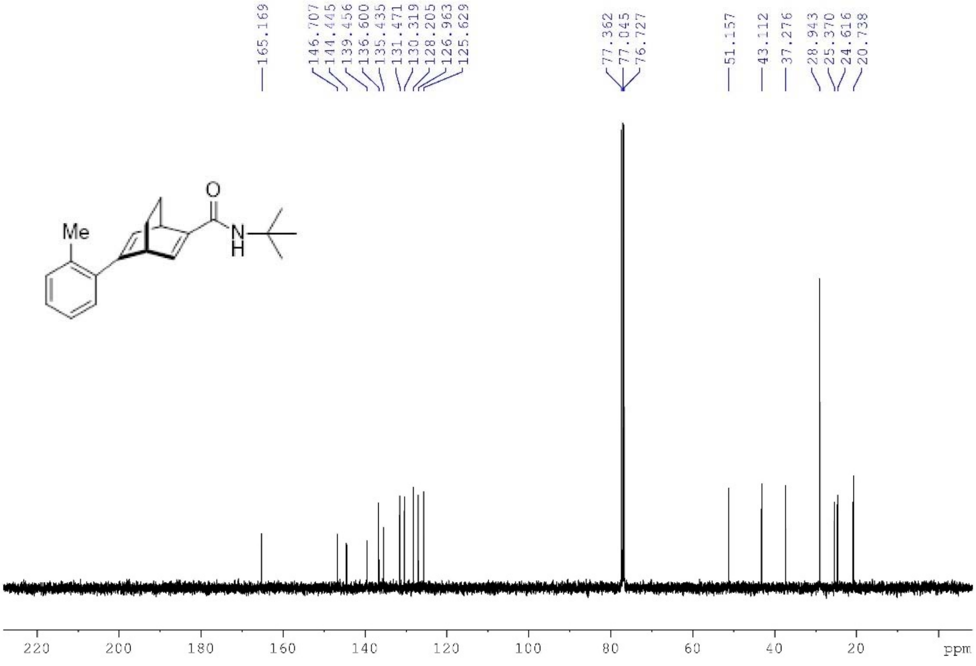
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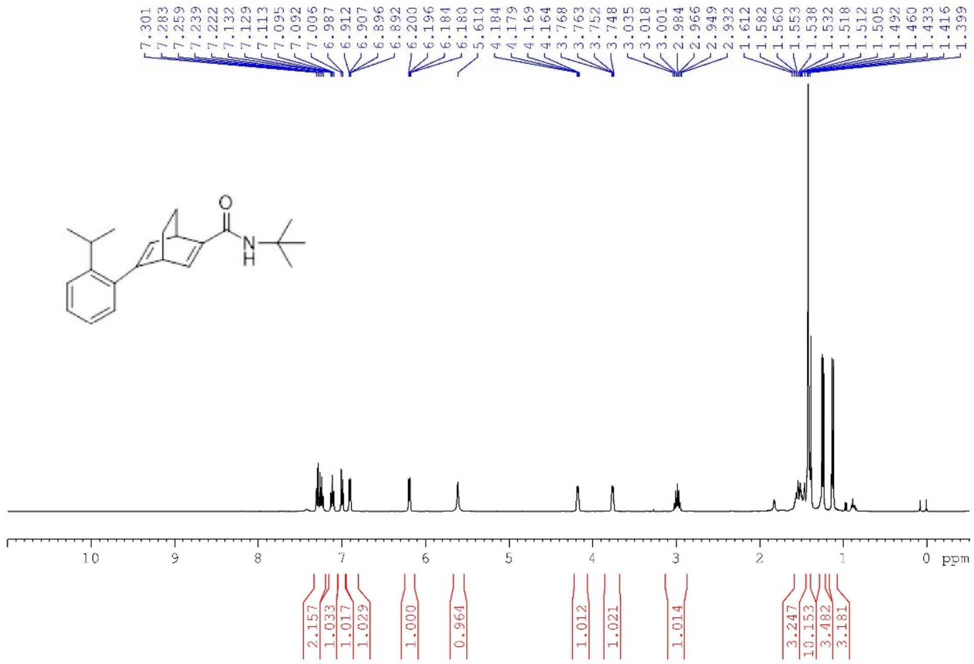
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6.907
6.896
6.892
6.200
6.196
6.184
6.180
5.610
4.184
4.179
4.169
4.164
3.768
3.763
3.752
3.748
3.035
3.018
3.001
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2.966
2.949
2.932
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1.560
1.553
1.538
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1.518
1.512
1.505
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N
H
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4
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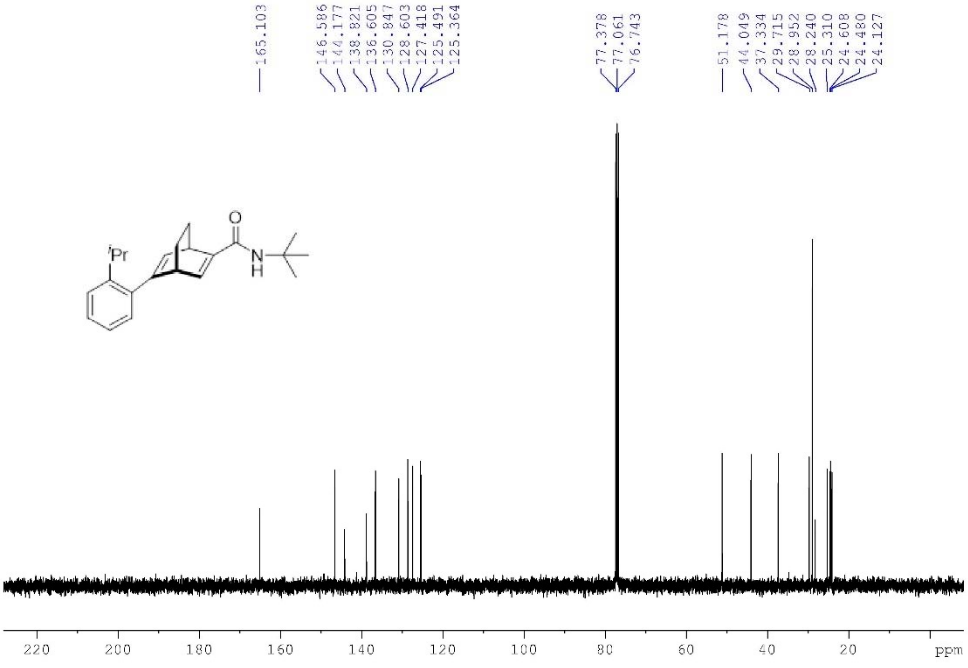
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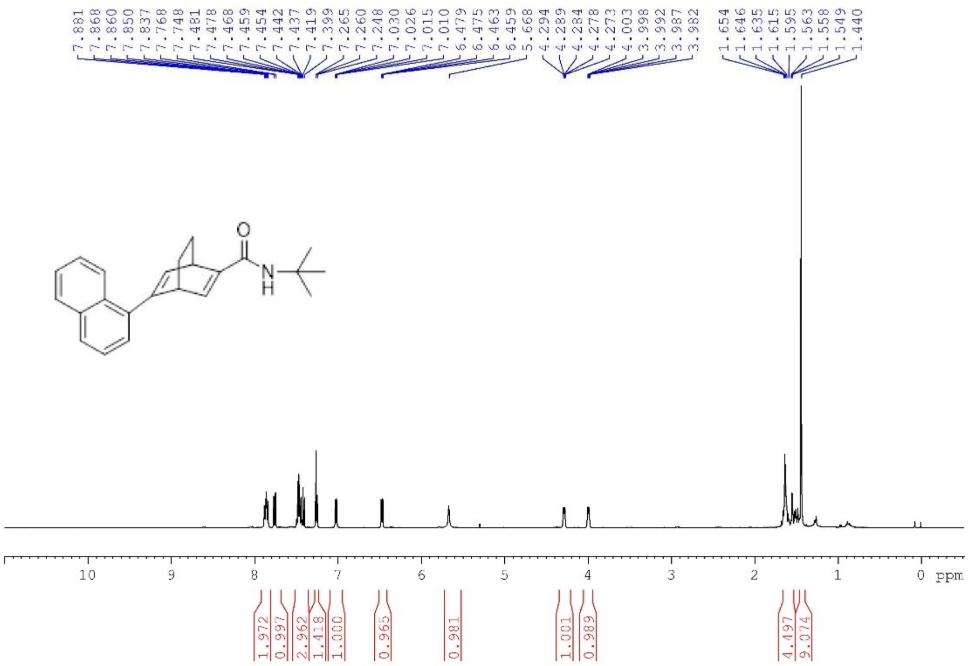
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H
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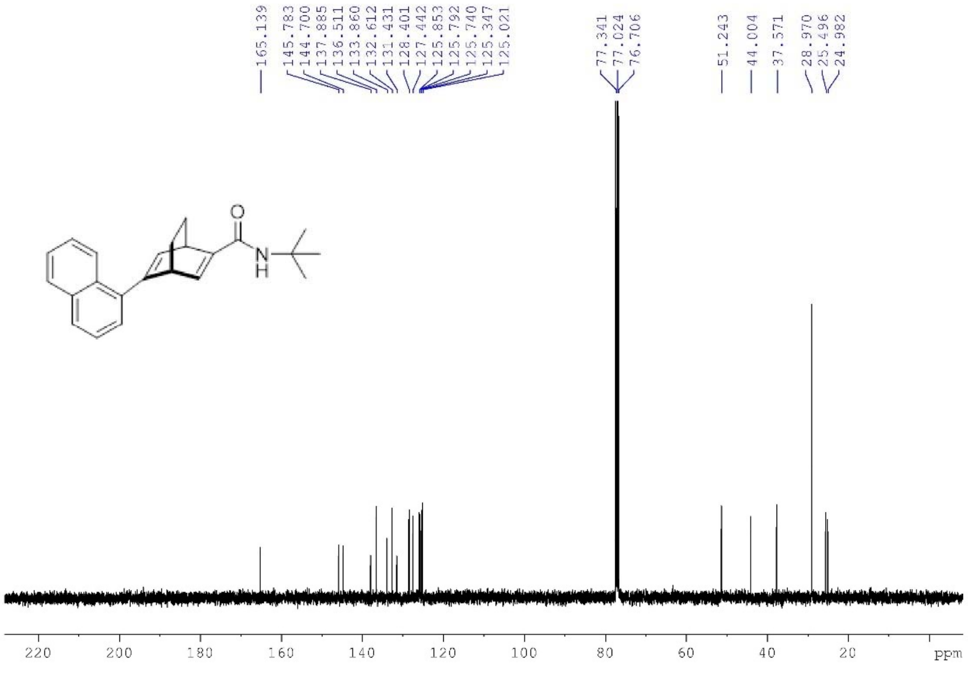
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76.706
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44.004
37.571
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H
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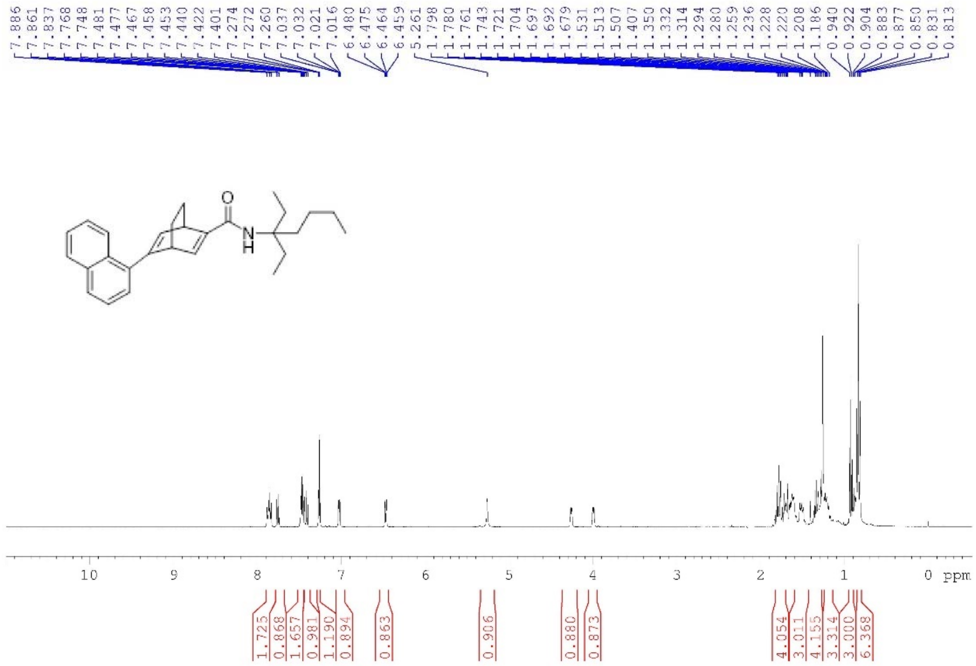
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7.401
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7.272
7.260
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6.459
5.261
1.798
1.780
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1.228
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1.208
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O
N
H
10
9
8
7
6
5
4
3
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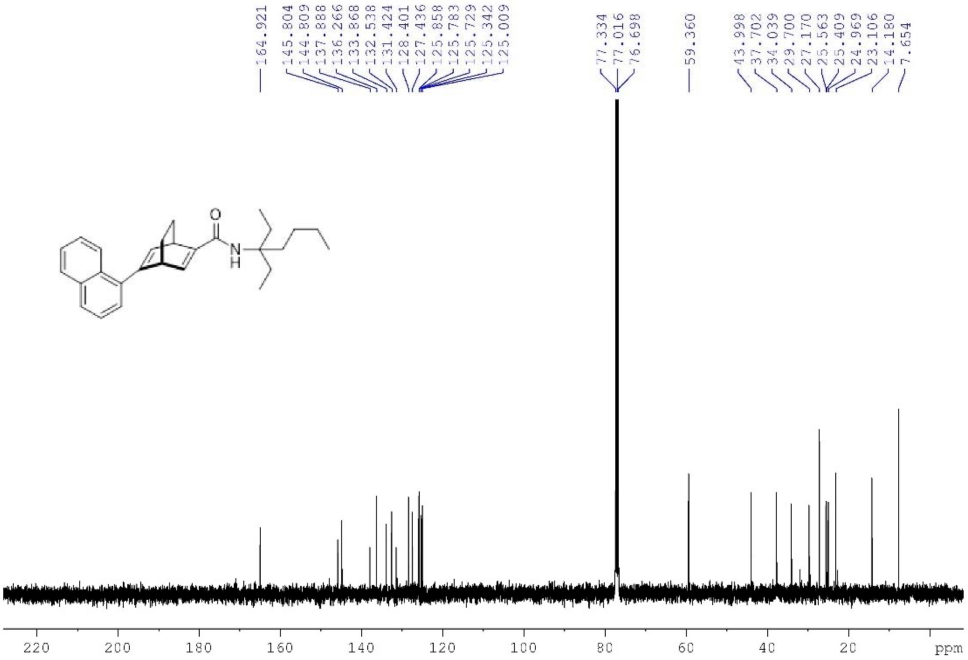
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77.016
76.698
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37.702
34.039
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25.563
25.409
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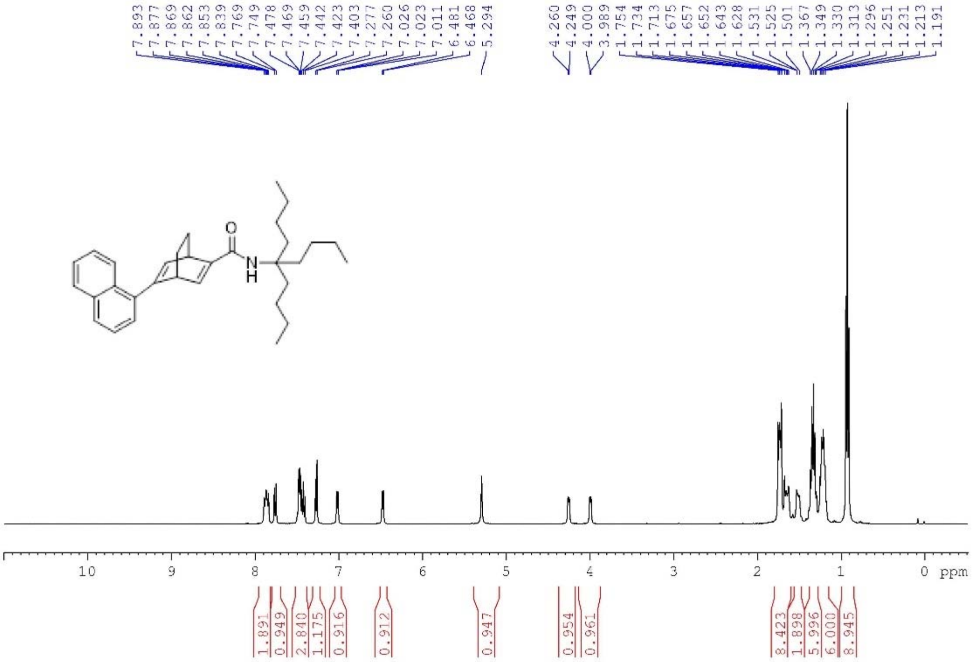
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1.231
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N
H
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8
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5
4
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2
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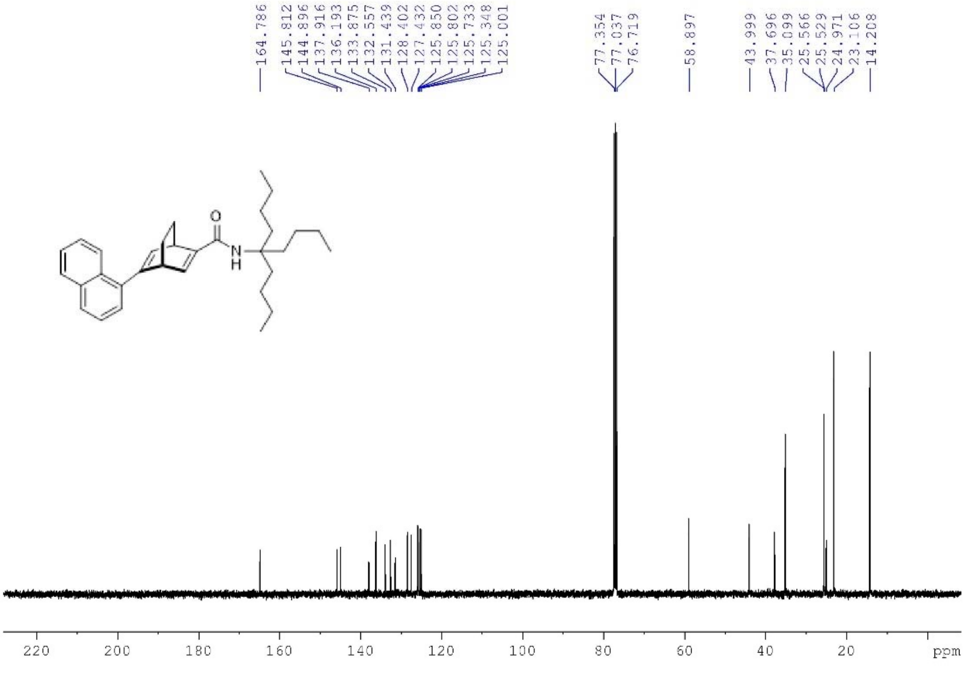
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58.897
43.999
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25.529
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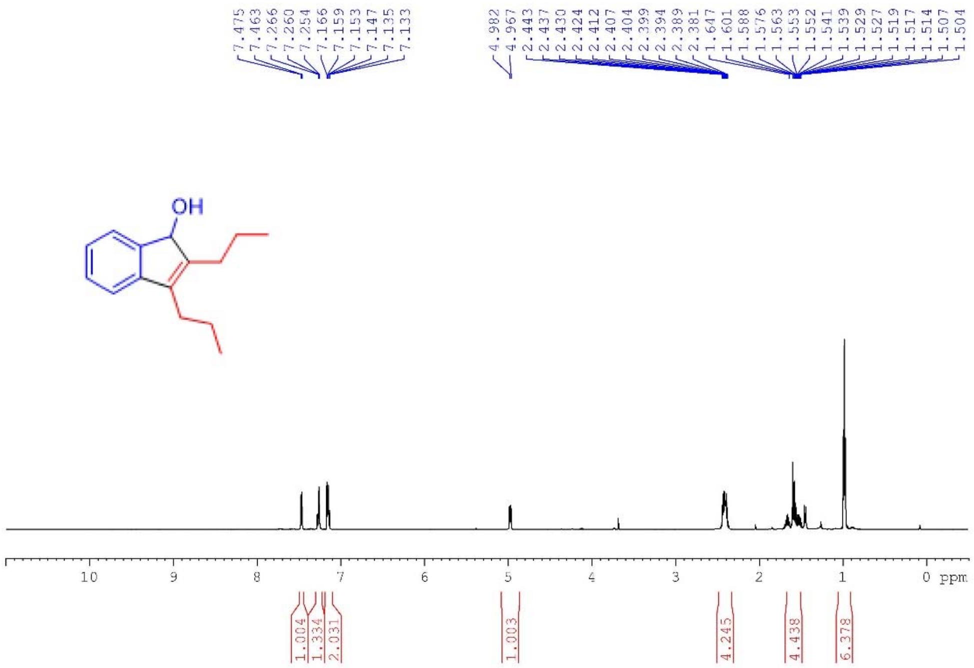
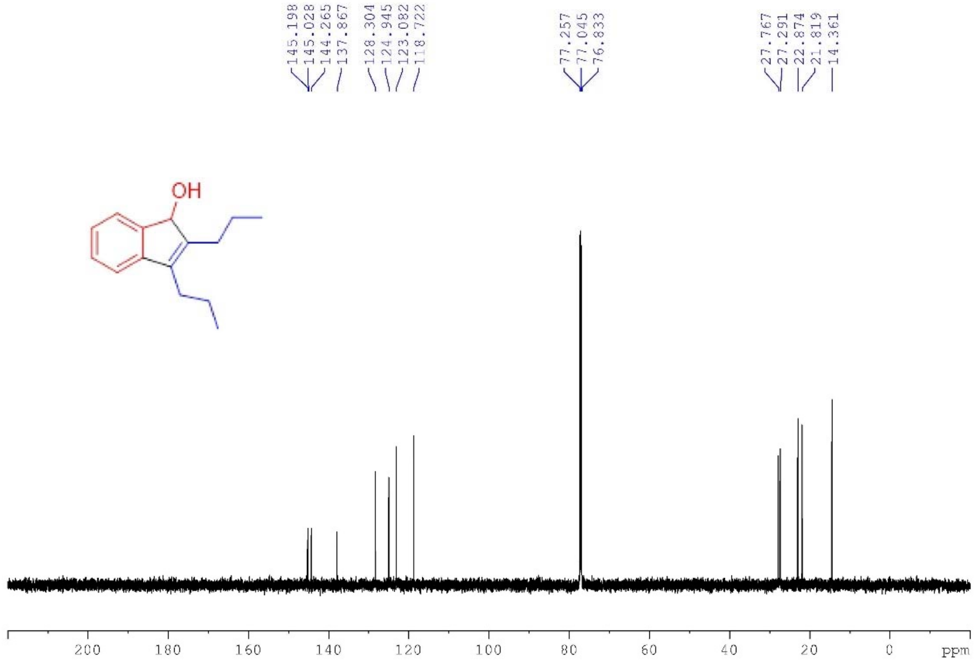
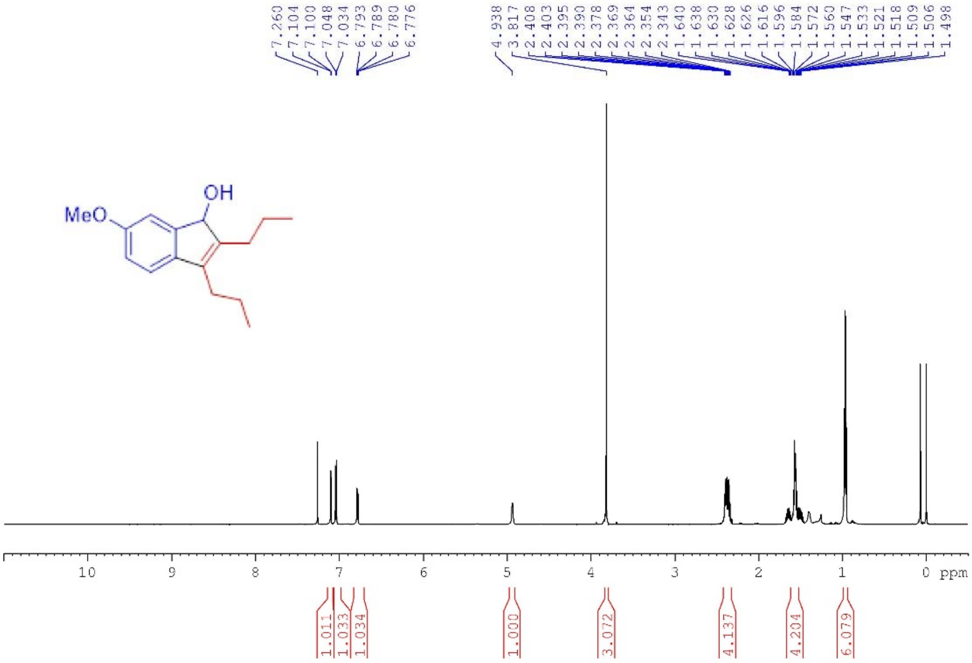


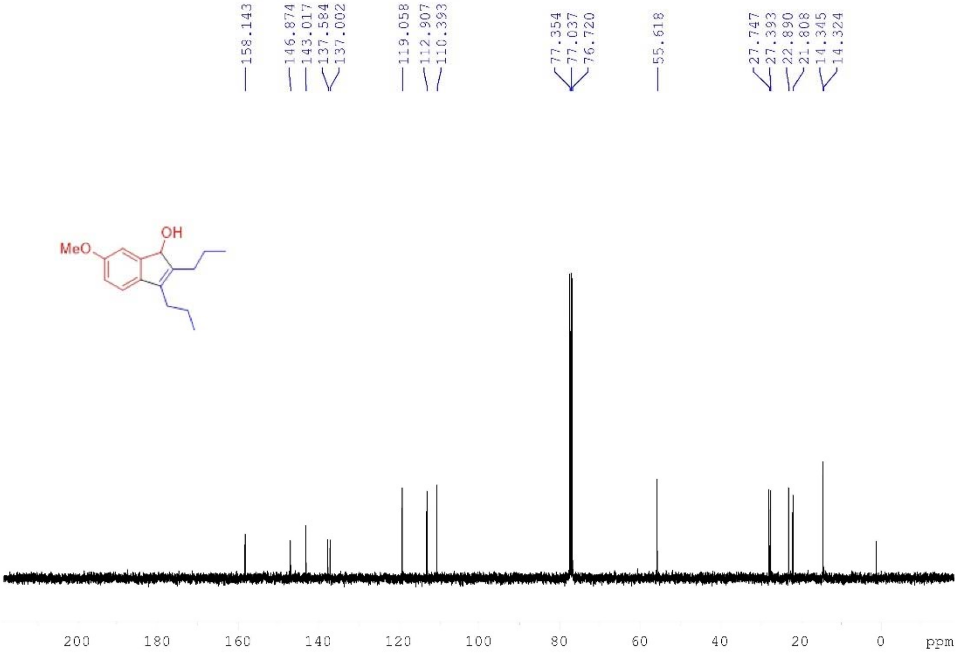
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3aa**



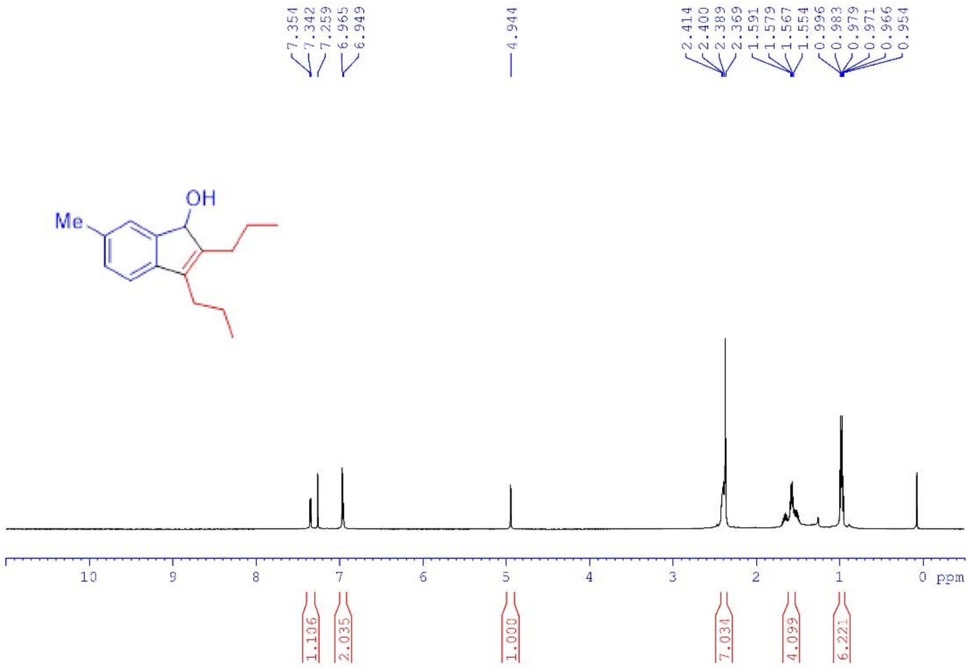
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3aa**



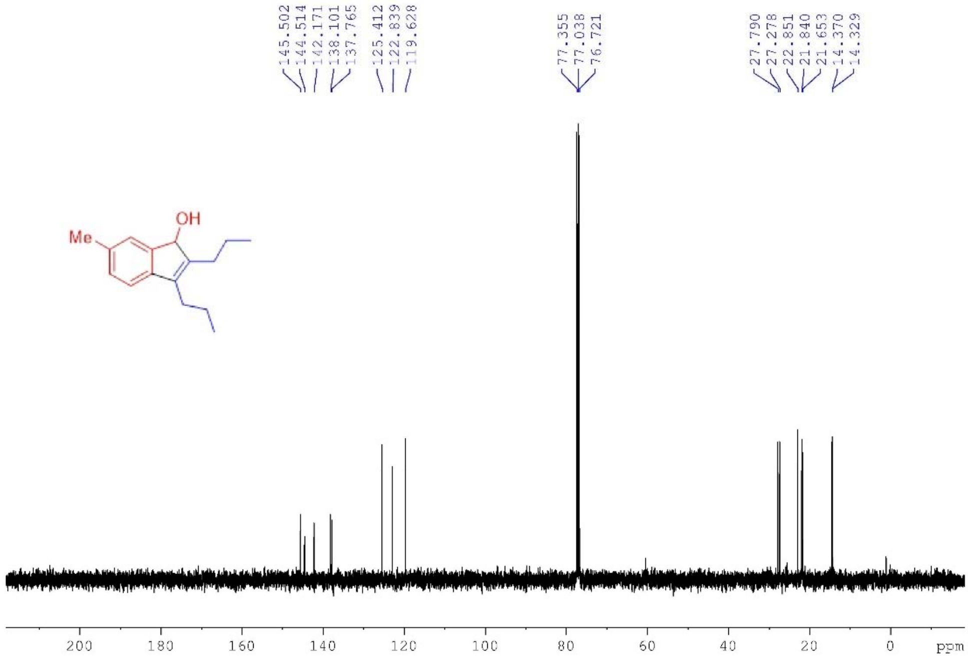
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ba**



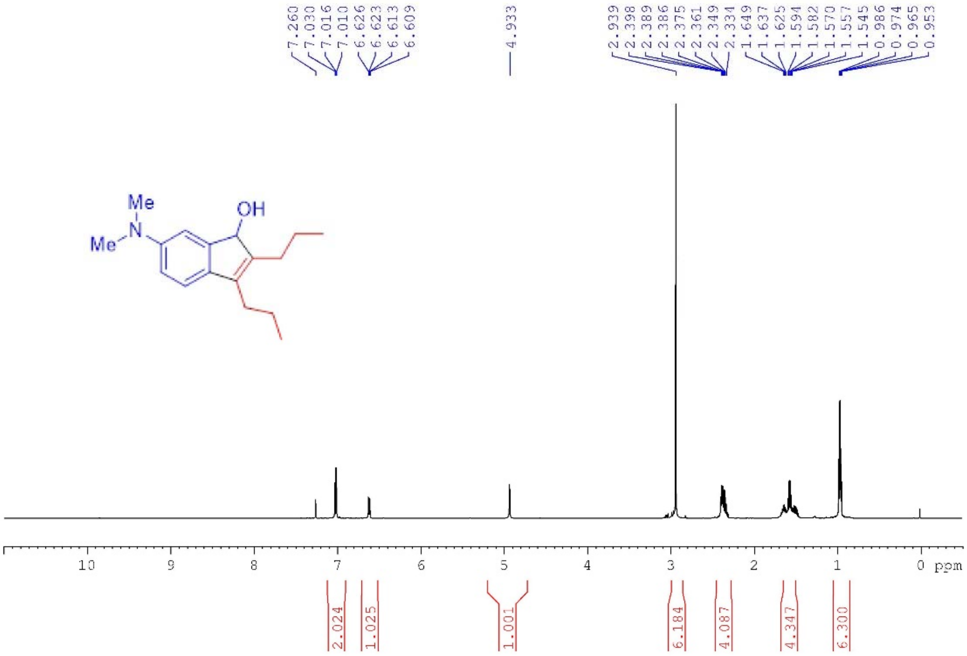
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ba**



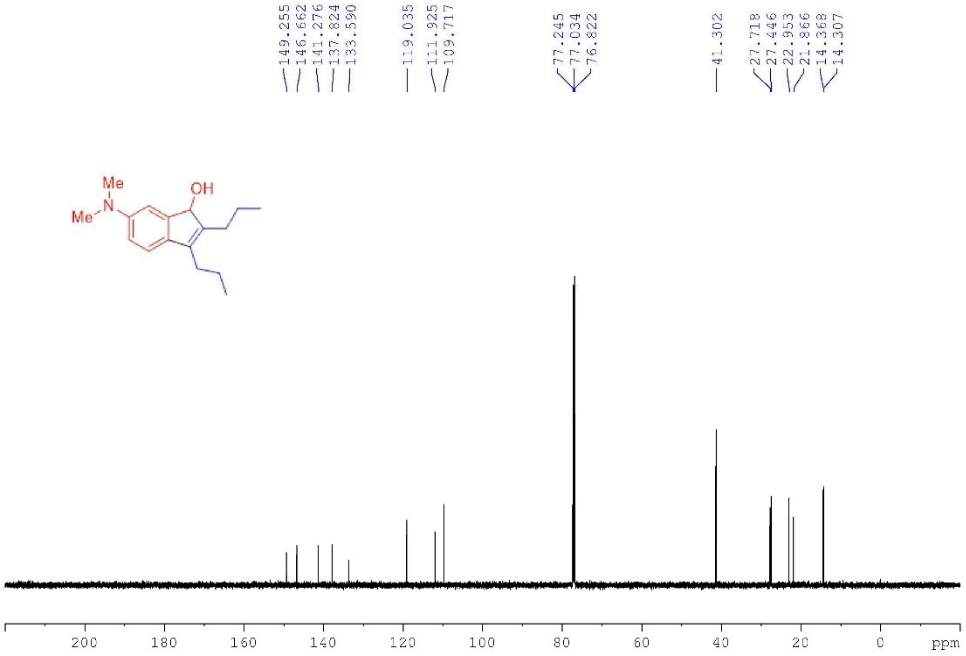
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3ca**



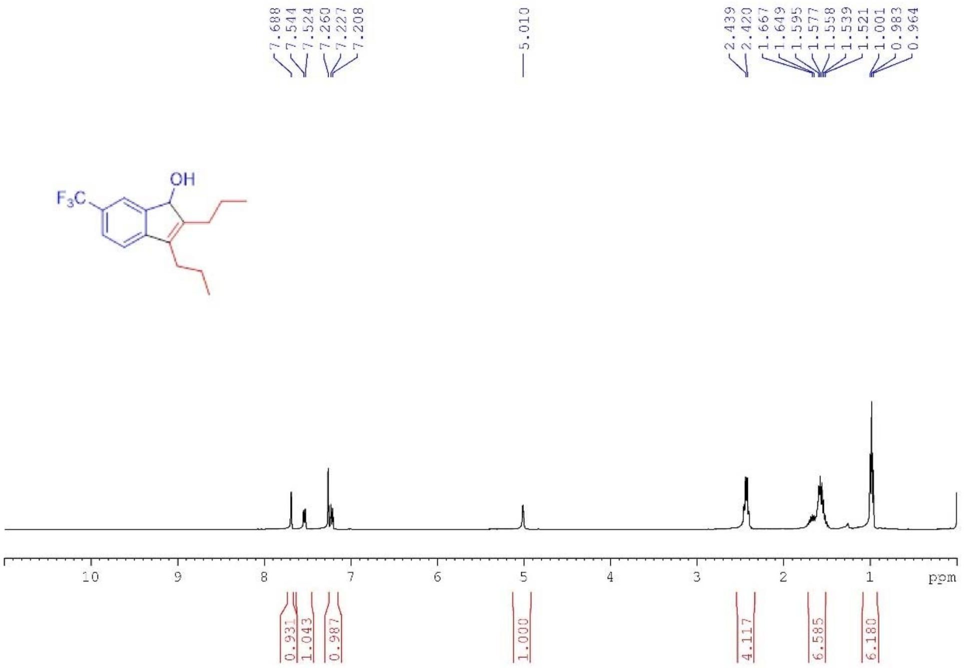
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **3ca**



^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3da**



^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3da**



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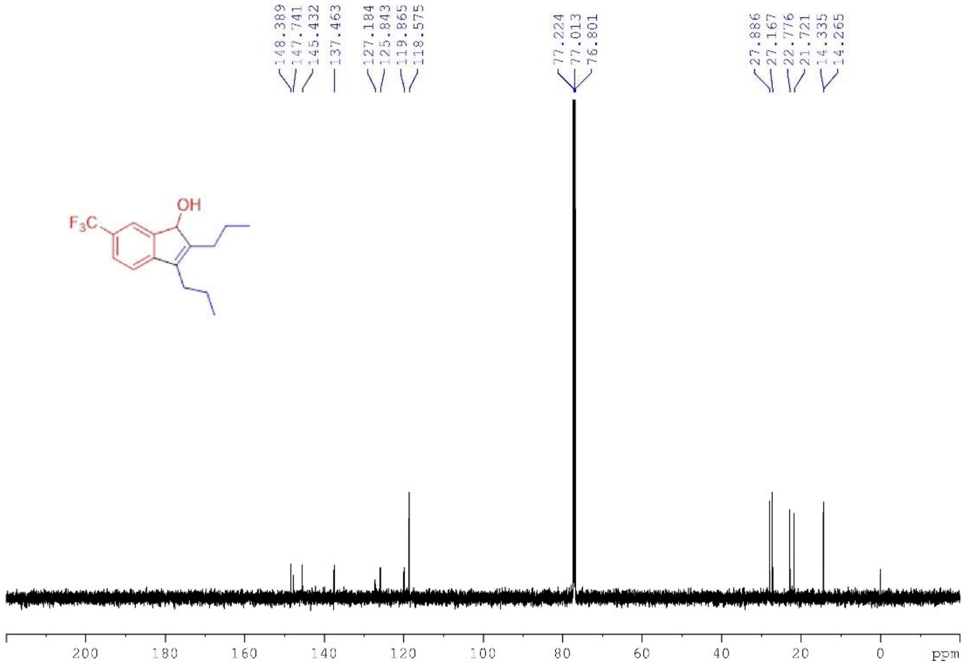
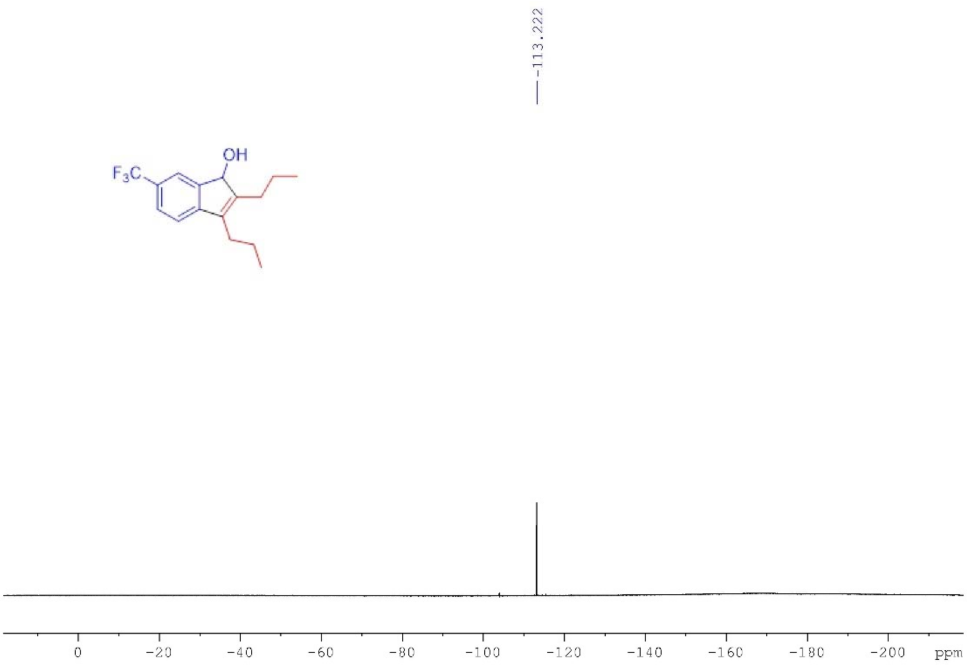
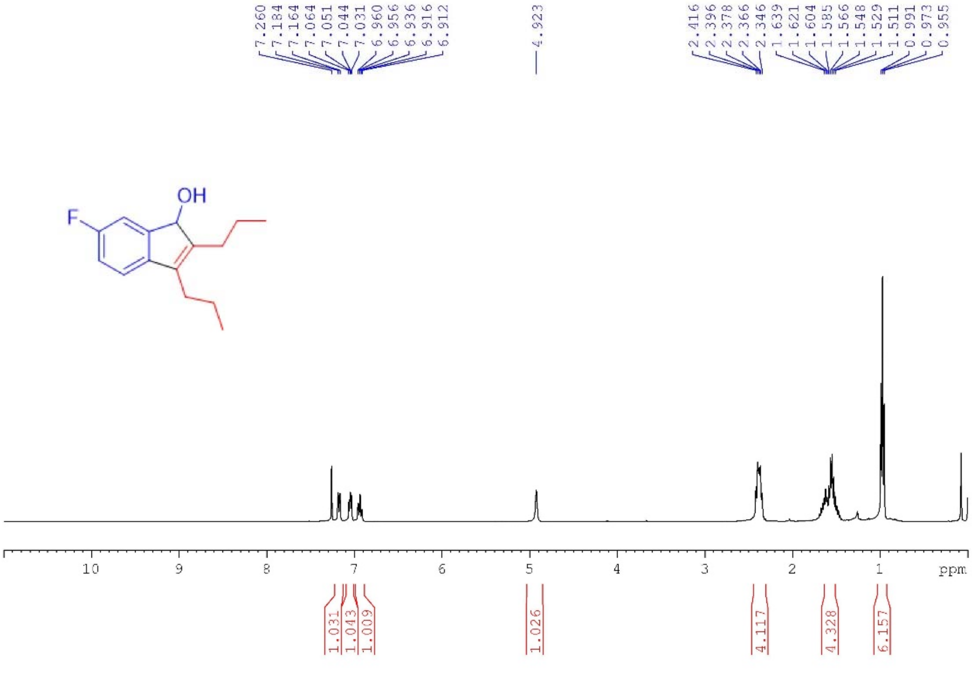


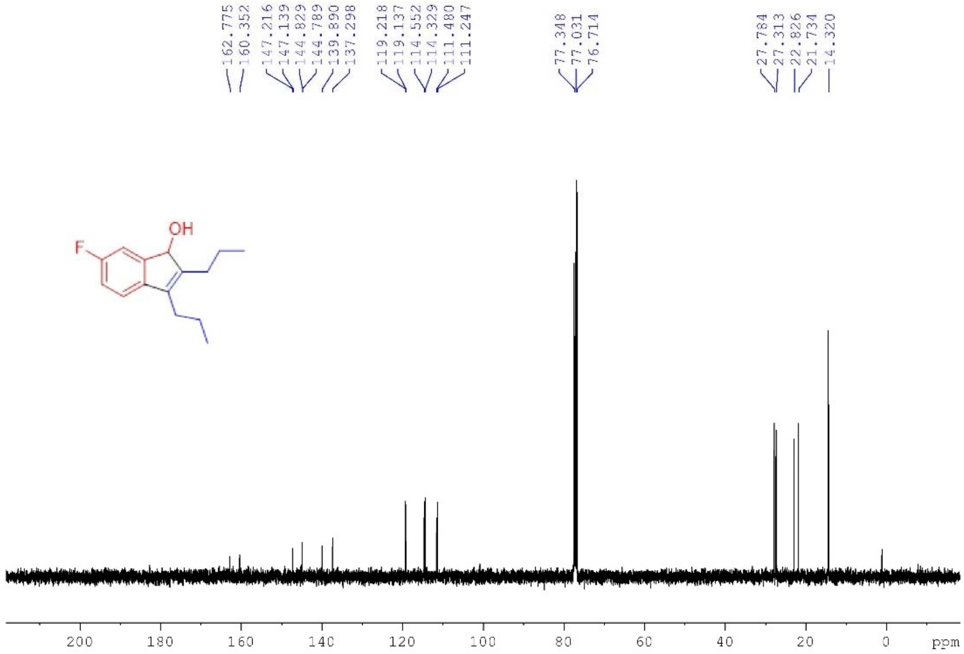
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ea**



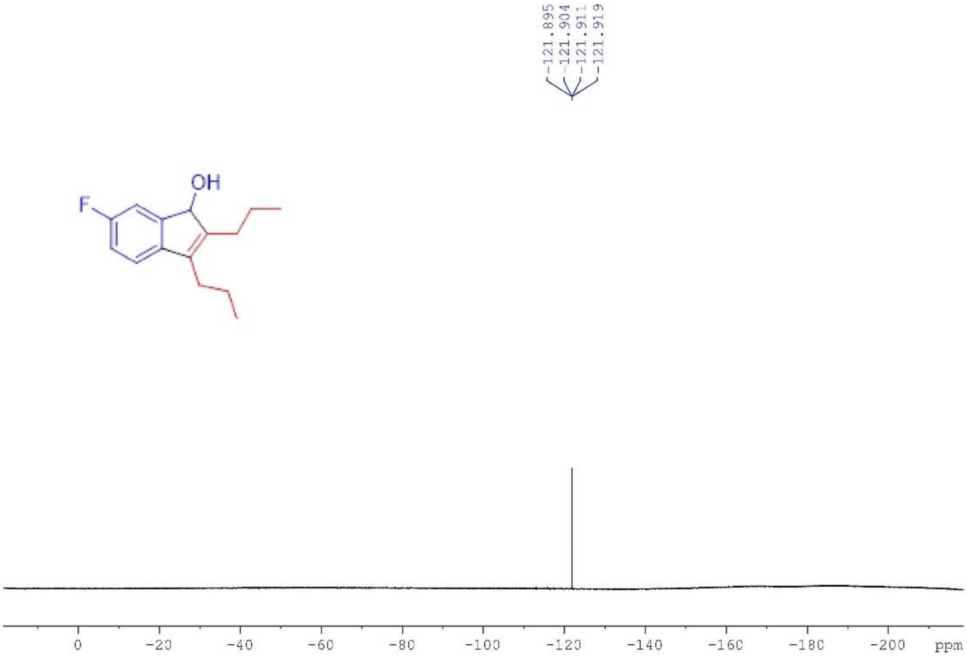
^{19}F NMR (565 MHz, $CDCl_3$,) spectrum of **3ea**



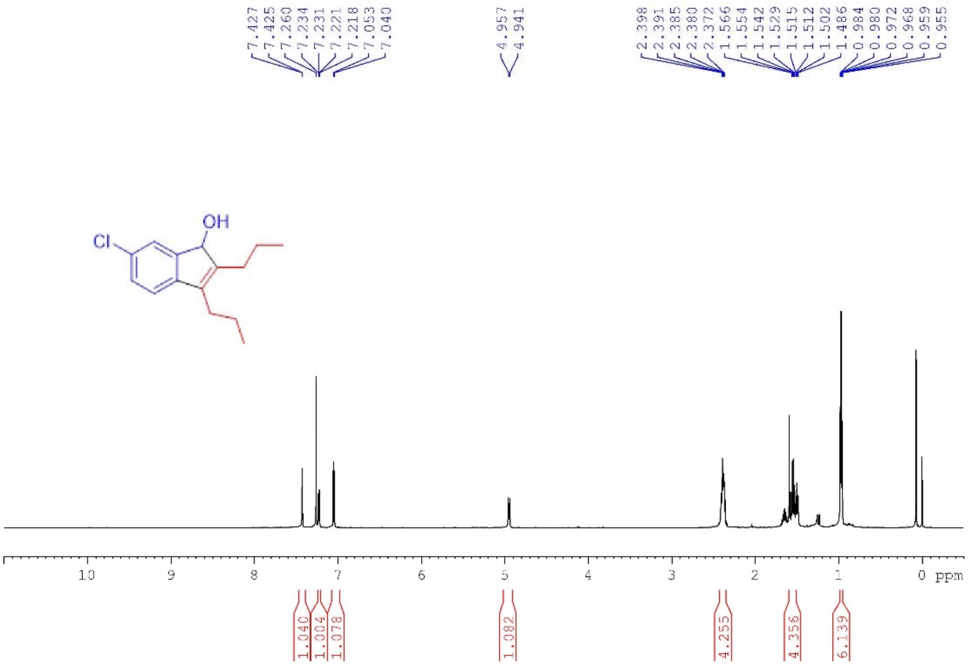
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3fa**



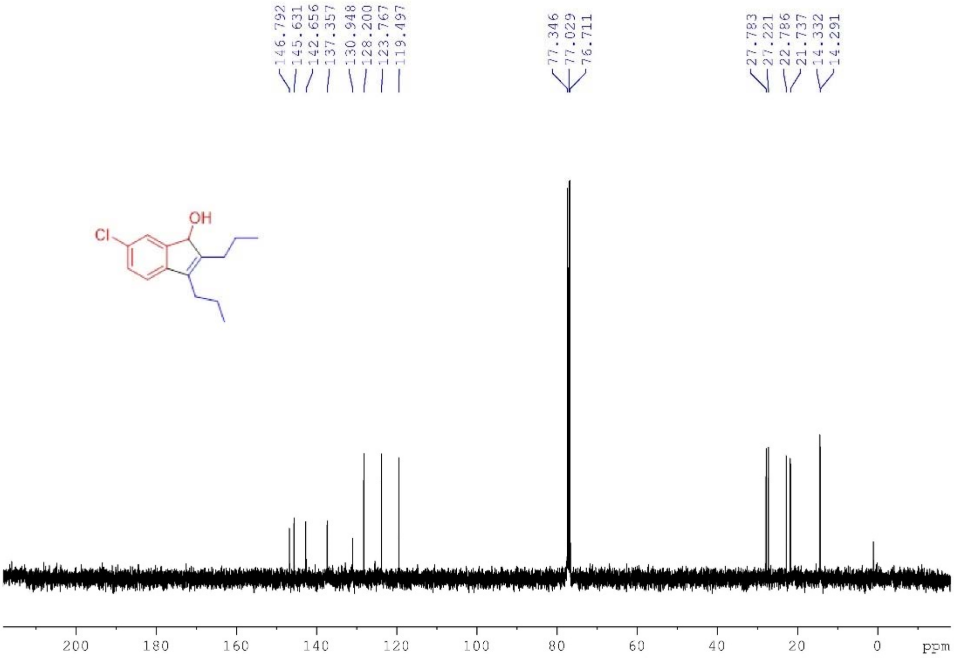
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3fa**



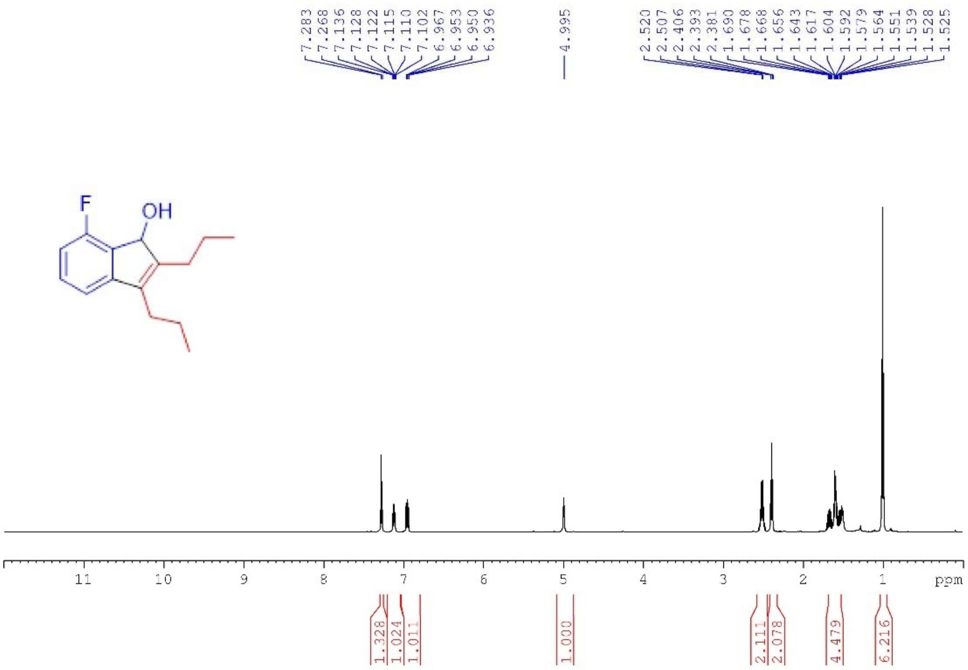
^{19}F NMR (565 MHz, CDCl$_3$,) spectrum of **3fa**



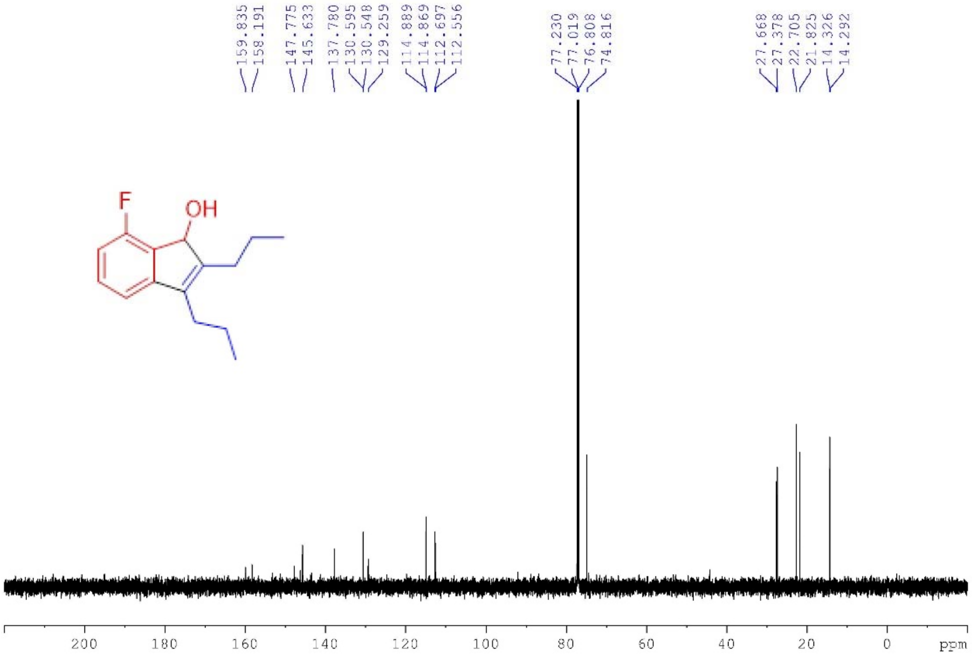
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3ga**



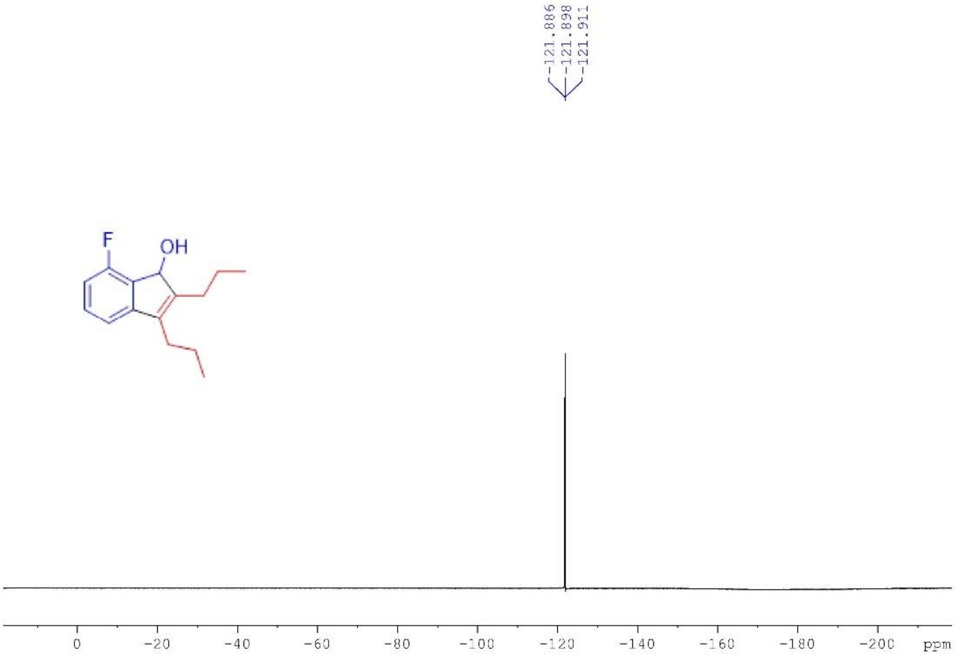
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **3ga**



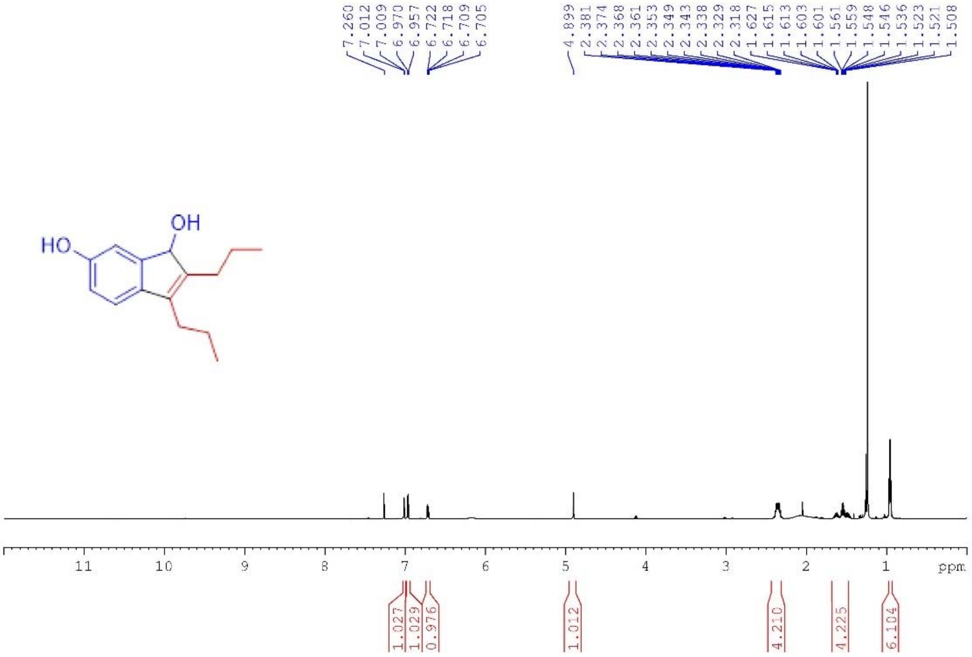
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ha**



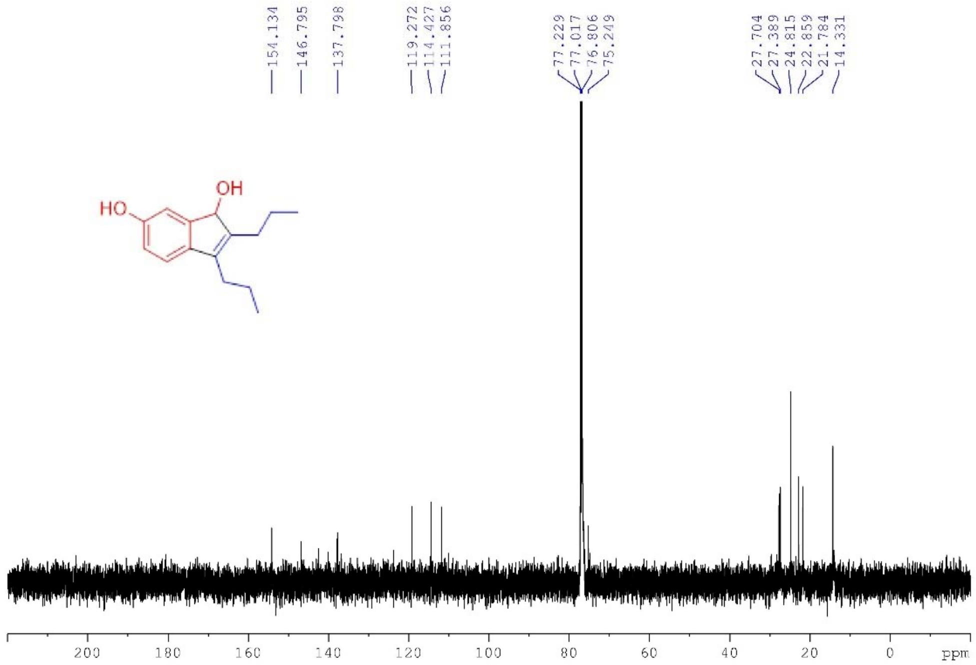
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ha**



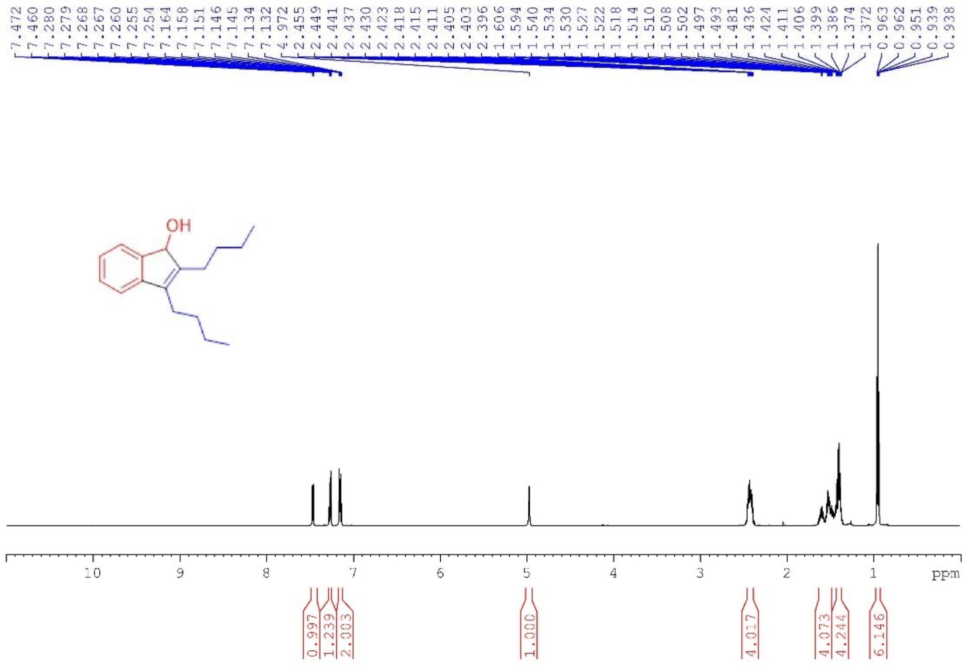
^{19}F NMR (565 MHz, CDCl$_3$,) spectrum of **3ha**



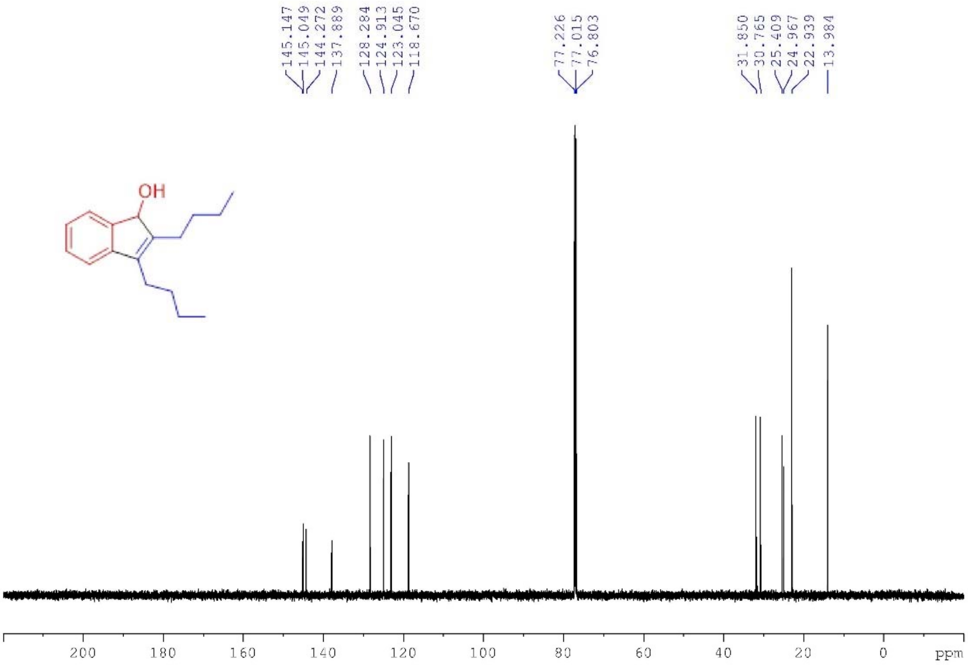
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ia**



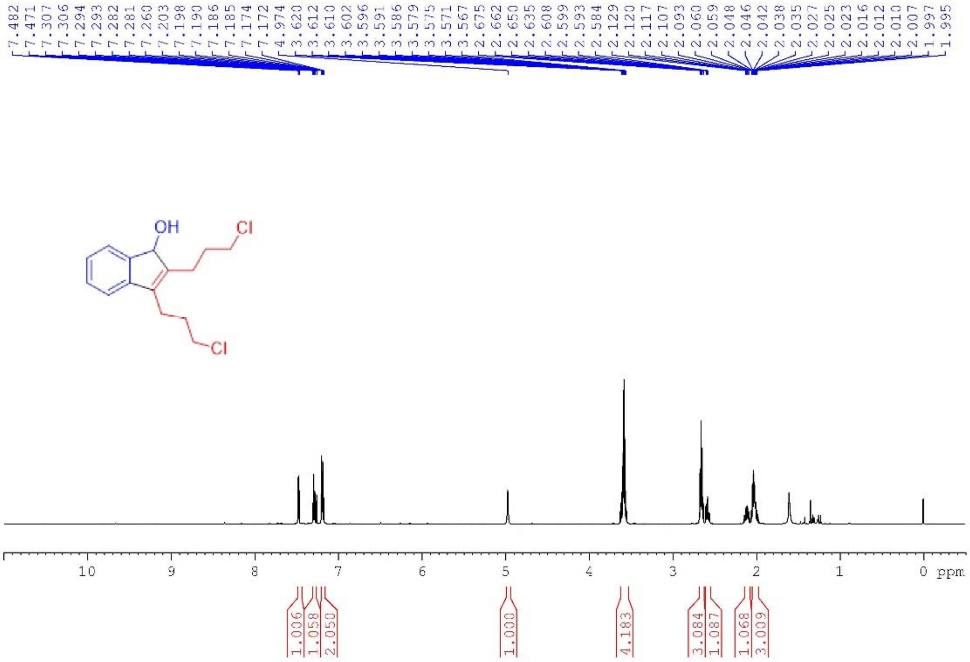
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ia**



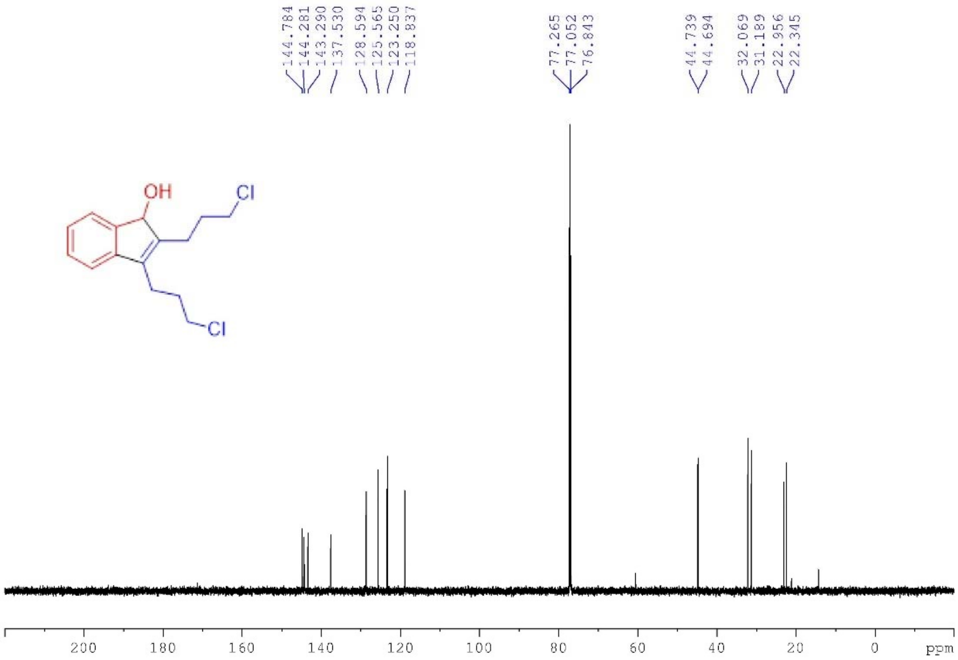
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ab**



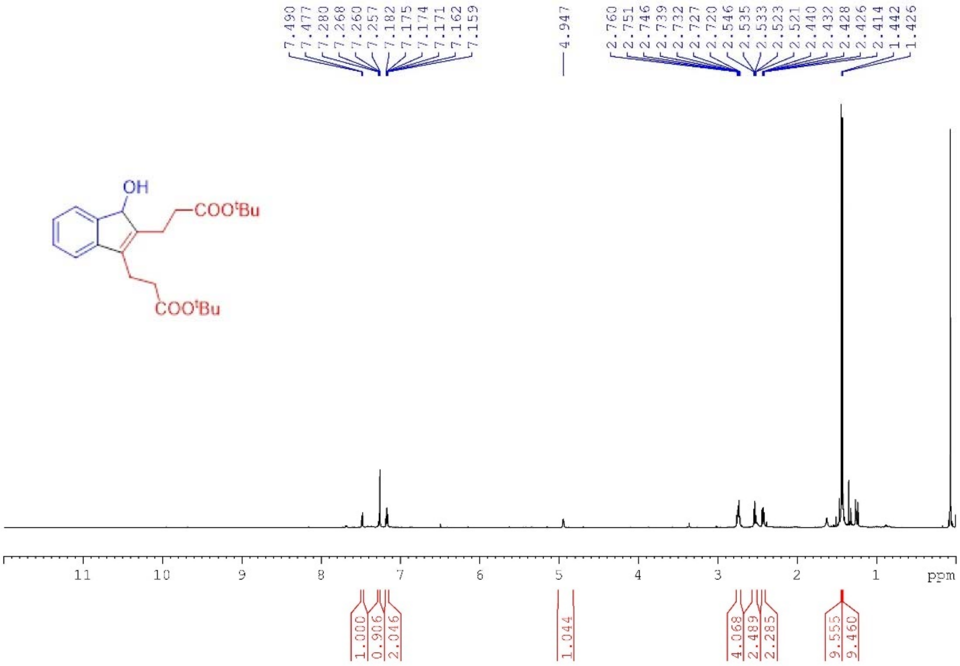
^{13}C NMR (151 MHz, $CDCl_3$) spectrum of **3ab**



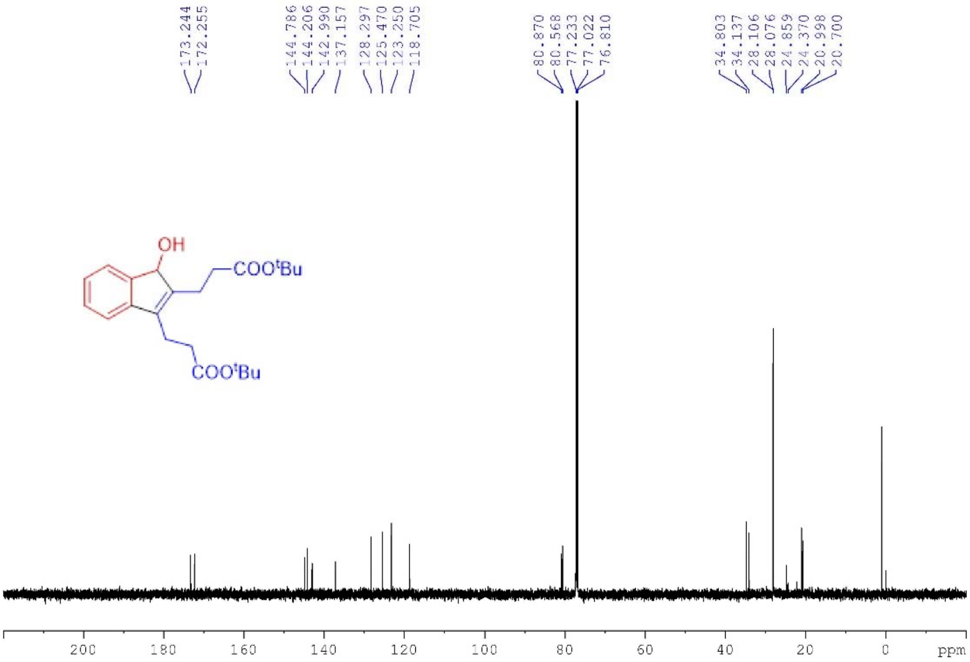
^{1}H NMR (600 MHz, $CDCl_3$) spectrum of **3ac**



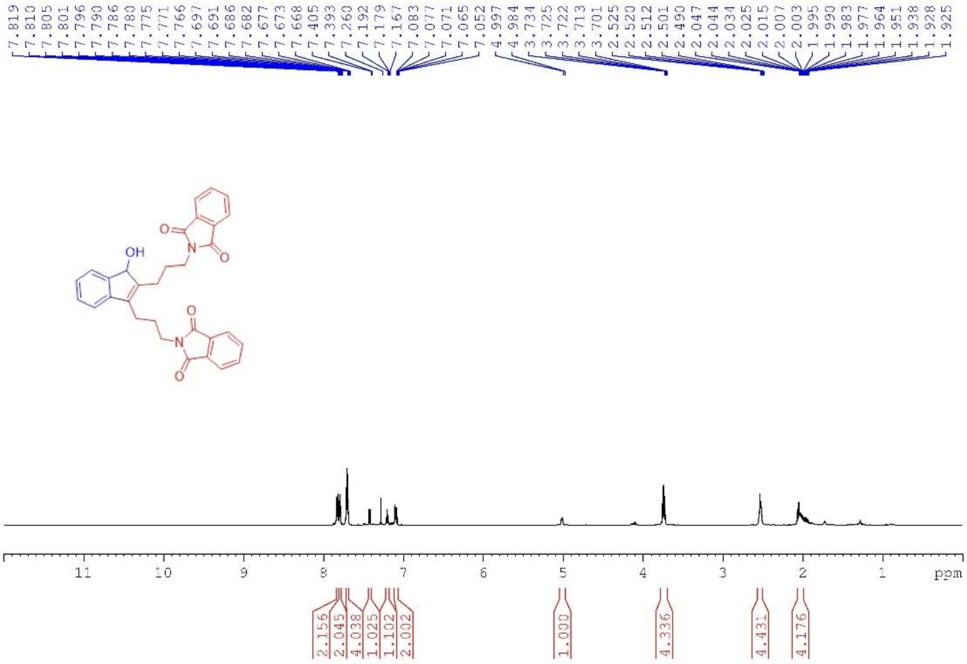
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ac**



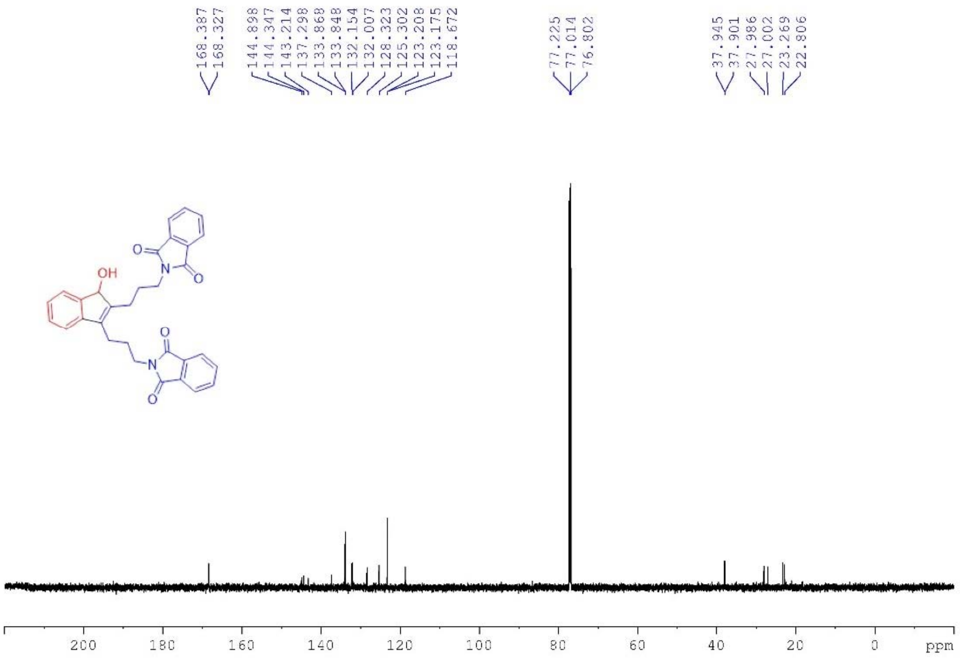
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ad**



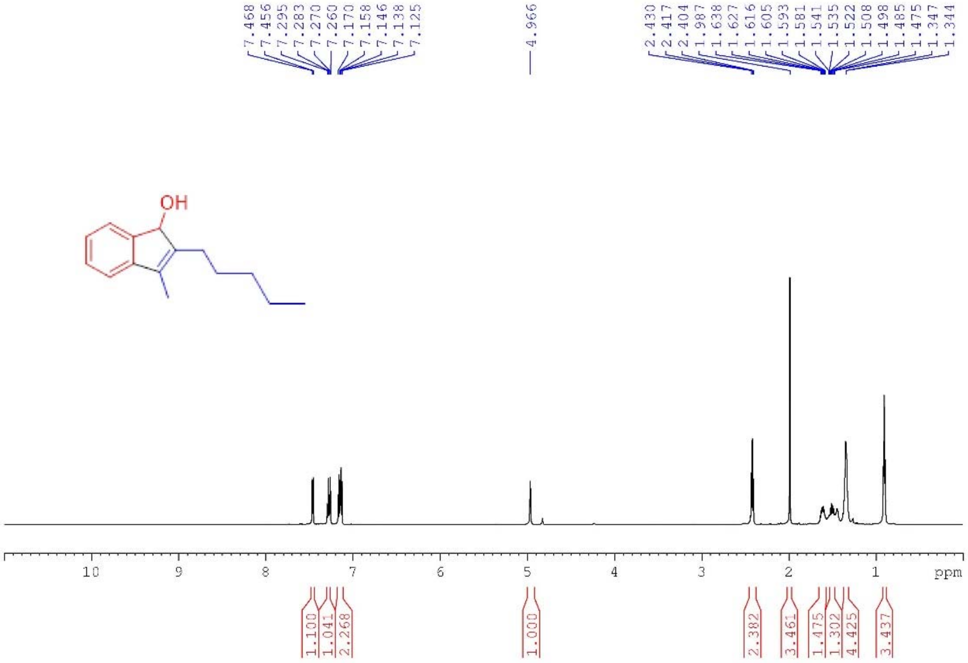
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ad**



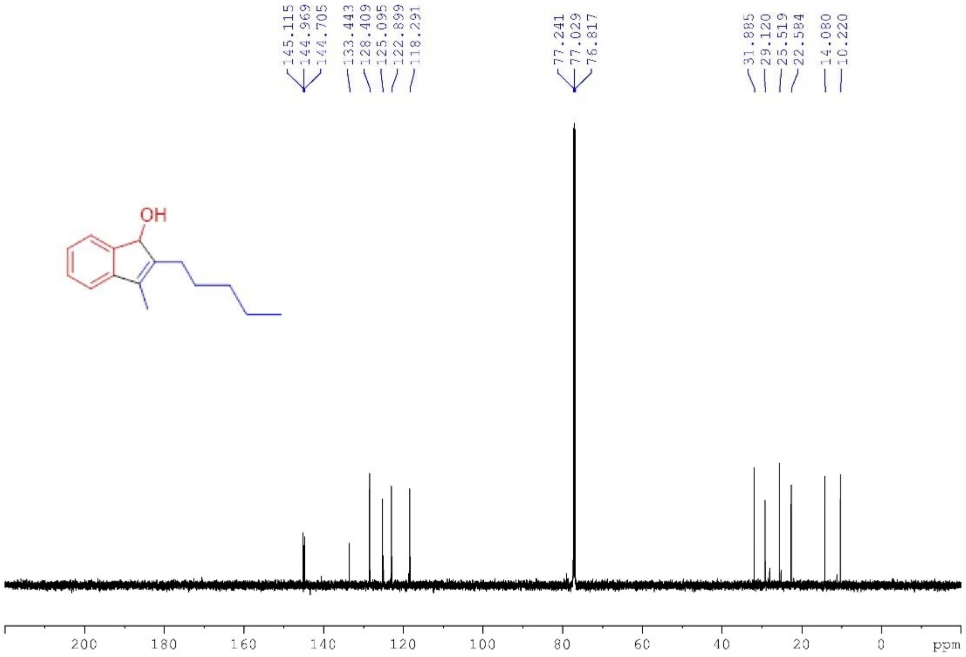
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ae**



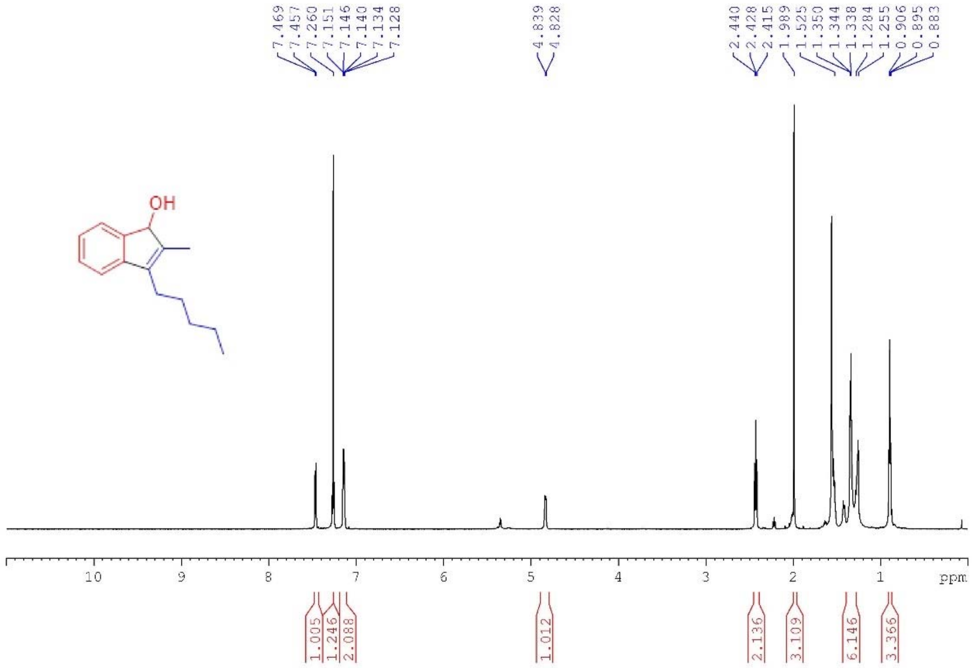
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ae**



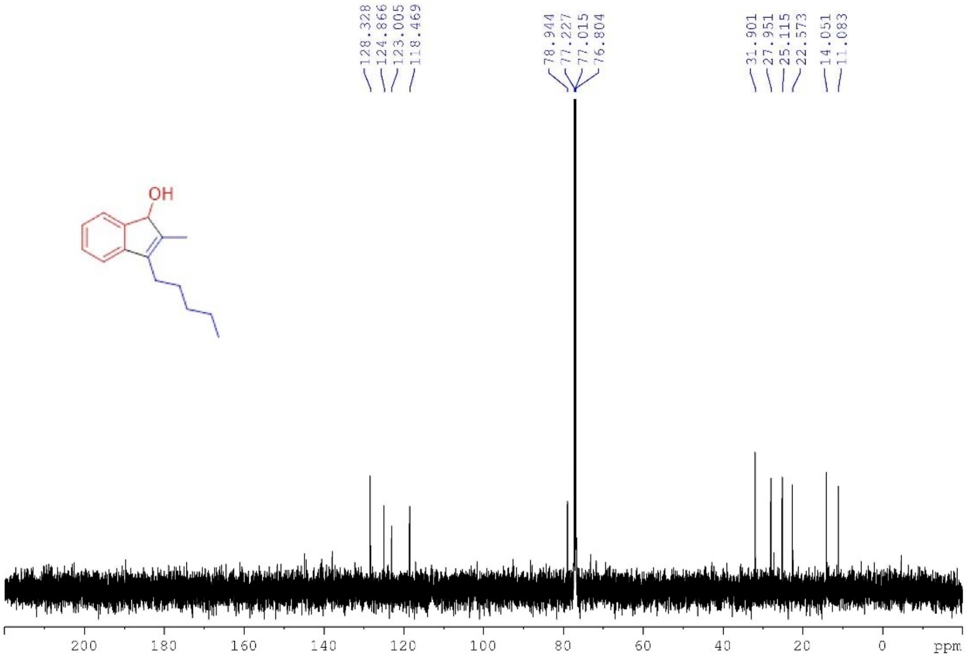
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3af**



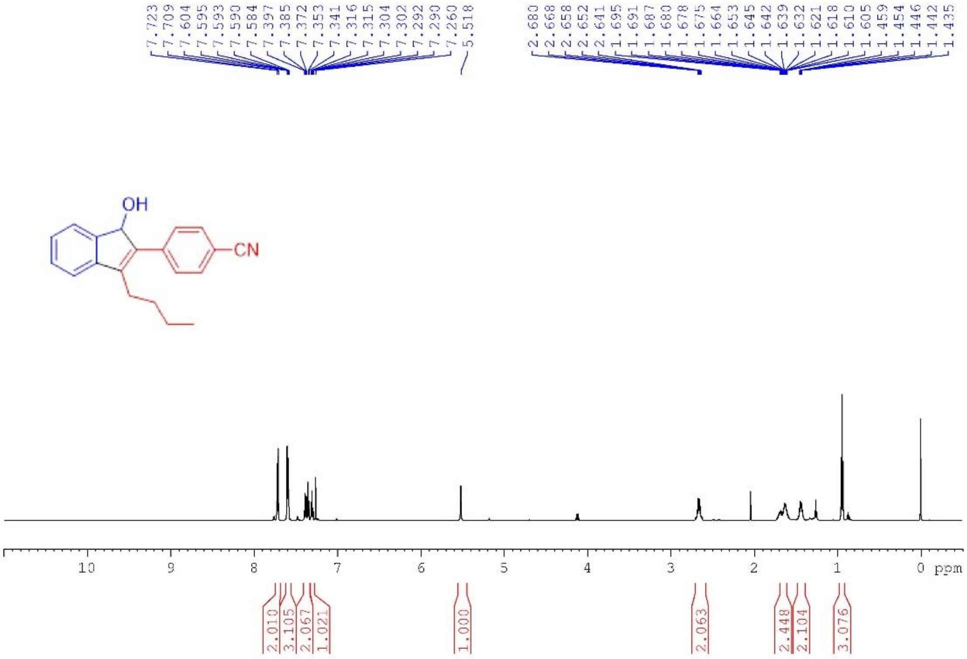
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3af**



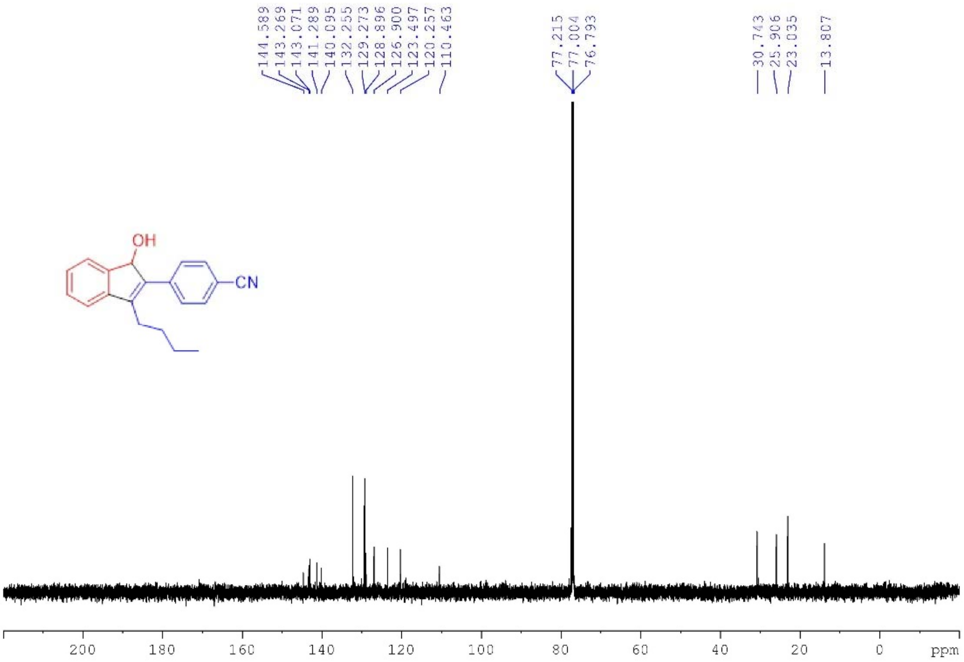
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ag**



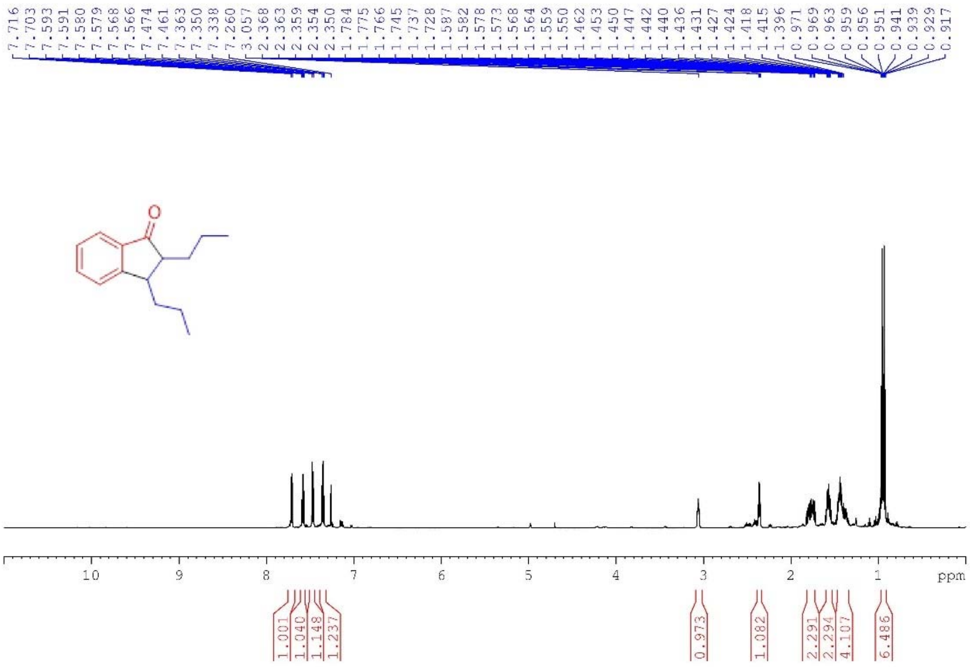
^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ag**



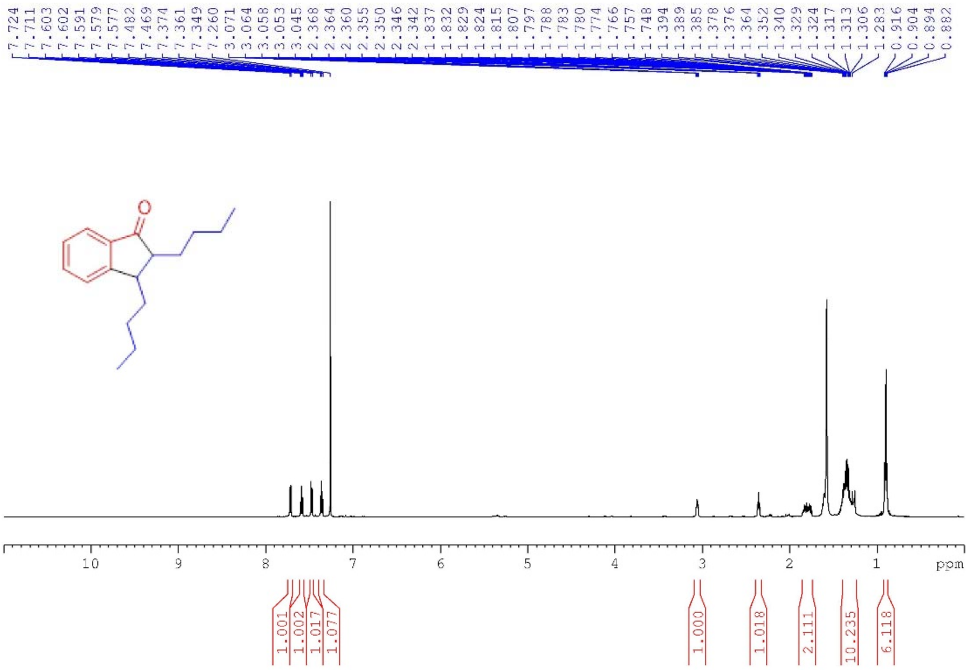
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **3ah**



^{13}C NMR (151 MHz, CDCl$_3$) spectrum of **3ah**

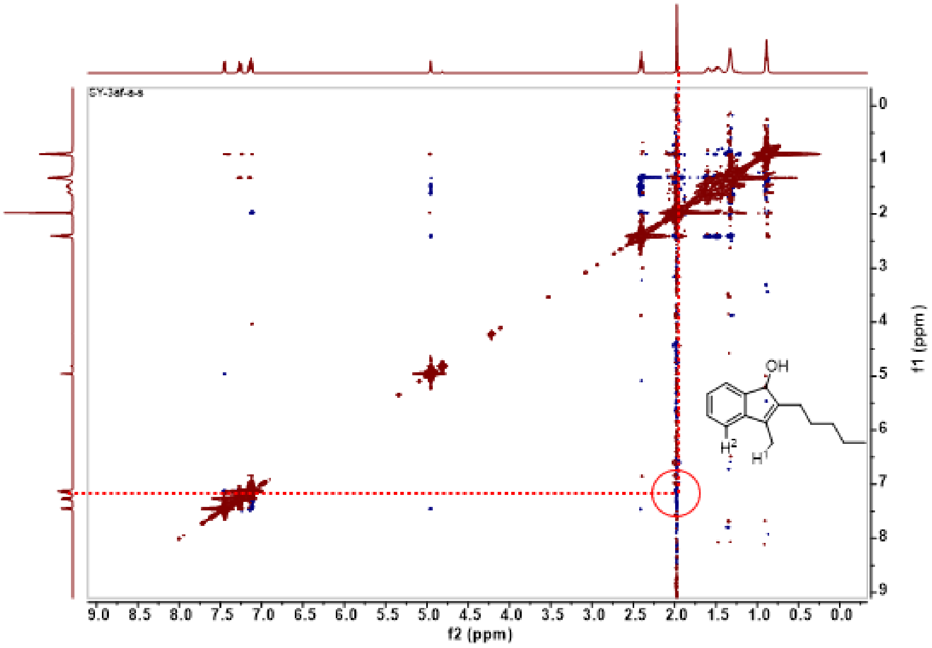


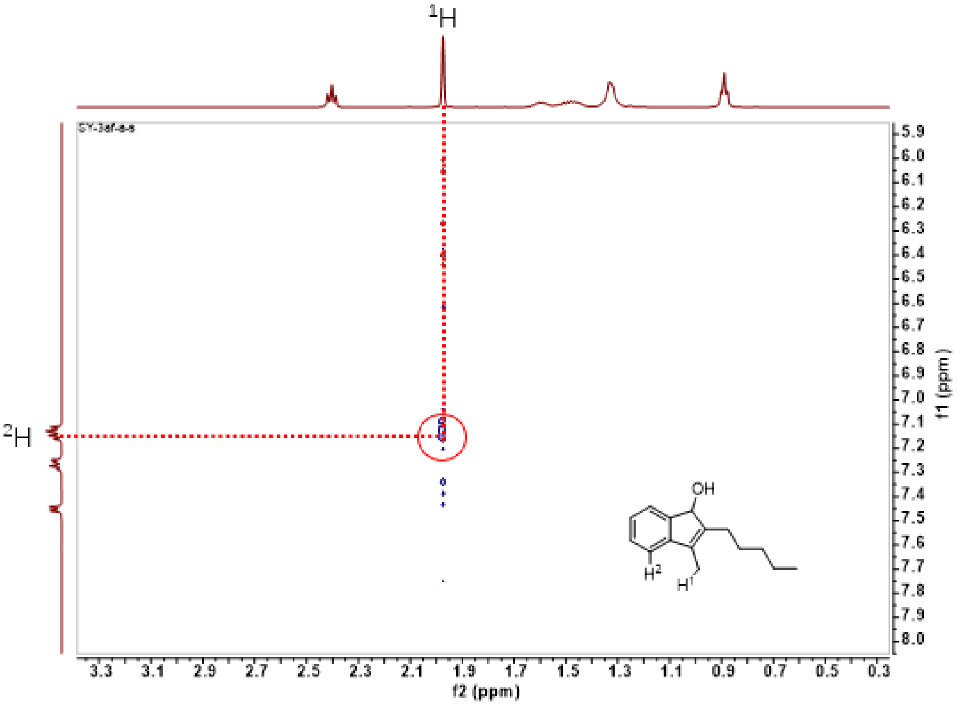
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **4a**

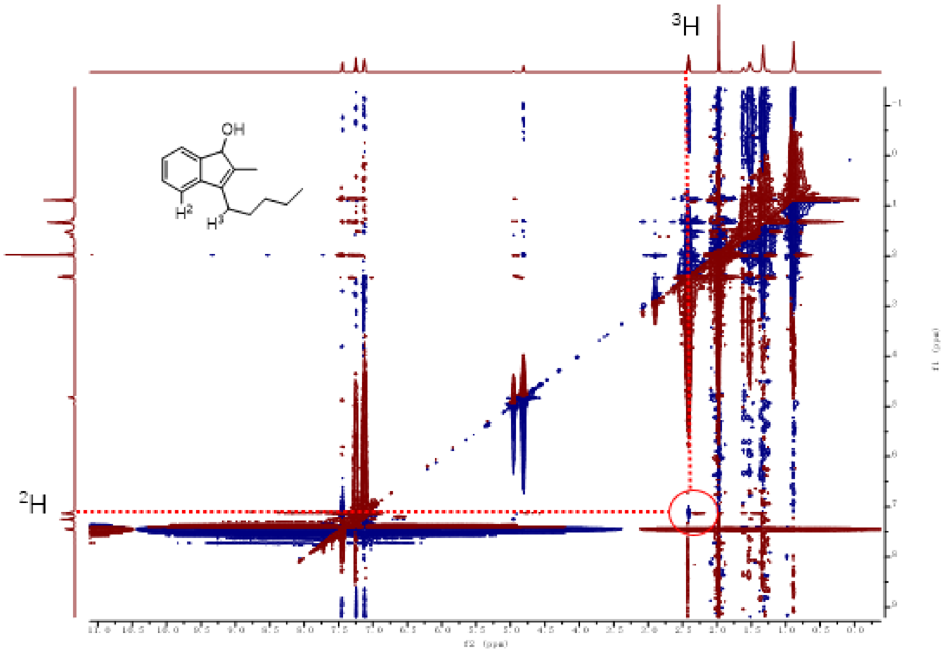


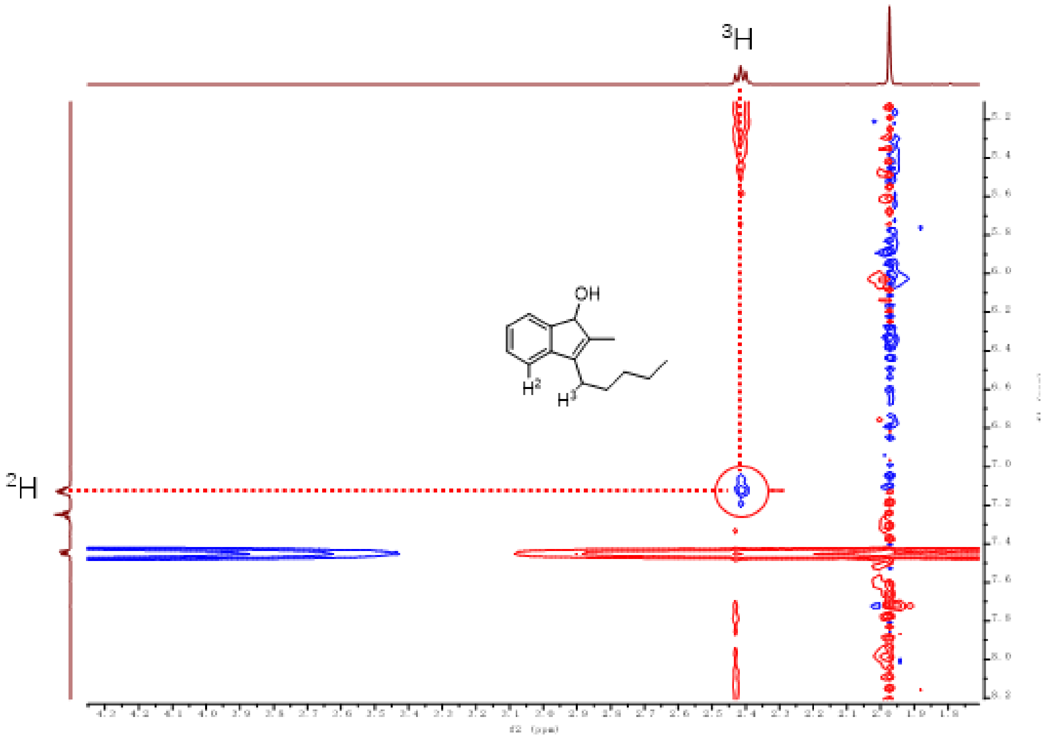
^{1}H NMR (600 MHz, CDCl$_3$) spectrum of **5a**

NOE NMR for 3af and 3af'




1H
2H
SY-38f-a-s
OH
H2
H1
5.9
6.0
6.1
6.2
6.3
6.4
6.5
6.6
6.7
6.8
6.9
7.0
7.1
7.2
7.3
7.4
7.5
7.6
7.7
7.8
7.9
8.0
f1 (ppm)
3.3
3.1
2.9
2.7
2.5
2.3
2.1
1.9
1.7
1.5
1.3
1.1
0.9
0.7
0.5
0.3
f2 (ppm)

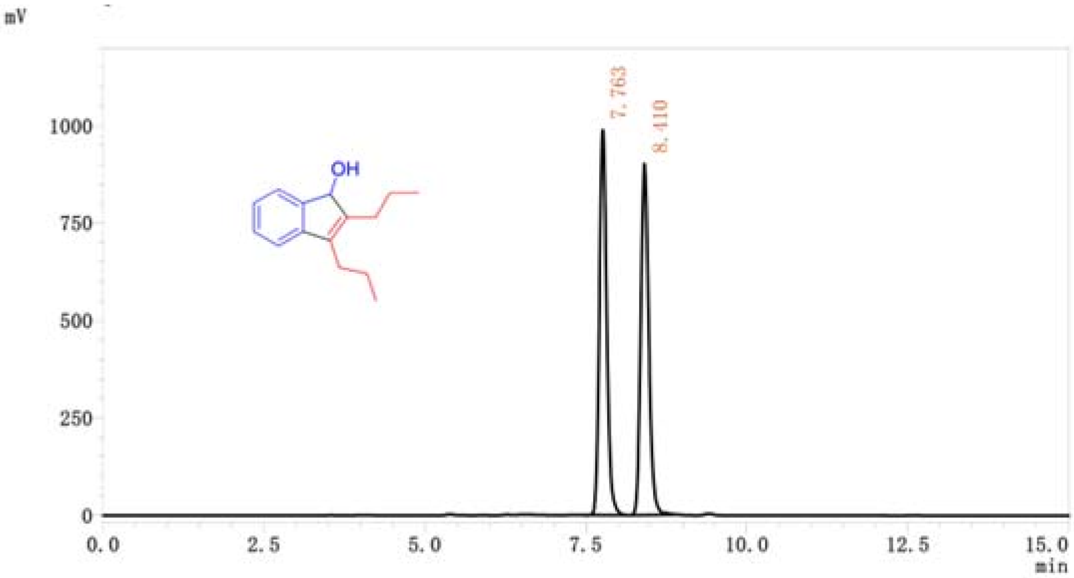

3H
2H
OH
H2
H3
f1 (ppm)
f2 (ppm)



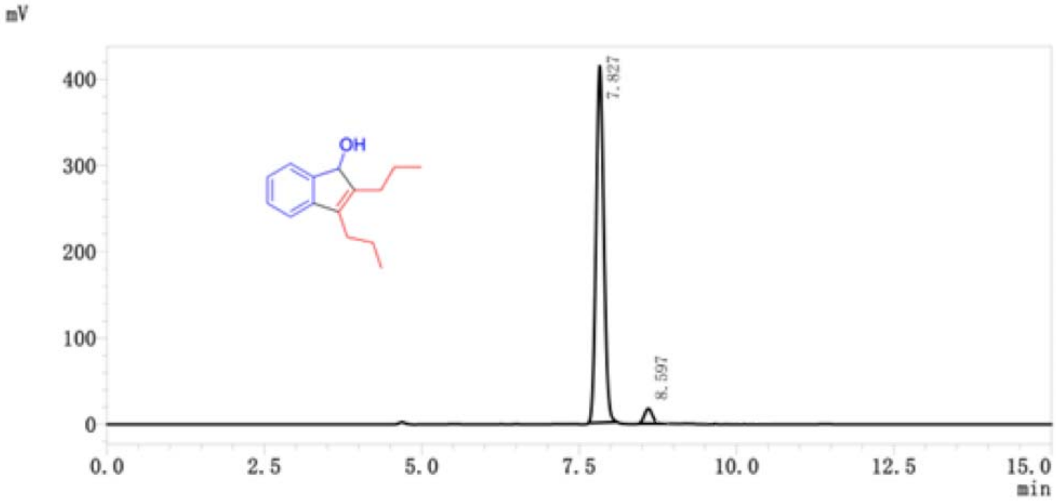
^{3}H
^{2}H
OH
H^2
H^3
5.2
5.4
5.6
5.8
6.0
6.2
6.4
6.6
6.8
7.0
7.2
7.4
7.6
7.8
8.0
8.2
f1 (ppm)
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
f2 (ppm)

10. HPLC Data

(*S*)-**3aa**

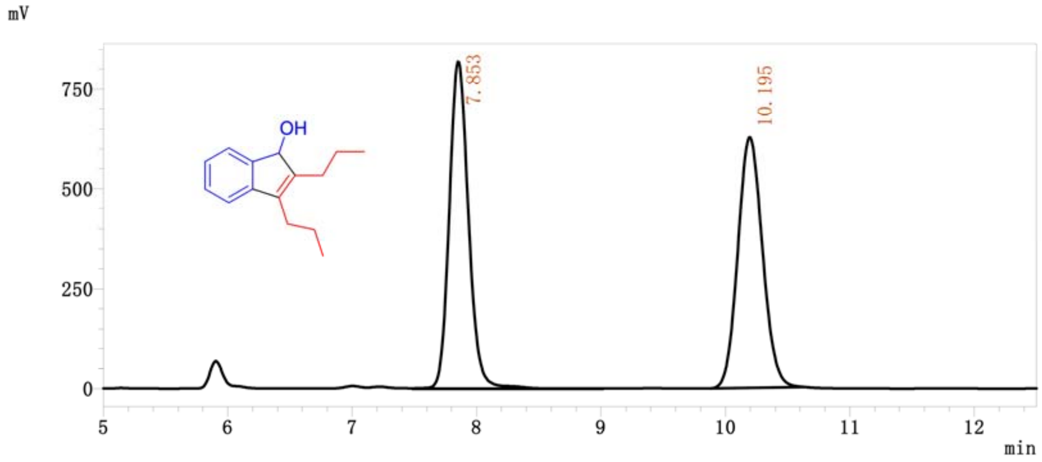


Peak#	Ret Time	Area	Height	Area%
1	7.763	7839775	987393	50.095
2	8.410	7809975	901247	49.905
Total		15649750	1888639	100.000

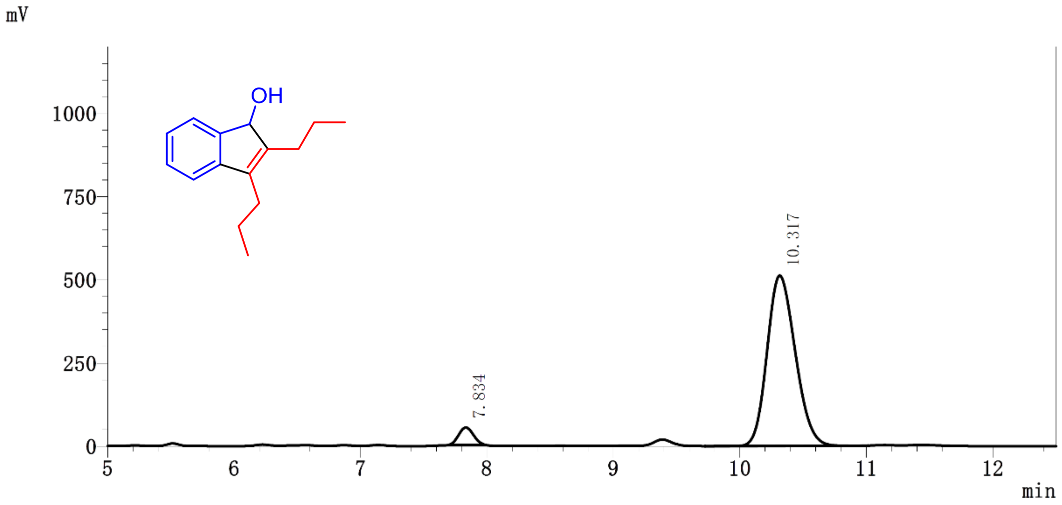


Peak%	Ret. Time	Area	Height	Area%
1	7.827	3520058	413283	95.897
2	8.597	150602	17204	4.103
Total		3670660	430487	

(R)-**3aa**

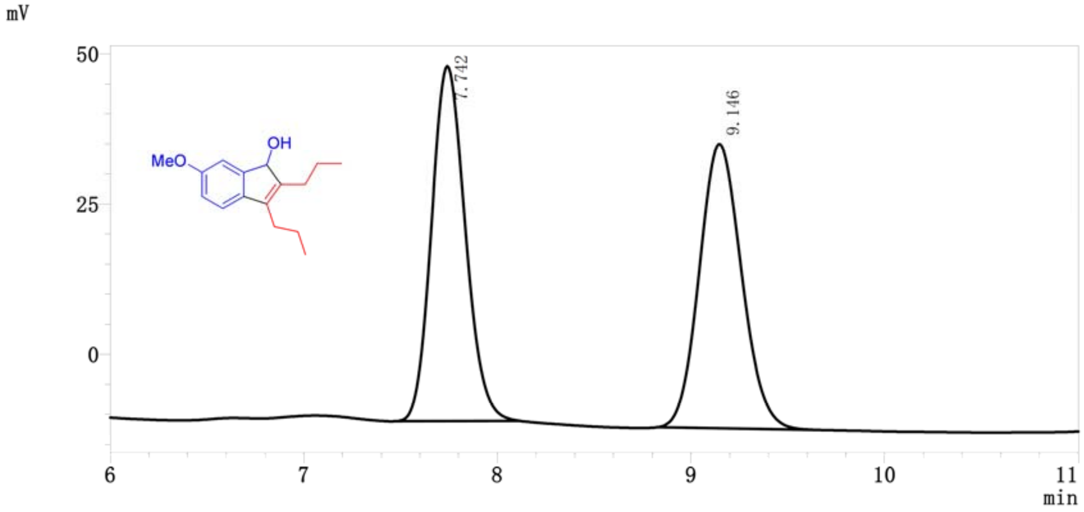


Peak#	Ret.Time	Area	Height	Area%
1	7.853	8814999	818607	50.458
2	10.195	8654891	627209	49.542
Total		17469890	1445816	

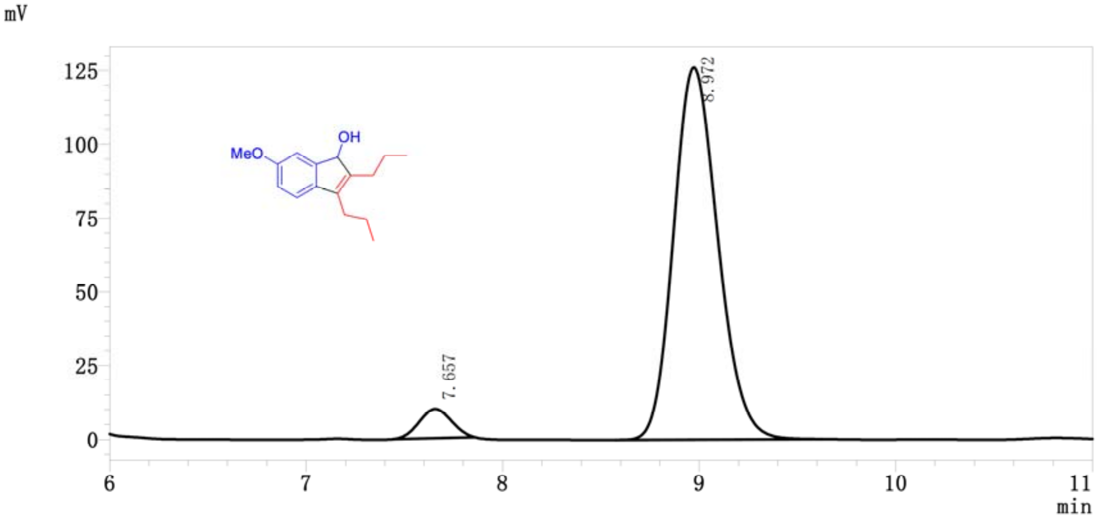


Peak#	Ret.Time	Area	Height	Area%
1	7.834	424435	52461	5.092
2	10.317	7910936	511553	94.908
总计		8335371	564014	

3ba:

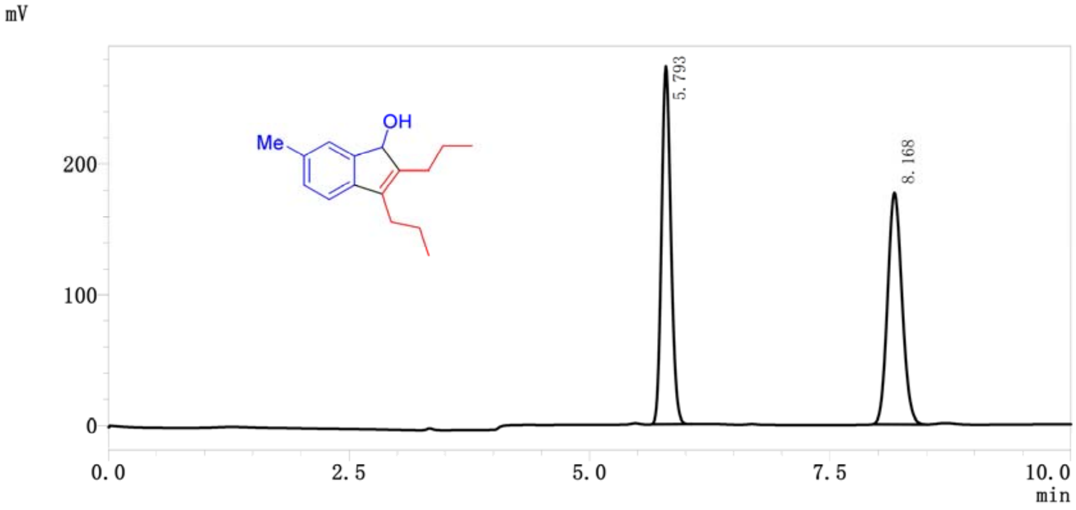


Peak#	Ret. Time	Area	Height	Area%
1	7.742	719410	59065	50.075
2	9.146	717263	47210	49.925
Total		1436673	106275	100.000

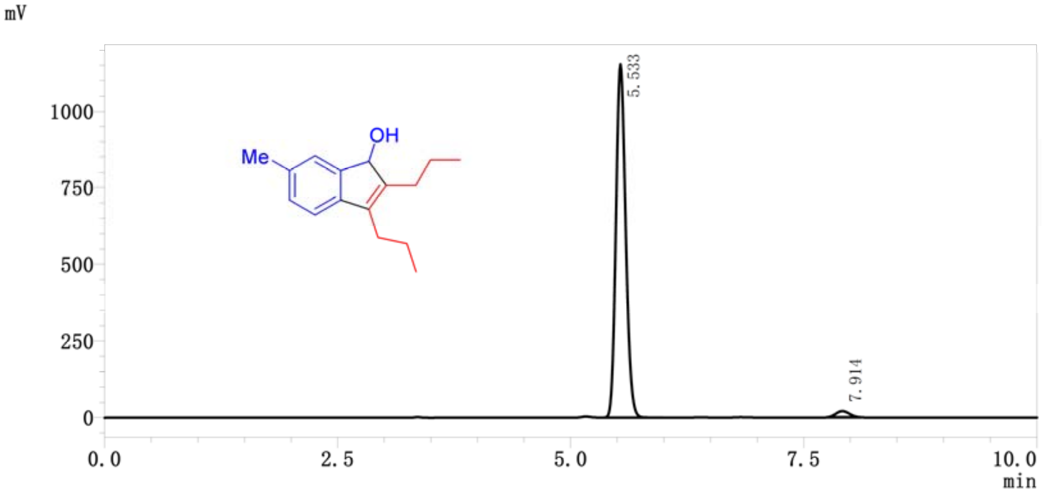


Peak#	Ret. Time	Area	Height	Area%
1	7.657	113672	9836	5.439
2	8.972	1976411	126091	94.561
Total		2090083	135927	

3ca:

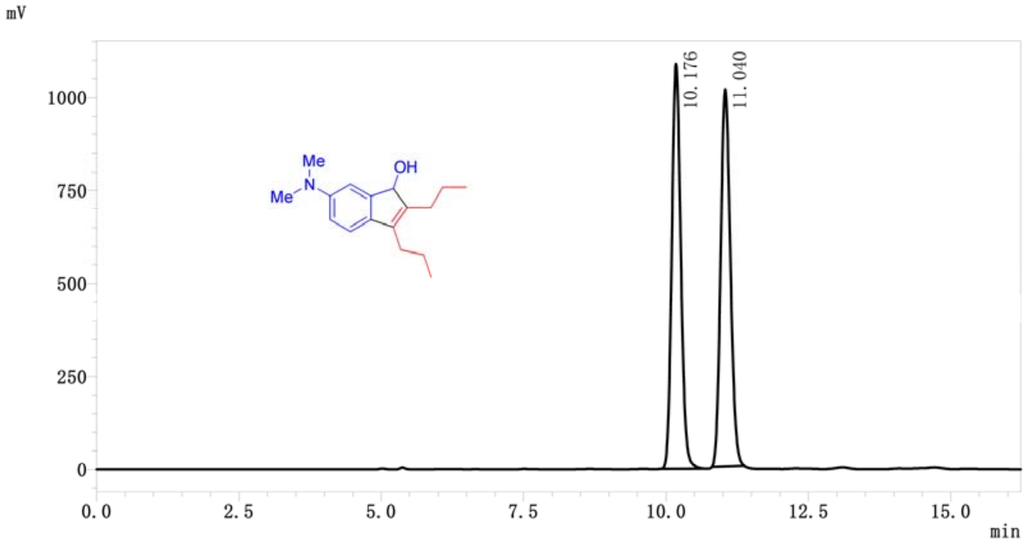


Peak#	Ret. Time	Area	Height	Area%
1	5.793	1845291	273526	50.027
2	8.168	1843315	176797	49.973
Total		3688606	450323	



Peak#	Ret. Time	Area	Height	Area%
1	5.533	8357479	1152818	97.632
2	7.914	202673	20113	2.368
Total		8560151	1172930	

3da



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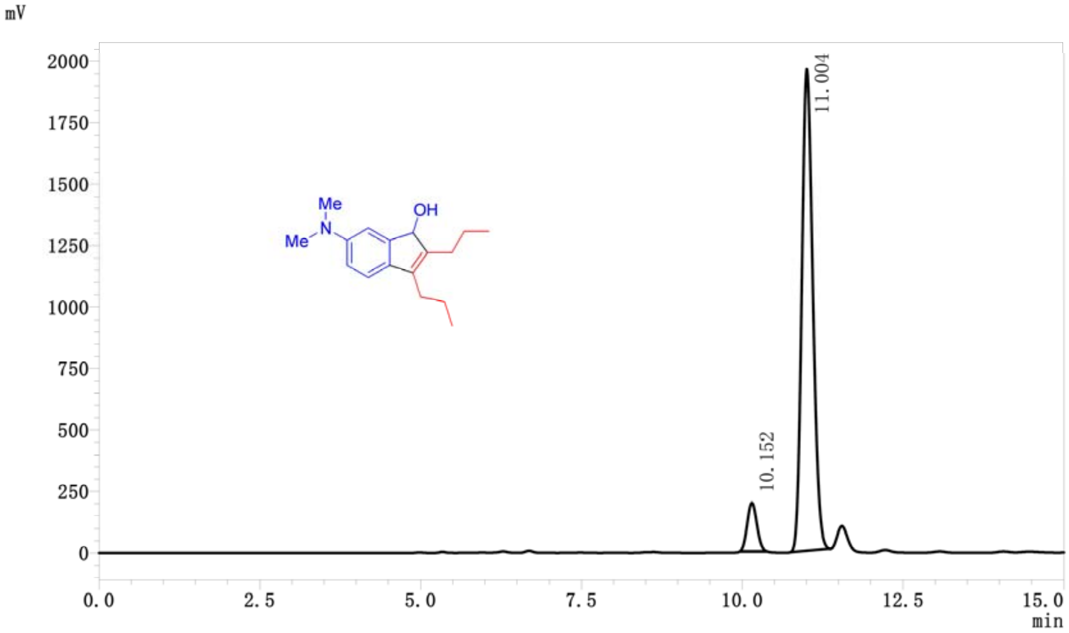
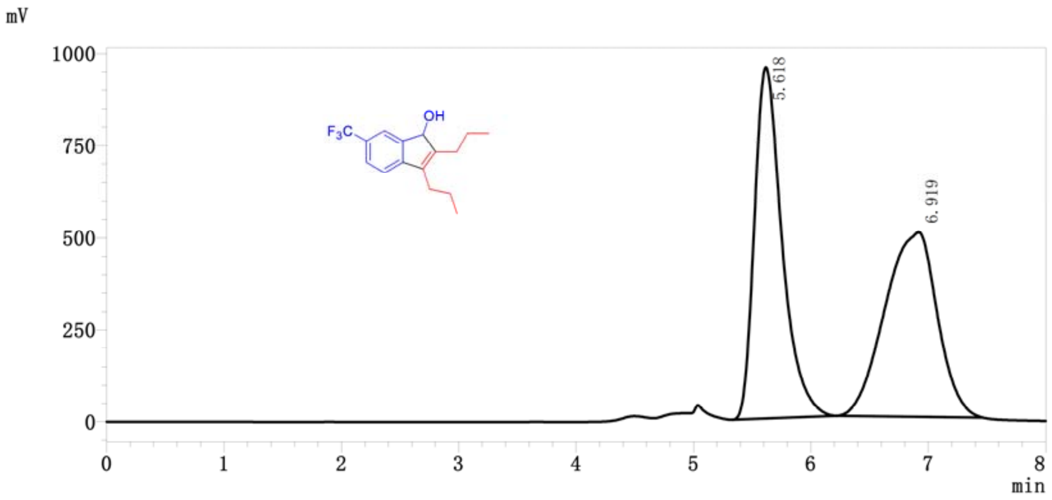
Peak#	Ret. Time	Area	Height	Area%
1	10. 176	11980919	1088933	49. 866
2	11. 040	12045273	1014226	50. 134
Total		24026191	2103159	100. 000

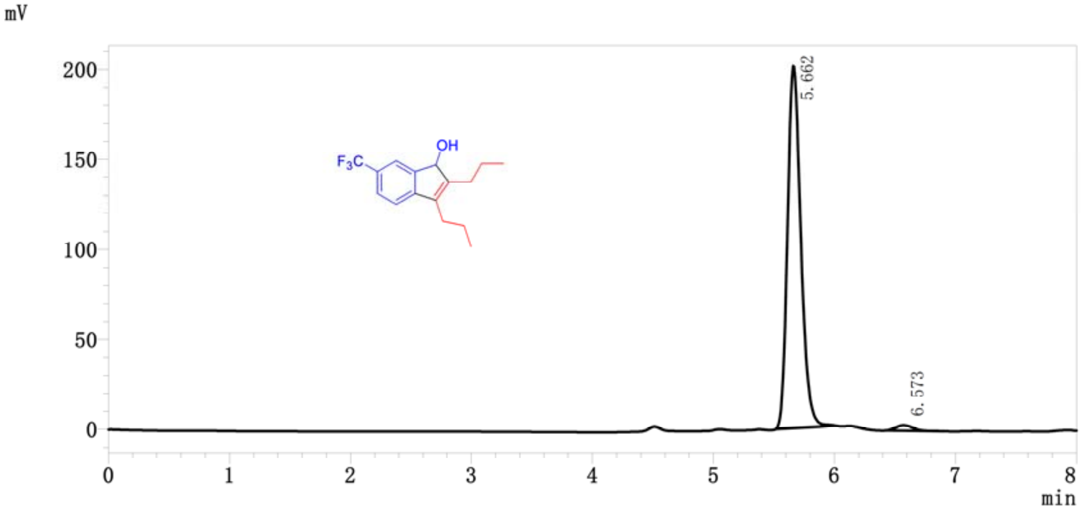


Peak#	Ret. Time	Area	Height	Area%
1	10. 152	2066931	197771	8. 139
2	11. 004	23329300	1958181	91. 861
Total		25396231	2155952	100. 000

3ea:

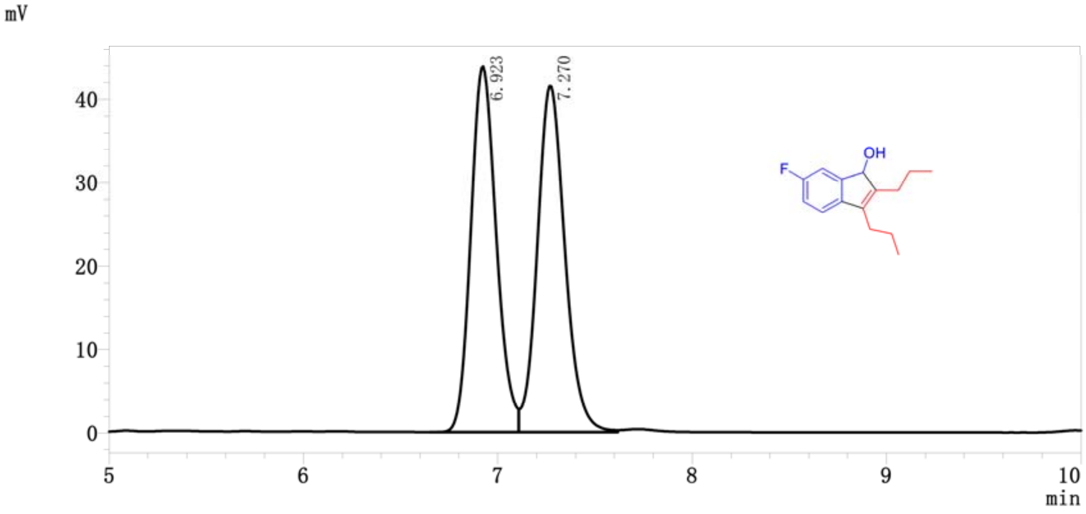


Peak#	Ret. Time	Area	Height	Area%
1	5.618	15595186	953384	50.053
2	6.919	15562122	501351	49.947
Total		31157308	1454735	100.000

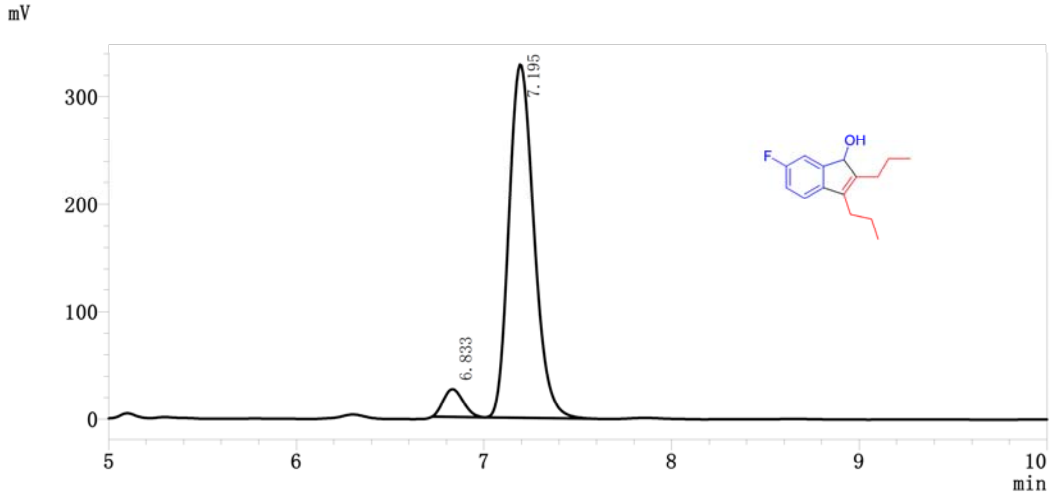


Peak#	Ret. Time	Area	Height	Area%
1	5.662	1540188	201056	98.178
2	6.573	28582	2919	1.822
Total		1568770	203975	100.000

3fa:

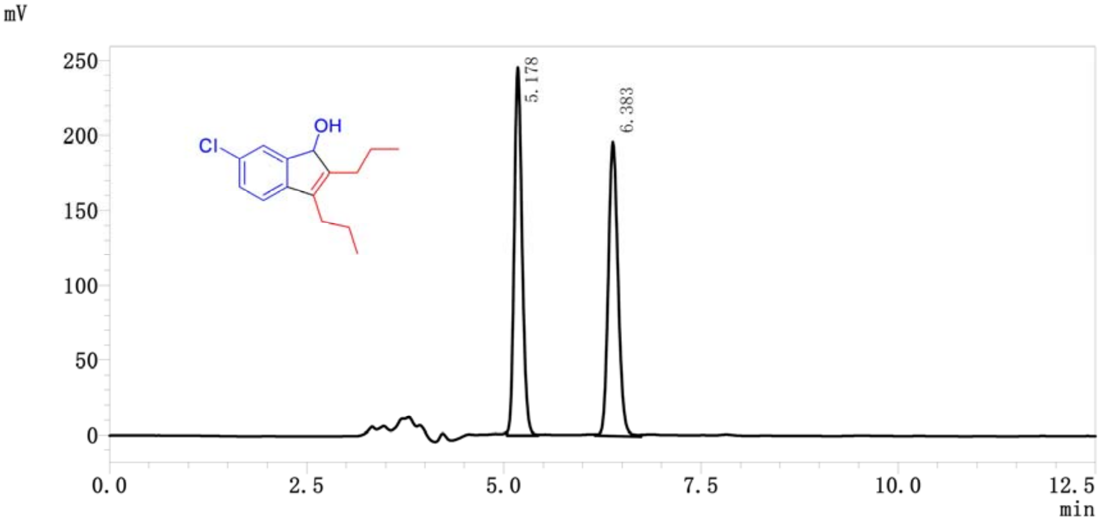


Peak#	Ret. Time	Area	Height	Area%
1	6.923	399669	43817	49.390
2	7.270	409533	41496	50.610
Total		809202	85314	

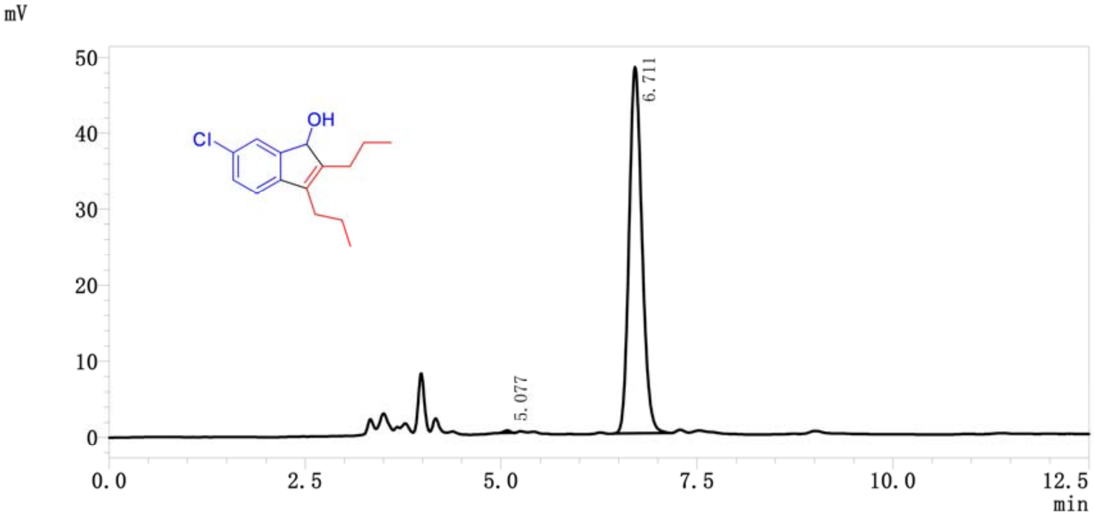


Prak#	Ret. Time	Area	Height	Area%
1	6.833	188781	25730	5.836
2	7.195	3046160	328464	94.164
Total		3234942	354194	

3ga:

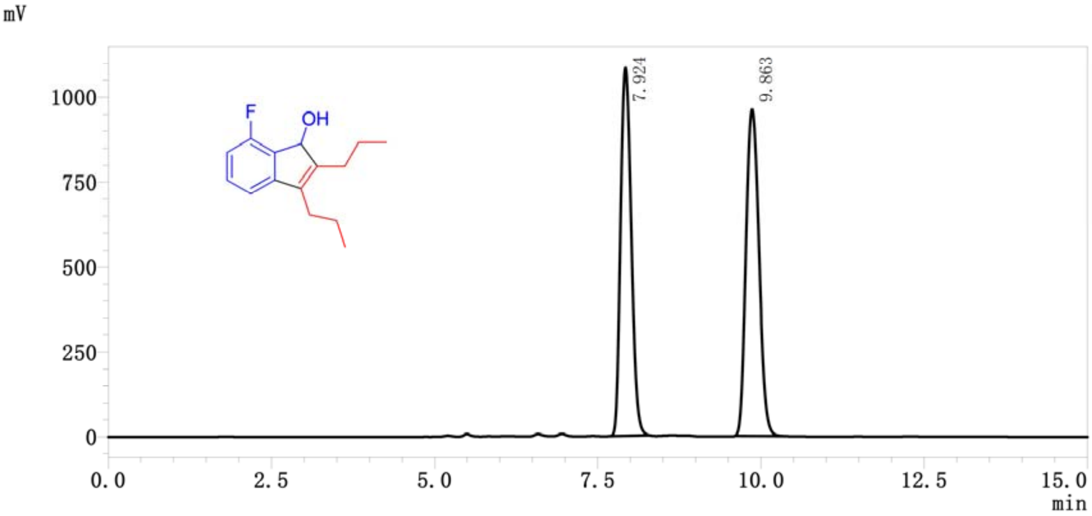


Peak#	Ret. Time	Area	Height	Area%
1	5.178	1700872	245324	50.203
2	6.383	1687106	195864	49.797
Total		3387978	441188	100.000

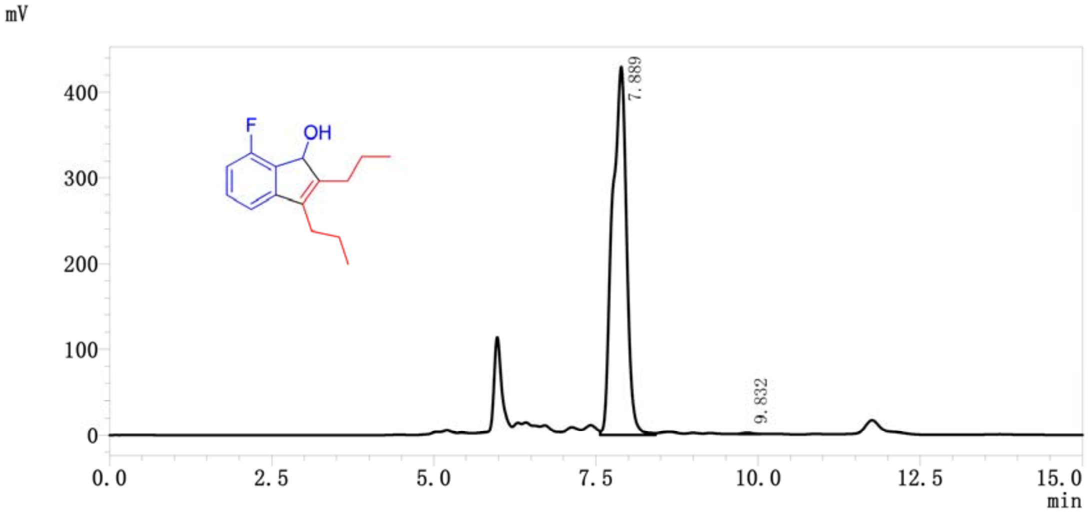


Peak#	Ret. Time	Area	Height	Area%
1	5.077	1560	316	0.282
2	6.711	551193	48149	99.718
Total		552753	48465	100.000

3ha:

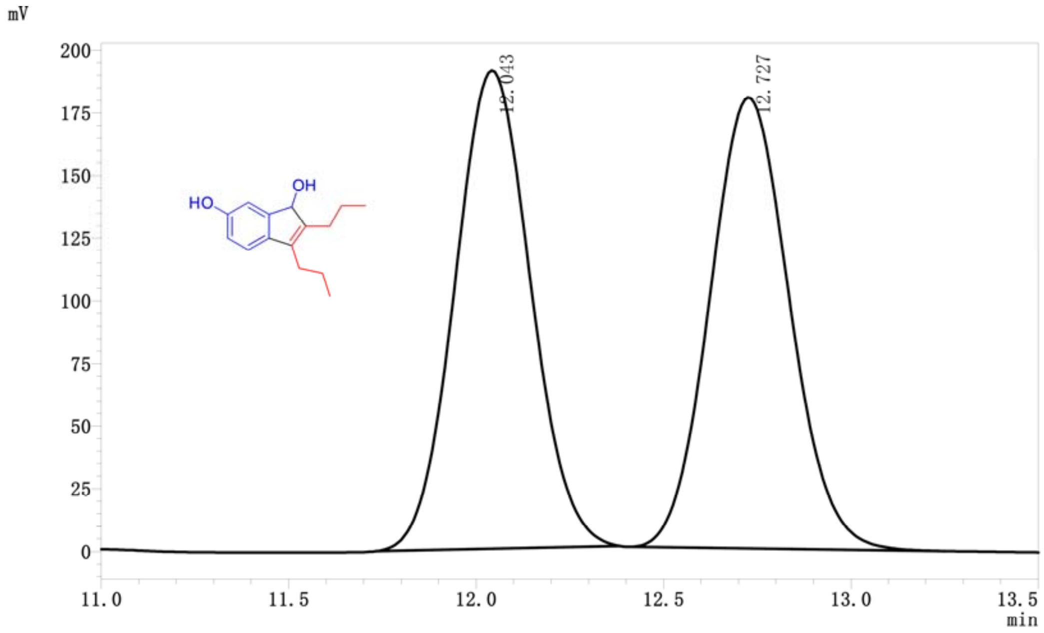


Peak#	Ret. Time	Area	Height	Area%
1	7. 924	12330995	1084282	47. 875
2	9. 863	13425555	961391	52. 125
Total		25756550	2045673	100. 000

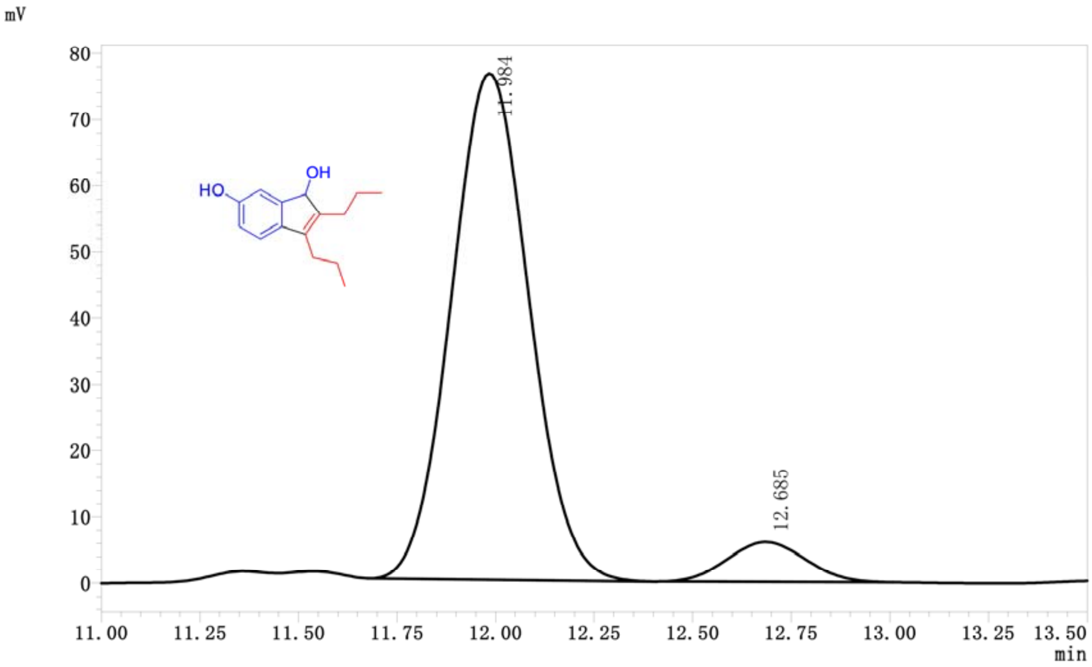


Peak#	Ret. Time	Area	Height	Area%
1	7. 889	6511364	429330	99. 816
2	9. 832	11998	1204	0. 184
Total		6523362	430534	100. 000

3ia:

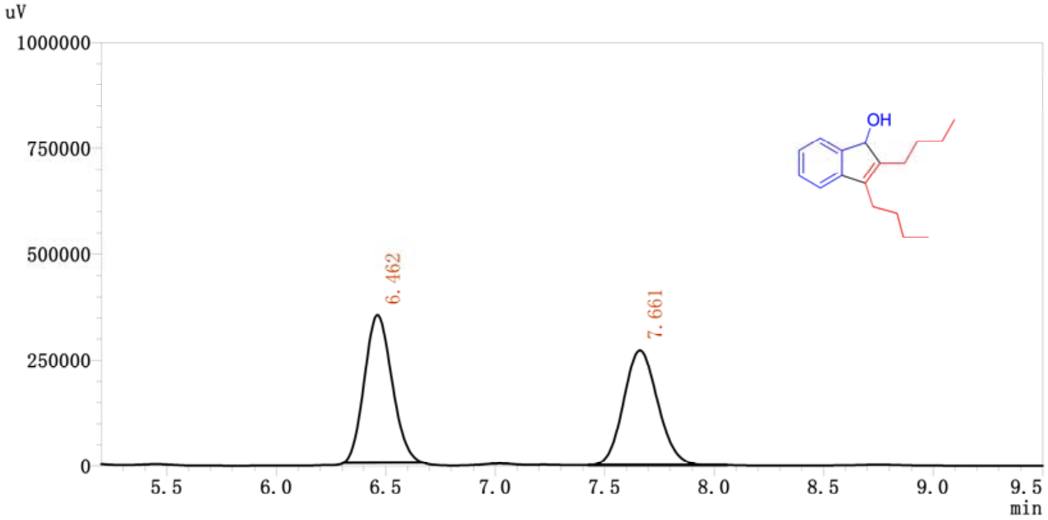


Peak#	Ret. Time	Area	Height	Area%
1	12.043	2674350	190824	50.169
2	12.727	2656339	179925	49.831
Total		5330689	370750	100.000

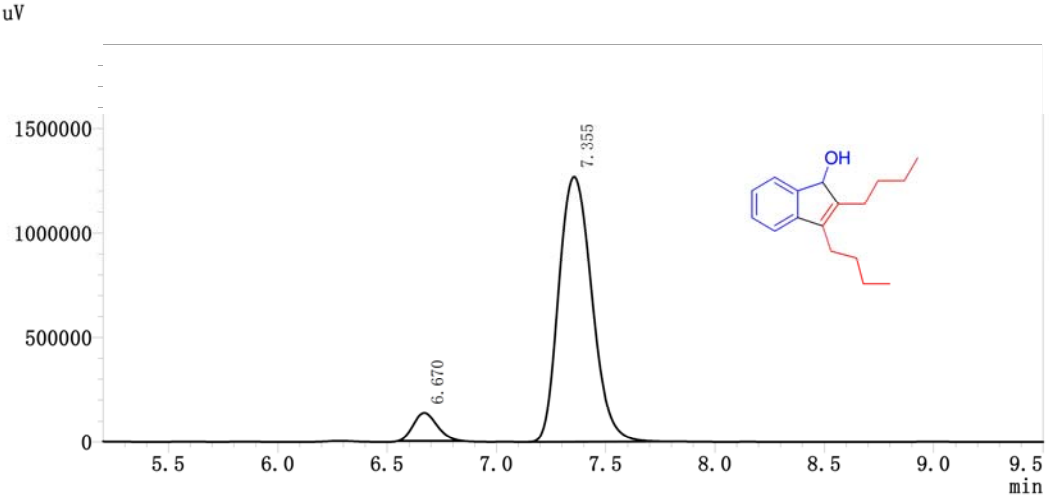


Peak#	Ret. Time	Area	Height	Area%
1	11.984	1049308	76485	92.625
2	12.685	83547	6027	7.375
Total		1132855	82512	

3ab:

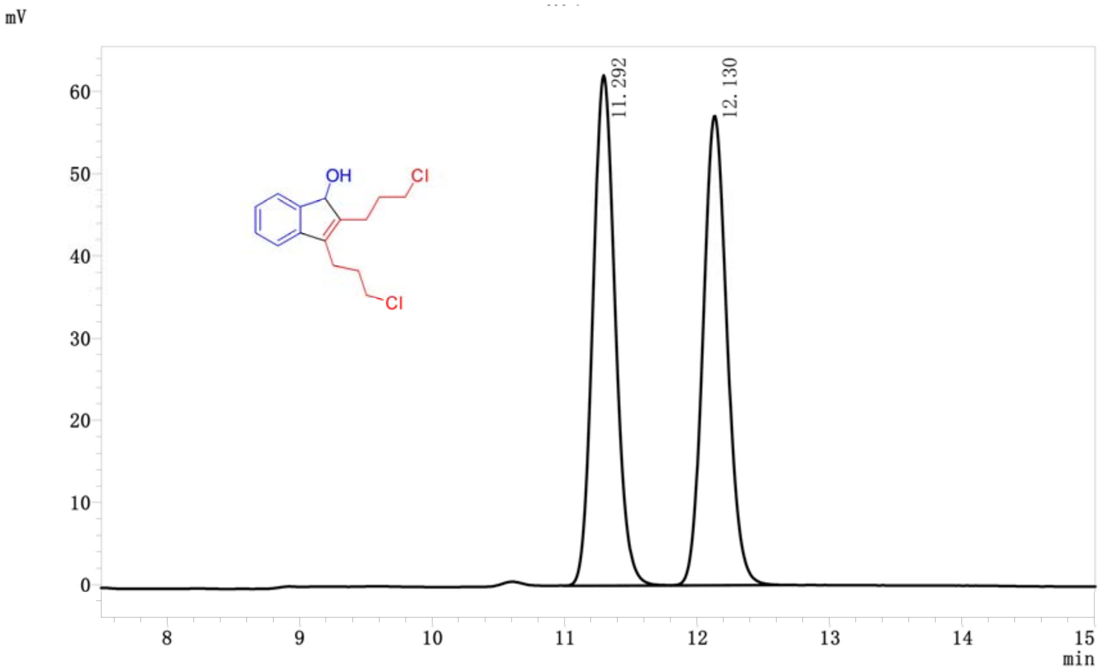


Peak#	Ret. Time	Area	Height	Area%
1	6.462	3048516	348158	50.869
2	7.661	2944309	271040	49.131
Total		5992825	619198	

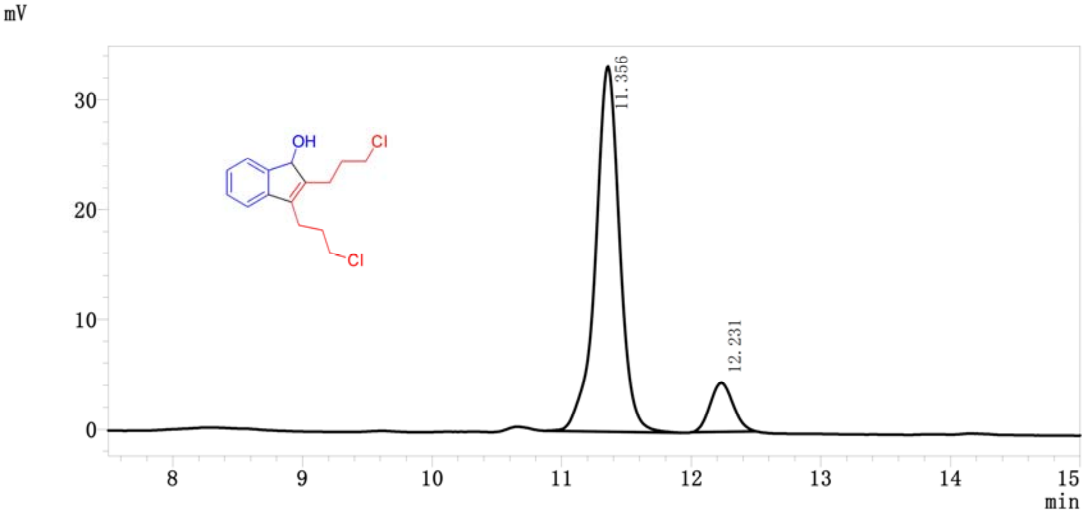


Peak#	Ret. Time	Area	Height	Area%
1	6.670	1015563	132299	7.086
2	7.355	13317014	1265620	92.914
Total		14332577	1397919	

3ac:

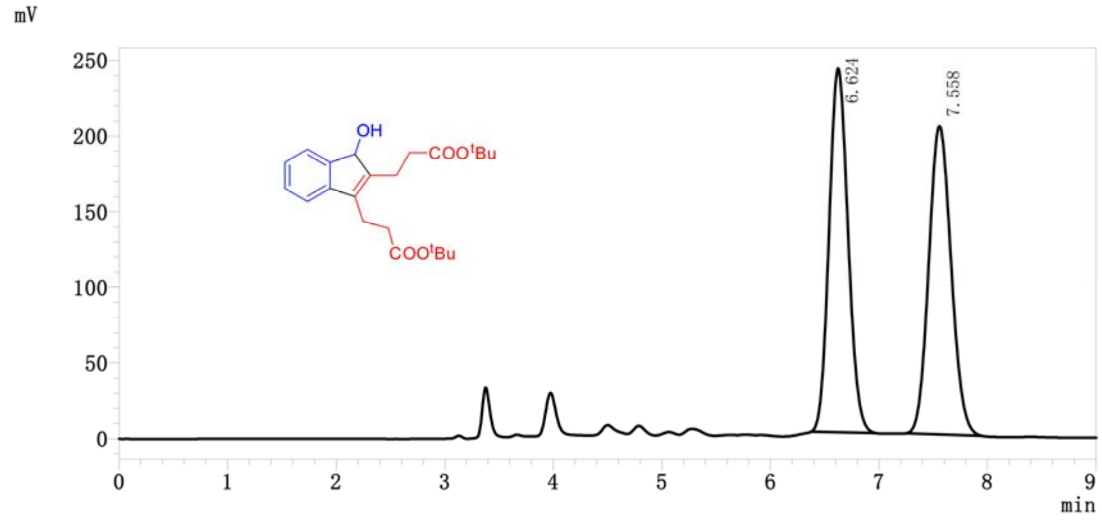


Peak#	Ret. Time	Area	Height	Area%
1	11.292	725283	62064	50.162
2	12.130	720590	57118	49.838
Total		1445873	119181	100.000

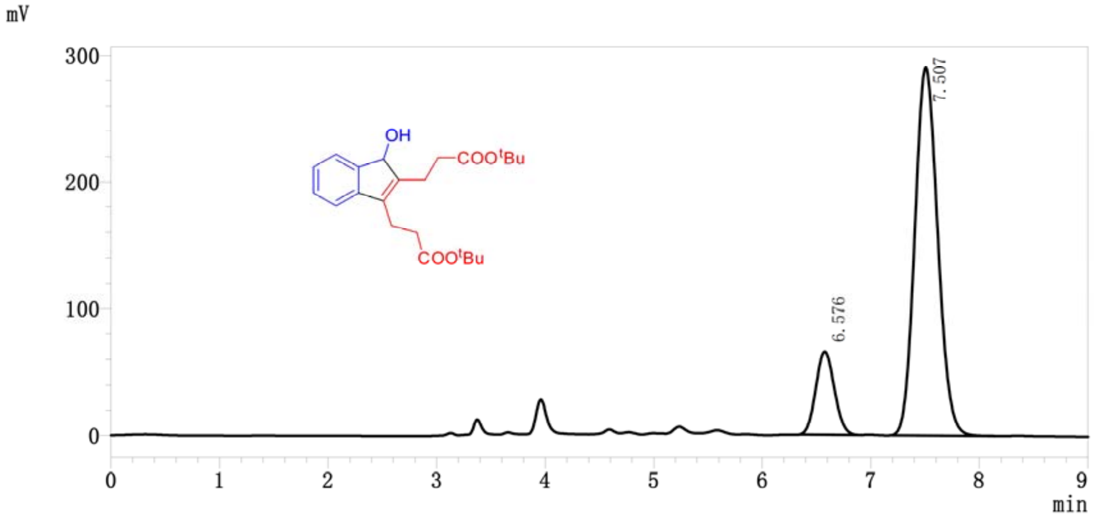


Peak#	Ret. Time	Area	Height	Area%
1	11.356	430341	33228	88.668
2	12.231	54999	4439	11.332
Total		485340	37667	100.000

3ad:

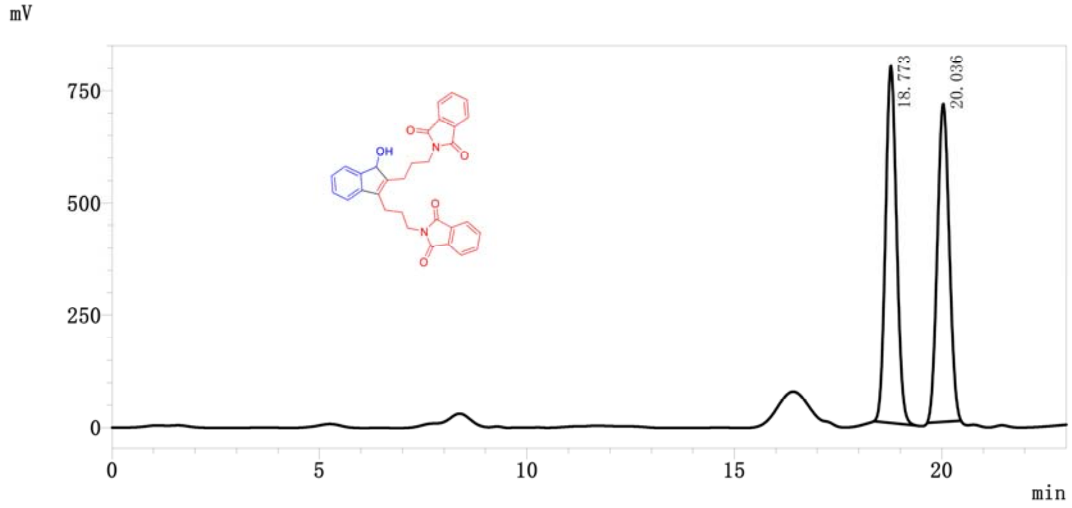


Peak#	Ret. Time	Area	Height	Area%
1	6.624	2910557	240288	49.979
2	7.558	2913032	203906	50.021
Total		5823589	444194	100.000

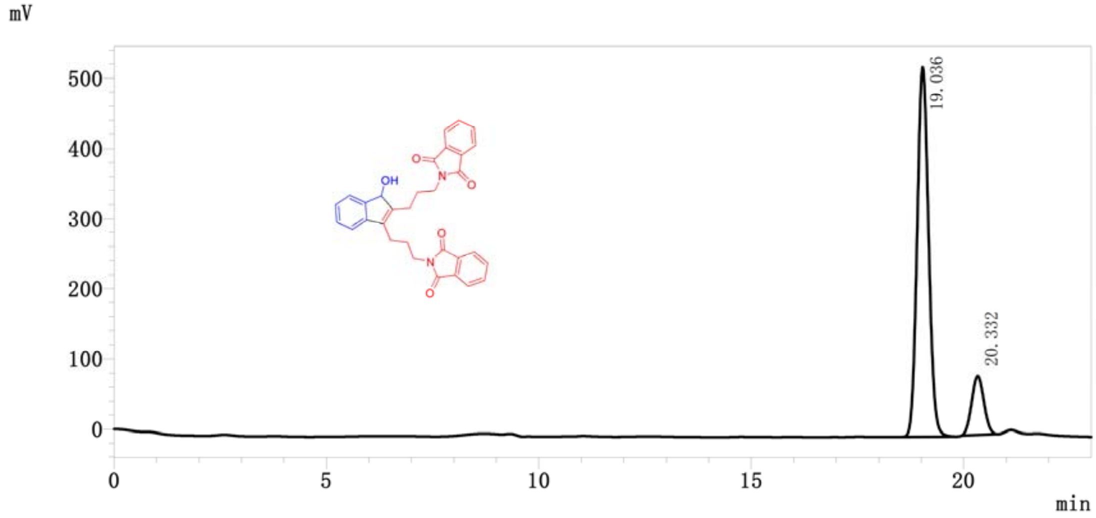


Peak#	Ret. Time	Area	Height	Area%
1	6.576	709175	62977	14.277
2	7.507	4258183	290529	85.723
Total		4967358	353507	

3ae:

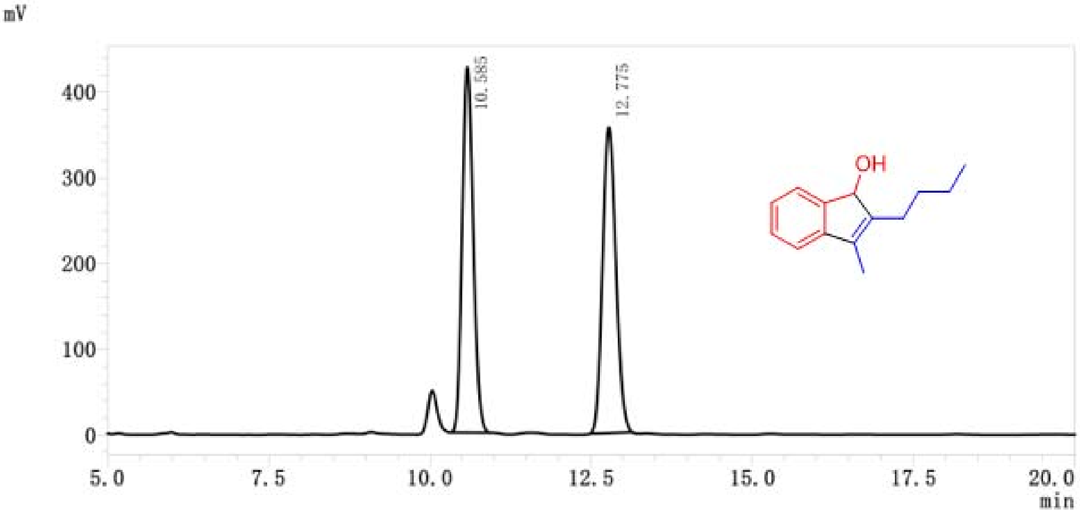


Peak#	Ret. Time	Area	Height	Area%
1	18.773	14707960	794762	50.921
2	20.036	14176023	707717	49.079
Total		28883982	1502479	

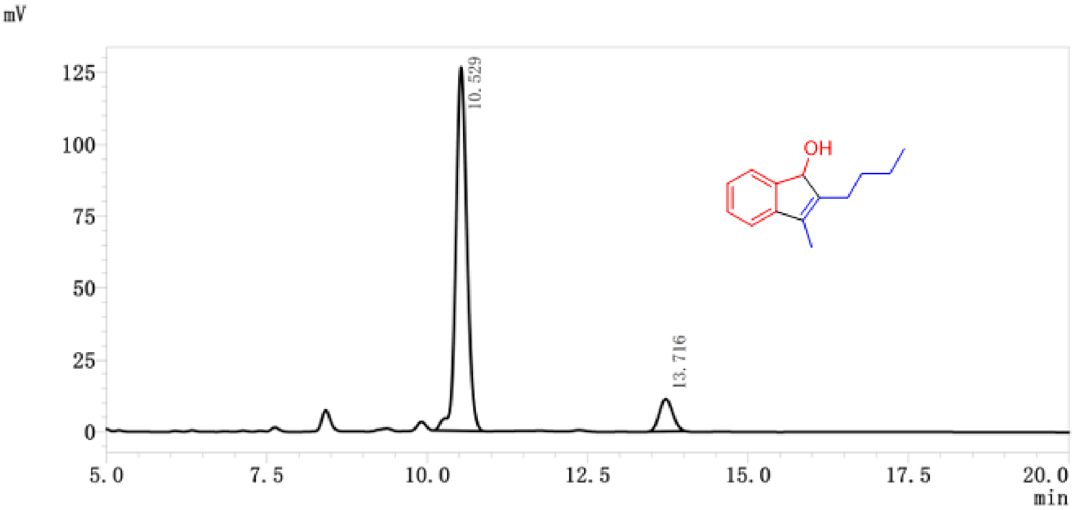


Peak#	Ret. Time	Area	Height	Area
1	19.036	9875934	526835	85.449
2	20.332	1681746	84129	14.551
Total		11557681	610964	

3af:

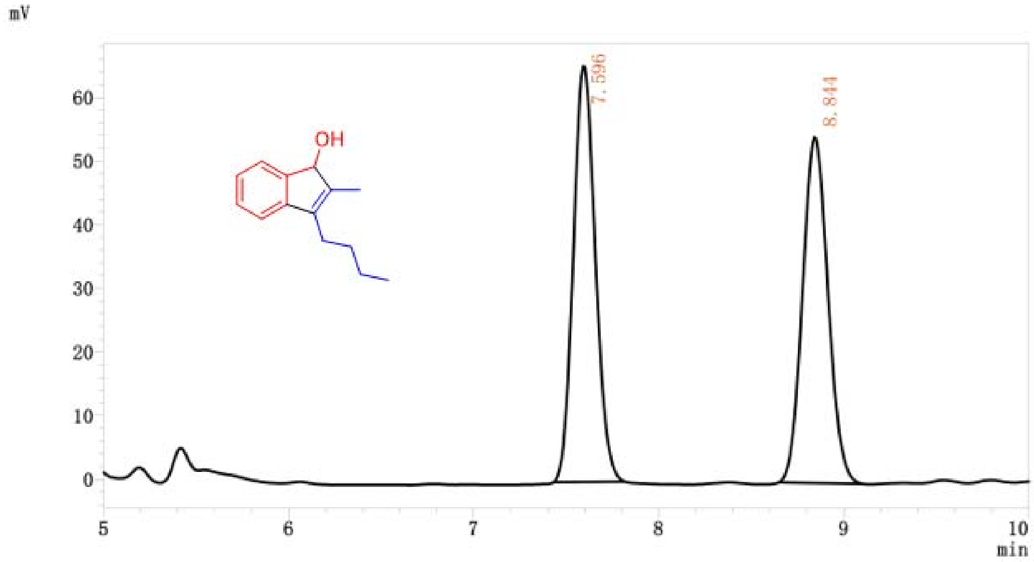


Peak#	Ret. Time	Area	Height	Area%
1	10.585	5072108	426109	49.691
2	12.775	5135215	356308	50.309
Total		10207323	782417	

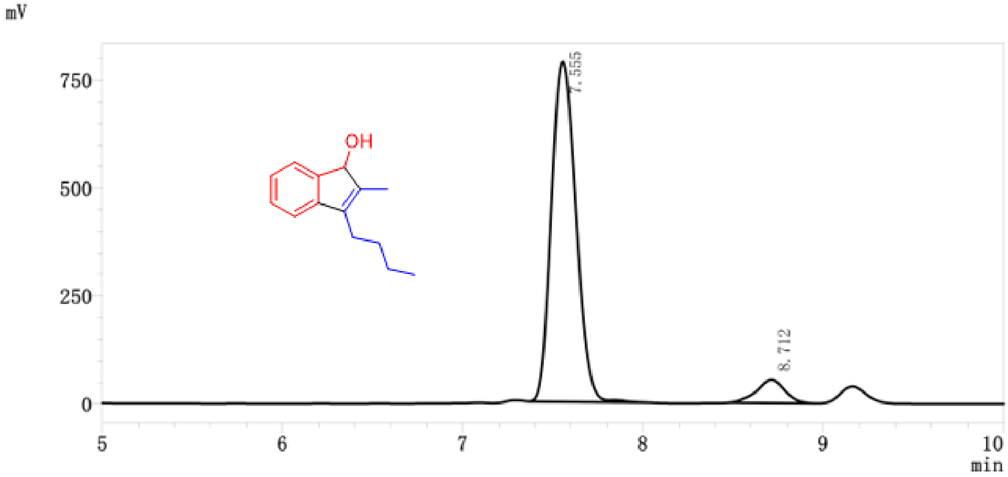


Peak#	Ret. Time	Area	Height	Area%
1	10.529	1508389	126409	90.125
2	13.716	165270	11339	9.875
Total		1673659	137748	

3af':

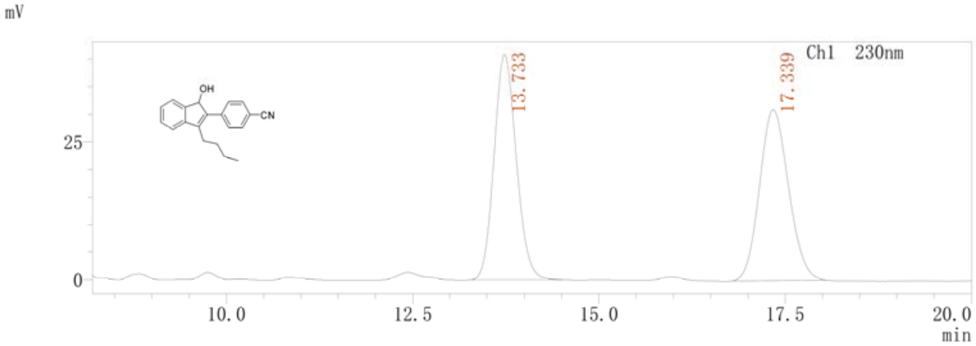


Peak#	Ret. Time	Area	Height	Area%
1	7.596	539134	65254	50.954
2	8.844	518950	54284	49.046
Total		1058084	119538	

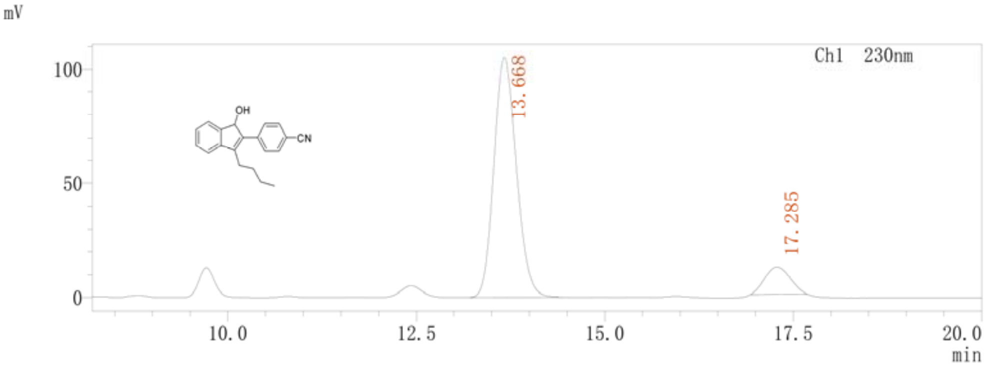


Peak#	Ret. Time	Area	Height	Area%
1	7.555	7453664	786870	92.655
2	8.712	590904	53875	7.345
Total		8044568	840745	

3ag:

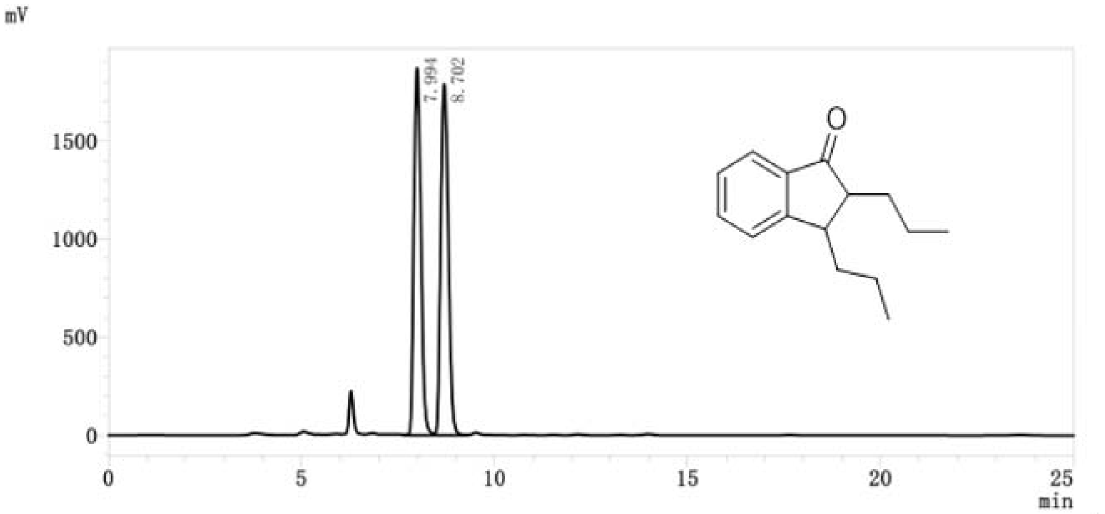


Peak#	Ret. Time	Area	Height	Area%
1	13.733	846777	40824	50.301
2	17.339	836642	30988	49.699
Tatol		1683419	71811	

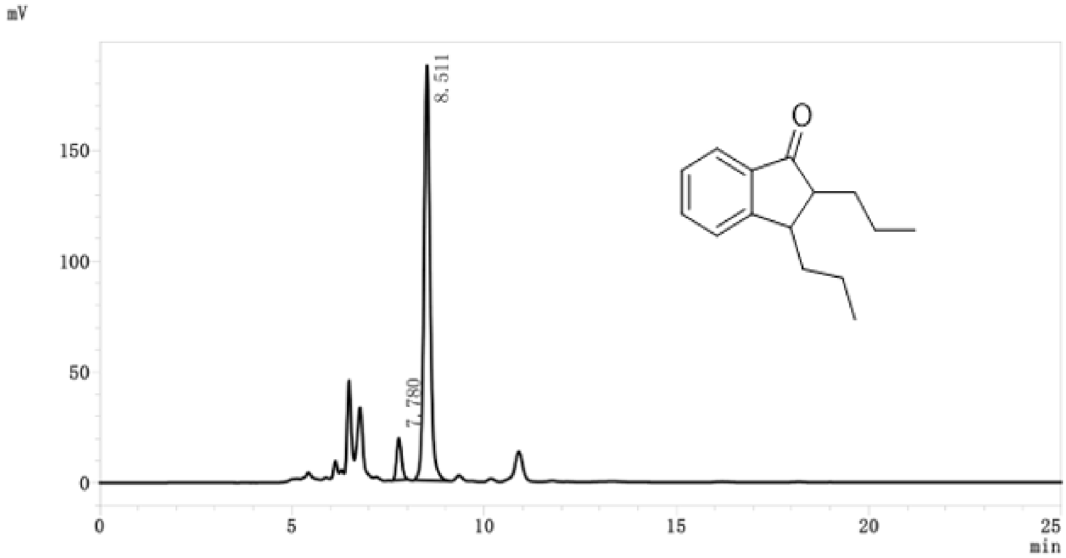


Peak#	Ret. Time	Area	Height	Area%
1	13.668	2180809	105090	88.647
2	17.285	279299	12001	11.353
Tatol		2460108	117091	

4a:

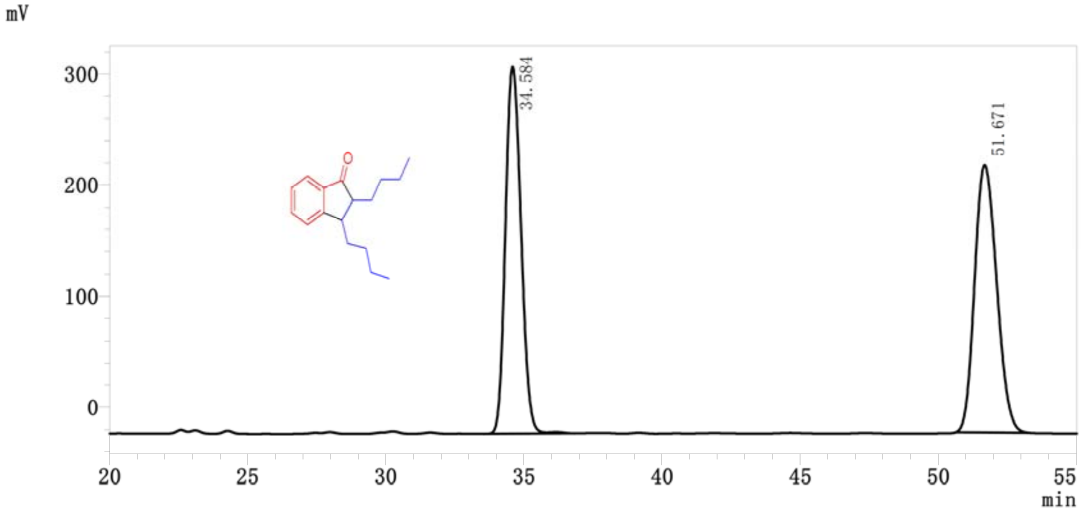


Peak#	Ret. Time	Area	Height	Area%
1	7.994	23805128	1869790	49.166
2	8.702	24612374	1790622	50.834
Total		48417503	3660412	

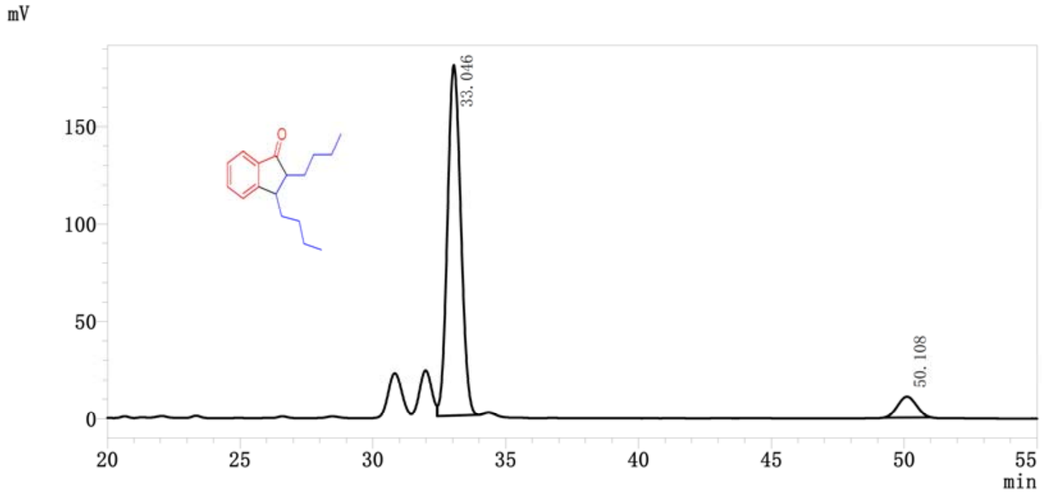


Peak#	Ret. Time	Area	Height	Area%
1	7.780	119044	15993	5.491
2	8.511	2048901	187050	94.509
Total		2167945	203043	100.000

5a:



Peak#	Ret. Time	Area	Height	Area%
1	34.584	12973098	330058	49.320
2	51.671	13331059	240014	50.680
Total		26304158	570073	



Peak#	Ret. Time	Area	Height	Area%
1	33.046	6271782	179767	92.291
2	50.108	523849	10570	7.709
Total		6795631	190337	