Supporting Information

Cobalt-Catalyzed Enantioselective Intramolecular Hydroacylation of Ketones and Olefins

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Contents

Materials and Methods

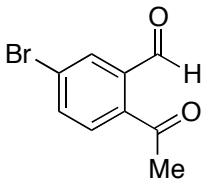
General. All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere or in the argon-filled glove box. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed as described by Still et al., using 40 – 63 μm silica gel (Si 60, Merck). ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on Bruker AV-400 (400 MHz) NMR spectrometers. ^{1}H and ^{13}C NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.1 ppm), respectively. Gas chromatographic (GC) analysis was performed on a Shimadzu GC-2010 system equipped with an FID detector and a capillary column, DB-5 (Agilent J&W, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). Chiral HPLC analysis was performed on a Shimadzu LC-20AD instrument using Daicel Chiralpak columns at room temperature (25–29 °C). Optical rotation was measured using a JASCO P-1030 polarimeter equipped with a sodium vapor lamp at 589 nm. High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer. Melting points were determined using a capillary melting point apparatus and are uncorrected.

Materials. Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Anhydrous $CoCl_2$ (99.7%) was purchased from Aldrich. Anhydrous $CoBr_2$ (99%) was purchased from Alfa Aesar. Manganese (-325 mesh, 99.95%), indium (-325 mesh, 99.99%), aluminum (-325 mesh, 99.5%), and magnesium (-100+200 mesh, 99.6%), were purchased from Alfa Aesar and used without further activation. Zinc (-100 mesh, 97+%) was purchased from Alfa Aesar and was washed successively with 1 M HCl, diethyl ether, and acetone, dried under vacuum, and stored under argon. THF was distilled over Na/benzophenone. MeCN was distilled over CaH_2 and stored under N_2. Anhydrous dioxane (Aldrich), DMF (Alfa Aesar) and 1,2-dichloroethane (Alfa Aesar) were used without further purification. Anhydrous toluene was collected from a solvent purification system (GlassContour) equipped with columns of activated alumina and copper catalyst.

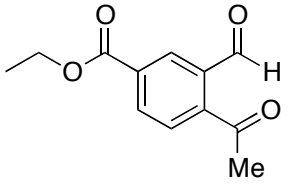
Preparation of Starting Materials

1. Preparation of 2-acylbenzaldehydes

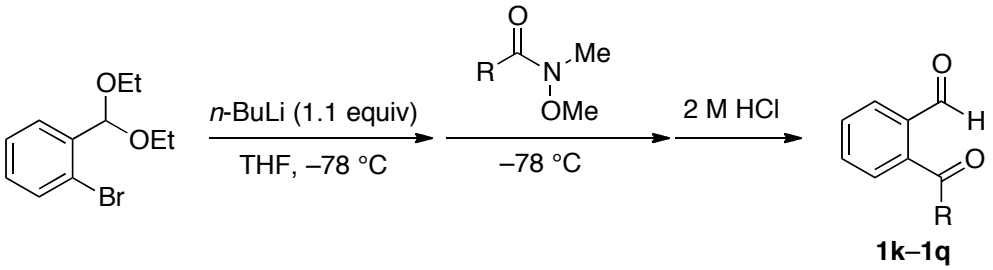
2-Acylbenzaldehyde derivatives **1a**–**1j** were prepared by lead tetraacetate-mediated rearrangement of *N*-acylhydrazones according to the literature procedure.[1] ^{1}H and ^{13}C NMR spectra of the compounds **1a**–**1e** and **1h**–**1j** showed good agreement with the literature data.[1] Below are characterization data for new compounds synthesized by this method.



2-Acetyl-5-bromobenzaldehyde (1f): Yellow solid; R_f 0.3 (hexane/EtOAc = 10/1); m.p. 77-78 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.00 (d, J = 2.0 Hz, 1H), 7.79 (dd, J = 8.2, 2.0 Hz, 1H), 6.54 (d, J = 8.2 Hz, 1H), 2.65 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 199.6, 190.9, 138.7, 138.2, 135.8, 132.5, 130.4, 127.2, 28.6; **HRMS** (ESI) Calcd for $C_9H_8BrO_2$ $[M + H]^+$ 226.9708, found 226.9716.



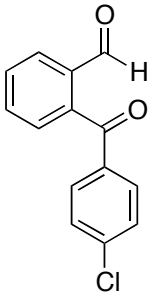
Ethyl 4-acetyl-3-formylbenzoate (1g): White solid; R_f 0.3 (hexane/EtOAc = 10/1); m.p. 72-73 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.51 (d, J = 1.0 Hz, 1H), 8.32 (dd, J = 8.0, 1.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 1H), 4.44 (q, J = 7.1 Hz, 2H), 2.66 (s, 3H), 1.43 (t, J = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 201.0, 191.1, 164.7, 144.1, 135.8, 134.0, 133.4, 131.2, 128.2, 61.9, 29.2, 14.3; **HRMS** (ESI) Calcd for $C_{12}H_{13}O_4$ $[M + H]^+$ 221.0814, found 221.0816.



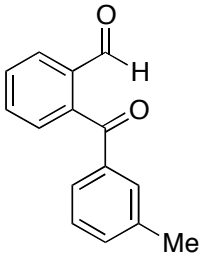
1k–1q

General procedure for the preparation of 2-acylbenzaldehydes 1k–1q (Scheme S1): To a solution of 1-bromo-2-(diethyoxymethyl)benzene (0.78 mL, 3.86 mmol) in THF (15 mL) was added a solution of *n*-butyllithium in hexane (1.6 M, 2.7 mL, 4.25 mmol) dropwise at –78 °C. After stirring for 1 h at this temperature, the resulting aryllithium solution was transferred to a cooled (–78 °C) solution of *N*-methoxy-*N*-methylamide (4.25 mmol) in THF (10 mL) via a cannula. The reaction mixture was stirred for 1 h at –78 °C, allowed to warm to room temperature, and stirred overnight. The reaction was quenched with 2 M HCl (5.5 mL). The resulting mixture was stirred for 3 h (monitored by TLC) and then neutralized with saturated aqueous $NaHCO_3$ solution. The crude reaction mixture was extracted with ethyl acetate (3 x 50 mL), and the combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified with silica gel chromatography to afford the desired 2-acylbenzaldehyde.

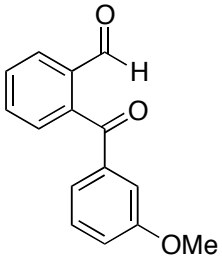
^1H and ^{13}C NMR spectra of the compounds **1k** and **1l** showed good agreement with the literature data.[1] Below are characterization data for new compounds synthesized by this method.



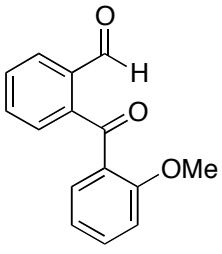
2-(4-Chlorobenzoyl)benzaldehyde (1m): Yellow solid (66% yield); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 110-120 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.03-8.01 (m, 1H), 7.74-7.69 (m, 4H) 7.49-7.42 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 195.5, 190.6, 140.8, 140.2, 135.5, 135.4, 133.6, 131.2, 130.9, 130.8, 129.1, 128.7; **HRMS** (ESI) Calcd for $C_{14}H_{10}ClO_2$ $[M + H]^+$ 245.0369, found 245.0374.



2-(3-Methylbenzoyl)benzaldehyde (1n): Yellow solid (58% yield); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 52-53 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.04-8.02 (m, 1H), 7.69-7.66 (m, 3H) 7.55-7.49 (m, 2H), 7.42 (d, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 1H), 3.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.8, 190.7, 141.7, 138.7, 137.3, 135.5, 134.6, 133.4, 130.7, 130.4, 130.0, 129.0, 128.6, 127.6, 21.4; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_2$ $[M + H]^+$ 225.0916, found 225.0907.

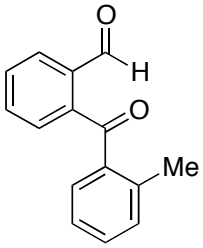


2-(3-Methoxylbenzoyl)benzaldehyde (1o): Yellow solid (59% yield); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 87-88 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.04-8.02 (m, 1H), 7.70-7.68 (m, 2H) 7.52-7.50 (m, 1H), 7.44 (d, J = 0.8 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.15 (dd, J = 8.2, 2.4 Hz, 1H), 3.86 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.4, 190.6, 160.0, 141.5, 138.6, 135.5, 133.4, 130.7, 130.2, 129.7, 128.9, 123.2, 120.4, 113.7, 55.6; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_3$ $[M + H]^+$ 241.0865, found 241.0861.



2-(2-Methoxylbenzoyl)benzaldehyde (1p): Yellow solid (42% yield); R_f 0.3 (hexane/EtOAc =

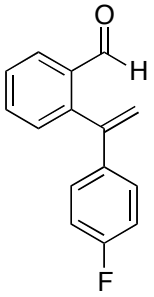
10/1); m.p. 82-84 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.22 (s, 1H), 8.00-7.98 (m, 1H), 7.66 (dd, J = 7.6, 1.8 Hz, 1H), 7.66-7.52 (m, 3H), 7.46-7.44 (m, 1H), 7.07 (td, J = 7.6, 0.7 Hz, 1H), 6.96 (d, J = 8.4 Hz, 1H), 3.62 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 196.3, 191.6, 158.8, 143.6, 135.7, 134.4, 132.9, 131.4, 130.8, 129.1, 128.6, 127.9, 120.9, 112.1, 55.7; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_3$ $[M + H]^+$ 241.0865, found 241.0860.



2-(2-Methylbenzoyl)benzaldehyde (1q): Yellow oil (15% yield); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 8.00-7.98 (m, 1H), 7.66-7.63 (m, 2H) 7.49-7.47 (m, 1H), 7.42 (td, J = 7.5, 1.3 Hz , 1H), 7.34-7.28 (m, 2H), 7.19 (t, J = 7.5 Hz, 1H), 2.59 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 198.5, 191.1, 142.4, 139.7, 137.2, 136.3, 133.2, 132.2, 132.0, 131.3, 131.2, 130.0, 129.7, 125.6, 21.2; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_2$ $[M + H]^+$ 225.0916, found 225.0911.

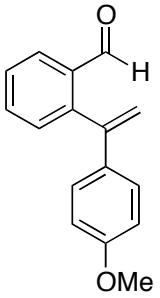
2. Preparation of 2-alkenylbenzaldehydes

2-Alkenylbenzaldehydes **3a**–**3d** were prepared by the Suzuki–Miyaura coupling of 2-formylphenylboronic acid and the corresponding alkenyl bromides according to the literature procedure.[2] ^{1}H and ^{13}C NMR spectra of the compounds **3a–3c** showed good agreement with the literature data.[2,3]

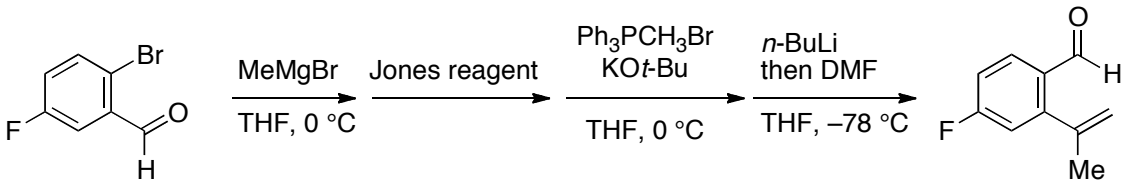


2-(1-(4-Fluorophenyl)vinyl)benzaldehyde (3d): Yellow oil (91% yield); R_f 0.3 (hexane/EtOAc

= 30/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.98 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.60 (td *J* = 7.4, 1.4 Hz, 1H), 7.49 (td, *J* = 7.5, 0.7 Hz, 1H), 7.34-7.32 (m, 1H), 7.27-7.23 (m, 2H), 7.03-6.98 (m, 2H), 5.91 (s, 1H), 5.26 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 191.9, 162.8 (d, $^1J_{C\text{-}F}$ = 247.0 Hz), 145.3, 145.0, 137.1 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 134.5, 133.9, 131.0, 128.7 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 128.4, 127.9, 117.8 (d, $^5J_{C\text{-}F}$ = 1.0 Hz), 115.7 (d, $^2J_{C\text{-}F}$ = 22.0 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$): δ -113.5; **HRMS** (ESI) Calcd for $C_{15}H_{12}FO$ $[M + H]^+$ 227.0872, found 227.0877.



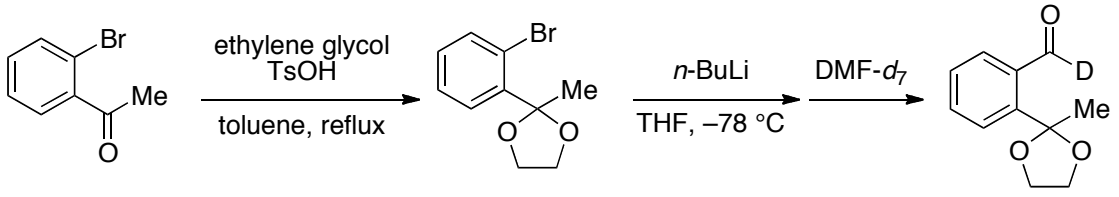
2-(1-(4-Methoxyphenyl)vinyl)benzaldehyde (3e): Yellow oil (59%); R_f 0.3 (hexane/EtOAc = 25/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.98 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 2H), 5.88 (s, 1H), 5.16 (s, 1H), 3.80 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.3, 159.8, 146.1, 145.3, 134.6, 133.8, 133.7, 131.0, 128.3, 128.2, 127.5, 116.2, 114.1, 55.5; **HRMS** (ESI) Calcd for $C_{16}H_{15}O_2$ $[M + H]^+$ 239.1072, found 239.1070.



4-Fluoro-2-(prop-1-en-2-yl)benzaldehyde (3f): Under nitrogen, methylmagnesium bromide (8 mL, 1.0 mol/L) was added to a solution of 2-bromo-5-fluorobenzaldehyde (1.31 g, 6.45 mmol) in THF (20 mL) at 0 °C. After stirring for 2 h, the reaction was quenched with aqueous NH_4Cl (10 mL) and warmed to room temperature. The organic phase was separated and washed with brine (2 x 10 mL). The organic solution was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to give the crude alcohol product, which was used in the next step without further purification. To the solution of the crude alcohol in acetone (10 mL) was added Jones

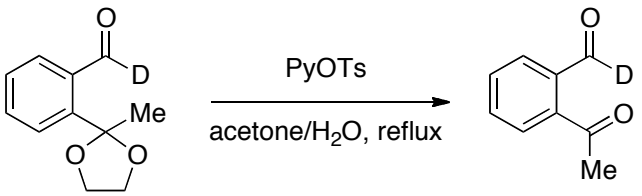
reagent (2.5 M, 3.0 mL) dropwise at 0 °C. After stirring for 30 min, *i*-PrOH (1.0 mL) was added. The reaction mixture was filtered through a pad of silica gel using additional diethyl ether (30 mL) as an eluent. The filtrate was concentrated under reduced pressure to give the crude ketone as a colorless oil, which was used in the next step without further purification. The crude ketone was added to a solution of Wittig reagent, which was prepared by the reaction of methyltriphenylphosphonium bromide (2.49 g, 7 mmol, 1.2 equiv) and KO*t*-Bu (0.78 g, 7 mmol, 1.2 equiv) in Et_2O (20 mL) at 0 °C for 30 min. The resulting mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was treated with hexane (50 mL), and the mixture was passed through a pad of silica gel using additional hexane (50 mL) as an eluent. The hexane solution was concentrated under reduced pressure to give the crude olefin as a colorless oil, which was used in the next step without further purification. To a solution of the olefin in THF (15 mL) was added a solution of *n*-butyllithium in hexane (1.6 M, 3.5 mL, 5 mmol) dropwise at -78 °C. After stirring for 30 min, anhydrous DMF (0.4 mL, 5 mmol) was added dropwise. The reaction mixture was stirred for another 30 min, followed by the addition of aqueous NH_4Cl (10 mL). The resulting mixture was allowed to room temperature. The organic phase was separated, washed with brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane/ethyl acetate = 25:1) to afford the title compound as a colorless oil (0.38 g, 36%). R_f 0.3 (hexane/EtOAc = 25/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.13 (s, 1H), 7.96 (dd, J = 8.7, 4.0 Hz, 1H), 7.11-7.06 (m, 1H), 7.02 (dd, J = 8.7, 2.5 Hz, 1H), 5.45 (s, 1H), 4.96 (s, 1H), 2.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 190.5, 165.6 (d, $J_{C\text{-}F}$ = 256.0 Hz), 150.5 (d, $J_{C\text{-}F}$ = 9.2 Hz), 140.7, 130.8 (d, $J_{C\text{-}F}$ = 10.0 Hz), 130.0 (d, $J_{C\text{-}F}$ = 3.0 Hz), 119.5, 115.3 (d, $J_{C\text{-}F}$ = 21.8 Hz), 115.0 (d, $J_{C\text{-}F}$ = 22.2 Hz), 24.7; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -103.8; **HRMS** (ESI) Calcd for $C_{10}H_{10}FO$ $[M + H]^+$ 165.0716, found 165.0715.

3. Preparation of deuterium-labeled substrates



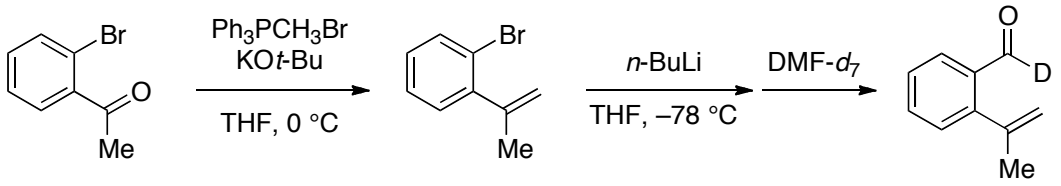
2-(2-Methyl-1,3-dioxolan-2-yl)benzaldehyde-1-*d*: To a solution of 2'-bromoacetophenone

(0.93 mL, 8.0 mmol) in toluene was added ethylene glycol (1.12 mL, 20 mmol) and *p*-toluenesulfonic acid (34.4 mg, 0.20 mmol). The resulting mixture was stirred at reflux for 18 h using Dean-Stark apparatus, then cooled to room temperature and quenched by the addition of saturated aqueous solution of $NaHCO_3$ (5 mL). The organic layer was separated, washed with brine (10 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford the crude acetal as a colorless oil, which was used for the next step without further purification. To a solution of the acetal in THF (10 mL) was added a solution of *n*-butyllithium in hexane (1.6 M, 6.0 mL, 9.6 mmol) dropwise at -78 °C. After stirring for 30 min, excess anhydrous DMF-d_7 (0.8 mL, 10.4 mmol) was added dropwise. The reaction mixture was stirred at for another 30 min, followed by the addition of aqueous NH_4Cl (10 mL). The resulting mixture was allowed to room temperature. The organic phase was separated, washed with brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane/ethyl acetate = 20:1) to afford the title compound as a colorless oil (0.95 g, 62 %). R_f 0.3 (hexane/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (dd, J = 7.7, 0.8 Hz, 1H), 7.66 (d, J = 7.7 Hz, 1H), 7.43 (td, J = 7.5, 1.2 Hz, 1H), 7.41 (dd, J = 7.5, 0.8 Hz, 1H), 4.09-4.02 (m, 2H), 3.79-3.73 (m, 2H), 1.82 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.8 (t, $^1J_{C\text{-}D}$ = 28.0 Hz), 145.3, 134.2 (t, $^2J_{C\text{-}D}$ = 4.0 Hz), 133.2, 128.6, 128.3, 126.5, 108.7, 64.5, 29.5; **HRMS** (ESI) Calcd for $C_{11}H_{12}DO_3$ $[M + H]^+$ 194.0927, found 194.0932.



2-Acetylbenzaldehyde-1-*d* (1a-*d*): To a solution of 2-(2-methyl-1,3-dioxolan-2-yl)benzaldehyde-1-*d* (868 mg, 4.5 mmol) in acetone (24 mL) and water (4 mL) was added pyridinium tosylate (169 mg, 0.67 mmol, 0.15 equiv). The resulting mixture was stirred at reflux for 12 h until the starting material disappeared, then cooled to room temperature and extracted with EtOAc (2 x 20 mL). The organic phase was washed with brine (2 x 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane/CH_2Cl_2 = 2:1) to afford the title compound as a colorless oil (0.30 g, 45 %). R_f 0.3 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90-7.87 (m, 1H),

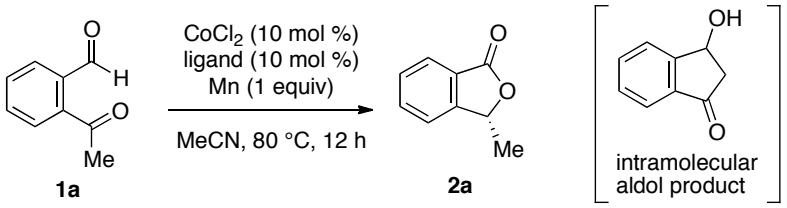
7,75-7.73 (m, 1H), 7.69-7.63 (m, 2H), 2.66 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 200.9, 191.9 (t, $^1J_{C\text{-}D}$ = 28.0 Hz), 140.6, 136.2 (t, $^2J_{C\text{-}D}$ = 4.0 Hz), 133.0, 131.9, 129.6, 128.5, 28.8; **HRMS** (ESI) Calcd for $C_9H_8DO_2$ $[M + H]^+$ 150.0665, found 150.0668.



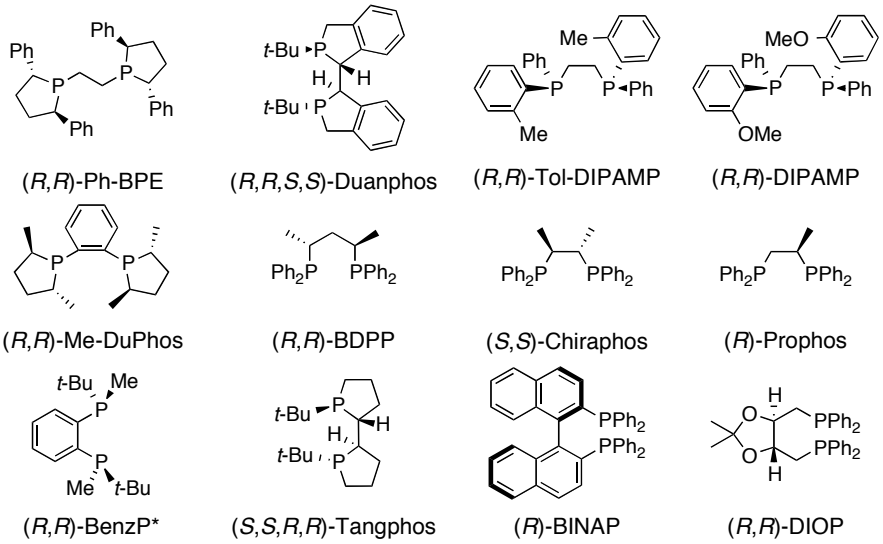
2-Isopropenyl-benzaldehyde-1-*d* (3b-*d*): KO*t*-Bu (0.67 g, 6.0 mmol) was added to a solution of methyltriphenylphosphonium bromide (2.13 g, 6.0 mmol) in Et_2O (20 mL) at 0 °C. After stirring for 30 min, to the mixture was added 2'-bromoacetophenone (0.67 mL, 5.0 mmol) in one portion. The resulting mixture was stirred overnight at room temperature and then concentrated under reduced pressure. The residue was treated with hexane (50 mL), and the mixture was passed through a pad of silica gel using additional hexane (50 mL) as an eluent. The hexane solution was concentrated under reduced pressure to give the crude olefin as a colorless oil, which was used in the next step without further purification. To a solution of the olefin in THF (10 mL) was added a solution of *n*-butyllithium in hexane (1.6 M, 7.5 mL, 12 mmol) dropwise at -78 °C. After stirring for 30 min, anhydrous DMF-d_7 (1.0 mL, 13 mmol) was added dropwise. The reaction mixture was stirred for another 30 min, followed by the addition of aqueous NH_4Cl (10 mL). The resulting mixture was allowed to room temperature. The organic phase was separated, washed with brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (hexane/ethyl acetate = 25:1) to afford the title compound as a colorless oil (0.50 g, 68%). R_f 0.3 (hexane/EtOAc = 25/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.6, 1.0 Hz, 1H), 7.54 (td, *J* = 7.6, 1.4 Hz, 1H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 5.42 (s, 1H), 4.91 (s, 1H), 2.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 192.0 (t, $^1J_{C\text{-}D}$ = 27.0 Hz), 147.8, 141.9, 133.6, 133.5 (t, $^2J_{C\text{-}D}$ = 3.0 Hz), 128.6, 127.9, 127.5, 119.1, 25.1; **HRMS** (ESI) Calcd for $C_{10}H_{10}DO$ $[M + H]^+$ 148.0873, found 148.0878.

Cobalt-Catalyzed Intramolecular Hydroacylation of Ketones

Table S1. Screening of Chiral Ligands[a]

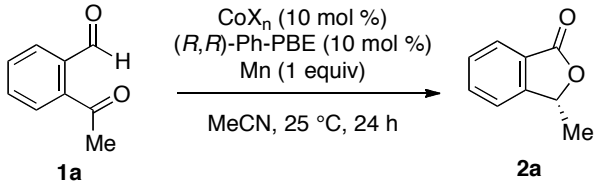


entry	ligand	conversion (%)[b]	yield (%)[b]	ee (%)[c]
1	(*R*,*R*)-Ph-BPE	100	70	95
2	(*R*,*R*,*S*,*S*)-Duanphos	90	37	85
3	(*R*,*R*)-Tol-DIPAMP	95	73	79
4	(*R*,*R*)-DIPAMP	75	4	ND
5	(*R*,*R*)-Me-DuPhos	90	12	ND
6	(*R*,*R*)-BDPP	55	15	ND
7	(*S*,*S*)-Chiraphos	83	0	–
8	(*R*)-Prophos	81	0	–
9	(*R*,*R*)-BenzP*	88	6	ND
10	(*S*,*S*,*R*,*R*)-Tangphos	86	0	–
11	(*R*)-BINAP	42	0	–
12	(*R*,*R*)-DIOP	35	0	–



[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. When the conversion was high but the yield of **2a** was low, no apparent byproduct except for a trace amount of the intramolecular aldol product was observed on the GC chromatogram. We speculate that intermolecular aldol condensation took place to produce nonvolatile oligomeric products. [c] Determined by chiral HPLC analysis. ND = not determined.

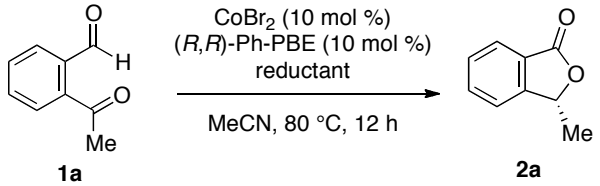
Table S2. Effect of Cobalt Precatalysts[a]



entry	CoX_n	yield (%)[b]	ee (%)[c]
1	$CoCl_2$	30	95
2	$CoBr_2$	66	94
3	CoI_2	42	92
4	$Co(OAc)_2$	12	93
5	$Co(OAc)_2•4H_2O$	0	–
6	$Co(acac)_2$	0	–
7	$Co(acac)_3$	0	–
8	CoF_2	0	–

[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis.

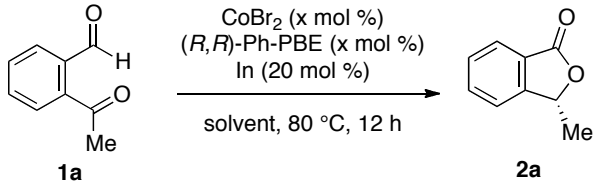
Table S3. Effect of Reductants[a]



entry	reductant	yield (%)[b]	ee (%)[c]
1	Mn (100 mol %)	71	95
2	Mn (50 mol %)	69	95
3	Mn (20 mol %)	59	95
4	Mn (10 mol %)	49	95
5	In (20 mol %)	92	95
6	Zn (20 mol %)	82	95
7	Al (20 mol %)	90	94
8	Mg (20 mol %)	3	ND

[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis. ND = not determined.

Table S4. Effect of Solvents and Catalyst Loading[a]

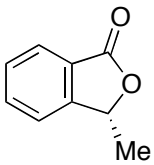


1a **2a**

entry	x	solvent	yield (%)[b]	ee (%)[c]
1	10	MeCN	92	95
2	10	toluene	67	95
3[d]	10	THF	28	95
4	10	DCE	6	ND
5	5	MeCN	95	95
6	2.5	MeCN	95	95
7	1	MeCN	67	ND

[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis. ND = not determined. [d] The reaction was performed at 60 °C.

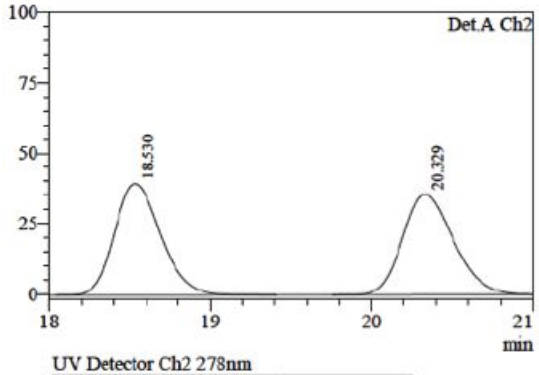
General procedure: In an argon-filled glove box, to a 4 mL vial were charged sequentially $CoBr_2$ (6.5 mg, 0.030 mmol), (*R,R*)-Ph-BPE (15.2 mg, 0.030 mmol) and indium powder (6.8 mg, 0.060 mmol). Then MeCN (0.6 mL) was added, and the mixture was stirred at room temperature for 5 min. To the resulting mixture was added a solution of 2-acylbenzaldehyde (0.30 mmol) in MeCN (0.6 mL). The vial was removed from the glove box and stirred for 12 h at 80 °C. Upon cooling to room temperature, the reaction mixture was diluted with ethyl acetate (5 mL) and filtered through a pad of silica gel with additional ethyl acetate (10 mL) as eluent. The solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.



(*R*)-3-Methylisobenzofuran-1(3*H*)-one (2a): Colorless oil (39.1 mg, 88%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.7 Hz, 1H), 7.69 (t, J = 7.5

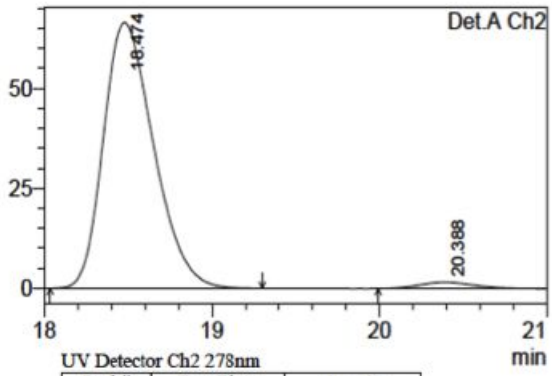
Hz, 1H), 7.53 (t, J = 7.5 Hz, 1H), 7.45 (d, J = 7.7 Hz, 1H), 5.57 (q, J = 6.7 Hz, 1H), 1.65 (d, J = 6.7 Hz, 3H); **HRMS** (ESI) Calcd for $C_9H_9O_2$ $[M + H]^+$ 149.0603, found 149.0607; $[\alpha]^{21}_D$ = +37.1° (c = 0.83 in $CHCl_3$, 95% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1] The absolute configuration was determined to be *R* by comparison of the optical rotation with the literature data ($[\alpha]^{25}_D$ = +48.4° (c = 0.93 in $CHCl_3$, > 99% ee sample).[4]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 95:5; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 18.5 min (major) and 20.4 min (minor), 95% ee.



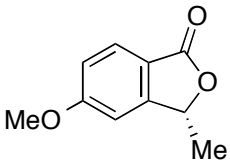
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	18.530	50.035
2	20.329	49.965
Total		100.000



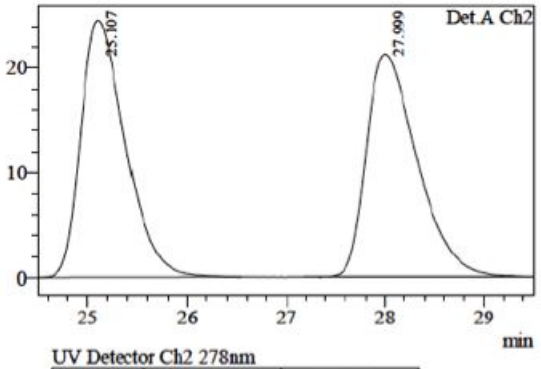
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	18.474	97.583
2	20.388	2.417
Total		100.000



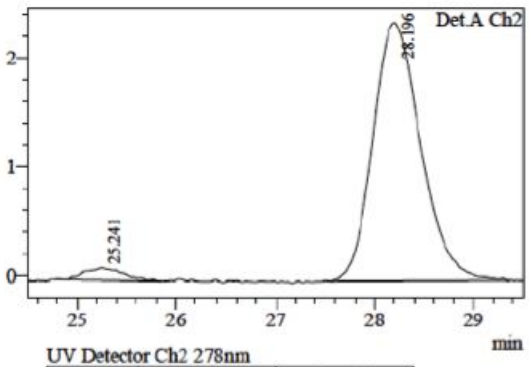
(*R*)-5-Methoxy-3-methylisobenzofuran-1(3*H*)-one (2b): Colorless oil (52.0 mg, 97%); R_f 0.3 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 1H), 7.02 (dd, J = 8.4, 2.0 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 5.48 (q, J = 6.7 Hz, 1H), 3.91 (s, 3H), 1.62 (d, J = 6.7 Hz, 3H); **HRMS** (ESI) Calcd for $C_{10}H_{11}O_3$ $[M + H]^+$ 179.0708, found 179.0712; $[\alpha]^{21}_D$ = +39.6° (c = 1.14 in $CHCl_3$, 93% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 98:2; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 25.2 min (minor) and 28.2 min (major), 93% ee.



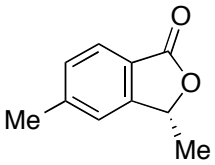
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	25.107	49.949
2	27.999	50.051
Total		100.000



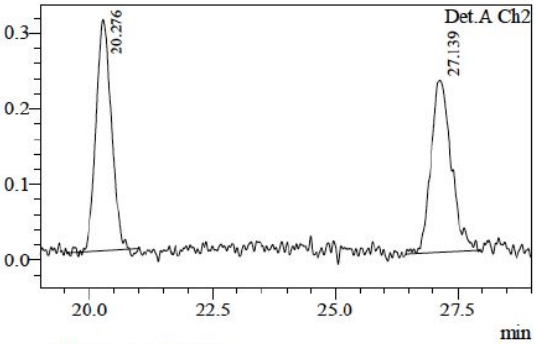
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	25.241	3.414
2	28.196	96.586
Total		100.000



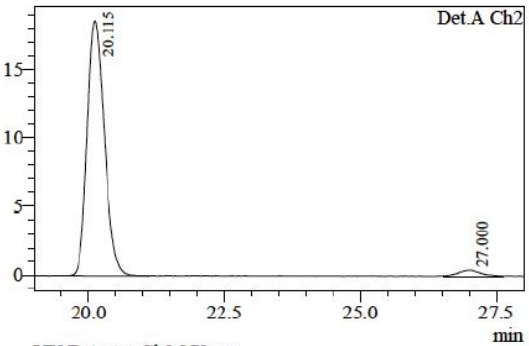
(*R*)-3,5-Dimethylisobenzofuran-1(3*H*)-one (2c): White solid (40.0 mg, 82%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.22 (s, 1H), 5.51 (q, *J* = 6.6 Hz, 1H), 2.50 (s, 3H), 1.62 (d, *J* = 6.6 Hz, 3H); **HRMS** (ESI) Calcd for $C_{10}H_{11}O_2$ $[M + H]^+$ 163.0759, found 163.0752; $[\alpha]^{21}_D$ = +35.8° (*c* = 1.05 in $CHCl_3$, 94% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 95:5; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 20.1 min (major) and 27.0 min (minor), 94% ee.



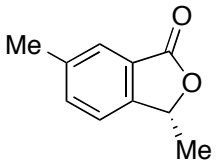
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	20.276	49.828
2	27.139	50.172
Total		100.000



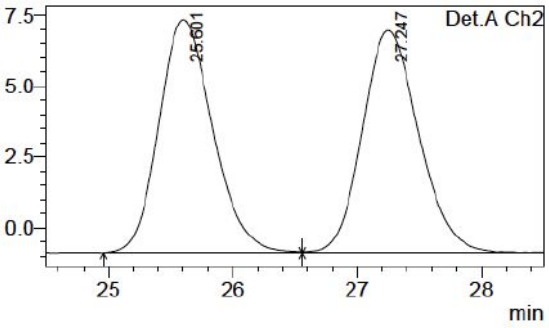
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	20.115	97.033
2	27.000	2.967
Total		100.000



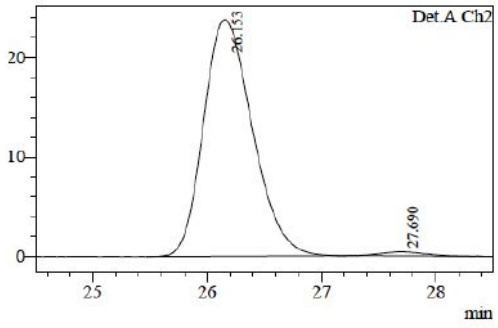
(*R*)-3,6-Dimethylisobenzofuran-1(3*H*)-one (2d): Colorless oil (41.0 mg, 84%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.48 (dd, *J* = 7.8, 0.7 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 5.52 (q, *J* = 6.7 Hz, 1H), 2.46 (s, 3H), 1.61 (d, *J* = 6.7 Hz, 3H); **HRMS** (ESI) Calcd for $C_{10}H_{11}O_2$ $[M + H]^+$ 163.0759, found 163.0764; $[\alpha]^{21}_D$ = +31.8° (*c* = 0.84 in $CHCl_3$, 97% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 98:2; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 26.1 min (major) and 27.7 min (minor), 97% ee.



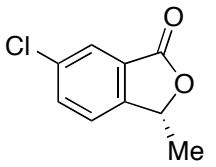
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	25.601	50.010
2	27.247	49.990
Total		100.000



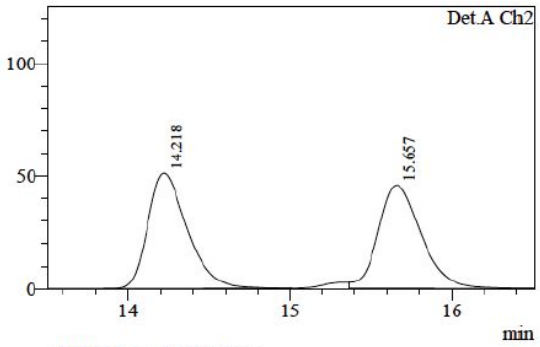
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	26.153	98.552
2	27.690	1.448
Total		100.000



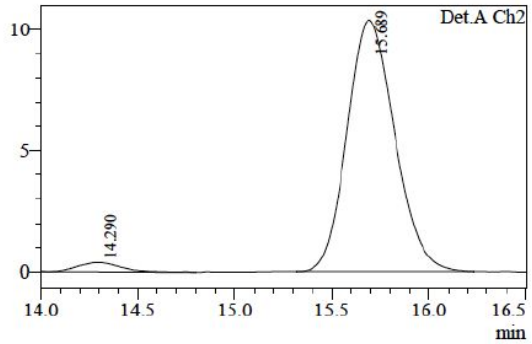
(*R*)-6-Chloro-3-methylisobenzofuran-1(3*H*)-one (2e): White solid (41.0 mg, 75%); R_f 0.3 (hexane/EtOAc = 7/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.65 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 5.55 (q, *J* = 6.7 Hz, 1H), 1.64 (d, *J* = 6.7 Hz, 3H); **HRMS** (ESI) Calcd for $C_9H_8ClO_2$ $[M + H]^+$ 183.0213, found 183.0208; $[\alpha]^{22}_D$ = +32.9° (*c* = 1.44 in $CHCl_3$, 93% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 98:2; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 14.3 min (minor) and 15.7 min (major), 93% ee.



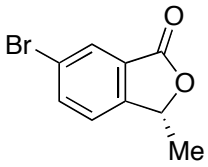
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	14.218	50.767
2	15.657	49.233
Total		100.000



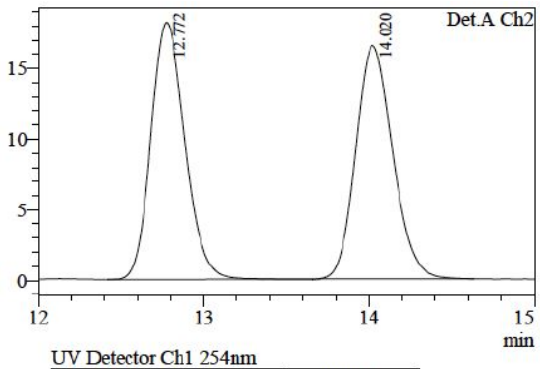
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	14.290	3.316
2	15.689	96.684
Total		100.000



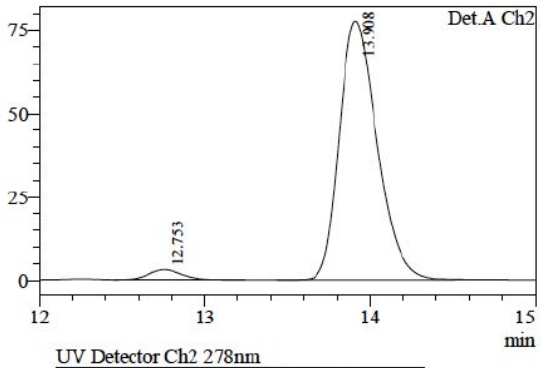
(*R*)-6-Bromo-3-methylisobenzofuran-1(3*H*)-one (2f): Colorless oil (41.0 mg, 61%); R_f 0.3 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 1.6 Hz, 1H), 7.79 (dd, *J* = 8.1, 1.6 Hz , 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 5.53 (q, *J* = 6.7 Hz, 1H), 1.63 (d, *J* = 6.7 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 168.9, 149.9, 137.2, 128.9, 128.1, 123.3, 123.2, 77.8, 20.4; **HRMS** (ESI) Calcd for $C_9H_8BrO_2$ $[M + H]^+$ 226.9708, found 226.9709; $[\alpha]^{22}_D$ = +34.7° (*c* = 0.68 in $CHCl_3$, 93% ee sample).

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 97:3; detection wavelengths = 254 and 278 nm; flow rate = 1.0 mL/min. t_R = 12.8 min (minor) and 13.9 min (major), 93% ee.



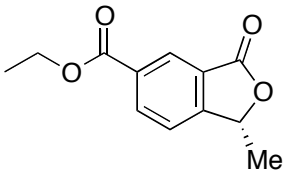
UV Detector Ch1 254nm

Peak#	Ret. Time	Area %
1	12.769	49.693
2	14.019	50.307
Total		100.000



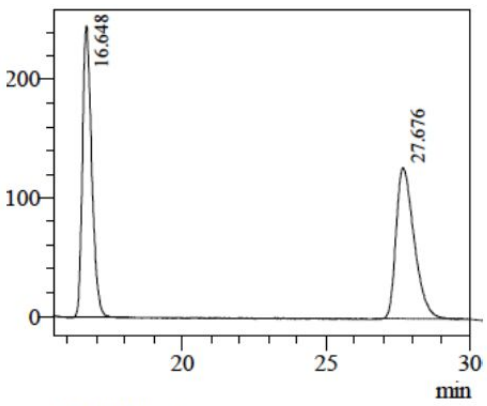
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	12.753	3.343
2	13.908	96.657
Total		100.000



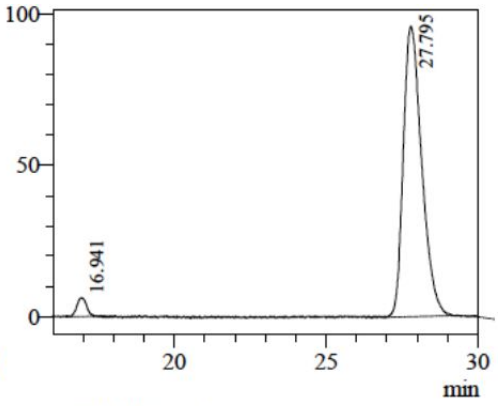
(*R*)-6-(Ethoxylcarbonyl)-3-methylisobenzofuran-1(3*H*)-one (2g): White solid (60.0 mg, 91%); R_f 0.3 (hexane/EtOAc = 4/1); m.p. 74-75 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.33 (dd, J = 8.0, 1.4 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 5.60 (q, J = 6.7 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.64 (d, J = 6.7 Hz, 3H), 1.39 (t, J = 7.1, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 169.5, 165.2, 155.1, 135.2, 132.1, 127.2, 126.4, 121.9, 77.8, 61.7, 20.3, 14.3; **HRMS** (ESI) Calcd for $C_{12}H_{13}O_4$ $[M + H]^+$ 221.0804, found 221.0806; $[\alpha]^{22}_D$ = +20.4° (c = 0.91 in $CHCl_3$, 93% ee sample).

HPLC analysis: Daicel CHIRALCEL OJ-H; hexane:*i*-PrOH = 85:15; detection wavelength = 190 nm; flow rate = 1.0 mL/min. t_R = 16.9 min (minor) and 27.8 min (major), 93% ee.



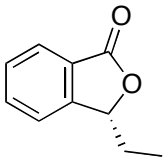
PDA Ch1 190nm 4nm

Peak#	Ret. Time	Area %
1	16.648	49.889
2	27.676	50.111
Total		100.000



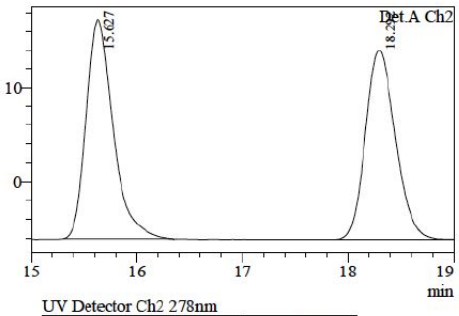
PDA Ch1 190nm 4nm

Peak#	Ret. Time	Area %
1	16.941	3.353
2	27.795	96.647
Total		100.000



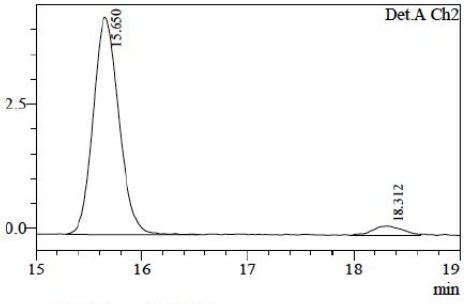
(*R*)-3-Ethylisobenzofuran-1(3*H*)-one (2h): Colorless oil (45.0 mg, 93%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.7 Hz, 1H), 7.67 (td, *J* = 7.5, 0.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.44 (dd, *J* = 7.7, 0.8 Hz, 1H), 5.45 (q, *J* = 4.4 Hz, 1H), 2.18-2.08 (m, 1H), 1.89-1.78 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H); **HRMS** (ESI) Calcd for $C_{10}H_{11}O_2$ $[M + H]^+$ 163.0759, found 163.0764; $[\alpha]^{22}_D$ = +64.1° (*c* = 0.88 in $CHCl_3$, 90% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 95:5; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 15.6 min (major) and 18.3 min (minor), 90% ee.



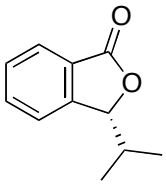
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	15.627	51.089
2	18.292	48.911
Total		100.000



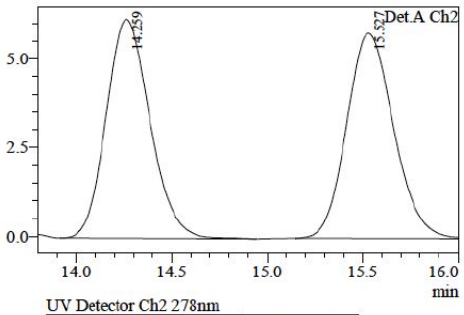
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	15.650	95.297
2	18.312	4.703
Total		100.000



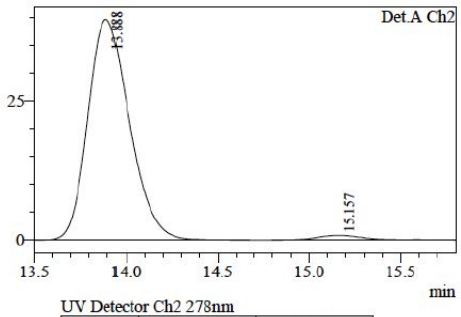
(*R*)-3-Isopropylisobenzofuran-1(3*H*)-one (2i): Colorless oil (48.0 mg, 91%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.65 (td, *J* = 7.5, 0.8 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 5.39 (d, *J* = 3.7 Hz, 1H), 2.35-2.27 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H); **HRMS** (ESI) Calcd for $C_{11}H_{13}O_2$ $[M + H]^+$ 177.0916, found 177.0915; $[\alpha]^{22}_D$ = +74.2° (*c* = 0.87 in $CHCl_3$, 95% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 95:5; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 13.9 min (major) and 15.1 min (minor), 95% ee.



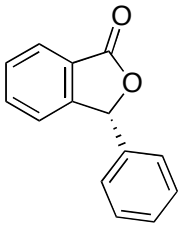
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	14.259	49.881
2	15.527	50.119
Total		100.000



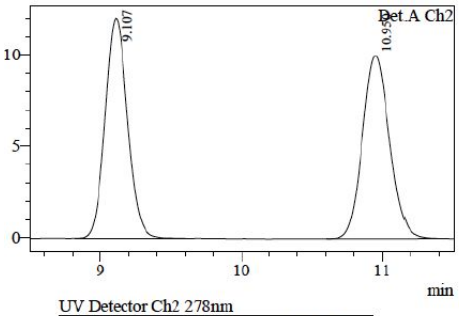
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	13.888	97.652
2	15.157	2.348
Total		100.000



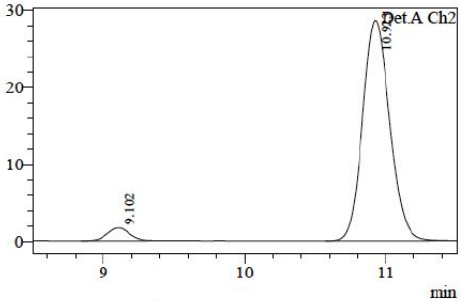
(*R*)-3-Phenylisobenzofuran-1(3*H*)-one (2j): Yellow solid (58.0 mg, 92%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.39-7.27 (m, 6H), 6.41 (s, 1H); **HRMS** (ESI) Calcd for $C_{14}H_{11}O_2$ $[M + H]^+$ 211.0759, found 211.0760; $[\alpha]^{22}_D$ = -42.1° (*c* = 1.05 in $CHCl_3$, 91% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 9.1 min (minor) and 10.9 min (major), 91% ee.



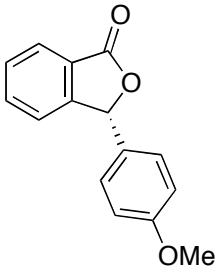
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	9.107	50.094
2	10.950	49.906
Total		100.000



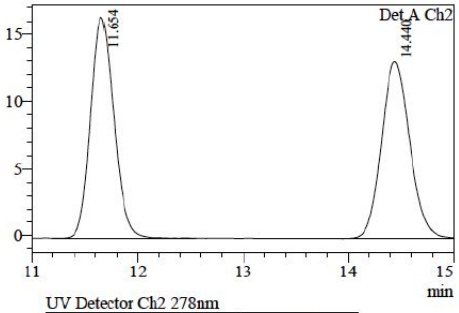
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	9.102	4.611
2	10.923	95.389
Total		100.000



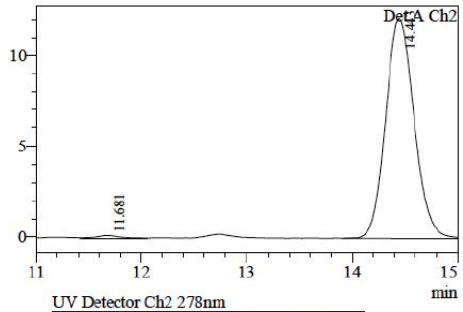
(*R*)-3-(4-Methoxyphenyl)isobenzofuran-1(3*H*)-one (2k): White solid (65.0 mg, 90%); R_f 0.3 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.32 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.19-7.17 (m, 2H), 6.90-6.88 (m, 2H), 6.37 (s, 1H), 3.81 (s, 1H); **HRMS** (ESI) Calcd for $C_{15}H_{13}O_3$ $[M + H]^+$ 241.0865, found 241.0867; $[\alpha]^{22}_D$ = +31.0° (*c* = 0.42 in $CHCl_3$, 98% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 11.7 min (minor) and 14.4 min (major), 98% ee.



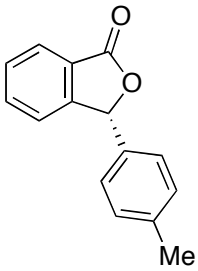
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	11.654	49.917
2	14.440	50.083
Total		100.000



UV Detector Ch2 278nm

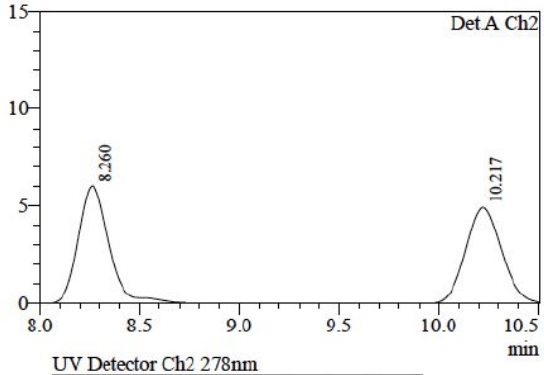
Peak#	Ret. Time	Area %
1	11.681	0.951
2	14.443	99.049
Total		100.000



(*R*)-3-(4-Methylphenyl)isobenzofuran-1(3*H*)-one (2l): White solid (57.0 mg, 86%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.4, 0.8 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.32 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.19-7.14 (m, 4H), 6.37 (s, 1H), 2.35 (s, 3H); **HRMS** (ESI) Calcd for $C_{15}H_{13}O_2$ $[M + H]^+$ 225.0916, found 225.0910; $[\alpha]^{22}_D$

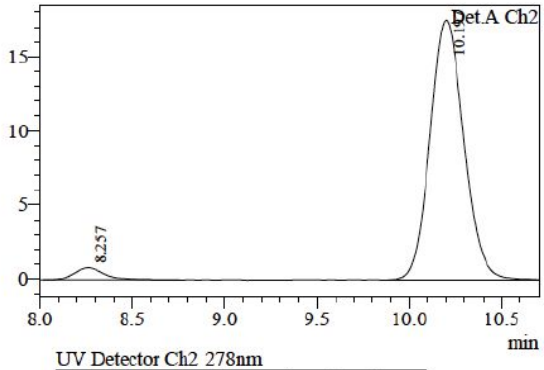
= -15.2° (c = 0.78 in $CHCl_3$, 92% ee sample). The ^1H NMR spectral data is in good agreement with the literature data (see attached).[1]

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 8.3 min (minor) and 10.2 min (major), 92% ee.



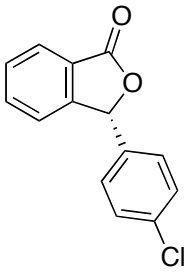
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	8.260	51.108
2	10.217	48.892
Total		100.000



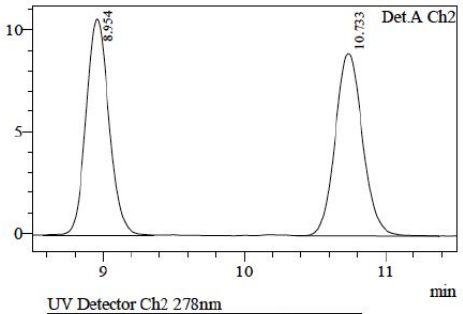
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	8.257	3.867
2	10.197	96.133
Total		100.000



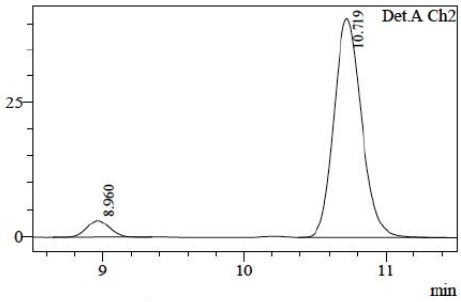
(*R*)-3-(4-Chlorophenyl)isobenzofuran-1(3*H*)-one (2m): White solid (60.0 mg, 83%); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 102-103 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, J = 7.6 Hz, 1H), 7.67 (t, J = 7.4 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.37-7.31 (m, 3H), 7.23-7.21 (m, 2H), 6.38 (s, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.3, 149.4, 135.5, 135.1, 134.6, 129.7, 129.4, 128.5, 126.0, 125.7, 122.9, 82.0; **HRMS** (ESI) Calcd for $C_{14}H_{10}ClO_2$ $[M + H]^+$ 245.0369, found 245.0363; $[\alpha]^{22}_D = -32.2°$ (c = 0.72 in $CHCl_3$, 88% ee sample).

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 8.9 min (minor) and 10.7 min (major), 88% ee.



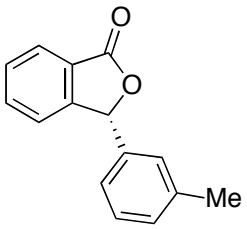
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	8.954	49.639
2	10.733	50.361
Total		100.000



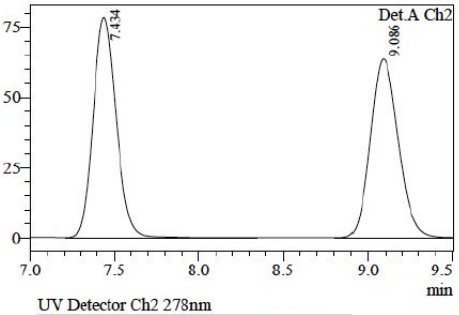
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	8.960	5.887
2	10.719	94.113
Total		100.000



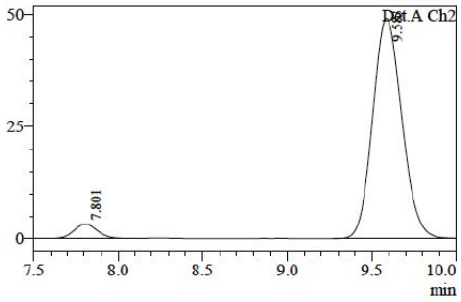
(*R*)-3-(3-Methylphenyl)isobenzofuran-1(3*H*)-one (2n): Yellow solid (58.0 mg, 86%); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 93-94 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.7 Hz, 1H), 7.64 (td, *J* = 7.5, 0.8 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.33 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.28-7.25 (m, 1H), 7.18-7.16 (m, 1H), 7.09-7.07 (m, 2H), 6.36 (s, 1H), 2.33 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.7, 149.9, 139.0, 136.5, 134.4, 130.2, 129.4, 129.0, 127.6, 125.7 (two overlapping peaks), 124.2, 123.0, 82.9, 21.5; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_2$ $[M + H]^+$ 225.0916, found 225.0924; $[\alpha]^{22}_D = -40.5^o$ (*c* = 1.18 in $CHCl_3$, 90% ee sample).

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 7.8 min (minor) and 9.6 min (major), 90% ee.



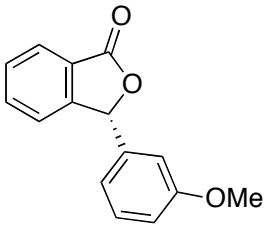
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	7.434	50.577
2	9.086	49.423
Total		100.000



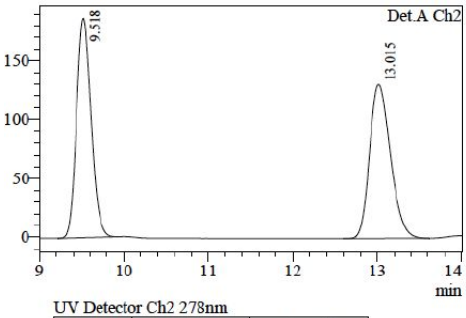
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	7.801	4.955
2	9.583	95.045
Total		100.000



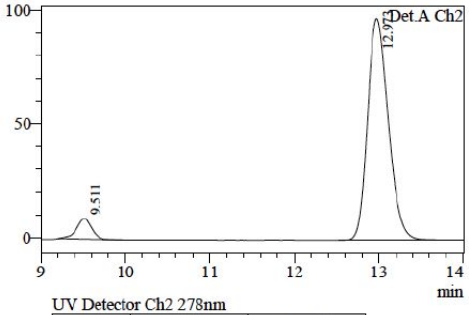
(*R*)-3-(3-Methoxyphenyl)isobenzofuran-1(3*H*)-one (2o): Yellow oil (38.0 mg, 53%); R_f 0.3 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.36-7.28 (m, 2H), 6.92-6.88 (m, 2H), 6.79 (t, *J* = 2.0 Hz, 1H), 6.37 (s, 1H), 3.78 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.6, 160.2, 149.8, 138.1, 134.5, 130.2, 129.5, 125.8, 125.7, 123.0, 119.3, 114.8, 112.6, 82.7, 55.5; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_3$ $[M + H]^+$ 241.0865, found 241.0873; $[\alpha]^{22}_D = -30.4°$ (*c* = 0.68 in $CHCl_3$, 87% ee sample).

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 9.5 min (minor) and 13.0 min (major), 87% ee.



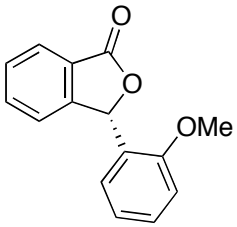
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	9.518	50.104
2	13.015	49.896
Total		100.000



UV Detector Ch2 278nm

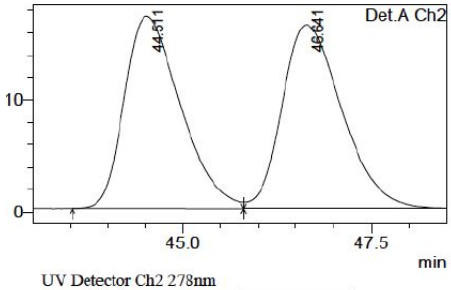
Peak#	Ret. Time	Area %
1	9.511	6.327
2	12.973	93.673
Total		100.000



(*R*)-3-(2-Methoxyphenyl)isobenzofuran-1(3*H*)-one (2p): White solid (66.0 mg, 98%); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 107-108 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 1H), 7.60 (td, *J* = 7.5, 1.0 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.44 (dd, *J* = 7.6, 0.5 Hz, 1H), 7.34-

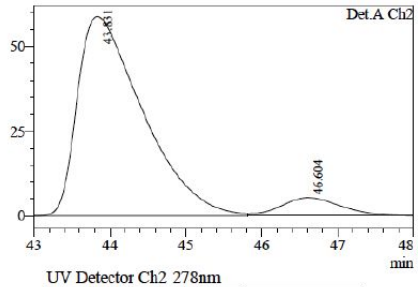
7.30 (m, 1H), 7.08 (dd, J = 7.6, 1.6 Hz, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.90 (td, J = 7.5, 0.7 Hz, 1H), 6.85 (s, 1H), 3.91 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 171.1, 157.1, 150.5, 134.2, 130.3, 129.1, 127.0, 125.8, 125.6, 125.2, 123.0, 121.0, 111.1, 78.2, 55.7; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_3$ $[M + H]^+$ 241.0865, found 241.0863; $[\alpha]^{22}_D$ = -136.1° (c = 1.33 in $CHCl_3$, 84% ee sample).

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 98:2; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 43.8 min (major) and 46.6 min (minor), 84% ee.



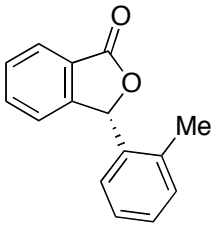
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	44.511	49.789
2	46.641	50.211
Total		100.000



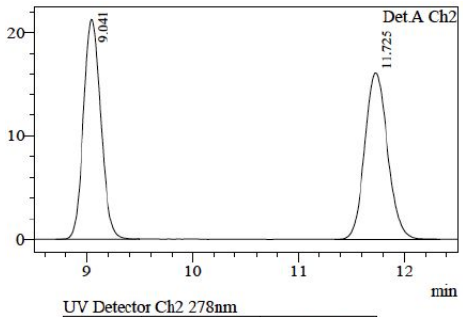
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	43.831	92.232
2	46.604	7.768
Total		100.000



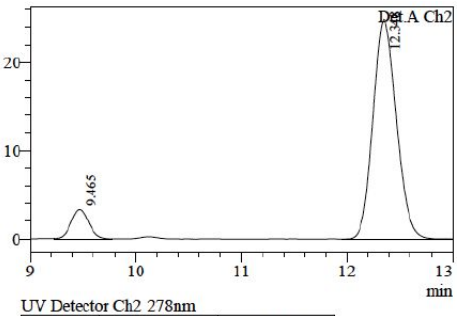
(*R*)-3-(2-Methylphenyl)isobenzofuran-1(3*H*)-one (2q): Yellow solid (36.0 mg, 54%); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 97-98 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 1H), 7.67 (td, J = 7.5, 1.1 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.34 (dd, J = 7.6, 0.7 Hz, 1H), 7.28-7.26 (m, 2H), 7.15-7.13 (m, 1H), 6.92 (d, J = 7.7 Hz, 1H), 6.68 (s, 1H), 2.50 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.7, 149.4, 137.3, 134.3, 134.2, 131.2, 129.5, 129.4, 127.4, 126.5 (two overlapping peaks), 125.8, 123.1, 80.6, 19.4; **HRMS** (ESI) Calcd for $C_{15}H_{13}O_2$ $[M + H]^+$ 225.0916, found 225.0923; $[\alpha]^{22}_D$ = +41.6° (c = 0.62 in $CHCl_3$, 82% ee sample).

HPLC analysis: Daicel CHIRALCEL OD-H; hexane:*i*-PrOH = 85:15; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 9.5 min (minor) and 12.3 min (major), 82% ee.



UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	9.041	49.940
2	11.725	50.060
Total		100.000

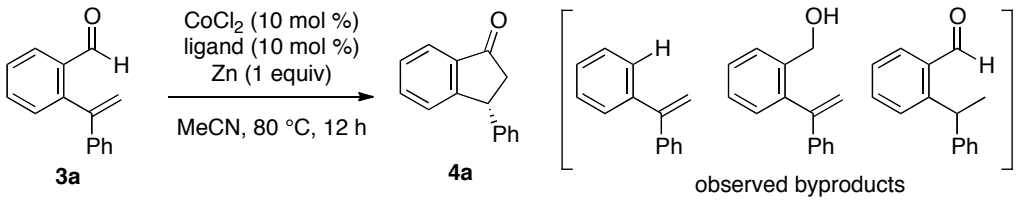


UV Detector Ch2 278nm

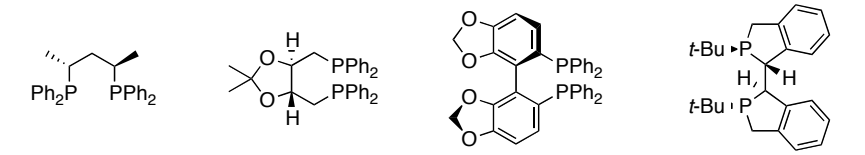
Peak#	Ret. Time	Area %
1	9.465	9.111
2	12.348	90.889
Total		100.000

Cobalt-Catalyzed Intramolecular Hydroacylation of Olefin

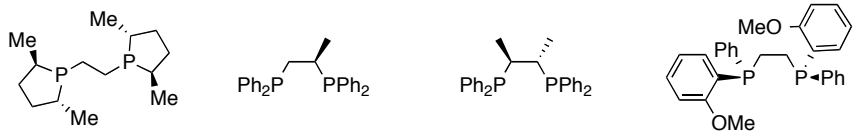
Table S5. Screening of Chiral Ligands[a]



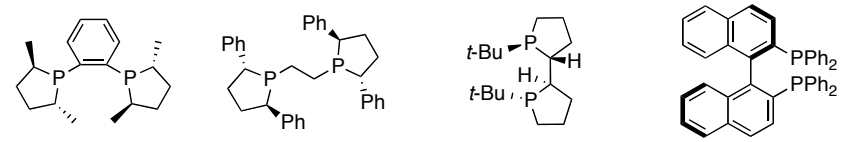
entry	ligand	conversion (%)[b]	yield (%)[b]	ee (%)[c]
1	(*R*,*R*)-BDPP	100	78	93
2	(*R*,*R*)-DIOP	100	87	53
3	(*R*)-SEGPHOS	81	17	52
4	(*R*,*R*,*S*,*S*)-Duanphos	100	50	51
5	(*R*,*R*)-Me-BPE	15	15	42
6	(*R*)-Prophos	42	22	31
7	(*S*,*S*)-Chiraphos	11	8	ND
8	(*R*,*R*)-DIPAMP	32	30	10
9	(*R*,*R*)-Me-DuPhos	0	0	–
10	(*R*,*R*)-Ph-BPE	53	0	–
11	(*S*,*S*,*R*,*R*)-Tangphos	0	0	–
12	(*R*)-BINAP	47	0	–



(*R*,*R*)-BDPP (*R*,*R*)-DIOP (*R*)-SEGPHOS (*R*,*R*,*S*,*S*)-Duanphos



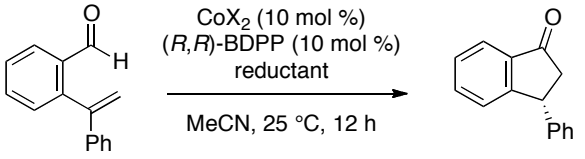
(*R*,*R*)-Me-BPE (*R*)-Prophos (*S*,*S*)-Chiraphos (*R*,*R*)-DIPAMP



(*R*,*R*)-Me-DuPhos (*R*,*R*)-Ph-BPE (*S*,*S*,*R*,*R*)-Tangphos (*R*)-BINAP

[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. When the conversion was high but the yield of **4a** was low, decarbonylation and aldehyde/olefin reduction products were typically observed. [c] Determined by chiral HPLC analysis. ND = not determined.

Table S6. Effect of Cobalt Precatalysts and Reductants[a]

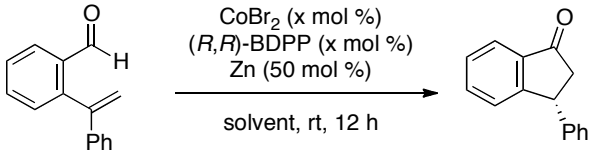


3a **4a**

entry	CoX_2	reductant	yield (%)[b]	ee (%)[c]
1	$CoCl_2$	Zn (100 mol %)	89	95
2	$CoCl_2$	Mn (100 mol %)	0	–
3	$CoCl_2$	In (100 mol %)	0	–
4	$CoBr_2$	Zn (100 mol %)	98	95
5	$CoBr_2$	Mn (100 mol %)	46	94
6	$CoBr_2$	In (100 mol %)	0	–
7	CoI_2	Zn (100 mol %)	17	ND
8	CoI_2	Mn (100 mol %)	0	–
9	CoI_2	In (100 mol %)	0	–
10	$CoCl_2$	Zn (50 mol %)	99	97
11	$CoCl_2$	Zn (20 mol %)	5	ND
12	$CoBr_2$	Zn (50 mol %)	58	95

[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis. ND = not determined.

Table S7. Effect of Solvents and Catalyst Loading[a]

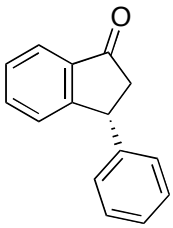


3a **4a**

entry	x	solvent	yield (%)[b]	ee (%)[c]
1	10	MeCN	99	97
2	10	toluene	0	–
3	10	THF	0	–
4	10	DCE	0	–
5	5	MeCN	89	ND
6	2.5	MeCN	47	ND

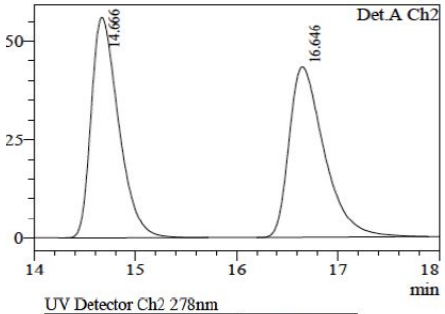
[a] The reaction was performed on a 0.1 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Determined by chiral HPLC analysis. ND = not determined.

General procedure: In an argon-filled glove box, to a 4 mL vial were charged sequentially $CoCl_2$ (3.9 mg, 0.030 mmol), (*R,R*)-BDPP (13.2 mg, 0.030 mmol) and zinc powder (9.8 mg, 0.15 mmol). Then MeCN (0.6 mL) was added and the mixture was stirred at room temperature (25 °C) for 5 min. To the resulting mixture was added a solution of 2-alkenylbenzaldehyde (0.30 mmol) in MeCN (0.6 mL). The vial was removed from the glove box, and the reaction mixture was stirred for 12 h at room temperature. Then the reaction mixture was diluted with ethyl acetate (5 mL) and filtered through a pad of silica gel with additional ethyl acetate (10 mL) as eluent. The solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel to afford the desired product.



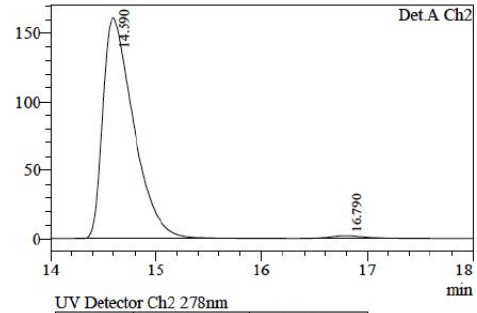
(*R*)-3-Phenyl-2,3-dihydro-1*H*-inden-1-one (4a): Colorless oil (59.0 mg, 95%); R_f 0.3 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.6 Hz, 1H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.33-7.25 (m, 4H), 7.13 (d, *J* = 7.2 Hz, 2H), 4.58 (dd, *J* = 8.0, 3.8 Hz, 1H), 3.23 (dd, *J* = 19.2, 8.0 Hz, 1H), 2.70 (dd, *J* = 19.2, 3.8 Hz, 1H); **HRMS** (ESI) Calcd for $C_{15}H_{13}O$ $[M + H]^+$ 209.0966, found 209.0969; $[\alpha]^{22}_D = -53.2°$ (*c* = 0.97 in $CHCl_3$, 97% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data (see attached).[5]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 99:1; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 14.6 min (major) and 16.8 min (minor), 97% ee.



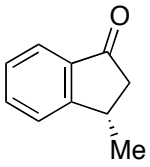
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	14.666	50.309
2	16.646	49.691
Total		100.000



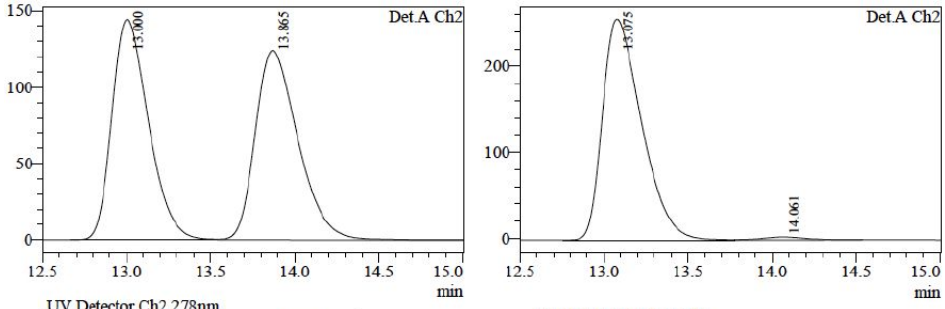
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	14.590	98.613
2	16.790	1.387
Total		100.000



(*S*)-3-Methyl-2,3-dihydro-1*H*-inden-1-one (4b): Colorless oil (41.0 mg, 94%); R_f 0.3 (hexane/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.7, 1.2 Hz, 1H), 7.51 (dd, *J* = 7.6, 0.6 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 3.50-3.40 (m, 1H), 2.95 (dd, *J* = 18.8, 7.5 Hz, 2H), 2.28 (dd, *J* = 18.8, 3.5 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 3H); **HRMS** (ESI) Calcd for $C_{10}H_{11}O$ $[M + H]^+$ 147.0810, found 147.0815; $[\alpha]^{22}_D$ = +15.9° (*c* = 0.80 in $CHCl_3$, 97% ee sample). The ^{1}H NMR spectral data is in good agreement with the literature data.[6] The absolute configuration was determined to be *S* by comparison of the optical rotation with the literature data ($[\alpha]^{25}_D$ = –6.67° (*c* = 1.05 in EtOH) for 92% ee sample).[5]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 99:1; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 13.1 min (major) and 14.1 min (minor), 97% ee.

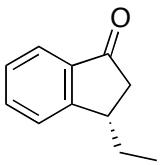


UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	13.000	49.920
2	13.865	50.080
Total		100.000

UV Detector Ch2 278nm

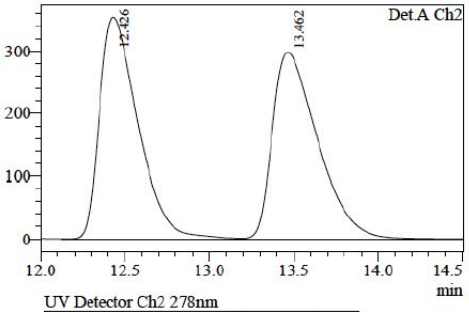
Peak#	Ret. Time	Area %
1	13.075	98.565
2	14.061	1.435
Total		100.000



(*S*)-3-Ethyl-2,3-dihydro-1*H*-inden-1-one (4c): Colorless oil (45.0 mg, 94%); R_f 0.3 (hexane/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.59 (td, *J* = 7.7, 1.1 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 1H), 3.36-3.30 (m, 1H), 2.85 (dd, *J* = 19.2, 7.5 Hz, 1H), 2.37 (dd, *J* = 19.2, 3.5 Hz, 1H), 2.01-1.95 (m, 1H), 1.60-1.52 (m, 1H), 0.98 (t, *J* = 7.4 Hz, 3H); **HRMS** (ESI) Calcd for $C_{11}H_{13}O$ $[M + H]^+$ 161.0966, found 161.0965; $[\alpha]^{22}_D$ =

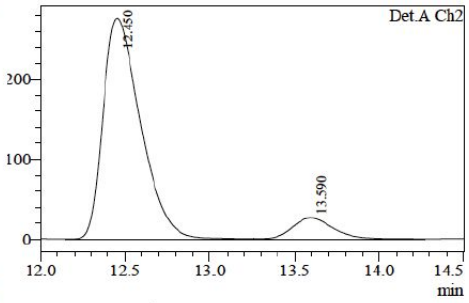
+23.6° (*c* = 0.80 in $CHCl_3$, 81% ee sample). The ^1H NMR spectral data is in good agreement with the literature data.[7]

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 99:1; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 12.4 min (major) and 13.6 min (minor), 81% ee.



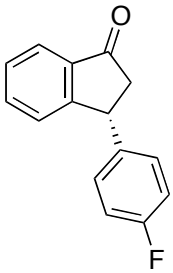
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	12.426	50.210
2	13.462	49.790
Total		100.000



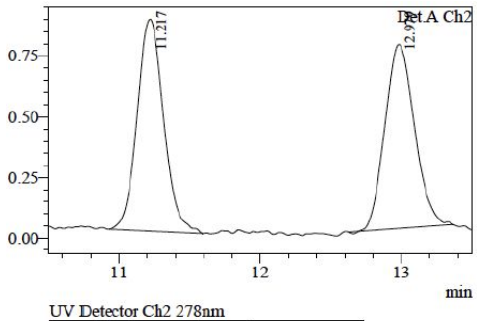
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	12.450	90.736
2	13.590	9.264
Total		100.000



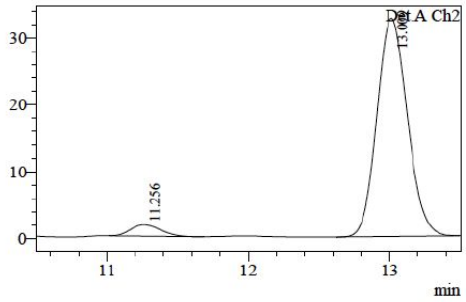
(*R*)-3-(4-Fluorophenyl)-2,3-dihydro-1*H*-inden-1-one (4d): The reaction was performed at 80 °C; Yellow solid (59.0 mg, 87%); R_f 0.3 (hexane/EtOAc = 10/1); m.p. 124-125 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.25 (d, *J* = 7.0 Hz, 1H), 7.10-7.07 (m, 2H), 7.00 (t, *J* = 8.6 Hz, 1H), 4.57 (dd, *J* = 8.0, 3.8 Hz, 1H), 3.23 (dd, *J* = 19.2, 8.0 Hz, 1H), 2.64 (dd, *J* = 19.2, 3.8 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 205.8, 161.9 (d, $^1J_{C\text{-}F}$ = 244.0 Hz), 157.8, 139.6 (d, $^4J_{C\text{-}F}$ = 4.0 Hz), 136.9, 135.3, 129.2 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 128.2, 126.9, 123.6, 115.9 (d, $^2J_{C\text{-}F}$ = 21.0 Hz), 47.1, 43.9; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -115.7; **HRMS** (ESI) Calcd for $C_{15}H_{12}FO$ $[M + H]^+$ 227.0872, found 227.0867; $[\alpha]^{22}_D$ = -59.6° (*c* = 0.69 in $CHCl_3$, 90% ee sample).

HPLC analysis: Daicel CHIRALPAK ID; hexane:*i*-PrOH = 98:2; detection wavelength = 278 nm; flow rate = 1.0 mL/min. t_R = 11.2 min (minor) and 13.0 min (major), 90% ee.



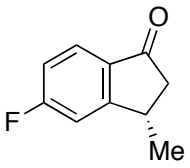
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	11.217	50.819
2	12.979	49.181
Total		100.000



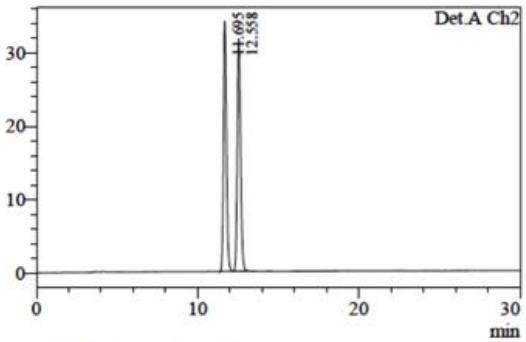
UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	11.256	4.876
2	13.009	95.124
Total		100.000



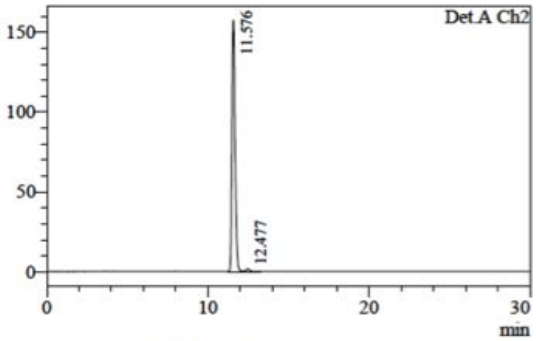
(*S*)-5-Fluoro-3-methyl-2,3-dihydro-1*H*-inden-1-one (4f): Colorless oil (40.0 mg, 81%); R_f 0.3 (hexane/EtOAc = 25/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 8.4, 5.4 Hz, 1H), 7.16 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.07 (td, *J* = 8.4, 2.2 Hz, 1H), 3.45-3.41 (m, 1H), 2.97 (dd, *J* = 19.0, 7.5 Hz, 1H), 2.31 (dd, *J* = 19.0, 2.6 Hz, 1H), 1.41 (d, *J* = 7.1 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 204.3, 168.6 (d, $J_{C\text{-}F}$ = 256.0 Hz), 162.8 (d, $J_{C\text{-}F}$ = 9.7 Hz), 132.8, 125.8 (d, $J_{C\text{-}F}$ = 10.3 Hz), 115.7 (d, $J_{C\text{-}F}$ = 23.9 Hz), 112.0 (d, $J_{C\text{-}F}$ = 22.2 Hz), 45.5, 32.7 (d, $J_{C\text{-}F}$ = 2.0 Hz), 21.1; **^{19}F NMR** (376 MHz, $CDCl_3$): δ -102.8; **HRMS** (ESI) Calcd for $C_{10}H_{10}FO$ $[M + H]^+$ 165.0716, found 165.0713. $[\alpha]^{21}_D$ = +8.2° (*c* = 1.15 in $CHCl_3$, 97% ee sample).

HPLC analysis: Daicel CHIRALCEL ID; hexanes: *i*-PrOH = 99:1; detection wavelength = 278 nm; flow rate = 1.0 mL/min). t_R = 11.6 min (major) and 12.4 min (minor), 97% ee.



UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	11.695	49.982
2	12.558	50.018
Total		100.000

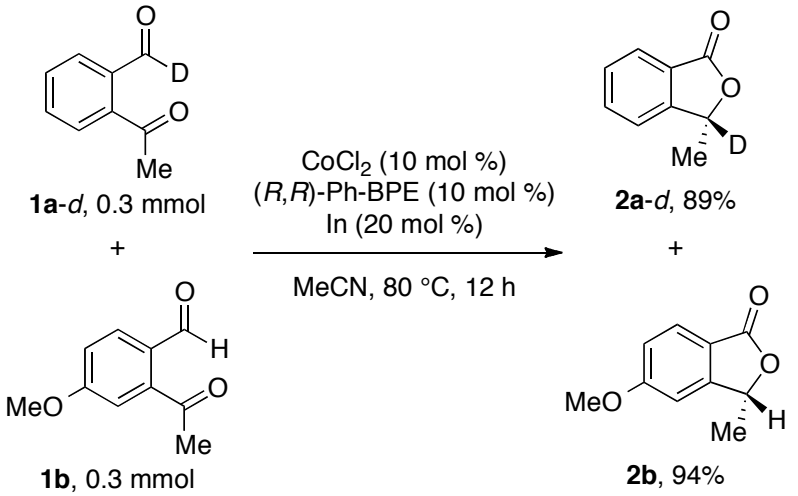


UV Detector Ch2 278nm

Peak#	Ret. Time	Area %
1	11.576	98.805
2	12.477	1.195
Total		100.000

Deuterium-Labeling Experiments

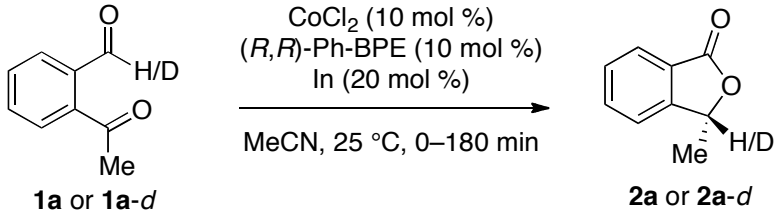
Crossover experiment (Scheme 4a)



A mixture of **1a**-*d* (0.30 mmol) and **1b** (0.30 mmol) were subjected to the standard reaction conditions. Purification of the crude mixture by silica gel chromatography (hexane/EtOAc = 6:1) afforded **2a**-*d* (40.0 mg, 89%) and **2b** (50.0 mg, 94%). ^{1}H NMR analysis of each product indicated that no H/D crossover took place during the reaction.

(*R*)-3-Methylisobenzofuran-1-one-3-*d* (2a-*d*): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.7 Hz, 1H), 7.68 (td, *J* = 7.5, 1.0 Hz, 1H), 7.52 (td, *J* = 8.0, 0.6 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 1.64 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 170.6, 151.2, 134.1, 129.2, 125.9, 125.8, 121.7, 77.5 (t, $^1J_{C\text{-}D}$ = 22.0 Hz), 20.4; **HRMS** (ESI) Calcd for $C_9H_8DO_2$ $[M + H]^+$ 150.0665, found 150.0668; $[\alpha]^{22}_D$ = +30.1° (*c* = 1.15 in $CHCl_3$).

Kinetic isotope effect experiments (Scheme 4b)



Parallel individual reactions of **1a** and **1a**-*d* were performed with the standard catalytic system at room temperature (25 °C) in the presence of *n*-tridecane as an internal standard for GC analysis. The progress of each reaction was monitored by GC analysis of periodically taken aliquots (0–180 min). As shown in Table S8 and Figure S1, the yields of the products **2a** and **2a**-*d* increased

linearly over time up to ca. 25% yield. The slopes for the yields of **2a** and **2a**-*d* were calculated to be 0.147 ± 0.012 and 0.136 ± 0.011 (the errors were given by 3σ), respectively, from which the H/D KIE was determined to be 1.1 ± 0.1.

Table S8. Progress of Individual Reactions of **1a** and **1a**-*d*[a]

time (min)	**2a** (%)	**2a**-*d* (%)
20	2.3	1.5
40	5.0	4.0
60	8.3	6.5
80	11.1	10.1
100	14.8	12.7
120	18.0	15.5
150	21.8	19.7
180	25.1	22.4

[a] The yield was determined by GC using *n*-tridecane as an internal standard.

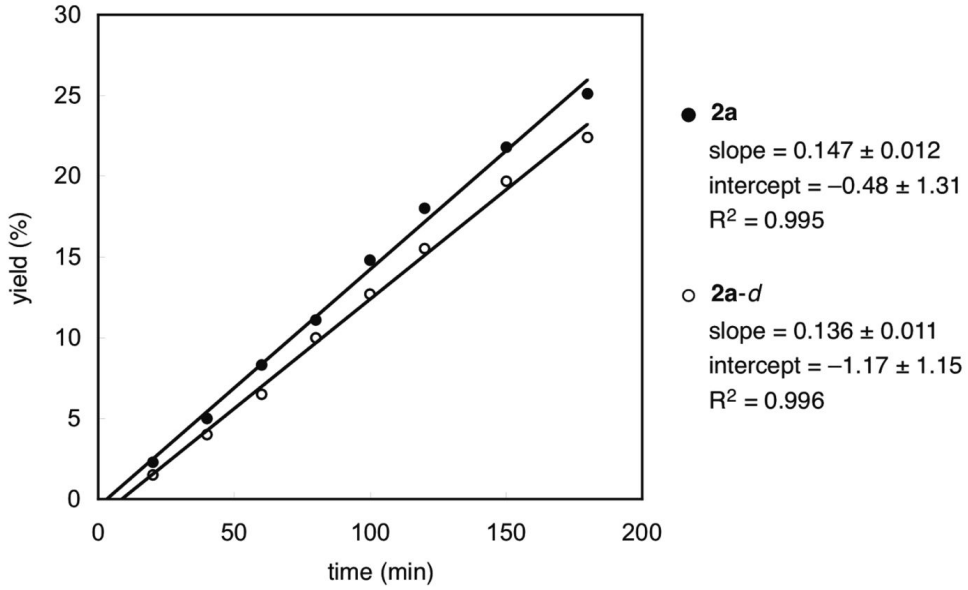
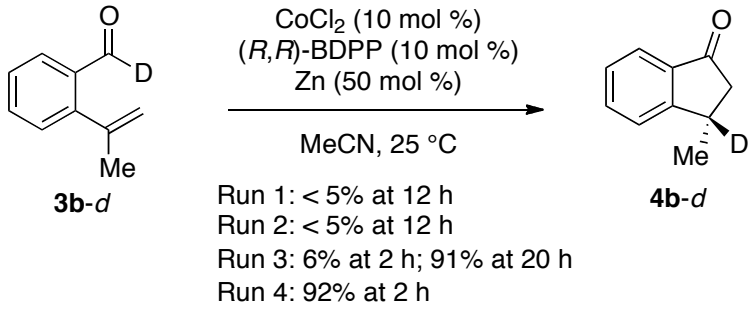


Figure S1. Plot of the yields of **2a** and **2a**-*d* against the reaction time.

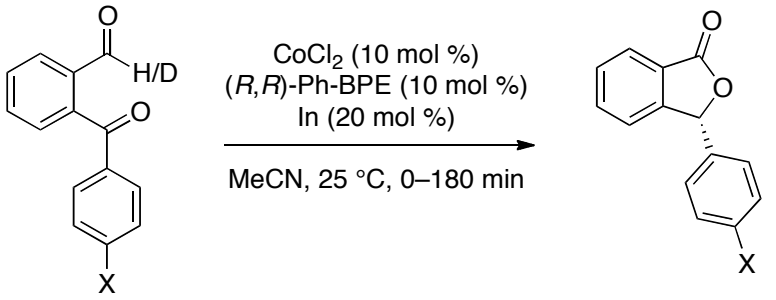
Reaction of deuterated 2-alkenylbenzaldehyde 3b-*d*

The deuterated substrate **3b**-*d* was subjected to the standard conditions for intramolecular olefin hydroacylation using *n*-tridecane as an internal standard for GC analysis (Scheme S1). The same experiments were performed four times. In runs 1 and 2, the yield was determined to be less than 5% after 12 h. In run 3, the reaction was monitored every 20 min for initial 2 hours. While the yield was only 6% at 2 h, upon further stirring, the yield reached 91% after 20 h. In run 4, the reaction was again monitored every 20 min for initial 2 hours. In this case, the yield reached 92% only after 2 h. Such a drastic fluctuation of yields would originate from the slow and heterogeneous nature of the precatalyst reduction, which would be sensitive to subtle changes of the reaction conditions and operation. The reaction of the parent substrate **3b** was also monitored twice, which showed similar fluctuating behavior in the early stage (2.4% and 7.7% yields at 20 min). However, in this case the yields of both the reactions reached to the same level (51% and 53%) after 2 h, which is consistent with the reproducibility of the preparative experiments using the non-deuterated substrates **3a**–**3f**.

Scheme S1.



Comparison of the Reaction Rates of 1j and 1k and Discussion on Rate-Limiting Step in Ketone Hydroacylation



1j (X = H) or **1k** (X = OMe) **2j** (X = H) or **2k** (X = OMe)

Parallel individual reactions of **1j** and **1k** were performed with the standard catalytic system at 60 °C in the presence of *n*-tridecane as an internal standard for GC analysis. The progress of each reaction was monitored by GC analysis of periodically taken aliquots (0–180 min). As shown in Table S9 and Figure S2, the yields of the products **2j** and **2k** increased linearly over time up to ca. 20% and 40%, respectively. The slopes for the yields of **2j** and **2k** were calculated to be 0.115 ± 0.007 and 0.237 ± 0.028 (the errors were given by 3σ), respectively, which indicates that **1k** reacts about twice as fast as **1j**.

Table S9. Progress of Individual Reactions of **1j** and **1k**[a]

time (min)	**2j** (%)	**2k** (%)
30	3.3	7.9
60	6.6	16.6
90	10.4	23.8
120	14.1	32.0
150	16.9	37.4
180	20.5	43.5

[a] The yield was determined by GC using *n*-tridecane as an internal standard.

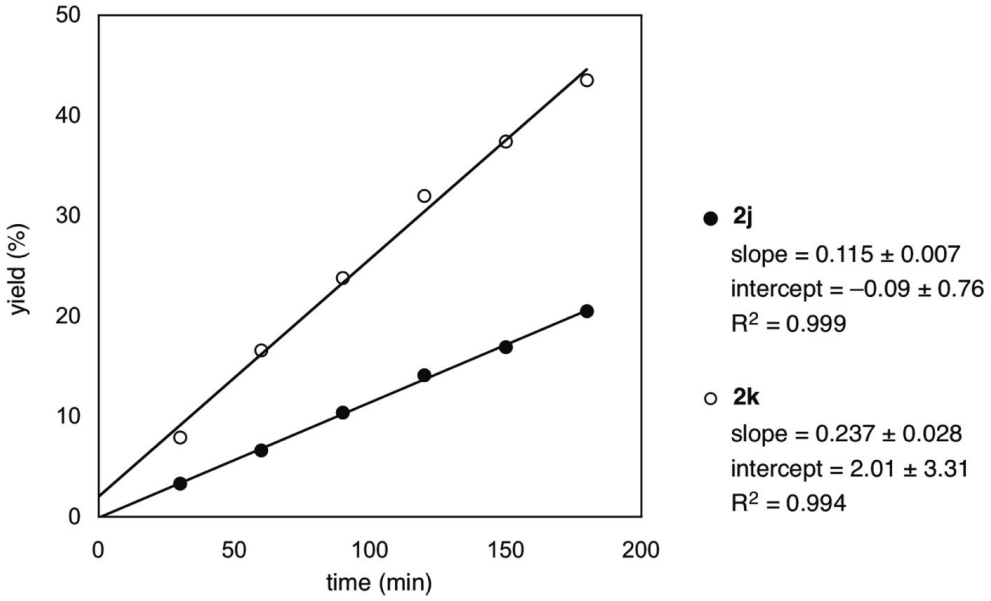
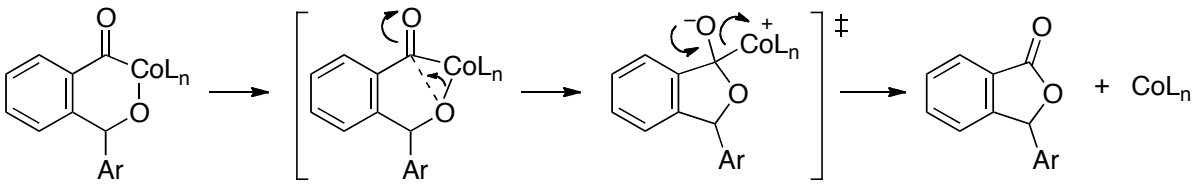


Figure S2. Plot of the yields of **2j** and **2k** against the reaction time.

The higher reactivity of the substrate bearing more electron-rich ketone moiety (**1k**) is in contrast to the trend observed in Dong's work on rhodium-catalyzed 7-membered ring-forming intramolecular hydroacylation.[8] Thus, in Dong's system, substrates bearing electron-poor ketones reacted faster, which, along with modest yet noticeable H/D KIE of 1.8, supported a proposal of rate-limiting ketone insertion (i.e., hydrometalation of C=O).

On the basis of the small KIE of 1.1 and the higher reactivity of **1k**, we are tempted to suggest rate-limiting reductive elimination. This proposal may be reasonable in light of the paring of the electron-withdrawing (electrophilic) acyl ligand and the electron-donating (nucleophilic) alkoxide ligand in the reductive elimination process (Scheme S1),[9] which would make the reaction of more donating alkoxide ligand faster. This model may also explain the lack of reactivity of the substrate **1t**, the 4-diethylamino group of which would make the acyl ligand much less electron-withdrawing and hence reluctant to undergo reductive elimination.

Scheme S2. Proposed Mechanistic Model of Acyl–Alkoxy Reductive Elimination



Reference

(1) Phan, D. H. T.; Kim, B.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 15608.

(2) Kundu, K.; McCullagh, J. V.; Morehead, A. T. *J. Am. Chem. Soc.* **2005**, *127*, 16042.

(3) Peyroux, E.; Berthiol, F.; Doucet, H.; Santelli, M. *Eur. J. Org. Chem.* **2004**, 1075.

(4) Kosaka, M.; Sekiguchi, S.; Naito, J.; Uemura, M.; Kuwahara, S.; Watanabe, M.; Harada, N.; Hiroi, K. *Chirality* **2005**, *17*, 218.

(5) Minatti, A.; Zheng, X.; Buchwald, S. L. *J. Org. Chem.* **2007**, *72*, 9253.

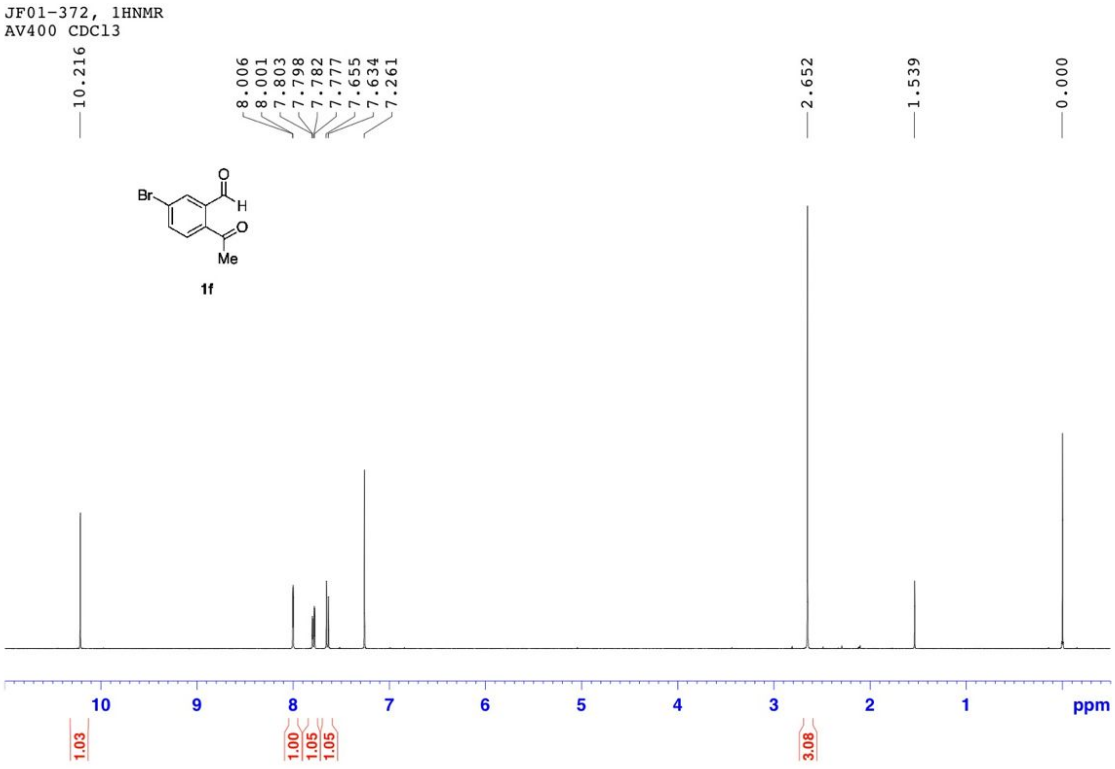
(6) Yun, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 767.

(7) Zheng, H.; Xie, X.; Yang, J.; Zhao, C.; Jing, P.; Fang, B.; She, X. *Org. Biomol. Chem.* **2011**, *9*, 7755.

(8) Shen, Z.; Dornan, P. K.; Khan, H. A.; Woo, T. K.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 1077.

(9) For electronic pairing in reductive elimination, see the following for example: (a) Widenhoefer, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 6504. (b) Shekhar, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 13016.

NMR Spectra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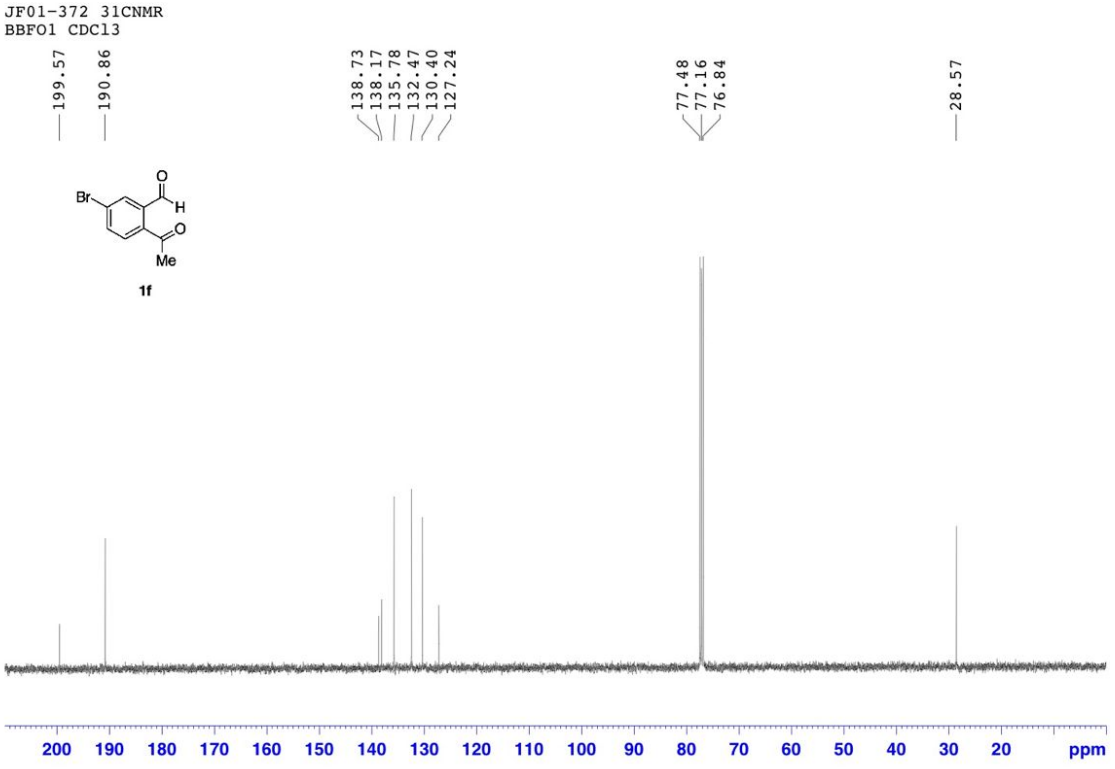
8.001
7.803
7.798
7.782
7.777
7.655
7.634
7.261
2.652
1.539
0.000
Br
O
H
O
Me
1f
10
9
8
7
6
5
4
3
2
1
ppm
1.03
1.00
1.05
1.05
3.08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77.16
76.84
28.57
Br
O
H
O
Me
1f
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130
120
110
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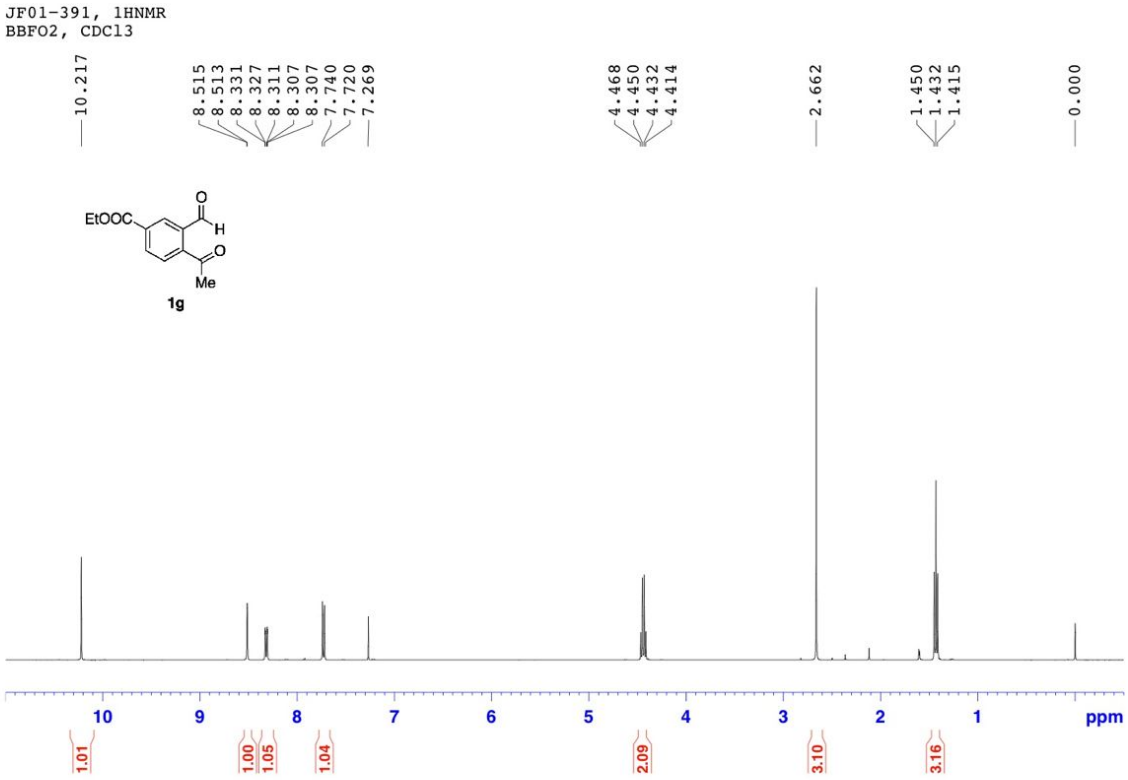
90
80
70
60
50
40
30
20
ppm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8.513
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8.327
8.311
8.307
8.307
7.740
7.720
7.269
4.468
4.450
4.432
4.414
2.662
1.450
1.432
1.415
0.000
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O
H
O
Me
1g
10
9
8
7
6
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3
2
1
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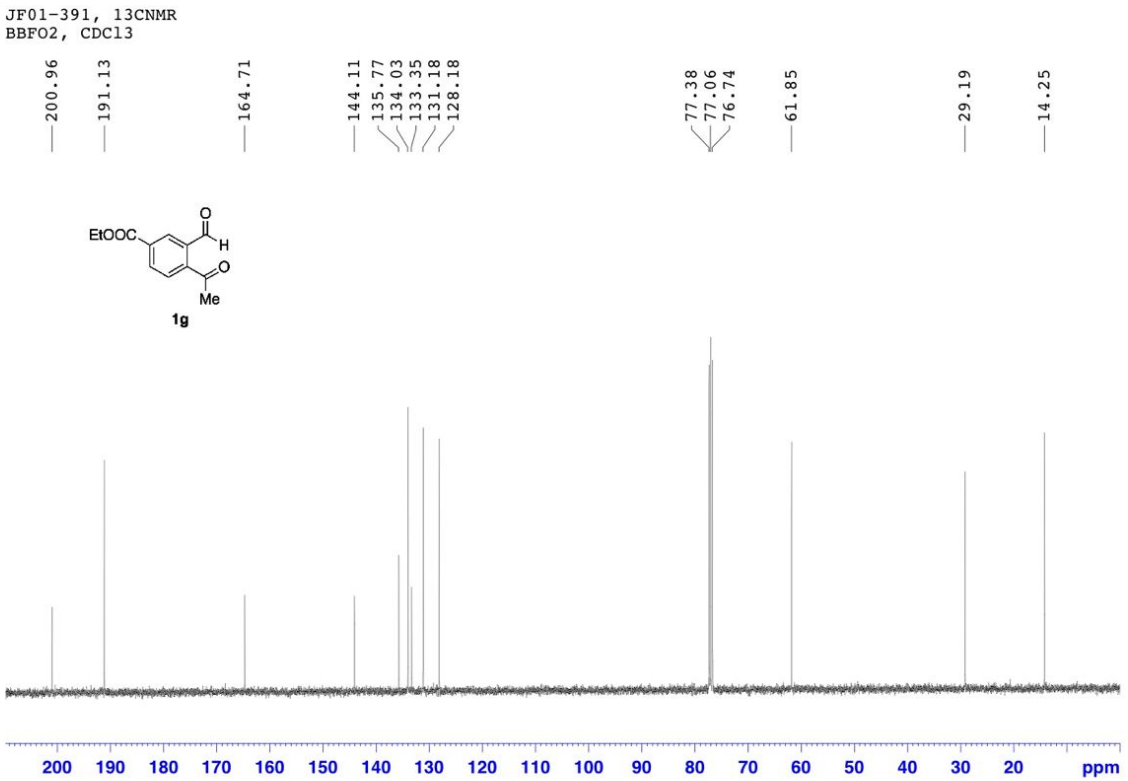
2.09
3.10
3.16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BBFO2, CDCl3
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191.13
164.71
144.11
135.77
134.03
133.35
131.18
128.18
77.38
77.06
76.74
61.85
29.19
14.25
EtOOC
O
H
O
Me
1g
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190
180
170
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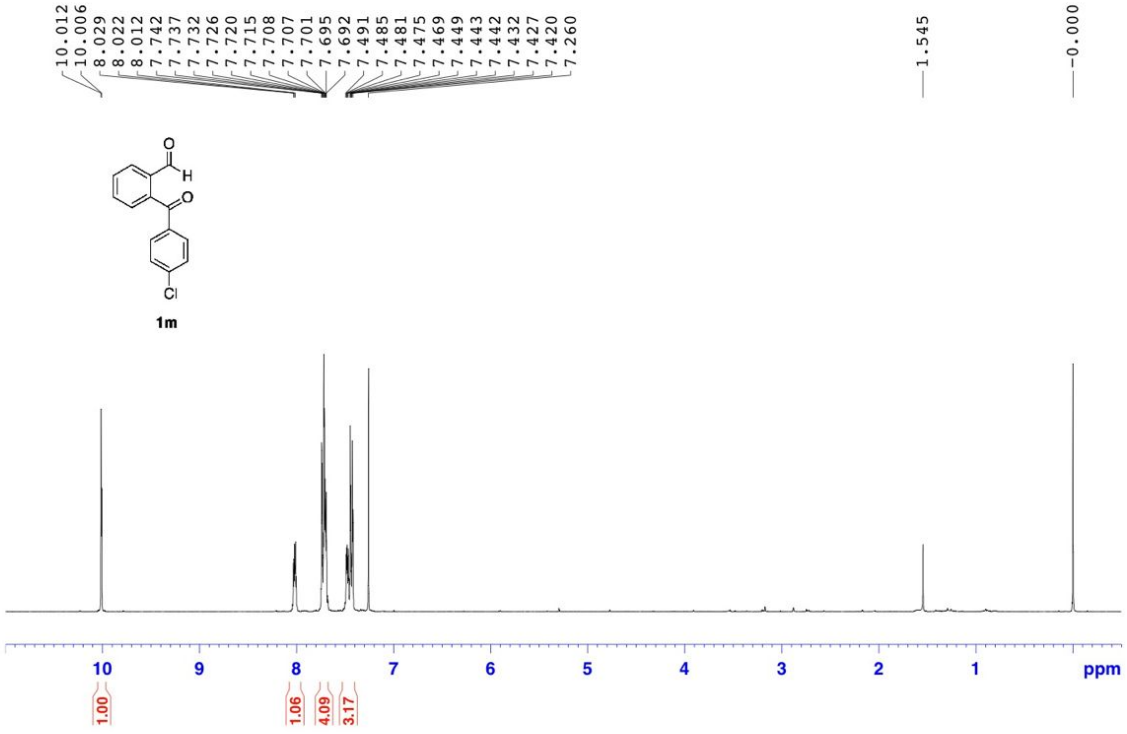
30
20
ppm

JF01-417 1HNMR
BBFO1 CDCl3



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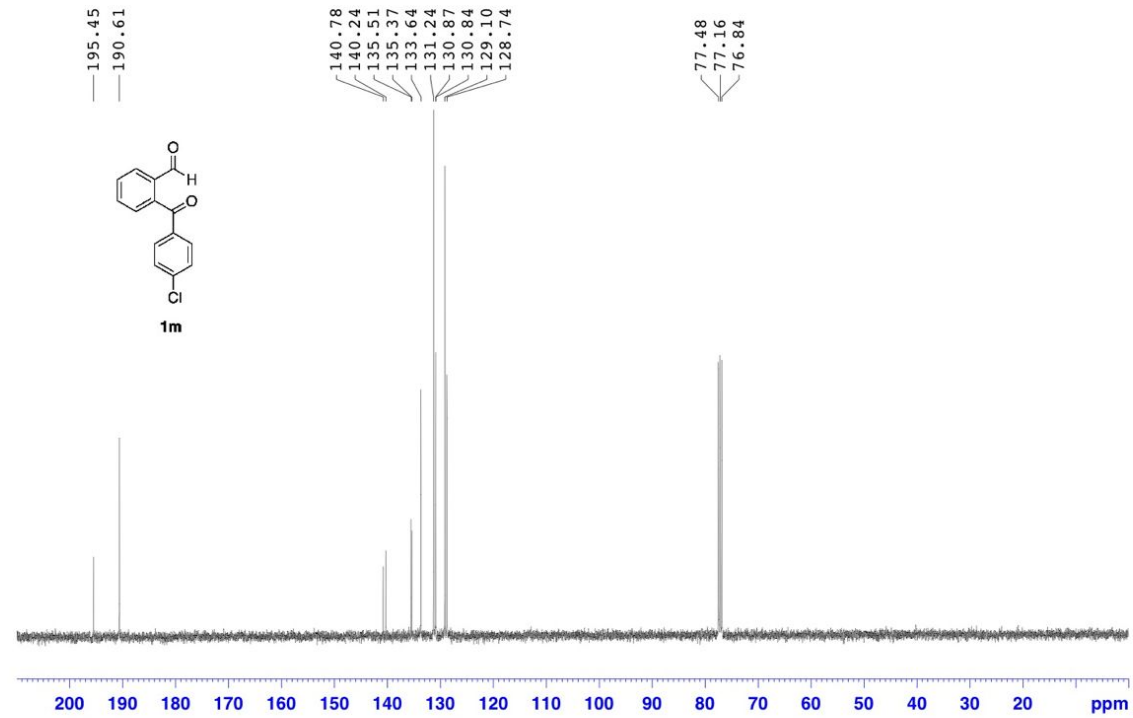
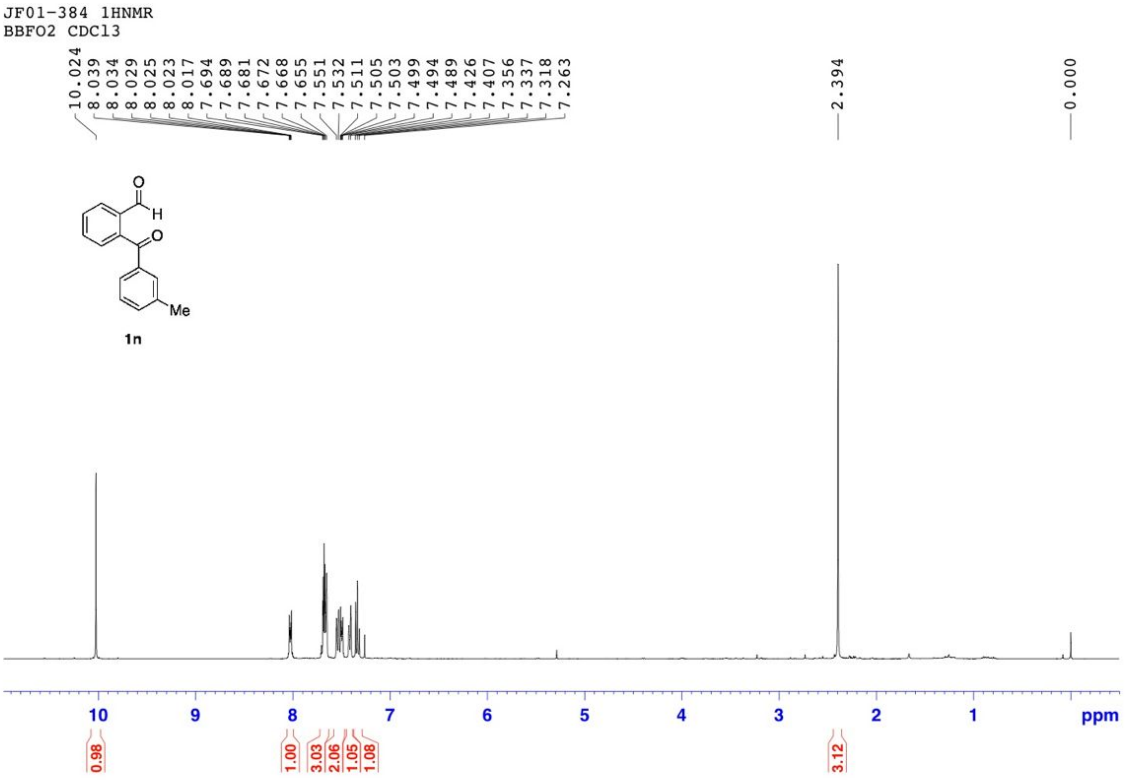
BBFO1 CDCl3

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7.672
7.668
7.655
7.551
7.532
7.511
7.505
7.503
7.499
7.494
7.489
7.426
7.407
7.356
7.337
7.318
7.263
2.394
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O
Me
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9
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ppm
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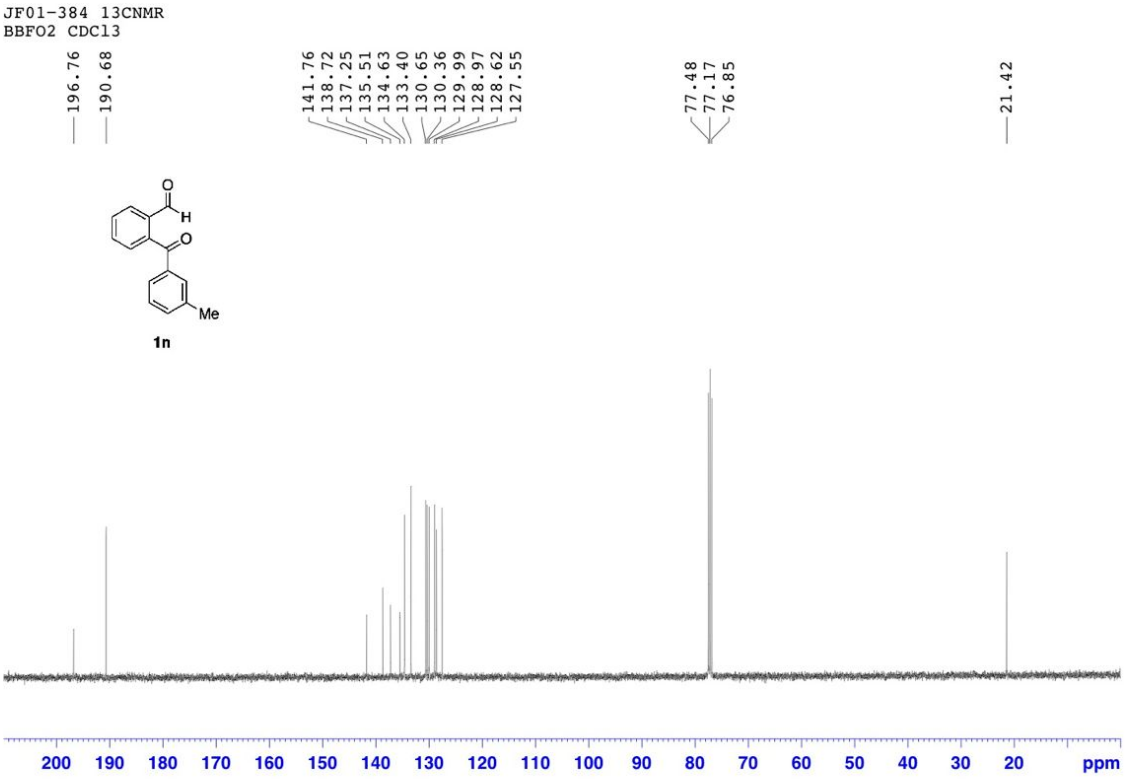
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130.36
129.99
128.97
128.62
127.55
77.48
77.17
76.85
21.42
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H
O
Me
1n
200
190
180
170
160
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90
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70
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50
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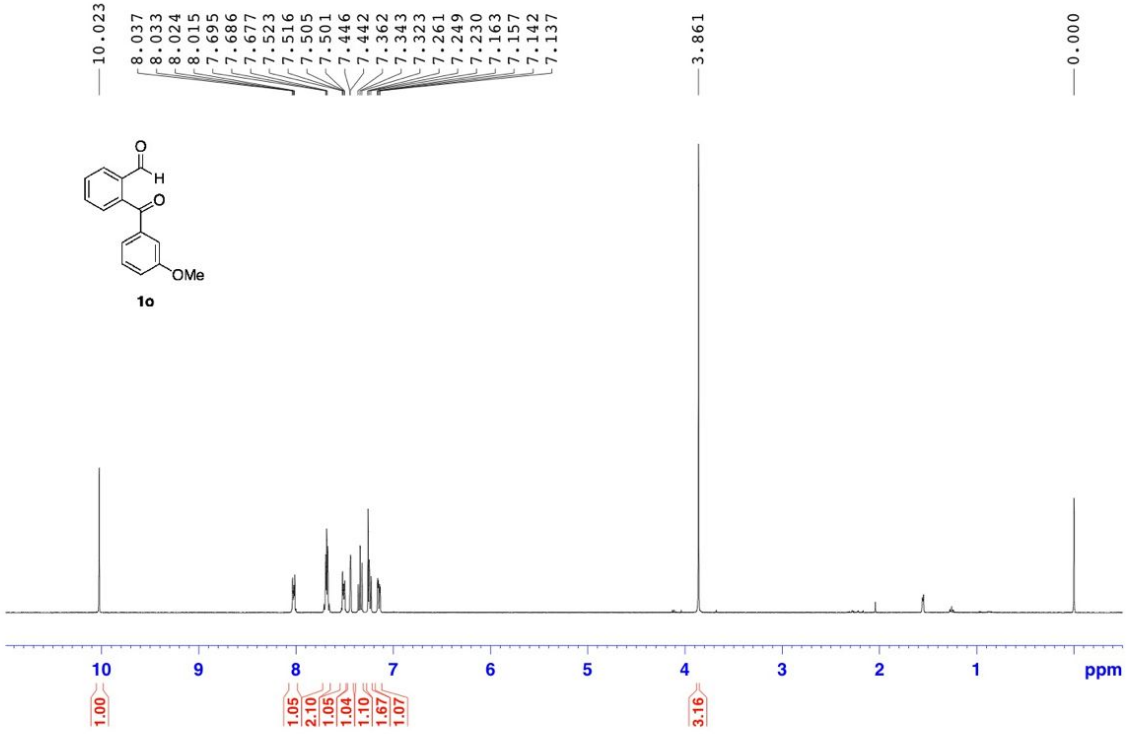
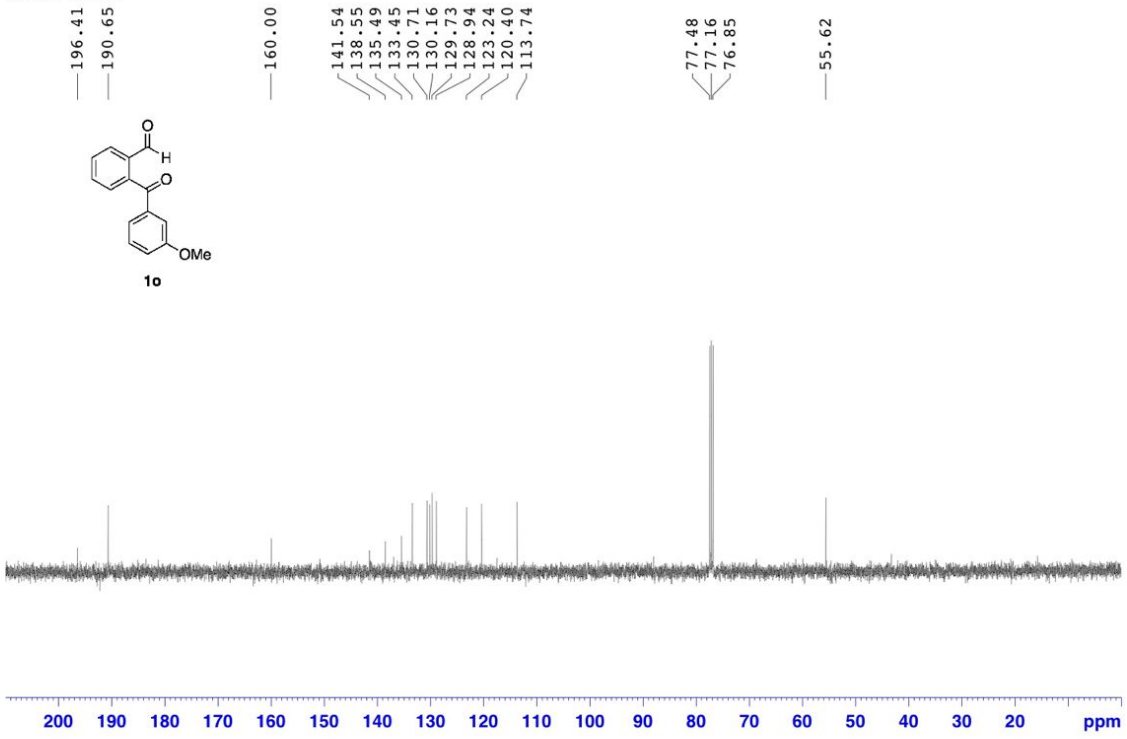
30
20
ppm

JF01-377 1HNMR
AV400 CDCl3

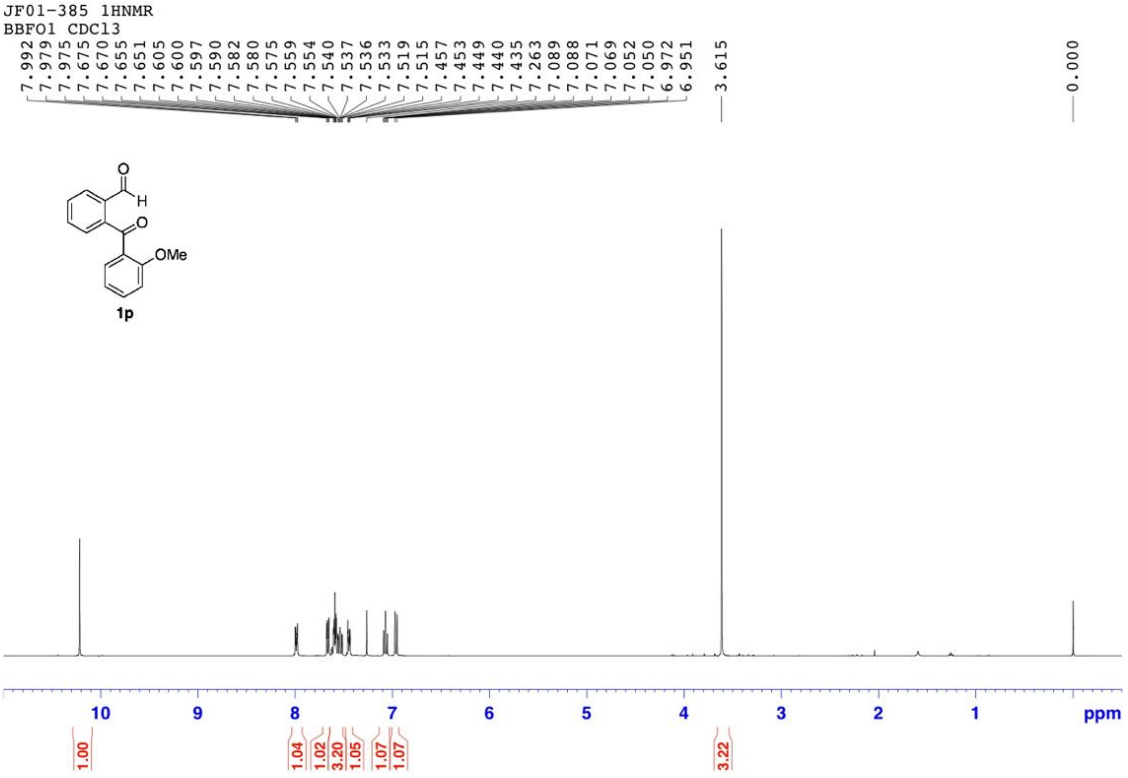


1o

JF01-377 13CNMR
BBFO1 CDCl3



1o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7.651
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7.597
7.590
7.582
7.580
7.575
7.559
7.554
7.540
7.537
7.536
7.533
7.519
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7.457
7.453
7.449
7.440
7.435
7.263
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7.088
7.071
7.069
7.052
7.050
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OMe
1p
10
9
8
7
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ppm
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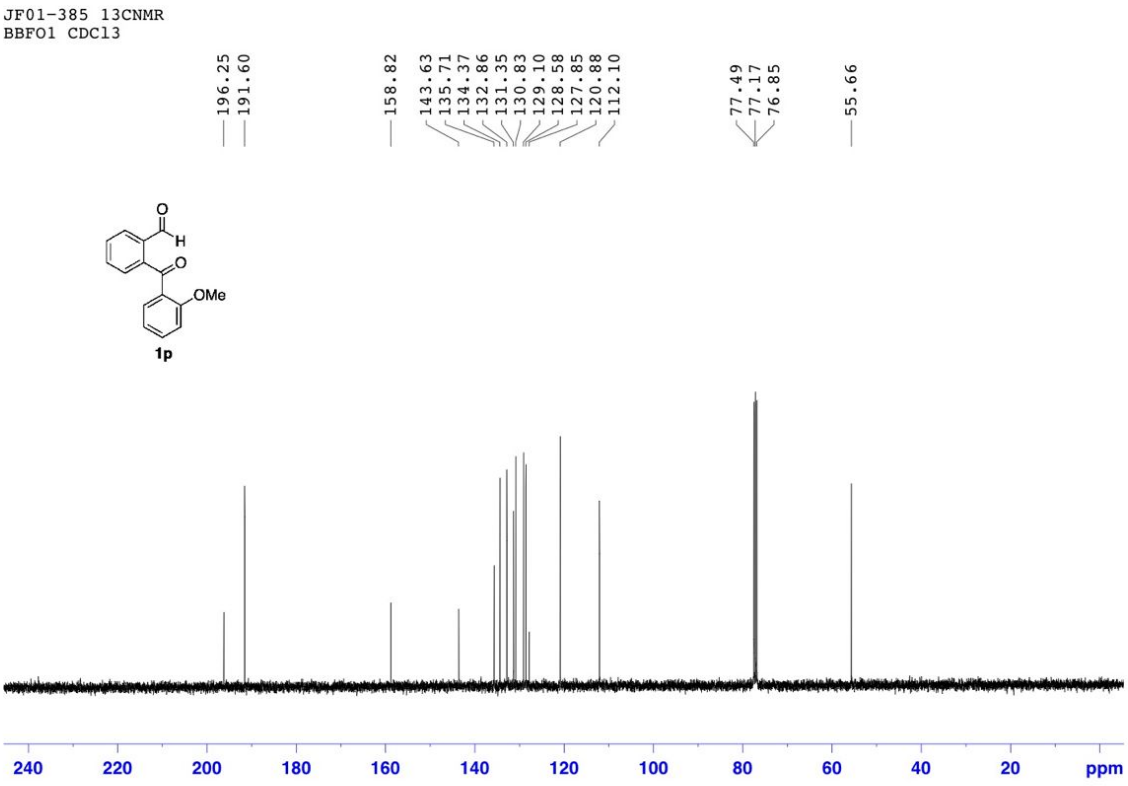
1.07
3.22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77.49
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OMe
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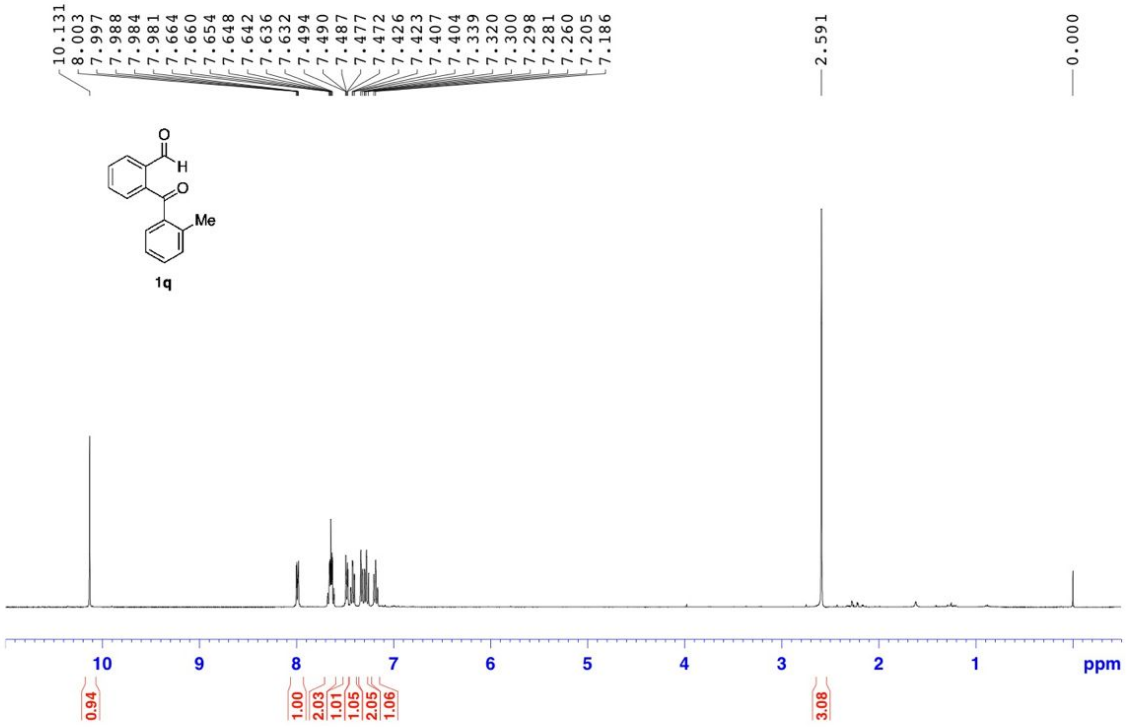

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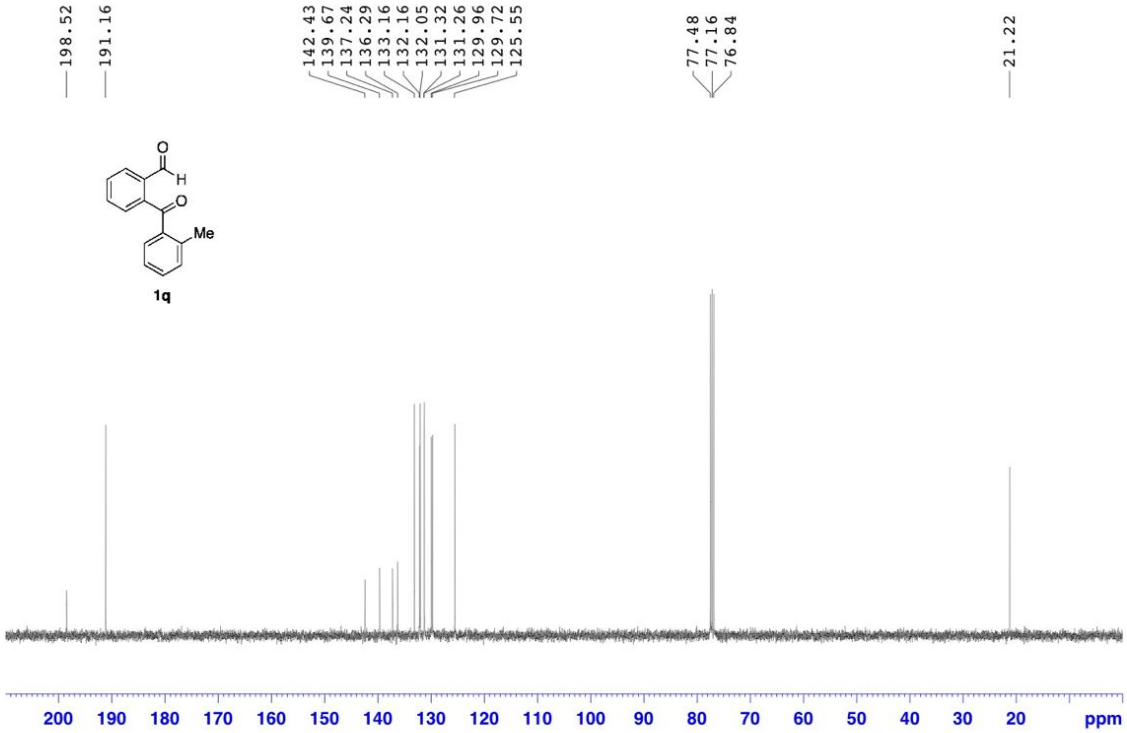
AV400 CDCl3



JF02-152, HNMR
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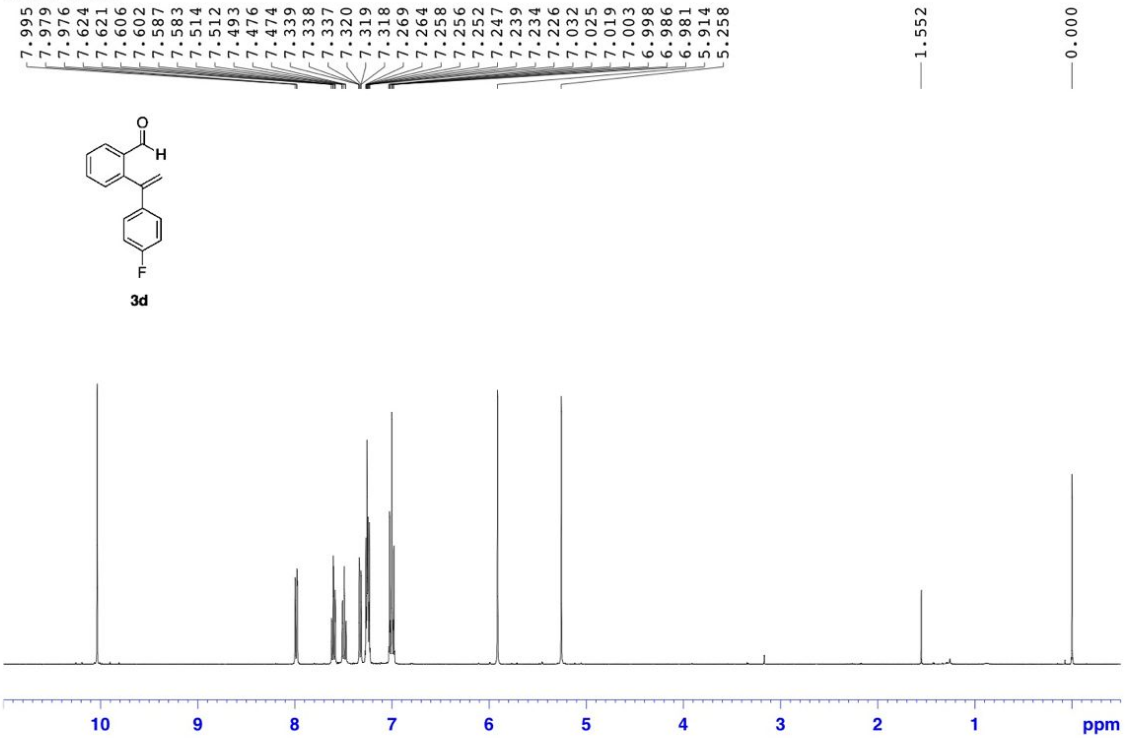

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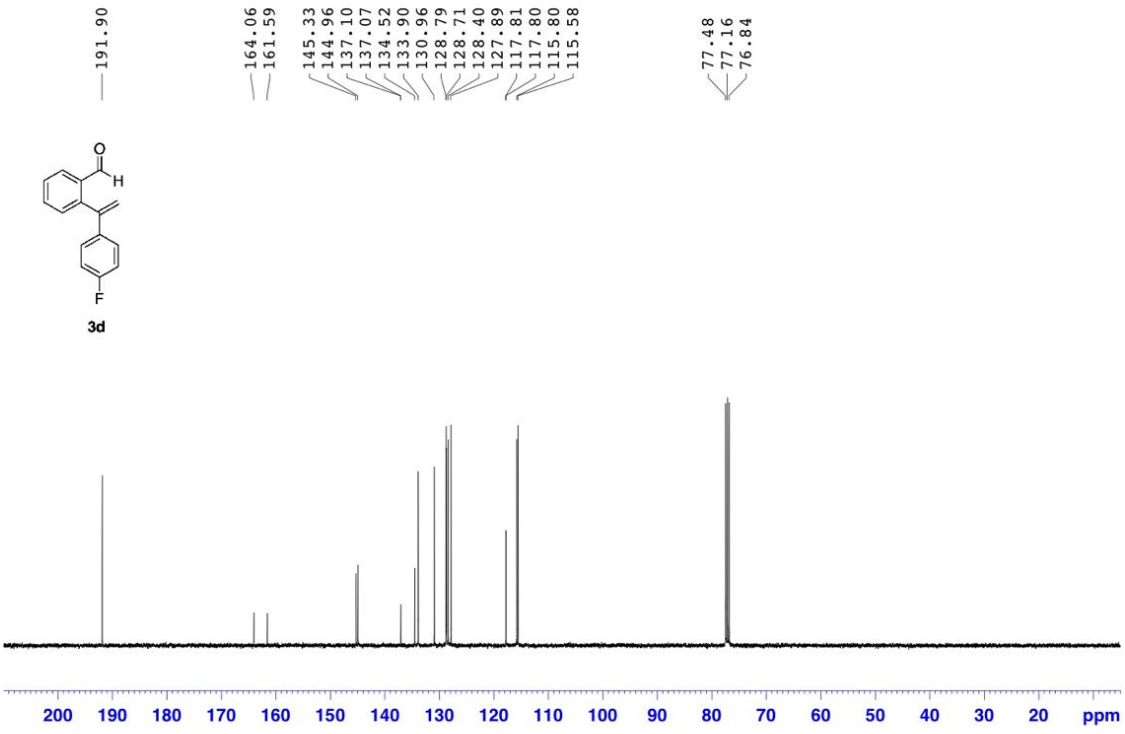
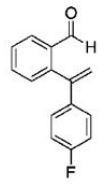
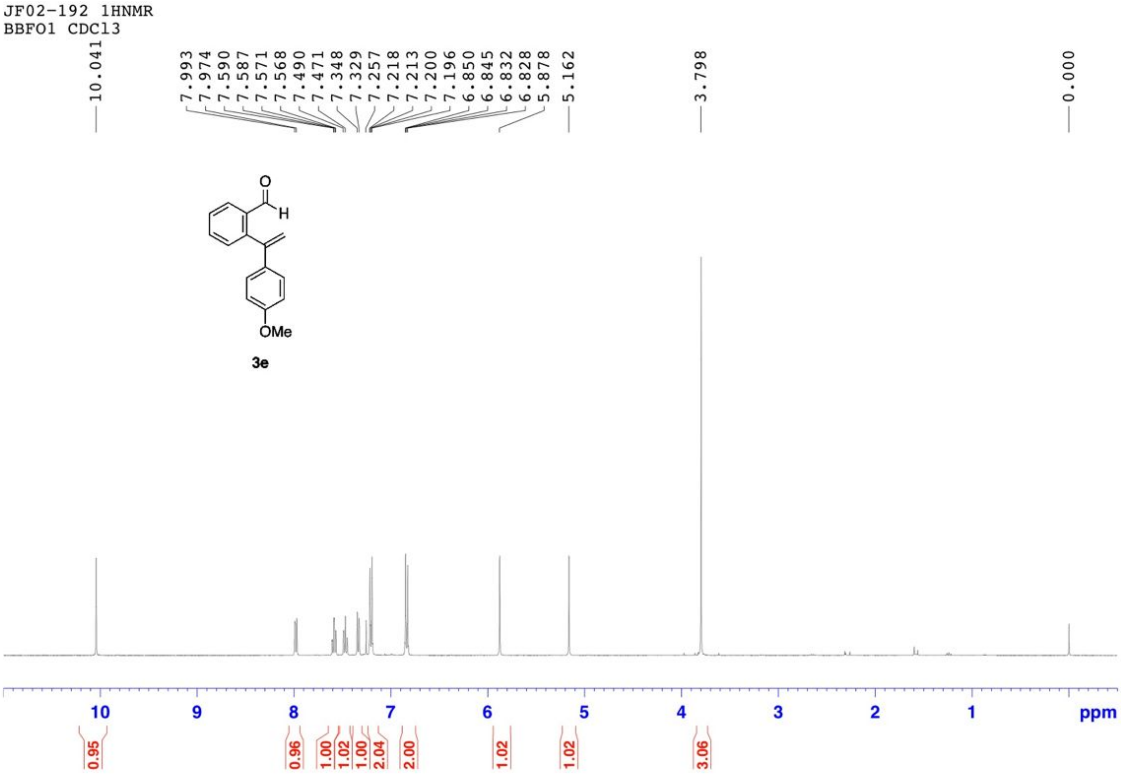
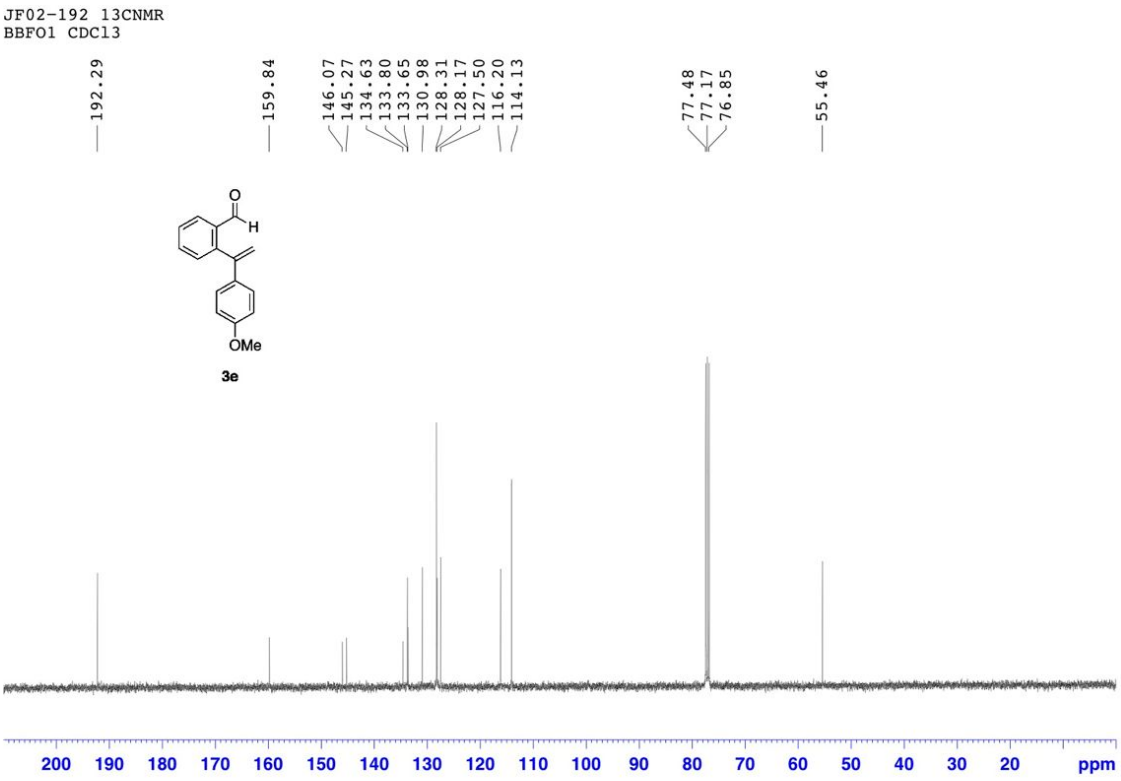


JF02-152 19FNMR
BBFO1 CDCl3

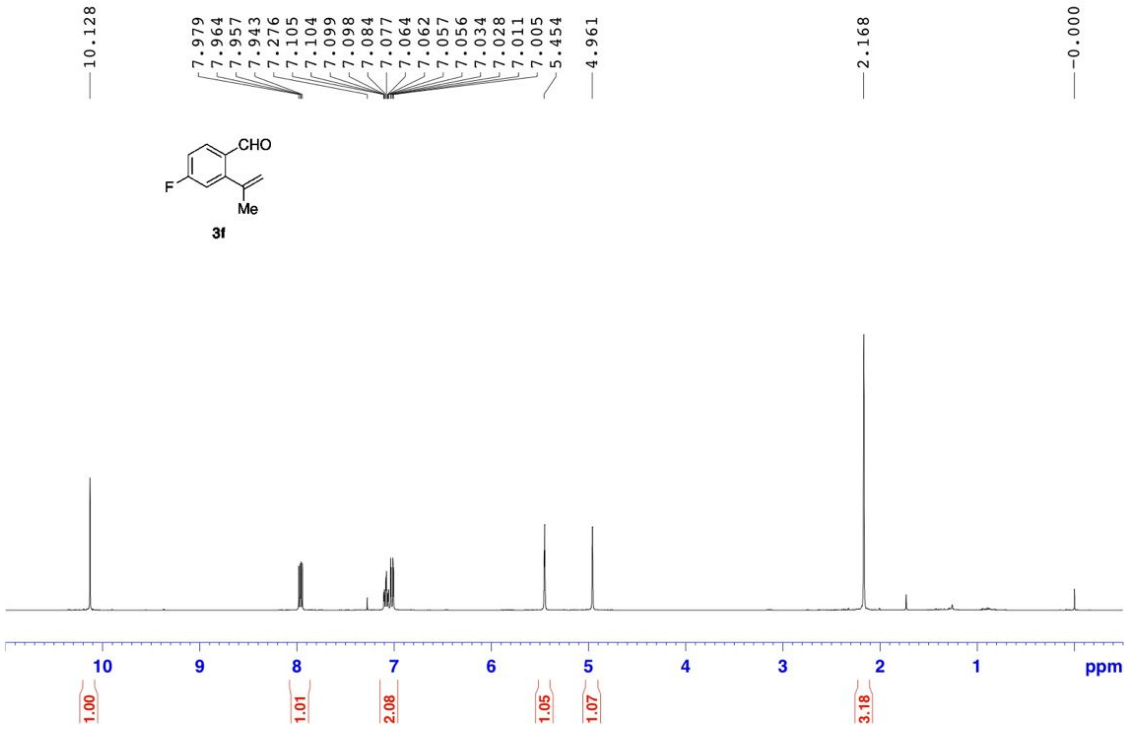


3d

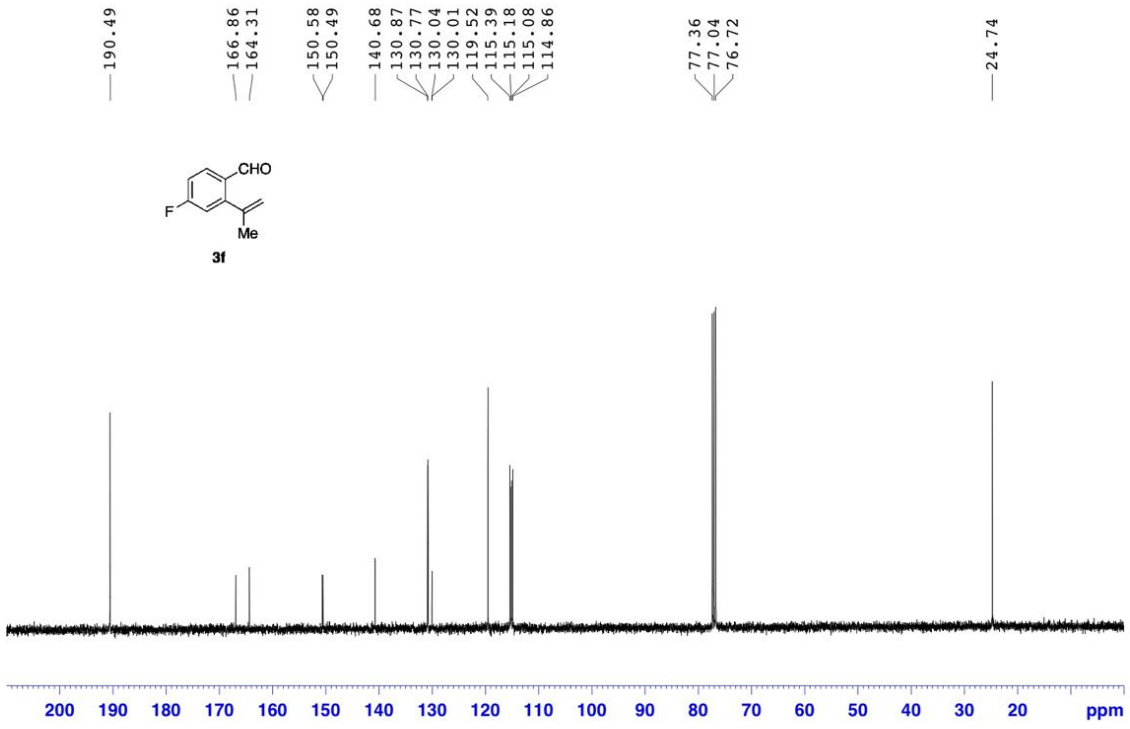

JF02-192 1HNMR
BBFO1 CDCl3
10.041
7.993
7.974
7.590
7.587
7.571
7.568
7.490
7.471
7.348
7.329
7.257
7.218
7.213
7.200
7.196
6.850
6.845
6.832
6.828
5.878
5.162
3.798
0.000
O
H
OMe
3e
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.96
1.00
1.02
1.00
2.04
2.00
1.02
1.02
3.06


JF02-192 13CNMR
BBFO1 CDCl3
192.29
159.84
146.07
145.27
134.63
133.80
133.65
130.98
128.31
128.17
127.50
116.20
114.13
77.48
77.17
76.85
55.46
O
H
OMe
3e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

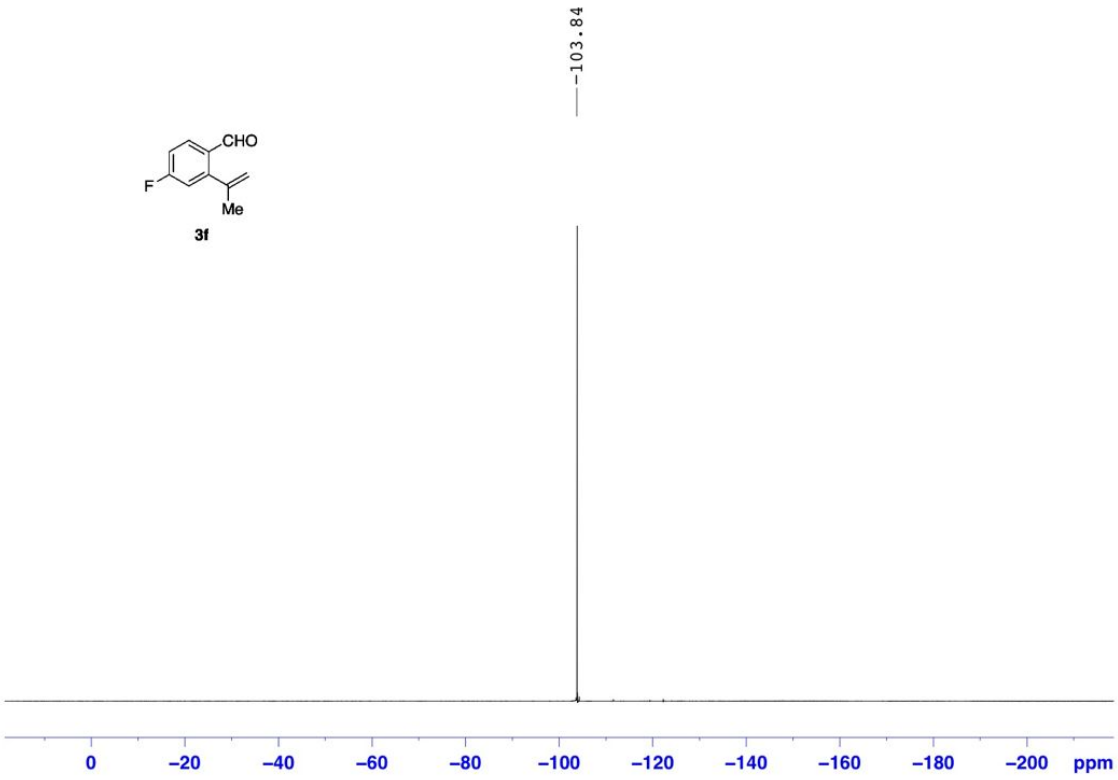
JF02-430 1HNMR
BBFO1 CDCl3

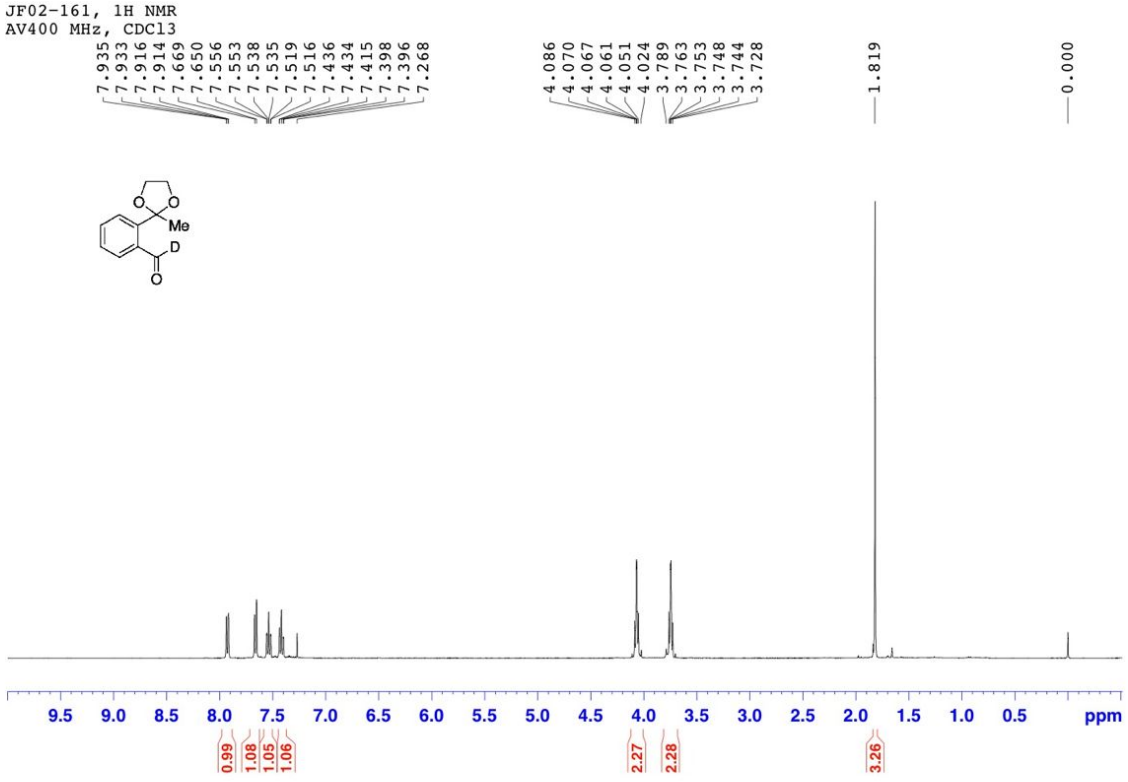


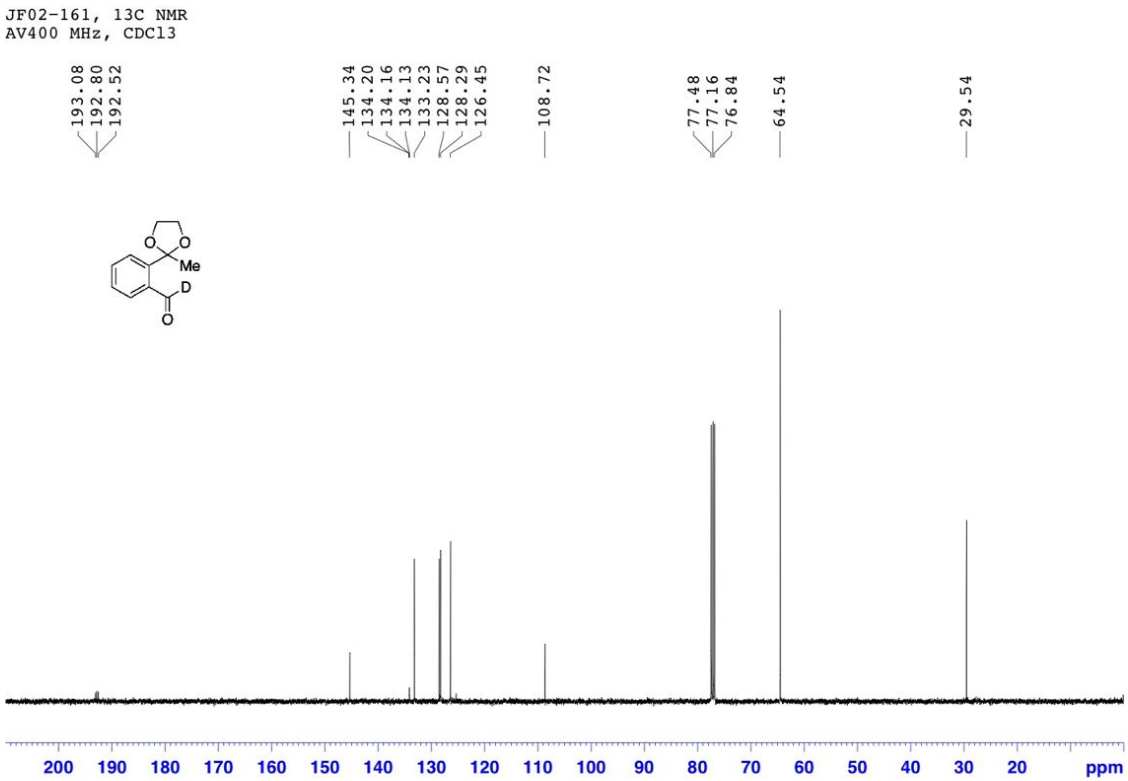
JF02-430 13CNMR
BBFO1 CDCl3

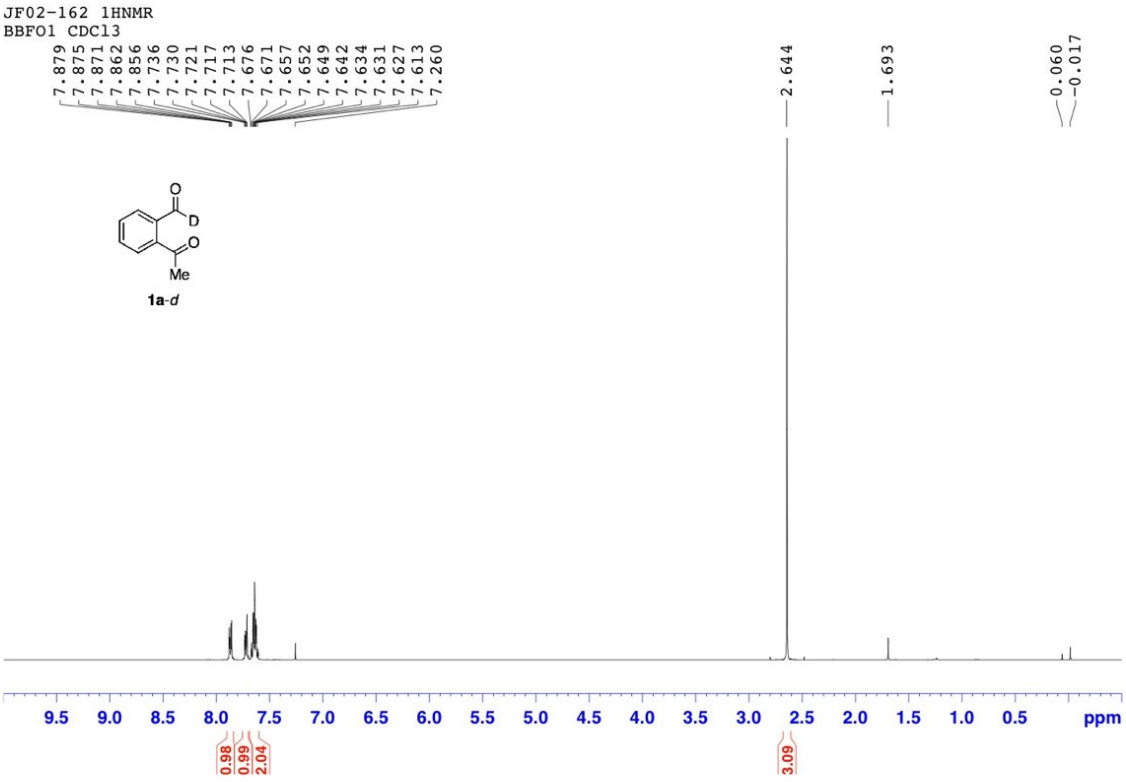


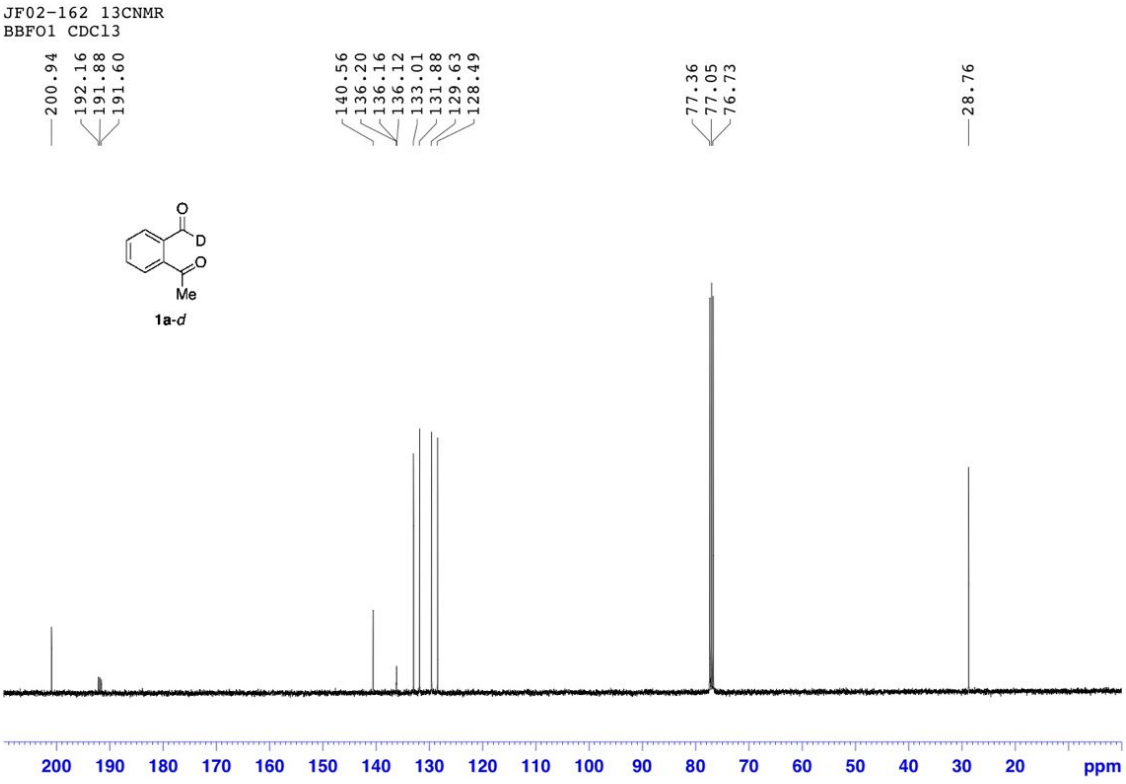
JF02-430 19FNMR
BBFO1 CDCl3



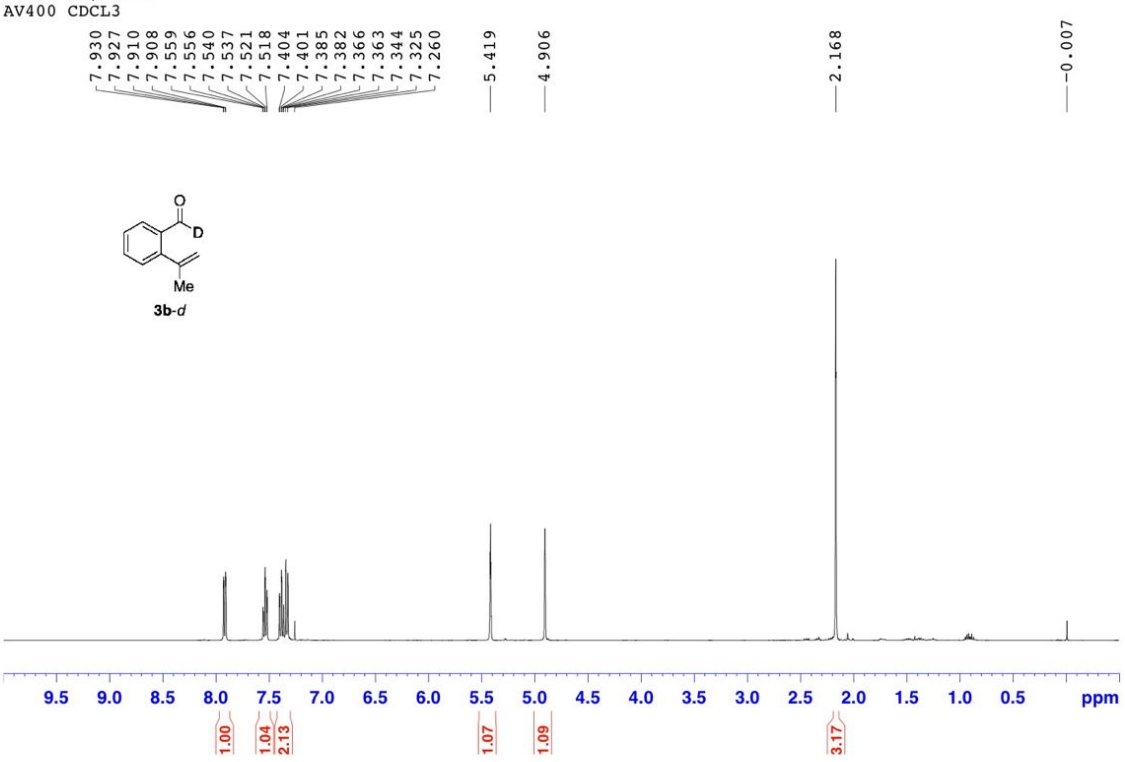

JF02-161, 1H NMR
AV400 MHz, CDCl3
7.935
7.933
7.916
7.914
7.669
7.650
7.556
7.553
7.538
7.535
7.519
7.516
7.436
7.434
7.415
7.398
7.396
7.268
4.086
4.070
4.067
4.061
4.051
4.024
3.789
3.763
3.753
3.748
3.744
3.728
1.819
0.000
Me
D
O
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.99
1.08
1.05
1.06
2.27
2.28
3.26


JF02-161, 13C NMR
AV400 MHz, CDCl3
193.08
192.80
192.52
145.34
134.20
134.16
134.13
133.23
128.57
128.29
126.45
108.72
77.48
77.16
76.84
64.54
29.54
Me
D
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

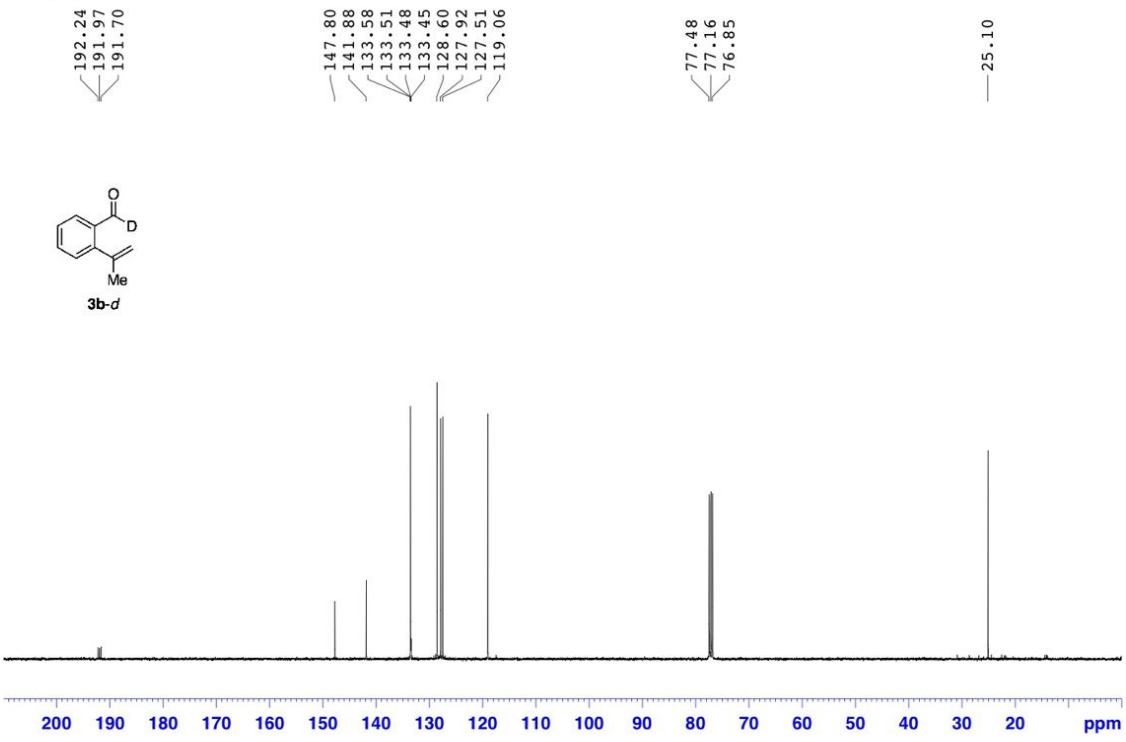

JF02-162 1HNMR
BBFO1 CDCl3
7.879
7.875
7.871
7.862
7.856
7.736
7.730
7.721
7.717
7.713
7.676
7.671
7.657
7.652
7.649
7.642
7.634
7.631
7.627
7.613
7.260
2.644
1.693
0.060
-0.017
O
D
O
Me
1a-d
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.98
0.99
2.04
3.09


JF02-162 13CNMR
BBFO1 CDCl3
200.94
192.16
191.88
191.60
140.56
136.20
136.16
136.12
133.01
131.88
129.63
128.49
77.36
77.05
76.73
28.76
O
D
O
Me
1a-d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

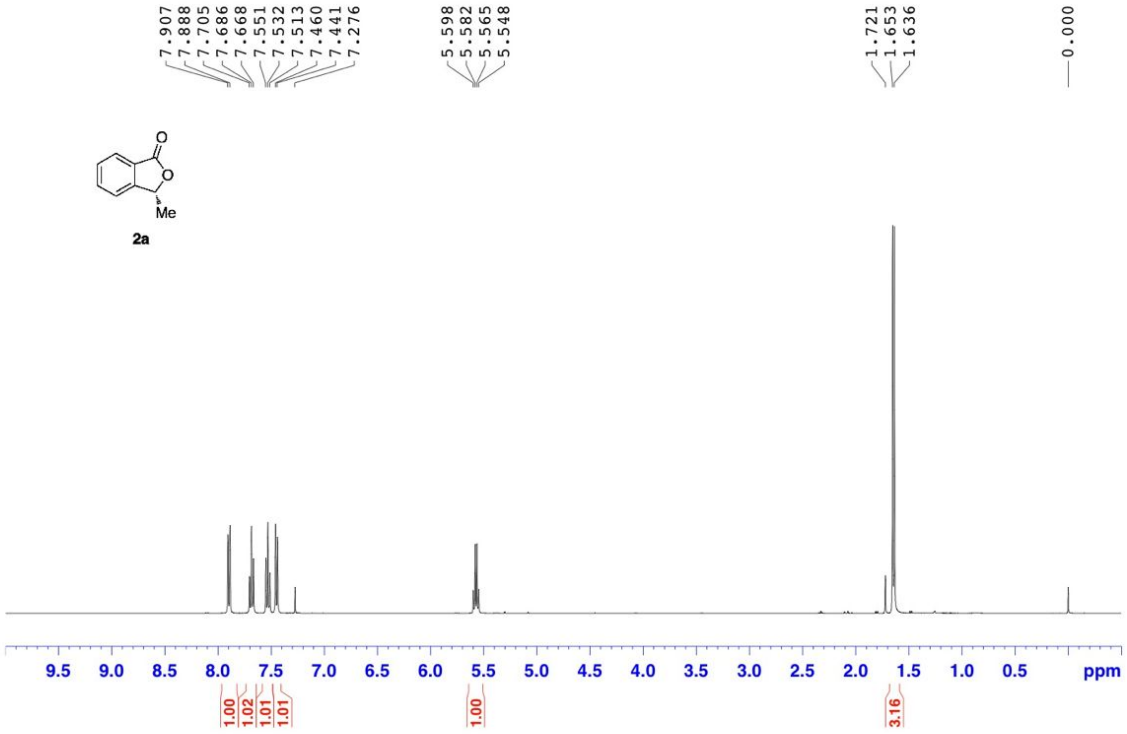
JF02-158, HNMR
AV400 CDCL3



JF02-158, 13CNMR
AV400 CDCL3

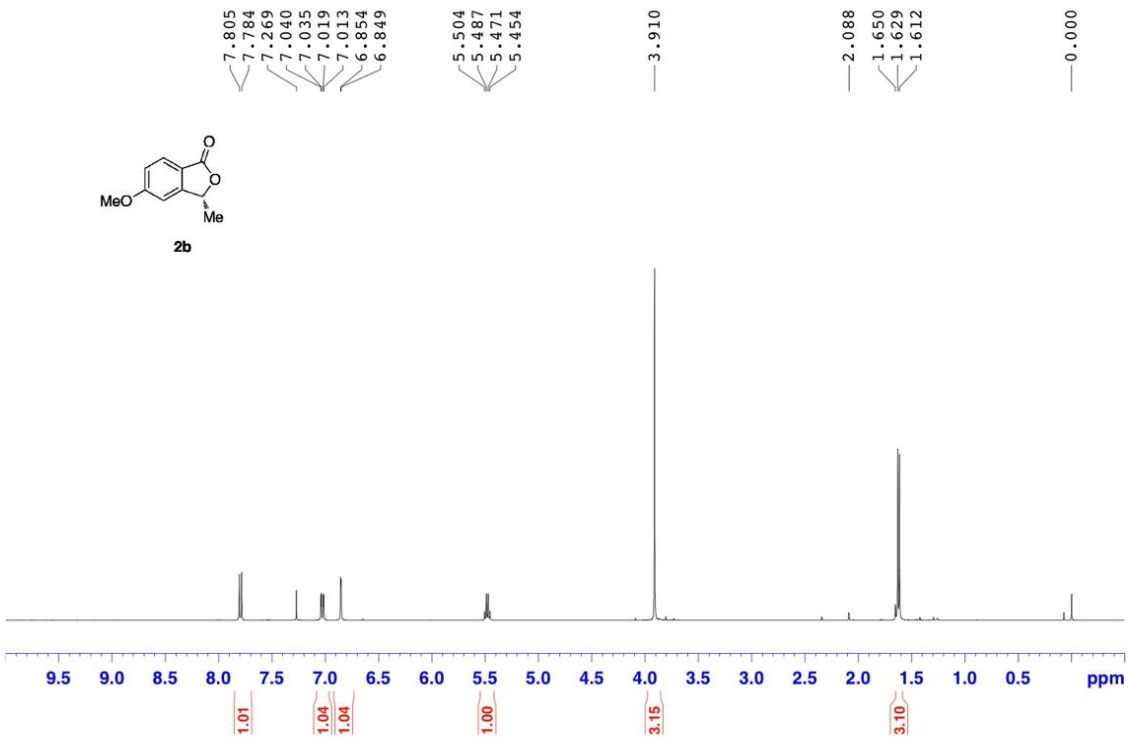


JF01-116 1HNMR
BBFO1 CDCl3



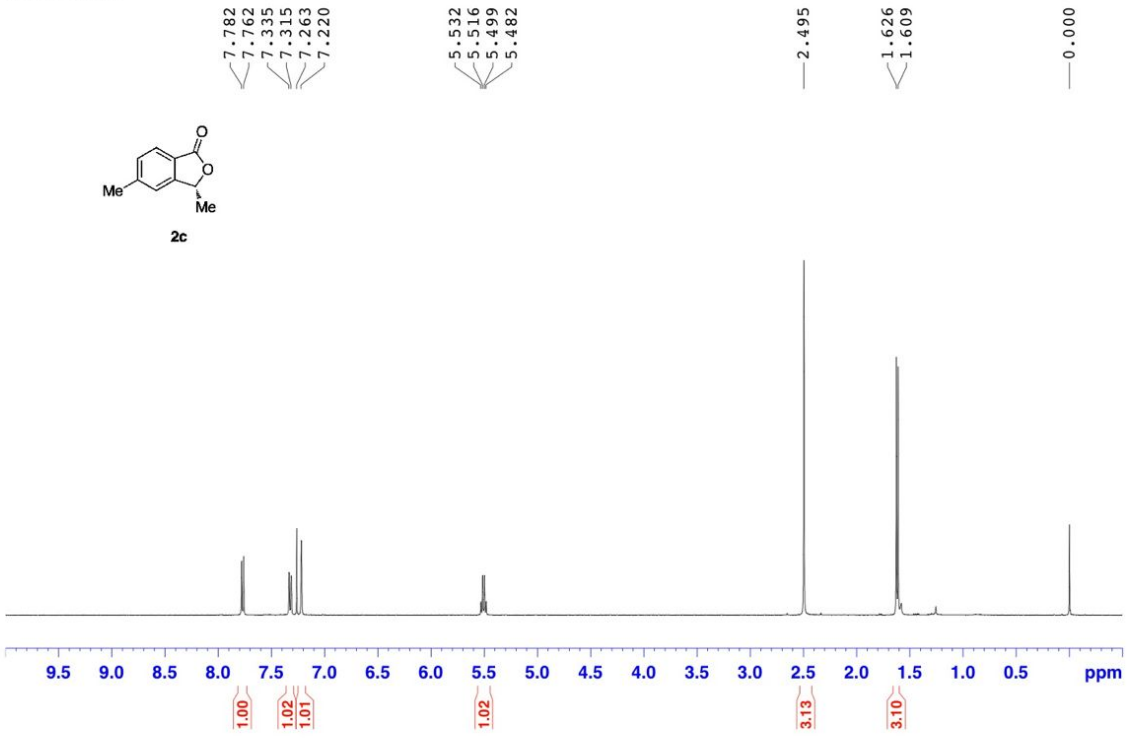
2a

JF01-335 1HNMR
BBFO1 CDCl3

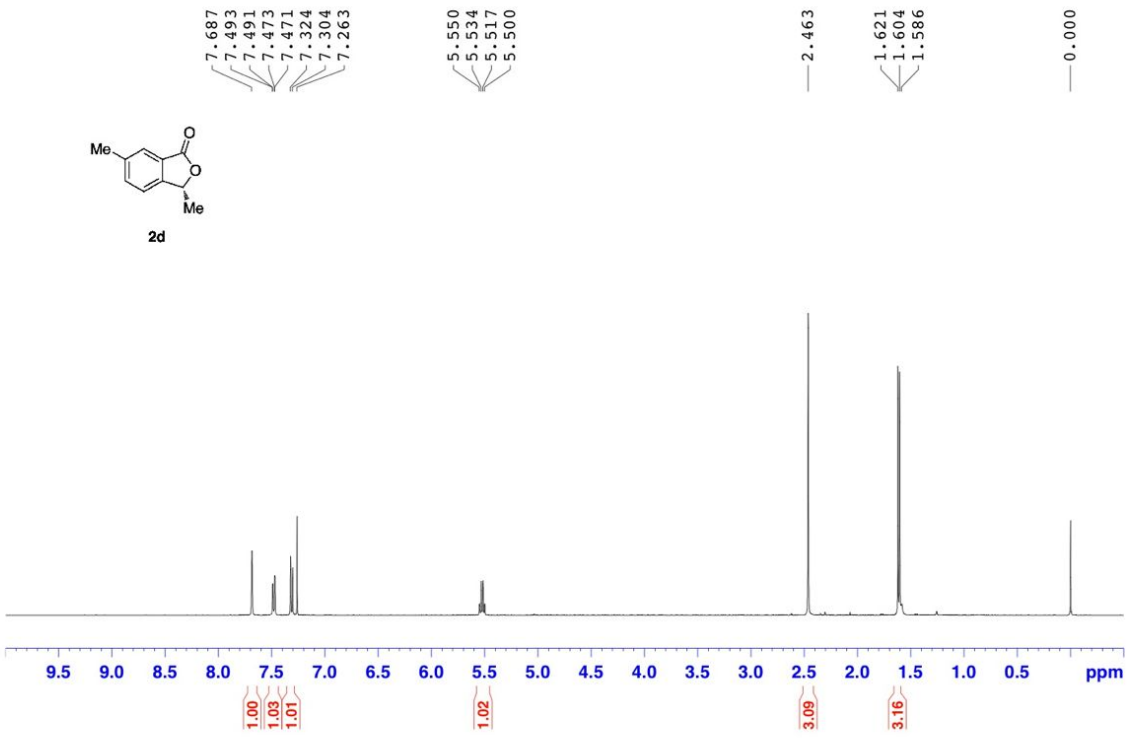


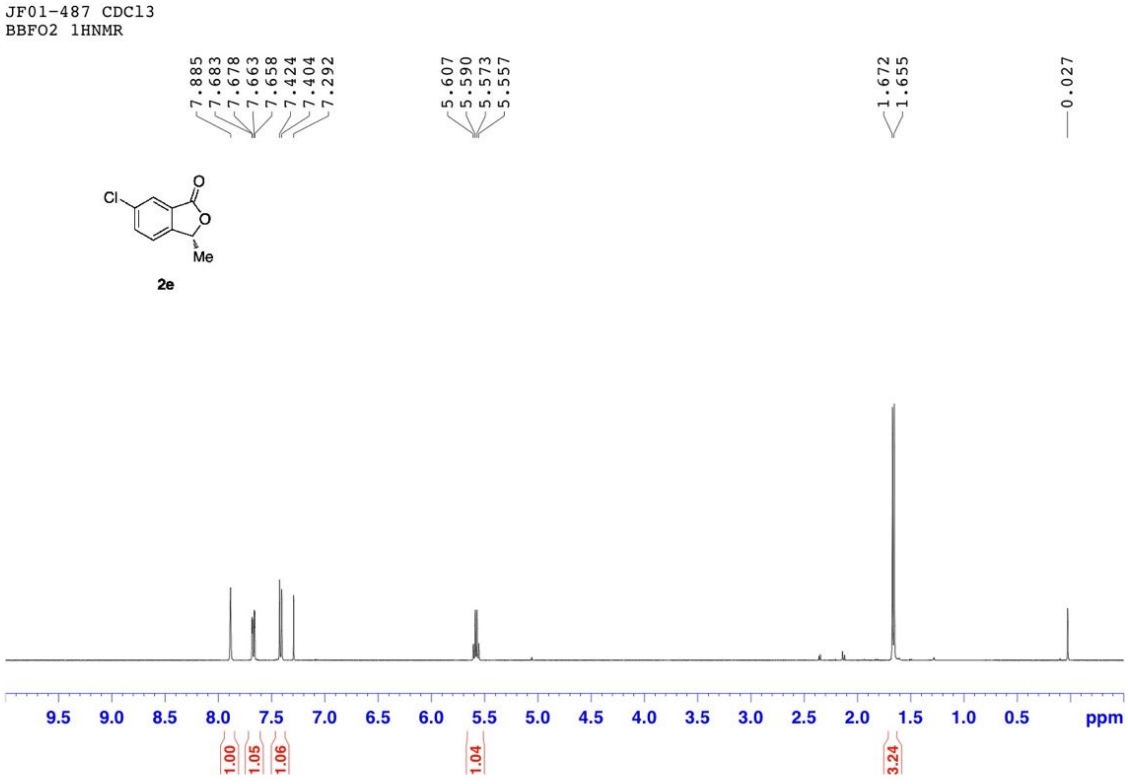
2b

JF01-337 1HNMR
BBFO1 CDCl3

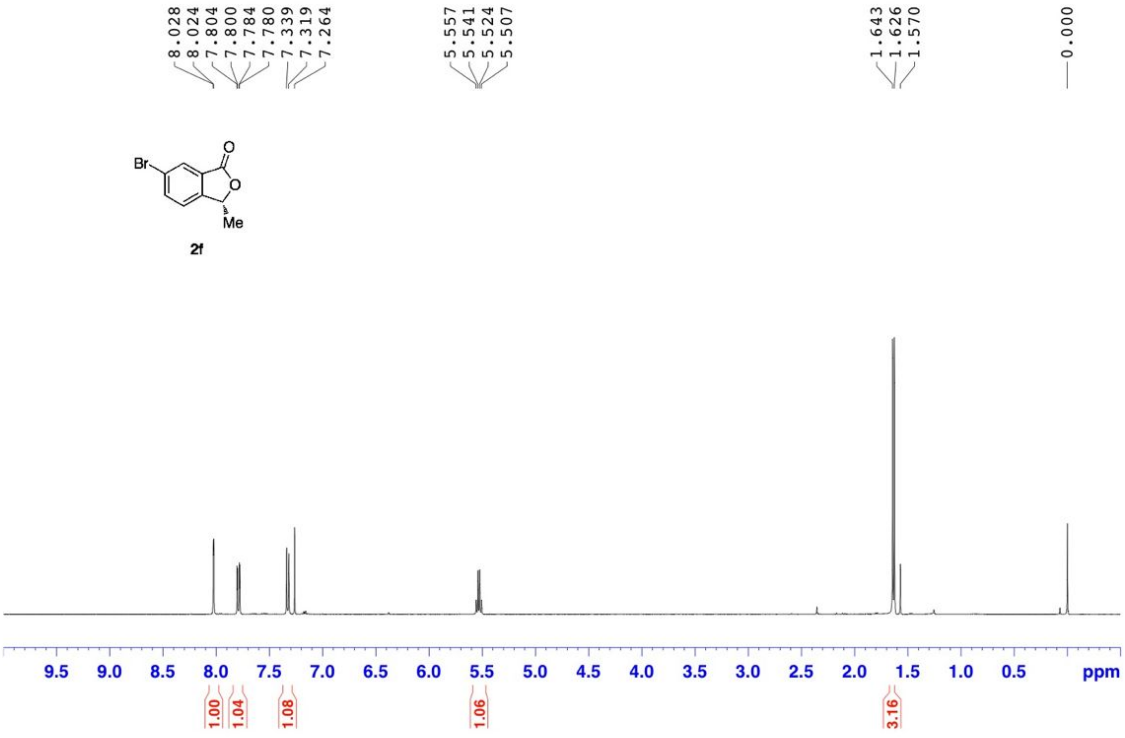


JF01-333 1HNMR
BBFO1 CDCl3

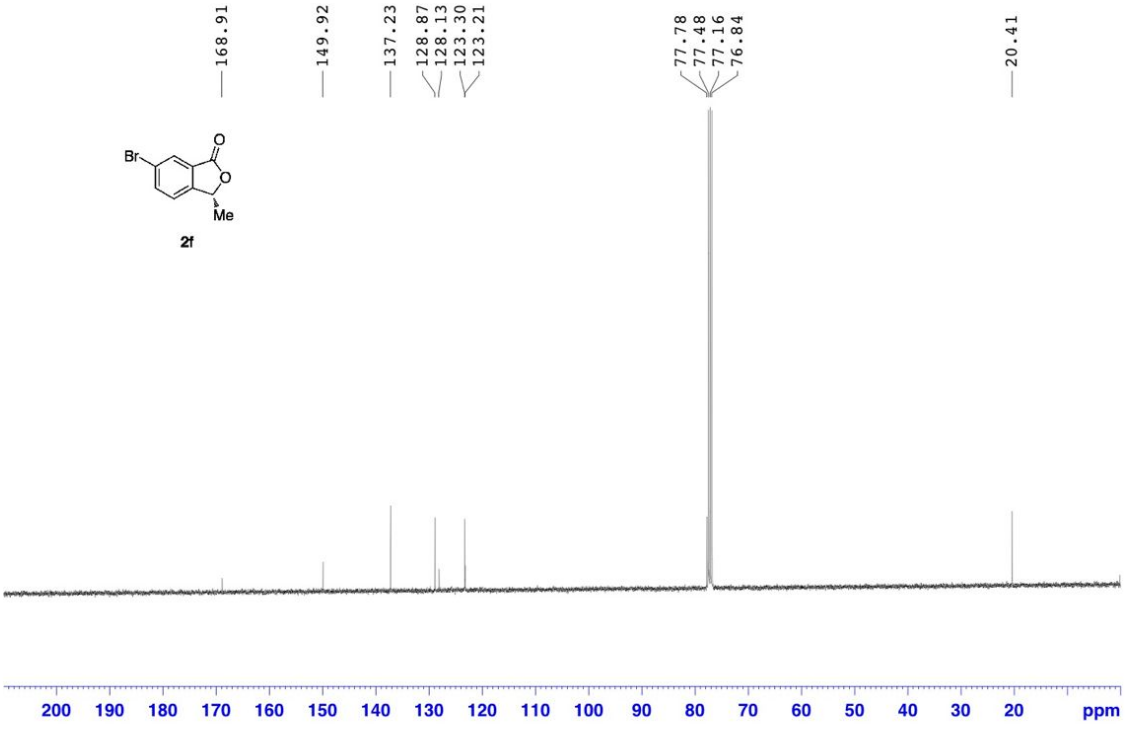



JF01-487 CDCl3
BBFO2 1HNMR
7.885
7.683
7.678
7.663
7.658
7.424
7.404
7.292
5.607
5.590
5.573
5.557
1.672
1.655
0.027
Cl
O
O
Me
2e
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.05
1.06
1.04
3.24

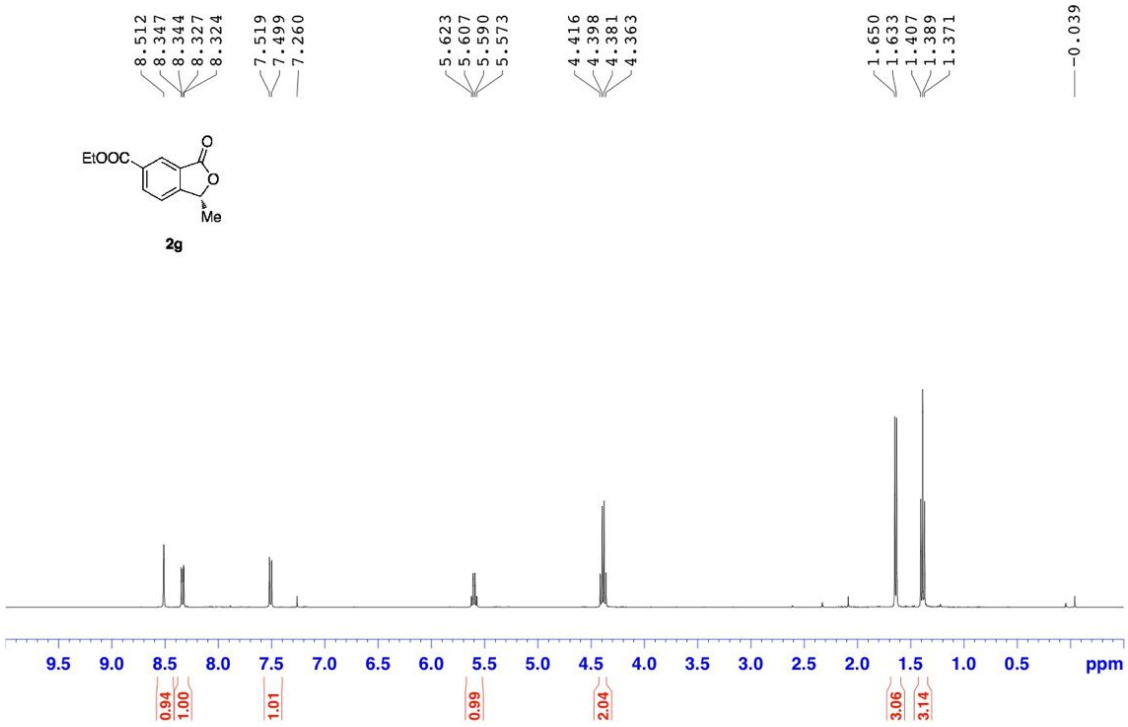
JF01-489 CDCl3
BBFO2 1HNMR



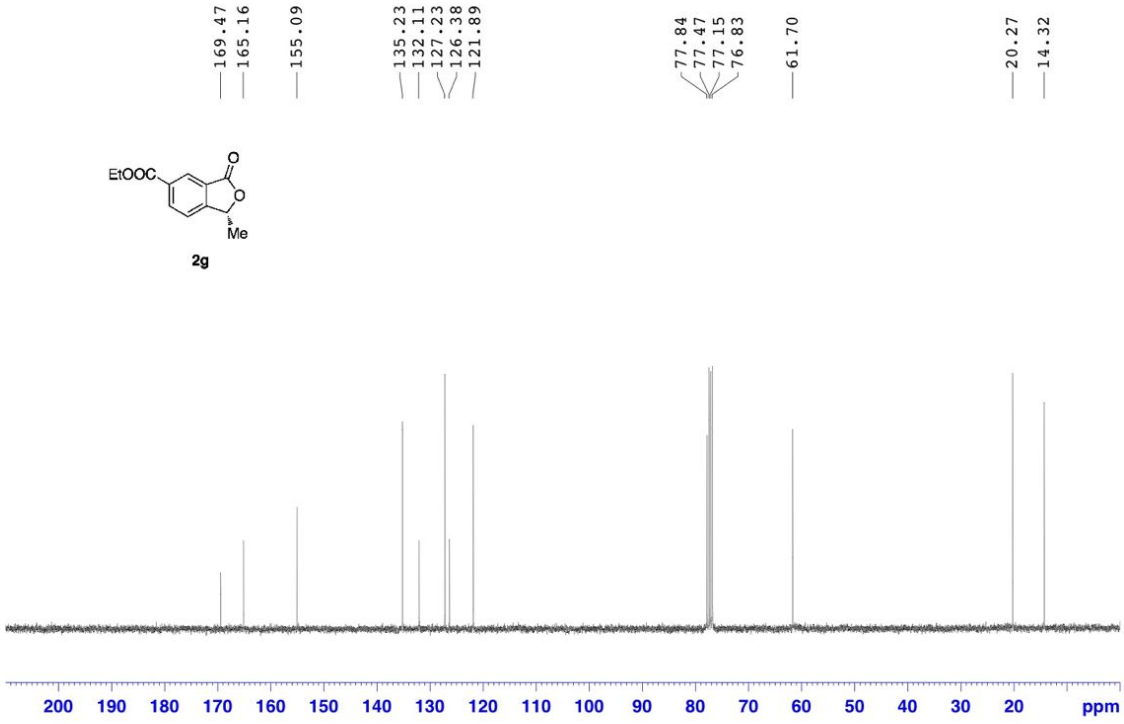
JF01-489 CDCl3
BBFO2 13CNMR



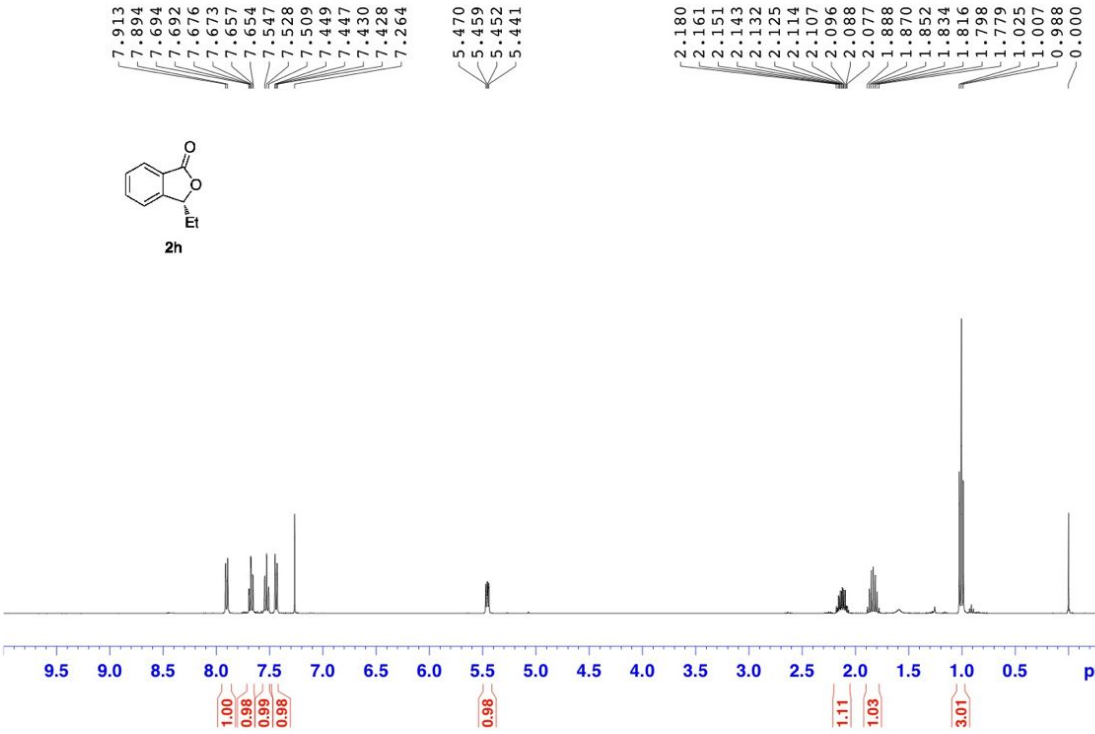
JF01-488 CDCl3
BBFO2 1HNMR



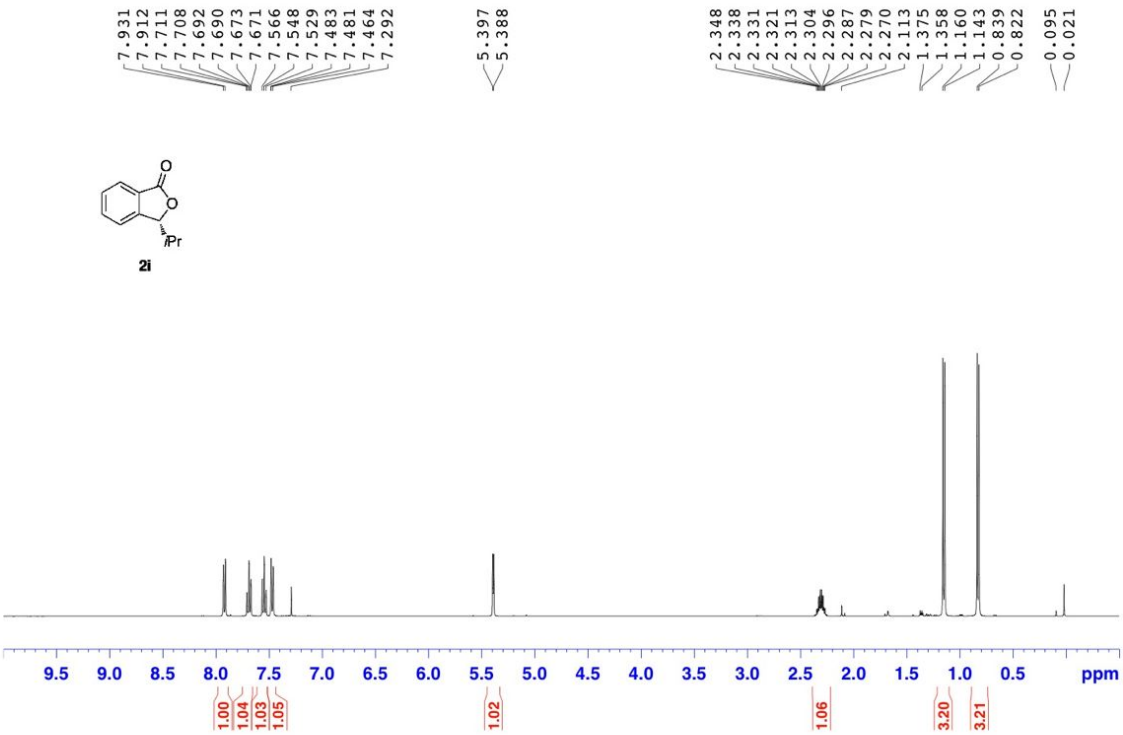
JF01-488 CDCl3
BBFO2 13CNMR



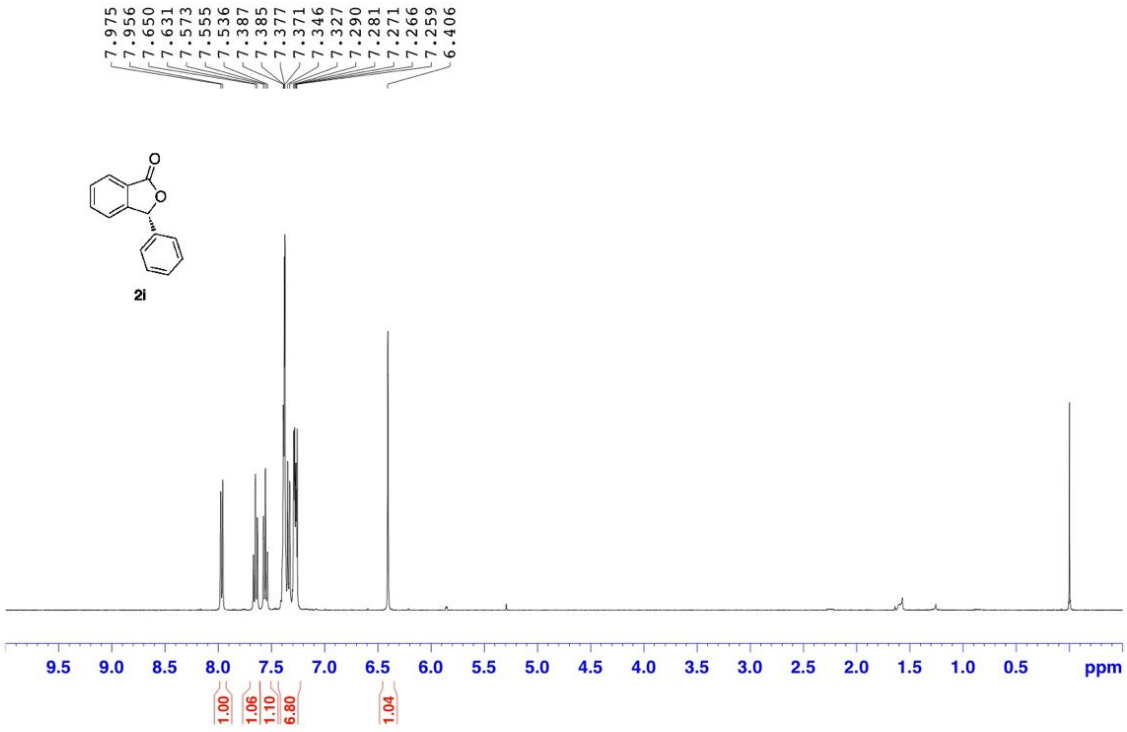
JF01-338 1HNMR
BBFO1 CDCl3



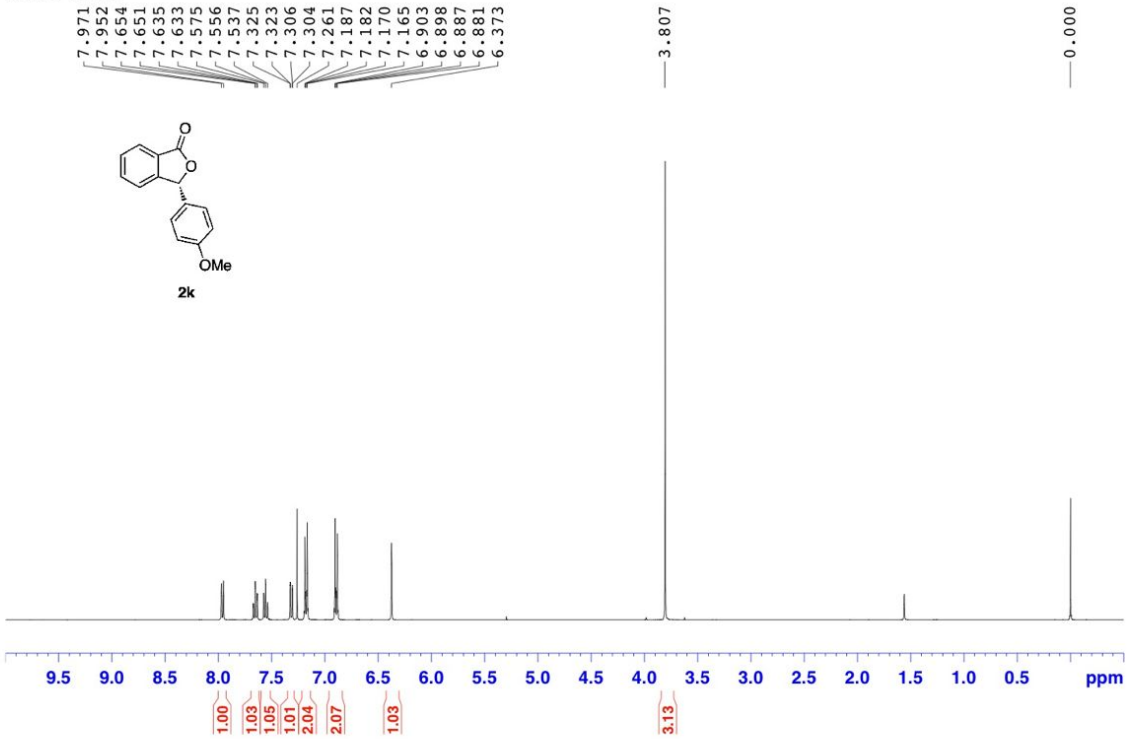
JF01-491 CDCl3
BBFO2 1HNMR

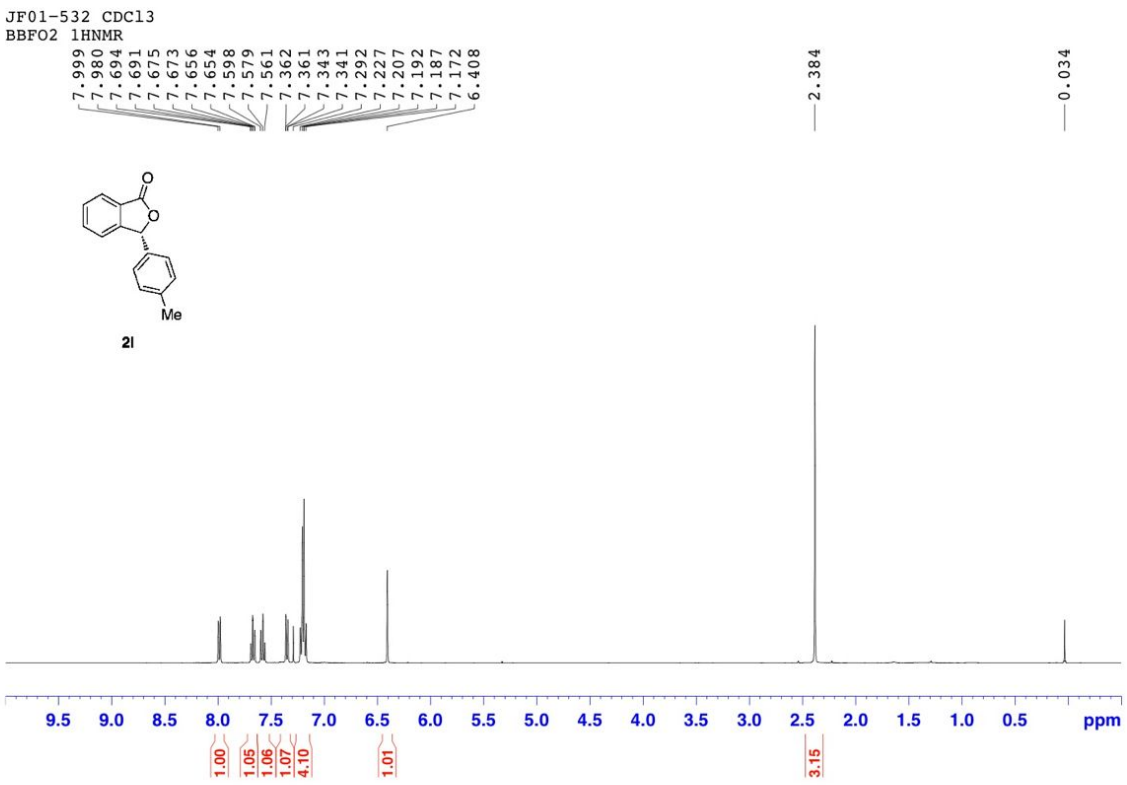


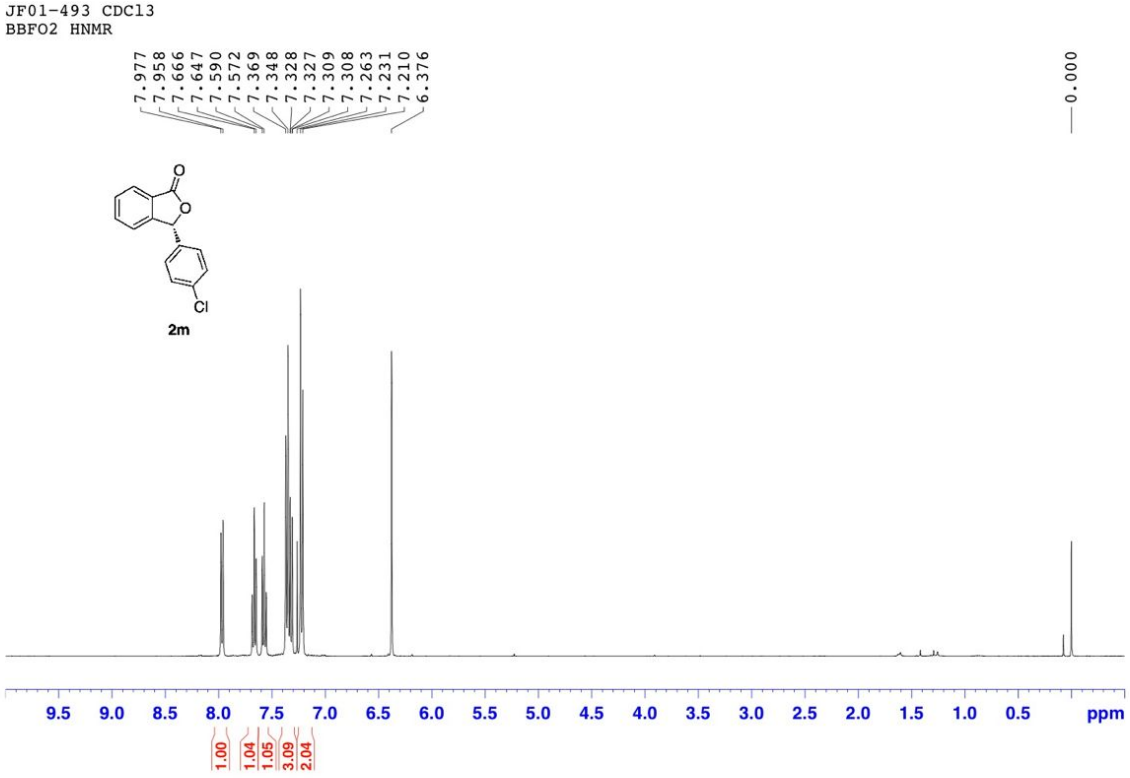
JF01-339 1HNMR
BBFO1 CDCl3

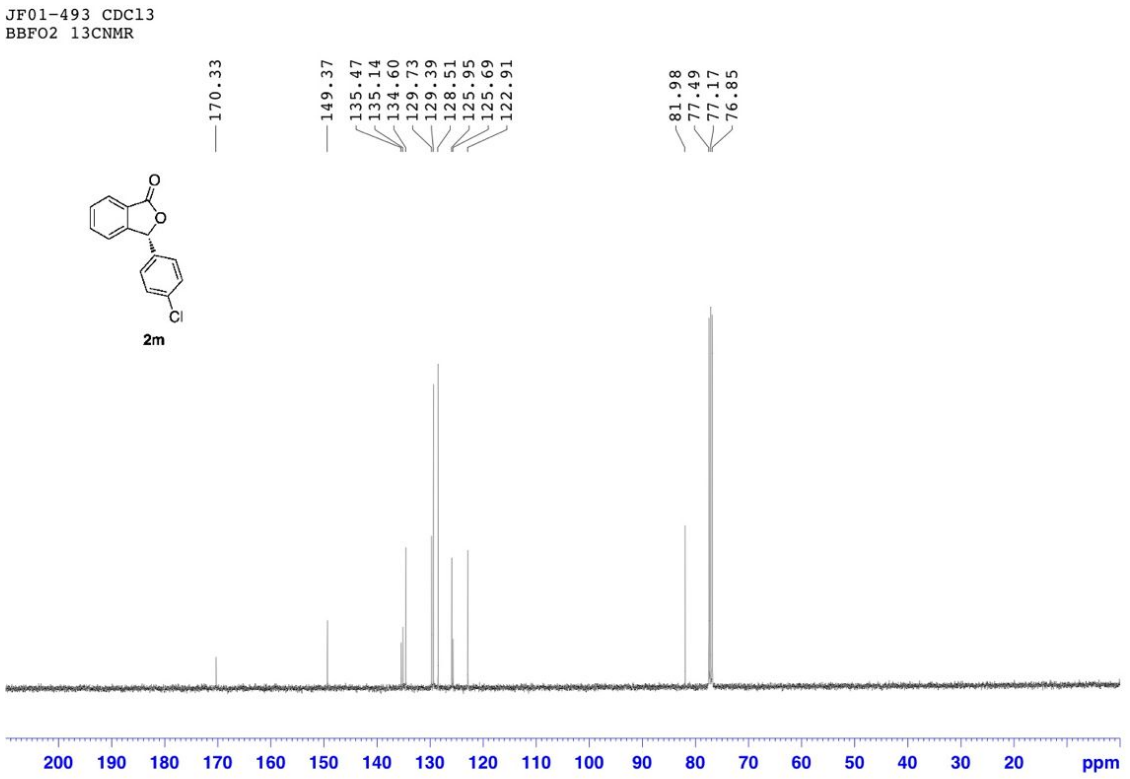


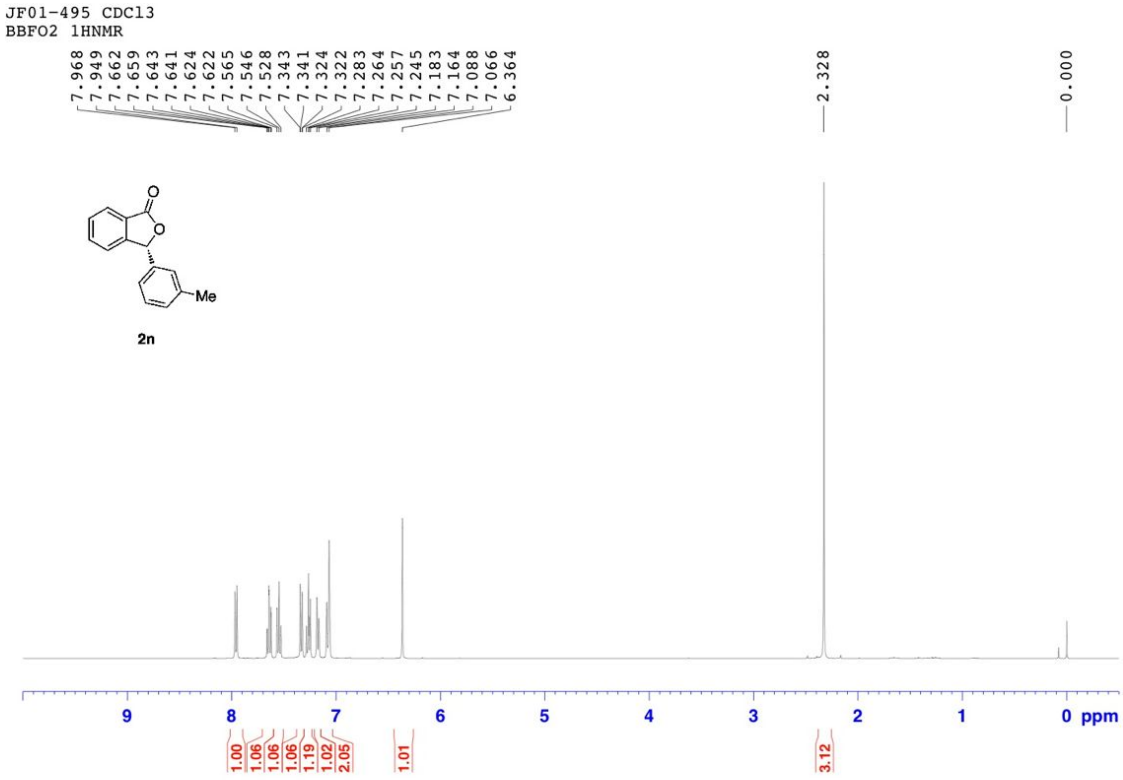
JF01-409 1HNMR
BBFO1 CDCl3

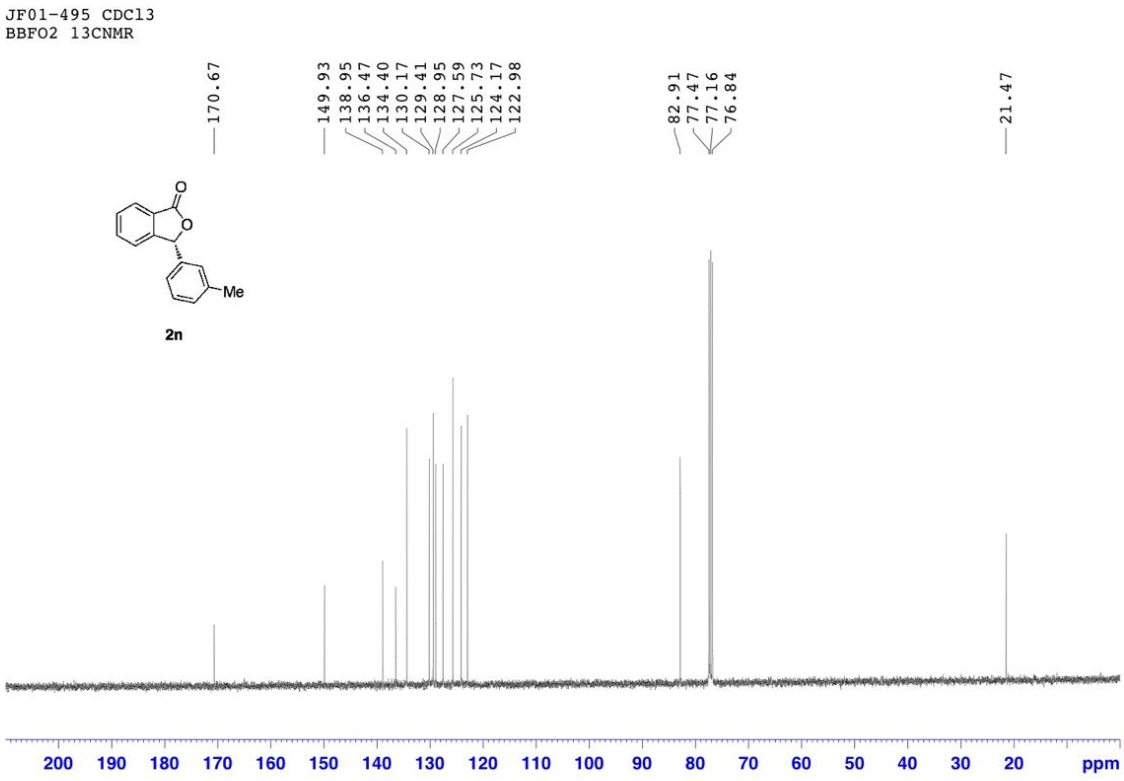



JF01-532 CDCl3
BBFO2 1HNMR
7.999
7.980
7.694
7.691
7.675
7.673
7.656
7.654
7.598
7.579
7.561
7.362
7.361
7.343
7.341
7.292
7.227
7.207
7.192
7.187
7.172
6.408
2.384
0.034
O
O
Me
2l
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.05
1.06
1.07
4.10
1.01
3.15

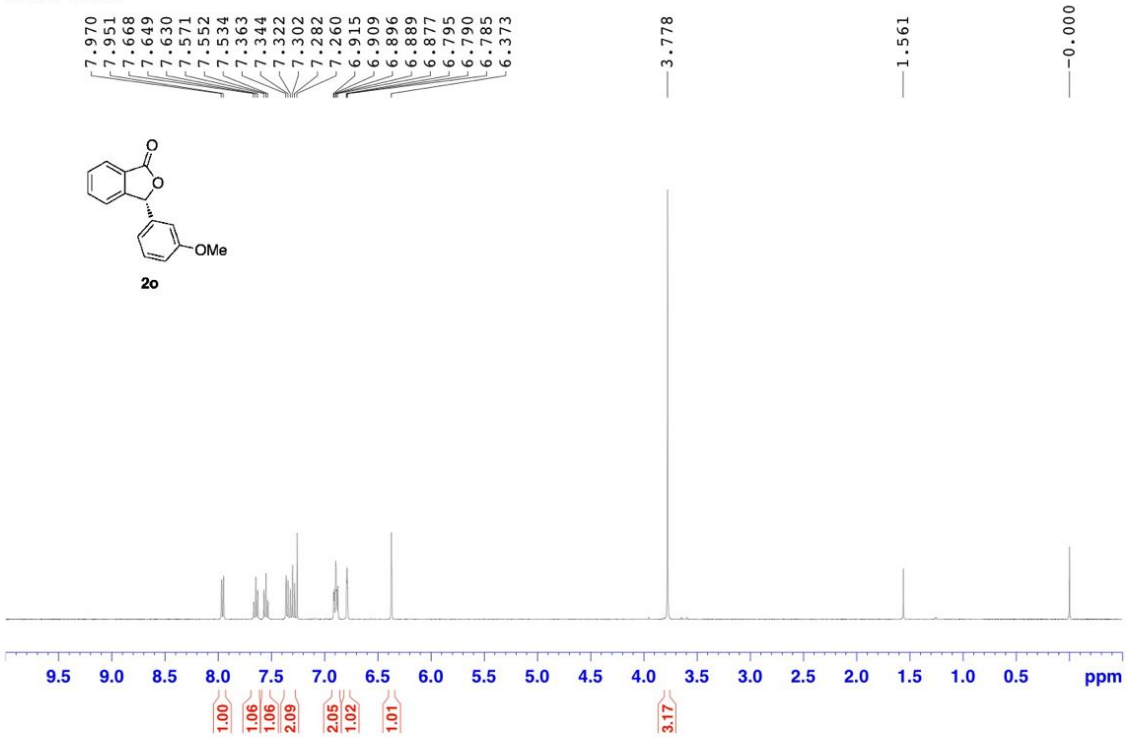

JF01-493 CDCl3
BBFO2 HNMR
7.977
7.958
7.666
7.647
7.590
7.572
7.369
7.348
7.328
7.327
7.309
7.308
7.263
7.231
7.210
6.376
0.000
2m
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.04
1.05
3.09
2.04


JF01-493 CDCl3
BBFO2 13CNMR
170.33
149.37
135.47
135.14
134.60
129.73
129.39
128.51
125.95
125.69
122.91
81.98
77.49
77.17
76.85
2m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

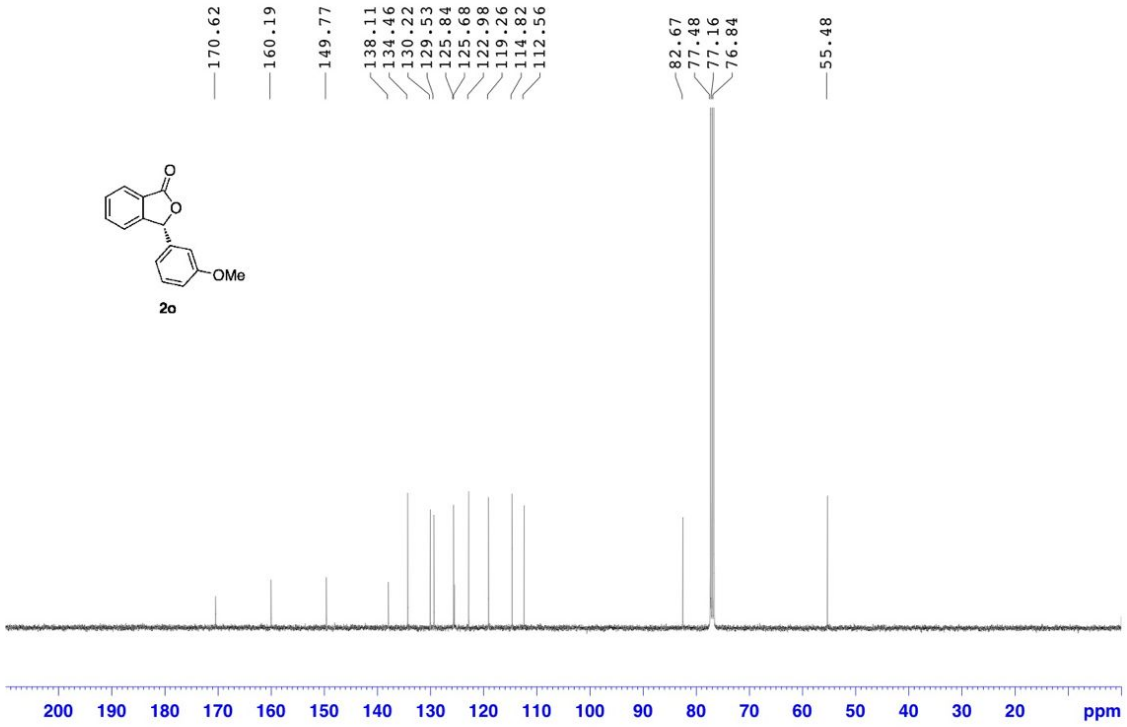

JF01-495 CDCl3
BBFO2 1HNMR
7.968
7.949
7.662
7.659
7.643
7.641
7.624
7.622
7.565
7.546
7.528
7.343
7.341
7.324
7.322
7.283
7.264
7.257
7.245
7.183
7.164
7.088
7.066
6.364
2.328
0.000
Me
2n
9
8
7
6
5
4
3
2
1
0 ppm
1.00
1.06
1.06
1.06
1.19
1.02
2.05
1.01
3.12


JF01-495 CDCl3
BBFO2 13CNMR
170.67
149.93
138.95
136.47
134.40
130.17
129.41
128.95
127.59
125.73
124.17
122.98
82.91
77.47
77.16
76.84
21.47
Me
2n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

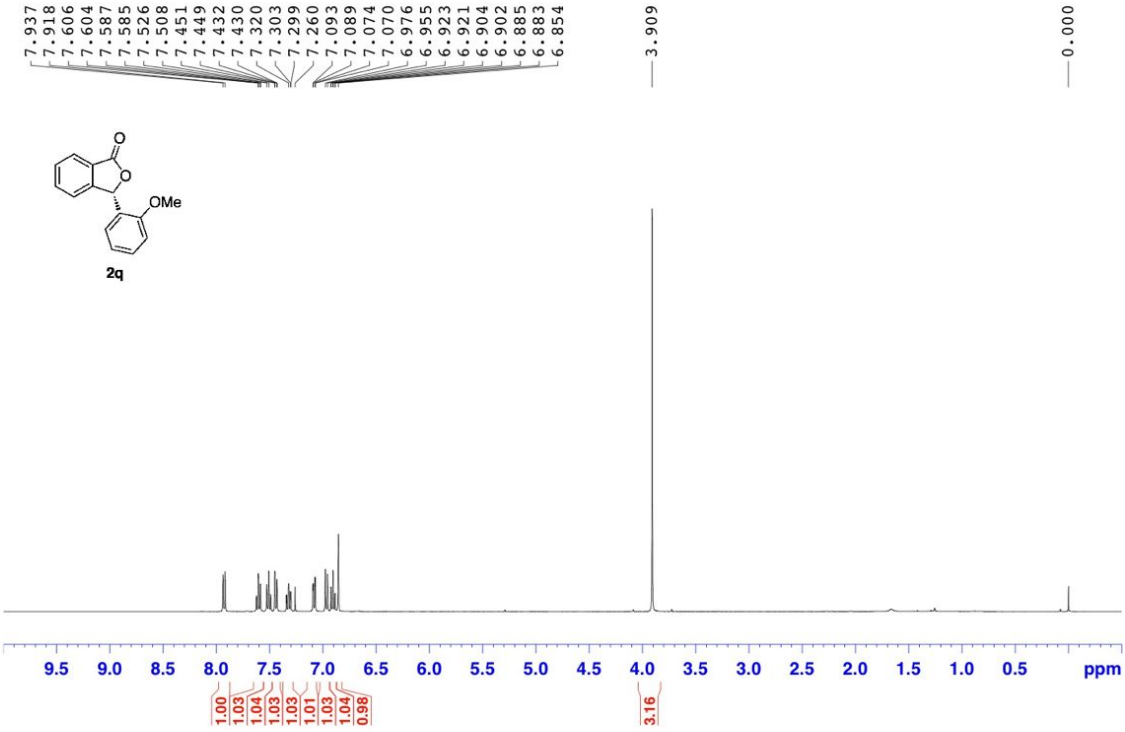
JF01-496, HNMR
AV400 CDCL3



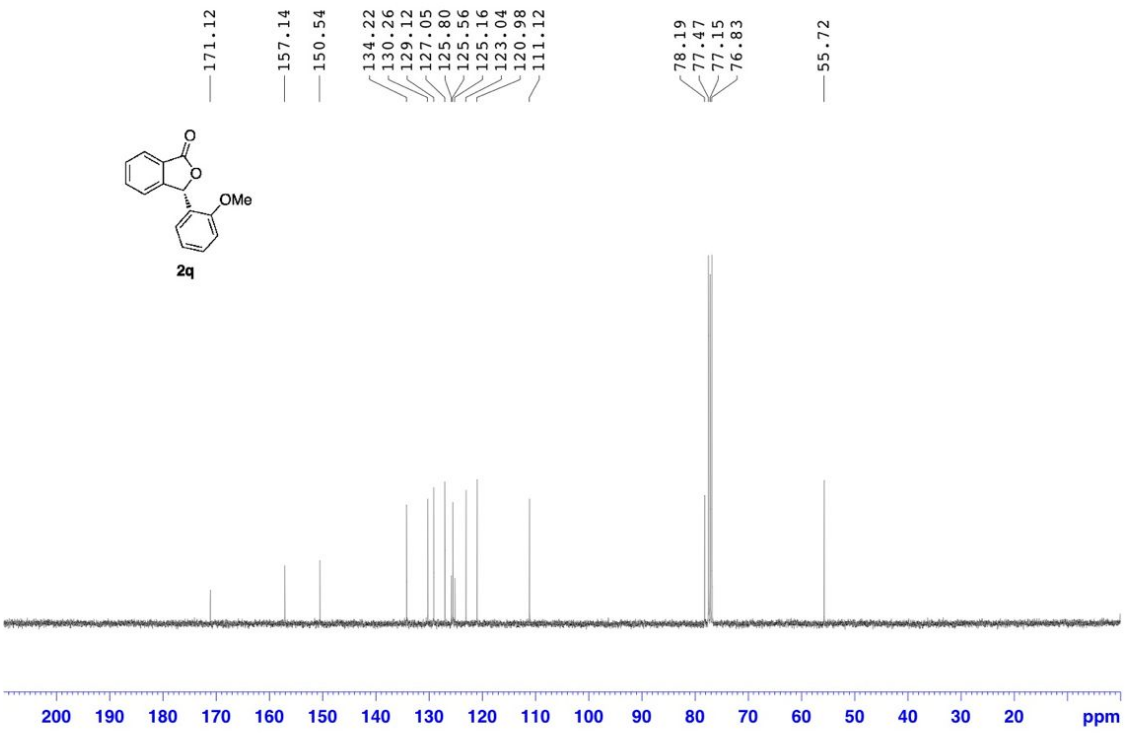
JF01-496, 13CNMR
AV400 CDCL3



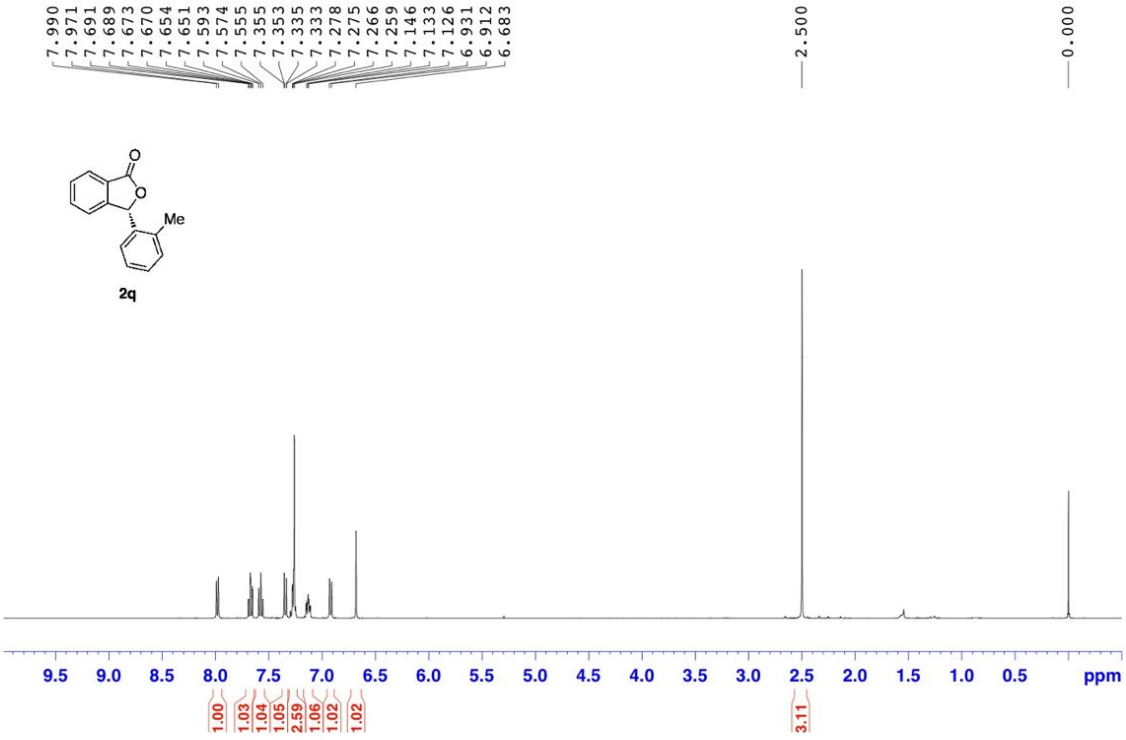
JF01-449 1HNMR
BBFO1 CDCl3



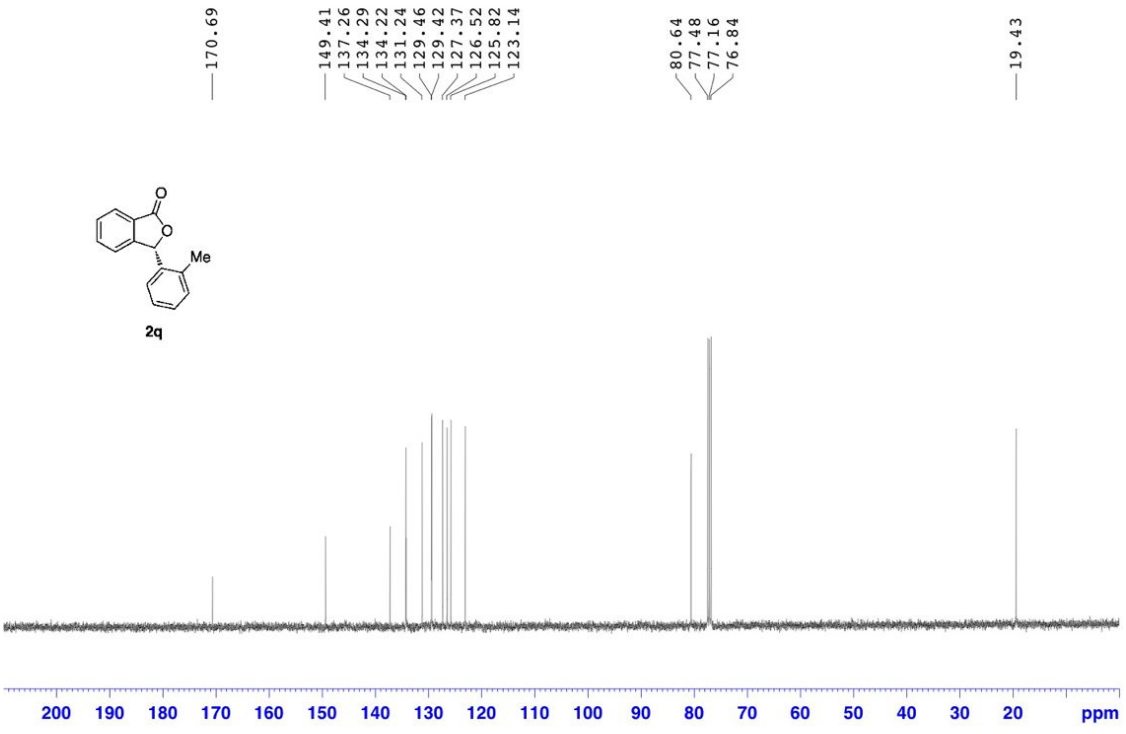
JF01-449 13CMR
BBFO1 CDCl3



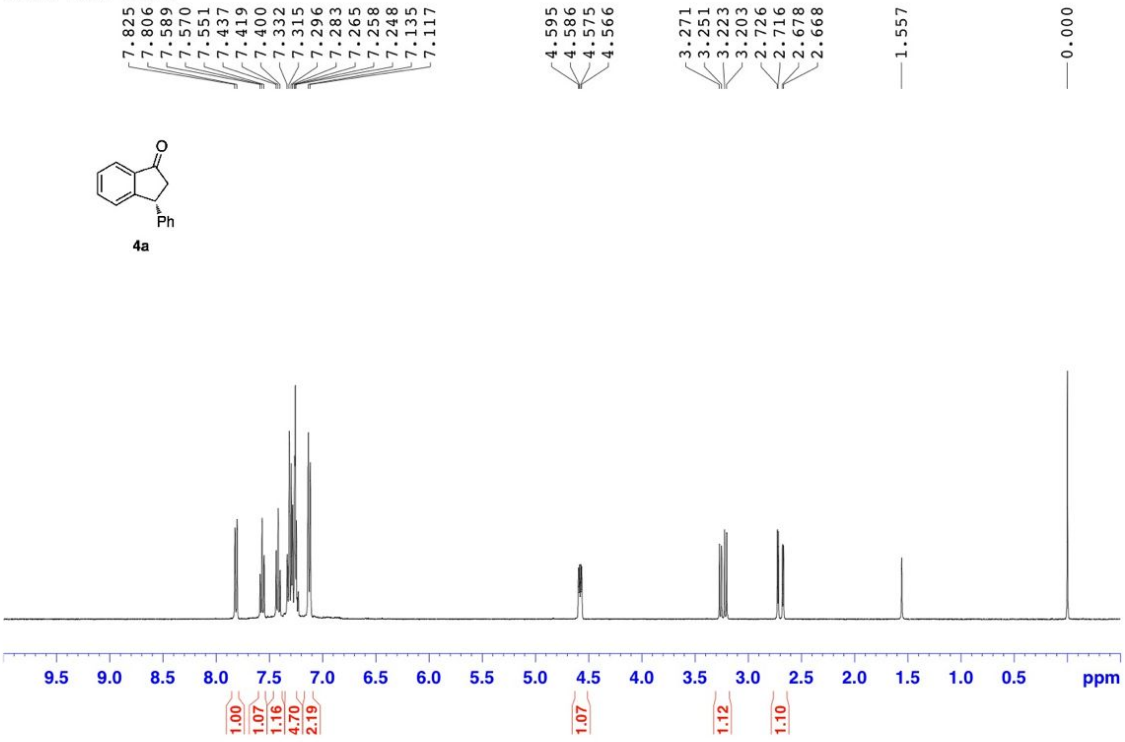
JF01-411 1HNMR
BBF01 CDCl3



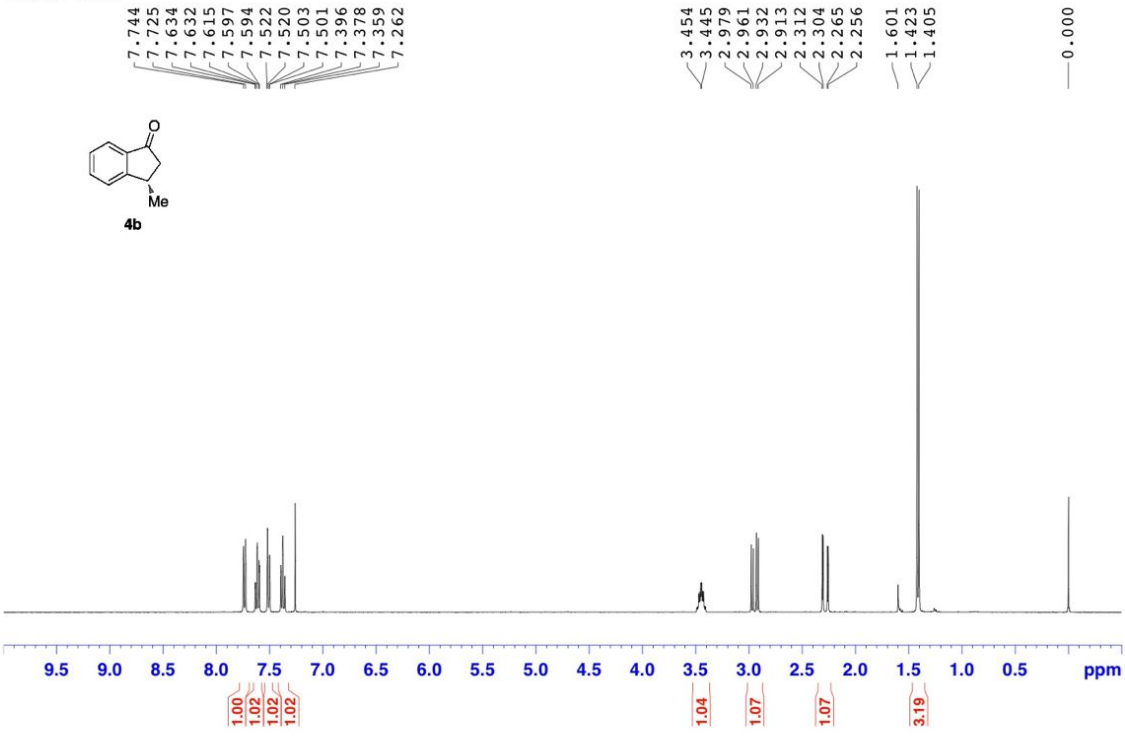
JF01-411, 13CNMR
BBF02, CDCl3

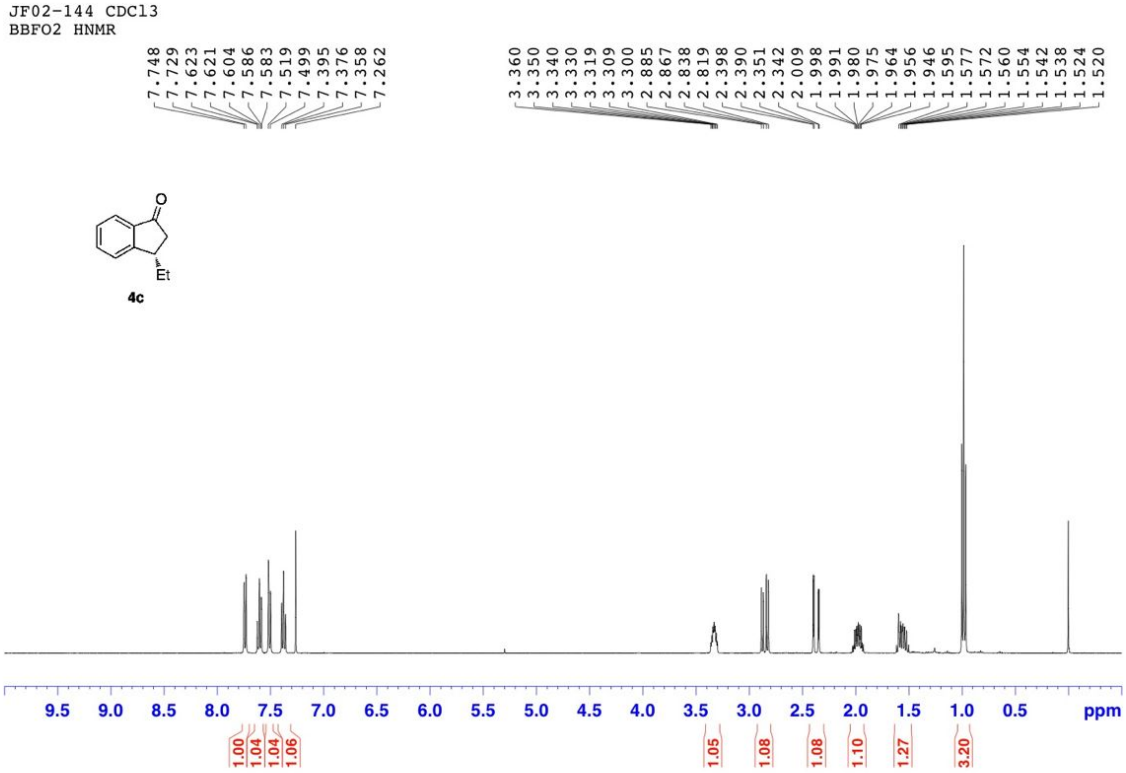


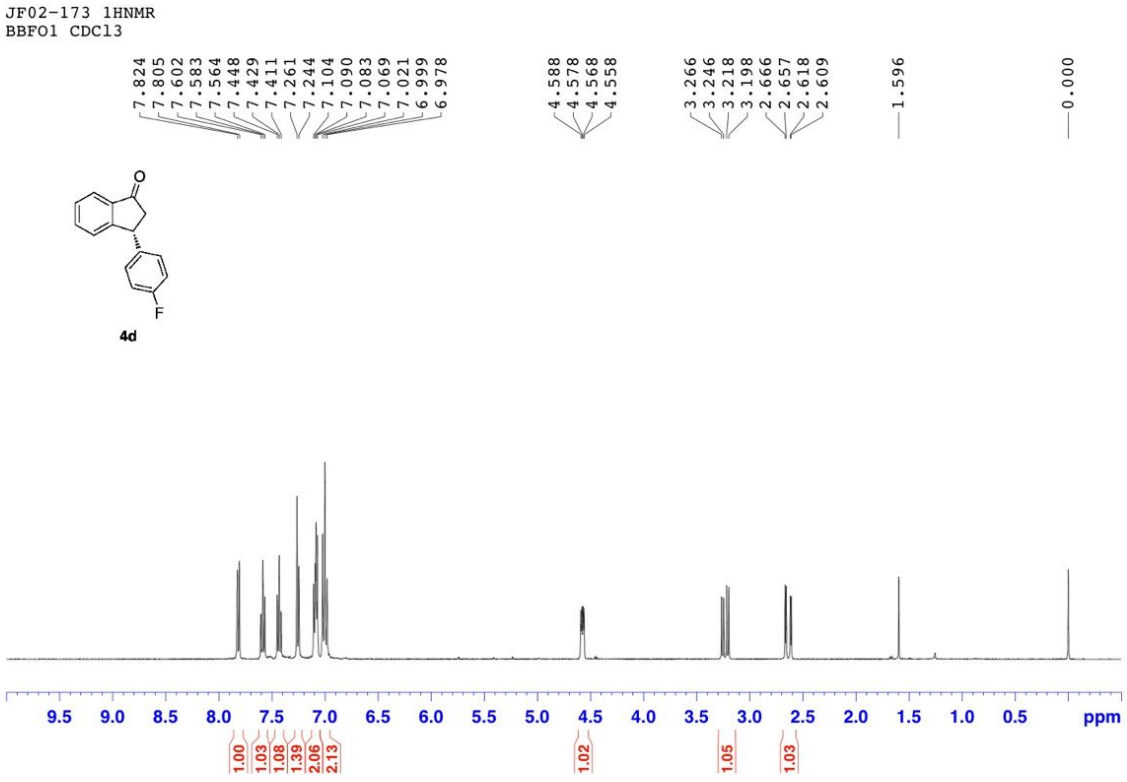
JF02-142, 1H NMR
AV400 MHz, CDCl3

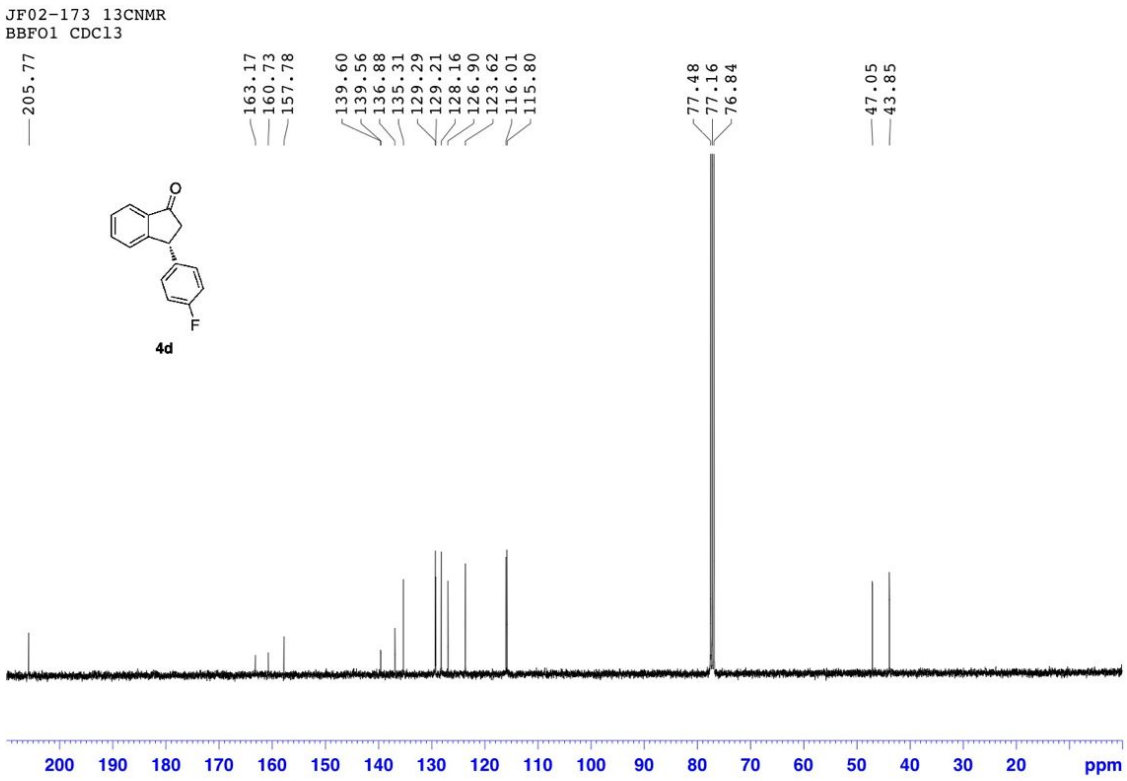


JF02-143 CDCl3
BBFO2 HNMR

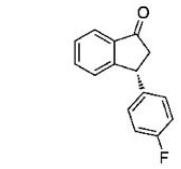



JF02-144 CDCl3
BBFO2 HNMR
7.748
7.729
7.623
7.621
7.604
7.586
7.583
7.519
7.499
7.395
7.376
7.358
7.262
3.360
3.350
3.340
3.330
3.319
3.309
3.300
2.885
2.867
2.838
2.819
2.398
2.390
2.351
2.342
2.009
1.998
1.991
1.980
1.975
1.964
1.956
1.946
1.595
1.577
1.572
1.560
1.554
1.542
1.538
1.524
1.520
O
Et
4c
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
ppm
1.00
1.04
1.04
1.06
1.05
1.08
1.08
1.10
1.27
3.20


JF02-173 1HNMR
BBFO1 CDCl3
7.824
7.805
7.602
7.583
7.564
7.448
7.429
7.411
7.261
7.244
7.104
7.090
7.083
7.069
7.021
6.999
6.978
4.588
4.578
4.568
4.558
3.266
3.246
3.218
3.198
2.666
2.657
2.618
2.609
1.596
0.000
4d
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 ppm
1.00
1.03
1.08
1.39
2.06
2.13
1.02
1.05
1.03

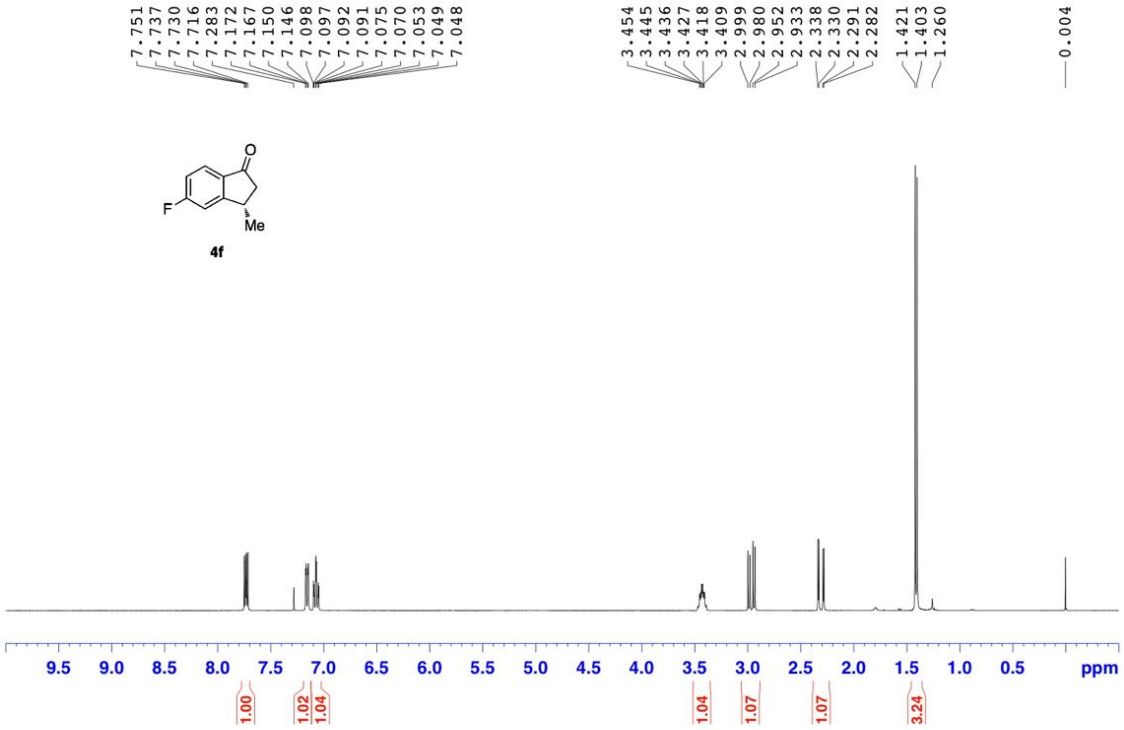

JF02-173 13CNMR
BBFO1 CDCl3
205.77
163.17
160.73
157.78
139.60
139.56
136.88
135.31
129.29
129.21
128.16
126.90
123.62
116.01
115.80
77.48
77.16
76.84
47.05
43.85
4d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

JF02-173 19FNMR
BBFO1 CDCl3

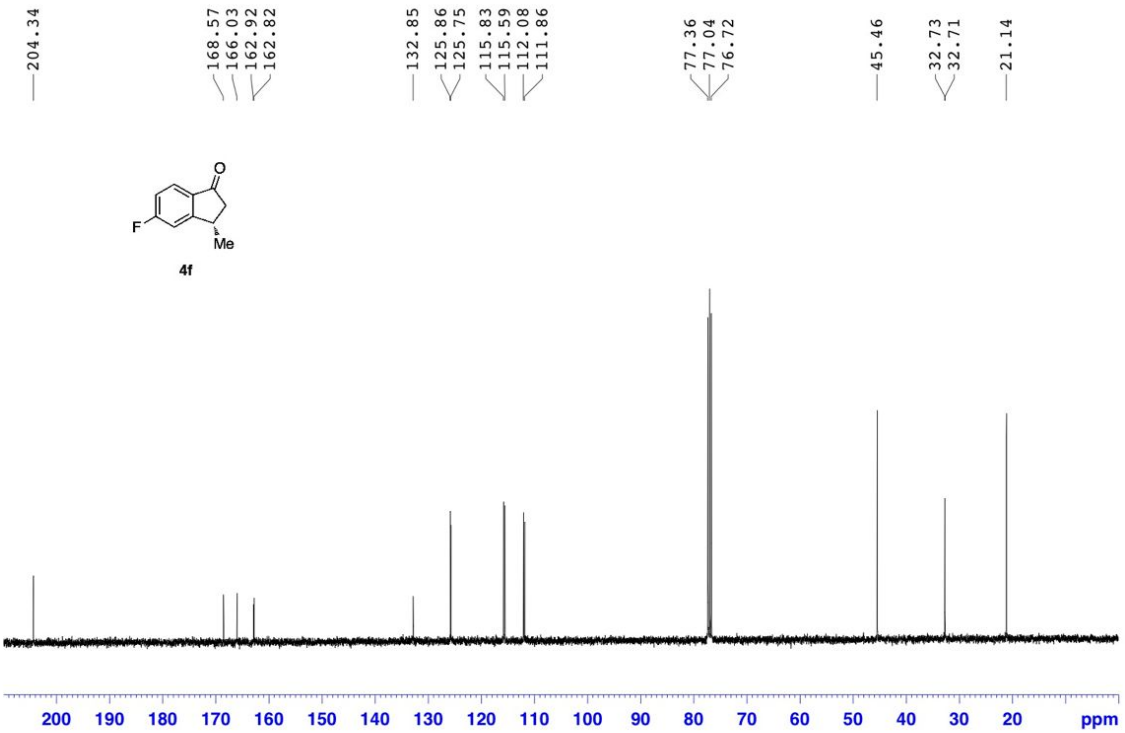


4d

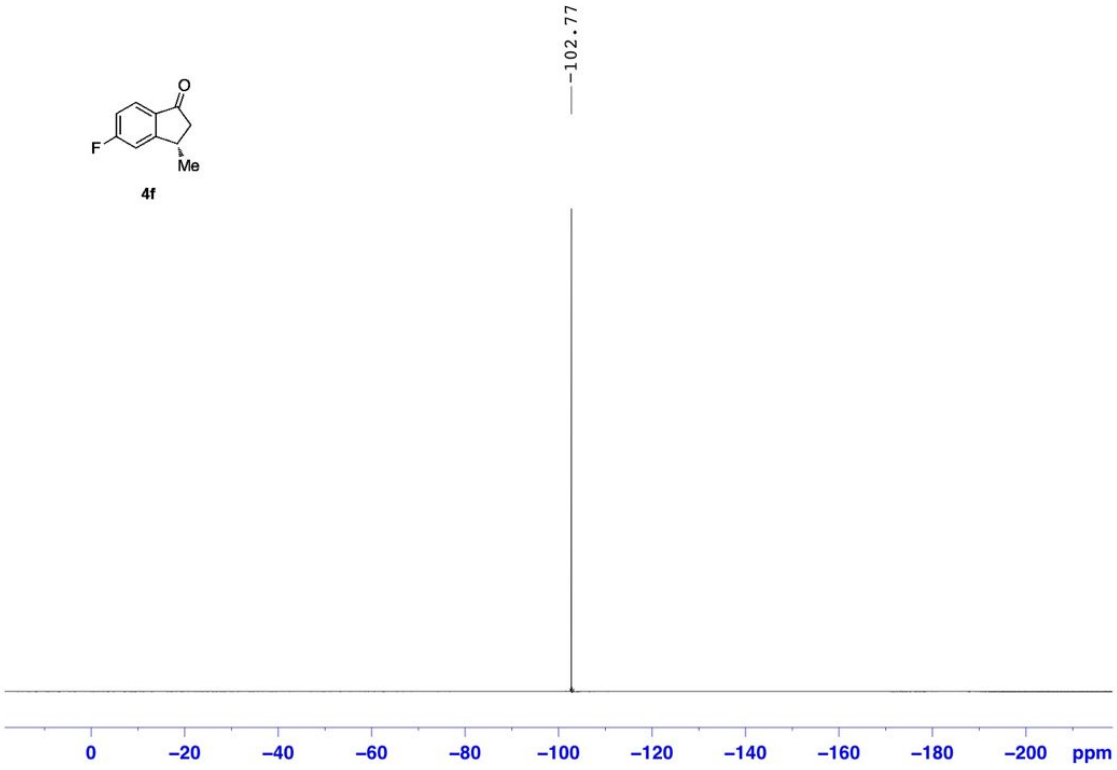
JF02-436 1HNMR
BBFO1 CDCl3

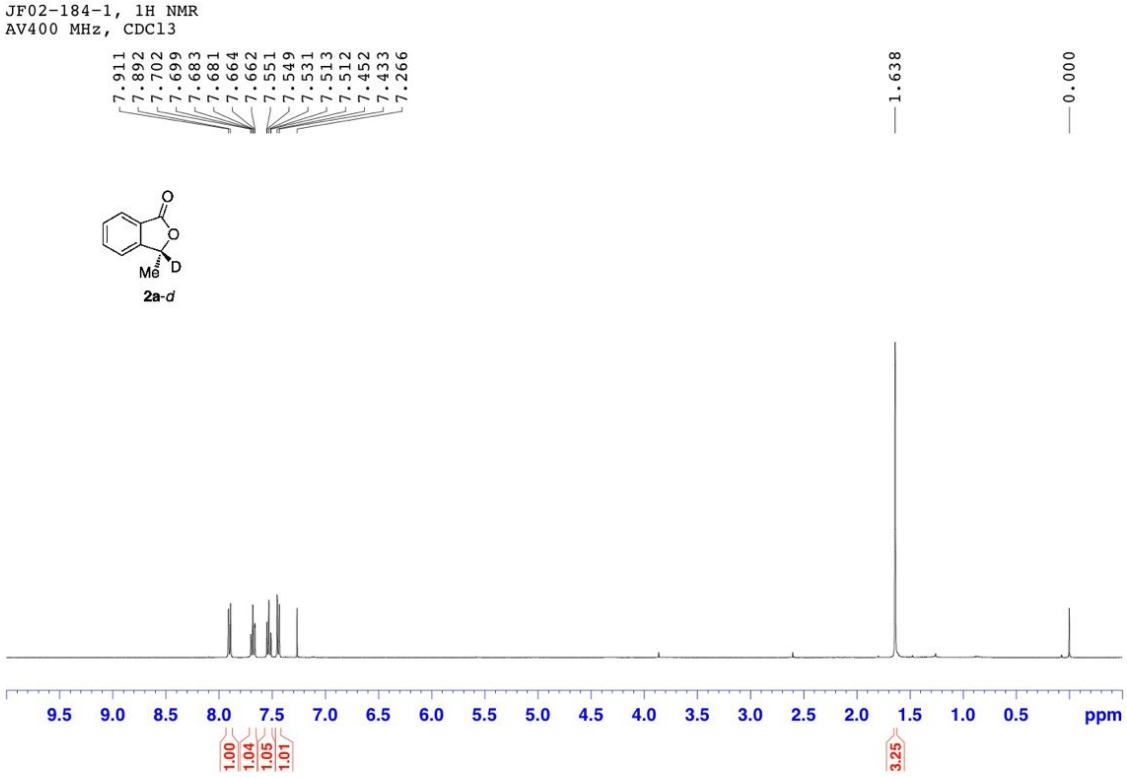


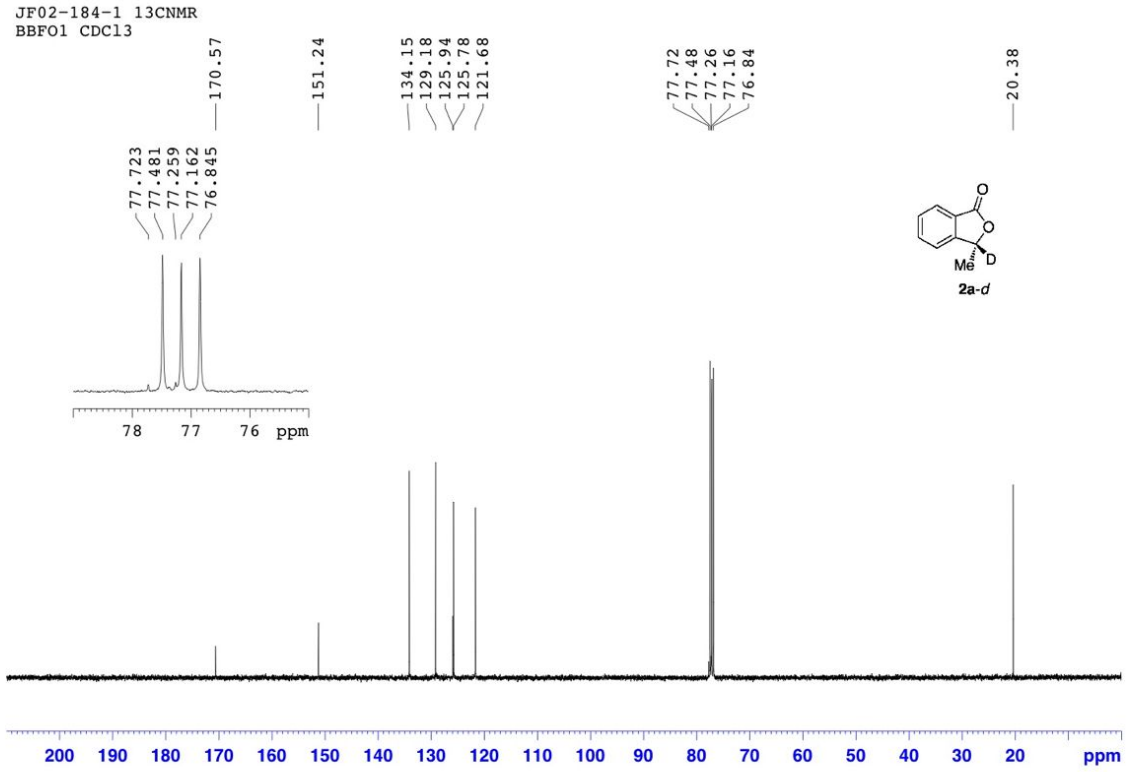
JF02-436 13CNMR
BBFO1 CDCl3



JF02-436 19FNMR
BBFO1 CDCl3




JF02-184-1, 1H NMR
AV400 MHz, CDCl3
7.911
7.892
7.702
7.699
7.683
7.681
7.664
7.662
7.551
7.549
7.531
7.513
7.512
7.452
7.433
7.266
1.638
0.000
Me
D
2a-d
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 ppm
1.00
1.04
1.05
1.01
3.25


JF02-184-1 13CNMR
BBFO1 CDCl3
170.57
151.24
134.15
129.18
125.94
125.78
121.68
77.72
77.48
77.26
77.16
76.84
20.38
77.723
77.481
77.259
77.162
76.845
78 77 76 ppm
Me
D
2a-d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm