Electronic Supplementary Material (ESI) for Chemical Communications


# Supplementary Information

# Cobalt-catalyzed arylation of aldimines via chelation-assisted C–H bond functionalization

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## Table of Contents

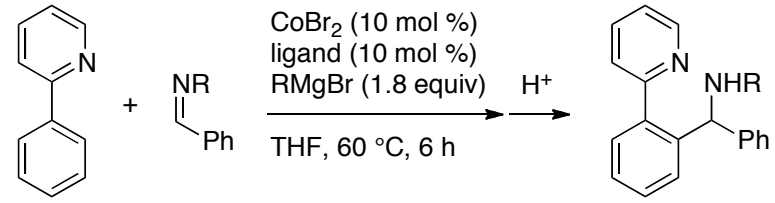
## Materials and Methods

**General.** All reactions dealing with air- or moisture-sensitive compound were performed by standard Schlenk techniques in oven-dried reaction vessels under nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Flash chromatography was performed 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 spectrometer. $^{1}H$ and $^{13}C$ NMR spectra are reported in parts per million (ppm) downfield from an internal standard, tetramethylsilane (0 ppm) and $CHCl_3$ (77.0 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). Gas chromatography–mass spectrometry (GC–MS) analysis was performed on a Shimadzu GCMS-QP2010 system equipped with a capillary column, Rxi®-5Sil MS (Restek, 0.25 mm i.d. x 30 m, 0.25 μm film thickness). High-resolution mass spectra (HRMS) were obtained with a Q-Tof Premier LC HR mass spectrometer. Melting points were measured on a Büchi M-565 apparatus and uncorrected.

**Materials.** Unless otherwise noted, commercial reagents were purchased from Aldrich, Alfa Aesar, and other commercial suppliers and were used as received. Anhydrous cobalt(II) bromide (>99%) was purchased from Alfa Aesar, and was used as received. THF was distilled over Na/benzophenone. Grignard reagents except MeMgCl (purchased from Aldrich) were prepared from the corresponding halides and magnesium turnings in anhydrous THF and titrated before use. The 2-arylpyridine derivatives were prepared by nickel-catalyzed cross-coupling according to the procedure reported by Mongin et al.[1] The aldimines were prepared by condensation of the corresponding aldehydes and aniline or *p*-anisidine in EtOH.

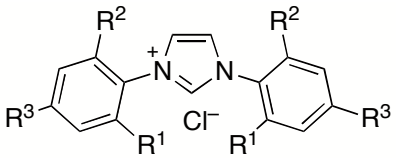
## Optimization of Reaction Conditions

**Table S1.** Screening conditions for the reaction of **1a** with **2a** or **2b**[a]




**1a** **2a** (R = Ph) **2b** (R = 4-MeOC$_6$H$_4$) **3a, b**

| Entry | Imine | Ligand | RMgX | Yield (%)[b] |
|---|---|---|---|---|
| 1 | **2a** | IPr•HCl | *t*BuCH$_2$MgBr | 84[c] |
| 2[d] | **2b** | IPr•HCl | *t*BuCH$_2$MgBr | 81[c] |
| 3 | **2a** | IMes•HCl | *t*BuCH$_2$MgBr | 21 |
| 4 | **2a** | **L1** | *t*BuCH$_2$MgBr | <1 |
| 5 | **2a** | **L2** | *t*BuCH$_2$MgBr | <1 |
| 6 | **2a** | IPr•HCl | MeMgCl | 14 |
| 7 | **2a** | IPr•HCl | *n*BuMgBr | 2 |
| 8 | **2a** | IPr•HCl | *i*PrMgBr | 2 |
| 9 | **2a** | IPr•HCl | Me$_3$SiCH$_2$MgCl | 4 |
| 10[e] | **2a** | IPr•HCl | *t*BuCH$_2$MgBr | 0 |

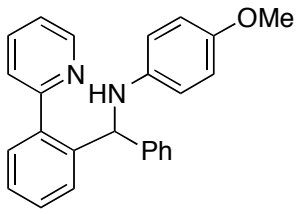



IPr•HCl ($R^1$ = $R^2$ = *i*Pr, $R^3$ = H)
IMes•HCl ($R^1$ = $R^2$ = $R^3$ = Me)
**L1** ($R^1$ = Me, $R^2$ = $R^3$ = H)
**L2** ($R^1$ = $R^2$ = H, $R^3$ = Ph)

[a] The reaction was performed on a 0.3 mmol scale. [b] Determined by GC using *n*-tridecane as an internal standard. [c] Isolated yield. [d] $CoCl_2$ was used instead of $CoBr_2$. The reaction time was 24 h. [e] $CoBr_2$ was omitted from the reaction.

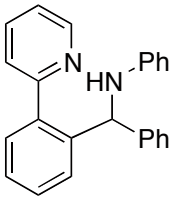
**Addition of 2-Arylpyridine to Aromatic Aldimine (Table 1)**

**A Typical Procedure: 4-Methoxy-*N*-(phenyl(2-(pyridin-2-yl)phenyl)methyl)aniline (3b).** In a Schlenk tube were placed $CoCl_2$ (3.9 mg, 0.030 mmol), IPr•HCl (12.8 mg, 0.030 mmol), 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol), and THF (0.64 mL). To the mixture was added a THF solution of *t*BuCH$_2$MgBr (0.63 M, 0.86 mL, 0.54 mmol) dropwise at 0 °C. After stirring for 30 min, (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) was added. The resulting mixture was stirred at 60 °C for 24 h, and then allowed to room temperature. The reaction was quenched by sequential addition of $Et_2O$ (1 mL) and saturated aqueous solution of $NH_4Cl$ (1 mL). The aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1) to afford the title compound as a brown oil (89.0 mg, 81 %).



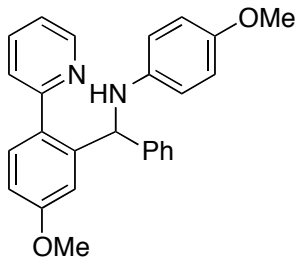

**3b:** $R_f$ 0.17 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.28 (brs, 1H), 5.88 (s, 1H), 6.51 (d, *J* = 8.8 Hz, 2H), 6.71 (d, *J* = 8.8 Hz, 2H), 7.13-7.22 (m, 7H), 7.36-7.40 (m, 3H), 7.53-7.59 (m, 2H), 8.65 (d, *J* = 4.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.8, 59.7, 114.6, 114.8, 122.0, 124.4, 126.9, 127.4, 127.7, 128.2, 128.4, 128.9, 130.2, 136.4, 140.5, 141.2, 141.8, 143.1, 149.1, 152.0, 159.7; HRMS (ESI) Calcd for $C_{25}H_{23}N_2O$ $[M + H]^+$ 367.1810, found 367.1812.

***N*-(Phenyl(2-(pyridin-2-yl)phenyl)methyl)aniline (3a):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-*N*-benzylideneaniline (**2a**, 65.2 mg, 0.36 mmol) using $CoBr_2$ (6.6 mg, 0.030 mmol) at 60 °C for 6 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1) of the crude product afforded the title compound as a yellow oil (84.3 mg, 84 %).



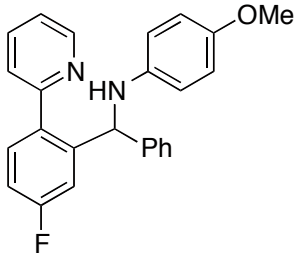

$R_f$ 0.15 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 4.56 (brs, 1H), 6.01 (s, 1H), 6.58(d, *J* = 8.0 Hz, 2H), 6.70 (t, *J* = 7.2 Hz, 1H), 7.11-7.23 (m, 9H), 7.39-7.44 (m, 3H), 7.55-7.59 (m, 2H), 8.66-8.67 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 59.0, 113.5, 117.4, 122.0, 124.3, 127.0, 127.4, 127.7, 128.2, 128.4, 128.9, 129.2, 130.3, 136.4, 140.5, 141.0, 142.9, 147.4, 149.1, 159.6; HRMS (ESI) Calcd for $C_{24}H_{21}N_2$ $[M + H]^+$ 337.1705, found 337.1702.

**4-Methoxy-*N*-((5-methoxy-2-(pyridin-2-yl)phenyl)(phenyl)methyl)aniline (3c):** The typical procedure was applied to 2-(4-methoxyphenyl)pyridine (**1b**, 55.6 mg, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 14 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–5/1/0.1) of the crude product afforded the title compound as a dark brown oil (90.4 mg, 76%).



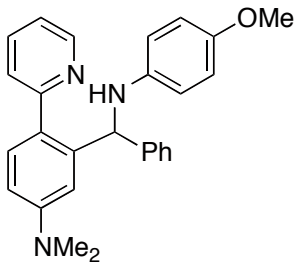

$R_f$ 0.15 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.79 (s, 3H), 4.28 (brs, 1H), 5.92 (s, 1H), 6.52 (app.d, *J* = 6.8 Hz, 2H), 6.71 (app.d, *J* = 6.8 Hz, 2H), 6.89 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.12-7.26 (m, 8H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.53-7.57 (m, 1H), 8.61-8.63 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.4, 55.8, 59.7, 112.2, 114.1, 114.7, 114.8, 121.7, 124.4, 127.0, 127.7, 128.4, 131.6, 133.2, 136.3, 141.8, 142.9, 143.0, 149.1, 152.1, 159.5, 160.0; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O_2$ $[M + H]^+$ 397.1916, found 397.1921.

***N*-((5-Fluoro-2-(pyridin-2-yl)phenyl)(phenyl)methyl)-4-methoxyaniline (3d):** The typical procedure was applied to 2-(4-fluorophenyl)pyridine (**1c**, 52.0 mg, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 14 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1) of the crude product afforded the title compound as a dark brown oil (73.3 mg, 64%).




$R_f$ 0.15 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.12 (brs, 1H), 5.88 (s, 1H), 6.52 (app.d, *J* = 6.8 Hz, 2H), 6.71 (app.d, *J* = 6.8 Hz, 2H), 7.03-7.09 (m, 4H), 7.16-7.21 (m, 4H), 7.32-7.36 (m, 2H), 7.55-7.59 (m, 1H), 8.62-8.64 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.9, 59.7, 114.3 (d, $^2J_{C\text{-}F}$ = 21 Hz), 114.8, 114.90 (d, $^2J_{C\text{-}F}$ = 20 Hz), 114.91, 122.2, 124.5, 127.3, 127.8, 128.6 (two signals overlapping), 132.1 (d, $^3J_{C\text{-}F}$ = 8 Hz), 136.5, 141.5, 142.5, 144.1 (d, $^3J_{C\text{-}F}$ = 7 Hz), 149.2, 152.3, 158.9, 163.3 (d, $^1J_{C\text{-}F}$ = 246 Hz); HRMS (ESI) Calcd for $C_{25}H_{22}FN_2O$ $[M + H]^+$ 385.1716, found 385.1719.

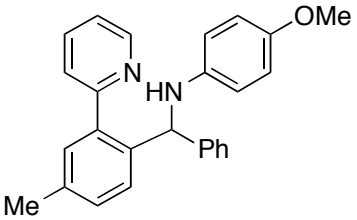
**3-(((4-Methoxyphenyl)amino)(phenyl)methyl)-*N*,*N*-dimethyl-4-(pyridin-2-yl)aniline (3e):** The typical procedure was applied to *N*,*N*-dimethyl-4-(pyridin-2-yl)aniline (**1d**, 59.5 mg, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 6/1/0.1–5/1/0.1) of the crude product afforded the title compound as a



brown solid (34.2 mg, 28%).

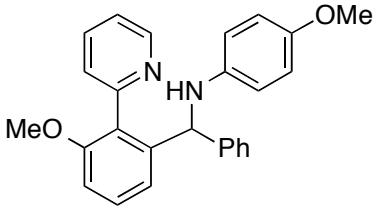
m.p. 125.0-126.1 ºC; $R_f$ 0.12 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.92 (s, 6H), 3.70 (s, 3H), 4.37 (brs, 1H), 5.92 (s, 1H), 6.51 (app.d, $J$ = 6.8 Hz, 2H), 6.68-6.71 (m, 3H), 6.82 (d, $J$ = 2.4Hz, 1H), 7.09-7.18 (m, 7H), 7.26-7.31 (m, 1H), 7.52-7.54 (m, 1H), 8.57-8.59 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 40.6, 55.9, 60.1, 111.2, 112.4, 114.7, 114.8, 121.2, 124.3, 126.7, 127.7, 128.3, 128.9, 131.4, 136.2, 142.1, 142.2, 143.5, 149.0, 150.9, 152.0, 160.1; HRMS (ESI) Calcd for $C_{27}H_{28}N_3O$ $[M + H]^+$ 410.2232, found 410.2230.

**4-Methoxy-*N*-((4-methyl-2-(pyridin-2-yl)phenyl)(phenyl)methyl)aniline (3f):** The typical procedure was applied to 2-(*m*-tolyl)pyridine (**1e**, 49 μL, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 16 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1) of the crude product afforded the title compound as a brown oil (53.9 mg, 47%).




$R_f$ 0.25 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 3H), 3.71 (s, 3H), 4.26 (brs, 1H), 5.77 (s, 1H), 6.49 (app.d, $J$ = 6.8 Hz, 2H), 6.70 (app.d, $J$ = 6.8 Hz, 2H), 7.13-7.22 (m, 9H), 7.38 (d, $J$ = 8.0 Hz, 1H), 7.54-7.58 (m, 1H), 8.63-8.65 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.2, 55.9, 59.5, 114.6, 114.8, 122.0, 124.3, 126.9, 127.8, 128.2, 128.4, 129.6, 130.9, 136.3, 137.0, 138.3, 140.4, 141.8, 143.3, 149.2, 152.0, 159.7; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1969.

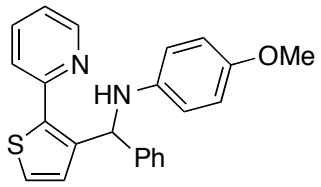
**4-Methoxy-*N*-((3-methoxy-2-(pyridin-2-yl)phenyl)(phenyl)methyl)aniline (3g):** The typical procedure was applied to 2-(2-methoxyphenyl)pyridine (**1f**, 52 μL, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–3/1/0.1) of the crude product afforded the title compound as a dark brown oil (83.4 mg, 70%).




$R_f$ 0.06 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 3.72 (s, 3H), 4.10 (d, $J$ = 4.0 Hz, 1H), 5.31 (d, $J$ = 4.4 Hz, 1H), 6.44 (app.d, $J$ = 6.8 Hz, 2H), 6.67 (app.d, $J$ = 6.8 Hz, 2H), 6.91 (d, $J$ =8.0 Hz, 1H), 6.96 (d, $J$ = 7.6 Hz, 1H), 7.04-7.06 (m, 2H), 7.13-7.18 (m, 5H), 7.34 (t, $J$ = 6.0 Hz, 1H), 7.51-7.53 (m, 1H), 8.62 (d, $J$ = 4.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.88, 55.91, 60.2, 110.1, 114.6, 114.8, 120.0, 122.0, 126.2, 127.1, 127.8, 128.4,

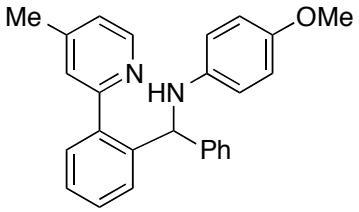
129.6, 129.7, 135.8, 141.9, 142.9, 143.0, 149.4, 152.0, 156.3, 157.3; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O_2$ $[M + H]^+$ 397.1916, found 397.1920.

**4-Methoxy-*N*-(phenyl(2-(pyridin-2-yl)thiophen-3-yl)methyl)aniline (3h):** The typical procedure was applied to 2-(thiophen-2-yl)pyridine (**1g**, 48.4 mg, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–7/1/0.1) of the crude product afforded the title compound as a dark brown solid (56.3 mg, 48%).




m.p. 104.1-105.9 ºC; $R_f$ 0.33 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.70 (s, 3H), 4.25 (brs, 1H), 6.17 (s, 1H), 6.52 (app.d, *J* = 6.8 Hz, 2H), 6.71 (app.d, *J* = 6.8 Hz, 2H), 7.01 (d, *J* = 5.2 Hz, 1H), 7.15-7.18 (m, 1H), 7.26 (t, *J* = 6.8 Hz, 2H), 7.31 (t, *J* = 7.2 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.61-7.63 (m, 1H), 8.63-8.65 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.8, 57.0, 114.7, 114.9, 122.0, 122.5, 126.2, 127.3, 127.5, 128.7, 129.6, 136.9, 139.4, 141.5, 141.9, 142.9, 149.7, 152.2, 152.8; HRMS (ESI) Calcd for $C_{23}H_{21}N_2OS$ $[M + H]^+$ 373.1375, found 373.1376.

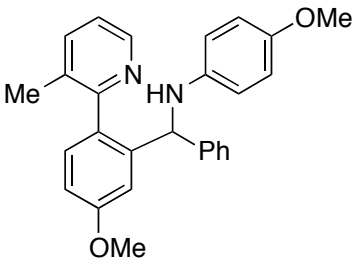
**4-Methoxy-*N*-((2-(4-methylpyridin-2-yl)phenyl)(phenyl)methyl)aniline (3i):** The typical procedure was applied to 4-methyl-2-phenylpyridine (**1h**, 50.8 mg, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 6/1/0.1) of the crude product afforded the title compound as a brown solid (76.5 mg, 67%).




m.p. 126.4-127.3 ºC; $R_f$ 0.20 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 3.71 (s, 3H), 4.26 (brs, 1H), 5.85 (s, 1H), 6.49 (app.d, *J* = 6.8 Hz, 2H), 6.70 (app.d, *J* = 6.8 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.16-7.21 (m, 5H), 7.35-7.41 (m, 4H), 7.49-7.51 (m, 1H), 8.48 (dd, *J* = 1.4, 0.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 18.3, 55.8, 59.6, 114.6, 114.8, 123.8, 126.9, 127.3, 127.7, 128.2, 128.4, 128.7, 130.2, 131.5, 136.9, 140.4, 141.2, 141.8, 143.2, 149.5, 152.0, 156.7; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1962.

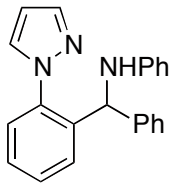
**4-Methoxy-*N*-((5-methoxy-2-(3-methylpyridin-2-yl)phenyl)(phenyl)methyl)aniline (3j):** The typical procedure was applied to 2-(4-methoxyphenyl)-3-methylpyridine (**1i**, 56 μL, 0.30 mmol) and (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 76.1 mg, 0.36 mmol) for 24 h. Silica gel

chromatography (eluent: hexane/EtOAc/$Et_3N$ = 6/1/0.1) of the crude product afforded the title compound as a yellow oil (62.6 mg, 51%).



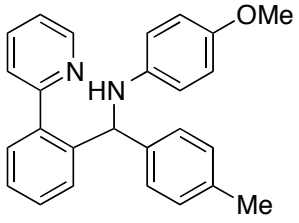

$R_f$ 0.16 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 1.63 (s, 3H), 3.70 (s, 3H), 3.80 (s, 3H), 4.32 (brs, 1H), 5.40 (s, 1H), 6.52 (brs, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.85 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.93 (brs, 2H), 7.08-7.13 (m, 5H), 7.19-7.23 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 8.45-8.47 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.0, 55.5, 55.9, 60.8, 111.9, 114.7, 114.8, 122.4, 124.9, 127.1, 127.7, 128.4, 129.2, 130.7, 132.4, 132.9, 138.0, 141.9, 142.3, 146.5, 152.1, 158.8, 159.7; HRMS (ESI) Calcd for $C_{27}H_{27}N_2O_2$ $[M + H]^+$ 411.2073, found 411.2076.

***N*-((2-(1*H*-pyrazol-1-yl)phenyl)(phenyl)methyl)aniline (3k):** The typical procedure was applied to 1-phenyl-1*H*-pyrazole (**1j**, 40 μL, 0.30 mmol) and (*E*)-*N*-benzylideneaniline (**2b**, 65.2 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 15/1/0.1–10/1/0.1) of the crude product afforded the title compound as a light yellow oil (59.3 mg, 61%).




$R_f$ 0.42 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 4.35 (d, *J* = 2.8 Hz, 1H), 5.85 (d, *J* = 3.2 Hz, 1H), 6.30 (t, *J* = 2.0 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 2H), 6.72 (t, *J* = 7.2 Hz, 1H), 7.08-7.10 (m, 2H), 7.12-7.16 (m, 2H), 7.21-7.25 (m, 4H), 7.35 (td, *J* = 7.2, 1.6 Hz, 1H), 7.41 (td, *J* = 7.2, 1.6 Hz, 1H), 7.44 (td, *J* = 7.2, 1.6 Hz, 1H), 7.69 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.74 (d, *J* = 1.6 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 57.6, 106.5, 113.6, 117.8, 127.2, 127.5, 127.6, 128.2, 128.59, 128.62, 129.26, 129.31, 131.2, 138.9, 139.5, 140.7, 142.1, 147.0; HRMS (ESI) Calcd for $C_{22}H_{20}N_3$ $[M + H]^+$ 326.1657, found 326.1658.

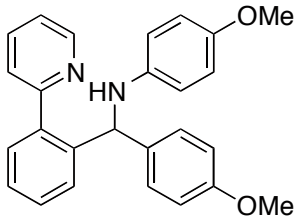
**4-Methoxy-*N*-((2-(pyridin-2-yl)phenyl)(p-tolyl)methyl)aniline (3l):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-4-methoxy-*N*-(4-methylbenzylidene)aniline (**2c**, 81.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 7/1/0.1) of the crude product afforded the title compound as a dark red solid (97.3 mg, 85%).




m.p. 89.3-91.6 ºC; $R_f$ 0.25 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 3.69 (s, 3H), 4.21 (brs, 1H), 5.83 (s, 1H), 6.49 (app.d, *J* = 9.2 Hz, 2H), 6.69 (app.d, *J* = 8.8 Hz, 2H), 7.02 (s, 4H), 7.18-7.23 (m, 2H), 7.33-7.39 (m, 3H), 7.53-7.56 (m, 2H), 8.62-8.64 (m, 1H);

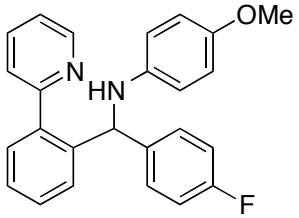
$^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.2, 55.8, 59.3, 114.6, 114.7, 122.0, 124.3, 127.2, 127.6, 128.0, 128.8, 129.1, 130.1, 136.3, 136.5, 140.1, 140.4, 141.3, 141.8, 149.1, 151.9, 159.6; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1970.

**4-Methoxy-*N*-((4-methoxyphenyl)(2-(pyridin-2-yl)phenyl)methyl)aniline (3m):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-4-methoxy-*N*-(4-methoxybenzylidene)aniline (**2d**, 86.9 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–5/1/0.1) of the crude product afforded the title compound as a dark brown oil (92.8 mg, 78%).




$R_f$ 0.13 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 3.75 (s, 3H), 4.22 (brs, 1H), 5.83 (s, 1H), 6.51 (d, $J$ = 9.2 Hz, 2H), 6.71-6.75 (m, 4H), 7.04 (d, $J$ = 8.4 Hz, 2H), 7.15-7.20 (m, 2H), 7.35-7.40 (m, 3H), 7.56-7.60 (m, 2H), 8.65 (d, $J$ = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.3, 55.8, 59.0, 113.7, 114.6, 114.7, 121.9, 124.3, 127.2, 127.8, 128.8 (two signals overlapping), 130.1, 135.3, 136.3, 140.4, 141.3, 141.8, 149.1, 151.9, 158.5, 159.7; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O_2$ $[M + H]^+$ 397.1916, found 397.1918.

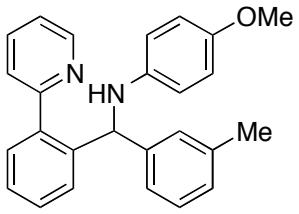
***N*-((4-Fluorophenyl)(2-(pyridin-2-yl)phenyl)methyl)-4-methoxyaniline (3n):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-*N*-(4-fluorobenzylidene)-4-methoxyaniline (**2e**, 82.5 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–7/1/0.1) of the crude product afforded the title compound as a brown oil (30.4 mg, 26%).




$R_f$ 0.17 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.25 (brs, 1H), 5.83 (s, 1H), 6.48 (app.d, $J$ = 9.2 Hz, 2H), 6.70 (app.d, $J$ = 9.2 Hz, 2H), 6.86 (t, $J$ = 8.8 Hz, 2H), 7.06-7.09 (m, 2H), 7.15 (d, $J$ = 8.0 Hz, 1H), 7.17-7.20 (m, 1H), 7.36-7.38 (m, 3H), 7.46-7.49 (m, 1H), 7.54-7.58 (m, 1H), 8.61-8.62 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.9, 59.0, 114.7, 114.9, 115.2 (d, $^2J_{C\text{-}F}$ = 21 Hz), 121.1, 124.3, 127.5, 128.2, 129.0, 129.3 (d, $^3J_{C\text{-}F}$ = 8 Hz), 130.3, 136.5, 138.9 (d, $^4J_{C\text{-}F}$ = 3 Hz), 140.5, 141.1, 141.6, 149.1, 152.2, 159.7, 161.8 (d, $^1J_{C\text{-}F}$ = 244 Hz); HRMS (ESI) Calcd for $C_{25}H_{22}FN_2O$ $[M + H]^+$ 385.1716, found 385.1718.

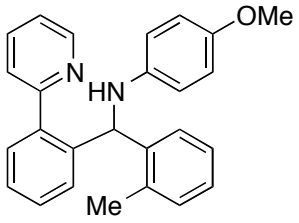
**4-Methoxy-*N*-((2-(pyridin-2-yl)phenyl)(*m*-tolyl)methyl)aniline (3o):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and

(*E*)-4-methoxy-*N*-(3-methylbenzylidene)aniline (**2f**, 81.1 mg, 0.36 mmol) for 13 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 7/1/0.1) of the crude product afforded the title compound as a dark red oil (87.8 mg, 77%).



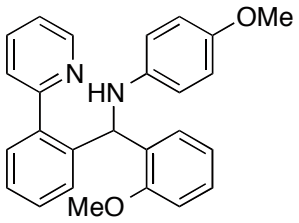

$R_f$ 0.20 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 3H), 3.71 (s, 3H), 4.21 (brs, 1H), 5.82 (s, 1H), 6.51 (app.d, *J* = 9.2 Hz, 2H), 6.71 (app.d, *J* = 9.2 Hz, 2H), 6.93 (s, 1H), 6.93 (d, *J* = 6.8 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 7.09 (t, *J* = 7.6 Hz, 1H), 7.16-7.21 (m, 2H), 7.36-7.40 (m, 3H), 7.53-7.58 (m, 2H), 8.65-8.66 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.5, 55.8, 59.7, 114.6, 114.8, 122.0, 124.4, 124.8, 127.3, 127.7, 128.1, 128.3, 128.4, 128.9, 130.1, 136.3, 137.9, 140.5, 141.3, 141.9, 143.0, 149.1, 152.0, 159.7; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1962.

**4-Methoxy-*N*-((2-(pyridin-2-yl)phenyl)(*o*-tolyl)methyl)aniline (3p):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-4-methoxy-*N*-(2-methylbenzylidene)aniline (**2g**, 81.1 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–5/1/0.1) of the crude product afforded the title compound as a light yellow solid (88.3 mg, 77%).




m.p. 120.0-121.3 ºC; $R_f$ 0.19 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 1.96 (s, 3H), 3.71 (s, 3H), 4.07 (brs, 1H), 5.85 (s, 1H), 6.45 (app.d, *J* = 8.8 Hz, 2H), 6.71 (app.d, *J* = 9.2 Hz, 2H), 7.05-7.06 (m, 1H), 7.10-7.15 (m, 2H), 7.14-7.17 (m, 2H), 7.25-7.27 (m, 1H), 7.36-7.39 (m, 2H), 7.43-7.46 (m, 2H), 7.50-7.52 (m, 1H), 8.60 (d, *J* = 4.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 19.1, 55.8, 56.7, 114.1, 114.8, 121.9, 124.0, 126.0, 127.1, 127.4, 127.6, 128.2, 128.7, 130.0, 130.5, 136.2, 136.3, 139.9, 140.8, 140.9, 141.8, 149.2, 151.9, 159.5; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O$ $[M + H]^+$ 381.1967, found 381.1972.

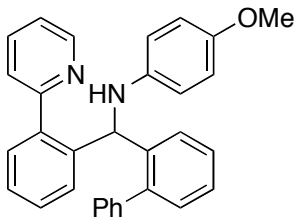
**4-Methoxy-*N*-((2-methoxyphenyl)(2-(pyridin-2-yl)phenyl)methyl)aniline (3q):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-4-methoxy-*N*-(2-methoxybenzylidene)aniline (**2h**, 86.9 mg, 0.36 mmol) for 24 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–5/1/0.1–3/1/0.1) of the crude product afforded the title compound as a dark brown oil (62.9 mg, 53%).




$R_f$ 0.13 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.52 (s, 3H), 3.70 (s, 3H), 4.22 (brs, 1H), 5.99 (s, 1H), 6.44 (app.d, *J* = 8.8 Hz, 2H), 6.67 (app.d, *J* = 8.8 Hz, 2H), 6.72 (d, *J* =

8.0 Hz, 1H), 6.84 (t, *J* = 7.2 Hz, 1H), 7.14-7.18 (m, 2H), 7.25-7.27 (m, 2H), 7.32-7.34 (m, 2H), 7.39-7.41 (m, 2H), 7.54-7.58 (m, 1H), 8.61-8.62 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 54.1, 55.3, 55.9, 110.6, 114.5, 114.8, 120.6, 121.8, 124.1, 127.2, 128.0, 128.21, 128.24, 128.6, 130.0, 130.9, 136.0, 140.76, 140.79, 141.9, 149.2, 151.9, 156.9, 159.7; HRMS (ESI) Calcd for $C_{26}H_{25}N_2O_2$ $[M + H]^+$ 397.1916, found 397.1911.

***N*-([1,1'-Biphenyl]-2-yl(2-(pyridin-2-yl)phenyl)methyl)-4-methoxyaniline (3r):** The typical procedure was applied to 2-phenylpyridine (**1a**, 43 μL, 0.30 mmol) and (*E*)-*N*-([1,1'-biphenyl]-2-ylmethylene)-4-methoxyaniline (**2i**, 103.4 mg, 0.36 mmol) for 48 h. Silica gel chromatography (eluent: hexane/EtOAc/$Et_3N$ = 10/1/0.1–7/1/0.1) of the crude product afforded the title compound as a light yellow solid (46.7 mg, 35%).

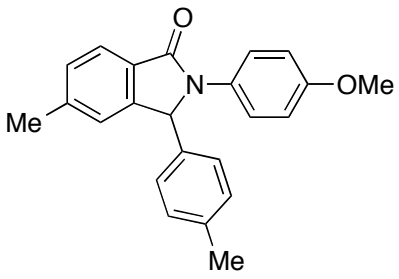



m.p. 142.1-143.1 ºC; $R_f$ 0.16 (hexane/EtOAc = 5/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.71 (s, 3H), 4.22 (brs, 1H), 5.69 (s, 1H), 6.41 (app.d, *J* = 8.8 Hz, 2H), 6.67 (app.d, *J* = 8.8 Hz, 2H), 6.73 (d, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.2 Hz, 2H), 6.99-7.01 (m, 1H), 7.12-7.16 (m, 3H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.24-7.27 (m, 3H), 7.28-7.32 (m, 2H), 7.34-7.47 (m, 2H), 7.47-7.49 (m, 1H), 8.27-8.28 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.8, 57.0, 114.5, 114.7, 121.6, 123.5, 126.9, 127.0, 127.3, 127.6, 128.0, 128.3, 128.4, 128.7, 129.1, 130.1, 130.4, 135.9, 139.9, 140.7, 140.8, 141.0, 141.5, 141.9, 149.0, 151.9, 159.0; HRMS (ESI) Calcd for $C_{31}H_{27}N_2O$ $[M + H]^+$ 443.2123, found 443.2127.

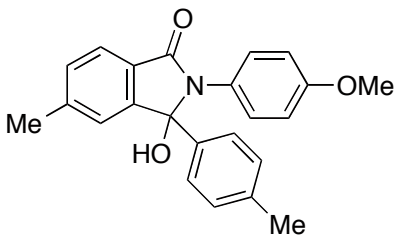
**Formation of Isoindolinones via Self-Coupling of Aldimine (Scheme 2)**

In a Schlenk tube were placed $CoBr_2$ (6.6 mg, 0.030 mmol), IPr•HCl (12.8 mg, 0.030 mmol), (*E*)-4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline (**2c**, 67.6 mg, 0.30 mmol), and THF (0.64 mL). To the mixture was added a THF solution of *t*BuCH$_2$MgBr (0.63 M, 0.86 mL, 0.54 mmol) dropwise at 0 °C. After stirring for 30 min, another portion of **2c** (67.6 mg, 0.30 mmol) was added. The resulting mixture was stirred at 60 °C for 6 h, and then allowed to room temperature. The reaction was quenched by the addition of ether (1 mL) and $H_2O$ (1 mL), followed by dilution with ethyl acetate (3 mL). The resulting mixture was stirred under air for 96 h, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluent: hexane/EtOAc = 5/1 to 3/1 to 1/1) to afford 2-(4-methoxyphenyl)-5-methyl-3-(*p*-tolyl)isoindolin-1-one (**5**, 16.3 mg, 16 %) and 3-hydroxy-2-(4-methoxyphenyl)-5-methyl-3-(*p*-tolyl)isoindolin-1-one (**6**, 52.8 mg, 49%) both as off-white solids. Note that GC-MS analysis of the crude mixture obtained just after quenching gave a major peak at *m*/*z* = 327, indicating the formation of isoindole **4** (see Scheme 2). Attempted isolation of **4** by silica gel chromatography was not successful, resulting in the formation of **5**, **6**, and other intractable products.

**2-(4-Methoxyphenyl)-5-methyl-3-(*p*-tolyl)isoindolin-1-one (5):** m.p. 161.3-162.4 ºC; $R_f$ 0.29 (hexane/EtOAc = 3/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.28 (s, 3H), 2.38 (s, 3H), 3.75 (s, 3H), 5.91 (s, 1H), 6.82 (app.d, *J* = 8.8 Hz, 2H), 7.01 (s, 1H), 7.04-7.09 (m, 4H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.42 (app.d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.3, 22.1, 55.5, 66.0, 114.3, 123.5, 123.9, 124.8, 127.3, 129.0, 129.7, 129.9, 130.9, 135.0, 138.3, 143.2, 146.4, 157.1, 168.1; HRMS (ESI) Calcd for $C_{23}H_{22}NO_2$ $[M + H]^+$ 344.1651, found 344.1650.



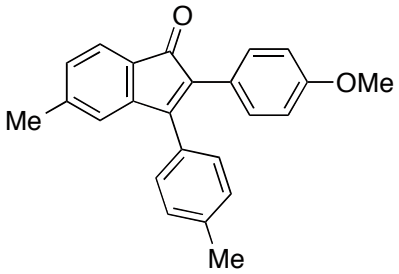

**3-Hydroxy-2-(4-methoxyphenyl)-5-methyl-3-(*p*-tolyl)isoindolin-1-one (6):** m.p. 208.8-210.1 ºC; $R_f$ 0.16 (hexane/EtOAc = 3/1); $^1$H NMR (400 MHz, DMSO-$d_6$): δ 2.21 (s, 3H), 2.34 (s, 3H), 3.68 (s, 3H), 6.82 (app.d, *J* = 9.2 Hz, 2H), 7.05-7.07 (m, 3H), 7.21 (app.d, *J* = 8.4 Hz, 2H), 7.32-7.36 (m, 3H), 7.44 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, DMSO-$d_6$): δ 21.1, 21.8, 55.6, 92.4, 114.0, 123.3, 123.5, 126.5, 128.0, 129.4 (two signals overlapping), 129.7, 130.5, 137.4,



137.7, 143.8, 150.6, 157.6, 166.8; HRMS (ESI) Calcd for $C_{23}H_{22}NO_3$ $[M + H]^+$ 360.1600, found 360.1596.

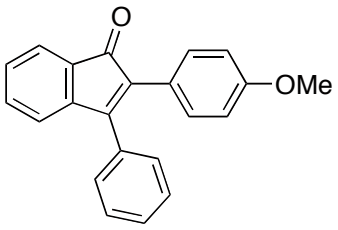
**Synthesis of Indenones via Self-Coupling of Aldimines (Scheme 2 and Table 2)**

**A Typical Procedure: 2-(4-Methoxyphenyl)-5-methyl-3-(*p*-tolyl)-1*H*-inden-1-one (7a).** In a Schlenk tube were placed $CoBr_2$ (6.6 mg, 0.030 mmol), IPr•HCl (12.8 mg, 0.030 mmol), (*E*)-4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline (**2c**, 67.6 mg, 0.30 mmol), and THF (0.71 mL). To the mixture was added a THF solution of *t*BuCH$_2$MgBr (0.68 M, 0.79 mL, 0.54 mmol) dropwise at 0 °C. After stirring for 30 min, another portion of **2c** (67.6 mg, 0.30 mmol) was added. The resulting mixture was stirred at room temperature for 12 h, followed by the addition of $H_2O$ (0.3 mL) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). After stirring for 1 h, aq. HCl (3 M, 1 mL) was added, and the resulting mixture was stirred at 60 °C for 12 h. The reaction was cooled to room temperature, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluent: hexane/EtOAc = 50/1) to afford the title compound as a red solid (72.0 mg, 71% based on **2c**).




**7a:** m.p. 173.5-174.3 ºC; $R_f$ 0.40 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.35 (s, 3H), 2.42 (s, 3H), 3.80 (s, 3H), 6.82 (app.d, $J$ = 8.8 Hz, 2H), 6.94 (s, 1H), 7.05 (d, $J$ = 7.2 Hz, 1H), 7.23-7.27 (m, 4H), 7.29 (app.d, $J$ = 8.0 Hz, 2H), 7.46 (d, $J$ = 7.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.7, 22.3, 55.3, 113.8, 122.4, 123.0, 123.6, 128.6 (two signals overlapping), 128.7, 129.7, 130.3, 131.4, 132.1, 139.3, 144.4, 146.2, 153.8, 159.2, 196.9; HRMS (ESI) Calcd for $C_{24}H_{21}O_2$ $[M + H]^+$ 341.1542, found 341.1540.

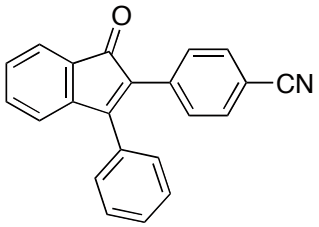
**2-(4-Methoxyphenyl)-3-phenyl-1*H*-inden-1-one (7b):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded the title compound as a light red solid (64.0 mg, 68%).




m.p. 116.8-117.5 ºC (lit. 118-119 °C);[2] $R_f$ 0.47 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz,

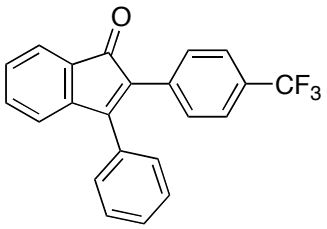
$CDCl_3$): δ 3.79 (s, 3H), 6.81 (app.d, *J* = 8.8 Hz, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 7.24-7.28 (m, 3H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.39-7.44 (m, 5H), 7.57 (d, *J* = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.4, 113.8, 121.1, 123.0, 123.3, 128.7, 128.8, 129.0, 129.3, 130.9, 131.5, 132.1, 133.2, 133.6, 145.7, 154.0, 159.4, 197.2; HRMS (ESI) Calcd for $C_{22}H_{17}O$ $[M + H]^+$ 313.1229, found 313.1226.

**4-(1-Oxo-3-phenyl-1*H*-inden-2-yl)benzonitrile (7c):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 4-cyanobenzaldehyde (78.7 mg, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 25/1) of the crude product afforded the title compound as a red solid (63.6 mg, 69%).



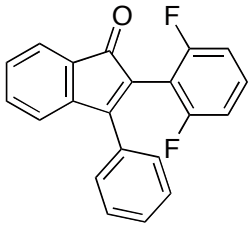

m.p. 139.1-139.9 ºC (lit. 142-144 °C);[3] $R_f$ 0.27 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 7.2 Hz, 1H), 7.34-7.37 (m, 4H), 7.38-7.41 (m, 2H), 7.43-7.47 (m, 3H), 7.53 (app.d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 7.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 111.2, 119.0, 122.1, 123.5, 128.5, 129.3, 129.9, 130.2, 130.5 (two signals overlapping), 130.7, 132.0, 132.1, 134.0, 135.9, 144.7, 158.0, 195.6; HRMS (ESI) Calcd for $C_{22}H_{14}NO$ $[M + H]^+$ 308.1075, found 308.1078.

**3-Phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-inden-1-one (7d):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 4-trifluoromethylbenzaldehyde (82 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 100/1) of the crude product afforded the title compound as a light red oil (66.3 mg, 63%).



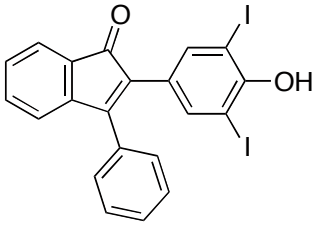

$R_f$ 0.53 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 7.18 (d, *J* = 7.2 Hz, 1H), 7.31-7.35 (m, 1H), 7.36-7.42 (m, 5H), 7.43-7.46 (m, 3H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 121.9, 123.5, 124.4 (q, $^1J_{C\text{-}H}$ =248 Hz), 125.2 (q, $^3J_{C\text{-}H}$ =4.0 Hz), 128.4 (q, $^2J_{C\text{-}H}$ =30 Hz), 128.6, 129.3, 129.7, 130.0, 130.2, 130.4, 130.8, 132.4, 133.9, 134.7, 145.0, 157.3, 196.0; HRMS (ESI) Calcd for $C_{22}H_{14}F_3O$ $[M + H]^+$ 351.0997, found 351.0999.

**2-(2,6-Difluorophenyl)-3-phenyl-1*H*-inden-1-one (7e):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 2,6-difluorobenzaldehyde (65 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded the title compound as a yellow solid (76.6 mg, 80%).



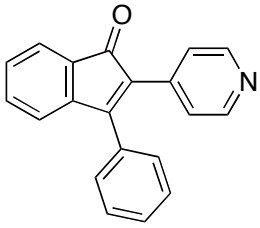

m.p. 133.3-134.5 ºC; $R_f$ 0.50 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 6.85-6.89 (m, 2H), 7.25-7.30 (m, 2H), 7.32-7.36 (m, 1H), 7.40-7.44 (m, 6H), 7.63 (d, $J$ = 6.8 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 109.2 (t, $^2J_{C\text{-}F}$ = 10 Hz), 111.7 (dd, $^2J_{C\text{-}F}$ = 19 Hz, $^4J_{C\text{-}F}$ = 6 Hz), 122.0, 123.5, 127.8, 128.9, 129.6, 130.1, 130.4 (t, $^3J_{C\text{-}F}$ = 10 Hz), 131.5, 132.6, 133.5, 144.8, 144.8, 160.1, 161.0 (dd, $^1J_{C\text{-}F}$ = 249 Hz, $^3J_{C\text{-}F}$ = 7 Hz), 194.4; HRMS (ESI) Calcd for $C_{21}H_{13}F_2O$ $[M + H]^+$ 319.0934, found 319.0933.

**2-(4-Methoxyphenyl)-3-phenyl-1*H*-inden-1-one (7f):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 3,5-diiodo-4-hydroxybenzaldehyde (224.3 mg, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 3/1) of the crude product afforded the title compound as a dark red solid (91.5 mg, 55%).




m.p. 177.2-178.4 ºC; $R_f$ 0.55 (hexane/EtOAc = 3/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 5.82 (brs, 1H), 7.13 (d, $J$ = 4.8 Hz, 1H), 7.30 (d, $J$ = 7.2 Hz, 1H), 7.36-7.39 (m, 3H), 7.46-7.47 (m, 3H), 7.57 (d, $J$ = 6.8 Hz, 1H), 7.59 (s, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 81.9, 121.7, 123.3, 127.2, 128.5, 128.8, 129.2, 129.5, 130.0, 130.6, 132.2, 133.9, 140.7, 145.0, 153.2, 156.0, 196.1; HRMS (ESI) Calcd for $C_{21}H_{13}I_2O_2$ $[M + H]^+$ 550.9005, found 550.9000.

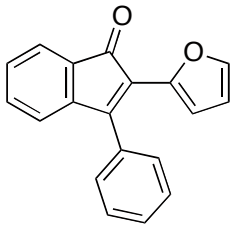
**3-Phenyl-2-(pyridin-4-yl)-1*H*-inden-1-one (7g):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and 4-pyridinecaboxaldehyde (56 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 5/1) of the crude product afforded the title compound as an orange solid (64.9 mg, 76%).




m.p. 131.3-132.5 ºC; $R_f$ 0.20 (hexane/EtOAc = 3/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 7.17-7.18 (m, 3H), 7.34-7.47 (m, 7H), 7.61 (dd, $J$ = 7.2, 0.8 Hz, 1H), 8.49 (d, $J$ = 2.4 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 122.2, 123.5, 124.4, 128.4, 129.3, 129.7, 130.0, 130.2, 130.8, 132.0, 133.9, 138.9, 144.7, 149.8, 158.7, 195.4; HRMS (ESI) Calcd for $C_{20}H_{14}NO$ $[M + H]^+$ 284.1075,

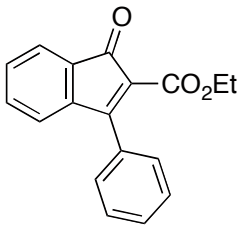
found 284.1078.

**2-(Furan-2-yl)-3-phenyl-1*H*-inden-1-one (7h):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and furfural (50 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded the title compound as a dark red solid (27.3 mg, 33%).



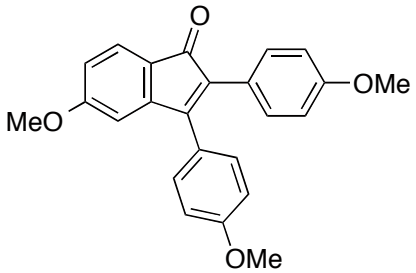
m.p. 92.3-93.7 ºC; $R_f$ 0.55 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 6.43-6.44 (m, 1H), 7.02 (d, $J$ = 7.2 Hz, 1H), 7.13 (d, $J$ = 3.2 Hz, 1H), 7.22 (t, $J$ = 7.2 Hz, 1H), 7.26-7.27 (m, 1H), 7.32 (td, $J$ = 7.6, 0.8 Hz, 1H), 7.47-7.50 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 111.7, 112.7, 121.7, 122.1, 123.2, 128.4, 128.8, 128.9, 129.4, 131.0, 133.2, 134.0, 143.1, 146.6, 147.3, 150.9, 195.2; HRMS (ESI) Calcd for $C_{19}H_{13}O_2$ $[M + H]^+$ 273.0916, found 273.0916.

**Ethyl 1-oxo-3-phenyl-1*H*-indene-2-carboxylate (7i):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 126.8 mg, 0.60 mmol) and ethyl glyoxalate (50% solution in toluene, 120 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 30/1–10/1) of the crude product afforded the title compound as a yellow solid (34.0 mg, 41%).



m.p. 84.0-84.8 ºC (lit. 87-88 °C);[4] $R_f$ 0.20 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 1.16 (t, $J$ = 7.2 Hz, 3H), 4.20 (q, $J$ = 6.8 Hz, 2H), 7.19-7.21 (m, 1H), 7.39-7.42 (m, 2H), 7.50-7.54 (m, 5H), 7.59-7.61 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 14.1, 61.1, 123.6, 124.6, 128.3, 128.6, 130.6 (two signals overlapping) 130.7, 131.2, 131.7, 133.7, 143.3, 163.2, 165.1, 192.3; HRMS (ESI) Calcd for $C_{18}H_{15}O_3$ $[M + H]^+$ 279.1021, found 279.1019.

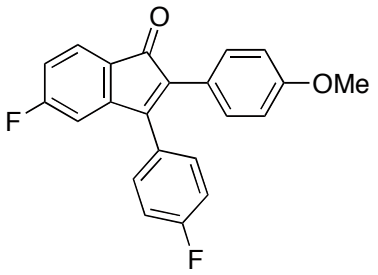
**5-Methoxy-2,3-bis(4-methoxyphenyl)-1*H*-inden-1-one (7j):** The typical procedure was applied to (*E*)-4-methoxy-*N*-(4-methoxybenzylidene)aniline (**2d**, 144.8 mg, 0.60 mmol) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 15/1 – 5/1) of the crude product afforded the title compound as an orange solid (94.9 mg, 81%).



m.p. 169.4-170.1 ºC (lit. 173-175 °C); [5] $R_f$ 0.21 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.78 (s, 3H), 3.81 (s, 3H), 3.83 (s, 3H),

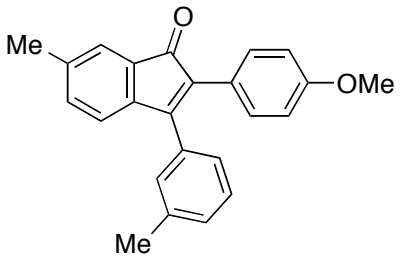
6.63 (dd, $J$ = 8.0, 2.0 Hz, 1H), 6.70 (d, $J$ = 2.0 Hz, 1H), 6.81 (app.d, $J$ = 8.8 Hz, 2H), 6.92 (app.d, $J$ = 8.8 Hz, 2H), 7.24 (d, $J$ = 9.2 Hz, 2H), 7.32 (d, $J$ = 8.8 Hz, 2H), 7.50 (d, $J$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.3, 55.4, 55.8, 110.0, 110.3, 113.7, 114.3, 123.7, 123.8, 124.7, 125.2, 130.3, 131.4, 132.7, 148.2, 151.7, 159.2, 160.3, 164.4, 195.7; HRMS (ESI) Calcd for $C_{24}H_{21}O_4$ $[M + H]^+$ 373.1440, found 373.1439. The $^1$H and $^{13}$C NMR spectra showed good agreement with the literature data.[6]

**5-Fluoro-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-1*H*-inden-1-one (7k):** The typical procedure was applied to (*E*)-*N*-(4-fluorobenzylidene)-4-methoxyaniline (**2e**, 137.6 mg, 0.60 mmol) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded the title compound as a light red solid (59.6 mg, 57%).




m.p. 180.4-181.3 ºC; $R_f$ 0.38 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.79 (s, 3H), 6.78-6.83 (m, 3H), 6.87-6.92 (m, 1H), 7.10-7.15 (m, 2H), 7.20-7.22 (m, 2H), 7.34-7.38 (m, 2H), 7.54 (dd, $J$ = 8.0, 5.2 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.4, 109.8 (d, $^2J_{C\text{-}F}$ = 26 Hz), 114.0, 114.4 (d, $^2J_{C\text{-}F}$ = 23 Hz), 116.4 (d, $^2J_{C\text{-}F}$ = 21 Hz), 122.7, 125.0 (d, $^3J_{C\text{-}F}$ = 9 Hz), 126.6 (d, $^4J_{C\text{-}F}$ = 3 Hz), 128.7 (d, $^4J_{C\text{-}F}$ = 3 Hz), 130.6 (d, $^3J_{C\text{-}F}$ = 9 Hz), 131.5, 133.6, 148.9 (d, $^3J_{C\text{-}F}$ = 9 Hz), 150.6, 159.7, 162.3 (d, $^1J_{C\text{-}F}$ = 249 Hz), 166.7 (d, $^1J_{C\text{-}F}$ = 253 Hz), 195.2; HRMS (ESI) Calcd for $C_{22}H_{15}F_2O_2$ $[M + H]^+$ 349.1040, found 349.1035.

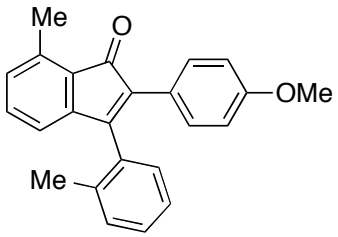
**2-(4-Methoxyphenyl)-6-methyl-3-(*m*-tolyl)-1*H*-inden-1-one (7l):** The typical procedure was applied to (*E*)-4-methoxy-*N*-(3-methylbenzylidene)aniline (**2f**, 135.2 mg, 0.60 mmol) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 50/1) of the crude product afforded a mixture of the title compound and its minor regioisomer (2-(4-methoxyphenyl)-4-methyl-3-(*m*-tolyl)-1*H*-inden-1-one) as a dark red solid (67.1 mg, 66%). The ratio of the regioisomers was determined to be 2.7:1 by $^1$H NMR analysis.




$R_f$ 0.48 (hexane/EtOAc = 8/1); $^1$H NMR (400 MHz, $CDCl_3$, major isomer): δ 2.36 (s, 3H), 2.37 (s, 3H), 3.79 (s, 3H), 6.81 (d, $J$ = 8.8 Hz, 2H), 6.99 (d, $J$ = 7.6 Hz, 1H), 7.10-7.16 (m, 2H), 7.17-7.26 (m, 3H), 7.28 (s, 1H), 7.32 (t, $J$ = 7.2 Hz, 1H), 7.38 (s, 1H); $^{13}$C NMR (100 MHz,

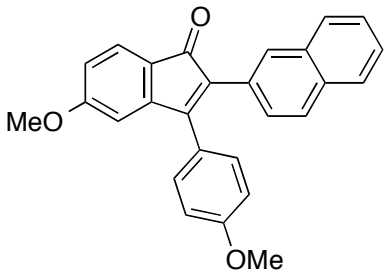
$CDCl_3$): δ 21.5, 21.6, 55.3, 113.7 (two signals overlapping), 121.0, 123.5, 124.1, 125.8, 128.6, 129.0, 130.0, 131.2, 131.28, 131.33, 133.5, 138.6, 139.0, 143.0, 154.5, 159.2, 197.6; HRMS (ESI) Calcd for $C_{24}H_{21}O_2$ $[M + H]^+$ 341.1542, found 341.1537.

**2-(4-Methoxyphenyl)-7-methyl-3-(*o*-tolyl)-1*H*-inden-1-one (7m):** The typical procedure was applied to (*E*)-4-methoxy-*N*-(2-methylbenzylidene)aniline (**2g**, 135.2 mg, 0.60 mmol) and 4-methoxybenzaldehyde (73 μL, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 100/1) of the crude product afforded the title compound as a light red oil (21.7 mg, 21%).



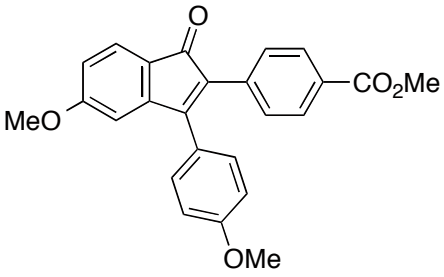

$R_f$ 0.45 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.09 (s, 3H), 2.64 (s, 3H), 3.78 (s, 3H), 6.62 (d, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.26-7.36 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 17.5, 20.1, 55.3, 113.8, 119.1, 124.1, 126.4, 126.9, 128.4, 128.8, 130.6, 131.0, 132.06, 132.14, 133.1, 133.4, 136.0, 137.8, 146.8, 153.4, 159.3, 198.5; HRMS (ESI) Calcd for $C_{24}H_{21}O_2$ $[M + H]^+$ 341.1542, found 341.1537.

**5-Methoxy-3-(4-methoxyphenyl)-2-(naphthalen-2-yl)-1*H*-inden-1-one (7n):** The typical procedure was applied to (*E*)-4-methoxy-*N*-(4-methoxybenzylidene)aniline (**2d**, 144.8 mg, 0.60 mmol) and 2-naphthaldehyde (93.7 mg, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 10/1 – 5/1) of the crude product afforded the title compound as a red solid (84.2 mg, 72%).



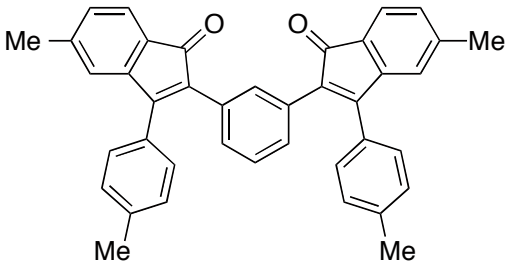

m.p. 59.6-60.8 ºC; $R_f$ 0.18 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.83 (s, 3H), 3.85 (s, 3H), 6.69 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.80 (d, *J* = 2.0 Hz, 1H), 6.90 (app.d, *J* = 8.8 Hz, 2H), 7.23 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.35 (app.d, *J* = 8.8 Hz, 2H), 7.44-7.47 (m, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.76-7.78 (m, 1H), 7.80-7.82 (m, 1H), 7.97 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 55.4, 55.9, 110.4, 110.7, 114.4, 124.0, 124.9, 125.0, 126.1, 126.4, 127.5, 127.6, 127.7, 128.6, 128.9, 129.9, 130.5, 132.8, 133.0, 133.4, 148.0, 153.4, 160.6, 164.5, 195.3; HRMS (ESI) Calcd for $C_{27}H_{21}O_3$ $[M + H]^+$ 393.1491, found 393.1496.

**Methyl 4-(5-methoxy-3-(4-methoxyphenyl)-1-oxo-1*H*-inden-2-yl)benzoate (7o):** The typical procedure was applied to (*E*)-4-methoxy-*N*-(4-methoxybenzylidene)aniline (**2d**, 144.8 mg, 0.60 mmol) and methyl 4-formylbenzoate (98.5 mg, 0.60 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 10/1 – 3/1) of the crude product afforded the title compound as an orange solid (88.7 mg, 74%).




m.p. 114.3-115.6 ºC; $R_f$ 0.30 (hexane/EtOAc = 3/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 3.825 (s, 3H), 3.833 (s, 3H), 3.88 (s, 3H), 6.68 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.91 (app.d, *J* = 8.8 Hz, 2H), 7.27 (app.d, *J* = 8.8 Hz 2H), 7.35 (app.d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.92 (app.d, *J* = 8.4 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 52.2, 55.5, 55.9, 110.8, 111.0, 114.5, 123.8, 124.4, 125.0, 129.0, 129.4, 130.1, 130.3, 132.1, 136.3, 147.5, 154.8, 160.8, 164.5, 167.1, 194.6; HRMS (ESI) Calcd for $C_{25}H_{21}O_5$ $[M + H]^+$ 401.1389, found 401.1386.

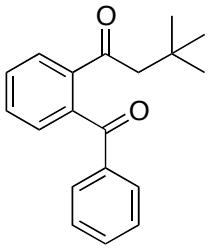
**2,2'-(1,3-Phenylene)bis(5-methyl-3-(*p*-tolyl)-1*H*-inden-1-one) (7p):** In a Schlenk tube were placed $CoBr_2$ (13.2 mg, 0.060 mmol), IPr•HCl (23.6 mg, 0.060 mmol), (*E*)-4-methoxy-*N*-(1-(*p*-tolyl)ethylidene)aniline (**2c**, 135.2 mg, 0.60 mmol), and THF (1.42 mL). To the mixture was added a THF solution of $(CH_3)_3CCH_2MgBr$ (0.68 M, 1.58 mL, 1.08 mmol) dropwise at 0 °C. After stirring for 30 min, another portion of **2c** (135.2 mg, 0.60 mmol) was added. The resulting mixture was stirred at room temperature for 12 h, followed by the addition of $H_2O$ (0.6 mL) and isophthalaldehyde (26.8 mg, 0.20 mmol). After stirring for 1 h, aq. HCl (3 M, 2 mL) was added, and the resulting mixture was stirred at 100 ºC for 12 h. The reaction was cooled to room temperature, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluent: hexane/EtOAc = 3/1) to afford the title compound as a dark red solid (75.3 mg, 69% based on isophthalaldehyde).




m.p. 193.4-194.5 ºC; $R_f$ 0.15 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 2.34 (s, 6H), 2.40 (s, 6H), 7.00 (s, 2H), 7.06 (d, *J* = 7.2 Hz, 2H), 7.09-7.12 (m, 3H), 7.21-7.26 (m, 8H), 7.32 (s, 1H), 7.44 (d, *J* = 7.2 Hz, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 21.7, 22.3, 122.7, 123.1,

127.9, 128.7 (two signals overlapping), 129.0, 129.4, 129.6, 129.9, 131.2, 131.8, 132.6, 139.5, 144.3, 145.9, 155.3, 196.2; HRMS (ESI) Calcd for $C_{40}H_{31}O_2$ $[M + H]^+$ 543.2324, found 543.2325.

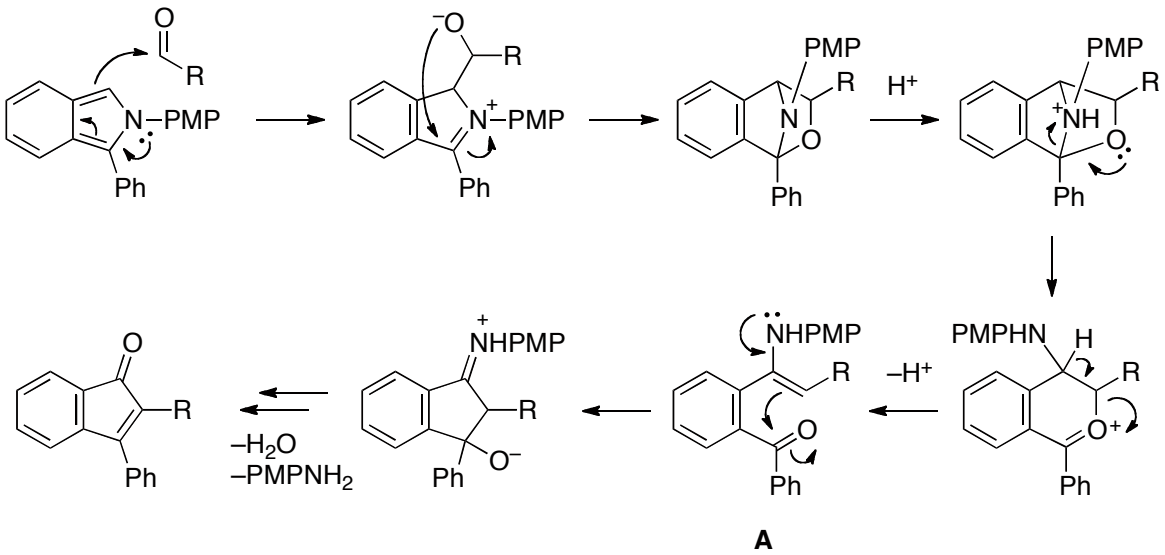
**1-(2-Benzoylphenyl)-3,3-dimethylbutan-1-one (7q):** The typical procedure was applied to (*E*)-*N*-benzylidene-4-methoxyaniline (**2b**, 63.4 mg, 0.30 mmol) and pivalaldehyde (65 μL, 0.6 mmol). Silica gel chromatography (eluent: hexane/EtOAc = 20/1–5/1) of the crude product afforded the title compound as a red oil (39.0 mg, 46%).



*R*$_f$ 0.20 (hexane/EtOAc = 10/1); $^1$H NMR (400 MHz, $CDCl_3$): δ 0.94 (s, 9H), 2.75 (s, 2H), 7.39-7.42 (m, 3H), 7.50-7.54 (m, 1H), 7.55-7.59 (m, 2H), 7.72-7.74 (m, 2H), 7.82-7.84 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 29.8, 31.7, 51.5, 128.5, 128.7, 129.0, 129.6, 129.8, 131.7, 133.0, 137.6, 139.9, 141.0, 198.0, 201.3; HRMS (ESI) Calcd for $C_{19}H_{21}O_2$ $[M + H]^+$ 281.1542, found 281.1545.

**Proposed Mechanism for the Formation of Indenone**

Below is shown a possible mechanism for the formation of indene, which is similar to that proposed for the reaction of isobenzofuran and benzaldehyde by Kuninobu and Takai.[6] Formation of the diketone product **7q** from pivalaldehyde can be explained by hydrolysis of the intermediate **A**.




**Scheme S1.** Proposed mechanism for the condensation of isoindole and aldehyde

(1) (a) Mongin, F.; Mojovic, L.; Guillamet, B.; Trécourt, F.; Quéguiner, G. *J. Org. Chem.* **2002**, *67*, 8991. (b) Rebstock, A.-S.; Mongin, F.; Trécourt, F.; Quéguiner, G. *Tetrahedron* **2003**, *59*, 4973.

(2) Bergman, E. D. *J. Org. Chem.* **1956**, *21*, 461.

(3) Koelsch, C. F. *J. Am. Chem. Soc.* **1936**, *58*, 1331.

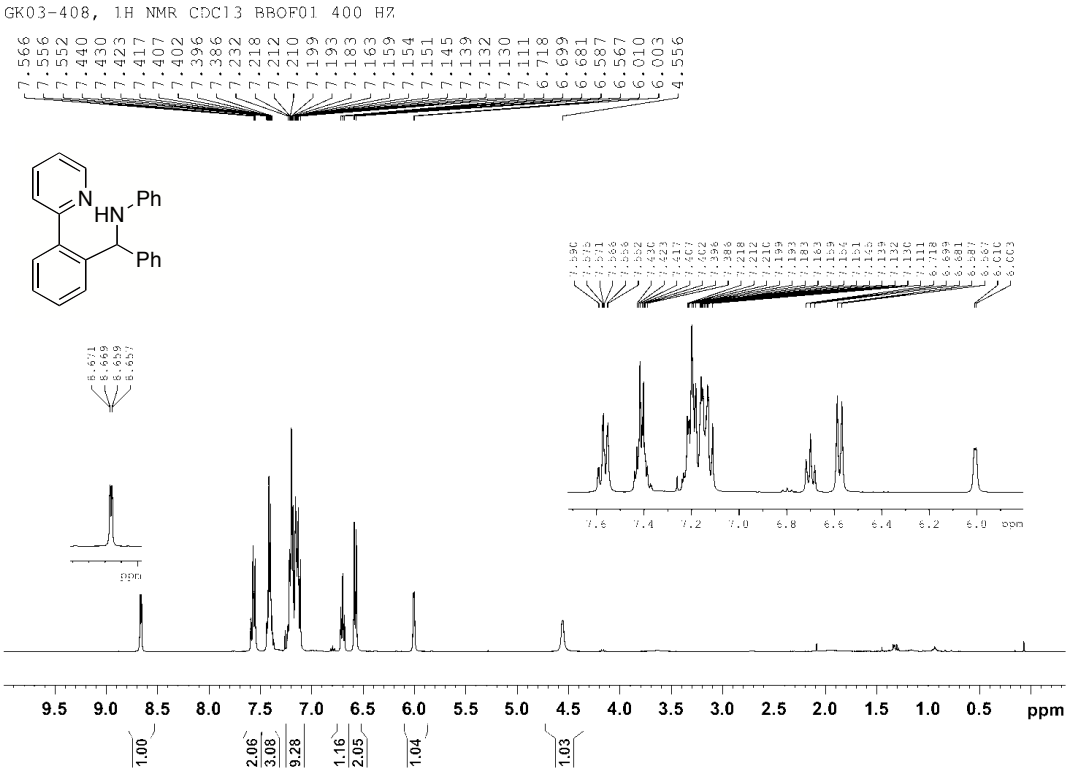
(4) Yost, W. L.; Burger, A. *J. Org. Chem.* **1950**, *15*, 1113.

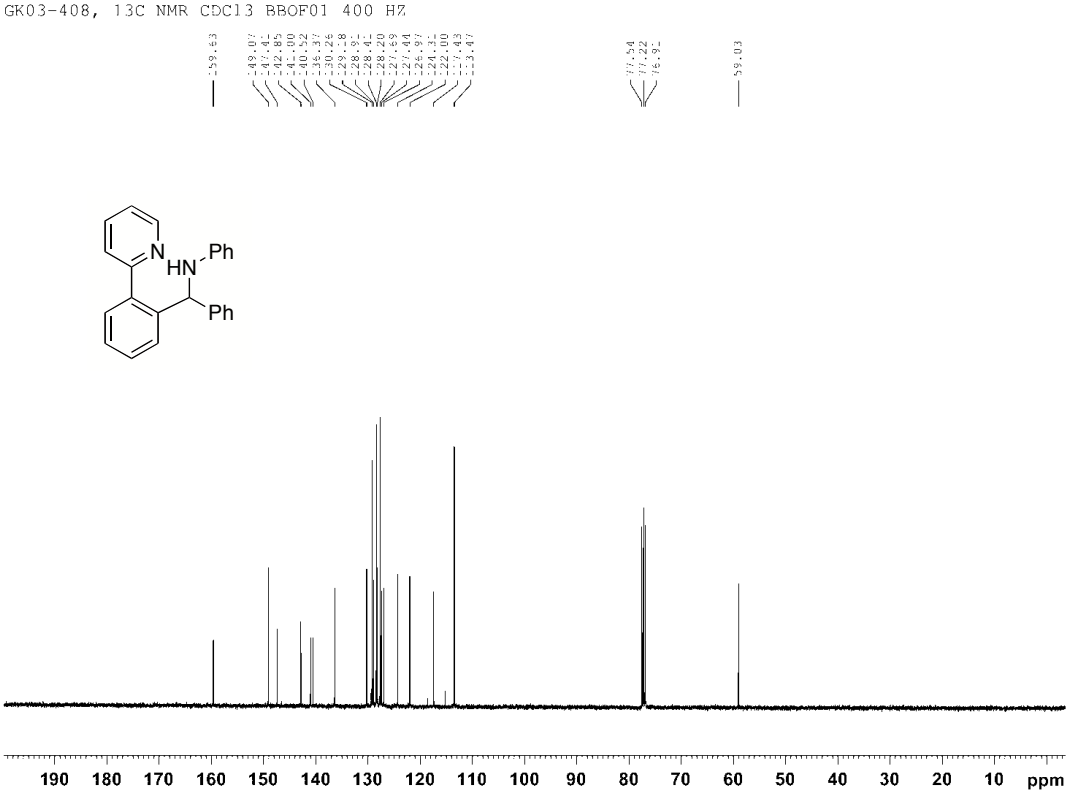
(5) Neunhoeffer, v. H.; Vötter, H.-D.; Gais-Mutterer, M. *Tetrahedron Lett.* **1973**, *14*, 219.

(6) Kuninobu, Y.; Matsuki, T.; Takai, K. *Org. Lett.* **2010**, *12*, 2948.

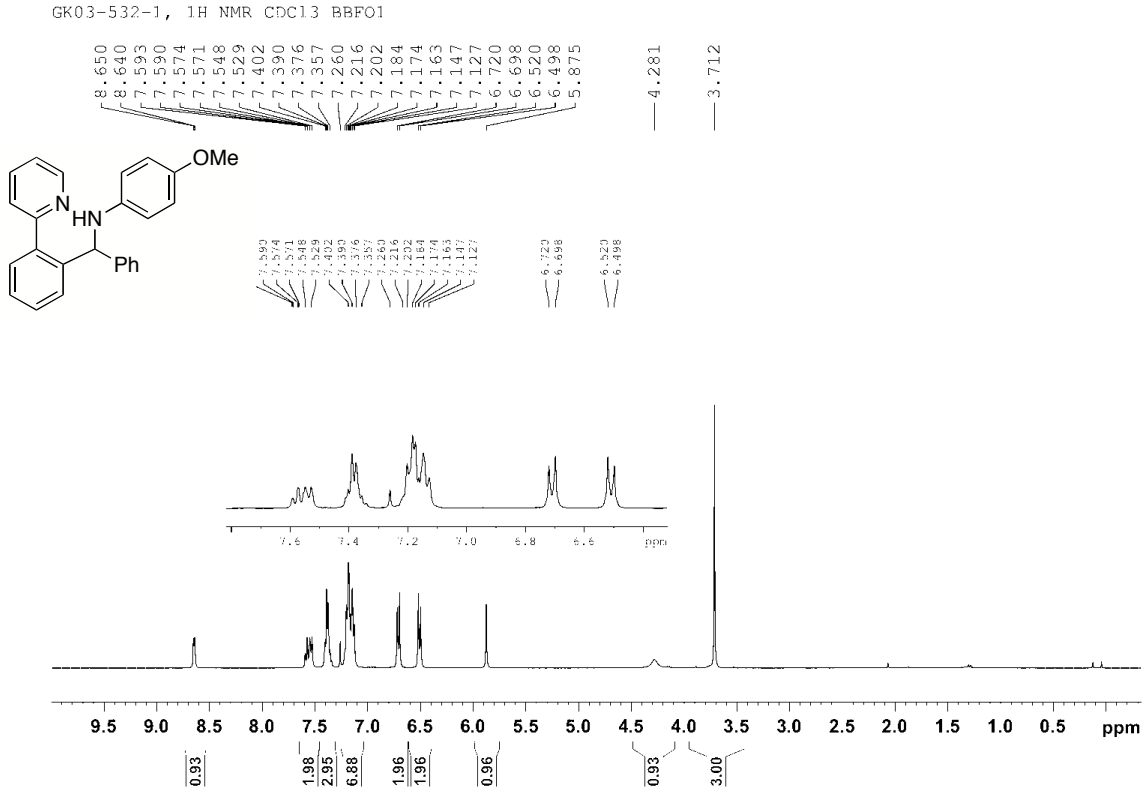
# NMR Spectra

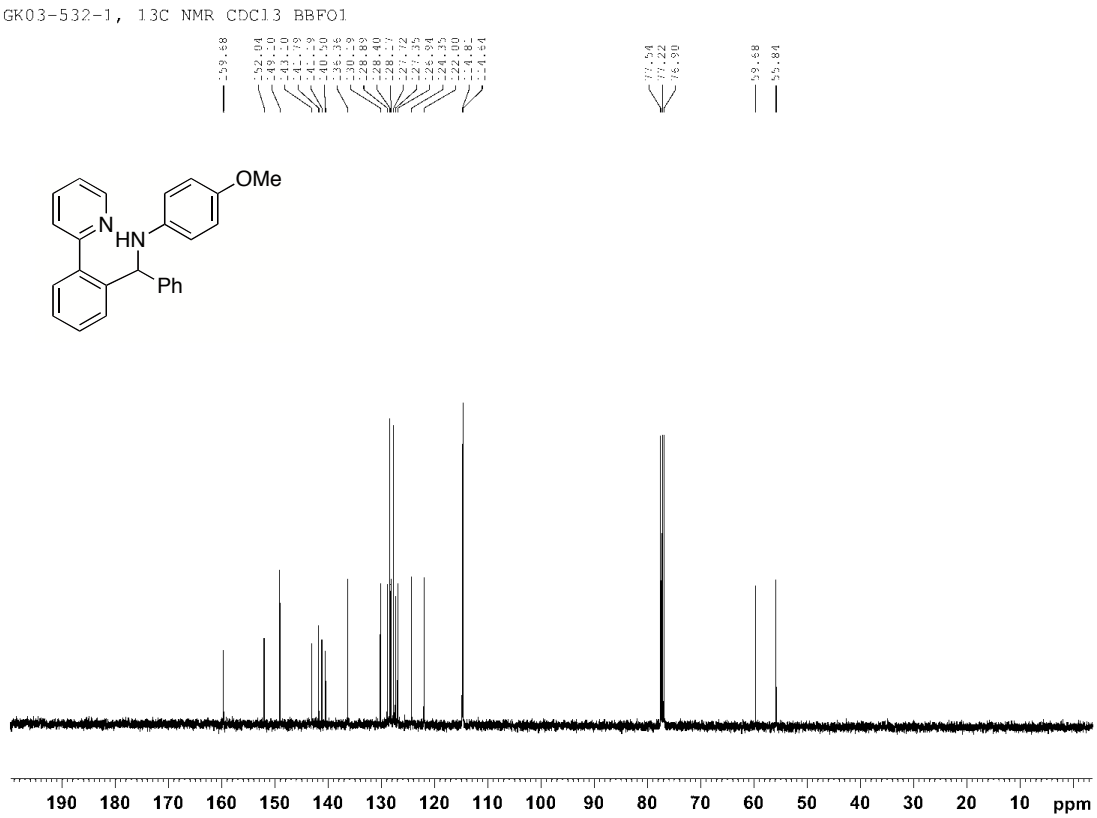
## 3a



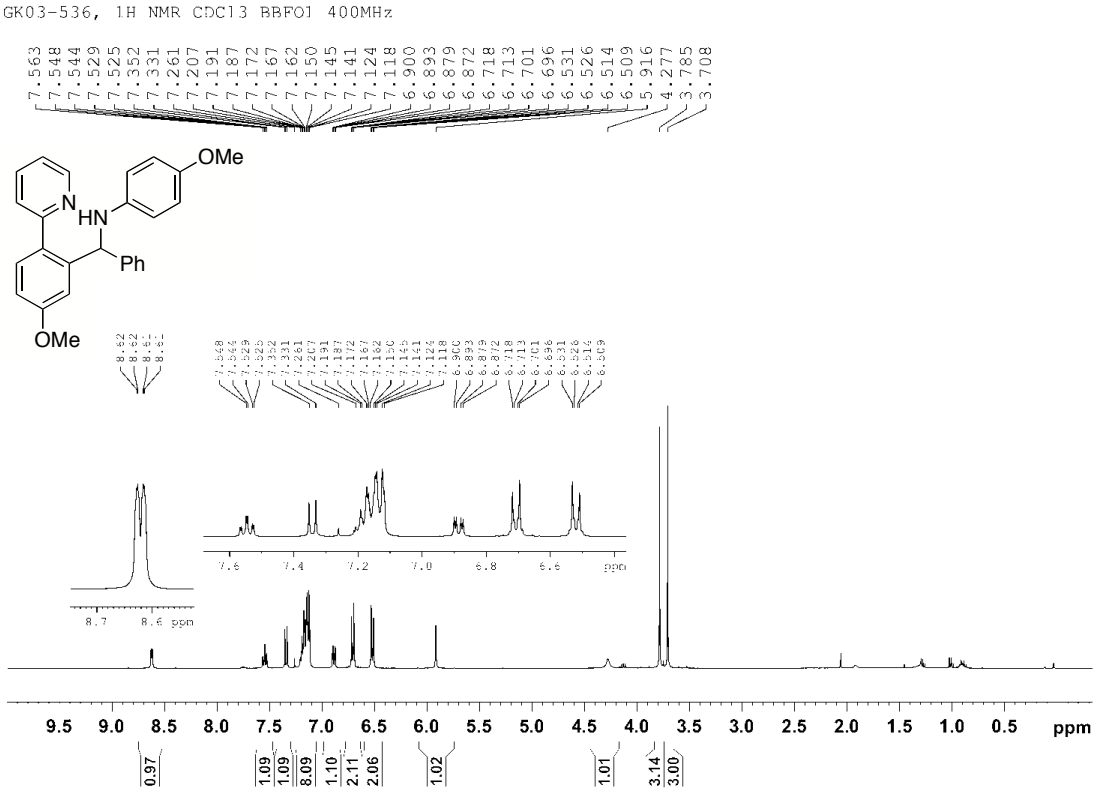



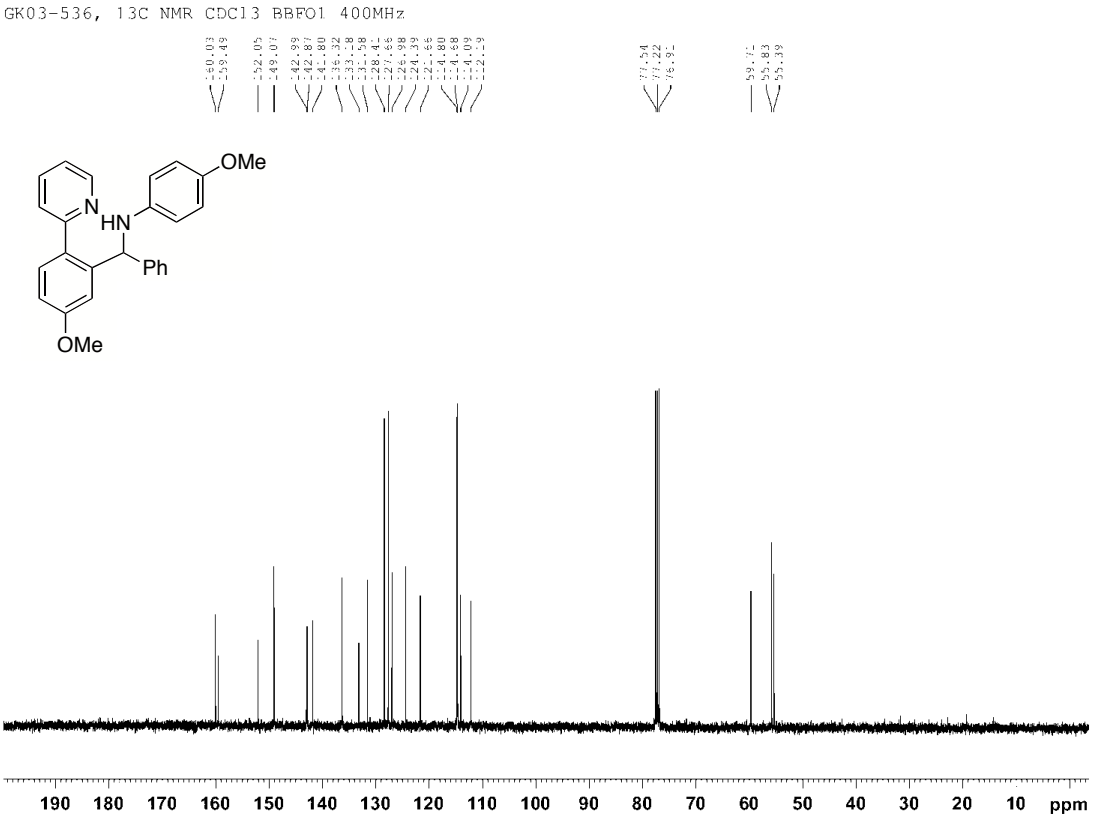
**3b**


GK03-532-1, 1H NMR CDCl3 BBFO1
8.650
8.640
7.593
7.590
7.574
7.571
7.548
7.529
7.402
7.390
7.376
7.357
7.260
7.216
7.202
7.184
7.174
7.163
7.147
7.127
6.720
6.698
6.520
6.498
5.875
4.281
3.712
OMe
N
HN
Ph
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
0.93
1.98
2.95
6.88
1.96
1.96
0.96
0.93
3.00

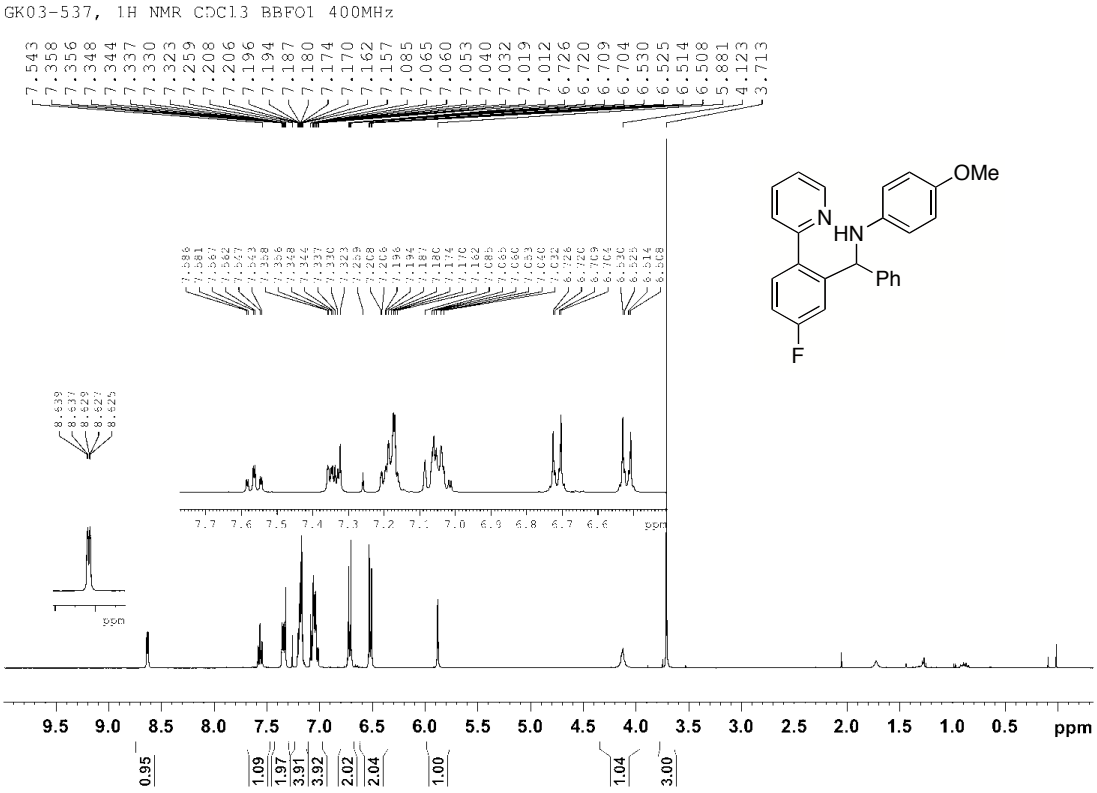

GK03-532-1, 13C NMR CDCl3 BBFO1
159.68
152.04
149.20
143.20
141.79
141.19
140.50
136.36
130.69
128.89
128.40
128.17
127.72
127.35
126.94
124.35
122.00
114.81
114.64
77.54
77.22
76.90
59.68
55.84
OMe
N
HN
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

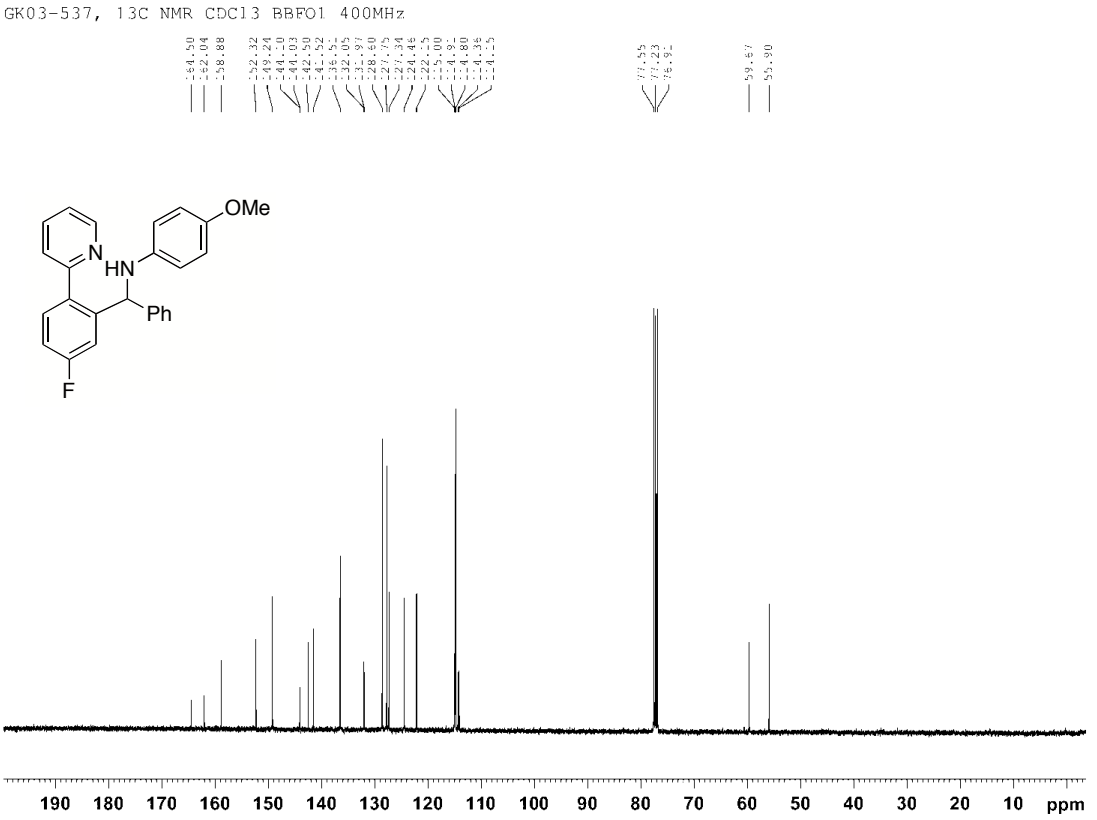
**3c**


GK03-536, 1H NMR CDCl3 BBFO1 400MHz
OMe
N
HN
Ph
OMe
ppm

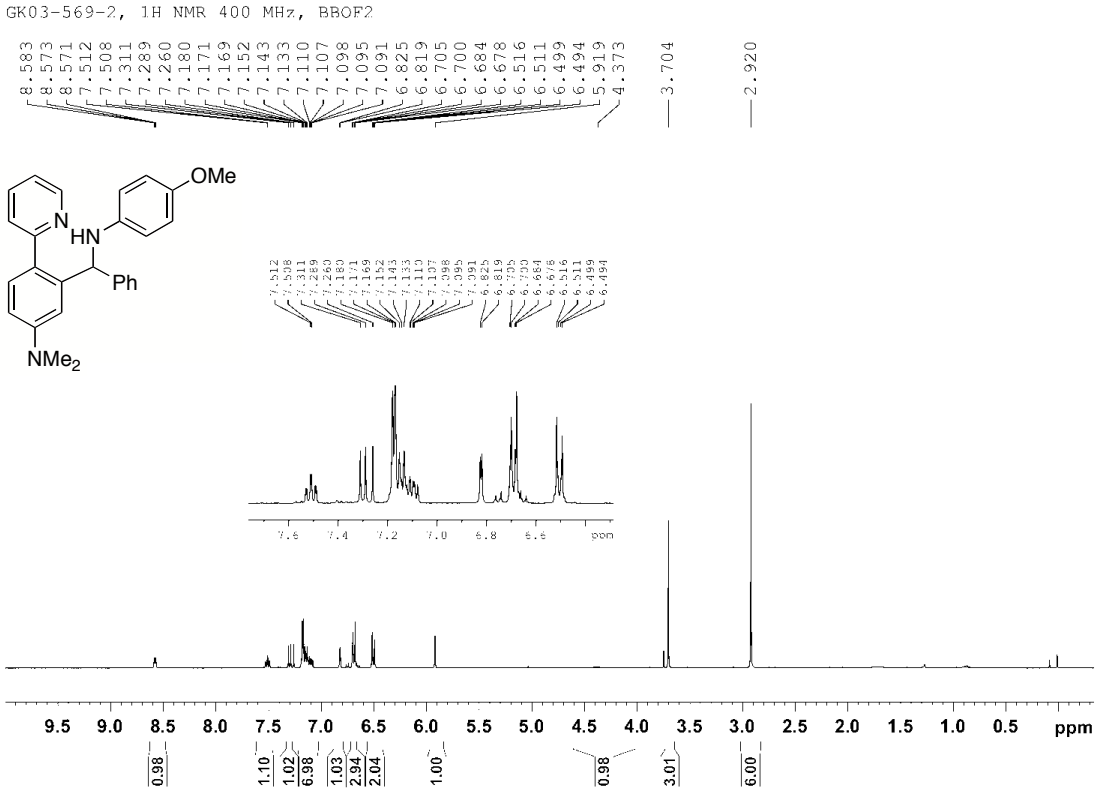

GK03-536, 13C NMR CDCl3 BBFO1 400MHz
OMe
N
HN
Ph
OMe
ppm

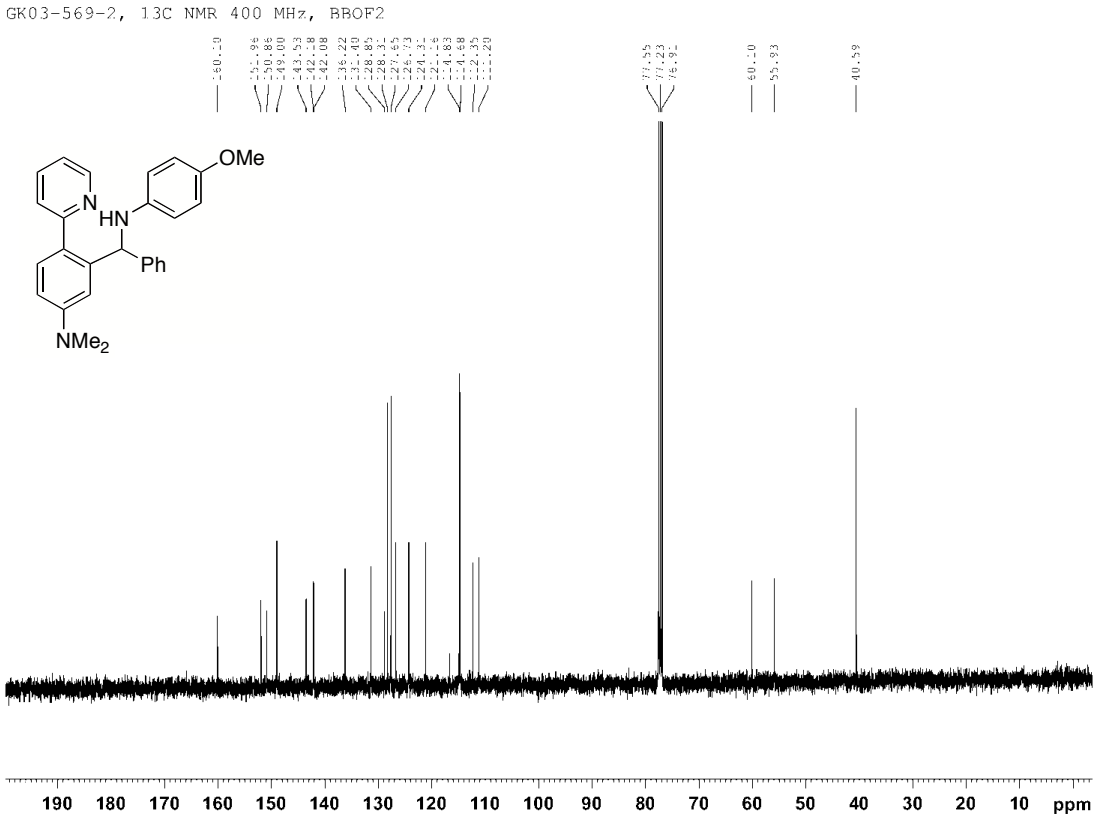
**3d**


GK03-537, 1H NMR CDCl3 BBFO1 400MHz
OMe
N
HN
Ph
F
ppm

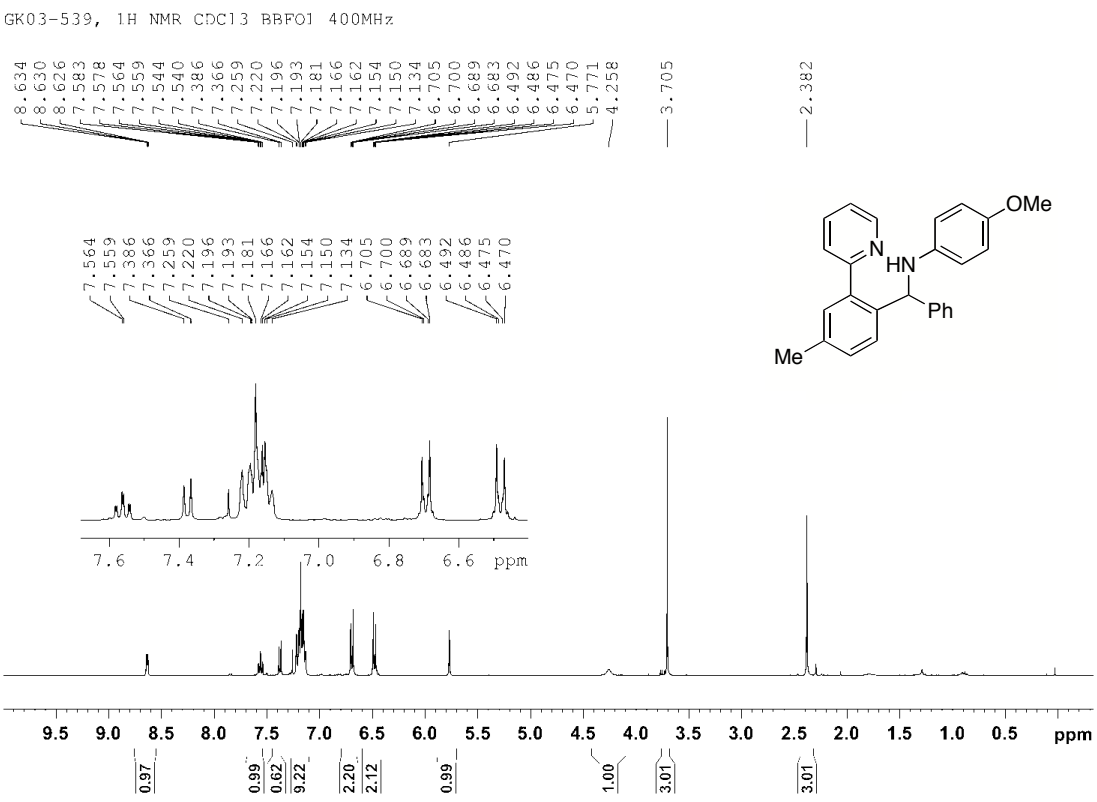

GK03-537, 13C NMR CDCl3 BBFO1 400MHz
OMe
N
HN
Ph
F
ppm

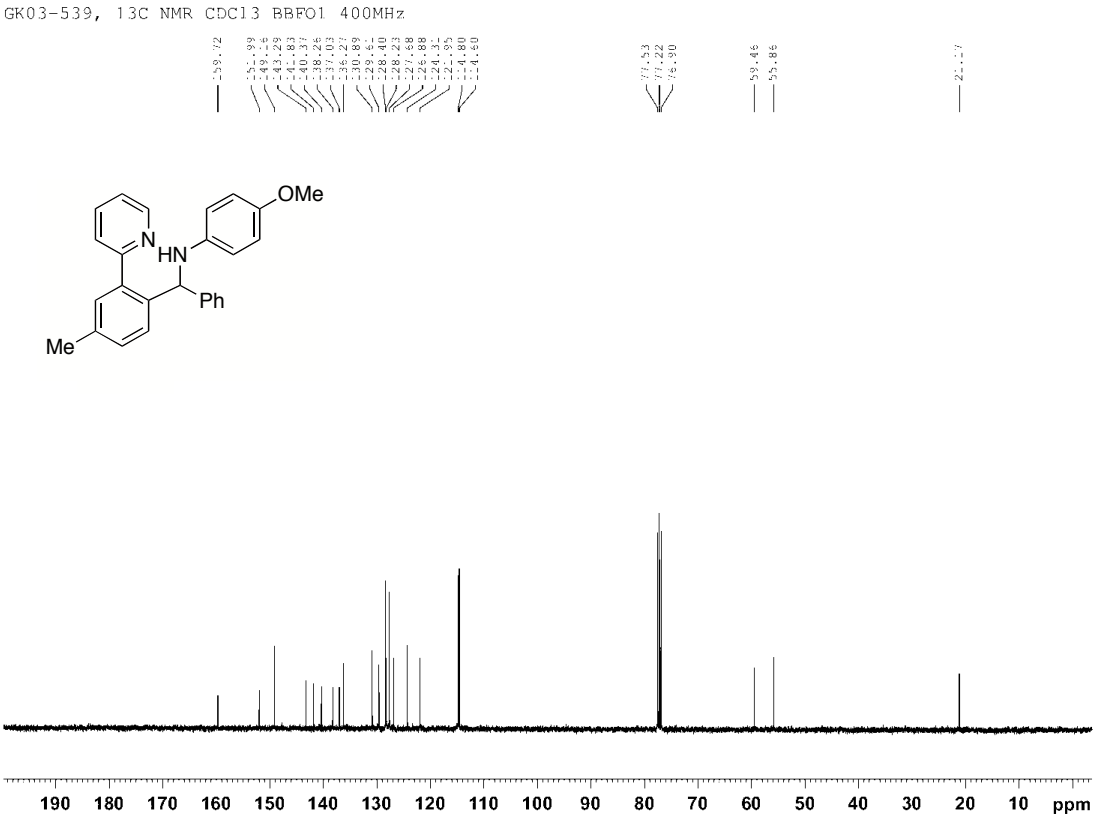
**3e**


GK03-569-2, 1H NMR 400 MHz, BBOF2
8.583
8.573
8.571
7.512
7.508
7.311
7.289
7.260
7.180
7.171
7.169
7.152
7.143
7.133
7.110
7.107
7.098
7.095
7.091
6.825
6.819
6.705
6.700
6.684
6.678
6.516
6.511
6.499
6.494
5.919
4.373
3.704
2.920
OMe
N
HN
Ph
NMe2
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
1.10
1.02
6.98
1.03
2.94
2.04
1.00
0.98
3.01
6.00

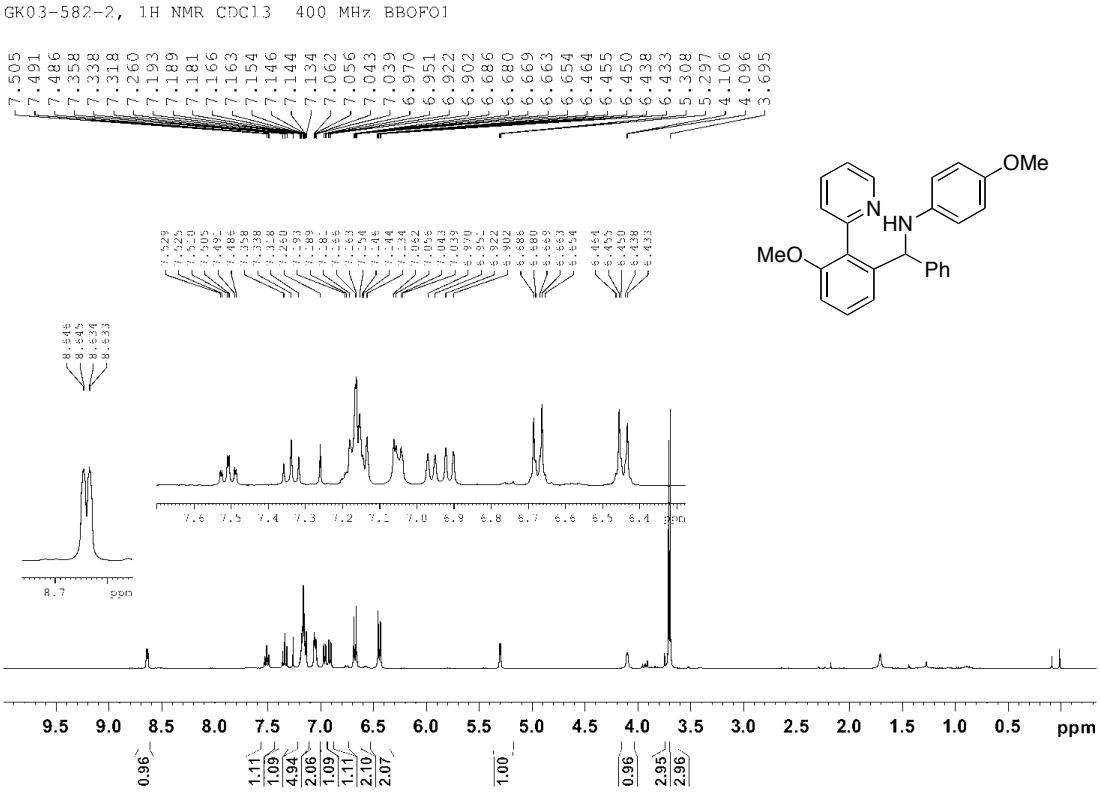

GK03-569-2, 13C NMR 400 MHz, BBOF2
160.19
135.96
130.86
129.00
143.53
142.18
142.08
136.22
131.40
128.85
128.32
127.65
126.73
126.32
124.83
124.68
122.35
122.20
77.55
77.23
76.92
60.10
55.93
40.59
OMe
N
HN
Ph
NMe2
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

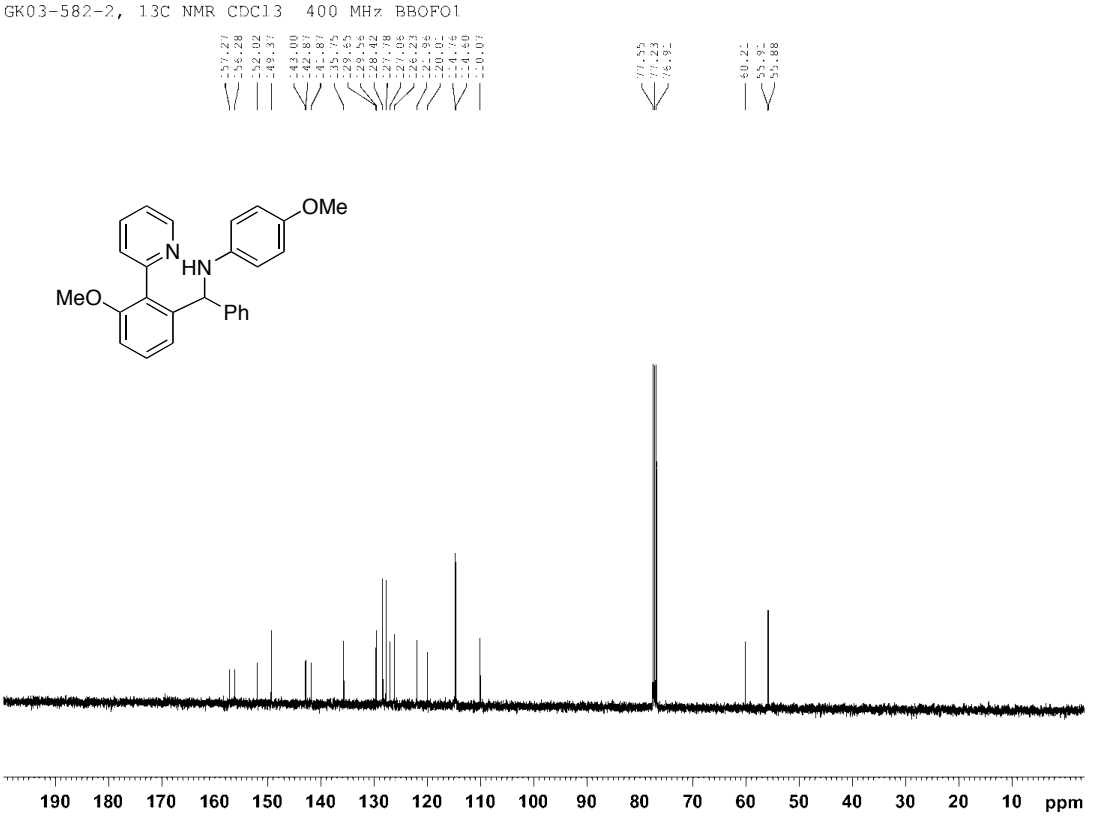
**3f**


GK03-539, 1H NMR CDCl3 BBFO1 400MHz
8.634
8.630
8.626
7.583
7.578
7.564
7.559
7.544
7.540
7.386
7.366
7.259
7.220
7.196
7.193
7.181
7.166
7.162
7.154
7.150
7.134
6.705
6.700
6.689
6.683
6.492
6.486
6.475
6.470
5.771
4.258
3.705
2.382
OMe
N
HN
Ph
Me
7.6
7.4
7.2
7.0
6.8
6.6
ppm
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
0.97
0.99
0.62
9.22
2.20
2.12
0.99
1.00
3.01
3.01

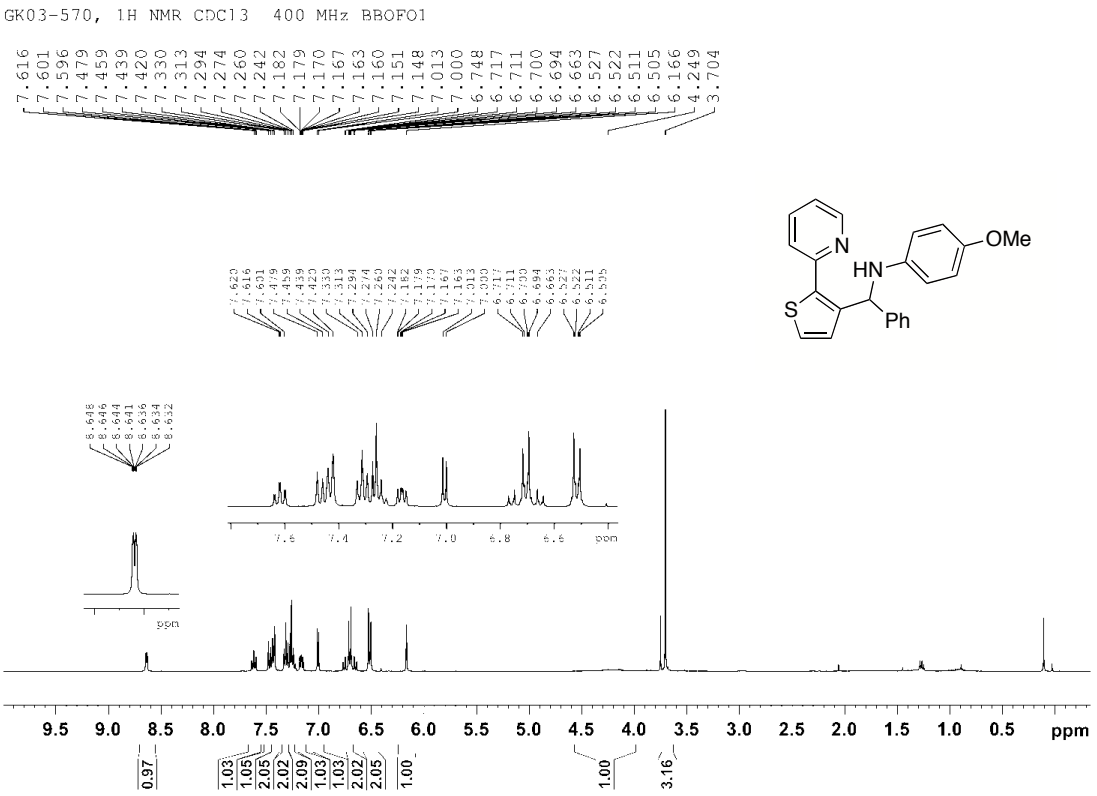

GK03-539, 13C NMR CDCl3 BBFO1 400MHz
OMe
N
HN
Ph
Me
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

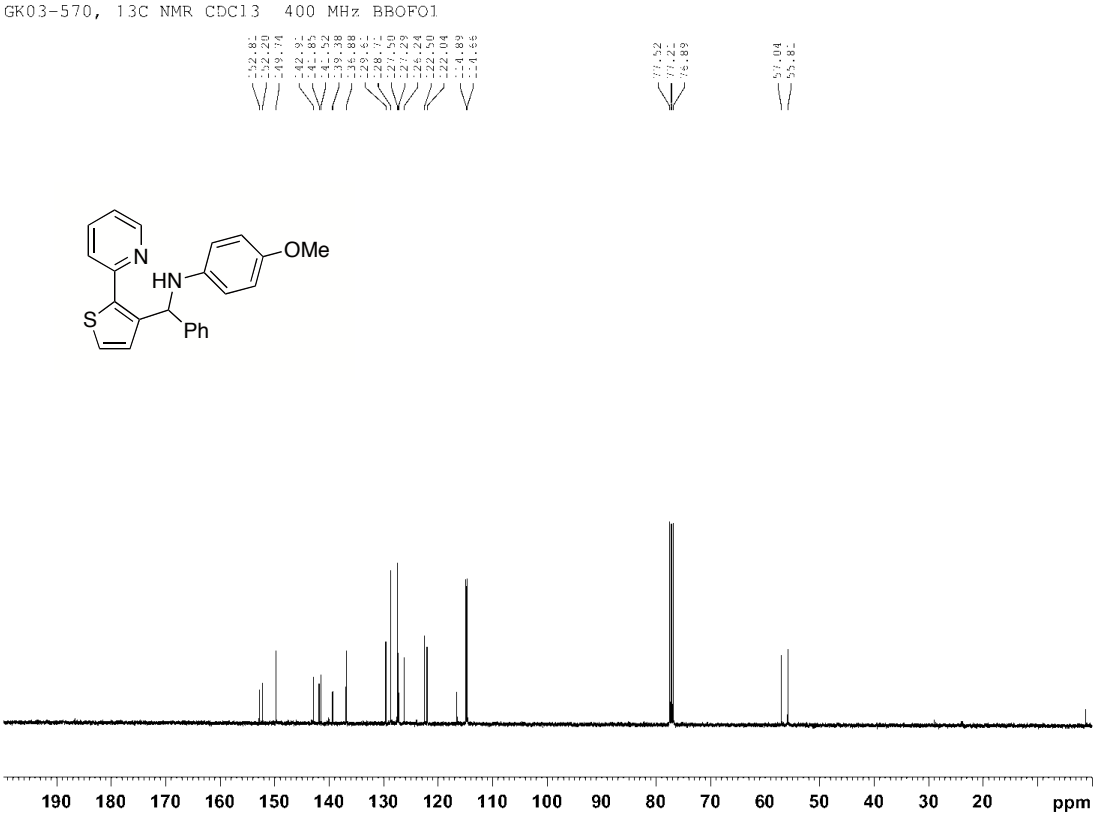
**3g**


GK03-582-2, 1H NMR CDCl3 400 MHz BBOFO1
OMe
N
HN
MeO
Ph
ppm

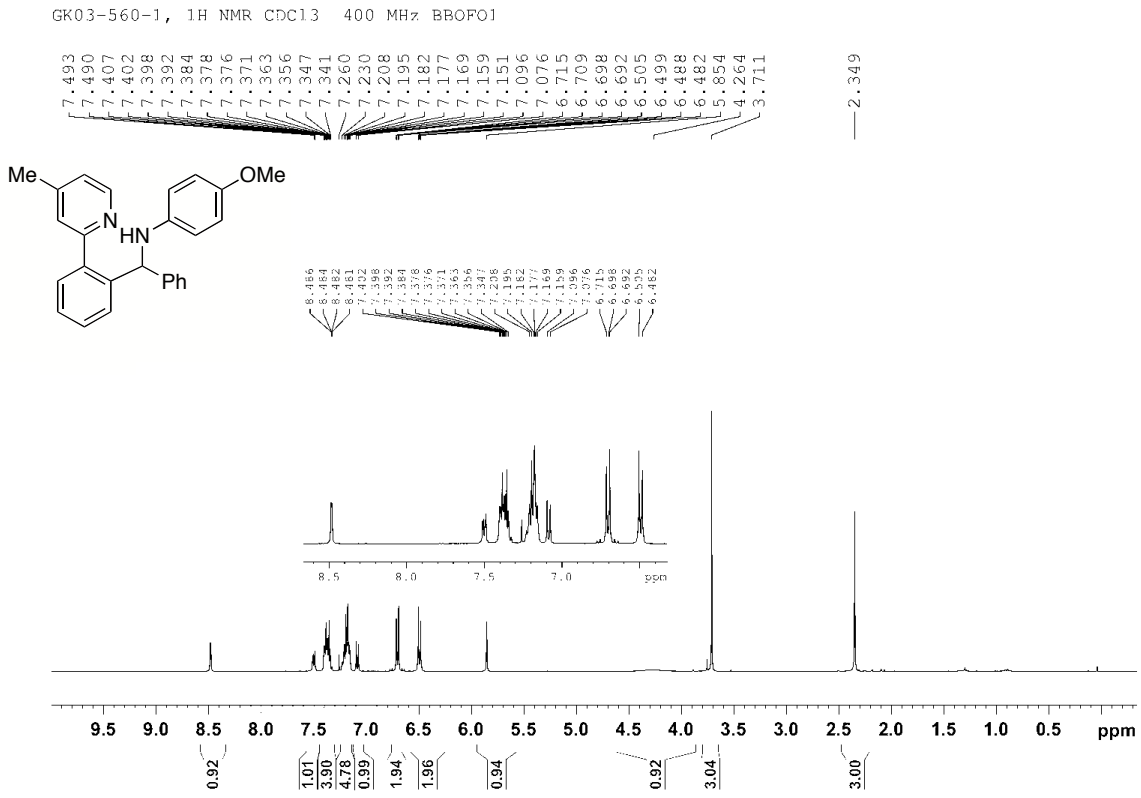

GK03-582-2, 13C NMR CDCl3 400 MHz BBOFO1
OMe
N
HN
MeO
Ph
ppm

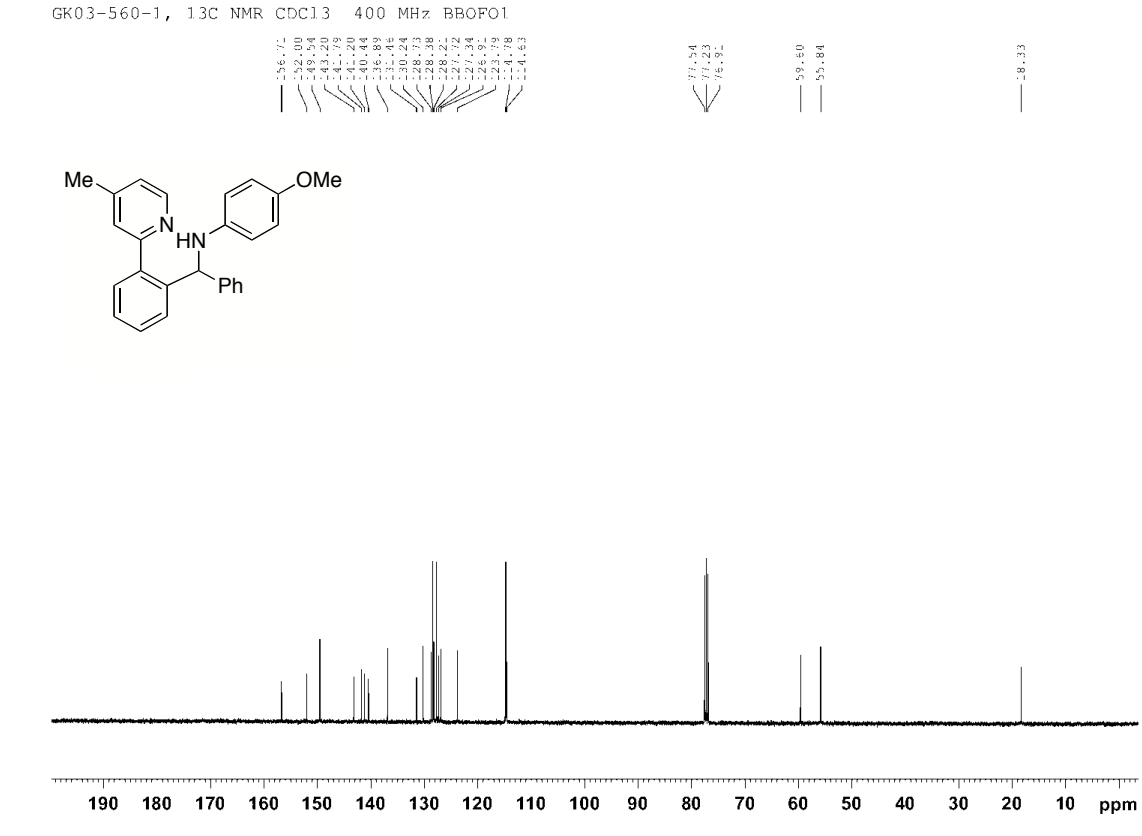
**3h**


GK03-570, 1H NMR CDCl3 400 MHz BBOFO1
N
HN
OMe
S
Ph
ppm


GK03-570, 13C NMR CDCl3 400 MHz BBOFO1
N
HN
OMe
S
Ph
ppm

**3i**


GK03-560-1, 1H NMR CDCl3 400 MHz BBOFO1
Me
OMe
N
HN
Ph
ppm
0.92
1.01
3.90
4.78
0.99
1.94
1.96
0.94
0.92
3.04
3.00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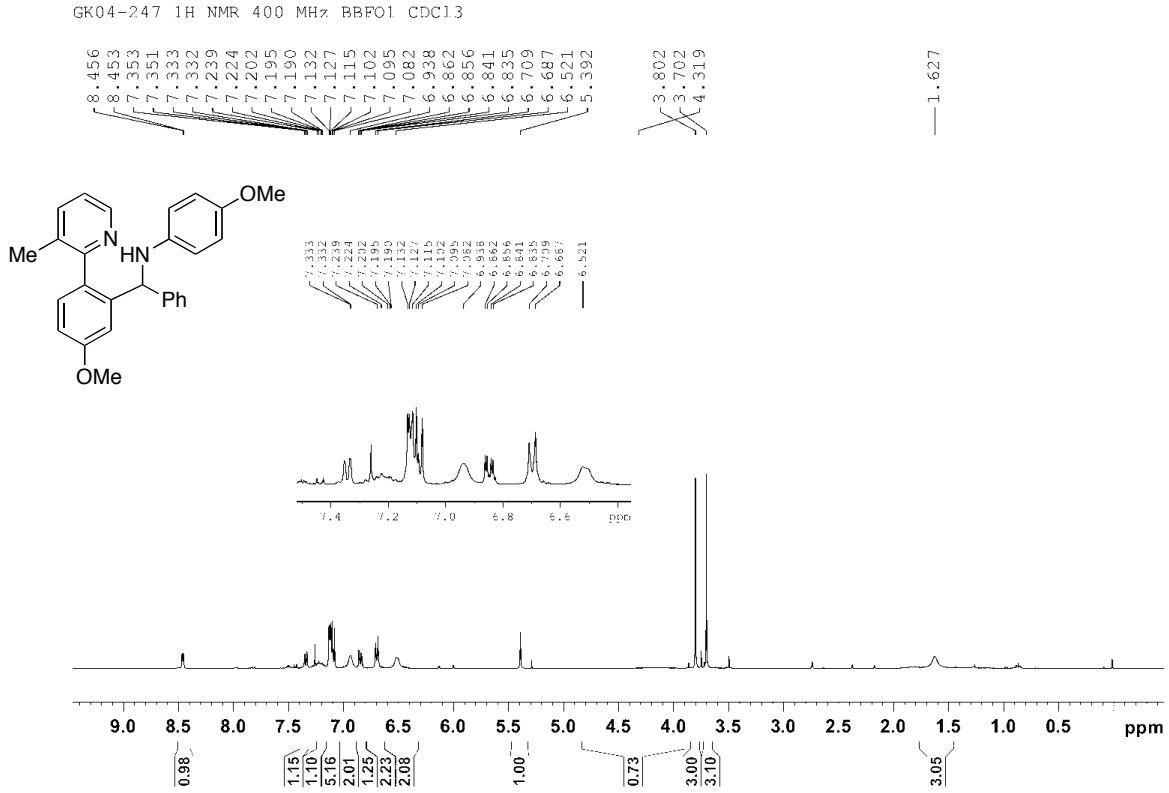
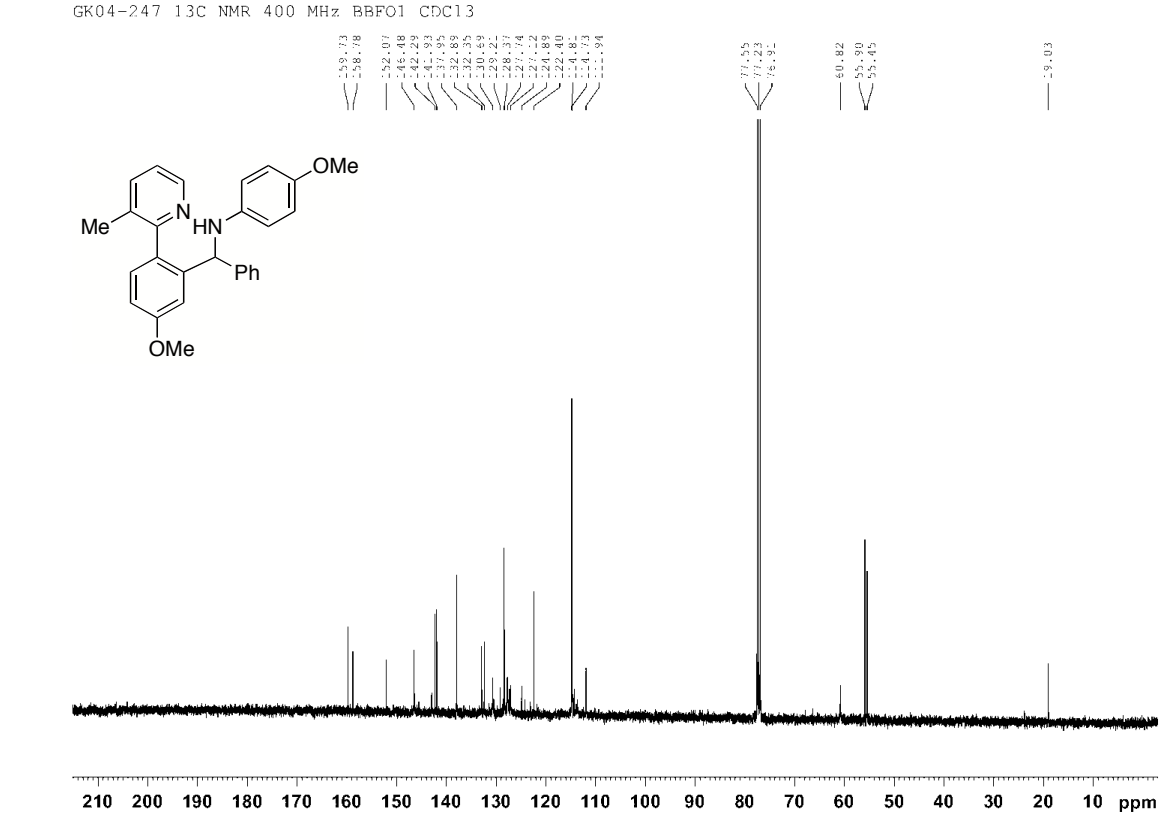
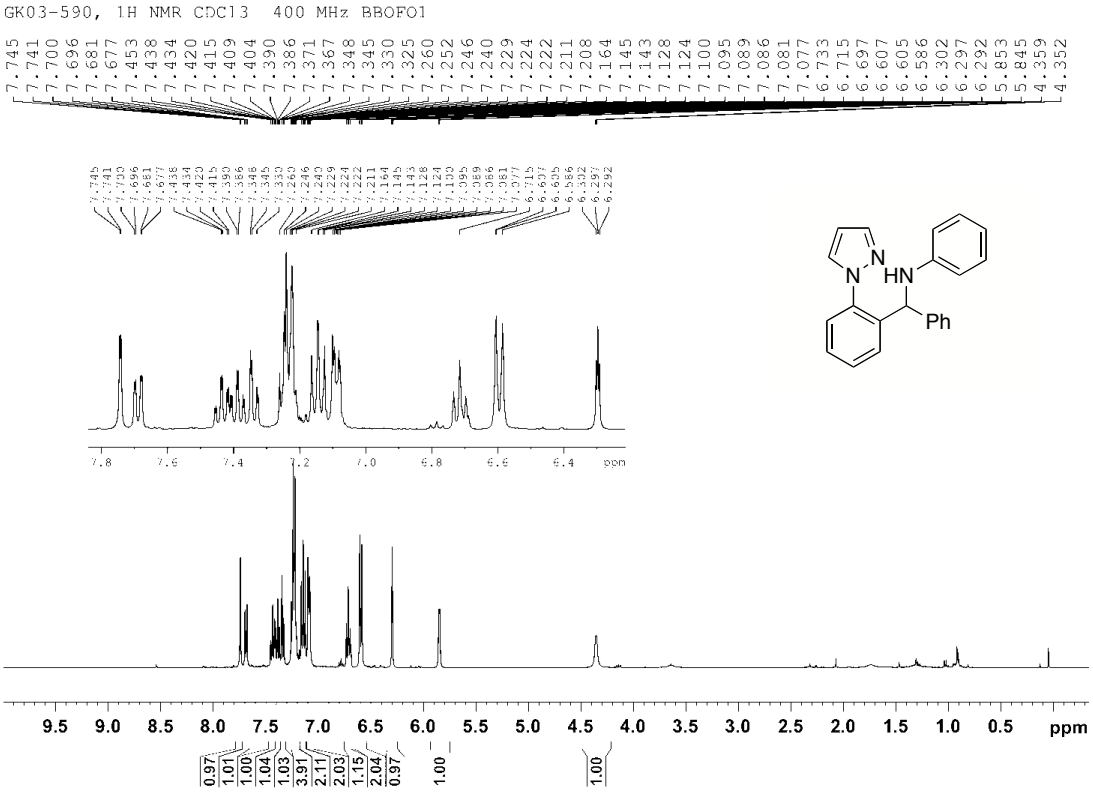
Me
OMe
N
HN
Ph
ppm

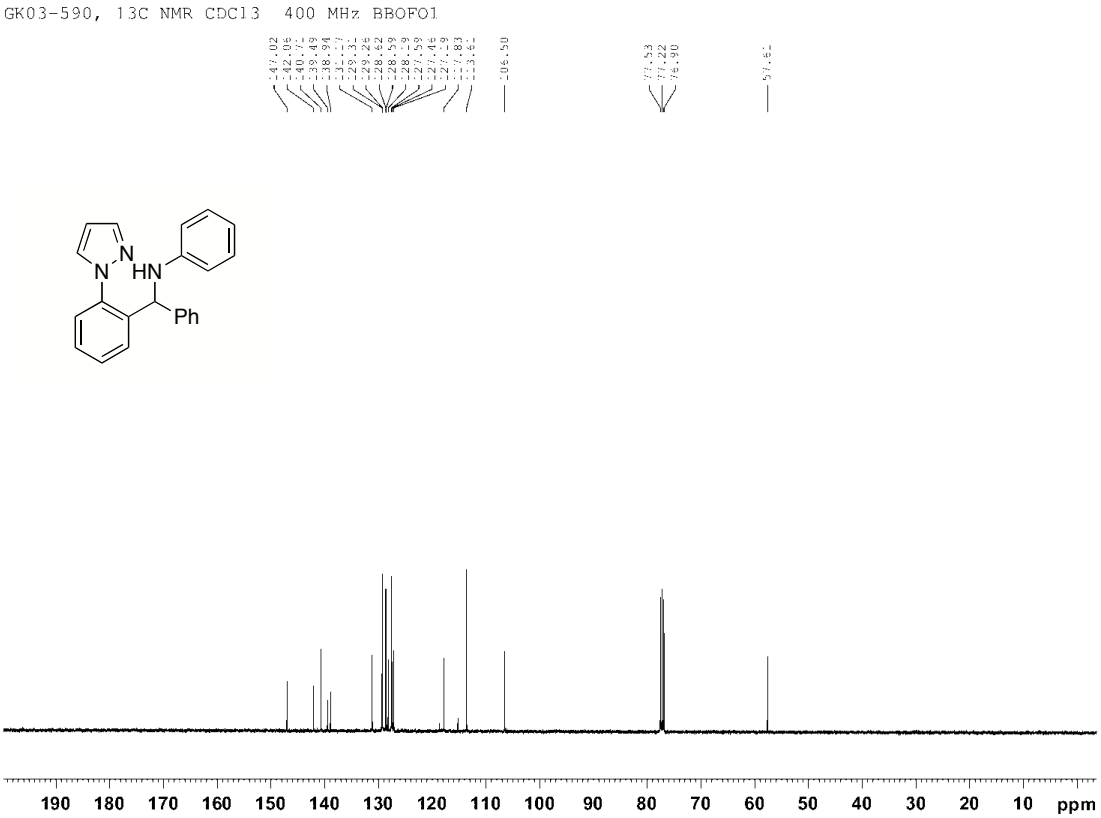
**3j**


GK04-247 1H NMR 400 MHz BBFO1 CDCl3
8.456
8.453
7.353
7.351
7.333
7.332
7.239
7.224
7.202
7.195
7.190
7.132
7.127
7.115
7.102
7.095
7.082
6.938
6.862
6.856
6.841
6.835
6.709
6.687
6.521
5.392
3.802
3.702
4.319
1.627
OMe
N
HN
Me
Ph
OMe
ppm
0.98
1.15
1.10
5.16
2.01
1.25
2.23
2.08
1.00
0.73
3.00
3.10
3.05

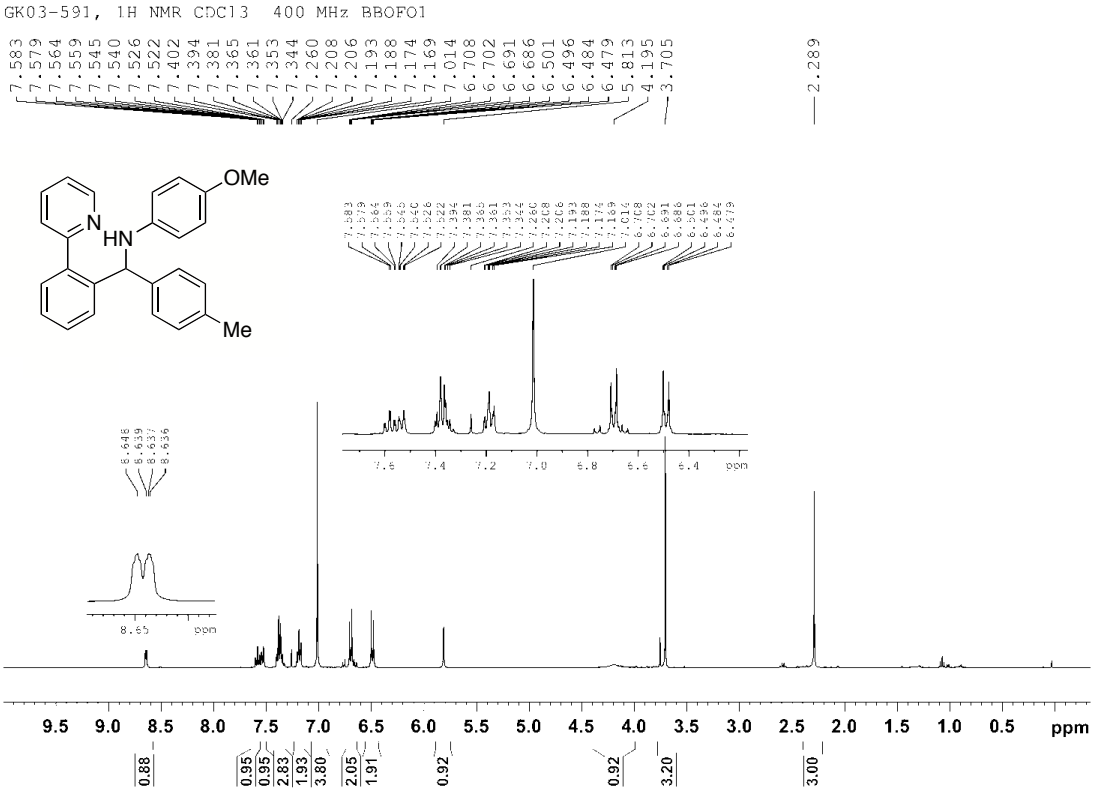

GK04-247 13C NMR 400 MHz BBFO1 CDCl3
159.73
158.78
152.07
146.48
142.29
141.93
137.95
132.89
132.35
130.69
129.22
128.37
127.74
127.22
124.89
122.40
114.93
111.94
77.55
77.23
76.92
60.82
55.90
55.45
19.03
OMe
N
HN
Me
Ph
OMe
ppm

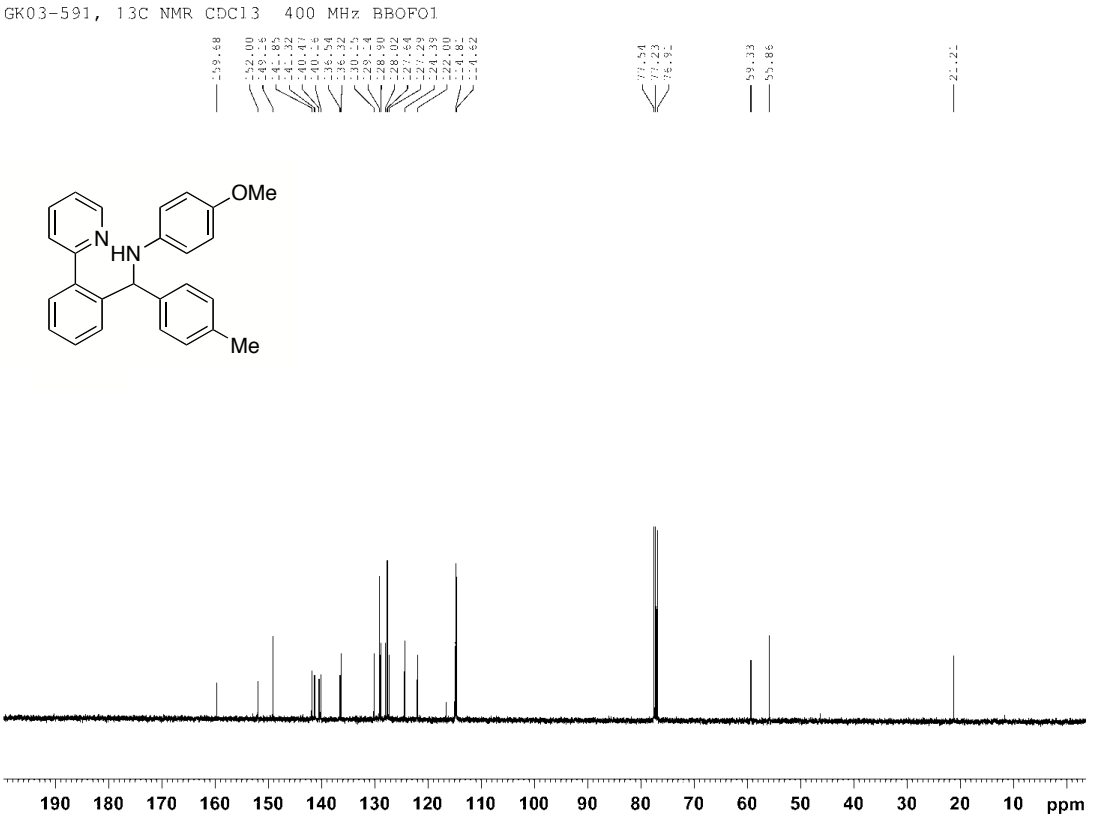
**3k**


GK03-590, 1H NMR CDCl3 400 MHz BBOFO1
7.745
7.741
7.700
7.696
7.681
7.677
7.453
7.438
7.434
7.420
7.415
7.409
7.404
7.390
7.386
7.371
7.367
7.348
7.345
7.330
7.325
7.260
7.252
7.246
7.240
7.229
7.224
7.222
7.211
7.208
7.164
7.145
7.143
7.128
7.124
7.100
7.095
7.089
7.086
7.081
7.077
6.733
6.715
6.697
6.607
6.605
6.586
6.302
6.297
6.292
5.853
5.845
4.359
4.352
N
N
HN
Ph
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
0.97
1.01
1.00
1.04
1.03
3.91
2.11
2.03
1.15
2.04
0.97
1.00
1.00

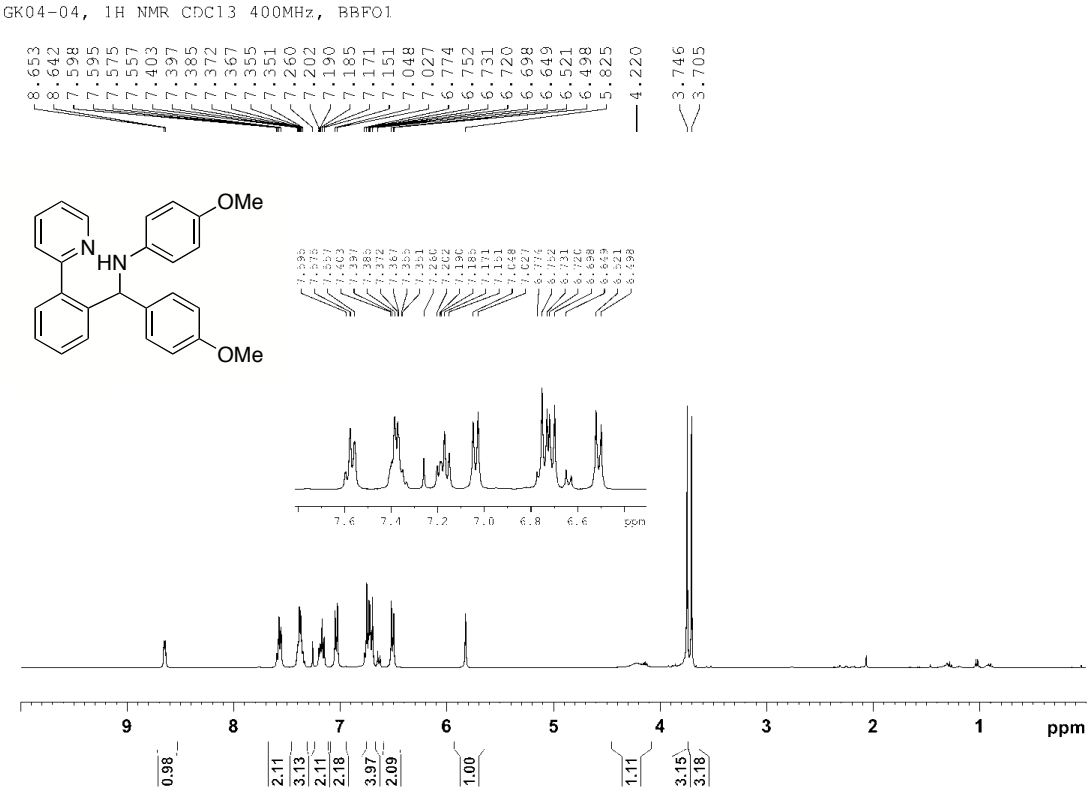

GK03-590, 13C NMR CDCl3 400 MHz BBOFO1
147.02
142.06
140.70
139.49
38.94
129.32
129.26
128.62
128.59
127.59
127.46
127.19
126.83
123.61
106.50
77.53
77.22
76.90
57.62
N
N
HN
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

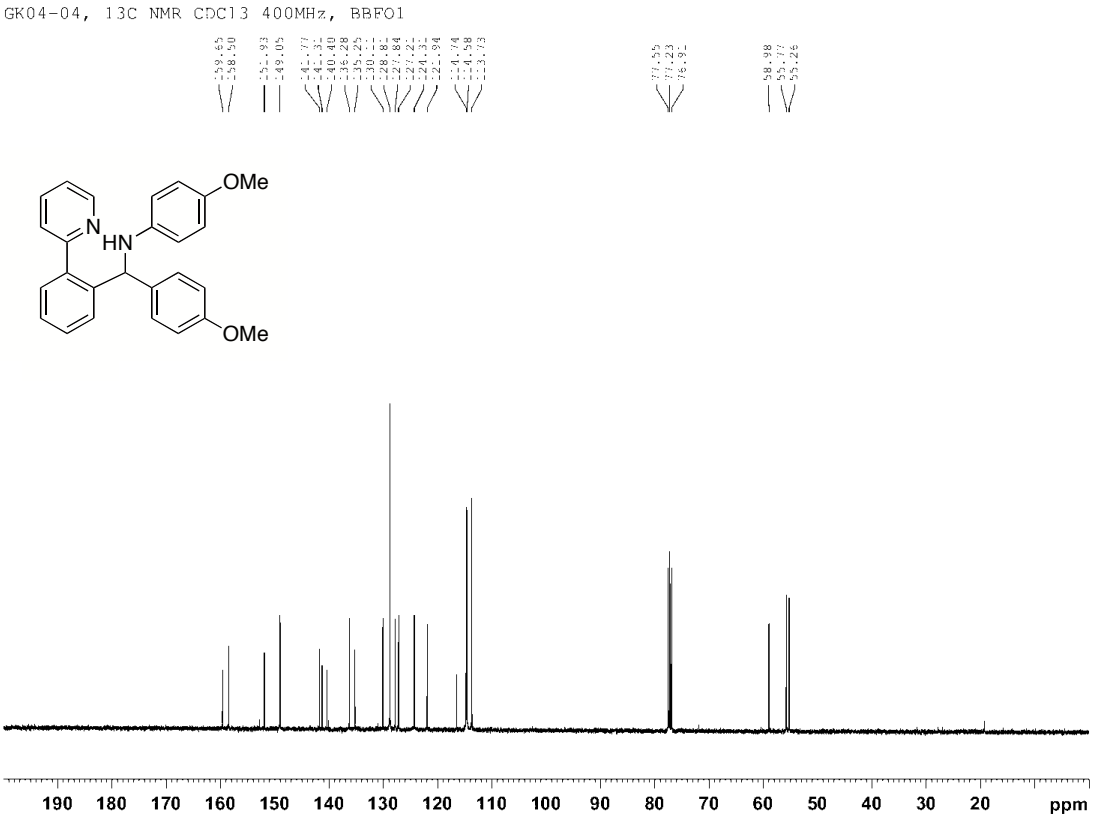
**3l**


GK03-591, 1H NMR CDCl3 400 MHz BBOFO1
OMe
N
HN
Me
ppm

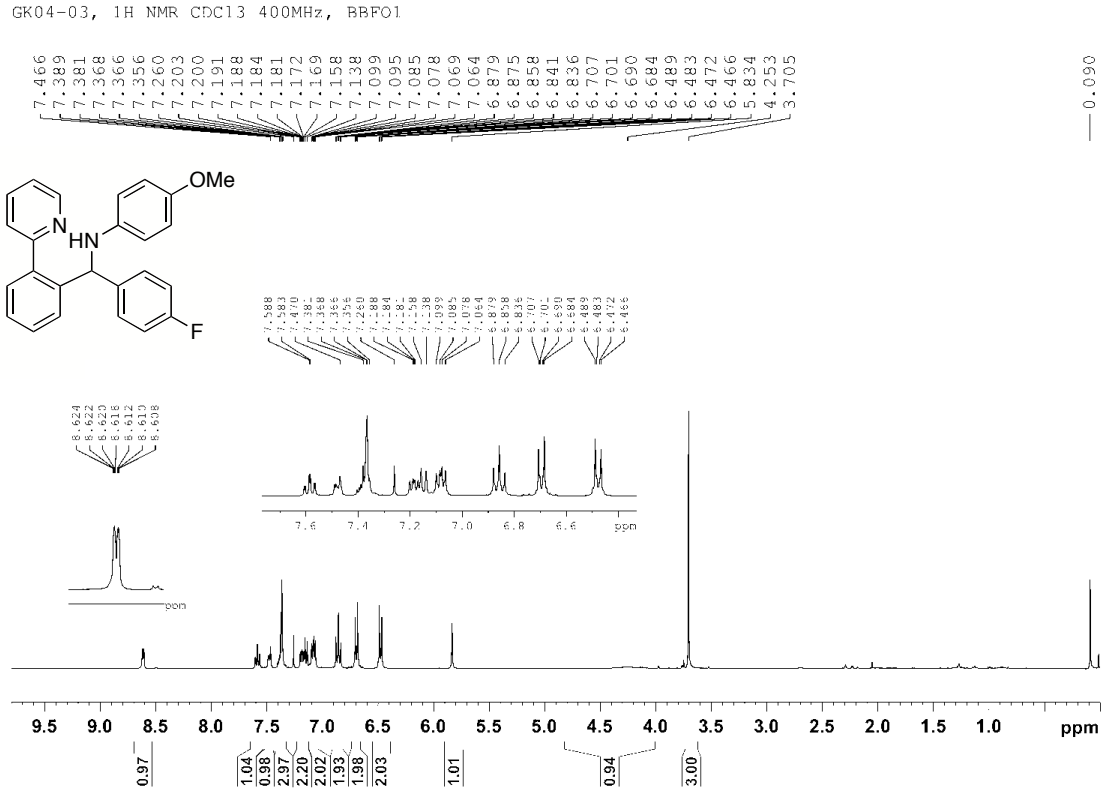

GK03-591, 13C NMR CDCl3 400 MHz BBOFO1
OMe
N
HN
Me
ppm

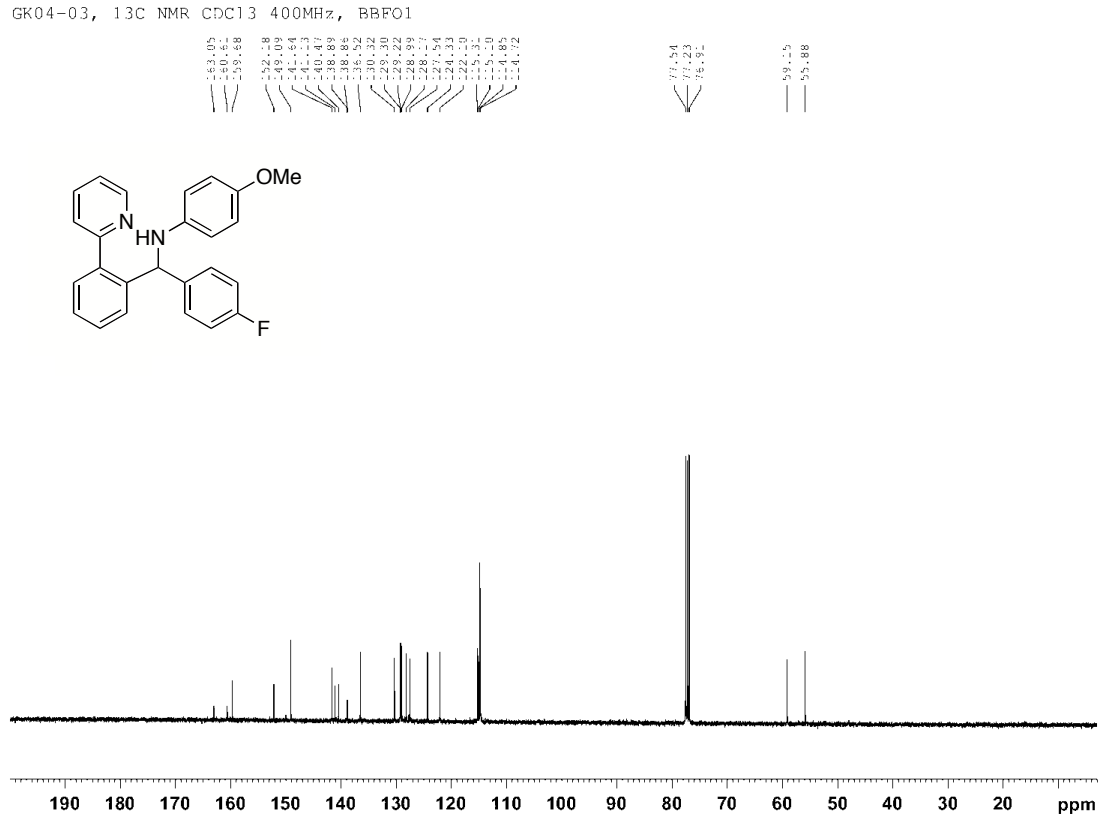
**3m**


GK04-04, 1H NMR CDCl3 400MHz, BBFO1
OMe
HN
OMe
ppm

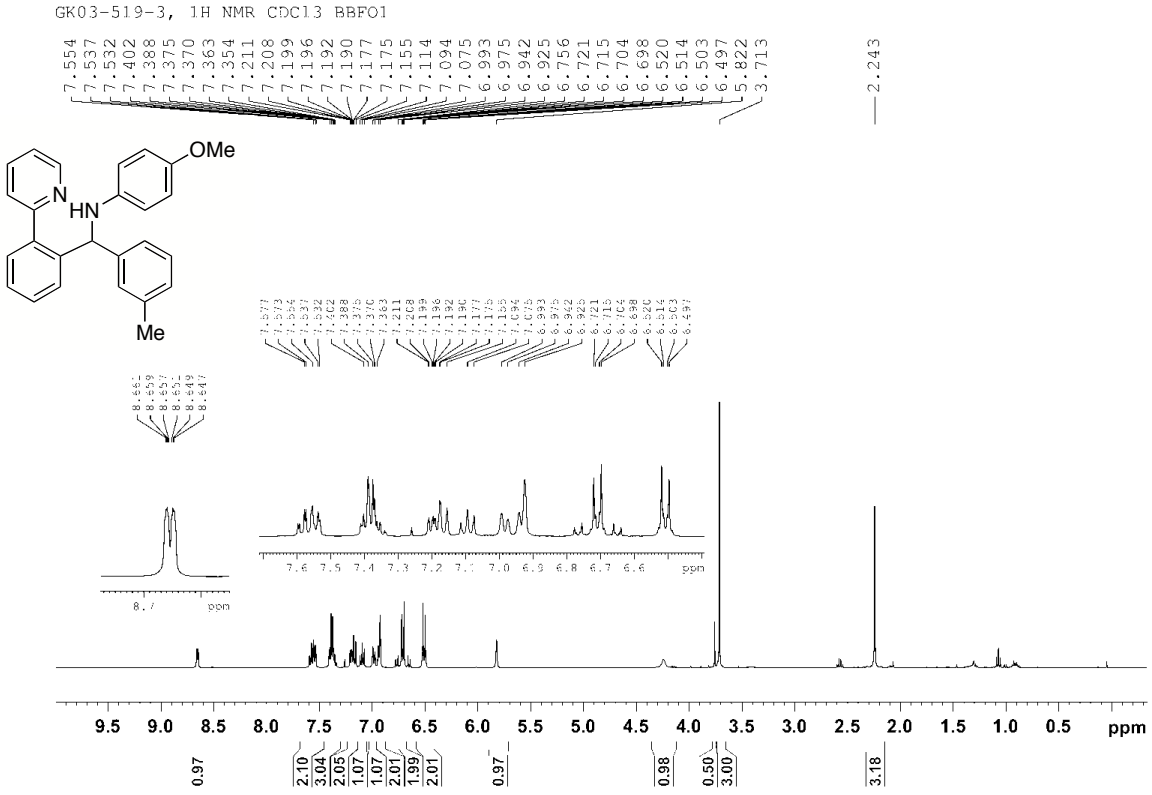

GK04-04, 13C NMR CDCl3 400MHz, BBFO1
OMe
HN
OMe
ppm

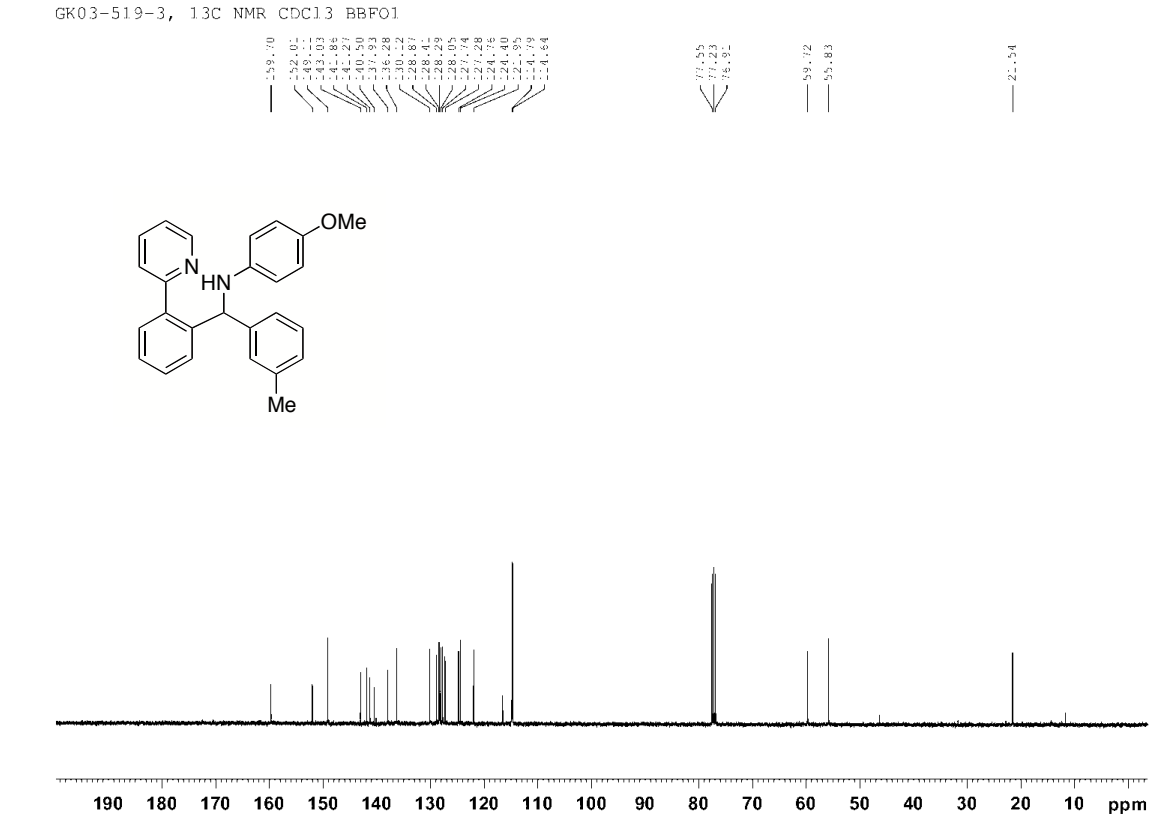
**3n**


GK04-03, 1H NMR CDCl3 400MHz, BBFO1
OMe
N
HN
F
ppm
0.97
1.04
0.98
2.97
2.20
2.02
1.93
1.98
2.03
1.01
0.94
3.00

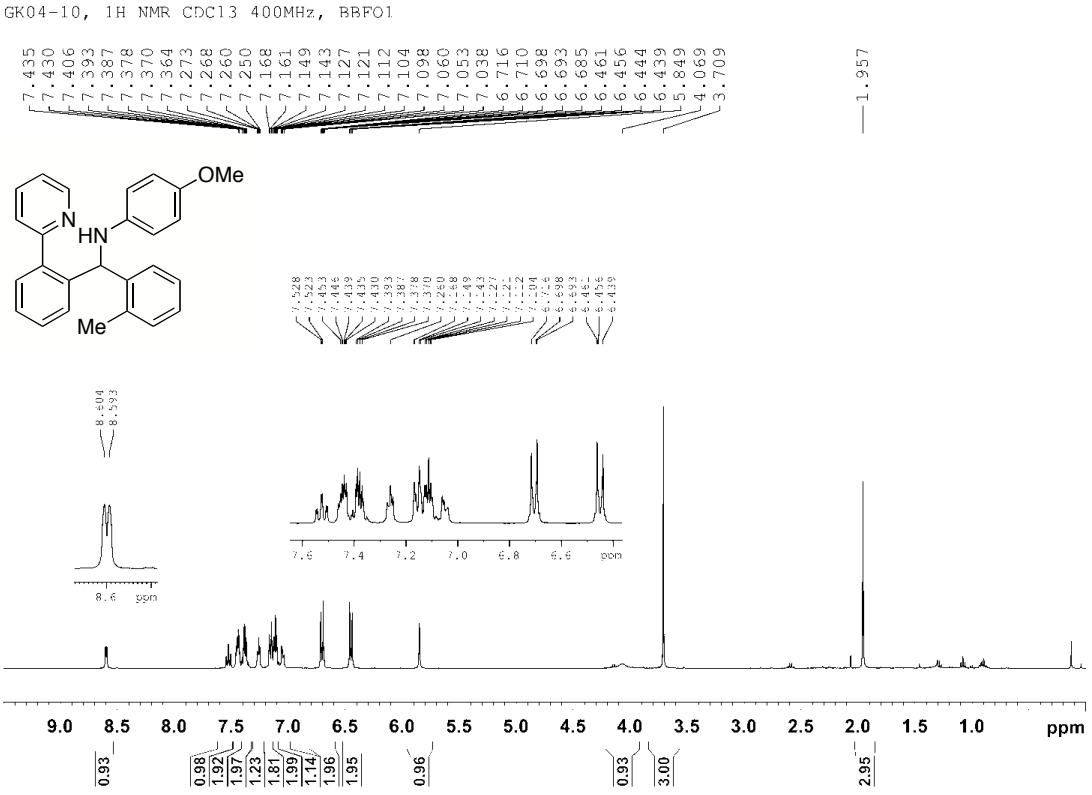

GK04-03, 13C NMR CDCl3 400MHz, BBFO1
OMe
N
HN
F
ppm

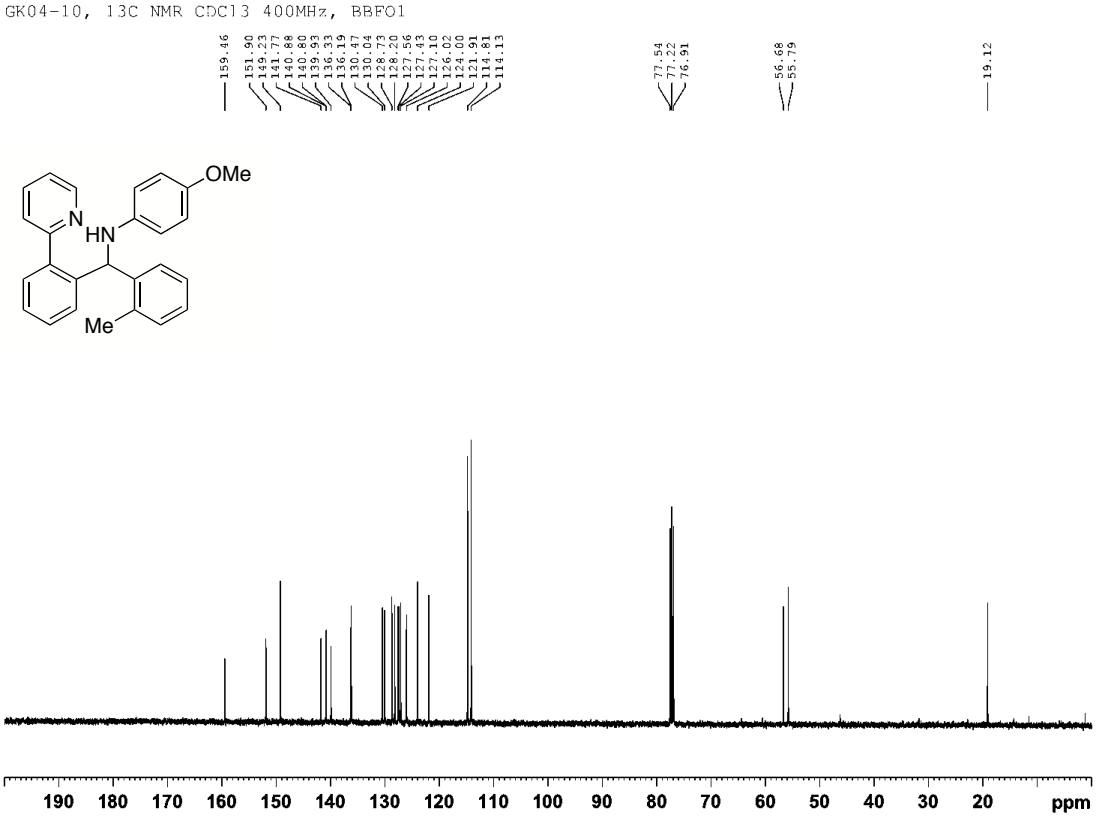
**3o**


GK03-519-3, 1H NMR CDCl3 BBFO1
OMe
N
HN
Me
ppm

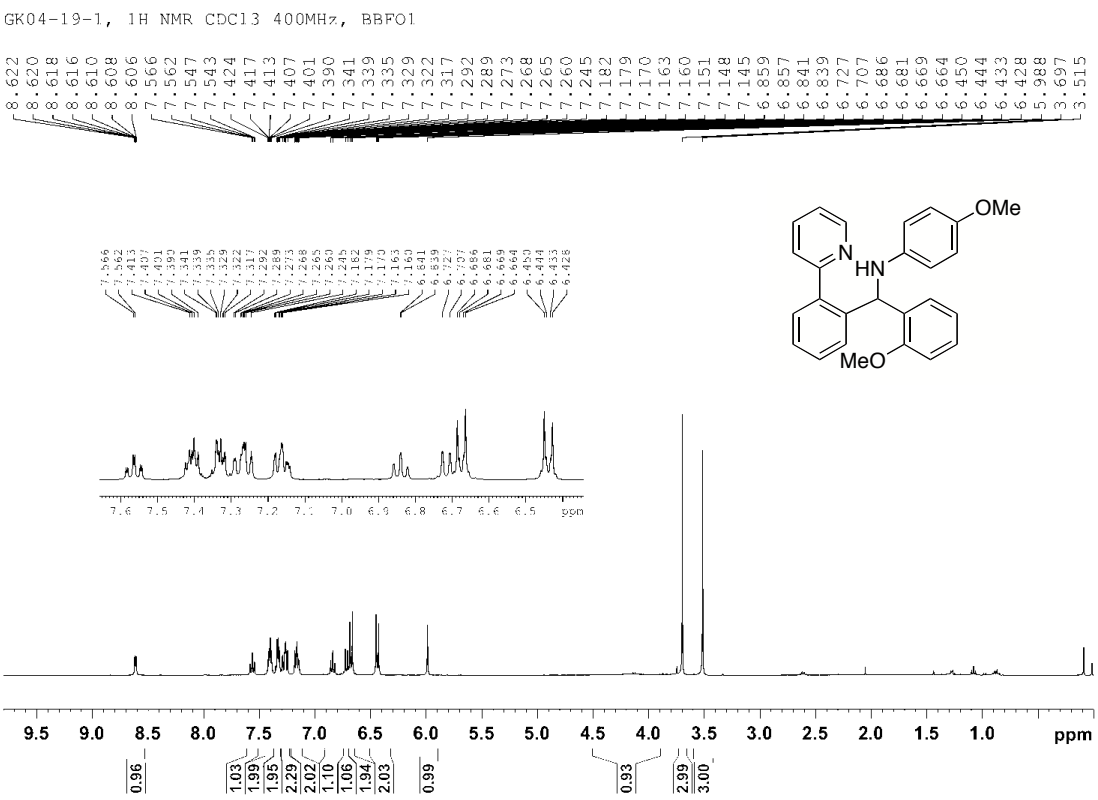

GK03-519-3, 13C NMR CDCl3 BBFO1
OMe
N
HN
Me
ppm

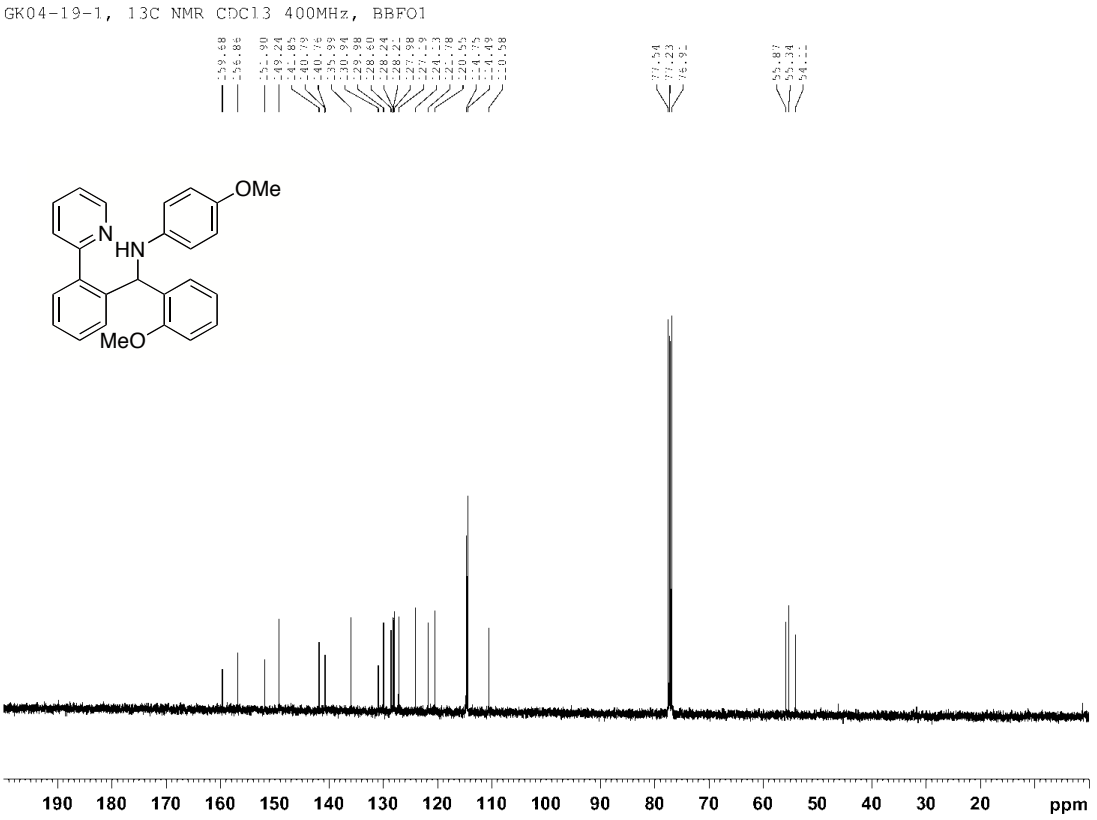
**3p**


GK04-10, 1H NMR CDCl3 400MHz, BBFO1
OMe
N
HN
Me
ppm

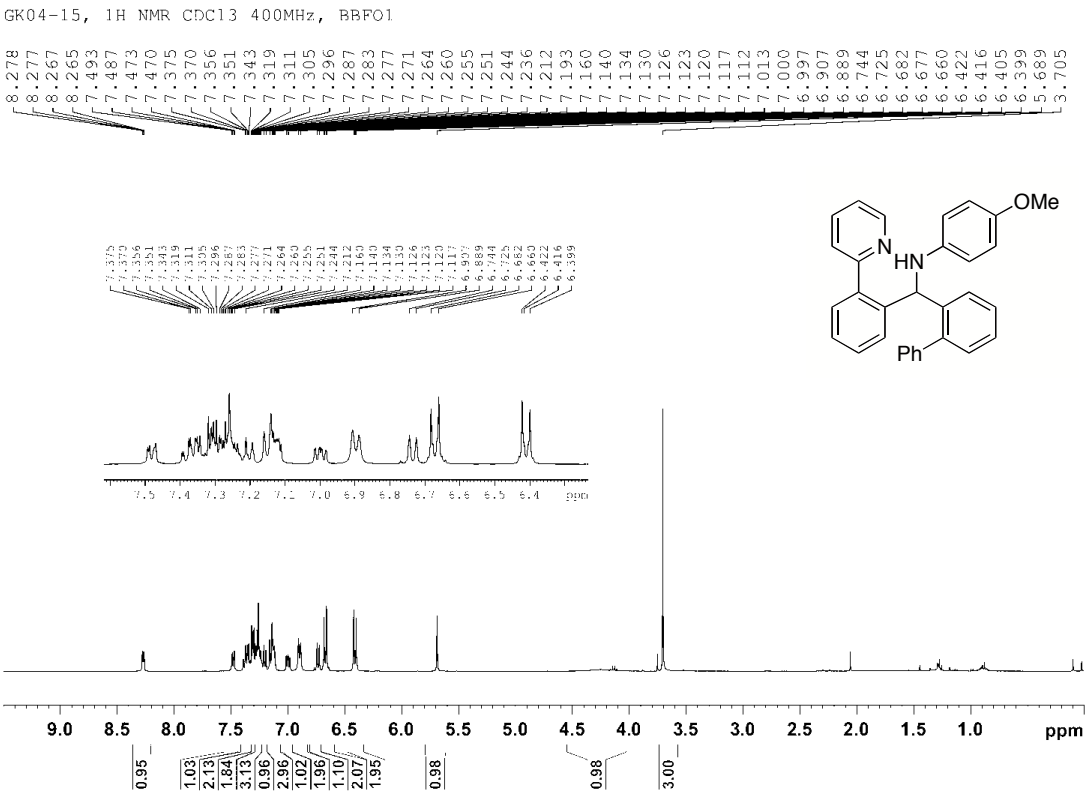

GK04-10, 13C NMR CDCl3 400MHz, BBFO1
OMe
N
HN
Me
ppm

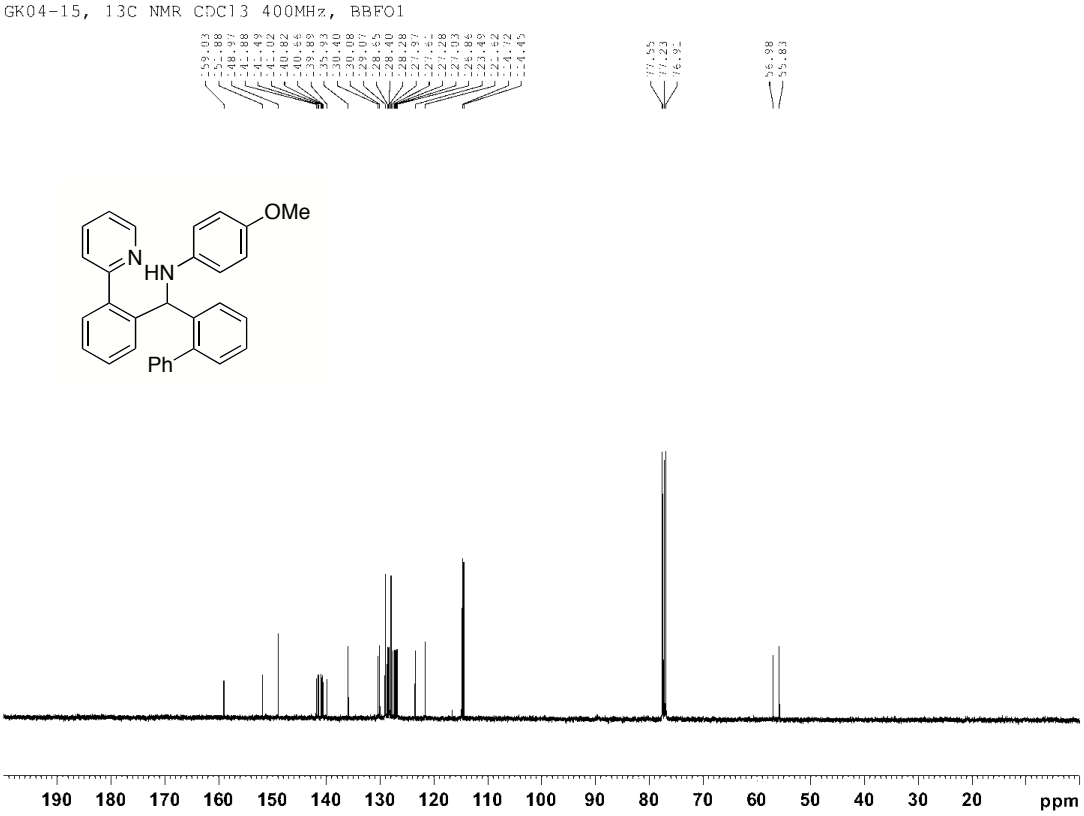
**3q**


GK04-19-1, 1H NMR CDCl3 400MHz, BBFO1
OMe
N
HN
MeO
ppm

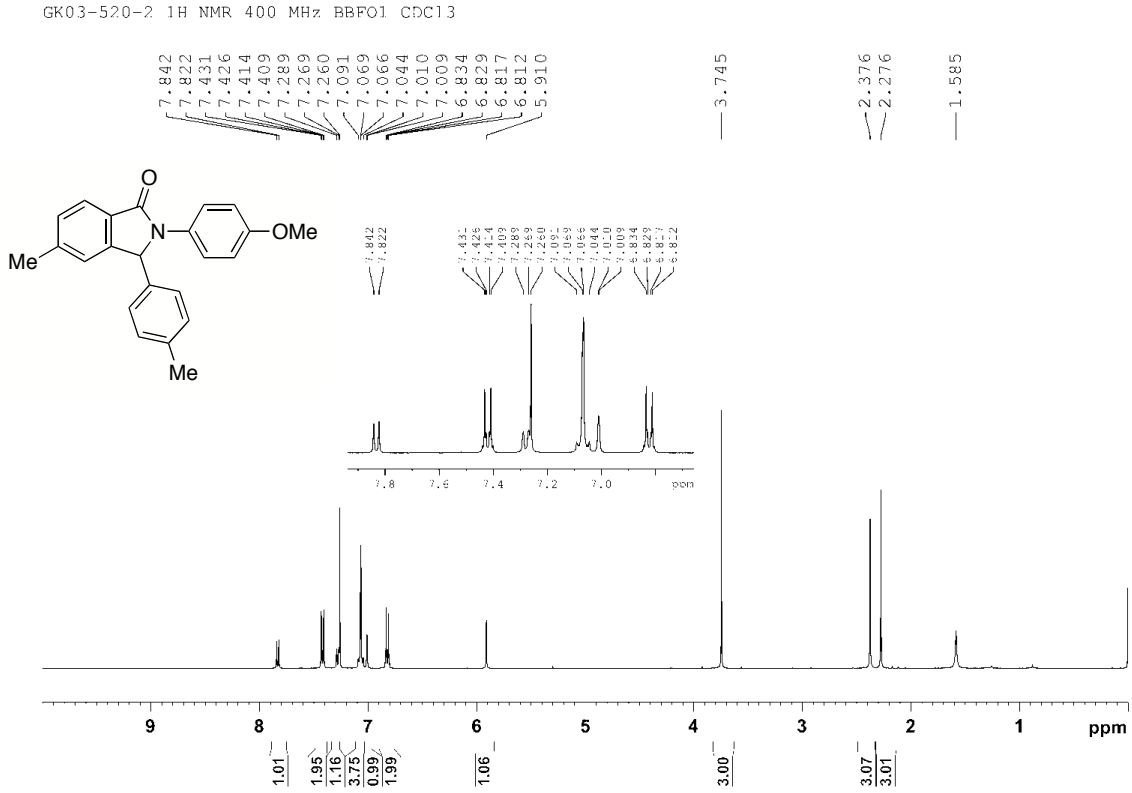

GK04-19-1, 13C NMR CDCl3 400MHz, BBFO1
OMe
N
HN
MeO
ppm

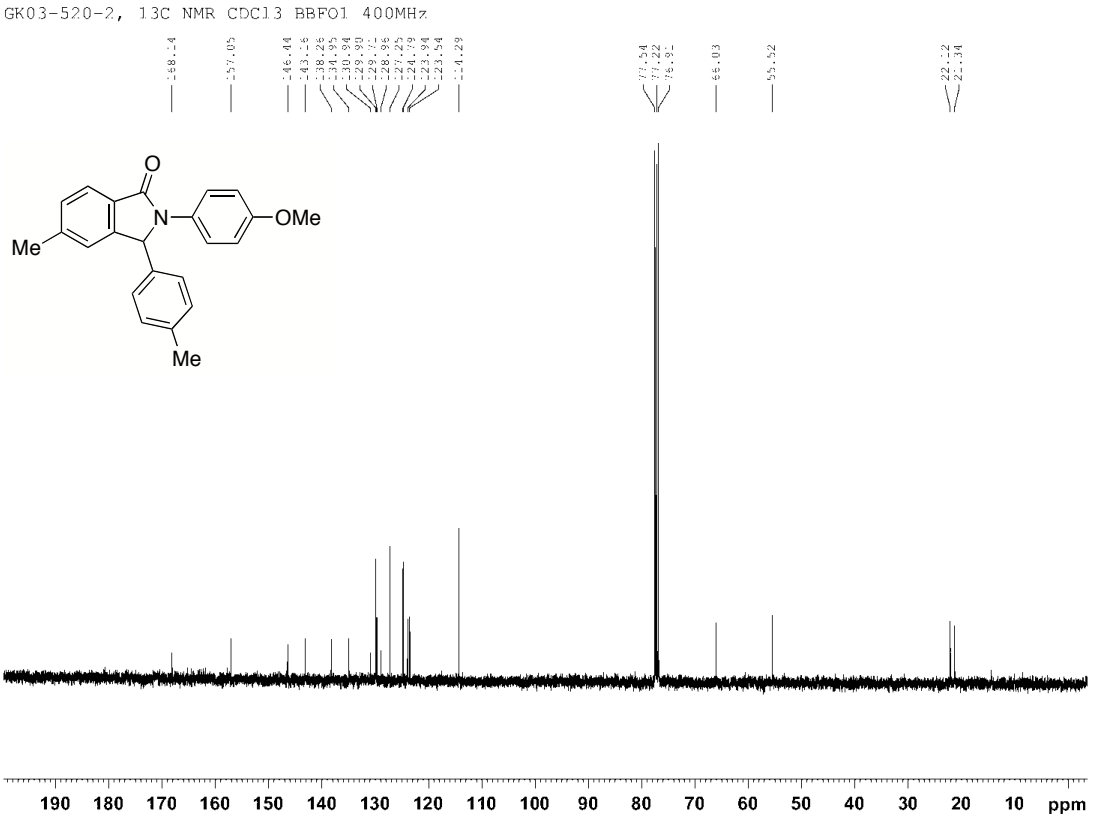
**3r**


GK04-15, 1H NMR CDCl3 400MHz, BBFO1
OMe
N
HN
Ph
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 ppm
0.95 1.03 2.13 1.84 3.13 0.96 2.96 1.02 1.96 1.10 2.07 1.95 0.98 0.98 3.00

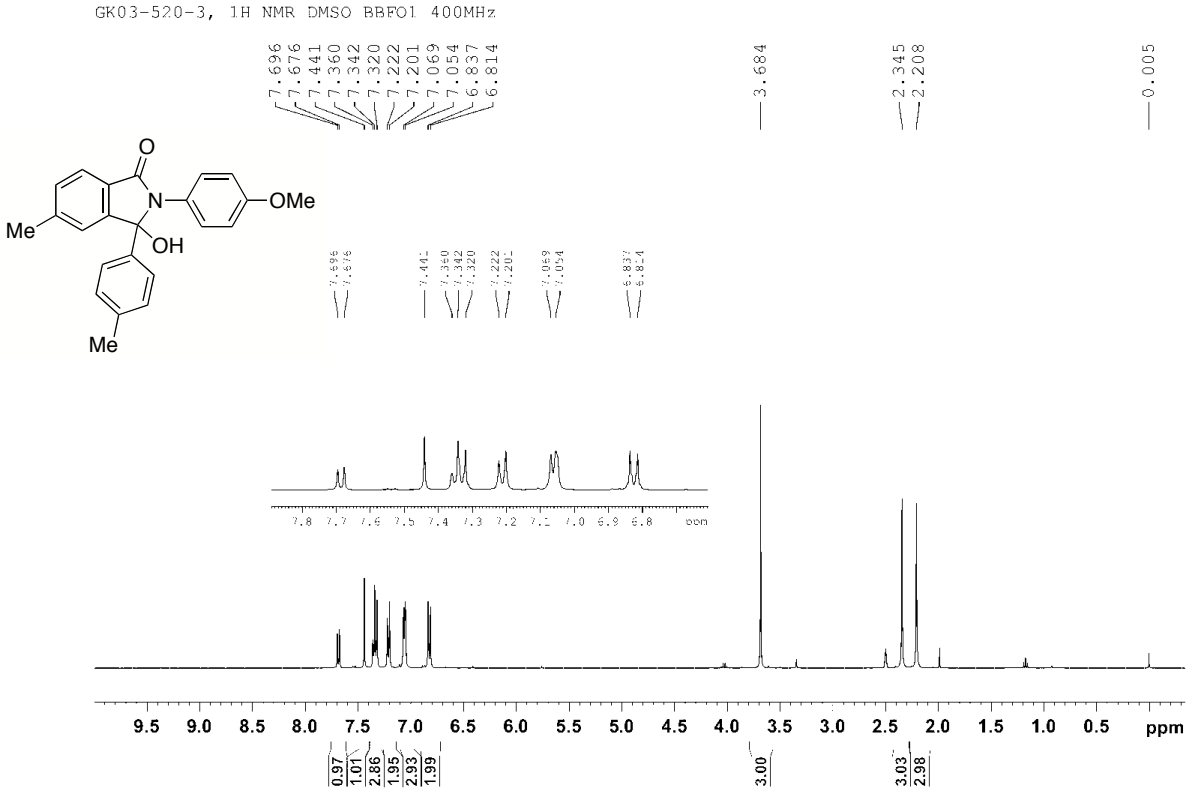

GK04-15, 13C NMR CDCl3 400MHz, BBFO1
OMe
N
HN
Ph
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

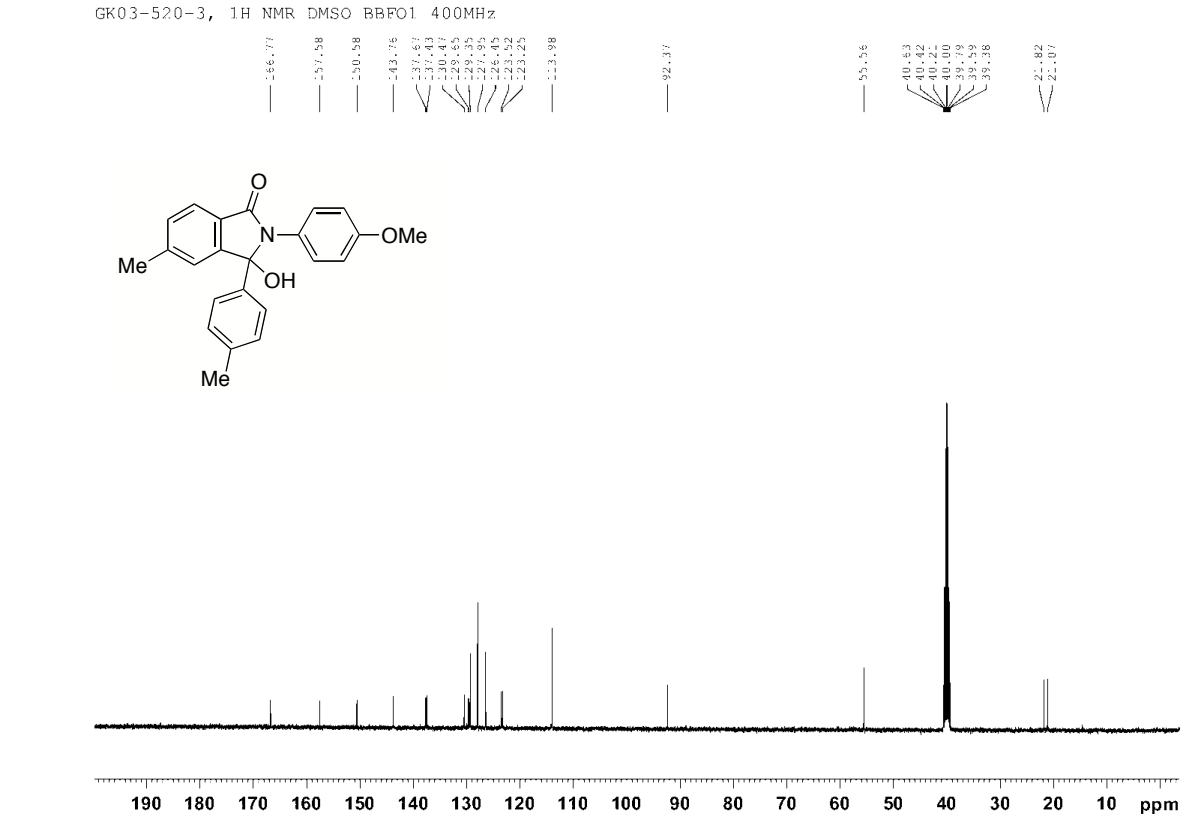
**5**


GK03-520-2 1H NMR 400 MHz BBFO1 CDCl3
7.842
7.822
7.431
7.426
7.414
7.409
7.289
7.269
7.260
7.091
7.069
7.066
7.044
7.010
7.009
6.834
6.829
6.817
6.812
5.910
3.745
2.376
2.276
1.585
O
N
OMe
Me
Me
ppm
1.01
1.95
1.16
3.75
0.99
1.99
1.06
3.00
3.07
3.01

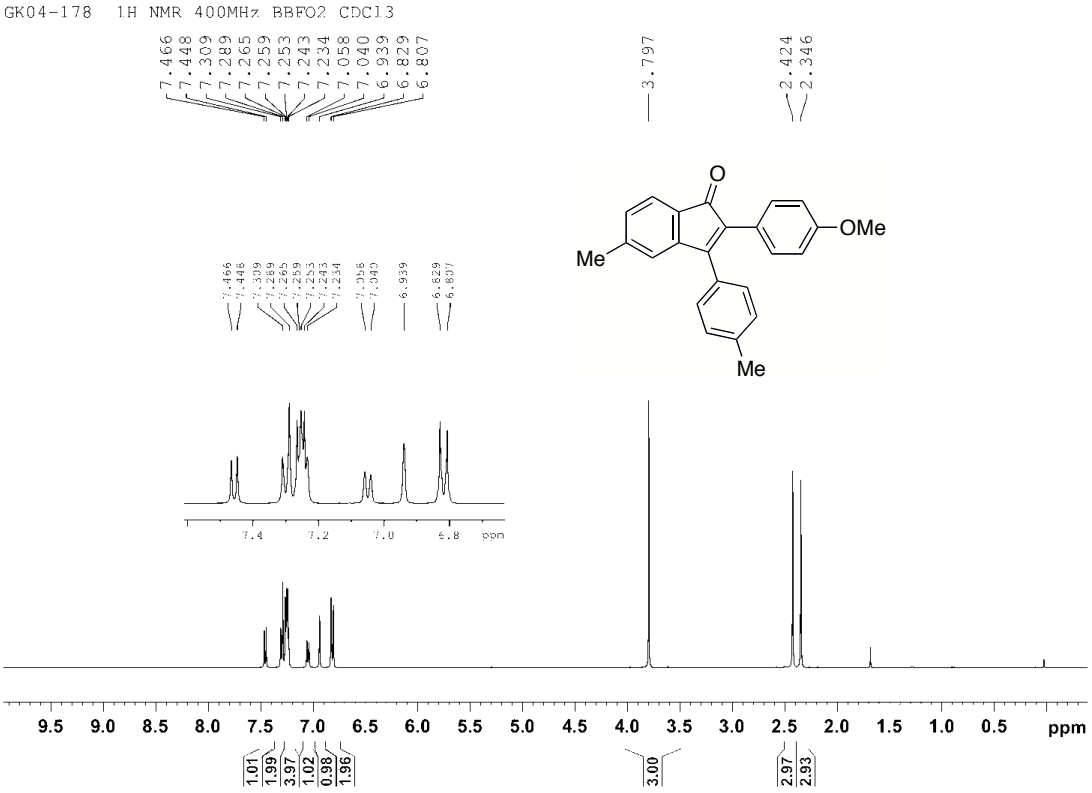

GK03-520-2, 13C NMR CDCl3 BBFO1 400MHz
168.24
157.05
146.44
143.56
138.26
134.95
130.94
129.90
128.96
127.25
124.79
123.94
123.54
114.29
77.54
77.22
76.92
66.03
55.52
22.12
21.34
O
N
OMe
Me
Me
ppm

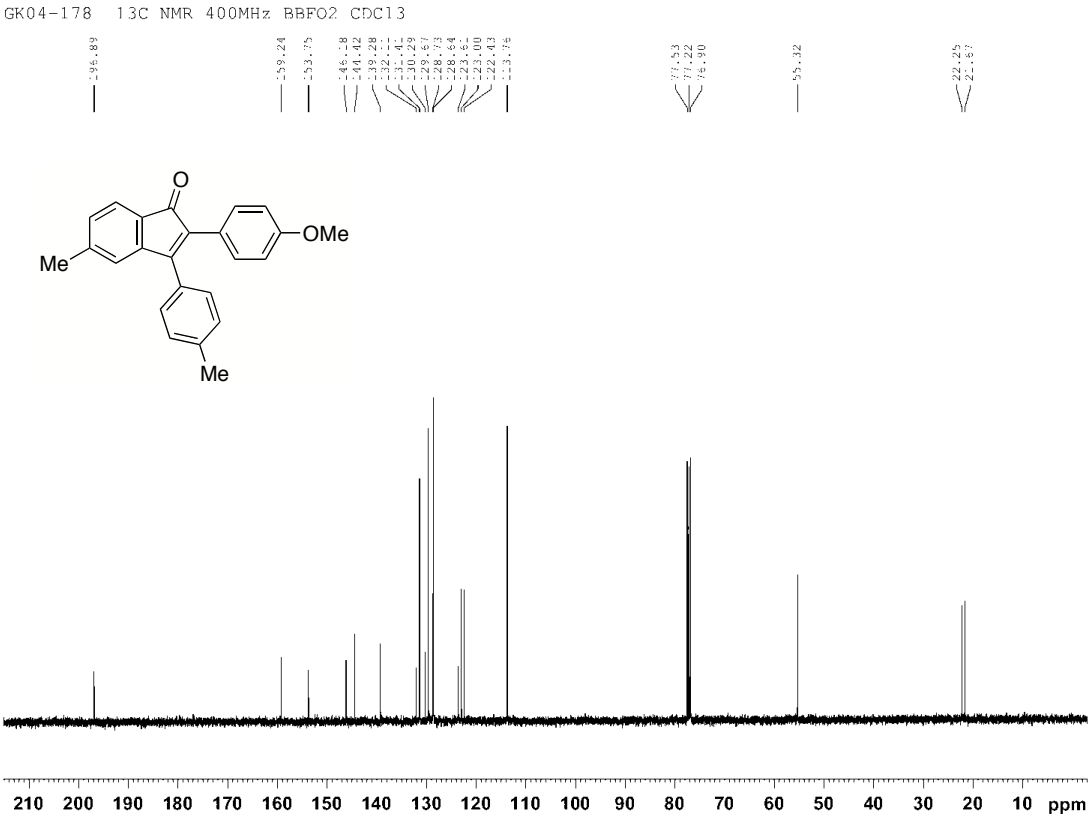
**6**


GK03-520-3, 1H NMR DMSO BBFO1 400MHz
7.696
7.676
7.441
7.360
7.342
7.320
7.222
7.201
7.069
7.054
6.837
6.814
3.684
2.345
2.208
0.005
O
N
OMe
Me
OH
Me
ppm
0.97
1.01
2.86
1.95
2.93
1.99
3.00
3.03
2.98

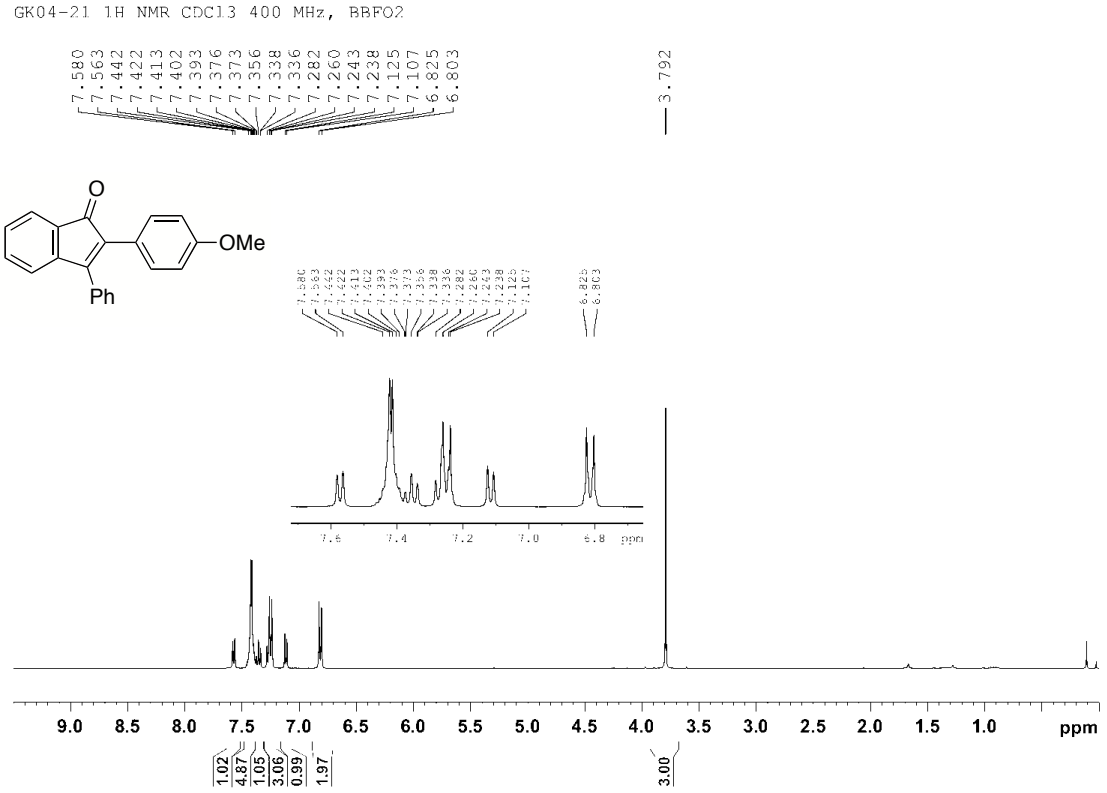

GK03-520-3, 1H NMR DMSO BBFO1 400MHz
166.77
157.58
150.58
143.76
137.67
137.43
130.47
129.65
127.95
127.45
126.45
123.52
123.25
113.98
92.37
55.56
40.63
40.42
40.22
40.00
39.79
39.59
39.38
21.82
21.07
O
N
OMe
Me
OH
Me
ppm

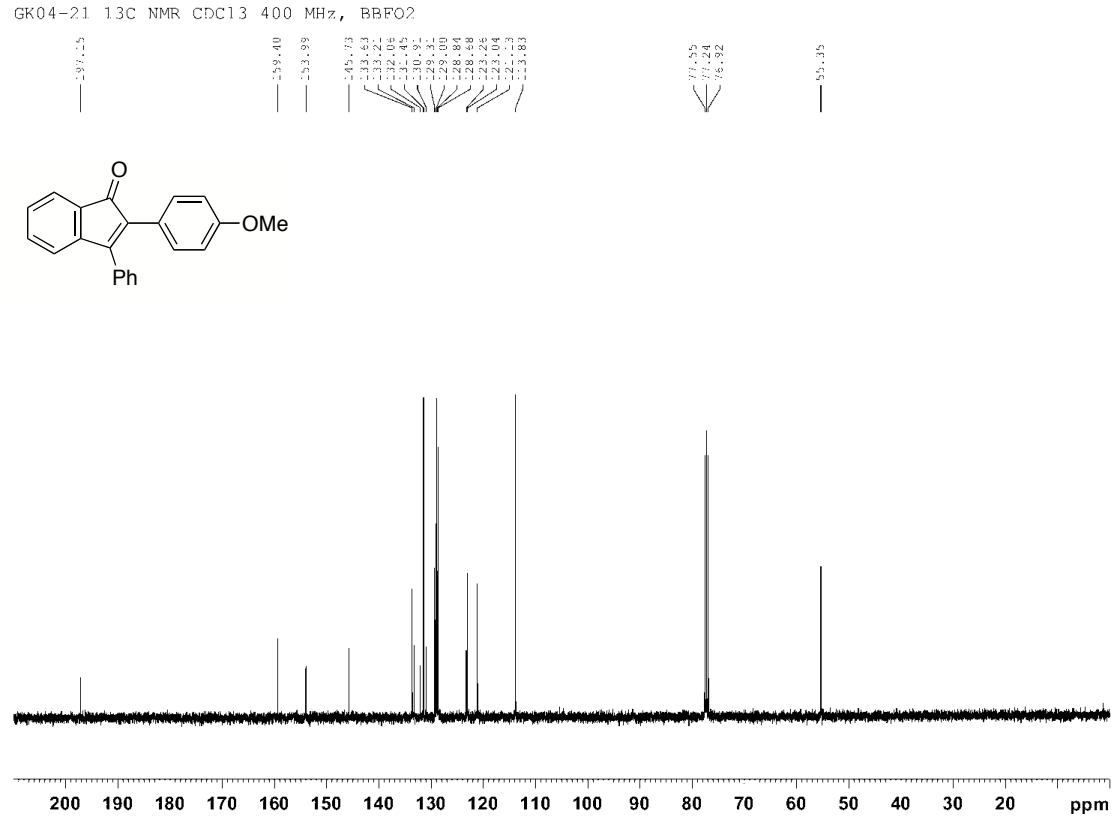
**7a**


GK04-178 1H NMR 400MHz BBFO2 CDCl3
7.466
7.448
7.309
7.289
7.265
7.259
7.253
7.243
7.234
7.058
7.040
6.939
6.829
6.807
3.797
2.424
2.346
O
OMe
Me
Me
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
1.01
1.99
3.97
1.02
0.98
1.96
3.00
2.97
2.93

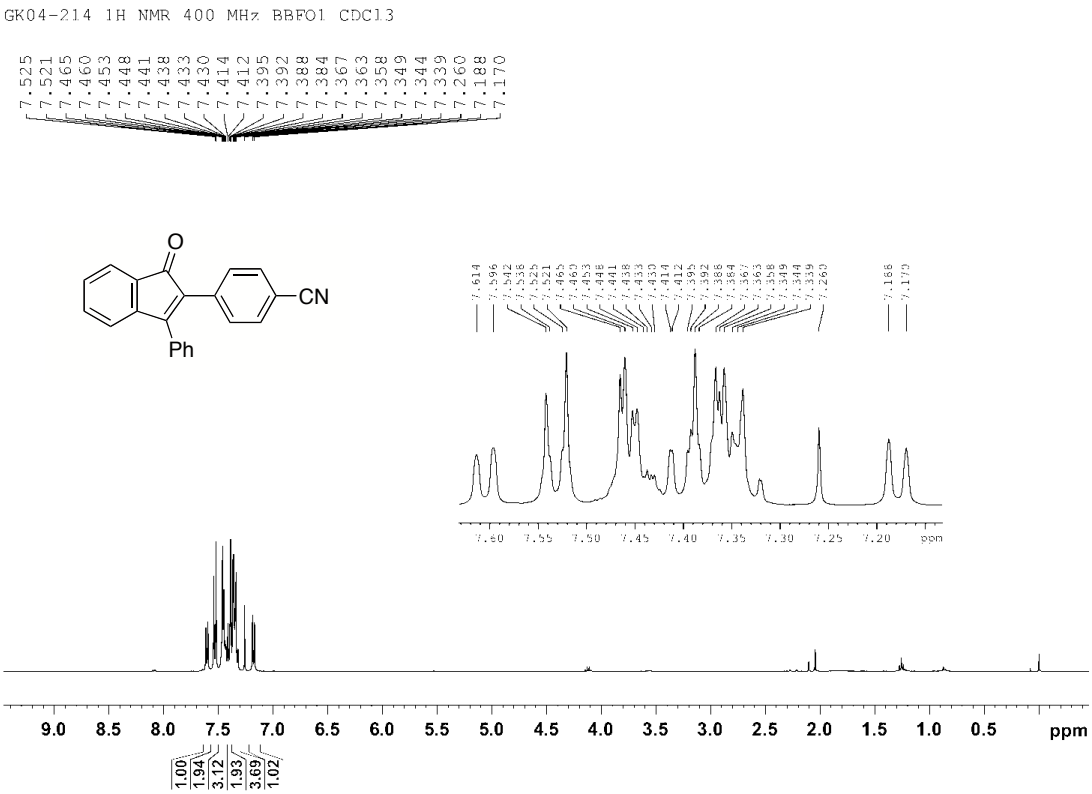

GK04-178 13C NMR 400MHz BBFO2 CDCl3
196.89
159.24
153.75
146.38
144.42
139.28
132.11
131.41
130.29
129.67
128.93
128.64
123.61
123.00
122.43
113.76
77.53
77.22
76.90
55.32
22.25
22.67
O
OMe
Me
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

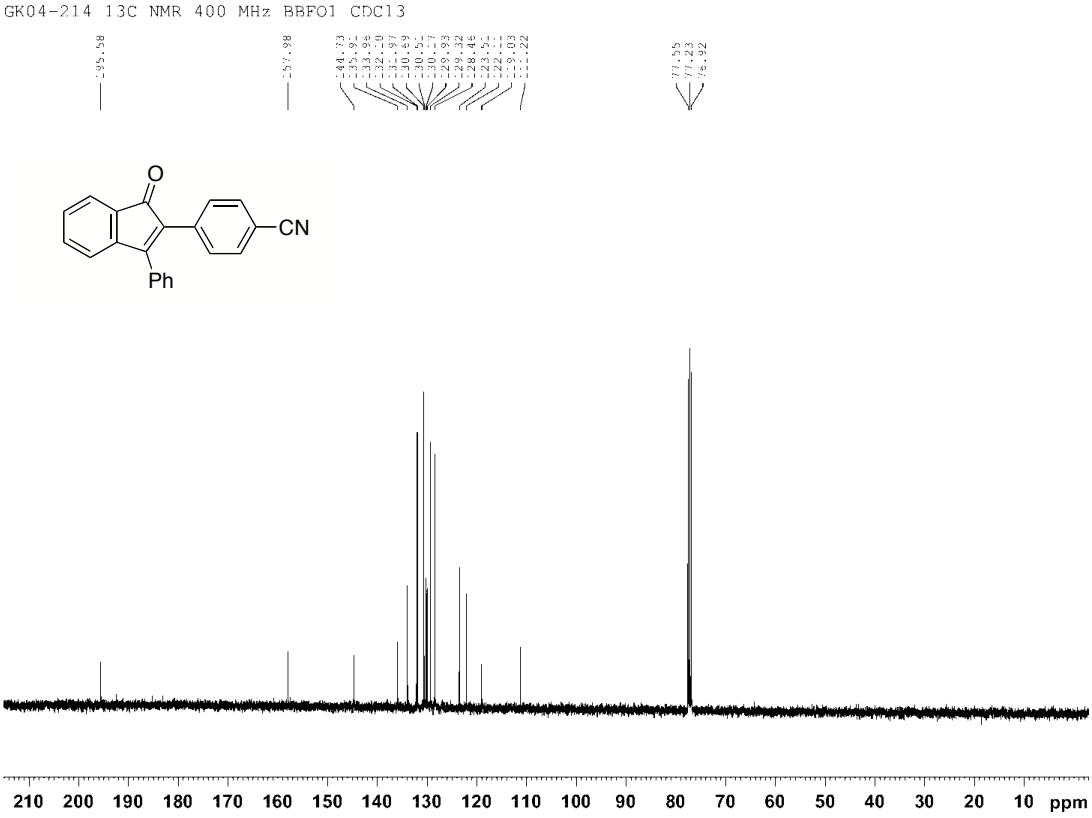
**7b**


GK04-21 1H NMR CDCl3 400 MHz, BBFO2
7.580
7.563
7.442
7.422
7.413
7.402
7.393
7.376
7.373
7.356
7.338
7.336
7.282
7.260
7.243
7.238
7.125
7.107
6.825
6.803
3.792
O
OMe
Ph
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 ppm
1.02
4.87
1.05
3.06
0.99
1.97
3.00

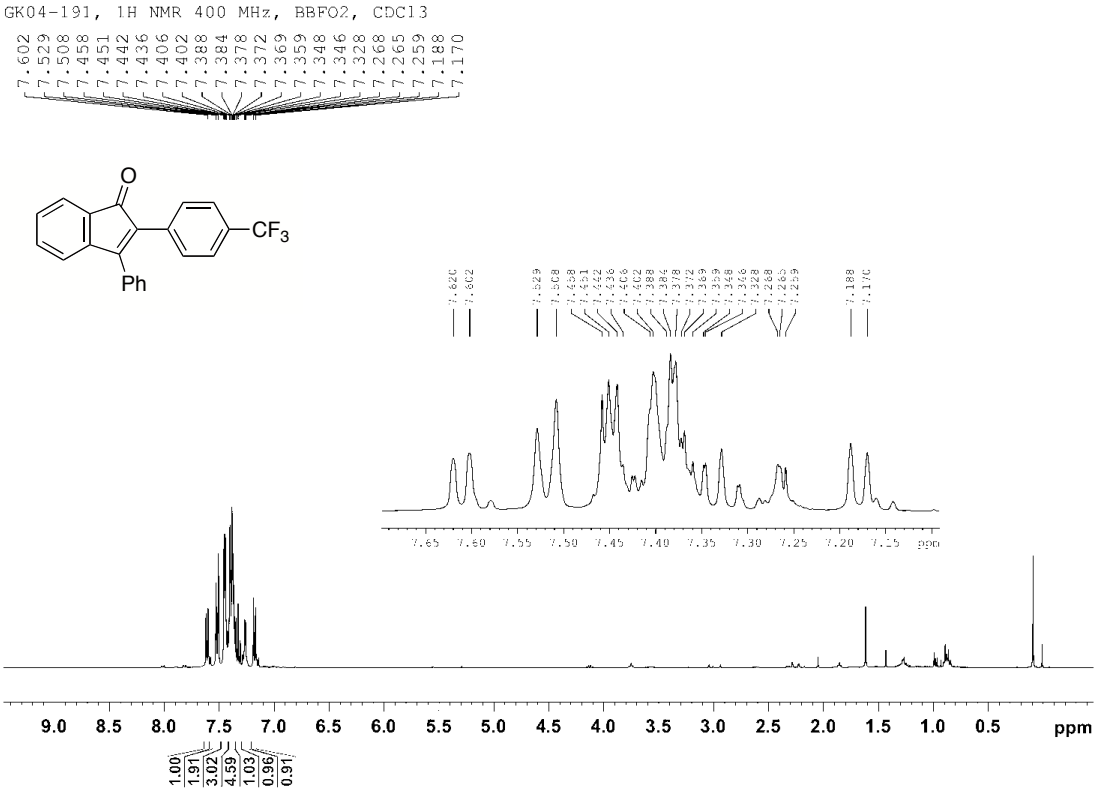

GK04-21 13C NMR CDCl3 400 MHz, BBFO2
197.25
159.40
153.99
145.73
133.63
133.22
132.06
131.45
130.92
129.31
129.00
128.84
128.58
123.26
123.04
122.13
113.83
77.55
77.24
76.92
55.35
O
OMe
Ph
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

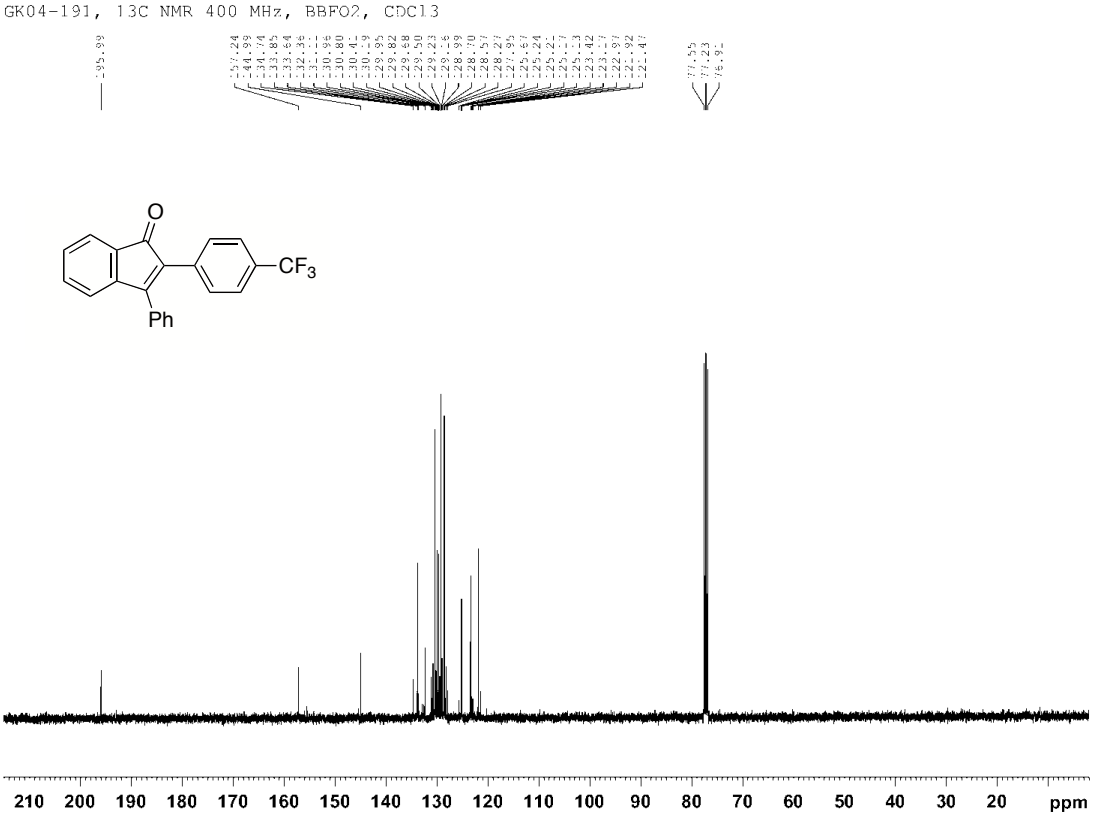
**7c**


GK04-214 1H NMR 400 MHz BBFO1 CDCl3
O
CN
Ph
ppm

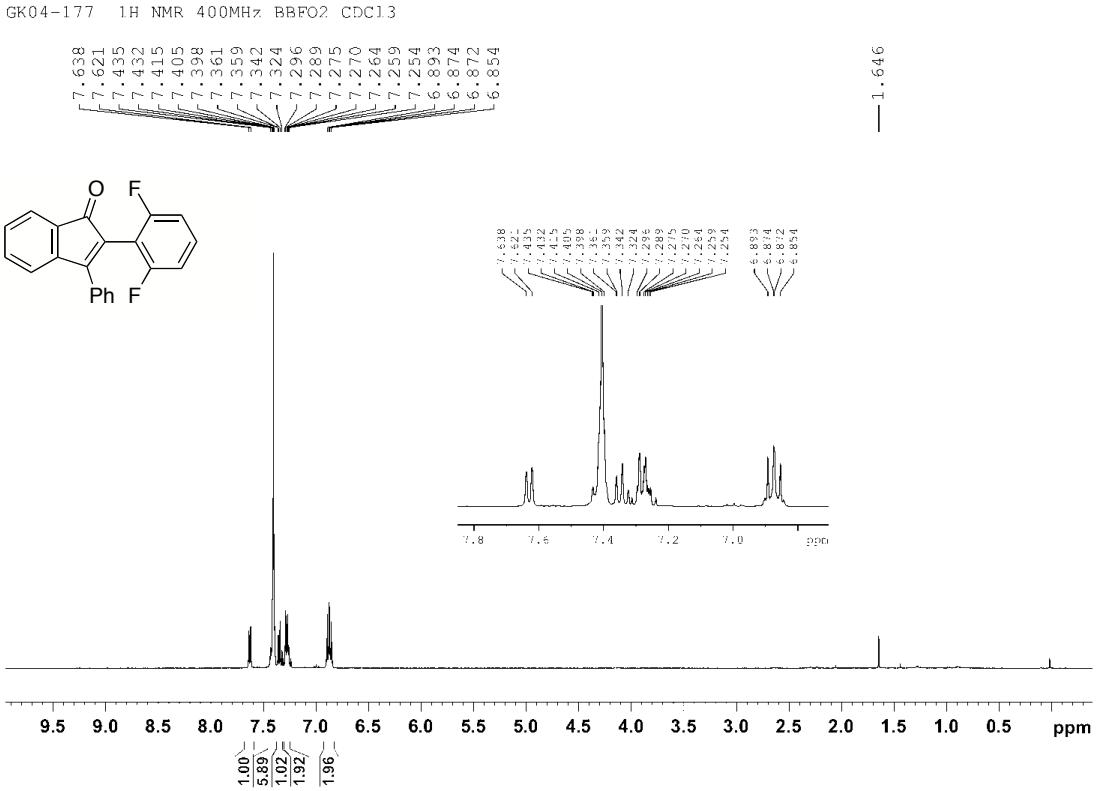

GK04-214 13C NMR 400 MHz BBFO1 CDCl3
O
CN
Ph
ppm

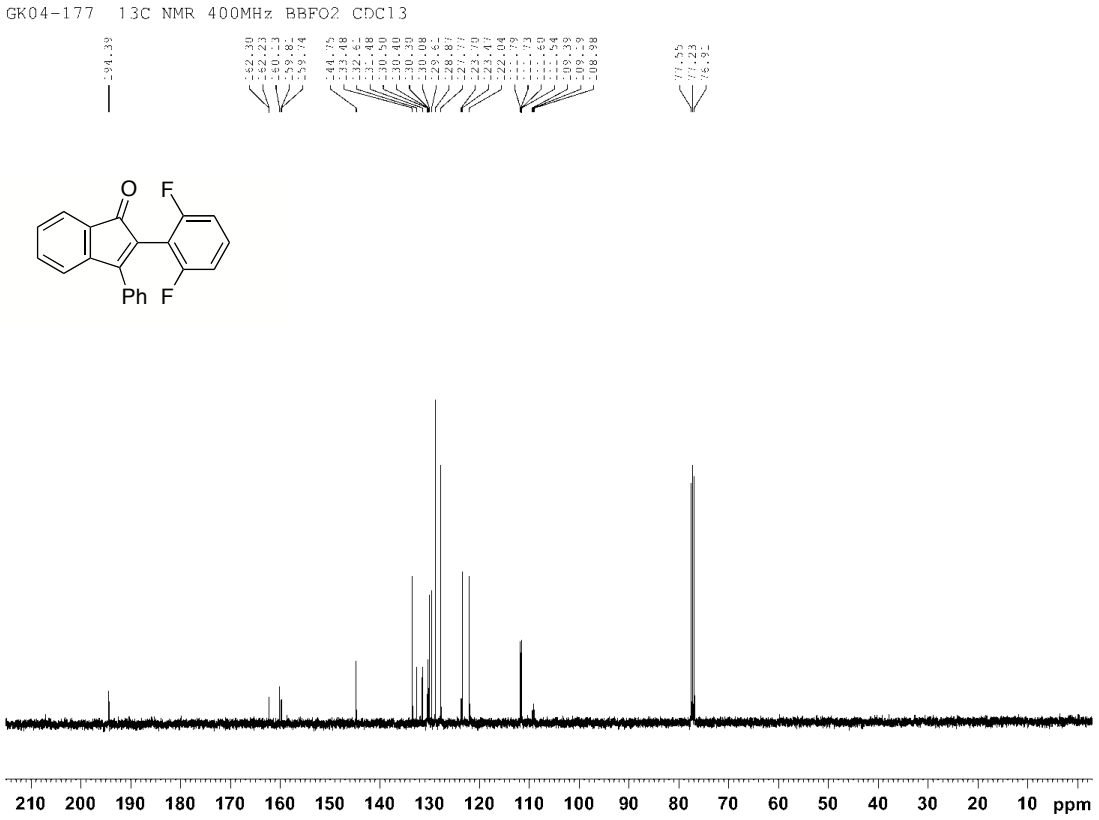
**7d**


GK04-191, 1H NMR 400 MHz, BBFO2, CDCl3
O
CF3
Ph
ppm

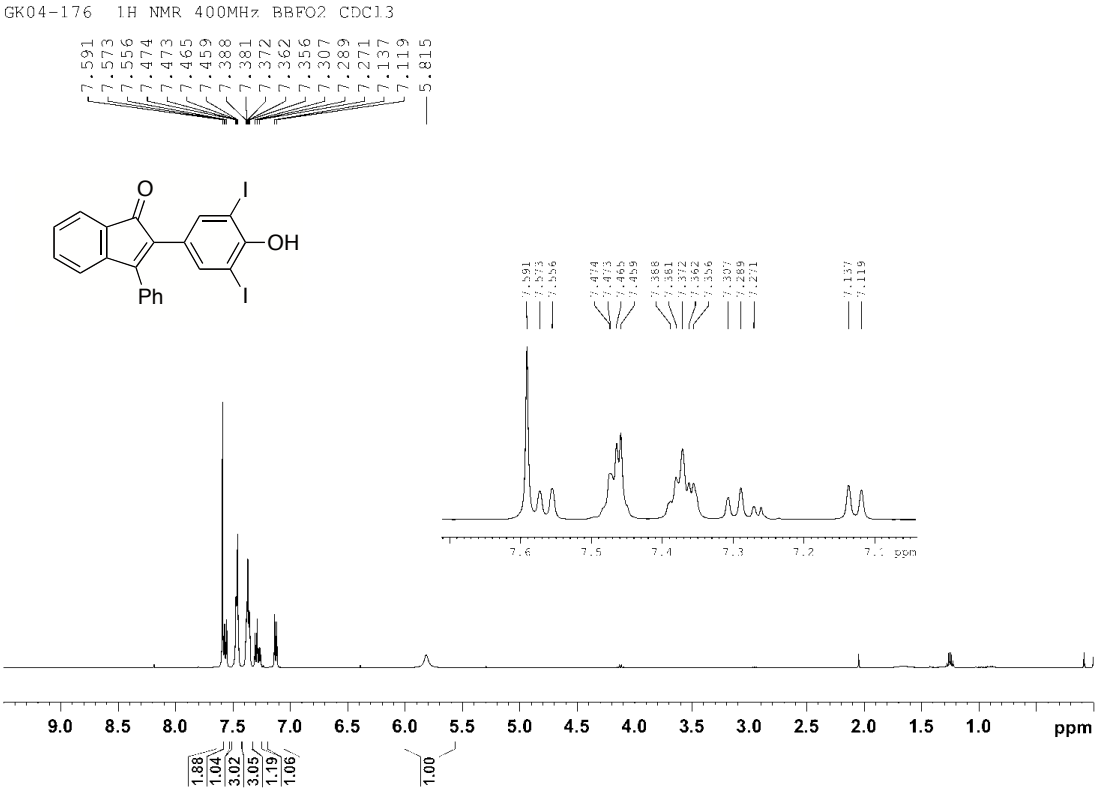

GK04-191, 13C NMR 400 MHz, BBFO2, CDCl3
O
CF3
Ph
ppm

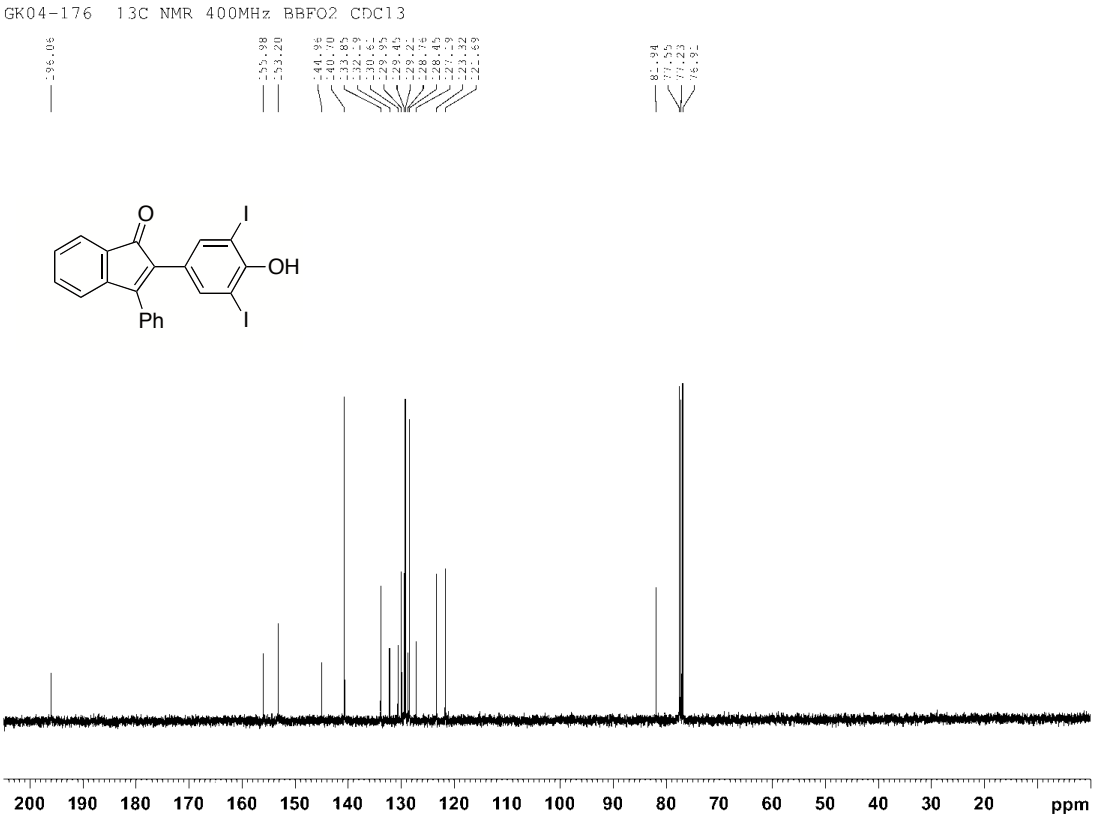
**7e**


GK04-177 1H NMR 400MHz BBFO2 CDCl3
7.638
7.621
7.435
7.432
7.415
7.405
7.398
7.361
7.359
7.342
7.324
7.296
7.289
7.275
7.270
7.264
7.259
7.254
6.893
6.874
6.872
6.854
1.646
O
F
Ph
F
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
5.89
1.02
1.92
1.96

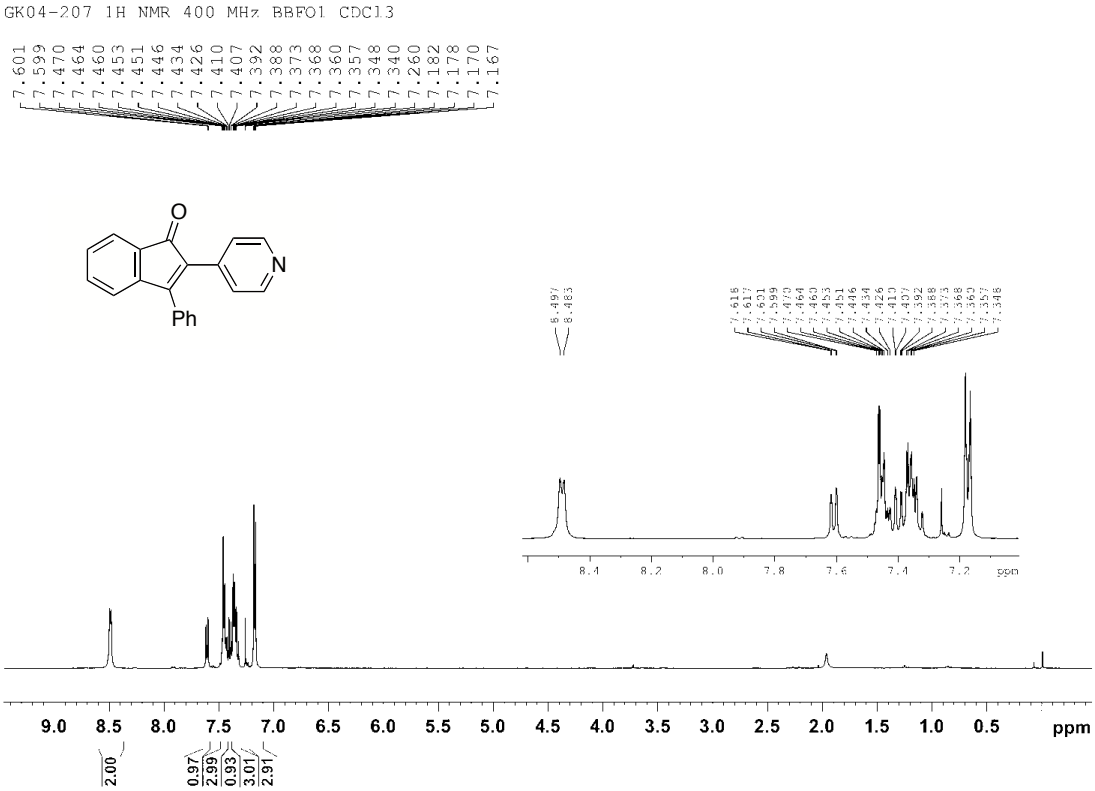

GK04-177 13C NMR 400MHz BBFO2 CDCl3
194.39
162.30
162.23
160.13
159.81
159.74
144.75
133.48
132.61
131.48
130.50
130.40
130.30
130.08
129.87
128.81
127.77
123.70
123.47
122.04
111.79
111.73
111.60
111.54
109.39
109.29
108.98
77.55
77.23
76.92
O
F
Ph
F
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

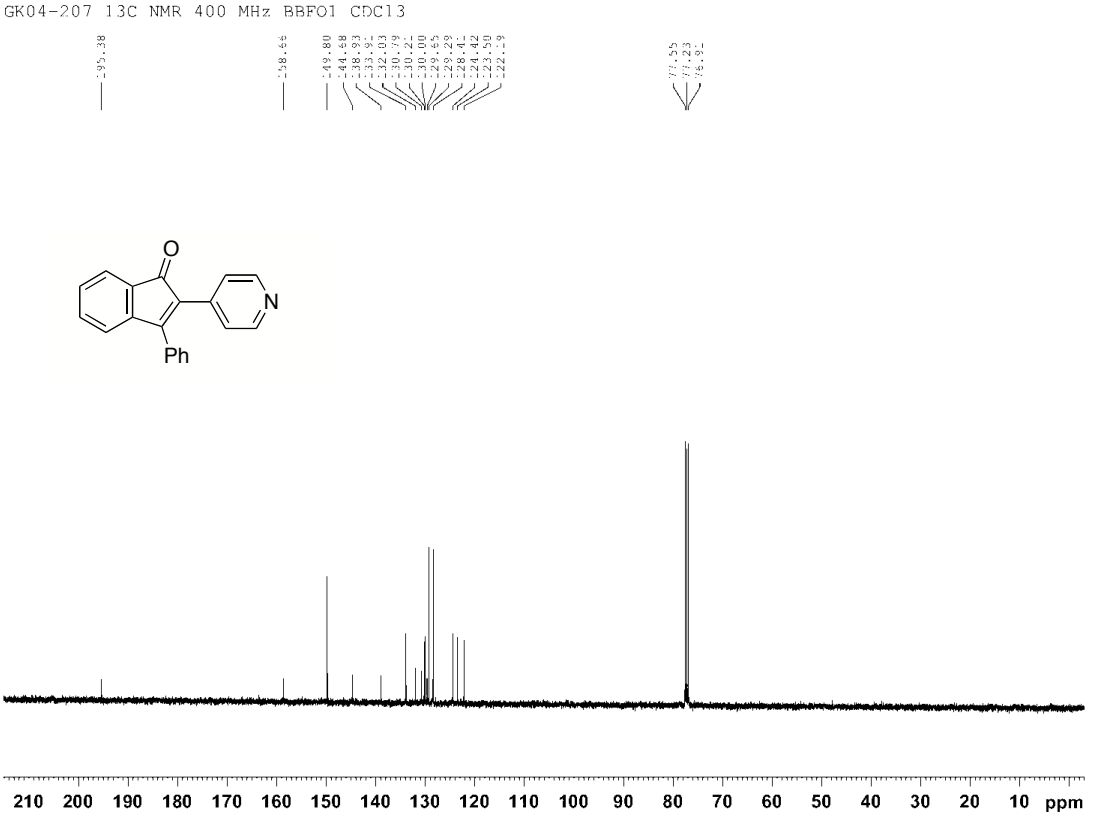
**7f**


GK04-176 1H NMR 400MHz BBFO2 CDCl3
7.591
7.573
7.556
7.474
7.473
7.465
7.459
7.388
7.381
7.372
7.362
7.356
7.307
7.289
7.271
7.137
7.119
5.815
O
I
OH
Ph
I
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 ppm
1.88
1.04
3.02
3.05
1.19
1.06
1.00

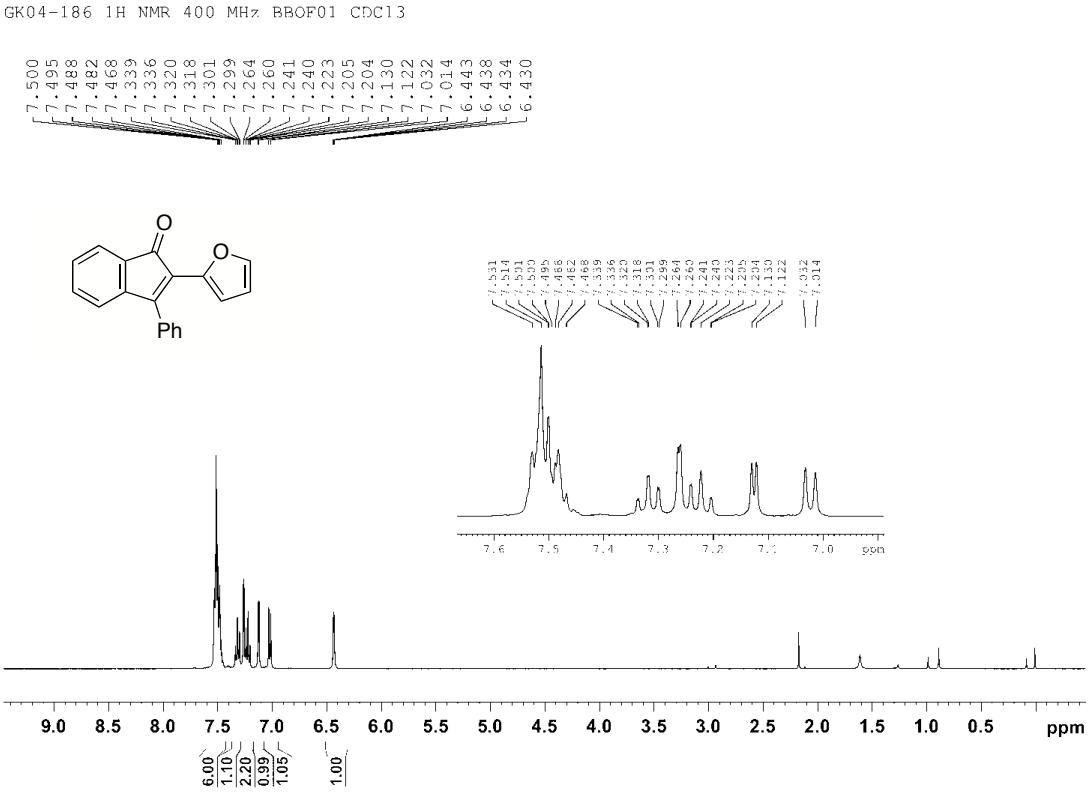

GK04-176 13C NMR 400MHz BBFO2 CDCl3
O
I
OH
Ph
I
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

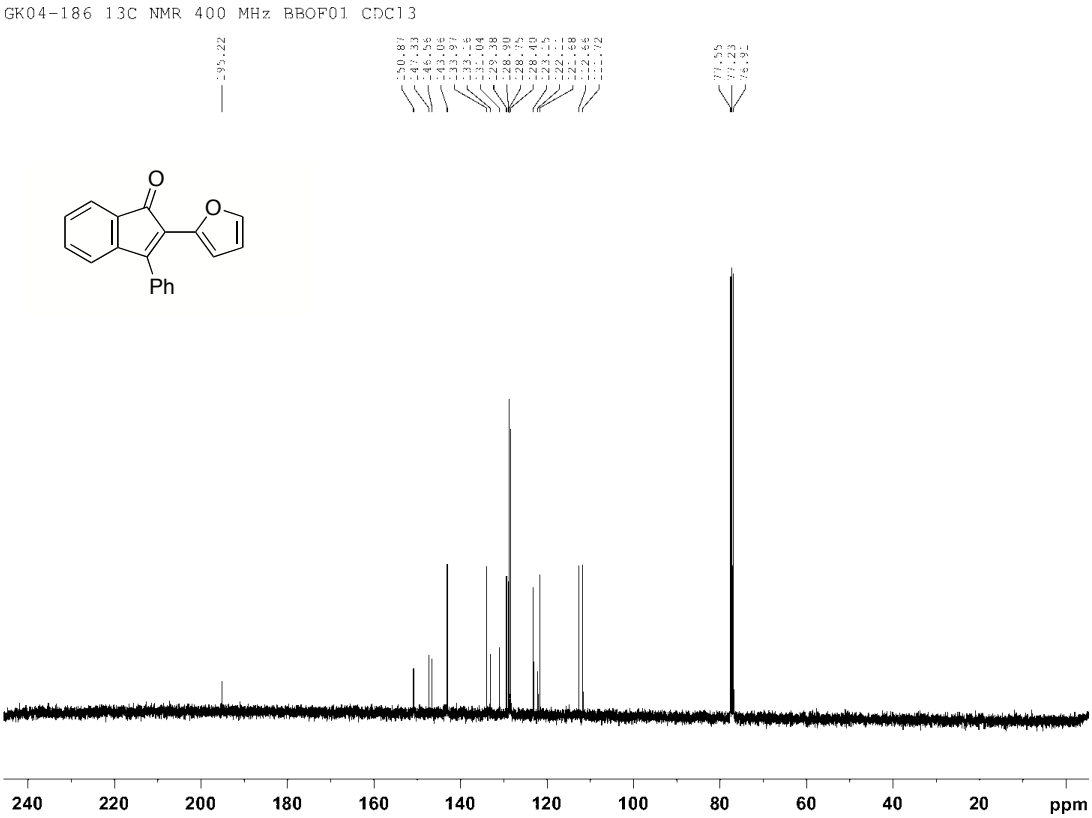
**7g**


GK04-207 1H NMR 400 MHz BBFO1 CDCl3
O
N
Ph
ppm

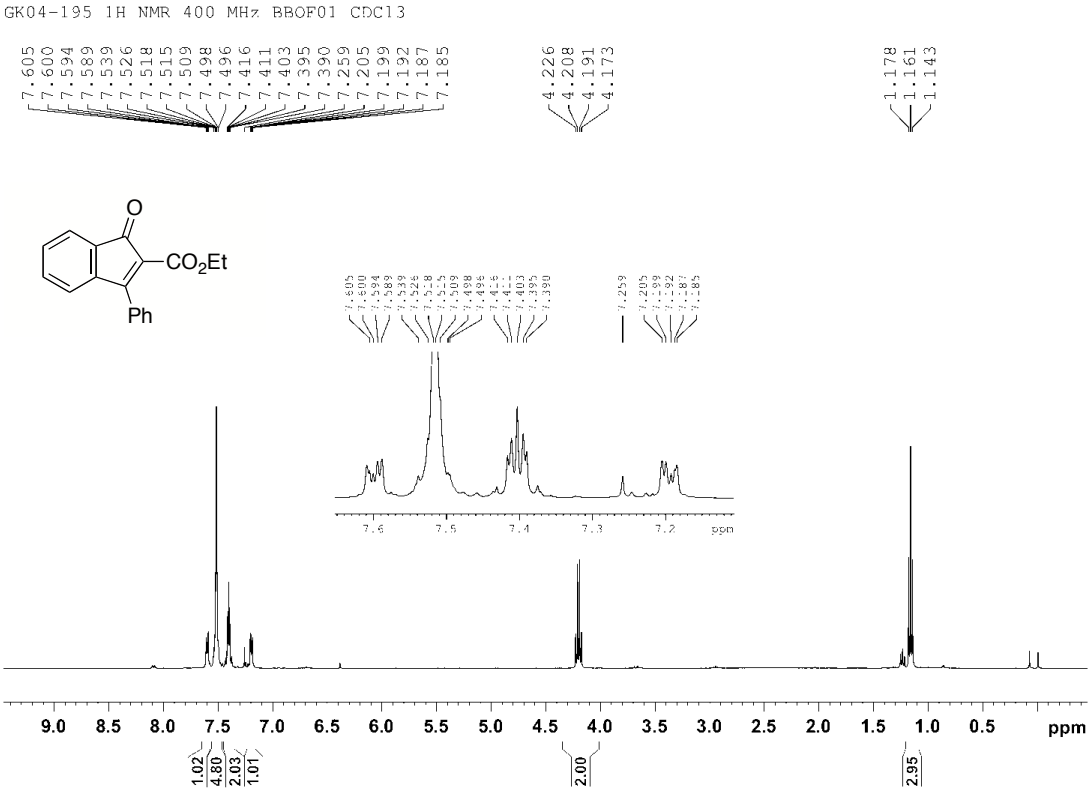

GK04-207 13C NMR 400 MHz BBFO1 CDCl3
O
N
Ph
ppm

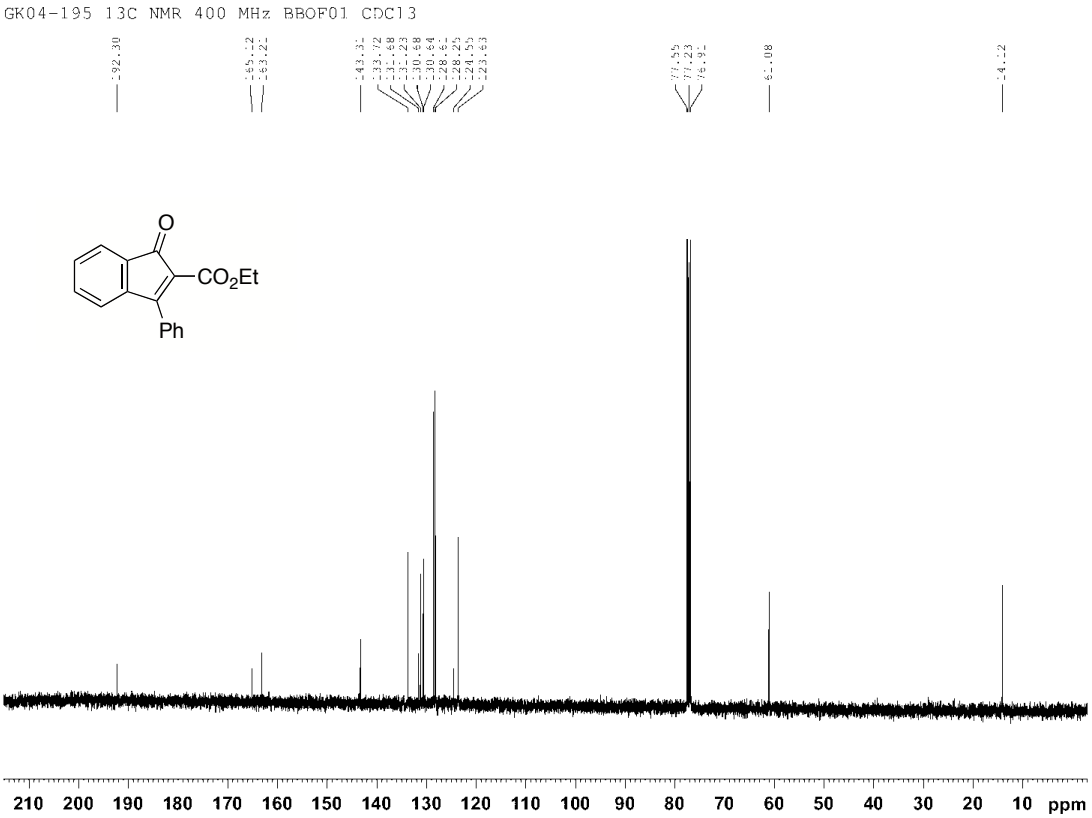
**7h**


GK04-186 1H NMR 400 MHz BBOF01 CDCl3
7.500
7.495
7.488
7.482
7.468
7.339
7.336
7.320
7.318
7.301
7.299
7.264
7.260
7.241
7.240
7.223
7.205
7.204
7.130
7.122
7.032
7.014
6.443
6.438
6.434
6.430
O
O
Ph
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
6.00
1.10
2.20
0.99
1.05
1.00

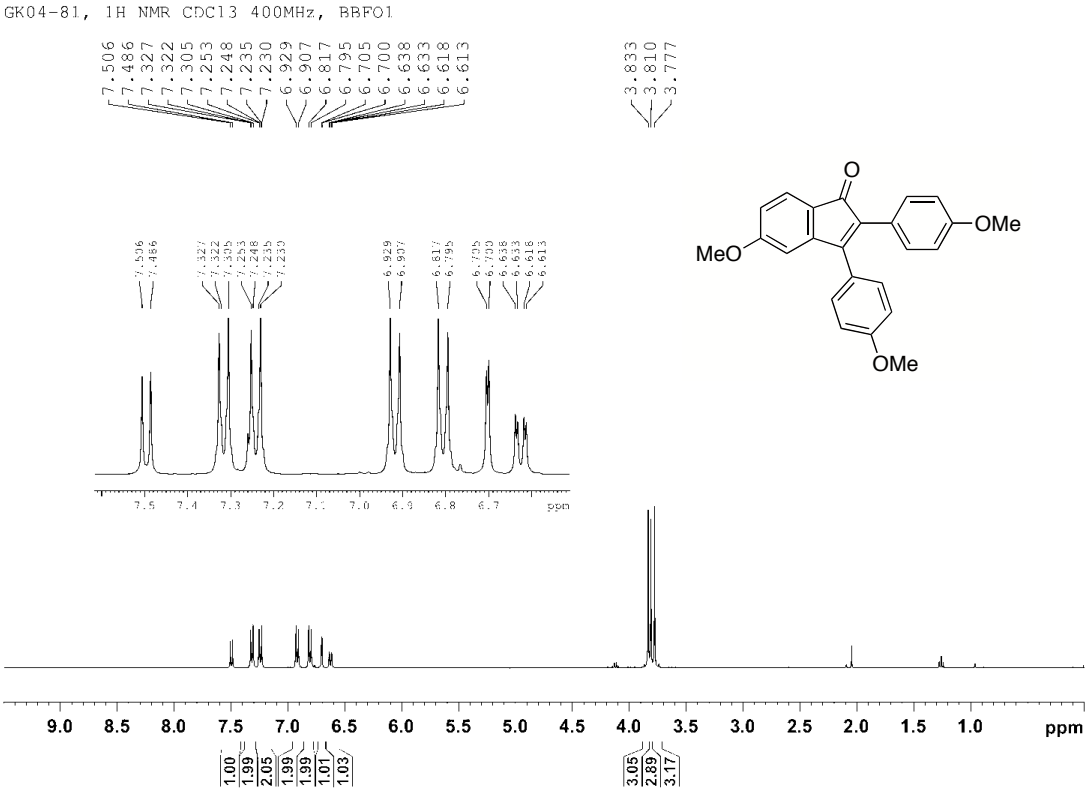

GK04-186 13C NMR 400 MHz BBOF01 CDCl3
195.22
150.87
147.33
146.56
143.06
133.97
133.56
131.04
129.38
128.90
128.75
128.40
123.15
122.68
122.66
111.72
77.55
77.23
76.92
O
O
Ph
240 220 200 180 160 140 120 100 80 60 40 20 ppm

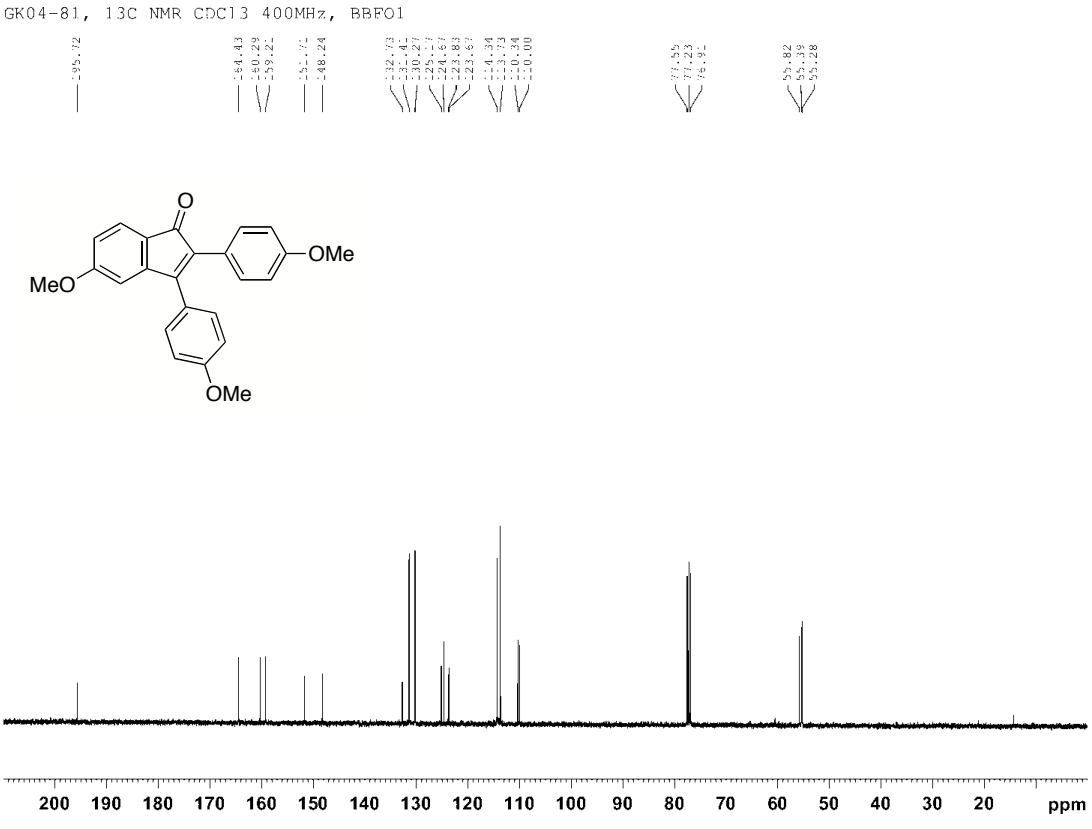
**7i**


GK04-195 1H NMR 400 MHz BBOF01 CDCl3
7.605
7.600
7.594
7.589
7.539
7.526
7.518
7.515
7.509
7.498
7.496
7.416
7.411
7.403
7.395
7.390
7.259
7.205
7.199
7.192
7.187
7.185
4.226
4.208
4.191
4.173
1.178
1.161
1.143
O
CO2Et
Ph
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
1.02
4.80
2.03
1.01
2.00
2.95

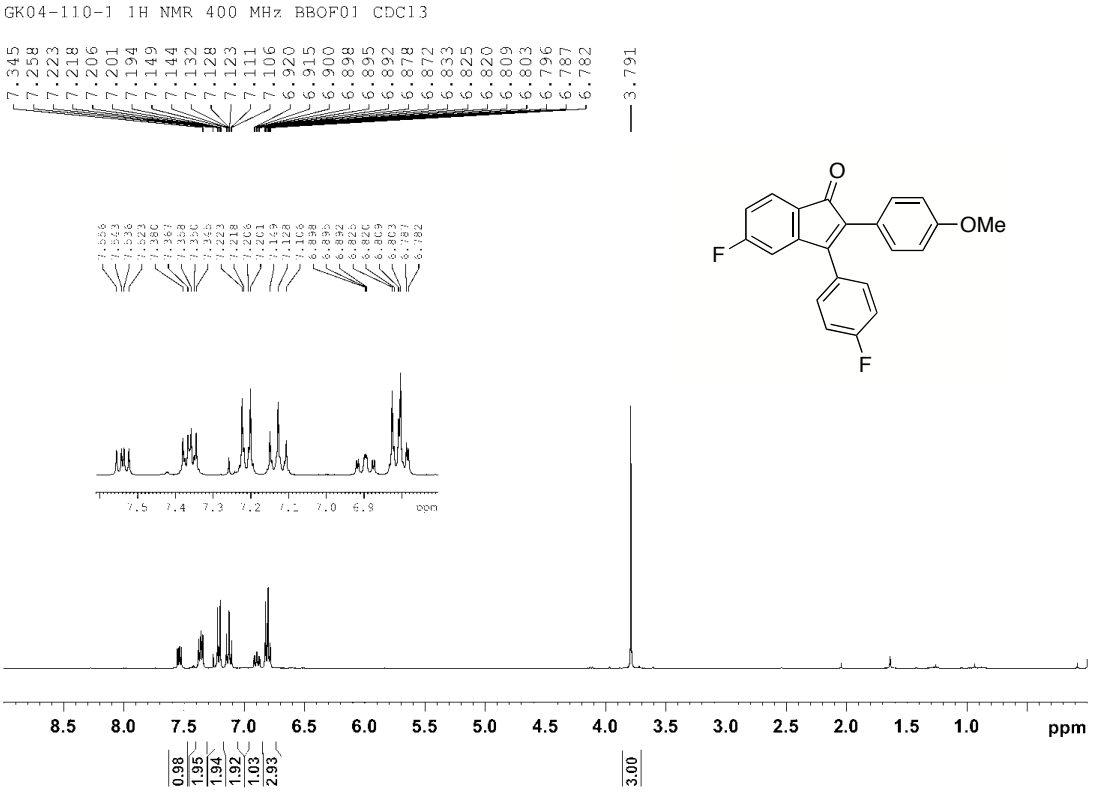

GK04-195 13C NMR 400 MHz BBOF01 CDCl3
O
CO2Et
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

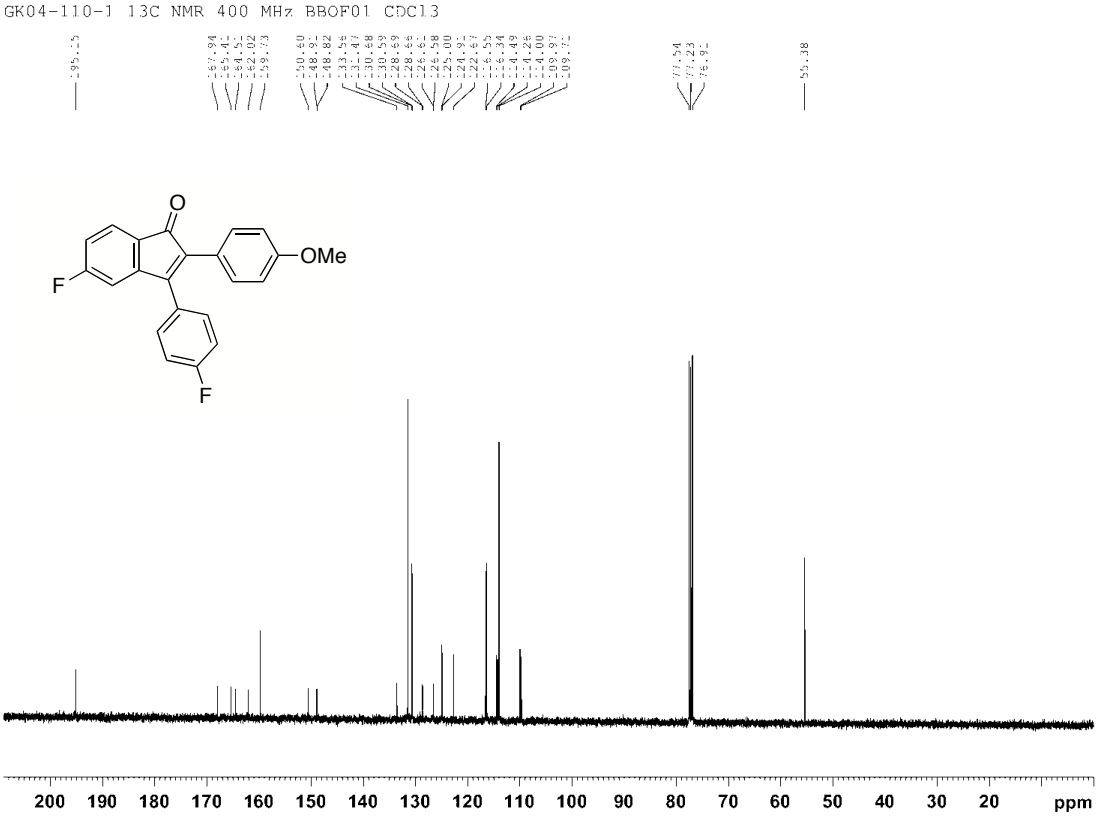
**7j**


GK04-81, 1H NMR CDCl3 400MHz, BBFO1
7.506
7.486
7.327
7.322
7.305
7.253
7.248
7.235
7.230
6.929
6.907
6.817
6.795
6.705
6.700
6.638
6.633
6.618
6.613
3.833
3.810
3.777
O
OMe
MeO
OMe
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 ppm
1.00 1.99 2.05 1.99 1.99 1.01 1.03
3.05 2.89 3.17

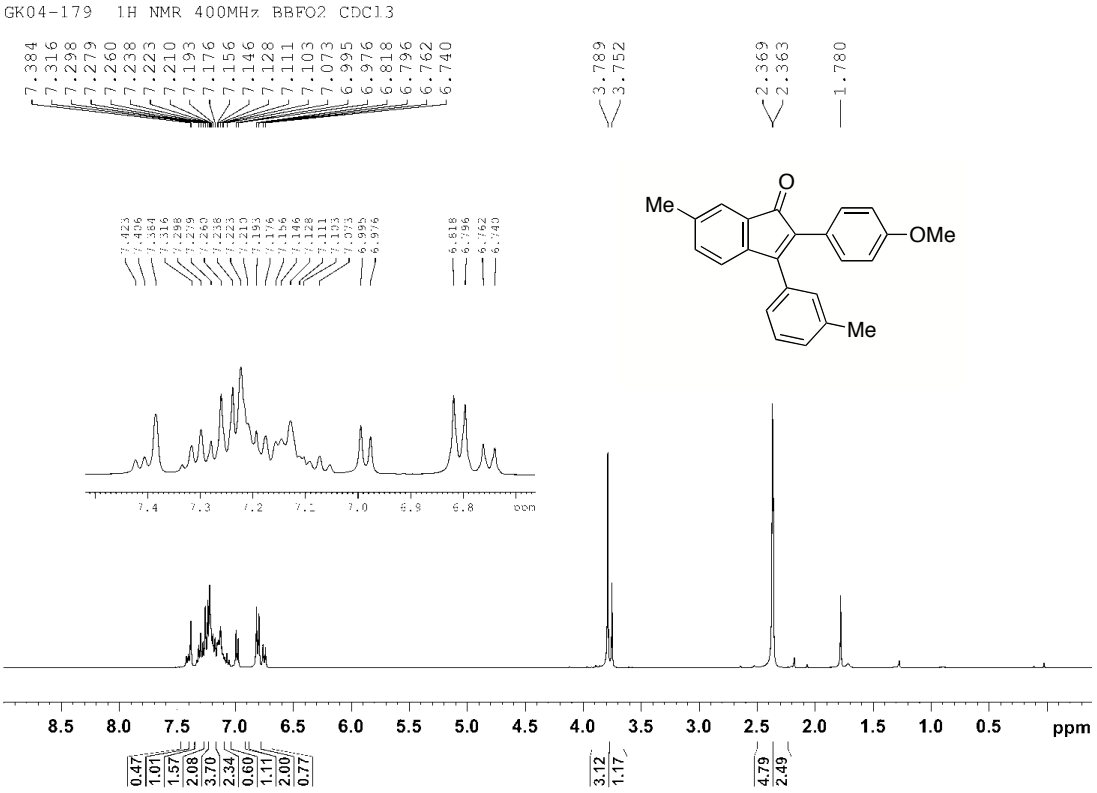

GK04-81, 13C NMR CDCl3 400MHz, BBFO1
O
OMe
MeO
OMe
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

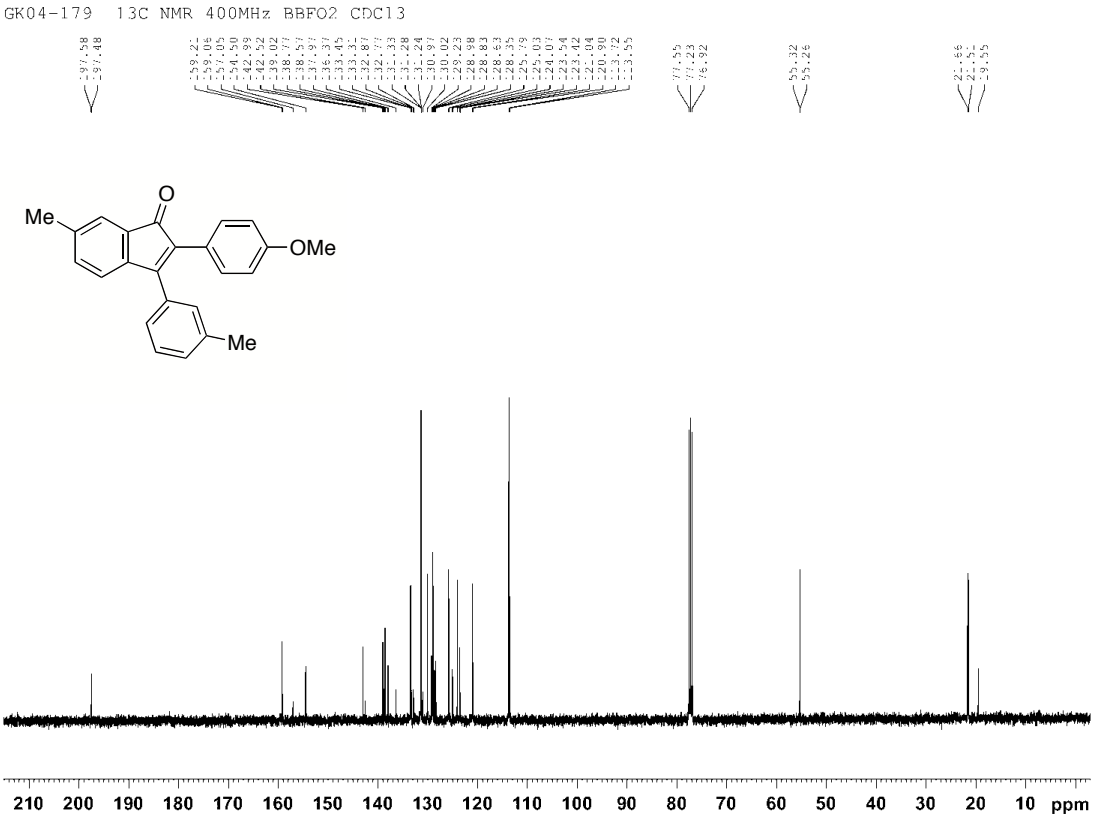
**7k**


GK04-110-1 1H NMR 400 MHz BBOF01 CDCl3
7.345
7.258
7.223
7.218
7.206
7.201
7.194
7.149
7.144
7.132
7.128
7.123
7.111
7.106
6.920
6.915
6.900
6.898
6.895
6.892
6.878
6.872
6.833
6.825
6.820
6.809
6.803
6.796
6.787
6.782
3.791
O
OMe
F
F
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 ppm
0.98 1.95 1.94 1.92 1.03 2.93 3.00

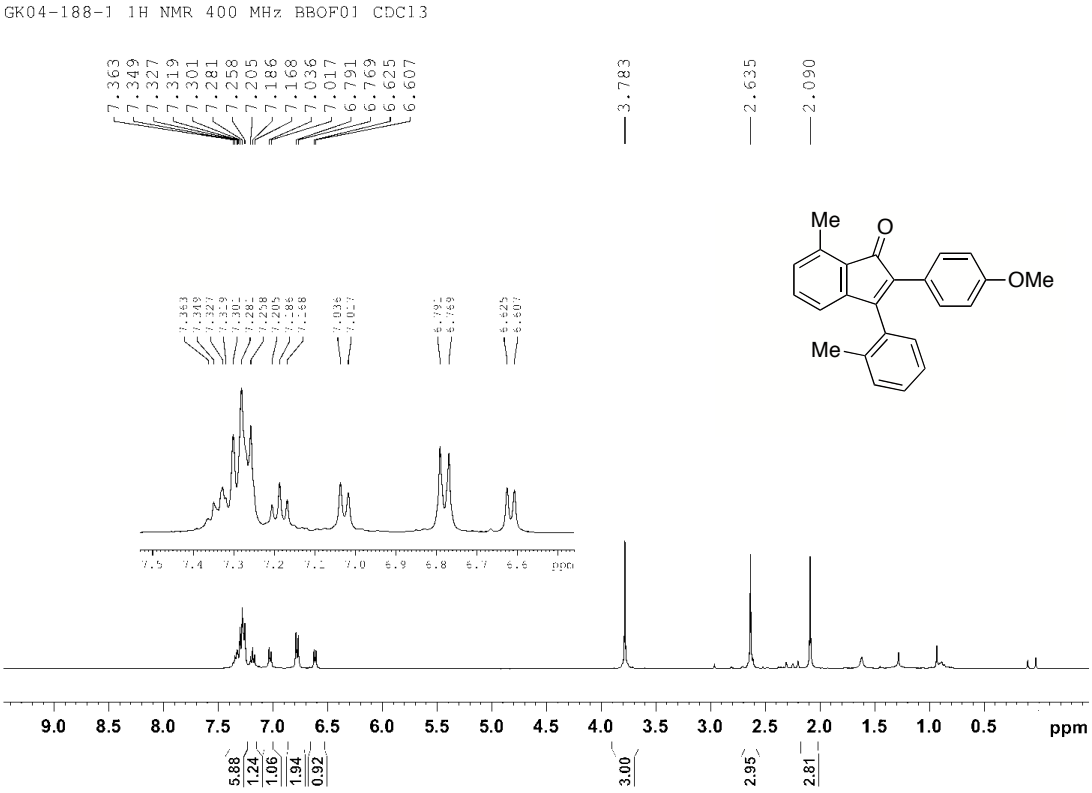

GK04-110-1 13C NMR 400 MHz BBOF01 CDCl3
195.5
167.94
165.41
164.52
162.02
159.73
150.60
148.90
148.82
133.56
131.47
130.58
130.59
128.69
128.46
126.62
126.58
125.00
124.97
122.67
116.55
116.34
114.49
114.26
114.00
109.97
109.72
77.54
77.23
76.92
55.38
O
OMe
F
F
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

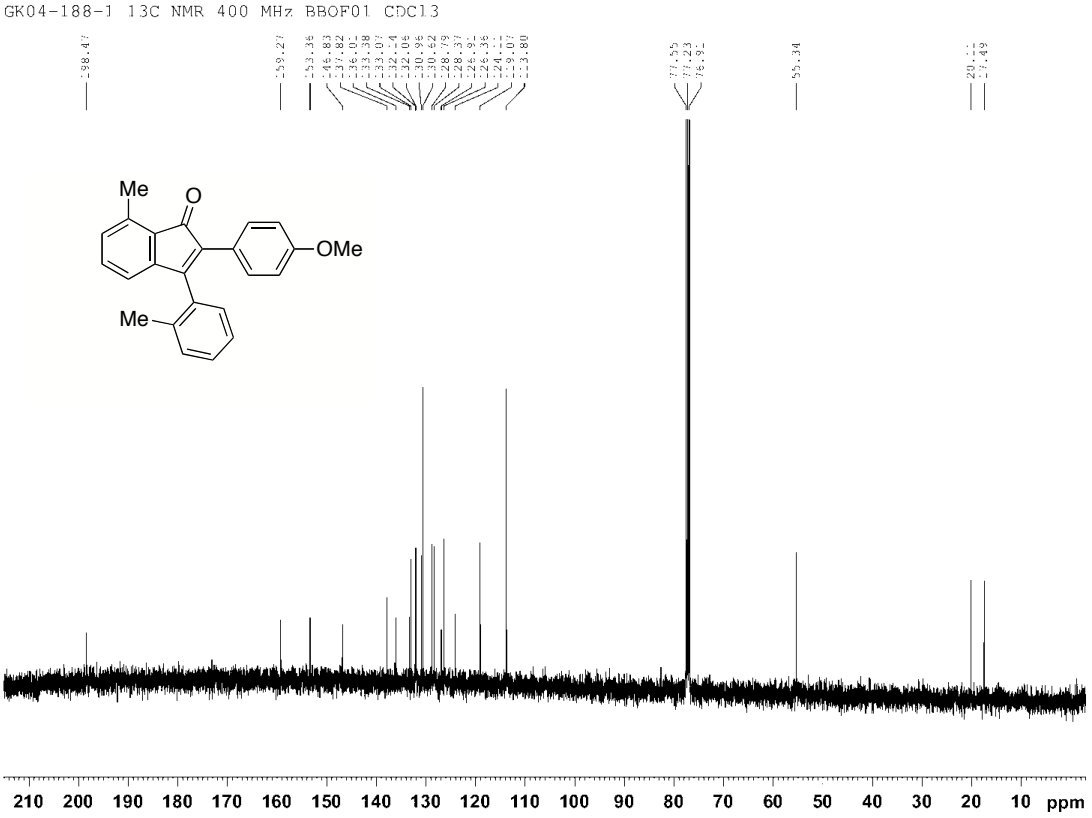
**7l**


GK04-179 1H NMR 400MHz BBFO2 CDCl3
7.384
7.316
7.298
7.279
7.260
7.238
7.223
7.210
7.193
7.176
7.156
7.146
7.128
7.111
7.103
7.073
6.995
6.976
6.818
6.796
6.762
6.740
3.789
3.752
2.369
2.363
1.780
Me
O
OMe
Me
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
0.47 1.01 1.57 2.08 3.70 2.34 0.60 1.11 2.00 0.77
3.12 1.17
4.79 2.49

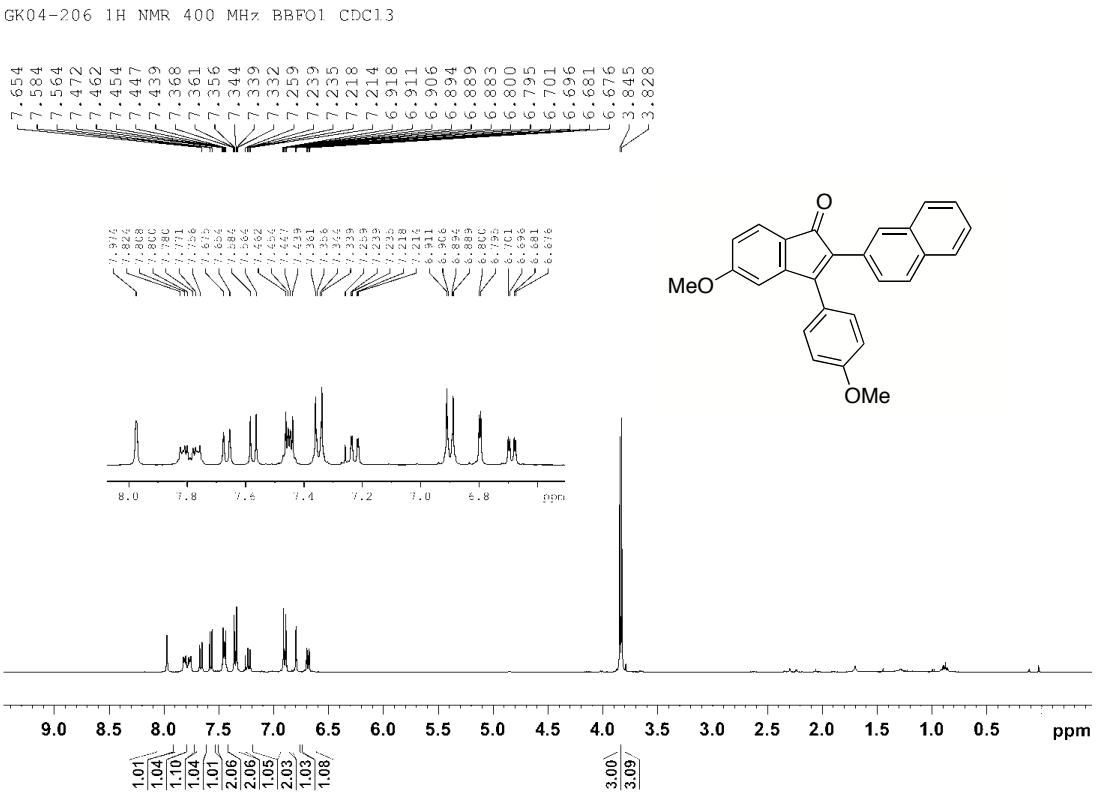

GK04-179 13C NMR 400MHz BBFO2 CDCl3
197.58
197.48
77.55
77.23
76.92
55.32
55.26
Me
O
OMe
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

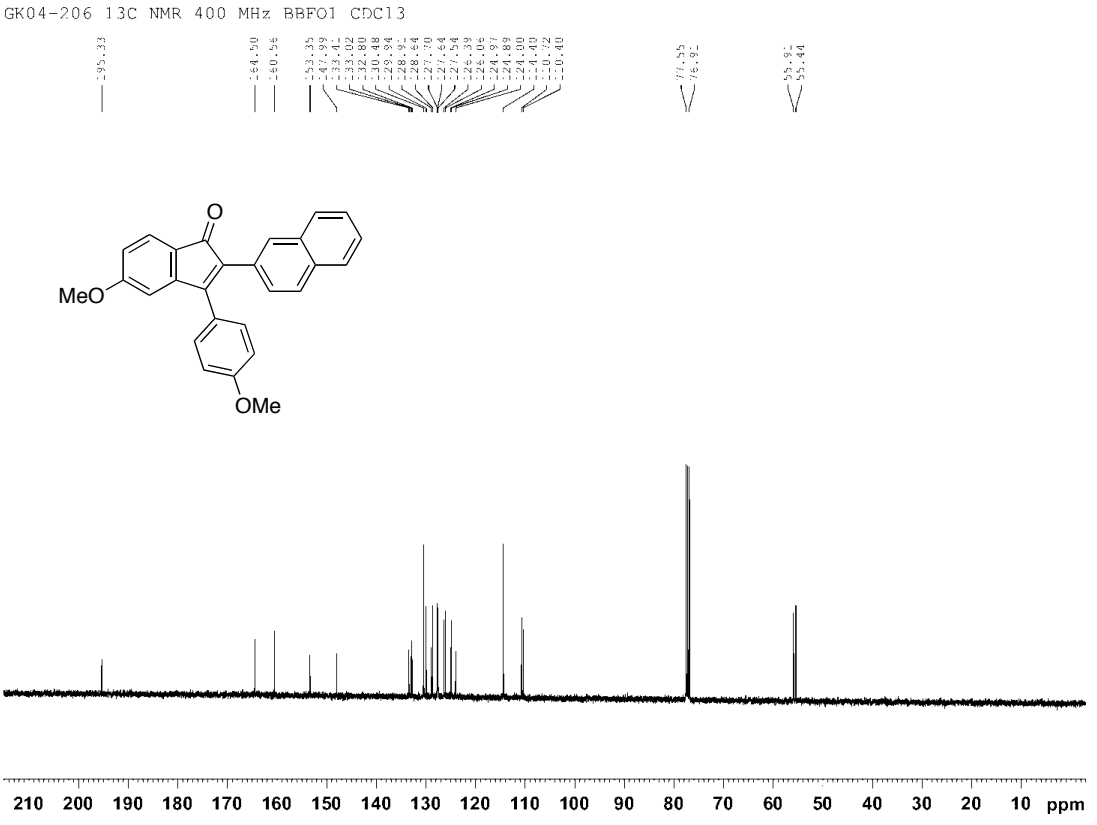
**7m**


GK04-188-1 1H NMR 400 MHz BBOF01 CDCl3
7.363
7.349
7.327
7.319
7.301
7.281
7.258
7.205
7.186
7.168
7.036
7.017
6.791
6.769
6.625
6.607
3.783
2.635
2.090
Me
O
OMe
Me
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
5.88
1.24
1.06
1.94
0.92
3.00
2.95
2.81

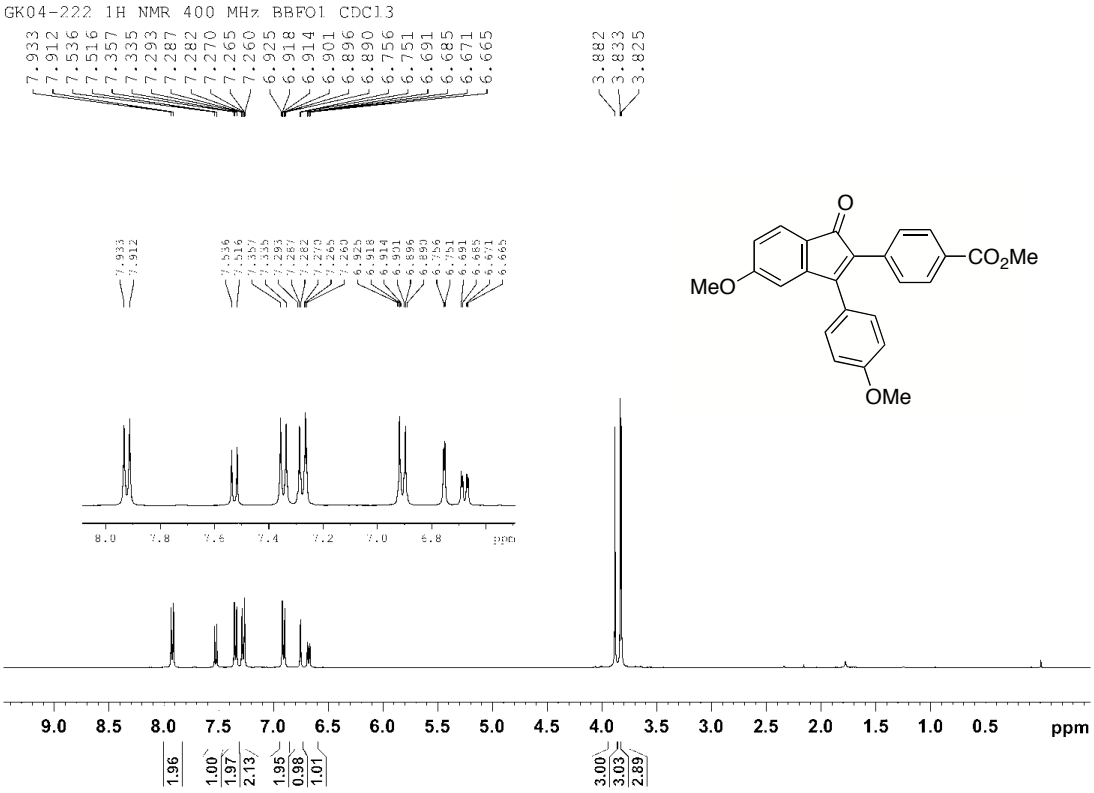

GK04-188-1 13C NMR 400 MHz BBOF01 CDCl3
198.47
159.27
153.36
77.55
77.23
76.92
55.34
20.11
17.49
Me
O
OMe
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

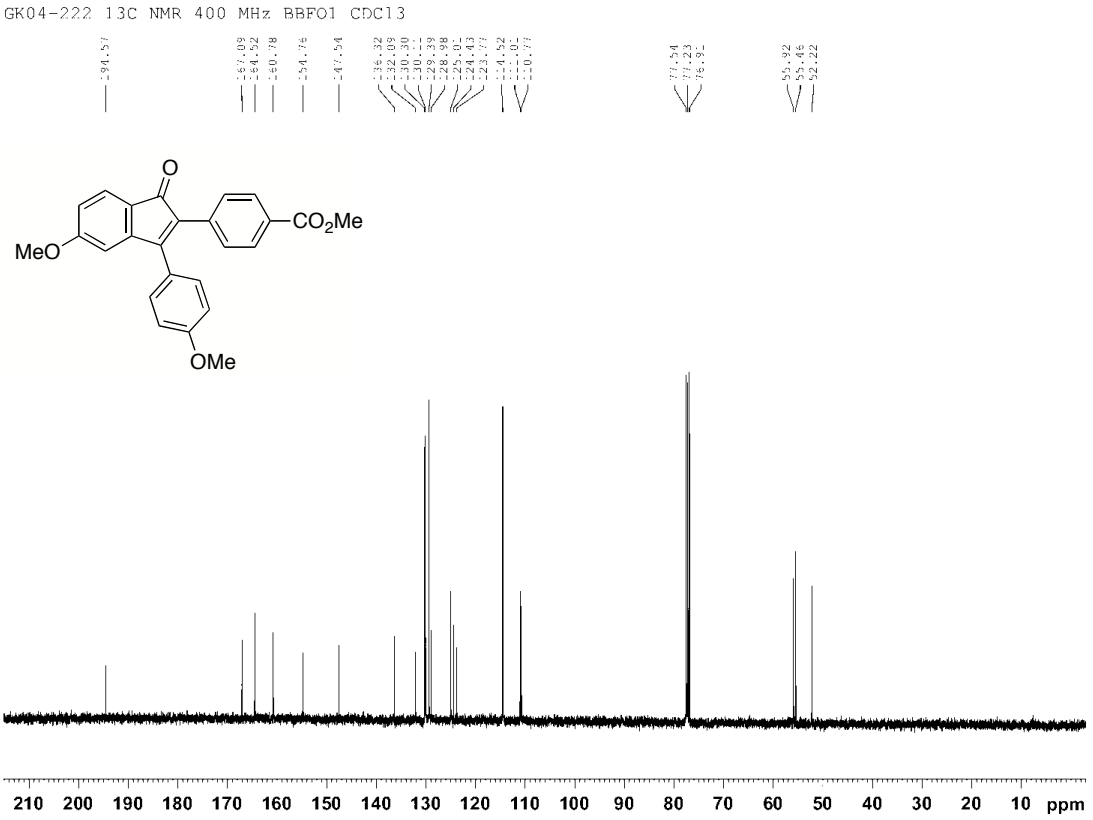
**7n**


GK04-206 1H NMR 400 MHz BBFO1 CDCl3
7.654
7.584
7.564
7.472
7.462
7.454
7.447
7.439
7.368
7.361
7.356
7.344
7.339
7.332
7.259
7.239
7.235
7.218
7.214
6.918
6.911
6.906
6.894
6.889
6.883
6.800
6.795
6.701
6.696
6.681
6.676
3.845
3.828
MeO
OMe
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
1.01 1.04 1.10 1.04 1.01 2.06 2.06 1.05 2.03 1.03 1.08
3.00 3.09

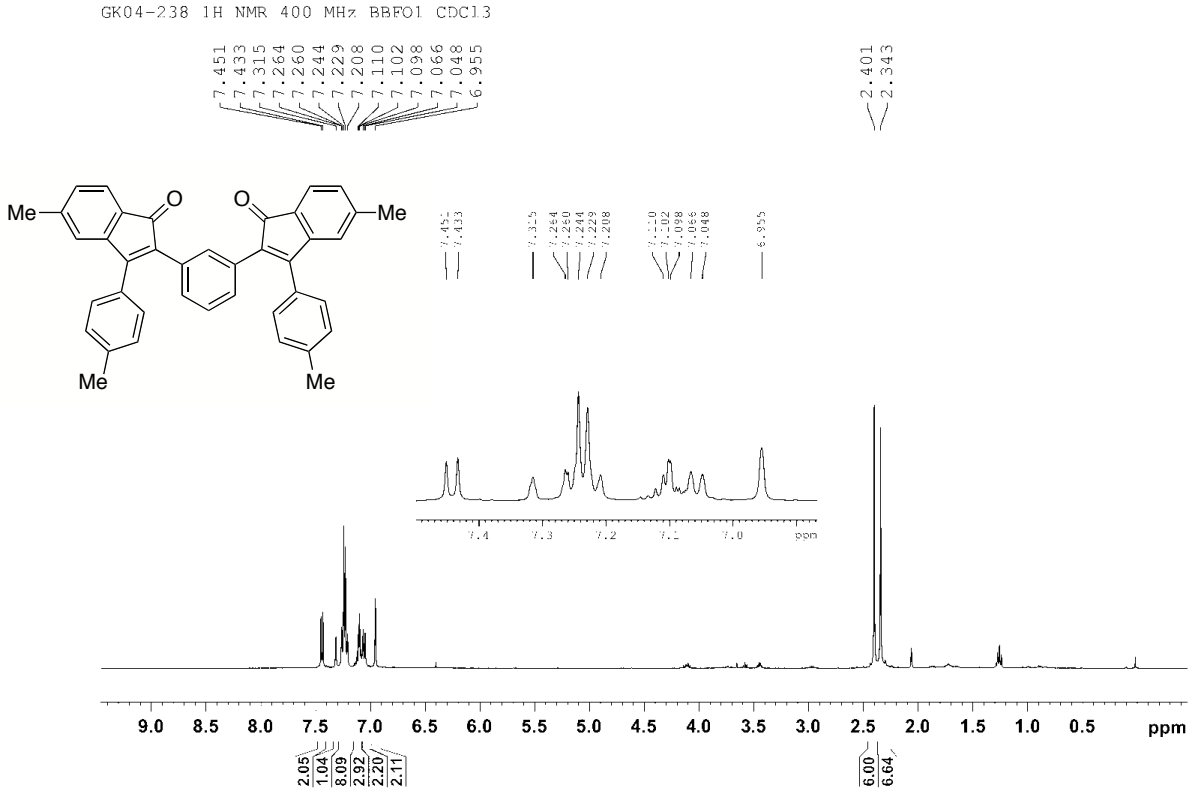

GK04-206 13C NMR 400 MHz BBFO1 CDCl3
195.33
164.50
160.56
153.35
147.99
143.42
133.02
132.80
130.48
129.94
128.92
128.64
127.70
127.64
127.54
126.39
126.06
124.97
124.89
124.00
114.40
110.72
110.40
77.52
76.92
55.92
55.44
MeO
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

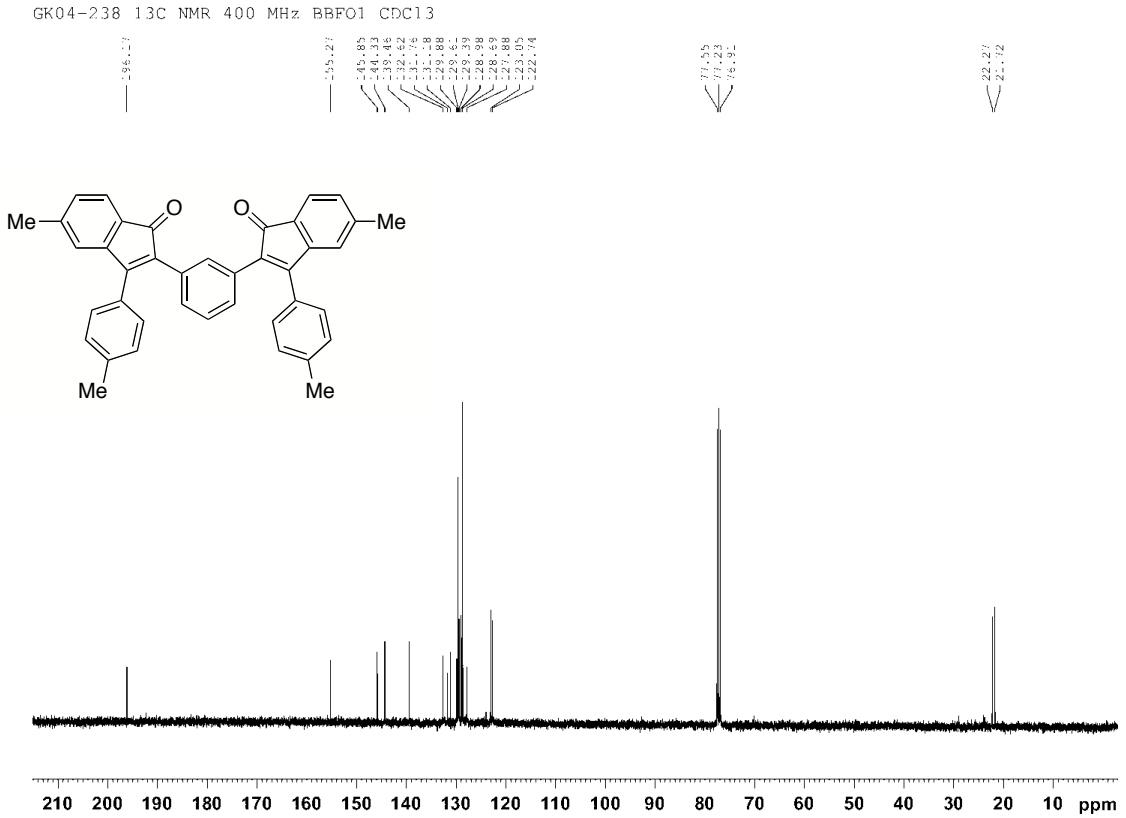
**7o**


GK04-222 1H NMR 400 MHz BBFO1 CDCl3
7.933
7.912
7.536
7.516
7.357
7.335
7.293
7.287
7.282
7.270
7.265
7.260
6.925
6.918
6.914
6.901
6.896
6.890
6.756
6.751
6.691
6.685
6.671
6.665
3.882
3.833
3.825
O
CO2Me
MeO
OMe
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
1.96
1.00
1.97
2.13
1.95
0.98
1.01
3.00
3.03
2.89

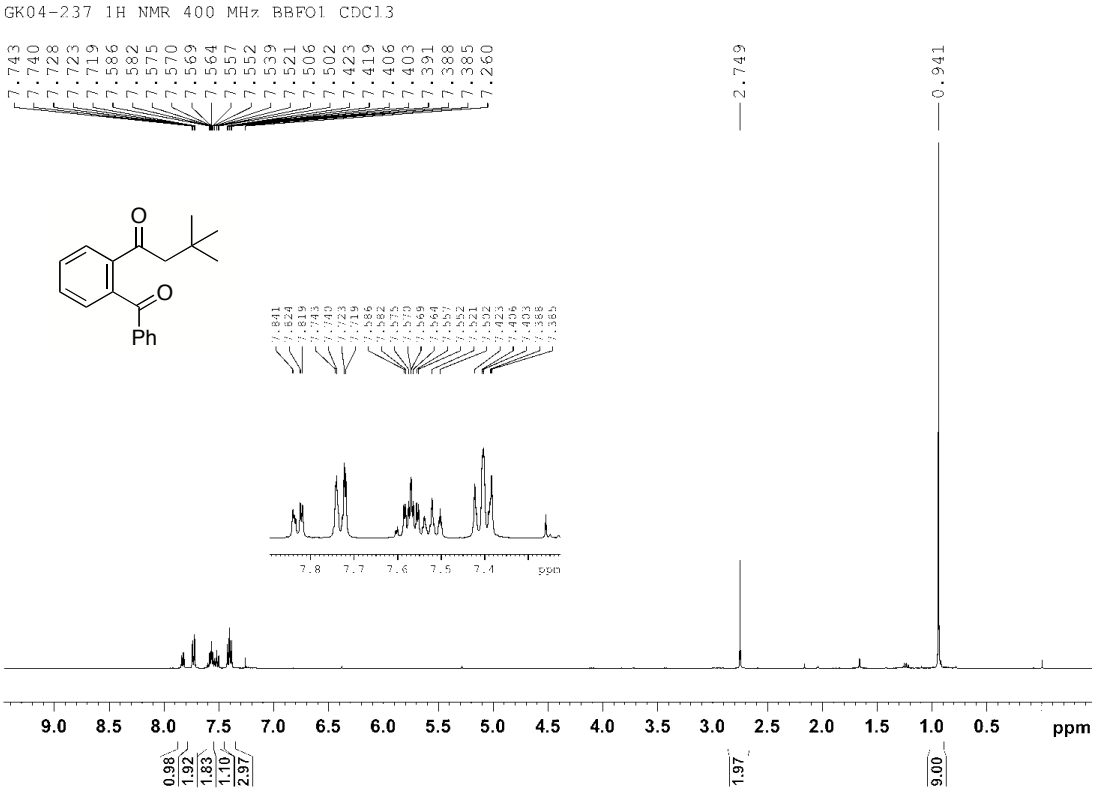

GK04-222 13C NMR 400 MHz BBFO1 CDCl3
O
CO2Me
MeO
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

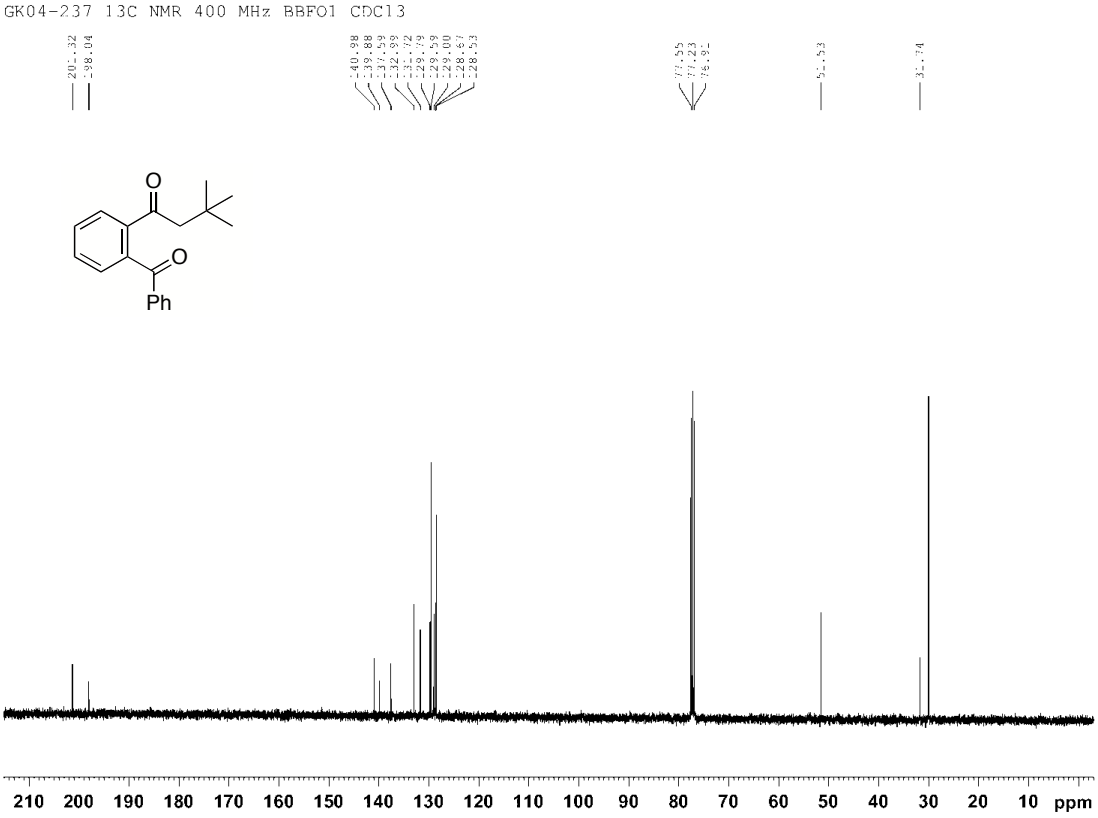
**7p**


GK04-238 1H NMR 400 MHz BBFO1 CDCl3
7.451
7.433
7.315
7.264
7.260
7.244
7.229
7.208
7.110
7.102
7.098
7.066
7.048
6.955
2.401
2.343
Me
O
O
Me
Me
Me
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
2.05
1.04
8.09
2.92
2.20
2.11
6.00
6.64


GK04-238 13C NMR 400 MHz BBFO1 CDCl3
145.85
144.33
139.46
132.62
131.18
129.88
129.61
129.39
128.98
128.69
127.88
123.05
122.14
77.55
77.23
76.92
22.27
22.12
Me
O
O
Me
Me
Me
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

**7q**


GK04-237 1H NMR 400 MHz BBFO1 CDCl3
7.743
7.740
7.728
7.723
7.719
7.586
7.582
7.575
7.570
7.569
7.564
7.557
7.552
7.539
7.521
7.506
7.502
7.423
7.419
7.406
7.403
7.391
7.388
7.385
7.260
2.749
0.941
O
O
Ph
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
1.92
1.83
1.10
2.97
1.97
9.00


GK04-237 13C NMR 400 MHz BBFO1 CDCl3
200.32
198.04
140.98
139.88
137.59
132.99
131.72
129.79
129.58
129.00
128.67
128.53
77.55
77.23
76.92
52.53
30.74
O
O
Ph
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm