Supporting Information

Synthesis of 1,2,4,5-*Tetra*-Substituted Benzenes via Copper-Catalyzed Dimerization of γ,δ-Unsaturated ketones

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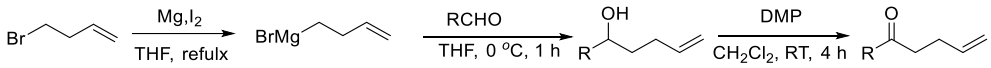
I General information

^{1}H NMR and **^{13}C NMR** spectra were recorded on a Bruker Avance 600 MHz instruments. Chemical shifts were reported in parts per million (ppm), and the residual solvent peak was used as an internal reference: proton (chloroform δ 7.26), carbon (chloroform δ 77.16) or tetramethylsilane (TMS δ 0.00) was used as a reference. Multiplicity was indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), bs (broad singlet). Coupling constants were reported in Hertz (Hz). All high resolution mass spectra (**HRMS**) were obtained on a Bruker Apex-2. For thin layer chromatography (**TLC**), Qingdao Haiyang Chemical was used, and compounds were visualized with a UV light at 254 nm. Further visualization was achieved by staining with iodine, or potassium permanganate solution followed by heating using a heat gun. Flash chromatography separations were performed on Qingdao Haiyang Chemical 200-300 mesh silica gel. All reactions were carried out under a nitrogen atmosphere. All commercially available reagents were used as received for the reactions without any purification. All solvents were dried on alumina columns using a solvent dispensing system.

II General procedure

General procedure for preparation of γ,δ-unsaturated ketones

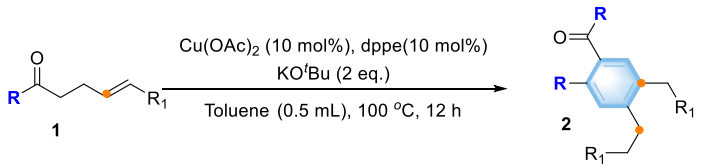


Step 1: To a 150 mL flame-dried and nitrogen-flushed, three-necked, round-bottomed flask equipped with a stirring bar was charged with Mg turnings and a grain of iodine, a constant pressure funnel was charged with 4-bromo-1-butene (26 mmol, 1.3 equiv.) solubilized in anhydrous 1.0 M THF and a condenser. 4-bromo-1-butene (26 mmol, 1.3 equiv.) in anhydrous 1.0 M THF was dropwise added to magnesium turnings (28 mmol, 1.4 equiv.) and a grain of iodine in THF (20 mL) which have preheating by heat gun, at such a rate to maintain a gentle reflux. Then, the freshly prepared solution of but-3-en-1-ylmagnesium bromide was slowly added to the aldehyde (20 mmol, 1.0 equiv.) in 0.25 M THF via a syringe dropwise under 0 °C. The mixture was allowed to warm to room temperature and stirred for 2 h. Saturated aqueous NH_4Cl was added,

and the mixture was diluted with ethyl acetate (EA). The layers were separated, and the organic layer was dried (Na_2SO_4), filtered and evaporated. Purification by column chromatography on silica gel.

Step 2: To a 100 mL flame-dried round-bottom flask equipped with a stir-bar was added Dess-Martin Periodinane (DMP) (18 mmol, 1.2 equiv.). It was solubilized in anhydrous 0.25 M DCM and stirred at room temperature. Then, the corresponding alcohol (15 mmol, 1.0 equiv.) was slowly added via a syringe and stirred for 4 hours. Saturated aqueous $NaHCO_3$ was added, and the mixture was diluted with ethyl acetate (EA). The layers were separated, and the organic layer was dried (Na_2SO_4), filtered and evaporated. Purification by column chromatography on silica gel to afford the corresponding ketones.

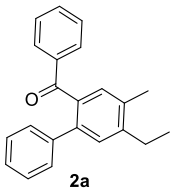
General procedure for the synthesis of 1,2,4,5-tetra-substituted benzenes



To a vial equipped with a dried stir bar was added unsaturated ketones **1** (0.1 mmol), $Cu(OAc)_2$ (10 mol%), dppe (20 mol%), KO^tBu (2.0 equiv), toluene (0.5 mL) in the glovebox. The reaction mixture was taken outside the glovebox and allowed to stir at 100 °C (oil bath) for 12 h. The reaction mixture was added to water (10 mL), and extracted with EtOAc (3 ×5 mL). The organic layer was washed with aqueous $NaHCO_3$ and brine and dried over Na_2SO_4. And the residue was purified by column chromatography with silica gel to give pure products **2**.

III The analytical and spectral characterization data

(5-Ethyl-4-methyl-[1,1'-biphenyl]-2-yl)(phenyl)methanone (2a)



2a

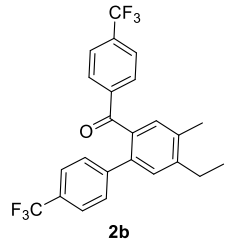
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 10.5 mg of yellow oil in 75% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.2 Hz, 1H), 7.30 (s, 1H), 7.24-7.23 (m, 3H), 7.17 (t, *J* = 7.2 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H), 2.74 (q, *J* = 7.8 Hz, 2H), 2.38 (s, 3H), 1.29 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.1, 145.2, 140.6, 139.2, 137.8, 136.5, 135.0, 132.7, 130.7, 130.1, 129.8, 129.1, 128.3, 128.1, 127.1, 26.4, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{22}H_{20}O$ $[M+H]^+$: 301.1587; Found: 301.1586.

(5-Ethyl-4-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)(4-(trifluoromethyl)ph-enyl)methanone (2b)



2b

The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 12.5 mg of yellow oil in 71% yield.

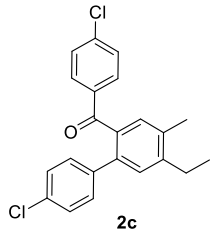
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.8 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.37-7.29 (m, 3H), 7.26 (s, 1H), 2.76 (q, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.4, 146.3, 144.1, 140.7, 138.3, 136.2, 135.6, 131.2, 130.2, 130.0, 129.6, 129.5, 125.4, 125.3, 125.3, 125.3, 26.4, 19.1, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.73, -63.27.

HRMS(ESI): m/z Calcd. for $C_{24}H_{18}F_6O$ $[M+Na]^+$: 459.1154; Found: 459.1152.

(4'-Chloro-5-ethyl-4-methyl-[1,1'-biphenyl]-2-yl)(4-chlorophenyl)methanone (2c)



2c

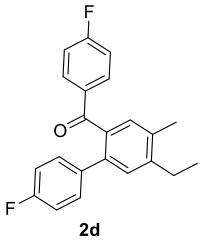
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 8.6 mg of yellow oil in 47% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 6.8 Hz, 1H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.31-7.23 (m, 4H), 7.19-7.14 (m, 4H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.9, 145.3, 139.2, 137.8, 136.4, 135.4, 133.3, 133.0, 130.8, 130.4, 130.1, 129.7, 128.5, 128.3, 26.4, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{12}H_{18}Cl_2O$ $[M+H]^+$: 369.0807; Found: 369.0805.

(5-Ethyl-4'-fluoro-4-methyl-[1,1'-biphenyl]-2-yl)(4-fluorophenyl)methanone (2d)



2d

The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.50 in hexane:ethyl acetate = 15:1) resulting in 7.9 mg of yellow oil in 47% yield.

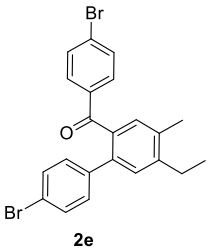
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (m, 2H), 7.28 (s, 1H), 7.21 (s, 1H), 7.20-7.17 (m, 2H), 6.93 (t, *J* = 8.4 Hz, 2H), 6.88 (t, *J* = 8.4 Hz, 2H), 2.74 (q, *J* = 7.8 Hz, 2H), 2.38 (s, 3H), 1.29 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.5, 166.4, 164.7, 163.0, 161.4, 145.4, 138.0, 136.6, 136.5, 135.4, 134.2, 132.6, 30.66, 130.7, 129.7, 128.2, 115.4, 26.40, 18.93, 14.35.

^{19}F NMR (376 MHz, $CDCl_3$) δ -105.46.

HRMS(ESI): m/z Calcd. for $C_{22}H_{18}F_2O$ $[M+H]^+$: 337.1398; Found: 337.1396.

(4'-Bromo-5-ethyl-4-methyl-[1,1'-biphenyl]-2-yl)(4-bromophenyl)methanone (2e)



2e

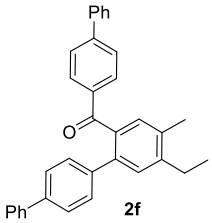
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 10:1) resulting in 7.3 mg of yellow oil in 32% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (m, 1H), 7.46-7.42 (m, 1H), 7.32-7.26 (m, 4H), 7.24-7.19 (m, 2H), 7.14-7.09 (m, 2H), 2.73 (q, *J* = 7.6 Hz, 3H), 2.37 (s, 3H), 1.26 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.7, 145.3, 139.6, 137.7, 135.4, 133.0, 131.4, 130.9, 130.7, 130.1, 129.7, 129.1, 128.3, 121.5, 26.4, 19.0, 14.4.

HRMS(ESI): m/z Calcd. for $C_{22}H_{18}Br_2O$ $[M+H]^+$: 456.9797; Found: 453.9795.

[1,1'-Biphenyl]-4-yl(5-ethyl-4-methyl-[1,1':4',1''-terphenyl]-2-yl)methanone (2f)



2f

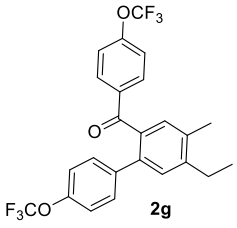
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (40:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 13.1 mg of yellow oil in 58% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 12 Hz, 2H), 7.58-7.46 (m, 6H), 7.46-7.39 (m, 5H), 7.39-7.31 (m, 7H), 2.77 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.6, 145.5, 145.2, 140.9, 140.2, 140.0, 139.7, 138.9, 136.7, 136.6, 135.1, 130.8, 130.7, 129.9, 129.6, 129.1, 129.0, 128.9, 128.8, 128.2, 127.4, 127.3, 127.2, 127.1, 126.9, 26.5, 19.0, 14.4.

HRMS(ESI): m/z Calcd. for $C_{38}H_{28}O$ $[M+H]^+$: 453.2213; Found: 453.2214.

(5-Ethyl-4-methyl-4'-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)(4-(trifluoromethoxy)phenyl)methanone (2g)



2g

The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 9.6 mg of yellow solid in 41% yield.

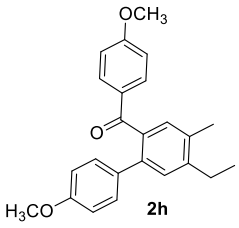
^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.4 Hz, 2H), 7.34 (s, 1H), 7.21 (t, *J* = 9 Hz, 3H), 7.06 (d, *J* = 7.2 Hz, 2H), 7.02 (d, *J* = 7.8 Hz, 2H), 2.75 (q, *J* = 7.2 Hz, 2H), 2.40 (s, 3H), 1.27 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.3, 152.3, 145.9, 139.2, 137.9, 136.2, 136.0, 135.9, 131.8, 130.9, 130.5, 129.7, 120.8, 120.0, 26.4, 19.0, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -57.78, -58.07.

HRMS(ESI): m/z Calcd. for $C_{24}H_{18}F_6O_3$ $[M+Na]^+$: 491.1052; Found: 491.1051.

(5-Ethyl-4'-methoxy-4-methyl-[1,1'-biphenyl]-2-yl)(4-methoxyphenyl)methanone (2h)



2h

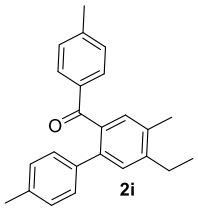
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (20:1) (R*f* = 0.40 in hexane:ethyl acetate = 10:1) resulting in 10.1 mg of yellow oil in 56% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.22-7.18 (m, 4H), 6.74 (t, *J* = 9.6 Hz, 4H), 3.80 (s, 3H), 3.73 (s, 3H), 2.74 (q, *J* = 7.8 Hz, 2H), 2.35 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 163.3, 158.8, 144.6, 138.3, 136.7, 134.5, 133.2, 132.5, 130.8, 130.3, 130.1, 129.6, 113.8, 113.4, 55.5, 55.3, 26.4, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}O_3$ $[M+Na]^+$: 383.1618; Found: 383.1615.

(5-Ethyl-4,4'-dimethyl-[1,1'-biphenyl]-2-yl)(p-tolyl)methanone (2i)



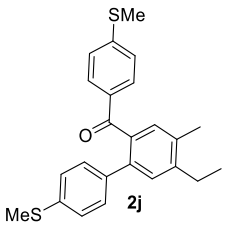
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.50 in hexane:ethyl acetate = 15:1) resulting in 10 mg of yellow oil in 61% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.24-7.22 (m, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.09 (d, *J* = 7.8 Hz, 2H), 7.00 (d, *J* = 7.8 Hz, 2H), 2.72 (q, *J* = 7.8 Hz, 2H), 2.35 (s, 3H), 2.33 (s, 3H), 2.25 (s, 3H), 1.28 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.8, 144.8, 143.6, 139.0, 137.8, 136.7, 136.6, 135.3, 134.5, 130.8, 130.4, 129.9, 129.1, 128.9, 128.9, 26.4, 21.8, 21.2, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}O$ $[M+Na]^+$: 351.1719; Found: 351.1714.

(5-Ethyl-4-methyl-4'-(methylthio)-[1,1'-biphenyl]-2-yl)(4-(methylthio)phenyl)met -hanone (2j)



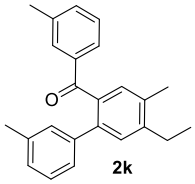
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 10.1 mg of yellow solid in 51% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.4 Hz, 2H), 7.23 (s, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 6.6 Hz, 4H), 2.72 (q, *J* = 7.8 Hz, 2H), 2.46 (s, 3H), 2.41 (s, 3H), 2.36 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.0, 145.7, 145.0, 138.4, 137.6, 137.5, 136.5, 135.0, 134.2, 130.5, 130.5, 129.7, 129.5, 126.8, 124.8, 26.4, 18.9, 16.1, 15.0, 14.4.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}OS_2$ $[M+Na]^+$: 415.1161; Found: 415.1162.

(5-Ethyl-4,4'-dimethyl-[1,1'-biphenyl]-2-yl)(p-tolyl)methanone (2k)



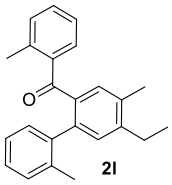
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (20:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 10.5 mg of yellow oil in 64% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.43 (m, 1H), 7.29-7.25 (m, 3H), 7.19-7.11 (m, 2H), 7.06-7.02 (m, 2H), 6.92 (d, *J* = 7.2 Hz, 1H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 2.26 (s, 3H), 2.23 (s, 3H), 1.29 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.3, 145.1, 140.7, 139.5, 137.9, 137.7, 137.7, 136.6, 134.9, 133.3, 130.8, 130.5, 129.9, 129.7, 128.1, 127.9, 127.8, 127.3, 126.2, 30.0, 26.4, 21.4, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}O$ $[M+H]^+$: 329.1900; Found: 329.1896.

(5-Ethyl-2',4-dimethyl-[1,1'-biphenyl]-2-yl)(o-tolyl)methanone (2l)



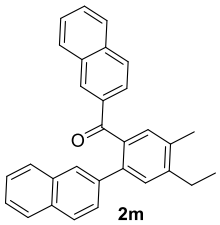
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 9.7 mg of yellow oil in 59% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.17-7.14 (m, 3H), 7.05-6.94 (m, 6H), 2.70 (q, J = 7.6 Hz, 2H), 2.38 (s, 3H), 2.26 (s, 3H), 2.08 (s, 3H), 1.30 (t, J = 7.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 200.6, 145.4, 139.4, 139.2, 138.1, 135.5, 134.8, 131.2, 131.1, 130.7, 130.3, 130.1, 129.9, 129.8, 127.2, 125.2, 124.7, 29.9, 26.3, 20.4, 19.0, 14.2.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}O$ $[M+H]^+$: 329.1900; Found: 329.1895.

(4-Ethyl-5-methyl-2-(naphthalen-2-yl)phenyl)(naphthalen-2-yl)methanone (2m)



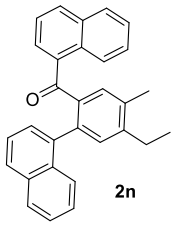
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.30 in hexane:ethyl acetate = 15:1) resulting in 7.6 mg of yellow solid in 38% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.80-7.75 (m, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 6 Hz, 2H), 7.64 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.50-7.47 (m, 1H), 7.44-7.40 (m, 3H), 7.39-7.30 (m, 3H), 2.80 (q, *J* = 7.2 Hz, 2H), 2.42 (s, 3H), 1.34 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.9, 145.2, 139.3, 138.2, 136.8, 135.5, 135.2, 135.1, 133.3, 132.4, 132.4, 132.3, 130.9, 130.3, 129.6, 128.4, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.2, 126.6, 126.2, 125.9, 125.2, 26.5, 19.0, 14.4.

HRMS(ESI): m/z Calcd. for $C_{30}H_{24}O$ $[M+H]^+$: 401.1900; Found: 401.1902.

(5-Benzyl-2-(naphthalen-2-yl)-4-phenethylphenyl)(naphthalen-2-yl)methanone (2n)



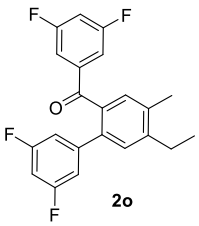
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.50 in hexane:ethyl acetate = 15:1) resulting in 7.6 mg of yellow oil in 40% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9 Hz, 1H), 7.70 (s, 1H), 7.63-7.62 (m, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.51-7.50 (m, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.32-7.30 (m, 2H), 7.28-7.20 (m, 4H), 7.02 (d, *J* = 6.6 Hz, 1H), 6.90-6.84 (m, 2H), 2.77 (q, *J* = 7.8 Hz, 2H), 2.48 (s, 3H), 1.28 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 200.4, 145.9, 139.7, 138.6, 138.4, 136.8, 135.6, 133.3, 131.9, 131.6, 131.2, 131.1, 130.2, 128.8, 128.1, 127.9, 127.8, 127.1, 127.1, 126.3, 126.0, 125.9, 125.6, 125.6, 124.7, 123.5, 26.5, 19.1, 14.3.

HRMS(ESI): m/z Calcd. for $C_{30}H_{24}O$ $[M+Na]^+$: 423.1719; Found: 423.1721.

(3,5-Difluorophenyl)(5-ethyl-3',5'-difluoro-4-methyl-[1,1'-biphenyl]-2-yl)methano-ne (2o)



The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (40:1) (R*f* = 0.40 in hexane:ethyl acetate = 10:1) resulting in 7.5 mg of yellow oil in 40% yield.

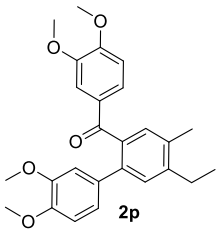
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 1H), 7.26 (s, 1H), 7.18-7.16 (m, 1H), 7.04 (s, 1H), 6.93-6.90 (m, 2H), 6.71-6.60 (m, 2H), 2.68 (q, *J* = 7.6 Hz, 2H), 2.29 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.1, 164.5, 164.3, 162.0, 161.9, 147.6, 146.6, 144.6, 138.5, 126.0, 120.4, 108.7, 108.4, 103.9, 103.7, 103.6, 103.3, 103.1, 102.8, 82.4, 26.5, 19.8, 14.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -109.50.

HRMS(ESI): m/z Calcd. for $C_{22}H_{16}F_4O$ $[M+H]^+$: 373.1210; Found: 373.1215.

(3,4-Dimethoxyphenyl)(5-ethyl-3',4'-dimethoxy-4-methyl-[1,1'-biphenyl]-2-yl)-methanone (2p)



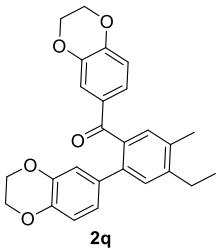
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.50 in hexane:ethyl acetate = 5:1) resulting in 11.1 mg of yellow oil in 53% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.30 (d, *J* = 4.3 Hz, 1H), 7.25-7.19 (m, 2H), 6.85-6.79 (m, 2H), 6.73-6.71 (m, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 3.80 (s, 3H), 3.73 (s, 3H), 2.74 (q, *J* = 7.6 Hz, 2H), 2.37 (s, 3H), 1.29 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.1, 153.2, 148.9, 148.7, 148.3, 144.6, 138.4, 136.8, 134.7, 133.6, 130.9, 130.2, 129.5, 125.8, 121.2, 112.7, 111.5, 111.2, 109.8, 56.1, 55.9, 18.9, 14.4, 14.2.

HRMS(ESI): m/z Calcd. for $C_{26}H_{28}O_5$ $[M+H]^+$: 421.2010; Found: 421.1012.

(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)(2-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-4-ethyl-5-methylphenyl)methanone (2q)



2q

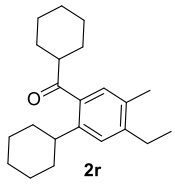
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 12 mg of yellow oil in 58% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30-7.22 (m, 2H), 7.19 (d, *J* = 12.6 Hz, 2H), 6.80 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 6.73-6.67 (m, 2H), 4.30-4.17 (m, 8H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.27 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 197.5, 147.8, 144.6, 143.3, 143.1, 142.9, 138.3, 136.5, 134.5, 134.3, 131.8, 130.3, 129.7, 124.5, 122.4, 119.6, 117.9, 117.1, 116.9, 64.8, 64.5, 64.4, 64.2, 26.4, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{23}H_{24}O_6$ $[M+H]^+$: 417.1697; Found: 417.1702.

Cyclohexyl(2-cyclohexyl-4-ethyl-5-methylphenyl)methanoness (2r)



2r

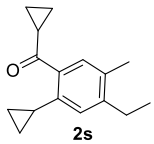
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (20:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 6 mg of yellow solid in 38% yield.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.12 (s, 1H), 7.08 (s, 1H), 2.94-2.89 (m, 1H), 2.70-2.66 (m, 1H), 2.62 (q, *J* = 7.2 Hz, 2H), 2.28 (s, 3H), 1.88-1.85 (m, 3H), 1.81-1.79 (m, 7H), 1.46-1.30 (m, 10H), 1.21 (t, *J* = 7.8 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 210.4, 144.7, 144.2, 137.5, 132.8, 128.2, 126.7, 50.3, 40.5, 35.0, 29.0, 27.1, 26.6, 26.4, 26.1, 26.0, 18.9, 14.4.

HRMS(ESI): m/z Calcd. for $C_{22}H_{32}O$ $[M+H]^+$: 313.2526; Found: 313.2529.

Cyclopropyl(2-cyclopropyl-4-ethyl-5-methylphenyl)methanone (2s)



2s

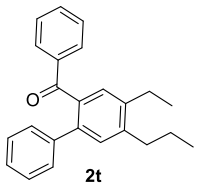
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.30 in hexane:ethyl acetate = 15:1) resulting in 4 mg of yellow oil in 34% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33 (s, 1H), 6.78 (s, 1H), 2.60 (q, *J* = 7.8 Hz, 2H), 2.53-2.49 (m, 1H), 2.31-2.29 (m, 4H), 1.18 (t, *J* = 7.8 Hz, 3H), 1.03-1.01 (m, 2H), 0.96-0.93 (m, 2H), 0.91-0.87 (m, 2H), 0.71-0.64 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 206.0, 145.5, 139.5, 139.3, 133.0, 129.6, 125.5, 26.5, 21.6, 18.7, 14.5, 13.4, 12.2, 8.9.

HRMS(ESI): m/z Calcd. for $C_{16}H_{20}O$ $[M+Na]^+$: 251.1406; Found: 251.1413.

(4-Ethyl-5-propyl-[1,1'-biphenyl]-2-yl)(phenyl)methanone (2t)



2t

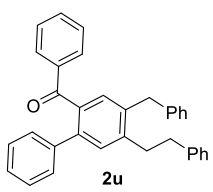
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (20:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 9.7 mg of yellow oil in 59% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.32 (s, 1H), 7.26-7.24 (m, 5H), 7.17 (t, *J* = 7.8 Hz, 2H), 7.12 (d, *J* = 7.2 Hz, 1H), 2.84-2.65 (m, 4H), 1.70 (q, *J* = 7.8 Hz, 2H), 1.36-1.27 (m, 3H), 1.04 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.2, 143.1, 141.1, 140.6, 138.9, 137.9, 136.7, 132.7, 131.0, 130.1, 129.2, 129.1, 128.3, 128.1, 127.1, 34.9, 25.3, 24.3, 15.3, 14.4.

HRMS(ESI): m/z Calcd. for $C_{24}H_{24}O$ $[M+Na]^+$:351.1719; Found: 351.1722.

(4-Benzyl-5-phenethyl-[1,1'-biphenyl]-2-yl)(phenyl)methanone (2u)



2u

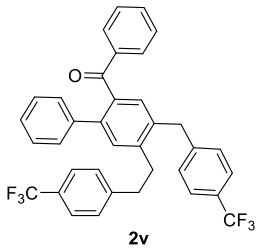
The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (30:1) (R*f* = 0.40 in hexane:ethyl acetate = 15:1) resulting in 11mg of yellow oil in 49% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.2 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 2H), 7.32-7.27 (m, 7H), 7.25-7.15 (m, 11H), 7.15-7.13 (m, 2H), 7.13-7.08 (m, 2H), 4.07 (s, 2H), 2.98 (t, *J* = 7.2 Hz, 2H), 2.80 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 202.3, 145.3, 142.1, 140.2, 139.9, 137.5, 137.3, 136.5, 133.6, 133.0, 131.78, 131.4, 130.0, 129.5, 129.1, 129.0, 128.7, 128.6, 128.4, 128.2, 127.5, 125.8, 125.5, 125.3, 54.6, 51.8, 40.8, 38.6, 36.9.

HRMS(ESI): m/z Calcd. for $C_{34}H_{28}O$ $[M+Na]^+$: 475.2032; Found: 475.2028

Phenyl(4-(4-(trifluoromethyl)benzyl)-5-(4-(trifluoromethyl)phenethyl)-[1,1'-biphenyl]-2-yl)methanone (2v)



2v

The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (15:1) (R*f* = 0.40 in hexane:ethyl acetate = 8:1) resulting in 8.8 mg of yellow oil in 30% yield.

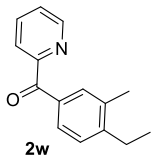
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.5 Hz, 1H), 7.63-7.28 (m, 12H), 7.25-7.15 (m, 5H), 6.92 (d, *J* = 7.9 Hz, 1H), 4.10 (s, 2H), 2.99-2.85 (m, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 202.3, 145.3, 142.1, 140.3, 139.9, 137.6, 137.4, 136.6, 133.6, 133.1, 131.8, 131.5, 130.1, 129.5, 129.2, 129.0, 128.7, 128.7, 128.5, 128.3, 127.6, 125.8, 125.6, 125.4, 54.6, 51.9, 40.8, 38.7, 36.9.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.38, -62.41.

HRMS(ESI): m/z Calcd. for $C_{36}H_{26}F_6O$ $[M+Na]^+$: 611.1780; Found: 611.1783.

(4-Ethyl-3-methylphenyl)(pyridin-2-yl)methanone (2w)



2w

The title compound was prepared according to the general procedure as described, silica gel flash column chromatography was performed using hexanes and ethyl acetate (40:1) (R*f* = 0.30 in hexane:ethyl acetate = 15:1) resulting in 6.8 mg of yellow oil in 60% yield.

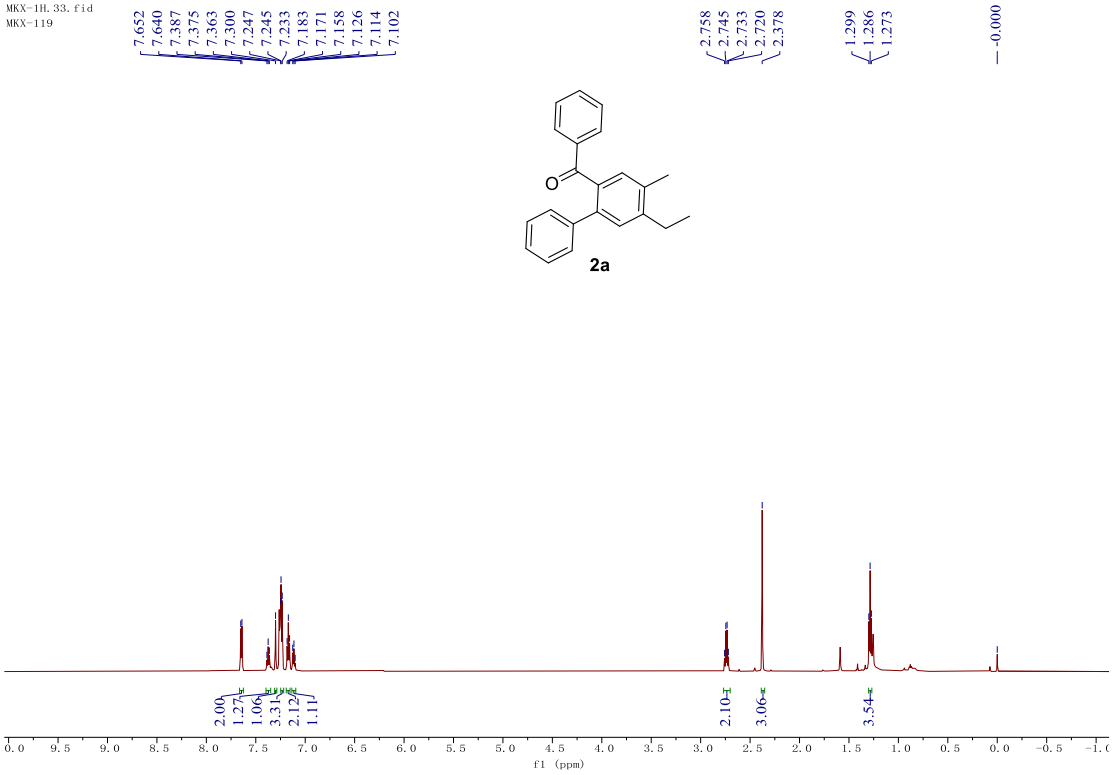
^{1}H NMR (600 MHz, DMSO-d_6) δ 8.63 (d, J = 4.2 Hz, 1H), 7.95-7.87 (m, 2H), 7.85-7.83 (m, 1H), 7.78 (d, J = 2.0 Hz, 1H), 7.32-7.29 (m, 1H), 7.24 (d, J = 7.8 Hz, 1H), 2.67 (q, J = 7.8 Hz, 2H), 2.31 (s, 3H), 1.21 (t, J = 7.6 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 156.7, 149.9, 142.7, 137.6, 137.0, 136.9, 130.8, 126.5, 124.3, 122.7, 120.4, 26.2, 19.1, 14.9.

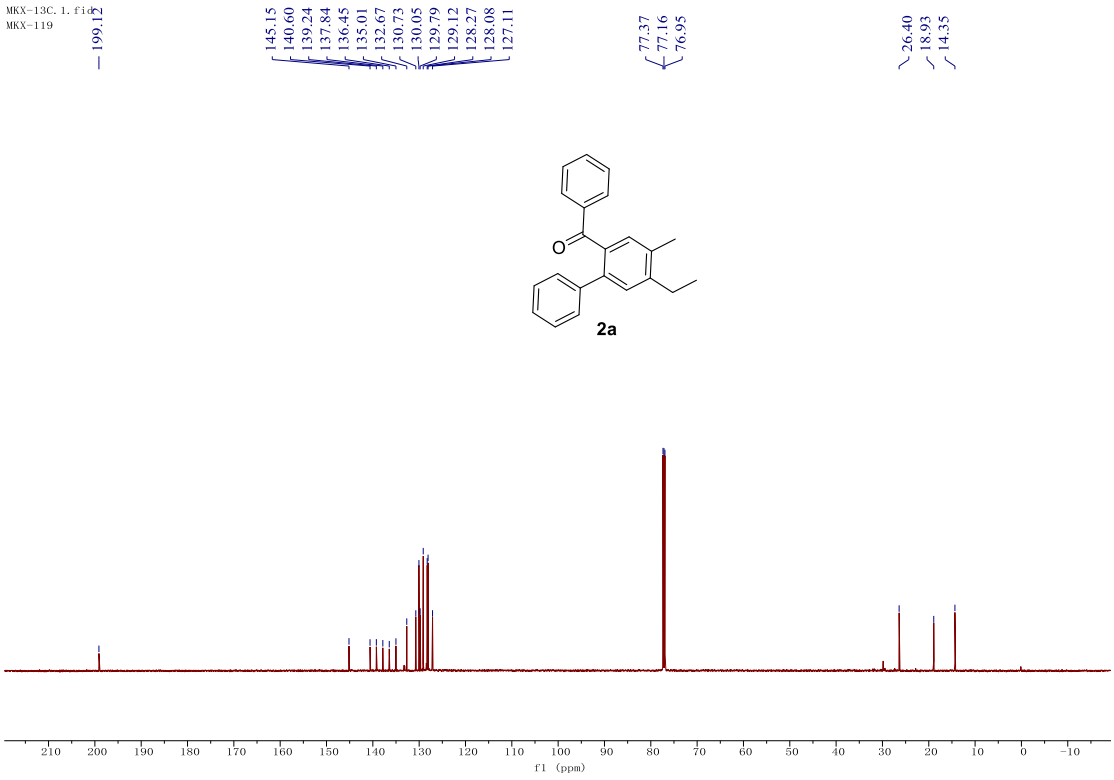
HRMS(ESI): m/z Calcd. for $C_{15}H_{15}NO$ $[M+H]^+$: 226.1226; Found: 226.1226.

IV NMR spectra

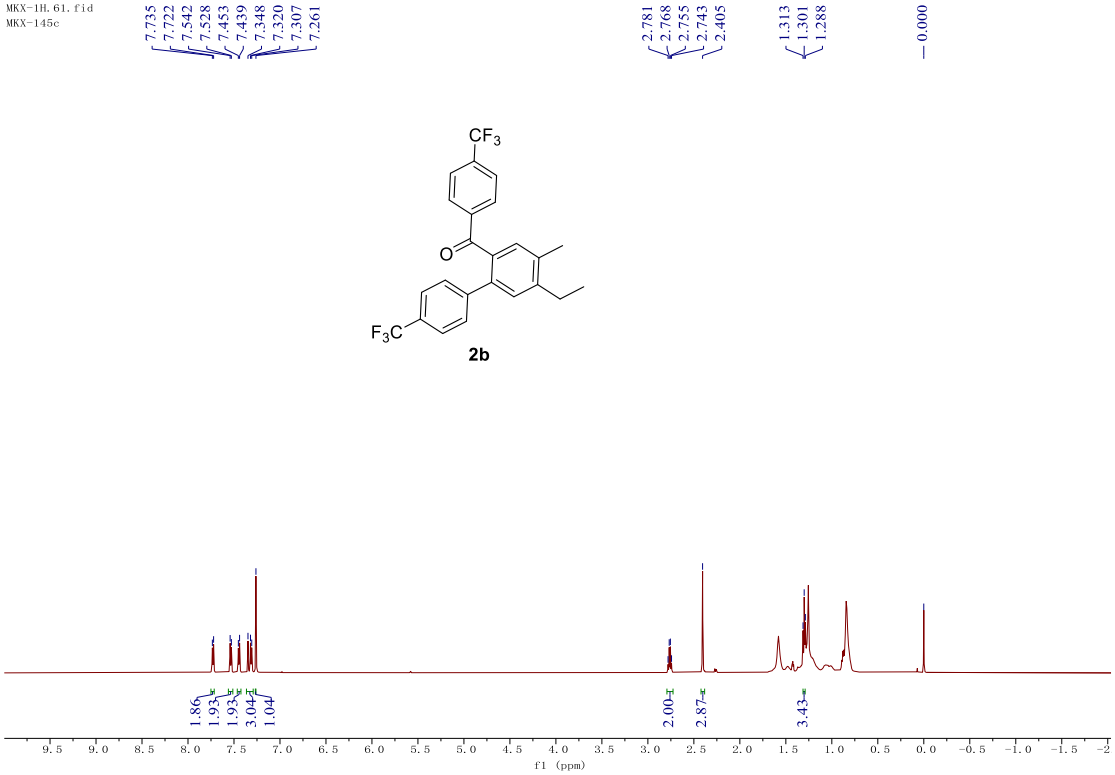
^{1}H NMR (400 MHz, $CDCl_3$) for **2a**



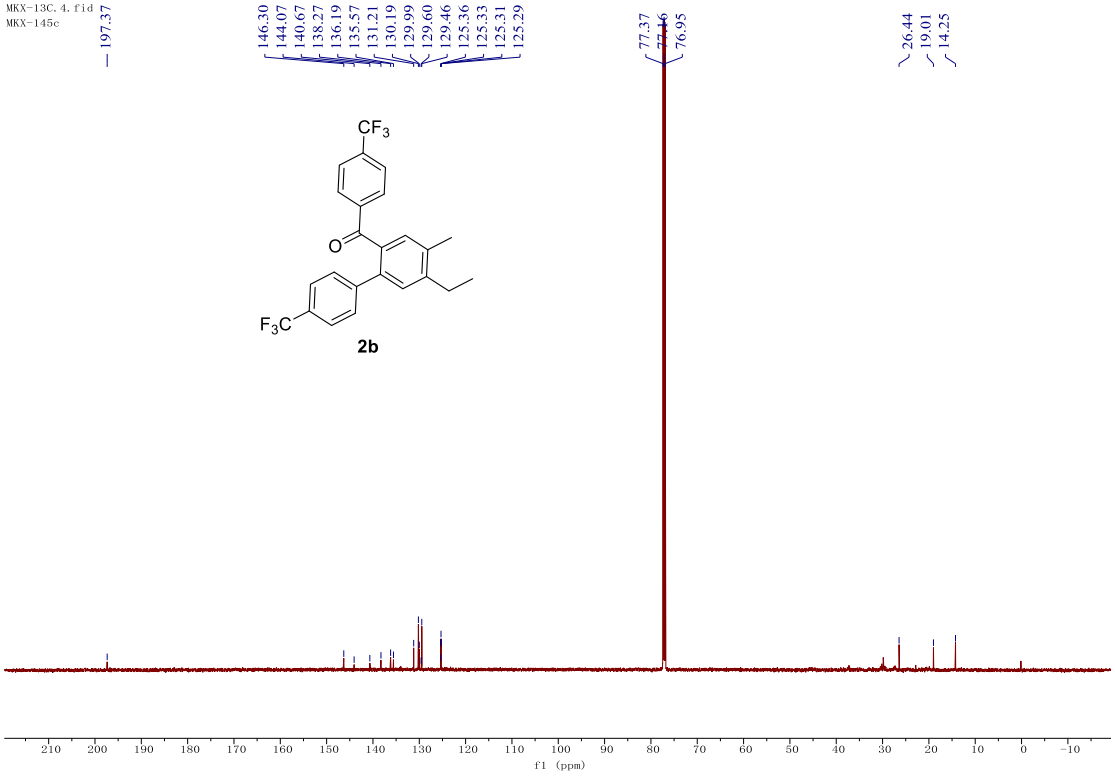
^{13}C NMR (101 MHz, $CDCl_3$) for **2a**



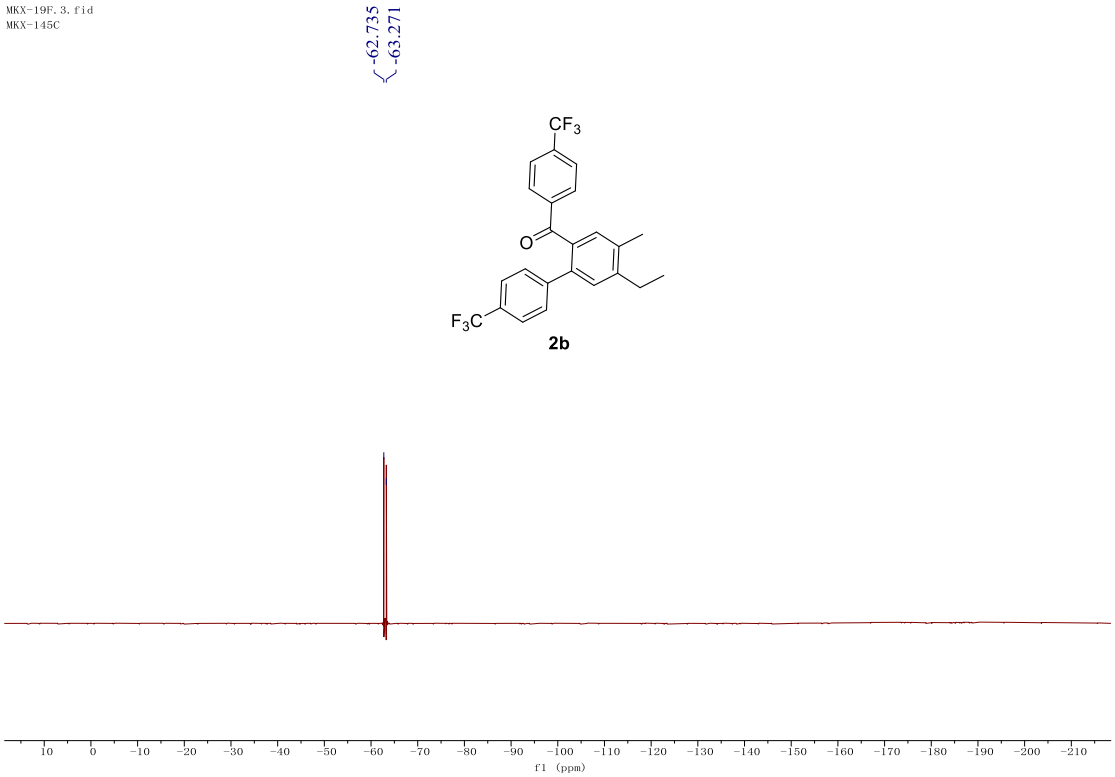
^{1}H NMR (400 MHz, $CDCl_3$) for **2b**



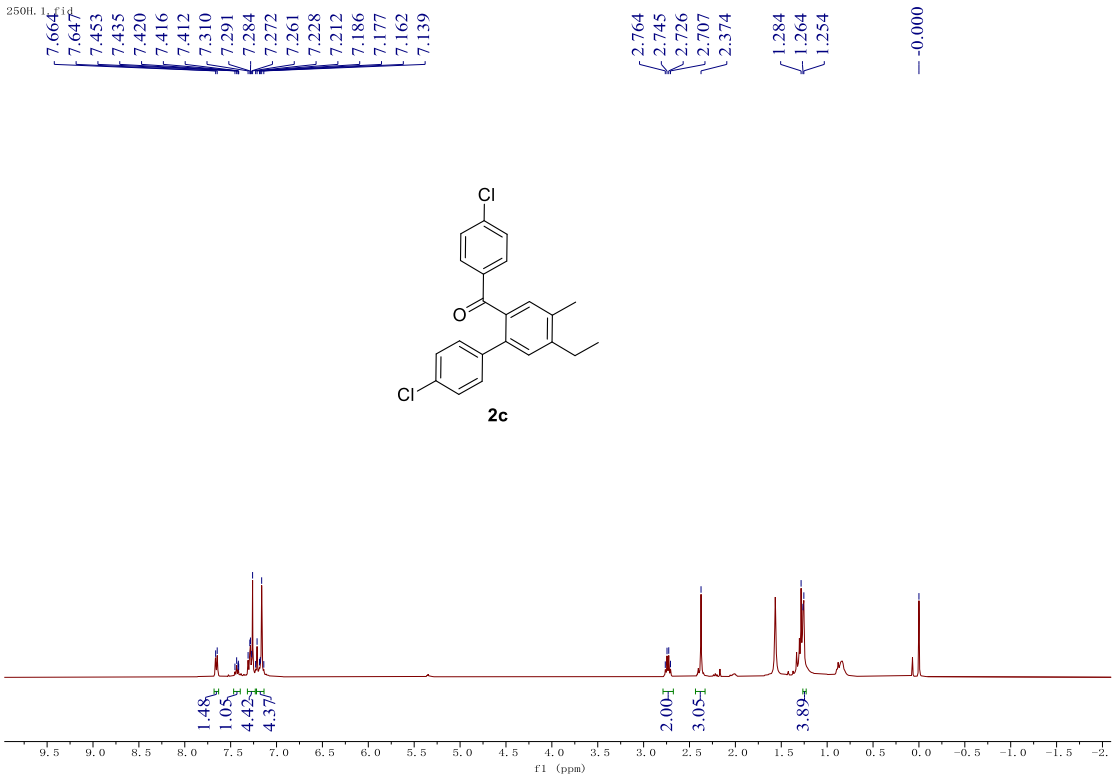
^{13}C NMR (101 MHz, $CDCl_3$) for **2b**



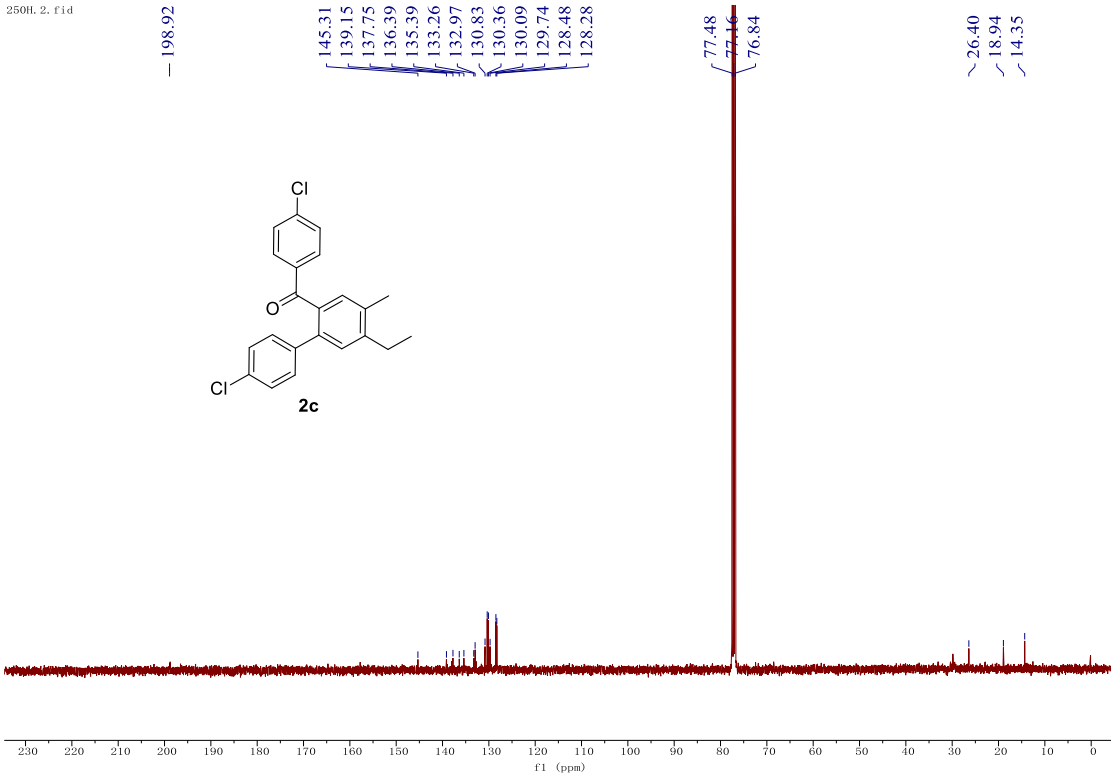
^{19}F NMR (376 MHz, $CDCl_3$) for **2b**



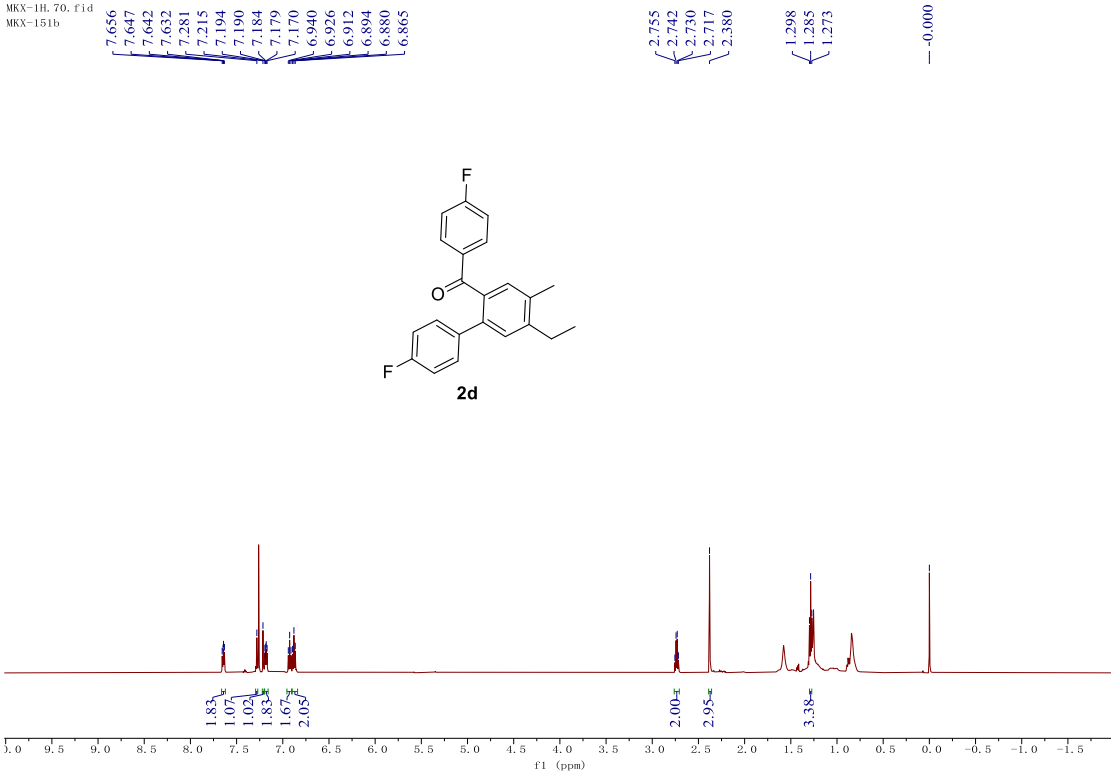
^{1}H NMR (400 MHz, $CDCl_3$) for **2c**



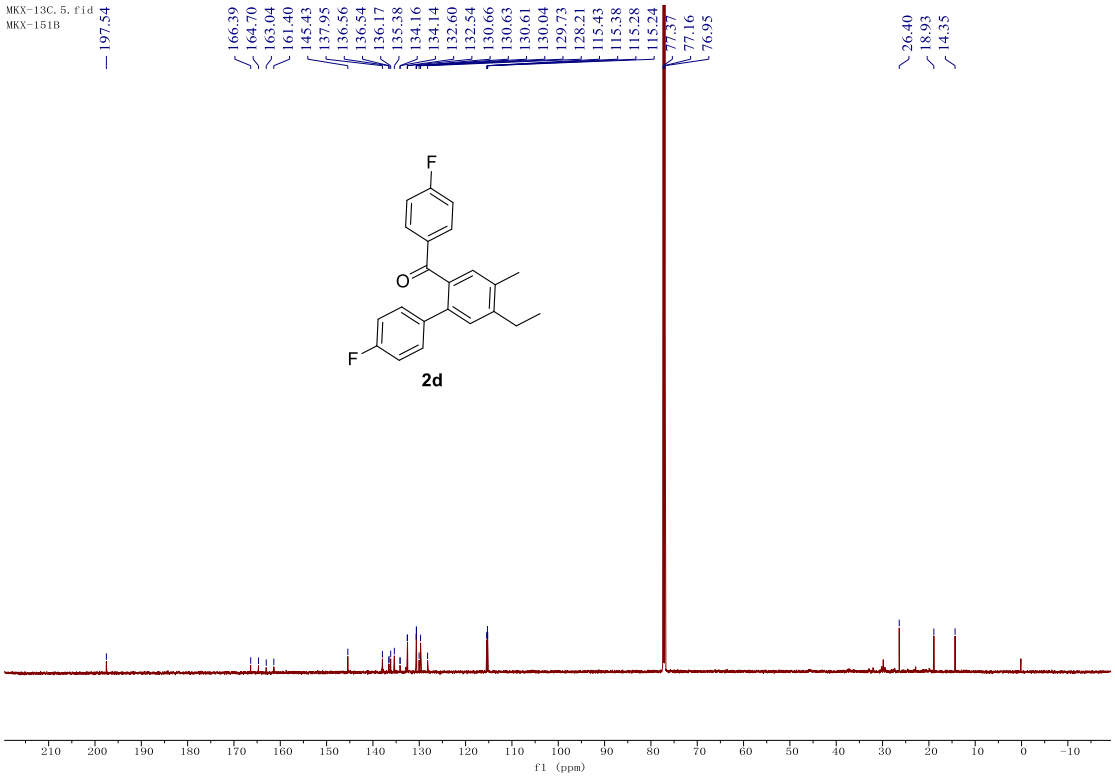
^{13}C NMR (151 MHz, $CDCl_3$) for **2c**



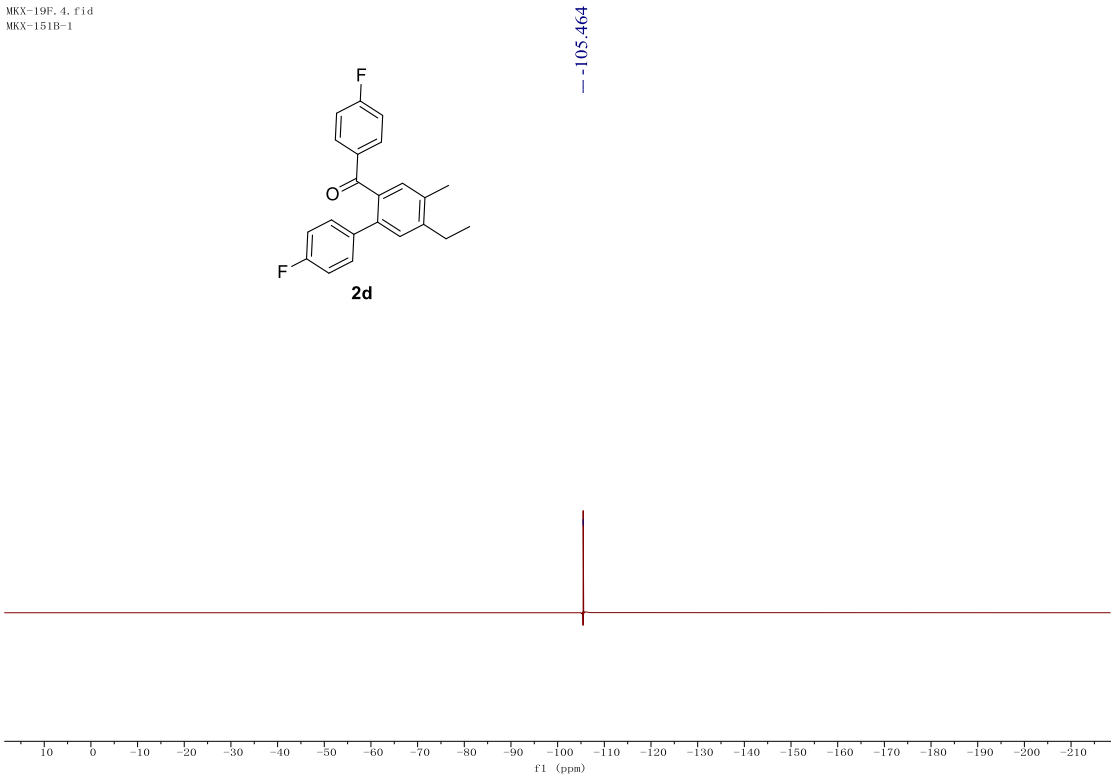
^{1}H NMR (400 MHz, $CDCl_3$) for **2d**



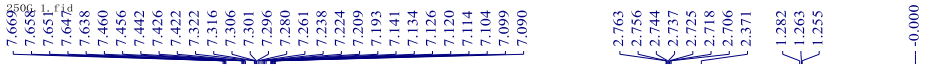
^{13}C NMR (151 MHz, $CDCl_3$) for **2d**

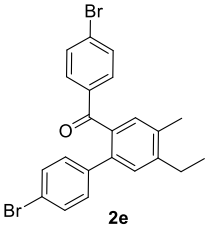


^{19}F NMR (376 MHz, $CDCl_3$) for **2d**

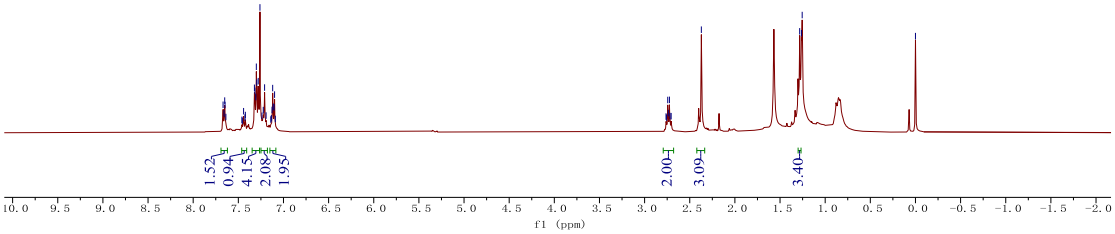


^{1}H NMR (400 MHz, $CDCl_3$) for **2e**

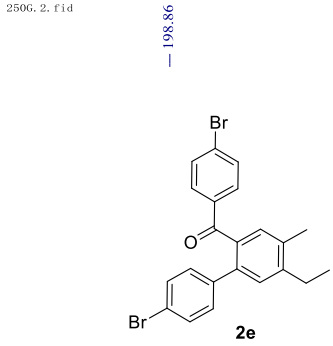




2e

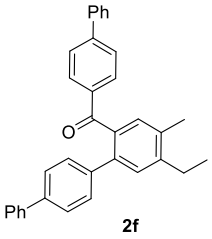


^{13}C NMR (101 MHz, $CDCl_3$) for **2e**

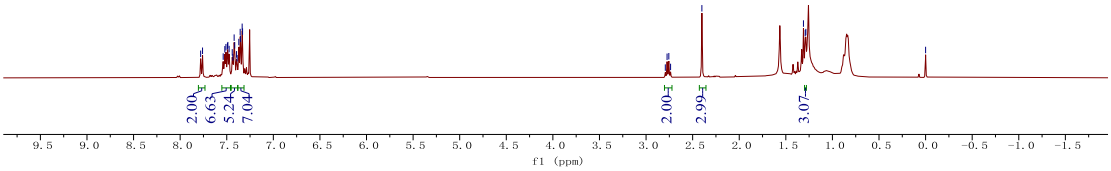


2e

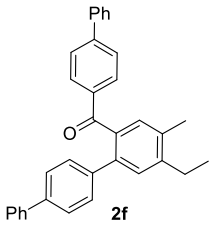
^{1}H NMR (400 MHz, $CDCl_3$) for **2f**



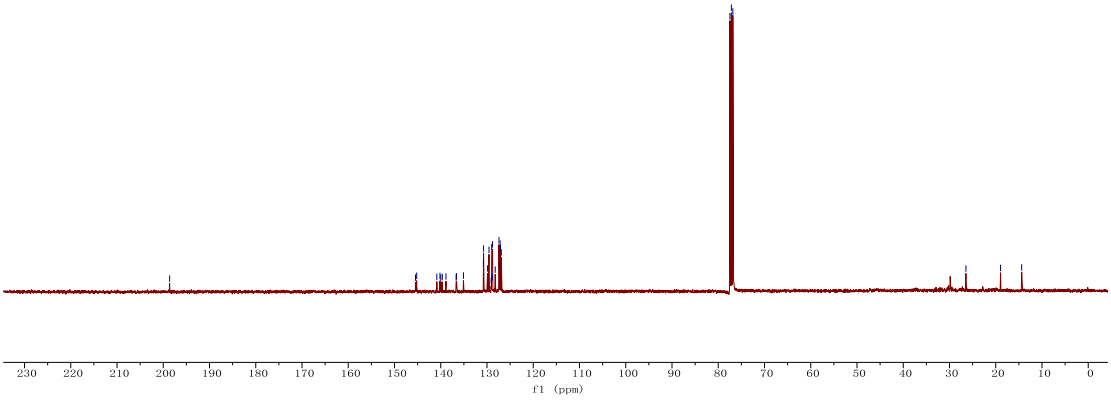
2f



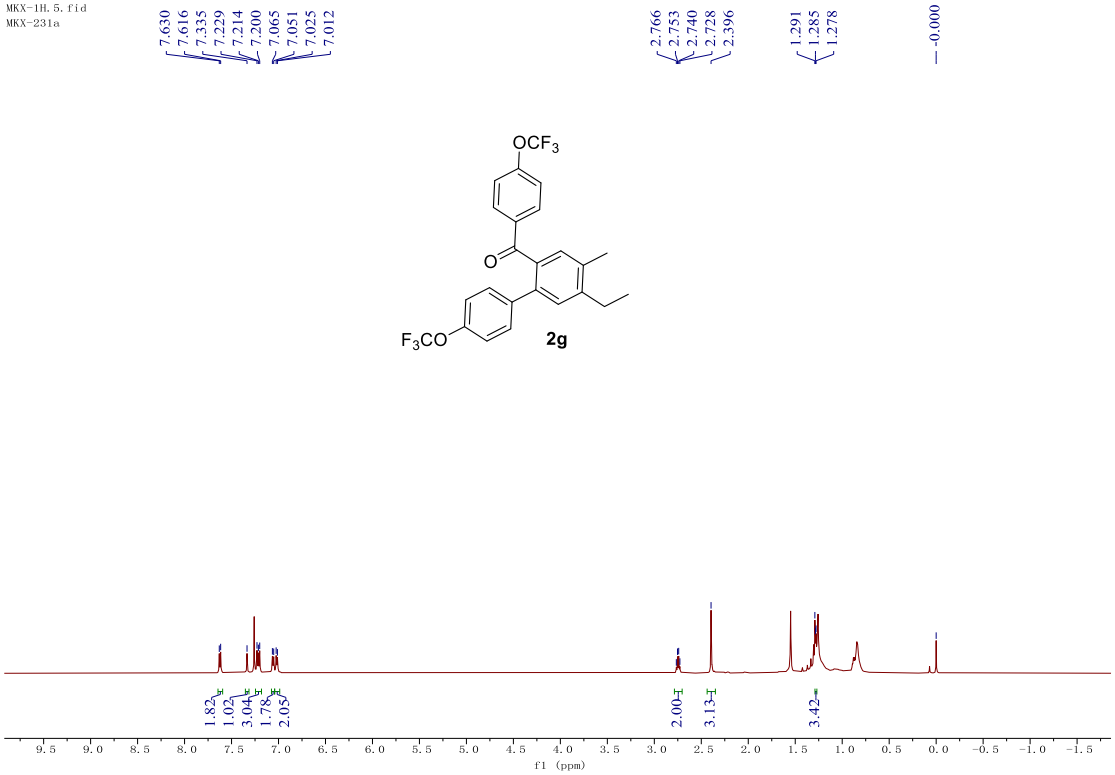
^{13}C NMR (101 MHz, $CDCl_3$) for **2f**



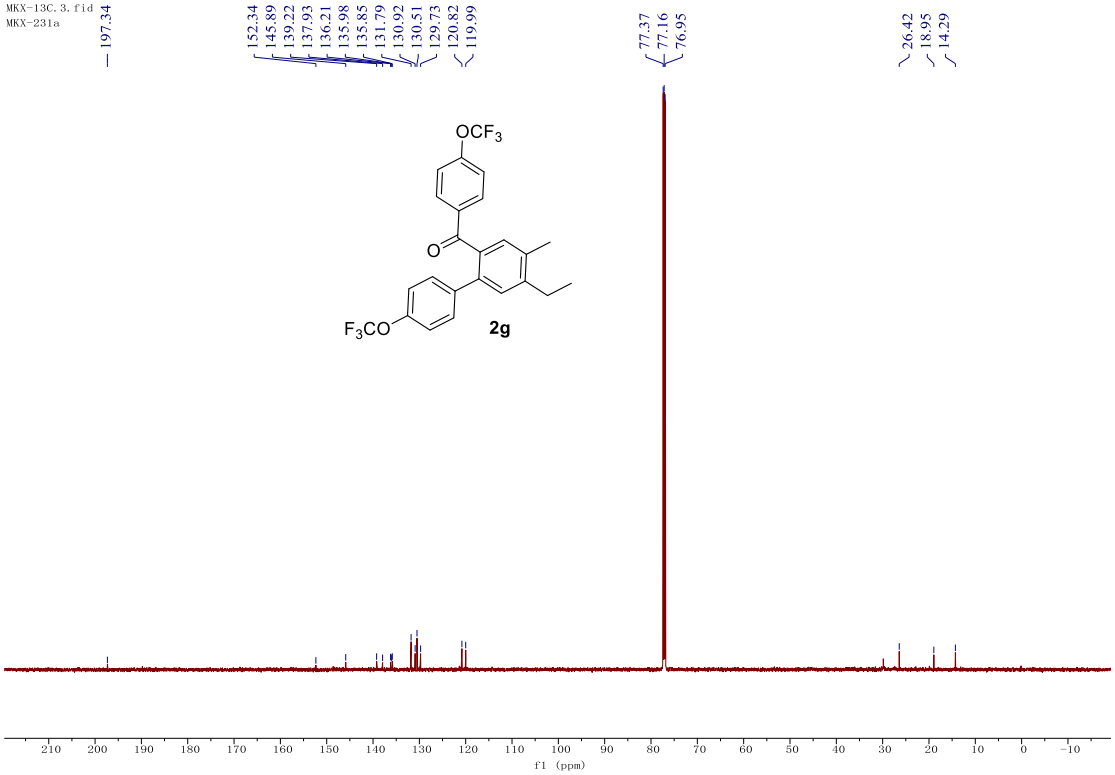
2f



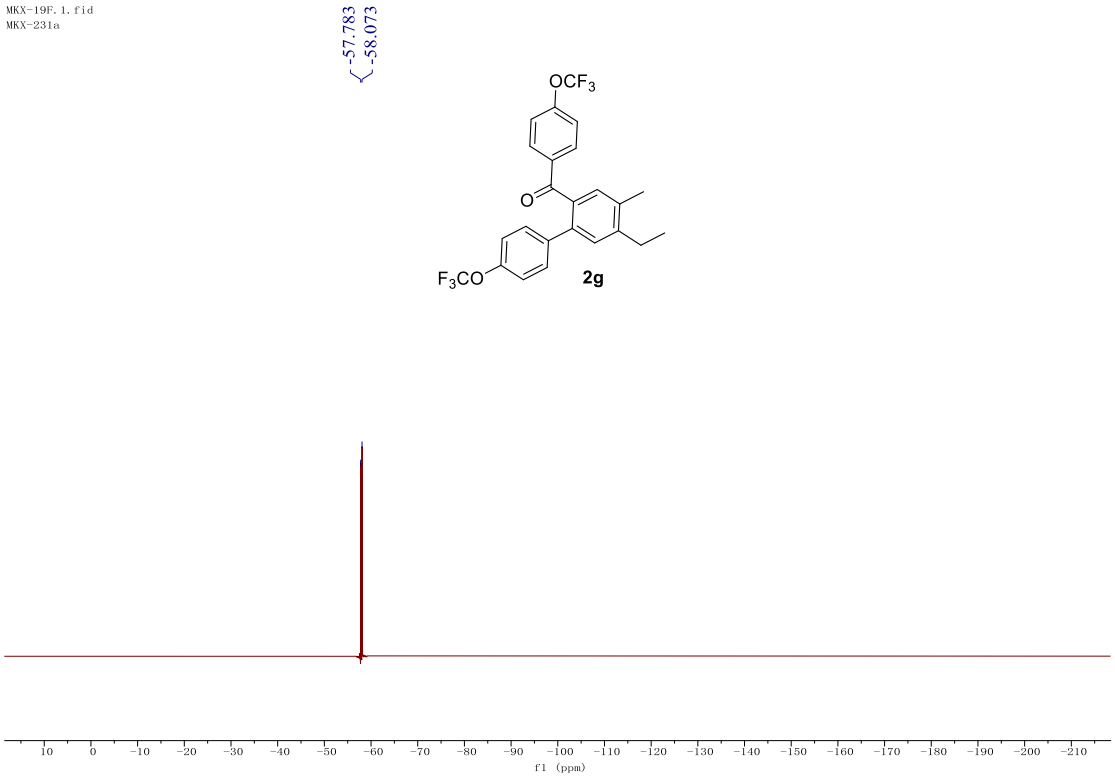
^{1}H NMR (400 MHz, $CDCl_3$) for **2g**



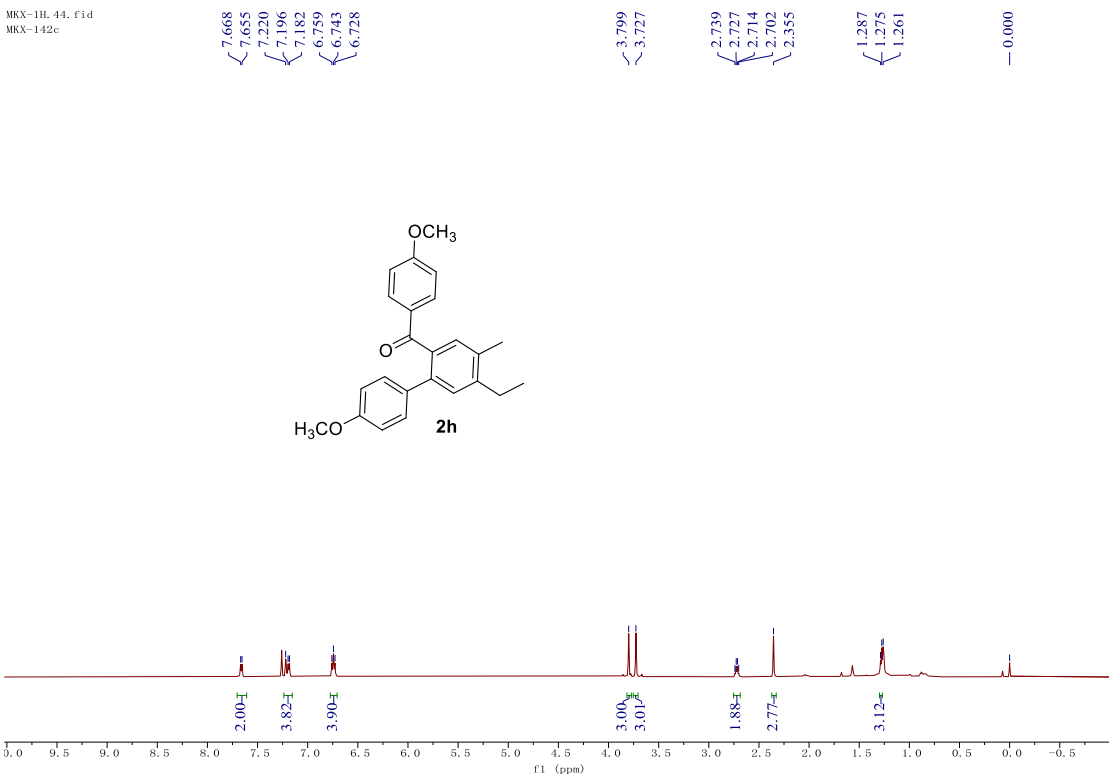
^{13}C NMR (101 MHz, $CDCl_3$) for **2g**



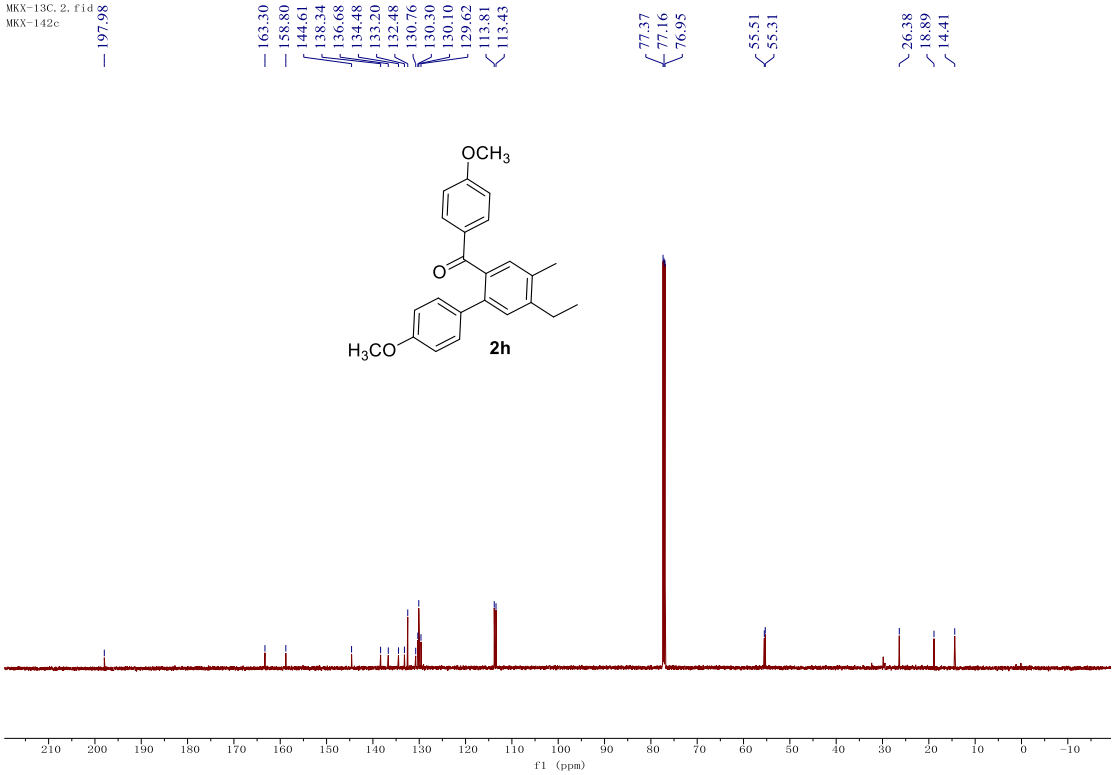
^{19}F NMR (376 MHz, $CDCl_3$) for **2g**



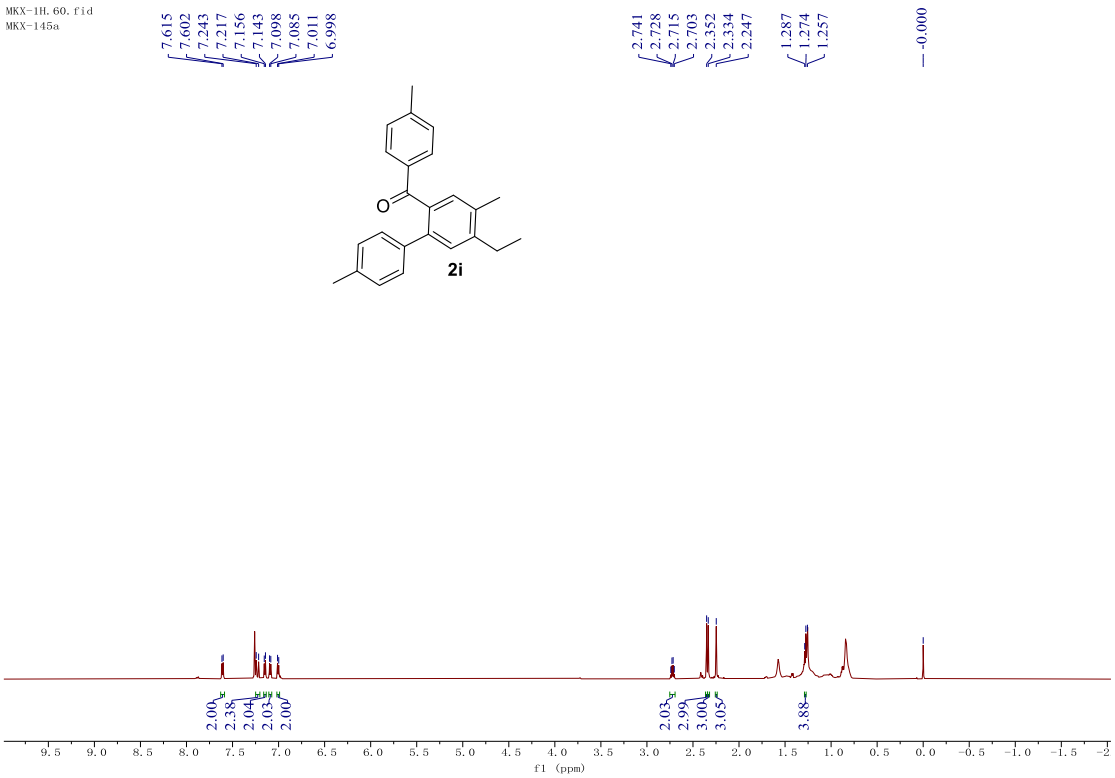
^{1}H NMR (400 MHz, $CDCl_3$) for **2h**



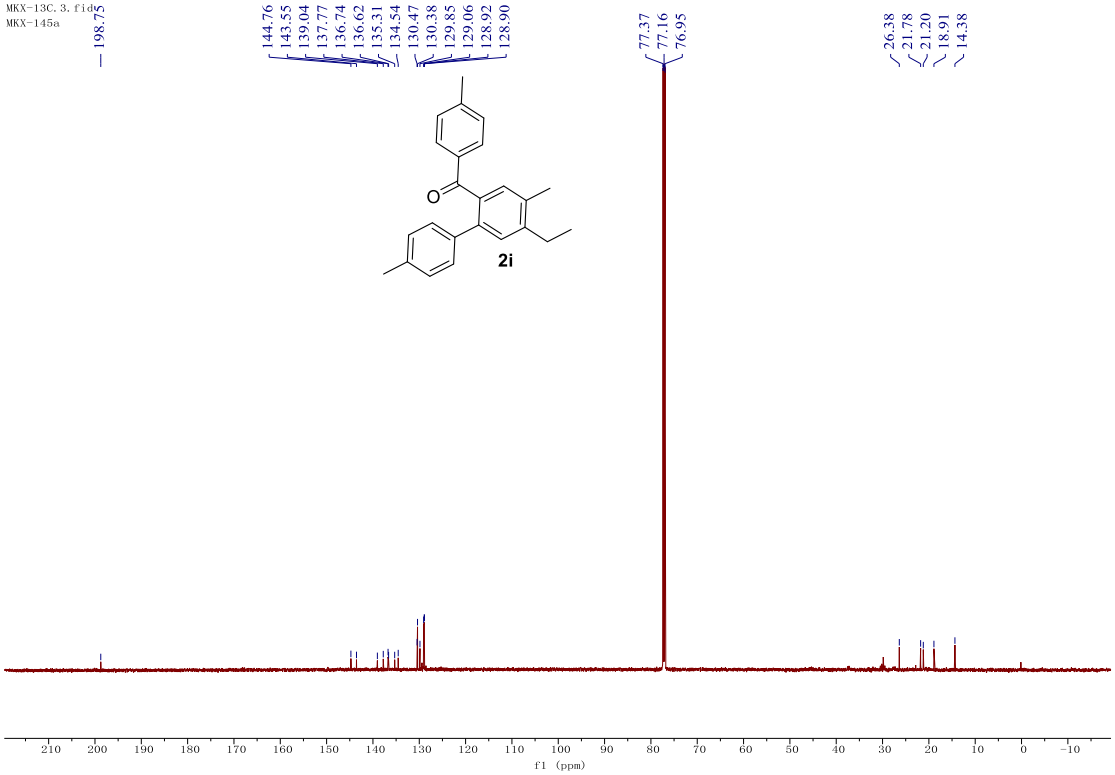
^{13}C NMR (101 MHz, $CDCl_3$) for **2h**



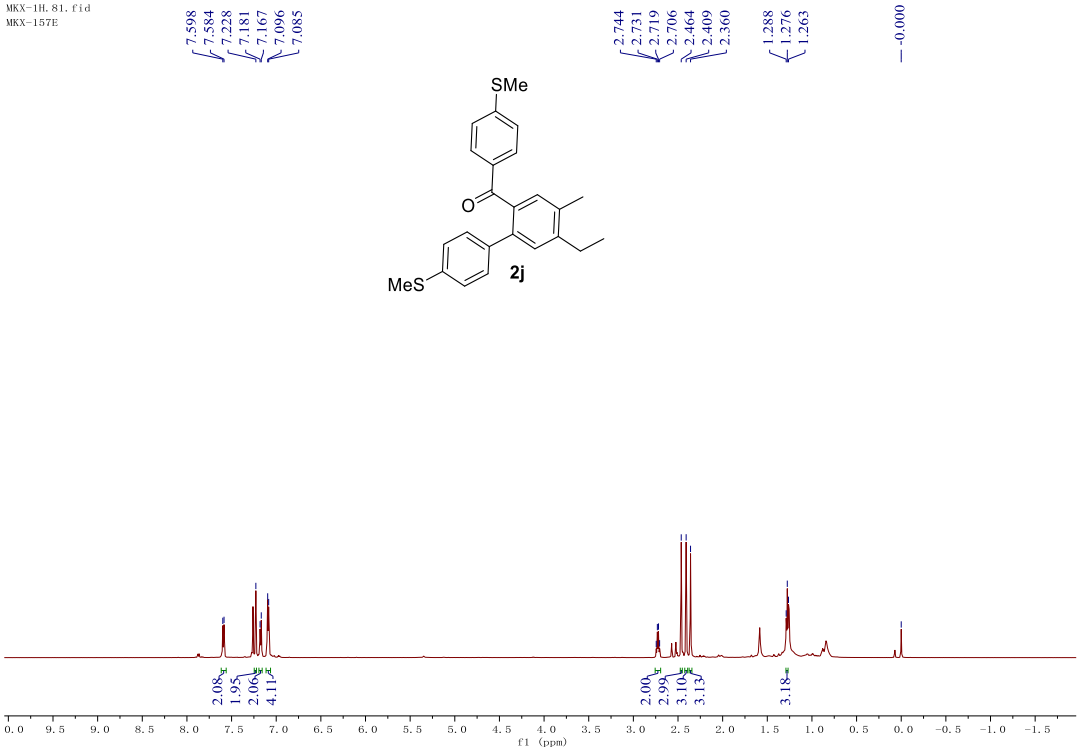
^{1}H NMR (400 MHz, $CDCl_3$) for **2i**



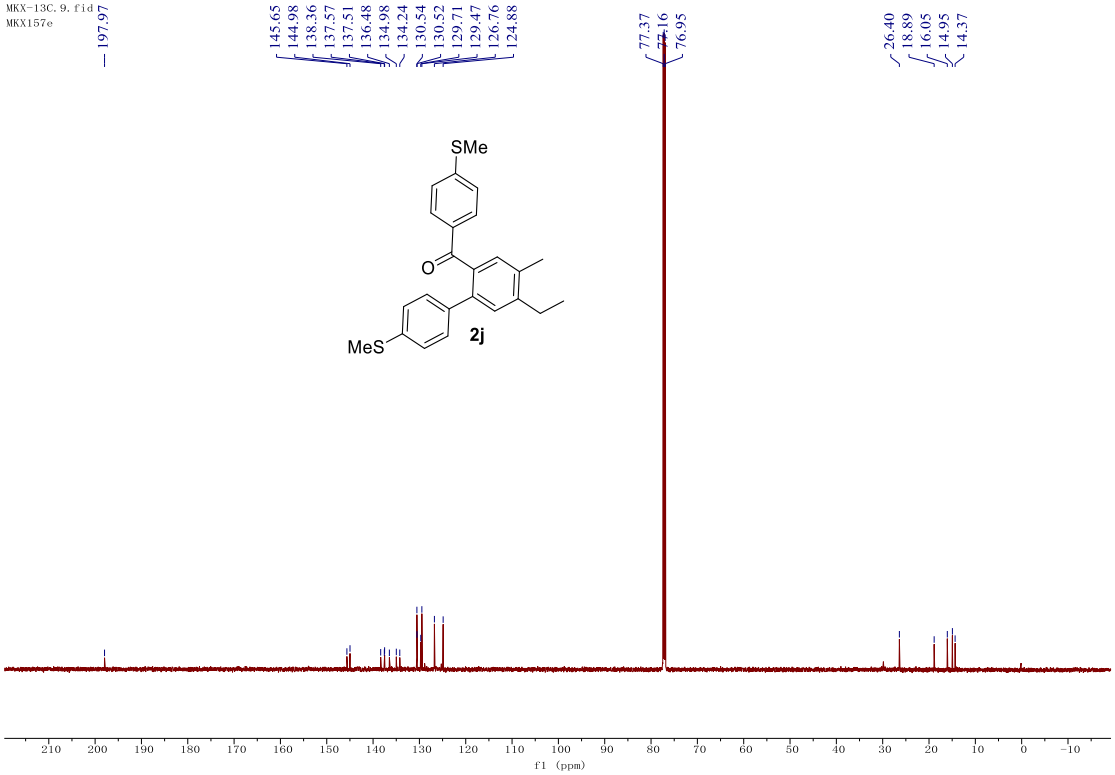
^{13}C NMR (101 MHz, $CDCl_3$) for **2i**



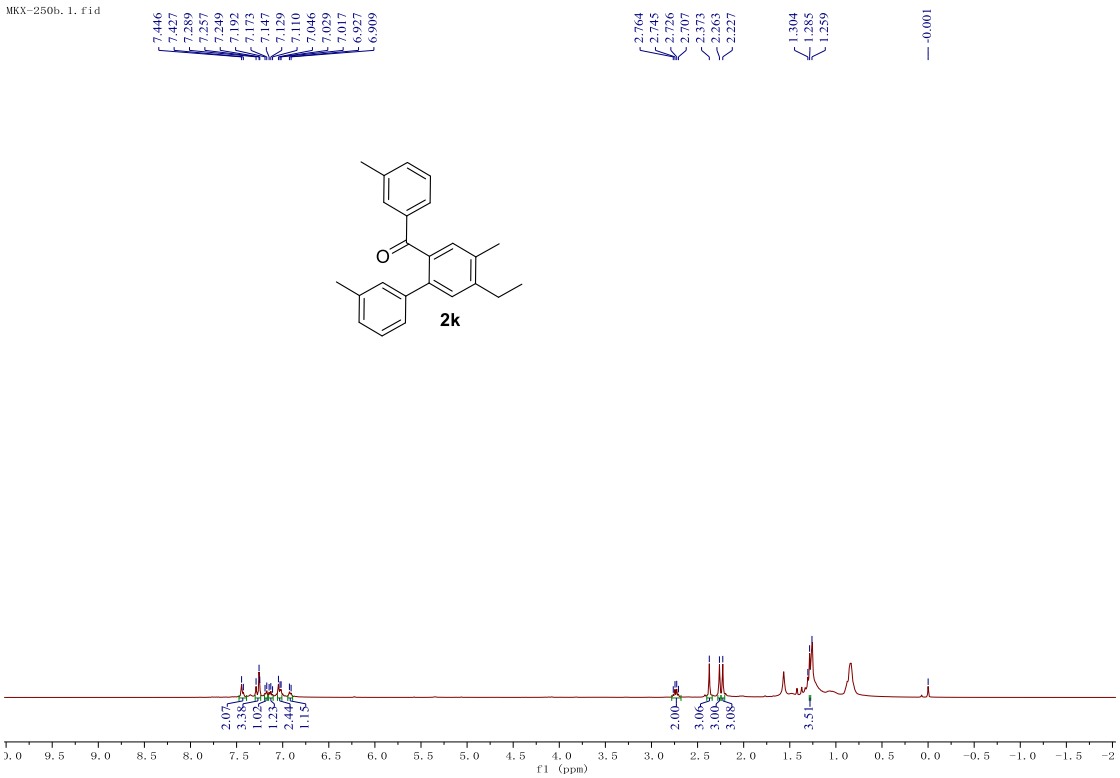
^{1}H NMR (400 MHz, $CDCl_3$) for **2j**



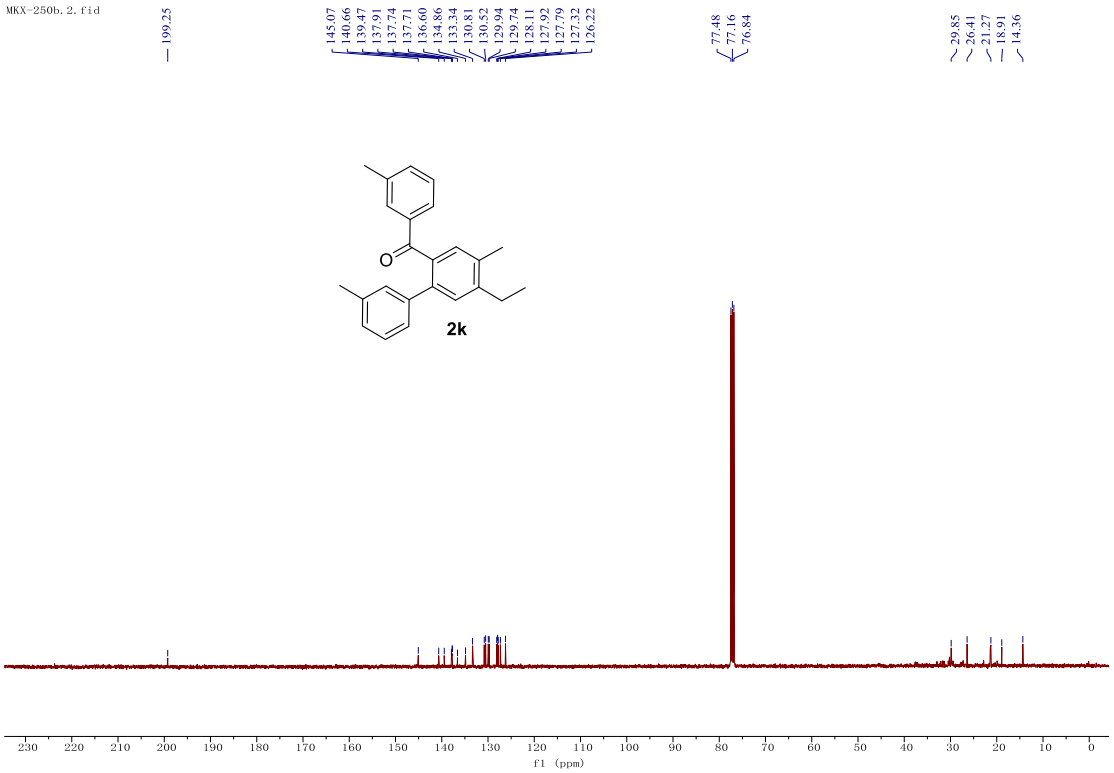
^{13}C NMR (101 MHz, $CDCl_3$) for **2j**



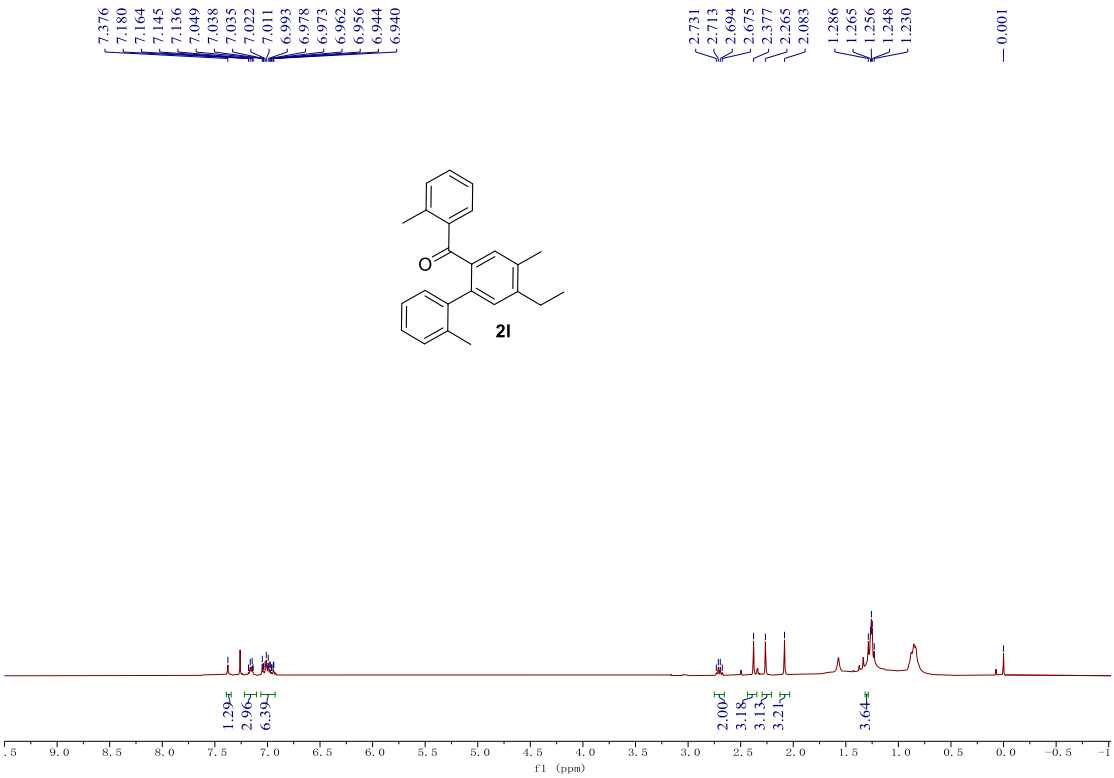
^{1}H NMR (400 MHz, $CDCl_3$) for **2k**



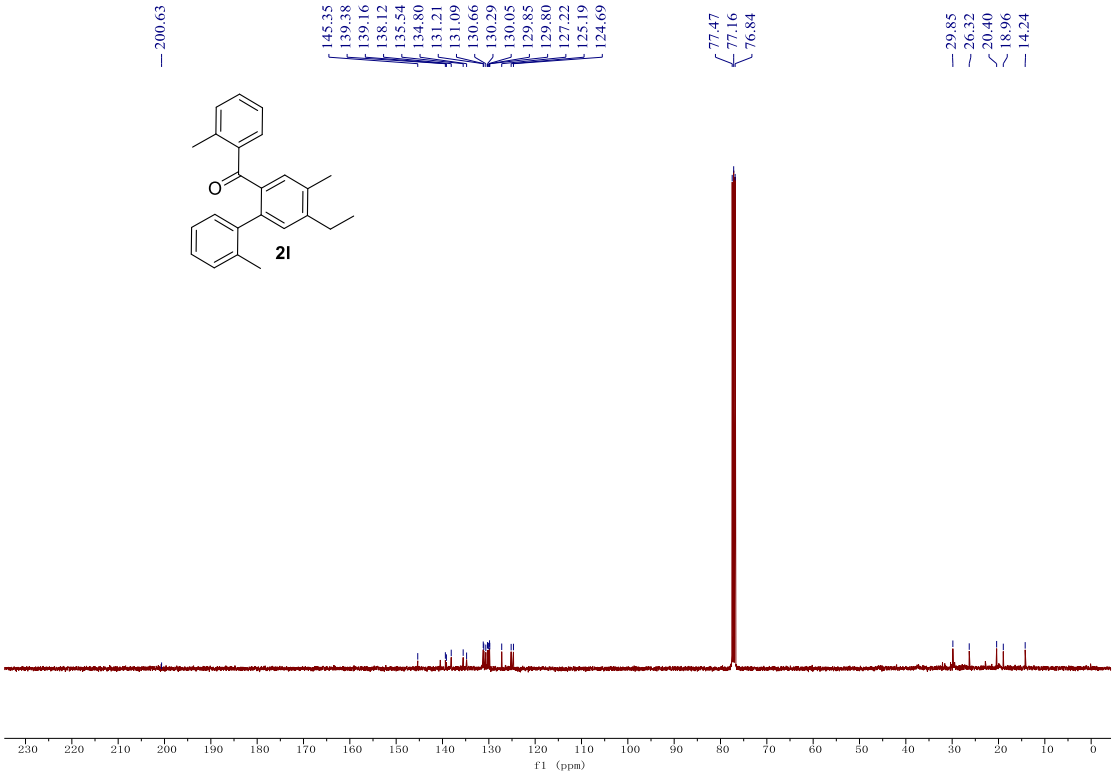
^{13}C NMR (101 MHz, $CDCl_3$) for **2k**



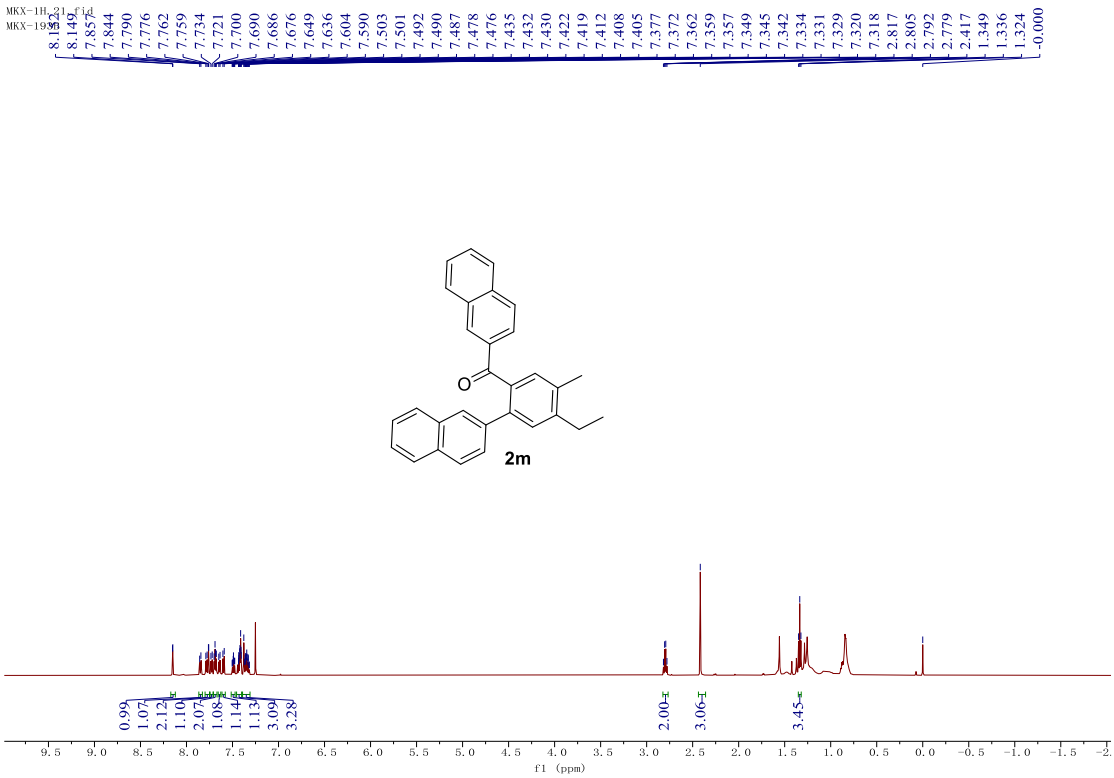
^{1}H NMR (400 MHz, $CDCl_3$) for **2l**



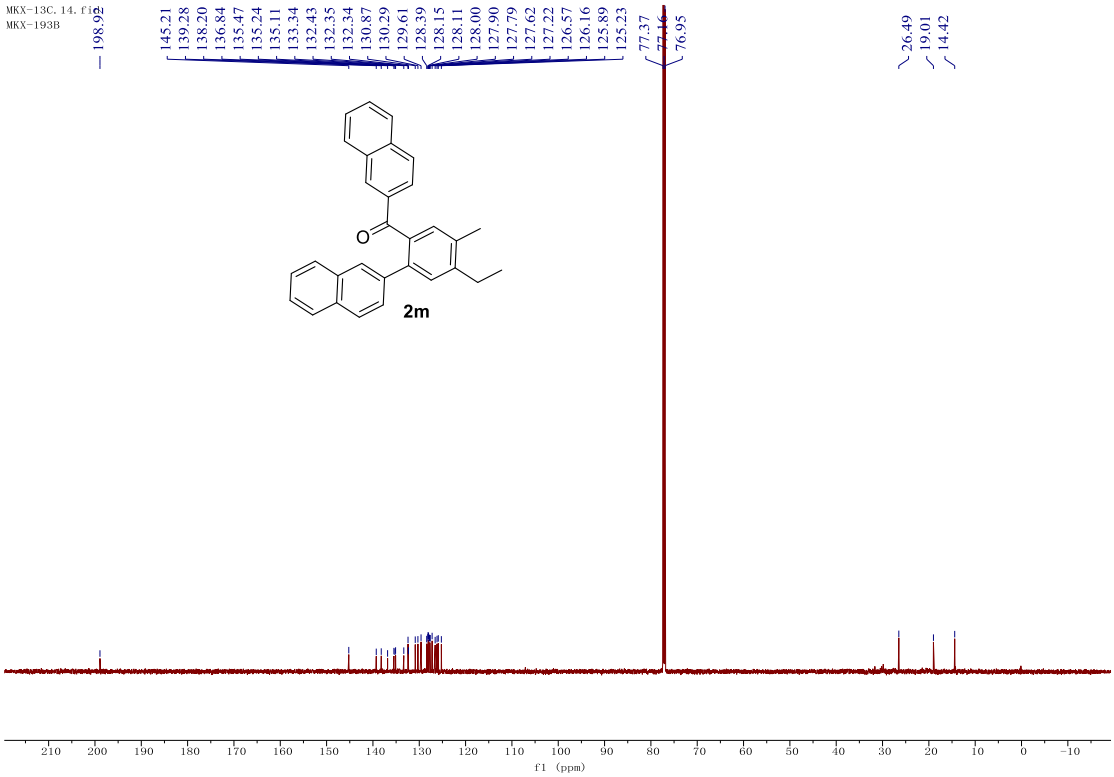
^{13}C NMR (151 MHz, $CDCl_3$) for **2l**



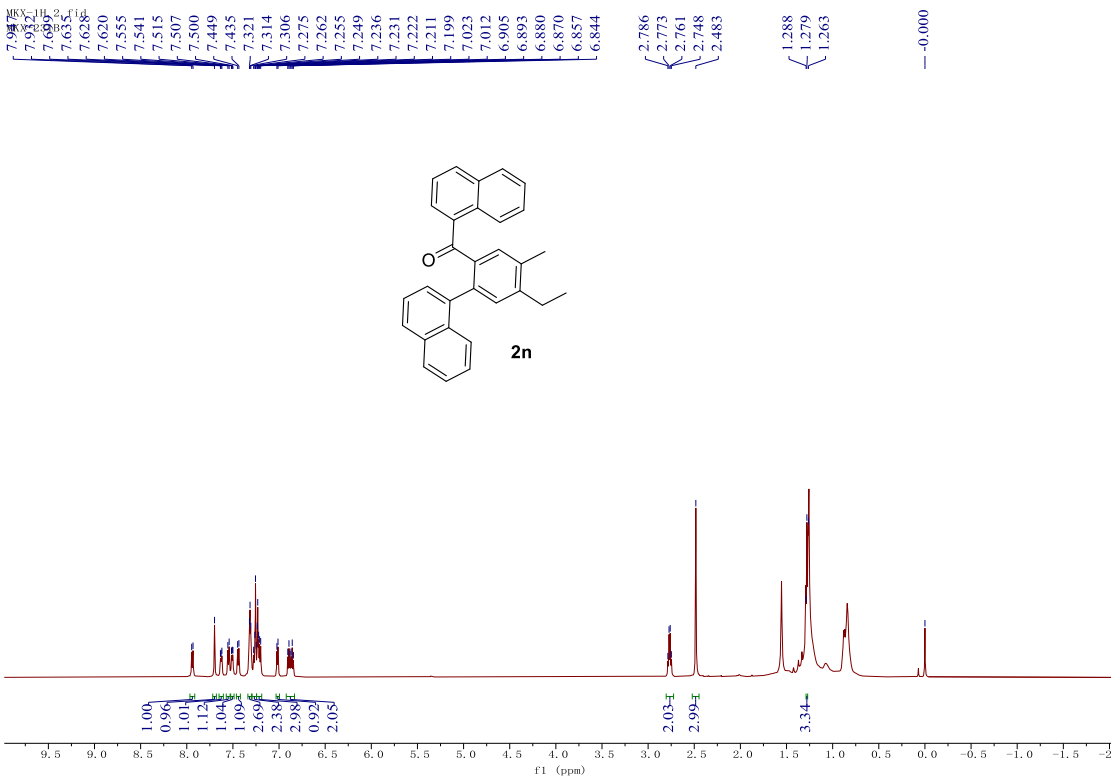
^{1}H NMR (400 MHz, $CDCl_3$) for **2m**



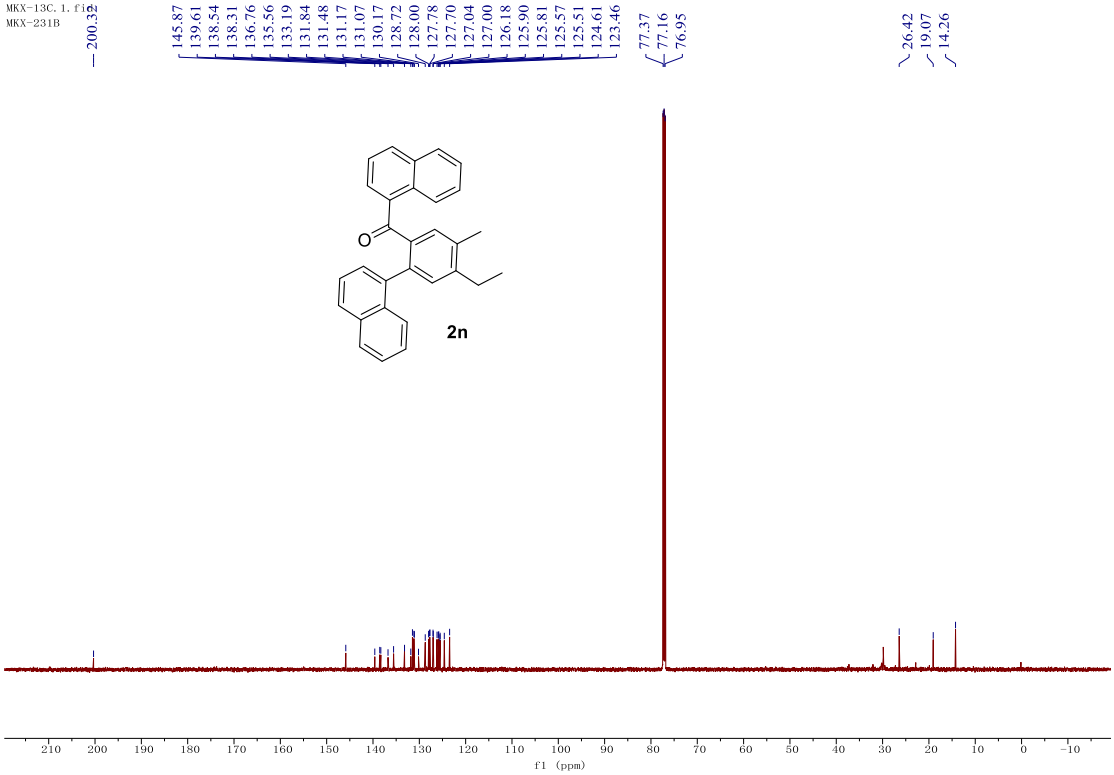
^{13}C NMR (151 MHz, $CDCl_3$) for **2m**



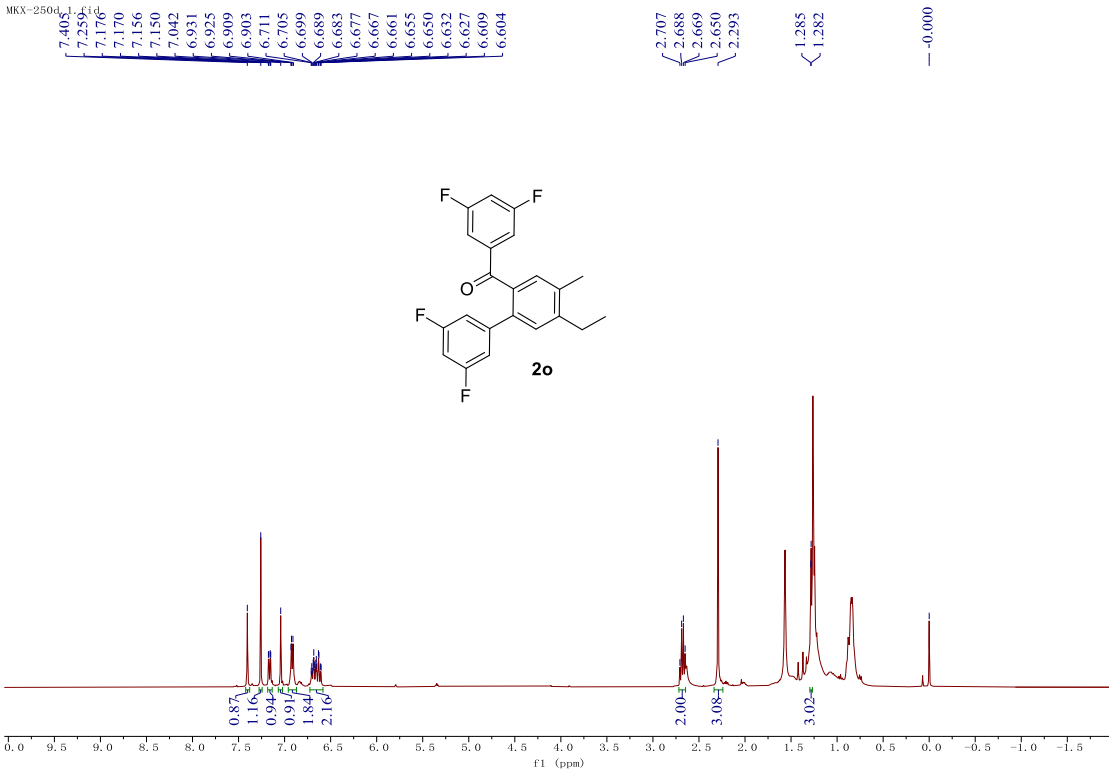
^{1}H NMR (400 MHz, $CDCl_3$) for **2n**



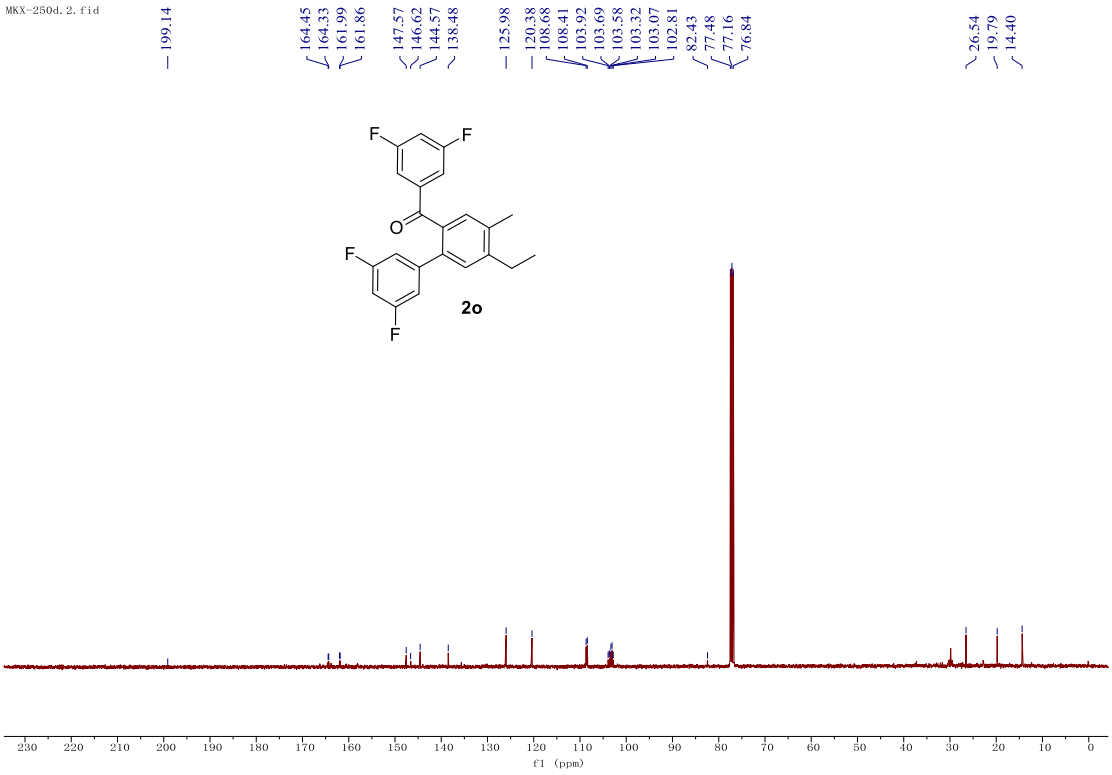
^{13}C NMR (151 MHz, $CDCl_3$) for **2n**



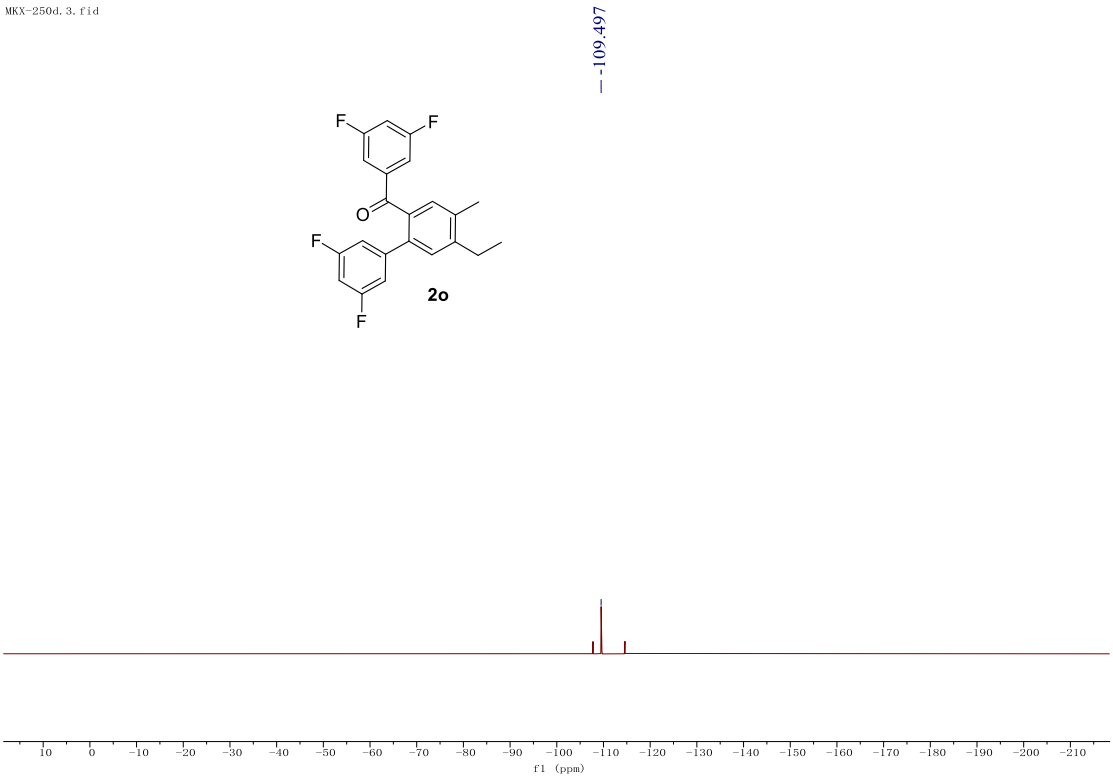
^{1}H NMR (400 MHz, $CDCl_3$) for **2o**



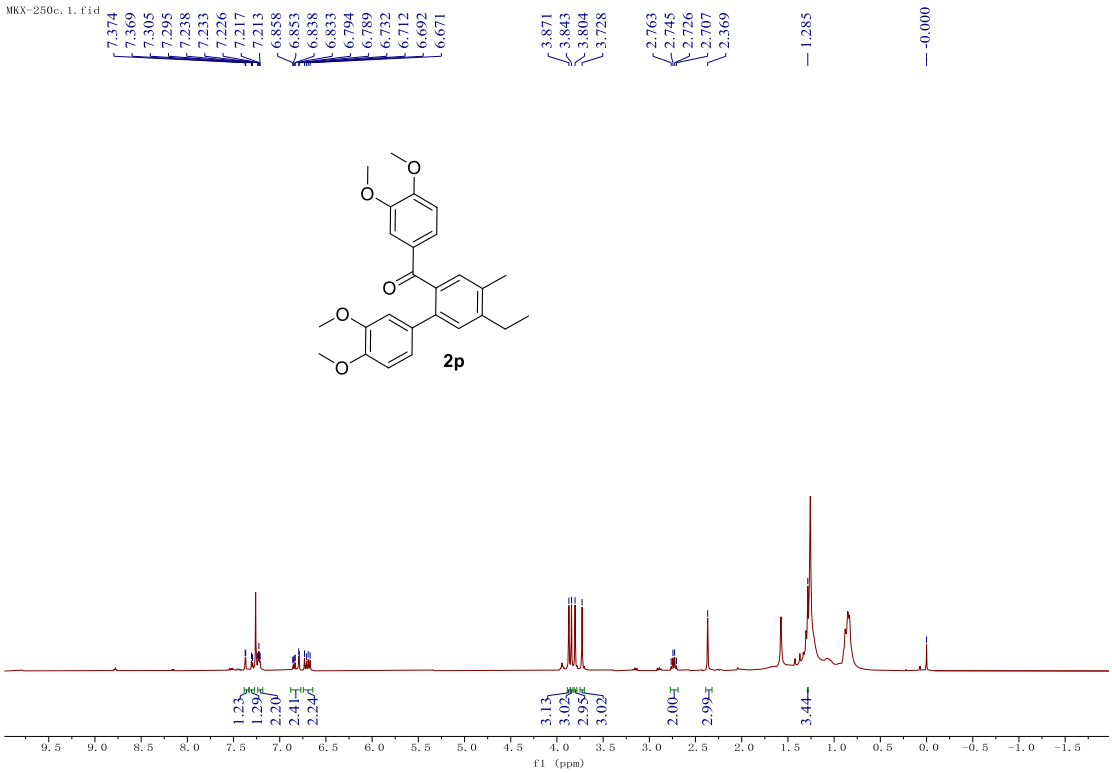
^{13}C NMR (101 MHz, $CDCl_3$) for **2o**



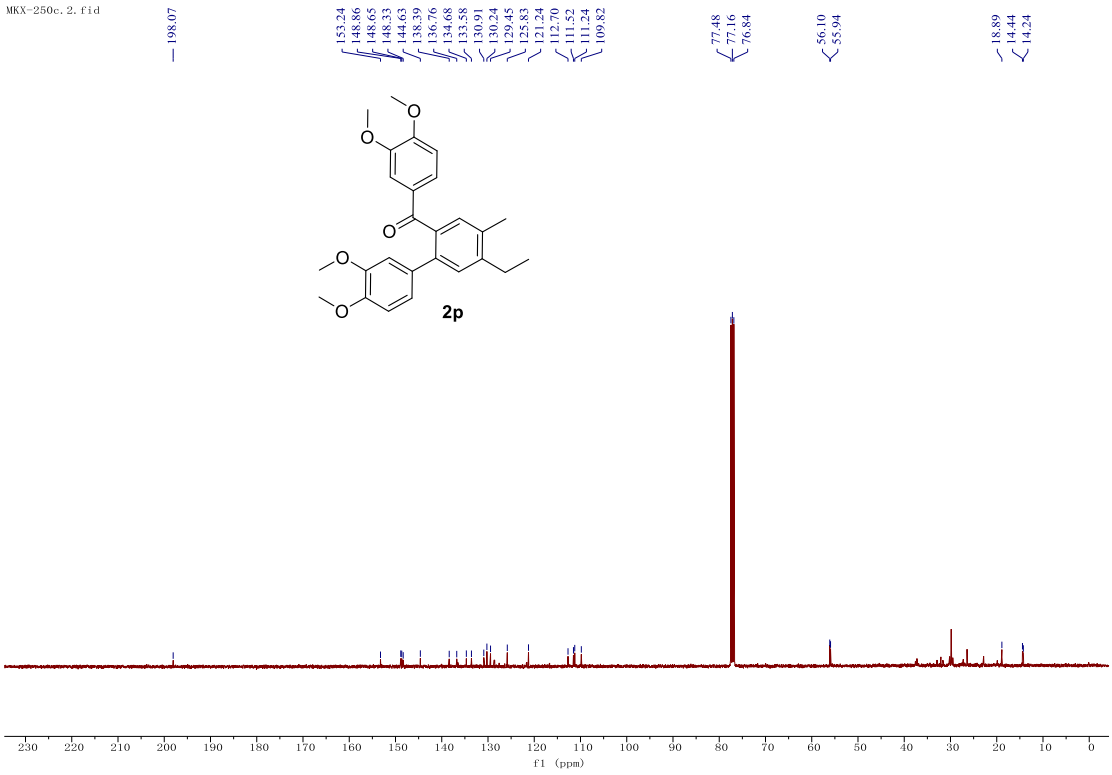
^{19}F NMR (376 MHz, $CDCl_3$) for **2o**



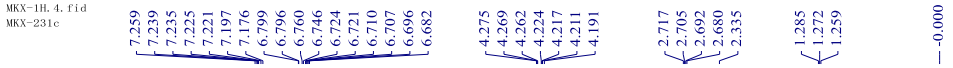
^{1}H NMR (400 MHz, $CDCl_3$) for **2p**

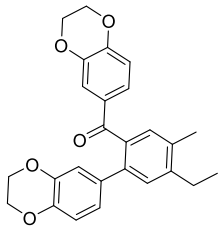


^{13}C NMR (101 MHz, $CDCl_3$) for **2p**

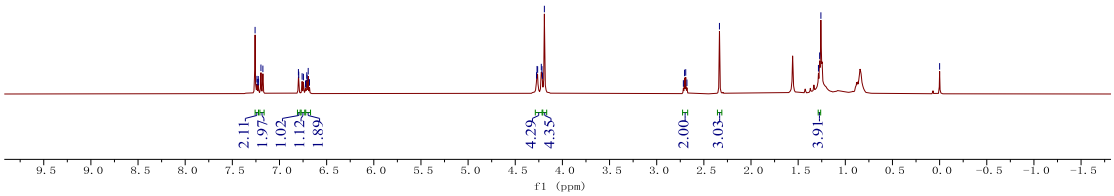


^{1}H NMR (400 MHz, $CDCl_3$) for **2q**

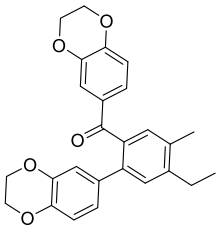




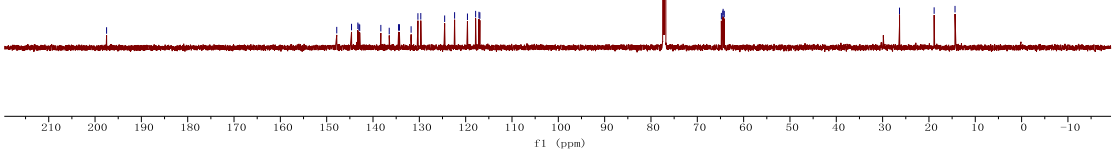
2q



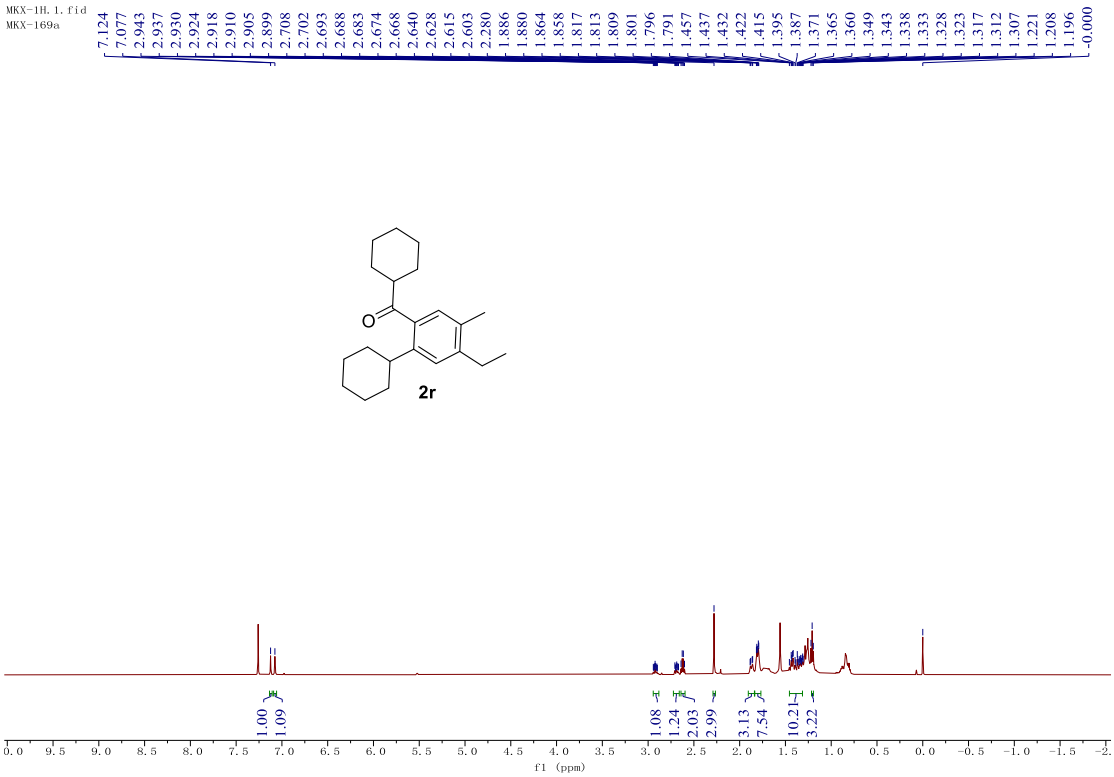
^{13}C NMR (101 MHz, $CDCl_3$) for **2q**



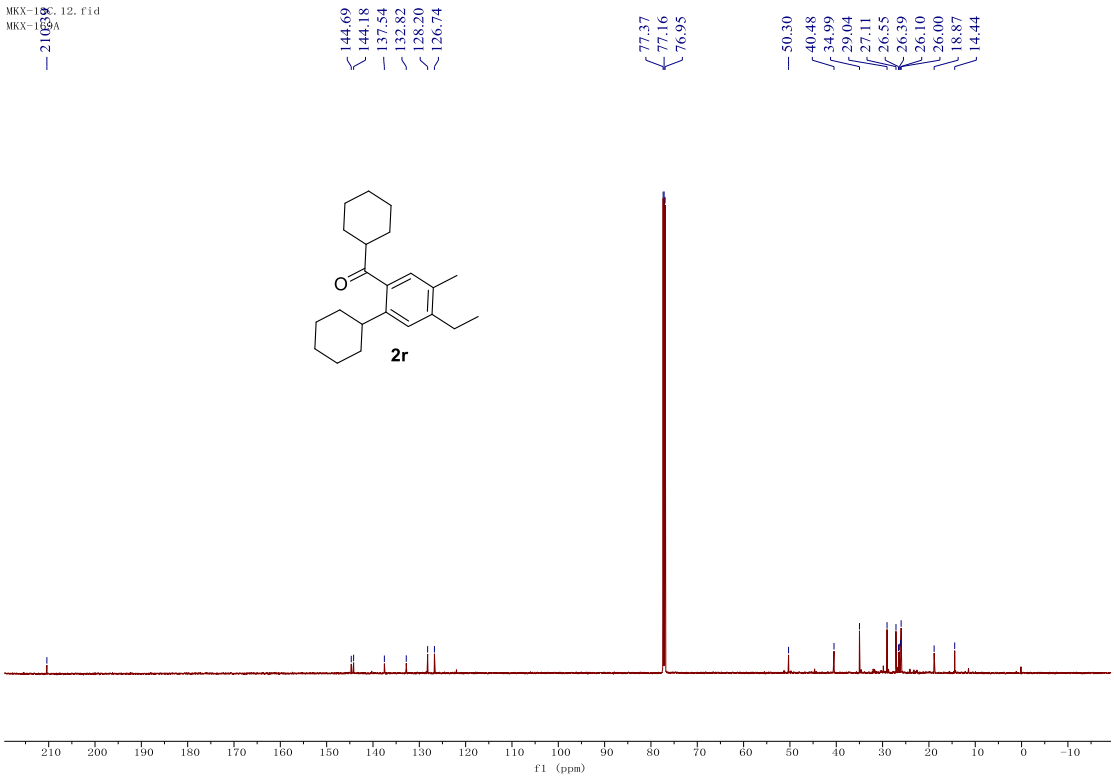
2q



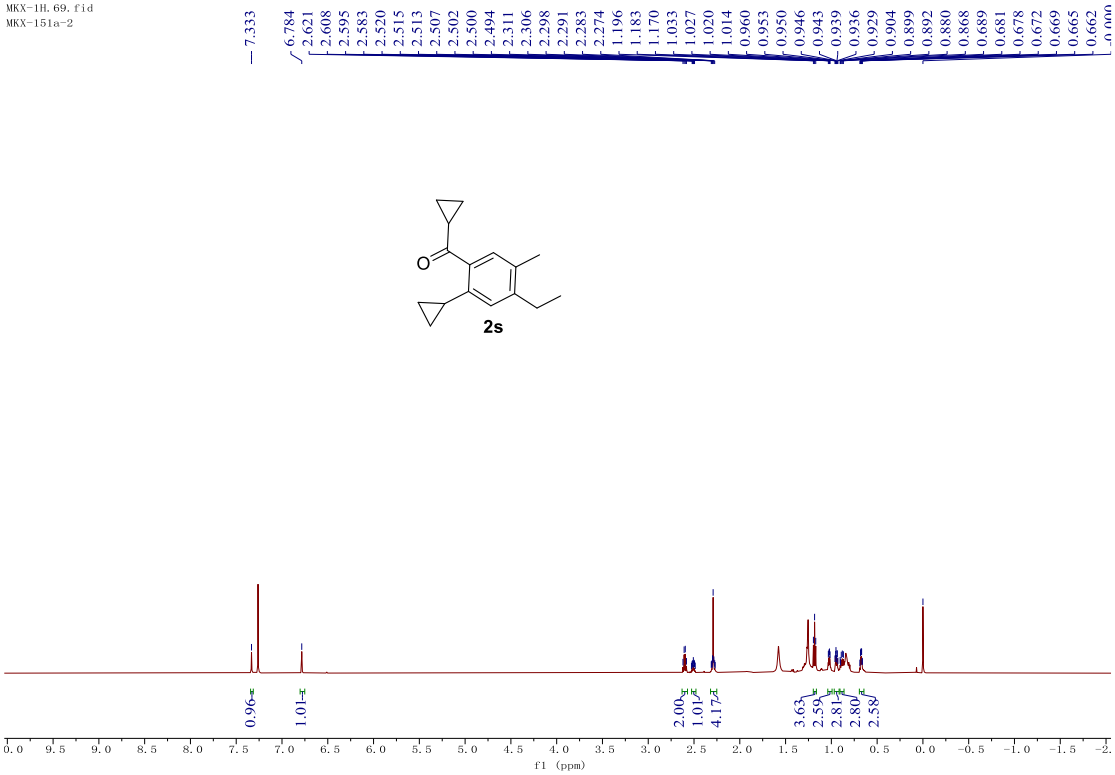
^{1}H NMR (400 MHz, $CDCl_3$) for **2r**



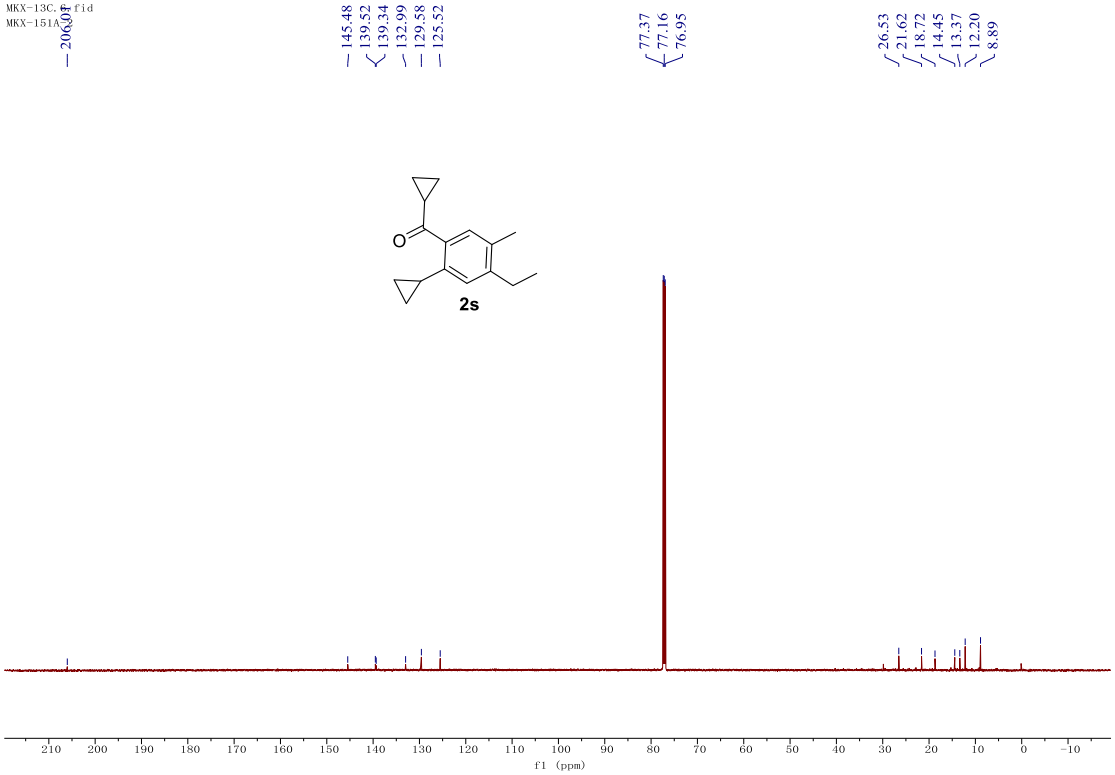
^{13}C NMR (101 MHz, $CDCl_3$) for **2r**



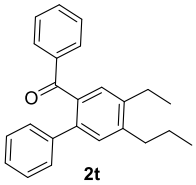
^{1}H NMR (400 MHz, $CDCl_3$) for **2s**

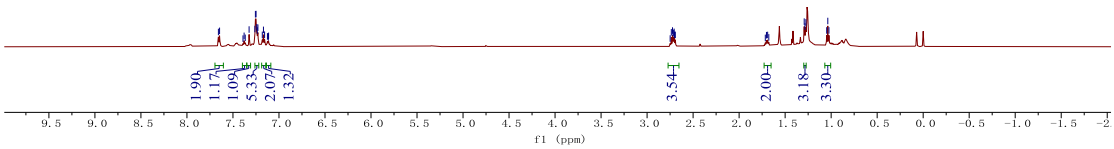


^{13}C NMR (101 MHz, $CDCl_3$) for **2s**

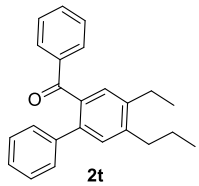


^{1}H NMR (400 MHz, $CDCl_3$) for **2t**

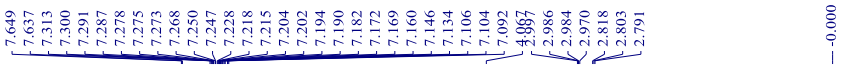


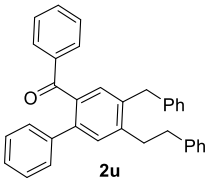


^{13}C NMR (101 MHz, $CDCl_3$) for **2t**

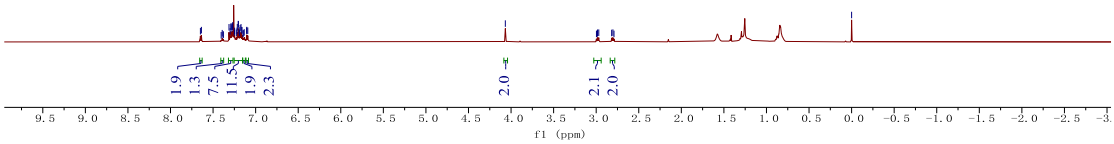


^{1}H NMR (400 MHz, $CDCl_3$) for **2u**

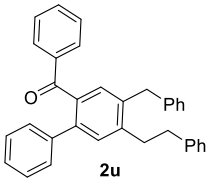




2u

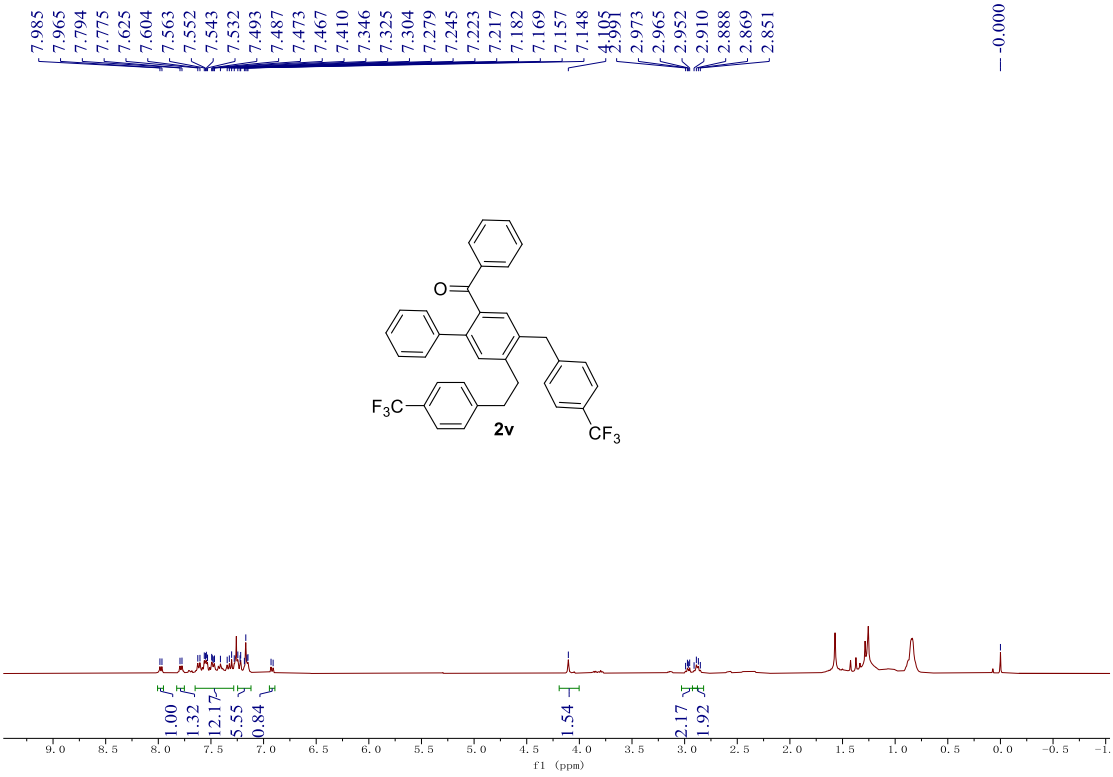


^{13}C NMR (101 MHz, $CDCl_3$) for **2u**

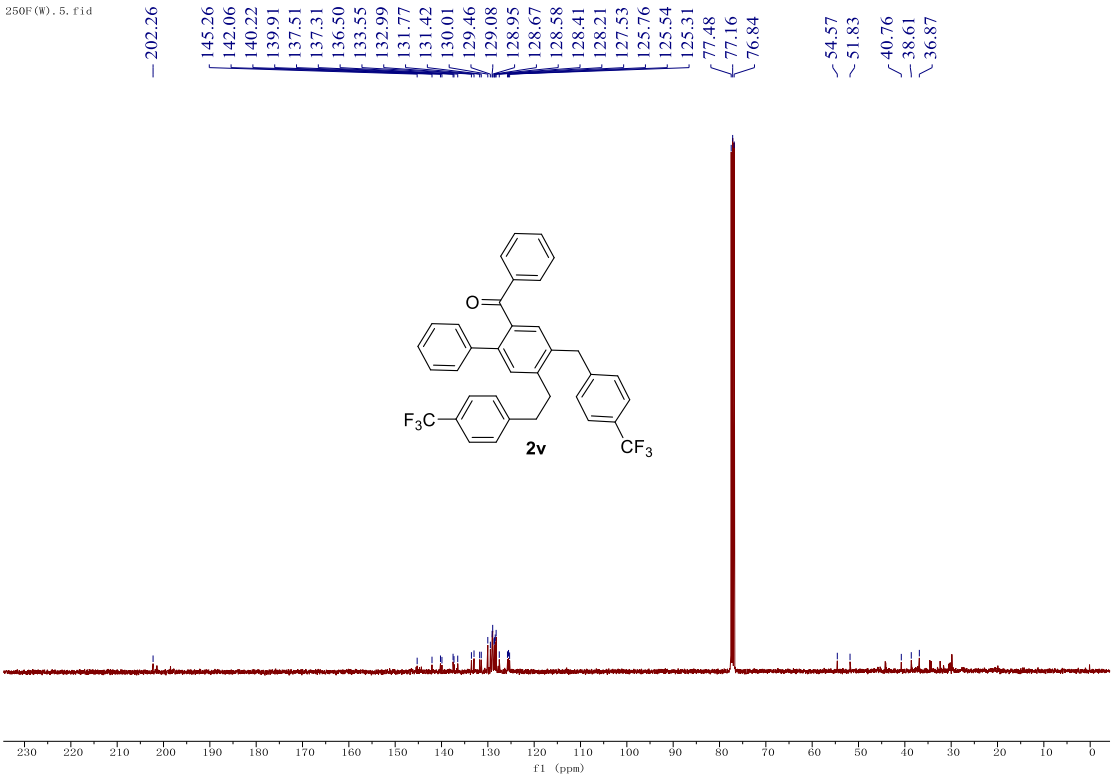


2u

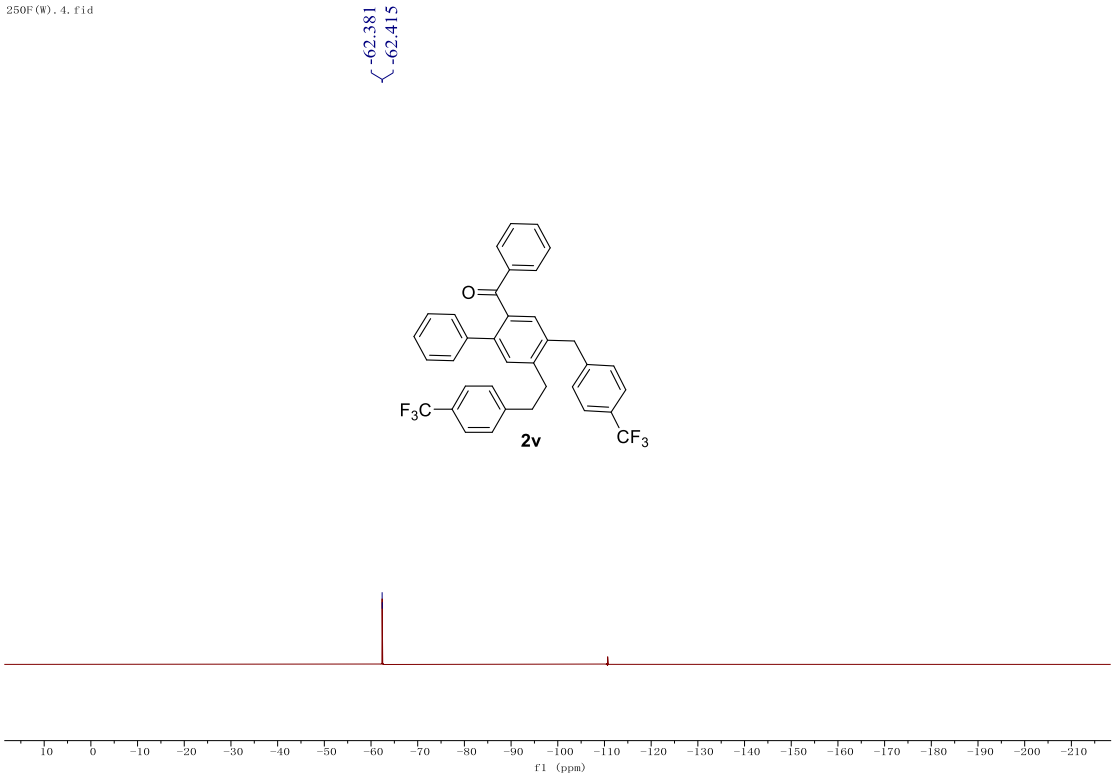
^{1}H NMR (400 MHz, $CDCl_3$) for **2v**



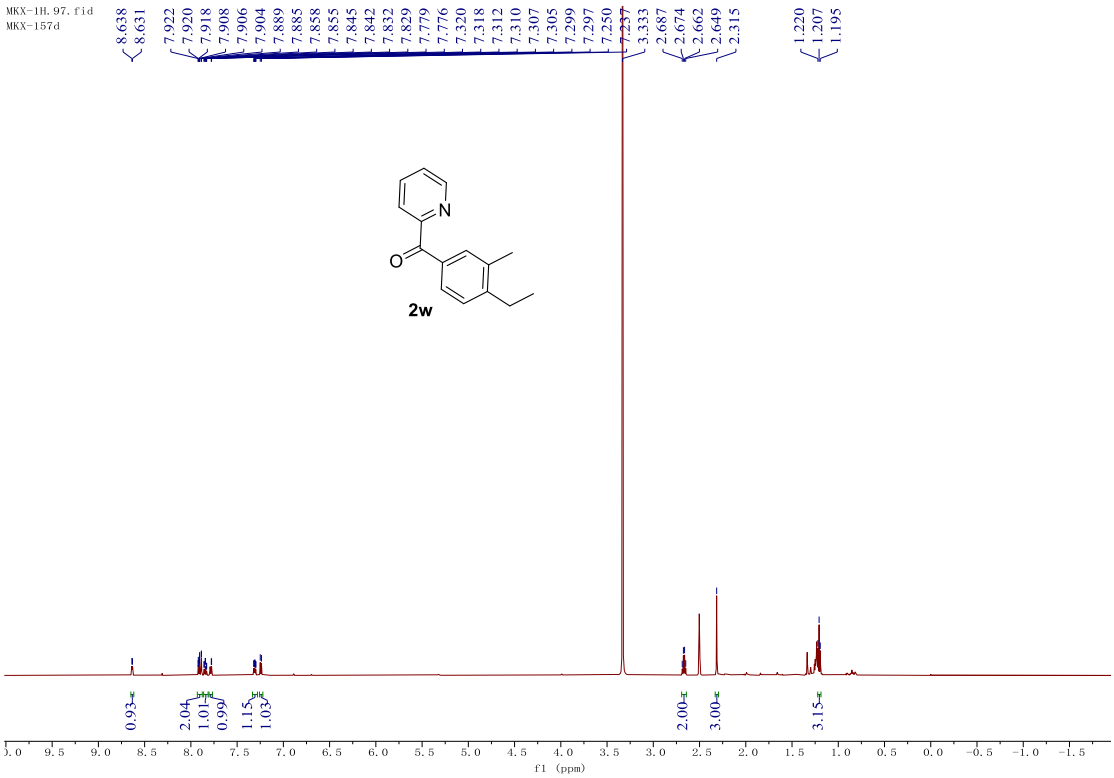
^{13}C NMR (101 MHz, $CDCl_3$) for **2v**



^{19}F NMR (376 MHz, $CDCl_3$) for **2v**



^{1}H NMR (400 MHz, DMSO-d_6) for **2w**



^{13}C NMR (101 MHz, DMSO-d_6) for **2w**