Electronic Supplementary Information

Nickel-catalyzed C-O bond reduction of aryl and benzyl 2-pyridyl ethers

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Contents

I. Experimental procedures and spectral data

General

All reactions were performed under nitrogen atmosphere using standard Schlenk and vacuum line techniques. Toluene, THF and Et_2O were purified by JC Meyer Phoenix Solvent Systems. 1,4-Dioxane and xylene were distilled over sodium under nitrogen. DMF was dried over 4 Å molecular sieve, fractionally distilled under reduced pressure and stored under nitrogen. $Ni(COD)_2$ was purchased from Strem Chemicals Inc and used as received. 3-(Biphenyl-4-yloxy)pyridine and 4-(biphenyl-4-yloxy)pyridine were purchased from Energy Chemical and used as received. NHC ligands,[2] aryl and benzyl 2-pyridyl ethers[3,4] and related starting materials[5] were prepared according to reported procedures. All other chemicals were obtained from commercial vendors and used as received. Gas chromatography (GC) analysis was conducted on a Aligent 7820A instrument. NMR spectra were recorded on a Bruker Avance III 400 spectrometer at ambient temperature. The chemical shifts of the ^1H NMR spectra were referenced to TMS or internal solvent resonance and the chemical shifts of the ^{13}C NMR spectra were referenced to internal solvent resonance.

1. Preparation of sodium isopropoxide[1]

Sodium (0.23 g, 10 mmol) and xylene (20 cm^3) were placed in a N_2-filled three-neck flask and heated until the sodium melted. The flask was closed with a rubber stopper, and the sodium was finely powdered by vigorous shaking. Then the xylene was removed by filtration and the powdered sodium was washed with two 10 cm^3 portions of diethyl ether. 30 cm^3 of diethyl ether was added, and the flask was placed on a 50 °C oil bath with a condenser. Anhydrous isopropanol (0.77 cm^3, 10 mmol) was added dropwise with stirring. The reaction mixture was refluxed with stirring for 8 h. The solvent was removed by filtration. The residual solid was washed twice with diethyl ether and dried under vacuum.

2. Typical procedure for the nickel-catalyzed hydrogenation of aryl 2-pyridyl ethers

A Schlenk tube was charged with $Ni(COD)_2$ (1.7 mg, 0.006 mmol), IPr·HCl (2.6 mg, 0.006 mmol), *i*-PrONa (25 mg, 0.30 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (49.4 mg, 0.2

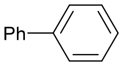
mmol) and THF (1 cm^3). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel or preparative thin layer chromatography (petroleum ether/EtOAc 60:1 v/v) to give 1,1'-biphenyl as a white solid, yield 30.5 mg (99%).

3. Nickel-catalyzed hydrogenation of 2-(biphenyl-4-yloxy)pyridine (4 mmol scale)

A Schlenk tube was charged with Ni(COD)$_2$ (33 mg, 0.12 mmol), IPr·HCl (51 mg, 0.12 mmol), *i*-PrONa (0.492 g, 6 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (0.988 g, 4 mmol) and THF (8 cm^3). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc 60:1 v/v) to give 1,1'-biphenyl as a white solid, yield 0.527 g (86%).

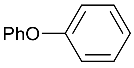
4. Spectral data for the cross-coupling products

(1) 1,1'-biphenyl (**2a**)[6]



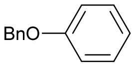
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 30.8 mg (99%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.67 (d, *J* = 8.0 Hz, 4H), 7.51 (t, *J* = 7.5 Hz, 4H), 7.41 (t, *J* = 7.2 Hz, 2H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 141.34, 128.88, 127.38, 127.29.

(2) oxydibenzene (**2c**)[6]



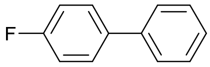
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 31.1 mg (90%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.42–7.30 (m, 4H), 7.13 (t, *J* = 7.4 Hz, 2H), 7.08–6.99 (m, 4H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 157.38, 129.87, 123.34, 119.02.

(3) (benzyloxy)benzene (**2d**)[6]



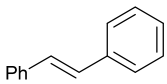
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 36.0 mg (98%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.36 (d, *J* = 7.2 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 2H), 7.27–7.16 (m, 3H), 6.95–6.83 (m, 3H), 4.98 (s, 2H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 158.89, 137.18, 129.62, 128.71, 128.07, 127.62, 121.06, 114.95, 70.01

(4) 4-fluoro-1,1'-biphenyl (**2f**)[7]



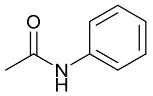
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 29.5 mg (86%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.59–7.50 (m, 4H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.39–7.32 (m, 1H), 7.13 (t, *J* = 8.7 Hz, 2H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 162.59 (d, *J* = 246.2 Hz), 140.39, 137.47 (d, *J* = 3.2 Hz), 128.96, 128.83 (d, *J* = 8.0 Hz), 127.40, 127.16, 115.75 (d, *J* = 21.4 Hz). ^{19}F NMR (376 MHz, CDCl$_3$): δ –115.85.

(5) (*E*)-1,2-diphenylethene (**2g**)[6]



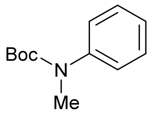
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 35.5 mg (99%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.57–7.46 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 4H), 7.29–7.21 (m, 2H), 7.11 (s, 2H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 137.43, 128.81, 127.75, 126.64.

(6) *N*-phenylacetamide (**2h**)[6]



Eluent: petroleum ether/ethyl acetate = 1:1 (v/v). White solid, yield 24.2 mg (90%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.99–7.62 (br, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.2 Hz, 1H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, CDCl$_3$): δ 168.87, 138.06, 129.03, 124.39, 120.13, 24.60.

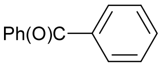
(7) *tert*-butyl methyl(phenyl)carbamate (**2i**)[6]



Eluent: petroleum ether/ethyl acetate = 5:1 (v/v). Colorless oil, yield 28.9 mg (70%). ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.25 (t, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.2

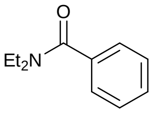
Hz, 1H), 3.19 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 154.92, 143.93, 128.67, 125.65, 125.50, 80.34, 37.44, 28.44.

(8) benzophenone (**2k**)[8]



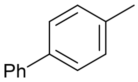
Eluent: petroleum ether/ethyl acetate = 20:1 (v/v). White solid, yield 35.7 mg (98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86–7.76 (m, 4H), 7.59 (t, J = 7.4 Hz, 2H), 7.48 (t, J = 7.6 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 196.91, 137.69, 132.55, 130.19, 128.40.

(9) *N,N*-diethylbenzamide (**2l**)[9]



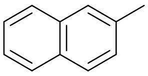
Eluent: petroleum ether/ethyl acetate = 2:1 (v/v). Colorless oil, yield 29.0 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.28 (m, 5H), 3.54 (br, 2H), 3.24 (br, 2H), 1.24 (br, 3H), 1.09 (br, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 171.39, 137.36, 129.17, 128.49, 126.34, 43.36, 39.30, 14.31, 13.00.

(10) 4-methyl-1,1'-biphenyl (**4a**)[10]



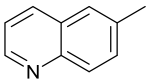
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 27.7 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65–7.58 (m, 2H), 7.53 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.35 (t, J = 7.4 Hz, 1H), 7.28 (d, J = 7.9 Hz, 2H), 2.43 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.29, 138.48, 137.16, 129.62, 128.85, 127.13, 127.11, 21.25.

(11) 2-methylnaphthalene (**4d**)[11]



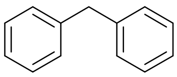
Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 23.4 mg (83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 7.8 Hz, 1H), 7.82–7.75 (m, 2H), 7.65 (s, 1H), 7.53–7.41 (m, 2H), 7.36 (dd, J = 8.4, 1.4 Hz, 1H), 2.56 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.56, 133.79, 131.82, 128.24, 127.82, 127.73, 127.36, 126.96, 125.99, 125.08, 21.85.

(12) 6-methylquinoline (**4e**)[12]



Eluent: petroleum ether/ethyl acetate = 5:1 (v/v). Colorless oil, yield 24.1 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (dd, *J* = 4.2, 1.5 Hz, 1H), 8.05 (d, *J* = 8.1 Hz, 1H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.61 – 7.49 (2 H, m), 7.34 (dd, *J* = 8.3, 4.2 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 149.63, 146.98, 136.51, 135.51, 131.87, 129.18, 128.43, 126.70, 121.18, 21.69.

(13) diphenylmethane (**4f**)[13]



Performed on 0.4 mmol scale. Eluent: petroleum ether/ethyl acetate = 60:1 (v/v). White solid, yield 25.1 mg (31%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.24 (m, 4H), 7.22–7.14 (m, 6H), 3.98 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.25, 129.07, 128.59, 126.20, 42.08.

II. Reaction mechanism

(1) Deuterium labeling experiment

A Schlenk tube was charged with $Ni(COD)_2$ (1.7 mg, 0.006 mmol), IPr·HCl (2.6 mg, 0.006 mmol), $(CD_3)_2CDONa$ (27 mg, 0.30 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (49.4 mg, 0.2 mmol) and THF (1 cm^3). The mixture was stirred at 60 °C for 2 h. Volatiles were removed by rotary evaporation. The residue was purified by preparative thin-layer chromatography (developing solvent: petroleum ether/EtOAc = 60:1 v/v) to give the reductive product as a white solid, yield 28.4 mg (92%). The deuterium content at the initial position of C-O bond was approximately 93% determined by ^{1}H NMR spectroscopy (Figure S1).

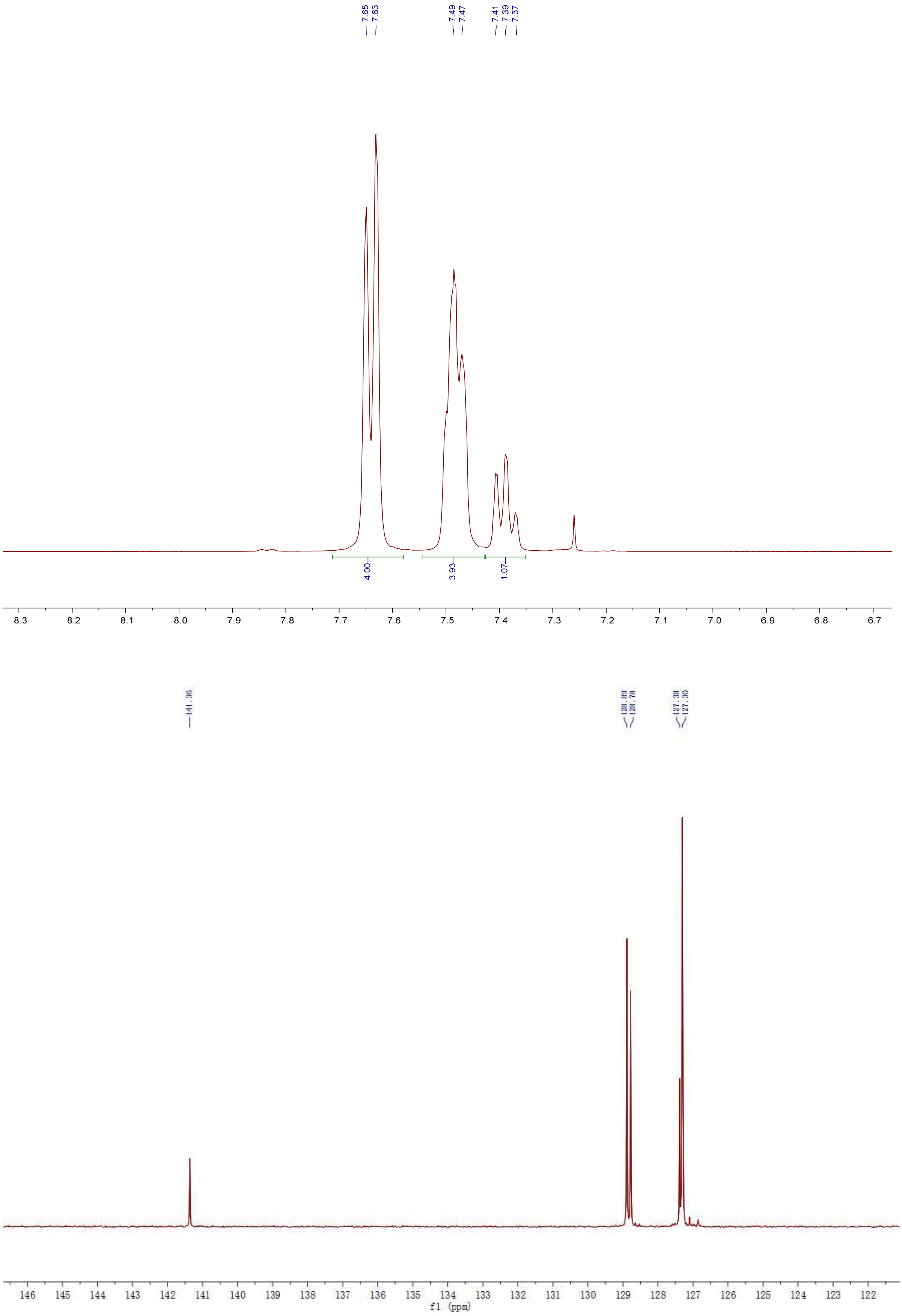
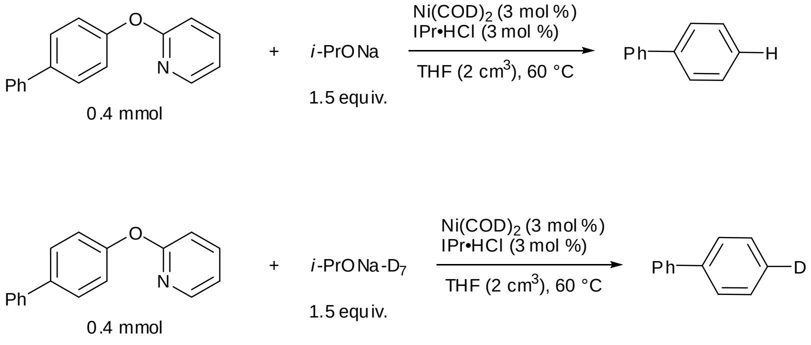


Figure S1 ^{1}H and ^{13}C NMR spectra of 1,1'-biphenyl-4-d.

(2) Kinetic isotope effect experiment



A Schlenk tube was charged with Ni(COD)$_2$ (3.3 mg, 0.012 mmol), IPr·HCl (5.2 mg, 0.012 mmol), *i*-PrONa (49.2 mg, 0.60 mmol), 2-([1,1'-biphenyl]-4-yloxy)pyridine (98.8 mg, 0.4 mmol , THF (2 cm^3) and dodecane (30 μl). The mixture was stirred at 60 °C. A 0.1 cm^3 aliquot was taken from the reaction mixture at 3, 6, 9, and 12 min., which were separately quenched with H$_2$O (1 cm^3) and diluted with EtOAc (3 cm^3). The GC yields were determined using dodecane as an internal standard. The reaction with *i*-PrONa-D$_7$ was carried out and monitored under exact same conditions. The experimental results are showed in Figure S2. The calculated KIE value is 1.41.

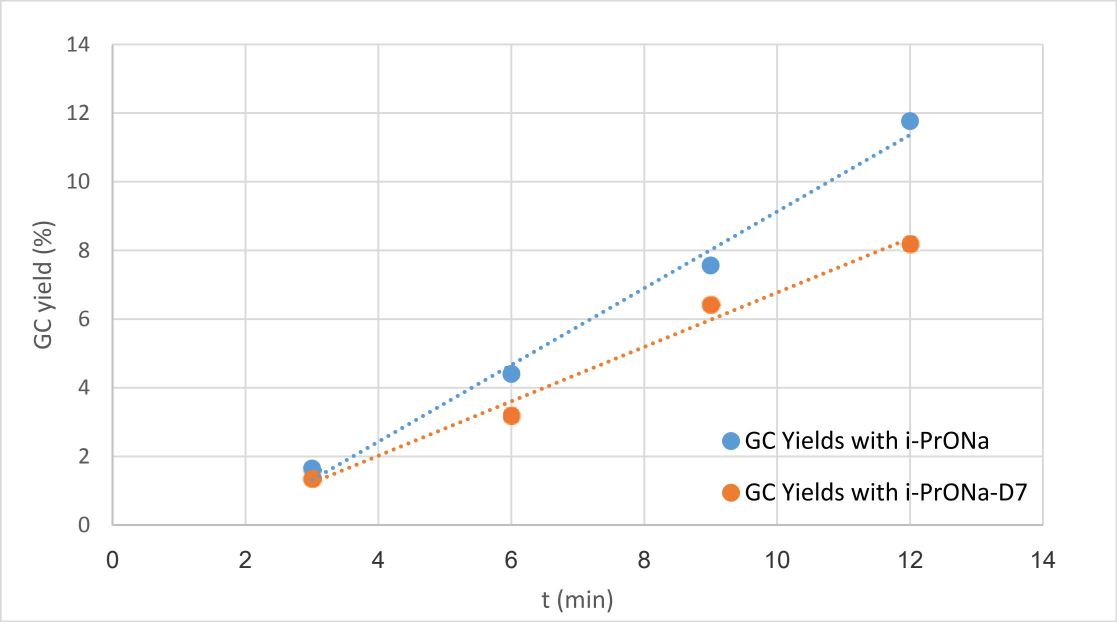


Figure S2 Intermolecular parallel KIE experiment with *i*-PrONa and *i*-PrONa-D$_7$.
For group with *i*-PrONa, $y = 1.117x - 2.0345$, $R^2 = 0.990$; For group with *i*-PrONa-D7, $y = 0.7915x - 1.1399$, $R^2 = 0.9858$. Thus KIE value is 1.41.

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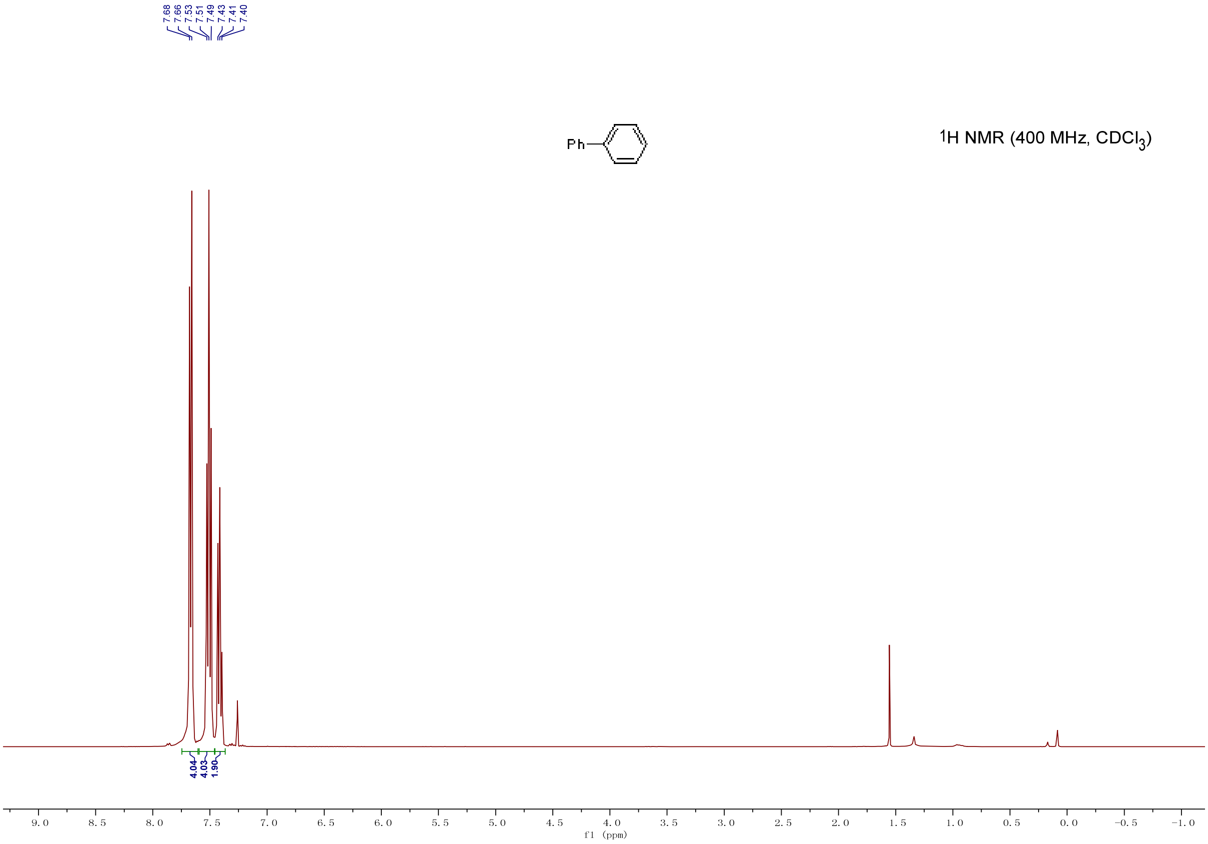
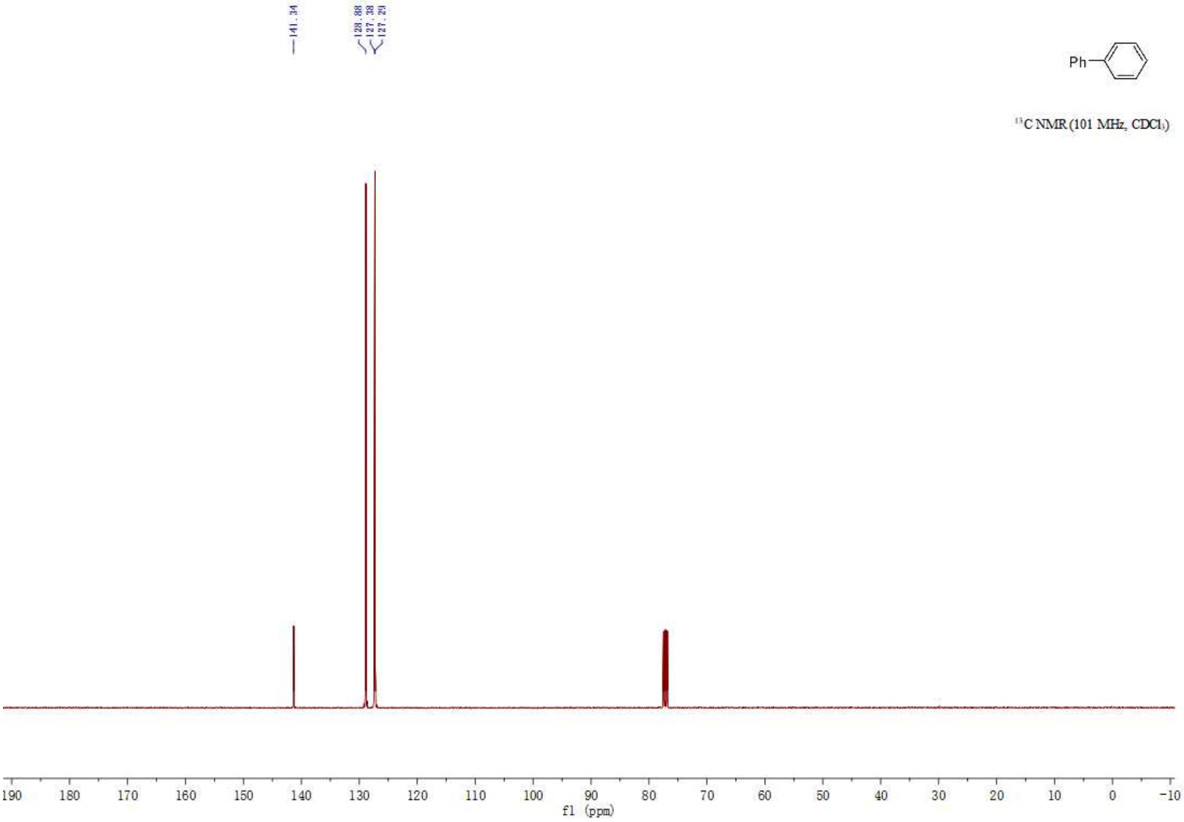
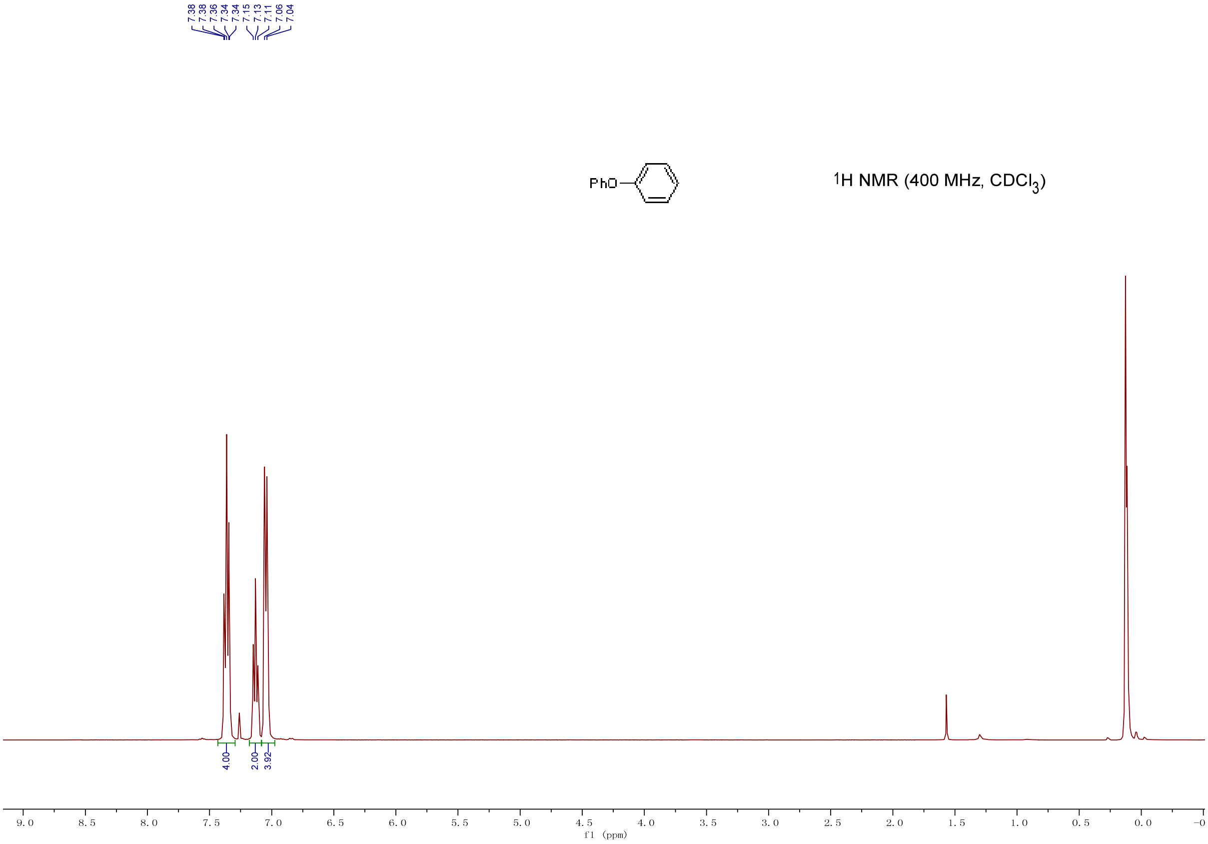
III. Copies of NMR spectra

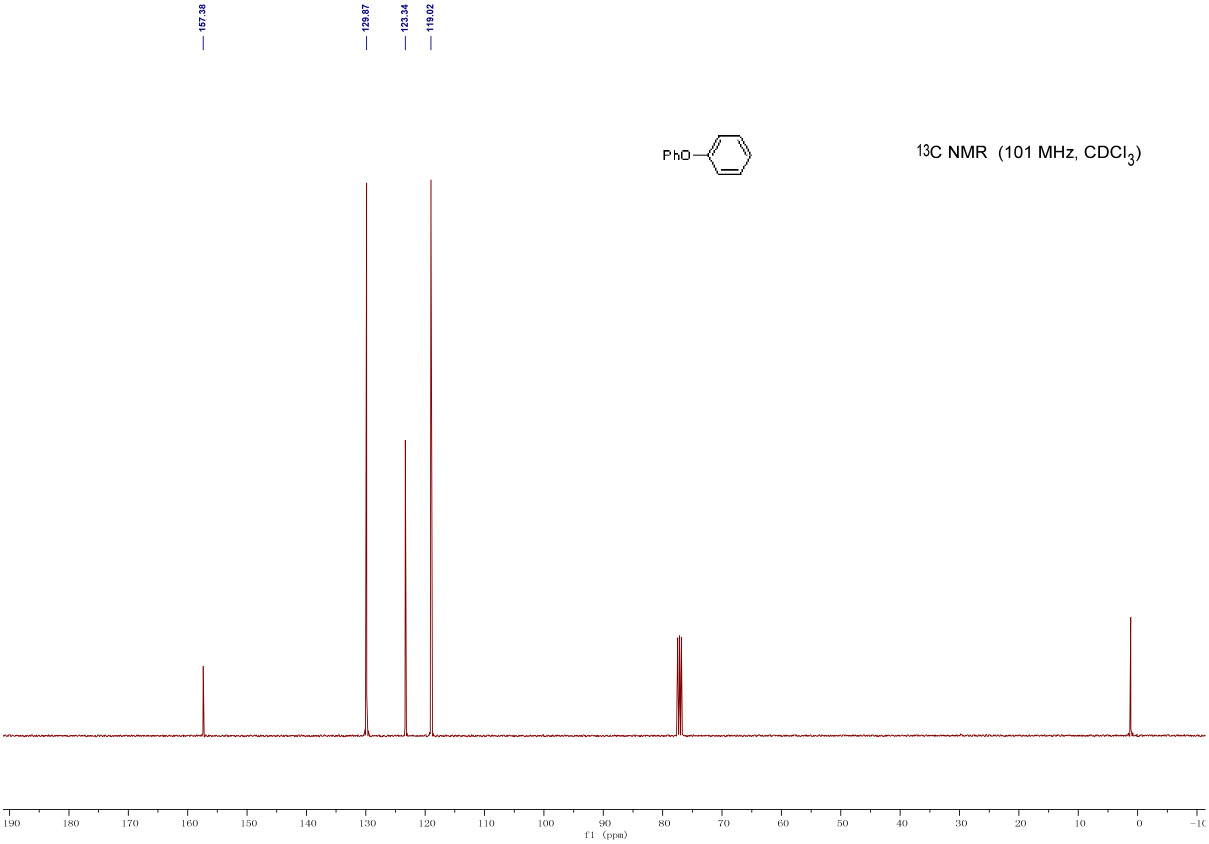
(1) 1,1'-biphenyl (**2a**)



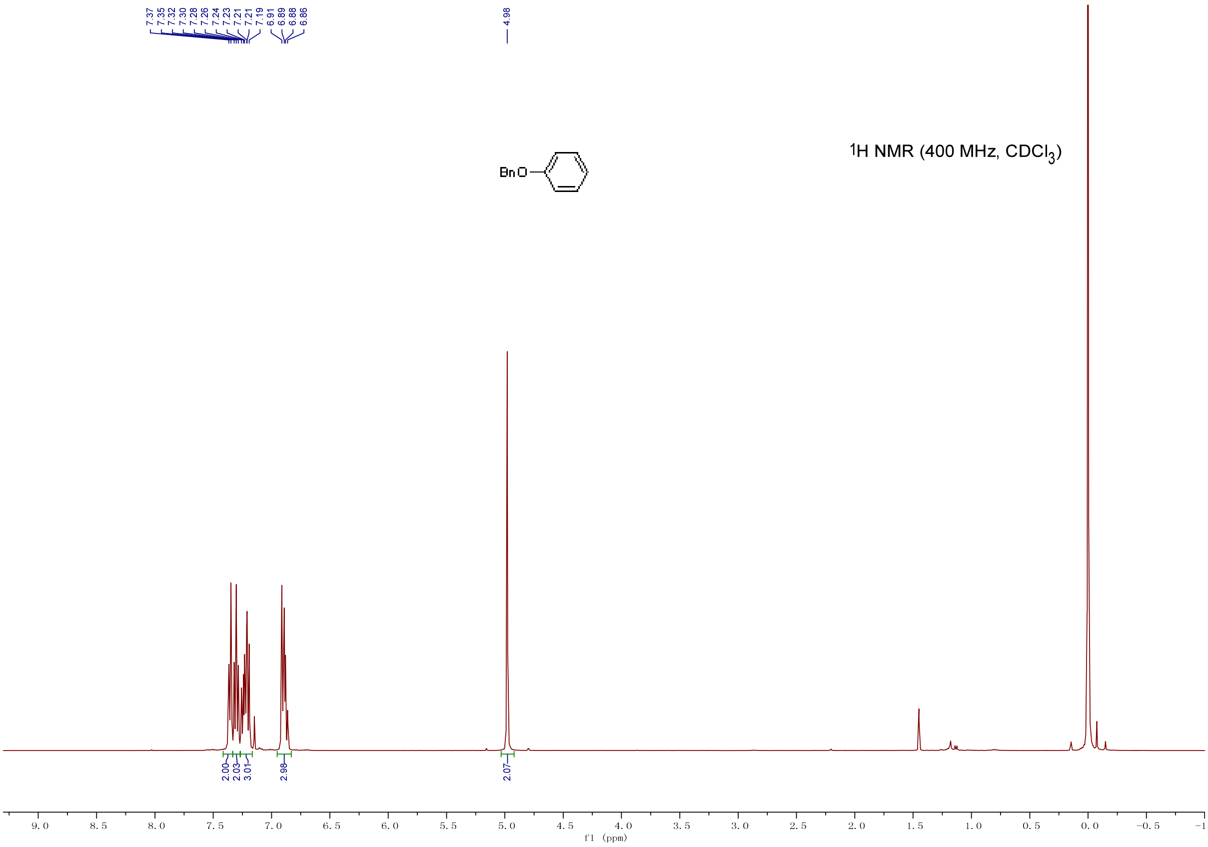


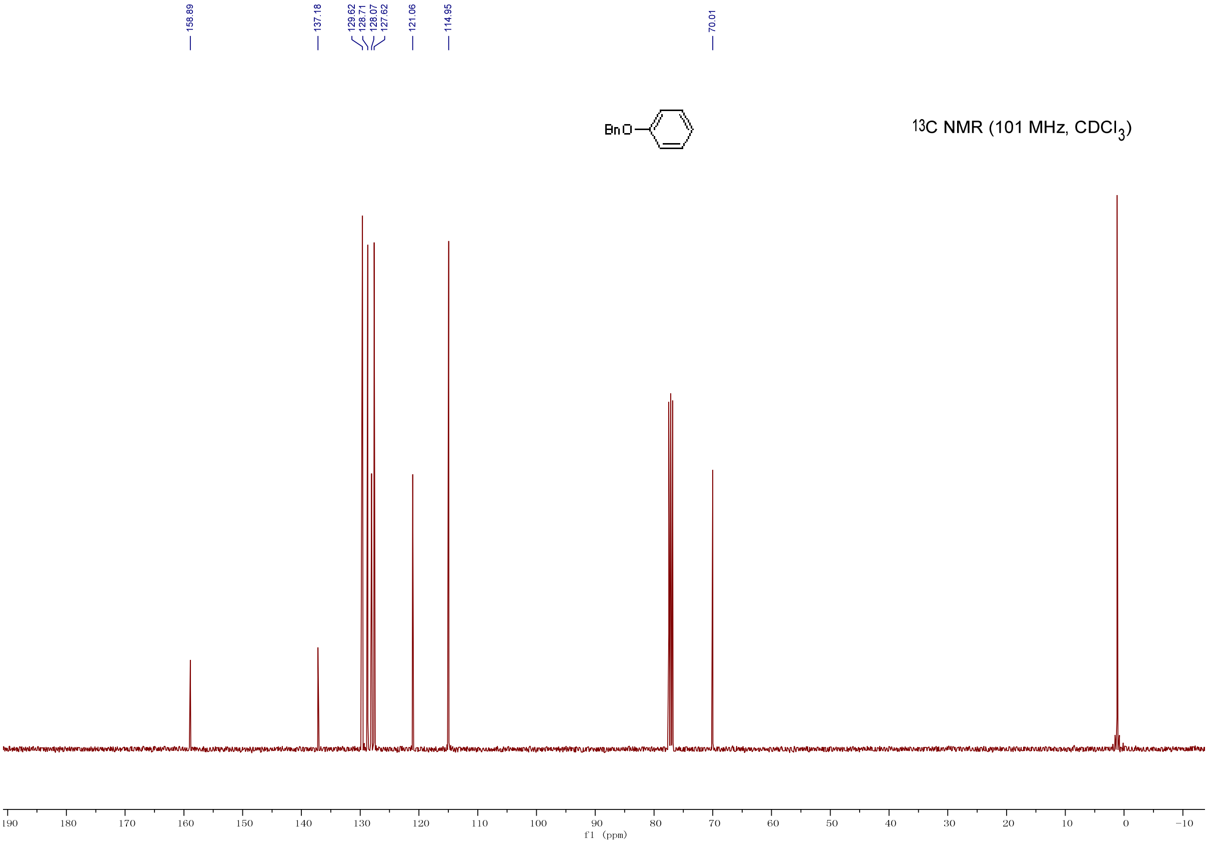
(2) oxydibenzene (**2c**)



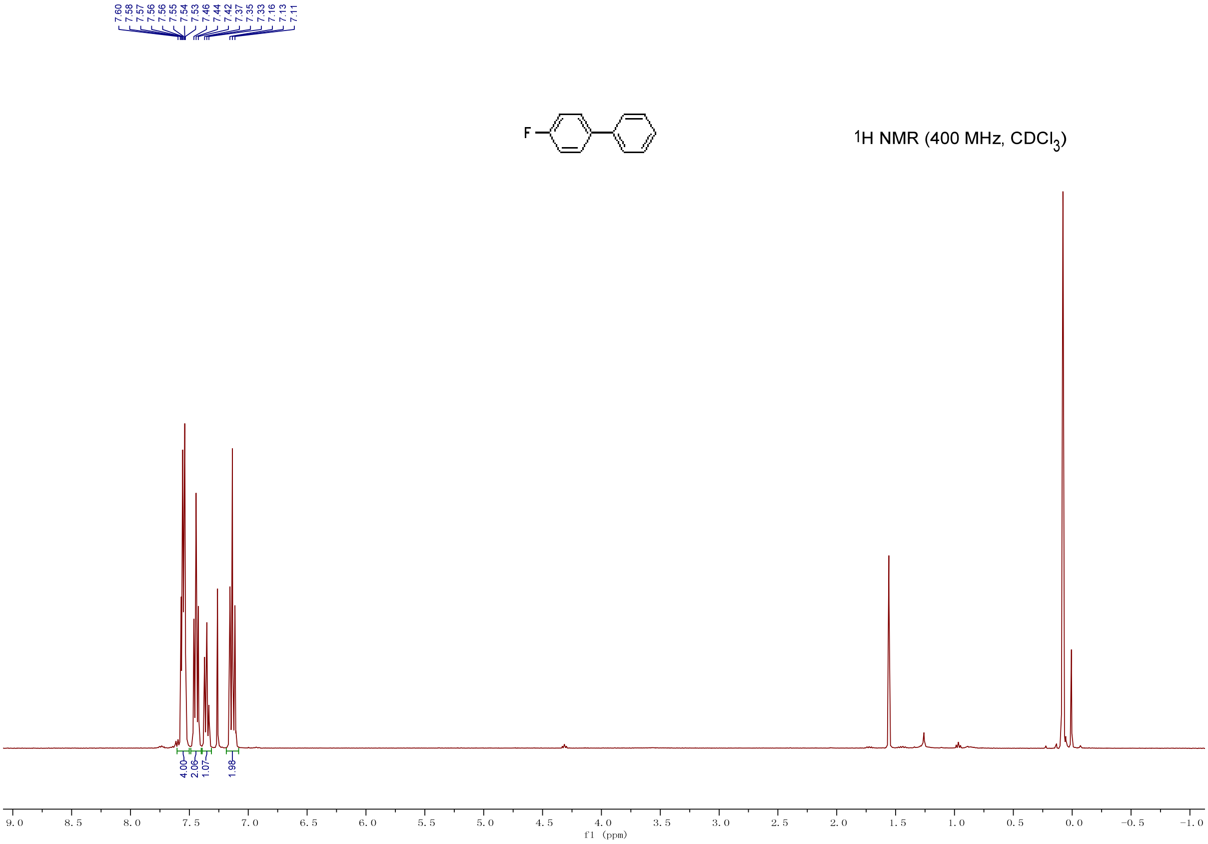


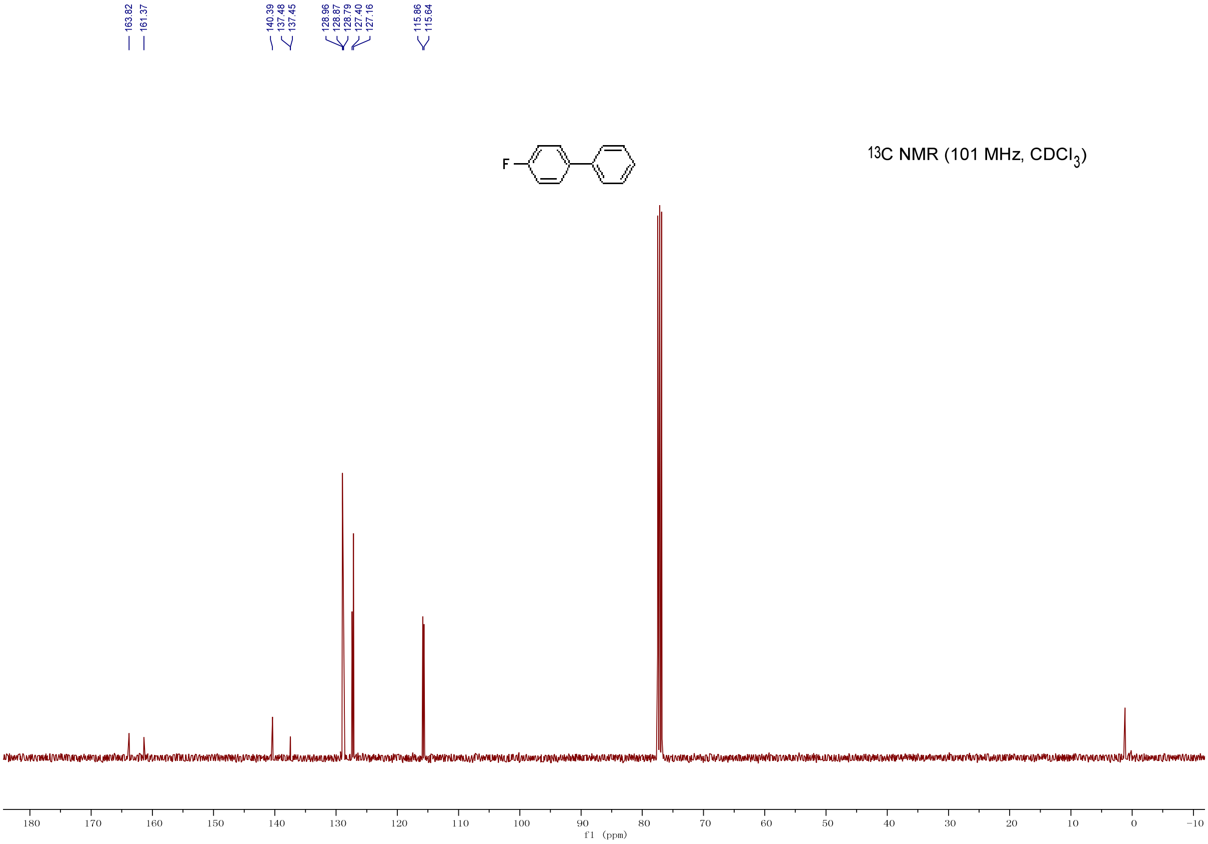
(3) (benzyloxy)benzene (**2d**)

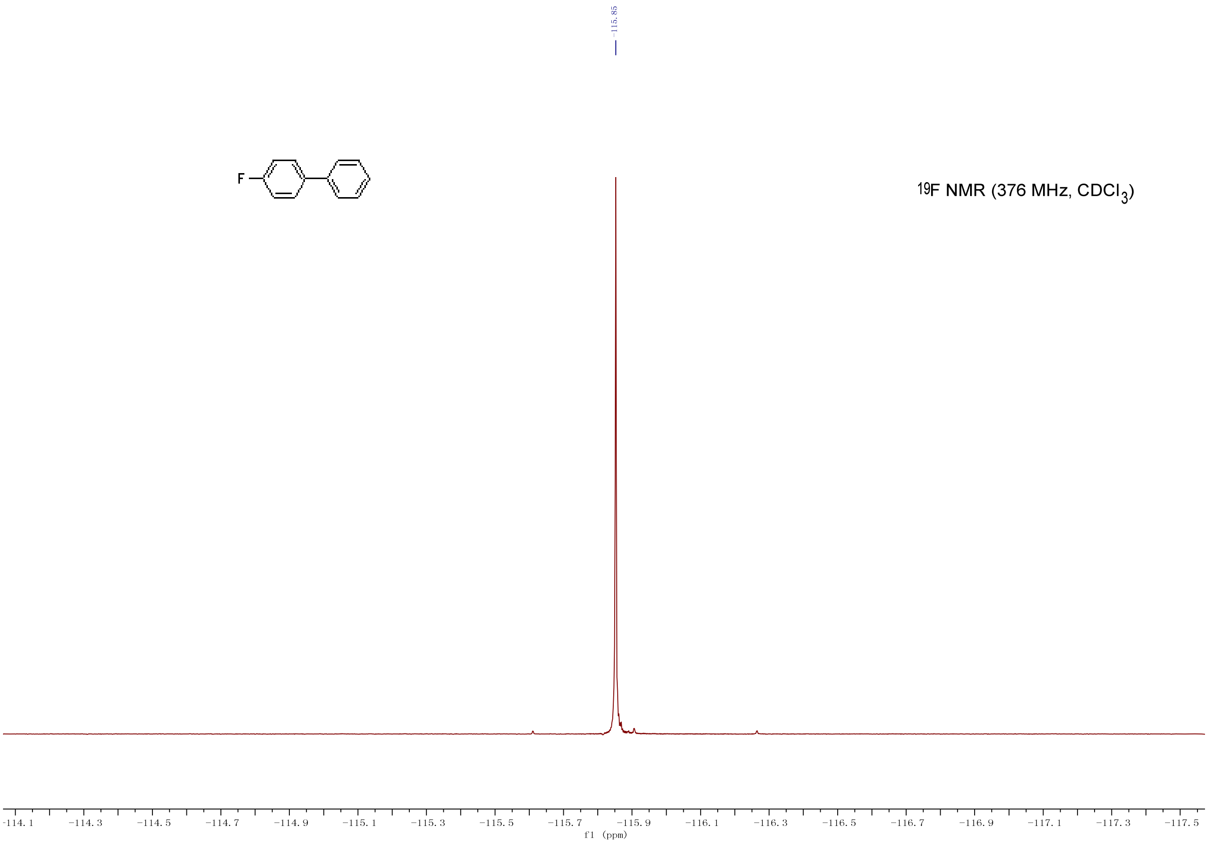




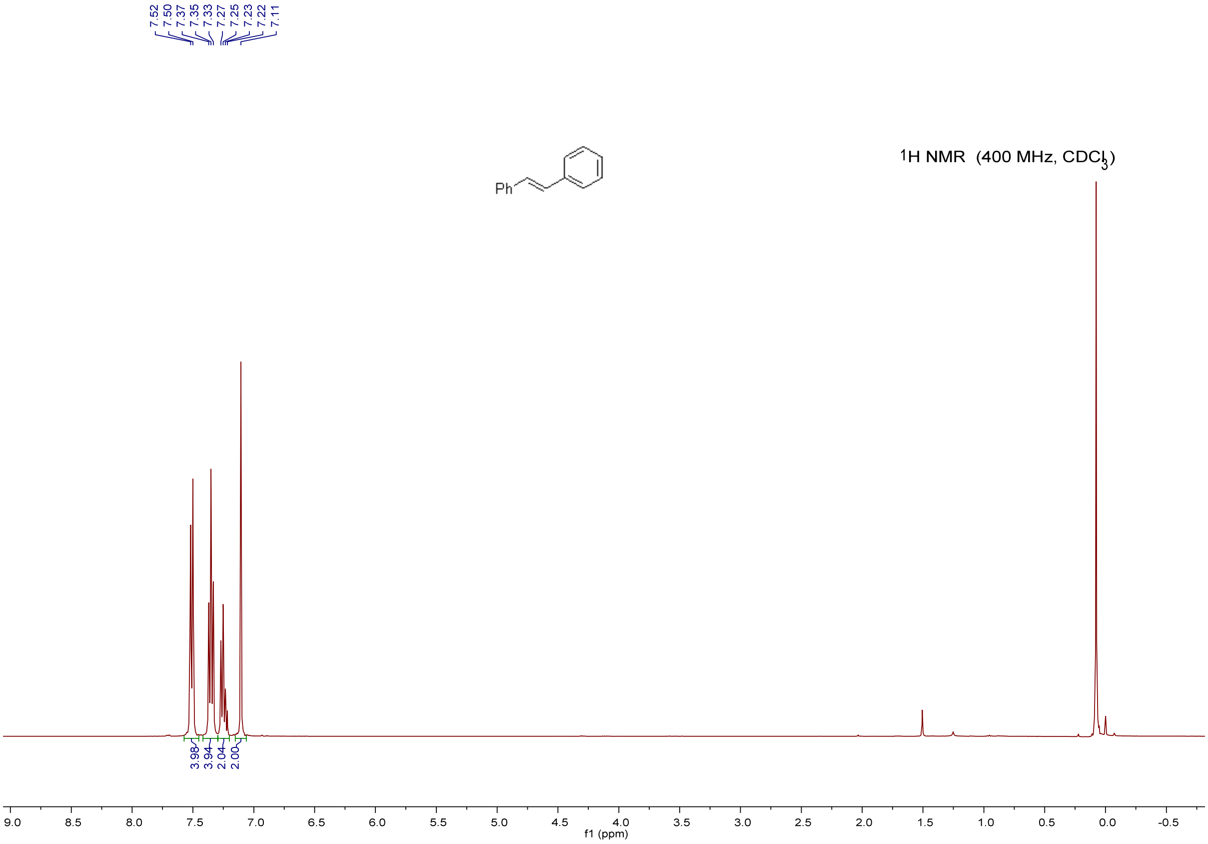
(4) 4-fluoro-1,1'-biphenyl (**2f**)

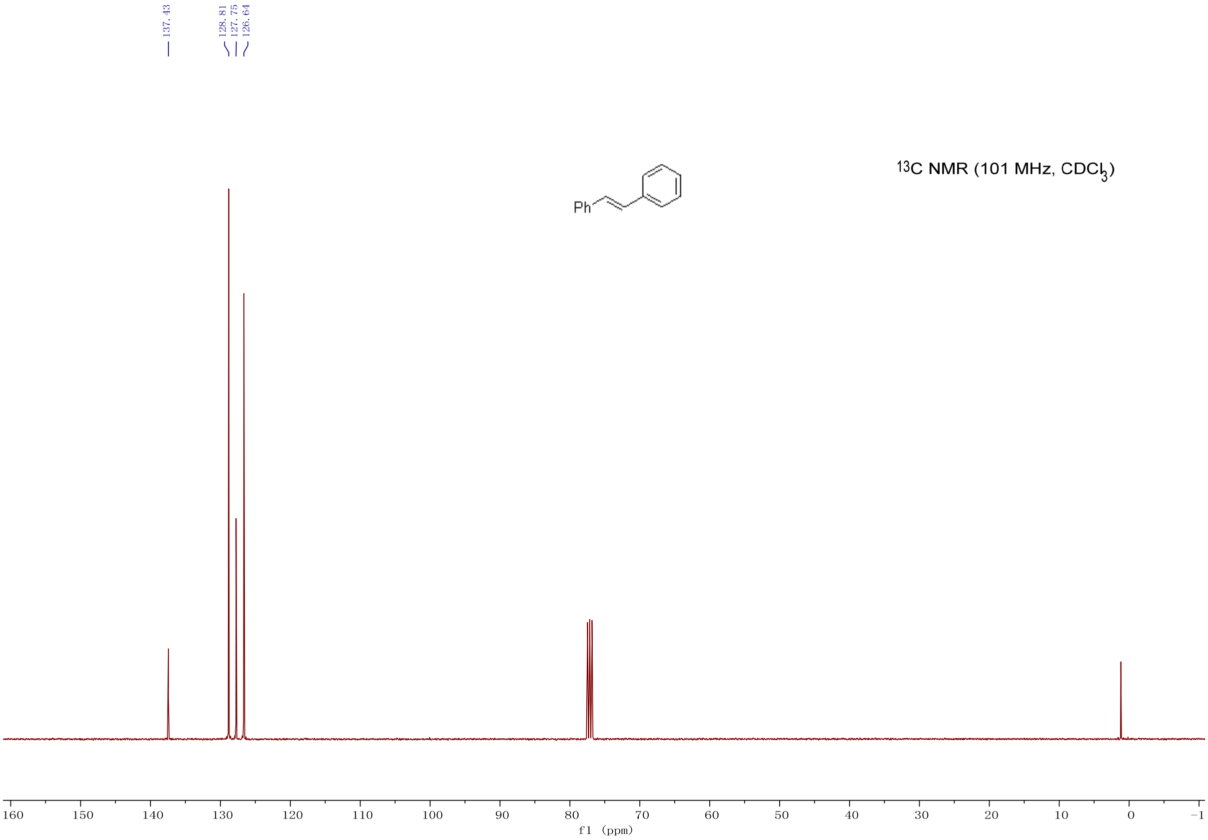




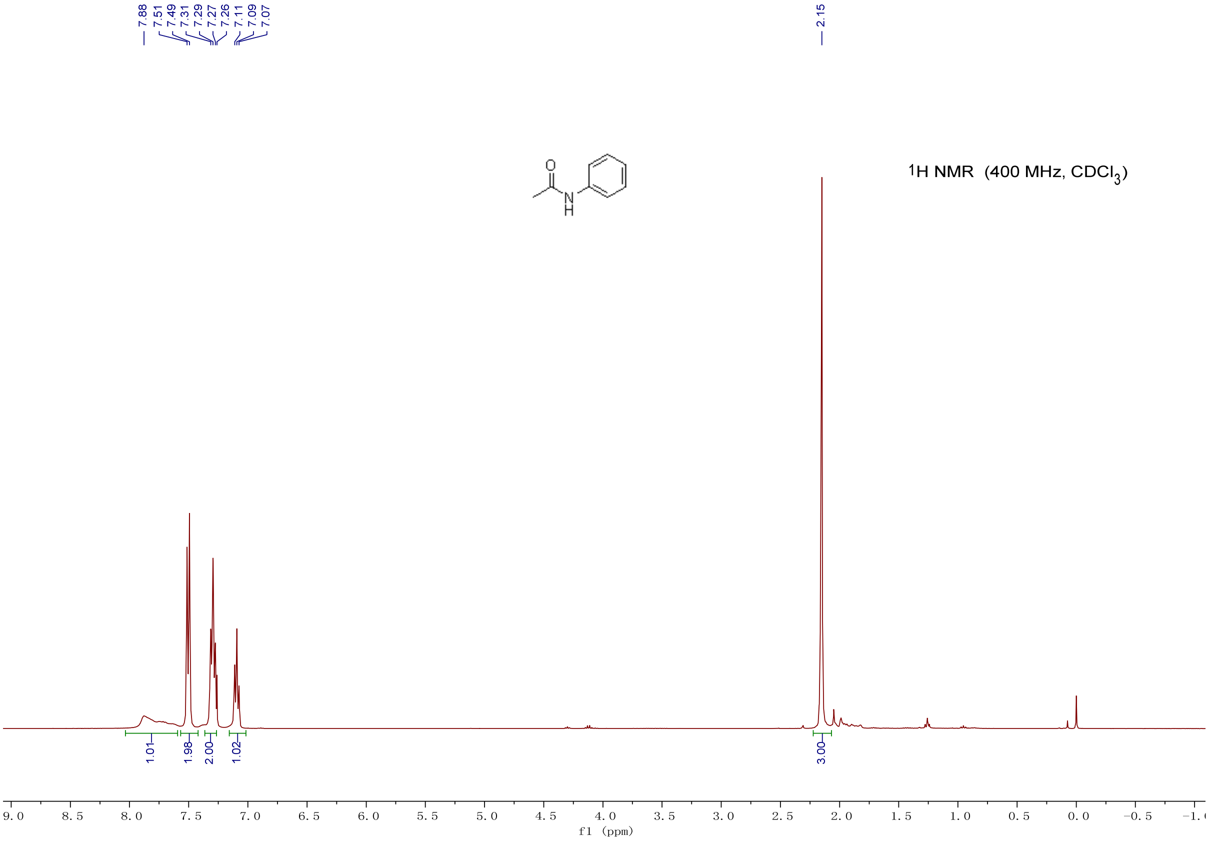

-115.85
F
^{19}F NMR (376 MHz, CDCl$_3$)
-114.1
-114.3
-114.5
-114.7
-114.9
-115.1
-115.3
-115.5
-115.7
-115.9
-116.1
-116.3
-116.5
-116.7
-116.9
-117.1
-117.3
-117.5
f1 (ppm)

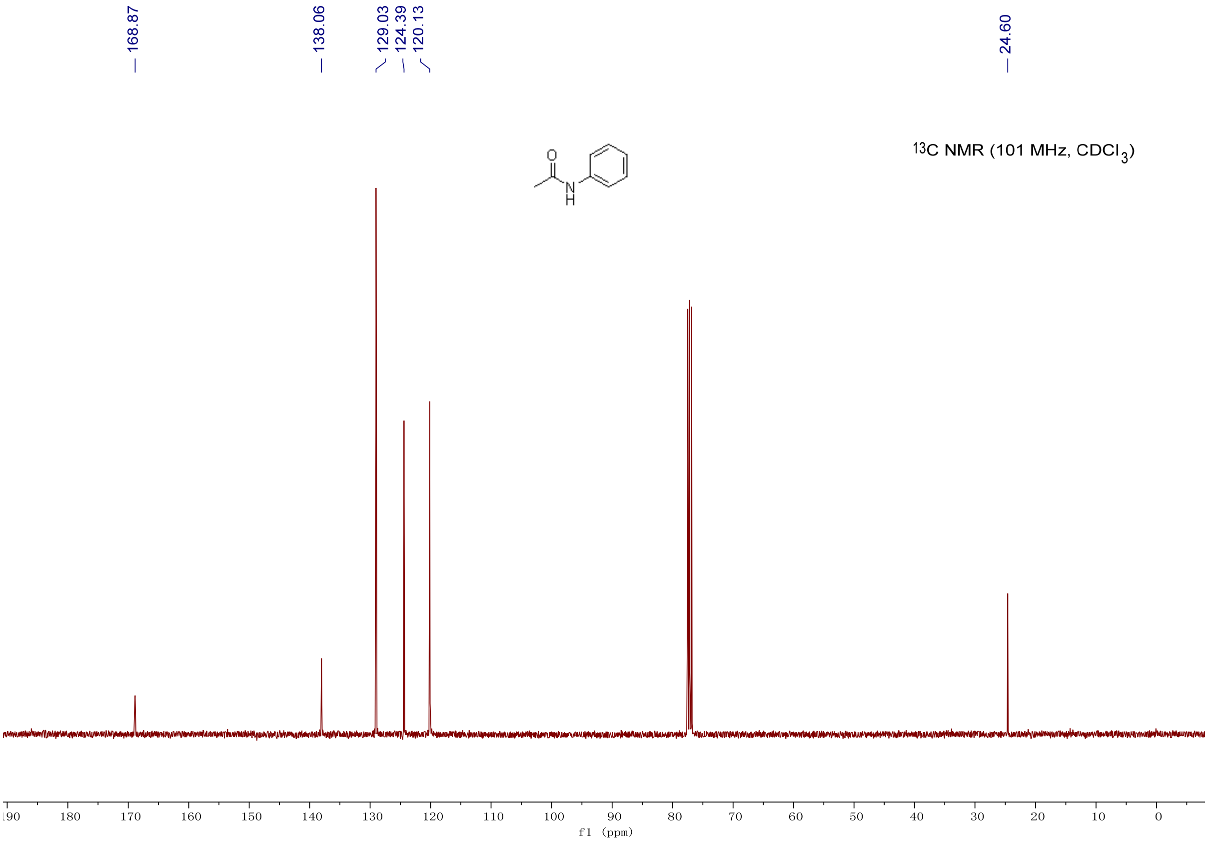
(5) (*E*)-1,2-diphenylethene (**2g**)



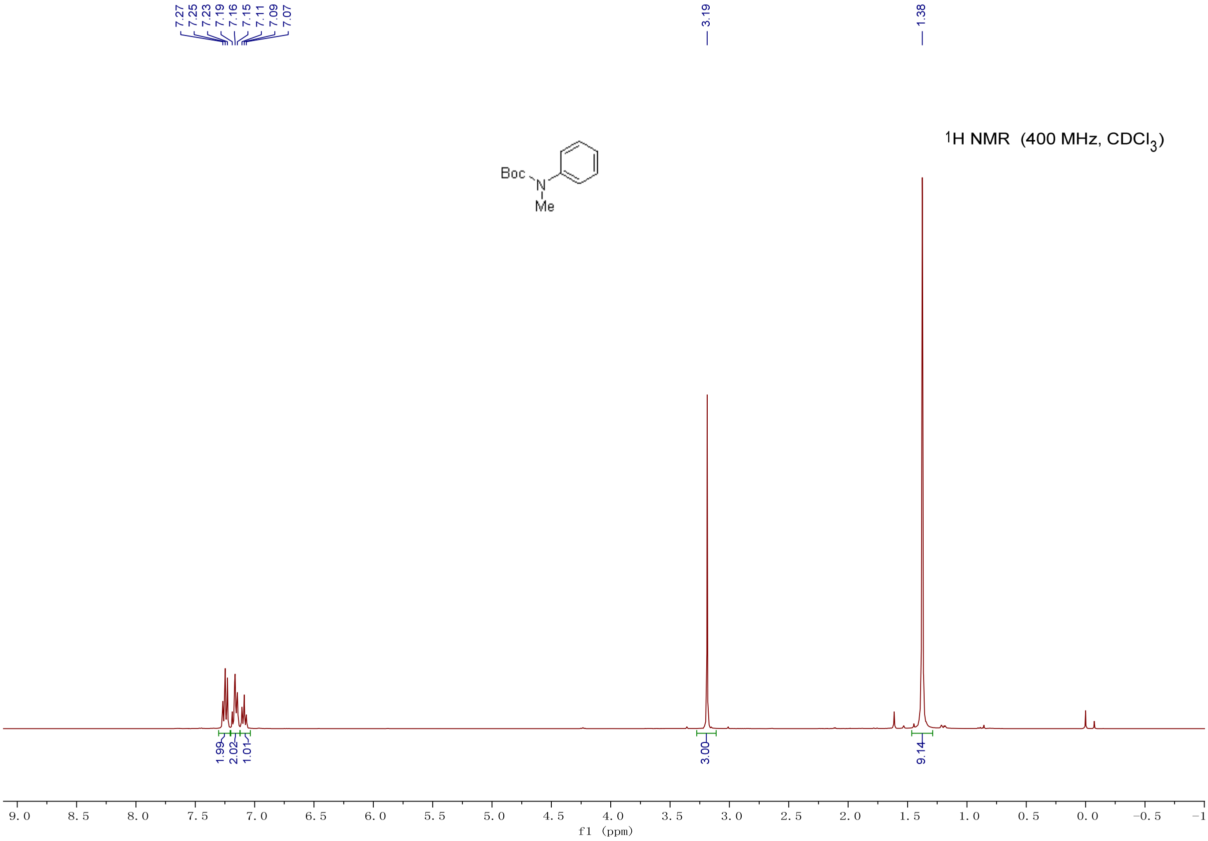


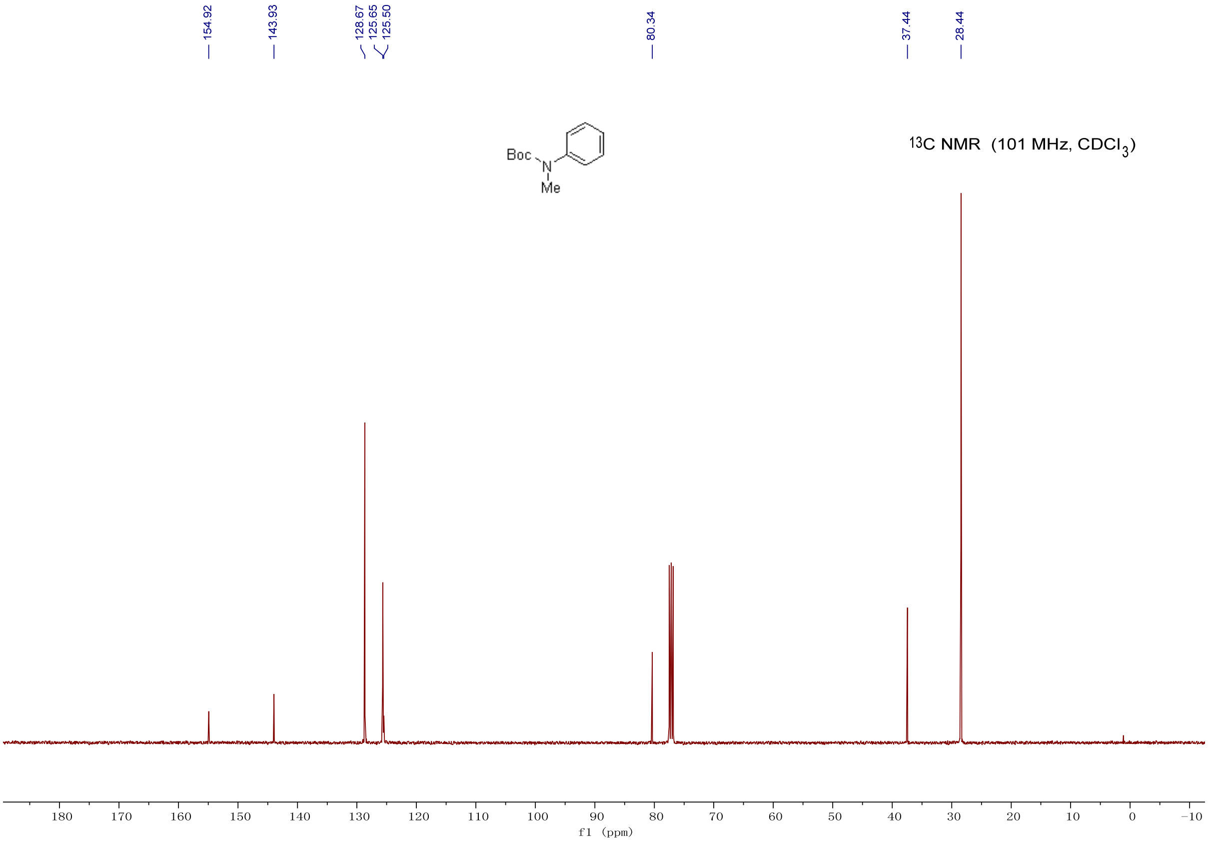
(6) *N*-phenylacetamide (**2h**)



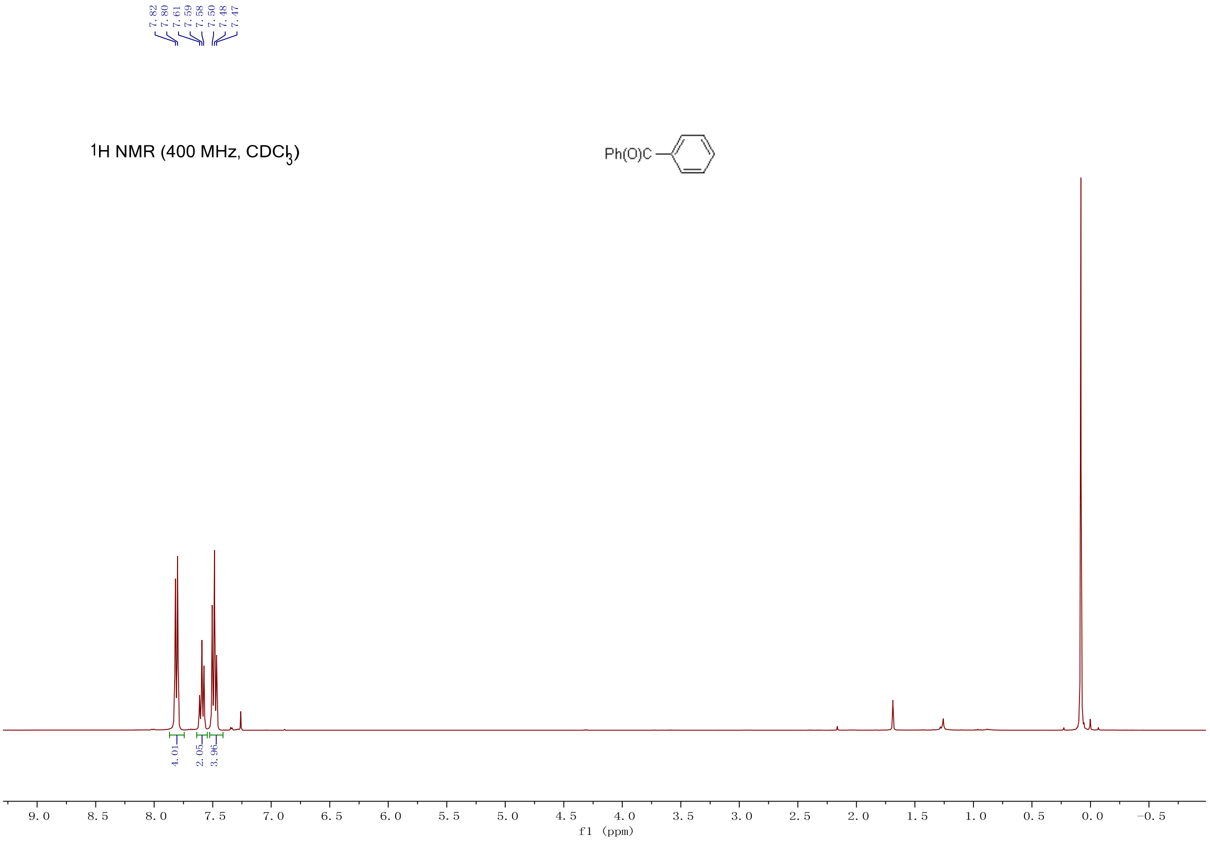


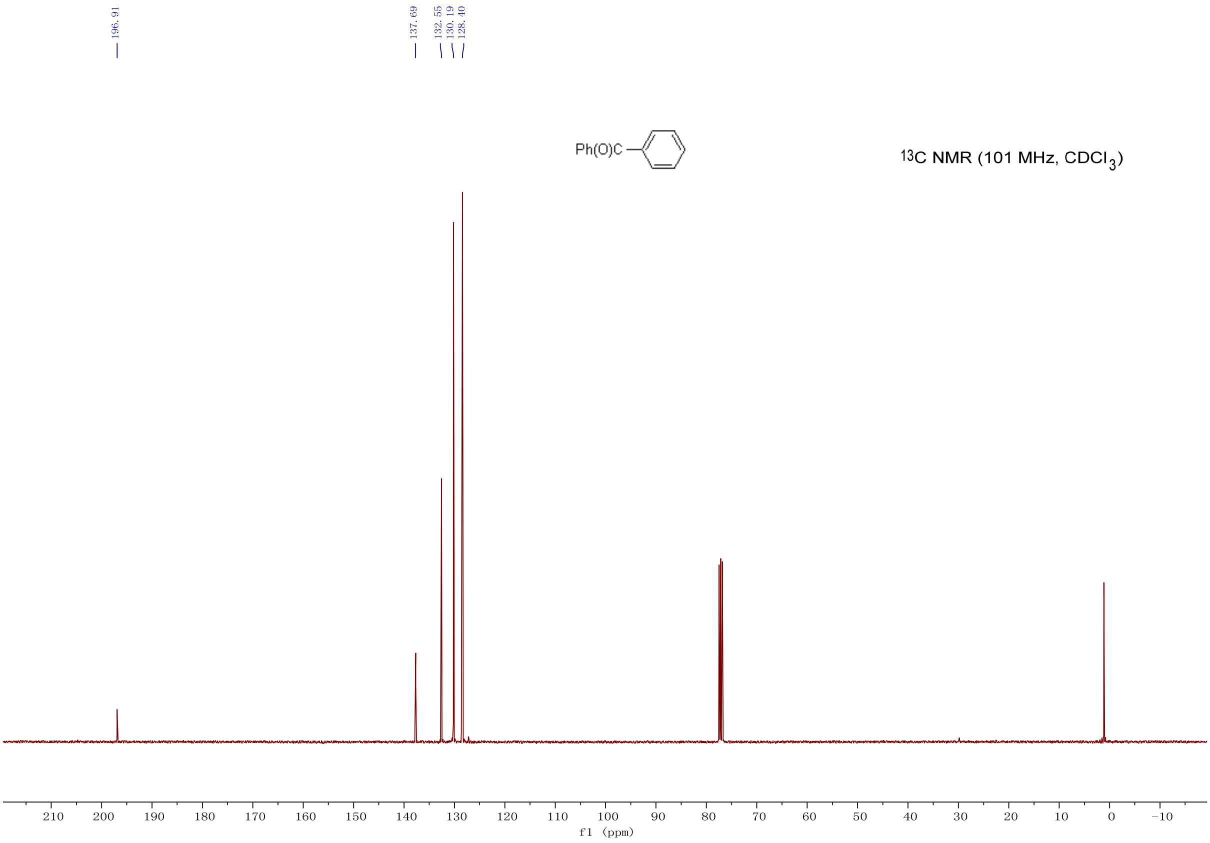
(7) *tert*-butyl methyl(phenyl)carbamate (**2i**)



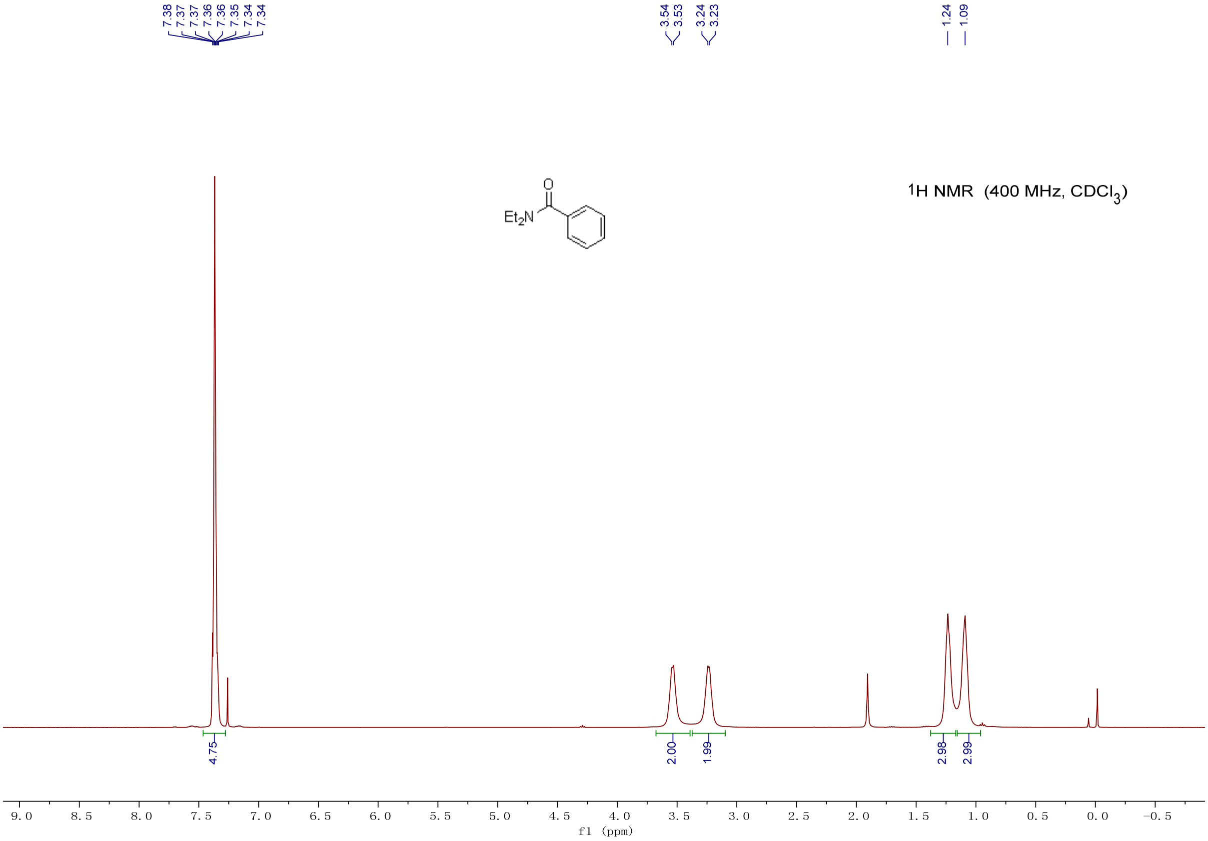


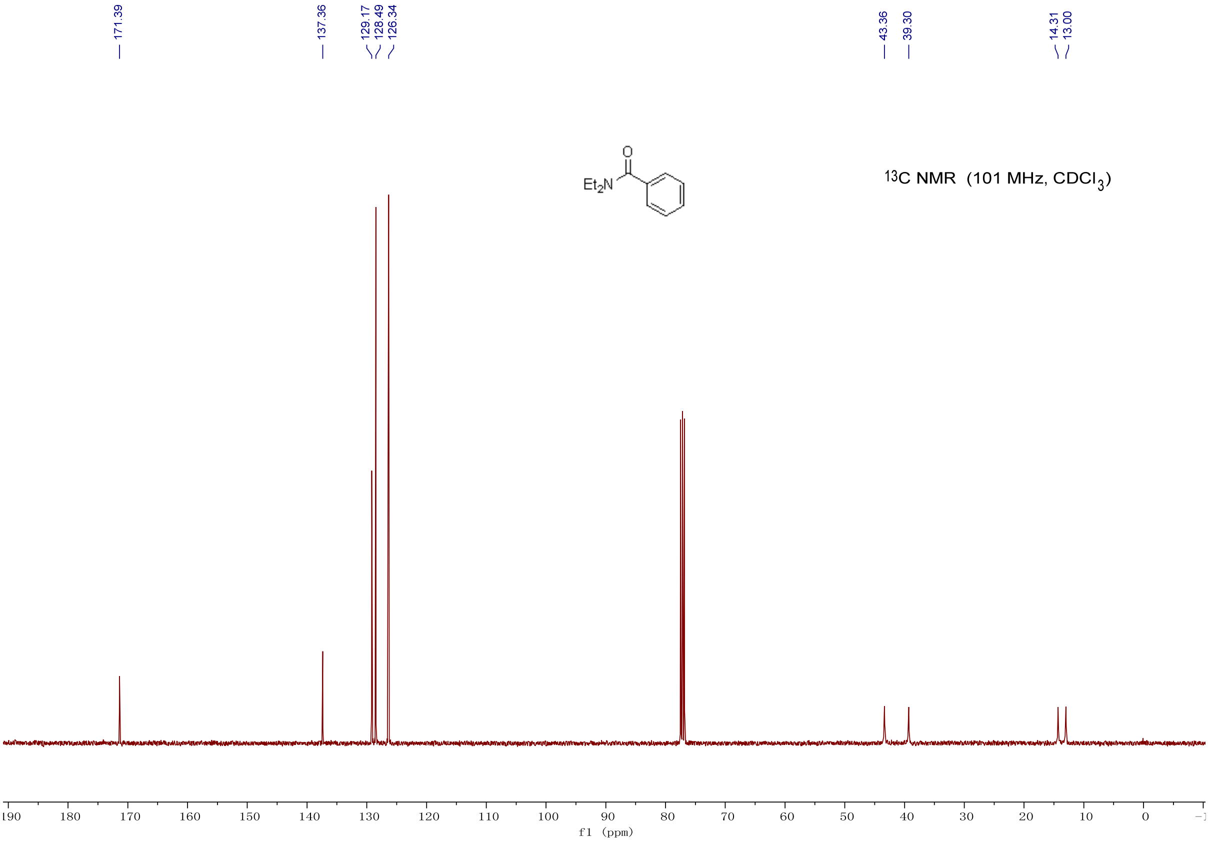
(8) benzophenone (**2k**)



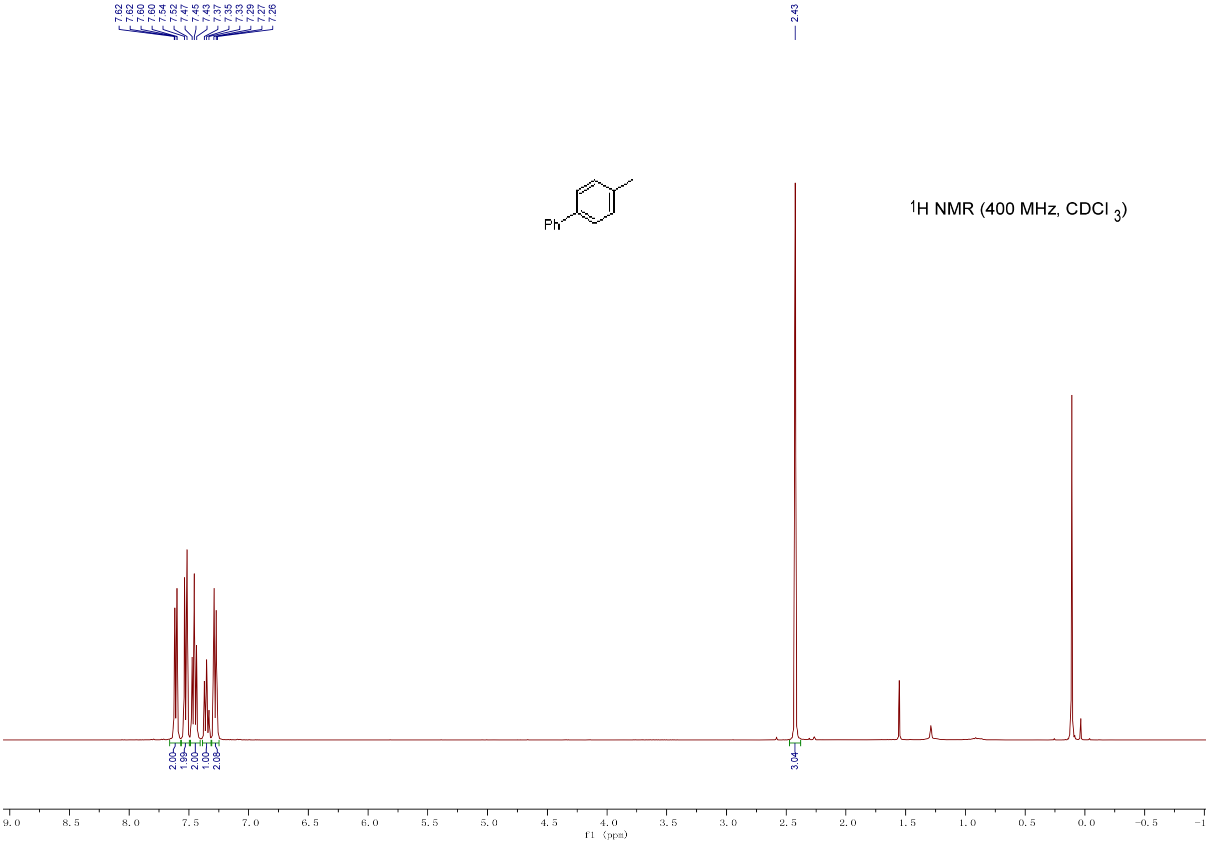


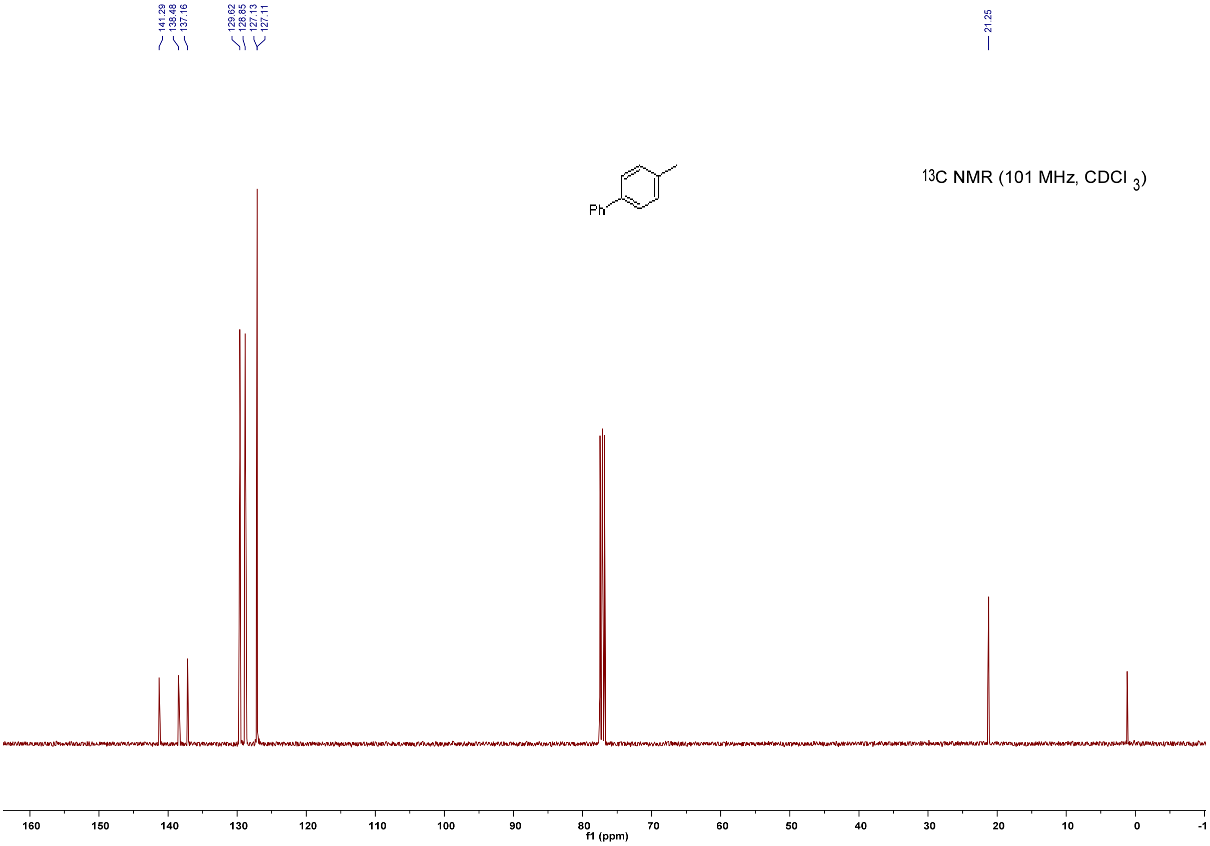
(9) *N*,*N*-diethylbenzamide (**2l**)



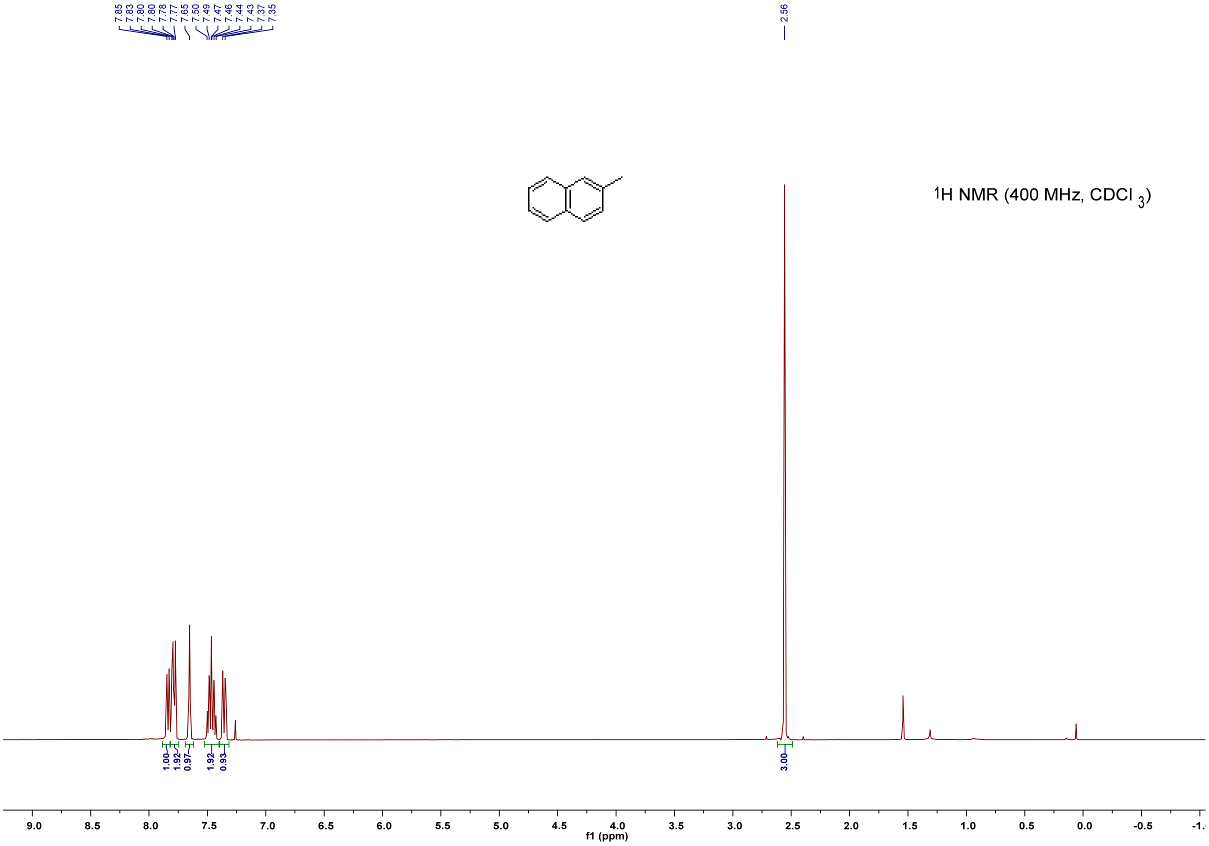


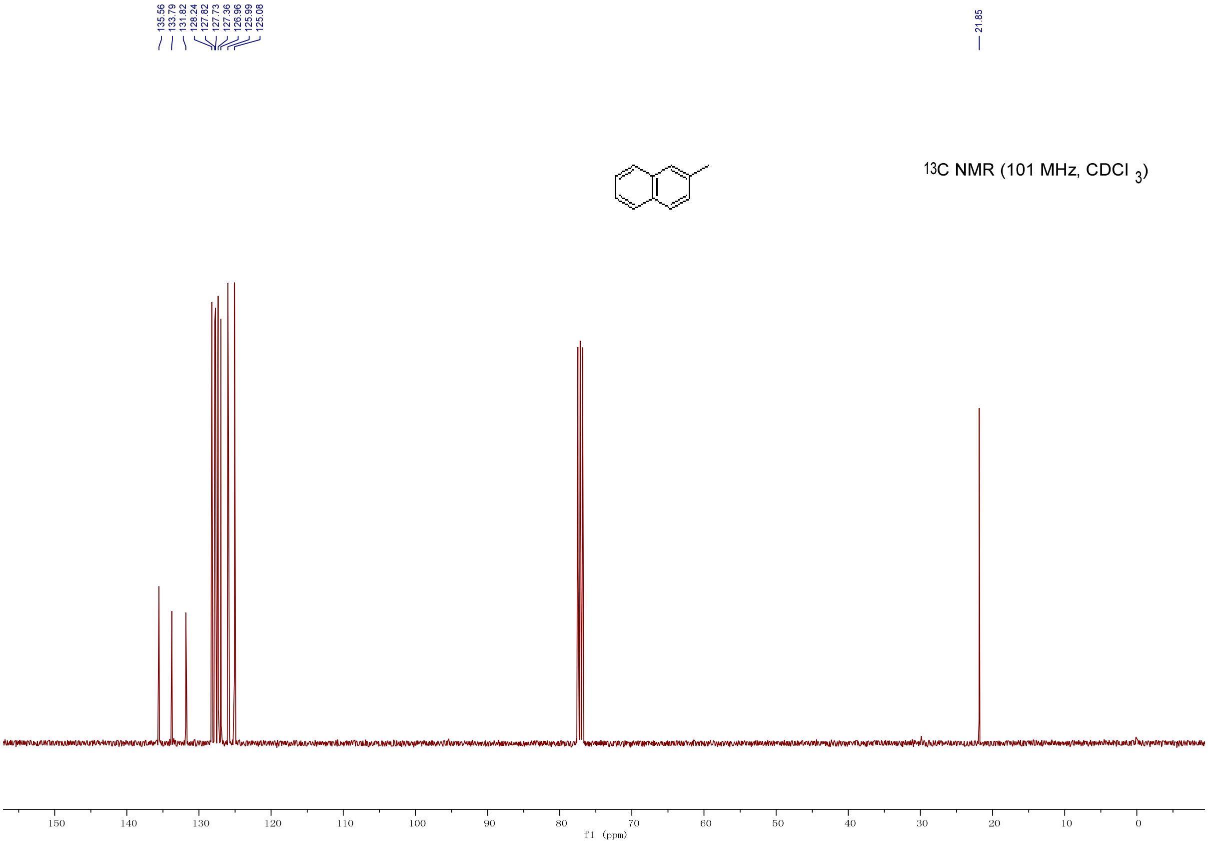
(10) 4-methyl-1,1'-biphenyl (**4a**)



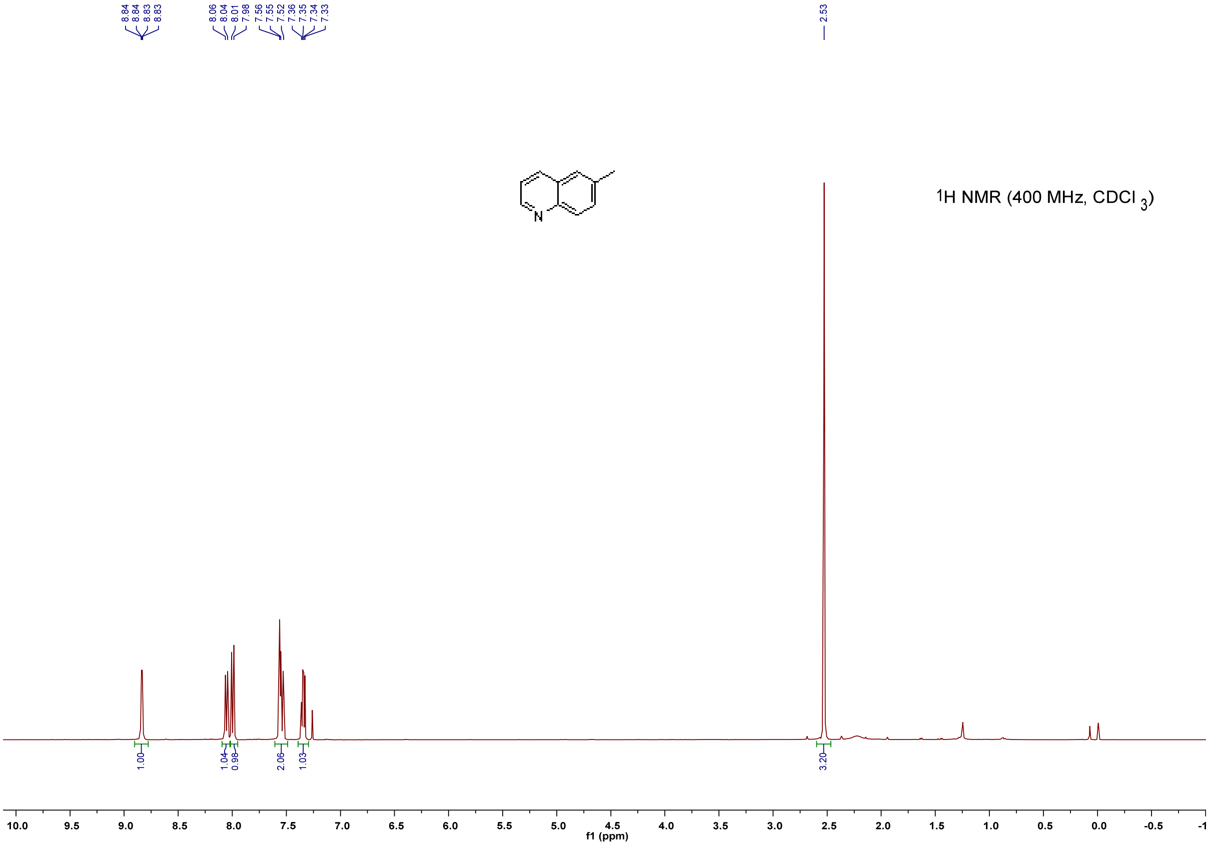


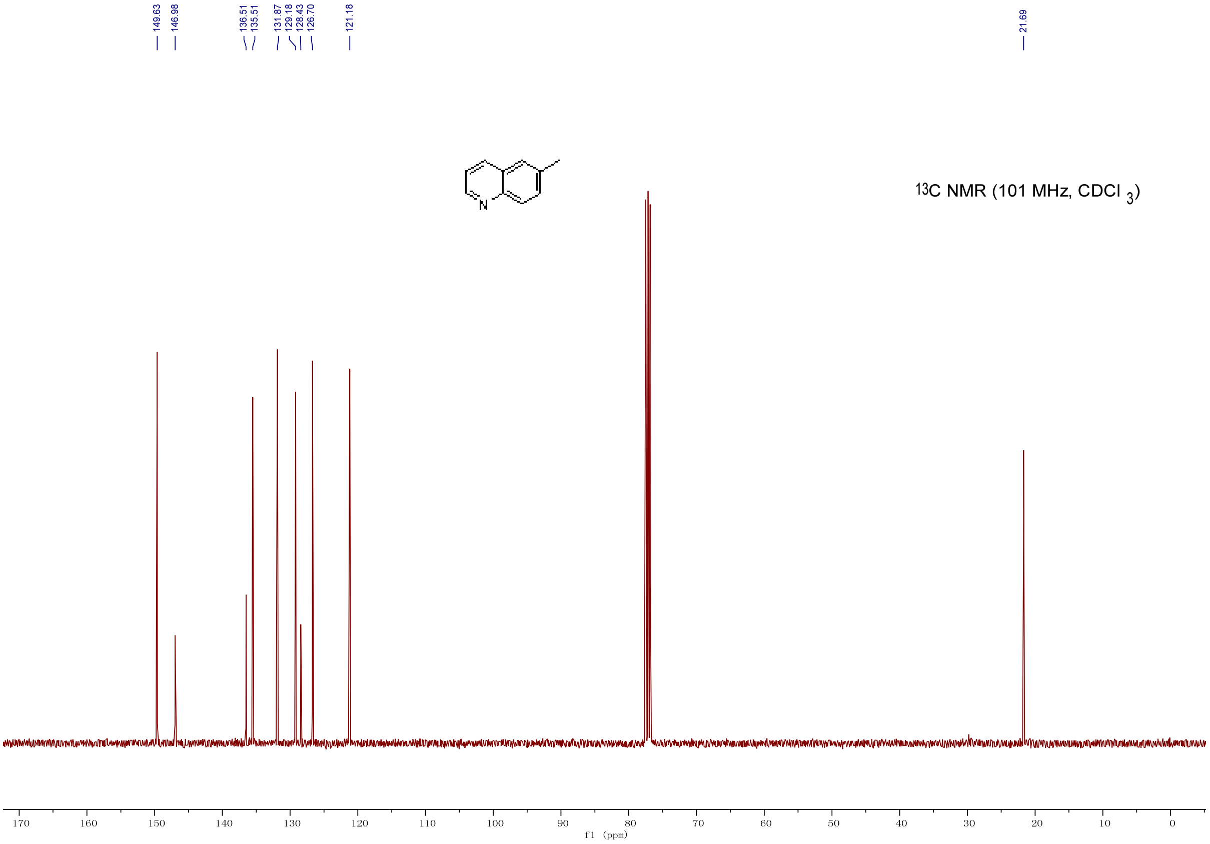
(11) 2-methylnaphthalene (**4d**)





(12) 6-methylquinoline (**4e**)





(13) diphenylmethane (**4f**)