Supporting Information

The synthesis of *meta*-arylphenol derivatives via acid-promoted rearrangement of cyclohexadienones

Hongyan Xie[a], Minxiang Zhang[a], Xueyu Fang, Zhaohua Yan*, Hua Yao*

[a] These authors made equal contributions to this work.

* To whom correspondence should be addressed. Email: yanzh@ncu.edu.cn; hyao@ncu.edu.cn

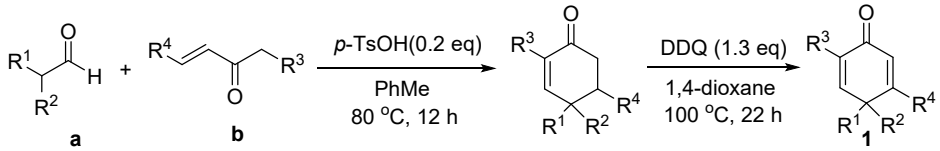
Contents

1 General Information

Unless otherwise stated, all reagents were commercially available and used without further purification. All reactions were performed in a double-necked flask. 400 MHz ^{1}H NMR and 101 MHz ^{13}C NMR spectra were measured on Agilent spectrometer, using $CDCl_3$, d_6-DMSO as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature and chemical shifts are expressed in δ ppm. HRMS spectra were recorded by Agilent 6545. Flash column chromatographic purification of products was accomplished by forced-flow chromatography on silica gel (300-400 mesh) using petroleum ether/ethyl acetate as eluent.

2 Experimental Section

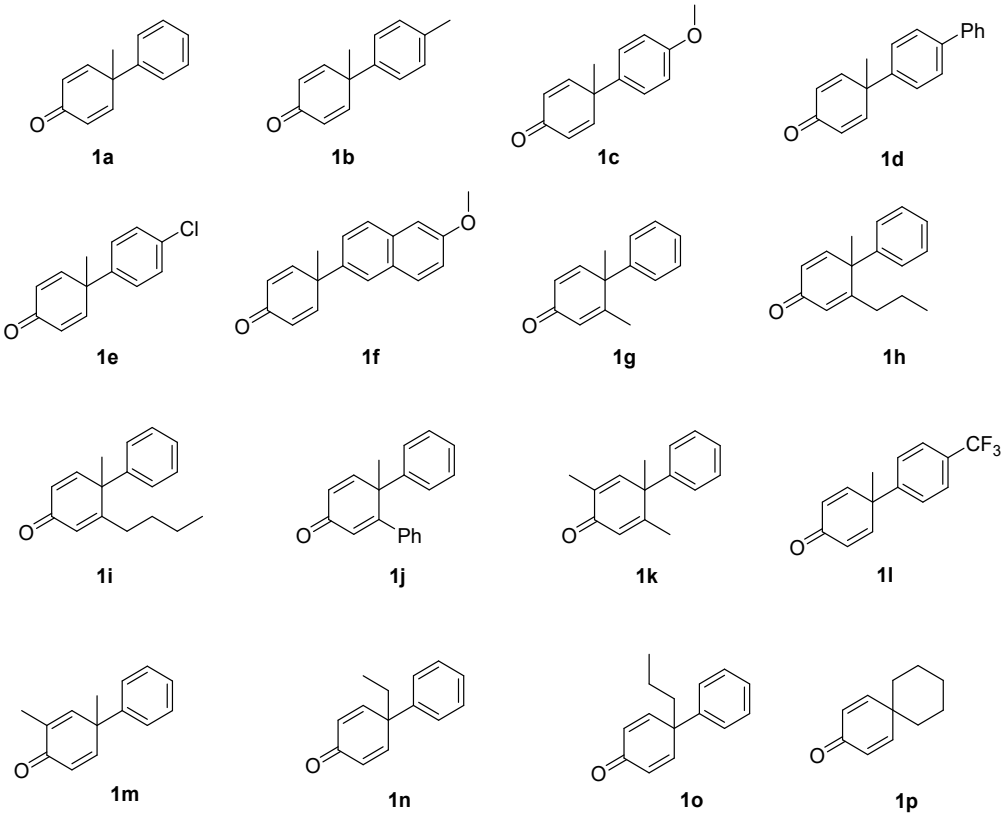
2.1 General procedure for the preparation of the starting materials

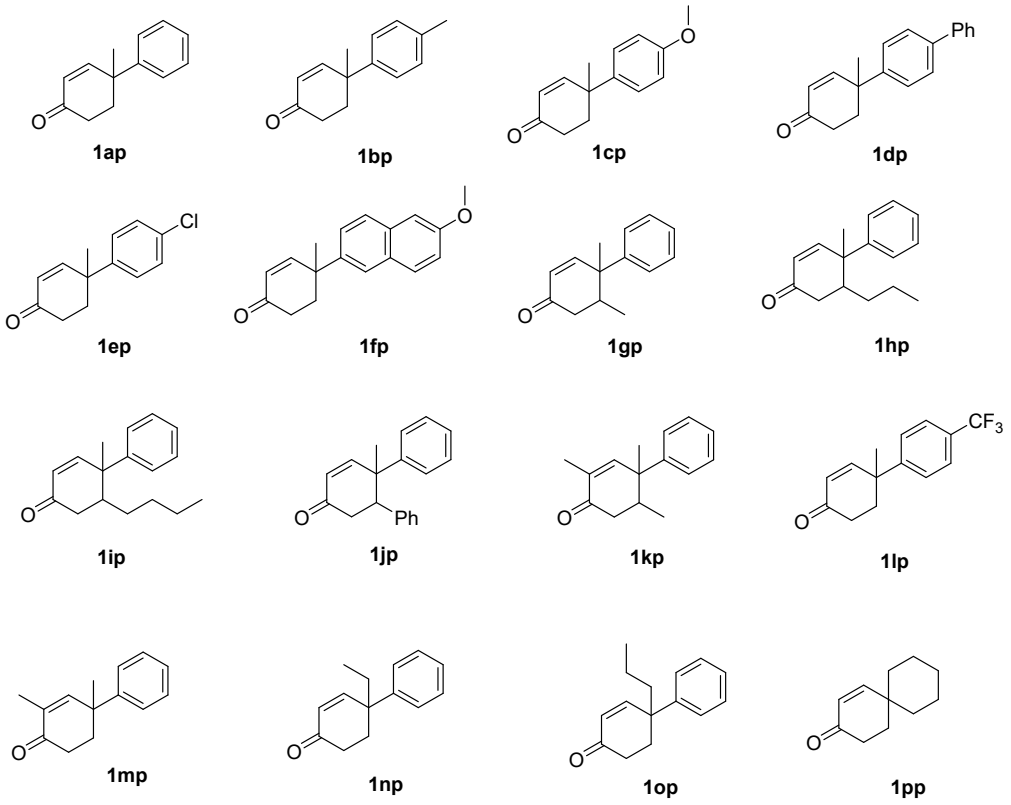


A solution of aldehyde (**a**, 20.0 mmol, 1.0 equiv) and alkyl vinylketone (**b**, 30.0 mmol, 1.5 equiv) in PhMe (15.0 mL) was cooled to 0°C, *p*-toluenesulfonic acid (4.0 mmol, 0.2 equiv) was added. The mixture was then heated in an oil bath at 80°C for 12 h. After cooled to room temperature, the reaction mixture was washed with 5% aqueous NaOH solution. The organic layer was dried over anhydrous Na_2SO_4. After filtration, the filtrate was evaporated in vacuo to afford the crude cyclohexanone which was further purified by flash column chromatography to furnish racemic cyclohexanone.

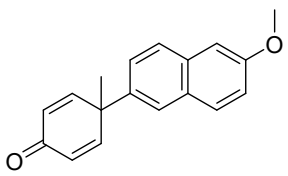
A solution of cyclohexenone (12.0 mmol, 1.0 equiv), DDQ (15.6 mmol, 1.3 equiv) in 1,4-dioxane (20.0 mL) was heated at 100°C and stirred for 22 h. The reaction mixture was then cooled down to room temperature and filtered through Celite®. The filtrates were diluted with ethyl acetate, washed with 5% aqueous NaOH solution, and water sequentially. The organic layer was dried over anhydrous Na_2SO_4, and filtered through Celite®. The volatiles were removed in vacuo to afford crude product which was further purified by flash column chromatography to furnish cyclohexadienone **(1)**.

The substrates of various 4,4-disubstituted cyclohexadienones **(1a-1e and 1l; 1ap-1ep and 1lp)**[1, 2]**; (1g, 1m-1p; 1gp, 1mp-1pp)**[3]**; (1ip and 1jp)**[4] were prepared following the previous literature procedures and obtained. The characterization data of substrates and intermediates were in alignment with the literature reported ones.





4-(6-methoxynaphthalen-2-yl)-4-methylcyclohexa-2,5-dien-1-one (1f)



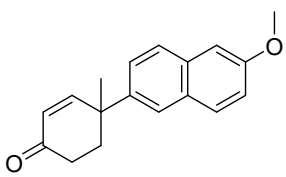
Isolated yield 86%. White solid, mp 110.1-110.3°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (t, *J* = 7.1 Hz, 3H), 7.29 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.15 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.09 (d, *J* = 2.3 Hz, 1H), 6.94 (d, *J* = 9.7 Hz, 2H), 6.30 (d, *J* = 9.7 Hz, 2H), 3.88 (s, 3H), 1.75 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 185.99, 158.05, 155.59, 134.69, 133.74, 129.40, 128.95, 127.48, 127.06, 125.09, 124.66, 119.32, 105.51, 55.31, 44.98, 23.75.

HRMS (ESI-TOF) m/z Calcd for $C_{18}H_{16}O_2$ $[M+Na]^+$: 287.1043, found: 287.1052.

4-(6-methoxynaphthalen-2-yl)-4-methylcyclohex-2-en-1-one (1fp)



Isolated yield 75%. White solid, mp 91.5-91.7°C.

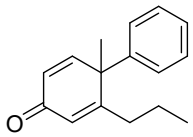
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.61 (m, 3H), 7.43 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.22 – 7.10 (m, 2H), 6.97 (dd, *J* = 10.2, 1.2 Hz, 1H), 6.17 (d, *J* = 10.2 Hz, 1H), 3.88 (s, 3H), 2.45 – 2.23 (m, 3H), 2.21 – 2.08 (m, 1H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.48, 157.80, 157.22, 140.13, 133.29, 129.41, 128.60,

127.40, 124.82, 124.71, 119.14, 105.50, 55.30, 40.55, 37.82, 34.66, 27.66.

HRMS (ESI-TOF) m/z Calcd for $C_{18}H_{18}O_2$ $[M+Na]^+$: 289.1207, found: 289.1205.

1-methyl-2-propyl-[1,1'-biphenyl]-4(1H)-one (1h)



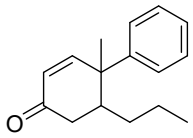
Isolated yield 86%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.7 Hz, 2H), 7.25 – 7.20 (m, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.76 – 6.70 (m, 1H), 6.24 (s, 1H), 6.18 (d, *J* = 9.9 Hz, 1H), 2.07 – 1.97 (m, 1H), 1.81 – 1.70 (m, 1H), 1.63 (s, 3H), 1.49 – 1.40 (m, 1H), 1.37 – 1.27 (m, 1H), 0.84 – 0.69 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.88, 167.88, 156.49, 139.49, 128.82, 127.43, 126.67, 125.28, 125.21, 48.04, 33.92, 22.22, 20.39, 13.72.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{18}O$ $[M+Na]^+$: 249.1255, found: 249.1258.

1-methyl-2-propyl-2,3-dihydro-[1,1'-biphenyl]-4(1H)-one (1hp)



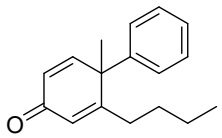
Isolated yield 78%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, *J* = 7.5 Hz, 2H), 7.25 (dd, *J* = 17.5, 7.4 Hz, 3H), 6.76 (d, *J* = 10.1 Hz, 1H), 6.04 (d, *J* = 10.1 Hz, 1H), 2.57 (d, *J* = 13.6 Hz, 1H), 2.32 – 2.16 (m, 2H), 1.43 (s, 3H), 1.29 (dt, *J* = 14.2, 6.9 Hz, 1H), 1.14 (q, *J* = 6.5, 5.1 Hz, 2H), 0.94 (dt, *J* = 13.1, 7.4 Hz, 1H), 0.69 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.87, 159.45, 146.21, 128.34, 127.07, 126.90, 126.68, 45.18, 44.36, 39.56, 31.82, 20.05, 16.92, 13.89.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{20}O$ $[M+Na]^+$: 251.1406, found: 251.1404.

2-butyl-1-methyl-[1,1'-biphenyl]-4(1H)-one (1i)



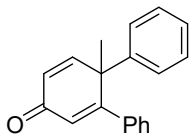
Isolated yield 84%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (t, *J* = 7.3 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.67 (d, *J* = 9.8 Hz, 1H), 6.20 (s, 1H), 6.12 (d, *J* = 9.9 Hz, 1H), 2.00 (ddd, *J* = 16.0, 9.6, 5.7 Hz, 1H), 1.74 (ddd, *J* = 16.4, 9.8, 5.8 Hz, 1H), 1.59 (s, 3H), 1.29 (dtt, *J* = 53.7, 14.8, 6.5 Hz, 2H), 1.16 – 0.97 (m, 2H), 0.70 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 186.74, 168.02, 156.38, 139.48, 128.79, 127.40, 126.65, 125.26, 125.22, 48.06, 31.50, 29.38, 22.18, 13.72.

HRMS (ESI-TOF) m/z Calcd for $C_{17}H_{20}O$ $[M+Na]^+$: 263.1412, found: 263.1416.

1'-methyl-[1,1':2',1''-terphenyl]-4'(1'H)-one (1j)



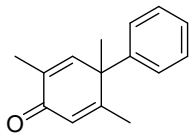
Isolated yield 84%. Yellow solid, mp 94.9-95.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.28 (m, 5H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 2H), 6.81 (d, *J* = 9.7 Hz, 1H), 6.75 (d, *J* = 7.6 Hz, 2H), 6.45 (d, *J* = 1.1 Hz, 1H), 6.27 (dd, *J* = 9.9, 1.3 Hz, 1H), 1.59 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.07, 164.68, 156.83, 138.50, 138.46, 129.06, 128.69, 128.28, 128.01, 127.90, 127.75, 127.17, 124.76, 47.62, 22.59.

HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{16}O$ $[M+Na]^+$: 283.1093, found: 283.1098.

1,2,5-trimethyl-[1,1'-biphenyl]-4(1H)-one (1k)



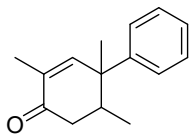
Isolated yield 84%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.27 – 7.21 (m, 1H), 7.18 (dd, *J* = 7.0, 1.5 Hz, 2H), 6.55 (d, *J* = 1.4 Hz, 1H), 6.19 (d, *J* = 1.3 Hz, 1H), 1.88 (d, *J* = 1.3 Hz, 3H), 1.70 (d, *J* = 1.2 Hz, 3H), 1.62 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 187.37, 163.63, 152.06, 140.42, 131.62, 128.82, 127.23, 126.97, 126.48, 47.82, 22.40, 19.69, 15.40.

HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{16}O$ $[M+Na]^+$: 235.1099, found: 235.1102.

1,2,5-trimethyl-2,3-dihydro-[1,1'-biphenyl]-4(1H)-one (1kp)



Isolated yield 80%. Yellow solid, mp 79.7-79.9°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.23 (m, 4H), 7.20 (dd, *J* = 7.7, 5.5 Hz, 1H), 6.53 (dt, *J* = 2.7, 1.4 Hz, 1H), 2.55 – 2.20 (m, 3H), 1.87 – 1.72 (m, 3H), 1.38 (d, *J* = 2.4 Hz, 3H), 0.87 – 0.68 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 199.70, 154.21, 146.92, 133.28, 128.26, 126.77, 126.50, 44.37, 42.50, 40.76, 17.18, 15.77, 15.69.

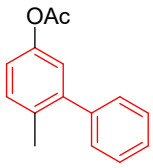
HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{18}O$ $[M+Na]^+$: 237.1250, found: 237.1252.

2.2 General procedure for acid-promoted rearrangement of cyclohexadienones

To a 50-mL round flask was added substrate **1** (0.5 mmol), 37% HCl (3.0 mmol, 6.0 equiv.), and Ac_2O (3.0 mL), and the reaction was stirred for 6 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (10 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was further purified through flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 20/1-10/1, v/v) to afford target compounds **2**.

The procedure for the gram-scale reaction of **1a** is similar to the above general procedure.

6-methyl-[1,1'-biphenyl]-3-yl acetate (2a)



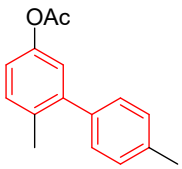
Isolated yield 90%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.43 (m, 2H), 7.41 – 7.36 (m, 3H), 7.31 (d, J = 9.2 Hz, 1H), 7.09 – 7.02 (m, 2H), 2.32 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.59, 148.64, 143.04, 141.10, 132.97, 131.20, 129.12, 128.20, 127.15, 122.71, 120.29, 21.08, 19.93.

HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{14}O_2$ $[M+Na]^+$: 249.0886, found: 249.0877.

4',6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2b)



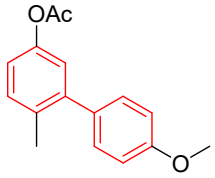
Isolated yield 92%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.8 Hz, 1H), 7.28 (s, 4H), 7.03 (d, *J* = 6.5 Hz, 2H), 2.45 (s, 3H), 2.33 (d, *J* = 0.7 Hz, 3H), 2.32 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.79, 148.57, 143.01, 138.14, 136.79, 133.09, 131.21, 129.03, 128.92, 122.74, 120.12, 21.25, 21.16, 20.06.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{16}O_2$ $[M+Na]^+$: 263.1043, found: 263.1044.

4'-methoxy-6-methyl-[1,1'-biphenyl]-3-yl acetate (2c)



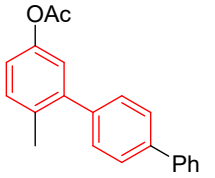
Isolated yield 94%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 3H), 7.03 – 6.92 (m, 4H), 3.85 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.64, 158.75, 148.55, 142.65, 133.45, 133.08, 131.11, 130.18, 122.69, 119.91, 113.56, 55.25, 21.07, 19.97.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{16}O_3$ $[M+Na]^+$: 279.0992, found: 279.0998.

6-methyl-[1,1':4',1''-terphenyl]-3-yl acetate (2d)

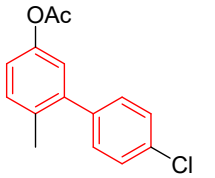


Isolated yield 88%. White solid, mp 79.5-79.9°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.3 Hz, 4H), 7.47 (t, J = 7.6 Hz, 2H), 7.39 (dd, J = 10.6, 8.4 Hz, 3H), 7.32 – 7.24 (m, 1H), 7.01 (d, J = 7.6 Hz, 2H), 2.31 (s, 3H), 2.31 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.77, 148.53, 142.54, 140.70, 139.96, 139.90, 133.09, 131.27, 129.54, 128.82, 127.36, 127.08, 126.85, 122.66, 120.30, 21.16, 20.04. HRMS (ESI-TOF) m/z Calcd for $C_{21}H_{18}O_2$ $[M+Na]^+$: 325.1199, found: 325.1207.

4'-chloro-6-methyl-[1,1'-biphenyl]-3-yl acetate (2e)



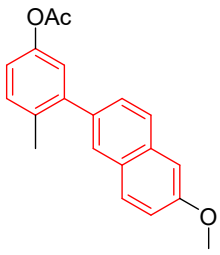
Isolated yield 82%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.4 Hz, 2H), 7.26 (t, J = 6.4 Hz, 3H), 7.00 (d, J = 6.4 Hz, 1H), 6.94 (s, 1H), 2.29 (s, 3H), 2.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.62, 148.57, 141.67, 139.40, 133.17, 132.90, 131.30, 130.41, 128.35, 122.53, 120.58, 21.08, 19.83.

HRMS (ESI-TOF) m/z Calcd for $C_{15}H_{13}ClO_2$ $[M+Na]^+$: 283.0498, found: 283.0496.

3-(6-methoxynaphthalen-2-yl)-4-methylphenyl acetate (2f)



Isolated yield 88%. White solid, mp 89.3-89.6°C.

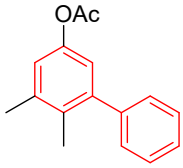
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, J = 17.6, 8.7 Hz, 3H), 7.47 (d, J = 8.4 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.22 (d, J = 10.3 Hz, 2H), 7.11 (s, 1H), 7.06 (d, J = 8.2 Hz, 1H), 3.96 (s, 3H), 2.33 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.73, 157.88, 148.63, 143.04, 136.36, 133.57, 133.26,

131.24, 129.57, 128.75, 127.94, 127.71, 126.50, 122.92, 120.22, 119.16, 105.65, 55.34, 21.13, 20.04.

HRMS (ESI-TOF) m/z Calcd for $C_{20}H_{18}O_3$ $[M+Na]^+$: 329.1148, found: 329.1158.

5,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2g)



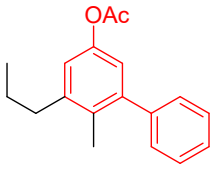
Isolated yield 86%. White solid, mp 64.7-65.0°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 9.0 Hz, 3H), 6.99 (s, 1H), 6.92 (s, 1H), 2.40 (s, 3H), 2.32 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.71, 147.99, 143.32, 141.77, 138.60, 131.72, 129.33, 128.12, 126.99, 121.81, 120.46, 21.08, 20.87, 16.61.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{16}O_2$ $[M+Na]^+$: 263.1043, found: 263.1038.

6-methyl-5-propyl-[1,1'-biphenyl]-3-yl acetate (2h)



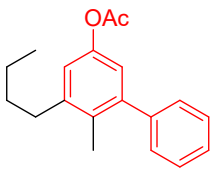
Isolated yield 85%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (t, J = 7.4 Hz, 2H), 7.37 – 7.29 (m, 3H), 6.92 (d, J = 2.1 Hz, 1H), 6.84 (d, J = 2.1 Hz, 1H), 2.74 – 2.59 (m, 2H), 2.29 (s, 3H), 2.17 (s, 3H), 1.68 (h, J = 7.4 Hz, 2H), 1.05 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.72, 148.00, 143.59, 142.85, 141.91, 131.06, 129.30, 128.02, 126.87, 120.78, 120.38, 36.12, 23.13, 21.11, 16.11, 14.22.

HRMS (ESI-TOF) m/z Calcd for $C_{18}H_{20}O_2$ $[M+Na]^+$: 291.1356, found: 291.1366.

5-butyl-6-methyl-[1,1'-biphenyl]-3-yl acetate (2i)



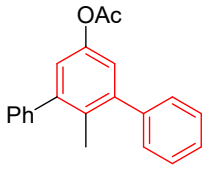
Isolated yield 82%. Yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.34 (t, J = 6.3 Hz, 3H), 6.95 (s, 1H), 6.87 (s, 1H), 2.77 – 2.65 (m, 2H), 2.30 (s, 3H), 2.19 (s, 3H), 1.66 (p, J = 7.6 Hz, 2H), 1.49 (h, J = 7.3 Hz, 2H), 1.02 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.72, 148.06, 143.62, 143.08, 141.94, 131.02, 129.32, 128.04, 126.90, 120.76, 120.38, 33.79, 32.24, 22.83, 21.12, 16.12, 14.06.

HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{22}O_2$ $[M+Na]^+$: 305.1620, found: 305.1625.

2'-methyl-[1,1':3',1''-terphenyl]-5'-yl acetate (2j)



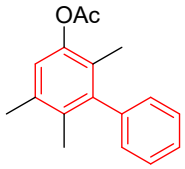
Isolated yield 85%. White solid, mp 126.8-127.2°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 4H), 7.41 – 7.33 (m, 6H), 7.01 (s, 2H), 2.30 (s, 3H), 2.11 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.62, 147.91, 143.96, 141.59, 130.71, 129.27, 128.15, 127.11, 121.87, 21.10, 18.28.

HRMS (ESI-TOF) m/z Calcd for $C_{21}H_{18}O_2$ $[M+Na]^+$: 325.1199, found: 325.1209.

2,5,6-trimethyl-[1,1'-biphenyl]-3-yl acetate (2k)



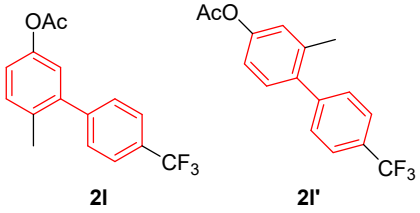
Isolated yield 82%. White solid, mp 75.2-75.8°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (t, J = 7.4 Hz, 2H), 7.38 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 7.4 Hz, 2H), 6.92 (s, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 1.96 (s, 3H), 1.86 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.67, 146.90, 143.32, 141.15, 135.08, 132.60, 129.21, 128.46, 126.80, 125.63, 121.99, 20.86, 20.45, 17.19, 14.03.

HRMS (ESI-TOF) m/z Calcd for $C_{17}H_{18}O_2$ $[M+Na]^+$: 277.1199, found: 277.1210.

6-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl acetate (2l) and 2-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl acetate (2l')



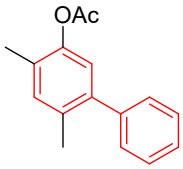
Isolated yield 80%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 4H), 7.43 (t, J = 7.1 Hz, 4H), 7.29 (d, J = 8.2 Hz, 1H), 7.21 (d, J = 9.1 Hz, 1H), 7.06 – 7.01 (m, 2H), 7.01 – 6.93 (m, 2H), 2.32 (d, J = 1.6 Hz, 3H, minor), 2.29 (d, J = 1.6 Hz, 3H, major), 2.25 (s, 3H, minor), 2.23 (s, 3H, major).

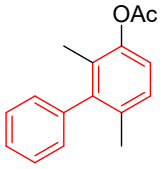
^{13}C NMR (101 MHz, $CDCl_3$) major regioisomer δ 169.62, 148.61, 144.75, 144.61, 136.90, 132.83, 131.41, 129.43, 125.14, 125.10, 125.07, 123.35, 120.96, 21.05, 19.74. minor regioisomer δ 169.60, 150.18, 141.44, 138.16, 130.58, 129.56, 125.18, 125.16, 125.12, 125.08, 125.05, 122.48, 119.07, 21.10, 20.42.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{13}F_3O_2$ $[M+Na]^+$: 317.0765, found: 317.0768.

4,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2m) and 2,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2m')



2m



2m'

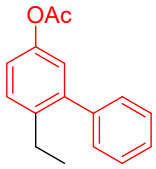
Isolated yield 85%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (q, J = 7.0 Hz, 4H), 7.43 (d, J = 4.8 Hz, 1H), 7.40 (s, 2H), 7.38 (s, 1H), 7.23 – 7.22 (m, 1H), 7.19 (d, J = 11.5 Hz, 3H), 7.03 (s, 1H), 7.01 (d, J = 4.6 Hz, 1H), 2.37 (s, 3H), 2.35 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H), 2.09 (s, 3H), 1.94 (s, 3H).

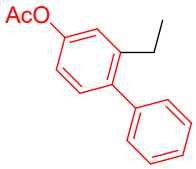
^{13}C NMR (101 MHz, $CDCl_3$) major regioisomer δ 169.50, 169.33, 147.53, 143.30, 140.51, 133.94, 133.01, 129.09, 128.57, 128.17, 126.99, 120.63, 20.84, 20.71, 14.08. minor regioisomer δ 169.52, 169.35, 147.30, 141.07, 140.68, 133.05, 129.24, 128.76, 128.32, 127.81, 123.02, 20.76, 19.86, 15.87.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{16}O_2$ $[M+Na]^+$: 263.1045, found: 263.1048.

6-ethyl-[1,1'-biphenyl]-3-yl acetate (2n) and 2-ethyl-[1,1'-biphenyl]-4-yl acetate (2n')



2n



2n'

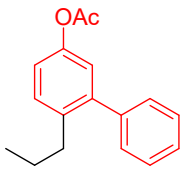
Isolated yield 75%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (t, J = 7.4 Hz, 2H), 7.38 (d, J = 7.1 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 8.3 Hz, 1H), 7.07 (d, J = 1.9 Hz, 1H), 7.00 (dd, J = 8.3, 2.3 Hz, 1H), 2.63 (q, J = 7.6 Hz, 2H), 2.34 (s, 2H, Major), 2.30 (s, 1H, Minor), 1.14 (t, J = 7.5 Hz, 3H).

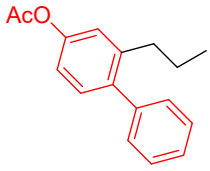
^{13}C NMR (101 MHz, $CDCl_3$) major regioisomer 169.67, 150.05, 143.20, 141.17, 139.33, 130.93, 129.28, 128.10, 126.93, 121.26, 118.66, 26.22, 21.18, 15.23. minor regioisomer δ 169.64, 148.29, 142.76, 141.04, 139.21, 129.50, 129.10, 127.07, 122.78, 120.47, 25.66, 21.11, 15.61.

HRMS (ESI-TOF) m/z Calcd for $C_{16}H_{16}O_2$ $[M+Na]^+$: 263.1048, found: 263.1049.

6-propyl-[1,1'-biphenyl]-3-yl acetate (2o) and 2-propyl-[1,1'-biphenyl]-4-yl acetate (2o')



2o



2o'

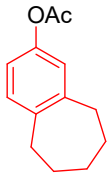
Isolated yield 75%. Colorless oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.38 (d, J = 6.8 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.24 (d, J = 8.3 Hz, 1H), 7.06 (dt, J = 4.4, 2.4 Hz, 1H), 7.02 – 6.97 (m, 1H), 2.58 (td, J = 9.6, 8.8, 3.9 Hz, 2H), 2.34 (d, J = 0.7 Hz, 2H, major), 2.30 (d, J = 0.7 Hz, 1H, minor), 1.58 – 1.49 (m, 2H), 0.85 (t, J = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) major regioisomer δ 169.61, 149.89, 141.71, 141.27, 139.56, 130.98, 129.32, 128.08, 126.90, 121.91, 118.66, 35.14, 24.14, 21.17, 13.97. minor regioisomer δ 169.58, 148.31, 142.99, 141.14, 137.71, 130.13, 129.14, 128.08, 127.04, 122.83, 120.30, 34.62, 24.45, 21.11, 14.03.

HRMS (ESI-TOF) m/z Calcd for $C_{17}H_{18}O_2$ $[M+Na]^+$: 277.1202, found: 277.1204.

6,7,8,9-tetrahydro-5H-benzo[7]annulen-2-yl acetate (2p)



Isolated yield 86%. White solid, mp 59.8-60.1°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.0 Hz, 1H), 6.88 – 6.79 (m, 2H), 2.80 (dt, *J* = 7.6, 4.1 Hz, 4H), 2.28 (s, 3H), 1.86 (p, *J* = 5.9 Hz, 2H), 1.68 (dp, *J* = 11.3, 5.8 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.65, 148.66, 144.79, 141.00, 129.84, 121.92, 118.46, 36.66, 36.10, 32.66, 28.20, 28.11, 21.09.

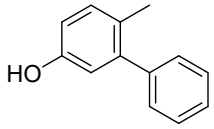
HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{16}O_2$ $[M+Na]^+$: 227.1043, found: 227.1048.

2.3 Procedure for the synthesis of polycyclic aromatic compounds

Synthesis of Compound 2a'

Add 4N HCl to the reaction stock solution of **2a**, Stir the mixture at at room temperature for 4 h until complete conversion of starting material (the progress of the reaction was monitored by TLC). After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (10 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was further purified through flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 5:1, v/v) to afford target compounds **2a'**.

6-methyl-[1,1'-biphenyl]-3-ol (2a')



Isolated yield 90%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.41 (m, 2H), 7.40 – 7.37 (m, 1H), 7.33 (d, *J* = 6.8 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 1H), 6.83 – 6.76 (m, 2H), 5.88 (s, 1H), 2.23 (s, 3H).

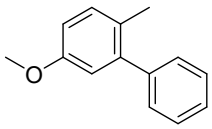
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.31, 143.09, 141.69, 131.46, 129.08, 128.12, 127.53, 126.92, 116.75, 114.29, 19.54.

HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{12}O$ $[M+H]^+$: 185.0966, found: 185.0963.

Synthesis of Compound 3[5]

A solution of phenol **2a'** (6.03 g, 32.6 mmol) and sodium hydroxide (3.26 g, 81.5 mmol) in DMF (20.0 mL) was treated with methyl iodide (5.0 mL, 81.5 mmol) and stirred at room temperature for 6 h. The reaction mixture was diluted with water (20 mL) and extracted with extracted with EtOAc (3×20 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The solvent was removed under reduced pressure to give **3**, a clear oil (6.0 g, 93%).

5-methoxy-2-methyl-1,1'-biphenyl (3)



Isolated yield 93%. Colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 2H), 7.37 (d, *J* = 7.6 Hz, 3H), 7.22 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 3.84 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.59, 142.88, 142.02, 131.19, 129.10, 128.10, 126.88, 115.15, 112.93, 55.34, 19.51.

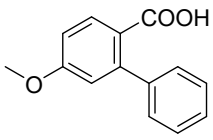
HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{14}O$ $[M+Na]^+$: 221.0924, found: 221.0929.

Synthesis of Compound 4[6]

A solution of compound **3** (5.0 g, 25.3 mmol) in 30 mL of pyridine and 50 mL of water containing 12.0 g of $KMnO_4$ (75.9 mmol) was heated at reflux for 12 h (12.0 g of $KMnO_4$ were added for four times). The hot solution (ca. 80°C) was filtered to remove the MnO_2 solid and the solid was washed with boiling water. The filtrate was

concentrated and the acid was recovered by addition of 1 M HCl. The precipitate was filtered and washed with water and dried in vacuum to afford the white solid of **4** (4.3 g, 75%).

5-methoxy-[1,1'-biphenyl]-2-carboxylic acid (4)



Isolated yield 75%. White solid, mp 174.5-174.8°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.7 Hz, 1H), 7.37 (d, *J* = 6.9 Hz, 3H), 7.32 (d, *J* = 7.3 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 1H), 6.83 (s, 1H), 3.86 (s, 3H).

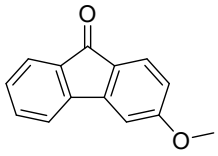
^{13}C NMR (101 MHz, $CDCl_3$) δ 172.70, 162.38, 146.35, 141.35, 133.45, 128.37, 127.88, 127.29, 121.09, 116.73, 112.59, 55.50.

HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{12}O_3$ $[M+Na]^+$: 251.0684, found: 251.0686.

Synthesis of Compound 5

In a flask equipped with a magnetic bar, compound **4** was dissolved in DCM containning 50 equiv. of methanesulfonic acid. A red brown color appeared quickly. The reaction mixture was heated at reflux until complete conversion of starting material (the progress of the reaction was controlled by TLC). The reaction mixture was then poured into 25 mL water. A yellow precipitate was observed. The mixture was extracted by 4×20 mL ethyl acetate, the organic phase was washed with 2×15 mL water and then with 15 mL of saturated sodium hydrogen carbonate aqueous solution, and finally with 15 mL of water. After drying the organic phase over $MgSO_4$, concentration in vacuo and recrystallization of the obtained residue (PE/EA = 30/1, v/v), pure compound **5** (yellow solid) was obtained. Yield: 80 %.

3-methoxy-9H-fluoren-9-one (5)



Isolated yield 80%. Yellow solid, mp 88.8-89.0°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.48 – 7.42 (m, 2H), 7.31 – 7.24 (m, 1H), 7.01 (d, *J* = 2.2 Hz, 1H), 6.73 (dd, *J* = 8.2, 2.2 Hz, 1H), 3.90 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.51, 165.38, 147.00, 143.33, 135.34, 134.10, 129.26,

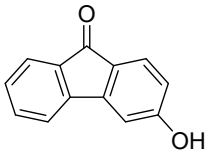
127.15, 126.27, 123.85, 120.09, 112.94, 107.07, 55.75.

HRMS (ESI-TOF) m/z Calcd for $C_{14}H_{10}O_2$ $[M+Na]^+$: 233.0573, found: 233.0572.

Synthesis of Compound 6

To a 25-mL Schlenk tube was added compound **5** (10.0 mmol), $PPh_3 \cdot Br_2$ (25.0 mm, 2.5 equiv.) and chlorobenzene (10.0 mL). The mixture was stirred at 130°C for 12 h. Then the mixture was cooled to room temperature, and the organic layer was separated and concentrated under reduced pressure. The residue was finally purified by flash silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to afford the desired products **6**. Yield: 68 %.

3-hydroxy-9H-fluoren-9-one (6)



Isolated yield 68%. Yellow solid, mp 216.2-216.4°C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.3 Hz, 2H), 7.44 (d, J = 8.1 Hz, 1H), 7.30 (t, J = 7.4 Hz, 1H), 7.10 (s, 1H), 6.67 (d, J = 8.1 Hz, 1H), 3.83 (s, 1H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 191.85, 164.87, 147.32, 143.29, 135.09, 134.85, 129.82, 126.74, 125.12, 123.58, 121.21, 115.64, 109.10.

HRMS (ESI-TOF) m/z Calcd for $C_{13}H_8O_2$ $[M+Na]^+$: 219.0417, found: 219.0415.

Synthesis of Compound 7[7].

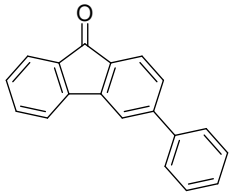
To a solution of **6** (0.98 g, 5.0 mmol) in 3 mL of pyridine and 10 mL of THF was added dropwise trifluoromethanesulfonic anhydride (1.25 mL, 7.5 mmol) at 0°C. The mixture was stirred for 4 h at 0 °C. The mixture was poured into ice water. The organic layer was washed with sat. $NaHCO_3$ aqueous solution, water and brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (PE/EA = 30/1, v/v) to afford 1.14 g (70%) of the compound trifluoromethanesulfonate as a yellow solid.

A mixture of trifluoromethanesulfonate (0.328 g, 1.0 mmol), phenylboronic acid (0.246 g, 2.0 mmol), tetrakis(triphenylphosphine)palladium (12 mg, 0.1 mmol), potassium phosphate tribasic (0.318 g, 1.5 mmol), and 5 mL of DMF was stirred for 12 h at 100°C under an argon atmosphere. The mixture was filtered and washed with

EtOAc. The organic layer was washed with water and brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (PE/EA = 50/1, v/v) to afford 0.192 g (75%) of the compound as a yellow solid.

The method of synthesizing compound **9** is similar to that of synthesizing compound **7**.

3-phenyl-9H-fluoren-9-one (7)



Isolated yield 53%. Yellow solid, mp 85.6-85.9°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.62 (m, 4H), 7.56 (dd, *J* = 7.4, 4.0 Hz, 1H), 7.50 – 7.46 (m, 3H), 7.43 (dd, *J* = 7.4, 4.0 Hz, 2H), 7.29 (ddd, *J* = 19.4, 9.9, 4.0 Hz, 1H), 7.23 – 7.11 (m, 1H).

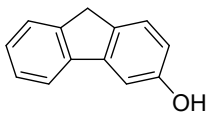
^{13}C NMR (101 MHz, $CDCl_3$) δ 193.48, 147.84, 145.14, 144.08, 140.18, 134.69, 134.61, 132.95, 129.20, 128.95, 128.42, 127.91, 127.19, 124.70, 124.25, 120.26, 119.18.

HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{12}O$ $[M+Na]^+$: 279.0780, found: 279.0781.

Synthesis of Compound 8[8]

Heat a mixture of reactant **6** (0.98 g, 5.0 mmol), $NaBH_4$ (0.57 g, 15.0 mmol), and anhydrous $AlCl_3$ (1.99 g, 15.0 mmol) in THF (15 mL) under reflux for 6 h. The reaction mixture was diluted with water (40 mL) and extracted with EtOAc (3×40 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residual was finally purified by flash silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to afford the desired products **8**.

9H-fluoren-3-ol (8)



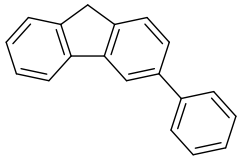
Isolated yield 75%. Yellow solid, mp 151.4-151.6 C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.36 (s, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.51 (d, J = 7.3 Hz, 1H), 7.33 (d, J = 7.4 Hz, 2H), 7.28 – 7.19 (m, 2H), 6.73 (d, J = 8.1 Hz, 1H), 3.75 (s, 2H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 157.13, 144.38, 142.75, 141.70, 133.62, 127.02, 126.05, 125.49, 120.20, 114.87, 106.98, 36.00.

HRMS (ESI-TOF) m/z Calcd for $C_{13}H_{10}O$ $[M+H]^+$: 183.0804, found: 183.0807.

3-phenyl-9H-fluorene (9)



Isolated yield 50%. White solid, mp 80.6-80.8°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.89 – 7.82 (m, 1H), 7.69 (d, *J* = 7.7 Hz, 2H), 7.63 – 7.52 (m, 3H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.44 – 7.31 (m, 3H), 3.95 (s, 2H).

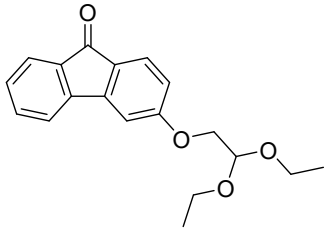
^{13}C NMR (101 MHz, $CDCl_3$) δ 143.59, 142.32, 142.31, 141.63, 141.53, 140.15, 128.75, 127.31, 127.13, 126.86, 126.78, 125.95, 125.22, 125.07, 119.90, 118.58, 36.67.

HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{14}$ $[M+H]^+$: 243.1168, found: 243.1176.

Synthesis of Compound 10[9]

A solution of phenol **6** (1.0 equiv) and K_2CO_3 (2.0 equiv) in DMF was stirred at 60°C for 1 h. Then 2-bromo-acetaldehyde ethyl acetal (1.5 equiv) was added. The mixture was stirred for about 10 h under reflux until the reaction was completed based on TLC analysis. It was cooled to room temperature and extracted with EtOAc (50 mL×3). The combined organic layers were subsequently washed with 5% NaOH aqueous solution and water, dried over $MgSO_4$ and concentrated under reduced pressure. The residual crude product was finally purified by flash silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to afford the desired compound **10**.

3-(2,2-diethoxyethoxy)-9H-fluoren-9-one (10)



Isolated yield 82%. Yellow solid, mp 135.2-135.4°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (t, J = 8.5 Hz, 2H), 7.44 (d, J = 4.1 Hz, 2H), 7.32 – 7.24 (m, 1H), 7.05 (d, J = 1.6 Hz, 1H), 6.74 (dd, J = 8.2, 1.6 Hz, 1H), 4.85 (t, J = 5.1 Hz, 1H), 4.09 (d, J = 5.1 Hz, 2H), 3.83 – 3.73 (m, 2H), 3.65 (p, J = 7.1 Hz, 2H), 1.25 (t, J = 7.0 Hz, 6H).

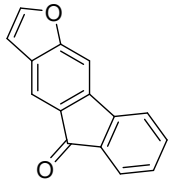
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.48, 164.33, 146.97, 143.31, 135.26, 134.15, 129.27, 127.37, 126.21, 123.87, 120.09, 113.71, 107.59, 100.29, 68.89, 62.84, 15.32.

HRMS (ESI-TOF) m/z Calcd for $C_{19}H_{20}O_4$ $[M+Na]^+$: 335.1254, found: 335.1261.

Synthesis of Compound 11[9]

To a 25 mL Schlenk tube was added compound **10** (1.0 mmol), phosphoric acid (300 μL, 4.8 equiv) and chlorobenzene (3.0 mL). The mixture was stirred at 130°C for 12 h. Then the mixture was cooled to room temperature, the organic layer was separated and concentrated under reduced pressure. The residual was finally purified by flash silica gel column chromatography (eluting with petroleum ether/ethyl acetate) to afford the desired products.

5H-fluoreno[3,2-b]furan-5-one (11)



Isolated yield 77%. Yellow solid, mp 151.4-151.6°C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.66 – 7.59 (m, 2H), 7.53 – 7.43 (m, 3H), 7.28 – 7.23 (m, 1H), 6.79 – 6.77 (m, 1H).

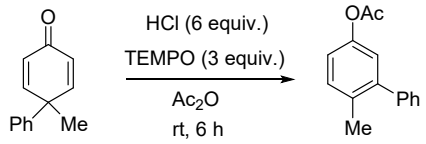
^{13}C NMR (101 MHz, $CDCl_3$) δ 192.97, 159.06, 146.49, 144.33, 141.34, 135.29, 134.69, 130.42, 128.84, 128.11, 124.09, 120.11, 118.48, 108.09, 104.26.

HRMS (ESI-TOF) m/z Calcd for $C_{15}H_8O_2$ $[M+Na]^+$: 243.0417, found: 243.0419.

2.4 Mechanistic Studies

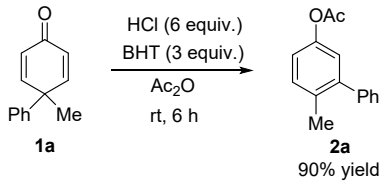
Control experiments A (Scheme 3, A, in the text)

Radical trapping experiments with TEMPO, BHT or 1,1-diphenylethylene

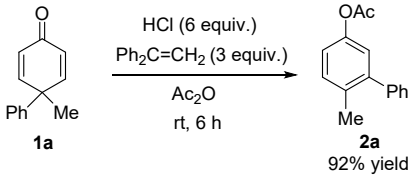


1a **2a** 90% yield

To a 25-mL round flask was added substrate **1a** (0.5 mmol), 37% HCl (3.0 mmol, 6 equiv.), TEMPO (1.5 mmol, 3 equiv.) and Ac_2O (1.5 mL), and the reaction was stirred for 6 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).

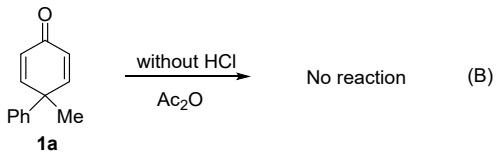


To a 25-mL round flask was added substrate **1a** (0.5 mmol), 37% HCl (3.0 mmol, 6 equiv.), BHT (1.5 mmol, 3 equiv.) and Ac_2O (1.5 mL), and the reaction was stirred for 6 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).



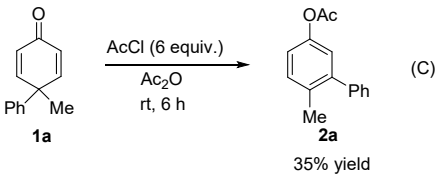
To a 25-mL round flask was added substrate **1a** (0.5 mmol), 37% HCl (3.0 mmol, 6 equiv.), 1,1-diphenylethylene (1.5 mmol, 3 equiv.) and Ac_2O (1.5 mL), and the reaction was stirred for 6 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (92% yield).

Control experiment B (Scheme 3, B, in the text)



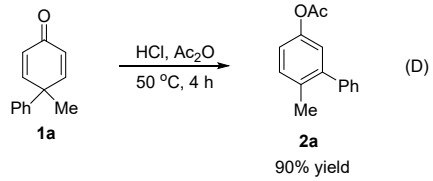
To a 25-mL round flask was added substrate **1a** (0.2 mmol), Ac_2O (0.5 mL), and the reaction was stirred for 12 h at room temperature. No reaction occurred and only **1a** was recovered.

Control experiment C (Scheme 3, C, in the text)



To a 25-mL round flask was added substrate **1a** (0.5 mmol), AcCl (3.0 mmol, 6 equiv.), Ac_2O (1.5 mL), and the reaction was stirred for 6 h at room temperature. The reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (35% yield).

Control experiment D (Scheme 3, D, in the text)



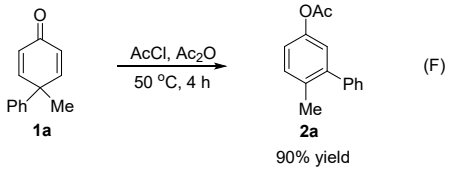
A solution of **1a** (0.5 mmol), 37% HCl (3.0 mmol, 6.0 equiv.), and Ac_2O (1.5 mL), and the reaction was stirred for 4 h at 50 ℃. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (10 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).

Control experiment E (Scheme 3, E, in the text)

A solution of 37% HCl (3.0 mmol, 6.0 equiv.) in Ac_2O (1.5 mL) was cooled to room temperature, and was stirred at rt for 30 min. **1a** (0.5 mmol) was then added. The

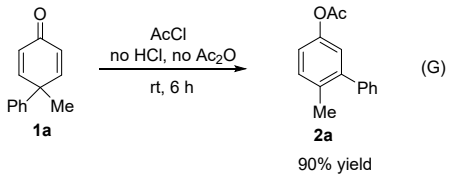
resulting mixture was then kept to stir for 6 h. The reaction mixture was poured into Na_2CO_3 aqueous solution (10 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (45% yield).

Control experiment F (Scheme 3, F, in the text)



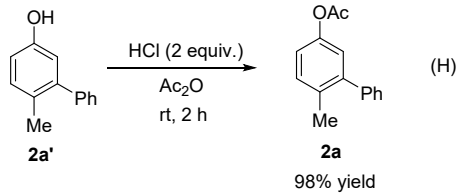
A solution of **1a** (0.5 mmol), AcCl (3.0 mmol, 6.0 equiv.), and Ac_2O (1.5 mL), and the reaction was stirred for 4 h at 50 ℃. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (10 mL) and extracted with ethyl acetate (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).

Control experiment G (Scheme 3, G, in the text)



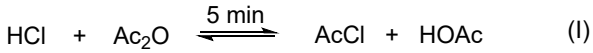
To a 25-mL round flask was added substrate **1a** (0.5 mmol), AcCl (0.5 mL), and the reaction was stirred for 6 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).

Control experiment H (Scheme 3, H, in the text)



To a 25-mL round flask was added **2a'** (0.5 mmol), Ac_2O (1.5 mL) and HCl (1.0 mmol, 2 equiv.), and the reaction mixture was stirred for 2 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (98% yield).

Control experiment I (Scheme 3, I, in the text)



To a 25-mL round flask was added 37% HCl (1.2 mmol) and Ac_2O (0.5 mL), and the reaction was stirred for 2 h at room temperature. The reaction of 37% HCl with Ac_2O was monitored through ^1H NMR.

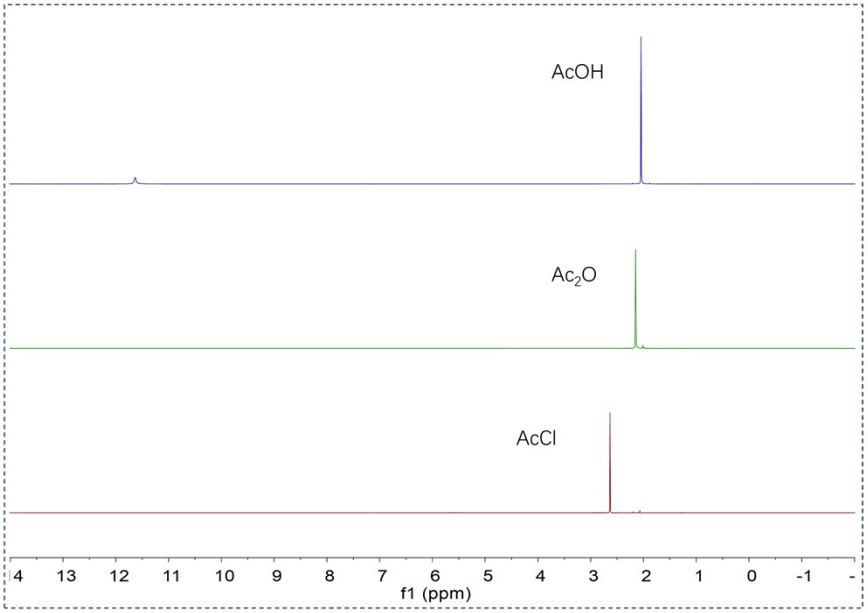


Figure S1. The standard ^1H NMR spectra of AcOH, Ac_2O and AcCl.

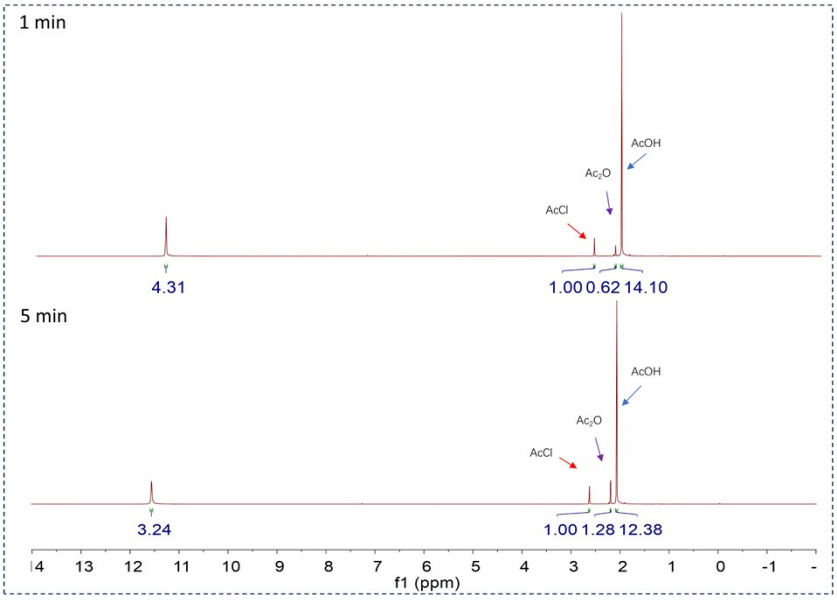


Figure S2. The H-1 NMR spectra of reaction mixture after 1 min and 5 min.

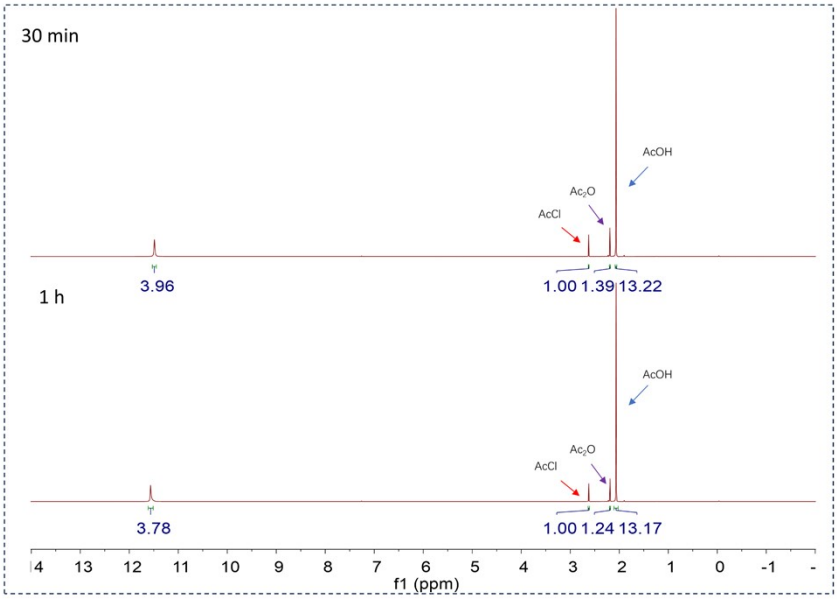
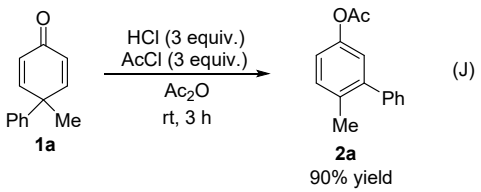


Figure S3. The H-1 NMR spectra of reaction mixture after 30 min and 1 h.

***From the above spectra, we can find that the integration of peaks in the H-1 NMR spectrum no longer changed after 5 min.

Control experiment J (Scheme 3, J, in the text)



(J)

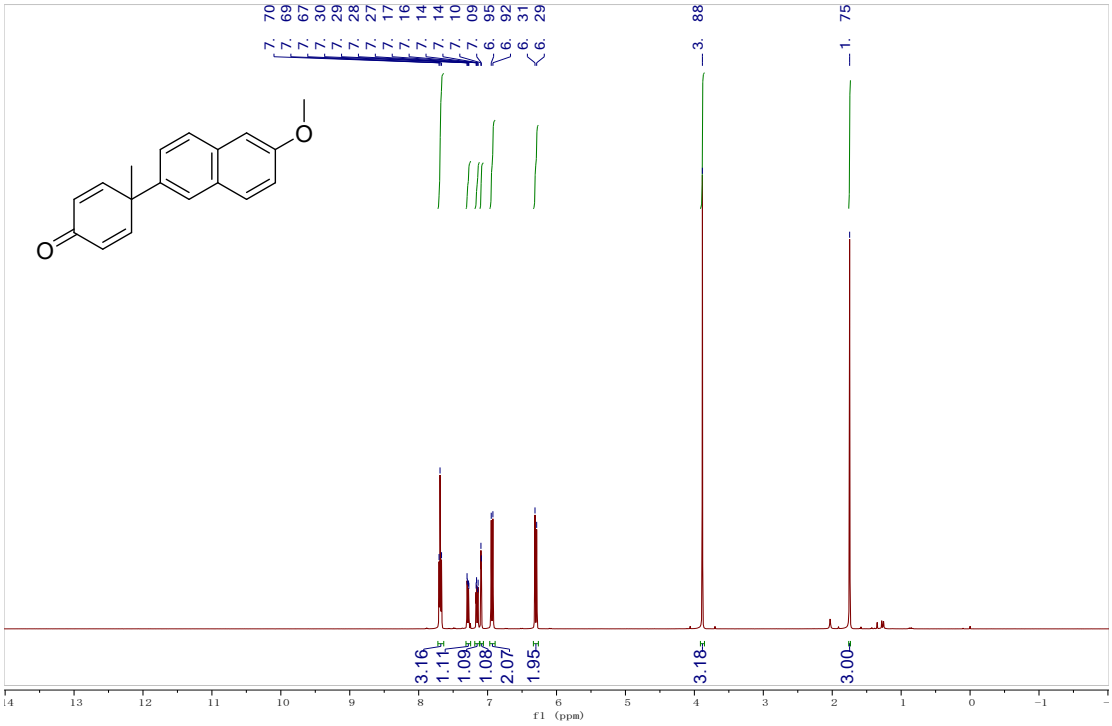
To a 25-mL round flask was added substrate **1a** (0.5 mmol), Ac_2O (0.5 mL), HCl (1.5 mmol, 3 equiv.), AcCl (1.5 mmol, 3 equiv.), and the reaction was stirred for 3 h at room temperature. After completion of the reaction, the reaction mixture was poured into Na_2CO_3 aqueous solution (15 mL) and extracted with ethyl acetate (15 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. Then the residue was purified by silica gel chromatography with a mixture of petroleum ether and ethyl acetate to afford the product **2a** (90% yield).

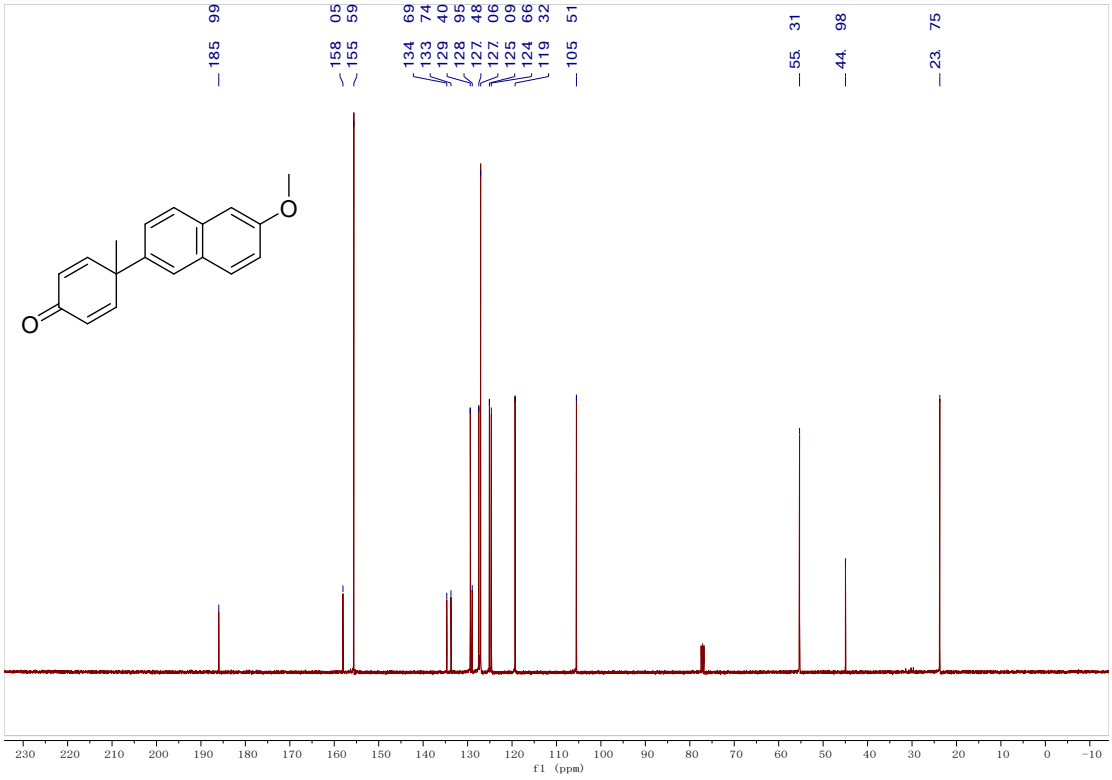
Notes and References

1. A. Bokka, J. X. Mao, J. Hartung, S. R. Martinez, J. A. Simanis, K. Nam, J. Jeon and X. Shen, *Org Lett*, 2018, **20**, 5158-5162.
2. N. Miyamae, N. Watanabe, M. Moritaka, K. Nakano, Y. Ichikawa and H. Kotsuki, *Org Biomol Chem*, 2014, **12**, 5847-5855.
3. G. Chen, Y. Shi, W. Tian, H. Xie, Z. Yan and J. Yu, *Tetrahedron Lett*, 2023, **117**.
4. H. Yang and R. G. Carter, *Org Lett*, 2010, **12**, 3108-3111.
5. N. J. HALES, H. HEANEY, J. H. HOLLINSHEAD and S. V. LEY, *Tetrahedron*, 1995, **51**, 7741-7754.
6. J. Yang, H. Huang and S. Lin, *J Org Chem*, 2009, **74**, 3974-3977.
7. K. Dodo, A. Aoyama, T. Noguchi-Yachide, M. Makishima, H. Miyachi and Y. Hashimoto, *Bioorgan Med Chem*, 2008, **16**, 4272-4285.
8. A. ONO, N. SUZUKI and J. KAMIMURA, *Synthesis-Stuttgart*, 1987, 736-738.
9. W. Ma, J. Huang, X. Huang, S. Meng, Z. Yang, C. Li, Y. Wang, T. Qi and B. Li, *Org Chem Front*, 2019, **6**, 493-497.

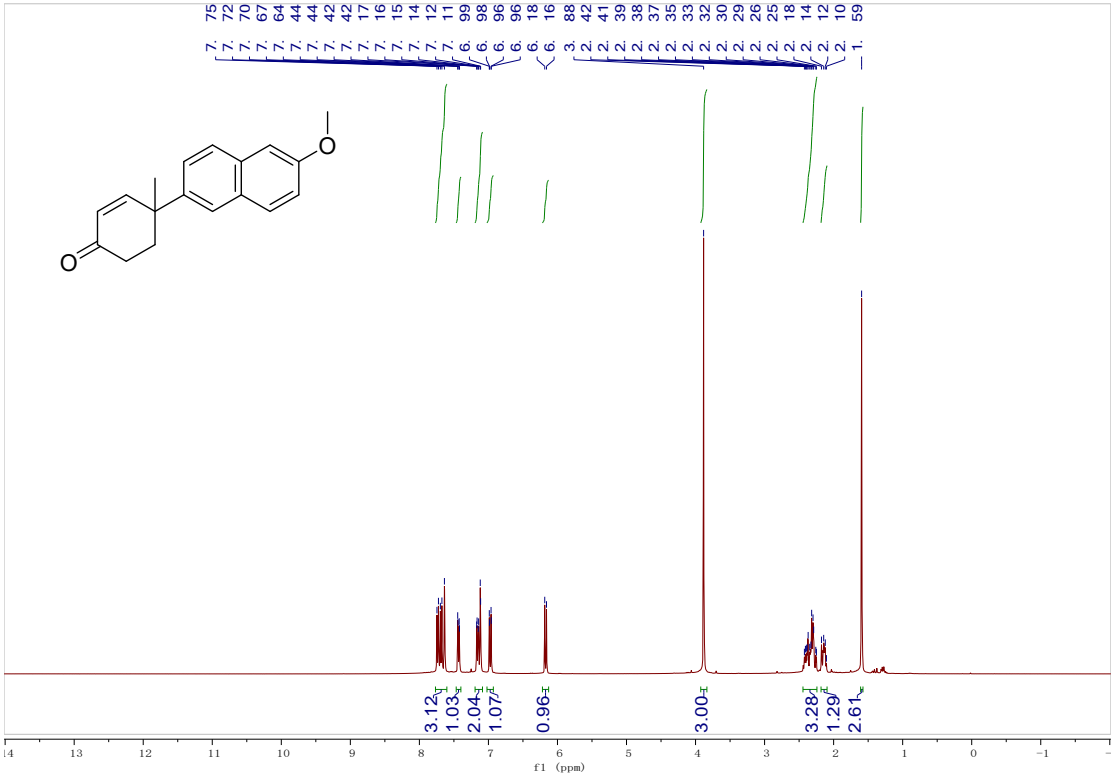
3 ^{1}H NMR and ^{13}C NMR spectra of products

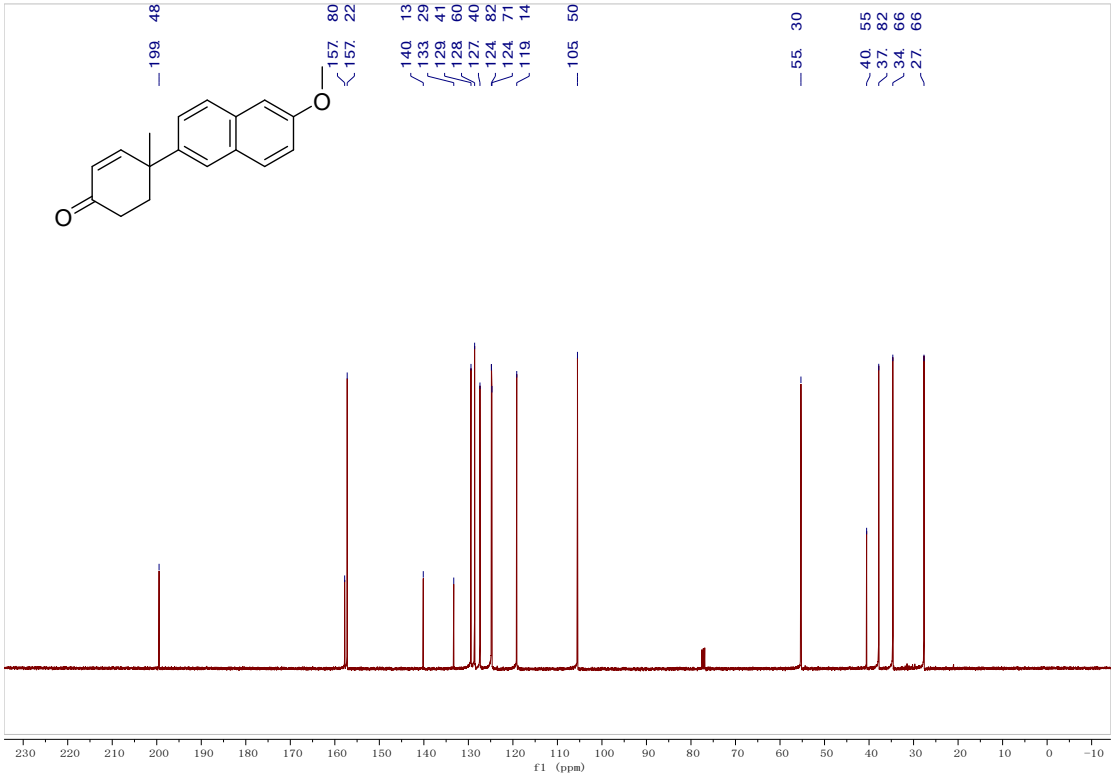
4-(6-methoxynaphthalen-2-yl)-4-methylcyclohexa-2,5-dien-1-one (1f)



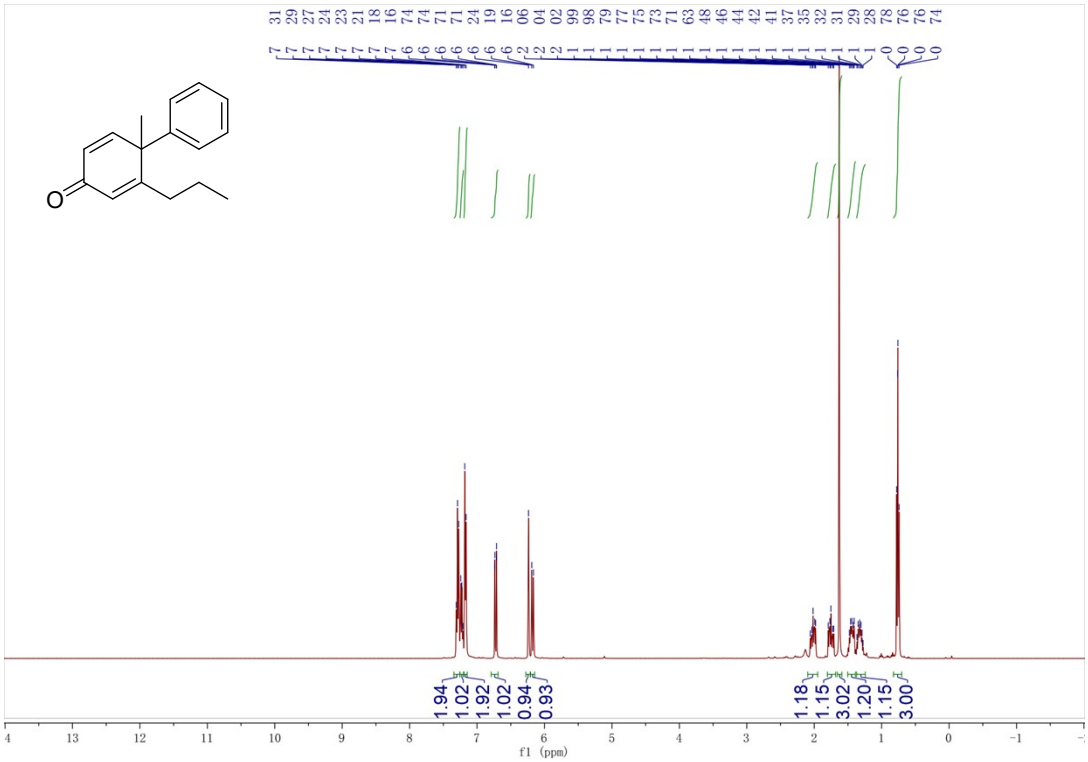


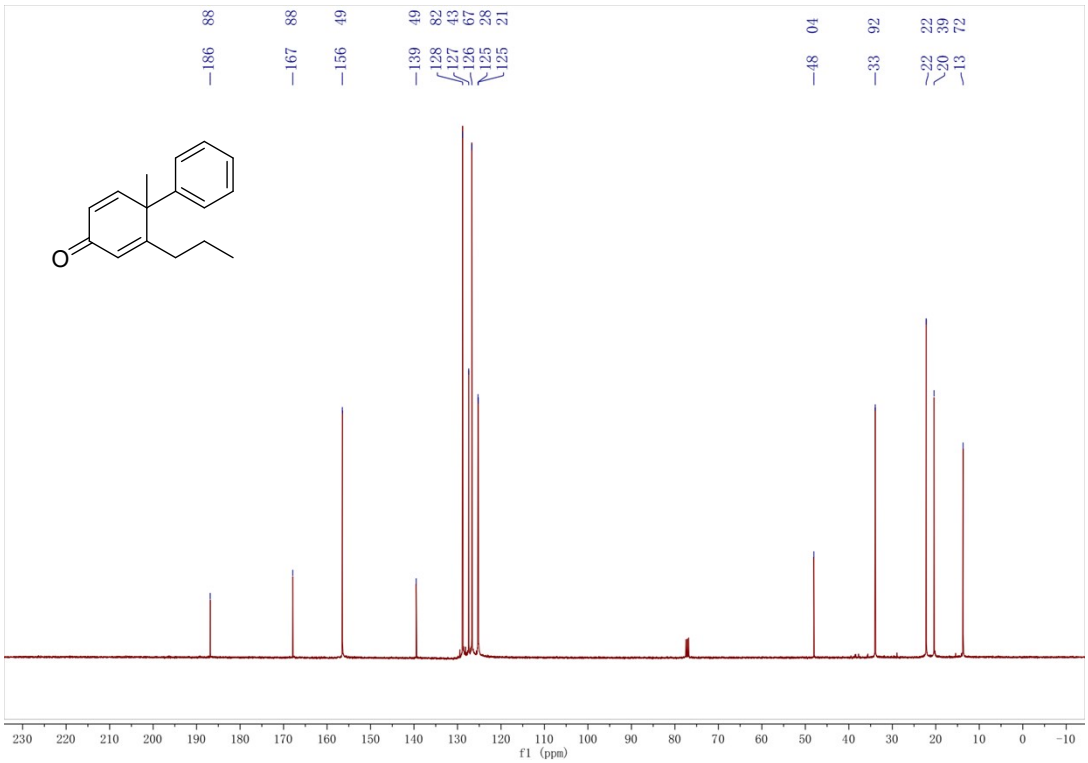
4-(6-methoxynaphthalen-2-yl)-4-methylcyclohex-2-en-1-one (1fp)



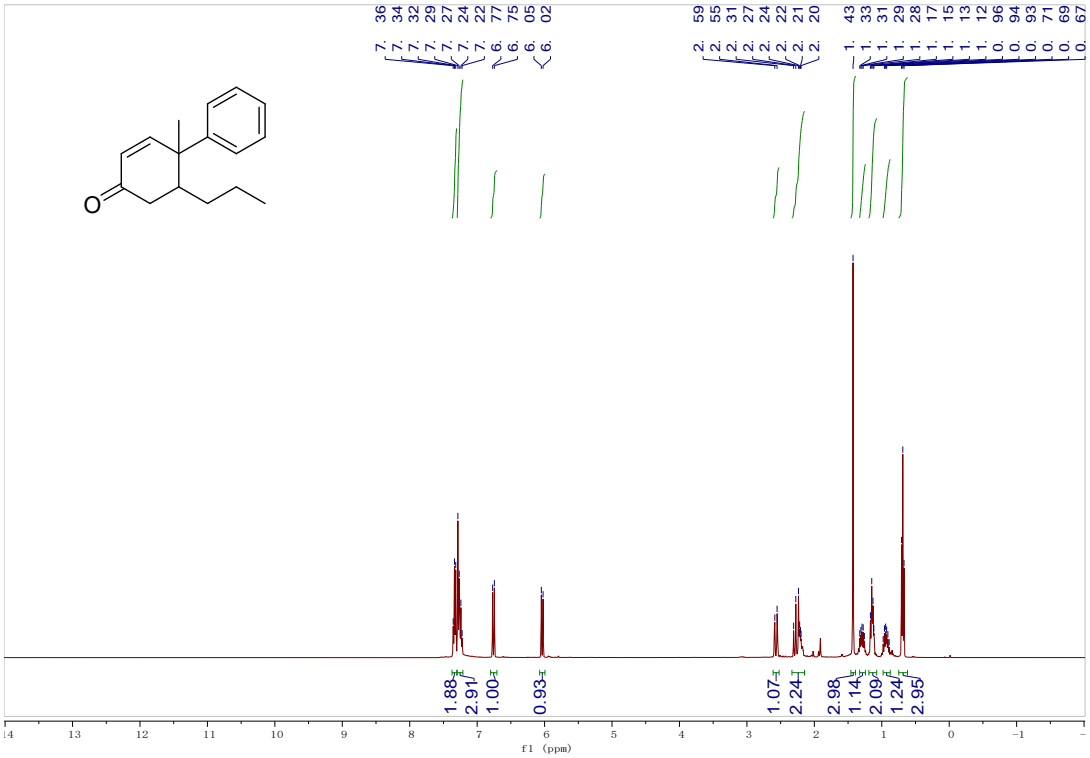


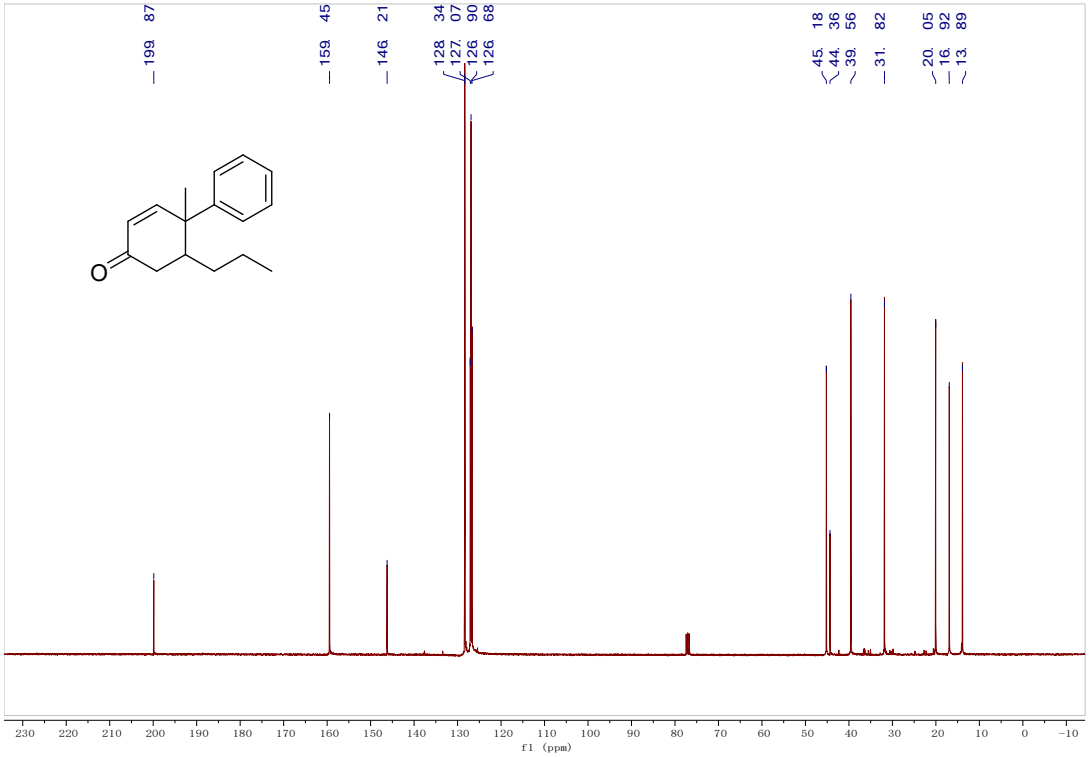
1-methyl-2-propyl-[1,1'-biphenyl]-4(1H)-one (1h)



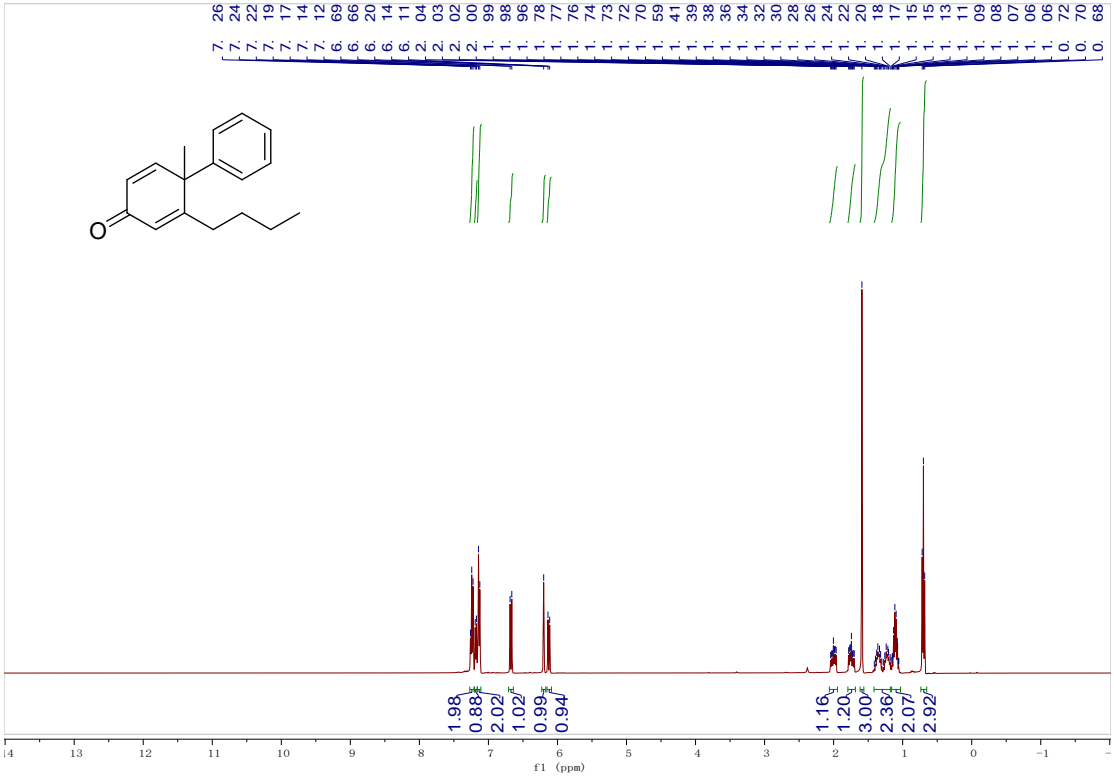


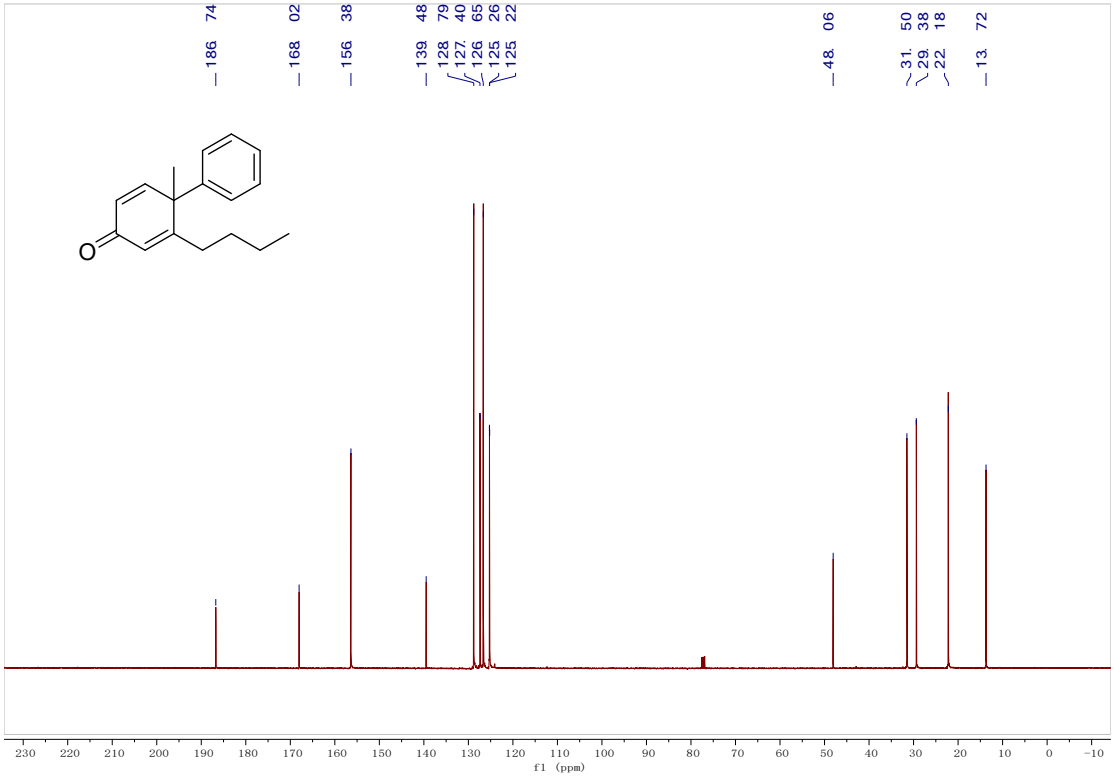
1-methyl-2-propyl-2,3-dihydro-[1,1'-biphenyl]-4(1H)-one (1hp)



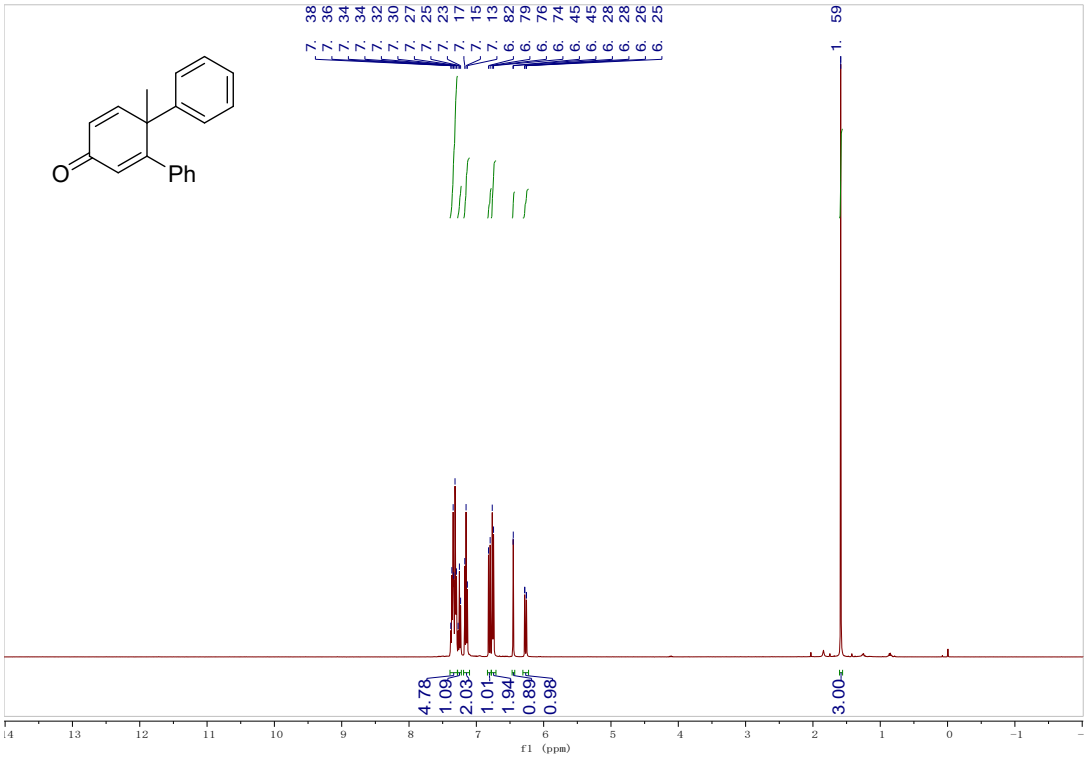


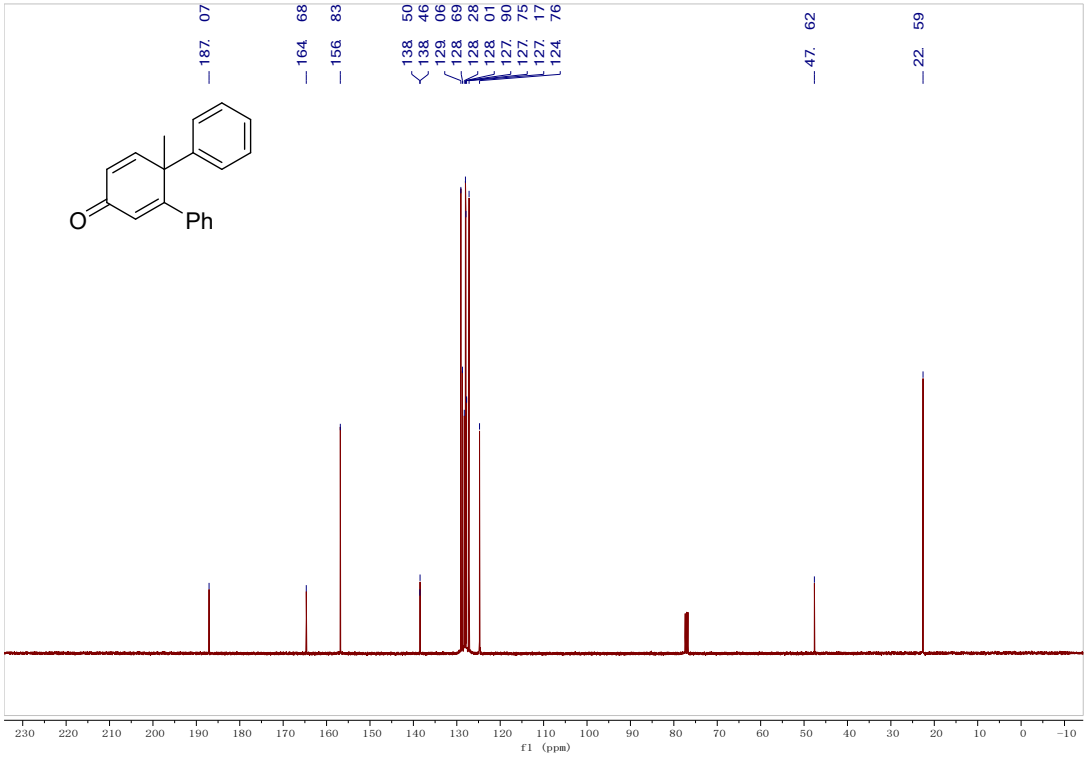
2-butyl-1-methyl-[1,1'-biphenyl]-4(1H)-one (1i)



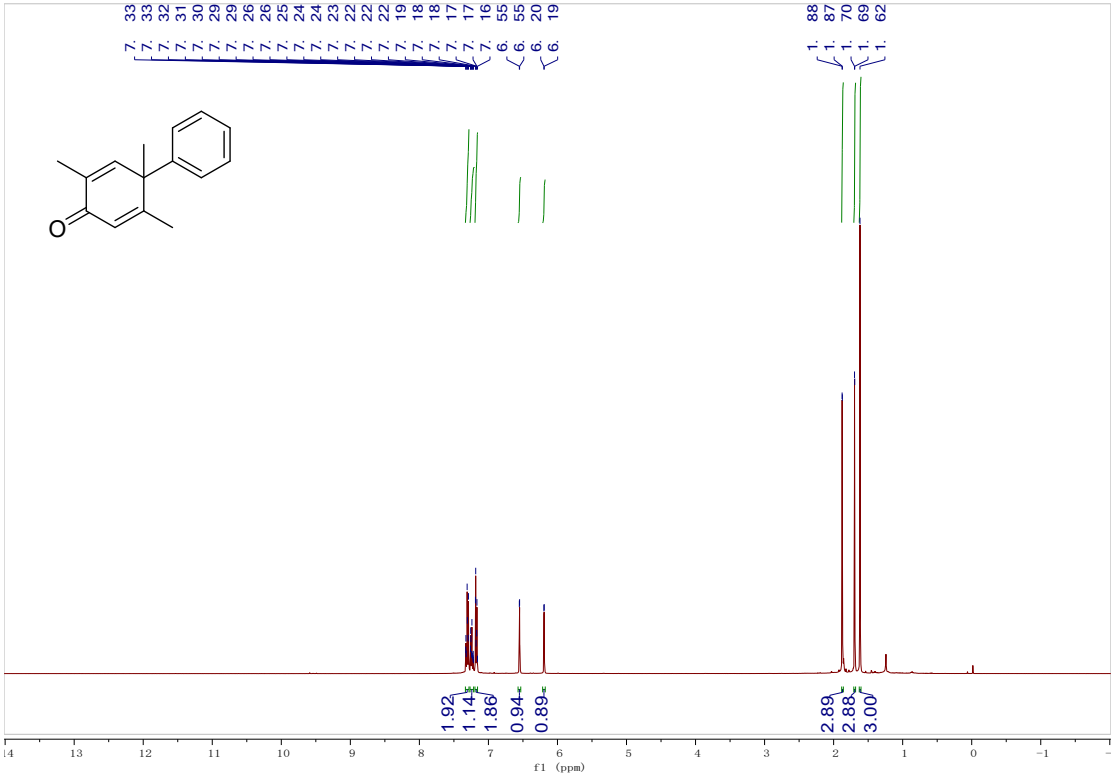


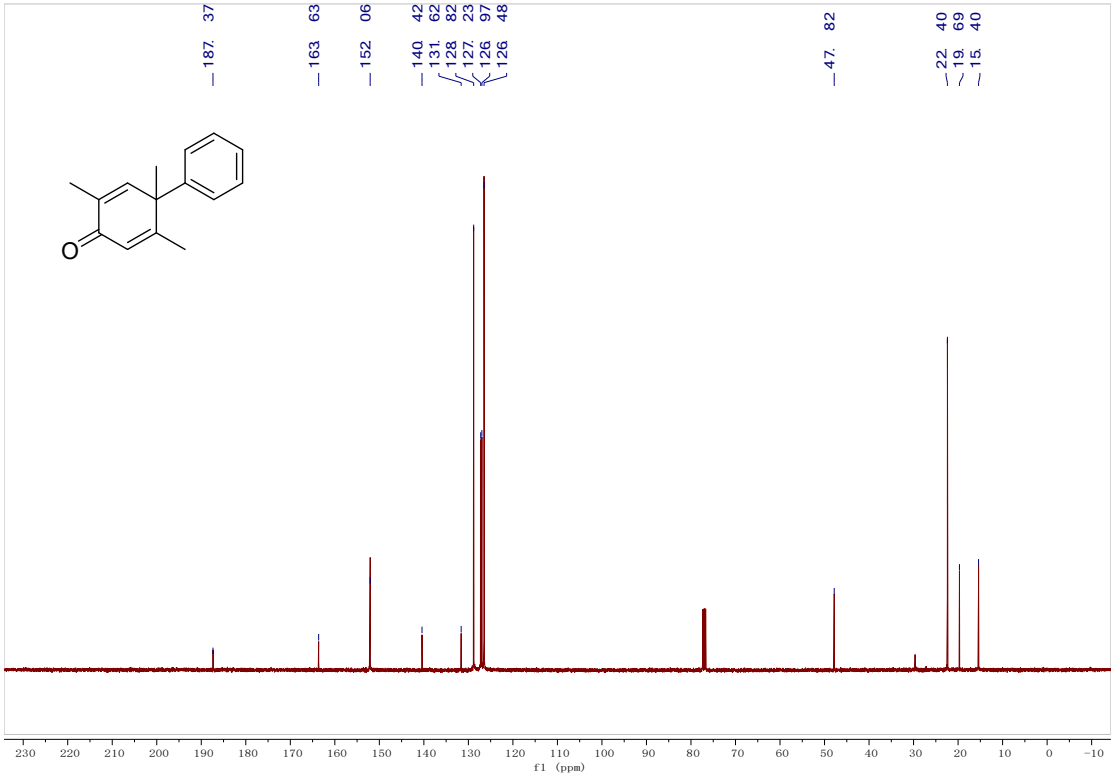
1'-methyl-[1,1':2',1''-terphenyl]-4'(1'H)-one (1j)



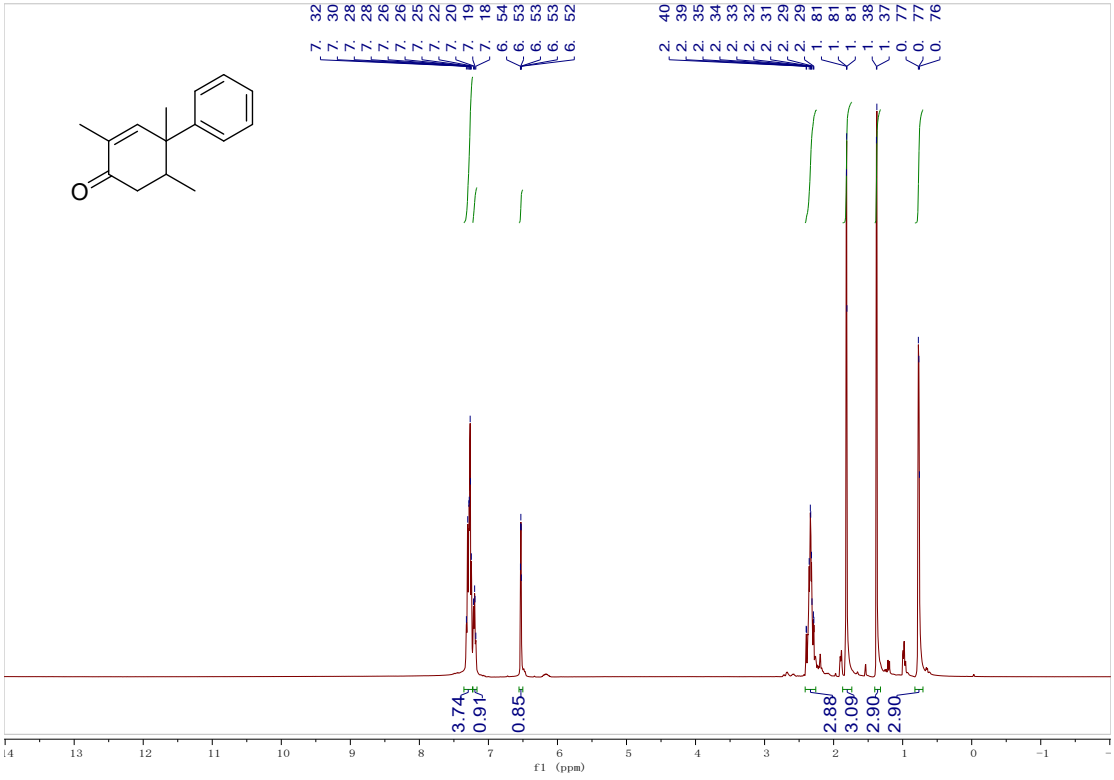


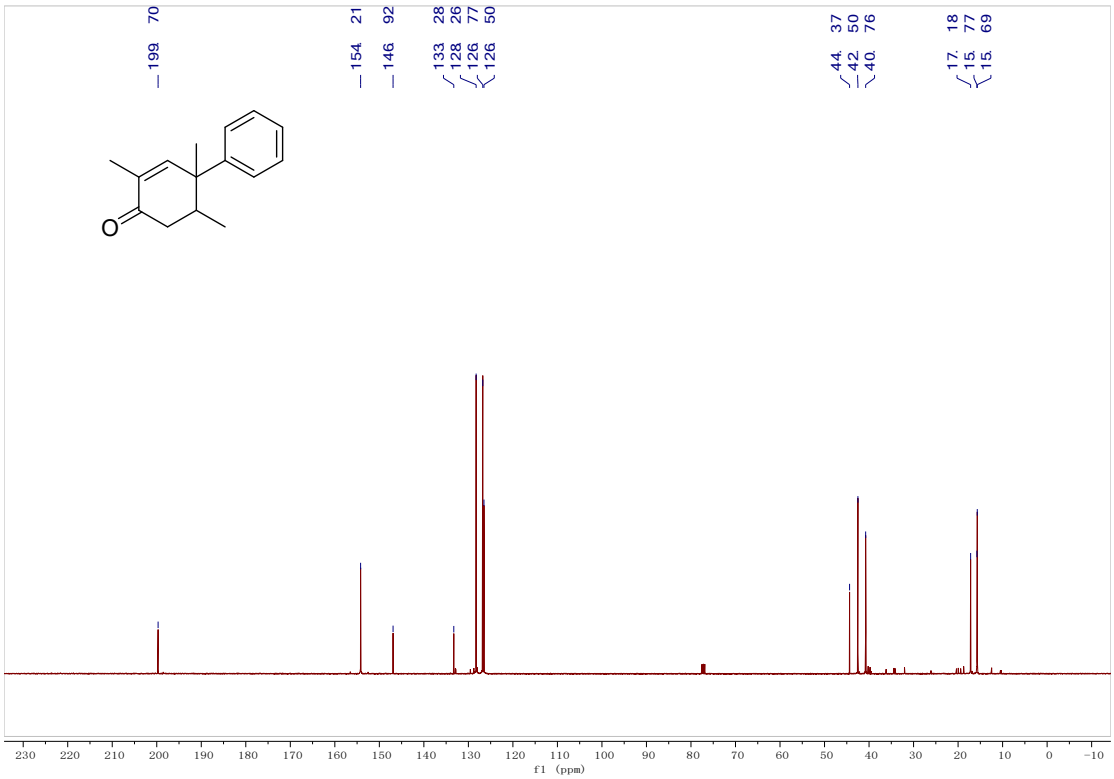
1,2,5-trimethyl-[1,1'-biphenyl]-4(1H)-one (1k)



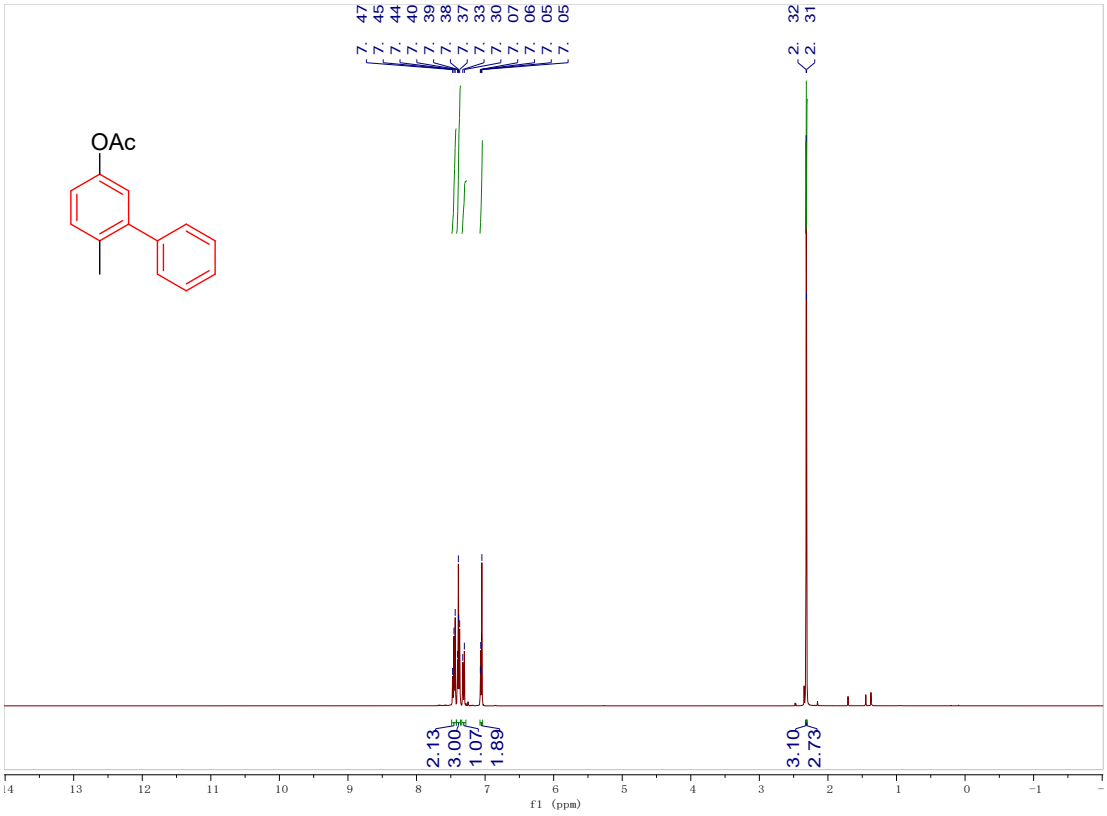


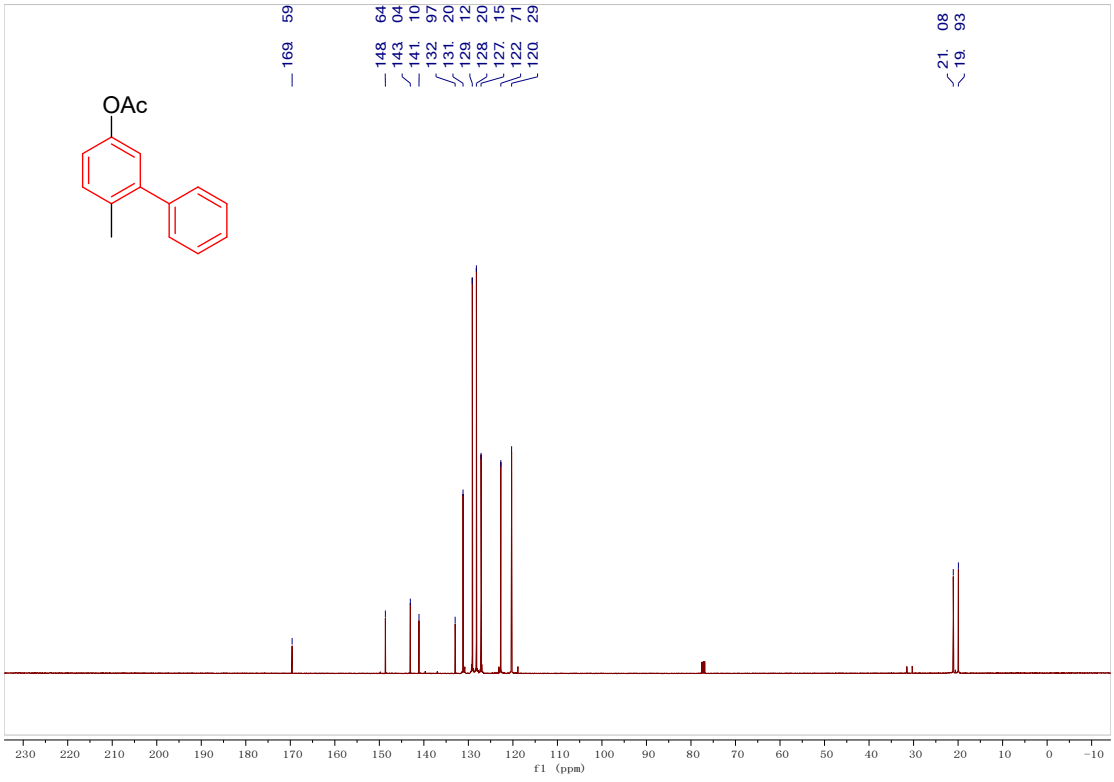
1,2,5-trimethyl-2,3-dihydro-[1,1'-biphenyl]-4(1H)-one (1kp)



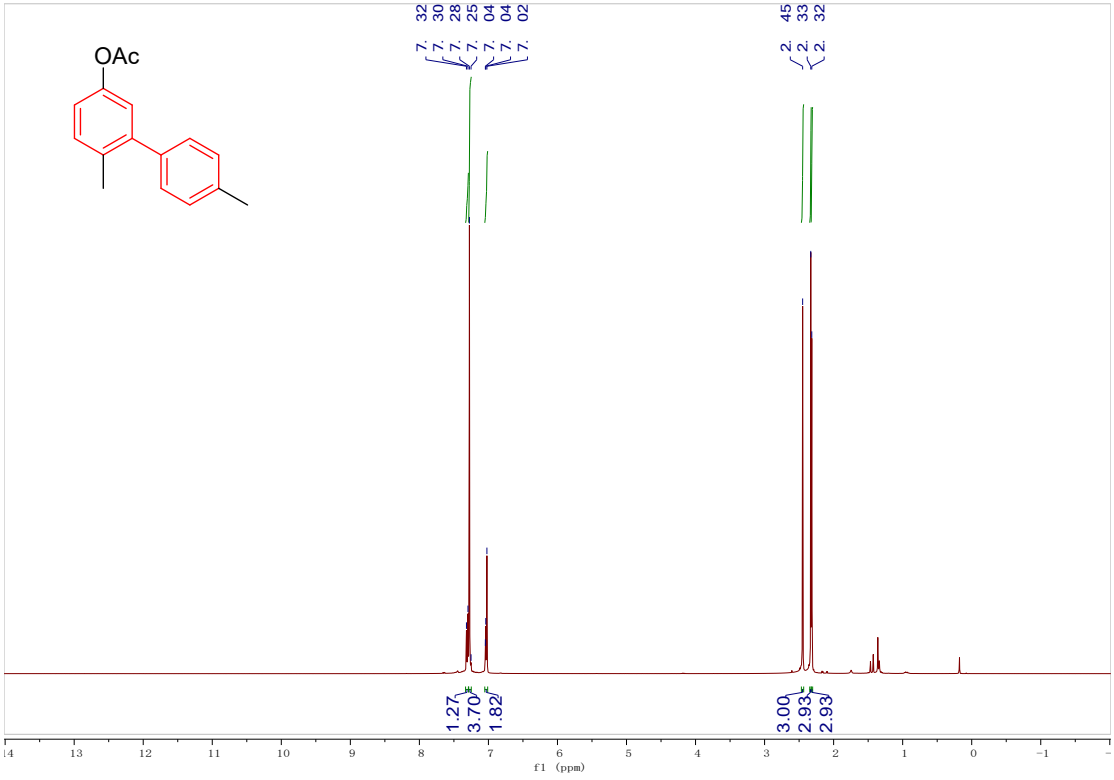


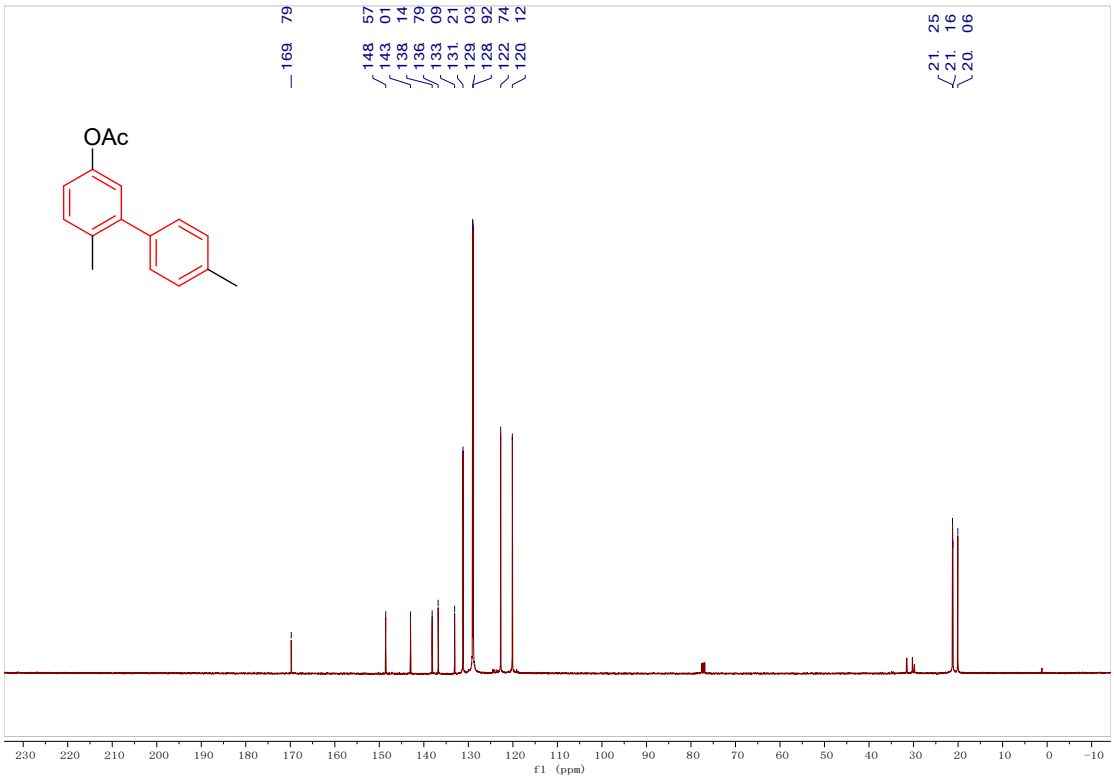
6-methyl-[1,1'-biphenyl]-3-yl acetate (2a)



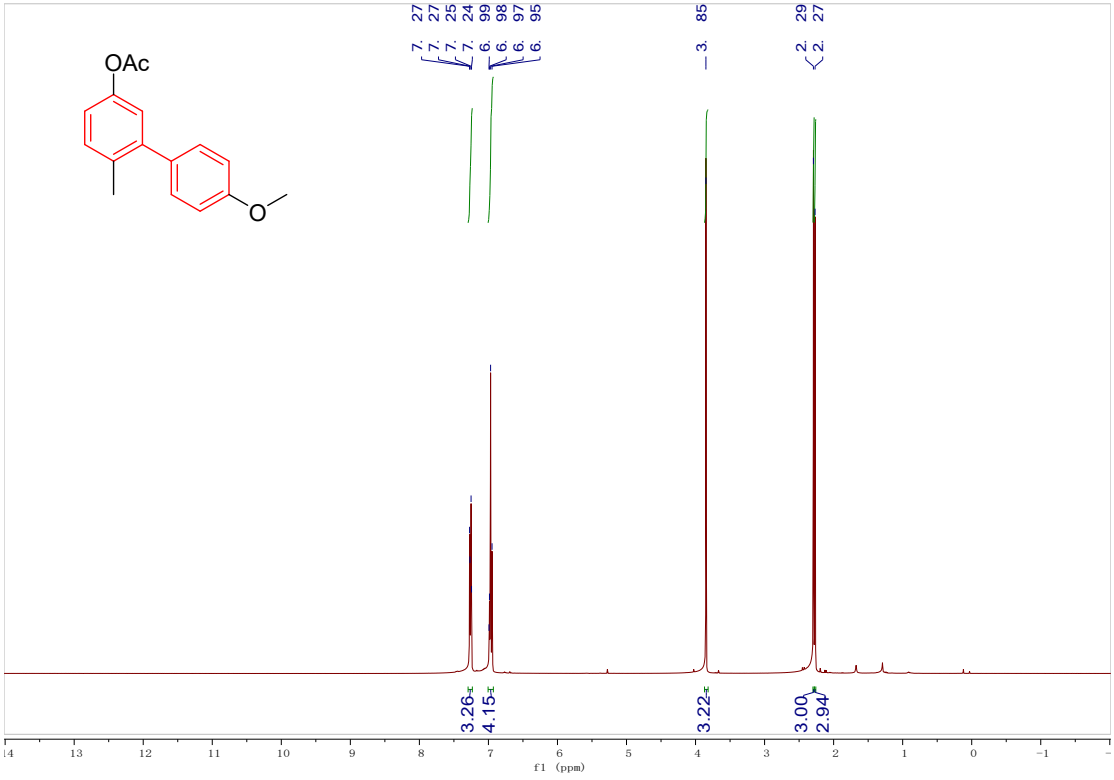


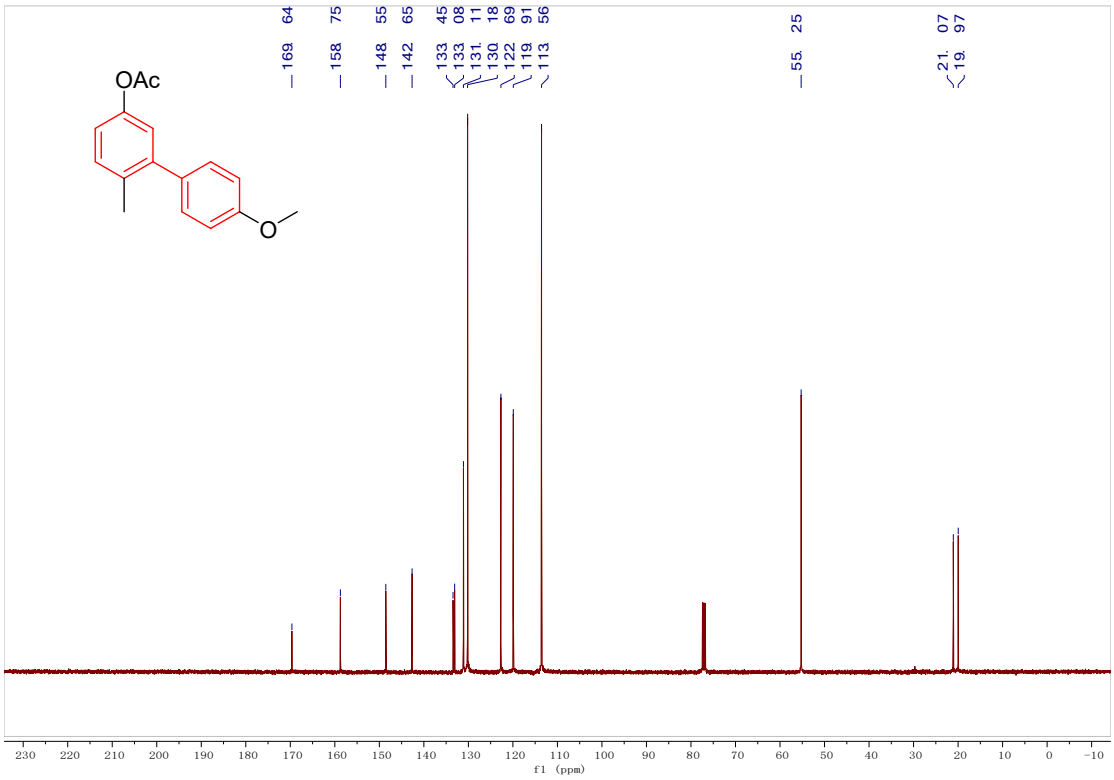
4',6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2b)



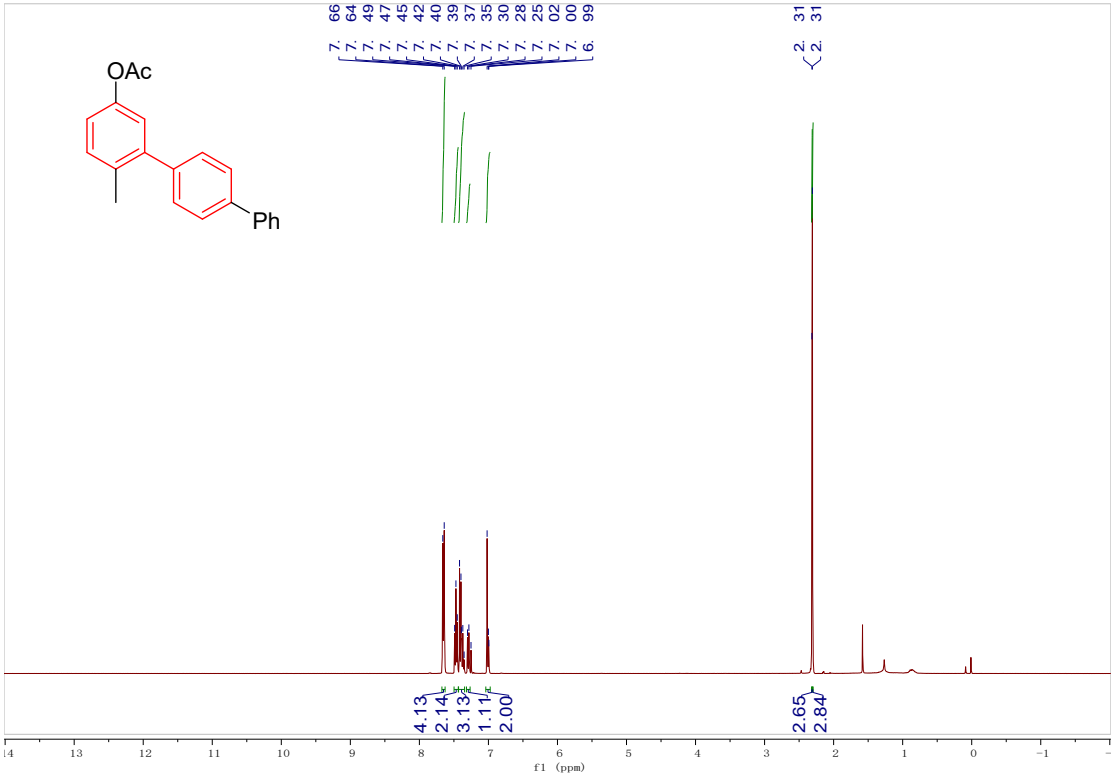


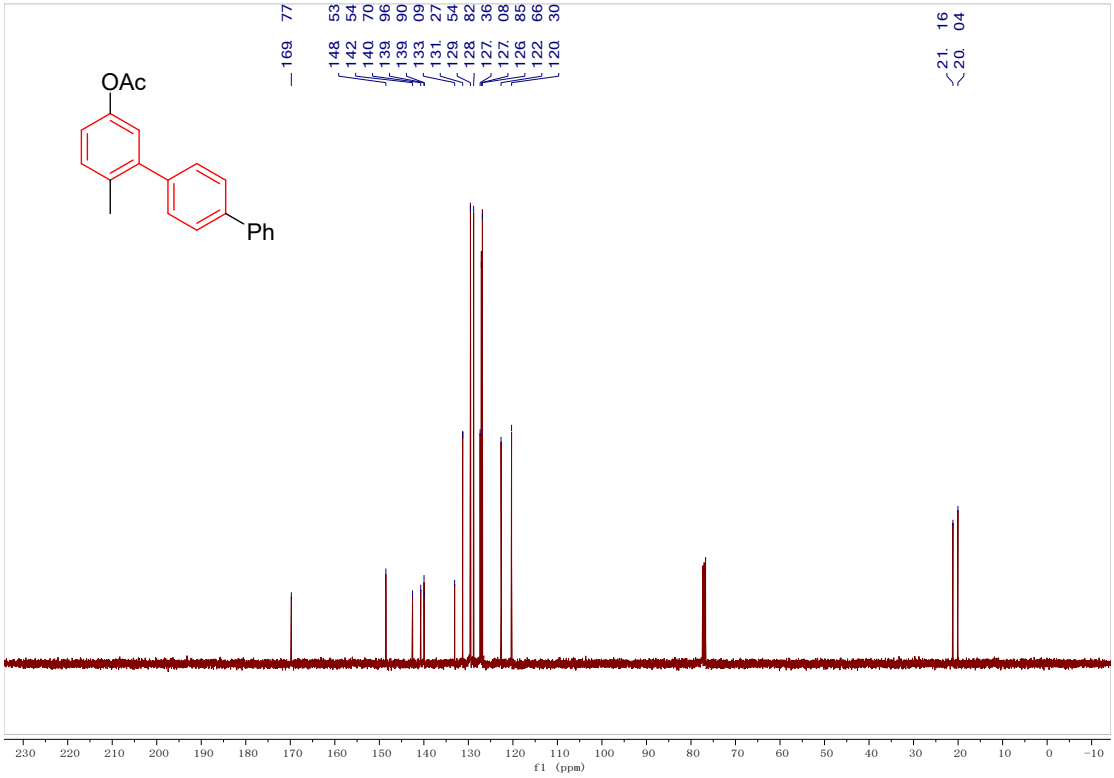
4'-methoxy-6-methyl-[1,1'-biphenyl]-3-yl acetate (2c)



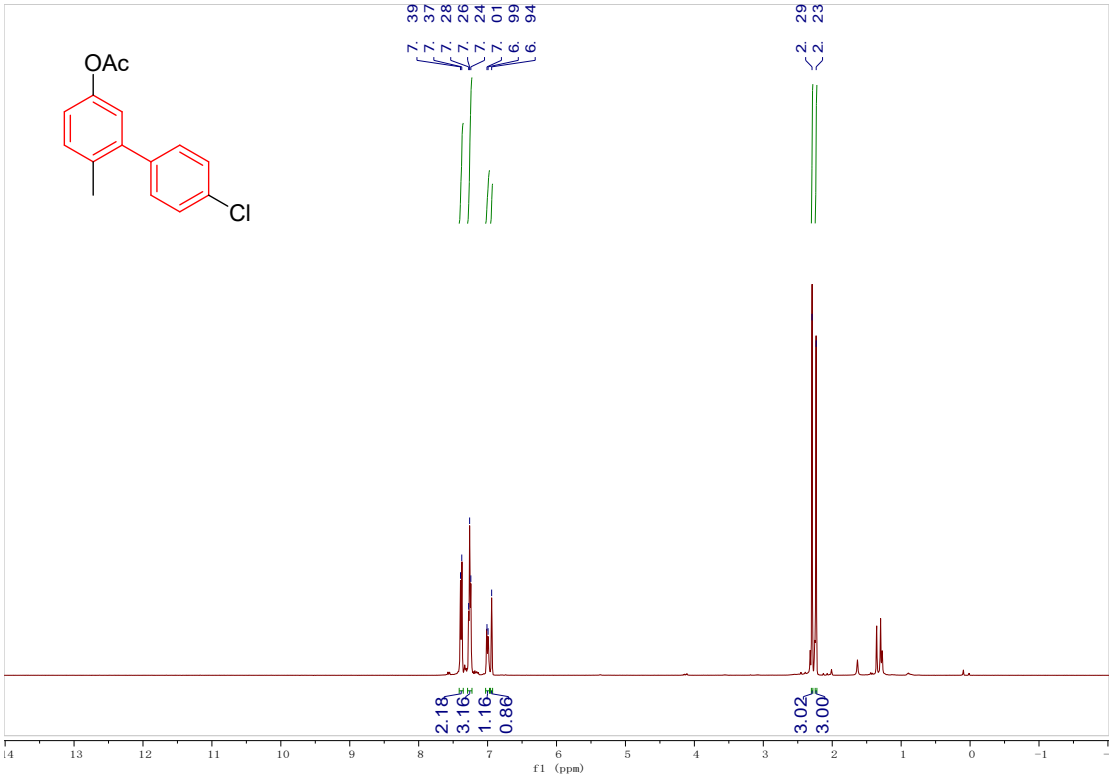


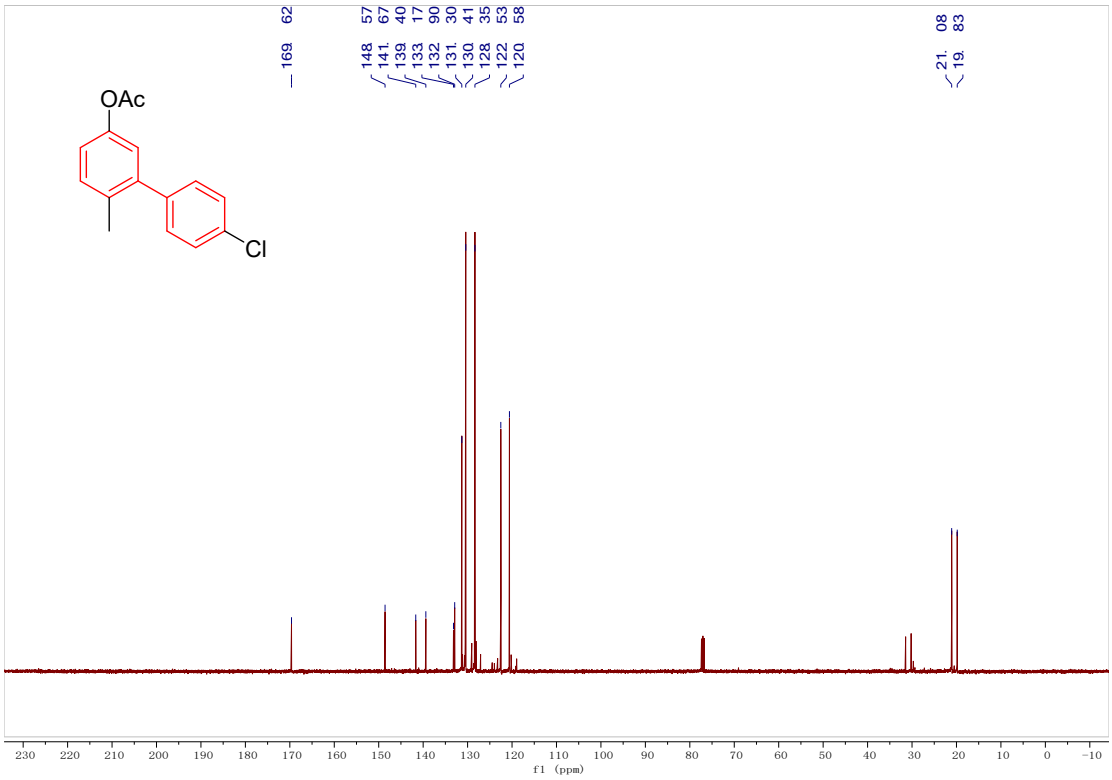
6-methyl-[1,1':4',1''-terphenyl]-3-yl acetate (2d)



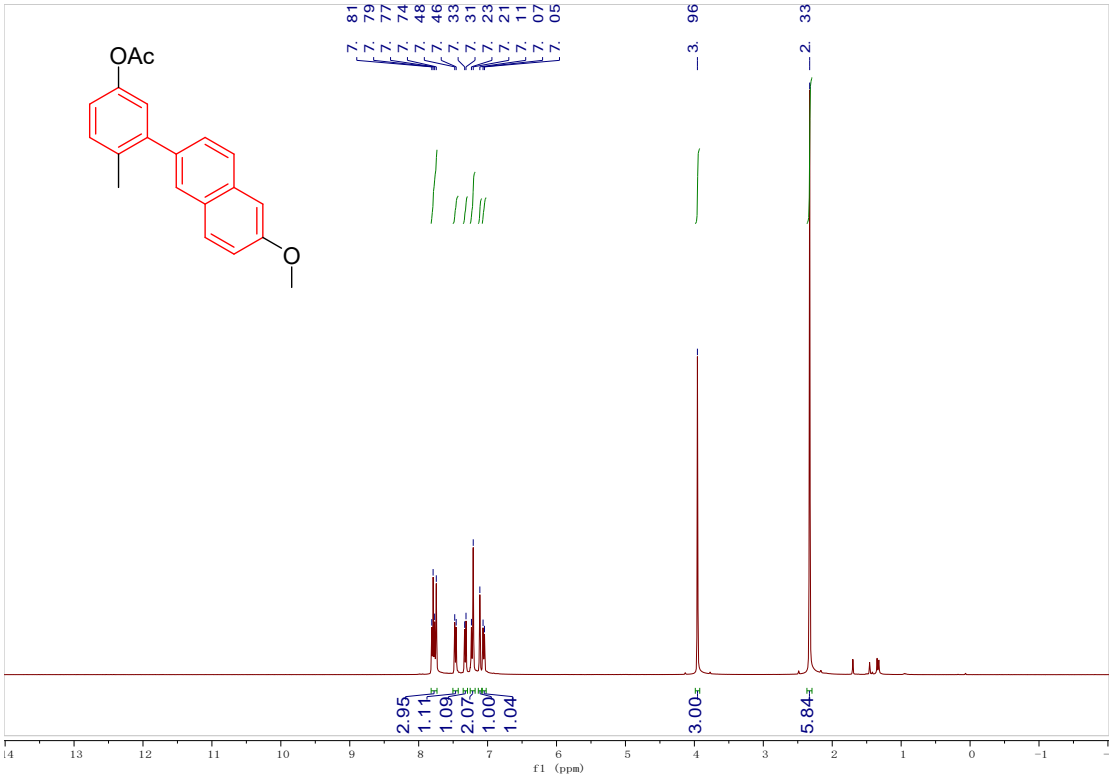


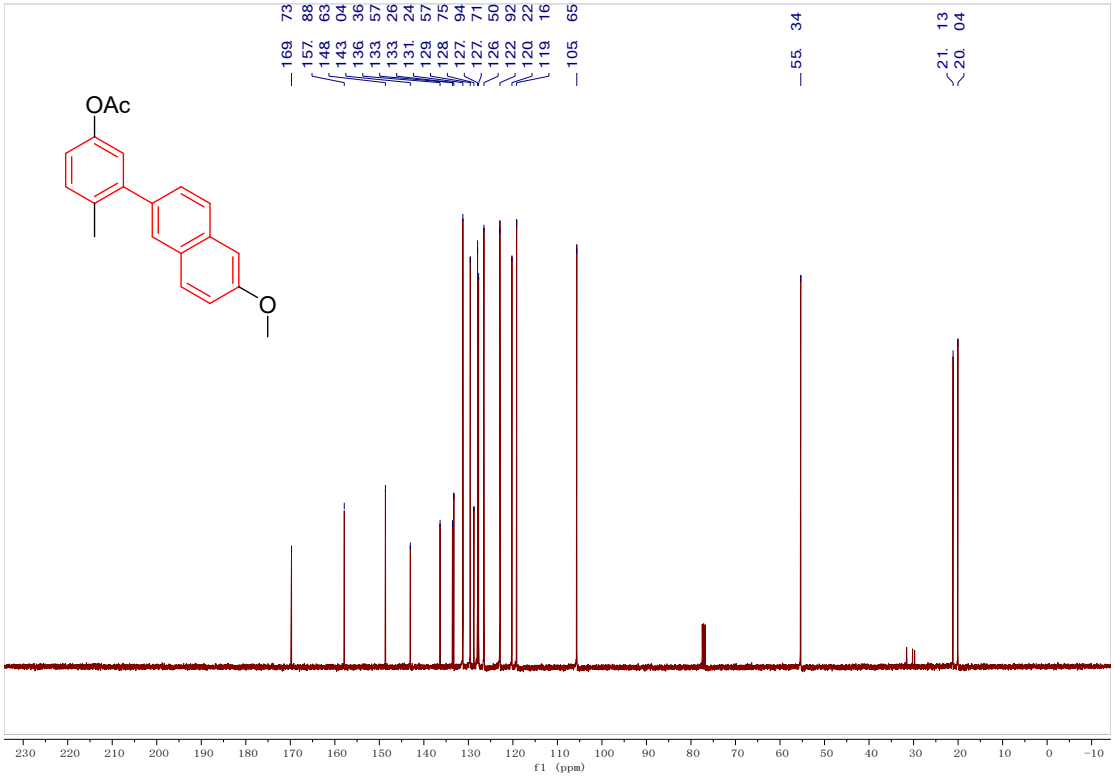
4'-chloro-6-methyl-[1,1'-biphenyl]-3-yl acetate (2e)



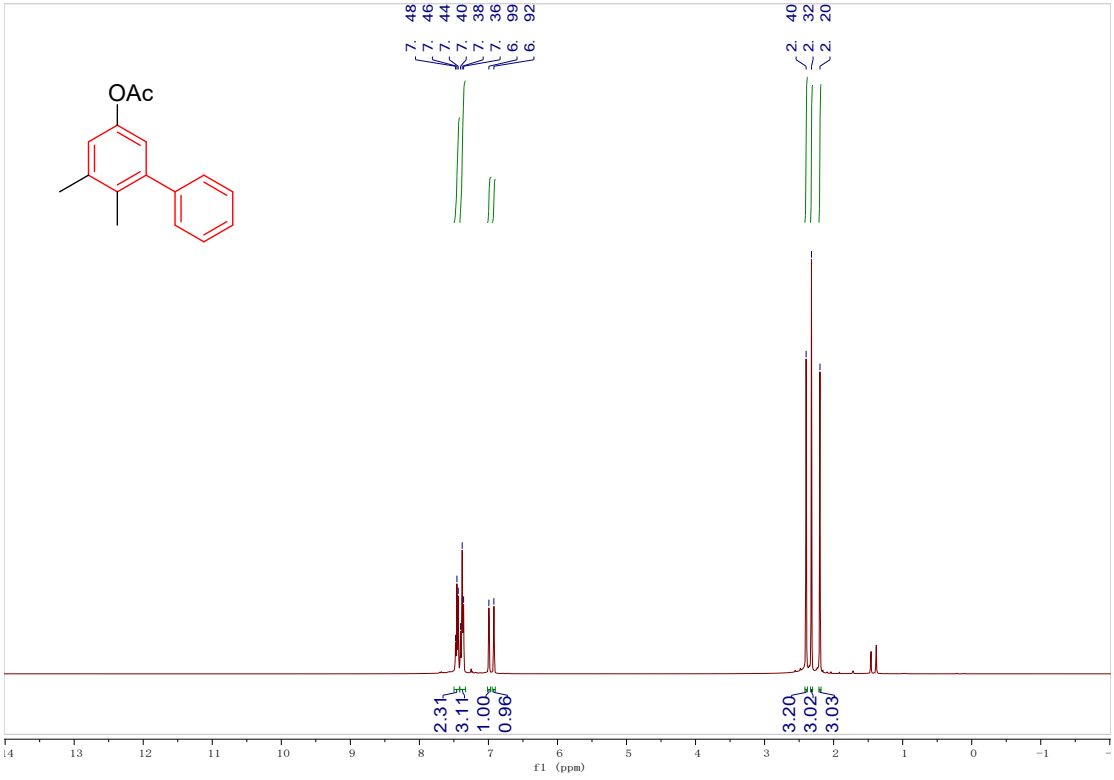


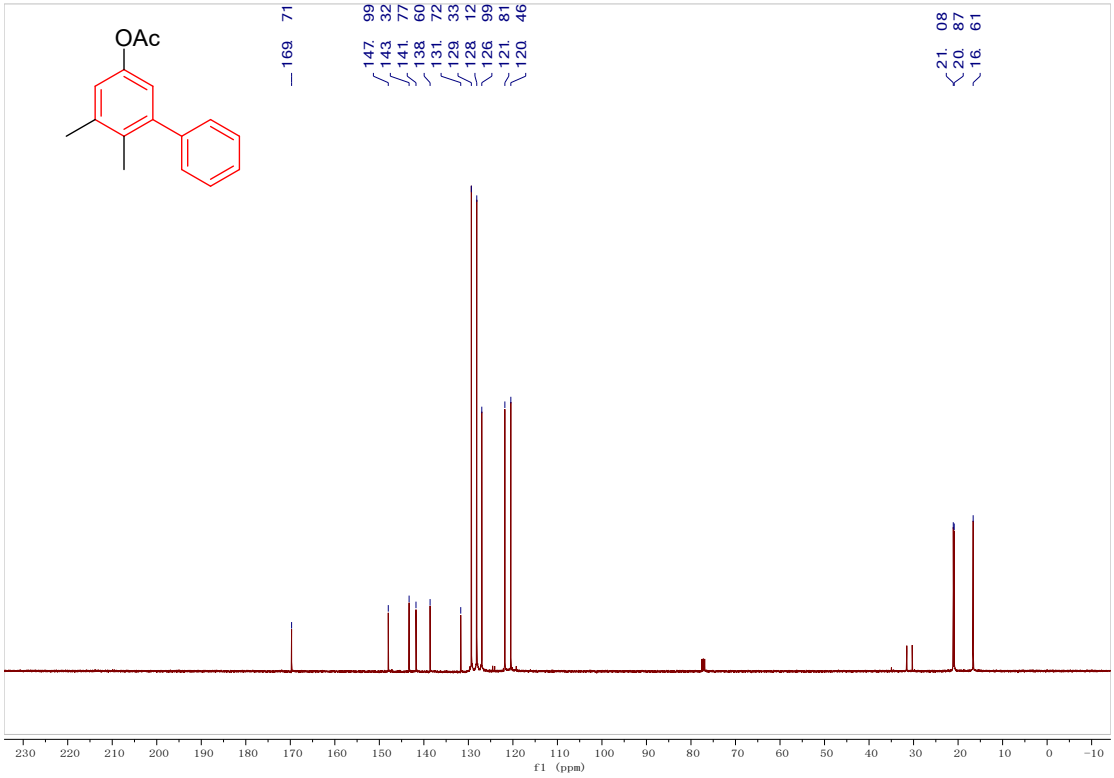
3-(6-methoxynaphthalen-2-yl)-4-methylphenyl acetate (2f)



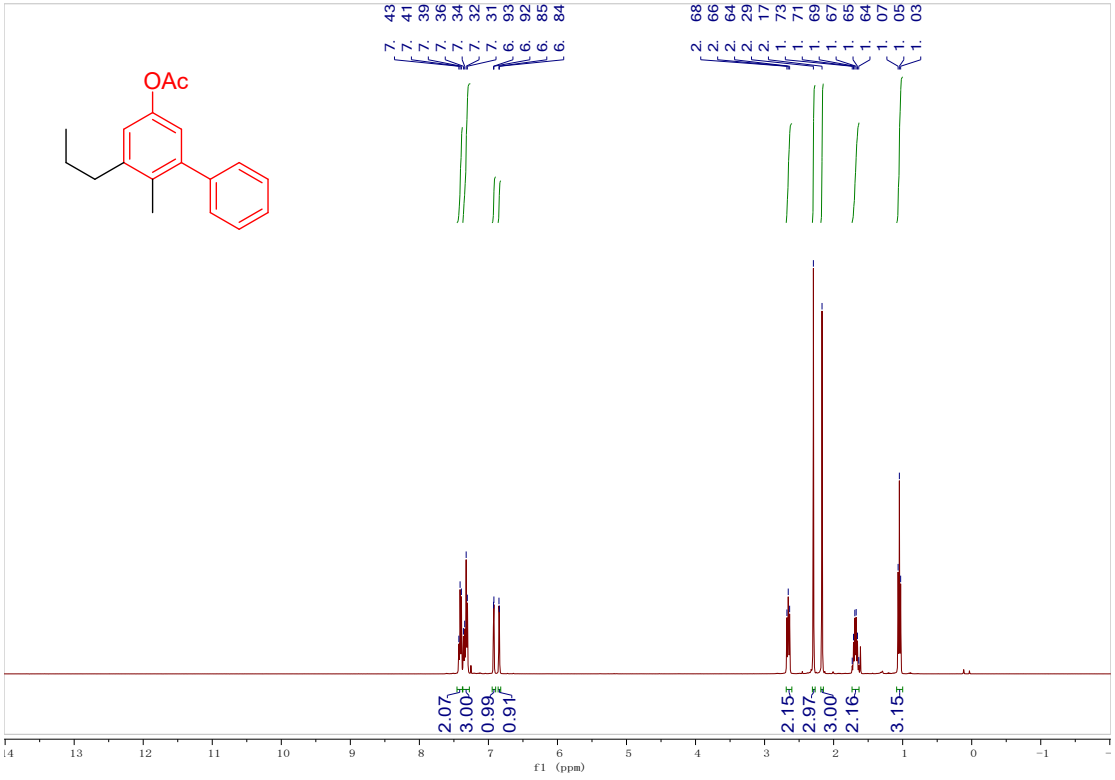


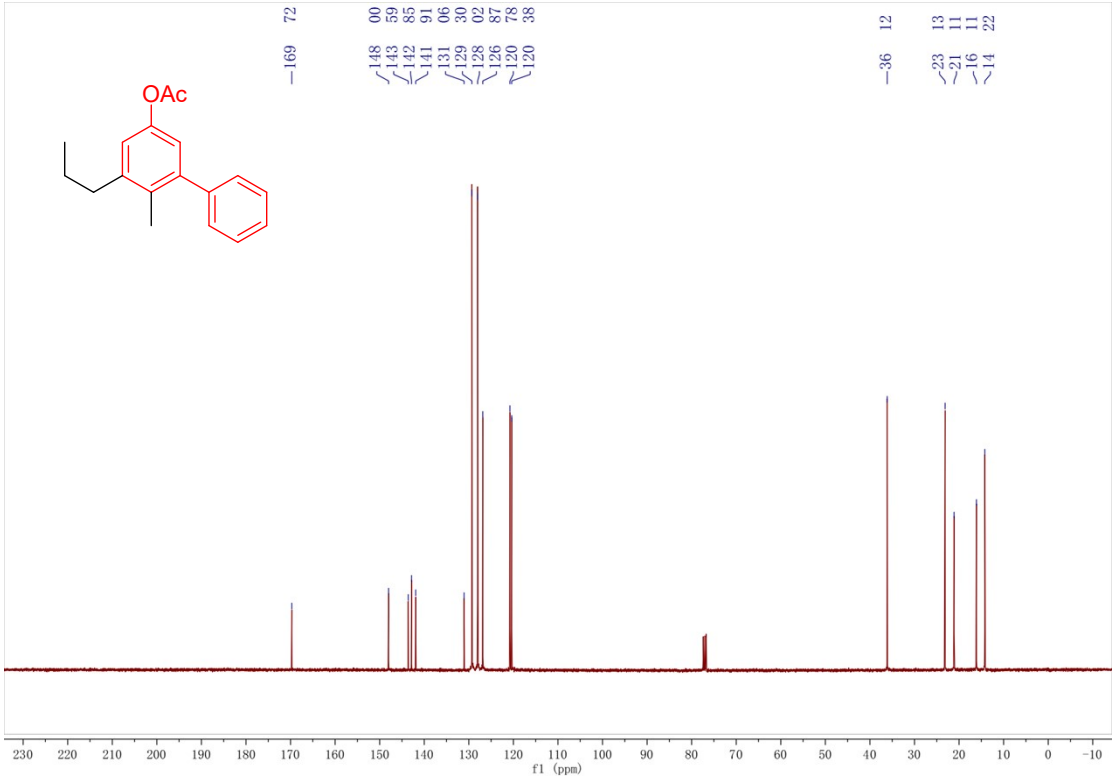
5,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2g)



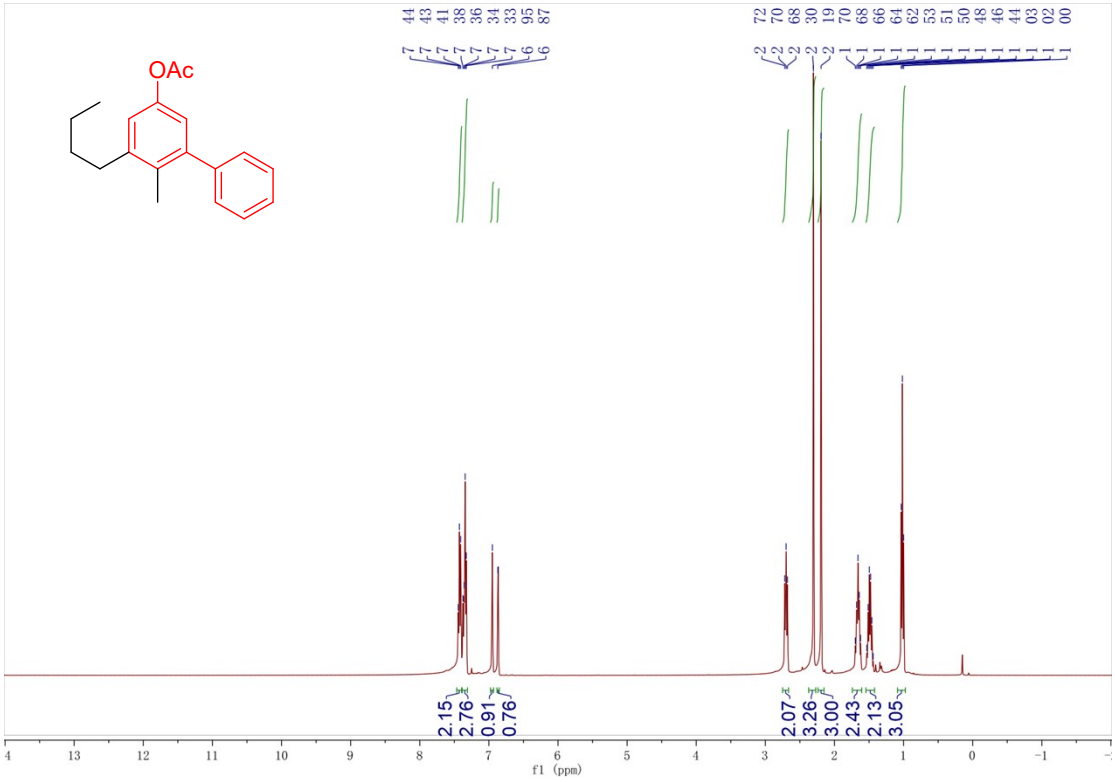


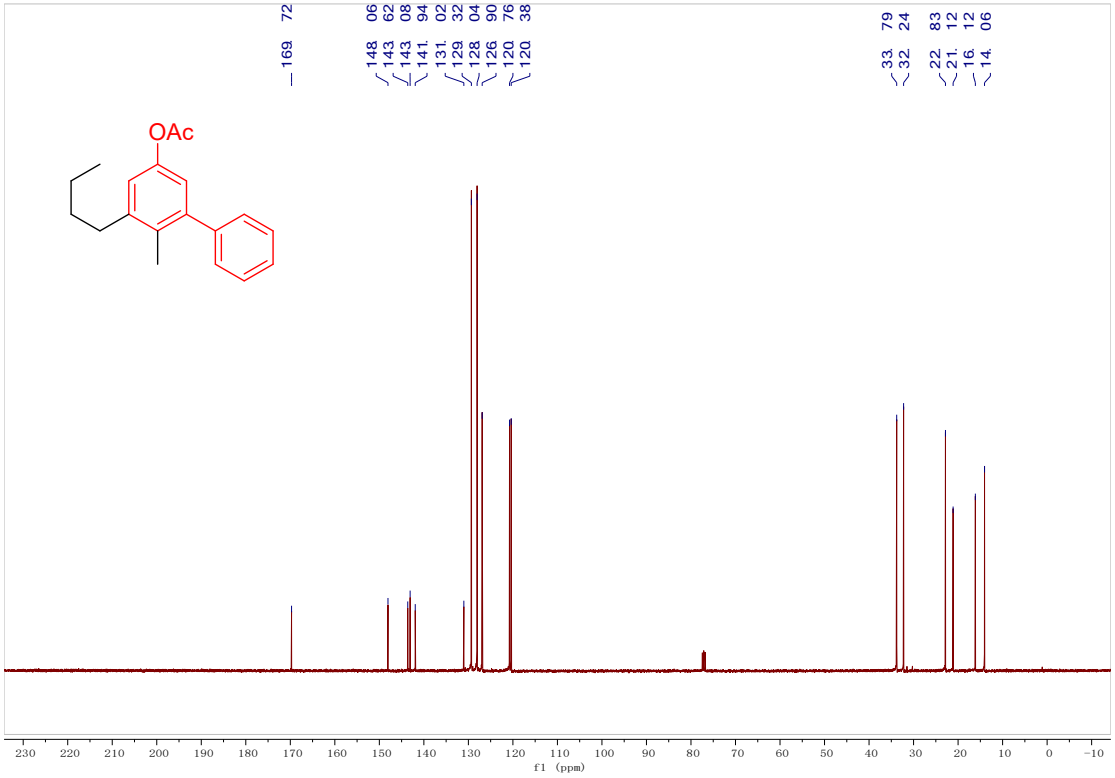
6-methyl-5-propyl-[1,1'-biphenyl]-3-yl acetate (2h)



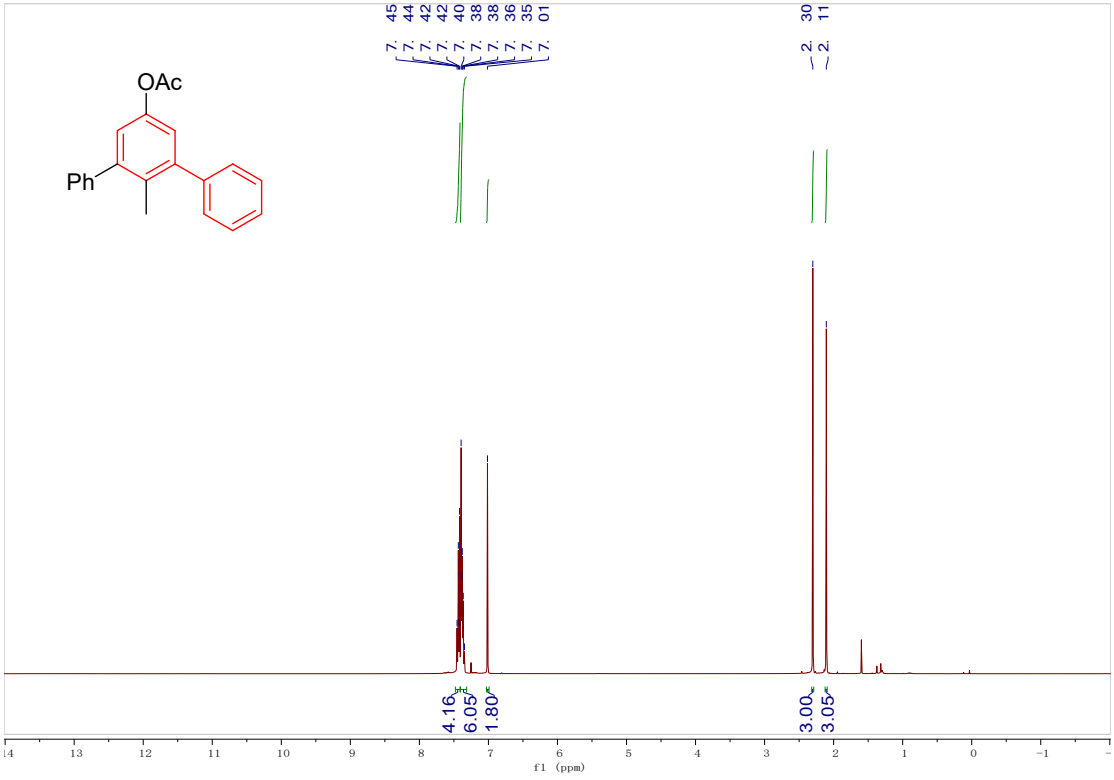


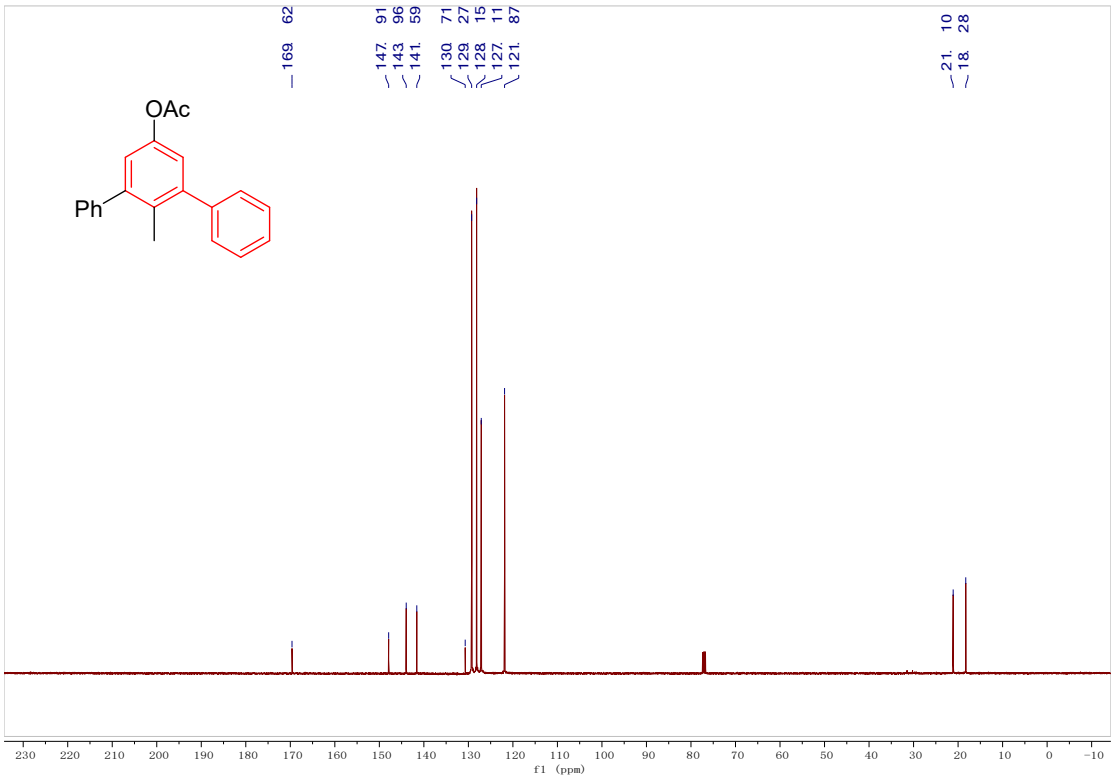
5-butyl-6-methyl-[1,1'-biphenyl]-3-yl acetate (2i)



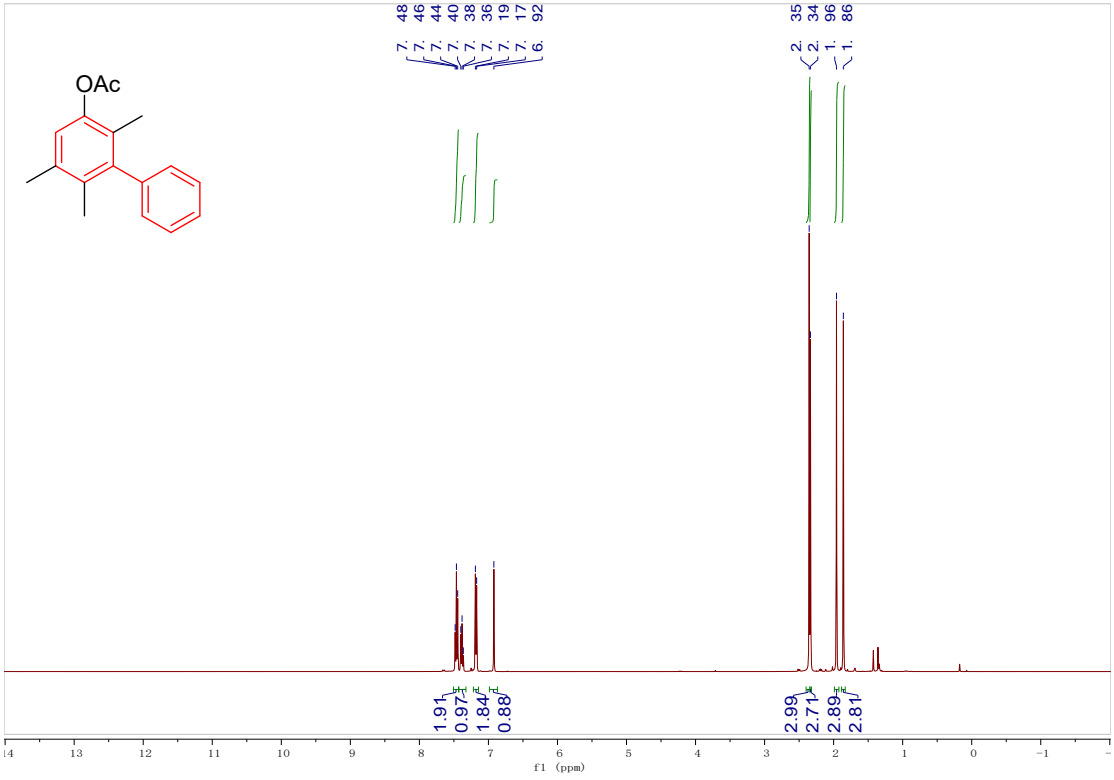


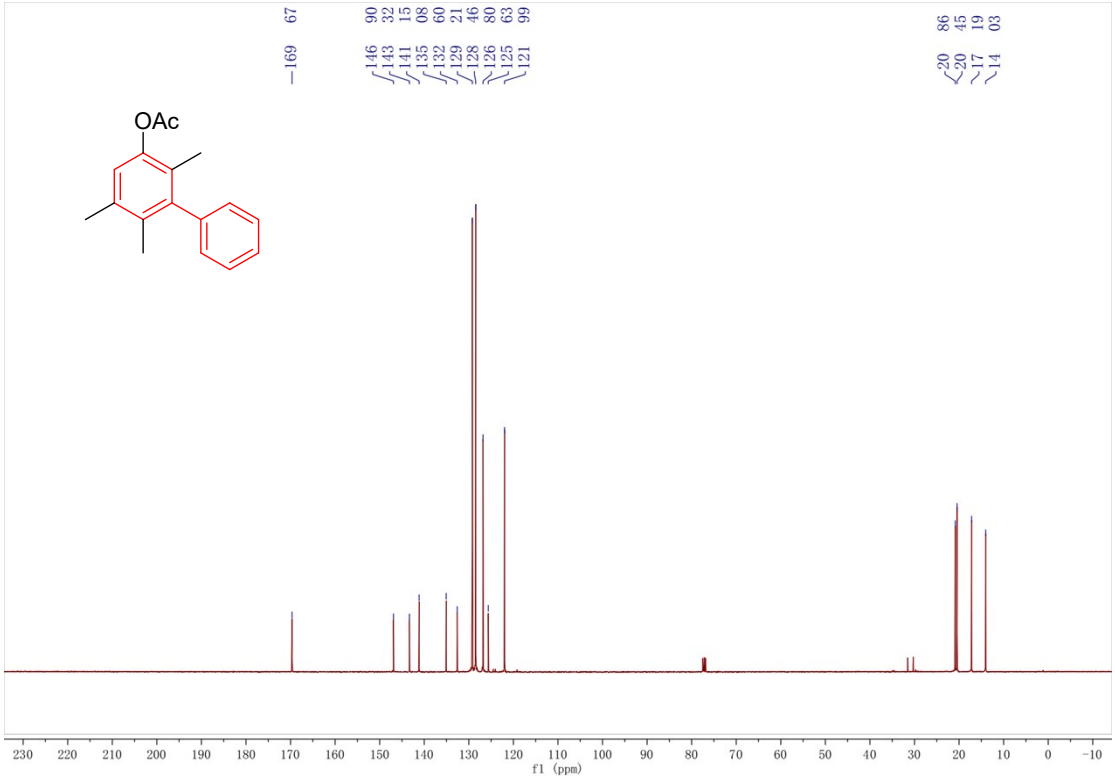
2'-methyl-[1,1':3',1''-terphenyl]-5'-yl acetate (2j)



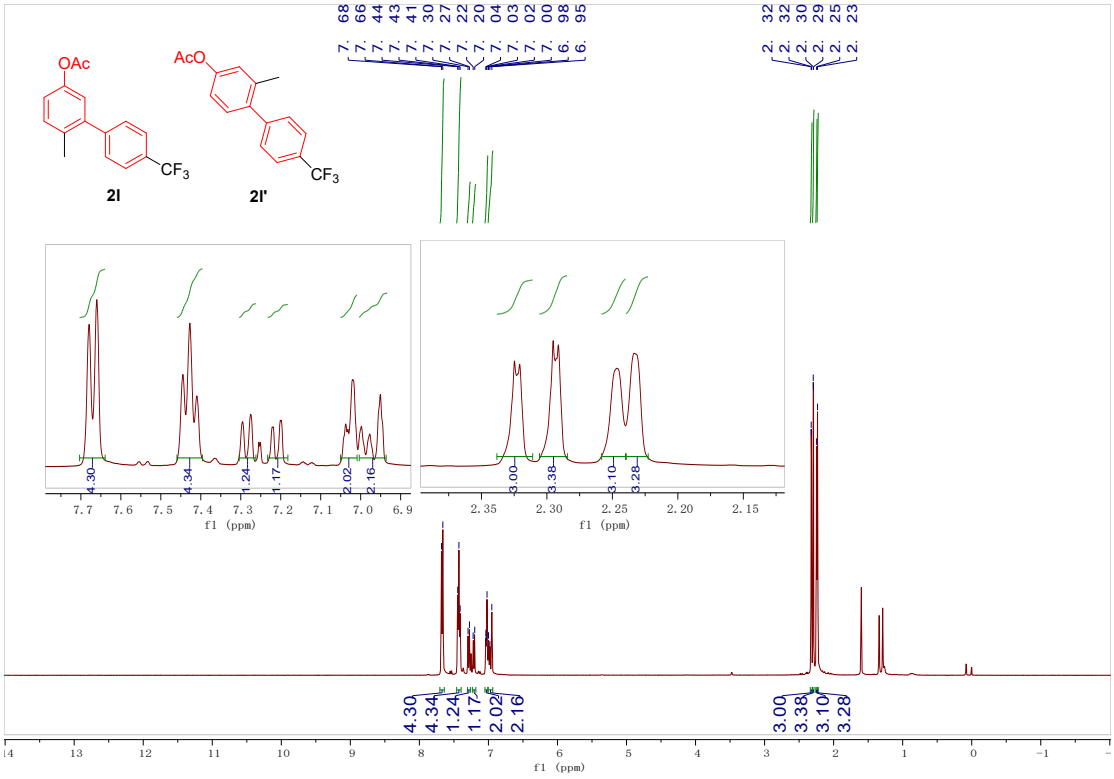


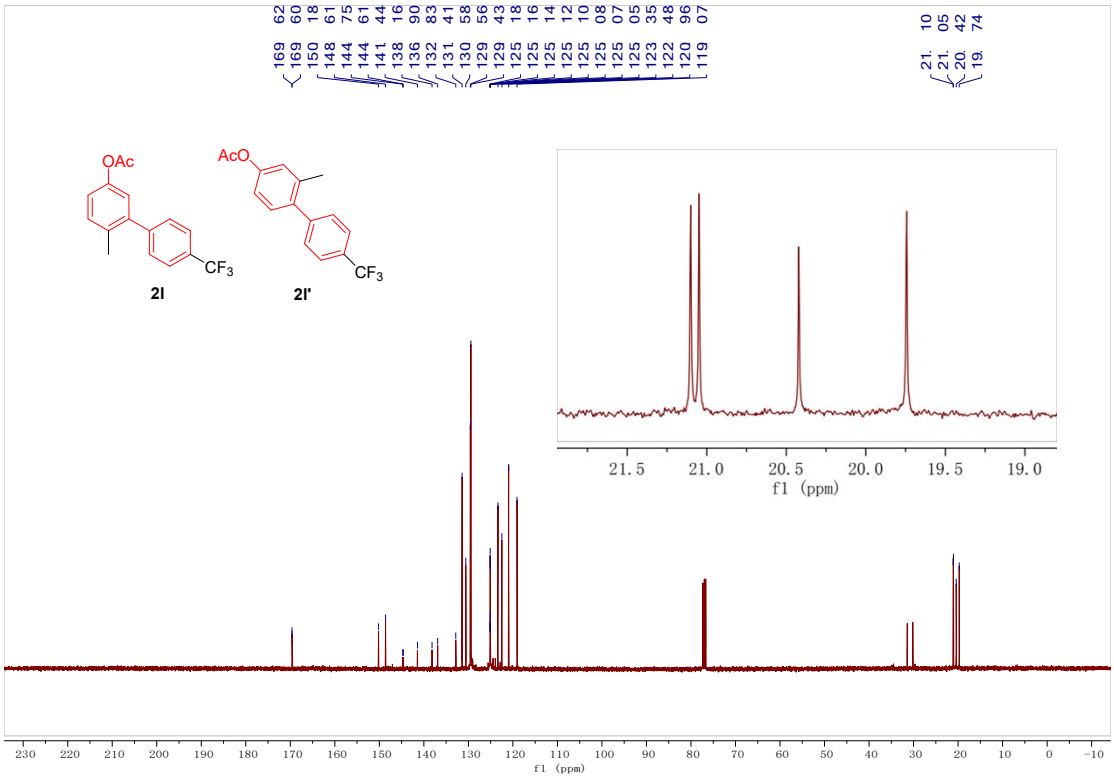
2,5,6-trimethyl-[1,1'-biphenyl]-3-yl acetate (2k)



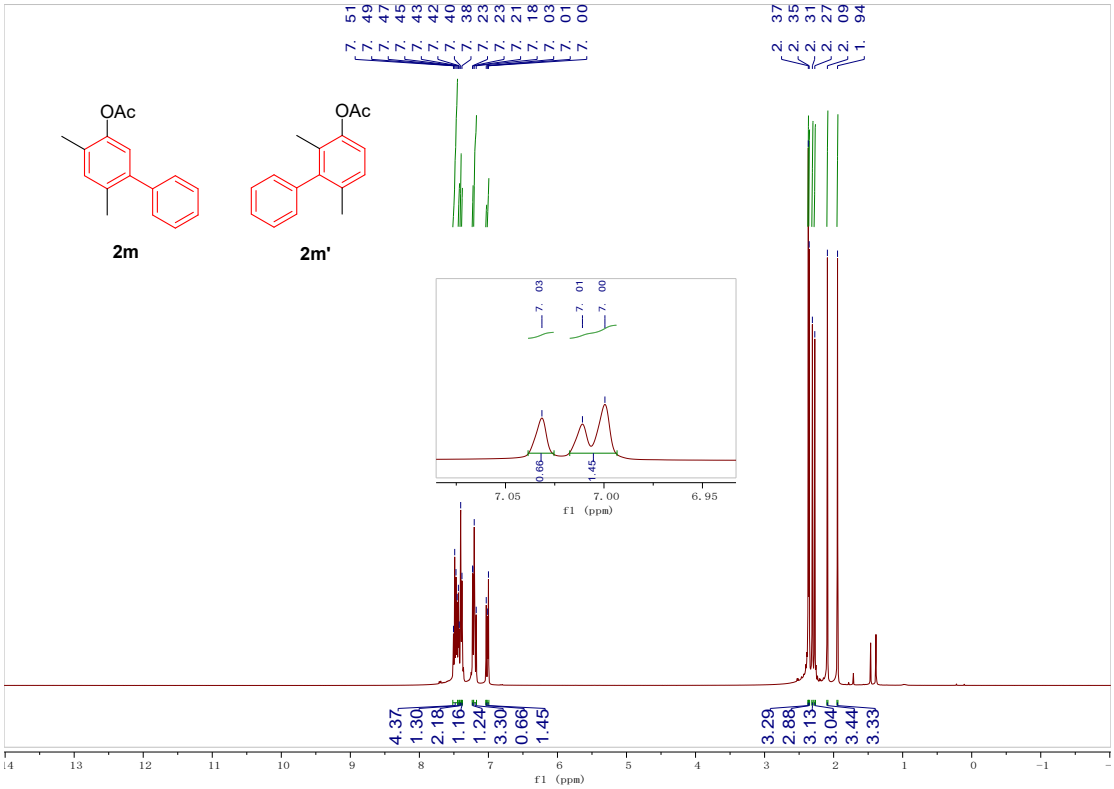


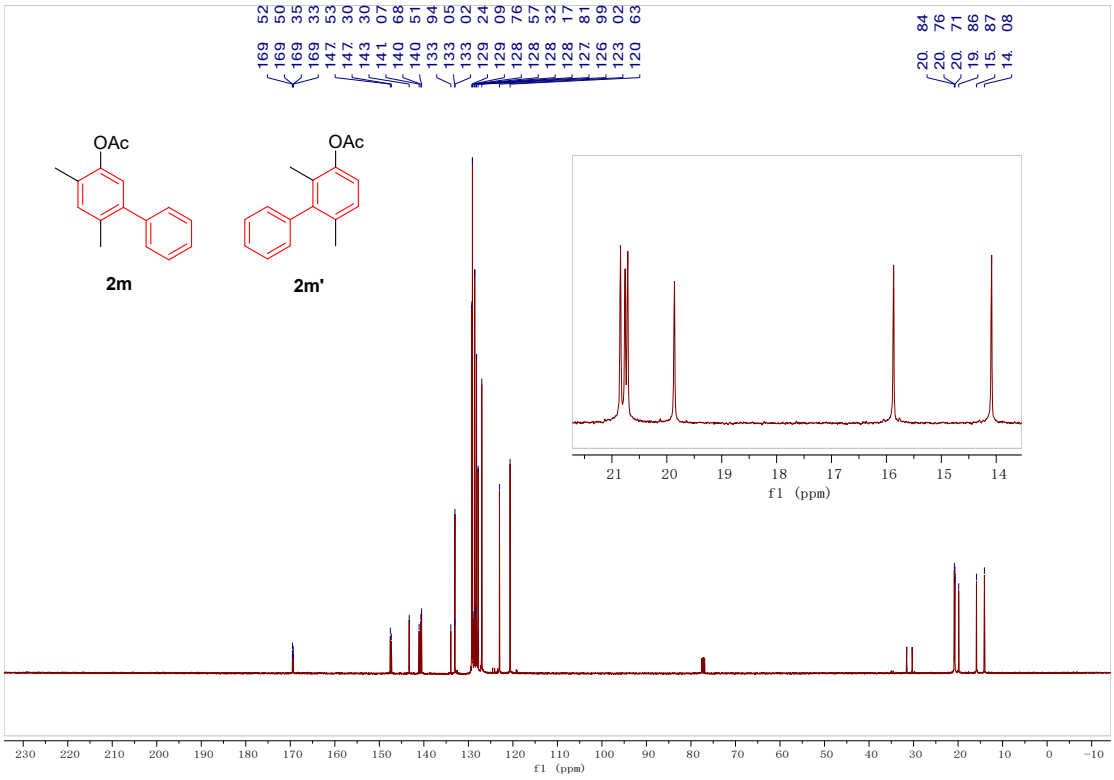
6-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-3-yl acetate (2l) and 2-methyl-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-yl acetate (2l')



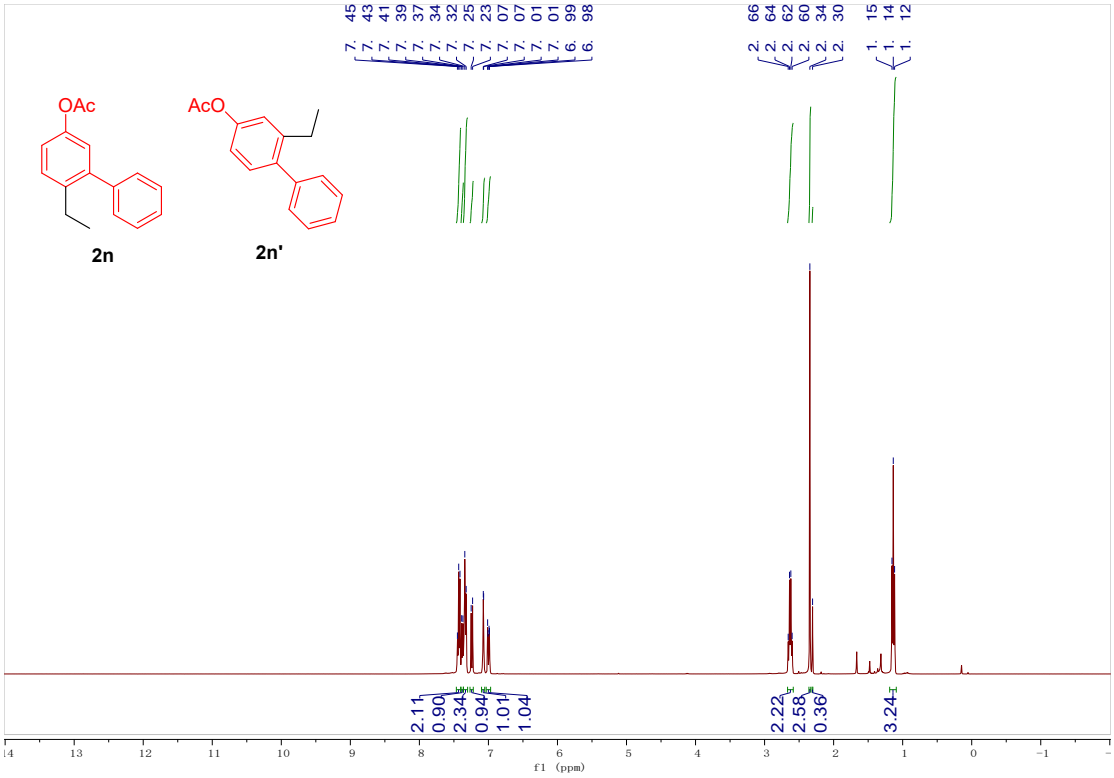


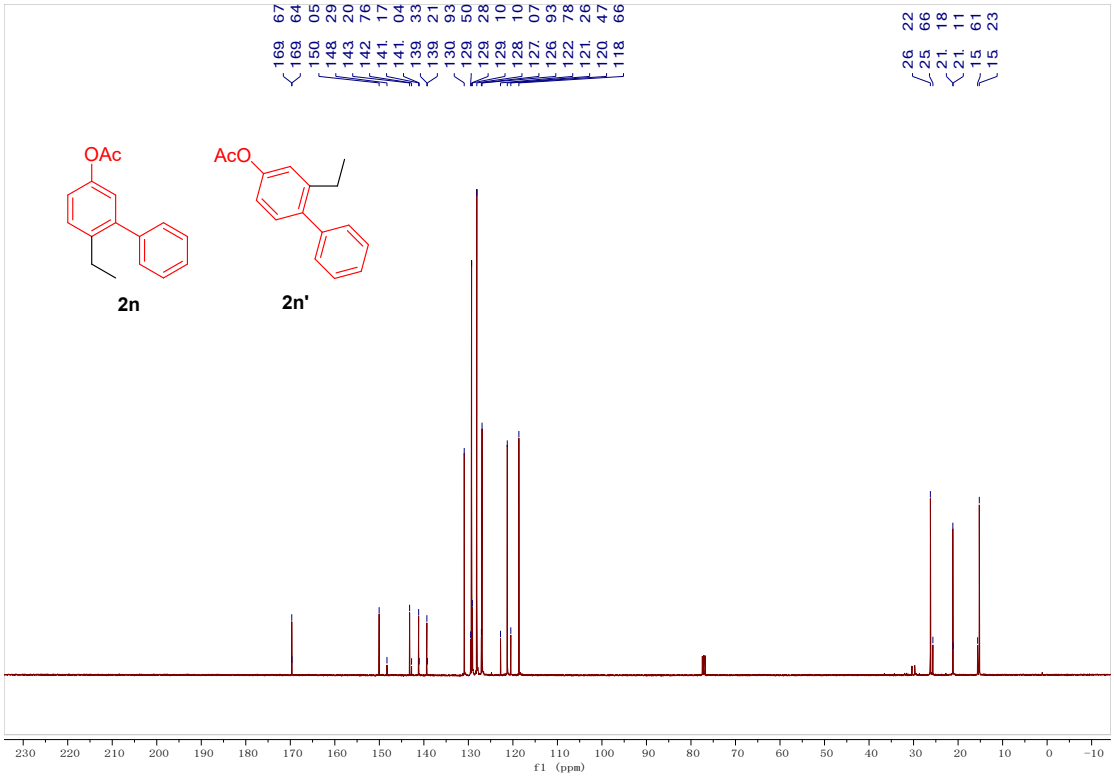
4,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2m) and 2,6-dimethyl-[1,1'-biphenyl]-3-yl acetate (2m')



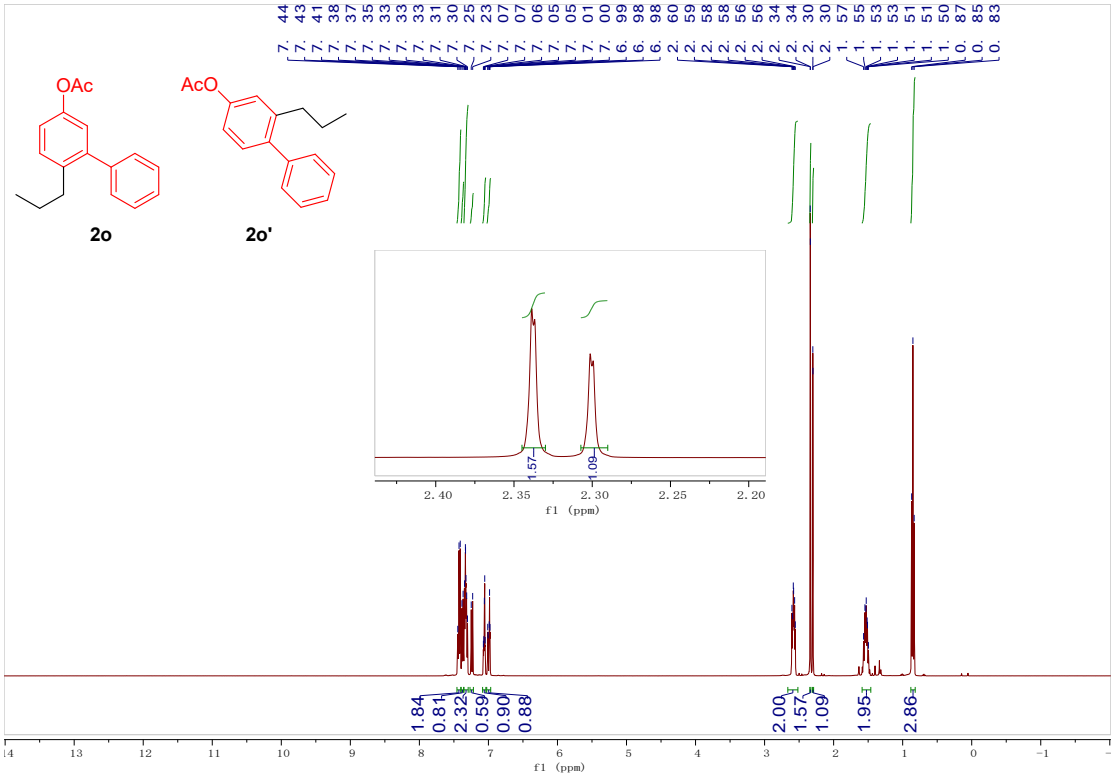


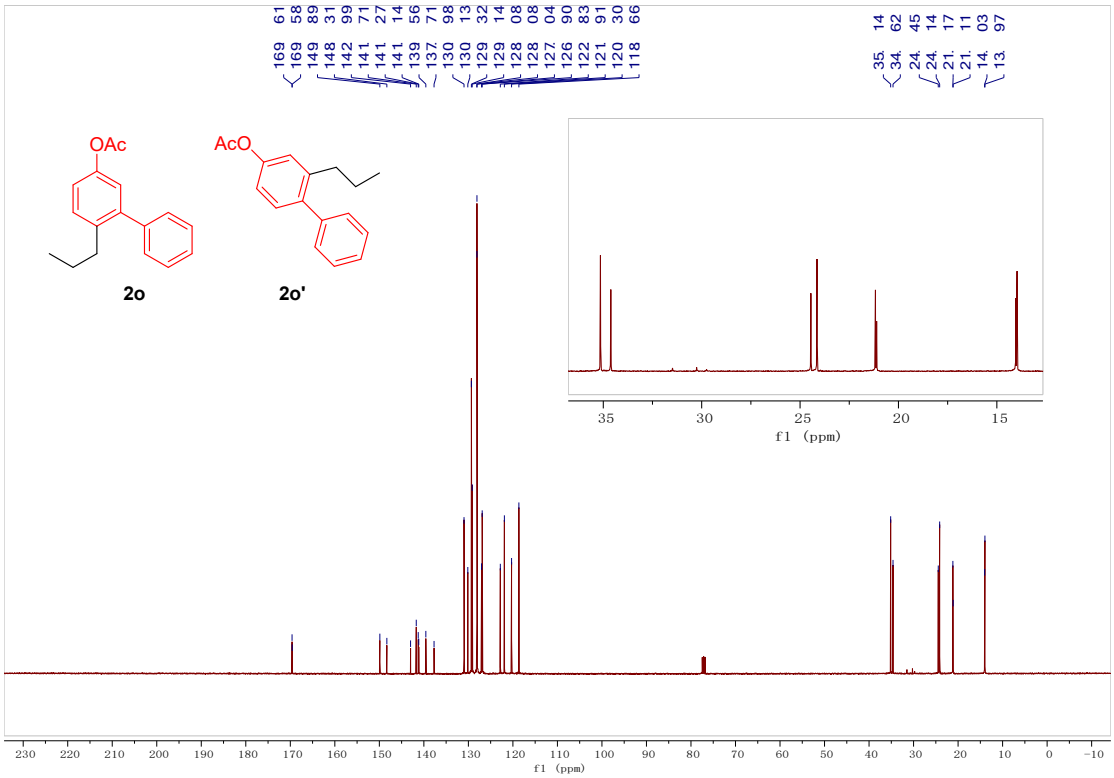
6-ethyl-[1,1'-biphenyl]-3-yl acetate (2n) and 2-ethyl-[1,1'-biphenyl]-4-yl acetate (2n')



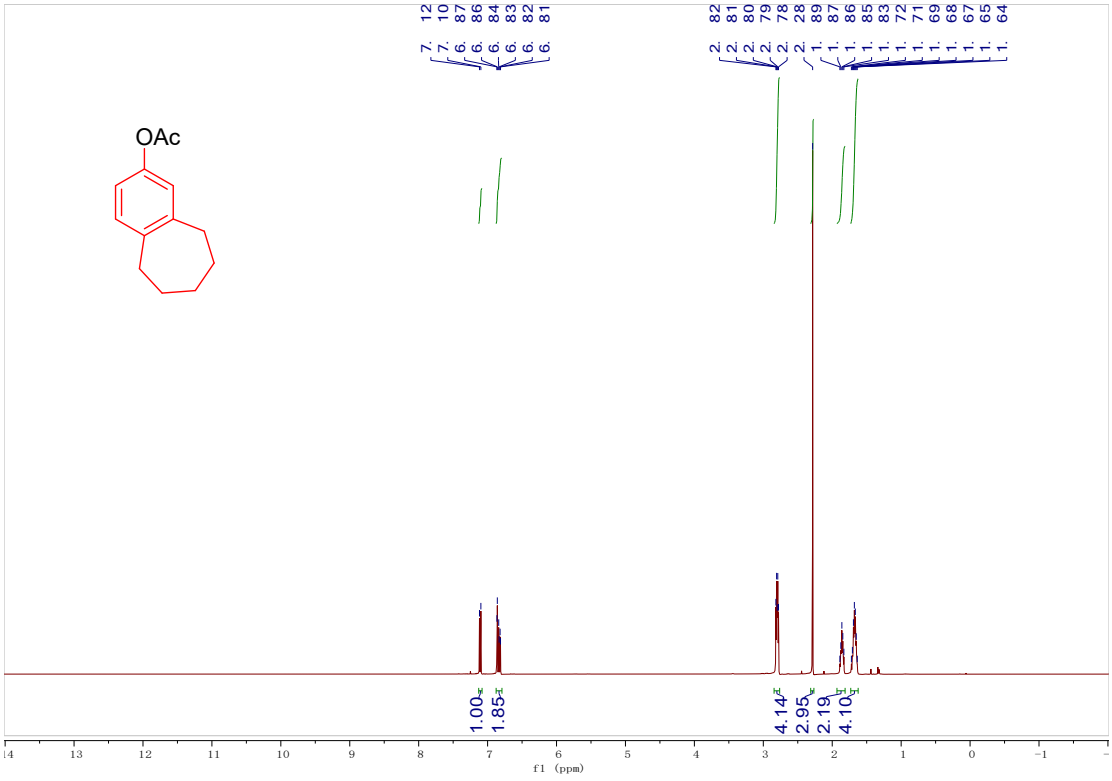


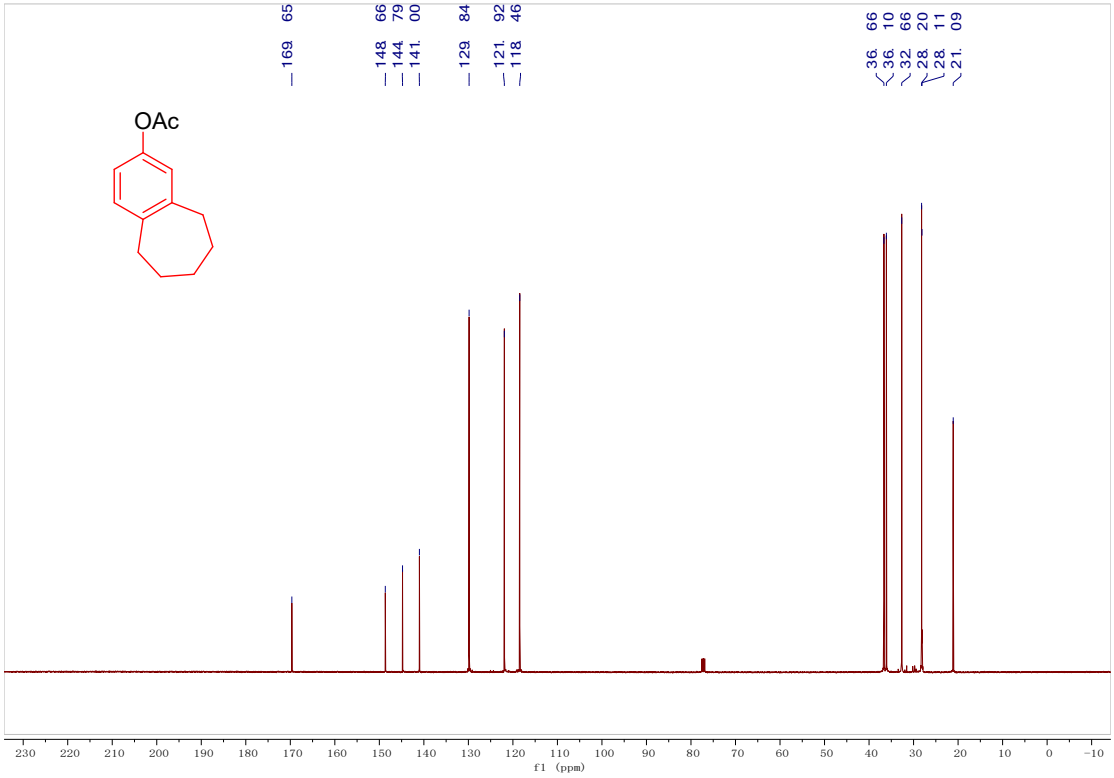
6-propyl-[1,1'-biphenyl]-3-yl acetate (2o) and 2-propyl-[1,1'-biphenyl]-4-yl acetate (2o')



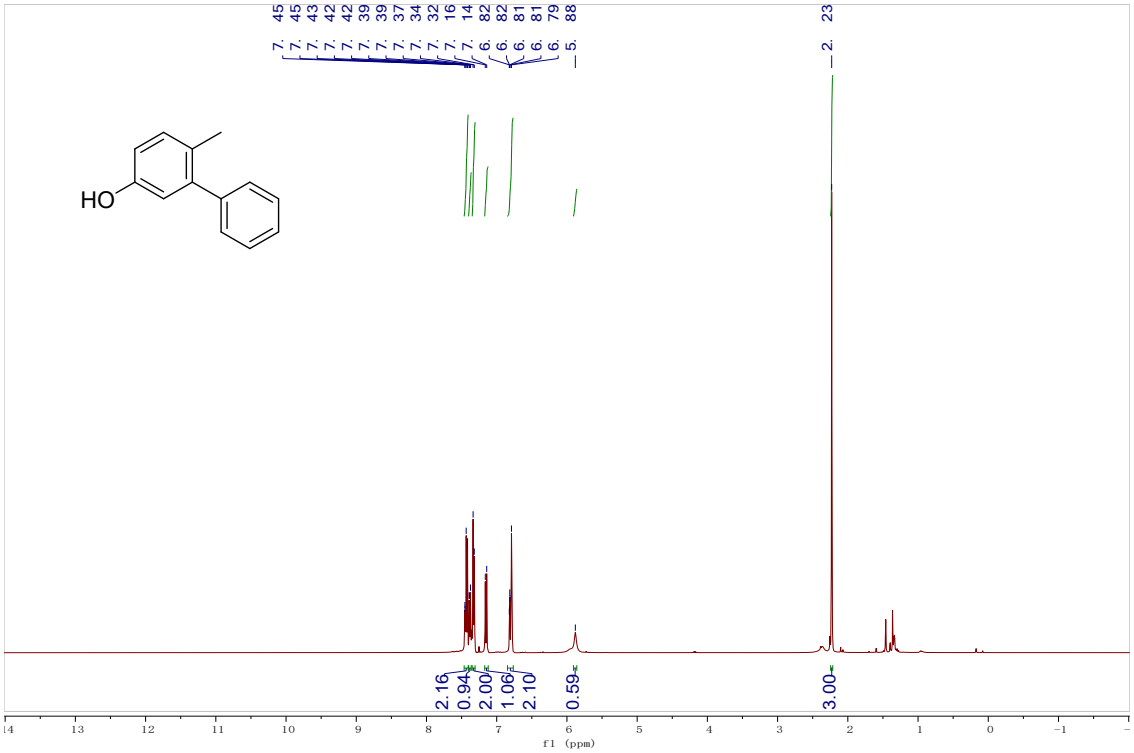


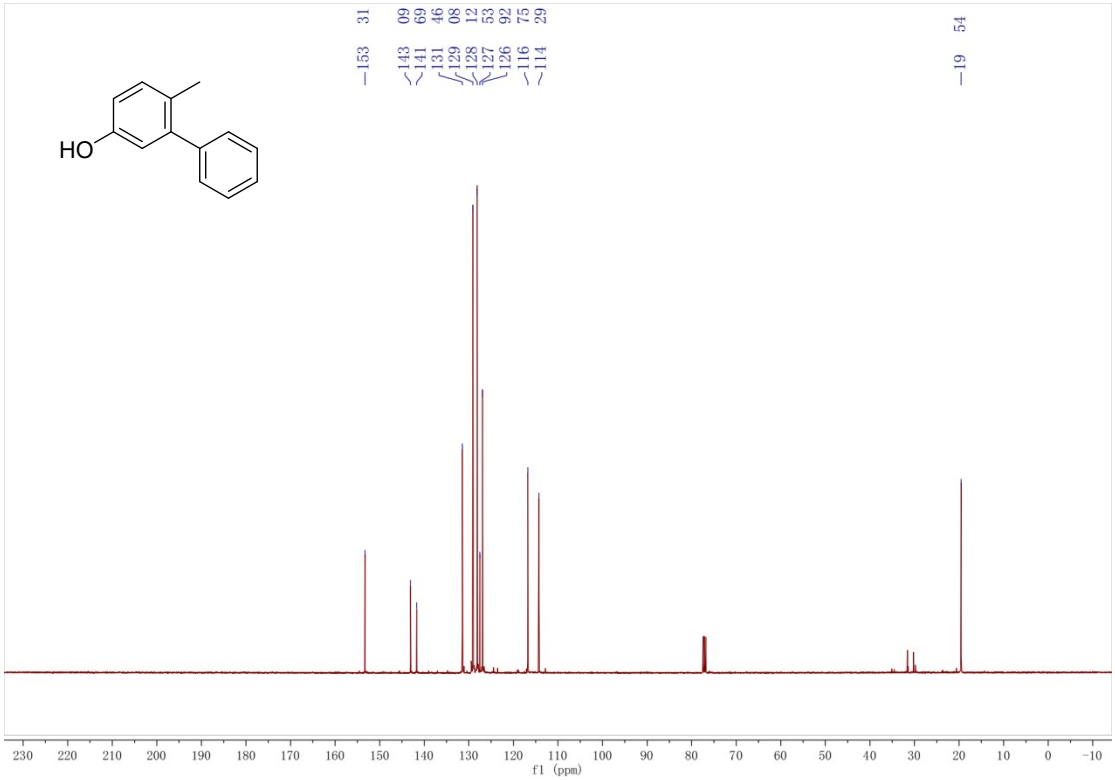
6,7,8,9-tetrahydro-5H-benzo[7]annulen-2-yl acetate (2p)



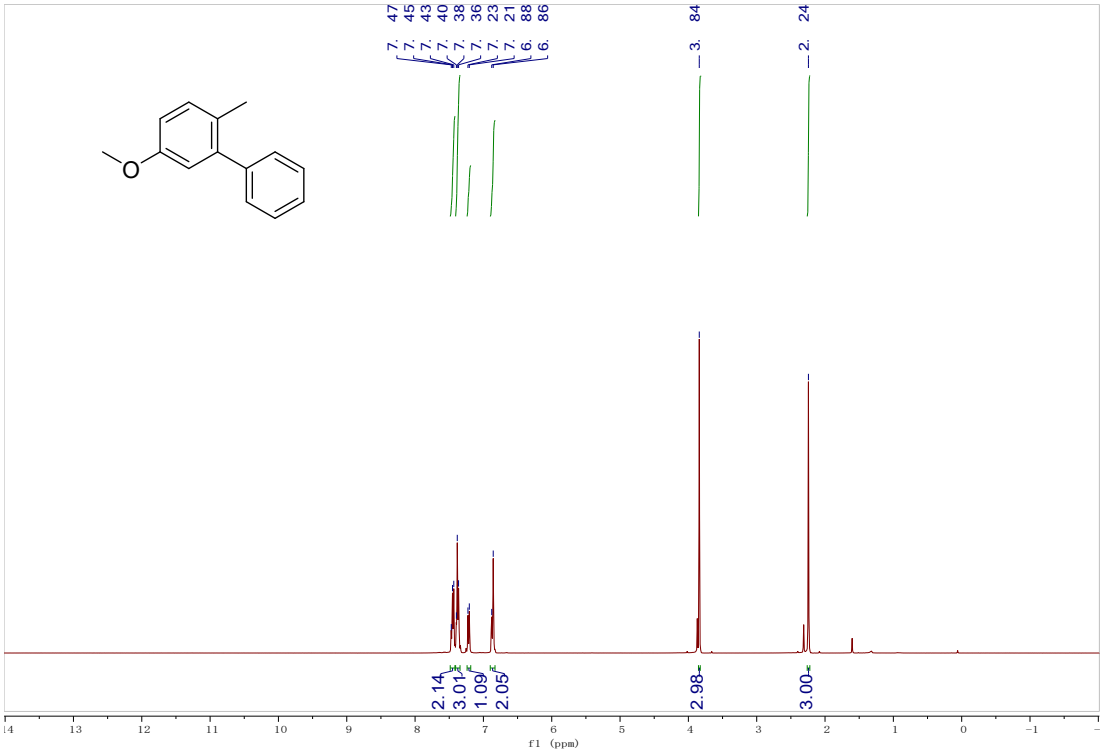


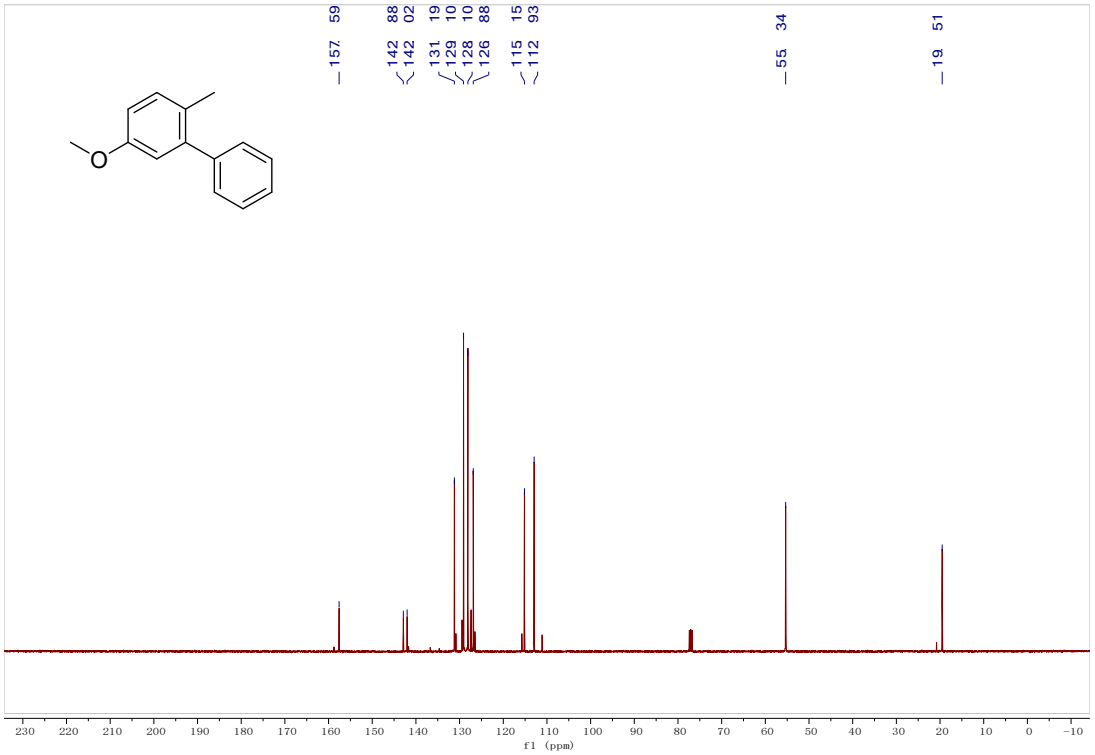
6-methyl-[1,1'-biphenyl]-3-ol (2a')



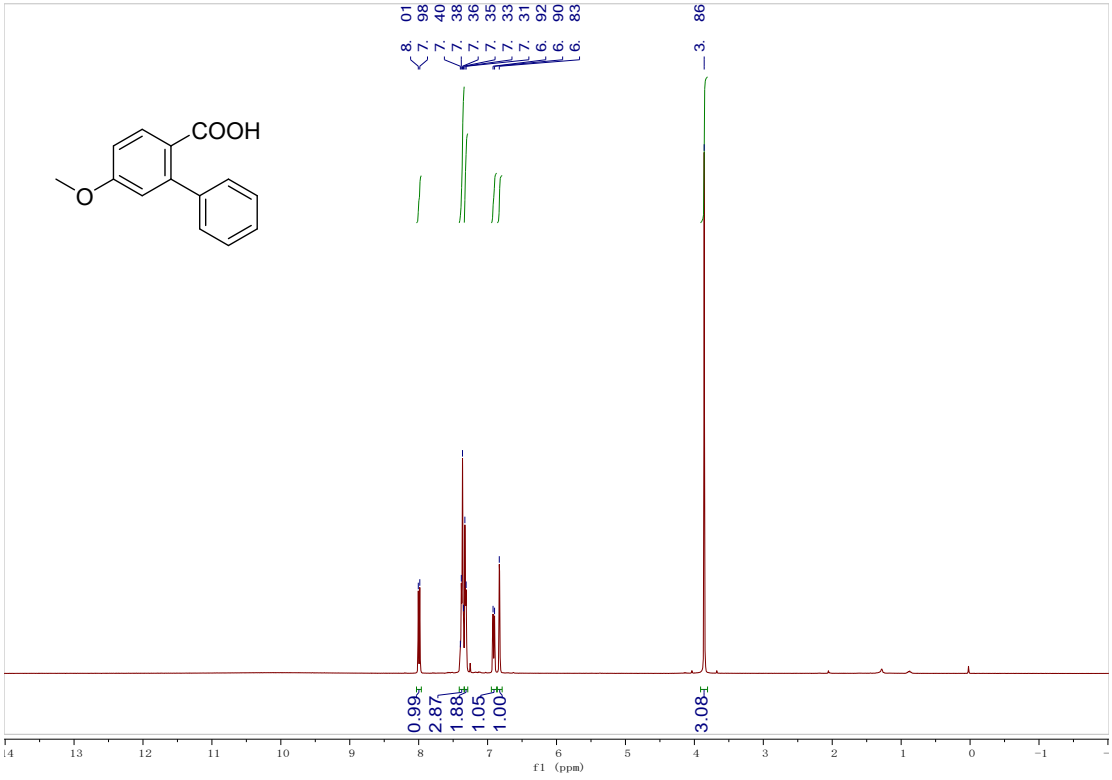


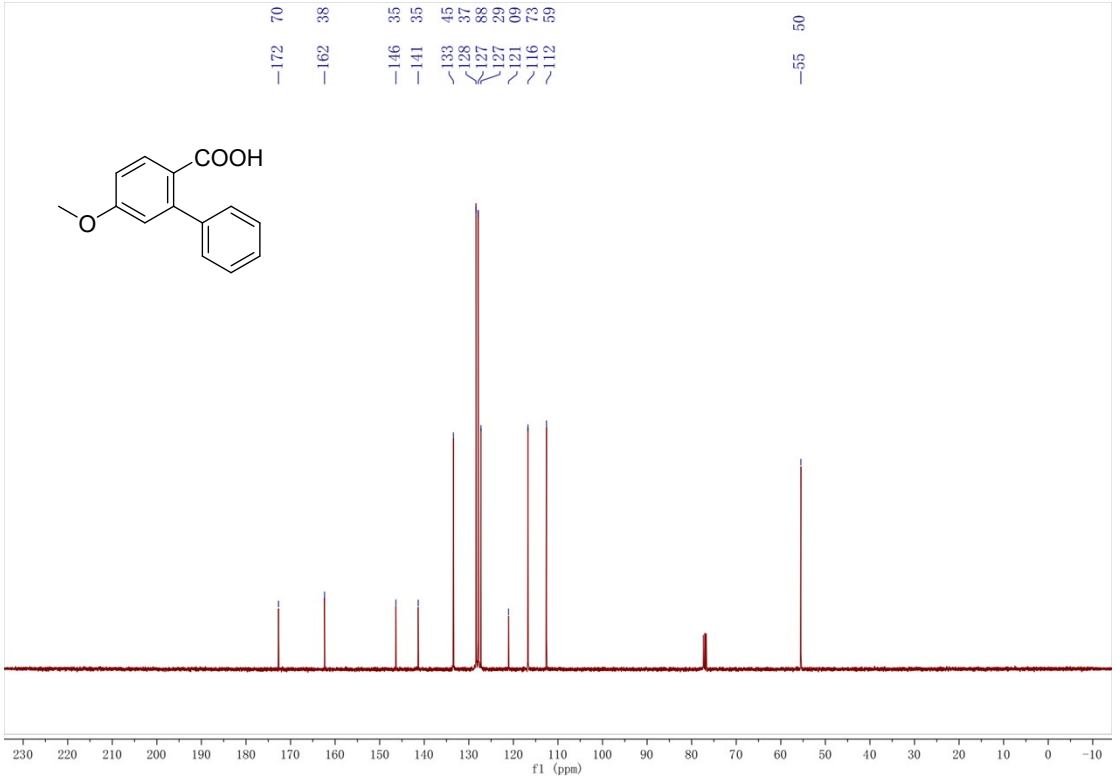
5-methoxy-2-methyl-1,1'-biphenyl (3)



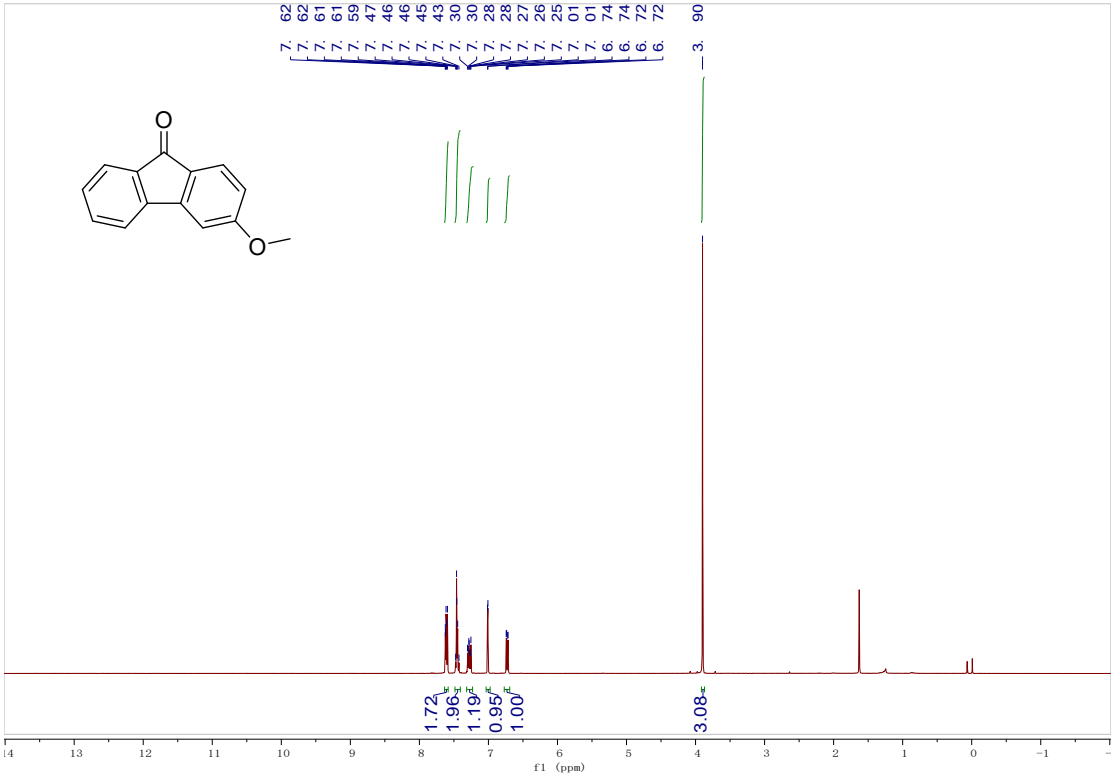


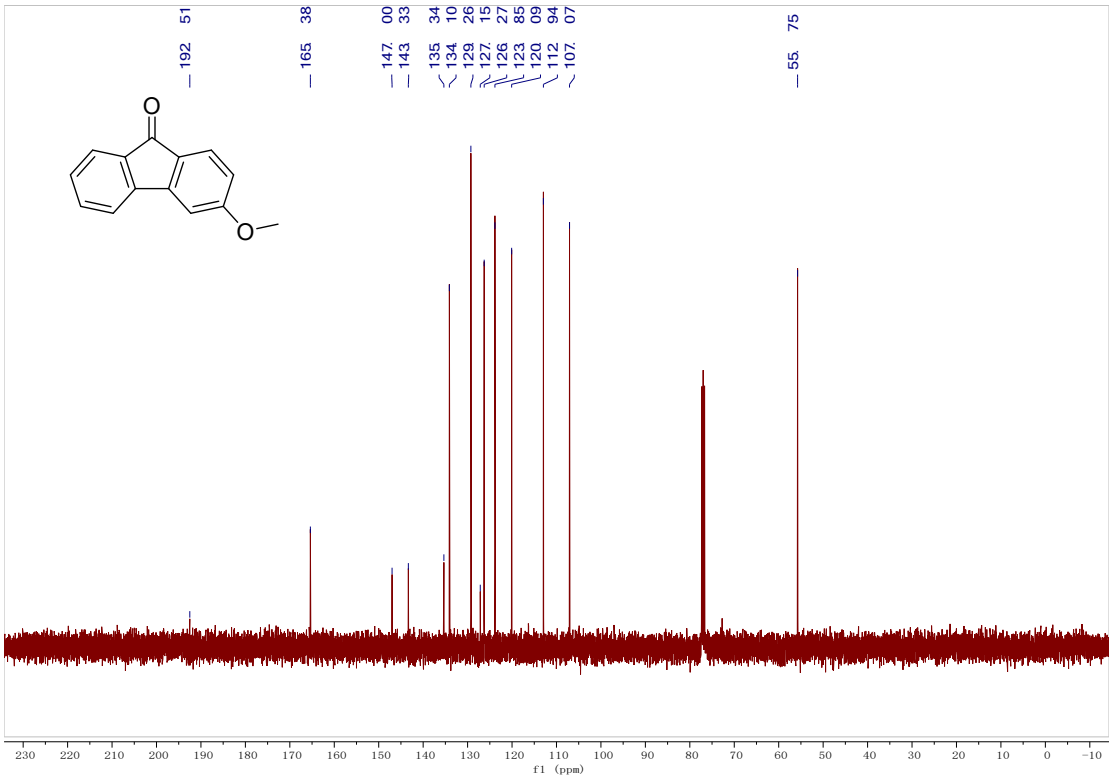
5-methoxy-[1,1'-biphenyl]-2-carboxylic acid (4)



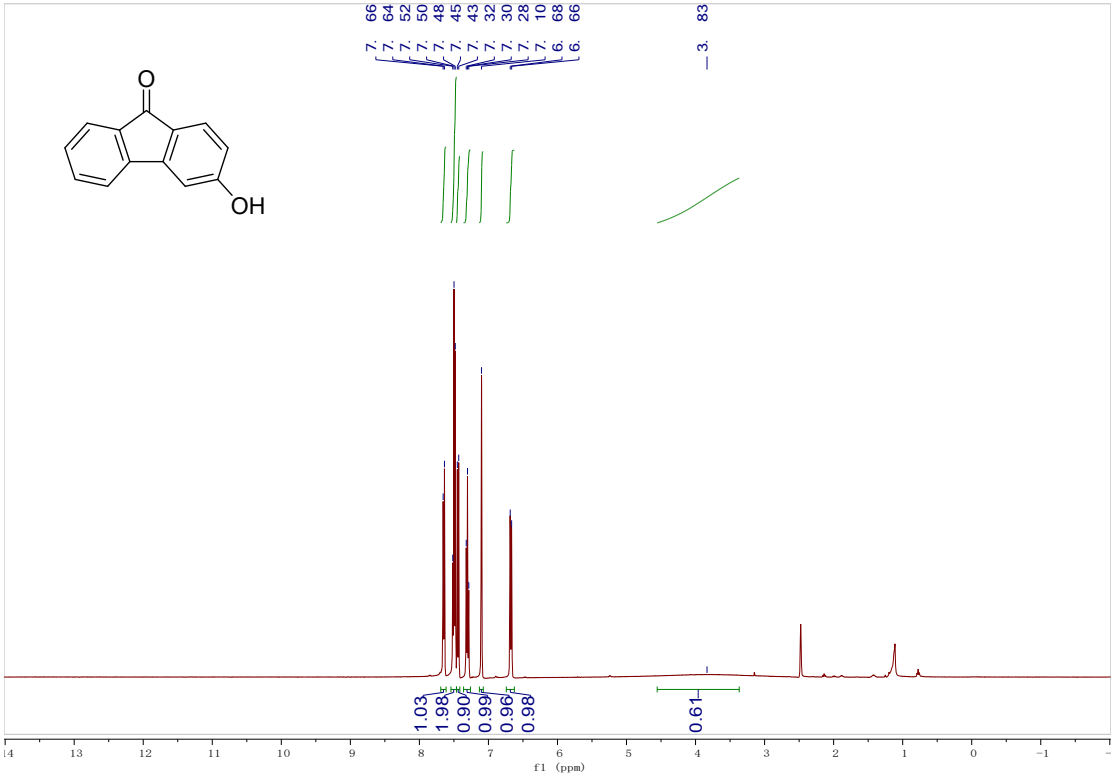


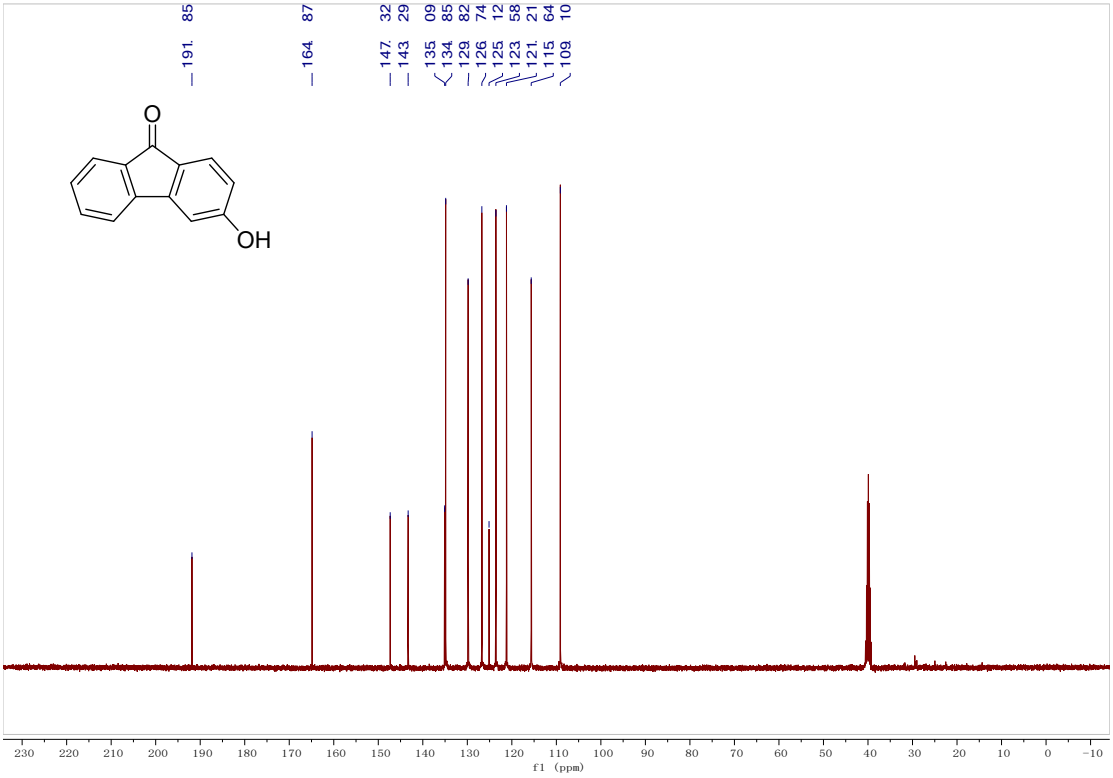
3-methoxy-9H-fluoren-9-one (5)



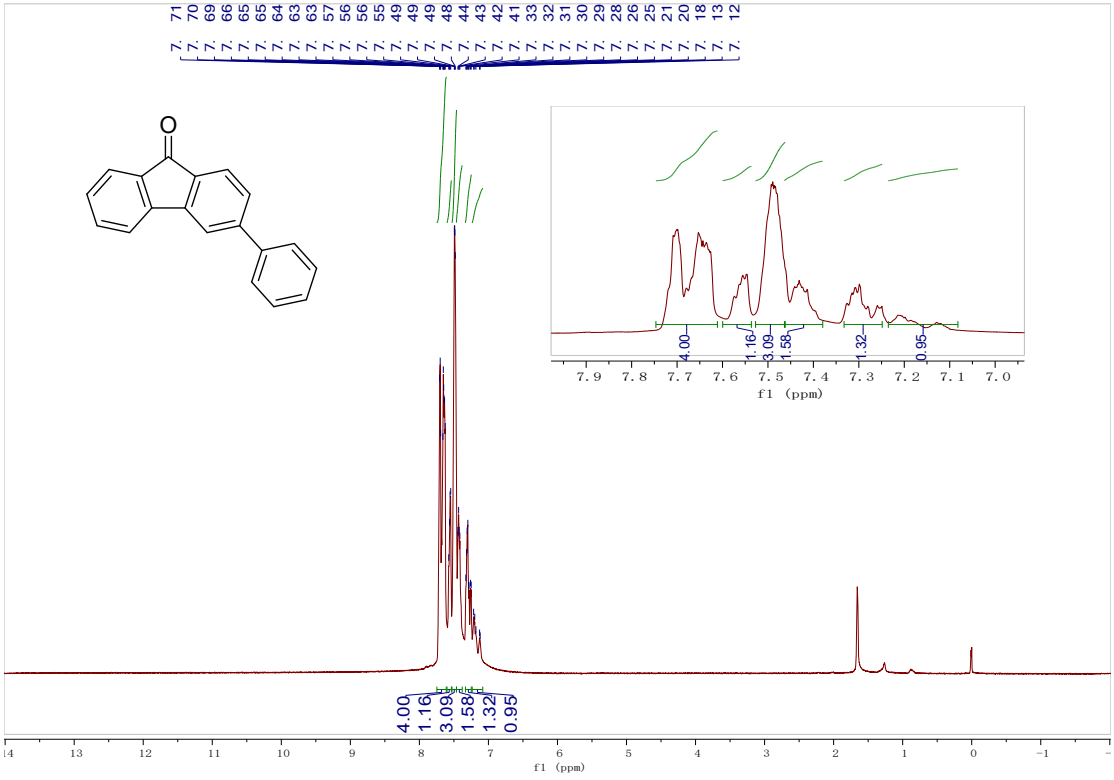


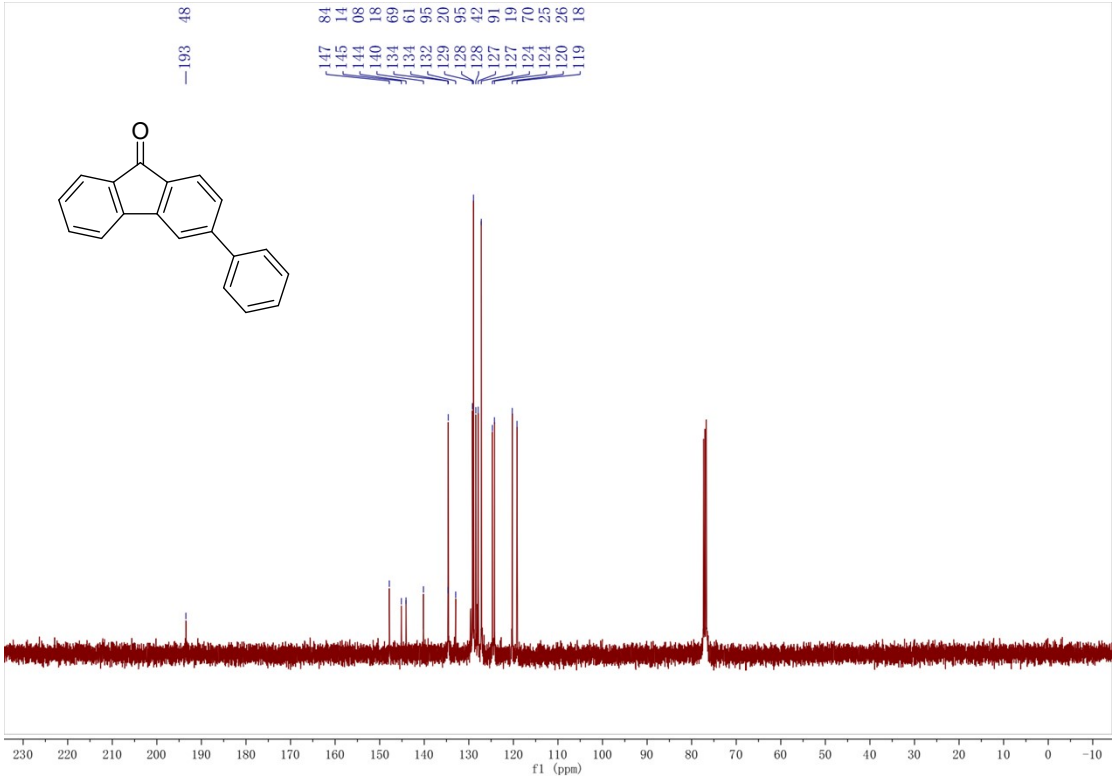
3-hydroxy-9H-fluoren-9-one (6)



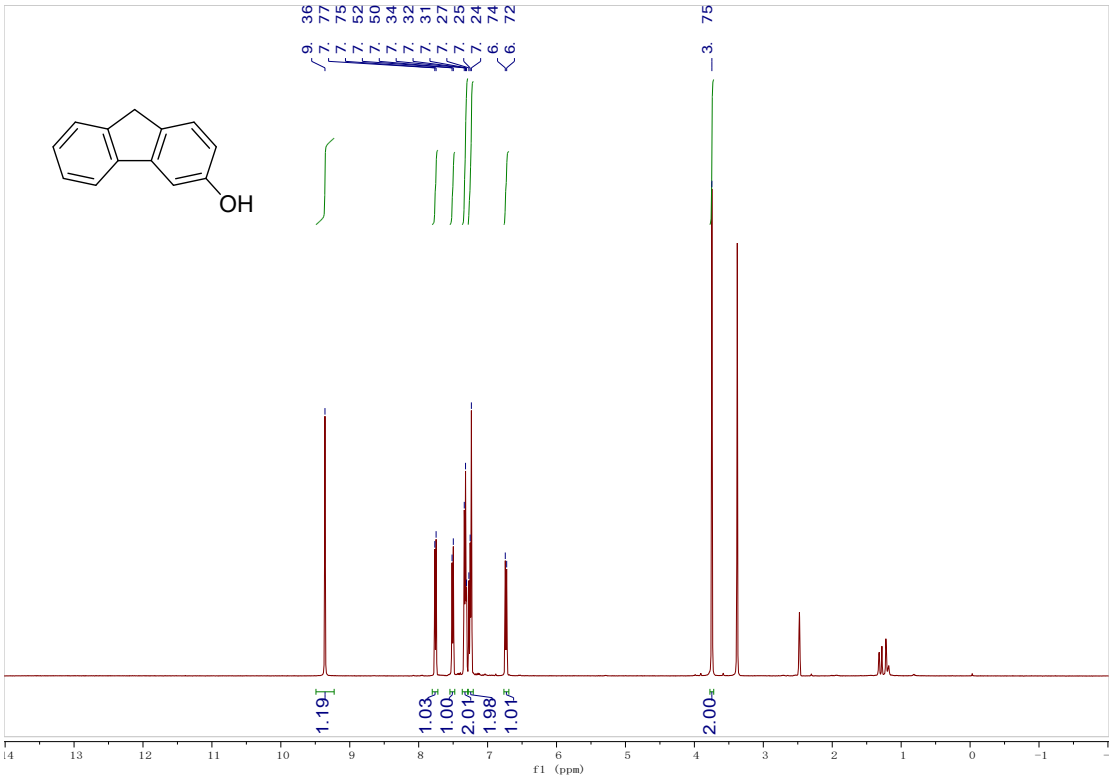


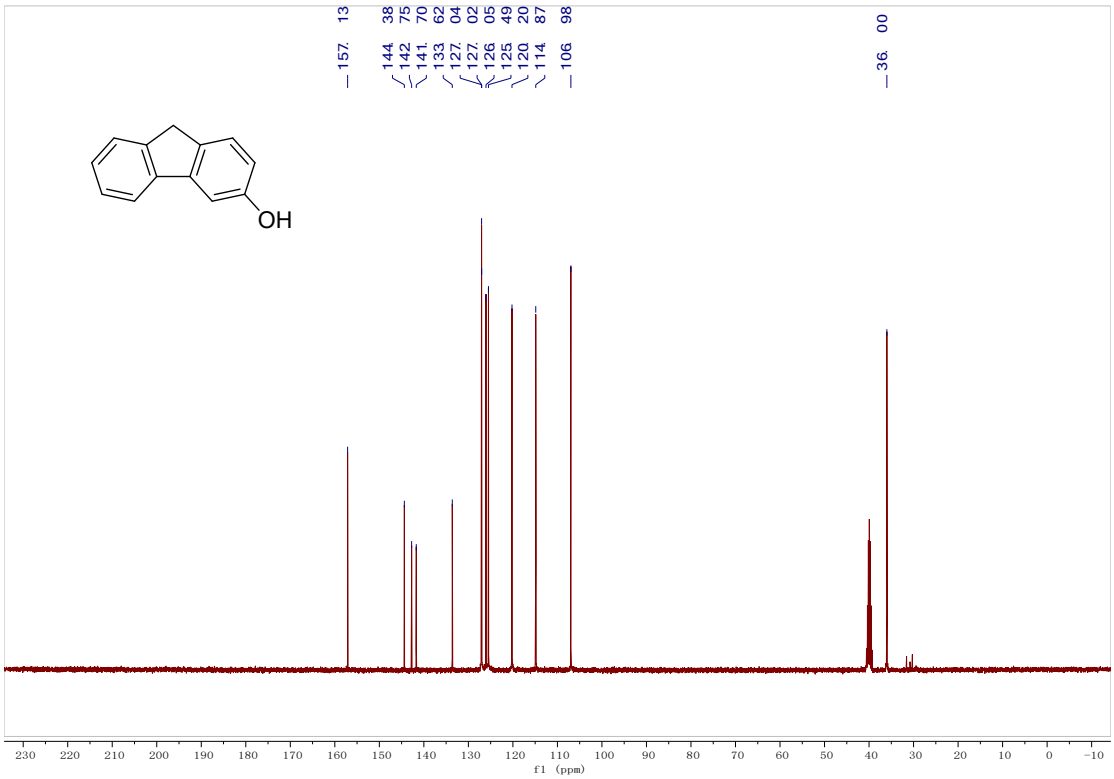
3-phenyl-9H-fluoren-9-one (7)



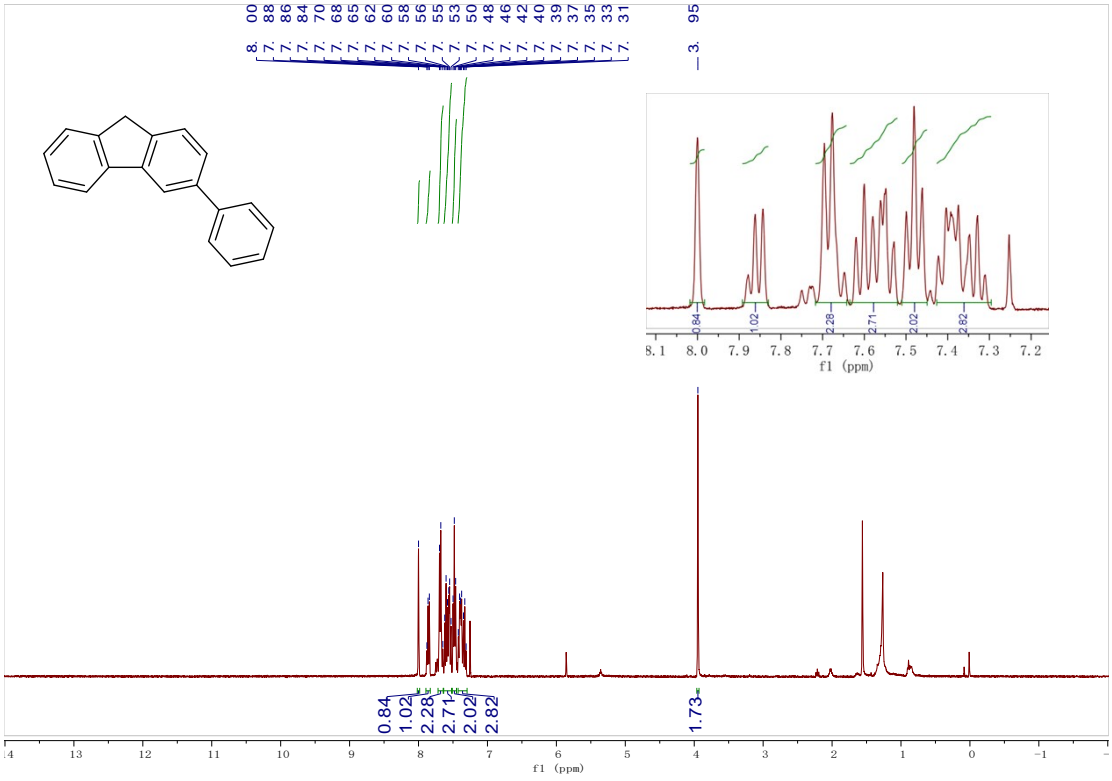


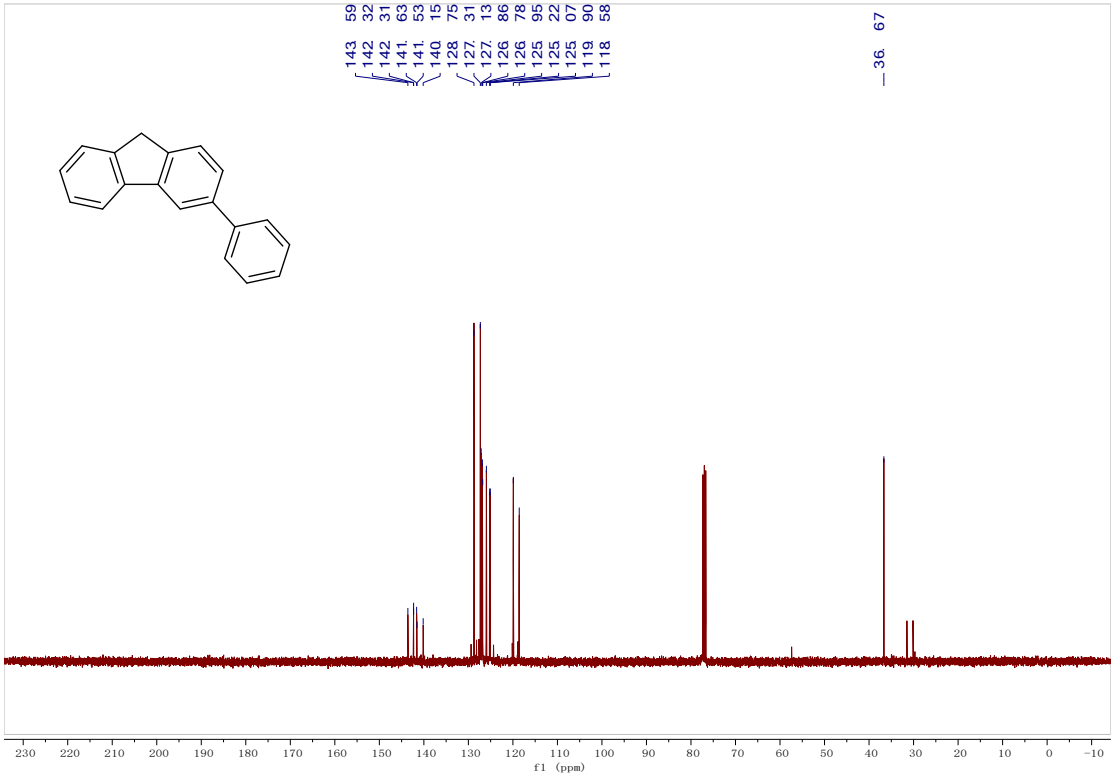
9H-fluoren-3-ol (8)



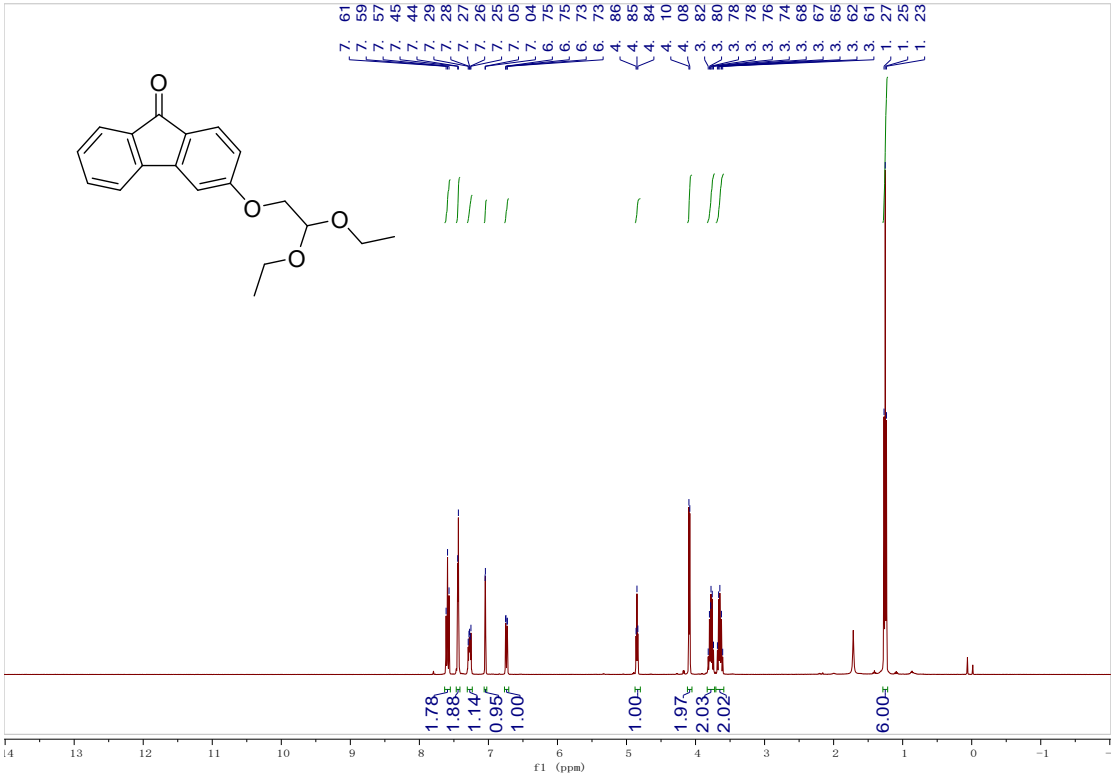


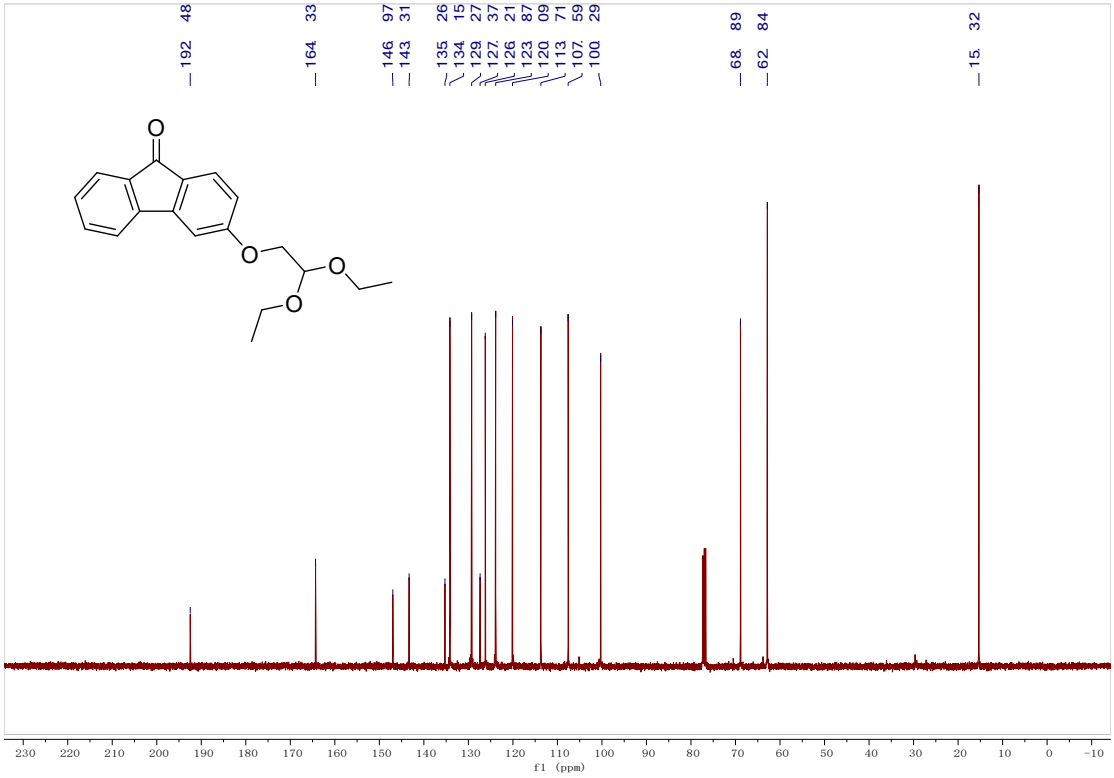
3-phenyl-9H-fluorene (9)





3-(2,2-diethoxyethoxy)-9H-fluoren-9-one (10)





5H-fluoreno[3,2-b]furan-5-one (11)