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Supporting Information (SI)

High-Yielding Aqueous Synthesis of Chloroacetophenones and Aroyl Chlorohydrins

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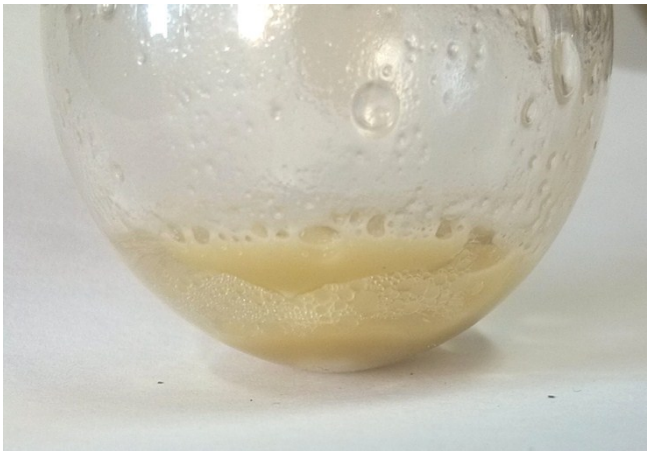
Picture 1. Phenomenon of the synthesis of **2a** in water under magnetic stirring.



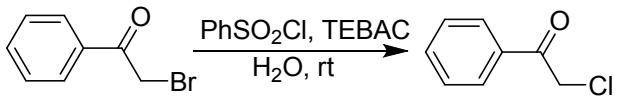
Picture 2. Phenomenon of the synthesis of **2a** in water after stopping magnetic stirring. Reaction conditions: bromoacetophenones (300 mg), benzenesulfonyl chloride (8.0 equiv), TEBAC (0.5 equiv) and H_2O (5 mL) at rt, 1.5 h.

General Experimental Information

All of the chemicals were obtained from commercial sources or prepared according to standard methods. NMR spectra were recorded with a 400 MHz spectrometer for ^{1}H NMR, and a 100 MHz spectrometer for ^{13}C NMR. TMS was used as an internal standard. Chemical shifts (δ) are reported relative to TMS (^{1}H) or $CDCl_3$ (^{13}C). Multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), dd (doublet of doublets) and dt (doublet of triplets). Coupling constants are reported in Hertz (Hz). Melting points were recorded with a micro melting point apparatus. Infrared analyses (KBr pellet) were performed on a FTIR spectrometer. High resolution mass spectra (HRMS) were recorded on a QTOF mass analyzer with electrospray ionization (ESI).

General procedure for all products

Procedure I: Typical 300 mg-scale synthesis of 2a using water as solvent



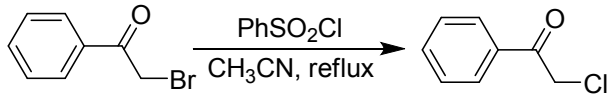
1a **2a**

Bromoacetophenone (300 mg), $PhSO_2Cl$ (8.0 equiv), TEBAC (0.5 equiv) and water (5.0 mL) were added to a 50-mL round-bottom flask. After the mixture was stirred at rt for 1.5 h and TLC indicated completion of the reaction, the reaction was stopped and cooled in an ice-bath. Then saturated Na_2CO_3 aq. (10 mL) was added to the reaction mixture with stirring until $PhSO_2Cl$ disappeared. The mixture was then extracted with ethyl acetate (3 x 10 mL), dried over Na_2SO_4 and evaporated to give a white product **2a** (235 mg, >99%).

Synthesis of 2a in 10 g scale

The synthesis of **2a** starting from 10 g of bromoacetophenone was performed in a 250-mL round-bottom flask using the same procedure as above to yield **2a** (7.8 g, >99%, t: 1.5 h).

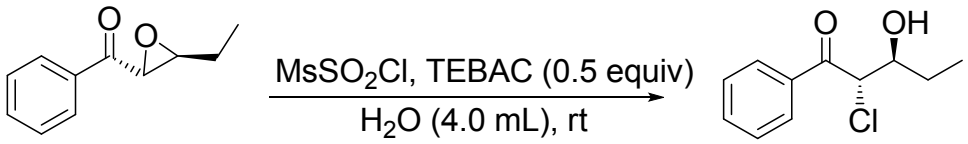
Procedure II: Typical 300 mg-scale synthesis of 2a using acetonitrile as solvent



1a **2a**

Bromoacetophenone (300 mg), $PhSO_2Cl$ (6.0 equiv) and acetonitrile (4.0 mL) were added to a 50-mL round-bottom flask. After the mixture was stirred at 85 ^oC for 2.5 h and TLC indicated completion of the reaction, the reaction mixture was concentrated under vacuum. Then saturated Na_2CO_3 aq. (10 mL) was added to the concentrate in an ice bath, which was stirred until $PhSO_2Cl$ disappeared. The mixture was then extracted with ethyl acetate (3 x 10 mL), dried over Na_2SO_4 and evaporated to give a white product **2a** (231 mg, >99%).

Typical 500 mg-scale synthesis procedure using the synthesis of 4a as an example



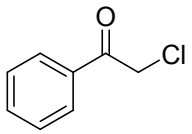
3a **4a**

In a 50-mL round-bottom flask, a mixture of **3a** (500 mg), MsCl (6.0 equiv), TEBAC (0.5 equiv) and water (4.0 mL) was stirred at rt for 5.5 h until TLC indicated completion of the reaction. Then the mixture was washed with ice water until MsCl disappeared. The product was then extracted with ethyl acetate (3 x 10 mL), and dried over Na_2SO_4. The ethyl acetate was evaporated to give **4a** (585 mg, 97%).

Synthesis of 4d in 10 g scale

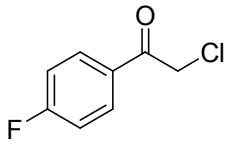
The synthesis of **4d** starting from 10 g of **3d** was performed in a 250-mL round-bottom flask using the same procedure as above to yield **4d** (11.3 g, >99%, t: 6.5 h).

Analytical data for all products



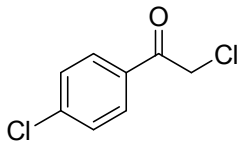
2a

Chloroacetophenone (2a):[1] 235 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.1 Hz, 2H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 2H), 4.69 (s, 2H)；**^{13}C NMR** (101 MHz, $CDCl_3$) δ 191.1, 134.3, 134.0, 128.9, 128.5, 46.1；**IR** (KBr) ν: 3676, 3063, 2939, 1703, 1597, 1449, 1226, 998, 770, 752 cm^{-1}.



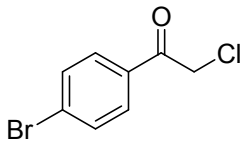
2b

2-Chloro-1-(4-fluorophenyl)ethanone (2b):[2] 244 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (m, 2H), 7.14 (t, *J* = 8.6 Hz, 2H), 4.64 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7, 167.5-164.9 (d, J_{CF} = 256.7 Hz), 131.4-131.3 (d, J_{CF} = 9.5 Hz), 130.7-130.6 (d, J_{CF} = 3.0 Hz), 116.3-116.0 (d, J_{CF} = 22.1 Hz), 45.6; **IR** (KBr) ν: 3679, 2996, 1694, 1600, 1507, 1395, 1221, 1160, 830, 591 cm^{-1}.



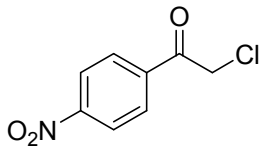
2c

2-Chloro-1-(4-chlorophenyl)ethanone (2c):[1] 247 mg, >99% yield; white solid**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.45 (d, *J* = 8.6 Hz, 2H), 4.64 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.1, 140.6, 132.5, 130.0, 129.3, 45.7; **IR** (KBr) ν: 3714, 2952, 1691, 1589, 1399, 1213, 1093, 997, 818, 780 cm^{-1}.



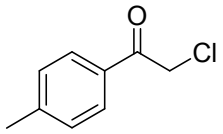
2d

1-(4-Bromophenyl)-2-chloroethanone (2d):[1] 251 mg, >99% yield; white solid**;** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 6.9 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 4.63 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.3, 132.9, 132.3, 130.1, 129.4, 45.6; **IR** (KBr) ν: 3559, 2953, 1699, 1587, 1557, 1401, 1211, 812, 775, 554 cm^{-1}.



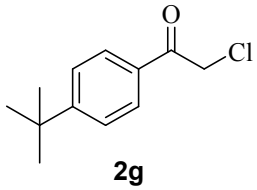
2e

2-Chloro-1-(4-nitrophenyl)ethanone (2e):[1] 247 mg, >99% yield; yellow solid**;** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 8.8 Hz, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 4.69 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.9, 150.8, 138.6, 129.8, 124.1, 45.7; **IR** (KBr) ν: 3501, 2947, 1705, 1522, 1368, 1204, 1002, 848, 772, 680 cm^{-1}.



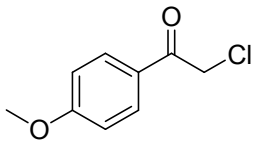
2f

2-Chloro-1-*p*-tolylethanone (2f):[1] 242 mg, >99% yield; white solid**;** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 4.67 (s, 2H), 2.41 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.7, 145.1, 131.8, 129.6, 128.7, 46.0, 21.8; **IR** (KBr) ν: 3731, 2952, 1698, 1608, 1403, 1221, 1180, 1000, 803, 587 cm^{-1}.



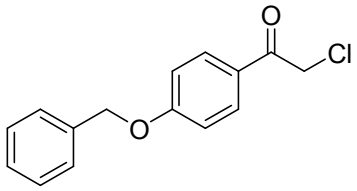
2g

2-Chloro-1-(4-*tert*-butylphenyl)ethanone (2g):[3] 253 mg, >99% yield; syrup; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.5 Hz, 2H), 7.47 (d, *J* = 8.5 Hz, 2H), 4.67 (s, 2H), 1.31 (s, 9H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.7, 157.9, 131.7, 128.5, 125.9, 46.0, 35.3, 31.0; **IR** (KBr) ν: 3684, 2965, 1702, 1604, 1406, 1288, 1218, 1108, 996, 529 cm^{-1}.



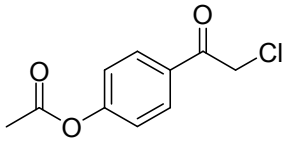
2h

2-Chloro-1-(4-methoxyphenyl)ethanone (2h):[1] 251 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 4.63 (s, 2H), 3.86 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7, 164.2, 130.9, 127.2, 114.1, 55.6, 45.8; **IR** (KBr) ν: 3727, 2977, 1691, 1599, 1221, 1172, 993, 842, 816, 561 cm^{-1}.



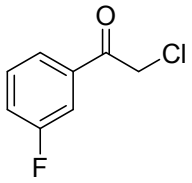
2i

1-(4-Benzyloxyphenyl)-2-chloroethanone (2i):[4] 255 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.6 Hz, 2H), 7.37 (m, 5H), 7.02 (d, *J* = 8.5 Hz, 2H), 5.13 (s, 2H), 4.63 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.7, 163.3, 136.0, 131.0, 128.8, 128.4, 127.5, 127.4, 115.0, 70.3, 45.8; **IR** (KBr) ν: 3457, 2942, 1695, 1596, 1212, 1170, 1002, 830, 744 cm^{-1}.



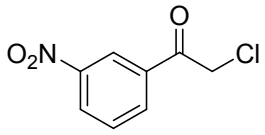
2j

1-(4-Acetyloxyphenyl)-2-chloroethanone (2j):[5] 253 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.8 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 4.66 (s, 2H), 2.31 (s, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.9, 168.7, 155.0, 131.8, 130.3, 122.2, 45.8, 21.2; **IR** (KBr) ν: 3687, 2959, 1763, 1700, 1599, 1396, 1195, 908, 663, 559 cm^{-1}.



2k

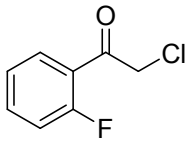
2-Chloro-1-(3-fluorophenyl)ethanone (2k):[6] 241 mg, >99% yield; colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 9.2 Hz, 1H), 7.52 (m, 1H), 7.35 (ddd, *J* = 10.0, 7.9, 1.8 Hz, 1H), 4.70 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 190.02-190.00 (d, J_{CF} = 2.2 Hz), 164.1-161.6 (d, J_{CF} = 249.0 Hz), 136.3-136.2 (d, J_{CF} = 6.5 Hz), 130.7-130.6 (d, J_{CF} = 7.7 Hz), 124.33-124.30 (d, J_{CF} = 3.1 Hz), 121.2-121.0 (d, J_{CF} = 21.4 Hz), 115.5-115.3 (d, J_{CF} = 22.7 Hz), 45.8; **IR** (KBr) ν: 3077, 2946, 1706, 1589, 1484, 1245, 1237, 1153, 834, 611cm^{-1}.



2l

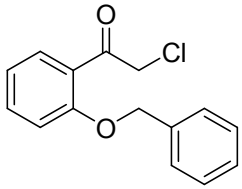
2-Chloro-1-(3-nitrophenyl)ethanone (2l):[7] 254 mg, >99% yield; white solid**; ^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.46 (d, *J* = 9.2 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 8.0 Hz, 1H), 4.71 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.4, 148.5, 135.4,

134.2, 130.3, 128.2, 123.5, 45.5; **IR** (KBr) ν: 3733, 3095, 2940, 1705, 1636, 1528, 1351, 1210, 1083, 679 cm^{-1}.



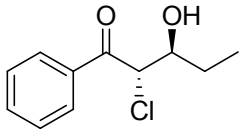
2m

2-Chloro-1-(2-fluorophenyl)ethanone (2m):[8] 242 mg, >99% yield; colorless oil; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 (t, *J* = 7.5 Hz, 1H), 7.57 (m, 1H), 7.27 (m, 1H), 7.16 (dd, *J* = 11.1, 8.5 Hz, 1H), 4.72 (d, *J* = 2.8 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 189.3-189.2 (d, J_{CF} = 4.3 Hz), 163.2-160.7 (d, J_{CF} = 254.1 Hz), 135.8-135.7 (d, J_{CF} = 9.2 Hz), 131.3-131.2 (d, J_{CF} = 2.5 Hz), 125.0-124.9 (d, J_{CF} = 3.2 Hz), 123.0-122.8 (d, J_{CF} = 14.3 Hz), 116.8-116.6 (d, J_{CF} = 23.7 Hz), 50.1-50.0 (d, J_{CF} = 11.9 Hz); **IR** (KBr) ν: 3688, 2950, 1703, 1610, 1481, 1428, 1314, 1212, 765, 627 cm^{-1}.



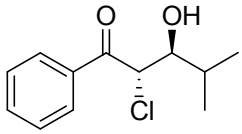
2n

1-(2-Benzyloxyphenyl)-2-chloroethanone (2n): 261 mg, >99% yield; white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.39 (m, 5H), 7.05 (t, *J* = 7.9 Hz, 2H), 5.17 (s, 2H), 4.70 (s, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.6, 158.1, 135.6, 134.8, 131.5, 128.9, 128.7, 127.8, 125.5, 121.4, 112.8, 71.1, 51.0; **IR** (KBr) ν: 3455, 1680, 1593, 1485, 1451, 1276, 1236, 1184, 991, 763 cm^{-1}.



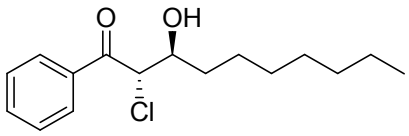
4a

2-Chloro-3-hydroxy-1-phenyl-1-pentanone (4a): 585 mg, 97% yield; *anti/syn* (7.3:1); mp: 36-39 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 5.08 (d, *J* = 3.8 Hz, 0.12H, *syn*), 4.91 (d, *J* = 7.9 Hz, 0.88H, *anti*), 4.15 (m,1H), 2.82 (s, 1H), 1.94 (m, 1H), 1.60 (m, 1H), 1.04 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.5, 134.7, 134.2, 129.12, 129.08 (*syn*), 128.9 (*syn*), 128.8, 73.0, 57.3, 25.8, 9.6; **IR** (KBr) ν: 3456, 2970, 1686, 1594, 1451, 1284, 1210, 978, 828, 689 cm^{-1}; **HRMS** (ESI) found: m/z 213.0682 $[M+H]^+$; calcd. for $C_{11}H_{13}ClO_2H^+$ 213.0677.



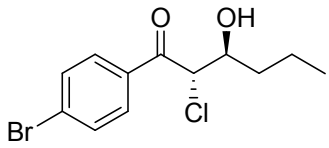
4b

2-Chloro-3-hydroxy-4-methyl-1-phenyl-1-pentanone (4b): 560 mg, 94% yield; *anti/syn* (15.7:1); mp: 52-54 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (m, 2H), 7.61 (m,1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.27 (d, *J* = 3.3 Hz, 0.06H, *syn*), 4.97 (d, *J* = 8.5 Hz, 0.94H, *anti*), 4.09 (m, 0.94H, *anti*), 3.83 (m, 0.06H, *syn*), 2.62 (d, *J* = 4.8 Hz, 1H), 2.23 (m, 1H), 1.06 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.7, 134.9, 134.1, 129.1, 128.8, 75.3, 54.6, 28.7, 19.9, 14.8. **IR** (KBr) ν: 3519, 2963, 1679, 1592, 1287, 1210, 997, 822, 685, 546 cm^{-1}; **HRMS** (ESI) found: m/z 227.0839 $[M+H]^+$; calcd. for $C_{12}H_{15}ClO_2H^+$ 227.0833.



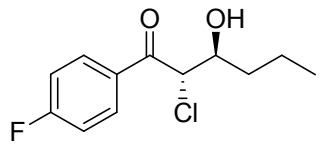
4c

2-Chloro-3-hydroxy-1-phenyl-1-decanone (4c):[9,10] 563 mg, 98% yield; *anti/syn* (4.5:1); white solid; mp: 50-51 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.52 (m, 2H), 5.10 (d, *J* = 3.9 Hz, 0.18H, *syn*), 4.95 (d, *J* = 7.8 Hz, 0.82H, *anti*), 4.24 (m, 1H), 2.70 (s, 1H), 1.86 (m, 1H), 1.59 (m, 2H), 1.33 (m, 9H), 0.90 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.5, 134.7, 134.2 (*syn*), 134.1, 129.09, 129.05 (*syn*), 128.9 (*syn*), 128.8, 71.9, 71.1 (*syn*), 60.8 (*syn*), 57.7, 33.7 (*syn*), 32.8, 31.81, 31.76 (*syn*), 29.43, 29.39 (*syn*), 29.2, 29.1 (*syn*), 25.6 (*syn*), 25.3, 22.7, 14.1; **IR** (KBr) ν: 3417, 2922, 2854, 1688, 1456, 1294, 1126, 826, 684, 556 cm^{-1}; **HRMS** (ESI) found: m/z 283.1465 $[M+H]^+$; calcd. for $C_{16}H_{23}ClO_2H^+$ 283.1459.



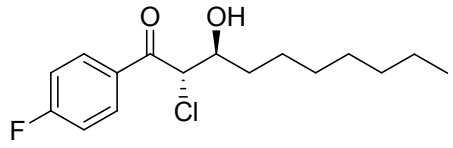
4d

1-(4-Bromophenyl)-2-chloro-3-hydroxy-1-hexanone (4d): 571 mg, >99% yield; *anti/syn* (4.5:1); white solid; mp: 66-69 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 4.96 (d, *J* = 3.8 Hz, 0.18H, *syn*), 4.81 (d, *J* = 7.9 Hz, 0.82H, *anti*), 4.19 (s, 1H), 3.04 (d, *J* = 2.5 Hz, 0.18H, *syn*), 2.75 (d, *J* = 4.8 Hz, 0.82H, *anti*), 1.84 (m, 1H), 1.65-1.41 (m, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 193.5, 133.4, 132.3 (*syn*), 132.2, 130.54, 130.51 (*syn*), 129.5, 71.6, 70.7 (*syn*), 60.8 (*syn*), 57.6, 35.7 (*syn*), 34.9, 18.8 (*syn*), 18.5, 13.9; **IR** (KBr) ν: 3429, 2958, 1667, 1582, 1401, 1216, 996, 852, 718, 526, 466 cm^{-1}; **HRMS** (ESI) found: m/z 304.9944 $[M+H]^+$; calcd. for $C_{12}H_{14}BrClO_2H^+$ 304.9938.



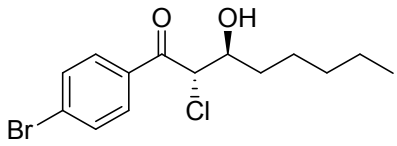
4e

2-Chloro-1-(4-fluorophenyl)-3-hydroxy-1-hexanone (4e): 558 mg, 95% yield; *anti/syn* (7.3:1); white solid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (m, 2H), 7.20 (m, 2H), 5.27 (d, *J* = 3.8 Hz, 0.12H, *syn*), 4.87 (d, *J* = 7.9 Hz, 0.88H, *anti*), 4.20 (m, 1H), 3.69 (s, 0.12H, *syn*), 2.80 (s, 0.88H, *anti*), 1.92-1.43 (m, 4H), 0.99 (t, *J* = 7.2 Hz, 2.64H, *anti*), 0.84 (t, *J* = 7.2 Hz, 0.36H, *syn*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.9, 167.6-165.0 (d, J_{CF} = 257.1 Hz), 132.0-131.9 (d, J_{CF} = 9.5 Hz), 131.7-131.6 (*syn,* d, J_{CF} = 9.6 Hz), 131.1-131.0 (d, J_{CF} = 2.6 Hz), 116.5-116.3 (*syn,* d, J_{CF} = 22.0 Hz), 116.2-116.0 (d, J_{CF} = 22.1 Hz), 76.4 (*syn*), 71.6, 63.0 (*syn*), 57.5, 34.9, 34.1 (*syn*), 19.5 (*syn*), 18.5, 13.9, 13.3 (*syn*); **IR** (KBr) ν: 3466, 2962, 1687, 1598, 1508, 1237, 1159, 1016, 854, 601 cm^{-1}; **HRMS** (ESI) found: m/z 245.0745 $[M+H]^+$; calcd. for $C_{12}H_{14}ClFO_2H^+$ 245.0739.



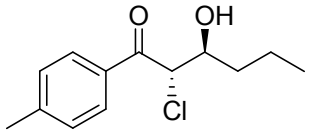
4f

2-Chloro-1-(4-fluorophenyl)-3-hydroxy-1-decanone (4f): 552 mg, 97% yield; *anti/syn* (8.1:1); white solid; mp: 49-50°C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (m, 2H), 7.15 (t, *J* = 6.9 Hz, 2H), 4.98 (d, *J* = 3.9 Hz, 0.11H, *syn*), 4.83 (d, *J* = 7.9 Hz, 0.89H, *anti*), 4.19 (m, 1H), 2.37 (s, 1H), 1.87 (m, 1H), 1.56 (m, 2H), 1.28 (m, 9H), 0.85 (m, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 192.9, 167.6-165.0 (d, J_{CF} = 257.1 Hz), 132.0-131.9 (d, J_{CF} =9.5 Hz), 131.09, 116.3-116.0 (*syn,* d, J_{CF} = 21.5 Hz), 116.2-115.9 (d, J_{CF} = 22.1 Hz), 71.9, 57.5, 32.8, 31.8, 29.4, 29.2, 25.2, 22.6, 14.1; **IR** (KBr) ν: 3415, 2924, 2856, 1688, 1597, 1507, 1411, 1235, 893, 555 cm^{-1}; **HRMS** (ESI) found: m/z 301.1362 $[M+H]^+$; calcd. for $C_{16}H_{22}ClFO_2H^+$ 301.1365.



4g

1-(4-Bromophenyl)-2-chloro-3-hydroxy-1-octanone (4g): 567 mg, >99% yield; *anti/syn* (9:1); white solid; mp: 88-90 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.5 Hz, 2H), 7.63 (d, *J* = 8.5 Hz, 2H), 4.96 (d, *J* = 3.8 Hz, 0.1H, *syn*), 4.81 (d, *J* = 7.9 Hz, 0.9H, *anti*), 4.18 (m, 1H), 3.01 (d, *J* = 2.0 Hz, 0.1H, *syn*), 2.68 (d, *J* = 5.4 Hz, 0.9H, *anti*), 1.88 (m, 1H), 1.57 (m, 2H), 1.40 (m, 5H), 0.87 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.5, 146.9, 133.4 (*syn*), 132.3 (*syn*), 132.2, 130.6, 129.6 (*syn*), 128.0, 127.3, 82.1 (*syn*), 71.8, 57.6, 32.7, 31.7, 24.9, 22.6, 14.1; **IR** (KBr) ν: 3426, 2927, 2857, 1688, 1586, 1399, 1285, 1071, 851, 702 cm^{-1}; **HRMS** (ESI) found: m/z 333.0257 $[M+H]^+$; calcd. for $C_{14}H_{18}BrClO_2H^+$ 333.0251.



4h

2-Chloro-3-hydroxy-1-*p*-tolyl-1-hexanone (4h): 542 mg, 92% yield; *anti/syn* (3.8:1); white solid; mp: 56-59°C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.90 (m, 2H), 7.33 (m, 2H), 5.32 (dd, *J* = 6.7, 3.3 Hz, 0.21H, *syn*), 4.93 (d, *J* = 7.7 Hz, 0.79H, *anti*), 4.22 (m, 1H), 3.87 (d, *J* = 6.9 Hz, 0.21H, *syn*), 2.86 (s, 0.79H, *anti*), 2.46 (m, 3H), 1.90-1.42 (m, 4H), 0.99 (t, *J* = 7.2 Hz, 2.37H, *anti*), 0.81 (t, *J* = 7.3 Hz, 0.63H, *syn*); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.1, 145.3, 132.2, 129.8 (*syn*), 129.5, 129.2, 128.9 (*syn*), 76.7 (*syn*). 71.8, 63.4 (*syn*), 57.6, 34.9, 33.7 (*syn*), 21.85 (*syn*), 21.78, 19.6 (*syn*), 18.6, 13.9, 13.3 (*syn*); **IR** (KBr) ν: 3462, 3036, 2872, 1682, 1606, 1293, 1182, 989, 849, 549 cm^{-1}; **HRMS** (ESI) found: m/z 241.0995 $[M+H]^+$; calcd. for $C_{13}H_{17}ClO_2H^+$ 241.0990.

References

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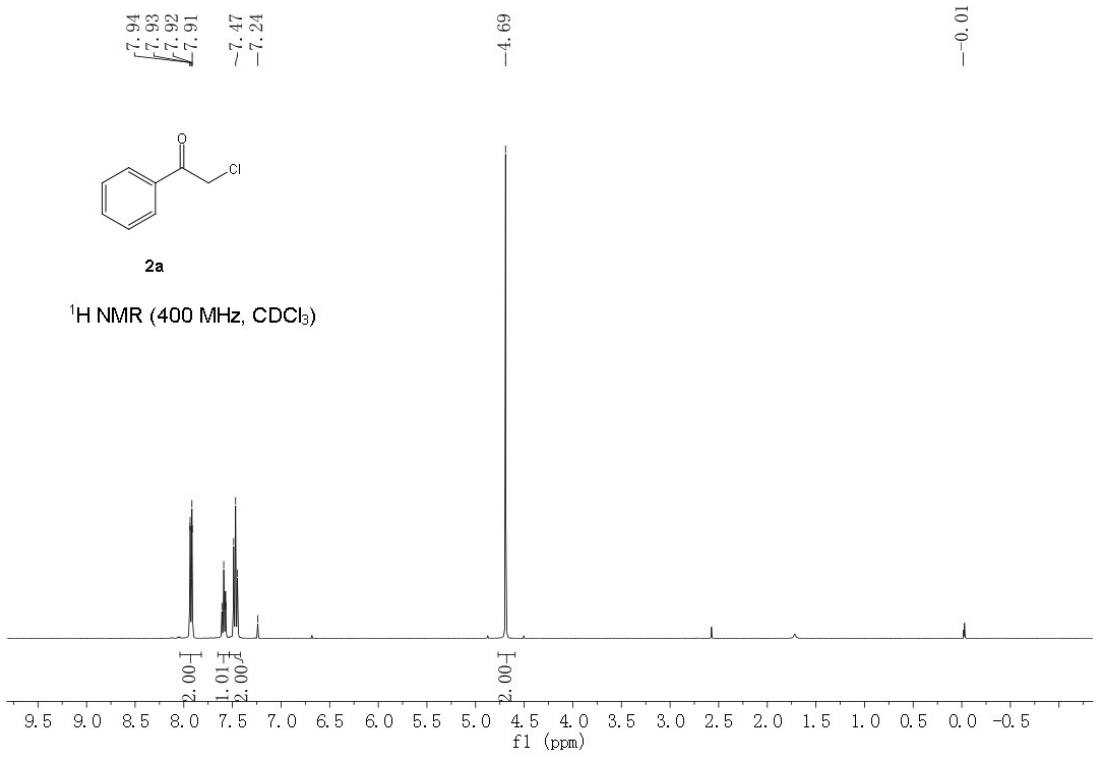
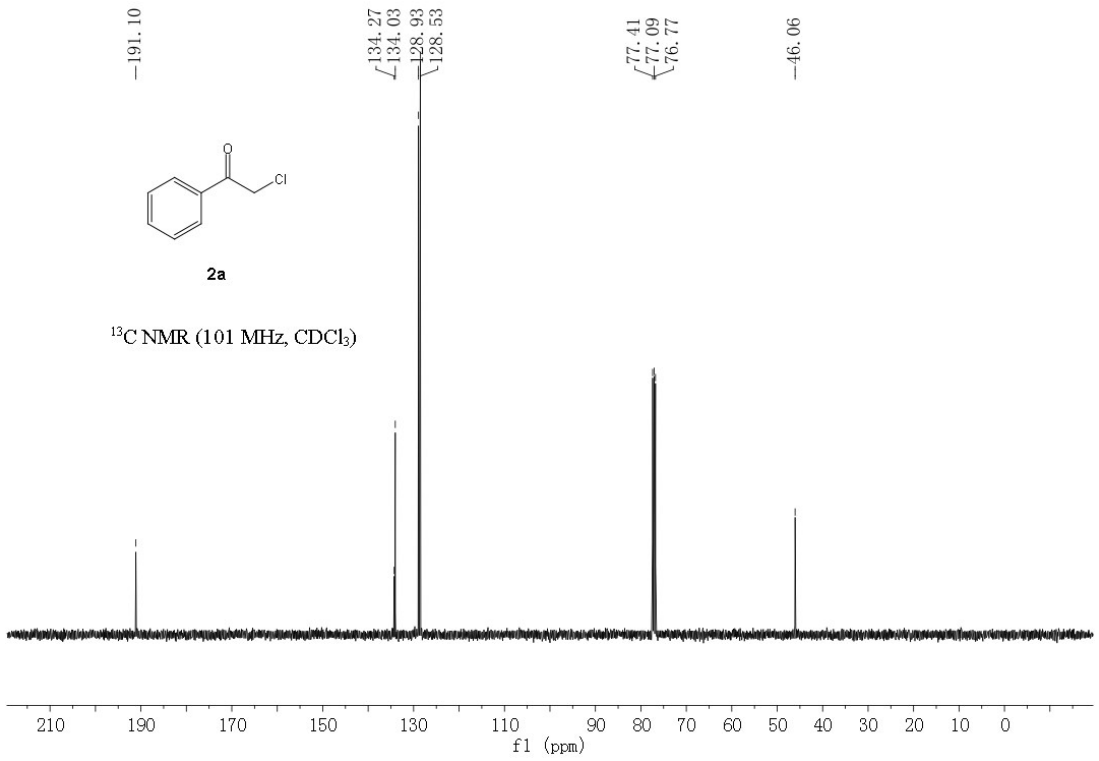
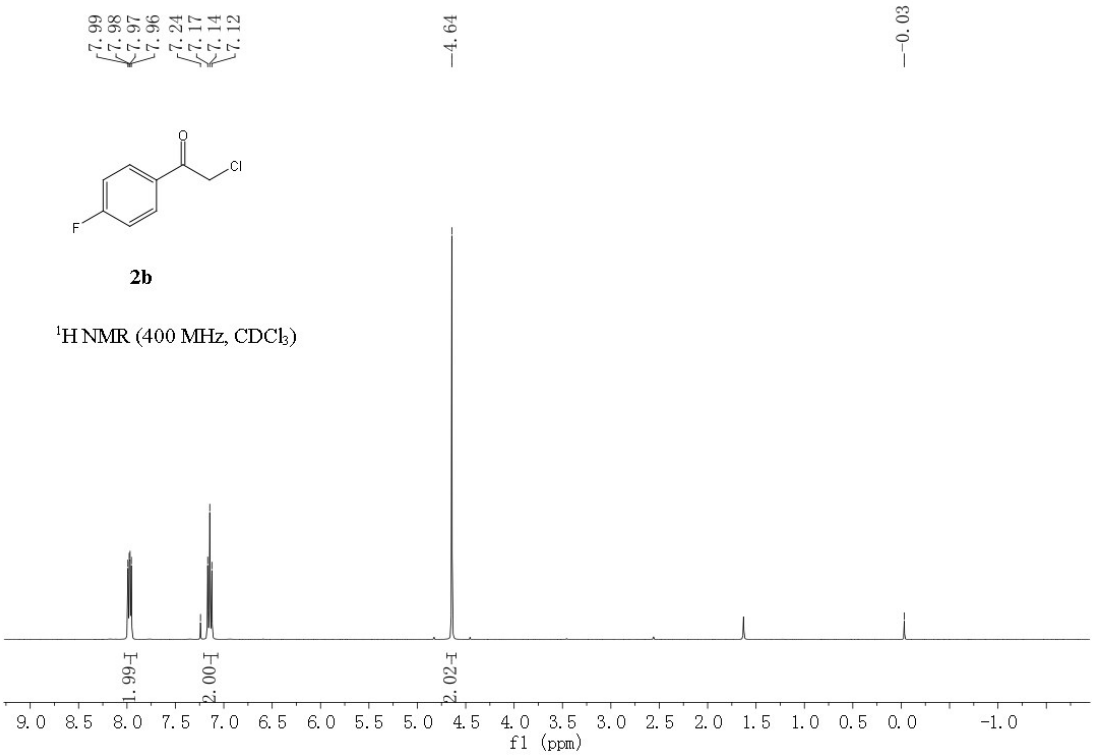
NMR spectra of the products:



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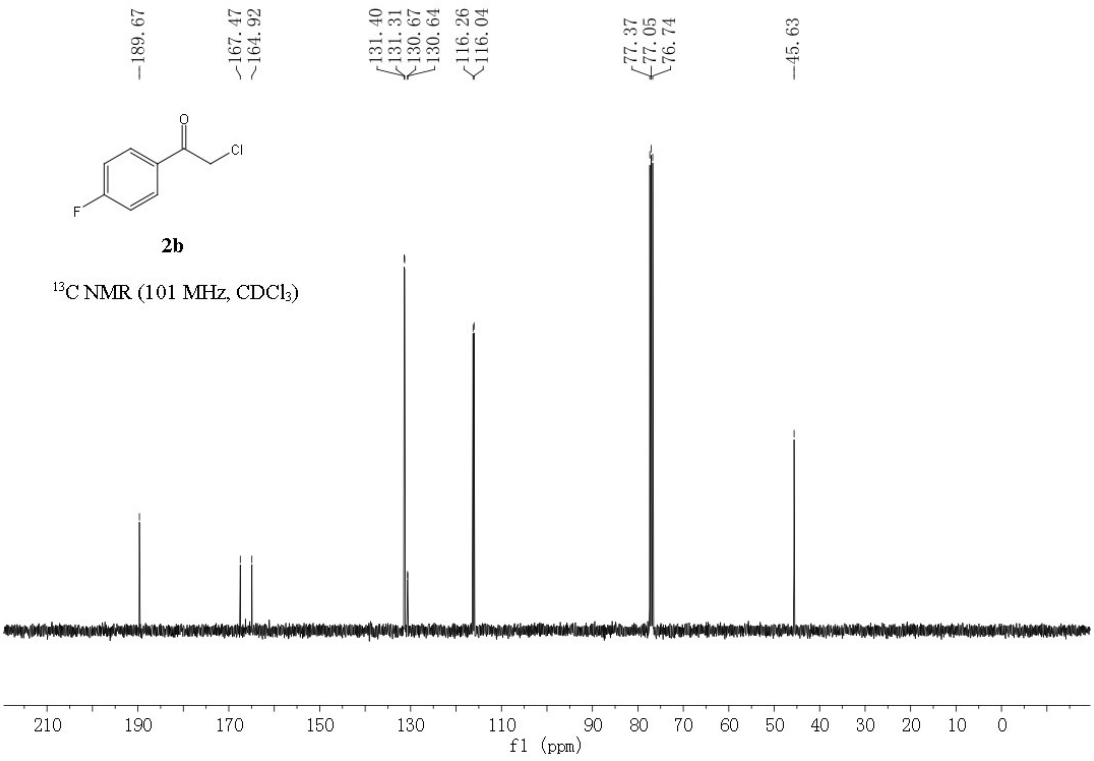
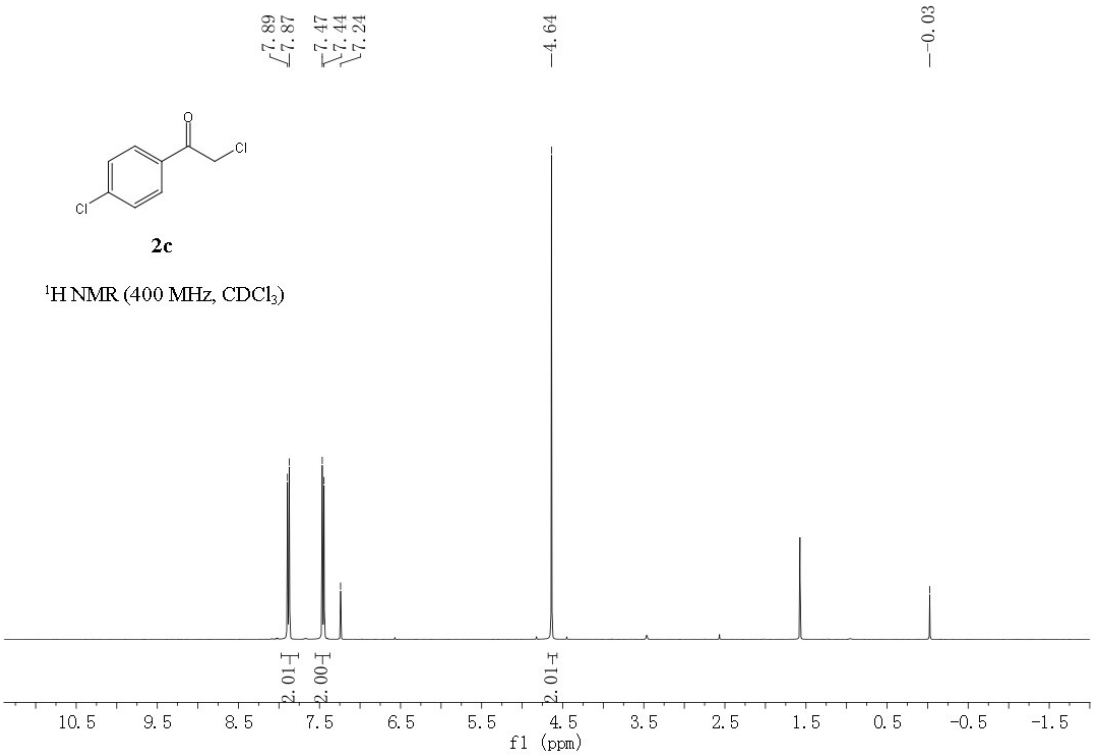
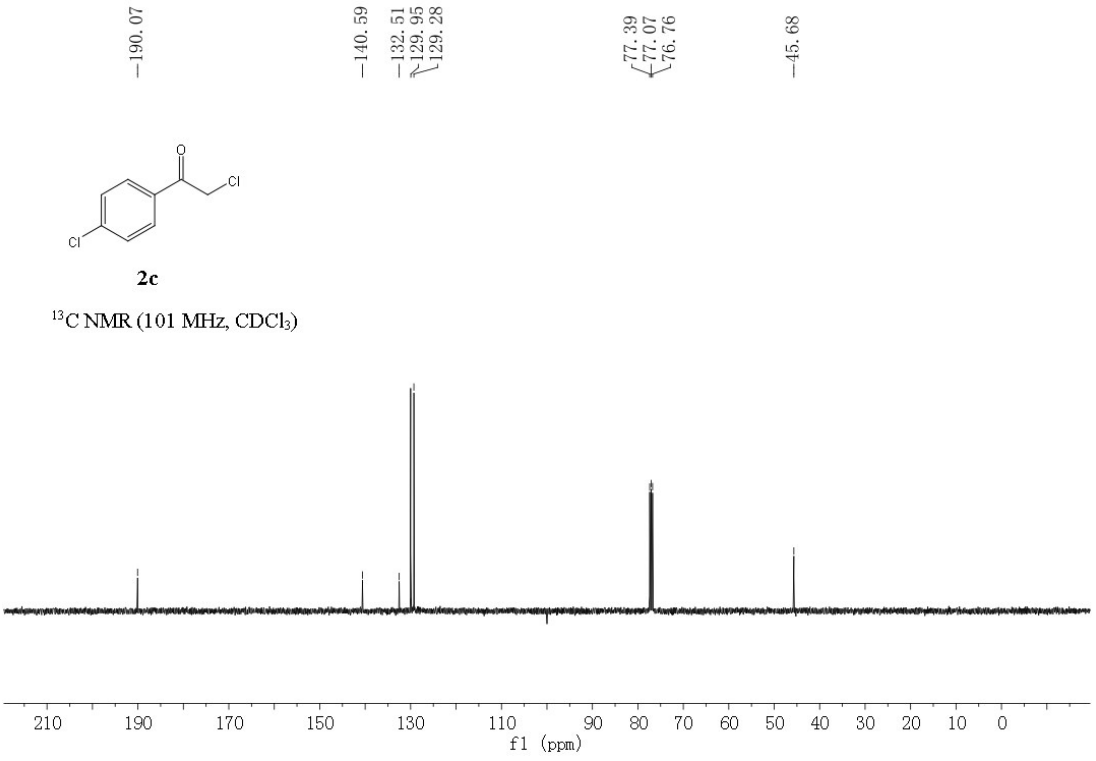
7.97
7.96
7.24
7.17
7.14
7.12
4.64
0.03
O
Cl
F
2b
1H NMR (400 MHz, CDCl3)
1.99
2.00
2.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -1.0
f1 (ppm)


189.67
167.47
164.92
131.40
131.31
130.67
130.64
116.26
116.04
77.37
77.05
76.74
45.63
O
Cl
F
2b
13C NMR (101 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



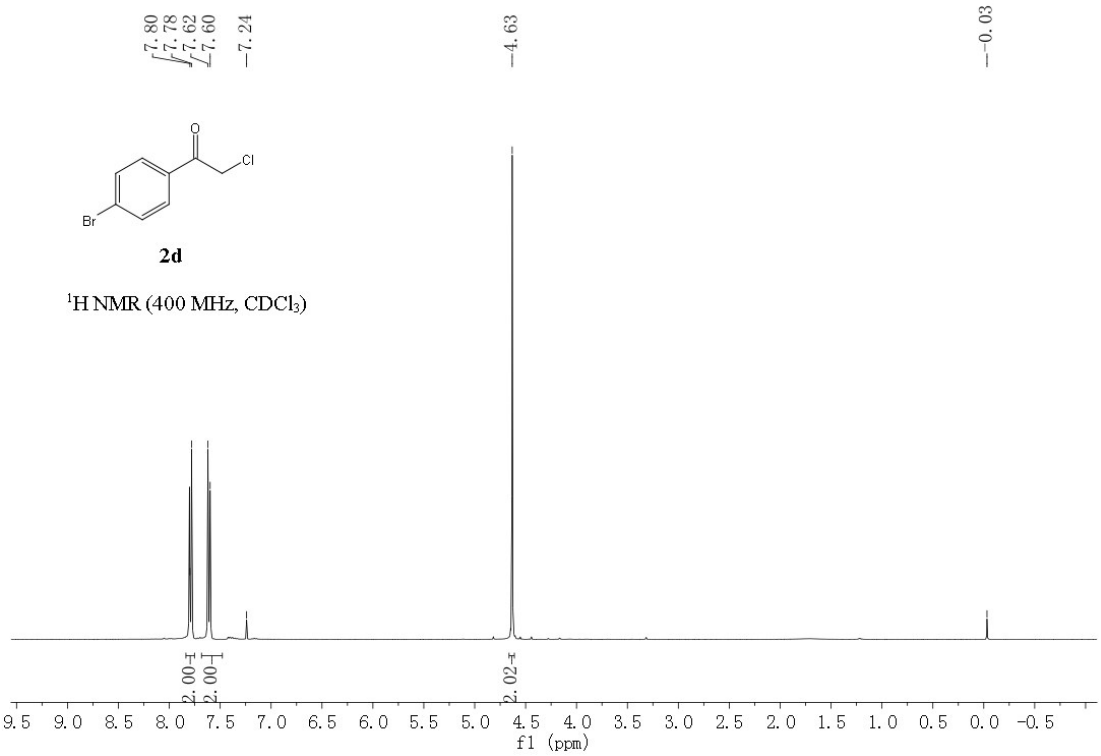
2c

^{1}H NMR (400 MHz, $CDCl_3$)



2c

^{13}C NMR (101 MHz, $CDCl_3$)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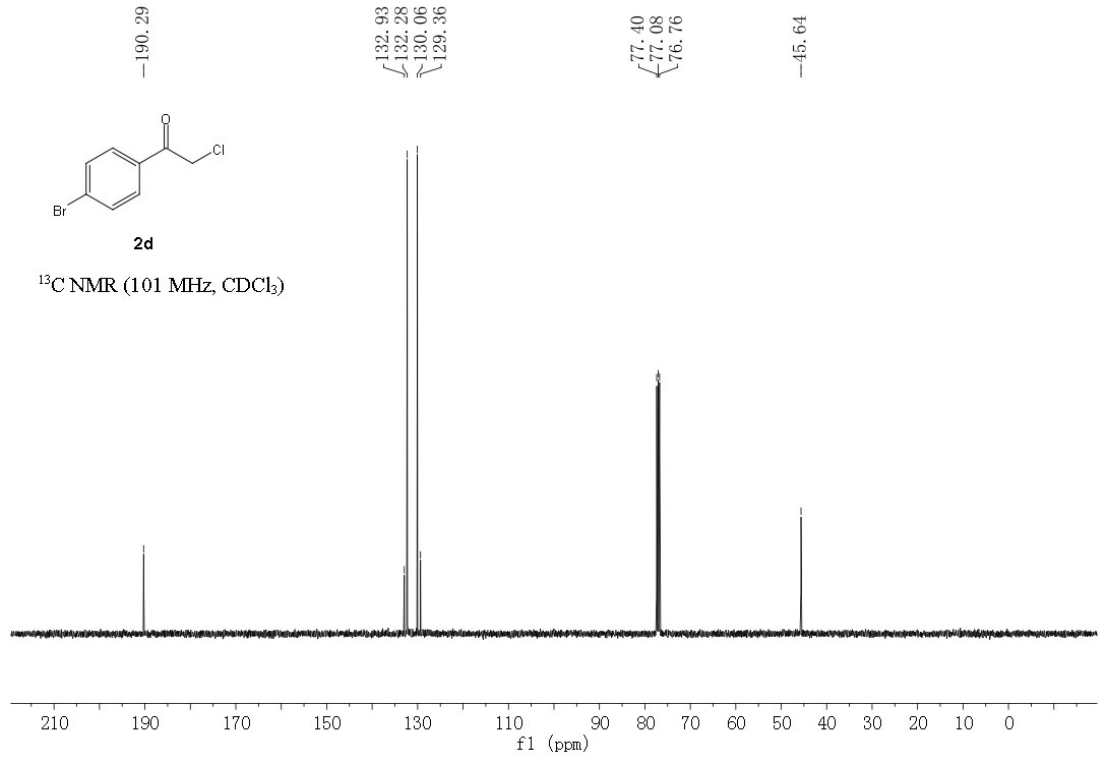
7.78
7.62
7.60
7.24
4.63
0.03
O
Cl
Br
2d
^{1}H NMR (400 MHz, CDCl$_3$)
2.00
2.00
2.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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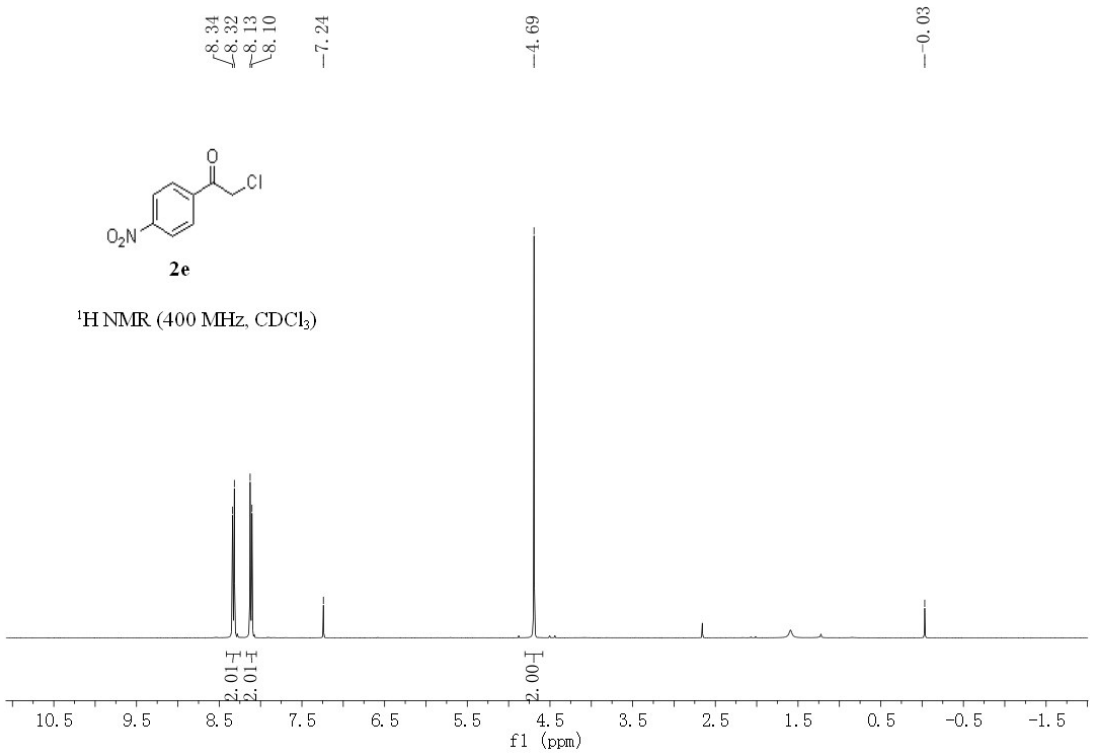
132.28
130.06
129.36
77.40
77.08
76.76
45.64
O
Cl
Br
2d
^{13}C NMR (101 MHz, CDCl$_3$)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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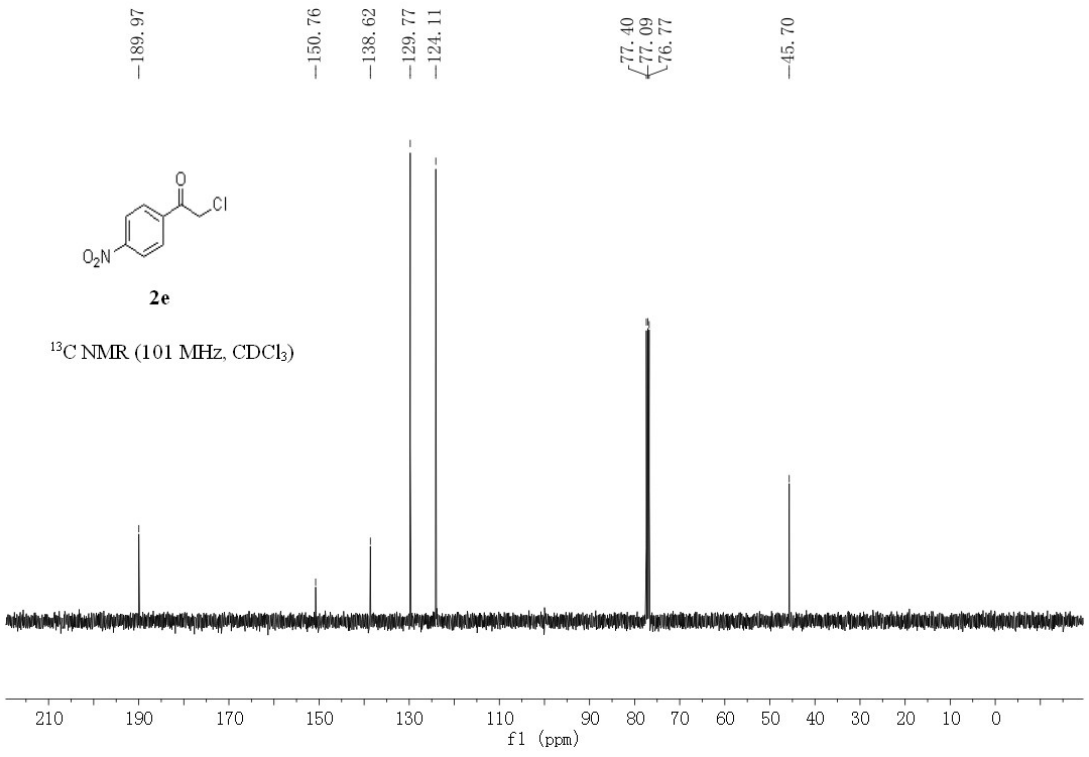
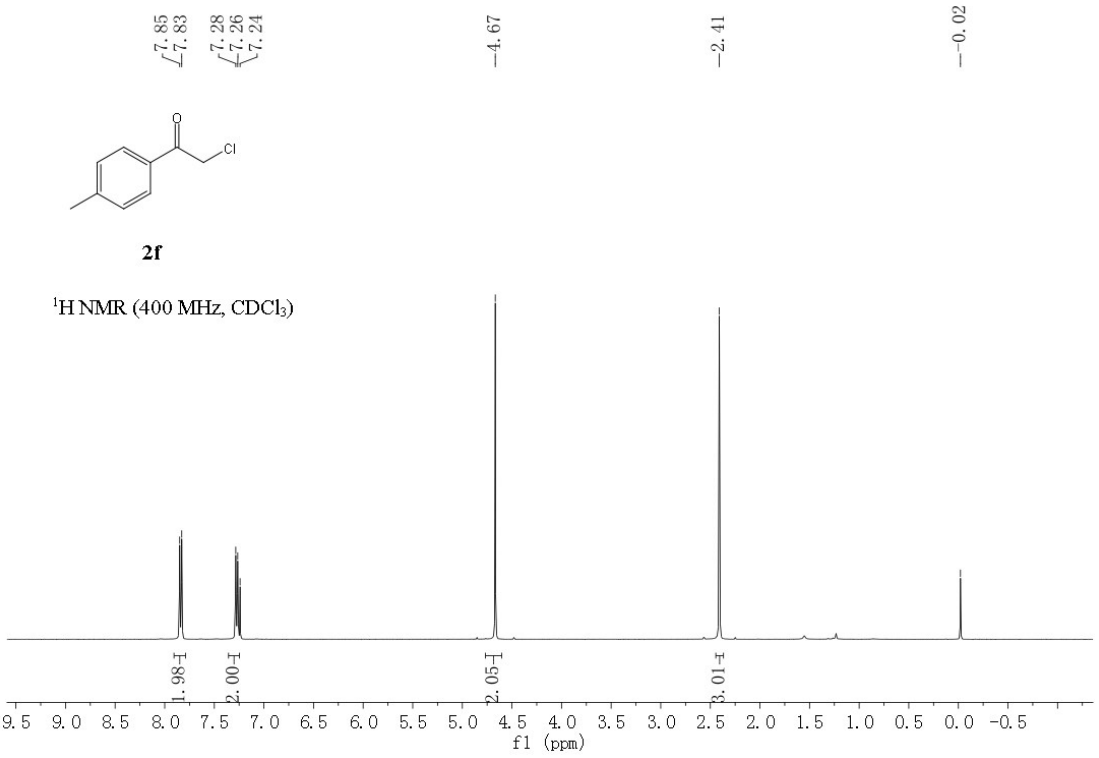
8.32
8.13
8.10
7.24
4.69
0.03
O
Cl
O2N
2e
1H NMR (400 MHz, CDCl3)
2.01
2.01
2.00
10.5
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
-1.5
f1 (ppm)


189.97
150.76
138.62
129.77
124.11
77.40
77.09
76.77
45.70
O
Cl
O2N
2e
13C NMR (101 MHz, CDCl3)
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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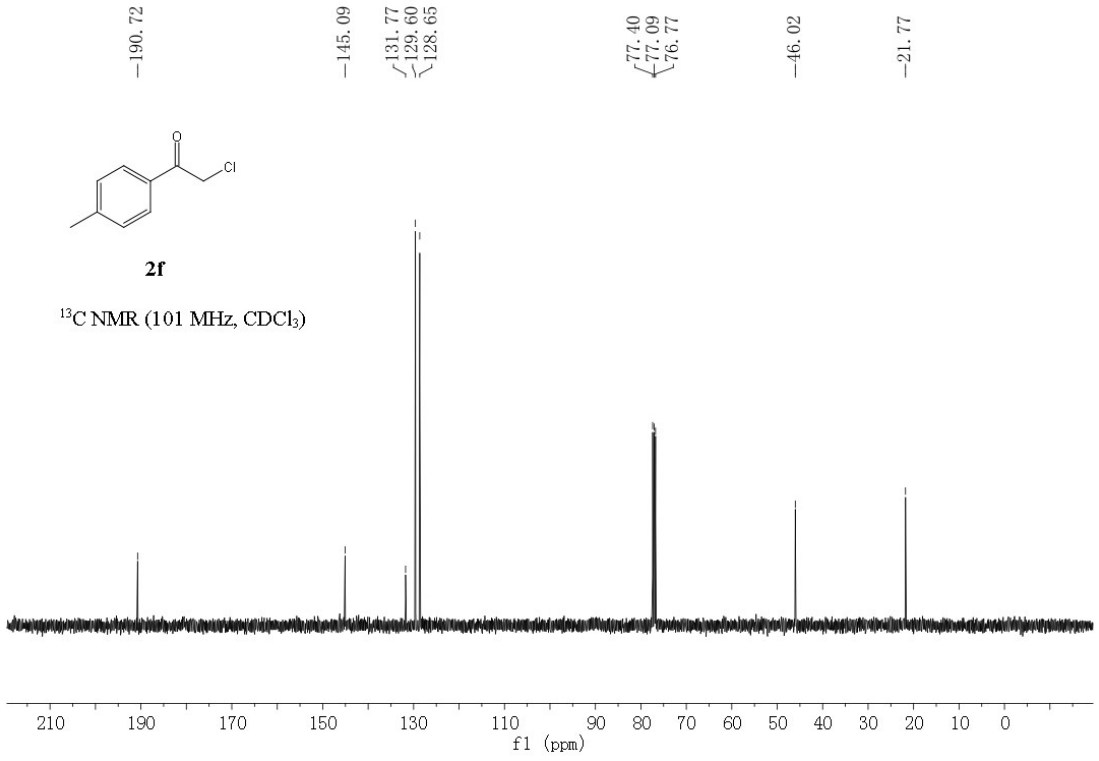
7.83
7.28
7.26
7.24
4.67
2.41
0.02
O
Cl
2f
^{1}H NMR (400 MHz, $CDCl_3$)
1.98
2.00
2.05
3.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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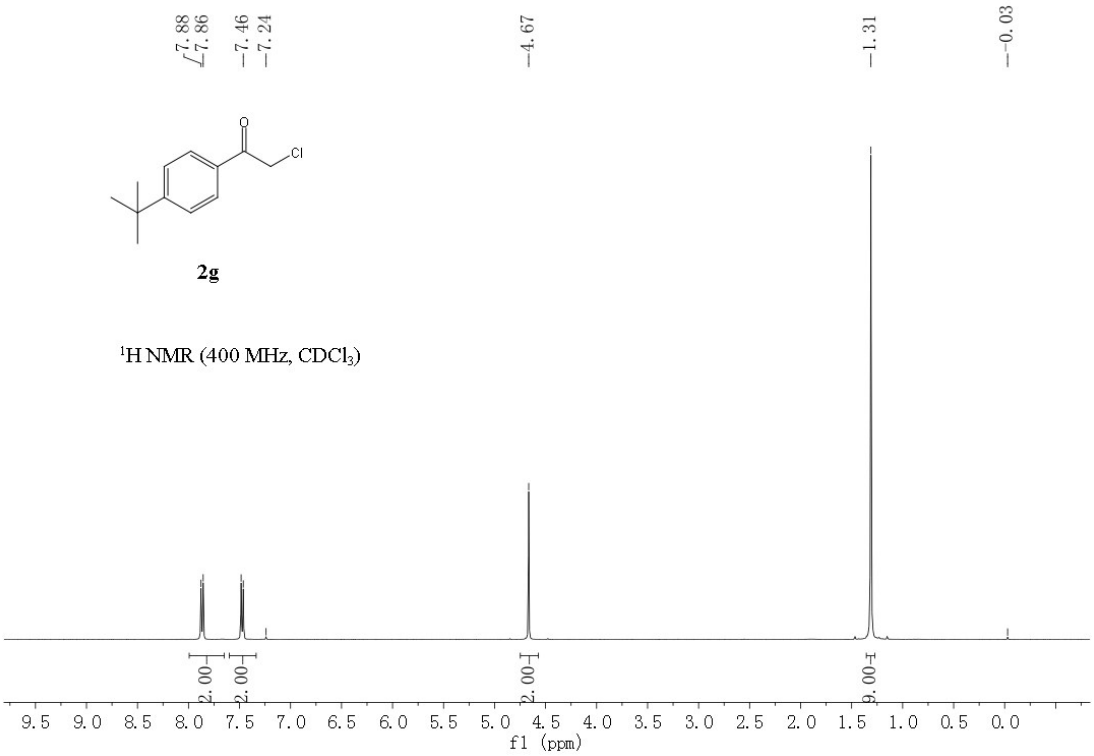
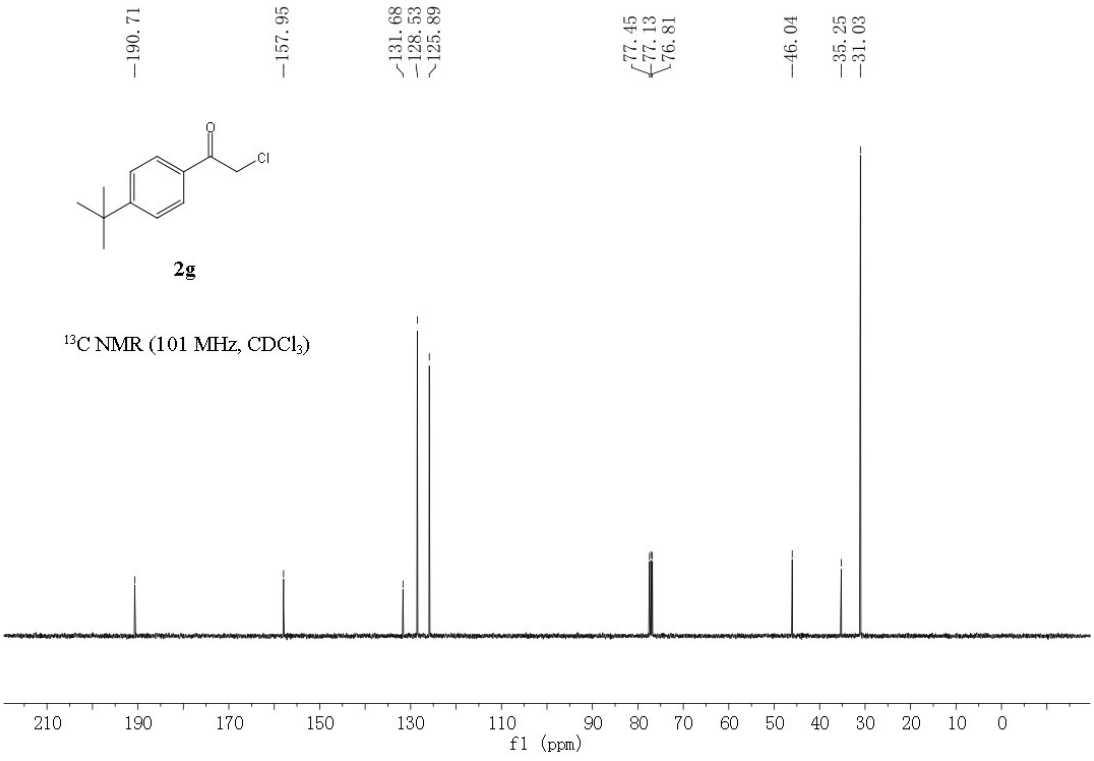
145.09
131.77
129.60
128.65
77.40
77.09
76.77
46.02
21.77
O
Cl
2f
^{13}C NMR (101 MHz, $CDCl_3$)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



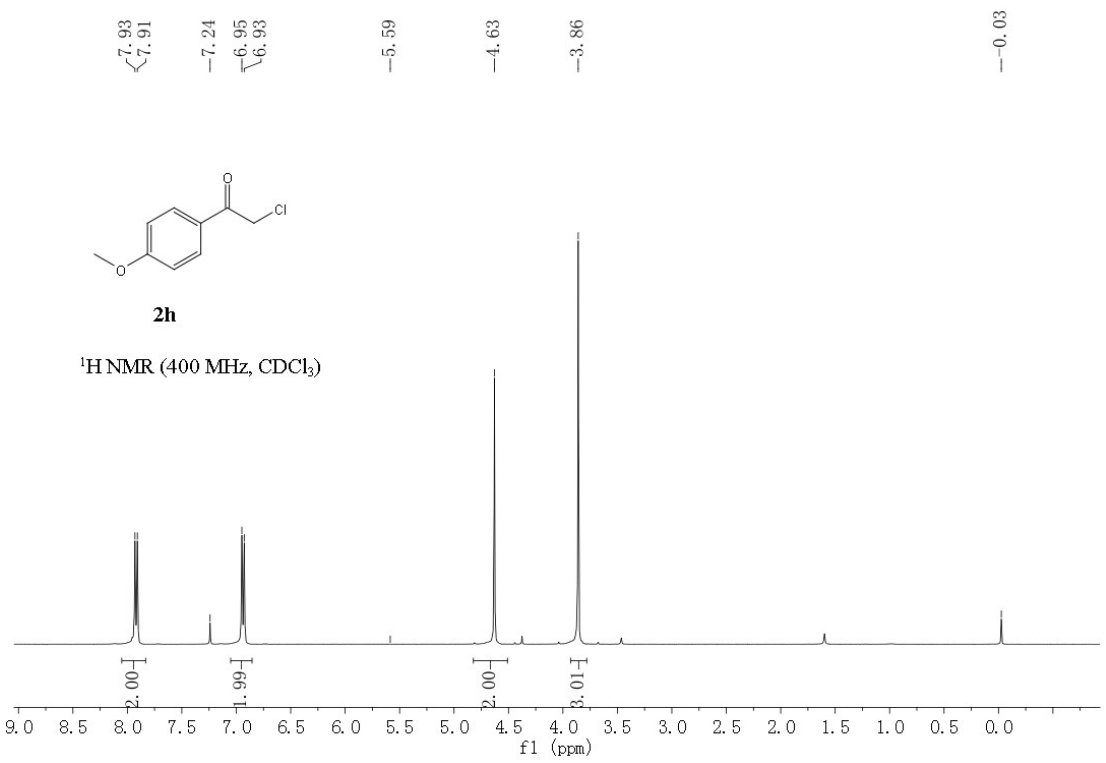
2g

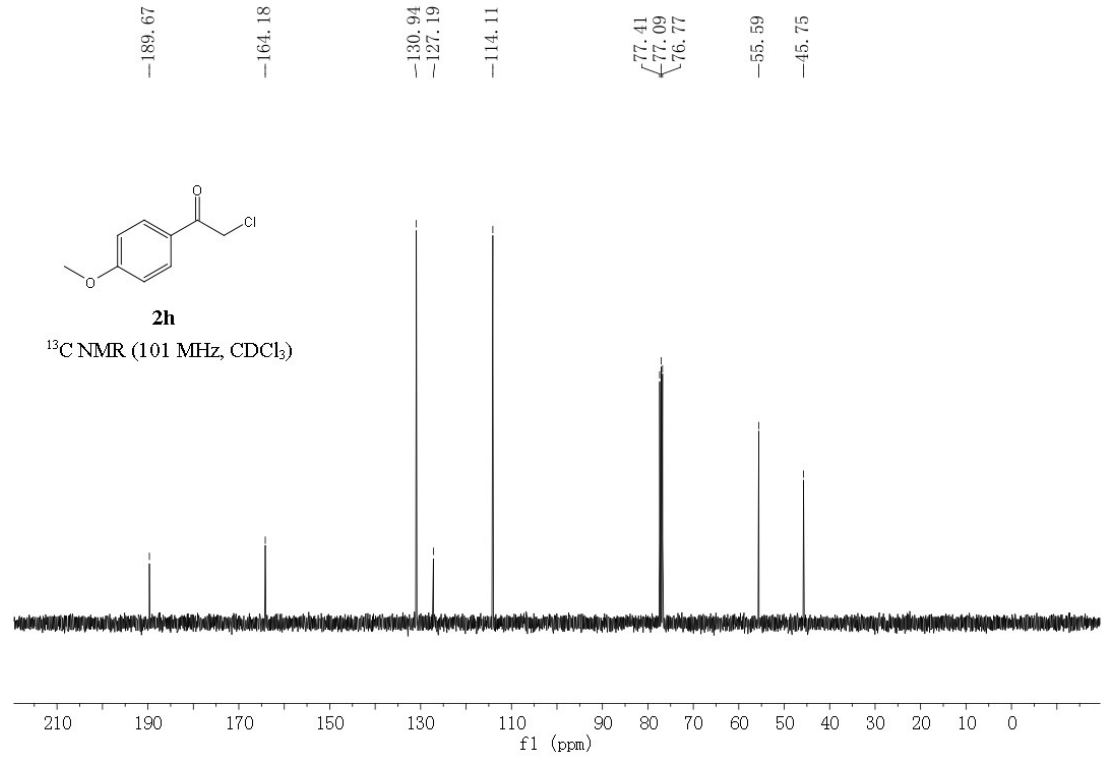
^{1}H NMR (400 MHz, $CDCl_3$)



2g

^{13}C NMR (101 MHz, $CDCl_3$)


7.93
7.91
7.24
6.95
6.93
5.59
4.63
3.86
0.03
O
Cl
O
2h
^{1}H NMR (400 MHz, $CDCl_3$)
2.00
1.99
2.00
3.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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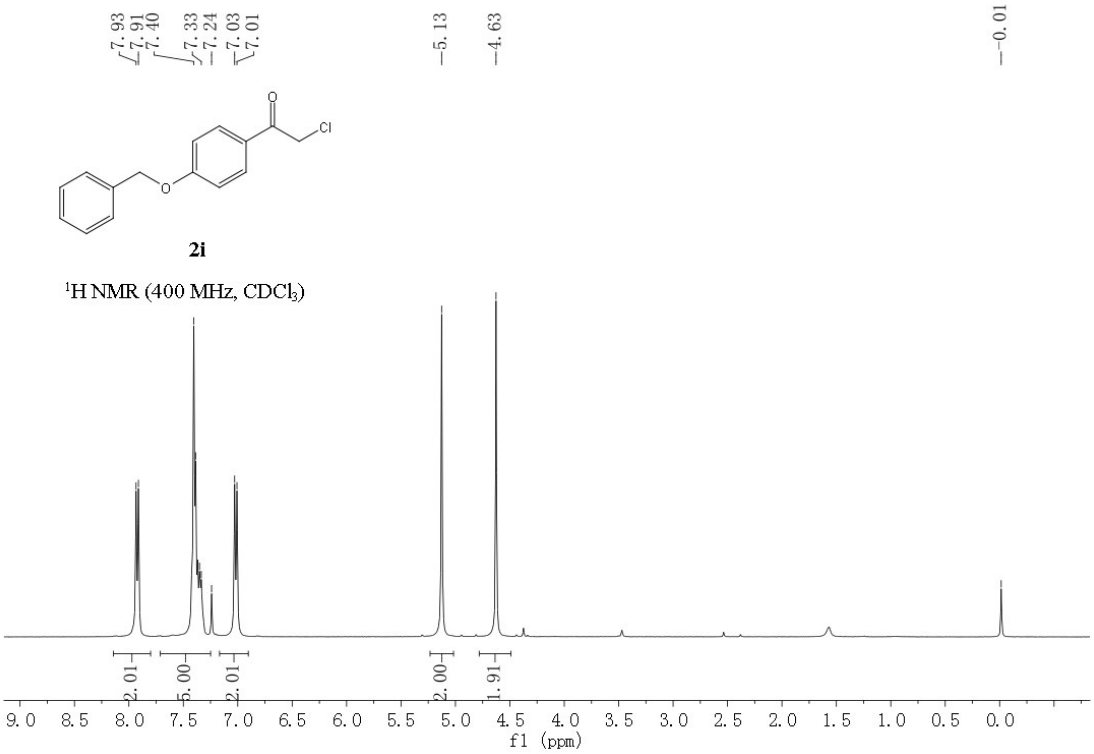
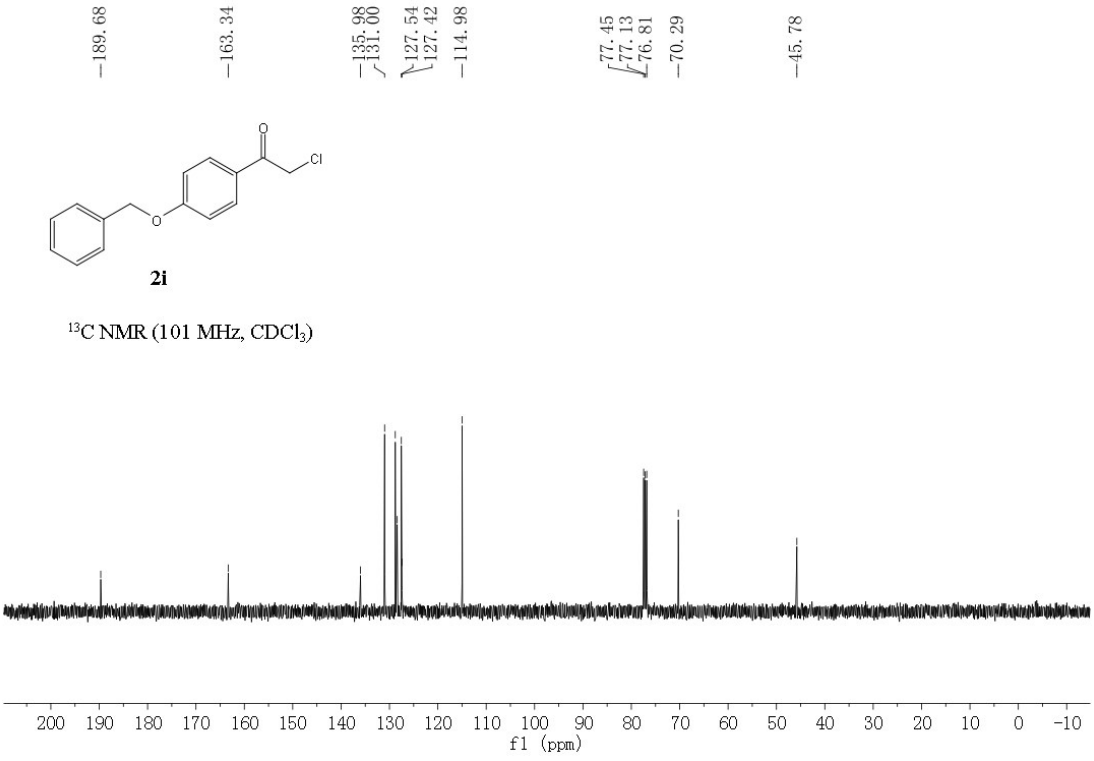
127.19
114.11
77.41
77.09
76.77
55.59
45.75
O
Cl
O
2h
^{13}C NMR (101 MHz, $CDCl_3$)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.93
7.91
7.40
7.33
7.24
7.03
7.01
5.13
4.63
0.01
Cl
O
O
2i
^{1}H NMR (400 MHz, $CDCl_3$)
2.01
5.00
2.01
2.00
1.91
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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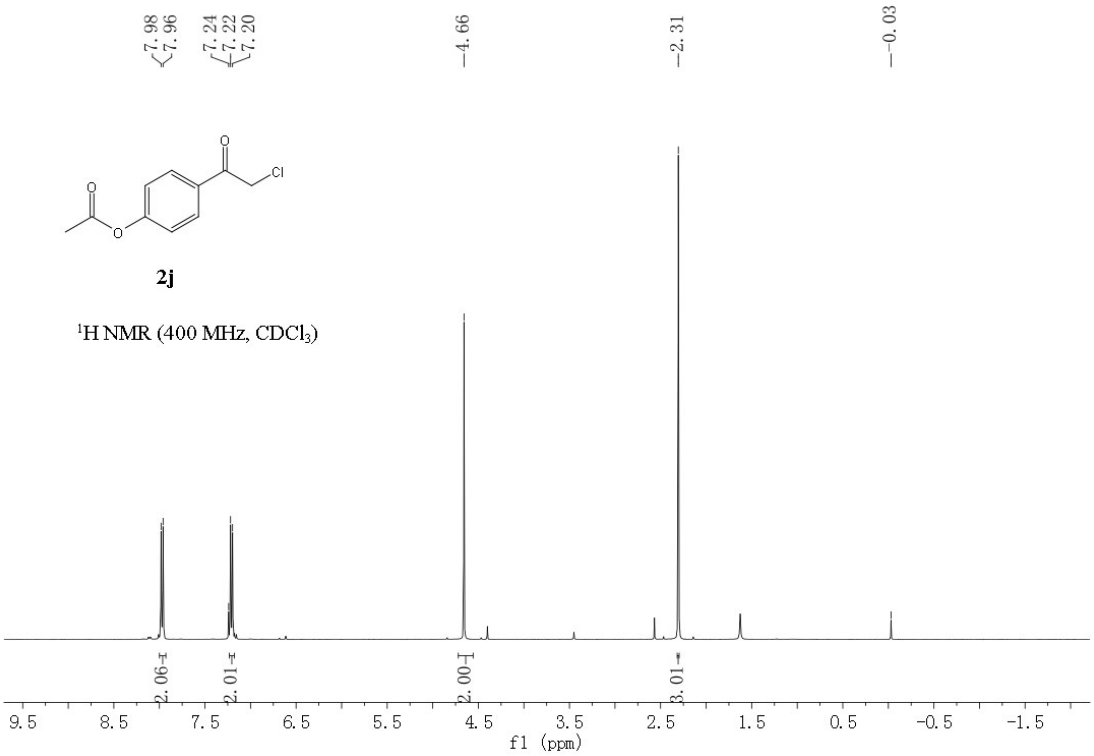
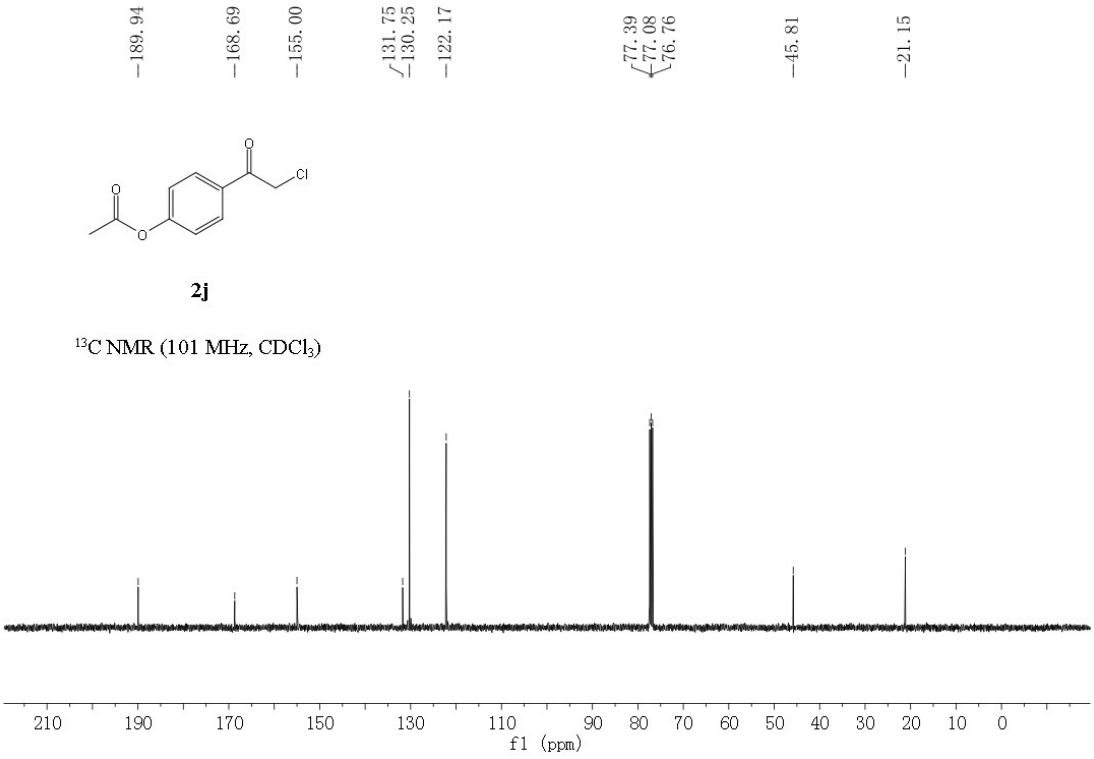
127.54
127.42
114.98
77.45
77.13
76.81
70.29
45.78
Cl
O
O
2i
^{13}C NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



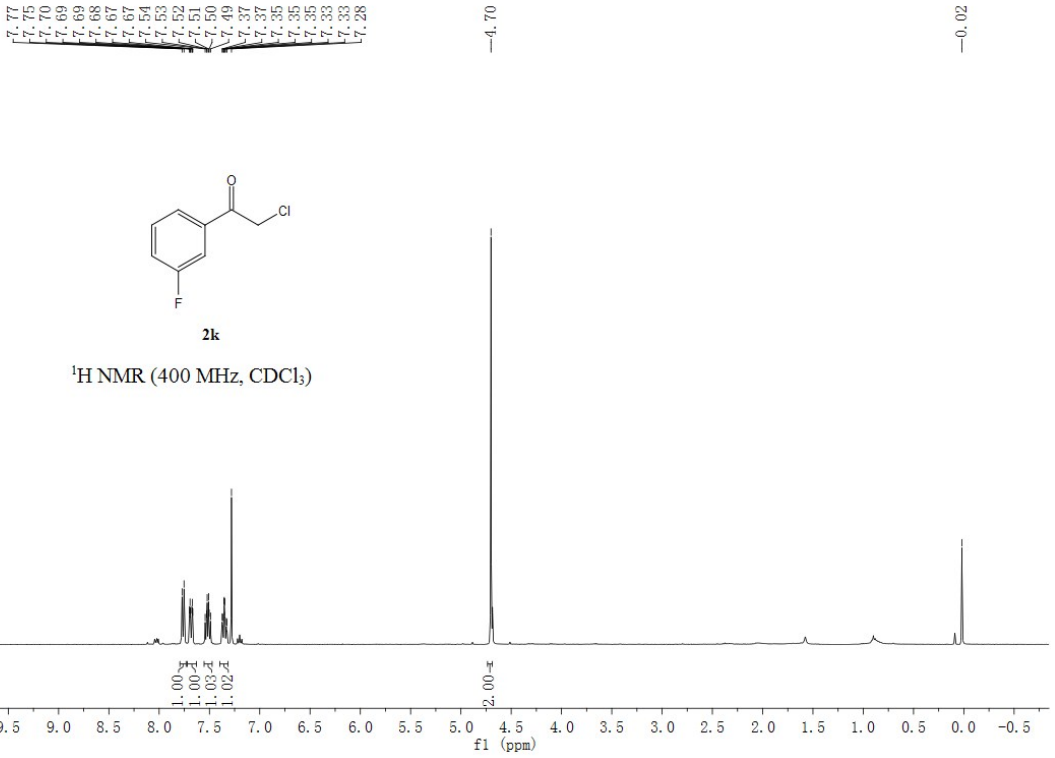
2j

^{1}H NMR (400 MHz, $CDCl_3$)



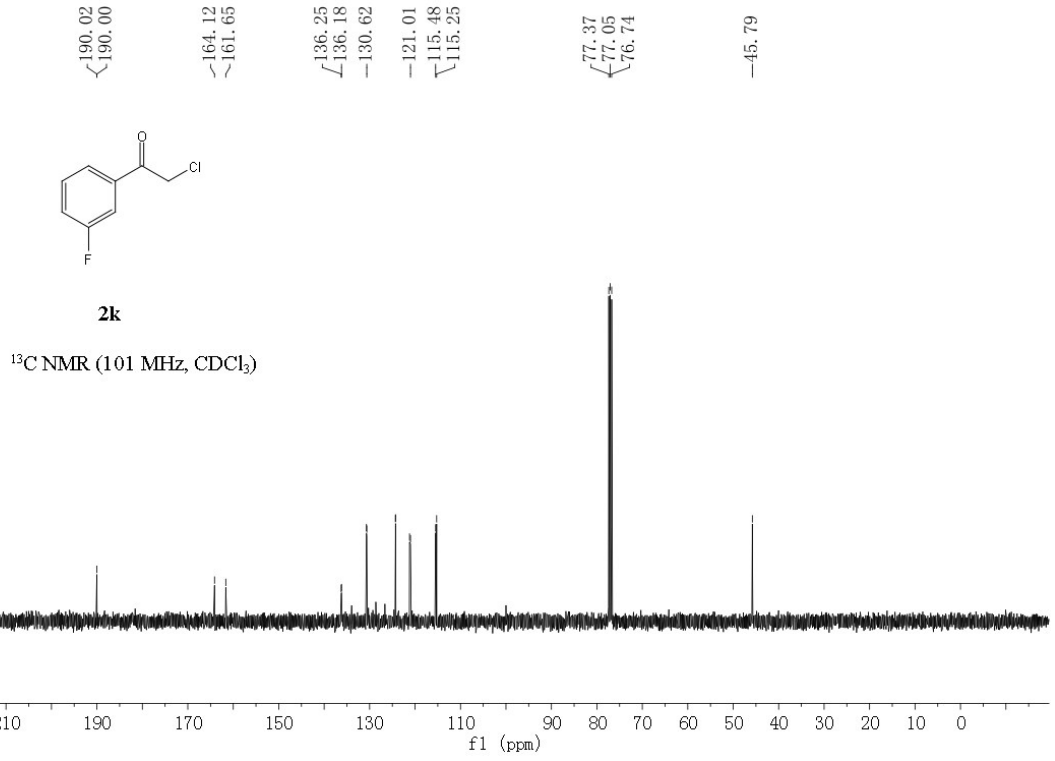
2j

^{13}C NMR (101 MHz, $CDCl_3$)



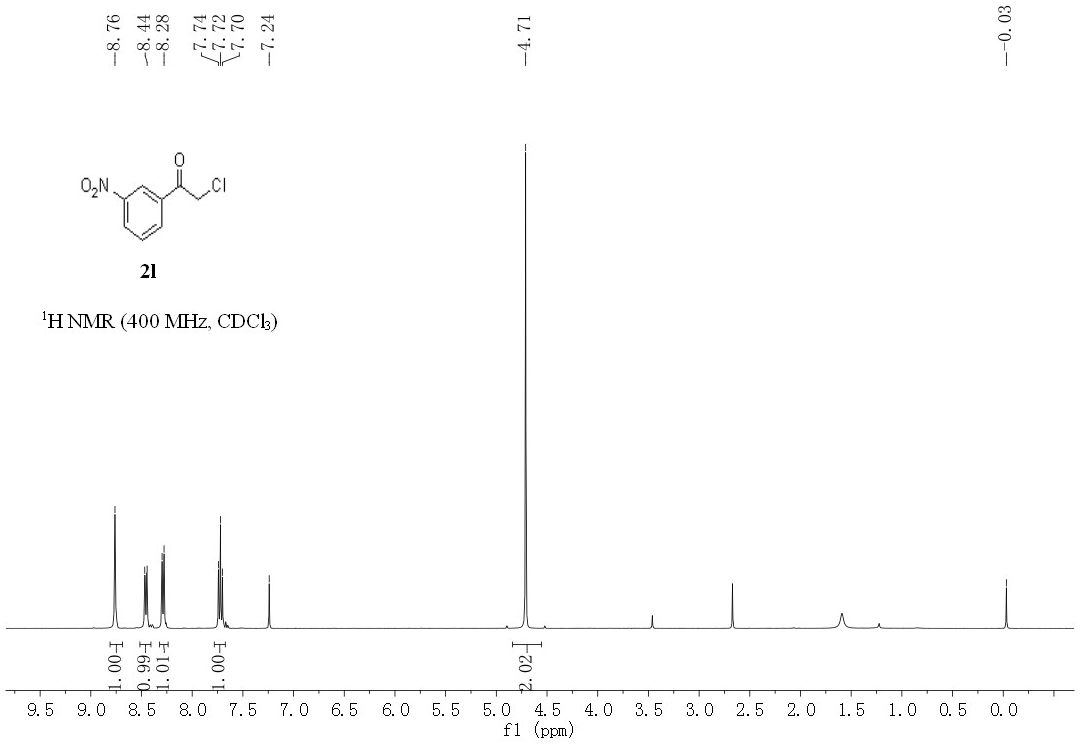
2k

^{1}H NMR (400 MHz, $CDCl_3$)



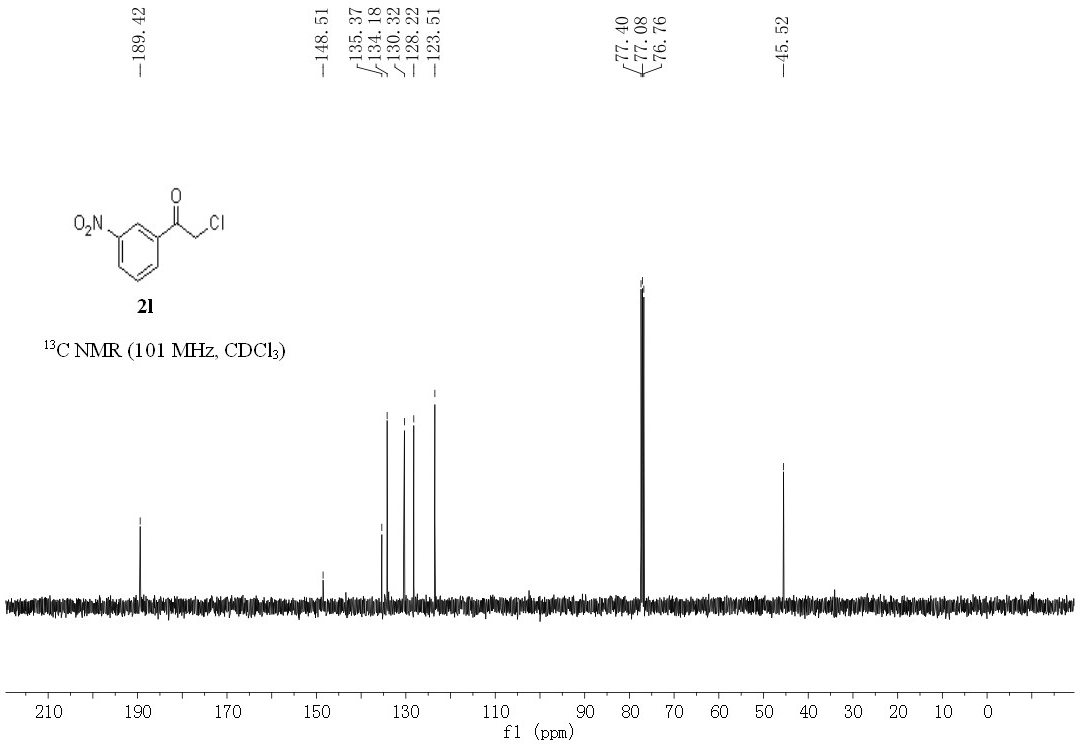
2k

^{13}C NMR (101 MHz, $CDCl_3$)



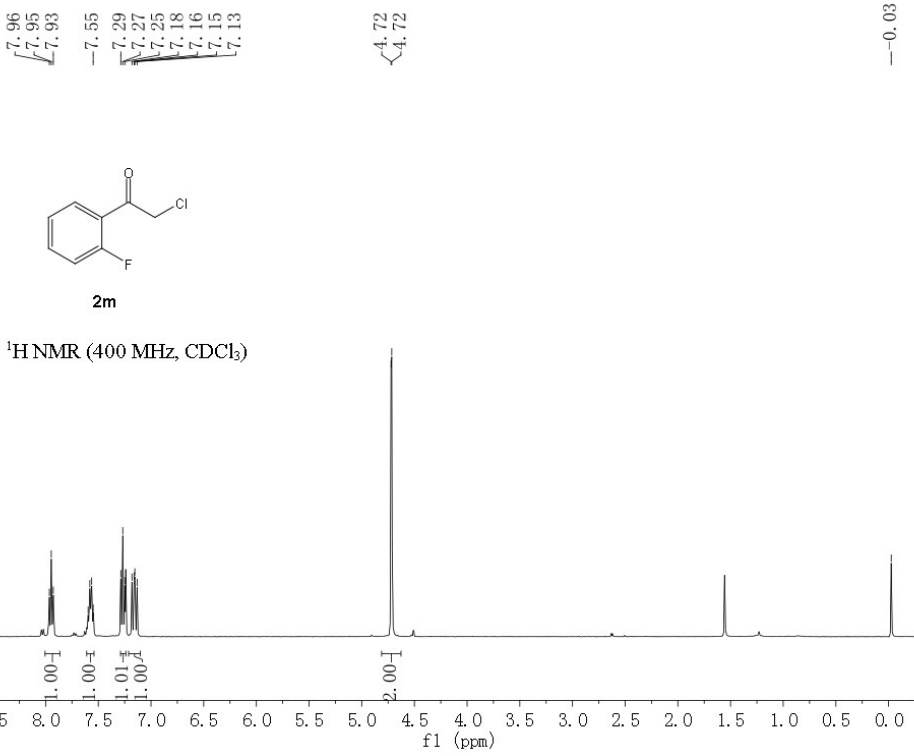
2l

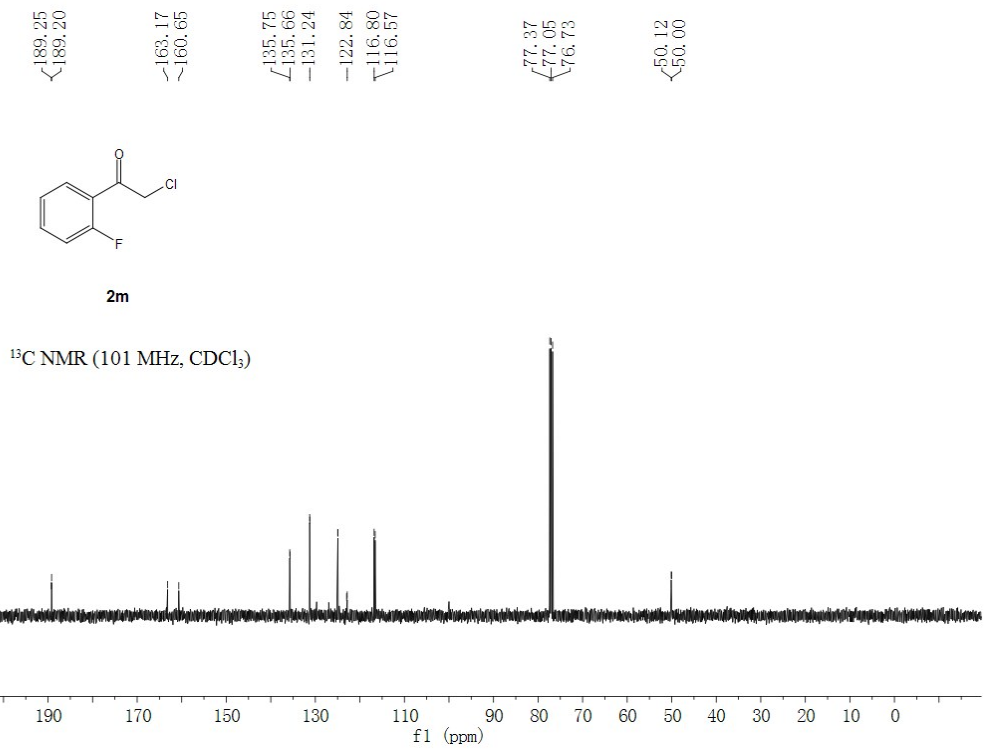
^{1}H NMR (400 MHz, $CDCl_3$)

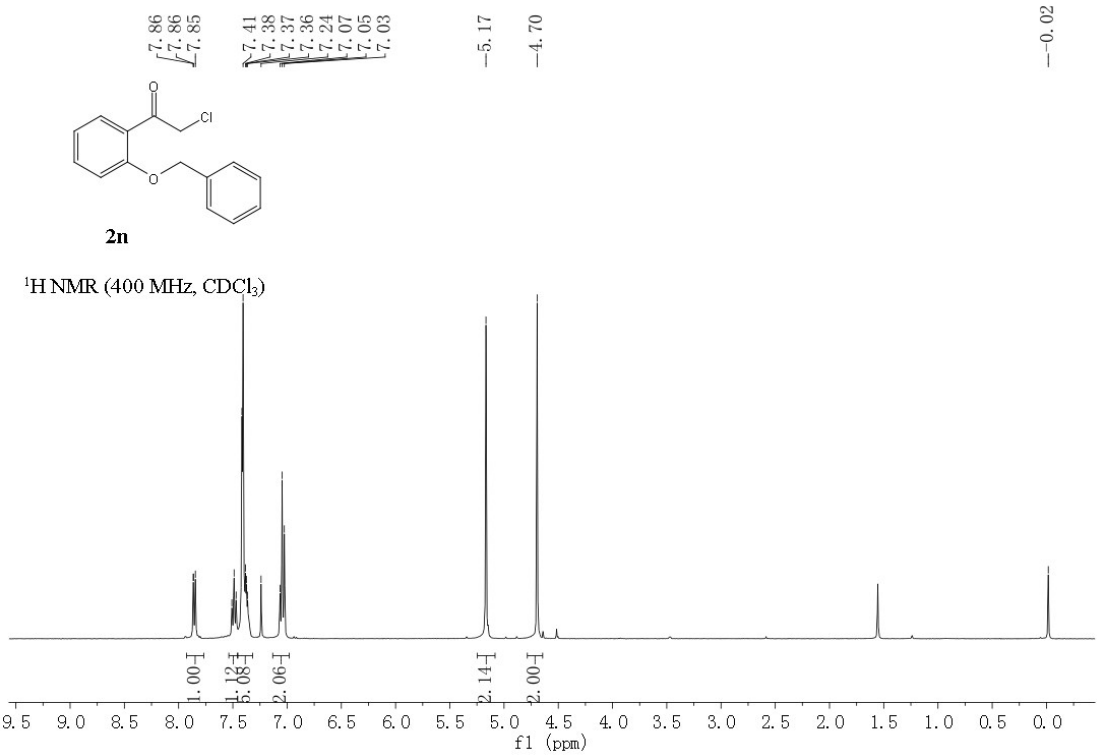


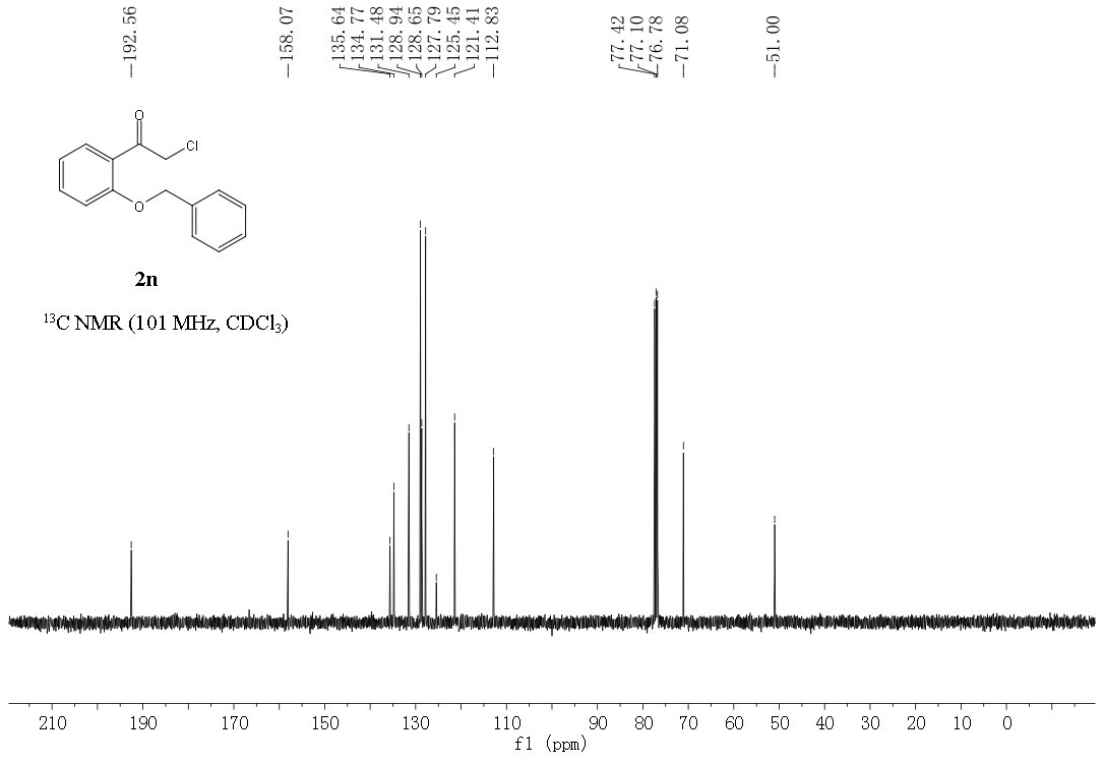
2l

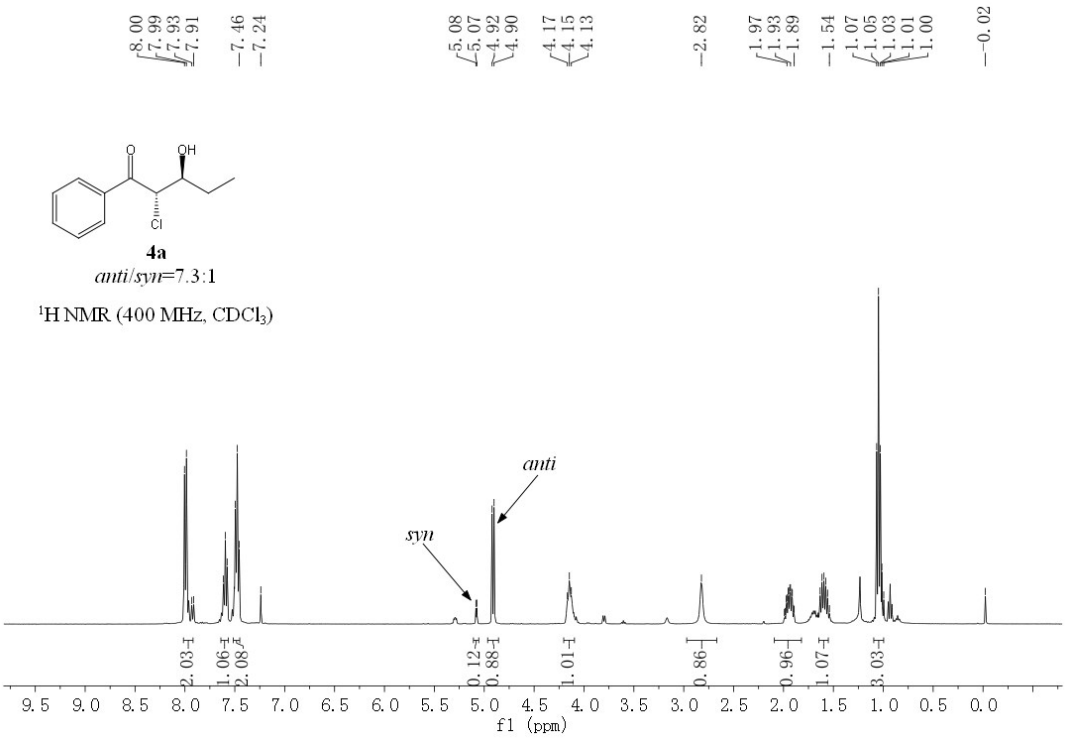
^{13}C NMR (101 MHz, $CDCl_3$)

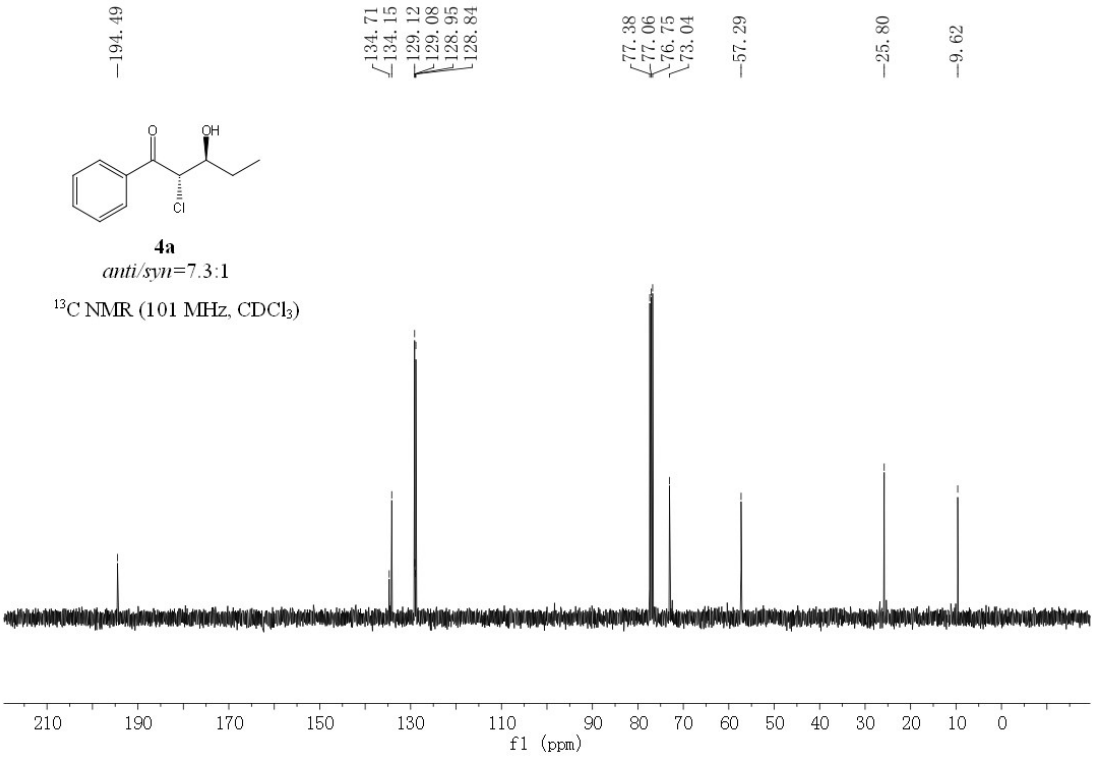

7.96
7.95
7.93
7.55
7.29
7.27
7.25
7.18
7.16
7.15
7.13
4.72
4.72
0.03
O
Cl
F
2m
^{1}H NMR (400 MHz, CDCl$_3$)
1.00
1.00
1.01
1.00
2.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

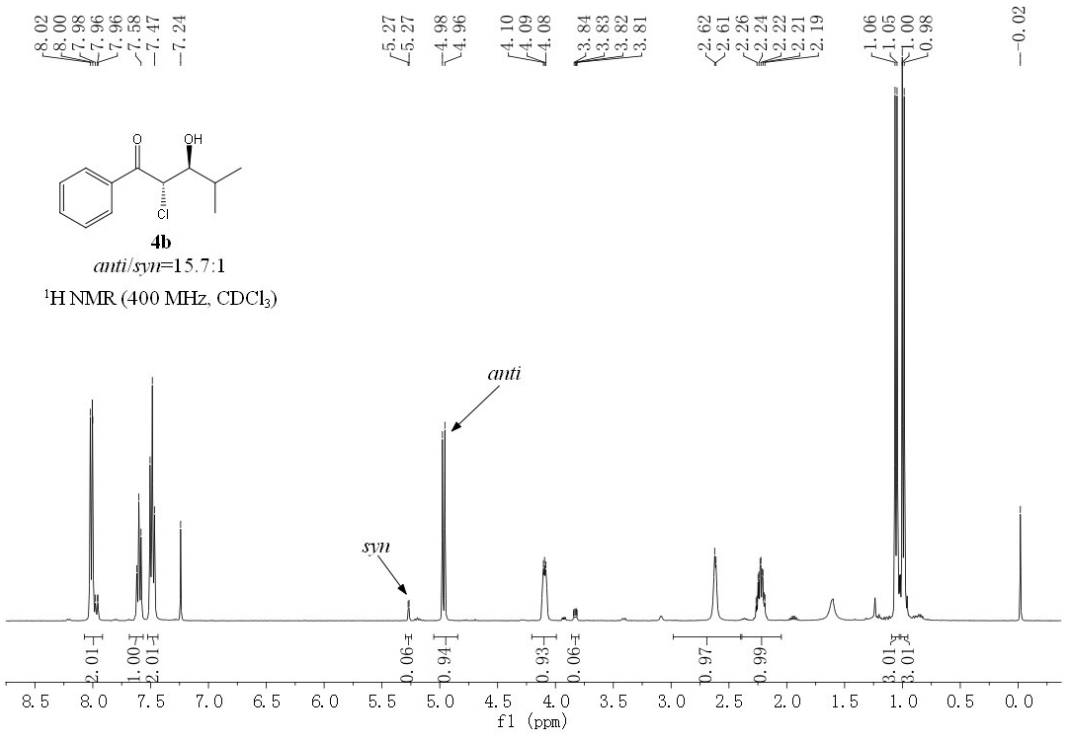

189.25
189.20
163.17
160.65
135.75
135.66
131.24
122.84
116.80
116.57
77.37
77.05
76.73
50.12
50.00
O
Cl
F
2m
^{13}C NMR (101 MHz, CDCl$_3$)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.86
7.86
7.85
7.41
7.38
7.37
7.36
7.24
7.07
7.05
7.03
5.17
4.70
0.02
Cl
O
O
2n
1H NMR (400 MHz, CDCl3)
1.00
1.12
6.08
2.06
2.14
2.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


192.56
158.07
135.64
134.77
131.48
128.94
128.65
127.79
125.45
121.41
112.83
77.42
77.10
76.78
71.08
51.00
Cl
O
O
2n
13C NMR (101 MHz, CDCl3)
210 190 170 150 130 110 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.00
7.99
7.93
7.91
7.46
7.24
5.08
5.07
4.92
4.90
4.17
4.15
4.13
2.82
1.97
1.93
1.89
1.54
1.07
1.05
1.03
1.01
1.00
0.02
O
OH
Cl
4a
anti/syn=7.3:1
1H NMR (400 MHz, CDCl3)
anti
syn
2.03
1.06
2.08
0.12
0.88
1.01
0.86
0.96
1.07
3.03
f1 (ppm)

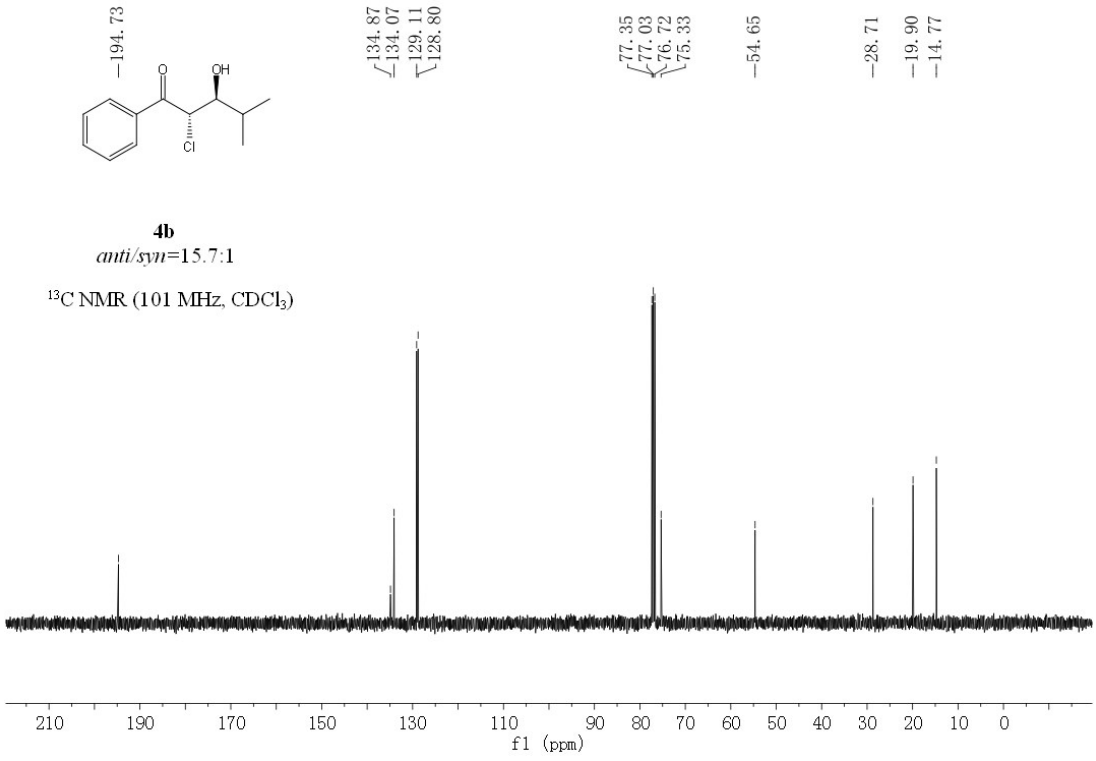

194.49
134.71
134.15
129.12
129.08
128.95
128.84
77.38
77.06
76.75
73.04
57.29
25.80
9.62
O
OH
Cl
4a
anti/syn=7.3:1
13C NMR (101 MHz, CDCl3)
f1 (ppm)



4b

anti/*syn*=15.7:1

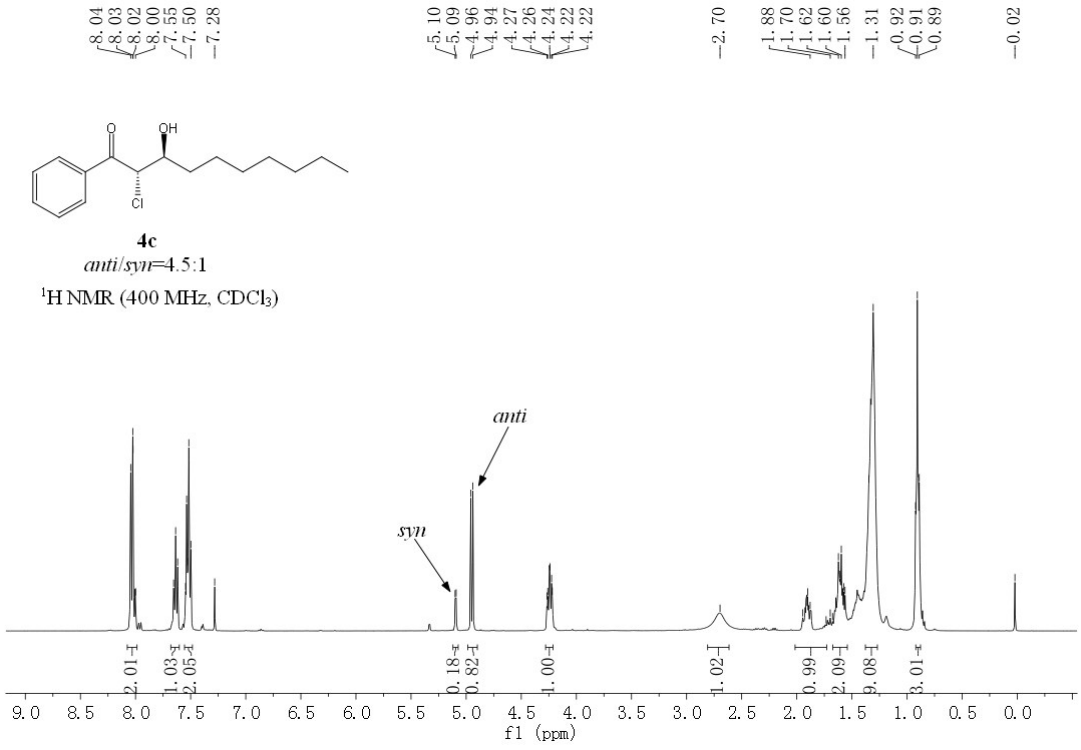
^{1}H NMR (400 MHz, $CDCl_3$)

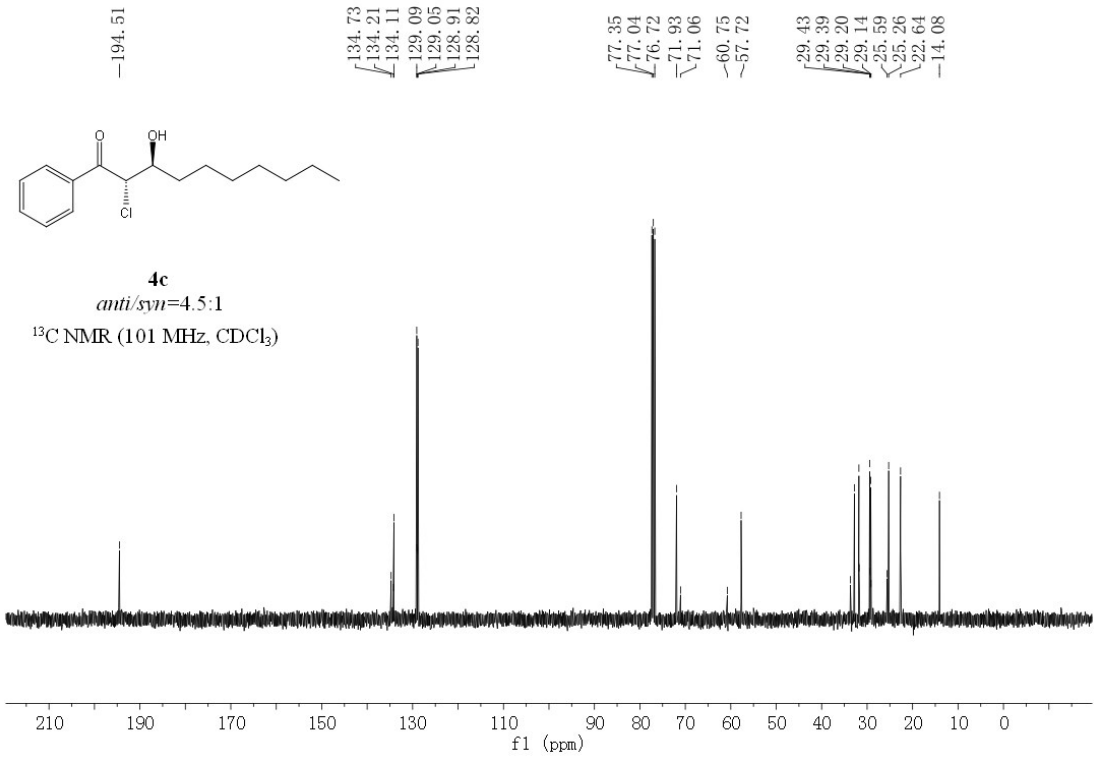


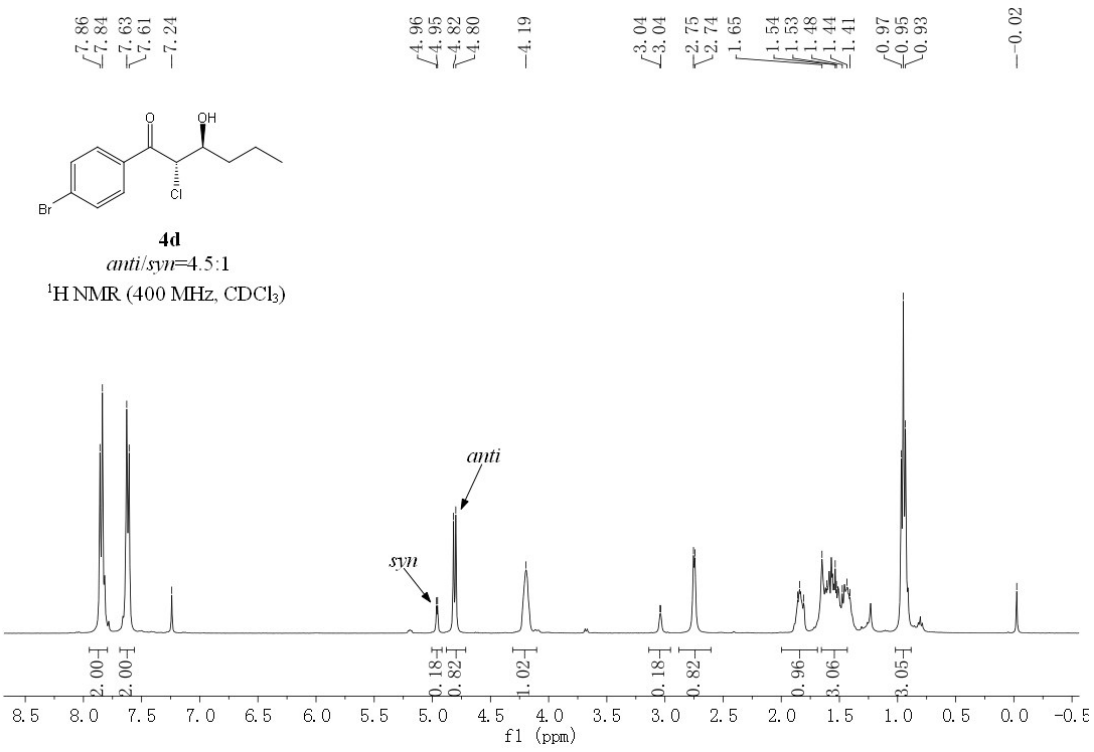
4b

anti/*syn*=15.7:1

^{13}C NMR (101 MHz, $CDCl_3$)


8.04
8.03
8.02
8.00
7.55
7.50
7.28
5.10
5.09
4.96
4.94
4.27
4.26
4.24
4.22
4.22
2.70
1.88
1.70
1.62
1.60
1.56
1.31
0.92
0.91
0.89
0.02
O
OH
Cl
4c
anti/syn=4.5:1
1H NMR (400 MHz, CDCl3)
anti
syn
2.01
1.03
2.05
0.18
0.82
1.00
1.02
0.99
2.09
9.08
3.01
f1 (ppm)

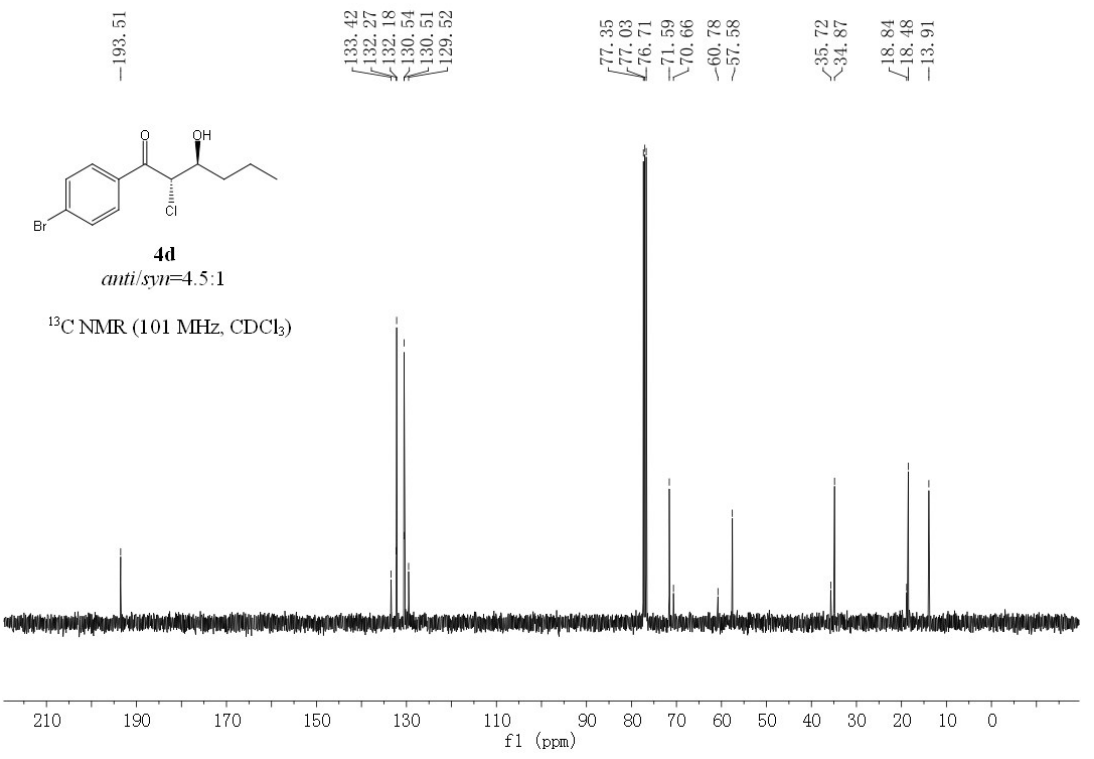

194.51
134.73
134.21
134.11
129.09
129.05
128.91
128.82
77.35
77.04
76.72
71.93
71.06
60.75
57.72
29.43
29.39
29.20
29.14
25.59
25.26
22.64
14.08
O
OH
Cl
4c
anti/syn=4.5:1
13C NMR (101 MHz, CDCl3)
f1 (ppm)



4d

anti/*syn*=4.5:1

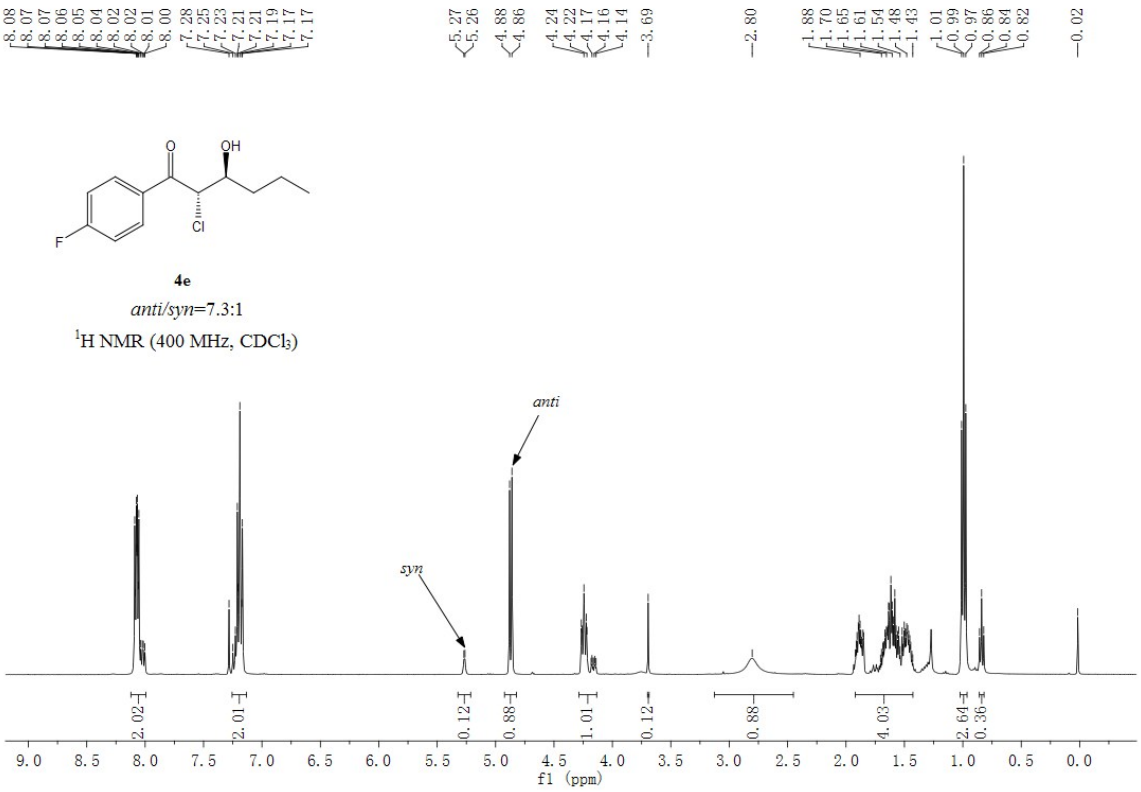
^{1}H NMR (400 MHz, $CDCl_3$)

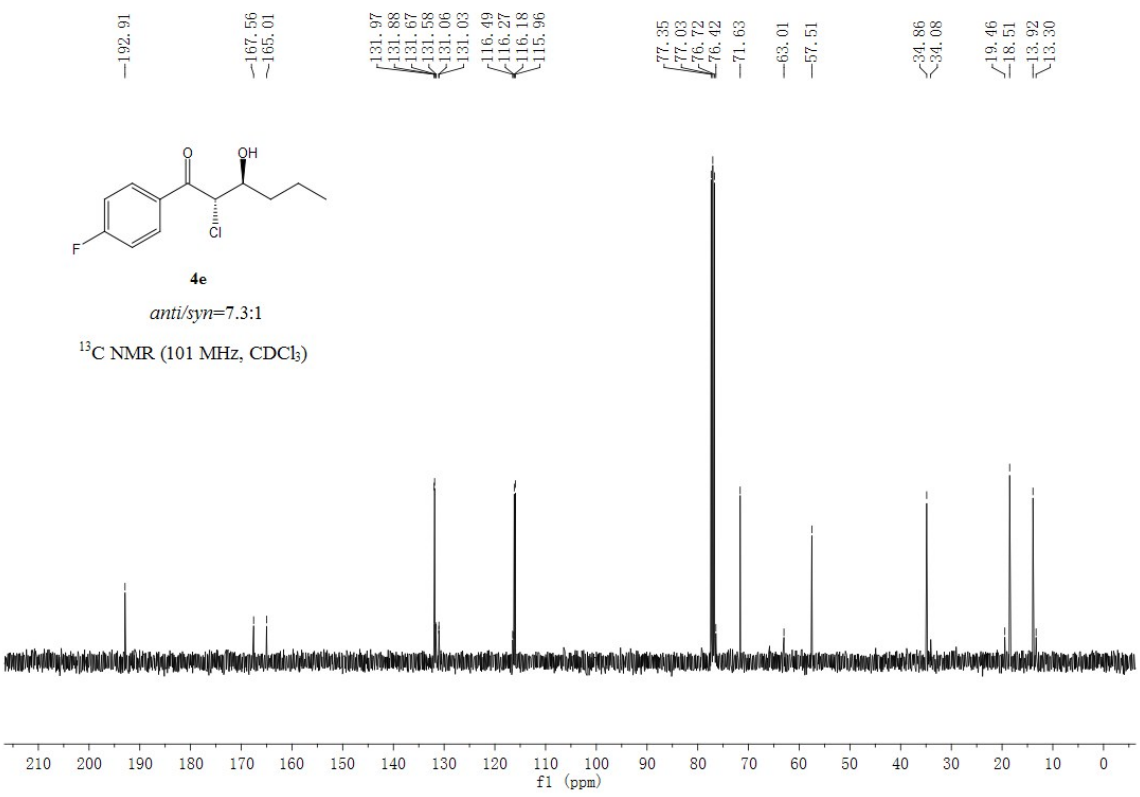


4d

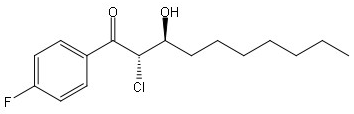
anti/*syn*=4.5:1

^{13}C NMR (101 MHz, $CDCl_3$)


8.08
8.07
8.07
8.06
8.05
8.04
8.02
8.02
8.01
8.00
7.28
7.25
7.23
7.21
7.21
7.19
7.17
7.17
5.27
5.26
4.88
4.86
4.24
4.22
4.17
4.16
4.14
3.69
2.80
1.88
1.70
1.65
1.61
1.54
1.48
1.43
1.01
0.99
0.97
0.86
0.84
0.82
0.02
O
OH
Cl
F
4e
anti/syn=7.3:1
1H NMR (400 MHz, CDCl3)
anti
syn
2.02
2.01
0.12
0.88
1.01
0.12
0.88
4.03
2.64
0.36
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


192.91
167.56
165.01
131.97
131.88
131.67
131.58
131.06
131.03
116.49
116.27
116.18
115.96
77.35
77.03
76.72
76.42
71.63
63.01
57.51
34.86
34.08
19.46
18.51
13.92
13.30
O
OH
Cl
F
4e
anti/syn=7.3:1
13C NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

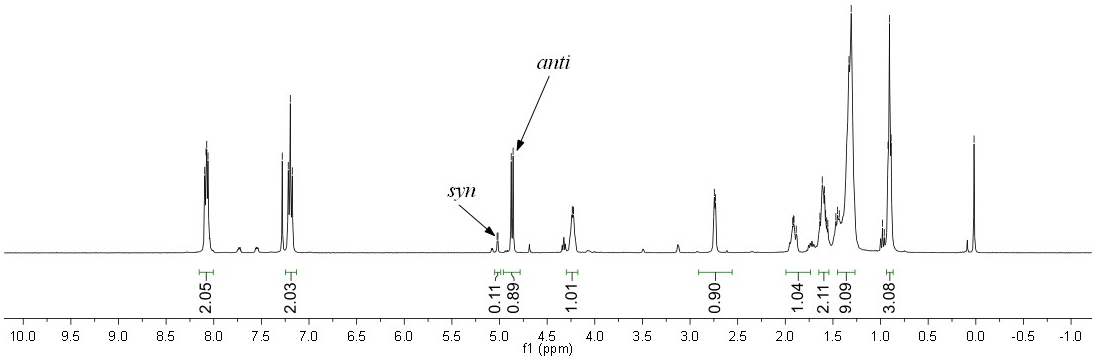
8.10
8.08
8.07
8.06
7.28
7.22
7.20
7.18
5.03
5.02
4.88
4.86
4.24
4.23
4.22
2.75
2.73
1.92
1.91
1.89
1.64
1.31
0.96
0.91
0.89
0.02



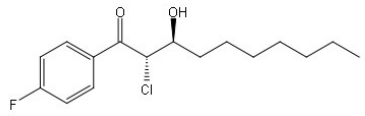
4f

anti/*syn*=8.1:1

^{1}H NMR (400 MHz, $CDCl_3$)



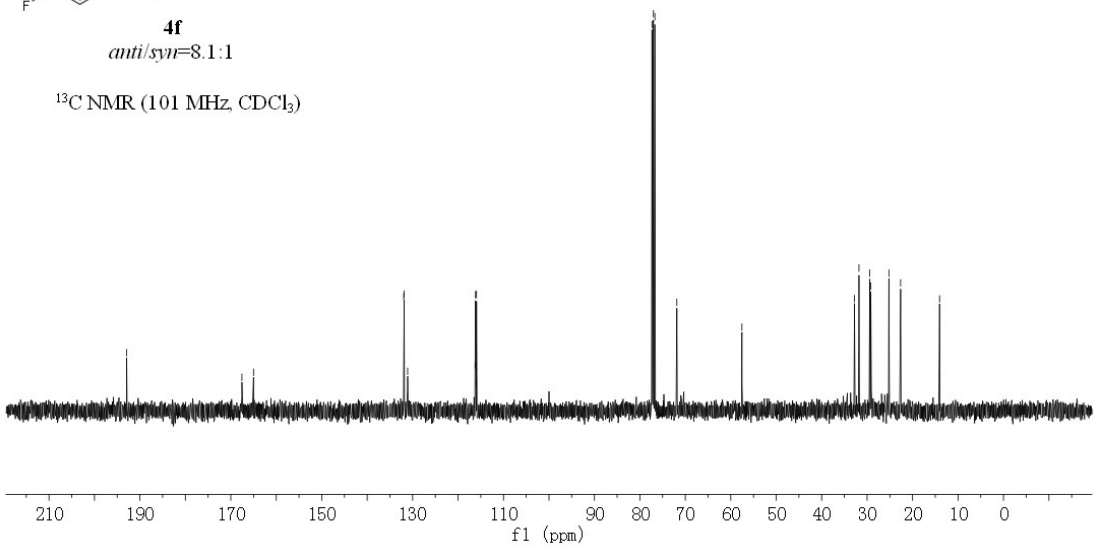
192.91
167.56
165.00
131.95
131.86
131.09
116.25
116.16
116.04
115.94
77.34
77.02
76.70
71.86
57.55
32.77
31.79
29.42
29.19
25.21
22.63
14.06

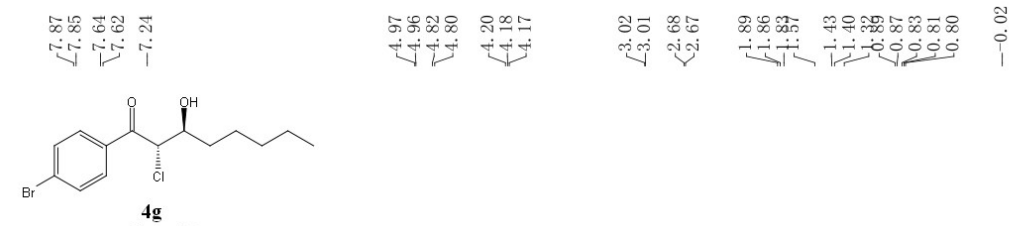


4f

anti/*syn*=8.1:1

^{13}C NMR (101 MHz, $CDCl_3$)

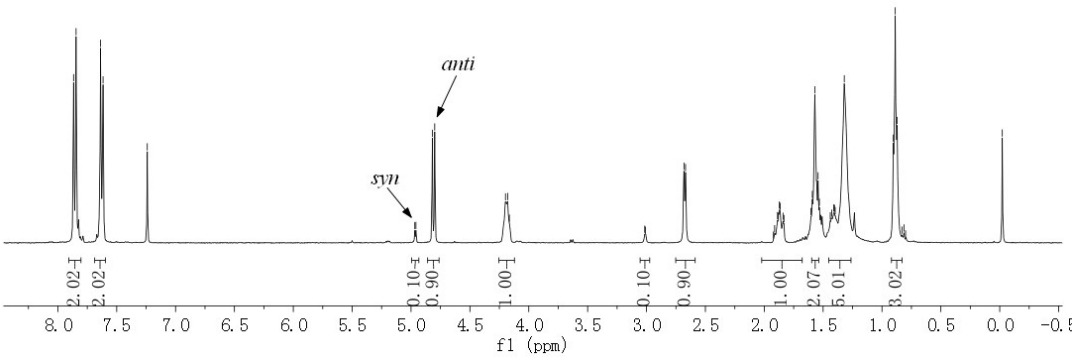


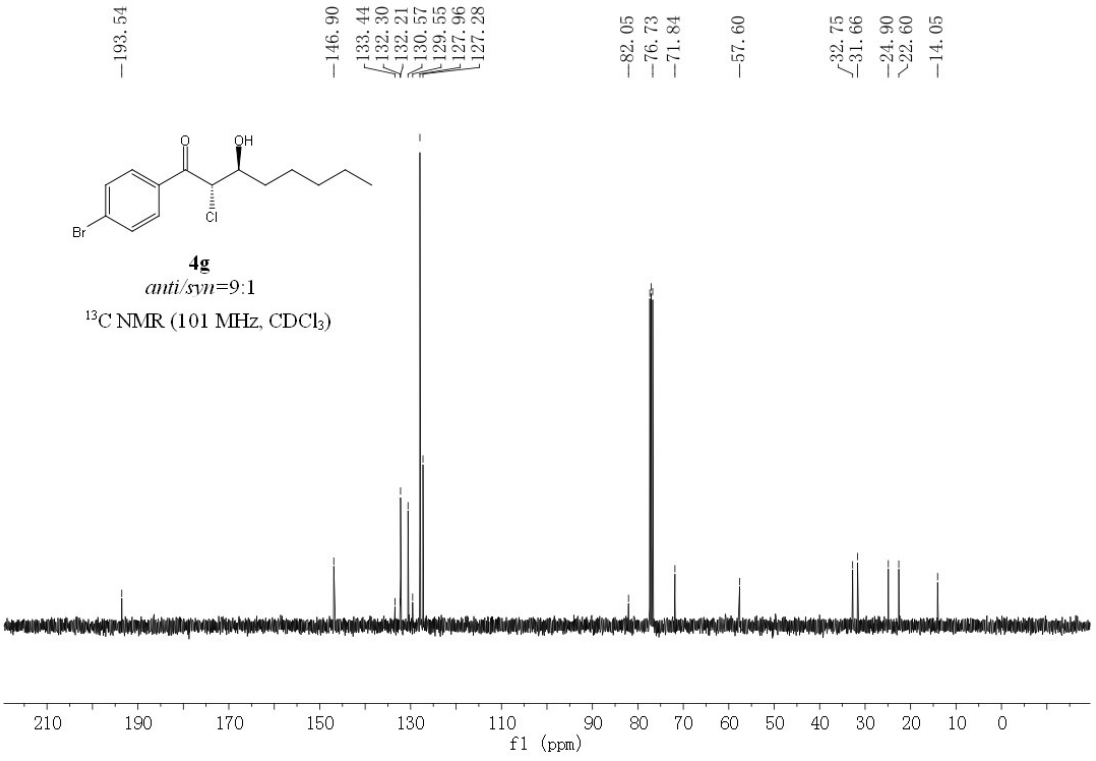


4g

anti/*syn*=9:1

^{1}H NMR (400 MHz, $CDCl_3$)

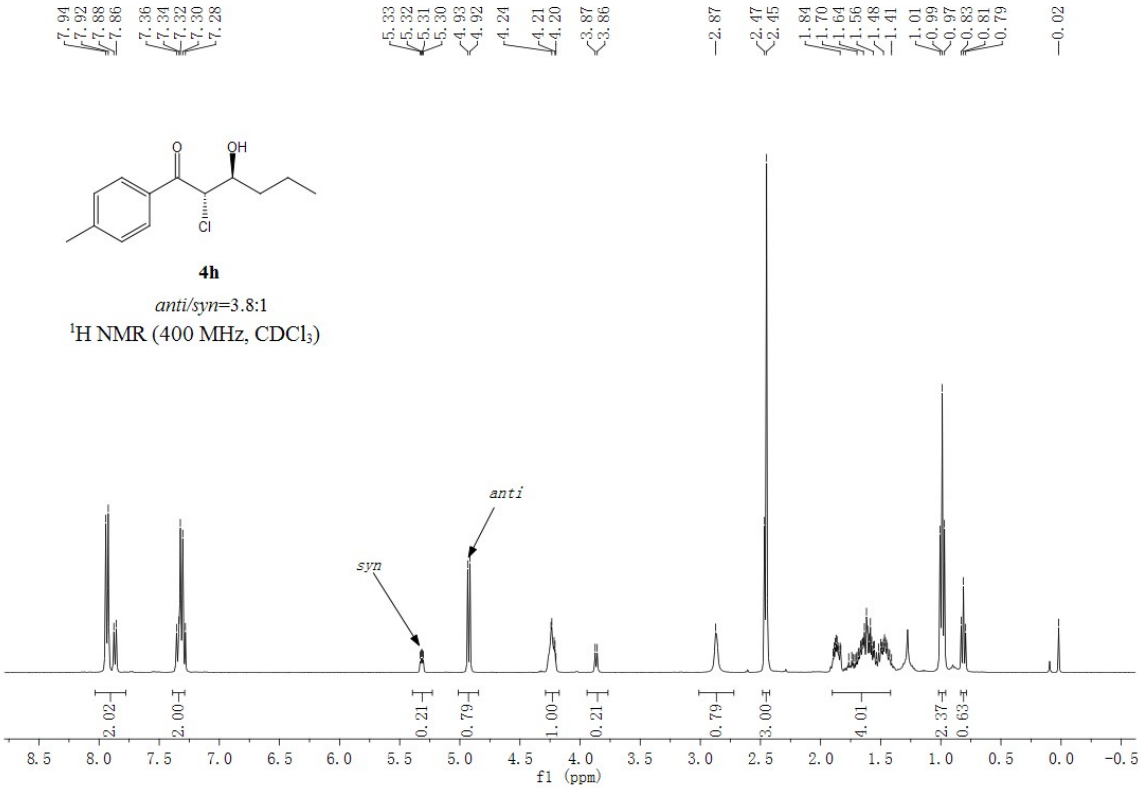




4g

anti/*syn*=9:1

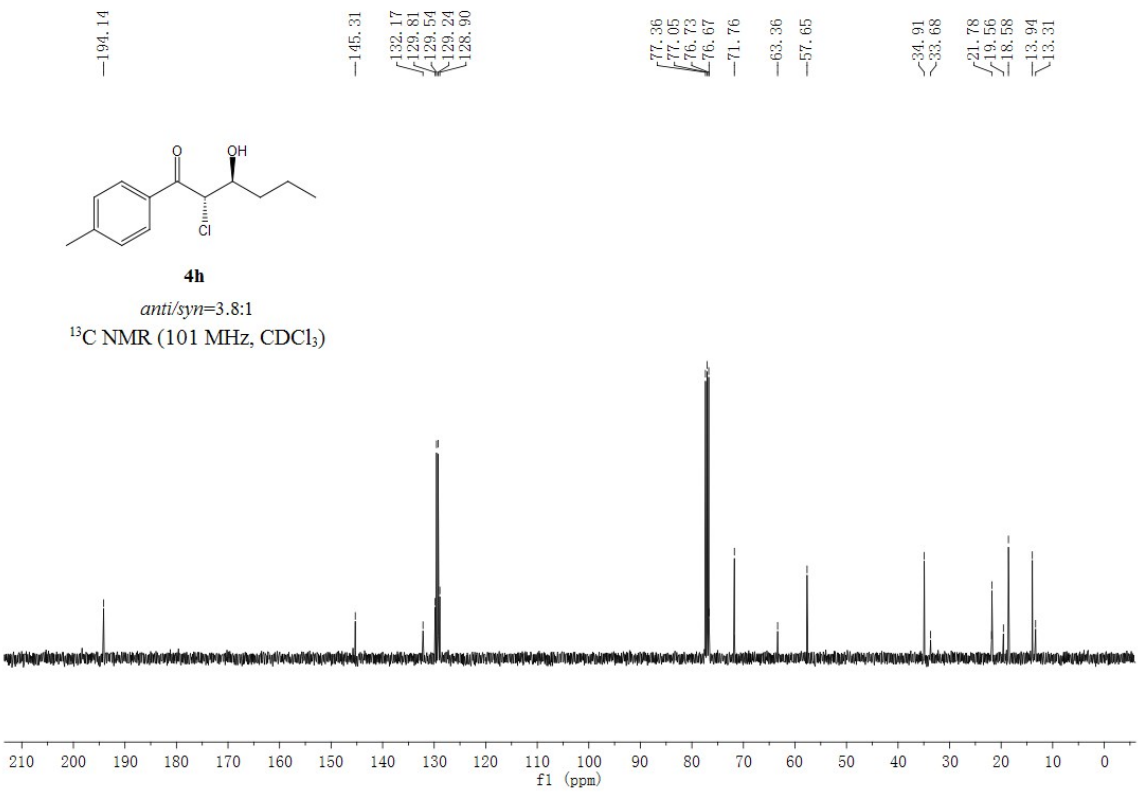
^{13}C NMR (101 MHz, $CDCl_3$)



4h

anti/syn=3.8:1

^{1}H NMR (400 MHz, $CDCl_3$)



4h

anti/syn=3.8:1

^{13}C NMR (101 MHz, $CDCl_3$)