

Supporting Information

Direct synthesis of α -Hydroxyacetophenones through molecule iodine activation of carbon–carbon double bond

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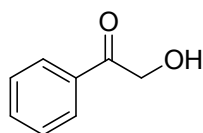
1. General remarks

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200–300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1} . ^1H spectra were recorded in CDCl_3 on 400/600 MHz NMR spectrometers and resonances (δ) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C spectra were recorded in CDCl_3 on 100 MHz NMR spectrometers and resonances (δ) are given in ppm. MS was carried out on a Finnigan Trace MS spectrometer (EI, 70 eV). The X-ray crystal-structure determinations of **2g** and **C** was obtained on a Bruker SMART APEX CCD system. Melting points were determined using XT-4 apparatus and not corrected.

2. General procedures for the synthesis of 2 and Characterization Data

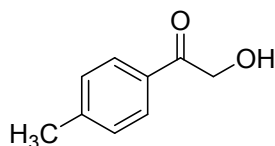
General procedure for synthesis of 2 (2a as an example): A mixture of styrene **1a** (1.0 mmol), iodine (1.0 mmol), and TBHP (4.0 mmol, 65% aq. Solution and purchase from Sinopharm Chemical Reagent Co., Ltd) in DMSO (3.0 mL) was stirred at room temperature till almost full conversion of the substrates by TLC analysis, then extracted with EtOAc 3 times ($3 \times 30\text{mL}$). The extract was washed with 10% $\text{Na}_2\text{S}_2\text{O}_3$. After drying over Na_2SO_4 and evaporation, The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **2a**.

Characterization of Products



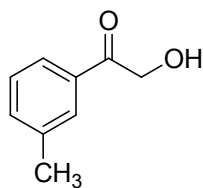
2-hydroxy-1-phenylethanone (**2a**):^[1]

Yield 80%; light yellow solid; mp 74–77°C; IR (KBr): 3426, 3389, 1686, 1447, 1405, 1233, 1106, 972, 757, 688, 615 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ (ppm) 7.93 (d, $J = 7.2$ Hz, 2H), 7.64 (t, $J = 7.2$ Hz, 1H), 7.51 (t, $J = 7.2$ Hz, 2H), 4.89 (s, 2H), 3.56 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 198.4, 134.3, 133.3, 128.9, 127.7, 65.4; MS (EI): m/z 137.17 (M+1, 0.25%), 136.10 (M, 2.26), 105.05 (100).



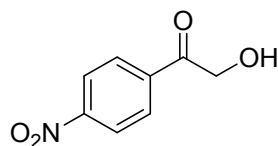
2-hydroxy-1-(p-tolyl)ethanone (**2b**):^[1]

Yield 83%; light yellow solid; mp 67–70°C; IR (KBr): 3440, 1679, 1608, 1416, 1284, 1178, 754 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.83 (d, $J = 8.4$ Hz, 2H), 7.64 (d, $J = 8.0$ Hz, 2H), 4.85 (s, 2H), 3.55 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 197.9, 130.8, 129.6, 129.3, 127.8, 65.3, 21.8; MS (EI): m/z 151.49 (M+1, 1.48%), 150.15 (M, 3.85), 149.17 (M-1, 44.37), 119.13 (100).



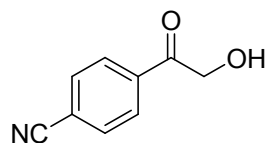
2-hydroxy-1-(m-tolyl)ethanone (2c): ^[2]

Yield 78%; yellow oily liquid; IR (KBr): 3451, 1689, 1287, 1098, 1032, 981, 787, 688 cm^{-1} ; ¹H NMR (600 MHz, CDCl_3): δ (ppm) 7.44 (s, 1H), 7.71 (t, $J = 7.2$ Hz, 1H), 7.44 (d, $J = 7.2$ Hz, 1H), 7.39 (t, $J = 7.2$ Hz, 1H), 4.87 (s, 2H), 3.59 (s, 1H), 2.43 (s, 3H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 198.5, 138.9, 135.1, 133.4, 128.8, 128.2, 124.9, 65.4, 21.3; MS (EI): m/z 150.12(M, 7.44%), 149.09(M-1, 4.99), 119.07 (100).



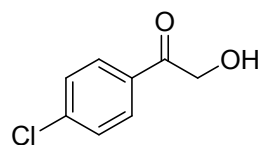
2-hydroxy-1-(4-nitrophenyl)ethanone (2d): ^[1]

Yield 65%; light yellow solid; mp 114–117°C; IR (KBr): 3437, 3386, 1687, 1605, 1543, 1348, 1320, 1228, 1108, 978, 856, 609 cm^{-1} ; ¹H NMR (600 MHz, CDCl_3): δ (ppm) 8.37 (d, $J = 7.8$ Hz, 2H), 8.11 (d, $J = 7.8$ Hz, 2H), 4.95 (s, 2H), 3.35 (s, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 197.2, 137.8, 130.9, 128.8, 124.2, 66.0; MS (EI): m/z 181.02(M, 0.31%), 150.07(100).



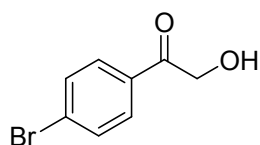
4-(2-hydroxyacetyl)benzonitrile (2e): ^[3]

Yield 60%; light yellow solid; mp 74–77°C; IR (KBr): 3448, 2231, 1696, 1289, 1229, 1100, 979, 836, 568 cm^{-1} ; ¹H NMR (600 MHz, CDCl_3): δ (ppm) 8.03 (d, $J = 8.4$ Hz, 2H), 7.83 (d, $J = 8.4$ Hz, 2H), 4.92 (s, 2H), 3.56 (s, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 197.3, 136.3, 132.8, 128.1, 117.5, 65.8; MS (EI): m/z 161.15(M, 2.95%), 130.07 (100).



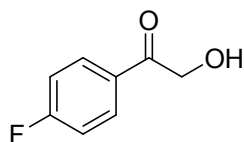
1-(4-chlorophenyl)-2-hydroxyethanone(2f): ^[1]

Yield 73%; light yellow solid; mp 109–112°C; IR (KBr): 3429, 3381, 1682, 1591, 1445, 1282, 1112, 1092, 978, 826, 616, 565, 525 cm^{-1} ; ¹H NMR (400 MHz, CDCl_3): δ (ppm) 7.87 (d, $J = 8.4$ Hz, 2H), 7.49 (d, $J = 8.4$ Hz, 2H), 4.85 (s, 2H), 3.48 (s, 1H); ¹³C NMR (100 MHz, CDCl_3) δ (ppm) 197.3, 140.8, 131.6, 129.3, 129.0, 65.4; MS (EI): m/z 170.14(M, 4.15%), 139.07 (100).



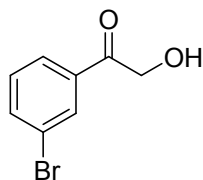
1-(4-bromophenyl)-2-hydroxyethanone (2g): ^[1]

Yield 71%; light yellow solid; mp 130–133°C; IR (KBr): 3426, 3380, 1683, 1585, 1412, 1231, 1108, 1069, 977, 822, 565 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.79 (d, J = 8.4 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 4.86 (s, 2H), 3.49 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 197.5, 132.2, 132.0, 129.5, 129.1, 65.4; MS (EI): m/z 216.11 (M+1, 5.28%), 214.04(M-1, 4.80), 185.03 (100).



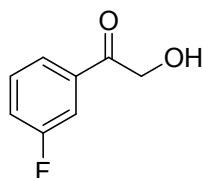
1-(4-fluorophenyl)-2-hydroxyethanone(2h): ^[3]

Yield 70%; light yellow solid; mp 104–107°C; IR (KBr): 3426, 3389, 1682, 1597, 1416, 1232, 1159, 1109, 979, 837, 602, 566 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.05–7.90 (m, 2H), 7.18 (t, J = 8.4Hz, 2H), 4.86 (s, 2H), 3.54 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 196.8, 167.5, 165.0, 130.4, 130.3, 116.3, 116.1, 65.3; MS (EI): m/z 154.13 (M, 3.69%), 123.05 (100).



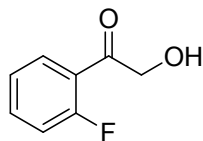
1-(3-bromophenyl)-2-hydroxyethanone (2i): ^[11]

Yield 70%; light yellow solid; mp 79–82 °C; IR (KBr): 3429, 3399, 1683, 1566, 1424, 1227, 1112, 788, 702 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.06 (s, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 8.0 Hz, 1H), 4.87 (s, 1H), 3.44 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 197.3, 137.1, 135.0, 130.7, 130.5, 126.1, 123.3, 65.5; MS (EI): m/z 216.11 (M+1, 7.51%), 214.11(M-1, 7.21), 183.03 (100).



1-(3-fluorophenyl)-2-hydroxyethanone (2j):

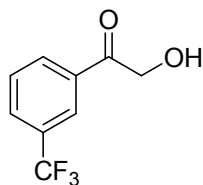
Yield 68%; yellow solid; mp 67–70°C; IR (KBr): 3433, 3396, 1686, 1589, 1453, 1259, 1099, 867, 793, 772, 680 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ (ppm) 7.70 (d, J = 7.2 Hz, 1H), 7.66–7.61 (m, 1H), 7.53–7.48 (m, 1H), 7.38–7.32 (m, 1H), 4.87 (s, 2H), 3.47 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 197.4, 164.1, 135.4, 130.8, 130.7, 123.4, 121.4, 121.2, 114.6, 114.4, 65.6; MS (EI): m/z 154.12 (M, 8.71%), 123.05 (100).



1-(2-fluorophenyl)-2-hydroxyethanone (2k): ^[3]

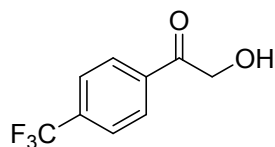
Yield 62%; yellow oily liquid; IR (KBr): 3448, 1699, 1611, 1486, 1356, 1279, 1222, 1094, 976,

761 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ (ppm) 8.07 (t, $J = 7.2$ Hz, 1H), 7.66-7.56 (m, 1H), 7.31 (t, $J = 7.2$ Hz, 1H), 7.19 (t, $J = 9.6$ Hz, 1H), 4.81 (s, 2H), 3.77 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 196.9, 164.1, 136.0, 135.9, 135.3, 130.6, 124.9, 124.8, 116.9, 116.7, 69.2; MS (EI): m/z 154.13 (M, 1.52%), 123.00 (100).



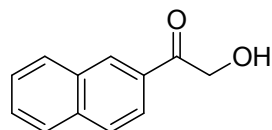
2-hydroxy-1-(3-(trifluoromethyl)phenyl)ethanone (2l):

Yield 67%; light yellow solid; mp 93–96°C; IR (KBr): 3429, 1701, 1334, 1174, 1127, 1072, 690 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ (ppm) 8.19 (s, 1H), 8.10 (s, 1H), 7.89 (s, 1H), 7.68 (s, 1H), 4.95 (s, 2H), 3.86 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 197.3, 133.9, 133.3, 130.8, 130.6, 130.2, 129.7, 129.2, 127.1, 124.6, 65.6; MS (EI): m/z 204.08 (M, 2.05%), 173.08 (100).



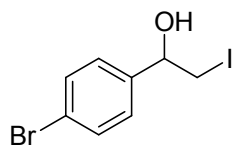
2-hydroxy-1-(4-(trifluoromethyl)phenyl)ethanone (2m):

Yield 62%; White solid; mp 110–113°C; IR (KBr): 3429, 3358, 1688, 1418, 1329, 1235, 1171, 1135, 1109, 1065, 981, 842, 765, 622, 600, 500 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3): δ (ppm) 8.05 (d, $J = 8.4$ Hz, 2H), 7.79 (d, $J = 8.4$ Hz, 2H), 4.93 (s, 2H), 3.42 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 197.6, 136.0, 135.6, 128.1, 126.1, 126.0, 124.7, 65.8; MS (EI): m/z 205.35 (M+1, 0.42%), 204.27 (M, 0.95), 73.09 (100).



2-hydroxy-1-(naphthalen-2-yl)ethanone (2n):

Yield 72%; light yellow solid; mp 108–111°C; IR (KBr): 3429, 3392, 1680, 1624, 1405, 1184, 1102, 1018, 855, 820, 744, 612, 478 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.42 (s, 1H), 7.95–7.87 (m, 4H), 7.63–7.24 (m, 2H), 5.02 (s, 2H), 3.61 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 198.3, 136.1, 132.4, 130.6, 129.6, 129.5, 129.0, 128.9, 127.9, 127.1, 123.0, 65.5; MS (EI): m/z 187.23 (M+1, 2.16%), 186.14 (M, 19.50), 155.10 (100).



1-(4-bromophenyl)-2-iodoethanol (C):

Yield 27%; brown solid; mp 76–79°C; IR (KBr): 3335, 1501, 1406, 1128, 1603, 1007, 967, 845 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.49 (d, $J = 6.0$ Hz, 2H), 7.23 (d, $J = 8.4$ Hz, 2H), 4.77 (d, $J = 7.8$ Hz, 1H), 3.46-3.42 (m, 1H), 3.34 (t, $J = 8.4$ Hz, 1H), 2.67 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 140.0, 131.7, 127.4, 122.1, 73.2, 14.9; MS (EI): m/z 326.10 (M, 5.13%),

185.15(100).

3.Reference:

- [1] Chen, C. Q.; Feng, G. Z.; Zhang, G. Z.; Zhao, Q.; Huang, G. S. *Synlett* **2008**, 3205-3208.
[2] Utsukihara, T.; Nakamura, H.; Watanabe, M.; Horiuchi, C. A.; *Tetrahedron Lett.* **2006**, 47, 9359-9364.
[3] Mclaughlin, M.; Belyk, K. M.; Qian, G.; Reamer, R. A.; Cheng, C. Y. *J. Org. Chem.* **2012**, 77, 5144-5148.

4. Crystallographic data and molecular structure of compounds **2g** and **C**

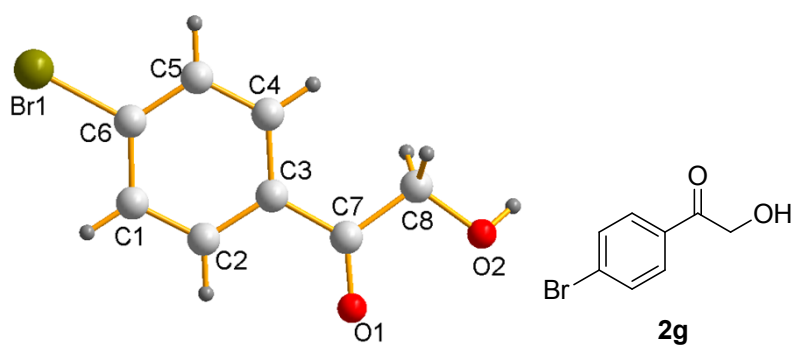


Fig. 1. X-ray crystal structure of compound **3ba**

Crystal structure data for compound **2g**: $C_8H_7BrO_2$, chemical formula weight: 215.05, Monoclinic space group $P2_1$, $a = 4.6871(6)$ Å, $b = 5.3721(7)$ Å, $c = 15.900(2)$ Å; $\alpha = 90^\circ$, $\beta = 97.381(2)^\circ$, $\gamma = 90^\circ$, $V = 397.03(9)$ Å³, $T = 298(2)$ K, $Z = 2$, $D_C = 1.799$ Mg/m³, $\mu = 5.119$ mm⁻¹, $\lambda = 0.71073$ Å, $F(000)$ 212, crystal size 0.16 x 0.12 x 0.10 mm³, 1460 independent reflections [$R(\text{int}) = 0.0226$], reflections collected 3959, refinement method: full-matrix least-squares on F^2 : goodness-of-fit on F^2 1.075, final R indices [$I > 2\sigma(I)$], $R_1 = 0.0282$, $wR_2 = 0.0707$, largest diff. peak and hole 0.326 and -0.290 e.Å⁻³. CCDC 973925 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

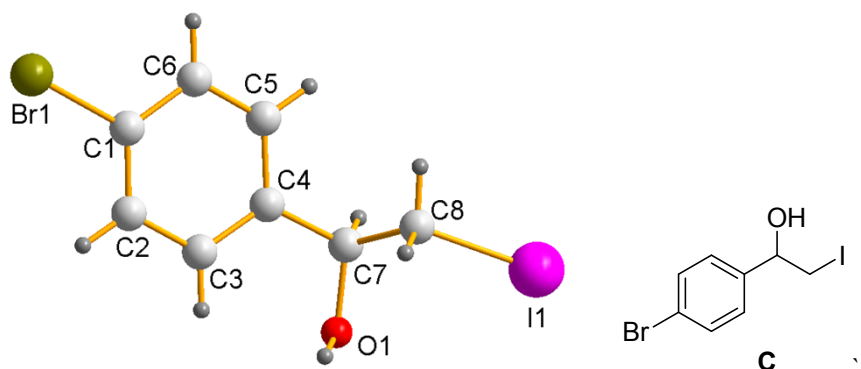


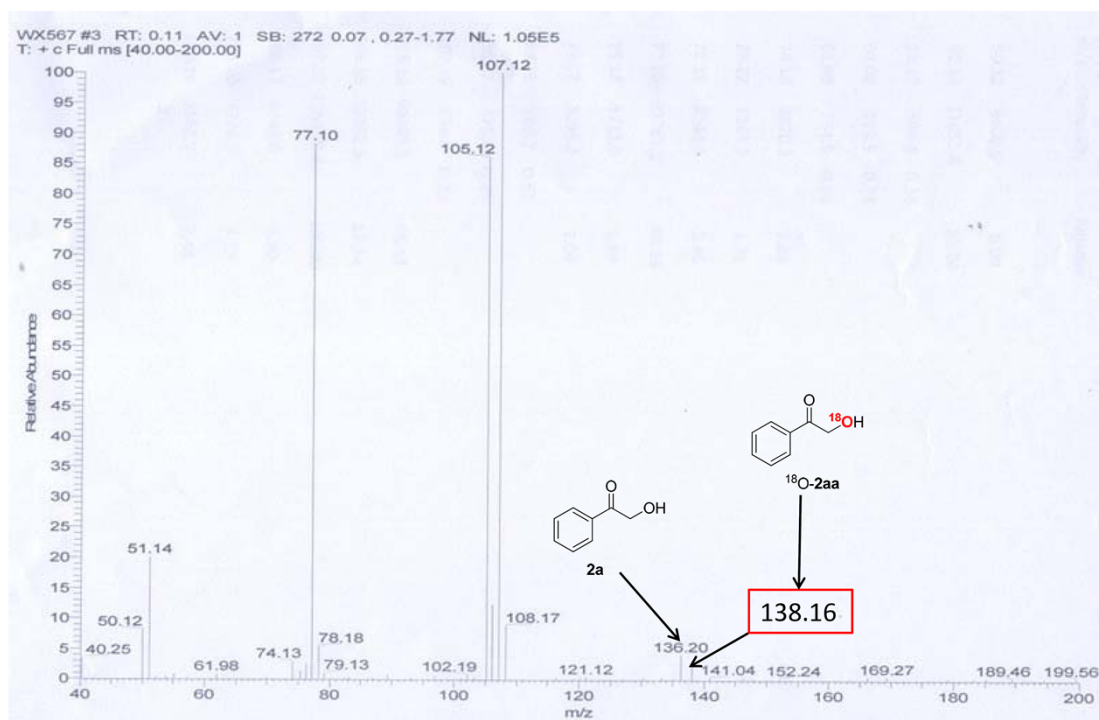
Fig. 2. X-ray crystal structure of compound **C**

Crystal structure data for compound **C**: C_8H_8BrIO , chemical formula weight: 326.95, Monoclinic space group $P2_1(1)/n$, $a = 13.414(3)$ Å, $b = 4.5553(8)$ Å, $c = 15.692(3)$ Å; $\alpha = 90^\circ$, $\beta = 100.321(3)^\circ$, $\gamma = 90^\circ$, $V = 943.3(3)$ Å³, $T = 296(2)$ K, $Z = 4$, $D_C = 2.302$ Mg/m³, $\mu = 7.573$ mm⁻¹, $\lambda = 0.71073$

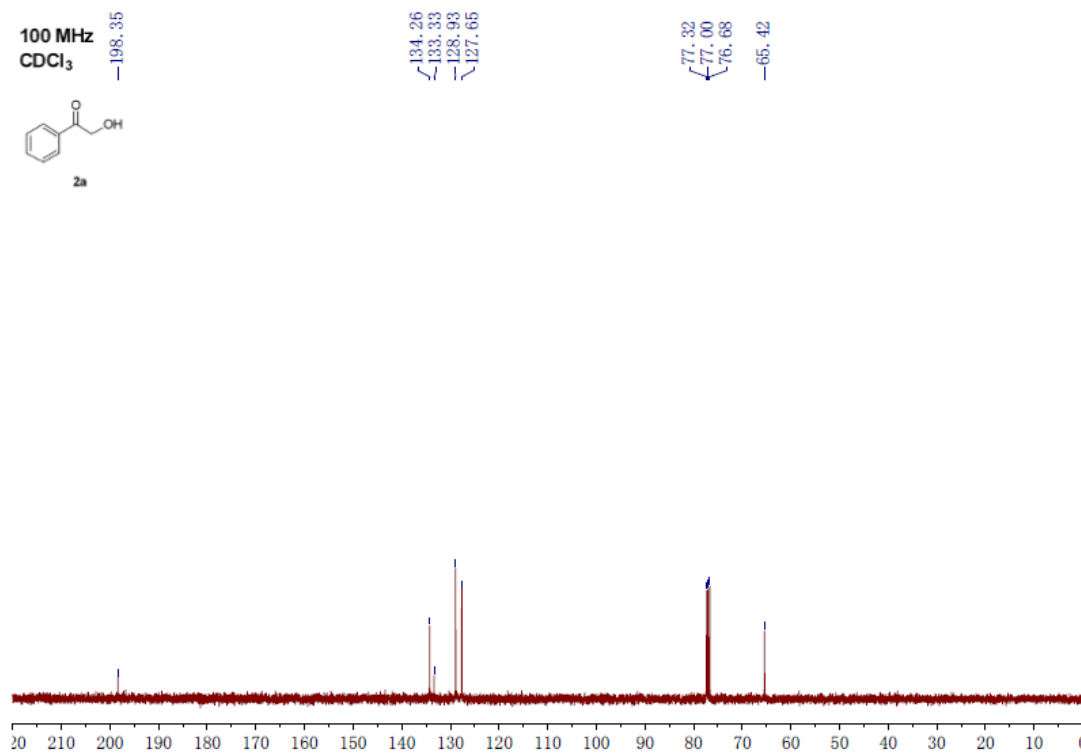
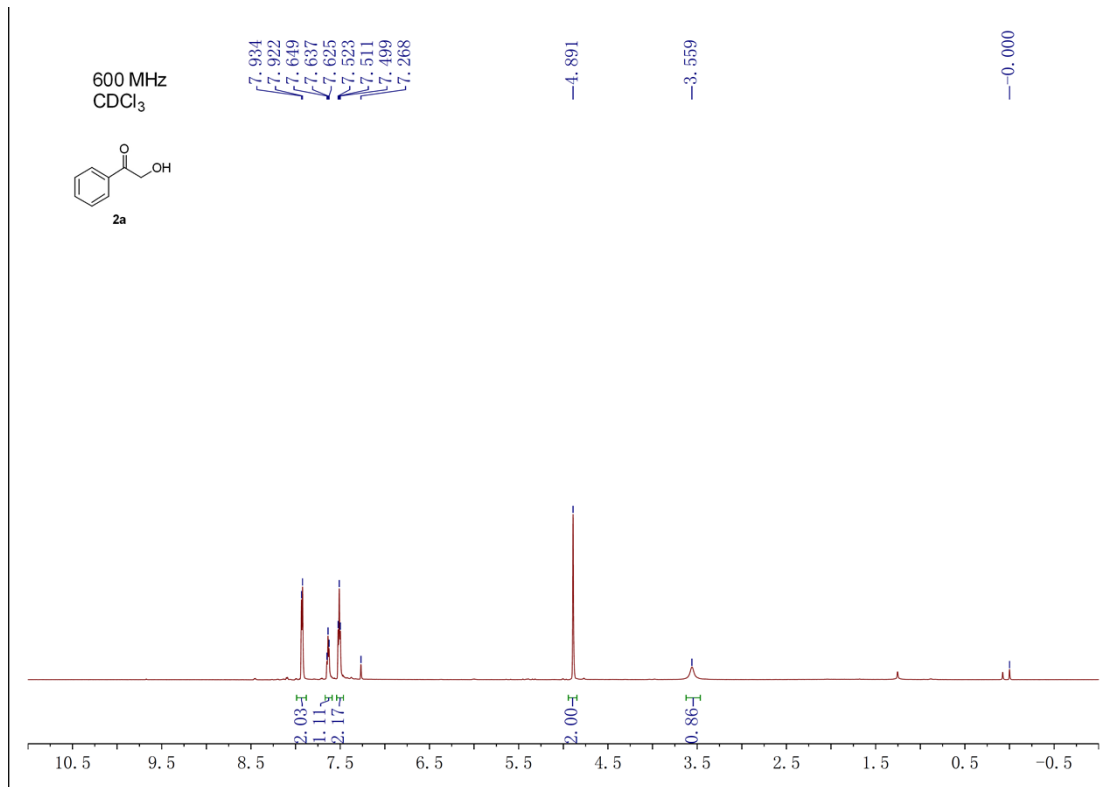
Å, F(000) 608, crystal size 0.20 x 0.10 x 0.10 mm³, 2724 independent reflections [R(int) = 0.0482], reflections collected 7986, refinement method: full-matrix least-squares on F²: goodness-of-fit on F² 1.075, final R indices [I > 2σ(I)], R1 = 0.0368, wR2 = 0.1089, largest diff. peak and hole 1.459 and -1.373 e.Å⁻³. CCDC 973926 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

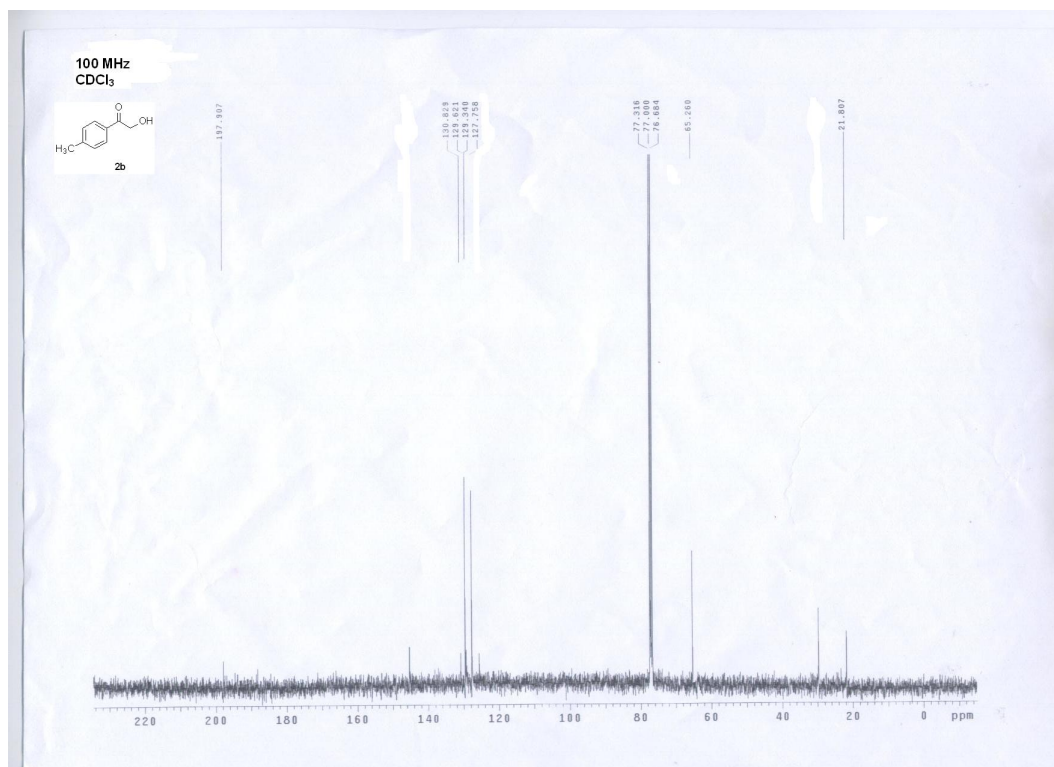
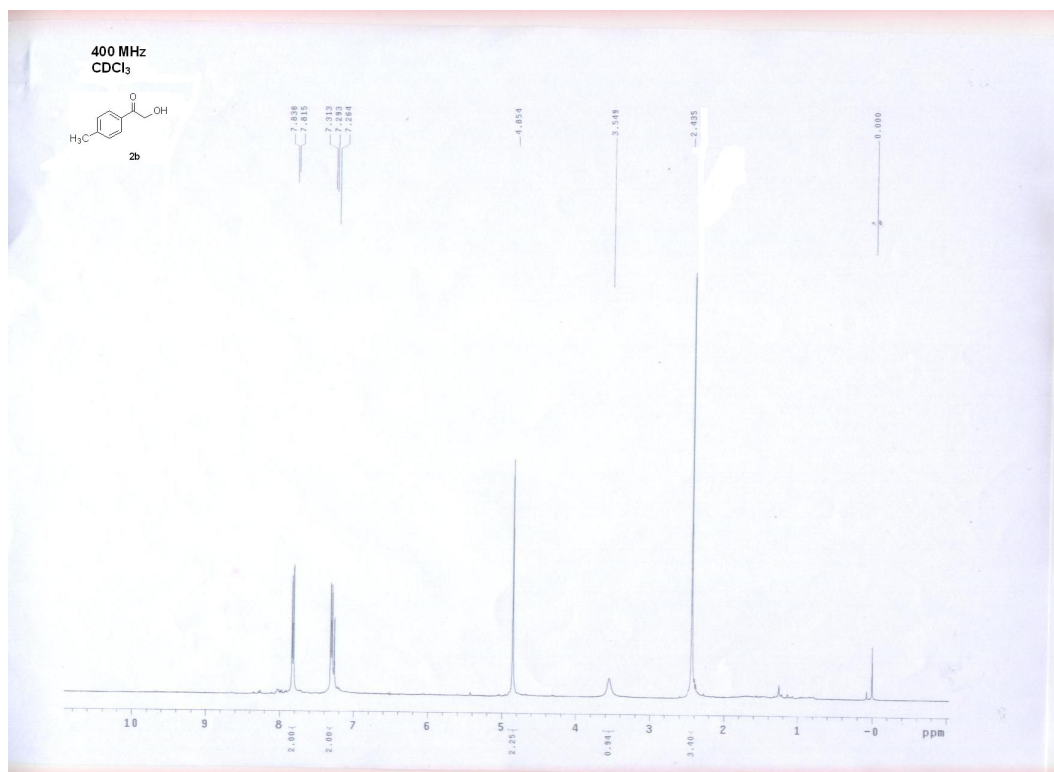
5. Labeling experiments

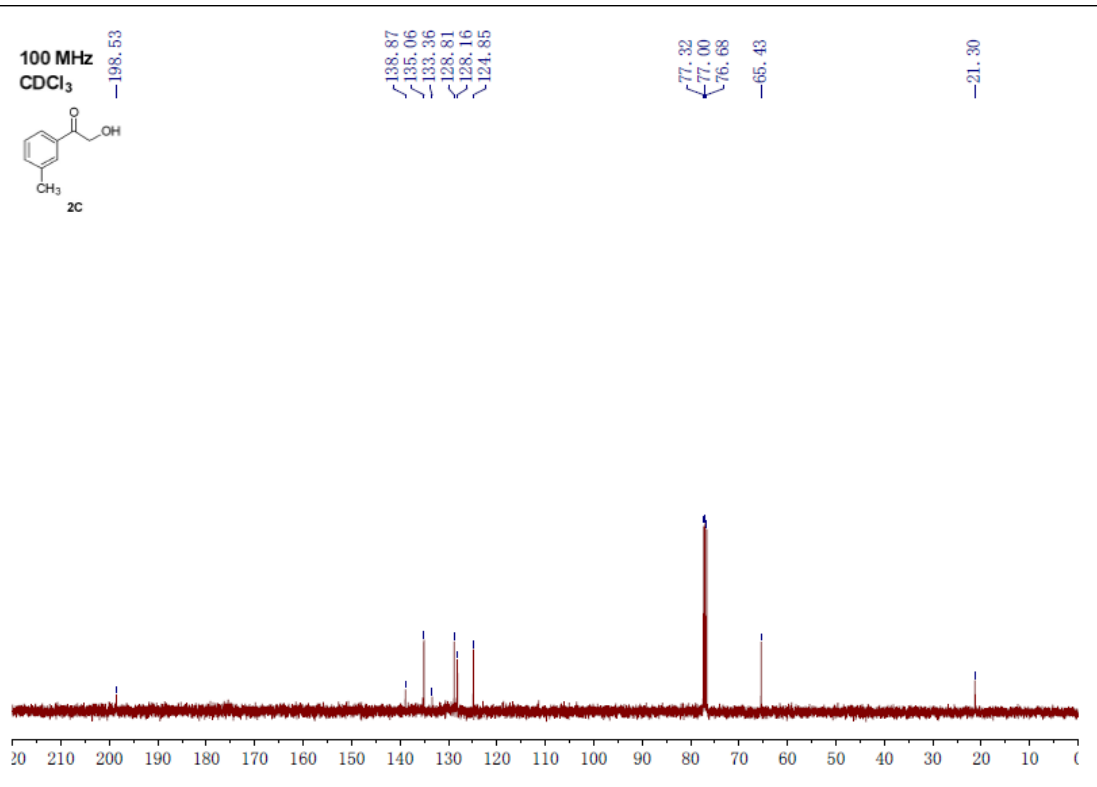
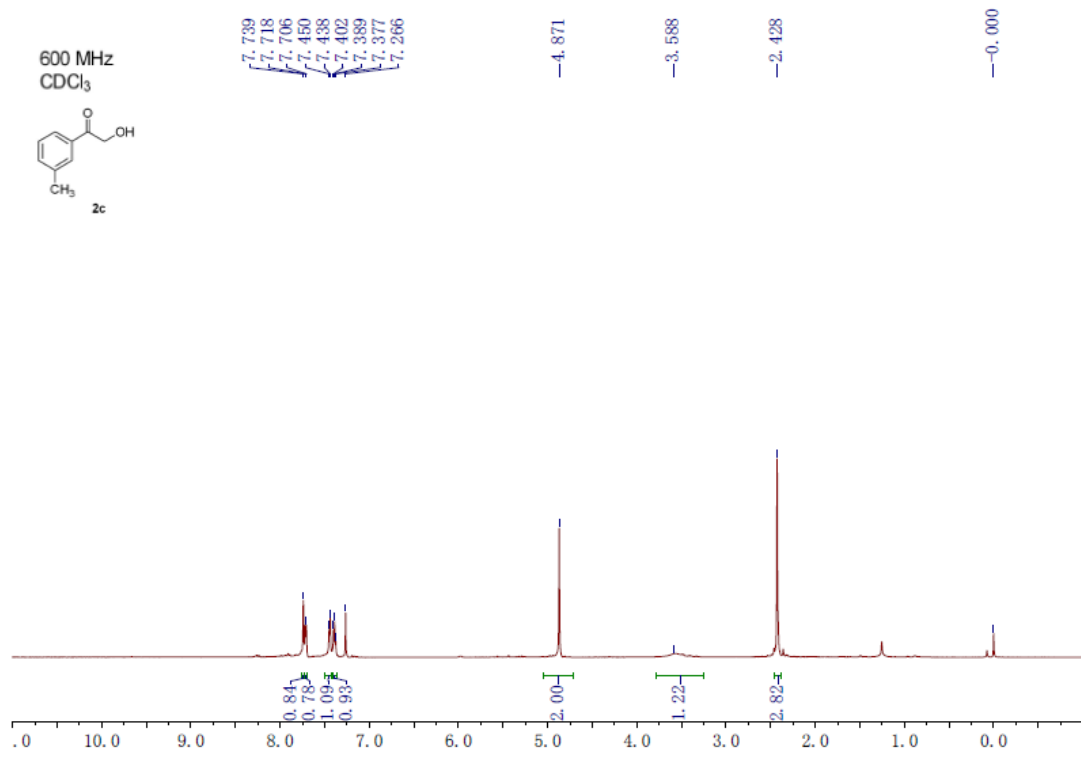
A mixture of styrene (1.0 mmol), I₂ (1.0 mmol), TBHP (4.0 mmol, dissolution in decane and purchase from Sigma-aldrich) and 0.15 mL H₂O¹⁸ (O¹⁸>90%) in anhydrous DMSO (3-4 mL) under at room temperature. After the reaction completed, the reaction mixture was filtered, diluted with water and extracted with EtOAc (3×20 mL). The extract was washed with Na₂S₂O₃ (5% w/w, aq.), and brine successively. After drying over Na₂SO₄ and evaporation, the crude product was purified by column chromatography on silica gel (eluent: petroleum ether/EtOAc) to afford the product **2aa** (78%).

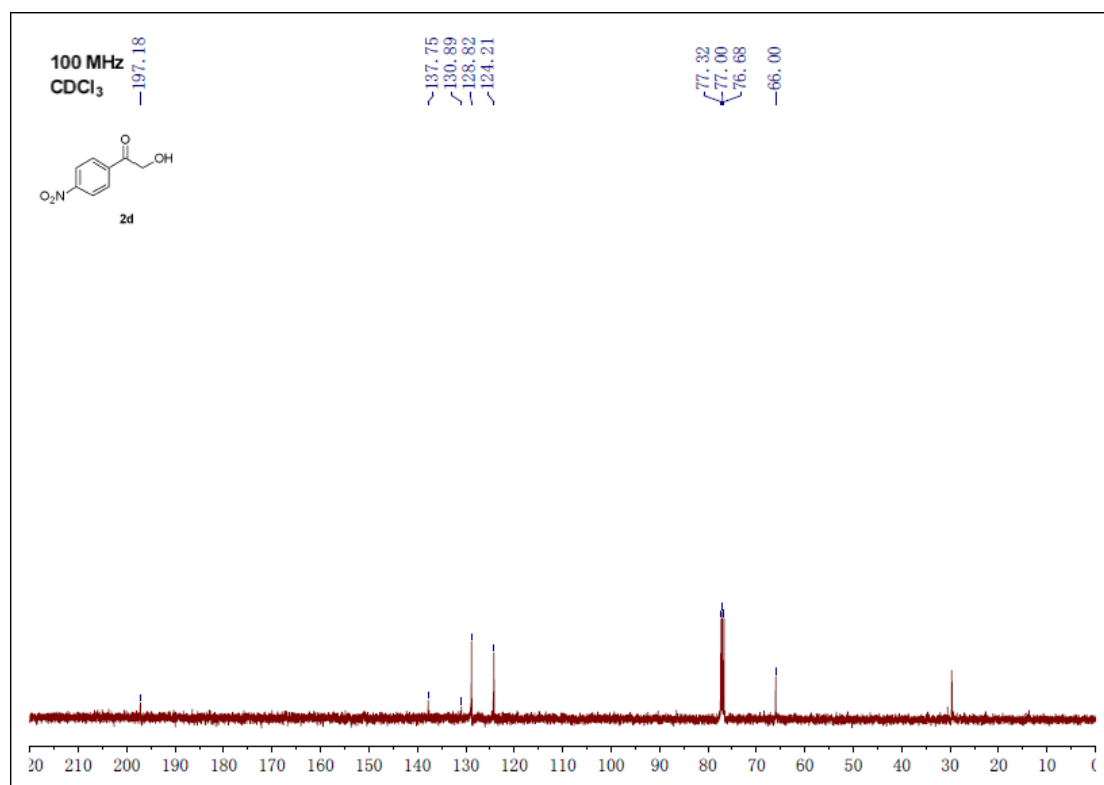
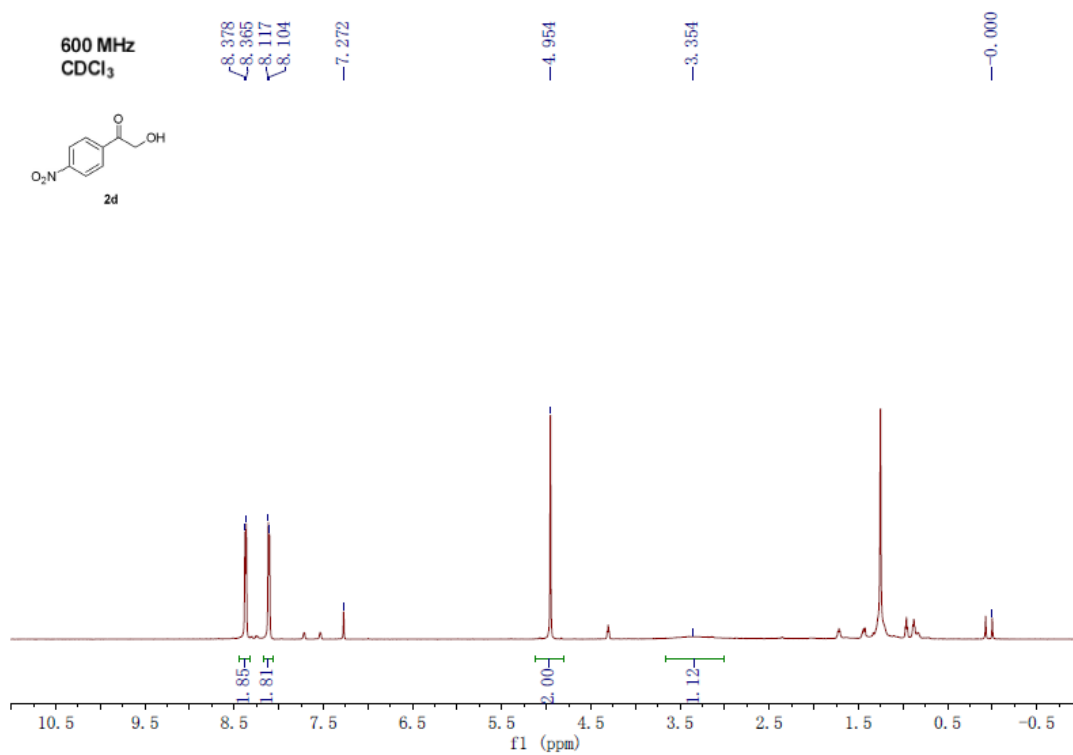


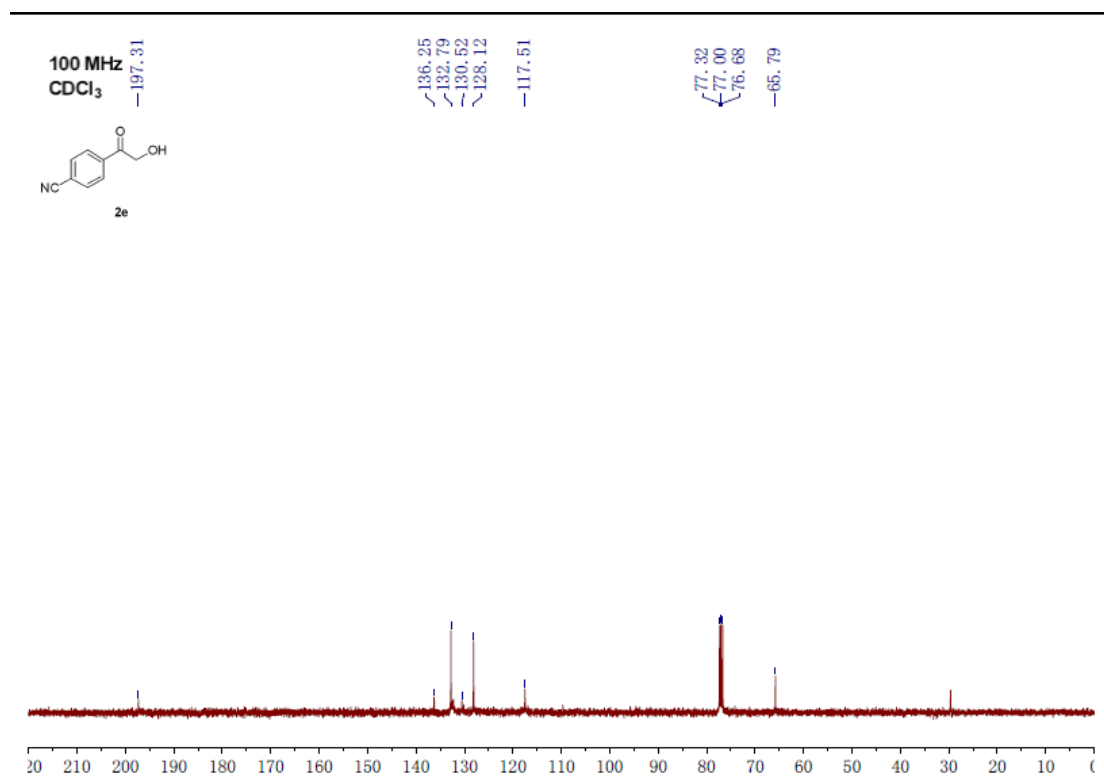
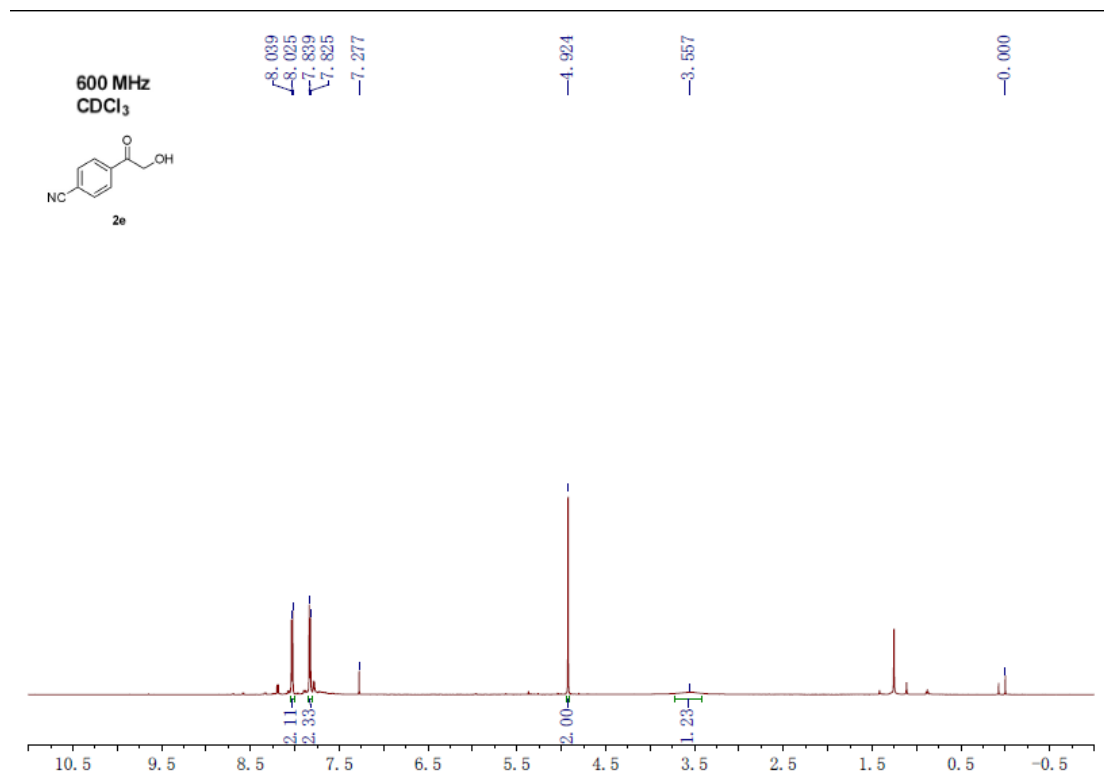
6. ¹H and ¹³C NMR spectra of compounds 2 and C

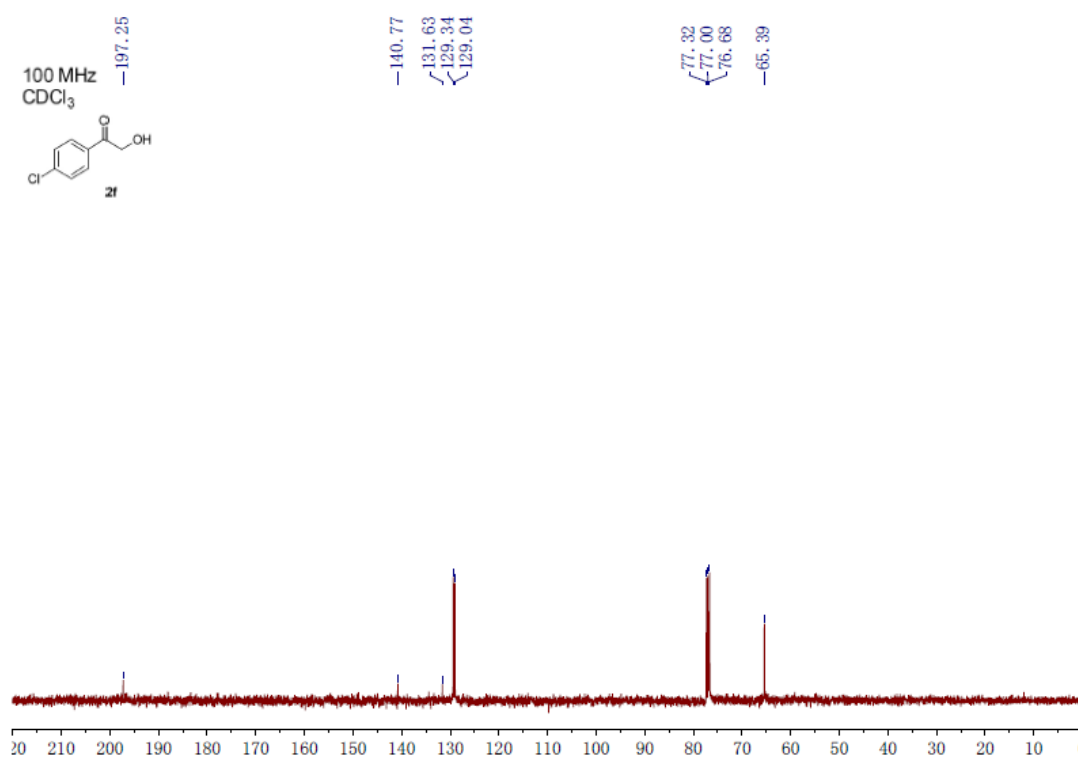
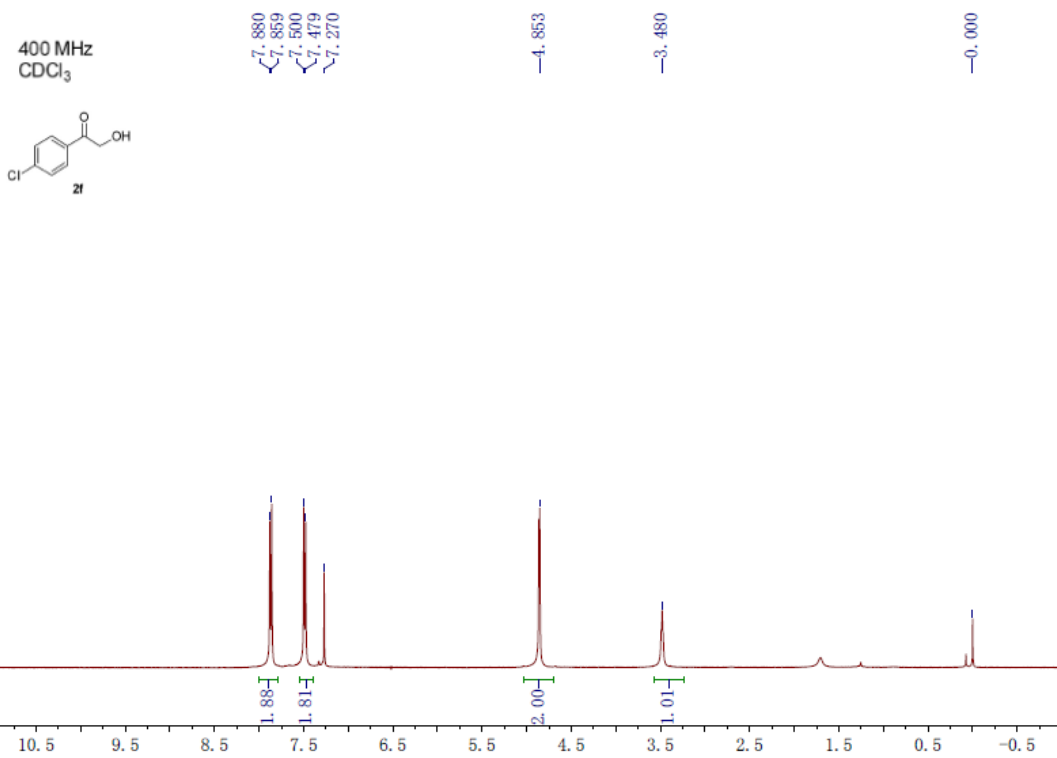


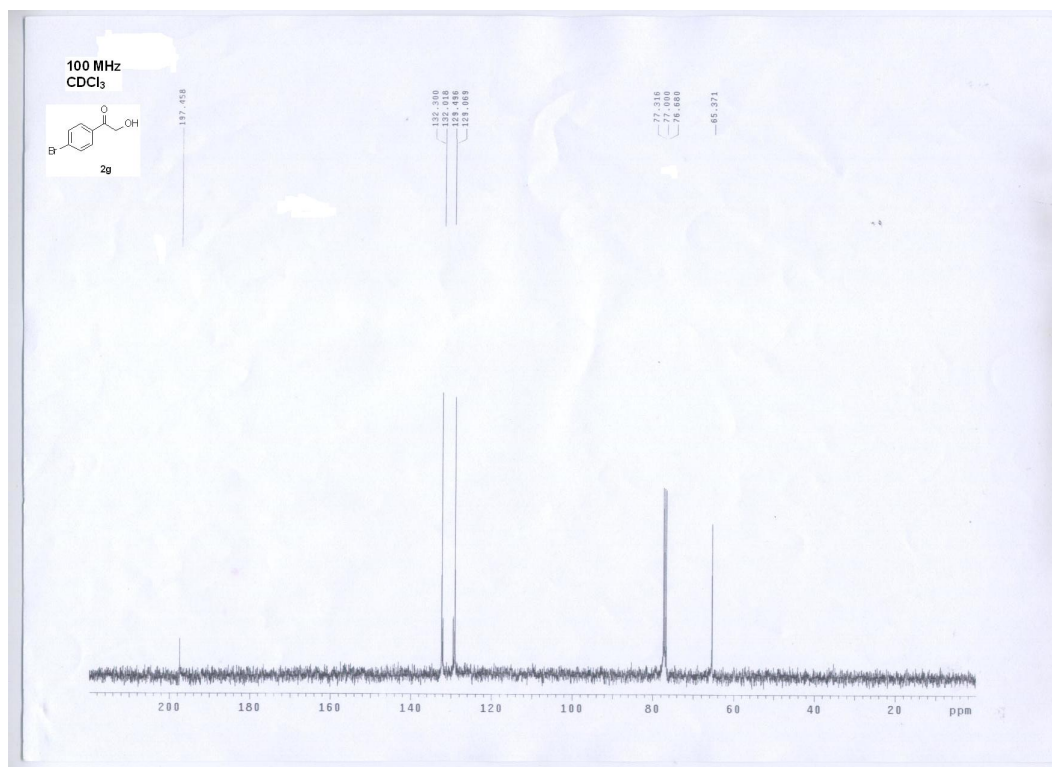
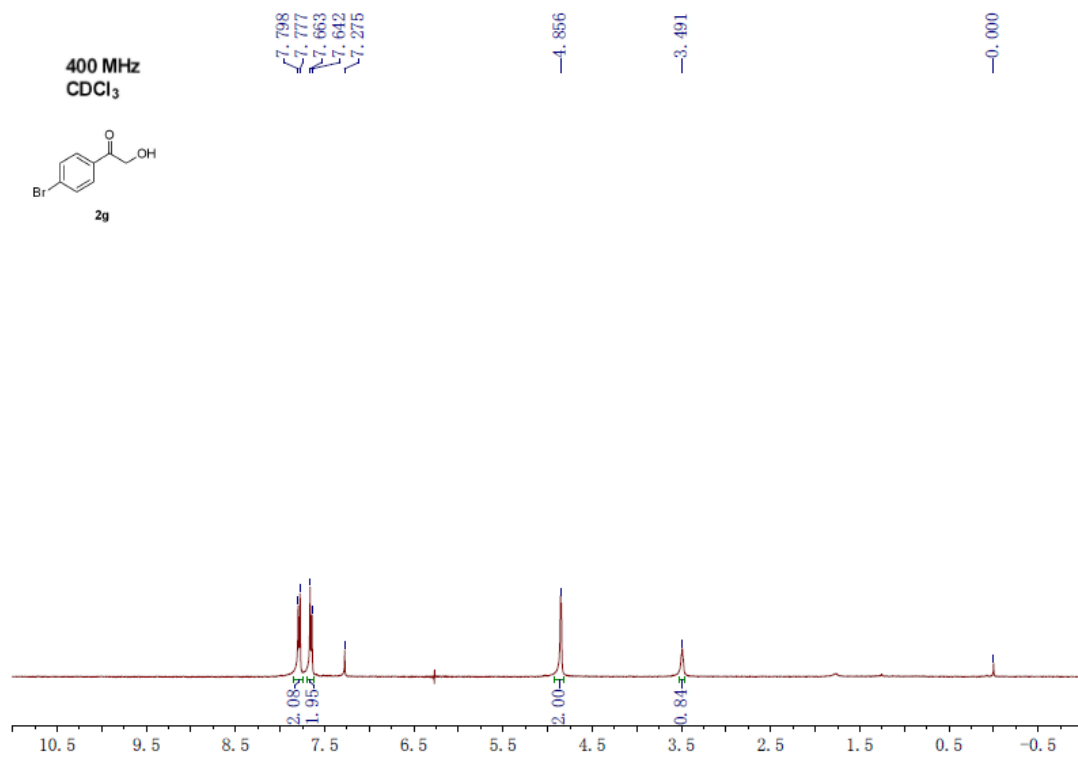


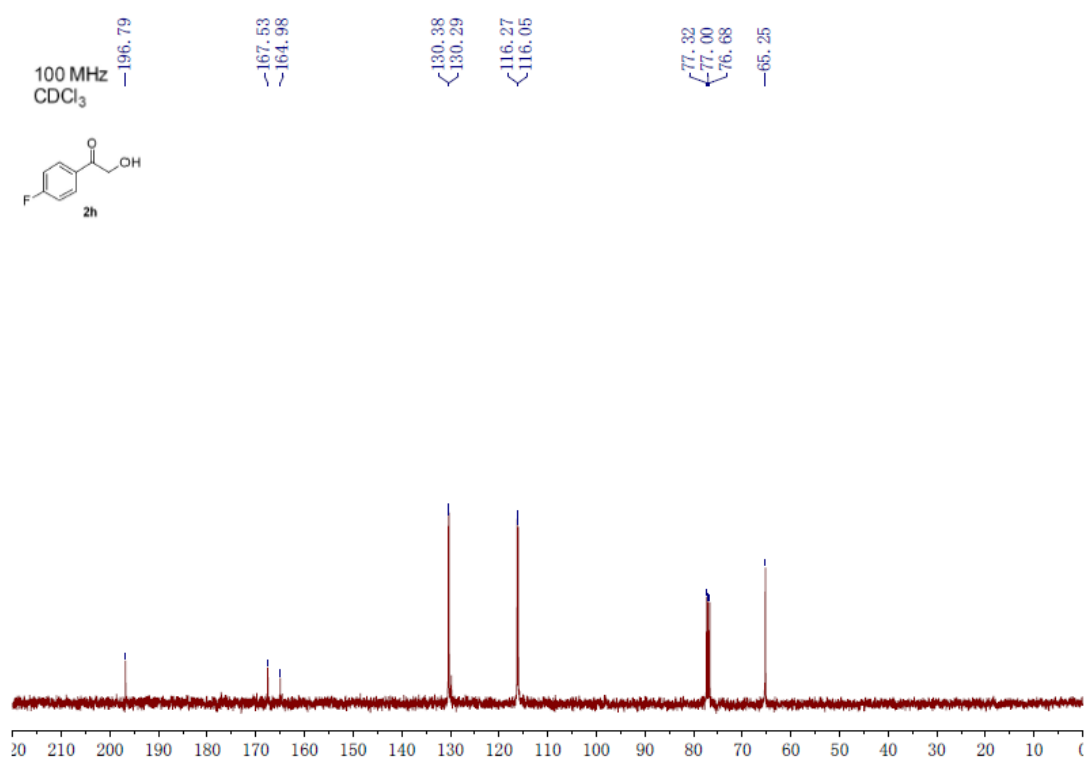
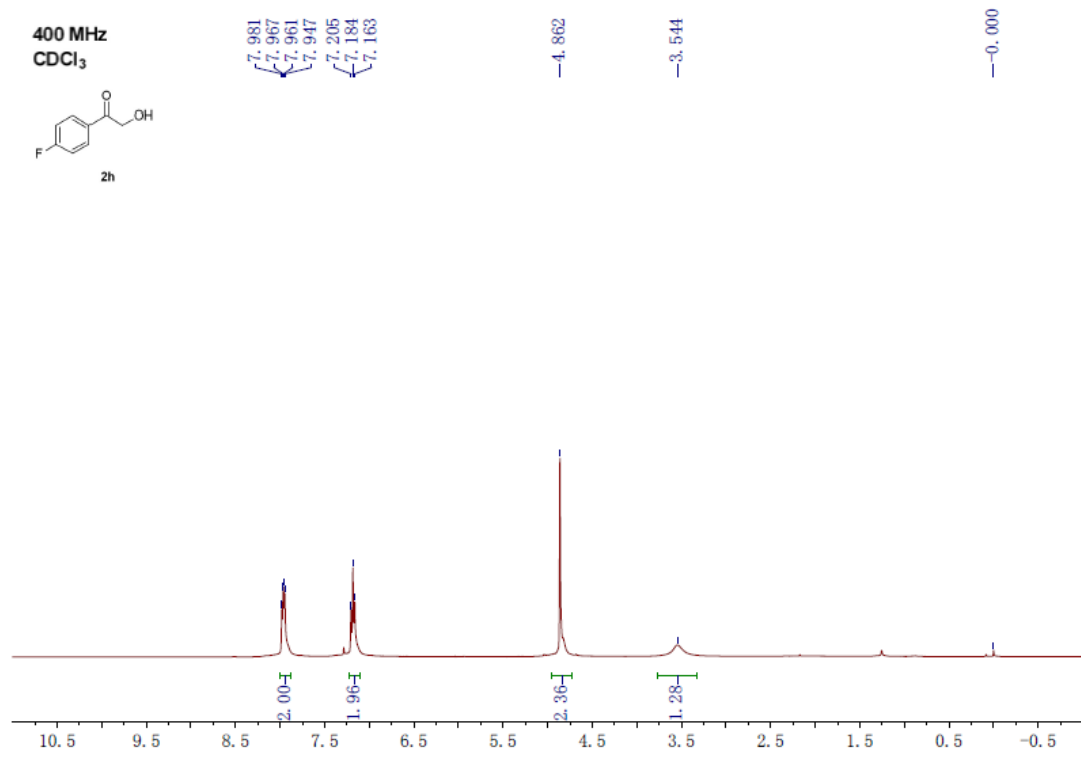


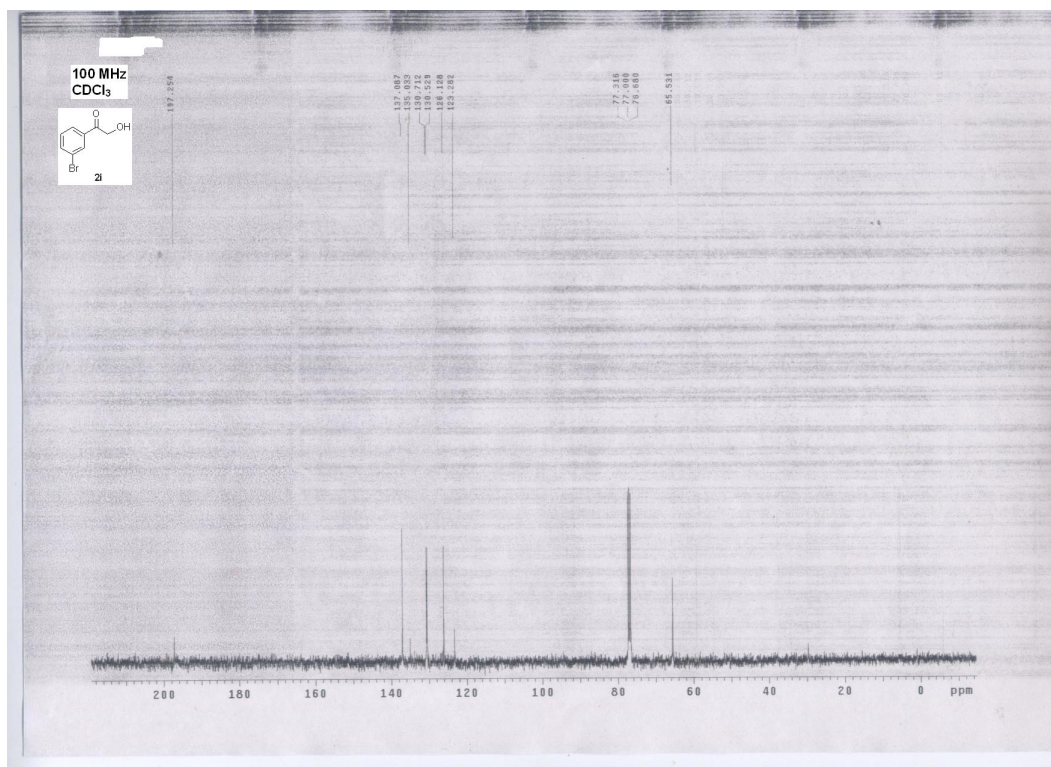
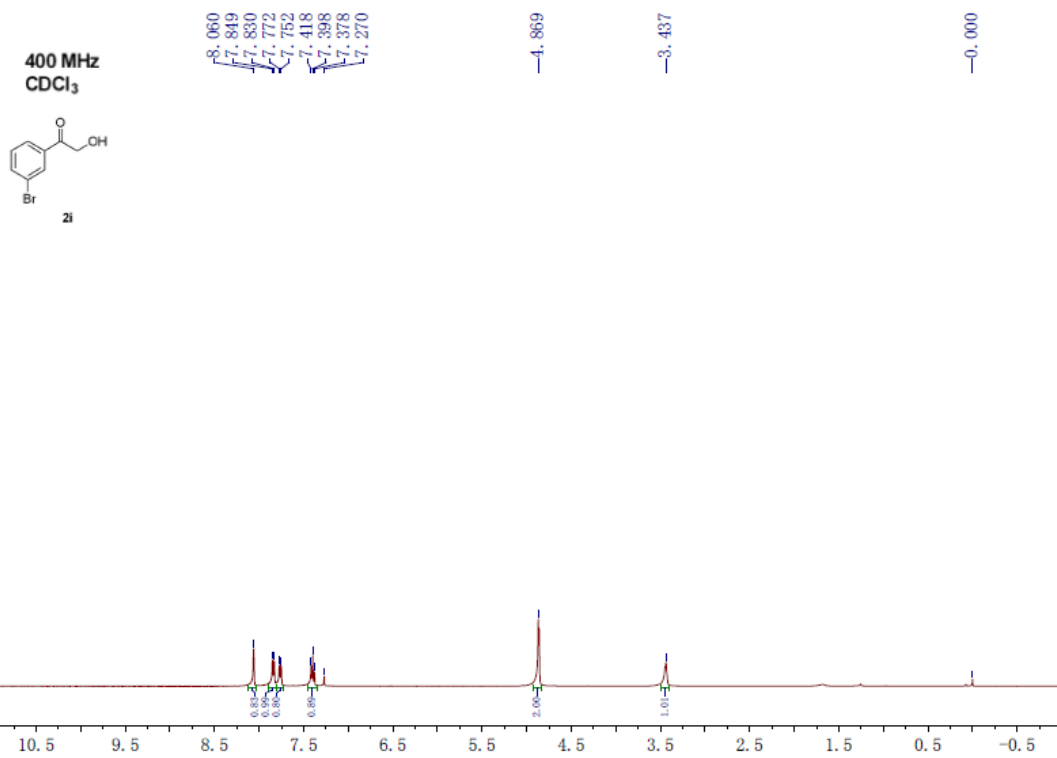


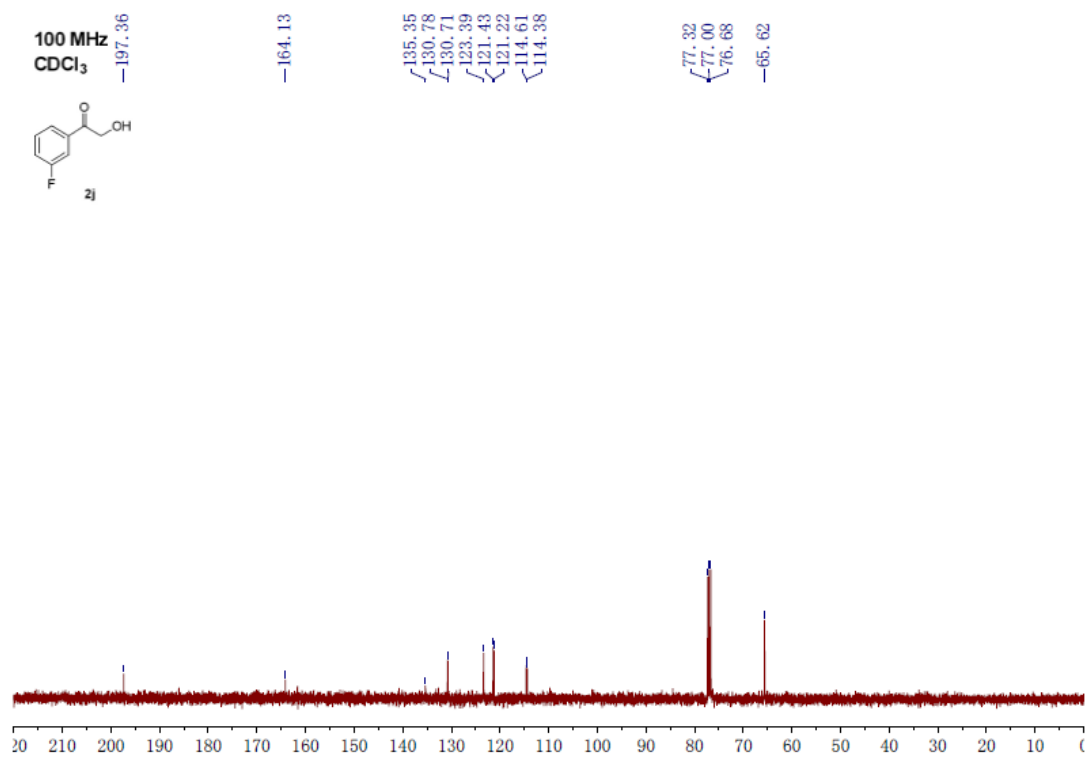
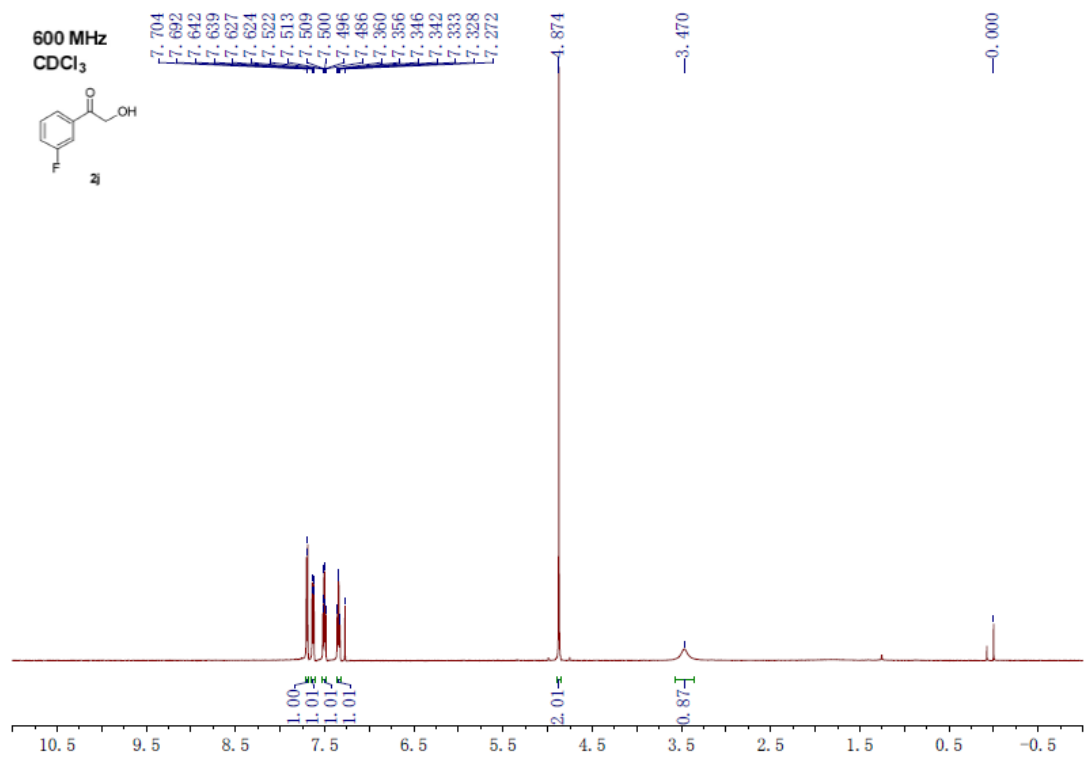


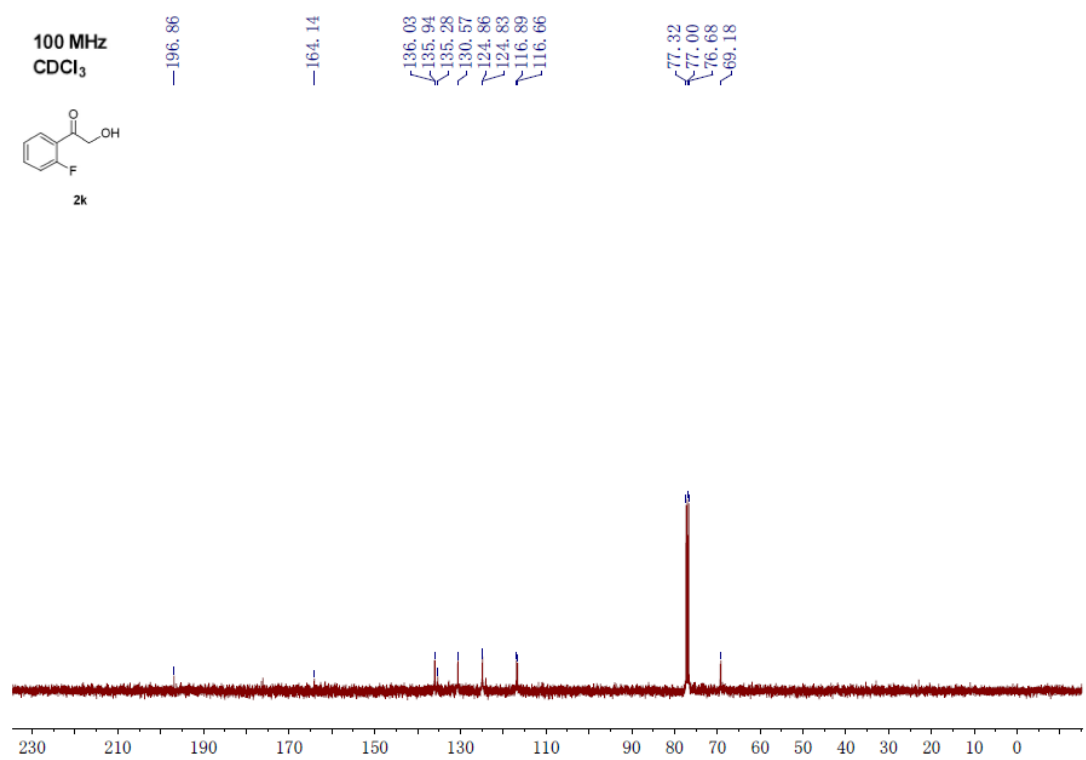
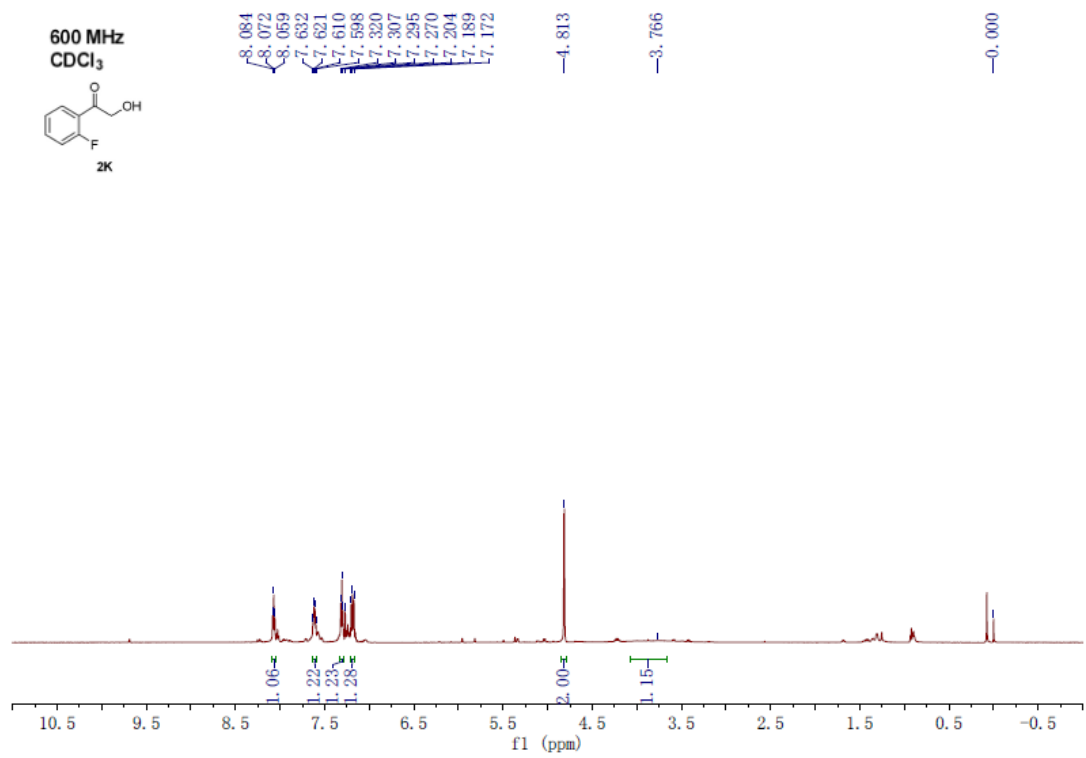




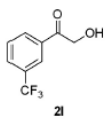








600 MHz
CDCl₃

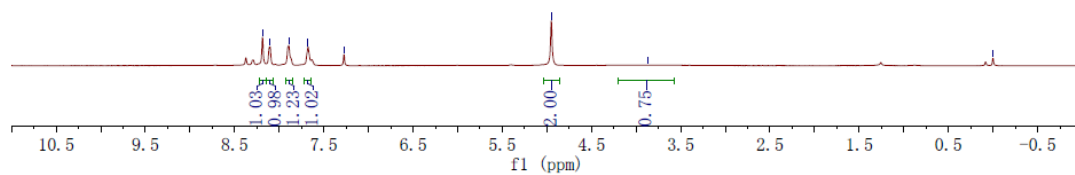


8.187
8.104
7.894
7.677
7.274

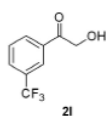
4.950

3.862

0.000



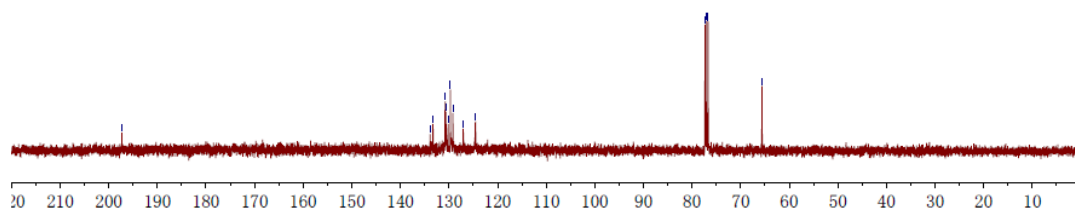
100 MHz
CDCl₃



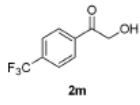
197.30

133.88
133.30
130.79
130.63
130.17
129.71
129.20
127.08
124.57

77.32
77.00
76.68
65.61



600 MHz
CDCl₃

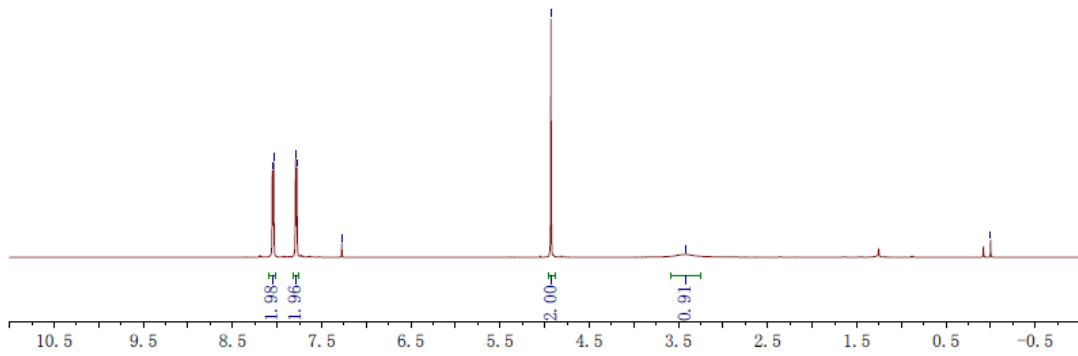


8.053
8.039
7.793
7.779
7.275

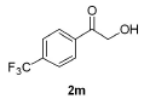
4.930

3.421

0.000



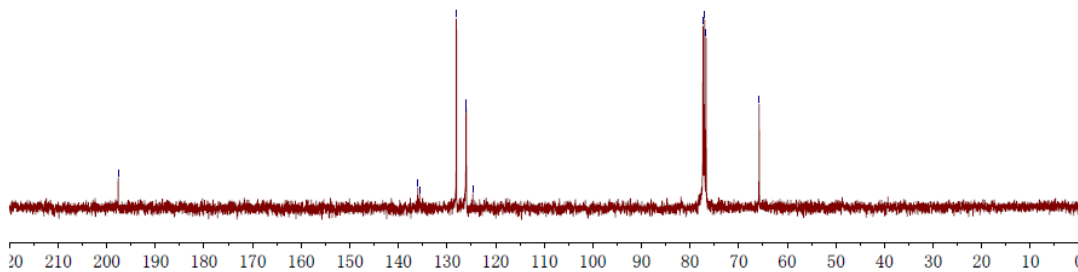
100 MHz
CDCl₃

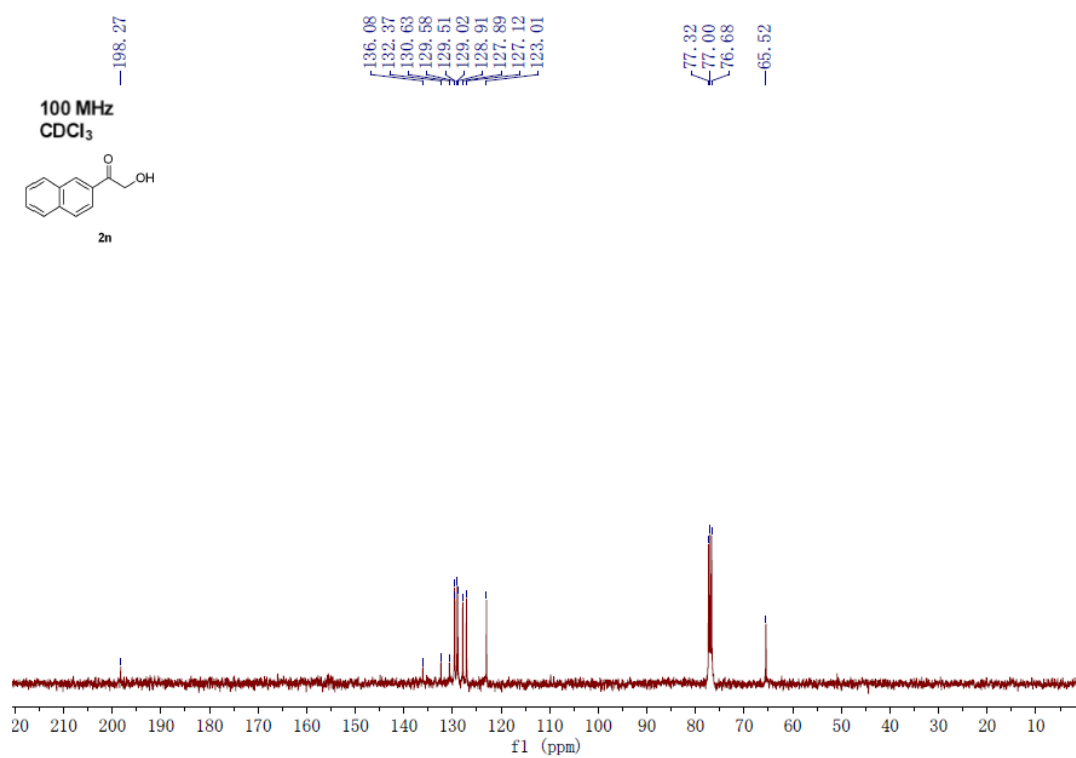
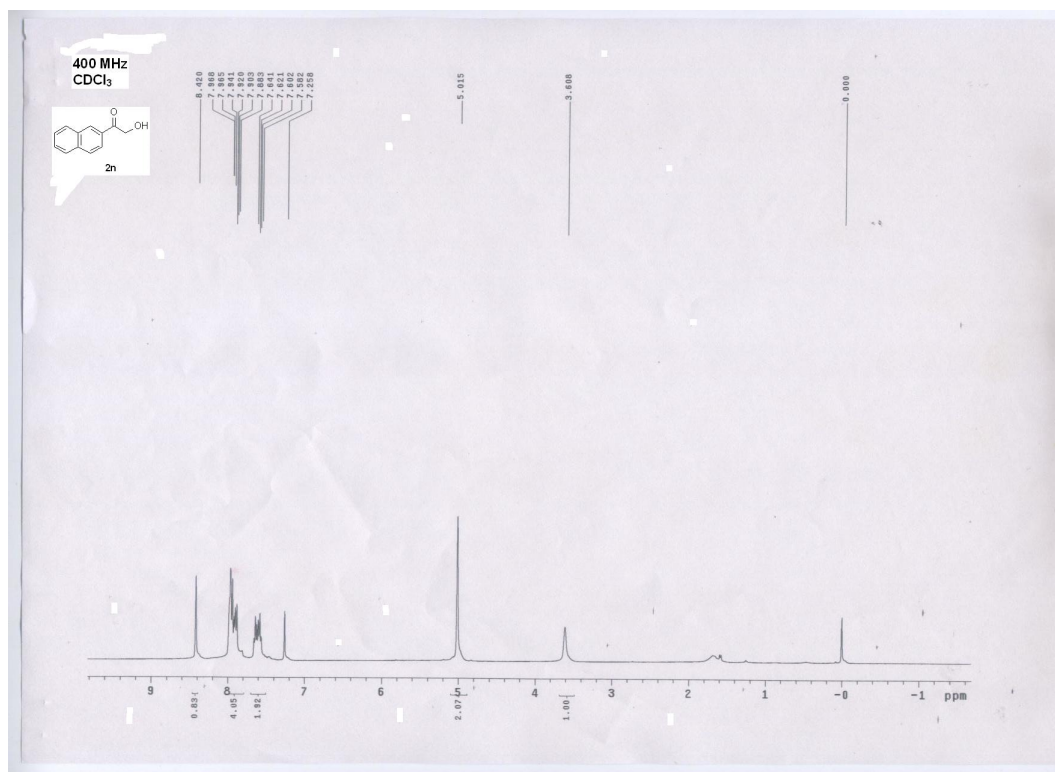


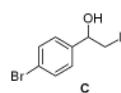
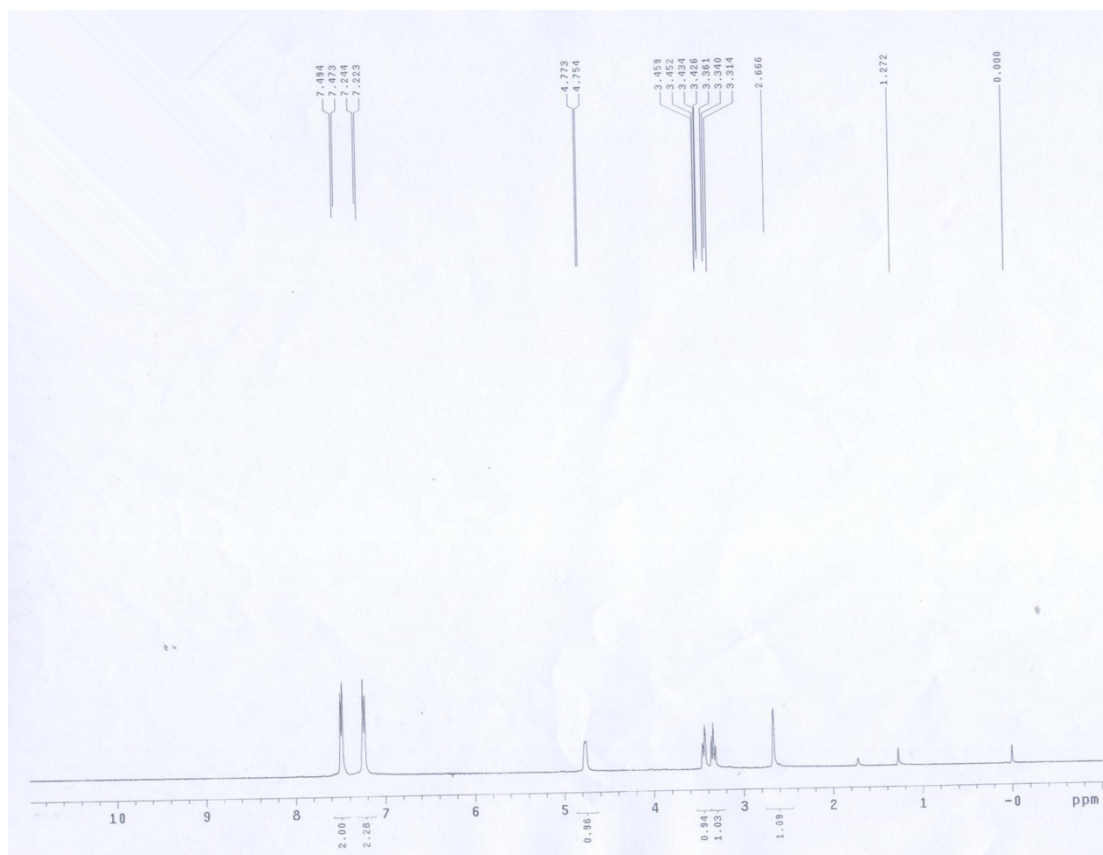
197.64

136.01
135.63
128.06
126.06
124.67

77.32
77.00
76.68
65.77







-140.00

131.72

127.41

122.14

77.32

77.00

76.68

73.21

-14.86

