Supporting Information

Palladium-Catalyzed *ortho*-CH-Bond Oxygenation of Aromatic Ketones

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1. General considerations

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All oxygenation reactions were performed in reaction tube (approx. 10 mL volume) equipped with a septum in the presence of Teflon coated magnetic stirrer bar (3 mm × 10 mm). Dichloroethane (DCE) was distilled under calcium hydride under reduced pressure. Dioxane and tetrahydrofuran (THF) were distilled from sodium under nitrogen. Acetonitrile was distilled from calcium hydride under nitrogen prior to use. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (Merck, 70-230 and 230-400 mesh) was used for column chromatography. ^{1}H NMR spectra were recorded on a Bruker (400 MHz) or Varian (500 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as part per million (ppm) in δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (*J*) were reported in Hertz (Hz). Mass spectra (EI-MS and ES-MS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were obtained on a Brüker APEX 47e FT-ICR mass spectrometer (ESIMS). GC-MS analysis was conducted on a HP 5973 GCD system using a HP5MS column (30 m × 0.25 mm). The products described in GC yield were accorded to the authentic samples/dodecane calibration standard from HP 6890 GC-FID system.

2. General procedures for initial reaction conditions screening

General Procedure for reaction condition screenings: $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), oxidant (1.0 mmol), benzophenone (0.5 mmol) and solvent (2.0 mL) were loaded into a reaction tube equipped with a septum in the presence of Teflon coated magnetic stirrer bar under air. The tube was then placed into a preheated oil bath (80 °C) and stirred for the time as indicated. After completion of reaction, the reaction tube was allowed to cool to room temperature. Ethyl acetate (~2 mL), dodecane (113 μL, internal standard) and water were added. The organic layer was subjected to GC analysis. The GC yield obtained was previously calibrated by authentic sample/dodecane calibration curve.

3. General procedures for oxygenation of aromatic ketones

General procedures for oxygenation of aromatic ketones (the Pd catalysts loading range from 5-10 mol%): $Pd(OAc)_2$, $PhI(OTFA)_2$ (1.0 mmol), aromatic ketones (0.5 mmol) and DCE (2.0 mL) were loaded into a reaction tube equipped with a septum in the presence of Teflon coated magnetic stirrer bar under air. The tube was then placed into a preheated oil bath (80 °C) and stirred for the time as indicated in Table 2 and 3. After completion of reaction as judged by GC analysis, the reaction tube was allowed to cool to room temperature and quenched with water. EtOAc was then added for dilution. The organic layer was separated and the aqueous layer was washed with EtOAc. The filtrate was concentrated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (230-400 mesh) to afford the desired product.

4. General procedures for further synthesis of flavones

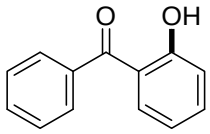
General procedures for further synthesis of flavones from hydroxylated products: $Pd(OAc)_2$ (10.0 mol%), $PhI(OTFA)_2$ (4.0 mmol), acetophenone (2.0 mmol) and DCE (8.0 mL) were loaded into a reaction tube equipped with a septum in the presence of Teflon coated magnetic stirrer bar under air. The tube was then placed into a preheated oil bath (80 °C) and stirred for 2 h. After isolation of the desired hydroxylated product, benzaldehyde was added with 50% NaOH and ethanol and further reaction was carried out by adding I_2 in DMSO to form flavones according to the literature procedures.[1]

5. General procedures for Hammett Correlation Study

$Pd(OAc)_2$ (10.0 mol%), $PhI(OTFA)_2$ (1.0 mmol), acetophenone or *para*-substituted acetophenone (*p*-OMe, *p*-Me, *p*-Cl, *p*-Br) (0.5 mmol) and DCE (2.0 mL) were loaded into a reaction tube equipped with a septum in the presence of Teflon coated magnetic stirrer bar under air. The tube was then placed into a preheated oil bath (80 °C) and stirred for 1 h. Ethyl acetate (~2 mL), dodecane (113 μL, internal standard) and water were added. The organic layer was subjected to GC analysis.

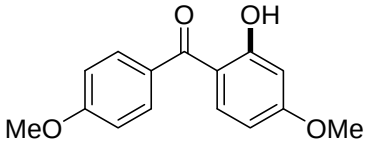
6. Characterization data of hydroxylated products

(2-Hydroxyphenyl)phenylmethanone (Table 2, entry 1, product 1a)[2]



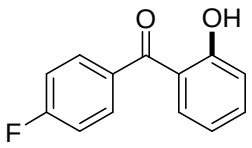
EA: Hexane = 1:9, R_f = 0.6, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (t, *J* = 7.6 Hz, 1H), 7.09-7.12 (m, 1H), 7.53 (t, *J* = 7.6 Hz, 3H), 7.59-7.62 (m, 2H), 7.70 (d, *J* = 7.2 Hz, 1H), 12.07 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.4, 118.6, 118.7, 118.8, 119.1, 119.8, 128.3, 129.1, 131.9, 133.0, 133.6, 135.9, 136.3, 137.9, 163.2, 201.6.

(2-Hydroxy-4-methoxyphenyl)(4-methoxyphenyl)methanone (Table 2, entry 2, product 2a)[3]



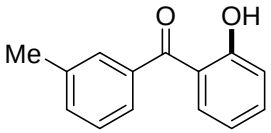
EA: Hexane = 1:9, R_f = 0.25, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.87 (d, *J* = 10.8 Hz, 6H), 6.42-6.53 (m, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 9.2 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 12.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 55.5, 101.1, 107.1, 113.2, 113.6, 130.7, 131.3, 134.4, 134.9, 162.5, 165.88, 166.0, 198.7.

(4-Fluorophenyl)(2-hydroxyphenyl)methanone (Table 2, entry 3, product 3a)[4]



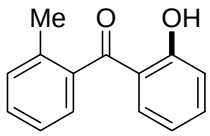
EA: Hexane = 1:9, R_f = 0.6, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 7.20 (t, *J* = 8.8 Hz, 2H), 7.53 (t, *J* = 7.2 Hz, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.73 (m, 2H), 11.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.4, 115.6, 118.5, 118.7, 119.0, 128.4, 129.0, 131.7, 131.8, 133.2, 134.0, 136.4, 163.1, 163.7, 166.2, 199.9.

(2-Hydroxyphenyl)(*m*-tolyl)methanone (Table 2, entry 4, product 4a)[5]



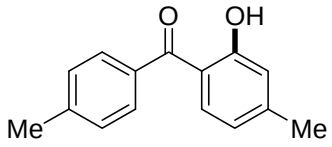
EA: Hexane = 1:9, R_f = 0.6, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 3H), 7.00 (d, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 8.4 Hz, 2H), 7.53 (t, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 2H) , 11.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 118.1, 118.8, 127.7, 128.3, 129.1, 131.7, 133.2, 137.3, 138.1, 161.1, 201.6.

(2-Hydroxyphenyl)(*o*-tolyl)methanone (Table 2, entry 5, product 5a)[6]



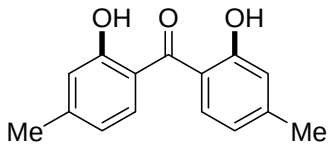
EA: Hexane = 1:9, R_f = 0.6, colorless liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 3H), 6.83 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.29-7.33 (m, 4H), 7.41-7.45 (m, *1*H), 7.52 (t, *J* = 7.6 Hz, 2H) , 12.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 118.3, 118.8, 119.9, 125.3, 127.4, 130.1, 130.8, 133.7, 135.5, 136.7, 137.8, 163.3, 204.4.

(2-Hydroxy-4-methylphenyl)(*p*-tolyl)methanone (Table 2, entry 6, product 6a)[7]



EA: Hexane = 1:9, R_f = 0.65, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.47 (s, 3H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.90 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 12.17 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 21.9, 117.9, 118.4, 119.8, 128.9, 129.3, 133.4, 135.3, 142.4, 147.7, 163.3, 200.8.

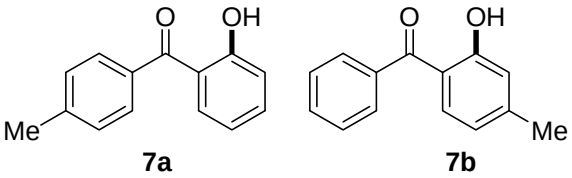
Bis(2-hydroxy-4-methylphenyl)methanone (Table 2, entry 7, product 6b)[8]



EA: Hexane = 1:9, R_f = 0.6, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 6H), 6.76 (d, *J* = 8.0 Hz, 2H), 6.90 (s, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 10.78 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 117.5, 118.6, 120.0, 132.9, 147.3, 161.9, 201.4.

(2-Hydroxyphenyl)(*p*-tolyl)methanone (Table 2, entry 8, product 7a)[9]

(2-Hydroxy-4-methylphenyl)(phenyl)methanone (Table 2, entry 8, product 7b)[9]

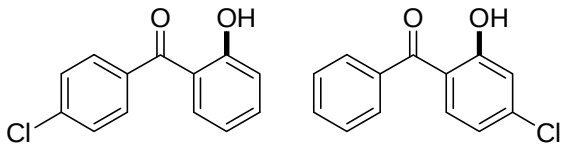


7a **7b**

EA: Hexane = 1:9, R_f = 0.5, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.47 (s,3H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.90 (d, *J* = 6.8 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.48-7.53 (m, 4H), 7.58-7.64 (m, 3H), 7.68 (d, *J* = 7.6 Hz, 3H), 12.05 (s, 1H), 12.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 22.0, 116.9, 118.3, 118.4, 118.5, 119.3, 119.9, 128.3, 129.0, 129.4, 131.7, 133.5, 135.1, 136.0, 138.1, 142.7, 148.0, 163.1, 163.4, 201.1, 201.3.

(4-Chlorophenyl)(2-hydroxyphenyl)methanone (Table 2, entry 9, product 8a)[9]

(4-Chloro-2-hydroxyphenyl)(phenyl)methanone (Table 2, entry 9, product 8b)[10]

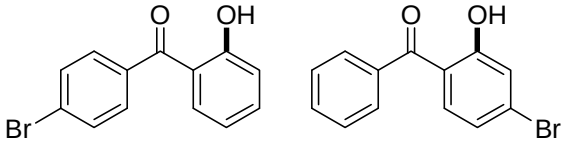


8a **8b**

EA: Hexane = 1:9, R_f = 0.5, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 1H), 7.47-7.57 (m, 4H), 7.67 (d, *J* = 7.2 Hz, 2H), 7.79 (d, *J* = 6.8 Hz, 1H), 11.9 (s, 1H), 12.21 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.5, 118.8, 118.9, 119.3, 128.4, 128.6, 128.7, 129.0, 129.9, 130.6, 131.4, 132.2, 133.2, 134.5, 136.1, 136.5, 138.4, 163.2, 200.1.

(4-Bromophenyl)(2-hydroxyphenyl)methanone (Table 2, entry 10, product 9a)[11]

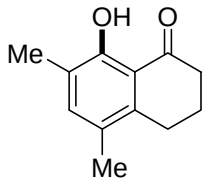
(4-Bromo-2-hydroxyphenyl)(phenyl)methanone (Table 2, entry 10, product 9b)[12]



9a **9b**

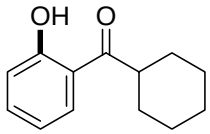
EA: Hexane = 1:9, R_f = 0.5, yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.90 (t, *J* = 8.0 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 1H), 7.51-7.58 (m, 4H), 7.67 (d, *J* = 8.4 Hz, 3H), 11.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.5, 118.8, 121.6, 122.2, 126.9, 128.4, 128.5, 129.1, 129.9, 130.7, 130.9, 131.5, 131.6, 132.2, 133.2, 134.4, 136.6, 163.2, 163.6, 200.3.

3,4-Dihydro-8-hydroxy-5,7-dimethylnaphthalen-1(2*H*)-one (Scheme 2, product 10a)[13]



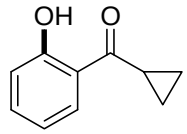
EA: Hexane = 1:9, R_f = 0.7, pale yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08-2.14 (m, 2H), 2.20 (d, *J* = 10.0 Hz, 6H), 2.67 (d, *J* = 6.8 Hz, 2H), 2.82 (d, *J* = 6.4 Hz, 2H), 7.16 (s, 1H), 12.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 18.6, 22.5, 26.6, 38.8, 116.3, 123.7, 124.8, 139.2, 139.9, 159.5, 205.6.

Cyclohexyl(2-hydroxyphenyl)methanone (Scheme 2, product 11a)[14]



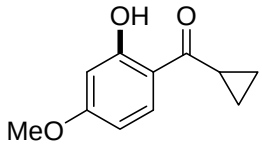
EA: Hexane = 1:9, R_f = 0.5, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28-1.65 (m, 5H), 1.78 (d, *J* = 11.2 Hz, 1H), 1.90 (s, 4H), 3.32 (t, *J* = 11.2 Hz, 1H), 6.91 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.80 (d, *J* = 7.2 Hz, 1H), 12.60 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 25.8, 29.5, 45.2, 118.2, 118.7, 129.7, 136.1, 163.1, 210.1.

Cyclopropyl(2-hydroxyphenyl)methanone (Scheme 2, product 12a)[15]



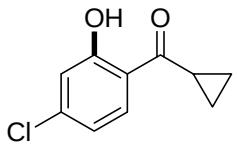
EA: Hexane = 1:9, R_f = 0.5, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.1-1.14 (m, 2H), 1.30-1.34 (m, 2H), 2.69-2.76 (m, 1H), 6.93-7.01 (m, 2H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 12.52 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.1, 16.4, 118.3, 118.8, 120.1, 130.0, 136.0, 162.1, 205.5.

Cyclopropyl(2-hydroxy-4-methoxyphenyl)methanone (Scheme 2, product 13a)



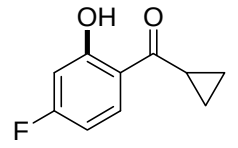
EA: Hexane = 1:9, R_f = 0.35, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06-1.09 (m, 2H), 1.26-1.30 (m, 2H), 2.57-2.63 (m, 1H), 3.86 (s, 3H), 6.44-6.51 (m, 2H), 7.88 (d, *J* = 9.2 Hz, 1H), 13.04 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 16.0, 55.5, 100.9, 107.5, 114.2, 131.5, 165.0, 165.8, 203.6; HRMS: calcd. for $C_{11}H_{13}O_3^+$: 193.0864, found 193.00869.

Cyclopropyl(2-hydroxy-4-chlorophenyl)methanone (Scheme 2, product 14a)



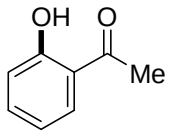
EA: Hexane = 1:9, R_f = 0.45, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12-1.17 (m, 2H), 1.31-1.35 (m, 2H), 1.59 (s, 1H), 2.61-2.68 (m, 1H), 6.93 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.02 (s, 1H), 7.91 (d, *J* = 8.4, 1H), 12.68 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 16.6, 118.4, 118.6, 119.5, 130.9, 141.7, 162.8, 182.6, 204.8; HRMS: calcd. for $C_{10}H_{10}O_2Cl^+$: 197.0369, found 197.0366.

Cyclopropyl(2-hydroxy-4-fluorophenyl)methanone (Scheme 2, product 15a)[16]



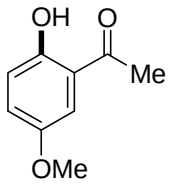
EA: Hexane = 1:9, R_f = 0.45, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12-1.15 (m, 2H), 1.31-1.63 (m, 2H), 2.60-2.66 (m, 1H), 6.64-6.69 (m, 2H), 7.99 (t, *J* = 6.8 Hz, 1H), 12.88 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.2, 16.5, 104.7, 105.0, 106.9, 107.1, 117.2, 132.2, 132.3, 164.6, 164.8, 166.1, 168.6, 204.4.

1-(2-Hydroxyphenyl)ethanone (Scheme 2, product 16a)[17]



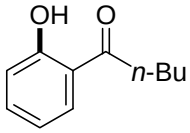
EA: Hexane = 1:9, R_f = 0.45, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (s, 3H), 6.92 (t, *J* = 7.6 Hz, 1H), 7.00 (t, *J* = 8.4 Hz, 1H), 7.49 (t, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 12.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 118.4, 118.9, 119.7, 130.6, 136.4, 162.4, 204.4.

1-(2-Hydroxy-5-methoxyphenyl)ethanone (Scheme 2, product 17a)[18]



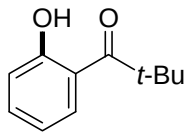
EA: Hexane = 1:9, R_f = 0.25, yellowish orange solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.65 (s, 3H), 3.92 (s, 3H), 6.86 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 12.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.0, 56.2, 117.0, 118.2, 119.7, 121.8, 148.9, 152.8, 204.9.

1-(2-hydroxyphenyl)pentan-1-one (Scheme 2, product 18a)[19]



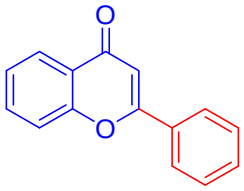
EA: Hexane = 1:9, R_f = 0.8, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.6 Hz, 3H), 1.40-1.50 (m, 2H), 1.72-1.79 (m, 2H), 2.97-3.03(m, 2H), 6.91 (t, *J* = 7.2 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 7.47(dd, *J* = 6.8, 1.2 Hz, 1H), 7.79 (d, *J* = 6.8 Hz, 1H), 12.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 22.4, 26.6, 38.0, 118.5, 118.8, 119.3, 128.0, 128.5, 130.0, 136.1, 162.5, 206.9.

1-(2-Hydroxyphenyl)-2,2-dimethylpropan-1-one (Scheme 2, product 19a)[6]



EA: Hexane = 1:9, R_f = 0.7, yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 6.86 (t, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 7.6 Hz, 1H), 12.71 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.7, 44.6, 117.5, 117.7, 119.3, 130.8, 135.3, 163.6, 212.1.

2-Phenyl-4H-chromen-4-one (Scheme 3, product 20)[20]



EA: Hexane = 1:4, R_f = 0.7, white solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.86 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.57 (m, 4H), 7.73 (t, *J* = 8.4 Hz, 1H), 7.96 (m, 2H), 8.26 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 107.5, 118.1, 123.9, 125.2, 125.7, 126.3, 129.0, 131.6, 131.8, 133.8, 156.2, 163.4, 178.4.

7. ^{1}H, ^{13}C NMR and HRMS spectra

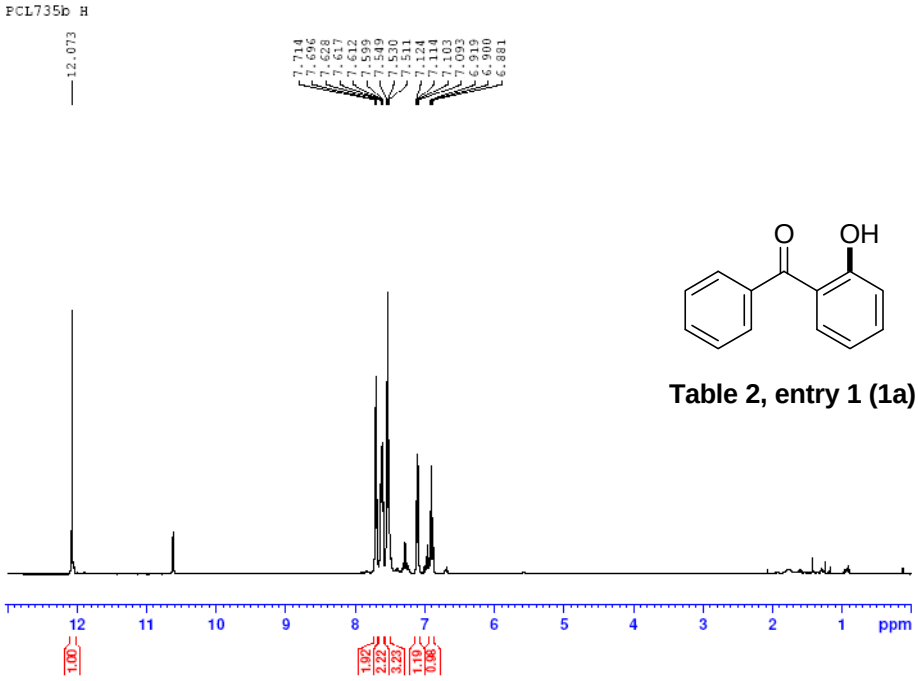
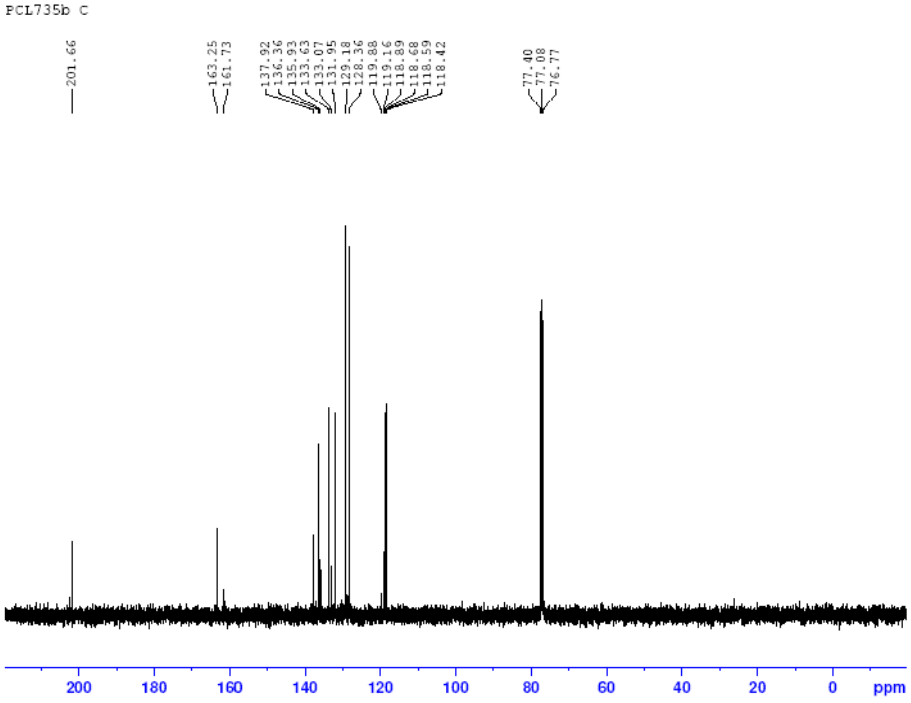


Table 2, entry 1 (1a)



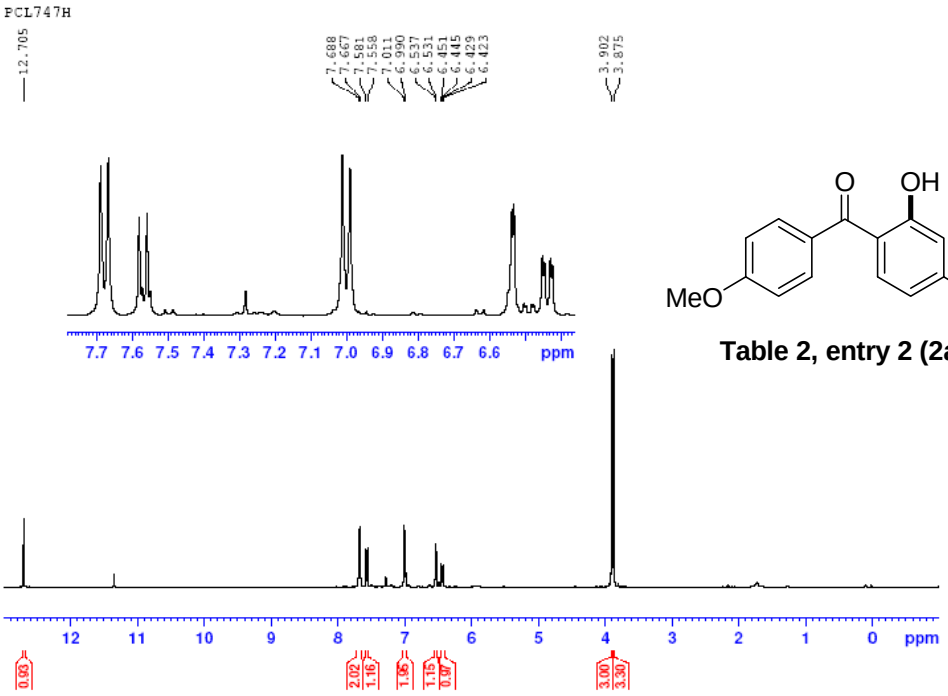
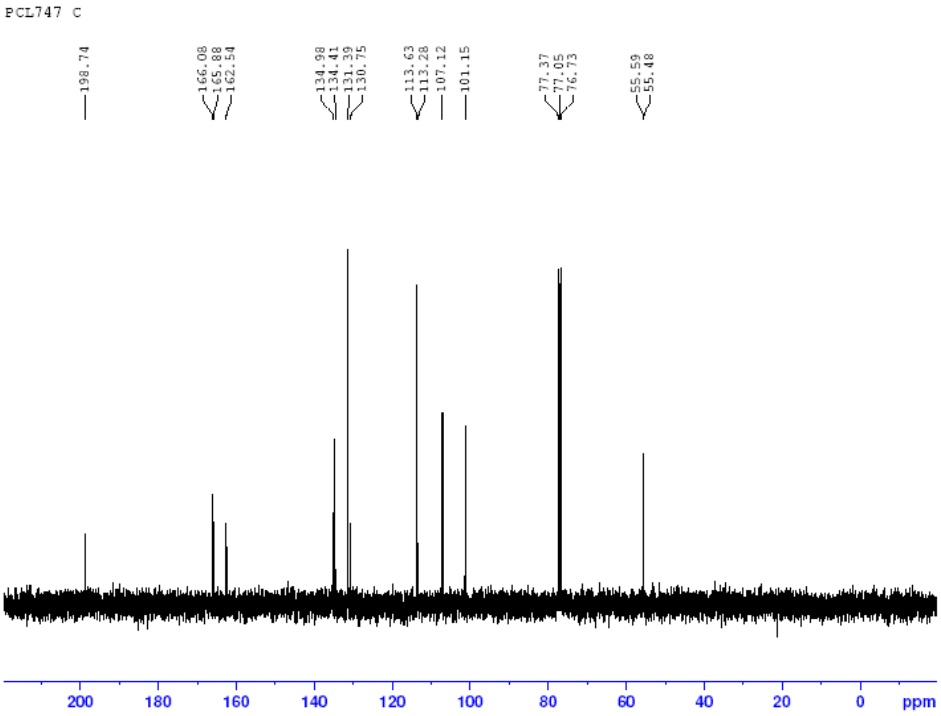
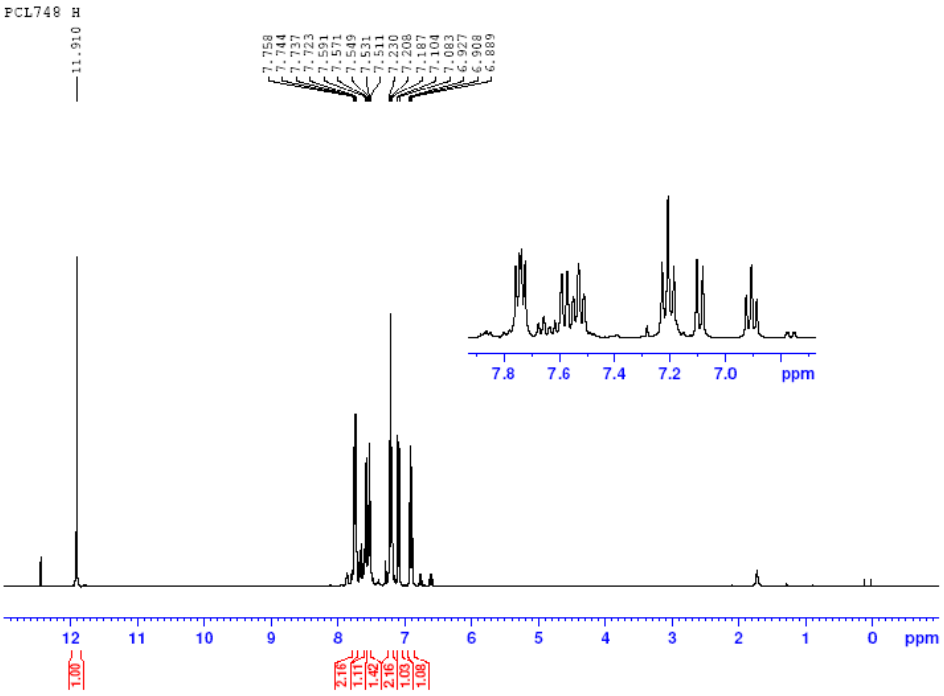


Table 2, entry 2 (2a)





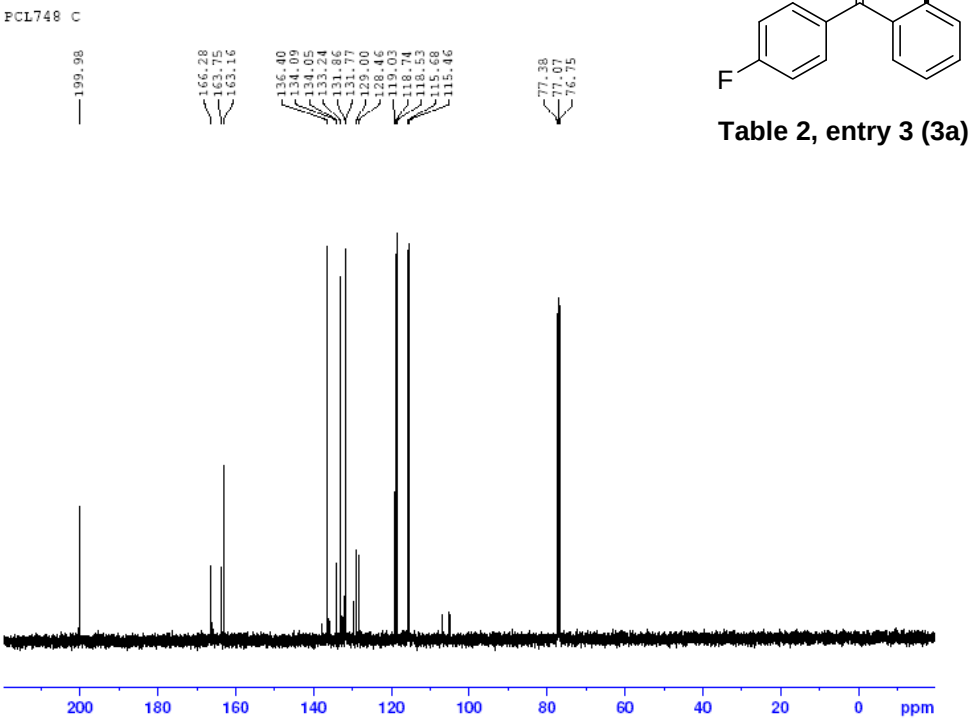


Table 2, entry 3 (3a)

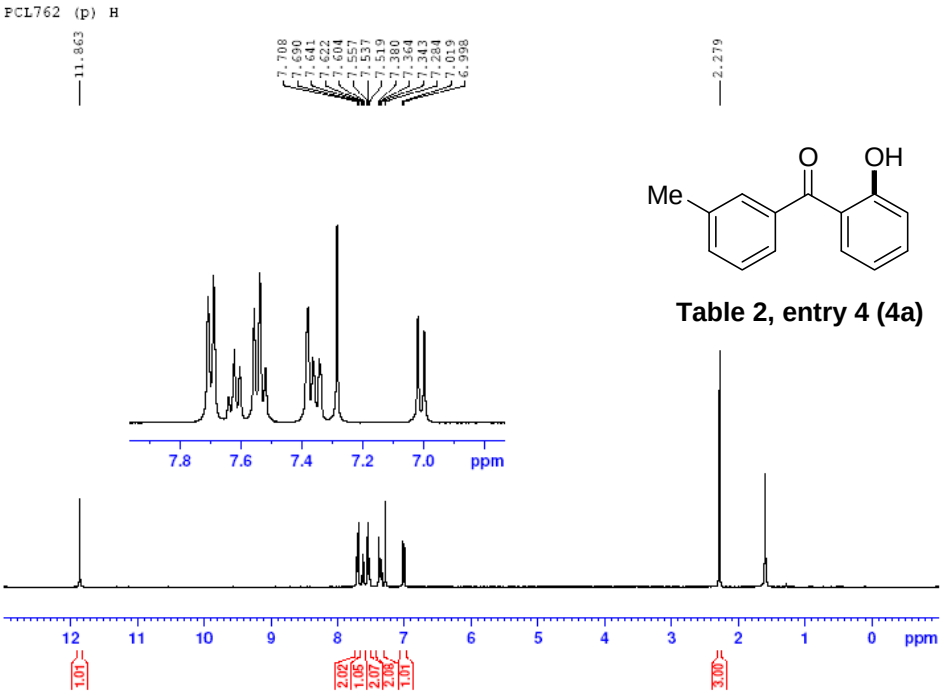
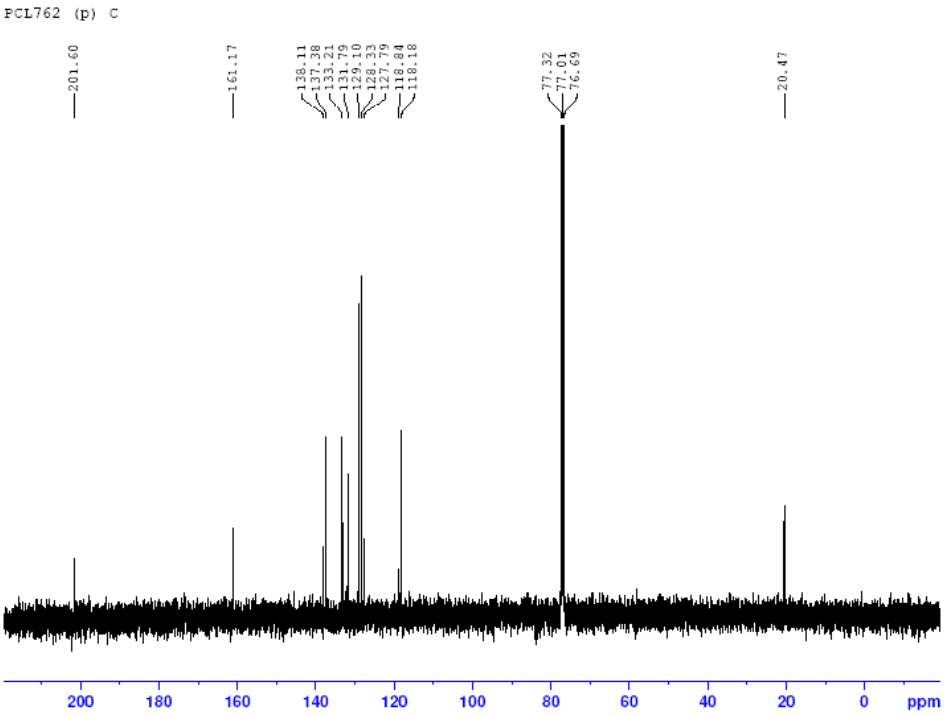


Table 2, entry 4 (4a)



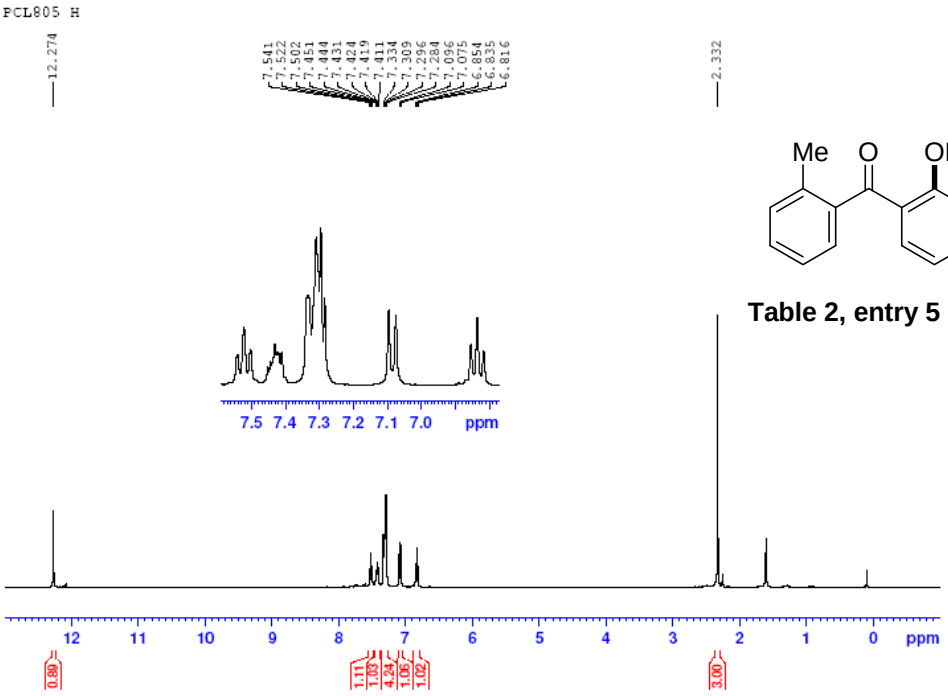
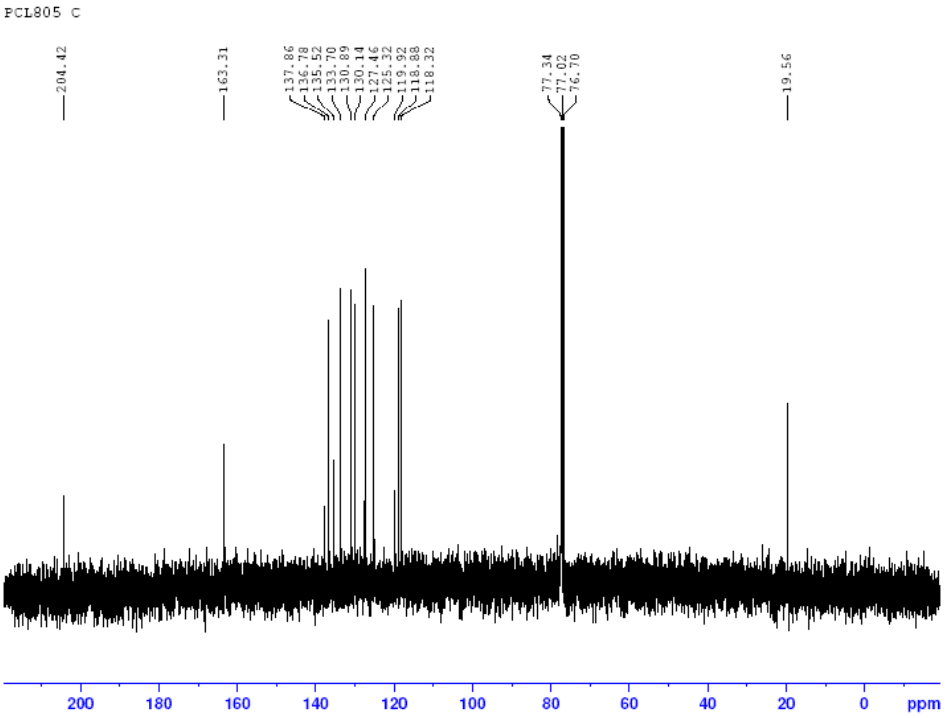


Table 2, entry 5 (5a)



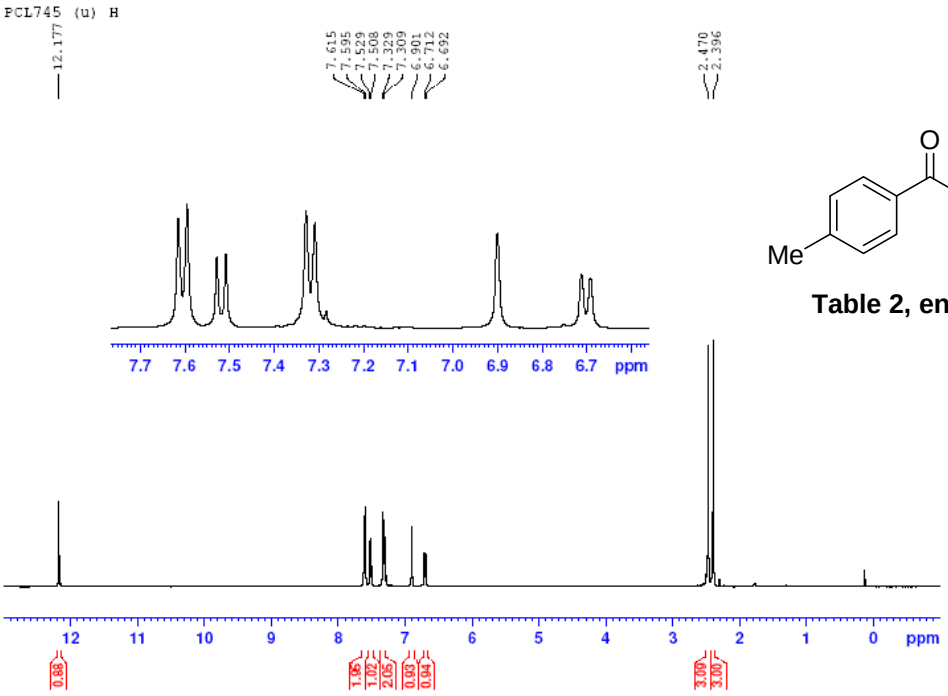
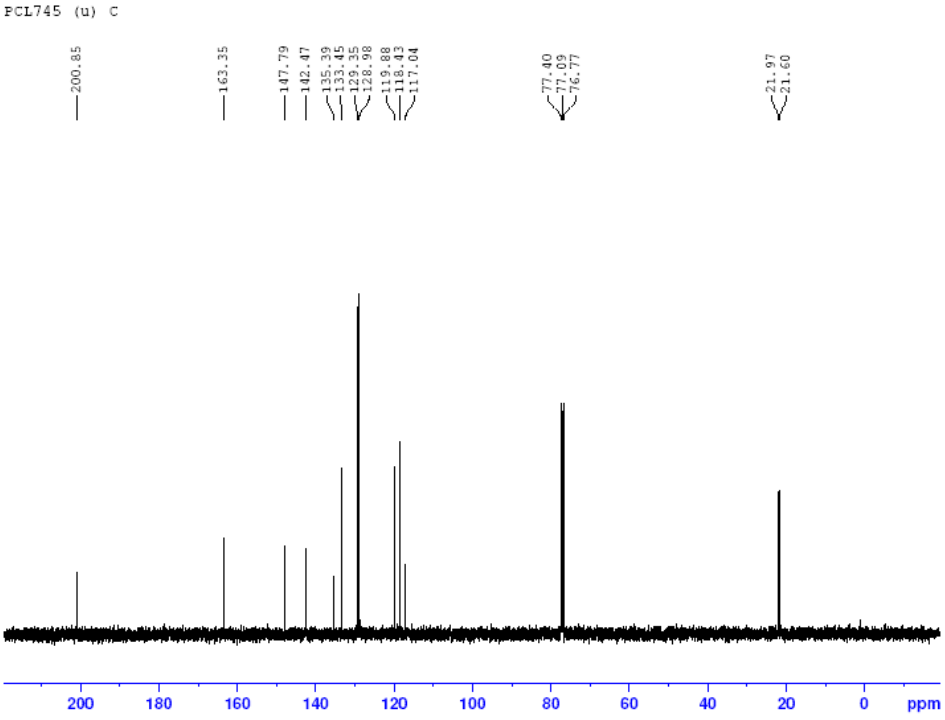


Table 2, entry 6 (6a)



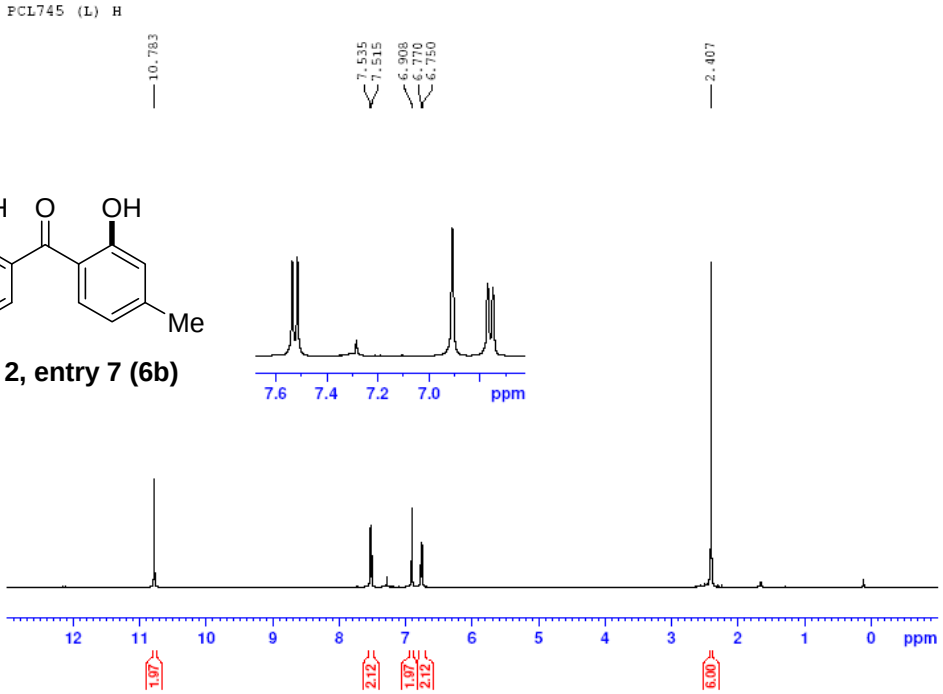
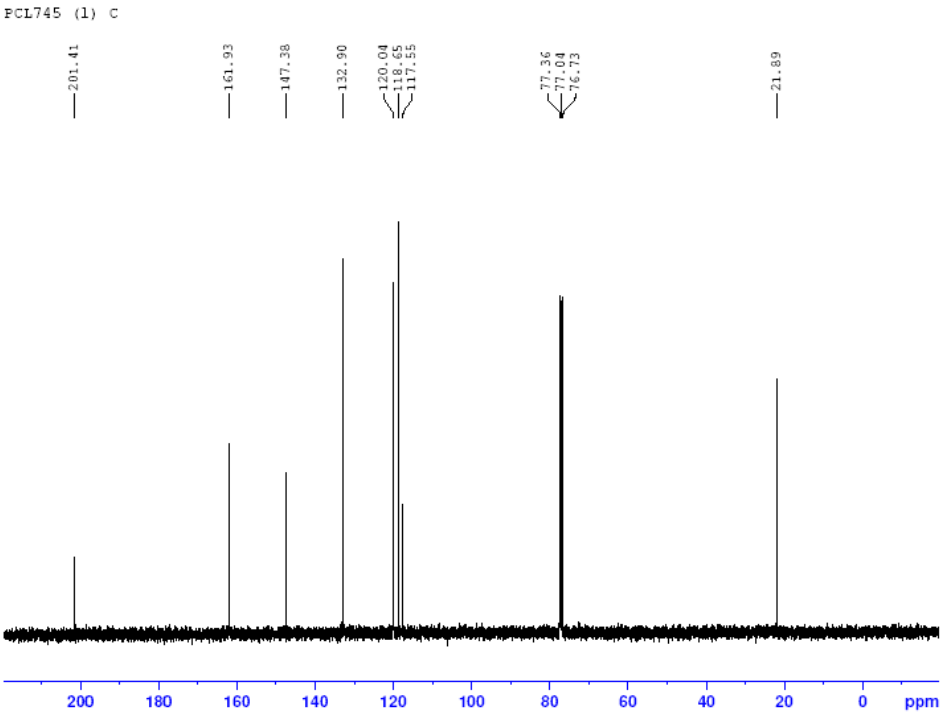


Table 2, entry 7 (6b)



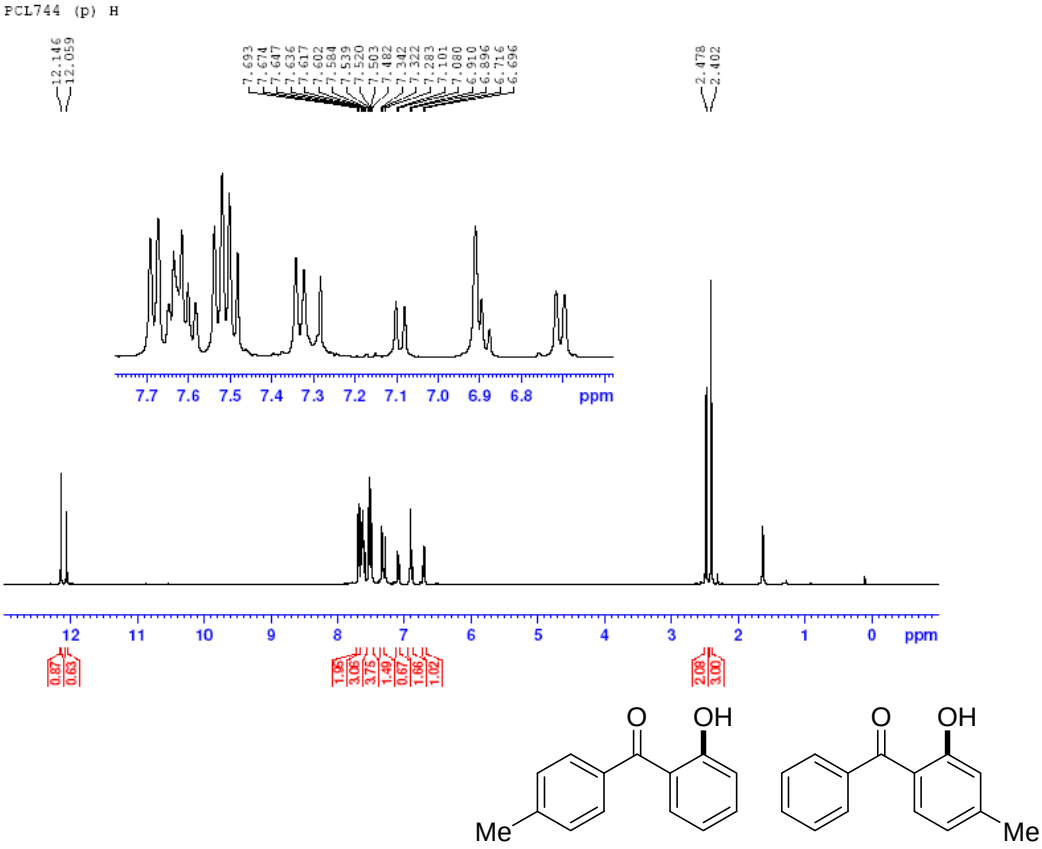
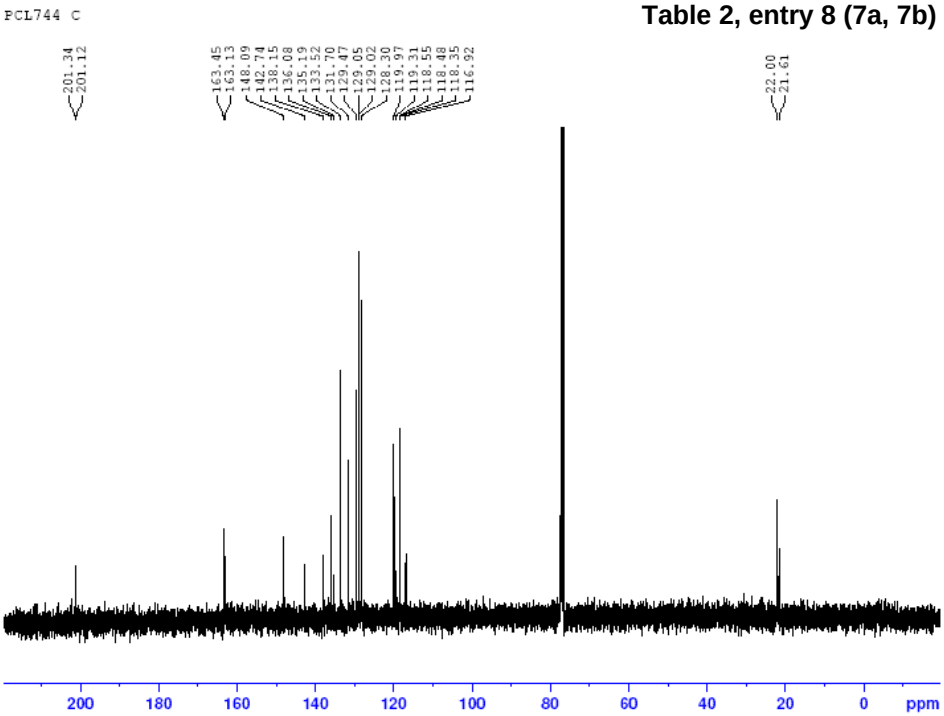
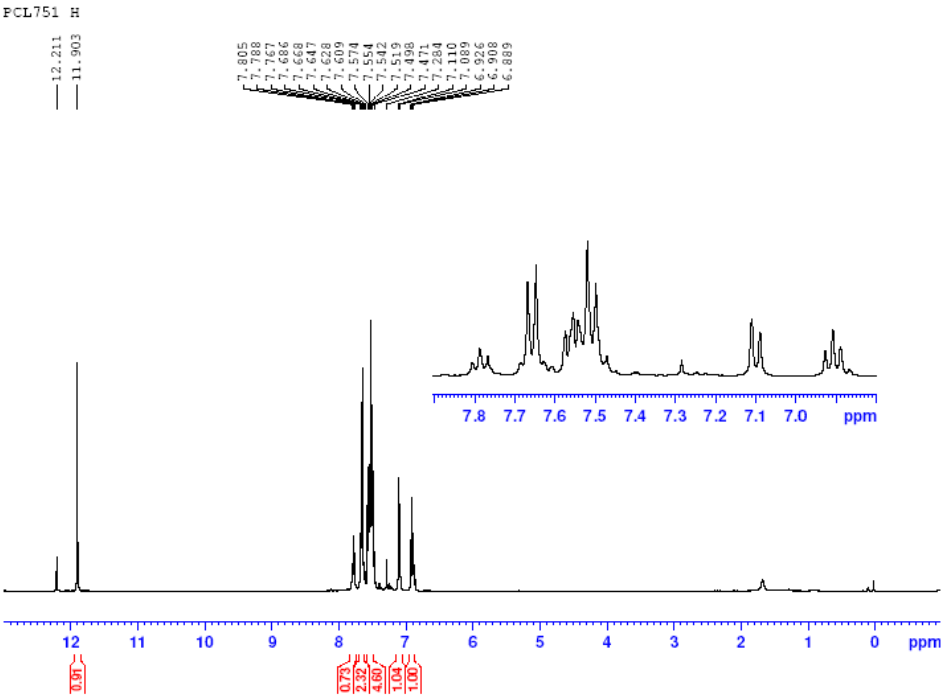


Table 2, entry 8 (7a, 7b)





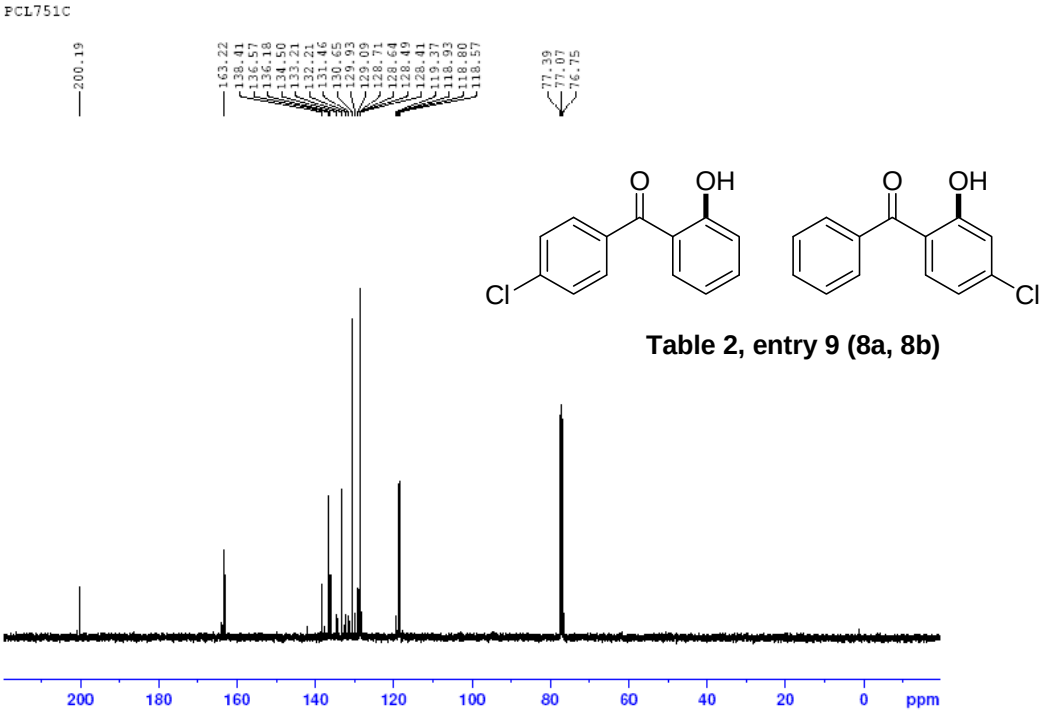
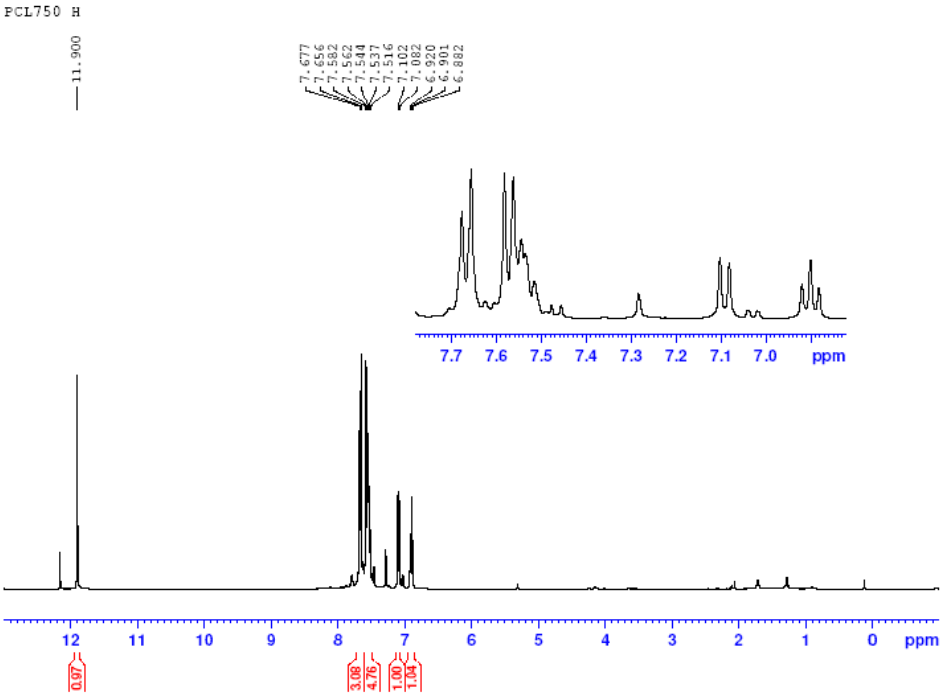


Table 2, entry 9 (8a, 8b)



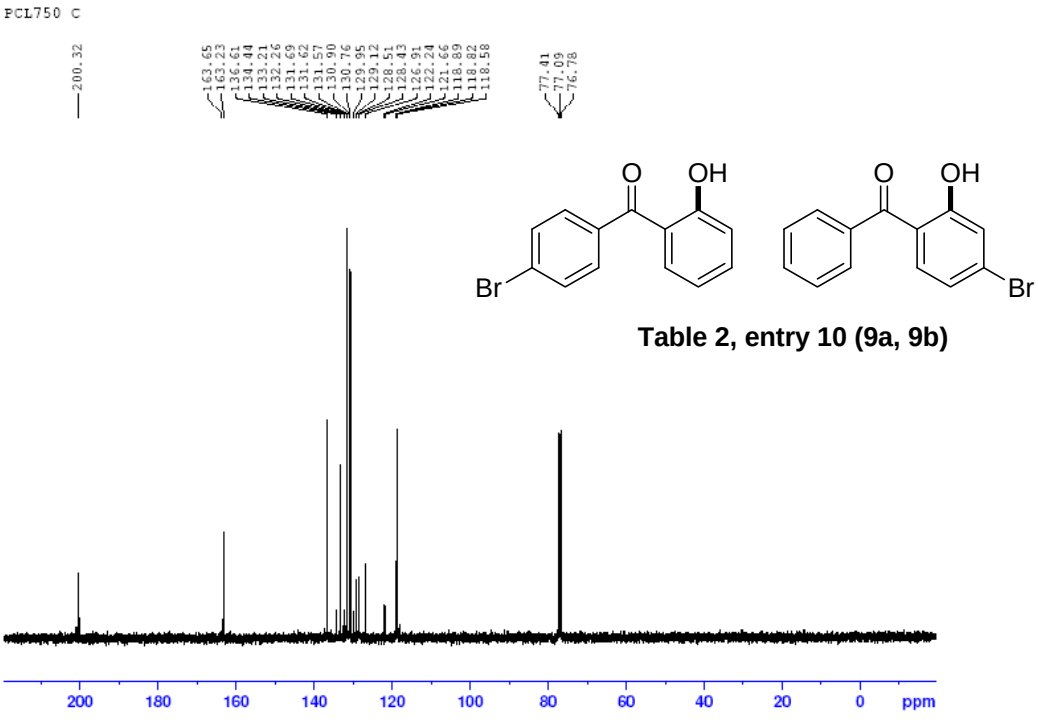
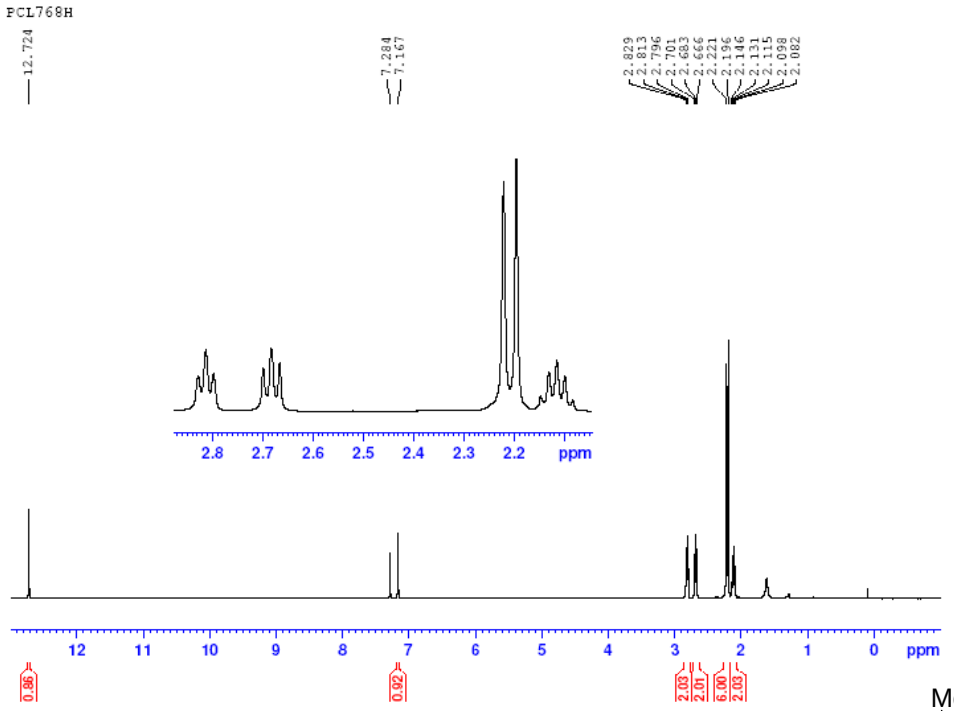
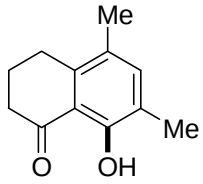
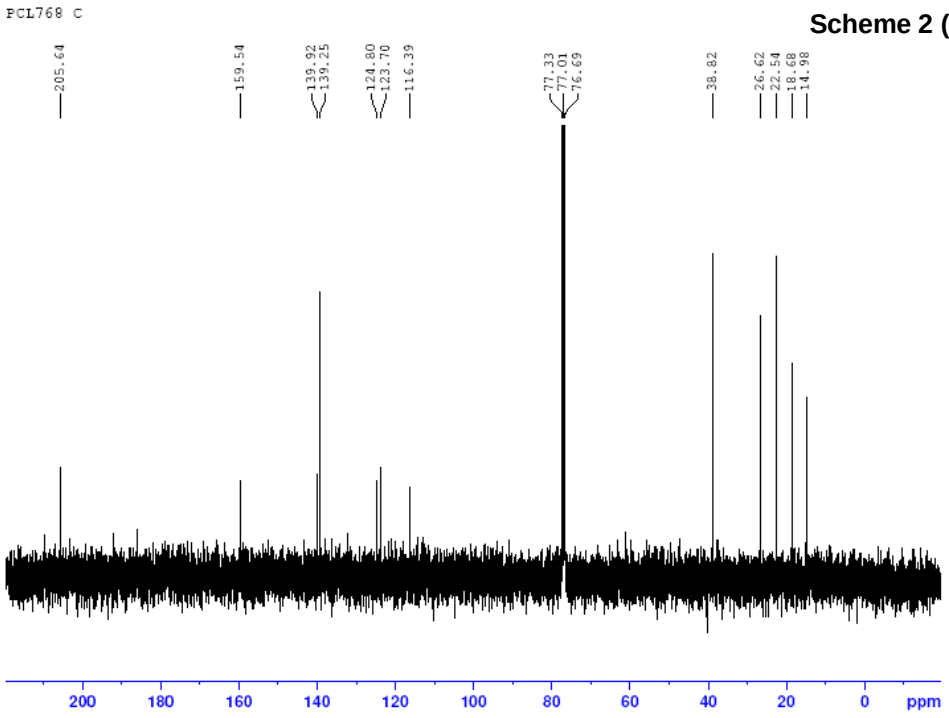


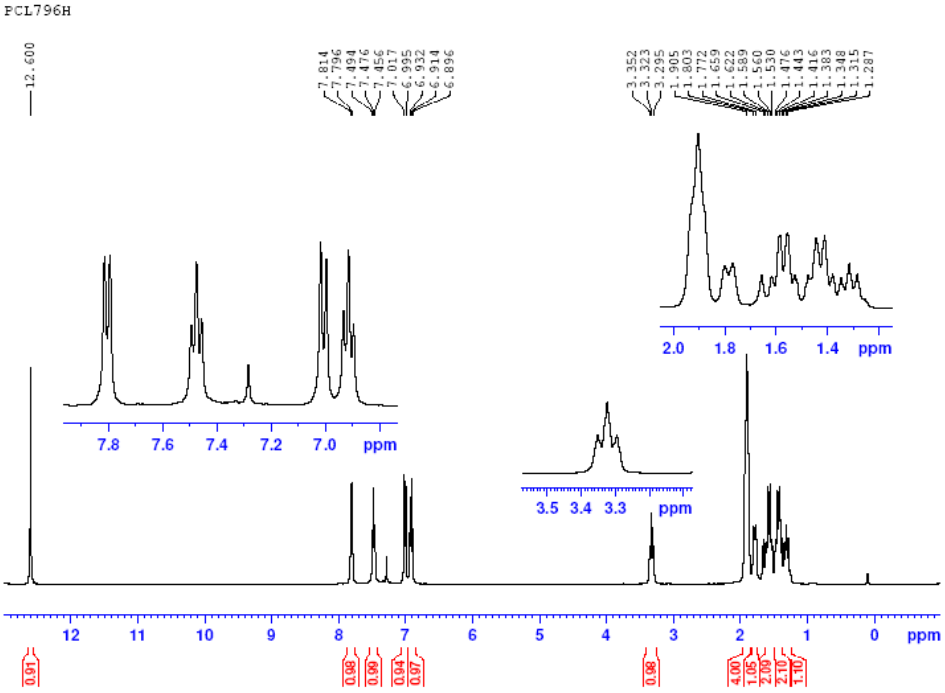
Table 2, entry 10 (9a, 9b)

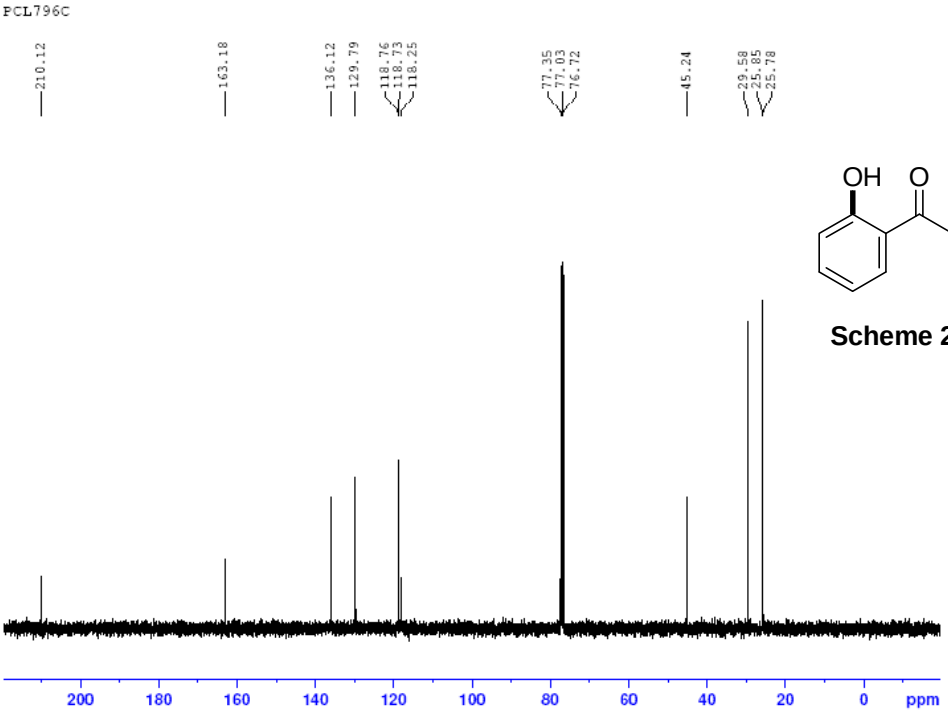

PCL768H
12.724
7.284
7.167
2.829
2.813
2.796
2.701
2.683
2.666
2.221
2.196
2.146
2.131
2.115
2.098
2.082
2.8 2.7 2.6 2.5 2.4 2.3 2.2 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.86
0.92
2.03
2.01
6.00
2.03


Me
Me
O
OH

Scheme 2 (10a)

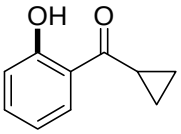

PCL768 C
205.64
159.54
139.92
139.25
124.80
123.70
116.39
77.33
77.01
76.69
38.82
26.62
22.54
18.68
14.98
200 180 160 140 120 100 80 60 40 20 0 ppm


PCL796H
12.600
7.814
7.796
7.494
7.476
7.456
7.017
6.995
6.932
6.914
6.896
3.352
3.323
3.295
1.905
1.803
1.772
1.659
1.622
1.589
1.560
1.530
1.476
1.443
1.416
1.383
1.348
1.315
1.287
7.8 7.6 7.4 7.2 7.0 ppm
2.0 1.8 1.6 1.4 ppm
3.5 3.4 3.3 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.91
0.98
0.99
0.94
0.97
0.98
4.00
1.05
2.09
2.10
1.10

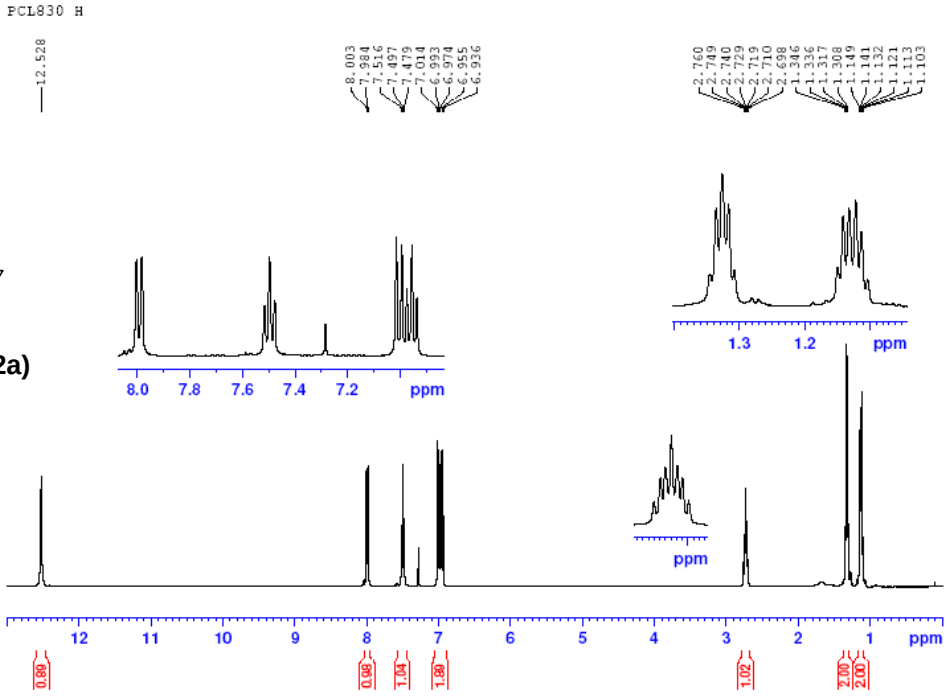

PCL796C
210.12
163.18
136.12
129.79
118.76
118.73
118.25
77.35
77.03
76.72
45.24
29.58
25.85
25.78
200 180 160 140 120 100 80 60 40 20 0 ppm

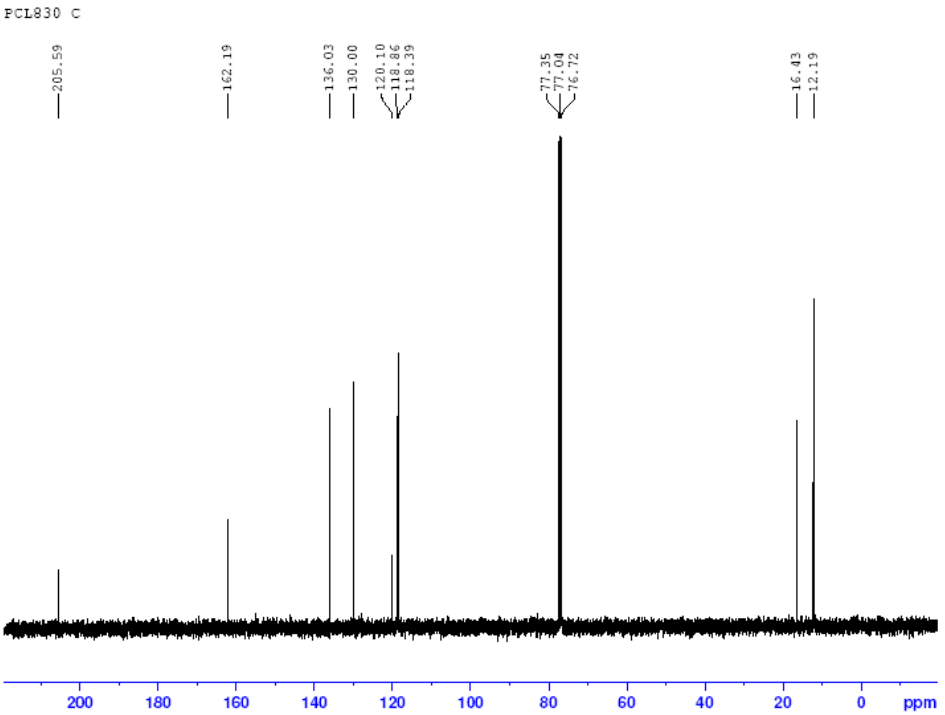
OH
O

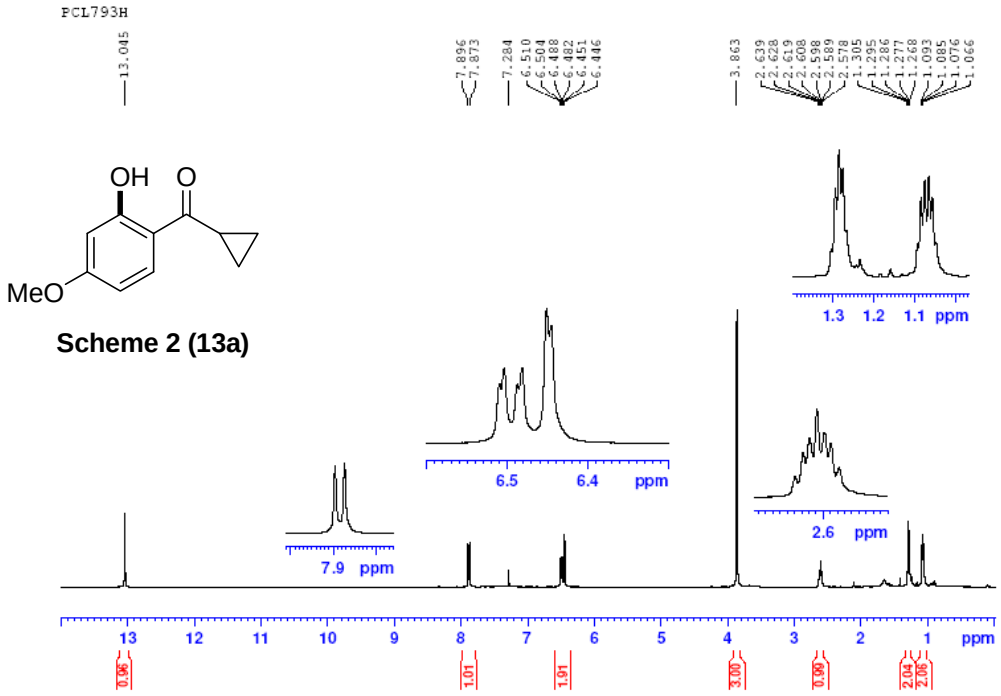
Scheme 2 (11a)


OH
O

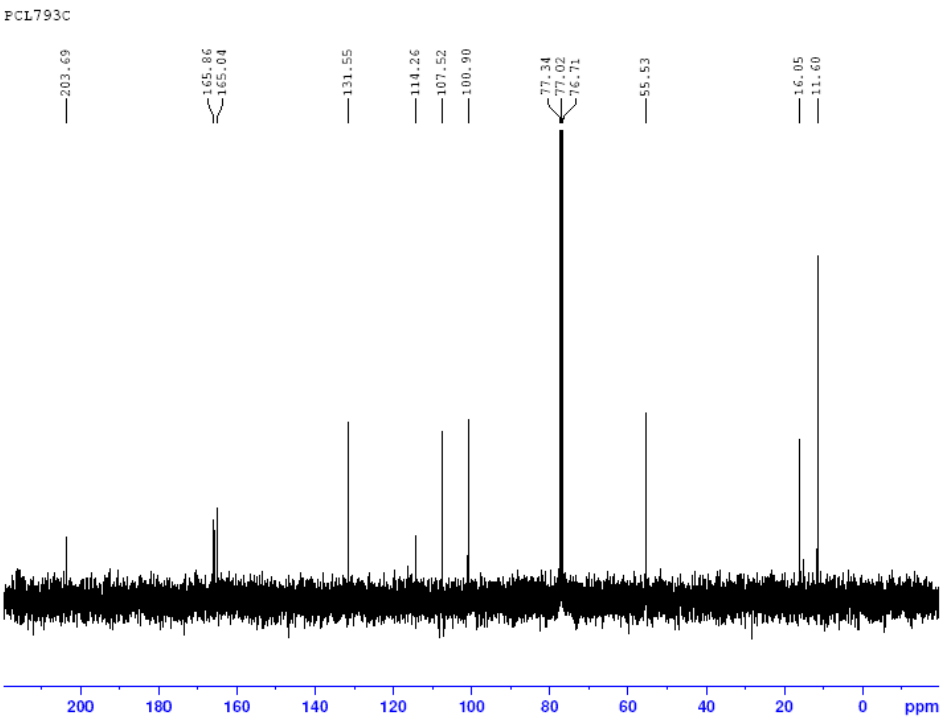
Scheme 2 (12a)

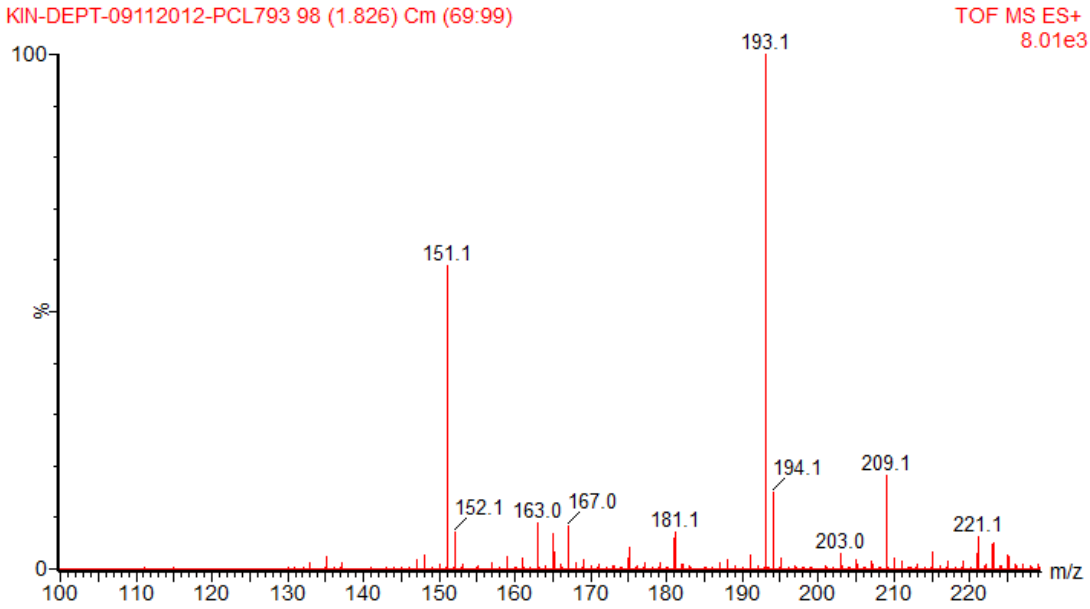

PCL830 H
12.528
8.003
7.984
7.516
7.497
7.479
7.014
6.993
6.974
6.955
6.936
2.760
2.749
2.740
2.729
2.719
2.710
2.698
1.346
1.336
1.317
1.308
1.149
1.141
1.132
1.121
1.113
1.103
8.0
7.8
7.6
7.4
7.2
ppm
1.3
1.2
ppm
ppm
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.89
0.98
1.04
1.80
1.02
2.00
2.00

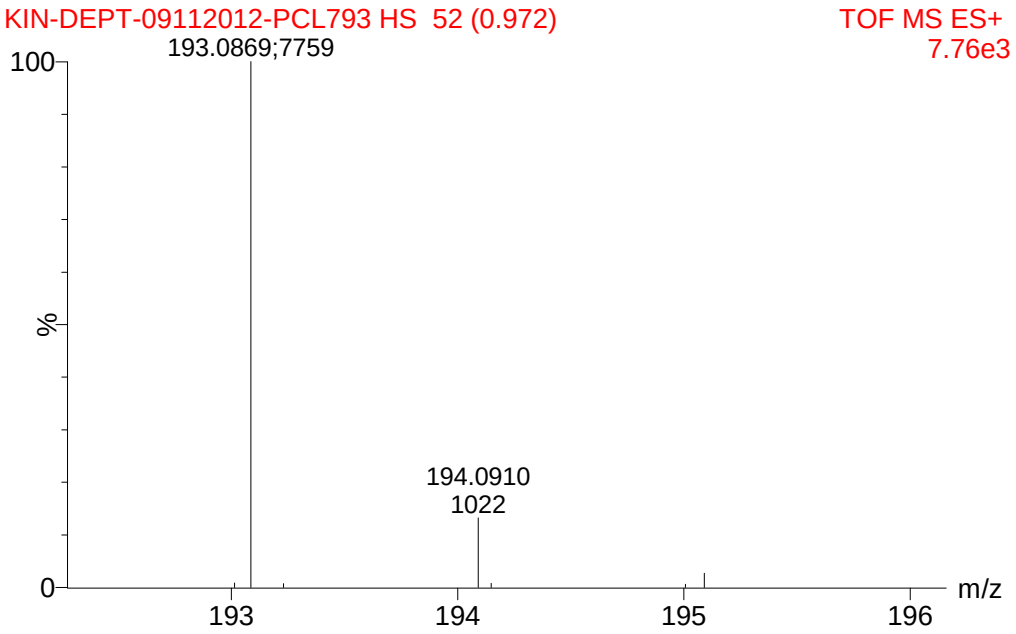

PCL830 C
205.59
162.19
136.03
130.00
120.10
118.86
118.39
77.35
77.04
76.72
16.43
12.19
200
180
160
140
120
100
80
60
40
20
0
ppm


PCL793H
13.045
7.896
7.873
7.284
6.510
6.504
6.488
6.482
6.451
6.446
3.863
2.639
2.628
2.619
2.608
2.598
2.589
2.578
1.305
1.295
1.286
1.277
1.268
1.093
1.085
1.076
1.066
OH
O
MeO
1.3 1.2 1.1 ppm
6.5 6.4 ppm
2.6 ppm
7.9 ppm
13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.96
1.01
1.91
3.00
0.90
2.04
2.06

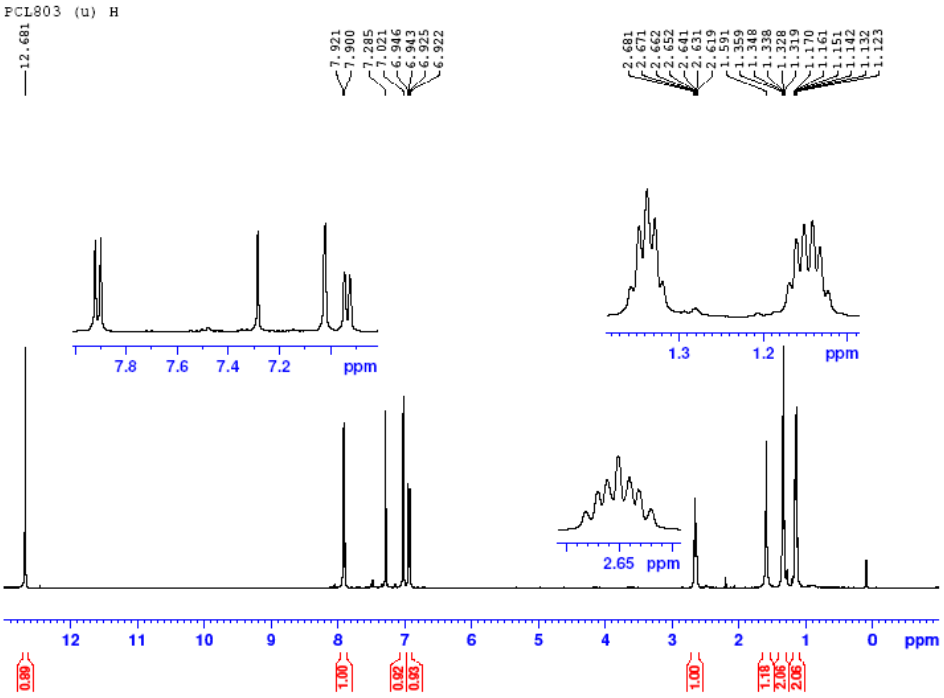
Scheme 2 (13a)

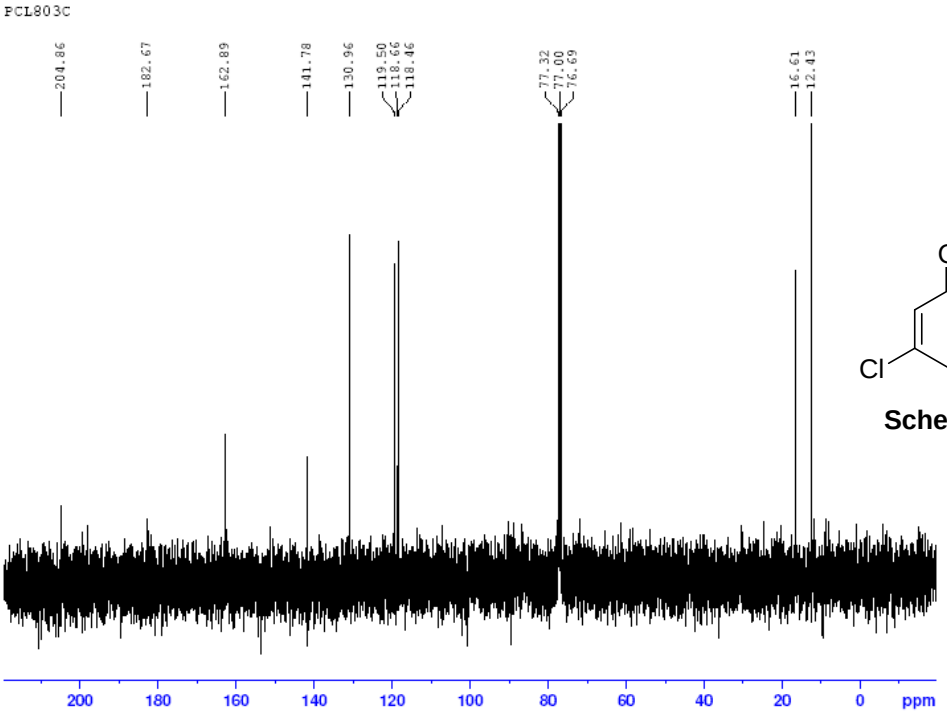

PCL793C
203.69
165.86
165.04
131.55
114.26
107.52
100.90
77.34
77.02
76.71
55.53
16.05
11.60
200 180 160 140 120 100 80 60 40 20 0 ppm

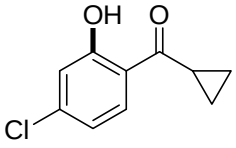




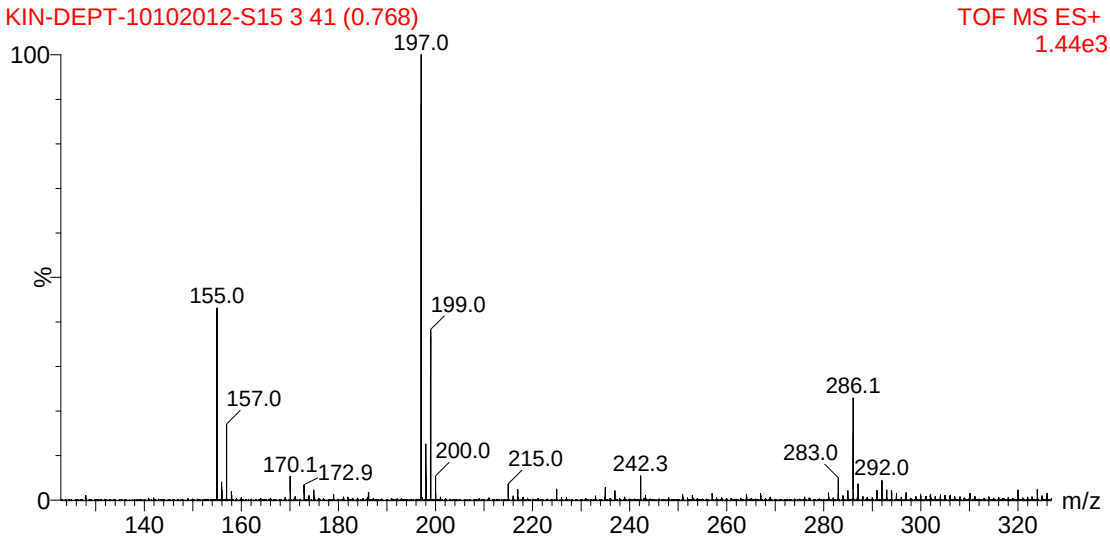
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
193.0869	193.0865	0.4	2.1	5.5	27.3	C11 H13 O3

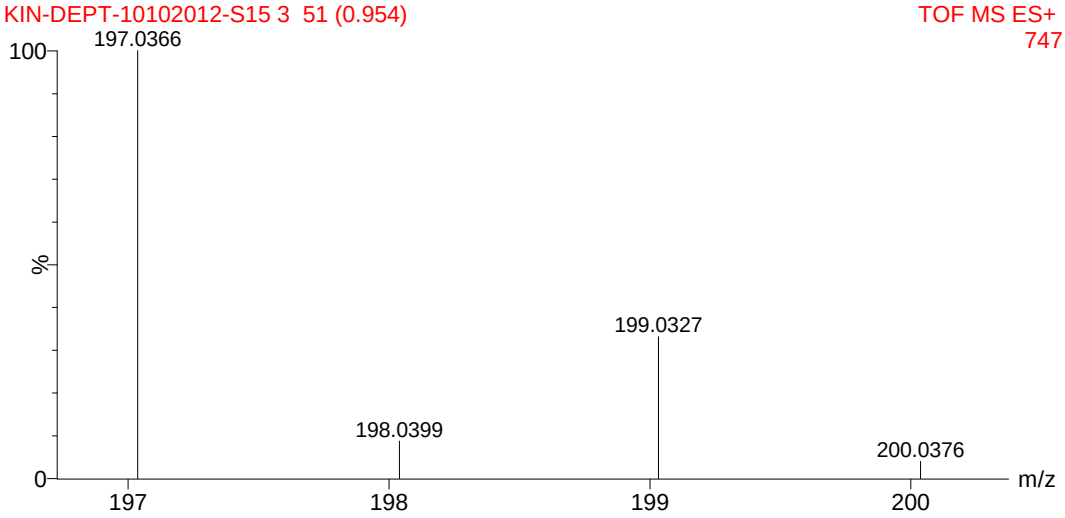

PCL803 (u) H
12.681
7.921
7.900
7.285
7.021
6.946
6.943
6.925
6.922
2.681
2.671
2.662
2.652
2.641
2.631
2.619
1.591
1.359
1.348
1.338
1.328
1.319
1.170
1.161
1.151
1.142
1.132
1.123
7.8
7.6
7.4
7.2
ppm
1.3
1.2
ppm
2.65 ppm
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
0.69
1.00
0.92
0.93
1.00
1.18
2.06
2.06


PCL803C
204.86
182.67
162.89
141.78
130.96
119.50
118.66
118.46
77.32
77.00
76.69
16.61
12.43
200
180
160
140
120
100
80
60
40
20
0
ppm

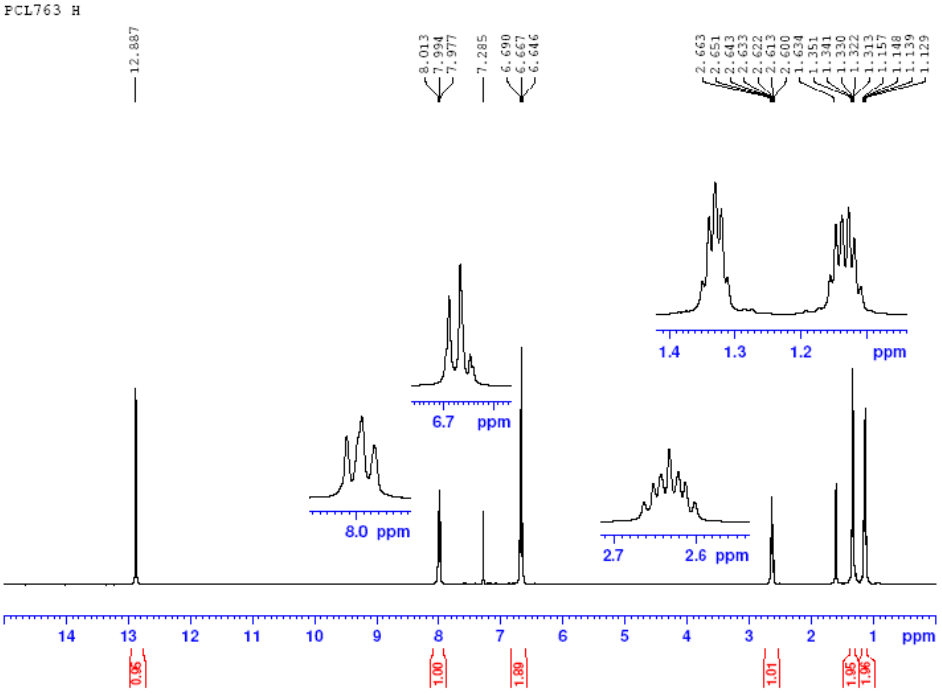

OH
O
Cl

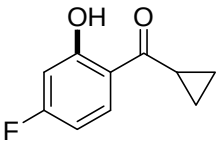
Scheme 2 (14a)



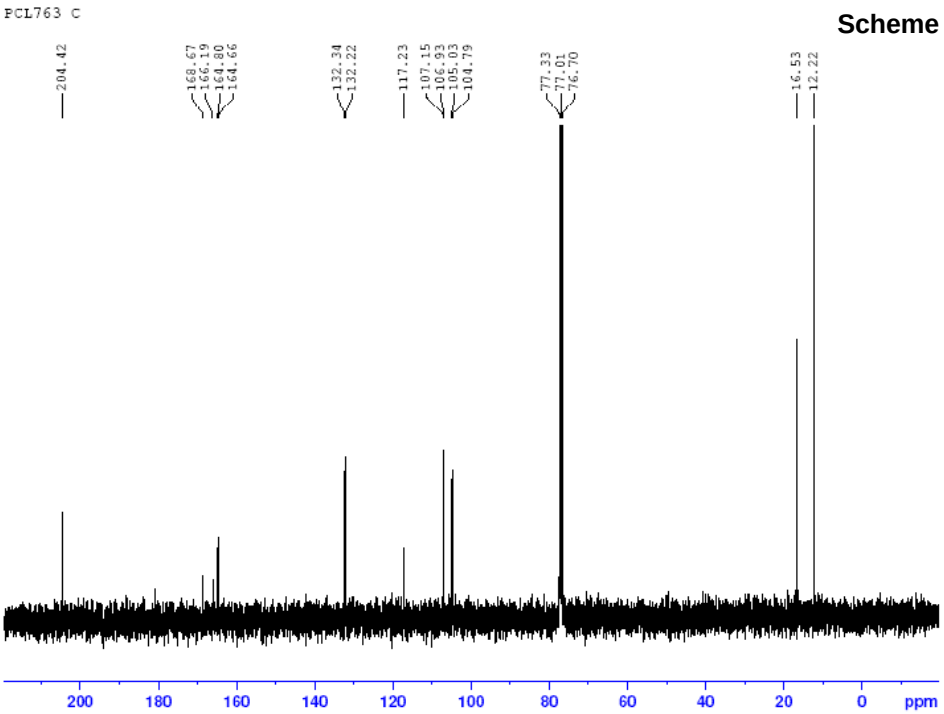


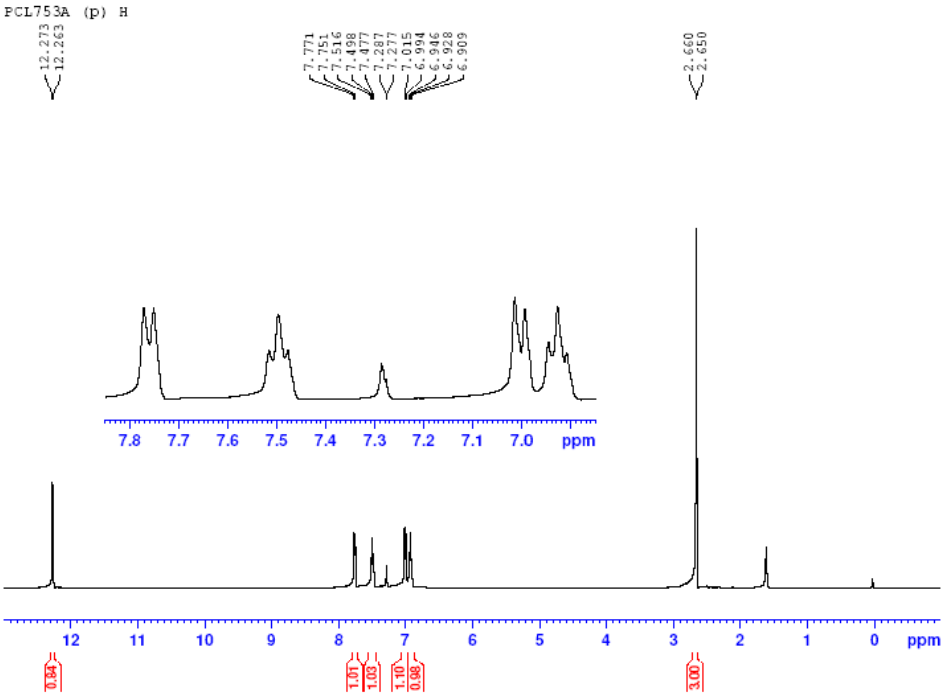
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
197.0366	197.0369	-0.3	-1.5	5.5	2.8	C10 H10 O2 Cl

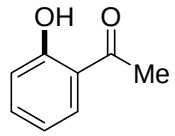

PCL763 H
12.887
8.013
7.994
7.977
7.285
6.690
6.667
6.646
2.663
2.651
2.643
2.633
2.622
2.613
2.600
1.634
1.351
1.341
1.330
1.322
1.313
1.157
1.148
1.139
1.129
1.4
1.3
1.2
ppm
6.7
ppm
8.0 ppm
2.7
2.6 ppm
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.95
1.00
1.89
1.01
1.95
1.96


OH
O
F

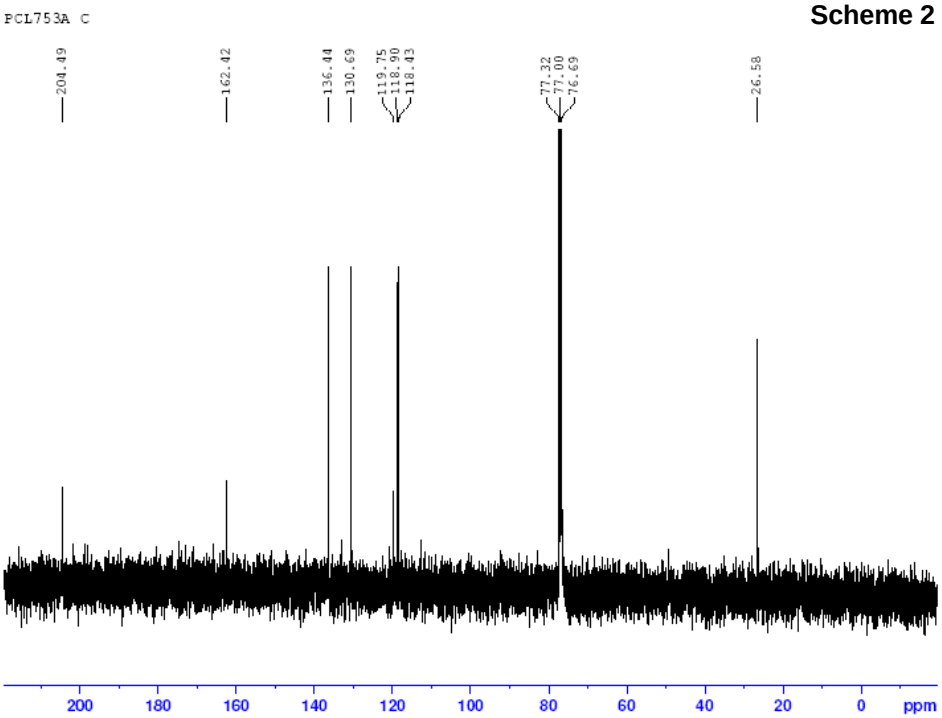
Scheme 2 (15a)

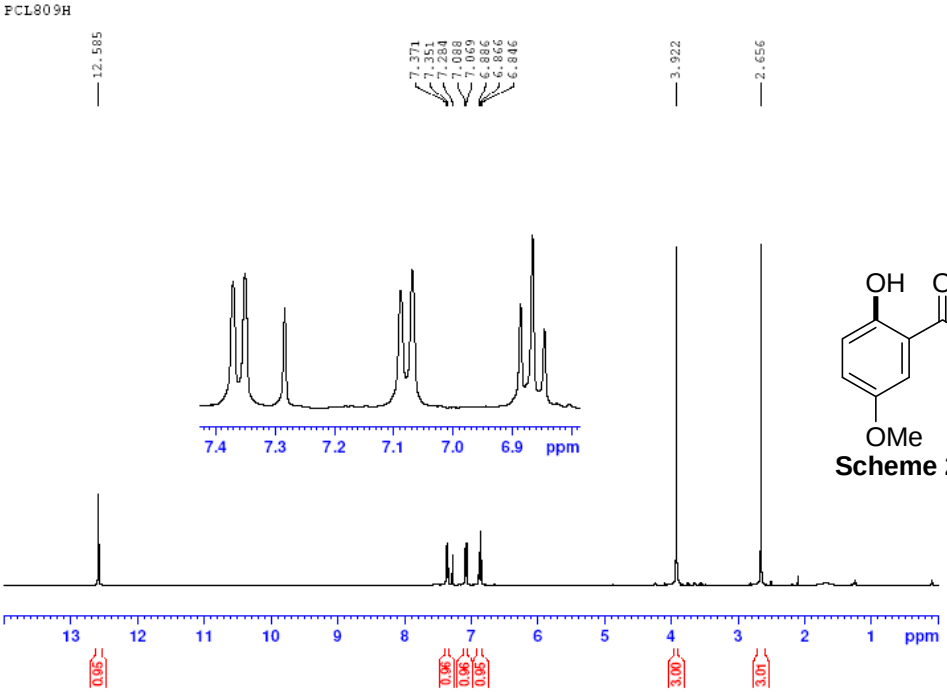

PCL763 C
204.42
168.67
166.19
164.80
164.66
132.34
132.22
117.23
107.15
106.93
105.03
104.79
77.33
77.01
76.70
16.53
12.22
200
180
160
140
120
100
80
60
40
20
0
ppm


PCL753A (p) H
12.273
12.263
7.771
7.751
7.516
7.498
7.477
7.287
7.277
7.015
6.994
6.946
6.928
6.909
2.660
2.650
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.84
1.01
1.03
1.10
0.98
3.00


OH
O
Me

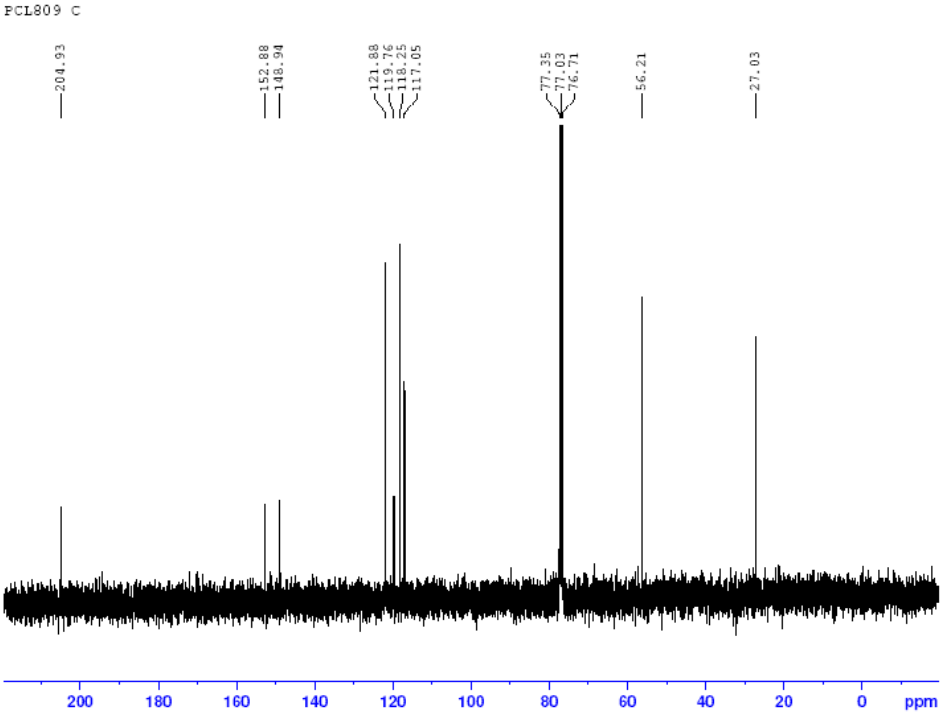
Scheme 2 (16a)

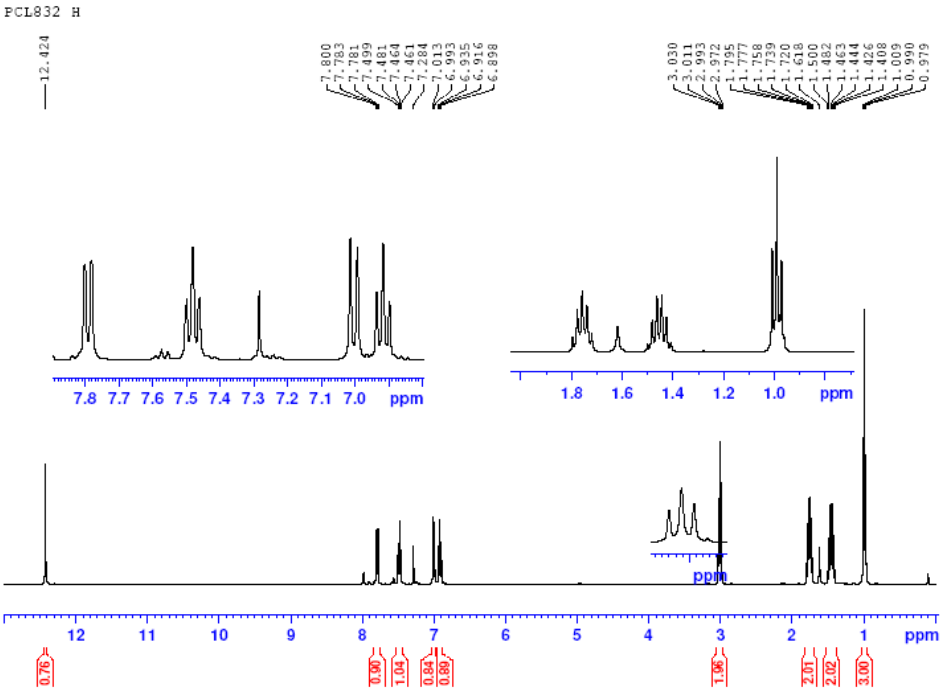

PCL753A C
204.49
162.42
136.44
130.69
119.75
118.90
118.43
77.32
77.00
76.69
26.58
200 180 160 140 120 100 80 60 40 20 0 ppm

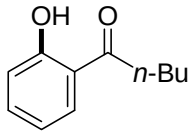

PCL809H
12.585
7.371
7.351
7.284
7.088
7.069
6.886
6.866
6.846
3.922
2.656
7.4
7.3
7.2
7.1
7.0
6.9
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.95
0.96
0.96
0.95
3.00
3.01

OH
O
Me
OMe

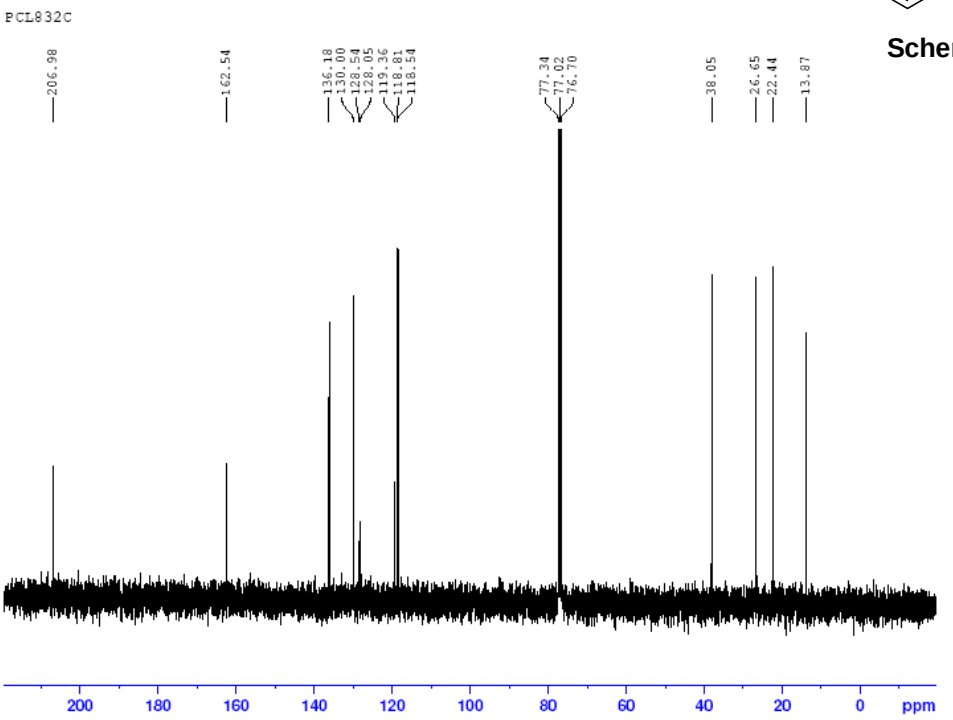
Scheme 2 (17a)

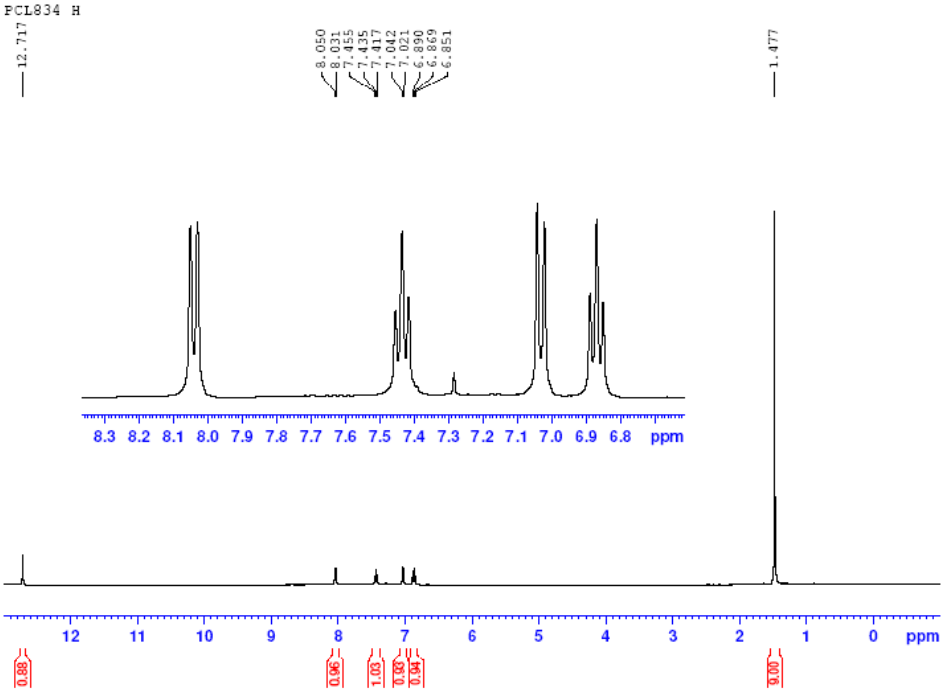

PCL809 C
204.93
152.88
148.94
121.88
119.76
118.25
117.05
77.35
77.03
76.71
56.21
27.03
200
180
160
140
120
100
80
60
40
20
0
ppm

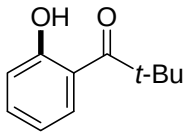

PCL832 H
12.424
7.800
7.783
7.781
7.499
7.481
7.464
7.461
7.284
7.013
6.993
6.935
6.916
6.898
3.030
3.011
2.993
2.972
1.795
1.777
1.758
1.739
1.720
1.618
1.500
1.482
1.463
1.444
1.426
1.408
1.009
0.990
0.979
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm
1.8 1.6 1.4 1.2 1.0 ppm
ppm
12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.76
0.90
1.04
0.84
0.89
1.96
2.01
2.02
3.00


OH
O
n-Bu

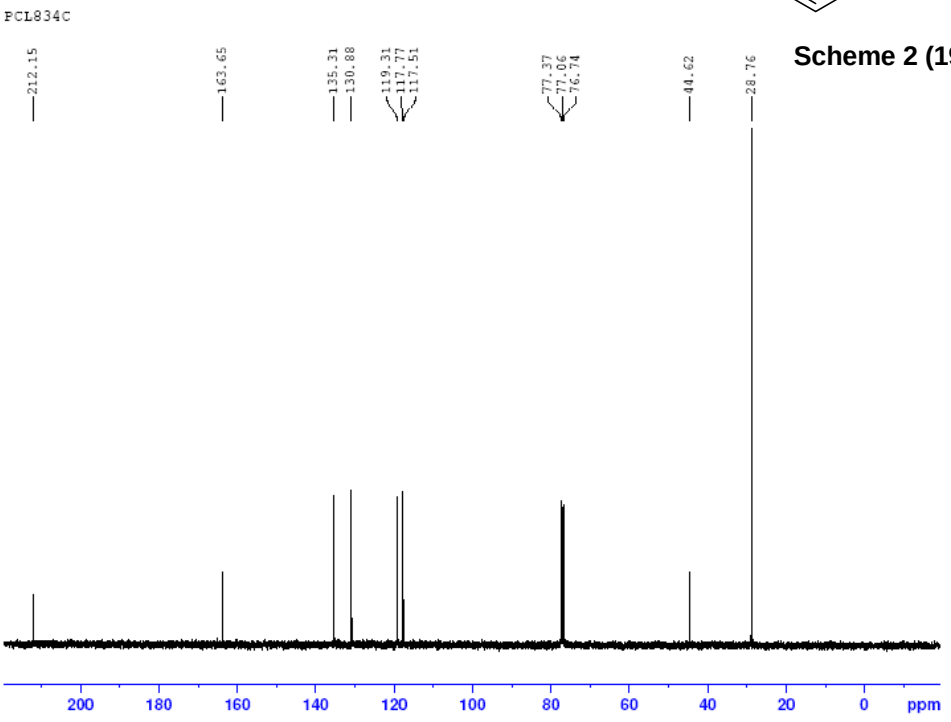
Scheme 2 (18a)

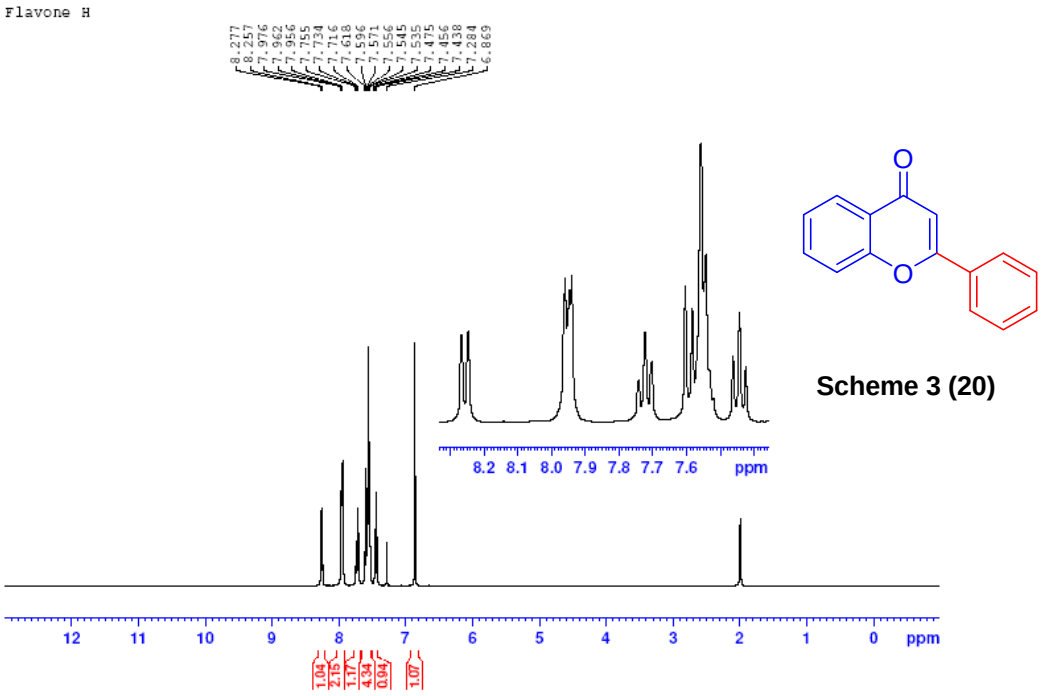

PCL832C
206.98
162.54
136.18
130.00
128.54
128.05
119.36
118.81
118.54
77.34
77.02
76.70
38.05
26.65
22.44
13.87
200 180 160 140 120 100 80 60 40 20 0 ppm


PCL834 H
12.717
8.050
8.031
7.455
7.435
7.417
7.042
7.021
6.890
6.869
6.851
1.477
8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.88
0.96
1.03
0.80
0.94
9.00

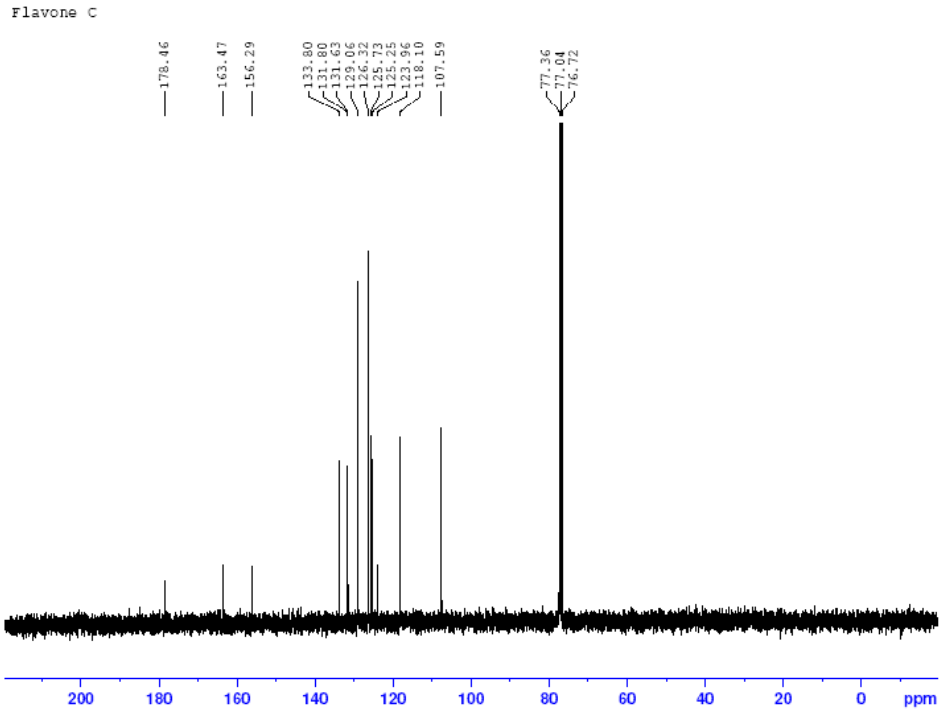

OH
O
t-Bu

Scheme 2 (19a)


PCL834C
212.15
163.65
135.31
130.88
119.31
117.77
117.51
77.37
77.06
76.74
44.62
28.76
200 180 160 140 120 100 80 60 40 20 0 ppm


Flavone H
8.277
8.257
7.976
7.962
7.956
7.755
7.734
7.716
7.618
7.596
7.571
7.556
7.545
7.535
7.475
7.456
7.438
7.284
6.869
8.2 8.1 8.0 7.9 7.8 7.7 7.6 ppm
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.04
2.15
1.17
4.34
0.94
1.07

Scheme 3 (20)


Flavone C
178.46
163.47
156.29
133.80
131.80
131.63
129.06
126.32
125.73
125.25
123.96
118.10
107.59
77.36
77.04
76.72
200 180 160 140 120 100 80 60 40 20 0 ppm

8. References

(1) Old, K. B.; Main, L. *J. Chem. Soc. Perkin Trans. II*, **1982**, 1309.

(2) Tsvelikhovsky, D.; Buchwald, S. L. *J. Am. Chem. Soc.* **2011**, *133,* 14228.

(3) Williams, J. L. R. *J. Org. Chem*. **1954**, *19*, 1205.

(4) Weng, F.; Wang, C.; Xu, B. *Tetrahedron Lett.* **2010**, *51*, 2593.

(5) Nguyen, T. B.; Wang, Q.; Gueritte, F. *Chem. Eur. J.* **2011**, *17*, 9576.

(6) Burns, N. Z.; Hackman, B. M.; Ng, P. Y.; Powelson, I. A.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2006**, *45*, 3811.

(7) Wang, Y.-Q.; Yu, C.-B.; Wang, D.-W.; Wang, X.-B.; Zhou, Y.-G. *Org. Lett.* **2008**, *10*, 2071.

(8) Wang, D. *U.S. Pat. Appl. Publ.* **2008**, US 20080271259 A1 20081106.

(9) Nguyen, T. B.; Wang, Q.; Gueritte, F. *Chem. Eur. J.* **2011**, *17*, 9576.

(10) Gabbutt, C. D.; Heron, B. M.; Instone, A. C. *Tetrahedron* **2006**, *62*, 737.

(11) Rao, H.-H.; Li, C.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 8936.

(12) Khanum, S. A.; Shashikanth, S.; Umesha, S.; Kavitha, R. *Eur. J. Med. Chem.* **2005,** *40*, 1156.

(13) Golumbic, C.; Orchin, M. *J. Am. Chem. Soc.* **1950**, *72,* 4145.

(14) Miranda, M. A.; Tormos, R. *J. Org. Chem*. **1993**, *58*, 3304.

(15) Beck, A. L.; Coates, W. J.; Moody, C. J. *J. Chem. Soc*., *Perkin Trans. 1*. **1990**, 689.

(16) Van Daele, G. *Eur. Pat. Appl.* **1983**, EP 76530 A2 19830413.

(17) Konishi, H.; Ueda, T.; Muto, T.; Manabe, K. *Org. Lett.* **2012**, *14,* 4722.

(18) Jackman, L. M.; Trewella, J. C.; Haddon, R. C *J. Am. Chem. Soc.* **1980**, *102*, 2519.

(19) Namba, K.; Kanaki, M.; Suto, H.; Nishizawa, M.; Tanino, K. *Org. Lett.* **2012**, *14,* 1222.

(20) Samanta, R.; Bauer, J. O.; Strohmann, C.; Antonchick, A. P. *Org. Lett.* **2012**, *14*, 5518.