One-pot synthesis of benzolactones and lactams via a cobalt-catalyzed regioselective [2+2+2] cocyclotrimerization of alkynyl alcohols and amines with propiolates

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Electronic Supplementary Information

Experimental Section

General procedure for the cobalt-catalyzed [2+2+2] cocyclotrimerization of alkynyl alcohols and propiolates:

A 25-mL round-bottom flask containing CoI_2(dppe) (0.050 mmol), Zn (2.75 mmol), DMAD **2** or propiolate **4** (2.2 mmol) was evacuated and purged with nitrogen gas three times. Freshly distilled solvents CH_3CN and THF (2.0 + 2.0 mL) and alkynyl alcohol **1** (1.0 mmol) were added. The reaction mixture was initially stirred at room temperature for 1 h to reduce Co(II) (pale green) to active species (dark green) species and then at 80 °C for 12 h (For Scheme 1, 2, 4, and 5 heat at 80 °C for 12 h, and Scheme 3 and 6 heat at 80 °C for 16 h). The reaction mixture was then filtered through Celite and silica gel, and eluted with dichloromethane. The filtrate was concentrated, and the residue was purified on a silica gel column using hexanes-ethyl acetate as eluent to afford the desired products **3** or **5**. Products **7a-b**, and **9** were synthesized according to similar procedures using propargyl amines **6** and propiolate **4c**, and unsymmetrical diyne **8** and propargyl alcohol **1a** as the reagents, respectively. In addition, product **13** was synthesized based on a similar procedure using Ni(dppe)Br_2 as the catalyst.

Product yields of these reactions are listed in Tables **1**, and **2**, while spectral data and the ^{1}H and ^{13}C NMR spectra of compounds **3a-g**, **5a-f**, **7a-b**, **9** and **13** are shown below.

Trimethyl 3-oxo-1,3-dihydro-4,5,6-isobenzofurantricarboxylate (**3a**)**:** Colorless solid; m.p 152 °C; IR (neat); 1771, 1738, 1731, 1723, 1339, 1295, 1283, 1260 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.95 (s, 1 H), 5.34 (s, 2 H), 3.95 (s, 3 H), 3.89 (s, 3 H), 3.86 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 166.8, 165.8, 165.3, 164.6, 148.4, 135.7, 132.8, 131.9, 125.6, 124.8, 69.0, 53.3, 53.3, 53.3; HRMS calcd for $C_{14}H_{12}O_8$ 308.0532 found 308.0535.

3'-Oxo-3'*H*-spiro[cyclohexane-1,1'-isobenzofuran]-4',5',6'-tricarboxylic acid trimethyl ester (**3b**)**:** Pale yellow solid; m.p 122 °C; IR (neat): 1779, 1747, 1742, 1731, 1341, 1290, 1264, 1233 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.86 (s, 1 H), 3.96 (s, 3 H), 3.90 (s, 3 H), 3.87 (s, 3 H), 1.85-1.75 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 165.8, 165.7, 165.5, 164.8, 156.5, 135.9, 132.6, 132.4, 125.4, 123.5, 86.8, 53.3, 53.2, 53.2, 35.9, 24.4, 21.9; HRMS calcd for $C_{19}H_{20}O_8$ 376.1158 found 376.1158.

Trimethyl 7-methyl-3-oxo-1,3-dihydro-4,5,6-isobenzofurantricarboxylate (**3c**)**:** Pale yellow solid; m.p 102 °C; IR (neat): 1776, 1732, 1341, 1297, 1252, 1218 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 5.28 (s, 2 H), 3.97 (s, 3 H), 3.91 (s, 3 H), 3.86 (s, 3 H), 2.31 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 167.4, 166.9, 165.2, 164.7, 149.4, 139.2, 132.4, 131.1, 128.7, 123.4, 68.7, 53.2, 53.2, 52.9, 15.0; HRMS calcd for $C_{15}H_{14}O_8$ 322.0689 found 322.0691.

Dimethyl 3,6-dioxo-1,3,6,8-tetrahydrofuro[3,4-*e*]isobenzofuran-4,5-dicarboxylate (3d): Colorless solid; m.p 130 °C; IR: 1791, 1766, 1744, 1733, 1310, 1221, 1210 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 5.42 (s, 4 H), 4.01 (s, 6 H); ^{13}C NMR (100 MHz, d-acetone)**;** δ 167.5, 165.1, 145.4, 131.7, 128.3, 69.4, 53.5; HRMS calcd for $C_{14}H_{10}O_8$ 306.0376 found 306.0376.

Trimethyl 1-oxo-3,4-dihydro-1*H*-6,7,8-isochromenetricarboxylate (**3e**)**:** Colorless solid; m.p 158 °C; IR (neat): 1749, 1318, 1283 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.80 (s, 1 H), 4.54 (t, J = 6.0 Hz, 2 H), 3.90 (s, 3 H), 3.90 (s, 3 H), 3.87 (s, 3 H), 3.11 (t, J = 6.0Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 166.8, 166.2, 165.2, 161.5, 142.2, 136.1, 133.9, 132.1, 129.6, 126.1, 66.8, 53.3, 53.2, 53.2, 28.2; HRMS calcd for $C_{15}H_{14}O_8$ 322.0689 found 322.0688.

Trimethyl 1-oxo-1,3,4,5-tetrahydro-2-benzoxepine-7,8,9-tricarboxylate (**3f**)**:** Colorless solid; m.p 126 °C; IR (neat): 1740, 173, 1328, 1283, 1248 cm^{-1}; ^{1}H NMR

(400 MHz, $CDCl_3$); δ 7.84 (s, 1 H), 4.20 (t, *J* = 6.4 Hz, 2 H), 3.88 (s, 3 H), 3.88 (s, 3 H), 3.82 (s, 3 H), 2.90 (t, *J* = 6.8 Hz, 2 H), 2.09 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 168.6, 167.0, 165.9, 164.9, 138.2, 135.4, 133.6, 132.7, 131.8, 131.7, 60.0, 53.3, 53.0, 53.0, 28.9, 26.8; HRMS calcd for $C_{16}H_{16}O_8$ 336.0845 found 336.0853.

Tetramethyl 5-(4-hydroxybutyl)-1,2,3,4-benzenetetracarboxylate (3g): Pale yellow viscous oil; IR (neat): 1735, 1326, 1299, 1263, 1247, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 7.92 (s, 1 H), 3.86 (s, 3 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 3.81 (s, 3 H), 3.59 (t, *J* = 6.4 Hz, 2 H), 2.67 (t, *J* = 7.2Hz, 2 H), 1.66-1.62 (m, 2 H), 1.56-1.54 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 167.5, 167.5, 165.7, 165.0, 142.5, 136.6, 133.8, 133.0, 129.9, 129.7, 61.9, 53.0, 52.9, 52.7, 52.7, 32.8, 31.9, 27.1; HRMS calcd for $C_{18}H_{22}O_9$ 382.1264 found 382.1266.

Methyl 1-oxo-6,7-dipentyl-1,3-dihydro-5-isobenzofurancarboxylate (**5a**)**:** Pale yellow viscous oil; IR (neat): 1755, 1730, 1312, 1218 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 7.54 (s, 1 H), 5.18 (s, 2 H), 3.91 (s, 3 H), 3.13 (t, *J* = 8.0 Hz, 2 H), 2.86 (t, *J* = 8.0 Hz, 2 H), 1.50-1.32 (m, 16 H), 0.91-0.87 (m, 6 H)**;** ^{13}C NMR (100 MHz, $CDCl_3$); δ 170.3, 168.6, 144.4, 144.1, 142.2, 136.9, 125.1, 120.4, 68.6, 52.5, 32.2, 32.2, 31.5, 31.2, 28.9, 26.9, 22.4, 22.3, 13.9, 13.9; HRMS calcd for $C_{20}H_{28}O_4$ 332.1988 found 332.1985.

Methyl 1-oxo-6,7-diphenyl-1,3-dihydro-5-isobenzofurancarboxylate (5b): Pale yellow solid; IR (neat): 1752, 1710, 1330, 1241 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 7.81 (s, 1 H), 7.20-7.17 (m, 3 H), 7.15-7.13 (m, 3 H), 7.00-6.98 (m, 2 H), 6.95-6.93 (m, 2 H), 5.36 (s, 2 H), 3.55 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 168.7, 168.4, 145.8, 142.5, 142.1, 138.4, 137.5, 134.1, 129.9, 129.7, 127.6, 127.5, 127.3, 127.2, 124.9, 121.3, 67.9, 52.4; HRMS calcd for $C_{22}H_{16}O_4$ 344.1049 found 344.1050.

Methyl 3-methyl-1-oxo-6,7-diphenyl-1,3-dihydro-5-isobenzofurancarboxylate (**5c**)**:** Pale yellow solid; m.p 141 °C; IR: 1763, 1737, 1327, 1222 cm^{-1}; ^1H NMR (400

MHz, $CDCl_3$); δ 7.73 (s, 1 H), 7.18-7.17 (m, 3 H), 7.15-7.13 (m, 3 H), 7.00-6.98 (m, 2 H), 6.98-6.94 (m, 2 H), 5.56 (q, *J* = 6.8 Hz, 1 H), 3.53 (s, 3 H), 1.70 (d, *J* = 6.8Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 168.5, 168.1, 150.5, 142.4, 142.0, 138.4, 137.5, 134.2, 129.9, 129.7, 127.5, 127.5, 127.3, 127.1, 124.9, 120.8, 75.8, 52.4, 20.5; HRMS calcd for $C_{23}H_{18}O_4$ 358.1205 found 358.1204.

Methyl 1-oxo-1,3-dihydro-5-isobenzofurancarboxylate (5d): Colorless solid; m.p 151 °C; IR (neat): 1755, 1719, 1285, 1208 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 8.17 (d, *J* = 8.0 Hz, 1 H), 8.15 (s, 1 H), 7.95 (d, *J* = 8.0 Hz, 1 H), 5.35 (s, 2 H), 3.95 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 169.9, 165.7, 146.4, 135.3, 130.3, 129.3, 125.7, 123.5, 69.6, 52.7; HRMS calcd for $C_{10}H_8O_4$ 192.0423 found 192.0421.

Methyl 3-methyl-1-oxo-1,3-dihydro-5-isobenzofurancarboxylate (**5e**)**:** Pale yellow solid; m.p 117 °C; IR (neat): 1764, 1724, 1284, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 8.15 (d, *J* = 7.6 Hz, 1 H), 8.08 (s, 1 H), 7.91 (d, *J* = 8.0 Hz, 1 H), 5.58 (q, *J* = 6.8Hz, 1 H), 3.94 (s, 3 H), 1.64 (d, *J* = 6.8Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 169.3, 165.7, 151.0, 135.3, 130.3, 129.4, 125.7, 122.9, 77.8, 52.7, 20.2; HRMS calcd for $C_{11}H_{10}O_4$ 206.0579 found 206.0580**.**

Methyl 1-oxo-3,4-dihydro-1*H*-6-isochromenecarboxylate (**5f**)**:** Colorless solid; m.p 112 °C; IR (neat): 1764, 1724, 1284, 1209 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 8.12 (d, *J* = 8.0 Hz, 1 H), 7.99 (d, *J* = 8.0 Hz, 1 H), 7.91 (s, 1 H), 4.53 (t, *J* = 6.0Hz, 2 H), 3.92 (s, 3 H), 3.09 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 165.9, 164.1, 139.5, 134.4, 130.5, 128.8, 128.4, 128.4, 67.3, 52.5, 27.7; HRMS calcd for $C_{11}H_{10}O_4$ 206.0579 found 206.0575.

Methyl 2-[(4-methylphenyl)sulfonyl]-1-oxo-5-isoindolinecarboxylate (**7a**)**:** Colorless solid; m.p 172 °C; IR (neat): 1739, 1707 1357, 1291, 1212 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$); δ 8.12 (s, 1 H), 8.11 (d, *J* = 9.6 Hz, 1 H), 8.00(d, *J* = 8.4 Hz, 2 H), 7.83 (d, *J* = 8.0Hz, 1 H), 7.32 (d, *J* = 8.0 Hz, 2 H), 4.92 (s, 2 H), 3.93 (s, 3 H), 2.39 (s,

3 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 165.7, 165.1, 145.5, 140.9, 135.1, 134.7, 130.0, 129.8, 128.2, 125.0, 124.7, 77.9, 52.7, 49.7, 21.7; HRMS calcd for $C_{17}H_{15}NO_5S$ 345.0671 found 345.0672.

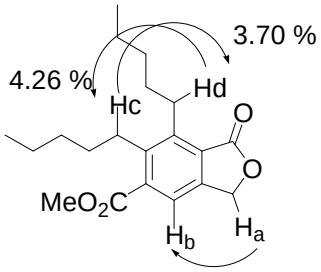
Methyl 2-[(*E*)-3-methoxy-3-oxo-1-propenyl]-1-oxo-5-isoindolinecarboxylate (**7b**)**:** Colorless solid; m.p 177 °C; IR (neat): 1726, 1708, 1637, 1295, 1266 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 8.34 (d, *J* = 14.4 Hz, 1 H), 8.19 (s, 1 H), 8.18 (d, *J* = 6.5 Hz, 1 H), 7.97 (d, *J* = 8.4 Hz, 1 H), 5.48 (d, *J* = 14.4 Hz, 1 H), 4.62 (s, 2 H), 3.96 (s, 3 H), 3.77 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) ; δ 167.3, 165.9, 140.6, 137.0, 134.8, 134.5, 130.2, 124.8, 124.5, 100.5, 52.7, 51.6, 47.9; HRMS calcd for $C_{14}H_{13}NO_5$ 275.0794 found 275.0793.

1,3,6,8-Tetrahydrofuro[3,4-*e*]isobenzofuran-1-one (**9**)**:** Colorless solid; m.p 73 °C; IR (neat): 1748, 1347, 1237, 1146 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.52 (d, *J* = 8.0 Hz, 1 H), 7.38 (d, *J* = 7.6 Hz, 1 H), 5.38 (s, 2 H), 5.35 (s, 2 H), 5.14 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 170.2, 146.0, 141.3, 138.4, 126.6, 121.2, 120.2, 72.8, 72.2, 70.4; HRMS calcd for $C_{10}H_8O_3$ 176.0473 found 176.0473.

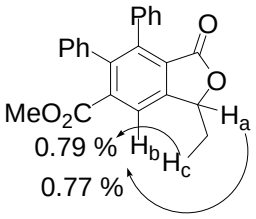
Dimethyl 4-(hydroxymethyl)-3,6-dipentylphthalate (**13**)**:** Pale yellow viscous oil; IR (neat): 1735, 1283, 1208, 1173 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$); δ 7.39 (s, 1 H), 4.73 (s, 2 H), 3.83 (s, 3 H), 3.83 (s, 3 H), 2.67-2.63 (m, 2 H), 2.62-2.59 (m, 2 H), 1.54-1.48 (m, 4 H), 1.32-1.22 (m, 8 H), 0.88-0.84 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$); δ 169.4, 168.8, 141.5, 139.7, 136.1, 132.9, 130.5, 130.1, 62.0, 52.2, 52.2, 33.6, 32.1, 31.7, 31.2, 30.8, 29.2, 22.4, 22.3, 13.9; HRMS calcd for $C_{21}H_{32}O_5$ 364.225 found 364.225.

The structures of [2+2+2] cocyclotrimerization products **5a-f**, **7a-b**, and **13** were established by ^{1}H NMR NOE experiments. For example compound **5a**, selective irradiation of the methylene protons H_a in the lactone ring at δ 5.30 led to an enhancement of the signal H_b at δ 7.04 by 0.86 % in the aromatic region, irradiation

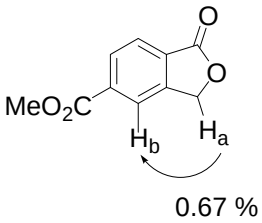
of the H_d signal at δ 2.84 caused an enhancement of the H_c signal at δ 2.64 by 4.26 % and irradiation of the Hc signal at δ 2.64 caused an enhancement of the H_d signal at δ 2.84 by 3.70 % for the methylene protons directly attached to aromatic ring. Similar NOE results were obtained for **5c, d, 7b** and **13** and were shown below. These NOE results strongly confirm the proposed structures of these compounds.



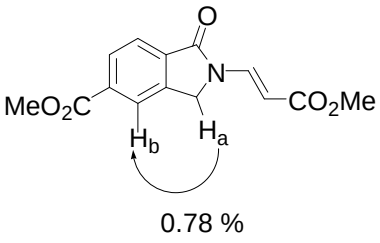
5a



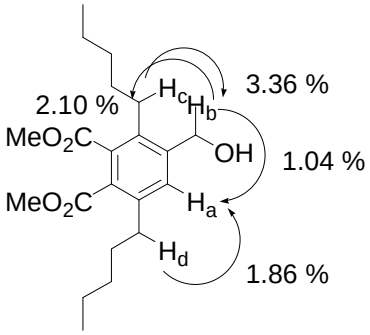
5c



5d

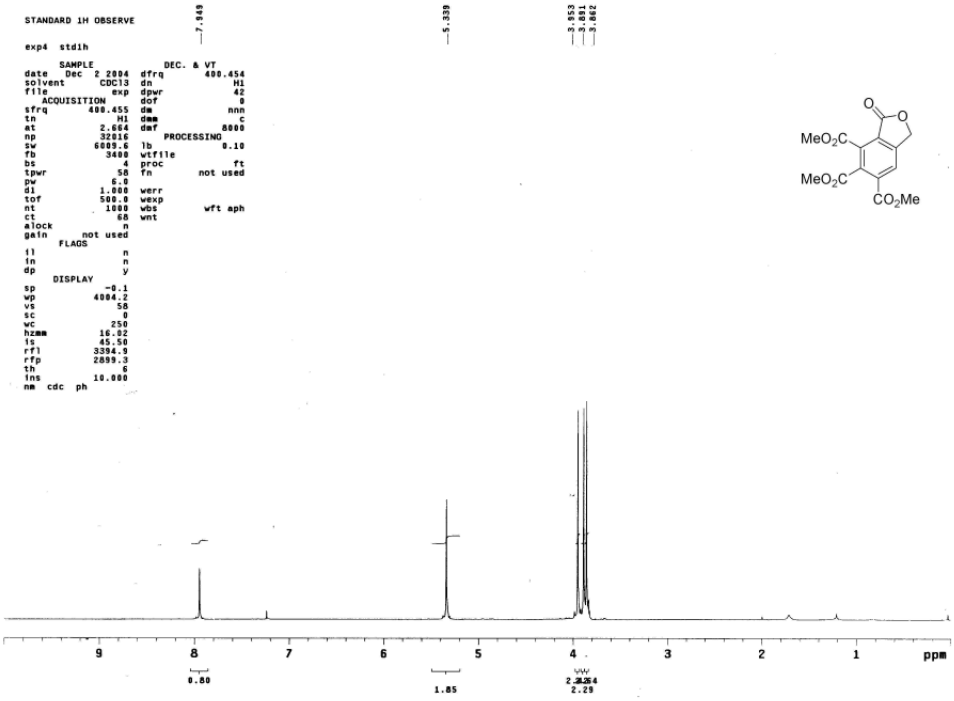


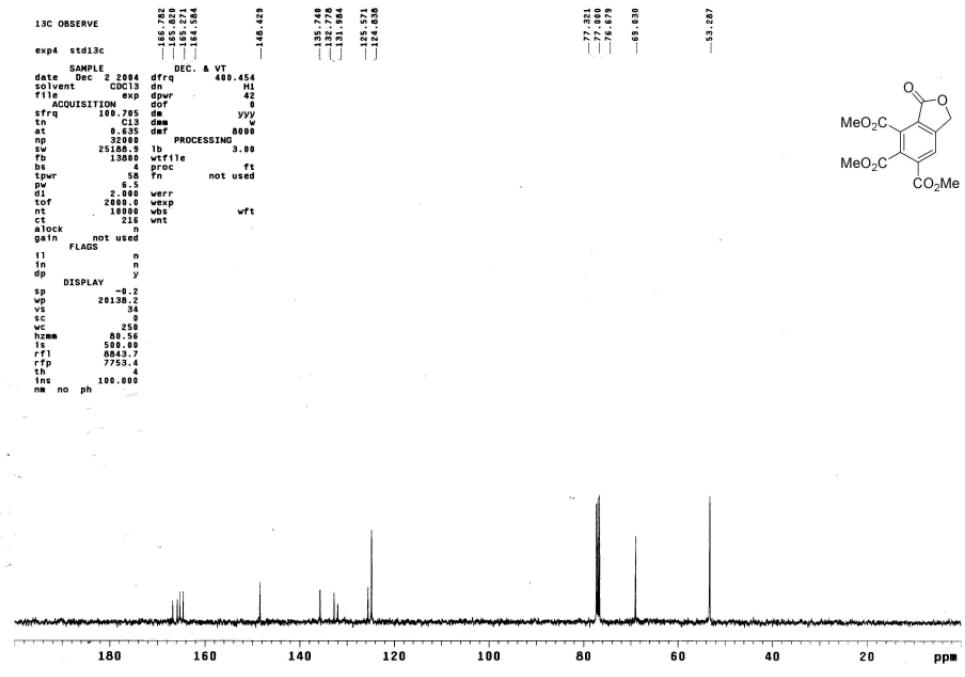
7b



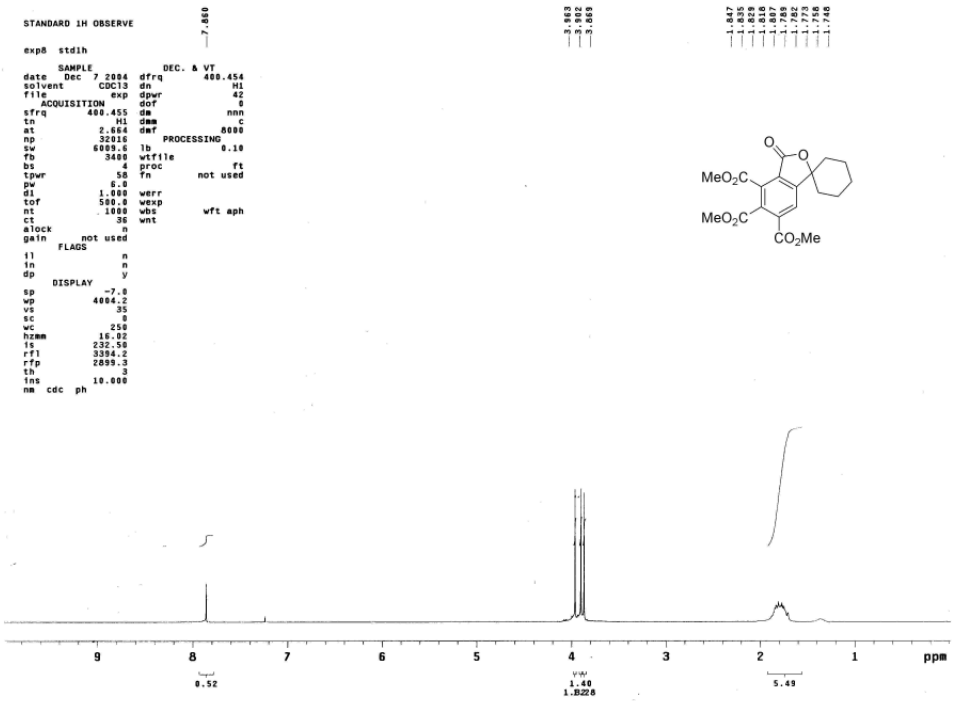
13

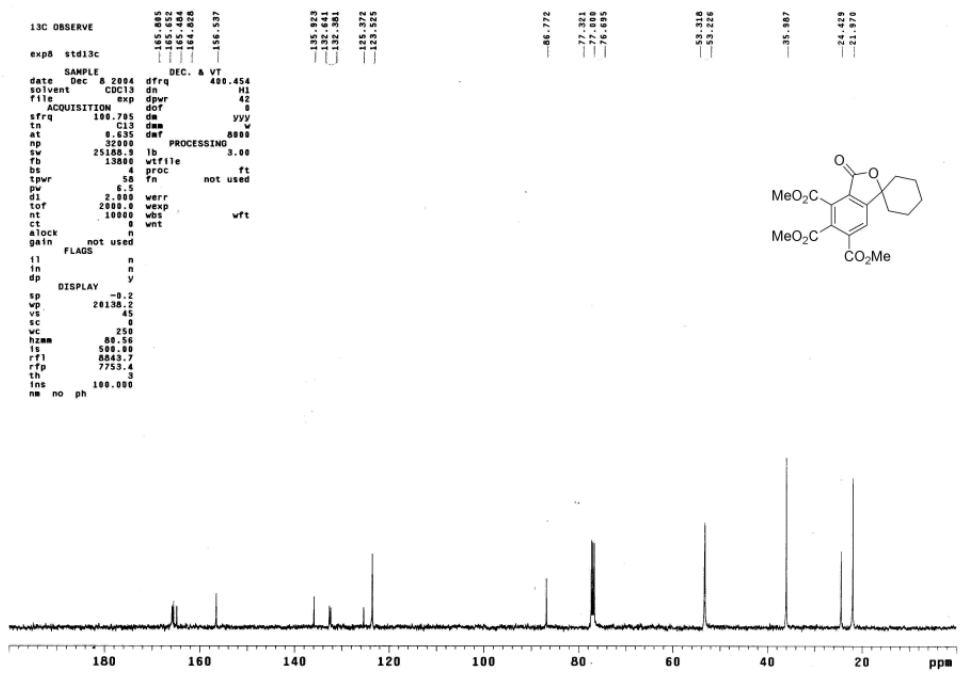
^{1}H and ^{13}C NMR Spectra of compound **3a**:



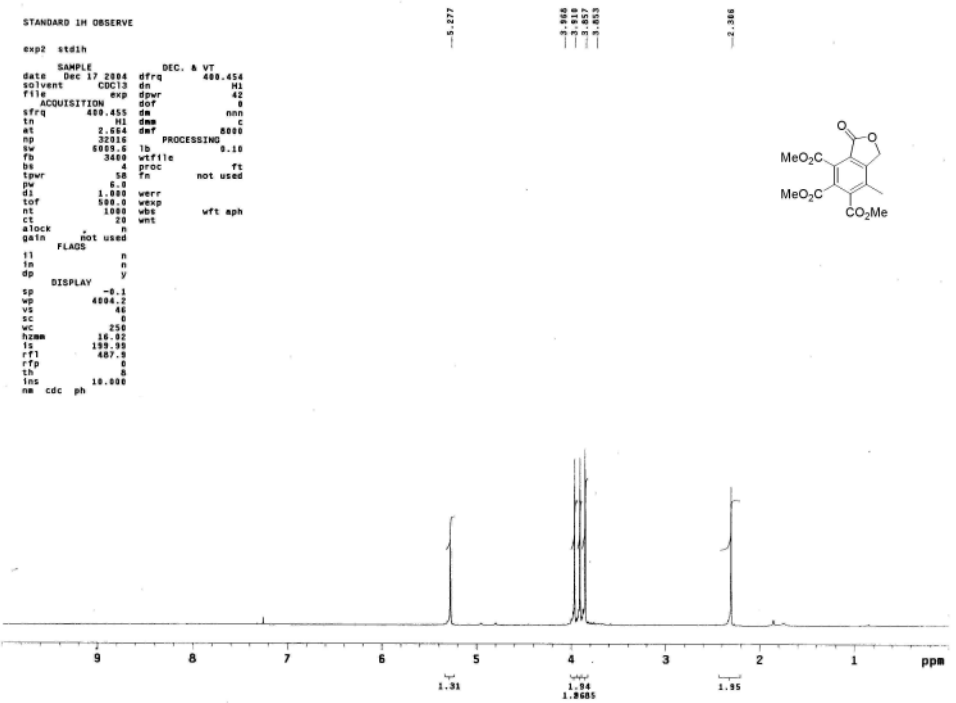


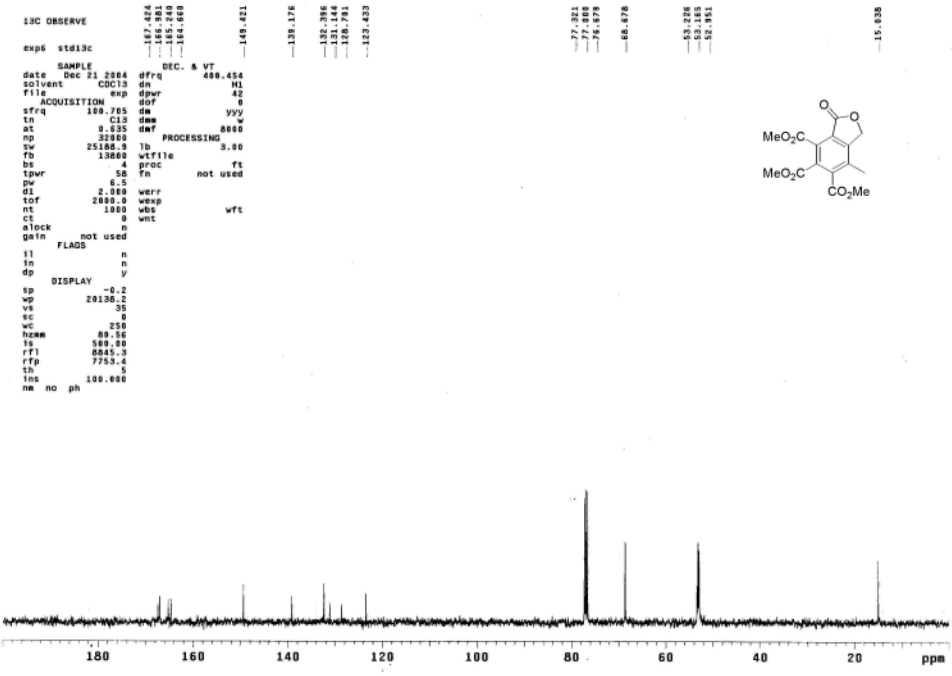
^{1}H and ^{13}C NMR Spectra of compound **3b**:



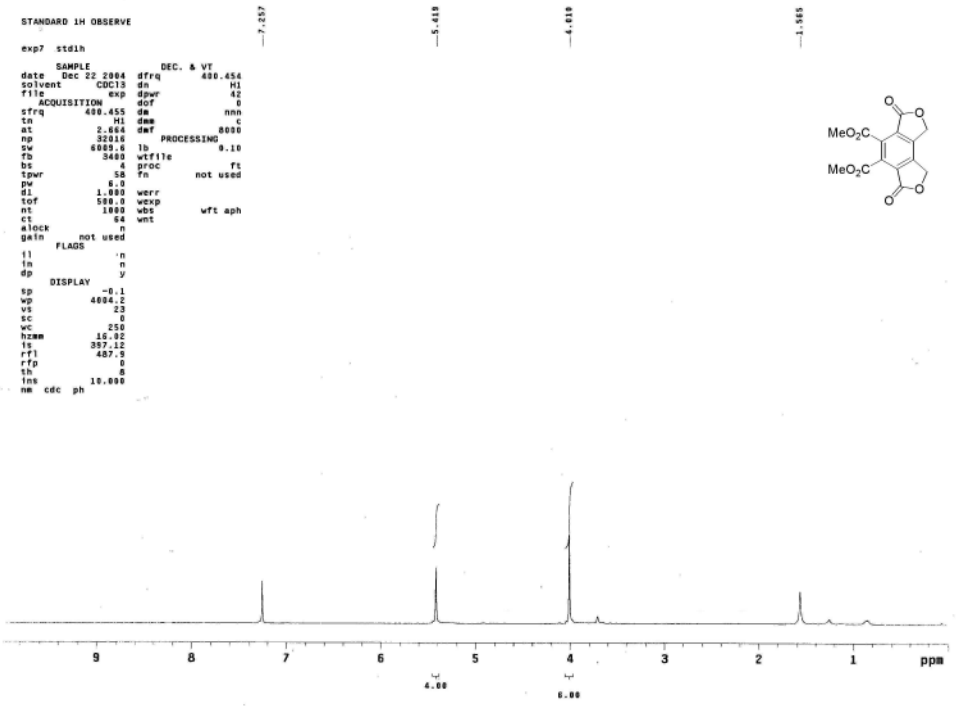


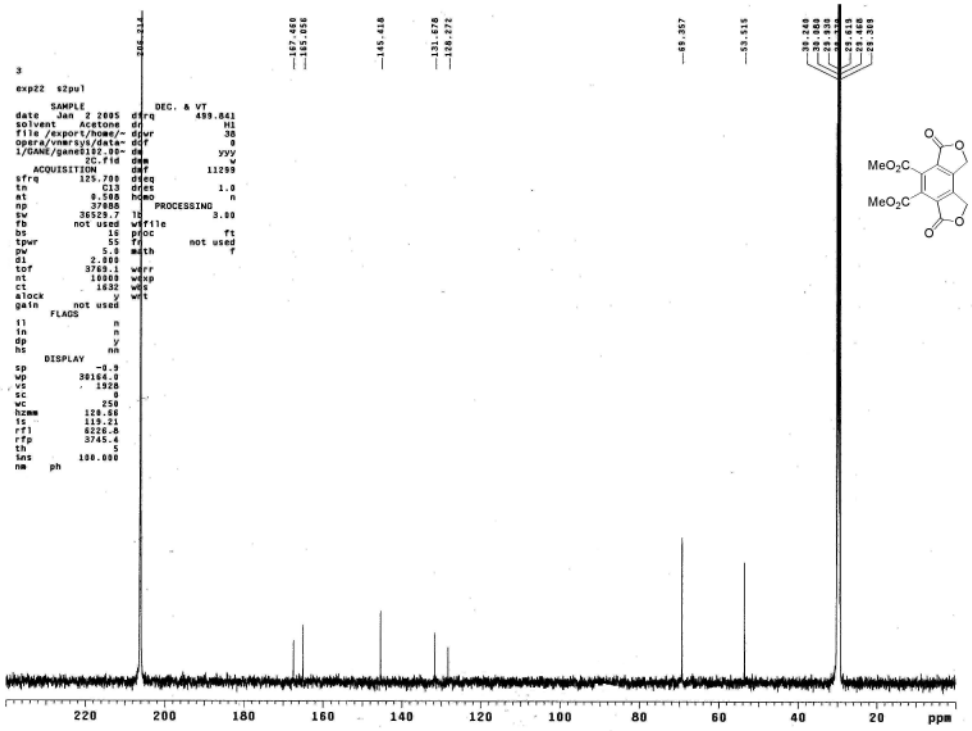
^{1}H and ^{13}C NMR Spectra of compound **3c**:



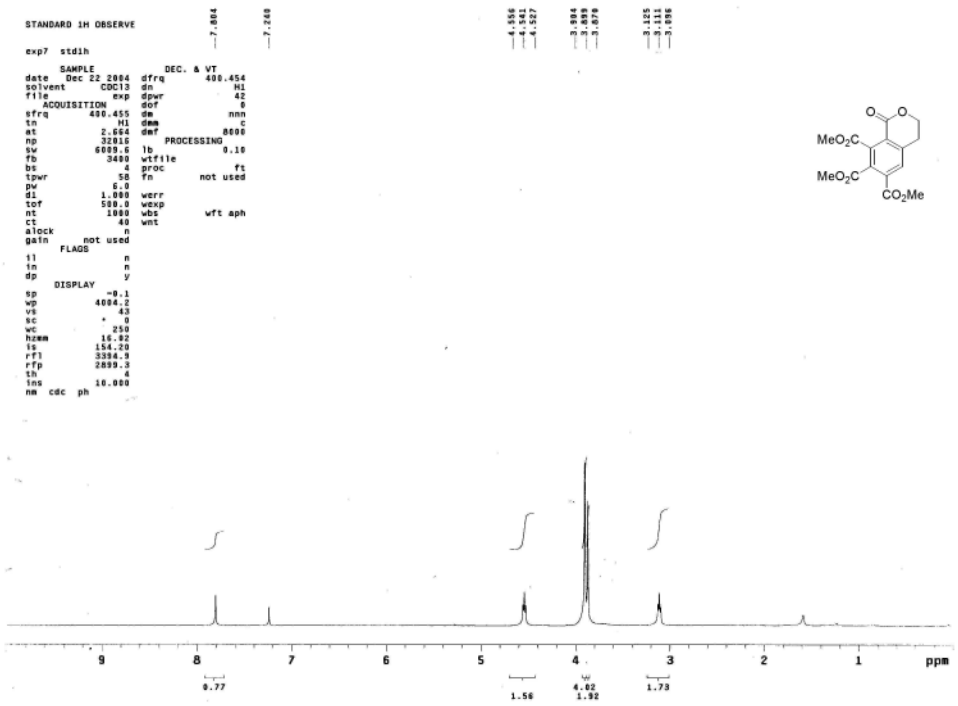


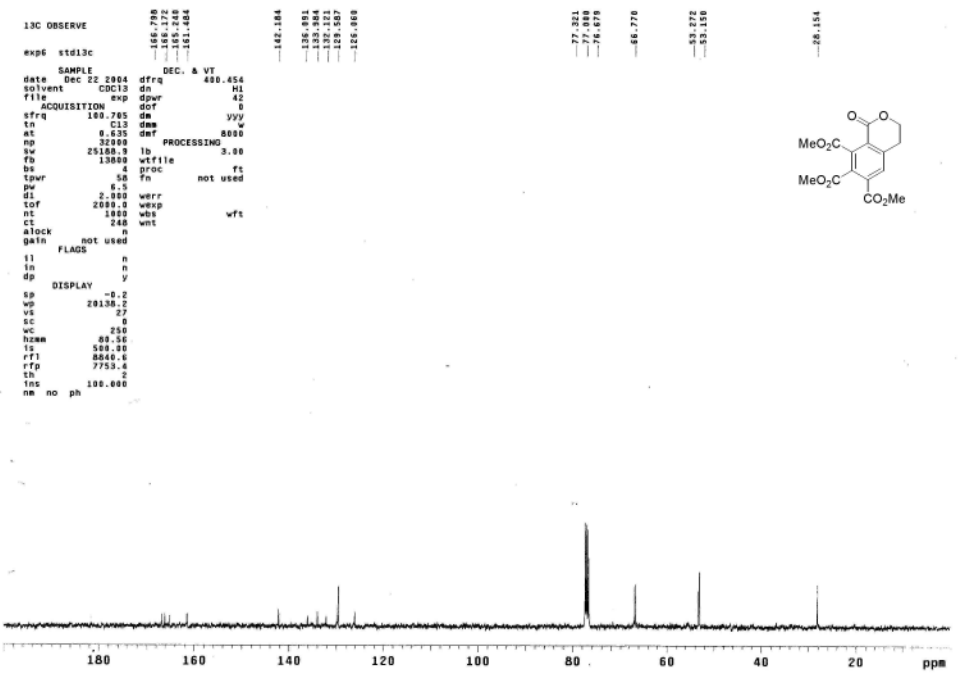
^{1}H and ^{13}C NMR Spectra of compound **3d**:



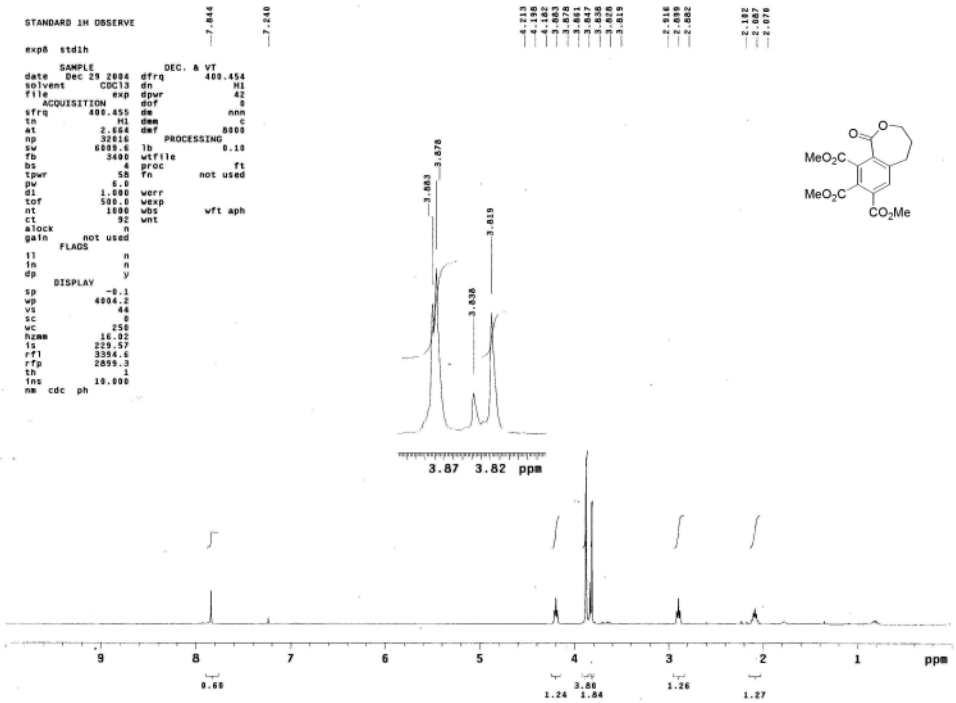


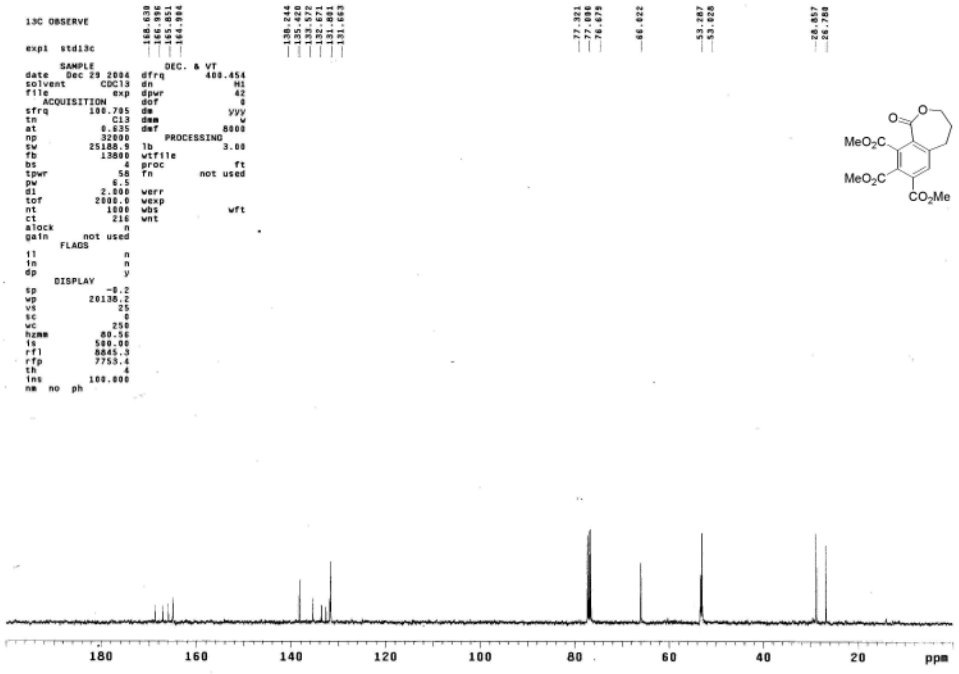
^{1}H and ^{13}C NMR Spectra of compound **3e**:



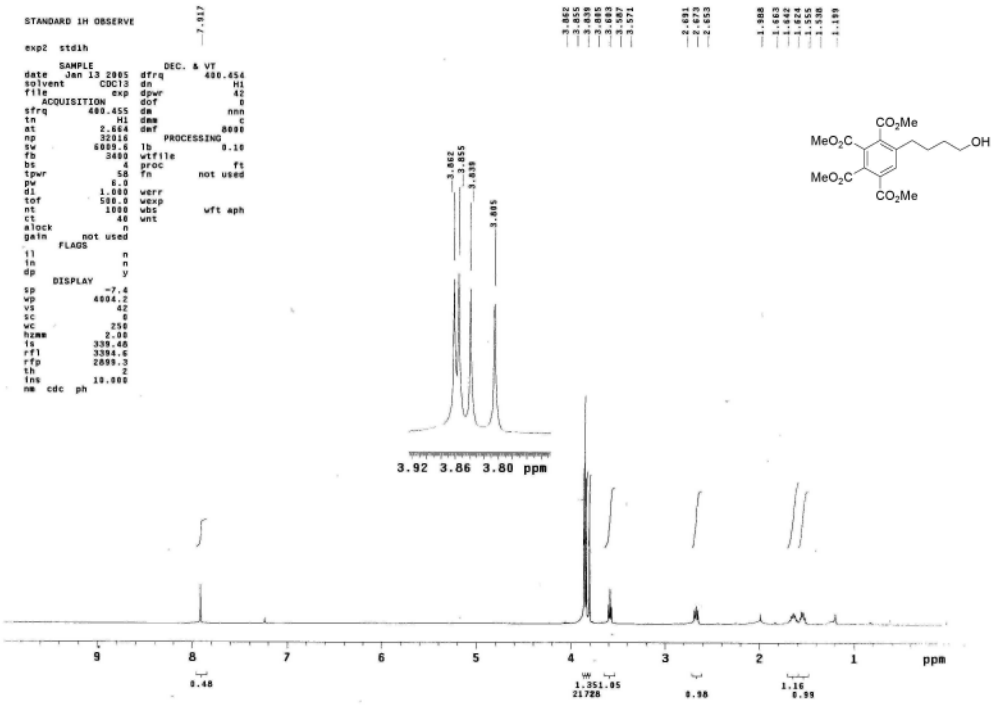


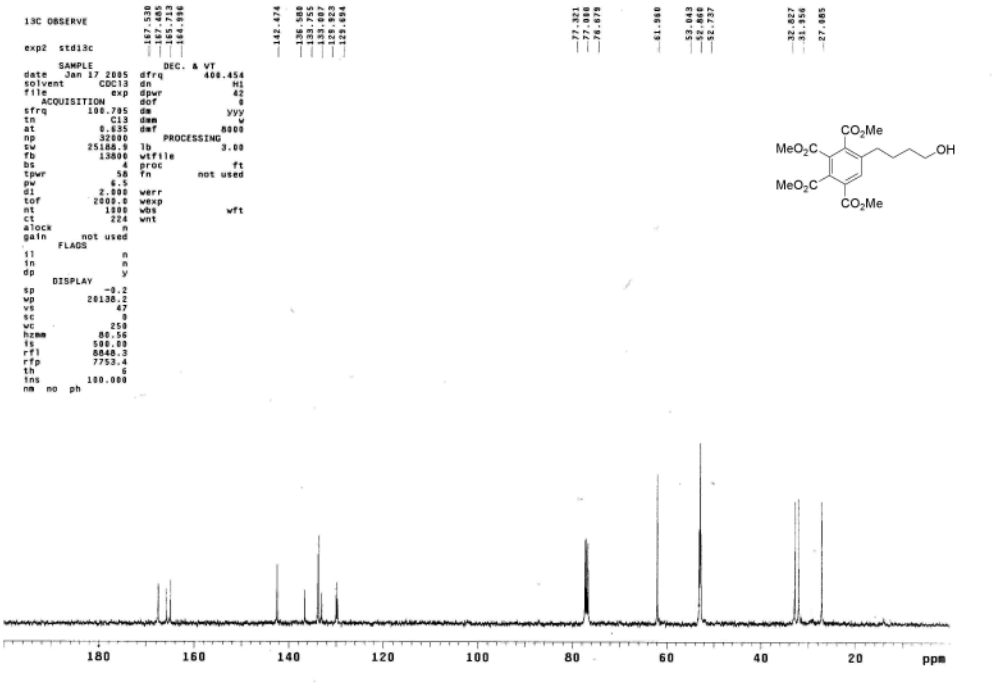
^{1}H and ^{13}C NMR Spectra of compound **3f**:



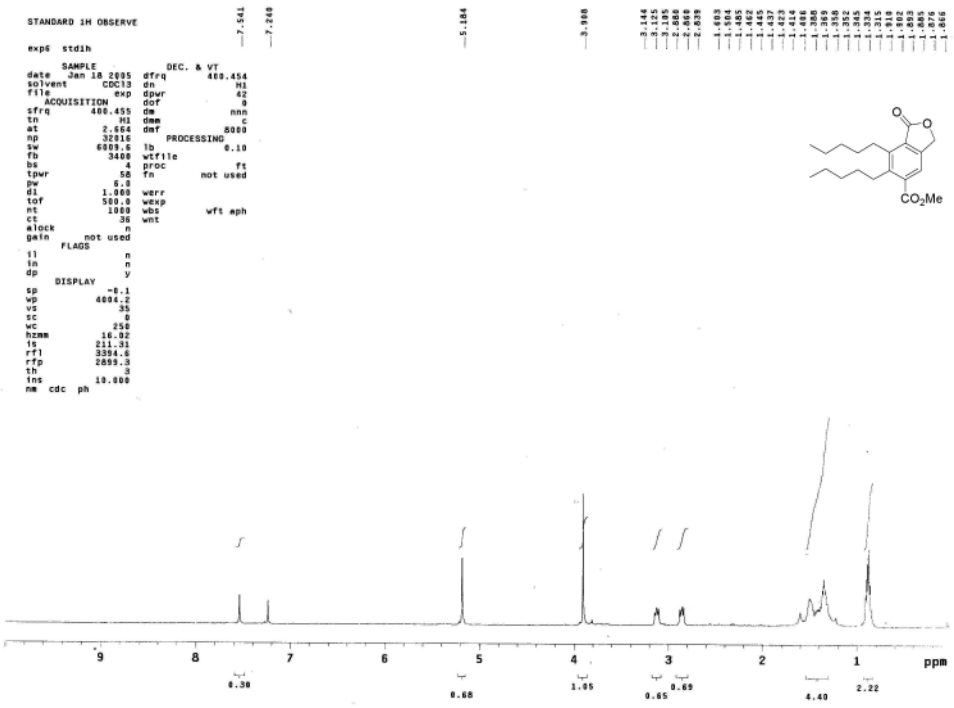


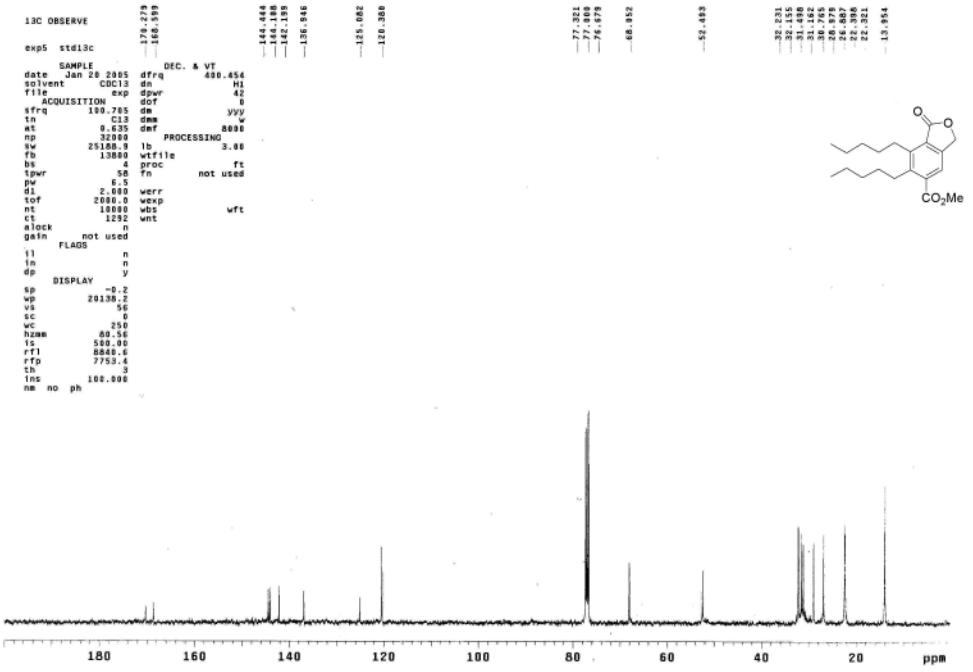
^{1}H and ^{13}C NMR Spectra of compound **3g**:



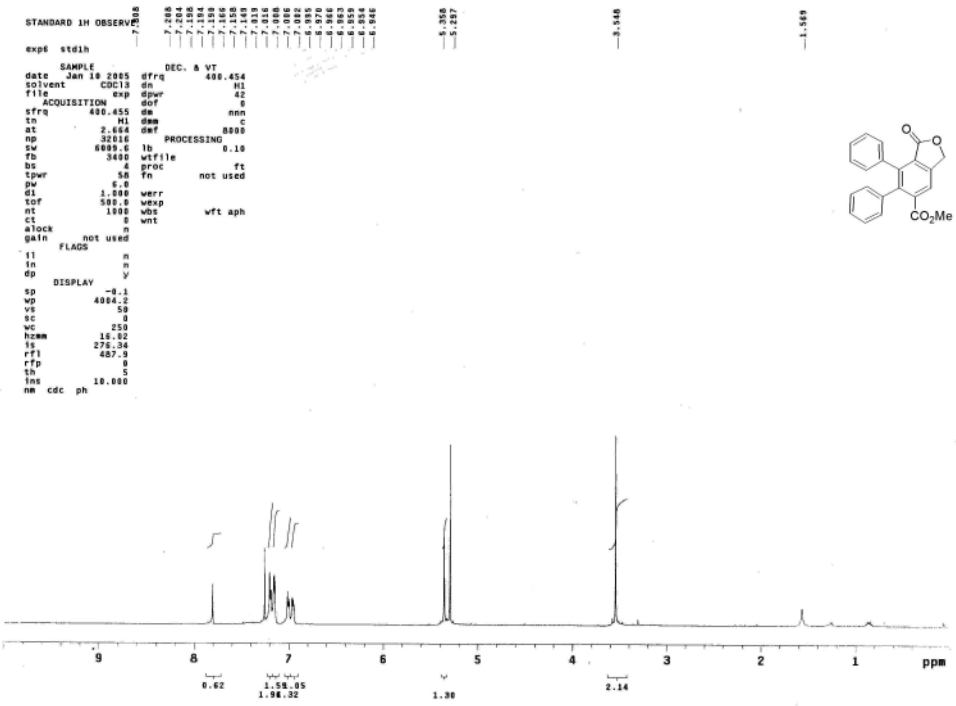


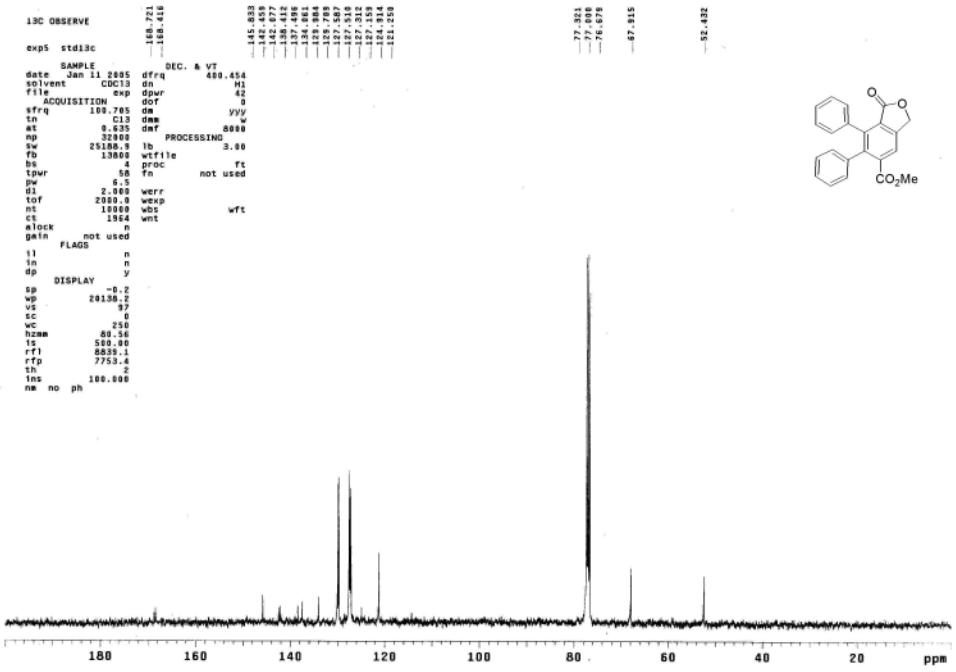
^{1}H and ^{13}C NMR Spectra of compound **5a**:



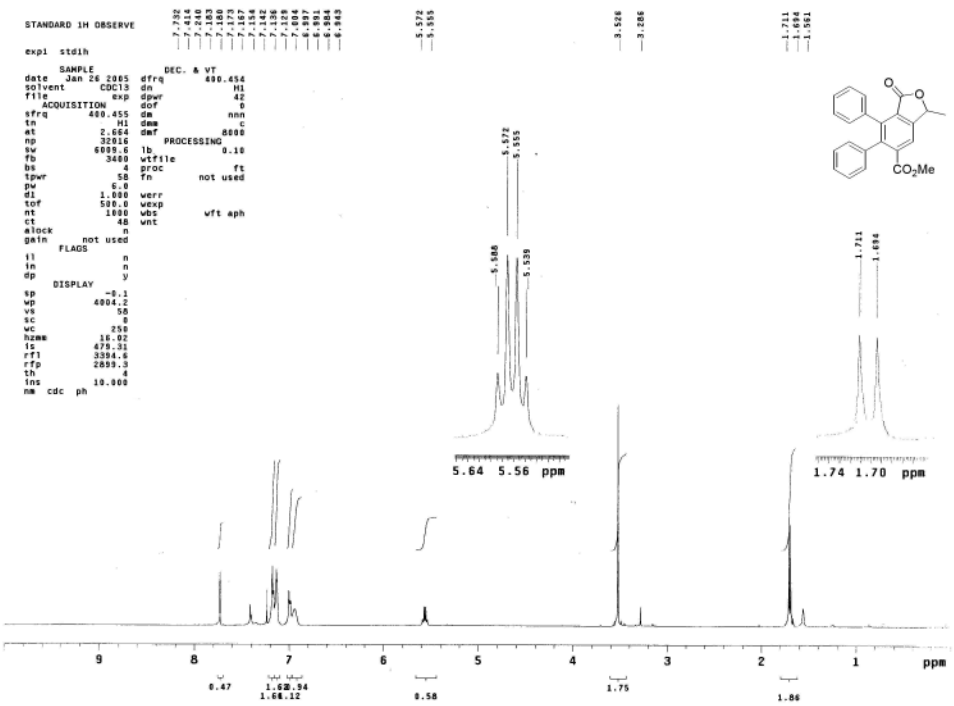


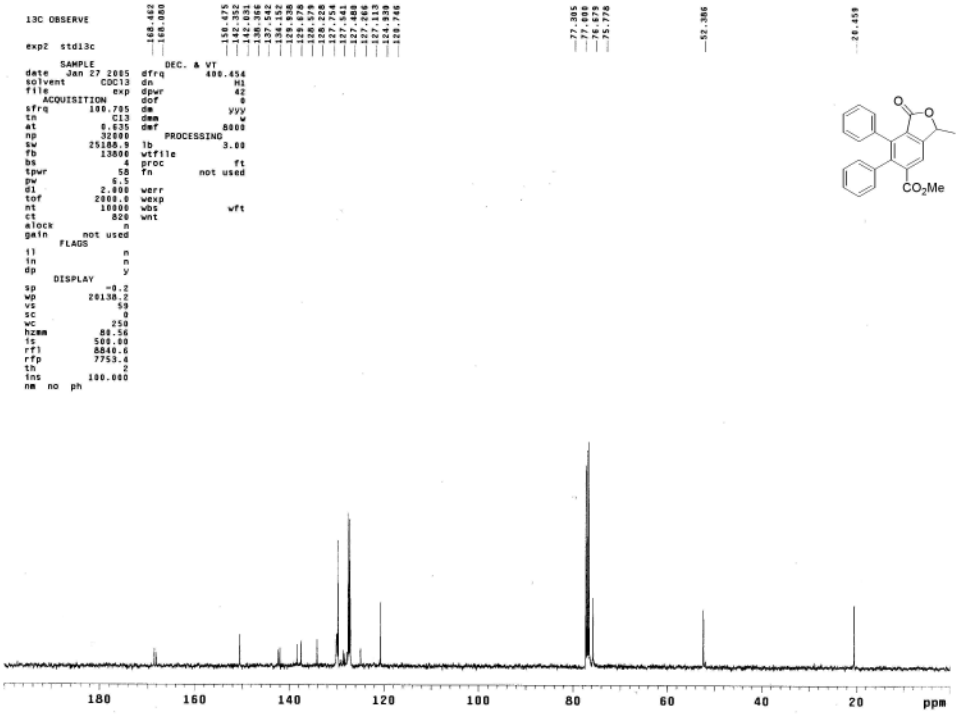
^{1}H and ^{13}C NMR Spectra of compound **5b**:



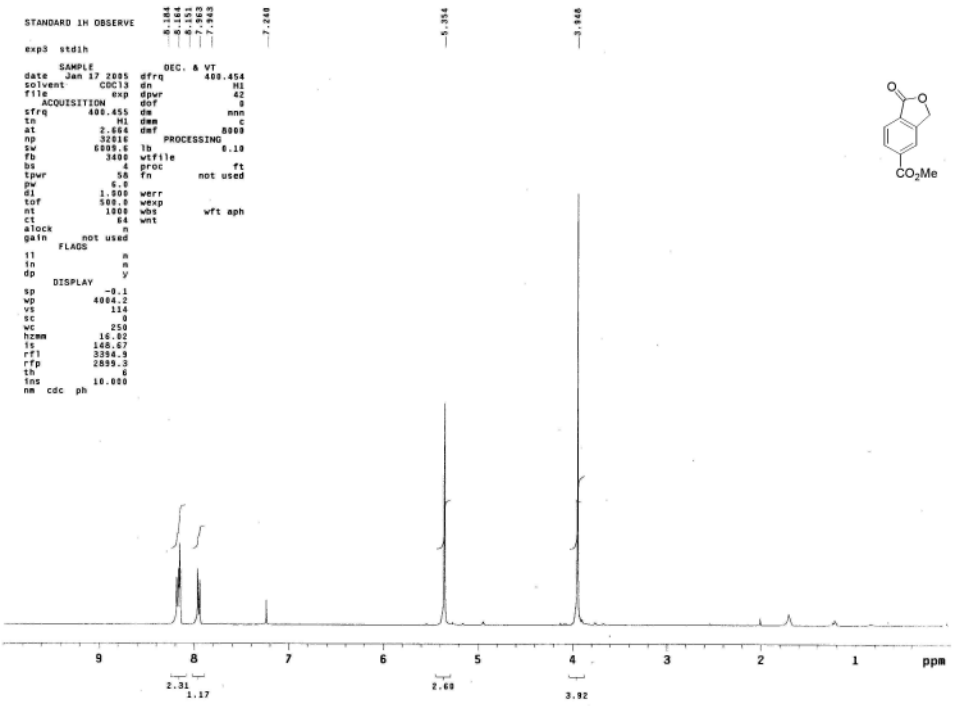


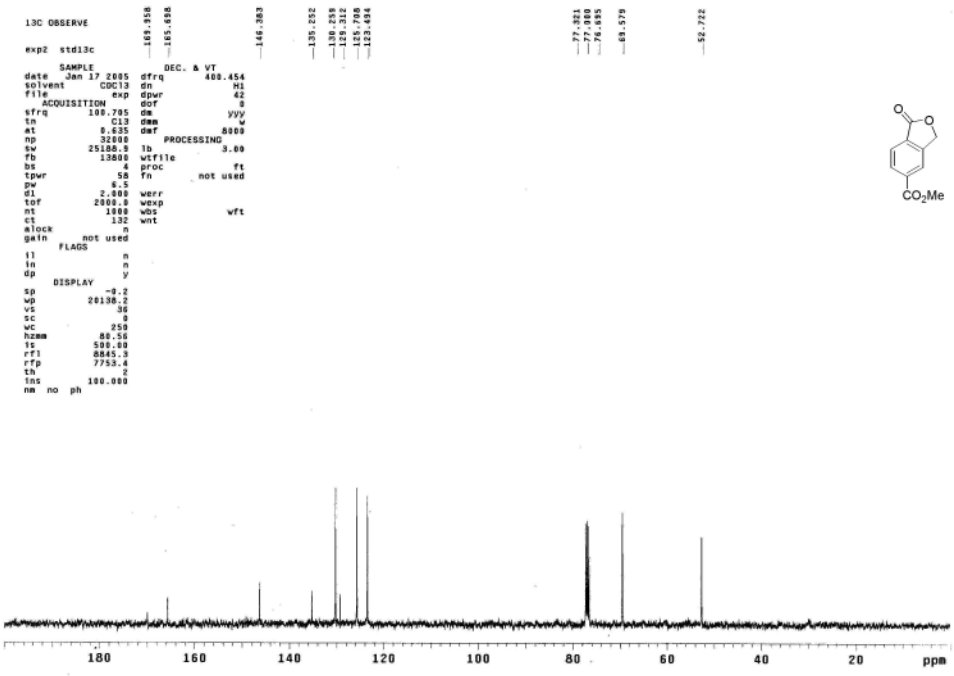
^{1}H and ^{13}C NMR Spectra of compound **5c**:



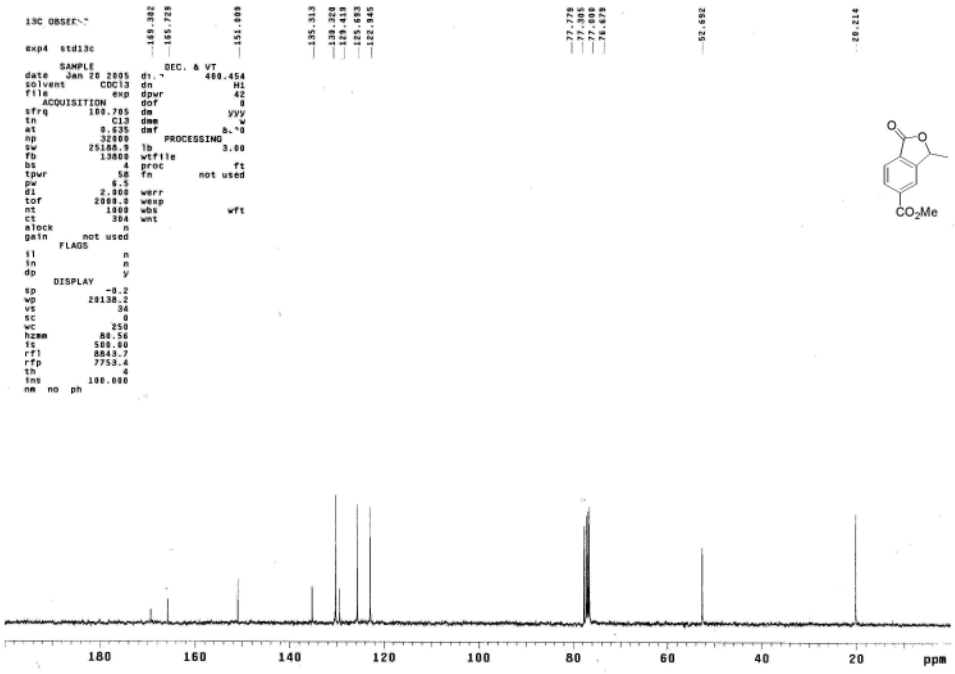


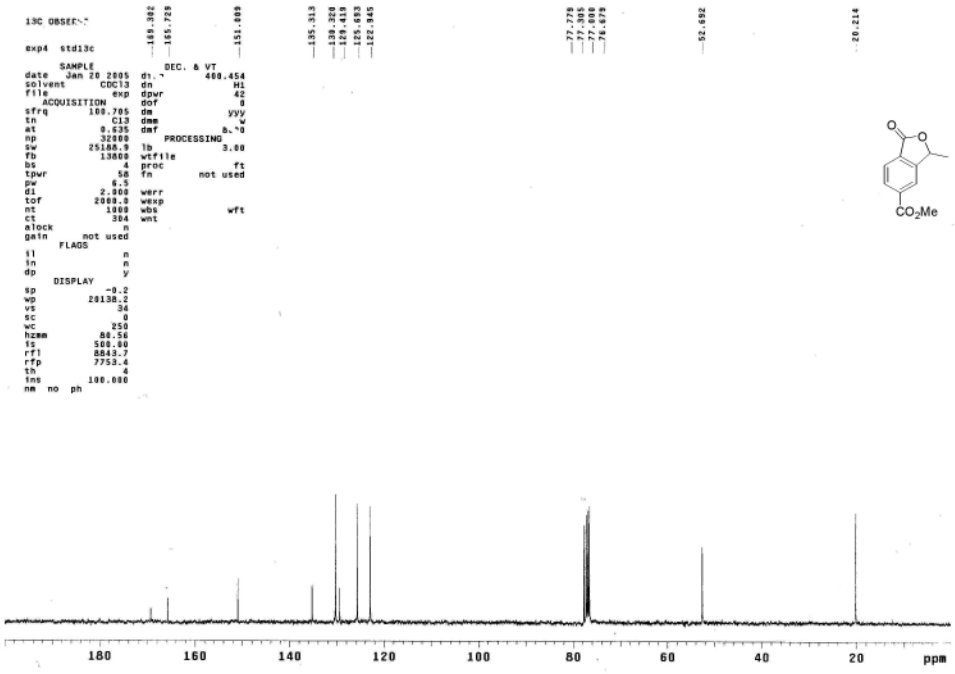
^{1}H and ^{13}C NMR Spectra of compound **5d**:



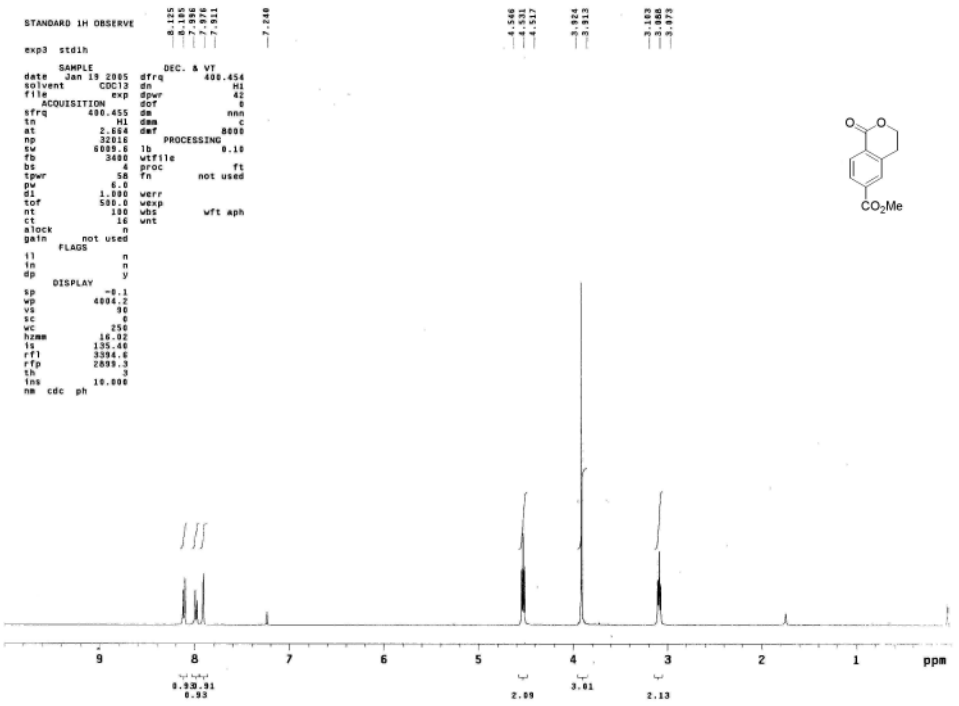


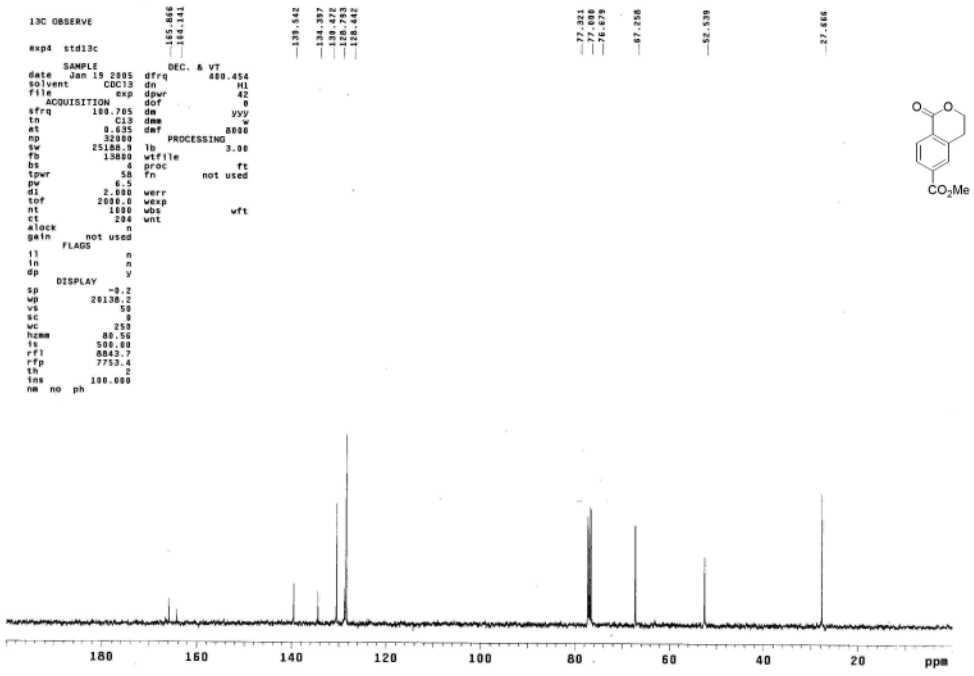
^{1}H and ^{13}C NMR Spectra of compound **5e**:



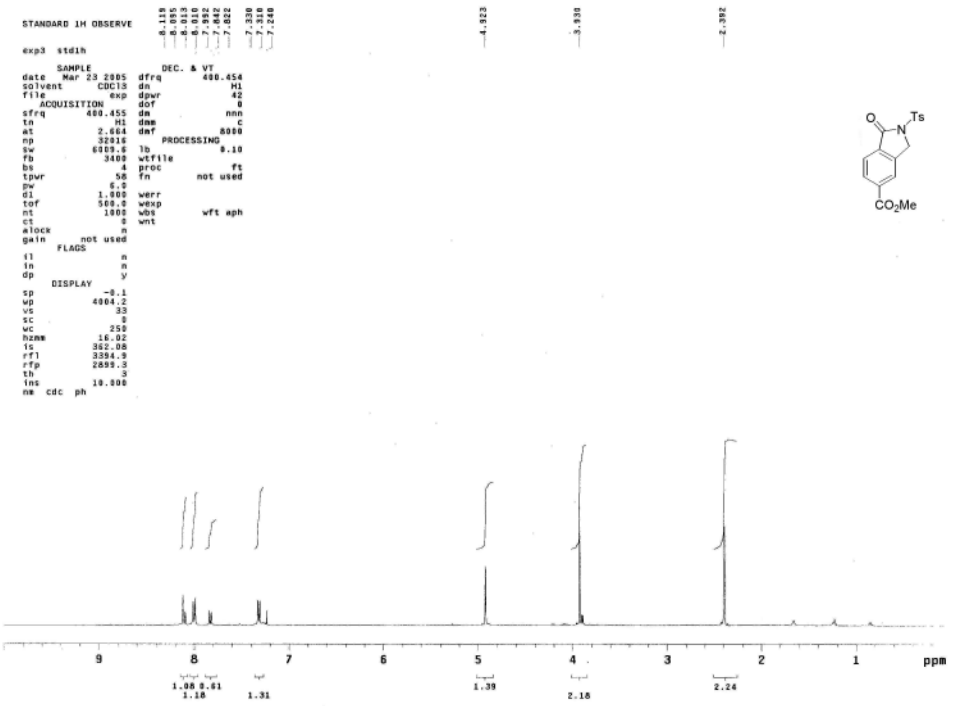


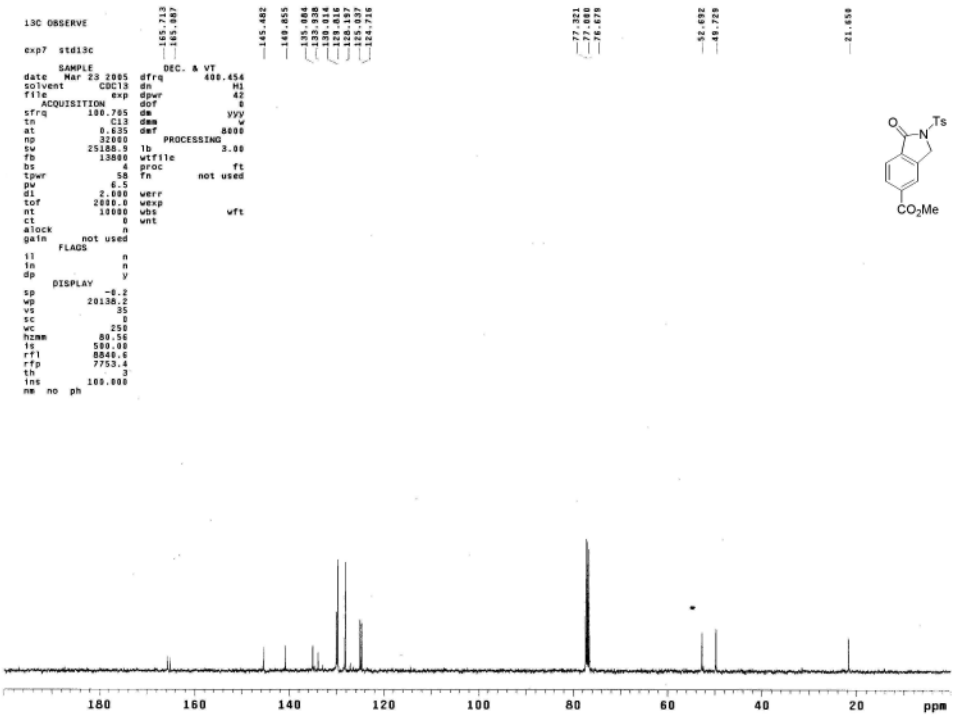
^{1}H and ^{13}C NMR Spectra of compound **5f**:



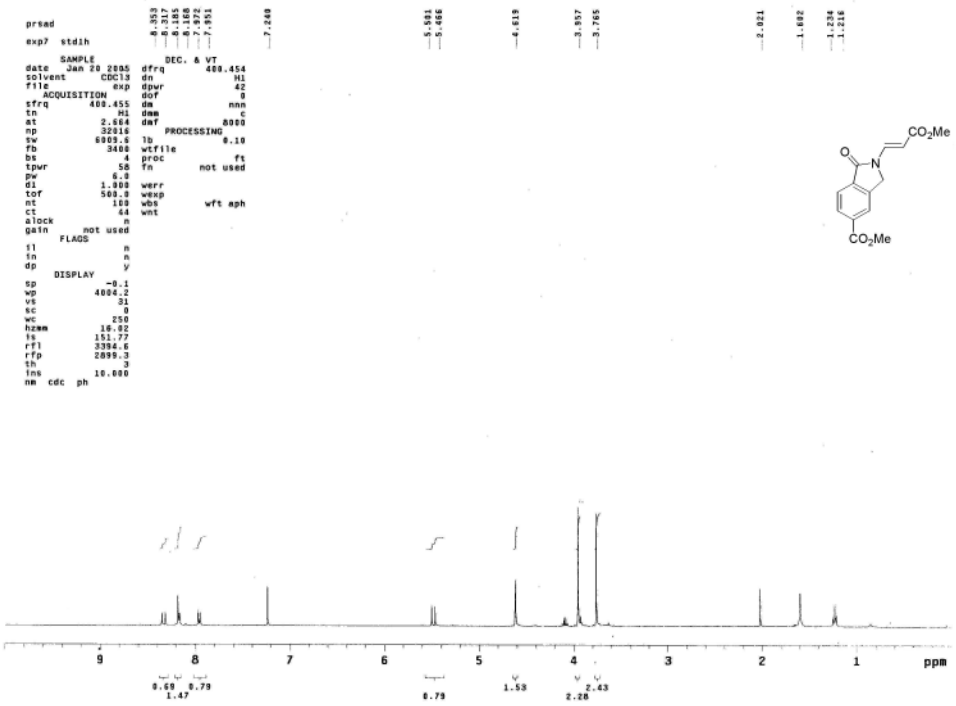


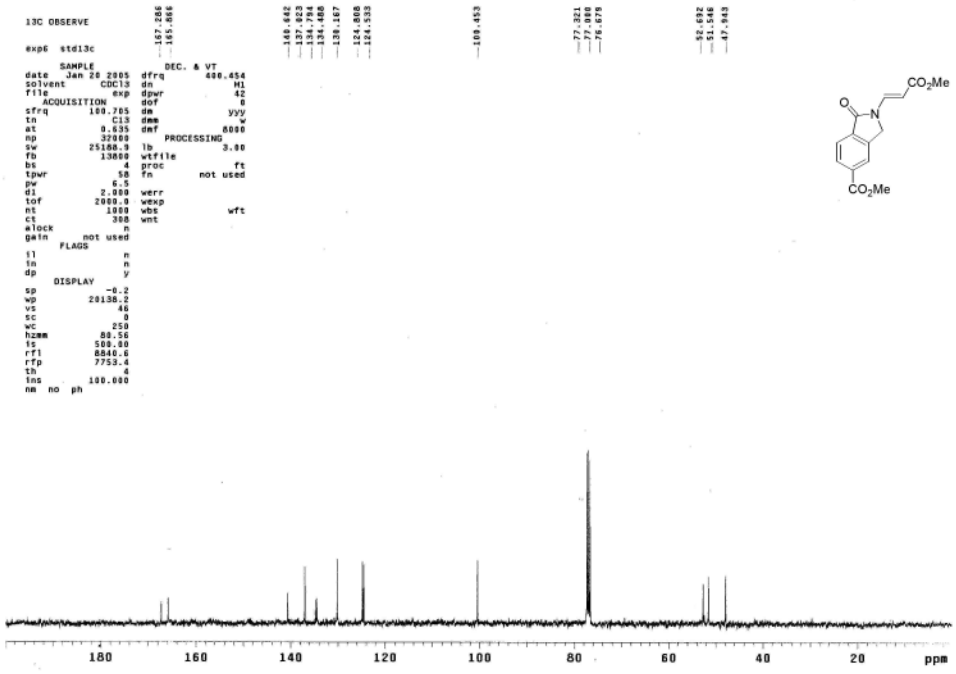
^{1}H and ^{13}C NMR Spectra of compound **7a**:



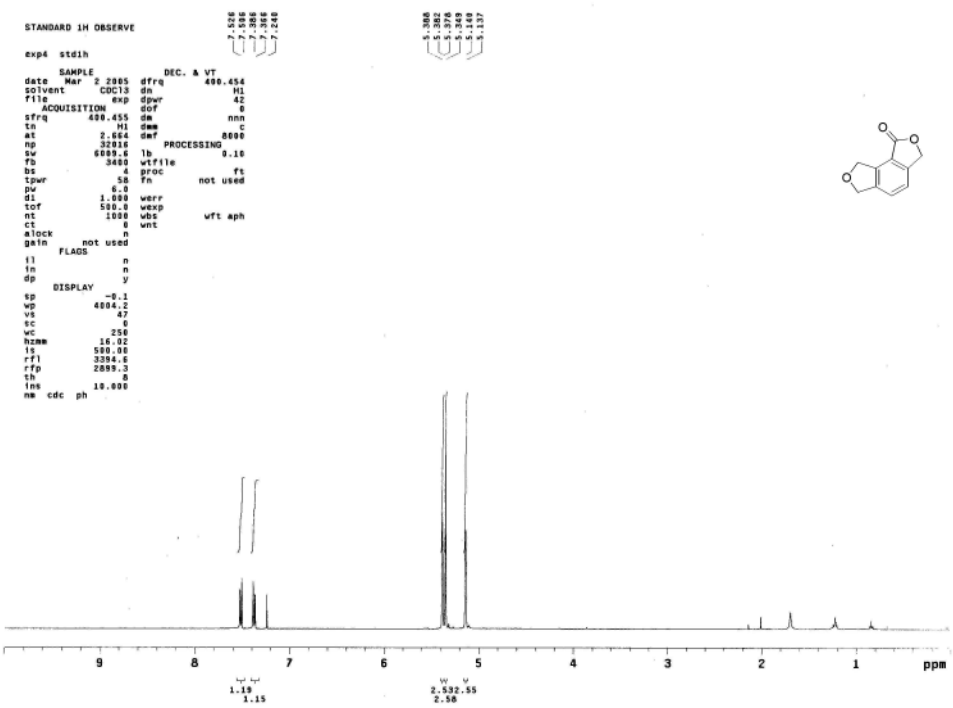


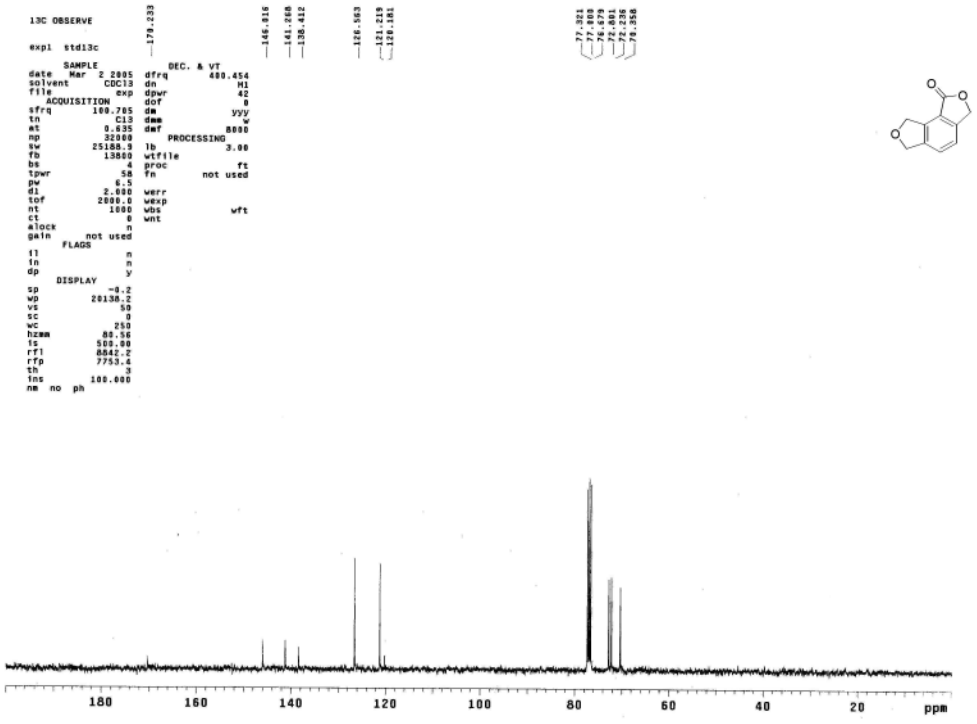
^{1}H and ^{13}C NMR Spectra of compound **7b**:





^{1}H and ^{13}C NMR Spectra of compound **9**:





^{1}H NMR Spectrum of compound **13**: