Electronic Supplementary Information (ESI)

A Simple and Efficient Synthesis of Isocoumarins and Alkylidenephthalides from 3-(1-Hydroxycarbethoxy/alkyl)phthalides with DEAD/PPh_3/TBHP System

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1. General description:

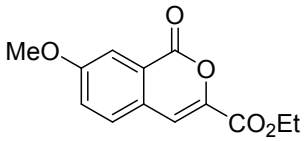
Solvents were purified and dried by standard procedures before use; petroleum ether of boiling range 60-80 °C was used. Melting points were uncorrected and recorded on a Buchi B-542 instrument. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. Infrared spectra were recorded on Shimadzu FTIR-8400 spectrometer and absorption is expressed in cm^{-1}. Elemental analysis was carried on a Carlo Erba CHNS-O analyzer. Purification was done using column chromatography (230-400 mesh).

2. Experimental procedure:

General experimental procedure for the preperation of 3-substituted isocoumarins (5a-j) and alkylidenephthalides (6k-t):

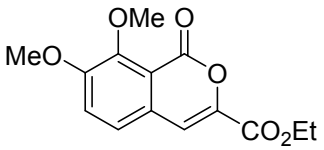
To a stirred solution of 3-(1-hydroxycarbethoxy/alkyl)phthalides derivatives (**4a-t**) (1 mmol) in THF (10 mL) was added diethyl azodicarboxylate (DEAD, 10 mol%), PPh_3 (1.5 mmol) and *tert*-butyl hydroperoxide (2 mmol) and the mixture allowed to stirred at 25 °C for 0.5 to 2 h. After the completion of reaction (as monitored by TLC), THF was distilled out to give the crude product. Chromatographic purification of the crude product [silica gel (230-400 mesh) and petrolium ether: ethyl acetate (7:3) as eluent] afforded 3-substituted isocoumarin derivatives (**5a-j**) or 3-substituted alkylidene phthalides (**6k-t**) as the case may be.

Ethyl 6-methoxy-1-oxo-1*H*-isochromene-3-carboxylate (5b):



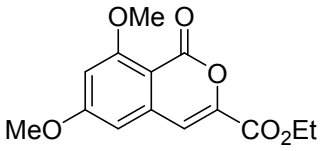
Yield: 96%; colorless solid; **mp**:128-129 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 669, 749, 785, 827, 1072, 1257, 1510, 1601, 1720, 1736, 2934, 3067; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.1 Hz, 3H), 3.94 (s, 3H), 4.41 (q, *J* = 7.1 Hz, 2H), 6.96 (d, *J* = 2.5 Hz, 1H), 7.16 (dd, *J* = 8.9 and 2.6 Hz, 1H), 7.4 (s, 1H), 8.26 (d, *J* = 9.0 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.3, 55.7, 62.2, 109.7, 112.0, 115.8, 118.6, 132.3, 137.4, 144.2, 160.2, 164.9; **Anal.** Calcd for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87. Found: C, 62.87; H, 4.85 %.

Ethyl 5,6-dimethoxy-1-oxo-1*H*-isochromene-3-carboxylate (5c):



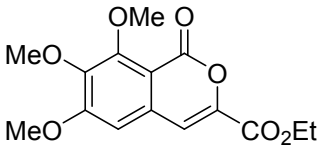
Yield: 92%; gum; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 695, 721, 997, 1018, 1119, 1194, 1261, 1360, 1437, 1473, 1592, 1655, 1719, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.3 Hz, 3H), 3.86 (s, 3H), 3.91 (s, 3H), 4.44 (q, *J* = 7.0 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 1H), 7.18 (s, 1H), 7.59 (d, *J* = 8.9 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.2, 61.6, 61.7, 65.2, 113.4, 121.8, 122.6, 131.0, 137.1, 152.2, 153.7, 162.2, 164.4; **Anal.** Calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.57; H, 5.05 %.

Ethyl 6,8-dimethoxy-1-oxo-1*H*-isochromene-3-carboxylate (5d):



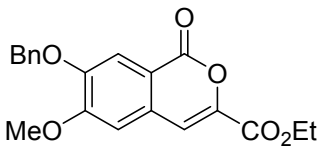
Yield: 92%; colorless solid; **mp**: 87-89 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 690, 711, 997, 1018, 1159, 1194, 1261, 1360, 1467, 1473, 1592, 1655, 1720, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.34 (t, *J* = 7.0 Hz, 3H), 3.86 (s, 3H), 3.92 (s, 3H), 4.33 (q, *J* = 7.0 Hz, 2H), 6.53 (d, *J* = 1.8 Hz, 1H), 6.58 (d, *J* = 1.8 Hz, 1H), 7.28 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.2, 55.8, 56.5, 62.2, 100.9, 102.3, 112.0, 120.4, 127.3, 135.7, 156.2, 163.5, 165.6; Anal. Calcd for $C_{14}H_{14}O_6$: C, 60.63; H, 5.07. Found: C, 60.75; H, 5.10 %.

Ethyl 6,7,8-trimethoxy-1-oxo-1*H*-isochromene-3-carboxylate (5e):



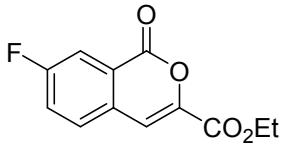
Yield: 90%; colorless solid; **mp**: 122-123 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 695, 721, 997, 1018, 1119, 1194, 1261, 1360, 1437, 1473, 1592, 1655, 1719, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.8 Hz, 3H), 3.96 (s, 1H), 3.97 (s, 1H), 3.99 (s, 1H), 4.44 (q, *J* = 7.2 Hz, 2H), 6.83 (s,1H), 7.17 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.1, 55.9, 61.2, 62.0, 62.1, 105.0, 110.2, 131.5, 133.6, 134.5, 144.2, 154.8, 157.3, 159.3, 161.2; **Anal.** Calcd for $C_{15}H_{16}O_7$: C, 58.44; H, 5.23. Found: C, 58.57; H, 5.30 %.

Ethyl 8-(benzyloxy)-7-methoxy-1-oxo-1*H*-isochromene-3-carboxylate (5f):



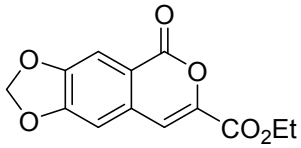
Yield: 92%; yellow solid; **mp**: 146-148 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 689, 765, 844, 1062, 1234, 1341, 1485, 1643, 1718, 1731, 2959, 3068; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.2 Hz, 3H), 4.01 (s, 3H), 4.40 (q, *J* = 7.1 Hz, 2H), 5.24 (s, 2H), 6.95 (s, 1H), 7.32-7.49 (m, 6H), 7.78 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.3, 56.3, 62.0, 71.1, 108.0, 111.7, 112.0, 116.5, 127.7, 128.4, 128.8, 130.5, 135.6, 142.7, 150.8, 155.6, 160.5; **Anal**. Calcd for $C_{20}H_{18}O_6$: C, 67.79; H, 5.12. Found: C, 67.74; H, 5.15 %.

Ethyl 7-fluoro-1-oxo-1*H*-isochromene-3-carboxylate (5g):



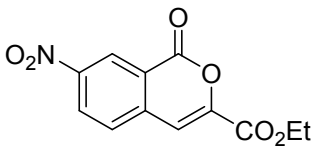
Yield: 95%; colorless solid; **mp**: 122-123 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 892, 1026, 1256, 1439, 1573, 1640, 1715, 1726, 2930, 3048; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.43 (t, *J* = 7.1 Hz, 3H), 4.43 (q, *J* = 7.1 Hz, 2H), 7.22-7.38 (m, 2H), 7.42 (s, 1H), 8.38 (dd, *J* = 5.5 and 8.7 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.3, 62.5, 111.1 (d, *J* = 2.6 Hz), 113.2 (d, *J* = 22.5 Hz), 118.7 (d, *J* = 22.6 Hz), 119.3 (d, *J* = 2.6 Hz), 133.6 (d, *J* = 10.2 Hz), 137.8 (d, *J* = 10.2 Hz), 144.8, 159.6, 159.9, 166.9 (d, *J* = 256.3 Hz); **Anal**. Calcd for $C_{12}H_9FO_4$: C, 61.02; H, 3.84. Found: C, 61.1; H, 3.88 %.

Ethyl 5-oxo-5*H*-[1,3]dioxolo[4,5-*g*]isochromene-7-carboxylate (5h):



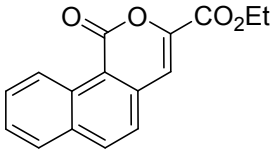
Yield: 95%; colorless solid; **mp**: 162-163 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 765, 832, 895, 955, 1065, 1160, 1341, 1482, 1643, 1718, 1724, 2928, 3054; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.42 (t, *J* = 7.8 Hz, 3H), 4.41 (q, *J* = 7.2 Hz, 2H), 6.16 (s, 2H), 6.93 (s, 1H), 7.36 (s, 1H), 7.68 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.2, 62.0, 102.7, 105.7, 108.1, 111.9, 118.2, 132.3, 142.6, 150.3, 153.7, 160.1; **Anal.** Calcd for $C_{13}H_{10}O_6$: C, 59.55; H, 3.84. Found: C, 59.57; H, 3.85 %.

Ethyl 7-nitro-1-oxo-1*H*-isochromene-3-carboxylate (5i):



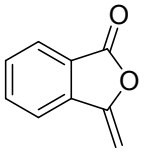
Yield: 90%; yellow solid; **mp**: 162-166 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 699, 755, 804, 1062, 1224, 1349, 1485, 1653, 1719, 1721, 2950, 3078; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.45 (t, *J* = 7.2 Hz, 3H), 4.45 (q, *J* = 7.0, 2H), 7.56 (s, 1H), 8.42 (dd, *J* = 2.2 and 8.6 Hz, 1H), 8.45 (d, *J* = 2.1 Hz, 1H), 8.52 (d, *J* = 8.7 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.3, 62.8, 110.6, 122.5, 124.5, 126.7, 132.2, 136.4, 145.6, 151.8, 158.8, 159.4; **Anal.** Calcd for $C_{12}H_9NO_6$: C, 54.76; H, 3.45, N, 5.32. Found: C, 54.57; H, 3.41, N, 5.31 %.

Ethyl 1-oxo-1*H*-benzo[*h*]isochromene-3-carboxylate (5j):



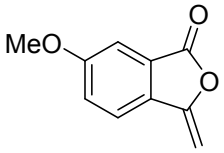
Yield: 93%; colorless solid; **mp**: 164-165 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 680, 748, 819, 852, 1065, 1185, 1368, 1488, 1632, 1718, 1732, 2935, 3054; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.46 (t, *J* = 7.3 Hz, 3H), 4.45 (q, *J* = 7.5 Hz, 2H), 7.54-7.57 (m, 2H), 7.68 (dt, *J* = 7.8 and 1.3 Hz, 1H), 7.79 (dt, *J* = 7.7 and 1.5 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H); 8.18 (d, *J* = 8.9 Hz, 1H), 9.74 (d, *J* = 8.6 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.3, 62.3, 112.4, 117.3, 124.3, 127.1, 128.0, 128.8, 129.9, 131.5, 134.1, 136.7, 137.5, 144.8, 159.8, 160.0; **Anal.** Calcd for $C_{16}H_{12}O_4$: C, 71.64; H, 4.51. Found: C, 71.96; H, 4.59 %.

3-methyleneisobenzofuran-1(3*H*)-one (6k):



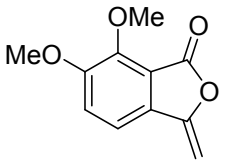
Yield: 95%; colorless solid; **mp**: 57-58 °C; IR ($CHCl_3$, cm^{-1}): υ_{max} 956, 1018, 1278, 1478, 1784, 2930; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 5.24 (dd, *J* = 3.0 and 6.2 Hz, 2H), 7.57-7.62 (m, 1H), 7.72 (d, *J* = 4.0 Hz, 2H), 7.92 (d, *J* = 8.0 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 91.1, 120.6, 125.2, 130.4, 134.4, 139.0, 151.8, 166.8; **Anal.** Calcd for $C_9H_6O_2$: C, 73.97; H, 4.14. Found: C, 73.9; H, 4.12 %.

6-methoxy-3-methyleneisobenzofuran-1(3*H*)-one (6l):



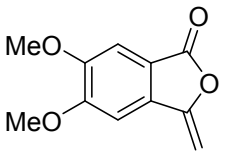
Yield: 95%; colorless solid; **mp**: 87-88 °C; IR ($CHCl_3$, cm^{-1}): υ_{max} 756, 1026, 1100, 1180, 1240, 1303, 1346, 1456, 1491, 1606, 1660, 1774, 2943, 3018; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.94 (s, 3H), 5.15 (d, *J* = 3.0 Hz, 1H), 5.18 (d, *J* = 2.9 Hz, 1H), 7.06-7.09 (m, 2H), 7.79 (dd, *J* = 7.9 and 1.2 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 55.9, 90.8, 103.7, 117.8, 118.5, 126.8, 141.6, 151.8, 165.0, 166.3; **Anal.** Calcd for $C_{10}H_8O_3$: C, 68.18; H, 4.58. Found: C, 68.16; H, 4.59 %.

5,6-dimethoxy-3-methyleneisobenzofuran-1(3*H*)-one (6m):



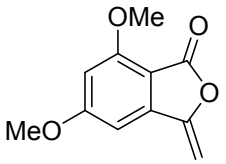
Yield: 94%; gum; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1024, 1275, 1458, 1499, 1719, 1773, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.94 (s, 3H), 4.14 (s, 3H), 5.02 (d, *J* = 2.8 Hz, 1H), 5.06 (d, *J* = 2.9 Hz, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 56.9, 62.5, 88.8, 115.3, 119.4, 121.4, 132.5, 148.1, 151.3, 153.7, 164.2; **Anal**. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.2; H, 5.00 %.

6,7-dimethoxy-3-methyleneisobenzofuran-1(3*H*)-one (6n):



Yield: 93%; gum; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1022, 1104, 1229, 1278, 1321, 1369, 1466, 1504, 1764, 2919; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.97 (s, 3H), 4.01 (s, 3H), 5.05 (d, *J* = 2.8 Hz, 1H), 5.13 (d, *J* = 2.9 Hz, 1H), 7.05 (s, 1H), 7.25 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 56.2, 56.7, 89.5, 101.5, 105.3, 117.8, 133.4, 151.8, 151.9, 155.1, 166.7; **Anal**. Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.10; H, 4.84 %.

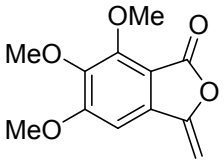
5,7-dimethoxy-3-methyleneisobenzofuran-1(3*H*)-one (6o):



Yield: 92%, colorless solid; **mp**: 228-229 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 779, 856, 1024, 1275, 1458, 1499, 1719, 1773, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.96 (s, 3H), 4.01 (s, 3H), 5.06 (d, *J* =

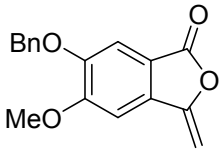
2.8 Hz, 1H), 5.12 (d, *J* = 2.9 Hz, 1H), 7.05 (s, 1H), 7.24 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 56.4, 56.4, 89.5, 101.5, 105.4, 118.0, 133.5, 151.9, 152.0, 155.2, 166.7; **Anal.** Calcd for $C_{11}H_{10}O_4$: C, 64.07; H, 4.89. Found: C, 64.10; H, 4.88 %.

5,6,7-trimethoxy-3-methyleneisobenzofuran-1(3*H*)-one (6p):



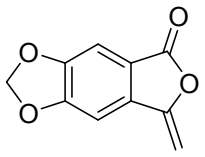
Yield: 94%; gum; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 1019, 1112, 1199, 1262, 1345, 1418, 1480, 1597, 1771, 2853, 2942; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.89 (s, 3H), 3.99 (s, 3H), 4.16 (s, 3H), 5.06 (d, *J* = 2.9 Hz, 1H), 5.11 (d, *J* = 3.2 Hz, 1H), 6.85 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 56.4, 61.4, 62.2, 89.6, 97.7, 109.9, 136.3, 151.5, 151.9, 159.9; **Anal.** Calcd for $C_{12}H_{12}O_5$: C, 61.01; H, 5.12. Found: C, 61.01; H, 5.09 %.

5-(benzyloxy)-6-methoxy-3-methyleneisobenzofuran-1(3*H*)-one (6q):



Yield: 93%; colorless solid; **mp**: 235-236 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 980, 1035, 1136, 1182, 1273, 1352, 1415, 1482, 1588, 1775, 2953, 3040; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 4.01 (s, 3H), 5.0 (d, *J* = 2.9 Hz, 1H), 5.1 (d, *J* = 2.9 Hz, 1H), 5.20 (s, 2H) 7.1 (s, 1H), 7.28-7.5 (m, 7H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 56.3, 71.0, 89.5, 101.8, 107.2, 117.8, 127.4, 128.3, 128.7, 133.7, 135.6, 151.0, 151.8, 155.6, 166.6; **Anal.** Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.31; H, 5.04 %.

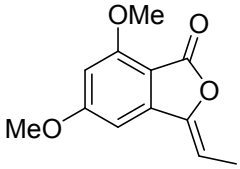
7-methylene-[1,3]dioxolo[4,5-*f*]isobenzofuran-5-(7*H*)-one (6r):



Yield: 94%; colorless solid; **mp**: 263-265 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 770, 866, 1024, 1275, 1458, 1499, 1719, 1773, 2943; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 5.01 (d, *J* = 3.0 Hz, 1H), 5.11 (d, *J* = 2.9 Hz, 1H), 6.15 (s, 2H), 7.01 (s, 1H), 7.18 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 90.1, 99.9,

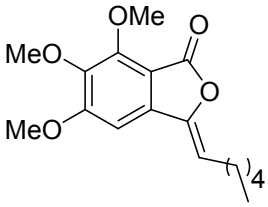
102.8, 103.4, 119.7, 135.6, 150.5, 151.6, 153.9, 166.1; **Anal**. Calcd for $C_{10}H_6O_4$: C, 63.16; H, 3.18. Found: C, 63.14; H, 3.18 %.

(*Z*)-3-ethylidene-5,7-dimethoxyisobenzofuran-1(3*H*)-one (6s):



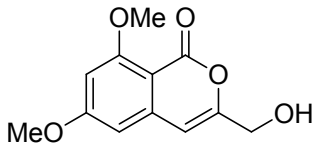
Yield; 94%; colorless solid; **mp**: 147-148 °C; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 668, 756, 1032, 1052, 1160, 1215, 1342, 1496, 1691, 1763, 3020; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 1.97 (d, *J* = 7.1 Hz, 3H), 3.90 (s, 3H), 3.95 (s, 3H), 5.56 (q, *J* = 7.1 Hz, 1H), 6.39 (d, *J* = 2.2 Hz, 1H), 6.57 (d, *J* = 2.2 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 11.2, 55.8, 55.8, 94.4, 99.5, 103.6, 105.7, 143.7, 146.2, 159.2, 164.6, 166.7; **Anal**. Calcd for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.41; H, 5.48 %.

(*Z*)-5,6,7-trimethoxy-3-pentylideneisobenzofuran-1(3*H*)-one (6t):



Yield: 91%; gum; **IR** ($CHCl_3$, cm^{-1}): υ_{max} 660, 760, 1052, 1152, 1160, 1215, 1342, 1496, 1691, 1764, 3030; **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 0.89 (t, *J* = 6.6 Hz, 3H), 1.34-1.52 (m, 6H), 1.55-1.66 (m, 4H), 3.87 (s, 3H), 3.95 (s, 3H), 4.14 (3H), 5.21 (d, *J* = 5.2 Hz, 1H), 6.68 (s, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.5, 22.7, 25.8, 29.2, 31.8, 61.3, 62.2, 62.3, 81.7, 99.8, 111.4, 142.0, 145.2, 152.5, 156.7, 167.9; **Anal.** Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.50; H, 7.34 %.

6,8-dimethoxy-3-hydroxymethylisocoumarin (7):

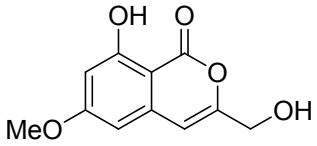


Sodium borohydride powder (0.054 g, 1.43 mmol) was added to a stirred solution of isocoumarin ester **5d** (0.2 g, 0.718 mmol) in THF (3 ml) at 0 °C. The resulting suspension was stirred at 25 °C for 15 min. Methanol (3 ml) was then added drop wise, after 4 h the reaction mixture was quenched with 2N HCl (10 ml). The organic layer was separated and the aqueous phase extracted

with ethyl acetate. The combined organic phase was dried (Na_2SO_4) and concentrated to obtain a solid residue. Further purification was done with column chromatography [silica gel (230-400 mesh) and petroleum ether: ethyl acetate (1:1) as eluent] to afford a pure product alcohol **7** as a colorless solid (0.147 g, yield: 87%, mp: 101-104 °C).

IR ($CHCl_3$, cm^{-1}): υ_{max} 1074, 1272, 1559, 1575, 1602, 1685, 1704, 1730, 2820, 2924, 3460; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 3.90 (s, 3H), 3.97 (s, 3H), 4.42 (s, 2H), 6.35 (s, 1H), 6.36 (d, *J* = 2.2 Hz, 1H), 6.45 (d, *J* = 2.2 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 55.6, 56.3, 61.4, 98.8, 100.3, 102.8, 107.7, 108.9, 128.6, 132.7, 169.6, 170.2; **Anal.** Calcd for $C_{12}H_{12}O_5$: C, 61.01; H, 5.12. Found: C, 61.1; H, 5.14%.

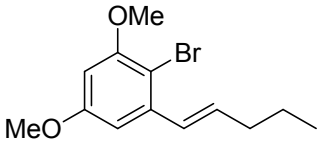
Cytogenin (1):



A solution of boron tribromide (0.22 mL (1M in dichloromethane), 1.27 mmol) was slowly added with a syringe to a stirred solution of alcohol **7** (0.1 g, 0.423 mmol) in dichloromethane (4 mL) under nitrogen at -5 °C. After complete addition, the mixture was stirred for 1 h and then $NaHCO_3$ was added. The organic layer was separated and an aqueous layer extracted with ethyl acetate twice, combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified using column chromatography [silica gel (230-400 mesh) and petroleum ether: ethyl acetate (4:1) as eluent] to afford pure product **1** as a colorless solid (0.071 g, yield: 76%, mp: 150-152 °C).

IR ($CHCl_3$, cm^{-1}): υ_{max} 741, 1162, 1271, 1480, 1580, 1665, 1685, 2650, 3460; **^{1}H NMR** (200 MHz, Acetone D_6): δ 3.92 (s, 3H), 4.40 (d, *J* = 5.6 Hz, 2H), 4.76 (t, *J* = 6.1 Hz, 1H), 6.49 (d, *J* = 2.2 Hz, 1H), 6.61 (d, *J* = 2.2 Hz, 1H), 6.66 (s, 1H), 11.11 (s, 1H); **^{13}C NMR** (50 MHz, Acetone D_6): δ 56.4, 61.1, 101.4, 102.6, 103.9, 110.0, 140.4, 158.4, 164.6, 166.8, 168.1; **Anal.** Calcd for $C_{11}H_{10}O_5$: C, 59.46; H, 4.54. Found: C, 59.45; H, 4.54%.

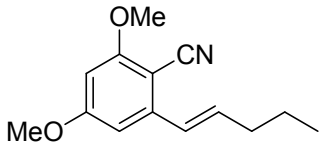
(*E*)-2-bromo-1,5-dimethoxy-3-(pent-1-en-1-yl)benzene (9):



To a stirred solution of 5-(butane- 1-sulfonyl)-1-phenyl-1H-tetrazole **A** (1.4 g, 5.28 mmol) in dry THF (25 mL) at -78 °C under N_2 was added drop wise the NaHMDS (5.8 mL, 1.0 M in THF, 5.80 mmol). After stirring at -78 °C for 30 min, neat aldehyde **8** (2.05 g, 7.92 mmol) was added. After stirring for 3 h the reaction mixture was allowed to warm slowly at 25 °C and stirred overnight, where upon H_2O and Et_2O were added and the mixture shaken well. The organic layer was separated and dried over Na_2SO_4 to get crude product, which was purified by column chromatography [silica gel (230-400 mesh) and petroleum ether: ethyl acetate (9:1) as eluent] to afford colorless oily product **9** (1.32 g, yield: 85%).

IR ($CHCl_3$ cm^{-1}): υ_{max} 770, 912, 1012, 1108, 1276, 1339, 1486, 1505, 1604, 1615, 2990, 3040; **^{1}H-NMR** (200 MHz, $CDCl_3$): δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.49-1.57 (m, 2H), 2.23 (q, *J* = 7.0 Hz, 2H), 3.81 (s, 3H), 3.86 (s, 3H), 6.0-6.15 (m, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 6.61 (d, *J* = 2.4 Hz, 1H), 6.73 (d, *J* = 15.6 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 113.9, 22.4, 35.2, 55.4, 56.2, 98.5, 102.8, 129.5, 134.0, 139.4, 156.8, 159.5; **Anal.** Calcd for $C_{13}H_{17}BrO_2$: C, 54.75; H, 6.01. Found: C, 54.74; H, 6.10%.

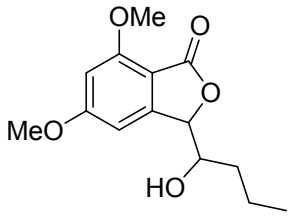
(*E*)-2,4-dimethoxy-6-(pent-1-en-1-yl)benzonitrile (10):



Olefin **9** (1 g, 3.52 mmol) was dissolved in dry DMF (15 mL) and CuCN (1.10 g, 12.32 mmol) was added to it. The entire solution was refluxed under N_2 for 12 h (monitored by TLC); the reaction mixture was then cooled to room temperature and diluted with water (10 mL) and EtOAc (15 mL). The organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude product which was purified by column chromatography [silica gel (230-400 mesh) and petroleum ether: Ethyl acetate (4:1) as eluent] to obtained colorless oily product **10** (0.68 g, yield: 84%).

IR ($CHCl_3$, cm^{-1}): υ_{max} 748, 876, 932, 1032, 1098, 1276, 1339, 1486, 1505, 1604, 1615, 2220, 2989, 3054; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.41-1.52 (m, 2H), 2.17 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 3.82 (s, 3H), 6.22 (d, *J* = 2.2 Hz, 1H), 6.27-6.39 (m, 1H), 6.54 (d, *J* = 2.2 Hz, 1H), 6.64 (d, *J* = 15.8 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 17.8, 22.2, 35.2, 55.5, 56.0, 93.4, 96.8, 101.5, 115.8, 126.4, 136.6, 144.1, 163.1, 163.8; **Anal.** Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.75; H, 7.40%.

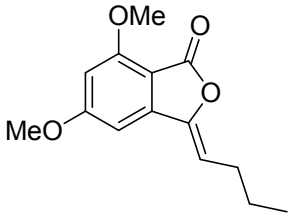
3-(1-hydroxybutyl)-5,7-dimethoxyisobenzofuran-1(3*H*)-one (11):



To the stirred solution of aryl cyanide **10** (0.6 g, 2.59 mmol) in acetone (12 mL) and water (4 mL) catalytic OsO_4 (0.010 g, 1 mol%) was added at 25 °C followed by the addition of NMO (0.426 g, 3.63 mmol). The reaction mixture was stirred for 12 h at 25 °C and quenched with sat. sodium thiosulphate (5 mL), the organic layer was seperated and the aquous layer was extracted with ethyl acetate (3 × 10 mL). Both the layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure, obtained crude product was purified using column chromatography [silica gel (230-400 mesh) and petroleum ether: ethyl acetate (3:2) as eluent] to afford pure colorless solid **11** (0.620 g, yield: 90%, mp: 110-112 °C).

IR ($CHCl_3$, cm^{-1}): υ_{max} 695, 720, 754, 992, 1022, 1061, 1217, 1231, 1312, 1372, 1438, 1600, 1695, 1731, 2852, 2922, 2990, 3242; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.92 (t, *J* = 6.8 Hz, 3H), 1.37-1.43 (m, 2H), 1.53-1.63 (m, 2H), 3.05 (d, *J* = 3.4 Hz, 1H), 3.72 (d, *J* = 3.4 Hz, 1H), 3.87 (s, 1H), 3.91 (s, 1H), 4.82 (t, *J* = 4.6 Hz, 1H), 6.36 (d, *J* = 2.3 Hz, 1H), 6.69 (d, *J* = 2.3 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 14.0, 19.0, 35.3, 55.7, 56.1, 74.8, 75.2, 92.8, 97.7, 104.0, 115.3, 149.1, 163.1, 164.4; **Anal.** Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.17; H, 6.84%.

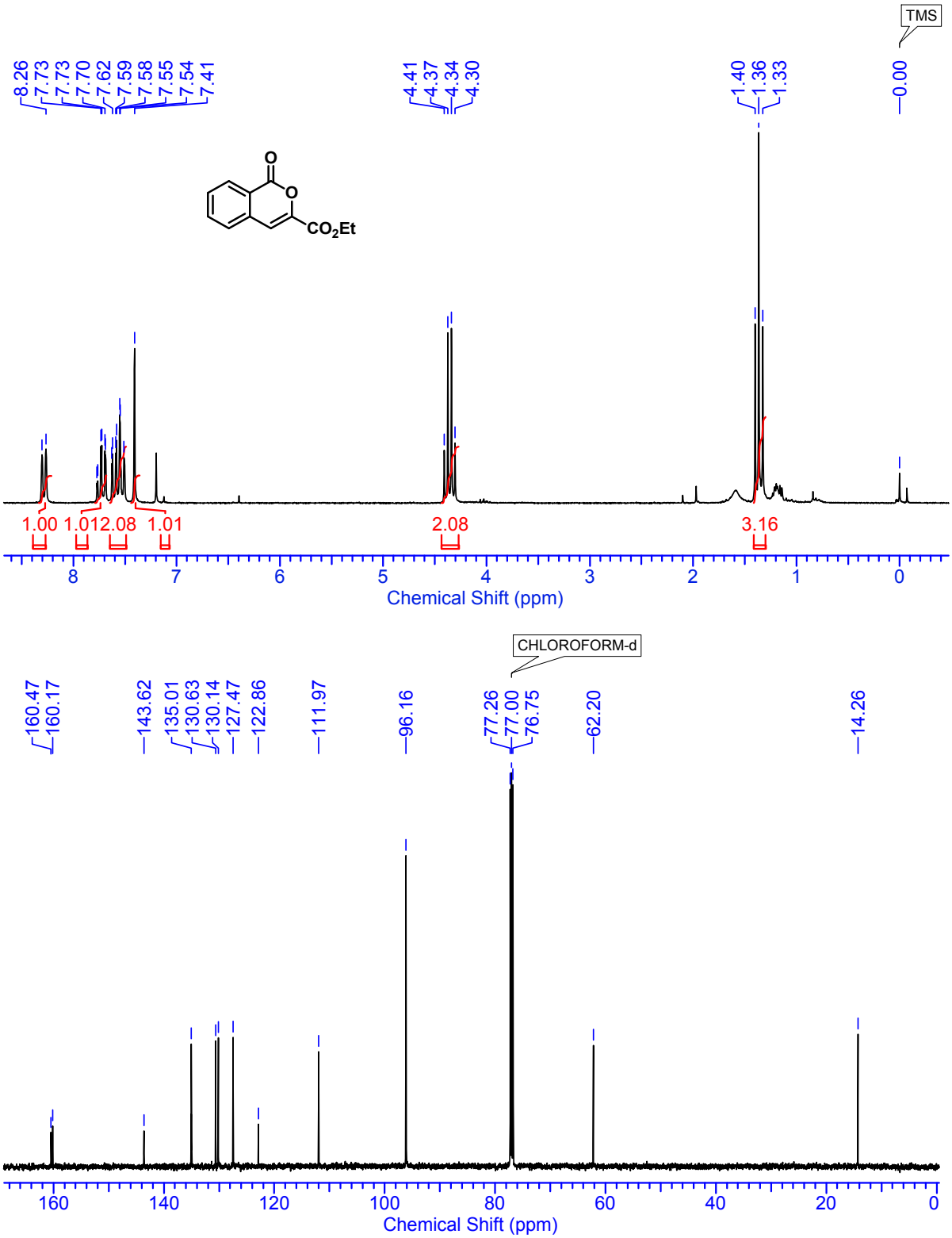
(*Z*)-3-butylidene-5-7-dimethoxyphthalide (12):



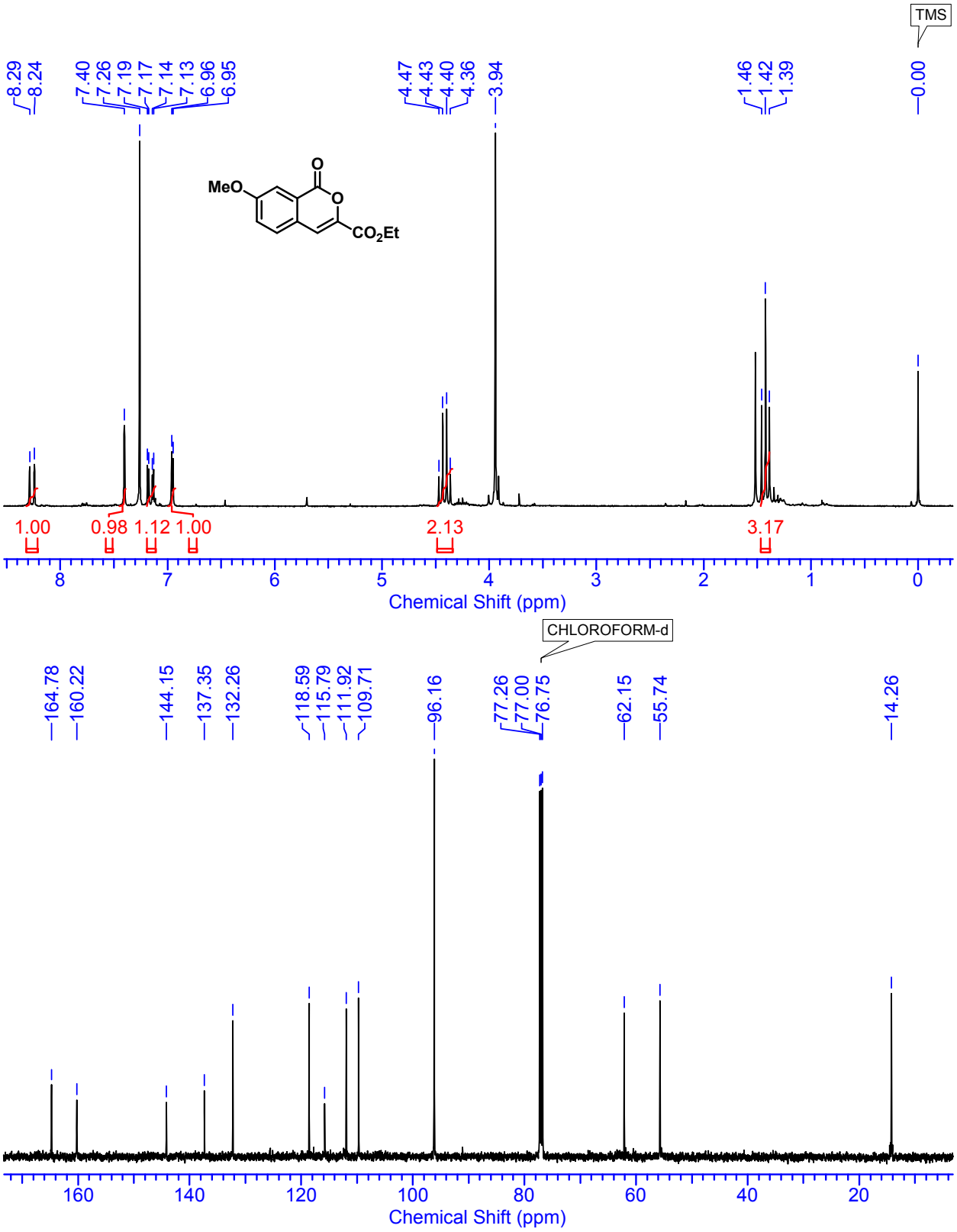
To a stirred solution of 3-substituted phthalide derivatives **11** (0.2 g, 0.751 mmol) in THF (10 mL) was added diethylazodicarboxylate (0.013 mL, 10 mol%) followed by the addition of PPh_3 (0.295 g, 1.5 mmol), tertiary butyl hydroperoxide (0.135 mL, 2 mmol) and allowed to stirred for 2 h at 25 °C. After the completion of reaction (as monitored by TLC), THF was distilled out to give crude product which was purified by chromatography [silica gel (230-400 mesh) and petrolium ether: ethyl acetate (7:3) as eluent] to afford viscous gum **12** (0.171 g, yield: 92%).

IR ($CHCl_3$, cm^{-1}): υ_{max} 695, 720, 992, 1022, 1120, 1217, 1312, 1438, 1598, 1760, 1606; **^{1}H NMR** (200 MHz, $CDCl_3$): δ 0.98-1.01 (t, *J* = 7.3 Hz, 3H), 1.45-1.66 (m, 2H), 1.90-2.03 (m, 2H), 3.90 (s, 3H), 3.94 (s, 3H), 5.52 (d, *J* = 5.6 Hz, 1H), 6.48 (d, *J* = 2.0 Hz, 1H), 6.63 (d, *J* = 2.0 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 13.5, 18.0, 35.9, 55.0, 56.3, 84.2, 98.9, 102.5, 114.7, 125.3, 143.4, 150.1, 163.7, 165.1; 164.4; **Anal.** Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.77; H, 6.50%.

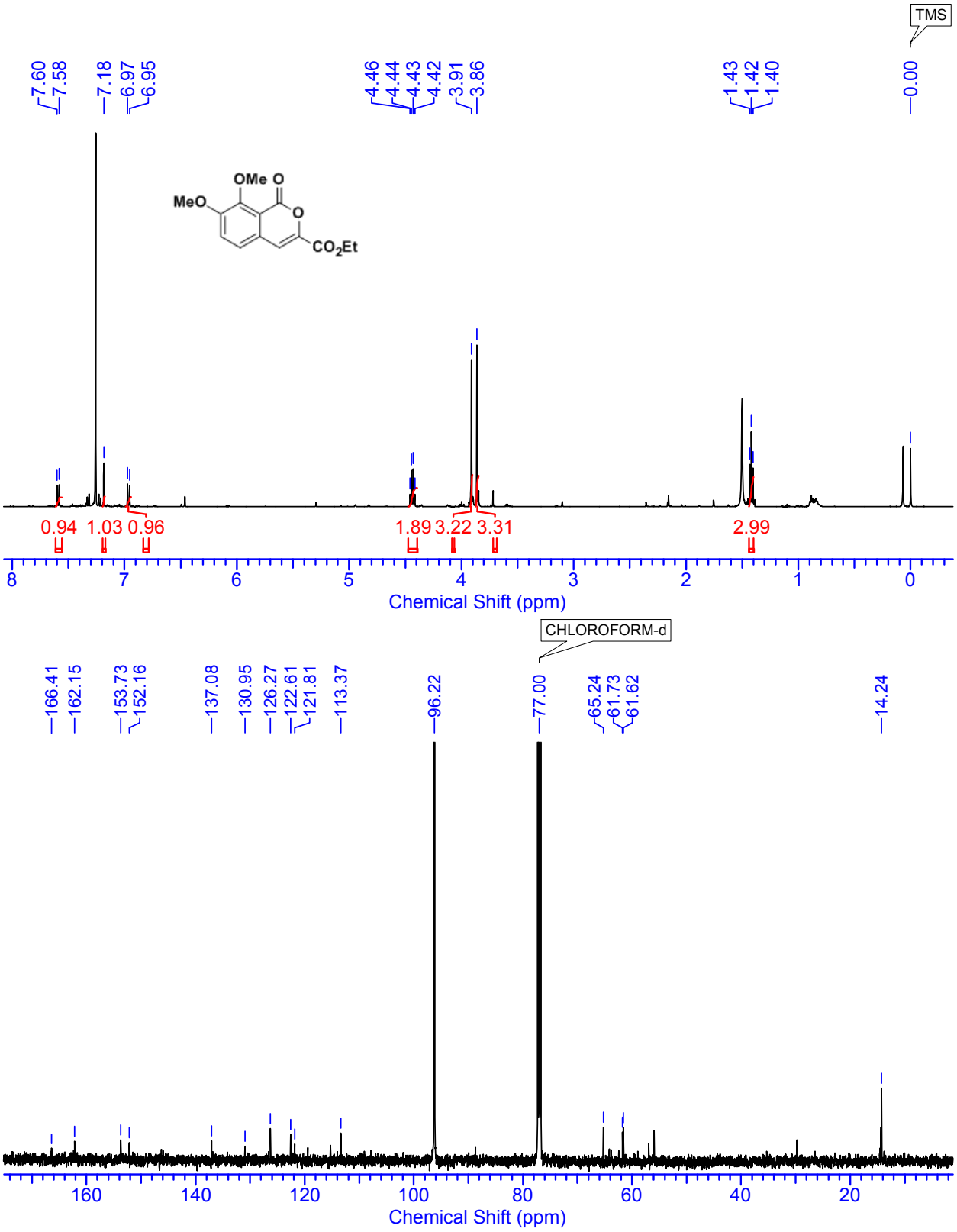
3. ^{1}H and ^{13}C-NMR charts of new compounds:



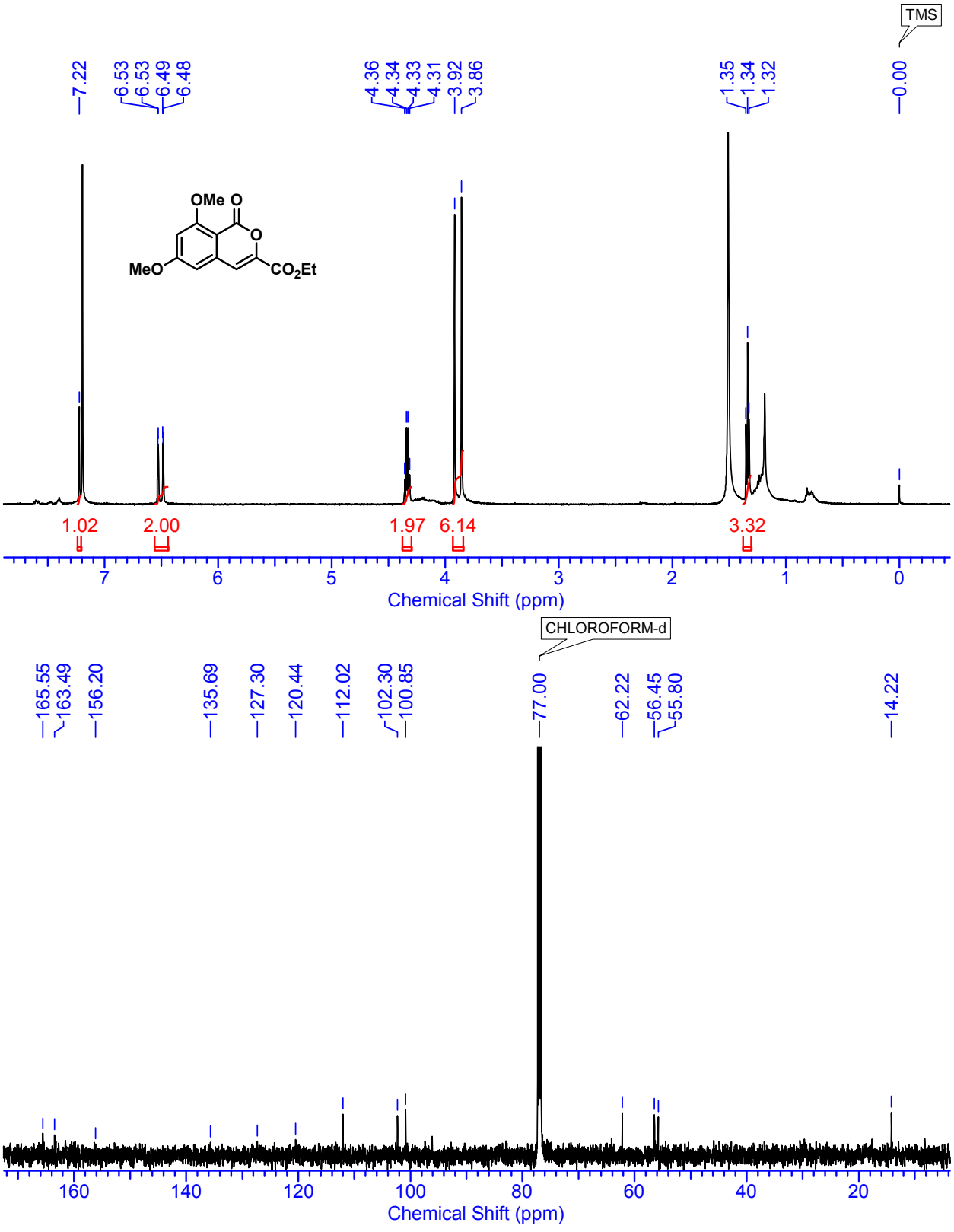
^{1}H and ^{13}C NMR Spectra of 5a



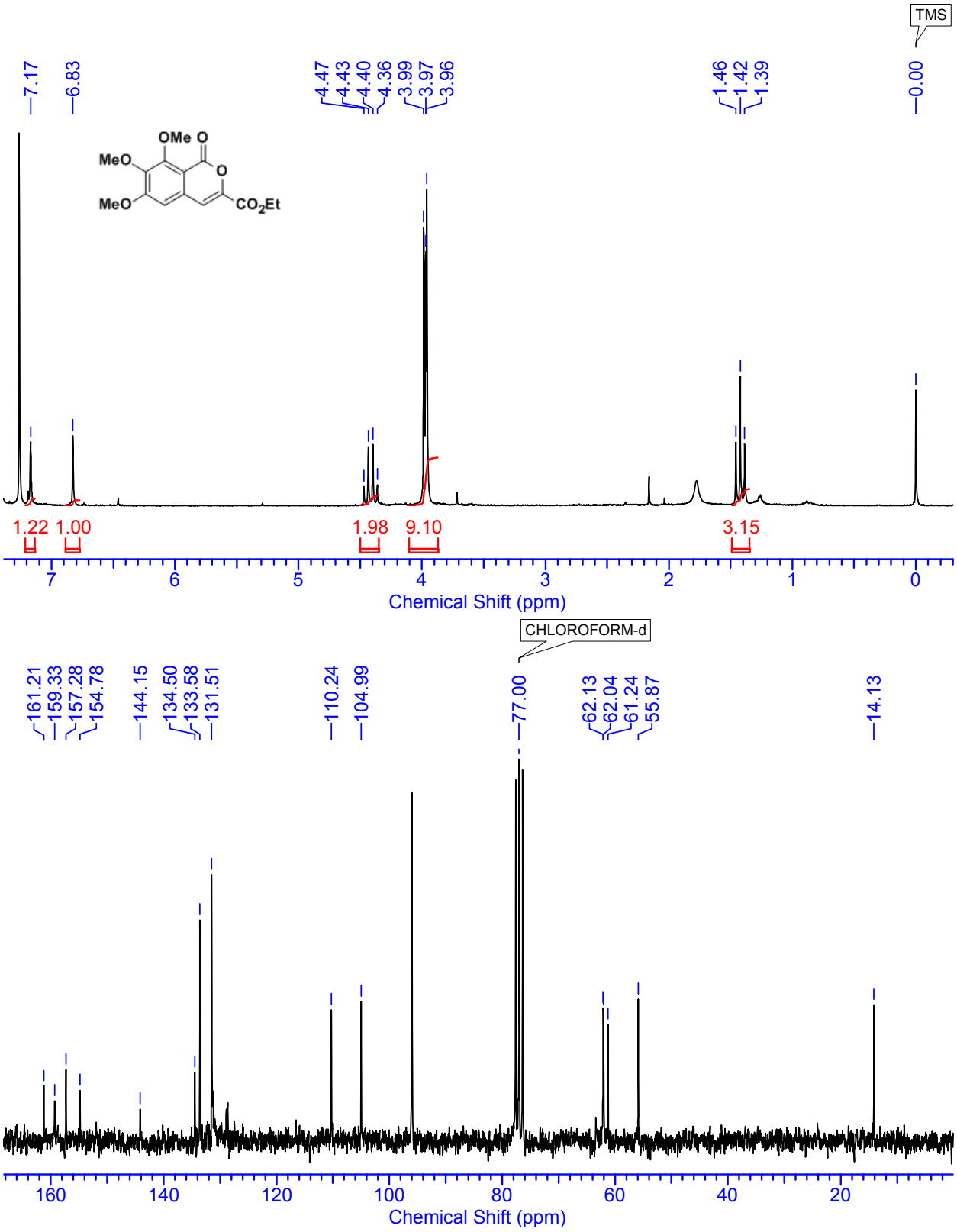
^{1}H and ^{13}C NMR Spectra of 5b



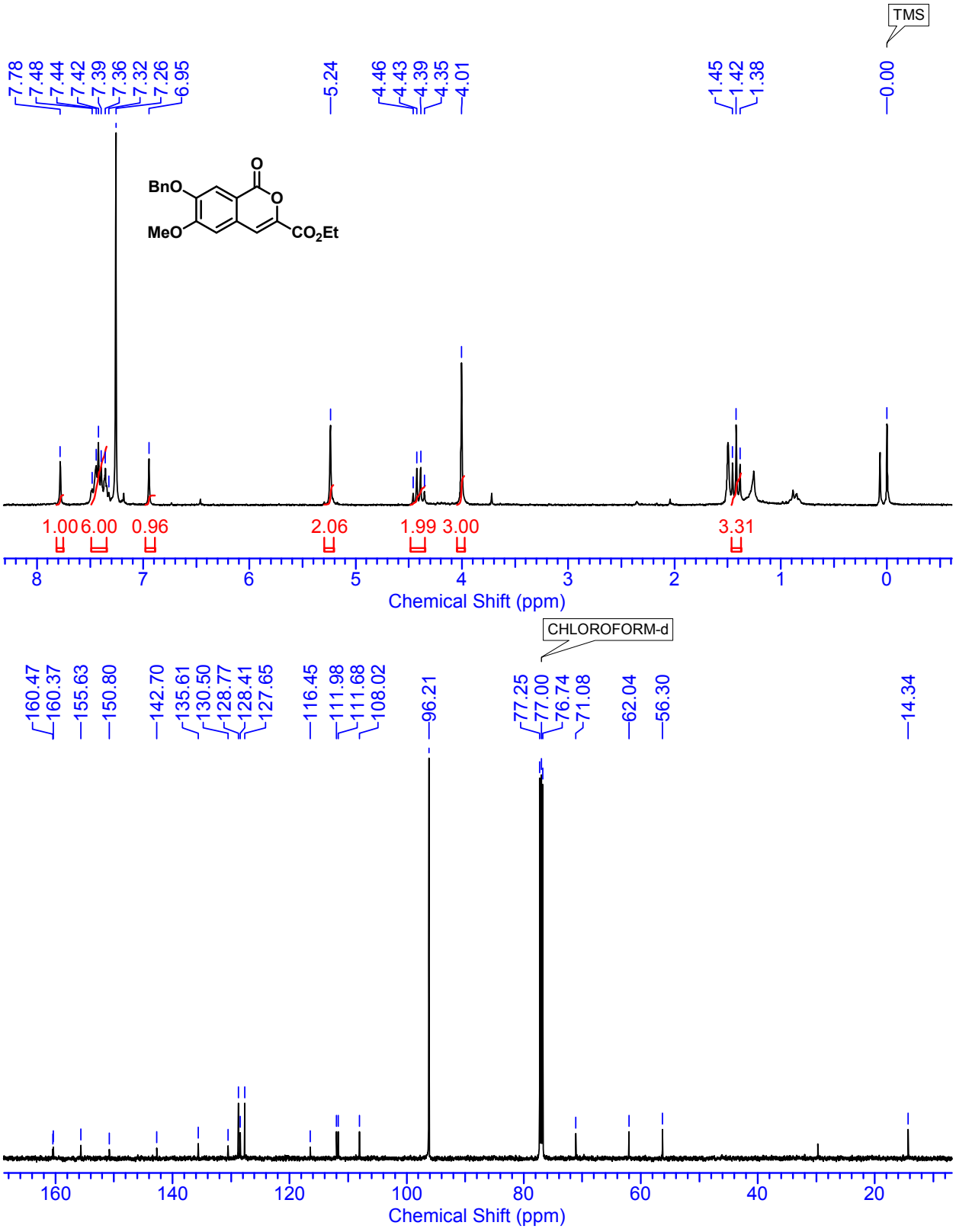
^{1}H and ^{13}C NMR Spectra of 5c



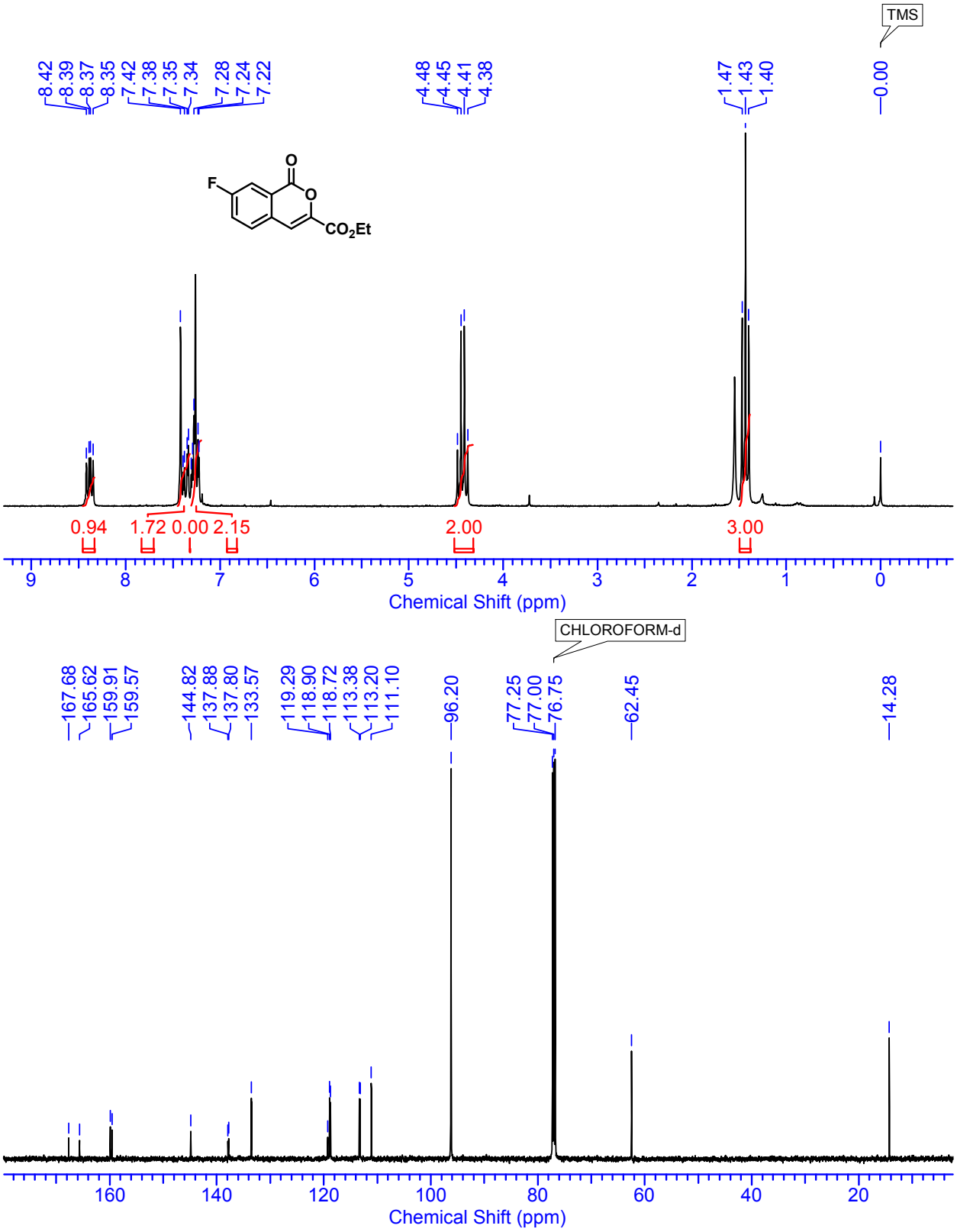
^{1}H and ^{13}C NMR Spectra of 5d



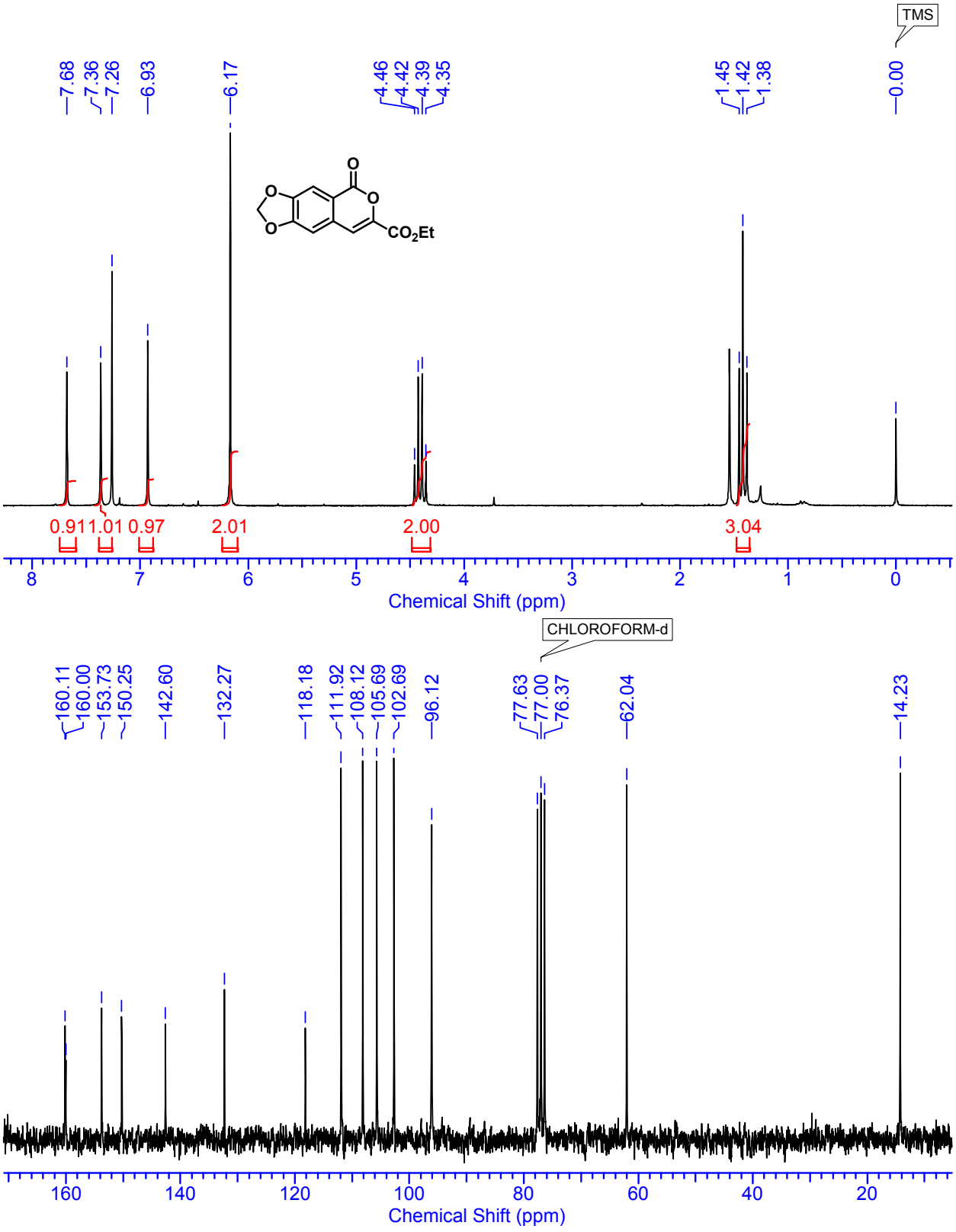
^{1}H and ^{13}C NMR Spectra of 5e



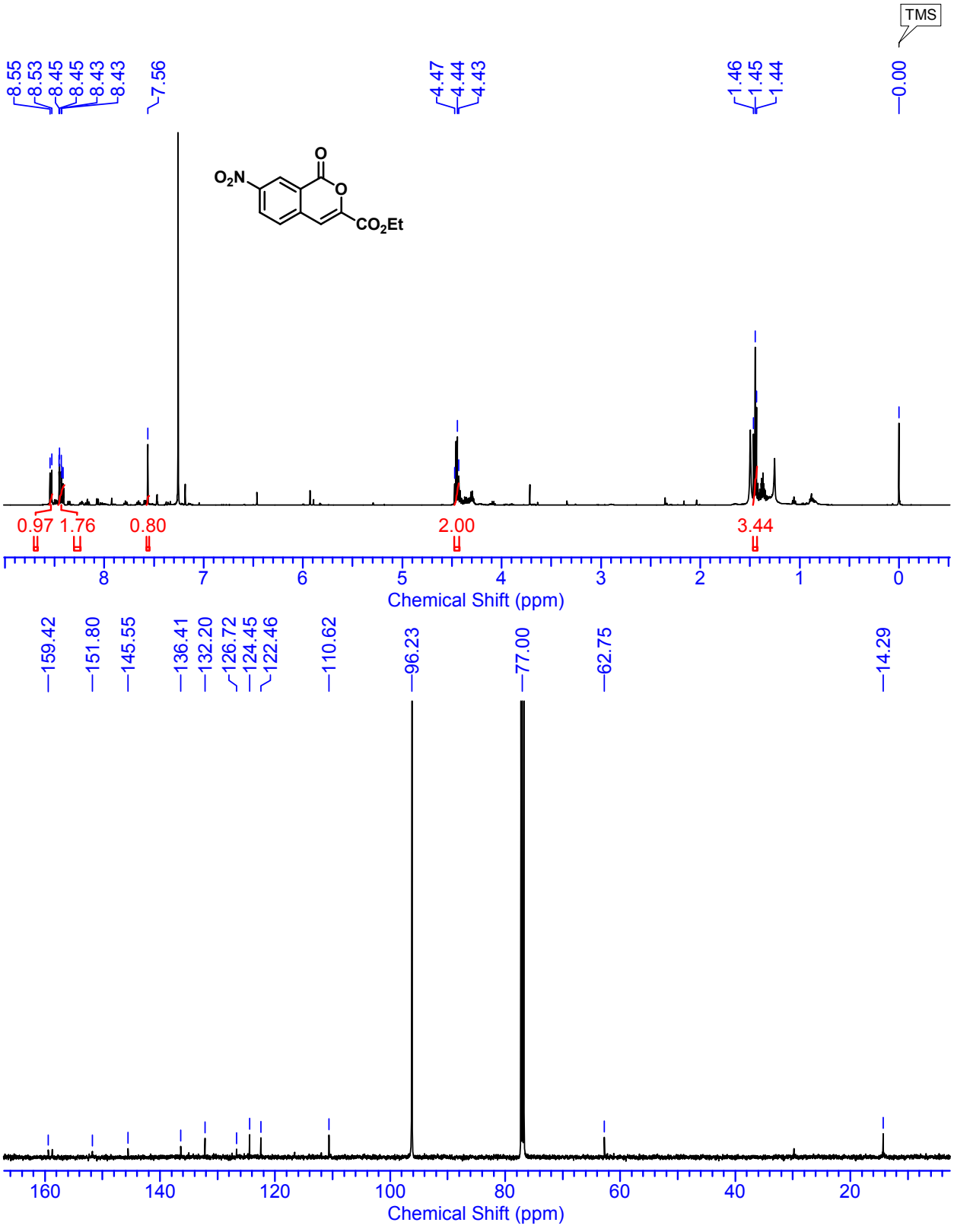
^{1}H and ^{13}C NMR Spectra of 5f



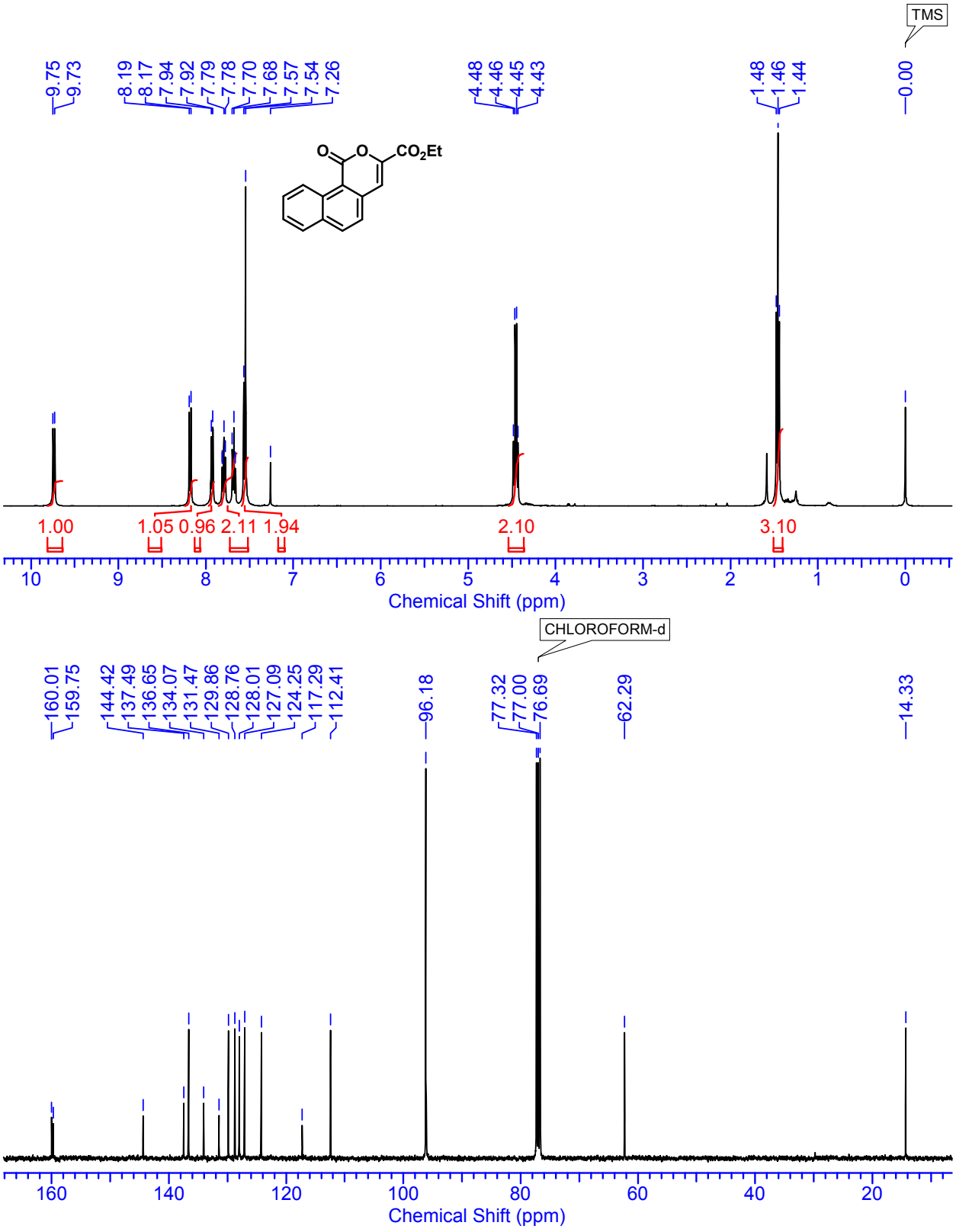
^{1}H and ^{13}C NMR Spectra of 5g



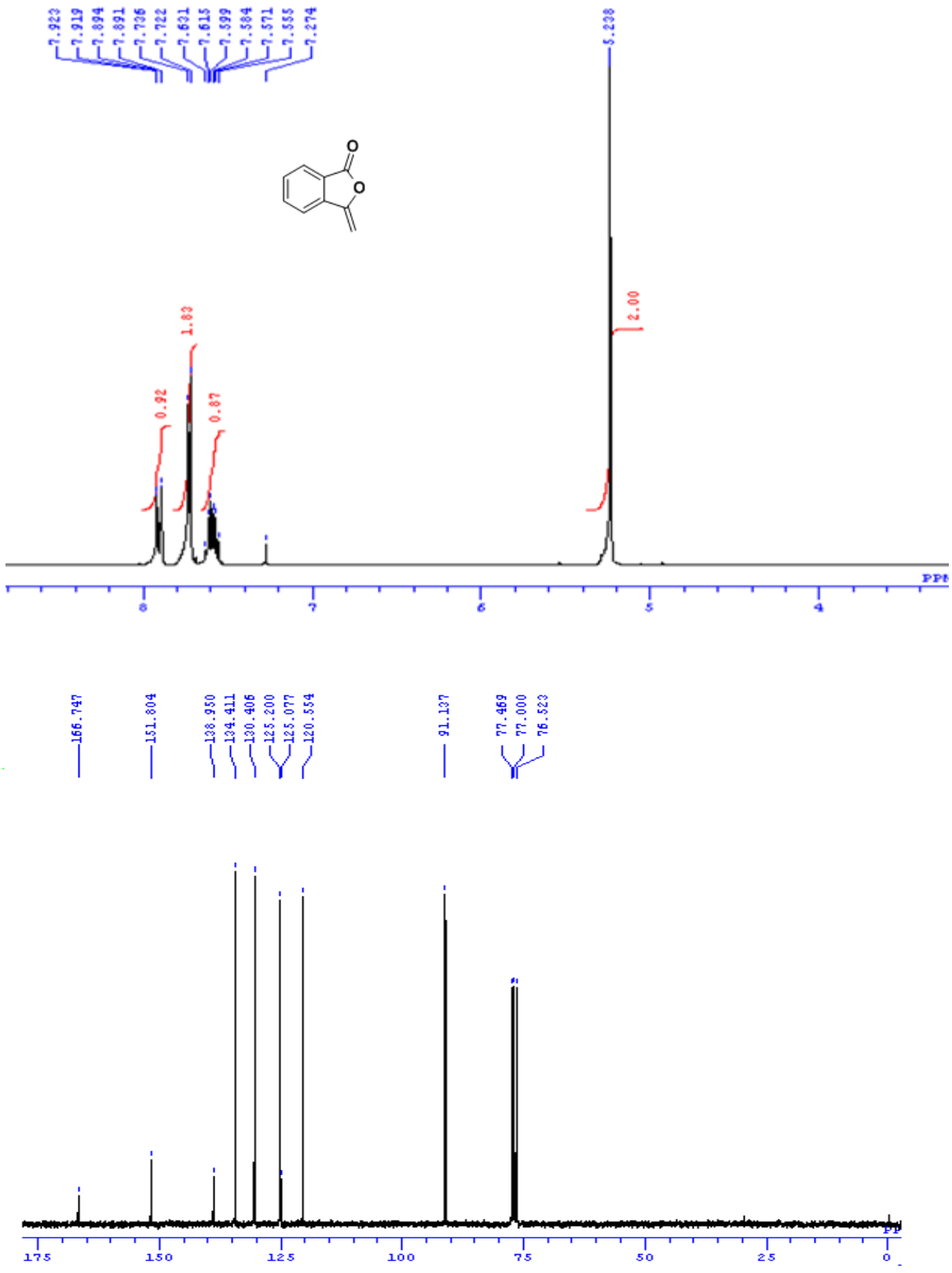
^{1}H and ^{13}C NMR Spectra of 5h



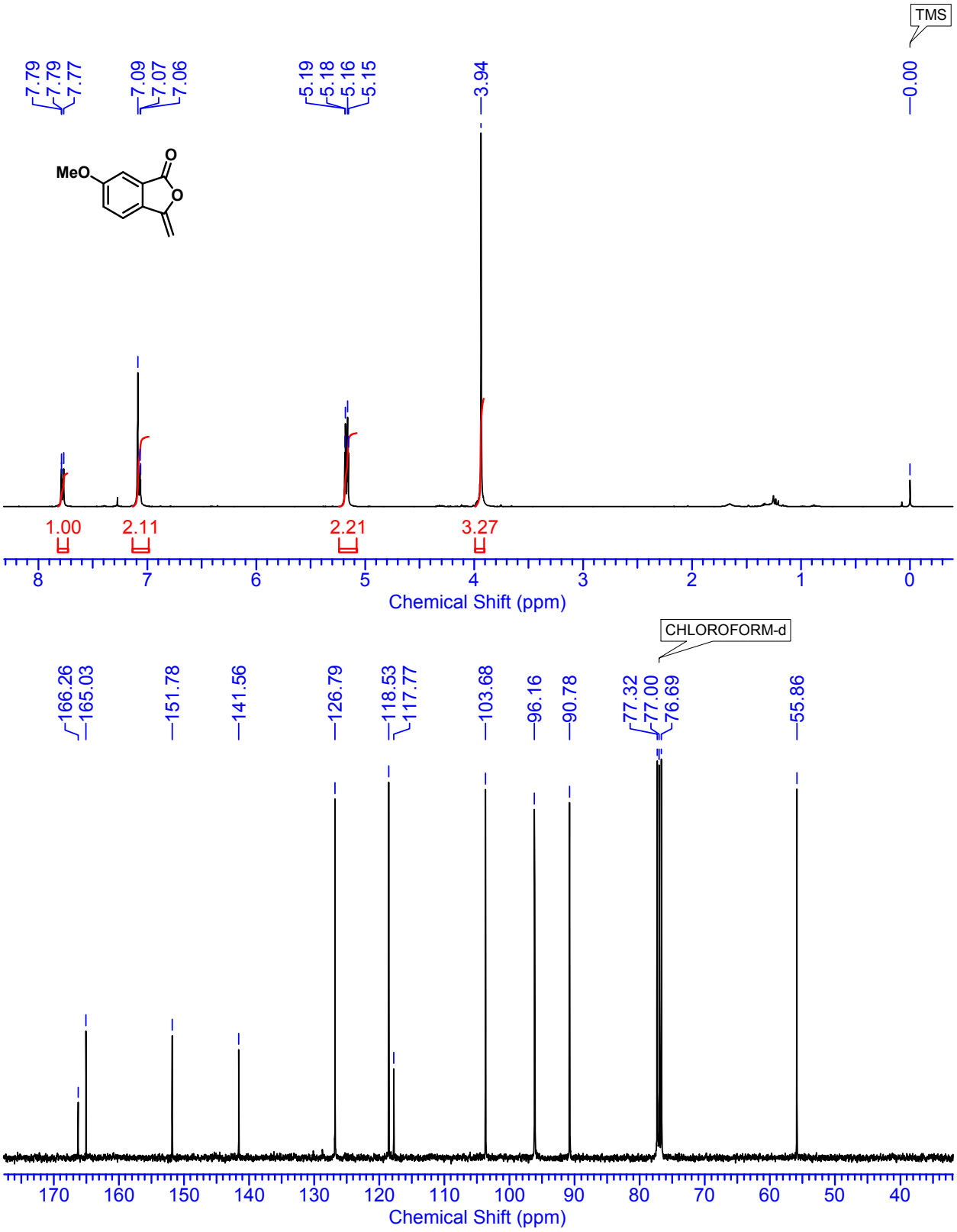
^{1}H and ^{13}C NMR Spectra of 5i



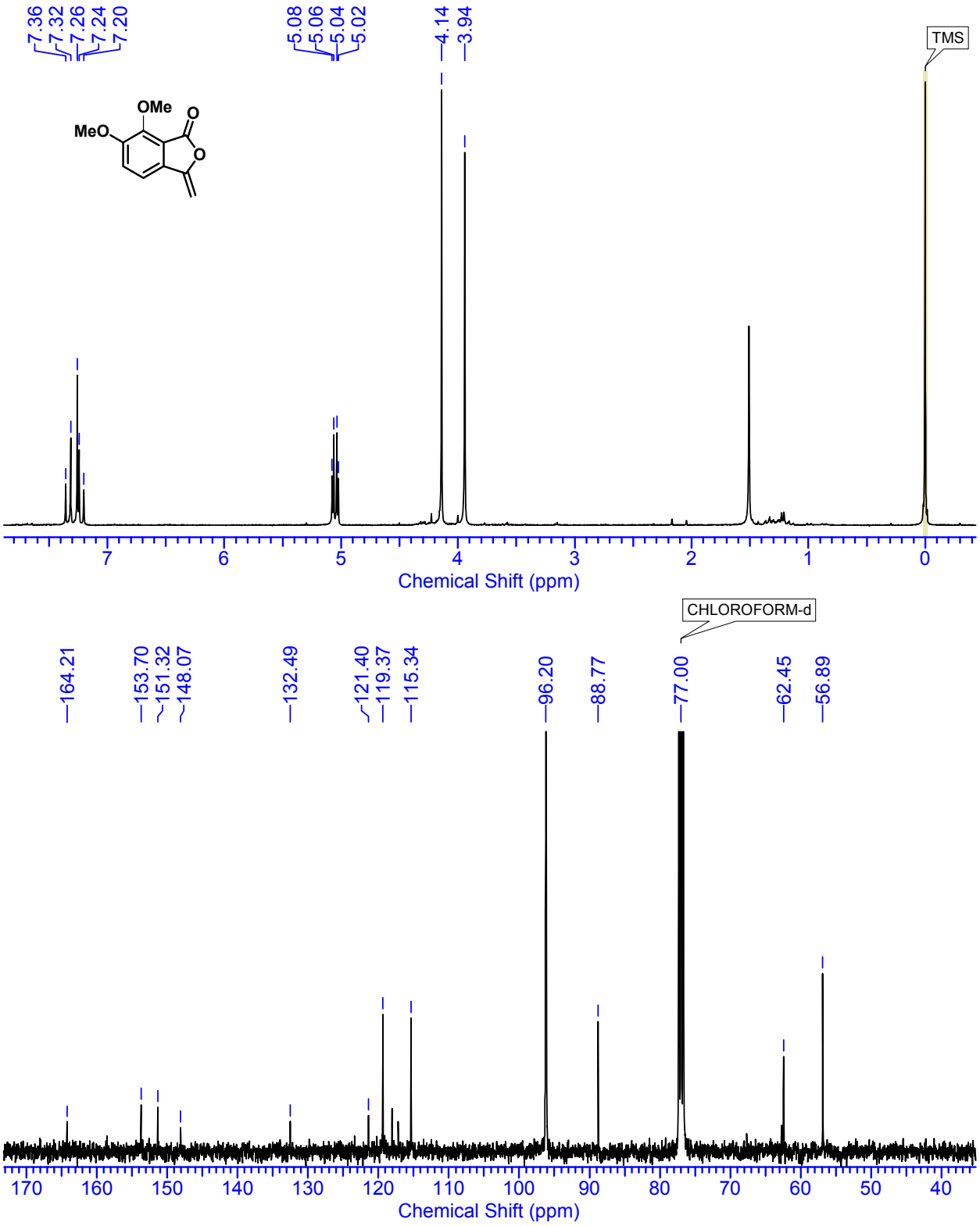
^{1}H and ^{13}C NMR Spectra of 5j



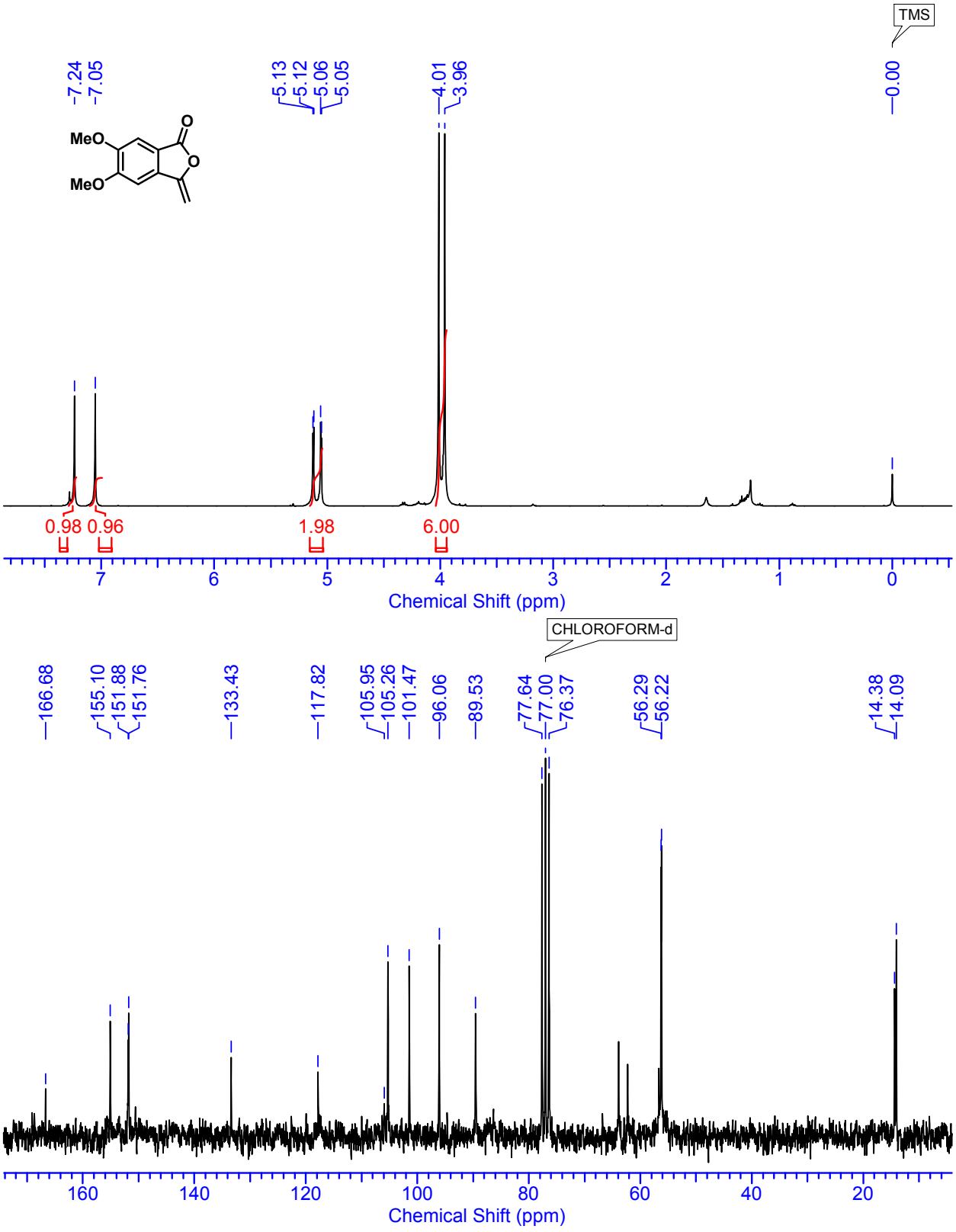
^{1}H and ^{13}C NMR Spectra of 6k



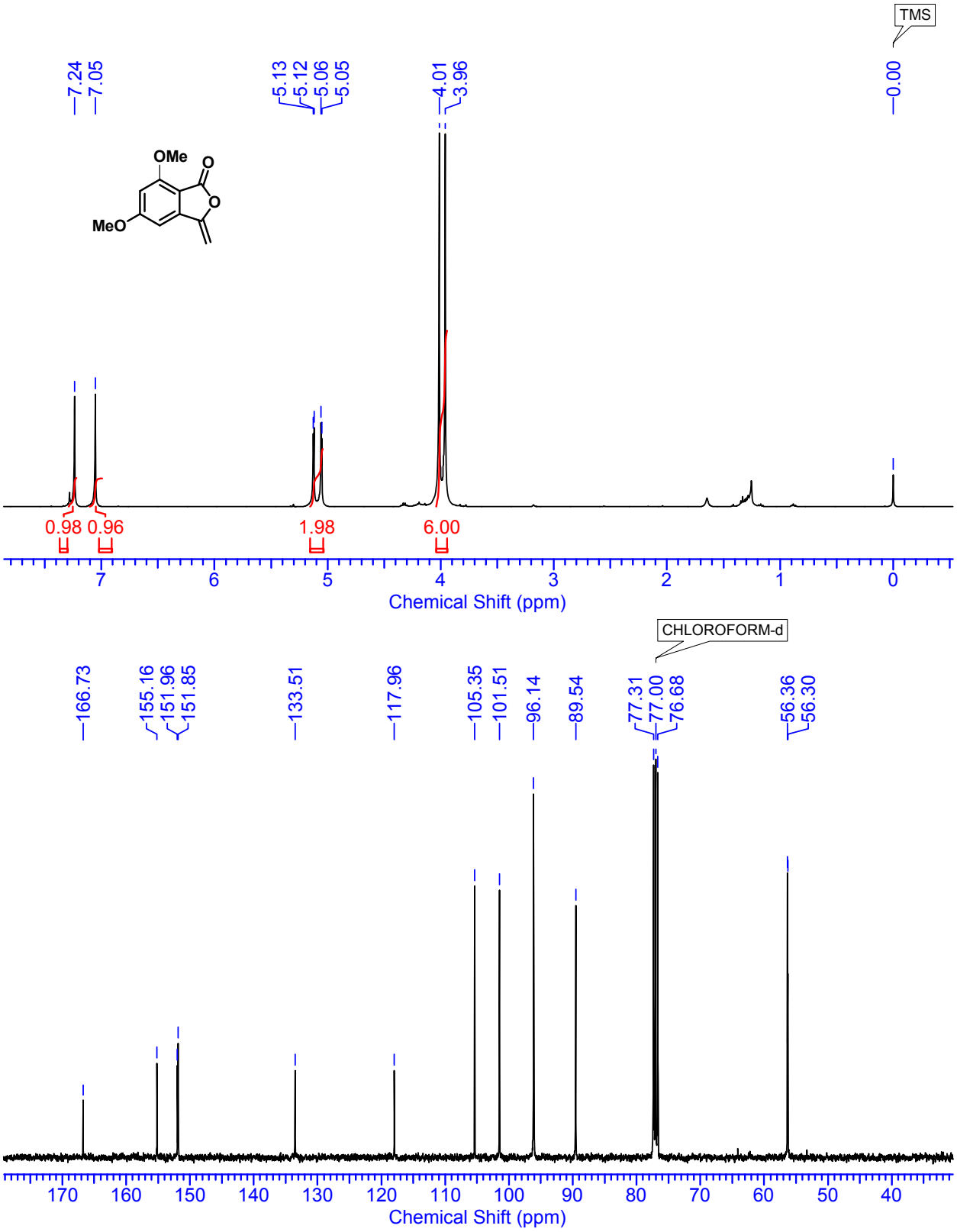
^{1}H and ^{13}C NMR Spectra of 6l



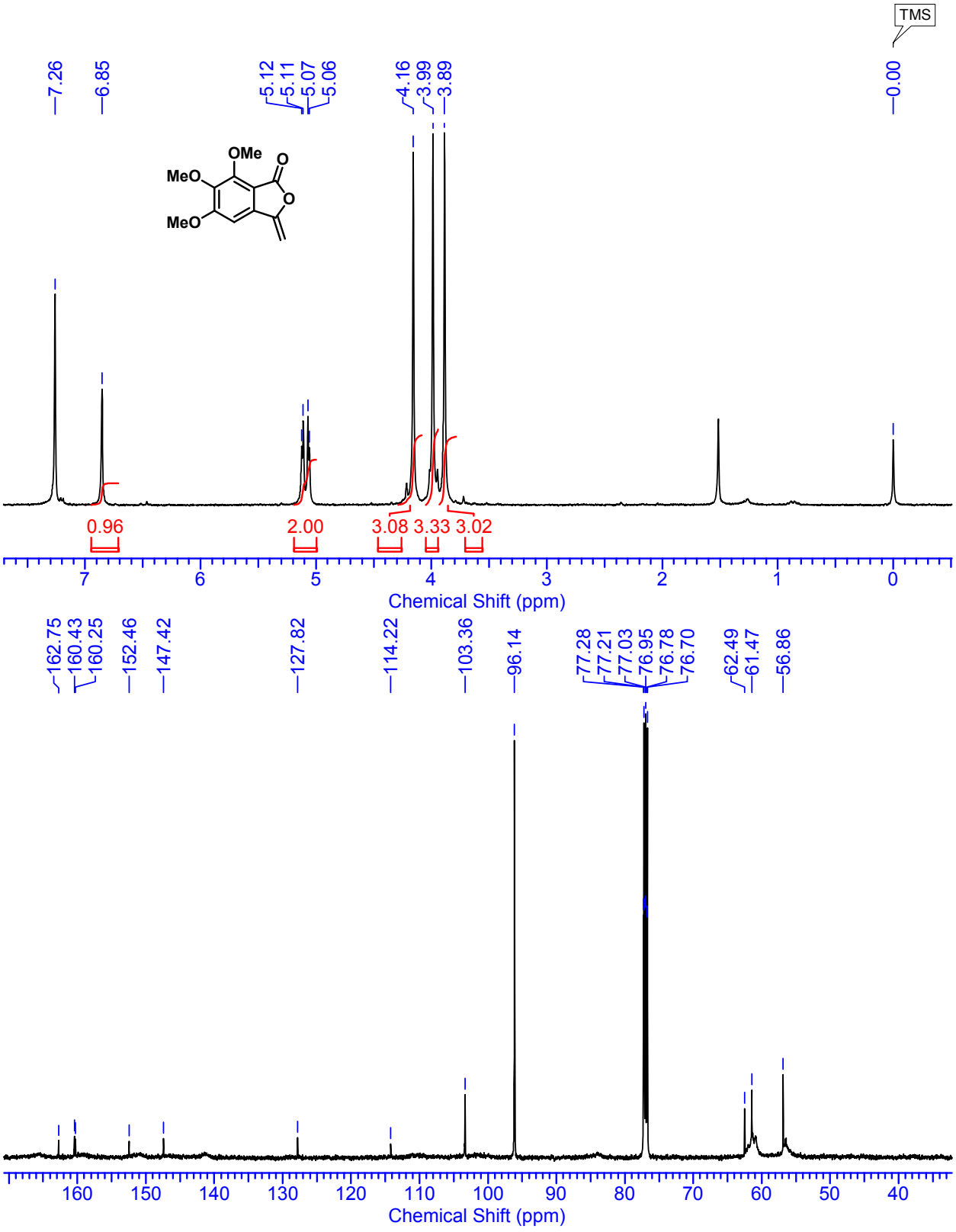
^{1}H and ^{13}C NMR Spectra of 6m



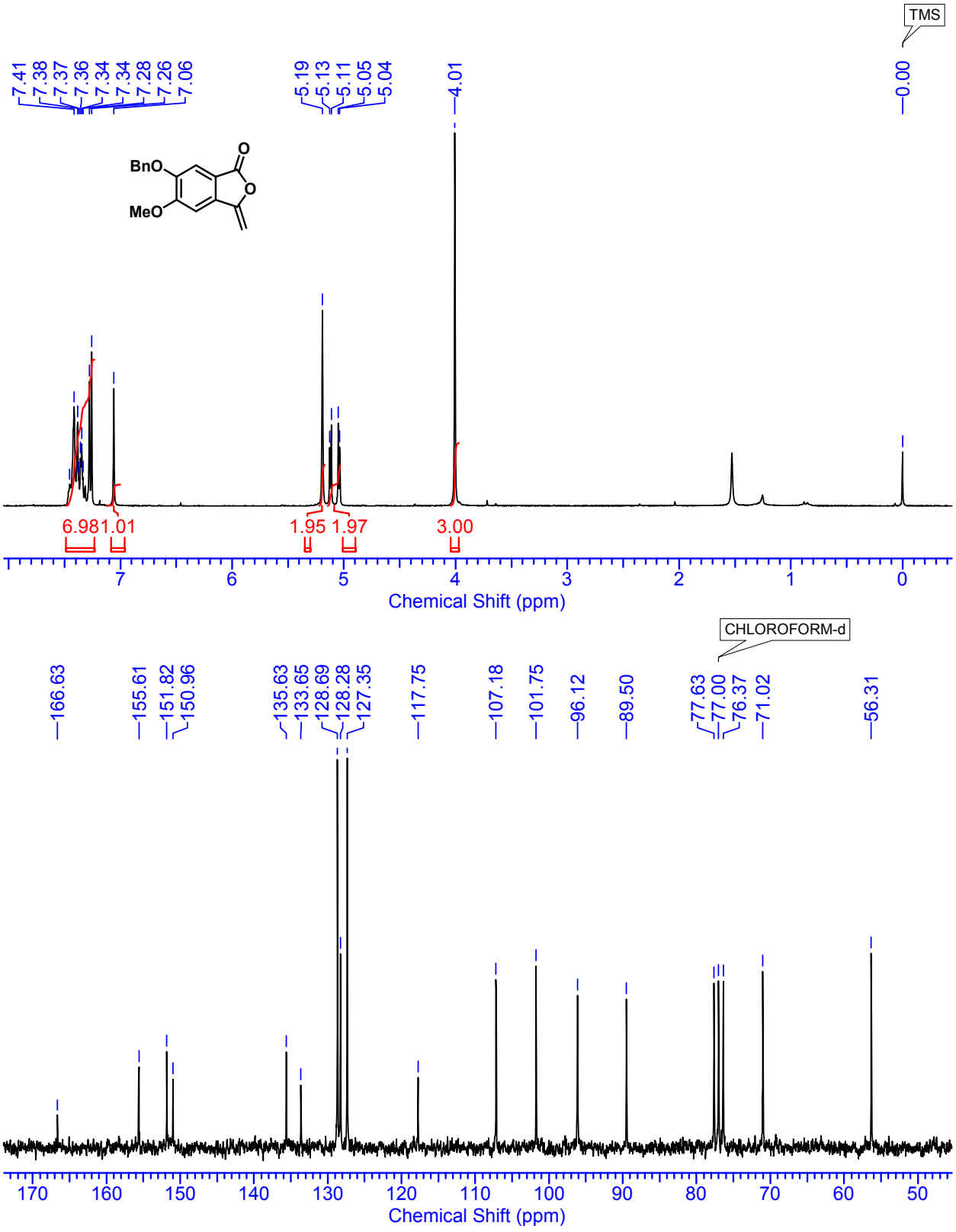
^{1}H and ^{13}C NMR Spectra of 6n



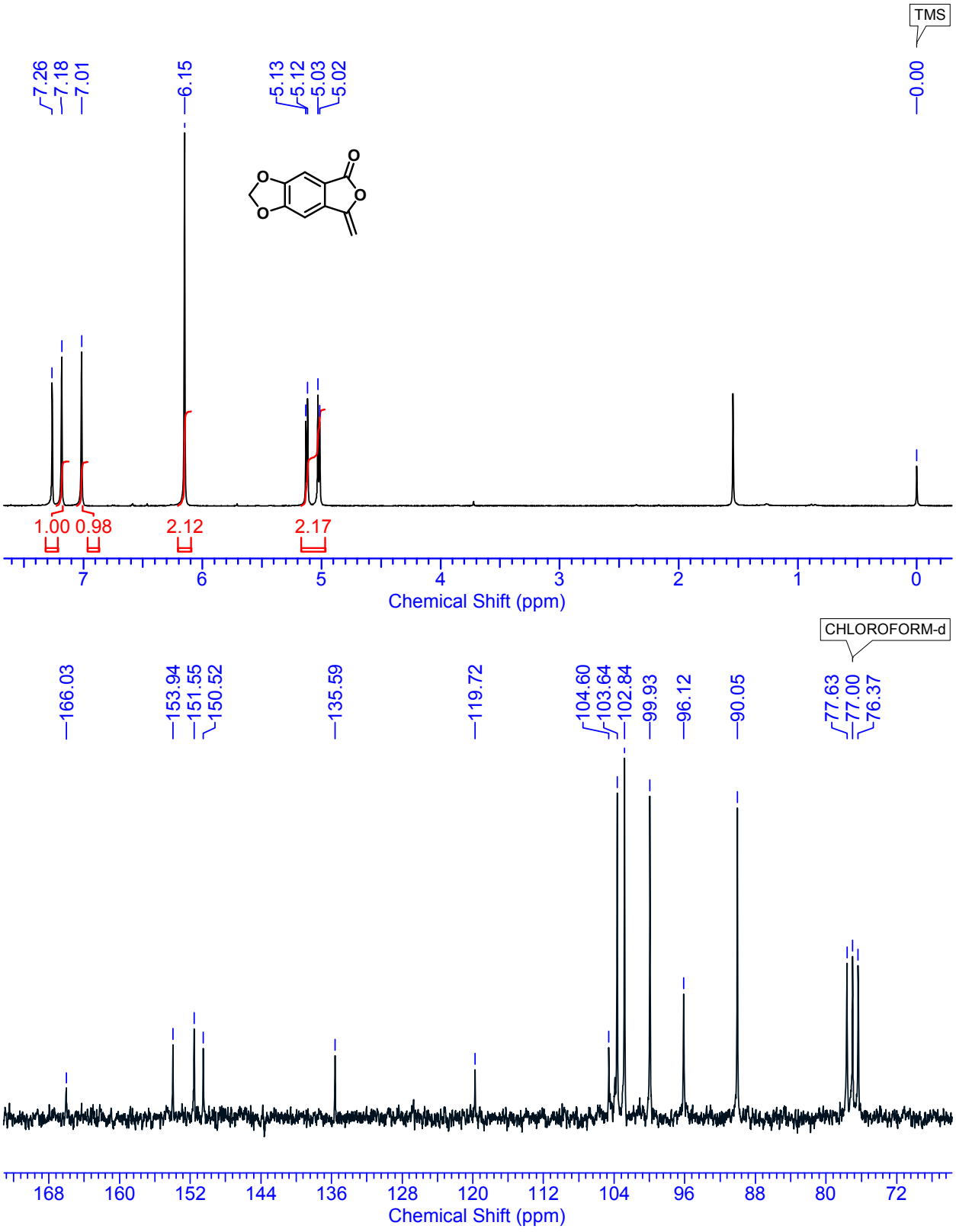
^{1}H and ^{13}C NMR Spectra of 6o



^{1}H and ^{13}C NMR Spectra of 6p

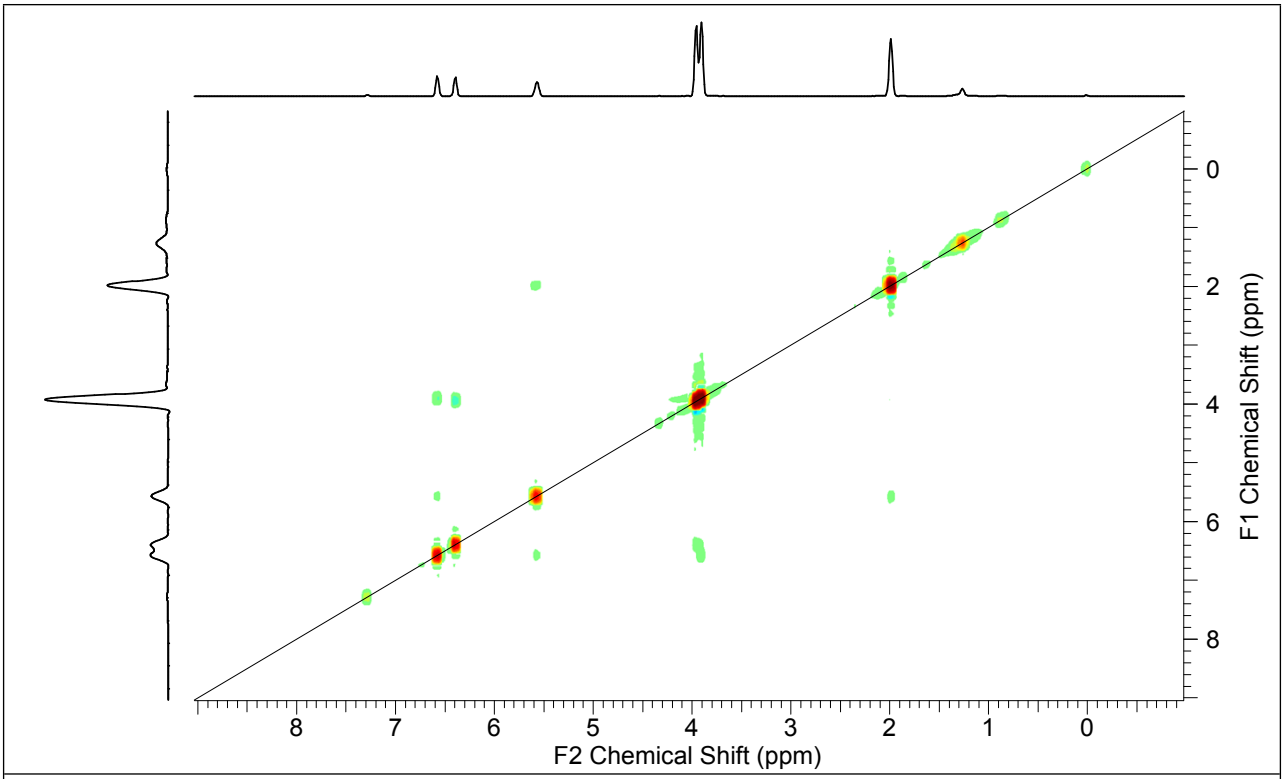


^{1}H and ^{13}C NMR Spectra of 6q

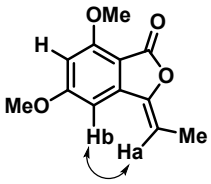


^{1}H and ^{13}C NMR Spectra of 6r

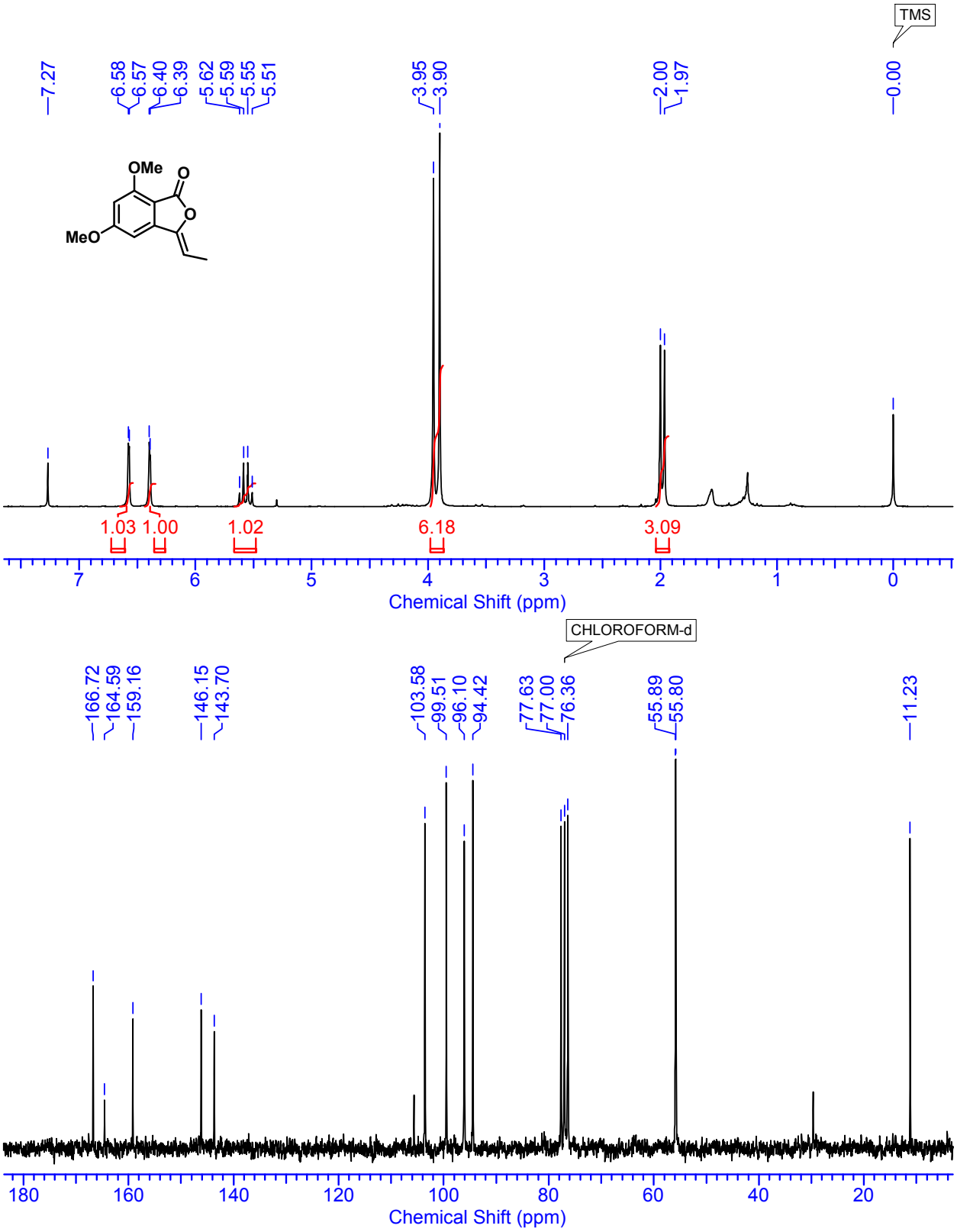
NOESY (500 MHz, $CDCl_3$)



NOESY Studies of Compound 6s.

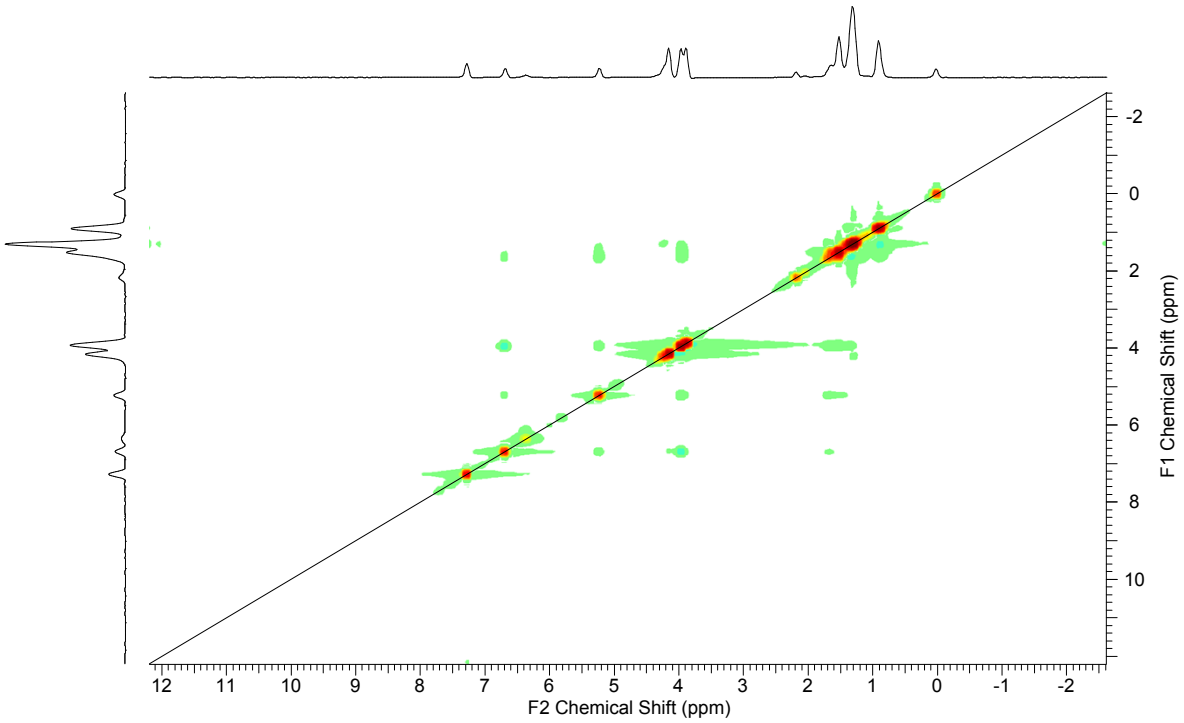


There is a NOE correlation between Ha (δ 5.56, J = 7.1 Hz, q) and Hb (δ 6.57, J = 2.2 Hz, d). These results clearly revealed that the *Z*-stereochemistry of compound 6s is correct.

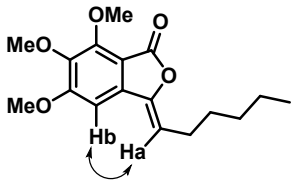


^{1}H and ^{13}C NMR Spectra of 6s

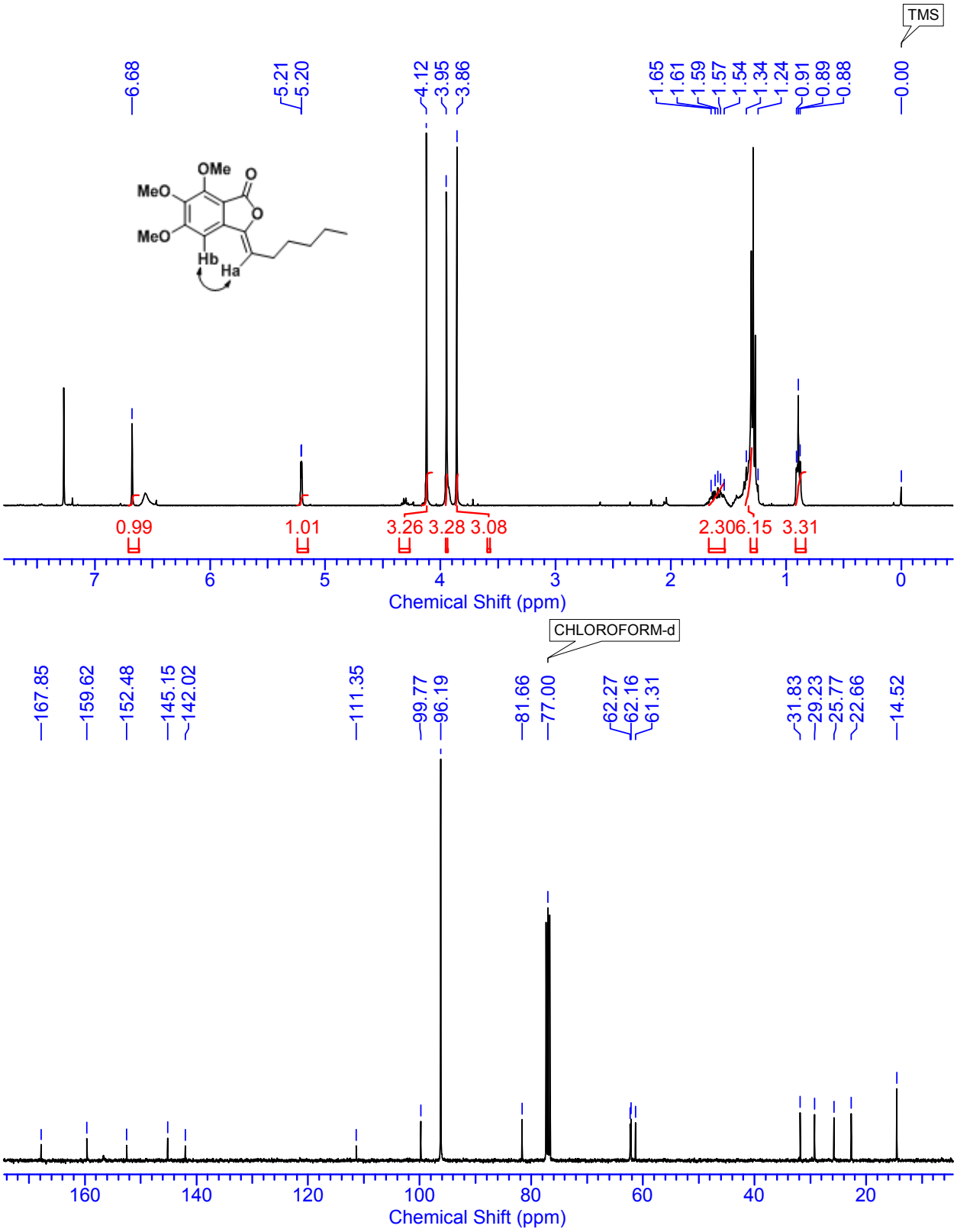
NOESY (500 MHz, $CDCl_3$)



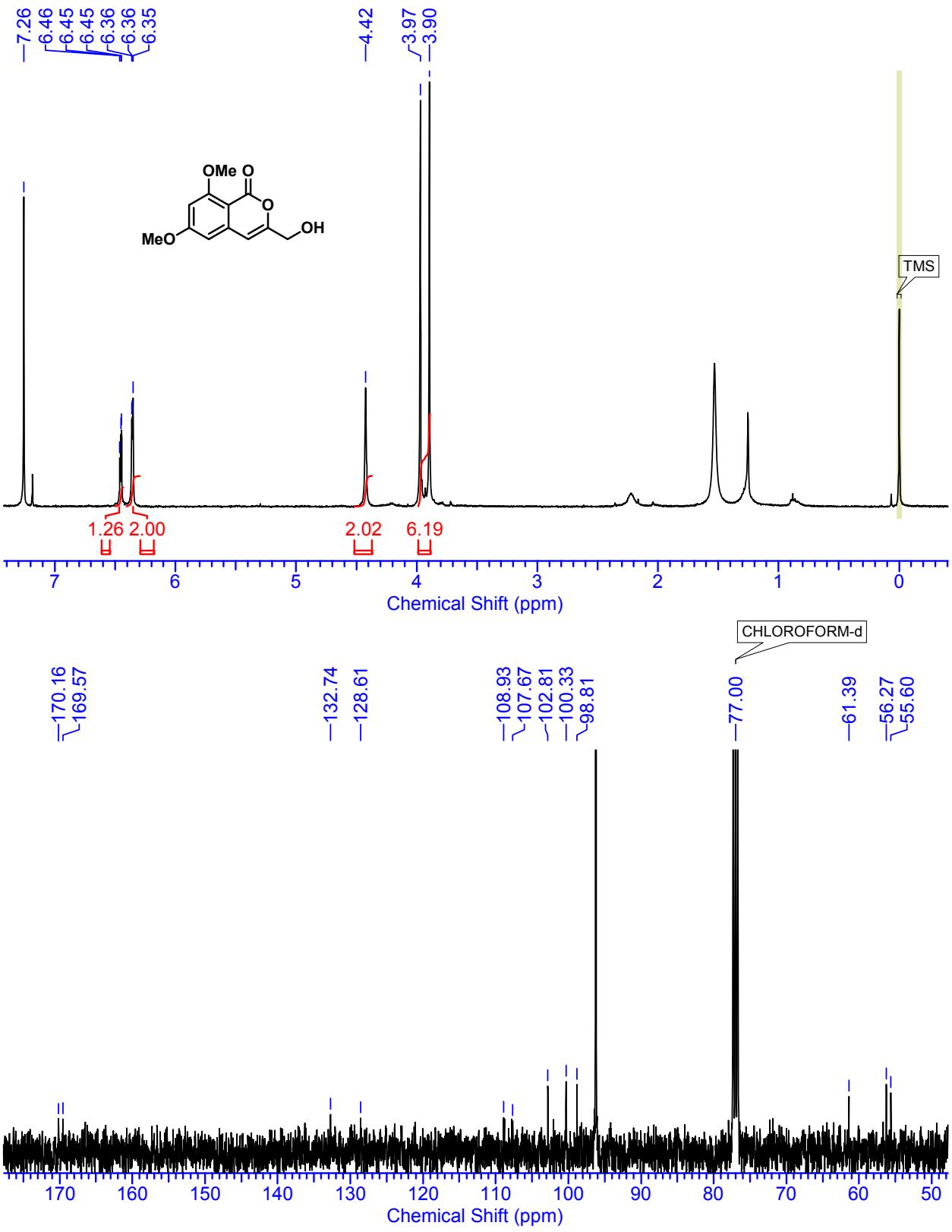
NOESY Studies of Compound 6t



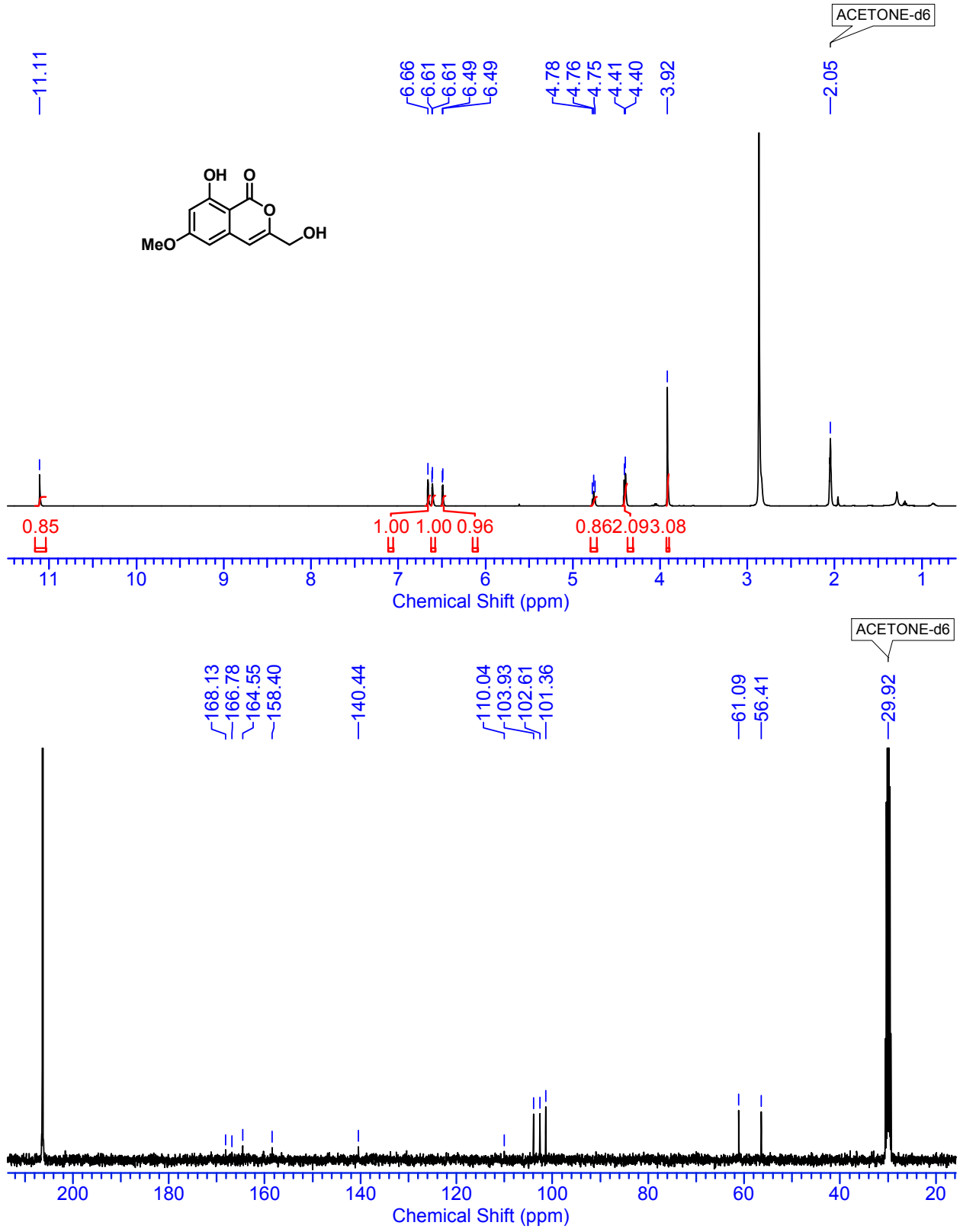
There is a NOE correlation between Ha (δ 5.21, J = 5.2 Hz, d) and Hb (δ 6.68, s). These results clearly revealed that the *Z*-stereochemistry of compound 6t is correct.



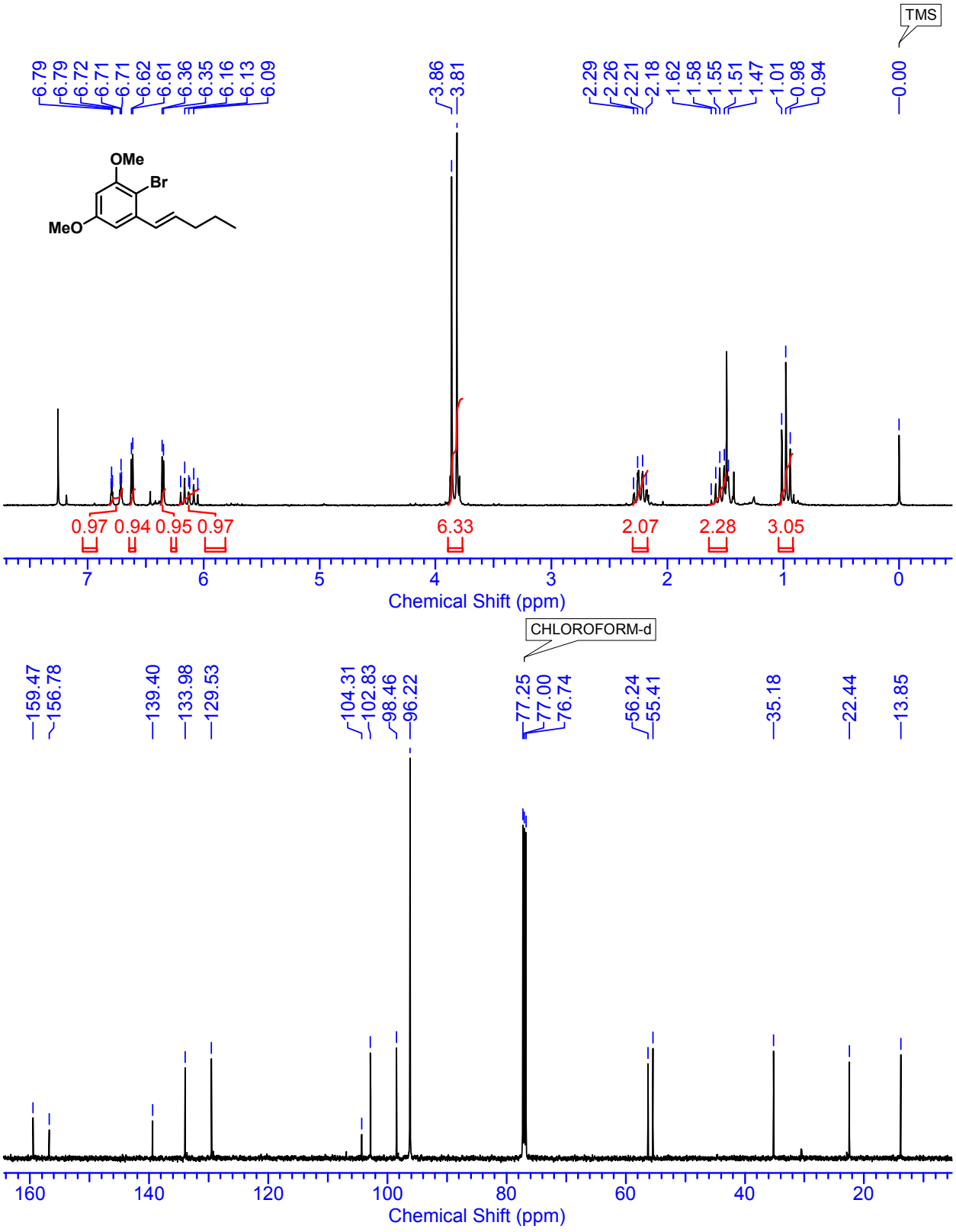
^{1}H and ^{13}C NMR Spectra of 6t



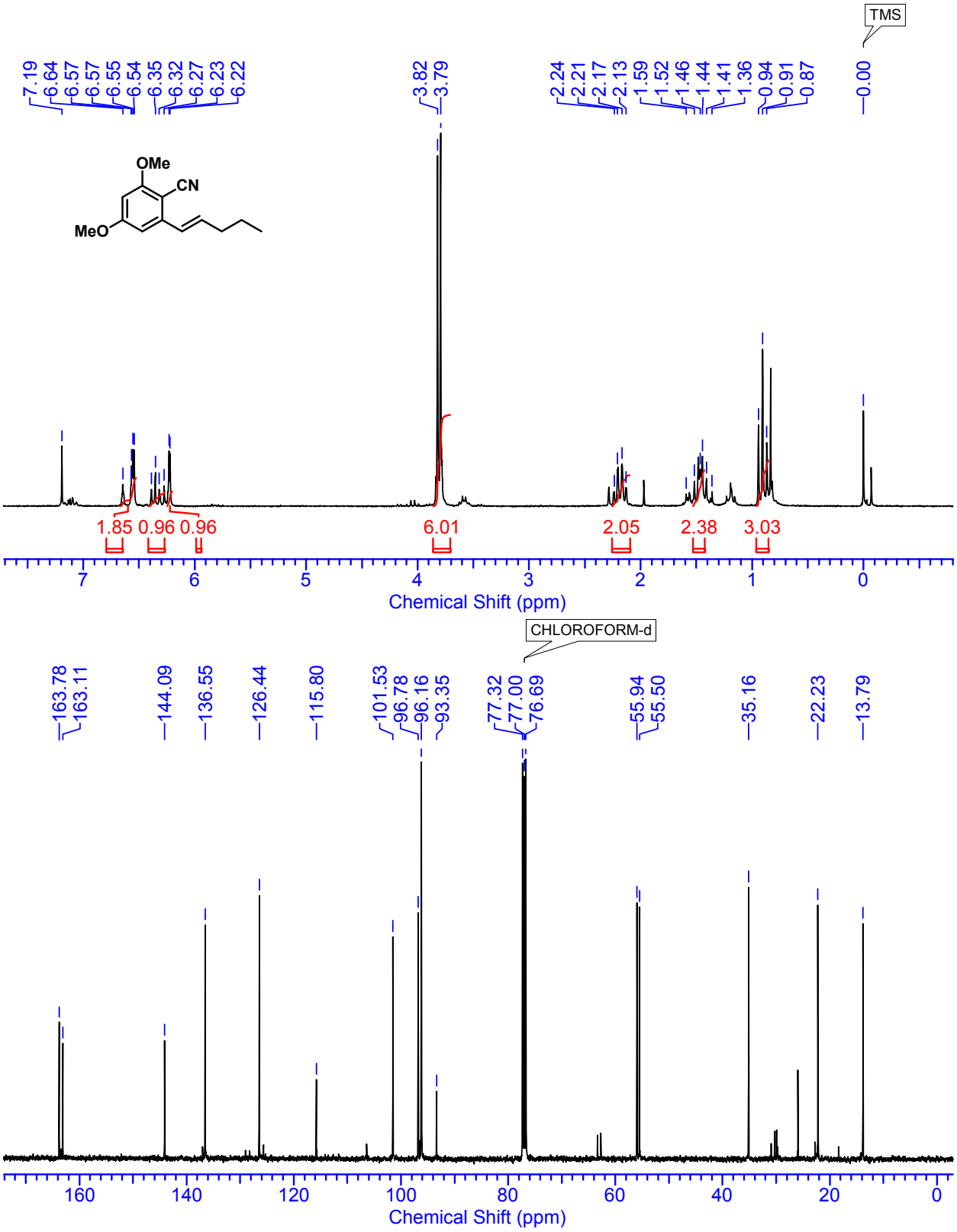
^{1}H and ^{13}C NMR Spectra of 7



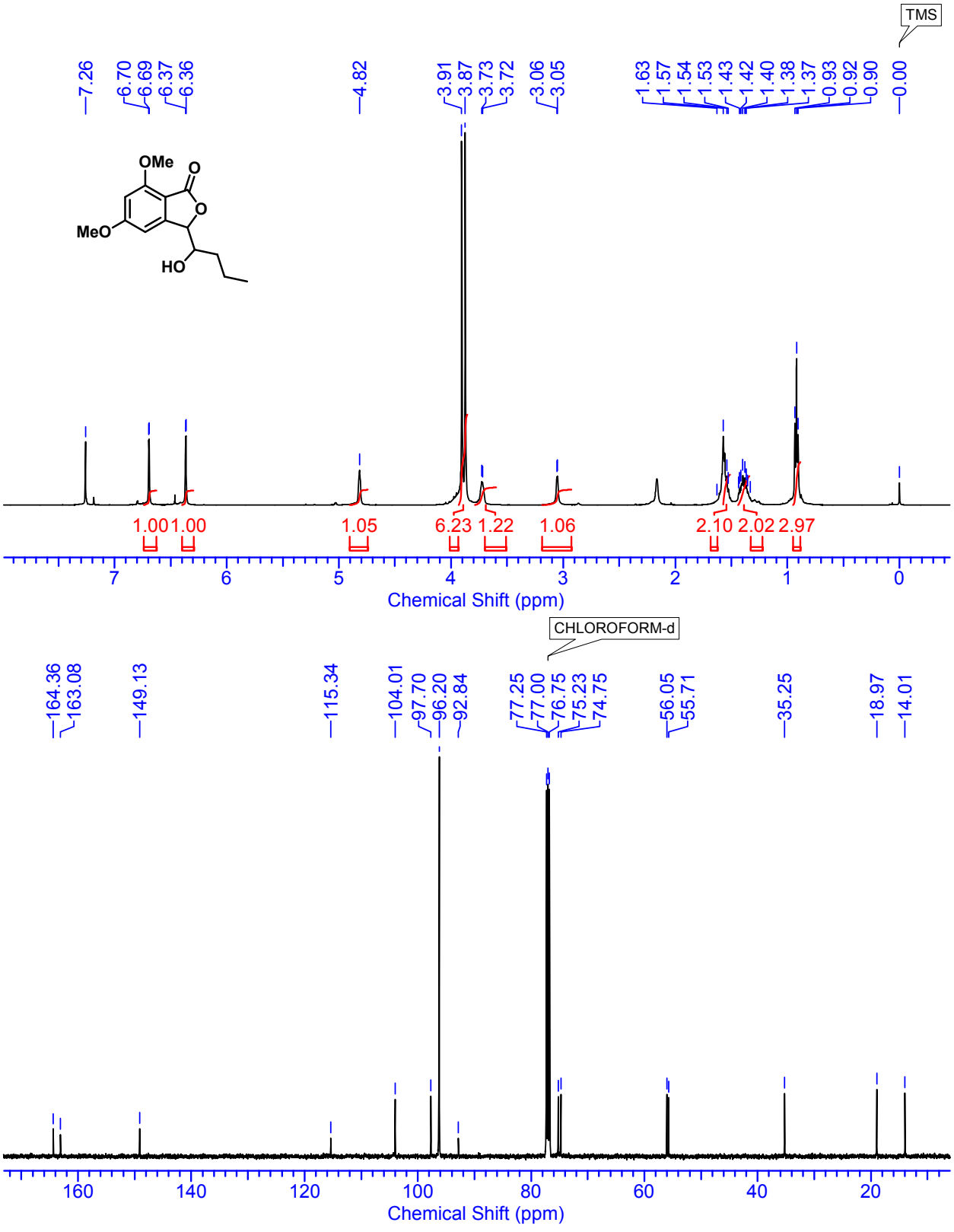
^{1}H and ^{13}C NMR Spectra of 1



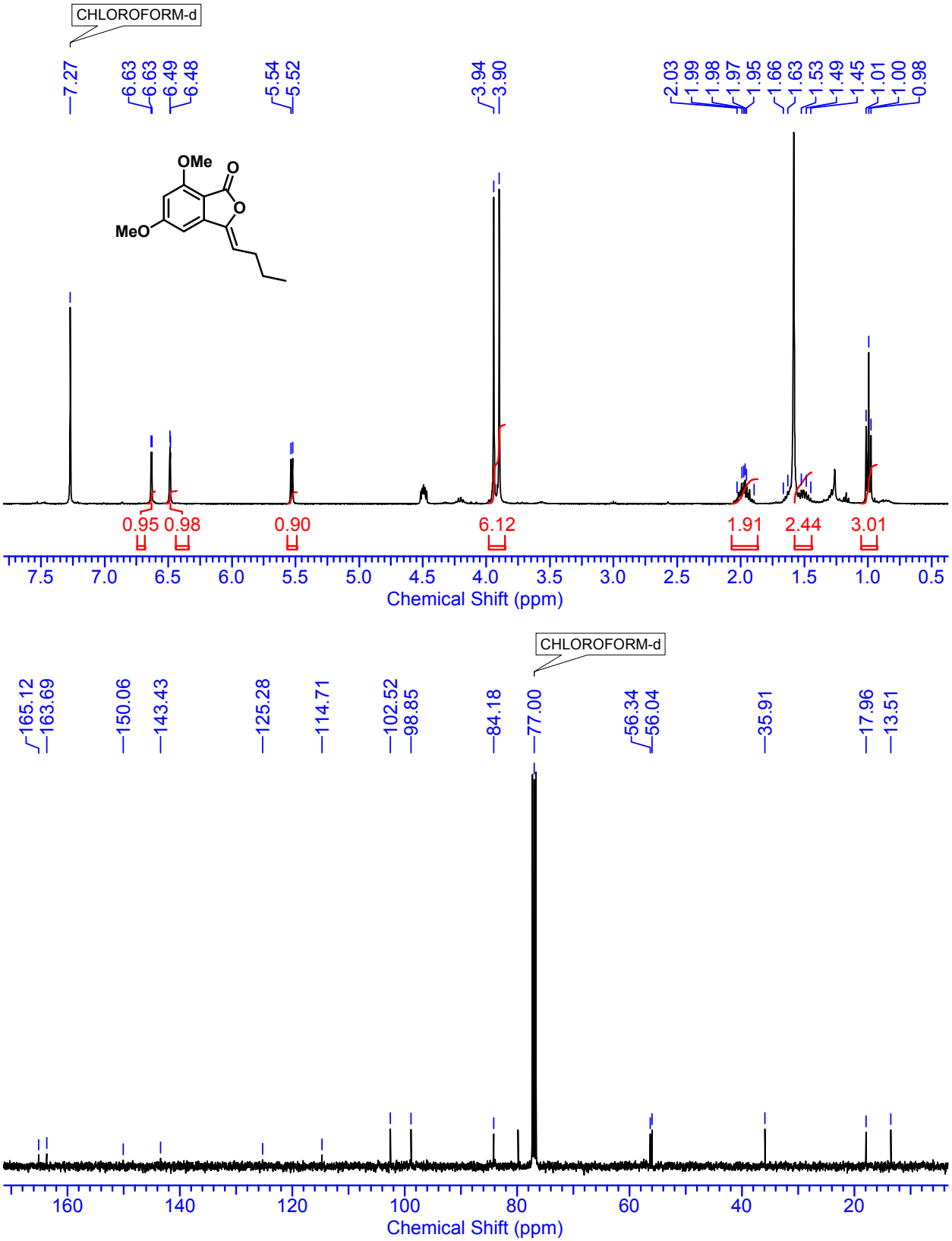
^{1}H and ^{13}C NMR Spectra of 9



^{1}H and ^{13}C NMR Spectra of 10



^{1}H and ^{13}C NMR Spectra of 11



^{1}H and ^{13}C NMR Spectra of 12