

Supplementary Information

Synthesis and Phytotoxicity of 4,5 Functionalized Tetrahydrofuran-2-one

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Synthetic procedures

5-isopropoxyfuran-2(5H)-one **2**

To a two neck round bottomed flask containing isopropyl alcohol (600 mL) 5-hydroxyfuran-2(5H)-one **1** (4 g, 39.9 mmol) and *p*-toluenesulfonic acid (2.30 g, 13.0 mmol) were added. The solution was refluxed at 100 °C for 5 h under N₂ atmosphere. The solvent was removed on rotary evaporator under vacuum and the reaction mixture was quenched with saturated NaHCO₃ (10 mL). After addition of distilled water (20 mL) the aqueous mixture was extracted with dichloromethane (DCM, 3 × 30.0 mL). The combined organic layers was dried with anhydrous Na₂SO₄, filtered and concentrated under reduced pressure. The oily residue was purified by flash column chromatography on silica gel with hexane/ethyl acetate 2:1 by volume (hex/EtOAc 2:1 v/v) as eluent to obtain a yellow oil (3.52 g; 24.8 mmol; 61% yield).

Thin layer chromatography (TLC) retention factor (R_f) 0.61 (hex/EtOAc 2:1 v/v); IR ν/cm⁻¹ 3102, 2979, 2936, 1790, 1754, 1614, 1468, 1383, 1336, 1318, 1111, 1078, 1008, 959, 927, 890, 845, 810; ¹H NMR (300 MHz, CDCl₃) δ 1.27 (3H, d, *J* 6.1 Hz, CH₃), 1.25 (3H, d, *J* 6.1 Hz, CH₃), 4.08 (1H, sep, *J* 6.1 Hz, H6), 5.98 (1H, dd, *J* 1.2 Hz, H5), 6.18 (1H, dd, *J* 1.2 Hz, *J* 5.7 Hz, H3), 7.16 (1H, dd, *J* 1.2 Hz, *J* 5.7 Hz, H4); ¹³C NMR (75 MHz, CDCl₃) δ 22.1 (CH₃), 23.3 (CH₃), 73.8 (C6), 102.3 (C5), 124.8 (C3), 151.0 (C4), 170.9 (C2); MS (EI) *m/z* (%) 127 (15); 115 (3); 98 (7); 83 (100); 71 (10); 55 (34).

5-acetoxifyfuran-2(5H)-one **3**

To an ice cooled solution of 5-hydroxyfuran-2(5H)-one **1** (2.00 g; 20.0 mmol) in DCM (100 mL) under magnetic stirring was added acetic anhydride (3.00 mL; 32.0 mmol) and a solution of 4-dimethylaminopyridine (DMAP,

0.770 g; 6.00 mmol) in DCM (5.00 mL). The volume was reduced to half under vacuum and distilled water (30.0 mL) was added to the mixture. The layers were separated and the aqueous residue was extracted with DCM (2 × 30.0 mL). The combined organic layers was dried with anhydrous Na₂SO₄ and the solvent evaporated under vacuum. The brown oil was purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v), resulting in a yellow oil (2.69 g, 19.0 mmol; 95% yield).

TLC R_f 0.59 (hex/EtOAc 1:1 v/v); IR ν/cm⁻¹ 3103, 2158, 2030, 1788, 1750, 1613, 1432, 1375, 1399, 1206, 1157, 1080, 1019, 997, 923, 875, 817; ¹H NMR (300 MHz, CDCl₃) δ 2.12 (3H, s, CH₃), 6.27 (1H, dd, *J* 1.2 Hz, *J* 5.7 Hz, H3), 6.94 (1H, dd, *J* 1.2 Hz, H5), 7.32 (1H, dd, *J* 1.2 Hz, *J* 5.7 Hz, H4); ¹³C NMR (75 MHz, CDCl₃) δ 20.8 (C7), 93.9 (C5), 125.3 (C3), 150.1 (C4), 169.1 (C6), 169.9 (C2); MS (EI) *m/z* (%): 113 (12); 100 (3); 83 (52); 82 (21); 55 (23); 53 (18); 43 (100); 38(2).

4-(1'-Hydroxy-1'-methylethyl)-5-isopropoxytetrahydrofuran-2-one **4**

A solution of 5-isopropoxyfuran-2(5H)-one **2** (1.00 g; 7.04 mmol) and isopropyl alcohol (250 mL) in a quartz tube was degassed with a flow of nitrogen for 30 min. The solution was irradiated with four low-pressure mercury lamps (4 × 15 W) for two hours. After this period, the solvent was removed under reduced pressure and the residue purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v) to give a colorless oil (1.30g; 6.92 mmol; 91% yield).

TLC R_f 0.54 (hex/EtOAc 1:1 v/v); IR ν/cm⁻¹ 3452, 2975, 2935, 2880, 2362, 2165, 2031, 1763, 1649, 1468, 1420, 1370, 1290, 1218, 1177, 1108, 1015, 937, 921, 873, 832, 793; ¹H NMR (300 MHz, CDCl₃) δ 1.17 (3H, s, CH₃), 1.19 (3H, d, *J* 6.2 Hz, CH₃), 1.20 (3H, d, *J* 6.2 Hz, CH₃), 1.24 (3H, s, CH₃), 2.06 (1H, s, OH), 2.27 (1H, ddd, *J* 9.8 Hz, *J* 6.9 Hz, *J* 3.9 Hz, H4), 2.52 (1H, dd, *J* 6.9 Hz, *J* 18.0 Hz,

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H3), 2.63 (1H, dd, *J* 9.8 Hz, *J* 18.0 Hz, H3'), 3.97 (1H, sep, *J* 6.2 Hz, H6), 5.58 (1H, d, *J* 3.87 Hz, H5); ¹³C NMR (CDCl₃, 75 MHz): δ 21.9 (CH₃), 23.5 (CH₃), 28.2 (CH₃), 28.3 (CH₃), 30.2 (C3), 52.2 (C4), 70.1 (C9), 72.7 (C6), 104.5 (C5), 176.1 (C2); MS (EI), *m/z* (%): 143 (5); 127 (7); 114 (11); 97 (24); 89 (44); 69 (58); 59 (100);.

4-(1'-Hydroxy-1'-methylethyl)-5-acetoxytetrahydrofuran-2-one **5**

A solution of 5-acetoxifyran-2(5*H*)-one **3** (0.428 g; 3.00 mmol) and isopropyl alcohol (250 mL) in a quartz tube was degassed with a flow of nitrogen for 30 min. The solution was irradiated with four low-pressure mercury lamps (4 × 15 W) for three hours. After this period, the solvent was removed under reduced pressure and the residue purified by flash column chromatography on silica gel (hex/EtOAc 1:2 v/v) to give a colorless oil (0.604 g; 2.90 mmol; 99% yield).

TLC R_f 0.44 (hex/EtOAc 1:1 v/v); IR ν/cm⁻¹ 3452, 3484, 2976, 2937, 2365, 2164, 2031, 2020, 1782, 1754, 1646, 1469, 1419, 1370, 1292, 1218, 1149, 1088, 1052, 972, 902, 868; ¹H NMR (300 MHz, CDCl₃) δ 1.09 (3H, s, CH₃), 1.13 (3H, s, CH₃), 2.00 (3H, s, CH₃), 2.37 (1H, ddd, *J* 9.6 Hz, *J* 5.1 Hz, *J* 2.6 Hz, H4), 2.48 (1H, dd, *J* 5.1 Hz, *J* 18.3 Hz, H3), 2.63 (1H, dd, *J* 9.6 Hz, *J* 18.3 Hz, H3'), 5.07 (1H, ls, OH); 6.46 (1H, d, *J* 2.6 Hz, H5); ¹³C NMR (CDCl₃, 75 MHz): δ 21.0 (C7), 27.3 (C10), 27.1 (C9), 29.2 (C3), 50.7 (C4), 69.7 (C8), 96.6 (C5), 169.5 (C6), 175.8 (C2); MS (EI), *m/z* (%): 127 (3), 115 (2), 97 (4), 84 (12), 71 (9), 69 (16), 59 (45), 43 (100), 41 (16).

Methyl 3-methoxy-4-oxobutanoate **6**

A solution of 5-isopropoxyfuran-2(5*H*)-one **2** (1.08 g; 7.60 mmol), anhydrous methanol (300 mL) and benzophenone (1.40g; 7.69 mmol) in a borosilicate reactor was degassed with a flow of nitrogen for 30 min. The solution was irradiated with a high pressure mercury lamp (125 W) for two hours. The solvent was removed under reduced pressure and the residue purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v) to give a yellow oil (0.650 g; 4.45 mmol; 58% yield).

TLC R_f 0.40 (hex/EtOAc 1:1 v/v); IR ν/cm⁻¹ 3443, 2953, 2834, 2359, 2158, 1730, 1438, 1366, 1266, 1200, 1166, 1108, 1068, 991, 887, 844, 735, 530; ¹H NMR (300 MHz, CDCl₃) δ 2.67 (1H, dd, *J* 6.6 Hz, *J* 16.5 Hz, H2), 2.78 (1H, dd, *J* 4.8 Hz, *J* 16.5 Hz, H2'), 3.49 (3H, s, CH₃), 3.69 (3H, s, CH₃), 3.95 (1H, ddd, *J* 4.8 Hz, *J* 6.6 Hz, *J* 0.8 Hz, H3), 9.70 (1H, s, H4); ¹³C NMR (CDCl₃, 75 MHz): δ 35.6 (C2), 52.0 (C5), 59.0 (C6), 81.9 (C3), 170.5 (C1), 202.5 (C4); MS (EI), *m/z* (%): 117 (43), 101 (10), 86 (24), 84 (45), 75 (100), 59 (32), 58 (43), 51 (27), 49 (83), 44 (61), 43 (22), 41 (20).

General method for the preparation of 4-Formyl-5,5-dimethyltetrahydrofuran-2-one **7**, 4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **8** and 4-(diethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **9**

A solution of 4-(1'-hydroxy-1'-methylethyl)-5-isopropoxytetrahydrofuran-2-one **4**, sulfuric acid (1.50 mL; 30% v/v) and either methanol, ethanol or acetonitrile (50.0 mL) was stirred and the solvent was removed under reduced pressure. The residue was neutralized with NaHCO₃ (20 mL; 20% m/v) and extracted with ethyl acetate (4 × 20 mL). The combined organic layers was dried with anhydrous Na₂SO₄, filtered and concentrated under vacuum. The residue was purified by flash column chromatography on silica gel (hex/EtOAc 1:2 v/v) to afford the aldehyde **7**, acetal **8** and **9** (Table S1).

Table S1. Yields and conditions for the synthesis of the aldehyde **7**, acetal **8** and acetal **9** from the reaction of compound **4** with sulfuric acid (1.50 mL; 30% v/v) in methanol, ethanol or acetonitrile (50 mL)

Compound 6 mass / g	Solvent	Reaction time / h	Yield / % 7	Yield / % 8	Yield / % 9
0.140	Methanol	2	15	48	–
0.100	Ethanol	55	28	–	54
0.144	Acetonitrile ^a	2	50	–	–

^aAldehyde **7** is unstable as observed by successive GC analysis, thus it was not purified anymore.

4-Formyl-5,5-dimethyltetrahydrofuran-2-one **7**:

TLC R_f 0.32 (hex/EtOAc 1:2 v/v); IR ν/cm⁻¹ 3429, 2980, 2936, 2362, 2161, 1755, 1719, 1464, 1421, 1389, 1376, 1266, 1251, 1120, 1044, 957, 936, 921, 836; ¹H NMR (300 MHz, CDCl₃) δ 1.38 (3H, s, CH₃), 1.66 (3H, s, CH₃), 2.65 (1H, dd, *J* 8.5 Hz, *J* 17.7 Hz, H3), 3.09 (1H, dd, *J* 9.3 Hz, *J* 17.7 Hz, H3'), 3.22 (1H, ddd, *J* 8.5 Hz, *J* 9.3 Hz, *J* 1.7 Hz, H4), 9.76 (1H, d, *J* 1.7 Hz, H8); ¹³C NMR (CDCl₃, 75 MHz): δ 24.0 (C7), 29.2 (C6), 29.3 (C3), 56.8 (C4), 84.0 (C5), 173.9 (C2), 197.5 (C8); MS (EI), *m/z* (%): 127 (25), 114 (8); 97 (11); 84 (62); 69 (50); 59 (100); 55 (87).

4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **8**:

TLC R_f 0.70 (hex/EtOAc 1:2 v/v); IR ν/cm⁻¹ 2977, 2938, 2834, 2158, 1976, 1765, 1445, 1422, 1385, 1372, 1273, 1256, 1225, 1186, 1119, 1069, 1052, 1011, 953, 936, 920, 837; ¹H NMR (300 MHz, CDCl₃) δ 1.30 (3H, s, CH₃), 1.46 (3H, s, CH₃), 2.46-2.63 (3H, m, H3 and H4), 3.30 (3H, s, CH₃), 3.34 (3H, s, CH₃), 4.35 (1H, d, *J* 9.0 Hz, H8); ¹³C NMR (CDCl₃, 75 MHz): δ 22.4 (C6), 28.9 (C7), 31.8 (C3), 46.9 (C4), 52.5 (CH₃), 54.1 (CH₃), 85.5 (C5), 103.9 (C8), 175.0 (C2). MS (EI), *m/z* (%): 157 (1), 141 (2), 131 (2), 113 (1), 99 (4), 75 (100), 71 (66), 55 (9), 47 (21), 43 (43), 41 (38).

4-(diethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **9:**

TLC R_f 0,88 (hex/EtOAc 1:2 v/v); IR ν/cm^{-1} 2976, 2932, 2882, 2159, 1976, 1767, 1445, 1422, 1385, 1372, 1270, 1254, 1225, 1186, 1119, 1069, 1052, 1011, 953, 936, 837, 796; ^1H NMR (300 MHz, CDCl_3) δ 1,18 (6H, t, J 14.0 Hz, H10 and H12), 1.30 (3H, s, CH_3), 1.47 (3H, s, CH_3), 2.50-2.61 (3H, m, H3 and H4), 3.37-3.75 (4H, m, H9 and H11), 4.46-4.48 (1H, m, H8); ^{13}C NMR (CDCl_3 , 75 MHz): δ 15.3 (CH_3), 15.5 (CH_3), 22.4 (C6), 29.0 (C7), 32.0 (C3), 47.8 (C4), 61.3 (CH_2), 62,8 (CH_2), 85.7 (C5), 102.4 (C8), 175.2 (C-2); MS (EI), m/z (%): 201 (0.1), 171 (2), 155 (3), 113 (10), 103 (69), 85 (88), 75 (51), 57 (60), 47 (100), 43 (65), 41 (36).

(Z)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **10 and (E)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **11****

An ice cooled solution of potassium *tert*-butoxyde (0.408 g, 3.60 mmol), trimethyl phosphonoacetate (290 μL , 1.75 mmol) in anhydrous tetrahydrofuran (THF, 10.0 mL) under nitrogen atmosphere was stirred for 40 minutes. The ice bath was removed and the crude aldehyde **7** (0.50 g) in dry THF (5.0 mL) was added to the reaction mixture. After 30 minutes the solvent was removed under vacuum and the residue diluted with water (5 mL). The aqueous mixture was extracted with diethyl ether (3 \times 10 mL) and ethyl acetate (1 \times 10 mL). The combined organic layers was dried with anhydrous Na_2SO_4 , filtered and concentrated under vacuum resulting in a yellow oil. After purification on flash column chromatography on silica gel (hex/EtOAc 2:1 v/v), the alkenes were obtained as a yellow solid (0.038 g; 0.19 mmol; 20% yield of isomer *Z*); (0.045 g; 0.23 mmol; 22% yield of isomer *E*) and (0.262 g; 1.32 mmol; mixture of *Z* and *E* isomers). The yields were calculated from the lactone **4**.

(Z)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **10:**

TLC R_f 0,49 (hex/EtOAc 2:1 v/v); melting point (mp): 78.9-79.8 $^\circ\text{C}$; IR ν/cm^{-1} 2980, 2952, 2362, 2166, 1769, 1717, 1650, 1439, 1389, 1376, 1264, 1248, 1209, 1174, 1118, 1076, 993, 978, 956, 934, 920, 899, 830; ^1H NMR (300 MHz, CDCl_3) δ 1.29 (3H, s, CH_3), 1.43 (3H, s, CH_3), 2.43 (1H, dd, J 9.3 Hz, J 17.6 Hz, H3'), 2.77 (1H, dd, J 8.4 Hz, J 17.6 Hz, H3), 3.70 (3H, s, OCH_3), 4.31-4.41 (1H, m, H4), 5.94 (1H, dd, J 0.7 Hz, J 11.5 Hz, H9), 6.06 (1H, dd, J 10.2 Hz, J 11.5 Hz, H8); ^{13}C NMR (CDCl_3 , 75 MHz): δ 23.1 (C7), 27.8 (C6), 35.8 (C3), 43.2 (C4), 51.6 (C11), 87.0 (C5), 123.0 (C9), 144.9 (C8), 166.2 (C10), 175.0 (C2); MS (EI), m/z (%): 183 (3), 167(1), 151 (6), 139 (4), 140 (43), 123 (17), 112 (31), 111 (31) 109 (13), 108 (43), 97

(31), 95 (10), 82 (38), 81 (73), 79 (16), 69 (11), 67 (10), 59 (12), 53 (80), 43 (100), 41 (34).

(E)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **11:**

TLC R_f 0,42 (hex/EtOAc 2:1 v/v); mp: 43.8-45.0 $^\circ\text{C}$; IR ν/cm^{-1} 2956, 2924, 2858, 2362, 2166, 1770, 1721, 1659, 1460, 1437, 1389, 1376, 1278, 1263, 1214, 1143, 1126, 1100, 1032, 977, 957, 936, 917, 866, 835; ^1H NMR (300 MHz, CDCl_3) δ 1.25 (3H, s, CH_3), 1.46 (3H, s, CH_3), 2.60 (1H, dd, J 11.1 Hz, J 17.4 Hz, H3'), 2.68 (1H, dd, J 8.3 Hz, J 17.4 Hz, H3), 3.03 (1H, dddd, J 11.1 Hz, J 8.4 Hz, J 8.3 Hz, J 1.1 Hz, H4), 3.73 (3H, s, OCH_3), 5.92 (1H, dd, J 1.1 Hz, J 15.6 Hz, H9), 6.80 (1H, dd, J 8.4 Hz, J 15.6 Hz, H8); ^{13}C NMR (CDCl_3 , 75 MHz): δ 23.0 (C7), 27.3 (C6), 34.3 (C3), 48.7 (C4), 52.0 (C11), 86.2 (C5), 124.4 (C9), 143.4 (C8), 166.1 (C10), 174.4 (C2); MS (EI), m/z (%): 183 (3), 167(1), 151 (6), 140 (39), 123 (2), 112 (45), 111 (31) 109 (12), 108 (34), 97 (31), 95 (7), 82 (41), 81 (97), 80 (16), 79 (11), 69 (9), 67 (12), 59 (17), 53 (83), 43 (100), 41 (34).

Methyl 3-(5-oxotetrahydrofuran-3-yl)propanoate **12**

A mixture of alkenes **10** and **11** (0.240 g; 1.21 mmol), Pd/C (0.030 g; 10%) and ethyl acetate (100 mL) was stirred at room temperature under hydrogen atmosphere for five hours. The mixture was filtered, the solvent evaporated under reduced pressure and the residue purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v) to give **12** as a white solid (0.238 g; 1.19 mmol; 98% yield).

TLC R_f 0,63 (hex/EtOAc 1:1 v/v); mp: 35.2-35.8 $^\circ\text{C}$; IR ν/cm^{-1} 2977, 2952, 2361, 2160, 1762, 1731, 1389, 1375, 1255, 1196, 1167, 1123, 1096, 1005, 956, 935, 917, 832; ^1H NMR (300 MHz, CDCl_3) δ 1.25 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.51-1.67 (1H, m, H8), 1.75-1.90 (1H, m, H8), 2.13-2.42 (4H, m, H9, H4 and H3'), 2.55-2.64 (1H, m, H3), 3.67 (3H, s, OCH_3); ^{13}C NMR (CDCl_3 , 75 MHz): δ 22.0 (C7), 24.9 (C8), 27.5 (C6), 32.3 (C9), 34.7 (C3), 45.3 (C4), 52.0 (C11), 86.7 (C5), 173.2 (C10), 175.3 (C2); MS (EI), m/z (%): 185 (7), 182 (6), 153 (15), 151 (6), 125 (7), 124 (7), 114 (41), 97 (9), 83 (15), 82 (46), 81 (12), 74 (13), 72 (16), 69 (16), 67 (13), 59 (35), 55 (100), 54 (33), 53 (14), 43 (91), 41 (59).

Methyl 3-(5-oxotetrahydrofuran-3-yl)propanoate **12 and 3-(5-oxotetrahydrofuran-3-yl)propanoic acid **13****

A mixture of alkenes **10** and **11** (0.232 g; 1.17 mmol), Pd/C (0.026 g; 10%) and ethyl acetate (100 mL) was stirred at room temperature under hydrogen atmosphere for five hours. The mixture was filtered under vacuum through a sintered funnel with a pad of celite (previously washed with

10% aqueous sulfuric acid), the solvent evaporated under reduced pressure and the residue purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v) to give **12** as a white solid (0.115 g; 0.57 mmol; 49% yield) and the acid **13** as a white solid (0.107 g; 0.57 mmol; 49% yield).

TLC R_f 0,25 (hex/EtOAc 1:1 v/v); mp: 90.1-90.9 °C; IR ν/cm^{-1} 3540-2500 (broad band), 2978, 2935, 1733, 1709, 1454, 1418, 1391, 1377, 1275, 1209, 1171, 1125, 1097, 986, 957, 936, 919, 833; ^1H NMR (300 MHz, CDCl_3) δ 1.27 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.54-1.71 (1H, m, H_8 '), 1.78-1.93 (1H, m, H_8), 2.18-2.49 (4H, m, H_9 , H_4 e H_3 '), 2.57-2.70 (1H, m, H_3); ^{13}C NMR (CDCl_3 , 75 MHz) δ 22.0 (C7), 24.6 (C8), 27.5 (C6), 32.7 (C9), 34.8 (C3), 45.2 (C4), 86.9 (C5), 175.5 (C2), 178.4 (C10); MS (EI), m/z (%): 171 (6), 153 (8), 124 (6), 111 (3), 100 (23), 97 (4), 83 (10), 82 (28), 81 (5), 69 (13), 67 (11), 59 (26), 58 (10), 56 (14), 55 (61), 54 (22), 43 (100), 41 (59).

5-isopropoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **14**

A solution of 5-isopropoxyfuran-2(5H)-one **2** (0.10 g; 0.70 mmol), anhydrous pyrrolidine (57.7 μL ; 0.70 mmol) and anhydrous DCM (10 mL) was stirred for 90 minutes and the solvent evaporated. The residue was purified by flash column chromatography on silica gel (hex/EtOAc 1:1 v/v) to give (**14**) as a yellow oil (0.097 g; 0.40 mmol; 65% yield).

TLC R_f 0,39 (hex/EtOAc 1:1 v/v); IR ν/cm^{-1} 2977, 2971, 2933, 2801, 2362, 2165, 1783, 1462, 1416, 1372, 1314, 1295, 1158, 1111, 1050, 952, 914, 863, 830; ^1H NMR (300 MHz, CDCl_3) δ 1.16 (3H, d, J 6.2 Hz, CH_3), 1.18 (3H, d, J 6.2 Hz, CH_3), 1.72-1.81 (4H, m, H_{10} and H_{11}); 2.43-2.53 (5H, m, H_3 , H_9 and H_{12}), 2.71 (1H, dd, J 7.8 Hz, J 17.6 Hz, H_3 '), 2.95 (1H, ddd, J 7.8 Hz, J 5.9 Hz, J 3.1 Hz, H_4), 3.93 (1H, sep, J 6.2 Hz, H_6), 5.43 (1H, d, J 3.1 Hz, H_5); ^{13}C NMR (CDCl_3 , 75 MHz): δ 21.8 (C8), 23.4 (C7),

23.4 (C10 and C11), 34.1 (C3), 52.0 (C9 and C12), 66.0 (C4), 72.7 (C6), 105.7 (C5), 174.5 (C2); MS (EI), m/z (%): 142 (21), 126 (8), 124 (3), 112 (16), 100 (4), 97 (100), 95 (27), 70 (8), 69 (50), 56(14), 55 (15), 54 (12), 44 (6), 43 (24), 42 (22), 41 (38).

5-acetoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **15**

A solution of 5-acetoxymfuran-2(5H)-one **3** (0.124 g; 0.87 mmol), anhydrous pyrrolidine (144.0 μL ; 1.75 mmol) and anhydrous DCM (10 mL) was stirred until finished of the reaction (15 minutes) and the solvent evaporated. The residue was purified by flash column chromatography on silica gel (hex/EtOAc 1:2 v/v) to give **15** as a yellow oil (0.011 g; 0.08 mmol; 6% yield) and a mixture of **15** and starting material (0.69 g).

TLC R_f 0,44 (hex/EtOAc 1:2 v/v); IR ν/cm^{-1} 2985, 2863, 2798, 1796, 1754, 1462, 1422, 1368, 1299, 1221, 1159, 1120, 1078, 1034, 984, 959, 928, 846, 791; ^1H NMR (300 MHz, CDCl_3) δ 1.79-1.86 (4H, m, H_9 and H_{10}), 2.13 (3H, s, CH_3), 2.53-2.68 (5H, m, H_3 , H_{11} and H_8), 2.83 (1H, dd, J 7.3 Hz, J 17.9 Hz, H_3 '), 3.24 (1H, ddd, J 7.3 Hz, J 3.4 Hz, J 1.8 Hz, H_4), 6.53 (1H, d, J 1.8 Hz, H_5); ^{13}C NMR (CDCl_3 , 75 MHz): δ 21.1 (C7), 23.5 (C9 and C-10), 32.5 (C3), 51.4 (C8 and C11), 64.4 (C4), 97.0 (C5), 169.0 (C6), 174.2 (C2); MS (EI), m/z (%): 153 (13), 142 (40), 125 (6), 112 (32), 99 (12), 97 (97), 96 (36), 83(11), 69 (73), 56(21), 55 (33), 54 (31), 44 (31), 43 (100), 42 (54), 41 (62), 40 (41).

Infrared, ^1H and ^{13}C NMR spectra for the synthesized compounds

Although all substances have been obtained in racemic form, some of the synthesized compounds were represented only by one enantiomer, since it was possible to establish the relative stereochemistry based on NOE experiments.

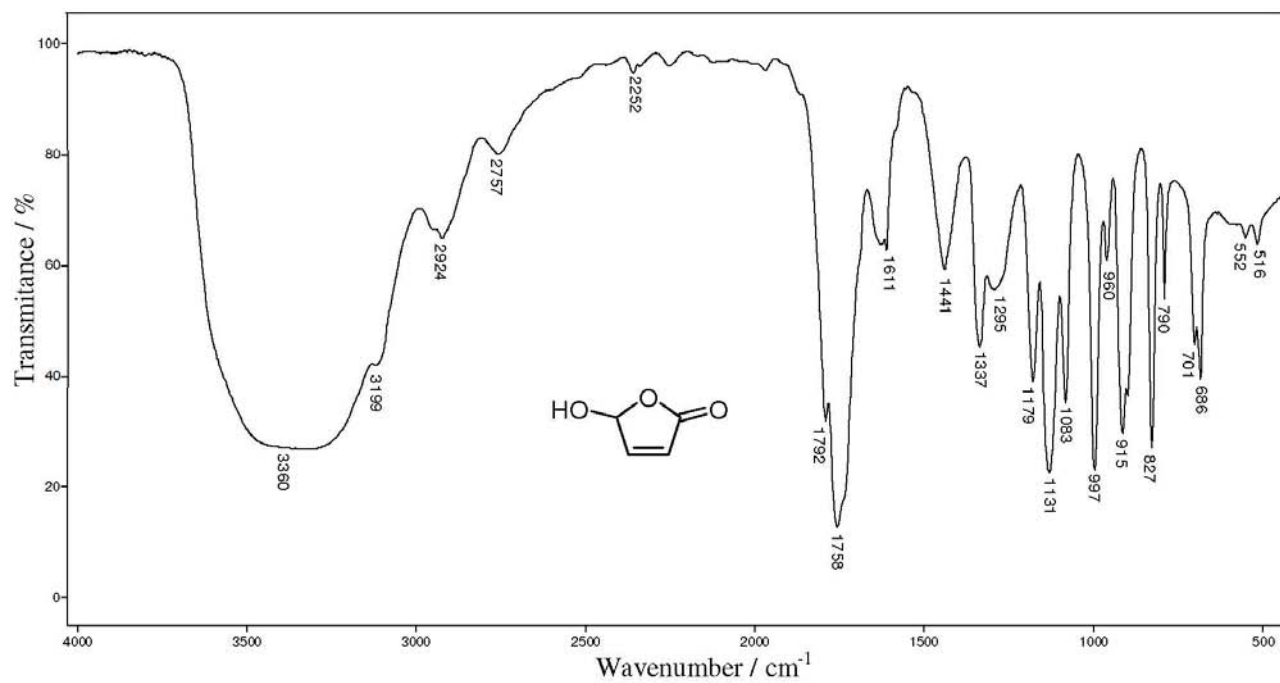
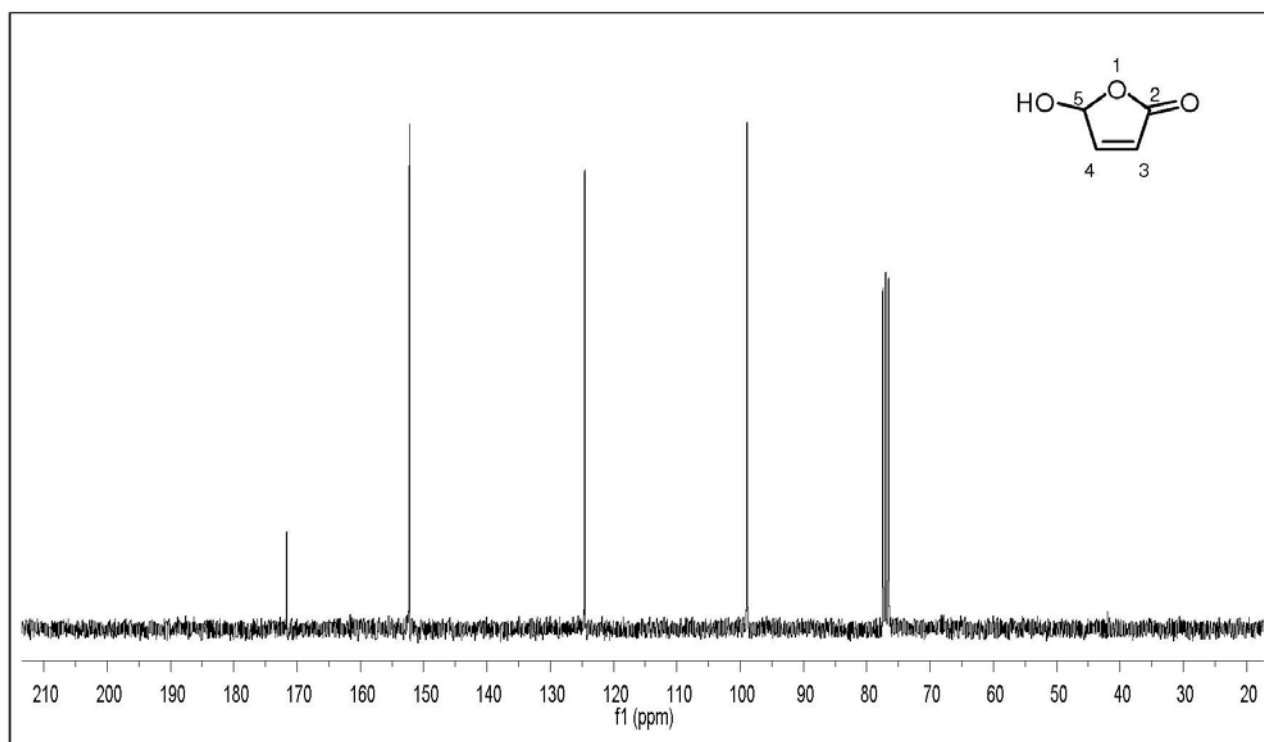


Figure S1. IR (reflectance) of 5-hydroxyfuran-2(5H)-one 1.

Figure S2. ^{13}C NMR spectrum (75 MHz, CDCl_3) of 5-hydroxyfuran-2(5H)-one 1.

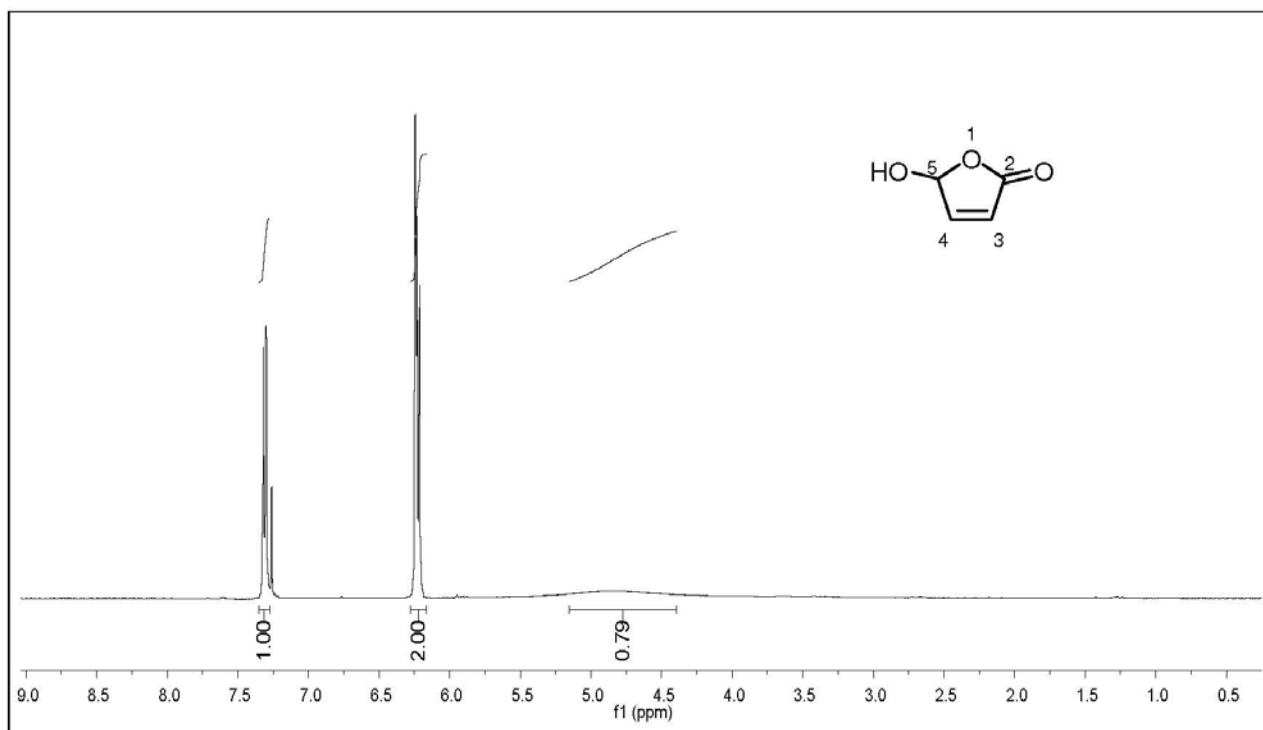


Figure S3. ^1H NMR spectrum (300 MHz, CDCl_3) of 5-hydroxyfuran-2(5H)-one **1**.

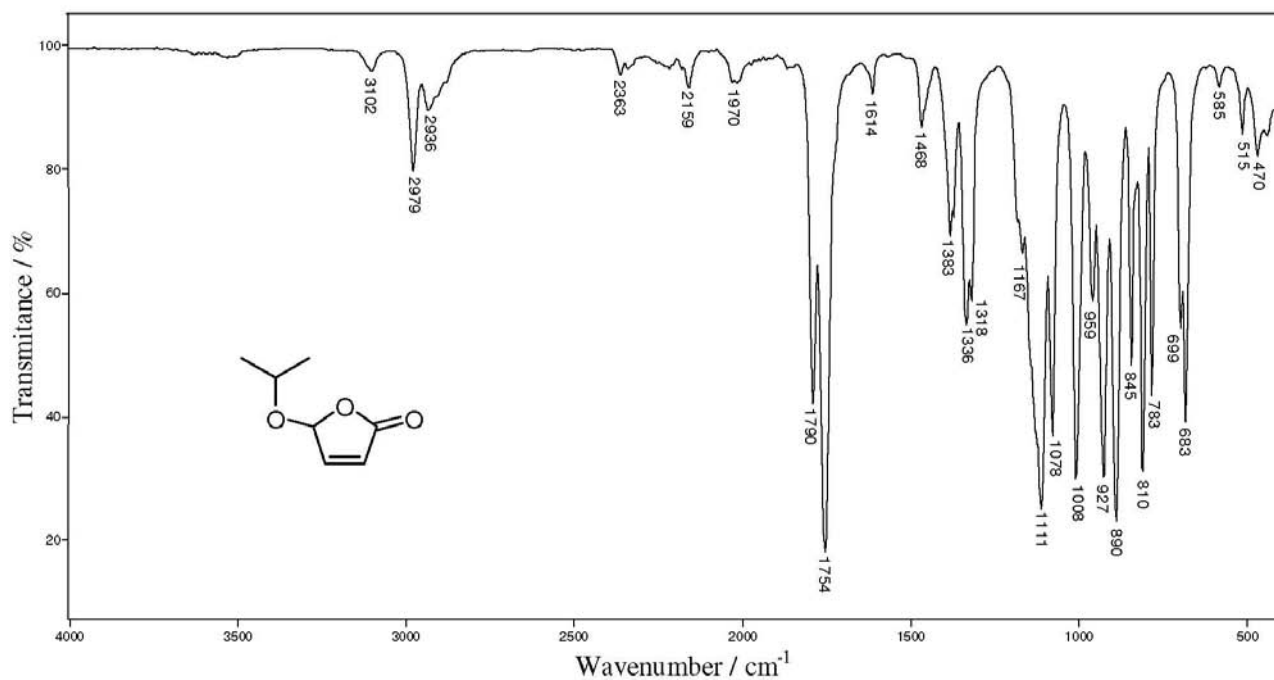


Figure S4. IR (reflectance) of 5-isopropoxyfuran-2(5H)-one **2**.

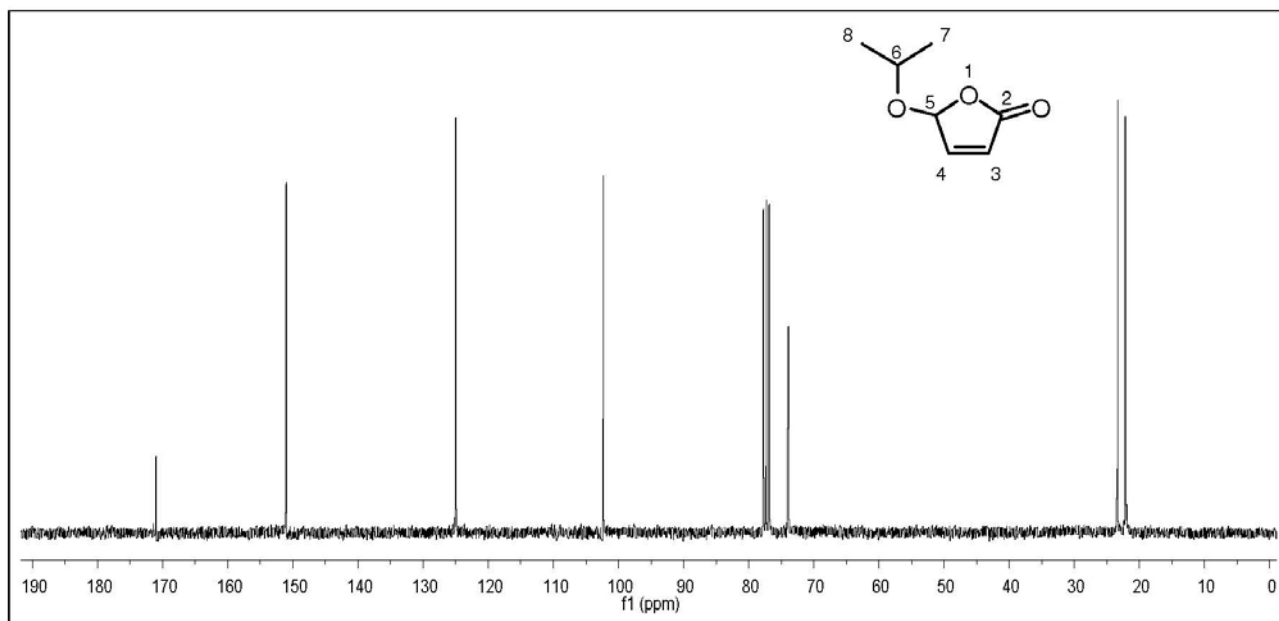


Figure S5. ^{13}C NMR spectrum (75 MHz, CDCl_3) of 5-isopropoxyfuran-2(5H)-one **2**.

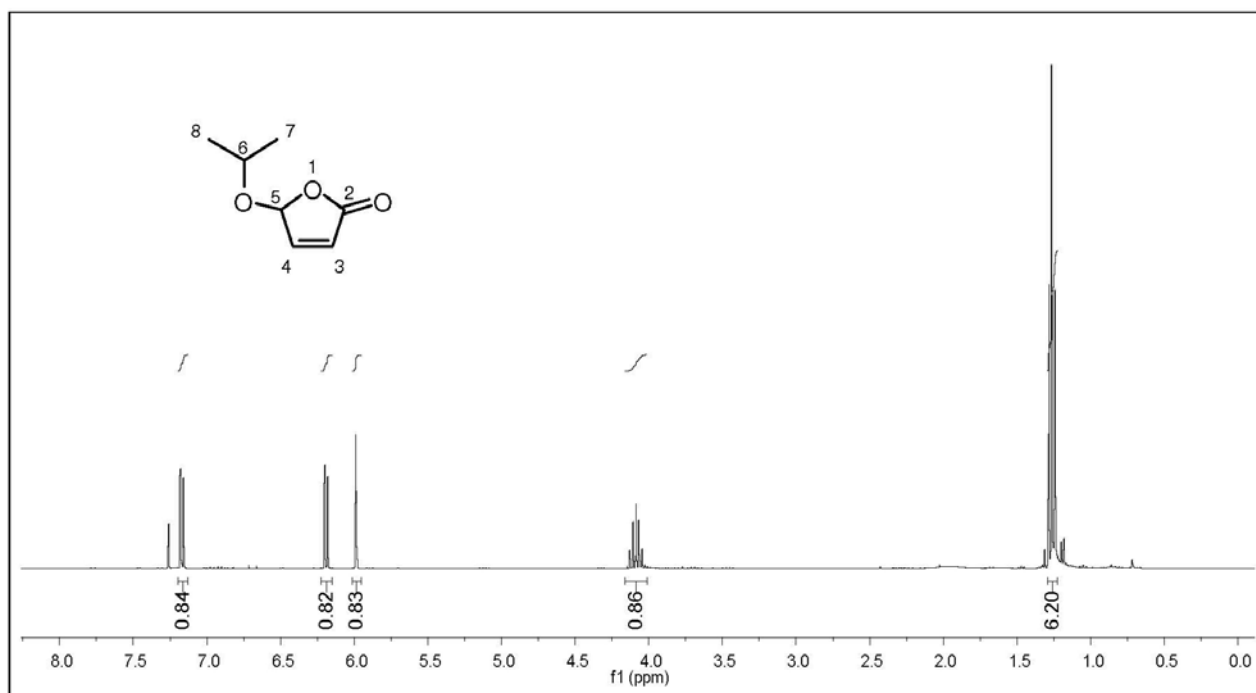


Figure S6. ^1H NMR spectrum (300 MHz, CDCl_3) of 5-isopropoxyfuran-2(5H)-one **2**.

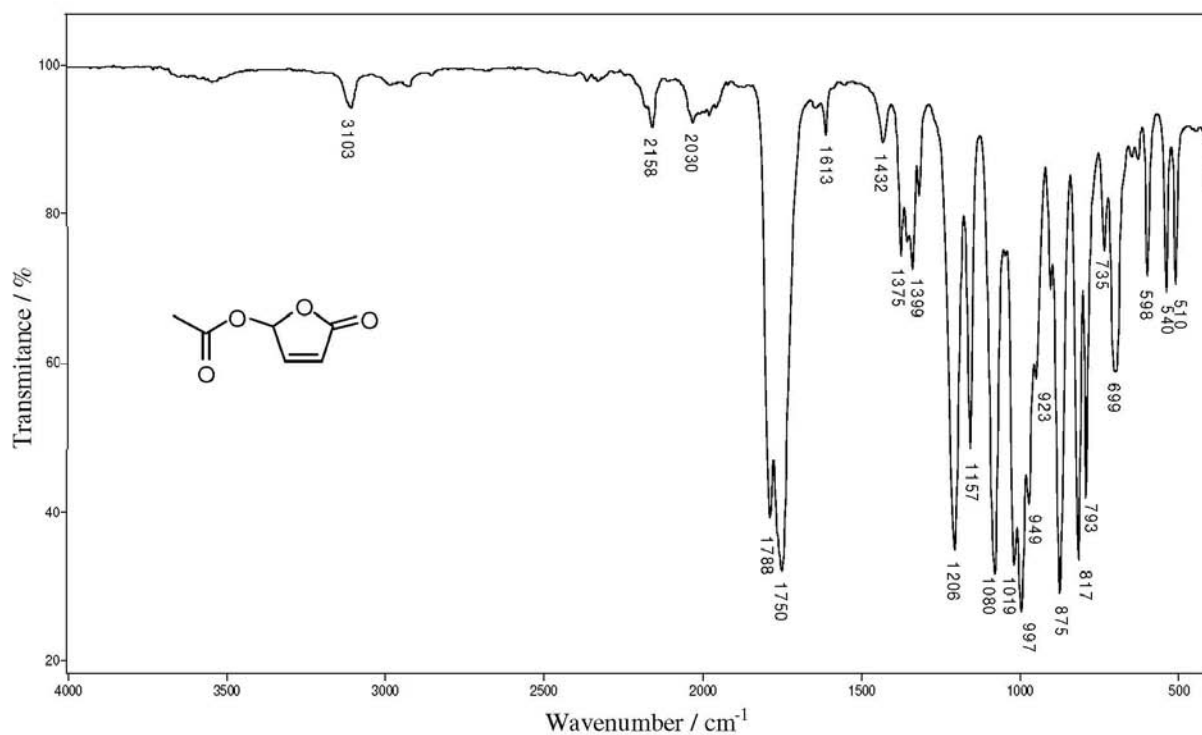


Figure S7. IR (reflectance) of 5-acetoxymethyl-2,5-dihydrofuran-2-one 3.

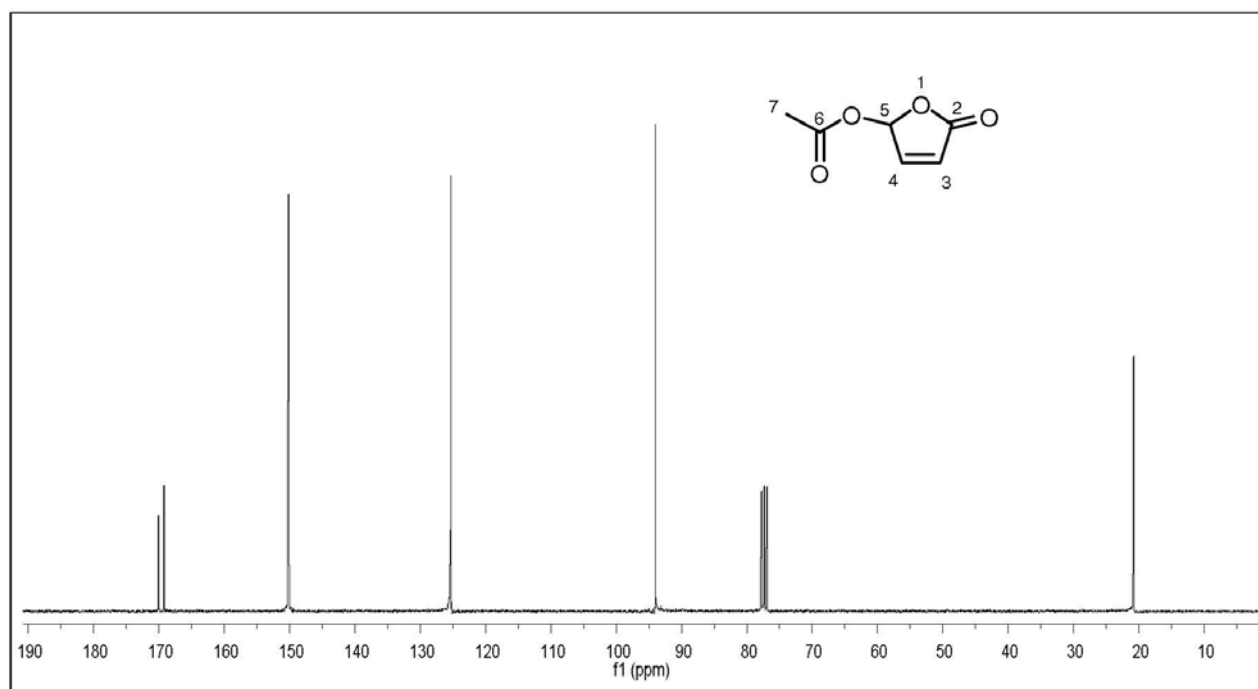


Figure S8. ^{13}C NMR spectrum (75 MHz, CDCl_3) of 5-acetoxymethyl-2,5-dihydrofuran-2-one 3.

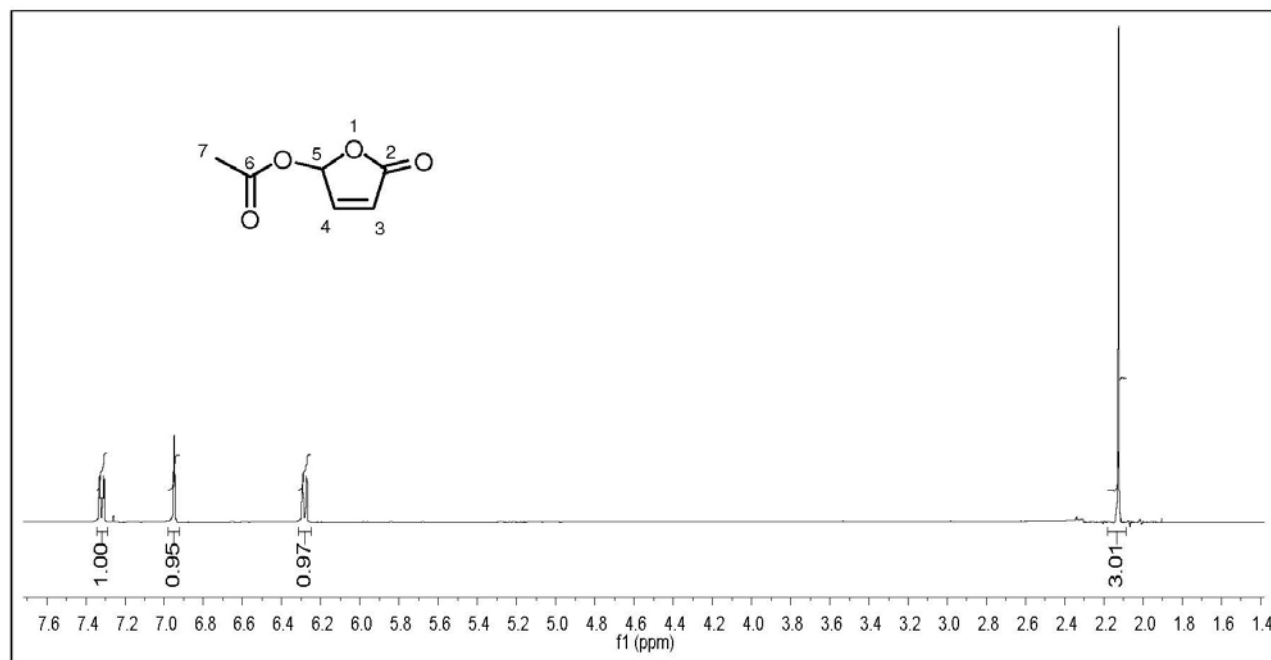


Figure S9. ¹H NMR spectrum (300 MHz, CDCl₃) of 5-acetoxymethyl-2(5H)-furanone 3.

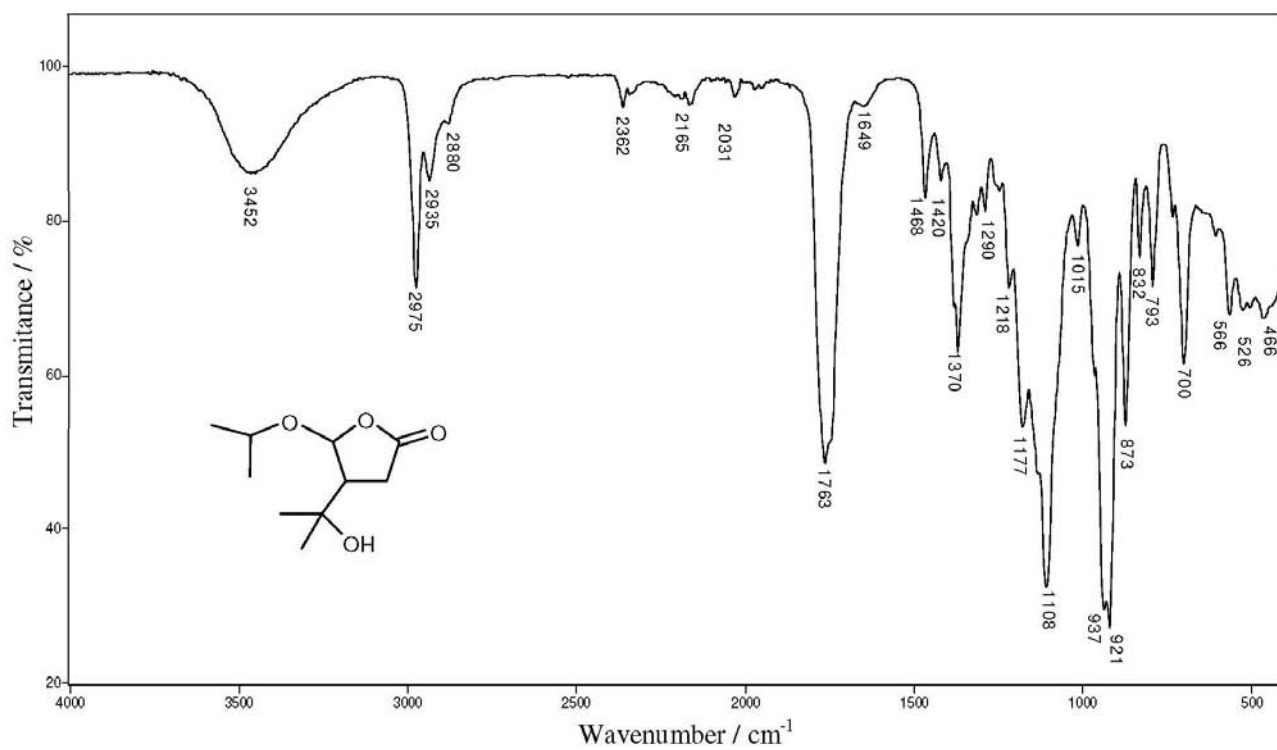


Figure S10. IR (reflectance) of 4-(1'-hydroxy-1'-methylethyl)-5-isopropoxytetrahydrofuran-2-one 4.

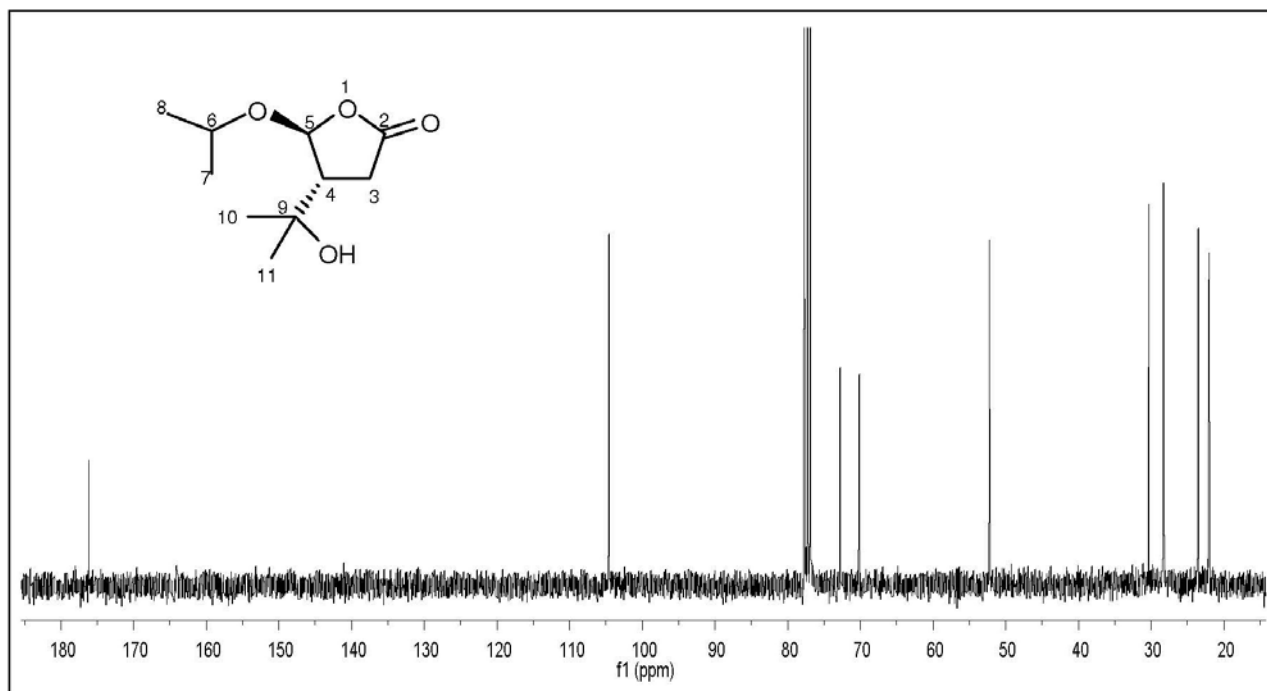


Figure S11. ¹³C NMR spectrum (75 MHz, CDCl₃) of 4-(1'-hydroxy-1'-methylethyl)-5-isopropoxytetrahydrofuran-2-one **4**.

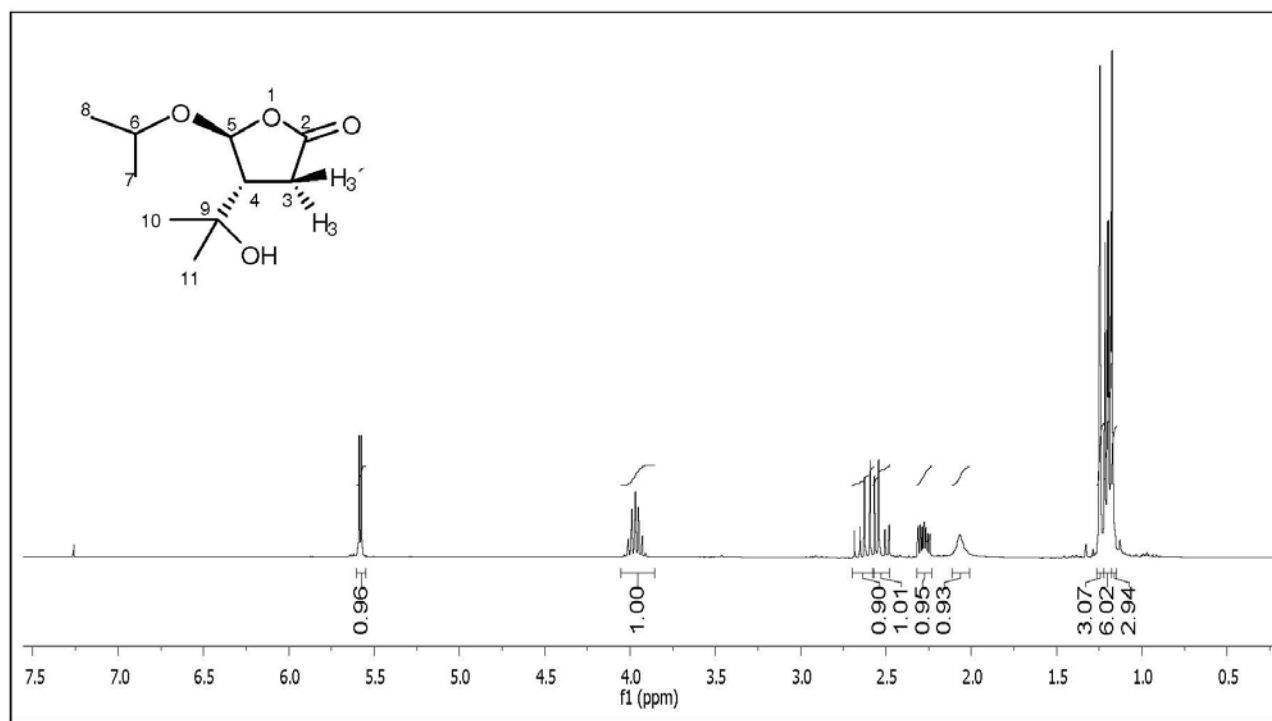


Figure S12. ¹H NMR spectrum (300 MHz, CDCl₃) of 4-(1'-hydroxy-1'-methylethyl)-5-isopropoxytetrahydrofuran-2-one **4**.

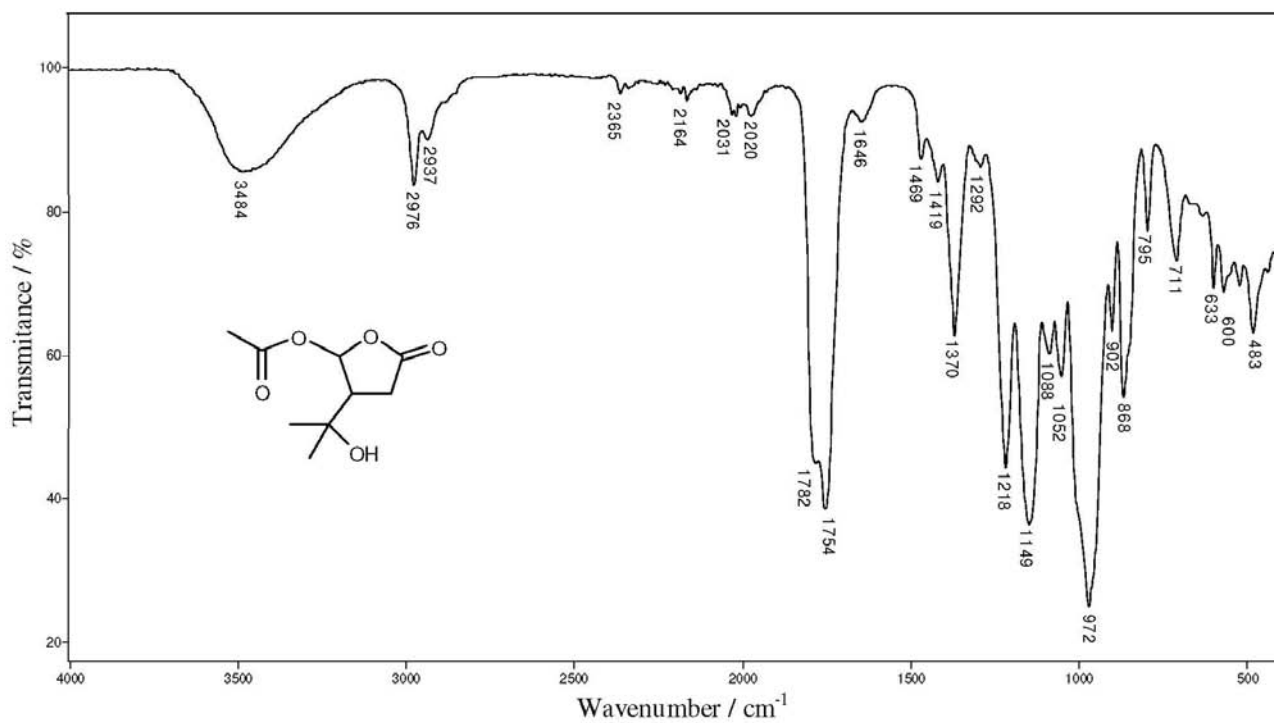


Figure S13. IR (reflectance) of 4-(1'-hydroxy-1'-methylethyl)-5-acetoxytetrahydrofuran-2-one **5**.

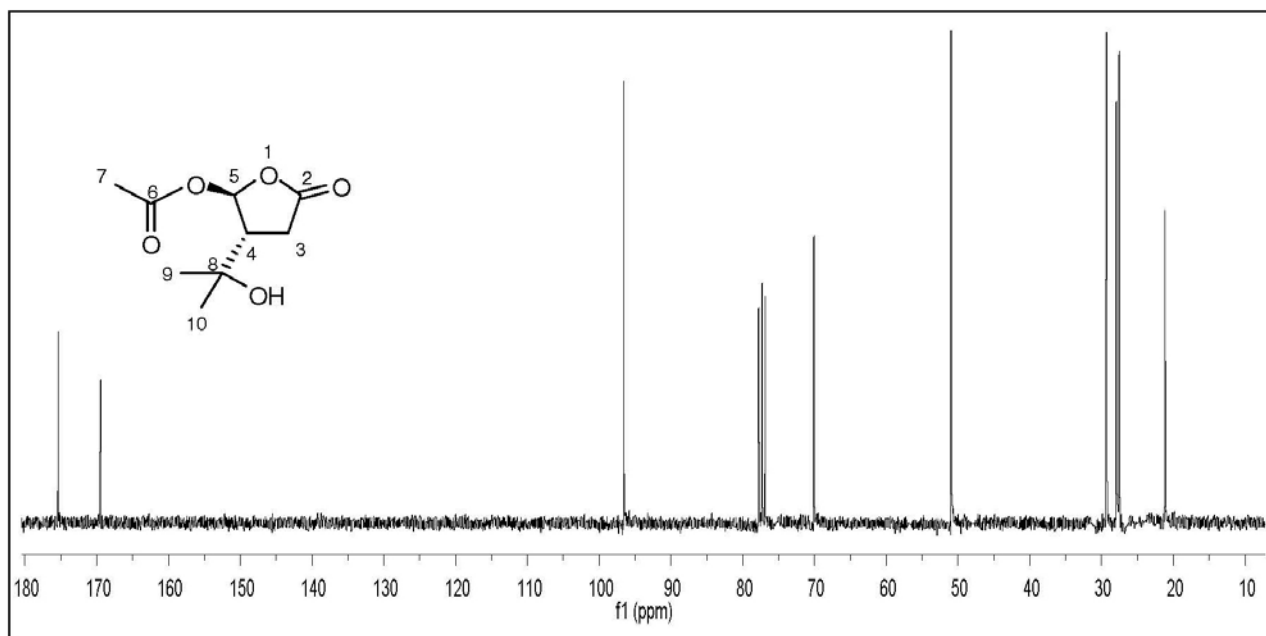


Figure S14. ¹³C NMR (75 MHz, CDCl₃) spectrum of 4-(1'-hydroxy-1'-methylethyl)-5-acetoxytetrahydrofuran-2-one **5**.

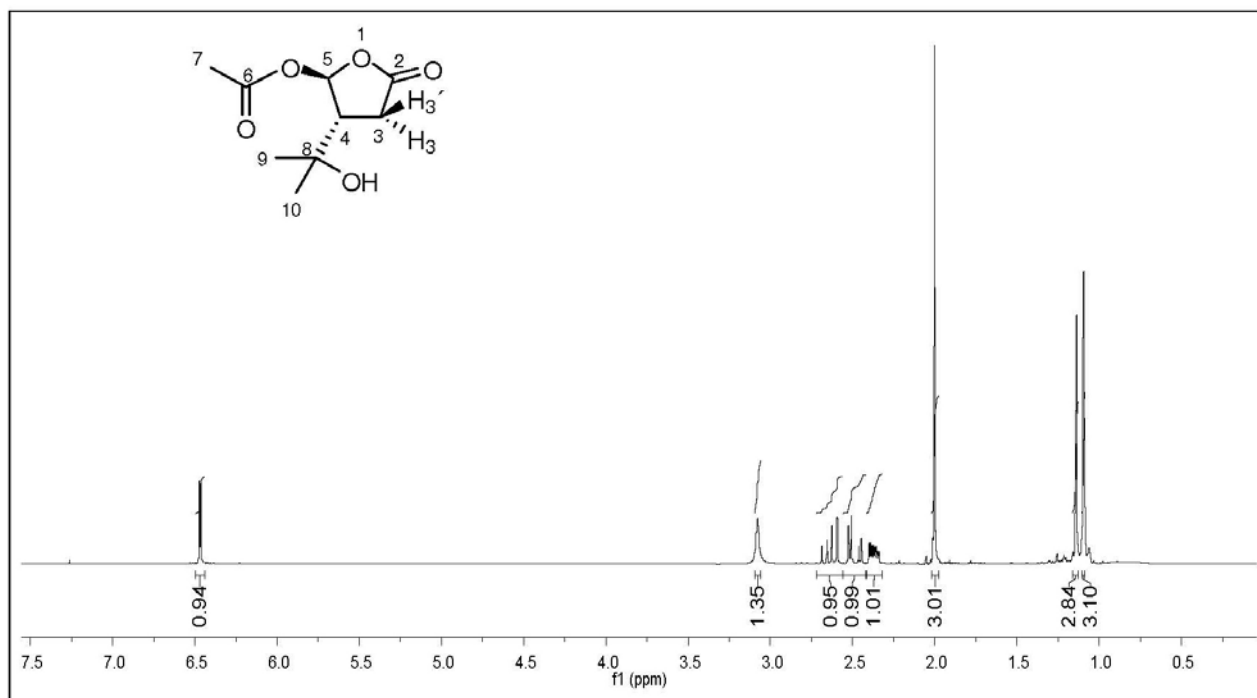


Figure S15. ¹H NMR spectrum (300 MHz, CDCl₃) of 4-(1'-hydroxy-1'-methylethyl)-5-acetoxytetrahydrofuran-2-one **5**.

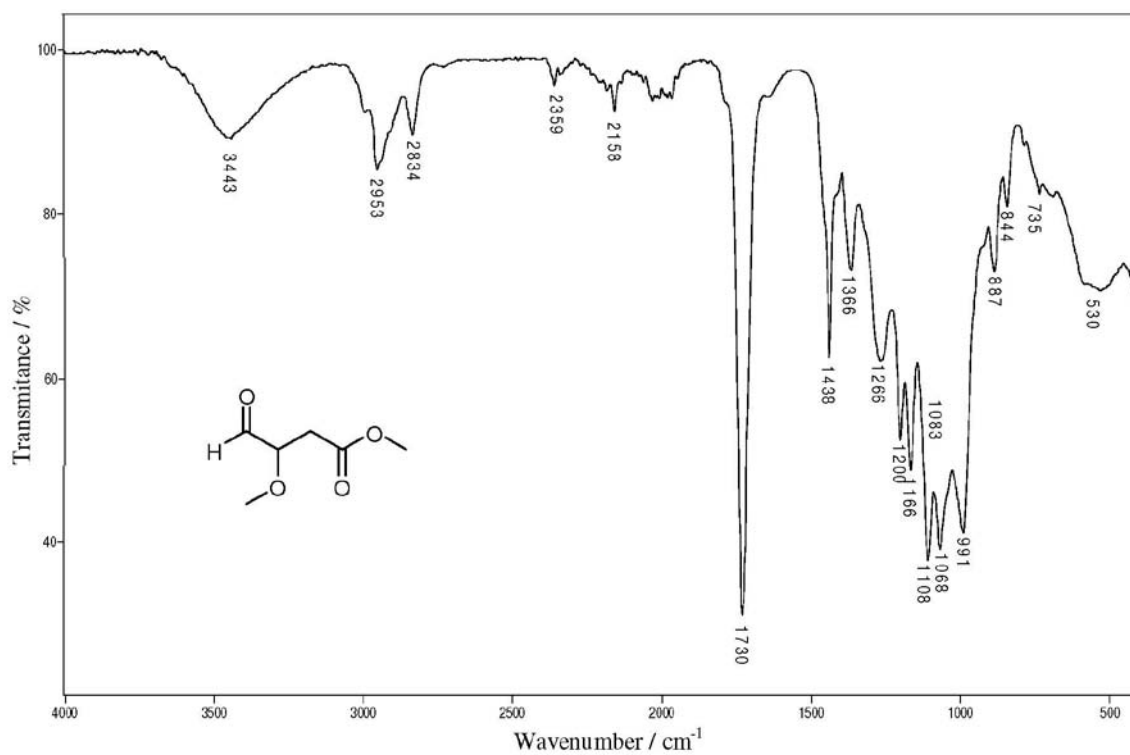


Figure S16. IR (reflectance) of 3-methoxy-4-oxobutanoate **6**.

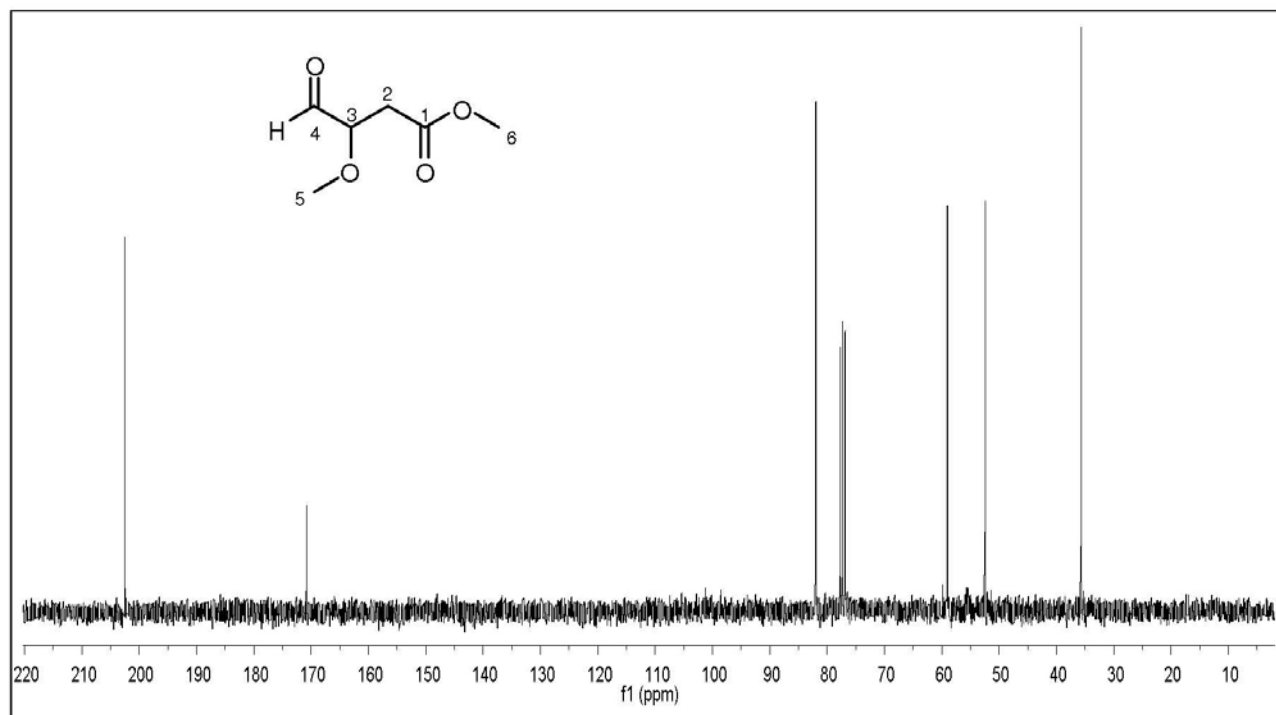


Figure S17. ^{13}C NMR spectrum (75 MHz, CDCl_3) of 3-methoxy-4-oxobutanoate **6**.

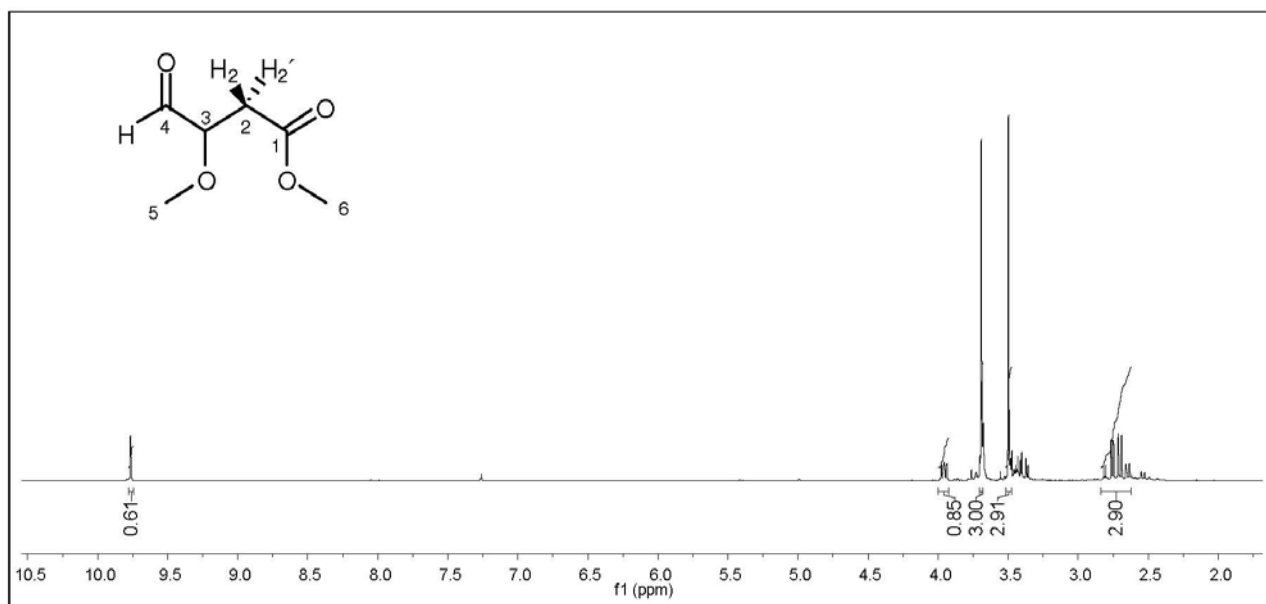


Figure S18. ^1H NMR spectrum (300 MHz, CDCl_3) of 3-methoxy-4-oxobutanoate **6**.

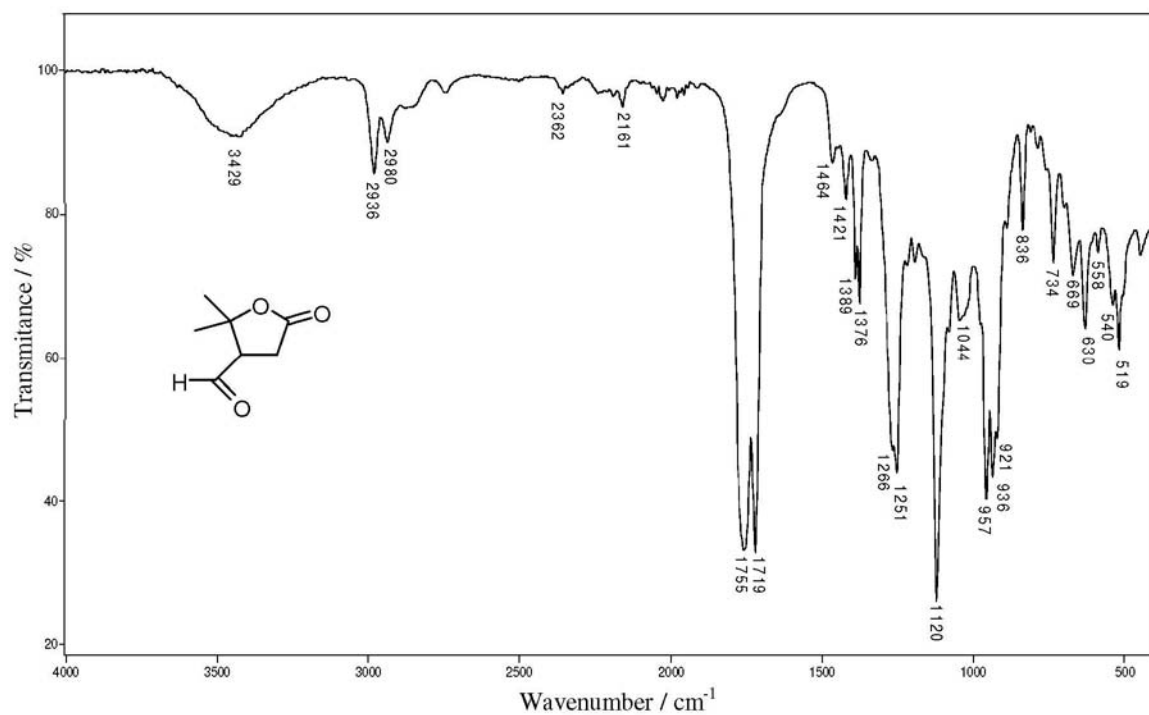


Figure S19. IR (reflectance) of 4-formyl-5,5-dimethyltetrahydrofuran-2-one 7.

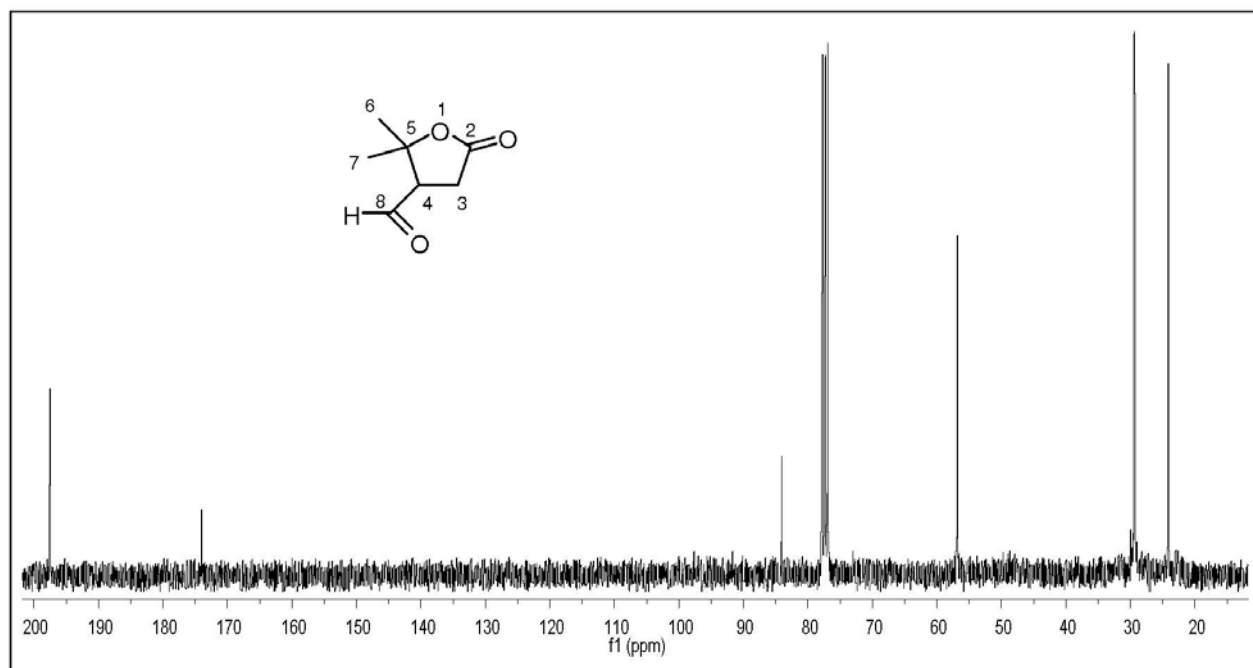


Figure S20. ^{13}C NMR spectrum (75 MHz, CDCl_3) of 4-formyl-5,5-dimethyltetrahydrofuran-2-one 7.

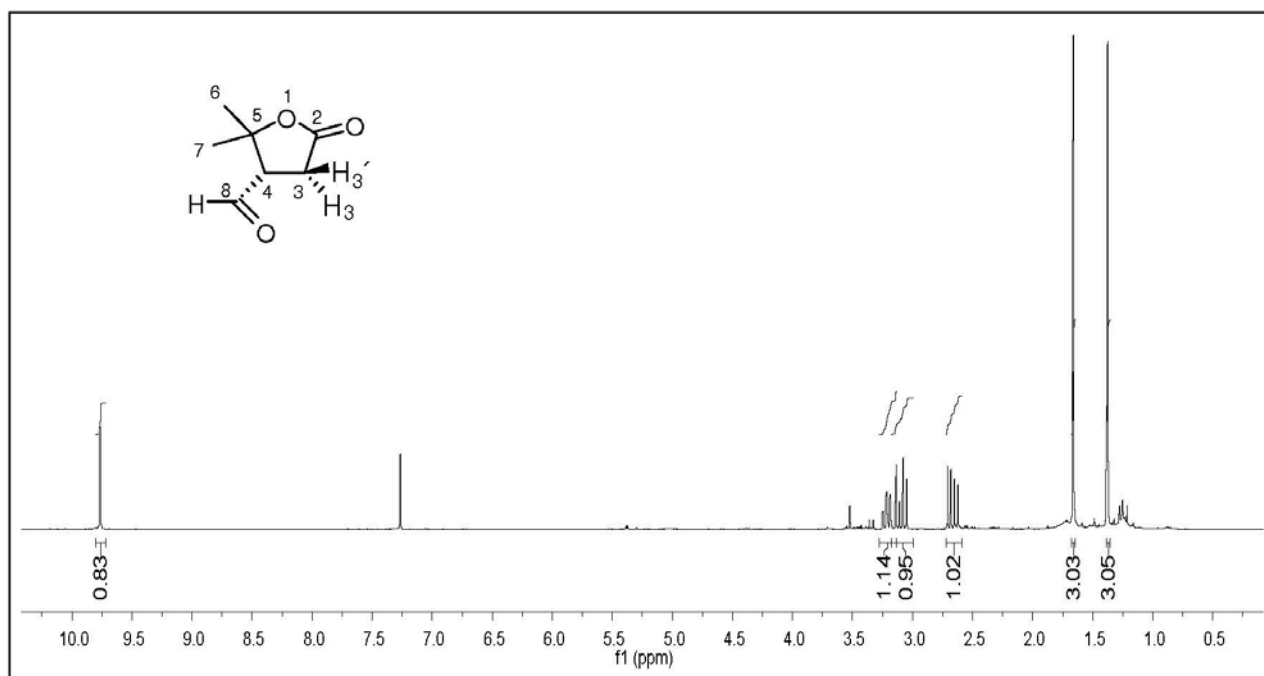


Figure S21. ¹H NMR spectrum (300 MHz, CDCl₃) of 4-formyl-5,5-dimethyltetrahydrofuran-2-one **7**.

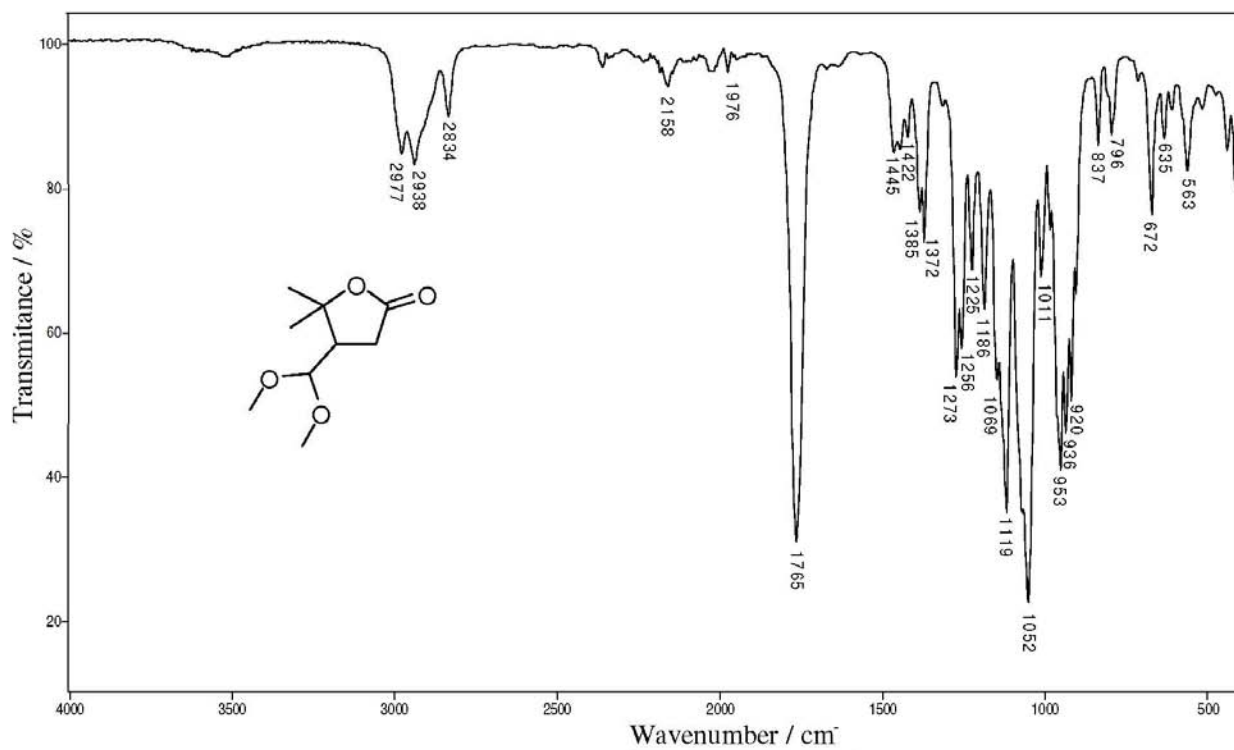


Figure S22. IR (reflectance) of 4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **8**.

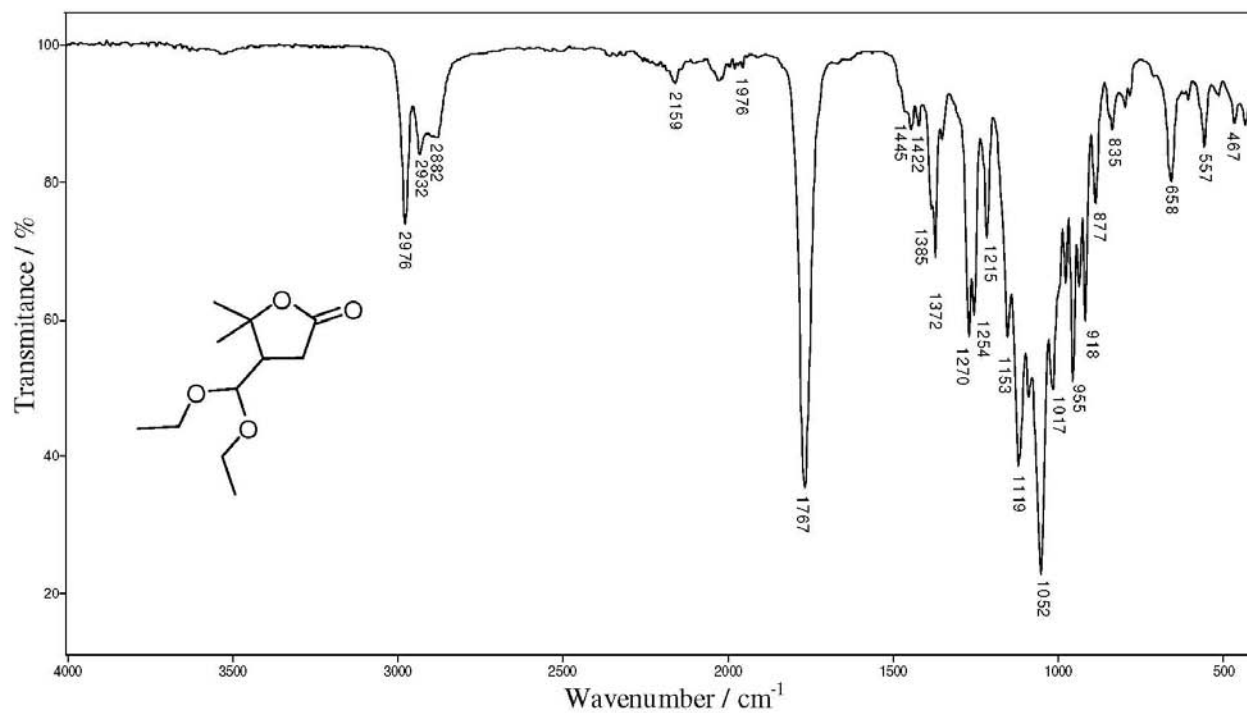


Figure S23. IR (reflectance) of 4-(diethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **9**.

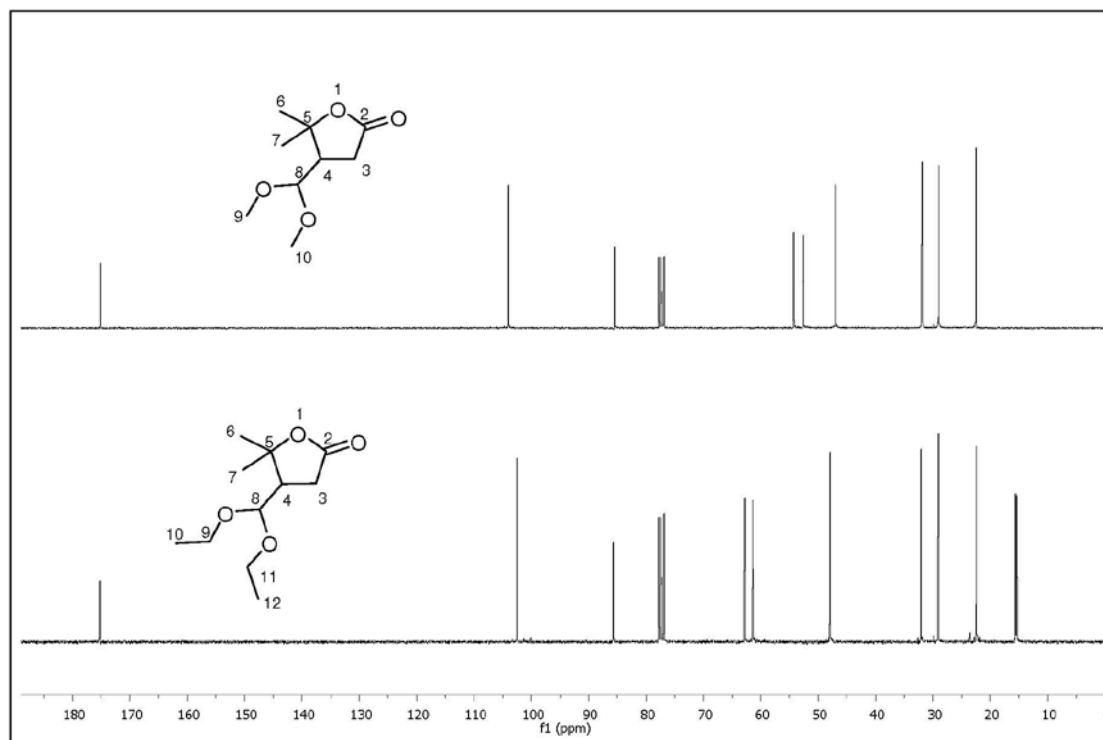


Figure S24. ¹³C NMR spectra (75 MHz, CDCl₃) of 4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **8** and 4-(diethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **9**.

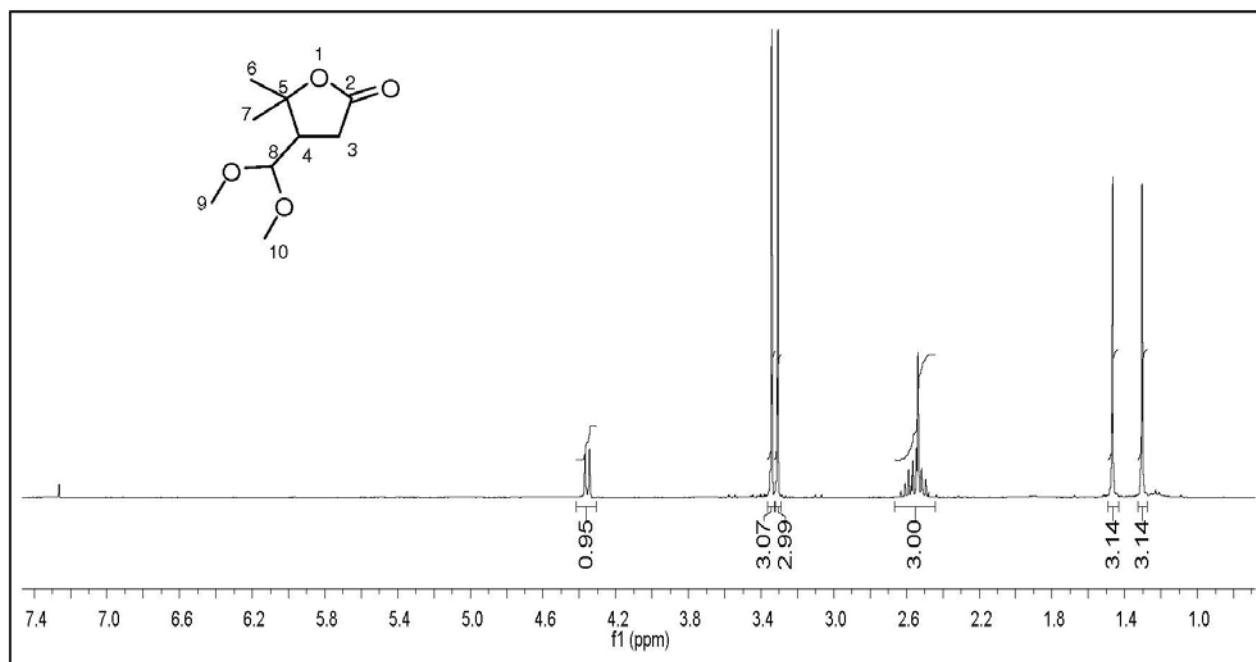


Figure S25. ¹H NMR spectrum (300 MHz, CDCl₃) of 4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **8**.

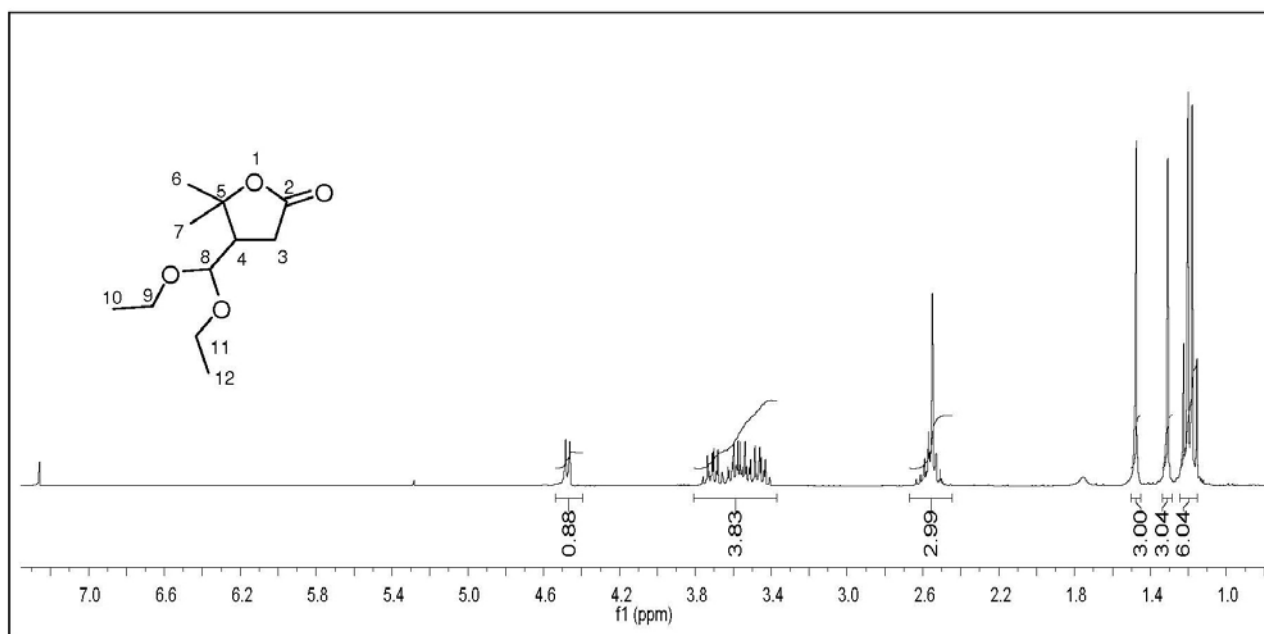


Figure S26. ¹H NMR spectrum (300 MHz, CDCl₃) of 4-(dimethoxymethyl)-5,5-dimethyltetrahydrofuran-2-one **9**.

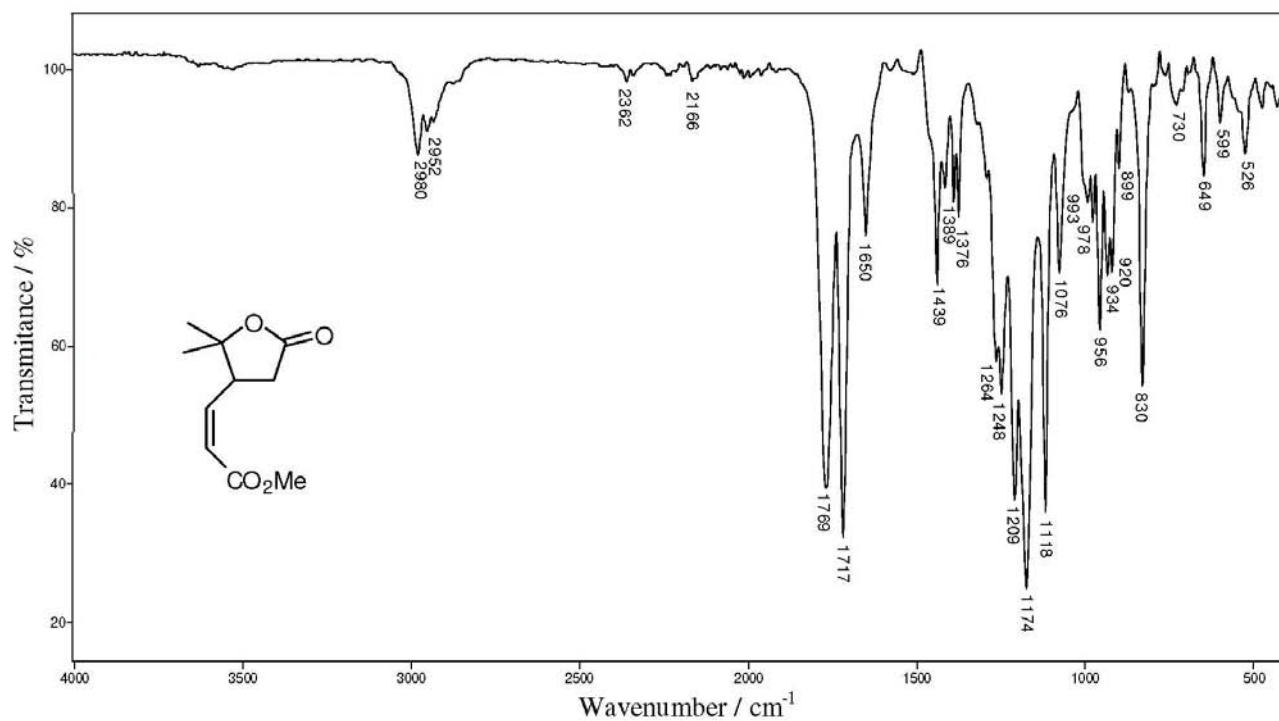


Figure S27. IR (reflectance) of (Z)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **10**.

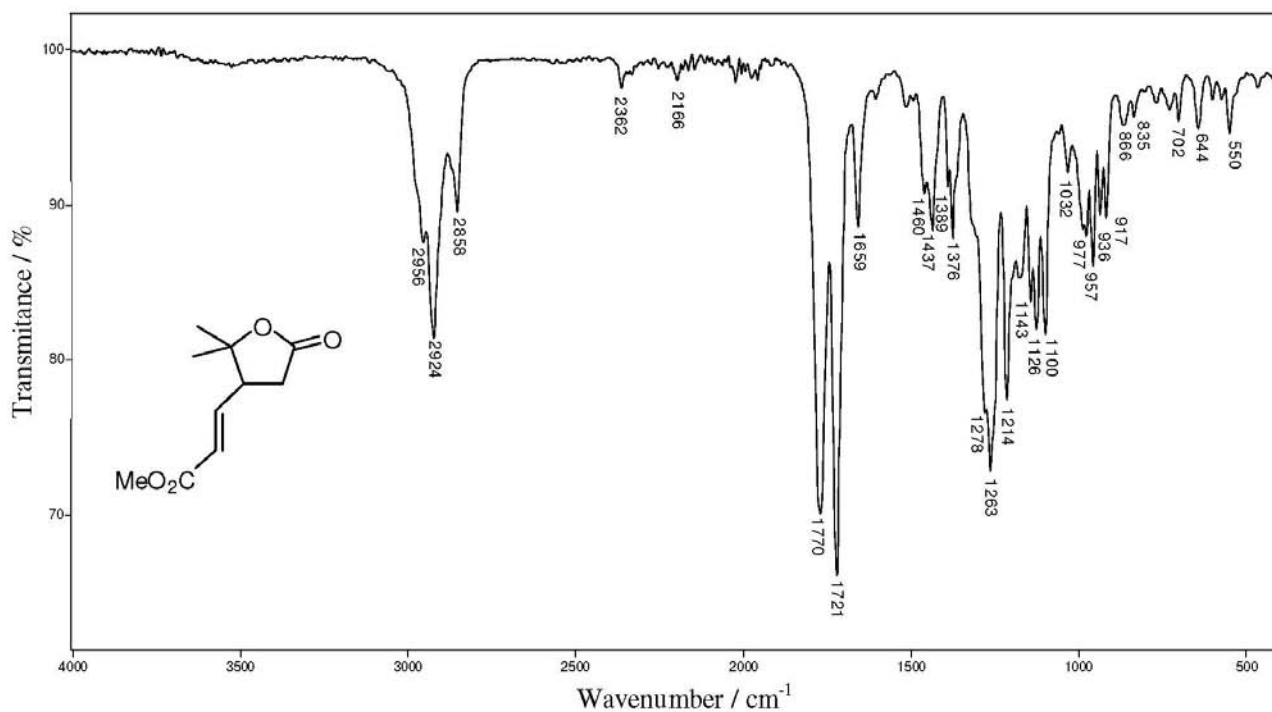


Figure S28. IR (reflectance) of (E)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **11**.

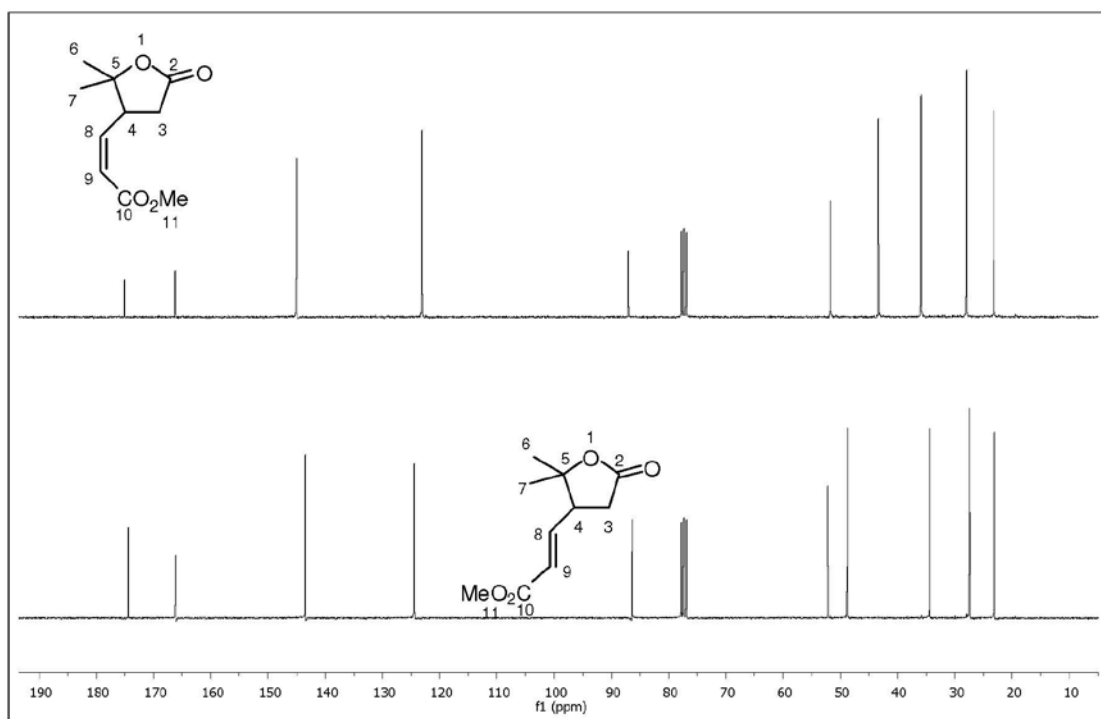


Figure S29. ^{13}C NMR spectra (75 MHz, CDCl_3) of (Z)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **10** and (E)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **11**.

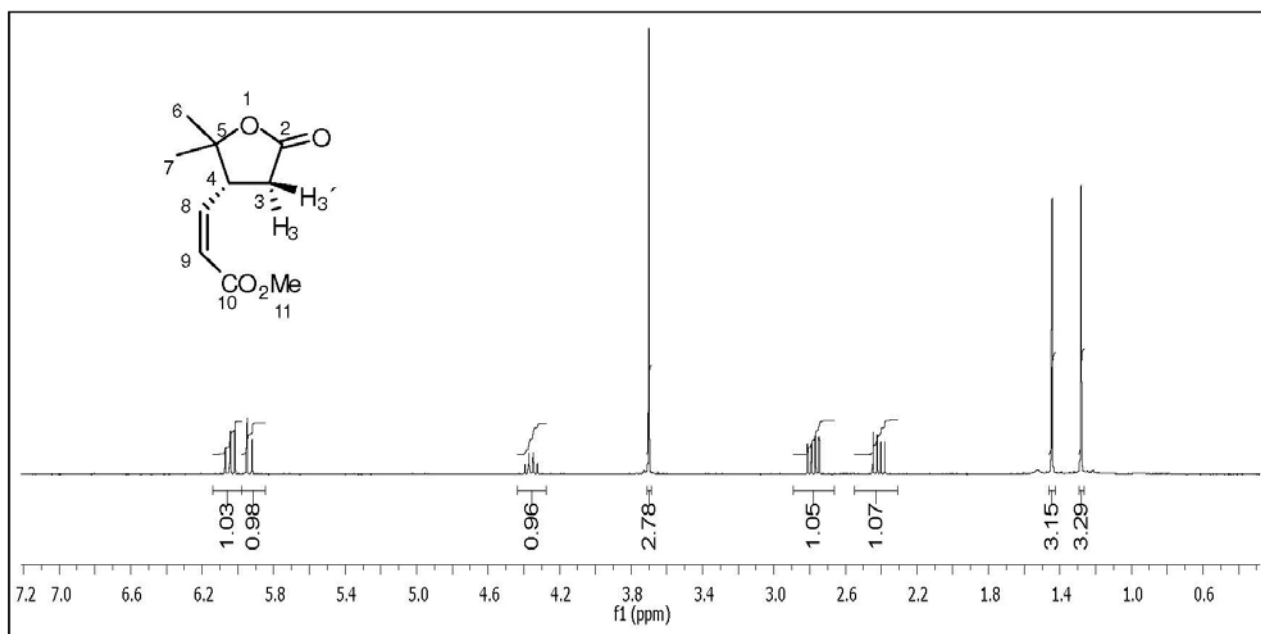


Figure S30. ^1H NMR spectrum (300 MHz, CDCl_3) of (Z)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **10**.

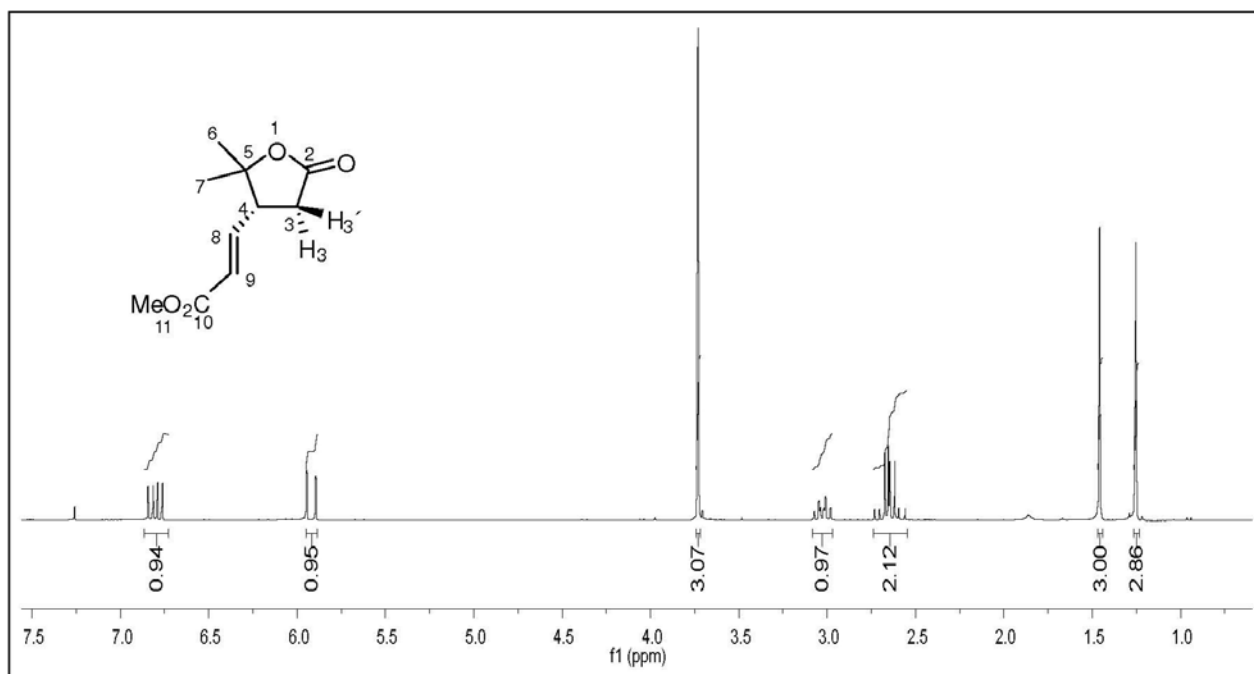


Figure S31. ¹H NMR spectrum (300 MHz, CDCl₃) of (*E*)-methyl 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)acrylate **11**.

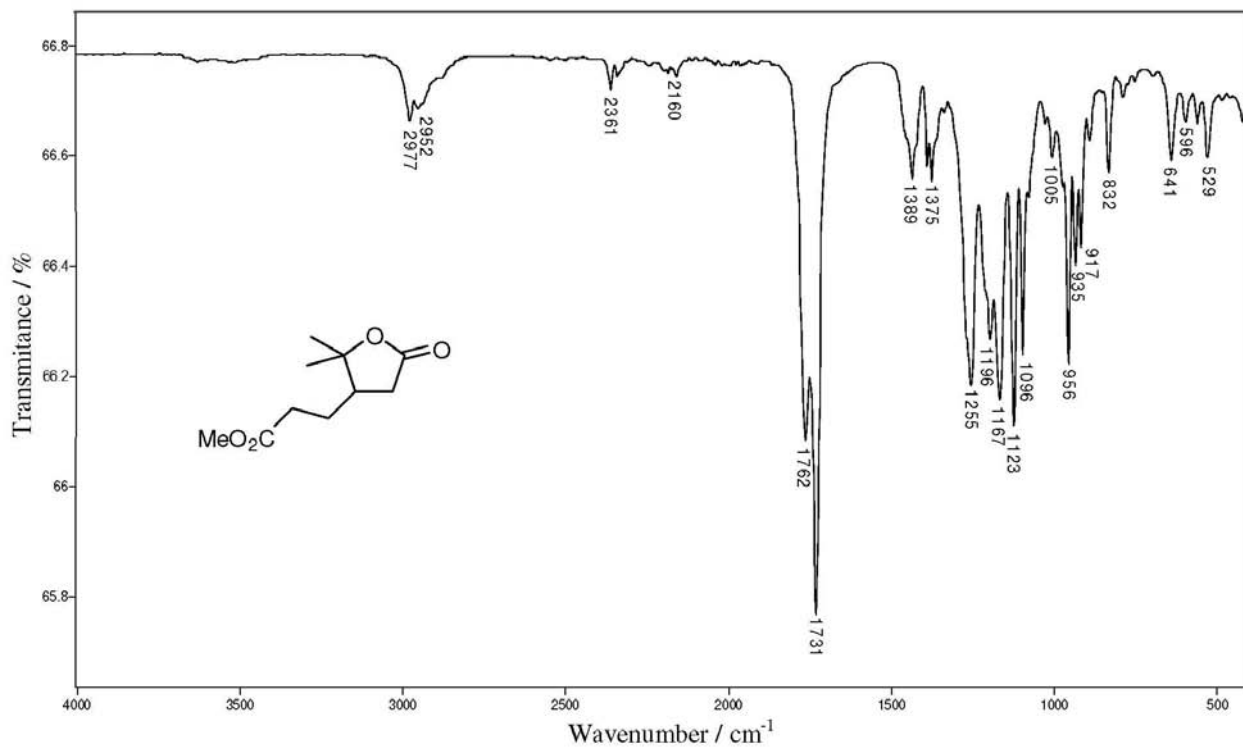


Figure S32. IR (reflectance) of 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoate **12**.

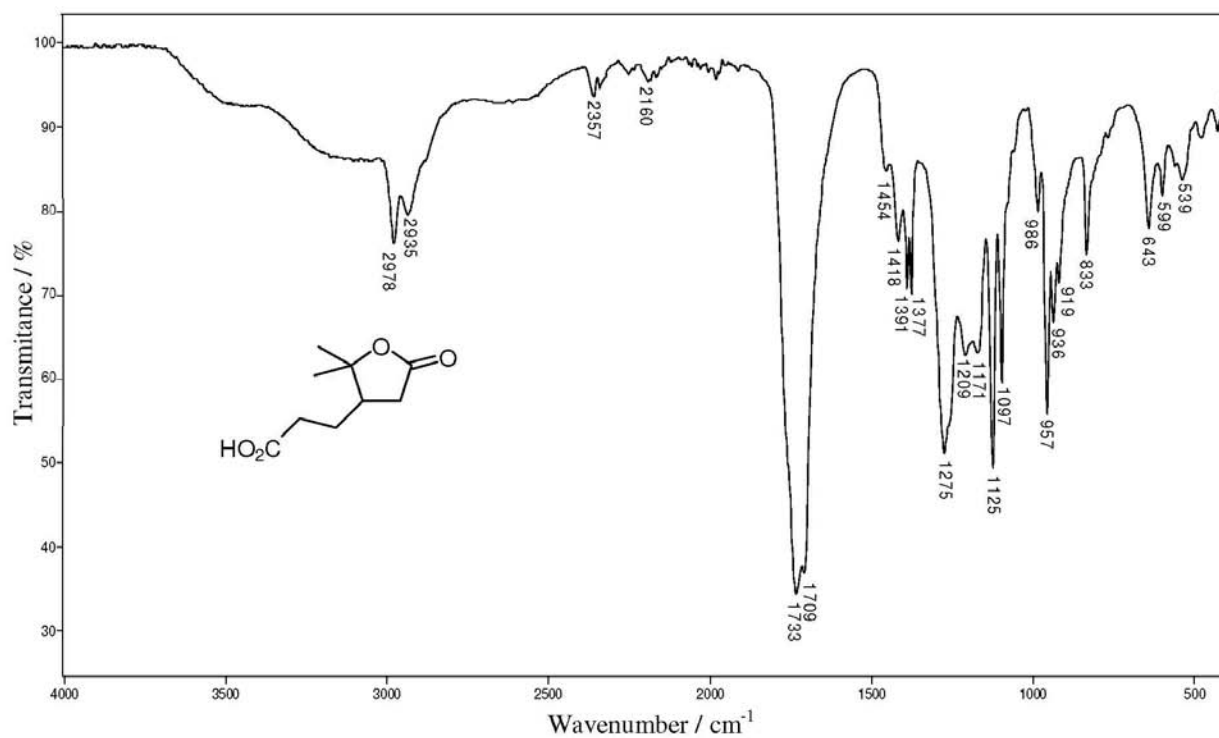


Figure S33. IR (reflectance) of 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoic acid **13**.

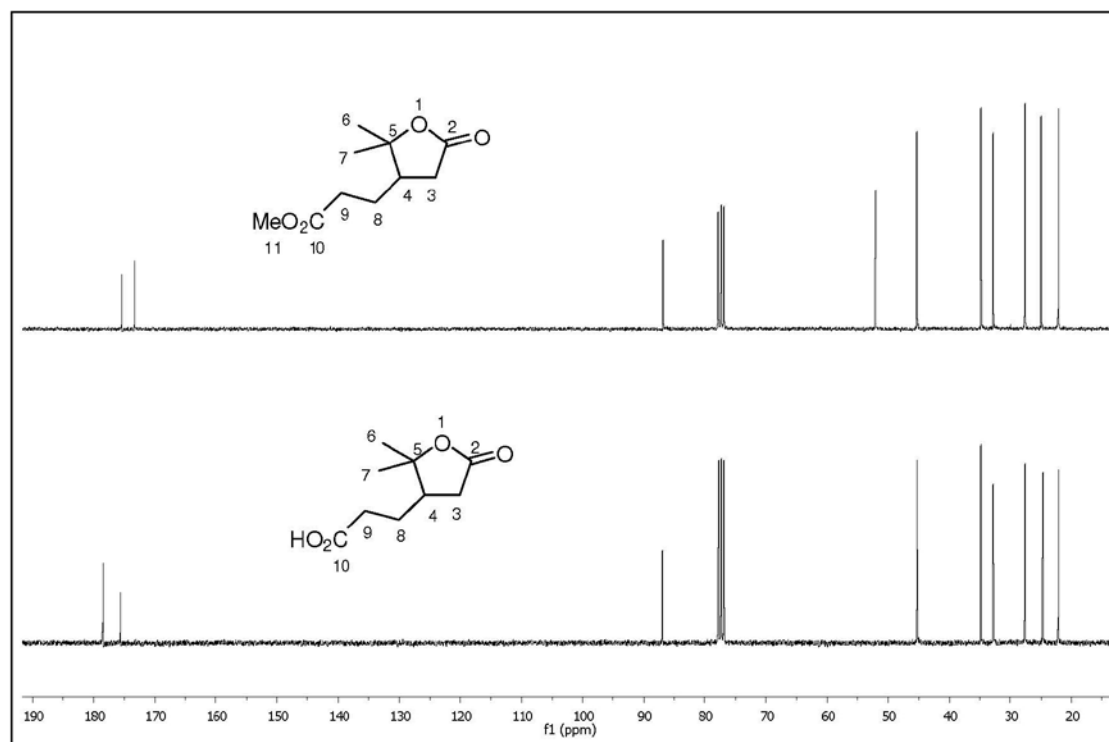


Figure S34. ^{13}C NMR spectra (75 MHz, CDCl_3) of 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoate **12** and 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoic acid **13**.

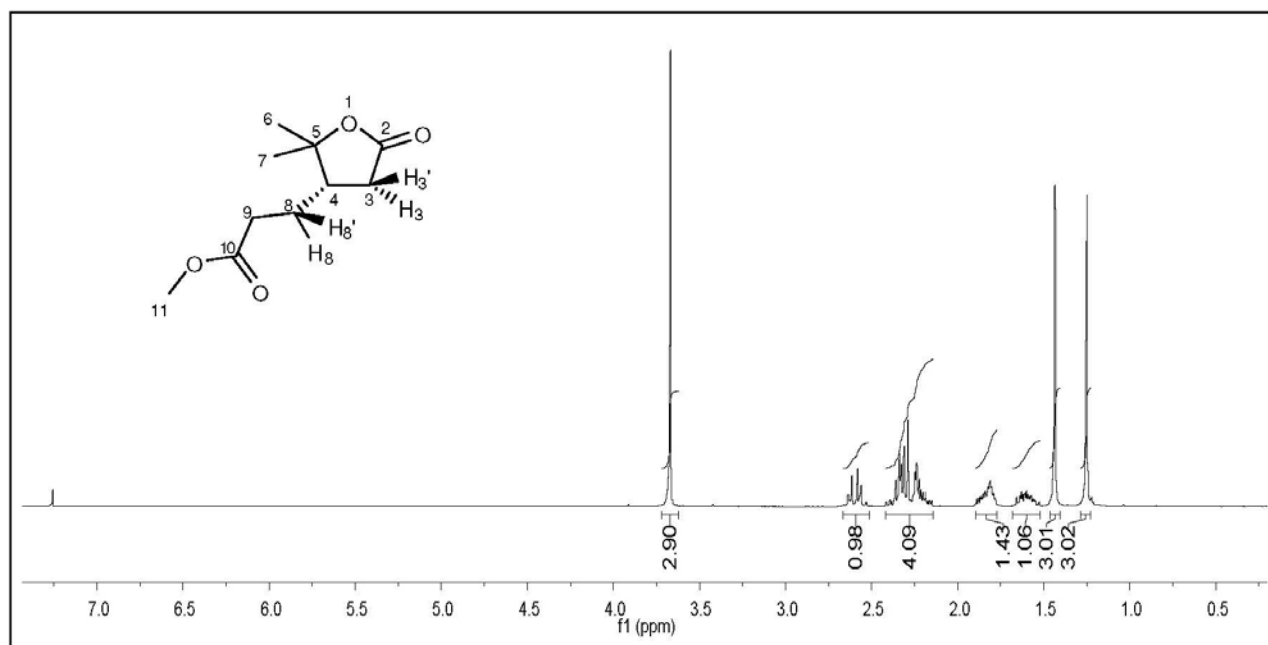


Figure S35. ¹H NMR spectrum (300 MHz, CDCl₃) of 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoate **12**.

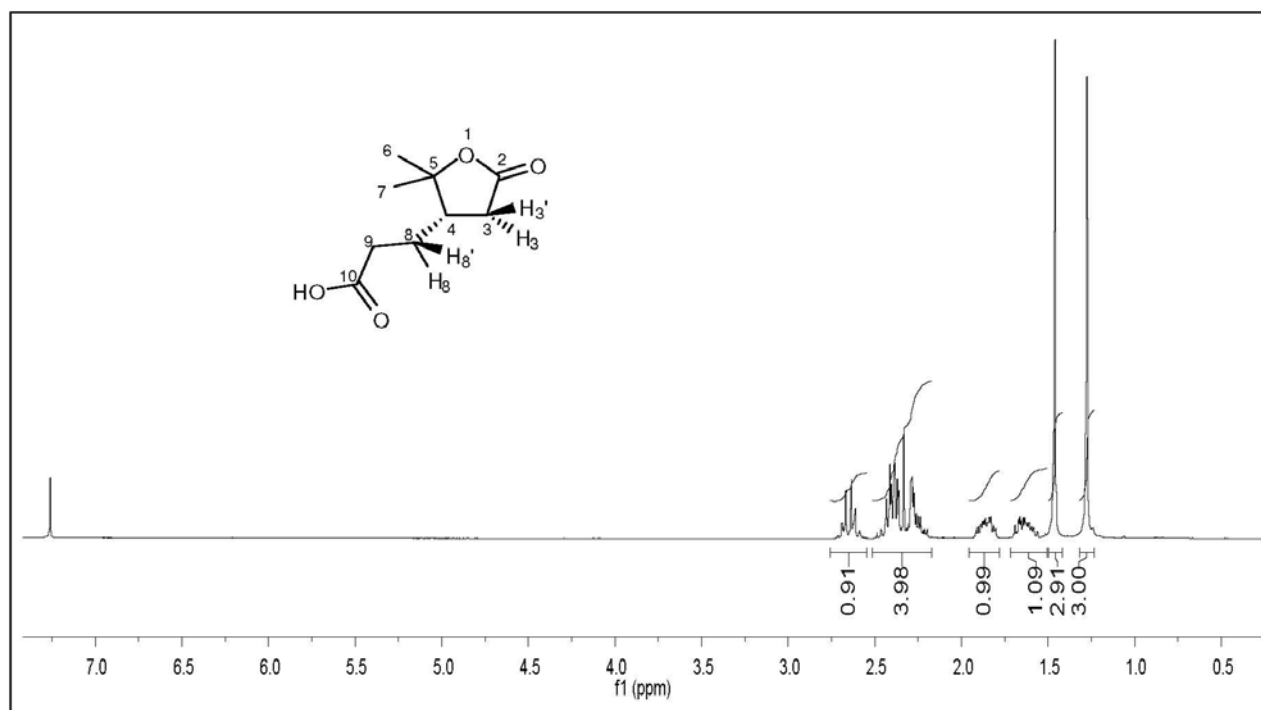


Figure S36. ¹H NMR spectrum (300 MHz, CDCl₃) of 3-(2,2-dimethyl-5-oxotetrahydrofuran-3-yl)propanoic acid **13**.

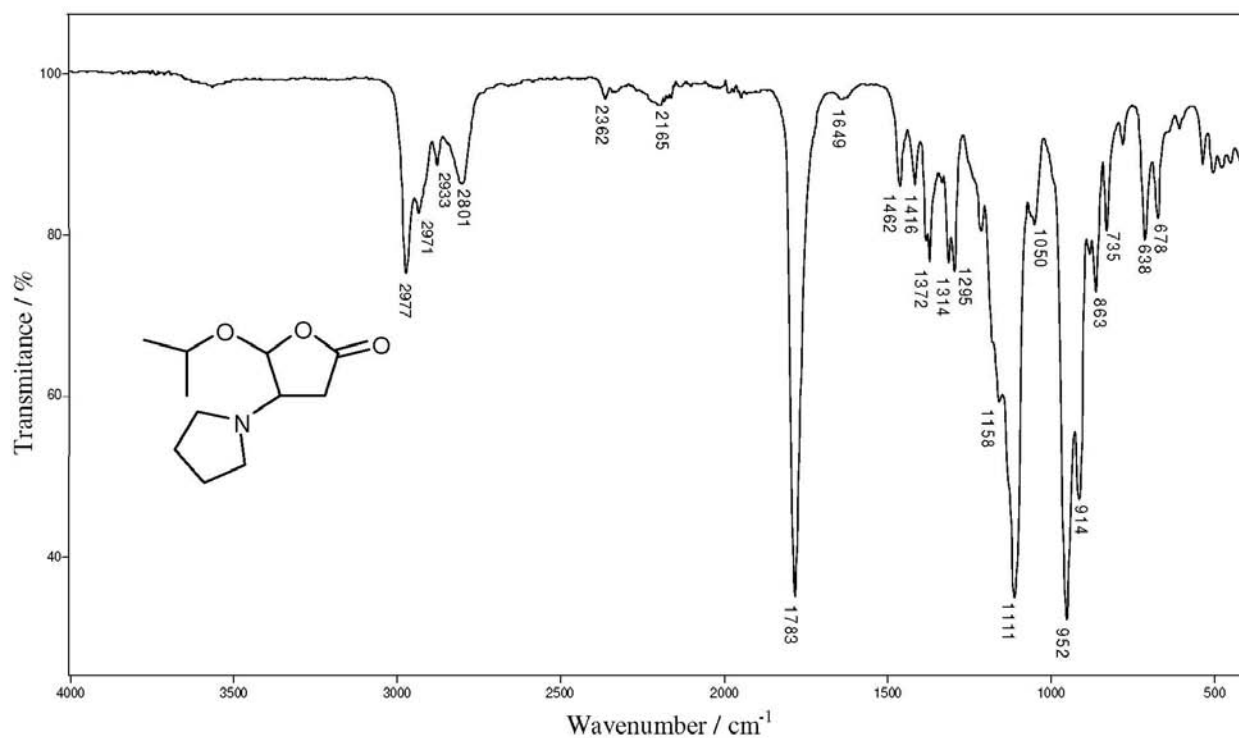


Figure S37. IR (reflectance) of 5-isopropoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **14**.

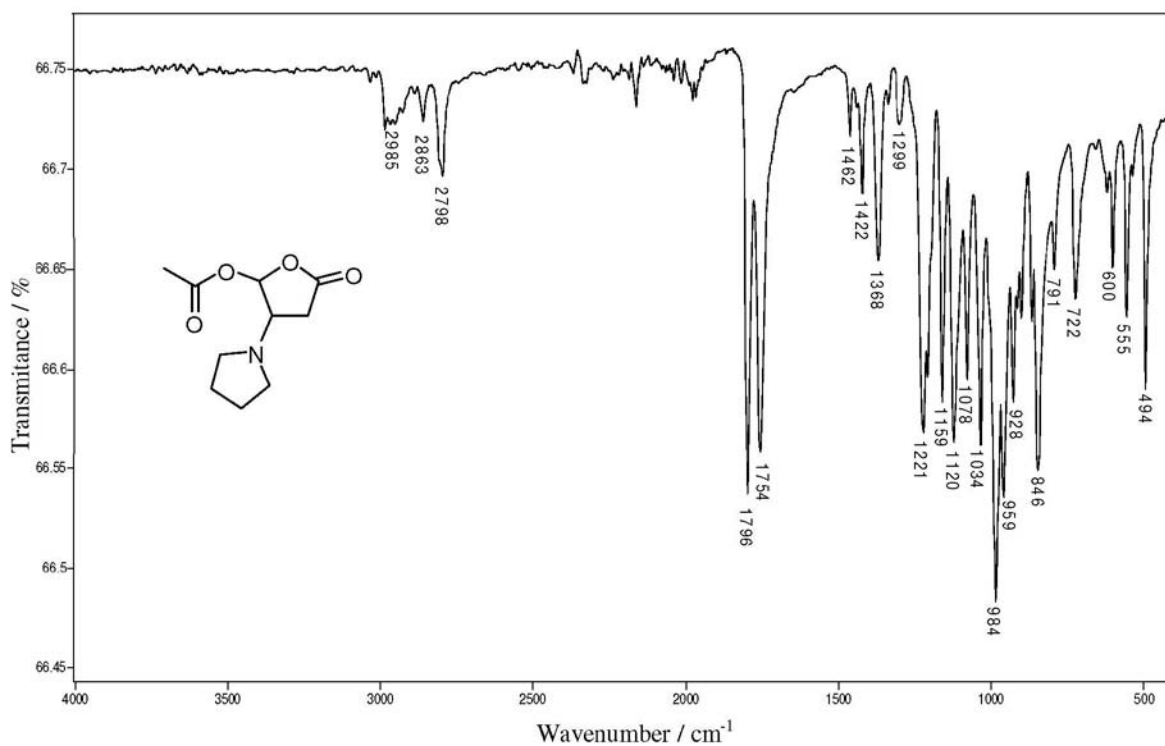


Figure S38. IR (reflectance) of 5-acetoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **15**.

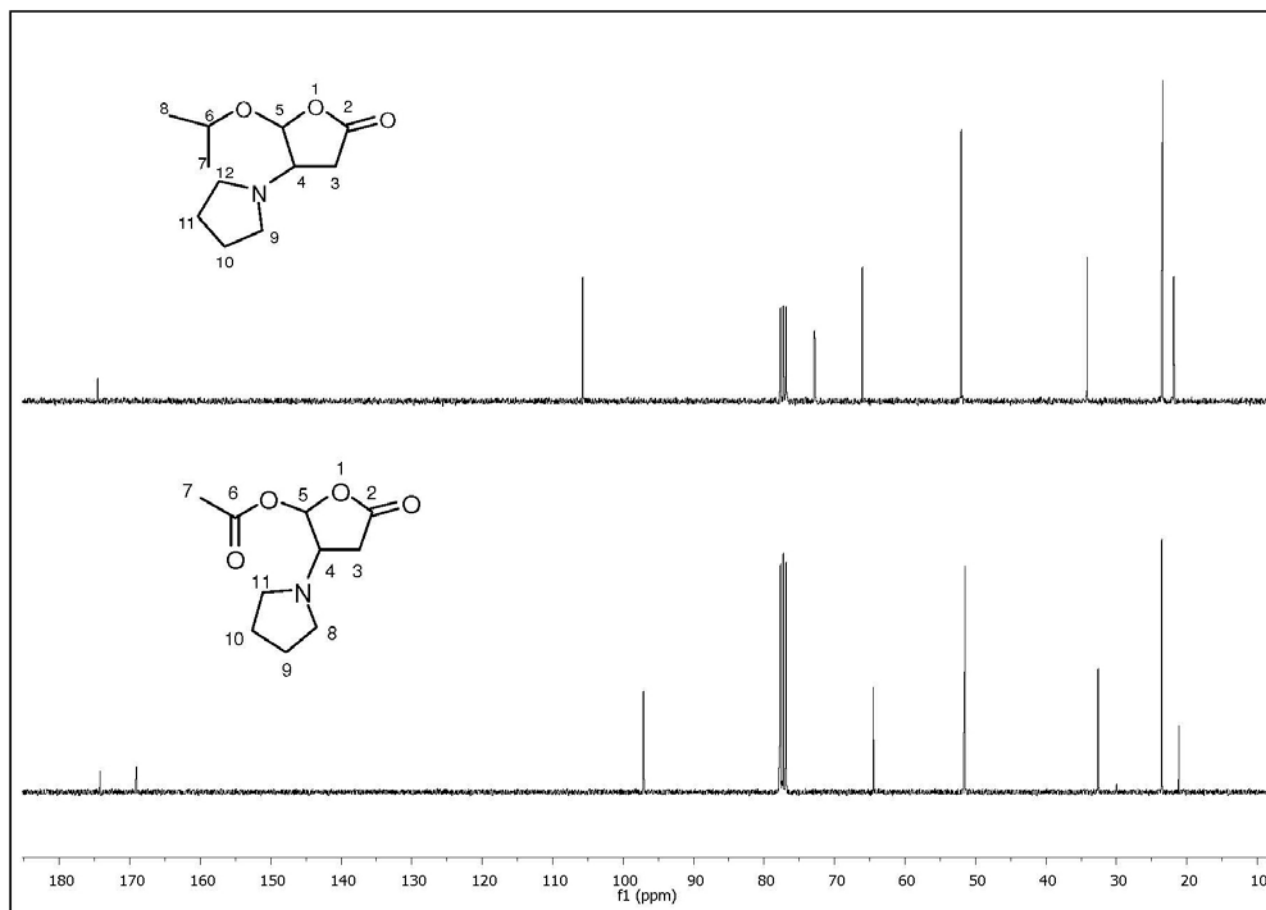


Figure S39. ^{13}C NMR spectra (75 MHz, CDCl_3) of 5-isopropoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **14** and 5-acetoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **15**.

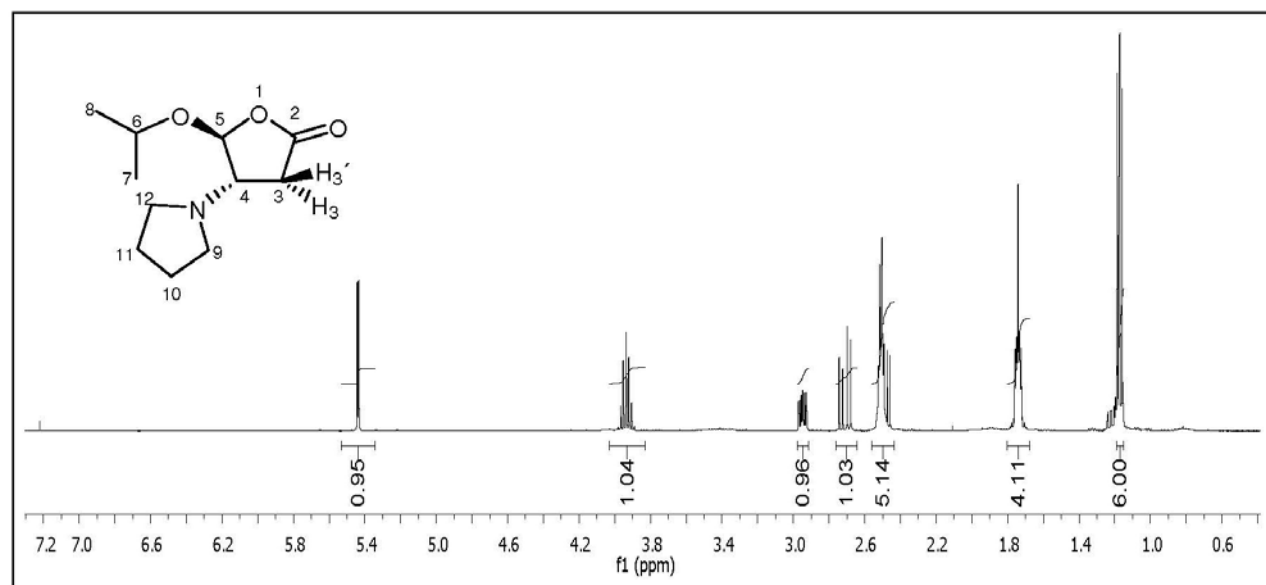


Figure S40. ^1H NMR spectrum (300 MHz, CDCl_3) of 5-isopropoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **14**.

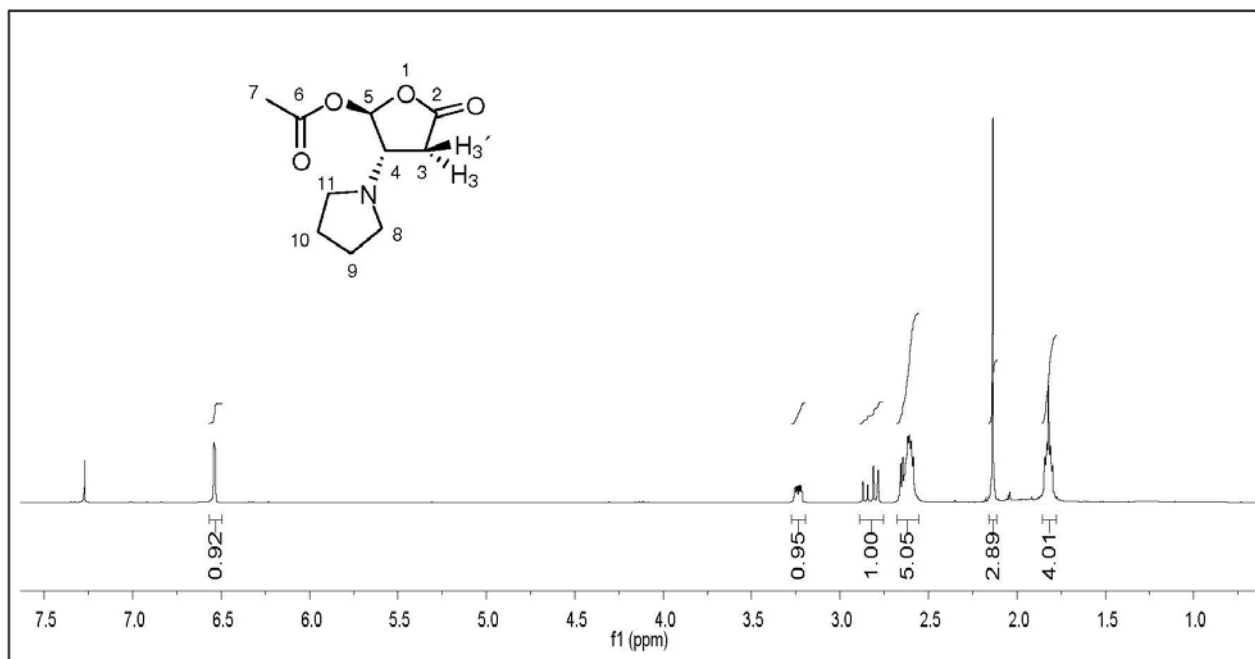


Figure S41. ¹H NMR spectrum (300 MHz, CDCl₃) of 5-acetoxy-4-(pyrrolidin-1-yl)tetrahydrofuran-2-one **15**.