

Supplementary Material

Synthesis of dihydropyranones and dihydropyrano[2,3-d][1,3]dioxine-diones by cyclization reaction of Meldrum's acid with arylaldehydes and 1,3-dicarbonyls under thermal and ultrasound irradiation

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Experimental

General. All chemicals were purchased from Aldrich and Merck with high-grade quality, and used without any purification. All melting points were obtained by Bamslead Electrothermal 9200 apparatus and are uncorrected. The reactions were monitored by TLC and all yields refer to isolated products. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 on a Bruker 300 MHz spectrometer. Infrared spectra were recorded on a Bruker FT-IR Equinax-55 spectrophotometer in KBr with absorption in Cm^{-1} . Elemental analyses were performed using a Carlo Erba EA 1108 instrument. All products were characterized by their spectra and physical data.

General procedure for the synthesis of dihydropyranone and dihydropyrano[2,3-d][1,3]dioxine-dione derivatives

Thermal conditions:

A mixture of the appropriate Meldrum's acid **1** (1.0 mmol), arylaldehydes **2** (1.0 mmol), and various 1,3-dicarbonyls (1.0 mmol) were stirred in $\text{H}_2\text{O}:\text{EtOH}$ (4 mL) in the presence of KOH (15%) as a base at 50 °C for an appropriate time. After completion of the reaction, determined by TLC, the solvent was removed under reduced pressure, and the resulting crude product was recrystallized from ethanol to give the pure compounds as a white solid.

Ultrasonic- Irradiation conditions:

A mixture of the appropriate Meldrum's acid **1** (1.0 mmol), arylaldehydes **2** (1.0 mmol), and various 1,3-dicarbonyls (1.0 mmol) in 2 mL of $\text{H}_2\text{O}:\text{EtOH}$ was irradiated under an ultrasonic processor at $25 \pm 1^\circ\text{C}$ and 100 W. After completion of the reaction, determined by TLC, the solvent was removed under reduced pressure, and the resulting crude product was recrystallized from ethanol to give the pure compounds as a white solid.

5-Acetyl-6-methyl-4-phenyl-3,4-dihydro-2H-pyran-2-one (4a). Mp 101-103 °C (102-104 °C, Lit.³⁴). IR ν/cm^{-1} (KBr): 1724, 1690, 1442, 1358, 1270, 1226, 1186, 1147. ^1H NMR (300 MHz, CDCl_3): δ 2.10 (s, 3H, COCH_3), 2.34 (s, 3H, CH_3), 2.68 (dd, $j = 2.1$ and 15.7 Hz, 1H, CH_2), 3.18 (dd, $j = 7.2$ and 15.7 Hz, 1H, CH_2), 4.31 (d, $j = 6.6$ Hz, 1H, CH), 7.16-7.36 (m, 5H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ 18.64, 29.70, 36.84, 37.33, 126.67, 127.35, 128.31, 129.07, 140.61, 159.62, 166.30, 197.62 ppm.

5-Acetyl-6-methyl-4-(o-tolyl)-3,4-dihydro-2H-pyran-2-one (4b). Mp 138-140 (137-139 °C, Lit.³⁴). IR ν/cm^{-1} (KBr): 1772, 1693, 1622, 1425, 1380, 1353, 1343, 1247, 1192. ¹H NMR (300 MHz, CDCl₃): δ 2.10 (s, 3H, COCH₃), 2.27 (s, 3H, CH₃), 2.34 (s, 3H, CH₃), 2.67 (dd, $j = 2.2$ and 15.7 Hz, 1H, CH₂), 3.16 (dd, $j = 7.2$ and 15.7 Hz, 1H, CH₂), 4.27 (d, $j = 6.5$ Hz, 1H, CH), 6.93-7.24 (m, 4H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 18.58, 21.00, 29.64, 36.83, 37.35, 117.24, 123.55, 127.28, 128.03, 128.90, 138.26, 140.57, 159.51, 166.25, 197.59 ppm.

5-Acetyl-4-(3-chlorophenyl)-6-methyl-3,4-dihydro-2H-pyran-2-one (4c). Mp 188-190 °C. IR ν/cm^{-1} (KBr): 1762, 1728, 1594, 1572, 1477, 1436, 1392, 1302, 1284, 1201. ¹H NMR (300 MHz, CDCl₃): δ 2.10 (s, 3H, COCH₃), 2.34 (s, 3H, CH₃), 2.67 (dd, $j = 2.2$ and 15.8 Hz, 1H, CH₂), 3.15 (dd, $j = 7.0$ and 15.8 Hz, 1H, CH₂), 4.29 (d, $j = 6.4$ Hz, 1H, CH), 7.14-7.41 (m, 4H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): $\delta = 18.61, 29.70, 36.86, 37.31, 117.14, 123.42, 127.32, 128.06, 128.88, 138.22, 140.59, 159.58, 166.28, 197.60$ ppm. Anal. Calcd for C₁₄H₁₃ClO₃ (264.71): C, 63.53; H, 4.95. Found: C, 63.79; H, 4.97 %.

Ethyl 6-methyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (6a). Mp 178-180 °C (Yellow oil, Lit.³³). IR ν/cm^{-1} (KBr): 1729, 1610, 1583, 1458, 1514, 1377, 1391, 1289, 1201, 1183. ¹H NMR (300 MHz, CDCl₃): δ 1.08 (t, $j = 6.9$ Hz, 3H, CH₃CH₂), 2.40 (s, 3H, CH₃), 2.68 (dd, $j = 2.1$ and 15.9 Hz, 1H, CH₂), 3.20 (dd, $j = 7.5$ and 15.8 Hz, 1H, CH₂), 4.05 (q, $j = 6.9$ Hz, 2H, OCH₂), 4.22 (d, $j = 6.9$ Hz, 1H, CH), 7.12-7.33 (m, 5H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 13.88, 18.43, 36.22, 37.01, 60.37, 126.44, 127.13, 127.99, 128.84, 141.04, 160.98, 165.52, 166.39 ppm.

Ethyl 6-methyl-2-oxo-4-(4-(trifluoromethyl)phenyl)-3,4-dihydro-2H-pyran-5-carboxylate (6b) Mp 192-194 °C. IR ν/cm^{-1} (KBr): 1733, 1712, 1619, 1465, 1376, 1331, 1246, 1160, 1118. ¹H NMR (300 MHz, CDCl₃): $\delta = 1.10$ (t, $j = 6.9$ Hz, 3H, CH₃CH₂), 2.48 (s, 3H, CH₃), 2.70 (dd, $j = 2.1$ and 15.9 Hz, 1H, CH₂), 3.23 (dd, $j = 7.5$ and 15.8 Hz, 1H, CH₂), 4.08 (q, $j = 6.9$ Hz, 2H, OCH₂), 4.25 (d, $j = 6.9$ Hz, 1H, CH), 7.53 (d, $j = 8.1$ Hz, 2H, ArH), 7.66 (d, $j = 8.1$ Hz, 2H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 13.91, 19.03, 36.16, 37.01, 61.35, 124.13, 125.94, 126.83, 128.09, 128.64, 140.14, 161.48, 165.48, 166.41 ppm. Anal. Calcd for C₁₆H₁₅F₃O₄ (328.29): C, 58.54; H, 4.61. Found: C, 58.39; H, 4.58 %.

7,7-Dimethyl-4-(m-tolyl)-4,6,7,8-tetrahydro-2H-chromene-2,5(3H)-dione (8a). Mp 118-120 °C. IR ν/cm^{-1} (KBr): 1786, 1655, 1373, 1294, 1158, 1147, 1112. ^1H NMR (300 MHz, CDCl_3): δ 1.06 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 2.24 (d, $j = 16.0$ Hz, 1H, CHH), 2.27 (s, 3H, CH_3), 2.33 (d, $j = 16.0$ Hz, 1H, CHH), 2.51 (d, $j = 17.8$ Hz, 1H, CHH), 2.62 (d, $j = 17.8$ Hz, 1H, CHH), 2.70 (dd, $j = 1.3$ and 15.9 Hz, 1H, CH_2), 3.22 (dd, $j = 7.8$ and 15.9 Hz, 1H, CH_2), 4.14 (d, $j = 7.5$ Hz, 1H, CH), 6.87-7.20 (m, 4H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ 21.03, 27.66, 27.83, 32.22, 33.14, 36.58, 49.96, 115.07, 123.24, 127.19, 127.72, 128.70, 137.98, 141.147, 166.18, 166.41, 195.81 ppm. Anal. Calcd for $\text{C}_{18}\text{H}_{20}\text{O}_3$ (284.36): C, 76.03; H, 7.09. Found: C, 75.90; H, 7.08 %.

4-(4-Chlorophenyl)-7,7-dimethyl-4,6,7,8-tetrahydro-2H-chromene-2,5(3H)-dione (8b). Mp 150-152 °C. IR ν/cm^{-1} (KBr): 1772, 1655, 1490, 1373, 1212, 1112. ^1H NMR (300 MHz, CDCl_3): δ 1.04 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 2.23 (d, $j = 16.0$ Hz, 1H, CHH), 2.31 (d, $j = 16.0$ Hz, 1H, CHH), 2.56 (d, $j = 17.8$ Hz, 1H, CHH), 2.61 (d, $j = 17.8$ Hz, 1H, CHH), 2.71 (dd, $j = 1.3$ and 16.0 Hz, 1H, CH_2), 3.26 (dd, $j = 7.9$ and 16.1 Hz, 1H, CH_2), 4.18 (d, $j = 7.5$ Hz, 1H, CH), 7.13 (d, $j = 7.2$ Hz, 2H, ArH), 7.36 (d, $j = 7.2$ Hz, 2H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ 27.71, 27.79, 32.19, 32.60, 36.21, 49.87, 114.71, 128.36, 128.77, 131.68, 140.20, 166.24, 166.44, 195.83 ppm. Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{ClO}_3$ (304.77): C, 67.00; H, 5.62. Found: C, 67.12; H, 5.65 %.

5-(4-Chlorophenyl)-6-(1-hydroxy-2-methylprop-1-en-1-yl)-2,2-dimethyl-5,6-dihydro-4H,7H-pyrano[2,3-d][1,3]dioxine-4,7-dione (10a). Mp 188-190 °C. IR ν/cm^{-1} (KBr): 1758, 1731, 1605, 1587, 1491, 1391, 1377, 1303, 1285, 1114. ^1H NMR (300 MHz, CDCl_3): δ 0.54 (s, 6H, 2 CH_3), 2.25 (s, 6H, 2 CH_3), 2.44 (m, 1H, CH), 3.44 (d, $j = 15.2$ Hz, 1H, CH), 4.01 (d, $j = 15.2$ Hz, 1H, CH), 6.92-7.27 (m, 4H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ 18.56, 20.95, 27.61, 42.32, 48.73, 59.78, 105.90, 125.30, 128.73, 128.89, 129.00, 137.36, 138.21, 164.78, 167.51, 206.54 ppm. Anal. Calcd for $\text{C}_{19}\text{H}_{19}\text{ClO}_6$ (378.81): C, 60.24; H, 5.06. Found: C, 60.18; H, 5.03 %.

5-(4-Bromophenyl)-6-(1-hydroxy-2-methylprop-1-en-1-yl)-2,2-dimethyl-5,6-dihydro-4H,7H-pyrano[2,3-d][1,3]dioxine-4,7-dione (10b). Mp 166-168 °C. IR ν/cm^{-1} (KBr): 1754, 1725, 1514, 1394, 1382, 1362, 1287, 1194. ^1H NMR (300 MHz, CDCl_3): δ 0.53 (s, 6H, 2 CH_3), 2.23 (s, 6H, 2 CH_3), 2.41 (m, 1H, CH), 3.46 (d, $j = 14.7$ Hz, 1H, CH), 4.00 (d, $j = 14.7$ Hz, 1H, CH), 7.02 (d, $j = 7.8$ Hz, 2H, ArH), 7.16 (d, $j = 7.8$ Hz, 2H, ArH) ppm. ^{13}C NMR (75 MHz, CDCl_3): δ 19.04, 20.50, 27.72, 48.42, 59.98, 105.85, 128.04, 129.42, 134.27, 137.81, 138.19,

164.76, 167.61, 206.56 ppm. Anal. Calcd for C₁₉H₁₉BrO₆ (423.26): C, 53.92; H, 4.52. Found: C, 53.80; H, 4.51 %.

5-(4-Methoxyphenyl)-2,2-dimethyl-5,6-dihydro-4H,7H-pyrano[2,3-d][1,3]dioxine-4,7-dione (12a). Mp 181-183 °C. IR ν/cm^{-1} (KBr): 1762, 1728, 1610, 1514, 1458, 1391, 1377, 1315, 1289, 1252, 1183. ¹H NMR (300 MHz, CDCl₃): δ 0.58 (s, 6H, 2CH₃), 2.43 (dd, $j = 4.4$ and 31.5 Hz, 1H, CH₂), 3.41 (dd, $j = 14.1$ and 31.3 Hz, 1H, CH₂), 3.69 (s, 3H, OCH₃), 4.12 (dd, $j = 4.3$ and 13.9 Hz, 1H, CH), 6.91 (d, $j = 8.7$ Hz, 2H, ArH), 7.05 (d, $j = 8.7$ Hz, 2H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 27.87, 42.56, 47.99, 55.19, 60.35, 105.90, 114.33, 117.41, 129.32, 159.22, 164.89, 167.84, 206.71 ppm. Anal. Calcd for C₁₆H₁₆O₆ (304.30): C, 63.15; H, 5.30. Found: C, 63.27; H, 5.33 %.

2,2-Dimethyl-5-(4-(trifluoromethyl)phenyl)-5,6-dihydro-4H,7H-pyrano[2,3-d][1,3]dioxine-4,7-dione (12b). Mp 218-220 °C. IR ν/cm^{-1} (KBr): 1731, 1621, 1428, 1394, 1328, 1280, 1171, 1121. ¹H NMR (300 MHz, CDCl₃): δ 0.50 (s, 6H, 2CH₃), 2.42 (dd, $j = 4.2$ and 31.0 Hz, 1H, CH₂), 3.42 (dd, $j = 15.1$ and 31.5 Hz, 1H, CH₂), 4.00 (dd, $j = 4.2$ and 13.7 Hz, 1H, CH), 7.39 (d, $j = 8.1$ Hz, 2H, ArH), 7.78 (d, $j = 8.1$ Hz, 2H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 27.57, 41.71, 48.33, 106.18, 122.09, 126.06, 129.04, 129.40, 155.79, 164.41, 167.22, 205.51 ppm. Anal. Calcd for C₁₆H₁₃F₃O₅ (342.27): C, 56.15; H, 3.83. Found: C, 56.21; H, 3.79 %.

5-(3-Fluorophenyl)-2,2-dimethyl-5,6-dihydro-4H,7H-pyrano[2,3-d][1,3]dioxine-4,7-dione (12c). Mp 173-175 °C. IR ν/cm^{-1} (KBr): 1733, 1570, 1475, 1434, 1395, 1304, 1200, 1110. ¹H NMR (300 MHz, CDCl₃): δ 0.53 (s, 6H, 2CH₃), 2.44 (dd, $j = 4.2$ and 31.1 Hz, 1H, CH₂), 3.43 (dd, $j = 15.0$ and 31.4 Hz, 1H, CH₂), 3.98 (dd, $j = 4.4$ and 13.7 Hz, 1H, CH), 7.13-7.23 (m, 4H, ArH) ppm. ¹³C NMR (75 MHz, CDCl₃): δ 27.75, 41.94, 48.22, 106.17, 115.32, 124.60, 131.31, 140.01, 160.57, 163.82, 164.51, 167.43, 205.79 ppm. Anal. Calcd for C₁₅H₁₃FO₅ (292.26): C, 61.64; H, 4.48. Found: C, 61.57; H, 4.45 %.