Polarizing the Nazarov cyclization: Efficient Catalysis under Mild Conditions

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Supporting information

General Methods: All reactions were carried out in vials without argon protection¹. Cu(OTf)₂ was stored in glove box before use. Dichloroethane and dichloromethane were purchased from Fisher and distilled over calcium hydride. Column chromatography was performed on EM Science silica gel 60 (230-400 mesh). Visualization was done with potassium permanganate or ceric ammonium molybdate.

Infrared spectra were recorded on a ATI Mattson Genesis FT-IR spectrometer. ¹H NMR and ¹³C NMR spectra were collected on a Bruker Amax 400 or an Avance 400 MHz spectrometer at ambient temperature. Chemical shift δ was reported in unit of parts per million downfield from tetramethylsilane. Elemental Analysis was done by MHW labs at Phoenix, AZ. HRMS was done on a ThermoFinnigan MAT 95XL with electrospray with 50% MeOH.

Preparation of substrates

All Nazarov substrates bearing ester group were prepared from Knoevenagel reaction between a β -keto ester which already contains the left olefin moiety and an aldehyde². Substrate **15a**, **15f**, **17a** and **17f** were prepared from condensation between a ketone which already contains the left olefin moiety and the corresponding aldehyde under basic conditions.

Spectroscopic data of substrates:

2-(5,6-Dihydro-4H-pyran-2-carbonyl)-3-(2,4,6-trimethoxy-phenyl)-acrylic acid methyl ester

3a ¹H NMR (400 MHz, CDCl₃) δ 7.90 (s, 1H), 5.98 (s, 2H), 5.79 (s, 1H), 3.98 (t, J = 4.6 Hz, 2H), 3.74 (s,

¹ While argon protection did not generally improve yield for most substrates, after submission we found that argon protection of fairly unreactive substrates **15f** and **17f** gave better yields.

² Desimoni, G., Faita, G., Ricci, M., Righetti, P., *Tetrahedron* **1998**, *54*, 9581

3H), 3.71 (s, 3H), 3.66 (s, 6H), 2.06 (d, $J = 4.5$ Hz, 2H), 1.75 (t, $J = 4.4$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 188.6, 166.7, 163.4, 159.3, 151.1, 135.3, 127.5, 111.1, 104.8, 90.0, 66.1, 55.2, 54.9, 51.8, 21.6, 20.6; IR (NaCl plate, cm^{-1}): 1712, 1603, 1460, 1336, 1255, 1206, 1156, 1127, 1056; Elemental analysis calculated for $\text{C}_{19}\text{H}_{22}\text{O}_7$: C 62.97%; H 6.12%. Found : C 62.79%; H 6.20%.

2-(5,6-Dihydro-4H-pyran-2-carbonyl)-3-(4-methoxy-phenyl)-acrylic acid methyl ester

3b ^1H NMR (400 MHz, CDCl_3) δ 7.59 (s, 1H), 7.16 (d, $J = 8.8$ Hz, 2H), 6.67 (d, $J = 8.8$ Hz, 2H), 5.87 (t, $J = 4.4$ Hz, 1H), 3.93 (t, $J = 5.6$ Hz, 2H), 3.62 (s, 6H), 1.98 (m, 2H), 1.65 (t, $J = 6$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 190.7, 165.3, 161.2, 150.9, 142.5, 132.0, 127.1, 125.2, 116.2, 114.0, 66.3, 55.1, 52.0, 21.0, 20.8; IR (NaCl plate, cm^{-1}): 1714, 1601, 1512, 1259, 1204, 1175, 734; HRMS calculated for $\text{C}_{17}\text{H}_{18}\text{O}_5$ ($\text{M}+\text{H}$) $^+$ 303.1224, Found : 303.1227.

2-(5,6-Dihydro-4H-pyran-2-carbonyl)-3-(3-methoxy-phenyl)-acrylic acid methyl ester

3c ^1H NMR (400 MHz, CDCl_3) δ 7.58 (s, 1H), 7.03 (t, $J = 3.6$ Hz, 1H), 6.75 (d, $J = 9.6$ Hz, 1H), 6.69 (s, 2H), 5.81 (t, $J = 4.4$ Hz, 1H), 3.86 (t, $J = 4.6$ Hz, 2H), 3.58 (s, 3H), 3.53 (s, 3H), 1.94 (d, $J = 6$ Hz, 2H), 1.57 (t, $J = 6.0$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 189.9, 164.8, 159.3, 150.9, 142.6, 133.9, 130.3, 129.5, 122.4, 116.4, 115.8, 114.3, 66.2, 54.7, 52.1, 21.0, 20.7; IR (NaCl plate, cm^{-1}): 1715, 1671, 1624, 1236, 1051; HRMS calculated for $\text{C}_{17}\text{H}_{18}\text{O}_5$ ($\text{M}+\text{H}$) $^+$ 303.1233 Found : 303.1227.

2-(5,6-Dihydro-4H-pyran-2-carbonyl)-3-phenyl-acrylic acid methyl ester

3d ^1H NMR (400 MHz, CDCl_3) δ 7.58 (s, 1H), 7.13 (m, 2H), 7.04 (m, 3H), 5.77 (t, $J = 4.1$ Hz, 1H), 3.79 (t, $J = 4.4$ Hz, 2H), 3.53 (s, 3H), 1.86 (m, 2H), 1.52 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 189.9, 164.8, 150.8, 142.6, 132.6, 131.1, 129.8, 128.4, 115.9, 66.1, 52.1, 52.1, 20.9, 20.6; IR (NaCl plate, cm^{-1}): 1714, 1257, 1201, 1051; Elemental analysis calculated for $\text{C}_{16}\text{H}_{16}\text{O}_4$: C 70.57%; H 5.92%. Found : C 70.80%; H 6.02%.

2-(5,6-Dihydro-4H-pyran-2-carbonyl)-3-furan-2-yl-acrylic acid methyl ester

3e ^1H NMR (400 MHz, CDCl_3) δ 7.34 (s, 1H), 7.28 (d, $J = 1.2$ Hz, 1H), 6.51 (d, $J = 3.6$ Hz, 1H), 6.26 (q, $J = 1.6$ Hz, 1H), 5.77 (t, $J = 3.6$ Hz, 1H), 3.91 (t, $J = 4.8$ Hz, 2H), 3.56 (s, 3H), 1.98 (m, 2H), 1.63 (t, $J = 5.2$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 189.0, 164.9, 151.1, 148.9, 146.0, 128.2, 125.8, 117.8, 115.5,

112.4, 66.2, 52.1, 22.1, 20.7; IR (NaCl plate, cm^{-1}): 1710, 1671, 1626, 1253, 1212; Elemental analysis calculated for $\text{C}_{14}\text{H}_{14}\text{O}_5$: C 64.12%; H 5.38%. Found : C 63.83%; H 5.42%.

3-Cyclohexyl-2-(5,6-dihydro-4H-pyran-2-carbonyl)-acrylic acid methyl ester

3f ^1H NMR (400 MHz, CDCl_3) δ 6.69 (d, $J = 10.8$ Hz, 1H), 5.85 (t, $J = 4.4$ Hz, 1H), 3.99 (t, $J = 5.2$ Hz, 2H), 3.60 (s, 3H), 2.08 (m, 2H), 2.03 (m, 1H), 1.76 (m, 2H), 1.54 (m, 5H), 1.02 (m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 189.1, 164.9, 152.7, 151.5, 130.4, 115.4, 66.2, 51.8, 38.4, 31.3, 25.3, 24.8, 21.1, 20.8; IR (NaCl plate, cm^{-1}): 2925, 2853, 1738, 1713, 1645, 1444, 1300, 1266, 1216, 1162, 1123, 1071, 1034; Elemental analysis calculated for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C 69.04%; H 7.97%. Found : C 69.17%; H 7.79%.

2-(Cyclohex-1-enecarbonyl)-3-(2,4,6-trimethoxy-phenyl)-acrylic acid methyl ester

5a ^1H NMR (400 MHz, CDCl_3) δ 7.98 (s, 1H), 6.62 (s, 1H), 6.06 (s, 2H), 3.78 (s, 3H), 3.76 (s, 3H), 3.71 (s, 6H), 2.25 (m, 2H), 2.04 (m, 2H), 1.52 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 194.8, 167.3, 163.1, 159.3, 141.5, 138.2, 134.9, 128.4, 105.3, 89.9, 55.2, 54.9, 51.9, 25.8, 22.8, 21.8, 21.6; IR (NaCl plate, cm^{-1}): 1710, 1603, 1251, 1206, 1157, 1128; Elemental analysis calculated for $\text{C}_{20}\text{H}_{24}\text{O}_6$: C 66.65%; H, 6.71%. Found : C 66.48%; H 6.56%.

2-(Cyclohex-1-enecarbonyl)-3-cyclohexyl-acrylic acid methyl ester

5f A separable mixture of E and Z stereoisomers were obtained in a ratio of 10:1 (ratio of mass after column on silica). The geometry was assigned by comparing the chemical shift of the vinylic proton at β' position. E isomer: ^1H NMR (400 MHz, CDCl_3) δ 6.63 (m, 2H), 3.56 (s, 3H), 2.10 (m, 4H), 1.88(m, 1H), 1.51(m, 9H), 1.02(m, 5H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 195.3, 165.1, 150.8, 144.6, 139.9, 131.2, 51.7, 38.5, 31.3, 25.9, 25.3, 24.8, 22.2, 21.5, 21.3; IR (NaCl plate, cm^{-1}): 2927, 2852, 1722, 1658, 1254, 1228; Elemental analysis calculated for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C 73.88%; H 8.75%. Found : C 74.12%; H 8.54%.

4-Methyl-3-oxo-2-(2,4,6-trimethoxy-benzylidene)-pent-4-enoic acid methyl ester

7a ^1H NMR (400 MHz, CDCl_3) δ 7.95 (s, 1H), 5.96 (s, 2H), 5.71 (s, 1H), 5.61(s, 1H), 3.76 (s, 3H), 3.71 (s, 3H), 3.65 (s, 6H), 1.85(s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 195.2, 167.2, 163.4, 159.5, 143.6, 135.0, 127.8, 125.8, 105.8, 90.1, 55.2, 54.9, 51.9, 16.8; IR (NaCl plate, cm^{-1}): 1710, 1664, 1603, 1462, 1436, 1252,

1208, 1158, 1129, 735; Elemental analysis calculated for $C_{17}H_{20}O_6$: C 63.74%; H 6.29%. Found : C 63.86%; H 6.35%.

2-(Benzo[1,3]dioxole-5-carbonyl)-3-(2,4,6-trimethoxy-phenyl)-acrylic acid methyl ester

9a 1H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.48 (q, J = 9.8 Hz, 1H), 7.44 (d, J = 1.6 Hz, 1H), 6.79 (d, J = 8.1 Hz, 1H), 6.03 (s, 2H), 5.96 (s, 2H), 3.79 (s, 3H), 3.72 (s, 3H), 3.53 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 191.8, 167.2, 163.4, 159.6, 151.0, 147.6, 135.5, 132.5, 128.0, 125.1, 108.2, 107.5, 105.0, 101.5, 90.7, 55.2, 54.6, 52.0; IR (NaCl plate, cm^{-1}): 1707, 1664, 1603, 1439, 1254, 1209, 1158, 1129, 1035; Elemental analysis calculated for $C_{21}H_{20}O_8$: C 63.00%; H 5.03%. Found : C 63.24%; H 4.99%.

2-(2-Methyl-cyclohex-1-enecarbonyl)-3-(2,4,6-trimethoxy-phenyl)-acrylic acid methyl ester

11a 1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 6.00 (s, 2H), 3.74 (s, 3H), 3.71 (s, 3H), 3.63 (s, 6H), 2.11 (m, 2H), 2.00 (m, 2H), 1.88 (s, 3H), 1.43 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 195.5, 166.9, 162.9, 159.1, 145.7, 134.6, 132.5, 131.8, 105.1, 90.2, 55.3, 55.2, 51.8, 34.2, 26.5, 22.5, 22.3, 22.0; IR (NaCl plate, cm^{-1}): 2935, 1726, 1602, 1459, 1336, 1232, 1208, 1157, 1129; Elemental analysis calculated for $C_{21}H_{26}O_6$: C 67.36%; H 7.00%. Found : C 67.50%; H 6.98%.

3-Oxo-2-(2,4,6-trimethoxy-benzylidene)-hex-4-enoic acid ethyl ester

13a As an unseparable mixture of Z and E stereoisomers (0.6: 1.0 according to the integration on 1H NMR). 1H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.78 (s, 0.6H), 7.00 (m, 0.6H), 6.68 (m, 1H), 6.19 (d, J = 1.6 Hz, 0.6H), 6.15 (d, J = 1.6 Hz, 1H), 6.08 (s, 1.2H), 6.04 (s, 2H), 4.24 (m, 2H), 4.13 (m, 1.2H), 3.88 (s, 2.4H), 3.83 (s, 3.6H), 3.79 (s, 6H), 3.73 (s, 6H), 1.92 (d, J = 1.6 Hz, 1.2H), 1.82 (d, J = 1.8 Hz, 2H), 1.28 (m, 1.8H), 1.24 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 193.0, 188.3, 167.8, 166.5, 163.5, 163.3, 159.8, 159.5, 143.7, 142.4, 136.1, 135.1, 133.0, 132.0, 129.6, 128.6, 105.8, 105.2, 90.2, 60.9, 60.4, 55.4, 55.3, 54.9, 18.4, 18.1, 14.2, 13.9; IR (NaCl plate, cm^{-1}): 1653, 1605, 1207, 1155, 1128, 500; Elemental analysis calculated for $C_{18}H_{22}O_6$: C 64.66%; H 6.63%. Found : C 64.75%; H 6.52%.

1-(5,6-Dihydro-4H-pyran-2-yl)-3-(2,4,6-trimethoxy-phenyl)-propenone

15a 1H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 16 Hz, 1H), 7.58 (d, J = 16 Hz, 1H), 6.08 (s, 2H), 6.02 (t,

$J = 3.6$ Hz, 1H), 4.11 (m, 2H), 3.85 (s, 6H), 3.82 (s, 3H), 2.23 (m, 2H), 1.86 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 186.7, 162.8, 161.5, 152.3, 134.8, 120.0, 109.6, 106.3, 90.2, 66.1, 55.6, 55.2, 21.5, 20.8; IR (NaCl plate, cm^{-1}): 1567, 1463, 1324, 1206, 1177, 1157, 1120, 1062; Elemental analysis calculated for $\text{C}_{17}\text{H}_{20}\text{O}_5$: C 67.09%; H 6.62%. Found : C 67.18%; H 6.69%.

3-Cyclohexyl-1-(5,6-dihydro-4H-pyran-2-yl)-propenone

15f ^1H NMR (400 MHz, CDCl_3) δ 6.96 (dd, $J_1 = 15.6$ Hz, $J_2 = 6.8$ Hz, 1H), 6.62 (d, $J = 15.6$ Hz, 1H), 6.02 (t, $J = 8$ Hz, 1H), 4.11 (m, 2H), 2.24 (m, 2H), 2.21 (m, 1H), 1.86 (m, 2H), 1.17-1.75 (m, 10H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 185.9, 153.8, 151.7, 121.4, 110.7, 66.25, 43.3, 31.7, 26.4, 26.2, 21.5, 20.8; IR (NaCl plate, cm^{-1}): 2926, 2853, 1725, 1632, 1448, 1309, 1280, 1243, 1176, 1062, 916; Elemental analysis calculated for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C 76.33%; H 9.15%. Found : C 76.18%; H 9.19%.

1-Cyclohex-1-enyl-3-(2,4,6-trimethoxy-phenyl)-propenone

17a ^1H NMR (400 MHz, CDCl_3) δ 8.02 (d, $J = 16$ Hz, 1H), 7.60 (d, $J = 16$ Hz, 1H), 6.91 (t, $J = 4$ Hz, 1H), 6.09 (s, 2H), 3.85 (s, 6H), 3.81 (s, 3H), 2.34 (m, 2H), 2.26 (m, 2H), 1.64 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 192.7, 162.4, 161.2, 140.3, 138.1, 133.5, 121.4, 106.5, 90.3, 55.6, 55.2, 26.0, 23.6, 22.0, 21.6; IR (NaCl plate, cm^{-1}): 2933, 1642, 1571, 1458, 1322, 1205, 1156, 1120; Elemental analysis calculated for $\text{C}_{18}\text{H}_{22}\text{O}_4$: C 71.50%; H 7.33%. Found : C 71.68%; H 7.25%.

1-Cyclohex-1-enyl-3-cyclohexyl-propenone

17f ^1H NMR (400 MHz, CDCl_3) δ 6.84 (br. m, 1H), 6.74 (dd, $J_1 = 15.2$ Hz, $J_2 = 7.8$ Hz, 1H), 6.52 (d, $J = 15.2$ Hz, 1H), 2.20 (m, 4H), 2.08 (m, 1H), 1.70 (m, 4H), 1.56 (m, 5H), 1.25 (m, 2H), 1.15 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 191.4, 151.6, 139.7, 139.4, 122.0, 40.6, 31.8, 25.9, 25.8, 25.6, 25.6, 23.2, 21.8, 21.4; IR (NaCl plate, cm^{-1}): 2924, 2852, 1659, 1613; Elemental analysis calculated for $\text{C}_{15}\text{H}_{22}\text{O}$: C 82.52%; H 10.16%. Found : C 82.19%; H 9.90%.

Representative procedure of $\text{Cu}(\text{OTf})_2$ catalyzed Nazarov cyclization

To a stirred suspension of $\text{Cu}(\text{OTf})_2$ (2.2 mg, 0.006 mmol, 0.02 eq.) in dichloroethane (0.5 mL) was added a solution of **5a** (110 mg, 0.304 mmol, 1.00 eq.) in dichloroethane (1 mL). The resulting mixture was heated to 40 °C under vigorous stirring. After 15 minutes, TLC found complete consumption of the starting material. The reaction was then cooled down to room temperature and purified by flash chromatography on

silica eluting with 20% EtOAc/Hexanes to give **6a-1** (43 mg 40%) and **6a-2** (49 mg, 45%).

Spectroscopic data of Nazarov products

1-Oxo-3-(2,4,6-trimethoxy-phenyl)-2,3,3a,4,5,6-hexahydro-1H-indene-2-carboxylic acid

methyl ester

6a-1 ^1H NMR (400 MHz, CDCl_3) δ 6.80 (dd, $J_1 = 6.4$ Hz, $J_2 = 3.2$ Hz, 1H), 6.14 (s, 2H), 4.30 (d, $J = 12.1$ Hz, 1H), 3.80 (t, $J = 12.1$ Hz, 1H), 3.77 (s, 3H), 3.74 (s, 6H), 3.65 (s, 3H), 2.93 (m, 1H), 2.04 (m, 2H), 1.80 (m, 2H), 1.25 (m, 1H), 1.13 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 199.4, 170.3, 159.9, 159.7, 140.6, 134.4, 107.5, 91.1, 91.0, 57.6, 55.2, 55.0, 52.0, 40.4, 39.6, 27.1, 25.6, 21.5; IR (NaCl plate, cm^{-1}): 1742, 1711, 1606, 1459, 1202, 1151, 1115; Elemental analysis calculated for $\text{C}_{20}\text{H}_{24}\text{O}_6$: C 66.65%; H, 6.71%. Found : C 66.80%; H 6.75%.

1-Oxo-3-(2,4,6-trimethoxy-phenyl)-2,3,4,5,6,7-hexahydro-1H-indene-2-carboxylic acid

methyl ester

6a-2 ^1H NMR (400 MHz, CDCl_3) δ 6.16 (d, $J = 2.4$ Hz, 1H), 6.06 (d, $J = 2.4$ Hz, 1H), 4.84 (m, 1H), 3.81 (s, 6H), 3.74 (s, 3H), 3.67 (s, 3H), 3.59 (d, $J = 5.8$ Hz, 1H), 2.00 (m, 2H), 1.73 (m, 1H), 1.71 (m, 1H), 1.63 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 201.6, 177.1, 170.7, 160.4, 159.4, 159.2, 134.9, 107.2, 90.7, 58.2, 56.0, 55.2, 55.1, 41.6, 26.2, 22.1, 21.5, 20.2; IR (NaCl plate, cm^{-1}): 2937, 1737, 1697, 1643, 1604, 1459, 1436, 1332, 1258, 1228, 1205, 1150, 1116, 733; Elemental analysis calculated for $\text{C}_{20}\text{H}_{24}\text{O}_6$: C 66.65%; H, 6.71%. Found : C 66.81%; H 6.62%.

7-Oxo-5-(2,4,6-trimethoxy-phenyl)-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid

methyl ester

4a ^1H NMR (400 MHz, CDCl_3) δ 6.11 (s, 1H), 6.04 (s, 1H), 4.78 (d, $J = 1.6$ Hz, 1H), 4.05 (t, $J = 4.6$ Hz, 2H), 3.74 (s, 6H), 3.69 (s, 3H), 3.64 (s, 3H), 3.54 (d, $J = 1.6$ Hz, 1H), 1.92 (m, 1H), 1.90 (m, 1H), 1.87 (m, 1H), 1.82 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 193.9, 170.0, 160.5, 149.5, 148.2, 106.2, 90.7, 66.6, 56.1, 55.9, 52.2, 37.1, 22.0, 21.3; IR (NaCl plate, cm^{-1}): 1738, 1708, 1605, 1205, 1150, 1120; X-ray crystallography please see attached cif file.

5-(4-Methoxy-phenyl)-7-oxo-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid methyl ester

4b ^1H NMR (400 MHz, CDCl_3) δ 7.01 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 4.13 (m, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.24 (d, J = 2.4 Hz, 1H), 2.10(m, 2H), 1.90(m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 193.0, 168.7, 158.9, 149.5, 147.8, 131.5, 128.2, 114.4, 66.9, 59.3, 55.2, 52.6, 46.8, 22.0, 22.1; IR (NaCl plate, cm^{-1}): 1738, 1713, 1648, 1512, 1250, 1162, 1122; HRMS calculated for $\text{C}_{19}\text{H}_{22}\text{O}_7$ ($\text{M}+\text{H}$) $^+$ 303.1216, Found : 303.1227.

5-(3-Methoxy-phenyl)-7-oxo-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid methyl ester

4c ^1H NMR (400 MHz, CDCl_3) δ 7.23 (t, J = 8 Hz, 1H), 6.78 (dd, J_1 = 8 Hz, J_2 = 6 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 6.64 (d, J = 1.6 Hz, 1H), 4.16 (br. s, 1H), 4.08 (m, 2H), 3.75 (s, 3H), 3.73 (s, 3H), 3.29 (br. s, 1H), 2.10 (m, 2H), 1.88 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 192.8, 168.6, 160.0, 149.7, 147.3, 141.3, 130.1, 119.4, 113.2, 112.6, 66.9, 58.9, 58.9, 55.1, 47.5, 22.1, 21.1; IR (NaCl plate, cm^{-1}): 1736, 1714, 439.3; Elemental analysis calculated for $\text{C}_{17}\text{H}_{18}\text{O}_5$: C 67.54%; H 6.00%. Found : C 67.62%; H 5.94%.

7-Oxo-5-phenyl-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid methyl ester

4d ^1H NMR (400 MHz, CDCl_3) δ 7.33 (t, J = 7.2 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 7.13 (d, J = 7.2 Hz, 2H), 4.20 (br. s, 1H), 4.15 (m, 2H), 3.75 (s, 3H), 3.32 (br. s, 1H), 2.13 (m, 1H), 2.08 (m, 1H), 1.93 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 192.8, 168.6, 149.7, 147.4, 139.7, 128.8, 127.6, 127.2, 66.9, 59.1, 52.8, 47.5, 22.1, 21.1; IR (NaCl plate, cm^{-1}): 1739, 1714, 1648, 1263, 1161, 1123; Elemental analysis calculated for $\text{C}_{16}\text{H}_{16}\text{O}_4$: C 70.57%; H 5.92%. Found : C 70.70%; H 5.78%.

5-Furan-2-yl-7-oxo-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid methyl ester

4e ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, J = 1.2 Hz, 1H), 6.31 (t, J = 1.2 Hz, 1H), 6.17 (d, J = 3.2 Hz, 1H), 4.35 (d, J = 2 Hz, 1H), 4.13 (m, 2H), 3.76 (s, 3H), 3.52 (d, J = 2 Hz, 1H), 2.27 (m, 1H), 2.19 (m, 1H), 1.94 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 192.0, 168.4, 151.7, 149.4, 144.7, 142.4, 110.3, 107.2, 66.9, 55.5, 52.8, 40.8, 22.2, 21.1; IR (NaCl plate, cm^{-1}): 1715, 1649, 524; Elemental analysis calculated for $\text{C}_{14}\text{H}_{14}\text{O}_5$: C 64.12%; H 5.38%. Found : C 64.00%; H 5.51%.

5-Cyclohexyl-7-oxo-2,3,4,5,6,7-hexahydro-cyclopenta[b]pyran-6-carboxylic acid methyl ester

4f ^1H NMR (400 MHz, CDCl_3) δ 4.16 (m, 1H), 4.03 (m, 1H), 3.72(s, 3H), 3.17 (d, $J = 2.4$ Hz, 1H), 3.03 (d, $J = 2.4$ Hz, 1H), 2.33 (m, 2H), 1.93 (m, 2H), 1.69-1.74 (m, 4H), 1.07-1.24 (m, 7H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 194.1, 170.0, 149.1, 147.8, 66.8, 52.6, 51.5, 47.4, 38.2, 31.0, 26.6, 26.3, 26.1, 26.0, 22.7, 21.2; IR (NaCl plate, cm^{-1}): 2359, 2337, 1711, 1033, 824, 614; Elemental analysis calculated for $\text{C}_{16}\text{H}_{22}\text{O}_4$: C 69.04%; H 7.97%. Found : C 68.84%; H 7.93%.

3-Cyclohexyl-1-oxo-2,3,3a,4,5,6-hexahydro-1H-indene-2-carboxylic acid methyl ester

6f-1 (53% isolated yield) ^1H NMR (400 MHz, CDCl_3) δ 6.79 (t, $J = 3.6$ Hz, 1H), 3.76 (s, 3H), 3.16 (d, $J = 11.6$, 1H), 2.36 (m, 2H), 2.20 (m, 2H), 2.12 (m, 1H), 1.76 (m, 1H), 1.65(m, 5H), 1.55(m, 2H), 1.15 (m, 6H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 199.2, 171.2, 140.2, 135.4, 57.8, 52.4, 51.1, 39.7, 38.7, 31.7, 29.3, 28.4, 26.7, 26.5, 26.3, 25.6, 21.7; IR (NaCl plate, cm^{-1}): 2925, 2853, 1744, 1713, 1651, 1447, 1336, 1259, 1149, 979, 422; Elemental analysis calculated for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C 73.88%; H 8.75%. Found : C 73.98%; H 8.69%.

1-Cyclohexyl-3-oxo-2,3,4,5,6,7-hexahydro-1H-indene-2-carboxylic acid methyl ester

6f-2 (17% isolated yield) ^1H NMR (400 MHz, CDCl_3) δ 3.75 (s, 3H), 3.22 (d, $J = 2.4$ Hz, 1H), 3.11 (br. s, 1H), 2.29 (m, 2H), 2.12 (m, 2H), 1.71 (m, 9H), 1.26 (m, 5H), 0.83 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 200.9, 175.6, 170.5, 137.6, 53.3, 52.3, 51.8, 37.9, 31.5, 26.7, 26.4, 26.2, 26.1, 26.0, 22.0, 21.4, 20.1; IR (NaCl plate, cm^{-1}) 2925, 2853, 1738, 1702, 1644, 1439, 1263, 1155, 897, 730; Elemental analysis calculated for $\text{C}_{17}\text{H}_{24}\text{O}_3$: C 73.88%; H 8.75%. Found : C 74.07%; H 8.60%.

3-Methyl-2-oxo-5-(2,4,6-trimethoxy-phenyl)-cyclopent-3-enecarboxylic acid methyl ester

8a ^1H NMR (400 MHz, CDCl_3) δ 7.20 (t, $J = 1.2$ Hz, 1H), 6.08 (s, 2H), 4.90 (q, $J = 2.4$ Hz, 1H), 3.76(s, 3H), 3.73 (s, 3H), 3.71 (s, 6H), 3.63 (d, $J = 2.4$ Hz, 1H), 1.80(s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 203.6, 170.2, 161.6, 160.4, 159.1, 137.3, 107.2, 90.7, 57.4, 55.5, 55.2, 52.2, 38.4, 9.9; IR (NaCl plate, cm^{-1}): 1738, 1704, 1636, 1605, 1459, 1436, 1333, 1256, 1221, 1204, 1151, 1119; Elemental analysis calculated for $\text{C}_{17}\text{H}_{20}\text{O}_6$: C 63.74%; H 6.29%. Found : C 63.57%; H 6.13%

5-Oxo-7-(2,4,6-trimethoxy-phenyl)-6,7-dihydro-5H-indeno[5,6-d][1,3]dioxole-6-carboxylic acid methyl ester

10a ^1H NMR (400 MHz, CDCl_3) δ 7.11 (s, 1H), 6.55 (s, 1H), 6.21 (s, 1H), 6.03 (s, 3H), 5.42 (d, $J = 3.6$ Hz, 1H), 4.00 (d, $J = 3.6$ Hz, 1H), 3.89 (s, 3H), 3.82 (s, 3H), 3.77 (s, 3H), 3.47 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 197.9, 170.2, 160.5, 156.2, 154.3, 147.9, 129.0, 109.0, 104.4, 102.0, 91.1, 90.6, 59.8, 56.0, 55.2, 55.1, 52.3, 37.6; IR (NaCl plate, cm^{-1}): 1738, 1700, 1607, 1497, 1467, 1329, 1294, 1248, 1205, 1151, 1118, 1035, 815, 734; Elemental analysis calculated for $\text{C}_{21}\text{H}_{20}\text{O}_8$: C 63.00%; H 5.03%. Found : C 62.99%; H 5.22%.

3a-Methyl-1-oxo-3-(2,4,6-trimethoxy-phenyl)-2,3,3a,4,5,6-hexahydro-1H-indene-2-carboxylic acid methyl ester

12a ^1H NMR (400 MHz, CDCl_3) δ 6.74 (t, $J = 4$ Hz, 1H), 6.15 (s, 2H), 4.90 (d, $J = 13.2$ Hz, 1H), 4.05 (d, $J = 13.2$ Hz, 1H), 3.81 (s, 3H), 3.77 (s, 6H), 3.66 (s, 3H), 2.21 (m, 2H), 1.63-1.71 (m, 4H), 1.24 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 200.0, 170.6, 159.9, 144.8, 134.4, 105.9, 91.5, 55.1, 52.1, 45.6, 41.9, 34.1, 25.5, 20.6, 18.1; IR (NaCl plate, cm^{-1}): 1740, 1707, 1646, 1606, 1459, 1203, 1152, 1115; X-ray crystallography please see attached cif file.

3-Methyl-5-oxo-2-(2,4,6-trimethoxy-phenyl)-cyclopent-3-enecarboxylic acid ethyl ester

14a ^1H NMR (400 MHz, CDCl_3) δ 6.15 (d, $J = 2.1$ Hz, 1H), 6.06 (s, 1H), 5.92 (s, 1H), 4.92 (br. s, 1H), 4.18 (m, 2H), 3.80 (s, 6H), 3.63 (m, 4H), 1.88 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 202.6, 182.4, 169.9, 160.6, 159.6, 159.2, 127.0, 106.4, 90.7, 90.5, 61.2, 59.1, 56.0, 55.3, 55.2, 43.8, 17.3, 14.2; IR (NaCl plate, cm^{-1}): 2939, 1732, 1700, 1606, 1461, 1420, 1331, 1205, 1150, 1120, 1058, 1035, 815; Elemental analysis calculated for $\text{C}_{18}\text{H}_{22}\text{O}_6$: C 64.66%; H 6.63%. Found : C 64.75%; H 6.52%.

5-(2,4,6-Trimethoxy-phenyl)-3,4,5,6-tetrahydro-2H-cyclopenta[b]pyran-7-one

16a ^1H NMR (400 MHz, CDCl_3) δ 6.13 (s, 1H), 6.07 (s, 1H), 4.43 (d, $J = 5.6$ Hz, 1H), 4.06 (m, 2H), 3.80 (s, 6H), 3.63 (s, 3H), 2.66 (dd, $J_1 = 18.4$ Hz, $J_2 = 6.4$ Hz, 1H), 2.47 (d, $J = 18.4$ Hz, 1H), 1.98 (m, 1H), 1.90 (m, 1H), 1.82-1.90 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 200.9, 160.0, 150.0, 148.7, 108.0, 91.7, 91.9, 66.6, 56.3, 55.2, 40.3, 32.4, 22.0, 21.6; IR (NaCl plate, cm^{-1}): 1705, 1649, 1604, 1461, 1224, 1202, 1151, 1116; Elemental analysis calculated for $\text{C}_{17}\text{H}_{20}\text{O}_5$: C 67.09%; H 6.62%. Found : C 66.97%; H 6.80%.

5-Cyclohexyl-3,4,5,6-tetrahydro-2H-cyclopenta[b]pyran-7-one

16f ^1H NMR (400 MHz, CDCl_3) δ 4.18 (m, 1H), 4.01 (m, 1H), 2.69 (m, 1H), 2.26 (m, 1H), 2.18 (m, 1H), 2.14 (m, 1H), 1.92 (m, 2H), 1.70 (m, 6H), 1.25-1.32 (m, 5H), 1.09 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 200.4, 151.2, 147.2, 66.6, 42.7, 38.6, 35.0, 31.2, 26.4, 26.3, 26.2, 26.1, 22.7, 21.4; IR (NaCl plate, cm^{-1}): 2922, 2851, 1708, 1644, 1117; Elemental analysis calculated for $\text{C}_{14}\text{H}_{20}\text{O}_2$: C 76.33%; H 9.15%. Found : C 76.06%; H 9.03%

3-(2,4,6-Trimethoxy-phenyl)-2,3,4,5,6,7-hexahydro-inden-1-one

18a A mixture of stereoisomers was detected by proton NMR, but only the major product could be isolated. The yield range was determined by weighing the mass of the crude product and that of the purified major product. ^1H NMR (400 MHz, CDCl_3) δ 6.70 (m, 1H), 6.16 (s, 2H), 3.80 (s, 3H), 3.78 (s, 6H), 3.45 (m, 1H), 3.14 (m, 1H), 3.05 (m, 1H), 2.31 (m, 2H), 2.29 (m, 1H), 1.87 (m, 2H), 1.83 (m, 1H), 1.43 (m, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 207.3, 159.6, 159.6, 142.4, 131.6, 109.3, 100.0, 55.6, 55.2, 41.9, 41.6, 36.6, 27.6, 25.5, 21.7; IR (NaCl plate, cm^{-1}): 1710, 1645, 1221, 1193, 1152, 1115, 597; HRMS calculated for $\text{C}_{18}\text{H}_{22}\text{O}_4$ ($\text{M}+\text{H}$) $^+$ 303.1582, Found : 303.1591.

3-Cyclohexyl-2,3,4,5,6,7-hexahydro-inden-1-one

18f A mixture of stereoisomers was detected by proton NMR, but only the major product could be isolated. The yield range was determined by weighing the mass of the crude product and that of the purified major product. ^1H NMR (400 MHz, CDCl_3) δ 6.67 (d, $J = 2.8$ Hz, 1H), 2.20-2.35 (m, 5H), 2.04 (m, 1H), 1.77 (m, 1H), 1.70 (m, 3H), 1.65 (m, 2H), 1.53 (m, 3H), 1.25 (m, 3H), 1.08 (m, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 205.81, 142.0, 132.0, 47.5, 41.4, 41.0, 40.4, 32.2, 29.4, 28.6, 26.5, 26.4, 26.3, 25.2, 21.7; IR (NaCl plate, cm^{-1}): 2922, 2852, 1718, 1651; Elemental analysis calculated for $\text{C}_{15}\text{H}_{22}\text{O}$: C 82.52%; H 10.16%. Found : C 82.71%; H 9.91%

ppm
 He-C13-28 07/07/2003 150.91
 He-(II)-165-p, clean 142.53
 H1 NMR He-590 132.05
 127.13
 125.17
 116.25
 113.99
 77.57
 77.25
 76.93
 66.26
 55.06
 52.05
 21.02
 20.76

He-Cl3-38 07/07/2003

He-(II)-167-p, clean

H1 NMR He-590

pyran/p-anisaldehyde: prod.

ppm

He-C13-53 08/11/2003
He-(II) 200-1, clean
for reeking PDF

207

18a

159.638

159.576

142.385

131.554

109.271

90.972

77.277

77.165

76.959

76.642

55.592

55.244

41.886

41.566

36.651

29.643

27.649

25.519

21.674