SUPPLEMENTARY MATERIALS

for the

communication

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A Lewis Acid Catalyzed Formal [3 + 3] Cycloaddition of α,β-Unsaturated Aldehydes with 4-Hydroxy-2-Pyrone, Diketones, and Vinylogous Esters.

authored by

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General Procedures. Column chromatography was performed on Bodman silica gel (60 Å, 230-400 mesh). Solvents were dried using MBrasun Drying Columns before use. Flasks were flame-dried under vacuum and purged with nitrogen before use. TLC plates (Whatman, polyester backed) were visualized with UV (254 nm) and either anisaldehyde or $KMnO_4$ stains. IR spectra were recorded on NaCl plates using a Midac M2000 FTIR. 500 MHz Spectra were recorded on a Varian Inova spectrometer. 300 MHz Spectra were recorded on a Varian Unity or Varian Inova instruments and are referenced to TMS at δ 0.00 ppm. All ^{13}C spectra were recorded on Varian Inova Spectrometers at 125 MHz and 75 MHz, and are referenced to the center chloroform peak with δ = 77.23 ppm. Electrospray (ESI) mass spectra were recorded on a Bruker Biotof II ESI-TOF/MS using either PPG or PEG as high-resolution internal standards. Unless noted, all reagents (Acros, TCI, Aldrich) were used as received.

A Representative General Procedure: The Annulation of 6-Methyl-4-hydroxy-2-pyrone Using BF_3-Et_2O for the Synthesis of Pyran 10.

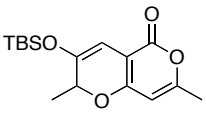
To the solution of aldehyde **9** (50.0 mg, 0.59 mmol) in anhy CH_2Cl_2 (4 mL) was added 6-methyl-4-hydroxy-2-pyrone **8** (74.0 mg, 0.59 mmol) and 4 Å MS (90 mg) followed by the dropwise addition of 1.0 *M* solution of $BF_3{\cdot}Et_2O$ in CH_2Cl_2 (0.60 mL, 0.59 mmol). The reaction mixture was stirred for 24 h at rt at which point it was poured into H_2Os (1 mL). The reaction was worked-up with sat aq $NaHCO_3$ until basic, washed with equal volume of sat aq NaCl and dried over Na_2SO_4. After the solvent was removed under the reduced pressure, the crude product was purified using flash silica gel column chromatography [10% EtOAc in hexanes] to give 78.2 mg of **10** (69% yield).

A Representative General Procedure: The Annulation of 1,3-Diketones Using a Strong Lewis Acid for the Synthesis of Pyran 12.

To the solution of aldehyde **9** (50.0 mg, 0.59 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added 1,3-diketone **11** (66.0 mg, 0.59 mmol) and 4 Å MS (45 mg) followed by the dropwise addition of 1.0 *M* solution of $TiCl_4$ in CH_2Cl_2 (0.060 mL, 0.059 mmol). The reaction mixture was stirred for 16 h at room temperature at which point it was poured into water (0.5 mL). The reaction was worked-up with sat aq $NaHCO_3$ until basic, washed with equal volume of sat aq NaCl and dried over Na_2SO_4. Evaporation of the solvent under the reduced pressure afforded 100.0 mg of **12** (95% yield).

A Representative General Procedure: The Annulation of 1,3-Diketones Using a Weak Lewis Acid for the Synthesis of Pyran 12.

To the solution of aldehyde **9** (50.0 mg, 0.59 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was added 1,3-diketone **11** (66.0 mg, 0.59 mmol) and 4 Å MS (45 mg) followed by the addition of $ZnBr_2$ (13.0 mg, 0.059 mmol). The reaction mixture was stirred for 48 h at rt at which point it was poured into water (0.5 mL). The reaction was worked-up with sat aq $NaHCO_3$ until basic, washed with an equal volume of sat aq NaCl and dried over Na_2SO_4. After the solvent was removed under the reduced pressure, the crude product was purified using flash silica gel column chromatography [20% EtOAc in hexanes] to give 76.0 mg of **12** (72% yield)



23

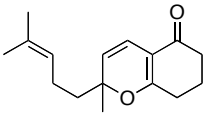
Lewis acid catalyzed formation of compound 23: To a flame-dried sealed tube were added 4 _ MS (1.0 g), 6-methyl-4-hydroxy-2-pyrone **8** (0.046 g, 0.25 mmol), and anhy toluene (10 mL). The solution was stirred for 5 min and aldehyde **22** (0.050 mL, 0.25 mmol) and then $TiCl_4$ (1M in CH_2Cl_2, 0.04 mmol, 0.04 ml) were added dropwise via syringe. The reaction mixture was sealed under nitrogen and heated at 120 °C for 24 h. After the solvent was removed under the reduced pressure, the crude product was purified using flash silica gel column chromatography [25% EtOAc in hexanes] (deactivated with 1% Et_3N) to give 54.0 mg of **23** (71% yield) as pale yellow oil.

R_f = 0.32 (25 % EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.21 (s, 6H), 0.92 (s, 9H), 1.40 (d, 3H, *J* = 6.5 Hz), 2.19 (s, 3H), 4.81 (q, 1H, *J* = 6.5 Hz), 5.55 (s, 1H), 5.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.6, –4.4, 19.4, 20.1, 25.8 (3 C), 26.7, 67.3, 69.9, 75.3, 93.1, 100.1, 147.1, 159.2, 159.7; IR (film) cm^{-1} 3054s, 2987s, 1704s, 1642m, 1424m, 838s; mass spectrum (APCI): *m/e* (% relative intensity) 309 (100) $(M + H)^+$, 241 (35), 225 (20), 128 (40); *m/e* calcd for $C_{16}H_{24}O_4Si$ $(M + H)^+$ 309.1522, found 309.1524.

A Representative General Procedure: The Annulation of Vinylogous Silyl Esters for the Synthesis of Pyran 35.

To the solution of aldehyde **34** (50.0 mg, 0.71 mmol) in anhydrous CH_2Cl_2 (1.5 mL) was vinylogous ester **33** (190.0 mg, 0.71 mmol) and 4 Å MS (50 mg) followed by the dropwise addition of 1.0 *M* solution of $TiCl_4$ in CH_2Cl_2 (0.71 mL, 0.71 mmol). The reaction mixture was stirred for 24 h at rt at which point it was poured into water (0.5 mL). The reaction was worked-

up with sat aq $NaHCO_3$ until basic, washed with an equal volume of sat aq NaCl and dried over Na_2SO_4. After the solvent was removed under the reduced pressure, the crude product was purified using flash silica gel column chromatography [20% EtOAc in hexanes] to give 110.0 mg of **35** (95% yield).



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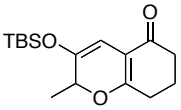
Compound 20: R_f = 0.41 (20 % EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 3H), 1.59 (s, 3H), 1.68 (s, 3H), 1.54–1.75 (m, 1H), 1.94–2.00 (m, 2H), 2.04 (d, 2H, *J* = 8.0, 16 Hz), 2.21–2.28 (m, 1H), 2.36–2.42 (m, 4H), 5.09 (t, 1H, *J* = 7.2 Hz), 5.18 (d, 1H, *J* = 9.9 Hz), 6.46 (d, 1H, *J* = 9.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.5, 20.5, 22.4, 25.5, 27.3, 28.4, 36.2, 41.5, 82.3, 105.3, 116.3, 121.6, 123.5, 131.9, 172.1, 194.9; IR (film) cm^{-1} 2969s, 2934s, 1723s, 1641s, 1591s; mass spectrum (ESI): *m/e* (% relative intensity) 247 (100) $(M + H)^+$, 245 (10), 239 (5), 197 (5); *m/e* calcd for $C_{16}H_{23}O_2$ $(M + H)^+$ 247.1698, found 247.1658.



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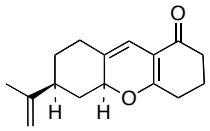
Compound 24:

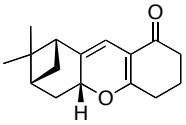
R_f = 0.40 (40 % EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.22 (s, 6H), 0.91 (s, 9H), 1.37 (d, 3H, *J* = 6.5 Hz), 1.92–1.97 (m, 2H), 2.33–2.39 (m, 4H), 4.74 (q, 1H, *J* = 6.5 Hz), 5.62 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ –4.5, –4.4, 19.4, 20.9, 25.7 (3 C), 26.7, 28.1, 36.5, 75.2, 92.5, 111.3, 145.5, 165.9, 195.3; IR (film) cm^{-1} 3056s, 2986s, 1649s, 1611m, 1424s, 1396s, 845s; mass spectrum (APCI): *m/e* (% relative intensity) 295 (15) $(M + H)^+$, 257 (10), 185 (60), 180 (15), 143 (100), 129 (10), 101 (10); *m/e* calcd for $C_{16}H_{26}O_3Si$ $(M + H)^+$ 295.1729, found 295.1746.



27

Compound 27: R_f = 0.28 (20% EtOAc in hexanes); $[\alpha]_D^{23}$ = –25.8 (c 0.57, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) _ 1.26 (ddd, 1H, *J* = 3.9, 14.7, 16.2 Hz), 1.70 (s, 3H), 1.61–1.82 (m, 2H),

1.87–2.20 (m, 3H), 2.15–2.21 (m, 2H), 2.30–2.45(m, 6H), 4.69 (s, 2H), 4.90 (dd, 1H, *J* = 4.8, 11.4 Hz), 6.10 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) _ 20.6, 20.7, 28.2, 31.9, 32.1, 36.4, 39.8, 43.4, 53.5, 79.1, 109.1, 109.3, 129.8, 148.0, 170.7, 194.7; IR (neat) cm^{-1} 2940m, 2866w, 1652s, 1608s, 1403s; mass spectrum (APCI): *m/e* (% relative intensity) 245.1 (100) $(M + H)^+$, 138 (12), 125 (31); *m/e* calcd for $C_{16}H_{21}O_2$ $(M + H)^+$ 245.1542, found 245.1519.



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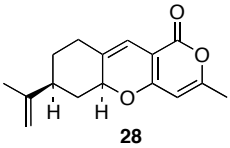
Compound 29: R_f = 0.28 (20% EtOAc in hexanes); $[\alpha]_D^{23}$= –36.2 (c 0.55, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) _ 0.85 (s, 3H), 1.28 (s, 3H), 1.37 (d, 1H, *J* = 10.2 Hz), 1.89–2.50 (m, 4H), 2.32–2.45 (m, 4H), 2.45–2.56 (m, 3H), 5.02 (ddd, 1H, *J* = 2.4, 6.3, 9.3 Hz), 6.08 (d, 1H, *J* = 2.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) _ 20.9, 21.9, 25.2, 25.6, 27.9, 31.8, 35.4, 40.2, 41.9, 48.4, 72.0, 110.9, 114.5, 133.0, 172.2, 195.7; IR (film) cm^{-1} 2948m, 2870m, 1654s, 1595s, 1400m; mass spectrum (APCI): *m/e* (% relative intensity) 245.1 (100) $(M + H)^+$, 245 (26), 277 (21), 203 (16), 149 (12); *m/e* calcd for $C_{16}H_{21}O_2$ $(M + H)^+$ 245.1542, found 245.1658.



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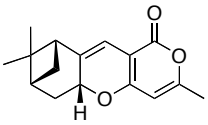
See: Hua, D. H.; Chen, Y.; Sin, H.-S.; Maroto, M. J.; Robinson, P. D.; Newell, S. W.; Perchellet, E. M.; Ladesich, J. B.; Freeman, J. A.; Perchellet, J.-P.; Chiang, P. K. *J. Org. Chem.* **1997**, *62*, 6888.



30

Compound 30: R_f = 0.38 (20% EtOAc in hexanes); mp 127–130 ºC; $[\alpha]_D^{23}$ = –254.7 (c 0.63, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) _ 0.89 (s, 3H), 1.33 (s, 3H), 1.43 (d, 1H, *J* = 10.5 Hz), 2.00–2.23 (m, 2H), 2.25 (d, 3H, *J* = 0.9), 2.35–2.48 (m, 1H), 2.58–2.69 (m, 2H), 5.16 (ddd, 1H, *J* = 2.6, 6.3, 9.3 Hz), 5.87 (d, 1H, *J* = 0.6 Hz), 6.13 (d, 1H, *J* = 2.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) _ 20.1, 21.7, 25.3, 25.4, 31.8, 40.0, 42.0, 48.7, 48.7, 71.9, 99.9, 111.3, 135.5, 161.2, 162.7,164.7; IR (film) cm^{-1} 2994m, 2361w, 1713s, 1636m, 1560m, 1448w; mass spectrum (APCI): *m/e* (% relative intensity) 259.3 (100) $(M + H)^+$, 258 (51), 215 (2), 541 (2); *m/e* calcd for $C_{16}H_{19}O_3$ $(M + H)^+$ 259.1334, found 259.1502.