Hydrazulene Ring Systems via Heteroatom-Assisted [1,2]-Shift of Oxonium and Sulfonium Ylides

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Supporting Information

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General. Reactions were carried out in flame-dried glassware under a positive nitrogen atmosphere unless otherwise stated. Transfer of anhydrous solvents and reagents was accomplished with oven-dried syringes or cannula. Solvents were distilled before use: methylene chloride from calcium hydride, tetrahydrofuran and diethylether from sodium/benzophenone ketyl, toluene from sodium metal. Ethereal diazomethane (hazard!) was prepared from Diazald according to literature procedures. Thin layer chromatography was performed on glass plates precoated with 0.25mm Kieselgel 60 F$_{254}$ (Merck). Flash chromatography columns were packed with 230-400 mesh silica gel (Merck). Radial chromatography was carried out on a Chromatotron 7924T (Harrison Research) with plates prepared using silica gel 60 F$_{254}$ with gypsum binder (EM) on glass rotors. Proton nuclear magnetic resonance spectra ($^1$H NMR) were recorded at 400 MHz or 500 MHz and coupling constants ($J$) are reported in Hertz (Hz). Carbon nuclear magnetic resonance spectra ($^{13}$C NMR) were recorded at 100 MHz or 125 MHz and are reported (ppm) relative to the center line of the triplet from chloroform-$d$ (77.23 ppm). Mass spectra were determined on a Finnigan Mat 95 high resolution gas chromatography/mass spectrometer with Finnigan Mat ICIS II operating system.

Ethyl Acetate Adducts 2a and 2b: Into a stirring solution of diisopropyl amine (3.66 mL, 26.1 mmol) in THF (30 mL) at $-78 \, ^{\circ}\text{C}$ was added nBuLi (10.9 mL of 2.4M solution, 26.1 mmol) and the resulting mixture was stirred at $-78 \, ^{\circ}\text{C}$ for 30 minutes. This was then warmed to 0 °C over several minutes and stirred for another 30 minutes before being cooled once again to $-78 \, ^{\circ}\text{C}$. Ethyl acetate (2.44 mL, 25 mmol) was added dropwise, and the mixture was stirred for 1 hour. A solution of 2-[(2,2-dimethoxy)ethyl]cyclopentanone 1 (4.0 g, 22.7 mmol) in THF (10 mL) was added dropwise to the above mixture and the
reaction mixture was stirred at –78°C until the reaction was complete by TLC analysis (4 h). The reaction mixture was quenched with saturated ammonium chloride (25 mL). After separation of the phases, the aqueous layer was extracted with Et₂O (3 x 15 mL) and the combined organic extracts were washed with water (50mL) and brine (50mL), dried (MgSO₄), filtered and concentrated. The crude product (5.64 g, 95.3 %), a 1.7 : 1 mixture of inseparable cis and trans isomers 2a and 2b (ratio determined by ¹H NMR integration of methoxy singlets), was carried on without further purification.

2a: R₆ 0.23 (3:7 EtOAc/hexanes); IR (CH₂Cl₂ cast) 3513, 2953, 2830, 1731, 1447, 1371, 1334, 1190, 1125, 1057, 964 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) □ [4.37 (dd, J = 7.8, 3.5 Hz, 1H), 4.14 (q, J=7.0 Hz, 2H) 3.28 (s, 6H), 3.23 (br.s, 1H), 2.66 (d, JAB=15.5 Hz, 1H), 2.33 (d, JAB=15.5 Hz, 1H), 1.88 – 1.65 (m, 5H), 1.60 – 1.50 (m, 4H), 1.25 (t, J=7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) □ 220.7, 103.3, 53.4, 52.8, 45.7, 37.9, 32.7, 30.4, 21.0; LRMS (ESI) calcd for C₁₃H₂₄O₅Na (M⁺) 283.1; found 283.1; Anal. Calcd for C₁₃H₂₄O₅: C, 59.98; H, 9.29. Found: C, 59.58; H, 10.01. (Data obtained from the inseparable mixture of diastereomers)

2b: R₆ 0.23 (3:7 EtOAc/hexanes); IR (CH₂Cl₂ cast) 3511, 2953, 2830, 1724, 1447, 1371, 1332, 1199, 1124, 1058, 966 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) □ [4.42 (dd, J = 7.1, 4.4 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H) 3.81 (br s, 1H) 3.30 and 3.26 (2s, 6H), 2.47 (d, JAB = 15.6 Hz, 1H), 2.38 (d, JAB = 15.6 Hz, 1H), 2.03 – 1.94 (m, 2H), 1.82 – 1.76 (ddd, J = 13.9, 7.1, 4.2 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.61 – 1.51 (m, 2H), 1.29 – 1.20 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) □ 173.7, 103.8, 80.7, 61.0, 53.5, 52.2, 45.6, 39.7, 38.4, 33.2, 29.3, 20.8, 14.4; LRMS (ESI) calcd for C₁₃H₂₄O₅Na (M⁺) 283.1; found 283.1; Anal. Calcd for C₁₃H₂₄O₅: C, 59.98; H, 9.29. Found: C, 59.85; H, 9.29. (Data obtained from a pure sample of 2b recovered after the formation of a mixture of 2a + 2b.)

Mixed Acetal 3a. To a solution of 2a and 2b (11.2 g, 43.3 mmol) in CH₂Cl₂ (1.0 L) at –15°C (acetone/ice bath) was added BF₃•OEt₂ (5.50 mL, 43.3 mmol) and the reaction was stirred for 20 minutes, at which time TLC showed consumption of 2a and a mixture of 2b and 3a. The reaction was quenched with Et₃N (6 mL) and water (500 mL) and the resulting phases were separated. The aqueous layer was extracted with CH₂Cl₂ and the combined organic extracts were washed with water and brine, then dried (MgSO₄), filtered and concentrated. The crude product was purified by column chromatography (silica gel; EtOAc/hexanes 3:7) to afford recovered 2b and 3a (3.85 g, 62 %; 4:4:1 mixture of □ and □ anomers; ratio based on integration of OMe singlets) as a yellow oil: R₆ 0.53 (3:7 EtOAc/hexanes); IR (CH₂Cl₂ cast) 2950, 2868, 2829, 1735, 1467, 1447, 1369, 1342, 1300, 1208, 1103, 1049 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) □ [4.97 (d, J = 5.2 Hz, 0.8H) overlapping with 4.96 (m, 0.2H) 4.11 (q, J = 7.1 Hz, 2H), 3.30 (s, 2.4H), 3.28 (s, 0.6H), 2.85 (d, JAB = 14.4 Hz, 0.8H), 2.67 – 2.61 (m, 0.8H), 2.64 (d, JAB = 14.4 Hz, 0.2H), 2.63 (d, JAB = 14.4 Hz, 0.8H), 2.56 (m, 0.2H), 2.52 (d, JAB = 14.4 Hz, 0.2H), 2.27 (ddd, J = 13.3, 9.5, 5.7 Hz, 0.2H), 2.20 (dd, J = 13.3, 9.3 Hz, 0.8H) 1.96 – 1.87 (m, 1H), 1.73 – 1.56 (m, 4.8H), 1.46 – 1.41 (m, 1.2H), 1.24 (t, J = 7.2 Hz, 2.4H), 1.23 (t, J = 7.2 Hz, 0.6H); ¹³C NMR (125 MHz, CDCl₃) □ MAJOR: 171.4, 106.7, 93.8, 60.4, 54.7, 46.2, 46.0, 41.4, 38.9, 33.6, 24.0, 14.5, MINOR: 171.2, 107.0, 94.9, 60.5, 54.9, 45.4, 44.9, 40.5,
40.4, 34.2, 24.5, 14.5; HRMS (EI) calc'd for C_{12}H_{20}O_{4} (M') 228.1362; found 228.1359; Anal. Calc'd for C_{12}H_{20}O_{4}: C, 63.14; H, 8.83. Found: C, 62.90; H, 9.43.

**Mixed Thiacetal 3b.** To a solution of 3a (50 mg, 0.22 mmol) and p-thiocresol (27 mg, 0.22 mmol) in CH_{2}Cl_{2} (22 mL) at -45°C was added BF_{3}•OEt_{2} (28 µL, 0.22 mmol) and the reaction was stirred until deemed complete by TLC. After 2 hours only a trace of 3a observed; the reaction was quenched with Et_{3}N (0.5 mL) and water (15 mL) and the resulting bi-layer was separated. The aqueous phase was extracted with CH_{2}Cl_{2} (15 mL) and the combined organic extracts were washed with water (30 mL), brine (30 mL), dried with magnesium sulfate, filtered and concentrated. The crude product was first passed through a pad of silica gel in a fritted filter, eluting with Et_{2}O, and then purified by radial chromatography (silica gel, 2 mm plate, solvent ramp: 100 mL each of 3%, 6% then 9% EtOAc/hexanes until the product was recovered) to afford the product, a yellow oil, as a 1:5 : 1 mixture of partially separable anomers (3b[α] and 3b[β]) in 88% yield (57 mg) based on recovered 3a (4 mg).

**Major Anomere 3b[α]:** R_{f} 0.63 (3:7 EtOAc/hexanes); IR (CH_{2}Cl_{2} cast) 2954, 2867, 1731, 1493, 1446, 1369, 1340, 1300, 1195, 1094, 1054, 1034 cm^{-1}; 1H NMR (500 MHz, CDCl_{3}) \[ 7.35 \ (d, \ J = 8.2 \ Hz, 2H), 7.04 \ (d, \ J = 8.2 \ Hz, 2H), 5.51 \ (dd, \ J = 6.9, 5.4 \ Hz, 1H), 4.09 \ (q, \ J = 7.2 \ Hz, 2H), 2.94 \ (d, J_{AB} = 14.6 \ Hz, 1H), 2.85 \ (d, J_{AB} = 14.6 \ Hz, 1H), 2.74 \ (ddd, \ J = 8.4, 5.2, 3.2 \ Hz, 1H), 2.29 – 2.24 \ (m, 1H), 2.28 \ (s, 3H), 2.08 \ (ddd, \ J = 13.6, 6.8, 5.2 \ Hz, 1H), 1.97 – 1.92 \ (m, 1H), 1.84 – 1.76 \ (m, 1H), 1.73 – 1.58 \ (m, 3H), 1.49 – 1.44 \ (m, 1H), 1.22 \ (t, \ J = 7.2 \ Hz, 3H); 13C NMR (125 MHz, CDCl_{3}) \[ 171.2, 137.2, 132.2, 131.8, 129.8, 95.0, 88.3, 60.5, 46.9, 44.8, 41.0, 39.2, 33.3, 24.5, 21.3, 14.4; HRMS (EI) calc'd for C_{18}H_{24}O_{4}S (M') 320.1446; found 320.1419; Anal. Calc'd for C_{18}H_{24}O_{4}S: C, 67.47; H, 7.55. Found: C, 67.24; H, 7.57.

**Minor Anomere 3b[β]:** R_{f} 0.63 (3:7 EtOAc/hexanes); IR (CH_{2}Cl_{2} cast) 3511, 2953, 2830, 1724, 1447, 1371, 1332, 1199, 1124, 1058, 966 cm^{-1}; 1H NMR (500 MHz, CDCl_{3}) \[ 7.33 \ (d, \ J = 8.0 \ Hz, 2H), 7.04 \ (d, \ J = 8.0 \ Hz, 2H), 5.25 \ (dd, \ J = 8.2, 6.4 \ Hz, 1H), 4.09 \ (q, \ J = 7.2 \ Hz, 2H), 2.61 \ (s, 2H), 2.66 – 2.53 \ (m, 3H), 2.29 \ (s, 3H), 2.04 \ (m, 1H), 1.78 – 1.50 \ (m, 6H), 1.22 \ (t, \ J = 8.0 \ Hz, 3H); 13C NMR (125 MHz, CDCl_{3}) \[ 171.1, 137.0, 131.7, 131.6, 129.7, 94.7, 86.2, 60.6, 46.8, 43.9, 41.0, 39.4, 33.8, 24.2, 21.3, 14.5; HRMS (EI) calc'd for C_{18}H_{24}O_{4}S (M') 320.1446; found 320.1428.

**Diazoketones 4a.** To a solution of mixed acetals 3a (1.00 g, 4.38 mmol) in THF (8 mL) and methanol (8 mL) was added a 2.0 M solution of LiOH (4.38 mL). The reaction was stirred for 16 hours at room temperature, during which time the reaction mixture turned slightly yellow. The reaction was diluted with water (20 mL) and Et_{2}O (20 mL) and transferred to a separatory funnel. The layers were separated and the aqueous layer was washed with ether (20 mL). The aqueous layer was then acidified with 0.5 M HCl to pH ~3, resulting in a cloudy suspension. This was then diluted with ethyl acetate (30 mL) and the resulting layers separated. The aqueous layer was washed with 3 portions of ethyl acetate (20 mL) and the combined organic extracts were washed with water then brine, dried over magnesium sulfate, filtered and concentrated to give the acid (mixture of anomers) as a yellow oil (870 mg, 99%): IR (CH_{2}Cl_{2} cast) 3600-2500, 2949, 1708, 1468, 1440, 1339, 1300, 1218 cm^{-1}; 1H NMR (500 MHz, CDCl_{3}) \[ 10.8 \ (br s, 1H), 4.99 \ (d, \ J = 5.2 \ Hz, 1.0H), 3.30 \ (s, 2.4H), 3.28 \ (s, 0.6H), 2.90 \ (d, J_{AB} = 14.9 \ Hz, 0.8H), S-3
2.64 (d, J<sub>AB</sub> = 14.6 Hz, 0.2H), 2.63 (d, J<sub>AB</sub> = 14.9 Hz, 0.8H), 2.56 (d, J<sub>AB</sub> = 14.6 Hz, 0.2H), 2.49 (ddd, J = 4.6, 1.2 Hz, 0.2H), 2.27 (ddd, J = 13.6, 9.8, 5.7 Hz, 0.2H), 2.20 (dd, J = 13.3, 9.2 Hz, 0.8H), 1.98 – 1.80 (m, 1.6H), 1.75 – 1.55 (m, 5.2H), 1.43 (m, 1.0H);<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) Major Anomer: 176.0, 107.1, 93.5, 55.0, 46.5, 46.0, 41.1, 38.9, 33.7, 24.0; Minor Anomer: 176.0, 107.2, 94.7, 55.1, 44.8, 40.2, 40.1, 34.0, 24.6; HRMS (EI) calcd for C<sub>16</sub>H<sub>16</sub>O<sub>4</sub>(M<sup>+</sup>) 200.1049; found 200.1051.

To a solution of the anomic acids (800 mg, 4.0 mmol) in Et<sub>2</sub>O (50 mL) at 0°C was added Et<sub>3</sub>N (585 L, 4.4 mmol) followed by isobutyl chloroformate (574 L, 4.4 mmol) and the reaction was stirred for 2.5 hours, resulting in the formation of an off-white precipitate. The reaction mixture was filtered through a fritted filter (D), rinsed with Et<sub>2</sub>O (50 mL) and concentrated to give the mixed anhydride (1.09 g, 91%) as a yellow oil: R<sub>f</sub> 0.62 (3.7 EtOAc/hexanes); IR (CH<sub>2</sub>Cl<sub>2</sub> cast) 2958, 2784, 2831, 1804, 1760, 1470, 1452, 1396, 1370 cm<sup>-1</sup>;<sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) Major Anomer: 5.00 (d, J = 5.3 Hz, 1H), 4.03 (d, J = 7.1 Hz, 2H), 3.31 (s, 3H), 3.03 (d, J<sub>AB</sub> = 15.3 Hz, 1H), 2.80 (d, J<sub>AB</sub> = 15.3 Hz, 1H), 2.66 (m, 1H), 2.23 (dd, J = 13.3, 9.2 Hz, 1H), 2.01 (sept, J = 6.8 Hz, 1H) 2.00 (m, 1H), 1.76 (m, 1H), 1.68 (ddd, J = 12.0, 7.5, 5.3 Hz, 1H), 1.63 (m, 3H), 1.46 (m, 1H), 0.95 (d, J = 6.8 Hz, 6H);<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) Major Anomer: 165.8, 149.4, 106.9, 93.1, 75.7, 54.8, 44.6, 45.7, 41.3, 38.8, 33.5, 27.8, 24.0, 19.0; Minor Anomer: 165.6, 149.4, 106.7, 94.4, 75.5, 54.8, 45.6, 44.6, 41.4, 38.9, 34.3, 33.6, 24.5, 19.0; HRMS (EI) calcd for C<sub>15</sub>H<sub>17</sub>O<sub>6</sub>(M+H)<sup>+</sup> 299.1495; found 299.1499.

A solution of anomic mixed anhydrides (624 mg, 2.2 mmol) in Et<sub>2</sub>O (10 mL) was added via cannula to a solution of freshly prepared diazomethane (20 mmol) in Et<sub>2</sub>O (60 mL) at –15°C, and the resulting mixture stirred for 16 hours as the cooling bath expired. A gentle stream of N<sub>2</sub> was applied to the system to allow for slow evaporation of both excess diazomethane and solvent, and the resulting yellow oil was diluted in ether (20 mL), passed through a short pad of silica gel in a fritted filter, eluting with copious ether. This was then concentrated and the resulting oil purified by radial chromatography (silica gel, 4 mm plate, solvent ramp: 100 mL each of 3%, 6%, 9% then 12% EtOAc/hexanes until the products were recovered) to yield 4a, an inseparable 4:7:1 mixture of anomers, (228 mg, 49%) as a bright yellow oil, as well as a trace of starting material (not quantified): R<sub>f</sub> 0.23 (3:7 EtOAc/hexanes); IR (CH<sub>2</sub>Cl<sub>2</sub> cast) 3087, 2949, 2868, 2829, 2102, 1817, 1735, 1637, 1440, 1361 cm<sup>-1</sup>;<sup>1</sup>H NMR (500 MHz, -40°C CDCl<sub>3</sub>) [5.67 (s, 0.8H), 5.52 (s, 0.2H), 5.01 (m, J = 5.1 Hz, 1H), 3.36 (s, 2.4H), 3.30 (s, 0.6H), 2.94 (d, J<sub>AB</sub> = 14.3 Hz, 0.8H), 2.69 (d, J<sub>AB</sub> = 13.5 Hz, 0.2H), 2.60 (m, 1H), 2.55 (d, J<sub>AB</sub> = 14.3 Hz, 0.8H), 2.47 (d, J<sub>AB</sub> = 13.5 Hz, 0.2H), 2.20 (dd, J = 13.5, 9.5 Hz, 1H), 1.90 (m, 1H), 1.70 – 1.45 (m, 6H);<sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>, -60°C) Major Anomer: 194.1, 106.4, 93.4, 56.0, 54.9, 52.8, 46.4, 40.3, 38.1, 32.5, 23.4; Minor Anomer: 194.1, 106.5, 95.4, 56.8, 54.7, 50.8, 44.2, 40.3, 39.9, 33.6, 24.2; HRMS (ESI) calcd for C<sub>11</sub>H<sub>10</sub>N<sub>2</sub>O<sub>3</sub>Na (M<sup>+</sup>) 247.1059; found 247.1060.

**Diazoketones 4b.** Preparation and characterization of individual acid anomers is given below. For convenience, they were usually prepared as a mixture of anomers and converted into the separable diazoketones, 4b[] and 4b[].
To a solution of mixed acetal 3b\[ (423 mg, 1.3 mmol) in THF (5 mL) and methanol (5 mL) was added a 2.0 M solution of LiOH (1.3 mL). The reaction was stirred for 16 hours at room temperature, during which time the reaction mixture turned slightly yellow. The reaction was diluted with water (20 mL) and Et\(_2\)O (20 mL) and transferred to a separatory funnel. The layers were separated and the aqueous layer was washed with ether (15 mL). The aqueous layer was then acidified with 0.5M HCl to pH ~3, resulting in a cloudy suspension. This was then diluted with ethyl acetate (40 mL) and the resulting layers separated. The aqueous layer was washed with 3 portions of ethyl acetate (20 mL) and the combined organic extracts were washed with water (50 mL) then brine (50 mL), dried over magnesium sulfate, filtered and concentrated to yield a yellow oil (333 mg, 86%): IR (CH\(_2\)Cl\(_2\) cast) 3500-2400, 2953, 2867, 1708,1597, 1493, 1443, 1408, 1300, 1231. 1133, 1093 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \[7.34 (d, \(J = 8.2\) Hz, 2H), 7.07 (d, \(J = 8.2\) Hz, 2H), 5.56 (dd, \(J = 6.0, 6.0\) Hz, 1H), 3.03 (d, \(J_{AB} = 14.8\) Hz, 1H), 2.74 (d, \(J_{AB} = 14.8\) Hz, 1H), 2.63 (m, 1H), 2.32 – 2.25 (m, 1H), 2.29 (s, 3H), 2.14 (ddd, \(J = 13.4, 6.8, 5.0\) Hz, 1H), 1.98 – 1.92 (m, 1H), 1.88 – 1.79 (m, 1H), 1.70 – 1.58 (m, 3H), 1.52 – 1.46 (m, 1H), (COOH peak not measured); \(^1\)C NMR (125 MHz, CDCl\(_3\)) \[186.8, 137.9, 132.5, 130.8, 130.0, 94.7, 88.7, 47.5, 44.9, 40.5, 39.0, 33.0, 24.5, 21.3; HRMS (EI) calcd for C\(_{16}\)H\(_{20}\)O\(_3\) (M\(^+\)) 292.1133; found 292.1135.

Following the same procedure as above, 3b\[ (142 mg, 0.44 mmol) was converted into the corresponding acid (100 mg, 78%) as a white solid: m.p. 115 – 116\(^\circ\)C; IR (CH\(_2\)Cl\(_2\) cast) 3500 - 2500, 2949, 2865, 1707, 1493, 1439, 1411, 1299, 1232. 1146, 1093 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \[9.4 (br s, 1H), 7.34 (d, \(J = 8.4\) Hz, 2H), 7.06 (d, \(J = 8.4\) Hz, 2H), 5.28 (dd, \(J = 8.2, 5.6\) Hz, 1H), 2.69 (d, \(J_{AB} = 14.8\) Hz, 1H), 2.57 (d, \(J_{AB} = 14.8\) Hz, 1H), 2.60 – 2.51 (m, 2H), 2.29 (s, 3H), 2.10 (m, 1H), 1.78 – 1.54 (m, 6H); \(^1\)C NMR (125 MHz, CDCl\(_3\)) \[186.8, 137.7, 132.4, 130.7, 129.9, 94.4, 86.5, 47.6, 43.6, 40.6, 39.0, 33.6, 24.3, 21.3; HRMS (EI) calcd for C\(_{16}\)H\(_{20}\)O\(_3\)S: C, 65.72; H, 6.89. Found: C, 65.21; H, 7.07.

To a solution of both anomers of the acids derived from 3b\[ and 3b\[ (1.0 g, 3.42 mmol) in CH\(_2\)Cl\(_2\) (140 mL) at −15\(^\circ\)C was added 2,6-lutidine (478 \[L, 4.1 mmol) followed by oxalyl chloride (36 \[L, 4.1 mmol) and DMF (2 drops, ~10 \[L), resulting in the evolution of copious amounts of gas. The reaction was stirred for 4 hours, and solven was removed by rotary evaporation to give a yellow oil entrained in a white precipitate. This material was redissolved in ether (50 mL) and the suspension filtered through a fritted filter (D), washing several times with ether (50 mL). The ethereal solution of the acid chloride was condensed to a lesser volume (~50 mL) and added via cannula to a solution of freshly prepared diazomethane (60 mmol) in Et\(_2\)O (200 mL) at −15\(^\circ\)C, and the resulting mixture stirred for 16 hours as the cooling bath expired. A gentle stream of N\(_2\) was applied to the system to allow for slow evaporation of both excess diazomethane and solvent, and the resulting yellow oil was diluted in ether (40 mL), passed through a short pad of silica gel in a fritted filter, eluting with copious ether. The filtrate was concentrated and the resulting oil purified by radial chromatography (silica gel, 4 mm plate, solvent ramp: 100 mL each of 3 %, 6 %, 9 % then 12 % EtOAc/hexanes until the products were recovered) to yield 4b\[ (410 mg) and 4b\[ (240 mg), as yellow oils in a combined overall yield of 60%.
Carbene Transfer Reaction of 4a; Preparation of 7a[\textsuperscript{\textbullet}] and 7a[\textdagger]. To a refluxing solution of Cu(hfacac)\textsubscript{2} (37 mg, 0.08 mmol, 10 mol %) in CH\textsubscript{2}Cl\textsubscript{2} (55 mL) was added a solution of 4a (168 mg, 0.75 mmol, 4.4:1 mixture of anomers) in CH\textsubscript{2}Cl\textsubscript{2} (25 mL), and the resulting mixture monitored by TLC. Upon consumption of diazoketone 4a (45 min) the reaction mixture was cooled to room temperature and quenched with 0.5 M K\textsubscript{2}CO\textsubscript{3} (25 mL). The layers were separated and the aqueous phase extracted with CH\textsubscript{2}Cl\textsubscript{2} (2 x 15 mL). The organic extracts were combined and washed with water (20 mL), pre-dried with brine (20 mL), dried with magnesium sulfate, filtered and concentrated. The resulting pale oil was purified by gradient column chromatography (silica gel; 5%, 10%, 15% then 20% EtOAc/hexanes until the products were recovered) to yield 7a[\textdagger] (68 mg) and 7a[\textsuperscript{\textbullet}] (25 mg) as pale yellow oils, in an overall yield of 67%. (This reaction was also carried out on small scale with pure samples of 4a[\textdagger] and 4a[\textsuperscript{\textbullet}]. 4a[\textsuperscript{\textbullet}] also furnished trace amounts of product A [see footnote 9 in the text].)
Side Product A (partial data): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.03 (d, $J = 2.3$ Hz, 1H), 5.56 (d, $J = 4.5$ Hz, 1H), 3.49 (s, 3H), 2.54 (dd, $J = 14.1$, 2.3 Hz, 1H), 2.42 (d, $J = 14.1$ Hz, 1H), 2.33 (dd, $J = 13.2$, 8.9 Hz, 1H), 2.24 (dddd, $J = 9.8$, 8.7, 6.4, 4.0 Hz, 1H), 2.01 – 1.83 (m, 3H), 1.74 (app dt, $J = 13.2$, 4.3 Hz, 1H), 1.70 – 1.56 (m, 2H), 1.35-1.27 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 136.2, 134.0, 102.9, 93.2, 60.1, 44.1, 40.9, 36.0, 34.2, 33.1, 25.7.

Carbene Transfer Reaction of 4b[]; Preparation of 7b[], 7b[] and 8. To a refluxing solution of Cu(hfacac)$_2$ (16 mg, 0.03 mmol, 10 mol %) in CH$_2$Cl$_2$ (33 mL) was added a solution of 4b[] (105 mg, 0.33 mmol) in CH$_2$Cl$_2$ (8 mL), and the resulting mixture monitored by TLC. Upon consumption of diazoketone 4b[] (30 min) the reaction mixture was cooled to room temperature and quenched with 0.5 M K$_2$CO$_3$ (25 mL). The layers were separated and the aqueous phase extracted with CH$_2$Cl$_2$ (2 x 15 mL). The organic extracts were combined and washed with water (25 mL), pre-dried with brine (25 mL), dried with magnesium sulfate, filtered and concentrated. The resulting pale yellow oil was diluted in ether (20 mL), passed through a short pad of silica gel in a fritted filter, rinsing with excess ether. This was then concentrated and the resulting oil purified by radial chromatography (silica gel, 2 mm plate, solvent ramp: 100 mL each of 2%, 5%, 7% then 10% EtOAc/hexanes until the products were recovered) to yield a mixture of 7b[] and 7b[] (59 mg, 68%, ca. 2:1 ratio) as pale yellow oils, as well as 8 (11 mg, 13%) as a white solid, in an overall yield of 80%. Minor diastereomer 7b[] could be obtained as a white solid, m.p.: 64 – 65 °C.

Diastereomers 7b[] and 7b[]: $R_f$ 0.41 (3:7 EtOAc/hexanes); IR (CH$_2$Cl$_2$ cast) 3019, 2955, 2869, 1785, 1711, 1492, 1447, 1401, 1343 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.35 (d, $J = 8.1$ Hz, 2H), 7.28 (d, $J = 8.1$ Hz, 1H), 7.07 (d, $J = 8.1$ Hz, 1H), 7.06 (d, $J = 8.1$ Hz, 2H), 4.01 (s, 0.5H), 3.86 (d, $J = 3.9$ Hz, 1H), 3.50 (ddd, $J = 13.2$, 5.4, 4.2 Hz, 1H), 3.27 (ddd, $J = 6.9$, 13.5, 1.7 Hz, 0.5H), 2.60 (d, $J_{AB} = 17.3$ Hz, 0.5H), 2.57 (d, $J_{AB} = 17.6$ Hz, 1H), 2.29 (s, 4.5H), 2.24 (d, $J_{AB} = 17.3$ Hz, 0.5H), 2.23 (d, $J_{AB} = 17.6$ Hz, 1H), 2.16 – 2.06 (m, 2H), 1.96 – 1.77 (m, 7.5H), 1.75 – 1.62 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ Major Diast: 213.5, 138.0, 133.3, 130.1, 129.9, 88.5, 79.8, 44.8, 44.4, 44.2, 34.5, 28.1, 27.5, 21.3; Minor Diast: 216.2, 137.8, 132.5, 131.4, 130.2, 89.1, 81.3, 45.8, 45.5, 43.0, 35.5, 31.4, 26.8, 22.3; HRMS (EI) calcd for C$_{17}$H$_{20}$O$_2$S (M$^+$) 288.1184; found 283.1180; Anal. Calcd for C$_{17}$H$_{20}$O$_2$S: C, 70.80; H, 6.99. Found: C, 70.36; H, 7.05.

Isomer 8: m.p. 95 °C; $R_f$ 0.44 (3:7 EtOAc/hexanes); IR (CH$_2$Cl$_2$ cast) 2953, 2866, 1711, 1493, 1448, 1404, 1345, 1301 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.32 (d, $J = 8.0$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 4.75 (d, $J = 7.3$ Hz, 1H), 3.43 (d, $J_{AB} = 14.8$ Hz, 1H), 3.32 (s, 1H), 2.32 (s, 3H), 2.26 – 2.21 (m, 1H), 2.24 (d, $J_{AB} = 14.8$ Hz, 1H), 2.16 (m, 1H), 2.13 (dd, $J = 12.4$, 9.1 Hz, 1H), 1.93 – 1.84 (m, 3H), 1.67 (m, 1H), 1.51 (ddd, $J = 13.4$, 9.8, 7.5 Hz, 1H), 1.40 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 203.4, 138.4, 132.9, 130.1, 93.9, 60.9, 48.9, 45.3, 39.9, 37.1, 34.8, 25.4, 21.4; HRMS (EI) calcd for C$_{17}$H$_{20}$O$_2$S (M$^+$) 288.1184; found 283.1183; Anal. Calcd for C$_{17}$H$_{20}$O$_2$S: C, 70.80; H, 6.99. Found: C, 70.90; H, 6.68.
Carbene Transfer Reaction of 4b[4]; Preparation of 7b[4] and 7b[7]. Diazoacetone 4b[4] was subjected to the procedure given above for 4b[4], to yield 85% of 7b[4] and 7b[7] in a 1:4.8 ratio. None of the isomeric product 8 was isolated.

Ketalization of 7b; Formation of 9[8] and 9[9]. To a mixture of diastereomers 7b[4] and 7b[7] (340 mg, 1.2 mmol, ca. 2.5:1) in CH₂Cl₂ (6 mL) at 0°C was added 1,2-bis(trimethylsiloxy)ethane (580 [4L, 2.4 mmol) followed by TMSOTf (12 [4L, 5 mol %) and the resulting mixture was warmed to room temperature over several hours. This was then heated to reflux for ca. 12 hours, after which TLC showed consumption of starting materials. The reaction was quenched with pyridine (1 mL) and saturated aqueous NaHCO₃ (5 mL), diluted with Et₂O (10 mL) and the resulting layers separated. The aqueous layer was washed with 3 portions of Et₂O (10 mL) and the combined organic extracts were washed with water (30 mL) then brine (30 mL), dried over magnesium sulfate, filtered and concentrated, giving the crude product as a yellow oil. This oil was diluted in ether (20 mL) and passed through a short pad of silica gel in a fritted filter, eluting with ether. This was then concentrated and the resulting oil purified by radial chromatography (silica gel, 2 mm plate, solvent ramp: 100 mL each of 3%, 6% then 10% EtOAc/hexanes until the products are recovered) to yield 9[8] (283 mg, 72%) as a pale oil, and 9[9] (102 mg, 26%) as a crystalline solid.

Ketal 9[8]: Rf 0.63 (3:7 EtOAc/hexanes); IR (CH₂Cl₂ cast) 2945, 2869, 1492, 1434, 1398, 1344, 1323, 1291 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.23 (d, J = 8.0 Hz, 2H), 7.06 (d, J = 8.0 Hz, 2H), 4.11 (m, 1H), 4.06 (m, 1H), 3.87, (d, J = 2.6 Hz, 1H), 3.84 (m, 1H), 3.76 (m, 1H), 3.31 (ddd, J = 12.7, 5.8, 3.5 Hz, 1H), 2.37 (d, J₂AB = 13.7 Hz, 1H), 2.42 – 2.34 (m, 1H), 2.32 (s, 3H), 2.10 (d, J₁AB = 13.7 Hz, 1H), 2.04 (dd, J = 14.0, 5.7 Hz, 1H), 1.80 – 1.74 (m, 5H), 1.65 – 1.57 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 136.8, 134.1, 131.1, 130.3, 116.9, 88.5, 83.1, 65.5, 64.6, 45.7, 45.3, 44.9, 34.6, 28.5, 28.4, 21.4, 21.2; HRMS (EI) calcd for C₁₉H₂₄O₂S (M⁺) 332.1146; found 332.1438; Anal. Calcd for C₁₉H₂₄O₂S: C, 68.64; H, 7.28; S, 9.60. Found: C, 68.78; H, 7.05; S, 9.79.

Ketal 9[9]: m.p. 78 – 79°C; Rf 0.54 (3:7 EtOAc/hexanes); IR (CH₂Cl₂ cast) 2951, 2871, 1492, 1445, 1433, 1398 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.29 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 3.92 – 3.87 (m, 2H), 3.78 (app q, J = 7.2 Hz, 1H), 3.63 (ddd, J = 11.5, 7.0, 4.5 Hz, 1H), 3.53 (app q, J = 7.4 Hz, 1H), 3.38 (ddd, J = 7.8, 6.1, 1.7 Hz, 1H), 2.29 (s, 3H), 2.24 (d, J₂AB = 13.4 Hz, 1H), 2.22 (m, 1H), 1.96 (d, J₁AB = 13.4 Hz, 1H), 1.92 – 1.74 (m, 8H); ¹³C NMR (125 MHz, CDCl₃) δ 137.2, 132.5, 132.4, 129.9, 116.7, 89.0, 83.4, 65.4, 64.3, 46.1, 44.1, 43.4, 36.5, 32.1, 27.4, 22.9, 21.3; HRMS (EI) calcd for C₁₉H₂₄O₂S (M⁺) 332.1446; found 332.1445; Anal. Calcd for C₁₉H₂₄O₂S: C, 68.64; H, 7.28; S, 9.60. Found: C, 68.61; H, 7.01; S, 9.76.

LDBB Reduction of 9[8]; Formation of 10 and 11: A large excess of LDBB was prepared according to Cohen’s procedure, using Li (8 mg, 6 equiv) and di-tert-butylbiphenyl (300 mg) in THF (3.2 mL). To a solution of 9[8] (57 mg, 0.19 mmol) and a crystal of phenanthroline in THF (0.7 mL) cooled to −78°C was added n-BuLi until the color turned deep red. LDBB was then added dropwise (without quantification) to the reaction mixture until the intense green color persisted, indicating the presence of excess LDBB. The reaction was stirred until consumption of starting material was observed by
TLC (ca. 2 hours). The reaction was then quenched by addition of saturated aqueous ammonium chloride (5 mL), further diluted in Et$_2$O (15 mL), and the resulting bi-layer was separated. The aqueous layer was back extracted once with Et$_2$O (10 mL) and the combined organic extracts were pre-dried with brine (30 mL), dried over anhydrous magnesium sulfate, filtered and concentrated. The crude product was purified by gradient column chromatography (silica gel, 0%, 20%, 60% EtOAc/hexanes) to give **10** (25 mg, 69 %) as a pale yellow oil, as well as a trace of isomer **11** (2 mg, 5.5 %), in an overall yield of 75%. The ratio of product isomers depended on the time allowed for the reaction: if the reaction was quenched after 30 minutes, the ratio of the products is **10** (19 %) and isomer **11** (45 %).

**Alcohol 10**: R$_f$ 0.36 (3:7 EtOAc/hexanes); IR (CH$_2$Cl$_2$ cast) 3513, 3025, 2959, 1653, 1445, 1425, 1397, 1344, 1316, 1281 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.89 (ddd, $J$ = 12.2, 8.9, 3.5 Hz, 1H), 5.65 (ddd, $J$ = 12.0, 3.1, 1.3 Hz, 1H), 4.19 (s, 1H) 3.93 (s, 4H), 2.29 (ddd, $J$ = 16.1, 11.8, 3.1, 3.1 Hz, 1H), 2.21 (d, $J_{AB}$ = 14.1 Hz, 1H), 2.04 (ddd, $J$ = 16.0, 8.8, 2.3 Hz, 1H), 1.86 (d, $J_{AB}$ = 14.1 Hz, 1H), 1.80 – 1.66 (m, 3H), 1.65 – 1.50 (m, 4H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 133.9, 133.6, 108.6, 78.6, 64.6, 63.9, 47.2, 44.9, 41.9, 30.9, 26.6, 19.8; HRMS (ESI) calc'd for C$_{12}$H$_{18}$O$_3$Na (M$^+$) 233.1148; found 233.1149.

**Isomer 11**: R$_f$ 0.09 (3:7 EtOAc/hexanes); IR (CH$_2$Cl$_2$ cast) 3428 (br), 2946, 2865, 1651, 1446, 1433, 1360, 1327 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 5.89 (ddd, $J$ = 12.2, 8.8, 3.5 Hz, 1H), 5.64 (d, $J$ = 12.2 Hz, 1H), 4.18 (s, 1H), 3.94 (s, 4H), 2.29 (app ddt, $J$ = 14.5, 11.3, 3.3, 3.3 Hz, 1H), 2.21 (d, $J_{AB}$ = 14.1 Hz, 1H), 2.04 (ddd, $J$ = 16.0, 8.8, 2.2 Hz, 1H), 1.86 (d, $J_{AB}$ = 14.1 Hz, 1H), 1.80 – 1.48 (m, 7H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 153.2, 99.4, 90.8, 74.1, 67.8, 61.3, 46.0, 46.9, 39.9, 37.1, 33.0, 24.8; HRMS (EI) calc'd for C$_{12}$H$_{18}$O$_3$ (M$^+$) 210.1256; found 210.1253.

Isomer 11 was found to reekatalize upon standing in CDCl$_3$ to give compound **12**: R$_f$ 0.40 (3:7 EtOAc/hexanes); IR (CH$_2$Cl$_2$ cast) 2951, 2869, 1350 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) δ 4.43 (dd, $J$ = 7.6, 4.3 Hz, 1H), 3.92 (app t, $J$ = 6.3 Hz, 2H), 3.81 (app t, $J$ = 6.3 Hz, 2H), 2.67 (app tt, $J$ = 9.2, 4.7 Hz, 1H), 2.31 (dd, $J$ = 12.2, 9.0 Hz, 1H), 2.08 (d, $J_{AB}$ = 13.5 Hz, 1H), 1.96 – 1.86 (m, 2H), 1.86 – 1.78 (m, 2H), 1.72 (dd, $J$ = 13.5, 2.0 Hz, 1H), 1.65 – 1.61 (m, 1H), 1.64 (ddd, $J$ = 13.8, 1.8, 1.8 Hz, 1H), 1.56 – 1.51 (m, 1H), 1.45 – 1.40 (m, 1H), 1.35 – 1.30 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 107.6, 91.5, 76.0, 64.3, 63.2, 44.5, 44.2, 40.7, 39.0, 37.4, 34.9, 25.1; HRMS (EI) calc'd for C$_{12}$H$_{18}$O$_3$ (M$^+$) 210.1256; found 210.1253.

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1H NMR 10 C13 in CDC13 (ref. to CDC13 @ 0.0 ppm), temp 27.0 C -> actual temp = 27.0 C, sw probe date:jul 28 2003 secpol=3ps pol = ho/mn:130.41 sweep width[Hz]:3128 swpt=auto/td:bd apd expt:acq.time[s]:1.0 relax time[s]:0.1 dig.res.[Hz/p]:8.24 # of scans: 46