Supporting Information

Samarium (II) Iodide Mediated Radical/Polar Crossover Reactions of Cyclobutenes. An Efficient Approach to the BCD Ring System of the Penitremes

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General Methods: All experiments were done under an atmosphere of argon. THF, DME, diethyl ether, and benzene were distilled from sodium/benzophenone. Dichloromethane was distilled from CaH₂. All NMR spectra were recorded on a Bruker model AC-300 or DPX-300 (¹H: 300 MHz, ¹³C: 75 MHz). Chemical shifts are reported in parts per million (ppm) from internal tetramethylsilane (¹H-NMR spectra, δ 0.00 ppm) or the residual solvent signal of CDCl₃ (¹³C-NMR spectra, δ 77.23 ppm). Spectra were taken in CDCl₃ unless noted otherwise. In reporting spectral data, the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double of doublets, bs = broad singlet, bd = broad doublet. Carbon multiplicities have been tentatively assigned by Distortionless Enhancement by Polarization Transfer (DEPT135) experiments and chemical shift. Infrared spectra were taken on a Matteson Genesis Series FTIR using thin film deposition. Peaks are reported in wavenumbers (cm⁻¹). High resolution mass spectra were taken on a VG 70/70 double focusing instrument under EI mode and are reported in units of *m/e*. Low resolution mass spectra were taken on a VG model 700 system and are reported in units of *m/e*. Flash chromatography was performed using ICN silica gel 60 (230-400 mesh). Thin layer chromatography (TLC) was done with Merck silica gel 60 F-254 aluminum-backed plates. Names for new compounds were generated by AutoNom Engine 2.1 and confirm to Beilstein nomenclature.

1-(*cis*-/*trans*-3-Chlorocyclobutyl)-2-(2-iodophenyl)ethanone (10-*trans*, 10-*cis*).

A solution of dibromoethane (0.157 g, 0.841 mmol) and zinc powder (5.52 g, 84.5 mmol) in THF (5 mL) was heated to reflux with a heat gun and allowed to cool to 25 °C. This was repeated two more times. The mixture was then sonicated at 5 °C while a solution of 2-iodobenzyl bromide (5.01 g, 16.8 mmol) in THF (30 mL) was slowly added. The consumption benzyl bromide was monitored by TLC (solvent: hexane). After 1-2 h of sonication at 5 °C, the benzyl zinc reagent was transferred to a solution of CuCN (1.81 g, 20.2 mmol) and anhydrous LiCl (1.72 g, 40.5 mmol) in dry THF (25 mL) at –78 °C. The resulting solution was warmed to –20 °C, stirred for 30 min, and recooled to –78 °C. Freshly distilled 3-chlorocyclobutane acid chloride **9** (2.84 g, 18.5 mmol) was added and the resulting solution warmed to –20 °C and stirred for 12 h. The reaction was quenched with water (50 mL) to the reaction mixture, and extracted with Et₂O (3 x 30 mL), and dried over sodium sulfate. Removal of the solvent followed by purification by silica gel column chromatography (pentane:EtOAc, 20:1) gave in order of elution 2.22 g (6.67 mmol, 40%) of **10-cis** as a yellow oil and 2.14 g (6.42 mmol, 38%) of **10-trans** as a white solid (Note: Following the procedure on a 20g scale of iodobenzyl bromide provided 9.11 g (39%) of **10-cis** and 8.62 g (37%) of **10-trans**).

10-cis: ¹H NMR (300 MHz, CDCl₃) δ 2.44-2.50 (m, 2 H), 2.86-2.91 (m, 2 H), 3.63 (ttd, 1 H, *J* = 5.3, 4.9, 0.9 Hz), 3.89 (s, 2 H), 4.42 (ttd, 1 H, *J* = 7.5, 6.5, 0.9 Hz), 6.98 (td, 1 H, *J* = 7.9, 1.7 Hz), 7.19 (dd, 1 H, *J* = 7.6, 1.4 Hz), 7.33 (td, 1 H, *J* = 7.5, 1.2 Hz), 7.85 (dd, 1 H, *J* = 7.9, 1 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 36.3 (CH₂), 40.9 (CH), 50.9 (CH), 53.1 (CH₂), 101.3 (C), 128.6 (CH), 129.1 (CH), 130.9 (CH), 137.7 (C), 139.6 (CH), 206.9 (C=O); IR 2944, 1712, 1466, 1435, 1350, 1277, 1013, 744.39 cm⁻¹; HRMS calcd for C₁₂H₁₂³⁵ClIO (M⁺) 333.9621, found 333.9635; LRMS (M⁺) 334 (30), 217 (45), 207 (60), 117 (95), 89 (100), 63 (15), 55(25).

10-trans: m.p. 45-46 °C; ¹H NMR (300 MHz, CDCl₃) δ 2.53-2.67 (m, 4 H), 3.06 (tt, 1 H, *J* = 9.8, 7.9 Hz), 3.85 (s, 2 H), 4.34 (tt, 1 H, *J* = 7.4, 8.7 Hz), 6.98 (td, 1 H, *J* = 7.7, 1.6 Hz), 7.20 (dd,

1 H, $J = 7.6, 1.6$ Hz), 7.30 (td, 1 H, $J = 7.5, 1.2$ Hz), 7.85 (dd, 1 H, $J = 7.8, 1.0$ Hz); ¹³C NMR (75 MHz, CDCl₃) δ 37.3 (CH₂), 39.6 (CH), 48.0 (CH), 53.0 (CH₂), 101.4 (C), 128.7 (CH), 129.2 (CH), 131.0 (CH), 137.7 (C), 139.7 (CH), 205.1 (C=O); IR 3052, 2944, 1705, 1563, 1466, 1398, 1360, 1317, 1277, 1152, 1114, 741.39 cm⁻¹; HRMS calcd for C₁₂H₁₂³⁵ClIO (M⁺) 333.9621, found 333.9629; LRMS (M⁺) 334 (30), 217 (35), 207 (55), 117 (100), 89 (90), 63 (18), 55 (15).

2-(*cis*-3-Chlorocyclobutyl)-2-(2-iodobenzyl)-[1,3]-dioxolane (11-*cis*).

Geometrically pure ketone **10-*cis*** (9.0 g, 26 mmol), ethylene glycol (3.2 g, 52 mmol), and *p*-toluenesulfonic acid monohydrate (0.1 g, 0.5 mmol) in benzene (400 mL) was refluxed with azeotropic removal of water with a Dean-Stark trap. After 14 h, the reaction mixture was cooled to room temperature, the benzene was evaporated and Et₂O (400 mL) was added followed by addition of a 20% NaOH solution (400 mL). The Et₂O layer was separated and the water layer extracted with Et₂O (3 × 150 mL). The combined ether extracts were dried over anhydrous sodium sulfate. Evaporation of the Et₂O under reduced pressure followed by purification by silica gel column chromatography (pentane:dichloromethane, 3:1) provided ketal **11-*cis*** in 91% yield (8.95 g, 23.7 mmol) as a clear oil: ¹H NMR (300 MHz, CDCl₃) δ 2.29-2.38 (m, 2 H), 2.53-2.62 (m, 2 H), 2.87 (ttd, 1 H, $J = 6.0, 5.5, 0.7$ Hz), 3.05 (s, 2 H), 3.69-3.71 (m, 2 H), 3.92-3.94 (m, 2 H), 4.48 (ttd, 1 H, $J = 6.5, 5.7, 0.8$ Hz), 6.90 (td, 1 H, $J = 7.7, 1.8$ Hz), 7.25 (td, 1 H, $J = 7.5, 1.2$ Hz), 7.32 (dd, 1 H, $J = 7.8, 1.8$ Hz), 7.82 (dd, 1 H, $J = 7.9, 1.2$ Hz); ¹³C NMR (75 MHz, CDCl₃) δ 35.6 (CH₂), 38.1 (CH), 46.0 (CH₂), 52.2 (CH), 66.1 (CH₂), 102.5 (C), 112.2 (C), 128.0 (CH), 128.5 (CH), 131.7 (CH), 139.7 (C), 139.8 (CH); IR 2948, 2883, 1561, 1463, 1362, 1268, 1121, 1071, 1059, 1032, 951, 752 cm⁻¹; LRMS (M⁺) 378 (0.35) 343 (5), 289 (50), 217 (80), 162 (90), 117 (85), 90 (100); HRMS calcd for C₁₄H₁₆IO₂ (M⁺ – Cl) 343.01951, found 343.0201.

2-(*trans*-3-Chlorocyclobutyl)-2-(2-iodobenzyl)-[1,3]-dioxolane (11-*trans*).

The reaction was carried out as above for **11-cis** using ethylene glycol and **10-trans**. Purification by silica gel column chromatography (pentane:dichloromethane, 3:1) provided 93% of ketal **11-trans** as a clear oil: ¹H NMR (300 MHz, CDCl₃) δ 2.26-2.35 (m, 2 H), 2.39-2.46 (m, 3 H), 3.03 (s, 2 H), 3.63-3.71 (m, 2 H), 3.85-3.92 (m, 2 H), 4.15-4.26 (m, 1 H), 6.88 (td, 1 H, *J* = 7.9, 1.8 Hz), 7.26 (td, 1 H, *J* = 7.8, 1.2 Hz), 7.26 (dd, 1 H, *J* = 7.6, 1.2 Hz), 7.82 (dd, 1 H, *J* = 7.8, 1.8 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 35.9 (CH₂), 37.1 (CH), 46.3 (CH₂), 48.6 (CH), 66.0 (CH₂), 102.6 (C), 110.8 (C), 127.9 (CH), 128.4 (CH), 131.5 (CH), 139.4 (C), 139.6 (CH); IR 2951, 2917, 1463, 1434, 1280, 1202, 1161, 1124, 1106, 1054, 1013, 752 cm⁻¹; LRMS (M⁺) 378 0.35) 343 (3), 289 (70), 217 (85), 162 (85), 117 (80), 90 (90); HRMS calcd for C₁₄H₁₆IO₂ (M⁺ – Cl) 343.0195, found 343.0191.

2-(2-Iodobenzyl)-2-(trans-3-phenylselanylcyclobutyl)-[1,3]-dioxolane (12-trans).

To a solution of diphenyldiselenide (36.9 g, 0.118 mol) in ethanol (400 mL) was slowly added sodium borohydride (6.28 g, 0.166 mol). The solvent was evaporated and the residual salt was dried under high vacuum for 1 h. The salt was then dissolved in anhydrous DME (200 mL) and **11-cis** (9.0 g, 0.024 mol) was added. The reaction mixture was then refluxed for 16 h. Afterwards, the DME was evaporated and Et₂O (200 mL) was added followed by addition of a 20% bicarbonate solution (200 mL). The organic layer was separated and the water layer extracted with Et₂O (3 × 150 mL). The combined ether extracts were dried over sodium sulfate. Evaporation of the solvent followed by purification by silica gel column chromatography (pentane:dichloromethane, 3:1) provided selenide **12-trans** in 67% yield (7.91 g, 15.8 mmol) as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 2.21-2.25 (m, 2 H), 2.39-2.43 (m, 2 H), 2.63 (tt, 1 H, *J* = 7.9, 7.8 Hz), 3.05 (s, 2 H), 3.57-3.60 (m, 2 H), 3.75-3.77 (m, 1 H), 3.78-3.81 (m, 2 H), 6.91 (td, 1 H, *J* = 7.7, 1.8 Hz), 7.24-7.27 (m, 4 H), 7.35 (dd, 1 H, *J* = 7.7, 1.8 Hz), 7.47-7.50 (m, 2 H), 7.82 (dd, 1 H, *J* = 7.9, 1.2 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 31.2 (CH), 32.8 (CH₂), 40.7 (CH), 46.1 (CH₂), 66.0 (CH₂), 102.8 (C), 111.1 (C), 127.0 (CH), 127.9 (CH), 128.4 (CH), 129.1 (C), 130.6 (CH), 131.6 (CH), 133.4 (CH), 139.7 (CH), 139.7 (C); IR 3054, 2976, 2935, 2883, 1579,

1560, 1476, 1435, 1254, 1203, 1122, 1104, 1053, 1014, 737 cm⁻¹; LRMS (M⁺) 500 (7), 283 (80), 217 (35), 171 (10), 157 (15), 125 (75), 99 (25) 85 (100); HRMS calcd for C₂₀H₂₁IO₂⁸⁰Se (M⁺) 499.9751, found 499.9773.

2-(2-Iodobenzyl)-2-(*cis*-3-phenylselanylcyclobutyl)-[1,3]-dioxolane (12-*cis*).

The reaction was carried out as above for **12-trans** using **11-trans**. Purification by silica gel column chromatography (pentane:dichloromethane, 3:1) provided selenide **12-cis** in 63% yield as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 2.13-2.18 (m, 2 H), 2.58-2.64 (m, 2 H), 2.95-2.98 (m, 1 H), 3.05 (s, 2 H), 3.64-3.67 (m, 2 H), 3.89-3.93 (m, 2 H), 3.97-3.98 (m, 1 H), 6.92 (td, 1 H, *J* = 7.9, 1.8 Hz), 7.23-7.28 (m, 4 H), 7.33 (dd, 1 H, *J* = 7.8, 1.8 Hz), 7.43-7.48 (m, 2 H), 7.83 (dd, 1 H, *J* = 7.8, 1.2 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 31.4 (CH₂), 32.5 (CH), 40.0 (CH₂), 46.0 (CH), 66.1 (CH₂), 102.6 (C), 112.3 (C), 126.8 (CH), 128.0 (CH), 128.4 (CH), 129.1 (CH), 131.1 (C), 131.7 (CH), 132.7 (CH), 139.7 (CH), 139.8 (C); IR 2974, 2934, 2879, 1579, 1476, 1435, 1227, 1121, 1102, 1013, 736 cm⁻¹; LRMS (M⁺) 500 (6), 283 (100), 217 (25), 171 (10), 161 (15), 125 (70), 99 (20); HRMS calcd for C₂₀H₂₁IO₂⁸⁰Se (M⁺) 499.9751, found 499.9774.

2-Cyclobut-2-enyl-2-(2-iodobenzyl)-[1,3]-dioxolane (13).

To a solution of **12-trans** (0.48 g, 0.97 mmol) in dichloromethane (10 mL) at 25 °C was added neat *m*-CPBA (0.237 g, 1.38 mmol). The solution was then warmed to 25 °C. A 5% bicarbonate solution (10 mL) was then added and the organic layer was separated and dried over anhydrous sodium sulfate. The solution was then concentrated under reduced pressure to provide the selenoxide intermediate which was used immediately without purification. A solution of the corresponding selenoxide of **12-trans** and diethylamine (0.3 mL) in anhydrous 1,2-dichloroethane (10 mL) was heated at 85 °C for 8 h in a sealed tube. Afterwards, the reaction mixture was concentrated and immediately purified by silica gel column chromatography (pentane:dichloromethane, 4:1) gave **13** in 60% yield (0.20 g, 0.58 mmol) as a clear oil: ¹H NMR (300 MHz, CDCl₃) δ 2.37 (d, 1 H, *J* = 13.8 Hz), 2.58 (dd, 1 H, *J* = 14, 4.3 Hz), 3.18 (s, 2

H), 3.25 (d, 1 H, $J = 4.3$), 3.53-3.54 (m, 1 H), 3.63-3.69 (m, 1 H), 3.79-3.91 (m, 2 H), 5.96 (d, 1 H, $J = 2.7$ Hz), 6.07 (d, 1 H, $J = 2.7$ Hz), 6.92 (td, 1 H, $J = 7.7, 1.6$ Hz), 7.24 (t, 1 H, $J = 7.8$ Hz), 7.40 (dd, 1 H, $J = 7.8, 1.6$ Hz), 7.82 (d, 1 H, $J = 7.8, 1.6$ Hz); ¹³C NMR (75 MHz, CDCl₃) δ 32.9 (CH₂), 46.4 (CH₂), 50.6 (CH), 65.8 (CH₂), 66.0 (CH₂), 102.8 (C), 111.1 (C), 127.7 (CH), 128.2 (CH), 131.7 (CH), 135.9 (CH), 138.0 (CH), 139.6 (CH), 139.9 (C); IR 3057, 2962, 2926, 2879, 1560, 1471, 1434, 1295, 1205, 1144, 1043, 1018, 744 cm⁻¹; LRMS (M⁺) 342 (1), 289 (40), 217 (35), 195 (25), 161 (25), 125 (100), 81 (55); HRMS calcd for C₁₄H₁₅IO₂ (M⁺ – cyclobutene) 288.9725, found 288.9723.

2-(3-[1,3]-Dioxolane)-cis-1,2,2a,3,4,8b-hexahydrocyclobuta[a]naphthalen-*exo*-1-yl]propan-2-ol (14).

A solution of anhydrous acetone (0.064 g, 1.12 mmol) and cyclobutene **13** (96 mg, 0.28 mmol) in THF (0.5 mL) was added to a mixture of HMPA (0.80 g, 4.5 mmol) and SmI₂ (0.1 M in THF, 11.2 mL, 1.12 mmol) at 23 °C. After 40 min, air was bubbled in, and 0.1 N HCl (10 mL) was added. After extraction with EtOAc (3 × 10 mL), the combined organic layers were dried over Na₂SO₄. Purification by silica gel chromatography (hexanes:EtOAc, 2:1) provided in order of elution **15** (1.2 mg, 0.0056 mmol, 2% yield), **16** (11.4 mg, 0.0527 mmol, 19 % yield), and **14** (45.2 mg, 0.165 mmol, 59% yield) as a clear oil: ¹H NMR (300 MHz, CDCl₃) δ 1.18 (s, 3 H), 1.25 (s, 3 H), 1.51 (bs, 1 H, OH), 2.08-2.17 (m, 3 H), 2.69-2.71 (m, 1 H), 2.82 (d, 1 H, $J = 15$), 3.32 (d, 1 H, $J = 15$ Hz), 3.66 (dd, 1 H, $J = 3.7, 3.6$ Hz), 3.95-4.01 (m, 4 H), 7.11-7.18 (m, 4 H); ¹³C NMR (75 MHz, CDCl₃) δ 20.9, 26.7, 27.2, 35.8, 37.0, 39.5, 51.2, 64.6, 64.9, 71.7, 110.5, 126.1, 126.9, 127.5, 129.2, 135.6, 139.9; IR 2968, 2933, 2876, 1664, 1597, 1462, 1368, 1223 cm⁻¹; LRMS (M⁺) 274 (3), 256 (8), 244 (8), 215 (8), 188 (80), 144 (55), 128 (47), 116 (85), 99 (100), 59 (71); HRMS calcd for C₁₇H₂₂O₃ (M⁺) 274.1568, found 274.1572.

3-[1,3]-dioxolane-cis-1,2,2a,3,4,8b-Hexahydrocyclobuta[a]naphthalene (15).

¹H NMR (300 MHz, CDCl₃) δ 1.92-2.29 (m, 3 H), 2.52-2.71 (m, 1 H), 2.81 (d, 1 H, *J* = 15 Hz), 2.83-2.93 (m, 1 H), 3.31 (d, 1 H, *J* = 15 Hz), 3.73-3.85 (m, 1 H), 3.97-4.07 (m, 4 H), 7.07 (d, 1 H, *J* = 6.4 Hz), 7.07-7.23 (m, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 20.5, 29.1, 37.1, 38.3, 40.0, 64.7, 65.2, 110.1, 126.1, 127.1, 127.7, 129.3, 134.9, 140.3; IR 3403, 2958, 1490, 1452, 1366, 1274, 1126, 1096, 1046, 749 cm⁻¹; LRMS (M⁺) 216 (55), 188 (50), 144 (60), 128 (65), 116 (80), 99 (70), 91 (65), 77 (37), 55 (80); HRMS calcd for C₁₄H₁₆O₂ (M⁺) 216.1150, found 216.1151.

2-Benzyl-2-cyclobut-2-enyl-[1,3]-dioxolane (16).

¹H NMR (300 MHz, CDCl₃) δ 2.40 (d, 1 H, *J* = 13 Hz), 2.52 (dd, 1 H, *J* = 13, 4.0 Hz), 2.93 (s, 2 H), 3.16 (d, 1 H, *J* = 4.0 Hz), 3.60-3.65 (m, 1 H), 3.70-3.72 (m, 1 H), 3.83-3.91 (m, 2 H), 5.94 (d, 1 H, *J* = 2.2 Hz), 6.17 (d, 1 H, *J* = 2.2 Hz), 7.21-7.29 (m, 5 H); ¹³C NMR (75 MHz, CDCl₃) δ 32.7, 42.8, 50.2, 65.8, 65.9, 110.7, 126.4, 128.0, 130.8, 136.0, 136.7, 137.8; IR 3045, 2953, 2922, 2879, 1605, 1496, 1454, 1313, 1286, 1207, 1126, 1075, 1045, 1014, 950, 700 cm⁻¹; LRMS (M⁺) 216 (1), 163 (100), 125 (95), 91 (96), 81 (98), 65 (55); HRMS calcd for C₁₄H₁₆O₂ (M⁺) 216.1150, found 216.1157.