***Comparative Diels-Alder Reactivities
within a Family of Valence Bond Isomers:
A Biomimetic Total Synthesis of (±)-UCS1025A***

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Supporting Information

Spectroscopic characterization data and experimental procedures for compounds **1-3**, **8-12**, and **14-19** (12 pp). Copies of ¹H and ¹³C NMR spectra of synthetic **1** and **3** (4 pages). (16 total pages).

General Experimental Protocols.

¹H and ¹³C NMR spectra were recorded on a Varian VI-500 or VI-300 spectrometer. Proton chemical shifts are referenced to TMS (0.00 ppm). “nfom” refers to a non-first order multiplet. Carbon chemical shifts are referenced to CDCl₃ (77.23 ppm). High resolution mass spectra were recorded on a Bruker Biotof II instrument. Infrared spectra were recorded on a Midac Corporation Prospect FT-IR spectrometer.

Preparation of (±)-(2a*R*,7*R*,7a*S*,7b*R*)-Hexahydro-7b-hydroxy-7-[(1*S*,2*S*,4a*R*,8a*S*)-1,2,4a,5,6,7,8,8a-octahydro-2-methyl-1-naphthalenyl]carbonyl]furo[2,3,4-*gh*]pyrrolizine-2,6-dione (1**)**

An ca. 1:1 mixture of **18** and **19** (25 mg, 0.049 mmol) was deprotected according to the procedure described for the preparation of **2**. A crude mixture of **1** and **3** (18 mg) was obtained. The same deprotection conditions were applied to an ca. 1.5:1 mixture of **15** and **16** (95 mg), which yielded an additional amount of the mixture of **1** and **3** (56 mg). Both of these mixtures were combined and fractionated using medium pressure liquid chromatography (MPLC) on silica gel as a stationary phase, hexanes/EtOAc 1:1 as eluent, and refractive index (RI) detection. The first component, the ketone tautomer of **3** (8 mg), containing minor amounts of **1** could be separated from the partially co-eluting mixture of the ketone tautomer of **1** and enol tautomers of **1** and **3** (cf., footnote 10 of the manuscript). This procedure was repeated two more times on the fractions enriched in **1**, which provided a 4:1 mixture of **1** and **3** (36 mg). Crystallization of this mixture from hexanes/acetone 4:1 solution produced a pure sample of, presumably, enol **4a** (12 mg). An equilibrium ratio of ketone (**1**) to enol (**4a**) (11:1) was achieved upon refluxing a solution of this material in CDCl₃ for one day. Heating for an additional 2 days did not lead to any appreciable changes in the ¹H NMR spectrum. mp: 185-195 °C. TLC: R_f (Hexanes/Acetone 2:1) = 0.35. ¹H NMR (500 MHz, CDCl₃): δ 5.59 (ddd, 1H, *J* = 9.6, 4.5, 2.4 Hz, H17), 5.41 (br d, 1H, *J* = 9.7 Hz, H16), 4.74 (s, 1H, H7a), 4.73 (s, 1H, OH), 4.07 (s, 1H, H7), 3.84 (ddd, *J* = 12.1, 9.6, 5.7 Hz, H_a4), 3.37 (ddd, 1H, *J* = 12.0, 10.0, 5.2 Hz, H_b4), 3.26 (dd, 1H, *J* = 9.3, 1.6 Hz, H2a), 3.18 (dd, 1H, *J* = 11.2, 5.4 Hz, H9), 2.92 (br q, *J* = 6 Hz, H18), 2.74 (dddd, *J* = 14.8, 9.8,

9.8, 5.7 Hz, H_a3), 2.57 (dddd, $J = 14.2, 9.3, 5.1, 2.1$ Hz, H_b3), 1.77 (m, 5H), 1.53 (dddd, $J = 11, 11, 11, 2.5$ Hz, H_{10}), 1.34 (m, 2H), 1.09 (br ddd, 1H, $J = 12, 12, 12$ Hz, H_{14}), 0.89 (nfom, 1H), and 0.79 (d, 3H, $J = 7.0$ Hz, CH_3). ^{13}C -NMR (75 MHz, $CDCl_3$): δ 209.2 (C8), 174.8 (C2), 167.3 (C6), 130.9 (C16), 130.6 (C17), 101.2 (C7b), 80.5 (C7a), 66.6, 59.0, 47.9, 42.4, 42.0, 36.9, 33.1, 30.3, 30.2, 30.1, 26.72, 26.66, and 17.8. (note: the ^{13}C NMR data reported for natural UCS1025Aⁱ were referenced to 77.05 ppm for the chemical shift of $^{13}CDCl_3$; the data here are referenced to 77.23 for that same resonance.) IR (KBr): 3196 (br), 3026, 3013, 2974, 2950, 2919, 2882, 2852, 2830, 1788, 1711, 1665, 1451, 1378, 1337, 1281, 1253, 1170, 1159, 1137, 1113, and 1023 cm^{-1} . MS: ESI-MS calcd for $C_{20}H_{25}NO_5Na$ ($M \cdot Na^+$) 382.1630, found 382.1636.

Preparation of Triene 2. To HF•pyridine (70% HF, 30% pyridine, 500 mg) in a polyethylene tube MeCN (0.5 mL) and then pyridine (520 μ L) were added. To this mixture tetraene **14** (53 mg, 0.079 mmol) in MeCN (0.5 mL) was added. The resulting mixture was stirred for ca. 48 h at room temperature and partitioned between water (30 mL) and CH_2Cl_2 (30 mL). The aqueous layer was extracted with CH_2Cl_2 (2x30 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to give a colorless oil (30 mg). To remove residual pyridine the mixture was filtered through a pad of silica gel using EtOAc as the eluent. Evaporation provided tetraene **2** (21 mg, 74%) as a pale yellow oil (ca. 90 % pure based on the 1H NMR spectrum, the other components corresponded to two diastereomers **1** and **3** resulting from some cyclization of **2**). TLC: R_f (Hexanes/EtOAc 1:1) = 0.22. 1H NMR (500 MHz, $CDCl_3$): δ 7.27 (dt, 1H, $J = 15.9, 6.9$ Hz), 6.29 (d, 1H, $J = 15.9$ Hz), 6.01 (m, 2H), 5.59 (dt, 1H, $J = 13.6, 6.7$ Hz), 5.52 (dq, 1H, $J = 14.1, 6.9$ Hz), 4.89 (s, 1H), 4.68 (br s, 1H), 4.34 (s, 1H), 3.83 (ddd, 1H, $J = 12.0, 9.4, 5.6$ Hz), 3.33 (ddd, 1H, $J = 12.0, 9.8, 5.2$ Hz), 3.28 (dd, 1H, $J = 9.4, 1.7$ Hz), 2.75 (dddd, 1H, $J = 14, 9.7, 9.7, 5.6$ Hz), 2.58 (dddd, 1H, $J = 14, 9.3, 5.2, 1.9$ Hz), 2.36 (dt, 2H, $J = 7, 7$ Hz), 2.08 (dt, 2H, $J = 7, 7$ Hz), 1.73 (d, 3H, $J = 6.4$ Hz), 1.54 (m, 2H), and 1.44 (m, 2H). ^{13}C -NMR (75 MHz, $CDCl_3$): δ 194.7, 175.1, 167.5, 156.9, 131.7, 131.2, 131.1, 129.2, 127.5, 101.1, 81.0, 61.6, 48.0, 41.8,

33.3, 32.4, 30.2, 29.1, 27.4 and 18.2. IR (thin film): 3439, 3014, 2928, 2855, 1788, 1716, and 1672 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_5\text{Na}$ ($\text{M}^+\cdot\text{Na}^+$) 382.1630, found 382.1622.

Preparation of ($\pm$)-(2a*R*,7*R*,7a*S*,7b*R*)-Hexahydro-7b-hydroxy-7-[(1*R*,2*R*,4a*S*,8a*R*)-1,2,4a,5,6,7,8,8a-octahydro-2-methyl-1-naphthalenyl]carbonyl]furo[2,3,4-*gh*]pyrrolizine-2,6-dione [3 (9,10,15,18-tetraepi)-UCS1025A]

A mixture of **18** and **19** (dr = 1:4, 80 mg), obtained from the $\text{ZnCl}_2\cdot\text{Et}_2\text{O}$ catalyzed cycloaddition reaction described below, was subjected to the same procedure as for the preparation of **2** (detailed above) to provide **1** and **3** (59 mg, 0.16 mmol, crude) in an ca. 1:4 ratio.

Chromatography on silica gel (hexanes/ EtOAc , 2:1) provided pure **3** (28 mg, 0.08 mmol, 56% from the bis-TIPS precursor **14**). This was the sample where we first observed the odd chromatographic behavior described in footnote 10 in the manuscript. mp: 133-135 $^\circ\text{C}$. TLC: R_f (Hexanes/Acetone 2:1) = 0.41; R_f (Hexanes/ EtOAc 1:1) = 0.46 (with streaking down to 0.3). ^1H NMR (500 MHz, CDCl_3): δ 5.58 (ddd, 1H, J = 9.8, 4.4, 2.6 Hz, H17), 5.45 (br d, 1H, J = 9.9 Hz, H16), 4.81 (s, 1H, H7a), 4.72 (br s, 1H, OH), 4.10 (s, 1H, H7), 3.84 (ddd, J = 1H, 12.1, 9.5, 5.6 Hz, H_a4), 3.36 (ddd, 1H, J = 12.0, 9.8, 5.4 Hz, H_b4), 3.29 (dd, 1H, J = 11.3, 5.8 Hz, H9), 3.28 (dd, 1H, J = 9.2, 2.1 Hz, H2a), 2.75 (dddd, 1H, J = 15.0, 9.7, 9.7, 5.5 Hz, H_a3), 2.73 (m, 1H, H18), 2.56 (dddd, 1H, J = 14.6, 9.2, 5.3, 2.0 Hz, H_b3), 1.73 (m, 5H), 1.46 (dddd, 1H, J = 11, 11, 11, 2.4 Hz, H10), 1.30 (m, 2H, H_{ax}12 and H_{ax}13), 1.08 (m, 1H, H_{ax}14), and 0.84 (d, 3H, J = 7.0 Hz, CH_3). ^{13}C -NMR (75 MHz, CDCl_3): δ 208.4 (C8), 174.9 (C2), 166.8 (C6), 131.9 (C16), 129.8 (C17), 101.2 (C7b), 80.3 (C7a), 65.4 (C7), 56.3 (C9), 48.0 (C2a), 42.1 (C4), 41.7 (C15), 35.8 (C10), 33.1 (C14), 31.2 (C18), 30.2 (C3), 29.1 (C11), 26.6 (C13), 26.5 (C12), and 18.5 (C19). IR (KBr): 3451 (br), 3007, 2966, 2928, 2853, 1792, 1720, 1698, 1425, 1340, 1287, 1252, 1166, 1120, 1096, and 1019 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{20}\text{H}_{25}\text{NO}_5\text{Na}$ ($\text{M}^+\cdot\text{Na}^+$) 382.1630, found 382.1616

Preparation of Lactam 8. Maleimide ester **7**ⁱⁱ (10.0 g, 50.8 mmol) was dissolved in CHCl_3 (100 mL) and Et_3N (14.1 mL, 101.5 mmol) was added. To this stirred solution TIPSOTf (22.5 mL, 83.8 mmol) was added dropwise at room temperature over ca. 5 minutes. A slight rise in the temperature was observed, and stirring was continued for 24 h. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed with a saturated solution of NaHCO_3 . The organic layer was dried over Na_2SO_4 and concentrated. The residue was chromatographed on silica gel with Hexanes/ EtOAc 4:1 as eluent to give **8** as a pale yellow oil (17.4 g, 49.3 mmol, 97%). TLC: R_f (Hexanes/ EtOAc 4:1) = 0.18. ^1H NMR (500 MHz, CDCl_3): δ 6.97 (d, 1H, J = 5.9 Hz), 5.98 (d, 1H, J = 5.9 Hz), 3.80 (ddd, 1H, J = 10.9, 8.7, 8.7 Hz), 3.58 (s, 3H), 3.31 (ddd, 1H, 10.9, 9.2, 2.8 Hz), 3.16 (dd, 1H, J = 7.1, 1.7 Hz), 2.66 (dddd, 1H, J = 13.2, 9.0, 9.0, 7.0 Hz), 2.50 (dddd, 1H, 13.2, 8.6, 2.8, 1.6 Hz), and 1.00-1.05 (21H, m). ^{13}C -NMR (75 MHz, CDCl_3): δ 173.2, 171.6, 147.2, 128.2, 100.6, 53.6, 52.1, 42.0, 31.2, 18.09, 18.05, and 12.9. IR (thin film): 2948, 2898, 2869, 1739, and 1723 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{18}\text{H}_{31}\text{NO}_4\text{SiNa}$ ($\text{M}\cdot\text{Na}^+$) 376.1915, found 376.1919.

Preparation of Lactam Acid 9. Ester **8** (683 mg, 1.93 mmol) was dissolved in THF (34 mL) and H_2O (34 mL) was added. To this stirred solution $\text{LiOH}\cdot\text{H}_2\text{O}$ (1.0 g, 23.8 mmol) was added. After TLC monitoring indicated complete consumption of the starting material, the reaction mixture was partitioned between CH_2Cl_2 (150 mL) and H_2O (100 mL) containing citric acid monohydrate (5.0 g, 23.8 mmol). The aqueous layer was washed with CH_2Cl_2 (2x100 mL) and the organic layers were combined and dried over Na_2SO_4 . Concentration of the organic extract yielded 634 mg (1.87 mmol, 97%) of pure acid **9** (>95 % pure based on the ^1H NMR spectrum). mp: 108-111 $^\circ\text{C}$. TLC: R_f (Hexanes/ EtOAc 1:1) = 0.32. ^1H NMR (500 MHz, CDCl_3): δ 7.04 (d, 1H, J = 5.9 Hz), 6.00 (d, 1H, J = 5.9 Hz), 4.56 (br s, 1H), 3.77 (ddd, 1H, J = 11.0, 8.7, 8.7 Hz),

3.30 (ddd, 1H, $J = 11.2, 9.0, 2.4$ Hz), 3.15 (dd, 1H, $J = 6.8, 1.5$ Hz), 2.67 (dddd, 1H, $J = 13.2, 9.0, 9.0, 6.9$ Hz), 2.53 (dddd, 1H, $J = 13.1, 8.6, 2.7, 1.6$ Hz), and 1.00-1.05 (m, 21H). ^{13}C -NMR (125 MHz, CDCl_3): δ 175.0, 173.9, 147.5, 128.2, 100.7, 53.5, 41.9, 31.3, 18.11, 18.06, and 12.9. IR (thin film): 3600-2400 (br), 2947, 2869, and 1731 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{17}\text{H}_{29}\text{NO}_4\text{SiNa}$ ($\text{M}\cdot\text{Na}^+$) 362.1739, found 362.1758.

Preparation of Lactam Lactone 10. A solution of acid **9** (several mg) in C_6D_6 was monitored by ^1H NMR spectroscopy for 3 days at room temperature and 1 day at reflux, at which time full conversion to lactone **10** was observed. Evaporation of the solvent provided a white crystalline solid that was judged to be essentially a single compound by ^1H NMR analysis. The compound could be chromatographed (MPLC on silica gel, 6:1 Hexanes/EtOAc). mp: 47-49 $^\circ\text{C}$. TLC: R_f (Hexanes/EtOAc 4:1) = 0.45. ^1H NMR (500 MHz, CDCl_3): δ 4.85 (d, 1H, $J = 4.4$ Hz), 3.88 (ddd, 1H, $J = 12.0, 9.5, 5.9$ Hz), 3.32 (dddd, 1H, $J = 11.9, 9.5, 5.2, 0.9$ Hz), 3.16 (dd, 1H, $J = 9.4, 2.5$ Hz), 3.12 (dd, 1H, 17.8, 4.4 Hz), 2.66 (dddd, 1H, $J = 14.0, 9.6, 9.6, 5.9$ Hz), 2.65 (d, 1H, $J = 17.8$ Hz), 2.56 (dddd, 1H, $J = 14.2, 9.4, 5.3, 2.4$ Hz), and 1.07 (m, 21H). ^{13}C -NMR (125 MHz, CDCl_3): δ 175.4, 173.8, 102.9, 81.0, 50.2, 42.9, 38.8, 30.2, 18.09, 18.08, and 13.0. IR (thin film): 2947, 2869, 1790, and 1725 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{18}\text{H}_{31}\text{NO}_4\text{SiNa}$ ($\text{M}\cdot\text{Na}^+$) 362.1759, found 362.1758.

Preparation of Iodolactone 11. Acid **9** (19.0 g, 56.0 mmol) was dissolved in CH_2Cl_2 (190 mL) and a saturated aqueous solution of NaHCO_3 (190 mL) was added. The reaction mixture was stirred for ca. 20 min until the evolution of CO_2 subsided and the reaction flask was covered with aluminum foil. Iodine (14.9 g, 58.8 mmol) was added in one portion during vigorous stirring of

the reaction mixture. After 6 h the reaction mixture was washed with a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ until the purple color of iodine disappeared. The organic layer was dried over Na_2SO_4 and concentrated to give iodolactone **11** as a bright white solid (24.1 g, 51.8 mmol, 93 %), which was used without purification. mp: 98-102 °C. TLC: R_f (Hexanes/EtOAc 4:1) = 0.27. ^1H NMR (500 MHz, CDCl_3): δ 5.03 (s, 1H), 4.45 (s, 1H), 3.95 (ddd, 1H, J = 12.2, 9.5, 5.1 Hz), 3.34 (ddd, 1H, J = 12.2, 9.8, 5.9 Hz), 3.17 (dd, 1H, J = 9.5, 2.7 Hz), 2.65 (dddd, 1H, J = 14.2, 9.4, 9.4, 4.9 Hz), 2.56 (dddd, 1H, J = 14.9, 8.4, 5.4, 2.7 Hz), and 1.10-1.15 (m, 21H). ^{13}C -NMR (125 MHz, CDCl_3): δ 174.4, 172.1, 102.2, 86.5, 49.7, 42.9, 30.6, 18.32, 18.26, 13.3, and 12.9. IR (thin film): 2945, 2893, 2867, 1796, and 1721 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{17}\text{H}_{28}\text{INO}_4\text{SiNa}$ ($\text{M}^+\cdot\text{Na}^+$) 488.0713, found 488.0701.

Preparation of Alkenyl iodide 12. Iodolactone **11** (5.13 g, 11.0 mmol) was dissolved in an anhydrous ether (100 mL), and triethylamine (1.89 mL, 13.5 mmol) was added followed by TIPSCl (2.52 mL, 11.8 mmol). The reaction mixture was stirred for 40 h at room temperature, and precipitation of triethylammonium hydrochloride was observed. The mixture was filtered through silica gel, and the silica gel bed was washed with additional fresh ether. The ethereal solutions were concentrated to give vinyl iodide as a white solid **12** (5.65 g, 9.1 mmol, 82%). mp: 83-87 °C. TLC: R_f (Hexanes/EtOAc 4:1) = 0.70. ^1H NMR (500 MHz, CDCl_3): δ 7.37 (s, 1H), 3.81 (ddd, 1H, J = 11.0, 8.6, 8.6 Hz), 3.39 (ddd, 1H, J = 11.6, 9.1, 2.8 Hz), 3.20 (dd, 1H, J = 6.9, 1.7 Hz), 2.63 (dddd, 1H, J = 13.1, 8.9, 8.9, 6.9 Hz), 2.48-2.53 (m, 1H), 1.26 (sept, 3H, J = 7.5 Hz), and 1.01-1.06 (m, 39H). ^{13}C -NMR (125 MHz, CDCl_3): δ 170.8, 169.0, 153.0, 101.4, 97.5, 55.2, 43.0, 31.4, 18.10, 18.55, 18.03, 13.0, and 12.1. IR (thin film): 2947, 2869, 1730 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{26}\text{H}_{48}\text{INO}_4\text{Si}_2\text{Na}$ ($\text{M}^+\cdot\text{Na}^+$) 644.2059, found 644.2054.

Preparation of bis-TIPS Tetraene 14. Alkenyl iodide **12** (100 mg, 0.16 mmol) was dissolved in anhydrous THF (1.0 mL) and cooled to $-50\text{ }^{\circ}\text{C}$. *i*-PrMgCl in ether (160 μL , 0.32 mmol, 2.0 M) was added. After the mixture was stirred for 10 min Weinreb amide **13**ⁱⁱⁱ (76 mg, 0.32 mmol) in anhydrous THF (0.3 mL) was added and the reaction mixture was stirred for 30 min at $-50\text{ }^{\circ}\text{C}$, warmed to rt, and quenched by addition of 5% aqueous solution of NaHCO_3 (1 mL) followed by CH_2Cl_2 (20 mL). This mixture was poured into 1M aqueous HCl (25 mL). After shaking the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2x30 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to give a yellow oil (140 mg). Chromatography on silica gel using Hexanes/EtOAc 50:1 as eluent yielded 39 mg (35%) of tetraene **14** as a pale yellow oil. TLC: R_f (Hexanes/EtOAc 4:1) = 0.77. ^1H NMR (500 MHz, CDCl_3): δ 7.66 (s, 1H), 7.08 (d, 1H, $J = 15.5\text{ Hz}$), 7.07 (dt, 1H, $J = 15.5, 5.5\text{ Hz}$), 5.96-6.05 (m, 2H), 5.59 (dt, 1H, $J = 13.5, 6.5\text{ Hz}$), 5.52 (dq, 1H, $J = 14.0, 7.0\text{ Hz}$), 3.83 (ddd, 1H, $J = 10.9, 8.6, 8.6\text{ Hz}$), 3.36 (ddd, 1H, $J = 11.7, 9.1, 2.8\text{ Hz}$), 3.25 (dd, 1H, $J = 6.8, 1.6\text{ Hz}$), 2.67 (dddd, 1H, $J = 13.1, 8.9, 8.9, 7.0\text{ Hz}$), 2.53 (dddd, 1H, $J = 13.0, 8.4, 2.3, 2.3$), 2.27 (dt, 2H, $J = 6.0, 7.5\text{ Hz}$), 2.07 (app q, 2H, $J = 7\text{ Hz}$), 1.73 (d, 3H, $J = 6.5\text{ Hz}$), 1.49 (m, 2H), 1.42 (m, 2H), 1.22 (sept, 3H, $J = 7.5\text{ Hz}$), and 0.99-1.04 (m, 39H). ^{13}C -NMR (75 MHz, CDCl_3): δ 184.5, 170.9, 169.6, 152.2, 151.0, 137.4, 131.8, 131.6, 130.8, 127.4, 127.2, 97.5, 55.2, 42.2, 32.8, 32.4, 31.3, 29.2, 27.7, 18.2, 18.11, 18.06, 17.94, 17.91, 13.0, and 12.0. IR (thin film): 3015, 2946, 2896, 2869, and 1721 cm^{-1} . MS: ESI-MS calcd for $\text{C}_{38}\text{H}_{65}\text{NO}_5\text{Si}_2\text{Na}$ ($\text{M}^+\cdot\text{Na}^+$) 694.4299, found 694.4266.

Preparation of a Mixture of the bis-TIPS Octalins 15 and 16. Tetraene **14** (35 mg, 0.052 mmol) was refluxed in CDCl_3 for 48 h. Evaporation produced a mixture (dr = 4:3) of **15** and **16** (24 mg, 0.036 mmol, 69%). These two isomers coeluted on normal (silica gel, hexanes/EtOAc 50:1) or reversed phase (cyanoethylated silica, acetonitrile/water gradient) chromatographic support. TLC: R_f (Hexanes/EtOAc 4:1) = 0.74. ^1H NMR (500 MHz, CDCl_3 , recorded for the mixture): δ 7.69 (s, 1H), 7.58 (s, 1H), 5.56 (ddd, 1H, $J = 11, 4.6, 2.5$ Hz), 5.54 (ddd, 1H, $J = 10, 4.6, 2.5$ Hz), 5.38 (br d, 1H, $J = 7$ Hz), 5.36 (br d, 1H, $J = 7$ Hz), 3.82 (dd, 1H, $J = 11.2, 5.4$ Hz), 3.81 (m, 1H), 3.76 (ddd, 1H, $J = 11.0, 8.4, 8.4$ Hz), 3.64 (dd, 1H, $J = 11.3, 5.6$ Hz), 3.32 (ddd, 1H+1H, $J = 11.5, 8.9, 2.7$ Hz), 3.23 (br d, 1H+1H, $J = 6.9$ Hz), 2.79 (m, 1H), 2.66 (m, 1H+1H), 2.57 (m, 1H), 2.54-2.44 (m, 1H+1H), 1.88 (br d, 1H+1H, $J = 11.6$ Hz), 1.80-1.68 (m, 5H+5H), 1.53 (dddd, 1H+1H, $J = 11, 11, 11, 2.0$ Hz), 1.40-1.28 (m, 4H+4H), 1.23 (m, 3H+3H), 1.04-1.01 (m, 39H+39H), 0.77 (d, 3H, $J = 7.2$ Hz), and 0.74 (d, 3H, $J = 7.1$ Hz). ^{13}C -NMR (75 MHz, CDCl_3): δ 198.2, 197.0; 170.72, 170.66; 169.7, 169.3; 152.4, 151.8; 138.3, 137.1; 131.44, 131.37; 130.80, 130.78; 97.3, 97.2; 55.3, 54.8; 53.8, 53.3; 42.4, 42.22, 42.19, 42.15; 36.8, 35.9; 33.40, 33.36; 31.8, 31.6; 31.3, 31.0; 29.9, 29.7; 26.93 (2C), 26.87 (2C), 18.15 (2C), 18.14, 17.98, 17.96, 17.92; 13.2, 13.1; and 12.0 (2C) MS: ESI-MS calcd for $\text{C}_{38}\text{H}_{65}\text{NO}_5\text{Si}_2\text{Na}$ ($\text{M}\cdot\text{Na}^+$) 694.4299, found 694.4297.

Preparation of Mono-TIPS Enol 17. Tetraene **14** (93 mg, 0.14 mmol) was dissolved in methanol (3.7 mL) and anhydrous KF (16 mg, 0.28 mmol) was added. After stirring for 5 min the reaction mixture was partitioned between water (20 mL) and CH₂Cl₂ (20 mL), and the aqueous layer was extracted with CH₂Cl₂ (2x20 mL). The combined organic extracts were dried over Na₂SO₄ and evaporated to give enol **17** (80 mg) as an oil, which was essentially a single heteraquinane-containing compound, contaminated with a portion of a TIPS-containing byproduct (likely, TIPSOH), as judged by ¹H NMR analysis. This sample was used directly in the following ZnCl₂•Et₂O catalyzed IMDA reaction. Other samples of this compound could be chromatographed on silica gel (Hexanes/EtOAc, 6:1). TLC: R_f (Hexanes/EtOAc 4:1) = 0.56. ¹H NMR (500 MHz, CDCl₃): δ 11.51 (br s, 1H), 6.77 (ddd, 1H, *J* = 15.4, 7.4, 7.4 Hz), 5.90-5.98 (m, 3H), 5.52 (dt, 1H, *J* = 13.6, 7.0 Hz), 5.46 (dq, 1H, *J* = 13.3, 6.7 Hz), 5.20 (s, 1H), 3.86 (ddd, 1H, *J* = 12.1, 9.2, 4.3 Hz), 3.35 (ddd, 1H, *J* = 12.0, 8.8, 7.1 Hz), 3.19 (dd, 1H, *J* = 10.1, 4.2 Hz), 2.60 (dddd, 1H, *J* = 13.9, 10.2, 8.8, 4.4 Hz), 2.37 (dddd, 1H, *J* = 13.6, 9.3, 7.1, 4.2 Hz), 2.19 (ddt, 2H, *J* = 7.2, 1.2, 7.2 Hz), 2.01 (dt, 2H, *J* = 7.0, 7.0 Hz), 1.66 (d, 3H, *J* = 6.3 Hz), 1.42 (m, 2H), 1.36 (m, 2H), and 0.97 (m, 21H). ¹³C-NMR (75 MHz, CDCl₃): δ 176.0, 175.8, 166.3, 145.3, 131.7, 131.5, 130.8, 127.2, 120.6, 102.3, 100.6, 81.9, 51.1, 45.1, 33.1, 32.4, 31.3, 29.1, 28.0, 18.2, 18.06, 18.05, and 12.9. IR (thin film): 3016, 2944, 2868, 1784, 1674, and 1611 cm⁻¹. MS: ESI-MS calcd for C₂₉H₄₅NO₅SiNa (M•Na⁺) 538.2959, found 538.2958.

Preparation of a Mixture of the mono-TIPS Octalin Enols **18 and **19** from **15** and **16**.** A mixture of **15** and **16** (dr = 4:3, 24 mg, 0.036 mmol) was subjected to the same selective silyl ester cleavage conditions described above for the preparation of **17** to yield a mixture of **18** and **19** (13 mg, 0.025 mmol, 70%). TLC: R_f (Hexanes/EtOAc 4:1) = 0.59. ^1H NMR (500 MHz, CDCl_3): δ 11.96 (br s, 1H), 11.93 (br s, 1H), 5.55 (m, 1H+1H), 5.43 (d, 1H, $J = 9.9$ Hz), 5.39 (d, 1H, $J = 9.9$ Hz), 5.23 (s, 1H), 5.22 (s, 1H), 3.91 (ddd, 1H+1H, $J = 12.7, 9.5, 4.3$ Hz), 3.41 (ddd, 1H+1H, $J = 11.8, 8.6, 7.3$ Hz), 3.26-3.22 (m, 1H+1H), 2.71-2.60 (m), 2.57-2.54 (m), 2.51-2.43 (m), 2.37 (m, 1H), 1.88 (br d, 1H, $J = 12.1$ Hz), 1.79-1.70 (m), 1.58 (br ddd, 1H, $J = 11, 11, 11$ Hz), 1.54 (br ddd, 1H, $J = 11, 11, 11$ Hz), 1.48-1.28 (m), and 1.10-0.99 (m). ^{13}C -NMR (75 MHz, CDCl_3): δ 178.6, 176.1; 175.4, 175.2; 131.8, 131.6, 131.0, 130.5; 102.1, 102.0; 82.5, 81.8; 51.2, 51.1; 47.7, 47.0; 44.92, 44.89; 42.9, 42.6; 36.4, 36.2, 35.0, 34.6; 33.3 (2C); 31.3, 31.1, 30.8, 30.0; 26.9, 26.8, 26.7, 26.6; 18.15, 18.13, 18.09, and 13.04. MS: ESI-MS calcd for $\text{C}_{29}\text{H}_{45}\text{NO}_5\text{SiNa}$ ($\text{M} \cdot \text{Na}^+$) 589.2959, found 589.2967.

Preparation of a Mixture of the mono-TIPS Octalin Enols **18 and **19** by IMDA of **17**.**

Thermal IMDA: Triene **17** (2 mg) was dissolved in CDCl_3 (0.6 mL). ^1H NMR spectra were periodically recorded in order to estimate $t_{1/2}$ of the reaction. It was found to be ca. 20 h. An ca. 1:2 ratio of the mixture of **18** and **19**, respectively, was produced.

Lewis acid catalyzed IMDA: ZnCl_2 (“anhydrous,” 246 mg, 1.80 mmol) was placed into a 50 mL round bottom reaction flask and heated *in vacuo* with a Bunsen burner until all of the white solid was molten. It was then left to cool to rt. This procedure was repeated two more times. CH_2Cl_2 (15 mL) was added while stirring followed by Et_2O (770 μL , 7.28 mmol) and pyridine (80 μL , 1.01 mmol). Enol **17** (80 mg, 0.16 mmol) in CH_2Cl_2 (4 mL) was added followed by TMSOTf (36 μL , 0.20 mmol). This two-phase reaction mixture was stirred for 18 h and partitioned between CH_2Cl_2 (30 mL) and water (30 mL). The aqueous layer was further extracted with CH_2Cl_2 (2x30 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated to give ca. 100 mg of a crude mixture of **18** and **19** (dr = 1:4).

References (for Supporting Information):

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1, synthetic UCS1025A

3, synthetic
(9,10,15,18-tetra*epi*)-UCS1025A