Acid-induced Rearrangement Reactions of Reduced Benzoquinone Cyclopentadiene Cycloadducts

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Supporting Information

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Experimental Section

General. ^1H and ^{13}C NMR: Bruker Avance 400, spectra were recorded in CDCl_3 , C_6D_6 , CD_3OD ; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: CDCl_3 (δH 7.25 ppm, δC 77.00 ppm), C_6D_6 (δH 7.16 ppm, δC 128.00 ppm), methanol- d_4 (δH 3.34 ppm, δC 49.86 ppm). Melting points: Büchi Melting Point B-540, uncorrected. IR: Jasco FT/IR-430. EI-MS: Finnigan Triple-Stage-Quadrupol (TSQ-70). HR-MS (EI): modified AMD Intectra MAT 711 A. Flash chromatography: J. T. Baker silica gel 43-60 μm . Thin-layer chromatography Machery-Nagel Polygram Sil G/UV₂₅₄. Solvents were distilled prior to use; petroleum ether with a boiling range of 40-60 °C was used; cyclopentadiene was generated from dicyclopentadiene freshly before use.

3-(3,6-Dioxo-cyclohexa-1,4-dienyl)-propionic acid (5). A solution of 3-(2-hydroxyphenyl)propionic acid (**4**) (2.0 g, 12 mmol) in a mixture of acetonitrile/water (4:1, 50 mL) was cooled to 0 °C under nitrogen and then [bis(trifluoroacetoxy)iodo]benzene (6.71 g, 15.6 mmol, 1.3 equiv) was added in one portion. The solution immediately became deep brown and after 10-15 minutes the color of the mixture brightened. The reaction was kept at this temperature for 8 h. Most of the acetonitrile was removed under vacuum and the residue treated with 5% NaHCO_3 solution (70 mL) and extracted with ethyl acetate (3×50 mL). The combined organic layers were washed with satd. NaCl solution, dried with MgSO_4 and filtered. Evaporation of the solvent gave a brown residue, which was chromatographed on silica gel (ethyl acetate/petroleum ether, 1:1) to give 0.97 g (45%) of the quinone **4** as a yellow-beige powder. Recrystallization from benzene gave orange crystals; m.p. 141 °C, lit.¹ 139-141 °C; TLC (ethyl acetate/petroleum ether, 1:1): R_f = 0.29; ^1H NMR ($[\text{D}_6]$ methanol): δ = 0.99 (t, J = 7.3 Hz, 2H, CH_2), 1.12 (t, J = 7.3 Hz, 2H, CH_2), 5.05 (s, 1H, quinone-H), 5.14-5.23 (m, 2H, quinone-H); ^{13}C NMR ($[\text{D}_6]$ methanol): δ = 24.5, 31.8 (CH_2), 132.8, 136.4, 137.1 (unsubst. alkene), 148.2 (subst. alkene), 175.0 (COO), 187.5, 188.1 (CO); IR (KBr): 1701 (COOH), 1654, 1598 cm^{-1} ; MS (EI), m/z (%): 178 (4) $[\text{M}]^+$, 162 (66) $[\text{M} - \text{H}_2\text{O}]^+$, 134 (100) $[\text{M} - \text{H}_2\text{O}, \text{CO}]^+$; $\text{C}_9\text{H}_8\text{O}_4$ (180.2): calcd C 60.00, H 4.48; found C 60.31, H 4.44; HRMS (EI): calcd for $\text{C}_9\text{H}_8\text{O}_4$ 180.04226, found 180.04323.

rel-(1R,4R,4aS,8aR)-6-Methyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (6a) was prepared according to the literature.²

¹ Borchardt, R. T.; Cohen, L. A. *J. Am. Chem. Soc.* **1972**, *94*, 9175-9182.

² (a) Ichihara, A.; Kobayashi, M.; Oda, K.; Sakamura, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 826-829;
(b) Alder, K.; Flock, F. H.; Beumling, H. *Chem. Ber.* **1960**, *93*, 1896-1899.

rel-(1R,4R,4aS,8aR)-6-Ethyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (6b). To a stirred solution of benzoquinone **2b** (651 mg, 4.78 mmol) in methanol (10 mL) was added cyclopentadiene (316 mg, 1 equiv) at room temperature. With the mixture being protected from light, stirring was continued at this temperature for 15 h. Thereafter, the solvent was removed in vacuo and the residue subjected to flash chromatography (petroleum ether/diethyl ether, 3:1) yielding 620 mg (64%) of **6b** as yellow oil. TLC (petroleum ether/diethyl ether, 4:1): $R_f = 0.22$; ^1H NMR (CDCl_3): $\delta = 0.97$ (t, $J = 7.4$ Hz, 3H, CH_3), 1.36 (dt, $J = 8.7, 1.7$ Hz, 1H, Cp- CH_2), 1.46 (dt, $J = 8.6, 1.7$ Hz, 1H, Cp- CH_2), 2.26 (q, $J = 7.5$ Hz, 2H, CH_2), 3.12-3.17 (m, 2H, CHR_3), 3.43-3.48 (m, 2H, CHR_3), 5.94-5.98 (m, 2H, Cp-alkene), 6.35 (s, 1H, quinone-alkene); ^{13}C NMR (CDCl_3): $\delta = 12.8$ (CH_3), 23.6 (CH_2), 49.6, 49.7, 49.8, 49.9, 50.3, 135.9, 136.5, 139.0 (unsubst. alkene), 157.8 (subst. alkene), 200.3, 200.5 (CO); IR (neat): 3068, 1661, 1620 cm^{-1} ; MS (EI), m/z (%): 202 $[\text{M}]^+$, 187, 173, 137, 66 [Cp]; HRMS (EI): calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2$ 202.10187, found 202.10314.

rel-(1R,4R,4aS,8aR)-6-Benzyl-1,4,4a,8a-tetrahydro-1,4-methanonaphthalene-5,8-dione (6c) was prepared according to the procedure of Bruce et al.³

rel-(1R,4R,4aS,5S,8R,8aR)-6-Methyl-1,4,4a,5,8,8a-hexahydro-1,4-methanonaphthalene-5,8-diol (7a). To a cooled (-5°C) solution of the cycloadduct **6a** (4.0 mmol) in a mixture of methanol/THF (2:1, 15 mL) was added NaBH_4 (0.45 g, 12 mmol, 3 equiv) within 5 min. The cooling bath was removed and stirring continued for 2.5 h at room temperature. Thereafter, the mixture was concentrated in vacuo, and the residue treated with ethyl acetate (40 mL). After washing the mixture twice with water, the organic layer was dried (MgSO_4), filtered, and concentrated. Purification of the residue by flash chromatography (ethyl acetate/petroleum ether, 2:3) provided the the known diol **7a** (0.67 g, 87%) as a sticky syrup.⁴ TLC (ethyl acetate/hexane, 5:8): $R_f = 0.11$; ^1H NMR (CDCl_3): $\delta = 1.35$ (d, $J = 7.8$ Hz, 1H, Cp- CH_2), 1.40 (dt, $J = 7.7, 1.7$ Hz, 1H, Cp- CH_2), 1.73 (s, 3H, CH_3), 2.50-2.57 (m, 2H, CHR_3), 2.84-2.89 (m, 2H, CHR_3), 4.10 (dd, 1H, $J = 5.6$ Hz, R_2CHOH), 4.29 (dd, $J = 4.5$ Hz, 1H, R_2CHOH), 5.56-5.57 (m, 1H, alkene-H), 6.02 (dd, $J = 11.6$ Hz, 2H, Cp-alkene); ^{13}C NMR (CDCl_3): $\delta = 20.8$ (CH_3), 45.1, 45.2, 45.6, 45.7 (CHR_3), 52.4 (Cp- CH_2), 66.6, 70.4 (R_2CHOH), 128.2, 134.1,

³ Al-Hamdany, R.; Bruce, J. M.; Heatley, F.; Khalafy, J. *J. Chem. Soc. Perkin Trans. 2* **1985**, 1395-1400.

⁴ (a) Shimizu, M.; Kamikubo, T.; Ogasawara, K. *Heterocycles* **1997**, 41, 21-26; (b) Wu, H.-J.; Chao, C.-S.; Lin, C.-C. *J. Org. Chem.* **1998**, 63, 7687-7693.

135.1 (unsubst. alkene), 143.2 (subst. alkene); IR (KBr): 3310 cm^{-1} (OH); MS (EI), m/z (%): 192 (5) $[\text{M}]^+$, 174 (17) $[\text{M} - \text{H}_2\text{O}]^+$; HRMS (EI): calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$ 192.13347, found 192.13579.

rel-(1R,4R,4aS,5S,8R,8aR)-6-Benzyl-1,4,4a,5,8,8a-hexahydro-1,4-methanonaphthalene-5,8-diol (7c). As described for **7a**, cycloadduct **6c** (4.0 mmol) was reduced to the diol **7c** (0.81 g, 76%), colorless solid. m.p. 121-122 $^{\circ}\text{C}$; TLC (ethyl acetate/hexane, 2:3): R_f = 0.47; ^1H NMR (CDCl_3): δ = 1.29 (d, J = 7.8 Hz, 1H, Cp- CH_2), 1.34-1.37 (dt, J = 7.8, 1.8 Hz, 1H, Cp- CH_2), 2.34-2.48 (m, 2H, CHR_3), 2.75-2.80 (m, 2H, CHR_3), 3.35 (s, 2H, benzyl- CH_2), 4.01-4.07 (m, 1H, R_2CHOH), 4.22-4.28 (m, 1H, R_2CHOH), 5.56-5.57 (m, 1H, alkene), 5.98-5.99 (m, 2H, Cp-alkene), 7.08-7.13 (m, 3H, aromat), 7.18-7.22 (m, 2H, aromat); ^{13}C NMR (CDCl_3): δ = 40.0 (Benzyl- CH_2), 44.2, 44.5, 44.5, 44.6 (CHR_3), 51.3 (Cp- CH_2), 65.3, 67.7 (R_2CHOH), 125.6, 127.8, 128.4, 128.9, 133.0, 133.8, 138.2 (unsubst. alkene, aromatic), 145.4 (subst. alkene); IR (KBr): 3298 (OH), 3058, 3027 cm^{-1} ; MS (EI), m/z (%): 268 (2) $[\text{M}]^+$, 250.2 (13) $[\text{M} - \text{H}_2\text{O}]^+$, 184 (22), 168 (28), 91 (100) [benzyl] $^+$; HRMS (EI): calcd for $\text{C}_{18}\text{H}_{20}\text{O}_2$ 268.14633, found 268.14859.

One-pot procedure for the preparation of 8a, 8b, 8c from the corresponding Diels-Alder adducts. To a cooled (-5°C) solution of the diketone **6** (3.0 mmol) in a mixture of methanol/water/THF (2:2:1, 15 mL) was added NaBH_4 (0.34 g, 9.0 mmol, 3 equiv). Following complete addition, the mixture was stirred at room temperature for 3 h. At this point, concentrated H_2SO_4 (0.5-0.8 mL) was added carefully in a dropwise fashion until a pH below 1 was reached (higher pH-values promote the formation of a complex mixture of side products). The mixture was stirred at 35°C for 30 h (**8a**) or for 9 h (for **8b** and **8c**), respectively. After filtration, most of the solvent was removed in vacuo, and the residue diluted with ethyl acetate (30 mL). The organic layer was washed twice with saturated NaHCO_3 solution, water, brine, and dried over MgSO_4 . After filtration and concentration of the filtrate, the residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1:1 for **8a** and **8b**; ethyl acetate/petroleum ether, 1:3 for **8c**).

Preparation of 8b from 6c in the presence of HBr. To a cooled (0°C) solution of the diol **7c** (0.4 g, 1.49 mmol) in methanol/water (2:1, 15 mL) was added HBr (48 % HBr solution, 0.9 mL) slowly within 5 minutes. Stirring was continued for 9 h at room temperature, before most of the solvent was removed in vacuo. The residue was diluted with ethyl acetate (30 mL) and washed twice with satd. NaHCO_3 solution, water and brine. The organic layer was dried (MgSO_4), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1:3) to provide **7c** (0.28 g, 66%).

Compound **8a**: yield 216 mg (35%), colorless gum, which formed a semi-crystalline solid upon standing for several days at room temperature; m.p. 81-82 $^{\circ}\text{C}$; TLC (ethyl acetate/hexane, 5:8): R_f =

0.37; IR (KBr): 3430 (OH), 3032 cm^{-1} ; ^1H NMR (CDCl_3): δ = 1.14 (s, 3H, CH_3), 2.12-2.20 (m, 2H, Cp- CH_2), 2.37 (d, J = 6.5 Hz, 1H, R_3CH), 3.16-3.18 (m, 2H, R_3CH), 3.31 (s, 3H, OCH_3), 3.79-3.80 (m, 1H, R_2CHOCH_3), 3.99 (d, J = 3.0 Hz, 1H, R_2CHOH), 5.34 (d, J = 9.3 Hz, 1H, alkene), 5.39-5.43 (m, 1H, alkene), 5.53-5.63 (m, 1H, alkene), 5.60 (m, 1H, alkene); ^{13}C NMR (CDCl_3): δ = 17.7 (CH_3), 30.8 (Cp- CH_2), 38.9 (Cp- CHR_3), 45.4 (CHR_3), 47.8 (CR_4), 55.7 (OCH_3), 60.5 (Cp- CHR_3), 77.2 (R_2CHOCH_3), 80.9 (R_2CHOH), 123.5 (alkene), 129.1 (Cp-alkene), 131.0 (Cp-alkene), 140.2 (alkene); MS (EI), m/z (%): 206 (21) $[\text{M}]^+$, 191 (100) $[\text{M} - \text{CH}_3]^+$, 175 (7) $[\text{M} - \text{OCH}_3]^+$; HRMS (EI): calcd for $\text{C}_{13}\text{H}_{18}\text{O}_2$ 206.13068, found 206.13340.

Compound **8b**: yield 263 mg (40%), colorless solid; m.p. 70-72 $^\circ\text{C}$ (from diethyl ether); TLC (ethyl acetate/hexane, 5:8): R_f = 0.51; ^1H NMR (CDCl_3): δ = 0.87 (t, J = 7.5 Hz, 3H, CH_3), 1.50-1.67 (m, 2H, CH_2), 2.11-2.17 (m, 2H, Cp- CH_2), 2.36-2.37 (m, 1H, CHR_3), 3.13-3.18 (m, 2H, CHR_3), 3.31 (s, 3H, OCH_3), 3.77-3.79 (m, 1H, R_2CHOCH_3), 4.12-4.13 (m, 1H, R_2CHOH), 5.36-5.38 (m, 1H, Cp-alkene), 5.41 (d, J = 10.0 Hz, 1H, alkene), 5.53-5.54 (m, 1H, Cp-alkene), 5.65-5.68 (m, 1H, alkene); ^{13}C NMR (CDCl_3): δ = 8.7 (CH_3), 24.5 (CH_2), 30.6 (Cp- CH_2), 38.7 (Cp- CHR_3), 45.4 (CHR_3), 52.1 (CR_4), 55.7 (OCH_3), 60.0 (Cp- CHR_3), 77.1 (R_2CHOCH_3), 77.9 (R_2CHOH), 124.5 (alkene), 129.8 (Cp-alkene), 130.8 (Cp-alkene), 138.3 (alkene); IR (KBr): 3433 (OH), 3046, 3021 cm^{-1} (alkene); MS (EI), m/z (%): 220 (28) $[\text{M}]^+$, 205 (100) $[\text{M} - \text{CH}_3]^+$, 189 (4) $[\text{M} - \text{OCH}_3]^+$, 177 (28); HRMS (EI): calcd for $\text{C}_{14}\text{H}_{20}\text{O}_2$ 220.14633, found 220.14865.

Compound **8c**: yield 347 mg (41%), colorless sticky oil; TLC (ethyl acetate/hexane, 1:3): R_f = 0.3; ^1H NMR (CDCl_3): δ = 2.03-2.21 (m, 2H, Cp- CH_2), 2.33-2.36 (m, 1H, CHR_3), 2.85, 2.92 (2 d, J = 13.4 Hz, 1H each, benzyl- CH_2), 3.15-3.24 (m, 1H, R_3CH), 3.25 (s, 3H, OCH_3), 3.38-3.43 (m, 1H, R_3CH), 3.73-3.74 (m, 1H, R_2CHOCH_3), 4.05 (d, J = 2.4 Hz, 1H, R_2CHOH), 5.06-5.08 (m, 1H, alkene), 5.46-5.48 (m, 1H, alkene), 5.57-5.58 (m, 2H, alkene), 7.11-7.21 (m, 5H, arom); ^{13}C NMR (CDCl_3): δ = 32.0 (Cp- CH_2), 39.3 (Benzyl- CH_2), 40.2 (Cp- CHR_3), 47.0 (CHR_3), 53.9 (CR_4), 57.1 (OCH_3), 61.3 (Cp- CHR_3), 78.2 (R_2CHOCH_3), 80.3 (R_2CHOH), 125.4 (Cp-alkene), 126.5, 128.6, 130.4, 131.0 (Cp-alkene), 132.4, 138.8 (alkene), 139.4 (CR_4 -aromat); IR (film): 3423 (OH), 3027 cm^{-1} (alkene); MS (EI), m/z (%): 282 (52) $[\text{M}]^+$, 250 (8) $[\text{M} - \text{CH}_3\text{OH}]^+$, 198 (20), 184 (84), 91 (100) [benzyl] $^+$; HRMS (EI): calcd for $\text{C}_{19}\text{H}_{22}\text{O}_2$ 282.16198, found 282.16393.

8-Ethyl-9-hydroxy-3,3a,4,5,8,8a-hexahydro-4,8-methanoazulen-5-yl acetate (9). To a cooled (-5°C) solution of the diketone **6b** (0.5 g, 2.47 mmol), dissolved in a mixture of methanol/water/THF (2:2:1, 15 mL) was added NaBH_4 (0.28 g, 7.41 mmol, 3 equiv). The suspension was stirred for 3 h at 25°C , followed by the addition of a mixture of glacial acetic acid and water (10:1, 22 mL) in order to dissolve the white solid. The resulting clear solution was then treated with conc. H_2SO_4 (0.7 mL) to

reach a pH < 1. After being stirred for 14 h at room temperature, most of the solvent was removed in vacuo. Ethyl acetate (30 mL) was added to the aqueous residue, the phases were separated, and the organic layer washed twice with satd. NaHCO₃ solution, water and brine. The organic layer was dried over MgSO₄, filtered, and evaporated. Flash chromatography (diethyl ether/petroleum ether, 1:1) of the residue yielded 0.21 g of **9** (34%) as colorless crystals (from hexane) together with 0.05 g (9%) of **8b**; Compound **9** slowly decomposed on air, it smells like acetic acid. It should be stored under nitrogen in a refrigerator. The peak at δ = 2.10 is probably due to acetic acid; m.p. 119-120 °C; TLC (ethyl acetate/hexane, 1:3): R_f = 0.4; ¹H NMR (CDCl₃): δ = 0.90 (t, *J* = 7.8 Hz, 3H, CH₃), 1.55-1.70 (m, 2H, CH₂), 1.98 (s, 3H, acetyl-CH₃), 2.22-2.23 (m, 2H, Cp-CH₂), 2.28-2.29 (m, 1H, CHR₃), 3.16-3.19 (m, 2H, Cp-CHR₃), 4.16 (d, *J* = 3.8 Hz, 1H, R₂CHOH), 5.35-5.36 (m, 2H, alkene), 5.49-5.60 (m, 3H, alkene, R₂CHOAc); ¹³C NMR (CDCl₃): δ = 10.1 (CH₃), 21.8 (acetyl-CH₃), 25.8 (CH₂), 32.1 (Cp-CH₂), 40.2 (Cp-CHR₃), 47.9 (CHR₃), 53.3 (CR₄), 61.3 (Cp-CHR₃), 72.1 (R₂CHOAc), 79.3 (R₂CHOH), 124.8 (alkene), 130.7 (Cp-alkene), 132.5 (Cp-alkene), 141.3 (alkene), 170.8 (COO); IR (KBr): 3497 (OH), 3043 (alkene), 1706 cm⁻¹ (COO); MS (EI), *m/z* (%): 248 (17) [M]⁺, 188 (43) [M - AcOH]⁺, 159 (49), 132 (57), 122 (100); HRMS (EI): calcd for C₁₅H₂₀O₃ 248.14125, found 248.14199.

rel-3-[(1*R*,4*R*,4*aS*,8*aR*)-5,8-Dioxo-1,4,4*a*,5,8,8*a*-hexahydro-1,4-methanonaphthalen-6-yl]propanoic acid (10**).** To a well stirred solution of acid **5** (5.0 g, 27.7 mmol) in methanol (15 mL) was added slowly freshly distilled cyclopentadiene (1.8 g, 1 equiv) at 0 °C. Within 1 h the solution turned bright orange. The mixture was allowed to stir for 15 h at 40 °C, then the solvent was removed in vacuo and the residue redissolved in ethyl acetate (50 mL). The organic phase was washed with water (3 × 20 mL), brine (20 mL), dried over MgSO₄, filtered, and concentrated in vacuo. The resulting bright yellow oil was purified by flash chromatography (gradient: ethyl acetate/petroleum ether, 1:1 to ethyl acetate) to yield 4.78 g (70%) of **10** as a cream-colored powder, which was recrystallized from diethyl ether, red-brownish needles; m.p. 106.5 °C. TLC (ethyl acetate/petroleum ether, 2:1): R_f = 0.21; ¹H NMR (CDCl₃): δ = 1.36 (dt, *J* = 8.6, 1.5 Hz, 1H, Cp-CH₂), 1.47 (dt, *J* = 8.6, 1.5 Hz, 1H, Cp-CH₂), 2.43-2.58 (m, 4H, CH₂CH₂), 3.16-3.17 (m, 2H, CHR₃), 3.46 (m, 2H, R₂CHCO), 5.93-5.98 (m, 2H, Cp-alkene), 6.40 (s, 1H, alkene); ¹³C NMR (CDCl₃): δ = 24.6 (CH₂), 31.4 (CH₂), 48.2, 48.6, 48.7, 48.7, 48.9 (Cp-CH₂, CHR₃), 134.7, 135.2 (Cp-alkene), 139.2 (unsubst. alkene), 152.7 (subst. alkene), 177.5 (COO), 198.8, 199.0 (CO); IR (KBr): 3100 (br, COOH), 1724 (COO), 1669, 1646 cm⁻¹ (CO); MS (EI), *m/z* (%): 246 (4) [M]⁺, 228 (12) [M - H₂O]⁺; HRMS (EI): calcd for [C₁₄H₁₄O₄ - H₂O] 228.07864, found 228.08096.

11-Hydroxy-1,2,7,7*a*,8,10*a*-hexahydro-3*H*,4*aH*-7,10*b*-methanoazuleno[5,4-*b*]pyran-3-one (12**).** Acid **10** (1.0 g, 4.06 mmol) was suspended in saturated NaHCO₃ solution (35 mL) and stirred for 20

minutes to get a homogeneous brown solution. The mixture was cooled to 0 °C and NaBH₄ (0.46 g, 12.2 mmol, 3 equiv) was carefully added. The mixture was stirred at this temperature for 1 h, and then for 2 h at room temperature. Thereafter, concentrated H₂SO₄ (1-2 mL) was carefully added drop by drop to reach a pH < 1. The mixture was heated at 75 °C for 45 minutes and then extracted with diethyl ether (3 × 35 mL). The bright yellow organic layer was dried over MgSO₄, filtered and concentrated in vacuo. Flash chromatography of the residue (ethyl acetate/petroleum ether, 2:1) yielded 0.4 g (43%) of **12** as a colorless sticky solid, which crystallized after 10-15 minutes at room temperature; m.p. 139-140 °C, colorless crystals. TLC (ethyl acetate/hexane, 3:2): R_f = 0.36; ¹H NMR (CDCl₃): δ = 1.93-1.98 (m, 1H, CH₂-lactone), 2.16-2.37 (m, 3H, CH₂-lactone, Cp-CH₂), 2.51-2.55 (m, 2H, CH₂-lactone), 2.63-2.66 (m, 1H, CHR₃), 3.15-3.20 (m, 2H, 2×Cp-CHR₃), 4.14 (d, *J* = 3.2 Hz, 1H, R₂CHOH), 4.69 (d, *J* = 3.6 Hz, 1H, COOCHR₂), 5.49-5.53 (m, *J* = 9.5 Hz, 1H, alkene), 5.56 (m, 2H, Cp-alkene), 5.93 (dd, *J* = 9.5, 7.3 Hz, 1H, alkene); ¹³C NMR (CDCl₃): δ = 26.2, 28.7 (CH₂-lactone), 33.7 (Cp-CH₂), 43.7 (Cp-CHR₃), 47.0 (CHR₃), 47.2 (CR₄), 58.8 (Cp-CHR₃), 76.5 (R₂CHOH), 82.6 (COOCHR₂), 125.4 (alkene), 129.1, 134.2 (Cp-alkene), 135.3 (alkene), 172.3 (COO); IR (KBr): 3425 (br, OH), 3039 (alkene), 1722 cm⁻¹ (CO-lactone); MS (EI), *m/z* (%): 232 (5) [M]⁺, 214 (7) [M - H₂O]⁺, 204 (17), 150 (100); HRMS (EI): calcd for C₁₄H₁₆O₃ 232.10995, found 232.11167.

11-Trimethylsilyloxy-1,2,7,7a,8,10a-hexahydro-3*H*,4*aH*-7,10*b*-methanoazuleno[5,4-*b*]pyran-3-one (13). A solution of lactone **12** (1.0 g, 4.31 mmol), dissolved in absolute pyridine (8 mL) was treated with HMDS (0.9 mL, 4.31 mmol) and TMSCl (0.27 mL, 2.15 mmol) at 0 °C, resulting in a white precipitate. The ice bath was removed and the mixture stirred for 2 h at room temperature. The suspension was diluted with ethyl acetate (30 mL) and the white solid filtered off. Then toluene (30 mL) was added to the filtrate which was then concentrated in vacuo. The last step was repeated three times to remove the pyridine. The residue was purified by flash chromatography on silica gel (ethyl acetate/petroleum ether, 1:2) to yield 1.21 g (92%) of **13** as a colorless crystalline solid; m.p. 92-93 °C. TLC (ethyl acetate/hexane, 1:4): R_f = 0.43; ¹H NMR ([D₆]benzene): δ = 0.00 (s, 9H, TMS), 1.50-1.53 (m, 1H, CH₂-lactone), 1.94-2.04 (m, 2H, CH₂-lactone), 2.10-2.21 (m, 1H, Cp-CH₂), 2.31-2.36 (m, 3H, CH₂-lactone, Cp-CH₂, CHR₃), 3.05-3.07 (m, 2H, 2 Cp-CHR₃), 4.13-4.14 (m, 1H, R₂CHOTMS), 4.45-4.46 (d, *J* = 3.7 Hz, 1H, COOCHR₂), 5.41-5.42 (m, 1H, alkene), 5.48-5.52 (m, 1H, Cp-alkene), 5.54 (dd, *J* = 9.4, 3.7 Hz, 1H, Cp-alkene), 5.64 (dd, *J* = 9.4, 7.3 Hz, 1H, alkene); ¹³C NMR ([D₆]benzene): δ = -0.01 (TMS), 26.2, 28.5 (CH₂-lactone), 33.2 (Cp-CH₂), 43.7 (Cp-CHR₃), 46.9 (CHR₃), 47.4 (CR₄), 59.3 (Cp-CHR₃), 77.5 (R₂CHOTMS), 80.6 (COOCHR₂), 125.8 (alkene), 129.5, 133.1 (Cp-alkene), 133.9 (alkene), 169.7 (COO); IR (KBr): 3043 (alkene), 1729 cm⁻¹ (CO-lactone); MS (FD), *m/z* (%): 303.9 (100) [M]⁺.

rel-(8a*S*,9a*R*)-10-[(Trimethylsilyl)oxy]-1,2,7,7a,8,8a,9a,9b-octahydro-3*H*,4a*H*-7,9c-methano-oxireno[2,3]azuleno[5,4-*b*]pyran-3-one (14). To a solution of the lactone **13** (0.9 g, 2.95 mmol) in degassed chloroform (6 mL) was added *m*CPBA (0.61 g, 1.2 equiv) in chloroform (4 mL) at $-5\text{ }^{\circ}\text{C}$ within 5 minutes. The ice-bath was removed and the mixture allowed to stir for 3 h at $25\text{ }^{\circ}\text{C}$. Then cyclohexene (2 mL) was added and stirring continued for 1 h at room temperature. The mixture was extracted with ethyl acetate ($3 \times 10\text{ mL}$), washed twice with satd. NaHCO_3 solution, water and brine. Drying over MgSO_4 , filtration and concentration of the filtrate afforded a colorless oil, which was purified by flash chromatography (ethyl acetate/petroleum ether, 5:2) to give 0.58 g (62%) of **14**, as a colorless solid. This material was recrystallized from methanol yielding transparent plates, m.p. $108\text{--}109\text{ }^{\circ}\text{C}$. TLC (ethyl acetate/petroleum ether, 1:1): $R_f = 0.57$; ^1H NMR ($[\text{D}_6]$ benzene): $\delta = 0.00$ (s, 9H, TMS), 1.40-1.44 (m, 2H, CH_2 -lactone, Cp- CH_2), 1.79-1.85 (m, 1H, CH_2 -lactone), 1.92-1.94 (m, 1H, Cp- CH_2), 2.15-2.22 (m, 1H, CH_2 -lactone), 2.27-2.34 (m, 2H, CH_2 -lactone, CHR_3), 2.75 (d, $J = 9.3\text{ Hz}$, 1H, Cp- CHR_3), 2.89-2.92 (m, 1H, Cp- CHR_3), 2.99-3.09 (m, 1H, epoxide), 3.22-3.27 (m, 1H, R_2CHOTMS), 4.07-4.10 (m, 1H, COOCHR_2), 4.28-4.43 (m, 1H, epoxide), 5.51-5.60 (m, 2H, alkene); ^{13}C NMR ($[\text{D}_6]$ benzene): $\delta = -0.0$ (TMS), 26.3, 28.5 (CH_2 -lactone), 29.0 (Cp- CH_2), 46.6 (Cp- CHR_3), 47.0 (CR_4), 47.1 (CHR_3), 54.1 (epoxide), 57.8 (Cp- CHR_3), 62.4 (epoxide), 78.2 (R_2CHOTMS), 79.4 (COOCHR_2), 124.7, 134.9 (alkene), 169.6 (COO); IR (KBr): 3044, 3022 (alkene), 1730 cm^{-1} (COO); MS (FD), m/z (%): 321.1 (100) $[\text{M}]^+$.

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Figure S1. Chem3D rendering of the crystal structure of **14**

4-(3-Hydroxypropyl)-9-[(trimethylsilyl)oxy]-1,3a,4,5,8,8a-hexahydro-4,8-methanoazuleno-5-ol (15). To a cooled ($0\text{ }^{\circ}\text{C}$) suspension of LiAlH_4 (0.3 g, 7.9 mmol, 1.2 equiv) in absolute THF (18 mL) was slowly added a solution of lactone **12** (2.0 g, 6.6 mmol) in absolute THF (10 mL). After complete addition, the mixture was stirred at $60\text{ }^{\circ}\text{C}$ for 1 h, then cooled to room temperature, and stirred for further 12 h at room temperature. The reaction was carefully quenched with water (10 mL) and extracted with ethyl acetate ($4 \times 30\text{ mL}$). The combined organic phases were dried over MgSO_4 ,

filtered, and concentrated in vacuo. The resulting yellow sticky oil was purified by flash chromatography (ethyl acetate/petroleum ether, 1:1) to give 1.52 g (75%) of the diol **15** as colorless powder, m.p. 144-145 °C. TLC (ethyl acetate/hexane, 3:2): R_f = 0.4; ^1H NMR (CDCl_3): δ = 0.00 (s, 9H, TMS), 1.57-1.65 (m, 4H, CH_2CH_2), 2.04-2.07 (m, 1H, Cp- CH_2), 2.10-2.19 (m, 1H, Cp- CH_2), 2.31 (m, 1H, CHR_3), 3.02-3.04 (m, 2H, $2 \times$ Cp- CHR_3), 3.56-3.58 (m, 1H, RCH_2OH), 3.65-3.67 (m, 1H, RCH_2OH), 3.86-3.88 (m, 1H, R_2CHOTMS), 4.05 (d, J = 3.8 Hz, 1H, R_2CHOH), 5.41-5.51 (m, 3H, alkene), 5.71-5.76 (m, 1H, alkene); ^{13}C NMR (CDCl_3): δ = 0.0 (TMS), 27.0, 27.4 (CH_2), 32.7 (Cp- CH_2), 44.1 (Cp- CHR_3), 46.8 (CHR_3), 52.8 (CR_4), 56.9 (Cp- CHR_3), 63.5 (CH_2OH), 70.0 (R_2CHOH), 79.5 (R_2CHOTMS), 128.7, 131.7, 132.2, 132.2 (alkene); IR (KBr): 3453 (OH), 3041, 3026 cm^{-1} (alkene); MS (FD), m/z (%): 308.1.

2,3,7,7a,8,10a-Hexahydro-1H,4aH-7,10b-methanoazuleno[5,4-b]pyran-11-ol (16). To a solution of the diol **15** (0.4 g, 1.3 mmol) in absolute THF (5 mL) was added $\text{BF}_3 \cdot \text{OEt}_2$ (0.16 mL, 1 equiv, 48% BF_3) slowly at 0 °C. Subsequently, the mixture was stirred for 24 h at room temperature. The solution was then treated with brine (5 mL) and extracted with ethyl acetate (2×10 mL). After drying of the organic phase over MgSO_4 , filtration, and evaporation of the solvent, the resulting yellow, gummy solid was purified by flash chromatography (ethyl acetate/petroleum ether, 2:3) to yield 0.21 g (74%) of **16** as a colorless solid (plates from methanol), m.p. 131-132 °C. TLC (ethyl acetate/hexane, 2:3): R_f = 0.37; ^1H NMR (CDCl_3): δ = 1.46-1.55 (m, 2H, CH_2), 1.63-1.76 (m, 1H, CH_2), 2.07-2.17 (m, 2H, Cp- CH_2 , CH_2), 2.23-2.25 (m, 1H, Cp- CH_2), 2.50-2.53 (m, 1H, CHR_3), 2.85-2.92 (m, 1H, Cp- CHR_3), 3.04-3.06 (m, 1H, Cp- CHR_3), 3.32 (td, J = 11.5, 2.5 Hz, 1H, CH_2OCHR_2), 3.70 (d, J = 4.4 Hz, 1H, R_2CHOH), 3.87-3.90 (m, 1H, $\text{RCH}_2\text{OCHR}_2$), 4.35-4.38 (m, 1H, R_2CHOR), 5.41 (dd, J = 9.5, 3.8 Hz, 1H, alkene), 5.48-5.52 (m, 1H, Cp-alkene), 5.61-5.63 (m, 1H, Cp-alkene), 5.81 (dd, J = 9.5, 7.2 Hz, 1H, alkene); ^{13}C NMR (CDCl_3): δ = 23.4 (CH_2), 27.9 (CH_2), 32.0 (Cp- CH_2), 42.1 (Cp- CHR_3), 45.9 (CHR_3), 47.5 (CR_4), 58.0 (Cp- CHR_3), 67.2 (CH_2OCHR_2), 75.7 (R_2CHOR), 77.9 (R_2CHOH), 126.1 (alkene), 128.8, 131.4 (Cp-alkene), 131.7 (alkene); IR (KBr): 3427 (OH), 3043, 3026 cm^{-1} (alkene); MS (EI), m/z (%): 218 (18) $[\text{M}]^+$, 199 (7) $[\text{M} - \text{H}_2\text{O}]^+$, 172 (9), 148 (42), 136 (100); HRMS (EI): calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ 218.13068, found 218.13185.

Figure S2. Chem3D rendering of the crystal structure of **16**

1,2,7,7a,8,10a-Hexahydro-3*H*,4*aH*-7,10*b*-methanoazuleno[5,4-*b*]pyran-3,11-dione (17). To a solution of oxalyl chloride (0.42 mL, 4.95 mmol) in absolute dichloromethane (15 mL) was slowly added dry DMSO (0.73 mL, 10.34 mmol) at $-60\text{ }^{\circ}\text{C}$. Stirring was continued for 5 min, before lactone **12** (1.0 g, 4.31 mmol), dissolved in absolute dichloromethane (10 mL) was added carefully, so that the temperature stayed between -50 to $-60\text{ }^{\circ}\text{C}$. After 15 minutes, triethylamine (3 mL) was added dropwise. The solution was further stirred for 10 minutes at $-55\text{ }^{\circ}\text{C}$ and then allowed to warm to room temperature. Water (25 mL) was added and the mixture extracted with diethyl ether ($4 \times 25\text{ mL}$). The combined organic layers were dried over MgSO_4 , filtered, and concentrated resulting in a sticky oil. Purification of the residue by flash chromatography (ethyl acetate/petroleum ether, 1:1) gave 882 mg (89%) of **17** as a colorless solid, m.p. $129\text{--}130\text{ }^{\circ}\text{C}$. TLC(ethyl acetate/hexane, 1:2): $R_f = 0.22$; ^1H NMR (CDCl_3): $\delta = 1.84\text{--}1.87$ (m, 1H, CH_2 -lactone), 2.36-2.48 (m, 4H, Cp- CH_2 , CH_2 -lactone), 2.85-2.89 (m, 3H, Cp- CHR_3 , CHR_3 , CH_2 -lactone), 3.10-3.13 (m, 1H, Cp- CHR_3), 5.12 (d, $J = 3.7\text{ Hz}$, 1H, COOCHR_2), 5.67-5.69 (m, 1H, Cp-alkene), 5.73 (dd, $J = 9.3, 3.6\text{ Hz}$, 1H, cis-alkene), 5.87-5.88 (m, 1H, Cp-alkene), 6.01 (dd, $J = 9.3, 7.5\text{ Hz}$, 1H, cis-alkene); ^{13}C NMR (CDCl_3): $\delta = 23.2, 26.5$ (CH_2 -lactone), 33.1 (Cp- CH_2), 36.6 (Cp- CHR_3), 46.6 (CR_4), 47.4 (CHR_3), 54.0 (Cp- CHR_3), 83.4 (COOCHR_2), 125.7, 126.4, 132.6, 135.3 (alkene), 169.8 (COO), 210.0 (CO); IR (KBr): 3473 (s, enol-OH), 3073, 3057, 3044 (alkene), 1748 cm^{-1} (br, COO, CO); MS (EI), m/z (%): 230 (6) $[\text{M}]^+$, 202 (100) $[\text{M} - \text{CO}]^+$, 174 (11), 162 (22); HRMS (EI): calcd for $\text{C}_{14}\text{H}_{14}\text{O}_3$ 230.09429, found 230.09585.

9-Hydroxy-3',3*a*,4,4',7,7*a*-hexahydro-3*H*,5'*H*-spiro[4,7-ethanoindene-8,2'-furan]-5'-one (18). To a solution of the lactone **13** (0.5 g, 1.6 mmol) in absolute THF (5 mL) was slowly added $\text{BF}_3 \cdot \text{OEt}_2$ (0.25 mL, 1.97 mmol, 1.2 equiv, 48% BF_3) at room temperature. The solution was stirred for 4 h at $25\text{ }^{\circ}\text{C}$, then brine was added and the mixture extracted with ethyl acetate ($2 \times 20\text{ mL}$). The combined organic layers were dried over MgSO_4 , filtered, and concentrated in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether, 1:3) to yield 0.31 g (84%) of the spiro lactone

18 as colorless crystals (recrystallization from diethyl ether), m.p. 156 °C. TLC (ethyl acetate/hexane, 2:5): R_f = 0.22; ^1H NMR (CDCl_3): δ = 1.85-1.93 (m, 2H, CH_2 -lactone, Cp- CH_2), 2.39-2.45 (m, 2H, Cp- CH_2 , CH-lactone), 2.57-2.71 (m, 5H, Cp- CHR_3 , $2 \times \text{CHR}_3$, $2 \times \text{CH}_2$ -lactone), 2.96-2.98 (m, 1H, Cp- CHR_3), 3.66-3.68 (m, 1H, R_2CHOH), 5.30-5.34 (m, 1H, Cp-alkene), 5.56-5.60 (m, 1H, Cp-alkene), 5.99-6.10 (m, 2H, alkene); ^{13}C NMR (CDCl_3): δ = 28.6 (CH_2), 30.1 (CH_2), 31.5 (Cp- CHR_3), 38.8 (Cp- CH_2), 45.4 (CHR_3), 45.8 (CHR_3), 47.4 (Cp- CHR_3), 76.7 (R_2CHOH), 91.2 (spiro-C), 129.5 (alkene), 131.3 (Cp-alkene), 132.9 (alkene), 133.2 (Cp-alkene) 177.6 (COO); IR (KBr): 3424, 3044 (alkene), 1735 cm^{-1} (COO); MS (FD), m/z (%): 232.2 $[\text{M}]^+$; HRMS (EI): calcd for $\text{C}_{14}\text{H}_{16}\text{O}_3$ 232.10995, found 232.11132.

Figure S3. Chem3D rendering of the crystal structure of **18**

3a,4,7,7a-Tetrahydro-3'*H*-spiro[4,7-ethanoindene-8,2'-furan]-5',9(3*H*,4'*H*)-dione (19). To a solution of oxalyl chloride (0.096 mL, 1.14 mmol) in dichloromethane (3 mL) was added dropwise DMSO (0.17 mL, 2.38 mmol) at $-60\text{ }^\circ\text{C}$. After 5 minutes, a solution of the spiro lactone **17** (0.23 g, 0.99 mmol) in dichloromethane (1 mL) added dropwise, in order to maintain the temperature of the solution between -50 to $-60\text{ }^\circ\text{C}$. Stirring was continued for 20 minutes, before triethylamine (0.69 mL) was added. After further stirring at $-50\text{ }^\circ\text{C}$ for 10 minutes, the mixture was slowly warmed up to room temperature. The yellow solution was treated with water (8 mL) and extracted with diethyl ether ($2 \times 40\text{ mL}$). The organic layer was dried over MgSO_4 , filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (ethyl acetate/petroleum ether, 1:5) afforded 0.20 g (88%) of **18** as white solid, m.p. $114\text{ }^\circ\text{C}$; TLC (ethyl acetate/hexane, 2:5): R_f = 0.24; ^1H NMR (CDCl_3): δ = 2.09-2.10 (m, 2H, CH_2 -lactone, Cp- CH_2), 2.20-2.23 (m, 1H, CH_2 -lactone), 2.43-2.62 (m, 2H, Cp- CH_2 , CH_2 -lactone), 2.65-2.72 (m, 1H, CH_2 -lactone), 2.88-2.93 (m, 2H, Cp- CHR_3 , CHR_3), 3.21-3.23 (m, 2H, Cp- CHR_3 , CHR_3), 5.39-5.43 (m, 1H, Cp-alkene), 5.63-5.67 (m, 1H, Cp-alkene), 6.04-6.07 (m, 1H, alkene), 6.29-6.32 (m, 1H, alkene); ^{13}C NMR (CDCl_3): δ = 28.9, 30.4 (CH_2), 35.9 (Cp- CHR_3), 39.4 (Cp- CH_2), 45.9 (CHR_3), 47.0 (Cp- CHR_3), 53.6 (CHR_3), 82.9 (spiro-C), 125.0, 130.5, 134.0, 136.0 (alkene), 176.5 (COO), 207.5 (CO); IR (KBr): 3045 (alkene), 1778 (COO), 1732 cm^{-1} (CO); MS (EI), m/z (%): 230

(22) $[M]^+$, 202 (77) $[M - CO]^+$, 184 (12), 165 (28), 117 (100); HRMS (EI): calcd for $C_{14}H_{14}O_3$ 230.09429, found 230.09541.