CHAPTER V: *EXPERIMENTAL PROCEDURES*

- *General*

Unless noted otherwise, materials were obtained from commercially available sources and used without further purification. Tetrahydrofuran (THF) and diethyl ether (Et_20) were distilled from sodium benzophenone ketyl under a nitrogen atmosphere. Benzene, toluene, dichloromethane (CH_2Cl_2), acetonitrile (CH_3CN) and pyridine were distilled from calcium hydride under a nitrogen atmosphere. Triethylamine (Et_3N) was distilled from barium oxide under an argon atmosphere and stored over potassium hydroxide. Chloroform ($CHCl_3$), carbon tetrachloride ($CC1_4$) and deuterated NMR solvents were dried over 1/16" bead 4Å molecular sieves. Alkyllithiums were titrated periodically employing 1,3-diphenylacetone-*p*-tosyl-hydrazone as described by Lipton.[188]

All operations involving moisture sensitive materials were conducted in oven and/or flame dried glassware under an atmosphere of anhydrous nitrogen. Hygroscopic solvents and liquid reagents were transferred using dry Gastight® syringes or cannulating needles. In cases where rigorous exclusion of dissolved oxygen was required, solvents were degassed via consecutive freeze, pump, thaw cycles. Photolyses were conducted in

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[188] (a) Lipton, M. F.; Soresen C. M.; Sadler A. C.; Shapiro R. H. *J. Organomet. Chem.* **1980**, *186*, 155. (b) Suffert,J. *J. Org. Chem.* **1989**, *54*, 509.

Pyrex vessels employing a 450 W medium pressure Hanovia (ultraviolet) lamp. Ozonolyses were carried out using an OREC V10-0 ozonator.

Flash Chromatography was performed on EM Science (E. Merck) 230-400 mesh, Baker 40 μm (J. T. Baker Inc.) or SA 40 μm (Scientific Adsorbents Inc.) silica gel as described by Still.[189] Thin layer chromatography utilized EM Science (E. Merck) 250 μm 60 F_{254} Silica plates. Compounds which did not absorb ultraviolet light were visualized by dipping the TLC plate in vanillin[190] or ceric sulfate / ammonium molybdate[191] solution followed by heating.

Infrared spectra were obtained on either a Nicolet SX Nicolet Magna 550 or Midac Corporation M series FTIR using samples prepared, neat or in chloroform solution, as 0.5 mm thin films between NaCl plates. Low resolution mass spectra were acquired on a Hewlett-Packard HP-5989 MS Engine mass spectrometer equipped with a direct injection or Vacuometrics™ Inc. desorption chemical ionization probe. GC / MS analyses were performed with a Hewlett-Packard 5890 Series II gas chromatograph (Supelco SPB-5 column; 30m x 0.25mm I. D. capillary column) interfaced with an HP 5971A mass selective detector. High resolution mass spectra were performed at the University of Illinois, Urbana-Champaign, School of Chemical Sciences mass apectrometry laboratory.

Nuclear magnetic resonance (NMR) spectra were recorded on either a General Electric QEPlus 300 or Bruker AM-500 spectrometer. ^{1}H chemical shifts are given in parts per million (δ) downfield from tetramethylsilane using the residual solvent signal

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[189] Still, W. C.; Kahn, M. *J. Org. Chem.* **1978**, *43*, 2923.

[190] Vanillin (27 g), dissolved in 20 mL H_2SO_4 (conc), 380 mL EtOH and 50 mL H_2O.

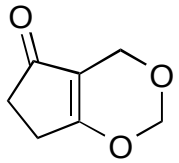
[191] $Ce(SO_4)_2$ (0.5-1.0 g) and $(NH_4)_6Mo_7O_{24}.4H_2O$ (24 g), dissolved in 500 mL of 10% aq. H_2SO_4.

($CHCl_3$ = δ 7.27, benzene = δ 7.15) as internal standard. Proton (^1H) NMR information is tabulated in the following format: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant(s) (*J*) in hertz and number of protons. The prefix *app.* is occasionally applied in cases where the true signal multiplicity is unresolved and *br* indicates that the signal in question is broadened. Proton decoupled ^{13}C NMR spectra are reported in ppm (δ) relative to $CDCl_3$ (δ 77.25) unless noted otherwise. Nuclear Overhauser Effect (NOE) difference spectroscopy measurements were made at 500 MHz in degassed $CDCl_3$ solution. Irradiation times were calculated based on measured T^1 relaxation time.

Melting points were measured on a Hoover Unimelt or Gallencamp digital apparatus and are uncorrected. Combustion Analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia 30091. When possible, compound nomenclature follows I.U.P.A.C. rules wuth the aid of the program ACD/Name[192] or else it was provided based on analogies taken from *Chemical Abstracts* entries.

[192] ACD/Name, version 2.51 copyright 1994 - 97 by Advanced Chemistry Development Inc. *www.acdlabs.com.*

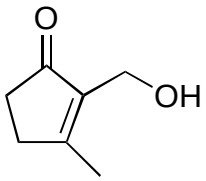
- *Specific Compounds*



Compound 7:[193] 4, 5, 6, 7-Tetrahydrocyclopenta-[a]-[1, 3]-dioxin-5-one

1,3-Cyclopentadione (5.3 g, 0.05 mol) and 1,3,5-trioxane (16.0 g, 0.18 mol) were suspended in CH_2Cl_2 (260 mL) in a dry flask, under nitrogen. The heterogeneous mixture was cooled in an ice bath. $BF_3.Et_2O$ (20 mL, 0.16 mol) was added slowly, *via* syringe, as the white solid suspension becomes a homogeneous orange solution. After addition, the reaction mixture was kept at 0 ^oC for another two hours and then allowed to warm to room temperature. The solution was kept stirring at room temperature for 30 h and then it was quenched cold (in an ice bath) by addition of NaOH (10% aq, 100 mL) and ice (50 mL) with constant stirring for 10 min. The resulting two phases were separated and the organic layer was washed with brine (2 x 50 mL). The aqueous phase was saturated with NaCl and back-extracted with EtOAc (4 x 100 mL). The organic layers were reuned, washed with brine (1 x 100 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated *in vacuo* and the orange oily residue was recrystalized from an acetone-pentane solution to yield 6.72 g (96 %) of the enone as a white solid: mp (acetone/ pentane) 73.3-73.6 ^oC; IR ($CHCl_3$, cm^{-1}) 3000, 1690, 1640, 1430, 1310, 1205, 1180, 1090, 910; ^1H NMR (500 MHz, $CDCl_3$) δ 5.21 (s, 2H); 4.44 (t, J = 2.0 Hz, 2H), 2.63 -

2.60 (m, 2H), 2.39 - 2.37 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 201.08, 181.95, 114.66, 92.68, 62.99, 32.56, 26.41; HRMS (EI) *m/z* (M^+) calcd 140.0473, obsd 140.0482.

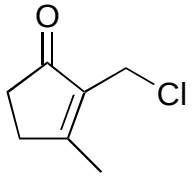


Compound 5:[193] 2-(Hydroxymethyl)-3-methyl-2-cyclopenten-1-one

Compound **7** (14 g, 0.1 mol) was dissolved in THF (250 mL) in a dry flask, under nitrogen, and the solution was cooled to -78 ^oC. A MeLi solution (250 mL, 0.225 mol, 0.9 M in diethyl ether) was added *via* syringe over 30 min. The reaction mixture turned yellow and was kept cold for another 1h. The solution was allowed to warm to 0 ^oC and ice cold HCl (4% aq., 440 mL) was added dropwise to the mixture. Hydrolysis was allowed to proceed at 0 ^oC for 1.5 h and at room temperature for another 2 h (reaction mixture turned dark orange). Reaction was quenched by addition of $NaHCO_3$ solid until pH neutral and saturated with NaCl. The layers were separated; the aqueous layer was acidified with a couple of drops of HCl (conc.) and extracted with EtOAc (3 x 100 mL). The organic layers were reuned and dried over anhydrous $MgSO_4$. Concentration and purification by flash chromatography using EtOAc as the eluent gave 9.93 g (79 %) of ketoalcohol **5** as a white needle-like solid: mp 52 - 53.5 ^oC; IR (CCl_4, cm^{-1}) 3453, 2917,

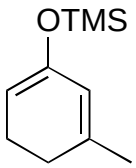
[193] Modification of procedure developed by Smith III, A. B.; Dorsey, B. D.; Ohba, M.; Lupo Jr., A. T.; Malames, M. S. *J. Org. Chem.* **1988**, *53*, 4314.

2862, 1696, 1664, 1488, 1387, 1337, 1011; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31, (*br* s, 2H), 3.07 (*br* s, 1H, exchange with D_2O), 2.56 - 2.53 (m, 2H), 2.39 - 2.36, (m 2H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 210.02, 173.29, 138.46, 54.58, 34.19, 31.79, 16.98; HRMS (EI) *m/z* (M^+) calcd 126.0681, obsd 126.0672.



Compound 18: 2-(Chloromethyl)-3-methyl-2-cyclopenten-1-one

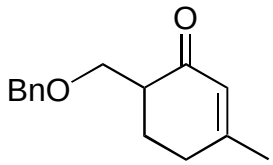
Compound **5** (4.5 g, 36 mmol) was dissolved in chloroform (45 mL) and the solution was cooled to 0 ^{o}C. Thionyl chloride (6.75 mL, 92 mmol) was added neat, dropwise, *via* syringe. The reaction mixture turned yellow. Solution was kept cold for another 20 min when there was no more starting material present in the medium. The reaction mixture was quenched by slow addition of $NaHCO_3$ (solid) and $NaHCO_3$ (sat., aq.) until pH neutral. Phases were separated; the organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash chromatography using methylene chloride as the eluent to give 5.02 g (96%) of chloride **18** as a pale yellow oil: IR ($CDCl_3$, cm^{-1}) 2964, 2917, 2858, 1698, 1650, 1438, 1385, 1346, 1263, 1178, 1078; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.19 (s, 2H), 2.62 - 2.60 (m, 2H), 2.46 - 2.43 (m, 2H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 206.51, 175.95, 136.72, 34.09, 32.77, 31.78, 17.40; HRMS (EI) *m/z* (M^+) calcd 144.0342, obsd 144.0351.



Compound 8:[194] 3-Trimethylsilyloxy-1-methyl-1, 3-cyclohexadiene

Lithium diisopropyl amide (LDA) was prepared at -78 ^{o}C by dissolving diisopropylamine (14 mL, 100 mmol) in THF (150 mL) and then adding butyllithium (10.6 mL, 106 mmol, 10 M in hexanes) slowly, to the cooled solution. 3-Methylcyclohexen-2-one (10 g, 91 mmol) was added to the cold base to afford a light yellow solution that was kept at -78 ^{o}C for 20 min. After that time, a solution of TMSCl (12.5 mL, 98 mmol) in THF (15 mL) was also added dropwise and set to react for another 20 min. The reaction mixture was then allowed to warm to room temperature and the THF was evaporated *in vacuo*. The residue was ressuspended in hexanes and washed with half saturated sodium bicarbonate (aqueous, 100 mL) and brine (2 x 200 mL), dried over anhydrous sodium sulfate and concentrated to give 16.2 g (98 %) of the enol ether **8** as a pale yellow oil, carried on with no further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.44 (t, J = 1.5Hz, 1H), 4.73 (*br* s, 1H), 2.19 - 2.15 (m, 2H), 2.05 - 1.99 (m, 2H), 1.79 (s, 3H), 0.19 (s, 9H).

[194] (a) Iwata, C.; Takemoto, Y.; Nakamura, A.; Imanish, T. *Tetrahedron Lett.*, **1985**, *26*, 3227 . (b) Rubboton, G. M.; Gruber, J. M. *J. Org. Chem.* **1978**, 43, 1599.



Compound 9: 6-(Benzyloxymethyl)-3-methyl-2-cyclohexen-1-one

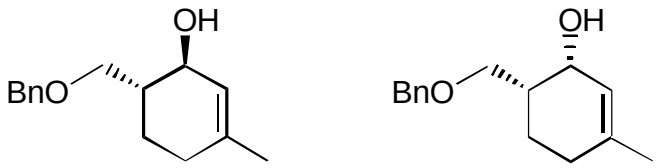
Method A (small scale): Compound **8** (510 mg, 2.8 mmol), benzyl-(chloromethyl)-ether (80%, 670 mg, 3.4 mmol) and methylene chloride (4 mL) were combined in a dry flask, under nitrogen, resulting in a yellow solution which was cooled to 0 ^{o}C. Freshly sublimed (flame heated, under 1 mm Hg) zinc bromide (68 mg, 0.3 mmol, 10 % eq.) was added to the reaction mixture in one portion. The solution turned orange-red, then brown and was kept stirring at 0 ^{o}C for 3 hours. At this point very little starting material was left but a second product started to form so the reaction was quenched, while the mixture was still cold, by the addition of $NaHCO_3$ (sat., aq., 2 mL). The layers were separated, the aqueous was extracted with more methylene chloride (2 x 5 mL) and the combined organic phase was dried over anhydrous $MgSO_4$ and concentrated. The residue was purified *via* flash chromatography using 1 % diethyl ether in methylene chloride to give 303 mg (49 %) of the enone **9**.

Method B (large scale): Zinc dust (12.3 g, 188 mmol) and cuprous chloride (2.6 g, 26 mmol) were suspended in methylene chloride (60 mL), in a dry flask, under nitrogen. The reaction mixture was heated to reflux for 30 min, then cooled to room temperature. Diiodo methane (8.3 mL, 102 mmol) was added neat and the new mixture was heated to reflux for another 1 h then cooled to 0 ^{o}C. Compound **8** (16.2 g, 89 mmol) was dissolved in CH_2Cl_2 (12 mL) and added to the reaction media, followed by slow addition of benzyl-

(chloromethyl)-ether (90%, 20 mL, 136 mmol) in methylene chloride (24 mL). The mixture was allowed to warm to room temperature over 2 h and then it was refluxed overnight. The reaction was quenched at 0 ^{o}C by addition of diethyl ether (300 mL) followed by sulfuric acid (10% aq., 300 mL, 0 ^{o}C). The phases were separated. The aqueous layer was extracted with diethyl ether (3 x 80 mL) and the combined organic layer was washed first with sodium bicarbonate (aq., sat.) until pH neutral and then with brine (2 x 100 mL). The final organic layer was filtered over a plug of silica gel and concentrated. The enone was isolated using dry chromatography[195] (solvent: hexanes to methylene chloride, 10% increments, 200 mL of each), 12 g (58%) of the enone **9** was purified as a pale yellow oil.

Compound **9**: IR (CCl_4, cm^{-1}) 3083, 3059, 3024, 2917, 2865, 1673, 1619, 1453, 1417, 1380, 1345, 1205, 1104; ^{1}H NMR (300 MHz, C_6D_6) δ 7.28 - 7.08 (m, 5H), 5.85 (s, 1H), 4.34 (s, 2H), 3.91 (dd, *J* = 9.3 Hz, 3.9 Hz, 1H), 3.66 (dd, *J* = 9.3 Hz, 7.8 Hz, 1H), 2.31 - 2.27 (m, 1H), 1.98 - 1.92 (m, 1H), 1.68 - 1.59 (m, 2H), 1.64 (s, 1H), 1.29 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 198.93, 162.16, 138.35, 128.20, 127.45, 127.39, 126.45, 73.13, 69.28, 45.90, 30.27, 25.83, 24.11; HRMS (EI) *m/z* (M^+) calcd 230.1307, obsd 230.1310.

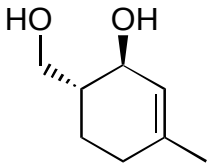
[195] Dry chromatography technique: *Aldrichimica Acta* **1985,** 18, 1.



Compounds 6a and 6b: (1R*, 6S*)-6-(Benzyloxymethyl)-3-methyl-2-cyclohex-2-ene-1-ol and (1R*, 6R*)-6-(Benzyloxymethyl)-3-methyl-2-cyclohex-2-ene-1-ol

Compound **9** (12 g, 52 mmol) was dissolved in diethyl ether (200 mL) in a dry flask, under nitrogen. The solution was cooled to -10 ^{o}C (ice, salt, EtOH). $LiAlH_4$ (0.65 g, 19.2 mmol) was added to this mixture in 3 portions of about 200 mg each, at 45 min intervals. The conversion from starting material was complete in 3 h and the reaction was quenched, cold, by slow addition of sodium sulfate (aq., sat). The reaction mixture was dried over anhydrous $MgSO_4$, filtered and concentrated. Crude ^{1}H NMR ($CDCl_3$) indicated a *trans*/*cis* ratio of 7.1: 1 by integration. Flash Chromatography in 1 % benzene and 5% diethyl ether in methylene chloride gave 9.22 g (76%) of pure *trans* alcohol **6a** and 1.1 g (9%) of the *cis* product **6b** as colorless oils. *Trans* alcohol **6a**: IR (CCl_4, cm^{-1}) 3613, 3523, 3085, 3060, 3031, 2914, 2858, 1484, 1444, 1369, 1364 1242, 1204, 1153 1089, 1075; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 - 7.23 (m, 5H), 5.38 (s, 1H), 4.56 (s, 2H), 4.14 (*br* d, *J* = 8.4 Hz, 1H), 3.60 (dd, *J* = 5.4 Hz, 3 Hz, 1H), 3.50 (dd, *J* = 5.7 Hz, 5.4 Hz, 1 H), 3.27 (*br* s, 1H, exchange with D_2O), 2.09 - 1.98 (m, 1H), 1.91 - 1.79 (m, 2H), 1.71 (s, 3H), 1.70 - 1.60 (m, 1H), 1.33 - 1.22 (m, 1H, 8 lines); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.81, 136.25, 128.37, 127.64, 127.51, 124.30, 75.27, 73.36, 71.87, 41.53, 29.36, 23.42, 23.04; HRMS (EI) *m/z* (M^+) calcd 232.1463, obsd 232.1451. *Cis* alcohol **6b**: IR ($CDCl_3$, cm^{-1}) 3611, 3478, 3102, 3066, 3033, 2917, 2863, 1668, 1602, 1497, 1453, 1423, 1369, 1365 1077, 1027; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 - 7.28 (m, 5H),

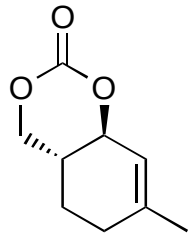
5.62 (s, 1H), 4.56 (s, 2H), 4.24 (t, *J* = 4.0 Hz, 1H), 3.64 (dd, *J* = 9.1 Hz, 8 Hz, 1H), 3.52 (dd, *J* = 9.1 Hz, 6.0 Hz, 1H), 1.98 (*br* t, *J* = 6.0 Hz, 2H), 1.91 - 1.83 (m, 2H), 1.71 (s, 3H), 1.57 - 1.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 139.66, 138.73, 128.70, 127.89, 123.38, 73.17, 72.02, 65.09, 38.75, 29.89, 23.18, 20.07; HRMS (EI) *m/z* (M^+) calcd 232.1463, obsd 232.1443.



Compound 10: 6-Hydroxymethyl-3-methyl-(1R*, 6S*)-2-cyclohexen-1-ol

A two-neck flask equipped with a dry ice condenser was flame dried and flushed with dry nitrogen. Ethylamine (4 mL, excess) was condensed onto the flask at -78 ^oC followed by addition of a solution of alcohol **6a** (200 mg, 0.86 mmol) in 4 mL of diethyl ether. Lithium wire (120 mg, 17.3 mmol), was cut in small pieces, and added to the reaction flask. The suspension of lithium pieces in ethereal ethylamine was stirred at -78 ^oC until a persistent dark blue color was observed (about 30 min). The suspension was allowed to stir at -78 ^oC for an additional 15 min before the blue color was discharged by addition of a few drops of 1-octyne. The remaining lithium pieces were removed with a spatula and the color of the resulting yellow solution was discharged by addition of methanol, dropwise. The mixture was allowed to warm to room temperature and was concentrated in a rotatory evaporator. The residue was resuspended in diethyl ether, dried over anhydrous $MgSO_4$ and filtered over a plug of silica gel. After that, the clear solution

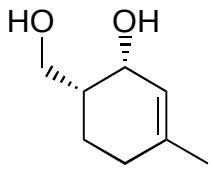
was again concentrated followed by purification of the residue by flash chromatography using 1:1 solution of diethyl ether and methylene chloride as the eluent. Obtained 119 mg (97%) of *trans* diol **10** as a white solid: mp 68.5 - 69 ^{o}C; IR ($CDCl_3$, cm^{-1}) 3614, 3500, 2928, 2886, 2837, 1678, 1444, 1374, 1262; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.32 (s, 1H), 4.12 (d, *J* = 7.5 Hz, 1H), 3.71 (dd, *J* = 10.5 Hz, 4.3 Hz, 1H), 3.63 (dd, *J* = 10.5 Hz, 8.5 Hz, 1H), 3.51 (*br* s, 1.5H, exchange with D_2O), 2.03 - 2.00 (m, 1H), 1.87 (dd, *J* = 12 Hz, 5.5 Hz, 1H), 1.68 - 1.59 (m, 2H), 1.66 (s, 3H), 1.30 - 1.21 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 136.75, 124.62, 72.36, 67.50, 43.29, 29.54, 23.39, 22.98.



Compound 11: 7-Methyl-(4aR*, 8aR*)-5H, 6H-benzo[a][1, 3]dioxin-2-one

A solution of compound **10** (50 mg, 0.352 mmol), pyridine (285 μL, 3.52 mmol) and DMAP (4 mg, 0.32 mmol) in 2.0 mL of THF was stirred at 0 ^{o}C in a dry flask, under nitrogen. A solution of triphosgene (52.0 mg, 0.176 mmol) in 0.8 mL of diethyl ether was added to the reaction mixture, *via* syringe pump, over 20 min. A white precipitate formed as addition of the reagent progressed. After addition was complete, the reaction mixture was kept at 0 ^{o}C for 1 h and at room temperature for 6 h. After this, the solvent was evaporated and the residue was suspended in 10 mL of water. The aqueous layer was extracted with methylene chloride (3 x 15 mL). The combined organic layers were dried

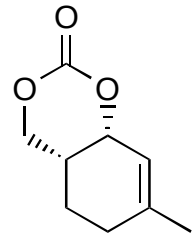
over anhydrous $MgSO_4$ and concentrated. Purification of the residue by flash chromatography was done using 10% diethyl ether in methylene chloride as the eluent and it afforded 56.2 mg (93%) of the *trans* cyclic carbonate **11** as a clear oil: IR ($CDCl_3$, cm^{-1}) 2976, 2928, 2869, 1749, 1667, 1480, 1406, 1353, 1308, 1237, 1203, 1154 1086; ^1H NMR (500 MHz, $CDCl_3$) δ 5.49 (s, 1H), 4.67 (d, *J* = 9.5 Hz, 1H), 4.43 (dd, *J* = 10.5 Hz, 5 Hz, 1H), 4.12 (dd, *J* = 12 Hz, 10.5 Hz, 1H), 2.23 - 2.16 (m, 1H), 2.10 - 2.01 (m, 2H), 1.89 - 1.84 (m, 1H), 1.74 (s, 3H), 1.43 - 1.34 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 149.26, 139.04, 119.09, 78.41, 73.06, 34.28, 29.29, 22.83, 21.37; HRMS (EI) *m/z* (M^+) calcd 168.0786, obsd 168.0795.



Compound 12: 6-Hydroxymethyl-3-methyl-(1R*, 6R*)-2-cyclohexen-1-ol

A two-neck flask equipped with a dry ice condenser was flame dried and flushed with dry nitrogen. Ethylamine (4 mL, excess) was condensed onto the flask at -78 °C. A solution of alcohol **6b** (100 mg, 0.43 mmol) in 4 mL of diethyl ether was added to the reaction media. Lithium wire (120 mg, 17.3 mmol), was cut in small pieces, and added to the flask. The suspension of lithium pieces in ethereal ethylamine was stirred at -78 °C until the presence of a persistent dark blue color was observed (about 30 min). The suspension was allowed to stir at -78 °C for an additional 15 min before the blue color was discharged by addition of a few drops of 1-octyne. The remaining lithium pieces were

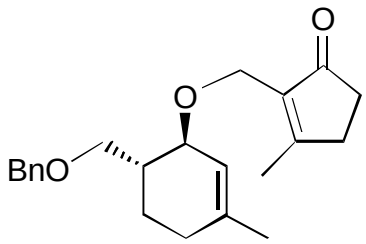
removed with a spatula and the color of the resulting yellow solution was discharged by addition of methanol, dropwise. The mixture was allowed to warm to room temperature and was concentrated in a rotatory evaporator. The residue was resuspended in ether, dried over anhydrous $MgSO_4$ and filtered over a plug of silica gel. After that the clear solution was concentrated followed by purification of the residue by flash chromatography, using 1:1 solution of diethyl ether and methylene chloride as the eluent. Obtained 56 mg (90%) of the *cis* diol **12** as a white solid: mp 63 – 65 ^oC; IR ($CDCl_3$, cm^{-1}) 3609, 3509, 2933, 2885, 2833, 1670, 1601, 1448, 1430, 1382; ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (s, 1H), 4.28 (s, 1H), 3.86 - 3.73 (m, 2H), 2.04 - 2.02 (m, 1H), 1.86 (*br* s, 2H, exchange with D_2O), 1.73 (s, 3H), 1.76 - 1.54 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 140.57, 123.18, 66.72, 65.24, 40.11, 30.02, 23.19, 19.7.



Compound 13: 7-Methyl-(4aR*, 8aS*)-5H, 6H-benzo[a][1, 3]dioxin-2-one

A solution of compound **12** (55 mg, 0.387 mmol) and pyridine (285 μL, 3.52 mmol) in 2.0 mL of THF was placed in a dry flask, under nitrogen, and was stirred at 0 ^oC. A solution of triphosgene (52.0 mg, 0.176 mmol) in 1 mL of THF was added to the reaction mixture, *via* syringe pump, over a period of 160 min. Observed formation of a white precipitate as the addition progressed. After addition was complete, the reaction

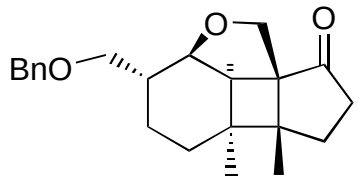
mixture was kept at 0 ^{o}C for 1 h and at room temperature for another 3 h. Reaction was quenched while mixture was still cold by addition of 5 mL of methanol. The solvent was evaporated and the residue was purified immediately by flash chromatography using 10% diethyl ether in methylene chloride as the eluent. Isolated 58 mg (89%) of the *cis* cyclic carbonate **13** as a clear colorless oil: IR ($CDCl_3$, cm^{-1}) 2937, 2918, 1743, 1672, 1476, 1405, 1386, 1216, 1184, 1140, 1118; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.60 (d, *J* = 2.5 Hz, 1H), 4.93 (dd, *J* = 4.3 Hz, 2.5 Hz, 1H), 4.47 (dd, *J* = 11 Hz, 3.5 Hz, 1H), 4.23 (dd, *J* = 11 Hz, 3.5 Hz, 1H), 2.15 - 2.08 (m, 3H), 1.86 - 1.72 (m, 2H), 1.77 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 149.16, 142.73, 118.44, 75.65, 69.99, 29.52, 28.51, 23.03, 20.20; HRMS (EI) *m/z* (M^{+}) calcd 168.0786, obsd 168.0809.



Compound 4: 2-(6-Benzyloxymethyl-3-methyl-(1R*, 6S*)-2-cyclohexenyloxymethyl)-3-methyl-2-cyclopenten-1-one

Reaction was set up in a flame-dried flask, under nitrogen atmosphere, containing about 2 g of activated molecular sieves 4Å. Alcohol **6a** (300 mg, 1.28 mmol) was dissolved in methylene chloride (3.0 mL), along with 2,6-di-tert-butylpyridine (850 μL, 3.84 mmol) and the clear solution was stirred for 30 min. Silver trifluoromethanesulfonate (1.0 g, 3.85 mmol) was added and the reaction flask was protected from light. Chloride **18** (185 mg, 1.28 mmol) was dissolved in 500 μL of methylene chloride and added to the

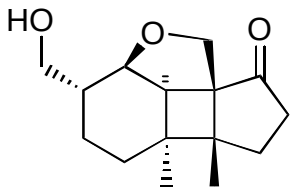
reaction mixture, *via* syringe pump, over a period of eight hours. The reaction was conducted at room temperature, protected from light, over 12 h. The reaction was quenched by addition of brine (25 mL), ammonium chloride (sat., aq., 7 mL) and stirred for 1 h. The reaction mixture was filtered over celite to give a dark yellow organic phase accompanied by a clear aqueous phase. The layers were separated and the aqueous was back-extracted with CH_2Cl_2 (2 x 10 mL) and EtOAc (2 x 5 mL). Organic phases were reuned, dried over anhydrous $MgSO_4$ and concentrated. (Brown residue). Flash Chromatography with 3% diethyl ether in methylene chloride gave 247 mg (57%) of the ether **4** as a clear oil: IR ($CDCl_3$, cm^{-1}) 3089, 3063, 3025, 2922, 2860, 1695, 1649, 1496, 1453, 1430, 1373, 1041; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 - 7.26 (m, 5H), 5.55 (s, 1H), 4.53 (s, 2H), 4.22 (d, *J* = 10.7 Hz, 1H), 4.10 (d, *J* = 10.7 Hz, 1H), 3.8 (*br* d, *J* = 5.7 Hz, 1H), 3.56 (dd, *J* = 8.9 Hz, 4.3 Hz, 1H), 3.44 (dd, *J* = 8.9 Hz, 6.6 Hz, 1H), 2.51 - 2.49 (m, 2H), 2.39 - 2.36 (m, 2H), 2.13 (s, 3H), 1.98 -1.90 (m, 4H), 1.69 (s, 3H), 1.62 - 1.51 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 208.16, 175.74, 138.76, 138.32, 137.34, 128.26, 127.50, 127.46, 121.05, 75.20, 73.02, 71.30, 58.59, 38.75, 34.37, 31.87, 28.91, 23.65, 23.45, 17.58; HRMS (EI) *m/z* (M^+) calcd 340.2038, obsd 340.2051; UV π-π* 210 – 250 nm, η-π* 310 – 330 nm. Some of starting material **6a** was also recovered (30%).



Compound 17: 3-[(Benzyloxy)-methyl]-5a, 5b-dimethyl-(2aR*, 3S*, 5aR*, 5bS*, 8aR*, 8bS*)-perhydro-2-xacyclopenta[4, 1]cyclobuta[c, d]-inden-8-one

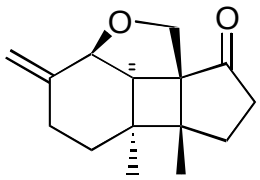
A solution prepared by dissolving compound **4** (1.19 g, 3.5 mmol) in 400 mL of benzene (photrex), was deoxygenated by flushing argon through the solution for 1 h. Photoaddition of this solution was conducted at room temperature, for 2 h, by irradiation with a 450 Watt, Hanovia, medium pressure mercury arc lamp until 50% conversion of the substrate. Solvent was evaporated under reduced pressure. Flash chromatography of the residue was conducted in 5% diethyl ether in methylene chloride and gave the photoadduct product, which was reserved, along with 2.18 g of unreacted starting material that was resubmited to the reaction conditions. The process was repeated 3 times. After 3 cycles, 928 mg (78%) of the photoadduct **17** was obtained as a clear oil: IR ($CDCl_3$, cm^{-1}) 3103, 3077, 3039, 2961, 2928, 2865, 1721, 1529, 1454, 1368, 1265 1104, 1059; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 - 7.16 (m, 5H), 4.38 (s, 2H), 3.76 (d, *J* = 9.9 Hz, 1H), 3.69 (d, *J* = 6.0 Hz, 1H), 3.64 (d, *J* = 9.9 Hz, 1H), 3.25 (dd, *J* = 9.0 Hz, 5.6 Hz, 1H), 3.18 (dd, *J* = 9.0 Hz, 6.3 Hz, 1H), 2.67 - 2.53 (m, 1H), 2.34 - 2.17 (m, 2H), 2.14 (d, *J* = 6Hz, 1H), 1.98 (td, *J* = 13 Hz, 3.1 Hz, 1H), 1.71 - 1.62 (m, 1H), 1.48 - 1.41 (m, 1H), 1.16 - 0.81 (m, 3H), 1.11 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 218.66, 138.68, 128.62, 127.79, 78.63, 73.33, 73.00, 66.29, 61.07, 51.54, 46.05,

39.05, 36.40, 36.17, 31.31, 27.29, 23.81, 20.91, 19.43; HRMS (EI) *m/z* (M^+) calcd 340.2038, obsd 340.2002.



Compound 39: 3-Hydroxymethyl-5a, 5b-dimethyl-(2aR*, 3S*, 5aR*, 5bS*, 8aR*, 8bS*)-perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]-inden-8-one

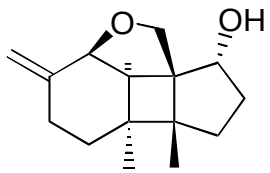
Compound **17** (827 mg, 2.43 mmol) was dissolved in absolute ethanol (70 mL), in a dry Parr shaker flask, under nitrogen. The catalyst, activated 10% palladium on carbon (50 mg, 6% w/w), was added to the solution. The suspension was then stirred at room temperature in a Parr Shaker Hydrogenator apparatus, under 40 psi of hydrogen, for 6 h, until there was no more starting material according to TLC analysis. The reaction mixture was filtered through a 1g SiO_2 plug. The filtrate was dried over anhydrous $MgSO_4$ and concentrated to give 600 mg (98 %) of alcohol **39** as a colorless oil: IR (CCl_4, cm^{-1}) 3640, 2969, 2928, 2865, 1729, 1462, 1454, 1405, 1216, 1132; ^1H NMR (300 MHz, $CDCl_3$) δ 3.76 (d, *J* = 9.9 Hz, 1H), 3.71 (d, *J* = 5.8 Hz, 1H), 3.63 (d, *J* = 9.9 Hz, 1H), 3.44 (dd, *J* = 10.5 Hz, 6.0 Hz, 1H), 3.32 (dd, *J* = 10.5 Hz, 6.9 Hz, 1H), 2.69 - 2.55 (m, 1H), 2.35 - 2.25 (m, 2H), 2.17 (d, *J* = 5.8 Hz, 1H), 2.12 - 1.95 (m, 2H), 1.72 - 1.62 (m, 1H), 1.51 - 1.39 (m, 1H), 1.12 (s, 3H), 1.06 (s, 3H), 1.14 - 0.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 218.31, 77.84, 65.80, 65.09, 60.64, 50.93, 45.78, 38.61, 38.41, 35.91, 30.90, 26.84, 23.34, 20.22, 19.01; HRMS (EI) *m/z* (M^+) calcd 250.1569, obsd 250.1551.



Compound 3: 5a, 5b-Dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 8aR*, 8bS*) perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-8-one

Alcohol **39** (240 mg, 0.96 mmol) and ortho-nitrophenylselenium cyanide (97% pure, 400 mg, 1.7 mmol) were dissolved in THF (6 mL) in a dry flask, under nitrogen. The dark yellow solution was cooled to 0^{o} C and then tri-*n*-butylphosphine (340 μL, 1.36 mmol) was added *via* syringe. The reaction mixture turned to a darker color while it was allowed to stir at 0^{o} C for 2 h and at room temperature for another 8 h. At that point all starting material had been consumed so the THF was evaporated in a rotatory evaporator. The residue was diluted with CH_2Cl_2 (100 mL) and transferred to a 3-neck flask. Diisopropyl amine (3 mL, 21 mmol) was added to the reaction mixture and the resulting solution was cooled to -78^{o} C and submitted to ozonolysis until a pale green color persisted. A stream of nitrogen was bubbled through this solution at -78^{o} C for 2 h to remove excess ozone, and another 5 mL of diisopropyl amine was added before it was allowed to warm to room temperature. The mixture was stirred at room temperature for 10 h. The solvent was evaporated and the residue was resuspended in diethyl ether (50 mL), washed with KOH (2M, 3 x 10 mL) and brine (2 x 10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated. Purification of the residue by flash chromatography, using 5% Et_2O in CH_2Cl_2 as the eluent afforded 167 mg (75 %) of keto-

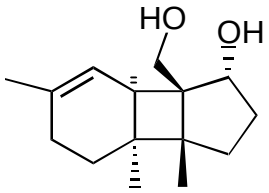
olefin **3** as a colorless oil: IR ($CDCl_3$, cm^{-1}) 2967, 2932, 2869, 1722, 1515, 1455, 1451, 1373, 1263, 1143, 1051, 1027; ^1H NMR (300 MHz, $CDCl_3$) δ 5.11 (*br* s, 1H), 5.06 (*br* s, 1H), 4.14 (d, *J* = 5.8 Hz, 1H), 3.95 (d, *J* = 10.2 Hz, 1H), 3.88 (d, *J* = 10.2 Hz, 1H), 2.76 - 2.64 (m, 1H), 2.55 - 2.27 (m, 3H), 2.41 (d, *J* = 5.8 Hz, 1H), 2.19 - 2.08 (m, 1H), 1.66 - 1.54 (m, 1H), 1.28 - 1.05 (m, 2H), 1.13 (s, 3H), 1.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 217.60, 142.13, 115.60, 79.71, 67.00, 61.39, 53.63, 46.06, 38.43, 35.77, 30.53, 28.05, 25.38, 22.79, 18.71; HRMS (EI) *m/z* (M^+) calcd 232.1463, obsd 232.1470.



Compound 91: 5a, 5b-Dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 8S*, 8aR*, 8bS*) perhydro-2-oxacyclopenta [4, 1] cyclobuta [c, d] inden-8-ol

A solution of ketone **3** (142 mg, 0.61 mmol) in 15 mL of diethyl ether was stirred at 0° C as $LiAlH_4$ (22 mg, 0.66 mmol) was added in small portions. The reaction mixture was kept at 0° C for 20 min. The suspension was diluted with 10 mL of diethyl ether, and the reaction was quenched at 0° C by dropwise addition of Na_2SO_4 (aq., sat.) until there was no more evolution of H_2. The suspension was filtered through a mixture of celite and anhydrous $MgSO_4$. Concentration of the filtrate and purification by flash chromatography using 10 % diethyl ether in methylene chloride as the eluent gave 127 mg (89 %) of alcohol **91** as a white solid: mp 115 - 116° C; IR ($CDCl_3$, cm^{-1}) 3615, 3443, 2956, 2928, 2867, 1645, 1602, 1450, 1374, 1327, 1301, 1282, 1244, 1208; ^1H NMR (300 MHz, $CDCl_3$) δ 5.09 (*br* s, 1H), 5.05 (*br* s, 1H), 4.02 (d, *J* = 5.1 Hz, 1H), 3.95 (d, *J* = 9.8 Hz,

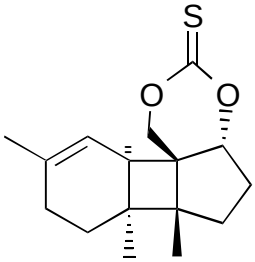
1H), 3.88 (dd, *J* = 10.2 Hz, 6.1 Hz, 1H), 3.57 (d, *J* = 9.8 Hz, 1H), 2.46 - 2.39 (m, 1H), 2.29 (td, *J* = 9.8 Hz, 3.5 Hz, 1H), 2.21 - 2.00 (m, 3H), 1.80 - 1.62 (m, 2H), 1.31 - 1.19 (m, 1H), 1.08 - 0.93 (m, 2H), 0.99 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 143.17, 115.45, 80.38, 72.81, 68.05, 60.39, 46.81, 44.25, 34.89, 34.50, 32.81, 27.22, 25.38, 19.90, 18.67; HRMS (EI) *m/z* (M^+) calcd 234.1619, obsd 234.1615.



Compound 92: 7b-(Hydroxymethyl)-3a, 3b, 6-trimethyl-(1R*, 3aR*, 3bS*, 7aR*, 7bS*)-2, 3, 3a, 3b, 4, 5, 7a, 7b-octahydro-1*H*-cyclopenta[3, 4] cyclobuta[a]benzen-1-ol

A solution of alcohol **91** (29 mg, 0.12 mmol) in 3 mL of diethyl ether was added to a 2-neck flask containing 3 mL of ethylamine, at -78^o C, and equipped with a dry ice condenser. The resulting clear solution was kept at -78^o C as lithium wire (20 mg, 2.88 mmol) was added. The reaction mixture was vigorously stirred for about 1 h until a stable dark blue color was observed and another 20 min after that. Reaction was then quenched, still cold, by addition of solid NH_4Cl until the blue color disappeared. The excess lithium pieces were removed with the aid of a spatula and a few drops of MeOH were added. Anhydrous $MgSO_4$ was added to the resulting suspension and it was allowed to warm to room temperature. The ethylamine was evaporated and the residue was resuspended in EtOAc, filtered and concentrated in a rotatory evaporator. Purification of the residue by flash chromatography using EtOAc as the eluent gave 26 mg (91%) of diol **92** as a white

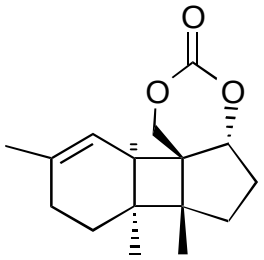
solid: mp 104.2 - 105° C; IR ($CDCl_3$, cm^{-1}) 3568, 3434, 2952, 2917, 2871, 1747, 1596, 1467, 1445, 1371, 1295, 1211, 1077, 983; ^1H NMR (300 MHz, $CDCl_3$) δ 5.41 (*br* s, 1H), 4.23 (dd, *J* = 10 Hz, 6.4 Hz, 1H), 4.14 (d, *J* = 10.3 Hz, 1H), 3.73 (d, *J* = 10.3 Hz, 1H), 2.57 (*br* s, 1H), 2.42 (*br* s, 1H), 2.05 - 1.61 (m, 6H), 1.73 (s, 3H), 1.36 - 1.25 (m, 3H), 0.90 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 136.82, 120.59, 78.96, 66.72, 52.90, 46.83, 39.40, 35.75, 33.43, 31.56, 30.93, 26.27, 24.13, 19.38, 18.22; HRMS (EI) *m/z* (M^+) calcd 236.1776, obsd 236.1782.



Compound 94: 6a, 6b, 9-Trimethyl-(4aR*, 6aR*, 6bS*, 10aR*, 10bS*)-4a, 5, 6, 6a, 6b, 7, 8, 10a-octahydrobenzo[3', 4']cyclobuta[2, 3]cyclopenta[d][1, 3]dioxin-3-thione

Diol **92** (20 mg, 0.084 mmol) and thionocarbonyl diimidazole (23 mg, 0.13 mmol) were dissolved in 2.5 mL of toluene in a dry flask, under nitrogen. The reaction mixture was heated to reflux for 10 h. Analysis by TLC showed that there was still some starting material present so an additional 11mg (0.065 mmol) of thionocarbonyl diimidazole was added and the reaction mixture was refluxed for another 8 h. At this point there was no more starting material left. The solvent was evaporated and the residue was immediately purified by flash chromatography using 10% EtOAc in hexanes as the eluent. Obtained 19.8 mg (85%) of the cyclic thionocarbonate **94** as a light yellow oil: IR (CCl_4, cm^{-1})

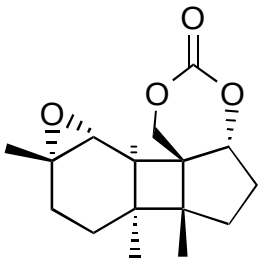
2973, 2957, 2914, 1549, 1253, 1216, 1067, 1005, 979; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.17 (*br* s, 1H), 4.82 (d, *J* = 9.9 Hz, 1H), 4.52, (d, *J* = 9.9 Hz, 1H), 4.35 (dd, *J* = 10.2 Hz, 6.9 Hz, 1H), 2.39 (*br* s, 1H), 2.33 - 2.14 (m, 3H), 1.96 - 1.83 (m, 2H), 1.72 (s, 3H), 1.58 - 1.38 (m, 3H), 0.93 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 191.26, 139.56, 117.69, 81.95, 79.43, 47.90, 47.19, 40.21, 36.94, 33.16, 30.92, 27.81, 26.00, 23.99, 19.17, 17.53; HRMS (EI) *m/z* (M^+) calcd 278.1341, obsd 278.1334.



Compound 95: 6a, 6b, 9-Trimethyl-(4aR*, 6aR*, 6bS*, 10aR*, 10bS*)-4a, 5, 6, 6a, 6b, 7, 8, 10a-octahydrobenzo[3', 4']-cyclobuta[2, 3]cyclopenta[d][1, 3]-dioxin-3-one

Compound **92** (26 mg, 0.11 mmol), and pyridine (50 μL, 0.61 mmol) were dissolved in methylene chloride (1.0 mL), in a dry flask, under nitrogen atmosphere. The transparent solution was cooled to 0^{o} C. A solution of triphosgene (12 mg, 0.04 mmol) in 1.6 mL of methylene chloride was added to the cold reaction mixture, *via* syringe, over a 20 min period. After addition, the reaction was allowed to proceed at 0^{o} C for another 150 min. Once there was no more starting material left, according to TLC analysis, the reaction was quenched by addition of brine (5 mL). The organic mixture was extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and concentrated. Purification by flash chromatography using 30% EtOAc in CH_2Cl_2 as the eluent gave 26 mg (90 %) of

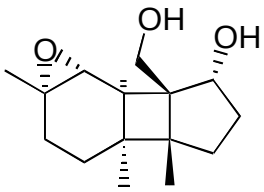
carbonate **95** as a clear oil: IR ($CDCl_3$, cm^{-1}) 2956, 2931, 2870, 1744, 1606, 1456, 1447, 1396, 1372, 1202, 1167, 1171; ^1H NMR (500 MHz, $CDCl_3$) δ 5.19 (*br* s, 1H), 4.67 (d, *J* = 9.5 Hz, 1H), 4.43 (dd, *J* = 10.5 Hz, 7.0 Hz, 1H), 4.40 (d, *J* = 9.5 Hz, 1H), 2.43 (*br* s, 1H), 2.28 (dd, *J* = 14 Hz, 7 Hz, 1H), 2.18 - 2.10 (m, 2H), 1.97 (*br* t, *J* = 14 Hz, 1H), 1.86 (dt, *J* = 16.5 Hz, 3.5 Hz, 1H), 1.73 (*br* s, 3H), 1.58 - 1.46 (m, 2H), 1.41 (dt, *J* = 12.5 Hz, 3.5 Hz, 1H), 0.97 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 149.95, 139.24, 118.18, 81.76, 75.24, 47.09, 40.00, 36.87, 33.62, 30.91, 29.66, 27.79, 26.01, 23.94, 19.20, 17.61; HRMS (EI) *m/z* (M^+) calcd 262.1569, obsd 262.1558.

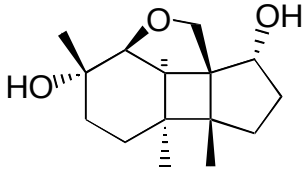


Compound 96: 1a, 3a, 3b-Trimethyl-(1aR*, 3aS*, 3bR*, 5aR*, 9aS*, 9bS*, 9cR*)-perhydrooxireno[2''', 3''':3'', 4'']benzo[3', 4']cyclobuta[2, 3]cyclopenta[d][1, 3] dioxin-7-one

Compound **95** (20 mg, 0.076 mmol) was dissolved in CH_2Cl_2 (2 mL), in a dry flask, under nitrogen, and the clear solution was cooled to 0^o C. *m*-CPBA (75% pure, 24 mg, 0.1 mmol) was dissolved in CH_2Cl_2 and this oxidizing solution was added dropwise to the reaction mixture. After addition was complete, the reaction mixture was stirred at 0^o C for 30 min (until no more starting material was detected by TLC analysis). The reaction was quenched by addition of 4 mL of $NaHCO_3$ (aqueous, sat.). The organic was extracted with diethyl ether, dried over anhydrous Na_2SO_4 and concentrated. Purification

of the residue with flash chromatography, using 10 % EtOAc in hexanes as the eluent yielded 19 mg (90 %) of the pure epoxy-carbonate **96** as white needle-like crystals: mp 108 – 110° C; IR ($CDCl_3$, cm^{-1}) 2974, 2927, 2829, 2252, 1751, 1602, 1474, 1441, 1386, 1369, 1193, 1170, 1111; ^{1}H NMR (500 MHz, C_6D_6) δ 4.01 (d, *J* = 10 Hz, 1H), 3.64 (d, *J* = 10. Hz, 1H), 3.33 (dd, *J* = 10 Hz, 7 Hz, 1H), 2.83 (d, *J* = 3 Hz, 1H), 2.25 (d, *J* = 3 Hz, 1H), 1.56 - 1.45 (m, 3 H), 1.26 (dd, *J* = 10 Hz, 4.5 Hz, 1H), 1.23 (t, *J* = 3.5 Hz, 1H), 1.19 (dd, *J* = 10 Hz, 4.5 Hz, 1H), 1.03 (s, 3H), 0.97 - 0.92 (m, 1 H), 0.67 - 0.58 (m, 1H), 0.57 (s, 3H), 0.30 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) ppm 148.84, 81.37, 73.87, 57.23, 56.60, 45.55, 44.13, 38.77, 35.01, 33.67, 28.78, 27.36, 27.29, 22.59, 22.33, 16.63; HRMS (EI) *m/z* (M^+) calcd 278.1518, obsd 278.1509.





Compounds 97 and 98: 6a-Hydroxymethyl-1a, 3a, 3b-trimethyl-(1aR*, 3aR*, 3bS*, 6S*, 6aR*, 6bS*, 6cS*)perhydrocyclopenta[3 , 4]cyclobuta[3, 4]benzo[b]oxiren-6-ol and 3, 5a, 5b-Trimethyl-(2aR*, 3R*, 5aR*, 5bS*, 8S*, 8aR*, 8bS*)-perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]indene-3, 8-diol

Method A: Compound **96** (40 mg, 0.146 mmol) was dissolved in THF (800 μL) and the solution was cooled to 0° C. A solution of LiOH (0.11M, aqueous, 800 μL) was added and the mixture was stirred at 4° C for 6h. The THF was removed in the rotatory evaporator and the residue was ressuspended in diethyl ether. The organic layer was washed with NH_4Cl (aqueous, sat.), until pH neutral, and then it was washed once with

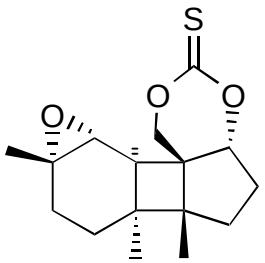
brine. The combined aqueous phase was back-extracted with ethyl acetate. The organic layers were reuned, dried over anhydrous Na_2SO_4 and concentrated. Purification *via* flash chromatography using 60 % EtOAc in CH_2Cl_2 as the eluent gave 6 mg of the diol epoxide **97** (0.024 mmol, 16 % yield) as a clear oil as well as 29 mg of the cyclic ether **98** (0.115 mmol, 79 % yield) as a white solid.

Method B: Sodium bicarbonate (20 mg, 0.24 mmol) was suspended in a solution of compound **92** (26 mg, 0.11 mmol) in chloroform (2 mL). The heterogeneous mixture was cooled to 0^o C. A solution of *m*-CPBA (75 % pure, 28 mg, 0.12 mmol) dissolved in 2 mL of chloroform was added dropwise to the reaction mixture. The mixture was kept at 0^o C for 20 min, and then the reaction was quenched by addition of 3 mL of Na_2CO_3 (sat., aqueous). The phases were separated and the aqueous was extracted with diethyl ether (3 x 5 mL). The combined organic layers were washed once with $NaHSO_3$ (aqueous, 10 %) and once with $NaHCO_3$ (aqueous, sat.) and then dried over anhydrous Na_2SO_4. Purification *via* flash chromatography using 40 % diethyl ether in methylene chloride as the eluent gave 19.2 mg (69 %) of epoxide **97** as a clear oil and 4.7 mg (17 %) of the cyclic ether **98** as a white solid.

Compound **97**: IR (CCl_4, cm^{-1}) 3560, 2958, 2935, 2880, 1468, 1452, 1374, 1370, 1296, 1073, 985; ^{1}H NMR (500 MHz, C_6D_6) δ 4.63 (d, *J* = 11 Hz, 1H), 4.08 (dd, *J* = 10 Hz, 6.5 Hz, 1 H), 3.62 (d, *J* = 11 Hz, 1H), 2.82 (*br* s, 1H), 2.79 (d, *J* = 4.5 Hz, 1H), 2.23 (d, *J* = 4.5 Hz, 1H), 2.19 (*br* s, 1H), 2.01 - 1.95 (m, 2H), 1.81 - 1.72 (m, 1H), 1.67 (dd, *J* = 13.5 Hz, 8 Hz, 1H), 1.57 (dt, *J* = 14.5 Hz, 3.5 Hz, 1H), 1.44 (td, *J* = 14.5 Hz, 3.5 Hz, 1H), 1.10 (s, 3H), 1.01 (td, *J* = 13.5 Hz, 6.5 Hz, 1H), 0.73 - 0.68 (m, 1H), 0.66 (s, 3H), 0.62 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) ppm 80.70, 67.02, 58.97, 56.00, 54.86, 47.48,

36.16, 34.46, 33.18, 31.48, 26.57, 26.20, 22.04, 18.78, 17.07; HRMS (EI) *m/z* (M^+) calcd 252.1726, obsd 252.1742.

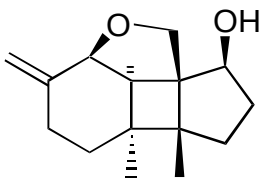
Compound **98**: mp 129.6 - 131.8° C; IR (CCl_4, cm^{-1}) 3626, 2950, 2908, 2856, 1733, 1457, 1371, 1058, 914; ^1H NMR (500 MHz, $CDCl_3$) δ 3.92 (d, *J* = 9.5 Hz, 1H), 3.84 (dd, *J* = 10 Hz, 7 Hz, 1H), 3.53 (d, *J* = 9.5 Hz, 1H), 3.51 (d, *J* = 6.5 Hz, 1H), 2.66 (*br* s, 2H), 2.41 (d, *J* = 6.5 Hz, 1H), 2.11 (m, 1H, 5 lines), 1.94 (dd, *J* = 14 Hz, 8 Hz, 1H), 1.88 - 1.80 (m, 2H), 1.78 - 1.73 (m, 1H), 1.42 - 1.34 (m, 1H), 1.34 (s, 3H), 1.21 - 1.08 (m, 2 H), 1.06 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 84.55, 73.16, 70.14, 68.80, 58.92, 46.21, 42.35, 34.85, 32.93, 32.62, 29.36, 28.12, 26.77, 22.41, 18.26; HRMS (EI) *m/z* (M^+) calcd 252.1726, obsd 252.1735.



Compound 99: 1a, 3a, 3b-Trimethyl-(1aR*, 3aS*, 3bR*, 5aR*, 9aS*, 9bS*, 9cR*)-perhydrooxireno [2''', 3''':3'', 4''] benzo [3', 4'] cyclobuta [2, 3] cyclopenta[d][1, 3] dioxin-7-thione

Compound **97** (24 mg, 0.095 mmol) and pyridine (80 μL, 0.99 mmol) were dissolved in toluene (10 mL). The solution was cooled to 0° C and to it, a solution of thiophosgene (95 % pure, 16 μL, 0.2 mmol) in 2 mL of toluene was added over a period of 1 h. After addition, the reaction mixture was stirred at 0° C for another 1 h and then was quenched by addition of 20 mL of brine. The aqueous phase was extracted with

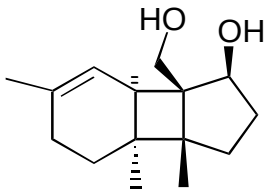
EtOAc and the organic was dried over anhydrous Na_2SO_4 and concentrated. Purification of the residue by flash chromatography using 10 % diethyl ether in CH_2Cl_2 as the eluent gave 12.8 mg (46 %) of thionocarbonate **99** as a light yellow oil: IR ($CDCl_3$, cm^{-1}) 2969, 2925, 2867, 2252, 1721, 1601, 1467, 1447, 1389, 1273; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.67 (d, *J* = 9.5 Hz, 1H), 4.51 (d, *J* = 9.5 Hz, 1H), 4.30 (dd, *J* = 11 Hz, 6 Hz, 1H), 2.93 (d, *J* = 4.5 Hz, 1H), 2.27 - 2.16 (m, 3H), 2.12 - 2.05 (m, 1H), 1.96 (td, *J* = 13 Hz, 4 Hz, 1H), 1.86 (dt, *J* = 14.5 Hz, 3.5 Hz, 1H), 1.77 (td, *J* = 14 Hz, 3.5 Hz, 1H), 1.41 (td, *J* = 13.5 Hz, 7 Hz, 1H), 1.32 (s, 3H), 1.03 (*br* d, *J* = 13.5 Hz, 1H), 0.98 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 191.65, 83.11, 79.38, 56.84, 51.29, 48.37, 48.00, 37.45, 36.50, 33.20, 27.69, 26.08, 25.84, 21.87, 19.26, 16.83; HRMS (EI) *m/z* (M^+) calcd 294.1290, obsd 294.1286.



Compound 100: 5a, 5b-Dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 8R*, 8aR*, 8bS*) perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-8-ol

Compound **91** (127 mg, 0.54 mmol), triphenyl phosphine (147 mg, 0.56 mmol) and benzoic acid (134 mg, 1.09 mmol) were dissolved in THF (2 mL) in a dry flask, under nitrogen. DEAD (95 μL, 0.60 mmol) was dissolved in 2 mL of THF and this solution was added to the reaction mixture, at room temperature, over a period of 100 min. The solution turned yellow. Reaction was allowed to proceed at room temperature for another

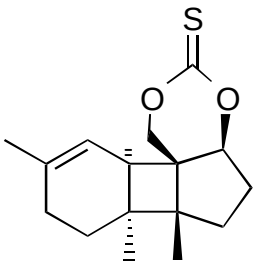
8h. TLC analysis showed no more change, but conversion was not complete. The solvent was evaporated and the residue was purified by flash chromatography using 30 % EtOAc in hexanes as the eluent to give 142 mg (78 %) of the benzoate and 19.8 mg (16 %) of unreacted starting material **91**. Hydrolysis of the ester was conducted by dissolving the benzoate (142 mg, 0.42 mmol) in 4 mL of methanol and adding this solution to KOH (aqueous, 3.6 M, 2 mL). The yellow color disappeared, and a precipitate formed. The reaction mixture was stirred for 8 h, at room temperature, and once the conversion was complete, according to TLC analysis, the methanol was evaporated. The remaining aqueous phase was extracted with CH_2Cl_2 (3 x 5 mL) and the combined organic layer was washed with brine, dried over anhydrous $MgSO_4$ and concentrated. Purification of the residue using flash chromatography with 30 % EtOAc in hexanes as the eluent gave 75 mg (75 %) of the inverted alcohol **100** as a white solid: mp 102 - 103.5^{o} C; IR (CCl_4, cm^{-1}) 3626, 2948, 2925, 2858, 1742, 1453, 1372, 1264, 1051, 1006, 942; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (*br* s, 1H), 5.04 (*br* s, 1H), 4.10 - 4.04 (m, 3H), 3.69 (d, *J* = 10 Hz, 1H), 2.42 (*br* d, *J* = 17 Hz, 1H), 2.31 (td, *J* = 13.5 Hz, 3.7 Hz, 1H), 2.13 - 2.10 (m, 2H), 2.08 - 1.97 (m, 1H), 1.83 (dd, *J* = 13.5 Hz, 7.5 Hz, 1H), 1.75 - 1.68 (m, 2H), 1.25 (*br* s, 1H), 1.07 (s, 3H), 1.02 (dt, *J* = 13.0 Hz, 3.7 Hz, 1H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 143.36, 115.70, 80.06, 79.10, 68.79, 61.68, 47.97, 47.88, 35.62, 34.49, 33.58, 26.89, 25.02, 20.68, 18.75; HRMS (EI) *m/z* (M^+) calcd 234.1619, obsd 234.1611.



Compound 101: 7b-(Hydroxymethyl)-3a, 3b, 6-trimethyl-(1R*, 3aS*, 3bR*, 7aS*, 7bR*)-2, 3, 3a, 3b, 4, 5, 7a, 7b-octahydro-1*H*-cyclopenta [3, 4] cyclobuta [a] benzen-1-ol

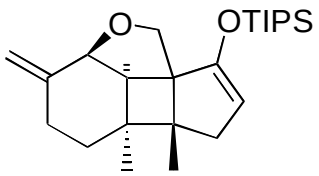
A solution of alcohol **100** (40 mg, 0.171 mmol) in 6 mL of diethyl ether was added to a 2-neck flask containing 6 mL of ethylamine, at -78^{o} C, and equipped with a dry ice condenser. The resulting clear solution was kept at -78^{o} C as lithium wire (20 mg, 2.88 mmol) was added. The reaction mixture was vigorously stirred for about 1 h until a stable dark blue color was observed and another 20 min after that. Reaction was then quenched, still cold, by addition of solid NH_4Cl until the blue color disappeared. The excess lithium pieces were removed with the aid of a spatula and a few drops of MeOH were added. Anhydrous $MgSO_4$ was added to the resulting suspension and it was allowed to warm to room temperature. The ethylamine was evaporated and the residue was resuspended in EtOAc, filtered and concentrated. Purification of the residue by flash chromatography using 5 % diethyl ether in methylene chloride as the eluent gave 39 mg (97%) of diol **101** as a clear oil: IR (CCl_4, cm^{-1}) 3625, 3524, 2954, 2926, 2884, 1731, 1449, 1436, 1370, 1263, 1032, 953; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.35 (s, 1H), 4.18 (d, J = 8.0 Hz, 1 H), 3.95 (s, 2H), 2.70 (*br* s, 1H, exchange with D_2O), 2.30 (*br* s, 1H, exchange with D_2O), 2.15 – 1.95 (m, 2H), 1.90 – 1.70 (m, 5H), 1.75 (s, 3H), 1.38 – 1.24 (m, 2H), 1.05 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 137.40, 119.11, 80.71, 63.46, 55.80,

48.21, 44.11, 35.78, 35.05, 33.78, 30.96, 26.49, 24.24, 20.69, 19.13; HRMS (EI) *m/z* (M^+) calcd 236.1776, obsd 236.1792.



Compound 102: 6a, 6b, 9-Trimethyl-(4aR*, 6aS*, 6bR*, 10aS*, 10bR*)-4a, 5, 6, 6a, 6b, 7, 8, 10a-octahydrobenzo[3', 4']-cyclobuta[2, 3] cyclopenta[d][1, 3]-dioxin-3-thione

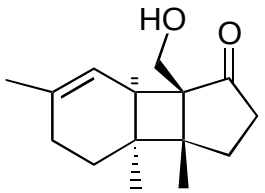
Diol **101** (7.0 mg, 0.03 mmol) and thiocarbonyl diimidazole (8 mg, 0.05 mmol) was dissolved in 2 mL of toluene in a dry flask, under nitrogen. The reaction mixture was heated to reflux for 10 h. At this point there was no more starting material left. The solvent was evaporated and the residue was immediately purified by flash chromatography using 10% EtOAc in hexanes as the eluent. Obtained 8 mg (95 %) of cyclic thionocarbonate **102** as a light yellow oil: IR (CCl_4, cm^{-1}) 2957, 2288, 1589, 1247, 1223, 1048, 1012, 979, 774; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.09 (s, 1H), 4.67 (d, *J* = 9.5 Hz, 1H), 4.33 (d, *J* = 9.5 Hz, 1H), 4.18 (*br* s, 1H), 2.09 (s, 1H), 2.01 – 1.82 (m, 3H), 1.67 – 1.49 (m, 2H), 1.38 (s, 3H), 1.24 – 1.03 (m, 4 H), 0.58 (s, 3H), 0.51 (s, 3H); HRMS (EI) *m/z* (M^+) calcd 278.1341, obsd 278.1328.



Compound 103: 5a, 5b-dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 8aR*, 8bS*)-[(2a, 3, 4, 5, 5a, 5b, 6, 8b-octahydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-8-yl)oxy](triisopropyl)silane

LDA was prepared at -78° C, in a dry flask, under nitrogen, by slow addition of BuLi (1.4M in hexanes, 1.5 mL, 2.1 mmol) to a solution of diisopropylamine (280 μL, 2.0 mmol) in THF (5 mL). Compound **3** (38 mg, 0.16 mmol) was dissolved in 1 mL of THF and this solution was cooled to -78° C. The freshly prepared LDA (800 μL, 0.24 mmol) was added *via cannula* and enolization was allowed to proceed for 30 min. The enol was trapped by addition of TIPSOTf (73 μL, 0.27 mmol) in one portion and the reaction mixture was stirred for 2 h. The reaction was quenched by addition of 1 mL of H_2O and the solution was allowed to warm to room temperature. The THF was evaporated under reduced pressure and the residue was extracted with diethyl ether. The organic phase was dried over anhydrous $MgSO_4$, concentrated and the residue was purified by flash chromatography using 30 % CH_2Cl_2 in hexanes as the eluent to give 54 mg (87 %) of the TIPS enol ether **103** as a clear oil: IR (CCl_4, cm^{-1}) 3071, 2953, 2869, 1638, 1465, 1370, 1325, 1251, 1178, 1026; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.03 (*br* s, 1H), 4.95 (*br* s, 1H), 4.63, (*br* s, 1H), 4.18 (d, *J* = 6.5 Hz, 1H), 3.93 (d, *J* = 9.0 Hz, 1H), 3.70 (d, *J* = 9.0 Hz, 1H), 2.65 - 2.58 (m, 2H), 2.4 (d, *J* = 6.5 Hz, 1H), 2.07 - 1.99 (m, 2H), 1.85 (dd, *J* = 16Hz, 1.5 Hz, 1H), 1.26 (s, 3H), 1.25 - 1.06 (m, 4H), 1.12 (s, 3H), 1.08 (d, *J* = 9.0 Hz,

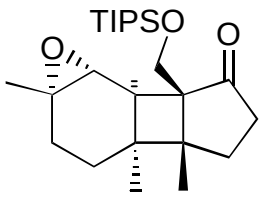
18H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 153.49, 145.93, 112.86, 102.31, 80.61, 68.34, 60.87, 53.66, 44.92, 38.79, 34.71, 32.52, 27.66, 27.36, 18.24, 17.68, 17.61, 12.01.



Compound 105: 7b-(Hydroxymethyl)-3a, 3b, 6-trimethyl-(3aR*, 3bS*, 7aR*, 7bS*)-2, 3, 3a, 3b, 4, 5, 7a, 7b-octahydro-1*H*-cyclopenta[3, 4]cyclobuta[a]benzen-1-one

A solution of compound **103** (54 mg, 0.14 mmol) in 6 mL of diethyl ether was added to a 2-neck flask containing 6 mL of ethylamine, at -78° C, and equipped with a dry ice condenser. The resulting clear solution was kept at -78° C as lithium wire (10 mg, 1.45 mmol) was added. The reaction mixture was vigorously stirred for about 30 min until a stable dark blue color was observed and another 25 min after that. Reaction was then quenched, still cold, by addition of solid NH_4Cl until the blue color disappeared. The excess lithium pieces were removed with the aid of a spatula and MeOH (2 mL) was added. The suspension was allowed to warm to room temperature, the ethylamine was allowed to evaporate and the residue was resuspended in EtOAc, washed with brine, dried over anhydrous $MgSO_4$ and concentrated. Obtained 52 mg (95%) of alcohol **104** as a light oil. This intermediate could be purified by flash chromatography using 5 % ethyl acetate in hexanes as the eluent for characterization, but for most cases it was carried on crude to the next step. The deprotection was carried out by addition of TBAF (1.0 M in THF, 1 mL) to the crude reduced product **104** at 0° C, allowing the mixture to warm to

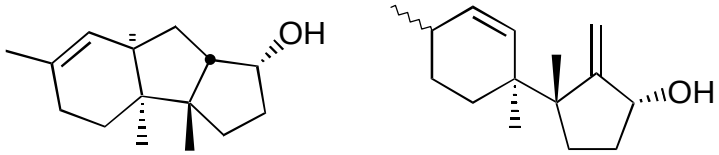
room temperature, and stirring it for 24 h. The reaction was quenched by addition of NH_4Cl (aqueous, sat., 3 mL). The mixture was extracted with diethyl ether (3 x 5 mL) and dried over anhydrous $MgSO_4$. Concentration and purification via flash chromatography using 5 % diethyl ether in CH_2Cl_2 as the eluent gave 24 mg (73 % overall) of keto-alcohol **105** as a light viscous oil: IR ($CDCl_3$, cm^{-1}) 3606, 3501, 2960, 2927, 2877, 1713, 1601, 1446, 1405, 1373, 1299, 1152, 1021; ^1H NMR (500 MHz, $CDCl_3$) δ 5.33 (*br* s, 1H), 3.95 (d, *J* = 12 Hz, 1H), 3.84 (d, *J* = 12 Hz, 1H), 2.73 - 2.66 (m, 1H, 5 lines), 2.42 - 2.31 (m, 2H), 2.29 (*br* s, 1H), 1.94 - 1.84 (m, 2H), 1.72 (s, 3H), 1.68 - 1.61 (m, 2H), 1.45 - 1.42 (m, 1H), 1.26 (*br* s, 1H), 1.10 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 224.19, 138.60, 117.85, 61.65, 57.22, 46.08, 44.53, 37.46, 37.17, 30.47, 29.95, 25.99, 23.80, 21.11, 18.20; HRMS (EI) *m/z* (M^+) calcd 234.1620, obsd 234.1602.



Compound 106: 1a, 3a, 3b-trimethyl-6a-{[(1, 1, 1-trimethylsilyl)oxy]methyl}-(1aR*, 3aR*, 3bS*, 6aR*, 6bS*, 6cS*)-perhydrocyclopenta[3 , 4]cyclobuta[3, 4] benzo[b]oxiren-6-one

Compound **105** (30 mg, 0.13 mmol), imidazole (20 mg, 0.29 mmol) and DMAP (4 mg, 0.03 mmol) were dissolved in 0.5 mL of dichloromethane, in a dry flask, under nitrogen. The reaction system was cooled to 0^oC and a solution of TIPSOTf (75 μL, 0.28

mmol) in 0.5 mL of CH_2Cl_2 was added *via* syringe. The reaction mixture was kept at 0^o C for 2 h until no more substrate was left. The reaction was quenched by addition of 2 mL of water followed by extraction with methylene chloride (3 x 3 mL). The organic layers were combined, washed once with NH_4Cl (sat., aqueous), dried over Na_2SO_4 and concentrated. Purification *via* flash chromatography using 1:1 ethyl acetate in hexanes gave 41.6 mg (81.5 %) of the TIPS protected hydroxy ketone intermediate. The protected intermediate (41.6 mg, 0.106 mmol) was dissolved in 1 mL of CH_2Cl_2, in a dry flask, under nitrogen. $NaHCO_3$ (15 mg, 0.178 mmol) was added and the suspension was cooled to 0^o C. A solution of *m*-CPBA (75 % pure, 30 mg, 0.130 mmol) dissolved in 1 mL of CH_2Cl_2 was added dropwise, *via* syringe, and the reaction mixture was stirred at 0^o C for 2 h. Reaction was quenched by addition of brine (1 mL) and Na_2CO_3 (solid). The layers were separated, and the aqueous was extracted with dichloromethane. The combined organic phase was dried over Na_2SO_4 and concentrated. Purification of the residue using flash chromatography with 5 % Et_2O in CH_2Cl_2 as the eluent gave 27 mg (62 %) of epoxide **106** as a light yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.22 (d, J = 8.0 Hz, 1H), 3.94 (d, J = 8.0 Hz, 1H), 2.80 (d, J = 4.0 Hz, 1H), 2.65 – 2.45 (m, 2H), 2.42 – 2.25 (m, 1H), 2.24 – 2.05 (m, 1H), 2.21 (d, J = 4.0 Hz, 1H), 2.04 – 1.88 (m, 1H) 1.73 – 1.50 (m, 3H), 1.60 (s, 3H), 1.45 – 1.18 (m, 2H), 1.35 (s, 3H), 1.32 (s, 3H), 1.15 –0.80 (m, 18 H); ^{13}C NMR (125MHz, $CDCl_3$) ppm 221, 62.8, 60.8, 57.5, 55.6, 47.2, 42.6, 37.4, 35.3, 31.7, 29.4, 28.1, 25.5, 22.5, 19.4, 17.5, 11.7; HRMS (EI) *m/z* (M^+) calcd 406.2903, obsd 406.2933.



Compounds 107 and 108: 3a, 3b, 6-Trimethyl-(1R*, 3aS*, 3bS*, 7aR*, 8aS*)-1, 2, 3, 3a, 3b, 4, 5, 7a, 8, 8a-decahydrocyclopenta[a]inden-1-ol and 3(1, 4-Dimethyl-(1R*)-2-cyclohexenyl)-3-methyl-2-methylene-(1R*, 3R*)-cyclopentan-1-ol

Toluene used in this reaction was first deoxygenated using the freeze-pump-thaw technique (3 cycles). A standard solution of Bu_3SnH / AIBN in toluene was prepared by dissolving Bu_3SnH (125 μL, 0.46 mmol) and AIBN (8 mg, 0.095 mmol) in toluene (10 mL). A solution of cyclic thionocarbonate **94** (24 mg, 0.09 mmol) in 28 mL of toluene was heated to reflux as 2.5 mL of the above standard solution was added *via* syringe pump over 6 h. After addition, the reaction mixture was allowed to reflux for an additional 60 min and it was then set to cool to room temperature. Solvent was evaporated *in vacuo*. The residue was ressuspended in 2.0 mL of wet ether and titrated with a saturated solution of iodine in ether until the orange color persisted.[196] A suspension of 1,8-diazabicyclo [5.4.0] undec-7-ene (60 mg, 0.39 mmol) in diethyl ether (4.0 mL) was added. Some white precipitate formed first and disappeared later. After this reaction mixture was stirred at room temperature for 1 h, water (40 mL) was added and the aqueous layer was extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. Purification of the residue by flash chromatography using 10 % diethyl ether in methylene chloride gave 9.0

[196] Curran, D. P.; Chang, C-T. *J. Org. Chem.* **1989**, 54, 3140.

mg (47%) of the tricyclic alcohol **107** and 3.5 mg (18%) of the diene-ol **108** as colorless oils.

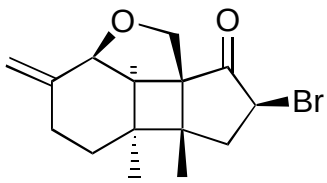
Tricyclic alcohol **107**: IR (CCl_4, cm^{-1}) 3631, 2959, 2926, 2854, 1771, 1455,1369, 1115; ^1H NMR (500 MHz, $CDCl_3$) δ 5.46 (*br* d, *J* = 4.5 Hz, 1H), 4.34 (q, *J* = 6.5Hz, 1H), 2.19 - 2.15 (m, 1H), 2.07 - 2.04 (m, 1H), 2.02 - 1.90 (m, 3H), 1.87 - 1.79 (m, 2H), 1.65 (s, 3H), 1.61 - 1.54 (m, 1H), 1.44 - 1.26 (m, 4H), 1.15 - 1.10 (m, 1H), 0.92 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 131.22, 124.14, 74.87, 52.64, 45.18, 43.55, 41.04, 33.64, 33.03, 31.85, 27.87, 27.63, 23.32, 21.66, 16.92; HRMS (EI) *m/z* (M^+) calcd 220.1827, obsd 220.1811.

Diene-ol **108** (3:1 mixture of diastereomers by GC-MS analysis): IR ($CHCl_3$, cm^{-1}) 3387, 3353, 1467, 1446, 1066, 1032; ^1H NMR (500 MHz, $CDCl_3$) δ 5.98 and 5.84 (d, *J* = 10.8 Hz, 1H), 5.57 and 5.53 (d, *J* = 10.8 Hz, 1H), 5.29 and 5.28 (s, 1H), 5.14 and 5.10 (s, 1H), 4.42 and 4.41 (s, 1H), 2.38–2.32 (m, 1H), 2.20–2.10 (m, 1H), 1.99–1.95 and 1.92–1.87 (m, 1H), 1.84 – 1.78 (m, 1H), 1.73 – 1.60 (m, 2H), 1.57 – 1.53 (m, 2H), 1.47, 1.43 (m, 1H), 1.37 and 1.36 (s, 3H), 1.16 –1.06 (m, 6 lines, 6H); HRMS (EI) *m/z* (M^+) calcd 220.1827, obsd 220.1793.

Fragmentation of compound 99

Toluene used in this reaction was first deoxygenated using the freeze-pump-thaw technique (3 cycles). A standard solution of Bu_3SnH / AIBN in toluene was prepared by dissolving Bu_3SnH (125 μL, 0.46 mmol) and AIBN (6.5 mg, 0.05 mmol) in toluene (10 mL). A solution of cyclic thionocarbonate **99** (7.7 mg, 0.026 mmol) in 10 mL of toluene

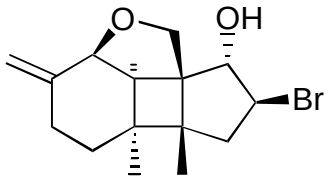
was heated to reflux as 735 μL of the above standard solution was added *via* syringe pump over 6 h. After addition, the reaction mixture was allowed to reflux for an additional 1 h and it was then cooled to room temperature. Solvent was evaporated *in vacuo*. The residue was ressuspended in 10 mL of wet diethyl ether and titrated with a saturated solution of iodine in ether until the orange color persisted.[196] A suspension of DBU (23 mg , 0.15 mmol) in diethyl ether (1 mL) was added. Some white precipitate formed first and disappeared later. After this reaction mixture was stirred at room temperature for 1 h, water (10 mL) was added and the aqueous layer was extracted with diethyl ether (3 x 8 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. Purification of the residue by flash chromatography using 10 % diethyl ether in methylene chloride gave 5.7 mg (78 %) of compound **96** as a colorless oil.



Compound 112: 7-Bromo-5a, 5b-dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 7R*, 8aR*, 8bS*)perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-8-one

Compound **3** (31 mg, 0.13 mmol) was dissolved in 5 mL of ethyl acetate, in a dry flask, under nitrogen. PhSeBr (80 mg, 0.34 mmol) was added to the reaction mixture and was let stir for 1 h. The solvent was removed in the rotatory evaporator and the dark brown residue was immediately purified by flash chromatography using 1:1 CH_2Cl_2 and hexanes as the eluent, 29mg (72 %) of the bromo-ketone **112** was obtained as a light

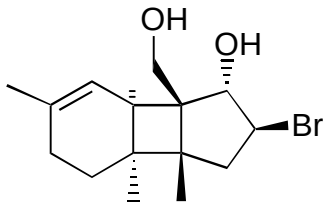
yellow oil: IR ($CDCl_3$, cm^{-1}) 3077, 2950, 2930, 2866, 1749, 1737, 1449, 1378, 1294, 1267, 1066,1027, 907; ^1H NMR (500 MHz, $CDCl_3$) δ 5.14 (s, 1H), 5.12 (s, 1H), 4.83 (t, *J* = 9.0 Hz, 1H), 4.16 (d, *J* = 6.0 Hz, 1H), 4.05 (d, *J* = 10.0 Hz, 1H), 3.95 (d, *J* = 10.0 Hz, 1H), 3.06 (dd, *J* = 15 Hz, 9 Hz, 1H), 2.51 (*br* d, *J* = 16.5 Hz, 1H), 2.39 (d, *J* = 6.0 Hz, 1H), 2.34 (td, *J* = 13.0, 8.0 Hz, 1H), 2.13 (*br* t, *J* = 13 Hz, 1H), 1.98 (dd, *J* = 15.0, 9.0 Hz, 1H), 1.23 (s, 3H), 1.19 (*br* t, *J* = 8.5 Hz, 1H), 1.15 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 209.32, 141.85, 116.75, 79.90, 67.57, 58.88, 53.45, 48.88, 45.83, 41.57, 36.00, 27.39, 24.97, 22.75, 18.55; HRMS (EI) *m/z* (M^+) calcd 310.0568, obsd 310.0557.



Compound 116: 7-Bromo-5a, 5b-dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 7S*, 8S*, 8aR*, 8bS*)perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-8-ol

Compound **112** (15 mg, 0.05 mmol) was dissolved in 2 mL of diethyl ether, in a dry flask, under nitrogen and the resulting light yellow solution was cooled to 0^o C. $LiAlH_4$ (2 mg, 0.06 mmol) was added to the reaction mixture in one portion. The reaction mixture was allowed to warm to room temperature and was let stir for 30 min. The suspension was cooled to 0^o C, diluted with 5 mL of diethyl ether, and the reaction was quenched by dropwise addition of Na_2SO_4 (aqueous, sat.) until there was no more evolution of H_2. The suspension was filtered through a mixture of celite and anhydrous $MgSO_4$. Concentration of the filtrate and purification by flash chromatography using 20

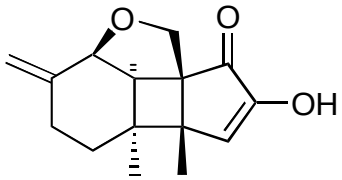
% diethyl ether in methylene chloride as the eluent gave 9.9 mg (63 %) of bromo-alcohol **116** as a clear oil: IR ($CDCl_3$, cm^{-1}) 3692, 3605, 2950, 2928, 2861, 2253, 1603, 1455, 1016; ^1H NMR (500 MHz, $CDCl_3$) δ 5.12 (s, 1H), 5.07 (s, 1H), 4.26 - 4.20 (m, 1H), 4.05 (d, *J* = 5.5 Hz, 1H), 3.99 (d, *J* = 9.5 Hz, 1H), 3.89 (*br* d, *J* = 9.0 Hz, 1H), 3.60 (d, *J* = 9.5 Hz, 1H), 2.62 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.44 (*br* d, *J* = 16.5 Hz, 1H), 2.28 (d, *J* = 13.5, 4.0 Hz, 1H), 2.23 (d, *J* = 5.5 Hz, 1H), 2.17 - 2.08 (m, 1H), 1.76 (dd, *J* = 14.0, 12.0 Hz, 1H), 1.06 - 1.01 (m, 1H), 1.02 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 142.87, 116.22, 80.41, 78.72, 67.72, 57.63, 54.56, 46.67, 44.31, 43.50, 34.83, 26.70, 24.95, 20.34, 18.01; HRMS (EI) *m/z* (M^+) calcd 312.0725, obsd 312.0720.



Compound 118: 7b-(Hydroxymethyl)-3a, 3b, 6-trimethyl-(1R*, 2R*, 3aR*, 3bS*, 7aR*, 7bS*)-2, 3, 3a, 3b, 4, 5, 7a, 7b-octahydro-1*H*-2-bromo-cyclopenta[3, 4] cyclobuta[a]benzen-1-ol

Compound **112** (15 mg, 0.05 mmol) was dissolved in 3 mL of ethanol, in a dry flask, under nitrogen. Sodium borohydride (3 mg, 0.08 mmol) was added to the reaction mixture in one portion and allowed to react for 4 h. Once there was no more starting material left the reaction was quenched by addition of half saturated solution of NaCl. The ethanol was evaporated and the residue was extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$ and the solvent was evaporated.

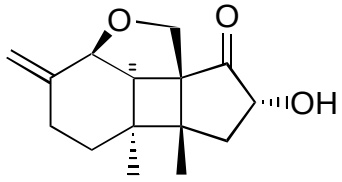
Purification by flash chromatography followed using 20 % diethyl ether in methylene chloride as the eluent to give 11 mg (70 %) of alcohol **118** as a light yellow oil: IR ($CDCl_3$, cm^{-1}) 3691, 3607, 3552, 2957, 2927, 2874, 1726, 1600, 1447, 1372, 1293, 1076; ^1H NMR (500 MHz, $CDCl_3$) δ 5.38 (*br* s, 1H), 4.32 – 4.29 (m, 1H), 4.22 (d, *J* = 8.5 Hz, 1H), 4.05 (d, *J* = 10.5 Hz, 1H), 3.78 (d, *J* = 10.5 Hz, 1H), 2.73 (*br* s, 1H), 2.58 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.33 (*br* s, 1H), 1.89 – 1.82 (m, 3H), 1-77 – 1.71 (m, 2H), 1.57 (s, 3H), 1.37 – 1.33 (m, 1H), 0.96 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (75MHz, $CDCl_3$) ppm 138, 119.5, 85, 65, 53, 52.5, 47, 45, 40.5, 36.5, 31, 26.5, 24.5, 20, 18; HRMS (EI) *m/z* (M^+) calcd 314.0881, obsd 314.0889.



Compound 114: 7-Hydroxy-5a, 5b-dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 8aR*, 8bS*)-2a, 3, 4, 5, 5a, 5b, 8, 8b-octahydro-2-oxacyclopenta[4, 1] cyclobuta[c, d]inden-8-one

Brederick's reagent (900 μL, 4.4 mmol) and compound **3** (75 mg, 0.32 mmol) were heated, neat, to 55° C, for 30 h. At this point, NMR of the crude mixture indicated formation of the enamine. The reaction mixture was let cool to room temperature and was diluted in 20 mL of dichloromethane. A tip of a spatula of rose bengal was added to the solution which was submitted to photolysis with a sun lamp, at -78° C, while oxygen was bubbled through the reaction mixture. After 5 h the photolysis was stopped, the solvent was evaporated and the residue was ressuspended in ethyl acetate (20 mL).

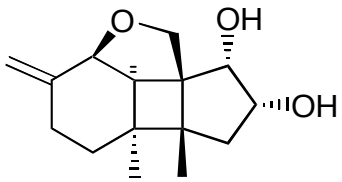
Work-up followed by washing the organic mixture with brine (1 x 10 mL), drying it over anhydrous $MgSO_4$ and concentrating it in the rota-vapor. Purification of the residue by flash chromatography using 20 % EtOAc in hexanes as the eluent gave 44 mg (56 %) of diketone **114** in its keto enol form: IR ($CDCl_3$, cm^{-1}) 3602, 3501, 2928, 2859, 1699, 1651, 1602, 1396, 1250; ^1H NMR (300 MHz, $CDCl_3$) δ 8.53 (*br* s, exchange with D_2O), 6.59 (s, 1H), 5.17 (*br* s, 1H), 5.12 (*br* s, 1H), 4.30 (d, *J* = 5.5 Hz, 1H), 3.97 (d, *J* = 10 Hz, 1H), 3.90 (d, *J* = 10 Hz, 1H), 2.51 (dt, *J* = 16 Hz, 4.3 Hz, 1H), 2.38 - 2.28 (m, 2H), 2.19 (d, *J* = 5.5 Hz, 1H), 2.16 - 2.09 (m, 1H), 1.72 - 1.57 (m, 1H), 1.13 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 217.53, 203.02, 142.37, 135.45, 116.53, 80.10, 67.08, 59.73, 50.52, 36.88, 33.0, 27.59, 25.07, 23.47, 14.40; HRMS (EI) *m/z* (M^+) calcd 246.1256, obsd 246.1274.



Compound 124: 5a, 5b-dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 7S*, 8aR*, 8bS*)-perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-7-ol-8-one

Compound **3** (30 mg, 0.13 mmol) was dissolved in 2.5 mL of methanol, in a dry flask, under nitrogen and this solution was cooled to 0^o C. A pre-cooled solution of KOH (52.5 mg, 0.94 mmol) in 1.2 mL of methanol was added to the cold reaction mixture and was let stir for 30 min. After this time, still at 0^o C, the $PhI(OAc)_2$ (83 mg, 0.26 mmol) was added in one portion and the reaction was allowed to proceed for another 3h. Once

there was no more starting material left the methanol was evaporated, the residue was resuspended in water (3 mL) and extracted with dichloromethane (3 x 5 mL). The organic layers were combined and washed with brine (1 x 5 mL), dried over anhydrous Na_2SO_4 and concentrated. Purification by flash chromatography using CH_2Cl_2 as the eluent gave 28 mg (73 %) of ketal-alcohol **125**. Hydrolysis of the ketal was conducted by dissolving the product in chloroform (2.0 mL) and adding trifluoroacetic acid (50%, aqueous, 750 μL). Reaction was conducted at 0^o C for 90 min and then it was diluted in chloroform (5 mL) and washed with $NaHCO_3$ (aqueous, sat.) until pH neutral. The organic phase was dried in anhydrous Na_2SO_4, concentrated and purified by flash chromatography using 10% diethyl ether in CH_2Cl_2 as the eluent to give 20 mg (62 % overall) of hydroxy ketone **124** as a light yellow oil: IR ($CDCl_3$, cm^{-1}) 3240, 2985, 2979, 1730, 1375, 1267, 1249, 1046; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.12 (*br* s, 1H), 5.04 (*br* s, 1H), 4.26 - 4.20 (m, 2H), 4.10 (d, J = 9.5 Hz, 1H), 3.79 (d, J = 9.5 Hz, 1H), 2.74 (*br* s, 1H), 2.64 (d, J = 5.5 Hz, 1H), 2.53 (*br* d, J = 17.5 Hz, 1H), 2.43 (td, J = 13 Hz, 5 Hz, 1H), 2.27 - 2.15 (m, 3H), 1.18 - 1.13 (m, 1H), 1.11 (s, 3H), 1.06 (s, 3H); HRMS (EI) *m/z* (M^+) calcd 248.1413, obsd 248.1415.



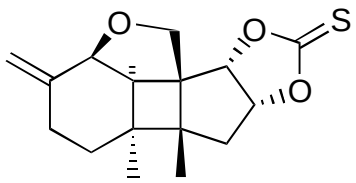
Compound 121: 5a, 5b-Dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 7S*, 8S*, 8aR*, 8bS*)-perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-7, 8-diol

Method A: Compound **114** (15 mg, 0.06 mmol) and a tip of a spatula of anhydrous potassium carbonate were suspended in ethanol (2.0 mL). $NaBH_4$ (20 mg, 0.52 mmol) was added to the reaction mixture in 4 portions, over a period of 18 h. One hour after the addition of the last portion of the reducing agent all the starting material had reacted, so the reagent was quenched by slow addition of water (1 mL) until no more gas evolution was observed. The ethanol was removed in the rota-vapor and the residue was ressuspended in EtOAc (5 mL). The layers were separated, the organic phase was washed with brine (1 x 2 mL), dried over anhydrous $MgSO_4$ and concentrated. Purification of the residue by flash chromatography afforded 13 mg (87 %) of *cis* diol **121** as a white solid.

Method B: Compound **124** (10 mg, 0.04 mmol) was dissolved in ethanol (1.0 mL) and $NaBH_4$ (10 mg, 0.26 mmol) was added to the solution, at 0^o C, in three portions, over 1h. After the addition was complete the reaction mixture was allowed to warm to room temperature and was stirred for another 1 h until reaction completion. Once all the starting material was consumed the ethanol was removed *in vacuo* and the residue was resuspended in EtOAc (5 mL), washed with brine, dried over anhydrous $MgSO_4$ and concentrated. Purification of the residue by flash chromatography using 30 % diethyl

ether in methylene chloride as the eluent gave 8 mg (80 %) of the *cis* diol **121** as a white solid.

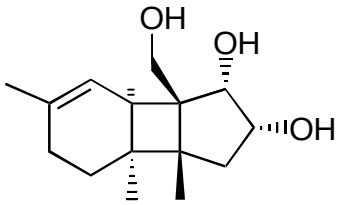
Compound **121**: mp 131-133^{o} C; IR ($CDCl_3$, cm^{-1}) 3627, 3552, 2976, 2927, 2869, 1730, 1644, 1602, 1446, 1381, 1207, 1112, 1039, 994; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.09 (*br* s, 1H), 5.03 (*br* s, 1H), 4.21 (td, *J* = 5.5 Hz, 1.5 Hz, 1H), 4.03 (d, *J* = 5.0 Hz, 1H), 4.01 (d, *J* = 10 Hz, 1H), 3.86 (d, *J* = 5.5 Hz, 1H), 3.58 (d, *J* = 10 Hz, 1H), 2.64 (d, *J* = 5.0 Hz, 1H), 2.51 (*br* d, *J* = 15 Hz, 1H), 2.43 (*br* d, *J* = 15 Hz, 1H), 2.32 (td, *J* = 13.5 Hz, 4 Hz, 1H), 2.18 (*br* t, *J* = 15 Hz, 1H), 1.58 (dd, *J* = 15 Hz, 5.5 Hz, 1H), 1.23 (*br* s, 2H), 1.14 (s, 3H), 1.01 (*br* d, *J* = 13.5 Hz, 1H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 143.48, 115.43, 81.26, 76.70, 73.25, 69.20, 59.00, 46.73, 44.34, 41.84, 34.29, 26.89, 24.88, 21.51, 18.66; HRMS (EI) *m/z* (M^{+}) calcd 250.1569, obsd 250.1536.



Compound 122: 5a, 5b-dimethyl-methylene-(2aR*, 5aR*, 5bS*, 6aS*, 9aR*, 9bR*, 9cS*)-perhydro[1]benzoxolo[3'', 4'':2', 3', 4']cyclobuta[4, 5] cyclopenta[d][1,3]dioxole-8-thione

Compound **121** (8 mg, 0.032 mmol) and thiocarbonyl diimidazole (15 mg, 0.084 mmol) were dissolved in dry toluene, in a dry flask, under nitrogen atmosphere and the yellow reaction mixture was heated to reflux for 24 h. The toluene was removed under reduced pressure and the residue was immediately purified by flash chromatography using 10 % EtOAc in hexanes as the eluent to give 7 mg (75 %) of the cyclic thionocarbonate

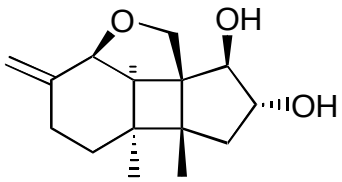
122 as a yellow oil: IR ($CDCl_3$, cm^{-1}) 2957, 2927, 2854, 1804, 1601, 1460, 1368, 1319, 1168, 1137, 1085, 1052; ^1H NMR (300 MHz, $CDCl_3$) δ 5.18 (s, 1H), 5.13 – 5.08 (m, 2H), 4.81 (d, *J* = 6.8 Hz, 1H), 4.15 – 4.10 (m, 2H), 3.42 (d, *J* = 11.2 Hz, 1H), 2.94 (d, *J* = 15.6 Hz, 1H), 2.45 (*br* d, *J* = 16.9 Hz, 1H), 2.31 (d, *J* = 6.0 Hz, 1H), 2.6 (td, *J* = 12.5, 3.1 Hz, 1H), 2.20 – 2.10 (m, 1H), 1.85 (dd, J = 15.6, 6.3 Hz, 1H), 1.12 (s, 3H), 1.11 – 1.06 (m, 1H), 1.05 (s, 3H); ^{13}C NMR (123 MHz, $CDCl_3$) ppm 156.30, 142.63, 117.01, 84.07, 83.48, 80.87, 69.43, 60.11, 49.86, 44.73, 40.32, 33.39, 28.95, 26.13, 24.51, 22.71, 18.32; HRMS (EI) *m/z* (M^+) calcd 292.1133, obsd 292.1139.



Compound 123: 7b-(Hydroxymethyl)-3a, 3b, 6-trimethyl-(1R*, 2S*, 3aR*, 3bS*, 7aR*, 7bS*)-2, 3, 3a, 3b, 4, 5, 7a, 7b-octahydro-1*H*-cyclopenta[3, 4] cyclobuta[a]benzen-1, 2-diol

A two-neck flask equipped with a dry ice condenser was flame dried and flushed with dry nitrogen. Ethylamine (3 mL, excess) was condensed onto the flask at -78° C. A solution of diol **121** (12 mg, 0.048 mmol) in 3 mL of diethyl ether was added to the reaction media. Lithium wire (10 mg, 1.4 mmol), was cut in small pieces, and added to the flask. The suspension of lithium pieces in ethereal ethylamine was stirred at -78° C until a persistent dark blue color was observed (about 30 min). The suspension was allowed to stir at -78° C for an additional 30 min before the blue color was discharged by

addition of a few drops of 1-octyne. The remaining lithium pieces were removed with a spatula and the color of the resulting yellow solution was discharged by addition of methanol, dropwise. The mixture was allowed to warm to room temperature and was concentrated in a rotatory evaporator. The residue was resuspended in ether, dried over anhydrous $MgSO_4$ and filtered over a plug of silica gel. The clear solution was again concentrated followed by purification of the residue by flash chromatography, using a solution of 1:1 diethyl ether and methylene chloride as the eluent. Obtained 4 mg (35 %) of triol **123** as a clear oil: IR (CCl_4, cm^{-1}) 3691, 3607, 3552, 2952, 2926, 2871, 1726,1622, 1436,1372, 1276, 1055.



Compound 126: 5a, 5b-Dimethyl-3-methylene-(2aR*, 5aR*, 5bS*, 7S*, 8R*, 8aR*, 8bS*)-perhydro-2-oxacyclopenta[4, 1]cyclobuta[c, d]inden-7, 8-diol

Compound **124** (15 mg, 0.06 mmol) was dissolved in acetic acid (glacial, 3 mL) and the solution was cooled to 0^o C. Tetramethylammonium triacetoxi-borohydride (42 mg, 0.15 mmol) was added in one portion. Reaction was allowed to warm to room temperature over 1 hour and them it was kept stirring for another 5h. Once there was no more starting material according to TLC analysis, the reaction mixture was diluted with brine (10 mL) and the aqueous phase was extracted with ethyl acetate (6 x 10 mL). The combined organic layers was dried over anhydrous $MgSO_4$, concentrated and the residue was purified using flash chromatography with a 1:1 solution of ethyl acetate and hexanes

used as the eluent. Obtained 11.3 mg (75 %) of *trans*-diol **126** along with 1.5 g (15 %) of the *cis*-diol **121**. Trans diol **126**: IR ($CDCl_3$, cm^{-1}) 3691, 3611, 2974, 2928, 2869, 1603, 1448, 1382, 1209, 1118, 1072, 1013; ^1H NMR (500 MHz, $CDCl_3$) δ 5.09 (*br* s, 1H), 5.03 (*br* s, 1H), 4.20 - 4.18 (m, 1H), 4.09 - 4.01 (m, 3H, 5 lines), 3.73 (d, *J* = 10 Hz, 1H), 2.51 (d, *J* = 5.5 Hz, 1H), 2.46 (*br* d, *J* = 18 Hz, 1H), 2.39 - 2.32 (m, 2H), 2.18 (*br* t, *J* = 14 Hz, 1H), 1.88 (dd, *J* = 15.0 Hz, 6.5 Hz, 1H), 1.56 (*br* s, 2H), 1.07 (s, 3H), 1.05 (s, 3H), 1.04 - 1.00 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) ppm 143.42, 115.31, 84.57, 80.75, 80.16, 68.52, 59.00, 49.44, 48.03, 42.59, 33.76, 26.91, 24.89, 21.40, 19.37; HRMS (EI) *m/z* (M^+) calcd 250.1569, obsd 250.1550.