

# SUPPORTING INFORMATION

for

## **Synthesis and characterization of norbornane diol isomers and their fluorinated analogs.**

Scott M. Grayson, Brian K. Long, Shiro Kusomoto, Brian P. Osborn, Ryan P.

Callahan, Charles R. Chambers, C. Grant Willson\*

*Department of Chemistry and Biochemistry,*

*University of Texas, Austin, Austin TX 78712*

### **CONTENTS:**

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Synthetic Procedures for 2, 6, 8-13	(S2-S4)

**General Methods and Materials:** Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded in CDCl<sub>3</sub> or CD<sub>2</sub>Cl<sub>2</sub> with TMS as the internal standard for <sup>1</sup>H (500 MHz) and CDCl<sub>3</sub> or CD<sub>2</sub>Cl<sub>2</sub> as the internal standard for <sup>13</sup>C (125 MHz), unless otherwise specified. All reactions were carried out under an atmosphere of nitrogen. Column chromatography was performed using 150-230 mesh silica gel

## Acid-Catalyzed Epoxynorbornane Ring Opening

**exo-2-syn-7-Dihydroxynorbornane<sup>1</sup> (6).** To a round bottom flask was added 1.5g of *exo*-norbornene oxide 100ml of dioxane, and 100 ml of 1M HCl (aq). The reaction mixture was stirred and heated to 90° C for 16 hour. The reaction mixture was worked up by washing with dichloromethane and extracting with sodium bicarbonate(aq), and brine, and the organic fractions reduced *in vacuo*. The crude reaction mixture was purified to remove oligomers by sublimation to yield a white amorphous solid (yield 62%). Product was a racemic mixture of (2R, 7S) and (2S, 7R) dihydroxynorbornane. mp 183-185 °C;<sup>2</sup> <sup>1</sup>H NMR 0.9-1.1 (m, 2H), 1.4-1.5 (m, 1H), 1.5-1.6 (m, 1H), 1.88 (m, 2H), 2.08 (d, 1H, J = 5.0 Hz), 2.18 (m, 1H), 3.84 (d, 1H, J = 4.5 Hz), 3.99 (d, 1H, J = 7.0 Hz), 4.02 (s, 1H), 4.28 (d, 1H, J = 4.5 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub> calibrated to 77.00): 21.3, 25.0, 39.4, 40.5, 45.8, 75.8, 80.4; LRMS (EI) *m/z* (%) 110 (60, M-18<sup>+</sup>), 95 (35), 92 (30), 81 (100), 79 (70), 66 (90); HRMS ([M+H]<sup>+</sup> calcd. = 129.0916 found = 129.0921) FTIR  $\nu$  = 3342 (br), 2958, 2875, 1083 cm<sup>-1</sup>; Anal Calcd for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>: C, 65.60%; H, 9.44%. Found: C, 65.20%; H, 9.47%.

## Base-Catalyzed Epoxynorbornane Ring Opening

**endo-3-Benzoxybicyclo[2.2.1]heptan-*exo*-2-ol (9).** To a dry 500 ml round bottom flask in an ice bath were added 200g (1.78 mol) of benzyl alcohol and a stir bar. Over 12h 13.64g (0.35 mol) of potassium metal was added in 1g increments and allowed to stir under a nitrogen atmosphere until the metal was fully dissolved. After all of the potassium was added, 33g of *exo*-norbornene epoxide (0.30 mol) was added and the reaction mixture heated to 150°C. The reaction mixture was allowed to stir for 20 days, at which point the reaction mixture was worked up by quenching with water, extracting with dichloromethane (3x), and organic layers combined and reduce *in vacuo*. The organic residue was then distilled under vacuum to remove the excess benzyl alcohol and the product was purified by column chromatography using 15% ethyl acetate in hexanes as eluent affording 39.4g of a transparent oil. Yield: 30% <sup>1</sup>H NMR: 1.1-1.3 (m, 3H), 1.5-1.8 (m, 3H), 2.01 (d, 1H, br), 2.10 (d, 1H, J = 5.0 Hz), 2.48 (br s, 1H), 3.51 (m, 1H), 3.63 (m, 1H), 4.51 (dd, 2H, J = 11.4 Hz, 31.7 Hz), 7.2-7.2 (m, 5H) <sup>13</sup>C NMR: 19.6, 25.3, 33.6, 39.0, 44.4, 71.3, 80.1, 89.7, 127.5, 127.7, 128.3, 138.4 LRMS (EI) *m/z* (%) 110 (60, M-18<sup>+</sup>), 95 (35), 92 (30), 81 (100), 66 (90); HRMS ([M+H]<sup>+</sup> calcd. = 219.1385 found = 219.1393) FTIR  $\nu$  = 3388, 3031, 2957, 1454, 1126 cm<sup>-1</sup>; Anal. Calcd. for C<sub>14</sub>H<sub>18</sub>O<sub>2</sub>: C, 77.03%; H, 8.31%. Found: C, 76.77%; H, 8.42%.

**trans-Bicyclo[2.2.1]heptan-2,3-diol (8).** To a 100ml cylindrical glass sleeve was added a stirbar, 1.30 g of *endo*-3-benzoxybicyclo[2.2.1]heptan-*exo*-2-ol (9),

<sup>1</sup> Kwart, H.; Vosburgh, W. G. *J. Am. Chem. Soc.* **1954**, 76, 5400.

<sup>2</sup> Crandall, J. K. *J. Org. Chem.* **1964**, 29, 2830.

50 ml of 1:1 ethanol/ethyl acetate, and 40mg of 10% Pd/C. The sleeve was placed inside a steel Parr reactor and charged with 400 psi of H<sub>2</sub>. The reaction vessel was allowed to stir vigorously for 12h, at which point the Parr reactor was depressurized, refreshed with an additional 20mg of Pd/C, recharged to 400 psi of H<sub>2</sub>, and the reaction allowed to react for an additional 12 h. The reaction vessel was then depressurized, and reaction mixture filtered through a Whatman 0.2 micron PTFE filter to remove the Pd/C catalyst. The clear solution was reduced *in vacuo* to yield the racemic product as a white amorphous solid. (yield 99%) mp 216-8 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub> calibrated to 7.29) 1.2-1.4 (m, 3H), 1.5-1.8 (m, 3H), 2.11 (d, 1H, J = 6 Hz), 2.31 (s, 1H), 2.68 (br s, 2H), 3.38 (s, 1H), 3.89 (d, 1H, J = 5.2 Hz) <sup>13</sup>C NMR (CDCl<sub>3</sub> calibrated to 77.00): 19.1, 25.3, 34.0, 41.5, 44.9, 82.4, 82.9; LRMS (EI) *m/z* (%) 128 (5, M<sup>+</sup>), 110 (25, M-18<sup>+</sup>), 95 (50), 81 (70), 67 (100), 57 (100); HRMS ([M+H]<sup>+</sup> calcd. = 129.0916 found = 129.0911) FTIR  $\nu$  = 3285 (br), 2956, 2873, 1048 cm<sup>-1</sup>; Anal Calcd for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>: C, 65.60%; H, 9.44%. Found: C, 65.30%; H, 9.40%.

### Alternate Route:

**2-exo-3-exo-Bicyclo[2.2.1]heptan-diol (2).** Prepared as reported in the literature.<sup>3</sup> Characterization data provided for comparison: mp 141-142 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub> calibrated to 7.29) 1.07 (m, 3H), 1.49 (m, 2H), 1.76 (m, 1H), 2.13 (m, 2H), 3.15 (s, 2H), 3.67 (s, 2H) <sup>13</sup>C NMR (CDCl<sub>3</sub> calibrated to 77.00): 24.48, 31.55, 43.00, 74.76. LRMS (M<sup>+</sup> calcd. = 128 found = 128) Anal Calcd for C<sub>7</sub>H<sub>12</sub>O<sub>2</sub>: C, 65.60%; H, 9.44%. Found: C, 65.56%; H, 9.48%.

**4-Phenyl-3,5-dioxatricyclo[5.2.1.0<sup>2,6</sup>]decane (10).** If the reaction was carried out at 60 degrees as previously reported<sup>4</sup> the product isolated was a 3:1 mixture of *exo* and *endo* benzylidene isomers. However, if the reaction was carried out in an ice bath under reduced pressure, the product formed was exclusively the *exo* isomer (99% yield). <sup>1</sup>H NMR (CDCl<sub>3</sub> calibrated to 7.29) 1.0-1.2 (m, 3H), 1.4-1.6 (m, 2H), 2.43 (m, 2H), 4.03 (d, 2H), 5.55 (s, 1H), 7.3-7.4 (m, 3H), 7.5-7.6 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub> calibrated to 77.00): 23.0, 31.8, 39.8, 76.6, 83.0, 102.6, 126.8, 128.4, 129.4, 129.5, 136.3. LRMS (EI) *m/z* (%) 215 (100, M-1<sup>+</sup>), 187 (15), 105 (35), 91 (40), 77 (25); HRMS ([M+H]<sup>+</sup> calcd. = 217.1229 found = 217.1223) FTIR  $\nu$  = 2964, 1718, 1450, 1137 cm<sup>-1</sup>; Anal Calcd for C<sub>14</sub>H<sub>16</sub>O<sub>2</sub>: C, 77.75%; H, 7.46 %. Found: C, 77.57%; H, 7.36%.

**exo-3-Benzoxybicyclo[2.2.1]heptan-exo-2-ol (11).** To a dry 250 ml round bottom flask were added 1.60 of **10** and a stirbar. The reactant was dried under vacuum for 24 h. To the dried reactant was added 45 ml of DIBAL solution (1.5M in toluene) and the reaction mixture was allowed to stir at 80°C under N<sub>2</sub> for 12 h. The product was purified by column chromatography using 6% ethyl acetate in hexanes as eluent affording 1.52g of a transparent oil. Yield: 94% <sup>1</sup>H NMR: 0.9-

<sup>3</sup> Shealy, Y. F.; Clayton, J. D. *J. Am. Chem. Soc.* **1969**, 91, 3075.

<sup>4</sup> Bazbouz, A.; Christol, H.; Coste, J.; Plenat, F. *Bull. Soc. Chim. Fr.* **1978**, 5-6, II, 305.

1.0 (m, 2H), 1.0-1.1 (m, 1H), 1.4-1.5 (m, 2H), 1.77 (m, 1H), 2.15 (s, 1H), 2.25 (s, 1H), 3.37 (m, 1H), 3.43 (m, 1H), 3.68 (m, 1H), 4.58 (dd, 2H,  $J = 16$  Hz, 31 Hz), 7.2-7.2 (m, 5H)  $^{13}\text{C}$  NMR: 24.0, 24.6, 31.9, 39.5, 43.0, 72.4, 74.8, 82.0, 127.5, 127.7, 128.3, 137.7; LRMS (EI)  $m/z$  (%) 215 (1,  $\text{M}-1^+$ ), 127 (45), 91 (100), 81 (90), 65 (20); HRMS ( $[\text{M}+\text{H}]^+$  calcd. = 219.1385 found = 219.1385) FTIR  $\nu = 3518, 3030, 2958, 1453, 1144, 1073\text{ cm}^{-1}$ ; Anal. Calcd. for  $\text{C}_{14}\text{H}_{18}\text{O}_2$ : C, 77.03%; H, 8.31%. Found: C, 76.94%; H, 8.34%.

**exo-3-Benzoxycyclo[2.2.1]heptan-2-one (12).** To a dry 50 ml round bottom flask were added 0.44g (0.20 mmole) of **11** and a stirbar. The reactant was diluted with 50 ml of dichloromethane and 0.66g (0.30mmole) of PCC was added. The transparent orange reaction mixture was allowed to stir for 12 h until a dark brownish precipitate was formed. The reaction mixture was diluted with a large excess of diethyl ether, and filter through celite to yield a light greenish oil. The product could be further purified by column chromatography using 5% ethyl acetate 95% hexane as eluent to yield 0.42g (96% yield) a transparent oil.  $^1\text{H}$  NMR ( $\text{CDCl}_3$  calibrated to 7.29) 1.42 (m, 2H), 1.57 (m, 2H), 1.81 (m, 2H), 2.26 (m, 1H), 2.60 (d, 1H,  $J = 1.5$  Hz), 3.28 (d, 1H,  $J = 1.5$  Hz), 4.70 (dd, 2H,  $J = 1.2$  Hz, 42 Hz), 7.2-7.2 (m, 5H)  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$  calibrated to 77.00): 23.6, 24.4, 34.6, 40.6, 48.0, 71.8, 81.0, 127.7, 127.9, 128.4, 137.9, 215.5 ppm; LRMS (EI)  $m/z$  (%) 216 (1,  $\text{M}^+$ ), 125 (10), 110 (30), 91 (100), 79 (30); HRMS ( $[\text{M}+\text{H}]^+$  calcd. = 217.1227 found = 217.1229) FTIR  $\nu = 3030, 2963, 1749, 1453, 1117\text{ cm}^{-1}$ ; Anal Calcd for  $\text{C}_{14}\text{H}_{16}\text{O}_2$ : C, 77.75%; H, 7.46%. Found: C, 78.11%; H, 7.54%.

**exo-3-Benzoxycyclo[2.2.1]heptan-2-endo-ol (13).** To a dry 50 ml round bottom flask were added 0.12 g of **12** and 1ml of 1M lithium triethylborohydride (superhydride) in THF. The reactions mixture was allowed to stir for 24h in an icebath at which time GC-MS of the crude product verified the starting material had been consumed, but two isomer of the product was observed. The product was purified by column chromatography using 5% ethyl acetate in hexanes as eluent affording 0.11g of a transparent oil. Yield: 92%  $^1\text{H}$  NMR: 1.1-1.3 (m, 3H), 1.5-1.6 (m, 1H), 1.6-1.8 (m, 2H), 2.08 (d, 1H,  $J = 4.5$  Hz), 2.45 (m, 1H), 2.45 (br s, 1H), 3.49 (m, 1H), 3.60 (m, 1H), 4.49 (dd, 2H,  $J = 12$  Hz, 37 Hz), 7.2-7.2 (m, 5H)  $^{13}\text{C}$  NMR: 19.6, 25.3, 33.6, 39.0, 44.4, 71.3, 80.2, 89.7, 127.5, 127.7, 128.3, 138.4 LRMS (EI)  $m/z$  (%) 215 (2), 127 (50), 93 (60), 91 (100), 81 (90); HRMS ( $[\text{M}+\text{H}]^+$  calcd. = 219.1385 found = 219.1383) FTIR  $\nu = 3518, 3030, 2958, 1454, 1128\text{ cm}^{-1}$ ; Anal. Calcd. for  $\text{C}_{14}\text{H}_{18}\text{O}_2$ : C, 77.03%; H, 8.31%. Found: C, 76.89%; H, 8.41%.

**trans-Bicyclo[2.2.1]heptan-2,3-diol (8).** Compound **8** was also prepared via procedure identical to that above, replacing **9** with its isomer **13**.