

## Supporting Information

### The C Ring Problem of Sterol Biosynthesis: $TiCl_4$ -Induced Rearrangement into the Anti-Markovnikov Cation Corresponding to the C-Ring

Mugio Nishizawa\*, Yoshihiro Iwamoto, Hiroko Takao, Hiroshi Imagawa, and Takumichi Sugihara

*Faculty of Pharmaceutical Sciences, Tokushima Bunri University, Yamashiro-cho, Tokushima 770-8514, Japan*

*mugi@ph.bunri-u.ac.jp*

#### *Experimental Procedure*

**Reaction of 3-Cyclopentylbutane-1,3-diol (8) with  $TiCl_4$ .** To a stirred solution of 3-cyclopentylbutane-1, 3-diol **8** (530 mg, 3.4 mmol) in  $CH_2Cl_2$  (10 mL) was added  $TiCl_4$  (1.97 g, 10.4 mmol, 3.1 equiv.) at 0 °C, and the mixture was stirred at 25 °C for 30 min. After addition of aqueous  $NH_4Cl$  solution, the mixture was extracted with  $CH_2Cl_2$ . The concentrated extract was subjected to column chromatography on silica gel eluted with hexane and ethyl acetate to give two fractions. Each fraction was further purified by HPLC using YMC-Pack R&D SIL D-SIL-5 column (250 x 20 mm) eluted with hexane-ethyl acetate to give **14** (74 mg, 16% yield), **17** (75 mg, 13% yield), **18** (148 mg, 26% yield), **19** (42 mg, 9% yield), **20** (92 mg, 16% yield), and **21** (39 mg, 7% yield) along with 1% of **12** (7 mg) as colorless oils.

**4-Methyl-1-oxaspiro[4.4]nonane (12):**  $^1H$  NMR (600 MHz in  $CDCl_3$ )  $\delta$  3.80 (1H, ddd,  $J$  = 8.5, 4.7, 4.7 Hz), 3.74 (1H, dd,  $J$  = 15.1, 7.7 Hz), 2.12 (1H, m), 2.04 (1H, m), 1.73 (3H, m), 1.55 (6H, m), 0.97 (3H, d,  $J$  = 6.6 Hz);  $^{13}C$  NMR (150 MHz in  $CDCl_3$ )  $\delta$  93.4s, 64.4t, 39.7d, 36.9t, 34.1t, 31.8t, 24.3t, 23.7t, 15.4q; HR-MS: calcd for  $C_9H_{16}O$ : 140.1201; found 140.1207.

**cis-3a-Methyloctahydrobenzofuran (14):**  $^1H$  NMR (600 MHz in  $CDCl_3$ )  $\delta$  3.92 (1H, dd,  $J$  = 8.5, 8.2 Hz), 3.84 (1H, ddd,  $J$  = 13.5, 8.5, 4.4 Hz), 3.43 (1H, dd,  $J$  = 3.3, 3.0 Hz), 1.83 (1H, m), 1.49 (2H, m), 1.32 (3H, m), 1.05 (3H, s);  $^{13}C$  NMR (150 MHz in  $CDCl_3$ )  $\delta$  82.1d, 64.9t, 40.7t, 39.3s, 32.9t, 26.3t, 22.2q, 21.9t, 20.5t; HR-MS calcd for  $C_9H_{16}O$  140.1201; found 140.1171.

**cis-2-(2-Chloro-1-methylcyclohexyl)ethanol (17):**  $^1H$  NMR (600 MHz in  $CDCl_3$ )  $\delta$  3.88 (1H, dd,  $J$  = 9.3, 3.8 Hz), 3.74 (2H, m), 1.97 (1H, m), 1.80 (5H, m),

1.47 (2H, m), 1.38 (1H, m), 1.29 (1H, br), 1.14 (1H, ddd,  $J = 14.0, 9.1, 4.9$  Hz), 1.08 (3H, s);  $^{13}\text{C}$  NMR (150 MHz in  $\text{CDCl}_3$ )  $\delta$  71.0d, 59.1t, 37.8t, 36.6s, 35.4t, 31.8t, 25.4q, 24.4t, 21.0t; HR-MS calcd. for  $\text{C}_9\text{H}_{18}\text{OCl} (\text{M}+1)^+$  177.1046, found 177.1033.

***trans*-2-(2-Chloro-1-methylcyclohexyl)ethanol (18):**  $^1\text{H}$  NMR (600 MHz in  $\text{CDCl}_3$ )  $\delta$  3.91 (1H, dd,  $J = 11.0, 4.1$  Hz), 3.75 (2H, m), 1.99 (1H, m), 1.80 (3H, m), 1.69 (1H, m), 1.63 (1H, m), 1.46 (3H, m), 1.33 (2H, m), 1.03 (3H, s);  $^{13}\text{C}$  NMR (150 MHz in  $\text{CDCl}_3$ )  $\delta$  69.5d, 58.9t, 44.1t, 38.4s, 36.6t, 32.6t, 25.9t, 21.0t, 18.6q; HR-MS calcd for  $\text{C}_9\text{H}_{18}\text{OCl} (\text{M}+1)^+$  177.1046, found 177.1041.

***cis*-7a-Methyloctahydrobenzofuran (19):**  $^1\text{H}$  NMR (600 MHz in  $\text{CDCl}_3$ )  $\delta$  3.89 (2H, m), 2.05 (1H, m), 1.57 (10H, m), 1.19 (3H, s);  $^{13}\text{C}$  NMR (150 MHz in  $\text{CDCl}_3$ )  $\delta$  80.5s, 64.5t, 42.8d, 34.3t, 3.07t, 27.2t, 25.7q, 23.0t, 22.5t; HR-MS calcd for  $\text{C}_9\text{H}_{16}\text{O}$  140.1201, found 140.1184.

***cis*-2-(2-Chloro-2-methylcyclohexyl)ethanol (20):**  $^1\text{H}$  NMR (600 MHz in  $\text{CDCl}_3$ )  $\delta$  3.75 (1H, ddd,  $J = 12.6, 7.5, 4.7$  Hz), 3.65 (1H, ddd,  $J = 14.5, 8.8, 5.8$  Hz), 1.98 (2H, m), 1.74 (2H, m), 1.67 (1H, m), 1.59 (3H, s), 1.56 (2H, m), 1.44 (3H, m), 1.35 (1H, m);  $^{13}\text{C}$  NMR (150 MHz in  $\text{CDCl}_3$ )  $\delta$  76.0s, 60.8t, 44.2d, 42.9t, 34.1t, 31.7q, 27.6t, 25.6t, 22.2t; HR-MS: calcd. for  $\text{C}_9\text{H}_{18}\text{OCl} (\text{M}+1)^+$  177.1046, found 177.1019.

***trans*-2-(2-Chloro-2-methylcyclohexyl)ethanol (21):**  $^1\text{H}$  NMR (600 MHz in  $\text{CDCl}_3$ )  $\delta$  3.76 (1H, ddd,  $J = 12.4, 7.7, 4.9$  Hz), 3.66 (1H, ddd,  $J = 14.4, 8.2, 6.3$  Hz), 2.14 (2H, m), 1.97 (1H, ddd  $J = 12.9, 3.8, 3.8$  Hz), 1.89 (1H, m), 1.83 (1H, m), 1.66 (2H, m), 1.50 (3H, s), 1.36 (4H, m), 1.13 (1H, m);  $^{13}\text{C}$  NMR (150 MHz in  $\text{CDCl}_3$ )  $\delta$  76.3s, 61.4t, 45.8d, 44.4t, 34.1t, 29.6t, 25.2t, 24.2t, 23.5q; HR-MS calcd for  $\text{C}_9\text{H}_{18}\text{OCl} (\text{M}+1)^+$  177.1046, found 177.1039.

**2-Cyclopentyl-2-methyloxetane (10).** A solution of diol **8** (500 mg, 3.16 mmol), *p*-toluenesulfonyl chloride (1.93 g, 10.02 mmol) in pyridine (15 mL) was stirred at room for 43 h. After addition of saturated sodium hydrogencarbonate solution, the mixture was extracted with ether. The dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 6:1) to give mono-tosylate (771 mg, 78% yield): FT-IR (film) 3560, 2954, 2870, 1360, 1176, 1097, 957  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  1.11 (3H, s), 1.58 (11H, m), 2.45 (3H, s), 4.23 (2H, t,  $J = 7.1$  Hz), 7.80 (2H, d,  $J = 6.6$  Hz), 7.85 (2H, d,  $J = 8.2$  Hz);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  21.7 (q), 24.5 (q), 25.9

(tx2), 26.6 (t), 27.1 (t), 39.4 (t), 50.2 (d), 67.7 (t), 73.0 (s), 128.0 (dx2), 129.9 (dx2), 133.2 (s), 144.9 (s); HR-MS (CI) calcd for  $C_{16}H_{25}O_4S$  ( $M^++1$ ) 313.1473, found 313.1476. To a THF (24 mL) solution of the above tosylate was added sodium hydride (297 mg, 4.4 mmol), and the mixture was stirred for 1.5 h at room temperature and then 1 h at reflux temperature. After cooling to 0 °C, reaction was quenched by the addition of water. The dried and concentrated extract was subjected to column chromatography on silica gel (pentane-ether 50:1) afforded oxetane **10** (275 mg, 95% yield): FT-IR (film) 2958, 2873, 1448, 1371, 1246, 995, 996, 858  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz in  $\text{CDCl}_3$ )  $\delta$  1.40-1.33 (1 H, m), 1.41 (3 H, s), 1.50-1.41 (1 H, m), 1.61-1.54 (2 H, m), 1.67-1.61 (2 H, m), 1.78-1.68 (2 H, m), 2.08 (1 H, ddd,  $J=17.2, 8.2, 0.8$  Hz), 2.23 (1 H, ddd,  $J=11.0, 9.1, 6.6$  Hz), 2.51 (1 H, ddd,  $J=10.9, 9.3, 7.1$  Hz), 4.36 (1 H, ddd,  $J=9.0, 6.0, 3.0$  Hz), 4.51 (1 H, ddd,  $J=8.7, 6.8, 6.0$  Hz);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  26.01 (t), 26.08 (t), 26.68 (t), 27.00 (q), 27.04 (t), 30.34 (t), 49.65 (d), 64.31 (t), 88.25 (s); MS (EI)  $m/z$  140 ( $M^+$ ), 122, 111, 95, 81, 67 (base), 55, 49, 41; HR-MS (EI) calcd for  $C_9H_{16}O$  140.1202, found 140.1219, as a colorless oil.

**Authentic 4-Methyl-1-oxaspiro[4.4]nonane (12).** A mixture of 1-(3-hydroxy-1-methyl-propyl)-cyclopentanol (200 mg, 1.26 mmol) and *p*-toluenesulfonyl chloride (480 mg, 2.52 mmol) in pyridine (10 mL) was stirred at room temperature for 43 h. After addition of sodium hydrogencarbonate, the mixture was extracted with ether, and the extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 30:1) to give **12** (167 mg, 95% yield) as a colorless oil.

**2-Allyl-2-methylcyclohexanone (23).** To a dioxane (50 mL) solution of acetic acid 2-methyl-cyclohex-1-enyl ester (**22**) (2.00g, 13.0 mmol) was successively added carbonic acid allyl ester methyl ester (2.95 g, 26.0 mmol), 1,2-bis(diphenylphosphino)-ethane (0.52 g, 1.3 mmol), and tris(dibenzylideneacetone)dipalladium chloroform adduct (0.67 g, 0.65 mmol), and the mixture was stirred at room temperature for 15 min. To this was added tributyltin methoxide (0.75 mL, 2.6 mmol) and the mixture was heated at reflux for 10 h. After addition of brine, organic materials were extracted with ether, and the washed and dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 10:1) to give **23** (1.78 g, 90% yield): FT-IR (film) 3076, 2935, 2868, 1712, 1639, 1452, 1377, 1313, 1215, 1124, 995, 914  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  1.07 (3 H, s), 1.91-1.53 (6 H, m), 2.42-2.04 (4 H, m), 5.08-4.98 (2 H, m), 5.80-5.58 (1 H, m);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  20.69 (e), 22.24 (o), 27.01 (e),

38.24 (e), 38.37 (e), 41.62 (e), 47.98 (e), 117.46 (e), 133.59 (o), 214.52 (e), as a colorless oil.

**cis-3a-Methyloctahydrobenzofuran-2-ol (24) and trans-(2-Hydroxy-1-methylcyclohexyl)acetaldehyde (25).** To a solution of ketone **23** (152 mg, 1.0 mmol) in 2-propanol (5 mL) was added sodium borohydride (57 mg, 1.5 mmol), and the mixture was stirred for 4 h at room temperature. After addition of 2N-HCl solution, organic materials were extracted with ether. The washed and dried extract was purified with column chromatography on silica gel (hexane and ethyl acetate 7:1). The resulting carbinol was dissolved in  $\text{H}_2\text{O}-\text{CH}_3\text{CN}$  (1:2, 6 mL), and to this was added 4-methylmorpholine *N*-oxide (194 mg, 1.66 mmol) and then 2% aq. solution of OsO<sub>4</sub> (4.0 mL, 0.08 mmol). After stirring at room temperature for 10 h, aq. sodium thiosulfate solution was added, and organic materials were extracted with ethyl acetate. The washed and dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 1:1) to give crude diols. The resulting material was dissolved in THF- $\text{H}_2\text{O}$  (3:1, 8 mL), and to this was added NaIO<sub>4</sub> (195 mg, 0.91 mmol). After stirring for 3.5 h at 0 °C,  $\text{H}_2\text{O}$  was added. The washed and dried ether extract were subjected to column chromatography on silica gel (hexane and ether 2:1). Concentrated fractions containing **24** and **25** were further purified by HPLC using YMC-Pack R&D SIL D-SIL-5 column (250 x 20 mm) eluted with hexane and ether 3:1 (flow rate 15 mL/min) to give hemiacetal **24**: <sup>1</sup>H NMR (300 MHz in CDCl<sub>3</sub>) δ 1.06 (3 H, s), 1.79-1.20 (8 H, m), 1.86 (1 H, dd, *J* = 3.6, 2.2 Hz), 2.07 (1 H, dd, *J* = 5.8, 5.7 Hz), 3.33 (1 H, br s), 3.88 (1 H, dd, *J* = 2.9, 2.4 Hz), 5.56 (1 H, ddd, *J* = 9.3, 4.9, 2.1 Hz); <sup>13</sup>C NMR (75 MHz in CDCl<sub>3</sub>) δ 19.84 (e), 20.91 (o), 21.63 (e), 25.25 (e), 39.89 (e), 40.13 (e), 49.89 (e), 80.24 (o), 96.80 (o), and aldehyde **25**: <sup>1</sup>H NMR (300 MHz in CDCl<sub>3</sub>) δ 0.92 (3H, s), 1.92-1.14 (8H, m), 2.09 (2H, dd, *J* = 12.6, 5.5 Hz), 3.30 (1H, br s), 3.47-3.42 (1H, m), 9.90 (1H, dd, *J* = 3.3, 2.7 Hz); <sup>13</sup>C NMR (75 MHz in CDCl<sub>3</sub>) δ 17.90 (o), 20.82 (e), 24.50 (e), 35.28 (e), 37.59 (e), 39.61 (e), 56.03 (e), 76.06 (o), 203.94 (e), as a colorless oils.

**Authentic cis-3a-methyl-octahydro-benzofuran (14).** To a stirred solution of triethylsilane (88 μL, 0.55 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL) was successively added trifluoroacetic acid (42 μL, 0.55 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (3 mL) solution of hemiacetal **24** (29 mg, 0.18 mmol) at -78°C. The mixture was slowly warmed to 0 °C and then stirred at this temperature for 2 h. After addition of saturated sodium hydrogencarbonate solution,

organic materials were extracted with ether. The dried extract was subjected to column chromatography on silica gel (pentane and ether 50:1) to give the ether **14** (21 mg, 83% yield) as a colorless oil.

**Authentic *trans*-2-(2-Chloro-1-methylcyclohexyl)ethanol (18).** To a solution of hemiacetal **24** (193 mg, 1.24 mmol) in 2-propanol (3 mL) was added NaBH<sub>4</sub> (23 mg, 0.62 mmol), and the mixture was stirred for 7 h at room temperature. After addition of sodium hydrogencarbonate solution, organic materials were extracted with ethyl acetate. The dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 2:1) to give cis-diol (163 mg, 83 % yield): FT-IR (film) 3327, 2933, 2868, 1565, 1454, 1379, 1053, 1024 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz in CDCl<sub>3</sub>) δ 1.02 (3 H, s), 1.72-1.11 (9 H, m), 2.01 (1 H, ddd, *J* = 5.3, 4.8, 4.4 Hz), 2.90 (2 H, br s), 3.83 (1 H, dd, *J* = 4.4, 3.9 Hz), 3.86-3.63 (2 H, m); <sup>13</sup>C NMR (75 MHz in CDCl<sub>3</sub>) δ 21.07 (e), 24.00 (e), 24.49 (o), 30.03 (e), 37.68 (e), 37.82 (e), 38.55 (e), 58.22 (e), 75.84 (o); MS (CI) *m/z* 159 (M<sup>+</sup>+1) (base), 141, 123, 96, 81; HR-MS (CI) calcd for C<sub>9</sub>H<sub>19</sub>O<sub>2</sub> (M<sup>+</sup>+1) 159.1385, found 159.1372, as a colorless oil.. Upon treatment of the above diol (24 mg, 0.15 mmol) with acetyl chloride (13 μL, 0.18 mmol) and pyridine (24 mL, 0.3 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (2 mL) at 0 °C for 30 min afforded mono-acetate (25 mg, 83 % yield): FT-IR (film) 3467, 2933, 2862, 1738, 1722, 1454, 1392, 1367, 1247, 1136, 1053, 1032 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz in CDCl<sub>3</sub>) δ 0.97 (3 H, s), 1.86-1.02 (10 H, m), 2.04 (3H, s), 3.40 (1 H, dd, *J* = 4.6, 3.0 Hz), 4.08-4.07 (2 H, m); <sup>13</sup>C NMR (75 MHz in CDCl<sub>3</sub>) δ 20.92 (e), 21.00 (o), 23.09 (e), 24.01 (o), 29.65 (e), 31.86 (e), 34.94 (e), 36.86 (e), 61.61 (e), 76.27 (o), 171.28 (e); MS (CI) *m/z* 201 (M<sup>+</sup>+1), 141, 123 (base), 96, 81; HR-MS (CI) calcd for C<sub>11</sub>H<sub>21</sub>O<sub>3</sub> (M<sup>+</sup>+1) 201.1490, found 201.1496, as a colorless oil after column chromatography on silica gel (hexane and ethyl acetate 10:1). The above mono-acetate and triphenylphosphine (49 mg, 0.19 mmol) were dissolved in CCl<sub>4</sub> (2.5 mL), and the mixture was heated to reflux for 68 h. To this was added pentane (2 mL), and the precipitates were removed by filtration through Celite. The concentrated filtrate was subjected to column chromatograph on silica gel (hexane and ethyl acetate 30:1) and then HPLC using YMC-Pack R&D SIL D-SIL-5 column (250 x 20 mm) eluted with hexane and ethyl acetate 40:1 (flow rate 15 mL/min) to give inverted chloro acetate **18a** (7 mg, 26% yield) as a colorless oil along with olefinic products. Hydrolysis of acetate with NaOMe-MeOH afforded **18**.

***trans*-3a-Methyloctahydrobenzofuran (15).** To a solution of aldehyde **25** (156

mg, 1.0 mmol) in 2-propanol (3 mL) was added  $\text{NaBH}_4$  (19 mg, 0.50 mmol), and the mixture was stirred at room temperature for 3.5 h. The dried and concentrated ethyl acetate extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 2.5:1) to give *trans*-diol (129 mg, 82 % yield): FT-IR (film) 3327, 2933, 2868, 1565, 1454, 1379, 1053, 1024  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  1.02 (3 H, s), 1.72-1.11 (9 H, m), 2.01 (1 H, ddd,  $J$  = 5.3, 4.8, 4.4 Hz), 2.90 (2 H, br s), 3.83 (1 H, dd,  $J$  = 4.4, 3.9 Hz), 3.86-3.63 (2 H, m);  $^{13}\text{C}$  NMR (75 MHz in  $\text{CDCl}_3$ )  $\delta$  21.07 (e), 24.00 (e), 24.49 (o), 30.03 (e), 37.68 (e), 37.82 (e), 38.55 (e), 58.22 (e), 75.84 (o); MS (CI)  $m/z$  159 ( $\text{M}^++1$ ) (base), 141, 123, 96, 81; HR-MS (CI) calcd for  $\text{C}_9\text{H}_{19}\text{O}_2$  ( $\text{M}^++1$ ) 159.1385, found 159.1372, as a colorless oil.. The *trans*-diol (78 mg, 0.49 mmol) was treated with *p*-toluenesulfonyl chloride (197 mg, 1.04 mmol) in pyridine (5 mL) at room temperature for 5 h. After aqueous work-up, the ether extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 15:1) to give *trans* fused ether **15** (23 mg, 33% yield): FT-IR (film) 2935, 2873, 2360, 1456, 1377, 1279, 1147, 1070, 1031  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  0.85 (3 H, s), 1.87-1.18 (10 H, m), 3.06 (1 H, dd,  $J$  = 3.8, 3.2 Hz), 3.87 (2 H, ddd,  $J$  = 8.4, 6.6, 3.2 Hz);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  16.77 (o), 21.15 (e), 24.57 (e), 25.42 (e), 35.83 (e), 40.06 (e), 40.25 (e), 65.04 (e), 84.65 (o); MS (CI)  $m/z$  139 ( $\text{M}^+-1$ ), 123, 109, 96, 81, 67, 41 (base); HR-MS (CI) calcd for  $\text{C}_9\text{H}_{16}\text{O}$  ( $\text{M}^+-1$ ) 139.1123, found 139.1133, as a colorless oil. This compound was not detected in the reaction product of diol **8** and  $\text{TiCl}_4$ .

**Authentic *cis*-2-(2-Chloro-1-methylcyclohexyl)ethanol (17).** *trans*-Diol (43 mg, 0.27 mmol) obtained by the  $\text{NaBH}_4$  reduction of aldehyde **25** was treated with acetyl chloride (23  $\mu\text{L}$ , 0.32 mmol) and pyridine (44  $\mu\text{L}$ , 0.54 mmol) in  $\text{CH}_2\text{Cl}_2$  (2 mL) to give mono-acetate (43 mg, 80 % yield): FT-IR (film) 3458, 2929, 2862, 1738, 1714, 1365, 1236, 1030  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  0.93 (3 H, s), 1.84-1.21 (10 H, m), 2.05 (3 H, s), 3.39 (1 H, dd,  $J$  = 6.4, 3.8 Hz), 4.19 (2 H, t,  $J$  = 7.8 Hz);  $^{13}\text{C}$  NMR (75 MHz in  $\text{CDCl}_3$ )  $\delta$  16.63(o), 20.86 (o), 20.95(e), 24.23 (o), 30.27 (e), 35.78 (e), 37.40 (e), 39.31 (e), 61.42 (e), 75.42 (o), 171.19 (e), as a colorless oil. A solution of this mono-acetate (50 mg, 0.25 mmol) and triphenylphosphine (98 mg, 0.37 mmol) in  $\text{CCl}_4$  (5 mL) was heated to reflux for 68 h. Precipitates formed by the addition of pentane were removed by filtration, and the concentrated filtrate was subjected to a column chromatography on silica gel (hexane and ethyl acetate 30:1) and then HPLC with YMS-Pack R&D SIL D-SIL-5 column (250 x 10mm) eluted with hexane and ethyl acetate (40:1)

(flow rate 15 mL/min) to give inverted cis chloro acetate **17a** (7 mg, 13 % yield): FT-IR (film) 2943, 2846, 1747, 1456, 1367, 1252, 1142, 1034  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (300 MHz in  $\text{CDCl}_3$ )  $\delta$  1.08 (3 H, s), 1.15 (1H, ddd,  $J$  = 9.4, 9.1, 8.6 Hz), 1.54-1.29 (3 H, m), 1.90-1.69 (6 H, m), 2.05 (3 H, s), 3.85 (1 H, dd,  $J$  = 9.3, 4.1 Hz), 4.21-4.07 (2 H, m);  $^{13}\text{C}$  NMR (75 MHz in  $\text{CDCl}_3$ )  $\delta$  21.01 (e), 21.17 (o), 24.70 (e), 25.53 (o), 31.96 (e), 31.96 (e), 35.44 (e), 37.87 (e), 61.22 (e), 70.88 (o), 171.24 (e), as a colorless oil along with olefinic products. Hydrolysis of the acetyl moiety by the treatment with NaOMe-MeOH afforded **17**.

**cis-2-Allyl-1-methylcyclohexanol (27).** To a stirred solution of 2-allylcyclohexanone (**26**) (700 mg 5.1 mmol) in THF (5 mL) was dropwise added allylmagnesium chloride (3.0 M THF solution, 4.2 mL, 12.4 mmol) at 0 °C, and the mixture was stirred an additional 40 min at the same temperature. After addition of aq.  $\text{NH}_4\text{Cl}$ , organic material was extracted with ether, and the washed and dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 15:1) to give carbinol **27** (585 mg, 73 % yield): FT-IR (film) 3365, 2937, 2862, 1651, 1446, 1377, 1265, 1159, 1056, 1018  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  1.24 (3 H, s), 1.73-1.03 (10 H, m), 1.93 (1 H, dddd,  $J$  = 8.0, 4.1, 1.2, 0.9 Hz), 2.45-2.37 (1 H, m), 5.07-4.97 (2 H, m), 5.89-5.75 (1 H, m);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  21.95 (e), 25.61 (e), 27.01 (e), 28.78 (o), 34.19 (e), 40.26 (e), 45.41 (o), 71.32 (e), 115.50 (e), 138.20 (o); MS (CI)  $m/z$  154 ( $\text{M}^++1$ ), 137, 95 (base), 81, 71, 43; HR-MS (CI) calcd for  $\text{C}_{10}\text{H}_{18}\text{O}$  ( $\text{M}^++1$ ) 154.1358, found 154.1338, as a colorless oil.

**cis-7a-Methyloctahydrobenzofuran-2-ol (28).** To a solution of carbinol **27** (305 mg, 2.0 mmol) in  $\text{CH}_3\text{CN}-\text{H}_2\text{O}$  (2:1, 15 mL) was added 4-methylmorpholine *N*-oxide (469 mg, 4.0 mmol) and then 2% aq. solution of  $\text{OsO}_4$  (1.0 mL, 0.02 mmol). After stirring at room temperature for 3 h, aq. sodium thiosulfate solution was added, and organic materials were extracted with ethyl acetate. The washed and dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 1:1) to give crude diols. The resulting material was dissolved in  $\text{THF}-\text{H}_2\text{O}$  (3:1, 16 mL), and to this was added  $\text{NaIO}_4$  (381 mg, 1.78 mmol). After stirring for 4 h at 0 °C,  $\text{H}_2\text{O}$  was added. The washed and dried ether extract was subjected to column chromatography on silica gel (hexane and ether 2:1) to give hemiacetal **28** (195 mg, 62 % yield):  $^1\text{H}$  NMR (major isomer, 300 MHz in  $\text{CDCl}_3$ )  $\delta$  1.35 (3 H, s), 1.74-1.21 (7 H, m), 2.28-1.89 (4 H, m), 2.93 (1 H, br s), 5.56-5.14 (1 H, m);  $^{13}\text{C}$  NMR (75 MHz in  $\text{CDCl}_3$ )  $\delta$  21.80 (e), 22.79

(e), 26.52 (e), 27.06 (o), 35.74 (e), 38.56 (e), 41.18 (o), 82.53 (e), 96.98 (o), as a colorless oil.

**Authentic *cis*-7a-methyloctahydrobenzofuran (19).** To a stirred solution of triethylsilane (151  $\mu$ L, 0.95 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was successively added trifluoroacetic acid (73  $\mu$ L, 0.95 mmol) and  $\text{CH}_2\text{Cl}_2$  (3 mL) solution of hemiacetal **28** (50 mg, 0.32 mmol) at  $-78$   $^{\circ}\text{C}$ . The mixture was slowly warmed to  $0$   $^{\circ}\text{C}$  and then stirred at this temperature for 1.5 h. After addition of saturated sodium hydrogencarbonate solution, organic materials were extracted with ether. The dried extract was subjected to column chromatography on silica gel (pentane and ether 50:1) to give the ether **20** (35 mg, 76% yield) as a colorless oil.

**Authentic *cis*-2-(2-chloro-2-methylcyclohexyl)ethanol (20).** To a solution of hemiacetal **28** (115 mg, 0.74 mmol) in 2-propanol (5 mL) was added  $\text{NaBH}_4$  (14 mg, 0.37 mmol), and the mixture was stirred at room temperature for 4 h. After addition of 2N-HCl solution, organic materials were extracted with ethyl acetate, and the washed and dried extract was subjected to column chromatography on silica gel (hexane and ethyl acetate 2:1) to give a diol (100 mg, 85 % yield): FT-IR (film) 3365, 2937, 2862, 1651, 1446, 1377, 1265, 1159, 1056, 1018  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz in  $\text{CDCl}_3$ )  $\delta$  1.26 (3 H, s), 1.76-1.28 (10 H, m), 3.82-3.56 (2 H, m);  $^{13}\text{C}$  NMR (50 MHz in  $\text{CDCl}_3$ )  $\delta$  21.98 (e), 25.68 (e), 26.92 (e), 28.74 (q), 32.47 (e), 40.03 (e), 43.45 (o), 59.56 (e), 70.89 (e), as a colorless oil. Above diol (75 mg, 0.47 mmol) was dissolved in ether (5 mL) and water 3 drops and then conc-HCl (5 drops) were added. After stirring for 15 min at room temperature, organic materials were extracted with ether. The washed and dried extract was subjected to a column chromatography on silica gel (hexane and ether 3:1) to give **20** (25 mg, 30 % yield) as a colorless oil. *trans*-Isomer **21** was not detected at all.