

## Model studies toward the synthesis of the bioactive diterpenoid, harringtonolide

Timothy P. O'Sullivan<sup>a\*</sup>, Hongbin Zhang<sup>b</sup> and Lewis N. Mander<sup>c</sup>

Receipt/Acceptance Data [DO NOT ALTER/DELETE THIS TEXT]

Publication data [DO NOT ALTER/DELETE THIS TEXT]

DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

### Experimental

#### 10 Methyl (1SR, 4RS, 4aSR, 9aSR)-1,4,4a,9a-tetrahydro-6-methoxy-3,9-dioxo-1,4-ethenoindeno[2,1-c]pyran-4(3H)-carboxylate (25).

The indenone **12** (550 mg, 3.44 mmol) and the pyrone **24** (504 mg, 3.27 mmol) were dissolved in dichloromethane (1 ml).  
15 The reaction mixture was then subjected to high pressure (19 Kbar) for 24 hours. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to yield the cycloadduct **25** (736 mg, 72%, based on pyrone).  
20 Recrystallisation from ethyl acetate afforded colourless crystals; mp 131-133 °C (from EtOAc); Found: C, 64.51%; H, 4.79%. Calc. for C<sub>17</sub>H<sub>14</sub>O<sub>6</sub>: C, 64.97%; H, 4.49%;  $\nu_{\max}/\text{cm}^{-1}$  3085 (ArH), 1763 (C=O), 1740 (C=O), 1256 (ArOCH<sub>3</sub>), 1092 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.62 (1H, d,  $J$  = 8.6 Hz, H-8),  
25 6.94 (1H, dd,  $J$  = 8.6 Hz,  $J$  = 2.2 Hz, H-7), 6.51 (1H, d,  $J$  = 2.0 Hz, H-5), 6.36 (2H, m, H-10, H-11), 5.45 (1H, ddd,  $J$  = 5.0 Hz,  $J$  = 5.4 Hz,  $J$  = 2.0 Hz, H-1), 4.32 (1H, d,  $J$  = 7.1 Hz, H-4a), 4.03 (3H, s, COOCH<sub>3</sub>), 3.85 (3H, s, CH<sub>3</sub>O-C6), 3.63 (1H, dd,  $J$  = 7.1 Hz,  $J$  = 5.0 Hz, H-9a);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>)  
30 199.00 (C9), 169.48 (C3), 168.13 (C12), 166.14 (C6), 154.00 (C4b), 132.03 (C8a), 130.57 (C11), 129.75 (C10), 126.24 (C8), 117.05 (C5), 109.87 (C7), 74.95 (C1), 59.90 (C4), 56.09 (CH<sub>3</sub>O-C6), 53.74 (COOCH<sub>3</sub>), 52.83 (C9a), 39.50 (C4a);  $m/z$   
35 314 (M<sup>+</sup>, 24%), 268 (3), 242 (27), 226 (4), 211 (100), 168 (20), 160 (93), 139 (29), 134 (29), 123 (6), 106 (35), 91 (3), 77 (10), 63 (26).

#### 40 Methyl (1SR, 4RS, 4aSR, 9RS, 9aRS)-1,4,4a,9a-tetrahydro-9-hydroxy-6-methoxy-3-oxo-1,4-ethenoindeno[2,1-c]pyran-4(3H)-carboxylate (29).

Sodium borohydride (3 mg, 0.31 mmol) was added to the ketone **25** (50 mg, 0.16 mmol) in a 1:1 solution of dichloromethane/methanol (5 ml) and stirred for 6 hours at room temperature. Acetone (1 ml) was added to decompose  
45 the excess borohydride. The solution was acidified with 2M HCl (1 ml) and extracted with ethyl acetate (3x20 ml). The organic phase was washed with brine (10 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on  
50 silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to yield the alcohol **130** (39 mg, 77%). Recrystallisation from ethyl acetate afforded colourless crystals; mp 139-141 °C (from EtOAc); Found: C, 64.72%; H, 5.17%. Calc. for

C<sub>17</sub>H<sub>16</sub>O<sub>6</sub>: C, 64.55%; H, 5.10%;  $\nu_{\max}/\text{cm}^{-1}$  3515 (OH), 3013  
55 (ArH), 1755 (C=O), 1268 (ArOCH<sub>3</sub>), 1109 (C-O), 1094 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.22 (1H, d,  $J$  = 8.4 Hz, H-8), 6.85 (1H, dd,  $J$  = 8.4 Hz,  $J$  = 2.2 Hz, H-7), 6.51 (1H, d,  $J$  = 2.2 Hz, H-5), 6.48 (1H, dd,  $J$  = 4.5 Hz,  $J$  = 4.1 Hz, H-11), 6.38 (1H, dd,  $J$  = 4.5 Hz,  $J$  = 2.1 Hz, H-10), 5.45 (1H, ddd,  $J$  = 4.0 Hz,  $J$   
60 = 4.1 Hz,  $J$  = 2.1 Hz, H-1), 5.34 (1H, d,  $J$  = 8.8 Hz, H-9), 4.27 (1H, d,  $J$  = 8.2 Hz, H-4a), 4.04 (3H, s, COOCH<sub>3</sub>), 3.75 (3H, s, CH<sub>3</sub>O-C6), 3.64 (1H, ddd,  $J$  = 8.2 Hz,  $J$  = 8.8 Hz,  $J$  = 4.0 Hz, H-9a);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 171.31 (C3), 169.11 (C12), 161.38 (C6), 140.68 (C4b), 138.16 (C8a), 131.41 (C11), 130.46  
65 (C10), 126.13 (C8), 115.91 (C5), 109.24 (C7), 76.26 (C1), 73.57 (C9), 60.88 (C4), 55.89 (CH<sub>3</sub>O-C6), 53.75 (COOCH<sub>3</sub>), 47.04 (C9a), 45.01 (C4a);  $m/z$  316 (M<sup>+</sup>, 28%), 290 (48), 272 (64), 254 (56), 240 (50), 223 (24), 211 (57), 195 (77), 184 (45), 162 (100), 152 (50), 135 (36), 115 (37), 102 (19), 91  
70 (27), 77 (29), 63 (17).

#### 75 Methyl (1SR, 4RS, 4aSR, 9RS, 9aRS, 10RS, 11SR)-1,4,4a,9a-tetrahydro-9-hydroxy-10,11-methano-6-methoxy-3-oxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (30).

The alcohol **29** (20 mg, 0.06 mmol) and palladium acetate (1 mg, 0.004 mmol) were dissolved in dichloromethane (5 ml). An excess of ethereal diazomethane (~10 equiv) was added  
80 over 30 minutes at 0°C. The solution was stirred at room temperature for 16 hours until the yellow colour had disappeared. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to yield the cyclopropyl product **30** (20 mg, 95%).  
85 Recrystallisation from ethyl acetate afforded colourless crystals. mp 129-130 °C (from EtOAc); Found: C, 65.03%; H, 5.32%. Calc. for C<sub>18</sub>H<sub>18</sub>O<sub>6</sub>: C, 65.45%; H, 5.49%;  $\nu_{\max}/\text{cm}^{-1}$  3530 (OH), 3005 (ArH), 1754 (C=O), 1269 (ArOCH<sub>3</sub>), 1095 (C-O), 1056 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.28 (1H, d,  $J$  = 8.4 Hz, H-8), 6.89 (1H, dd,  $J$  = 8.4 Hz,  $J$  = 2.2 Hz, H-7), 6.56 (1H, d,  $J$  = 2.4 Hz, H-5), 5.49 (1H, d,  $J$  = 8.9 Hz, H-9), 5.06 (1H, d,  $J$  = 3.3 Hz, H-1), 4.09 (1H, d,  $J$  = 9.2 Hz, H-4a), 3.97 (3H, s, COOCH<sub>3</sub>), 3.77 (3H, s, CH<sub>3</sub>O-C6), 3.34 (1H, ddd,  $J$  = 9.2 Hz,  $J$  = 8.9 Hz,  $J$  = 3.3 Hz, H-9a), 1.52 (1H, m,  $J$  = 8.0  
95 Hz,  $J$  = 4.2 Hz, H-11), 1.07 (1H, m,  $J$  = 7.9 Hz,  $J$  = 4.2 Hz, H-10), 0.57-0.50 (2H, m, 2x H-13);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 171.09 (C3), 170.83 (C12), 160.95 (C6), 140.5 (C4b), 138.28 (C8a), 126.08 (C8), 115.44 (C5), 109.92 (C7), 75.13 (C1), 73.92 (C9), 57.18 (C4), 55.97 (CH<sub>3</sub>O-C6), 53.69 (COOCH<sub>3</sub>), 47.27  
100 (C9a), 46.03 (C4a), 10.21 (C11), 9.43 (C10), 3.46 (C13);  $m/z$

330 (M<sup>+</sup>, 87%), 299 (4), 280 (4), 270 (5), 253 (6), 225 (10), 209 (14), 197 (5), 175 (6), 162 (100), 147 (36), 139 (12), 126 (11), 115 (10), 102 (7), 91 (12), 77 (11), 59 (8)

105 **Methyl 4-methyl-2-oxo-2H-pyran-3-carboxylate (32).**

The pyrone **24** (5 g, 32.5 mmol) was dissolved in dichloromethane (100 ml) and cooled to 0°C. Ethereal diazomethane was added in portions over 1 hour until all the starting material had been consumed as monitored by TLC. 110 Stirring at room temperature was continued for a further 16 hours. The solvent was removed under reduced pressure and the residue was purified by flash chromatography directly on silica gel (petroleum ether : ethyl acetate = 1:1) to yield the pyrone **32** (4.525 g, 82%). Recrystallisation from ethyl acetate 115 afforded colourless crystals; mp 86-88 °C (from EtOAc); Found: C, 56.88%; H, 4.73%. Calc. for C<sub>8</sub>H<sub>8</sub>O<sub>4</sub>: C, 57.14%; H, 4.80%;  $\nu_{\max}/\text{cm}^{-1}$  3070 (=CH), 2970 (CH), 1701 (C=O), 1268 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.44 (1H, d,  $J$  = 5.4 Hz, H-6), 6.14 (1H, d,  $J$  = 5.4 Hz, H-5), 3.91 (3H, s, COOCH<sub>3</sub>), 2.26 120 (3H, s, CH<sub>3</sub>-C4);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 165.49 (COOCH<sub>3</sub>), 159.51 (C2), 156.02 (C4), 151.85 (C6), 119.89 (C3), 110.33 (C5), 53.25 (COOCH<sub>3</sub>), 20.74 (CH<sub>3</sub>-C4);  $m/z$  168 (M<sup>+</sup>, 73%), 140 (89), 137 (100), 125 (13), 112 (72), 109 (92), 97 (33), 82 (45), 67 (31), 59 (17).

125 **Methyl (1SR, 4SR, 4aSR, 9aSR)-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-3,9-dioxo-1,4-ethenoindeno[2,1-c]pyran-4(3H)-carboxylate (33).**

The indenone **12** (500 mg, 1.05 mmol) and the pyrone **32** (500 130 mg, 1 mmol) were dissolved in a minimum of dichloromethane (1 ml). The reaction mixture was then subjected to high pressure (19 Kbar) for 20 hours. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to yield the cycloadduct 135 **33** (713 mg, 73%, based on pyrone). Recrystallisation from ethyl acetate afforded colourless crystals; mp 129-131 °C (from EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3000 (ArH), 1745 (C=O), 1258 (ArOCH<sub>3</sub>), 1095 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.63 (1H, d,  $J$  = 8.5 Hz, H-8), 7.12 (1H, d,  $J$  = 2.2 Hz, H-5), 6.95 (1H, dd,  $J$  = 8.5 Hz,  $J$  = 2.2 Hz, H-7), 5.97 (1H, d,  $J$  = 5.0 Hz, H-11), 5.56 (1H, dd,  $J$  = 4.9 Hz,  $J$  = 5.0 Hz, H-1), 4.39 (1H, d,  $J$  = 6.8 Hz, H-4a), 4.03 (3H, s, COOCH<sub>3</sub>), 3.86 (3H, s, CH<sub>3</sub>O-C6), 3.53 (1H, dd,  $J$  = 6.8 Hz,  $J$  = 4.9 Hz, H-9a), 1.55 (3H, s, CH<sub>3</sub>-C10); 145  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 200.35 (C9), 170.55 (C3), 168.75 (C12), 166.29 (C6), 154.69 (C4b), 140.59 (C10), 132.64 (C8a), 126.54 (C8), 124.29 (C11), 117.11 (C5), 111.26 (C7), 74.54 (C1), 63.78 (C4), 56.40 (CH<sub>3</sub>O-C6), 53.69 (COOCH<sub>3</sub>), 53.34 (C9a), 39.80 (C4a), 20.44 (CH<sub>3</sub>-C10);  $m/z$  328 (M<sup>+</sup>, 29%), 282 150 (3), 253 (4), 225 (89), 210 (4), 184 (10), 160 (100), 153 (12), 134 (14), 106 (17), 63 (14).

155 **Methyl (1SR, 4SR, 4aSR, 9RS, 9aRS)-1,4,4a,9a-tetrahydro-9-hydroxy-6-methoxy-10-methyl-3-oxo-1,4-ethenoindeno[2,1-c]pyran-4(3H)-carboxylate (34).**

The ketone **33** (400 mg, 1.2 mmol) was dissolved in a 1:1 solution of dichloromethane/methanol (20 ml). Sodium borohydride (46 mg, 1.2 mmol) was added and the reaction mixture was stirred at room temperature for 16 hours. Acetone

160 (2 ml) was added to decompose the excess borohydride. The solvent was removed under reduced pressure and the residue was redissolved in ethyl acetate (100 ml). The solution was acidified with 2M HCl (10 ml) and washed with water (20 ml), brine (20 ml) and dried over magnesium sulfate. After 165 filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the alcohol **34** (342 mg, 85%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3486 (OH), 3012 (ArH), 2953 (CH), 1749 (C=O), 1273 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.22 (1H, d,  $J$  = 8.3 Hz, H-8), 6.85 (1H, dd,  $J$  = 8.3 Hz,  $J$  = 2.3 Hz, H-7), 6.80 (1H, d,  $J$  = 2.3 Hz, H-5), 6.04 (1H, d,  $J$  = 4.4 Hz, H-11), 5.33 (1H, d,  $J$  = 8.4 Hz, H-9), 5.31 (1H, dd,  $J$  = 4.1 Hz,  $J$  = 4.5 Hz, H-1), 4.34 (1H, d,  $J$  = 8.1 Hz, H-4a), 4.03 (3H, s, COOCH<sub>3</sub>), 3.77 (3H, s, CH<sub>3</sub>O-C6), 170 3.52 (1H, ddd,  $J$  = 8.1 Hz,  $J$  = 3.8 Hz,  $J$  = 8.4 Hz, H-9a), 1.63 (3H, s, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 171.67 (C3), 169.12 (C12), 161.03 (C6), 140.79 (C4b), 140.52 (C10), 138.31 (C8a), 125.98 (C8), 125.50 (C11), 115.65 (C5), 110.36 (C7), 75.26 (C1), 73.80 (C9), 64.49 (C4), 56.01 (CH<sub>3</sub>O-C6), 53.47 (COOCH<sub>3</sub>), 49.31 (C9a), 46.83 (C4a), 20.81 (CH<sub>3</sub>-C10);  $m/z$  330 (M<sup>+</sup>, 24%), 300 (1), 286 (17), 268 (9), 254 (45), 236 (14), 225 (71), 209 (59), 195 (17), 184 (10), 175 (58), 162 (100), 147 (42), 135 (54), 119 (15), 102 (15), 91 (21), 77 (17), 65 (12).

185 **Methyl (1RS, 4SR, 4aSR, 9RS, 9aRS, 10RS, 11SR)-1,4,4a,9a-tetrahydro-9,11-dihydroxy-6-methoxy-10-methyl-3-oxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (35).**

190 2M Borane-dimethyl sulfide in tetrahydrofuran (2 ml, 4 mmol) was added dropwise over 5 minutes to the alkene **34** (815 mg, 2.47 mmol) in tetrahydrofuran (25 ml) at 0°C. Stirring was continued at room temperature for 10 hours. Triethylamine *N*-oxide (900 mg, 8.1 mmol) was added and the 195 mixture was heated under for 16 hours. The solution was filtered through a short pad of silica gel and the solvent was removed under vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 1:1) to afford the alcohol **35** (423 mg, 49%) as a 200 colourless oil and starting material (80 mg);  $\nu_{\max}/\text{cm}^{-1}$  3445 (OH), 3010 (ArH), 2951 (CH), 1738 (C=O), 1271 (ArOCH<sub>3</sub>), 1114 (C-O), 1034 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.29 (1H, d,  $J$  = 8.7 Hz, H-8), 6.92 (1H, dd,  $J$  = 8.7 Hz,  $J$  = 1.7 Hz, H-7), 6.85 (1H, d,  $J$  = 1.7 Hz, H-5), 5.50 (1H, d,  $J$  = 9.5 Hz, H-9), 4.94 (1H, d,  $J$  = 4.2 Hz, H-1), 4.13 (1H, d,  $J$  = 9.9 Hz, H-4a), 4.08 (1H, d,  $J$  = 5.5 Hz, H-11), 3.96 (3H, s, COOCH<sub>3</sub>), 3.77 (3H, s, CH<sub>3</sub>O-C6), 3.31 (1H, ddd,  $J$  = 9.9 Hz,  $J$  = 4.2 Hz,  $J$  = 9.5 Hz, H-9a), 2.31 (1H, dq,  $J$  = 7.2 Hz,  $J$  = 5.5 Hz, H-10), 0.60 (3H, d,  $J$  = 7.2 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 210 173.54 (C3), 170.02 (C12), 161.01 (C6), 141.27 (C4b), 136.59 (C8a), 126.52 (C8), 116.21 (C5), 112.06 (C7), 83.19 (C11), 73.69 (C9), 72.49 (C1), 59.27 (C4), 56.04 (CH<sub>3</sub>O-C6), 53.50 (COOCH<sub>3</sub>), 44.85 (C9a), 42.29 (C4a), 41.98 (C10), 16.53 (CH<sub>3</sub>-C10);  $m/z$  348 (M<sup>+</sup>, 100%), 330 (25), 317 (10), 299 (8), 215 271 (19), 258 (29), 241 (46), 227 (49), 211 (34), 199 (22), 185 (30), 175 (59), 158 (32), 145 (42), 127 (24), 115 (28), 102 (12), 91 (12), 77 (12), 59 (11).

**Methyl (1RS, 4SR, 4aSR, 9aSR, 10RS)-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-3,9,11-trioxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (36).**

*tert.*-Butyl alcohol (990  $\mu$ l, 10.34 mmol) was added to the Dess Martin periodinane (2.14 g, 5.17 mmol) in tetrahydrofuran (50 ml) and the solution was stirred for 20 minutes. The diol **35** (600 mg, 1.72 mmol) in tetrahydrofuran (5 ml) was added via syringe over 10 minutes. The solution was stirred for a further 2 hours at room temperature. A 1:1 mixture of saturated aqueous sodium thiosulfate and sodium bicarbonate (20 ml) was added and stirring was continued for 20 minutes. The product was extracted with ethyl acetate (3x50 ml) and the combined organic phase was washed with saturated sodium thiosulfate (20 ml) and brine (20 ml). After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the diketone **36** (285 mg, 48%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3006 (ArH), 2950 (CH), 1772 (C=O), 1741 (C=O), 1258 (ArOCH<sub>3</sub>), 1152 (C-O), 1098 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.15 (1H, d,  $J = 8.6$  Hz, H-8), 7.07 (1H, d,  $J = 2.1$  Hz, H-5), 7.01 (1H, dd,  $J = 8.6$  Hz,  $J = 2.1$  Hz, H-7), 5.09 (1H, d,  $J = 5.4$  Hz, H-1), 4.55 (1H, d,  $J = 8.7$  Hz, H-4a), 4.03 (3H, s, COOCH<sub>3</sub>), 3.87 (3H, s, CH<sub>3</sub>O-C6), 3.71 (1H, dd,  $J = 8.7$  Hz,  $J = 5.4$  Hz, H-9a), 3.17 (1H, q,  $J = 7.3$  Hz, H-10), 0.49 (3H, d,  $J = 7.3$  Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 203.20 (C11), 196.45 (C9), 170.01 (C3), 168.07 (C12), 166.93 (C6), 154.65 (C4b), 131.02 (C8a), 127.54 (C8), 117.98 (C5), 112.22 (C7), 81.89 (C1), 60.16 (C4), 56.52 (CH<sub>3</sub>O-C6), 54.13 (COOCH<sub>3</sub>), 51.58 (C9a), 44.36 (C10), 39.41 (C4a), 12.45 (CH<sub>3</sub>-C10);  $m/z$  344 (M<sup>+</sup>, 100%), 312 (33), 300 (3), 285 (6), 268 (17), 257 (61), 248 (33), 241 (53), 229 (27), 213 (21), 200 (27), 190 (39), 174 (16), 161 (37), 145 (12), 127 (74), 115 (21), 102 (15), 89 (10), 77 (13), 59 (19).

**Methyl (1RS, 4SR, 4aSR, 9aSR, 10SR)-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-3,9,11-trioxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (37).**

DBU (10  $\mu$ l, 0.07) was added to a solution of diketone **36** (200 mg, 0.58 mmol) in tetrahydrofuran (20 ml) and stirred for 16 hours. The solvent was removed under reduced pressure and the residue was purified using MPLC (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the epimer **37** (144 mg, 72%) as a colourless oil and starting material (41 mg);  $\nu_{\max}/\text{cm}^{-1}$  3005 (ArH), 2955 (CH), 1773 (C=O), 1741 (C=O), 1258 (Ar-OCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.73 (1H, d,  $J = 8.7$  Hz, H-8), 7.04 (1H, dd,  $J = 8.7$  Hz,  $J = 2.2$  Hz, H-7), 6.59 (1H, d,  $J = 2.2$  Hz, H-5), 4.96 (1H, d,  $J = 5.1$  Hz, H-1), 4.54 (1H, d,  $J = 8.4$  Hz, H-4a), 4.05 (3H, s, COOCH<sub>3</sub>), 3.88 (3H, s, CH<sub>3</sub>O-C6), 3.70 (1H, dd,  $J = 8.4$  Hz,  $J = 5.1$  Hz, H-9a), 2.34 (1H, q,  $J = 7.4$  Hz, H-10), 1.35 (3H, d,  $J = 7.4$  Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 203.14 (C11), 196.14 (C9), 168.13 (C3), 168.10 (C12), 167.04 (C6), 152.31 (C4b), 131.14 (C8a), 127.67 (C8), 117.79 (C5), 110.32 (C7), 82.05 (C1), 58.37 (C4), 56.46 (CH<sub>3</sub>O-C6), 53.93 (COOCH<sub>3</sub>), 50.50 (C9a), 42.68 (C10), 42.42 (C4a), 14.72 (CH<sub>3</sub>-C10);  $m/z$  344 (M<sup>+</sup>, 100%), 312 (22), 299 (2), 285 (4), 268 (7), 257 (70), 241 (28), 229 (26), 213 (13), 200 (26), 190 (54), 174 (13), 161 (35), 145 (11), 127 (82), 115 (15), 95 (10), 77 (8), 59 (13).

**Methyl (1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-1,4,4a,9a-tetrahydro-9,11-dihydroxy-6-methoxy-10-methyl-3-oxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (38).**

Sodium borohydride (109 mg, 2.87 mmol) was added to the diketone **37** (330 mg, 0.96 mmol) in a 10:1 solution of tetrahydrofuran/methanol (20 ml) and stirred for 6 hours. The solution was acidified with 2M HCl (10 ml) and extracted with ethyl acetate (3x80 ml). The combined organic phase was washed with brine (30 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 1:1) to afford the diol **38** (221 mg, 66%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3392 (OH), 2953 (ArH), 1732 (C=O), 1260 (Ar-OCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.35 (1H, d,  $J = 8.3$  Hz, H-8), 6.92 (1H, dd,  $J = 8.3$  Hz,  $J = 1.9$  Hz, H-7), 6.44 (1H, d,  $J = 1.9$  Hz, H-5), 5.35 (1H, d,  $J = 9.9$  Hz, H-9), 4.92 (1H, d,  $J = 3.8$  Hz, H-1), 4.13 (1H, d,  $J = 10.3$  Hz, H-4a), 3.96 (3H, s, COOCH<sub>3</sub>), 3.78 (3H, s, CH<sub>3</sub>O-C6), 3.77 (1H, d,  $J = 3.4$  Hz, H-11), 3.49 (1H, ddd,  $J = 10.3$  Hz,  $J = 3.8$  Hz,  $J = 9.9$  Hz, H-9a), 2.04 (1H, dq,  $J = 7.0$  Hz,  $J = 3.4$  Hz, H-10), 1.27 (3H, d,  $J = 7.0$  Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 169.98 (C3), 169.43 (C12), 161.23 (C6), 138.93 (C4b), 138.61 (C8a), 126.11 (C8), 115.75 (C5), 110.02 (C7), 78.64 (C11), 74.34 (C9), 74.26 (C1), 60.99 (C4), 55.93 (CH<sub>3</sub>O-C6), 53.40 (COOCH<sub>3</sub>), 45.98 (C9a), 45.59 (C4a), 38.34 (C10), 14.76 (CH<sub>3</sub>-C10);  $m/z$  348 (M<sup>+</sup>, 100%), 330 (48), 317 (6), 299 (13), 271 (11), 258 (24), 253 (25), 241 (36), 225 (41), 213 (19), 202 (21), 186 (39), 175 (62), 162 (38), 145 (52), 127 (47), 115 (31), 102 (15), 96 (15), 77 (16), 59 (13).

**Methyl (1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-epoxy-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-3-oxo-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylate (31).**

The diol **38** (210 mg, 60 mmol) and *p*-toluenesulfonic acid (115 mg, 60 mmol) were dissolved in tetrahydrofuran (20 ml) and stirred for 2 hours. The solution was filtered through a short pad of silica gel and the solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the ether **31** (142 mg, 71%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2998 (CH), 1766 (C=O), 1258 (ArOCH<sub>3</sub>), 1152 (C-O), 1098 (C-O), 1065 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.33 (1H, d,  $J = 8.5$  Hz, H-8), 6.86 (1H, dd,  $J = 8.5$  Hz,  $J = 1.9$  Hz, H-7), 6.48 (1H, d,  $J = 1.9$  Hz, H-5), 5.22 (1H, d,  $J = 5.0$  Hz, H-9), 5.15 (1H, dd,  $J = 5.6$  Hz,  $J = 5.7$  Hz, H-1), 4.10 (1H, d,  $J = 8.8$  Hz, H-4a), 3.96 (1H, d,  $J = 5.7$  Hz, H-11), 3.93 (3H, s, COOCH<sub>3</sub>), 3.78 (3H, s, CH<sub>3</sub>O-C6), 3.57 (1H, ddd,  $J = 8.8$  Hz,  $J = 5.6$  Hz,  $J = 5.0$  Hz, H-9a), 2.16 (1H, q,  $J = 7.5$  Hz, H-10), 1.10 (3H, d,  $J = 7.5$  Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 169.04 (C3), 168.36 (C12), 161.40 (C6), 141.85 (C4b), 136.80 (C8a), 126.48 (C8), 115.33 (C5), 110.20 (C7), 82.79 (C11), 79.66 (C1), 79.58 (C9), 57.55 (C4), 55.63 (CH<sub>3</sub>O-C6), 52.69 (COOCH<sub>3</sub>), 49.23 (C9a), 45.86 (C4a), 37.42 (C10), 17.36 (CH<sub>3</sub>-C10);  $m/z$  330 (M<sup>+</sup>, 100%), 299 (6), 271 (8), 241 (15), 226 (4), 214 (11), 197 (10), 186 (62), 175 (22), 158 (15), 146 (39), 127 (58), 115 (21), 102 (15), 89 (3), 77 (5), 59 (9).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-1,4-ethanoindeno[2,1-c]pyran-4(3H)-carboxylic acid (39).**

Tetrahydrothiophene (320  $\mu$ l, 3.64 mmol) was added to a solution of aluminum tribromide (194 mg, 0.728 mmol) in dichloromethane (10 ml) at 0°C. The mixture was stirred for 5 minutes and the ester **31** (120 mg, 0.364 mmol) in dichloromethane (2 ml) was then added dropwise over 10 minutes. Stirring was continued for 20 hours at room temperature. 4M HCl (10 ml) was added and the product was extracted with dichloromethane (4x50 ml). The combined organic phase was washed with brine (10 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate : acetic acid = 1:2:0.03) to afford the acid **39** (79 mg, 69%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3500 (COOH), 2957 (CH), 1764 (C=O), 1261 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.33 (1H, d,  $J$  = 8.2 Hz, H-8), 6.86 (1H, dd,  $J$  = 8.2 Hz,  $J$  = 1.9 Hz, H-7), 6.72 (1H, d,  $J$  = 1.9 Hz, H-5), 5.24 (1H, d,  $J$  = 5.2 Hz, H-9), 5.20 (1H, dd,  $J$  = 5.6 Hz,  $J$  = 5.6 Hz, H-1), 4.03 (1H, d,  $J$  = 8.7 Hz, H-4a), 4.01 (1H, d,  $J$  = 5.6 Hz, H-11), 3.76 (3H, s, CH<sub>3</sub>O-C6), 3.62 (1H, ddd,  $J$  = 8.7 Hz,  $J$  = 5.6 Hz,  $J$  = 5.4 Hz, H-9a), 2.21 (1H, q,  $J$  = 7.4 Hz, H-10), 1.10 (3H, d,  $J$  = 7.4 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 171.42 (C12), 170.76 (C3), 161.46 (C6), 141.25 (C4b), 136.46 (C8a), 126.39 (C8), 116.32 (C5), 110.55 (C7), 82.74 (C11), 79.84 (C1), 79.21 (C9), 56.99 (C4), 55.74 (CH<sub>3</sub>O-C6), 49.23 (C9a), 46.29 (C4a), 37.64 (C10), 17.12 (CH<sub>3</sub>-C10);  $m/z$  316 (M<sup>+</sup>, 100%), 272 (2), 244 (3), 226 (7), 213 (5), 197 (12), 186 (31), 175 (48), 158 (9), 146 (25), 128 (6), 115 (16), 102 (12), 89 (2), 77 (5).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,4,4a,9a-tetrahydro-4-hydroxymethyl-6-methoxy-10-methyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (40).**

Oxalyl chloride (194  $\mu$ l, 2.23 mmol) was added to the acid **39** (140 mg, 0.446 mmol) in dry benzene (25 ml). A few drops of DMF were added and stirring was continued for 2 hours. After removal of the solvent, the residue was dissolved in benzene (10 ml) which was subsequently removed under vacuum. This last step was repeated twice. The residue was redissolved in tetrahydrofuran (15 ml) and cooled to 0°C. A suspension of sodium borohydride (20 mg, 0.535 mmol) in tetrahydrofuran (5 ml) was added over 5 minutes. Stirring was continued for 4 hours at room temperature. Ethyl acetate (100 ml) was added and the mixture was acidified with 2M HCl (10 ml), separated and washed with brine (10 ml). The organic phase was dried over magnesium sulfate, filtered and the solvent was removed. The residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the alcohol **40** (95 mg, 71%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3414 (OH), 2946 (CH), 1767 (C=O), 1261 (ArOCH<sub>3</sub>), 1150 (C-O), 1081 (ArOCH<sub>3</sub>), 1056 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.32 (1H, d,  $J$  = 8.4 Hz, H-8), 6.98 (1H, d,  $J$  = 2.1 Hz, H-5), 6.85 (1H, dd,  $J$  = 8.4 Hz,  $J$  = 2.1 Hz, H-7), 5.22 (1H, d,  $J$  = 5.4 Hz, H-9), 5.12 (1H, dd,  $J$  = 5.5 Hz,  $J$  = 5.6 Hz, H-1), 4.16 (1H, d,  $J$  = 12.1 Hz, H-1' $\alpha$ ), 3.92 (1H, d,  $J$  = 9.0 Hz, H-4a), 3.84 (1H, d,  $J$  = 5.5 Hz, H-11), 3.81 (3H, s, CH<sub>3</sub>O-C6),

3.54 (1H, ddd,  $J$  = 9.0 Hz,  $J$  = 5.6 Hz,  $J$  = 5.4 Hz, H-9a), 3.38 (1H, d,  $J$  = 12.1 Hz, H-1' $\beta$ ), 1.61 (1H, q,  $J$  = 7.6 Hz, H-10), 0.84 (3H, d,  $J$  = 7.6 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 175.71 (C3), 161.38 (C6), 142.82 (C4b), 136.47 (C8a), 126.22 (C8), 115.28 (C5), 111.75 (C7), 83.16 (C11), 79.72 (C1), 79.59 (C9), 60.45 (C1'), 55.79 (CH<sub>3</sub>O-C6), 50.20 (C4), 46.14 (C9a), 42.25 (C4a), 37.51 (C10), 16.19 (CH<sub>3</sub>-C10);  $m/z$  302 (M<sup>+</sup>, 100%), 284 (1), 255 (6), 243 (4), 227 (9), 216 (7), 199 (11), 188 (21), 175 (37), 159 (58), 139 (39), 128 (13), 115 (31), 99 (23), 77 (9).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-4-formyl-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (41).**

*tert*.-Butyl alcohol (68  $\mu$ l, 0.714 mmol) was added to the Dess Martin periodinane (171 mg, 0.357 mmol) in tetrahydrofuran (10 ml) and stirred for 5 minutes. The alcohol **167** (72 mg, 0.238 mmol) in tetrahydrofuran (1 ml) was added *via* syringe over 5 minutes and the solution was stirred for a further 2 hours at room temperature. A 1:1 mixture of saturated aqueous sodium thiosulfate and sodium bicarbonate (5 ml) was added and stirring was continued for 5 minutes. The product was extracted with ethyl acetate (3x30 ml) and the combined organic phase was washed with saturated sodium thiosulfate (10 ml) and brine (10 ml). After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to afford the aldehyde **168** (66 mg, 92%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2955 (CH), 2838 (CHO), 1751 (C=O), 1728 (C=O), 1258 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 10.09 (1H, s, H-1'), 7.31 (1H, d,  $J$  = 8.4 Hz, H-8), 6.85 (1H, dd,  $J$  = 8.4 Hz,  $J$  = 2.1 Hz, H-7), 6.45 (1H, d,  $J$  = 2.0 Hz, H-5), 5.23 (1H, d,  $J$  = 5.2 Hz, H-9), 5.17 (1H, dd,  $J$  = 5.4 Hz,  $J$  = 5.6 Hz, H-1), 3.99 – 3.94 (2H, m, H-4a, H-11), 3.77 (3H, s, CH<sub>3</sub>O-C6), 3.64 (1H, ddd,  $J$  = 8.9 Hz,  $J$  = 5.4 Hz,  $J$  = 5.2 Hz, H-9a), 2.17 (1H, q,  $J$  = 7.6 Hz, H-10), 0.95 (3H, d,  $J$  = 7.6 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 196.88 (C1'), 170.52 (C3), 160.93 (C6), 140.61 (C4b), 136.33 (C8a), 126.23 (C8), 115.61 (C5), 111.50 (C7), 82.48 (C11), 79.45 (C1), 79.04 (C9), 58.55 (C4), 55.56 (CH<sub>3</sub>O-C6), 46.48 (C9a), 46.09 (C4a), 35.25 (C10), 16.20 (CH<sub>3</sub>-C10);  $m/z$  300 (M<sup>+</sup>, 100%), 272 (14), 254 (6), 243 (20), 226 (24), 213 (19), 197 (35), 186 (25), 175 (21), 159 (21), 145 (39), 127 (15), 115 (37), 97 (32), 77 (11), 57 (12).

**(1RS, 4RS, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,4,4a,9a-tetrahydro-6-methoxy-4-[(Z)-2'-methoxyethenyl]-10-methyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (42).**

A 1M solution of lithium hexamethyldisilazide (396  $\mu$ l, 0.396 mmol) was added dropwise to a stirred suspension of (methoxymethyl)triphenylphosphonium chloride (135 mg, 0.396 mmol) in dry tetrahydrofuran (8 ml) at room temperature under nitrogen. After 10 minutes, the deep red solution was cooled to 0°C and the aldehyde **41** (66 mg, 0.22 mmol) in tetrahydrofuran (2 ml) was added dropwise over 30 minutes. The mixture was allowed to warm to room temperature and stirred for 1.5 hours. Water (2 ml) was added and stirring was continued for 2 minutes. The solution was

acidified with 2M HCl (10 ml) and extracted with ethyl acetate (3x20 ml). The combined organic phase was washed with brine (10 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to afford the enol ether **42** (42 mg, 58%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2937 (CH), 1754 (C=O), 1257 (ArOCH<sub>3</sub>), 1087 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.30 (1H, d,  $J$  = 8.7 Hz, H-8), 6.89 – 6.82 (2H, m, H-5, H-7), 6.16 (1H, d,  $J$  = 7.0 Hz, H-2'), 5.20 (1H, d,  $J$  = 5.2 Hz, H-9), 5.07 (1H, dd,  $J$  = 5.4 Hz,  $J$  = 5.6 Hz, H-1), 4.35 (1H, d,  $J$  = 6.9 Hz, H-1'), 3.94 (1H, d,  $J$  = 5.6 Hz, H-11), 3.81 – 3.77 (4H, m, H-4a, CH<sub>3</sub>O-C6), 3.52 – 3.48 (4H, m, H-9a, CH<sub>3</sub>O-C13), 2.14 (1H, q,  $J$  = 7.5 Hz, H-10), 0.89 (3H, d,  $J$  = 7.6 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 172.76 (C3), 160.66 (C6), 149.71 (C2'), 143.95 (C4b), 137.19 (C8a), 125.60 (C8), 114.10 (C5), 112.99 (C7), 100.21 (C1'), 82.93 (C11), 79.25 (C1), 78.98 (C9), 60.12 (CH<sub>3</sub>O-C2'), 55.67 (CH<sub>3</sub>O-C6), 50.53 (C4), 48.42 (C9a), 46.50 (C4a), 39.18 (C10), 16.54 (CH<sub>3</sub>-C10);  $m/z$  328 (M<sup>+</sup>, 64%), 314 (4), 286 (6), 268 (2), 242 (4), 223 (2), 197 (3), 186 (55), 175 (12), 159 (100), 145 (62), 127 (13), 115 (17), 102 (16), 77 (5).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-4-(2'-oxoethyl)-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (43).**

The enol ether **42** (30 mg, 0.091 mmol), water (500  $\mu$ l), and 1M HCl (25  $\mu$ l) were stirred in tetrahydrofuran (2 ml) for 24 hours. The solvent was removed under reduced pressure and the residue was redissolved in ethyl acetate (10 ml). The organic phase was separated, washed with brine (2 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to afford the aldehyde **43** (24 mg, 83%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2959 (CH), 2852 (CHO), 1753 (C=O), 1717 (C=O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 10.4 (1H, d,  $J$  = 3.3 Hz, H-2'), 7.33 (1H, d,  $J$  = 8.1 Hz, H-8), 6.89 (1H, d,  $J$  = 2.2 Hz, H-5), 6.87 (1H, dd,  $J$  = 8.1 Hz,  $J$  = 2.2 Hz, H-7), 5.21 (1H, d,  $J$  = 5.4 Hz, H-9), 5.12 (1H, dd,  $J$  = 5.4 Hz,  $J$  = 5.2 Hz, H-1), 3.93 (1H, d,  $J$  = 5.2 Hz, H-11), 3.89 (1H, d,  $J$  = 8.8 Hz, H-4a), 3.81 (3H, s, CH<sub>3</sub>O-C6), 3.51 (1H, ddd,  $J$  = 8.8 Hz,  $J$  = 5.2 Hz,  $J$  = 5.4 Hz, H-9a), 3.05 (1H, d,  $J$  = 15.5 Hz, H-1' $\alpha$ ), 2.29 (1H, dd,  $J$  = 15.5 Hz,  $J$  = 3.3 Hz, H-1' $\beta$ ), 1.68 (1H, q,  $J$  = 7.6 Hz, H-10), 0.92 (3H, d,  $J$  = 7.7 Hz, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 202.20 (C2'), 173.68 (C3), 161.21 (C6), 142.46 (C4b), 137.05 (C8a), 126.45 (C8), 115.36 (C5), 111.85 (C7), 83.02 (C11), 79.72 (C1), 79.32 (C9), 55.75 (CH<sub>3</sub>O-C6), 48.39 (C9a), 47.39 (C4), 46.13 (C4a), 42.44 (C1'), 40.27 (C10), 16.21 (CH<sub>3</sub>-C10);  $m/z$  314 (M<sup>+</sup>, 24%), 286 (30), 256 (4), 187 (20), 175 (19), 159 (100), 145 (33), 128 (18), 115 (30), 102 (24), 83 (35), 69 (24).

**(1'RS, 4'SR, 4a'SR, 9'RS, 9a'RS, 10'SR, 11'RS)-9',11'-Epoxy-1',3',4',4a',9',9a'-hexahydro-6'-methoxy-10'-methyl-3'-oxo-1',4'-ethanoindeno[2',1'-c]pyran-yl-acetic acid (44).**

The aldehyde **43** (16 mg, 0.051 mmol), 30% hydrogen peroxide (270  $\mu$ l, 0.82 mmol) and sodium hydrogenphosphate (2 mg, 0.017 mmol) were dissolved in a 1:1 solution of acetonitrile/water (1 ml) and cooled to 0°C. Sodium chlorite (7.5 mg, 0.082 mmol) in water (100  $\mu$ l) was added dropwise. The mixture was warmed to room temperature and stirred for 2.5 hours. The reaction was quenched with sodium sulfate (20 mg, 0.168 mmol) and acidified with 6M HCl (1 ml). The mixture was extracted with dichloromethane (4x15 ml) and the combined organic phase was washed with brine (5 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate : acetic acid = 1:1:0.02) to afford the acid **44** (11 mg, 65%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3500 (COOH), 2931 (CH), 1755 (C=O), 1260 (ArOCH<sub>3</sub>), 1031 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.33 (1H, d,  $J$  = 8.2 Hz, H-8'), 6.89 (1H, s, H-5'), 6.87 (1H, d,  $J$  = 8.2 Hz, H-7'), 5.22 (1H, d,  $J$  = 5.5 Hz, H-9'), 5.12 (1H, dd,  $J$  = 5.5 Hz,  $J$  = 5.8 Hz, H-1'), 4.30 (1H, d,  $J$  = 9.4 Hz, H-4a'), 3.94 (1H, d,  $J$  = 5.6 Hz, H-11'), 3.81 (3H, s, CH<sub>3</sub>O-C6'), 3.53 (1H, ddd,  $J$  = 9.4 Hz,  $J$  = 5.5 Hz,  $J$  = 5.5 Hz, H-9a'), 2.96 (1H, d,  $J$  = 15.9 Hz, H-1' $\alpha$ ), 2.34 (1H, d,  $J$  = 16.0 Hz, H-1' $\beta$ ), 1.67 (1H, q,  $J$  = 7.2 Hz, H-10'), 0.88 (3H, d,  $J$  = 7.5 Hz, CH<sub>3</sub>-C10');  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 176.74 (C2), 174.83 (C3'), 161.32 (C6'), 142.74 (C4b'), 137.01 (C8a'), 126.41 (C8'), 115.10 (C5'), 111.91 (C7'), 83.20 (C11'), 79.70 (C1'), 79.48 (C9'), 55.78 (CH<sub>3</sub>O-C6'), 47.76 (C9a'), 46.29 (C4'), 46.01 (C4a'), 40.38 (C10'), 33.98 (C1), 16.11 (CH<sub>3</sub>-C10');  $m/z$  330 (M<sup>+</sup>, 9%), 296 (100), 271 (33), 256 (35), 242 (15), 229 (53), 214 (12), 201 (11), 187 (6), 175 (58), 161 (12), 149 (8), 128 (7), 115 (13), 83 (43), 57 (21).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-4-(3'-Diazo-2'-oxopropyl)-9,11-epoxy-1,4,4a,9a-tetrahydro-6-methoxy-10-methyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (45).**

Oxalyl chloride (15.5  $\mu$ l, 0.18 mmol) was added to the acid **44** (6 mg, 0.018 mmol) in dry benzene (1 ml). A drop of DMF was added and stirring was continued for 2 hours. The solvent was removed under reduced pressure. Benzene (1 ml) was added and removed under vacuum. This step was repeated twice. The residue was redissolved in tetrahydrofuran (2 ml), which was then added dropwise to an excess of ethereal diazomethane at 0°C and stirred for 6 hours. The mixture was warmed to room temperature and stirred for a further 16 hours. The solvent was removed and the residue was directly chromatographed on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the diazoketone **45** (4 mg, 62%) as a pale yellow oil;  $\nu_{\max}/\text{cm}^{-1}$  3099 (ArH), 2930 (CH), 2104 (CHN<sub>2</sub>), 1753 (C=O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.34 (1H, d,  $J$  = 8.4 Hz, H-8), 7.15 (1H, d (br),  $J$  = 2.5 Hz, H-5), 6.87 (1H, dd,  $J$  = 8.4 Hz,  $J$  = 2.4 Hz, H-7), 5.22 (1H, d,  $J$  = 5.3 Hz, H-9), 5.10 (1H, dd,  $J$  = 6.2 Hz,  $J_{1,11}$  = 5.4 Hz, H-1), 4.90 (1H, s (br) C2'-CHN<sub>2</sub>), 4.45 (1H, d,  $J$  = 8.8 Hz, H-4a), 3.93 (1H, d,  $J_{11,1}$  = 5.4 Hz, H-11), 3.82 (3H, s, CH<sub>3</sub>O-C6), 3.51 (1H, ddd,  $J$  = 8.8 Hz,  $J$  = 6.1 Hz,  $J$  = 5.4 Hz, H-9a), 2.83 (1H, d (br),  $J$  = 15.5 Hz, H-1' $\alpha$ ), 2.25 (1H, d,  $J$  = 15.5 Hz, H-1' $\beta$ ), 1.68 (1H, q,  $J$  = 7.6 Hz, H-10), 0.89 (3H, d,  $J$  = 7.6 Hz, CH<sub>3</sub>-C10);  $m/z$  354 (M<sup>+</sup>, 3%), 326 (100), 313 (31), 298 (18), 269 (7), 241 (10),

225 (7), 213 (12), 199 (7), 186 (42), 173 (38), 159 (51), 145 (35), 128 (11), 115 (20), 102 (1), 91 (8), 71 (5).

**Methyl (1'*RS*, 4'*SR*, 4a'*SR*, 9'*RS*, 9a'*RS*, 10'*SR*, 11'*RS*)-9',11'-epoxy-1',3',4',4a',9',9a'-hexahydro-6'-methoxy-10'-methyl-3'-oxo-1',4'-ethanoindeno[2',1'-c]pyranyl-acetate (46).**

The acid **44** (15 mg, 0.045 mmol) was dissolved in dichloromethane (500  $\mu$ l) and added dropwise to an excess of ethereal diazomethane at 0°C. The solution was warmed to room temperature and stirring was continued for 16 hours. The solvent was removed under reduced pressure and the residue was directly chromatographed on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the ester **46** (15 mg, 96%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2950 (CH), 1756 (C=O), 1261 (ArOCH<sub>3</sub>), 1120 (C-O), 1047 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.34 (1H, d,  $J$  = 8.3 Hz, H-8'), 6.86 (1H, dd,  $J$  = 8.3 Hz,  $J$  = 2.2 Hz, H-7'), 5.73 (1H, d,  $J$  = 2.2 Hz, H-5'), 5.21 (1H, d,  $J$  = 5.4 Hz, H-9'), 5.10 (1H, dd,  $J$  = 5.5 Hz,  $J$  = 5.6 Hz, H-1'), 4.51 (1H, d,  $J$  = 8.9 Hz, H-4a'), 3.92 (1H, d,  $J$  = 5.6 Hz, H-11'), 3.80 (3H, s, CH<sub>3</sub>O-C6'), 3.79 (3H, s, COOCH<sub>3</sub>), 3.52 (1H, ddd,  $J$  = 8.8 Hz,  $J$  = 5.6 Hz,  $J$  = 5.4 Hz, H-9a'), 2.88 (1H, d,  $J$  = 16.8 Hz, H-1 $\alpha$ ), 2.27 (1H, d,  $J$  = 16.9 Hz, H-1 $\beta$ ), 1.66 (1H, q,  $J$  = 7.7 Hz, H-10'), 0.88 (3H, d,  $J$  = 7.7 Hz, CH<sub>3</sub>-C10');  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 173.16 (C3'), 171.49 (C2), 160.88 (C6'), 143.01 (C4b'), 137.04 (C8a'), 126.22 (C8'), 114.07 (C5'), 111.83 (C7'), 82.92 (C11'), 79.57 (C1'), 79.09 (C9'), 55.43 (CH<sub>3</sub>O-C6'), 51.92 (COOCH<sub>3</sub>), 47.15 (C9a'), 45.79 (C4'), 45.74 (C4a'), 39.99 (C10'), 32.60 (C1), 15.91 (CH<sub>3</sub>-C10');  $m/z$  344 (M<sup>+</sup>, 100%), 313 (17), 270 (7), 241 (6), 227 (18), 213 (11), 199 (9), 186 (21), 175 (15), 171 (12), 159 (16), 145 (25), 128 (12), 115 (19), 102 (14), 91 (13), 81 (9), 57 (14).

**4-Methyl-2-oxo-2H-pyran-3-carboxylic acid (47).**

A mixture of hexamethyldisilane (2.5 ml, 12.2 mmol) and iodine (1.55 g, 12.2 mmol) was carefully heated to 50°C in a dry 250 ml round-bottomed flask equipped with a reservoir and a long reflux condenser. A violent exothermic reaction occurred, and a homogeneous reddish brown solution resulted, which was heated under reflux for 1.5 hours to form a colourless liquid. The pyrone **32** (2 g, 11.9 mmol) in 50 ml of dry chloroform was added, and the mixture was heated at reflux for 24 hours. The reaction mixture was cooled to 25°C, and 2 ml of water was added. The mixture was stirred for 10 minutes and then diluted with dichloromethane (100 ml). Saturated aqueous sodium thiosulfate (5 ml) was added, and the mixture was stirred until colourless. The organic layer was separated and the aqueous layer was extracted with dichloromethane (3x100 ml). The combined organic solution was then washed with saturated aqueous sodium thiosulfate solution (20 ml), dried with magnesium sulfate, filtered and removed under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate : acetic acid 1:1:0.02) to yield the acid **47** (1.381 g, 75 %). Recrystallisation from ethyl acetate afforded colourless crystals; mp 116-117 °C (from EtOAc); Found: C, 54.28%; H, 4.00%. Calc. for C<sub>7</sub>H<sub>6</sub>O<sub>4</sub>: C, 54.55%; H, 3.92%;  $\nu_{\max}/\text{cm}^{-1}$  3500 (COOH), 3074 (=CH), 2971 (CH), 1725

(C=O), 1618 (=CH);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.61 (1H, d,  $J$  = 5.2 Hz, H-5), 6.46 (1H, d,  $J$  = 5.1 Hz, H-4), 2.78 (3H, s, CH<sub>3</sub>-C4);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 167.90 (COOH), 166.02 (C2), 163.40 (C4), 152.06 (C6), 114.37 (C5), 112.85 (C3), 23.78 (CH<sub>3</sub>-C4);  $m/z$  154 (M<sup>+</sup>, 54%), 136 (100), 126 (32), 110 (79), 108 (63), 98 (54), 81 (31), 69 (19), 67 (20), 52 (47).

**5-Methoxy-7-methyl-1H-inden-1-one and 3-Bromo-5-methoxy-7-methyl-1H-inden-1-one (4).**

*N*-Bromosuccinimide (1.2 g, 6.74 mmol) was added to a solution of the indanone **48** (1.2 g, 6.82 mmol) in carbon tetrachloride (100 ml). The resulting suspension was stirred at reflux with irradiation from a tungsten lamp for 1.5 hours. Triethylamine (4 ml) was added and the reaction mixture was stirred at 85°C (oil bath) for a further 2 hours. The mixture was filtered through a short column of silica gel and washed with ethyl acetate. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 30:1→10:1) to afford 5-methoxyindenone **4** (750 mg, 63%) as a yellow oil, and starting material (96 mg);  $\nu_{\max}/\text{cm}^{-1}$  3010 (ArH), 2941 (CH), 1695 (C=O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.23 (1H, d,  $J$  = 5.9 Hz, H-3), 6.35 (1H, d,  $J$  = 2.2 Hz, H-4), 6.25 (1H, d,  $J$  = 2.2 Hz, H-6), 5.73 (1H, d,  $J$  = 5.9 Hz, H-2), 3.72 (3H, s, CH<sub>3</sub>O-C5), 2.37 (3H, s, CH<sub>3</sub>-C7);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 198.27 (C1), 163.91 (C5), 147.88 (C3a), 146.72 (C3), 139.95 (C7), 129.14 (C2), 120.09 (C7a), 113.35 (C6), 109.53 (C4), 55.71 (CH<sub>3</sub>O-C5), 17.69 (CH<sub>3</sub>-C7);  $m/z$  174 (M<sup>+</sup>, 100%), 159 (13), 146 (20), 131 (29), 120 (14), 115 (26), 103 (29), 102 (24), 87 (12), 77 (29), 63 (20).

**(1*SR*, 4*SR*, 4a*SR*, 9a*SR*)-1,4,4a,9a-tetrahydro-6-methoxy-8,10-dimethyl-3,9-dioxo-1,4-ethenoindeno[2,1-c]pyran-4(3H)-carboxylic acid (49).**

The indenone **4** (1.42 g, 9.22 mol) and the pyrone **47** (1.604 g, 9.22 mol) were dissolved in a minimum of dichloromethane (10 ml). The reaction mixture was then subjected to high pressure (19 Kbar) for 16 hours. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate : acetic acid = 1:2:0.03) to yield the cycloadduct **49** (2.07 g, 68%, based on pyrone). Recrystallisation from ethyl acetate afforded colourless crystals; mp 158-160 °C (from EtOAc); Found: C, 65.84%; H, 4.93%. Calc. for C<sub>18</sub>H<sub>16</sub>O<sub>6</sub>: C, 65.85%; H, 4.91%; Found: C, 68.54%; H, 6.11%. Calc. for C<sub>18</sub>H<sub>18</sub>O<sub>5</sub>: C, 68.78%; H, 5.77%;  $\nu_{\max}/\text{cm}^{-1}$  3430 (COOH), 3003 (ArH), 2959 (CH), 1750 (C=O), 1695 (C=O), 1251 (ArOCH<sub>3</sub>);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 7.08 (1H, s, H-7), 6.58 (1H, s, H-5), 5.85 (1H, d,  $J$  = 4.9 Hz, H-11), 5.30 (1H, dd,  $J$  = 4.7 Hz,  $J$  = 4.9 Hz, H-1), 4.24 (1H, d,  $J$  = 6.7 Hz, H-4a), 3.75 (3H, s, CH<sub>3</sub>O-C6), 3.38 (1H, dd,  $J$  = 6.7 Hz,  $J$  = 4.7 Hz, H-9a), 2.45 (3H, s, CH<sub>3</sub>-C8), 1.56 (3H, s, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 200.63 (C9), 171.47 (C12), 170.11 (C3), 165.01 (C6), 156.78 (C4b), 141.45 (C10), 141.34 (C8), 130.00 (C8a), 123.31 (C11), 117.88 (C5), 108.70 (C7), 74.44 (C1), 63.48 (C4), 55.86 (CH<sub>3</sub>O-C6), 53.37 (C9a), 38.99 (C4a), 20.29 (CH<sub>3</sub>-C10), 18.82 (CH<sub>3</sub>-C8);  $m/z$  328 (M<sup>+</sup>, 3%), 239 (100), 225 (26), 196 (7), 174 (28), 165 (11), 148 (28), 120 (27), 84 (37), 78 (31), 66 (46).

690 **(1SR, 4SR, 4aSR, 9aSR)-1,4,4a,9a-Tetrahydro-4-hydroxymethyl-6-methoxy-8,10-dimethyl-9-oxo-1,4-ethenoindeno[2,1-c]pyran-3(4H)-one (50).**

Oxalyl chloride (1.73 ml, 20 mmol) was added to the acid **49** (1.3 g, 4 mmol) in dry tetrahydrofuran (150 ml). DMF (150  $\mu$ l) was added and stirring was continued for 2 hours. After removal of the solvent, the residue was dissolved in benzene (50 ml) which was subsequently removed under vacuum. This step was repeated twice. The residue was redissolved in tetrahydrofuran (150 ml) and cooled to 0°C. A solution of sodium borohydride (454 mg, 11.9 mmol) in DMF (5 ml) was added over 5 minutes. Stirring was continued for 5 hours at room temperature. The mixture was acidified with 2M HCl (50 ml) and the solvent was removed under reduced pressure. The product was extracted with dichloromethane (3x250 ml) and the combined organic phase was washed with brine (50 ml), dried over magnesium sulfate and filtered. The solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to yield the alcohol **50** (820 mg, 66%) and starting material (86 mg). Recrystallisation from ethyl acetate afforded colourless crystals; mp 146-148 °C (from EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  3508 (OH), 3008 (ArH), 2942 (CH), 1743 (C=O), 1150 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 6.86 (1H, s, H-7), 6.66 (1H, s, H-5), 6.04 (1H, d,  $J = 4.9$  Hz, H-11), 5.41 (1H, dd,  $J = 4.9$  Hz,  $J = 4.9$  Hz, H-1), 4.45 (1H, d,  $J = 12.2$  Hz, H-1' $\alpha$ ), 4.19 (1H, d,  $J = 12.2$  Hz, H-1' $\beta$ ), 3.87 (1H, d,  $J = 6.6$  Hz, H-4a), 3.86 (3H, s, CH<sub>3</sub>O-C6), 3.48 (1H, dd,  $J = 6.6$  Hz,  $J = 4.9$  Hz, H-9a), 2.52 (3H, s, CH<sub>3</sub>-C8), 1.38 (3H, s, CH<sub>3</sub>-C10);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 201.11 (C9), 176.02 (C3), 164.89 (C6), 154.85 (C4b), 141.80 (C10), 140.74 (C8), 130.17 (C8a), 124.82 (C11), 117.86 (C5), 108.70 (C7), 74.29 (C1), 59.42 (C1'), 55.98 (CH<sub>3</sub>O-C6), 55.46 (C4), 53.43 (C9a), 36.42 (C4a), 18.84 (CH<sub>3</sub>-C8), 16.83 (CH<sub>3</sub>-C10);  $m/z$  315 (M<sup>+</sup> + H, 2%), 239 (32), 225 (5), 196 (3), 174 (100), 165 (6), 148 (3), 120 (8), 115 (7), 103 (4), 91 (5), 77(7).

730 **(1SR, 4SR, 4aSR, 9aSR)-4-(tert.-Butyldimethylsilyloxymethyl)-1,4,4a,9a-tetrahydro-6-methoxy-8,10-dimethyl-9-oxo-1,4-ethenoindeno[2,1-c]pyran-3(4H)-one (51).**

*tert.*-Butyldimethylsilyl trifluoromethanesulfonate (272  $\mu$ l, 1.18 mmol) was added dropwise over 10 minutes to the alcohol **50** (310 mg, 0.99 mmol) and *N,N*-diisopropylethylamine (258  $\mu$ l, 1.49 mmol) in dichloromethane (30 ml) at 0°C. Stirring was continued at room temperature for 2 hours. The mixture was diluted with dichloromethane (150 ml), washed with 2M HCl (20 ml), brine (20 ml) and dried over magnesium sulfate. The solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 6:1) to yield the ether **51** (350 mg, 83%). Recrystallisation from ethyl acetate afforded colourless crystals; mp 155-157 °C (from EtOAc);  $\nu_{\max}/\text{cm}^{-1}$  2951 (CH), 1758 (C=O), 1250 (ArOCH<sub>3</sub>), 1149 (C-O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 6.99 (1H, s, H-7), 6.66 (1H, s, H-5), 5.99 (1H, d,  $J = 5.1$  Hz, H-11), 5.36 (1H, dd,  $J = 4.9$  Hz,  $J = 5.1$  Hz, H-1), 4.49 (1H, d,  $J = 10.5$  Hz, H-1' $\alpha$ ), 4.12 (1H, d,  $J = 10.5$  Hz, H-

1' $\beta$ ), 4.01 (1H, d,  $J = 7.0$  Hz, H-4a), 3.85 (3H, s, CH<sub>3</sub>O-C6), 3.48 (1H, dd,  $J = 6.9$  Hz,  $J = 4.9$  Hz, H-9a), 2.53 (3H, s, CH<sub>3</sub>-C8), 1.32 (3H, s, CH<sub>3</sub>-C10), 0.97 (9H, s, (CH<sub>3</sub>)<sub>3</sub>-C), 0.26 (3H, s, CH<sub>3</sub>-Si), 0.24 (3H, s, CH<sub>3</sub>-Si);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 201.87 (C9), 173.71 (C3), 164.95 (C6), 155.87 (C4b), 141.46 (C10), 140.75 (C8), 130.39 (C8a), 125.13 (C11), 118.11 (C5), 108.18 (C7), 73.46 (C1), 58.42 (C1'), 55.92 (CH<sub>3</sub>O-C6), 55.30 (C4), 53.20 (C9a), 35.75 (C4a), 26.15 ((CH<sub>3</sub>)<sub>3</sub>-C), 18.81 (CH<sub>3</sub>-C8), 18.53 ((CH<sub>3</sub>)<sub>3</sub>-C), 17.03 (CH<sub>3</sub>-C10), -5.05 (CH<sub>3</sub>-Si), -5.23 (CH<sub>3</sub>-Si);  $m/z$  371 (M<sup>+</sup> - C<sub>4</sub>H<sub>9</sub>, 6%), 325 (72), 252 (64), 239 (100), 223 (39), 197 (36), 179 (13), 165 (21), 153 (7), 115 (10), 89 (22), 77 (57), 75 (56).

760 **(1SR, 4SR, 4aSR, 9RS, 9aRS)-4-(tert.-Butyldimethylsilyloxymethyl)-1,4,4a,9a-tetrahydro-9-hydroxy-6-methoxy-8,10-dimethyl-1,4-ethenoindeno[2,1-c]pyran-3(4H)-one (52).**

Sodium borohydride (117 mg, 3.08 mmol) was added to the ketone **51** (880 mg, 2.06 mmol) in tetrahydrofuran (50 ml) and methanol (1 ml) and the reaction mixture was stirred at room temperature for 3 hours. Acetone (5 ml) was added to decompose the excess borohydride. The solution was acidified with 2M HCl (30 ml) and extracted with ethyl acetate (3x100 ml). The organic phase was washed with brine (20 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 4:1) to yield the alcohol **52** (787 mg, 89%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3543 (OH), 2951 (CH), 1750 (C=O), 1731 (C=O);  $\delta_{\text{H}}$  (300MHz, CDCl<sub>3</sub>) 6.78 (1H, s, H-7), 6.63 (1H, s, H-5), 6.13 (1H, d,  $J = 3.2$  Hz, H-11), 5.34 - 5.25 (2H, m, H-1, H-9), 4.52 (1H, d,  $J = 10.7$  Hz, H-1' $\alpha$ ), 4.23 (1H, d,  $J = 10.4$  Hz, H-1' $\beta$ ), 3.96 (1H, d,  $J = 8.9$  Hz, H-4a), 3.77 (3H, s, CH<sub>3</sub>O-C6), 3.54 (1H, ddd,  $J = 8.7$  Hz,  $J = 4.2$  Hz,  $J = 8.5$  Hz, H-9a), 2.34 (3H, s, CH<sub>3</sub>-C8), 1.46 (3H, s, CH<sub>3</sub>-C10), 0.95 (9H, s, (CH<sub>3</sub>)<sub>3</sub>-C), 0.25 (3H, s, CH<sub>3</sub>-Si), 0.23 (3H, s, CH<sub>3</sub>-Si);  $\delta_{\text{C}}$  (75MHz, CDCl<sub>3</sub>) 175.03 (C3), 160.96 (C6), 141.59 (C4b), 140.51 (C10), 137.43 (C8), 136.54 (C8a), 126.35 (C11), 116.79 (C5), 107.20 (C7), 74.20 (C1), 73.63 (C9), 58.64 (C1'), 55.97 (CH<sub>3</sub>O-C6), 55.61 (C4), 48.67 (C9a), 43.52 (C4a), 26.12 ((CH<sub>3</sub>)<sub>3</sub>-C), 18.80 (CH<sub>3</sub>-C8), 18.51 ((CH<sub>3</sub>)<sub>3</sub>-C), 17.42 (CH<sub>3</sub>-C10), -5.06 (CH<sub>3</sub>-Si), -5.24 (CH<sub>3</sub>-Si);  $m/z$  429 (M<sup>+</sup> - H, 1%), 413 (1), 397 (1), 373 (9), 327 (12), 311 (6), 254 (31), 237 (43), 223 (17), 197 (100), 176 (28), 159 (25), 105 (13), 75 (21).

795 **(1RS, 4SR, 4aSR, 9RS, 9aRS, 10RS, 11SR)-4-(tert.-Butyldimethylsilyloxymethyl)-1,4,4a,9a-tetrahydro-9,11-dihydroxy-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (53).**

2M Borane-dimethyl sulfide in tetrahydrofuran (1.02 ml, 2.04 mmol) was added dropwise over 30 minutes to the alkene **52** (350 mg, 0.814 mmol) in dichloromethane (25 ml) at 0°C. Stirring was continued at room temperature for 5 hours. Triethylamine *N*-oxide (700 mg, 6.3 mmol) was added and the mixture was heated under reflux for 16 hours. The solution was filtered through a short pad of silica gel and the solvent was removed under reduced vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether 40-

60°C : ethyl acetate = 1:1) to afford the alcohol **53** (140 mg, 38%) as a colourless oil and starting material (42 mg);  $\nu_{\max}/\text{cm}^{-1}$  3400 (OH), 2929 (CH), 1752 (C=O), 1142 (C-O), 1104 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.64 (1H, s, H-7), 6.62 (1H, s, H-5), 5.46 (1H, d,  $J = 9.6$  Hz, H-9), 4.90 (1H, d,  $J = 4.0$  Hz, H-1), 4.35 (1H, d,  $J = 5.2$  Hz, H-1' $\alpha$ ), 4.11 (1H, d,  $J = 3.2$  Hz, H-11), 3.96 (1H, d,  $J = 5.2$  Hz, H-1' $\beta$ ), 3.73 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.54 (1H, d,  $J = 10.4$  Hz, H-4a), 3.21 (1H, ddd,  $J = 10.3$  Hz,  $J = 4.0$  Hz,  $J = 9.7$  Hz, H-9a), 2.34 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.66 (1H, dq,  $J = 7.3$  Hz,  $J = 3.2$  Hz, H-10), 0.86 (9H, s,  $(\text{CH}_3)_3\text{-C}$ ), 0.61 (3H, d,  $J = 7.3$  Hz,  $\text{CH}_3\text{-C10}$ ), 0.15 (3H, s,  $\text{CH}_3\text{-Si}$ ), 0.13 (3H, s,  $\text{CH}_3\text{-Si}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 177.15 (C3), 160.56 (C6), 142.53 (C4b), 138.47 (C8), 134.92 (C8a), 116.57 (C5), 108.33 (C7), 81.90 (C11), 74.42 (C9), 72.79 (C1), 60.11 (C1'), 55.56 ( $\text{CH}_3\text{-O-C6}$ ), 51.35 (C4), 44.71 (C9a), 40.60 (C4a), 39.89 (C10), 26.06 ( $(\text{CH}_3)_3\text{-C}$ ), 18.95 ( $\text{CH}_3\text{-C8}$ ), 18.48 ( $(\text{CH}_3)_3\text{-C}$ ), 14.19 ( $\text{CH}_3\text{-C10}$ ), -5.19 ( $\text{CH}_3\text{-Si}$ ), -5.27 ( $\text{CH}_3\text{-Si}$ );  $m/z$  449 ( $\text{M}^+ + \text{H}$ , 1%), 432 (2), 420 (2), 414 (2), 391 (57), 373 (11), 329 (9), 311 (10), 271 (6), 254 (40), 237 (58), 225 (25), 214 (17), 199 (53), 189 (26), 171 (76), 160 (49), 135 (10), 107 (23), 85 (53), 75 (100), 66 (57).

**(1RS, 4SR, 4aSR, 9aSR, 10RS)-4-(tert.-Butyldimethylsilyloxymethyl)-1,4,4a,9a-tetrahydro-6-methoxy-8,10-dimethyl-9,11-dioxo-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (54).**

The diol **53** (316 mg, 0.705 mmol) in tetrahydrofuran (5 ml) was added dropwise over 10 minutes to the Dess Martin periodinane (1.35 g, 2.82 mmol) in tetrahydrofuran (30 ml). The solution was stirred for 16 hours at room temperature. A 1:1 mixture of saturated aqueous sodium thiosulfate and sodium bicarbonate (5 ml) was added and stirring was continued for 1 hour. The product was extracted with ethyl acetate (3x100 ml) and the combined organic phase was washed with saturated sodium thiosulfate (20 ml) and brine (20 ml). After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 5:1) to afford the diketone **54** (182 mg, 58%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2951 (CH), 1775 (C=O), 1748 (C=O), 1700 (C=O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.91 (1H, s, H-7), 6.74 (1H, s, H-5), 5.04 (1H, d,  $J = 5.6$  Hz, H-1), 4.25 (1H, d,  $J = 10.3$  Hz, H-1' $\alpha$ ), 4.11 (1H, d,  $J = 10.4$  Hz, H-1' $\beta$ ), 4.03 (1H, d,  $J = 8.7$  Hz, H-4a), 3.87 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.66 (1H, dd,  $J = 8.7$  Hz,  $J = 5.7$  Hz, H-9a), 2.57 (3H, s,  $\text{CH}_3\text{-C8}$ ), 2.53 (1H, q,  $J = 7.4$  Hz, H-10), 0.96 (9H, s,  $(\text{CH}_3)_3\text{-C}$ ), 0.45 (3H, d,  $J = 7.4$  Hz,  $\text{CH}_3\text{-C10}$ ), 0.24 (3H, s,  $\text{CH}_3\text{-Si}$ ), 0.23 (3H, s,  $\text{CH}_3\text{-Si}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 204.53 (C11), 197.98 (C9), 172.75 (C3), 165.40 (C6), 155.54 (C4b), 142.84 (C8), 128.71 (C8a), 118.26 (C5), 109.00 (C7), 80.74 (C1), 59.38 (C1'), 55.85 ( $\text{CH}_3\text{-O-C6}$ ), 52.43 (C4), 52.06 (C9a), 43.13 (C10), 36.54 (C4a), 25.89 ( $(\text{CH}_3)_3\text{-C}$ ), 18.76 ( $\text{CH}_3\text{-C8}$ ), 18.35 ( $(\text{CH}_3)_3\text{-C}$ ), 9.65 ( $\text{CH}_3\text{-C10}$ ), -5.35 ( $\text{CH}_3\text{-Si}$ ), -5.42 ( $\text{CH}_3\text{-Si}$ );  $m/z$  387 ( $\text{M}^+ - \text{C}_4\text{H}_9$ , 73%), 369 (1), 343 (3), 295 (3), 267 (5), 239 (3), 213 (3), 199 (20), 187 (100), 171 (7), 159 (36), 129 (5), 116 (6), 75 (22).

**(1RS, 4SR, 4aSR, 9aSR, 10SR)-4-(tert.-Butyldimethylsilyloxymethyl)-1,4,4a,9a-tetrahydro-6-**

**methoxy-8,10-dimethyl-9,11-dioxo-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (55).**

DBU (2  $\mu\text{l}$ , 0.013) was added to a solution of diketone **54** (182 mg, 0.41 mmol) in tetrahydrofuran (10 ml) and stirred for 1.5 hours. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 5:1) to afford the epimer **55** (179 mg, 98%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2951 (CH), 2929 (CH), 1772 (C=O), 1254 ( $\text{ArOCH}_3$ ), 1150 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.99 (1H, s, H-7), 6.74 (1H, s, H-5), 4.93 (1H, d,  $J = 5.4$  Hz, H-1), 4.36 (1H, d,  $J = 10.8$  Hz, H-1' $\alpha$ ), 4.25 (1H, d,  $J = 10.8$  Hz, H-1' $\beta$ ), 3.86 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.65 (1H, d,  $J = 8.8$  Hz, H-4a), 3.63 (1H, dd,  $J = 8.8$  Hz,  $J = 5.4$  Hz, H-9a), 2.55 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.83 (1H, q,  $J = 7.6$  Hz, H-10), 0.98 (3H, d,  $J = 7.6$  Hz,  $\text{CH}_3\text{-C10}$ ), 0.97 (9H, s,  $(\text{CH}_3)_3\text{-C}$ ), 0.25 (6H, s,  $(\text{CH}_3)_2\text{-Si}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 203.74 (C11), 198.68 (C9), 172.32 (C3), 165.89 (C6), 154.66 (C4b), 142.66 (C8), 129.19 (C8a), 118.57 (C5), 109.08 (C7), 81.03 (C1), 60.25 (C1'), 56.01 ( $\text{CH}_3\text{-O-C6}$ ), 52.19 (C4), 50.51 (C9a), 41.98 (C10), 37.50 (C4a), 26.10 ( $(\text{CH}_3)_3\text{-C}$ ), 18.93 ( $\text{CH}_3\text{-C8}$ ), 18.48 ( $(\text{CH}_3)_3\text{-C}$ ), 11.78 ( $\text{CH}_3\text{-C10}$ ), -5.07 ( $\text{CH}_3\text{-Si}$ ), -5.23 ( $\text{CH}_3\text{-Si}$ );  $m/z$  387 ( $\text{M}^+ - \text{C}_4\text{H}_9$ , 84%), 369 (1), 343 (4), 295 (3), 267 (5), 239 (3), 213 (4), 199 (17), 187 (100), 171 (5), 159 (30), 129 (3), 116 (5), 75 (17).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-4-(tert.-Butyldimethylsilyloxymethyl)-9,11-epoxy-1,4,4a,9a-tetrahydro-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (56).**

Sodium borohydride (51 mg, 1.35 mmol) was added to the diketone **55** (260 mg, 0.585 mmol) in tetrahydrofuran (20 ml) and methanol (1 ml). The mixture was stirred at 3 hours at room temperature. Acetone (2 ml) was added and stirred for 10 minutes. The solution was acidified with 2M HCl to pH 2 and extracted with ethyl acetate (3x100 ml). The combined organic phase was washed with brine (30 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 5:1) to afford the ether **56** (160 mg, 64%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2951 (CH), 1764 (C=O), 1254 ( $\text{ArOCH}_3$ ), 1102 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.89 (1H, s, H-7), 6.66 (1H, s, H-5), 5.30 (1H, d,  $J = 5.5$  Hz, H-9), 5.06 (1H, dd,  $J = 5.5$  Hz,  $J = 5.4$  Hz, H-1), 4.13 (1H, d,  $J = 10.3$  Hz, H-1' $\alpha$ ), 3.90 (1H, d,  $J = 8.9$  Hz, H-4a), 3.84 (1H, d,  $J = 5.3$  Hz, H-11), 3.76 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.45 (1H, ddd,  $J = 9.0$  Hz,  $J = 5.5$  Hz,  $J = 5.5$  Hz, H-9a), 3.32 (1H, d,  $J = 10.3$  Hz, H-1' $\beta$ ), 2.35 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.63 (1H, q,  $J = 7.6$  Hz, H-10), 0.96 (9H, s,  $(\text{CH}_3)_3\text{-C}$ ), 0.78 (3H, d,  $J = 7.6$  Hz,  $\text{CH}_3\text{-C10}$ ), 0.21 (3H, s,  $\text{CH}_3\text{-Si}$ ), 0.19 (3H, s,  $\text{CH}_3\text{-Si}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 173.32 (C3), 161.39 (C6), 143.14 (C4b), 136.22 (C8), 135.99 (C8a), 116.39 (C5), 108.61 (C7), 81.85 (C11), 80.34 (C1), 79.15 (C9), 60.82 (C1'), 55.68 ( $\text{CH}_3\text{-O-C6}$ ), 49.96 (C4), 45.27 (C9a), 45.19 (C4a), 38.11 (C10), 26.15 ( $(\text{CH}_3)_3\text{-C}$ ), 18.79 ( $\text{CH}_3\text{-C8}$ ), 18.50 ( $(\text{CH}_3)_3\text{-C}$ ), 15.78 ( $\text{CH}_3\text{-C10}$ ), -5.16 ( $\text{CH}_3\text{-Si}$ ), -5.19 ( $\text{CH}_3\text{-Si}$ );  $m/z$  415 ( $\text{M}^+ - \text{CH}_3$ , 1%), 373 (100), 343 (1), 315 (4), 286 (2), 253 (2), 225 (6), 213 (3), 197 (4), 171 (11), 159 (15), 141 (4), 129 (5), 75 (27).



**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,4,4a,9a-tetrahydro-4-hydroxymethyl-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (57).**

1M Tetrabutylammonium fluoride in tetrahydrofuran (331  $\mu$ l, 0.331 mmol) was added to the ether **56** (95 mg, 0.221 mmol) in tetrahydrofuran (10 ml) and stirred at room temperature for 2 hours. The mixture was diluted with ethyl acetate (100 ml), washed with 2M HCl (10 ml), brine (10 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to afford the alcohol **253** (66 mg, 95%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3480 (OH), 2941 (CH), 1751 (C=O), 1277 (CO), 1138 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.78 (1H, s, H-7), 6.60 (1H, s, H-5), 5.30 (1H, d,  $J = 5.5$  Hz, H-9), 5.10 (1H, dd,  $J = 5.6$  Hz,  $J = 5.5$  Hz, H-1), 4.13 (1H, d,  $J = 9.6$  Hz, H-1' $\alpha$ ), 3.90 – 3.80 (2H, m, H-4a, H-11), 3.79 (3H, s,  $\text{CH}_3\text{-C6}$ ), 3.49 (1H, ddd,  $J = 8.8$  Hz,  $J = 5.6$  Hz,  $J = 5.5$  Hz, H-9a), 3.39 (1H, d,  $J = 9.6$  Hz, H-1' $\beta$ ), 2.35 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.61 (1H, q,  $J = 7.5$  Hz, H-10), 0.83 (3H, d,  $J = 7.6$  Hz,  $\text{CH}_3\text{-C10}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 175.81 (C3), 161.42 (C6), 142.48 (C4b), 136.75 (C8), 135.75 (C8a), 116.17 (C5), 108.99 (C7), 81.75 (C11), 80.13 (C1), 79.68 (C9), 60.46 (C1'), 55.70 ( $\text{CH}_3\text{-O-C6}$ ), 50.21 (C4), 45.60 (C9a), 45.32 (C4a), 37.51 (C10), 18.80 ( $\text{CH}_3\text{-C8}$ ), 16.22 ( $\text{CH}_3\text{-C10}$ );  $m/z$  316 ( $\text{M}^+$ , 100%), 298 (4), 285 (2), 269 (6), 241 (9), 230 (5), 213 (10), 200 (40), 189 (56), 173 (62), 160 (48), 141 (9), 128 (14), 115 (21), 99 (20), 77 (5), 65 (2).

**(1RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-4-Dichloroacetoxymethyl-9,11-epoxy-1,4,4a,9a-tetrahydro-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3(4H)-one (58).**

Dichloroacetyl chloride (25.5  $\mu$ l, 0.266 mmol) was added to the alcohol **57** (70 mg, 0.222 mmol) and pyridine (25  $\mu$ l, 0.310 mmol) in dichloromethane (5 ml) and stirred for 1 hour at room temperature. The mixture was acidified with 2M HCl (5 ml) and extracted with dichloromethane (3x25 ml). The combined organic phase was washed with brine (10 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 3:1) to afford the acetate **58** (91 mg, 96%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2961 (CH), 1764 (C=O), 1279 ( $\text{ArOCH}_3$ );  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.67 (1H, s, H-7), 6.52 (1H, s, H-5), 6.09 (1H, s,  $\text{COCHCl}_2$ ), 5.32 (1H, d,  $J = 5.4$  Hz, H-9), 5.11 (1H, dd,  $J = 5.6$  Hz,  $J = 5.4$  Hz, H-1), 4.87 (1H, d,  $J = 11.4$  Hz, H-1' $\alpha$ ), 3.93 – 3.80 (3H, m, H-4a, H-11, H-1' $\beta$ ), 3.73 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.54 (1H, ddd,  $J = 8.8$  Hz,  $J = 5.7$  Hz,  $J = 5.6$  Hz, H-9a), 2.36 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.76 (1H, q,  $J = 7.7$  Hz, H-10), 0.88 (3H, d,  $J = 7.6$  Hz,  $\text{CH}_3\text{-C10}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 172.09 (C3), 163.95 ( $\text{COCHCl}_2$ ), 161.54 (C6), 141.54 (C4b), 137.00 (C8), 135.89 (C8a), 116.58 (C5), 108.03 (C7), 81.77 (C11), 79.89 (C1), 79.33 (C9), 64.63 ( $\text{COCHCl}_2$ ), 64.49 (C1'), 55.70 ( $\text{CH}_3\text{-O-C6}$ ), 48.15 (C4), 45.63 (C9a), 45.33 (C4a), 38.02 (C10), 18.86 ( $\text{CH}_3\text{-C8}$ ), 16.05 ( $\text{CH}_3\text{-C10}$ );  $m/z$  430 ( $\text{M}^+$ ,  $^{37}\text{Cl}_2$ , 16%), 428 ( $\text{M}^+$ ,  $^{37}\text{Cl}^{35}\text{Cl}$ , 71%), 426 ( $\text{M}^+$ ,  $^{35}\text{Cl}_2$ , 100%), 392 (7), 299 (14), 269 (6), 241 (11), 213 (9), 200 (25), 189 (10), 173 (14), 159 (23), 115 (7), 81 (5).

**(1RS, 3SR, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-4-Dichloroacetoxymethyl-9,11-epoxy-1,3,4,4a,9,9a-hexahydro-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3-ol and (1RS, 3SR, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-9,11-Epoxy-1,3,4,4a,9,9a-hexahydro-4-hydroxymethyl-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran-3-ol (59).**

1M Diisobutylaluminum hydride in heptane (351  $\mu$ l, 0.351 mmol) was added dropwise to the lactone **58** (100 mg, 0.234 mmol) in toluene (5 ml) at -40°C and stirred for 20 minutes. Methanol (200  $\mu$ l) was added to quench the reaction, followed by 10% HCl (1 ml) also at -40°C. The mixture was warmed to room temperature and diluted with ethyl acetate (10 ml). The product was extracted with ethyl acetate (3x25 ml) and the combined organic phase was washed with brine (5 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 2:1) to afford the hemi-acetal **59** (57 mg, 57%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  3391 (OH), 2959 (CH), 2853 (w), 2840 (w), 1750 (C=O), 1141 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.94 (1H, s, H-7), 6.64 (1H, s, H-5), 6.01 (1H, s,  $\text{COCHCl}_2$ ), 5.29 (1H, s, H-3), 5.27 (1H, d,  $J = 5.4$  Hz, H-9), 4.76 (1H, d,  $J = 11.5$  Hz, H-1' $\alpha$ ), 4.56 (1H, dd,  $J = 5.4$  Hz,  $J_{1,11} = 5.6$  Hz, H-1), 4.08 (1H, d,  $J = 11.5$  Hz, H-1' $\beta$ ), 3.96 (1H, d,  $J = 8.9$  Hz, H-4a), 3.77 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.67 (1H, d,  $J = 5.6$  Hz, H-11), 3.22 (1H, ddd,  $J = 8.8$  Hz,  $J = 5.3$  Hz,  $J = 5.4$  Hz, H-9a), 2.37 (3H, s,  $\text{CH}_3\text{-C8}$ ), 1.52 (1H, q,  $J = 7.6$  Hz, H-10), 0.94 (3H, d,  $J = 7.7$  Hz,  $\text{CH}_3\text{-C10}$ );  $\delta_{\text{C}}$  (75MHz,  $\text{CDCl}_3$ ) 164.36 ( $\text{COCHCl}_2$ ), 160.97 (C6), 144.66 (C4b), 136.71 (C8), 136.33 (C8a), 115.03 (C5), 108.98 (C7), 91.14 (C3), 82.71 (C11), 80.56 (C9), 74.05 (C1), 68.37 (C1'), 64.72 ( $\text{COCHCl}_2$ ), 55.63 ( $\text{CH}_3\text{-O-C6}$ ), 44.10 (C9a), 41.37 (C4a), 40.23 (C4), 38.17 (C10), 18.96 ( $\text{CH}_3\text{-C8}$ ), 14.74 ( $\text{CH}_3\text{-C10}$ );  $m/z$  432 ( $\text{M}^+$ ,  $^{37}\text{Cl}_2$ , 9%), 430 ( $\text{M}^+$ ,  $^{37}\text{Cl}^{35}\text{Cl}$ , 44%), 428 ( $\text{M}^+$ ,  $^{35}\text{Cl}_2$ , 60%), 392 (21), 347 (16), 301 (19), 271 (9), 254 (18), 239 (23), 225 (48), 213 (15), 200 (34), 189 (91), 173 (22), 160 (100), 128 (13), 115 (17), 95 (7), 83 (15).

**(1RS, 3RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-3-(tert.-Butyldimethylsilyloxymethyl)-4-dichloroacetoxymethyl-9,11-epoxy-1,3,4,4a,9,9a-hexahydro-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran (60).**

*tert.*-Butyldimethylsilyl trifluoromethanesulfonate (30  $\mu$ l, 0.13 mmol) was added dropwise to the alcohol **59** (11 mg, 0.26 mmol) and *N,N*-diisopropylethylamine (46  $\mu$ l, 0.26 mmol) in dichloromethane (1 ml). Stirring was continued at room temperature for 1 hour. Methanol (1 ml) was added and the solvent was removed under reduced pressure. The residue was purified by flash chromatography directly on silica gel (petroleum ether 40-60°C : ethyl acetate = 20:1) to yield the ether **60** (10 mg, 72%) as a colourless oil;  $\nu_{\max}/\text{cm}^{-1}$  2954 (CH), 1750 (C=O), 1141 (C-O);  $\delta_{\text{H}}$  (300MHz,  $\text{CDCl}_3$ ) 6.62 (1H, s, H-7), 6.55 (1H, s, H-5), 5.91 (1H, s,  $\text{COCHCl}_2$ ), 5.28 (1H, s, H-3), 5.26 (1H, d,  $J = 5.4$  Hz, H-9), 4.51 (1H, dd,  $J = 5.6$  Hz,  $J = 5.5$  Hz, H-1), 4.43 (1H, d,  $J = 11.5$  Hz, H-1' $\alpha$ ), 4.34 (1H, d,  $J = 11.7$  Hz, H-1' $\beta$ ), 3.85 (1H, d,  $J = 8.9$  Hz, H-4a), 3.77 (3H, s,  $\text{CH}_3\text{-O-C6}$ ), 3.66 (1H, d,  $J = 5.5$  Hz, H-11), 3.14 (1H, ddd,  $J = 8.8$  Hz,  $J = 5.5$  Hz,  $J = 5.5$  Hz, H-9a), 2.36

(3H, s,  $CH_3$ -C8), 1.58 (1H, q,  $J = 7.6$  Hz, H-10), 0.98 (3H, d,  $J = 7.7$  Hz,  $CH_3$ -C10), 0.93 (9H, s,  $(CH_3)_3$ -C), 0.18 (3H, s,  $CH_3$ -Si), 0.12 (3H, s,  $CH_3$ -Si);  $\delta_C$  (75MHz,  $CDCl_3$ ) 164.20 (COCHCl<sub>2</sub>), 160.88 (C6), 144.96 (C4b), 136.80 (C8), 136.22 (C8a), 115.23 (C5), 108.57 (C7), 90.73 (C3), 82.60 (C11), 81.01 (C9), 73.79 (C1), 70.02 (C1'), 64.43 (COCHCl<sub>2</sub>), 55.67 ( $CH_3$ O-C6), 44.22 (C9a), 42.31 (C4), 41.95 (C4a), 38.53 (C10), 26.05 ( $(CH_3)_3$ -C), 18.93 ( $CH_3$ -C8), 18.20 ( $(CH_3)_3$ -C), 15.27 ( $CH_3$ -C10), -3.83 ( $CH_3$ -Si), -4.60 ( $CH_3$ -Si);  $m/z$  432 ( $M^+$  -  $C_4H_9$ ,  $^{37}Cl_2$ , 9%), 430 ( $M^+$  -  $C_4H_9$ ,  $^{37}Cl$   $^{35}Cl$ , 44%), 428 ( $M^+$  -  $C_4H_9$ ,  $^{35}Cl_2$ , 60%), 392 (21), 347 (16), 301 (19), 271 (9), 254 (18), 239 (23), 225 (48), 213 (15), 200 (34), 189 (91), 173 (22), 160 (100), 128 (13), 115 (17), 95 (7), 83 (15).

**(1RS, 3RS, 4SR, 4aSR, 9RS, 9aRS, 10SR, 11RS)-3-(tert.-Butyldimethylsilyloxymethyl)-9,11-epoxy-1,3,4,4a,9,9a-hexahydro-4-hydroxymethyl-6-methoxy-8,10-dimethyl-1,4-ethanoindeno[2,1-c]pyran (61).**

The dichloroacetate **60** (10 mg, 0.018 mmol), triethylamine (20  $\mu$ l, 0.144 mmol) and water (5  $\mu$ l) were stirred in methanol (1 ml) for 16 hours. The mixture was diluted with ethyl acetate (20 ml), washed with brine (2x5 ml) and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by flash chromatography on silica gel (petroleum ether 40-60°C : ethyl acetate = 10:1) to afford the alcohol **61** (7 mg, 90%) as a colourless oil;  $\nu_{max}/cm^{-1}$  3400 (OH), 2955 (CH), 2928 (CH), 1139 (C-O);  $\delta_H$  (300MHz,  $CDCl_3$ ) 6.91 (1H, s, H-5), 6.62 (1H, s, H-7), 5.29 (1H, s, H-3), 5.28 (1H, d,  $J = 5.4$  Hz, H-9), 4.51 (1H, dd,  $J = 5.4$  Hz,  $J = 5.6$  Hz, H-1), 3.97 (1H, d,  $J = 9.1$  Hz, H-4a), 3.79 (3H, s,  $CH_3$ O-C6), 3.60 (1H, d,  $J = 5.5$  Hz, H-11), 3.44 (1H, d,  $J = 11.1$  Hz, H-1' $\alpha$ ), 3.14 (1H, ddd,  $J = 9.1$  Hz,  $J = 5.5$  Hz,  $J = 5.4$  Hz, H-9a), 2.95 (1H, d,  $J = 11.0$  Hz, H-1' $\beta$ ), 2.36 (3H, s,  $CH_3$ -C8), 1.35 (1H, q,  $J = 7.6$  Hz, H-10), 0.95 (9H, s,  $(CH_3)_3$ -C), 0.82 (3H, d,  $J = 7.7$  Hz,  $CH_3$ -C10), 0.23 (3H, s,  $CH_3$ -Si), 0.22 (3H, s,  $CH_3$ -Si);  $\delta_C$  (75MHz,  $CDCl_3$ ) 160.87 (C6), 145.16 (C4b), 136.29 (C8), 135.66 (C8a), 115.02 (C5), 108.73 (C7), 93.52 (C3), 82.52 (C11), 80.57 (C9), 74.14 (C1), 64.38 (C1'), 55.41 ( $CH_3$ O-C6), 43.63 (C9a), 41.52 (C4a), 38.30 (C10), 37.26 (C4), 25.84 ( $(CH_3)_3$ -C), 18.64 ( $CH_3$ -C8), 17.84 ( $(CH_3)_3$ -C), 14.06 ( $CH_3$ -C10), -3.65 (2x  $CH_3$ -Si);  $m/z$  432 ( $M^+$ , 1%), 375 (40), 329 (6), 283 (16), 275 (12), 265 (14), 255 (23), 237 (12), 225 (26), 213 (21), 197 (16), 173 (20), 169 (22), 159 (100), 149 (24), 138 (26), 110 (27), 97 (33), 83 (43), 77 (29), 57 (42).