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# TOWARDS THE SYNTHESIS OF POLYOXYGENATED LABDANE DITERPENES: FURAN AS BUILDING BLOCK FOR THE C-RING

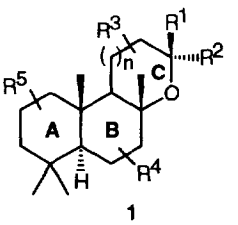
**Udo Lange, Winfried Plitzko, Siegfried Blechert***

Institut für Organische Chemie, Technische Universität Berlin,
Straße des 17. Juni 135, D-10623 Berlin, Germany

***Abstract:*** *The highly functionalized cis-decalin system **11** is prepared by an intramolecular Michael addition reaction of the hydroxydihydropyranone derivative **4** which is obtained by oxidative ring-opening of furfuryl alcohol **9**. The three carbonyl groups of **11** are differentiated by the use of neighbour-group effects giving **12** which is transformed into the tricyclic compound **13** an interesting precursor for the synthesis of various labdane diterpenes.*

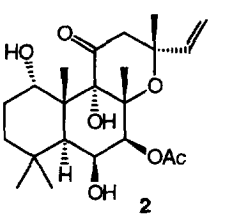
## INTRODUCTION

Within recent years, there has been a continuous high interest in the total synthesis of certain polyoxygenated labdane diterpenes **1**,[1] most prominently forskolin **2**.[2] Many of these labdanes exhibit interesting biological activities,[3] but are of limited availability from natural resources. We were interested in designing a new synthesis for the basic skeleton of these diterpenes that allows the introduction of various functional groups, especially in the C-ring.




**1**

n = 0, 1

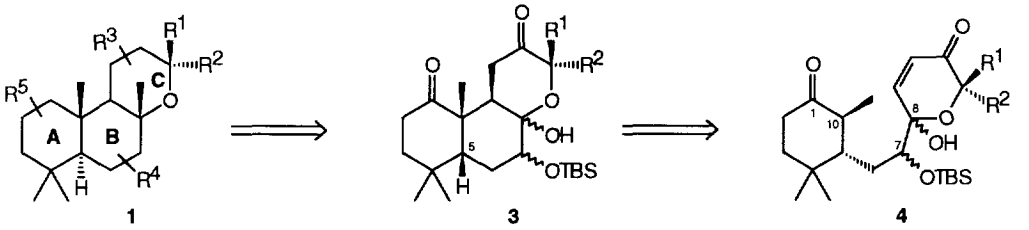



**2**

The retrosynthetical analysis of the labdane skeleton **1** showed that the tricyclic ringsystem could be build up by an intramolecular Michael addition from an A,C-ring precursor of type **4** (scheme 1). The carbonyl group

in the A-ring at C-1 establishes the required C,H-acidity at C-10 and can be used to introduce a variety of functional groups. The Michael acceptor in the C-ring can easily be obtained by an oxidative ring-opening of a furfuryl alcohol. The furan was chosen as a precursor for the C-ring because this latent 1,4-dicarbonyl is a very flexible building block permitting the construction of different substitution patterns[4] and should therefore allow the synthesis of various labdane diterpenes. The envisaged *cis*-annulation of the A,B-ring system in the cyclization product **3**[5] should prove beneficial for the selective introduction of substituents from the β-face of the molecule. At a later stage of the synthesis the stereochemistry at C-5 will have to be inverted.

**Scheme 1**



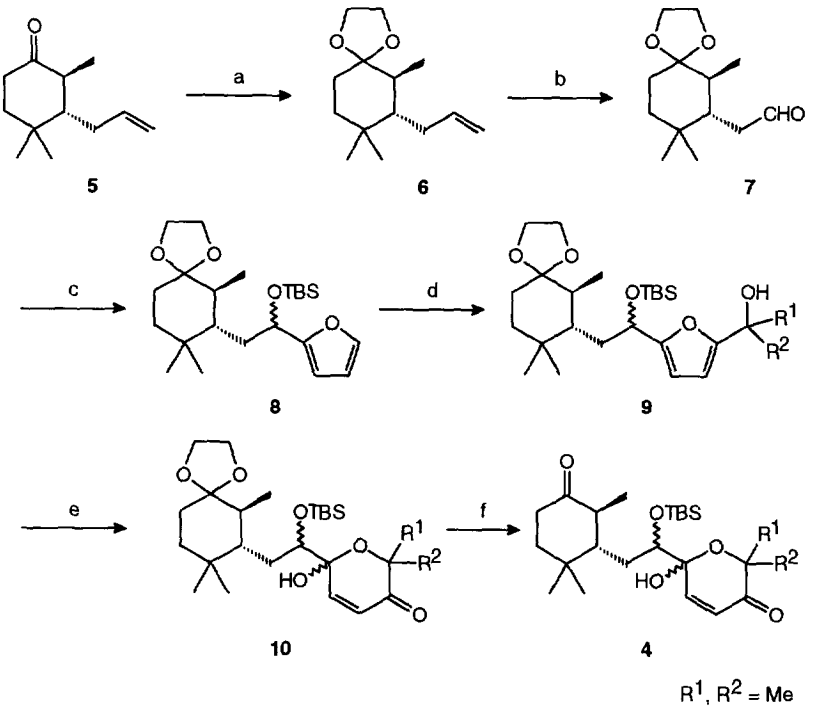

## RESULTS AND DISCUSSION

The requisite A,C-ring precursor **4** for the planned intramolecular Michael addition was prepared as depicted in scheme 2. Starting from ketone **5**[6] ketalization, subsequent ozonolysis and reductive work-up with zinc dust and acetic acid afforded aldehyde **7** in 88% overall yield as a 1:4.4 mixture of diastereoisomers. The mixture of the diastereoisomers could be used for the next steps without separation because the stereogenic centre C-10 was to be planarized in the envisioned intramolecular Michael addition. 1,2-Addition of 2-furyllithium to aldehyde **7** and trapping of the intermediate alcoholate with *t*-butyldimethylsilyl chloride furnished the furan derivative **8** as a mixture of four diastereoisomers. In principle, the newly formed stereogenic centre C-7 could be epimerized or planarized at an advanced stage of the synthesis. Deprotonation of furan **8** with *t*-butyllithium and reaction with acetone yielded furfuryl alcohol **9** in 77% yield. Based on consumed starting material the yield of **9** was 98%.

For our initial studies we chose acetone for the sake of simplicity ($R^1$, $R^2$ = Me), anticipating that in the reaction sequence shown in scheme 2 differently functionalized side chains ($R^1 \neq R^2$) are tolerated, too.

The desired hydroxydihydropyranone **4** was prepared by oxidative ring-opening of the furan in **9** followed by deketalization as a complex mixture of diastereoisomers. By this route **4** was obtained in multigram quantities and could be used for the following cyclization reaction without purification or protection of the anomeric alcohol at C-8.

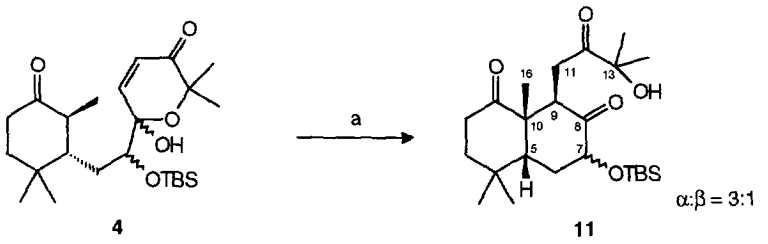
**Scheme 2**[g]




a) Ethylene glycol, *p*-TsOH, benzene, Δ, 12 h, 98 %; b) $O_3$, $CH_2Cl_2$:MeOH = 9:1, -78 °C then Zn, HOAc, -78 °C to r.t., 90 %; c) 1. 2-furyllithium, THF, -78 °C, 3 h, 2. TBSCl, THF, 0 °C to r.t., 12 h, 72 %; d) 1. *t*-BuLi, THF, -78 °C, 2 h, 2. acetone, -78 °C to r.t., 2.5 h, 77 % (98 % based on consumed starting material); e) *m*CPBA, $CH_2Cl_2$, 0 °C to r.t., 12 h, 92 %; f) PyHOTs, acetone: water = 9:1, Δ, 9 h, 98 %; g) *In scheme 2 only the major trans-isomers are shown.*

Treatment of **4** with catalytic amounts of potassium carbonate in methanol at room temperature furnished the highly functionalized *cis*-decalin **11** as a 3:1 mixture of diastereoisomers in an intramolecular Michael addition (scheme 3).

**Scheme 3**



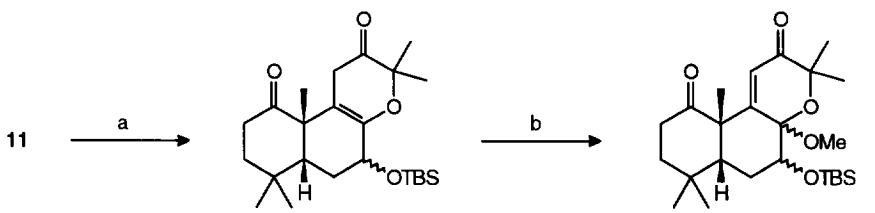

a) $K_2CO_3$, MeOH, r.t., 12 h, 33-55 %.

The expected *cis*-annulation of the A,B-ring moiety[5] was confirmed by NOE effects between the proton signals of the angular methyl group (H-16) at C-10 and the methin proton H-5. The relative stereochemistry at C-7 and C-9 was also assigned on the basis of NOE effects. While the NOE spectra of both stereoisomers exhibited effects between H-16 and H-11 the main stereoisomer showed an additional effect between H-5 and H-7 and the minor stereoisomer between H-7 and H-9, respectively. Three singulets in the $^{13}C$ NMR spectrum of the cyclization product above 200 ppm which were assigned to three saturated carbonyl groups indicated the opening of the semiketal at C-9 during the cyclization.

Despite the low yield in the cyclization step the product of the Michael addition **11** was obtained in 7 steps and 19-31 % overall yield starting from ketone **5** in multigram quantities.

After the successful cyclization the pivotal problem was the differentiation of the three carbonyl groups in the cyclization product **11**. A differentiation by means of chemoselective reducing agents could not be achieved. Reactivity studies of **11** encouraged us, however, to attempt a selective protection of the carbonyl group at C-8 with the help of the neighbour-group effect displayed by the hydroxy group at C-13. Treatment of **11** with boron trifluoride etherate afforded glycal **12** among other products in low yield. This useful reaction was optimized by switching from the Lewis acid $BF_3{\cdot}OEt_2$ to a Brønstedt acid and strong dehydrating conditions. Best results were obtained with phosphorus pentoxide in dichloromethane (scheme 4).

**Scheme 4**




a) $P_4O_{10}$, $CH_2Cl_2$, r.t., 1 h, 72 %; b) $PhI(OAc)_2$, NaOH, MeOH, r.t., 1 h, 56 %.

In a tandem reaction consisting of an electrophilic attack of a hypervalent iodine species on the double bond of the glycal, trapping of the formed cation with methanolate and elimination of iodobenzene **12** was transformed into **13**. In compound **13** the three former carbonyl groups of **11** can be easily distinguished. The carbonyl group at C-8 is protected as a ketal and the two carbonyl groups in the A- and C-ring should display very different reactivities because the C-ring carbonyl is α,β-unsaturated.[7] Furthermore, the newly introduced double bond between C-9 and C-11 in **13** is useful for further transformations in this molecular region.

In summary, a concise synthesis of a highly functionalized intermediate for the preparation of polyoxygenated labdane diterpenes has been described. The key step of the reaction sequence is an intramolecular Michael addition reaction. The requisite Michael acceptor was obtained by oxidative ring-opening of a furfuryl alcohol.

We currently investigate whether this strategy can be extended to systems bearing an additional oxygen functionality at C-6 and different substituents at C-13.

## EXPERIMENTAL

$^1$H NMR spectra were measured in $CDCl_3$ with $CHCl_3$ ($\delta$ = 7.26 ppm) as internal standard on a Bruker AM 400 (400 MHz) or a Bruker AC 200 spectrometers, respectively. $^{13}$C NMR spectra were recorded on a Bruker AM 400 (100.6 MHz), a Bruker AM 270 (67.5 MHz) or a Bruker AC 200 (50.1 MHz) spectrometers, respectively. Infrared spectra were obtained on a Perkin-Elmer model 881 spectrophotometer. Mass spectra were recorded on a Varian MAT 711 mass spectrometer (70 eV) using a direct inlet. Melting points are uncorrected and were obtained on a Büchi SMP-20. THF was freshly distilled from potassium and dichloromethane from calcium hydride. All reactions were carried out in an atmosphere of argon unless stated otherwise.

**7-Allyl-6,8,8-trimethyl-1,4-dioxaspiro[4.5]decane (6).** 3-Allyl-2,4,4-trimethyl-cylcohexanone[5] **(5)** (37.3 g, 207 mmol), ethylene glycol (34 mL, 610 mmol) and *p*-toluenesulfonic acid (0.3 g) were heated in benzene (500 mL) for 12 h under reflux. The excess ethylene glycol was removed and the solution of the crude product was washed successively with sat. aqu. $NaHCO_3$ (2 x) and water (2 x). After drying ($MgSO_4$) the solvent was removed under reduced pressure. The product was used for the next step without further purificaton. Yield 45.5 g (98 %), mixture of diastereoisomers, *cis:trans* = 1:4.4, pale yellow oil. Spectroscopic data of the *trans*-diastereoisomer: $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 0.85 (3H, s); 0.89 (3H, d, J = 7 Hz); 0.94 (3H, s); 1.25-1.66 (5H, m); 1.76 (1H, dq, J = 12, 7 Hz); 1.96 (1H, m); 2.22 (1H, m); 3.93 (4H, m); 4.90 (1H, dddd, J = 10, 1.5, 1.5, 1.5 Hz); 4.99 (1H, dddd, J = 17, 1.5, 1.5, 1.5 Hz); 5.85 (1H, dddd, J = 17, 10, 7, 7 Hz). MS: m/z (%) = 224 (6, $M^{+\cdot}$); 209 (3); 183 (3); 153 (6); 139 (3); 100 (10); 99 (100); 86 (12). HRMS calc. for $C_{14}H_{24}O_2$ ($M^{+\cdot}$) 224.1776, found 224.1776.

**(6,8,8-Trimethyl-1,4-dioxaspiro[4.5]dec-7-yl)-ethanal (7).** A solution of olefin **6** (10.2 g, 45.5 mmol) in $CH_2Cl_2$/MeOH = 9:1 (500 mL) was ozonized at -78 °C until the solution had a persistent blue colour. The excess ozon was removed by bubbling argon through the solution. Zinc dust (30 g) and acetic acid (45 mL) were added and the mixture slowly warmed to r.t. After stirring at r.t. for 1.5 h the zinc was removed by filtration through a pad of Celite. The filtrate was washed neutral with sat. aqu. $NaHCO_3$, water and brine and dried ($MgSO_4$). The solvent was removed under reduced pressure. The product was used without further purification for the next step. Yield 9.2 g (90 %), pale yellow oil. $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 0.78 (3H, d, J = 6.5 Hz); 0.84 (3H, s); 0.92 (3H, s); 1.34-1.68 (4H, m); 1.74 (1H, dq, J = 6.5, 12 Hz); 1.95 (1H, ddd, J = 3, 7, 12 Hz); 2.24 (1H, ddd, J = 3, 7, 17 Hz); 2.40 (1H, ddd, J = 1, 3, 17 Hz); 3.95 (4H, m); 9.76 (1H, dd, J = 1, 3 Hz). IR ($CCl_4$): $\nu$ = 1735 cm$^{-1}$. MS: m/z (%) = 226 (2, $M^{+\cdot}$); 155 (8); 127 (10); 99 (100); 86 (16). HRMS calc. for $C_{13}H_{22}O_3$ ($M^{+\cdot}$) 226.1569, found 226.1569.

**7-(2-Furan-2-yl-2-*t*-butyldimethylsiloxyethyl)-6,8,8-trimethyl-1,4-dioxaspiro[4.5]decane (8).** A solution of furan (4.2 mL, 57.7 mmol) in THF (50 mL) was treated with a 1.6 M solution of *n*-butyllithium in *n*-hexane (27.2 mL, 43.5 mmol) at 0 °C. After stirring at 0 °C for 30 min the solution was warmed to r.t. and stirring was continued for another 30 min. Upon cooling to -78 °C a solution of aldehyde **7** (6.56 g, 29.0 mmol) in THF (50 mL) was added over 20 min. The reaction mixture was slowly warmed to r.t. over 3 h. After cooling to 0 °C *t*-butyldimethylsilyl chloride (8.74 g, 58.0 mmol) was added and the mixture stirred for another 12 h while gradually warming to r.t. Water was added and the aqueous layer was extracted with MTBE (5 x). The combined extracts were washed neutral with brine and were dried ($MgSO_4$). The solvent was evaporated under reduced pressure and the crude product purified by flash column chromatography (silica, PE:MTBE = 95:5). Yield 8.50 g (72 %), 4:2:1 mixture of diastereoisomers, yellow oil. Spectroscopic data of the main stereoisomer: $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = -0.13 (3H, s); 0.07 (3H, s); 0.80 (3H, s); 0.86 (9H, s); 0.86 (3H, d, J = 6.5 Hz); 0.98 (3H, s); 0.90-2.10 (8H, m); 3.85-4.00 (4H, m); 4.66 (1H, dd, J = 3, 10 Hz); 6.13 (1H, dbr, J = 3 Hz); 6.28 (1H, dd, J = 1, 3 Hz); 7.33 (1H, dbr, J = 1 Hz). $^{13}$C NMR ($CDCl_3$, 50.1 MHz): $\delta$ = 158.0 (C); 141.0 (CH); 110.9 (C); 109.9, 105.1, 69.3 (3 x CH); 65.0 (2 x $CH_2$); 44.7, 42.3 (2 x CH); 38.7, 38.4, 31.4 (3 x $CH_2$); 33.7 (C); 27.0, 19.3, 11.2 (3 x $CH_3$); 25.8 ($CH_3$, *t*-Bu); 18.1 (C); -4.7, -5.0 (2 x $CH_3$). MS: m/z (%) = 408 (1, $M^{+\cdot}$); 393 (1); 351 (5); 257 (25); 211 (30); 197 (5); 161 (5); 139 (10); 137 (12); 119 (49); 99 (100); 75 (70); 55 (36). HRMS calc. for $C_{19}H_{31}O_4Si$ (M-Bu) 351.1992, found 351.1992.

**2-{5-[1-*t*-Butyldimethylsiloxy-2-(6,8,8-trimethyl-1,4-dioxaspiro[4.5.]dec-7-yl)ethyl]-furan-2-yl} propan-2-ol (9).** A solution of furan **8** (8.40 g, 20.6 mmol) in THF (150 mL) was treated with a 1.65 M solution of *t*-butyllithium in *n*-pentane (15.2 mL, 25.0 mmol) at 0 °C. After stirring for 2 h at 0 °C the mixture was cooled to -78 °C. Acetone (1.8 mL, 24.5 mmol) was added and stirring was continued for 2.5 h. Sat. aqu. $NH_4Cl$ (40 mL) was added and the mixture warmed to r.t. The aqueous layer was extracted with MTBE (5 x). The combined extracts were washed neutral with brine and dried ($MgSO_4$). The crude product was purified by flash column chromatography (silica, PE:MTBE = 6:4). Yield 7.38 g (77%), 4:2:1 mixture of diastereoisomers, pale yellow oil. 1.74 g, 21 % of the starting material was recovered. Spectroscopic data of the main stereoisomer: $^1H$ NMR ($CDCl_3$, 400 MHz): δ = -0.10 (3H, s); 0.07 (3H, s); 0.80 (3H, d, J = 6.5 Hz); 0.84 (3H, s); 0.87 (9H, s); 0.98 (3H, s); 1.58 (6H, s); 0.90-2.20 (8H, m); 3.80-4.00 (4H, m); 4.50-4.65 (1H, m); 6.05-6.15 (2H, m). $^{13}C$ NMR ($CDCl_3$, 50.1 MHz): δ = 158.9, 158.6, 110.9 (3 x C); 105.8, 103.9 (2 x CH); 77.2 (C); 68.8 (CH); 65.0, 64.8 (2 x $CH_2$); 44.6, 42.1 (2 x CH); 38.6, 38.1, 31.3 (3 x $CH_2$); 33.8 (C); 30.3, 28.8, 26.8 19.3, 11.0 (5 x $CH_3$); 25.8 ($CH_3$, *t*-Bu); 18.1 (C); -4.6, -5.0 (2 x $CH_3$). IR ($CCl_4$): ν = 3610 $cm^{-1}$. MS: m/z (%) = 409 (40, $[M\text{-}Bu]^+$); 317 (22); 269 (100); 251 (16); 225 (20); 183 (98); 137 (22); 99 (62); 75 (32); 73 (58). HRMS calc. for $C_{22}H_{37}O_5Si$ (M-Bu) 409.2410, found 409.2410.

**6-Hydroxy-6-[1-*t*-butyldimethylsiloxy-2-(6,8,8-trimethyl-1,4-dioxaspiro[4.5]dec-7-yl)ethyl]-2,2-dimethyl-6H-pyran-3-one (10).** A solution of furfuryl alcohol **9** (7.38 g, 15.8 mmol) in $CH_2Cl_2$ (200 mL) was cooled to 0 °C and treated with 70 % *m*CPBA (4.29 g, 17.4 mmol). The solution was gradually warmed to r.t. over 12 h and then was washed with sat. aqu. $NaHCO_3$ (4 x 100 mL) and with brine (2 x 100 mL). The solvent was evaporated under reduced pressure and the crude product was used without further purification. Yield 6.99 g (92 %), 6:3:1:1 mixture of stereoisomers, pale yellow oil. For analytical purposes a small sample was purified by flash column chromatography, silica gel, PE:MTBE = 75:25. Spectroscopic data of the main stereoisomer: $^1H$ NMR ($CDCl_3$, 200 MHz): δ = 0.17 (3H, s); 0.21 (3H, s); 0.75 (3H, s); 0.87 (3H, s); 0.92 (3H, d, J = 6.5 Hz); 0.94 (9H, s); 1.36 (3H, s); 1.52 (3H, s); 0.90-1.90 (8H, m); 3.45 (1H, sbr, OH); 3.80-4.00 (5H, m); 6.09 (1H, d, J = 10 Hz); 6.98 (1H, d, J = 10 Hz). $^{13}C$ NMR ($CDCl_3$, 67.5 MHz): δ = 199.6 (C); 144.4, 126.6 (2 x CH); 110.8, 94.8, 78.9 (3 x C); 78.8 (CH); 65.5, 64.9 (2 x $CH_2$); 43.7, 42.5 (2 x CH); 38.5, 31.3, 29.7 (3 x $CH_2$); 33.8 (C); 29.8, 28.0, 25.3, 19.5, 11.6 (5 x $CH_3$); 26.3 ($CH_3$, *t*-Bu); 18.5 (C); -2.7, -3.8 (2 x $CH_3$). IR ($CCl_4$): ν = 3587, 3508, 1697, 1636 $cm^{-1}$. MS: m/z (%) = 482 (5, $M^{+\cdot}$); 425 (10, $[M\text{-}Bu]^+$); 407 (6); 341 (74); 292 (4); 279 (6); 256 (4); 241 (5); 209 (6); 183 (48); 147 (6); 139 (7); 123 (4); 121 (4); 109 (4); 99 (100); 75 (32); 73 (32). HRMS calc. for $C_{26}H_{46}O_6Si$ ($M^{+\cdot}$) 482.3064, found 482.3064.

**6-[1-*t*-Butyldimethylsiloxy-2-(2,6,6-trimethyl-5-oxo-cyclohexyl)-ethyl]-6-hydroxy-2,2-dimethyl-6H-pyran-3-one (4).** A solution of ketone **10** (6.854 g, 14.2 mmol) and pyridinium *p*-toluenesulfonate (1.072 g, 4.3 mmol) in acetone:water (150 mL, 9:1) was heated under reflux for 9 h. The solution was concentrated under reduced pressure. MTBE (500 mL) was added. The organic layer was washed with sat. aqu. $NaHCO_3$ (3 x 100 mL) and with brine (100 mL). The solution was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The crude product was used without further purification. Yield 6.078 g (98%), pale yellow oil. For analytical purposes a small sample was purified by flash column chromatography, silica gel, PE:MTBE = 75:25. Spectroscopic data of the main stereoisomer: $^1H$ NMR ($CDCl_3$, 200 MHz): δ = 0.09 (3H, s); 0.17 (3H, s); 0.88 (3H, s); 0.90 (9H, s); 0.91 (3H, s); 1.00 (3H, d, J = 6.5 Hz); 1.36 (3H, s); 1.52 (3H, s); 0.90-2.60 (8H, m); 3.28 (1H, sbr, OH); 3.60-3.80 (1H, m); 6.12 (1H, d, J = 10 Hz); 6.88 (1H, d, J = 10 Hz). $^{13}C$ NMR ($CDCl_3$, 50.1 MHz): δ = 212.7, 199.3 (2 x C); 143.9, 126.7 (2 x CH); 94.8 (C); 79.0 (CH); 78.5 (C); 47.8, 47.3 (2 x CH); 41.3, 38.2, 34.7 (3 x $CH_2$); 34.7 (C); 27.9, 26.9, 25.3, 19.5, 12.9 (5 x $CH_3$); 26.2 ($CH_3$, *t*-Bu); 18.4 (C); -3.0, -3.9 (2 x $CH_3$). IR ($CCl_4$): ν = 3500, 1714, 1699 $cm^{-1}$. MS: m/z (%) = 381 (5, $[M\text{-}Bu]^+$); 363 (6); 335 (4); 323 (4); 297 (24); 253 (6); 213 (6); 199 (5); 139 (16); 97 (16); 75 (20); 73 (100); 57 (50). HRMS calc. for $C_{20}H_{33}O_5Si$ (M-Bu) 381.2097, found 381.2097.

**6-*t*-Butyldimethylsiloxy-8-(3-hydroxy-3-methyl-2-oxo-butyl)-4,4,8a-tri-methyloctahydronaphthalene-1,7-dione (11).** A solution of ketone **4** (6.078 g, 13.9 mmol) in methanol (500 mL) was treated with $K_2CO_3$ (100 mg) at r.t. for 20 h. The solution was concentrated under reduced pressure. The solution was

diluted with MTBE (300 mL) and water was added (150 mL). The aqueous layer was extracted with MTBE and the combined extracts were washed neutral with brine. The solution was dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (silica gel, PE:MTBE = 1:1). Yield 2.002 g (33%), 3:1 mixture of diastereoisomers, pale yellow oil. On a 0.2 mmol scale the yield of purified **11** was 55%. $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.09 (3H, s); 0.11 (3H, s); 0.88 (9H, s); 0.96 (3H, s); 1.00 (3H, s); 1.03 (3H, s); 1.36 (3H, s); 1.42 (3H, s); 1.70 (1H, ddbr, J = 5, 13 Hz); 1.83 (1H, ddd, J = 6.5, 9, 14 Hz); 2.01 (1H, ddd, J = 5, 5, 13 Hz); 2.07 (1H, ddd, J = 6, 9, 14 Hz); 2.12 (1H, ddd, J = 11.5, 13, 13.5 Hz); 2.19 (1H, dd, J = 3, 17.5 Hz); 2.46 (1H, ddd, J = 6, 9.5, 18 Hz); 2.52 (1H, ddd, J = 6, 9, 18 Hz); 3.03 (1H, dd, J = 8.5, 17.5 Hz); 3.66 (1H, sbr, OH); 3.73 (1H, dd, J = 3, 8.5 Hz); 3.84 (1H, dd, J = 5, 11.5 Hz). $^{13}C$ NMR (50.1 MHz, $CDCl_3$): δ = 214.9, 212.6, 209.7, 76.4 (4 x C); 72.6, 52.4 (2 x CH); 48.6 (C); 46.1 (CH); 34.3 ($CH_2$); 33.6 (C); 33.1, 31.6, 30.7 (3 x $CH_2$); 29.0, 26.8, 26.5, 25.4, 24.2 (5 x $CH_3$); 25.7 ($CH_3$, *t*-Bu); 18.3 (C); -4.9, -5.3 (2 x $CH_3$). IR ($CCl_4$): ν = 3508, 1733, 1709 $cm^{-1}$. MS: m/z (%) = 423 (2); 381 (36); 363 (24); 335 (16); 297 (70); 253 (22); 243 (24); 155 (22); 139 (52); 97 (22); 75 (92); 73 (96); 69 (48); 59 (100). HRMS calc. for $C_{20}H_{33}O_5Si$ (M-Bu) 381.2097, found 381.2097.

**5-*t*-Butyldimethylsiloxy-3,3,7,7,10a-pentamethyl-1,5,6,6a,7,8,9,10a-octa-hydrobenzo[f]chromene-2,10-dione (12). 11** (23 mg, 53 μmol) was dissolved in dry $CH_2Cl_2$ (4 mL) and treated with phosphorus pentoxide (10 mg, 70 μmol) at r.t. for 1 h. The solution of the crude product was purified by filtration through a short column (silica gel, $CH_2Cl_2$ then MTBE). The solvent was evaporated under reduced pressure. Yield 16 mg (72%), 3:1 mixture of stereoisomers, pale yellow oil. Spectroscopic data of the main stereoisomer: $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.13 (3H, s); 0.14 (3H, s); 0.93 (9H, s); 1.02 (3H, s); 1.13 (3H, s); 1.23 (3H, s); 1.33 (3H, s); 1.35 (3H, s); 1.50-1.58 (1H, m); 1.68 (1H, ddbr, J = 6, 6 Hz); 1.95 (1H, ddd, J = 4.5, 6, 15 Hz); 2.10 (1H, ddd, J = 6, 6, 15 Hz); 2.20-2.47 (3H, m); 2.61 (1H, dd, J = 1, 20.5 Hz); 2.77 (1H, dd, J = 2.5, 20.5 Hz); 4.15 (1H, m). $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 214.7, 209.7, 149.0, 108.5, 80.7 (5 x C); 64.7 (CH); 51.3 (C); 50.5 (CH); 35.9, 35.1, 34.7, 31.8 (4 x $CH_2$); 33.5 (C); 30.9, 27.6, 24.5, 23.9, 23.4 (5 x $CH_3$); 26.0 ($CH_3$, *t*-Bu); 18.4 (C); -4.4, -4.8 (2 x $CH_3$). IR ($CCl_4$): ν = 1730, 1710, 1691 $cm^{-1}$. MS: m/z (%) = 420 (2, $M^{+\cdot}$); 419 (3); 379 (20); 363 (20); 321 (5); 288 (26); 259 (22); 225 (12); 149 (20); 139 (10); 97 (10); 95 (8); 91 (8); 77 (10); 75 (100); 73 (74); 69 (72). HRMS calc. for $C_{20}H_{31}O_4Si$ (M-Bu) 363.1991, found 363.1991.

**5-*t*-Butyldimethylsiloxy-4a-methoxy-3,3,7,7,10a-pentamethyl-4a,5,6,6a,7,8,9,10a-octahydrobenzo [f]chromene-2,10-dione (13).** A solution of **12** (17 mg, 40 μmol) in methanol (2 mL) was treated with iodobenzene diacetate (14 mg, 45 μmol) and sodium hydroxide (2 mg, 50 μmol) at r.t. for 1 h. The mixture was diluted with MTBE (30 mL) and washed neutral with water and brine. The solution was dried ($MgSO_4$), the solvent was evaporated under reduced pressure and the crude product was purified by preparative thin layer chromatography (silica gel, PE:MTBE = 1:1). Yield 10 mg (56%), 3:3:1:1 mixture of stereoisomers. Spectroscopic data of more polar main stereoisomer: $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.02 (3H, s); 0.09 (3H, s); 0.87 (9H, s); 1.12 (3H, s); 1.23 (3H, s); 1.39 (3H, s); 1.43 (3H, s); 1.45 (3H, s); 1.68 (1H, ddd, J = 6, 9, 14 Hz); 1.77 (1H, ddbr, J = 8, 12 Hz); 1.90 (2H, m); 2.01 (1H, ddd, J = 6.5, 6.5, 14 Hz); 2.38 (1H, ddd, J = 6, 6.5, 17 Hz); 2.62 (1H, ddd, J = 6.5, 9, 17 Hz); 3.47 (3H, s); 3.52 (1H, dd, J = 6.5, 9.5 Hz); 6.04 (1H, s). $^{13}C$ NMR (67.5 MHz, $CDCl_3$): δ = 209.4; 199.6; 160.1; 123.0; 95.2; 77.2; 77.0; 53.1; 51.7; 48.3; 35.6; 33.9; 33.1; 32.6; 32.0; 30.1; 28.1; 25.7; 24.9; 18.1; -4.4; -4.8. IR ($CCl_4$): ν = 1713, 1693 $cm^{-1}$. MS: m/z (%) = 450 (1, $M^{+\cdot}$); 393 (38); 361 (26); 335 (54); 318 (18); 303 (18); 275 (14); 260 (36); 243 (25); 213 (22); 189 (18); 173 (26); 167 (32); 149 (100); 145 (14); 133 (16); 105 (14); 95 (14); 89 (20); 83 (14); 75 (46); 73 (74). HRMS calc. for $C_{25}H_{42}O_5Si$ ($M^{+\cdot}$) 450.2852, found 450.2852.

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