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A simple and efficient synthesis of enantiomeric (3a*RS*,4*RS*,6a*SR*)-4-hydroxy-3,3a,4,6a-tetrahydro-1*H*-cyclopenta[*c*]furan-1-ones

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ABSTRACT

Diastereomeric amides produced via the cleavage of easily available (±)-7,7-dichloro-4-*exo*-trimethylsilylbicyclo[3.2.0]hept-2-en-6-one by treatment with (+)-α-methylbenzylamine were transformed into bicyclic lactam-aminals, which can easily be separated by column chromatography on SiO_2. The latter products lead to enantiomeric (3a,6a)-4-hydroxy-3,3a,4,6a-tetrahydro-1*H*-cyclopenta[*c*]furan-1-ones after the removal of the chiral auxiliary and epoxidation.

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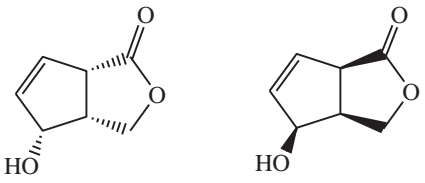
1. Introduction

In the synthesis of natural and unnatural biologically active cyclopentanoids, the preparation of chiral orthogonally functionalized cyclopentane (cyclopentene) block-synthons is important.[1] They are required in the synthesis of monocyclic cyclopentanoids (prostaglandins,[2] carbanucleosides,[3] pheromones,[4] cyclopentenone antibiotics[5]) as well as in approaches to the more complex bi- and polycyclic compounds containing a fragment of the cyclopentane ring (Brefeldin A,[6] Hitachimycin,[7] Didemenones,[8] Hybridalactone,[9] Retigeranic Acid,[10] Quadrone,[11] Ginkgolide[12]).

In this paper, we describe the synthesis of new enantiomeric γ-lactones (3a*R*,4*R*,6a*S*)-**1** and (3a*S*,4*S*,6a*R*)-**1**, which may find various applications in approaches to a variety of the cyclopentanoids (Fig. 1).



(3a*R*,4*R*,6a*S*)-**1** (3a*S*,4*S*,6a*R*)-**1**

Fig. 1. Target hydroxylactones (3a*R*,4*R*,6a*S*)-**1** and (3a*S*,4*S*,6a*R*)-**1**.

2. Results and discussion

As a basic starting compound in the synthesis of compounds **1**, an easily available racemic bicyclic adduct **2** was selected.[13] Optical resolution of **2** was carried out using (+)-α-methylbenzylamine by the method previously described by us[14] for the analogue of **2** without the TMS-group. A cleavage of the dichlorocyclobutane ring of **2** by treatment with (+)-α-methylbenzylamine gave an inseparable mixture of diastereomers **3** and **4**. Hydrolysis of the *gem*-dichloromethyl group in **3** and **4** gave bicyclic aminals **5** and **6**, which were easily separated by column chromatography on SiO_2 (Scheme 1). Each of these bicyclic acetals was stereochemically pure and did not contain any C3-epimer. Compounds **5** and **6** were characterized as the less hindered *exo*-epimers. Thus, in the ^{1}H NMR spectrum a doublet resonance for the 3-H at 1.82 ppm appeared with $J_{3,3a}$=4.0 Hz, which is characteristic for **5**.

The individual aminals **5** and **6** were transformed into lactones **9**[15] by the consecutive operations of the borohydride reduction and acidic hydrolysis of amides **7** and **8**.

Treatment of compounds **9** with *m*-CPBA gave the unstable *endo*-epoxides **10**. The epoxidation in this case proceeds

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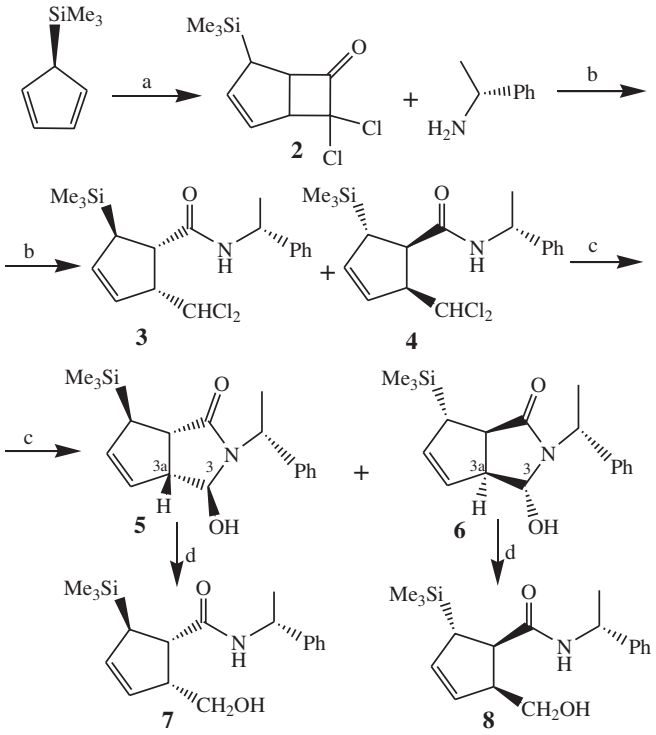


a) $Cl_2CHCOCl$, NEt_3, hexane, 0 ^{0}C, 5 h, 70%; b) benzene, rt, 4 h, 92%; c) MeCN:H_2O, 4:1, reflux, 8 h, 93%; d) $NaBH_4$, dioxane:H_2O, 5:1, reflux, 5 h, 91-92%.

Scheme 1. Optical resolution of (±)-7,7-dichloro-4-*exo*-trimethylsilylbicyclo[3.2.0] hept-2-en-6-one 2..

stereoselectively, due to steric factor.[13] Finally, removal of the TMS-group by the fragmentation of *endo*-epoxides **10** led to targets hydroxylactones (3a*R*,4*R*,6a*S*)-**1** and (3a*S*,4*S*,6a*R*)-**1** (Scheme 2).

The stereochemistry of the stereogenic centers of compounds (3a*R*,4*R*,6a*S*)-**1** and (3a*S*,4*S*,6a*R*)-**1** and their precursors was assigned based on X-ray data for lactone (3a*R*,6*R*,6a*S*)-**9**. The structure of (3a*R*,6*R*,6a*S*)-**9** was determined by single-crystal XRD study (see Experimental). The values of Flack parameter of −0.07(13) and Hooft parameter of −0.02(11) identified the absolute configuration as (3a*R*,6*R*,6a*S*) (Fig. 2).

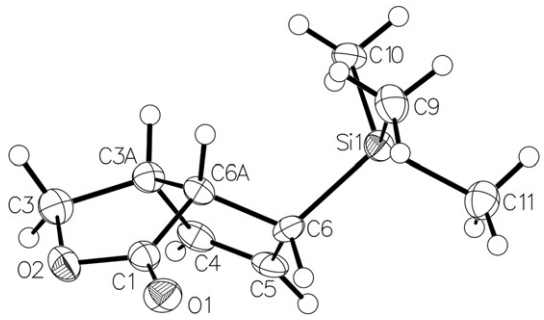


Fig. 2. The general view of molecule (3a*R*,6*R*,6a*S*)-**9** in crystal. Atoms are represented by thermal displacement ellipsoids (p=50%).

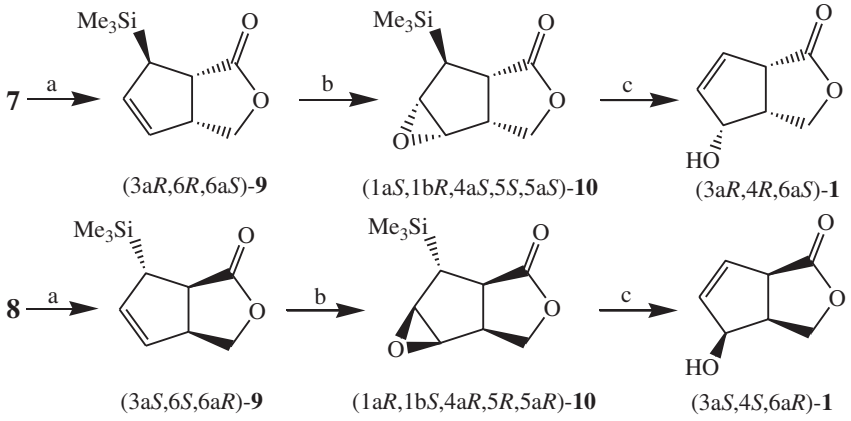
3. Conclusion

We have developed a convenient route to enantiomeric hydroxylactones (3a*R*,4*R*,6a*S*)-**1** and (3a*S*,4*S*,6a*R*)-**1** from a common source. Prepared compounds may find applications as key building blocks in the design and synthesis of a wide range of biologically active cyclopentanoids.

4. Experimental

4.1. General

Solvents were purified and dried by standard procedures before use. Reagents were generally of the best quality commercial grade and used without further purification unless otherwise indicated. All reactions were carried out in oven-dried glassware. Dichloroacetyl chloride was prepared as described in the literature.[16] Cyclopentadiene was obtained by thermal cracking of dicyclopentadiene. Trimethylsilylcyclopentadiene was prepared as described in the literature.[17] TLC was performed using Sorbfil STC-1A 110 μm layer, silica gel 5-17 precoated foil plates. Column chromatography was conducted using 210–280 mesh silica gel. Optical rotations were measured using the sodium D line at 589 nm on a Perkin–Elmer, Model 241MC polarimeter at 20 °C. IR (infrared spectra) were recorded on a Shimadzu IRPrestige-21 spectrometer as Nujol mull or as neat thin films on KBr plates (film) and were reported in reciprocal centimeters (cm^{-1}). ^{1}H and ^{13}C NMR spectra were obtained using a Bruker AM-300 (300 MHz for ^{1}H and



a) 9N H_2SO_4:dioxane, 1:5, reflux, 4 h, 89%;b) m-CPBA, $NaHCO_3$, CH_2Cl_2, from 0 ^{0}C to rt, 8h;
c) 9N H_2SO_4:THF, 1:5, rt, 2 h, 87% (two steps).

Scheme 2. Synthesis of target hydroxylactones **1**.

75.47 MHz for ^{13}C) as solutions in $CDCl_3$ (Aldrich Chemical Company; spectra grade). Chemical shifts are reported in δ unit—parts per million (ppm) downfield from tetramethyl silane (TMS) as the internal reference. Splitting patterns are designated as s, singlet; br s, broad singlet; d, doublet, t, triplet; q, quartet; quint., quintet. Mass spectra were recorded on Shimadzu LCMS QP-2010EV (APCI) spectrometer. Elemental analyses were carried on an Euro EA 3000 CHNS-analyzer. Melting points were recorded on a Mel-Temp apparatus.

4.2. General protocol for (±)-7,7-dichloro-4-*exo*-trimethylsilylbicyclo[3.2.0]-hept-2-en-6-ones 2

To a flame-dried, nitrogen-purged flask were added hexane (150 mL), trimethylsilylcyclopentadiene (10.3 g, 0.075 mol) and dichloroacetyl chloride (15 g, 0.1 mol). Triethylamine (10.2 g, 0.1 mol) in hexane (100 mL) was added via syringe at 0 °C in a period of 1.5 h and allowed to stir for 3 h at the same temperature. The triethylammonium hydrochloride salt was removed by filtration through a short pad of Celite and washed with hexane (2×50 mL). The combined filtrates were concentrated under reduced pressure and the residue was purified by distillation to furnish **2** (13.1 g, 70%) as a yellow oil, bp 71–73 °C/0.3 mmHg (lit.[13] 71–73 °C/0.3 mmHg). Found: C, 48.19; H, 5.51; Cl, 28.49. $C_{10}H_{14}Cl_2OSi$ requires C, 48.19; H, 5.62; Cl, 28.63%; ν_{max} (liquid film) 1805, 1674, 1568 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 5.97–6.00 (1H, m, CH=C*H*CHSi$(CH_3)_3$), 5.63–5.66 (1H, m, C*H*=CHCHSi$(CH_3)_3$), 4.06–4.09 (1H, m, C*H*$CHCl_2$), 3.96–3.99 (1H, m, C*H*C=O), 2.45–2.47 (1H, m, C*H*Si$(CH_3)_3$), 0.01 (9H, s, Si$(CH_3)_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$): 197.8, 139.0, 124.5, 88.7, 60.1, 59.7, 34.7, −3.5; *m*/*z* (APCI) 249 (100, MH^+, ^{35}Cl), 177 (68), 149 (13.3%).

4.3. General protocol for 2-(dichloromethyl)-*N*-[(1*R*)-1-phenylethyl]-5-(trimethylsilyl)-cyclopent-3-ene-1-carboxamides 3 and 4

To a stirred solution of (2.0 g, 8 mmol) **2** in benzene (40 mL) at room temperature under nitrogen was added dropwise a solution (+)-α-methylbenzylamine (ee 99.9%, Aldrich) (1.09 g, 9 mmol) in benzene (10 mL). The reaction was monitored by TLC (1:5 ethyl acetate/petroleum ether) and after stirring 4 h at room temperature the solution was concentrated under reduced pressure, and the residue was diluted with CH_2Cl_2 (50 mL) and washed with water, 5% aqueous solution HCl, water and brine, then dried over $MgSO_4$. Removal of the solvent under reduced pressure afforded an inseparable 1:1 mixture of the *title compounds* **3** and **4** (2.73 g, 92%) as a yellow solid, mp 126–132. Found: C, 58.24; H, 6.62; N, 3.64; Cl, 18.91. $C_{18}H_{25}Cl_2NOSi$ requires C, 58.38; H, 6.76; N, 3.78; Cl, 19.11%; R_f (ethyl acetate/petroleum ether=1:5) 0.7; ν_{max} (Nujol mull) 3332, 2956, 2852, 1635, 1527, 1249, 840, 756, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 7.28–7.41 (5H, m, Ph), 6.20 (0.5H, d, *J* 9.5 Hz, C*H*Cl_2), 6.16 (0.5H, d, *J* 9.3 Hz, C*H*Cl_2), 5.89–5.97 (1H, m, C*H*=CHCHSi$(CH_3)_3$), 5.63–5.83 (2H, m, CH=C*H*CHSi$(CH_3)_3$ and N*H*), 5.13 (1H, quint., *J* 6.8 Hz, C*H*Ph), 3.48–3.69 (1H, m, C*H*$CHCl_2$), 2.93–2.99 (1H, m, C*H*C=O), 2.23–2.35 (1H, m, C*H*Si$(CH_3)_3$), 1.51 (3H, d, *J* 6.9 Hz, CH_3), 0.03–0.08 (9H, m, Si$(CH_3)_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 171.9, 143.0, 142.5, 135.3, 129.0, 127.5, 127.4, 126.5, 126.1, 125.9, 125.8, 74.3, 74.1, 61.5, 61.3, 48.9, 48.7, 41.9, 21.3, 21.0, −3.1, −1.9; *m*/*z* (APCI) 370 (100, MH^+, ^{35}Cl). Anal. Calcd for $C_{18}H_{25}Cl_2NOSi$: C, 58.38; H, 6.76; N, 3.78; Cl, 19.11. Found: C, 58.24; H, 6.62; N, 3.64; Cl, 18.91.

4.4. General protocol for aminals 5 and 6

To a stirred solution of 1:1 mixture **3** and **4** (1.5 g, 4 mmol) in CH_3CN (20 mL) at room temperature was added a solution $NaHCO_3$ (0.75 g, 11.5 mmol) in H_2O (5 mL). After being stirred at room temperature for 0.5 h, the reaction solution was refluxed for 7.5 h, monitored by TLC (1:3 ethyl acetate/petroleum ether), cooled to room temperature, and concentrated under vacuum. The residue was diluted with water (15 mL) and extracted with 3×20 mL ethyl acetate. The combined ethyl acetate extracts were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification of the products by column chromatography (1:3 ethyl acetate/petroleum ether) afforded **5** (0.6 g, 47%) as a white crystalline solid and **6** (0.59 g, 46%) as a yellow crystalline solid.

*4.4.1. (3aR,6R,6aS)-3S-Hydroxy-2-[(1R)-phenylethyl]-6-(trimethylsilyl)-3,3a,6,6a-tetrahydrocyclopenta[c]pyrrol-1(2H)-one (**5**).* Mp=116–118 °C. Found: C, 68.43; H, 7.77; N, 4.32. $C_{18}H_{25}NO_2Si$ requires C, 68.57; H, 7.93; N, 4.44%; R_f (ethyl acetate/petroleum ether=1:3) 0.4; $[\alpha]_D^{20}$ −54.6 (*c* 1.3, CH_2Cl_2); ν_{max} (Nujol mull) 3250, 2929, 2852, 1651, 1454, 1330, 1274, 1251, 1058, 837, 700 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 7.23–7.45 (5H, m, Ph), 5.73–5.77 (1H, m, C*H*=CHCHSi$(CH_3)_3$), 5.41–5.46 (1H, m, CH=C*H*CHSi$(CH_3)_3$), 5.35 (1H, q, *J* 7.1 Hz, C*H*Ph), 5.08 (1H, d, *J* 4.0 Hz, C*H*OH), 3.04–3.07 (2H, br s, C*H*CHOH, C*H*C=O), 2.36–2.39 (1H, br s, C*H*Si$(CH_3)_3$), 1.82 (1H, d, *J* 4.0 Hz, O*H*), 1.50 (3H, d, *J* 7.1 Hz, CH_3), 0.0 (9H, s, Si$(CH_3)_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 177.7, 141.3, 135.2, 128.9, 127.9, 127.3, 124.6, 84.5, 53.3, 50.0, 45.0, 38.8, 16.9, −3.3; *m*/*z* (APCI) 316 (69, MH^+), 298 (100), 194 (27%).

*4.4.2. (3aS,6S,6aR)-3R-Hydroxy-2-[(1R)-phenylethyl]-6-(trimethylsilyl)-3,3a,6,6a-tetrahydrocyclopenta[c]pyrrol-1(2H)-one (**6**).* Mp=134–136 °C. Found: C, 68.31; H, 7.75; N, 4.25. $C_{18}H_{25}NO_2Si$ requires C, 68.57; H, 7.93; N, 4.44%; R_f (ethyl acetate/petroleum ether=1:3) 0.3; $[\alpha]_D^{20}$ −0.1 (*c* 1.01, CH_2Cl_2); ν_{max} (Nujol mull) 3265, 2925, 2852, 1649, 1444, 1377, 1271, 1247, 1053, 835, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 7.23–7.35 (5H, m, Ph), 5.73–5.77 (1H, m, C*H*=CHCHSi$(CH_3)_3$), 5.37 (1H, q, *J* 6.9 Hz, C*H*Ph), 5.25–5.30 (1H, m, CH=C*H*CHSi$(CH_3)_3$), 4.66–4.69 (1H, br s, C*H*OH), 3.22–3.27 (1H, br s, O*H*), 3.05–3.15 (2H, m, C*H*CHOH, C*H*C=O), 2.39–2.81 (1H, br s, C*H*Si$(CH_3)_3$), 1.69 (3H, d, *J* 7.1 Hz, CH_3), 0.04 (9H, s, Si$(CH_3)_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 177.6, 140.0, 132.3, 128.4, 127.4, 125.5, 124.7, 85.2, 54.2, 50.0, 44.9, 38.8, 18.7, −3.3; *m*/*z* (APCI) 316 (65, MH^+), 298 (100), 194 (33%).

4.5. General protocol for (1*S*,2*R*,5*R*)-2-(hydroxymethyl)-*N*-[(1*R*)-1-phenylethyl]-5-(trimethylsilyl)-cyclopent-3-ene-1-carboxamide 7

To a suspension of sodium borohydride (0.61 g, 16 mmol) in a water/dioxane mixture (4 mL/20 mL) was added a solution of **5** (1.0 g, 3.2 mmol) in 3 mL of dioxane. The mixture was heated under refluxed for 5 h and monitored by TLC (1:1 ethyl acetate/petroleum ether). The excess hydride was decomposed by the successive addition of 1 mL of water, 1.5 mL of 15% sodium hydroxide, and 3 mL of water; the suspension was filtered. The filtrate was extracted with 3×10 mL methylene chloride. The combined methylene chloride extracts were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification of the product by column chromatography (1:1 ethyl acetate/petroleum ether) afforded the *title compound* **7** (0.93 g, 92%) as a white crystalline solid, mp=107–109 °C. Found: C, 68.03; H, 8.42; N, 4.28. $C_{18}H_{27}NO_2Si$ requires C, 68.14; H, 8.52; N, 4.42%; R_f (ethyl acetate/petroleum ether=1:1) 0.3; $[\alpha]_D^{20}$ −77.8 (*c* 1.39, CH_2Cl_2); ν_{max} (Nujol mull) 3292, 2955, 2852, 1629, 1525, 1458, 1377, 1247, 1036, 867, 839, 698 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 7.19–7.31 (5H, m, Ph), 6.46 (1H, d, *J* 7.8 Hz, N*H*), 5.78 (1H, d, *J* 5.8 Hz, C*H*=CHCHSi$(CH_3)_3$), 5.37–5.44

(1H, m, CH=C*H*CHSi(CH_3)$_3$), 5.11 (1H, quint., *J* 6.9 Hz, C*H*Ph), 3.38–3.48 (3H, m, CH_2O*H*), 2.96–3.02 (1H, m, C*H*CH_2OH), 2.9 (1H, dd, *J* 7.3, 9.3 Hz, C*H*C=O), 2.29–2.35 (1H, m, C*H*Si(CH_3)$_3$), 1.47 (3H, d, *J* 6.8 Hz, CH_3), −0.1 (9H, s, Si(CH_3)$_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 174.4, 142.8, 133.3, 128.5, 127.4, 127.3, 126.3, 62.9, 52.6, 49.6, 49.0, 38.9, 21.4, −3.2; *m*/*z* (APCI) 318 (100, MH^+), 300 (27.4), 229 (12.5), 214 (15.7), 197 (61.2%).

4.6. General protocol for (1*R*,2*S*,5*S*)-2-(hydroxymethyl)-*N*-[(1*R*)-1-phenylethyl]-5-(trimethylsilyl)-cyclopent-3-ene-1-carboxamide 8

Compound **6** (1.5 g, 4.8 mmol), treated with sodium borohydride as described in the synthesis of **7**, afforded the *title compound* **8** (1.39 g, 91%) as a white crystalline solid, mp=159–161 °C. Found: C, 67.93; H, 8.33; N, 4.35. $C_{18}H_{27}NO_2Si$ requires C, 68.14; H, 8.52; N, 4.42%; R_f (ethyl acetate/petroleum ether=1:1) 0.3; $[\alpha]_D^{20}$ +183.5 (*c* 1.24, CH_2Cl_2); ν_{max} (Nujol mull) 3263, 2951, 2852, 1637, 1546, 1455, 1377, 1247, 1056, 839, 696 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 7.19–7.30 (5H, m, Ph), 6.22 (1H, d, *J* 6.4 Hz, N*H*), 5.75 (1H, d, *J* 5.5 Hz, C*H*=CHCHSi(CH_3)$_3$), 5.35–5.39 (1H, m, CH=C*H*CHSi(CH_3)$_3$), 5.10 (1H, quint., *J* 7.1 Hz, C*H*Ph), 3.50 (1H, dd, *J* 2.8, 12.1 Hz, CH_aH_bOH), 3.40 (1H, dd, *J* 5.2, 12.3 Hz, CH_aH_bOH), 3.10–3.25 (1H, br s, O*H*), 2.81–2.97 (2H, m, *J* 9.3 Hz, C*H*C=O, C*H*CH_2OH), 2.28–2.33 (1H, m, C*H*Si(CH_3)$_3$), 1.43 (3H, d, *J* 6.9 Hz, CH_3), −0.06 (9H, s, Si(CH_3)$_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 174.5, 142.8, 133.2, 128.4, 127.6, 127.5, 126.2, 62.9, 52.6, 49.9, 48.9, 39.1, 21.2, −3.1; *m*/*z* (APCI) 318 (100, MH^+), 300 (29.2), 229 (13.8), 214 (14.5), 197 (65.7%).

4.7. General protocol for (3a*R*,6*R*,6a*S*)-9

To a stirred solution of **7** (0.5 g, 1.6 mmol) in dioxane (15 mL) at room temperature was added a 9 N solution of H_2SO_4 (3 mL). The mixture was heated under refluxed for 4 h and monitored by TLC (1:5 ethyl acetate/petroleum ether), cooled to room temperature, and concentrated under vacuum. The residue was diluted with water (5 mL) and extracted with 3×15 mL ethyl acetate. The combined organic extracts were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification of the products by column chromatography (1:5 ethyl acetate/petroleum ether) afforded (3a*R*,6*R*,6a*S*)-**9** (0.28 g, 89%) as a white crystalline solid.

*4.7.1. (3aR,6R,6aS)-6-(Trimethylsilyl)-3,3a,6,6a-[3.3.0]oct-6-en-2-one ((3aR,6R,6aS)-**9**).* Mp=65–67 °C. Found: C, 61.03; H, 8.10. $C_{10}H_{16}O_2Si$ requires C, 61.22; H, 8.16%; R_f (ethyl acetate/petroleum ether=1:5) 0.5; $[\alpha]_D^{20}$ −175.1 (*c* 1.36, CH_2Cl_2); ν_{max} (Nujol mull) 3045, 2954, 2862, 1751, 1447, 1379, 1249, 1145, 1051, 987, 958, 835, 715 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 5.77–5.84 (1H, m, C*H*=CHCHSi(CH_3)$_3$), 5.44–5.49 (1H, m, CH=C*H*CHSi(CH_3)$_3$), 4.36 (1H, ddd, *J* 4.4, 7.1, 9.1 Hz, CH_aH_bOC=O), 4.19 (1H, dd, *J* 3.8, 9.2 Hz, CH_aH_bOC=O), 3.45 (1H, t, *J* 6.9 Hz, C*H*CH=CH), 2.87 (1H, dd, *J* 4.2, 8.0 Hz, C*H*C=O), 2.37–2.41 (1H, br s, C*H*Si(CH_3)$_3$), 0.0 (s, 9H, Si(CH_3)$_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 181.5, 134.9, 126.5, 71.9, 46.5, 43.7, 39.9, −3.4; *m*/*z* (APCI) 197 (MH^+).

4.8. General protocol for (3a*S*,6*S*,6a*R*)-9

Compound **8** (0.6 g, 1.9 mmol), treated as described in the synthesis of (3a*R*,6*R*,6a*S*)-**9**, afforded (3a*S*,6*S*,6a*R*)-**9** (0.31 g, 89%) as a white crystalline solid.

*4.8.1. (3aS,6S,6aR)-6-(Trimethylsilyl)-3,3a,6,6a-[3.3.0]oct-6-en-2-one ((3aS,6S,6aR)-**9**).* Mp=65–67 °C. Found: C, 61.08; H, 8.02. $C_{10}H_{16}O_2Si$ requires C, 61.22; H, 8.16%; R_f (ethyl acetate/petroleum ether=1:5) 0.5; $[\alpha]_D^{20}$ +174.5 (*c* 1.3, CH_2Cl_2); ν_{max} (Nujol mull) 3048, 2955, 2862, 1755, 1462, 1377, 1251, 1168, 1053, 981, 960, 839, 717 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 5.75–5.84 (1H, m, C*H*=CHCHSi(CH_3)$_3$), 5.43–5.48 (1H, m, CH=C*H*CHSi(CH_3)$_3$), 4.35 (1H, ddd, *J* 4.2, 7.0, 9.0 Hz, CH_aH_bOC=O), 4.20 (1H, dd, *J* 3.9, 9.0 Hz, CH_aH_bOC=O), 3.44 (1H, t, *J* 6.9 Hz, C*H*CH=CH), 2.85 (1H, dd, *J* 4.1, 8.0 Hz, C*H*C=O), 2.35–2.40 (1H, br s, C*H*Si(CH_3)$_3$), −0.01 (s, 9H, Si(CH_3)$_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 181.5, 134.9, 126.5, 71.9, 46.6, 43.7, 39.9, −3.4; *m*/*z* (APCI) 197 (MH^+).

4.9. General protocol for (1a*S*,1b*R*,4a*S*,5*S*,5a*S*)-10 and (3a*R*,4*R*,6a*S*)-1

A solution of 1.04 g (6.0 mmol) of *m*-chloroperoxybenzoic acid and 0.51 g (6.0 mmol) of $NaHCO_3$ in 10 mL of methylene chloride was added to a solution of 0.4 g (2.0 mmol) of lactone (3a*R*,6*R*,6a*S*)-**9** in 10 mL of methylene chloride at 0 °C. After being stirred at 0 °C for 2 h, the reaction solution was heated to room temperature and stirred for 6 h, monitored by TLC (1:1 ethyl acetate/petroleum ether). To a solution was then added 15 mL of a saturated solution of $Na_2S_2O_3$ and the mixture stirred for 1 h. Organic layer was separated and washed with 15 mL of 5% aqueous solution of $NaHCO_3$. Aqueous layer was extracted with 3×15 mL methylene chloride, the combined organic extracts dried over $MgSO_4$ and evaporated under reduced pressure. To the received low stable epoxide (1a*S*,1b*R*,4a*S*,5*S*,5a*S*)-**10** without purification were added 15 mL tetrahydrofuran, 3 mL 9 N solution of H_2SO_4 and the mixture was stirred 2 h at room temperature. The residue was diluted with water (10 mL) and extracted with 3×15 mL ethyl acetate. The combined organic extracts were washed with saturated brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. Purification of the products by column chromatography (3:1 ethyl acetate/petroleum ether) afforded (3a*R*,4*R*,6a*S*)-**1** (0.24 g, 87%) as a transparent viscous oily liquid.

*4.9.1. (1aS,1bR,4aS,5S,5aS)-5-(Trimethylsilyl)-hexahydro-4H-oxireno[3,4]-cyclopenta[1,2-c]furan-4-one ((1aS,1bR,4aS,5S,5aS)-**10**).* Viscous oily liquid; R_f (ethyl acetate/petroleum ether=3:1) 0.7; δ_H (300 MHz, $CDCl_3$/TMS) 4.57 (1H, d, *J* 9.4 Hz, CH_aH_bOC=O), 4.43 (1H, dd, *J* 6.5, 9.4 Hz, CH_aH_bOC=O), 3.65 (1H, t, *J* 2.1 Hz, CHOC*H*CHSi(CH_3)$_3$), 3.52 (1H, d, *J* 2.4 Hz, C*H*OCHCHSi(CH_3)$_3$), 2.70–2.82 (2H, m, *J* 9.6 Hz, C*H*CH_2O, C*H*C=O), 2.13 (1H, s, C*H*Si(CH_3)$_3$), 0.11 (s, 9H, Si(CH_3)$_3$); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 176.7, 70.1, 68.2, 61.1, 42.5, 40.4, 31.9, −2.6.

*4.9.2. (3aR,4R,6aS)-4-Hydroxy-3,3a,4,6a-tetrahydro-1H-cyclopenta[c]furan-1-one ((3aR,4R,6aS)-**1**).* Found: C, 59.85; H, 5.54. $C_7H_8O_3$ requires C, 59.99; H, 5.75%; R_f (ethyl acetate/petroleum ether=3:1) 0.3; $[\alpha]_D^{20}$ +163.1 (*c* 1.095, CH_2Cl_2); ν_{max} (liquid film) 3423, 2976, 2920, 1759, 1479, 1381, 1188, 1109, 1018, 952 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 5.91–5.96 (2H, br s, C*H*=C*H*), 5.03 (1H, d, *J* 7.5 Hz, C*H*OH), 4.65 (1H, dd, *J* 5.2, 9.6 Hz, CH_aH_bOC=O), 4.36 (1H, t, *J* 9.4 Hz, CH_aH_bOC=O), 3.62 (1H, d, *J* 8.5 Hz, C*H*C=O), 3.29 (1H, qd, *J* 5.8, 8.2 Hz, C*H*CH=CH), 1.91–2.09 (1H, br s, O*H*); δ_C (75 MHz, $CDCl_3$/$CHCl_3$) 177.0, 136.3, 129.2, 67.0, 66.9, 51.2, 41.0; *m*/*z* (APCI) 141 (100, MH^+), 111 (19.6), 83 (13.1%).

4.10. General protocol for (1a*R*,1b*S*,4a*R*,5*R*,5a*R*)-10 and (3a*S*,4*S*,6a*R*)-1

Compound (3a*S*,6*S*,6a*R*)-**9** (0.6 g, 3.0 mmol), treated as described in the synthesis of (1a*S*,1b*R*,4a*S*,5*S*,5a*S*)-**10** and (3a*R*,4*R*,6a*S*)-**1**, afforded epoxide (1a*R*,1b*S*,4a*R*,5*R*,5a*R*)-**10** and then hydroxylactone (3a*S*,4*S*,6a*R*)-**1** (0.36 g, 87%) as a transparent viscous oily liquid.

*4.10.1. (1aR,1bS,4aR,5R,5aR)-5-(Trimethylsilyl)-hexahydro-4H-oxireno [3,4]-cyclopenta[1,2-c]furan-4-one ((1aR,1bS,4aR,5R,5aR)-**10**).* Viscous oily liquid; R_f (ethyl acetate/petroleum ether=3:1) 0.7; δ_H (300 MHz, $CDCl_3$/TMS) 4.54 (1H, d, *J* 9.4 Hz, $CH_aH_bOC{=}O$), 4.40 (1H, dd, *J* 6.6, 9.6 Hz, $CH_aH_bOC{=}O$), 3.64 (1H, t, *J* 2.2 Hz, $CHOCHCHSi(CH_3)_3$), 3.50 (1H, d, *J* 2.8 Hz, $CHOCHCHSi(CH_3)_3$), 2.70–2.82 (2H, m, *J* 8.9 Hz, $CHCH_2O$, $CHC{=}O$), 2.09 (1H, s, $CHSi(CH_3)_3$), 0.09 (s, 9H, $Si(CH_3)_3$); δ_C (75 MHz, $CDCl_3/CHCl_3$) 176.5, 70.0, 68.1, 61.0, 42.2, 40.4, 32.6, −2.8.

*4.10.2. (3aS,4S,6aR)-4-Hydroxy-3,3a,4,6a-tetrahydro-1H-cyclopenta [c]furan-1-one ((3aS,4S,6aR)-**1**).* Found: C, 59.82; H, 5.61. $C_7H_8O_3$ requires C, 59.99; H, 5.75%; R_f (ethyl acetate/petroleum ether=3:1) 0.3; $[\alpha]_D^{20}$ −162.5 (*c* 1.08, CH_2Cl_2); ν_{max} (liquid film) 3423, 2976, 2920, 1759, 1477, 1379, 1186, 1097, 1020, 960 cm^{-1}; δ_H (300 MHz, $CDCl_3$/TMS) 5.91–5.96 (2H, br s, $CH{=}CH$), 5.02 (1H, d, *J* 7.5 Hz, CHOH), 4.62 (1H, dd, *J* 5.3, 9.7 Hz, $CH_aH_bOC{=}O$), 4.38 (1H, t, *J* 9.1 Hz, $CH_aH_bOC{=}O$), 3.61 (1H, d, *J* 8.5 Hz, $CHC{=}O$), 3.29 (1H, qd, *J* 5.5, 8.8 Hz, $CHCH{=}CH$), 2.20–2.33 (1H, br s, OH); δ_C (75 MHz, $CDCl_3/CHCl_3$) 176.8, 136.3, 129.2, 67.0, 66.9, 51.2, 41.0; *m/z* (APCI) 141 (100, MH^+), 111 (21.4), 83 (17.9%).

4.11. X-ray crystallographic analysis of (3a*R*,6*R*,6a*S*)-9

Single crystals of $C_{10}H_{16}O_2Si$ ((3a*R*,6*R*,6a*S*)-**9**) were grown from mixture petroleum ether/ethyl acetate. A suitable crystal was selected and studied on a Bruker SMART 1000 diffractometer. The crystal was kept at 120 K during data collection. Using Olex2,[18] the structure was solved with the XS[19] structure solution program using Direct Methods and refined with the XL[20] refinement package using Least Squares minimization.

*4.11.1. Crystal data for (3aR,6R,6aS)-**9**.* $C_{10}H_{16}O_2Si$, *M*=196.32, orthorhombic, *a*=8.175(3) Å, *b*=10.280(4) Å, *c*=26.455(8) Å, *V*=2223.2 (13) $Å^3$, *T*=120 K, space group $P2_12_12_1$ (no. 19), *Z*=8, μ(Mo Kα)=0.180, 16,634 reflections measured, 5524 unique (R_{int}=0.0997), which were used in all calculations. The final wR_2 was 0.0860 (all data) and R_1 was 0.0474 ($>2\sigma(I)$). CCDC 865270 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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