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Olefin Metathesis: A Reversible Stimulus for a Conformational Switch

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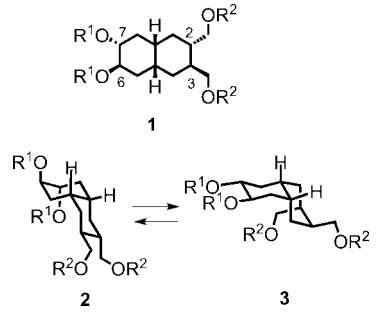
A ring-closing olefin metathesis (RCM) to an eight-membered ring is suitable to induce a conformational switch of a 2,3,6,7-tetrasubstituted *cis*-decalin. The double-ring flip of the decalin scaffold can be reversed by a ring-opening metathesis. The corresponding RCM to a 14-membered ring does not force the double ring flip to occur. A ring-size competition experiment resulted in the exclusive formation of an eight-membered ring.

Introduction

Biconformational *cis*-decalins[1] and *cis,anti,cis*-perhydroanthracenes[2] have been explored as molecular switches[3] and used as conformational transducers for signal transduction by conformational transmission.[4] The use of substituted pyranose sugars[5] and substituted cyclohexanes[6] as building blocks for molecular switches has also been reported. For 2,3,6,7-tetrasubstituted *cis*-decalins of type **1** a double-ring flip converts the conformer **2** into the conformer **3** and vice versa (Scheme 1).



Scheme 1. Decalin **1** and the double-ring flip interconverting conformers **2** and **3**.

The choice of C-substituents at C2,3 and O-substituents at C6,7 shifts this equilibrium to the left and makes conformer **2** the only observable species.

Molecular maneuvers that direct the C6,7 substituents from their axial into equatorial positions induce the double ring flip (**2** → **3**) leading to a switch of the C2,3 substituents into axial positions. A bis(acetal) clamp[1,2a] and the formation of a metal complex[1a,2b] was successfully used as a stimulus for the conformational switch. Because of its reversibility, the olefin metathesis reaction is another candidate for controlling the double ring-flip between **2** and **3**. Here, we report on the use of a ring-closing metathesis (RCM)[7] and the effect of the ring size to induce the double ring flip.

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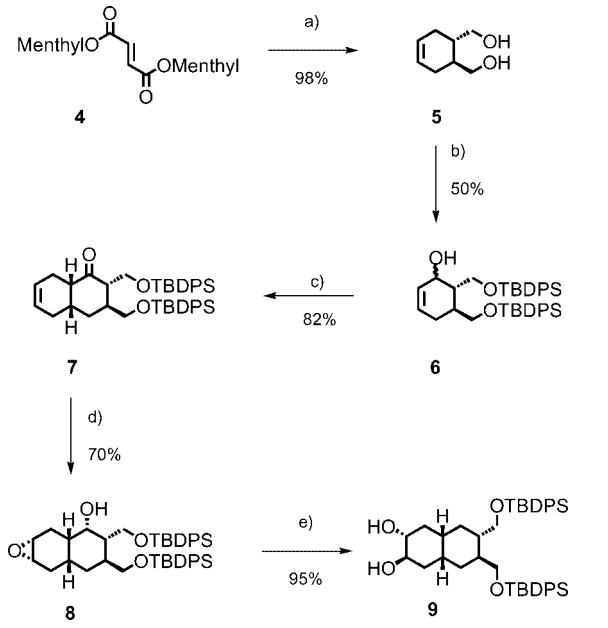
Results and Discussion

Synthesis of the Tetrasubstituted Decalin

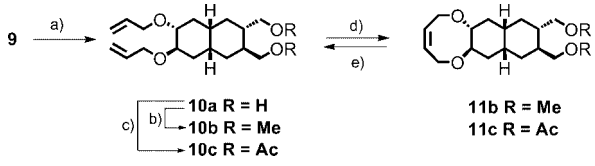
In order to avoid problems with the formation of stereoisomeric mixtures in an intermolecular metathesis, the enantiomerically pure decalins were required. The enantioselective synthesis of the tetrasubstituted decalin (Scheme 2) combined an earlier racemic route[1a] with an asymmetric Diels–Alder entry from the studies[1b] on the conformational coupling of two decalin units. Starting with dimenthyl fumarate (**4**), a Lewis acid catalyzed stereoselective Diels–Alder reaction followed by reductive cleavage of the chiral auxiliaries gave the diol **5** (95% *ee* by HPLC). TBDPS protection and subsequent allylic oxidation afforded the allylic alcohol **6**, which was oxidized to the corresponding cyclohexenone. The latter was converted in a second Lewis acid catalyzed stereoselective Diels–Alder reaction into the *cis*-decalin derivative **7**. The reduction of the ketone with $NaBH_4$ led to the α-alcohol only. An α-selective epoxidation with *m*CPBA provided the epoxide **8**. Removal of the secondary hydroxy group by the Barton–McCombie method[8] and epoxide opening gave the desired tetrasubstituted, enantiopure *cis*-decalin **9** with a *trans*-diaxial diol in positions 6,7 and *trans*-diequatorial $CH_2OTBDPS$ substituents in positions 2,3.



Scheme 2. Enantioselective synthesis of decalin **9**: a) i) 1,3-butadiene, Et_2AlCl, toluene, –78 → 20 °C; ii) $LiAlH_4$,THF; b) i) TBDPSCl, imidazole, CH_2Cl_2; ii) SeO_2, dioxane/water; c) i) MnO_2, CH_2Cl_2; ii) 1,3-butadiene, $AlCl_3/AlMe_3$, toluene, –78 → 20 °C; d) i) $NaBH_4$, CH_2Cl_2/MeOH; ii) *m*CPBA, CH_2Cl_2, –30 → 20 °C, α/β = 9:1; e) i: *n*BuLi, PhOCSCl; ii) nBu_3SnH, AIBN; iii) $HClO_4$, acetone.

RCM Leading to an Eight-Membered Ring

The formation of an eight-membered ring by an olefin metathesis reaction was chosen as the first experiment to study the RCM-induced conformational switch of the decalin scaffold (Scheme 3). Towards this end, the two hydroxy groups at C6,7 of compound **9** were converted into two allyl ethers. After TBDPS deprotection, the diol **10a** was obtained. Protection of the primary hydroxy groups led to the bis(methyl ether) **10b** and the bis(acetate) **10c**, respectively.



Scheme 3. RCM reaction of the bis(allyl ethers) **10** to the eight-membered ring products **11**: a) i) allyl bromide, NaH, DMF, 16 h; ii) TBAF, THF, 2 h 40 °C, 93% **10a** in two steps; b) MeI, NaH, DMF, 16 h, 93% **10b**; c) Ac_2O, Py, DMAP, 6 h, 88% **10c**; d) **10b** → **11b**, Grubbs I catalyst, toluene, 140 °C, sealed tube, 30 min, 98%; **10c** → **11c**, Grubbs I catalyst, $ClCH_2CH_2Cl$, 85 °C, 1 h, 76%; e) **11c** → **10c**, Grubbs I catalyst, CH_2Cl_2, room temp., 4 bar ethylene, 22 h, 62%.

Treatment of the bis(allyl ether) **10b** with 20% benzylidenebis(tricyclohexylphosphane)ruthenium dichloride (Grubbs I catalyst)[7a] in toluene at 140 °C (sealed tube) for 30 min gave the eight-membered RCM product **11b** in nearly quantitative yield.

An NMR-structural analysis (Figures 1 and 2) showed that the RCM reaction (**10b** → **11b**) induced a double ring flip of the tetrasubstituted *cis*-decalin from the conformer **12** to the conformer **13**. The conformational analysis in $CDCl_3$ is based on the change of the diagnostic ^3J coupling constants of H-C6,7 (Figure 1) and the analysis of the significant NOE data (Figure 2). In conformer **12** the ^3J coupling constants of the two equatorial protons at C6,7 were 2.4 and 2.7 Hz, while in conformer **13**, the *trans*-diaxial protons at C6,7 exhibited characteristic coupling constants (for H-C6: 11.1, 8.5, 5.2 Hz).

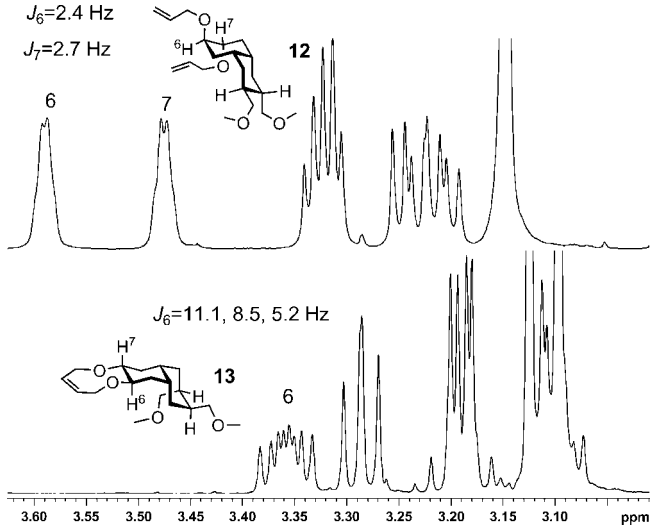


Figure 1. Parts of the ^{1}H NMR spectra of compounds **10b** (top) and **11b** (bottom) showing the presence of the conformers **12** and **13**. The diagnostic coupling constants of H-C6,7 are highlighted.

As a result of the RCM reaction (**10b** → **11b**), the methoxymethyl groups at positions 2,3 have been switched from equatorial into axial positions.

Reversibility is an important condition for each switching device.[3] The reversibility of the conformational switch by an olefin metathesis reaction was demonstrated for the case of the bis(acetates) **10c/11c** (Scheme 3). The Grubbs I catalyst mediated ring-closing metathesis **10c** → **11c** resulted in a double ring flip of the decalin scaffold, which could be switched back by ring-opening metathesis **11c** → **10c**. The ring opening metathesis was performed with an excess of ethylene and the Grubbs I catalyst.

RCM Leading to a 14-Membered Ring

Having proven that the ring closure of the eight-membered ring induces a double ring flip, it was of interest to investigate the effect of increasing the ring size. A 14-membered ring would be a representative example of a large ring size. Therefore, the RCM reaction leading to a 14-membered ring was investigated next.

To investigate the RCM reaction leading to the 14-membered ring, the bis(allyl ether) **15** was prepared (Scheme 4). Starting from the alkene **11b** an ozonolysis with a subsequent $NaBH_4$ reduction yielded the diol **14**. The

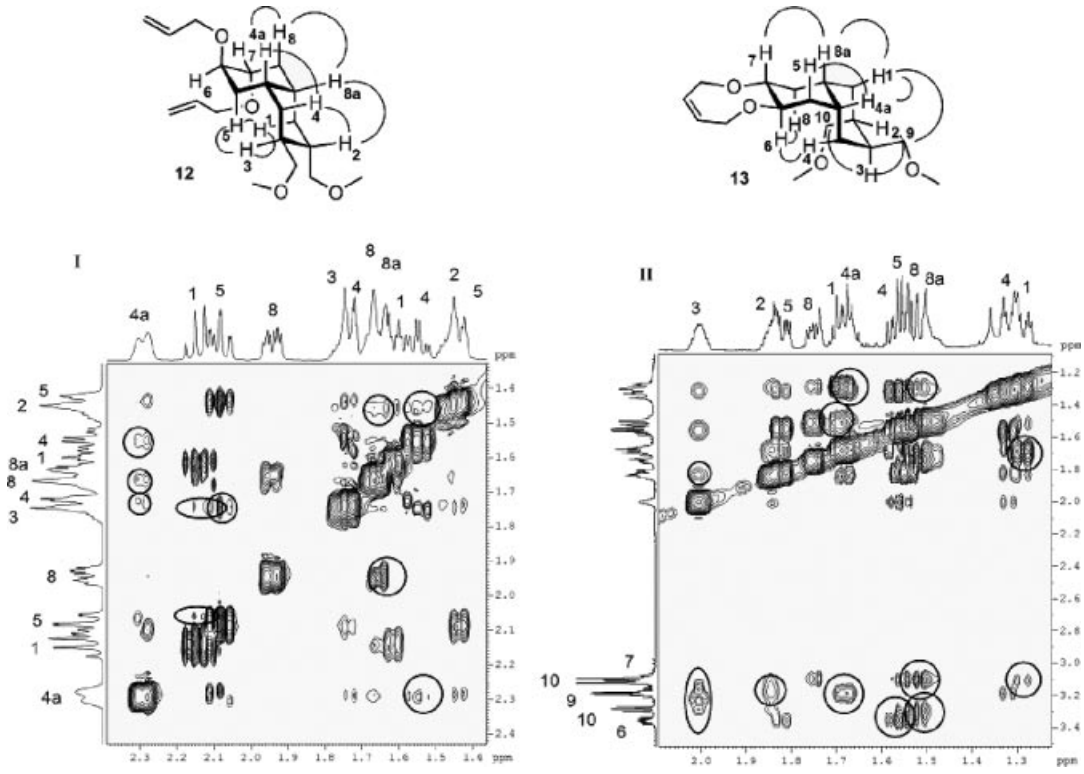
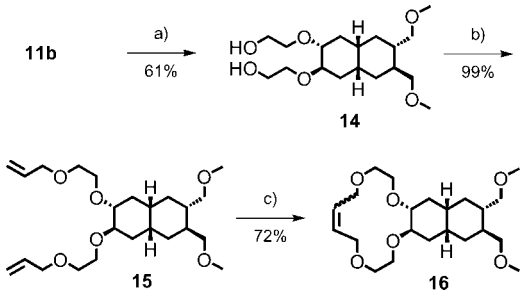


Figure 2.Sections of the NOESY spectra of **10b** (left) and **11b** (right) in $CDCl_3$ and structures of their corresponding conformers **12** and **13** with significant NOE contacts.

ozonolytic cleavage of the eight-membered ring was associated with a double-ring flip back (of type **3** → **2**). Bis(allylation) of **14** led to **15**, the precursor for the intended larger-ring-size RCM experiment. The RCM of **15** using Grubbs I catalyst led to the 14-membered tetraoxacycloalkenes **16**. Compound **16** was obtained as an inseparable 7:2 mixture of the (*E*)/(*Z*) stereoisomers.



Scheme 4. Synthesis and RCM reaction of the bis(allyl ether) **15** to the 14-membered-ring product **16**: a) O_3, $NaBH_4$, CH_2Cl_2/MeOH (1:1), 16 h; b) allyl bromide, NaH, DMF, 16 h; c) Grubbs I, toluene, 140 °C, sealed tube, 30 min.

Inspection of the ^{1}H NMR spectra of compounds **15** and **16** indicated the presence of the conformers **17** and **18** (Figure 3). No change for the ^3J coupling constants of the diagnostic signals at C6,7 was observed.

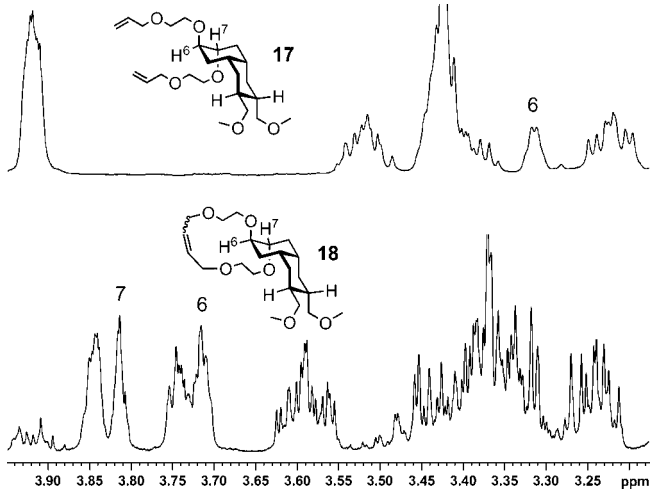


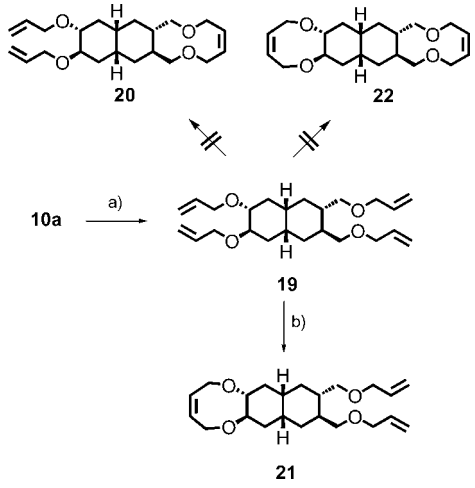
Figure 3. Parts of the ^{1}H NMR spectra of compounds **15** (bottom) and **16** (top) showing the presence of the conformers **17** and **18**. The diagnostic signals of H-C6,7 are highlighted.

The formation of the 14-membered ring did not induce the double-ring flip to occur, neither in the case of the (*Z*) olefin, nor the (*E*) olefin. The higher conformational flexibility of the 14-membered ring compared to the eight-membered ring left the 6,7 substituents in their diaxial positions and the double-chair conformation of the decalin unaffected.

RCM with Competing Ring Sizes

The examples above are two separate cases of RCM reactions leading to different ring sizes. What are the conformational consequences of two competing RCM reactions in the same molecule leading to two competing ring sizes?

The tetraallyl-substituted *cis*-decalin **19** would be a good candidate to look at this problem (Scheme 5). As shown by NMR spectroscopy, compound **19**, whose synthesis was straightforward from **10a**, exists as the conformer **23** with diequatorial 2,3 substituents and diaxial 6,7 substituents (Figure 4). An RCM reaction at the 2,3 substituents could lead to the product **20** with a 10-membered ring and no double ring flip of the *cis*-decalin. In contrast, an RCM at the 6,7 positions leading to the eight-membered ring **21** strictly requires the double ring flip as has been shown for the reaction (**10** → **11**). A priori, compound **19** could also form the double-RCM product **22**.



Scheme 5. Synthesis and RCM reaction of **19** leading to **21**: a) allyl bromide, NaH, DMF, 16 h, 61%; b) Grubbs I catalyst, toluene, 140 °C, sealed tube, 30 min, 45%.

The RCM reaction of **19** using Grubbs I catalyst gave compound **21** with the eight-membered ring as the only isolable product. No product with a 10-membered ring was formed.

The olefin metathesis (**19** → **21**) induced a double ring flip (**23** → **24**), which was was evident from the inspection of the ^{1}H NMR spectra (Figure 4). In conformer **23** the ^3J coupling of the two equatorial protons at C6,7 was 2.7 Hz, while in conformer **24**, the *trans*-diaxial protons at C6,7 exhibited characteristic coupling constants (for H-C6: 11.3, 8.7, 5.4 Hz, H-C7: 10.9, 8.6, 5.4 Hz).

In this competion experiment, the formation of the eight-membered ring clearly dominates over the formation of the 10-membered ring although it requires the extra energy for the double ring flip.

Conclusions

The formation of an eight-membered ring by RCM (**10** → **11**) can enforce the double ring flip of the *cis*-decalin,

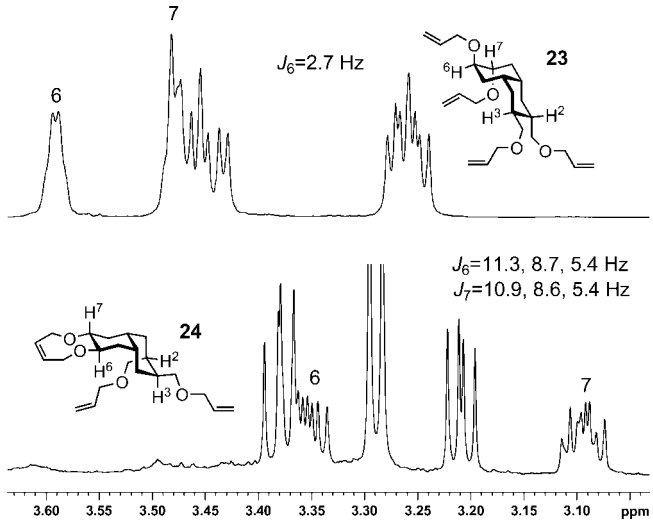


Figure 4. Parts of the ^{1}H NMR spectra of compounds **19** (top) and **21** (bottom) showing the presence of the conformers **23** and **24**. The diagnostic coupling constants of H-C6,7 are highlighted.

while the formation of a 14-membered ring is not sufficient (**15** → **16**). In the competition experiment with compound **19**, the eight-membered-ring formation (**19** → **21**) dominates over the 10-membered ring-closure reaction. These studies establish the RCM reaction as a suitable reversible stimulus for conformational switches of the decalin and perhydroanthracene type. Future work will focus on the implementation of the metathesis reaction as a stimulus into supramolecular devices.

Experimental Section

General Methods and Materials: All non-aqueous reactions were carried out under argon in flame-dried glassware. Solvents for non-aqueous reactions were dried as follows prior to use: THF was dried with KOH and subsequently distilled from sodium/benzophenone, toluene from a potassium/sodium alloy (K/Na, 4:1); CH_2Cl_2 was distilled from CaH_2; DMF was distilled from 4 Å molecular sieves; $CHCl_3$ (for measuring optical rotations) was dried by passage through basic alumina, MeOH was dried by refluxing with Mg turnings (5 g/L) and subsequent distillation; acetone and DMSO were purchased from Acros (ultra dry quality), "MnO_2 precipitated active" was purchased from Merck. All commercially available reagents and reactants were used without purification unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC) using Merck Silica Gel 60 F_{254} glass-plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained using a cerium sulfate/phosphomolybdic acid reagent. Chromatographic purification of products was performed on Merck Silica Gel 60 (230–400 mesh), unless otherwise noted using a forced flow of eluents. Neutral silica was purchased from Fuji Silysia (Chromatorex MB 100-40/75). Concentration under reduced pressure was performed by rotary evaporation at 40 °C and the appropriate pressure. Yields refer to purified and spectroscopically pure products, unless otherwise noted. Optical rotations were measured with a Perkin–Elmer 241 polarimeter using dried solvents and a 1 dm path-length cell. IR spectra

were recorded with a Bruker IFS 200 or a Nicolet Magna-IR 750 spectrometer. The absorption bands are given in wave numbers (cm^{-1}), intensities are reported as follows: s = strong, m = medium, w = weak, br. = broad band. NMR spectra were recorded with a Bruker ARX300, DRX500 or DRX600 spectrometer at room temperature. Chemical shifts are reported in ppm with the solvent resonance as internal standard. Data are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, m_c = symmetrical multiplet, br. = broad signal, p = pseudo. Mass spectra were recorded with a Finnigan MAT TSQ 700, MAT 95S, or an Applied Biosystems Model Q-Star.

(1*S*,2*S*)-1,2-Bis(hydroxymethyl)cyclohex-4-ene (5). Diels–Alder Reaction: Dimenthyl fumarate (**4**) (20 g, 50.95 mmol) was dissolved in toluene (100 mL) in a Schlenk tube. At –78 °C, a solution of diethylaluminium chloride (50.9 mL, 50.9 mmol, 1 M in hexane) and 1,3-butadiene (44.0 mL, 0.51 mol) was added. The vessel was sealed and the reaction mixture was warmed up to 20 °C. After stirring for 35 h, a saturated K/Na tartrate solution (20 mL) was slowly added, and the mixture was filtered through a pad of Celite. The filter pad was washed with *tert*-butylmethyl ether (TBME) (10 mL) and the aqueous layer was extracted with TBME (3 × 20 mL). The combined organic layers were washed with brine (2 × 30 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by CC on silica gel (250 g, pentane/TBME, 20:1) to give 22.16 g (49.61 mmol, 97%) of the corresponding diester as a colorless oil. R_f = 0.41 (pentane/TBME, 20:1). $[\alpha]_D$ = 25.1 (*c* = 4.18, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.72 (d, *J* = 6.9 Hz, 6 H), 0.89 (dd, *J* = 6.9 Hz, 14 H), 0.92–1.12 (m, 4 H), 1.33–1.58 (m, 4 H), 1.61–1.72 (m, 4 H), 1.79–1.94 (m, 2 H), 1.95–2.04 (m, 2 H), 2.08–2.23 (m, 2 H), 2.34–2.49 (m, 2 H), 2.77–2.92 (m, 2 H), 4.59 (dt, *J* = 4.3, 10.9 Hz, 2 H), 5.62–5.73 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.1, 21.0, 22.2, 23.4, 26.1, 28.0, 31.5, 34.5, 40.9, 41.4, 47.2, 74.5, 125.1, 174.6 ppm. IR (film): $\tilde{\nu}$ = 3030 (w), 2955 (s), 2870 (s), 1731 (s), 1456 (m), 1369 (m), 1302 (m), 1178 (m), 1014 (m), 1013 (m), 983 (m), 658 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{46}O_4Na$ [M + Na^+] 469.3288; found 469.3295. **Reduction:** To a suspension of $LiAlH_4$ (3.40 g, 89.6 mmol) in THF (100 mL) was added dropwise at 0 °C a solution of the diester (20.0 g, 44.8 mmol) in THF (180 mL). After stirring for 40 min at 0 °C, the reaction mixture was heated to reflux for 2 h. After cooling to 20 °C, water (25 mL) and NaOH (10 mL, 1.0 M) were added and the reaction mixture was heated to reflux for 1 h, the organic phase was separated and to the residue was added THF (200 mL) and the mixture heated again for 30 min, filtered through a pad of Celite and the aqueous phase was extracted with AcOEt (6 × 20 mL). The combined organic layers were washed first with a saturated aqueous NH_4Cl solution (50 mL) and then with brine (50 mL). After drying with $MgSO_4$, the solvent was evaporated in vacuo and the subsequent flash chromatography (200 g, $CHCl_3$/MeOH, 30:1) afforded 6.36 g of the diol **5** (44.8 mmol, 99%) as a colorless oil. R_f = 0.29 ($CHCl_3$/MeOH, 9:1). $[\alpha]_D$ = +68.02 (*c* = 3.75, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.55–2.08 (m, 6 H), 3.46–3.57 (m, 2 H), 3.61–3.69 (m, 2 H), 4.74 (b, 2 H), 5.53–5.71 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.9, 39.0, 65.6, 125.8 ppm. IR (film): $\tilde{\nu}$ = 3326 (br.), 3025 (s), 2893 (s), 1655 (w), 1471 (w), 1436 (m), 1069 (m), 1024 (m), 995 (m), 958 (m), 663 (m) cm^{-1}. HRMS (ESI): calcd. for $C_8H_{14}O_2Na$ [M + Na^+] 165.0886; found 165.0885. $C_8H_{14}O_2$ (142.10): calcd. C 67.25, H 9.60; found C 67.57, H 9.92.

(1*RS*,2*S*,3*S*)-2,3-Bis(*tert*-butyldiphenylsilyloxymethyl)cyclohex-5-en-1-ol (6). Silyl Protection: To a solution of diol **5** (6.70 g, 47.2 mmol) and imidazole (8.02 g, 117.9 mmol) in CH_2Cl_2 (250 mL) was added dropwise at 0 °C a solution of TBDPSCl (23.2 mL, 99.0 mmol) in CH_2Cl_2 (50 mL). The reaction mixture was warmed up to 20 °C within 12 h, then a saturated aqueous NH_4Cl solution (50 mL) was added, the mixture extracted with CH_2Cl_2 (3 × 50 mL), washed with a saturated aqueous NH_4Cl solution(20 mL) and brine (20 mL). After drying with $MgSO_4$, the solvent was evaporated and the crude residue was purified by flash chromatography (500 g, pentane/TBME, 50:1) to obtain 33.02 g of the bis(silyl ether) (46.95 mmol, 99%) as a colorless oil. R_f = 0.36 (pentane/ethyl acetate, 19:1). $[\alpha]_D$ = +18.82 (*c* = 3.92, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17 (s, 18 H), 2.05–2.33 (m, 6 H), 3.72–3.91 (m, 4 H), 5.65–5.81 (m, 2 H), 7.41–7.55 (m, 12 H), 7.74–7.81 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 27.0, 27.4, 37.2, 66.1, 126.0, 127.7, 129.6, 134.1, 135.7 ppm. IR (film): $\tilde{\nu}$ = 3070 (m), 3023 (m), 2932 (s), 2959 (s), 2931 (s), 2894 (s), 2857 (s), 1428 (m), 1112 (s), 823 (m), 739 (m), 702 (s), 505 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{40}H_{50}O_2Si_2Na$ [M + Na^+] 641.3242; found 641.3242. **Allylic Oxidation:** To a solution of cyclohexene (11.50 g, 16.86 mmol) in dioxane/water (10:1) (1.1 L), selenium dioxide (2.34 g, 21.08 mmol) was added. The reaction mixture was stirred at 90 °C for 36 h; after 18 h, another portion of selenium dioxide (2.34 g, 21.08 mmol) was added. Brine (100 mL) and TBME were added until both phases separated. The aqueous phase was extracted with TBME (3 × 50 mL), and the combined organic phases were washed with $NaHCO_3$ (50 mL) and brine (3 × 50 mL), and dried with $MgSO_4$. After evaporation of the solvents, the residue was purified by flash chromatography (250 g, pentane/ethyl acetate, 19:1) to afford 6.83 g of **6** (9.18 mmol, 54%) of a 2:1 mixture of C-1 epimers and 4.01 g (5.88 mmol, 35%) of reisolated starting material. R_f = 0.28 (pentane/ethyl acetate, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.96 (s, 9 H), 1.04 (s, 9 H), 1.82–2.20 (m, 4 H), 2.54 (d, *J* = 4.5 Hz, 1 H), 3.40–3.57 (m, 2 H), 3.83 (t, *J* = 9.4 Hz, 1 H), 3.98 (dd, *J* = 10.2, 4.5 Hz, 1 H), 4.46–4.55 (m, 1 H), 5.82–5.93 (m, 2 H), 7.25–7.68 (m, 20 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2, 26.8, 26.9, 28.8, 33.5, 42.3, 63.9, 65.2, 65.3, 127.6, 127.8, 128.0, 129.5, 129.7, 129.9, 130.2, 133.1, 133.2, 133.5, 135.5 ppm. IR (film): $\tilde{\nu}$ = 3465 (br.), 3070 (m), 2958 (s), 2930 (s), 2856 (s), 1739 (m), 1428 (m), 1113 (s), 823 (m), 740 (m), 703 (s), 505 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{40}H_{50}O_3Si_2Na$ [M + Na^+] 657.3191; found 657.3193.

(2*S*,3*S*,4a*S*,8a*S*)-2,3-Bis(*tert*-butyldiphenylsilyloxymethyl)-3,4,4a,5,8,8a-hexahydro-2*H*-naphthalen-1-one (7). MnO_2 Oxidation: To a solution of allylic alcohol **6** (19.54 g, 30.77 mmol) in CH_2Cl_2 (250 mL) was added MnO_2 (21.31 g, 0.24 mol) and the solution was heated to reflux for 2 h. After cooling to 20 °C, more MnO_2 (21.31 g, 0.24 mol) was added and the reaction was heated to reflux for 1 h again. This addition was repeated 7 times, then the reaction mixture was filtered through a pad of Celite, and the filtrate concentrated in vacuo. After purification by column chromatography with silica gel (500 g, pentane/ethyl acetate, 19:1), 16.80 g (26.54 mmol, 86%) of the corresponding enone was obtained as a colorless oil. R_f = 0.48 (pentane/ethyl acetate, 9:1). $[\alpha]_D$ = +23.30 (*c* = 3.08, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.09 (s, 9 H), 1.13 (s, 9 H), 2.49–2.82 (m, 4 H), 3.52–3.68 (m, 3 H), 4.36 (dd, *J* = 10.1, 3.9 Hz, 1 H), 6.14 (d, *J* = 10.0 Hz, 1 H), 6.99 (dt, *J* = 9.9, 4.1 Hz, 1 H), 7.34–7.53 (m, 12 H), 7.64–7.84 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 26.9, 27.0, 27.8, 37.5, 50.3, 60.4, 64.9, 127.7, 127.8, 129.7, 129.8, 133.3, 133.5, 133.7, 135.6, 135.8, 149.1, 198.9 ppm. IR (film): $\tilde{\nu}$ = 3071 (w), 2957 (m), 2930 (m), 2889 (m), 2857 (m), 1679 (m), 1472 (w), 1427 (m), 1113 (s), 1006 (m), 823 (m), 740 (m), 702 (s), 613 (w), 505 (m), 488 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{40}H_{48}O_3Si_2Na$ [M + Na^+] 655.3034; found 655.3049. **Diels–Alder Reaction:** $AlCl_3$ (1.55 g, 11.63 mmol) and Me_3Al (1.22 mL in 2 M toluene, 2.34 mmol) were dissolved in

toluene (30 mL) in a Schlenk tube. At –78 °C, a solution of enone (17.12, 27.05 mmol) in toluene (200 mL) and sunsequently 1,3-butadiene (35 mL, 406 mmol) were added. Then the flask was sealed and the reaction mixture warmed up to 20 °C within 36 h. The reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (100 mL). A saturated aqueous solution of NH_4Cl (100 mL) was added, and the mixture was filtered through a pad of Celite. The aqueous phase was extracted with TBME (3 × 80 mL), and the combined organic phases were washed with brine (2 × 30 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (200 g, pentane/TBME, 19:1) to obtain 17.69 g (25.75 mmol, 95%) of ketone **7** as a colorless oil. R_f = 0.43 (pentane/ethyl acetate, 19:1). $[\alpha]_D$ = –14.26 (c = 5.19, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.97 (s, 9 H), 1.05 (s, 9 H), 1.82–2.07 (m, 4 H), 2.18–2.35 (m, 1 H), 2.43–2.57 (m, 3 H), 2.64–2.76 (m, 2 H), 3.52 (dd, J = 10.3, 2.9 Hz, 1 H), 3.65–3.78 (m, 2 H), 4.09–4.18 (m, 1 H), 5.59–5.74 (m, 2 H), 7.24–7.48 (m, 12 H), 7.54–7.68 (m, 6 H), 7.69–7.75 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 19.6, 24.3, 26.7, 26.9, 27.1, 33.1, 34.5, 37.9, 47.8, 52.0, 58.8, 65.4, 125.1, 125.2, 127.6, 127.8, 129.5, 129.6, 129.8, 133.7, 133.8, 134.1, 135.7, 136.0, 209.7 ppm. IR (film): $\tilde{\nu}$ = 3064 (br.), 3070 (w), 2934 (s), 2863 (s), 1712 (w), 1612 (m), 1587 (m), 1513 (m), 1463 (m), 1427 (m), 1248 (m), 1112 (s), 1011 (w), 822 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{54}O_3Si_2Na$ [M + Na^+] 709.3504; found 709.3525.

(1*S*,2*S*,3*S*,4a*R*,6*S*,7*R*,8a*S*)-2,3-Bis(*tert*-butyldiphenylsilyloxymethyl)-6,7-epoxydecalin-1-ol (8). $NaBH_4$ Reduction: To a solution of ketone **7** (7.54 g, 10.97 mmol) in a mixture of CH_2Cl_2/MeOH (1:1) (100 mL) was added portionwise $NaBH_4$ (1.66 g, 43.90 mmol) at 0 °C, and the resulting mixture warmed up to 20 °C within 16 h. A saturated aqueous solution of NH_4Cl (30 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL), and the combined organic phases were washed with saturated aqueous solution of NH_4Cl (30 mL) and brine (30 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (150 g, pentane/ethyl acetate, 19:1) to obtain 6.59 g (9.56 mmol, 87%) of the corresponding alcohol as a colorless solid. R_f = 0.57 (pentane/ethyl acetate, 9:1). $[\alpha]_D$ = +57.79 (c = 3.08, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 9 H), 1.16 (s, 9 H), 1.79–2.69 (m, 11 H), 3.62 (dd, J = 10.2, 4.9 Hz, 1 H), 3.71 (dd, J = 10.2, 3.0 Hz, 1 H), 3.93 (dd, J = 10.0, 7.5 Hz, 1 H), 4.06 (dd, J = 10.2, 4.3 Hz, 1 H), 4.41 (br., 1 H), 5.84–5.99 (m, 2 H), 7.35–7.53 (m, 12 H), 7.65–7.82 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3, 19.4, 27.0, 29.3, 29.6, 30.3, 31.1, 35.0, 37.3, 46.3, 64.3, 66.4, 74.8, 125.9, 127.6, 127.7, 128.4, 129.5, 129.6, 129.7, 133.5, 133.7, 133.9, 135.6, 135.7 ppm. IR (film): $\tilde{\nu}$ = 3070 (w), 2957 (m), 2929 (m), 2893 (m), 2856 (m), 1471 (w), 1427 (m), 1112 (s), 823 (m), 740 (m), 702 (s), 505 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{56}O_3Si_2Na$ [M + Na^+] 711.3660; found 711.3664. **Epoxidation:** To a solution of the alcohol (6.422 g, 9.32 mmol) in CH_2Cl_2 (150 mL) was added *m*CPBA (70%, 4.59 g, 26.63 mmol) at –30 °C and the mixture warmed up to 0 °C within 2.5 h. A solution of Na_2SO_3 (40 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (4 × 20 mL), the combined organic phases were washed with $NaHCO_3$ (40 mL) and brine (40 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (150 g, pentane/ethyl acetate, 9:1 → 4:1) to obtain 5.33 g (7.55 mmol, 81%) of the desired α-epoxide **8** as a colorless solid, and 1.17 g (1.66 mmol, 18%) of the β-epoxide **8′** as a colorless solid. **8:** R_f = 0.22 (pentane/ethyl acetate, 9:1). $[\alpha]_D$ = +12.2 (c = 1.00, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.89 (s, 9 H), 0.91 (s, 9 H), 1.31–1.48 (m, 2 H), 1.58–1.86 (m, 5 H), 1.90–2.05 (m, 1 H), 2.06–2.23 (m, 2 H), 3.16 (br., 1 H), 3.24–3.36 (m, 2 H), 3.55–3.76 (m, 3 H), 3.90 (br., 1 H), 4.32 (m, 1 H), 7.15–7.33 (m, 12 H), 7.46–7.61 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 26.6, 27.0, 28.7, 29.2, 31.6, 34.7, 38.2, 47.6, 52.0, 53.5, 64.1, 66.8, 69.5, 127.6, 127.7, 129.4, 129.5, 129.6, 134.0, 134.1, 134.2, 134.4, 135.7, 135.8 ppm. IR (KBr): $\tilde{\nu}$ = 3391 (br), 2929 (m), 2855 (m), 1739 (w), 1472 (w), 1427 (m), 1112 (s), 823 (m), 741 (m), 702 (s), 613 (w), 504 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{56}O_4Si_2Na$ [M + Na^+] 727.3609; found 727.3623. **8′:** R_f = 0.12 (pentane/ethyl acetate, 9:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 9 H), 1.10 (s, 9 H), 1.79–2.63 (m, 10 H), 3.50–4.38 (m, 6 H), 5.35 (m, 1 H), 5.72 (br., 1 H), 7.26–7.51 (m, 12 H), 7.52–7.69 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.2, 19.4, 26.9, 27.0, 28.2, 28.9, 29.4, 32.5, 35.0, 38.2, 43.6, 64.7, 65.4, 65.8, 75.2, 75.3, 127.7, 127.9, 128.0, 129.7, 129.8, 130.2, 132.4, 132.7, 132.9, 133.7, 134.6, 135.6, 135.8 ppm. IR (KBr): $\tilde{\nu}$ = 3398 (br.), 2929 (m), 2856 (m), 1719 (w), 1472 (w), 1427 (m), 1112 (s), 823 (w), 740 (w), 702 (s), 612 (w), 504 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{56}O_4Si_2Na$ [M + Na^+] 727.3609; found 727.3630.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-2,3-Bis(*tert*-butyldiphenylsilyloxymethyl)decalin-6,7-diol (9). Thiocarbonate Formation: To a solution of epoxide **8** (5.16 g, 7.31 mmol) in THF (100 mL) was added dropwise at –78 °C a 2.5 M solution of *n*BuLi in hexane (3.51 mL, 8.78 mmol). After stirring for 10 min, *O*-phenyl chlorothioformate (1.28 mL, 9.51 mmol) was added and the reaction mixture was warmed up to 20 °C within 12 h. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (50 mL), and extracted with TBME (3 × 30 mL). The combined organic layers were washed with brine (2 × 30 mL), dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by flash chromatography (150 g, pentane/TBME, 10:1) to obtain the corresponding thiocarbonate (5.88 g, 6.99 mmol, 96%) as a colorless solid. R_f = 0.17 (pentane/ethyl acetate, 15:1). $[\alpha]_D$ = +10.91 (c = 2.10, $CHCl_3$, 20 °C). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.95 (s, 9 H), 1.03 (s, 9 H), 1.46–1.59 (m, 2 H), 1.68–1.77 (m, 3 H), 1.82–2.00 (m, 4 H), 2.76–2.83 (m, 1 H), 3.02–3.05 (m, 1 H), 3.16–3.20 (m, 1 H), 3.35 (dd, J = 10.4, 5.3 Hz, 1 H), 3.45 (dd, J = 10.4, 4.4 Hz, 1 H), 3.53 (dd, J = 9.2, 9.7 Hz, 1 H), 3.84 (dd, J = 10.2, 5.5 Hz, 1 H), 6.04 (m, 1 H), 7.12–7.18 (m, 2 H), 7.20–7.43 (m, 15 H), 7.51 (dd, J = 11.9, 7.9 Hz, 4 H), 7.65 (dd, J = 20.8, 8.0 Hz, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.3, 19.4, 26.3, 27.0, 27.1, 27.2, 29.6, 33.2, 37.4, 46.2, 50.0, 51.1, 62.5, 66.4, 82.6, 122.6, 126.2, 127.7, 127.8, 129.3, 129.6, 129.7, 133.6, 133.7, 133.8, 133.9, 135.7, 135.8, 135.9, 153.9, 195.2 ppm. IR (KBr): $\tilde{\nu}$ = 3428 (br.), 3070 (w), 2928 (m), 2855 (m), 1471 (w), 1427 (m), 1289 (m), 1202 (m) 1112 (s), 1085 (m), 823 (w), 740 (w), 702 (s), 613 (w), 505 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{51}H_{60}O_5SSi_2Na$ [M + Na^+] 863.3592; found 863.3613. **Bu_3SnH Reduction:** A solution of the thiocarbonate (1.60 g, 1.90 mmol) in toluene (50 mL) was degassed at –78 °C. The solution was heated to 90 °C and *n*Bu_3SnH (1.54 mL, 5.71 mmol) and AIBN (cat.) were added and the mixture was stirred at this temperature for 30 min. The solvent was evaporated in vacuo and the residue was purified by flash chromatography (100 g, pentane/ethyl acetate, 10:1) to yield 1.25 g (18.20 mmol, 96%) of the corresponding epoxide as a colorless oil. R_f = 0.31 (pentane/ethyl acetate, 19:1). $[\alpha]_D$ = +14.13 (c = 3.23, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (s, 9 H), 1.14 (s, 9 H), 1.45–1.97 (m, 10 H), 2.00–2.18 (m, 3 H), 3.18–3.24 (m, 1 H), 3.28–3.35 (m, 1 H), 3.54–3.66 (m, 2 H), 3.69–3.81 (m, 2 H), 7.38–7.53 (m, 12 H), 7.68–7.79 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 24.8, 27.0, 30.4, 30.5, 32.0, 33.6, 34.6, 35.4, 42.4, 52.1, 52.2, 66.5, 66.6, 127.6, 129.5, 129.6, 134.0, 134.1, 134.2, 135.6, 135.7, 135.8 ppm. IR (KBr): $\tilde{\nu}$ = 3447 (m), 3070 (m), 3048 (m), 2929 (s), 1471 (w), 1427 (m), 1390 (w), 1361 (w), 1111 (br.), 1009 (w), 823 (m), 802 (w), 739 (m), 702 (m), 613 (m),

504 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{56}O_3Si_2Na$ [M + Na^+] 711.3660; found 711.3669. **Epoxide Opening:** To a solution of the epoxide (3.45 g, 5.01 mmol) in acetone (50 mL) was added perchloric acid (0.5 mL, 3% in water) at 0 °C and the reaction mixture stirred for 2 h. $NaHCO_3$ (5 mg) was added. The organic layer was dried with $MgSO_4$, and after evaporation of the solvents in vacuo, diol **9** (3.53 g, 4.99 mmol, 99%) was obtained as a colorless solid. R_f = 0.39 (pentane/ethyl acetate, 1:1). $[\alpha]_D$ = –16.66 (c = +2.45, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 18 H), 1.31–1.99 (m, 12 H), 3.44–3.71 (m, 6 H), 7.29–7.46 (m, 12 H), 7.64–7.70 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 27.0, 27.1, 29.4, 30.5, 33.8, 35.2, 36.7, 38.9, 65.9, 67.2, 71.7, 73.6, 127.7, 129.6, 134.1, 135.7, 135.8 ppm. IR (KBr): $\tilde{\nu}$ = 3382 (br.), 3070 (w), 2955 (m), 2929 (m), 2857 (m), 1471 (w), 1427 (m), 1111 (s), 823 (m), 740 (m), 701 (s), 613 (w), 504 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{44}H_{58}O_4Si_2Na$ [M + Na^+] 729.3766; found 729.3777.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-6,7-Bis(allyloxy)-2,3-bis(hydroxymethyl)decalin (10a). Allyl Ether Formation: To a solution of diol **9** (500 mg, 0.71 mmol) and allyl bromide (0.98 mL, 11.31 mmol) in DMF (50 mL) at 0 °C was added NaH (60%, 339 mg, 14.13 mmol) and the mixture warmed up to 20 °C within 16 h. A saturated aqueous solution of NH_4Cl (20 mL) was added and the aqueous layer was extracted with TBME (3 × 30 mL). The combined organic layers were washed with brine (2 × 20 mL), dried with $MgSO_4$ and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography (150 g, pentane/TBME, 19:1) to afford 545 mg (0.69 mmol, 98%) of the corresponding bis(allyl ether) as a colorless oil. R_f = 0.30 (pentane/ethyl acetate, 19:1). $[\alpha]_D$ = +5.35 (c = 3.85, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (s, 18 H), 1.24–1.13 (m, 12 H), 3.36–3.59 (m, 6 H), 3.79–4.02 (m, 4 H), 4.96–5.24 (dd, J = 21.8, 10.2, Hz, 4 H), 5.71–5.91 (dddd, J = 20.8, 17.2, 5.2 Hz, 2 H), 7.15–7.31 (m, 12 H), 7.46–7.55 (m, 8 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 19.5, 26.6, 27.0, 27.1, 29.0, 30.3, 31.2, 34.5, 35.2, 36.1, 42.2, 66.5, 66.7, 69.8, 75.1, 76.3, 116.2, 116.3, 127.6, 129.5, 134.2, 135.6, 135.7 ppm. IR (KBr): $\tilde{\nu}$ = 3071 (w), 3041 (w), 2928 (m), 2856 (m), 1472 (w), 1427 (m), 1489 (w), 1361 (w), 1111 (s), 1087 (s), 1007 (w), 921 (w), 823 (m), 740 (m), 702 (s), 614 (w), 505 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{50}H_{66}O_4Si_2Na$ [M + Na^+] 809.4392; found 809.4383. **Silyl Deprotection:** To a solution of the bis(allyl ether) (439 mg, 0.56 mmol) in THF (25 mL) was added TBAF trihydrate (528 mg, 1.67 mmol) and the reaction mixture was stirred at 50 °C for 4 h. A saturated aqueous solution of NH_4Cl (20 mL) was added and the aqueous layer was extracted with TBME (3 × 20 mL). The combined organic layers were washed with brine (20 mL), dried with $MgSO_4$ and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography (100 g, pentane/TBME, 1:1) to afford 148 mg (0.48 mmol, 86%) of the diol **10a** as a colorless oil. R_f = 0.35 (pentane/ethyl acetate, 1:1). $[\alpha]_D$ = –4.69 (c = 2.96, $CHCl_3$, 20 °C). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.14–2.09 (m, 12 H), 3.41–3.69 (m, 6 H), 3.85–4.06 (m, 4 H), 5.13 (dddd, J = 10.4, 4.6, 3.1, 1.4 Hz, 2 H), 5.24 (dddd, J = 17.2, 8.5, 3.4, 1.7 Hz, 2 H), 5.88 (dddd, J = 17.2, 10.4, 9.3, 5.3 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2, 28.7, 29.9, 31.2, 34.5, 35.5, 39.4, 45.6, 67.9, 68.0, 69.6, 69.8, 74.6, 75.8, 116.2, 116.5, 135.4 ppm. IR (KBr): $\tilde{\nu}$ = 3364 (br.), 2913 (m), 1646 (w), 1426 (w), 1197 (w), 1065 (s), 1014 (w), 922 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{30}O_4Na$ [M + Na^+] 333.2036; found 333.2035.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-6,7-Bis(allyloxy)-2,3-bis(methoxymethyl)decalin [10b (Conformer 12)]. Methyl Ether Formation: To a solution of the diol **10a** (117 mg, 0.38 mmol) and methyl iodide (237 µL, 3.77 mmol) in DMF (25 mL) at 0 °C was added NaH (60%, 151 mg, 6.28 mmol) and the mixture warmed up to 20 °C within 16 h. A saturated aqueous solution of NH_4Cl (10 mL) was added and the aqueous layer was extracted with TBME (3 × 15 mL). The combined organic layers were washed with brine (2 × 10 mL), dried with $MgSO_4$ and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography (20 g, pentane/TBME, 19:1) to afford 119 mg of the bis(methyl ether) **10b** (0.35 mmol, 93%) as a colorless oil. R_f = 0.15 (pentane/ethyl acetate, 19:1). $[\alpha]_D$ = +19.44 (c = 3.22, $CHCl_3$, 20 °C). ^1H NMR (500 MHz, C_6D_6): δ = 1.40–1.79 (m, 8 H), 1.94 (ddd, J = 14.4, 3.7, 5.5 Hz, 1 H), 2.08 (dt, J = 13.6, 2.3 Hz 1 H), 2.14 (q, J = 12.8 Hz, 1 H), 2.26–2.33 (m, 1 H), 3.15 (s, 6 H), 3.22 (ddd, J = 16.7, 9.2, 6.1 Hz, 2 H), 3.30–3.35 (m, 2 H), 3.46–3.49 (m, 1 H), 3.57–3.61 (m, 1 H), 3.70–3.78 (m, 2 H), 3.83–3.90 (m, 2 H), 5.02 (ddd, J = 10.4, 1.6, 3.1 Hz, 2 H), 5.24 (dddd, J = 17.1, 13.7, 3.3, 1.5 Hz, 2 H), 5.82 (dddd, J = 17.2, 13.4, 10.4, 5.2 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 26.8, 29.6, 30.9, 32.5, 35.4, 35.5, 36.6, 41.8, 59.0, 70.0, 70.1, 75.7, 76.7, 76.8, 77.0, 115.9, 136.3, 136.5 ppm. IR (KBr): $\tilde{\nu}$ = 2977 (m), 2916 (s), 2866 (s), 1460 (m), 1385 (w), 1346 (w), 1289 (w), 1263 (w), 1193 (m), 1122 (s), 1093 (s), 995 (w), 956 (w), 921 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{34}O_4Na$ [M + Na^+] 361.2349; found 361.2347.

(2*S*,3*S*,4a*R*,5a*R*,8*Z*,11a*R*,12a*S*)-2,3-Bis(methoxymethyl)-5a,7,10,11a-tetrahydro-6,11-dioxacycloocta[*b*]decalin [11b (Conformer 13)]: To a solution of the diallyl compound **10b/12** (23 mg, 68.2 µmol) in toluene (80 mL) was added Grubbs I catalyst (12 mg, 13.6 µmol) in a Schlenk tube, then the flask was sealed and the reaction mixture was heated to 140 °C for 30 min. After cooling to 20 °C, $Pb(OAc)_4$ (6 mg, 13.6 µmol) was added and the reaction mixture was stirred at 20 °C for 1 h. The mixture was filtered through a pad of Celite, the filtrate concentrated in vacuo, and the residue was purified by flash chromatography (5 g, pentane/TBME, 5:1) to obtain 21 mg (67.6 µmol, 98%) of the alkene **11b** as a colorless oil. R_f = 0.39 (pentane/TBME, 5:1). $[\alpha]_D$ = –28.1 (c = 2.51, $CHCl_3$, 20 °C). ^1H NMR (500 MHz, C_6D_6): δ = 1.25–1.35 (m, 2 H), 1.52–1.60 (m, 4 H), 1.66–1.78 (m, 3 H), 1.80–1.88 (m, 2 H), 1.98–2.03 (m, 1 H), 3.10 (s, 3 H), 3.10–3.11 (m, 2 H), 3.12 (s, 3 H), 3.18 (dd, J = 7.2, 3.1 Hz, 2 H), 3.28 (dd, J = 7.9, 8.8 Hz, 1 H), 3.35 (ddd, J = 11.2, 8.6, 5.3 Hz, 1 H), 4.19–4.34 (m, 4 H), 5.51–5.59 (m, 2 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 25.6, 30.2, 30.4, 33.9, 34.9, 35.7, 35.8, 37.7, 57.8, 68.4, 68.5, 75.4, 77.8, 80.7, 84.5, 130.5, 130.6 ppm. HRMS (ESI): calcd. for $C_{18}H_{30}O_4Na$ [M + Na^+] 333.2036; found 333.2035.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-2,3-Bis(acetoxymethyl)-6,7-bis(allyloxy)decalin (10c): To a solution of diol **10a** (155 mg, 499 µmol) in acetic anhydride (1.5 mL) and pyridine (4.5 mL) was added DMAP (5 mg) and the reaction mixture was stirred at 40 °C for 6 h. 1 M HCl (5 mL) was added and the aqueous layer was extracted with diethyl ether (4 × 10 mL). The combined organic layers were washed with 1 M HCl (5 mL) and brine (2 × 10 mL), dried with Na_2SO_4 and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography [15 g, petroleum ether (PE)/ethyl acetate, 4:1] to afford 173 mg of the diacetate **10c** (439 µmol, 88%) as a colorless oil. R_f = 0.58 (hexane/ethyl acetate, 2:1). $[\alpha]_D$ = +11.1 (c = 1.00, $CHCl_3$, 23 °C). ^1H NMR (600 MHz, $CDCl_3$): δ = 1.37–1.44 (m, 4 H), 1.5 (dt, J = 13.5 and 3.0 Hz, 1 H), 1.82 (ddd, J = 14.6, 5.5, 3.4 Hz, 1 H), 1.89 (dt, J = 13.8, 2.5 Hz, 1 H), 1.91 (q, J = 13.5 Hz, 1 H), 2.00 (s, 3 H), 2.01 (s, 3 H), 2.09–2.15 (m, 1 H), 3.46–3.49 (m, 1 H), 3.58–3.61 (m, 1 H), 3.85–4.05 (m, 8 H), 5.11 (dq, J = 14.5 and 1.6 Hz, 2 H), 5.12 (dq, J = 14.2 und 1.6 Hz, 1 H), 5.23 (dq, J = 17.2 and 1.8 Hz, 1 H), 5.25 (dq, J = 17.2 and 1.7 Hz, 1 H), 5.81–5.92 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 25.9, 28.3, 29.6, 31.0, 33.6, 34.0, 35.2, 39.8, 67.4,

69.4, 69.6, 75.5, 75.6, 115.9, 116.4, 135.2, 135.3, 171.1 ppm. IR (KBr): $\tilde{\nu}$ = 3081 (w), 2916 (s), 2964 (s), 1733 (s), 1655 (m), 1462 (m), 1430 (m), 1367 (m), 1246 (s), 1127 (m), 1077 (s), 926 (m), 736 (w), 607 (w) cm^{-1}. HRMS (EI): calcd. for $C_{22}H_{34}O_6$ [M^+] 394.2355; found 394.2356.

(2*S*,3*S*,4a*R*,5a*R*,8*Z*,11a*R*,12a*S*)-2,3-Bis(acetoxymethyl)-5a,7,10,11a-tetrahydro-6,11-dioxacycloocta[*b*]decalin (11c): To a solution of the diallyl compound **10c** (20 mg, 51 μmol) in 1,2-dichoroethane (60 mL) was added Grubbs I catalyst (10 mg, 12 μmol) and the reaction mixture was heated to 85 °C for 1 h. Afterwards, more of Grubbs I catalyst (3 mg) was added and the reaction mixture was stirred for 45 min. After cooling to 20 °C, $Pb(OAc)_4$ (8 mg) was added and the reaction mixture was stirred at 20 °C for 12 h. The mixture was filtered through a pad of Celite, the filtrate concentrated in vacuo, and the residue was purified by flash chromatography (2 g, PE/ethyl acetate, 2:1) to obtain 14 mg (38 μmol, 76%) of **11c** as a colorless oil. R_f = 0.22 (hexane/ethyl acetate, 2:1). $[\alpha]_D$ = –35.1 (*c* = 1.00, $CHCl_3$, 22 °C). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.28 (dt, *J* = 13.7 and 3.0 Hz, 1 H), 1.31 (dt, *J* = 14.2 and 3.7 Hz, 1 H), 1.38 (q, *J* = 12.4 Hz, 1 H), 1.48 (ddd, *J* = 13.6, 11.3, 5.4 Hz, 1 H), 1.69 (td, *J* = 13.7 and 5.4 Hz, 1 H), 1.72–1.83 (m, 2 H), 1.86 (dt, *J* = 14.2 and 6.3 Hz, 1 H), 1.86–1.90 (m, 1 H), 1.91–1.97 (m, 1 H), 2.01 (s, 3 H), 2.03 (s, 3 H), 3.11 (ddd, *J* = 11.3, 8.7 and 4.6 Hz, 1 H), 3.28 (ddd, *J* = 11.2, 8.7 and 5.1 Hz, 1 H), 3.90 (dd, *J* = 10.9 and 5.9 Hz, 1 H), 4.06 (d, *J* = 7.4 Hz, 2 H), 4.15 (dd, *J* = 10.9 and 8.4 Hz, 2 H), 4.25–4.35 (m, 4 H), 5.66–5.72 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 24.5, 29.2, 29.5, 32.7, 33.1, 34.2, 34.7, 36.5, 65.8, 667.9, 68.0, 79.8, 83.3, 129.6, 129.7, 170.9, 171.1 ppm. IR (KBr): $\tilde{\nu}$ = 2927 (m), 1736 (s), 1446 (w), 1367 (m), 1244 (s), 1099 (m), 1035 (m), 735 (w), 60 w (w). HRMS (ESI): calcd. for $C_{20}H_{30}O_6$ [M] 366.2042; found 366.2043.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-2,3-Bis(acetoxymethyl)-6,7-bis(allyloxy)decalin (10c) by Ring-Opening Metathesis: To a solution of the dioxacyclooctene **11c** (19 mg, 52 μmol) in dichloromethane (60 mL) was added Grubbs I catalyst (10 mg, 12 μmol) in a pressure-vessel at 20 °C. The reaction mixture was stirred under ethylene (4 bar) for 22 h. Then $Pb(OAc)_4$ (10 mg) was added. After stirring at 25 °C for 12 h, the mixture was filtered through a pad of Celite, the filtrate concentrated in vacuo, and the residue was purified by flash chromatography (4 g, PE/TBME, 1:1) to obtain 12.5 mg (32.0 μmol, 62%) of **10c** as a colorless oil. The analytic data of the product are identical with those of the compound obtained from **10a**.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-6,7-Bis(2-hydroxyethoxy)-2,3-bis(methoxymethyl)decalin (14): Olefin **11b** (22 mg, 70.8 μmol) was dissolved in CH_2Cl_2/MeOH (1:1) (10 mL) at –78 °C and a stream of ozone was introduced into the solution for 5 min until the color turned blue. Then the mixture was purged with a stream of argon until it was colorless again and $NaBH_4$ (16 mg, 42.5 mmol) was added. The reaction mixture was warmed up to 20 °C within 16 h. After aqueous workup with a saturated solution of NH_4Cl (3 × 5 mL) and brine (2 × 5 mL), the combined organic phases were dried with $MgSO_4$. After evaporation of the solvents, the residue was purified by column chromatography (5 g, $CHCl_3$/MeOH, 19:1) to afford 15 mg of diol **14** (43.3 mmol, 61%) as a colorless oil. R_f = 0.32 ($CHCl_3$/MeOH, 9:1). $[\alpha]_D$ = +0.45 (*c* = 1.1, $CHCl_3$, 20 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.35–1.46 (m, 3 H), 1.52–1.66 (m, 4 H), 1.69–1.74 (m, 2 H), 1.78–1.84 (m, 1 H), 1.87–1.95 (m, 1 H), 2.01–2.08 (m, 1 H), 2.21–2.24 (br., 2 H), 3.25 (dd, *J* = 9.1, 6.1 Hz, 2 H), 3.30 (s, 6 H), 3.33 (m, 2 H), 3.43–3.52 (m, 3 H), 3.55–3.59 (m, 1 H), 3.61–3.74 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 27.7, 28.9, 30.5, 31.4, 33.7, 34.1, 34.6, 39.8, 58.9, 59.0, 62.3, 70.0, 70.3, 76.1, 76.5 ppm. HRMS (ESI): calcd. for $C_{18}H_{34}O_6Na$ [M + Na^+] 369.2248; found 369.2247.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-6,7-Bis(2-allyloxyethoxy)-2,3-bis(methoxymethyl)decalin [15 (Conformer 17)]: To a solution of diol **14** (10 mg, 28.9 μmol) and allyl bromide (39.9 μL, 461.7 μmol) in DMF (25 mL) at 0 °C was added NaH (13.1 mg, 545.8 μmol) and the reaction mixture was warmed up to 20 °C within 16 h. A saturated aqueous solution of NH_4Cl (10 mL) was added and the aqueous layer was extracted with TBME (3 × 10 mL). The combined organic layers were washed with brine (2 × 20 mL), dried with $MgSO_4$ and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography (5 g, pentane/ethyl acetate, 9:1) to afford 12.2 mg of bis(allyl ether) **15** (28.6 μmol, 99%) as a colorless oil. R_f = 0.10 (pentane/ethyl acetate, 9:1). $[\alpha]_D$ = +6.20 (*c* = 1.0, $CHCl_3$, 20 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27–1.60 (m, 7 H), 1.65–1.70 (m, 1 H), 1.74–1.95 (m, 3 H), 2.01–2.14 (m, 1 H), 3.15–3.26 (m, 2 H), 3.29 (s, 6 H), 3.33–3.42 (m, 2 H), 3.44–3.52 (m, 1 H), 3.53–3.62 (m, 7 H), 3.63–3.70 (m, 2 H), 4.00–4.05 (m, 4 H), 5.13–5.20 (m, 2 H), 5.22–5.32 (m, 2 H), 5.83–5.98 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.5, 28.7, 30.0, 31.6, 34.4, 35.1, 35.4, 41.0, 58.9, 68.3, 68.4, 69.9, 72.3, 76.2, 76.6, 76.9, 77.4, 116.9, 135.1, 135.2 ppm. IR (KBr): $\tilde{\nu}$ = 3078 (m), 2919 (m), 1102 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{42}O_6Na$ [M + Na^+] 449.2874; found 449.2870.

(2*S*,3*S*,4a*S*,5a*R*,11*Z*/*E*,17a*R*,18a*R*)-2,3-Bis(methoxymethyl)-5a,7,8,10,13,15,16,17a-octahydro-6,9,14,17-tetraoxacyclotetradeca-[*b*]decalin [16 (Conformer 18)]: To a solution of the bis(allyl ether) **15** (12 mg, 28.1 μmol) in toluene (80 mL) was added Grubbs I catalyst (4.6 mg, 5.6 μmol) in a Schlenk tube. Then the flask was sealed and the reaction mixture was heated to 140 °C for 30 min. After cooling to 20 °C, $Pb(OAc)_4$ (3 mg, 5.6 μmol) was added and the reaction mixture was stirred at 20 °C for 1 h. The mixture was filtered through a pad of Celite, the filtrate concentrated in vacuo, and the residue was purified by flash chromatography (5 g, pentane/TBME, 5:1) to afford 8 mg (20.1 μmol, 72%) of the olefin **16** [(*E*)/(*Z*) = 2:7] as a white solid. R_f = 0.25 (pentane/ethyl acetate, 1:1). ^{1}H NMR (500 MHz, C_6D_6): δ = 1.39–2.22 (m, 11 H), 2.34–2.41 (m, 1 H), 3.24 (s, 3 H), 3.25 (s, 3 H), 3.34 (ddd, *J* = 13.6, 9.0, 6.1 Hz, 2 H), 3.40–3.56 (m, 8 H), 3.65–3.73 (m, 2 H), 3.79–3.86 (m, 3 H), 3.88–3.96 (m, 3 H), 5.77–5.89 (m, 2 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 27.1, 29.6, 30.9, 32.3, 35.4, 35.6, 36.1, 41.6, 59.0, 68.2, 68.3, 70.5, 70.8, 76.8, 77.1, 77.8, 130.2, 130.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{38}O_6Na$ [M + Na^+] 421.2561; found 421.2561.

(2*S*,3*S*,4a*R*,6*R*,7*R*,8a*S*)-6,7-Bis(allyloxy)-2,3-bis(allyloxymethyl)decalin [19 (Conformer 23)]: To a solution of diol **10a** (32 mg, 10.3 μmol) and allyl bromide (89 μL, 1.03 mmol) in DMF (25 mL) at 0 °C was added NaH (60%, 41.2 mg, 1.72 mmol) and the mixture warmed up to 20 °C within 16 h. A saturated aqueous solution of NH_4Cl (20 mL) was added and the aqueous layer was extracted with TBME (3 × 15 mL). The combined organic layers were washed with brine (2 × 10 mL), dried with $MgSO_4$ and after evaporation of the solvents in vacuo, the residue was purified by flash chromatography (10 g, pentane/TBME, 19:1) to afford 27 mg of the tetrakis(allyl ether) **19** (68.4 μmol, 66%) as a colorless oil. R_f = 0.38 (pentane/ethyl acetate, 9:1). $[\alpha]_D$ = +15.07 (*c* = 4.61, $CHCl_3$, 20 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29–1.48 (m, 3 H), 1.50–1.74 (m, 5 H), 1.76–1.99 (m, 3 H), 2.04–2.16 (m, 1 H), 3.26 (ddd, *J* = 9.2, 6.1, 2.8 Hz, 2 H), 3.41–3.51 (m, 3 H), 3.58–3.62 (m, 1 H), 3.86–4.09 (m, 8 H), 5.09–5.18 (m, 4 H), 5.20–5.25 (m, 2 H), 5.26–5.31 (m, 2 H), 5.82–5.98 (m, 4 H) ppm. ^{13}C NMR (75 MHz,

$CDCl_3$): δ = 26.5, 28.8, 30.1, 31.7, 34.3, 35.1, 35.6, 41.1, 69.6, 69.7, 72.1, 74.0, 74.1, 76.2, 116.1, 116.4, 116.5, 135.4, 135.5, 135.6 ppm. IR (KBr): $\tilde{\nu}$ = 3078 (m), 2919 (m), 1102 (m) cm^{-1}. IR (KBr): $\tilde{\nu}$ = 3468 (w), 3079 (w), 2920 (s), 2855 (s), 1828 (w), 1646 (w), 1460 (w), 1345 (w), 1265 (w), 1196 (w), 1087 (s), 997 (w), 920 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{38}O_4Na$ [M + Na^+] 413.2662; found 413.2661.

(2*S*,3*S*,4a*R*,5a*R*,8*Z*,11a*R*,12a*S*)-2,3-Bis(allyloxymethyl)-5a,7,10,11a-tetrahydro-6,11-dioxacycloocta[*b*]decalin [21 (Conformer 24)]: To a solution of the tetrakis(allyl ether) **19** (27 mg, 68 μmol) in toluene (80 mL) was added Grubbs I catalyst (11 mg, 13.7 μmol) in a Schlenk tube, then the flask was sealed and the reaction mixture was heated to 140 °C for 30 min. After cooling to 20 °C, $Pb(OAc)_4$ (6 mg, 13.6 μmol) was added and the reaction mixture was stirred at 20 °C for 1 h. The mixture was filtered through a pad of Celite, the filtrate concentrated in vacuo, and the residue was purified by flash chromatography (5 g, pentane/ethyl acetate, 9:1 → 4:1) to obtain the cyclic olefin **21** (10 mg, 27.6 μmol, 41%) as a colorless oil. R_f = 0.21 (pentane/ethyl acetate, 4:1). ^1H NMR (600 MHz, C_6D_6): δ = 1.28–1.37 (m, 4 H), 1.55–1.61 (m, 2 H), 1.68–1.77 (m, 3 H), 1.80–1.85 (m, 1 H), 1.86–1.91 (m, 1 H), 2.01–2.06 (s, 1 H), 3.09 (ddd, *J* = 10.9, 8.6, 4.6 Hz, 1 H), 3.21 (dd, *J* = 9.0, 6.5 Hz, 1 H), 3.29 (d, *J* = 7.3 Hz, 2 H), 3.36 (ddd, *J* = 11.3, 8.7, 5.4 Hz, 1 H), 3.77 (tdd, *J* = 5.4, 3.9, 1.5 Hz, 2 H), 3.81 (td, *J* = 5.3, 1.6 Hz, 2 H), 4.19–4.25 (m, 2 H), 4.26–4.29 (m, 2 H), 5.16 (dddd, *J* = 10.4, 8.8, 3.3, 1.5 Hz, 2 H), 5.36 (dddd, *J* = 17.2, 10.6, 3.6, 1.8 Hz, 2 H), 5.66 (ddd, *J* = 16.9, 11.7, 3.8 Hz, 2 H), 5.96 (dddd, *J* = 17.3, 10.4, 5.2, 1.9 Hz, 2 H) ppm. ^{13}C NMR (125 MHz, C_6D_6): δ = 25.7, 30.3, 30.5, 33.8, 35.0, 35.7, 36.0, 37.7, 65.4, 68.4, 68.5, 72.2, 75.4, 80.8, 84.5, 116.2, 127.3, 127.8, 128.9, 130.5, 136.2, 142.3 ppm. HRMS (ESI): calcd. for $C_{22}H_{34}O_4Na$ [M + Na^+] 385.2349; found 385.2351.

Supporting Information (see also the footnote on the first page of this article): NMR spectra for compounds **5**–**9**, **10b**, **11b**, **14**–**16**, **19**, and **21**.

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