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A highly stereoselective route to medium-ring-sized *trans*-alkenolides via oxidative fragmentation of bicyclic oxycyclopropane precursors: application to the synthesis of (+)-recifeiolide

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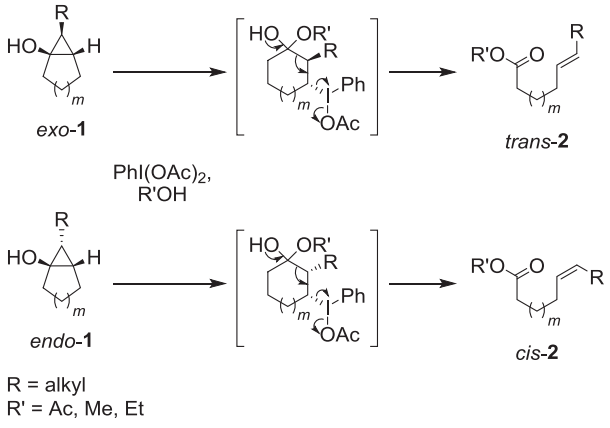
ABSTRACT

A new approach to the synthesis of medium-ring-sized *trans*-alkenolides, based on the oxidative fragmentation of a three-carbon ring in hydroxyalkyl substituted bicyclo[*n*.1.0]alkan-1-ols readily available from 2-alkylidenecycloalkanones, is described. This methodology was applied to the six-step transformation of cyclooctanone to the natural 12-membered *trans*-alkenolide antibiotic (+)-recifeiolide.

1. Introduction

Oxycyclopropanes are reactive, easily available compounds that are used as intermediates in the synthesis of other organic compounds owing to their ability to undergo synthetically useful transformations based upon the cleavage of the strained cyclopropane ring. Cleavage of either of the two adjacent to alcohol group bonds of the cyclopropane usually results in the formation of corresponding carbonyl compounds, whereas cleavage of the opposite carbon–carbon bond of the ring leads to allylic alcohols or related compounds.[1] Oxidative fragmentation of the substituted cyclopropanols with $Pb(OAc)_4$ or $PhI(OAc)_2$, occurring via the splitting of both carbon–carbon bonds adjacent to oxygen and leading to the corresponding carboxylic acids and alkenes, is also known.[2,3] An essential feature of the latter transformations is its high diastereoselectivity. This occurs, particularly, in the transfer of the relative configuration of substituents at the cyclopropane ring in bicyclic cyclopropanols **1** to the stereochemistry of the disubstituted carbon–carbon double bond in the products of their fragmentation, for example, *exo*-**1** is exclusively converted into *trans*-alkene **2**, whereas *endo*-**1** converts to *cis*-alkene **2** (Scheme 1).[2–4] This sort of substrate diastereocontrol has made it possible to efficiently use this oxidative fragmentation of the cyclopropane ring in appropriate bicyclic precursors to perform the stereoselective generation of carbon–carbon double bonds in the syntheses of the alkaloid (−)-pinidine,[3b] capsaicin[4] and some monoene insect pheromones.[5]



Scheme 1.

Since hydroxylic solvents are involved in the formation of a carbon–oxygen bond in this reaction (Scheme 1), we assumed that the oxidation of bicyclo[*n*.1.0]alkan-1-ols **1**, bearing a hydroxyl

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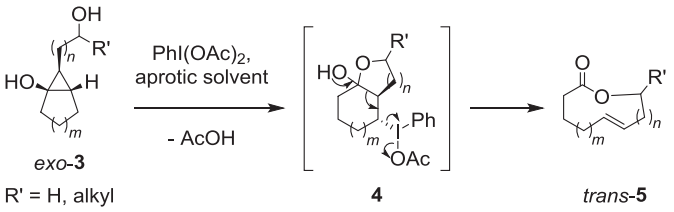
group in alkyl substituent R, in aprotic solvents would afford the corresponding lactones. In this case, the less sterically hindered *exo*-diastereomers of bicyclo[*n*.1.0]alkan-1-ols **3** might form the corresponding fused bicyclic intermediates **4**, and the fragmentation of the bridge carbon–carbon bond in the latter should provide alkenolides **5** with *trans*-configuration of the double bond (Scheme 2).



Scheme 2.

Similar diastereocontrol in the formation of *trans*-alkenolides was observed during the oxidation of fused oxabicycloalkenes,[6–9] as well as trialkylstannyl-substituted bicyclic lactols.[10] However, the formation of the double bond in these transformations was not highly regioselective or the required substrates for the oxidation were not readily available. At the same time, macrolactonization or ring-closing methathesis, which are both frequently employed in the synthesis of natural bioactive *trans*-alkenolides, quite often gave products in low yields or with low stereoselectivity, which required optimization of the reaction conditions.[11,12] In this work, we report a convenient method for the preparation of oxy-substituted *exo*-bicyclo[*n*.1.0]alkan-1-ols **3** and their application to the synthesis of medium-ring *trans*-alkenolides **5**.

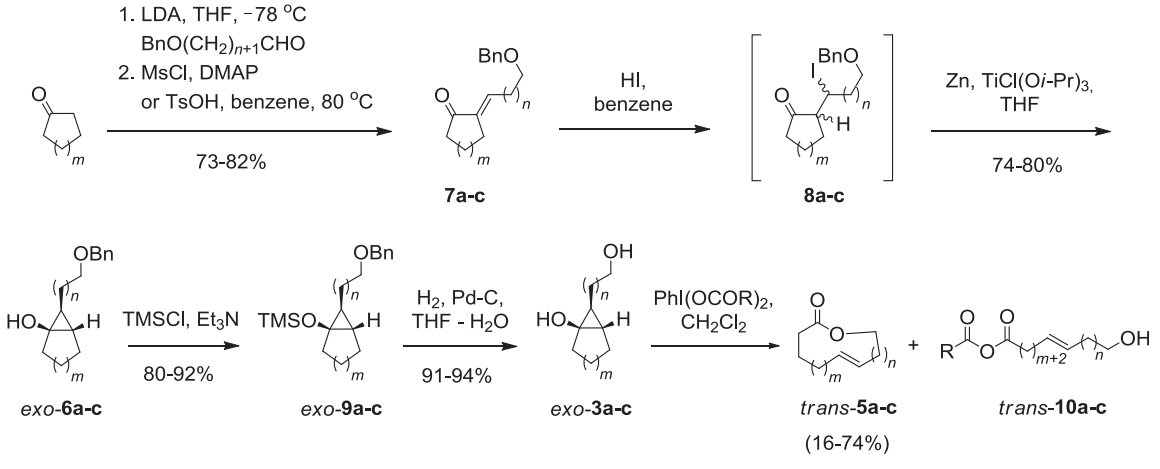
2. Results and discussion

Bicyclic cyclopropanols **6a**–**c**, bearing benzyl-protected hydroxyalkyl substituents, were obtained from unsaturated ketones **7a**–**c**, which are readily available via aldol condensation (Scheme 3). The treatment of unsaturated ketones **7a**–**c** with hydrogen iodide in dry benzene, followed by the reaction of intermediate β-iodoketones **8a**–**c** with zinc dust in the presence of $TiCl(Oi\text{-}Pr)_3$, under the previously described conditions,[4] led to the formation of the corresponding bicyclic cyclopropanols **6a**–**c** in high (74–91%) overall yields.[13] It is noteworthy that, unlike the transformations of 2-alkylidenecycloalkanones without functional groups in the side chain,[4] the reductive cyclization of compounds **7a**,**b** led to *exo*-bicyclo[*n*.1.0]alkan-1-ols **6a**,**b** exclusively.[14] In the case of ketone **7c**, which contains a remote benzyloxy substituent, a chromatographically readily separable mixture of *exo*/*endo*-isomers **6c** in the ratio of 82:18 was obtained. We suggest that the exclusive formation of *exo*-isomers **6a**,**b** was favored due to the intramolecular chelation of a metal atom with oxygen of the benzyloxy group in intermediate β-metaloketones.[15]

Debenzylation of compounds **6a**–**c** by hydrogenolysis was performed in the presence of 5 mol % of Pd–C following a silyl protection of the tertiary hydroxyl group. The benzyl group in TMS-protected cyclopropanols **9a**–**c** was smoothly removed in aq tetrahyfrofuran with the retention of a three-carbon ring, and was accompanied by the removal of the TMS-protecting group to give hydroxyalkyl substituted cyclopropanols **3a**–**c**. It is noteworthy that unprotected cyclopropanols **6** were involved in Pd-catalyzed three-carbon ring opening reactions[16] and yields of the target products **3** did not exceed 50%.

The oxidative fragmentation of *exo*-bicyclo[*n*.1.0]alkan-1-ol **3b** with phenyliodine(III) diacetate in anhydrous dichloromethane or deuterochloroform was completed in 1 h to give *trans*-alkenolide **5b**[9] in 70% yield (Scheme 3). The signals of the olefinic protons in the homodecoupled ^1H NMR spectrum of *trans*-**5b** displayed mutual splitting with a coupling constant of 15.4 Hz,[17] which corresponded to the *trans*-configuration of the double bond. The presence of an absorption band at 975 cm^{-1} in the IR spectrum of *trans*-**5b** provided further support for the stereochemistry assignment. The more reactive phenyliodine(III) bis(trifluoroacetate), as was shown by ^1H NMR inspection, reacted with diol *exo*-**3b** significantly faster to complete the reaction within 12 min. However, only a minor increase in the yield of lactone *trans*-**5b** (to 74%) was observed.[18] Under the same conditions, *exo*-bicyclo[*n*.1.0]alkan-1-ol **3a** gave the corresponding *trans*-alkenolide **5a** in 60% isolated yield.[19] At the same time, according to ^1H NMR spectroscopy, *exo*-bicyclo[*n*.1.0]alkan-1-ol **3c** in reaction with $PhI(OCOCF_3)_2$ in $CDCl_3$ was converted to the target macrolactone *trans*-**5c** in 23% yield (16% isolated yield).

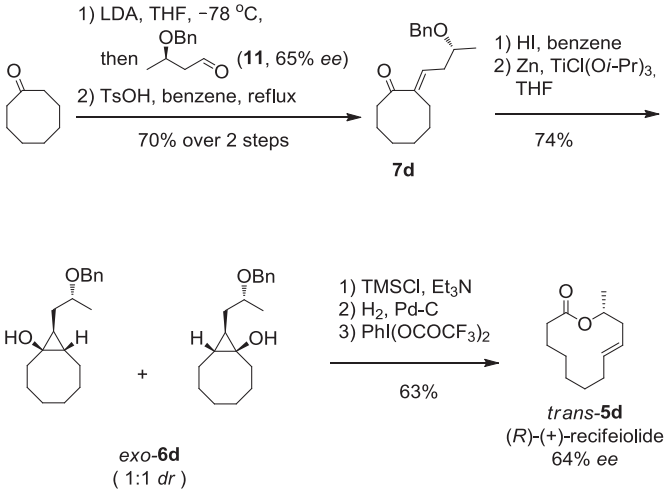
^1H NMR analysis of the reaction mixtures also indicated the formation of mixed anhydrides **10a**–**c**[20] of the corresponding *trans*-ω-hydroxyalkenoic acids as initial side products, which were transformed gradually to acyclic *trans*-ω-acyloxyalkenoic acids as a result of the cross-acylation reactions. As an example, in the reaction *exo*-**3c** with $PhI(OCOCF_3)_2$ in $CDCl_3$, the primary reaction



Scheme 3.

product *trans*-**10c** demonstrated in ^{1}H NMR an easily visible triplet at δ 3.75 ppm, typical of the protons of the CH_2OH group. The intensity of this signal gradually decreased in conjunction with an increase in a triplet at δ 4.34 ppm attributed to methylene protons of the CH_2OCOCF_3 group.[21] It should be noted that mixed trifluoroacetic acid anhydride *trans*-**10c** could also be employed as a potential precursor for the macrolactonization reactions.[22]

Using the methodology described above, we implemented the synthesis of a natural antibiotic (*R*)-(+)-recifeiolide (*trans*-**5d**), isolated from the fungus *Cephalosporium recifei*,[23] starting from cyclooctanone and enantiomerically enriched (*R*)-3-benzyloxy butanal (**11**) (Scheme 4).[6,24] The latter was prepared in three steps in 43% yield and with 65% ee from ethyl acetoacetate by successive asymmetric reduction of the β-keto group with a sodium borohydride/(L)-tartaric acid system,[25] benzylation of the hydroxyl group[26] and DIBAL reduction of the obtained ester. Aldol coupling of (*R*)-3-benzyloxybutanal and cyclooctanone, followed by dehydration, resulted in the formation of (*R*)-2-(3-(benzyloxy)butylidene)cyclooctan-1-one (**7d**) in 70% yield over two steps.



Scheme 4.

A reductive cyclization of unsaturated ketone **7d** via its preliminary conversion to the corresponding β-iodoketone gave a mixture of diastereomeric cyclopropanols **6d** in 87% combined yield and with *exo*/*endo* diastereoselectivity of 85:15. The formation of minor *endo*-**6d** isomers[27] in this case can be explained by the greater steric bulk at the benzylic oxygen bonded to the secondary carbon, which may have hindered the chelation of the metal atom in the β-metaloketone intermediate. After debenzylation of diastereomeric *exo*-bicyclo[6.1.0]alkan-1-ol **6d**, in a manner analogous to that described above, and subsequent oxidation of the obtained diols *exo*-**3d** with $PhI(OCOCF_3)_2$, the target (*R*)-(+)-recifeiolide **5d** was obtained in 33% total yield, based on the starting cyclooctanone. The enantiomeric purity of the obtained product *trans*-**5d** (ee 64%) was virtually identical to that of aldehyde **11** (ee 65%), which indicated that no significant racemization of the chiral center occurred during the synthesis.[28]

3. Conclusion

In conclusion, we present a new methodology for the synthesis of *trans*-alkenolides based on the stereoselective preparation of *exo*-hydroxyalkyl-substituted bicyclo[*n*.1.0]alkan-1-ols, followed by the stereoselective oxidative fragmentation of the three-carbon ring in these compounds with phenyliodine dicarboxylates in dry dichloromethane. Under these conditions, medium-sized *trans*-alkenolides **5** were obtained in good yields from *exo*-bicyclo[*n*.1.0]alkan-1-ols **3a**,**b**,**d** bearing β-hydroxyalkyl substituents at the cyclopropane ring, which favored the formation of bicyclic hemiketal intermediate **4**. The methodology was successfully applied to the six-step synthesis of the enantiomerically enriched antibiotic (*R*)-(+)-recifeiolide (*trans*-**5d**) from cyclooctanone in 33% overall yield.

4. Experimental section

4.1. General

All solvents were purified and dried by conventional methods prior to use. Titanium(IV) chlorotriisopropoxide was prepared from distilled titanium(IV) chloride and titanium(IV) isopropoxide.[29] Zinc dust was activated by successive washings with dilute hydrochloric acid, water, ethanol, acetone, and anhydrous diethyl ether and dried under reduced pressure at 100 °C for 1–2 h. Phenyliodine(III) bis(trifluoroacetate) was synthesized according to the literature procedure.[30] Other reagents were used as purchased from commercial suppliers. All the reactions with organometallics were carried out under dry argon. Silica gel Sorbfil plates were used for TLC. Chromatographic separations were performed on Merck 60 silica gel (70–230 mesh). In the case of isolation of acidophobic compounds (**3**, **6**, **9**) silica gel was pretreated with triethylamine (ca. 0.2 mL per 2 g of SiO_2). The mixture of petroleum ether and ethyl acetate in various ratios was used as an eluent. ^{1}H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were taken on a Bruker AC 400 spectrometer in $CDCl_3$ as a solvent. Chemical shifts were given in δ value with $CHCl_3$ (δ=7.26 ppm) and $CDCl_3$ (δ=77.16 ppm) as internal standards for ^{1}H NMR and ^{13}C NMR spectra, respectively. The multiplicity of signals in ^{13}C NMR spectra was determined by DEPT-135 experiment. IR spectra were taken on a Bruker Vertex 70 spectrometer. Optical rotation was measured on a PerkinElmer 141 polarimeter.

4.2. General procedure for the preparation of ketones 7

To the cooled −78 °C stirred solution of lithium diisopropylamide (39.8 mmol) in THF (40 mL), a solution of corresponding cycloalkanone (38.3 mmol) in THF (7 mL) was added dropwise over 15 min via syringe. After 20 min, a solution of benzyloxyaldehyde (38.3 mmol) in THF (15 mL) was added dropwise over 30 min. After 1.5 h, the reaction mixture was quenched by the addition of $NaHCO_3$ solution (35 mL, satd aq) and was allowed to warm to room temperature. The aqueous layer was separated and extracted with ether (4×40 mL). The combined organic phases were washed with cold HCl solution (1% aq), $NaHCO_3$ solution (satd aq), brine (2×30 mL) and dried (Na_2SO_4). Solvents were removed in vacuo and the obtained crude aldols were used in the next step without further purification.

Compound **7a** was obtained according to the following dehydration procedure: methanesulfonyl chloride (5.92 mL, 76.5 mmol) was added in one portion to the cooled (0°C) and stirred solution of crude aldol (30.6 mmol) and DMAP (14.9 g, 122 mmol) in dichloromethane (240 mL). After the completion of the reaction (TLC-monitoring), $NaHCO_3$ (150 mL, satd aq) and H_2O (150 mL) were added to the reaction mixture. The aqueous layer was separated and extracted with dichloromethane (3×40 mL). The combined organic phases were washed with brine (20 mL) and dried (Na_2SO_4). Evaporation and chromatography of the residue (from 1:13 to 1:7 ethyl acetate/petroleum ether) gave compound **7a** as a light yellow liquid.

Compounds **7b**–**d** were obtained according to the following dehydration procedure: the solution of a crude aldol (30.6 mmol) in benzene (150 mL) was refluxed in the presence of a catalytic amount of *p*-toluenesulfonic acid monohydrate using a Dean–Stark

trap. After the completion of the reaction (TLC-monitoring), the reaction mixture was cooled to room temperature, washed with $NaHCO_3$ solution (2×20 mL, satd aq), and dried (Na_2SO_4). Evaporation and chromatography of the residue (from 1:13 to 1:7 ethyl acetate/petroleum ether) gave compounds **7b**–**d** as light yellow liquids.

*4.2.1. (E)-2-(3-(Benzyloxy)propylidene)cyclopentanone (**7a**).* Yield 73%. Found: C, 78.18; H, 7.90. $C_{15}H_{18}O_2$ requires C, 78.23; H, 7.88%; R_f (25% EtOAc/petroleum ether) 0.53; ν_{max} (liquid film) 3092, 3063, 3030, 1717, 1652 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.55–7.18 (5H, m, Ph), 6.62–6.52 (1H, m, H-olef.), 4.52 (2H, s, CH_2Ph), 3.58 (2H, t, J=6.7 Hz, CH_2OBn), 2.65–2.55 (2H, m), 2.54–2.41 (2H, m), 2.33 (2H, t, J=7.7 Hz), 1.98–1.88 (2H, m); δ_C (100 MHz, $CDCl_3$) 207.0 (*C*=O), 139.0 ($C_{quart.}$), 138.3 ($C_{quart.}$), 132.4 (CH-olef.), 128.5 (CH-arom.), 127.8 (2CH-arom.), 127.8 (2CH-arom.), 73.3 (CH_2), 68.7 (CH_2), 38.7 (CH_2), 30.6 (CH_2), 27.0 (CH_2), 19.9 (CH_2).

*4.2.2. (E)-2-(3-(Benzyloxy)propylidene)cyclohexanone (**7b**).* Yield 81%. Found: C, 78.57; H, 8.27. $C_{16}H_{20}O_2$ requires C, 78.65; H, 8.25%; R_f (25% EtOAc/petroleum ether) 0.63; ν_{max} (CCl_4) 3090, 3067, 3032, 1691, 1620 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.38–7.27 (5H, m, Ph), 6.66–6.59 (1H, m, H-olef.), 4.52 (2H, s, CH_2Ph), 3.57 (2H, t, J=6.7 Hz, CH_2OBn), 2.53–2.37 (6H, m), 1.89–1.79 (2H, m), 1.79–1.68 (2H, m); δ_C (100 MHz, $CDCl_3$) 201.0 (*C*=O), 138.3 ($C_{quart.}$), 137.9 ($C_{quart.}$), 135.6 (CH-olef.), 128.5 (CH-arom.), 127.8 (2CH-arom.), 127.8 (2CH-arom.), 73.2 (CH_2), 68.8 (CH_2), 40.3 (CH_2), 28.7 (CH_2), 27.0 (CH_2), 23.6 (CH_2), 23.4 (CH_2).

*4.2.3. (E)-2-(6-(Benzyloxy)hexylidene)cyclohexanone (**7c**).* Yield 82%. Found: C, 79.61; H, 9.17. $C_{19}H_{26}O_2$ requires C, 79.68; H, 9.15%; R_f (25% EtOAc/petroleum ether) 0.61; ν_{max} (liquid film) 3087, 3063, 3030, 1686, 1613 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.20 (5H, m, Ph), 6.65–6.55 (1H, m, H-olef.), 4.49 (2H, s, CH_2Ph), 3.45 (2H, t, J=6.5 Hz, CH_2OBn), 2.52–2.35 (4H, m), 2.17–2.03 (2H, m), 1.90–1.78 (2H, m), 1.78–1.68 (2H, m), 1.68–1.55 (2H, m), 1.53–1.32 (4H, m); δ_C (100 MHz, $CDCl_3$) 201.3 (*C*=O), 139.6 (CH-olef.), 138.7 ($C_{quart.}$), 136.4 ($C_{quart.}$), 128.5 (2CH-arom.), 127.7 (2CH-arom.), 127.6 (CH-arom.), 73.0 (CH_2), 70.4 (CH_2), 40.3 (CH_2), 29.7 (CH_2), 28.4 (CH_2), 27.8 (CH_2), 26.8 (CH_2), 26.2 (CH_2), 23.7 (CH_2), 23.5 (CH_2).

*4.2.4. (R,E)-2-(3-(Benzyloxy)butylidene)cyclooctanone (**7d**).* Yield 70%. Found: C, 79.63; H, 9.17. $C_{19}H_{26}O_2$ requires C, 79.68; H, 9.15%; R_f (20% EtOAc/petroleum ether) 0.63; $[\alpha]_D^{17}$ −2.6 (*C* 3.0, $CHCl_3$); ν_{max} (CCl_4) 3095, 3066, 3031, 1684, 1617 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.38–7.21 (5H, m, Ph), 6.64 (1H, t, J=7.4 Hz, H-olef.), 4.57 (1H, d, J=11.7 Hz, CH_2Ph), 4.49 (1H, d, J=11.7 Hz, CH_2Ph), 3.72–3.55 (1H, m, C*H*(OBn)Me), 2.71–2.38 (5H, m), 2.36–2.26 (1H, m), 1.83–1.71 (2H, m), 1.61–1.49 (4H, m), 1.46–1.33 (2H, m), 1.22 (3H, d, J=6.1 Hz, Me); δ_C (100 MHz, $CDCl_3$) 206.1 (*C*=O), 141.1 ($C_{quart.}$), 138.8 ($C_{quart.}$), 136.1 (CH-olef.), 128.5 (2CH-arom.), 127.8 (2CH-arom.), 127.6 (CH-arom.), 74.3 (*C*H(OBn)Me), 70.7 (CH_2), 39.5 (CH_2), 35.7 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 26.4 (CH_2), 25.8 (CH_2), 25.2 (CH_2), 20.1 (Me).

4.3. General procedure for the preparation of bicyclo[*n*.1.0] alkan-1-ols 6[4]

Intermediate β-iodoketones **8** were generated by the addition of an equivalent amount of hydrogen iodide (solution in dry benzene, ca. 0.5–1.5 M)[31] to the solution of unsaturated ketones **7** (25 mmol) in dry benzene (15 mL). A solution of TiCl(O*i*-Pr)$_3$ in THF (1 M, 25 mmol, 25 mL) was added to the suspension of zinc dust[32] (3.25 g, 50 mmol) in THF (25 mL) and then a fresh-prepared solution of β-iodoketone **8** (25 mmol) in dry benzene was added via syringe in one portion. After few minutes, the reaction mixture spontaneously warmed up and turned dark brown. When the reaction was completed (TLC monitoring), a solution of NH_4Cl (10 mL, satd aq) was added, precipitate was filtered off and washed thoroughly with Et_2O (5×15 mL). The filtrate was washed with brine (15 mL), dried (Na_2SO_4), the solvent was evaporated and chromatography of the residue (from 1:10 to 1:6 ethyl acetate/petroleum ether) gave compounds **6a**–**d** as colorless or pale-yellow liquids.

*4.3.1. exo-6-(2-(Benzyloxy)ethyl)bicyclo[3.1.0]hexan-1-ol (exo-**6a**).* Yield 74%. Found: C, 77.49; H, 8.70. $C_{15}H_{20}O_2$ requires C, 77.55; H, 8.68%; R_f (25% EtOAc/petroleum ether) 0.52; ν_{max} (liquid film) 3409, 3088, 3064, 3029 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.43–7.23 (5H, m, Ph), 4.59 (1H, d, J=12.2 Hz, CH_2Ph), 4.54 (1H, d, J=12.2 Hz, CH_2Ph), 4.05 (1H, br s, O*H*), 3.61 (1H, dt, J=8.7, 3.6 Hz, CH_2OBn), 3.46 (1H, ddd, J=11.3, 8.7, 2.5 Hz, CH_2OBn), 2.09–1.95 (2H, m), 1.95–1.81 (2H, m), 1.71–1.57 (2H, m), 1.57–1.48 (1H, m), 1.18–1.00 (1H, m), 0.95 (1H, t, J=4.0 Hz, H-cycloprop.), 0.76 (1H, dt, J=10.6, 4.0 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.0 ($C_{quart.}$ arom.), 128.6 (2CH-arom.), 127.9 (CH-arom.), 127.8 (2CH-arom.), 73.5 (CH_2), 70.7 (CH_2), 66.6 ($C_{quart.}$ cycloprop.), 34.4 (CH_2), 30.0 (CH cycloprop.), 28.6 (CH_2), 26.9 (CH_2), 23.9 (CH cycloprop.), 21.6 (CH_2).

*4.3.2. exo-7-(2-(Benzyloxy)ethyl)bicyclo[4.1.0]heptan-1-ol (exo-**6b**).* Yield 80%. Found: C, 77.95; H, 9.02. $C_{16}H_{22}O_2$ requires C, 78.01; H, 9.00%; R_f (25% EtOAc/petroleum ether) 0.52; ν_{max} (CCl_4) 3478, 3090, 3068, 3033, 3006, 2978 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.39–7.27 (5H, m, Ph), 4.57 (1H, d, J=12.0 Hz, CH_2Ph), 4.54 (1H, d, J=12.0 Hz, CH_2Ph), 3.77 (1H, br s, O*H*), 3.58 (1H, dt, J=8.7, 3.7 Hz, CH_2OBn), 3.46 (1H, ddd, J=11.3, 8.7, 2.6 Hz, CH_2OBn), 2.08–1.86 (4H, m), 1.66–1.54 (1H, m), 1.53–1.44 (1H, m), 1.43–1.33 (1H, m), 1.32–1.15 (2H, m), 1.12–0.98 (1H, m), 0.79 (1H, ddd, J=7.5, 5.7, 1.3 Hz, H-cycloprop.), 0.51 (1H, ddd, J=10.0, 5.7, 4.5 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.1 ($C_{quart.}$ arom.), 128.6 (2CH-arom.), 127.9 (3CH-arom.), 73.6 (CH_2), 70.8 (CH_2), 56.5 ($C_{quart.}$ cycloprop.), 33.1 (CH_2), 29.3 (CH_2), 27.9 (CH cycloprop.), 25.8 (CH cycloprop.), 24.5 (CH_2), 21.9 (CH_2), 21.8 (CH_2).

*4.3.3. exo-7-(5-(Benzyloxy)pentyl)bicyclo[4.1.0]heptan-1-ol (exo-**6c**).* Yield 75%. Found: C, 79.07; H, 9.80. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.78%; R_f (25% EtOAc/petroleum ether) 0.63; ν_{max} (liquid film) 3397, 3088, 3064, 3030, 2996 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.22 (5H, m, Ph), 4.51 (2H, s, CH_2Ph), 3.54–3.40 (2H, m, CH_2OBn), 2.12–1.91 (3H, m), 1.90–1.78 (1H, m), 1.73–1.53 (2H, m), 1.53–1.31 (8H, m), 1.29–1.15 (2H, m), 1.13–0.99 (1H, m), 0.66 (1H, ddd, J=7.6, 6.0, 1.3 Hz, H-cycloprop.), 0.39 (1H, dt, J=6.3, 6.0 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.7 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.8 (2CH-arom.), 127.6 (CH-arom.), 73.0 (CH_2), 70.6 (CH_2), 58.1 ($C_{quart.}$ cycloprop.), 32.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.4 (CH cycloprop.), 27.3 (CH_2), 25.9 (CH_2), 24.8 (CH cycloprop.), 24.5 (CH_2), 21.9 (CH_2), 21.6 (CH_2).

*4.3.4. endo-7-(5-(Benzyloxy)pentyl)bicyclo[4.1.0]heptan-1-ol (endo-**6c**).* Yield 16%. Found: C, 79.05; H, 9.81. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.78%; R_f (25% EtOAc/petroleum ether) 0.43; ν_{max} (liquid film) 3384, 3088, 3064, 3029, 3006 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.39–7.22 (5H, m, Ph), 4.51 (2H, s, CH_2Ph), 3.47 (2H, t, J=6.7 Hz, CH_2OBn), 2.19–1.96 (2H, m), 1.96–1.78 (2H, m), 1.72–1.54 (2H, m), 1.54–1.03 (11H, m), 1.11 (1H, ddd, J=10.5, 9.3, 2.2 Hz, H-cycloprop.), 0.94–0.84 (1H, m, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.8 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.8 (2CH-arom.), 127.6 (CH-arom.), 73.1 (CH_2), 70.6 (CH_2), 55.9 ($C_{quart.}$ cycloprop.), 30.0 (CH_2), 29.9 (CH_2), 29.1 (CH_2), 28.7 (CH cycloprop.), 26.3 (CH_2), 23.7 (CH_2), 22.5 (CH_2), 22.2 (CH_2), 21.6 (CH cycloprop.), 19.1 (CH_2).

*4.3.5. exo-9-((R)-2-(Benzyloxy)propyl)bicyclo[6.1.0]nonan-1-ol (exo-**6d**).* Mixture of two diastereomers in a ratio of 1:1. Yield 74%. $[\alpha]_D^{13}$

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−11.5 (*C* 3.0, $CHCl_3$); ν_{max} (CCl_4) 3460, 3095, 3067, 3032 cm^{-1}. Found: C, 79.07; H, 9.81. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.78%.

Diastereomer 1: R_f (20% EtOAc/petroleum ether) 0.67; δ_H (400 MHz, $CDCl_3$) 7.37–7.22 (5H, m, Ph), 4.63 (1H, d, *J*=11.5 Hz, C*H*$_2$Ph), 4.46 (1H, d, *J*=11.5 Hz, C*H*$_2$Ph), 3.63–3.53 (1H, m, C*H*(OBn)Me), 3.27 (1H, br s, O*H*), 2.54–2.18 (1H, m), 2.02–1.85 (2H, m), 1.82–0.88 (10H, m), 1.18 (3H, *J*=6.1 Hz, Me), 0.84–0.69 (1H, m), 0.50–0.41 (1H, m, H-cycloprop.), 0.22 (1H, ddd, *J*=10.1, 5.7, 4.3 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.4 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 128.1 (2CH arom.), 127.8 (CH-arom.), 76.3 (*C*H(OBn)Me), 71.1 (CH_2), 58.7 ($C_{quart.}$ cycloprop.), 36.4 (CH_2), 34.2 (CH_2), 31.2 (CH cycloprop.), 29.2 (CH_2), 28.7 (CH_2), 27.5 (CH cycloprop.), 26.5 (CH_2), 26.3 (CH_2), 25.3 (CH_2), 19.8 (Me).

Diastereomer 2: R_f (20% EtOAc/petroleum ether) 0.58; δ_H (400 MHz, $CDCl_3$) 7.41–7.19 (5H, m, Ph), 4.62 (1H, d, *J*=12.0 Hz, C*H*$_2$Ph), 4.47 (1H, d, *J*=12.0 Hz, C*H*$_2$Ph), 3.72–3.62 (1H, m, C*H*(OBn)Me), 3.21 (1H, br s, O*H*), 2.11–2.03 (1H, m), 2.02–1.87 (2H, m), 1.84–1.11 (10H, m), 1.23 (3H, d, *J*=6.1 Hz, Me), 1.11–0.72 (1H, m), 0.55–0.45 (1H, m, H-cycloprop.), 0.34 (1H, dt, *J*=10.4, 5.2 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 138.7 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.7 (3CH-arom.), 74.6 (*C*H(OBn)Me), 70.5 (CH_2), 58.8 ($C_{quart.}$ cycloprop.), 34.5 (CH_2), 34.2 (CH_2), 31.6 (CH cycloprop.), 29.2 (CH_2), 28.8 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 25.4 (CH_2), 24.8 (CH cycloprop.), 18.1 (Me).

*4.3.6. endo-9-((R)-2-(Benzyloxy)propyl)bicyclo[6.1.0]nonan-1-ol (endo-**6d**).* Mixture of two diastereomers in a ratio of 1:1. Yield 13%. Found: C, 79.08; H, 9.79. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.78%; R_f (20% EtOAc/petroleum ether) 0.41; $[\alpha]_D^{18}$ −7.5 (*C* 2.0, $CHCl_3$); ν_{max} (liquid film) 3400, 3088, 3064, 3030 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.23 (5H, m, Ph), 4.59 (0.5H, d, *J*=11.8 Hz, C*H*$_2$Ph), 4.58 (0.5H, d, *J*=12.0 Hz, C*H*$_2$Ph), 4.49 (0.5H, d, *J*=11.8 Hz, C*H*$_2$Ph), 4.48 (0.5H, d, *J*=12.0 Hz, C*H*$_2$Ph), 3.58–3.47 (1H, m, C*H*(OBn)Me), 2.64 (1H, q, *J*=7.1 Hz), 1.97–1.25 (11H, m), 1.22 (3H, d, *J*=6.1 Hz, Me), 1.10 (2H, t, *J*=7.2 Hz), 1.05–0.94 (1H, m), 0.94–0.73 (2H, m); δ_C (100 MHz, $CDCl_3$) 139.2 (2$C_{quart.}$ arom.), 128.5 (2CH-arom.), 128.4 (2CH-arom.), 127.9 (2CH-arom.), 127.8 (2CH-arom.), 127.6 (CH-arom.), 127.5 (CH-arom.), 75.4 (*C*H(OBn)Me), 75.1 (*C*H(OBn)Me), 70.6 (CH_2), 70.5 (CH_2), 58.6 ($C_{quart.}$ cycloprop.), 58.6 ($C_{quart.}$ cycloprop.), 46.3 (CH_2), 46.3 (CH_2), 31.2 (CH_2), 31.2 (CH_2), 28.9 (CH_2), 28.4 (CH_2), 28.3 (CH_2), 27.9 (2CH cycloprop.), 26.6 (CH_2), 26.2 (CH_2), 26.2 (CH_2), 24.9 (2CH_2), 24.4 (CH cycloprop.), 24.2 (CH cycloprop.), 23.3 (2 CH_2), 19.8 (Me), 19.7 (Me).

4.4. General procedure for the preparation of trimethylsilyl ethers 9

Trimethylchlorosilane (6.27 mL, 49.5 mmol) was added to the cooled (0°C) and stirred solution of cyclopropanol **6** (16.5 mmol) and triethylamine (9.18 mL, 66 mmol) in anhydrous THF (55 mL). The resulted mixture was stirred until the completion of the reaction (TLC-monitoring) and then was treated with water (15 mL). The aqueous layer was separated and extracted with ethyl acetate (2×10 mL). The combined organic phases were washed with brine (5 mL) and dried (Na_2SO_4). Evaporation and chromatography of the residue (1:40 ethyl acetate/*n*-hexane) gave compounds **9a**–**d** as colorless liquids.

*4.4.1. exo-6-(2-(Benzyloxy)ethyl)-1-trimethylsiloxybicyclo[3.1.0]hexane (exo-**9a**).* Yield 80%. Found: C, 70.95; H, 9.29. $C_{18}H_{28}O_2Si$ requires C, 71.00; H, 9.27%; R_f (2.4% EtOAc/petroleum ether) 0.36; ν_{max} (liquid film) 3088, 3064, 3029 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.45–7.23 (5H, m, Ph), 4.56 (1H, d, *J*=12.2 Hz, C*H*$_2$Ph), 4.52 (1H, d, *J*=12.2 Hz, C*H*$_2$Ph), 3.60–3.51 (2H, m, C*H*$_2$OBn), 2.04–1.78 (4H, m), 1.68–1.48 (3H, m), 1.20–1.03 (1H, m), 0.94 (1H, t, *J*=4.0 Hz, H-cycloprop.), 0.77 (1H, ddd, *J*=9.0, 5.7, 4.0 Hz, H-cycloprop.), 0.14 (9H, s, Si*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 139.0 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.7 (2CH-arom.), 127.6 (CH-arom.), 73.0 (CH_2), 70.7 (CH_2), 68.9 ($C_{quart.}$ cycloprop.), 34.5 (CH_2), 29.2 (CH cycloprop.), 28.0 (CH_2), 27.0 (CH_2), 21.7 (CH_2), 21.0 (CH-cycloprop.), 1.2 (Si*Me*$_3$).

*4.4.2. exo-7-(2-(Benzyloxy)ethyl)-1-trimethylsiloxybicyclo[4.1.0]heptane (exo-**9b**).* Yield 92%. Found: C, 71.57; H, 9.51. $C_{19}H_{30}O_2Si$ requires C, 71.64; H, 9.49%; R_f (2.4% EtOAc/petroleum ether) 0.36; ν_{max} (CCl_4) 3089, 3067, 3031, 3006 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.20 (5H, m, Ph), 4.56 (1H, d, *J*=12.2 Hz, C*H*$_2$Ph), 4.52 (1H, d, *J*=12.2 Hz, C*H*$_2$Ph), 3.61–3.50 (2H, m, C*H*$_2$OBn), 2.11–2.02 (1H, m), 2.02–1.92 (1H, m), 1.92–1.79 (2H, m), 1.60–1.50 (1H, m), 1.49–1.38 (2H, m), 1.32–1.17 (2H, m), 1.16–1.01 (1H, m), 0.72 (1H, ddd, *J*=7.4, 6.0, 1.4 Hz, H-cycloprop.), 0.52 (1H, dt, *J*=7.9, 6.0 Hz, H-cycloprop.), 0.14 (9H, s, Si*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 139.0 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.7 (2CH-arom.), 127.5 (CH-arom.), 72.9 (CH_2), 70.7 (CH_2), 59.4 ($C_{quart.}$ cycloprop.), 33.2 (CH_2), 28.6 (CH_2), 25.2 (CH cycloprop.), 25.0 (CH cycloprop.), 24.5 (CH_2), 21.8 (CH_2), 21.7 (CH_2), 1.5 (Si*Me*$_3$).

*4.4.3. exo-7-(5-(Benzyloxy)pentyl)-1-trimethylsiloxybicyclo[4.1.0]heptane (exo-**9c**).* Yield 90%. Found: C, 73.21; H, 10.09. $C_{22}H_{36}O_2Si$ requires C, 73.28; H, 10.06%; R_f (2.4% EtOAc/petroleum ether) 0.36; ν_{max} (liquid film) 3089, 3065, 3030, 3002 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.42–7.23 (5H, m, Ph), 4.51 (2H, s, C*H*$_2$Ph), 3.48 (2H, t, *J*=6.7 Hz, C*H*$_2$OBn), 2.12–1.92 (2H, m), 1.91–1.80 (1H, m), 1.73–1.58 (2H, m), 1.57–1.33 (7H, m), 1.30–1.16 (3H, m), 1.15–1.03 (1H, m), 0.66 (1H, ddd, *J*=7.5, 5.9, 1.4 Hz, H-cycloprop.), 0.37 (1H, dt, *J*=8.1, 5.9 Hz, H-cycloprop.), 0.14 (9H, s, Si*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 138.9 ($C_{quart.}$ arom.), 128.5 (2CH-arom.), 127.7 (2CH-arom.), 127.6 (CH-arom.), 73.0 (CH_2), 70.7 (CH_2), 59.7 ($C_{quart.}$ cycloprop.), 33.3 (CH_2), 29.9 (CH_2), 29.6 (CH_2), 28.2 (CH cycloprop.), 28.0 (CH_2), 26.3 (CH_2), 25.3 (CH cycloprop.), 24.6 (CH_2), 21.9 (CH_2), 21.8 (CH_2), 1.5 (Si*Me*$_3$).

*4.4.4. exo-9-((R)-2-(Benzyloxy)propyl)-1-trimethylsiloxybicyclo[6.1.0]nonane (exo-**9d**).* Mixture of two diastereomers in a ratio of 1:1. Yield 90%. Found: C, 73.23; H, 10.08. $C_{22}H_{36}O_2Si$ requires C, 73.28; H, 10.06%; R_f (2.4% EtOAc/petroleum ether) 0.36; $[\alpha]_D^{13}$ −6.2 (*C* 3.0, $CHCl_3$); ν_{max} (CCl_4) 3090, 3067, 3031 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.40–7.22 (5H, m, Ph), 4.61 (0.5H, d, *J*=11.7 Hz, C*H*$_2$Ph), 4.53 (1H, s, C*H*$_2$Ph), 4.48 (0.5H, d, *J*=11.7 Hz, C*H*$_2$Ph), 3.66–3.54 (1H, m, C*H*(OBn)Me), 2.25–2.12 (1H, m), 2.01–1.85 (1.5H, m), 1.82–1.57 (3.5H, m), 1.57–1.35 (4H, m), 1.25 (3H, t, *J*=6.1 Hz, Me), 1.33–1.03 (3H, m), 0.91–0.69 (1H, m), 0.44–0.28 (1.5H, m, H-cycloprop.), 0.26–0.19 (0.5H, m, H-cycloprop.), 0.17 (4.5H, s, Si*Me*$_3$), 0.16 (4.5H, s, Si*Me*$_3$); δ_C (100 MHz, $CDCl_3$) 139.3 (2$C_{quart.}$ arom.), 128.5 (4CH-arom.), 127.8 (2CH-arom.), 127.7 (2CH-arom.), 127.5 (CH-arom.), 127.5 (CH-arom.), 76.1 (*C*H(OBn)Me), 75.7 (*C*H(OBn)Me), 70.8 (CH_2), 70.4 (CH_2), 63.3 ($C_{quart.}$ cycloprop.), 63.1 ($C_{quart.}$ cycloprop.), 36.7 (CH_2), 35.1 (CH_2), 34.3 (CH_2), 34.2 (CH_2), 30.6 (CH cycloprop.), 30.6 (CH cycloprop.), 28.9 (CH_2), 28.9 (2 CH_2), 28.8 (CH_2), 26.9 (CH cycloprop.), 26.5 (CH_2), 26.5 (CH_2), 26.3 (2 CH_2), 25.9 (CH cycloprop.), 25.8 (CH_2), 25.8 (CH_2), 20.2 (Me), 19.9 (Me), 2.0 (2 Si*Me*$_3$).

4.5. General procedure for the preparation of diols 3

A solution of trimethylsilyl ether **9** (13.2 mmol) in a mixture of THF (200 mL) and water (10 mL) was stirred under a hydrogen atmosphere at room temperature in the presence of 10% palladium on charcoal (0.702 g, 0.660 mmol, 5% mol.) until the completion of the reaction (TLC-monitoring, approximately 1 h). Then the catalyst was filtered off and washed cautiously with ethyl acetate, the filtrate was dried (Na_2SO_4) in the presence of a few drops of triethylamine. Evaporation and chromatography of the residue (from 1:5 to 1:1 ethyl acetate/petroleum ether) gave the title compounds as colorless liquids (**3a**–**c** and one of the diastereomers of **3d**) or a colorless solid (one of the diastereomers of **3d**).

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*4.5.1. exo-6-(2-Hydroxyethyl)bicyclo[3.1.0]hexan-1-ol (exo-**3a**).* Yield 91%. Found: C, 67.49; H, 9.94. $C_8H_{14}O_2$ requires C, 67.57; H, 9.92%; R_f (50% EtOAc/petroleum ether) 0.32; ν_{max} (liquid film) 3305 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.79 (1H, ddd, *J*=10.0, 4.4, 3.5 Hz, CH_2OH), 3.63 (1H, ddd, *J*=10.9, 10.0, 2.9 Hz, CH_2OH), 3.42 (2H, br s, 2 O*H*), 2.13–1.77 (4H, m), 1.72–1.46 (3H, m), 1.18–1.00 (1H, m), 0.95 (1H, t, *J*=4.0 Hz, H-cycloprop.), 0.77 (1H, dt, *J*=10.2, 4.0 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 62.8 (CH_2), 46.1 ($C_{quart.}$ cycloprop.), 34.4 (CH_2), 30.6 (CH_2), 30.1 (CH cycloprop.), 26.9 (CH_2), 23.5 (CH cycloprop.), 21.6 (CH_2).

*4.5.2. exo-7-(2-Hydroxyethyl)bicyclo[4.1.0]heptan-1-ol (exo-**3b**).* Yield 94%. Found: C, 69.13; H, 10.35. $C_9H_{16}O_2$ requires C, 69.19; H, 10.32%; R_f (50% EtOAc/petroleum ether) 0.32; ν_{max} (CCl_4) 3487, 2976 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.90 (1H, br s, O*H*), 3.75 (1H, ddd, *J*=10.0, 4.4, 3.8 Hz, CH_2OH), 3.60 (1H, ddd, *J*=10.8, 10.0, 3.1 Hz, CH_2OH), 2.98 (1H, br s, O*H*), 2.08–1.93 (3H, m), 1.93–1.84 (1H, m), 1.58–1.42 (2H, m), 1.42–1.33 (1H, m), 1.28–1.15 (2H, m), 1.13–0.98 (1H, m), 0.78 (1H, ddd, *J*=7.7, 5.7, 1.7 Hz, H-cycloprop.), 0.50 (1H, ddd, *J*=10.1, 5.7, 4.6 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 62.7 (CH_2), 56.8 ($C_{quart.}$ cycloprop.), 32.9 (CH_2), 31.2 (CH_2), 27.4 (CH cycloprop.), 25.7 (CH cycloprop.), 24.5 (CH_2), 21.9 (CH_2), 21.7 (CH_2).

*4.5.3. exo-7-(5-Hydroxypentyl)bicyclo[4.1.0]heptan-1-ol (exo-**3c**).* Yield 91%. Found: C, 72.60; H, 11.20. $C_{12}H_{22}O_2$ requires C, 72.68; H, 11.18%; R_f (50% EtOAc/petroleum ether) 0.30; ν_{max} (liquid film) 3350 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.71–3.58 (2H, m, CH_2OH), 2.10–2.01 (1H, m), 2.00–1.92 (1H, m), 1.92–1.82 (2H, m), 1.64–1.52 (3H, m), 1.52–1.31 (8H, m), 1.27–1.17 (2H, m), 1.13–1.00 (1H, m), 0.67 (1H, ddd, *J*=7.8, 6.0, 1.7 Hz, H-cycloprop.), 0.41 (1H, dt, *J*=6.4, 6.0 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 63.1 (CH_2), 58.1 ($C_{quart.}$ cycloprop.), 33.0 (CH_2), 32.7 (CH_2), 29.8 (CH_2), 29.3 (CH cycloprop.), 27.5 (CH_2), 25.5 (CH_2), 25.0 (CH cycloprop.), 24.6 (CH_2), 22.0 (CH_2), 21.6 (CH_2).

*4.5.4. exo-9-((R)-2-Hydroxypropyl)bicyclo[6.1.0]nonan-1-ol (exo-**3d**).* mixture of two diastereomers in a ratio of 1:1. Yield 92%. $[\alpha]_D^{18}$ −9.1 (*C* 2.9, $CHCl_3$); Found: C, 72.58; H, 11.21. $C_{12}H_{22}O_2$ requires C, 72.68; H, 11.18%.

Diastereomer 1: colorless solid, mp 73–74°C. R_f (50% EtOAc/petroleum ether) 0.63; ν_{max} (CCl_4) 3488 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.87–3.76 (1H, m, C*H*(OH)Me), 3.52 (1H, br s, O*H*), 2.87 (1H, br s, O*H*), 2.08 (1H, dt, *J*=14.6, 3.5 Hz), 1.96 (1H, dq, *J*=14.3, 3.5 Hz, 1H), 1.89 (1H, ddd, *J*=14.6, 4.4, 2.6 Hz), 1.82–1.55 (3H, m), 1.54–1.08 (7H, m), 1.16 (3H, d, *J*=6.1 Hz, Me), 0.88–0.69 (1H, m), 0.46 (1H, ddd, *J*=12.0, 5.8, 3.3 Hz, H-cycloprop.), 0.22 (1H, ddd, *J*=10.3, 5.8, 4.5 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 68.8 (*C*H(OH)Me), 59.1 ($C_{quart.}$ cycloprop.), 37.6 (CH_2), 34.1 (CH_2), 31.2 (CH cycloprop.), 29.1 (CH_2), 28.6 (CH_2), 27.7 (CH cycloprop.), 26.5 (CH_2), 26.4 (CH_2), 25.3 (CH_2), 24.3 (Me).

Diastereomer 2: colorless liquid. R_f (50% EtOAc/petroleum ether) 0.49; ν_{max} (CCl_4) 3473 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 4.02–3.87 (1H, m, C*H*(OH)Me), 3.40 (1H, br s, O*H*), 2.83 (1H, br s, O*H*), 2.15–2.06 (1H, m), 2.04–1.92 (1H, m), 1.87–1.08 (11H), 1.18 (3H, d, *J*=6.1 Hz, Me), 0.89–0.70 (1H, m), 0.48 (1H, ddd, *J*=11.9, 5.5, 3.5 Hz, H-cycloprop.), 0.27 (1H, dt, *J*=9.4, 5.5 Hz, H-cycloprop.); δ_C (100 MHz, $CDCl_3$) 67.3 (*C*H(OH)Me), 59.0 ($C_{quart.}$ cycloprop.), 35.9 (CH_2), 33.9 (CH_2), 31.3 (CH cycloprop.), 29.1 (CH_2), 28.7 (CH_2), 26.5 (CH_2), 26.3 (CH_2), 25.2 (CH_2), 24.7 (CH cycloprop.), 22.1 (Me).

4.6. General procedure for the preparation of *trans*-alkenolides 5

Phenyliodine(III) bis(trifluoroacetate) $PhI(OCOCF_3)_2$ (2.71 g, 6.30 mmol) was added in one portion to the stirred solution of *exo*-diol **3** (6.00 mmol) in dry dichloromethane (200 mL, 0.03 M solution). After the completion of the reaction (TLC-monitoring, usually within 15 min) the reaction mixture was washed with $NaHCO_3$ solution (2×50 mL, satd aq), brine (2×10 mL) and dried (Na_2SO_4). Evaporation and chromatography of the residue (from pure petroleum ether to 1:20 ethyl acetate/petroleum ether) gave compounds **5a**–**d** as colorless liquids.

*4.6.1. trans-Oxacyclonon-6-ene-2-one (trans-**5a**).* Yield 60% (from *exo*-**3a**). Spectral data are in accordance with those previously reported.[9]

*4.6.2. trans-Oxacyclodec-7-ene-2-one (trans-**5b**).* Yield 74% (from *exo*-**3b**). Spectral data are in accordance with those previously reported.[9]

trans-9-(2,2,2-Trifluoroacetoxy)non-6-enoic acid and *trans*-9-((9-(2,2,2-trifluoroacetoxy)non-6-enoyl)oxy)non-6-enoic acid in a ratio of about 1.25:1 were isolated as minor products. Yield 25% (from *exo*-**3b**). R_f (50% EtOAc/petroleum ether) 0.30; ν_{max} (CCl_4) 3107, 1789, 1737, 1711, 970 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 10.53 (ca. 2H, br s, COOH), 5.65–5.29 (6.5H, m, H-olef.), 4.34 (4.5H, t, *J*=6.7 Hz, CH_2OCOCF_3), 4.06 (2H, t, *J*=6.8 Hz, CH_2OCOCH_2), 2.55–2.25 (13H, m, CH_2), 2.09–1.96 (6.5H, m, CH_2), 1.70–1.54 (6.5H, m, CH_2), 1.47–1.31 (6.5H, m, CH_2).

*4.6.3. trans-Oxacyclotridec-7-en-2-one (trans-**5c**).* Yield 16% (from *exo*-**3c**). Spectral data are in accordance with those previously reported.[33]

*4.6.4. trans-(12R)-Methyloxacyclododec-9-ene-2-one (trans-**5d**, (R)-(+)-recifeiolide).* Yield 76% (from *exo*-**3d**) and 64% ee. R_f (9% EtOAc/petroleum ether) 0.59; $[\alpha]_D^{18}$ +40 (*c* 1.0, $CHCl_3$) 64% ee; lit:[24a] $[\alpha]_D$ +70 (*c* 1.0, $CHCl_3$) 100% ee. δ_H (400 MHz, $CDCl_3$) 5.27 (m, 2H, CH olef.), 5.15 (m, 1H, MeC*H*O), 2.05–2.42 (m, 5H, CH_2), 1.96 (m, 1H, CH_2), 1.80 (m, 1H, CH_2), 1.30–1.57 (m, 5H, CH_2), 1.23 (d, *J*=6.3 Hz, 3H, Me), 1.14 (m, 2H, CH_2); δ_C (100 MHz, $CDCl_3$) 173.5 (CO), 133.6 (CH), 127.1 (CH), 68.6 (CH), 41.1 (CH_2), 33.0 (CH_2), 30.4 (CH_2), 25.0 (CH_2), 24.8 (CH_2), 24.3 (CH_2), 23.3 (CH_2), 20.7 (Me). Spectral data are in accordance with those previously reported.[24e,f]

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14. Stereochemical configuration was confirmed by 1D NOESY experiments. Low values of ^{3}J coupling constants between the cyclopropyl protons (for example, J=4.0 Hz for *exo*-**6a**) were also in agreement with the stereochemical assignment.
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19. The smaller isolated yield of *trans*-**5a**, compared to that of *trans*-**5b**, may have been due to its greater volatility and losses due to evaporation during isolation.
20. The formation of mixed anhydrides in the reaction of TMS-derivatives of cyclopropanols **1** with $PhI(OAc)_2$ in acetic acid was observed by Kirihara et al. (see Ref. 3a).
21. In the case of the oxidative fragmentation of cyclopropanol *exo*-**3b** under the used conditions, the mixture of *trans*-9-(2,2,2-trifluoroacetoxy)non-6-enoic acid and *trans*-9-((9-(2,2,2-trifluoroacetoxy)non-6-enoyl)oxy)non-6-enoic acid was isolated in 25% yield after the completion of the reaction (after approx. 24 h; see Experimental part).
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