Synthesis of 1-substituted cis-bicyclo[3.3.0]octane-3,7-dione derivatives as potential precursors of polyquinanes

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Dedicated to Prof. James Cook on the occasion of his 65th anniversary

Abstract
The synthesis of several 1-substituted cis-bicyclo[3.3.0]octane-3,7-dione derivatives as potential precursors of a triquinacene having a pyramidalized C=C bond from ethyl cis-3,7-dioxobicyclo[3.3.0]octane-1-carboxylate is described.

Keywords: 1-Substituted cis-bicyclo[3.3.0]octane-3,7-diones, polycyclic compounds, cis-dihydroxylation, Swern oxidation, epoxidation, alkylation

Introduction

For several years, we have been working on the generation, trapping and dimerization of highly pyramidalized alkenes containing the skeleton of tricyclo[3.3.0.03,7]oct-1(5)-ene 2.1 These alkenes are very reactive and can not be isolated, but they can be trapped as Diels-Alder adducts with various dienophiles. In the absence of a dienophile, these pyramidalized alkenes usually dimerize in a [2+2] cycloaddition to give cyclobutane dimers 3, which under the standard reaction conditions of their generation (molten sodium in boiling 1,4-dioxane) are transformed into diene dimers 4 (Scheme 1).

R = H, Me
R, R = CH2OCH2, CH2OC(CH3)2OCH2

Scheme 1. Generation and dimerization of pyramidalized bicyclo[3.3.0.03,7]oct-1(5)-ene derivatives 2. (i) Molten Na, 1,4-dioxane, reflux, 3 h. (ii) n-Pentane, hv, 6 h.
Scheme 2. Generation and [2+2+2+2] dimerization of pentacyclo[6.4.0.0^2,10.0^3,7.0^4,9]dodeca-5,8,11-triene (6). (i) Molten Na, 1,4-dioxane, reflux, 3 h.

We were also able to perform [2+2] cross-couplings among different pyramidalized alkenes by simultaneously generating them in the same pot. However, in one case, in which the pyramidalized alkene contained additional, relatively close alkene functionalities, dimerization took place through a [2+2+2+2] process to give a complex polycyclic product 7 (Scheme 2).

This observation led us to envision a similar process in a triquinacene derivative containing a pyramidalized C=C bond that might lead to a dodecahedrane derivative 10 (see Scheme 3).

Scheme 3. Potential [2+2+2+2+2+2] dimerization of a bridged triquinacene containing a pyramidalized C=C bond to dodecahedrane derivative 10. (i) Molten Na, 1,4-dioxane, reflux.
Scheme 4. Retrosynthetic analysis for compound 11 (= 8, X = CH₂OCH₂).

The preparation of the precursor 11 (= 8, X = CH₂OCH₂) was envisaged, as shown in Scheme 4, to be formed from dihydroxydione 12. Substitution of two vicinal bridgehead hydroxyl groups by iodine atoms in related systems has been previously described. Also the conversion of two keto groups into two alkene functions in connection with the preparation of triquinacene derivatives has been described. We envisaged the preparation of dihydroxydione 12 through a double intramolecular condensation from tetraketo 13, a compound which might be prepared from dimethyl acetonedicarboxylate 18 and ethyl 2,3-dioxopropanoate 17 by standard procedures through the shown intermediates and the required protecting group transformations.

Results and Discussion

Compound 17 was prepared as described from oxalic acid monoethyl ester chloride by reaction with diazomethane, followed by oxidation of the formed α-diazoketone with dimethyldioxirane. Reaction of 17 with dimethyl acetonedicarboxylate 18 in water containing sodium bicarbonate gave a mixture of compounds 19 and 20 as previously described. Analytically pure samples of compounds 19 (9%) and 20 (11%) were isolated from the reaction mixture by column chromatography. For the preparation of diketone 22, the reaction mixture obtained from 17 and 18 was directly submitted to hydrolysis and decarboxylation under the Krapcho conditions. Column chromatography of the resulting mixture gave the new diketo ester 22 and a compound that was characterized as ethyl 2-methyl-4-oxocyclopent-2-enecarboxylate 21 (Scheme 5).
Scheme 5. Preparation of intermediates 24 and 25. (i) NaHCO₃, H₂O, r.t., 4 d, 19 (11%), 20 (9%). (ii) NaCl, H₂O, DMSO, 180 °C, 4 h, 22 (36%), 21 (19%). (iii) 2,2-Dimethylpropane-1,3-diol, p-TsOH, toluene, reflux, 2 h, 23 (90%). (iv) LAH, Et₂O, rt, 1.5 h, 24 (98%). (v) TsCl, pyridine, 4 °C, 23 h, 25 (100%).

The keto functions of diketoester 22 were protected with 2,2-dimethylpropane-1,3-diol to give acetal 23 in high yield, which was reduced with lithium aluminum hydride (LAH) to alcohol 24. Tosylation of alcohol 24 gave the corresponding tosylate 25 (Scheme 5).

For the introduction of the (3-cyclopentenyl)methyl group in alcohol 24, (3-cyclopentenyl)-methanol 26 and the corresponding tosylate 27 were prepared as described. Reaction of cis-1,4-dichloro-2-butene with the lithium salt of dimethyl malonate gave dimethyl 3-cyclopentene-1,1-dicarboxylate.⁵ Hydrolysis and decarboxylation of this diester gave 3-cyclopentenecarboxylic acid, which was reduced with LAH to alcohol 26.⁶ Reaction of alcohol 26 with tosyl chloride gave the corresponding tosylate 27.⁷

First, we synthesized ether 28 by reaction of alcohol 24 with tosylate 27. However and to our surprise, the yield of ether 28 was only 19%, tosylate 25 was isolated in 27% yield, and a large
amount of alcohol 24 (38%) was recovered. This means that tosyl transfer between alcohol 24 and tosylate 27 is taking place to a large extent (Scheme 6).

Scheme 6. Preparation of 31. (i) NaH, toluene, reflux, 3.5 h, 28 (19%), 25 (27%), 24 (38% recovered). (ii) NaH, toluene, reflux, 19 h, 28 (44%, from 25), 24 (44%, from 25), 29 (52%, from 26). (iii) K₂OsO₄·2H₂O (0.02 equiv), NMO (1.2 equiv), H₂O/t-BuOH, 0 °C, 15 min, r.t., 4 h, 30. (iv) Oxalyl chloride, DMSO, Et₃N, DCM, 31 (41% from 28).

Then, we carried out the reaction of alcohol 26 and tosylate 25. In this case, ether 28 was obtained from 25 with an improved yield (44%), although tosyl transfer was also observed; alcohol 24 and ether 29 were obtained from 25 (44%) and from 26 (52%), respectively. Dihydroxylation of compound 28 using a catalytic amount of dipotassium osmate and N-methylmorpholine N-oxide (NMO) as the stoichiometric oxidant gave a mixture of stereoisomeric alcohols (1r,2c,4c)- and (1r,2c,4t)-35, which was characterized as such.
Scheme 7. Transformations of 28. (i) MCPBA, DCM, rt, 1 h, 32 (94%). (ii) Ce(NH₄)₂(NO₃)₆, CH₃CN/H₂O, 65 ºC, 5 min, 14 (44%). (iii) 35% HCl, THF, rt, 2 h, 33 (61%). (iv) MCPBA, DCM, rt, 1.5 h, 34 (63%). (v) LiHMDS (2.4 equiv), toluene, −68 ºC to rt, 24 h; or LiHMDS (2.4 equiv), toluene, Sc(OTf)₃ (1.2 equiv), −68 ºC to rt, 24 h; or LiHMDS (2.4 equiv), THF, BF₃·Et₂O (1.2 equiv), −78 ºC to rt, 24 h.

Swern oxidation of this mixture gave the expected product 31, which exists essentially in the enol form, as evidenced by the comparison of significant ¹³C NMR signals of the 2-hydroxycyclopent-2-en-1-one moiety of 31 (δ₁-C 203.0, δ₂-C 153.2, δ₃-C 130.5) with the corresponding signals of a model compound, 4-(n-hexyl)-2-hydroxycyclopent-2-en-1-one (δ₁-C 203.3, δ₂-C 152.0, δ₃-C 133.3). Attempts to convert enol 31 into dihydroxydione 12 (hydrolysis and two intramolecular aldol condensations) or into the corresponding acetal with p-TsOH in acetone gave a mixture, in which 31 had disappeared but the expected products were not detected.
Noteworthy, dihydroxydione 12 is by far the most stable among 12 possible stereoisomers derived from enol 31 by hydrolysis and double intramolecular aldol condensation, as established by theoretical methods (MM3, AM1, and PM3). However, among the 16 stereoisomers of hydrolysis and monocondensation products derived from enol 31, the precursor of dihydroxydione 12 and several other stereoisomers showed similar stabilities according to the above theoretical methods.

In view of this result and having ether 28 in hand, we attempted an alternative approach to the skeleton of compound 12 in a stepwise way (Scheme 7). To this end, ether 28 was epoxidized with m-chloroperoxybenzoic acid (MCPBA) to give a mixture of stereoisomeric epoxides 32 in a ratio close to 1:3 (1H NMR). Attempts to hydrolyze this mixture under various acidic conditions (MsOH, H2SO4, p-TsOH) gave complex product mixtures with not only the acetal functions hydrolyzed but also the epoxide reacted. When the hydrolysis was carried out with 35% HCl in THF, a stereoisomeric mixture of chlorohydrins 33 was obtained. In order to obtain epoxide 34, we first carried out the hydrolysis of the acetal functions of compound 28 by reaction with Ce(IV) ammonium nitrate. Under these conditions, diketone 14 was obtained in 44% yield. Epoxidation of diketone 14 with MCPBA gave a mixture of stereoisomeric epoxides 34 in 63% yield. However, all attempts to transform this compound into the tricyclic derivative 35 on reaction with an excess of lithium hexamethyldisilazide (LiHMDS) in toluene or THF, in the presence of Sc(III) triflate or boron trifluoride etherate were fruitless, always leading to complex mixtures of unidentified products.

Conclusions

In conclusion we have prepared a series of 1-substituted cis-bicyclo[3.3.0]octane-3,7-dione derivatives as potential precursors of a triquinacene having a pyramidalized C=C bond. In spite of very favorable expectations based on different theoretical calculations, the double aldol condensation of compound 31 that should provide the tetracyclic dihydroxydione 12 failed to give any defined product. Also, the intramolecular condensation of diketoepoxide 34 to diketoalcohol 35 failed to give any defined product. Work is in progress to prepare a derivative of general structure through other synthetic approaches.

Experimental Section

General. Melting points were determined with a MFB 595010 M Gallenkamp melting point apparatus. 1H NMR spectra were recorded on Varian-Gemini 200 (200 MHz), Varian Gemini-300 (300 MHz), Varian Mercury-400 (400 MHz), or Varian VXR-500 (500 MHz) spectrometers. 13C NMR spectra were recorded on Varian Gemini-200 (50.3 MHz) and Varian Gemini-300 (75.4 MHz) spectrometers. The 1H/1H homocorrelation spectra (COSY and NOESY) and the one
bond and long range $^1$H/$^{13}$C heterocorrelation spectra (gHSQC and gHMBC, respectively) were performed on a Varian VXR-500 spectrometer. Chemical shifts are given in δ scale and the coupling constants in Hz. IR spectra were registered on a FTIR Perkin–Elmer model 1600 or a Perkin–Elmer Spectrum RX1 spectrometer. MS and GC/MS analyses were carried out on a Hewlett-Packard HP-5988A spectrometer, the sample being introduced directly or through a gas chromatograph (Hewlett-Packard model 5890 Series II) using a 30-m column (HP-45, 5% diphenyl-95% dimethylpolysiloxane), conditions: 10 psi, initial temperature 100 °C (2 min), then heating at a rate of 10 °C/min up to 250 °C, then isothermic. The electron impact (EI, 70 eV) or chemical ionization (CI, CH$_4$) techniques were used. Where not indicated, the electron impact ionization technique was used. Only significant ions are given: those with higher relative ratio, except for the ions with higher m/z values. High resolution MS spectra were performed in an Autospec Micromass spectrometer at the University of Santiago de Compostela. The elemental analyses were determined in a Carlo Erba model 1106 equipment at the IIQAB (CSIC) of Barcelona, Spain. For the column chromatography, silica gel 60 AC (35–70 µM, SDS, ref. 2000027 or 70–200 µM, SDS, ref. 2100027) or neutral aluminium oxide (Macherey-Nagel) were used. Except where otherwise indicated, 35–70 µM silica gel was used. Thin-layer chromatography (TLC) was performed on aluminium-backed sheets with silica gel 60 F$_{254}$ (Merck, ref. 1.05554) and spots were visualized with UV light, a 1% aqueous solution of KMnO$_4$ or by placing the sheets in an iodine atmosphere.

**Ethyl cis-3,7-dioxobicyclo[3.3.0]octane-1-carboxylate (22) and ethyl 2-methyl-4-oxocyclopent-2-enecarboxylate (21).** To a solution of NaHCO$_3$ (6.41 g, 76.3 mmol) in water (460 mL), dimethyl acetone-1,3-dicarboxylate 18 (23.9 g, 137 mmol) and ethyl 2,3-dioxopropanoate (17; 10.2 g, 69 mmol) were added; the mixture was vigorously stirred at room temperature for 4 d. The mixture was acidified to pH 1 with 6N HCl and then extracted with DCM (3×275 mL). The organic extracts were combined, dried (anhydrous Na$_2$SO$_4$), and concentrated in vacuo to give a residue (30.8 g). Part of this residue (4.9 g) was subjected to column chromatography (silica gel, 100 g; hexane/EtOAc 85:15); 20 (0.46 g, 9%) and 19 (0.48 g, 11%) were eluted in this order. The $^1$H and $^{13}$C NMR data of compounds 19 and 20 matched those previously described.$^5$ The rest of the above residue (25.9 g) was taken up in DMSO (47 mL); water (12 mL) and finely ground NaCl (3.5 g) were added, the mixture was heated to 180 °C for 4 h, then allowed to cool to room temperature and concentrated in vacuo. The residue (18.9 g) was subjected to column chromatography (silica gel, 190 g; hexane/EtOAc 9:1); 21 (1.9 g, 19%) and 22 (4.3 g, 36%) were eluted in this order. Analytical samples were obtained as colorless oils by distillation in a rotary microdistillation equipment at 130 °C/0.1 Torr and 150 °C/0.1 Torr, respectively.

**Compound 21.** IR (NaCl): ν 2982, 2932, 1625, 1436, 1369, 1327, 1257, 1230, 1185, 1031, 857 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): δ 1.27 (t, $J = 7.5$ Hz, 3H, OCH$_2$CH$_3$), 2.14 (s, 3H, 2-CH$_3$), 2.60 (dd, $J = 18.5$ Hz, $J' = 7.0$ Hz, 1H, 5-H$_{trans}$), 2.68 (dd, $J = 18.5$ Hz, $J' = 2.5$ Hz, 1H, 5-H$_{cis}$), 3.63 (dm, $J = 7.0$ Hz, 1H, 1-H), 4.19 (m, 2H, OCH$_2$CH$_3$), 6.00 (s, 1H, 3-H). $^{13}$C
NMR (50.3 MHz, CDCl₃): δ 14.2 (OCH₃CH₂), 18.0 (2-CH₃), 39.3 (5-C), 49.9 (1-C), 61.5 (OCH₂CH₃), 132.1 (3-C), 171.2, 173.6 (COOEt, 2-C), 206.8 (4-C). GC/MS (tᵣ = 12.6 min): m/z (%) 168 (M⁺, 38), 123 (15), 122 (54), 96 (43), 95 (95), 94 (51), 67 (100). Anal. calcd. for C₃H₁₂O₂·0.2H₂O: C, 62.92; H, 7.28. Found: C, 62.83; H, 7.09.

**Compound 22.** IR (NaCl): ν 2981, 2926, 1744, 1405, 1319, 1289, 1253, 1228, 1178, 1163, 1105, 1059, 1022 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 1.29 (t, J = 7.0 Hz, 3H, OCH₂CH₃), 2.19 [ddd, J = 19.0 Hz, J' = 5.5 Hz, J" = 1.0 Hz, 2H, 4(6)-Hendo], 2.37 [ddd, J = 19.0 Hz, J' = 1.0 Hz, 2H, 2(8)-Hendo], 2.79 [ddd, J = 19.0 Hz, J' = 9.0 Hz, J" = 1.5 Hz, 2H, 4(6)-Hexo], 3.05 [dd, J = 19.0 Hz, J' = 1.5 Hz, 2H, 2(8)-Hexo], 3.19 (tt, J = 9.0 Hz, J' = 5.5 Hz, 1H, 5-H), 4.21 (q, J = 7.0 Hz, 2H, OCH₂CH₃). ¹³C NMR (75.4 MHz, CDCl₃): δ 14.1 (OCH₂CH₃), 40.9 (5-C), 43.7 [4(6)-C], 46.4 [2(8)-C], 52.6 (1-C), 62.0 (OCH₂CH₃), 174.2 (COOEt), 214.5 [3(7)-C]. GC/MS (tᵣ = 16.4 min): m/z (%) 210 (M⁺, 17), 164 (14), 141 (72), 137 (23), 136 (16), 113 (100), 85 (44). Anal. calcd. for C₁₁H₄O₂·0.1H₂O: C, 62.31; H, 6.75. Found: C, 62.23; H, 6.74.

**Ethyl 3,3:7,7-bis(2,2-dimethyl-1,3-propylenedioxy)-cis-bicyclo[3.3.0]octane-1-carboxylate (23).** A mixture of diketone 22 (2.31 g, 11.0 mmol), 2,2-dimethyl-1,3-propanediol (4.44 g, 42.6 mmol) and p-TsOH·H₂O (72 mg) in toluene (100 mL) was heated under reflux for 2 h with continuous removal of the formed water using a Dean-Stark equipment. The cold solution was washed with water (3×40 mL), dried (anhydrous Na₂SO₄) and concentrated in vacuo to give acetal 23 as a white solid (3.79 g, 90%). White crystals (from Et₂O); mp 87.4 °C. IR (KBr): ν 2979, 2951, 2867, 1717, 1473, 1364, 1323, 1304, 1132, 1111, 1043 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 0.89 (s, 6H, 2 syn-CH₃), 1.01 (s, 6H, 2 anti-CH₃), 1.25 (t, J = 7.0 Hz, 3H, OCH₂CH₃), 1.99 [ddd, J = 13.0 Hz, J' = 6.0 Hz, J" = 1.0 Hz, 2H, 4(6)-Hendo], 2.02 [ddd, J = 13.5 Hz, J' = 1.0 Hz, 2H, 2(8)-Hendo], 2.10 [ddd, J = 13.0 Hz, J' = 9.0 Hz, J" = 1.5 Hz, 2H, 4(6)-Hexo], 2.64 [ddd, J = 13.5 Hz, J' = 1.5 Hz, 2H, 2(8)-Hexo], 3.02 (tt, J = 9.0 Hz, J' = 6.0 Hz, 1H, 5-H), 3.39 (ddd, J = 11.0 Hz, J' = 1.0 Hz, 2H, 2 CHexo,anti dioxane substructure), 3.46 (dd, J = 11.0 Hz, J' = 1.0 Hz, 2H, 2 CHendo,anti dioxane substructure), 3.49 (d, J = 11.5 Hz, 2H, 2 CHendo,syn dioxane substructure), 3.51 (dd, J = 11.5 Hz, 2H, 2 CHexo,syn dioxane substructure), 4.14 (q, J = 7.0 Hz, 2H, OCH₂CH₃). ¹³C NMR (75.4 MHz, CDCl₃): δ 14.1 (CH₃, OCH₂CH₃), 22.4 (CH₃, syn-CH₃), 22.6 (CH₃, anti-CH₃), 30.0 [C, 2 CH₂(CH₃)₂], 40.6 [CH₂, 4(6)-C], 40.7 (CH, 5-C), 42.0 [CH₂, 2(8)-C], 55.0 (C, 1-C), 60.7 (CH₂, OCH₂CH₃), 71.9 (CH₂, exo-CH₂ dioxane substructure), 72.1 (CH₂, endo-CH₂ dioxane substructure), 108.5 [C, 3(7)-C], 176.9 (C, COOEt). GC/MS (tᵣ = 23.7 min): m/z (%) 382 (M⁺, 14), 309 (59), 227 (64), 155 (27), 141 (28), 113 (28), 69 (100). Anal. calcd. for C₂₁H₃₅O₃: C, 65.94; H, 8.96. Found: C, 66.07; H, 9.02.

**[3,3:7,7-Bis(2,2-dimethyl-1,3-propylenedioxy)-cis-bicyclo[3.3.0]oct-1-yl]methanol (24).** To a suspension of LAH (0.36 g, 9.5 mmol) in anhydrous Et₂O (12 mL), a solution of acetal 23 (1.18 g, 3.1 mmol) in anhydrous Et₂O (40 mL) was added and the mixture was stirred at room temperature for 1.5 h. Water (3 mL) was slowly added and the formed suspension was filtered. Concentration of the filtrate in vacuo gave alcohol 24 (1.03 g, 98%) as white solid. White crystals (from Et₂O); mp 109.5–110.8 °C. IR (KBr): ν 3495, 2961, 2932, 2858, 1474, 1323, 1308, 1145, 1108, 1084, 1073, 1042, 1011 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 0.95 (s, 6H),
0.97 (s, 6H) [2 C(CH$_3$)$_3$], 1.93 [ddd, $J$ = 13.0 Hz, $J'$ = 6.5 Hz, $J''$ = 1.0 Hz, 2H, 4(6)-H$_{endo}$], 2.01 (dd, $J$ = 13.5 Hz, $J'$ = 1.0 Hz, 2H) and 2.05 [dd, $J$ = 13.5 Hz, $J'$ = 1.0 Hz, 2H] [2(8)-H$_{endo}$ and 2(8)-H$_{exo}$], 2.22 [ddd, $J$ = 13.5 Hz, $J'$ = 8.5 Hz, $J''$ = 1.0 Hz, 2H, 4(6)-H$_{exo}$], 2.40 (tt, $J$ = 8.5 Hz, $J'$ = 6.5 Hz, 1H, 5-H), 2.89 (broad s, 1H, OH), 3.44–3.50 (complex signal, 10H, 4 CH$_2$ of 2
dioxane substructures plus CH$_2$OH). $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ 22.4 (CH$_3$) and 22.5 (CH$_3$
[2 C(CH$_3$)$_3$], 30.0 [C, 2 C(CH$_3$)], 39.5 [CH$_2$, 4(6)-C], 39.8 (CH, 5-C), 44.5 [CH$_2$, 2(8)-C], 50.4
(C, 1-C), 70.4 (CH$_2$, CH$_2$OH), 71.7 (CH$_2$ and 72.1 (CH$_2$) (2H 2 dioxane substructures), 109.1
[C, 3(7)-C]. GC/MS ($t_R$ = 23.5 min): m/z (%) 340 (M$^+$, 5), 309 (17), 155 (23), 128 (26), 99 (18),
69 (100). Anal. calcd. for C$_{10}$H$_{12}$O$_2$: C, 67.03; H, 9.47. Found: C, 66.93; H, 9.48.

[3,3:7,7-Bis(2,2-dimethyl-1,3-propyldenedioxy)-cis-bicyclo[3.3.0]oct-1-yl)methyl tosylate (25). To a cold (0
°C) solution of alcohol 24 (1.00 g, 2.9 mmol) in pyridine (3.5 mL), tosyl chloride (0.71 g, 3.7 mmol) was added in portions for 15 min. The mixture was stirred at 0 °C for
1.5 h and then it was kept at 4 °C for 21 h. The mixture was poured on to a mixture of ice (15 g)
and 0.94 (s, 6H) [2 C(CH$_3$)$_3$], 1.82 [complex signal, 4H, cis-2(8)-H and 2(8)-H$_{endo}$], 1.98 - 2.12
[complex signal, 5H, 2(8)-H$_{exo}$, 4(6)-H$_{exo}$ and 5-H], 2.42 (s, 3H, Ar-CH$_3$), 3.26 (s, 4H, 2 CH$_2$
and 3.38 (s, 4H, 2 CH$_2$) (4 CH$_2$ of 2 dioxane substructures), 3.85 (s, 2H, CH$_2$OTs), 7.32 [d, $J$ =
8.5 Hz, 2H, Ar-3(5)-H], 7.77 [d, $J$ = 8.5 Hz, 2H, Ar-2(6)-H]. $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ
21.6 (CH$_3$, Ar-CH$_3$), 22.4 (CH$_3$) and 22.6 (CH$_3$) [2 C(CH$_3$)$_3$], 30.0 [C, 2 C(CH$_3$)], 39.5 (CH, 5-
C), 40.6 (CH$_2$) and 41.5 (CH$_2$) [2(8)-C and 4(6)-C], 48.9 (C, 1-C), 71.4 (CH$_2$) and 72.2 (CH$_2$
(2×2 CH$_2$ of 2 dioxane substructures), 77.2 (CH$_2$, CH$_2$OTs), 108.7 [C, 3(7)-C], 128.0 [CH, Ar
2(6)-C], 129.8 [CH, Ar 3(5)-C], 132.9 (C, Ar 1-C), 144.6 (C, Ar 4-C). GC/MS ($t_R$ = 21.4 min):
m/z (%) 324 (20), 323 [(M–TsO)$^+$, 100], 322 (20), 321 (39), 237 (45), 151 (57). Anal. calcd. for
C$_{26}$H$_{38}$O$_5$: C, 63.13; H, 7.74, S, 6.48. Found: C, 63.28; H, 7.74, 6.40.

1-[(Cyclopent-3-enyl)methoxymethyl]-3,3:7,7-bis-(2,2-dimethyl-1,3-propyldenedioxy)-cis-
bicyclo[3.3.0]octane (28). Procedure 1. To a magnetically stirred suspension of NaH (12 mg,
60% content, 0.28 mmol) in anhydrous toluene (0.5 mL) under an argon atmosphere, a solution of
alcohol 24 (85 mg, 0.25 mmol) in the same solvent (0.5 mL) was added and the mixture was
stirred until no more hydrogen was evolved. Then, a solution of tosylate 27 (76 mg, 0.30 mmol)
in anhydrous toluene (0.5 mL) was added dropwise and the mixture was heated under reflux for
3.5 h, following the evolution of the reaction by TLC. The mixture was allowed to cool to room
temperature, was washed with water (3×2 mL). The organic phase was dried (anhydrous
Na$_2$SO$_4$) and concentrated in vacuo to give a residue (123 mg) that was subjected to column
chromatography (neutral aluminum oxide, 6 g; hexane). In order of elution, ether 28 (20 mg,
19%), tosylate 25 (33 mg, 27%) and starting alcohol 24 (32 mg, 38% recovery) were isolated.
28: White crystals (sublimed); mp 74.8–76.6 °C. IR (NaCl): ν 3054, 2952, 2931, 2852, 1472,
1362, 1324, 1309, 1110, 1042 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): δ 0.88 (s, 6H) and 0.97 (s, 6H)
[2 C(CH$_3$)$_2$], 1.86 [dd, $J = 13.5$ Hz, $J' = 1.0$ Hz, 2H, 2(8)-H$_{endo}$], 1.91 [ddd, $J = 13.0$ Hz, $J' = 7.0$ Hz, $J'' = 1.0$ Hz, 2H, 4(6)-H$_{endo}$], 2.05 [ddd, $J = 13.0$ Hz, $J' = 9.0$ Hz, $J'' = 1.0$ Hz, 2H, 4(6)-H$_{exo}$], 2.08 [m, 2H, 2'(5')-H$_{cis}$], 2.15 [m, 1H, 5-H], 2.20 [dd, $J = 13.5$ Hz, $J' = 1.5$ Hz, 2H, 2(8)-H$_{exo}$], 2.42 [m, 2H, 2'(5')-H$_{trans}$], 2.55 (m, 1H, 1'-H), 3.22 (s, 2H, C1-CH$_2$O), 3.28 (d, $J = 7.5$ Hz, 2H, C1'-CH$_2$O), 3.39–3.47 (m, 8H, 4 CH$_2$ of 2 dioxane substructures), 5.62 [s, 2H, 3'(4')-H].

$^{13}$C NMR (75.4 MHz, CDCl$_3$): δ 22.5 (CH$_3$) and 22.7 (CH$_3$) [2 C(CH$_3$)$_2$], 30.0 [C, 2 C(CH$_3$)], 35.9 [CH$_2$, 2'(5')-C], 36.5 (CH, 1'-C), 40.3 (CH, 5-C), 40.4 [CH$_2$, 4(6)-C], 42.5 [CH$_2$, 2(8)-C], 49.9 (C, 1-C), 71.7 (CH$_2$) and 72.1 (CH$_2$) (2×2 CH$_2$ of 2 dioxane substructures), 75.5 (CH$_2$, 1'-C-CH$_2$O), 78.1 (CH$_2$, 1-C-CH$_2$O), 109.4 [C, 3(7)-C], 129.5 [CH, 3'(4')-C]. GC/MS ($t_R = 28.9$ min):

$m/z$ (%) 420 (M$^+$, 9), 341 (13), 309 [(M-C$_3$H$_7$CH$_2$OCH$_3$)$^+$, 94], 128 (26), 81 (54), 79 (32), 69 (100). Anal. calcld. for C$_{25}$H$_{40}$O$_5$: C, 71.39; H, 9.59. Found: C, 71.84; H, 9.55.

**Procedure 2.** To a magnetically stirred suspension of NaH (127 mg, 55% content, 2.9 mmol) in anhydrous toluene (1 mL) under an argon atmosphere, a solution of alcohol 26 (228 mg, 2.3 mmol) in anhydrous toluene (1 mL) was added and the mixture was stirred until no more hydrogen was evolved. Then, a solution of tosylate 25 (960 mg, 1.93 mmol) in anhydrous toluene (2 mL) was added dropwise and the mixture was heated under reflux for 19 h, following the evolution of the reaction by TLC. The mixture was allowed to cool to room temperature and was washed with water (2×10 mL). The organic phase was dried (anhydrous Na$_2$SO$_4$) and concentrated in vacuo to give a residue (857 mg) that was subjected to column chromatography (neutral aluminum oxide, 35 g; hexane/EtOAc mixtures). Ether 29 (106 mg, 52% from 26) was eluted with hexane, the expected ether 28 (355 mg, 44% from 25) was eluted with hexane/EtOAc 95:5 and alcohol 24 (287 mg, 44% from 25) was eluted with EtOAc.

**Compound 29.** Oil, bp 120 °C / 1 Torr. IR (NaCl): ν 2923, 2853, 1459, 1376, 1116 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.04–2.15 (m, 4H) and 2.42–2.64 (complex signal, 6H) [2(5)-H$_2$ and 1-H], 3.32 (d, $J = 6.9$ Hz, 4H, CH$_2$O), 5.65 [m, 4H, 3(4)-H]. $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ 36.0 [CH$_2$, 2(5)-C], 36.6 (CH, 1-C), 75.3 (CH$_2$, CH$_2$O), 129.5 [CH, 3(4)-C]. GC/MS ($t_R = 12.3$ min, CI):


**Mixture of (1r,2c,4t)- and (1r,2c,4c)-4-{[3,3:7,7-bis-(2,2-dimethyl-1,3-propylienedioxy)-cisis-bicyclo[3.3.0]oct-1-yl]methoxymethyl}cyclopentane-1,2-diol (30).** To a cold (0 °C) suspension of K$_2$OsO$_4$·2H$_2$O (7.6 mg, 0.02 mmol) and N-methylmorpholine N-oxide (NMO, 161 mg, 1.37 mmol) in a mixture of water/t-BuOH 1:1 (1.3 mL), a solution of ether 28 (474 mg, 1.13 mmol) in acetone (3 mL) was added dropwise and the mixture was magnetically stirred for 15 min at 0 °C and then for 4 h at room temperature. The mixture was concentrated in vacuo and the residue (553 mg), containing mainly one stereoisomeric diol, was used as such in the next step. An analytical sample of diol 30 was obtained by taking the product in DCM, filtering the solution through a 0.45 µm polytetrafluoroethylene (PTFE) filter and concentrating the filtrate in vacuo. IR (NaCl): ν 3435, 2952, 2932, 2855, 1473, 1395, 1362, 1323, 1308, 1107 cm$^{-1}$. $^1$H NMR (300 MHz, CDCl$_3$) (data of the main diastereomer of 30): δ 0.92 (s, 6H) and 0.98 (s, 6H) [2 C(CH$_3$)$_2$], 1.50–2.60 [complex signal, 14H, 2'(8')-H$_2$, 4'(6')-H$_2$, 5'-H, 3(5)-H$_2$ and 4-H], 3.23 (s, 2H, C1'-
CH₂O), 3.27 (d, J = 6.0 Hz, C4-CH₂O), 3.34–3.50 (complex signal, 10H, CH₂ from 2 dioxane substructures and 1(2)-H, 4.13 (broad t, J = 4.2 Hz, 2H, 2 OH). ¹³C NMR (75.4 MHz, CDCl₃): (data of the main diastereomer of 30): δ 22.4 (CH₃) and 22.5 (CH₃) [2 C(CH₃₂), 34.4 (CH, 4-C), 34.5 (CH₂) and 39.9 (CH₂) [2'(8')-C and 4'(6')-C], 40.3 (CH, 5'-C), 42.7 [CH₂, 3(5)-C], 49.6 (C, 1'-C), 71.6 (CH₂) and 71.9 (CH₂) [1'-C-CH₂O and 4-C-CH₂O], 73.7 [CH, 1(2)-C], 75.2 (CH₂) and 78.0 (CH₂) (4 CH₂ of 2 dioxane substructures), 109.2 [C, 3'(7')-C]. GC/MS (tR = 25.8 min): m/z (%) 454 (M⁺, 16), 351 (18), 309 [(M−(C₅H₇O₂)CH₂OCH₂)⁺, 100], 267 (19), 223 (20), 128 (19), 69 (56). HRMS: calcd. for [C₂₅H₄₂O₇⁺H]⁺: 455.3009. Found: 455.3007.

4-[[3,3:7,7-Bis(2,2-dimethyl-1,3-propylenedioxy)-cis-bicyclo[3.3.0]oct-1-yl)methoxymethyl]-2-hydroxycyclopent-2-en-1-one (31). To a magnetically stirred cold (−70 °C, acetone/CO₂ bath) solution of oxalyl chloride (270 µL, 3.1 mmol) in DCM (7 mL) under an argon atmosphere, a solution of anhydrous DMSO (470 µL, 6.6 mmol) in DCM (1.5 mL) was added. The mixture was stirred for 30 min and then a solution of diol 30 (451 mg, 1.0 mmol) in DCM (2 mL) was added dropwise keeping the temperature below −65 °C. The mixture was stirred for 2 h at −65 °C, then anhydrous Et₃N (1.5 mL) was added and stirring was continued for 1.5 h at this temperature. The reaction mixture was allowed to warm to room temperature, was acidified with cold 1N HCl (20 mL) and was diluted with DCM (20 mL). The organic phase was separated and the aqueous phase was extracted with DCM (20 mL). The organic phase and extracts were combined, washed with brine (2×20 mL), dried (anhydrous Na₂SO₄) and concentrated in vacuo to give a residue (364 mg) that was subjected to column chromatography (silica gel, 70–200 µm; hexane/EtOAc mixtures). Upon elution with hexane/EtOAc 8:2, slightly impure enol 31 (182 mg, 41%) was isolated as an oil. IR (NaCl): ν 3448, 2953, 2924, 2859, 1736, 1400, 1267, 1111, 1080, 1045 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 0.93 (s, 6H), 0.97 (s, 6H) [2 C(CH₃₂), 1.8–2.2 [complex signal, 12H, 2'(8')-H₂, 4'(6')-H₂, 5'-H, 4-H and 5-H₂], 3.27 (s, 2H) and 3.45 (s, 10H) (4 CH₂ of 2 dioxane substructures, C1'-CH₂O and C4-CH₂O), 6.50 (d, J = 3.5 Hz, 1H, 3-H). ¹³C NMR (50.3 MHz, CDCl₃): δ 22.5 (CH₃) and 22.6 (CH₃) [2 C(CH₃₂), 30.0 [2 C(CH₃₂), 35.1 (CH, 5'-C), 36.4 [CH₂, 4'(6')-C], 39.9 [CH₂, 2'(8')-C], 40.4 (CH, 4-C), 42.8 (CH₂, 5-C), 49.6 (C, 1'-C), 71.7 (CH₂) and 72.0 (CH₂) (4 CH₂ of 2 dioxane substructures), 74.2 (CH₂, 4-C-CH₂O), 78.4 (CH₂, 1'-C-CH₂O), 109.2 [C, 3'(7')-C], 130.5 (CH, 3-C), 153.2 (C, 2-C), 203.1 (C, 1-C).

Attempted conversion of (31) into (12)
To a solution of enol 31 (45 mg, 0.1 mmol) in acetone (1.4 mL), p-TsOH·H₂O (5 mg) was added and the mixture was magnetically stirred at room temperature for 24 h. The solution was concentrated in vacuo, water (5 mL) and EtOAc were added, the organic phase was separated and the aqueous one was extracted with EtOAc (2×2 mL). The combined organic phases were dried (anhydrous Na₂SO₄) and concentrated in vacuo to give and oily residue in which no defined product could be detected (¹H NMR).
Mixture of 3,3:7,7-bis(2,2-dimethyl-1,3-propylidenedioxy)-1-[(trans-3,4-epoxycyclopentyl) methoxymethyl]-cis-bicyclo[3.3.0]octane (trans-32) and its stereoisomer (cis-32). To a magnetically stirred solution of ether 28 (420 mg, 1.0 mmol) in DCM (10 mL) at room temperature, MCPBA (449 mg, 77% content, 2.0 mmol) was added portionwise in 5 min and stirring was continued for 1 h. The organic solution was washed with saturated aqueous NaHCO₃ solution (3×10 mL), was dried (anhydrous Na₂SO₄) and concentrated in vacuo to give an oily residue of the mixture of epoxides 32 (412 mg, 94%) in a ratio close to 1:3 (H and C NMR). IR (NaCl): ν 2951, 2857, 1473, 1395, 1362, 1308, 1108, 838 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) (data of the main diastereomer of 32): δ 0.91 (s, 6H) and 0.92 (s, 6H) [2 CH₃], 1.83–2.22 [complex signal, 14H, 2(8)-H, 4(6)-H, 5-H, 1’-H and 2’(5’)-H2], 3.21 (s, 2H, C1-CH₂O), 3.34 (broad d, J = 4.5 Hz, 2H, C1-CH₂O), 3.45 (broad s, 10H, 3'(4’)-H and 4 CH₃ of 2 dioxane substructures). ¹³C NMR (75.4 MHz, CDCl₃) (data of the main diastereomer of 32): δ 22.5 (CH₃) and 22.6 (CH₃) [2 C(CH₃)₂], 30.0 [C, 2 C(CH₃)₂], 31.1 [CH₂, 2(5’)-C], 33.1 (CH, 1’-C), 40.1 [CH₂, 4(6)-C], 40.4 (CH, 5-C), 42.8 [CH₂, 2(8)-C], 49.7 (C, 1-C 57.0 [CH, 3’(4’)-C], 71.7 (CH₂) and 72.0 (CH₂) (4 CH₂ of 2 dioxane substructures), 73.4 (1’-C-CH₂O), 78.2 (1-C-CH₂O), 109.3 [C, 3(7)-C]. GC/MS (tᵣ = 28.7 min): m/z (%) 436 (M⁺, 2), 309 ([M-(C₃H₇O)CH₂OCH₃]⁺, 22), 128 (33), 69 (100). HRMS (ESI-TOF): calced. for [C₂₃H₄₀O₆]+: 437.2898. Found: 437.2895.

Mixture of (1r,3c,4t)- and (1r,3t,4c)-1-[(3-chloro-4-hydroxycyclopentyl)methoxymethyl]-cis-bicyclo[3.3.0]octane-3,7-dione (33). To a solution of the stereoisomeric mixture of epoxides 32 (77 mg, 0.18 mmol) in THF (5 mL), 35% HCl (50 µL) was added and the mixture was stirred for 2 h at room temperature. After diluting with water (5 mL), the mixture was extracted with EtOAc (3×10 mL). The combined organic extracts were washed with saturated aqueous NaHCO₃ solution (2×5 mL) and brine (2×5 mL), dried (anhydrous Na₂SO₄) and concentrated in vacuo to give an oily residue (67 mg) that was subjected to column chromatography (silica gel, 7 g; hexane/EtOAc mixtures). Upon elution with hexane/EtOAc 2:3 a slightly impure stereoisomeric mixture of chlorohydrins 33 was isolated (51 mg, 61%). ¹H NMR (200 MHz, CDCl₃): δ 1.6–3.0 [complex signal, 14H, 2(8)-H, 4(6)-H, 5-H, 1’-H, 2’-H2 and 5’-H2], 3.41 (d, J = 6.2 Hz, 2H, C1’-CH₂O), 3.47 (s, 2H, C1-CH₂O), 3.51 (d, J = 4.0 Hz, 1H, O-H), 3.95 (m, 1H, C1’-CH₂O). ¹³C NMR (50.3 MHz, CDCl₃) (data of the main diastereomer of 33) δ 34.5 (CH₂, 2’-C), 34.9 (CH, 1’-C), 36.8 (C, 5’-C), 39.7 (CH, 5-C), 44.8 [CH₂, 4(6)-C], 46.7 [CH₂, 2(8)-C], 47.9 (C, 1-C), 64.3 (CH, 3’-C), 75.7 (CH₂, 1’-C-CH₂O), 77.3 (1-C-CH₂O), 79.4 (CH, 4’-C), 217.0 [C, 3(7)-C]. GC/MS (tᵣ = 25.0 min): m/z (%) 264 ([M–HCl]⁺, 3), 151 (27), 150 (26), 137 (100), 83 (53), 79 (82), 69 (64), 55 (65).

1-[(Cyclopent-3-enyl)methoxymethyl]-cis-bicyclo[3.3.0]octane-3,7-dione (14). To a warm (70 °C), magnetically stirred solution of ether 28 (119 mg, 0.28 mmol) in acetonitrile (4 mL), a solution of Ce(NH₄)₂(SO₄)₆ (769 mg, 1.4 mmol) in water (4 mL) was added. The stirred mixture was heated to 65 °C for 5 min and was then allowed to cool to room temperature. The mixture was extracted with DCM (3×15 mL), the organic extracts were combined, dried (anhydrous Na₂SO₄) and concentrated in vacuo to give a residue (54 mg) that was subjected to column
chromatography (silica gel, 5.4 g; heptane/EtOAc mixtures). Upon elution with heptane/EtOAc, diketone 14 (31 mg, 44%) was isolated. An analytical sample was obtained by distillation in a rotary microdistillation equipment. Colorless oil, bp 175 °C/0.1 Torr. IR (KBr): v 3052, 2925, 2891, 1740, 1403, 1114 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): δ 2.02 [broad dd, J = 13.5 Hz, J' = 5.5 Hz, 2H, 2'(5')-H$_{cis}$], 2.09 [dd, J = 19.0 Hz, J' = 5.5 Hz, 2H, 4(6)-H$_{endo}$], 2.25 [dd, J = 18.5 Hz, J' = 1.0 Hz, 2H, 2(8)-H$_{endo}$], 2.39 [dd, J = 18.5 Hz, J' = 1.5 Hz, 2H, 2(8)-H$_{exo}$], 2.38–2.45 [m, 2H, 2'(5')-H$_{trans}$], 2.47–2.54 [m, 1H, 1'-H], 2.72 [ddd, J = 19.0 Hz, J' = 9.0 Hz, J'' = 1.5 Hz, 2H, 4(6)-H$_{endo}$], 2.85 (tt, J = 9.0 Hz, J' = 5.5 Hz, 1H, 5-H), 3.32 (d, J = 7.0 Hz, 2H, C1'-CH$_2$O), 3.43 (s, 2H, C1-CH$_2$O), 5.62 [s, 2H, 3'(4')-H]. $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ 35.8 [CH$_2$, 2'(5')-C], 36.5 (CH, 1'-C), 39.7 (CH, 5-C), 44.8 [CH$_2$, 4(6)-C], 46.7 [CH$_2$, 2(8)-C], 47.9 (C, 1-C), 75.8 (CH$_2$, 1'-C-CH$_2$O), 77.1 (CH$_2$, 1-C-CH$_2$O), 129.4 [CH, 3'(4')-C], 216.8 [C, 3(7)-C]. MS (Cl): m/z (%): 250 (30), 249 [M+H]$^+$, 67), 201 (69), 199 (88), 179 (80), 169 (65), 151 (100), 137 (39), 109 (54), 81 (99), 80 (75). Anal. calcd. for C$_{13}$H$_{20}$O$_3$: C, 71.52; H, 8.16. Found: C, 71.61; H, 8.20. HRMS: calcd. for [C$_{13}$H$_{20}$O$_3$+H]$^+$: 249.1491. Found: 249.1492.

1-[(trans-3,4-Epoxycyclopentyl)methoxymethyl]-cis-bicyclo[3.3.0]octane-3,7-dione (trans-34). To a magnetically stirred solution of diketone 14 (99 mg, 0.40 mmol) in DCM (6 mL) at room temperature, MCPBA (359 mg, 77% content, 1.6 mmol) was added portionwise within 5 min and stirring was continued for 1.5 h. The organic solution was washed with 10% aqueous Na$_2$SO$_4$ solution (3×5 mL) and saturated aqueous NaHCO$_3$ solution (3×5 mL), dried (anhydrous Na$_2$SO$_4$) and concentrated in vacuo to give an oily residue of the mixture of epoxides cis- and trans-34 (96 mg), which was subjected to column chromatography (silica gel, 10 g; heptane/EtOAc mixtures). Upon elution with heptane/EtOAc 1:1, pure epoxide trans-34 (13 mg, 12%) and a mixture of epoxides trans-34/cis-34 in a ratio close to 1:3 (38 mg, 36%) were isolated. The analytical samples of epoxide trans-34 and of the mixture of epoxides trans-34/cis-34 were obtained by distillation in a rotary microdistillation equipment at 200 °C/0.1 Torr.

trans-34. IR (NaCl): v 2924, 2854, 1738, 1401, 1101, 839 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): δ 1.76–1.84 [m, 4H, 2'(5')-H$_2$], 2.10 [dd, J = 19.0 Hz, J' = 5.5 Hz, 2H, 4(6)-H$_{endo}$], 2.24 [dd, J = 19.0 Hz, J' = 0.5 Hz, 2H, 2(8)-H$_{endo}$], 2.22–2.32 (m, 1H, 1'-H), 2.38 [dd, J = 19.0 Hz, J' = 1.5 Hz, 2H, 2(8)-H$_{exo}$], 2.71 [ddd, J = 19.0 Hz, J' = 9.0 Hz, J'' = 1.5 Hz, 2H, 4(6)-H$_{exo}$], 2.85 (tt, J = 9.0 Hz, J' = 5.5 Hz, 1H, 5-H), 3.23 (d, J = 8.0 Hz, 2H, C1'-CH$_2$O), 3.39 (s, 2H, C1-CH$_2$O), 3.45 [s, 2H, 3'(4')-H]. $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ 30.3 [CH$_2$, 2'(5')-C], 35.0 (CH, 1'-C), 39.7 (CH, 5-C), 44.8 [CH$_2$, 2(8)-C], 46.8 [CH$_2$, 2(8)-C], 48.0 (C, 1-C), 58.5 [CH, 3'(4')-C], 76.9 (CH$_2$, 1'-C-CH$_2$O), 77.8 (CH$_2$, 1-C-CH$_2$O), 216.9 [C, 3(7)-C]. MS (Cl): m/z (%): 265 (100), 264 ([M+H]$^+$), 25), 199 (14), 191 (13), 179 (51), 169 (21), 151 (100), 97 (38), 79 (66). HRMS (Cl): calcd. for [C$_{13}$H$_{20}$O$_3$+H]$^+$: 265.1440. Found: 265.1440.

Mixture of epoxide stereoisomers trans-34/cis-34 (ratio of 1:3). IR (NaCl): v 2926, 2855, 1739, 1402, 1120, 837 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): (data of cis-34 epoxide from the mixture): δ 1.37 [dd, J = 13.0 Hz, J' = 9.0 Hz, 2H, 2'(5')-H$_{cis}$], 2.01 (m, 1H, 1'-H), 2.04–2.12 [m, 4H, 2'(5')-H$_{trans}$ and 4(6)-H$_{endo}$], 2.24 [dd, J = 19.0 Hz, 2H, 2(8)-H$_{endo}$], 2.35 [ddd, J = 19.0 Hz, J' = 1.5 Hz, 2H, 2(8)-H$_{exo}$], 2.69 [ddd, J = 19.0 Hz, J' = 8.5 Hz, J'' = 1.5 Hz, 2H, 4(6)-H$_{exo}$], 2.83 (tt, J =
9.0 Hz, $J' = 6.0$ Hz, 1H, 5-H), 3.36 (d, $J = 5.5$ Hz, 2H, C1'-CH$_2$O), 3.41 (s, 2H, C1-CH$_2$O), 3.43 [s, 2H, 3'(4')-H]. $^{13}$C NMR (75.4 MHz, CDCl$_3$): (data of epoxide cis-34 from the spectrum of the mixture) $\delta$ 31.0 [CH$_2$, 2'(5')-C], 32.9 (CH, 1'-C), 39.8 (CH, 5-C), 44.8 [CH$_2$, 4(6)-C], 46.7 [CH$_2$, 2(8)-C], 47.9 (C, 1-C), 56.9 [CH, 3'(4')-C], 73.9 (CH$_2$, 1'-C-CH$_2$O), 77.3 (CH$_2$, 1-C-CH$_2$O), 216.5 [C, 3(7)-C]. HRMS (Cl): calcd. for [C$_{15}$H$_{20}$O$_4$]+H$: 265.1440$. Found: 265.1443.

Anal. calcd. for C$_{15}$H$_{20}$O$_4$: C, 68.16; H, 7.63. Found: C, 67.77; H, 7.84.

**Attempted conversion of epoxide (34) into alcohol (35)**

**Procedure 1.** A solution of (LHMDS) was prepared by adding a solution of $n$-BuLi (2.5 M in hexanes, 90 µL, 0.23 mmol) to a cold (−68 °C, acetone/CO$_2$ bath) solution of hexamethyldisilazane (HMDS, 56 µL, 0.27 mmol) in anhydrous toluene (0.5 mL). After stirring for 10 min, a solution of the stereoisomeric mixture of epoxide 34 (24 mg, 0.09 mmol) in anhydrous toluene (0.5 mL) was added dropwise. The reaction mixture was stirred at −68 °C for 1 h and then allowed to warm to room temperature for 24 h. The reaction mixture was quenched by addition of saturated aqueous solution of NH$_4$Cl (1 mL) and was extracted with Et$_2$O (3×10 mL). The combined organic extracts were dried (anhydrous Na$_2$SO$_4$) and concentrated in vacuo to give a residue (12 mg) containing mainly epoxide 34 (1H NMR) The aqueous phase was acidified with 1N HCl (5 mL) and was extracted with Et$_2$O (3×10 mL). The combined organic extracts were dried (anhydrous Na$_2$SO$_4$) and concentrated in vacuo to give a residue (19 mg) consisting mainly of epoxide 34.

**Procedure 2.** The reaction was carried out as in procedure 1 and after the addition of 34, Sc(OTf)$_3$ (1.2 equiv) was added. Epoxide 34 was the main component of the crude product.

**Procedure 3.** The reaction was carried out as in procedure 1 using THF instead of toluene as the solvent, with similar result.

**Procedure 4.** The reaction was carried out as in procedure 3 and after the addition of 34, BF$_3$Et$_2$O in THF (1.2 equiv) was added. Epoxide 34 was the main component of the crude product.

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**Supplementary Materials**

Possible pathways from 17 and 18 to the side product 21 (Scheme S1) can be found as supplementary material.
References


