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Synthesis of a chiral building block for highly functionalized polycyclic ethers†

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An efficient procedure for preparing enantiopure polycyclic ethers is reported. The protocol is based on the photo-oxidation/conjugate addition sequence over a chiral functionalized furan, which was prepared from commercially available tri-*O*-acetyl-D-glucal. The Michael addition step afforded two products with the same absolute configuration from a mixture of diastereomers.

Introduction

Polycyclic ethers are the structural basis of many natural products such as the so-called marine ladder toxins, a family of red tide toxins with a highly complex unusual molecular architecture, a series of fused cyclic ethers having regular *trans–syn–trans* stereochemistry.[1] Some representative examples including the brevetoxins (**1** and **2**),[2] ciguatoxin (**3**),[3] and yessotoxin (**4**),[4] among others, are depicted in Fig. 1. In addition to the interesting biological properties including the neurotoxicity and antimicrobial activity of these compounds, their challenging molecular architecture and their scarcity in natural sources have attracted the attention of the synthetic community. This family of compounds indeed represents challenging synthetic targets for organic chemists, chemical synthesis being a practical way of supplying samples to allow further investigation of their biological activities. Among the different total syntheses of this type of compound it is worth citing the impressive work of Nicolaou and co-workers on brevetoxins A and B,[2a–d] and that of Hirama and co-workers on ciguatoxin.[3] Due to the highly repetitive nature of these structures, many research groups designed iterative approaches to access these rings.[1f] We recently developed a new method for the synthesis of oxacyclic compounds from furan, we coined the furan approach.[5] We successfully applied this method to the synthesis of chiral butenolides,[6] natural products,[7] racemic polyoxepanes[8] and *trans*-fused bistetrahydropyrans.[9] The scope and limitations of this powerful methodology continue to be our main concern. Here we report its extension to the synthesis of enantiopure *trans*-fused polycyclic tetrahydropyrans **5** and **6**, structural motifs which are commonly present in the ladder toxins and related natural products.

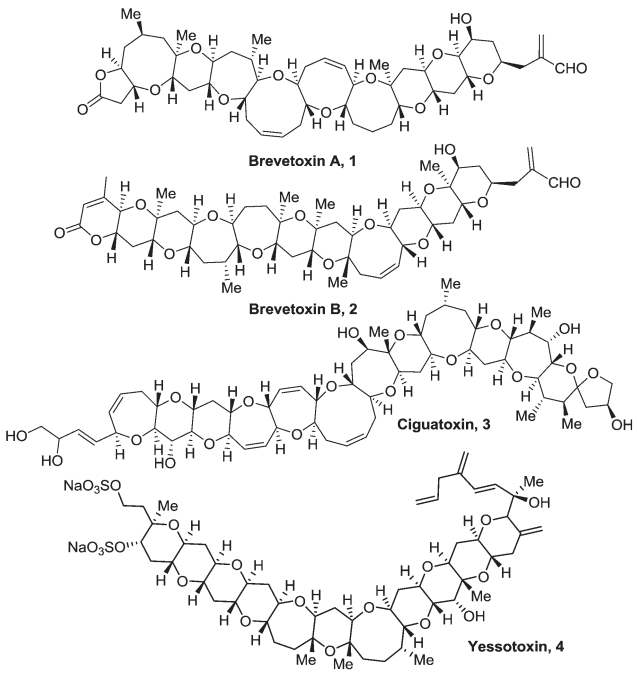

Fig. 1 Structures of some marine ladder toxins.

Results and discussion

Our retrosynthetic strategy for the synthesis of **5** and **6** is depicted in Scheme 1.

We anticipated that we could easily access three of the chiral centers present in ketone **8**, starting from commercially available tri-*O*-acetyl-D-glucal and using a Claisen rearrangement

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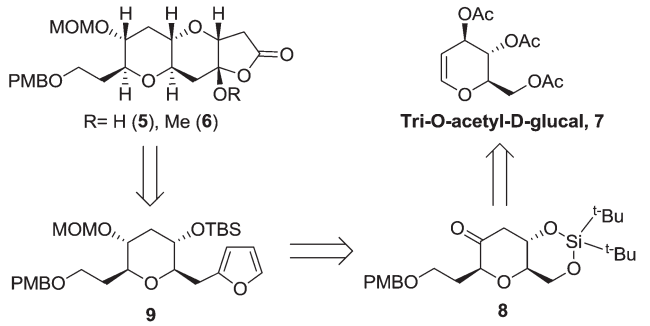
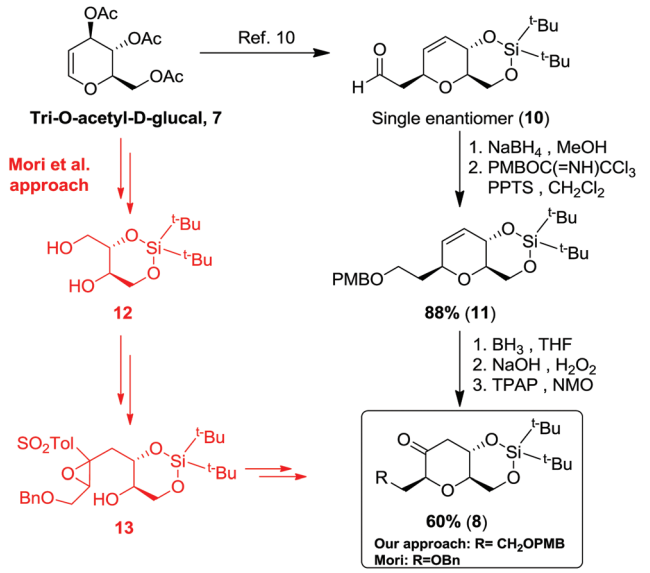
†Electronic supplementary information (ESI) available: Experimental procedures and full spectroscopic data for all new compounds. CCDC 988171. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ob01439a



Scheme 1 Retrosynthetic analysis of *trans*-fused tetrahydropyrans **5** and **6**.

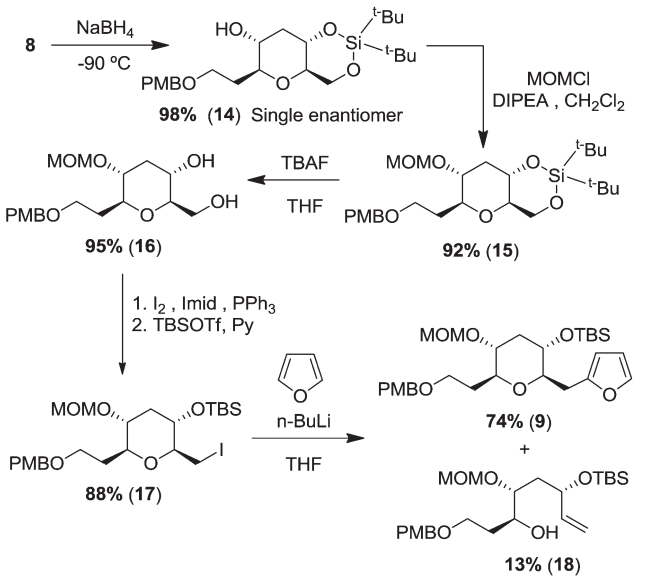


Scheme 2 Synthesis of ketone **8**.

as we already showed in our recently published synthesis of isolaurepan.[10] Accordingly, as outlined in Scheme 2, enantiopure aldehyde **10** was obtained in high yield through a thermal Claisen rearrangement. Reduction of aldehyde **10** followed by orthogonal protection of the resulting alcohol afforded compound **11** in 88% overall yield. The hydroboration of the double bond followed by oxidation gave a mixture of inseparable alcohols in positions 4 and 5. After TPAP oxidation of the mixture of alcohols, the resulting ketones could be separated by chromatography over silica gel, affording the desired ketone **8** in 60% overall yield, together with 30% of its regioisomer. Mori *et al.*[11] used the same starting material (tri-*O*-acetyl-D-glucal) but a different strategy to prepare a similar ketone (Scheme 2).

Our strategy competes favorably with Mori's approach and can be carried out on a large scale. With ketone **8** in hand, the stage was then set for the preparation of chiral furan **9** as outlined in Scheme 3.

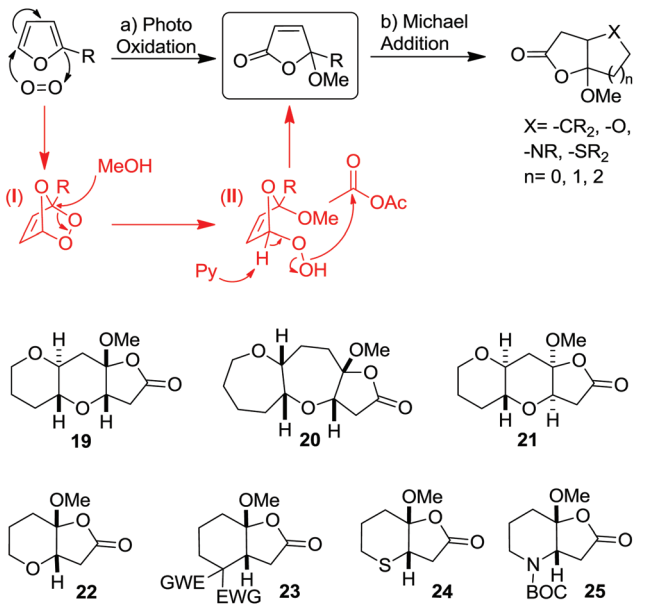
Reduction of ketone **8** with sodium borohydride afforded chiral alcohol **14**. The protection with MOMCl and subsequent



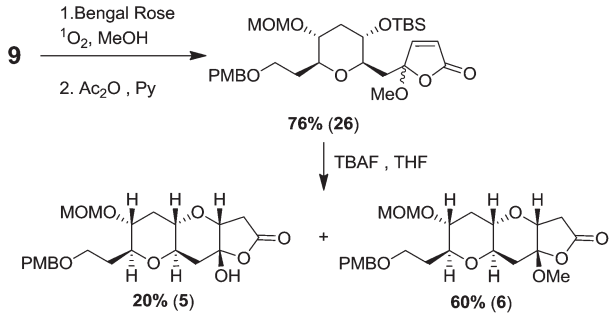
Scheme 3 Synthesis of chiral furan **9**.

deprotection of the silyl ethers with TBAF gave the diol **16** in 87% overall yield. The selective iodination of the primary hydroxyl group of diol **16**, followed by protection of the secondary hydroxyl group as TBS ether using *t*-butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) gave iodide **17** in 88% overall yield. Iodide **17**, on reaction with lithiated furan afforded the targeted chiral furan **9** in 74% yield, together with alkene **18** in 13% yield.

During the last ten years we used our furan approach to access racemic heterocyclic compounds,[5,12] some of them are depicted in Scheme 4.



Scheme 4 Fall *et al.* approach to polycyclic compounds.



Scheme 5 Synthesis of polyoxacycles **5** and **6**.

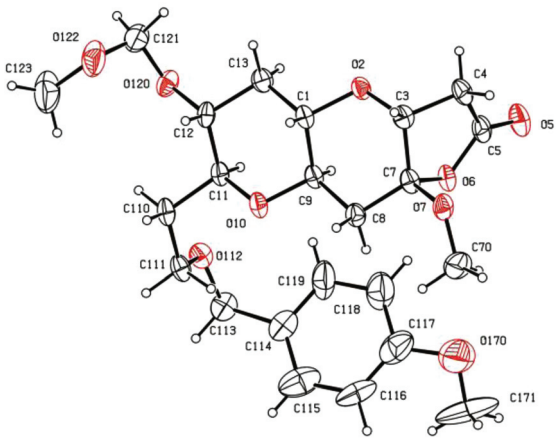


Fig. 2 X-ray structure (ORTEP) of **6**.

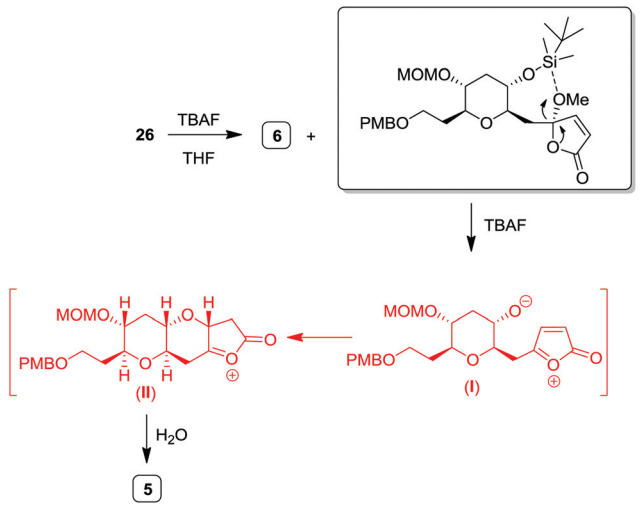
We now wanted to further enlarge the scope of our strategy by tackling the synthesis of enantiopure polycyclic ethers. Accordingly, as outlined in Scheme 5, chiral furan **9** was subjected to singlet oxygen oxidation affording 76% yield of methoxybutenolide **26** as a 60/40 diastereoisomeric mixture.

TBAF mediated cyclization furnished a mixture of lactones **5** and **6** which were separated by chromatography on silica gel affording **5** in 20% yield and **6** in 60% yield. The structure of the major product **6** was confirmed unambiguously as shown in Fig. 2, by X-ray crystallographic analysis of the crystals obtained by recrystallization from a mixture of hexane and ethyl ether.[13]

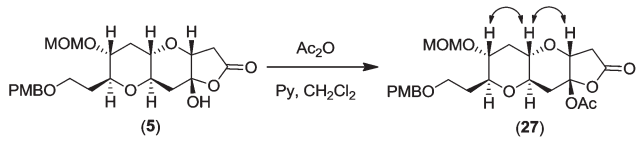
Formation of compound **5** can be rationalized by the loss of the methoxy group (intermediate I) followed by a hetero Michael addition (intermediate II) and final addition of H_2O (Scheme 6).

Compound **5** was transformed into the more stable acetate derivative **27** and the relative stereochemistry was confirmed by 2D-NOESY experiments (Scheme 7).

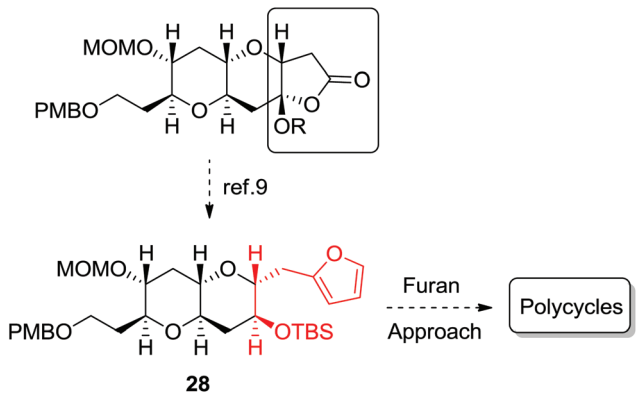
Lactones **5** and **6** can be opened and transformed into chiral furan **28**,[9] which through the photo-oxidation/conjugate addition sequence would lead to new polycyclic compounds (Scheme 8).



Scheme 6 Proposed mechanism for the formation of **5**.



Scheme 7 Confirmation of the stereochemistry of **5**.



Scheme 8 Iterative polyether synthesis through the furan approach.

Conclusions

In conclusion, starting from commercially available tri-*O*-acetyl-D-glucal, we developed a highly flexible approach towards chiral *trans*-fused polycyclic tetrahydropyrans, structural motifs which are commonly present in the ladder toxins and related natural products. Work is now in progress for the synthesis of marine toxins using our furan approach as an iterative strategy.

Experimental

General

Solvents were purified and dried by standard procedures before use. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker ARX-400 spectrometer (400 MHz for ^{1}H NMR, 100.61 MHz for ^{13}C NMR) using TMS as the internal standard (chemical shifts in δ values, J in Hz). Flash chromatography (FC) was performed on silica gel (Merck 60, 230–400 mesh); analytical TLC was performed on plates precoated with silica gel (Merck 60 F254, 0.25 mm); mass spectra (FAB, EI) were recorded using a FISONS VG and electrospray ionization (ESI-MS) spectra were recorded using a Bruker FTMS APEXIII. Melting points were obtained in open capillary tubes and are not corrected. Optical rotations were obtained using a Jasco P-2000 polarimeter. IR spectra were recorded with a JASCO FT/I(R)-6100 spectrophotometer.

(1*S*,6*R*,8*S*)-3,3-Ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]dec-9-ene (11). To a solution of aldehyde **10** (6.28 g, 20.12 mmol) in MeOH (30 mL) cooled at 0 °C was slowly added $NaBH_4$ (913 mg, 24.15 mmol) and the mixture was stirred for 30 min under the same conditions. Then, water (30 mL) was added and the product was extracted with EtOAc (3 × 50 mL). The organic phase was washed with water (3 × 150 mL) and brine (150 mL), dried over Na_2SO_4 and the solvent was evaporated under reduced pressure affording a white solid.

To a solution of PMBOH (3.76 mL, 30.18 mmol) in THF (50 mL) cooled at 0 °C was added NaH (60%) (72 mg, 3 mmol) and the mixture was stirred for 1 h under the same conditions. Then, CCl_3CN (3 mL, 3.18 mmol) was added and stirred for 30 min and a saturated aqueous solution of $NaHCO_3$ (30 mL) was added. The resulting mixture was extracted with EtOAc (2 × 40 mL) and the combined organic phases were washed with brine (70 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure affording a residue which was dissolved in CH_2Cl_2 (40 mL). The alcohol which was obtained in the first step and a catalytic amount of PPTS were added and the mixture stirred was for 48 h. Then, a saturated aqueous solution of $NaHCO_3$ (40 mL) was added and the resulting organic phase was washed with water (3 × 40 mL) and brine (40 mL), filtered and evaporated to yield a residue which was chromatographed on silica gel using 1% EtOAc–hexane as the eluent, affording compound **11** (7.52 g, 89%) as a white solid; m.p. = 60 °C; R_f: 0.55 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2960.30, 2933.69, 2880.69, 2859.36, 1647.83, 1132.58; $[\alpha]_D^{22}$ = −14.51 (*c* 1.43, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.26 (2H, d, J = 8.7 Hz, Ho-PMB), 6.88 (2H, d, J = 8.7 Hz, Hm-PMB), 5.83 (1H, d, J = 10.3 Hz, H-9, H-10), 5.64 (1H, d, J = 10.3 Hz, H-9, H-10), 4.43 (2H, s, CH_2-PMP), 4.37 (2H, m, H-1, H-8), 4.16 (1H, dd, J = 10.0, 5.1 Hz, H-5), 3.85 (1H, t, J = 10.0 Hz, H-5), 3.80 (3H, s, OCH_3-PMB), 3.54 (3H, m, 2H-2′, H-6), 1.85 (1H, m, H-1′), 1.74 (1H, m, H-1′), 1.06 (9H, s, CH_3-^{t}Bu), 1.00 (9H, s, CH_3-^{t}Bu); ^{13}C-NMR ($CDCl_3$, δ): 159.1 (Cp-PMB), 130.5 (C-PMB), 129.7 (CH-9, CH-10), 129.6 (CH-9, CH-10), 129.2 (CHo-PMB), 113.7 (CHm-PMB), 74.6 (CH-6), 72.8 (CH-1), 72.6 (CH_2-PMP), 70.3 (CH-8), 67.2 (CH_2-5), 65.9 (CH_2-2′), 55.2 (OCH_3-PMB), 35.4 (CH_2-1′), 27.5 (CH_3-*t*Bu), 27.1 (CH_3-^{t}Bu), 22.6 (C-^{t}Bu), 20.0 (C-*t*Bu); MS (ESI) [*m*/*z*, (%)]: 457 (M^+ + Na, 100), 315 (17); HRMS (ESI): 457.2380 calcd for $C_{24}H_{38}NaO5Si$, found 457.2390.

(1*S*,6*R*,8*S*)-3,3-Ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]decan-10-ol (11a) and (1*S*,6*R*,8*S*)-3,3-ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]decan-9-ol (11b). To a solution of **11** (4 g, 9.21 mmol) in THF (40 mL) cooled at 0 °C was added BH_3·THF (18.42 mL of a 1 M solution in THF, 18.42 mmol) and stirring was continued for 30 min. Then, 3 M aqueous solution of NaOH (7.5 mL) and 30% aqueous solution of H_2O_2 (2.04 mL) were added; the reaction was allowed to reach room temperature and was stirred for 12 h. The reaction was quenched with water (30 mL) and the product was extracted with EtOAc (3 × 40 mL). The combined organic phases were dried, filtered and evaporated. Finally, the residue was filtered through silica gel (30% EtOAC–hexane) to give a mixture of alcohols **11a** and **11b**.

(1*S*,6*R*,8*S*)-3,3-Ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]dec-9-one (8) and(1*S*,6*R*,8*S*)-3,3-ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]dec-10-one (8a). To a solution of a mixture of alcohols **11a** and **11b** (4 g, 8.83 mmol) in CH_2Cl_2 (40 mL) were added 4 Å molecular sieves (2 g), NMO (3.10 g, 25 mmol) and a catalytic amount of TPAP. The resulting greenish solution was stirred at room temperature for 12 h. The solvent was rotatory evaporated to afford a residue which was chromatographed on silica gel using 5% EtOAc–hexane as the eluent, affording ketone **8** (2.4 g, 60%) along with its isomeric ketone **8a** (1.23 g, 31%).

Compound **8**. White solid, m.p. = 81 °C, R_f: 0.62 (30% EtOAc–hexane); IR (NaCl, cm^{-1}): 2962.13, 2934.16, 2880.17, 2859.92, 1727.91, 1513.85, 1132.05; $[\alpha]_D^{26}$ = −16.54 (*c* 1.86, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.23 (2H, d, J = 8.6 Hz, Ho-PMB), 6.87 (2H, d, J = 8.6 Hz, Hm-PMB), 4.42 (1H, d, J = 11.6 Hz, CH_2-PMP), 4.38 (1H, d, J = 11.6 Hz, CH_2-PMP), 4.19 (1H, dd, J = 10.3, 5.0 Hz, H-5), 4.09 (1H, ddd, J = 10.9, 9.4, 5.7 Hz, H-1), 3.98 (1H, dd, J = 7.7, 4.2 Hz, H-8), 3.85 (1H, t, J = 10.2 Hz, H-5), 3.80 (3H, s, OCH_3-PMB), 3.57 (3H, m, 2H-2′, H-6), 2.97 (1H, dd, J = 15.7, 5.7 Hz, H-10), 2.42 (1H, dd, J = 15.7, 11.0 Hz, H-10), 2.19 (1H, m, H-1′), 1.77 (1H, m, H-1′), 1.04 (9H, s, CH_3-^{t}Bu), 1.01 (9H, s, CH_3-^{t}Bu); ^{13}C-NMR ($CDCl_3$, δ): 205.1 (C═O), 159.2 (Cp-PMB), 130.4 (C-PMB), 129.2 (CHo-PMB), 113.7 (CHm-PMB), 79.6 (CH-8), 76.1 (CH-6), 73.1 (CH-1), 72.4 (CH_2-PMP), 66.5 (CH_2-5), 65.2 (CH_2-2′), 55.2 (OCH_3-PMB), 48.1 (CH_2-10), 29.4 (CH_2-1′), 27.3 (CH_3-^{t}Bu), 27.0 (CH_3-^{t}Bu), 22.6 (C-^{t}Bu), 19.9 (C-^{t}Bu); MS (ESI) [*m*/*z*, (%)]: 473 (M^+ + Na, 100), 313 (30); HRMS (ESI): 473.2329 calcd for $C_{24}H_{38}NaO_6Si$, found 473.2319.

Compound **8a**. White solid, m.p. = 76 °C, R_f: 0.5 (30% EtOAc–hexane); IR (NaCl, cm^{-1}): 2961.98, 2933.69, 2880.17, 2858.24, 1736.58, 1512.79, 1247.57, 1133.94; $[\alpha]_D^{24}$ = −19.34 (*c* 1.60, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.22 (2H, d, J = 8.3 Hz, Ho-PMB), 6.87 (2H, d, J = 8.3 Hz, Hm-PMB), 4.41 (3H, m, CH_2-PMB, H-1), 4.16 (1H, dd, J = 10.0, 4.6 Hz, H-5), 3.95 (1H, t,

J = 10.2 Hz, H-5), 3.88 (1H, m, H-6), 3.79 (3H, s, OCH_3-PMB), 3.52 (3H, 2H-2′, H-8), 2.51 (1H, dd, J = 13.7, 2.4 Hz, H-9), 2.43 (1H, m, H-9), 1.83 (2H, m, 2H-1′), 1.04 (9H, s, CH_3-^{t}Bu), 1.00 (9H, s, CH_3-^{t}Bu); ^{13}C-NMR ($CDCl_3$, δ): 202.4 (C=O), 159.2 (Cp-PMB), 130.2 (C-PMB), 129.2 (CHo-PMB), 113.7 (CHm-PMB), 80.1 (CH-1), 77.0 (CH-8), 75.7 (CH-6), 72.6 (CH_2-PMP), 66.7 (CH_2-5), 65.3 (CH_2-2′), 55.2 (OCH_3-PMB), 47.3 (CH_2-9), 36.0 (CH_2-1′), 27.3 (CH_3-^{t}Bu), 26.9 (CH_3-^{t}Bu), 22.6 (C-^{t}Bu), 20.1 (C-^{t}Bu); MS (ESI) [m/z, (%)]: 473 (M^+ + Na, 100), 338 (21), 313 (12); HRMS (ESI): 473.2329 calcd for $C_{24}H_{38}NaO_6Si$, found 473.2328.

(1*S*,6*R*,8*S*,9*R*)-3,3-Ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-2,4,7-trioxy-3-silinebicyclic[4,4,0]dec-9-ol (14). To a solution of ketone **8** (2.33 g, 5.15 mmol) in MeOH (20 mL) and CH_2Cl_2 (20 mL) cooled at −78 °C was slowly added $NaBH_4$ (292 mg, 7.72 mmol) and the mixture was stirred for 1 h under the same conditions. Then, water (40 mL) was added and the product was extracted with EtOAc (3 × 40 mL) and the organic phases were washed with water (3 × 100 mL) and brine (100 mL), dried over Na_2SO_4 and the solvent was evaporated under reduced pressure affording alcohol **14** (2.34 g, 99%) as a white solid; m.p. = 115 °C, R_f: 0.25 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 3420.14, 2960.23, 2933.87, 2859.92, 1513.85, 1092.48; $[\alpha]_D^{25}$ = −25.13 (c 1.48, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.24 (2H, d, J = 8.5 Hz, Ho-PMB), 6.88 (2H, d, J = 8.5 Hz, Hm-PMB), 4.46 (1H, d, J = 11.4 Hz, CH_2-PMP), 4.43 (1H, d, J = 11.4 Hz, CH_2-PMP), 4.08 (1H, dd, J = 10.0, 4.8 Hz, H-5), 3.79 (3H, s, OCH_3-PMB), 3.73 (2H, m, H-1, H-5), 3.58 (2H, m, 2H-2′), 3.39 (1H, m, H-9), 3.22 (2H, m, H-6, H-8), 2.44 (1H, m, H-10), 1.99 (1H, m, H-1′), 1.84 (1H, m, H-1′), 1.47 (1H, dd, J = 22.3, 11.1 Hz, H-10), 1.03 (9H, s, CH_3-^{t}Bu), 0.98 (9H, s, CH_3-^{t}Bu); ^{13}C-NMR ($CDCl_3$, δ): 159.3 (Cp-PMB), 129.4 (CHo-PMB), 128.5 (C-PMB), 113.8 (CHm-PMB), 81.0 (CH-8), 77.1 (CH-6), 72.8 (CH_2-PMB), 72.5 (CH-1), 69.2 (CH-9), 66.8 (CH_2-5), 66.5 (CH_2-2′), 55.2 (OCH_3-PMB), 41.1 (CH_2-10), 33.5 (CH_2-1′), 27.4 (CH_3-^{t}Bu), 27.1 (CH_3-^{t}Bu), 22.5 (C-^{t}Bu), 19.8 (C-^{t}Bu); MS (ESI) [m/z, (%)]: 475 (M^+ + Na, 100); HRMS (ESI): 475.2486 calcd for $C_{24}H_{40}NaO_6Si$, found 475.2486.

(1*S*,6*R*,8*S*,9*R*)-3,3-Ditert-butyl-8-(2′-*p*-methoxybenzyloxyethyl)-9-(methoxymethoxy)-2,4,7-trioxy-3-silinebicyclic[4,4,0]decane (15). To a solution of alcohol **14** (1 g, 2.21 mmol) in CH_2Cl_2 (10 mL) was added DIPEA (1.93 mL, 11.06 mmol) and the mixture was stirred for 10 min, cooled to 0 °C and MOMCl (839 μL, 11.06 mmol) was added. Stirring was continued for 12 h allowing the mixture to gradually reach room temperature. The reaction was quenched with water (10 mL) and was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with H_2O (30 mL) and brine (30 mL) and were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was chromatographed on silica gel using 3% EtOAc–hexane as the eluent, affording compound **15** (1.01 g, 93%) as a colourless liquid; R_f: 0.51 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2960.65, 2932.78, 2859.15, 1512.89, 1092.47, 854.35; $[\alpha]_D^{26}$ = −43.56 (c 2.80, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.25 (2H, d, J = 8.6 Hz, Ho-PMB), 6.87 (2H, d, J = 8.6 Hz, Hm-PMB), 4.72 (1H, d, J = 6.9 Hz, CH_2-MOM), 4.60 (1H, d, J = 6.9 Hz, CH_2-MOM), 4.47 (1H, d, J = 11.6 Hz, CH_2-PMP), 4.40 (1H, d, J = 11.6 Hz, CH_2-PMP), 4.05 (1H, dd, J = 10.1, 4.9 Hz, H-5), 3.80 (3H, s, OCH_3-PMB), 3.74 (1H, t, J = 10.1 Hz, H-5), 3.73 (1H, m, H-9), 3.55 (2H, dd, J = 7.9, 6.1 Hz, 2H-2′), 3.37 (3H, s, OCH_3-MOM), 3.33 (2H, m, H-1, H-8), 3.24 (1H, dt, J = 10.1, 4.9 Hz, H-6), 2.58 (1H, m, H-10), 2.16 (1H, m, H-1′), 1.55 (1H, m, H-10), 1.47 (1H, m, H-1′), 1.03 (9H, s, CH_3-^{t}Bu), 0.99 (9H, s, CH_3-^{t}Bu); ^{13}C-NMR ($CDCl_3$, δ): 159.1 (Cp-PMB), 130.6 (C-PMB), 129.2 (CHo-PMB), 113.7 (CHm-PMB), 95.2 (CH_2-MOM), 77.5 (CH-8), 76.8 (CH-6), 74.5 (CH-1), 72.4 (CH_2-PMP), 72.3 (CH-9), 66.8 (CH_2-5), 66.1 (CH_2-2′), 55.6 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 39.3 (CH_2-10), 31.9 (CH_2-1′), 27.4 (CH_3-^{t}Bu), 27.0 (CH_3-^{t}Bu), 22.6 (C-^{t}Bu), 19.9 (C-^{t}Bu); MS (ESI) [m/z, (%)]: 520 (M^+ + 1 + Na, 27), 519 (M^+ + Na, 100); HRMS (ESI): 519.2748 calcd for $C_{26}H_{44}NaO_7Si$, found 519.2747.

(1*S*,2*R*,4*S*,5*R*)-2-Hydroxymethyl-4-(2′-*p*-methoxybenzyloxyethyl)-5-(methoxymethoxy)-3-tetrahydro-2*H*-pyran-1-ol (16). To a solution of **16** (1 g, 2.04 mmol) in THF (10 mL) was added TBAF (6.6 mL of a 1 M solution in THF, 6.6 mmol) and the mixture was stirred at room temperature for 12 h, quenched with an aqueous saturated solution of NH_4Cl (15 mL) and the product was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 70% EtOAc–hexane as the eluent, affording diol **16** (690 mg, 96%) as a colourless liquid; R_f: 0.30 (EtOAc); IR (NaCl, cm^{-1}): 3428.36, 2920.98, 2884.25, 1512.89, 1248.96, 1098.36; $[\alpha]_D^{30}$ = +37.35 (c 1.69, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.25 (2H, d, J = 8.6 Hz, Ho-PMB), 6.87 (2H, d, J = 8.6 Hz, Hm-PMB), 4.69 (1H, d, J = 6.9 Hz, CH_2-MOM), 4.59 (1H, d, J = 6.9 Hz, CH_2-MOM), 4.46 (1H, d, J = 11.6 Hz, CH_2-PMP), 4.40 (1H, d, J = 11.6 Hz, CH_2-PMP), 3.79 (3H, s, OCH_3-PMB), 3.72 (2H, m, CH_2-OH), 3.58 (3H, m, 2H-2′, H-5), 3.35 (3H, s, OCH_3-MOM), 3.29 (2H, m, H-1, H-4), 3.12 (1H, m, H-2), 2.95 (1H, s, OH), 2.50 (1H, m, H-6), 2.17 (1H, m, H-1′), 1.60 (1H, m, H-1′), 1.45 (1H, dd, J = 22.2, 11.3 Hz, H-6); ^{13}C-NMR ($CDCl_3$, δ): 159.1 (Cp-PMB), 130.4 (C-PMB), 129.3 (CHo-PMB), 113.7 (CHm-PMB), 95.3 (CH_2-MOM), 80.7 (CH-2), 77.3 (CH-4), 74.5 (CH-1), 72.5 (CH_2-PMP), 66.3 (CH-5), 66.2 (CH_2-2′), 62.9 (CH_2-OH), 55.6 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 39.1 (CH_2-6), 31.9 (CH_2-1′); MS (ESI) [m/z, (%)]: 379 (M^+ + Na, 100); HRMS (ESI): 379.1727 calcd for $C_{18}H_{28}NaO_7$, found 379.1726.

(2*S*,3*R*,5*S*,6*S*)-5-(*tert*-Butyldimethylsililoxy)-2-(2′-*p*-methoxybenzyloxyethyl)-3-(methoxymethoxy)-6-iodomethyl-1-tetrahydro-2*H*-pyrane (17). To a solution of diol **16** (570 mg, 1.6 mmol) in THF (15 mL) were added PPh_3 (630 mg, 2.4 mmol) and imidazole (326 mg, 4.80 mmol). When the mixture was completely dissolved, I_2 (487 mg, 1.92 mmol) was added at 0 °C. The solution was stirred till it reached room temperature for 2 h and then a saturated aqueous solution of $NaHCO_3$ (30 mL) was added. The resulting mixture was extracted with EtOAc (2 × 30 mL) and the organic phases were washed with a 10% aqueous solution of $Na_2S_2O_4$ (60 mL) and brine (60 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. The obtained residue was dissolved in CH_2Cl_2

(10 mL) and pyridine (2 mL), cooled to 0 °C and TBSOTf (441 μL, 1.92 mmol) was added and the mixture was stirred to room temperature for 2 h. Water (15 mL) was added and the organic phase was washed with a 10% aqueous solution of HCl (2 × 10 mL) and brine (10 mL), dried over Na_2SO_4 and the solvent was filtered and evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc–hexane as the eluent, affording iodide **17** (750 mg, 80%) as a colourless liquid; R_f: 0.52 (30% EtOAc–hexane); IR (NaCl, cm^{-1}): 2920.98, 2884.17, 1512.66, 1247.58, 1095.78, 789.37; $[\alpha]_D^{26}$ = −1.10 (*c* 1.20, CHCl3); ^{1}H-NMR ($CDCl_3$, δ): 7.28 (2H, d, *J* = 8.6 Hz, Ho-PMB), 6.87 (2H, d, *J* = 8.6 Hz, Hm-PMB), 4.69 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.59 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.47 (2H, s, CH_2-PMB), 3.80 (3H, s, OCH_3-PMB), 3.66 (2H, m, 2H-2′), 3.47 (1H, m, H-3), 3.35 (3H, s, OCH_3-MOM), 3.34 (3H, m, H-2, H-5, H-6), 3.16 (1H, dd, 1H, *J* = 10.3, 7.4 Hz, CH_2-I), 2.94 (1H, m, CH2-I), 2.39 (1H, m, H-4), 2.16 (1H, m, H-1′), 1.62 (1H, m, H-1′), 1.49 (1H, dd, *J* = 22.4, 11.0 Hz, H-4), 0.88 (9H, s, CH_3-^{t}Bu), 0.10 (3H, s, CH_3-Si), 0.09 (3H, s, CH_3-Si); ^{13}C-NMR ($CDCl_3$, δ): 159.0 (Cp-PMB), 130.7 (C-PMB), 129.3 (CHo-PMB), 113.6 (CHm-PMB), 95.3 (CH_2-MOM), 80.3 (CH-6), 77.3 (CH-2), 74.5 (CH-5), 72.6 (CH_2-PMP), 70.2 (CH-3), 66.2 (CH_2-2′), 55.5 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 39.7 (CH_2-4), 31.9 (CH_2-1′), 25.7 (CH_3-*t*Bu), 17.8 (C-^{t}Bu), 7.9 (CH_2-I), −4.0 (CH_3-Si), −4.6 (CH_3-Si); MS (ESI) [*m*/*z*, (%)]: 603 (M^+ + Na, 100), 580 (M^+ + 1, 26), 519 (48), 283 (60); HRMS (ESI): 603.1609 calcd for $C_{24}H_{41}INaO_6Si$, found 603.1617.

(2*R*,3*S*,5*R*,6*S*)-3-(*tert*-Butyldimethylsilyloxy)-2-(furanylmethyl)-6-(2′-*p*-methoxybenzyloxyethyl)-5-(methoxymethoxy)-1-tetrahydro-2*H*-pyrane (9) and(3*S*,4*R*,6*S*)-6-(*tert*-butyldimethylsilyloxy)-1-(2′-*p*-methoxybenzyloxyethyl)-4-(methoxymethoxy)-oct-7-en-3-ol (18). To a solution of furan (320 μL, 4.40 mmol) in THF (5 mL) at 0 °C was added *n*-BuLi (1.76 mL of a 2.5 M solution in hexanes, 4.40 mmol) and the mixture was stirred for 30 min affording a yellow solution. Iodide **17** (640 mg, 1.10 mmol) in THF (4 mL) was added *via* a cannula and the mixture was stirred at 0 °C for 3 h. After quenching with water (15 mL), the product was extracted with EtOAc (3 × 20 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 2% EtOAc–hexane as the eluent, affording compound **9** (420 mg, 74%) and alcohol **18** (85 mg, 13%).

Compound **9**. Yellow liquid, R_f: 0.35 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2920.25, 2884.15, 1614.78, 1244.08, 1095.15; $[\alpha]_D^{26}$ = −5.95 (*c* 1.41, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.27 (1H, d, *J* = 1.8, H-5 furan), 7.22 (2H, d, *J* = 8.6 Hz, Ho-PMB), 6.87 (2H, d, *J* = 8.6 Hz, Hm-PMB), 6.27 (1H, dd, *J* = 2.9, 1.9 Hz, H-4 furan), 6.05 (1H, d, *J* = 2.9 Hz, H-3), 4.70 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.58 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.33 (2H, s, CH_2-PMP), 3.80 (3H, s, OCH_3-PMB), 3.54–3.25 (6H, m, H-2, 2H-2′, H-3, H-5, H-6), 3.36 (3H, s, OCH_3-MOM), 3.13 (1H, dd, *J* = 15.4, 1.5 Hz, CH_2-furan), 2.59 (1H, dd, *J* = 15.4, 9.3 Hz, CH_2-furan), 2.41 (1H, dt, *J* = 10.8, 4.2 Hz, H-4), 2.15 (1H, m, H-1′), 1.56 (1H, m, H-1′), 1.49 (1H, dd, *J* = 22.2, 10.9 Hz, H-4), 0.90 (9H, s, CH_3-^{t}Bu), 0.09 (6H, s, CH_3-Si); ^{13}C-NMR ($CDCl_3$, δ): 159.1 (Cp-PMB), 153.3 (C-2 furan), 140.6 (CH-5 furan), 130.7 (C-PMB), 129.2 (CHo-PMB), 113.6 (CHm-PMB), 110.2 (CH-4 furan), 106.1 (CH-3 furan), 95.2 (CH_2-MOM), 80.4 (CH-6), 77.1 (CH-2), 74.7 (CH-5), 72.6 (CH_2-PMP), 70.0 (CH-3), 66.3 (CH_2-2′), 55.5 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 40.2 (CH_2-4), 32.1 (CH_2-1′), 30.6 (CH_2-furan), 25.7 (CH_3-*t*Bu), 17.9 (C-*t*Bu), −4.1 (CH_3-Si), −4.8 (CH_3-Si); MS (ESI) [*m*/*z*, (%)]: 543 (M^+ + Na, 100), 521 (M^+ + 1, 18); HRMS (ESI): 543.2748 calcd for $C_{28}H_{44}NaO_7Si$, found 543.2745.

Compound **18**. Yellow liquid, R_f: 0.16 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 3469.31, 2953.45, 2930.31, 2882.78, 2856.06, 1513.85, 1034.62; $[\alpha]_D^{30}$ = −6.13 (*c* 1.75, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.25 (2H, d, *J* = 8.6 Hz, Ho-PMB), 6.87 (2H, d, *J* = 8.6 Hz, Hm-PMB), 5.79 (1H, ddd, *J* = 17.1, 10.3, 6.6 Hz, H-7), 5.15 (1H, d, 17.1 Hz, H-8), 5.06 (1H, d, 10.3 Hz, H-8), 4.67 (1H, d, *J* = 6.8 Hz, CH_2-MOM), 4.61 (1H, d, *J* = 6.8 Hz, CH_2-MOM), 4.45 (2H, s, CH_2-PMP), 4.29 (1H, dd, *J* = 12.2, 6.6 Hz, H-6), 3.79 (3H, s, OCH_3-PMB), 3.75 (1H, ddd, *J* = 12.3, 5.8, 3.1 Hz, H-4), 3.62 (3H, m, H-3, 2H-1), 3.40 (3H, s, OCH_3-MOM), 1.86 (1H, m, H-5), 1.74 (2H, m, 2H-2), 1.62 (1H, ddd, *J* = 14.3, 7.5, 3.8 Hz, H-5), 0.89 (9H, s, CH_3-^{t}Bu), 0.06 (3H, s, CH_3-Si), 0.04 (3H, s, CH_3-Si); ^{13}C-NMR ($CDCl_3$, δ): 159.1 (Cp-PMB), 141.0 (CH-7), 130.3 (C-PMB), 129.2 (CHo-PMB), 114.5 (CH_2-8), 113.7 (CHm-PMB), 97.2 (CH_2-MOM), 80.5 (CH-3), 72.7 (CH_2-PMP), 71.4 (CH-4, CH-6), 71.3 (CH-4, CH-6), 67.9 (CH_2-1), 55.7 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 39.3 (CH_2-5), 31.8 (CH_2-2), 25.8 (CH_3-^{t}Bu), 18.1 (C-^{t}Bu), −4.4 (CH_3-Si), −4.9 (CH_3-Si); MS (ESI) [*m*/*z*, (%)]: 477 (M^+ + Na, 100), 455 (M^+ + 1, 76); HRMS (ESI): 477.2642 calcd for $C_{24}H_{42}NaO_6Si$, found 477.2638.

(2′*R*,3′*S*,5′*R*,6′*S*)-5-[3′-(*tert*-Butyldimethylsilyloxy)-6′-(2″-*p*-methoxybenzyloxyethyl)-5′-(methoxymethoxy)-1′-(tetrahydro-2*H*-pyran-2-yl)methyl]-5-methoxy-5*H*-furan-2-one (26). A solution of compound **9** (370 mg, 0.71 mmol) and a catalytic amount of 4,5,6,7-tetrachloro-2′,4′,5′,7′-tetraiodofluorescein disodium salt (Rose Bengal) in MeOH (5 mL), previously purged with O_2, was cooled at −78 °C, irradiated with a 200 W lamp for 1 h, and stirred under an oxygen atmosphere. The solvent was evaporated, and the residue was rapidly filtered through a column on silica gel (50% EtOAc–hexane) in order to get rid of the catalyst. After solvent evaporation the residue was dissolved in pyridine (4 mL) and Ac_2O (452 μL) and DMAP (catalytic) were added at 0 °C. The reaction mixture was stirred for 12 h at room temperature, then water (20 mL) was added and the product was extracted with EtOAc (3 × 20 mL). The combined organic phases were washed with a 10% aqueous solution of HCl (2 × 50 mL) and brine (50 mL), dried over Na_2SO_4 and the solvent was filtered and evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc–hexane as the eluent, affording compound **26** (305 mg, 76%) as a colourless liquid; R_f: 0.27 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2953.45, 2932.23, 2886.92, 2857.99, 1776.12, 1249.65, 1100.19; ^{1}H-NMR ($CDCl_3$, δ): (major diastereomer); 7.25 (2H, m, Ho-PMB), 7.00 (1H, d, *J* = 5.6 Hz, H-4), 6.87 (2H, m, Hm-PMB), 5.93 (1H, d, *J* = 5.6 Hz, H-3), 4.69 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.58 (1H, d, *J* = 6.9 Hz, CH_2-MOM), 4.44 (2H, s, CH_2-PMP), 3.78 (3H, s, OCH_3-PMB), 3.54 (1H, dd, *J* = 7.3 5.8 Hz), 3.45 (2H, m), 3.34 (3H, s, OCH_3-MOM), 3.26 (2H, m), 3.18 (1H, s, OCH_3),

2.90 (1H, m), 2.71 (1H, m, H-1), 2.38 (1H, m, H-1), 2.16 (2H, m, H-1″, H-4′), 1.49 (2H, m, H-1″, H-4′), 0.87 (9H, s, CH_3-*t*Bu), 0.05 (6H, s, CH_3-Si); ^{13}C-NMR ($CDCl_3$, δ):(major diastereomer); 170.1 (C═O), 159.1 (Cp-PMB), 155.3 (CH-4), 130.3 (C-PMB), 129.2 (CHo-PMB), 122.4 (CH-3), 113.7 (CHm-PMB), 110.0 (C-5), 95.2 (CH_2-MOM), 77.5 (CH-6′), 77.2 (CH-2′), 74.4 (CH_2-PMB), 72.5 (CH-5′), 69.6 (CH-3′), 66.5 (CH_2-2″), 55.5 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 51.1 (OCH_3), 39.9 (CH_2-4′), 39.3 (CH_2-1), 31.9 (CH_2-1″), 25.6 (CH_3-^{t}Bu), 17.8 (C-^{t}Bu), −4.1 (CH_3-Si), −4.8 (CH_3-Si); MS (ESI) [*m*/*z*, (%)]: 589 (M^+ + Na, 100); HRMS (ESI): 589.2803 calcd for $C_{29}H_{46}NaO_9Si$, found 589.2801.

(1*S*,3*R*,7*R*,9*R*,11*S*,12*R*)-7-Methoxy-11-(2′-*p*-methoxybenzyloxyethyl)-12-(methoxymethoxy)-2,6,10-trioxytricyclic[7,4,0,03,7]tridecan-5-one (6) and (1*S*,3*R*,7*R*,9*R*,11*S*,12*R*)-7-hydroxy-11-(2′-*p*-methoxybenzyloxyethyl)-12-(methoxymethoxy)-2,6,10-trioxytricyclic[7,4,0,03,7]tridecan-5-one (5). To a solution of **26** (275 mg, 0.49 mmol) in THF (2 mL) was added TBAF (1.47 mL of a 1 M solution in THF, 1.47 mmol) and the mixture was stirred at room temperature for 24 h. Then it was quenched with an aqueous saturated solution of NH_4Cl (10 mL) and the product was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 5% EtOAc–hexane as the eluent, affording compound **2** (129 mg, 60%) and compound **1** (40 mg, 20%).

Compound **6**: white solid; m.p. = 115 °C, R_f: 0.21 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2933.20, 2887.88, 1796.37, 1425.89, 1090.55, 1036.55; $[\alpha]_D^{21}$ = −39.88 (*c* 1.45, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.24 (2H, d, *J* = 8.6 Hz, Ho-PMB), 6.87 (2H, d, *J* = 8.6 Hz, Hm-PMB), 4.68 (1H, d, *J* = 6.9 Hz, CH_2-OMOM), 4.59 (1H, d, *J* = 6.9 Hz, CH_2-OMOM), 4.47 (1H, d, *J* = 11.7 Hz, CH_2-PMB), 4.38 (1H, d, *J* = 11.7 Hz, CH_2-PMB), 3.96 (1H, d, *J* = 4.4 Hz, H-9), 3.80 (3H, s, OCH_3-PMB), 3.55 (2H, m, 2H-2′), 3.36 (3H, s, OCH_3), 3.34 (3H, s, OCH_3-OMOM), 3.32 (2H, m, H-1, H-11), 3.07 (2H, m, H-3, H-12), 2.88 (1H, dd, *J* = 17.3, 4.5 Hz, H-8), 2.72 (1H, dd, *J* = 13.1, 4.5 Hz, H-4), 2.45 (1H, m, H-13), 2.39 (1H, d, *J* = 17.3 Hz, H-8), 2.16 (1H, m, H-1′), 1.57 (2H, m, H-1′, H-4), 1.43 (1H, m, H-13); ^{13}C-NMR ($CDCl_3$, δ): 175.1 (C═O), 159.1 (Cp-PMB), 130.5 (C-PMB), 129.2 (CHo-PMB), 113.6 (CHm-PMB), 106.5 (C-7), 95.4 (CH_2-MOM), 77.4 (CH-1), 76.7 (CH-9), 74.6 (CH-11), 73.8 (CH-12), 73.0 (CH-3), 72.4 (CH_2-PMP), 65.8 (CH_2-2′), 55.6 (OCH_3-OMOM), 55.2 (OCH_3-PMB), 49.8 (OCH_3), 36.3 (CH_2-8), 35.6 (CH_2-13), 33.6 (CH_2-4), 31.9 (CH_2-1′); MS (ESI) [*m*/*z*, (%)]: 476 (M^+ + 1 + Na, 31), 475 (M^+ + Na, 100), 338 (44); HRMS (ESI): 475.1911 calcd for $C_{23}H_{32}NaO_9$, found 475.1917.

Compound **5**: white solid; m.p. = 140–143 °C, R_f: 0.13 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 3359.39, 2928.38, 1785.76, 1729.83, 1611.23, 1512.88, 1105.98, 1037.52, 909.27, 822.49; $[\alpha]_D^{21}$ = −25.6 (*c* 1.0, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.25 (2H, d, *J* = 7.2 Hz, Ho-PMB), 6.91 (2H, d, *J* = 8.8 Hz, Hm-PMB), 4.65 (2H, m, CH_2-OMOM), 4.44 (2H, m, CH_2-PMP), 4.03 (1H, d, *J* = 4.3 Hz, H-3), 3.82 (3H, s, CH_3-PMB), 3.56 (2H, m, H-2′), 3.35 (3H, s, CH_3-OMOM), 3.09 (2H, m), 2.95 (1H, m), 2.51 (4H, m), 2.16 (2H, m), 1.75 (1H, m), 1.57 (2H, m), 0.86 (1H, m); ^{13}C-NMR ($CDCl_3$, δ): 175.36 (C-5), 159.23 (C-PMB), 130.65 (C-PMB), 129.54 (CHo-PMB), 113.90 (CHm-PMB), 104.24 (C-7), 95.61 (CH_2-OMOM), 77.41 (CH), 76.58 (CH), 74.71 (CH), 74.06 (CH), 73.04 (CH), 72.47 (CH_2-PMB), 65.89 (CH_2-2′), 55.71 (CH_3-OMOM), 55.36 (CH_3-PMB), 38.04 (CH_2), 36.33 (CH_2), 35.68 (CH_2), 31.89 (CH_2); MS (ESI) [*m*/*z*, (%)]: 503.18 (26), 461.17 (M^+ + 1 + Na, 100), 445.18 (10); HRMS (ESI): 475.17962 calcd for $C_{22}H_{30}NaO_9$, found 461.17820.

(1*S*,3*R*,7*R*,9*R*,11*S*,12*R*)-7-Acetoxy-11-(2′-*p*-methoxybenzyloxyethyl)-12-(methoxymethoxy)-2,6,10-trioxytricyclic[7,4,0,03,7]tridecan-5-one (27). To a solution of alcohol (**1**) (25 mg, 0.06 mmol) in DCM (1.0 mL) was added Py (77 μL, 0.30 mmol) and Ac_2O (13 μL, 0.12 mmol) at r.t. The reaction mixture was stirred at r.t. for 16 h. Then it was quenched with water (5 mL) and the product was extracted with EtOAc (3 × 10 mL). The combined organic phases were dried, filtered and evaporated to give a residue which was chromatographed on silica gel using 10% EtOAc–hexane as the eluent, affording compound **27** (23 mg, 80%) as a colourless oil; R_f: 0.13 (20% EtOAc–hexane); IR (NaCl, cm^{-1}): 2932.58, 1789.23, 1732.56, 1611.87, 1513.45, 1039.26, 825.36; $[\alpha]_D^{21}$ = −45.5 (*c* 1.0, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, δ): 7.24 (2H, d, *J* = 8.7 Hz, Ho-PMB), 6.85 (2H, d, *J* = 8.7 Hz, Hm-PMB), 4.41 (4H, m, CH_2-OMOM, CH_2-PMP), 3.95 (1H, d, *J* = 3.9 Hz, H-3), 3.71–3.56 (2H, m; CH-2′), 3.38 (3H, s, CH_3-PMB), 3.30 (1H, m, H-11), 3.24–3.12 (3H, m, H-12, H-8), 3.10 (3H, s, CH_3-OMOM), 2.97 (1H, m, H-9), 2.81 (1H, m, H-1), 2.31 (2H, m, 1H-13, 1H-1′), 2.22 (1H, m, H-4), 2.09 (1H, m, H-4), 1.68 (1H, m, 1H-1′), 1.38 (3H, s, CH_3-OAc), 1.30 (1H, m, 1H-13); ^{13}C-NMR ($CDCl_3$, δ): 173.24 (C-OAc), 167.74 (C═O), 159.82 (C-PMB), 131.34 (C-PMB), 129.46 (Co-PMB), 114.13 (Cm-PMB), 106.70 (C-7), 95.57 (CH_2-OMOM), 77.55 (CH-11), 75.16 (CH-12, CH-3), 74.20 (CH-1), 73.07 (CH-9), 72.83 (CH_2-PMP), 66.28 (CH_2-2′), 55.32 (CH_3-OMOM), 54.87 (CH_3-PMB), 35.95 (CH_2-13), 35.11 (CH_2-8), 35.00 (CH_2-4), 32.71 (CH-1′), 21.01 (CH_3-OAc); MS (ESI) [*m*/*z*, (%)]: 503.23 (M^+ + 1 + Na, 100), 427.25 (13), 415.89 (28); HRMS (ESI): 503.14856 calcd for $C_{24}H_{32}NaO_{10}$, found 503.14867.

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Notes and references

1 (*a*) Y. Shimizu, *Chem. Rev.*, 1993, **93**, 1685–1698; (*b*) E. Alvarez, M.-L. Candenas, R. Pérez, J. Ravelo and J. D. Martín, *Chem. Rev.*, 1995, **95**, 1953–1980; (*c*) K. Fujiwara, N. Hayashi, T. Tokiwano and A. Murai, *Heterocycles*, 1999, **50**, 561–593; (*d*) M. Murata and T. Yasumoto, *Nat. Prod. Rep.*, 2000, **17**, 293–314; (*e*) T. Yasumoto, *Chem. Rec.*, 2001, **1**, 228–242;

(*f*) F. P. Marmsater and F. G. West, *Chem. – Eur. J.*, 2002, **8**, 4346–4353; (*g*) T. Nakata, *Chem. Rev.*, 2005, **105**, 4314–4347; (*h*) A. R. Gallimore and J. B. Spencer, *Angew. Chem., Int. Ed.*, 2006, **45**, 4406–4413; (*i*) M. Sasaki and H. Fuwa, *Nat. Prod. Rep.*, 2008, **25**, 401–426; (*j*) K. C. Nicolaou, M. O. Frederick and R. J. Aversa, *Angew. Chem., Int. Ed.*, 2008, **47**, 7182–7225; (*k*) M. Isobe and A. Hamajima, *Nat. Prod. Rep.*, 2010, **27**, 1204–1226.

2 (*a*) K. C. Nicolaou, F. P. J. T. Rutjes, E. A. Theodorakis, J. Tiebes, M. Sato and E. Untersteller, *J. Am. Chem. Soc.*, 1995, **117**, 10252–10263; (*b*) K. C. Nicolaou, *Angew. Chem., Int. Ed.*, 1996, **35**, 589–607; (*c*) K. C. Nicolaou, Z. Yang, G.-Q. Shi, J. L. Gunzner, K. A. Agrios and P. Gartner, *Nature*, 1998, **392**, 264–269; (*d*) K. C. Nicolaou, J. L. Gunzner, G.-Q. Shi, K. A. Agrios, P. Gartner and Z. Yang, *Chem. – Eur. J.*, 1999, **5**, 646–658; (*e*) G. Matsuo, K. Kawamura, N. Hori, H. Matsukura and T. Nakata, *J. Am. Chem. Soc.*, 2004, **126**, 14374–14376.

3 (*a*) M. Hirama, T. Oishi, H. Uehara, M. Inoue, M. Maruyama, H. Oguri and M. Satake, *Science*, 2001, **294**, 1904–1907; (*b*) M. Inoue and M. Hirama, *Acc. Chem. Res.*, 2004, **37**, 961–968.

4 (*a*) M. Murata, M. Kumagai, J. S. Lee and T. Yasumoto, *Tetrahedron Lett.*, 1987, **28**, 5869–5872; (*b*) M. Satake, K. Terasawa, Y. Kadowaki and T. Yasumoto, *Tetrahedron Lett.*, 1996, **37**, 5955–5958; (*c*) H. Takahashi, T. Kusumi, Y. Kan, M. Satake and T. Yasumoto, *Tetrahedron Lett.*, 1996, **37**, 7087–7090; (*d*) B. M. Trost and Y. H. Rhee, *Org. Lett.*, 2004, **6**, 4311–4313.

5 (*a*) Y. Fall, B. Vidal, D. Alonso and G. Gómez, *Tetrahedron Lett.*, 2003, **44**, 4467–4469; (*b*) For the mechanism involved in the photooxidation step see: *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*, ed. A. Berkessel, vol. 38, pp. 100–101; (*c*) D. Alonso, M. Pérez, G. Gómez, B. Covelo and Y. Fall, *Tetrahedron*, 2005, **61**, 2021–2026.

6 (*a*) M. Teijeira, P. L. Suárez, G. Gómez, C. Terán and Y. Fall, *Tetrahedron Lett.*, 2005, **46**, 5889–5892; (*b*) M. González, Z. Gándara, G. Pazos, G. Gómez and Y. Fall, *Synthesis*, 2013, 0625–0632.

7 (*a*) I. García, G. Gómez, M. Teijeira, C. Terán and Y. Fall, *Tetrahedron Lett.*, 2006, **47**, 1333–1335; (*b*) C. Álvarez, M. Pérez, A. Zúñiga, G. Gómez and Y. Fall, *Synthesis*, 2010, **22**, 3883–3890; (*c*) M. González, Z. Gándara, B. Covelo, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2011, **52**, 5983–5986; (*d*) M. González, Z. Gándara, A. Martínez, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2013, **54**, 3647–3650; (*e*) M. González, Z. Gándara, A. Martínez, G. Gómez and Y. Fall, *Synthesis*, 2013, 1693–1700.

8 P. Canoa, M. Pérez, B. Covelo, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2007, **48**, 3441–3443.

9 P. Canoa, N. Vega, M. Pérez, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2008, **49**, 1149–1151.

10 (*a*) G. Pazos, M. Pérez, Z. Gándara, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2009, **50**, 5285–5287; (*b*) G. Pazos, M. Pérez, Z. Gándara, G. Gómez and Y. Fall, *Tetrahedron*, 2012, **68**, 8994–9003.

11 Y. Mori and H. Hayashi, *J. Org. Chem.*, 2001, **66**, 8666–8668.

12 (*a*) G. Gómez, H. Rivera, I. García, L. Estévez and Y. Fall, *Tetrahedron Lett.*, 2005, **46**, 5819–5822; (*b*) I. García, M. Pérez, Z. Gándara, G. Gómez and Y. Fall, *Tetrahedron Lett.*, 2008, **49**, 3609–3612; (*c*) S. Boullosa, Z. Gándara, M. Pérez, G. Gómez and Y. Fall, *Tetrahedron*, 2008, **49**, 4040–4042.

13 Crystallographic data were collected on a Bruker Smart 1000 CCD diffractometer at CACTI (Universidade de Vigo) at 20 °C using graphite monochromated Mo Kα radiation (λ = 0.71073 Å), and were corrected for Lorentz and polarisation effects. The frames were integrated with the Bruker SAINT software package and the data were corrected for absorption using the program SADABS. The structures were solved by direct methods using the program SHELXS97. All non-hydrogen atoms were refined with anisotropic thermal parameters by full-matrix least-squares calculations on F^2 using the program SHELXL97. Hydrogen atoms were inserted at calculated positions and constrained with isotropic thermal parameters. The structural data are deposited with the Cambridge Crystallographic Data Centre (CCDC) with reference number CCDC 988171.

