Sequential radical cyclization of β-functionalized allyl bromomethyldimethylsilyl ethers. Application to the regio- and stereo-specific synthesis of an isoprostanoid precursor

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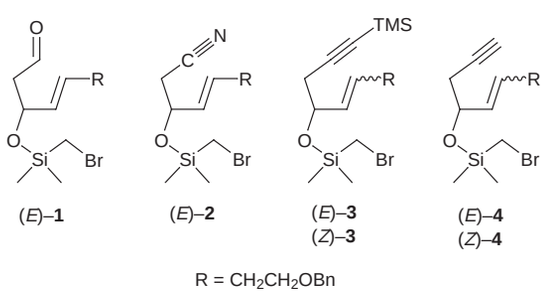
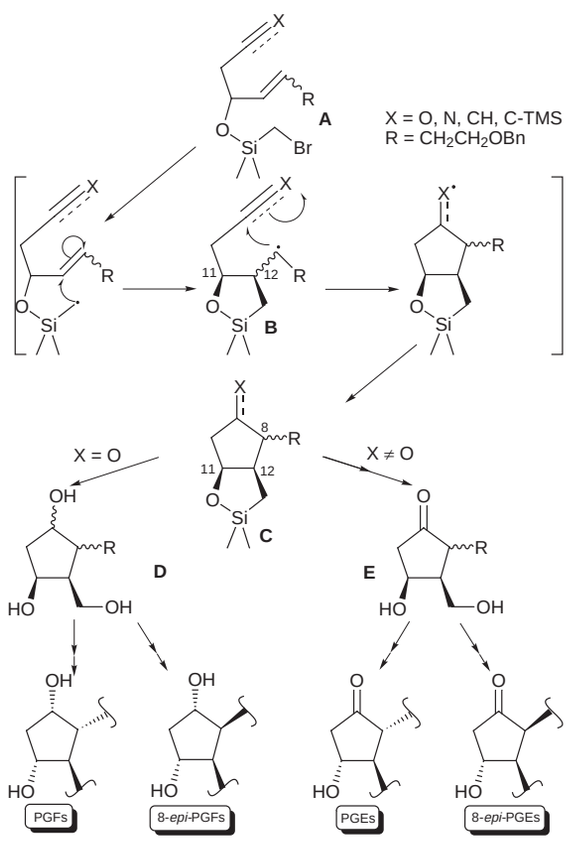
The behaviour of allyl bromomethyldimethylsilyl ethers β-substituted by various radical trapping functions (aldehyde, nitrile or acetylenic) is studied in tandem radical cyclizations. Only homopropargylic ethers (but-3-ynylic ethers) lead to the formation of cyclic compounds *via* a 5-*exo-trig*, 5-*exo-dig* or 5-*exo-trig*, 6-*endo-dig* mode. The influence of the TMS group located on the acetylenic moiety is shown to be determinant for the regio- and stereo-specific C5 ring closure (5-*exo-dig* mode).

Intra- and inter-molecular free radical reactions have proved in the past years to be valuable tools to create carbon–carbon bonds.[1–9] Their increasing use has contributed to a better knowledge of the factors which govern their outcome in terms of regio- and stereo-selectivity.[10–12] The emergence of serial radical cyclizations has attracted much attention for the obtention of natural and unnatural polycyclic molecules with high regio- and stereo-control.[6,10,13–17] The use of the temporary silicon connection approach allowing the introduction of a hydroxymethyl equivalent to a stereogenic olefinic center has received considerable attention in recent years.[18–22] This paper is devoted to the study of the behaviour of the six racemic allylic bromomethyldimethylsilyl ethers **1**–**4** in sequential radical cyclizations, using



both the well-known tri-*n*-butyltin hydride method and a tethered silicon reactant in order to obtain functionalized cyclic precursors of (iso)prostanoid targets of biological interest.[23–25] We focused our efforts on the elaboration of a new synthetic approach (Scheme 1) leading to PGFs (or isoPGFs) and PGEs (or isoPGEs) starting from a single acyclic chiral template **A**, which differs only in its terminal function (C≡X). The key step of this strategy is the radical cascade cyclization under the 5-*exo-trig*, 5-*exo-dig* (or *trig*) mode, applied to allylic bromomethyldimethylsilyl ethers **A** (Stork–Nishiyama reaction). The first 5-*exo-trig* cyclization provides the two isomeric *trans* and *cis* silafuran radicals **B**; the latter gives, after a 5-*exo* cyclization and hydrogen atom transfer, the bicyclo[3.3.0]octane **C**, where the benzyloxyethyl chain located on the C_8 carbon (PGs numbering) adopts either an *endo* or an *exo* configuration, which has to be determined. Finally, further steps give either a disubstituted cyclopentanediol **D** (from aldehydic moiety) or a disubstituted 4-hydroxycyclopentanone **E** (from nitrile and

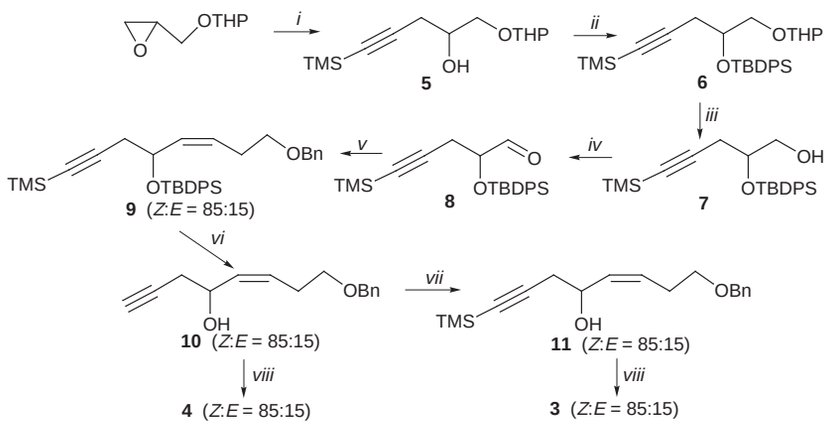


Scheme 1

acetylenic functions) to reach respectively (iso)PGFs and (iso)PGEs frameworks.

Results

The syntheses of silylated ethers **1**–**4** of *E* configuration have been reported in a preliminary paper;[26] the homopropargylic silyl ethers (*Z*)-**3** and (*Z*)-**4** were prepared from glycidol as shown in Scheme 2. For comparison purposes all the radical cyclizations were performed using similar experimental conditions, using tri-*n*-butyltin hydride with a motor-driven syringe

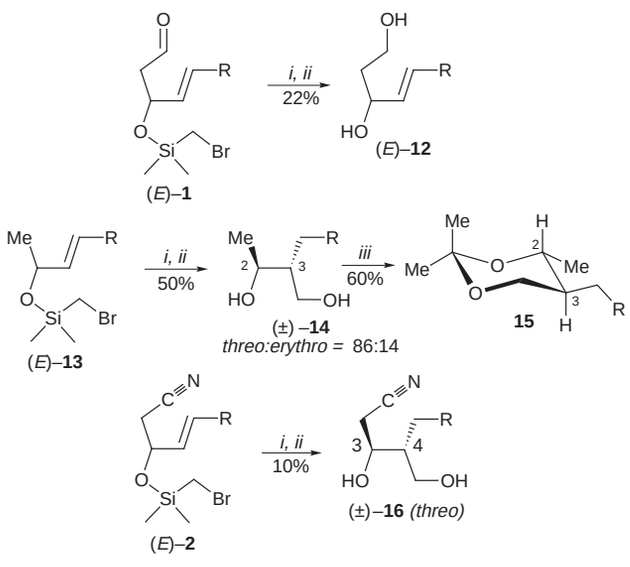


Scheme 2 *Reagents and conditions*: i, trimethylsilylacetylene (3 equiv.), Bu^{n}Li (3.1 equiv.), tetrahydropyranylglycidol (ref. 27) (1 equiv.), THF, −78 °C to reflux, 20 h (70%); ii, TBDPSCl (1.5 equiv.), imidazole (2 equiv.), DMAP (0.1 equiv.), THF, room temp., 24 h (96%); iii, Ogawa procedure (ref. 28: Me_2AlCl (2 equiv.), dichloromethane, −30 °C to room temp., 7.5 h (93%); iv, Swern (quant.); v, I^- $Ph_3P^+(CH_2)_3OBn$ (ref. 29) (1.7 equiv.), $(TMS)_2NNa$ (3 equiv.), toluene, −78 °C to room temp., 3 h (85%) (*Z*:*E* = 85:15); vi, TBAF (2 equiv.), THF, 0 °C, 4 h (89%) (*Z*:*E* = 85:15); vii, Bu^{n}Li (2.2 equiv.), TMSCl (5 equiv.), NaI (0.1 equiv.), THF, −78 °C to reflux, 2 h (51%) (*Z*:*E* = 85:15); viii, $BrCH_2SiMe_2Cl$ (1 equiv.), Et_3N (1.1 equiv.), DMAP (0.1 equiv.), dichloromethane, 0 °C, 2 h (quant.) (*Z*:*E* = 85:15).

for better control of the hydride–AIBN addition speed (v_{add} = 2×10^{-4} mol h^{-1}). The crude silafuran intermediates were directly subjected to the standard Tamao oxidation. The yields of acyclic and cyclic diols were generally low and this was partly due to the tedious separation (very close R_f) and the necessary two or three successive chromatographic separations for the removal of tin byproducts.

Radical cyclization of allyl ethers (*E*)-1, (*E*)-13 and (*E*)-2

When the aldehyde ether (*E*)-**1** was submitted to the above cyclization conditions, it did not undergo any ring closure but gave the reduction compound (*E*)-**12** as the sole isolated product (22% yield) (Scheme 3). Furthermore, the catalytic tin

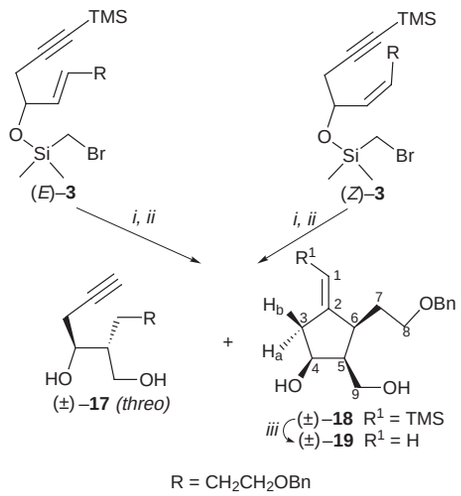


Scheme 3 *Reagents and conditions*: i, $HSnBu_3$ (1.3 equiv.), AIBN (0.2 equiv.), benzene, reflux, 12 h; ii, H_2O_2 (2.6 equiv.), KF (7.7 equiv.), DMF, 60 °C, 5 h.

hydride method developed by Stork [tri-*n*-butyltin chloride (Bu$^n_3$SnCl), sodium cyanoborohydride ($NaBH_3CN$), AIBN, Bu^{t}OH, reflux][30] afforded a similar result. The possible implication of the carbonyl function accounted for these disappointing results and led us to attempt the same typical reaction on ether (*E*)-**13**, which was lacking an aldehydic moiety (product obtained by the 1,2-addition of methyllithium to (*E*)-benzyloxypent-2-enal and subsequent standard etherification). This time, we were able to isolate the 5-*exo-trig* cyclization product **14** as a diastereomeric mixture (50% yield) in an 86:14 ratio (*threo*:*erythro*), which was determined by a careful ^{1}H NMR study of the corresponding 1,3-dioxane derivative mixture **15** (major *threo* isomer: $J_{2a\text{-}3a}$ 9.9 Hz). This outcome, in complete accordance with the pioneering Nishiyama stereochemical results,[18] showed that the aldehyde function was responsible for the absence of 5-*exo-trig* ring closure from (*E*)-**1**, and this result could be explained by an exclusive pathway proceeding with the formation of a transient *O*-stannyl ketyl species[31–33] which was not susceptible to a further evolution through the disfavoured 5-*endo-trig* cyclization mode[34] according to Baldwin's rules.[35] The radical cyclization of the nitrile ether (*E*)-**2** was carried out under conditions similar to those described above, and a single 5-*exo-trig* cyclization diol **16** was isolated (10% yield), the configuration of which was assumed to be *threo* by comparison with **14**, since its ^{1}H NMR spectrum did not allow us to measure the $J_{3\text{-}4}$ coupling constant due to unresolved overlapping signals. The nitrile function seemed to be slightly more favourable than the aldehyde for the first 5-*exo-trig* ring closure step, but the second 5-*exo-dig* cyclization was not observed; both aldehyde and nitrile functions apparently acted as poor radical traps,[36] even if some authors succeeded in serial radical cyclizations involving cyclic related structures.[37,38]

Radical cyclization of allyl homopropargyl ethers (*E*/*Z*)-3 and (*E*/*Z*)-4

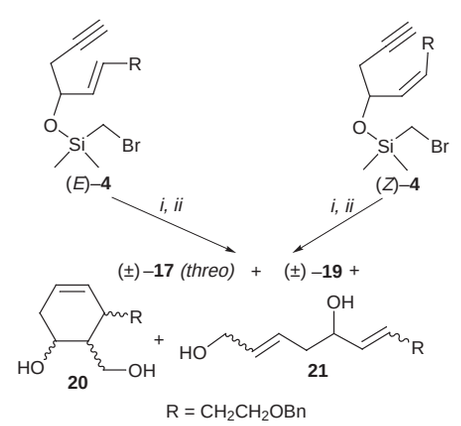
Tandem radical cyclizations involving a 5-*exo-dig*, 5-*exo-trig* process from an initial carbon-centered α-silicon radical have been well documented.[39] Our attempts focus on the reverse strategy, 5-*exo-trig*, 5-*exo-dig*, where the acetylenic function acts as the final radical trap, and to the best of our knowledge this approach in the field of silicon-tethered reactions is unprecedented. We have reported our preliminary results[40] on the cascade radical cyclization of silyl ethers **3** bearing a TMS group at the distal propargylic position. Both ethers (*E*)-**3** and (*Z*)-**3** underwent successive radical cyclizations *via* a 5-*exo-trig*, 5-*exo-dig* mode and afforded the expected TMS-vinylcyclopentanol **18** (30% yield) with total regio- and stereo-control together with the desilylated acyclic *threo* diol **17** (10% yield) as a byproduct (Scheme 4). The all *cis* stereochemistry of the substituted five-membered ring **18** was established *via* chemical and NMR spectroscopic evidence. Firstly, only the *cis* silafuran radical **B** (Scheme 1, X = C-TMS) was able to undergo a cyclization *via* a 5-*exo-dig* mode and this was established for obvious geometrical reasons; consequently the silafuran radical **B** afforded the transient bicyclo[3.3.0]octane **C** implying a neces-



Scheme 4 *Reagents and conditions*: i, $HSnBu_3$ (1.3 equiv.), AIBN (0.2 equiv.), benzene, reflux, 12 h; ii, H_2O_2 (2.65 equiv.), KF (7.74 equiv.), DMF, 60 °C, 5 h; iii, $PhSO_2H$ (1 equiv.), acetonitrile–water (50 : 1), room temp., 2 h.

sary *cis* relationship between the resulting hydroxy and hydroxymethyl groups located respectively at the C_4 and C_5 positions. At this stage the relative configuration of H_5 and H_6 remained to be determined. NMR study of compound **18** in [^{2}H]chloroform and [$^2H_6$]benzene at 250 and 400 MHz, by the way of COSY, COSYLR and ^{1}H/^{13}C-HMQC pulse sequences, allowed all the ^{1}H and ^{13}C signals to be assigned. Due to strong mixing of signals, the obtention of $J_{5\text{-}6}$ required some simulation experiments[41,42] of the 9-spin system of hydrogens H_4, H_5, H_{9a}, H_{9b}, H_6, H_{7a}, H_{7b}, H_{8a} and H_{8b}. The large value found, 9.3 Hz, suggested a *cis* arrangement of H_5 and H_6, as for H_4 and H_5 ($J_{4\text{-}5}$ 7.7 Hz). The relative configuration of C_6 has been confirmed by the detection of a small NOE enhancement of signals of H_4 and H_1 under saturation of H_6 and by a similar enhancement of $H_{3\alpha}$, H_5 and H_6 under saturation of H_4. These experiments proved at the same time the assignment of the pair $H_{3\alpha}/H_{3\beta}$ and the *E* configuration of the double bond C_1–C_2.

Both silylated ethers (*E*)-**4** and (*Z*)-**4** were subjected to the standard cascade radical cyclization conditions and each of them gave an acyclic diol (**17**, 16% isolated yield) and an inseparable mixture (48% overall yield) of three compounds (**19**, **20**, **21**) made of two cyclic derivatives together with another acyclic compound (Scheme 5). First of all, the all-*cis*



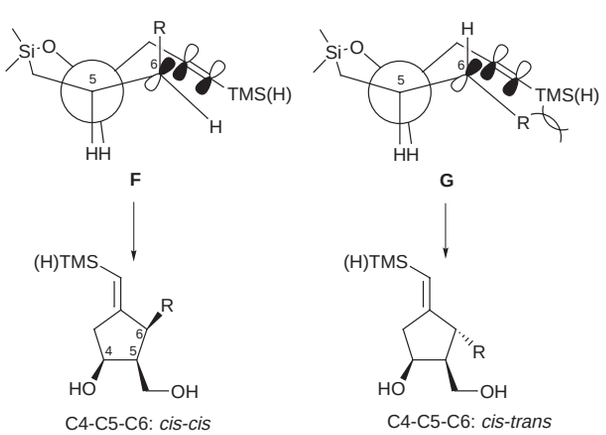
Scheme 5 *Reagents and conditions*: see Scheme 4.

vinylcyclopentanol **19** (14%) was identified and came from a 5-*exo-trig*, 5-*exo-dig* cyclization. The structure and stereochemistry of **19** were ascertained by comparison with an authentic sample obtained after the removal of the TMS protecting group of **18** by an acidic treatment[43] (benzenesulfinic acid, acetonitrile–water, 24% yield) (Scheme 4); some relevant characteristic ^{1}H and ^{13}C NMR data for **19** are worth noting: two ethylenic hydrogens as singlets at 4.65 and 4.80 ppm with the corresponding CH_2 C_1 signal at 107.5 ppm (*versus* a *C*H signal at 120.5 ppm in **18**). Furthermore, we identified a single substituted cyclohexenol **20** (15%), which originated from a 5-*exo-trig*, 6-*endo-dig* mode cyclization, by means of two ^{1}H signals at 5.55 and 5.61 ppm bearing the coupling constant typical of a cyclohexene ring and by two ^{13}C signals of *C*H type at 123.4 and 130.0 ppm. The *cis* or *trans* arrangement of the hydroxy and hydroxymethyl groups, located at the 1 and 2 positions respectively, cannot be chemically resolved as easily as in the case of **18**, which derives from a necessary *cis* junction in the parent bicyclo[3.3.0]octane, while it can be either *cis* or *trans* in the bicyclo[4.3.0]nonane leading to **20**. The complexity of the ^{1}H NMR spectra due to strong mixing of signals did not allow us to gain additional data to ascertain the relative configurations of the three stereogenic centers of **20**. Finally, we identified a third minor compound **21** (5%) whose linear structure has been determined from its ^{1}H COSY spectra. This acyclic dienediol would be the result of a 7-*endo-dig* cyclization[44] involving the reaction of the α-silyl radical with the distal position of the acetylenic function. Finally, the acyclic diol **17** already characterized in the preceding radical cyclization of ethers (*E*)-**3** and (*Z*)-**3** was isolated in 16% yield.

Discussion

Regioselectivity (5-*exo-dig vs.* 6-*endo-dig*) and stereoselectivity of the second radical cyclization step

The above results showed that an acetylenic silyl ether protected with a TMS group underwent a regio- and stereo-specific 5-*exo-trig*, 5-*exo-dig* cyclization leading to the all *cis* substituted cyclopentanol **18**; in the case where the TMS group was missing from the acetylenic moiety, the cyclization was less regioselective (formation of one C5 ring **19** and one C6 ring **20**) but remained stereoselective since only one diastereomer was formed in each case. In hexyn-5-yl radical cyclizations, the 5-*exo-dig* mode generally predominated[45] and to the best of our knowledge, only three examples of 6-*endo-dig* cyclizations have been reported as minor processes by Hart,[46] Hoffmann[47] and Marco-Contelles.[48] In our case, the regioselectivity of the second radical cyclization (**B**→**C**) could partially be due to the steric effect[46] of the TMS group, favouring the 5-*exo-dig* mode by impeding the approach of the incoming radical on the acetylenic terminus (6-*endo-dig* mode). If we assume an early transition state, as is generally expected[2,36] for radical cyclizations, one set of transition states (**F**, **G**) involving a *cis* junction of the intermediate silafuran **B** could be considered in the case of the TMS-containing ethers **3** (Scheme 6). The orbital overlap is



Scheme 6

appropriate for C5 ring formation but not for C6 ring closure. Moreover, the strong steric interaction developing between the

R and TMS groups in model **G** favours the transition state **F** (weaker interaction H_6/TMS) towards the stereoselective formation of the all *cis* TMS-vinylcyclopentanol **18**, and this result is in accordance with experience.

Experimental

Elemental analyses were performed by the 'Service de Microanalyse de l'Ecole Supérieure de Chimie de Montpellier'. ^{1}H NMR and ^{13}C NMR spectra were determined on a Bruker AC 250 or AC 400 spectrometer; *J* values are in Hz. Mass spectra were obtained with a JEOL JMS-DX-300 by the FAB ionization method with thioglycerol (GT) or *p*-nitrobenzyl alcohol (NBA) as the matrix.

1-Tetrahydropyranyloxy-5-trimethylsilylpent-4-yn-2-ol 5

To a stirred solution of *n*-butyllithium (1.6 mol dm^{-3} in hexanes) in anhydrous THF (32 cm^3, 52 mmol) under argon, trimethylsilylacetylene (5 g, 51 mmol) was added at 0 °C. After 30 min, tetrahydropyranylglycidol[27] (2.63 g, 16.7 mmol) dissolved in THF (10 cm^3) was added at −78 °C and the reaction refluxed for 20 h. After hydrolysis with water (17 cm^3) at 0 °C, the aqueous phase was extracted with diethyl ether, the organic phases dried on Na_2SO_4 and the solvents evaporated under reduced pressure. Chromatography on silica gel and elution with hexane–diethyl ether (9:1) afforded the *title compound* as an oily diastereomeric mixture (1:1) (2.98 g, 70%); R_f 0.42 [hexane–diethyl ether (6:4), 2 elutions]; δ_H(400 MHz; $CDCl_3$) 0.0 (9 H, s, Me_{TMS}), 1.4–1.8 (6 H, m, $CH_{2\text{-}THP}$), 2.27 (1 H, dd, $J_{3\text{-}3'}$ 16.8, $J_{3\text{-}4}$ 5.7, 3-H), 2.37 (1 H, dd, $J_{3'\text{-}3}$ 16.8, $J_{3'\text{-}4}$ 7.5, 3′-H), 2.78 (1 H, d, *J* 5.9, OH_a), 3.1 (1 H, d, *J* 3.9, OH_b), 3.37 (1 H, m, 2-H), 3.47 (1 H, dd, $J_{1\text{-}2}$ 7.0, $J_{1\text{-}1'}$ 10.9, 1-H), 3.65 (1 H, dd, $J_{1'\text{-}2}$ 3.6, $J_{1'\text{-}1}$ 10.6, 1′-H), 3.75 (2 H, m, CH_2O_{THP}), 4.43 (1 H, m, OCHO); δ_C(400 MHz, $CDCl_3$) 0.0 (3 C, Me_{TMS}), 20.2 (1 C, $CH_{2\text{-}THP}$), 24.5 (1 C, $CH_{2\text{-}THP}$), 26.3 (1 C, 3-C), 30.5 (1 C, $CH_{2\text{-}THP}$), 62.5 (1 C, 1-C), 68.3 (1 C, 4-C), 71.1 (1 C, CH_2O_{THP}), 86.5 (1 C, 2-C), 99.8 (1 C, OCHO) and 102.5 (1 C, 5-C); all signals except C_{TMS} and 2-C were split due to the diastereomeric mixture; *m*/*z* (GT) 257 $[M + H]^+$ (Found: C, 61.1; H, 9.2. $C_{13}H_{24}O_3Si$ requires C, 60.9; H, 9.4%).

1-Tetrahydropyranyloxy-2-*tert*-butyldiphenylsilyloxy-5-trimethylsilylpent-4-yne 6

To the alcohol **5** (5.48 g, 21.4 mmol) dissolved in THF (110 cm^3) were added at room temperature imidazole (2.9 g, 42.8 mmol), 4-dimethylaminopyridine (DMAP) (0.26 g, 2.1 mmol) and *tert*-butyldiphenylchlorosilane (TBDPSCl) (8.8 g, 32.1 mmol). After 24 h the reaction was hydrolyzed with water (10 cm^3) and extracted with diethyl ether. The organic phases were pooled, dried on Na_2SO_4 and concentrated under reduced pressure. Chromatography on silica gel and elution with hexane–diethyl ether (9:1) afforded the *title compound* as an oily diastereomeric mixture (1:1) (10.14 g, 96%); R_f 0.74 [hexane–diethyl ether (9:1)]; δ_H(400 MHz; $CDCl_3$) 0.15 (9 H, s, Me_{TMS}), 1.1 (9 H, s, Me_{tBu}), 1.3–1.8 (6 H, m, $CH_{2\text{-}THP}$), 2.45 (2 H, m, 3-H), 3.4 (2 H, m, CH_2O_{THP}), 4.05 (1 H, m, 2-H), 4.5 (1 H, dt, *J* 3.3, *J* 9.0, OCHO), 4.75 (2 H, m, 1-H), 7.4 (6 H, m, 4 × *m*-H and 2 × *p*-H) and 7.75 (4 H, m, 4 × *o*-H); δ_C(400 MHz, $CDCl_3$) 0.2 (3 C, Me_{TMS}), 20.1 (1 C, $C_{q\text{-}tBu}$), 20.8 (1 C, $CH_{2\text{-}THP}$), 26.1 (1 C, 3-C), 27.0 (1 C, $CH_{2\text{-}THP}$), 28.3 (3 C, Me_{tBu}), 31.5 (1 C, $CH_{2\text{-}THP}$), 60.4 (1 C, 1-C), 70.2 (1 C, CH_2O_{THP}), 71.5 (1 C, 2-C), 85.8 (1 C, 4-C), 99.3 (1 C, OCHO), 104.8 (1 C, 5-C) and 127.0–144.1 (12 C, aromatics); all signals except C_{TMS} and 2-C were split due to the diastereomeric mixture; *m*/*z* (NBA) 517 $[M + Na]^+$, 495 $[M + H]^+$ (Found: C, 70.2; H, 8.4. $C_{29}H_{42}O_3Si_2$ requires C, 70.4; H, 8.5%).

2-*tert*-Butyldiphenylsilyloxy-5-trimethylsilylpent-4-ynol 7

To compound **6** (5.43 g, 11 mmol) dissolved in anhydrous dichloromethane (40 cm^3) was added under argon at −30 °C dimethylaluminium chloride (1 mol dm^{-3} in hexanes) (22 cm^3, 22 mmol). After 3.5 h at this temperature and 4 h at room temperature the reaction was hydrolyzed with a saturated solution of $NaHCO_3$ at −20 °C and extracted with dichloromethane. The organic phases were dried on Na_2SO_4, pooled and concentrated *in vacuo*. The residual oil was chromatographed on silica gel with with hexane–diethyl ether (95:5) to give the *title compound* as an oil (4.18 g, 93%); R_f 0.16 [hexane–diethyl ether (9:1)]; δ_H[250 MHz; $(CD_3)_2SO$] 0.1 (9 H, s, Me_{TMS}), 1.0 (9 H, s, Me_{tBu}), 1.8 (1 H, t, *J* 5.4, OH), 2.4 (2 H, m, 3-H), 3.5 (2 H, m, 1-H), 3.75 (1 H, m, 2-H), 7.4 (6 H, m, 4 × *m*-H and 2 × *p*-H) and 7.75 (4 H, m, *o*-H); δ_C(400 MHz, $CDCl_3$) 0.2 (3 C, Me_{TMS}), 20.1 (1 C, $C_{q\text{-}tBu}$), 25.9 (1 C, 3-C), 27.0 (3 C, Me_{tBu}), 65.0 (1 C, 1-C), 70.9 (1 C, 2-C), 86.7 (1 C, 4-C), 104.6 (1 C, 5-C) and 127.7–146.0 (12 C, aromatics); *m*/*z* (NBA) 433 $[M + Na]^+$, 411 $[M + H]^+$ (Found: C, 69.9; H, 8.5. $C_{24}H_{34}O_2Si_2$ requires C, 70.2; H, 8.3%).

2-*tert*-Butyldiphenylsilyloxy-5-trimethylsilylpent-4-ynal 8

To a solution of oxalyl chloride (1.42 g, 11.21 mmol) in anhydrous dichloromethane (34 cm^3) cooled to −60 °C under nitrogen was added dimethyl sulfoxide (1.91 g, 24.47 mmol) in dichloromethane (5 cm^3). The reaction was stirred for 10 min at this temperature and the alcohol **7** (4.18 g, 10.19 mmol) dissolved in dichloromethane (11 cm^3) was added dropwise followed after 10 min by the addition of triethylamine (5.15 g, 51 mmol) over 5 min. The reaction was hydrolyzed at room temperature with water (42 cm^3) and extracted with dichloromethane. The organic phases were pooled, dried on Na_2SO_4 and concentrated under reduced pressure. Chromatography on silica gel with hexane–diethyl ether (9:1) gave the *title compound* as an oil (4.16 g, 100%); R_f 0.7 [hexane–diethyl ether (8:2)]; δ_H(250 MHz; $CDCl_3$) 0.1 (9 H, s, Me_{TMS}), 1.1 (9 H, s, Me_{tBu}), 2.55 (2 H, 2d, $J_{3\text{-}4}$ 5.9, $J_{3'\text{-}4}$ 7.1, 3-H), 4.1 (1 H, td, $J_{2\text{-}1}$ 1.3, $J_{2\text{-}3}$ 5.8, 2-H), 7.3 (6 H, m, 4 × *m*-H and 2 × *p*-H), 7.7 (4 H, m, *o*-H) and 9.6 (1 H, d, $J_{1\text{-}2}$ 1.3, 1-H); δ_C(400 MHz, $CDCl_3$) 0.2 (3 C, Me_{TMS}), 20.1 (1 C, $C_{q\text{-}tBu}$), 25.8 (1 C, 3-C), 27.7 (3 C, Me_{tBu}), 75.6 (1 C, 2-C), 86.7 (1 C, 4-C), 102.8 (1 C, 5-C), 127–135 (12 C, aromatics) and 203.2 (1 C, 1-C); *m*/*z* (NBA) 409 $[M + H]^+$ (Found: C, 70.3; H, 8.0. $C_{24}H_{32}O_2Si_2$ requires C, 70.5; H, 7.8%).

(*Z*)- and (*E*)-8-Benzyloxy-4-*tert*-butyldiphenylsilyloxy-1-trimethylsilyloct-5-en-1-yne 9

To a stirred solution of the phosphonium iodide $[I^-Ph_3P^+(CH_2)_3OBn]$[29] (448 mg, 0.83 mmol) in anhydrous toluene (3.7 cm^3) cooled to 0 °C was added dropwise under argon sodium bis(trimethylsilyl)amide (1 mol dm^{-3} in THF) (1.47 cm^3, 1.47 mmol). After 30 min at room temperature the solution was cooled to −78 °C and added dropwise to the aldehyde **8** (200 mg, 0.49 mmol) dissolved in toluene (7 cm^3). After acidic hydrolysis (HCl 1 mol dm^{-3}), the aqueous phase was extracted with diethyl ether and the pooled organic phases were dried on Na_2SO_4 and concentrated under reduced pressure. The crude residue was chromatographed on silica gel with hexane–diethyl ether (95:5) to give the *title compound* (*Z*:*E* = 85:15) as an oil (215 mg, 81%); R_f 0.71 [hexane–diethyl ether (8:2)]; δ_H(400 MHz; $CDCl_3$) 0.0 (9 H, s, Me_{TMS}), 0.95 (9 H, s, Me_{tBu}), 1.8 (2 H, m, 7-H), 2.3 (2 H, 2dd, $J_{3\text{-}3'}$ 16.2, $J_{3\text{-}4}$ 5.7, $J_{3'\text{-}4}$ 6.2, 3-H), 3.05 [2 H, t, $J_{8\text{-}7}$ 7.2, 8(*Z*)-H], 3.2 [2 H, t, $J_{8\text{-}7}$ 7.0, 8(*E*)-H], 4.25 (2 H, s, CH_2Ph_Z), 4.35 (2 H, s, CH_2Ph_E), 4.4 (1 H, m, 4-H), 5.2–5.35 [2 H, 2dt, $J_{6Z\text{-}5Z}$ 11.0, $J_{6E\text{-}5E}$ 15.7, $J_{6\text{-}7}$ 7.2, 6(*E*)-H and 6(*Z*)-H], 5.45–5.6 [2 H, 2dd, $J_{5Z\text{-}6Z}$ 11.0, $J_{5E\text{-}6E}$ 15.7, $J_{5\text{-}4}$ 9.3, 5(*E*)-H and 5(*Z*)-H] and 7.2–7.6 (15 H, m, aromatics); *Z* isomer δ_C(400 MHz, $CDCl_3$) 0.2 (3 C, Me_{TMS}), 19.8 (1 C, $C_{q\text{-}tBu}$), 26.5 (1 C, 3-C), 27.7 (3 C, Me_{tBu}), 30.2 (1 C, 7-C), 68.0 (1 C, 4-C), 69.5 (1 C, 8-C), 73.0 (1 C, CH_2Ph), 85.5 (1 C, 2-C), 103.7 (1 C, 1-C), 126.3 (1 C, 6-C), 127–136 (18 C, aromatics) and 138.5 (1 C,

5-C); *m/z* (NBA) 563[M + Na]$^+$, 541 [M + H]$^+$ (Found: C, 75.8; H, 8.3. $C_{34}H_{44}O_2Si_2$ requires C, 75.5; H, 8.2%).

(*Z*)- and (*E*)-8-Benzyloxyoct-5-en-1-yn-4-ol 10

To a stirred solution of the silylated ether **9** (941 mg, 1.74 mmol) in anhydrous THF (2 cm^3) cooled to 0 °C was added TBAF (1 mol dm^{-3} in THF) (3.5 cm^3, 3.5 mmol). After 4 h at room temperature the solution was concentrated under reduced pressure to give a residue which was then chromatographed on silica gel with hexane–diethyl ether (6:4) to give the *title compound* (*Z*:*E* = 85:15) as an oil (357 mg, 89%); R_f 0.19 [hexane–diethyl ether (6:4)]; δ_H(400 MHz; $CDCl_3$) 1.95 [1 H, t, $J_{1\text{-}3}$ 2.6, 1(*Z*)-H], 1.98 [1 H, t, $J_{1\text{-}3}$ 2.6, 1(*E*)-H], 2.25 (2 H, m, 7-H), 2.37 (1 H, m, 3-H), 2.5 (1 H, m, 3′-H), 2.7 (1 H, m, OH), 3.37 (1 H, m, 8-H), 3.46 (1 H, m, 8′-H), 4.2 [1 H, m, 4(*E*)-H], 4.45 (2 H, s, CH_2Ph), 4.55 [1 H, m, 4(*Z*)-H], 5.6 [2 H, m, 5-H and 6(*Z*)-H], 5.7 [1 H, dt, $J_{6\text{-}5}$ 15.6, $J_{6\text{-}7}$ 6.5, 6(*E*)-H] and 7.3 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) 26.1 [1 C, 3(*E*)-C], 26.6 [1 C, 3(*Z*)-C], 28.8 (1 C, 7-C), 63.0 (1 C, 1-C), 67.5 (1 C, 4-C), 69.0 (1C, 8-C), 71.5 (1 C, CH_2Ph), 79.8 [1 C, 2(*E*)-C], 80.0 [1 C, 2(*Z*)-C], 127.0–128.0 (6 C, aromatics), 129.1 [1 C, 6(*Z*)-C], 129.5 [1 C, 6(*E*)-C], 131.2 [1 C, 5(*E*)-C] and 132.5 [1 C, 5(*Z*)-C]; *m/z* (GT) 231 [M + H]$^+$, 213 [M + H − H_2O]$^+$ (Found: C, 78.4; H, 7.8. $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.9%).

(*Z*)- and (*E*)-8-Benzyloxy-4-bromomethyldimethylsilyloxyoct-5-en-1-yne 4

The *title compound* (*Z*:*E* = 85:15) was obtained as an oil according to the published procedure[26] in 87% yield; R_f 0.62 [hexane–diethyl ether (9:1)]; δ_H(400 MHz; $CDCl_3$) 0.15 (6 H, s, Me), 1.8 [1 H, t, $J_{1\text{-}3}$ 2.7, 1(*Z*)-H], 1.9 [1 H, t, $J_{1\text{-}3}$ 2.6, 1(*E*)-H], 2.2 (2 H, m, 3-H), 2.3 (2 H, m, 7-H), 2.36 (2 H, s, CH_2Br), 3.4 (2 H, t, $J_{8\text{-}7}$ 6.9, 8-H), 4.15 [1 H, m, 4(*E*)-H], 4.4 (2 H, s, CH_2Ph), 4.55 [1 H, m, 4(*Z*)-H], 5.4 [2 H, m, 5-H and 6(*Z*)-H], 5.6 [1 H, dt, $J_{6\text{-}5}$ 15.5, $J_{6\text{-}7}$ 6.7, 6(*E*)-H] and 7.3 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) −2.2 (2 C, Me), 17.0 (1 C, 7-C), 28.0 [1 C, 3(*Z*)-C], 28.2 [1 C, 3(*E*)-C], 28.5 (1 C, CH_2Br), 68.2 (1 C, 4-C), 69.8 [1 C, 1(*Z*)-C], 70.1 [1 C, 1(*E*)-C], 70.3 [1 C, 8(*Z*)-C], 70.5 [1 C, 8(*E*)-C], 73.4 (1 C, CH_2Ph_E), 73.5 (1 C, CH_2Ph_Z), 81.5 (1 C, 2-C), 128.1–133.5 (6 C, aromatics), 138.7 [1 C, 5(*Z*)-C] and 138.8 [1 C, 5(*E*)-C]; *m/z* (NBA) 381 and 383 [M + H]$^+$, 213 [M + H − HO − $SiMe_2CH_2Br$]$^+$ (Found: C, 56.5; H, 6.4. $C_{18}H_{25}BrO_2Si$ requires C, 56.7; H, 6.6%).

(*Z*)- and (*E*)-8-Benzyloxy-1-trimethylsilyloct-5-en-1-yn-4-ol 11

To a stirred solution of the alcohol **10** (795 mg, 3.46 mmol) in THF (15 cm^3) cooled to −78 °C was added sodium iodide (51 mg, 0.34 mmol) and *n*-butyllithium (1.6 mol dm^{-3} in hexanes) (4.75 cm^3, 7.6 mmol). After 30 min at −78 °C, trimethylsilyl chloride (1.87 g, 17.88 mmol) was added dropwise and the reaction mixture refluxed for 2 h then hydrolyzed with a saturated solution of $NaHCO_3$. The aqueous phase was extracted with diethyl ether and the organic phases were pooled, dried on Na_2SO_4 and concentrated under reduced pressure. Chromatography on silica gel with hexane–diethyl ether (4:6) gave the *title compound* (*Z*:*E* = 85:15) as an oil (528 mg, 51%); R_f 0.55 diethyl ether–hexane (6:4)]; δ_H(250 MHz; $CDCl_3$) 0.15 (9 H, s, Me_{TMS}), 1.55 (1 H, m, OH), 2.3–2.6 (4 H, m, 3-H and 7-H), 3.5 (2 H, m, 8-H), 4.2 [1 H, m, 4(*E*)-H], 4.5 (2 H, s, CH_2Ph), 4.55 [1 H, m, 4(*Z*)-H], 5.55–5.65 (2 H, m, 5-H and 6-H) and 7.35 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) 0.0 (3 C, Me_{TMS}), 28.0 [1 C, 7(*Z*)-C], 28.5 [1 C, 7(*E*)-C], 33.0 (1 C, 3-C), 65.0 (1 C, 4-C), 72.8 (1 C, CH_2Ph_Z), 73.0 (1 C, CH_2Ph_E), 79.2 [1 C, 8(*Z*)-C], 79.5 [1 C, 8(*E*)-C], 86.8 [1 C, 2(*Z*)-C], 87.0 [1 C, 2(*E*)-C], 103.0 [1 C, 1(*E*)-C], 103.6 [1 C, 1(*Z*)-C], 126.8 (1 C, 5-C), 127.0–147.8 (6 C, aromatics), 129.6 (1 C, 6-C); *m/z* (GT) 303 [M + H]$^+$, 285 [M + H − H_2O]$^+$ (Found: C, 71.3; H, 8.7. $C_{18}H_{26}O_2Si$ requires C, 71.5; H, 8.7%).

(*Z*)- and (*E*)-8-Benzyloxy-4-bromomethyldimethylsilyloxy-1-trimethylsilyloct-5-en-1-yne 3

The *title compound* (*Z*:*E* = 85:15) was obtained according to the aforementioned procedure for **4** in 94% yield; R_f 0.83 [hexane–diethyl ether (6:4)]; δ_H(250 MHz; $CDCl_3$) 0.15 (9 H, s, Me_{TMS}), 0.35 (6 H, s, MeSi), 2.3–2.5 (6 H, m, 3-H and 7-H and CH_2Br), 3.5 (2 H, t, $J_{8\text{-}7}$ 6.7, 8-H), 4.3 [1 H, q, $J_{4E\text{-}3} = J_{4E\text{-}5}$ 6.3, 4(*E*)-H], 4.5 (2 H, s, CH_2Ph), 4.65 [1 H, q, $J_{4Z\text{-}3} = J_{4Z\text{-}5}$ 6.8, 4(*Z*)-H], 5.35–5.8 (2 H, m, 5-H and 6-H), 7.3 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) −2.0 (3 C, Me_{TMS}), 1.0 (2 C, MeSi), 17.2 (1 C, 7-C), 29.3 (1 C, 3-C), 30.0 (1 C, CH_2Br), 68.0 (1 C, 4-C), 69.8 [1 C, 8(*Z*)-C], 70.1 [1 C, 8(*E*)-C], 73.6 (1 C, CH_2Ph_Z), 73.8 (1 C, CH_2Ph_E), 86.8 [1 C, 2(*Z*)-C], 86.9 [1 C, 2(*E*)-C], 103.8 [1 C, 1(*Z*)-C], 103.9 [1 C, 1(*E*)-C], 127.6–128.4 (5 C, aromatics), 129.6 (1 C, 6-C), 132.6 (1 C, 5-C), 138.0 (1 C, $C_{q\text{-phenyl}}$); *m/z* (NBA) 453 and 455 [M + H]$^+$ (Found: C, 55.7; H, 7.5. $C_{21}H_{33}BrO_2Si_2$ requires C, 55.6; H, 7.3%).

(*E*)-6-Benzyloxy-2-bromomethyldimethylsilyloxyhex-3-ene 13

To a stirred solution of methyllithium (1.6 mol dm^{-3} in diethyl ether) (1.1 cm^3, 1.73 mmol) cooled to −80 °C under argon was added 5-benzyloxypent-2-enal (300 mg, 1.58 mmol) in THF (6 cm^3), the temperature was maintained for 1 h and then raised to room temperature, and then the reaction was hydrolyzed with aqueous HCl (1 mol dm^{-3}) to pH 7. The aqueous phase was extracted with diethyl ether and the pooled organic phases dried on Na_2SO_4 and concentrated under reduced pressure. The resulting oil was chromatographed on silica gel with hexane–diethyl ether (8:2) to afford *6-benzyloxyhex-3-en-2-ol* as an oil (120 mg, 36%); R_f 0.3 [hexane–diethyl ether (1:1)]; δ_H(250 MHz; $CDCl_3$) 1.3 (3 H, d, $J_{1\text{-}2}$ 6.5, 1-H), 1.65 (1 H, m, OH), 2.4 (2 H, q, $J_{5\text{-}6} = J_{5\text{-}4}$ 6.7, 5-H), 3.55 (2 H, t, $J_{6\text{-}5}$ 6.8, 6-H), 4.3 (1 H, m, 2-H), 4.5 (2 H, s, CH_2Ph), 5.5–5.9 (2 H, m, 3-H and 4-H) and 7.4 (5 H, m, aromatics). This allylic alcohol was silylated according to the aforementioned procedure for **4** to give the *title compound* as an oil in 90% yield; R_f 0.84 [hexane–diethyl ether (1:1)]; δ_H(250 MHz; $CDCl_3$) 0.3 (6 H, s, MeSi), 1.25 (3 H, d, $J_{1\text{-}2}$ 6.3, 1-H), 2.35 (2 H, q, $J_{5\text{-}6} = J_{5\text{-}4}$ 6.6, 5-H), 2.5 (2 H, s, CH_2Br), 3.55 (2 H, t, $J_{6\text{-}5}$ 6.7, 6-H), 4.3 (1 H, m, 2-H), 4.5 (2 H, s, CH_2Ph), 5.4–5.8 (2 H, m, 3-H and 4-H), 7.3 (5 H, m, aromatics) (Found: C, 53.5; H, 6.9. $C_{16}H_{25}BrO_2Si$ requires C, 53.8; H, 7.0%).

General procedure for radical cyclizations followed by the Tamao oxidation

To a refluxed stirred solution of the allylic silylated ether (1.05 mmol) and AIBN (8 mg, 0.05 mmol) in degassed benzene (42 cm^3) under argon was added with a motor-driven syringe ($v = 2 \times 10^{-4}$ mol h^{-1}) a mixture of tri-*n*-butyltin hydride (0.37 cm^3, 1.37 mmol) and AIBN (25 mg, 0.15 mmol) in benzene (14 cm^3). The reflux was maintained for 12 h and the solvent evaporated under reduced pressure to give a crude material which was, without purification, oxidized by a mixture of hydrogen peroxide (9 wt% in water) (1 cm^3, 2.65 mmol) and potassium fluoride (0.45 g, 7.74 mmol) in DMF (4.3 cm^3) at 60 °C during 5 h. The solvent was evaporated and the crude residue hydrolyzed with a saturated solution of NaCl and extracted with dichloromethane; the organic phases were pooled, dried on Na_2SO_4 and concentrated under reduced pressure to give a crude residue which was further chromatographed on silica gel with dichloromethane–methanol (98:2) to afford the products of radical cyclization.

(*E*)-7-Benzyloxyhept-4-ene-1,3-diol 12

The *title compound* was obtained from (*E*)-**1** according to the aforementioned cyclization general procedure in 22% yield as an oil; R_f 0.43 [dichloromethane–methanol (98:2)]; δ_H(400 MHz; $CDCl_3$) 1.5 (1 H, s, OH), 1.71 (2 H, q, $J_{2\text{-}1} = J_{2\text{-}3}$ 5.8, 2-H),

2.14 (1 H, s, OH), 2.3 (2 H, q, $J_{6\text{-}5} = J_{6\text{-}7}$ 6.4, 6–H), 3.44 (2 H, t, $J_{7\text{-}6}$ 6.4, 7-H), 3.75 (2 H, m, 1-H), 4.27 (1 H, m, 3-H), 4.45 (2 H, s, CH_2Ph), 5.54 (1 H, dd, $J_{4\text{-}3}$ 6.5, $J_{4\text{-}5}$ 15.6, 4-H), 5.65 (1 H, dt, $J_{5\text{-}4}$ 15.5, $J_{5\text{-}6}$ 6.4, 5-H), 7.2 (5 H, m, aromatics) (Found: C, 71.0; H, 8.4. $C_{14}H_{20}O_3$ requires C, 71.2; H, 8.5%).

1-Benzyloxy-4-hydroxymethylhexan-5-ol 14

The *title compound* was obtained from (*E*)-**13** according to the aforementioned cyclization general procedure in 50% yield as an oil (*threo*:*erythro* = 86:14); R_f 0.31 [hexane–diethyl ether (6:4)]; δ_H(400 MHz; $CDCl_3$) 1.2 (3 H, d, $J_{1\text{-}2}$ 6.4, 1-H), 1.3–1.8 (5 H, m, 3-H, 2 × 4-H and 2 × 5-H), 2.3 (1 H, m, OH), 2.6 (1 H, m, OH), 3.4 (2 H, t, $J_{6\text{-}5}$ 6.4, 6-H), 3.6 (1 H, dd, J_{gem} 11.1, $J_{CH_2OH\text{–}3}$ 5.3, CH_2OH), 3.85 (2 H, m, 2-H and CH_2OH), 4.4 (2 H, s, CH_2Ph), 7.3 (5 H, m, aromatics) (Found: C, 70.3; H, 9.1. $C_{14}H_{22}O_3$ requires C, 70.6; H, 9.3%).

5-(3′-Benzyloxypropyl)-2,2,4-trimethyl-1,3-dioxane 15

The diol **14** (40 mg, 0.17 mmol) was reacted overnight at room temperature with 2,2-dimethoxypropane (1 cm^3, 8.13 mmol) in the presence of a catalytic quantity of toluene-*p*-sulfonic acid. After neutralization with solid $NaHCO_3$ and evaporation of the solvent, the residue was purified by preparative thick layer chromatography with hexane–diethyl ether (8:2) as the eluent to afford the *title compound* as an oil (*threo*:*erythro* = 85:15) (29 mg, 60%); R_f 0.48 [hexane–diethyl ether (8:2)]; δ_H(400 MHz; $CDCl_3$) 1.1 (3 H, d, $J_{1\text{-}2}$ 6.1, 1-H), 1.3 (3 H, s, Me), 1.35 (3 H, s, Me), 1.4–1.7 (5 H, m, 3-H, 2 × 4-H and 2 × 5-H), 3.5 (2 H, m, 6-H), 3.45 (1 H, t, $J_{7a\text{-}7e} = J_{7a\text{-}3}$ 11.4, 7a-H), 3.6 (1 H, qd, $J_{2\text{-}3}$ 9.9, $J_{2\text{-}1}$ 6.1, 2-H), 3.75 (1 H, dd, $J_{7a\text{-}7e}$ 11.7, $J_{7e\text{-}3}$ 5.0, 7e-H), 4.43 (2 H, s, CH_2Ph) and 7.2–7.4 (5 H, m, aromatics) (Found: C, 73.1; H, 9.2. $C_{17}H_{26}O_3$ requires C, 73.3; H, 9.4%).

threo-6-Benzyloxy-1-cyano-3-hydroxymethylhexan-2-ol 16

The *title compound* was obtained from (*E*)-**2** according to the aforementioned cyclization general procedure in 10% yield as an oil; R_f 0.17 [dichloromethane–methanol (98:2)]; δ_H(400 MHz; $CDCl_3$) 1.3–1.7 (5 H, m, 3-H, 2 × 4-H and 2 × 5-H), 2.3 (1 H, m, OH), 2.6 (2 H, d, $J_{1\text{-}2}$ 6.1, 1-H), 3.4 (2 H, m, 6-H), 3.65 (1 H, dd, J_{gem} 11.3, $J_{CH_2\text{–}3}$ 5.6, CH_2OH), 3.7 (1 H, m, OH), 3.8 (1 H, dd, J_{gem} 11.2, $J_{CH_2\text{–}3}$ 2.9, CH_2OH), 4.0 (1 H, q, $J_{2\text{-}1} = J_{2\text{-}3}$ 5.9, 2-H), 4.4 (2 H, s, CH_2Ph) and 7.1–7.4 (5 H, m, aromatics); *m*/*z* (NBA) 264 $[M + H]^+$, 237 $[M + H - HCN]^+$ (Found: C, 68.2; H, 8.2. $C_{15}H_{21}NO_3$ requires C, 68.4; H, 8.0%).

threo-8-Benzyloxy-5-hydroxymethyloct-1-yn-4-ol 17

The *title compound* was obtained from (*E*/*Z*)-**3** and (*E*/*Z*)-**4** according to the aforementioned general procedure in 15% yield as an oil; R_f 0.14 [dichloromethane–methanol (98:2)]; δ_H(400 MHz; $CDCl_3$) 1.42 (2 H, m, 6-H), 1.6 (3 H, m, 5-H and 2 × 7-H), 1.95 (1 H, t, $J_{1\text{-}3}$ 2.7, 1-H), 2.25 (1 H, m, OH), 2.42 (2 H, m, 3-H), 2.80 (1 H, t, $J_{OH\text{-}4}$ 4.8, OH), 3.4 (2 H, t, $J_{8\text{-}7}$ 6.3, 8-H), 3.61 (1 H, dd, $J_{9\text{-}9'}$ 11.3, $J_{9\text{-}5}$ 5.7, 9-H), 3.75 (1 H, m, 4-H), 3.82 (1 H, dd, $J_{9'\text{-}9}$ 11.3, $J_{9'\text{-}5}$ 2.9, 9′-H), 4.4 (2 H, s, CH_2Ph) and 7.2 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) 26.9 (1 C, 6-C), 27.5 (1 C, 3-C), 29.4 (1 C, 7-C), 45.0 (1 C, 5-C), 66.3 (1 C, CH_2OH), 72.5 (1 C, 8-C), 73.2 (1 C, 1-C), 75.0 (1 C, CH_2Ph), 76.2 (1 C, 4-C), 83.1 (1 C, 2-C) and 130–138 (6 C, aromatics); *m*/*z* (GT) 263 $[M + H]^+$ (Found: C, 73.0; H, 8.3. $C_{16}H_{22}O_3$ requires C, 73.2; H, 8.4%).

3-Benzyloxyethyl-2-hydroxymethyl-4-trimethylsilylvinylcyclopentanol 18

The *title compound* was obtained from (*E*/*Z*)-**3** according to the aforementioned cyclization general procedure in 30% yield as an oil; R_f 0.42 [dichloromethane–methanol (95:5)]; δ_H(400 MHz; C_6D_6) 1.80 (1 H, $J_{7a\text{-}6}$ 5.8, $J_{7a\text{-}7b}$ 14.2, $J_{7a\text{-}8a}$ 5.4, $J_{7a\text{-}8b}$ 7.7, 7a-H), 1.87 (1 H, $J_{5\text{-}4}$ 7.7, $J_{5\text{-}6}$ 9.3, $J_{5\text{-}9a}$ 7.7, $J_{5\text{-}9b}$ 5.0, 5-H), 2.05 (1 H, $J_{7b\text{-}6}$ 6.6, $J_{7b\text{-}7a}$ 14.2, $J_{7b\text{-}8a}$ 7.8, $J_{7b\text{-}8b}$ 4.6, 7b-H), 2.30 (1 H, $J_{6\text{-}1}$ 1.9, $J_{6\text{-}3\beta}$ 1.9, $J_{6\text{-}5}$ 9.3, $J_{6\text{-}7a}$ 5.8, $J_{6\text{-}7b}$ 6.6, 6-H), 2.45 (1 H, $J_{3\beta\text{–}1}$ 2.7, $J_{3\beta\text{–}3\alpha}$ 16.0, $J_{3\beta\text{-}4}$ 8.8, $J_{3\beta\text{-}6}$ 1.9, 3β-H), 2.82 (1 H, $J_{3\alpha\text{-}1}$ 1.9, $J_{3\alpha\text{-}3\beta}$ 16.0, $J_{3\alpha\text{-}4}$ 6.9, 3α-H), 3.42–3.45 (2 H, 8a-H and 8b-H), 3.46 (1 H, $J_{9a\text{-}5}$ 7.7, $J_{9a\text{-}9b}$ 10.5, 9a-H), 3.70 (1 H, $J_{9b\text{-}5}$ 5.0, $J_{9b\text{-}9a}$ 10.5, 9b-H), 3.95 (1 H, $J_{4\text{-}3\alpha}$ 6.9, $J_{4\text{-}3\beta}$ 8.8, $J_{4\text{-}5}$ 7.7, 4-H), 5.50 (1 H, $J_{1\text{-}3\alpha}$ 1.9, $J_{1\text{-}3\beta}$ 2.7, $J_{1\text{-}6}$ 1.9, 1-H), 7.1–7.3 (5 H, aromatics); δ_C(400 MHz, $CDCl_3$) 0.0 (3 C, Me_{TMS}), 33.4 (1 C, 7-C), 41.2 (1 C, 3-C), 43.9 (1 C, 6-C), 53.2 (1 C, 5-C), 65.5 (1 C, 9-C), 68.2 (1 C, 8-C), 73.2 (1 C, CH_2Ph), 75.8 (1 C, 4-C), 120.5 (1 C, 1-C), 127.1 (1 C, *p*-C), 128.0 (2 C, *o*-C), 130 (2 C, *m*-C), 138.1 (1 C, $C_{q\text{-phenyl}}$) and 159.5 (1 C, 2-C); *m*/*z* (GT) 335 $[M + H]^+$ (Found: C, 68.3; H, 8.9. $C_{19}H_{30}O_3Si$ requires C, 68.2; H, 9.0%).

3-Benzyloxyethyl-2-hydroxymethyl-4-vinylcyclopentanol 19

Method (*a*). To the TMS-vinylcyclopentanol **18** (32 mg, 0.1 mmol) dissolved in a mixture of acetonitrile (1 cm^3) and water (20 μl) was added benzenesulfinic acid (3 mg, 0.1 mmol), and the reaction stirred for 2 h at room temperature. After evaporation of the acetonitrile, the aqueous phase was extracted with diethyl ether and the organic phases were pooled, dried on Na_2SO_4 and concentrated under reduced pressure to afford an oil, which was chromatographed *via* preparative thick layer chromatography with dichloromethane–methanol (97:3) as the eluent, and the *title compound* was obtained as an oil (6 mg, 24%); R_f 0.2 [dichloromethane–methanol (98:2), 2 elutions]; δ_H(400 MHz; $CDCl_3$) 1.65–1.9 (3 H, m, 5-H, 7-H and 7′-H), 2.2 (2 H, m, 3-H and 6-H), 2.43 (1 H, m, OH), 2.5 (1 H, dd, $J_{3'\text{-}3}$ 15.4, $J_{3'\text{-}4}$ 6.8, 3′-H), 2.9 (1 H, m, OH), 3.4 (3 H, m, 2 × 8-H and 9-H), 3.6 (1 H, dd, $J_{9'\text{-}9}$ 10.4, $J_{9'\text{-}5}$ 5.1, 9′-H), 3.7 (1 H, dt, $J_{4\text{-}3} = J_{4\text{-}5}$ 7.2, 4-H), 4.35 (2 H, s, CH_2Ph), 4.65 (1 H, s, 1-H), 4.8 (1 H, s, 1′-H) and 7.2 (5 H, m, aromatics); δ_C(400 MHz, $CDCl_3$) 33.9 (1 C, 7-C), 41.0 (1 C, 6-C), 41.7 (1 C, 3-C), 54.1 (1 C, 5-C), 65.5 (1 C, 9-C), 68.2 (1 C, 8-C), 73.1 (1 C, CH_2Ph), 75.4 (1 C, 4-C), 107.5 (1 C, 1-C), 130–138 (6 C, aromatics) and 150.8 (1 C, 2-C); *m*/*z* (NBA) 263 $[M + H]^+$ (Found: C, 73.1; H, 8.5. $C_{16}H_{22}O_3$ requires C, 73.2; H, 8.4%).

Method (*b*). The *title compound* was obtained (14% yield estimated by ^1H NMR) from (*E*/*Z*)-**4** according to the aforementioned cyclization general procedure.

2-Hydroxymethyl-3-benzyloxyethylcyclohex-4-enol 20

The *title compound* was obtained (15% yield estimated by ^1H NMR) from (*E*/*Z*)-**4** according to the aforementioned cyclization general procedure; R_f 0.39 [dichloromethane–methanol (95:5)]; δ_H(400 MHz; C_6D_6) 1.5 (2 H, 2-H and CH_2CH_2OBn), 1.9 (1 H, CH_2CH_2OBn), 2.1 (2 H, $J_{3a\text{-}5}$ 1.3, $J_{3a\text{-}4}$ 2.5, 3-H and 6a-H), 2.2 (1 H, $J_{6e\text{-}5}$ 5.4, 6e-H), 2.5 (1 H, OH), 2.6 (1 H, OH), 3.35 (2 H, $J_{CH_2CH_2}$ 6.6, CH_2OBn), 3.6 (1 H, J_{gem} 10.9, $J_{CH_2OH\text{-}2}$ 7.4, CH_2OH), 3.8 (1 H, 1-H), 3.95 (1 H, J_{gem} 10.9, CH_2OH), 4.3 (2 H, CH_2Ph), 5.55 (1 H, $J_{4\text{-}5}$ 9.9, $J_{4\text{-}3a} = J_{4\text{-}6a}$ 2.5, 4-H), 5.61 (1 H, $J_{5\text{-}4}$ 9.9, $J_{5\text{-}6e}$ 5.4, $J_{5\text{-}6a}$ 1.7, $J_{5\text{-}3a}$ 1.3, 5-H), 7.1–7.4 (5 H, m, aromatics); δ_C(400 MHz, C_6D_6) 33.4 (1 C, CH_2CH_2OBn), 34.4 (1 C, 6-C), 34.6 (1 C, 3-C), 47.0 (1 C, 2-C), 65.1 (1 C, CH_2OH), 65.3 (1 C, 1-C), 67.9 (1 C, CH_2OBn), 73.0 (1 C, CH_2Ph), 123.4 (1 C, 5-C), 129.8 (1 C, 4-C) and 130.0–139.1 (6 C, aromatics).

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