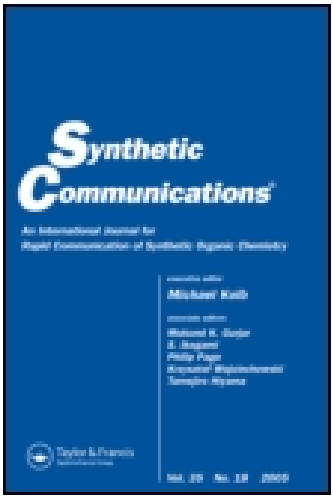


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

New Acyclic β-Functionnalized (E) Allyl Alcohols and their Bromomethyldimethylsilyl Ethers as Cyclopentanoids Precursors

Florence Belval [a] , Claude Chavis [a] , Jean-Louis Montero [a] & Marc Lucas [a]
[a] Laboratoire de Chimie Biomoléculaire, associé au CNRS, Case 073, Université de Montpellier II, Place Eugène Bataillon , 34095, Montpellier, Cédex 05, France
Published online: 20 Aug 2006.

SYNTHETIC COMMUNICATIONS, 28(10), 1823-1837 (1998)

NEW ACYCLIC β-FUNCTIONNALIZED (E) ALLYL ALCOHOLS AND THEIR BROMOMETHYLDIMETHYLSILYL ETHERS AS CYCLOPENTANOIDS PRECURSORS

Florence Belval, Claude Chavis, Jean-Louis Montero and Marc Lucas*

Laboratoire de Chimie Biomoléculaire, associé au CNRS, Case 073, Université de Montpellier II, Place Eugène Bataillon, 34095 Montpellier Cédex 05 (France)

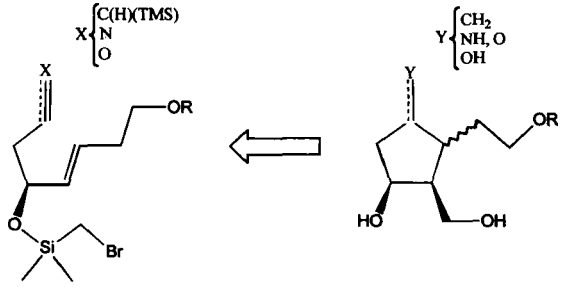
ABSTRACT : The syntheses of new acyclic (*E*) allyl alcohols β-functionnalized by various radical trapping functions and their corresponding bromomethyldimethylsilyl ethers are reported.

Bromomethyldimethylsilyl ethers as versatile reagents in radical chemistry were originally developped by Stork[1] and Nishiyama.[2] They allowed the stereoselective introduction of a hydroxymethyl group on the olefinic moiety of an allylic alcohol which otherwise could be β-functionnalized by either a simple double bond,[3] an unsaturated carboxylic ester,[4] an unsaturated alcohol,[4] a hemiacetalic oxygen[5] or an acetal.[6] In the course of a research project on prostanoïd precursors, we needed a specific acyclic seven carbon chain length bearing the bromomethyldimethylsilyl ether flanked on one side by an ω-benzyloxybutenyl chain and on the other side in the β position by various radical

* To whom all correspondence should be addressed

trapping functions such as alcyne, nitrile or aldehyde, in order to study subsequently their behaviour in tandem radical cyclisations (scheme 1).

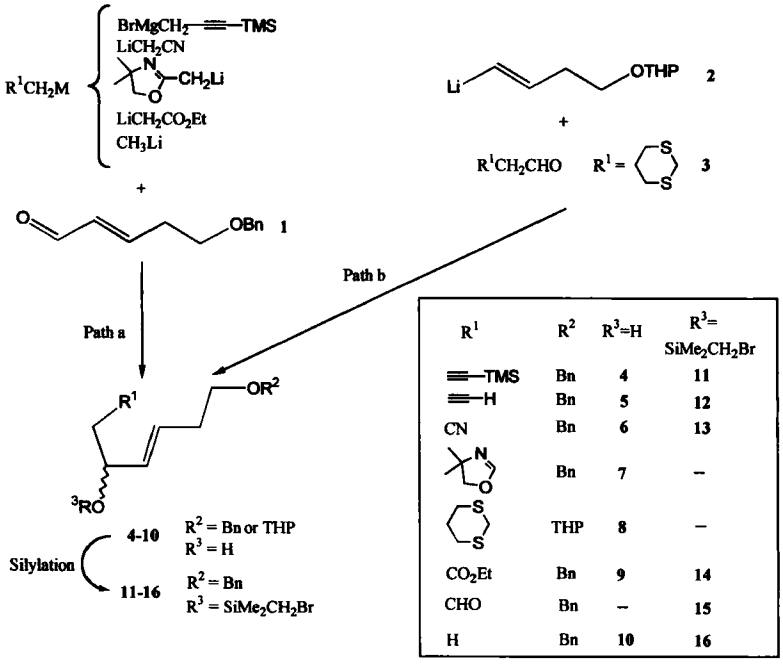
SCHEME 1



The present paper deals with the preparation of new racemic series of acyclic β-functionnalized (*E*) allyl alcohols together with their corresponding bromomethyldimethylsilyl ethers.

For our purpose, we devised a general route (scheme 2, path a) in order to reach the allylic alcohols **4** and **6** which beared respectively a TMS-alcyne (R^1= C≡C-TMS) or a cyano (R^1= C≡N) functionnality; this was achieved by 1,2-addition of the suitable organometallic reagents on (*E*) 5-benzyloxypent-2-enal **1** which in turn was available by a three steps sequence from 1,3-propanediol (monobenzylation,[7] Swern oxidation[7], Wittig condensation[8]). Although the β-functionnalized allyl alcohols **4** and **6** were obtained in 50 and 84% yields respectively, it is worth noting that Grignard condensation of the trimethylsilylpropargyl bromide on the conjugated aldehyde **1** gave, besides the desired compound **4**, a 40% yield in the corresponding trimethylsilyl allenic derivative as a by-product and in agreement with earlier reports.[9]

SCHEME 2



In order to avoid the formation of the allenic compound during the synthesis of **5** (R^1= C≡CH), we preferred the more convenient desilylation reaction of the TMS-acetylenic derivative **4** with tetrabutylammonium fluoride in THF which gave the expected acetylenic alcohol **5** in 62% yield.

In view of the β-functionnalization with an aldehydic moiety, we planned to use dimethyloxazoline, 1,3-dithiane and carboxylic ester as masked aldehydes to reach the corresponding target allyl alcohols **7**, **8** and **9**. The compounds **7** (R^1= oxazolinyl, 70% yield) and **9** (R^1= CO_2Et, 60% yield) were prepared according to the strategy described above (scheme 2, path a), by condensation of

deprotonated 2,4,4-trimethyloxazoline and ethyl acetate respectively with the conjugated aldehyde **1**.

The allyl dithianyl alcohol **8** was synthesized (scheme 2, path b) in a 37% yield by reaction of 2[2(1,3-dithianyl)]acetaldehyde **3**[10] with (*E*) vinylic lithium derivative **2**; this reagent was prepared[11] by hydrostannylation of the tetrahydro-2(3-butynyloxy)2*H*-pyran[12] ($HSnBu_3$, AIBN, benzene, 76% yield, mainly *E*-isomer) followed by a transmetallation reaction with *n*BuLi in THF.

The unfunctionnalized benzyloxyhexenol **10** (36% yield) was synthesized by addition of MeLi on aldehyde **1** (scheme 2, path a) in order to study the propency of its silylated derivative **16** (R^1= H) to the radical cyclisation and to compare its behaviour with all other β-function containing ethers ($R^1 \neq$ H).

TABLE

R^1	R^2	R^3 = H (% yield)[a]	R^3 = $SiMe_2CH_2Br$ (% yield)[a]
C≡C-TMS	Bn	**4** (50)[b]	**11** (quant.)
C≡CH	Bn	**5** (62)[c]	**12** (quant.)
C≡N	Bn	**6** (84)[d]	**13** (quant.)
2-(dimethyl oxazolinyl)	Bn	**7** (70)[e]	-------
2(1,3-dithianyl)	THP	**8** (37)[f]	-------
CO_2Et	Bn	**9** (60)[g]	**14** (quant.)
CH=O	Bn	-------	**15** (80)[i]
H	Bn	**10** (36)[h]	**16** (90)

a) non optimized yields; b) **1**+$BrCH_2C{\equiv}C$-TMS, Mg/Et_2O; c) **4**+TBAF/THF; d) **1**+acetonitrile, LDA/THF; e) **1**+2,4,4-trimethyl-2-oxazoline, *n*BuLi/THF; f) **3**+(*E*) Bu_3Sn-CH=CH-$(CH_2)_2$OTHP, *n*BuLi/THF; g) **1**+ethyl acetate, LDA/THF; h) **1**+MeLi/Et_2O/THF; i) **14**+ DIBAH/hexane.

We noticed that α,β-unsaturated alcohols **4-9** (especially **7**) were very prone to give the corresponding (*E,E*)-dienes by dehydration when either purified on silica gel or stored at -20°C. The whole allylic alcohols were obtained with non optimized yields ranging from 36 to 84% (see table) and their *E* configuration was ascertained by the coupling constant of the two ethylenic protons ($J \approx 15.5$ Hz).

All the experimental conditions used to liberate aldehydic function from the oxazolinyl and dithianyl derivatives **7** and **8** failed and afforded respectively the sole dehydration compound or an untractable mixture of degradation products; all attempts to enhance their stabilities by temporary protection of the hydroxyl group gave similar results.

We finally succeeded in the obtention of the aldehydic moiety, by the following two steps sequence: *i.e.* silylation of the β-hydroxyester **9** with the Nishiyama reagent ($ClSiMe_2CH_2Br$) into silylated ether **14** (quant. yield) and reduction of this compound with DIBAH at -80°C which cleanly afforded the desired aldehyde ether **15** in 80% yield.

The silylated ethers **11-16** (except **15** as outlined above) were obtained by treatment of the corresponding free alcohols **4-6, 9, 10** with the Nishiyama reagent (1 eq.) in dichloromethane at 0°C and triethylamine (1.1 eq.); a catalytic amount of DMAP was necessary in order to achieve a complete reaction[3] and to prevent the use of a cumbersome excess of the reagent which was always difficult to remove in the purification step. Silylated ethers purifications are generally performed on silica gel,[2-6] but compounds **11-16** appeared very unstable on this adsorbent or on neutral alumina and afforded the starting parent alcohols; this degradation was

circumvented by carrying out a flash column chromatography on Florisil (100-200 mesh) with hexane.

The bromomethyldimethylsilyl ethers **11**, **12**, **13** and **15** are currently studied for their propency to generate, under stereoselective tandem radical cyclisations, the racemic trisubstituted cyclopentanols as valuable prostanoïd precursors. Sequential cyclisations are actually in progress and this work is being extented to the optically active series starting from (R)-glycidol.

EXPERIMENTAL

^{1}H NMR spectra were performed on a Brüker avance DPX 200 and avance DRX 400. Mass spectra were obtained on a JEOL JMS.DX 300 (accelerating voltage 3KeV) by the FAB ionization method.

(E) 8-Benzyloxy-1-trimethylsilyloct-5-ene-1-yne-4-ol ***4***.- To the stirred Grignard reagent solution prepared from *1-bromo-3-trimethylsilylprop-2-yne* (7.09 g, 37.1 mmol) and magnesium (1.78 g, 74.21 mmol) in anhydrous diethyl ether (20 cm^3) was added dropwise at 0°C *(E) 5-benzyloxypent-2-enal* **1** (4.7 g, 24.74 mmol) in diethyl ether (3 cm^3). The reaction was stirred overnight at room temp. and hydrolysed at 0°C with saturated aq. NH_4Cl and extracted with diethyl ether. The extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford an oily residue which was chromatographed on silica gel with hexane-diethyl ether (95:5) to give the title compound **4** as an oil (3.7 g, 50% yield). R_f = 0.21 (6:4 hexane:diethyl ether); ^{1}H NMR ($CDCl_3$), δ (ppm): 0.2 (s, 9H, 3Me); 2 (d, J_4-

$_{OH}$ 4.52 Hz, 1H, OH); 2.4 (td, $J_{7\text{-}8}$=$J_{7\text{-}6}$ 6.6 Hz, 2H, H_7); 2.5 (m, 2H, H_3); 3.55 (t, $J_{8\text{-}7}$ 6.8 Hz, 2H, H_8); 4.2 (m, 1H, H_4); 4.5 (s, 2H, CH_2Ph); 5.6 (ddt, $J_{5\text{-}6}$ 15.51, $J_{5\text{-}4}$ 6.11, $J_{5\text{-}7}$ 1 Hz, 1H, H_5); 5.8 (dtd, $J_{6\text{-}5}$ 15.49, $J_{6\text{-}7}$ 6.55, $J_{6\text{-}4}$ 0.77 Hz, 1H, H_6); 7.3 (m, 5H, H_{ar}); FAB$^+$ (NOBA): m/z 303 $(M+H)^+$, 285 $(M+H\text{-}H_2O)^+$. (Found: C, 71.63; H, 8.52. $C_{18}H_{26}O_2Si$ requires C, 71.47; H, 8.66%).

(E) 8-Benzyloxyoct-5-ene-1-yne-4-ol ***5***.- The trimethylsilyl derivative **4** (213 mg, 0.7 mmol) was dissolved in a solution of tetrabutylammonium fluoride (1.1 M in THF) (25 cm^3, 2.75 mmol) and left at room temp. 4 h. The solvent was then removed under reduced pressure and the resulting crude residue was chromatographed on silica gel with hexane-diethyl ether (1:1) to afford the desired desilylated compound **5** as a colorless oil (100 mg, 62% yield); R_f = 0.17 (1:1 hexane:diethyl ether); ^{1}H NMR ($CDCl_3$), δ (ppm): 2 (s, 1H, OH); 2.1 (t, $J_{1\text{-}3}$ 2.64 Hz, 1H, H_1); 2.4 (m, 2H, H_7); 2.45 (2dd, $J_{3\text{-}3'}$ 16.65, $J_{3\text{-}4}$ 5.98, $J_{3'\text{-}4}$ 5.65 Hz, 2H, H_3, $H_{3'}$); 3.55 (t, $J_{8\text{-}7}$ 6.72 Hz, 2H, H_8); 4.3 (m, 1H, H_4); 4.55 (s, 2H, CH_2Ph); 5.6 (ddt, $J_{5\text{-}4}$ 6.1, $J_{5\text{-}6}$ 15.5, $J_{5\text{-}7}$ 1 Hz, 1H, H_5); 5.8 (dtd, $J_{6\text{-}7}$ 6.4, $J_{6\text{-}5}$ 15.48, $J_{6\text{-}4}$ 0.6 Hz, 1H, H_6); 7.3 (m, 5H, H_{ar}); FAB$^+$ (NOBA): m/z 231 $(M+H)^+$, 213 $(M+H\text{-}H_2O)^+$. (Found: C, 78.32; H, 7.95. $C_{15}H_{18}O_2$ requires C, 78.23; H, 7.88%).

(E) 6-Benzyloxy-1-cyanohex-3-ene-2-ol ***6***.- To a stirred solution of acetonitrile (129 mg, 0.17 ml, 3.16 mmol) in anhydrous THF (5 cm^3) cooled to -80°C was added under nitrogen, lithium diisopropylamide (1.5 M in THF) (2.2 cm^3, 3.3 mmol). After 30 min *(E) 5-benzyloxypent-2-enal* **1** (300 mg, 1.58 mmol) dissolved in THF (1 cm^3) was added dropwise. After 3 h at room temp. the reaction was hydrolysed with dilute HCl (1 N) until pH 7 and extracted with

diethyl ether and the extracts dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude oil was chromatographed on silica gel with hexane-diethyl ether (1:1) as eluent to afford the title compound **6** as a colorless oil (308.5 mg, 84% yield). R_f = 0.26 (6:4 hexane:diethyl ether). ^{1}H NMR ($CDCl_3$), δ (ppm): 2 (bs, 1H, OH); 2.3 (m, 2H, H_5); 2.5 (2dd, $J_{1\text{-}1'}$ 16.56, $J_{1\text{-}2}$ 5.62, $J_{1'\text{-}2}$ 6.06 Hz, 2H, H_1, $H_{1'}$); 3.5 (t, $J_{6\text{-}5}$ 6.48 Hz, 2H, H_6); 4.3 (m, 1H, H_2); 4.4 (s, 2H, CH_2Ph); 5.55 (dd, $J_{3\text{-}4}$ 15.47, $J_{3\text{-}2}$ 6.9 Hz, 1H, H_3); 5.8 (dt, $J_{4\text{-}3}$ 15.5, $J_{4\text{-}5}$ 6.7 Hz, 1H, H_4); 7.3 (m, 5H, H_{ar}). (Found: C, 72.63; H, 7.52. $C_{14}H_{17}NO_2$ requires C, 72.7; H, 7.41%).

(E) 1[2(4,4-dimethyloxazolinyl)]6-benzyloxyhex-3-ene-2-ol **7**.- To a stirred solution of 2,4,4-trimethyloxazoline (270 mg, 2.39 mmol) in anhydrous THF (2 cm^3) cooled to -78°C, was added dropwise under nitrogen, *n*BuLi (1.6 M in hexanes) (1.65 cm^3, 2.65 mmol). After 30 min, *(E) 5-benzyloxypent-2-enal* **1** (0.5 g, 2.63 mmol) dissolved in THF (1 cm^3) was added at -78°C and the reaction was maintained 24 h at room temp. then hydrolysed with dilute HCl (1 N) until pH 7, extracted with diethyl ether and the extracts dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude oil was chromatographed on silica gel with hexane-diethyl ether (1:1) to afford the title compound **7** as a colorless oil (507 mg, 70% yield); R*f* = 0.51 (diethyl ether). ^{1}H NMR ($CDCl_3$), δ (ppm): 1.3 (s, 6H, 2Me); 2.4 (m, 2H, H_5); 2.42 (2dd, $J_{1\text{-}1'}$ 16.24, $J_{1\text{-}2}$ 4.7, $J_{1'\text{-}2}$ 7.82 Hz, 2H, H_1, $H_{1'}$); 3.6 (t, $J_{6\text{-}5}$ 6.8 Hz, 2H, H_6); 3.9 (s, 2H, $CH_2O_{oxazoline}$); 4.2 (s, 1H, OH); 4.45 (m, 1H, H_2); 4.55 (s, 2H, CH_2Ph); 5.6 (dd, $J_{3\text{-}4}$ 15.46, $J_{3\text{-}2}$ 6.04 Hz, 1H, H_3); 5.8 (dt, $J_{3\text{-}4}$ 15.44, $J_{4\text{-}5}$ 6.63 Hz, 1H, H_4); 7.4 (m, 5H, H_{ar}). (Found: C, 71.35; H, 8.45; N, 4.59. $C_{18}H_{25}NO_3$ requires C, 71.26; H, 8.31; N, 4.62%).

(E) 1[2(1,3-dithianyl)]6-tetrahydropyranyloxyhex-3-ene-2-ol **8**[11]. -To a mixture of *4-tetrahydro-2(3-butynyloxy)2H-pyran*[12] (7.67 g, 50 mmol) and AIBN (50 mg) dissolved in anhydrous benzene (333 cm^3) was added tributyltin hydride (15.3 cm^3, 55 mmol) and the reaction refluxed 2 h. The solvent was evaporated under reduced pressure to give a crude oil (26 g). A portion (2 g) was purified by chromatography on silica gel with hexane-diethyl ether (9:1) to afford the corresponding pure *(E) 4-tributyltin-1-tetrahydropyranyloxybut-3-ene* as a colorless oil (1.52 g, 76% yield); ^1H NMR ($CDCl_3$), δ (ppm): 0.7-0.9 (m, 9H, 3Me); 1.1-1.9 (m, 24H, $9CH_{2\text{-Bu}}$, $3CH_{2\text{-THP}}$); 2.45 (m, 2H, H_2); 3.5 (m, 2H, H_1); 3.8 (m, 2H, CH_2O_{THP}); 4.6 (m, 1H, OCHO); 5.8-6 (m, 2H, H_3, H_4). To a stirred solution of the previous tributyltin derivative (1.35 g, 3.03 mmol) in anhydrous THF (5 cm^3) cooled to -78°C, was added dropwise under nitrogen *n*BuLi (1.6 M in hexanes) (2.1 cm^3, 3.36 mmol). After 15 min *2[2(1,3-dithianyl)]acetaldehyde* **3**[10] (427 mg, 2.64 mmol) in THF (5 cm^3) was added at -78°C dropwise and the reaction was maintained 1 h at low temperature and 24 h at room temp. After hydrolysis with water, extraction with diethyl ether, the extracts were dried (Na_2SO_4) and concentrated under reduced pressure, then chromatographed on silica gel with hexane-diethyl ether (8:2) to afford the title compound **8** (311 mg, 37% yield); R_f =0.72 (hexane-diethyl ether); ^1H NMR ($CDCl_3$), δ (ppm): 1.5 (m, 6H, $3CH_{2\text{-THP}}$); 1.9 (m, 4H, H_5, $CH_{2\text{-dithiane}}$); 2.3 (m, 2H, H_1); 2.8 (m, 4H, CH_2S); 3.4 (m, 2H, CH_2O_{THP}); 3.8 (m, 2H, H_6); 4.2 (t, *J* 7.1 Hz, 1H, SCHS); 4.4 (m, 1H, H_2); 4.5 (s, 1H, OCHO); 4.7 (bs, 1H, OH); 5.5 (dd, $J_{3\text{-}4}$ 15.4, $J_{3\text{-}2}$ 6.6 Hz, 1H, H_3);

5.7 (dt, $J_{4\text{-}3}$ 15.6, $J_{4\text{-}5}$ 6.6 Hz, 1H, H_4). (Found: C, 56.43; H, 8.37. $C_{15}H_{26}O_3S_2$ requires C, 56.57; H, 8.23%).

(E) Ethyl 7-benzyloxy-3-hydroxyhept-4-enoate ***9***.- To a stirred solution of ethyl acetate (2.43 g, 27.6 mmol) in anhydrous THF (20 cm^3) cooled to -78°C, was added dropwise under nitrogen, lithium diisopropylamide (1.5 M in cyclohexane) (19.3 cm^3, 28.96 mmol). After 30 min at -78°C, *(E) 5-benzyloxypent-2-enal* **1** (2.62 g, 13.8 mmol) dissolved in THF (25 cm^3) was added dropwise. After 3 h at room temp. the reaction was hydrolysed with dilute HCl (1 N), extracted with diethyl ether and the extracts dried (Na_2SO_4) and concentrated under reduced pressure. The crude oil was chromatographed on silica gel with hexane-diethyl ether (1:1) as eluent to afford the pure title compound **9** (2.3 g, 60% yield) as an oil. R_f = 0.41 (75:25 diethyl ether:hexane); ^{1}H NMR ($CDCl_3$) δ (ppm): 1.2 (t, $J_{Me\text{-}CH2O}$ 7.1 Hz, 3H, Me); 2.3 (m, 2H, H_6); 2.5 (2dd, $J_{2\text{-}2'}$ 16.15, $J_{2\text{-}3}$ 4.61, $J_{2'\text{-}3}$ 7.76 Hz, 2H, H_2, $H_{2'}$); 2.8 (d, $J_{3\text{-}OH}$ 4.07 Hz, 1H, OH); 3.4 (t, $J_{7\text{-}6}$ 6.75 Hz, 2H, H_7); 4.15 (q, $J_{OCH2\text{-}Me}$ 7.1 Hz, 2H, OCH_2); 4.45 (m, 3H, H_3, CH_2Ph); 5.55 (ddt, $J_{4\text{-}5}$ 15.53, $J_{4\text{-}3}$ 6.2, $J_{4\text{-}6}$ 1.1 Hz, 1H, H_4); 5.7 (dtd, $J_{5\text{-}4}$ 15.56, $J_{5\text{-}6}$ 6.6, $J_{5\text{-}3}$ 0.85 Hz, 1H, H_5); 7.2-7.3 (m, 5H , H_{ar}); FAB$^+$ (thioglycerol): m/z 279 $(M+H)^+$, 261 $(M+H\text{-}H_2O)^+$. (Found: C, 69.15; H, 8.12. $C_{16}H_{22}O_4$ requires C, 69.04; H, 7.97%).

(E) 6-benzyloxyhex-3-ene-2-ol ***10***.-To a stirred solution of methyllithium (1,6 M in diethyl ether) (1.1 cm^3; 1.73 mmol) in anhydrous THF (4 cm^3) cooled to -80°C, was added dropwise under nitrogen, *(E) 5-benzyloxypent-2-enal* **1** (0.3 g, 1.58 mmol) dissolved in THF (2 cm^3). After 1 h at -80°C, the reaction was

hydrolysed with dilute HCl (1 N) until pH 7, extracted with diethyl ether and the extracts dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude oil was chromatographed on silica gel with hexane-diethyl ether (8:2) as eluent to afford the title compound **10** (118 mg, 36% yield) as an oil. R_f = 0.3 (1:1 hexane:diethyl ether). ^{1}H NMR ($CDCl_3$), δ (ppm): 1.3 (d, $J_{1\text{-}2}$ 6.46 Hz, 3H, Me); 1.65 (bs, 1H, OH); 2.4 (td, $J_{5\text{-}6}$=$J_{5\text{-}4}$ 6.7 Hz, 2H, H_5); 3.55 (t, $J_{6\text{-}5}$ 6.78 Hz, 2H, H_6); 4.3 (m, 1H, H_2); 4.5 (s, 2H, CH_2Ph); 5.5-5.9 (m, 2H, H_3, H_4); 7.4 (m, 5H, H_{ar}). (Found: C, 54.67; H, 6.42. $C_{13}H_{18}O_2$ requires C, 54.56; H, 6.34%).

General Procedure for the silylation of allylic alcohols.-To a stirred solution of the alcohol (3.96 mmol), triethylamine (0.61 cm^3, 4.35 mmol), DMAP (0.4 mmol) in anhydrous dichloromethane (15 cm^3) cooled to 0°C, was added dropwise under nitrogen, bromomethyldimethylchlorosilane (0.742 g, 3.96 mmol). After 2 h at 0°C, the reaction mixture was hydrolysed with saturated aq. NaCl, extracted with dichloromethane and the extracts dried (Na_2SO_4). The solvent was removed under reduced pressure and the oily residue was rapidly filtrated on Florisil (100-200 mesh) with dichloromethane as the eluent to afford the desired silylated ethers as colorless oils.

(E) 8-Benzyloxy-4-bromomethyldimethylsilyloxy-1-trimethylsilyloct-5-ene-1-yne ***11***.-: 98% yield; R_f = 0.77 (8:2 hexane:diethyl ether). ^{1}H NMR ($CDCl_3$), δ (ppm): 0.1 (s, 9H, 3Me); 0.15 (s, 6H, 2Me); 2.2-2.4 (m, 6H, H_3, H_7, CH_2Br); 3.35 (t, $J_{8\text{-}7}$ 6.75 Hz, 2H, H_8); 4.1 (m, 1H, H_4); 4.4 (s, 2H, CH_2Ph); 5.4 (ddt, $J_{5\text{-}6}$ 15.46,

$J_{5\text{-}4}$ 6.3, $J_{5\text{-}7}$ 1.1 Hz, 1H, H_5); 5.55 (dtd, $J_{6\text{-}5}$ 15.49, $J_{6\text{-}7}$ 6.25, $J_{6\text{-}4}$ 0.7 Hz, 1H, H_6); 7.2 (m, 5H, H_{ar}); FAB^+ (NOBA): m/z 453, 455 $(M+H)^+$. (Found: C, 55.57; H, 7.48. $C_{21}H_{33}BrO_2Si_2$ requires C, 55.61; H, 7.33%).

(E) 8-Benzyloxy-4-bromomethyldimethylsilyloxyoct-5-ene-1-yne ***12***.-quant. yield; R_f= 0.66 (1:1 hexane:diethyl ether). ^1H NMR ($CDCl_3$), δ (ppm): 0.3 (s, 6H, 2Me); 2 (t, $J_{1\text{-}3}$ 2.65 Hz, 1H, H_1); 2.3-2.5 (m, 4H, H_3, H_7); 2.55 (s, 2H, CH_2Br); 3.55 (t, $J_{8\text{-}7}$ 6.65 Hz, 2H, H_8); 4.3 (m, 1H, H_4); 4.55 (s, 2H, CH_2Ph); 5.6 (ddt, $J_{5\text{-}6}$ 15.42, $J_{5\text{-}4}$ 6.11, $J_{5\text{-}7}$ 0.86 Hz, 1H, H_5); 5.75 (dtd, $J_{6\text{-}5}$ 15.47, $J_{6\text{-}7}$ 5.85, $J_{6\text{-}4}$ 0.65 Hz, 1H, H_6); 7.3-7.5 (m, 5H, H_{ar}); FAB^+ (NOBA): m/z 381, 383 $(M+H)^+$. (Found: C, 56.87; H, 6.78. $C_{18}H_{25}BrO_2Si$ requires C, 56.69; H, 6.61%).

(E) 6-Benzyloxy-1-cyano-2-bromomethyldimethylsilyloxyhex-3-ene ***13***.-99% yield; R_f= 0.58 (1:1 hexane:diethyl ether). ^1H NMR ($CDCl_3$), δ (ppm): 0.25 (s, 6H, 2Me); 2.4 (m, 2H, H_5); 2.5 (s, 2H, CH_2Br); 2.6 (m, 2H, H_1); 3.6 (t, $J_{6\text{-}5}$ 6.49 Hz, 2H, H_6); 4.4 (m, 1H, H_2); 4.5 (s, 2H, CH_2Ph); 5.55 (dd, $J_{3\text{-}4}$ 15.59, $J_{3\text{-}2}$ 6.98 Hz, 1H, H_3); 5.8 (dt, $J_{4\text{-}3}$ 15.55, $J_{4\text{-}5}$ 6.6 Hz, 1H, H_4); 7.3 (m, 5H, H_{ar}); FAB^+ (thioglycerol): m/z 382, 384 $(M+H)^+$. (Found: C, 53.28; H, 6.48. $C_{17}H_{24}BrNSiO_2$ requires C, 53.4; H, 6.33%).

(E) Ethyl 7-benzyloxy-3-bromomethyldimethylsilyloxyhept-4-enoate ***14***.-quant. yield; R_f= 0.69 (6:4 hexane:diethyl ether); ^1H NMR ($CDCl_3$) δ (ppm): 0.3 (s, 6H, 2Me); 1.3 (t, $J_{Me\text{-}CH2O}$ 7.15 Hz, 3H, Me); 2.35 (td, $J_{6\text{-}5}$ 6.5, $J_{6\text{-}7}$ 6.6 Hz, 2H, H_6); 2.45 (s, 2H, CH_2Br); 2.65 (2dd, $J_{2\text{-}2'}$ 16.65, $J_{2\text{-}3}$ 8.51, $J_{2'\text{-}3}$ 5.67 Hz, 2H, H_2, $H_{2'}$); 3.55 (t, $J_{7\text{-}6}$ 6.65 Hz, 2H, H_7); 4.15 (m, 2H, CH_2O); 4.55 (s, 2H, CH_2Ph);

4.65 (m, 1H, H_3); 5.55 (ddt, J_{4-3} 6.82, J_{4-5} 15.43, J_{4-6} 1.3 Hz, 1H, H_4); 5.75 (dtd, J_{5-4} 15.41, J_{5-6} 6.65, J_{5-3} 0.7 Hz, 1H, H_5); 7.35 (m, 5H, H_{ar}). (Found: C, 53.2; H, 6.72. $C_{19}H_{29}BrO_4Si$ requires C, 53.14; H, 6.81%).

(E) 7-Benzyloxy-3-bromomethyldimethylsilyloxyhept-4-enal ***15***.-To a stirred solution of the ester ether **14** (3.85 g, 8.97 mmol) in anhydrous hexane was added dropwise under nitrogen at -78°C, diisobutylaluminium hydride (1 M in hexane) (9.9 cm^3, 9.87 mmol). After 1 h at -78°C, methanol (9.7 cm^3) was added and the reaction was then hydrolysed with an aqueous saturated solution of NH_4Cl, extracted with diethyl ether and the extracts dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was chromatographed on silica gel with hexane-diethyl ether (8:2) to afford the aldehyde **15** as a colorless oil (2.76 g, 80% yield); R_f = 0.43 (1:1 hexane:diethyl ether). ^1H NMR ($CDCl_3$), δ (ppm): 0.2 (s, 6H, 2Me); 2.3 (td, J_{6-7}=J_{6-5} 6.5 Hz, 2H, H_6); 2.4 (s, 2H, CH_2Br); 2.45 (m, 1H, $H_{2'}$); 2.6 (ddd, $J_{2-2'}$ 13.7, J_{2-3} 7.7, J_{2-1} 2.3 Hz, 1H, H_2); 3.4 (t, J_{7-6} 6.54 Hz, 2H, H_7); 4.4 (s, 2H, CH_2Ph); 4.6 (m, 1H, H_3); 5.45 (dd, J_{4-5} 15.47, J_{4-3} 6.8 Hz, 1H, H_4); 5.6 (dt, J_{5-4} 15.55, J_{5-6} 6.56 Hz, 1H, H_5); 7.25 (m, 5H, H_{ar}); 9.7 (t, J_{1-2} 2.04 Hz, 1H, H_1)); FAB^+ (thioglycerol): m/z 385, 387 $(M+H)^+$. (Found: C, 52.81; H, 6.48. $C_{17}H_{25}BrO_3Si$ requires C, 52.98; H, 6.54%).

(E) 6-Benzyloxy-2-bromomethyldimethylsilyloxyhex-3-ene ***16***.- 90% yield; R_f= 0.84 (1:1 hexane:diethyl ether). ^1H NMR ($CDCl_3$), δ (ppm): 0.3 (s, 6H, 2Me); 1.25 (d, J_{1-2} 6.31 Hz, 3H, H_1); 2.35 (q, J_{5-6}= J_{5-4} 6.63 Hz, 2H, H_5); 2.5 (s, 2H, CH_2Br); 3.55 (t, J_{6-5} 6.74 Hz, 2H, H_6); 4.3 (m, 1H, H_2); 4.5 (s, 2H, CH_2Ph); 5.4-

5.8 (m, 2H, H_3, H_4); 7.3 (m, 5H, H_{ar}). (Found: C, 53.85; H, 7.2. $C_{16}H_{25}BrO_2Si$ requires C, 53.78; H, 7.05%).

Acknowledgements:

We are deeply grateful to the « Ministère de l'Enseignement Supérieur et de la Recherche » for a grant (to F. B) and to C.N.R.S and « Ministère de l'Education Nationale » and « La Ligue Régionale contre le Cancer » for generous support.

REFERENCES

1. Stork, G.; Kahn, M. *J. Am. Chem. Soc.*, **1985**, *107*, 500.
2. Nishiyama, H.; Kitajima, T.; Matsumoto, M.; Itoh, K. *J. Org. Chem.*, **1984**, *49*, 2298.
3. Journet, M.; Malacria, M. *J. Org. Chem.*, **1992**, *57*, 3085. Bogen, S.; Journet, M.; Malacria, M. *Synlett*, **1994**, 958. Journet, M.; Lacote, E.; Malacria, M. *J. Chem. Soc., Chem. Commun.*, **1994**, 461. Wu, S.; Journet, M.; Malacria, M. *Tetrahedron Lett.*, **1994**, *35*, 8601.
4. Lopez, J. C.; Gomez, A. M.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.*, **1994**, 1533.
5. Gomez, A. M.; Lopez, J. C.; Fraser-Reid, B. *J. Org. Chem.*, **1995**, *60*, 3859. Pedretti, V.; Mallet, J. M.; Sinay, P. *Carbohydrate Res.*, **1993**, *244*, 247.
6. Crimmins, M. T.; O'Mahony, R. *J. Org. Chem.*, **1989**, *54*, 1157.
7. Wei, Z. Y.; Wang, D.; Li, J. S. *J. Org. Chem.*, **1989**, *54*, 5768.

8. Le Merrer, Y.; Gravier-Pelletier, C.; Micas-Languin, D.; Mestre, F.; Duréault, A.; Depezay, J. C. *J. Org. Chem.*, **1989**, *54*, 2411.

9. Mesnard, D.; Miginiac, L. *J. Organometal. Chem.*, **1990**, *397*, 127.

10. Trost, B. M.; Kung, R. A. *J. Am. Chem. Soc.*, **1975**, *97*, 7152.

11. Parrain, J. L.; Duchene, A.;. Quintard, J. P. *Tetrahedron Lett.*, **1990**, *31*, 1857. Stille, J. K.; *Angew. Chem. Int. Ed. Engl.*, **1986**, *25*, 508.

12. Nicolaou, K. C.; Webber, S. E.; Ramphal, J.; Abe, Y. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1019.

13. Nordin, I. C. *J. Heterocyclic Chem.*, **1966**, *3*, 531.

14. Meyers, A. I.; Shimano, M. *Tetrahedron Lett.*, **1993**, *34*, 4893.

(Received in the UK 3 November 1997)