Factors Affecting Reaction of 1,6-Anhydrohexos-2-ulose Derivatives

Takatoshi Kawai,^A Minoru Isobe^B and Steven C. Peters^{B,C}

^A Eisai Co. Ltd, Tsukuba Research Laboratories,
1-3, Tokodai 5, Tsukuba, Ibaraki 300-26, Japan.
^B School of Agricultural Sciences, Nagoya University,
Chikusa, Nagoya 464-01, Japan.
^C To whom correspondence should be addressed.
Present address: School of Chemistry, The University of Melbourne,
Parkville, Vic. 3052.

Abstract

1,6-Anhydrohexos-2-ulose derivatives undergo reaction with (trimethylsilyl)diazomethane in the presence of boron trifluoride etherate to afford structurally isomeric products. Ion-dipole interactions involving the 1,6-anhydro bridge and C4 substituents control reactivity.

Introduction

We recently became interested in the development of methodologies for ring expansion of pyranoses as part of our synthetic studies of ciguatoxin and related polycyclic ether containing marine natural products. Laevoglucosenone (1,6-anhydro-3,4-dideoxy- β -D-glycerohex-3-enopyranos-2-ulose) (1) was particularly appealing to us as a starting material because of its availability and low cost, and



potential for stereocontrolled introduction of oxygen functionality. We considered that the carbonyl moiety of 1,6-anhydrohexos-2-ulose derivatives readily accessible from (1) may be amenable to a diazomethane-type homologation methodology to afford products of ring expansion. (Trimethylsilyl)diazomethane (Me₃SiCHN₂) is a safe and commercially available alternative to diazomethane and typically affords products of homologation in better yield and increased regioselectivity on reaction with ketones in the presence of Lewis acid catalysts.^{1,2}

Results and Discussion

Treatment of the 4-methoxylaevoglucosenone derivative $(2)^3$ with Me₃SiCHN₂ and boron trifluoride etherate (BF₃.Et₂O) at 0° afforded a mixture of the structural isomers (3), (4) and (5) in 30, 35, and 14% yields, respectively [equation (1)].

¹ Hashimoto, N., Aoyama, T., and Shioiri, T., *Tetrahedron Lett.*, 1980, **21**, 4619; Uyehara, T., Kabasawa, Y., and Kato, T., *Bull. Chem. Soc. Jpn*, 1986, **59**, 2521; for a review see Anderson, R., and Anderson, S. B., *Adv. Silicon Chem.*, 1991, **1**, 303.

² Hashimoto, N., Aoyama, T., and Shioiri, T., Chem. Pharm. Bull., 1982, 30, 119.

³ Shafizadeh, F., Furneaux, R. H., and Stevenson, T. T., Carbohydr. Res., 1979, 71, 169.

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Fig. 1. Molecular diagram of (3a) showing the crystallographic labelling scheme. Ellipsoids are at the 50% probability level. Carbon atoms are denoted by numerals only.

Table 1. Final fractional atomic coordinates and equivalent isotropic temperature factors for(3a)

Estimated standard deviations are given in parentheses $B_{\rm eq} = \frac{4}{3} \sum \sum B_{ij} a_i^* a_j^* a_i \cdot a_j$

Atom	$10^4 x$	$10^4 y$	$10^4 z$	$B_{\rm eq}$ (Å ²)
Si	2253(2)	3926(1)	939.4(9)	3.07(2)
O(2)	1316(5)	5310(4)	2650(2)	$3 \cdot 92(8)$
O(4)	3076(4)	7723(4)	322(2)	3.78(7)
O(5)	4315(4)	7691(4)	2149(3)	$3 \cdot 50(7)$
O(6)	2506(5)	8105(4)	3246(2)	4.53(9)
C(1)	3267(7)	7081(5)	2763(3)	$3 \cdot 4(1)$
C(2)	2136(6)	6315(5)	2175(3)	2.75(8)
C(3)	1217(6)	7171(5)	1540(4)	$3 \cdot 14(9)$
C(4)	2242(6)	8230(5)	1096(3)	$3 \cdot 24(9)$
C(5)	3402(7)	8730(5)	1786(4)	$3 \cdot 5(1)$
C(6)	2625(8)	9245(6)	2671(4)	$4 \cdot 5(1)$
C(7)	2575(6)	4960(5)	2001(3)	$3 \cdot 15(9)$
C(8)	439(7)	4261(6)	301(4)	$4 \cdot 2(1)$
C(9)	3973(8)	4250(6)	207(4)	$4 \cdot 6(1)$
C(10)	2228(8)	2219(5)	1368(5)	$4 \cdot 5(1)$
C(11)	2216(8)	7730(7)	-522(4)	$4 \cdot 9(1)$

Table 2. Selected torsion angles (degrees) for (3a) Estimated standard deviations are given in parentheses

Atoms	Angle	Atoms	Angle
$\overline{C(1)}$ - $C(2)$ - $C(3)$ - $C(4)$	$39 \cdot 9(5)$	C(3)-C(2)-C(7)-Si	$4 \cdot 1(8)$
C(3) - C(4) - C(5) - O(5)	$56 \cdot 2(6)$	C(3) - C(2) - C(7) - H(7)	152(3)
C(5) - O(5) - C(1) - C(2)	$75 \cdot 7(5)$	$\dot{C(11)} - \dot{O(4)} - \dot{C(4)} - \dot{C(3)}$	$84 \cdot 3(5)$
C(3)-C(4)-C(5)-C(6)	$-56 \cdot 3(6)$	C(7)-C(2)-C(3)-C(4)	$-108 \cdot 4(6)$
O(6)-C(1)-C(2)-C(3)	$53 \cdot 0(5)$	O(2) - C(2) - C(3) - C(4)	$178 \cdot 5(4)$

Although lower temperature favoured oxiran formation, a mixture was always obtained.



The oxiran (3) was produced as a mixture of two diastereomers possessing almost identical spectral characteristics. Selective crystallization of (3a) permitted structure elucidation by X-ray crystallography as shown in Fig. 1, with atomic coordinates and equivalent isotropic temperature factors in Table 1 and torsion angles in Table 2. The carbon [C(7)] bearing the trimethylsilyl group is located in the α -configuration corresponding to reaction of Me₃SiCHN₂ at the α -face of the carbonyl of (2). A syn relationship with respect to the plane of the oxiran moiety between the trimethylsilyl group and C(3) is indicated by the torsion angle C(3)-C(2)-C(7)-Si of $4 \cdot 1(8)^{\circ}$ (Table 2).

Nuclear Overhauser enhancement (n.O.e.) between H7, H1 and H3 α , and the trimethylsilyl group (Fig. 2) is consistent with the X-ray data of (3a). Examination of the mother liquors of (3) showed an n.O.e. between H7 and H3 α . Expected anisotropy associated with opposite absolute stereochemistry at C2 indicated that the mother liquors contained the diastereomer (3b) (Fig. 2) differing from (3a) by opposite absolute stereochemistry at C7.



Fig. 2. Nuclear Overhauser enhancements of (3a) and (3b).

The major product (4) arising from ring expansion was obtained as a single diastereomer. The potential energy minimized conformations of hypothetical diastereomers differing by opposite absolute stereochemistry at C 2 were calculated,⁴ and predicted coupling constants compared with observed values (Fig. 3). Only the conformation possessing the trimethylsilyl group in the β -configuration was consistent with observed coupling constants. In addition, an n.O.e. between H 4 β and the trimethylsilyl group was consistent with the calculated distance of 2 · 5 Å.

The minor product (5) arising from ring expansion was also produced diastereospecifically. On the basis of observed ¹H n.m.r. coupling constants and similar calculations⁴ to those described above for (4), the trimethylsilyl group was assigned the β -configuration (Fig. 4).

⁴ Biograf. v.3.1, Molecular Simulations Inc., 200 Fifth Avenue, Waltham, Massachusetts 02154.



Fig. 3. Potential energy minimized conformation of (4) and the C2 diastereomer.



potential energy 159 kJ/mol

potential energy 162 kJ/mol

Protons		Selected coupling constants (Hz)	
	Calculated	Observed	Calculated
H 3, H 4α	5.3	5	3.1
Η 3, Η 4β	12.4	11	3.7
H 4a, H 5	4.5	5	3.2
Η 4β, Η 5	2.2	2	3.5
Η 4α, Η 6	—	1	—

Fig. 4. Potential energy minimized conformation of (5) and the C3 diastereomer.

Shioiri² has suggested that if oxirans are produced in reactions of ketones with Me₃SiCHN₂, BF₃.OEt₂ would effect conversion into structurally isomeric homologated products. However, attempted conversion of (3) into (4) and (5) by treatment with BF₃.OEt₂ was unsuccessful [equation (2)]. In addition, extended reaction times of (2), Me₃SiCHN₂ and BF₃.OEt₂ did not effect structural isomerization. Diastereospecific formation of (4) and (5) is also consistent with formation of (3)–(5) by unique reaction pathways of (2).



The reaction mechanism of (2) presumably involves approach of Me_3SiCHN_2 at the α -face of the carbonyl. The involvement of a chair-like conformation of the pyranose ring in transition states is implied by similar conformations of (2) and (3) (Scheme 1). Diastereofacial specificity is presumably effected by ion-dipole interaction involving the C4 and C5 oxygens which stabilize transition states leading to the oxiran (3). Conformational restriction and ring strain associated with the 1,6-anhydro bridge of (2) is presumably another factor affecting epoxidation and diastereofacial specificity. The regioselective formation of (4) and (5) is indicative of relatively higher electron density at C1 than C3 of (2) and steric interaction between the trimethylsilyl and methoxy groups in transition states leading to (5).

In order to examine the effect of a bulkier substituent at C 4, the 1,6-anhydro-4benzyloxyhexos-2-ulose derivative $(6)^5$ was synthesized in 92% yield by treatment of laevoglucosenone (1) with benzyl alcohol and triethylamine. Interestingly, when a high concentration of laevoglucosenone (1) and triethylamine was employed in reaction with benzyl alcohol, the bispyranose (7)⁶ was isolated in higher yield (32%) than (6) (19%). Under such conditions, (6) is presumably deprotonated at C 3 and undergoes condensation with laevoglucosenone (1) followed by elimination of benzyl alcohol [equation (3)].



Treatment of (6) with Me_3SiCHN_2 and $BF_3.OEt_2$ afforded a mixture of the structural isomers (8), (9) and (10) as the major products in the ratio 3:4:1 and

⁵ Furneaux, R. H., Gainsford, G. J., Shafizadeh, F., and Stevenson T. T., *Carbohydr. Res.*, 1986, 146, 113.

⁶ Shafizadeh, F., Furneaux, R. H., Pang, D., and Stevenson, T. T., *Carbohydr. Res.*, 1982, 100, 303.





isolated in 22, 38, and 2% yields, respectively [equation (4)]. The oxiran (8) was produced with diastereofacial selectivity of c. 9:1, from reaction preferentially at the α -face (Fig. 5). Increased steric bulk of the C4 substituent of (6) compared with (2) is presumably responsible for decrease in diastereofacial selectivity.



Replacement of an alkoxy substituent with a proton at C4 was also investigated. Reaction of $(11)^7$ with Me₃SiCHN₂ and BF₃.OEt₂ afforded (12) and (13) [equation (5)], which indicates the importance of alkoxy substitution at C4 for high diastereofacial selectivity.



Reaction of (2) with sodium borohydride in water afforded the alcohols (14) and (15) in 33 and 30% yields, respectively [equation (6)]. The product (14) with the hydroxy group in the α -configuration was less polar than (15), and as a solution in CDCl₃ showed coupling of 12 Hz between H2 and the hydroxy

⁷ Shafizadeh, F., and Chin, P. P. S., *Carbohydr. Res.*, 1977, 58, 79.



proton in the ¹H n.m.r. spectrum. Intramolecular hydrogen bonding in $(14)^{\dagger}$ is consistent with ion-dipole interaction in transition states of reactions of the 1,6-anhydrohexos-2-ulose derivatives (2) and (6) with Me₃SiCHN₂ (Fig. 6).



Fig. 6. Intramolecular hydrogen bonding in (14) compared with the proposed ion-dipole interaction.

As part of the initial aim of our project we investigated reaction of the pyranose (16) with Me₃SiCHN₂ and BF₃.OEt₂ [equation (7)]. Although the product of ring expansion (17) was isolated from the reaction mixture in only moderate yield (40%), analysis of crude reaction mixtures by ¹H n.m.r. spectroscopy indicated that products derived from epoxidation of (16) were not formed. To the best of our knowledge reactions of the 1,6-anhydrohexos-2-ulose derivatives (2), (6) and (11) are the first examples of epoxidation of ketones with Me₃SiCHN₂ and BF₃.OEt₂. Indeed the synthetic utility is typically a high yield of homologated ketones. Regardless of the details of the mechanism, it is apparent that the 1,6-anhydro bridge exerts a strong influence on the nature of reaction.



In a related series of experiments, 3-bromolaevoglucosenone $(18)^9$ was treated with Me₃SiCHN₂ in the presence of BF₃.OEt₂. Although the initial products of reaction were too unstable to isolate, spectral data indicated that the alcohol (20) was formed on concentration after workup [equation (8)]. Presumably (20) is produced by reaction of the oxiran (19) with HBr, formed by decomposition of

 $[\]dagger$ Intramolecular hydrogen bonding in 1,6-anhydro-2-hydroxypyranoses has been reported previously. 3,8

⁸ Pecka, J., Stanek, J., and Cerny, M., Collect. Czech. Chem. Commun., 1974, 39, 1192.

⁹ Ward, D. D., and Shafizadeh, F., Carbohydr. Res., 1981, 93, 284.

an unidentified component on concentration. The relative regiochemistry of the C2–Br and C7–OH groups is inferred from expected positive charge development at C2 of (19), consistent with reported acid-catalysed reactions of α -silyloxirans.¹⁰ Conformational restrictions imposed on (20) presumably preclude coupling of H7 and the hydroxy proton in (CD₃)₂SO.



Treatment of laevoglucosenone (1) with Me₃SiCHN₂ and BF₃.OEt₂ afforded a mixture of the oxiran (21) and the cyclopropane derivative (22) as major products of reaction [equation (9)], as indicated by spectral characteristics. Competing 1,2- and 1,4-addition of Me₃SiCHN₂ to laevoglucosenone (1) presumably results in formation of (21) and (22), respectively.



Reaction of the α,β -enone (23) under similar conditions afforded the labile compound (24) as the sole product [equation (10)]. 1,3-Dipolar cycloaddition of Me₃SiCHN₂ to the olefinic moiety of (23) followed by expulsion of N₂ from the pyrazoline intermediate presumably affords (24). Although cyclopropane formation and 1,3-dipolar cycloaddition reactions of α,β -enones and Me₃SiCHN₂ are common,¹¹ epoxidation is apparently associated with the 1,6-anhydro bridge of (1) and (18). The results indicate that the 1,6-anhydro bridge also affects chemoselectivity in reactions with Me₃SiCHN₂ and BF₃.OEt₂.



In summary, diastereofacial selectivity in reactions of 1,6-anhydrohexos-2-ulose derivatives can not be rationalized solely on the basis of the steric bulk of,

¹⁰ Stork, G., and Colvin, E., J. Am. Chem. Soc., 1971, 93, 2080.

¹¹ Aoyama, T., Iwamoto, Y., Nishigaki, S., and Shioiri, T., Chem. Pharm. Bull., 1989, **37**, 253; Aoyama, T., Nakano, T., Nishigaki, S., and Shioiri, T., Heterocycles, 1990, **30**, 375; Ikuina, J., Yoshida, K., Tagata, H., Kumakura, S., and Tsunetsugu, J., J. Chem. Soc., Perkin Trans. 1, 1989, 1305. and conformational rigidity imposed by, the 1,6-anhydro bridge, and ion-dipole interaction in transition states is presumably important in reactions involving Me_3SiCHN_2 and $BF_3.OEt_2$. We expect the improved understanding of reactivity will be of value in synthetic studies employing 1.6-anhydrohexos-2-ulose derivatives.

Experimental

General

Melting points were determined by using a Yanaco MP-S3 apparatus and are uncorrected. Infrared spectra were measured on a JASCO F.t.i.r. 7000S spectrophotometer. Proton and carbon nuclear magnetic resonance spectra were recorded on a JEOL EX270 spectrometer. All samples were dissolved in CDCl₃ and chemical shifts are reported as δ values in parts per million relative to tetramethylsilane as internal standard, unless otherwise indicated. E.i. mass spectra were measured on a JEOL D-100 or DX-705 mass spectrometer. High resolution mass spectra (h.r.m.s.) were measured with a JEOL DX-705 instrument. Optical rotation was determined with a JASCO DIP-370 digital polarimeter. Elemental analyses and h.r.m.s. were performed by the Analytical Laboratory at the School of Agriculture, Nagoya University.

Analytical thin-layer chromatography (t.l.c.) was performed on precoated plates: silica gel 60 F-254, layer thickness 0.25 mm, supplied by E. Merck (Art 5715), Darmstadt, Germany. Preparative t.l.c. was conducted on precoated plates: silica gel 60 F-254 (Art 5774), layer thickness 0.5 mm, or prepared silica gel 60 FP-254 (Art 7747), layer thickness 2.0 mm, supplied by E. Merck, Darmstadt, Germany. Silica gel columns for chromatography were prepared with Fuji Devison (BW 820-MH).

Synthesis of (2)

The ketone (2) was prepared according to a modified procedure of Shafizadeh *et al.*³ A solution of laevoglucosenone (1) (0.17 g, 1.35 mmol) and triethylamine (0.10 ml, 0.72 mmol) in methanol (10 ml) was stirred at room temperature for 3 h. Concentration and filtration (silica, 3:1 dichloromethane/ethyl acetate elution) afforded (2) as a pale yellow oil (0.20 g, 94%). ¹H n.m.r. δ 2.51, dm, J 17 Hz, 1H, H 3 α ; 2.69, dd, J 5, 17 Hz, 1H, H 3 β ; 3.37, d, J 1 Hz, 3H, OMe; 3.71, d, J 5 Hz, 1H, H4; 3.87, d, J 8 Hz, 1H, 1×H6; 3.91, dd, J 5, 8 Hz, 1H, 1×H6; 4.77, m, 1H, H5; 5.08, s, 1H, H1. ¹³C n.m.r. δ 36.9, 56.5, 65.0, 74.2, 78.5, 101.2, 198.3.

Reaction of (2) with (Trimethylsilyl)diazomethane and Boron Trifluoride Etherate

To a solution of (2) (0.40 g, 2.5 mmol) and (trimethylsilyl)diazomethane (2.0 M in hexanes, 1.4 ml, 2.8 mmol) in dichloromethane (3 ml) at 0° under an inert atmosphere was added boron trifluoride etherate (0.2 M in dichloromethane, 0.63 ml, 0.13 mmol). On completion of vigorous gas expulsion, water (5 ml) was added and the mixture was stirred vigorously for 0.1 h. The aqueous fraction was extracted with dichloromethane $(2 \times 5 \text{ ml})$ and the combined organics were concentrated to a residual yellow oil (0.67 g). Chromatography of the mixture on silica (65 g, ether/hexane gradient elution) permitted separation of the components.

Compound (3) ($R_{\rm F}$ 0.38, 4:1 ether/hexane elution) was obtained as a mixture of two diastereomers possessing almost identical spectral characteristics, as a colourless oil (185 mg, 30%) [Found: m/z 244.1144. $C_{11}H_{20}O_4Si$ ($M^{+\bullet}$) requires 244.1131]. ¹H n.m.r. δ 0.17, s, 9H, Me₃Si; 1.73, dddd, J 2, 2, 2, 15 Hz, 1H, H 3 α ; 2.23, dd, J 5, 15 Hz, 1H, H 3 β ; 2.23(1), s, 1H, H 7; 3.40, m, 1H, H 4; 3.43, s, 3H, OMe; 3.83, m, 2H, H 6; 4.71, m, 2H, H 1, H 5. ¹³C n.m.r. δ -2.3, 26.9, 56.6, 56.7, 60.4, 65.6, 73.4, 76.9, 106.3. $\nu_{\rm max}$ (KBr) 2955, 2898, 2823, 1251, 1123, 1102, 920, 881, 845 cm⁻¹. Mass spectrum m/z 244 (1%, M), 243 (1), 229 (15), 213 (15), 201 (43), 183 (100).

Repeated crystallization of a portion (81 mg) from ether/hexane afforded (3a) as colourless crystals (35 mg), m.p. 79–80° (Found: C, 54·1; H, 8·3. C₁₁H₂₀O₄Si requires C, 54·1; H, 8·3%). ¹H n.m.r. (difference n.O.e.) δ 2·23(1) (H7), 4·71 (H1); 0·17 (Me₃Si), 1·73 (H3 α). $[\alpha]_{D}^{29}$ (CHCl₃) -110·4° (c, 23 mM).

The mother liquors containing (3b) showed different n.O.e. characteristics to the crystalline material: $\delta 2 \cdot 23(1)$ (H 7), $1 \cdot 73$ (H 3 α); $2 \cdot 23$ (H 3 β), $1 \cdot 73$ (H 3 α).

Compound (4) ($R_{\rm F}$ 0·23, 4:1 ether/hexane elution) was obtained as colourless crystals from ether/hexane (215 mg, 35%), m.p. 59–61° (Found: C, 54·1; H, 8·2%; M^{+•}, 244·1136. C₁₁H₂₀O₄Si requires C, 54·1; H, 8·3%; M^{+•}, 244·1131). ¹H n.m.r. δ 0·13, s, 9H, Me₃Si; 2·68, d, J 3 Hz, 1H, H2; 2·78, ddd, J 1·5, 5, 13 Hz, 1H, H4 α ; 2·84, dd, J 2·5, 13 Hz, 1H, H4 β ; 3·36, ddd, J 2·5, 2·5, 5 Hz, 1H, H5; 3·43, s, 3H, OMe; 3·93, dd, J 4, 8 Hz, 1×H7; 3·96, dd, J 2, 8 Hz, 1×H7; 4·62, m, 1H, H6; 5·54, d, J 3 Hz, 1H, H1. ¹H n.m.r. (difference n.O.e.) δ 0·13 (Me₃Si), 2·68 (H2); 0·13, 2·84 (H4 β); 0·13, 5·54 (H1). ¹³C n.m.r. δ -1·9, 43·4, 56·3, 56·8, 67·1, 76·7, 77·7, 103·5, 206·5. $\nu_{\rm max}$ (KBr) 2955, 2831, 1706, 1681, 1374, 1253, 1144, 1110, 1032, 850 cm⁻¹. Mass spectrum m/z 229 (60%), 212 (48), 201 (40), 185 (76), 183 (100). [α]_D²⁷ (CHCl)₃ -256·2° (c, 23 mM).

The desilylated analogue of (4), possessing a proton at C2 instead of a trimethylsilyl group, was isolated as a colourless solid (19 mg, 4%), m.p. 87–103° [Found: m/z 172·0742. C₈H₁₂O₄ (M^{+•}) requires 172·0736]. ¹H n.m.r. δ 2·67–2·98, cm, 4H, H 2, H 4; 3·4, m, 1H, H 5; 3·44, s, 3H, OMe; 3·97, m, 2H, H 7; 4·69, m, 1H, H 6; 5·62, br d, J 3 Hz, 1H, H 1. $\nu_{\rm max}$ (KBr) 2944, 2889, 1745w, 1702, 1443, 1393, 1252, 1190, 1152, 1087, 1028, 1010, 884, 875 cm⁻¹. Mass spectrum m/z 172 (100%, M), 140 (98, M – CH₃OH), 94 (97), 85 (95), 71 (93), 58 (100).

Compound (5) ($R_{\rm F}$ 0.44, 4:1 ether/hexane elution) was obtained as a colourless *oil* (88 mg, 14%) [Found: m/z 244.1132. $C_{11}H_{20}O_4Si$ ($M^{+\bullet}$) requires 244.1131]. ¹H n.m.r. δ 0.09, s, 9H, Me₃Si; 1.94, ddd, J 2, 11, 15 Hz, 1H, H 4 β ; 1.98, dddd, J 1, 1, 5, 15 Hz, 1H, H 4 α ; 2.39, dd, J 5, 11 Hz, 1H, H 3; 3.40, s, 3H, OMe; 3.47, m, 1H, H 5; 3.86, dd, J 5, 8 Hz, 1H, 1×H7; 3.89, dd, J 2, 8 Hz, 1H, 1×H7; 4.74, m, 1H, H 6; 5.05, s, 1H, H1. ¹³C n.m.r. δ -2.1 (Me₃Si), 22.8 (C4), 33.9 (C3), 56.3 (OMe), 66.6 (C7), 77.1 (C6), 79.3 (C5), 104.6 (C1), 207.6 (C 2). $\nu_{\rm max}$ (KBr) 2947, 2833, 1693, 1251, 1147, 1101, 857 cm⁻¹. Mass spectrum m/z 244 (30%, M), 229 (17), 199 (83), 198 (82), 197 (80), 185 (100), 183 (87).

When the reaction was performed under similar conditions to those described above, analysis of the crude reaction mixture by ¹H n.m.r. spectroscopy indicated that (3), (4) and (5) were produced in the ratio $2 \cdot 6 : 5 \cdot 2 : 1 \cdot 0$, respectively.

In an alternative experiment, a mixture of (2) (0.29 g, 1.8 mmol), boron trifluoride etherate (45 ml, 0.37 mmol) and (trimethylsilyl)diazomethane (2.0 M in hexanes, 1.0 ml, 2.0 mmol) in dichloromethane (16 ml) at -78° under an inert atmosphere afforded (3) (174 mg, 40%), (4) (48 mg, 11%) and (5) (24 mg, 5%). Analysis by ¹H n.m.r spectroscopy, of a crude mixture from a reaction performed under similar conditions, indicated formation of (3), (4) and (5) as the major products in the ratio 6:2:1, respectively. The ratio did not vary for reaction times between 0.1 and 1 h.

Reaction of (3) with Boron Trifluoride Etherate

To a solution of (3) (185 mg, 0.76 mmol) in dichloromethane (5 ml) at room temperature under an inert atmosphere was added boron trifluoride etherate (0.2 M in dichloromethane, 0.38 ml, 76 mmol). Analysis of the reaction mixture by t.l.c. (4:1 ether/hexane elution) at various intervals over 15 h indicated slow reaction to afford baseline material. The mixture was cooled to 0° and boron trifluoride etherate (80 ml, 0.68 mmol) was added. T.l.c. analysis at 0.1 h indicated almost complete consumption of (3) and concomitant formation of mainly lower $R_{\rm F}$ material. The regioisomers (4) and (5) were not detected throughout the reaction.

Reaction of Laevoglucosenone (1) with Benzyl Alcohol and Triethylamine

A mixture of laevoglucosenone (1) $(1 \cdot 26 \text{ g}, 10 \text{ mmol})$ and triethylamine $(0 \cdot 70 \text{ ml}, 5 \text{ mmol})$ in benzyl alcohol (40 ml) was stirred overnight at room temperature. Concentration and chromatography on silica (250 g, 1:1 ether/hexane elution) afforded (6) as a yellow oil (2·16 g, 92%) with spectral characteristics consistent with those reported previously.⁵ Mass spectrum m/z 234 (35%, M), 206 (100), 167 (33), 162 (73), 160 (44).

In an alternative experiment, a mixture of laevoglucosenone (1) $(2 \cdot 0 \text{ g}, 16 \text{ mmol})$, triethylamine $(3 \cdot 0 \text{ ml}, 22 \text{ mmol})$ and benzyl alcohol (3 ml, 29 mmol) was stirred at room temperature for 40 h. The reaction mixture was diluted with dichloromethane (200 ml),

washed with 5% aqueous hydrochloric acid $(2 \times 60 \text{ ml})$, saturated aqueous sodium bicarbonate $(2 \times 80 \text{ ml})$ and brine (100 ml), and dried (Na_2SO_4) . Concentration to a brown oily residue $(7 \cdot 4 \text{ g})$ and chromatography on silica (300 g, 1:1 ether/hexane elution) afforded (6) as a yellow oil $(0 \cdot 71 \text{ g}, 19\%)$. Further chromatography and recrystallization from ethyl acetate/hexane gave the bispyranose (7) as colourless crystals $(0 \cdot 64 \text{ g}, 32\%)$, m.p. $173-175^{\circ}$ (lit.⁶ $170-172^{\circ}$) with spectral characteristics consistent with those reported previously.

Reaction of (6) with (Trimethylsilyl)diazomethane and Boron Trifluoride Etherate

To a solution of (6) (0.23 g, 1.0 mmol) and (trimethylsilyl)diazomethane (2.0 M in hexanes, 0.55 ml, 1.1 mmol) in dichloromethane (1.2 ml) at 0° under an inert atmosphere was added boron trifluoride etherate (0.2 M in dichloromethane, 0.25 ml, 0.05 mmol). Water (2 ml) was added and the mixture was stirred to room temperature. The aqueous fraction was extracted with dichloromethane (3 ml) and the combined organics were dried (Na₂SO₄) and concentrated. Chromatography of the residual yellow solid (0.28 g) on silica (40 g, 1:2 ether/hexane elution) afforded (10) as a colourless oil (8 mg, 2%) [Found: m/z 320·1430. $C_{17}H_{24}O_4\text{Si}$ (M^{+•}) requires 320·1444]. ¹H n.m.r. δ 0·10, s, 9H, Me₃Si; 1·94, m, 2H, H 4; 2·49, dd, J 8, 8 Hz, 1H, H3; 3·64, q, J 3 Hz, 1H, H5; 3·85, m, 2H, H7; 4·63, d, J 2 Hz, 2H, PhCH₂; 4·73, m, 1H, H6; 5·09, s, 1H, H1; 7·22–7·42, cm, 5H, ArH. ¹³C n.m.r. δ -2·1, 23·4, 34·2, 66·7, 70·3, 77·2, 77·7, 104·7, 127·7, 127·9, 128·5, 207·7 (1×ArC not observed). ν_{max} (KBr) 2924, 2864, 1719w, 1687, 1252, 1116, 837 cm⁻¹. Mass spectrum m/z 320 (5%, M), 275 (4, M - CO₂H), 229 (17, M - PhCH₂), 168 (22), 91 (100), 73 (100).

Further chromatography and recrystallization from ether/hexane afforded (9) as colourless platelets (121 mg, 38%), m.p. 127–129° (Found: C, 63·7; H, 7·6%; M^{+•}, 320·1448. C₁₇H₂₄O₄Si requires C, 63·7; H, 7·6%; M^{+•} 320·1444). ¹H n.m.r. δ 0·15, s, 9H, SiMe₃; 2·74, d, J 3 Hz, 1H, H2; 2·81, ddd, J 2, 5, 14 Hz, 1H, H4 α ; 2·87, dd, J 3, 14 Hz, 1H, H4 β ; 3·50, m, 1H, H5; 3·91, m, 2H, H7; 4·57, m, 1H, H6; 4·58, d, J 12 Hz, 1H, 1×PhCH₂; 4·77, d, J 12 Hz, 1H, 1×PhCH₂; 5·57, d, J 3 Hz, 1H, H1; 7·22–7·40, cm, 5H, ArH. ¹H n.m.r. (DIFNOE) δ 0·15 (Me₃Si), 2·74 (H2); 0·15, 2·87 (H4 β); 0·15, 5·57 (H1). ¹³C n.m.r. δ –1·8, 43·5, 56·9, 67·2, 69·8, 74·3, 77·4, 103·5, 127·8, 128·0, 128·4, 137·6, 206·7. ν_{max} (KBr) 2957, 2897, 1742w, 1676, 1253, 1142, 1117, 848 cm⁻¹. Mass spectrum m/z 320 (19%, M), 229 (18, M – PhCH₂), 168 (43), 113 (52), 91 (100), 73 (100). $[\alpha]_D^{27}$ (CHCl₃) –163·7° (c, 11 mM).

Further chromatography afforded (8), as a mixture of mainly two diastereomers possessing almost identical spectral characteristics, as a colourless oily solid (72 mg, 22%), m.p. <63° (Found: C, 63·1; H, 7·6. C₁₇H₂₄O₄Si requires C, 63·7; H, 7·6%). ¹H n.m.r. δ 0·15, s, 9H, Me₃Si; 1·75, dddd, J 2, 2, 2, 14 Hz, 1H, H 3 α ; 2·25, br dd, J 5, 14 Hz, 1H, H 3 β ; 2·26, br s, 1H, H7; 3·58, m, 1H, H4; 3·79, m, 2H, H6; 4·62, s, 2H, PhCH₂; 4·67, m, 1H, H5; 4·73, br, 1H, H1; 7·25–7·42, cm, 5H, ArH. ¹³C n.m.r. δ –2·1, 27·5, 56·8, 60·6, 65·8, 70·8, 74·0, 74·2, 106·5, 127·7, 127·8, 128·4 (1×ArC not observed). ν_{max} 2952, 2896, 1250, 1123, 1098, 923, 843 cm⁻¹. Mass spectrum m/z 319 (0·1%, M-H), 229 (3, M-PhCH₂), 129 (2), 113 (2), 92 (3), 91 (100), 73 (80).

Analysis of a portion of the crude reaction mixture by 1 H n.m.r. spectroscopy indicated formation of (8), (9) and (10) in the ratio 3:4:1, respectively, as the major products of reaction.

The formation of c. 10% of two oxirans, diastereomeric with (8), was indicated by ¹H n.m.r. spectroscopic analysis of (8) and the crude reaction mixture. ¹H n.m.r. δ 0.13, s, Me₃Si; 0.19, s, Me₃Si; 1.58, dm, J 15 Hz, 1×H 3; 2.34, dd, J 5, 15 Hz, 1×H 3; 2.44, dd, J 5, 15 Hz, 1×H 3; 3.50, m, H 4; 3.66, m, H 4.

Synthesis of (11)

Laevoglucosenone (1) was hydrogenated to afford (11) according to the procedure of Shafizadeh and Chin.⁷ A mixture of (1) (161 mg, 1.3 mmol), 5% Pd/BaSO₄ (300 mg) and ethyl acetate (5 ml) was maintained under an atmosphere of hydrogen for 3 h at room temperature. T.l.c. analysis (1:1 ether/hexane elution) indicated complete consumption of (1). The mixture was filtered through Celite and concentrated to afford (11) as a colourless liquid (150 mg, 92%). ¹H n.m.r. $\delta 2.03$, m, $J_{4\beta,3\alpha}$ 1, $J_{4\beta,3\beta}$ 6, $J_{4\beta,4\alpha}$ 13 Hz, 1H, H4 β ; 2.31,

m, $J_{4\alpha,3\alpha}$ 7, $J_{4\alpha,3\beta}$ 11, $J_{4\alpha,4\beta}$ 13 Hz, 1H, H 4 α ; 2·40, m, $J_{3\alpha,1}$ 1, $J_{3\alpha,5}$ 1, $J_{3\alpha,4\beta}$ 1, $J_{3\alpha,4\alpha}$ 7, $J_{3\alpha,4\beta}$ 15 Hz, 1H, H 3 α ; 2·65, m, $J_{3\beta,4\beta}$ 6, $J_{3\beta,4\alpha}$ 11, $J_{3\beta,3\alpha}$ 15 Hz, 1H, H 3 β ; 3·98, ddd, J 1, 5, 7 Hz, 1H, 1×H 6; 4·05, dd, J 1, 7 Hz, 1H, 1×H 6; 4·70, m, 1H, H 5; 5·11, br s, 1H, H 1.

Reaction of (11) with (Trimethylsilyl)diazomethane and Boron Trifluoride Etherate

To a solution of the ketone (11) (141 mg, $1 \cdot 1$ mmol) in dichloromethane (3 $\cdot 5$ ml) under an atmosphere of nitrogen at -78° was added boron trifluoride etherate (0 $\cdot 4$ M in dichloromethane, 0 $\cdot 27$ ml, 0 $\cdot 11$ mmol) and (trimethylsilyl)diazomethane (2 $\cdot 0$ M in hexanes, 0 $\cdot 55$ ml, 1 $\cdot 1$ mmol). Water (2 ml) was added and the mixture was stirred vigorously to room temperature. The organic fraction was washed with brine (5 ml), dried (Na₂SO₄) and concentrated to a colourless oil (191 mg). Chromatography on silica (30 g, 1 $\cdot 2$ ether/hexane elution) afforded a diastereomeric mixture of the oxiran (12) as a colourless oil (75 mg, 31%) (Found: C, 56 $\cdot 0$; H, $8 \cdot 7\%$; M^{+•}, 214 $\cdot 1040$. C₁₀H₁₈O₃Si requires C, 56 $\cdot 0$; H, $8 \cdot 5\%$; M^{+•}, 214 $\cdot 1025$). ¹H n.m.r. δ 0 $\cdot 08$, s, 8%×9H, Me₃Si; 0 $\cdot 11$, s, 62%×9H, Me₃Si; 0 $\cdot 13$, s, 17%×9H, Me₃Si; 0 $\cdot 13$ (4), s, 13%×9H, Me₃Si; 1 $\cdot 1 - 2 \cdot 5$, cm, 5H, H 3, H 4, H 7; 3 $\cdot 7 - 4 \cdot 0$, cm, 2H, H 6; 4 $\cdot 55$, m, 1H, H 5; 4 $\cdot 59$, s, 8%×1H, H 1; 4 $\cdot 63$, s, 62%×1H, H 1; 4 $\cdot 85$, s, 30%×1H, H 1. ¹³C n.m.r. δ $-2 \cdot 1$, $-2 \cdot 0$, $-1 \cdot 9$, $-0 \cdot 7$ (Me₃Si); 21 $\cdot 7$, 22 $\cdot 5$, 25 $\cdot 7$, 26 $\cdot 1$, 26 $\cdot 8$, 27 $\cdot 4$, 28 $\cdot 5$, 28 $\cdot 6$ (C 3, C 4); 54 $\cdot 9$, 55 $\cdot 4$, 56 $\cdot 4$, 58 $\cdot 8$ (C 7); 61, 61 $\cdot 6$, 63 (C 2); 66 $\cdot 8$, 66 $\cdot 9$, 67 $\cdot 7$, 67 $\cdot 9$ (C 6); 72 $\cdot 5$, 72 $\cdot 6$, 72 $\cdot 8$, 73 $\cdot 2$ (C 5); 103 $\cdot 0$, 103 $\cdot 6$, 106 $\cdot 0$, 106 $\cdot 6$ (C 1). ν_{max} (KBr) 2952, 2900, 1251, 1116, 991, 918, 874, 839 cm⁻¹. Mass spectrum m/z 214 (14%, M), 199 (15, M - CH₃), 184 (100, M - CH₂O), 169 (76), 155 (79), 103 (100), 79 (100), 59 (100).

Further chromatography afforded a c. 2:1 mixture of diastereomers of the ketone (13) as a colourless oil (15 mg, 6%) [Found: m/z 214·1033. $C_{10}H_{18}O_3Si$ (M^{+•}) requires 214·1025]. ¹H n.m.r. δ 0·15, s, 67%×9H, Me₃Si; 0·17, s, 33%×9H, Me₃Si; 1·60-2·94, cm, 5H, H2, H4, H5; 3·85-3·96, cm, 1H, 1×H7; 4·02, d, J 8 Hz, 33%×1H, 1×H7; 4·08, d, J 8 Hz, 67%×1H, 1×H7; 4·49-4·61, cm, 1H, H6; 5·50, d, J 2 Hz, 33%×1H, H1; 5·52, d, J 3 Hz, 67%×1H, H1. ¹³C n.m.r. δ -1·8, -1·3 (Me₃Si); 28·8, 30·1 (C5); 40·0, 41·1 (C4); 55·6, 57·4 (C2); 68·8, 69·1 (C7); 74·5, 74·6 (C6); 102·9, 103·4 (C1); 210·3 (C3). ν_{max} (KBr) 2954, 2918, 1675, 1251, 1168, 1133, 843 cm⁻¹. Mass spectrum m/z 214 (12%, M), 199 (22, M - CH₃), 184 (14, M - CH₂O), 156 (17), 155 (16), 143 (15), 103 (100), 79 (42), 75 (79), 73 (75).

A fraction containing a mixture of (12) and (13) (28 mg, 12%) was also collected.

In a separate experiment performed under similar conditions to those described above, analysis of the crude reaction mixture by ¹H n.m.r. spectroscopy and t.l.c. (1:2 ether/hexane elution, phosphomolybdic acid and anisaldehyde visualization) indicated that (12) and (13) were the major products of reaction.

Synthesis of (14) and (15)

A mixture of the 4-methoxylaevoglucosenone derivative (2) (0.30 g, 1.9 mmol), sodium borohydride (0.30 g, 8 mmol) and water (30 ml) was stirred at room temperature for 0.2 h. Acetone (10 ml) and dichloromethane (10 ml) were added with vigorous stirring. The aqueous fraction was saturated with salt and extracted with chloroform $(5\times30 \text{ ml})$ and the combined organics were dried (Na₂SO₄), concentrated and chromatographed (silica, 3:1 dichloromethane/ether elution) to afford (14) ($R_{\rm F}$ 0.19) as a colourless oil (0.10 g, 33%) (Found: C, 52.5; H, 7.7%; M^{+•}, 160.0721; M^{+•} - C₂H₄O, 116.0488. C₇H₁₂O₄ requires C, 52.5; H, 7.6%; M^{+•}, 160.0736; M^{+•} - C₂H₄O, 116.0473). ¹H n.m.r. δ 1.94, m, 2H, H 3; 2.90, d, J 12 Hz, 1H, OH; 3.27, m, 1H, H4; 3.44, s, 3H, OCH₃; 3.52, dm, J 12 Hz, 1H, H2; 3.77, dd, J 2, 8 Hz, 1H, 1×H6; 3.85, dd, J 5, 8 Hz, 1H, 1×H6; 4.64, m, 1H, H5; 5.37, d, J 2 Hz, 1H, H1. ¹³C n.m.r. δ 27.6, 56.6, 65.4, 67.1, 73.5, 75.9, 102.5. Mass spectrum m/z 160 (2%, M), 116 (100, M - C₂H₄O), 114 (100), 87(81), 71 (100).

Further chromatography afforded (15) ($R_{\rm F}$ 0.09) as a colourless oil (0.09 g, 30%) [Found: m/z 160.0753. $C_7H_{12}O_4$ (M^{+•}) requires 160.0736. Found: m/z 116.0497. $C_5H_8O_3$ (M^{+•} - C_2H_4O) requires 116.0473]. ¹H n.m.r. δ 1.46, ddd, J 5, 11, 15 Hz, 1H, H3 β ; 2.13, dm, J 15 Hz, 1H, H3 α ; 2.81, br, 1H, OH; 3.26, m, 1H, H4; 3.33, s, 3H, OMe; 3.67, dd, J 1, 8 Hz, 1H, 1×H6; 3.74, dd, J 6, 8 Hz, 1H, 1×H6; 3.75, m, 1H, H2; 4.52, m, 1H, H5; 5.27, s, 1H, H1. ¹H n.m.r. [(CD₃)₂SO] δ 1.48, ddd, J 5, 11, 14 Hz, 1H, H3 β ; 1.82, dm, J 14 Hz, 1H, H3α; 3·25, s, 3H, OMe; 3·27, m, 1H, H4; 3·49, dtd, J 11, 6, 2 Hz, 1H, H2; 3·58, dd, J 5, 8 Hz, 1H, $1 \times H6$; 3·65, br d, J 8 Hz, 1H, $1 \times H6$; 4·53, m, 1H, H5; 4·79, d, J 6 Hz, 1H, OH; 5·09, br s, 1H, H1. ¹³C n.m.r. δ 29·9, 56·3, 66·1, 66·4, 73·4, 76·6, 102·6. Mass spectrum m/z 161 (6%, M+H), 116 (100, M - C₂H₄O), 114 (100), 87 (100), 71 (100).

Preparation of (23)

To a solution of a previously described diol[†] (1.00 g, 5.3 mmol) and imidazole (1.74 g, 25.6 mmol) in *N*,*N*-dimethylformamide (20 ml) at room temperature was gradually added over 24 h sufficient t-butyldiphenylsilyl chloride (c. 5.3 mmol) until complete consumption was effected, as indicated by t.l.c. analysis (ether elution). Water (10 ml) was added to the mixture and stirring continued for 2 h. The aqueous phase was extracted with dichloromethane (3×20 ml), and the combined organics washed were with brine (20 ml), dried (Na₂SO₄) and concentrated. Column chromatography of the residual oil on silica (100 g, ether/hexane gradient elution) afforded a silylated alcohol as a colourless oil (1.96 g, 87%). ¹H n.m.r. δ 1.07, s, 9H, Bu^t; 1.15, d, *J* 6 Hz, 3H, 1×CHMe₂; 1.16, d, *J* 6 Hz, 3H, 1×CHMe₂; 2.59, d, *J* 5 Hz, 1H, OH; 3.80–3.92, cm, 3H, H5, H6; 3.92, dq, *J* 6, 6 Hz, 1H, CHMe₂; 4.22, m, 1H, H4; 5.04, m, 1H, H1; 5.72, dt, *J* 10, 2 Hz, 1H, H2 or H3; 5.94, dt, *J* 10, 1 Hz, 1H, H2 or H3; 7.35–7.46, cm, 6 ArH; 7.66–7.75, cm, 4×ArH. ¹³C n.m.r. δ 19.1, 21.8, 23.7, 26.8, 65.7, 66.5, 69.9, 70.4, 92.3, 126.6, 127.8, 129.8, 132.6, 132.8, 135.5, 135.6.

Without further purification, the silvlated alcohol $(1\cdot82 \text{ g}, 4\cdot3 \text{ mmol})$ was dissolved in dichloromethane (30 ml). Pyridinium dichromate (9.63 g, 25.6 mmol) was added to the mixture and stirring continued at room temperature for 40 h. Filtration through a column of silica/sand/Celite and concentration afforded a pale yellow oil (1.96 g) which was chromatographed (silica, 1:10:10, ethyl acetate/dichloromethane/hexane elution) to afford the enone (23) as a colourless oil (1.71 g, 94%) (Found: C, 70.7; H, 7.6%; M^{+•} – Bu[†], 367.1350. C₂₅H₃₂O₄Si requires C, 70.7; H, 7.6%; M^{+•} – Bu[†], 367.1366). ¹H n.m.r. δ 1.02, s, 9H, Bu[†]; 1.23, d, J 6 Hz, 3H, 1×CHMe₂; 1.27, d, J 6 Hz, 3H, 1×CHMe₂; 4.02–4.15, cm, 3H, CHMe₂, H6; 4.56, dd, J 3, 5 Hz, 1H, H5; 5.42, d, J 3 Hz, 1H, H1; 6.10, d, J 10 Hz, 1H, H3; 6.86, dd, J 3, 10 Hz, 1H, H2; 7.33–7.44, cm, 6×ArH; 7.66–7.74, cm, 4×ArH. ¹³C n.m.r. δ 19.2, 21.7, 23.2, 26.6, 63.3, 70.8, 75.9, 91.3, 127.6, 127.8, 129.6, 133.2, 133.4, 135.6, 135.6(1), 144.5, 194.8. ν_{max} (KBr) 3071, 2968, 2934, 2859, 1693, 1474, 1429, 1383, 1318, 1220, 1106, 1025 cm⁻¹. Mass spectrum m/z 367 (54%, M – Bu[†]), 199 (100). $[\alpha]_D^{29}$ (CHCl₃) –18.1° (c, 15 mM).

Preparation of (16)

A mixture of the α,β -enone (23) (473 mg, 1.1 mmol), triethylamine (0.15 ml, 1.1 mmol) and benzyl alcohol (10 ml) was stirred at room temperature for 40 h. Concentration and chromatography on silica (400 g, 1:4 ether/hexane elution) afforded a c. 3:1 diastereomeric mixture of the ketone (16) as a colourless oil (239 mg, 41%) [Found: m/z 532 · 2632. C₃₂H₄₀O₅Si $(M^{+\bullet})$ requires 532·2645]. ¹H n.m.r. δ 1·04, s, 9H, Bu^t; 1·18–1·28, cm, 6H, CHMe₂; 2·58, dd, J 5, 16 Hz, 25%×1H, 1×H 3; 2 73, dd, J 7, 15 Hz, 75%×1H, 1×H 3; 2 78, dd, J 5, 15 Hz, $75\% \times 1H$, $1 \times H3$; $2 \cdot 93$, dd, J 5, 16 Hz, $25\% \times 1H$, $1 \times H3$; $3 \cdot 76$, ddd, J 3, 5, 7 Hz, $75\% \times 1H$, H2; 3.93, ddd, J 4, 5, 5 Hz, 25%×1H, H2; 3.95-4.16, cm, 4H, H5, H6, CHMe₂; 4.54-4.67, cm, 2H, PhCH₂; 4.88, d, J 4 Hz, 25%×1H, H 1; 5.17, d, J 3 Hz, 75%×1H, H 1; 7.25–7.43, cm, 11H, ArH; 7 · 65–7 · 75, cm, 4H, ArH. ¹³C n.m.r. δ 19 · 2 (CMe₂), 21 · 4 (1×CHMe₂, major), 21.6 (1×CHMe₂, minor), 23.3 (1×CHMe₂, major), 23.5, (1×CHMe₂, minor), 26.7 (CMe₃), 42.0 (C3, major), 53.4 (C3, minor), 63.2 (C6, major), 63.7 (C6, minor), 69.3 (C5, major), 70.7 (C5, minor), 71.1 (PhCH₂, major), 71.5 (PhCH₂, minor), 76.4, 76.5 (C2, CHMe₂, major), 77.0 (CHMe2, minor), 80.4 (C2, minor), 97.6 (C1, major), 100.4 (C1, minor), $127 \cdot 5(9), \ 127 \cdot 6, \ 127 \cdot 7, \ 128 \cdot 4, \ 129 \cdot 6, \ 133 \cdot 2, \ 133 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 135 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 137 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 137 \cdot 6, \ 135 \cdot 6(1), \ 137 \cdot 7 \ (ArC), \ 207 \cdot 33 \cdot 3, \ 137 \cdot 6, \ 137 \cdot 6$ (C4, minor), 207.4 (C4, major). ν_{max} (KBr) 2969, 2931, 2858, 1735, 1429, 1114, 702 cm⁻¹. Mass spectrum m/z 532 (0.2%, M), 475 (22, M – Bu^t), 265 (34), 91 (100).

† Compound (19; $R = Pr^i$, R', R'' = H), see ref. 12.

¹² Isobe, M., Ichikawa, Y., Funabashi, Y., Mio, S., and Goto, T., *Tetrahedron*, 1986, **42**, 2863.

Synthesis of (17)

To a solution of the ketone (16) (163 mg, 0.31 mmol) in dichloromethane (5 ml) at -23° was added boron trifluoride etherate (0.41 M in dichloromethane, 0.75 ml, 0.31 mmol) and (trimethylsilyl)diazomethane (2.0 M in hexanes, 0.16 ml, 0.31 mmol). Portions (0.05 ml)were removed at 2 and 10 min, washed with water and dried (Na_2SO_4) . T.l.c. analysis (1:4)ether/hexane elution, u.v., phosphomolybdic acid and anisaldehyde visualization) indicated complete consumption of (16) $(R_{\rm F} \ 0.35)$ and formation of one component $(R_{\rm F} \ 0.31)$, which underwent some decomposition at the longer reaction time. Water (2 ml) was added and the mixture was stirred vigorously to room temperature. The organic fraction was washed with brine, dried (Na₂SO₄) and concentrated to a residual yellow oil (140 mg). Purification of the major component by preparative t.l.c. afforded mainly one diastereomer of (17) as a colourless oil (76 mg, 40%) [Found: m/z 618 3195. C₃₆H₅₀O₅Si₂ (M^{+•}) requires 618 3197]. ¹H n.m.r. δ 0 · 12, s, 9H, Me₃Si; 0 · 90, d, J 6 Hz, 6H, Me₂CH; 1 · 06, s, 9H, Bu^t; 2 · 75, d, J 1 · 5 Hz, 1H, H5; 2 · 82, dd, J 9, 15 Hz, 1H, 1×H3; 2 · 97, dd, J 1 · 5, 15 Hz, 1H, 1×H3; 3 · 49, ddd, J 1.5, 4, 9 Hz, 1H, H2; 3.59, dd, J 8, 10 Hz, 1H, 1×H7; 3.70, dd, J 6, 10 Hz, 1H, $1\times H~7;~3\cdot 89,~\mathrm{dq},~J~6,~6~\mathrm{Hz},~1\mathrm{H},~\mathrm{CHMe_2};~4\cdot 0,~\mathrm{m},~1\mathrm{H},~\mathrm{H}~6;~4\cdot 59,~\mathrm{br}~\mathrm{s},~2\mathrm{H},~\mathrm{PhCH_2};~4\cdot 87,~\mathrm{H},~\mathrm{H}~\mathrm{H}~\mathrm{H}^{-1}$ d, J 4 Hz, 1H, H1; $7 \cdot 25 - 7 \cdot 50$, cm, 11H, ArH; $7 \cdot 62 - 7 \cdot 77$, cm, 4H, ArH. ¹³C n.m.r. $\delta 1 \cdot 0$, 19 \cdot 1, 20 · 9, 23 · 2, 26 · 9, 45 · 6, 51 · 1, 65 · 5, 67 · 9, 68 · 4, 71 · 7, 76 · 3, 98 · 0, 127 · 6, 127 · 7, 127 · 8, 128·3, 129·8, 133·1, 135·6, 137·7, 210·4. ν_{\max} (KBr) 2960, 2931, 2859, 1718, 1684, 1428, 1251, 1112, 840, 700 cm⁻¹. Mass spectrum m/z 618 (<1%, M), 604 (1, M - CH₂), 561 (13, $M - C_4H_9$), 489 (16), 349 (62), 199 (100), 91 (100).

Reaction of 3-Bromolaevoglucosenone (18) with (Trimethylsilyl)diazomethane

To a solution of 3-bromolaevoglucosenone (18) (125 mg, 0.61 mmol) in dichloromethane (5 ml) at -78° under an atmosphere of nitrogen was added (trimethylsilyl)diazomethane $(2 \cdot 0 \text{ M})$ in hexanes, 0.39 ml, 0.78 mmol) and boron trifluoride etherate (0.4 M in dichloromethane, 0.15 ml, 0.06 mmol). After stirring for 0.2 h, water (5 ml) was added and the mixture was allowed to warm to room temperature with vigorous stirring. Ether (30 ml) was added and the organics were washed with brine (10 ml) and dried (Na_2SO_4) . T.l.c. analysis (silica, 1:2) ether/hexane elution, molybdophosphoric acid and anisaldehyde-sulfuric acid visualization) indicated at least two major components ($R_{\rm F}$ 0.29, 0.35). On concentration, t.l.c. analysis of the residual oil (167 mg) indicated the presence of a newly formed component ($R_{\rm F}$ 0.18). Chromatography on silica (20 g, ether/hexane elution) afforded the alcohol (20) as a colourless solid (18 mg, 10%), m.p. 90–95° [Found: m/z 308.8959. $C_8H_{11}^{79}Br_2OSi$ (M^{+•} -C₂H₄O) requires 308 · 8947]. ¹H n.m.r. δ 0 · 24, s, 9H, Me₃Si; 3 · 10, br s, 1H, OH; 3 · 74, dd, J 5, 7 Hz, 1H, 1×H6; 3·75, s, 1H, H7; 3·92, d, J 7 Hz, 1H, 1×H6; 4·67, t, J 5 Hz, 1H, H5; 5·75, s, 1H, H1; 6·42, d, J 5 Hz, 1H, H4. ¹H n.m.r. [(CD₃)₂SO] δ 0·20, s, 9H, Me₃Si; 3·57, s, 1H, H7; 3.62, dd, J 5, 7 Hz, 1H, 1×H6; 3.85, d, J 7 Hz, 1H, 1×H6; 4.83, t, J 5 Hz, 1H, H5; 5.48, s, 1H, H 1 or OH; 5.60, s, 1H, H 1 or OH; 6.55, d, J 5 Hz, 1H, H 4. ¹³C n.m.r. δ -0.9, $46 \cdot 4, \ 69 \cdot 8, \ 73 \cdot 0, \ 75 \cdot 7, \ 101 \cdot 1, \ 128 \cdot 8, \ 132 \cdot 3. \ \nu_{\max} \ (\text{KBr}) \ 3492, \ 2955, \ 2901, \ 1625, \ 1334, \ 1250, \$ 1126, 1058, 989, 901, 862, 844 cm⁻¹. Mass spectrum m/z 324 (<1%, M - CO₂H), 309 (4, $M - C_2H_4O$, 252 (5), 245 (22), 229 (7), 166 (100), 94 (74), 73 (66).

Reaction of (1) with (Trimethylsilyl)diazomethane and Boron Trifluoride Etherate

To a solution of (1) (75 mg, 0.59 mmol) in dichloromethane (5 ml) at -78° under an atmosphere of nitrogen was added (trimethylsilyl)diazomethane (2.0 M in hexanes, 0.45 ml, 0.90 mmol) and boron trifluoride etherate (0.4 M in dichloromethane, 0.35 ml, 0.14 mmol). Saturated aqueous sodium bicarbonate solution (4 ml) was added and the mixture was allowed to stir vigorously to room temperature for 0.5 h. The aqueous fraction was extracted with dichloromethane (3 ml) and the combined organics were dried (Na₂SO₄) and concentrated. Chromatography of the residual oil on silica (20 g, 1:2 ether/hexane elution) afforded a c. 1:1 mixture of (21) and (22) (60 mg, 48%) as indicated by t.l.c. and ¹H n.m.r., ¹³C n.m.r. and i.r. spectroscopic analysis. Preparative t.l.c. (silica, 2:1 dichloromethane/hexane elution) permitted separation of (21) and (22). Compound (21): ¹H n.m.r. δ 0.20, s, 9H, Me₃Si;

2.29, s, 1H, CHSiMe₃; 3.80, dd, J 4, 7 Hz, 1H, $1 \times H6$; 3.99, d, J 7 Hz, 1H, $1 \times H6$; 4.78, t, J 4 Hz, 1H, H5; 5.17, d, J 2 Hz, 1H, H1; 5.31, dd, J 2, 10 Hz, 1H, H3; 6.33, dd, J 4, 10 Hz, 1H, H4. Compound (22): ¹H n.m.r. δ 0.12, s, 9H, Me₃Si; 0.48, dd, J 9, 12 Hz, 1H, CHSiMe₃; 1.68, m, 1H, CHCHO; 1.89, dd, J 7, 12 Hz, 1H, CHC=O; 3.90, dd, J 5, 7 Hz, 1H, $1 \times CH_2$; 4.02, d, J 7 Hz, 1H, $1 \times CH_2$; 4.90, br d, J 5 Hz, 1H, CHCH2; 4.95, s, 1H, OCHO. Compounds (21) and (22) failed to give mass spectra suitable for analysis by h.r.m.s.

Synthesis of (24)

To a solution of the enone (23) (0.33 g, 0.78 mmol) in dichloromethane (15 ml) at -78° under an atmosphere of nitrogen was added boron trifluoride etherate (0.15 ml, 1.22 mmol). After stirring for 0.1 h, a solution of (trimethylsilyl)diazomethane in hexanes (10%, 1.4 ml, 1.22 mmol) was added dropwise over 0.5 h and the mixture was maintained at -78° for 0.75 h. Saturated aqueous sodium bicarbonate solution (10 ml) was added and the mixture was allowed to warm to room temperature with stirring over 1 h. The aqueous fraction was extracted with dichloromethane $(2 \times 20 \text{ ml})$ and the combined organics were washed with brine (30 ml), dried (Na₂SO₄), filtered (silica, ether elution) and concentrated. T.l.c. and ¹H n.m.r. analysis of the residue (0.34 g) indicated that the β -substituted enone (24) was the major product. Repeated column chromatography (silica, ether/hexane and dichloromethane/hexane elution) afforded (24) as a colourless oil (0.13 g, 33%) [Found: m/z 510.2658. C₂₉H₄₂O₄Si₂ $(M^{+\bullet})$ requires 510.2621. Found: m/z 454.1987. $C_{25}H_{34}O_4Si_2$ $(M^{+\bullet} - C_4H_8)$ requires 454 · 1996]. ¹H n.m.r. δ 0 · 12, s, 9H, Me₃Si; 1 · 02, s, 9H, Bu^t; 1 · 23, d, J 6 Hz, 3H, 1×CHMe₂; $\begin{array}{l} 1 \cdot 26, d, J \ 6 \ Hz, \ 3H, \ 1 \times CHMe_2; \ 1 \cdot 76, d, J \ 12 \ Hz, \ 1H, \ 1 \times CH_2; \ 1 \cdot 84, d, J \ 12 \ Hz, \ 1H, \ 1 \times CH_2; \\ 4 \cdot 08, \ dq, \ J \ 6, \ 6 \ Hz, \ 1H, \ CHMe_2; \ 4 \cdot 09, \ d, \ J \ 4 \ Hz, \ 2H, \ H \ 6; \ 4 \cdot 43, \ t, \ J \ 4 \ Hz, \ 1H, \ H \ 5; \ 5 \cdot 10, \ s, \\ 1H, \ H \ 1; \ 5 \cdot 78, \ s, \ 1H, \ H \ 3; \ 7 \cdot 3 - 7 \cdot 5, \ m, \ 6 \times ArH; \ 7 \cdot 6 - 7 \cdot 8, \ m, \ 4 \times ArH. \ ^{13}C \ n.m.r. \ \delta \ - 1 \cdot 2, \ 19 \cdot 2, \\ \end{array}$ 21.5, 23.2, 25.7, 26.7, 63.4, 70.5, 74.6, 94.9, 122.1, 127.5, 129.5, 133.4, 133.6, 135.6, $135 \cdot 7, 161 \cdot 0, 193 \cdot 9. \nu_{\text{max}}$ (CHCl₃) 2900, 1660, 1630, 1380, 1320, 1120, 1020, 850 cm⁻¹. $\nu_{\rm max}$ (KBr) 2960, 2932, 2895, 2859, 1683, 1629, 1428, 1251, 1114, 1030, 850 cm⁻¹. Mass spectrum m/z 454 (100%, M – C₄H₈), 321 (80).

Single-Crystal X-Ray Analysis of (3a)

Colourless crystals were grown from ether/hexane. Unit cell parameters were determined from 25 reflections in the range $20^{\circ} \leq \theta \leq 44^{\circ}$, measured with Cu K α (graphite monochromatized) radiation ($\lambda = 1.54184$ Å).

Crystal data. C₁₁H₂₀O₄Si, M 244·37, orthorhombic, space group $P2_{1}2_{1}2_{1}$ (No. 19), a 8·689(2), b 10·342(1), c 14·429(2) Å, V 1296·6 Å³, Z 4, D_{x} 1·25 g cm⁻³, F(000) 528, μ 15·9 cm⁻¹; T 293 K.

Structure determination. Intensity data were measured from a crystal of dimensions 0.40 by 0.33 by 0.31 mm aligned on an Enraf-Nonius CAD4 diffractometer with Cu K α radiation and employing the $\bar{\omega}:2\theta$ scan method. A total of 1538 unique reflections were measured, $2 \cdot 4^{\circ} \leq 2\theta \leq 75 \cdot 0^{\circ}$, $(0 \leq h \leq 10, 0 \leq k \leq 12, 0 \leq l \leq 18)$ of which 1376 reflections with $I \geq 3\sigma(I)$ were used for refinement. Full-matrix least squares refinement was carried out with anisotropic thermal parameters assigned to each of the non-hydrogen atoms. The positional parameters of all of the hydrogen atoms, initially calculated geometrically, were allowed to vary, with each being given the $B_{\rm eq}$ value of the parent carbon atom; a weighting scheme of the type $1/\sigma(F_{\rm o})$ was used. At convergence, $R \ 0.064$, and $wR \ 0.092$, where $R = \Sigma \Delta / \Sigma F_{\rm o}$, $wR = (\Sigma w \Delta^2 / \Sigma w F_{\rm o}^2)^{1/2}$, and $\Delta = ||F_{\rm o}| - |F_{\rm c}||$. In the final difference map the maximum peak height was 0.37 e Å⁻³.

Final atomic coordinates are given in Table 1. The atomic scattering factors of C, H, O and Si were those incorporated in the MolEN/VAX program system;¹³ corrections were made for anomalous dispersion. Calculations were carried out on a VAX 11/750 computer. Fig. 1

¹³ MolEN, An Interactive Structure Solution Procedure, Enraf-Nonius, Delft, The Nederlands, 1990. was prepared from the output of ORTEP II.¹⁴ Material deposited[†] includes hydrogen atom positions, bond lengths, angles and torsion angles, thermal parameters, and a listing of the observed and calculated structure factor amplitudes.

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[†] Copies are available on application to the Australian Journal of Chemistry, P.O. Box 89, East Melbourne, Vic. 3002.

¹⁴ Johnson, C. K., ORTEP II, 'Fortran Thermal Ellipsoid Plot Program', Report ORNL-5138, Oak Ridge National Laboratories, Tennessee, U.S.A., 1976.