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The Synthesis of Some Octenoses as Potential Precursors to Lincosamine, a Derived Portion of the Antibiotic Lincomycin

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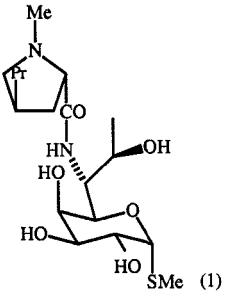
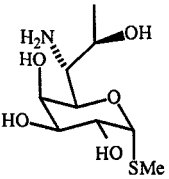
Abstract

Methyl (*E*)-2,3-di-*O*-benzyl-6,7,8-trideoxy-α-D-*galacto*-oct-6-enopyranoside, a potential precursor to lincosamine, has been prepared from both methyl α-D-galactopyranoside and methyl α-D-glucopyranoside, with the required inversion at C4 in the latter sequence being effected by a conventional oxidation–reduction. As well, (*E*)-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enose and (*E*)- and (*Z*)-6,7,8-trideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-oct-6-enose have been prepared from 1,2:3,4-di-*O*-isopropylidene-α-D-galactose.

Lincomycin (1)[1,2] is an effective agent for the treatment of Gram-positive bacterial infections in humans,* inhibiting bacterial protein synthesis by binding to a region of the peptidyl transferase.[2] Partial degradation of lincomycin gives the thioglycoside (2), and it is a derivative of (2), lincosamine (3), that



(1)



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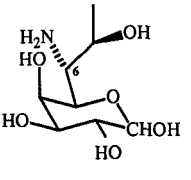

(3)

* One of us (R.V.S.) attests to the effectiveness of lincomycin in the treatment of tooth abscess while on study leave!

[1] Magerlein, B. J., Birkenmeyer, R. D., Herr, R. R., and Kagan, F., *J. Am. Chem. Soc.*, 1967, **89**, 2459.
[2] Monro, R. E., Fernandez-Muñoz, R., Celma, M. L., and Vazquez, D., in 'Drug Action and Drug Resistance in Bacteria, 1. Macrolide Antibiotics and Lincomycin' (Ed. S. Mitsuhashi) p. 305 (University of Tokyo Press, 1971).

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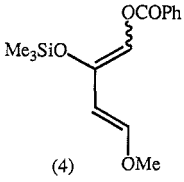
has been the main synthetic target for organic chemists. Most syntheses[3–9] of (3) have involved the addition of two carbons (or alternatively, two consecutive additions of one carbon) to C 6 of a modified D-galactose unit, with consequent lack of stereochemical control at both C 6 and C 7 in the product. The only stereoselective synthesis of lincosamine, albeit as a racemate, has been reported by Danishefsky.[10] The eight-carbon framework was elegantly assembled by boron trifluoride etherate-mediated cyclocondensation of (*E*)-but-2-enal and the mixture of dienes (4) (the now familiar hetero Diels–Alder reaction), giving the (±)-pyrone (5). This was elaborated straightforwardly into the octoside (6). Bromohydrin methodology then provided the epoxide (7), but the subsequent introduction of nitrogen (Me_3SiN_3) occurred at C 7 rather than the desired C 6, and with the wrong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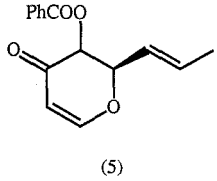
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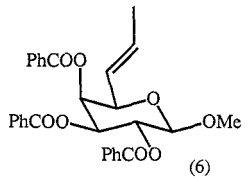
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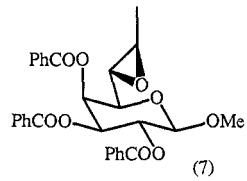
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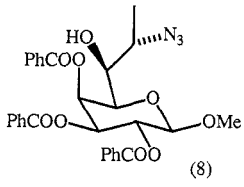
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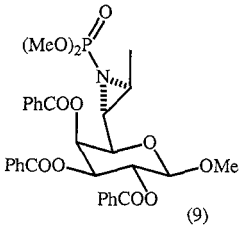
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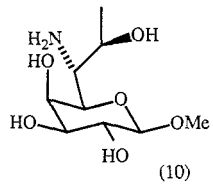
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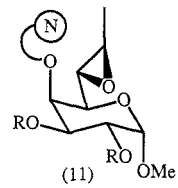
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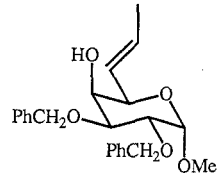
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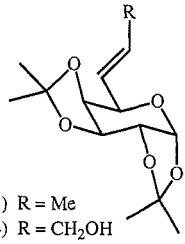
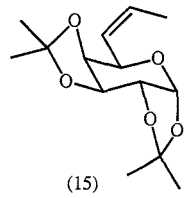

(13) R = Me
(14) R = CH_2OH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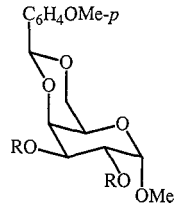
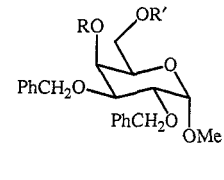
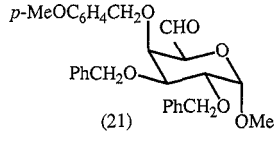

(16) R = H
(17) R = CH_2Ph



	R	R'
(18)	$CH_2C_6H_4OMe$-*p*	H
(19)	H	$CH_2C_6H_4OMe$-*p*
(20)	H	H


(21)

[3] Magerlein, B. J., *Tetrahedron Lett.*, 1970, 33.
[4] Woolard, G. R., Rathbone, E. B., Szarek, W. A., and Jones, J. K. N., *J. Chem. Soc., Perkin Trans. 1*, 1976, 950.
[5] Saeki, H., and Ohki, E., *Chem. Pharm. Bull.*, 1970, **18**, 789.
[6] Atsumi, T., Fukumaru, T., and Matsui, M., *Agric. Biol. Chem.*, 1973, **32**, 2627.
[7] David, S. M., and Fischer, J.-C., *Carbohydr. Res.*, 1974, **38**, 147.
[8] Hoppe, I., and Schöllkopf, U., *Liebigs Ann. Chem.*, 1980, 1474.
[9] Czernecki, S., and Valery, J.-M., *Carbohydr. Res.*, 1988, **184**, 121.
[10] Danishefsky, S. J., Larson, E., and Springer, J. P., *J. Am. Chem. Soc.*, 1985, **107**, 1274.

relative stereochemistry (8). A rather circuitous route, via the aziridine (9), then gave racemic methyl β-lincosaminide (10).

It occurred to us that a synthesis of lincosamine was possible through the intramolecular delivery of a nitrogen atom, somehow attached to O4, at C6 in an octoside such as (11). This paper describes the synthesis of various octenoses (12–15), one suitable for transformation into an epoxide such as (11). The following paper outlines our attempts to convert such an epoxide, and some of the octenoses, into derivatives of lincosamine.

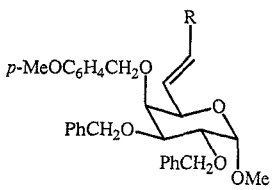
Our first synthetic target was the octenoside (12), having the (*E*) double bond necessary for obtaining the correct stereochemistry at C7 in lincosamine, and O4 available for functionalization with some type of nitrogen-delivery group. Thus, methyl α-D-galactopyranoside was converted into the *p*-methoxybenzylidene acetal (16) by use of our transacetalization methodology,[11] and the dibenzyl ether (17) easily followed.[12] Treatment of (17) with chlorotrimethylsilane/sodium cyanoborohydride in acetonitrile,[12] in our hands, gave only a 54% yield of the desired alcohol (18), together with 11% of the unwanted regioisomer (19); the remainder of the product appeared to be the diol (20). However, the alcohol (18) was obtained from (17) in high yield (81%) by using chloroalane, generated from lithium aluminium hydride/aluminium chloride;[13,14] only 5% of the unwanted alcohol (19) was formed. Oxidation of the primary alcohol (18) under Swern[15] conditions then gave the aldehyde (21).

We next needed to convert the aldehyde (21) stereoselectively into the octenoside (22), and naturally turned to the Wittig reaction. Not unexpectedly, treatment of (21) with ethylidenetriphenylphosphorane (generated *in situ*) in tetrahydrofuran gave only the (*Z*)-alkene (23) in 65% yield. The configuration of the double bond was assigned from an analysis of the ^{13}C n.m.r. spectrum, which showed a methyl resonance at δ 13·58 characteristic of a (*Z*)-alkene [the (*E*)-alkene typically shows the methyl resonance at δ 17–18].[16a–18] The Schlosser modification[19] of the Wittig reaction was hopeless, consuming all of the starting material and yielding virtually no alkenes as product.

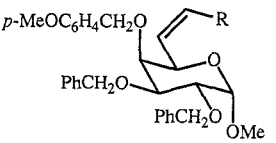
Attention was now directed towards stabilized ylides, such as ethoxycarbonylmethylenetriphenylphosphorane, in an effort to obtain an (*E*)-alkene; this necessitated additional steps to reduce the ester to a methyl group, presumably a straightforward exercise. By following the protocols established by Tronchet[20] and Brimacombe[21] for Wittig extension of the aldehyde (24), the aldehyde (21) was treated with ethoxycarbonylmethylenetriphenylphosphorane

[11] Ferro, V., Mocerino, M., Stick, R. V., and Tilbrook, D. M. G., *Aust. J. Chem.*, 1988, **41**, 813.
[12] Johansson, R., and Samuelsson, B., *J. Chem. Soc., Perkin Trans. 1*, 1984, 2371.
[13] Lipták, A., Jodál, I., and Nánási, P., *Carbohydr. Res.*, 1975, **44**, 1.
[14] Joniak, D., Košiková, B., and Kosáková, L., *Collect Czech. Chem. Commun.*, 1978, **43**, 769.
[15] Omura, K., and Swern, D., *Tetrahedron*, 1978, **34**, 1651.
[16] Silverstein, R. M., Bassler, G. C., and Morrill, T. C. in 'Spectrometric Identification of Organic Compounds' 4th Edn, (*a*) p. 261; (*b*) p. 235 (John Wiley: New York 1981).
[17] Lance, D. G., and Szarek, W. A., *Carbohydr. Res.*, 1969, **10**, 306.
[18] Lance, D. G., Szarek, W. A., Jones, J. K. N., and Howarth, G. B., *Can. J. Chem.*, 1969, **47**, 2871.
[19] Schlosser, M., Christmann, K.-F., and Piskala, A., *Chem. Ber.*, 1970, **103**, 2814.
[20] Tronchet, J. M. J., and Massoud, M. A. M., *Helv. Chim. Acta*, 1979, **62**, 1632.
[21] Brimacombe, J. S., Hanna, R., Kabir, A. K. M. S., Bennett, F., and Taylor, I. D., *J. Chem. Soc., Perkin Trans. 1*, 1986, 815.

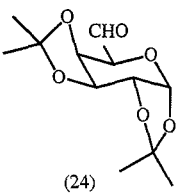
in methanol at 4°; only the (*Z*)-α,β-unsaturated ester (25) was isolated, in 74% yield. Here, the geometry of the double bond was assigned from an analysis of the ^{1}H n.m.r. spectrum ($J_{6,7}$ 11·8 Hz).[16b] A change in reaction conditions to benzene at reflux gave a mixture of the (*Z*)- and (*E*)-esters (25) and (26) in 66% yield, in a ratio of 1:4 [δ 6·24, H6; 5·65, H7 for (25); 6·71, H6; 6·07, H7, $J_{6,7}$ 15·6 Hz for (26)]. Treatment of the aldehyde (21) with formylmethylenetriphenylphosphorane in benzene at reflux gave a single alkene, but only in 46% yield. The ^{1}H n.m.r. (300 MHz) spectrum could not be used to determine the geometry of the alkene because H6 and H7 were isochronous. The structure of the alkene was tentatively assigned as the (*E*)-α,β-unsaturated aldehyde (27) on the basis of Brimacombe's[21] work, and this was later confirmed by conversion into an alkene of known geometry (see below).



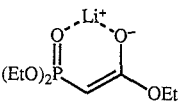
(22) R = CH_3
(26) R = CO_2Et
(27) R = CHO
(29) R = CH_2OH
(30) R = CH_2Cl



(23) R = CH_3
(25) R = CO_2Et



(24)



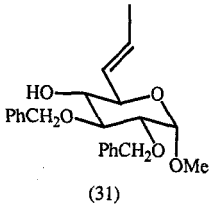
(28)

In view of the undesired stereochemistry or poor yield of the above reactions, we decided to investigate the utility of phosphonate anions (the Emmons–Wadsworth reaction)[22] for the synthesis of our alkene. Thus, according to the methodology developed by Masamune and Roush,[23] the aldehyde (21) was treated with triethyl phosphonoacetate/lithium bromide/ethyldiisopropylamine in acetonitrile [a source of the salt (28)] to give the (*E*)-ester (26) in 70% yield.

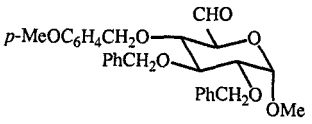
A sequence of simple reactions was now required to convert the ester group in (26) into the methyl group of the alkene (22). Thus, reduction of (26) with diisobutylaluminium hydride gave the alcohol (29), and subsequent treatment with Viehe's salt ($Me_2N^+{=}CCl_2\ Cl^-$)[24] gave the chloride (30). Reduction of (30) with lithium aluminium hydride then gave the desired alkene (22). The overall yield of (22) from the alcohol (18) was 59%, and both the ^{1}H (300 MHz) and ^{13}C (75·4 MHz) n.m.r. spectra of (22) conclusively demonstrated the (*E*) geometry of the alkene: H6 resonated at δ 5·45 and H7 at 5·67 with $J_{6,7}$ 15·4 Hz, and C8 resonated at δ 17·87. Reduction of (27) with diisobutylaluminium hydride gave an alcohol identical in all respects to (29), thus confirming the (*E*) geometry of (27) alluded to above. Removal of the 4-methoxybenzyl ether from (22) was achieved by using cerium(IV) ammonium nitrate in acetonitrile,[12] and the desired octenoside (12) was obtained in 94%

[22] Wadsworth, W. S., Jr, and Emmons, W. D., *J. Am. Chem. Soc.*, 1961, **83**, 1733.
[23] Blanchette, M. A., Choy, W., Davis, J. T., Essenfeld, A. P., Masamune, S., Roush, W. R., and Sakai, T., *Tetrahedron Lett.*, 1984, **25**, 2183.
[24] Viehe, H. G., and Janousek, Z., *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 806.

yield. 2,3-Dichloro-5,6-dicyanobenzoquinone[25] was an inferior reagent for the same transformation (64%).



(31)



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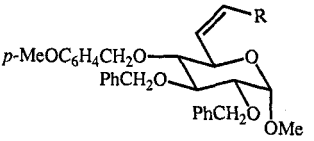
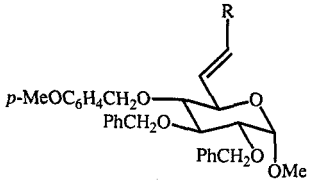
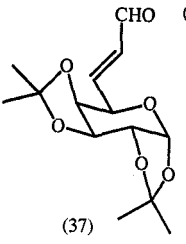


(33) R = CH_3
(35) R = CO_2Et



(34) R = CH_3
(36) R = CO_2Et



(37)

At this stage it seemed to us that the octenoside (12) would also be available from the alkene (31) (requiring only inversion of configuration at C4), and (31) should be obtainable from the very cheap methyl α-D-glucopyranoside. Thus, in a series of reactions parallel to those already described above, methyl α-D-glucopyranoside was converted into the aldehyde (32). The direct ethylidenation of (32) gave a mixture of the (*Z*)- and (*E*)-alkenes (33) and (34) (54%, 4:1). Again the stereochemistry of the double bonds was assigned from an analysis of the ^{13}C n.m.r. spectra [δ 13·87, Me for (33); 18·06, Me for (34)]. Treatment of the aldehyde (32) with ethoxycarbonylmethylenetriphenylphosphorane in methanol at 4° gave a mixture of the (*Z*)- and (*E*)-esters (35) and (36) (50%, 3:17), whereas a solvent change to benzene at reflux resulted in the formation of only the (*E*)-ester (36) (83%, ^1H n.m.r. $J_{6,7}$ 15·7 Hz). The ester (36) was then routinely converted into the alkene (34), and removal of the O4 protecting group gave the alcohol (31).

For the inversion of the stereochemistry at C4 in (31) a Mitsunobu[26] reaction with benzoic acid proved ineffective, and a conventional oxidation–reduction sequence was considered. Thus, oxidation of the alcohol (31) under Swern conditions gave the ketone, but subsequent reduction with lithium aluminium hydride gave a mixture of the alcohols (12) and (31) (13:7). However, reduction of the ketone with lithium tri-t-butoxyaluminium hydride[27] gave only the desired octenoside (12). These last two steps proceeded in a combined yield of only 57% and, coupled with an overall yield of 38% for methyl α-D-glucopyranoside to the alcohol (31), made the D-galactoside sequence still the more favourable (36% *versus* 22% for the D-glucoside sequence).

With the octenoside (12), designed specifically for our intramolecular approach, in hand, we decided to prepare the octenoses (13–15) for use in more direct approaches to lincosamine. For the synthesis of the allylic alcohol (14),

[25] Oikawa, Y., Yoshioka, T., and Yonemitsu, O., *Tetrahedron Lett.*, 1982, **23**, 885.
[26] Mitsunobu, O., *Synthesis*, 1981, 1.
[27] Hudlicky, M., 'Reductions in Organic Chemistry' (Ellis Horwood: Chichester 1984).

the aldehyde (24) was treated with formylmethylenetriphenylphosphorane in benzene at reflux to yield the α,β-unsaturated aldehyde (37), and subsequent reduction with diisobutylaluminium hydride gave (14). Treatment of (14) with methanesulfonyl chloride presumably gave the mesylate that was subsequently reduced by lithium aluminium hydride to the alkene (13).[28] Although the ^1H and ^{13}C n.m.r. data supported the structure of (13), especially when compared with similar data obtained for (15) (see below), our physical constants (m.p., $[\alpha]_D$) were in disagreement with those reported by Valverde.[28] Finally, the alkene (15) was prepared from the aldehyde (24) by utilizing ethylidenetriphenylphosphorane generated *in situ* in tetrahydrofuran.[17]

Experimental

Experimental details have been given previously.[29]

Methyl 2,3-Di-O-benzyl-4-O-(4-methoxybenzyl)-α-D-galactoside (18)

The 4-methoxybenzylidene compound (17)[11,12] (3·2 g, 6·4 mmol) was added to a suspension of $LiAlH_4$ (1·2 g, 30 mmol) in Et_2O/CH_2Cl_2 (1:1, 70 ml, N_2 atmosphere), and the mixture heated at reflux. To this mixture was added a solution of $AlCl_3$ (2·5 g, 24 mmol) in Et_2O (35 ml) as quickly as possible, followed by EtOAc (20 ml) *cautiously* but quickly. The mixture was then diluted with Et_2O, and water (5 ml) added to destroy any remaining hydride. Washing with water (×3) and brine, followed by drying and concentration, gave a colourless oil (3·85 g). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave firstly the 6-*O*-(4-methoxybenzyl) ether (19) (160 mg, 5%), R_F 0·50 (EtOAc/petrol, 1:1), $[\alpha]_D$ +33·4° (lit.[12] +33°). The second compound to elute was the 4-*O*-(4-methoxybenzyl) ether (18) (2·6 g, 81%), R_F 0·27 (EtOAc/petrol, 1:1), $[\alpha]_D$ −4·1° (lit.[12] −3·8°).

Oxidation of the Alcohol (18) to the Aldehyde (21)

To a solution of oxalyl chloride (345 μl, 4·0 mmol) in dry CH_2Cl_2 (2 ml, −70°) was added a solution of dimethyl sulfoxide (565 μl, 8 mmol) in dry CH_2Cl_2 (2 ml) dropwise. This solution was stirred (5 min) and then the primary alcohol (18) (1·0 g, 2·0 mmol) in CH_2Cl_2 (3 ml) added dropwise. After a short time (15 min), ethyldiisopropylamine (1·25 ml, 9·0 mmol) was added and the mixture allowed to warm (room temperature). Normal workup (CH_2Cl_2) gave a pale-yellow oil (965 mg), shown to be essentially the aldehyde (21) by infrared and ^1H n.m.r. spectroscopy. $\bar{\nu}_{max}$ (thin film) 1715 cm^{-1} (CO). ^1H n.m.r. (60 MHz) δ 3·25, s, OMe; 3·6, s, ArO**Me**; 9·35, s, H6.

Methyl (Z)-2,3-Di-O-benzyl-6,7,8-trideoxy-4-O-(4-methoxybenzyl)-α-D-galacto-oct-6-enoside (23)

(i) Ethyltriphenylphosphonium bromide (1·10 g, 3·0 mmol) was suspended in dry tetrahydrofuran (5 ml, 0°, argon atmosphere), BuLi (1·5 ml of 1·65 M, 2·5 mmol) added and the mixture stirred (5 min). A solution of the aldehyde (21) (965 mg, 2 mmol) in dry tetrahydrofuran (5 ml) was added dropwise and the stirring continued (30 min); t.l.c. then showed the absence of starting material. The mixture was poured into petrol, and filtered through Celite. The filter pad was washed with Et_2O/petrol (50 ml, 1:1), and concentration of the filtrate and washings gave a yellow oil (1·26 g). Flash chromatography (EtOAc/petrol, 2:8) of this oil gave *methyl (Z)-2,3-di-O-benzyl-6,7,8-trideoxy-4-O-(4-methoxybenzyl)-α-D-galacto-oct-6-enoside* (23) (640 mg, 65%) as an oil, $[\alpha]_D$ −8·6°. $\bar{\nu}_{max}$ (thin film) 1605 cm^{-1} (C=C); R_F 0·40 (EtOAc/petrol, 4:6) (Found: C, 73·8; H, 7·3. $C_{31}H_{36}O_6$ requires C, 73·8; H, 7·2%). ^1H n.m.r.

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[29] Rodriguez, E. B., and Stick, R. V., *Aust. J. Chem.*, 1990, **43**, 665.

(300 MHz) δ 1·61–1·64, m, Me; 3·40, s, OMe; 3·72, dd, $J_{3,4}$ 2·8, $J_{4,5}$ 1·5 Hz, H4; 3·78, s, ArO**Me**; 3·96, dd, B part of ABMX system, $J_{2,3}$ 10·1 Hz, H3; 4·07, dd, A part of ABMX system, $J_{1,2}$ 3·6 Hz, H2; 4·51–4·54, m, H5; 4·55-4·87, m, 3×ABq, 6H, Ar**CH**$_2$; 4·73, d, H1; 5·53–5·65, m, H6, 7; 6·79–6·84, 7·22–7·42, 2m, 14H, Ar. ^{13}C n.m.r. (75·4 MHz) δ 13·58, C8; 55·26, 55·56, 2C, OMe; 66·09, 76·26, 77·48, 79·05, C2,3,4,5; 73·21, 73·50, 74·58, 3C, Ar**CH**$_2$; 99·09, C1; 113·51, 2C, **Ar**OMe; 127·08, 127·44, 127·66, 127·74, 128·08, 128·34, 129·84, 130·76, 14C, Ar, C7; 138·58, 138·94, 2C, Ar; 144·3, C6; 159·12, Ar.

(ii) Ethyltriphenylphosphonium bromide (564 mg, 1·52 mmol) was suspended in dry tetrahydrofuran (5 ml, −78°, argon atmosphere), BuLi (0·92 ml of 1·65 M, 1·52 mmol) added and the mixture stirred (5 min). A solution of the aldehyde (21) (747 mg, 1·5 mmol) in dry tetrahydrofuran (5 ml) was added dropwise and the orange colour discharged. More BuLi (0·92 ml of 1·65 M, 1·52 mmol) was added and the orange colour regenerated. After a short time (5 min), saturared NH_4Cl solution was aded and the mixture allowed to warm (room temperature). Workup as for (i) gave a yellow oil (580 mg). Flash chromatography (EtOAc/petrol, 2:8) of this oil gave the (*Z*)-alkene (23) (16 mg, 1·6%); the ^{1}H n.m.r. spectrum was identical to that in (i) above.

Ethyl [Methyl (Z)*-2,3-Di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enosid]uronate (25)*

(i) The primary alcohol (18) (1·0 g, 2·0 mmol) was oxidized as above to give the aldehyde (21) as a yellow oil (955 mg). This oil was dissolved in methanol (20 ml, 0°), ethoxycarbonylmethylenetriphenylphosphorane (780 mg, 2·2 mmol) added and the mixture kept (4°, 24 h). Concentration gave a white solid (1·83 g). Flash chromatography (EtOAc/petrol, 3:7) of this solid gave *ethyl [methyl* (Z)*-2,3-di-*O*-benzyl-6,7-dideoxy-4-O-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enosid]uronate* (25) (844 mg, 74%) as an oil, $[\alpha]_D$ −158°. $\bar{\nu}_{max}$ (thin film) 1605 (C=C), 1705 cm^{-1} (CO); R_F 0·35 (EtOAc/petrol, 4:6) (Found: C, 70·2; H, 6·9. $C_{33}H_{38}O_8$ requires C, 70·4; H, 6·8%). ^{1}H n.m.r. (300 MHz) δ 1·24, t, *J* 7·1 Hz, CH$_2$**Me**; 3·34, s, OMe; 3·74, s, ArO**Me**; 4·06–4·14, m, H2,3, C**H**$_2$Me; 4·19–4·20, m, H4; 4·31–4·32, m, H5; 4·47–4·89, 3×ABq, 6H, ArC**H**$_2$; 4·73, d, H1; 5·65, dd, $J_{5,7}$ 1·5, $J_{6,7}$ 11·8 Hz, H7; 6·24, dd, $J_{5,6}$ 6·9 Hz, H6; 6·76–6·80, 7·14–7·18, 7·24–7·43, 3m, 14H, Ar. ^{13}C n.m.r. (75·4 MHz) δ 14·11, CH$_2$**Me**; 55·13, 55·46, 2C, OMe; 60·30, **C**H$_2$Me; 68·23, 76·14, 76·79, 78·85, C2,3,4,5; 73·30, 73·48, 74·35, 3C, Ar**C**H$_2$; 98·92, C1; 113·42, 2C, **Ar**OMe; 119·78, C7; 127·44, 127·62, 128·02, 128·29, 128·33, 130·15, 130·41, 13C, Ar; 137·54, 139·60, 2C, Ar; 147·35, C6; 159·22, Ar; 165·45, CO.

(ii) The primary alcohol (18) (1·0 g, 2·0 mmol) was oxidized as above to give the aldehyde (21) as a yellow oil (980 mg). This oil was dissolved in benzene (30 ml), ethoxycarbonylmethylenetriphenylphosphorane (780 mg, 2·2 mmol) added and the mixture heated at reflux (4 h). The mixture was then concentrated to give an orange oil, passage of which through a plug of alumina (EtOAc/petrol, 3:7) and concentration gave a yellow oil (800 mg). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave the α,β-unsaturated ester fraction as an oil (740 mg, 66%). The ^{1}H n.m.r. (300 MHz) spectrum showed the (*Z*)-ester (25) and the (*E*)-ester (26) (see below) to be present in the ratio of 1:4.

Methyl (E)*-2,3-Di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enodialdo-1,5-pyranoside (27)*

The primary alcohol (18) (1·0 g, 2·0 mmol) was oxidized as above to give the aldehyde (21) as a yellow oil (995 mg). This oil was dissolved in benzene (30 ml), formylmethylenetriphenylphosphorane (610 mg, 2·0 mmol) added, and the mixture heated at reflux (1·5 h). The mixture was then concentrated to give an orange oil, and flash chromatography (EtOAc/petrol, 2:8) of this oil gave *methyl* (E)*-2,3-di-*O*-benzyl-6,7-dideoxy-4-O-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enodialdo-1,5-pyranoside (27)* as an oil (480 mg, 46%), $[\alpha]_D$ +34·5°. $\bar{\nu}_{max}$ (thin film) 1610 (C=C), 1685 cm^{-1} (CO); R_F 0·40 (EtOAc/petrol, 1:1) (Found: C, 71·7; H, 6·7. $C_{31}H_{34}O_7$ requires C, 71·8; H, 6·6%). ^{1}H n.m.r. (300 MHz) δ 3·34, s, OMe; 3·78, s, ArO**Me**; 3·85–3·87, m, H4; 3·97, dd, B part of ABMX system, $J_{2,3}$ 10·2, $J_{3,4}$ 2·8 Hz, H3; 4·07, dd, A part of ABMX system, $J_{1,2}$ 3·6 Hz, H2; 4·61–4·38, m, H5;

4·56–4·87, 3×ABq, 6H, ArC**H**$_2$; 4·74, d, H1; 6·21–6·24, m, H6,7; 6·80–6·84, 7·12–7·18, 7·24–7·45, 3m, 14H, Ar; 9·30–9·33, m, H8. ^{13}C n.m.r. (75·4 MHz) δ 55·16, 55·59, 2C, OMe; 69·48, 75·54, 76·15, 78·50, C2,3,4,5; 73·61, 73·95, 3C, Ar**C**H$_2$; 98·86, C1; 113·59, 2C, **Ar**OMe; 127·56, 127·65, 127·73, 127·98, 128·31, 128·40, 129·73, 130·44, 131·63, 13C, C7, Ar; 138·22, 138·48, 2C, Ar; 152·92, C6; 159·41, Ar; 193·02, CO.

Ethyl [Methyl (E)*-2,3-Di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-*α*-*D*-*galacto-*oct-6-enosid]uronate (26)*

The primary alcohol (18) (14·2 g, 28·8 mmol) was oxidized as above to give the aldehyde (21) as a yellow oil (14·7 g). This oil was dissolved in dry MeCN (80 ml), then ethyldiisopropylamine (9·1 ml, 51 mmol), lithium bromide (4·6 g, 53 mmol) and triethyl phosphonoacetate (9·1 ml, 46·5 mmol) were added and the mixture stirred (room temperature, overnight). Normal workup (CH_2Cl_2) gave a dark-yellow oil (20 g). Passage through a plug of alumina (CH_2Cl_2/petrol, 1:1) followed by crystallization gave *ethyl [methyl* (E)*-2,3-di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-*D*-*galacto*-oct-6-enosid]uronate* (26) (10·4 g) as white crystals. Flash chromatography (EtOAc/petrol, 4:6) of the mother liquors gave a further amount of (26) (900 mg; total 11·3 g, 70%), m.p. 63·5–65° (Pr^i_2O/petrol), $[\alpha]_D$ +40·5°. $\bar{\nu}_{max}$ (thin film) 1605 cm^{-1} (C=C); R_F 0·32 (EtOAc/petrol, 4:6) (Found: C, 70·5; H, 6·9. $C_{33}H_{38}O_8$ requires C, 70·4; H, 6·8%). ^{1}H n.m.r. (300 MHz) δ 1·28, t, J 7·1 Hz, CH$_2$**Me**; 3·33, s, OMe; 3·77, s, ArO**Me**; 3·83–3·84, m, H4; 3·94, dd, B part of ABMX system, $J_{2,3}$ 10, $J_{3,4}$ 2·8 Hz, H3; 4·06, dd, A part of ABMX system, $J_{1,2}$ 3·6 Hz, H2; 4·09–4·25, m, C**H**$_2$Me; 4·31–4·32, m, H5; 4·56–4·87, 3×ABq, 6H, ArC**H**$_2$; 4·73, d, H1; 6·07, dd, $J_{5,7}$ 1·9, $J_{6,7}$ 15·6 Hz, H7; 6·71, dd, $J_{5,6}$ 4·2 Hz, H6; 6·77–6·83, 7·12–7·21, 7·23–7·46, 3m, 14H, Ar. ^{13}C n.m.r. (20·1 MHz) δ 14·3, CH$_2$**Me**; 55·2, 55·6, 2C, OMe; 60·3, **C**H$_2$Me; 69·6, 76·2. 76·3, 78·9, C2,3,4,5; 73·4, 73·7, 78·9, 3C, Ar**C**H$_2$; 99·0, C1; 113·8, 2C, **Ar**OMe; 122·1, C7; 127·7, 127·8, 128·3, 128·5, 129·4, 130·2, 13C, Ar; 138·6, 139·9, 2C, Ar; 144·3, C6; 159·5, Ar; 166·1, CO.

Methyl (E)*-2,3-Di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enoside (29)*

(i) To a solution of the unsaturated ester (26) (11·3 g, 20·2 mmol) in dry tetrahydrofuran (100 ml, 0°) was added a solution of diisobutylaluminium hydride in toluene (19·3 ml of 2·1 M, 40·5 mmol), and the mixture stirred (5 min). Dilute sulfuric acid (1 M) was added until a clear solution resulted. Normal workup (EtOAc) gave the the *allylic alcohol* (29) as an oil (10·2 g). A sample purified by preparative t.l.c. gave a colourless oil, $[\alpha]_D$ +10·9°. $\bar{\nu}_{max}$ (thin film) 1610 cm^{-1} (C=C); R_F 0·10 (EtOAc/petrol, 1:1) (Found: C, 71·6; H, 7·0. $C_{31}H_{36}O_7$ requires C, 71·5; H, 7·0%). ^{1}H n.m.r. (80 MHz) δ 1·69, br s, OH; 3·34, s, OMe; 3·77, s, ArO**Me**; 3·75–4·17, m, H2,3,4,5,8,8; 4·35–5·02, m, 7H, ArC**H**$_2$, H1; 5·36–6·00, m, H6,7; 6·75–6·91, 7·10–7·72, 2m, 14H, Ar. ^{13}C n.m.r. (20·1 MHz) δ 55·4, 55·5, 2C, OMe; 63·1, C8; 73·5, 73·6, 74·3, 3C, ArC**H**$_2$; 70·5, 76·5, 77·2, 79·0, C2,3,4,5; 99·1, C1; 113·7, 2C, **Ar**OMe; 127·7, 128·2, 128·5, 130·4, 130·8, 131·6, 15C, Ar, C6,7: 138·7, 139·1, Ar; 159·5, Ar.

(ii) To a solution of the unsaturated aldehyde (27) (340 mg, 0·66 mmol) in dry tetrahydrofuran (12 ml, 0°, argon atmosphere) was added a solution of diisobutylaluminium hydride in toluene (340 μl of 2·07 M, 0·7 mmol), and the mixture stirred (5 min). Dilute H_2SO_4 (1 M) was added until a clear solution resulted. Normal workup (EtOAc) gave a colourless oil (285 mg). Flash chromatography (EtOAc/petrol, 8:2) gave the allylic alcohol (29) (220 mg, 65%), $[\alpha]_D$ +10·1°.

Methyl (E)*-2,3-Di-*O*-benzyl-6,7,8-trideoxy-4-*O*-(4-methoxybenzyl)-α-*D*-galacto-oct-6-enoside (22)*

To a solution of the allylic alcohol (29) (10·2 g, 20 mmol) in dry CH_2Cl_2 (110 ml) were added triethylamine (4·2 ml, 30 mmol) and Viehe's salt (3·9 g, 26 mmol), and the mixture was stirred (2 h). Normal workup (CH_2Cl_2) gave a yellow oil (11·0 g), presumably the chloride (30).

This oil was dissolved in dry tetrahydrofuran (100 ml), $LiAlH_4$ (1·9 g, 50 mmol) added and the suspension heated at reflux (6 h). Cooling (0°), sequential treatment with water (1·9 ml), 3 M NaOH (1·9 ml) and water (5·7 ml), filtration and concentration gave an oil (9·6 g). Flash chromatography (EtOAc/petrol, 2:8) gave the *trideoxy compound* (22) as an oil [8·5 g, 84%, 59% from the the primary alcohol (18)], $[\alpha]_D$ +9·9°. $\bar{\nu}_{max}$ (thin film) 1605 cm^{-1} (C=C); R_F 0·45 (EtOAc/petrol, 4:6) (Found: C, 74·0; H, 7·2. $C_{31}H_{36}O_6$ requires C, 73·8; H, 7·2%). ^1H n.m.r. (300 MHz) δ 1·64, dd, $J_{7,Me}$ 6·4, $J_{6,Me}$ 0·8 Hz, Me; 3·35, s, OMe; 3·70–3·72, m, H4; 3·79, s, ArO**Me**; 3·92, dd, $J_{2,3}$ 10·1, $J_{3,4}$ 2·9 Hz, H3; 4·02–4·08, m, H2,5; 4·56–4·91, m, 6H, ArCH_2; 4·69, d, $J_{1,2}$ 3·7 Hz, H1; 5·45, ddq, $J_{5,6}$ 6·9, $J_{6,7}$ 5·4 Hz, H6; 5·67, ddq, $J_{5,7}$ 0·9 Hz, H7; 6·80–6·85, 7·21–7·46, 2m, 14H, Ar. ^{13}C n.m.r. (75·5 MHz) δ 17·87, Me; 55·26, 55·38, 2C, OMe; 71·29, 76·34, 77·44, 79·02, C2,3,4,5; 73·21, 73·56, 74·31, 3C, ArCH_2; 98·89, C1; 113·48, 2C, **Ar**OMe; 127·50, 127·66, 127·95, 128·10, 128·33, 128·38, 128·49, 130·07, 130·70, 15C, Ar, C6,7; 138·57, 138·92, 2C, Ar; 159·15, Ar.

Methyl (E)-*2,3-Di-O-benzyl-6,7,8-trideoxy-α-*D-galacto-*oct-6-enopyranoside (12)*

(i) To a solution of the 4-methoxybenzyl ether (22) (500 mg, 1·0 mmol) in CH_2Cl_2/water (20:1, 15 ml) was added 2,3-dichloro-5,6-dicyanobenzoquinone (340 mg, 1·5 mmol), and the mixture stirred (1·5 h, room temperature). The mixture was then filtered (Celite), the filtrate washed with water, $NaHCO_3$ (×2) and brine, dried and concentrated to give a yellow oil (505 mg). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave the *octenoside* (12) as a colourless oil (250 mg, 64%), $[\alpha]_D$ +37·0°. $\bar{\nu}_{max}$ (thin film) 1625 cm^{-1} (C=C); R_F 0·40 (EtOAc/petrol, 4:6) (Found: C, 71·8; H, 7·4. $C_{23}H_{28}O_5$ requires C, 71·8; H, 7·4%). ^1H n.m.r. (80 MHz) δ 1·72, d, $J_{7,Me}$ 4·7 Hz, Me; 2·37, br s, OH; 3·37, s, OMe; 3·82–4·30, m, H2,3,4,5; 4·59–4·91, m, 5H, PhCH_2, H1; 5·48–6·05, m, H6,7; 7·22–7·41, m, 10H, Ph. ^{13}C n.m.r. (20·1 MHz) δ 17·9, Me; 55·4, OMe; 70·2, 70·5, 75·6, 77·8, C2,3,4,5; 72·8, 73·1, 2C, PhCH_2; 98·8, C1; 127·1, 128·0, 128·2, 128·6, 128·7, 129·5, 12C, Ph, C6,7; 138·4, 138·6, 2C, Ph.

(ii) To a well stirred solution of the 4-methoxybenzyl ether (22) (210 mg, 0·41 mmol) in MeCN/water (9:1, 6 ml) was added cerium(IV) ammonium nitrate (500 mg, 0·9 mmol), and the stirring continued (3 h). The reaction mixture was diluted with CH_2Cl_2 (25 ml), washed with water (×2), $NaHCO_3$ and brine, dried and concentrated to give an oil (200 mg). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave the octenoside (12) as a colourless oil (150 mg, 94%), $[\alpha]_D$ +36·3°.

(iii) A solution of triphenylphosphine (285 mg, 1·1 mmol) and the secondary alcohol (31) (426 mg, 1·1 mmol) in dry Et_2O (5 ml) was added to a solution of diethyl azodicarboxylate (172 μl, 192 mg, 1·1 mmol) and benzoic acid (132 mg, 1·1 mmol) in dry Et_2O (5 ml, argon atmosphere, 25°). After standing (3 days) t.l.c. showed no reaction. The reaction mixture was concentrated, triturated with Et_2O, the precipitated triphenylphosphine oxide removed by filtration, and the filtrate concentrated to give a yellow oil (930 mg). Flash chromatography of this oil gave a colourless oil (325 mg) identical with the starting material (31) (^1H n.m.r.).

(iv) To a solution of oxalyl chloride (370 μl, 4·0 mmol) in dry CH_2Cl_2 (5 ml, −70°) was added dimethyl sulfoxide (2·9 ml of 20% in CH_2Cl_2, 8·0 mmol) dropwise, and the mixture stirred (5 min). The alcohol (31) (780 mg, 2·0 mmol) in dry CH_2Cl_2 (5 ml) was then added dropwise and the stirring continued (15 min). Ethyldiisopropylamine (1·6 ml, 8·8 mmol) was added and the mixture allowed to warm (room temperature). Normal workup (CH_2Cl_2) presumably gave the ketone as a yellow oil (720 mg). This oil was dissolved in dry Et_2O (10 ml, 0°), and $LiAlH_4$ (100 mg, 3·0 mmol) was added to the stirred solution. After a short time (5 min), workup proceeded by sequential treatment with water (100 μl), NaOH (100 μl of 3 M) and water (300 μl). Filtration and concentration gave an oil (660 mg). Flash chromatography (EtOAc/petrol, 3:7) then gave a colourless oil (570 mg, 73%). ^{13}C n.m.r. (75·4 MHz) spectroscopy showed the oil to be a mixture of the D-*gluco* alcohol (31) and the desired D-*galacto* alcohol (12) in the ratio of 7:13.

(v) The alcohol (31) (430 mg, 1·1 mmol) was oxidized in the same manner as above to give again the ketone as a yellow oil (400 mg). This oil was dissolved in Et_2O (2 ml), and added to a suspension of lithium tri-t-butoxyaluminium hydride (2·63 mmol) [prepared from $LiAlH_4$ (100 mg, 2·63 mmol) and dry t-butyl alcohol (740 μl, 7·9 mmol)] in dry Et_2O

(10 ml, 0°). After a short time (5 min), dilute sulfuric acid (1 M) was added until a clear solution resulted. Normal workup (EtOAc) then gave an oil (350 mg). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave a colourless oil (245 mg, 57%). The ^{13}C n.m.r. (75·4 MHz) spectrum was identical to that of the D-*galacto* alcohol (12).

Methyl 2,3-Di-O-benzyl-4-O-(4-methoxybenzyl)-α-D-glucoside

Methyl 2,3-di-*O*-benzyl-4,6-*O*-(4-methoxybenzylidene)-α-D-glucoside[11,12] (6·94 g, 14·1 mmol) was added to a suspension of $LiAlH_4$ (2·65 g, 66 mmol) in Et_2O/CH_2Cl_2 (1:1, 160 ml, N_2 atmosphere), and the mixture heated at reflux. To this mixture was added a solution of $AlCl_3$ (4·0 g, 52 mmol) in Et_2O (70 ml) as quickly as possible, followed by EtOAc (60 ml) *cautiously*. The mixture was diluted with Et_2O (300 ml), water (20 ml) added and the mixture filtered through Celite. The filtrate was dried and concentrated to give a syrup (6·8 g) that crystallized on standing. Recrystallization gave methyl 2,3-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α-D-glucoside (5·0 g, 72%), m.p. 65·5–66·5° (Pr^i_2O/petrol), $[\alpha]_D$ +19·0° (lit.[12] +19·3°), R_F 0·25 (EtOAc/petrol, 1:1).

Oxidation of Methyl 2,3-Di-O-benzyl-4-O-(4-methoxybenzyl)-α-D-glucoside to the Aldehyde (32)

To a solution of oxalyl chloride (345 μl, 4·0 mmol) in dry CH_2Cl_2 (2 ml, −70°) was added a solution of dimethyl sulfoxide (565 μl, 8·0 mmol) in dry CH_2Cl_2 (2 ml) dropwise. This solution was stirred (5 min), and methyl 2,3-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α-D-glucoside (1·0 g, 2·0 mmol) in CH_2Cl_2 (3 ml) then added dropwise. After a short time (15 min), ethyldiisopropylamine (1·25 ml, 9·0 mmol) was added and the mixture allowed to warm (room temperature). Normal workup (EtOAc) gave the aldehyde (32) as a pale-yellow oil (970 mg). $\bar{\nu}_{max}$ (thin film) 1715 cm^{-1} (CO). ^1H n.m.r. (60 MHz) δ 3·25, s, OMe; 3·3–4·1, m, H2,3,4,5; 3·60, s, ArO**Me**; 4·3–4·9, m, 7H, H1, Ar$\mathbf{CH_2}$; 6·4–7·3, m, 14H, Ar; 9·35, s, H6.

Methyl (Z)- and (E)-2,3-Di-O-benzyl-6,7,8-trideoxy-4-O-(4-methyoxybenzyl)-α-D-gluco-oct-6-enoside (33) and (34)

Ethyltriphenylphosphonium bromide (1·10 g, 3·0 mmol) was suspended in dry tetrahydrofuran (5 ml, 0°, argon atmosphere), BuLi (1·5 ml of 1·65 M, 2·5 mmol) added, and the mixture stirred (5 min). A solution of the aldehyde (32) (965 mg) in dry tetrahydrofuran (5 ml) was added dropwise (resulting in a red solution) and the stirring continued (30 min). T.l.c. then showed the absence of starting material. The mixture was poured into petrol, and filtered through a pad of Celite. The pad was washed with Et_2O/petrol (1:1, 50 ml), and the filtrate and washings were concentrated to give a yellow oil (690 mg). Flash chromatography (EtOAc/petrol, 2:8) gave methyl (*Z*)-2,3-di-O-benzyl-6,7,8-trideoxy-4-*O*-(4-methoxybenzyl)-α-D-*gluco*-oct-6-enoside (33) and methyl (*E*)-2,3-di-*O*-benzyl-6,7,8-trideoxy-4-*O*-(4-methoxybenzyl)-α-D-*gluco*-oct-6-enoside (34) (540 mg, 54%) as an inseparable mixture in the ratio of 4:1 [the data for the (*Z*)-alkene (33) were obtained from the n.m.r. spectra after a comparison with the data for the (*E*)-alkene (34) formed in a later reaction]. ^1H n.m.r. (300 MHz) for (33) δ 1·74, dd, $J_{6,Me}$ 1·8, $J_{7,Me}$ 7·0 Hz, Me; 3·28, t, $J_{3,4} = J_{4,5}$ 9·5 Hz, H4; 3·40, s, OMe; 3·52, dd, $J_{1,2}$ 3·6, $J_{2,3}$ 9·7 Hz, H2; 3·77, s, ArO**Me**; 3·98, dd, H3; 4·48, m, H5; 4·55, d, H1; 4·54–4·97, m, 6H, Ar$\mathbf{CH_2}$; 5·38, ddq, $J_{5,6}$ 9·0, $J_{6,7}$ 10·8 Hz, H6; 5·42, ddq, $J_{5,7}$ 0·9 Hz, H7; 6·79–6·85, 7·14–7·39, 2m, 14H, Ar. ^{13}C n.m.r. for (33) (75·4 MHz) δ 13·87, C8; 55·22, 55·27, 2C, OMe; 65·89, 79·82, 81·64, 82·31, C2,3,4,5; 73·41, 74·81, 75·86, 3C, Ar$\mathbf{CH_2}$; 99·29, C1; 113·68, 2C, **Ar**OMe; 127·56, 127·66, 127·96, 128·07, 128·11, 128·37, 128·42, 129·66, 130·76, 15C, Ar, C6,7; 138·24, 138·94, 2C, Ar; 159·22, Ar.

Ethyl [Methyl (E)-2,3-Di-O-benzyl-6,7-dideoxy-4-O-(4-methoxybenzyl)-α-D-gluco-oct-6-enosid]uronate (36)

(i) The aldehyde (32) (955 mg, 2 mmol) was dissolved in methanol (20 ml, 0°), ethoxycarbonylmethylenetriphenylphosphorane (780 mg, 2·2 mmol) added, and the mixture

kept cold (4°, 24 h). The resulting mixture was concentrated to give a white solid (1·83 g). Passage through a plug of Al_2O_3 (Et_2O/petrol), and concentration gave a pale-yellow oil (900 mg). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave a mixture of ethyl [methyl (*Z*)-2,3-di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-D-*gluco*-oct-6-enosid]uronate (35) and ethyl [methyl (*E*)-2,3-di-*O*-benzyl-6,7-dideoxy-4-*O*-(4-methoxybenzyl)-α-D-*gluco*-oct-6-enosid]uronate (36) (565 mg, 50%) as an oil, in the ratio of 3:17. ^{1}H n.m.r. (300 MHz) δ 3·44, s, OMe; 3·74, s, ArO**Me** for (*Z*)-alkene (35); 3·34, s, OMe; 3·78, s, ArO**Me** for (*E*)-alkene (36) (see below).

(ii) The aldehyde (32) (8·2 g, 16 mmol) was dissolved in benzene (140 ml), ethoxycarbonylmethylenetriphenylphosphorane (6·05 g, 17·4 mmol) added, and the mixture heated at reflux (30 min). The mixture was concentrated, the residue triturated with Et_2O, and the Et_2O extract filtered and concentrated. This process was repeated with EtOAc/petrol (2:8). Flash chromatography (EtOAc/petrol, 2:8) of the combined residues gave the (E)-*ester* (36) as an oil (7·72 g, 86%). A sample purified by preparative t.l.c. gave a clear oil, $[\alpha]_D$ +49·0°. $\bar{\nu}_{max}$ (thin film) 1705 (CO), 1605 cm^{-1} (C=C); R_F 0·37 (EtOAc/petrol, 4:6) (Found: C, 70·3; H, 6·9. $C_{33}H_{38}O_8$ requires C, 70·4; H, 6·8%). ^{1}H n.m.r. (300 MHz) δ 1·29, t, *J* 7·2 Hz, CH_2**Me**; 3·22, dd, $J_{2,3}$ 9·7, $J_{3,4}$ 9·2 Hz, H3; 3·34, s, OMe; 3·51, dd, $J_{1,2}$ 3·5 Hz, H2; 3·78, s, ArO**Me**; 4·00, dd, $J_{4,5}$ 9·3 Hz, H4; 4·20, q, C**H**$_2$Me; 4·23, ddd, $J_{5,6}$ 4·7, $J_{5,7}$ 1·7 Hz, H5; 4·48–5·00, 3×ABq, 6H, ArC**H**$_2$; 4·60, d, H1; 6·11, dd, $J_{6,7}$ 15·7 Hz, H7; 7·02, dd, H6; 6·83–6·86, 7·18–7·23, 7·28–7·40, 3m, 14H, Ar. ^{13}C n.m.r. (20·1 MHz) δ 14·3, CH_2**Me**; 55·2, 55·3, 2C, OMe; 60·4, **C**H$_2$Me; 69·3, 79·9, 81·5, 81·8, C2,3,4,5; 73·4, 75·1, 75·8, 3C, Ar**C**H$_2$; 98·2, C1; 114·0, 2C, **Ar**OMe; 122·0, C7; 127·8, 128·0, 128·2, 128·6, 129·7, 130·0, 13C, Ar; 138·2, 138·9, 2C, Ar; 144·1, C6; 159·6, Ar; 166·3, CO.

Methyl (E)-*2,3-Di-O-benzyl-6,7-dideoxy-4-O-(4-methoxybenzyl)-α-D-gluco-oct-6-enopyranoside*

A solution of diisobutylaluminium hydride in toluene (12·3 ml of 2·2 M, 27·4 mmol) was added to a solution of the ester (36) (7·72 g, 13·7 mmol) in dry tetrahydrofuran (100 ml, N_2 atmosphere). After a short time (10 min), dilute sulfuric acid (1 M) was added until a clear solution resulted. Normal workup (EtOAc) gave a white solid (7·66 g). A portion of this was recrystallized to give *methyl* (E)-*2,3-di-O-benzyl-6,7-dideoxy-4-O-(4-methoxybenzyl)-α-D-gluco-oct-6-enopyranoside* as white crystals, m.p. 94–95° (Pr^i_2O), $[\alpha]_D$ +19·7°. $\bar{\nu}_{max}$ (thin film) 1605 cm^{-1} (C=C); R_F 0·20 (EtOAc/petrol, 1:1) (Found: C, 71·4; H, 6·8. $C_{31}H_{36}O_7$ requires C, 71·5; H, 7·0%). ^{1}H n.m.r. (80 MHz) δ 1·57, br s, OH; 3·2–4·0, m, H2,3,4,5; 3·36, s, OMe; 3·78, s, ArO**Me**; 4·09, t, H8,8; 4·5–5·1, m, 7H, ArC**H**$_2$, H1; 5·6–6·2, m, H6,7; 6·7–7·3, m, 14H, Ar. ^{13}C n.m.r. (20·1 MHz) δ 55·1, 2C, OMe; 62·6, C8; 70·8, 80·1, 81·7, 81·9, C2,3,4,5; 73·3, 74·7, 75·8, 3C, Ar**C**H$_2$; 98·1, C1; 113·8, 2C, **Ar**OMe; 127·7, 128·1, 128·5, 129·9, 130·5, 14C, Ar, C7; 133·3, C6; 138·3, 139·0, 2C, Ar; 159·4, Ar.

Methyl (E)-*2,3-Di-O-benzyl-6,7,8-trideoxy-4-O-(4-methoxybenzyl)-α-D-gluco-oct-6-enoside (34)*

To a solution of the above allylic alcohol (7·6 g, 14 mmol) in CH_2Cl_2 (100 ml, 0°) were added triethylamine (10·5 ml, 75 mmol) and Viehe's salt (3·6 g, 21 mmol), and the mixture was stirred (5 min). The mixture was then poured into water, extracted with CH_2Cl_2, and the organic extracts were washed with brine, dried and concentrated to give a yellow oil (7·6 g). This oil was then dissolved in tetrahydrofuran (100 ml), $LiAlH_4$ (2·0 g, 50 mmol) added, and the suspension heated at reflux (6 h). Workup by sequential treatment with water (2 ml), NaOH (2 ml of 3 M) and water (6 ml), followed by filtration and concentration gave a yellow oil (6·1 g). Flash chromatography (EtOAc/petrol, 2:8) of this oil gave the *trideoxy compound* (34) [5·02 g, 72%, 62% from methyl 2,3-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-α-D-glucoside] which crystallized on standing, m.p. 78·5–79·5° (petrol), $[\alpha]_D$ −1·3°, R_F 0·32 (EtOAc/petrol, 2:8) (Found: C, 73·8; H, 7·0. $C_{31}H_{36}O_6$ requires C, 73·8; H, 7·2%). ^{1}H n.m.r. (300 MHz) δ 1·74, dd, $J_{6,Me}$ 1·5, $J_{7,Me}$ 6·5 Hz, Me; 3·25, t, $J_{3,4} = J_{4,5}$ 9·3 Hz, H4; 3·36, s, OMe; 3·50, dd, $J_{1,2}$ 3·6, $J_{2,3}$ 9·7 Hz, H2; 3·78, s, ArO**Me**; 3·91–4·02, m, H3,5; 4·55, d, H1; 4·51–4·96, 3×ABq, 6H, ArC**H**$_2$; 5·40, ddq, $J_{5,6}$ 7·7, $J_{6,7}$ 15·2 Hz, H6; 5·84, ddq, $J_{5,7}$ 0·6 Hz, H7; 6·80–6·85, 7·15–7·43, 2m, 14H, Ar. ^{13}C n.m.r. (75·4 MHz) δ 18·04, C8; 55·11, 55·26, 2C, OMe; 71·73, 79·60, 80·60, 81·85, C2,3,4,5; 73·37, 74·69, 75·84, 3C, Ar**C**H$_2$; 98·09, C1; 113·73, 2C,

ArOMe; 127·58, 127·86, 128·00, 128·10, 128·39, 128·43, 129·73, 130·45, 130·81, 15C, Ar, C6,7; 138·21, 138·90, 2C, Ar; 159·26, Ar.

Methyl (E)-*2,3-Di-O-benzyl-6,7,8-trideoxy-α-D-gluco-oct-6-enopyranoside (31)*

A solution of the trideoxy compound (34) (1·15 g, 4·3 mmol) and cerium(IV) ammonium nitrate (5·12 g, 9·4 mmol) in MeCN/water (30 ml, 9:1) was stirred (30 min). The reaction mixture was then diluted with CH_2Cl_2, washed with water (×2), $NaHCO_3$ and brine, dried and concentrated to yield a yellow oil (2·13 g). Flash chromatography (EtOAc/petrol, 2:8) of this oil gave the *secondary alcohol* (31) (1·6 g, 97%) as a colourless oil. A sample purified by preparative t.l.c. gave a heavy oil, $[\alpha]_D$ +7·5°. $\bar{\nu}_{max}$ (thin film) 1620 cm^{-1} (C=C); R_F 0·40 (EtOAc/petrol, 4:6) (Found: C, 72·0; H, 7·1. $C_{23}H_{28}O_5$ requires C, 71·8; H, 7·4%). ^1H n.m.r. (80 MHz) δ 1·73, dd, $J_{6,Me}$ 1·1, $J_{7,Me}$ 6·1 Hz, Me; 2·25, br s, OH; 3·19–3·47, 3·81–4·01, 2m, H3,4,5; 3·38, s, OMe; 3·57, d, $J_{1,2}$ 3·4 Hz, H2; 4·60, d, H1; 4·55–5·08, 2×ABq, 4H, Ph**CH$_2$**; 5·45, ddq, B part of ABMX, $J_{5,6}$ 6·9, $J_{6,7}$ 15·4 Hz, H6; 5·84, ddq, A part of ABMX, H7; 7·25–7·60, m, 10H, Ph. ^{13}C n.m.r. (20·1 MHz) δ 18·0, C8; 55·3, OMe; 72·1, 73·2, 73·8, 75·5, C2,3,4,5; 79·8, 81·2, 2C, Ph**C**H$_2$; 98·4, C1; 128·2, 128·3, 128·6, 128·7, 12C, Ph, C6,7; 138·3, 139·0, 2C, Ph.

(E)-*6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-oct-6-enodialdo-1,5-pyranose (37)*

To a solution of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexosdialdo-1,5-pyranose (24)[30] (4·1 g, 16 mmol) in benzene (100 ml) was added formylmethylenetriphenylphosphorane (4·7 g, 18 mmol), and the mixture heated at reflux (12 h). The solution was concentrated, the residue triturated with EtOAc/petrol (3:7), filtered and the filtrate concentrated to give an orange oil (5·5 g). Flash chromatography (EtOAc/petrol, 3:7) of this oil gave the α,β-unsaturated aldehyde (37) (4·05 g, 90%), m.p. 95–96° (petrol; lit.[21] 94·5–95·5°), $[\alpha]_D$ −135·5° (lit.[21] −137°), R_F 0·43 (EtOAc/petrol, 1:1). ^{13}C n.m.r. (20·1 MHz) δ 24·5, 24·8, 25·8, 26·0, 4C, C**Me$_2$**; 67·7, 70·4, 71·0, 72·7, C2,3,4,5; 96·5, C1; 108·9, 110·0, 2C, **C**Me$_2$; 132·9, C7; 151·6, C6; 193·5, CO.

(E)-*6,7-Dideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-oct-6-enose (14)*

To a solution of the unsaturated aldehyde (37) (2·56 g, 9·0 mmol) in dry tetrahydrofuran (50 ml, 0°) was added a solution of diisobutylaluminium hydride in toluene (10 ml of 1 M, 10 mmol), and the mixture stirred (5 min). Dilute H_2SO_4 (1 M) was added until a clear solution resulted. Dilution with Et_2O, and washing with water (×3), $NaHCO_3$ and brine, followed by drying and concentration, gave the allylic alcohol (14) as a colourless oil (2·49 g, 98%), $[\alpha]_D$ −104·2° (lit.[21] −108°), R_F 0·25 (EtOAc/petrol).

(E)-*6,7,8-Trideoxy-1,2:3,4-di-O-isopropylidene-α-D-galacto-oct-6-enose (13)*

The allylic alcohol (14) (870 mg, 3·2 mmol) was dissolved in dry CH_2Cl_2 (20 ml); triethylamine (2 ml) and mesyl chloride (310 μl, 4·0 mmol) were added, and the mixture was allowed to stand (overnight). T.l.c. showed the formation of a less polar material. Normal workup (EtOAc) and rapid silica chromatography (EtOAc/petrol, 1:1) of the reaction mixture gave, presumably, the mesylate as an oil (605 mg). This oil was dissolved in dry tetrahydrofuran (30 ml), $LiAlH_4$ (380 mg, 10 mmol) added, and the mixture heated at reflux (6 h). T.l.c. showed only one compound to be present, and this was not the starting material. Normal workup and flash chromatography (EtOAc/petrol, 3:7) of the reaction mixture gave the (*E*)-alkene (13) [350 mg, 43% from (14)] as a crystalline solid, m.p. 42–43° (lit.[28] 235–237°), $[\alpha]_D$ −139·9° (lit·[28] −99°). $\bar{\nu}_{max}$ (thin film) 1670w cm^{-1} (C=C); R_F 0·62 (EtOAc/petrol, 1:1) (Found: C, 62·4; H, 8·3. $C_{14}H_{22}O_5$ requires C, 62·2; H, 8·2%). ^1H n.m.r. (300 MHz) δ 1·34, 1·35, 1·48, 1·58, 4s, 12H, CMe_2; 1·72–1·75, m, Me; 4·18, dd, $J_{3,4}$ 7·8, $J_{4,5}$ 1·9 Hz, H4; 4·21–4·24, m, H5; 4·30, dd, $J_{1,2}$ 5·1, $J_{2,3}$ 2·4 Hz, H2; 4·60, dd, H3; 5·55, d, H1; 5·63, ddq, B part of ABMX, $J_{5,6}$ 7·2, $J_{6,7}$ 15·5, $J_{6,Me}$ 1·5 Hz, H6; 5·80, ddq, A part of ABMX, $J_{5,7}$

[30] Czernecki, S., Dieulesaint, A., and Valery, J.-M., *J. Carbohydr. Chem.*, 1986, **5**, 469.

0·8, $J_{7,Me}$ 6·4 Hz, H7. ^{13}C n.m.r. (75·4 MHz) δ 17·98, C8; 24·30, 24·95, 25·98, 26·14, 4C, C**Me**$_2$; 66·08, 70·39, 70·87, 73·72, C2,3,4,5; 96·50, C1; 108·37, 109·12, 2C, **C**Me$_2$; 126·06, 130·13, C6,7.

(Z)-*6,7,8-Trideoxy-1,2 : 3,4-di*-O-*isopropylidene*-α-D-galacto-*oct-6-enose (15)*

Ethyltriphenylphosphonium bromide (4·65 g, 12·5 mmol) was suspended in dry tetrahydrofuran (30 ml, 0°, argon atmosphere), BuLi (6·9 ml of 1·6 M, 11·0 mmol) added, and the mixture stirred (5 min). A solution of the aldehyde (24) (2·37 g, 9·2 mmol) in dry tetrahydrofuran (10 ml) was then added and the mixture stirred (5 min). T.l.c. showed no starting material remaining. The mixture was allowed to warm (room temperature), and acetone was added (the red colour was discharged). The mixture was poured into petrol and filtered; the filtrate was then passed through a short plug of alumina (petrol), and concentrated. The residue was then passed through a short plug of silica (EtOAc/petrol, 1 : 9), and concentrated to give a pale-yellow oil (2·06 g). Distillation of this oil by using a Kugelrohr apparatus (120°/0·07 mm) gave the (*Z*)-alkene (15) (1·72 g, 70%), $[\alpha]_D$ −114·8° (lit.[17] −117°). ^{1}H n.m.r. (300 MHz) δ 1·35, 1·48, 1·58, 3s, 12H, CMe$_2$; 1·72, dd, $J_{7,Me}$ 6·7, $J_{6,Me}$ 1·6 Hz, Me; 4·17, dd, $J_{3,4}$ 7·9, $J_{4,5}$ 2·0 Hz, H4; 4·32, dd, $J_{1,2}$ 5·1, $J_{2,3}$ 2·4 Hz, H2; 4·60–4·65, m, H3,5; 5·56, d, H1; 5·63, ddq, B part of ABMX, $J_{5,6}$ 7·9 Hz, H6; 5·74, ddq, A part of ABMx, $J_{5,7}$ 0·8, $J_{6,7}$ 11·0 Hz, H7. ^{13}C n.m.r. (75·4 MHz) δ 13·64, C8; 24·34, 24·93, 25·98, 26·13, 4C, C**Me**$_2$; 63·57, 70·27, 70·89, 73·29, C2,3,4,5; 96·59, C1; 108·33, 109·10, 2C, **C**Me$_2$; 126·14, 128·60, C6,7.

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