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A CONVENIENT, HIGH-YIELD SYNTHESIS OF L-OLEANDROSE AND L-OLEANDRAL*

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ABSTRACT

A short, practical synthesis of L-oleandrose (2,6-dideoxy-3-*O*-methyl-L-*arabino*-hexose) from L-arabinose has been achieved. The synthesis is satisfactory for large-scale preparation of oleandrosylating intermediates, and employs dithiolane formation for protection of the aldehyde group during deoxygenation and methylation steps, and Wittig chain-extension to 2-deoxyhexose derivatives. Useful intermediates in the introduction of oleandrose glycosides into natural products, such as the 1,4-dibenzoates and the methyl glycosides, were prepared and characterized. L-Oleandral (1,5-anhydro-2,6-dideoxy-3-*O*-methyl-L-*arabino*-hex-1-enitol), another useful intermediate for glycosylation, was prepared from 3,4-di-*O*-acetyl-L-rhamnal by deacetylation, and regioselective methylation with stannous chloride–diazomethane.

INTRODUCTION

Since the discovery and characterization[1] of the oleandrosylated macrolides, the avermectins, and their potent anthelmintic activity, there has been renewed interest in the synthesis of oleandrosides although such other oleandrose-containing natural products as oleandomycin[2] have been known for decades. Recent syntheses of avermectins have resolved the problem of glycosylation of the macrolide by utilization of oleandrose saccharides isolated from avermectin degradation[3], or by the synthesis of oleandrosylating intermediates[4–6] by lengthy or tedious methods not suited to large-scale preparation. Since the classic, but lengthy, syntheses of D-[7] and L-oleandrose[8] by Reichstein *et al.*, there have been a number of other syntheses of oleandrose, but these have suffered the disadvantage of racemic products[9,10], dependence upon not readily available L-sugar intermediates[11], or extensive separation chemistry[12,13]. We decided to attempt to devise a simple synthesis, modelled on Reichstein's, which would use readily available starting-materials, require minimal chromatography, and be readily adaptable to large-scale synthesis. We

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found that the regioselective methylation which we developed during the course of this work is also useful in the preparation of another oleandrosylating intermediate, namely, L-oleandral (1,5-anhydro-2,6-dideoxy-3-*O*-methyl-L-*arabino*-hex-1-enitol).

RESULTS AND DISCUSSION

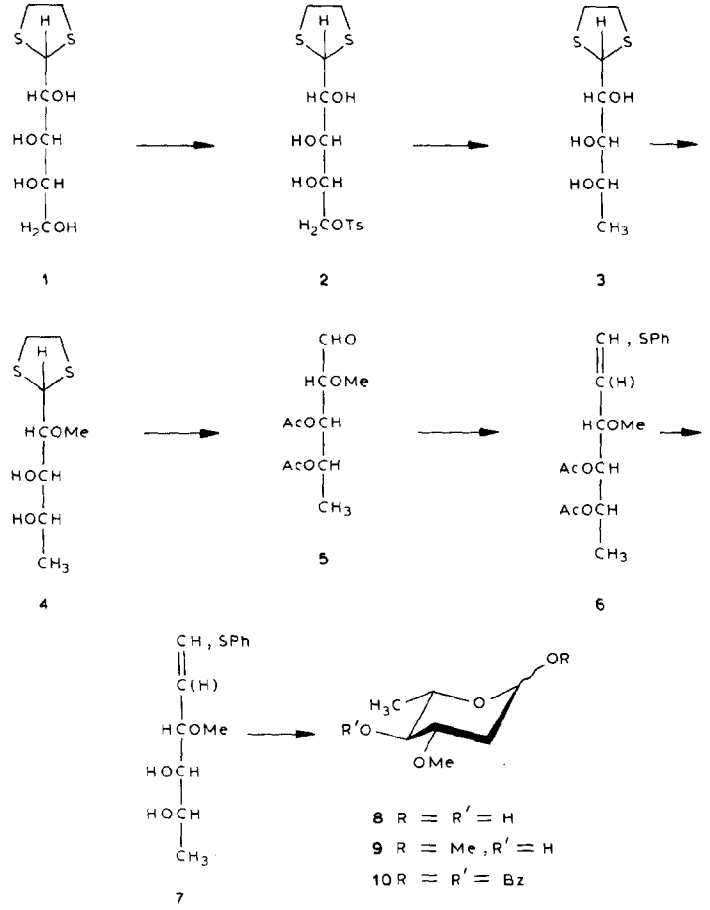
The Reichstein synthesis first homologates L-arabinose to a hexose, then introduces the 3-*O*-methyl group, and finally deoxygenates at C-6 and C-2. We envisaged accomplishing deoxygenation at the terminal carbon atom first, in order to simplify regiospecific methylation, and then combining the homologation and 2-deoxygenation steps.

Protection of the aldehyde group of L-arabinose as the diethyl dithioacetal proceeded as described in the literature, but the compound did not seem to be very stable at room temperature. Ethanethiol vapors were present even 24 h after recrystallization, and reaction side-products were isolated that could only have arisen from loss of the aldehyde-protecting group. Protection[14,15] of the aldehyde group as the dithiolane (**1**), an ethylene dithioacetal, proved to be satisfactory, as **1** was found to be completely stable for many months at ambient temperature. Tosylation of **1** by conventional methods[16] gave the 5-tosylate (**2**) exclusively, and this compound underwent facile reduction with lithium aluminum hydride to furnish the 5-deoxy-L-arabinose derivative **3**. Regiospecific methylation of the 2-hydroxyl group[17] of **3** with diazomethane in dimethoxyethane in the presence of stannous chloride[18–21] gave only the 2-*O*-methyl-L-arabinose derivative **4** in excellent yields. Methylation with tributyltin oxide–methyl iodide[5] was also satisfactorily regioselective, whereas other methylation procedures, such as use of methyl iodide–aqueous sodium hydroxide, gave many products. Acetylation of **4** and then deprotection of the aldehyde group with boron trifluoride etherate–mercuric oxide[22], gave the *aldehydo*-sugar 3,4-diacetate (**5**). The dithiolane derivative **4** was found to be resistant[23] to conventional dithioacetal cleavage with mercuric chloride–mercuric oxide in acetone.

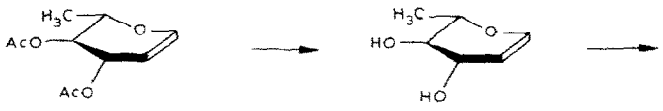
Although Bestmann *et al.*[24,25] published their finding that Wittig extension of other sugar derivatives goes well in the absence of hydroxyl protection, we found that only the protected 2-*O*-methyl-L-arabinose derivative **5** could successfully undergo Wittig homologation with the ylid obtained from triphenyl(phenylthiomethyl)phosphonium chloride. The synthesis may be brought to this point without the need for chromatography, but the Wittig product **6** requires chromatographic purification if good-quality **8** is desired. The *E*/*Z* isomers of **6** can be resolved by conducting the chromatography slowly and with a low ratio of product weight:silica gel.

Difficulty was encountered with the hydrolysis of the vinyl sulfide linkage of **6** with mercuric chloride. Following the reports of Trost and Stanton[26], and others[27], that an allylic or homoallylic hydroxyl group is necessary (in order to assist in the liberation of aldehydes, but not ketones[28], from vinyl thioethers), we deacetylated

the Wittig product **6** (to give **7**) and found that the desired deoxy sugar (**8**) could be obtained in good yield by conventional mercuric chloride–mercuric oxide treatment. Use of the conditions of Grieco *et al.*[27] with **6** for addition of benzenethiol to vinyl sulfides to produce diphenyl dithioacetals gave, instead, in an apparent addition–elimination reaction, another unsaturated sugar (presumably the 2-ene) as the major product, which had eliminated the elements of methanol.



L-Oleandrose (**8**) was characterized as the mixture of methyl glycopyranosides (**9**), which were shown to be identical to an authentic sample, and by conversion into the α and β 1,4-dibenzoates (**10a,b**), which were separated, and characterized spectroscopically. These derivatives are useful either as glycosylation substrates in the syntheses of disaccharides, or in the preparation of the glycosylating intermediates, the halides or 1-thioglycosides.



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It occurred to us that the regiospecific methylation observed for **3** might also be useful in the preparation of another intermediate for glycosylation, namely, L-oleandral. Deacetylation of commercial 3,4-di-*O*-acetyl-L-rhamnal gave L-rhamnal (**11**), but methylation was only regioselective. Under optimized conditions in ether, instead of dimethoxyethane, a 7:1 mixture favoring the 3-*O*-methyl derivative (**12**) was obtained. N.m.r. studies of the 4-*O*-benzoyl derivative (**13**), which showed a downfield shift of the signal of H-4 (adjacent to the benzoate), confirmed that the methylation had occurred on the 3-hydroxyl group. The glycal **13** can be used to generate the 2-deoxyglycopyranosyl halide directly[29], or in a glycosylation strategy[30] employing addition of bromine to the double bond, or in the efficient glycosylation conditions described by Thiem *et al.*[31–33], which utilize *N*-iodosuccinimide.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover apparatus and are uncorrected. Optical rotations were measured at 25–27° with a Perkin–Elmer 241 polarimeter. T.l.c. was conducted on Analtech plates of silica gel GF; the components were located either by exposure to u.v. light or by spraying the plates with 5% H_2SO_4 in ethanol and heating. The silica gel used for column chromatography was E. Merck Silica Gel 60. Organic solutions were generally dried with anhydrous Na_2SO_4. Elemental analyses were performed at Merck Sharp & Dohme Research Laboratories, Rahway, NJ. N.m.r. spectra were recorded at 25° with a Varian T-60A or an HR-300 instrument; the positions of the peaks are expressed from the Me_4Si signal.

5-O-p-Tolylsulfonyl-L-arabinose ethylene dithioacetal (**2**). — A solution of 6.78 g (30 mmol) of L-arabinose ethylene dithioacetal[14] in 50 mL of pyridine was cooled in an ice bath with stirring; a solution of 6.5 g (34 mmol) of tosyl chloride in pyridine was added dropwise during 0.5 h, and the solution kept for 18 h at 5° and poured into 600 mL of ice water. A precipitate formed which did not crystallize. The mixture was extracted three times with dichloromethane, and the extracts were combined, successively washed with M HCl (~600 mL), water, 10% $NaHCO_3$, and

saturated NaCl, dried ($MgSO_4$), filtered, concentrated to ~100 mL, and hexane added, giving a crystalline precipitate that was filtered off, and washed with hexane and a small amount of ether; dry wt. 8.0 g; m.p. 128–130° (dec.). The foamed residue from evaporation of the filtrate and washes weighed 2.5 g, and gave a single spot in t.l.c. (3:97 MeOH–CH_2Cl_2); total yield, 92%. This material was used immediately in reactions; ^{1}H-n.m.r. (Me_2SO-d_6): δ 2.4 (s, 3 H, CH_3 of Ts), 3.15 (s, 4 H, SCH_2), 3.3–4.4 (m, 5 H, OC*H*), 4.5 (d, 1 H, $J_{1,2}$ 10 Hz, H-1), and 7.6 (q, 4 H, C_6H_4 of Ts).

Anal. Calc. for $C_{14}H_{20}O_6S_3$ (380.49): C, 44.19; H, 5.30. Found: C, 44.14; H, 5.20.

*5-Deoxy-*L*-arabinose ethylene dithioacetal* (**3**). — To a suspension of lithium aluminum hydride (3 g) in tetrahydrofuran (75 mL) was slowly added a solution of 9.5 g of tosylate **2** in tetrahydrofuran (50 mL); foaming occurred, and the temperature rose to 55°. The mixture was boiled under reflux overnight; t.l.c. then showed that no starting material remained. The mixture was cautiously treated with ethyl acetate (250 mL were added finally), and then with a small amount of water. More ethyl acetate and 20 mL of water were added, and the mixture was stirred until all suspended solids were white. The mixture was filtered through a bed of Supercel, and the cake was well washed with ethyl acetate. Water was separated from the combined filtrate and washes and the organic phase was washed with saturated sodium chloride, dried, and evaporated under diminished pressure to a residue which solidified. The residue was broken up in ether, the suspension filtered, and the solid washed with ether, and dried; wt. 2.78 g, 53%, m.p. 103–104°. T.l.c. with 1:19 MeOH–CH_2Cl_2 showed a single spot. Additional product could be obtained by chromatography of the filtrates (total yield, 83%); $[\alpha]_D$ +10.7° (*c* 0.7, MeOH); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.1 (d, 3 H, $J_{4,5}$ 5 Hz, H-5), 3.2 (s, 4 H, SCH_2), 3.2–3.9 (m, 3 H, OC*H*), and 4.6 (d, 1 H, $J_{1,2}$ 10 Hz, H-1).

Anal. Calc. for $C_7H_{14}O_3S_2$ (210.31): C, 39.98; H, 6.71. Found: C, 39.90; H, 6.97.

*5-Deoxy-2-*O*-methyl-*L*-arabinose ethylene dithioacetal* (**4**). — To a solution of 5.7 g (27 mmol) of the 5-deoxy derivative **3** in dimethoxyethane (120 mL) was added stannous chloride (177 mg, 0.82 mmol), and then a solution of diazomethane (from 120 mmol of nitrosomethylurea) in dimethoxyethane was added dropwise until the yellow color persisted and gas evolution stopped. The remaining color was dispersed by the addition of 0.28 mL (5 mmol) of acetic acid. A light precipitate was filtered off and discarded, and the filtrate was evaporated to a glass under diminished pressure (yield, 94%). T.l.c. with 3:97 MeOH–CH_2Cl_2 showed a single spot. Analytically pure material could be obtained by column chromatography with the same solvent system; ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.1 (d, 3 H, $J_{4,5}$ 5 Hz, H-5), 3.2 (s, 4 H, SCH_2), 3.5 (s, 3 H, OCH_3), 3.2–3.7 (m, 3 H, OC*H*), 4.4 (d, 1 H, $J_{1,2}$ 9 Hz, H-1), and 4.3–4.8 (m, 2 H, O*H*).

Anal. Calc. for $C_8H_{16}O_3S_2$ (224.33): C, 42.83; H, 7.19. Found: C, 42.79; H, 7.06.

*4,5-Di-O-acetyl-1,2-didehydro-1,2,6-trideoxy-3-O-methyl-1-(phenylthio)-*L-arabino-*hexose* (**6**). — A solution of 5-deoxy-2-*O*-methyl-L-arabinose ethylene dithioacetal (5.6 g, 25 mmol) in 1:1 acetic anhydride–pyridine (60 mL) was stirred overnight at ambient temperature, and then evaporated under diminished pressure to a residue that was mixed with cold water, and after 30 min, extracted several times with ethyl acetate. The extracts were combined, washed with dilute $NaHCO_3$ solution, dried, and evaporated to give the crude diacetate, which was dissolved in 125 mL of 1:9 tetrahydrofuran–water, and 10.9 g (50 mmol) of yellow mercuric oxide was added. After cooling (in an ice bath) under a nitrogen atmosphere, boron trifluoride etherate (16 mL, 18 g, 125 mmol) was added during 45 min, the temperature being maintained below 10°. After stirring for 18 h, t.l.c. (3:9 MeOH–CH_2Cl_2) showed starting diacetate to have been consumed, and the mixture was diluted with two volumes of ether, and filtered. The yellow solid was washed with ether, and the filtrate and washes were washed alternately with saturated sodium chloride and 10% $NaHCO_3$ solution (3 × 25 mL each). The aqueous phases were combined, and back-extracted with ethyl acetate (3 × 50 mL). The ethyl acetate and ether phases were combined, dried, and evaporated to a residue which became a hard foam after repeated evaporation of ethyl acetate under diminished pressure [5.1 g, 22 mmol, 88%; 3,4-di-*O*-acetyl-5-deoxy-2-*O*-methyl-*aldehydo*-L-arabinose (**5**)]; ^{1}H-n.m.r. ($CDCl_3$): δ 1.2 (d, 3 H, $J_{4,5}$ 6 Hz, H-5), 2.0–2.05 (2 s, 6 H, OAc), 3.45 (s, 3 H, OCH_3), 3.3–3.8 (m, 2 H, OC*H*), 5.2 (m, 1 H, H-2), and 9.7 (d, 1 H, $J_{1,2}$ 1 Hz, H-1). The product was taken immediately to the next step.

A mixture of 60 mL of redistilled dimethyl sulfoxide and 4.0 g (96 mmol) of a 57% suspension of sodium hydride was heated under nitrogen with stirring at 75° until gas evolution ceased (1 h). The mixture was cooled, and 39 g (93 mmol) of triphenyl(phenylthiomethyl)phosphonium chloride was added in portions. During the addition, the temperature was maintained at ~27° with a cooling bath. The resultant clear, red solution was stirred for 1 h with cooling. A solution of **5** (17.0 g, 74 mmol) in freshly distilled dimethyl sulfoxide (30 mL) was added dropwise during 45 min, a cooling bath being used to maintain the temperature at 20° during the addition, and the mixture was then stirred overnight at ambient temperature. Ice-cold water (150 mL) and hexane (120 mL) were added with cooling, whereupon triphenylphosphine oxide crystallized out. The mixture was filtered, and the precipitate was washed with ether and discarded. The layers of the combined filtrate and washings were separated, and the aqueous phase was extracted with ether. The ether and hexane solutions were combined, washed with saturated sodium chloride solution, dried, and evaporated to a residue, column chromatography of which with dichloromethane resolved the major component from other materials. Combination and evaporation of product-containing fractions gave a residue which was extracted with hexane; the suspension was filtered, and the filtrate evaporated to a clear, straw-colored glass (12.8 g, 51%; *E*:*Z* 8:1 by n.m.r.; more cautious chromatography resolved the geometric isomers); ^{1}H-n.m.r. ($CDCl_3$) *E*-isomer: δ 1.2 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 2.0–2.05 (2 s, 6 H, 2 OAc), 3.3 (s, 3 H, OCH_3), 5.6 (q,

1 H, $J_{2,3}$ 7 Hz, H-2), 6.5 (d, 1 H, $J_{1,2}$ 15 Hz, H-1), and 7.4 (s, 5 H, S-Ph); Z-isomer: δ 1.2 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 2.0–2.05 (2 s, 6 H, 2 OAc), 3.35 (s, 3 H, OCH_3), 5.65 (t, 1 H, $J_{2,3}$ 9 Hz, H-2), 6.8 (d, 1 H, $J_{1,2}$ 9 Hz, H-1), and 7.4 (s, 5 H, S-Ph).

Anal. Calc. for $C_{17}H_{23}O_5S$ (339.43): C, 60.16; H, 6.83. Found: C, 59.98; H, 6.77.

*1,2,6-Trideoxy-1,2-didehydro-3-*O*-methyl-1-(phenylthio)-*L-arabino*-hexose* (**7**) — *Method 1.* To 2.66 g (8 mmol) of **6** was added methanolic ammonia (25 mL, saturated at 10°). The solution was stirred overnight at ambient temperature in a sealed pressure-vessel. After 20 h, t.l.c.(3:97 MeOH–CH_2Cl_2) showed that complete reaction had occurred, and the solution was evaporated under diminished pressure to a residue. Ether and saturated sodium chloride solution were added. The ether layer was separated, and the aqueous phase was back-extracted with ether. The ether solutions were combined, dried, and concentrated to 1–2 mL. After hexane addition, and induction of crystallization by scratching, the product crystallized. It was filtered off, and washed with petroleum ether, to give 1.61 g (79%) of **7**; m.p. 72–76°; ^{1}H-n.m.r. ($CDCl_3$): δ 1.27 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 2.3–4.4 (m, 5 H, OC*H* & O*H*), 3.4 (s, 3 H, OCH_3), 5.5–6.6 (overlapping m's, 2 H, =C*H*), and 7.35 (s, 5 H, S-Ph).

Anal. Calc. for $C_{13}H_{18}O_3S$ (254.34): C, 61.39; H, 7.13. Found: C, 61.22; H, 7.34.

Method 2. A solution of 11.8 g (35 mmol) of **6** in methanol (125 mL) was treated with 216 mg (4 mmol) of sodium methoxide. The resulting solution, which became somewhat colored, was stirred overnight at ambient temperature. T.l.c. confirmed occurrence of complete reaction, and carbon dioxide was then bubbled through the solution for 10 min; it was evaporated to a residue that did not crystallize well. Purification by column chromatography (3:97 MeOH–CH_2Cl_2), and recrystallization from ether–petroleum ether, provided 5.9 g of product (66%; m.p. 63–64°) identical in all respects to that from Method 1.

Anal. Found: C, 61.22; H, 7.34.

*2,6-Dideoxy-3-*O*-methyl-*L-arabino*-hexopyranose* (L-*oleandrose,* **8**). — A solution of **7** (2.54 g, 10 mmol) in 1:3 water–acetone (200 mL) was treated with yellow mercuric oxide (7.5 g, 34.5 mmol) and mercuric chloride (5.45 g, 20 mmol). The mixture was stirred under nitrogen for 3 h at 50°, and then cooled and filtered. The insoluble material was washed well with acetone, and discarded. To the combined filtrate and washes were added water (40 mL) and pyridine (10 mL), and the solution was concentrated under diminished pressure; a new precipitate formed. It was filtered off, and washed with water, and pyridine (10 mL) was added to the combined aqueous solutions. Hydrogen sulfide was bubbled through the solution for 20 min, the mixture filtered twice through Supercel, the filter cake washed with water, and the solutions combined, evaporated *in vacuo,* and lyophilized. The residue, which weighed 2.67 g, was extracted several times with ether. Evaporation of the combined extracts gave 1.53 g of L-oleandrose, which did not crystallize.

Methyl glycosides (**9**) *of* **8**. — To a solution of 325 mg of L-oleandrose (2

mmol) was added 10 mL of methanol containing 1% of sulfuric acid. After 18 h at ambient temperature, sufficient $NaHCO_3$ solution was added to neutralize the acid, and the mixture was concentrated to a small volume under diminished pressure (bath temperature <20°). Ether extracts (3 × 25 mL) were combined, dried, and evaporated under vacuum to a residue which was confirmed by n.m.r. to be a mixture of the methyl α- and β-glycosides. After purification by column chromatography (1:9 THF–$CHCl_3$), a comparison of spectral properties with those of an authentic sample[3] showed them to be identical. Chromatographic comparisons in two solvent systems also confirmed the products to be identical with authentic material (solvent systems: 3:97 MeOH–CH_2Cl_2 and 1:9 THF–$CHCl_3$).

1,4-Dibenzoates (**10**) *of* **8**. — L-Oleandrose (325 mg, 2 mmol) was dissolved in pyridine (5 mL), and stirred with cooling while 0.6 mL (5.2 mmol) of benzoyl chloride was added dropwise. The mixture was stirred for 18 h at ambient temperature, water was added, and stirring was continued for 1 h. Dichloromethane (50 mL) was added, and the organic phase was successively washed with M hydrochloric acid (2 × 25 mL) and 10% aqueous $NaHCO_3$ (1 × 25 mL), dried, and evaporated. Chromatography of the residue with 1:99 THF–CH_2Cl_2 removed impurities and separated the anomers. The α anomer (**10a**) crystallized upon standing (244 mg, 33%); m.p. 116–120°; $[\alpha]_D$ −51.5° (MeOH); ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 1.27 (d, 3 H, $J_{5,6}$ 7 Hz, H-6), 2.02 (octet, 1 H, $J_{2a,2e}$ 12, $J_{2a,3}$ 4, $J_{1,2}$ 2 Hz, H-2*a*), 2.56 (octet, 1 H, $J_{2e,3}$ 6 Hz, H-2*e*), 3.42 (s, 3 H, OCH_3), 3.95 (octet, 1 H, $J_{3,4}$ 10 Hz, H-3), 4.17 (octet, 1 H, $J_{4,5}$ 10 Hz, H-4), 5.13 (t, 1 H, H-4), 6.56 (d, 1 H, H-1), and 7.9 (m, 10 H, 2 Bz).

Anal. Calc. for $C_{21}H_{22}O_6$ (370.40): C, 68.09; H, 5.99. Found: C, 67.82; H, 5.86.

The β anomer (**10b**) was an amorphous solid (155 mg, 21%); ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 1.32 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 1.97 (octet, 1 H, $J_{2a,2e}$ 13, $J_{2a,3}$ 2, $J_{1,2a}$ 10 Hz, H-2*a*), 2.38 (octet, 1 H, $J_{2e,3}$ 6, $J_{1,2e}$ 2 Hz, H-2*e*), 3.42 (s, 3 H, OCH_3), 3.68 (octet, 1 H, $J_{3,4}$ 9 Hz, H-3), 3.80 (octet, 1 H, $J_{4,5}$ 9 Hz, H-4), 5.06 (t, 1 H, H-4), 6.09 (q, 1 H, H-1), and 7.8 (m, 10 H, 2 Bz).

Anal. Found: C, 68.21; H, 5.78.

1,5-Anhydro-2,6-dideoxy-L-arabino-*hex-1-enitol* (**11**, L-rhamnal). — This was prepared by the procedure of Roth and Pigman[34] (84%; m.p. 73–75°); one spot in t.l.c. (1:19 MeOH–CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): δ 1.3 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 3.2–4.3 (m, 5 H, OC*H* & O*H*), 4.6 (q, 1 H, $J_{1,2}$ 7, $J_{2,3}$ 3 Hz, H-2), and 6.3 (d, 1 H, H-1).

*1,5-Anhydro-2,6-dideoxy-3-*O*-methyl*-L-arabino-*hex-1-enitol* (L-oleandral, **12**). — A solution of diazomethane (from 156 mmol of nitrosomethylurea) in ether was added dropwise at ambient temperature to a mixture of **11** (2.1 g, 16 mmol) and stannous chloride (0.2 g, 0.89 mmol) in 220 mL of ether. After half of the addition of diazomethane had been made, an additional 0.2 g of stannous chloride in 20 mL of ether was added, and stirring was continued for 18 h. The remaining diazomethane color was then dispersed by the addition of 0.28 mL (5 mmol) of

acetic acid. T.l.c. (1:19 MeOH–CH_2Cl_2) showed a small amount of starting material remaining. A light precipitate was filtered off and discarded, and the filtrate was successively washed with 5% $NaHCO_3$ solution and saturated NaCl solution, dried, and evaporated to a glass under diminished pressure. Chromatography with 3:97 MeOH–CH_2Cl_2 gave good resolution, and 1.78 g (yield 77%) of product[6,8] was isolated; ^{1}H-n.m.r. ($CDCl_3$): δ 1.4 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 3.4 (s, 3 H, OC*H*$_3$), 3.4–4.0 (m, 3 H, OC*H*), 4.8–5.0 (m, 2 H, H-2 & O*H*-4), and 6.4 (d, 1 H, $J_{1,2}$ 6 Hz, H-1).

Anal. Calc. for $C_7H_{12}O_3$ (144.17): C, 58.32; H, 8.39. Found: C, 58.54; H, 8.4.

*1,5-Anhydro-4-*O*-benzoyl-2,6-dideoxy-3-*O*-methyl-*L-arabino*-hex-1-enitol (4-*O*-benzoyl-*L*-oleandral,* **13**). — A solution of syrupy **12** (983 mg, 6.8 mmol) in pyridine (10 mL) was stirred with cooling while 1.0 mL (8.64 mmol) of benzoyl chloride was added dropwise. The mixture was stirred for 18 h at ambient temperature, water (1 mL) was added, and stirring was continued for 1 h. Dichloromethane (50 mL) was added, and the organic phase was successively washed with M hydrochloric acid (2 × 25 mL) and 10% aqueous $NaHCO_3$ (1 × 25 mL), dried, and evaporated. Chromatography of the residue with 1:99 THF–CH_2Cl_2 removed impurities and afforded the product in 59% yield (1.0 g); $[\alpha]_D$ +89.7° (*c* 0.7, MeOH); ^{1}H-n.m.r. (300 MHz, $CDCl_3$): δ 1.37 (d, 3 H, $J_{5,6}$ 6 Hz, H-6), 3.40 (s, 3 H, OC*H*$_3$), 4.1–4.3 (m, 2 H, H-3,5), 4.92 (q, 1 H, H-4), 5.32 (q, 1 H, $J_{1,2}$ 8, $J_{2,3}$ 3 Hz, H-2), 6.48 (d, 1 H, H-1), and 7.9 (m, 10 H, 2 Bz).

Anal. Calc. for $C_{14}H_{16}O_4$ (248.28): C, 67.73; H, 6.50. Found: C, 67.41; H, 6.39.

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