[Chem. Pharm. Bull.
25(10)2676—2680(1977)]

UDC 547.457.057 : 547.466.23.04

Stereochemical Studies. XLVIII.[1] Stereoselective Synthesis of 6-Deoxy-L-hexose Derivatives from L-Alanine without a Resolution Step[2]

MASAKATSU OHZEKI,[3a)] TOMISHIGE MIZOGUCHI,[3a)] KENJI KOGA,[3b,c)]
and SHUN-ICHI YAMADA[3b)]

Organic Chemistry Research Laboratory, Tanabe Seiyaku Co., Ltd.[3a)] *and Faculty of Pharmaceutical Sciences, University of Tokyo*[3b)]

(Received February 22, 1977)

A new stereoselective synthesis of methyl α-L-amicetoside (**11**), methyl α-L-mycaminoside (**14**) and methyl α-L-oleandroside (**17**) starting from L-alanine is described. It is shown that methyl 2,3,6-trideoxy-α-L-hex-2-enopyranosid-4-ulose (**8**) is readily accessible from L-alanine in optically pure state and is a potential intermediate for the synthesis of various kinds of 6-deoxy-L-hexoses.

Keywords——total synthesis; stereoselective synthesis; 6-deoxy-L-hexoses; deamination; methyl α-L-amicetoside; methyl α-L-mycaminoside; methyl α-L-oleandroside

The isolation of a number of antibiotics containing carbohydrates of unique and unusual structures as well as their potentiality in clinical applications have stimulated widespread investigations on the chemistry of these substances.[4] Studies on the synthesis of their component sugars have also been a matter of intensive investigations either by chemical modification of naturally occurring carbohydrates or by total synthesis from non-carbohydrate precursors.[5] In general, synthesis of monosaccharides starting from non-carbohydrate precursors is considered to have an advantage that the method could be short in synthesis steps and applicable widely to various type of compounds, but also have a disadvantage that resolution should be carried out at some stage of the synthesis. The choice of an optically active starting material, however, will eliminate the necessity of resolution, as in the previous synthesis of various D-pentoses from L-glutamic acid.[6] The present paper describes a new stereoselective synthesis of 6-deoxy-L-hexose derivatives, *i.e.*, methyl α-L-amicetoside (**11**), methyl α-L-mycaminoside (**14**), and methyl α-L-oleandroside (**17**) from L-alanine (**1**), by making use of the chiral center of **1** as those at C-5 of the target compounds *via* a key intermediate, methyl 2,3,6-trideoxy-α-L-hex-2-enopyranosid-4-ulose (**8**), as shown in Chart 1.

---

[1] Part XLVII: M. Kitamoto, K. Kameo, S. Terashima, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **25**, 1273 (1977).

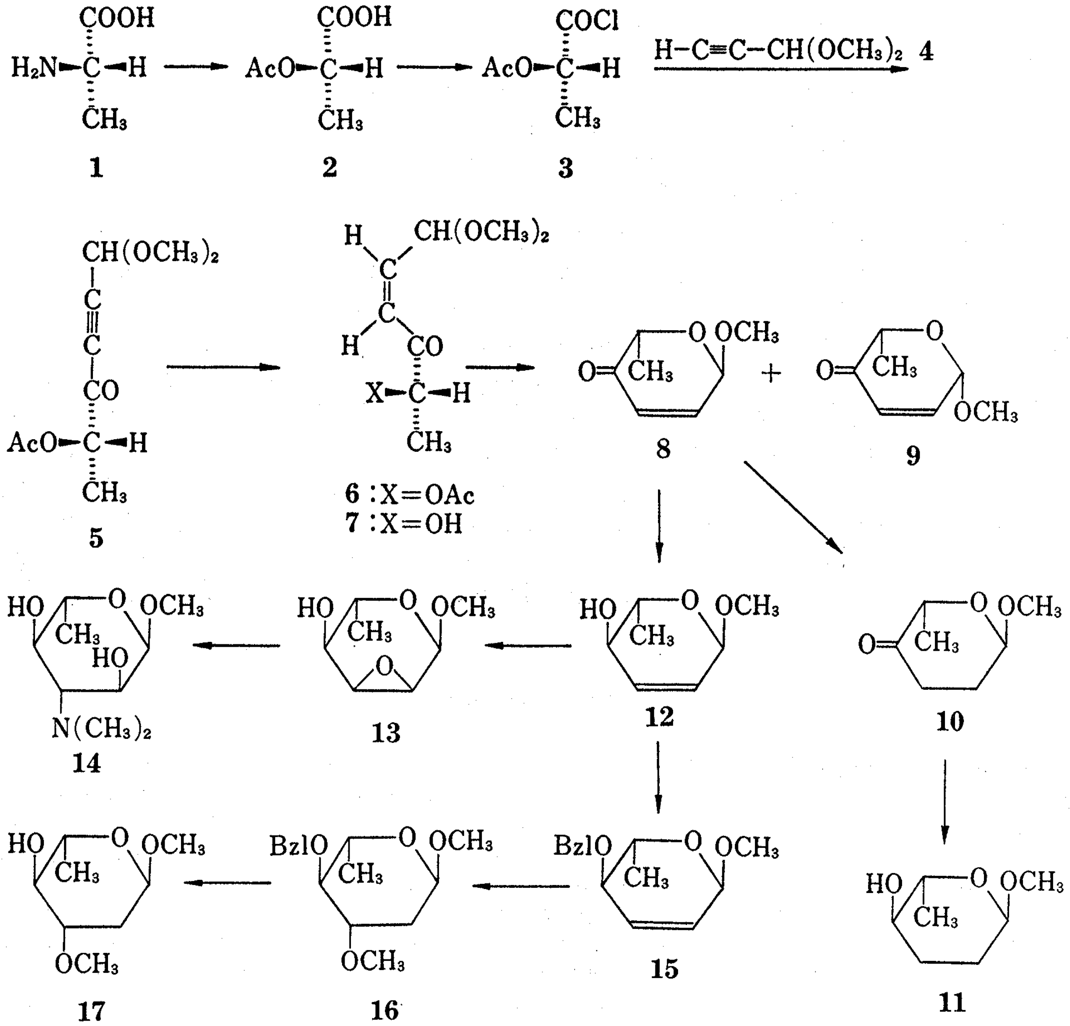
[2] Preliminary communication: K. Koga, S. Yamada, M. Yoh, and T. Mizoguchi, *Carbohyd. Res.*, **36**, C9 (1974).

[3] Location: *a) 2-2-50, Kawagishi, Toda, Saitama, 335, Japan*; *b) 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113, Japan*; *c)* Address correspondence to this author at the University of Tokyo.

[4] *a)* H. Umezawa, "Recent Advances in Chemistry and Biochemistry of Antibiotics," Microbial Chemistry Research Foundation, Tokyo, 1964, p. 67; *b)* S. Hanessian and T.H. Haskell, "The Carbohydrates; Chemistry and Biochemistry," Vol. IIA, ed. by W. Pigman and D. Horton, Academic Press, New York, 1970, p. 139; *c)* S. Umezawa, "Advances in Carbohydrate Chemistry and Biochemistry," Vol. 30, ed. by S. Tipson and D. Horton, Academic Press, New York, 1974, p. 111.

[5] *a)* L. Hough and A.C. Richardson, "Rodd's Chemistry of Carbon Compounds," Vol. IF, ed. by S. Coffey, Elsevier, Amsterdam, 1967, p. 198; *b)* J.S. Brimacombe, *Angew. Chem. Internat. Edit.*, **10**, 236 (1971); *c)* J.K.N. Jones and W.A. Szarek, "The Total Synthesis of Natural Products," Vol. 1, ed. by J. Apsimon, Wiley-Interscience, New York, 1973, p. 1.

[6] *a)* K. Koga, M. Taniguchi, and S. Yamada, *Tetrahedron Lett.*, **1971**, 263; *b)* M. Taniguchi, K. Koga, and S. Yamada, *Tetrahedron*, **30**, 3547 (1974); *c)* M. Taniguchi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **22**, 2318 (1974).



Bzl: benzyl

Chart 1

Nitrous acid deamination of L-alanine (**1**) in acetic acid afforded 2-acetoxypropionic acid (**2**) with at least 96% retention of configuration. Nitrous acid deamination of usual α-amino acids is known to give the corresponding α-substituted product with full retention of configuration due to the participation of the neighboring α-carboxylate group.[7] The reaction of **2** with thionyl chloride gave the corresponding acid chloride (**3**), which was coupled with the Grignard reagent prepared from propiolaldehyde dimethyl acetal (**4**) and ethylmagnesium bromide in the presence of cuprous chloride[8] to the acetylenic compound (**5**). This reaction proceeded even in the absence of the catalyst giving in a lower yield, but the use of other Lewis acid such as $AlCl_3$ and $FeCl_3$ afforded **5** in poor yields. Partial hydrogenation of **5** over palladium on barium sulfate in ethyl acetate containing quinoline afforded the cis-olefin (**6**) in good yield. Treatment of **6** with an equimolar amount of sodium hydroxide in aqueous dioxane gave the olefinic alcohol (**7**), which on heating in carbon tetrachloride in the presence of phosphoric acid afforded a mixture of methyl 2,3,6-trideoxy-α-L- and β-L-hex-2-enopyranosid-4-uloses (**8** and **9**) in a yield of over 70% from **5**. This cyclization reaction was found to

---

[7] *a*) P. Brewster, F. Hiron, E.D. Hughes, C.K. Ingold, and P.A.D.S. Rao, *Nature*, **166**, 179 (1950); *b*) S. Yamada, M. Taniguchi, and K. Koga, *Tetrahedron Lett.*, **1969**, 25; *c*) M. Taniguchi, K. Koga, and S. Yamada, *Chem. Pharm. Bull.* (Tokyo), **20**, 1483 (1972); *d*) K. Koga, C.C. Wu, and S. Yamada, *ibid.*, **20**, 1282 (1972); *e*) M. Yoh, K. Koga, and S. Yamada, *ibid.*, **20**, 2017 (1972).

[8] *a*) N.C. Cook and W.C. Percival, *J. Am. Chem. Soc.*, **71**, 4141 (1949); *b*) W.C. Percival, P.B. Wagner, and N.C. Cook, *ibid.*, **75**, 3731 (1953).

proceed smoothly by eliminating the liberated methanol azeotropically to avoid its addition to the double bond of **8** and **9**.

Racemic **8** and **9** have already been reported as useful intermediates for the chemical synthesis of monosaccharides.[9] The anomeric mixture obtained in the present synthesis was found to be composed of **8** and **9** in a ratio of 2: 1 based on the nuclear magnetic resonance (NMR) analysis. Separation of this mixture by column chromatography on silica gel followed by recrystallization afforded α-anomer (**8**), which was proved to be optically pure by the following experiments. β-Anomer (**9**) was not obtained in a pure state.

Catalytic hydrogenation of **8** over 10% palladium on charcoal in methanol, followed by reduction of the product (**10**) with lithium aluminum hydride afforded methyl α-L-amicetoside (**11**) in 57% yield. Reduction of **8** with lithium aluminum hydride in ether afforded an unsaturated alcohol (**12**), from which methyl α-L-mycaminoside (**14**) and methyl α-L-oleandroside (**17**) were obtained as reported previously for the racemic compounds.[10] The monosaccharides thus obtained were found to be optically pure judging from their optical rotations.

The present results clearly show that optically pure enone (**8**) is readily accessible and serves as a potential intermediate for the synthesis of various kinds of optically active 6-deoxyhexose derivatives that are abundant in nature, especially as component sugars of antibiotics.

Experimental[11]

(*S*)-(−)-α-Acetoxypropionic Acid (2)——To a suspension of L-alanine (1) (100 g, 1.12 mol) in AcOH (600 ml) was added $NaNO_2$ (100 g, 1.45 mol) by portions under stirring at room temperature in the course of 3 days. The resulting solution was evaporated *in vacuo* below 60°. The residue was taken up in AcOEt (700 ml) and the whole was washed with 10% aqueous (aq.) HCl (150 ml). The aq. layer was separated, acidified with conc. aq. HCl to pH below 1, and then filtered to remove the precipitated NaCl. The filtrate was used for washing the above organic layer. This operation was repeated several times until the pH of the aq. layer became below 1. The organic layer was washed with a small volume of saturated (satd.) aq. NaCl and dried over Na_2SO_4. Removal of the solvent left an oily residue, which was taken up in ether (300 ml) and some insoluble materials were filtered off. Evaporation of the filtrate left a yellow oil, which was distilled to give **2** (70.0 g, 47%) as a colorless liquid of bp 101—104° (3 mmHg) (reported[12] bp 115—117° (2 mmHg)), $[\alpha]_D^{22}$ −47.3° (c=6.8, $CHCl_3$) (reported[12] $[\alpha]_D^{22}$ −49.3° (c=7.3, $CHCl_3$)). *Anal.* Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10. Found: C, 45.31; H, 6.05.

(*S*)-α-Acetoxypropionyl Chloride (3)[13]——A mixture of **2** (36.0 g, 0.273 mol) and $SOCl_2$ (40 ml, 0.55 mol) was stirred at 40° for 1.5 hr, and then under reflux for 0.5 hr. After evaporating to dryness, the residue was distilled to give **3** (34.3 g, 83.5%) as a colorless liquid of bp 58—63° (19 mmHg) (reported[12] bp 78° (22 mmHg)), IR ν_{max}^{film} cm^{-1}: 1790 (–COCl), 1755 (–OAc). This sample was used in the next step without further purification.

(*S*)-(−)-5-Acetoxy-1,1-dimethoxy-2-hexyn-4-one (5)——A solution of propiolaldehyde dimethyl acetal (**4**) (18.0 g, 0.18 mol) in tetrahydrofuran (THF) (80 ml) was added dropwise to an ice-cooled solution of ethylmagnesium bromide in THF (prepared from Mg (4.37 g, 0.18 mol) and ethyl bromide (20.0 g, 0.184 mol) in THF (80 ml)), and the whole was stirred at room temperature for 4 hr. The Grignard solution thus obtained was added under ice-cooling to a stirred suspension of **3** (29.2 g, 0.194 mol) and CuCl (0.4 g, 0.004 mol) in tetrahydrofuran (THF) (30 ml) over a period of 3 hr. After the addition was completed, the mixture was stirred at room temperature for 30 min, poured into ice-water (1.2 l), and the whole was extracted with four 150 ml portions of benzene. The combined organic layer was washed with H_2O, satd. aq. NaCl, and

---

9) O. Achmatowicz Jr., P. Bukowski, B. Szechner, Z. Zwierzchowska, and A. Zamojski, *Tetrahedron*, **27**, 1973 (1971).

10) *a*) S. Yasuda and T. Matsumoto, *Tetrahedron Lett.*, **1969**, 4393; *b*) *Idem*, *ibid.*, **1969**, 4397; *c*) *Idem*, *Tetrahedron*, **29**, 4087 (1973).

11) All melting and boiling points are uncorrected. Infrared absorption (IR) spectra were measured with a JASCO DS-402G or a Hitachi 215 Spectrometer. NMR spectra were measured with a JNM-3H-60 (60 MHz) or a JNM-PS-100 (100 MHz) Spectrometer using TMS as an internal standard. MS were measured with a Hitachi RMS-4 Mass Spectrometer. Optical rotations were measured with a JASCO DIP-180 or a Yanaco OR-50 Automatic Polarimeter.

12) S.G. Cohen, J. Crossley, E. Khedouri, R. Zand, and L.H. Klee, *J. Am. Chem. Soc.*, **85**, 1685 (1963).

13) By skipping over the distillation of **2**, the acid chloride (**3**) was obtained in 56% net yield from **1**.

dried over $MgSO_4$. Evaporation of the solvent left a brown oil, which was distilled to give **5** (25.7 g, 67%) as a pale yellow liquid of bp 115—125° (4 mmHg), $[\alpha]^{20}_{D}$ $-19.5°$ ($c=2.0$, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 2240 ($-C\equiv C-$), 1750 (–OAc), 1700 (–CO–). NMR (CCl_4) δ: 1.44 (3H, d, $J=7$ Hz, $-CH-C\underline{H}_3$), 2.08 (3H, s, $-OCOC\underline{H}_3$), 3.32 (6H, s, two $O C\underline{H}_3$) 5.04 (1H, q, $J=7$ Hz, $-C\underline{H}-CH_3$), 5.20 (1H, s, $-C\underline{H}(OCH_3)_2$). *Anal.* Calcd. for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59. Found: C, 55.97; H, 6.74.

(2*Z*,5*S*)-(−)-5-Acetoxy-1,1-dimethoxy-2-hexen-4-one (6)——A mixture of **5** (10.7 g, 0.05 mol), 5% Pd-$BaSO_4$ (2.0 g) and quinoline (2.0 ml) in AcOEt (200 ml) was stirred under atmospheric pressure of H_2 for 14 hr at room temperature. The catalyst was filtered off and the filtrate was washed with 5% aq. HCl, H_2O, satd. aq. NaCl, and dried over $MgSO_4$. Evaporation of the solvent afforded crude **6** in quantitative yield as a brown liquid, which was distilled to a colorless liquid of bp 117—119° (4 mmHg), $[\alpha]^{20}_{D}$ $-30.0°$ ($c=2.0$, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 1750 (–OAc), 1715 (–CO–), 1645 (–CH=CH–). NMR (CCl_4) δ: 1.36 (3H, d, $J=7$ Hz, $-CH-C\underline{H}_3$), 2.04 (3H, s, $-OCOC\underline{H}_3$), 3.28 (6H, s, two $-OC\underline{H}_3$), 5.02 (1H, q, $J=7$ Hz, $-C\underline{H}-CH_3$), 5.40 (1H, d, $J=7$ Hz, $=CH-C\underline{H}(OCH_3)_2$), 5.90 (1H, double d, $J=7$ and 12 Hz, $-CH=C\underline{H}-CH(OCH_3)_2$), 6.20 (1H, d, $J=12$ Hz, $-CO-C\underline{H}=CH-$). *Anal.* Calcd. for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.20; H, 7.30.

(2*Z*,5*S*)-5-Hydroxy-1,1-dimethoxy-2-hexen-4-one (7)——To an ice-cooled solution of crude **6** (10.96 g) in H_2O (15 ml) and dioxane (45 ml) was added aq. 1 N NaOH (50 ml, 0.05 mol) all at once, and the resulting solution was stirred for 1 min under ice-cooling. The solution was acidified with AcOH, and extracted with four 70 ml portions of AcOEt. The combined extracts were washed with satd. aq. NaCl, dried over $MgSO_4$, and evaporated *in vacuo* to give crude **7** (8.82 g) as a brown liquid of IR ν^{film}_{max} cm^{-1}: 3460 (OH), 1700 (–CO–), 1640 (–CH=CH–). This sample was used in the next step without further purification.

Methyl 2,3,6-Trideoxy-α-L-hex-2-enopyranosid-4-ulose (8)——A mixture of phosphoric acid (1.5 g) and CCl_4 (300 ml) in a flask equipped with Dean-Stark apparatus was refluxed for 10 min. After cool. crude **7** obtained above (8.82 g) was added and the whole was heated to boil for 10 min, during which time about 50 ml of distillate was collected. The reaction mixture was washed with H_2O, satd. aq. NaCl, dried over $MgSO_4$, and evaporated to give an anomeric mixture of **8** and **9** as a brown liquid (5.5 g, 77% yield based on **5**), which was chromatographed on silica gel (120 g) with petr. ether–AcOEt (20: 1). The fractions containing faster-moving isomer were combined and evaporated to give α-anomer (**8**) (2.24 g, 30% yield based on **5**) as pale yellow needles. Recrystallization from hexane afforded colorless needles (1.20 g) of mp 50—52°, $[\alpha]^{24}_{D}$ $-16.6°$ ($c=2.2$, $CHCl_3$). IR ν^{Nujol}_{max} cm^{-1}: 1700 (–CO–), 1630 (–CH=CH–). NMR (CCl_4)[9] δ: 1.32 (3H, d, $J=7$ Hz, $-CH-C\underline{H}_3$), 3.44 (3H, s, $-OC\underline{H}_3$), 4.40 (1H, q, $J=7$ Hz, $-C\underline{H}-CH_3$), 4.94 (1H, d, $J=3.5$ Hz, $CH_3O-C\underline{H}(O-)-CH=$), 5.93 (1H, d, $J=10$ Hz, $-CO-C\underline{H}=CH-$), 6.70 (1H, double d, $J=3.5$ and 10 Hz, $-CO-CH=C\underline{H}-$). Elemental analysis gave unsatisfactory results because of the sublimating nature of **8**.

Methyl 2,3,6-Trideoxy-α-L-*erythro*-hexopyranoside (Methyl α-L-Amicetoside) (11)——A mixture of **8** (0.50 g, 3.52 mmol) and 10% Pd–C (50 mg) in MeOH was shaken under the atmospheric pressure of H_2 until the absorption of H_2 ceased. The catalyst was filtered off, and the filtrate was evaporated to give crude **10** (0.45 g) as a colorless liquid (IR ν^{film}_{max} cm^{-1}: 1725 (–CO–)). To a solution of this material (**10**) (0.45 g) in ether (20 ml) was added $LiAlH_4$ (170 mg, 4.5 mmol) and the resulting mixture was stirred at room temperature for 1 hr. H_2O (0.2 ml), 15% aq. NaOH (0.2 ml), H_2O (0.4 ml) and ether (50 ml) were successively added to the reaction mixture under ice-cooling, and the whole was filtered. The filtrate was dried over $MgSO_4$ and evaporated to dryness *in vacuo* to give a pale yellow residue, which was chromatographed on silica gel (60 g) with petr. ether–AcOEt (2: 3) to afford **11** (0.29 g, 57.5% based on **8**) as a colorless liquid of bp 110° (bath temperature) (10 mmHg), $[\alpha]^{20}_{D}$ $-147°$ ($c=0.70$, H_2O), $[\alpha]^{20}_{D}$ $-173°$ ($c=0.3$, $CHCl_3$) (reported $[\alpha]^{18}_{D}$ $+142\pm1°$ ($c=1.2$, H_2O)[14] for the D-enantiomer, $[\alpha]^{20}_{D}$ $-144°$ ($c=0.23$, $CHCl_3$),[15] $[\alpha]_{D}$ $-139\pm1°$ ($c=1.3$, $CHCl_3$)[16]). IR ν^{film}_{max} cm^{-1}: 3400 (OH). NMR ($CDCl_3$) δ: 1.29 (3H, d, $J=6$ Hz, $-CH-C\underline{H}_3$), 1.6—2.0 (4H, m, $-CH(OH)-C\underline{H}_2-C\underline{H}_2-$), 2.18 (1H, broad s, $-O\underline{H}$), 3.39 (3H, s, $-OC\underline{H}_3$), 3.18—3.76 (2H, m, $-C\underline{H}(OH)-C\underline{H}(O-)-$), 4.66 (1H, broad s, $CH_3O-C\underline{H}(O-)-$). MS *m/e*: 146 ($M^+$).

3,5-Dinitrobenzoate: mp 97.5—99.5° (from MeOH) (reported mp 100—101°[14] for the D-enantiomer, mp 96—98°,[15] mp 97—98°[16]), $[\alpha]^{22}_{D}$ $-134°$ ($c=0.4$, $CHCl_3$) (reported $[\alpha]^{20}_{D}$ $+134\pm1°$ ($c=0.4$, $CHCl_3$)[14] for the D-enantiomer, $[\alpha]_{D}$ $-131°$ ($c=0.97$, $CHCl_3$),[15] $[\alpha]_{D}$ $-130°$ ($c=0.5$, $CHCl_3$)[16]). NMR ($CDCl_3$) δ: 1.13 (3H, d, $J=6$ Hz, $-CH-C\underline{H}_3$), 1.7—2.0 (4H, m, $-CH(O-)-C\underline{H}_2-C\underline{H}_2-$), 3.30 (3H, s, $-OC\underline{H}_3$), 3.70—4.20 (1H, m, $CH_3-C\underline{H}(O-)-$), 4.50—4.90 (2H, m, $CH_3O-C\underline{H}(O-)-$ and $CH_3-CH-C\underline{H}-$), 8.85—9.10 (3H, m, aromatic protons). MS *m/e*: 340 (M^+). *Anal.* Calcd. for $C_{14}H_{16}O_8N_2$: C, 49.41; H, 4.74; N, 8.23. Found: C, 49.72; H, 4.83; N, 8.33.

Methyl 2,3,6-Trideoxy-α-L-*erythro*-hex-2-enopyranoside (12)——To a solution of **8** (0.50 g, 3.51 mmol) in ether (20 ml) was added $LiAlH_4$ (0.15 g, 3.94 mmol) and the resulting mixture was stirred for 20 min under ice-cooling. H_2O (0.2 ml), 15% aq. NaOH (0.2 ml), H_2O (0.4 ml) and ether (100 ml) were added successively to the reaction mixture under ice-cooling, and the whole was mixed with $MgSO_4$. Evaporation of the filtrate left an oily residue, which was chromatographed on silica gel (18 g) with petr. ether–AcOEt (8: 3) to give **12**

---

[14] E.L. Albano and D. Horton, *J. Org. Chem.*, **34**, 3519 (1969).

[15] A.H. Haines, *Carbohyd. Res.*, **21**, 99 (1972).

[16] J.S. Brimacombe, L.W. Doner, and A.J. Rollins, *J. Chem. Soc., Perkin I*, **1972**, 2977.

(0.38 g, 74%) as a colorless glass of $[\alpha]_D^{24}$ −103° (c=0.9, $CHCl_3$) (reported[16] $[\alpha]_D$ −94° (c=1, $CHCl_3$)). IR ν_{max}^{film} cm^{-1}: 3400 (OH), 1660 (–CH=CH–). NMR (CCl_4) δ: 1.23 (3H, d, J=6 Hz, $C\underline{H}_3$–CH–), 3.00 (1H, broad s, –O$\underline{H}$), 3.35 (3H, s, –OC$\underline{H}_3$), 3.46—3.80 (2H, m, CH_3–C$\underline{H}$–C$\underline{H}$–), 4.65 (1H, d, J=2 Hz, CH_3O–C$\underline{H}$–CH=), 5.55 (1H, double d, J=2 and 10 Hz, CH_3O–CH–C$\underline{H}$=), 5.80 (1H, d, J=10 Hz, CH_3O–CH–CH=C$\underline{H}$–).

Benzoate: mp 56° (from hexane) (reported[16] mp 53—54.5°), $[\alpha]_D^{20}$ −219° (c=1.0, $CHCl_3$) (reported[16] $[\alpha]_D$ −225° (c=1, $CHCl_3$)). NMR (CCl_4) δ: 1.25 (3H, d, J=6.5 Hz, $C\underline{H}_3$–CH–), 3.38 (3H, s, –OC$\underline{H}_3$), 3.98 (1H, octet, J=6.5 and 9 Hz, CH_3–C$\underline{H}$–CH–), 4.76 (1H, broad s, CH_3O–C$\underline{H}$–CH=), 5.18 (1H, double d, J=2 and 9 Hz, CH_3–CH–C$\underline{H}$–), 5.68 (1H, m, CH_3O–CH–C$\underline{H}$–), 5.86 (1H, d, J=10 Hz, CH_3O–CH–CH=C$\underline{H}$–), 7.22—8.04 (5H, m, aromatic protons). *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.51. Found: C, 67.80; H, 6.40.

Methyl 2,3-Anhydro-6-deoxy-α-L-allopyranoside (13)——To a solution of **12** (0.29 g, 2.0 mmol) in benzene (10 ml) was added *m*-chloroperbenzoic acid (0.45 g, 2.6 mmol), and the mixture was stirred at room temperature for 40 hr. *m*-Chlorobenzoic acid formed was filtered off, and the filtrate was evaporated. The residue was taken up in CCl_4, some insoluble materials were filtered off, and the CCl_4 was evaporated. The residual solid was chromatographed on silica gel (15 g) with benzene–AcOEt (5: 1) to give **13** (0.25 g, 77%) as a colorless solid. Recrystallization from AcOEt–petr. ether afforded colorless needles of mp 98.0—99.5°, $[\alpha]_D^{17}$ −165° (c=1.0, $CHCl_3$). NMR spectral data agreed well with those reported for racemic **13**.[10] MS m/e: 129 (M^+−OCH_3). *Anal.* Calcd. for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.47; H, 7.49.

Methyl 3,6-Dideoxy-3-dimethylamino-α-L-glucopyranoside (Methyl α-L-Mycaminoside) (14)——A solution of **13** (0.15 g) in 40% aq. dimethylamine (10 ml) was heated at 80° for 8 hr. Evaporation to dryness gave a residue, which was taken up in $CHCl_3$ (50 ml), and the whole was dried over $MgSO_4$. Evaporation of the $CHCl_3$ left a solid, which was chromatographed on silica gel (8 g) with $CHCl_3$–MeOH (10: 1) to give **14** (0.13 g, 67%) as a pale yellow solid. Recrystallization from hexane gave colorless plates of mp 83.5—86°, $[\alpha]_D^{22}$ −125° (c=0.4, H_2O) (reported[17] mp 81—82°, $[\alpha]_D$ +123° (c=0.43, H_2O) for the D-enantiomer). NMR spectral data agreed well with those reported for racemic **14**.[10] MS m/e: 205 (M^+). *Anal.* Calcd. for $C_9H_{19}NO_4$: C, 52.66; H, 9.33; N, 6.82. Found: C, 52.84; H, 9.36; N, 6.87.

Methyl 4-O-Benzyl-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (15)——A mixture of **12** (0.36 g, 2.5 mmol), benzyl chloride (3.0 ml, 26 mmol) and powdered NaOH (0.32 g, 8.0 mmol) was stirred at 80—90° for 4 hr. After cooling, ether (50 ml) was added, and insoluble materials were filtered off. The filtrate was washed with satd. aq. NaCl, dried over $MgSO_4$, and evaporated to dryness *in vacuo*. The residue was chromatographed on silica gel (10 g) with hexane–AcOEt (20: 1) to give **15** (0.47 g, 80.5%) as a pale yellow liquid of $[\alpha]_D^{22}$ −170° (c=2.1, $CHCl_3$) (reported[15] $[\alpha]_D^{23}$ −168° (c=2.1, $CHCl_3$)). NMR data agreed well with those reported for racemic **15**.[10] MS m/e: 203 (M^+–OCH_3). *Anal.* Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 72.39; H, 7.84.

Methyl 4-O-Benzyl-2,6-dideoxy-3-O-methyl-α-L-arabinohexopyranoside (16)——A solution of **15** (0.43 g) and *p*-toluenesulfonic acid (60 mg) in MeOH (10 ml) was refluxed for 3 hr. After evaporation of the solvent, the residue was taken up in AcOEt (50 ml), and the whole was washed with satd. aq. $NaHCO_3$, satd. aq. NaCl and dried over $MgSO_4$. Removal of the solvent gave a pale yellow liquid, which was shown to be a mixture (*Rf* 0.31 and 0.28) by thin–layer chromatography (TLC) (silica gel, hexane–AcOEt (5: 1)). Separation of this mixture by preparative TLC afforded **16** (*Rf* 0.31) (0.24 g, 49%) as a pale yellow liquid of $[\alpha]_D^{23}$ −100° (c=1.1, $CHCl_3$). NMR spectral data agreed well with those reported for racemic **16**.[10] *Anal.* Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.90; H, 8.34.

Methyl 2,6-Dideoxy-3-O-methyl-α-L-arabino-hexopyranoside (Methyl α-L-Oleandroside) (17)——A mixture of **16** (0.18 g) and 10% Pd-C (20 mg) in MeOH (15 ml) was shaken under atmospheric pressure of H_2 for 2 hr. The catalyst was filtered off, and the filtrate was evaporated to dryness. The residue was chromatographed on silica gel (7 g) with hexane–AcOEt (5: 1) to give **17** (85 mg, 71%) as a colorless liquid of $[\alpha]_D^{24}$ −105° (c=0.7, $CHCl_3$). NMR spectral data agreed well with those reported for the racemic **17**.[10] MS m/e: 145 (M^+–OCH_3).

3,5-Dinitrobenzoate: mp 122—123° (from MeOH), $[\alpha]_D^{20}$ −63.5° (c=0.7, $CHCl_3$). NMR ($CDCl_3$) δ: 1.24 (3H, d, J=6 Hz, $C\underline{H}_3$–CH–), 1.70 (1H, m, CH_3O–CH–C$\underline{H}_2$–CH–), 2.40 (1H, m, CH_3O–CH–C$\underline{H}_2$–CH–), 3.32 (3H, s, –OC$\underline{H}_3$), 3.42 (3H, s, –OC$\underline{H}_3$), 3.66—4.18 (2H, m, C$\underline{H}$–CH–C$\underline{H}$–CH_3), 4.88 (1H, q, J=1 and 3.5 Hz, CH_3O–C$\underline{H}$–CH_2–), 4.98 (1H, t, J=9 Hz, –C$\underline{H}$–CH–CH_3), 9.04—9.18 (3H, m, aromatic protons). MS m/e: 370 (M^+). *Anal.* Calcd. for $C_{15}H_{18}N_2O_9$: C, 48.65; H, 4.90; N, 7.57. Found: C, 48.59; H, 5.09; N, 7.51.

---

[17] A.B. Foster, T.D. Inch, J. Lehmann, M. Stacey, and J.M. Webber, *J. Chem. Soc.*, **1962**, 2116.