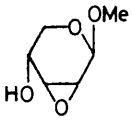
Synthesis of Methyl Gentosaminide, Methyl 3-Deoxy-3-methylamino-arabinopyranoside, and Related Amino-sugars

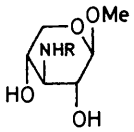
By **David J. Cooper,†** **D. Huw Davies, Alan K. Mallams,*** and **Albert S. Yehaskel,** Research Division, Schering Corporation, Bloomfield, New Jersey 07003, U.S.A.

The synthesis of both α- and β-anomers of methyl gentosaminide (methyl 3-deoxy-3-methylamino-D-xylopyranoside), a component of the amino-glycoside antibiotics gentamicin A and 66-40B, is described. A number of novel 3-alkylamino-analogues of gentosamine have been prepared and the synthesis of the L-enantiomer is also discussed. The preparation of methyl 3-deoxy-3-methylamino-α-D-arabinopyranoside and of the L-enantiomer, involving use of novel epoxy-ketone intermediates, is described. The L-enantiomer has recently been demonstrated to be a component of the amino-glycoside antibiotics 66-40D and gentamicins A_1, A_3, and B_2.

In recent years a wide variety of novel amino-glycoside antibiotics have been isolated from various *Micromonospora* species and the structures have been elucidated in these laboratories. Gentamicin A [1,2] was thus shown to contain 3-deoxy-3-methylamino-D-xylose (gentosamine) as one of the amino-sugar components. The structure and absolute stereochemistry of methyl gentosaminide were established independently in these laboratories [3,4] and by the Rutgers group.[2] The synthesis of methyl β-gentosaminide (2) was reported independently by both groups,[2-4] using the same route [reaction of methyl 2,3-anhydro-β-D-ribopyranoside (1) [5] with methylamine]. Gentosamine has subsequently been found as a sugar component of the unsaturated amino-glycoside antibiotic 66-40B.[6] During ^{13}C n.m.r. studies on the latter

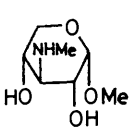


(1)



(2) R = Me
(3) R = H
(4) R = Et
(5) R = Pr^n
(6) R = Pr^i

(7) R =



(8)

antibiotic,[6] it was necessary to prepare methyl α-gentosaminide (8) in order to assign unambiguously the carbon resonances in that sugar unit in 66-40B. This was readily achieved in the laboratory by epimerization of methyl β-gentosaminide (2) in refluxing methanolic hydrogen chloride. Chromatography of the resulting equilibrium mixture of anomers afforded crystalline methyl α-gentosaminide (8), which has not previously been described. The c.d. spectra of methyl α- and β-gentosaminides in TACu and Cupra A were recorded. The α-anomer (8) exhibited a very weak negative extremum at 290—310 nm suggesting almost equal complexing between the 3-methylamino-group and the 2-hydroxy-group and between the 3-methylamino-group and the 4-hydroxy-group. The former complex would be expected to give a negative extremum whereas that of the latter would be expected to be positive.[7,8] In the β-anomer (2) the amplitude of the negative extremum is greater, indicating a preference for 2,3-complexing over 3,4-complexing, presumably owing to the absence of the axial anomeric substituent in (2). The c.d. spectra were consistent with a 3-deoxy-3-methylamino-D-*xylo*-structure for (2) and (8), as were the molecular rotations (Table 1).

The ease of preparation of the methyl 3-deoxy-3-amino-β-D-xylopyranosides from the anhydro-sugar (1) led us to prepare a series of these *xylo*-sugars for part of a mass spectral study of amino-glycoside antibiotics [9] and for screening as antiviral agents. Thus methyl 3-amino- (3),[10,11] 3-ethylamino- (4), 3-n-propylamino- (5), 3-isopropylamino- (6), and 3-adamantylamino- (7) 3-deoxy-β-D-xylopyranoside were prepared, and their physical constants are given in Table 2. The physical constants for (3) were in good agreement with those published.[10,11]

The L-enantiomer of methyl β-gentosaminide [methyl 3-deoxy-3-methylamino-β-L-xylopyranoside (9)] was prepared in a similar manner by treatment of methyl 2,3-anhydro-β-L-ribopyranoside (10) [12] with methylamine. This amino-sugar (9) was prepared as a model compound to demonstrate the lack of reactivity of the vicinal *trans*-3-amino-4-alcohol group towards benzaldehyde both at ambient temperature and upon heating. This was offered as chemical evidence for

† *Present address:* Smith, Kline and French Laboratories, Philadelphia. Pennsylvania 19101, U.S.A.

[1] H. Maehr and C. P. Schaffner, *J. Amer. Chem. Soc.*, 1967, **89**, 6787.
[2] H. Maehr and C. P. Schaffner, *J. Amer. Chem. Soc.*, 1970, **92**, 1697.
[3] D. J. Cooper, H. M. Marigliano, M. D. Yudis, A. S. Yehaskel, and J. Weinstein, Abstracts 158th National Meeting, American Chemical Society, 7—12th September, 1969, CARB 19.
[4] D. J. Cooper, *Pure Appl. Chem.*, 1971, **28**, 455.
[5] P. W. Kent, M. Stacey, and L. F. Wiggins, *J. Chem. Soc.*, 1949, 1232.
[6] D. H. Davies, D. Greeves, A. K. Mallams, J. B. Morton, and R. W. Tkach, following paper.
[7] S. T. K. Bukhari, R. D. Guthrie, A. I. Scott, and A. D. Wrixon, *Chem. Comm.*, 1968, 1580.
[8] S. T. K. Bukhari, R. D. Guthrie, A. I. Scott, and A. D. Wrixon, *Tetrahedron*, 1970, **26**, 3653.
[9] P. J. L. Daniels, A. K. Mallams, J. Weinstein, and J. J. Wright, *J.C.S. Perkin I*, in preparation.
[10] C. D. Anderson, L. Goodman, and B. R. Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 5247.
[11] T. Tsuchiya, K. Suo, and S. Umezawa, *Bull. Chem. Soc. Japan*, 1970, **43**, 531.
[12] J. Honeyman, *J. Chem. Soc.*, 1946, 990.

the fact that the tertiary 4-hydroxy-group in garosamine [4,13] was in a vicinal *cis*-orientation to the 3-methylamino-group, as the reaction between methyl garosaminide and benzaldehyde to form the oxazolidine [13] proceeded exothermically at room temperature. In order to confirm the ease of formation of the oxazolidine in the *arabino*-series, methyl 3-deoxy-3-methylamino-α-D-arabinopyranoside (11) was prepared; this reacted exothermically with benzaldehyde thus lending chemical support for the stereochemistry of the tertiary C-4 in garosamine. The model compound (11) was prepared in the following manner.

Mild oxidation of methyl 2,3-anhydro-β-L-ribopyranoside (10) [12] with ruthenium tetraoxide afforded a high yield of methyl 2,3-anhydro-β-L-*erythro*-pentopyranosid-4-ulose (12). The ^{1}H n.m.r. spectrum of (12) showed a singlet at δ 4·78 for the anomeric proton, and H-2 and -3 gave rise to singlets at δ 3·21 and 3·22 which were not unambiguously assigned. The C-5 methylene group gave rise to a singlet at δ 3·94. The i.r. spectrum exhibited characteristic carbonyl absorption at 1750 cm^{-1}. The foregoing represents a ready preparation of the novel epoxy-ketone (12), which is stable and crystalline. Reduction of the ketone (12) with sodium borohydride gave methyl 2,3-anhydro-α-D-lyxopyranoside (13) [14] together with methyl 2,3-anhydro-β-L-ribopyranoside (10).[12] Treatment of the *lyxo*-epoxide (13) with methylamine in a bomb gave the desired methyl 3-deoxy-3-methylamino-α-D-arabinopyranoside (11) together with methyl 2-deoxy-2-methylamino-α-D-xylopyranoside (14), the latter being formed by nucleophilic opening of the epoxide at C-2.† The ^{1}H n.m.r. spectrum of (14) exhibited resonances at δ 2·42 (NMe), 3·41 (OMe), and 4·92 (d, anomeric H, $J_{1,2}$ 3·5 Hz, consistent with an α-D-*xylo*-configuration). The molecular rotation was also con-

TABLE 1

Molecular rotations

Compound	$[M]_D$(°)	Reference compound	$[M]_D$(°)
(2)	−110	Methyl 3-amino-3-deoxy-β-D-xylopyranoside [a]	−103
(8)	+218	Methyl 3-amino-3-deoxy-α-D-xylopyranoside [b]	+258
(9)	+107	Methyl 3-amino-3-deoxy-β-L-xylopyranoside [c]	+100
(11)	−38	Methyl α-D-arabinopyranoside [d]	−30
(14)	+251	Methyl α-D-xylopyranoside [e]	+252
(15)	+62	Methyl 3-amino-3-deoxy-α-L-arabinopyranoside, HCl [f]	+49
(18)	−261		*ca.* −252 *
(20)	+416	Methyl 3-amino-3-deoxy-β-L-arabinopyranoside, HCl [f]	+403

[a] Ref. 10. [b] Ref. 11. [c] B. R. Baker and R. E. Schaub, *J. Org. Chem.*, 1954, **19**, 646. [d] H. G. Fletcher and C. S. Hudson, *J. Amer. Chem. Soc.*, 1950, **72**, 4173. [e] C. S. Hudson, *J. Amer. Chem. Soc.*, 1925, **47**, 265. [f] H. H. Baer and A. Ahammad, *Canad. J. Chem.*, 1963, **41**, 2931.

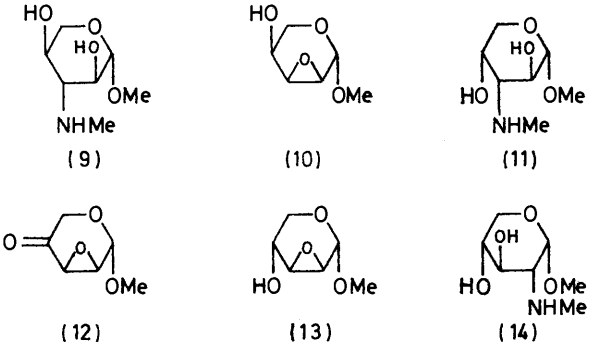
* Approximate value based on methyl α-D-xylopyranoside (footnote *e*).

TABLE 2

Properties of the amino-sugars (4)—(7)

			Required (%)			Found (%)			δ (D_2O) (*J* in Hz)		
Compd.	M.p. (°C)	$[\alpha]_D$ [a] (°)	C	H	N	C	H	N	1-OCH_3	H-1	Other
(4)	131—133	−53·6 [b]	50·3	9·0	7·3	50·15	9·1	7·2	3·50 (3H, s)	4·31 (1H, d, *J* 8)	1·07 (3H, t, *J* 7, CH_3·CH_2·NH), 2·78 (2H, q, *J* 7, CH_3·CH_2·NH)
(5)	122—123	−51·4	52·8	9·3	6·8	52·9	9·5	6·8	3·50 (3H, s)	4·32 (1H, d, *J* 8)	0·89 (3H, t, *J* 7, CH_3·CH_2·CH_2·NH), 1·42 (2H, tq, *J* 7, CH_3·CH_2·CH_2·NH), 2·71 (2H, t, *J* 7, CH_3·CH_2·CH_2·NH)
(6)	111—113	−57·7	52·8	9·3	6·8	52·8	9·3	6·9	3·48 (3H, s)	4·32 (1H, d, *J* 7)	1·03 [6H, d, *J* 6, $(CH_3)_2$CH·NH]
(7)	178—179	−71·8	64·5	9·15	4·7	64·8	9·0	4·7	3·40 (3H, s) [d]	4·88 (1H, d, *J* 3) [d]	

[a] In MeOH. [b] *c* 0·2%. [c] *c* 0·1%. [d] In [$^2H_5$]pyridine.



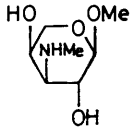
† T.l.c. confirmed the presence of only two products. No isolable substances were observed corresponding to the products of base catalysed migration of the epoxide to the 3,4-position with subsequent ring opening.

[13] D. J. Cooper, M. D. Yudis, R. D. Guthrie, and A. M. Prior, *J. Chem. Soc.* (*C*), 1971, 960.

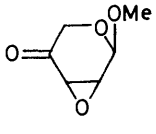
[14] J. G. Buchanan and R. Fletcher, *J. Chem. Soc.* (*C*), 1966, 1926.

sistent with that expected for an α-D-xylopyranoside (Table 1).

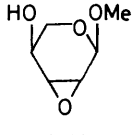
The synthesis of methyl 3-deoxy-3-methylamino-α-L-arabinopyranoside (15) was undertaken [3] prior to its recognition as a component sugar of several aminoglycoside antibiotics, notably 66-40D [6] and gentamicins A_1,[15] A_3,[15] and B_2.[16] The synthesis was achieved by a route similar to that just described for the D-enantiomer. Oxidation of methyl 2,3-anhydro-β-D-ribopyranoside (1) [5] with ruthenium tetraoxide afforded methyl 2,3-anhydro-β-D-*erythro*-pentopyranosid-4-ulose (16). The ^{1}H n.m.r. spectrum of the latter exhibited signals at δ 4·70 (d, anomeric H, $J_{1,2}$ 1·3 Hz), 3·10 (dd, $J_{1,2}$ 1·3, $J_{2,3}$ 4 Hz), 3·20 (d, $J_{2,3}$ 4 Hz), and 3·92 (s, 5-H_2). The keto-group absorbed at 1750 cm^{-1} in the i.r. spectrum. Reduction of the epoxy-ketone (16) with sodium borohydride afforded methyl 2,3-anhydro-α-L-lyxopyranoside (17) together with methyl 2,3-anhydro-β-D-ribopyranoside (1). Treatment of the *lyxo*-epoxide (17) with methylamine gave the



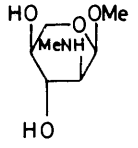
(15)



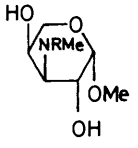
(16)



(17)

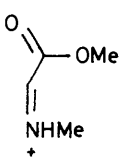


(18)

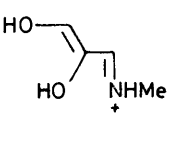


(19) R = Ac
(20) R = H

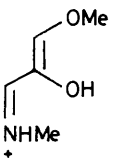
desired methyl 3-deoxy-3-methylamino-α-L-arabinopyranoside (15) thus completing the first synthesis of this novel antibiotic sugar. The molecular rotation (Table 1) and the c.d. spectra (in TACu and Cupra A) were consistent with an L-*arabino*-configuration. Nucleophilic opening of the epoxide at C-2 also occurred to give methyl 2-deoxy-2-methylamino-α-L-xylopyranoside (18).† The ^{1}H n.m.r. spectrum of the latter exhibited signals at δ 2·39 (NMe), 3·40 (OMe), and 4·29 (d, anomeric H, $J_{1,2}$ 3·5 Hz, as expected for an α-L-xylopyranoside). The molecular rotation agreed with the value expected (Table 1). The c.d. spectra of (18) in TACu and Cupra A showed positive extrema at 290 nm consistent with the proposed structure. The mass spectrum contained a peak at *m/e* 102 due to the fragment ions *a* and/or *b* while the 3-methylaminopyranosides (8) and (15) gave fragment ions (*c*) at *m/e* 116. The ^{13}C n.m.r. spectrum of (18) was recorded (Table 3); the assignments are in agreement with the proposed α-L-*xylo*-configuration and correlate well with the values assigned by Perlin [17] for methyl α-D-xylopyranoside. The spectrum at pH 1 (Table 3) clearly demonstrated the presence of the methylamino-group at C-2: the C-1 and -3 signals both



a



b



c

showed the expected upfield shifts [18] associated with *N*-protonation.

Epimerization of methyl 3-deoxy-3-methylamino-α-L-arabinopyranoside (15) by refluxing with methanolic

TABLE 3

^{13}C Chemical shifts (δ_C) of (18) in D_2O

Carbon	(18)	(18) pH 1	Δ(Base ⟶ pH 1)
C-1	99·1	95·7	−3·4
C-2	63·4	61·9 [a]	−1·5
C-3	73·4	70·1 [b]	−3·3
C-4	70·8	70·8 [b]	
C-5	61·8	61·7 [a]	−0·1
NCH_3	34·0	32·2	−1·8
OCH_3	55·9	56·0	+0·1

[a,b] Values not unambiguously assigned.

hydrogen chloride gave an equilibrium mixture of the α- and β-anomers which were inseparable in several chromatographic systems. The anomeric mixture was *N*-acetylated and the resulting mixture was chromatographed to give pure methyl 3-deoxy-3-methylacetamido-β-L-arabinopyranoside (19). The latter upon hydrazinolysis afforded crystalline methyl 3-deoxy-3-methylamino-β-L-arabinopyranoside (20), the molecular rotation of which was in good agreement with the expected value (Table 1). ^{13}C N.m.r. studies on (15) and (20) are described in the following paper.[6]

EXPERIMENTAL

Unless otherwise stated, optical rotations were recorded at 26° in water (*c* 0·3%). I.r. spectra were recorded on a Perkin-Elmer 221 spectrometer. ^{1}H N.m.r. spectra were obtained at 60 MHz for solutions in D_2O on a Varian A60A spectrometer with internal or external sodium 4,4-dimethyl-4-silapentane-1-sulphonate as standard. ^{13}C N.m.r. spectra were recorded for solutions in D_2O with an internal dioxan reference and shifts are reported in p.p.m. downfield from Me_4Si (δ_C for dioxan = −67·4). The spectra were obtained on a Varian XL100-12 spectrometer by Fourier transform with a Varian 620L-16K computer. Mass spectra were recorded on a Varian MAT CH5 spectrometer. C.d. spectra were recorded on a Cary 61 spectrometer.

Methyl 3-Deoxy-3-methylamino-β-D-xylopyranoside (2).—Methyl 2,3-anhydro-β-D-ribopyranoside (1) (3·0 g) was dissolved in absolute ethanol (50 ml) saturated with methylamine. The solution was heated in a bomb at 140° for 16 h, cooled, and evaporated, affording methyl 3-*deoxy*-3-(*methylamino*)-β-D-*xylopyranoside* (2) (2·5 g, 69%) as

† Same footnote as on page 786.

[15] T. L. Nagabhushan, W. N. Turner, P. J. L. Daniels, and J. B. Morton, *J. Org. Chem.*, in preparation.

[16] P. J. L. Daniels, C. Luce, and R. W. Tkach, unpublished observations.

[17] A. S. Perlin, B. Casu, and H. J. Koch, *Canad. J. Chem.*, 1970, **48**, 2596.

[18] G. Kotowycz and R. U. Lemieux, *Chem. Rev.*, 1973, **73**, 669.

crystals (from ethanol), m.p. 144—145° (Found: C, 47·75; H, 8·7; N, 7·8. $C_7H_{15}NO_4$ requires C, 47·45; H, 8·5; N, 7·9%), $[\alpha]_D$ −62·1°; δ 2·43 (3H, s, NCH_3), 3·51 (3H, s, OCH_3), and 4·33 (1H, d, $J_{1.2}$ 8 Hz, H-1), $[\theta]_{290}$ −2380 (TACu), $[\theta]_{290}$ −1860 (Cupra A), identical with methyl β-gentosaminide prepared from gentamicin A.

By essentially the procedure described above a number of *N*-substituted derivatives [(4)—(7)] of methyl 3-amino-3-deoxy-β-D-xylopyranoside were prepared; physical constants are recorded in Table 2.

Methyl 3-Deoxy-3-methylamino-α-D-xylopyranoside (8).—A solution containing methyl 3-deoxy-3-methylamino-β-D-xylopyranoside (2) (1·4 g) in dry methanol (120 ml) saturated with hydrogen chloride gas was heated under reflux for 92 h. The mixture was concentrated and passed over Amberlite IRA 45 ion-exchange resin. The equilibrium mixture of anomers was chromatographed on a silica gel column (110 × 2·5 cm) with 50% methanol in chloroform as eluant to give *methyl 3-deoxy-3-methylamino-α-D-xylopyranoside* (8) (0·5 g, 36%) as crystals (from ethanol), m.p. 110—112° (Found: C, 47·2; H, 8·5; N, 7·7. $C_7H_{15}NO_4$ requires C, 47·45; H, 8·5; N, 7·9%), $[\alpha]_D$ +122·9°; δ 2·43 (3H, s, NCH_3), 3·41 (3H, s, OCH_3), and 4·74 (1H, d, $J_{1.2}$ 4 Hz, H-1), $[\theta]_{290}$ −194 (TACu), $[\theta]_{310}$ −150 (Cupra A).

Methyl 3-Deoxy-3-methylamino-β-L-xylopyranoside (9).—Methyl 2,3-anhydro-β-L-ribopyranoside (10) (1·5 g), dissolved in a 7% (w/v) solution of methylamine in absolute ethanol (30 ml), was heated in a bomb at 150° for 16 h. The cooled solution was evaporated to give *methyl 3-deoxy-3-methylamino-β-L-xylopyranoside* (9) (1·25 g, 69%) as needles (from ethanol), m.p. 141—142° (Found: C, 47·6; H, 8·7; N, 7·9. $C_7H_{15}NO_4$ requires C, 47·45; H, 8·5; N, 7·9%), $[\alpha]_D$ +60·6° (*c* 1%), δ 2·43 (3H, s, NCH_3), 3·52 (3H, s, OCH_3), and 4·31 (1H, d, $J_{1.2}$ 7·5 Hz, H-1).

Methyl 2,3-Anhydro-β-L-erythro-pentopyranosid-4-ulose (12).—Ruthenium tetraoxide, prepared by treating ruthenium dioxide dihydrate (6·7 g) with sodium periodate (105·1 g) in water (1 l), was extracted into carbon tetrachloride. The resulting solution was added dropwise during 1·5 h to a solution of methyl 2,3-anhydro-β-L-ribopyranoside (10) (7·8 g) in dichloromethane (100 ml) at 25°. The mixture set aside for 1 h, filtered, and evaporated to dryness to give *methyl 2,3-anhydro-β-L-erythro-pentopyranosid-4-ulose* (12) (7·5 g, 97%) as needles after sublimation, m.p. 45—46° (Found: C, 49·2; H, 5·6. $C_6H_8O_4$ requires C, 50·0; H, 5·6%), $[\alpha]_D$ +107·5° (CH_3OH), $\nu_{max.}$ (Nujol) 1750 cm^{-1}, δ (C_6D_6) 3·14 (3H, s, OCH_3), 3·21 and 3·22 (2H, s,* H-2 and -3), 3·94 (2H, s, 5-H_2), and 4·78 (1H, s,* H-1).

Methyl 2,3-Anhydro-α-D-lyxopyranoside (13).—Methyl 2,3-anhydro-β-L-*erythro*-pentopyranosid-4-ulose (12) (8·2 g) in methanol (410 ml) was treated with sodium borohydride (2·3 g) and the mixture was stirred at 0° for 2 h. The solution was evaporated to dryness, the residue was taken up in chloroform, and the solution was filtered and evaporated to dryness. The residue was chromatographed on a silica gel column (110 × 5 cm) with ethyl acetate as eluant to give methyl 2,3-anhydro-α-D-lyxopyranoside (13) (1·3 g, 16%) as crystals, m.p. 61—62° (lit.,[14] 62—63°), the physical constants of which were in good agreement with those reported [14,19] and methyl 2,3-anhydro-β-L-ribopyranoside (10) (2·1 g, 25%), identical with an authentic sample.[12]

Methyl 3-Deoxy-3-methylamino-α-D-arabinopyranoside (11) *and Methyl 2-Deoxy-2-methylamino-α-D-xylopyranoside* (14).—Methyl 2,3-anhydro-α-D-lyxopyranoside (13) (870 mg) was dissolved in dry methanol (15 ml) saturated with methylamine and heated in a bomb at 135° for 24 h. The cooled solution was evaporated and the residue was chromatographed on a silica gel column (60 × 1 cm) with the lower phase of a chloroform–methanol–concentrated ammonium hydroxide solution (2 : 1 : 1) as eluant to give *methyl 2-deoxy-2-methylamino-α-D-xylopyranoside* (14) (0·36 g, 34%), which crystallized, m.p. 163—165° (Found: C, 46·55; H, 8·7; N, 7·7. $C_7H_{15}NO_4$,0·5H_2O requires C, 46·9; H, 8·4; N, 7·3%), $[\alpha]_D$ +141·6° (MeOH), δ 2·42 (3H, s, NCH_3), 3·41 (3H, s, OCH_3), and 4·92 (1H, d, $J_{1.2}$ 3·5 Hz, H-1); and *methyl 3-deoxy-3-methylamino-α-D-arabinopyranoside* (11) (0·5 g, 47%) as a syrup (Found: C, 47·2; H, 8·5; N, 7·65. $C_7H_{15}NO_4$ requires C, 47·4; H, 8·5; N, 7·9%), $[\alpha]_D$ −21·3° (MeOH), δ 2·35 (3H, s, NCH_3), 3·52 (3H s, OCH_3), and 4·25 (1H, d, $J_{1.2}$ 8 Hz, H-1).

Methyl 2,3-Anhydro-β-D-erythro-pentopyranosid-4-ulose (16).—Ruthenium tetraoxide, prepared by treating ruthenium dioxide dihydrate (3·4 g) with sodium periodate (52·6 g) in water (500 ml), was extracted into carbon tetrachloride. The resulting solution was added dropwise during 1·5 h to a solution of methyl 2,3-anhydro-β-D-ribopyranoside (1) (5·0 g) in dichloromethane (100 ml) at 25°. The mixture was set aside for 1 h, filtered, and evaporated to dryness to give *methyl 2,3-anhydro-β-D-erythro-pentopyranosid-4-ulose* (16) (4·2 g, 85%), which was sublimed; m.p. 45—46° (Found: C, 49·65; H, 5·6. $C_6H_8O_4$ requires C, 50·0; H, 5·6%), $[\alpha]_D$ −107·4° (MeOH), $\nu_{max.}$ (Nujol) 1750 cm^{-1}, δ (C_6D_6) 3·08 (3H, s, OCH_3), 3·10 (1H, dd, $J_{1.2}$ 1·3, $J_{2.3}$ 4 Hz, H-2), 3·20 (1H, d, $J_{2.3}$ 4 Hz, H-3), 3·92 (2H, s, 5-H_2), and 4·70 (1H, d, $J_{1.2}$ 1·3 Hz, H-1).

Methyl 2,3-Anhydro-α-L-lyxopyranoside (17).—Methyl 2,3-anhydro-β-D-*erythro*-pentopyranosid-4-ulose (16) (7·0 g) in methanol (100 ml) was treated with sodium borohydride (0·6 g) and the mixture was stirred at 25° for 0·5 h. Water (20 ml) was added and the solution was extracted with chloroform. The extract was dried ($MgSO_4$) and evaporated to dryness to give a viscous oil which was chromatographed on a silica gel column (160 × 2·5 cm) with 50% ethyl acetate in hexane as eluant to give *methyl 2,3-anhydro-α-L-lyxopyranoside* (17) (3·0 g, 42%) as crystals (from ethyl acetate–hexane), m.p. 62—63° (Found: C, 49·1; H, 7·0. $C_6H_{10}O_4$ requires C, 49·2; H, 6·9%), $[\alpha]_D$ −140·8° (MeOH), δ ($CDCl_3$) 3·47 (3H, s, OCH_3) and 4·78 (1H, s, H-1) and methyl 2,3-anhydro-β-D-ribopyranoside (1) (2·1 g, 30%), identical with an authentic sample.

Methyl 3-Deoxy-3-methylamino-α-L-arabinopyranoside (15) *and Methyl 2-Deoxy-2-methylamino-α-L-xylopyranoside* (18).—Methyl 2,3-anhydro-α-L-lyxopyranoside (17) (2·7 g), dissolved in absolute ethanol (50 ml) saturated with methylamine, was heated in a bomb at 140° for 16 h. The cooled solution was evaporated and the residue was chromatographed on a silica gel column (160 × 2·5 cm) with 50% methanol in chloroform as eluant to give *methyl 3-deoxy-3-methylamino-α-L-arabinopyranoside* (15) (0·95 g, 29%) as crystals, m.p. 81—84° (Found: C, 47·5; H, 8·3; N, 7·85. $C_7H_{15}NO_4$ requires C, 47·45; H, 8·5; N, 7·9%), $[\alpha]_D$ +35·2°, δ 2·40 (3H, s, NCH_3), 3·58 (3H, s, OCH_3), and 4·27 (1H, d, $J_{1.2}$ 8 Hz, H-1), $[\theta]_{290}$ −9170 (TACu), $[\theta]_{290}$ −8720 (Cupra A); and *methyl 2-deoxy-2-methylamino-α-L-xylopyranoside* (18) (0·93 g, 28%), which crystallized from ethanol; m.p. 161—163° (Found: C, 46·5; H, 7·8; N, 6·9%; M^+, 177·1017.

* Slight coupling (*J* 0·5 Hz) was observed for these protons, but could not be accurately measured at 60 MHz.

[19] J. G. Buchanan, R. Fletcher, K. Parry, and W. A. Thomas, *J. Chem. Soc.* (*B*), 1969, 377.

$C_7H_{15}NO_4,0{\cdot}5H_2O$ requires C, 46·9; H, 8·4; N, 7·3%; $C_7H_{15}NO_4$ requires *M*, 177·1001), $[\alpha]_D$ −147·4°, δ 2·39 (3H, s, NCH_3), 3·40 (3H, s, OCH_3), and 4·92 (1H, d, $J_{1.2}$ 3·5 Hz, H-1), $[\theta]_{290}$ +7100 (TACu), $[\theta]_{290}$ +4490 (Cupra A).

Methyl 3-*Deoxy*-3-*methylamino*-β-L-*arabinopyranoside* (20). —A solution containing methyl 3-deoxy-3-methylamino-α-L-arabinopyranoside (15) (0·95 g) in dry methanol (40 ml) saturated with hydrogen chloride gas was heated under reflux for 60 h. The mixture was concentrated and passed over Amberlite IRA 45 ion-exchange resin. The equilibrium mixture of anomers was chromatographed on a silica gel column (110 × 2·5 cm) with 40% methanol in chloroform as eluant to give a mixture of the α- and β-anomers in the ratio 30 : 70 (340 mg). The mixture (340 mg) was treated with acetic anhydride (600 mg) in dry methanol (30 ml) and the solution was allowed to remain at 0° for 20 min. Evaporation, followed by azeotropic distillation of the residue with toluene, afforded the anomeric mixture of *N*-acetates, which were separated by chromatography on a silica gel column (160 × 2 cm) with 8% methanol in chloroform as eluant to give methyl 3-deoxy-3-methylacetamido-β-L-arabinopyranoside (19) (120 mg). The latter on heating with 90% hydrazine hydrate (3 ml) in a bomb at 100° for 16 h, followed by evaporation and chromatography on a silica gel column (110 × 1 cm) with the lower phase of a chloroform–methanol–7% ammonium hydroxide solution (2 : 1 : 1) as eluant, gave *methyl* 3-*deoxy*-3-*methylamino*-β-L-*arabinopyranoside* (20) (60 mg, 6%) as crystals, m.p. 97—99° (Found: C, 42·85; H, 8·3; N, 7·3. $C_7H_{15}NO_4,H_2O$ requires C, 43·1; H, 8·8; N, 7·2%), $[\alpha]_D$ +235·1°, δ 2·36 (3H, s, NCH_3), 3·40 (3H, s, OCH_3), and 4·78 (1H, d, $J_{1.2}$ 4 Hz, H-1).

We thank Dr. M. D. Yudis and his staff for the spectral and analytical data and Dr. P. J. L. Daniels for discussions and for his critical review of the manuscript.

[4/2336 *Received*, 8*th November*, 1974]