# The Megalomicins. Part III.[1] D-Rhodosamine, a New Dimethylamino-sugar

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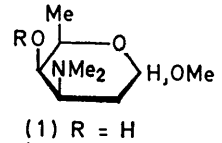
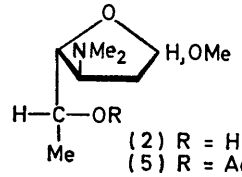
D-Rhodosamine. a new dimethylamino-sugar isolated from megalomicins A. B. $C_1$. and $C_2$. a new family of macrolide antibiotics elaborated by *Micromonospora megalomicea* sp. n., has been shown to be 2,3,6-trideoxy-3-dimethylamino-D-*lyxo*-hexopyranose.

DURING the structural elucidation of the macrolide antibiotics [2-4] megalomicins A, B, $C_1$, and $C_2$, a new dimethylamino-sugar [1,5] was isolated which has been shown to be 2,3,6-trideoxy-3-dimethylamino-D-*lyxo*-hexopyranose. This has been named D-rhodosamine by analogy with L-rhodosamine (2,3,6-trideoxy-3-dimethylamino-L-*lyxo*-hexopyranose), which occurs in rhodomycins A,[6] B,[6] and $\gamma$,[7] pyrromycin,[8] and cinnerubins A and B.[9]

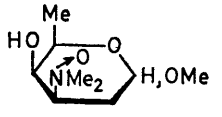
Methanolysis of megalomicin A [1,5] afforded anomeric mixtures of methyl α- and β-glycosides of the pyranose (1) and furanose (2) forms of D-rhodosamine. The pyranosides and furanosides were readily separable by column chromatography, but no separation of the α- and β-anomers was observed. In order to separate the methyl α- and β-pyranosides (1), the anomeric mixture was converted into the *N*-oxides (3) with hydrogen peroxide, and the latter were separated chromatographically to give the pure α- and β-anomers. On heating with triethyl phosphite the α- and β-anomers of the *N*-oxide (3) afforded the methyl α-glycoside (1α) and the methyl β-glycoside (1β), respectively. The i.r. spectra of methyl α- and β-D-rhodosaminide (1) indicated the presence of hydroxy- and dimethylamino-groups in the molecule, and the $pK_a$ value (8·8) was consistent with that of a β-dimethylamino-alcohol. The n.m.r. spectrum of the α-anomer (1α) revealed the presence of a secondary methyl group (δ 1·34, $J_{5a,6}$ 7 Hz), a dimethylamino-group (δ 2·30), and a methoxy-group (δ 3·38). The anomeric proton gave rise to a doublet of doublets at δ 4·80 ($J_{1eq,2ax} = J_{1eq,2eq} = 3$ Hz) consistent




(1) R = H
(4) R = Ac




(2) R = H
(5) R = Ac

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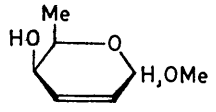


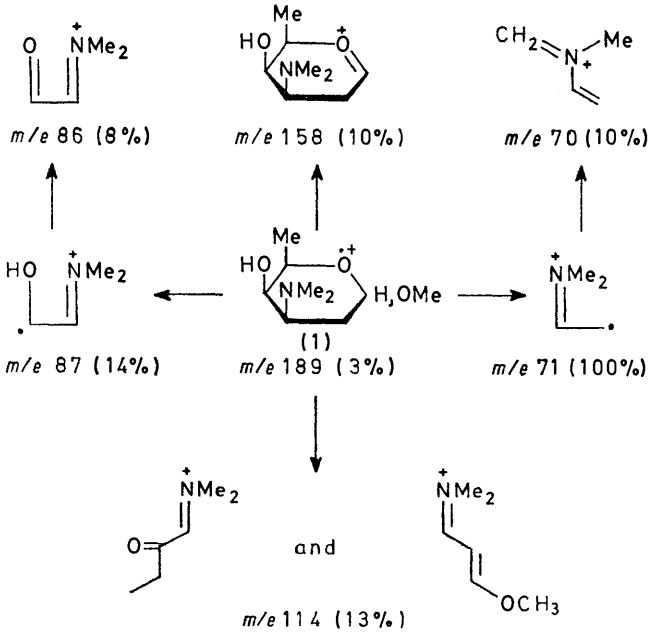

(6)

with a 2-deoxy-structure. The 3-proton gave a doublet of doublets of doublets at δ 2·63 ($J_{3ax,4eq}$ 3, $J_{2ax,3ax}$ 8·5, $J_{2eq,3ax}$ 7·5 Hz), H-4 gave a doublet of doublets at δ 3·71 ($J_{4eq,5ax}$ 2·5, $J_{3ax,4eq}$ 3 Hz), and H-5 gave a doublet of quartets at δ 4·07 ($J_{5ax,6}$ 7, $J_{4eq,5ax}$ 2·5 Hz) in agreement with structure (1α). The c.d. curve of a cuprammonium solution of methyl D-rhodosaminide (1α) † showed, as

† Kindly run by Dr. R. D. Guthrie and Miss S. T. K. Bukhari, University of Sussex, Brighton.

[1] Part II, A. K. Mallams, R. S. Jaret, and H. Reimann, *J. Amer. Chem. Soc.*, 1969, **91**, 7506.
[2] M. J. Weinstein, G. H. Wagman, J. A. Marquez, R. T. Testa, E. Oden, and J. A. Waitz, *J. Antibiotics*, 1969, **22**, 253.
[3] J. A. Marquez, A. Murawski, G. H. Wagman, R. S. Jaret, and H. Reimann, *J. Antibiotics*, 1969, **22**, 259.
[4] J. A. Waitz, E. L. Moss, jun., E. Oden, and M. J. Weinstein, *J. Antibiotics*, 1969, **22**, 265.
[5] A. K. Mallams, *J. Amer. Chem. Soc.*, 1969, **91**, 7505.
[6] H. Brockmann, E. Spohler, and T. Waehneldt, *Chem. Ber.*, 1963, **96**, 2925.
[7] H. Brockmann and T. Waehneldt, *Naturwiss.*, 1961, **48**, 717.
[8] H. Brockmann and W. Lenk, *Chem. Ber.*, 1959, **92**, 1904.
[9] L. Ettlinger, E. Gäumann, R. Hütter, W. Keller-Schierlein, P. Kradolfer, L. Neipp, V. Prelog, P. Reusser, and H. Zähner, *Chem. Ber.*, 1959, **92**, 1867.

expected, a positive band at 570 and a negative band at 290 nm corresponding to the formation of a *k* chelate [10] (*i.e.* there is a negative dihedral angle between the dimethylamino- and hydroxy-groups), thus confirming the D-*lyxo*-configuration for (1). The amplitude of the 570 nm band was in agreement with the value expected for a β-dimethylamino-alcohol.[11] The n.m.r. spectrum of the β-anomer was also consistent with the proposed structure (1), showing a secondary methyl group at δ 1·29 ($J_{5ax,6}$ 6·5 Hz), a dimethylamino-group at δ 2·31, and a methoxy-group at δ 3·39. The axial anomeric proton gave rise to a doublet of doublets at δ 4·66 ($J_{1ax,2ax}$ 8, $J_{1ax,6eq}$ 5 Hz), and the methylene group at C-2 gave two multiplets due to H-2$_{ax}$ at δ 1·55 ($J_{1ax,2ax}$ 8, $J_{2ax,2eq} = J_{2ax,3ax} = 12·5$ Hz) and H-2*eq* at δ 1·99 ($J_{1ax,2eq}$ 5, $J_{2eq,2ax}$ 12·5, $J_{2eq,3ax}$ 4, $J_{2eq,4eq}$ 1·5 Hz). The 3-proton gave a doublet of doublets of doublets at δ 2·31 ($J_{2ax,3ax}$ 12·5, $J_{3ax,4eq} = J_{2ax,3ax} = 4$ Hz), H-4 gave a doublet of doublets of doublets at δ 3·54 ($J_{4ax,5eq}$ 4·5, $J_{3ax,4eq}$ 4, $J_{2eq,4eq}$ 1·5 Hz), and H-5 gave a doublet of quartets at δ 3·93 ($J_{5ax,6}$ 6·5, $J_{4eq,5ax}$ 4·5 Hz). The long-range 1,3-diequatorial coupling between H-2*eq* and H-4*eq* confirmed the axial orientation of the 4-hydroxy-group. The mass spectrum of methyl α- and β-D-rhodosaminide (1) gave a molecular ion at *m/e* 189 ($C_9H_{19}NO_3$), and showed fragmentation patterns (Scheme 1) in agreement with structure (1).




SCHEME 1

When the methyl pyranoside (1) was subjected to mild acidic hydrolysis under a variety of aqueous acidic conditions, as well as acetolysis conditions, extensive decomposition occurred and no free sugar was isolated. In contrast L-rhodosamine is stable under hydrolytic conditions in 0·5N-hydrochloric acid.[6] Acetylation of the methyl pyranoside (1) gave a monoacetate (4), identical with the product obtained in high yield on attempted oxidation of (1) with acetic anhydride–dimethyl sulphoxide. Extensive *O*-acetylation by the above reagent had not been noted in the literature at the time these observations were recorded. However, Richardson *et al.*[12] recently reported extensive *O*-acetylation, when using the reagent to oxidize carbohydrates in which the hydroxy-group was β to either a *trans*-equatorial acylamino-group, or a *cis*-acylamino-group. The formation of the acetates (4) and (5) by use of the reagent suggests that the reaction is more general than proposed by Richardson *et al.*[12] Dmitriev *et al.*[13] have also recently reported *O*-acylation in the oxidation of carbohydrates using the dimethyl sulphoxide–acetic anhydride reagent. When Pfitzner–Moffatt oxidation conditions were employed to oxidize (1), only unchanged starting material was obtained. The decrease of the p$K_a$ value from 8·8 to 7·5 on acetylation of (1) to give (4) clearly indicated the presence of the β-dimethylamino-group in methyl D-rhodosaminide (1).

The anomeric mixture of *N*-oxides (3) was subjected to a Cope elimination to give a mixture consisting of methyl D-rhodosaminide (1) * and methyl 2,3,6-trideoxy-D-*threo*-hex-2-enopyranoside (6). The latter was identical with the olefin formed from methyl D-rhodosaminide methiodide on heating with sodium hydride in tetrahydrofuran. The formation of the olefin (6) rather than an epoxide on base-catalysed elimination of the quaternary salt confirmed the *cis*-orientation of the dimethylamino- and hydroxy-groups at C-3 and C-4, respectively, in D-rhodosamine. Catalytic reduction of the olefin (6) gave methyl 2,3,6-trideoxy-D-*threo*-hexopyranoside (7),[14] which on oxidation with ruthenium tetroxide gave methyl 2,3,6-trideoxy-D-hexopyranosid-4-ulose (8). The c.d. curve of the ketone (8) in methanol exhibited a negative Cotton curve at $\lambda_{max.}$ 298 nm, indicating a D-configuration. No racemization would be expected to occur at C-5 under the mild oxidation conditions used to prepare the ketone (8), as was found to be the case.†

The furanose form (2) of methyl D-rhodosaminide, obtained from the methanolysis of megalomicin A, consisted of a 1 : 1 ratio of the α- and β-anomers. The n.m.r. spectrum of the furanoside (2) indicated the presence of a secondary methyl group (δ 1·21, *J* 6 Hz; δ 1·24, *J* 6 Hz), a dimethylamino-group (δ 2·23 and δ 2·29), and a methoxy-group (δ 3·36 and 3·38). The anomeric proton gave rise to a doublet of doublets (δ 5·08, $J_{1.2} = J_{1.2'} = 3$ Hz) and (δ 4·99, $J_{1.2}$ 3·5,

* The *N*-oxide (3) used in the reaction contained no free amine (1); the latter must therefore have been generated from the *N*-oxide under the conditions of the Cope elimination.

† The c.d. curve of a cuprammonium solution of (1), described earlier, confirmed this hypothesis.

[10] S. T. K. Bukhari, R. D. Guthrie, A. I. Scott, and A. D. Wrixon, *Chem. Comm.*, 1968, 1580.

[11] R. D. Guthrie, personal communication.

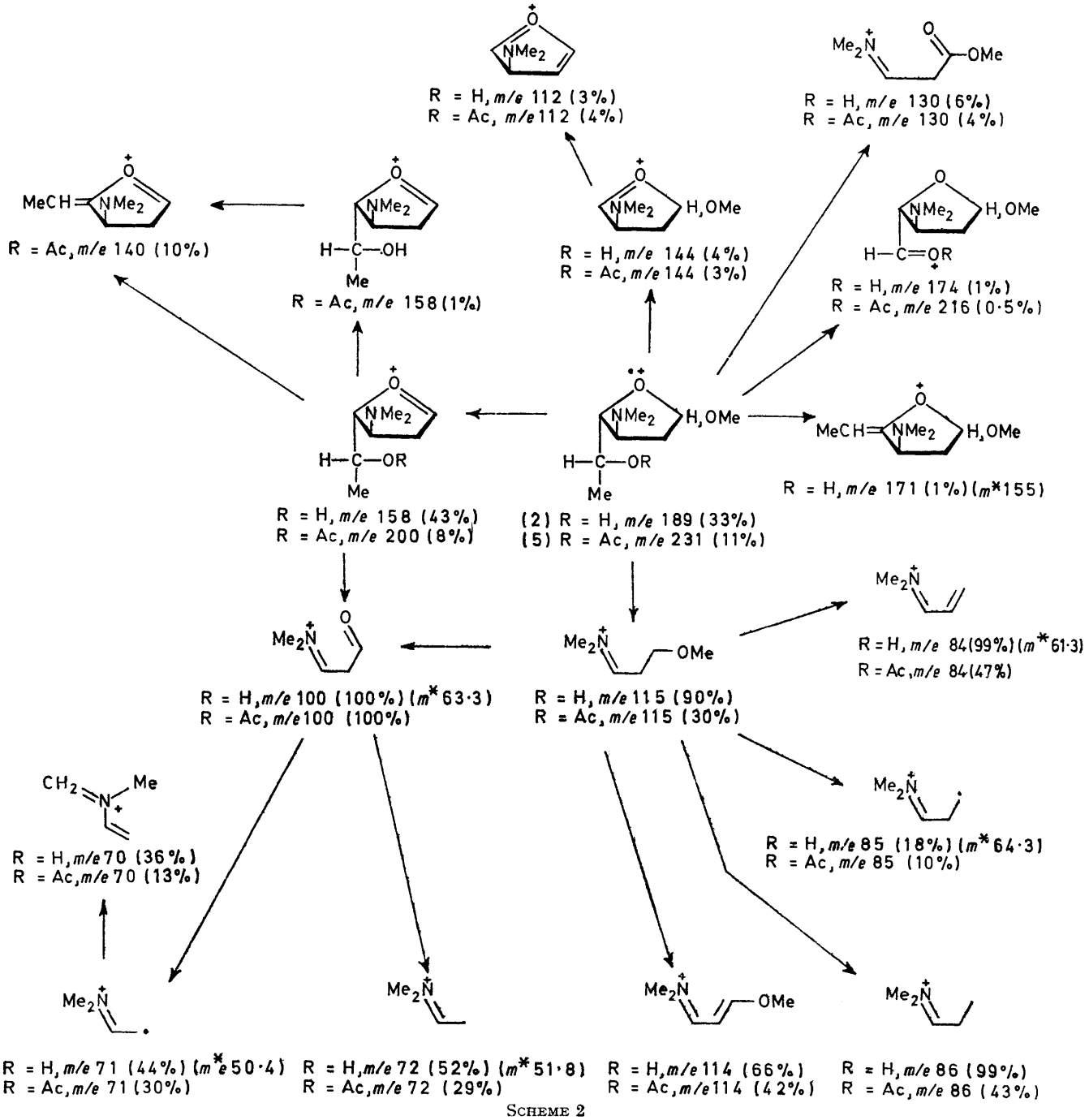
[12] Y. Ali and A. C. Richardson, *J. Chem. Soc.* (*C*), 1969, 320.

[13] B. A. Dmitriev, A. A. Krost, and N. K. Kochetkov, *Bull. Acad. Sci., U.S.S.R., Chem. Ser.*, 1969, 903.

[14] C. L. Stevens, P. Blumbergs, and D. L. Wood, *J. Amer. Chem. Soc.*, 1964, **86**, 3592.

$J_{1.2'}$ 5 Hz) as expected for a 2-deoxyfuranoside. The mass spectral fragmentation pattern (Scheme 2) was consistent with the furanoside structure (2). Attempted acidic hydrolysis of the methyl furanoside (2) under mild conditions led to extensive decomposition.

support to the formulation of (2) and (5) as furanosides. Distillation of the acetate (5) gave predominantly the α-anomer, the n.m.r. spectrum of which in deuteriobenzene was spin decoupled at 60 MHz leading to confirmation of the structure. Irradiation at the frequency

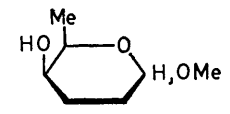



SCHEME 2

Acetylation of the furanoside (2) gave a monoacetate (5), identical with the product obtained in high yield from the attempted oxidation of (2) with acetic anhydride–dimethyl sulphoxide. The acetate (5) exhibited a $pK_a$ of 7·6 [*cf.* 7·9 for the alcohol (2)], giving additional

of the methyl group gave a doublet for H-5 ($J$ 6·5 Hz), and irradiation at the frequency of the latter led to a doublet of doublets for H-4 ($J_{3.4}$ 4·5, $J_{4.6}$ 1·5 Hz), and a doublet for the methyl group ($J_{4.6}$ 1·5 Hz). The long-range coupling of H-4 to the protons of the methyl

group was not apparent prior to irradiation at the frequency of H-5. When the H-4 frequency was irradiated, the signal due to H-5 became a quartet ($J$ 6·5 Hz) coupling with the neighbouring methyl protons. Irradiation at the frequency of H-3 caused the signal due to H-4 to collapse to a doublet ($J_{4,5}$ 6·5 Hz).

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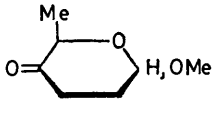


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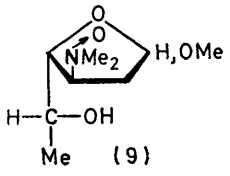


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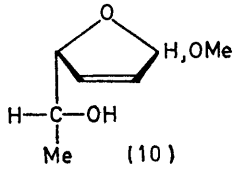


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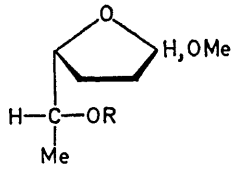
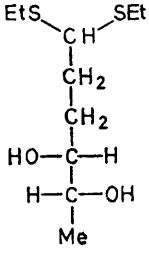



(11) R = H
(12) R = Me




(13)

The furanoside (2) on treatment with hydrogen peroxide gave an anomeric mixture of *N*-oxides (9) from which the α-anomer readily crystallized. The latter (9α) on subjection to a Cope elimination gave a mixture consisting of methyl D-rhodosaminide (2α), and methyl 2,3,6-trideoxy-α-D-*threo*-hex-2-enofuranoside (10α). Catalytic hydrogenation of an anomeric mixture of the latter (10) gave methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hexofuranoside (11), which on methylation gave the permethylated derivative (12). Thiolysis of the furanoside (11) with ethanethiol gave the diethyl thioacetal (13).

## EXPERIMENTAL

Unless otherwise stated, optical rotations were recorded at 26° for solutions in ethanol. N.m.r. spectra were obtained at 60 MHz for solutions in deuteriochloroform, with an internal tetramethylsilane standard, on a Varian A60A spectrometer. I.r. spectra were recorded for solutions in carbon tetrachloride on a Perkin-Elmer Infracord 137 instrument. p$K_a$ Values were obtained coulometrically for solutions in 66% aqueous dimethylformamide. Mass spectra were run on a Perkin-Elmer RMU-6D spectrometer.

*Methyl α- and β-D-Rhodosaminide* (1) *and* (2).—Megalomicin A (30 g) was dissolved in 0·6N-hydrogen chloride in methanol (750 ml). The solution was kept at 25° for 48 h, then passed through an Amberlite IR 45 ion-exchange resin. The methanolic eluate was evaporated, and the resulting gum was dried by azeotropic distillation with benzene. The crude gum was chromatographed by gradient elution (2, 10, and 20% methanol in chloroform) on a silica gel column (140 × 3·5 cm) to give, in order of elution, methyl α- and β-L-mycaroside [15] (5·4 g), erythralosamine [16,17] (17·9 g), methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (2), obtained as an oil (650 mg) after two short-path distillations (b.p. 54—55° at 0·5 mmHg) (Found: C, 57·0; H, 10·3; N, 7·4. Calc. for $C_9H_{19}NO_3$: C, 57·1; H, 10·1; N, 7·4%), $[\alpha]_D$ +12·4°, p$K_a$ 7·9, $\nu_{max.}$ ($CHCl_3$) 3400, 2770, and 1035 $cm^{-1}$, and methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (1), obtained as an oil (360 mg) after short-path distillation (b.p. 65—66° at 0·5 mmHg) (Found: C, 57·0; H, 9·9; N, 7·5%), $[\alpha]_D$ +20·3°, p$K_a$ 8·8, $\nu_{max.}$ ($CHCl_3$) 3420, 2780, and 1045 $cm^{-1}$.

*Methyl 2,3,6-Trideoxy-3-dimethylamino-α- and -β-D-lyxo-hexopyranoside N-Oxide* (3).—Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (1) (1·4 g) was dissolved in methanol (50 ml) and treated with a mixture of 30% hydrogen peroxide (10 ml) and water (10 ml). The mixture was kept at 25° for 24 h, the methanol was distilled off under reduced pressure, and the excess of hydrogen peroxide was destroyed by addition of 5% palladium–carbon. The solution was filtered and evaporated to give the *N*-oxide (3) as a gum (1·4 g) (Found: C, 52·4; H, 9·55; N, 6·6. Calc. for $C_9H_{19}NO_4$: C, 52·7; H, 9·3; N, 6·8%), *m/e* 205 ($M^{+\bullet}$, 0·1%), 189 ($M$ − O, 2), 187 ($M$ − $H_2O$, 1·3), 174 ($M$ − $CH_3O$ and $M$ − O − $CH_3$, 0·4), 158 ($M$ − O − $CH_3O$, 8), 156 ($M$ − $CH_3O$ − $H_2O$, 5), 114 (19), 87 (17), 86 (17), 71 (69), and 70 (16), $[\alpha]_D$ +36·3°. The anomeric mixture of *N*-oxides was chromatographed on silica gel (140 × 2·5 cm) with 10% methanol in chloroform as eluant. The less polar *methyl 2,3,6-trideoxy-3-dimethylamino-α-D-lyxo-hexopyranoside N-oxide* (3α) (616 mg) crystallized from methanol–acetone–hexane as needles, m.p. 162—163°, $[\alpha]_D$ +117·3° ($CH_3OH$), $\nu_{max.}$ (Nujol) 3300 and 1050 $cm^{-1}$, δ ($CD_3OD$) 1·37 (3H, d, $J_{5ax,6}$ 7·5 Hz, 6-$CH_3$), 3·18 and 3·30 (6H, s, 3-$Me_2N\rightarrow O$), 3·40 (3H, s, 1-$OCH_3$), and 4·97 (1H, dd, $J_{1eq,2ax}$ 4, $J_{1eq,2eq}$ 2 Hz, H-1). The more polar β-*glycoside N-oxide* (3β) (630 mg) crystallized from methanol–acetone–hexane as needles, m.p. 178—179°, $[\alpha]_D$ −37·2° ($CH_3OH$), $\nu_{max.}$ (Nujol) 3300 and 1035 $cm^{-1}$, δ ($CD_3OD$) 1·27 (3H, s, $J$ 6·5 Hz, 6-$CH_3$), 3·24 and 3·31 (6H, s, 3-$Me_2N\rightarrow O$), and 3·42 (3H, s, 1-$OCH_3$).

*Methyl 2,3,6-Trideoxy-3-dimethylamino-α-D-lyxo-hexopyranoside* (1α).—Methyl 2,3,6-trideoxy-3-dimethylamino-α-D-*lyxo*-hexopyranoside *N*-oxide (3α) (230 mg) and triethyl phosphite (3 ml) in methanol (3 ml) were heated on a steam-bath for 5 h. The methanol was removed under reduced pressure and the residue was chromatographed on silica gel (110 × 2·5 cm) with 10% methanol in chloroform as eluant. The *product* was obtained as an oil (175 mg), $[\alpha]_D$ +119·1° ($CH_3OH$), $\nu_{max.}$ (film) 3410, 2770, and 1045 $cm^{-1}$.

*Methyl 2,3,6-Trideoxy-3-dimethylamino-β-D-lyxo-hexopyranoside* (1β).—Methyl 2,3,6-trideoxy-3-dimethylamino-β-D-*lyxo*-hexopyranoside *N*-oxide (3β) (250 mg) was treated as in the case of the α-anomer to give the *product* as an oil (198 mg), $[\alpha]_D$ −58·8° ($CH_3OH$), $\nu_{max.}$ (film) 3440, 2780, and 1070 $cm^{-1}$.

[15] D. M. Lemal, P. D. Pacht, and R. B. Woodward, *Tetrahedron*, 1962, **18**, 1275.

[16] E. H. Flynn, M. V. Sigal, jun., P. F. Wiley, and K. Gerzon, *J. Amer. Chem. Soc.*, 1954, **76**, 3121.

[17] P. F. Wiley, K. Gerzon, E. H. Flynn, M. V. Sigal, jun., O. Weaver, U. C. Quarck, R. R. Chauvette, and R. Monahan, *J. Amer. Chem. Soc.*. 1957 **79**. 6062.

*Methyl* 4-O-*Acetyl*-2,3,6-*trideoxy*-3-*dimethylamino*-α- *and* -β-D-lyxo*hexopyranoside* (4).—Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (1) (50 mg) was dissolved in dry pyridine (5 ml), treated with acetic anhydride (0·5 ml), and kept at 25° for 16 h. The mixture was poured into aqueous sodium hydrogen carbonate and extracted with chloroform; the extract was washed with water and dried ($Na_2SO_4$). The crude *product* was distilled (air bath; 100° at 0·5 mmHg) to give an oil (40 mg), p$K_a$ 7·5, $\nu_{max.}$ ($CHCl_3$) 2780, 1725, 1240, and 1040 $cm^{-1}$, δ 1·31 and 1·41 (3H, d, $J_{5,6}$ 7 Hz, 6-$CH_3$), 1·12 (3H, s, 4-OAc), 2·31 (6H, s, 3-$Me_2N$), 3·40 and 3·46 (3H, s, 1-$OCH_3$), 4·72 (1H, dd, $J_{1ax,2eq}$ 4, $J_{1ax,2ax}$ 8 Hz, H-1*ax*), and 4·86 (1H, dd, $J_{1eq,2ax} = J_{1eq,2eq}$ = 3 Hz, H-1*eq*).

*Attempted Oxidation of Methyl* 2,3,6-*Trideoxy*-3-*dimethylamino*-α- *and* -β-D-lyxo-*hexopyranoside* (1).—(a) *Dimethyl sulphoxide–acetic anhydride method.* The glycoside mixture (1) (60 mg) was dissolved in dimethyl sulphoxide (2 ml) and acetic anhydride (0·5 ml), and the mixture was kept at 25° for 20 h. The solution was evaporated under reduced pressure to 0·5 ml, treated with aqueous sodium hydrogen carbonate, and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated, and the resulting oil was distilled (air bath; 120° at 0·5 mmHg) to give methyl 4-*O*-acetyl-2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (4) as an oil (36 mg) (Found: C, 55·8; H, 8·9; N, 6·5. Calc. for $C_{11}H_{21}NO_4$: C, 57·1; H, 9·15; N, 6·1%), *m/e* 231 ($M^+$, 1·5%), 200 ($M$ − $CH_3O$, 6), 171 ($M$ − AcOH, 4), 156 (6), 114 (22), 71 (100), 70 (8), and 43 (58), $[\alpha]_D$ +43·0° ($CH_3OH$). The i.r. and n.m.r. spectra were identical with those of the acetate (4), prepared by direct acetylation, and mixed t.l.c. on Kieselgel with 30% methanol in chloroform as eluant showed only one spot.

(b) *Pfitzner–Moffatt method.* The glycoside mixture (1) (55 mg) was dissolved in anhydrous dimethyl sulphoxide (10 ml), treated with dicyclohexylcarbodi-imide (247 mg) and anhydrous phosphoric acid (17 mg), and stirred under anhydrous conditions at 25° for 18 h. The mixture was evaporated under reduced pressure and extracted with chloroform; the extract was washed with sodium hydrogen carbonate and water, dried ($MgSO_4$), and evaporated to leave unchanged starting material (1). The i.r. spectrum of the crude product showed no carbonyl band.

*Methyl* 2,3,6-*Trideoxy*-α- *and* -β-D-threo-*hex*-2-*enopyranoside* (6).—(a) *Cope elimination.* Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside *N*-oxide (3) (180 mg), on short-path distillation (air bath; 170—180° at 0·5 mmHg), gave a pale yellow oil (84 mg) which was shown by t.l.c. on Kieselgel (in both 3% methanol in chloroform and 40% methanol in chloroform) to be a mixture of methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hex-2-enopyranoside (6) (*ca.* 70%) and methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (1) (30%). Preparative t.l.c. on Kieselgel with 3% methanol in chloroform as eluant gave the olefin (6) as an oil (17 mg), *m/e* 144 ($M^+$, 0·06), 126 (1), 113 (16), 100 (100), 95 (7), and 71 (67%), $\nu_{max.}$ 3400 and 1055 $cm^{-1}$, δ 1·33 and 1·37 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), 2·19 (1H, disappears on deuteriation, 4-OH), 3·43 and 3·47 (3H, s, 1-$OCH_3$), 4·83 (1H, d, $J_{1ax,2}$ 2 Hz, H-1*ax*), and 5·04 (1H, unresolved m, H-1*eq*) and methyl-D-rhodosaminide (1) (3 mg).

(b) *Base elimination.* Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexopyranoside (1) (150 mg) was stirred with methyl iodide (5 ml) at 25° for 48 h. The mixture was evaporated to dryness, and tetrahydrofuran (25 ml) and sodium hydride (300 mg) were added. The mixture was heated under reflux for 24 h, then filtered, and the filtrate was evaporated. Preparative t.l.c. on Kieselgel with 3% methanol in chloroform as eluant gave methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hex-2-enopyranoside (6) (11 mg) as an oil. The i.r., n.m.r., and mass spectra of the product were identical with those of the corresponding product from the Cope elimination (a).

*Methyl* 2,3,6-*Trideoxy*-α- *and* -β-D-threo-*hexopyranoside* (7).—The crude methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hex-2-enopyranoside (6) obtained directly from the Cope elimination of the *N*-oxide (3) (500 mg) was dissolved in methanol (50 ml), and hydrogenated over platinum oxide at 25° and 1 atm. Preparative t.l.c. on Kieselgel with 2% methanol in chloroform as eluant gave the product as an oil (127 mg), *m/e* 146 ($M^+$, 1%), $[\alpha]_D$ −56·8°, $\nu_{max.}$ (film) 3440 and 1055 $cm^{-1}$, δ 1·25 and 1·31 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), 2·19 (1H, disappears on deuteriation, 4-OH), 3·32 and 3·46 (3H, s, 1-$OCH_3$), 4·37 (1H, dd, $J_{1ax,2a7}$ 8·5, $J_{1ax,2eq}$ 3 Hz, H-1*ax*), and 4·62 (1H, dd, $J_{1eq,2ax} = J_{1eq,2eq}$ = 2 Hz, H-1*eq*).

*Methyl* 2,3,6-*Trideoxy*-α- *and* -β-D-*hexopyranosid*-4-*ulose* (8).—Methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hexopyranoside (7) (80 mg) was dissolved in carbon tetrachloride (5 ml) and treated with an excess of ruthenium tetroxide [from ruthenium dioxide dihydrate (80 mg) by treatment with excess of sodium periodate] in carbon tetrachloride (100 ml). The mixture was kept at 25° for 2 h, then filtered and evaporated. Preparative t.l.c. on Kieselgel with 0·5% methanol in chloroform as eluant gave the product as an oil (30 mg), *m/e* 144 ($M^+$, 16%), $\nu_{max.}$ (film) 1730 and 1060 $cm^{-1}$, $\lambda_{max.}$ ($CH_3OH$) 298 nm (Δε − 1·07).

*Methyl* 5-O-*Acetyl*-2,3,6-*trideoxy*-3-*dimethylamino*-α- *and* -β-D-lyxo-*hexofuranoside* (5).—Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (2) (60 mg) in dry pyridine (5 ml) was treated with acetic anhydride (0·5 ml) and kept at 25° for 16 h. The mixture was poured into aqueous sodium hydrogen carbonate and extracted with chloroform; the extract was washed with water and dried ($MgSO_4$). The crude oil was distilled (air bath; 100° at 0·5 mmHg) to give the acetate as an oil (50 mg) (Found: C, 57·0; H, 9·0; N, 5·9. Calc. for $C_{11}H_{21}NO_4$: C, 57·1; H, 9·15; N, 6·1%), $[\alpha]_D$ +46·6° ($CH_3OH$), p$K_a$ 7·6, $\nu_{max.}$ ($CHCl_3$) 2780, 1730, and 1245 $cm^{-1}$, δ ($C_6D_6$) 1·31 (3H, d, $J_{5.6}$ 6·5 Hz, 6-$CH_3$), 1·78 (3H, s, 4-OAc), 2·03 (6H, s, 3-$NMe_2$), 3·18 (3H, s, 1-$OCH_3$), 3·99 (1H, dd, $J_{4.5}$ 6·5, $J_{3.4}$ 4·5 Hz, H-4), 4·86 (1H, dd, $J_{1.2'} = J_{1.2}$ = 4 Hz, H-1), and 5·23 (1H, dq, $J_{5.6} = J_{4.5}$ = 6·5 Hz, H-5).

*Attempted Oxidation of Methyl* 2,3,6-*Trideoxy*-3-*dimethylamino*-α- *and* -β-D-lyxo-*hexofuranoside* (2).—Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (2) (60 mg) was treated with dimethyl sulphoxide and acetic anhydride as for the corresponding pyranoside (1), to give methyl 5-*O*-acetyl-2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (5) as an oil (23 mg), showing physical data in agreement with those for the corresponding acetate prepared by direct acetylation of the furanoside (2).

*Methyl* 2,3,6-*Trideoxy*-3-*dimethylamino*-α- and -β-D-lyxo-*hexofuranoside* N-*Oxide* (9).—Methyl 2,3,6-trideoxy-3-dimethylamino-α- and -β-D-*lyxo*-hexofuranoside (2) (600 mg) was dissolved in methanol (15 ml), treated with a mixture of water (12 ml) and 30% hydrogen peroxide (3 ml), and kept at 25° for 24 h. The methanol was distilled off under reduced pressure, and the excess of hydrogen peroxide was destroyed with 5% palladium–carbon. The solution was

filtered and evaporated to give the product as a gum (620 mg). The latter on addition of acetone deposited needles of the α-*anomer* (328 mg), m.p. 129—131° (Found: C, 52·4; H, 9·4; N, 7·0. $C_9H_{19}NO_4$ requires C, 52·7; H, 9·3; N, 6·8%), *m/e* 205 ($M^{+\cdot}$, 0·1%), 190 (2), 189 (7), 187 (3), 158 (11), 144 (4), 130 (2), 115 (22), 114 (22), 112 (3), 100 (100), 86 (42), 85 (14), 84 (44), 72 (25), and 71 (27), $[\alpha]_D$ +94·1°, $pK_a$ 6·0, $\nu_{max.}$ ($CHCl_3$) 3100 and 1050 $cm^{-1}$, δ 1·31 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), 3·13 and 3·20 (6H, s, 3-$Me_2N\rightarrow O$), 3·32 (3H, s, 1-$OCH_3$), 3·62 (1H, dq, $J_{4.5}$ 8, $J_{5.6}$ 6 Hz, H-5), 4·07 (1H, dd, $J_{3.4}$ 5, $J_{4.5}$ 8 Hz, H-4), and 5·05 (1H, dd, $J_{1.2}$ 2·5, $J_{1.2'}$ 3·5 Hz, H-1).

*Methyl* 2,3,6-*Trideoxy*-α-D-threo-*hex*-2-*enofuranoside* (10α).—Methyl 2,3,6-trideoxy-3-dimethylamino-α-D-*lyxo*-hexofuranoside *N*-oxide (9α) (250 mg) was heated at 180—190° (air bath) and 0·5 mmHg, and the mixture of products was distilled directly out of the vessel. T.l.c. on Kieselgel with 2% methanol in chloroform as eluant showed the product to be a mixture of the amine (2α) and the desired product (10α) in a ratio of *ca.* 1 : 9. Fractional short-path distillation (air bath; 90—100° at 0·5 mmHg) gave the *olefin* (10α) as an oil (170 mg) (Found: C, 58·45; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%), *m/e* 144 ($M^{+\cdot}$, 1%). 113 (4), 100 (32), 99 (20), and 68 (100), $[\alpha]_D$ +147·5°, $\nu_{max.}$ (film) 3440 and 1050 $cm^{-1}$, δ 1·18 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), 3·02 (1H, disappears on deuteriation, 5-OH), 3·49 (3H, s, 1-$OCH_3$), 3·90 (1H, dq, $J_{4.5}$ 3·5, $J_{5.6}$ 6 Hz, H-5), 4·70 (1H, ddd, $J_{2.4}$ 1·5, $J_{3.4}$ *ca.* 3, $J_{4.5}$ 3·5 Hz, H-4), 5·61 (1H, dd, $J_{1.2} = J_{1.3}$ = 1·5 Hz, H-1), 5·91 (1H, ddd, $J_{1.3}$ 1·5, $J_{2.3}$ 6·5, $J_{3.4}$ *ca.* 3 Hz, H-3), and 6·19 (1H, ddd, $J_{1.2} = J_{2.4}$ = 1·5, $J_{2.3}$ 6·5 Hz, H-2).

*Methyl* 2,3,6-*Trideoxy*-α- *and* -β-D-threo-*hexofuranoside* (11).—Methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hex-2-enofuranoside (10) (2·31 g) was dissolved in methanol (150 ml) and hydrogenated at 25° and 1 atm over platinum oxide (400 mg). Filtration, evaporation, and chromatography on preparative Kieselgel plates with 5% methanol in chloroform as eluant gave the product as an oil (2·0 g) (Found: C, 57·7; H, 9·7. Calc. for $C_7H_{14}O_3$: C, 57·5; H, 9·65%), *m/e* 146 ($M^{+\cdot}$, 0·4%), 101 (100), and 69 (96), $[\alpha]_D$ +38·3°, $\nu_{max.}$ (film) 3430 and 1045 $cm^{-1}$, δ 1·12 and 1·14 (3H, d, $J_{5.6}$ 6·5 Hz, 6-$CH_3$), 2·82 (1H, disappears on deuteriation, 5-OH), and 3·33 and 3·38 (3H, s, 1-$OCH_3$).

*Methyl* 2,3,6-*Trideoxy*-5-O-*methyl*-α- *and* -β-D-threo-*hexofuranoside* (12).—Methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hexofuranoside (11) (2 g) and sodium hydride (4 g) in tetrahydrofuran (100 ml) were heated under reflux at 35° for 30 min. Methyl iodide (25 ml) was then added, and the mixture was stirred at 35° for 16 h, and filtered. The residue was washed with tetrahydrofuran, and the filtrate was evaporated. The resulting oil was dissolved in carbon tetrachloride; the solution was filtered and evaporated, and the residue was purified by preparative t.l.c. on Kieselgel with 1% methanol in chloroform as eluant to give the methyl ether (12) as an oil (1·1 g) (Found: C, 60·1; H, 9·9. Calc. for $C_8H_{16}O_3$: C, 60·0; H, 10·1%), *m/e* 160 ($M^{+\cdot}$, 0·03%), 101 (100%), and 69 (70), $[\alpha]_D$ +49·2°, $\nu_{max.}$ (film) 1090 and 1045 $cm^{-1}$, δ 1·13 and 1·22 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), and 3·31 and 3·37 (6H, s, 2 × OMe).

2,3,6-*Trideoxy*-D-threo-*hexose Diethyl Dithioacetal* (13).—Methyl 2,3,6-trideoxy-α- and -β-D-*threo*-hexofuranoside (11) (35 mg) was dissolved in 0·3N-hydrogen chloride in benzene (25 ml) and treated with ethanethiol (20 ml); the mixture was stirred at 25° for 65 h, the benzene and the excess of ethanethiol were evaporated off under a stream of nitrogen, and the resulting oil was chromatographed on preparative Kieselgel plates with 3% methanol in chloroform as eluant to give the *thioacetal* (13) as an oil (27 mg), *m/e* 238 ($M^{+\cdot}$, 7%), $[\alpha]_D$ +12·1°, $\nu_{max.}$ (film) 3390 and 1070 $cm^{-1}$, δ 1·16 (3H, d, $J_{5.6}$ 6 Hz, 6-$CH_3$), 1·26 (6H, t, *J* 7·5 Hz, $CH_3{\cdot}CH_2$), and 2·65 (4H, q, *J* 7·5 Hz, $CH_3{\cdot}CH_2$).

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