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EFFICIENT SYNTHESIS OF UNSATURATED AZIDO SUGAR DERIVATIVES

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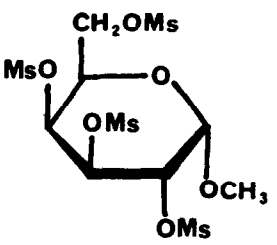
Nitrogen containing 2,3 unsaturated hexopyranosides are important intermediates [1] for the synthesis of the carbohydrate moieties of diverse antibiotics such as Blasticidine S [2] and the gentamicin group of amino-glycoside antibiotics [3,4]. In connection with a number of synthetic problems now under study in our laboratory, it became apparent that an efficient method for preparing this class of substances would be of considerable interest.

This communication reports the synthesis of methyl 4,6-diazido-2,3,4,6-tetradeoxy-α-D-erythro-hex-2-enopyranoside 10 and methyl 4,6-diazido-2,3,4,6-tetradeoxy-α-D-threo-hex-2-enopyranoside 12 from methyl α-D-galactopyranoside and glucopyranoside.

Our synthesis is based on the successive modification of the mesyloxy-groups in 1 and 2 as shown in the scheme.

When methyl 2,3,4,6-tetra-O-methylsulphonyl-α-D-galactopyranoside 1, m.p. 68-70°, $[\alpha]_D$ + 86° (c 1 in $CHCl_3$), (readily obtained from methyl-α-D-galactopyranoside by exhaustive methansulphonylation) was heated with sodium azide in DMF for 1.5 h. at 120°, crystalline methyl 4,6-diazido-4,6-dideoxy-2,3-di-O-methyl sulphonyl-α-D-glucopyranoside 3 was isolated in 85 % yield, m.p. 70-72°, $[\alpha]_D$ + 194° (c 1.16 in $CHCl_3$). Treatment of the diazide 3 with two moles of sodium methoxide in dichloromethane over five days at room temperature furnished as the major product, methyl 2,3-anhydro-4,6-diazido-4,6-dideoxy-α-D-allopyranoside 5 (63 %), m.p. 79-80°, $[\alpha]_D$ + 201 (c 1.08 in $CHCl_3$).



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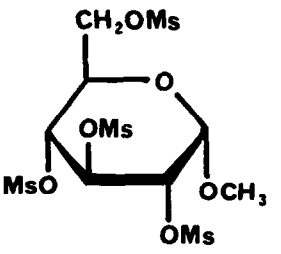

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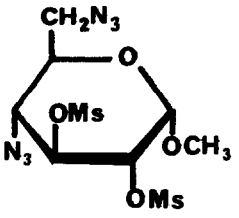

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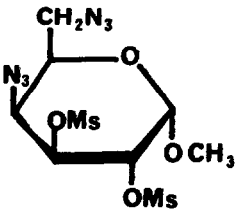

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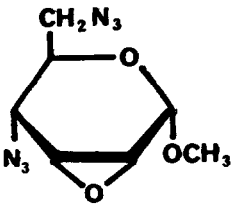

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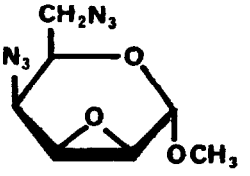

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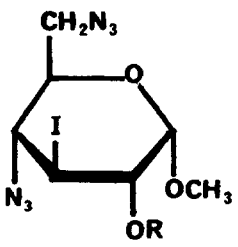
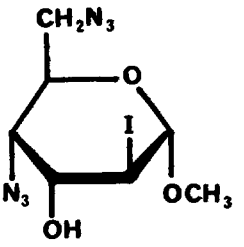


7 R= H

8 R= OAc



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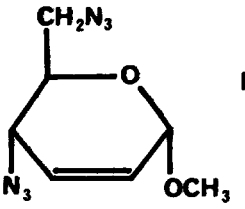

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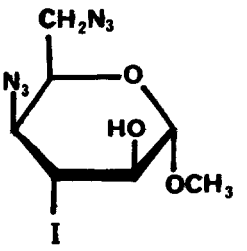

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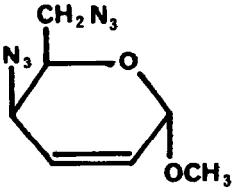

12

The doublet in its N.M.R. Spectrum at δ 4.15 ($J_{1,2}$ = 2.5 c.p.s.) assigned unequivocally to H-1, excludes the opposite manno-configuration. Opening of the epoxide 5 with sodium iodide-sodium acetate and acetic acid in acetone afforded a mixture of two iodohydrins 7 and 9 in a ratio of 1 : 1.67 in almost quantitative yield. The minor crystalline iodohydrin 7 had m.p. 107-108°, $[\alpha]_D$ + 200° (c 0.9 in $CHCl_3$) ; its gluco- configuration was established by N.M.R. study of its O-acetate 8.

Reaction of the mixture of 7 and 9 with phosphorus oxychloride in pyridine solution [5] at 0° for 30 minutes yielded methyl 4,6-diazido-2,3,4,6-tetradeoxy-α-D-erythro-hex-2-enopyranoside 10, as an oil b.p.$_{0.8\ mm\ Hg}$ 95°, $[\alpha]_D$ + 176° (c 1.6 in $CHCl_3$) in 72 % yield.

The preparation of the olefin 10 can also be achieved in two steps, without isolation of the intermediates in 55 % overall yield from methyl 2,3,4,6-tetra-O-methylsulphonyl-α-D-galactopyranoside 1.

By an analogous series of reactions the methyl 4,6-diazido-4,6-dideoxy-α-D-threo-hex-2-enopyranoside 12 was readily obtained from the known methyl 4,6-diazido-4,6-dideoxy-2,3-di-O-methylsulphonyl-α-D-galactopyranoside [6] 4.

Refluxing the disulphonate 4 with two moles of methanolic sodium methoxide for 4 h. afforded the methyl-2,3-anhydro-4,6-diazido-4,6-dideoxy-α-D-talo-pyranoside 6, m.p. 52-53°, $[\alpha]_D$ - 178° (c 1.26 in $CHCl_3$) in 76 % yield. The presence of a singlet at δ 4.98 ($J_{1,2}$ = O) in the N.M.R. Spectrum of 6 suggested that the adjacent protons at C_1-C_2 must have a trans relationship [7,8].

Reaction of the epoxide 6 with sodium iodide-sodium acetate and acetic acid in acetone gave the oily iodohydrin 11, regiospecifically in a yield of 85 %. The N.M.R. data of the iodohydrin were consistent with ido configuration. Treatment of 11 with phosphorous oxychloride in pyridine gave the desired methyl-4,6-diazido-2,3,4,6-tetradeoxy-α-D-threo-hex-2-enopyranoside 12 in quantitative yield, b.p.$_{0.04\ mm\ Hg}$ 72-75° $[\alpha]_D$ -323° (c 1.9 in $CHCl_3$). Overall yield is 65 % from the di-O-sulphonate 4.

Further modification of allylic azides 10 and 12 by thermal rearrangement leading to derivatives of purpurosamine and epi-purpurosamine will be reported elsewhere.

It is clear from the reactions described that this new approach presents definite advantages over the previously reported methods for preparing nitrogen-containing hexopyranosides [1-4].

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REFERENCES

1. R.J. Ferrier, (1965), Adv.Carbohyd.Chem., 20, 67
(1969), Adv.Carbohyd.Chem., 24, 199

2. J.J. Fox and K.A. Watanabe, (1971), Pure and Applied Chemistry, 28, 475

3. R.J. Ferrier and N. Vethaviyaser, (1971), J.Chem.Soc./C/, 1907

4. R.D. Guthrie and G.J. Williams, (1972), J.C.S. Perkin I., 2619

5. P. Crabbé and A. Guzman, (1972), Tetrahedron Letters, 115

6. A.J. Dick and J.K.N. Jones, (1965), Can.J.Chem., 43, 977
(1966), Can.J.Chem., 44, 79

7. K.A. Watanabe, R.S. Goody and J.J. Fox (1970), Tetrahedron, 26, 3883.

8. D.H. Buss, L. Hough, L.D. Hall and J.F. Manville, (1965), Tetrahedron, 21, 69.