Syntheses of Derivatives of 2,6-Diamino-2,3,4,6-tetradeoxy-D-*erythro*-hexose (Purpurosamine C), a Component of Gentamycin C_{1a}

By **John S. Brimacombe,* Ibrahim Da'aboul,** and **Leslie C. N. Tucker,** Chemistry Department, The University, Dundee DD1 4HN

Two routes have been used to synthesize methyl 2,6-diacetamido-2,3,4,6-tetradeoxy-α-D-*erythro*-hexopyranoside (methyl *NN'*-diacetyl-α-purpurosaminide C) (13), a derivative of a component sugar of gentamicin C_{1a}. The first route was based on a previous synthesis of DL-(13), whereas the alternative route relied on an azide displacement reaction of methyl 3,4-dideoxy-2,6-bis-*O*-methylsulphonyl-α-D-*threo*-hex-3-enopyranoside (19).

THE broad spectrum antibiotic complex gentamicin C [1] contains three closely related, non-reducing pseudotrisaccharides designated as gentamicins C_1, C_2, and C_{1a}.[2,3] Each pseudotrisaccharide comprises the branched-chain amino-sugar garosamine,[4-6] deoxystreptamine,[5] and one of three different 2,6-diamino-2,3,4,6-tetradeoxyaldoses,[7] which have been named purpurosamines A, B, and C from gentamicins C_1, C_2, and C_{1a}, respectively. Whereas the detailed stereochemistry of purpurosamines A (1) and B (2) has yet to be elucidated, Guthrie and Williams [8] have prepared derivatives of epipurpurosamine C (4) that permitted the natural sugar (purpurosamine C) to be identified as 2,6-diamino-2,3,4,6-tetradeoxy-D-*erythro*-hexose (3). Methyl α-purpurosaminide C has been synthesized [9] from derivatives of neamine C, obtained from the antibiotics neomycin and kanamycin, but no stereochemical correlation was made with the natural sugar. More recently, derivatives

[1] M. J. Weinstein, G. H. Luedemann, E. M. Oden, and G. H. Wagman, 'Antibacterial Agents and Chemotherapy,' American Society for Microbiology, 1963, p. 1.

[2] M. J. Weinstein, G. H. Luedemann, E. M. Oden, G. H. Wagman, J. P. Rosselet, J. A. Marquez, C. T. Coniglio, W. Charney, H. L. Herzog, and J. Black, *J. Medicin. Chem.*, 1963, **6**, 463; G. H. Wagman, J. A. Marquez, and M. J. Weinstein, *J. Chromatog.*, 1968, **34**, 210.

[3] D. J. Cooper, H. Marigliano, M. D. Yudis, and T. Traubel, *J. Infectious Diseases*, 1969, **114**, 342.

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

[5] D. J. Cooper, P. J. L. Daniels, M. D. Yudis, H. M. Marigliano, R. D. Guthrie, and S. T. K. Bukhari, *J. Chem. Soc.* (*C*), 1971, 3126.

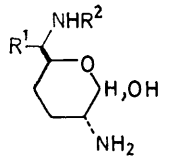
[6] W. Meyer zu Reckendorf and E. Bischof, *Tetrahedron Letters*, 1970, 2475; *Chem. Ber.*, 1972, **105**, 2546.

[7] D. J. Cooper, M. D. Yudis, H. M. Marigliano, and T. Traubel, *J. Chem. Soc.* (*C*), 1971, 2876.

[8] R. D. Guthrie and G. J. Williams, *Chem. Comm.*, 1971, 923; *J.C.S. Perkin I*, 1972, 2619.

[9] S. Umezawa, T. Tsuchiya, and Y. Okazaki, *Bull. Chem. Soc. Japan*, 1971, **44**, 3494.

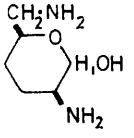
of both purpurosamine C (3) and epipurpurosamine C (4) have been obtained by Gero *et al.*;[10] the route used will be discussed later, since it impinges on one of



(1) $R^1 = R^2 = Me$ (purpurosamine A)

(2) $R^1 = Me$, $R^2 = H$ (purpurosamine B)

(3) $R^1 = R^2 = H$ (purpurosamine C)



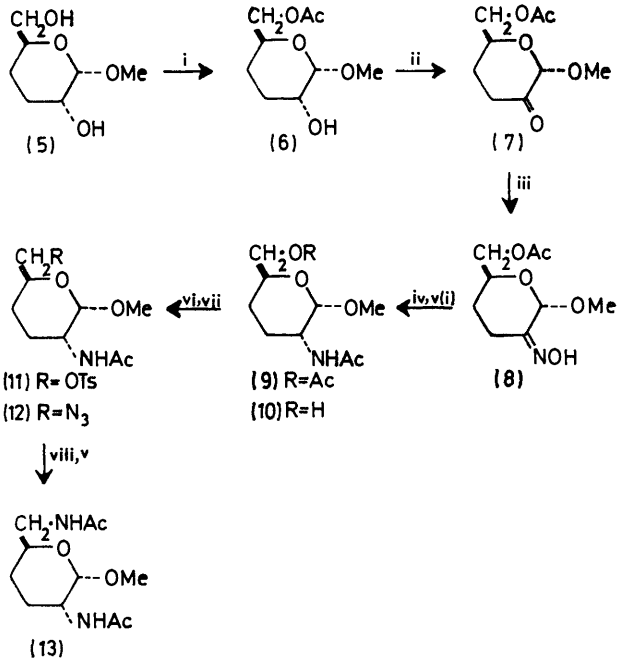
(4)

the routes adopted in the present work. Methyl *NN'*-diacetyl-α-DL-purpurosaminide C [DL-(13)] has also been synthesized.[11] Another amino-glycoside antibiotic, sisomicin, has been found[12,13] to contain a 2,6-diamino-2,3,4,6-tetradeoxyhex-4-enopyranose, which afforded a glycosidically linked 2,6-diamino-2,3,4,6-tetradeoxy-β-L-*threo*-hexopyranose [L-(4)] on catalytic reduction of the unsaturated linkage.

In our synthesis[11] of methyl *NN'*-diacetyl-α-DL-purpurosaminide C [DL-(13)], a key intermediate was the oxime DL-(8), prepared *via* the addition of nitrosyl chloride to 2-acetoxymethyl-3,4-dihydro-2*H*-pyran (obtained in two steps from acrylaldehyde dimer). Although an analogous route to the optically pure oxime (8) eluded us, it was possible to synthesize the oxime by an alternative route (Scheme 1). Thus, preferential acetylation of the primary hydroxy-group of methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (5) [prepared by hydrogenation of the corresponding olefin[14] (14)] gave the 6-acetate (6), which was oxidized (ruthenium tetraoxide in carbon tetrachloride) to methyl 6-*O*-acetyl-3,4-dideoxy-α-D-*glycero*-hexopyranosid-2-ulose (7). The anomeric proton signal appeared as a singlet at τ 5·40 in the n.m.r. spectrum of the hexosidulose (7), thereby establishing that the carbonyl group is located at position 2. The hexosidulose (7) was then converted (hydroxylamine hydrochloride in boiling methanol–pyridine) into the oxime (8), the n.m.r. spectrum of which was identical in all essential features with that of the racemic form.[11] The oxime (8) was then transformed into methyl *NN'*-diacetyl-α-purpurosaminide C (13) as previously described;[11] the sequence [(8) → (10) → (11) → (12) → (13)] is outlined in Scheme 1 and is further delineated in the Experimental section. The final product (13) was indistinguishable (physical and spectroscopic properties) from the same derivative obtained from natural purpurosamine C, and its n.m.r. spectrum was identical with that of the racemic form (see Figure 1 in ref. 11).

One feature of the oximation of the hexosidulose (7) is worthy of comment: when the oximation was carried out in ethanol and pyridine, the ethyl analogue of the hydroxyiminoglycoside (8) was isolated. This transglycosidation was not examined in detail, but could conceivably occur *via* the 2-deoxy-2-nitrosoglycal,[15] formed by isomerization of the oxime (8) and loss of methanol. Although a related transglycosidation will no doubt take place when the oximation is carried out in methanol, the α-configuration of the ensuing products is assured from comparisons with known compounds.

In the second approach used to obtain derivatives of purpurosamine C, resort was made to the displacement



SCHEME 1 Reagents: i, Ac_2O–C_5H_5N; ii, RuO_4–CCl_4; iii, NH_2OH–MeOH–C_5H_5N; iv, Pd–H_2 or $LiAlH_4$; v, Ac_2O–MeOH; vi, TsCl–C_5H_5N; vii, NaN_3–Me_2SO; viii, Pd–H_2

of allylic sulphonyloxy-groups introduced into the pyranoid ring. Nucleophilic displacements of sulphonyloxy-groups at C-2 of saturated, pyranoid rings are notoriously difficult to effect, owing to a combination of adverse steric and electronic factors[16] (but see later). However, it was envisaged that a displacement with

[10] J. Cleophax, J. Leboul, A. Olesker, and S. D. Gero, *Tetrahedron Letters*, 1973, 4911.

[11] J. S. Brimacombe, I. Da'aboul, and L. C. N. Tucker, *J.C.S. Perkin I*, 1974, 263.

[12] D. J. Cooper, R. S. Jaret, and H. Reimann, *Chem. Comm.*, 1971, 285.

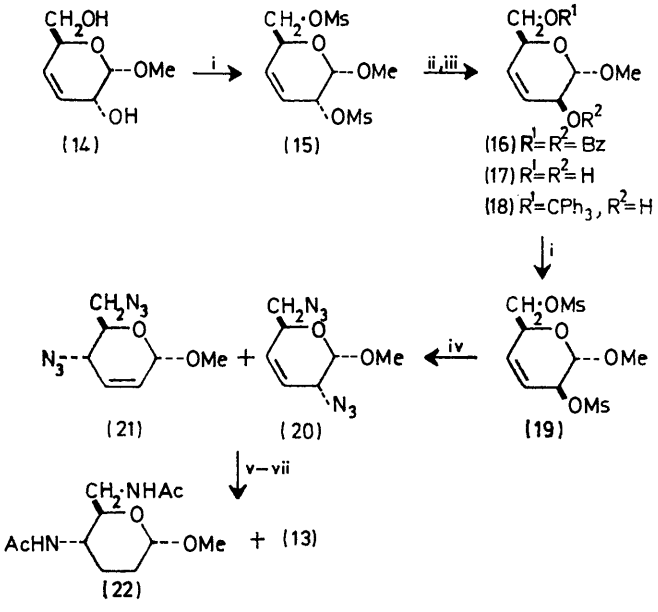
[13] H. Reimann, R. S. Jaret, and D. J. Cooper, *Chem. Comm.*, 1971, 924.

[14] N. L. Holder and B. Fraser-Reid, *Canad. J. Chem.*, 1973, **51**, 3357.

[15] See, for example, R. U. Lemieux, Y. Ito, K. James, and T. L. Nagabhushan, *Canad. J. Chem.*, 1973, **51**, 7.

[16] A. C. Richardson, *Carbohydrate Res.*, 1969, **10**, 395.

azide ion on an appropriate hex-3-enopyranoside 2-sulphonate would proceed much more readily,[17,18] subsequently permitting the introduction of an acetamido-group at C-2. Methyl 3,4-dideoxy-2,6-bis-*O*-methylsulphonyl-α-D-*threo*-hex-3-enopyranoside (19) was synthesized, therefore, as follows. Sulphonation of



SCHEME 2 Reagents: i, MsCl–C_5H_5N; ii, NaOBz–Me_2N·CHO; iii, basic resin; iv, NaN_3–Me_2SO; v, Pt–H_2; vi, Ac_2O–MeOH; vii, fractional crystallisation

methyl 3,4-dideoxy-α-D-*erythro*-hex-3-enopyranoside (14) (prepared by a modification of the literature procedure[14]) gave the bismethanesulphonate (15), which furnished methyl 2,6-di-*O*-benzoyl-3,4-dideoxy-α-D-*threo*-hex-3-enopyranoside (16) when heated with sodium benzoate in *NN*-dimethylformamide. Debenzoylation of (16) afforded the *threo*-enediol (17), which was characterized as the trityl ether (18) having physical constants in good agreement with those reported for an authentic compound, prepared[14] by an unambiguous route from a derivative of methyl α-D-altropyranoside. This information establishes that the displacement of the allylic sulphonyloxy-group had occurred with inversion of configuration and without rearrangement. Sulphonylation of the diol (17) then gave the required bismethanesulphonate (19). On heating the bismethanesulphonate (19) with azide ion in dimethyl sulphoxide at 140° for 2 h, a mixture of methyl 2,6-diazido-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-3-enopyranoside (20) and the isomeric 4,6-diazide (21) was obtained in the ratio *ca.* 2 : 1 (n.m.r. evidence). The formation of the diazides (20) and (21) can be attributed to a [3,3] sigmatropic rearrangement involving the azido-group introduced at C-2 by displacement of the methylsulphonyloxy-group. There is now an abundant literature[8,18,19] on related rearrangements, but, more pertinently, our route impinges at this point on a synthesis of methyl *NN'*-diacetyl-α-purpurosaminide reported by Gero *et al.*[10] in which isomerization of the 4,6-diazide (21) was used to introduce the azido-group at C-2. Whereas the sigmatropic rearrangement (21) ⇌ (20) is a calculated step in the synthesis described by Gero *et al.*,[10] the reverse rearrangement is an unwanted, although not unexpected, reaction in our approach. Unfortunately, it was not possible to find conditions for displacing both methylsulphonyloxy-groups from the disulphonate (19) which eliminated the accompanying sigmatropic rearrangement.*

Gero *et al.*[10] have reported the conversion of the *erythro*-diazides (20) and (21) into methyl *NN'*-diacetyl-α-purpurosaminide C (13) and its isomer (22) in which a separation of the two isomers was achieved following their conversion into methyl 2(4),6-diacetamido-2,3,4,6-α-D-*erythro*-hex-3(2)-enopyranosides. In our approach, no attempt was made to separate the isomers until the final stage was reached. Thus, the mixture of diazides (20) and (21) was hydrogenated over platinum to give, following *N*-acetylation of the resulting diamines, a mixture of compounds (13) and (22). Fractional crystallisation then furnished methyl *NN'*-diacetyl-α-purpurosaminide C (13), which was indistinguishable (i.r. and n.m.r. spectra, m.p., and $[\alpha]_D$) from the compound prepared previously.

A related sigmatropic rearrangement was encountered when methyl 3,4-dideoxy-2,6-bis-*O*-methylsulphonyl-α-D-*erythro*-hex-3-enopyranoside (15) was heated with sodium azide in dimethyl sulphoxide. N.m.r. spectroscopy of the products clearly showed that two diazides [presumably (23) and (24)] had been formed. Since Gero *et al.*[10] have already reported on the conversion of these *threo*-diazides into derivatives of epipurpurosamine C (25) and the 4,6-isomer (26), we did not pursue our study further.

Both of the foregoing routes to methyl *NN'*-diacetyl-α-purpurosaminide C (13) have drawbacks in terms of the overall efficiencies of the conversions. In the first route (Scheme 1), reduction of the oxime (8) also yields derivatives of epipurpurosamine C (*cf.* ref. 11), whereas a significant proportion of the required diazide (20) is lost *via* the sigmatropic rearrangement in the other route (Scheme 2). These factors prompted us to examine an azide-exchange reaction on the *erythro*-bismethanesulphonate (27), prepared from the saturated diol (5), since there is evidence[20] that nucleophilic

* It is obviously more efficient from a synthetic standpoint if both sulphonyloxy-groups can be displaced from the bismethanesulphonate (19) with azide ion in the same operation. However, displacement of the primary methylsulphonyloxy-group presumably requires more vigorous conditions, thereby promoting the sigmatropic rearrangement of the azido-group already introduced at C-2.

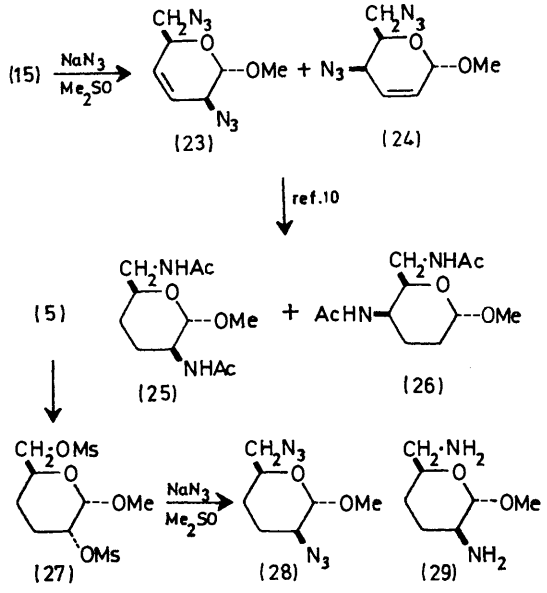
[17] S. Laland, W. G. Overend, and M. Stacey, *J. Chem. Soc.*, 1950, 738; D. M. Ciment, R. J. Ferrier, and W. G. Overend, *J. Chem. Soc.* (*C*), 1966, 446.

[18] R. J. Ferrier, *Adv. Carbohydrate Chem.*, 1969, **24**, 199; R. J. Ferrier and N. Vethaviyasar, *J. Chem. Soc.* (*C*), 1971, 1907.

[19] R. J. Ferrier and N. Vethaviyasar, *J.C.S. Perkin I*, 1973, 1791.

[20] See, for example, M. Nakajima, N. Shibata, K. Kitahara, S. Takahashi, and A. Hasegawa, *Tetrahedron Letters*, 1968, 2271.

displacements at C-2 of α-glycosides can be accomplished in the absence of an electron-withdrawing substituent at C-3. The bismethanesulphonate (27) was found to undergo smooth displacements of both sulphonyloxy-groups with azide in dimethyl sulphoxide at 100° to give methyl 2,6-diazido-2,3,4,6-tetradeoxy-α-D-*threo*-hexopyranoside (28). Unfortunately, no characterizable products were obtained following reduction



of the *threo*-diazide (28) over platinum. While the reason for this is not clear, the orientation of the amino-groups in the expected product (29) may possibly lead to some form of complexing with the platinum catalyst [*cf.* the corresponding reduction of the *erythro*-diazide (20)]. Fortunately, other ways of reducing an azido-group exist. This approach, which appears to hold considerable promise for the synthesis of derivatives of purpurosamine C and its epimer, is under investigation.

EXPERIMENTAL

T.l.c. was performed on Kieselgel G, and detection was effected with vanillin–sulphuric acid.[21] I.r. spectra were usually recorded for Nujol mulls with a Perkin-Elmer Infracord spectrometer and n.m.r. spectra for solutions in deuteriochloroform with 1% tetramethylsilane as internal standard using a Perkin-Elmer R10 (60 MHz) spectrometer. Optical rotations were measured at ambient temperature with a Perkin-Elmer 141 automatic polarimeter. Light petroleum refers to the fraction having b.p. 60—80°.

Methyl 6-O-*Acetyl*-3,4-*dideoxy*-α-D-erythro-*hexopyranoside* (6).—A solution of the *erythro*-diol [22] (5) (6·85 g) in dry pyridine (30 ml) containing acetic anhydride (4·8 g, 1·1 mol) was set aside for 2 h at room temperature, after which time t.l.c. (acetone–light petroleum, 2 : 1) revealed that most of the starting material had reacted. Water (5 ml) was added and, after 30 min, the mixture was partitioned between chloroform and water. The separated organic layer was washed with dilute solutions of hydrochloric acid and sodium hydrogen carbonate, and water. Concentration of the dried ($MgSO_4$) extract and chromatography of the residue on silica gel (elution with acetone–light petroleum, 1 : 2) gave the *monoacetate* (6) (5·8 g, 67%), b.p. 120—125° (bath) at *ca.* 0·2 mmHg, $[\alpha]_D$ +110° (*c* 1 in $CHCl_3$), $\nu_{max.}$ (film) 3400br (OH) and 1740 cm^{-1} (OAc) (Found: C, 53·0; H, 8·0. $C_9H_{16}O_5$ requires C, 52·9; H, 7·8%); τ 5·25 (1H, d, $J_{1,2}$ *ca.* 3 Hz, H-1), 6·52 (3H, s, OMe), and 7·90 (3H, s, OAc).

Methyl 6-O-*Acetyl*-3,4-*dideoxy*-α-D-glycero-*hexopyranosid*-2-*ulose* (7).—To a vigorously stirred solution of the previous acetate (3·95 g) in carbon tetrachloride (100 ml) was added a solution of ruthenium tetraoxide in carbon tetrachloride [400 ml; prepared [23] from the hydrated dioxide (2 g)]. The solution was then stirred for 1 h, after which t.l.c. (ether–light petroleum, 2 : 1) showed that all the starting material had been consumed. Propan-2-ol (60 ml) was then added, and solids were filtered off after 30 min and washed thoroughly with carbon tetrachloride and hot acetone. Removal of the solvents furnished the *hexosidulose* (7) (2·65 g, 68%), b.p. 65—68° (bath) at *ca.* 0·2 mmHg, $[\alpha]_D$ +83° (*c* 0·9 in $CHCl_3$), $\nu_{max.}$ (film) 1740br cm^{-1} (C=O and OAc) (Found: C, 53·8; H, 6·9. $C_9H_{14}O_5$ requires C, 53·5; H, 6·9%); τ 5·40 (1H, s, H-1), 6·50 (3H, s, OMe), and 7·88 (3H, s, OAc).

Methyl 6-O-*Acetyl*-3,4-*dideoxy*-α-D-glycero-*hexopyranosid*-2-*ulose Oxime* (8).—To a solution of the hexosidulose (7) (1·2 g) in dry methanol (20 ml) and pyridine (20 ml) was added hydroxylamine hydrochloride (1 g) and the mixture was heated under gentle reflux for 2 h. The cooled solution was concentrated and the residue was dispersed in dilute hydrochloric acid, which was extracted with chloroform (3 × 100 ml); the combined organic extracts were washed with a solution of sodium hydrogen carbonate (2 × 100 ml) and dried ($MgSO_4$). Removal of the solvent and chromatography of the residue on silica gel (elution with acetone–light petroleum, 1 : 2) gave the *oxime* (8) (1·1 g, 85%), $[\alpha]_D$ +132·5° (*c* 1 in $CHCl_3$), $\nu_{max.}$ (film) 3400 (OH) and 1730 cm^{-1} (OAc), as a syrup that could not be induced to crystallise. The n.m.r. spectrum of this material was essentially indistinguishable from that of the racemic oxime [11] obtained previously, although it indicated that the latter was contaminated with another component.

When the foregoing oximation was performed in ethanol, a single oxime (89%), $[\alpha]_D$ +115° (*c* 1 in $CHCl_3$), was obtained, which appeared from the n.m.r. spectrum to be derived from the corresponding ethyl glycoside: τ 4·93 (1H, s, H-1), 6·38 (2H, q, O·CH_2·CH_3), 7·90 (3H, s, OAc), and 8·72 (3H, t, O·CH_2·CH_3).

Methyl 2-*Acetamido*-6-O-*acetyl*-2,3,4-*trideoxy*-α-D-erythro-*hexopyranoside* (9).—A solution of the oxime (8) (0·9 g) in dry methanol (100 ml) containing a suspension of 30% palladised charcoal (*ca.* 0·5 g) was shaken under hydrogen (40 atm) for 3 days at room temperature; t.l.c. (acetone–light petroleum, 1 : 1) then showed that all the starting material had been reduced. The catalyst was filtered off, and acetic anhydride (5 ml) was added to the filtrate, which was kept for 1 h at room temperature. Removal of the solvents, with repeated additions of toluene, left a syrup (containing several components), which was chromatographed on silica gel (elution with acetone–light petroleum, 1 : 1) to give, *inter alia*, the erythro-*glycoside* (9) (0·24 g,

[21] 'Chromatography,' E. Merck AG, Darmstadt, 2nd edn., p. 30.

[22] K. Bock and C. Pedersen, *Acta Chem. Scand.*, 1971, **25**, 1021.

[23] P. J. Beynon, P. M. Collins, P. T. Doganges, and W. G. Overend, *J. Chem. Soc.* (*C*), 1966, 1131.

24%), m.p. 99—100° (from ether–light petroleum), $[\alpha]_D$ +98° (*c* 0·8 in $CHCl_3$), $\nu_{max.}$ 3300 (NH), 1750 (OAc), and 1650 and 1540 cm^{-1} (NHAc) (Found: C, 53·4; H, 7·9; N, 5·9. $C_{11}H_{19}NO_5$ requires C, 53·9; H, 7·7; N, 5·7%). The n.m.r. spectrum of this material was indistinguishable from that obtained previously for the racemic compound.[11]

Methyl 2-*Acetamido*-2,3,4-*trideoxy*-α-D-erythro-*hexopyranoside* (10).—A solution of the oxime (8) (1·5 g) in dry ether (15 ml) containing lithium aluminium hydride (0·2 g) was heated under gentle reflux for 4 h, during which time all the starting material reacted. The excess of hydride was then destroyed by careful addition of a few drops of water, and solids were filtered off and washed thoroughly with ether and chloroform. The combined filtrate and washings were dried ($MgSO_4$) and concentrated, and the residue was dissolved in methanol (20 ml) and treated with acetic anhydride (2 ml) for 2 h at room temperature. After removal of the solvents, with repeated additions of toluene, the residue was chromatographed on silica gel (elution with acetone–light petroleum, 1 : 1) to give the *alcohol* (10) (0·35 g, 25%), $[\alpha]_D$ +74·5° (*c* 1·1 in $CHCl_3$); τ 5·32 (1H, d, $J_{1,2}$ *ca.* 3·5 Hz, H-1), 6·60 (3H, s, OMe), and 8·02 (3H, s, NAc).

Acetylation of the alcohol (10) gave methyl 2-acetamido-6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hexopyranoside (9), m.p. and mixed m.p. 99—100°, $[\alpha]_D$ +98° (*c* 1 in $CHCl_3$), identical (i.r. and n.m.r. spectroscopy) with that prepared by catalytic reduction of the oxime (8).

Methyl 2-*Acetamido*-6-*azido*-2,3,4,6-*tetradeoxy*-α-D-erythro-*hexopyranoside* (12).—A solution of the alcohol (10) (0·45 g) in dry pyridine (10 ml) containing toluene-*p*-sulphonyl chloride (0·8 g) was set aside overnight at room temperature; work-up in the usual manner afforded methyl 2-acetamido-2,3,4-trideoxy-6-*O*-*p*-tolylsulphonyl-α-D-*erythro*-hexopyranoside (11) (0·7 g, 89%), $[\alpha]_D$ +45° (*c* 1 in $CHCl_3$).

A stirred solution of the sulphonate (0·7 g) in dimethyl sulphoxide (15 ml) containing sodium azide (0·3 g) was heated overnight at 100°; t.l.c. (acetone–light petroleum, 1 : 1) then showed that no starting material remained. On cooling, the mixture was dispersed in water (50 ml), and the aqueous solution was extracted with chloroform (3 × 50 ml). Concentration of the dried ($MgSO_4$) organic extracts furnished the *azide* (12) (0·4 g, 87%), m.p. 150—151° (from ether), $[\alpha]_D$ +134·5° (*c* 0·8 in $CHCl_3$), $\nu_{max.}$ 2100 (N_3), and 1650 and 1540 cm^{-1} (NHAc) (Found: C, 47·1; H, 7·2; N, 24·6. $C_9H_{16}N_4O_3$ requires C, 47·4; H, 7·0; N, 24·6%). The n.m.r. and i.r. spectra of the azide (12) were indistinguishable from those of the racemic form obtained in earlier work.[11]

Methyl 3,4-*Dideoxy*-α-D-erythro-*hex*-3-*enopyranoside* (14).—A rapidly stirred solution of methyl 2,6-di-*O*-benzoyl-3,4-bis-*O*-methylsulphonyl-α-D-glucopyranoside [14] (15 g) in dry *NN*-dimethylformamide (300 ml) containing suspended sodium iodide (33·5 g) and zinc dust (27 g) was heated overnight at *ca.* 100°, after which it was poured into ice–water. Solids were filtered off through a pad of Celite, which was washed thoroughly with chloroform and then with water. The separated chloroform layer was washed with sodium thiosulphate solution and water, and dried ($MgSO_4$). The solvents were removed at *ca.* 0·5 mmHg, and the residual syrup in methanol (300 ml) was stirred with Deacidite FF-IP (HO^-) resin for 1 h to effect debenzoylation. The resin was then filtered off, the filtrate was concentrated, and the residue was chromatographed on silica gel (elution with acetone–light petroleum, 1 : 5) to give the erythro-*enediol* (14) (3·8 g, 84%), b.p. 80—85° (bath) at 0·2 mmHg. The distillate slowly crystallized and after recrystallization from ether had m.p. 61—62°, $[\alpha]_D$ +62·5° (*c* 1 in $CHCl_3$) (Found: C, 53·0; H, 7·6. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%); this compound has previously been obtained as an oil.[14]

The unsaturated glycoside (14) was further characterized as the 2,6-bis-*O*-(*p*-nitrobenzoate) (72%), m.p. 149—151° (from chloroform–light petroleum), $[\alpha]_D$ −42° (*c* 0·6 in $CHCl_3$) {lit.,[14] m.p. 152—153°, $[\alpha]_D$ −57·7° (*c* 5 in $CHCl_3$)}.

Methyl 2,6-*Di*-O-*benzoyl*-3,4-*dideoxy*-α-D-threo-*hex*-3-*enopyranoside* (16).—To a cooled (0°) solution of the unsaturated sugar (14) (1 g) in dry pyridine (10 ml) was gradually added methanesulphonyl chloride (3 ml), and the solution was then kept at 0° for 1 h and at room temperature for 2 h. Work-up in the usual manner furnished methyl 3,4-dideoxy-2,6-bis-*O*-methylsulphonyl-α-D-*erythro*-hex-3-enopyranoside (15) (1·8 g, 91%), $[\alpha]_D$ +120° (*c* 0·9 in $CHCl_3$), as a syrup that was used in the next step without further purification; τ 4·10 (1H, s, H-1), 6·45 (3H, s, OMe), and 6·90 and 6·93 (each 3H, s, 2 × OMs).

A solution of the disulphonate (15) (2·9 g) in *NN*-dimethylformamide (100 ml) containing sodium benzoate (5 g) was heated overnight at 140°; t.l.c. (acetone–light petroleum, 1 : 5) then showed that the reaction was essentially complete. After pouring into water, the product was extracted with light petroleum (3 × 200 ml), and the combined extracts were dried ($MgSO_4$) and concentrated. Recrystallisation of the residue from light petroleum gave the threo-*dibenzoate* (16) (2·75 g, 81%), m.p. 67—68°, $[\alpha]_D$ +95·5° (*c* 1 in $CHCl_3$), $\nu_{max.}$ 1730 (OBz) and 1650 cm^{-1} (C=C) (Found: C, 68·3; H, 5·5. $C_{21}H_{20}O_6$ requires C, 68·5; H, 5·4%); τ 2·10 (10H, m, aromatic) and 6·40 (3H, s, OMe).

Methyl 3,4-*Dideoxy*-α-D-threo-*hex*-3-*enopyranoside* (17).—A solution of the dibenzoate (16) (2·7 g) in dry methanol (40 ml) was stirred overnight at room temperature with Deacidite FF-IP(HO^-) resin (*ca.* 5 g) to effect debenzoylation. After filtration and removal of the solvents, the residue was chromatographed on silica gel (elution with acetone–light petroleum, 1 : 5) to give the threo-*enediol* (17) (1·1 g, 94%), b.p. 90—95° (bath) at 0·1 mmHg. The distillate slowly crystallised and after recrystallisation from ether–light petroleum had m.p. 71—72°, $[\alpha]_D$ +205° (*c* 1 in $CHCl_3$), $\nu_{max.}$ 3400 (OH) and 1650 cm^{-1} (C=C) (Found: C, 52·7; H, 7·7. $C_7H_{12}O_4$ requires C, 52·5; H, 7·5%); τ 4·00 (2H, m, H-3 and -4), 5·14 (1H, s, H-1), and 6·48 (3H, s, OMe).

The trityl derivative (18) (70%), prepared from (17) in the usual way, had m.p. 149—151° (from methanol), $[\alpha]_D$ +39° (*c* 1·1 in $CHCl_3$) {lit.,[14] m.p. 152—153°, $[\alpha]_D$ +38° (*c* 5 in $CHCl_3$)}.

Preparation of Methyl 3,4-*Dideoxy*-2,6-*bis*-O-*methylsulphonyl*-α-D-threo-*hex*-3-*enopyranoside* (19) *and its Reaction with Sodium Azide*.—The title bismethanesulphonate (94%), $[\alpha]_D$ +115° (*c* 1·1 in $CHCl_3$), was prepared from the *threo*-enediol (17), essentially as described for the *erythro*-isomer (14), and was suitable for use in the next step without further purification; τ 4·95 (1H, s, H-1), 6·45 (3H, s, OMe), and 6·86 (6H, s, 2 × OMs).

The disulphonate (19) (1·7 g) in dimethyl sulphoxide (25 ml) containing sodium azide (1 g) was stirred and heated at 100° for 2 h; t.l.c. (acetone–light petroleum, 1 : 2) then showed that all the starting material had reacted. The cooled solution was extracted with light petroleum (5 × 50

ml), and the combined extracts were dried ($MgSO_4$) and concentrated. Chromatography of the oily residue on silica gel (elution with acetone–light petroleum, 1 : 5) furnished a mixture (0·85 g, 75%), b.p. 60—62° at 0·1 mmHg, $\nu_{max.}$ (film) 2100 cm^{-1} (N_3), shown (n.m.r. spectroscopy) to contain methyl 2,6-diazido-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-3-enopyranoside (20) (2 parts) and methyl 4,6-diazido-2,3,4,6-tetradeoxy-α-D-*erythro*-hex-2-enopyranoside (21) (1 part) (Found: C, 40·4; H, 5·1; N, 39·5. $C_7H_{10}N_6O_2$ requires C, 40·0; H, 4·8; N, 40·0%). Separation of the diazides (20) and (21) was not attempted at this stage.

Methyl 2,6-*Diacetamido*-2,3,4,6-*tetradeoxy*-α-D-erythro-*hexopyranoside* (*Methyl* NN′-*Diacetyl*-α-*purpurosaminide C*) (13).—(a) *From the monoazide* (12). A solution of the monoazide (12) (0·38 g) in dry methanol (15 ml) containing 5% palladised charcoal (*ca.* 0·3 g) was shaken overnight at room temperature with a slight overpressure of hydrogen. The catalyst was then filtered off and a few drops of acetic anhydride were added to the filtrate to acetylate the amine. After 2 h, the solvents were removed, with repeated additions of toluene. Chromatography of the residue on silica gel (elution with methanol–toluene, 1 : 5) gave the *purpurosaminide* (13) (0·11 g, 27%), m.p. 195—197° (from ethyl acetate), $[\alpha]_D$ +166° (*c* 0·8 in MeOH) (Found: C, 54·0; H, 8·1; N, 11·6. $C_{11}H_{20}N_2O_4$ requires C, 54·1; H, 8·2; N, 11·5%) {lit.,[10] m.p. 200—208°, $[\alpha]_D$ +161° (*c* 0·9 in MeOH)}. The n.m.r. spectrum of the synthetic material was indistinguishable from that of the racemic compound (see Figure 1, ref. 11) and from that of an authentic sample.

(b) *From the diazide* (20). A mixture (0·5 g) of the diazides (20) and (21) (obtained above) in dry methanol (20 ml) containing Adams catalyst (0·1 g) was shaken for 3 h at room temperature under a slight overpressure of hydrogen. Work-up, as described in (a), and chromatography on silica gel (elution with methanol–toluene, 1 : 4) furnished a crystalline residue (0·35 g) containing (n.m.r. evidence) both (13) and (22). Fractional crystallisation (twice) from ethyl acetate yielded methyl *NN′*-diacetyl-α-purpurosaminide C (13) (0·16 g, 28%), m.p. and mixed m.p. 197—199°, $[\alpha]_D$ +164° (*c* 1 in MeOH), indistinguishable (i.r. and n.m.r. spectroscopy) from the material obtained in the previous experiment.

Reaction of Methyl 3,4-*Dideoxy*-2,6-*bis*-O-*methylsulphonyl*-α-D-erythro-*hex*-3-*enopyranoside* (15) *with Sodium Azide*.—The bismethanesulphonate (15) (1·6 g) in dimethyl sulphoxide (25 ml) containing sodium azide (1 g) was heated for 2 h at 100°, whereafter the mixture was processed as already described for the isomeric compound. Distillation of the oily residue, b.p. 64—66° (bath) at 0·2 mmHg, $\nu_{max.}$ (film) 2100 cm^{-1} (N_3), afforded a mixture (0·98 g, 92%), shown (n.m.r. spectroscopy) to contain both methyl 2,6-diazido-2,3,4,6-tetradeoxy-α-D-*threo*-hex-3-enopyranoside (23) and methyl 4,6-diazido-2,3,4,6-tetradeoxy-α-D-*threo*-hex-2-enopyranoside (24) (Found: C, 40·0; H, 4·9; N, 39·8%). An effective way of separating these isomers has been reported by Gero *et al.*,[10] who also reported the subsequent conversion of the diazide (23) into methyl *NN′*-diacetyl-α-epipurpurosaminide C (25).

Methyl 2,6-*Diazido*-2,3,4,6-*tetradeoxy*-α-D-threo-*hexopyranoside* (28).—A cooled (0°) solution of methyl 3,4-dideoxy-α-D-*erythro*-hexopyranoside (5) (1·4 g) [prepared by catalytic hydrogenation of the unsaturated sugar (14) [14]] in dry pyridine (30 ml) was treated with a cold solution of methanesulphonyl chloride (*ca.* 3·5 ml) at 0° for 1 h and afterwards at room temperature for 3 h. Work-up in the usual manner furnished methyl 3,4-dideoxy-2,6-bis-*O*-methylsulphonyl-α-D-*erythro*-hexopyranoside (27) (2·2 g, 80%), $[\alpha]_D$ +55° (*c* 1 in MeOH), as a syrup that was suitable for the next step.

A solution of the disulphonate (27) (1·3 g) in dimethyl sulphoxide (25 ml) containing sodium azide (0·8 g) was heated overnight at 100°, during which time complete reaction had occurred. The cooled mixture was partitioned between light petroleum and water, and the separated and dried ($MgSO_4$) organic layer was concentrated. Distillation of the residue gave the threo-*diazide* (28) (0·62 g, 71%), b.p. 60—62° (bath) at 0·2 mmHg, $[\alpha]_D$ +84° (*c* 0·8 in $CHCl_3$), $\nu_{max.}$ (film) 2100 cm^{-1} (N_3) (Found: C, 40·9; H, 6·1; N, 39·3. $C_7H_{12}N_6O_2$ requires C, 39·6; H, 5·7; N, 39·6%).

Hydrogenation of the diazide (28) in methanol over platinum produced a low yield of an intractable mixture of products from which characterizable compounds could not be obtained.

We thank Dr. P. J. L. Daniels (Schering Corporation), Dr. S. D. Gero (C.N.R.S., Gif-sur-Yvette), and Professor R. D. Guthrie (Griffith University) for a number of n.m.r. spectra of derivatives of purpurosamine C and its epimer, and Professor J. G. Buchanan (Heriot-Watt University) for discussion. One of us (I. D.) is indebted to the University of Aleppo for financial support through a grant administered by the Ford Foundation.

[4/2411 *Received*, 18*th November*, 1974]