Synthesis of a (2,3-Dideoxyglyc-2-enopyranosyl)thymine and a (2,3-Dideoxyglycopyranosyl)thymine *via* a 2,2'-Anhydro-nucleoside

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2,2'-Anhydro-1-(4,6-*O*-benzylidene-3-*O*-methylsulphonyl-β-D-mannopyranosyl)thymine (5), prepared quantitatively from the 2',3'-bismethanesulphonate (3), was converted into the corresponding unsaturated nucleoside (8) in 56% yield by the action of sodium iodide in boiling *NN*-dimethylformamide. Debenzylidenation of (8) with acid gave a free unsaturated nucleoside (12) in 91% yield. Reduction of (12) over palladium–carbon gave the (2,3-dideoxyhexopyranosyl)thymine (14). A mechanism for the formation of unsaturated nucleoside is described.

NUCLEOSIDES containing a 2,3-dideoxyglyc-2-enopyranosyl unit exist in nature in antibiotics such as blasticidin S.[1] Such nucleosides may be useful as intermediates in the synthesis of biologically important new compounds, and serve as key intermediates in the synthesis of amicetin and plicacetin,[1] because of their ready con-

[1] R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley–Interscience, New York, 1970, p. 170.

version into 2,3-dideoxyglycopyranosyl derivatives. Studies on the introduction of 2′,3′-unsaturation in pyranosyl nucleosides have generally involved (i) axial ring opening of epoxides and *trans*-elimination of the resulting halogenohydrins,[2] or (ii) condensation accompanied by allylic rearrangement of a nucleoside base and an acylated glycal in the presence or absence of a Lewis acid.[3] However, there has been no previous report of the direct preparation of 2′,3′-unsaturated nucleosides from the readily available glucopyranosyl nucleosides.

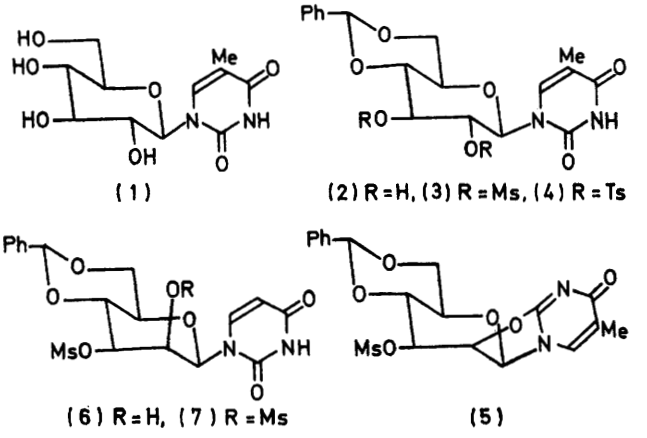
Recently, Freestone *et al.*[4] reported that treatment of 7-(4,6-*O*-benzylidene-2,3-di-*O*-methylsulphonyl-β-D-glucopyranosyl)theophylline under Tipson–Cohen conditions[5] gave a syrup containing several components, Fox *et al.*[6] obtained a similar result on attempting to prepare a 2′-ene analogue of cytosine.

We have demonstrated[7] the formation of a 2′,3′-unsaturated pyranosylthymine from a 2,2′-anhydronucleoside, prepared quantitatively from a disulphonated glucopyranosyl nucleoside. We now describe a new route to a (2,3-dideoxyglyc-2-enopyranosyl)thymine and a (2,3-dideoxyglycopyranosyl)thymine, and discuss the mechanism of the introduction of unsaturation.

1-(β-D-Glucopyranosyl)thymine (1), prepared easily and in high yield by the nitromethane–mercury cyanide method,[8] was converted into a benzylidene derivative (2) by shaking with a catalytic amount of zinc chloride in benzaldehyde. The product (2) was sulphonated with a sulphonyl chloride in pyridine. Although the bismethanesulphonate (3) was obtained in 90% yield, the bistoluene-*p*-sulphonate (4) was obtained only in low yield, presumably as a result of the greater bulk of the *p*-tolylsulphonyloxy-group. T.l.c. indicated the accumulation of the mono-*p*-tolylsulphonyl derivative. The 2,2′-anhydro-nucleoside (5) was prepared quantitatively by treatment of the bis-sulphonate (3) with 1 equiv. of sodium benzoate in heated *NN*-dimethylformamide. When the bis-sulphonate (3) was treated with 1 equiv. of sodium methoxide in methanol, some starting material remained undissolved even on heating, and the yield of (5) was about 60%. Formation of the C(2)–O–C(2′) linkage was confirmed by the characteristic u.v. absorption spectra.[9] Treatment of the anhydro-nucleoside (5) with 1 equiv. of sodium hydroxide in aqueous 75% ethanol gave a monomethanesulphonate (6) (in 96% yield), which has the *manno*-configuration. The n.m.r. spectrum of (6) showed the anomeric proton signal at δ 5.90 with $J_{1',2'}$ *ca.* 0.[10] The sulphonate (6) was methylsulphonylated by heating with methanesulphonyl chloride in pyridine for 1 h, and gave the *manno*-type bismethanesulphonate (7), a 2′-epimer of (3), in 55% yield. The n.m.r. spectrum of (7) showed the anomeric proton signal at δ 6.16, with $J_{1',2'}$ 0,[10] and $MeSO_2$ signals at δ 3.24 and 3.26.

The Tipson–Cohen reaction (sodium iodide–zinc in dimethylformamide) is useful for the preparation of methyl 4,6-*O*-benzylidene-α- and -β-D-*erythro*-hex-2-enopyranosides from the corresponding disulphonated sugars. In a preliminary experiment we applied this reaction to the 2′,3′-disulphonated nucleoside (3).

Treatment of the bismethanesulphonate (3) with a 20-fold excess of sodium iodide and zinc dust[11] in *NN*-dimethylformamide (DMF) for 0.5 h resulted in the disappearance of the starting material (R_F 0.65) and the appearance of two major products (R_F 0.25 and 0.7) and several minor products (t.l.c. in benzene–ethanol, 5 : 1).



Extraction of the reaction mixture with chloroform and subsequent fractional crystallisation gave the 2,2′-anhydro-derivative (5) (the more polar product) and the 2′,3′-unsaturated derivative (8) (the less polar product), both in 10% yield. The reaction of the toluene-*p*-sulphonate (4) with the same reagents under reflux for 1 h gave compound (8) in 30% yield. This result is as anticipated, because the *p*-tolylsulphonyloxy-group is generally more readily eliminated than the methylsulphonyloxy-group.[12] The n.m.r. spectrum of (8) showed the presence of two vinylic protons (δ 5.76 and 6.50, $J_{2',3'}$ 10.5 Hz). The signals for (8) were easily assigned by reference to Ferrier's data.[13]

[2] C. L. Stevens, N. A. Neilsen, and P. Blumbers, *J. Amer. Chem. Soc.*, 1964, **86**, 1894; K. A. Watanabe, I. Wempen, and J. J. Fox, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 2368; K. A. Watanabe, T. M. K. Chiu, D. H. Hollenberg, and J. J. Fox, *J. Org. Chem.*, 1974, **39**, 2482.

[3] T. Kondo, H. Nakai, and T. Goto, *Agric. and Biol. Chem.*, 1970, **35**, 1990; *Tetrahedron Letters*, 1972, 1881; *Tetrahedron*, 1973, **29**, 1801; K. J. Ferrier and M. M. Ponpipom, *J. Chem. Soc.* (*C*), 1971, 560, 563.

[4] A. J. Freestone, L. Hough, and A. C. Richardson, *Carbohydrate Res.*, 1975, **45**, 3.

[5] R. S. Tipson and A. Cohen, *Carbohydrate Res.*, 1965, **1**, 338.

[6] K. A. Watanabe, R. S. Goody, and J. J. Fox, *Tetrahedron*, 1970, **26**, 3883.

[7] T. Yamazaki, H. Shiraishi, K. Matsuda, H. Sugiyama, S. Seto, and N. Yamaoka, *J.C.S. Chem. Comm.*, 1975, 518.

[8] N. Yamaoka, K. Aso, and K. Matsuda, *J. Org. Chem.*, 1965, **30**, 149; K. A. Watanabe and J. J. Fox, *J. Heterocyclic Chem.*, 1969, **6**, 109; H. Shiraishi, N. Yamaoka, H. Sugiyama, and K. Tuzimura, *Agric. and Biol. Chem.*, 1971, **35**, 1151.

[9] R. Fecher, J. F. Codington, and J. J. Fox, *J. Amer. Chem. Soc.*, 1961, **83**, 1889.

[10] N. Yamaoka, H. Sugiyama, and K. Tuzimura, *Bull. Chem. Soc. Japan*, 1971, **44**, 1442; N. Yamaoka, E. Takahashi, and K. Tuzimura, *Carbohydrate Res.*, 1971, **19**, 262.

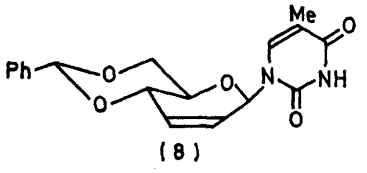
[11] L. F. Fieser and M. Fieser, ' Reagents for Organic Synthesis,' Wiley, New York, 1967, vol. 1, p. 1276.

[12] E. Albano, D. Horton, and T. Tsuchiya, *Carbohydrate Res.*, 1966, **2**, 349.

[13] R. J. Ferrier and M. M. Ponpipom, *J. Chem. Soc.* (*C*), 1971, 553.

Similar treatment of the bis-sulphonate (3) at lower temperature (80—90 °C) gave the anhydro-nucleoside (5) in 27% yield, with a small amount of (8). The predominant formation of (5) suggested that it was an intermediate in the formation of the unsaturated nucleoside (8).

Treatment of the anhydro-nucleoside (5) with a 20-fold excess of sodium iodide and zinc dust in refluxing DMF for 2 h gave the unsaturated nucleoside (8) in 44% yield. Use of lithium iodide in place of sodium iodide decreased the yield of (8) to 21%. Although we previously reported that both sodium iodide and zinc were essential for this reaction, our new finding showed that only the iodide ion was essential: compound (8) was



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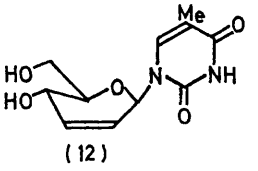

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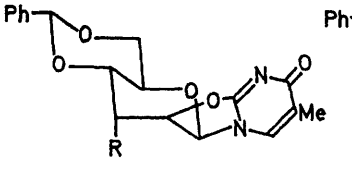
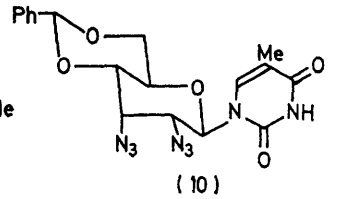
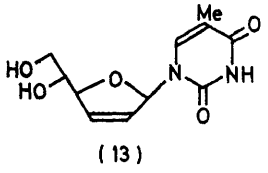


(9) R = N_3, (11) R = I



(10)



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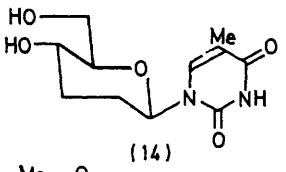
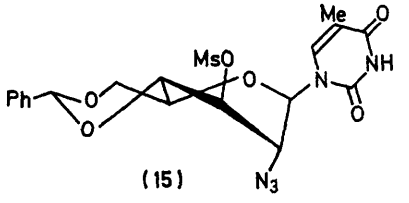


(14)

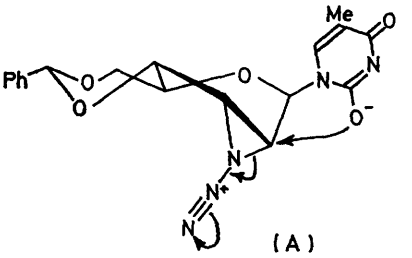


(15)

obtained in 56% yield when a mixture containing (5) and a 20-fold excess of sodium iodide was refluxed for 4 h. Thus, the 2,2′-anhydro-derivative (5) is an intermediate in the reaction of the disulphonated nucleoside, and a better precursor for introducing 2′,3′-unsaturation into a pyranosylthymine.

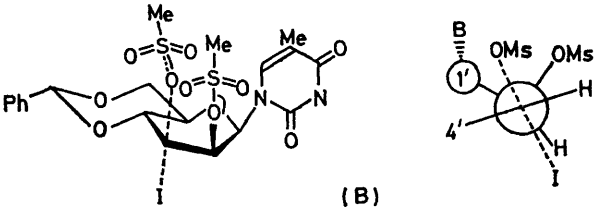
Application of this reaction to the *manno*-type disulphonate (7) gave several unidentified compounds, and did not give the unsaturated compound (8).

In order to determine the reaction mechanism, we needed to know which of the two positions C-2′ or C-3′ is more easily attacked by the nucleophile. As it was difficult to isolate the presumed iodinated intermediate, we attempted to use azide ion as a nucleophile for the replacement reaction. The azido-substituent, normally introduced by S_N2 replacement of a suitable leaving group,[14] can easily be detected by its characteristic i.r. band at *ca.* 2 100 cm^{-1}. When the anhydro-nucleoside (5) was treated with sodium azide in refluxing DMF for 1 h, two products were observed by t.l.c. [benzene–ethanol (5 : 1)]. These were separated by preparative t.l.c. The more polar was the 2,2′-anhydro-3′-azido-3′-deoxy-*altro*-nucleoside (9), obtained crystalline in 10%



(A)

yield. The less polar was the 2′,3′-diazido-2′,3′-dideoxy-*allo*-nucleoside (10), also obtained crystalline in 10% yield. Since no other product was detected by t.l.c., this result appears to exclude the possibility of migration of the azido group from C-2′ to C-3′. If such a migration were to occur [see (A)], the 2′-azido-*gluco*-nucleoside having *trans*-diequatorial substitution at C-2′ and -3′ must change its conformation into a boat form (15), which should require much more energy for conversion than the original form, and the 2′-azido-*gluco*-nucleoside should be detectable by t.l.c. Thus, in the pyranoside series, migration of the azido-function could not be readily achieved, although recent work [15] has provided an example of the formation of an azidonium intermediate in furanosyl nucleoside reactions. In the light of the above results, in the production of the unsaturated nucleoside the initial attack by iodide ion should occur at the C-3′, to yield the 3′-iodinated intermediate (11) which is better suited for reductive elimination with iodide ion or zinc. This hypothesis offers a convenient explanation of why the 2,2′-anhydro-precursor (5) changes smoothly into the



(B)

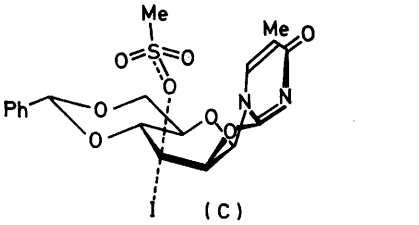
unsaturated nucleoside (8) whereas the *manno*-type precursor (7) does not. Axial attack of iodide ion on the C-3′ of (7) will result in a strong eclipsing effect and an electrostatic interaction amongst the leaving 3′- and 2′-methylsulphonyloxy-groups and the thymine base, owing to flattening of the pyranose ring [see (B)]. Consequently, there is a resistance to the replacement of a nucleophile at C-3′, and side reactions might occur.

When the iodide ion attacks C-3′ in the anhydro-

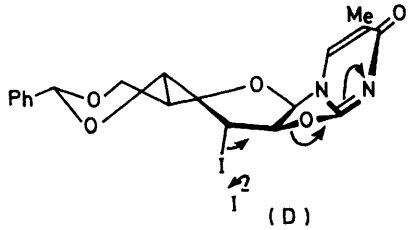
[14] J. Hill, L. Hough, and A. C. Richardson, *Carbohydrate Res.*, 1968, **8**, 7; Y. Ali and A. C. Richardson, *J. Chem. Soc.* (*C*), 1968, 1764; 1969, 320.

[15] T. Sasaki, K. Minamoto, T. Sugiura, and M. Niwa, *J. Org. Chem.*, 1976, **41**, 3138.

nucleoside (5) from the axial direction, formation of a transition state [see (C)] will be easy because of the characteristic conformation in which the bulky 1′- and 2′-substituents have been constrained by eclipsing in the 2,2′-anhydro-bridge. Substituents at C-2′ and -3′ in the



(C)



(D)

2,2′-anhydro-3′-iodinated intermediate (11) have a *trans*-diaxial configuration, and elimination should occur rapidly [see (D)]. This explanation is endorsed by the fact that the Tipson–Cohen reaction of methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulphonyl-β-D-mannopyranoside was slower than that of the corresponding β-D-glucopyranoside.[16] Thus, steric and electrostatic effects predominate over other factors in this reaction and, as in the elimination reactions of methyl pyranoside derivatives,[16] the initial replacement should be the rate-determining step in the reaction of the anhydro-nucleoside (5).

Watanabe and others[17] have shown that the sugar

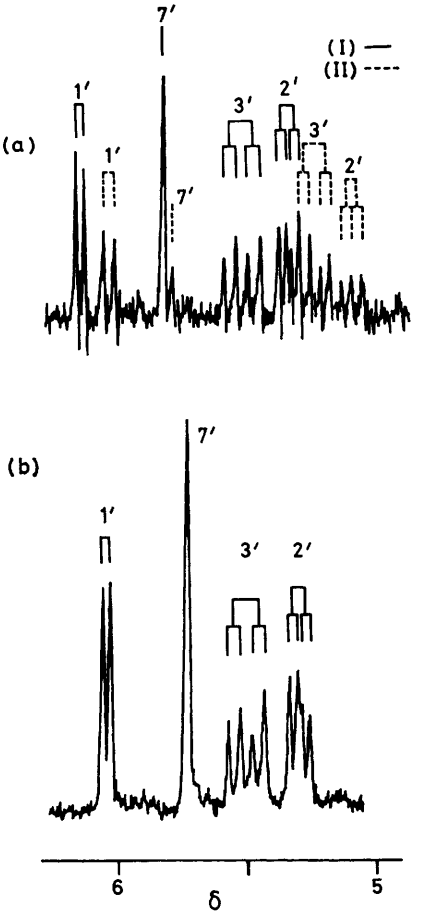
N.m.r. spectra of compounds (5) and its high-temperature conformers (I) and (II)

	δ				*J*/Hz		
	H-1′	H-2′	H-3′	PhC*H*	1′, 2′	2′, 3′	3′, 4′
Room temp.							
(5)	6.05	5.18	5.50	5.75	3.0	5.0	10
150 °C							
(I)	6.17	5.36	5.53	5.84	3.0	5.0	9.0
(II)	6.04	5.10	5.25	5.80	4.0	4.0	8.0

moiety in 2,2′-anhydro-1-(3-acetamido-3-deoxy-4,6-*O*-benzylidene-β-D-mannopyranosyl)uracil can exist in the $^4C_1$ form, but other conformations are also possible, although less likely, for this compound. For this reason, n.m.r. spectra of the 2,2′-anhydro-nucleoside (5) were measured at room temperature and at 150 °C (Figure and Table). The anomeric proton signal was easily assigned as a doublet with $J_{1',2'}$ 3.0 Hz, and the 2′-proton signal was identified as a quartet, $J_{1',2'}$ 3.0, $J_{2',3'}$ 5.0 Hz. The H-3′ signal was identified as a quartet with $J_{2',3'}$ 5.0 and $J_{3',4'}$ 10 Hz (room temperature J values). Compound

[16] T. Yamazaki, H. Sugiyama, N. Yamaoka, K. Matsuda, and S. Seto, *Carbohydrate Res.*, 1976, **50**, 279; *J.C.S. Perkin I*, in the press.

(5) was found to exist in the $^4C_1$ form at room temperature, as Watanabe and others stated, from a molecular model. However, a high-temperature measurement of the n.m.r. spectrum indicated the presence of two new conformers. In one (I) all signals were shifted to lower field than in the spectrum taken at room temperature. In the other (II) the anomeric proton signal has not moved and that of the benzylidene proton is at lower field but the signals of the other protons appear at higher field. The corresponding coupling constants in these conformers are similar, but the differences in chemical shift show that conformational changes can occur; this might not have



N.m.r. spectra of the anhydro-nucleoside (a) at 150 °C and (b) at room temperature

been expected for a 2,2′-anhydro-derivative constrained by the benzylidene group and the 2,2′-bridge.

For the preparation of the debenzylidenated unsaturated nucleoside, compound (8) was treated with aqueous 80% acetic acid under reflux for 0.5 h; a crystalline product (12) was obtained in 91% yield. Although Albano *et al.*[12] reported that methyl 4,6-*O*-benzylidene-α-D-*erythro*-hex-2-enopyranoside changed rapidly into furfural under acidic conditions, compound (8) did not change into a furfural derivative. The n.m.r. spectrum of (12) showed that elimination of the benzylidene group

[17] K. A. Watanabe and J. J. Fox, *J. Org. Chem.*, 1966, **31**, 211.

had occurred and vinylic proton signals were observed at δ 6.08 and 5.58 ($J_{2',3'}$ 10 Hz). The possibility of ring cleavage and recyclisation of (12) to a furanosyl derivative (13) was excluded by the results of a periodate consumption test. In the n.m.r. spectrum of (12) the C-4′ hydroxy-proton signal appeared as a doublet at δ 5.18, J 6.0 Hz, and the C-6′ hydroxy-proton signal as a triplet at δ 4.60, J 6.0 Hz. These assignments were confirmed from the fact that when compound (12) was stored in [$^2H_6$]dimethyl sulphoxide for a long time, the hydroxy-proton peaks became broadened, while other peaks remained unchanged; also only hydroxy-proton signals were shifted at high temperature.

The unsaturated nucleoside (12) was hydrogenated over 10% palladium–carbon for 1 h, giving the 2′,3′-dideoxy-nucleoside (14) in 83% yield. Compound (14) could serve as an intermediate for the synthesis of antibiotic analogues such as amicetosylthymine. In its n.m.r. spectrum, the hydroxy-proton signals appeared at δ 4.85 and 4.48, J 5.0 and 6.0 Hz, respectively. The yield of (14) from the glucosylthymine (1) was 26%.

EXPERIMENTAL

N.m.r. data were recorded at 100 MHz with a JEOL PS-100 spectrometer. I.r. spectra were taken with a Hitachi EPI-G2 spectrometer. Mass spectra were obtained by direct insertion into the ion source of a Shimadzu LKB-9000 instrument.

1-(β-D-*Glucopyranosyl*)*thymine* (1).—A mixture of thymine (10 g) and mercury(II) cyanide (30 g) in dry nitromethane (1 l) was dried by azeotropic distillation. Tetra-*O*-acetyl-α-D-glucopyranosyl chloride (60 g, 2 equiv.) was added to the suspension, and the mixture was refluxed for 4 h. The clear solution was concentrated to a syrup *in vacuo*, and the residue was extracted with chloroform (400 ml). The extract was filtered, washed with aqueous 30% potassium iodide (500 ml × 2) and water (500 ml × 2), dried (Na_2SO_4), and evaporated. Crystallisation of the residual syrup from ethanol gave 1-(tetra-*O*-acetyl-β-D-glucopyranosyl)-thymine (32 g, 88%), m.p. 154—155° (lit.,[18] 154.5—155.5°).

The acetylated nucleoside (26 g) was dissolved in dry methanol (300 ml) saturated with ammonia gas, and the mixture was stored overnight at 5 °C. Evaporation gave a syrup. Crystallisation from ethanol afforded the product (1) (13.3 g, 81%), m.p. 265—268°, $[\alpha]_D^{21}$ +19° (*c* 1.0 in water) (lit.,[18] m.p. 269—271°, $[\alpha]_D^{25}$ +18.3°) (Found: C, 45.6; H, 5.65; N, 9.65. $C_{11}H_{16}N_2O_7$ requires C, 45.85; H, 5.55; N, 9.7%).

1-(4,6-O-*Benzylidene*-β-D-*glucopyranosyl*)*thymine* (2).—A mixture of compound (1) (13 g), dried zinc chloride (39 g), and benzaldehyde (210 ml; distilled under nitrogen) was shaken for 36 h at room temperature, then transferred into ether (900 ml) with stirring. The white precipitate was filtered off and washed with ether (yield 15 g, 88%). Crystallisation from ethanol afforded the *product* (2) (11.5 g, 68%), m.p. 297—299° (decomp.), $[\alpha]_D^{21}$ −12° (*c* 1.0 in dimethylformamide) (Found: C, 57.0; H, 5.35; N, 7.5. $C_{18}H_{20}N_2O_7$ requires C, 57.45; H, 5.3; N, 7.45%).

1-(4,6-O-*Benzylidene*-2,3-*di*-O-*methylsulphonyl*-β-D-*glucopyranosyl*)*thymine* (3).—To a solution of compound (2) (10 g) in dry pyridine (360 ml) at room temperature, methanesulphonyl chloride (5.5 ml) was added, and the mixture was stirred overnight at room temperature. The solution was concentrated to a small volume and then poured into ice–water (1 l). The precipitate was collected and crystallised from acetone–ethanol to give the *product* (3) (12.7 g, 89%), m.p. 206—208° (decomp.), $[\alpha]_D^{21}$ −18° (*c* 1.0 in dimethylformamide), $\lambda_{max.}$ (EtOH) 266 nm (ε 9 160), δ [$(CD_3)_2SO$] 11.4 (1 H, s, N^3-H), 7.70 (1 H, s, H-6), 7.40 (5 H, s, ArH), 6.12 (1 H, d, $J_{1',2'}$ 7.5 Hz, H-1′), 5.69 (1 H, s, PhC*H*), 5.15—5.50 (2 H, m, H-2′ and -3′), 3.40—4.50 (4 H, m, H-4′ and -5′, and H_2-6′), 3.22 (3 H, s, $MeSO_2$), 3.18 (3 H, s, $MeSO_2$), and 1.80 (3 H, s, 5-Me) (Found: C, 45.35; H, 4.6; N, 4.65. $C_{20}H_{24}N_2O_{11}S_2,0.5C_2H_5OH$ requires C, 45.4; H, 4.85; N, 5.05%).

1-(4,6-O-*Benzylidene*-2,3-*bis*-O-p-*tolylsulphonyl*-β-D-*glucopyranosyl*)*thymine* (4).—A solution of compound (2) (7 g) in dry pyridine (250 ml) was treated with toluene-*p*-sulphonyl chloride (10.7 g) at 0 °C. The mixture was stirred at room temperature for 6 days, and evaporated to a syrup which was applied to a silica gel column in chloroform. Elution with benzene–ethanol (1 : 1) afforded the crystalline *product* (4), m.p. 144—145°, $[\alpha]_D^{21}$ −26° (*c* 1.0 in chloroform), δ [$(CD_3)_2SO$] 7.0—7.70 (13 H, m, ArH), 6.10br (1 H, d, $J_{1',2'}$ 9 Hz, H-1′), 5.20—5.55 (3 H, m, H-2′ and -3′ and PhC*H*), 3.50—4.35 (4 H, m, H-4′ and -5′ and H_2-6′), 2.40 (3 H, s, ArMe), 2.25 (3 H, m, ArMe), and 1.72 (3 H, s, 5-Me) (Found: C, 54.4; H, 4.7; N, 3.95. $C_{32}H_{32}N_2O_{11}S_2,H_2O$ requires C, 54.7; H, 4.85; N, 4.0%).

2,2′-*Anhydro*-1-(4,6-O-*benzylidene*-3-O-*methylsulphonyl*-β-D-*mannopyranosyl*)*thymine* (5).—A mixture of compound (3) (3.8 g) and sodium benzoate (1.8 g, 1 equiv.) in dry DMF (160 ml) was heated at 120 °C for 1 h. The mixture was then poured into ice–water (1.8 l) and the white precipitate was collected and washed with water. Crystallisation from acetone gave pure *product* (5) (2.98 g, quantitative), m.p. 249—251° (decomp.), $[\alpha]_D^{18}$ −176° (*c* 1.0 in dimethyl sulphoxide), $\lambda_{max.}$ (EtOH) 248 nm (ε 10 360), δ [$(CD_3)_2SO$] 7.80 (1 H, s, H-6), 7.40 (5 H, s, ArH), 6.05 (1 H, d, $J_{1',2'}$ 3.0 Hz, H-1′), 5.75 (1 H, s, PhC*H*), 5.50 (1 H, q, $J_{2',3'}$ 5.0, $J_{3',4'}$ 10 Hz, H-3′), 5.18 (1 H, q, $J_{1',2'}$ 3.0, $J_{2',3'}$ 5.0 Hz, H-2′), 3.70—4.35 (4 H, m, H-4′ and -5′ and H_2-6′), 3.25 (3 H, s, $MeSO_2$), and 1.83 (3 H, s, 5-Me) (Found: C, 52.15; H, 4.6; N, 6.4. $C_{19}H_{20}N_2O_8S$ requires C, 52.3; H, 4.6; N, 6.4%).

1-(4,6-O-*Benzylidene*-2,3-*bis*-O-*methylsulphonyl*-β-D-*mannopyranosyl*)*thymine* (7).—Compound (5) (800 mg) was suspended in aqueous 75% ethanol (106 ml) containing M-sodium hydroxide (3.7 ml). The suspension was kept for 6.5 h at 40 °C. The clear solution was then neutralised with Dowex-50 (H^+) resin. Evaporation of the deionised solution gave 1-(4,6-O-*benzylidene*-3-O-*methylsulphonyl*-β-D-*mannopyranosyl*)*thymine* (6), which crystallised during concentration of the solution (800 mg, 96%), m.p. 214—217° (decomp.), $\lambda_{max.}$ (EtOH) 262 nm, $\lambda_{min.}$ (EtOH) 233 nm, δ [$(CD_3)_2SO$] 5.90 (1 H, s, H-1′).

To a solution of compound (6) (600 mg) in dry pyridine (50 ml) was added methanesulphonyl chloride (1.8 ml), and the mixture was stirred for 1 h at 60 °C, then poured into ice–water (700 ml). The white precipitate (700 mg) was crystallised from acetone–ethanol to give the *product* (7) (385 mg, 55%), m.p. 182—184°, $[\alpha]_D^{21}$ + 5° (*c* 0.5 in chloroform), $\lambda_{max.}$ (EtOH) 266 nm (ε 10 100), δ [$(CD_3)_2SO$] 7.40 (5 H, s, ArH), 7.28 (1 H, s, H-6), 6.16 (1 H, s, H-1′), 5.82 (1 H, s, PhC*H*), 5.61 (1 H, q, $J_{2',3'}$ 4.0, $J_{3',4'}$ 9.0 Hz, H-3′), 5.16 (1 H, d, $J_{2',3'}$ 4.0 Hz, H-2′), 3.80—4.40 (4 H, m, H-4′

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and -5′ and H_2-6′), 3.26 (3 H, s, $MeSO_2$), 3.24 (3 H, s, $MeSO_2$), and 1.80 (3 H, s, 5-Me) (Found: C, 44.35; H, 4.6; N, 5.2. $C_{20}H_{24}N_2O_{11}S_2,0.5H_2O$ requires C, 44.65; H, 4.35; N, 5.2%).

Reaction of the Anhydronucleoside (5) *with Sodium Iodide and Zinc*.—A suspension of compound (5) (440 mg, 1 mmol), sodium iodide (3 g, 20 mmol), and zinc (1.3 g, 20 mmol) in dry DMF (25 ml) was refluxed for 2 h with stirring. After cooling, water (150 ml) and chloroform (150 ml) were added and the mixture was filtered. The organic layer was washed with water and dried (Na_2SO_4). Evaporation, and trituration of the residue with 50% aqueous ethanol, gave a homogeneous crystalloid mass, which was filtered off and recrystallised from acetone to yield 1-(4,6-O-*benzylidene*-2,3-*dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)*thymine* (8) (151 mg, 44%), m.p. 242.5—243.5° (decomp.), $[\alpha]_D^{18}$ +85.3° (*c* 0.75 in acetonitrile), $\lambda_{max.}$ (EtOH) 266 nm (ε 10 050), δ [$(CD_3)_2SO$] 7.45 (5 H, ArH), 7.18 (1 H, s, H-6), 6.65 (1 H, d, $J_{1',2'}$ 2.2 Hz, H-1′), 6.50 (1 H, d, $J_{2',3'}$ 10.5 Hz, H-3′), 5.76 (1 H, q, $J_{1',2'}$ 2.2, $J_{2',3'}$ 10.5 Hz, H-2′), 5.72 (1 H, s, PhC*H*), 3.80—4.70 (4 H, m, H-4′ and -5′, and H_2-6′), and 1.90 (3 H, s, 5-Me), *m/e* 342 (M^+) (Found: C, 62.85; H, 5.35; N, 8.05. $C_{18}H_{18}N_2O_5$ requires C, 63.15; H, 5.25; N, 8.2%).

Reaction of the Anhydro-nucleoside (5) *with Sodium Iodide*.—A mixture of compound (5) (440 mg, 1 mmol) and sodium iodide (3 g, 20 mmol) in dry DMF (20 ml) was refluxed for 4 h with stirring. The usual procedures gave crystals of the product (8) (190 mg, 56%), m.p. 239—241° (decomp.), identified by i.r. spectrum.

Reaction of the Bis-sulphonate (4) *with Sodium Iodide and Zinc*.—A mixture of compound (4) (600 mg, 0.9 mmol), sodium iodide (3 g, 20 mmol), and zinc (1.3 g, 20 mmol) in dry DMF (20 ml) was refluxed for 1 h with stirring. The usual procedures gave crystals of compound (8) (89 mg, 30%), m.p. 239—241° (decomp.), identified by i.r. spectrum.

Reaction of the Bis-sulphonate (3) *with Sodium Iodide and Zinc*.—To a suspension of sodium iodide (9 g, 20 equiv.) and zinc (5.5 g, 20 equiv.) in DMF (40 ml) under reflux was added compound (3) (1.3 g). After 0.5 h, the mixture was filtered hot and to the filtrate were added chloroform (100 ml) and water (100 ml). The organic layer was dried (Na_2SO_4) and evaporated to a small volume; addition of ethanol (10 ml) to the residue gave a precipitate, which was crystallised from acetone, to afford the product (5) (100 mg, 10%), identical (m.p. and i.r. spectra) with that described above. The mother liquor was evaporated to a small volume; addition of 50% aqueous ethanol afforded crystalloid material (8) (90 mg, 10%), m.p. 241—243° (decomp.), identified by i.r. and n.m.r. spectra.

Reaction of the Anhydro-nucleoside (5) *with Sodium Azide*.—A mixture of compound (5) (200 mg, 0.46 mmol) and sodium azide (60 mg, 0.92 mmol) in dry DMF (10 ml) was refluxed for 1 h with stirring. After cooling, ethyl acetate (100 ml) and water (100 ml) were added and the organic layer was washed with water, dried (Na_2SO_4], and evaporated. The residual syrup was subjected to preparative t.l.c. Compound (5) (identified by i.r. spectrum) was recovered (65 mg). The next most polar product, 2,2′-*anhydro*-1-(3-*azido*-4,6-O-*benzylidene*-3-*deoxy*-β-D-*altropyranosyl*)*thymine* (9), was crystallised from ethyl acetate; yield 18 mg (10%), m.p. 226—228° (decomp.), $\lambda_{max.}$ (EtOH) 246 nm, $\lambda_{min.}$ (EtOH) 218 nm, $\nu_{max.}$ 2 100 cm^{-1} (no OH or SO_2R absorbance), *m/e* 232 ($M - N_2$ base), 255 ($M - N_2$), and 383 (M^+). The least polar product, 1-(2,3-*diazido*-4,6-O-*benzylidene*-2,3-*dideoxy*-β-D-*allopyranosyl*)*thymine* (10), was crystallised from ether–hexane; yield 20 mg (10%), m.p. 194—196° (decomp.), $\lambda_{max.}$ (EtOH) 260 nm, $\lambda_{min.}$ (EtOH) 233 nm, $\nu_{max.}$ 2 100 cm^{-1} (no OH or SO_2R absorbance), *m/e* 246 ($M - N_4$ + base), 370 ($M - N_4$), 398 ($M - N_2$), and 426 (M^+).

1-(2,3-*Dideoxy*-β-D-erythro-*hex*-2-*enopyranosyl*)*thymine* (12).—Compound (8) (540 mg) in 80% acetic acid (20 ml) was refluxed for 20 min; after cooling, the solution was evaporated to a syrup. Crystallisation occurred on dropwise addition of ethyl acetate (3 ml). Preparative t.l.c. gave pure *product* (12) (366 mg, 91%), m.p. 194—196° (decomp.), $[\alpha]_D^{21}$ +125° (*c* 0.5 in ethanol), $\lambda_{max.}$ (EtOH) 262 nm (ε 10 030), δ [$(CD_3)_2SO$] 7.10 (1 H, s, H-6), 6.24 (1 H, q, $J_{1',2'}$ 2.0, $J_{1',3'}$ 2.0, $J_{1',4'}$ 2.0 Hz, H-1′), 6.08 (1 H, dt, $J_{1',3'}$ 2.0, $J_{2',3'}$ 10, $J_{3',4'}$ 2.0 Hz, H-3′), 5.60 (1 H, dt, $J_{1',2'}$ 2.0 $J_{2',3'}$ 10, $J_{2',4'}$ 2.0 Hz, H-2′), 5.18 (0.6 H, d, *J* 6.0 Hz, 4′-OH), 4.60 (0.7 H, t, *J* 6.0 Hz, 6′-OH), 4.04 (1 H, m, H-4′), 3.40—3.80 (3 H, m, H-5′ and H_2-6′), and 1.80 (3 H, s, 5-Me) (Found: C, 51.9; H, 5.4; N, 10.95. $C_{11}H_{14}N_2O_5$ requires C, 51.95; H, 5.55; N, 11.0%).

1-(2,3-*Dideoxy*-β-D-erythro-*hexopyranosyl*)*thymine* (14).—To a prehydrogenated suspension of 10% palladium–charcoal (10 mg) in ethanol (10 ml) was added the unsaturated nucleoside (12) (100 mg), and hydrogenation was continued. After 1 h, the catalyst was removed and the filtrate was evaporated *in vacuo* to give a syrup. Trituration with ethyl acetate gave the *product* (14) as crystalline material (83 mg). Preparative t.l.c. gave a sample with m.p. 203—204°, $[\alpha]_D^{21}$ +48° (*c* 0.25 in ethanol), $\lambda_{max.}$ (EtOH) 265 nm (ε 10 100), δ [$(CD_3)_2SO$] 7.54 (1 H, s, H-6), 5.55 (1 H, q, $J_{1',2'a} = J_{1',2'e}$ = 6.0 Hz, H-1′), 4.85 (0.8 H, d, *J* 5.0 Hz, 4′-OH), 4.48 (0.9 H, t, *J* 6.0 Hz, 6′-OH), 3.40—3.85 (4 H, m, H-4′ and -5′ and H_2-6′), 1.40—2.20 (4 H, m, H-2′a, -2′e, -3′a, and 3′e), and 1.90 (3 H, s, 5-Me) (Found: C, 51.35; H, 6.4; N, 10.55. $C_{11}H_{16}N_2O_5$ requires C, 51.55; H, 6.25; N, 10.95%).

[6/2116 *Received*, 17*th November*, 1976]