Phenyloxazoline Derivatives of Amino-sugars

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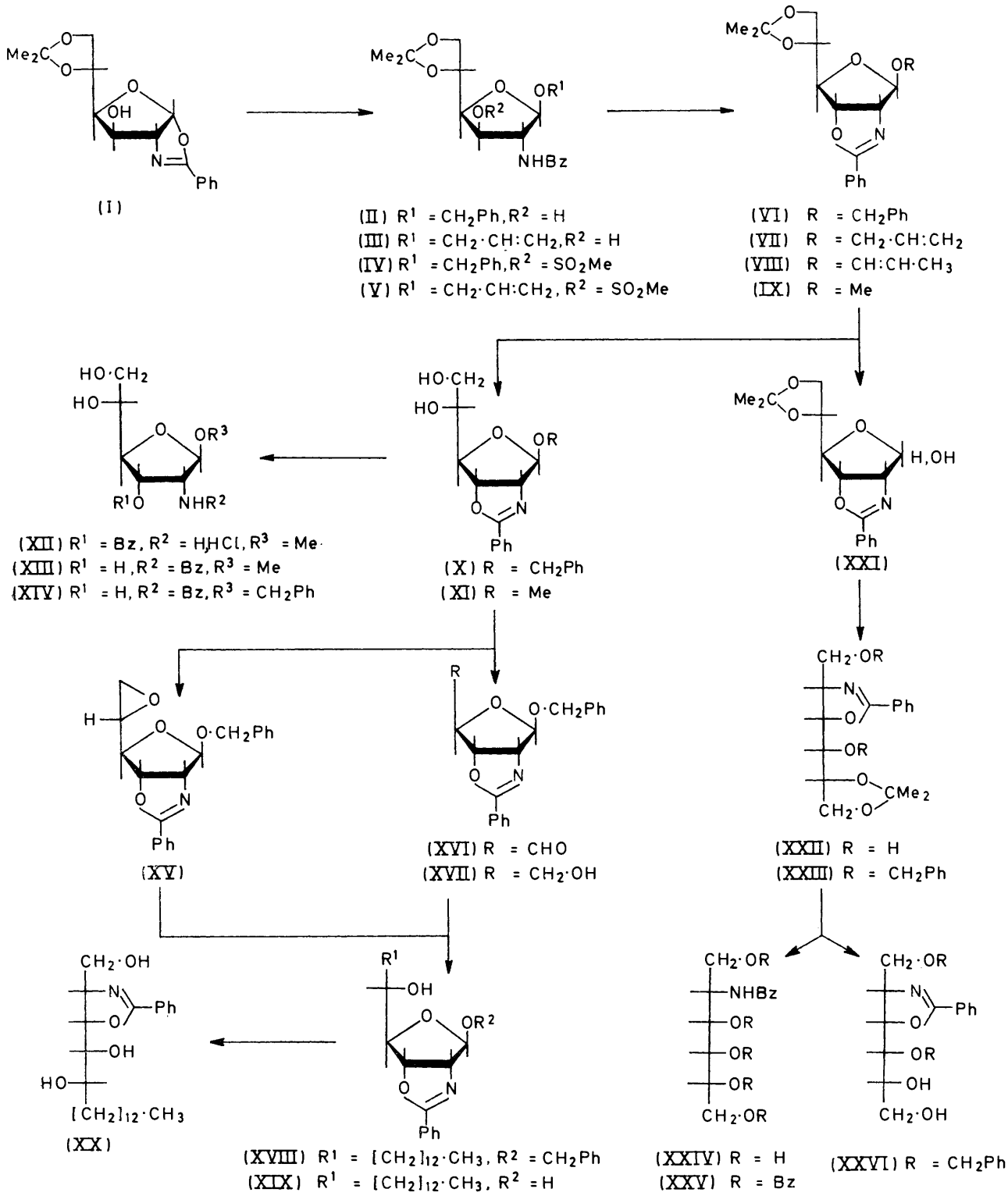
The preparation and borohydride reduction of 2,3-dideoxy-5,6-*O*-isopropylidene-2′-phenyl-D-allofuranoso-[2,3-*d*]-$\Delta^{2'}$-oxazoline (XXI) are described. The reduction product was a derivative of 2-amino-2-deoxy-D-allitol, indicating that no isomerisation of the sugar system in compound (XXI) had occurred during its formation and reduction. A derivative of muramic acid containing a reduced side chain was synthesised from a phenyloxazoline derivative of 2-amino-2-deoxy-D-glucofuranose. A convenient method for the preparation of the 5,6-carbonate of 1,2-*O*-isopropylidene-D-glucofuranose and related sugars was also developed.

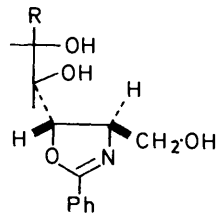
THE long-chain base sphingosine is a component of many phospholipids and glycolipids, and until recently [1] no stereospecific synthesis has been available. As an extension of our studies [2] on the synthesis of phytosphingosine from the D-glucosamine derivative (I) we considered that a synthesis of sphingosine from this compound would also be valuable. For this work we aimed for the intermediate (XX), and a route to it from the phenyloxazoline derivative (X) of D-allosamine *via* the 5,6-epoxide (XV) or the 5-aldehyde (XVI) was envisaged. The final stage, conversion of the 5-tridecanyl-5-ol (XVIII) into the open-chain derivative (XX) would involve the preparation and borohydride reduction of a free sugar (XIX) (or its pyranoside form) containing a phenyloxazoline system on carbon atoms 2 and 3.

In compound (XIX) the substituents on the 4- and 5-positions of the oxazoline ring are in a *cis*-relationship, similar to that in the derivative (XXVIII) of allothreonine. Compound (XXVIII) is rapidly and com-

[1] E. J. Reist and P. H. Christie, *J. Org. Chem.*, 1970, **35**, 4127.
[2] J. Gigg, R. Gigg, and C. D. Warren, *J. Chem. Soc.* (*C*), 1966, 1872.


(I)
(II) R¹ = CH₂Ph, R² = H
(III) R¹ = CH₂·CH:CH₂, R² = H
(IV) R¹ = CH₂Ph, R² = SO₂Me
(V) R¹ = CH₂·CH:CH₂, R² = SO₂Me
(VI) R = CH₂Ph
(VII) R = CH₂·CH:CH₂
(VIII) R = CH:CH·CH₃
(IX) R = Me
(X) R = CH₂Ph
(XI) R = Me
(XII) R¹ = Bz, R² = H,HCl, R³ = Me
(XIII) R¹ = H, R² = Bz, R³ = Me
(XIV) R¹ = H, R² = Bz, R³ = CH₂Ph
(XV)
(XVI) R = CHO
(XVII) R = CH₂·OH
(XVIII) R¹ = [CH₂]₁₂·CH₃, R² = CH₂Ph
(XIX) R¹ = [CH₂]₁₂·CH₃, R² = H
(XX)
(XXI)
(XXII) R = H
(XXIII) R = CH₂Ph
(XXIV) R = H
(XXV) R = Bz
(XXVI) R = CH₂Ph

pletely isomerised [3] under basic conditions to the threonine derivative (XXIX), owing to the lability of the proton at C-4 of the oxazoline ring and the favoured stereochemistry of the threonine derivative (XXIX). In compound (XIX), the potential aldehyde group



(XXVII)

(XXVIII) (XXIX)

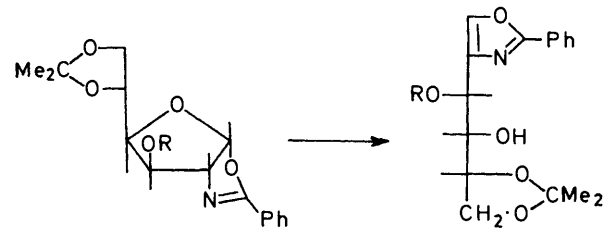
attached to C-4 of the oxazoline ring would be expected to increase the lability of the proton at C-4, and the possibility existed that during the preparation and reduction of compound (XIX) inversion would occur to give the *trans*-isomer (XXVII) rather than the required product (XX). Before embarking on this route to sphingosine it was decided to investigate the stability of the D-allosamine derivative (XXI) and the products obtained from it on borohydride reduction.

The 2,3-fused oxazoline (VI) was prepared from the 1,2-fused oxazoline (I) by way of the ring-opened amides (II) and (IV), by use of the method developed previously [4] for the preparation of the corresponding methyl glycoside (IX). Acidic hydrolysis of the furanoso[2,3-*d*]-Δ^2-oxazoline (VI) removed the isopropylidene group and opened the oxazoline ring, and subsequent treatment with alkali gave the amide (XIV). Hydrogenolysis of the amide (XIV) gave 2-benzamido-2-deoxy-D-allose identical, with material prepared previously [4] by hydrolysis of the methyl glycoside (IX). Borohydride reduction of the 2-benzamido-2-deoxy-D-allose gave crystalline 2-benzamido-2-deoxy-D-allitol.

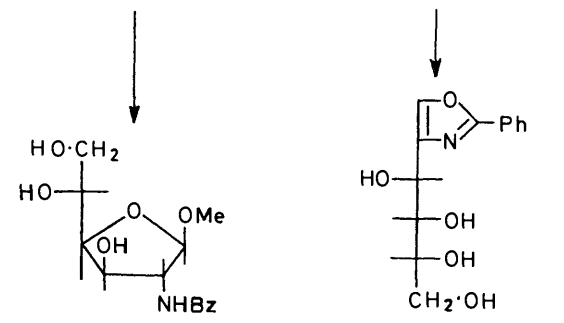
The removal of the benzyl group from the glycoside (VI), to give the free sugar (XXI), proved difficult and led to a mixture of products during the prolonged hydrogenolysis; an alternative route to the sugar (XXI) *via* the allyl glycoside (VII) was therefore investigated. Compound (VII) was prepared from the 1,2-fused oxazoline (I) by the method used for the preparation of the corresponding methyl and benzyl glycosides. The opening of the oxazoline ring of compound (I) by allyl alcohol in the presence of 0·0001N-acid must be carefully followed by t.l.c.

[3] D. F. Elliott, *J. Chem. Soc.*, 1949, 589; 1950, 62; E. E. Hamel and E. P. Painter, *J. Amer. Chem. Soc.*, 1953, **75**, 1362; H. E. Carter, J. B. Harrison, and D. Shapiro, *ibid.*, p. 4705; M. Viscontini, G. Odasso, and W. Freitag, *Helv. Chim. Acta*, 1966, **49**, 1720.

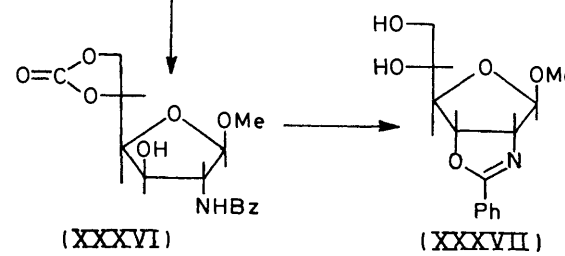
We had previously shown [5b] that the 3-*O*-allyl compound (XXX) was very sensitive to the action of potassium t-butoxide in dimethyl sulphoxide at room



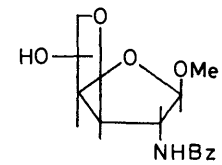
(XXX) R = $CH_2{\cdot}CH{:}CH_2$ (XXXII) R = $CH_2{\cdot}CH{:}CH_2$
(XXXI) R = H (XXXIII) R = H



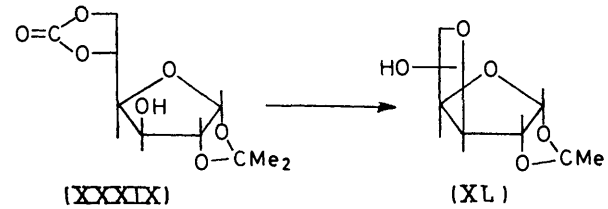
(XXXV) (XXXIV)



(XXXVI) (XXXVII)



(XXXVIII)



(XXXIX) (XL)

temperature, and was converted into the oxazole (XXXII) before the allyl group was isomerised. We

[4] R. Gigg and C. D. Warren, *J. Chem. Soc.*, 1965, 1351.
[5] (*a*) J. Gigg and R. Gigg, *J. Chem. Soc.* (*C*), 1966, 82; (*b*) R. Gigg and C. D. Warren, *ibid.*, 1968, 1903.

have subsequently observed that the corresponding alcohol (XXXI) is much more stable to these conditions, and can only be converted into the oxazole (XXXIII) at higher temperatures. Presumably the alkoxide ion formed on interaction of the potassium t-butoxide with the free hydroxy-group hinders the removal of a proton from C-4 of the oxazoline ring, which is the initial step in the formation of the oxazole. Preliminary investigations of the action of potassium t-butoxide in dimethyl sulphoxide on the 2,3-fused oxazoline (IX) also showed that the phenyloxazoline group in this compound was much more stable to these conditions than the 1,2-fused oxazoline (XXX), and this encouraged us to look at the behaviour of the oxazoline allyl glycoside (VII). When compound (VII) was treated with potassium t-butoxide in dimethyl sulphoxide at room temperature the allyl group was isomerised [5] to give the crystalline prop-1-enyl glycoside (VIII) in high yield. At higher temperatures however, further reactions occurred, and the nature of the products is being investigated.

The hydrolysis of the prop-1-enyl group with mercury(II) chloride in the presence of mercury(II) oxide [5b] gave a single product (t.l.c.), which was reduced with sodium borohydride to give the crystalline open-chain oxazoline (XXII). Acid hydrolysis of compound (XXII) and subsequent benzoylation gave a crystalline hexabenzoyl amide (XXV), which on alkaline hydrolysis gave the crystalline *N*-benzoyl derivative (XXIV). Compounds (XXIV) and (XXV) were identical with the corresponding derivatives prepared from 2-benzamido-2-deoxy-D-allose by borohydride reduction and benzoylation, thus establishing that the conversion of the allyl glycoside (VII) into the open-chain alcohol (XXII) occurred without inversion at C-2 of the intermediate sugar (XXI).

The 5,6-diol (XI) was a valuable intermediate in the synthesis [2] of phytosphingosine and was originally prepared,[4] in low yield, by acid hydrolysis of the isopropylidene derivative (IX). A further route to compound (XI) was also developed [2] during work on the synthesis of phytosphingosine. Since the diol (X) was required for the proposed synthesis of sphingosine we have reinvestigated the preferential hydrolysis of the isopropylidene groups from compounds (VI) and (IX) and have developed conditions that allow the preparation of the diols (X) and (XI) in high yield by this method.

The 1,4-diol (XXII) was converted into the dibenzyl ether (XXIII). It was anticipated that acidic hydrolysis of the latter, under the conditions worked out for the preferential hydrolysis of the isopropylidene groups from compounds (VI) and (IX), would give the 5,6-diol (XXVI), which would also be a potentially useful intermediate for the synthesis of the tridecanyl-1,4,5-triol (XX). However, under these hydrolytic conditions, the oxazoline ring and the isopropylidene group were hydrolysed at similar rates and only a small yield of the 5,6-diol (XXVI) was obtained.

Before the satisfactory conditions for the preferential hydrolysis of the isopropylidene groups from compounds (VI) and (IX) had been established, a further route to the oxazoline [(XI) ≡ (XXXVII)], *via* the cyclic carbonate (XXXVI) was considered. It was envisaged that the carbonate (XXXVI) could be prepared from the 3,5,6-triol (XXXV) [4] by the methods used previously for the preparation of the carbonate (XXXIX) of 1,2-*O*-isopropylidene-D-glucofuranose. Since the first preparation of the latter compound (XXXIX) by Haworth and Porter,[6a] several other methods have been investigated [7] in order to improve the yield and ease of preparation. One method which has not previously been used is an exchange reaction between 1,2-*O*-isopropylidene-D-glucofuranose and ethylene carbonate. In view of the success achieved [8] in the preparation of glycerol carbonate from glycerol and ethylene carbonate, we investigated this exchange reaction with the 3,5,6-triol (XXXV). When this compound (XXXV) and ethylene carbonate were heated together at 120° in the presence of a trace of sodium hydrogen carbonate, t.l.c. indicated almost complete conversion into the carbonate (XXXVI) in 5 min. Continued heating of the mixture was accompanied by the evolution of gas and after 30 min the carbonate was completely converted into a new product which was assumed to be the anhydride (XXXVIII) although it was not characterised. The conversion of the carbonate (XXXIX) into the anhydride (XL) in the presence of base has been described.[7a,b] The carbonate (XXXVI) was most readily obtained (in 70% yield) by heating the 5,6-diol (XXXV) with ethylene carbonate at 140° in a soda-glass tube for 20 min in the absence of sodium hydrogen carbonate. The carbonate (XXXIX) was also obtained in a similar way from 1,2-*O*-isopropylidene-D-glucofuranose in good yield; this is therefore the most convenient way of obtaining compounds of this type.

We have previously shown [9] that the phenyloxazoline (I) is a useful intermediate for the synthesis of muramic acid (XLV). The corresponding alcohol (XLIV) has been isolated [10] as a sodium borohydride reduction product of the 'lactam' of muramic acid which occurs in the mucopeptide of bacterial spores. For a convenient synthesis of the alcohol (XLIV) the methyl ester (XLI) [11]

[6] (*a*) W. N. Haworth and C. R. Porter, *J. Chem. Soc.*, 1929, 2796; (*b*) W. G. Overend, M. Stacey, and L. F. Wiggins, *ibid.*, 1949, 1358.

[7] (*a*) K. Freudenberg, H. Eich, C. Knoevenagel, and W. Westphal, *Ber.*, 1940, **73**, 441; E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, 1958, **23**, 1958; (*b*) L. D. Hall and L. Hough, *J. Chem. Soc.*, 1963, 5301; (*c*) G. Hanisch and G. Henseke, *Chem. Ber.*, 1967, **100**, 3225; B. S. Shasha, W. M. Doane, C. R. Russell, and C. E. Rist, *Carbohydrate Res.*, 1967, **5**, 346.

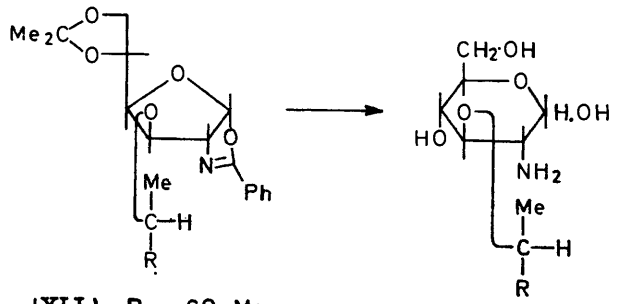
[8] J. B. Bell, V. A. Currier, and J. D. Malkemus, U.S.P. 2,915,529/1959; J. Cunningham and R. Gigg, *J. Chem. Soc.*, 1965, 1553.

[9] R. Gigg and P. M. Carroll, *Nature*, 1961, **191**, 495; R. Gigg, P. M. Carroll, and C. D. Warren, *J. Chem. Soc.*, 1965, 2975.

[10] A. D. Warth and J. L. Strominger, *Proc. Nat. Acad. Sci. U.S.A.*, 1969, **64**, 528.

[11] R. Gigg and C. D. Warren, *J. Chem. Soc.* (*C*), 1969, 295.

was reduced by lithium aluminium hydride to give the alcohol (XLII), which gave a crystalline acetate (XLIII). Acidic hydrolysis of the acetate gave the hydrochloride of the ' reduced muramic acid ' (XLIV), with properties similar to those reported previously.[12]



(XLI) R = CO_2Me
(XLII) R = CH_2·OH
(XLIII) R = CH_2·OAc
(XLIV) R = CH_2·OH
(XLV) R = CO_2H

EXPERIMENTAL

Solvents were evaporated off under reduced pressure. Optical rotations were measured at 22—24° (unless otherwise stated) with a Bendix automatic polarimeter. T.l.c. was carried out with microscope slides coated with silica gel G. The light petroleum used had b.p. 40—60° unless otherwise stated.

Benzyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-β-D-glucofuranoside (II).—A solution of 1,2-dideoxy-5,6-*O*-isopropylidene-2′-phenyl-α-D-glucofuranoso[2,1-*d*]-$\Delta^{2'}$-oxazoline (I) (30 g) [4,13] and toluene-*p*-sulphonic acid (210 mg) in benzyl alcohol (900 ml) was stirred at room temperature and the course of the reaction was followed by t.l.c. (ethyl acetate) (a portion of the solution was neutralised with sodium hydrogen carbonate and the benzyl alcohol was evaporated off). After 24 h when the starting material (R_F 0·7) had been completely converted into a product (R_F 0·8), a solution of sodium hydrogen carbonate was added to neutralise the acid and the alcohol was evaporated off). The product was extracted from the residue with chloroform and recrystallised from 50% aqueous methanol to give the *furanoside* (II) (31 g, 76%), m.p. 141—143°, $[\alpha]_D$ −53° (*c* 1 in $CHCl_3$) (Found: C, 67·0; H, 6·5; N, 3·5. $C_{23}H_{27}NO_6$ requires C, 66·8; H, 6·6; N, 3·4%).

When the foregoing reaction was allowed to continue, a new product (R_F 0·3) appeared. During evaporation of the benzyl alcohol this material crystallised out and was recrystallised from methanol to give benzyl 2-benzamido-2-deoxy-β-D-glucopyranoside, m.p. 240°, $[\alpha]_D$ −40·8° (*c* 0·68 in pyridine) (Found: C, 64·6; H, 6·3; N, 3·8. Calc. for $C_{20}H_{33}NO_6$: C, 64·3; H, 6·2; N, 3·75%) {lit.,[14] m.p. 236°, $[\alpha]_D^{24}$ −44° (*c* 1—2 in pyridine)}.

Benzyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-3-O-methylsulphonyl-β-D-glucofuranoside (IV).—Methanesulphonyl chloride (3·5 ml) was added to a solution of compound (II) (10 g) in dry pyridine (100 ml) at 0°. After 2 h, ice–water was added and the oil which precipitated was extracted with ether. The extract was washed with N-hydrochloric acid at 0°, potassium chloride solution, and sodium hydrogen carbonate solution, and dried ($MgSO_4$). Evaporation left a crystalline product which yielded the *methanesulphonate* (IV) (10 g), m.p. 124—125° (from methanol), $[\alpha]_D$ −45° (*c* 0·45 in Me_2N·CHO) (Found: C, 58·65; H, 5·95; N, 2·85; S, 6·5. $C_{24}H_{29}NO_8S$ requires C, 58·6; H, 6·0; N, 2·85; S, 6·5%).

Benzyl 2,3-Dideoxy-5,6-O-isopropylidene-2′-phenyl-β-D-allofuranosido[2,3-d]-$\Delta^{2'}$-*oxazoline* (VI).—A solution of the methanesulphonate (IV) (10 g) in pyridine (100 ml) was heated at 100° until t.l.c. (ether) indicated that conversion of the starting material (R_F 0·7) into the product (R_F 1·0) was complete (*ca.* 7 h). Water was added to the cooled solution and the crystalline product was filtered off and washed with water. Recrystallisation from aqueous methanol gave the *oxazoline* (VI) (6·5 g, 81%), m.p. 89—91°, $[\alpha]_D$ −60° (*c* 0·87 in $CHCl_3$) (Found: C, 70·1; H, 6·5; N, 3·6. $C_{23}H_{25}NO_5$ requires C, 69·85; H, 6·4; N, 3·5%).

Benzyl 2,3-Dideoxy-2′-phenyl-β-D-allofuranosido[2.3-d]-$\Delta^{2'}$-*oxazoline* (X).—A solution of the oxazoline (VI) (10 g) and toluene-*p*-sulphonic acid monohydrate (7 g) in methanol (1·7 l) was kept at 20° for 20 h; t.l.c. (chloroform–methanol, 10 : 1) then showed complete conversion of the starting material (R_F 1·0) into the product (R_F 0·52). An excess of sodium hydrogen carbonate was added and the solution was evaporated to dryness. The product was extracted from the residue with chloroform and crystallised from methanol to give the *oxazoline* (X) (7·2 g, 80%), m.p. 179—181°, $[\alpha]_D$ −84·6° (*c* 0·6 in Me_2N·CHO) (Found: C, 67·5; H, 5·8; N, 3·9. $C_{20}H_{21}NO_5$ requires C, 67·6; H, 6·0; N, 3·9%). The *diacetate*, prepared by the action of acetic anhydride–pyridine, had m.p. 112—113° [from light petroleum (b.p. 60—80°)], $[\alpha]_D$ −84·6° (*c* 1 in $CHCl_3$) (Found: C, 66·0; H, 5·7; N, 3·3. $C_{24}H_{25}NO_7$ requires C, 65·6; H, 5·7; N, 3·2%).

Benzyl 2,3-Dideoxy-2′-phenyl-β-D-ribofuranosido[2,3-d]-$\Delta^{2'}$-*oxazoline* (XVII).—A 50% aqueous solution of periodic acid (640 mg) was added to a solution of the oxazoline (X) (500 mg) in ethanol (80 ml) and the solution was stirred at 20° for 15 min. Potassium hydrogen carbonate (140 mg) and sodium borohydride (1 g) were added and the solution was stirred at 20° for 1 h. Water (80 ml) was added and the ethanol was evaporated off to give an oily product which was extracted with ether. Crystallisation from light petroleum (b.p. 60—80°) gave the *oxazoline* (XVII), m.p. 92—94°, $[\alpha]_D$ −124·2° (*c* 0·7 in $CHCl_3$) (Found: C, 70·3; H, 6·1; N, 4·2. $C_{19}H_{19}NO_4$ requires C, 70·1; H, 5·9; N, 4·3%).

Methyl 2,3-Dideoxy-2′-phenyl-β-D-allofuranosido[2,3-d]-Δ^{2}-*oxazoline* (XI).[2,4]—A solution of methyl 2,3-dideoxy-5,6-*O*-isopropylidene-2′-phenyl-β-D-allofuranosido[2,3-*d*]-$\Delta^{2'}$-oxazoline (IX) [4] (3·76 g) and toluene-*p*-sulphonic acid monohydrate (3·25 g) in methanol (750 ml) was kept at 20° for 24 h. Excess of sodium hydrogen carbonate was added and the solution was evaporated to dryness. Water (250 ml) was added to the residue and the product was filtered off and washed with water. Recrystallisation from aqueous methanol gave the oxazoline (XI) (2·7 g, 82%), m.p. and mixed m.p. 200°.

2-Benzamido-2-deoxy-D-allose.[4]—A solution of the oxazoline (XI) (2 g) in methanol (72 ml) and N-hydrochloric acid (7·2 ml) was heated under reflux for 30 min; t.l.c.

[12] R. W. Jeanloz and E. Walker, *Carbohydrate Res.*, 1967, **4**, 504.

[13] S. Konstas, I. Photaki, and L. Zervas, *Chem. Ber.*, 1959, **92**, 1288; B. Lindberg and H. Agback, *Acta Chem. Scand.*, 1964, **18**, 185.

[14] P. H. Gross, K. Brendel, and H. K. Zimmerman, *Annalen*, 1965, **683**, 175; H. Weidmann, E. Fauland, R. Helbig, and H. K. Zimmerman, *ibid.*, 1966, **694**, 183.

(ethyl acetate–methanol, 9 : 2) then showed almost complete conversion of the starting material (R_F 0·75) into the ester (XII) (R_F 0·35—0·5). An excess of potassium carbonate was added, the solution was evaporated to dryness, and the product was extracted with methanol. T.l.c. then showed the presence of the amide (XIII) (R_F 0·65) together with a trace of starting material. Water (25 ml) was added to the crude product and the oxazoline (XI) (180 mg) which separated was filtered off. 2N-Hydrochloric acid (8 ml) was added to the filtrate and the solution was heated under reflux for 20 min. On cooling, crystals of 2-benzamido-2-deoxy-D-allose (1·2 g) separated, and were recrystallised from ethanol–water (2 : 1); m.p. 204° (decomp.), $[\alpha]_D$ −24° (*c* 1 in $Me_2N{\cdot}CHO$ or Me_2SO) (Found: C, 55·4; H, 6·0; N, 4·7. Calc. for $C_{13}H_{17}NO_6$: C, 55·1; H, 6·05; N, 4·9%) {lit.,[4] m.p. 201—204° (decomp.), $[\alpha]_D$ −16° (*c* 1 in H_2O)}.

2-Benzamido-2-deoxy-D-allitol (XXIV).—(*a*) 2-Benzamido-2-deoxy-D-allose (500 mg) was stirred with a solution of sodium borohydride (1 g) in water (10 ml) for 4 h at 20°. Acetic acid was added to decompose the excess of sodium borohydride and the solution was passed through a column of Amberlite IR 120 (H^+) resin; the eluate was then evaporated to dryness. Several portions of methanol were added to and evaporated from the residue and the crystalline product was recrystallised from n-butanol to give *2-benzamido-2-deoxy-D-allitol* (400 mg), m.p. 142—143°, $[\alpha]_D^{28}$ −7·5° (*c* 1 in H_2O) (Found: C, 54·5; H, 6·3; N, 4·9. $C_{13}H_{19}NO_6$ requires C, 54·7; H, 6·7; N, 4·9%). This compound was treated with benzoyl chloride in pyridine, as described later, to give *2-benzamido-1,3,4,5,6-penta-O-benzoyl-2-deoxy-D-allitol* (XXV), m.p. 178—180°, $[\alpha]_D^{28}$ −6·3° (*c* 1 in $CHCl_3$) (Found: C, 71·6; H, 4·9; N, 2·0. $C_{48}H_{39}NO_{11}$ requires C, 71·5; H, 4·9; N, 1·7%).

(*b*) A solution of the oxazoline (VI) (2 g) in methanol (50 ml) and 0·1N-hydrochloric acid (50 ml) was heated under reflux for 1 h. Sodium hydrogen carbonate (500 mg) was added and the solvents were evaporated off. Glacial acetic acid (50 ml) and 10% palladium–charcoal (1 g) were added and the solution was stirred under hydrogen at atmospheric pressure for 15 h. Filtration and evaporation gave a solid residue. Recrystallisation of a portion from water gave 2-benzamido-2-deoxy-D-allose, m.p. 202—204° (decomp.). Water (20 ml) and sodium borohydride (1 g) were added to the residue and the solution was stirred at 20° for 2 h. Acetic acid was added to decompose the excess of borohydride and the solution was passed through a column of Amberlite IR 120 (H^+) resin; the eluate was evaporated to dryness. Several portions of methanol were added to and evaporated from the residue, and the crystalline product was recrystallised from ethanol to give 2-benzamido-2-deoxy-D-allitol, m.p. and mixed m.p. 142—144°, $[\alpha]_D$ −8·1° (*c* 1 in H_2O) (Found: C, 54·7; H, 6·75; N, 4·95%).

Allyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-β-D-glucofuranoside (III).—A solution of the oxazoline (I) (10 g) in redistilled allyl alcohol (450 ml) containing toluene-*p*-sulphonic acid (100 mg) was kept at 20°, and the course of the hydrolysis was followed by t.l.c. (acetone–toluene, 1 : 1) (sodium hydrogen carbonate was added to a portion of the solution and the allyl alcohol was then evaporated off). After 17 h the starting material (R_F 0·5) had been converted into a single product (R_F 0·6); an excess of sodium hydrogen carbonate was added and the allyl alcohol was evaporated off. The product was extracted from the residue with chloroform and crystallised from ether–light petroleum to give the *allyl furanoside* (III) (5·5 g), m.p. 107—108°, $[\alpha]_D$ −24·4° (*c* 1 in $CHCl_3$) (Found: C, 62·5; H, 6·9; N, 3·8). $C_{19}H_{25}NO_6$ requires C, 62·8; H, 6·9; N, 3·9%).

Allyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-3-O-methylsulphonyl-β-D-glucofuranoside (V).—The *methanesulphonate* (V), prepared as described for compound (IV), had m.p. 125—126° (from ethanol), $[\alpha]_D$ −30° (*c* 1 in $CHCl_3$) (Found: C, 54·6; H, 6·1; N, 3·7; S, 7·0. $C_{20}H_{27}NO_8S$ requires C, 54·4; H, 6·2; N, 3·2; S, 7·3%).

Allyl 2,3-Dideoxy-5,6-O-isopropylidene-2′-phenyl-β-D-allofuranosido[2,3-d]-$\Delta^{2'}$-*oxazoline* (VII).—The methanesulphonate (V) was heated in pyridine at 80° for 5 h; t.l.c. (toluene–acetone, 5 : 2) then showed complete conversion of the starting material (R_F 0·5) into a product (R_F 0·7). The product was isolated as described for compound (VI) and crystallised from ether–light petroleum (4 : 1) to give the *oxazoline* (VII), m.p. 59·5—61°, $[\alpha]_D$ −20·7° (*c* 1 in $CHCl_3$) (Found: C, 66·4; H, 6·6; N, 4·2. $C_{19}H_{23}NO_5$ requires C, 66·1; H, 6·7; N, 4·1%).

Prop-1-enyl 2,3-Dideoxy-5,6-O-isopropylidene-2′-phenyl-β-D-allofuranosido[2,3-d]-$\Delta^{2'}$-*oxazoline* (VIII).—A solution of the oxazoline (VII) (2·8 g) in dry dimethyl sulphoxide (100 ml) containing potassium t-butoxide (2 g) was kept at 20° for 3 h; t.l.c. (toluene–acetone, 9 : 1) then showed conversion of the starting material (R_F 0·5) into a product (R_F 0·6). Water was added to the solution and the product was extracted with ether and chromatographed on alumina. Elution with ether–light petroleum (1 : 5) gave the *prop-1-enyl glycoside* (VIII) (1·8 g), m.p. 58—59°, $[\alpha]_D$ +67·4° (*c* 1 in $CHCl_3$) (Found: C, 66·1; H, 6·5; N, 4·1. $C_{19}H_{23}NO_5$ requires C, 66·1; H, 6·7; N, 4·1%).

2,3-Dideoxy-5,6-O-isopropylidene-2′-phenyl-D-allitolo-[2,3-d]-$\Delta^{2'}$-*oxazoline* (XXII).—A solution of mercury(II) chloride (1·7 g) in acetone–water (9 : 1; 20 ml) was added to a solution of the prop-1-enyl glycoside (VIII) (1·7 g) in acetone–water (9 : 1; 30 ml). After 5 min at 20°, t.l.c. (toluene–acetone, 9 : 1) indicated complete conversion of the starting material (R_F 0·6) into a single product (R_F 0·1). The mixture was filtered and evaporated. The residue was extracted with ether; the extract was washed with potassium iodide solution and evaporated to give a solid residue which was stirred in a solution of sodium borohydride (1·8 g) in ethanol (25 ml) for 4 h at 20°. T.l.c. (toluene–acetone, 5 : 2) then indicated conversion of the starting material (R_F 0·5) into a single product (R_F 0·4). Water was added and the precipitated product was extracted with chloroform and crystallised from benzene to give the *oxazoline* (XXII) (830 mg), m.p. 147·5—149·5°, $[\alpha]_D$ −14·3° (*c* 1 in $CHCl_3$) (Found: C, 62·9; H, 6·9; N, 4·4. $C_{16}H_{21}NO_5$ requires C, 62·5; H, 6·9; N, 4·6%).

2-Benzamido-1,3,4,5,6-penta-O-benzoyl-2-deoxy-D-allitol (XXV).—A solution of the oxazoline (XXII) (800 mg) in 2N-sulphuric acid (20 ml) was heated under reflux for 2 h, cooled, extracted with ether, neutralised with barium carbonate, and filtered. The filtrate and washings were evaporated to dryness and the residue was dissolved in dry pyridine (20 ml) and cooled to 0°. Benzoyl chloride (3 ml) was added and the solution was stirred at 0° for 15 min and at 20° for 12 h. Water (0·5 ml) was added and the solution was stirred at 20° for 3 h (to decompose benzoic anhydride) and then poured into ice–water. The product was filtered off and recrystallised from benzene–light petroleum to give the hexabenzoyl derivative (XXV)

(1·2 g), m.p. and mixed m.p. (with material already described) 178—180°, $[\alpha]_D$ −5·9° (*c* 1 in $CHCl_3$) (Found: C, 71·6; H, 5·0; N, 2·0. Calc. for $C_{48}H_{39}NO_{11}$: C, 71·5; H, 4·9; N, 1·7%).

A mixture of the hexabenzoyl derivative (XXV) (1 g), methanol (100 ml), and sodium hydroxide (350 mg) was heated under reflux for 10 min. The solution was evaporated to *ca.* 10 ml and water (100 ml) was added. The solution was acidified (to pH 2), extracted with ether to remove benzoic acid, and passed through columns of Amberlite IR 120 (H^+) and Amberlite IR 400 (OH^-) resins. The eluate was evaporated and the product crystallised from ethanol to give 2-benzamido-2-deoxy-D-allitol, m.p. and mixed m.p. (with material already described) 142—144°, $[\alpha]_D$ −8·6° (*c* 0·7 in H_2O) (Found: C, 54·7; H, 6·9; N, 5·0. Calc. for $C_{13}H_{19}NO_6$: C, 54·7; H, 6·7; N, 4·9%).

Action of Potassium t-Butoxide in Dimethyl Sulphoxide on the Oxazoline [(I) ≡ (XXXI)].—A solution of the oxazoline (XXXI) (1 g) and potassium t-butoxide (1·5 g) in dimethyl sulphoxide (25 ml) was kept at 100° for 6 h. T.l.c. (ether) then showed a major product (R_F 0·65) and a trace of starting material (R_F 0·4). The solution was cooled, diluted with water, and extracted with ether and the product was recrystallised from light petroleum to give the oxazole acetal (XXXIII),[5b] m.p. and mixed m.p. 96—98°. This compound was hydrolysed as described previously [5b] to give the oxazole (XXXIV), m.p. and mixed m.p. 206—208°.

Methyl 2-Deoxy-2-benzamido-β-D-glucofuranoside 5,6-Carbonate (XXXVI) *and 1,2-O-Isopropylidene-α-D-glucofuranose 5,6-Carbonate* (XXXIX).—The methyl glycoside (XXXV) [4] (740 mg) and ethylene carbonate (1·4 g) were heated in an open soda-glass tube at 140°. T.l.c. (ethyl acetate) after 20 min showed almost complete conversion of the starting material (R_F 0·2) into a product (R_F 0·85). The mixture was cooled, water was added, and the product (570 mg, 70%) was filtered off, washed with water and dried. Recrystallisation from 50% aqueous methanol gave the *carbonate* (XXXVI), m.p. 162—164° (decomp.), $[\alpha]_D$ −89·8° (*c* 0·56 in $Me_2N{\cdot}CHO$) (Found: C, 55·8; H, 5·2; N, 4·3. $C_{15}H_{17}NO_7$ requires C, 55·7; H, 5·3; N, 4·3%), $\nu_{max.}$ 1780—1800 cm^{-1} (C=O). Continued heating of the mixture resulted in the appearance of a new product (R_F 0·5), which was considered to be the anhydride (XXXVIII). This product was also obtained by heating the mixture at 120° in the presence of traces of sodium hydrogen carbonate.

1,2-*O*-Isopropylidene-D-glucofuranose (1 g) and ethylene carbonate (2 g) were heated together in a soda-glass tube at 140° for 20 min; t.l.c. (ethyl acetate) then showed complete conversion of the starting material (R_F 0·2) into the product (R_F 0·85). Water was added to the cooled mixture and the carbonate (XXXIX) which separated was filtered off (660 mg, 60%); m.p. 220° (decomp), $[\alpha]_D$ −29·8° (*c* 1 in Me_2CO) (Found: C, 48·8; H, 5·7. Calc. for $C_{10}H_{14}O_7$: C, 48·8; H, 5·7%) {lit.,[7b] m.p. 224—225°, $[\alpha]_D$ −31·8° (*c* 0·5 in Me_2CO)}.

3-O-(2-*Acetoxy*-1-*methylethyl*)-1,2-*dideoxy*-5,6-O-*isopropylidene*-2′-*phenyl*-α-D-*glucofuranoso*[2,1-d]-$\Delta^{2'}$-*oxazoline* (XLIII).—A solution of the oxazoline ester (XLI) [11] (1·1 g) in dry ether (10 ml) was added dropwise to a solution of lithium aluminium hydride (100 mg) in ether (30 ml) at 0°, and the resulting solution was stirred for 30 min. T.l.c. (ether–light petroleum, 1 : 1) then showed complete conversion of the starting material (R_F 0·5) into the alcohol (XLII) (R_F 0·13). The excess of lithium aluminium hydride was decomposed by the addition of ethyl acetate, and water was then added dropwise until the inorganic material was in the form of a white precipitate which was filtered off. Evaporation of the filtrate gave the alcohol (XLII) as an oil, which was acetylated with acetic anhydride–pyridine to give the *acetate* (XLIII) (750 mg), m.p. 83—85° (from light petroleum), $[\alpha]_D$ −5·4° (*c* 0·8 in $CHCl_3$) (Found: C, 62·1; H, 6·8; N, 3·6. $C_{21}H_{27}NO_7$ requires C, 62·2; H, 6·7; N, 3·45%).

2-*Amino*-2-*deoxy*-3-O-[(S)-1-(*hydroxymethyl*)*ethyl*]-D-*glucose Hydrochloride* [(XLIV)HCl].—The oxazoline (XLIII) (1 g) in 3N-hydrochloric acid (50 ml) was heated at 100° for 5·5 h, cooled, extracted with ether (to remove benzoic acid), and evaporated to give a syrup. The last traces of water were removed by azeotropic distillation with ethanol–benzene and the syrupy residue slowly crystallised. Recrystallisation from acetone–methanol gave the hydrochloride of compound (XLIV) (600 mg), m.p. 180—183° (decomp.), $[\alpha]_D$ +69·4° (5 min) ⟶ +48·3° (24 h) (*c* 1 in H_2O) (Found: C, 39·5; H, 6·8; Cl, 12·8; N, 5·3. Calc. for $C_9H_{20}ClNO_6$: C, 39·5; H, 7·4; Cl, 12·95; N, 5·1%) {lit.,[12] m.p. 176—178° (decomp.), $[\alpha]_D^{24}$ +68 (4 min) ⟶ +48° (10 h) (*c* 0·99 in H_2O)}.

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