235. *New Syntheses of 2-Amino-2-deoxy-*D*-allose* (D-*Allosamine*), *2-Amino-2-deoxy-*D*-ribose* (D-*Ribosamine*), *and 2-Amino-2-deoxy-*D*-xylose* (D-*Xylosamine*).

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The 2-amino-2-deoxy-sugars mentioned in the title have been synthesised from the oxazoline (I) derived from 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose.

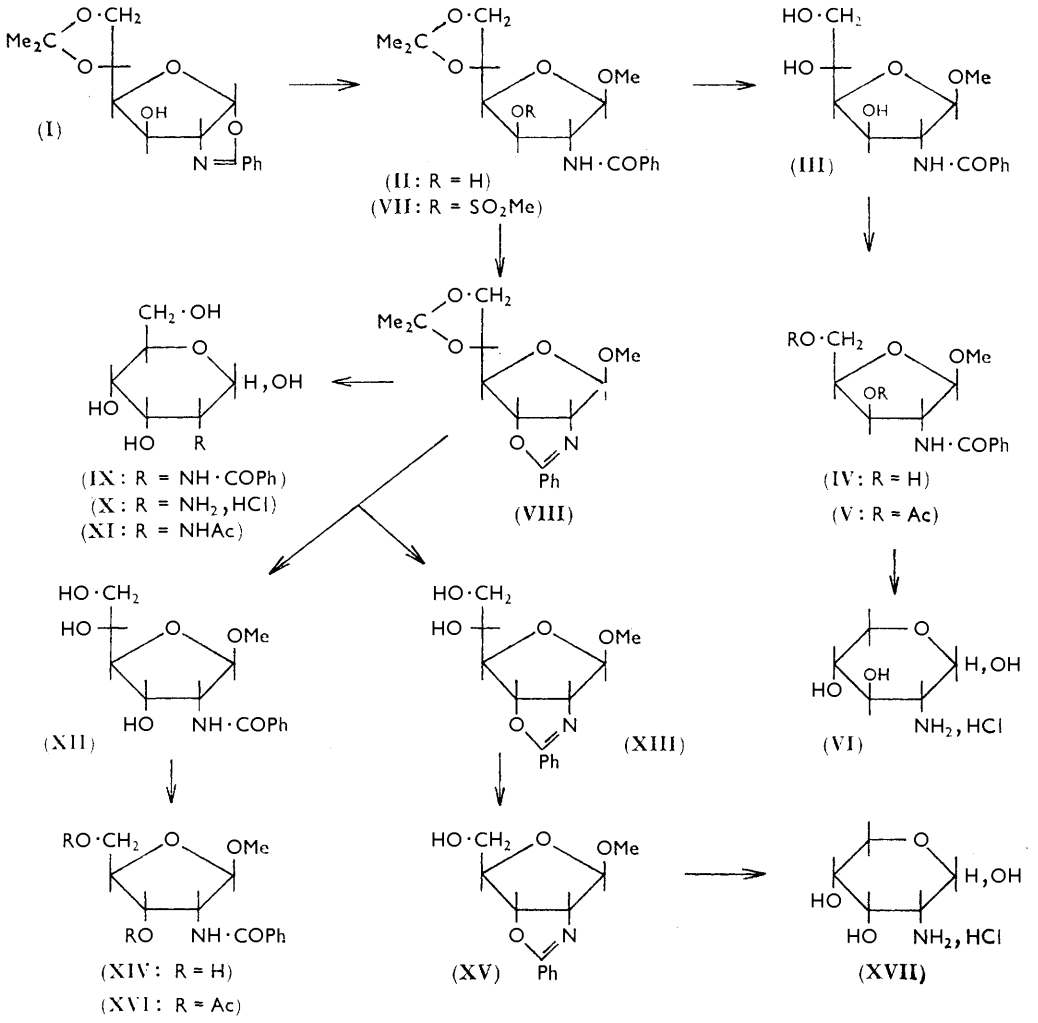
Since Zervas and his co-workers [1] introduced the readily available, crystalline oxazoline (I), derived from 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-D-glucofuranose, it has been used by several workers [2] for the synthesis of derivatives of 2-amino-2-deoxy-D-glucose. Zervas and his co-workers [1] also showed that the oxazoline (I) could be converted into the crystalline methyl furanosides (II) and (III) by the action of acid in methanol. These intermediates have been used in the present work for new syntheses of the amino-sugars mentioned in the title.

Methyl 2-benzamido-2-deoxy-β-D-glucofuranoside (III) was oxidised by sodium periodate, and the aldehyde formed was reduced by sodium borohydride to give methyl 2-benzamido-2-deoxy-β-D-xylofuranoside (IV) as a syrup. This was purified by conversion into the crystalline di-*O*-acetate (V), which gave D-xylosamine hydrochloride (VI) on acid hydrolysis. D-Xylosamine has been prepared previously by a similar degradation of ethyl 2-acetamido-2-deoxy-1-thio-α-D-glucofuranoside,[3] and by a synthesis from D-threose.[4]

Methyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (II) was converted into its crystalline 3-*O*-methanesulphonate (VII) by reaction with methanesulphonyl chloride in pyridine at 0°. On warming the pyridine solution after the completion of the reaction, the methanesulphonate was converted into the oxazoline derivative (VIII) of methyl 2-benzamido-2-deoxy-β-D-allofuranoside. The crystalline oxazoline (VIII) was also obtained from the methanesulphonate (VIII) by the action of sodium methoxide in methanol.

[1] S. Konstas, I. Photaki, and L. Zervas, *Chem. Ber.*, 1959, **92**, 1288.
[2] R. Gigg and P. M. Carroll, *Nature*, 1961, **191**, 495; W. Meyer zu Reckendorf, and W. A. Bonner, *Chem. Ber.*, 1962, **95**, 996; W. Meyer zu Reckendorf, *Tetrahedron*, 1963, **19**, 2033; B. Lindberg and H. Agback, *Acta Chem. Scand.*, 1964, **18**, 185.
[3] M. L. Wolfrom and A. Thompson, "Methods in Carbohydrate Chemistry," Academic Press, New York, 1962, Vol. 1, p. 209.
[4] R. Kuhn and G. Baschang, *Annalen*, 1959, **628**, 193.

Partial hydrolysis of the oxazoline (VIII) with acid gave 2-benzamido-2-deoxy-D-allose (IX) and this on further hydrolysis gave D-allosamine hydrochloride (X) as a hygroscopic solid. For characterisation this was converted into the crystalline *N*-acetyl derivative (XI) using *N*-acetoxyphthalimide.[5] D-Allosamine has been prepared previously



by several procedures,[6] and the conversion of methyl 2-benzamido-2-deoxy,4,6-*O*-benzylidene-β-D-glucopyranoside into methyl 2-benzamido-2-deoxy-4,6-*O*-benzylidene-β-D-allopyranoside by way of an oxazoline has also been reported.[7]

Hydrolysis of the oxazoline (VIII) under very mild acidic conditions gave a mixture of methyl 2-benzamido-2-deoxy-β-D-allofuranoside (XII) and its oxazoline derivative (XIII), as well as a small quantity of 2-benzamido-2-deoxy-D-allose (IX). The compounds (XII) and (XIII) were both crystalline and could be separated easily because of their different solubilities in water. The furanoside (XII) was converted into 2-benzamido-2-deoxy-D-allose (IX) in high yield.

For the preparation of D-ribosamine, compounds (XII) and (XIII) were oxidised by

[5] (*a*) G. H. L. Nefkens, G. I. Tesser, and R. J. F. Nivard, *Rec. Trav. chim.*, 1962, **81**, 683; (*b*) P. M. Carroll, *Nature*, 1963, **197**, 694.

[6] (*a*) R. W. Jeanloz, ref. 3, p. 212; (*b*) R. Kuhn and J. C. Jochims, *Annalen*, 1961, **641**, 143.

[7] W. Meyer zu Reckendorf and W. A. Bonner, *Chem. Ber.*, 1962, **95**, 1917.

sodium periodate and the products reduced with sodium borohydride to give the corresponding derivatives of D-ribose (XIV) and (XV), respectively. Acid hydrolysis of the crystalline oxazoline (XV) gave D-ribosamine hydrochloride (XVII) in good yield. The syrupy methyl 2-benzamido-2-deoxy-β-D-ribofuranoside (XIV) was converted into its crystalline di-*O*-acetate (XVI) which also gave D-ribosamine hydrochloride on acid hydrolysis. Since the oxazoline (XV) is crystalline and is obtained in good yield, it is superior to the compound (XIV) as an intermediate for the preparation of D-ribosamine.

D-Ribosamine has been prepared previously by replacement of the 2-*O*-toluene-*p*-sulphonate in a derivative of D-arabinose by hydrazine,[8] by synthesis from D-erythrose,[4] and by degradation of derivatives of 3-amino-3-deoxy-D-allose or 3-amino-3-deoxy-D-altrose.[9]

Experimental

Thin-layer chromatography (t.l.c.) was carried out on microscope slides coated with silica gel G (E. Merck). Compounds were detected by spraying with aqueous sulphuric acid (50% v/v) and heating at 200°. Melting points are uncorrected. Specific rotations were measured at 22—23°. Paper chromatography was carried out by the descending method, at room temperature on Whatman No. 1 filter paper with n-butyl acetate–pyridine–water (5 : 3 : 1, v/v) as the mobile phase. The amino-sugars were detected with the ninhydrin spray reagent.[10]

Oxazoline (I) *Derived from* 2-*Benzamido*-2-*deoxy*-5,6-O-*isopropylidene*-D-*glucofuranose*.[1]—2-Benzamido-2-deoxy-D-glucose was prepared as described previously.[1] The product, which contained potassium chloride, was dried thoroughly over phosphorus pentoxide *in vacuo* until it was in the form of a fine, free-running powder and was used without recrystallisation. The crude 2-benzamido-2-deoxy-D-glucose (84 g.) was added to a solution of dry hydrogen chloride (57 g.) in dry acetone (2·5 l.) and the mixture stirred for 3 hr. at room temperature and then kept for 24 hr. The stirred solution was cooled in ice, and ammonia gas was passed over it until the hydrogen chloride was neutralised. After filtering, the acetone was removed by evaporation under reduced pressure and the residue extracted with light petroleum (b. p. 60—80°) to remove condensation products of acetone. The crude product was recrystallised from ethyl acetate–cyclohexane (1 : 2) to give the oxazoline (I) (40 g.), m. p. 161° (lit.,[1] 159—160°).

Methyl 2-*Benzamido*-2-*deoxy*-5,6-O-*isopropylidene*-β-D-*glucofuranoside* (II).[1]—A solution of the oxazoline (I) (35 g.) in dry methanolic hydrogen chloride (1·5 l.; 0·0005N) was kept at room temperature and the course of the hydrolysis was followed by t.l.c. (ether as mobile phase) of small portions of the solution, after making alkaline with aqueous ammonia. After 15 hr., the oxazoline (R_F 0·5) had disappeared and a single spot (R_F 0·3) indicated complete hydrolysis to the furanoside (II). A solution of potassium hydroxide in methanol (10 ml.; 0·1N) was added and the excess of hydroxide destroyed by the addition of solid carbon dioxide. After evaporation of the methanol under reduced pressure, the residue was recrystallised from ethyl acetate to give the methyl furanoside (30 g., 79%), m. p. 133° (lit.,[1] 133—134°).

Methyl 2-*Benzamido*-2-*deoxy*-β-D-*glucofuranoside* (III).[1]—A solution of methyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (II) (1·75 g.) in methanolic sulphuric acid (100 ml.; 0·01N) was refluxed for 25 min. T.l.c. (ethyl acetate as mobile phase) of a portion of the solution, after making alkaline with aqueous ammonia, showed absence of starting material (R_F 0·65) and a single product (R_F 0·1). After neutralisation with barium carbonate, the solution was filtered and the filtrate concentrated under reduced pressure. The solid residue was recrystallised from light petroleum (b. p. 60—80°)–ethanol (2 : 1) to give the methyl glucofuranoside (1·25 g., 81%) as fine needles, m. p. 149—150° (lit.,[1] 146—148°).

Methyl 3,5-*Di*-O-*acetyl*-2-*benzamido*-2-*deoxy*-β-D-*xylofuranoside* (V).—An aqueous solution of sodium metaperiodate (20 ml.; 0·25M) was added to a solution of methyl 2-benzamido-2-deoxy-β-D-glucofuranoside (1 g.) in water (50 ml.). After 1 hr. at room temperature, a solution of sodium borohydride (1 g.) in water (25 ml.) was added, with stirring, and the solution was kept for 1 hr. at room temperature. Glacial acetic acid was added to decompose the excess of sodium borohydride and the solution was evaporated under reduced pressure. Several portions of methanol–toluene (1 : 1) were evaporated from the residue to remove boric acid as methyl

[8] F. Shafizadeh, ref. 3, p. 206.
[9] B. Coxon and L. Hough, *J.*, 1961, 1463, 1643.
[10] J. J. Pratt and J. L. Auclair, *Science*, 1948, **108**, 213.

borate, and the solid residue was then extracted with ethyl acetate. Evaporation of the extract gave crude methyl 2-benzamido-2-deoxy-β-D-xylofuranoside (IV) (0·6 g.) as a syrup. A solution of the syrup in pyridine (15 ml.) and acetic anhydride (12 ml.) was left at room temperature for 12 hr. then poured on to ice and extracted with chloroform. The chloroform solution was washed with sodium hydrogen carbonate solution, dried ($MgSO_4$), and evaporated to give crude *methyl 3,5-di-O-acetyl-2-benzamido-2-deoxy-β-D-xylofuranoside* which was recrystallised from ethanol–cyclohexane (1 : 2) to give rosettes (0·4 g., 34%), m. p. 142—143°, $[\alpha]_D$ +21° (*c* 1 in chloroform) (Found: C, 58·4; H, 6·1; N, 3·9. $C_{17}H_{21}NO_7$ requires C, 58·1; H, 6·0; N, 4·0%).

2-Amino-2-deoxy-D-xylose Hydrochloride.—Methyl 3,5-di-*O*-acetyl-2-benzamido-2-deoxy-β-D-xylofuranoside (0·4 g.) in hydrochloric acid (10 ml.; 2·6N) was heated under reflux for 4 hr. After cooling, the solution was extracted with ether to remove benzoic acid, and the aqueous layer was evaporated to dryness under reduced pressure. A solution of the residual syrup in ethanol was decolourised with charcoal and concentrated to 2 ml. After 1 hr. at 5° the crystals of 2-amino-2-deoxy-D-xylose hydrochloride (0·19 g., 88%) were collected, m. p. 168—170° (decomp.), $[\alpha]_D$ +79 ⟶ +40° (*c* 0·94 in H_2O), paper chromatography *R*(Glucosamine HCl) 1·6 (Found: C, 32·5; H, 6·6; N, 7·3. Calc. for $C_5H_{11}NO_4$,HCl: C, 32·3; H, 6·5; N, 7·5%) (lit.,[3] m. p. 165—167°, $[\alpha]_D^{31}$ + 80 ⟶ +40°).

Methyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-3-O-methanesulphonyl-β-D-glucofuranoside (VII).—Methanesulphonyl chloride (0·5 ml.) was added slowly with stirring to a solution of methyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (1 g.) in pyridine (8 ml.) at 0°. The mixture was kept at 4° for 24 hr. and poured into stirred ice–water. The solid which precipitated was recrystallised from aqueous ethanol giving the *methanesulphonate* (VII) (0·6 g.) as needles, m. p. 116—117°, $[\alpha]_D$ −1·6° (*c* 1 in $CHCl_3$) (Found: C, 52·1; H, 6·2; N, 3·2; S, 7·3. $C_{18}H_{25}NO_8S$ requires C, 52·1; H, 6·0; N, 3·4; S, 7·7%).

Oxazoline (VIII) *Derived from Methyl 2-Benzamido-2-deoxy-5,6-O-isopropylidene-β-D-allofuranoside*.—(*a*) A solution of the methanesulphonate (VII) (1·3 g.) in pyridine (8 ml.) was kept at 60° for 4 hr. After this time, analysis of the solution by t.l.c. (ether as mobile phase) showed absence of starting material (R_F 0·6) and the presence of a single product (R_F 0·9). The mixture was poured into water and the product extracted with chloroform. After evaporation of the extract under reduced pressure, the crude product was recrystallised from aqueous methanol to give the *oxazoline* (VIII) (0·9 g.) as needles, m. p. 92—93°, $[\alpha]_D$ 0° (*c* 1 in $CHCl_3$) $\nu_{max.}$ 1642 cm.$^{-1}$ (C=N) (Found: C, 63·7; H, 6·6; N, 4·4. $C_{17}H_{21}NO_5$ requires C, 63·9; H, 6·6; N, 4·4%).

(*b*) Sodium methoxide (0·05 g.) was added to a solution of the methanesulphonate (VII) (0·02 g.) in methanol (1 ml.). After 30 min. at room temperature, analysis by t.l.c. as in (*a*) showed complete conversion into the oxazoline (VIII). Water (10 ml.) was added and the precipitated solid recrystallised as above, m. p. 92—93°.

(*c*) (Preparative method). Methanesulphonyl chloride (13 ml.) was added slowly, with stirring, to a solution of methyl 2-benzamido-2-deoxy-5,6-*O*-isopropylidene-β-D-glucofuranoside (27 g.) in pyridine (100 ml.) at 0°. The temperature was allowed to rise to 20° and the solution kept for 2 hr. The precipitated solid was removed by filtration, the solution was kept at 60° for 4 hr. and poured into ice–water, and the solid which precipitated was recrystallised from aqueous methanol to give the oxazoline (VIII) (25 g.) as needles, m. p. 92—93°.

2-Benzamido-2-deoxy-D-allose (IX). A solution of the oxazoline (VIII) (1 g.) in methanol (5 ml.) and sulphuric acid (5 ml.; 0·2N) was heated under reflux for 20 min. After neutralisation with barium carbonate, the solution was concentrated to 2 ml. and diluted with water (5 ml.). The *2-benzamido-2-deoxy-D-allose* (0·45 g., 51%) which separated was recrystallised from ethanol–water (2 : 1) as needles, m. p. 201—204° (deomp.), $[\alpha]_D$ −16° (*c* 1 in H_2O) (Found: C, 55·3; H, 6·3; N, 4·7. $C_{13}H_{17}NO_6$ requires C, 55·1; H, 6·0; N, 4·9%).

2-Amino-2-deoxy-D-allose Hydrochloride (X).—A solution of the oxazoline (VIII) (0·4 g.) in hydrochloric acid (10 ml.; 2·6N) was heated under reflux for 4 hr. The cooled solution was extracted with ether and the aqueous layer evaporated to dryness under reduced pressure. A solution of the syrupy residue in methanol was decolourised with charcoal and evaporated to dryness. The product was treated with absolute ethanol to give D-allosamine hydrochloride as a hygroscopic solid (0·2 g., 74%), $[\alpha]_D$ +26 ⟶ +17° (*c* 1 in H_2O), paper chromatography *R*(Glucosamine HCl), 0·86 (lit.,[6a] $[\alpha]_D^{22}$ +26 ⟶ +17°).

2-Acetamido-2-deoxy-D-allose (XI).—Triethylamine (3 ml.) was added to a solution of

D-allosamine hydrochloride (0·6 g.) in water (30 ml.) at 0°. A solution of *N*-acetoxyphthalimide [5a] (1·5 g.) in dioxan (60 ml.) was added immediately and, after 20 min., the deep red solution was passed successively through columns of Amberlite IR-120 (H^+) and IR-4B (OH^-) resins. The effluent was concentrated to 10 ml., diluted with water (20 ml.), and extracted with ethyl acetate. The aqueous layer was concentrated to a syrup which was dissolved in ethanol. Crystals of 2-acetamido-2-deoxy-D-allose (0·45 g., 73%) separated, m. p. 207—208°, $[\alpha]_D$ −47° (after 1·5 min.) (lit.,[11] m. p. 201—203°, $[\alpha]_D$ −57 ⟶ −48°).

Oxazoline (XIII) *Derived from Methyl* 2-*Benzamido*-2-*deoxy*-β-D-*allofuranoside*.—A solution of the oxazoline (VIII) (14 g.) in methanol (500 ml.) and sulphuric acid (500 ml.; 0·04N) was heated under reflux. Analysis of the solution by t.l.c. (ether as mobile phase) after 3 hr. indicated three products, R_F 0·3, 0·1, and 0·05, respectively. The solution was neutralised with barium carbonate and concentrated to 500 ml. On cooling to 0°, a crystalline product separated and this was recrystallised from aqueous methanol to give the *oxazoline derivative* (XIII) (5 g.) as needles, m. p. 200°, $[\alpha]_D$ −22° (*c* 1 in pyridine), t.l.c. (ether as mobile phase) R_F 0·3, $\nu_{max.}$ 1642 $cm.^{-1}$ (C=N) (Found: C, 60·3; H, 6·0; N, 5·0. $C_{14}H_{17}NO_5$ requires C, 60·2; H, 6·1; N, 5·0%).

The filtrate was evaporated to dryness under reduced pressure and the residue dissolved in ethanol (40 ml.). Ethyl acetate (20 ml.) was added and the crystalline material (0·15 g.) which separated was recrystallised from ethanol–water (3 : 1) to give 2-benzamido-2-deoxy-D-allose as fine needles, m. p. 201—204° (decomp.), t.l.c. (ether as mobile phase), R_F 0·05.

Methyl 2-*Benzamido*-2-*deoxy*-β-D-*allofuranoside* (XII).—The ethyl acetate–ethanol mother-liquor from the previous preparation was concentrated to 20 ml. and ethyl acetate (20 ml.) was added. *Methyl* 2-*benzamido*-2-*deoxy*-β-D-*allofuranoside* (XII) (3·4 g.) separated as needles, m. p. 130—131°, $[\alpha]_D$ −24° (*c* 1 in MeOH), t.l.c. (ether as mobile phase) R_F 0·1, $\nu_{max.}$ 1693, 1583 cm^{-1}. (amide) (Found: C, 56·4; H, 6·4; N, 4·6. $C_{14}H_{19}NO_6$ requires C, 56·5; H, 6·4; N, 4·7%).

2-*Benzamido*-2-*deoxy*-D-*allose* (IX) *from* (XII).—A solution of methyl 2-benzamido-2-deoxy-β-D-allofuranoside (XII) (1·75 g.) in sulphuric acid (60 ml.; 0·1N) was heated under reflux for 30 min. The solution was cooled to 0° and the precipitate (1·4 g.) recrystallised from ethanol–water (2 : 1) to give needles of 2-benzamido-2-deoxy-D-allose, m. p. 201—204°, $[\alpha]_D$ −16° (*c* 1 in H_2O).

Oxazoline (XV) *Derived from Methyl* 2-*Benzamido*-2-*deoxy*-β-D-*ribofuranoside*.—An aqueous solution of sodium metaperiodate (11 ml.; 0·25M) was added to a solution of the oxazoline (XIII) (0·75 g.) in methanol (20 ml.) and water (10 ml.). After 30 min. at room temperature, sodium borohydride (0·7 g.) was added with stirring. After 15 min. the solution was cooled to 0° and the precipitated solid was recrystallised from aqueous methanol to give the *oxazoline* (XV) (0·55 g., 87·5%) as needles, m. p. 99—100°, $[\alpha]_D$ −65° (*c* 1·6 in $CHCl_3$) (Found: C, 62·6; H, 6·2; N, 5·6. $C_{13}H_{15}NO_4$ requires C, 62·6; H, 6·0; N, 5·6%).

Methyl 3,5-*Di*-O-*acetyl*-2-*benzamido*-2-*deoxy*-β-D-*ribofuranoside* (XVI).—An aqueous solution of sodium metaperiodate (30 ml.; 0·25M) was added to a solution of methyl 2-benzamido-2-deoxy-β-D-allofuranoside (2·5 g.) in water (20 ml.). After 1 hr. at room temperature a solution of sodium borohydride (2 g.) in water (50 ml.) was added and after a further 1 hr. the product was isolated and acetylated as described for the corresponding xylose derivative (V). The crude *diacetate* was recrystallised from ethanol–cyclohexane (1 : 2) to give rosettes (1·2 g., 41%), m. p. 115°, $[\alpha]_D$ +29° (*c* 1 in $CHCl_3$) (Found: C, 58·1; H, 6·1; N, 4·1. $C_{17}H_{21}O_7$ requires C, 58·1; H, 6·0; N, 4·0%).

2-*Amino*-2-*deoxy*-D-*ribose Hydrochloride*.—(*a*) A mixture of the oxazoline (XV) (0·35 g.) and hydrochloric acid (5 ml.; 2·6N) was heated under reflux for 4 hr. The cooled solution was extracted with ether and the aqueous layer concentrated to a syrup. The residue was recrystallised from ethanol (1 ml.) to give 2-amino-2-deoxy-D-ribose hydrochloride (0·14 g., 54%) as needles, m. p. 147—148° (decomp.), $[\alpha]_D$ +14 ⟶ −3° (*c* 1 in H_2O) (Found: C, 32·6; H, 6·6; N, 7·3. Calc. for $C_5H_{11}NO_4$,HCl: C, 32·3; H, 6·5; N, 7·5%), paper chromatography *R*(Glucosamine HCl), 1·28 (lit.,[8] m. p. 144—149°, $[\alpha]_D$ +14 ⟶ −3°).

(*b*) Methyl 3,5-di-*O*-acetyl-2-benzamido-2-deoxy-β-D-ribofuranoside was hydrolysed and the product isolated as described above to give D-ribosamine hydrochloride, m. p. 147—148° (decomp.), $[\alpha]_D$ +14 ⟶ −3° (*c* 1 in H_2O).

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[11] R. W. Jeanloz, *J. Amer. Chem. Soc.*, 1957, **79**, 2591.