compound such as an alkali benzenesulphonate cannot be computed accurately (for example, it would be necessary to know the Madelung constant for the crystal structure, and the charge distribution of the polyatomic anion).

However, an empirical correlation between anion hydration heat and lyotropic number has been observed and substantiated.[3-5] The lyotropic number, developed by Buchner *et al.*[6-8] is a quantitative expression of the position of an anion in the lyotropic (Hofmeister) series. When known hydration heats of anions are plotted against the corresponding lyotropic numbers, a linear relationship is observed (Fig. 1). If the lyotropic number of the benzenesulphonate ion can be obtained therefore, the hydration heat of the ion may be determined by interpolation.

The lyotropic number of the benzenesulphonate ion can be derived from the graph due to Buchner and Postma[9] on the flocculation of gelatin sols (Fig. 2). If θ is the angle between the line for $C_6H_5SO_3^-$ and the abscissa, then

$$N - 4{\cdot}78 \cot \theta + 11{\cdot}55 \qquad (3)$$

From the measurement of θ it can be calculated that $N = 14{\cdot}95$, and by interpolation in Fig. 1 it follows that the heat of hydration of the benzenesulphonate ion $W_{\bar{X}} = 56{\cdot}4$ kcal/g ion (298°K).

The procedure illustrated here appears to be the only possible one available at present for the accurate derivation of the hydration heats of various unsymmetrical polyatomic anions.

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Synthesis of methyl 2-acetamido-2-deoxy-β-D-glucofuranoside

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DESPITE the wide distribution of glucosamine in natural products, the ring form and mode of linkage is known only in a few cases and in these, only the pyranose modification has so far been found.[1-3]

The stability which many polysaccharides containing glucosamine show towards acidic hydrolysis is consistent with the behaviour of known pyranosides of glucosamine under identical conditions[4,5] and this is often taken as evidence of the predominance of pyranose form of the amino-sugar in polysaccharide chains.

It is now of interest to examine the stability of furanoside derivatives of glucosamine with a view to assessing the contribution that this form of the amino-sugar may make in polysaccharide structures, particularly as potential sites of acid-labile linkages.

The failure of glucosamine to form glycosides with methanolic hydrogen chloride has led to the investigation of an alternative synthesis via the neutral scission of the sugar mercaptal. Wolfrom *et al.*[6] synthesised a methyl β-thioglycoside of glucosamine and by an analogous route we have now obtained in a crystalline form methyl 2-acetamido-2-deoxy-β-D-glucofuranoside from N-acetyl

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D-glucosamine diethylthioacetal[7,8] by the action of mercuric oxide in methanol.[9] The N-benzyloxycarbonyl-furanoside was obtained in the same way from the appropriately N-substituted mercaptal.

The structure of the new glucoaminides has been assigned on the basis of the following evidence:—

(i) The glycosides were hydrolysed rapidly by mineral acids (0·04 $N \cdot H^+$) with the formation of N-acetyl and N-benzyloxycarbonyl glucosamine respectively. Under identical conditions the corresponding pyranosides were not hydrolysed.

(ii) In the course of hydrolysis, the optical rotation became more dextrorotatory and the glycoside was provisionally designated a β-configuration.

(iii) A series of comparative oxidations was performed simultaneously on the new methyl N-acetyl, and methyl N-benzyloxycarbonyl-β-furanosides and the corresponding pyranosides (methyl N-acetyl-β-glucosaminide, methyl N-benzyloxycarbonyl-α-glucosaminide) N-benzyloxycarbonyl-glucosamine and N-acetylglucosamine. The oxidation with periodate ion was non-stoicheiometrical and in the case of the furanosides was shown to be accompanied in the early stages by the liberation of formaldehyde which is consistent with the presence of a terminal glycol group. In contrast to the pyranoside glycosides, the furanosides were oxidised rapidly by lead tetracetate, one mole of oxidising agent being consumed by one mole of the methyl N-benzyloxycarbonyl furanoside in 6 hr. In the same time, 1 mole of the authentic N-benzyloxycarbonyl pyranoside consumed only 0·3 mole of lead tetracetate. The N-acetyl furanoside was oxidised under identical conditions at a much faster rate than methyl 2-acetamido-2-deoxy-β-D-glucopyranoside.

(iv) The new N-acetyl and N-benzyloxycarbonyl methyl furanosides were methylated with methyl sulphate and sodium hydroxide. Only after acetylation[10] were products obtained containing the calculated methoxyl content for fully etherified substances. Without acetylation, only 90 per cent substitution was effected. The N-substitutent was removed from the fully methylated N-benzyloxycarbonyl furanoside by catalytic hydrogenation and the glycosidic group cleared by hot aqueous acid. In the absence of an N-substitutent, the glycoside was more resistant to hydrolysis and this is in agreement with the findings of Moggridge and Neuberger.[4] The resulting trimethyl glucosamine, formed a crystalline phenylosazone indistinguishable from authentic 3:5:6-trimethyl-D-glucosazone (X-ray powder photograph). Oxidation of trimethyl glucosamine with sodium metaperiodate or ninhydrin yielded a non-crystalline trimethyl pentose chromatographically identical with 2:4:5-trimethyl-D-arabinose.[11]

The new N-acetyl furanoside gave no indication of alkali sensitivity though it gave a weakly positive Elson and Morgan test.

EXPERIMENTAL

C.H.N. analyses were carried out by Drs. Strauss and Weiler (Oxford). Chromatographic examinations were performed on Whatman No. 1 paper with butanol-ethanol-water (4 : 1 : 5) as the elution system, and the sugars revealed with aniline hydrogen phthalate or iodine vapour.

Methyl 2-acetamido-2-deoxy-β-D-glucofuranoside (I)

N-acetyl D-glucosaminediethylthioacetal (5 g) prepared by the method of Whitehouse *et al.*[11] was shaken for 6 hr with mercuric oxide (6·7 g) and mercuric chloride (8·3 g) in dry methanol (50 ml). After heating to 55° for 35 min, the filtered solution was shaken with metallic mercury for 5 days. The inorganic material was separated centrifugally and the supernatant solution evaporated, giving a syrup which crystallised spontaneously. The product, recrystallised from *iso*propanol, had m.p. 193° $[\alpha]_D^{18}$ −20° (*c*, 0·6 in H_2O), R_F 0·31. (Found: C, 42·5; H, 7·33; N, 5·0; OMe, 13·6; $C_9H_{17}O_6$ requires: C, 46·0; H, 7·24; N, 5·95; OMe, 13·2%).

Neuberger and Pitt-Rivers[14] report m.p. 196°, $[\alpha]_D$ −43° (H_2O) for methyl 2-acetamido-2-deoxy-β-D-glucopyranoside.

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Methyl 2-benzyloxycarbonylamino-2-deoxy-β-D-glucofuranoside (II)

N-Benzyloxycarbonyl-D-glucosaminediethylthioacetal (5 g) was dissolved in dry methanol (50 ml) and treated with freshly prepared yellow mercuric oxide (5·5 g) and mercuric chloride (6·25 g) at 37° for 12 hr. A syrupy product was isolated in the above manner, yield 3 g, n_D^{15} 1·5201, $[\alpha]_D^{19}$ −38° (*c*, 0·12 in EtOH), $[\alpha]_D^{23}$ −16° (*c*, 0·65 in H_2O), R_F 0·88 (Found: OMe, 9·7; $C_{15}H_{21}O_7N$ requires: OMe 9·5%).

Acidic hydrolysis of N-*substituted methyl*-D-*glucosaminides*

(i) The N-acetyl-furanoside (I, 120 mg) was heated with sulphuric acid (0·04 N, 25 ml) on a boiling water-bath.

Time (hr)	0	0·5	1	3	6
$[\alpha]_D^{23}$	−20°	+4	+12·5	+30	+41·5

The hydrolysate, which reduced Fehlings solution, was neutralised with barium carbonate and filtered, yielding on evaporation a reducing sugar $[\alpha]_D^{18}$ +44° (H_2O, *c*, 0·48) R_F 0·23. N-acetyl-D-glucosamine shows $[\alpha]_D^{18}$ +42; R_F 0·24. (Authentic methyl 2-acetamido-2-deoxy-β-D-glucopyranoside under identical conditions showed $[\alpha]_D^{23}$ −37 → +31° in 6 hr.)

(ii) N-Benzyloxycarbonyl-furanoside (III, 120 mg) in sulphuric acid (0·04 N, 25 ml) was heated at 100°.

Time (hr)	0	0·5	1·0	2
$[\alpha]_D^{18}$	−15·5	+11·5	+23	+27

The hydrolysate, neutralised with barium carbonate, filtered and evaporated, yielded crystalline N-benzyloxycarbonyl-glucosamine, m.p. 200°, (decomp) chromatographically identical with an authentic specimen.

Authentic methyl 2-benzyloxycarbonylamino-2-deoxy-β-D-glucopyranoside treated with identical reagents was not hydrolysed after 6 hr.

Oxidations with lead tetra-acetate[13]

50–100 mg of glycoside was dissolved in 100 ml of 10% acetic anhydride glacial acetic acid containing 0·77 g lead tetra-acetate. At intervals, 5 ml aliquots were withdrawn, transferred into 10 ml of an iodide buffer (20 g potassium iodide and 250 g anhydrous sodium acetate in 1 l. solution) and the iodine liberated was titrated with 0·02 N sodium thiosulphate. A control consisting of lead tetra-acetate alone was maintained under identical conditions.

(i) *Methyl 2-acetamido-2-deoxy-β-D-glucofuranoside* (I, 57 mg)

Time (hr)	1	2·5	7·5	8·5
$Pb(OAc)_4$ consumed (mole/mole)	0·11	0·22	0·33	0·66

(ii) *Methyl 2-benzyloxycarbonylamino-2-deoxy-β-D-glucofuranoside* (II, 44 mg)

Time (hr)	1	2	3	4	11	22	34	58	82
$Pb(OAc)_4$ consumed (mole/mole)	0·31	0·62	0·80	0·83	0·88	0·92	1·12	1·65	1·80

The presence of formaldehyde (detected by chromatropic acid) and another aldehyde (chromatography) was demonstrated after 12 hr. No N-acetylglucosamine was detected.

(iii) *Methyl N-benzloxycarbonylamino-2-deoxy-α-D-glucopyranoside* (70 mg)

Time (hr)	1	2	3	4	11	22	34	46	58	70
$Pb(OAc)_4$ consumed (mole/mole)	0·05	0·10	0·16	0·23	0·33	0·37	0·55	0·68	0·75	0·80

No formaldehyde was detectable.

(iv) *Methyl 2-acetamido-2-deoxy-β-D-glucopyranoside* (56·8 mg)

Time (hr)	1	7·5	20	32
$Pb(OAc)_4$ consumed (mole/mole)	0·01	0·02	0·04	0·05

(v) *N-benzyloxycarbonyl-D-glucosamine* (50·8 mg)

Time (hr)	1	2	3	4	11	22	34	46	58
$Pb(OAc)_4$ consumed (mole/mole)	0·09	0·16	0·21	0·25	0·38	0·78	1·30	1·68	2·26

(vi) *N-acetyl-D-glucosamine* (38 mg)

Time (hr)	1	2	3	4	11	22	34	46	58
$Pb(OAc)_4$ consumed (mole/mole)	0·04	0·07	0·11	0·15	0·16	0·17	0·23	0·25	0·26

Methylation of 2-benzyloxycarbonylamino-2-deoxy-β-D-glucofuranoside (III)

The glycoside (III, 1·8 g) was acetylated with pyridine (10 ml) and acetic anhydride (4·5 ml) at room temp. After two days, the reaction mixture was poured into ice-water and the oily product extracted with ether and washed with water. After drying, the solvent was removed and the acetylated glycoside (n_D^{22} 1·4930, OMe 6·54% 2·2 g), dissolved in chloroform (20 ml), was treated with dimethyl sulphate (30 ml) and sodium hydroxide (30%, 90 ml) added at 45° over a period of 4 hr with continuous stirring. The reaction mixture was stirred for a further 4 hr, saturated with CO_2 and heated on a boiling water bath for 10 min. The cooled solution was neutralised (pH 7·2) with H_2SO_4 and the product separated by repeated extraction with chloroform. The dried extracts were evaporated giving a syrup (1·4 g), OMe, 20·6%.

This product was subjected to remethylation three times by the same procedure. The final product had R_F 0·94 and OMe, 31·6%. The fully methylated derivative requires OMe, 33·6%.

Hydrogenolysis of fully methylated N-*benzyloxycarbonyl-amino furanoside* (IV)

0·6 g of the glycoside in acetone (10 ml) was shaken with freshly prepared palladium black (0·5 g) in a slow stream of hydrogen.[14,15] After 3 hr when no further CO_2 was evolved, the solution was filtered and evaporated to a syrup $[\alpha]_D^{21}$ −32° MeOH, *c*, 1·2, R_F 0·76. (Found: OMe 39·8; $C_{11}H_{21}O_7N$ (amine carbonate) requires: OMe, 40·4%.)

3:5:6-*trimethyl*-D-*glucosamine hydrochloride* (V)

The above free amino glycoside was not hydrolysed readily by 0·04 N mineral acid, but at 100°, the glycosidic group was removed by 1·5 N HCl, $[\alpha]_D^{18}$ −25 → +31 (12 hr).

The product which reduced Fehlings solution, was extracted by chloroform from the reaction mixture which had been made alkaline (pH 8·5) with NaOH. The extracts were dried over anhydrous sodium carbonate and concentrated to a syrup n_D^{17} 1·4645; R_F 0·65, (Found: OMe, 38·8. $C_9H_{19}O_5N$ (free amine) requires: OMe, 40·2%.)

Isolation of 3:5:6-*trimethyl*-D-*glucosazone*

3:5:6-trimethyl glucosamine (V, 30 mg) was dissolved in water (2 ml) containing sodium acetate (0·2 g) and phenylhydrazine (70 mg) and the solution was heated on a boiling water bath for 2·5 hr. After filtration, the solution was evaporated under reduced pressure to a syrup and the product extracted with ethanol. To this a little water was added and a crystalline product separated m.p. 55–57°, which had an X-ray powder diagram identical with that of authentic 3:5:6-trimethyl D-glucosazone.[16] (The authentic material, crystallised once from aqueous ethanol had m.p. 56–58°.)

Oxidation of 3:5:6-*trimethyl*-D-*glucosamine*

A solution of the trimethyl sugar (5 mg) in acetone was added to an aqueous solution of ninhydrin (0·1 g in 10 ml) containing a little sodium bicarbonate. The solution heated on a boiling water bath acquired the characteristic purple coloration and then a brown precipitate was formed which was removed centrifugally after 1½ hr. The solution was concentrated and chromatographed. A substance having the same R_G value (0·96) as 2:4:5-trimethyl-D-arabinose[16] (VII) was found.

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