Aminosugars and Related Compounds

Part VI*. The Action of Alkali on Some Benzyloxycarbonylamino Derivatives

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The action of aqueous ethanolic sodium hydroxide on methyl 2-benzyloxycarbonylamino-2-deoxy-6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside (II) yields an unexpected product to which the structure methyl 2-amino-3:6-anhydro-2-*N*:4-*O*-carbonyl-2-deoxy- α -D-glucopyranoside (IV) has been allocated. The susceptibility of benzyloxycarbonylamino alkyl derivatives towards alkali appears to be influenced by the presence of hydroxyl groups in the same molecule. Benzyloxycarbonylamino*cyclohexane* is converted to a mixture of *dicyclohexylurea* and *ethoxycarbonylamino*cyclohexane** by the action of alkali. Several new derivatives of methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside are described.

The action of alkali on suitable 6-*O*-toluene-*p*-sulphonyl-D-glycopyranoside derivatives yields 3:6-anhydro-D-glucopyranoside compounds¹. The reaction occurs in other hexopyranose derivatives and has been well studied². 2-Amino-3:6-anhydro-2-deoxy-D-glucose and its derivatives are however unknown and an attempted synthesis of a derivative by the alkaline treatment of methyl 2-benzyloxycarbonylamino-2-deoxy-6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside (II) gave unexpected results.

Treatment of methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside (I) with one mole of toluene-*p*-sulphonyl chloride in pyridine gave, as anticipated³, the 6-*O*-toluene-*p*-sulphonate (II). That the C₆ hydroxyl group had been substituted in this reaction was indicated by the ready exchange of the toluene-*p*-sulphonyloxy residue for iodine on treatment of (II) with sodium iodide in acetone at 100° for 2 h to yield methyl 2-benzyloxycarbonylamino-2:6-di-deoxy-6-iodo- α -D-glucopyranoside (III). This type of exchange

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reaction is generally characteristic of primary toluene-*p*-sulphonates ^{3,4}. The consumption of approximately 1 mole of lead tetra-acetate by the 6-*O*-toluene-*p*-sulphonate (II) indicated the presence of a vicinal glycol grouping in the molecule and confirmed the allocated structure. When methyl 2-benzyloxy-carbonylamino-2-deoxy-6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside (II) was treated with 0.33 N sodium hydroxide in boiling aqueous ethanol (water-ethanol 1:2 v/v)* a rapid reaction took place ($[M]_D + 445^\circ \rightarrow + 93^\circ$ during 30 min). An almost identical change in $[M]_D$ occurred during 36 h when the reaction was carried out at room temperature. Only one compound, *A*, could be isolated from the reaction and it appeared to be the major if not the sole product. Compound *A* has been allocated the structure methyl 2-amino-3:6-anhydro-2-*N*:4-*O*-carbonyl-2-deoxy- α -D-glucopyranoside (IV) on the basis of the following arguments and observations.

Elemental analysis was consistent with the formula $C_8H_{10}O_5N$ and the molecular weight (196) obtained by cryoscopy in water indicated a monomeric structure.

Evidence, which may be interpreted as indicating the presence of a 3:6-anhydro ring in compound *A*, is provided by infra-red spectra measurements. The spectra of a series of 3:6-anhydrohexopyranosides have been studied by Barker and Stephens ⁵, who found that, in general the spectrum of a 3:6-anhydro compound in the region 700—900 cm^{-1} was more complex than that of the parent glycoside. Further, the 3:6-anhydrohexopyranosides showed apparently characteristic absorptions in the ranges 870 ± 7 , 838 ± 16 , 798 ± 21 and 747 ± 11 cm^{-1} (for a discussion of the assignment of these absorptions reference should be made to the original paper ⁵). The absorptions at 878, 860, 820 and 755 cm^{-1} shown by compound *A* provide a reasonably close parallel with these findings and are suggestive of a 3:6-anhydro hexopyranoside structure.

Table 1 illustrates the similarities in the infra-red spectra in the region 700—900 cm^{-1} of methyl 3:6-anhydro- α -D-glucopyranoside, Compound *A* and the respective parent compounds.

Table 1.

Methyl α -D-glucopyranoside ^a	896 s		840 s		745 s
Methyl 3:6-anhydro- α -D-glucopyranoside ^a	909 vs 892 vs	868 s	842 s	815 vs	742 vs
Methyl 2-benzyloxycarbonyl-amino-2-deoxy- α -D-glucopyranoside ^{b,c}	902 w 910 w		850 w		740 m 764 m
Methyl 2-amino-3:6-anhydro-2- <i>N</i> :4- <i>O</i> -carbonyl-2-deoxy- α -D-glucopyranoside (Compound <i>A</i>) ^b	900 w 914 s	878 w	860 m	820 w	755 m 762 m

^a Data taken from Ref. ⁵ and measured in "Nujol" mulls.

^b Measured in KBr discs.

^c Also showed absorption at 779 cm^{-1} (w).

Key: w weak, m medium, s strong, v very.

* Unless otherwise stated, subsequent reference to alkali implies a reagent of this composition.

Further evidence suggesting the presence of a 3:6-anhydro-ring in compound *A* is the similar changes in optical rotation which occur when methyl 6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside¹ and methyl 2-benzyloxycarbonylamino-2-deoxy-6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside (II) are treated with alkali. The ready conversion, under these conditions, of the former compound to methyl 3:6-anhydro- α -D-glucopyranoside is well established¹.

Proof of the presence of a 3:6-anhydro ring in compound *A* followed when, on vigorous acidic hydrolysis a product *B*, presumably 2-amino-3:6-anhydro-2-deoxy-D-glucofuranose, was obtained which appeared homogeneous and displayed properties anticipated for an anhydro aminosugar on examination by paper chromatography and zone electrophoresis (ionophoresis). Reaction of *B* with phenylhydrazine yielded a compound identical with 3:6-anhydro-D-glucose phenylosazone obtained by treatment of authentic 3:6-anhydro-D-glucofuranose with phenylhydrazine.

Absorption in the range 1700–1736 cm⁻¹ (amide I band) of a series of carbamates (R—O.CO.NH.R') has been associated with the carbonyl group⁶. Thus the strong absorption at 1708 cm⁻¹ in the spectrum of compound *A* is consistent with the presence of a carbamate grouping. However, the absence of absorption at *ca.* 1540 cm⁻¹ indicated that the carbamate grouping, if present, was part of a cyclic structure. Although an adequate explanation is lacking, it is well established⁶ that the amide II band (N—H deformation) characteristic of acyclic amides is not shown when the NH—CO grouping is part of a cyclic system. This is true of tetrahydro-1:3-oxazine-2-one⁷, the simplest cyclic carbamate analogue of compound *A*, and of a wide range of other related compounds^{6,8}. The absorption at 3280 cm⁻¹ in the spectrum of compound *A* is therefore most likely due to an N—H bond and not to an O—H bond, an inference substantiated by the fact that compound *A* could not be converted to an *O*-acetate or *O*-toluene-*p*-sulphonate.

Since a 3:6-anhydro-ring is present in compound *A*, then, in a pyranoside structure, a cyclic carbamate grouping can involve only the amino and hydroxyl groups on C₂ and C₄ respectively. That the C₄-hydroxyl group is blocked is suggested by the resistance of compound *A* to cold dilute acid. Methyl 3:6-anhydro- α - and β -D-glucopyranoside¹ (and related compounds²) readily undergo an acid catalysed intramolecular rearrangement to yield the corresponding furanoside compounds. However, this rearrangement does not occur if the C₄-hydroxyl group is blocked, *e.g.* by methylation¹ (or in the galactose series⁹ where the C₄-hydroxyl group is located in a sterically unfavourable position).

The presence of the carbamate grouping in compound *A* was confirmed when vigorous acidic hydrolysis liberated carbon dioxide.

Formation of the 3:6-anhydro-ring during the action of alkali on methyl 2-benzyloxycarbonylamino-2-deoxy-6-*O*-toluene-*p*-sulphonyl- α -D-glucopyranoside (II) probably precedes the formation of the cyclic carbamate since, under similar alkaline reaction conditions, methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside (I), in which 3:6-anhydro-ring formation is precluded, does not form a cyclic carbamate but undergoes rapid (*ca.* 30 min) decarboxylation (separation of sodium carbonate). Examination of accurate scale models shows that initial formation of the 3:6-anhydro-ring, following

the action of alkali on the 6-*O*-toluene-*p*-sulphonate (II), would bring the benzyloxycarbonylamino and hydroxyl groups at C₂ and C₄, respectively, into *meta* axial positions so that the hydroxyl group would be very favourably situated for nucleophilic attack on the carbonyl group of the benzyloxycarbonylamino residue with consequent expulsion of the benzyloxy group.

The stability of benzyloxycarbonylaminoalkyl groups towards alkali appears to be significantly influenced by the presence of hydroxyl groups in the same molecule. This is illustrated by the examples quoted above and by the facts that both 2-benzyloxycarbonylaminoethanol and 3-benzyloxycarbonylamino-1-propanol underwent rapid decarboxylation (30 min) on treatment with alkali. On the other hand benzyloxycarbonylamino-*cyclohexane* was much more resistant. Treatment of this compound (readily obtained from the reaction of *cyclohexylamine* and benzylchloroformate) with alkali for 12 h did not cause complete reaction since 8 % of pure starting material could be recovered. The main product (59 %) formed together with benzyl alcohol was dicyclohexylurea, identical with the compound obtained by the reaction of dicyclohexyl carbodi-imide and phosphoric acid. Also produced in the reaction was ethoxycarbonylamino-*cyclohexane* (*N*-carbethoxycyclohexylamine) identical with the product obtained by the action of ethylchloroformate on *cyclohexylamine*. No reaction occurred when benzyloxycarbonylamino-*cyclohexane* was treated with 0.33 N sodium hydroxide in aqueous dioxan (66 % dioxan).

The preceding observations indicate that care must be exercised in the selection of the amine protecting group in aminosugar syntheses where the use of alkaline reagents is contemplated.

Parallel with the above investigations a number of derivatives of methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside were prepared. Treatment¹⁰ of methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside with benzaldehyde at 140° yielded methyl 4:6-*O*-benzylidene-2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside which gave a crystalline 3-*O*:methyl ether, 3-*O*-benzoate, 3-*O*-methanesulphonate and 3-*O*-toluene-*p*-sulphonate. The location of the benzylidene residue across the C₄:C₆-hydroxyl groups in these compounds was shown on acidic hydrolysis of the 3-*O*-methyl derivative when known¹¹ 2-amino-2-deoxy 3-*O*-methyl-D-glucose hydrochloride was formed. This latter compound was readily converted to crystalline *N*-(2:4-dinitrophenyl) and *N*-(2-hydroxynaphthylidene-1) derivatives.

- I, R = OH
 II, R = CH₂ · C₆H₄ · SO₂ · O
 III, R = I

IV

EXPERIMENTAL

Methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-toluene-p-sulphonyl- α -D-glucopyranoside. A solution of methyl 2-benzyloxycarbonylamino-2-deoxy- α -D-glucopyranoside¹² (1 g, m. p. 159°, $[\alpha]_D +89^\circ$ in pyridine) in dry pyridine (10 ml) was cooled (0°) and treated gradually with a solution of freshly recrystallized toluene-*p*-sulphonyl chloride (0.58 g) in dry pyridine (2 ml). After storage at 0° for 2 h and then at room temperature overnight the reaction mixture was poured into ice water (150 ml). The oily compound which separated solidified after vigorous agitation of the suspension for 1 h. It was collected (0.73 g, 50 %) and recrystallized from aqueous-ethanol (50 %, v/v) to yield the product, m. p. 103°, $[\alpha]_D +96^\circ$ (c, 1.0 in ethanol). Kyi¹³ reports m. p. 103–104° for this product.

A solution of the above toluene-*p*-sulphonate (96 mg) in glacial acetic acid (20 ml) was treated with a 2.9 % solution (25 ml) of lead tetra-acetate in glacial acetic acid and the volume rapidly adjusted to 50 ml. Aliquots were withdrawn at suitable time intervals and the consumption of oxidant determined by a standard procedure¹⁴; the following results were obtained.

Time (h)	1	24	48	72	96	120
Oxidant consumed (mole)	0.096	0.29	0.483	0.725	0.918	0.918

Methyl 2-benzyloxycarbonylamino-2:6-dideoxy-6-iodo- α -D-glucopyranoside. A solution of methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-toluene-*p*-sulphonyl- α -D-glucopyranoside (0.8 g) and sodium iodide (1.6 g) in acetone (16 ml) was heated in a sealed tube at 100° for 2 h. Sodium *p*-toluenesulphonate was precipitated. After filtration the reaction mixture was diluted to turbidity with water and stored at 0°. The product (0.7 g, 96 %) separated and after recrystallization from alcohol it had m. p. 156°, $[\alpha]_D +77^\circ$ (c, 1.0 in acetone). (Found: C 41.5; H 4.7; N 3.1; I 29.0. $C_{15}H_{20}O_6NI$ requires C 41.2; H 4.6; N 3.2; I 29.1.)

Action of alkali on methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-toluene-p-sulphonyl- α -D-glucopyranoside. A solution of methyl 2-benzyloxycarbonylamino-2-deoxy-6-O-toluene-*p*-sulphonyl- α -D-glucopyranoside (1 g) in ethanol (10 ml) and N sodium hydroxide (5 ml) was boiled under reflux. $[\alpha]_D$ changed $+92.5 \rightarrow +19.4^\circ$ (based on the weight of the 6-O-toluene-*p*-sulphonate) during 30 min. After cooling and neutralisation with carbon dioxide the reaction solution was concentrated at 45° (bath)/15 mm, the residue extracted with boiling acetone (20 ml) for 15 min and the extract clarified by filtration through a carbon pad. Evaporation of the filtrate yielded a syrup which crystallized on trituration with ethyl acetate (3 ml) and heating. *Methyl 2-amino-3:6-anhydro-2-N:4-O-carbonyl-2-deoxy- α -D-glucopyranoside* (0.27 g, 65 %) obtained thus had m. p. 172°, $[\alpha]_D +46.4^\circ$ (c, 1.0 in water). (Found: C 47.5; H 5.5; N 6.6. $C_8H_{11}O_6N$ requires C 47.8; H 5.5; N 7.0.)

When the reaction was allowed to proceed at room temperature $[\alpha]_D$ changed $+92.5^\circ \rightarrow +19.2^\circ$ (final constant value) during 36 h. From the solution a product (0.29 g, 69.5 %) was isolated and found to be identical with that described above.

A solution of methyl 2-amino-3:6-anhydro-2-N:4-O-carbonyl-2-deoxy- α -D-glucopyranoside (0.1304 g) in deionized water (4.8137 g) depressed the freezing point by 0.255°. Employing a freezing point constant of 18.5 (determined using 2-acetamido-2-deoxy-D-glucose as a standard) these results indicate a molecular weight of 196 (calc. 201).

Acidic hydrolysis of methyl 2-amino-3:6-anhydro-2-N:4-O-carbonyl-2-deoxy- α -D-glucopyranoside. A solution of (a) the cyclic carbamate (0.1 g) in 0.1 N sulphuric acid (5 ml) showed no change in $[\alpha]_D$ during 24 h storage at room temperature; neutralisation and evaporation of the solution gave unchanged starting material, (b) the cyclic carbamate (0.13 g) in 3 N hydrochloric acid (10 ml) was boiled under reflux in a stream of nitrogen for 3 h. The carbon dioxide evolved was collected as barium carbonate (105.4 mg, 83.5 %) which was formed on passage of the effluent gases through barium hydroxide solution.

The hydrolysate was freed from hydrochloric acid by prolonged codistillation with water at 40° (bath)/14–16 mm. Final evaporation yielded amorphous B, presumably 2-amino-3:6-anhydro-2-deoxy-D-glucofuranose hydrochloride (0.075 g). The infra red

spectrum (KBr disc) of the product showed absorption at 825 and 878 cm^{-1} indicative ⁵ of furanose configuration. The hydrolysate was examined by zone electrophoresis (ionophoresis) on Whatman No. 3 paper using the enclosed strip technique ¹⁵. With a borate buffer ¹⁶ (pH 10) a single compact zone, M_G 0.9, was detected with aniline hydrogen phthalate. Under the same conditions 2-amino-2-deoxy-D-glucose affords a rather diffuse zone. In an acetate buffer (pH 5) a single zone of higher mobility than that of 2-amino-2-deoxy-D-glucose could be detected with ninhydrin.

Paper chromatographic analysis of the hydrolysate using the *tert*-butanol-acetic acid-water (2:1:1) solvent system ¹⁷ revealed a single component, detected with ninhydrin with R_F value (0.497) significantly higher than that of 2-amino-2-deoxy-D-glucose (0.327) but similar to that of 2-amino-1:6-anhydro-2-deoxy-D-gulopyranose ¹⁸ and the altrose analogue ¹⁸. A solution of *B* (57.8 mg) in water (1 ml) was treated with acetic acid (0.1 ml), phenylhydrazine (0.12 g) and sodium acetate (0.18 g) and the mixture maintained at 95° for 1.5 h. The solid which separated on cooling was dissolved in methanol (2 ml) and diluted with water (20 ml). 3:6-Anhydro-D-glucose phenylosazone (5.9 mg) separated and after collection and washing with water it gave an infra-red spectrum (KBr disc) identical with that of authentic material described below.

Under identical reaction conditions 2-amino-2-deoxy-D-glucose hydrochloride (50 mg) yielded D-glucosephenylosazone (15.6 mg).

3:6-Anhydro-D-glucosephenylosazone. Crystalline 3:6-anhydro-D-glucose (50 mg) was treated at 75–80° for 2 h with a solution (3 ml) prepared from water (25 ml), sodium acetate (2 g), acetic acid (1 ml) and phenylhydrazine (1 g). On cooling a mixture of crystals and oil separated. The crystals were freed from oil by trituration with aqueous methanol yielding 3:6-anhydro-D-glucose phenylosazone (27.4 mg), m. p. 185–187°. A further amount (13.5 mg) of product was obtained on dilution of the combined mother liquors with water.

Benzylloxycarbonylaminocyclohexane. Sodium hydrogen carbonate (21 g) was added to a solution of cyclohexylamine (25 g) in water (150 ml) followed by benzyl chloroformate (43 g) gradually during 1 h with continuous vigorous stirring. The crude product was collected, washed successively with light petroleum (60–80°) and water, then dissolved in ether and the solution dried (MgSO_4). Addition of light petroleum (60–80°) gave *benzylloxycarbonylaminocyclohexane*. (39 g, 66 %), m. p. 93° (Found: C 72.4; H 8.0; N 6.0. $\text{C}_{14}\text{H}_{23}\text{O}_2\text{N}$ requires C 72.1; H 8.15; N 6.0). Infra-red spectrum (KBr disc) showed absorptions at 1 545 cm^{-1} (amide II band) and 1 688 cm^{-1} (amide carbonyl).

Action of alkali on benzylloxycarbonylaminocyclohexane. (a) A solution of benzylloxycarbonylaminocyclohexane (25 g) in N sodium hydroxide (125 ml) and ethanol (250 ml) was boiled under reflux for 12 h. On cooling sodium carbonate (2.4 g) separated. The solution was neutralised with carbon dioxide, freed from insoluble material and fractionally distilled using a 12" column packed with nickel gauze. Ethyl alcohol was collected at 78° followed by a fraction at 98° which after condensation separated into three phases *B*, *C* and *D* of increasing density, respectively. *N:N'*-Dicyclohexyl urea (7.1 g) separated after dissolution of the still residue in aqueous alcohol; it had, after recrystallization from alcohol, m. p. 236° alone or in admixture with an authentic specimen. (Found: C 69.4; H 10.75; Calc. for $\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}$: C 69.5; H 10.7.) The identity of the compound was confirmed by infra-red spectroscopy. From the mother liquors by dilution with water unchanged benzylloxycarbonylaminocyclohexane (1.6 g, 8 %) separated with m. p. 92° alone or in admixture with authentic material.

Examination of fractions *B* and *D* by gas phase chromatography (Perkin-Elmer apparatus with packing A at 155° with a flow rate of 15 ml/min) revealed a single component with properties closely similar to those of benzyl alcohol.

The infra-red spectra (liquid film) of fractions *B* and *D* revealed a very close similarity indeed and both showed strong absorptions at 1 692 (amide carbonyl ⁹), 1 572 (amide II band, characteristic of acyclic amides) and 697 and 738 cm^{-1} (aromatic group).

Portions of fractions *B* and *D* were combined (2 ml total volume), diluted with 50 % aqueous ethanol (3 ml) and stored at 0°. Ethoxycarbonylaminocyclohexane separated and after recrystallization from ethanol-ether it had m. p. 56° alone or in admixture with an authentic sample. Identity was confirmed by infra-red spectroscopy.

The infra-red spectrum (liquid film) of a solution of ethoxycarbonylaminocyclohexane (1 g) in benzyl alcohol (2 ml) was virtually identical with the spectra of fractions *B* and *D*.

Ethoxycarbonylamino-cyclohexane. To a solution of cyclohexylamine (20 g) and sodium hydrogen carbonate (18 g) in water (100 ml), ethyl chloroformate (22 g) was gradually added during 1 h with constant vigorous stirring of the mixture. The crude product was collected, washed with water and a small volume of cold ethanol. Recrystallization from ethanol-ether afforded ethoxycarbonylamino-cyclohexane (23 g, 66.5 %) m. p. 55–56°. (Gillibrand and Lamberton¹⁹ record m. p. 56° for this compound prepared by a different procedure.) The infra-red spectrum (KBr disc) showed absorptions at 1537 cm⁻¹ (amide II absorption) and 1700 cm⁻¹ (amide carbonyl).

N:N'-Dicyclohexylurea. A solution of dicyclohexylcarbodi-imide (1 g) in ether (4 ml) was added to a solution of phosphoric acid (0.86 g) in ether (20 ml). Recrystallization, of the product which separated, after 30 min from ethanol yielded N:N'-dicyclohexyl urea (0.7 g, 64 %), m. p. 235°. (Skita and Rolfes²⁰ record m. p. 230° for this compound prepared by a different method.) The infra-red spectrum (nujol mull) showed absorptions at 1541 cm⁻¹ (amide II absorption) and 1633 cm⁻¹ (amide carbonyl).

Methyl 4:6-O-benzylidene-2-benzylloxycarbonylamino-2-deoxy-α-D-glucopyranoside. Methyl 2-benzylloxycarbonylamino-2-deoxy-α-D-glucopyranoside (2 g) was heated with freshly distilled benzaldehyde at 140–145° for 5 h whilst a stream of carbon dioxide was passed through the reaction mixture. The cooled mixture was then diluted with light petroleum (10 vol, 60–80°) and the precipitate (2.0 g) collected, washed with light petroleum and recrystallized from chloroform-acetone. *Methyl 4:6-O-benzylidene-2-benzylloxycarbonylamino-2-deoxy-α-D-glucopyranoside* (1.82 g, 71.5 %) was obtained, m. p. 209–210° [α]_D +51° (c, 1.0 in chloroform). (Found: C 63.3; H 5.8; N 3.7. C₂₅H₂₅O₇N requires C 63.6; H 6.0; N 3.4.)

By the usual methods the benzylidene compound was converted to a 3-O-toluene-*p*-sulphonate, m. p. 116°, after softening at 60–65°, [α]_D +8° (c, 1.0 in CHCl₃). (Found: C 61.1; H 5.5; N 2.2; S 5.9. C₂₅H₃₁O₉NS requires C 61.2; H 5.45; N 2.5; S 5.6); 3-O-benzoate, m. p. 165–166°, [α]_D +43° (c, 1.0 in CHCl₃). (Found: C 67.3; H 5.6; N 2.4. C₂₉H₂₉O₈N requires C 67.1; H 5.6; N 2.7); 3-O-methanesulphonate, m. p. 138–140°, [α]_D +38° (c, 1.0 in CHCl₃). (Found: C 55.7; H 5.3; N 2.8; S 6.7. C₂₃H₂₇O₉NS requires C 56.0; H 5.5; N 2.8; S 6.5.)

Methylation of methyl 4:6-O-benzylidene-2-benzylloxycarbonylamino-2-deoxy-α-D-glucopyranoside. A solution of methyl 4:6-O-benzylidene 2-benzylloxycarbonylamino-2-deoxy-α-D-glucopyranoside (0.5 g) in methyl iodide (6 ml) was boiled under reflux in the presence of dry silver oxide (1 g) for 2 h. During this period two additional amounts (1 g) of silver oxide were added. After filtration through a carbon pad the reaction mixture was evaporated and the residue recrystallized from a methanol-chloroform mixture. *Methyl 4:6-O-benzylidene-2-benzylloxycarbonylamino-2-deoxy-3-O-methyl-α-D-glucopyranoside* (0.32 g) was obtained, m. p. 223–224°. (Found: C 64.3; H 6.2; N 3.1. C₂₃H₂₇O₇N requires C 64.3; H 6.3; N 3.3.)

A solution of the above methyl ether (1 g) in 2.5 N hydrochloric acid (15 ml) was boiled under reflux for 4 h. After filtration through a carbon pad the hydrolysate was diluted with water and twice extracted with light petroleum (60–80°). Subsequent evaporation of the aqueous solution gave a syrupy residue which crystallized from methanol-acetone to yield 2-amino-2-deoxy-3-O-methyl-D-glucose hydrochloride (0.25 g, 47 %), m. p. 210–215° (decomp.) with discoloration at ca. 175°. (Neuberger¹¹ records m. p. 215° for this compound prepared by a different method.) Examination of the crystalline methyl ether by paper chromatography using the organic phase of a butanol-ethanol-water (4:1:5) system revealed that it contained a trace of the parent amino sugar.

2-Amino-2-deoxy-3-O-methyl-D-glucose hydrochloride was readily converted to an *N*-(2,4-dinitrophenyl) derivative which darkened at ca. 174° and had m. p. 184°. (Found: C 42.6; H 4.5; N 11.7. C₁₃H₁₇O₉N₃ requires C 43.45; H 4.7; N 11.7) and an *N*-(2-hydroxynaphthylidene-1) derivative, m. p. 184–185° (decomp.). (Found: C 62.6; H 6.0; N 4.1. C₁₈H₂₁O₈N requires C 62.3; H 6.05; N 4.0.)

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