ACTA CHEMICA SCANDINAVICA 15 (1961) 87–95

Phenyl*iso*cyanate Derivatives of Carbohydrates

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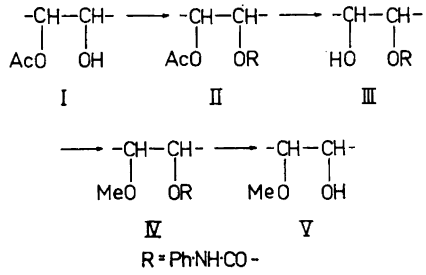
An investigation was made of a method of locating the acetyl groups in partially acetylated carbohydrates using phenyl*iso*cyanate for introducing protective substituents. It was found that the derived phenylcarbamoyl groups sometimes undergo acyl migration but that generally the reagent is suitable for use in the determination of the substituent distribution in partially acetylated 1→4-linked xylans and glucans.

Locating the *O*-acetyl groups in partially acetylated carbohydrates is complicated by their lability. It seemed that locating these groups might be facilitated by using phenyl*iso*cyanate for the introduction of protective groups. In the procedure used here the acetyl groups are replaced by methyl groups according to the reaction sequence I—V (R = phenylcarbamoyl group, Ph · NH · CO—). The *O*-methyl groups are then easily localised by standard methods.



Such a procedure must satisfy the following requirements: (a) Phenyl*iso*cyanate should react quantitatively with the free hydroxyl groups under conditions that do not affect the acetyl groups; (b) The derived phenylcarbamoyl groups should not be affected by the deacetylation; (c) The phenylcarbamoyl groups should not migrate on methylation of the deacetylated products; (d) The phenylcarbamoyl groups should be easily removed to give the partially methylated compound.

To investigate these points the reaction sequence I—V or part of it was applied to the following D-glucose derivatives:

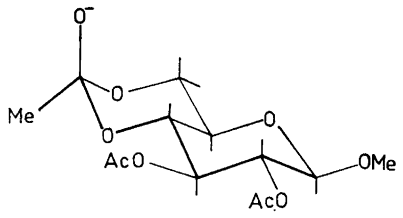
Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside;
Methyl 6-*O*-acetyl-β-D-glucopyranoside;
Methyl β-D-glucopyranoside 2,3-di(phenylcarbamate);
1,2-*O*-*iso*propylidene-3-*O*-acetyl-α-D-glucofuranose;
1,2-*O*-*iso*propylidene-6-*O*-acetyl-α-D-glucofuranose.

Phenyl*iso*cyanate is known to react quantitatively with hydroxyl groups and it is possible to prepare fully substituted glycosides quite readily.[1] The reaction is usually carried out in pyridine but neutral solvents such as benzene can also be used[2]. It has been claimed[3,4] that when partially acetylated carbohydrates are treated with phenyl*iso*cyanate, no migration of the acetyl groups takes place. The absence of migration was confirmed by conversion of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside to 2,3,4-tri-*O*-methyl-D-glucose by application of the reaction sequence I—V followed by hydrolysis.

After substitution of the free hydroxyl groups in the partially acetylated derivative, deacetylation was carried out at room temperature in methanol or ethanol-acetone containing about 2 % of sulphuric or hydrochloric acid. The reaction was complete after 20—50 h. The stability of the phenylcarbamoyl group to acid hydrolysis was shown by treating methyl α-D-glucopyranoside 6-phenylcarbamate for 20 h with 3 % sulphuric acid at 100°. Only a faint trace of glucose was detected on chromatography of the hydrolysate.

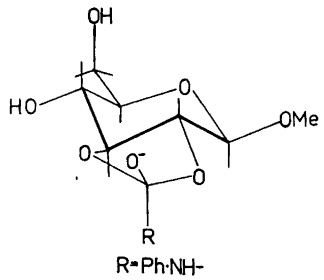
Boiling sodium methoxide solution has been used to remove phenylcarbamoyl groups in carbohydrates[2]. Thus methyl α-D-glucopyranoside 6-phenylcarbamate, prepared by treatment of methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside with phenyl*iso*cyanate followed by deacetylation[3], gave methyl α-D-glucopyranoside in good yield when treated for 1 h with 1.5 equivalents of sodium methoxide in boiling methanol. Phenylcarbamates are, however, rapidly N-methylated when treated with iodomethane and silver oxide in *N*,*N*-dimethylformamide (DMFA) and this increases the resistance to alkaline hydrolysis. Lithium aluminium hydride (LAH) has previously been used for reductive removal of phenylcarbamoyl groups[5]. It was now found that *N*-methyl-phenylcarbamoyl groups also reacted smoothly with LAH using dioxan or tetrahydrofuran as solvent. The reductive removal was complete in 3—4 h.

The phenylcarbamates are carboxylic esters. These groups would therefore be expected to undergo acyl migration when the steric conditions are favourable, in an analogous way to the ready migration of the otherwise extremely stable mesitoyl group to the C_2 hydroxyl when 1-*O*-mesitoyl-2,3,4,6-tetra-*O*-acetyl-α-D-glucose is deacetylated in methanolic ammonia at 0°[6]. Acyl migration in carbohydrates has been reviewed by Pacsu[7] and Sugihara[8]. Lately Bonner[9] has devoted a series of investigations to the subject. The migration is assumed to proceed over an orthoester intermediate[10] and it is noticeable that it is possible to construct molecular models of orthoester intermediates in all cases where the course of an acyl migration has been established.



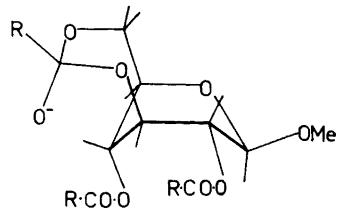
VI

Migration of an acetyl group from the C_4 to the C_6 hydroxyl group in D-glucose is known to take place very easily, for instance on methylation of its 2,3,4-tri-*O*-acetyl derivatives [11,12]. The assumed intermediate (VI) consists of two strainless 6-membered rings with the glucose in the C*1* conformation. To test whether phenylcarbamoyl groups are liable to migrate or not, an examination was made of the products formed on methylation of methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate), prepared by treatment of methyl 6-*O*-acetyl-β-D-glucopyranoside with phenyl*iso*cyanate and subsequent deacetylation. The main methylation product was a crystalline compound (yield 67 %, calculated as methyl mono-*O*-methyl-β-D-glucopyranoside tri-(*N*-methyl-phenylcarbamate) which on reduction with LAH gave crystalline methyl 4-*O*-methyl-β-D-glucopyranoside. In addition to the crystalline compound, which must be assigned a methyl 4-*O*-methyl-β-D-glucopyranoside 2,3,6-tri-(*N*-methyl-phenylcarbamate) structure, there was also obtained some non-crystalline material. On reduction with LAH and subsequent hydrolysis this gave 4-*O*-methyl-D-glucose as main product together with a quantity of 6-*O*-methyl-D-glucose corresponding to 5—10 % of the original methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). It is thus obvious that the phenylcarbamate group can migrate. The small amount of 6-*O*-methyl-D-glucose found indicates, however, that some methylation of the 6-positions occurred before the migration took place. The methyl 4-*O*-methyl-β-D-glucopyranoside obtained on methylation of methyl 2,3,4-tri-*O*-acetyl-β-D-glucopyranoside [12] was also accompanied by a small amount of the 2-*O*-methyl isomer showing that in this case some migration from the C_2 to the C_4 hydroxyl took place before the methylation of the C_4 hydroxyl was completed.



VII

The main purpose of the present investigation was to find a suitable procedure for determining the distribution of substituents in the partially acetylated xylan from birch wood [13] and in partially acetylated cellulose. A migration of acyl groups from the C_2 to the C_3 hydroxyl groups does not seem to be possible by the accepted mechanism as the formation of an intermediate orthoester (VII) would require a considerable distortion of bonds. The same applies for migration from the C_2 to the C_6 hydroxyl in cellulose. Inspection of molecular models shows that migration might be possible over a somewhat hindered intermediate (VIII) from the C_3 to the C_6 hydroxyl groups in



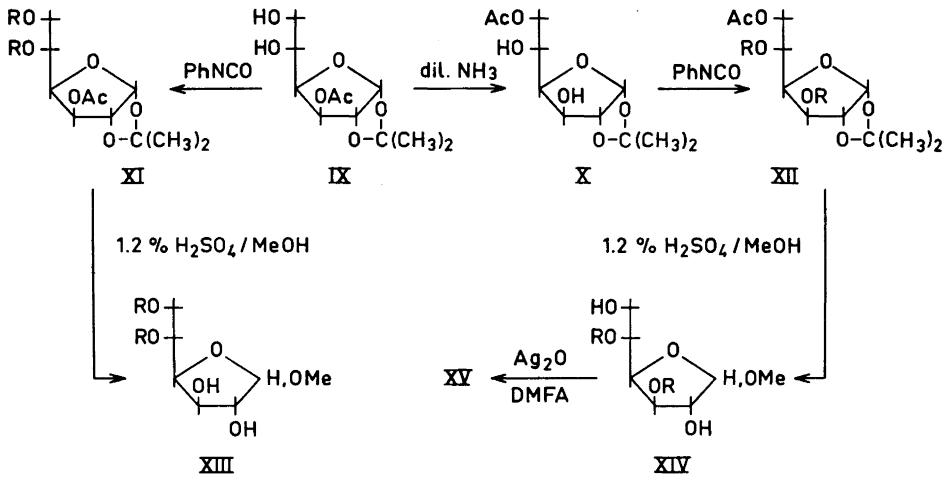
R= Ph·NH-

VIII

glucopyranose structures with 1 C and 1 B conformations. To investigate this, methyl β-D-glucopyranoside 2,3-di(phenylcarbamate) was methylated with iodomethane and silver oxide in DMFA and the product was reduced with LAH and hydrolysed. Crystalline 4,6-di-*O*-methyl-D-glucose was the sole product. This shows that neither $C_3 \rightarrow C_6$ nor $C_3 \rightarrow C_4$ migration took place. As no $C_3 \rightarrow C_4$ migration occurred the inference might be drawn that neither would $C_2 \rightarrow C_3$ migration occur in glucose or xylose as the $C_2 - C_3$ and $C_3 - C_4$ groupings are conformationally similar. It appears from this that the reaction sequence I—V should therefore be applicable to the determination of the substituent distribution in partially acetylated 1 → 4-linked xylans and glucans.

Josephson [14] has investigated the kinetics of the rearrangement of 1,2-*O*-*iso*propylidene-3-*O*-acetyl-α-D-glucofuranose (IX) to the 6-*O*-acetyl isomer (X). For an intended comparison of the rates of migration of acetate and phenylcarbamoyl groups, analoguous 3- and 6-phenylcarbamoyl D-glucofuranose derivatives were prepared. IX and X were treated with phenyl*iso*cyanate to give the 5,6- (XI) and 3,5-di(phenylcarbamates) (XII), respectively. These were then deacetylated with simultaneous glycosidation according to Haworth and Porter [15] yielding the amorphous 5,6- and 3,5-di(phenylcarbamates) of methyl D-glucofuranoside (XIII and XIV, respectively), mainly as the β-anomers [15]. It was anticipated that the 3-*O*-phenylcarbamoyl group in XIV would migrate to the 6-position by analogy with the behaviour of the 3-*O*-acetyl group in IX. No change in the optical rotation was, however, observed when XIV was treated with saturated ammoniacal methanol. On treatment with silver oxide in DMFA the specific rotation in methanol changed from —35° to —26°. The same treatment of XIII had no effect on its rotation (—14°).

The infrared spectra of XIV and of its derived product XV were very similar except that XIV showed a weak band at 1 800 cm^{-1} and XV a weak band



at 1 650 cm^{-1}. These spectra were, however, easily distinguished from that of XIII, especially in the regions for the amide I (1 700 — 1 725 cm^{-1}) and amide II (1 540 — 1 550 cm^{-1}) bands, the bands for the C-O stretching vibration of the ester groups (1 200 — 1 260 cm^{-1}) and the bands associated with the stretching mode of C-O bonds in hydroxyl groups (1 040 — 1 125 cm^{-1})[16].

XV, on acetylation with acetic anhydride in pyridine solution, gave a heterogeneous product which probably consisted of a mixture of the acetates obtained on acetylation of XIII and XIV.

XIV was methylated twice with iodomethane and silver oxide in DMFA solution. The syrupy methylation product was reduced with LAH and then hydrolysed. The hydrolysate contained a mixture of 2-*O*-methyl-D-glucose (21 %), 2,3-di-*O*-methyl-D-glucose (55 %) and 2,6-di-*O*-methyl-D-glucose (24 %). Only traces of mono-*O*-methyl-D-glucoses other than 2-*O*-methyl-D-glucose were observed.

The 2,3-di-*O*-methyl-D-glucose results from methylation of the C_3 hydroxyl subsequent to the migration of the 3-*O*-phenylcarbamate group. The not unsignificant amount of 2,6-di-*O*-methyl-D-glucose found shows that methylation of the C_6 hydroxyl takes place at a rate comparable to that of the migration. The presence of 2-*O*-methyl-D-glucose among the products is difficult to explain. The interpretation of this and of the ambiguous results from the IR studies and from the acetylation experiments must await further investigation.

EXPERIMENTAL

All melting points were corrected. All evaporations were done under reduced pressure.

Methyl α-D-glucopyranoside 6-phenylcarbamate. Methyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside 6-phenylcarbamate[3], m.p. 146—148° (2.0 g), was dissolved in 2 % methanolic hydrochloric acid (40 ml). The solution was stored at room temperature until the optical rotation was constant (30 h). It was then neutralised and concentrated to a small volume. The product that crystallised (1.25 g, 87 %) was recrystallised several times from etha-

nol, m.p. 182—184°, $[\alpha]_D^{20}$ +93° (*c*, 0.5 in ethanol). Hearon *et al.*[3] report m.p. 131—133° for methyl α-D-glucopyranoside 6-phenylcarbamate. (Found: C 52.1; H 6.2; N 4.3. Calc. for $C_{14}H_{19}O_7N$: C 53.7; H 6.1; N 4.5.)

Methylation of methyl α-D-glucopyranoside 6-phenylcarbamate. Methyl α-D-glucopyranoside 6-phenylcarbamate (0.98 g) was methylated with iodomethane and silver oxide in DMFA [17]. The reaction mixture was filtered and the filtrate taken to dryness. Extraction of the residue with hot chloroform and concentration of the extract gave the methylation product as a light-coloured glass (1.07 g).

2,3,4-Tri-O-methyl-D-glucose. Part of the methylated methyl α-D-glucopyranoside 6-phenylcarbamate was used in less successful attempts to remove the *N*-methyl-phenylcarbamoyl group by alkaline hydrolysis. A portion (0.20 g) was instead treated for 3 h with excess lithium aluminium hydride (LAH) in hot dioxan. Excess water and then dilute sulphuric acid were added to the cooled reaction mixture. It was filtered, the filtrate was taken to dryness and the product obtained was dissolved in 0.5 N sulphuric acid and kept at 100° overnight. After neutralisation and concentration of the solution the product was purified by distillation to give a colourless syrup (87 mg), $[\alpha]_D^{20}$ +96° (*c*, 0.5 in chloroform). The product was indistinguishable from 2,3,4-tri-*O*-methyl-D-glucose on chromatography and its aniline derivative had m.p. 144—146°, undepressed on admixture with authentic 2,3,4-tri-*O*-methyl-D-glucosyl-*N*-phenylamine.

Methyl 6-O-acetyl-β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). Methyl 6-*O*-acetyl-β-D-glucopyranoside was prepared by treatment of methyl β-D-glucopyranoside (15 g) with 0.9 equiv. of acetic anhydride in pyridine at room temperature overnight. Water was then added and the mixture was concentrated with further addition of water to remove the acetic acid. The resulting aqueous solution of the reaction product was then extracted continuously with hot chloroform, first for 3 h and then exhaustively. The 3-hour extract contained mainly di-, tri- and tetraacetylated products. The second extract was concentrated to dryness and then dissolved in ethanol-ether. On scratching, crude methyl 6-*O*-acetyl-β-glucopyranoside (3.33 g, 18 %) crystallised. It was recrystallised from ethanol-ether, $[\alpha]_D^{20}$ —34° (*c*, 2.0 in water), m.p. 128—129°, undepressed on admixture with an authentic specimen [18].

The methyl 6-*O*-acetyl-β-D-glucopyranoside (2.00 g) was treated for 3 h with phenyl*iso*cyanate (1.2 equiv.) in anhydrous pyridine (25 ml) at 100°. Anhydrous methanol was then added to destroy excess phenyl*iso*cyanate and the solution was boiled for another 10 min. and then poured into cold water. The crystalline precipitate formed was collected on a glass filter and dried. It was recrystallised from ethanol-acetone giving needles, m.p. 221—221.5°, $[\alpha]_D^{20}$ —19° (*c*, 1.0 in pyridine). Yield 4.55 g (91 %). (Found: C 60.6; H 5.1; N 7.4. Calc. for $C_{30}H_{31}O_{10}N_3$. C 60.1; H 5.1; N 7.2.)

Methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). Methyl 6-*O*-acetyl-β-D-glucopyranoside 2,3,4-tri(phenylcarbamate) (3.8 g) was dissolved in acetone (100 ml) and ethanol containing 10 % concentrated hydrochloric acid (100 ml). When the optical rotation was constant (24 h) the solution was neutralised with aqueous sodium hydrogen carbonate. After concentration to about one third the solution was poured into water. The precipitated product was recrystallised from aqueous acetone giving large needles, m.p. 218—219°, $[\alpha]_D^{20}$ —3° (*c*, 1.0 in pyridine). Hearon *et al.*[4] report somewhat different constants for methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate) and for the methyl β-D-glucopyranoside 2,3-di(phenylcarbamate) described below. To make sure that no migration had occurred during the isolation of methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate) it was reacetylated to give a crystalline material, m.p. 220.5—221°, undepressed on admixture with methyl6-*O*-acetyl-β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). (Found: C 61,1; H 5.3; N 7.4. Calc. for $C_{28}H_{29}O_9N_3$: C 61.1; H 5.3; N 7.6.)

Methylation of methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). Methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate) (2.36 g) was methylated twice with iodomethane and silver oxide in DMFA. The reaction product was isolated as previously described. It crystallised on concentration of a methanolic solution. Recrystallisation from aqueous methanol gave large prisms, m.p. 133—134°, $[\alpha]_D^{20}$ +25° (*c*, 1.0 in pyridine). Yield 1.75 g (67 %). (Found: C 63.1; H 5.8; N 7.0; OCH_3 10.4; (N)-CH_3 7.1. Calc. for methyl mono-

O-methyl-β-D-glucopyranoside tri-(*N*-methyl-phenylcarbamate) ($C_{32}H_{37}O_9N_3$): C 63.1; H 6.1; N 6.9; OCH_3 10.2; (N)-CH_3 7.1.)

Reduction of methylated methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate). The above compound (1.64 g) in dioxan was refluxed for 4 h with excess LAH. After removal of inorganic material the solution was taken to dryness to give a rapidly crystallising glass (0.58 g = 96 %). Recrystallisation from ethyl acetate gave large, non-dichroic plates, m.p. 90—91°, $[\alpha]_D^{20}$ —17° (*c*, 1.0 in water). The molten compound solidified to fan-like dichroic crystals, m.p. 102—104°. The latter melting point and the optical rotation are in agreement with the values reported for methyl 4-*O*-methyl-β-D-glucopyranoside [12].

A hydrolysed sample of the product was indistinguishable from authentic 4-*O*-methyl-D-glucose on paper chromatography and paper electrophoresis in borate buffer.

The non-crystalline material in the mother liquors from the methylated methyl β-D-glucopyranoside 2,3,4-tri(phenylcarbamate), on reduction with LAH and subsequent hydrolysis gave a syrupy product (0.16 g). Paper electrophoresis of this product in borate buffer showed the presence of 4-*O*-methyl-D-glucose and 6-*O*-methyl-D-glucose in proportions of about 3 : 1, together with a faint trace of D-glucose.

Methyl 4,6-O-ethylidene-β-D-glucopyranoside 2,3-di(phenylcarbamate). Methyl 4,6-*O*-ethylidene-β-D-glucopyranoside 2,3-di(phenylcarbamate) was prepared from methyl 4,6-*O*-ethylidene-β-D-glucopyranoside following the procedure previously described. It had m.p. 224—225°, $[\alpha]_D^{20}$ —165° (*c*, 1.0 in pyridine). (Found: C 60.1; H 5.5; N 6.4. Calc. for $C_{23}H_{26}O_8N_2$: C 60.3; H 5.7; N 6.1.)

Methyl β-D-glucopyranoside 2,3-di(phenylcarbamate). Methyl 4,6-*O*-ethylidene β-D-glucopyranoside di(phenylcarbamate) (4.37 g) was dissolved in hot ethanol (60 ml) and 0.5 N sulphuric acid (30 ml). After boiling for 3 h the solution was neutralised with barium carbonate and filtered. The filtrate was taken to dryness. The residue was triturated with ether giving small needles, m.p. 195°. This product was recrystallised from aqueous acetone, m.p. 205—207°, $[\alpha]_D^{20}$ —118° (*c*, 1.0 in pyridine). Yield 3.24 g (79 %). Found: C 56.3; H 5.6; N 6.7. Calc. for $C_{21}H_{24}O_8N_2$. C 58.3; H 5.6; N 6.5.) A sample of the substance was acetylated with acetic anhydride in pyridine solution to give a product that melted at 215—216° in good agreement with the value [3] previously reported for methyl 4,6-di-*O*-acetyl β-D-glucopyranoside 2,3-di(phenylcarbamate).

Methylation of methyl β-D-glucopyranoside 2,3-di(phenylcarbamate(. The methyl β-D-glucopyranoside 2,3-di(phenylcarbamate) was methylated with iodomethane and silver oxide in DMFA. After isolation in the usual manner the product was obtained as a glass, $[\alpha]_D^{20}$ +24° (*c*, 1.0 in pyridine), which did not crystallise.

Methyl 4,6-di-O-methyl-β-D-glucopyranoside and 4,6-di-O-methyl-D-glucose. The above methylation product was treated with excess LAH and the reduced product was worked up as usual. After removal of inorganic material it crystallised on concentration of its ethereal solution. Recrystallisation from ethyl ether-*iso*propyl ether gave long needles, m.p. 73.5—75°, $[\alpha]_D^{20}$ —28° (*c*, 1.0 in chloroform).

A portion of this compound was hydrolysed in 0.5 N sulphuric acid. The isolated product crystallised from ethyl acetate-ethyl ether as small needles, $[\alpha]_D^{20}$ +109° → +64° (*c*, 0.5 in water), m.p. 155—157°. The m.p. agrees with that reported for the expected 4,6-di-*O*-methyl-α-D-glucose [19], and it was not depressed on admixture with an authentic specimen of this ether. M.p. 52—54°and $[\alpha]_D^{20}$ —28° are reported for its methyl β-glucopyranoside. The m.p. reported above for this substance indicates that it was obtained as a different crystal modification.

*1,2-O-*Iso*propylidene-3-O-acetyl-α-D-glucofuranose 5,6-di(phenylcarbamate) (XI).* 1,2-*O*-*Iso*propylidene-3-*O*-acetyl-α-D-glucofuranose, m.p. 124—125°, $[\alpha]_D^{20}$ —27° (*c*, 1.0 in ethanol) prepared as described by Josephson [14] was treated for 2.5 h with 2.4 equiv. of phenyl*iso*cyanate in hot DMFA solution. The product was isolated as previously described and appeared as microscopic needles, melting at 186—188° with partial recrystallisation. The molten sample crystallised on cooling and was used for inoculating a hot methanolic solution of the product which then crystallised as long, silky needles, m.p. 196—196.5°,

$[\alpha]_D^{20}$ +42° (*c*, 1.0 in pyridine). (Found: C 60.1; H 5.7; N 5.7. Calc. for $C_{25}H_{28}O_9N_2$. C 60.0; H 5.6; N 5.6.)

1,2-O-Isopropylidene-6-O-acetyl-α-D-glucofuranose 3,5-di(phenylcarbamate) (XII). 1,2-*O-Iso*propylidene-3-*O*-acetyl-α-D-glucofuranose was dissolved in a minimum of aqueous ethanol and a few drops of ammonia were added. Crystals started immediately to separate from the solution. It was concentrated and the product was filtered off. The yield of 1,2-*O-iso*propylidene-6-*O*-acetyl-α-D-glucofuranose was 85 %, m.p. 144—145°, $[\alpha]_D^{20}$ −4° (*c*, 1.0 in ethanol). It was treated with phenyl*iso*cyanate giving the 3,5-di(phenylcarbamate) as flat needles, crystallised from methanol, m.p. 218—219°, $[\alpha]_D^{20}$ +9° (*c*, 1.0 in pyridine). (Found: C 60.0; H 5.7; N 5.7. Calc. for $C_{25}H_{28}O_9N_2$: C 60.0; H 5.6; N 5.6.)

Methyl (α,β)-D-glucofuranoside 3,5- and 5,6-di(phenylcarbamates). XI and XII were deacetylated with simultaneous glycosidation in dry methanol containing 1.2 % sulphuric acid.[15] The reactions were followed polarimetrically and were complete in 50 h. The solutions were neutralised by slowly adding dilute methanolic ammonia until a precipitate of ammonium sulphate formed. After filtration the solutions were taken to dryness and the residues extracted with warm ethyl ether. On concentration of the extracts the products were obtained as amorphous powders soluble in ethanol and warm ether and insoluble in chloroform. The methyl (α,β)-D-glucofuranoside 5,6-di(phenylcarbamate) (XIII) had $[\alpha]_D^{20}$ −14° (*c*, 1.0 in methanol) and the methyl (α,β)-D-glucofuranoside 3,5-di(phenylcarbamate) (XIV) $[\alpha]_D^{20}$ −35° (*c*, 1.0 in methanol).

Treatment of XIII with saturated methanolic ammonia or with silver oxide in DMFA, as expected, had no effect on its optical rotation. Saturated methanolic ammonia had no effect on XIV but silver oxide in DMFA changed its specific rotation in methanol to −26°. This compound (XV) was obtained as an amorphous powder after isolation and purification in the same way as the products from methylations with iodomethane and silver oxide in DMFA.

Acetylation of XIII, XIV and XV. These were acetylated with acetic anhydride in pyridine. The products were recrystallised from ethanol-ether. Acetylated XIII formed non-dichroic needles recrystallising at 150° to larger, dichroic crystals, m.p. 189—191°. Acetylated XIV formed small non-dichroic needles, m.p. 179—180°. Acetylated XV consisted of small non-dichroic needles, melting at 180° leaving larger dichroic crystals which melted at 189°. Too little material was available for further investigations but it seemed probable that the latter acetate consisted of a mixture of the first two.

Methylation of methyl (α,β)-D-glucofuranoside 3,5-di(phenylcarbamate). The amorphous 3,5-di(phenylcarbamate) XIV (1.87 g) was methylated twice with iodomethane and silver oxide in DMFA. The product (1.80 g) was treated with excess LAH. The reduced material was then hydrolysed in 0.1 N sulphuric acid at 100° overnight. After neutralisation and concentration a lightcoloured syrup (0.75 g) was obtained. This was shown by paper chromatography to contain a mixture of three components indistinguishable from authentic 2-*O*-, 2,3-di-*O*- and 2,6-di-*O*-methyl-D-glucose. The proportions of the three ethers (21, 55 and 24 %, respectively) were estimated quantitatively by hypoiodite oxidation [20] after fractionation on thick filter paper. The 2,3-di-*O*-methyl-D-glucose appeared considerably enriched in the extract on continuous extraction of an aqueous solution of the ethers with hot chloroform. The 2-*O*-methyl-D-glucose and 2,6-di-*O*-methyl-D-glucose were separated by chromatography on thick filter paper.

The 2-*O*-methyl-D-glucose had m.p. 153—154° underpressed on admixture with an authentic specimen. It was indistinguishable from the authentic ether on electrophoresis in borate buffer of pH 10. The 2,3-di-*O*-methyl-D-glucose was characterised as the 1,4,6-triazobenzoate, m.p. 183—185°, $[\alpha]_D^{20}$ −29° (*c*, 1.0 in chloroform) and the 2,6-di-*O*-methyl-D-glucose as the 1,3,4-triazobenzoate, m.p. 203—205°, $[\alpha]_D^{20}$ −250° (*c*, 1.0 in chloroform).

Acknowledgements: The author is indebted to Professor Bengt Lindberg for many valuable discussions throughout this work, to Miss Anita Myhrman for skilful assistance and to Dr. D. J. Bell, Edinburgh, for a gift of 4,6-di-*O*-methyl-D-glucose.

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Received September 22, 1960.