MECHANISMS FOR THE REACTIONS OF THE ANOMERIC TETRA-*O*-ACETYL-D-GLUCOPYRANOSYL BROMIDES WITH PYRIDINE AND 2-PYRIDONE

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Received January 25, 1965

ABSTRACT

Reaction of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) with pyridine at high dilution gives a high yield of *N*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-pyridinium bromide (II). The addition of tetra-*n*-butylammonium bromide diverts the reaction to the formation of the highly strained α-anomer (III) of II. It is contended that III arises from the β-anomer (IV) of I by way of a rearrangement of an intermediate formed between pyridine and the 1,2-acetoxonium ion (VIII) which readily arises by dissociation of IV. The formation of 2-pyridyl tetra-*O*-acetyl-α-D-glucopyranoside in >60% yield in the reactions of I with either 2-ethoxypyridine or 2-pyridone in the presence of tetra-*n*-butylammonium bromide is taken as supporting evidence for this novel type of rearrangement.

INTRODUCTION

Fischer and Raske (1) prepared *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-pyridinium bromide (II), through the reaction of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) with pyridine in the presence of phenol. On repeating the preparation, II was obtained in 47% yield and its anomeric configuration was confirmed by the n.m.r. spectrum (2). Since the role of the phenol in the reaction mixture was not evident, it was decided to examine the course of the reaction in its absence. When a 34.4% solution of I in pyridine was allowed to react to constant rotation, a syrupy, water-soluble product was obtained. The n.m.r. spectrum in deuterium oxide showed doublet signals at τ 3.60 (spacing 8 c.p.s.) and τ 3.12 (spacing 3 c.p.s.). These signals were found to arise from the anomeric protons of II and its α-anomer (III), respectively (2, 3). The relative intensities of the signals indicated that the two compounds were present in the ratio 11:9 in favour of the α-anomer.

The change in optical rotation during the reaction of I with pyridine was followed polarimetrically. When the initial concentration was low, 1.95% (w/v), the rate of change corresponded closely to a first-order process and virtually only the β-anomer (II) was formed. The yield was greater than 90% as judged from the n.m.r. spectrum of the product in pyridine. When the initial concentration of I was 34.4%, an induction period in the polarimetric change was noted and, therefore, it was apparent that the product of the initial reaction became involved in a faster process. The induction period was also present when the initial concentration of I was about 16%, and the anomers were formed in about equal amounts. The same course of reaction was obtained when half of the pyridine was replaced by acetonitrile, although the more polar solvent gave rise to a somewhat increased rate of reaction. When the reaction of I (16% initial concentration) was carried out in pyridine containing 1 mole of tetra-*n*-butylammonium bromide per mole of I, the rate of the reaction was greater and the induction period was not present. Virtually only the α-pyridinium glucoside (III) was formed as judged from the n.m.r. spectrum of the product. When tetra-*n*-butylammonium perchlorate was used instead of the bromide, the induction period reappeared and the product comprised a 3:2 mixture of the α- and β-forms, respectively. These results are summarized in Table I.

[1]*Presented in part in a thesis by A. R. M. in partial fulfillment of the requirements for the degree of Doctor of Philosophy, University of Alberta, 1964.*

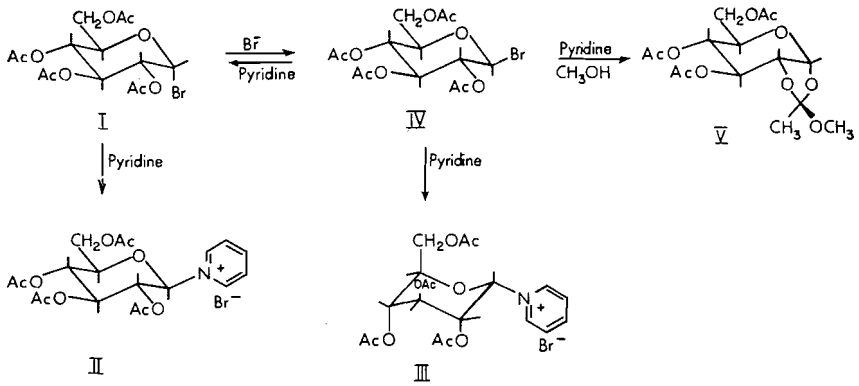


TABLE I

Effect of concentration and the addition of bromide ion on the rate and stereochemical route of the reaction of tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I) with pyridine

Experiment	Concentration of I, % w/v	Final specific rotation, deg	Time for completion of reaction, h	Yields of *N*-glucosides, %	
				α-Anomer	β-Anomer
1	1.95	7.2	30	—	>90
2	34.4	13.4	9	55	45
3	16.3	10.3	12	50	50
4	15.8*	18.4	5	>90	—
5	15.9†	9.65	—	60	40

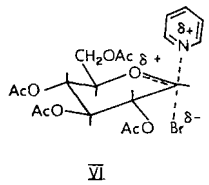
*The solution contained 13.5% tetra-*n*-butylammonium bromide.
†The solution contained 13.2% tetra-*n*-butylammonium perchlorate.

The most reasonable interpretation of these results was that initially I underwent nucleophilic attack by pyridine with inversion of the anomeric center to produce the β-pyridinium bromide (II). The bromide ion, thus liberated, then participated in a faster process involving a nucleophilic attack on I to form its anomer, tetra-*O*-acetyl-β-D-glucopyranosyl bromide (IV), and the latter compound was the precursor of the α-pyridinium glucoside (III). To test this hypothesis, tetra-*O*-acetyl-β-D-glucopyranosyl chloride was reacted with pyridine at room temperature. Five days were required for the rotation of the solution to reach a constant value. To the syrupy product obtained, water was added, and the mixture was extracted with chloroform. The chloroform extract gave a syrup (40% yield), the n.m.r. spectrum of which showed it to be virtually pure tetra-*O*-acetyl-α-D-glucopyranosyl chloride. Evaporation of the aqueous phase gave a syrup which was assigned the structure of *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-pyridinium chloride in view of the very close similarity of its n.m.r. spectrum to that of compound III. No evidence was present in the spectrum for the formation of the β-anomer. When the reaction of the β-chloride with pyridine was repeated under the same conditions, except that tetraethylammonium chloride was added, a time of about 2 d was required for the rotation to reach a constant value and the only product found in appreciable amount was that of anomerization, the α-chloride. That the bromide ion can catalyze the anomerization of the tetra-*O*-acetyl-D-glucopyranosyl bromides was supported by a recent study of the anomerization of the anomeric chloride (4). It was found that, in acetonitrile, the rate of anomerization was first-order in tetraethylammonium chloride. The more rapid exchange of the chlorine of the β-anomer with ^{36}Cl-labelled chloride ion was interpreted as resulting from

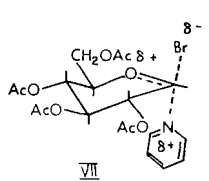
dissociation of the β-chloride to 1,2-acetoxonium ion (4). The β-bromide (IV) has recently been isolated (5), and its reaction properties correspond closely to those previously established for tetra-*O*-acetyl-β-D-glucopyranosyl chloride (6).

Since the reaction of this β-chloride in pyridine containing an alcohol leads to the formation of tri-*O*-acetyl-α-D-glucopyranose 1,2-(alkyl orthoacetate) (6, 7), the observations related to the formation of the α-pyridinium glucoside (III) led to the prediction that the addition of I to pyridine containing methanol would result in the formation of the 1,2-(methyl orthoacetate) (V). In fact, the reaction of I in pyridine containing 3 moles of methanol per mole of I, under conditions which in the absence of methanol provided the α- and β-pyridinium glucosides in the ratio 3:2, respectively, gave a mixture of the methyl orthoacetate (V) and the β-pyridinium glucoside (II). That is, the presence of the methanol blocked the route to the formation of the α-pyridinium glucoside (III), precisely the result expected should the latter compound arise from the β-bromide (IV). The n.m.r. spectrum of the crude 1,2-orthoacetate (V) showed the presence of the two possible diastereoisomers arising from a change in the configuration of the new asymmetric center in the dioxalane ring (8). It thus became apparent why Fischer and Raske (1) found it useful to add phenol to the reaction mixture to form the β-pyridinium glucoside (II). That is, the phenol prevented the formation of the α-anomer. In fact, the n.m.r. spectrum of the reaction product showed the presence of only II and the phenyl orthoesters (9).

The formation of the β-pyridinium glucoside (II) undoubtedly involves nucleophilic attack by pyridine at the anomeric center of I. Bimolecular reactions of this type at the anomeric center of glycosyl halides are known to occur (10, 11). The mechanism for the formation of the α-pyridinium glucoside (III) is more difficult to anticipate. An obvious possibility is attack by pyridine at the anomeric center of the β-bromide (IV). However, this course of reaction seems unattractive for a number of reasons. First of all, it is to be noted that compound III is highly strained (2) and must be thermodynamically considerably less stable than the β-anomer (II). Consequently, the mechanism must account for the ability of bromide ion to divert the reaction to the formation of a less stable product. That is, the formation of III is kinetically controlled. It is well established that I is more stable than the β-anomer (IV) and is the anomer with the bromine in axial orientation (n.m.r. spectrum). Judging from the yields of I obtained from reactions mixtures where it must have been at equilibrium with IV (12), the equilibrium constant for the anomerization must be at least 9. The equilibrium constant for the $\beta \rightleftarrows \alpha$ anomerization of the acetochloroglucoses is about 16 (4). Assuming that, in the presence of tetra-*n*-butylammonium bromide, compounds I and IV were at equilibrium throughout the course of reaction, then the concentration of I was at least nine times that of IV. Control experiments showed that the presence of the β-*N*-glucoside (II) in mixtures of II with its α-anomer (III) could easily be detected when II formed 10% of the mixture. Therefore, the yield of III in the experiment using tetra-*n*-butylammonium bromide as catalyst must have been greater than 90%. It is seen therefore that the reaction of IV with pyridine would have to be at least 80 times faster than the reaction of the α-anomer (I) with pyridine.

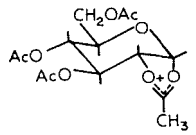


VI



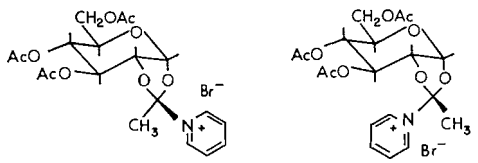
VII

Assuming that the reactions proceed by nucleophilic attack at the anomeric centers of I and IV, the transition states depicted in VI and VII, respectively, would be anticipated and the transition state VII would have to be at least 1 kcal/mole more stable than VI. In fact, VII must be expected to be less stable than VI especially if those factors related to the anomeric effect are important in the transition states (2). Evidence in support of this contention was obtained by reaction of tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl bromide (13) with pyridine in the presence of tetra-*n*-butylammonium bromide. The main product of the reaction had the n.m.r. spectrum expected for 2-chloro-D-glucal triacetate. This product of dehydrobromination (11) was formed in about 78% yield. *N*-(Tri-*O*-acetyl-2-chloro-2-deoxy-β-D-glucopyranosyl)-pyridinium bromide crystallized directly from the reaction mixture in 17% yield. Therefore, if the reaction mixture contained the equilibrium amounts of the α- and β-glucosyl bromides, the reaction of the α-bromide with pyridine was substantially faster than that of the β-anomer. Although it was not possible to obtain direct evidence for the rates of anomerization of the 2-chloroglucosyl bromides under these reaction conditions, the α-bromide reacts rapidly with tetraethylammonium chloride in acetonitrile to yield tri-*O*-acetyl-2-chloro-2-deoxy-β-D-glucopyranosyl chloride and this reaction is substantially faster than the analogous reaction of I under comparable conditions (13). Thus, there is no reason to doubt that the bromide ion led to equilibration of the 2-chloroglucosyl bromides as was observed in the reactions of I with pyridine in the presence of bromide ion. On this basis, the results obtained in the reaction of tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl bromide with pyridine in the presence of a high concentration (0.51 *M*) of tetra-*n*-butylammonium bromide support the contention that nucleophilic attack by pyridine at the anomeric center of the β-bromide (IV) leads to a less favorable transition state (VII) than that (VI) involving attack of the α-anomer (I).



VIII

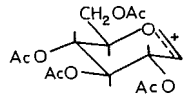
It seems more likely that the ready formation of III from IV relative to the formation of II from I is related to the ability of IV to readily dissociate to the 1,2-acetoxonium ion (VIII). This is consistent with the observation that the cation VIII is formed more rapidly than the α-glucoside (III) and can be a precursor of III. The experimental results require the reaction of the acetoxonium ion (VIII) with pyridine to form the β-glucoside (II) to be much slower than the process which leads to the formation of the α-anomer (III).



IX X

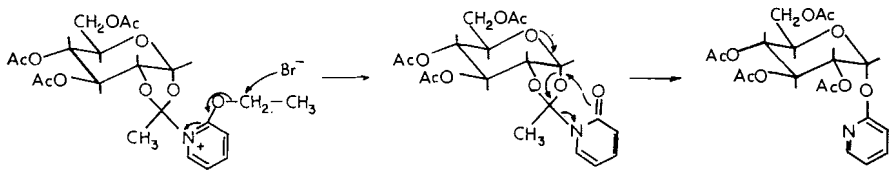
In pyridine, the 1,2-cyclic carbonium ion must lead rapidly to the complexes IX and X. In view of the ease of the acid-catalyzed hydrolysis or alcoholysis of orthoesters, these complexes must be expected to be highly labile and of only transient existence. For

example, tri-*O*-acetyl-α-D-glucopyranose 1,2-(phenyl orthoacetate) was found to be solvolyzed in *sym*-collidine saturated with water (9). Therefore, IX and X can be expected to readily revert to the acetoxonium ion.



XI

Formation of III from the acetoxonium ion (VIII) would have to involve rearrangement of the acetoxonium ion *toward* the glucosyloxocarbonium ion (XI) in the first stage of the reaction. It is reasonable to expect that this would be a facile process since it is first-order process and merely involves a reallocation of the positive charge. In contrast, the formation of the transition state VII requires charge separation in a second-order process conducted in a weakly polar solvent. It could be speculated that the ion XI is closer to the 1C- than the C1-conformation and provides α-pyridinium glucoside (III) for this reason. However it is well established that the 1,2-acetoxonium ion is formed in the anomerization of both penta-*O*-acetyl-β-D-glucopyranose (14) and tetra-*O*-acetyl-β-D-glucopyranosyl chloride (4) and that the ion does not offer a facile route to the formation of the α-anomers. For this reason, it seems best to assume that the α-glucoside (III) is formed by a rearrangement of a pyridine – acetoxonium ion complex. That is, an intimate ion–molecule pair could be involved as an intermediate in a 1,3-shift of the pyridine via the *endo*-complex X. Thus, an energetically economical route for the formation of the highly-strained α-glucoside (III) would be provided.



XII XIII XIV

In view of the unexpected conformational properties of III, it was desired to examine the conformation of *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl) 2-pyridone. Therefore, I was reacted with 2-ethoxypyridine in an excess of tetra-*n*-butylammonium bromide; n.m.r. examination of the product showed the presence of a complex mixture containing about 60% of an acetylated *O*-glucoside. The compound was readily isolated by chromatography on silicic acid and found to be 2-pyridyl tetra-*O*-acetyl-α-D-glucopyranoside, m.p. 84–84.5°, $[\alpha]_D$ +147° (*c*, 0.5 in chloroform). The anomeric proton gave a doublet signal at τ 3.22 with a spacing of 3.5 c.p.s. The four aromatic protons gave signals with chemical shifts and structures very similar to those in the spectrum of 2-ethoxypyridine. The signal for H-3 was a triplet (spacing 9.5 c.p.s.) at τ 4.24, about 0.5 p.p.m. to lower field than the signals for H-2 and H-4. It was therefore evident that the compound was the α-anomer in the C1-conformation. The tetra-*O*-acetyl-α- and -β-*N*-glucosides of 2-pyridone were also formed but did not separate on the silicic acid column. The n.m.r. spectrum of the mixture isolated from the chromatogram indicated that β-anomer was formed to about three times the extent of the α-form. Spin-decoupling experiments at 100 Mc.p.s. showed the anomeric protons of the α- and β-forms to give doublet signals at τ 3.44 and τ 3.60, respectively.

The spacings were 2.5 and 9.0 c.p.s., respectively. It was not possible to draw conclusions as to the structures of the signals for other ring-protons of the α-anomer. The spectra were devoid of signals for the ethyl group which, as expected (15), was lost in the course of the reaction. In these reactions, the ethyl group must be lost after the nitrogen has been quaternized. The quaternization which was involved in producing the α-*O*-glucoside must have taken place at a position other than the anomeric center. It seems probable *in view of the high yield of the O-glucoside*, that the 2-ethoxypyridine attacked the 1,2-acetoxonium ion to yield the intermediate (XII). This would activate the nucleophilic attack by bromide ion to remove the ethyl group and yield the *N*-orthoacetyl pyridone derivative (XIII). Such a compound can be expected to be highly labile and its rearrangement to the *O*-glucoside (XIV) following a route similar to that described above for the formation of the α-pyridinium glucoside (III) appears plausible. Reaction of I with 2-pyridone in *sym*-collidine containing tetra-*n*-butylammonium bromide gave a 70% yield of the *O*-α-glucoside (XIV) but none of the *N*-glycosides. The formation of an α-glucoside under these conditions is abnormal and presumably arose by way of the intermediate XIII. The small amount of the *N*-α-glucoside which was formed in the reaction of I with 2-ethoxypyridine in the presence of bromide ion was likely the result of nucleophilic attack by the 2-ethoxypyridine at the anomeric center of the β-bromide (IV).

EXPERIMENTAL

The experimental methods were similar to those previously described (9, 11, 16).

Reactions of Pyridine with Tetra-O-acetyl-α-D-glucopyranosyl Bromide (I)

Solutions of I in pyridine, with or without the addition of salt, were made up in the concentrations reported in Table I. The solutions were kept at room temperature and their optical rotations were determined from time to time. The initial specific rotations, 194.5°, were those expected for I. The reaction times reported in Table I correspond to the time required for the rotational change to become near asymptotic. The rotational changes observed in experiments 2, 3 and 5 showed points of inflection indicating increases in the rates of optical change in the first periods of the reactions.

After the solutions had achieved constant rotations, the pyridine was rapidly removed *in vacuo* and a sample of the residue was dissolved in deuterium oxide for analysis by n.m.r. spectroscopy. The relative amounts of the α- and β-anomers of *N*-(tetra-*O*-acetyl-D-glucopyranosyl)-pyridinium bromide were estimated from the relative intensities of the signals for the anomeric protons at τ 2.8–3.1 and 3.4–3.6, respectively, depending on the salt concentration. When the α-anomer (III) was dissolved in pyridine, the n.m.r. spectrum showed a signal for one of the acetoxy to lower field, τ 7.47, than the signals for the other acetyl groups centered at τ 7.86. Under the same conditions, the acetyl groups of the β-anomer all gave their signals above τ 7.9. The relative amounts of the anomers in mixtures could therefore be estimated by integrating over the acetyl group signals. This method of analysis confirmed in each case the results obtained by comparing the intensities of the signals from the anomeric protons.

Reactions of Tetra-O-acetyl-β-D-glucopyranosyl Chloride

(*a*) The compound, 0.25 g, was dissolved in 5 ml of dry pyridine. After 2.5 min, the observed rotation was −1.09° and the rotation steadily rose to a constant value of 4.50° after 125 h. Most of the pyridine was evaporated *in vacuo* and the product was distributed between 20 ml of water and 20 ml of chloroform. The solutions were taken to dryness. The chloroform layer gave 0.10 g of tetra-*O*-acetyl-α-D-glucopyranosyl chloride (40% yield) identified by its n.m.r. spectrum. The residue from the aqueous layer was dissolved in deuterium oxide for examination by n.m.r. spectroscopy. The spectrum was that expected for *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-pyridinium chloride. It was therefore concluded that the yield of this compound was about 60%. No indication of the β-anomer was present in the n.m.r. spectrum.

(*b*) The compound, 0.25 g, was taken up in 5 ml of dry pyridine saturated with tetraethylammonium chloride. After 15 min the observed rotation was −0.5° and the rotation rose to +6.52° in 45 h. The pyridine was evaporated *in vacuo* and the product was worked up as described above. The chloroform layer contained 0.19 g of virtually pure tetra-*O*-acetyl-α-D-glucopyranosyl chloride (n.m.r. spectrum). The aqueous layer gave a crystalline solid which had the n.m.r. spectrum of tetraethylammonium chloride. The spectrum indicated that a mere trace of *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-pyridinium chloride had formed.

Tri-O-acetyl-α-D-glucopyranose 1,2-(Methyl Orthoacetate)

Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (I), 3.03 g, was dissolved in 10 ml of pyridine containing 0.89 ml of methanol and the solution was kept at room temperature. The observed rotation after 5 min was

47° and fell to a constant value of 2.81° after 19 h. An induction period was noted in the rotational change. The solvent was removed *in vacuo* and the residue was partitioned between water and chloroform. The chloroform layer gave a sirupy product, the n.m.r. spectrum of which showed it to be tri-*O*-acetyl-α-D-glucopyranose 1,2-(methyl orthoacetate) (9). Evaporation of the aqueous layer left a residue which was dissolved in deuterium oxide for n.m.r. spectroscopy. Except for pyridinium hydrobromide, the substance was virtually pure *N*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-pyridinium bromide (2).

Reaction of Tri-O-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl Bromide

The compound, m.p. 97–98°, $[\alpha]_D$ +250° (*c*, 3 in chloroform) (13), 0.94 g, and 0.83 g of tetra-*n*-butylammonium bromide were taken up in pyridine to give 5 ml of solution. The solution was kept at room temperature. After 40 min, the observed rotation had fallen to 11.3° at which time the solution became turbid due to deposition of a crystalline solid. After 16 h, the crystals were collected and washed with pyridine. The n.m.r. spectrum of this product required it to be *N*-(tri-*O*-acetyl-2-chloro-2-deoxy-β-D-glucopyranosyl)-pyridinium bromide contaminated by tetra-*n*-butylammonium bromide. It was estimated that the β-*N*-glucoside was formed in 17% yield based on the starting material. Recrystallization of the compound from ethanol – ethyl acetate gave material, m.p. 129.5–131.5°, $[\alpha]_D$ +67° (*c*, 0.5 in water). The n.m.r. spectrum in deuterium oxide showed the signal for the anomeric proton at τ 3.55 with a spacing of 9.2 c.p.s. The signals for H-3 and H-4 were broadly (about 9 c.p.s.) spaced triplets centered at τ 4.24 and 4.60, probably respectively. The presence of ethanol in the crystals was indicated.

The filtrate was evaporated to dryness *in vacuo* and the residue was partitioned between water and chloroform. The aqueous layer was evaporated to dryness and taken up in deuterium oxide for analysis by n.m.r. The material was mainly a mixture of tetra-*n*-butylammonium bromide and pyridinium hydrobromide. The spectrum was devoid of signals for the above mentioned β-*N*-glucoside. However, weak signals at τ 2.75 and 4.5 can be taken as evidence that some of the *N*-(tri-*O*-acetyl-2-chloro-2-deoxy-α-D-glucopyranosyl)-pyridinium bromide had formed.

The chloroform layer was taken to dryness to leave 1.19 g of syrup. The n.m.r. spectrum in chloroform showed this product to be an equimolar mixture of tetra-*n*-butylammonium bromide and 2-chloro-D-glucal triacetate. On this basis the yield of the latter compound was estimated to be 78%. The identity of the 2-chloro-D-glucal triacetate was evident from its n.m.r. spectrum which had a one-proton singlet at τ 3.22 and was otherwise virtually identical to that of 2-acetoxy-D-glucal triacetate (17).

2-Pyridyl Tetra-O-acetyl-α-D-glucopyranoside and N-(Tetra-O-acetyl-D-glucopyranosyl)-2-pyridone

(*a*) Tetra-*O*-acetyl-α-D-glucopyranosyl bromide, 5.91 g, and tetra-*n*-butylammonium bromide, 3.96 g, were dissolved in 2-ethoxypyridine, 10 ml, and the homogeneous solution obtained at 75° was allowed to react for 1 d. The volatile components were then removed *in vacuo* and the residue was dissolved in chloroform. The chloroform solution was washed three times with 2 *N* hydrochloric acid and finally with aqueous sodium bicarbonate solution. The n.m.r. spectrum of the syrup obtained from the chloroform layer showed the mixture to consist essentially of 2-pyridyl tetra-*O*-acetyl-α-D-glucopyranoside (60%) and *N*-(tetra-*O*-acetyl-D-glucopyranosyl)-2-pyridone (<40%). This was determined in the following manner. The *p*-anisidin spray reagent (18) revealed only two spots when a sample of the syrup was chromatographed on a thin layer of silicic acid. A 0.42 g sample was therefore chromatographed on a column of silicic acid, 25 g (100 mesh), with reagent chloroform as the eluant. The bands which could be observed to separate on the column were collected. The first band corresponded to ~10% yield of 2-acetoxy-D-glucal triacetate as determined by the direct comparison of n.m.r. spectra (17).

The second band showed absorptions in the ultraviolet, λ_{max} 266 mμ (ε 3 670) and 208 mμ [2-ethoxypyridine, λ_{max} 270 mμ (ε 4 500) and 214 mμ]. The n.m.r. spectrum was that expected for 2-pyridyl tetra-*O*-acetyl-α-D-glucopyranoside and this was confirmed by crystallization of the syrup. Recrystallization from ethanol–water to constant physical properties resulted in material of m.p. 84–84.5°, $[\alpha]_D$ +148° (*c*, 0.5 in chloroform).

Anal. Calcd. for $C_{19}H_{23}NO_{10}$: C, 53.64; H, 5.45; N, 3.29. Found: C, 53.70; H, 5.77; N, 3.20.

The n.m.r. spectrum contained a doublet at τ 3.22, spacing 3.5 c.p.s., and signals in the τ 1.7 to 3.2 region closely resembling those in the spectrum of 2-ethoxypyridine. The remainder of the spectrum was that expected for a tetra-*O*-acetyl-α-D-glucopyranoside.

The material in the third band absorbed in the ultraviolet, λ_{max} 300 mμ (ε 4 720) and 226 mμ (2-pyridone, λ_{max} 300 mμ (ε 6 120) and 224 mμ). The n.m.r. spectrum at 100 Mc.p.s. showed the material to be a mixture, and it was established by integration of the signals and by spin-decoupling experiments that the compounds were both *N*-(tetra-*O*-acetyl-D-glucopyranosyl) 2-pyridones. The signal for the anomeric proton of the α-anomer was a doublet at τ 3.44, spacing 2.5 c.p.s., and that for the β-form was a doublet at τ 3.60, spacing 9 c.p.s. The ratio of the α- to β-forms was estimated to be about 1:3. Pure compounds were not obtained.

(*b*) Tetra-*O*-acetyl-α-D-glucopyranosyl bromide, 0.21 g, 0.19 g of 2-pyridone, and 0.16 g of tetra-*n*-butylammonium bromide were dissolved in 0.4 ml of *sym*-collidine. The solution was kept at 75° for 18 h. Chloroform was added and the solution was washed three times with dilute hydrochloric acid and then with aqueous bicarbonate. Solvent removal gave a syrup. Integration of the n.m.r. spectrum required the material to be about 70% 2-pyridyl tetra-*O*-acetyl-α-D-glucopyranoside. There was no evidence that *N*-glycosides had formed.

ACKNOWLEDGMENTS

The research was supported by grants (N.R.C.-T 172) to R. U. Lemieux and three North Atlantic Treaty Organization Studentships to A. R. M. (1961–1964). The n.m.r. spectra were determined by Mrs. G. Conway (60 Mc.p.s.) and G. Bigam (100 Mc.p.s.) of this department.

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