The Formation of Acetylated Oxazolines through the Action of Zinc Chloride and Acetic Anhydride on 2-Acylamino-2-deoxyaldoses

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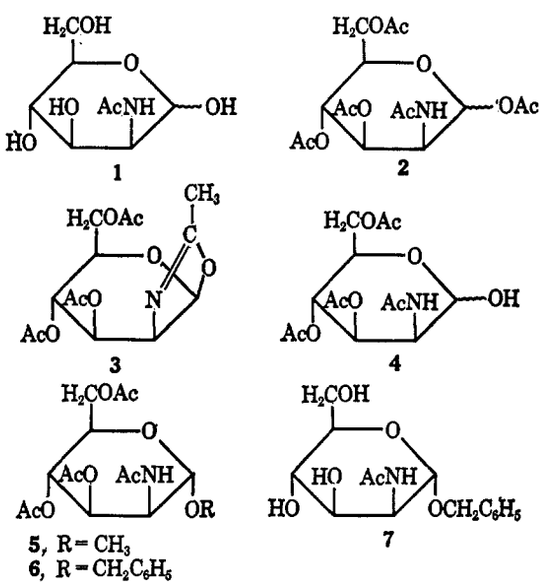
Brief treatment of 2-acetamido-2-deoxy-D-mannose (**1**) with acetic anhydride in the presence of a moderate quantity of anhydrous zinc chloride results in normal acetylation, a mixture of the two anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-mannopyranoses (**2**) being formed. With a larger proportion of zinc chloride and a longer reaction time, these products are accompanied by 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-Δ^2-oxazoline (**3**). The nature of this product was demonstrated through its conversion into both methyl and benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranosides (**5** and **6**). That oxazoline formation under these conditions is not restricted to the D-mannopyranose series has been demonstrated by the preparation of analogous oxazolines from 2-benzamido-2-deoxy-D-glucose (**8**) and 2-acetamido-2-deoxy-D-galactose (**12**). A mechanism for the formation of oxazolines of this class under these conditions is proposed.

In the course of a recent investigation of the nmr spectra of various *N*-acyl derivatives of 2-acylamino-2-deoxyhexoses[3] the need arose for 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-mannopyranose (α **2**) as an intermediate for further syntheses. In the hope of maximizing the yield of this substance (with respect to that of its anomer, β **2**), 2-acetamido-2-deoxy-D-mannose (**1**) was acetylated with acetic anhydride in the presence of a nearly equal weight of anhydrous zinc chloride. Evidence available at that time indicated that the product consisted, as expected, of a mixture of the anomeric forms of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-mannopyranose (**2**) and, in the course of the present research, we have confirmed this fact. We have now examined this acetylation reaction more closely and have found that the use of a higher proportion of zinc chloride, a longer reaction time, and subsequent chromatography of the products on silica gel lead to the isolation, in addition to **2**, of two new crystalline substances. The infrared absorption spectrum of one of these substances showed the presence of a C=N bond as well as of *O*-acetyl groups; this evidence, together with the elementary analysis (which corresponded to $C_{14}H_{19}NO_8$), suggested that the product was the oxazoline, 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-Δ^2-oxazoline (**3**). The chemical behavior of the substance readily substantiated this view; with benzyl alcohol containing a trace of *p*-toluenesulfonic acid it gave benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside (**6**). Removal of the *O*-acetyl groups from **6** afforded the parent glycoside **7** which was found to consume 1.21 molar equiv of sodium metaperiodate. Removal of the benzyl group from **7** by hydrogenolysis over palladium gave 2-acetamido-2-deoxy-D-mannose (**1**), identified by glpc of its trimethylsilyl ether. The pyranose structure and *manno* configuration of **3** was thus established. Another acetylated glycoside (**5**) was made from **3** through the action of methanol in the presence of *p*-toluenesulfonic acid. The anomeric configurations of **5**, **6**, and **7** were assigned on the basis of their optical rotations and in the light of the mechanism by which they were formed.

With water, containing a trace of acid, the oxazoline ring of **3** was opened to give 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyranose (**4**), and this crystalline substance appeared to be identical with the second product obtained on chromatography of the original acetylation mixture. It seems highly likely that **4** was formed by the spontaneous hydrolysis of the oxazoline **3** in the course of the isolation procedure.



It was of interest to ascertain whether the formation of an oxazoline such as **3** is dependent upon the configuration of the system. Since the oxazoline **9** derived from 2-benzamido-2-deoxy-D-glucose (**8**) had been made by other workers,[4,5] we treated **8** with acetic anhydride in the presence of a large excess of anhydrous zinc chloride. Some of the normal acetylation product, a mixture of the anomeric 1,3,4,6-tetra-*O*-acetyl-2-benzamido-2-deoxy-D-glucopyranoses (**10**), was formed, but the main product, 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyrano)-2-phenyl-Δ^2-oxazoline (**9**), was obtained in 82% yield. While **9** was isolated only as a chromatographically homogeneous syrup (rather than as crystals, mp 56°, as reported[4,5]), its physical and chemical properties clearly identified it as the expected oxazoline; with methanol in the presence of *p*-toluenesulfonic acid, it rapidly gave the known methyl 3,4,6-

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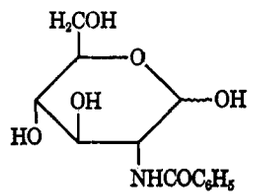
(3) T. D. Inch, J. R. Plimmer, and H. G. Fletcher, Jr., *J. Org. Chem.*, **31**, 1825 (1966).

(4) F. Micheel and H. Köchling, *Ber.*, **90**, 1597 (1957).

(5) T. Osawa, *Chem. Pharm. Bull.* (Tokyo), **8**, 597 (1960).

tri-*O*-acetyl-2-benzamido-2-deoxy-β-D-glucopyranoside (**11**)[4] in high yield (83%).

An analogous acetylation of 2-acetamido-2-deoxy-D-galactose (**12**) gave 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-galactopyranose (α **13**)[3,6] in 45% yield and 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-galactopyrano)-2-methyl-Δ^2-oxazoline (**14**) in 26% yield. The latter



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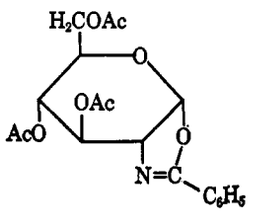

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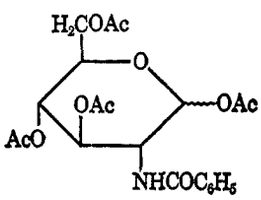

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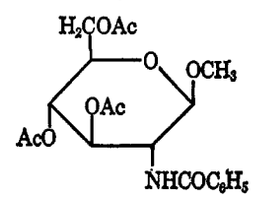

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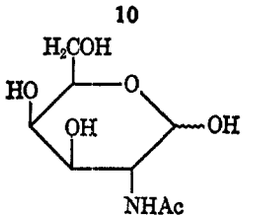

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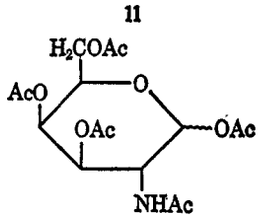

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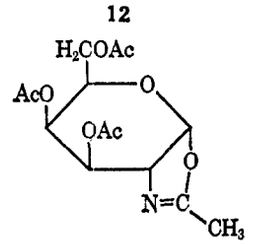

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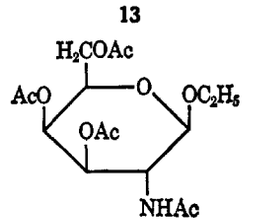

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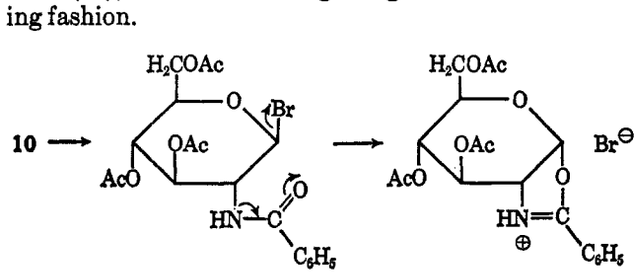
substance was converted into the known ethyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (**15**).[7]

Discussion

Micheel and his co-workers[4,8] have shown that treatment of 1,3,4,6-tetra-*O*-acetyl-2-benzamido-2-deoxy-D-glucopyranose (**10**) with hydrogen bromide in glacial acetic acid gives rise to the formation of the hydrobromide of the oxazoline **9**. This transformation may take place directly or proceed through 3,4,6-tri-*O*-acetyl-2-benzamido-2-deoxy-β-D-glucopyranosyl bromide (**16**), the oxazoline ring being formed in the following fashion.

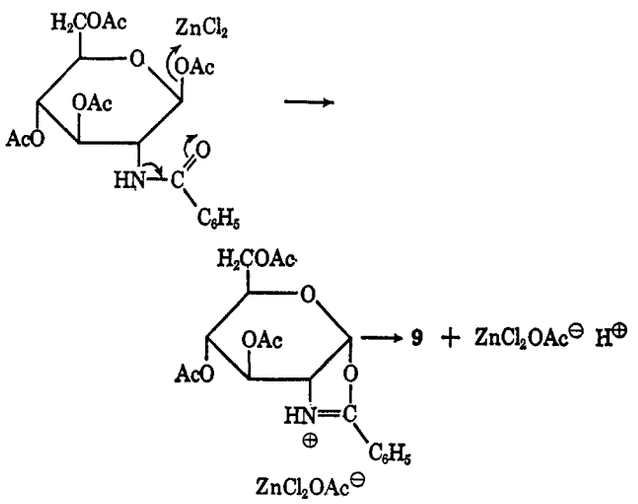


16 **17**

(6) M. Stacey, *J. Chem. Soc.*, 272 (1944).

The free oxazoline **9** may be prepared from its salt (**17**) through the action of pyridine.[4]

The formation of an oxazoline through the action of zinc chloride and acetic anhydride has not, to our knowledge, been observed before. The fact that a lower proportion of zinc chloride leads to normal acetylation while a larger proportion yields an oxazoline, together with the known affinity of zinc chloride for the acetate ion,[9] suggests that the following mechanism may be operative after initial *O*-acetylation.



The acetic acid formed in the course of *O*-acetylation would not only diminish the activity of the zinc chloride for this purpose but, by reacting directly with the oxazoline, would also tend to reverse the reaction; hence the dependency of oxazoline formation on the proportion of zinc chloride used.

Osawa[5] prepared **9** through the action of aluminum chloride on **10**; the mechanism of this conversion is probably similar to that with zinc chloride, although aluminum chloride is doubtless more effective than zinc chloride in this reaction.

The yield of pure **3** was only 11% but the mixture of reaction products was not wholly resolved by column chromatography and, as stated, **4** (obtained in 10% yield) probably represents **3** which was hydrolyzed during the isolation procedure; the actual yield of **3** is, therefore, probably in excess of 21%. The other two oxazolines, **9** and **14**, were isolated in 82 and 26% yields, respectively. While the wide variation in the yields of these oxazolines might tempt one to speculate on the steric factors at play in the reaction mixture, attention should be drawn to the marked variation in the reactivity of these substances toward alcohols. In the presence of *p*-toluenesulfonic acid, the oxazoline from the D-mannopyranose series (**3**) required some 70 hr for complete reaction with methanol while the D-glucopyranose derivative **9** required only about 10 min under the same conditions.[10] Finally, the D-galactopyranose-related oxazoline (**14**) required 2 hr for reaction with ethanol. In view of these apparently wide variations in reactivity, conclusions based on the yields of these oxazolines, obtained after comparatively

(7) Z. Tarasiejska and R. W. Jeanloz, *J. Am. Chem. Soc.*, **80**, 6325 (1958).
(8) F. Micheel, F. P. van de Kamp, and H. Petersen, *Ber.*, **90**, 521 (1957).
(9) H. Meerwein, *Ann.*, **455**, 244 (1927).
(10) Steric factors aside, one would expect **9** to be less reactive than **3** inasmuch as the phenyl group at position two in **9** should confer resonance stabilization on the oxazoline ring.

lengthy preparative chromatography, did not appear justified.

In conclusion, the reactions reported here may, on one hand, serve as a convenient method for the preparation of oxazolines directly from 2-acylamino-2-deoxyaldoses or, on the other hand, constitute a warning to those who wish simply to acetylate these sugars with this combination of reagents.

Experimental Section[11]

Reaction of 2-Acetamido-2-deoxy-D-mannose (1) with Zinc Chloride and Acetic Anhydride. A. Using a Lower Proportion of Zinc Chloride.—A solution of 2-acetamido-2-deoxy-D-mannose monohydrate[12] (1, 0.5 g) in acetic anhydride (10 ml) containing anhydrous zinc chloride (0.5 g) was heated at 85–90° (bath) for 10 min. The cooled solution was then poured into ice–water and the product extracted with dichloromethane; the combined extracts were washed with water, aqueous sodium bicarbonate, and water. Moisture was removed with sodium sulfate and the solution was concentrated *in vacuo* to a syrup from which toluene was distilled *in vacuo*. Thin layer chromatography (benzene–ether–methanol, 14:14:1, v/v) of the product showed it to be essentially pure 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-mannopyranose (2);[13] by crystallization from ether the pure β anomer (β 2) was obtained: 105 mg (13%), mp 163–164°;[14] nmr peaks at τ 4.12 (doublet, 1.8 cps, H-1), 7.90, 7.94, and 8.00 (Ac). The amorphous material remaining in the mother liquor was rich in the α anomer (α 2); its lower-field signal for H-1 at τ 3.98 distinguished it from the β anomer.

B. Using a Higher Proportion of Zinc Chloride.—A solution of 2-acetamido-2-deoxy-D-mannose monohydrate (1, 5.0 g) in acetic anhydride (35 ml) containing anhydrous zinc chloride (12 g) was stirred and heated at 85–90° (bath) for 20 min. The cooled solution was diluted with dichloromethane (*ca.* 100 ml), washed with water and sodium bicarbonate solution, and dried with sodium sulfate. Solvent was removed *in vacuo* and toluene was repeatedly distilled *in vacuo* from the residual syrup to remove traces of acetic acid. Examination by tlc (benzene–ether–methanol, 14:14:1, v/v) revealed 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-mannopyranose (2) and a component which moved slightly faster. The crude product was chromatographed on a column of silica gel (450 ml) using benzene–ether–methanol (14:14:1, v/v) as eluent.

The first product isolated (fractions 63–74) was crystallized from ether: 0.77 g (11%), mp 133–134°, $[\alpha]^{20}D$ −31° (*c* 1.1, $CHCl_3$); infrared absorption (Nujol) at 1750 (OAc) and 1665 cm^{-1} (C=N); nmr signals at τ 4.22 (doublet, 5.5 cps, H-1), 7.85, 7.88, and 7.93 (OAc). The elementary analysis and physical properties of the substance suggested that it was **4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-Δ^2-oxazoline (3)**.

Anal. Calcd for $C_{14}H_{19}NO_8$ (mol wt, 329.31): C, 51.06; H, 5.82; N, 4.25. Found: C, 51.51; H, 5.64; N, 4.14.

Fractions 75–85 (1.6 g) contained a mixture of 2 and 3. Fractions 86–100 contained a mixture of the two anomeric forms of 2 (2.3 g, 28%); its chromatographic behavior was indistinguishable from that of an authentic specimen of the two anomers. Fractions 101–124 contained **2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyranose** (4, 0.73 g, 10%) which was crystallized from ethanol–hexane (1:1): mp 144–148°, $[\alpha]^{20}D$ +27.3° (*c* 0.50, $CHCl_3$); infrared absorption ($CHCl_3$) at 3620 (OH), 3450 (NH), 1755 (OAc), and 1685 and 1510 cm^{-1} (NAc). The substance reduced Fehling solution on heating.

Anal. Calcd for $C_{14}H_{21}NO_9$ (mol wt, 347.33): C, 48.41; H, 6.09; N, 4.03. Found: C, 48.26; H, 6.00; N, 3.86.

Hydrolysis of 4,5-(3,4,6-Tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-Δ^2-oxazoline (3).—A sample of 3 (200 mg) was dissolved in water (5 ml) containing *p*-toluenesulfonic acid (*ca.* 10 mg) and the solution was stored at room temperature, the course of the hydrolysis being monitored by tlc (ether–acetone, 5:1, v/v, and benzene–ether–methanol, 14:14:1, v/v). After 1 hr the oxazoline could no longer be detected. Water was removed *in vacuo* and the syrup thus obtained was triturated with chloroform which was then evaporated. The residue was crystallized from ethanol–hexane to give 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyranose (4): 180 mg (85%), mp 134–137°, $[\alpha]^{19}D$ +30.4° (*c* 0.82, $CHCl_3$). A mixture melting point with 4, isolated by chromatography of the acetylation mixture as described earlier, was 134–142°. The differences in melting point and specific rotation of samples prepared *via* the two different routes is probably attributable to the fact that 4 may exist in two anomeric forms; the chromatographic behavior and infrared spectra of the two samples were indistinguishable.

Methyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside (5).—A solution of 3 (390 mg) in absolute methanol (10 ml) containing *p*-toluenesulfonic acid monohydrate (10 mg) was left at room temperature, the reaction being monitored by tlc using ether–methanol (19:1, v/v). After 70 hr the presence of a main product, together with some 4, was evident. The solution was concentrated *in vacuo* to a syrup which was chromatographed on a column of silica gel (100 ml) using benzene–ether–methanol (5:5:1, v/v). Fractions 12–14 contained methyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside (5) which was obtained as a syrup: 145 mg (34%), $[\alpha]^{24}D$ +45° (*c* 0.3, $CHCl_3$); infrared absorption (Nujol) at 3400 (NH), 1740 (OAc), 1560 (NAc), and 1525 cm^{-1} (amide II); nmr signals at τ 6.63 (OCH_3), 7.92, 7.99, and 8.05 (Ac).

Anal. Calcd for $C_{15}H_{23}NO_9$ (mol wt, 361.36): C, 49.86; H, 6.42; N, 3.88. Found: C, 49.96; H, 6.31; N, 3.94.

Benzyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside (6).—A solution of 4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-mannopyrano)-2-methyl-Δ^2-oxazoline (3, 400 mg) in freshly distilled benzyl alcohol (4 ml) containing *p*-toluenesulfonic acid monohydrate (4 mg) was kept at room temperature, and the reaction was monitored by tlc using ether–methanol (19:1, v/v). After 30 hr the reaction was complete and the mixture was then chromatographed directly on a column of silica gel (400 ml) using ether–methanol (19:1, v/v). Benzyl alcohol was eluted first, and then the main product of the reaction (6), which was obtained as a fine powder after trituration with hexane: 390 mg (73%), $[\alpha]^{20}D$ +72.2° (*c* 0.53, $CHCl_3$); infrared absorption ($CHCl_3$) at 3440 (NH), 1750 (OAc), 1690 (NAc), and 1600 and 1500 cm^{-1} (phenyl); nmr signals at τ 2.61 (aromatic), 4.15 (doublet, J = 9.0 cps, NH), 7.88, 7.92, and 8.00 (Ac).

Anal. Calcd for $C_{21}H_{27}NO_9$ (mol wt, 437.45): C, 57.66; H, 6.22; N, 3.20. Found: C, 57.84; H, 6.22; N, 3.07.

Benzyl 2-Acetamido-2-deoxy-α-D-mannopyranoside (7).—Benzyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-α-D-mannopyranoside (6, 300 mg) was de-*O*-acetylated with sodium methoxide in conventional fashion to give a material which solidified on trituration with hexane: 210 mg (98%), mp 73–78°, $[\alpha]^{20}D$ +97.3° (*c* 0.37, $CHCl_3$). All attempts to recrystallize the substance were unsuccessful.

Anal. Calcd for $C_{15}H_{21}NO_6$ (mol wt, 311.35): C, 57.87; H, 6.80; N, 4.50. Found: C, 57.78; H, 7.00; N, 4.61.

A sample (70.0 mg) of 7 was found to have consumed 1.21 molar equiv of sodium metaperiodate after 24 hr at room temperature. Another sample (40 mg) was hydrogenated in methanol in the presence of palladium black; after removal of the catalyst and solvent, the product was trimethylsilylated[15] and examined by glpc.[16] Its behavior was identical in all respects with the product from the trimethylsilylation of 1. A sample of 7 was trimethylsilylated; the product proved to be chromatographically homogeneous on glpc and had a shorter retention time than the corresponding furanoside.[17]

Reaction of 2-Benzamido-2-deoxy-D-glucose (8) with Zinc Chloride and Acetic Anhydride.—A mixture of 8[18] (1.0 g), acetic anhydride (8 ml), and zinc chloride (2.5 g) was stirred and heated at 85–90° (bath) for 20 min. The cooled solution was diluted

(11) Melting points are corrected. Thin layer chromatography was conducted on silica gel G (E. Merck AG, Darmstadt) using the solvent systems specified, components being detected by spraying with 10% sulfuric acid and heating at 100°. Column chromatography was carried out with Merck AG silica gel (0.05–0.20 mm), 15-ml fractions being collected. Nmr spectra were obtained in $CDCl_3$ solution using a Varian A-60 spectrometer and tetramethylsilane as an internal standard. Infrared spectra were recorded on Perkin-Elmer Model 137 and Model 221 spectrometers.

(12) Pfanstiehl Laboratories, Inc., Waukegan, Ill.

(13) The anomeric forms of 2 are not separable in the solvent system used or, indeed, in any solvent system tried.

(14) A. N. O'Neill, *Can. J. Chem.*, **37**, 1747 (1959), reported mp 162–163°.

(15) The Tri-Sil reagent of the Pierce Chemical Co., Rockford, Ill., was used for this purpose.

(16) An F & M Model 500 instrument, with a flame ionization detector, was used for glpc; the column employed (0.25 in. × 6 ft) was filled with 3% SE 52 on Gaschrom A (Applied Science Laboratories, Inc., State College, Pa.).

(17) J. R. Plimmer, N. Pravdić, and H. G. Fletcher, Jr., *J. Org. Chem.*, **32**, 1978 (1967).

(18) S. Konstas, I. Photaki, and L. Zervas, *Ber.*, **92**, 1288 (1959).

with dichloromethane (*ca.* 50 ml) and washed with water and sodium bicarbonate solution. Moisture was removed with sodium sulfate and the solution was concentrated *in vacuo* to a syrup from which toluene was distilled *in vacuo*. The syrup was then chromatographed on a column of silica gel (110 ml) using benzene–ether–methanol (14:14:1, v/v) as eluent. Fractions 8–11 contained **4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyrano)-2-phenyl-Δ^2-oxazoline** (**9**)[19] which was obtained as a chromatographically homogeneous syrup: 1.14 g (82%); infrared absorption (Nujol) at 1755 (OAc) and 1660 cm^{-1} (C=N);[20] nmr signals at τ 3.88 (doublet, J = 7.8 cps, H-1), 7.87, 7.95, and 8.00 (OAc).

Fractions 13–15 contained a second product (250 mg, 16%) which proved to be chromatographically identical with 1,3,4,6-tetra-*O*-acetyl-2-benzamido-2-deoxy-D-glucopyranose (**10**): nmr signals at τ 3.67 (doublet, J = 3.8 cps) and 4.15 (doublet, J = 9.0 cps), corresponding to H-1 of the α anomer of **10** and H-1 of the β anomer of **10**, respectively.[21]

Methyl 3,4,6-Tri-*O*-acetyl-2-benzamido-2-deoxy-β-D-glucopyranoside (**11**).—4,5-(3,4,6-Tri-*O*-acetyl-2-deoxy-D-glucopyrano)-2-phenyl-Δ^2-oxazoline (**9**, 470 mg) was dissolved in absolute methanol (10 ml) containing *p*-toluenesulfonic acid monohydrate (10 mg), and the solution was stored at room temperature. After 10 min, crystallization of the product began. After cooling, **11** was removed by filtration: 420 mg (83%), mp 221–222°, $[\alpha]^{20}D$ +28.5° (*c* 1.33, $CHCl_3$); nmr signals at τ 2.2–2.8 (aromatic), 3.50 (doublet, J = 9.0 cps, NH), 6.53 (OCH_3), 7.93, 7.99, and 8.07 (OAc). Micheel and Köchling[4] reported mp 222° and $[\alpha]^{24}D$ +29.6° (*c* 1.05, $CHCl_3$) for methyl 3,4,6-tri-*O*-acetyl-2-benzamido-2-deoxy-β-D-glucopyranoside (**11**).

Reaction of 2-Acetamido-2-deoxy-D-galactose (**12**) **with Zinc Chloride and Acetic Anhydride.**—A mixture of 2-acetamido-2-deoxy-D-galactose[12] (**12**, 1.0 g), acetic anhydride (8 ml), and anhydrous zinc chloride (2.5 g) was stirred and heated at 85–90° (bath) for 20 min. The cooled reaction mixture was diluted with dichloromethane and washed with cold water and then twice with aqueous sodium bicarbonate. Moisture was removed with sodium sulfate, and the solution was concentrated *in vacuo* to a syrup from which toluene was distilled *in vacuo*. The partially crystalline residue was treated with ether (*ca.* 50 ml), and the crystals were removed by filtration: 790 mg (45%), mp 180–184°; nmr peaks at τ 3.72 (doublet, J = 3.5 cps, H-1), 7.82, 7.96, and 8.03 (Ac). The nmr and infrared spectra and the chromatographic properties of the substance were identical with those of an authentic sample of 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-galactopyranose (α **13**).[3,6]

Examination of the ethereal filtrate by tlc (benzene–ether–methanol (14:14:1, v/v) showed the presence of a small quantity of **13** and a larger quantity of a faster moving component. The material was chromatographed on a column of silica gel (100 mg) using benzene–ether–methanol (14:14:1, v/v) as eluent. Fractions 15–19 contained **4,5-(3,4,6-tri-*O*-acetyl-2-deoxy-D-galactopyrano)-2-methyl-Δ^2-oxazoline** (**14**) which was isolated as a syrup: 390 mg (26%), $[\alpha]^{20}D$ +25.5° (*c* 1.25, $CHCl_3$); infrared absorption (neat) at 1770 (OAc) and 1675 cm^{-1} (C=N); nmr peaks at τ 4.09 (doublet, J = 6.5 cps, H-1), 7.92, 7.96, and 8.02 (Ac).

Anal. Calcd for $C_{14}H_{19}NO_8$ (mol wt, 329.31): C, 51.06; H, 5.82; N, 4.25. Found: C, 51.29; H, 6.15; N, 4.21.

Fractions 25–53 contained β **13** (230 mg), mp (from ethanol–hexane) 230° dec, lit.[6] mp 235°. The chromatographic behavior (tlc) of the material was identical with that of α **13**.

Ethyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (**15**).—A solution of **14** (160 mg) in absolute ethanol (2 ml) was kept at room temperature for 2 days and then concentrated *in vacuo*. The chromatographic behavior and infrared absorption spectrum of the syrup showed it to be unchanged **14**. It was redissolved in absolute ethanol (5 ml) and *p*-toluenesulfonic acid monohydrate (*ca.* 5 mg) was added. Thin layer chromatography (ether–methanol, 19:1, v/v) showed that the reaction was complete at room temperature in 2 hr. On cooling, the product (**15**) crystallized: 95 mg (52%). It was twice recrystallized from ethanol: mp 218–219°, $[\alpha]^{20}D$ −26.3° (*c* 0.3, $CHCl_3$), $[\alpha]^{20}D$ −21° (*c* 0.60, CH_3OH). Tarasiejska and Jeanloz[7] reported mp 225–226° and $[\alpha]^{24}D$ −19° (CH_3OH).

An attempt to prepare the picrate of **14** in ethanol solution led to the isolation of **15**.

Registry No.—β **2**, 6730-10-5; **3**, 10385-48-5; α **4**, 10353-11-4; **5**, 10353-12-5; **6**, 10375-65-2; **7**, 10380-86-6; **9**, 10380-87-7; α **10**, 10380-88-8; β **10**, 10385-49-6; **11**, 10380-89-9; α **13**, 10385-50-9; **14**, 10378-06-0; **15**, 10353-13-6; zinc chloride, 7646-85-7; acetic anhydride, 108-24-7.

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(19) Micheel and Köchling[4] obtained this substance in crystalline form, mp 56°.

(20) Micheel *et al.*,[3] published the infrared spectrum of the hydrobromide of **9**.

(21) T. D. Inch and H. G. Fletcher, Jr., *J. Org. Chem.*, **31**, 1821 (1966).

The Favored Conformation of Tri-*O*-acetyl-β-D-xylopyranosyl Chloride. An All-Axial Tetrasubstituted Six-Membered Ring[1-3]

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It is shown that tri-*O*-acetyl-β-D-xylopyranosyl chloride (**1**) does not adopt the all-equatorial (*C1*) chair form (**3**) as the favored conformation in solution. The evidence of nmr indicates that the favored conformation of **1**, in chloroform, benzene, or acetone solution, is the all-axial (*1C*) chair form (**2**).

The thermodynamically stable anomers of the tri-*O*-acetylpentopyranosyl bromides are the β-D- (or L-) *arabino*, α-D- (or L-) *lyxo*, β-D- (or L-) *ribo*, and α-D- (or L-) *xylo*.[2] In an earlier paper[2] it was shown that the favored conformation of these derivatives in chloroform solution is, in each case, that chair form in which the halogen atom is axial. In the case of tri-*O*-acetyl-β-D- (or L-) ribopyranosyl bromide, two of the three acetoxy groups are also axial in the favored conformation. This indicates that the unfavorable polar interaction between electron clouds of the ring oxygen atom and an equatorial C-1–halogen dipole (anomeric effect)[5,6] outweighs the steric effects of three axial sub-

(1) Part II in the series "Conformational and Configurational Studies on Some Acetylated Aldopyranosyl Halides." For part I, see ref 2.

(2) Previous publication in this series: D. Horton and W. N. Turner, *J. Org. Chem.*, **30**, 3387 (1965).

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(4) To whom inquiries should be addressed.

(5) R. U. Lemieux in "Molecular Rearrangements," part II, P. deMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, pp 735–743.

(6) S. J. Angyal in "Conformational Analysis," E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, Ed., Interscience Publishers, Inc., New York, N. Y., 1965, Chapter 6.