The authors are indebted to the members of Central Analysis Room of Faculty of Pharmaceutical Sciences, University of Tokyo, for elementary analyses.

Summary

Comparative studies on the acid hydrolysis and periodate oxidation of methyl N-acyl-β-D-glucosaminides were carried out. Results of these reactions were discussed in relation to the properties of N-acyl groups.

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103. Toshiaki Osawa: Nitrogen-containing Sugars. IX.*2 Influence of the Substituent at C-2 on the Chlorination at C-1 in N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines.

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The two methods most usually used for the preparation of glycosyl chloride from C-1-acylated sugars are treatment of acylated sugar with hydrogen chloride in acetic acid or acetic anhydride, and that with titanium tetrachloride in refluxing chloroform. These methods give the stable form of the poly-O-acylglycosyl chloride as the final product, irrespective of the anomeric configuration of the starting material. For example, α-glycosyl chlorides are obtained from both α- and β-acylated glucose derivatives by either of these methods.

In 1926, Schlubach[1] found that a brief treatment of the normal α-acetobromo-D-glucose in ether with freshly prepared silver chloride yielded the unstable acetochloro-β-D-glucose. This reaction has been commonly used to obtain unstable β-glycosyl chlorides. In 1954, Zémplen and co-workers[2] found that the reaction of penta-O-acetyl-β-D-glucose with anhydrous aluminium chloride in cold chloroform gave acetochloro-β-D-glucose. Recently, Korytnyk and Mills[3] applied this reaction on several 1,2-*trans*-acetylated sugars and found that this reaction was a convenient method for the preparation of 1,2-*trans*-acetylglycosyl chlorides from 1,2-*trans*-acetylated sugars. Lemieux and Brice[4] have recently found that the reaction of penta-O-acetyl-β-D-glucose with titanium tetrachloride at 40° results in a rapid formation of acetochloro-β-D-glucose followed by a relatively much slower rearrangement of the latter to the α-anomer.

In the preceding papers of this series,[5,6] several methods of chlorination were applied on both N,N-phthaloyl and N,N-succinyl derivatives of D-glucosamine and only β-glycosyl chlorides were obtained. In this paper, several new observations on the chlorination at C-1 of other N-acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines will be de-

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*2 Part Ⅷ: This Bulletin, 8, 592(1960).

1) H. H. Schlubach: Ber., **59**, 840(1926).
2) G. Zémplen, L. Mester: Acta Chim. Acad. Sci. Hung., **4**, 73(1954).
3) W. Korytnyk, J. A. Mills: J. Chem. Soc., **1959**, 636.
4) R. U. Lemieur, C. Brice: Can. J. Chem., **30**, 295(1952).
5) Part. Ⅵ. S. Akiya, T. Osawa: This Bulletin, 8, 583(1960).
6) Part. Ⅶ. *Idem*: *Ibid.*, 8, 588(1960).

scribed. These chlorination reactions were conducted in the following fashion unless otherwise stated:

(1) A solution of 1 g. of acetylated sugar dissolved in 10 cc. of anhydrous chloroform was shaken for 40 min. with 0.7 g. of anhydrous aluminium chloride. (2) A solution of 1 g. of acetylated sugar dissolved in 10 cc. of anhydrous chloroform was boiled for 4 hr. with 0.3 cc. titanium tetrachloride. (3) A solution of 1 g. of acetylated sugar dissolved in 15 cc. acetic anhydride saturated with hydrogen chloride at 0° was left to stand for 18 hr. at room temperature.

It has been known[7] that penta-O-acetyl-β-D-glucosamine[8] (I) gives α-acetochloro-D-glucosamine (II) on treatment with hydrogen chloride in acetic anhydride. The treatment of (I) with titanium tetrachloride in boiling chloroform also gave (II). In the reaction of (I) with aluminium chloride in cold chloroform (due to the relative insolubility of (I) in cold chloroform, larger amounts of both chloroform and aluminium chloride than those described above were used), the product (III) was a syrup which was positive to the Beilstein test for halogen and its optical rotation, $[\alpha]_D^{20}$ +19.6° ($CHCl_3$), increased gradually on standing. Treatment of (III) with titanium tetrachloride in boiling chloroform yielded (II) and the reaction of (III) with methanol gave methyl N-acetyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (IV). On being kept in water-saturated chloroform in the presence of a catalytic amount of hydrogen chloride, (III) easily underwent rearrangement to 1,3,4,6-tetra-O-acetyl-α-D-glucosamine hydrochloride (V) which was converted into N-phthaloyl-1,3,4,6-tetra-O-acetyl-α-D-glucosamine (VI). (III) was transformed to (I) by treatment with silver acetate in refluxing benzene. Further, on treatment of (I) with titanium tetrachloride in chloroform at 40°, it was rapidly converted into a syrupy product, $[\alpha]_D^{20}$ +20.0° ($CHCl_3$), and the properties of this product were entirely the same as those of (III).

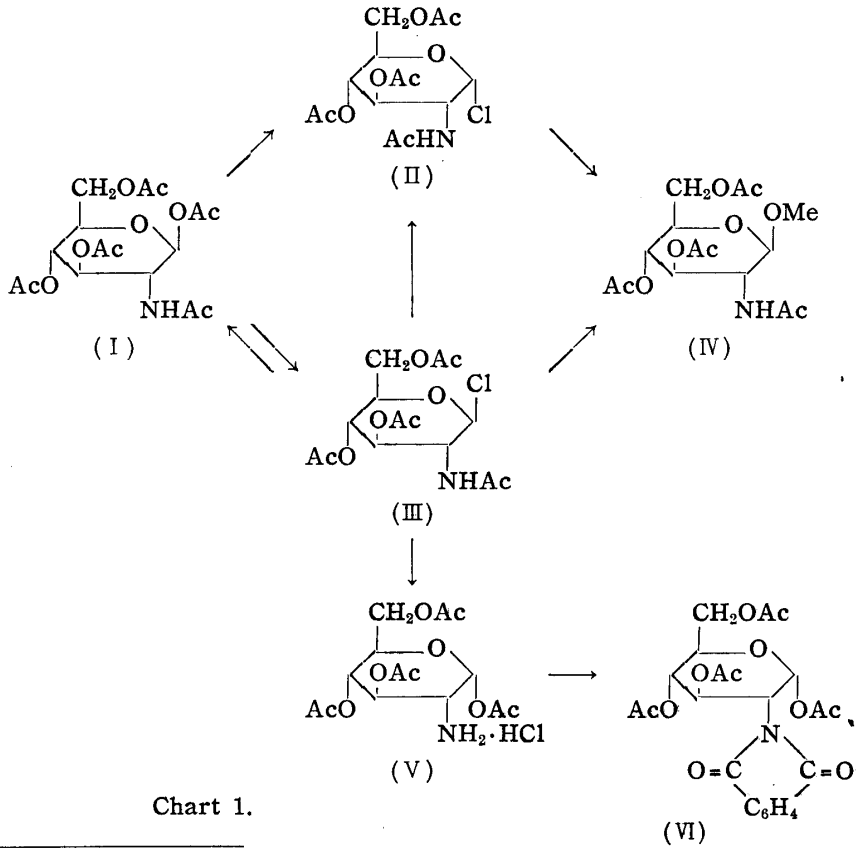


Chart 1.

7) D. H. Leaback, P. G. Walker: J. Chem. Soc., **1957**, 4754.
8) M. Bergmann, L. Zervas: Ber., **64B**, 975(1931).

From the foregoing experiments, (III) was assumed to be acetochloro-β-D-glucosamine. Thus, (I) behaved as ordinary sugars in chlorination reactions to give β-glycosyl chloride in the reaction with aluminium chloride and α-glycosyl chloride on treatment with both titanium tetrachloride in boiling chloroform and hydrogen chloride in acetic anhydride. However, in the case of N-chloroacetyl derivative, introduction of a chlorine atom into N-acetyl group changed the features of these chlorination reactions and, in each case of these three methods of chlorination, N-chloroacetyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine[8] (VII) gave only one crystalline product (VIII), m.p. 143°, $[\alpha]_D^{22}$ +115.7° ($CHCl_3$). Reaction of (VIII) with methanol in the presence of silver carbonate as acid-acceptor gave methyl N-chloroacetyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (IX). Infrared spectrum of (VIII) revealed the presence of NH (3300 cm^{-1}) and secondary amide (1665 cm^{-1}) groups. From these observations and its high rotational property, (VII) was clearly 1-chloro-N-chloroacetyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine. (VII) is the first example of 1,2-*trans*-acylated sugar hitherto known which yields α-glycosyl chloride in the reaction with anhydrous aluminium chloride in cold chloroform. Moreover, even brief treatment of (VII) with titanium tetrachloride in chloroform at 40° resulted in the formation of (VIII).

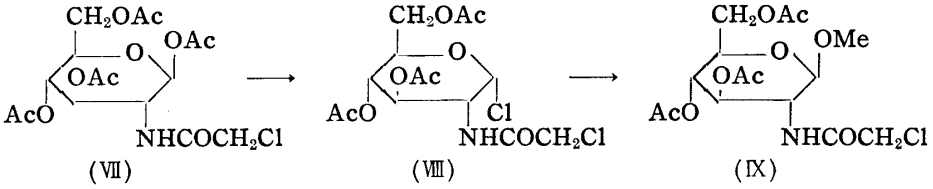


Chart 2.

On the other hand, N-aroyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine showed remarkable characteristic in these chlorination reactions compared with N-acetyl or N-chloroacetyl derivatives, giving oxazoline derivatives. Recently, Micheel[9] showed facile rearrangement of 1-bromo-N-benzoyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine to 2-phenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline hydrobromide.

In the reaction with aluminium chloride in cold chloroform, N-benzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine[9] (X) and N-anisoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XVIII)

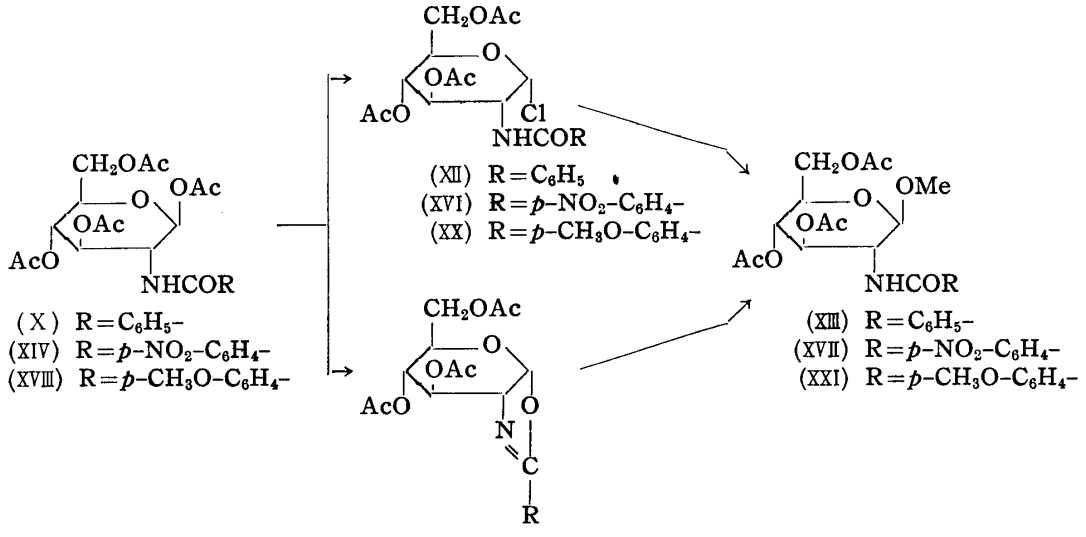


Chart 3.

9) F. Micheel, F.-P. van de Kamp, H. Petersen: Ber., **90**, 521(1957).

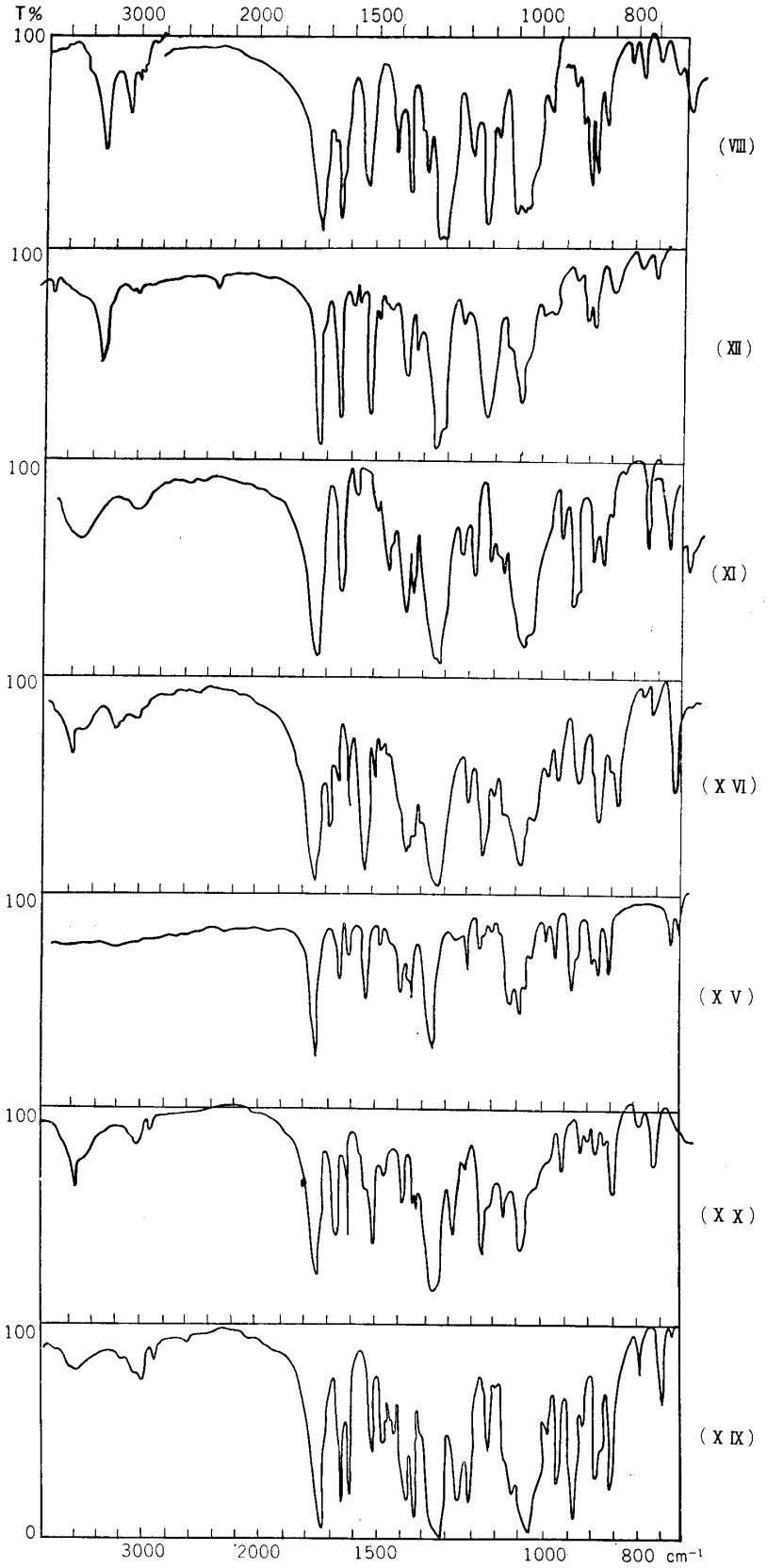


Fig. 1. Infrared Spectra of α-Glycosyl Chlorides and Oxazoline Derivatives obtained from 1,3,4,6-Tetra-O-acetyl-N-acyl-β-D-glucosamines (KBr disc)

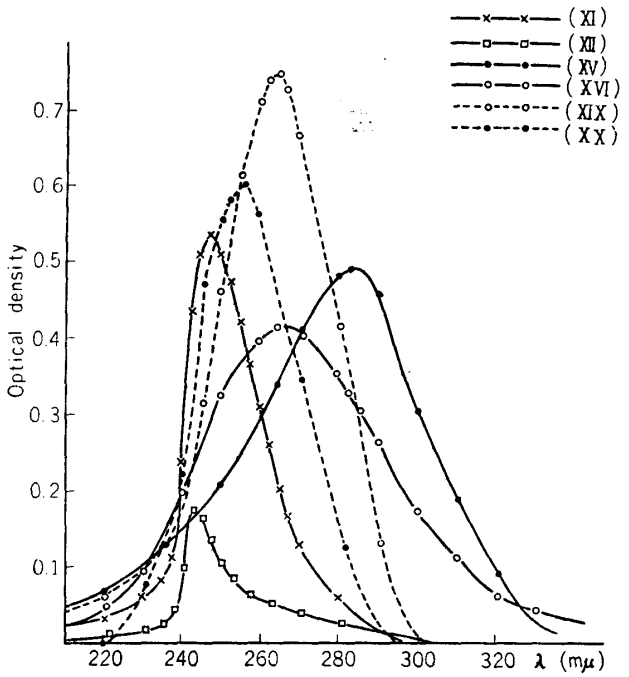
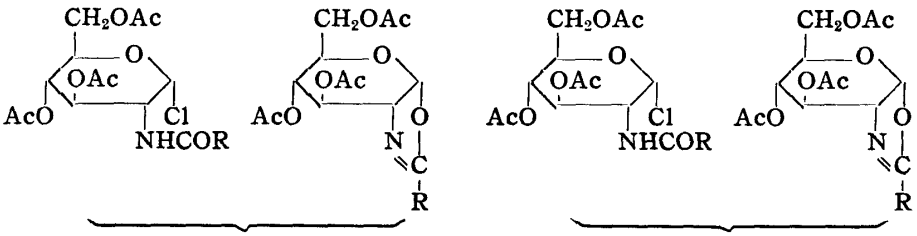


Fig. 2.

Ultraviolet Spectra of α-Glycosyl Chlorides and Oxazoline Derivatives obtained from 1,3,4,6-Tetra-O-acetyl-N-acyl-β-D-glucosamines (in $CHCl_3$)

TABLE I. Yield (%) of Reaction Products in the Chlorination of 1,3,4,6-Tetra-O-acetyl-N-acyl-β-D-glucosamines



Reagent	R	40 min.		15 min.	
$AlCl_3$	-OMe	—	74		
	-	—	69		
	$-NO_2$	53	34	21	66
		4 hr. reflux		5 min. at 40°	
$TiCl_4$	-OMe	7	69		
	-	32	29	—	63
	$-NO_2$	53	6	7	76
		18 hr.		10 min.	
HCl/Ac_2O	-OMe	11	69		
	-	53	17	5	63
	$-NO_2$	86	—	42	34

yielded the corresponding oxazoline derivatives as the only product, while N-*p*-nitrobenzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XIV) yielded both oxazoline derivative and α-glycosyl chloride. Titanium tetrachloride in refluxing chloroform converted (X), (XIV), and (XVIII) into mixtures of corresponding oxazoline derivatives and α-glycosyl chlorides. With hydrogen chloride in acetic anhydride, (X) and (XVIII) gave both oxazoline derivatives and α-glycosyl chlorides, while (XIV) gave only α-glycosyl chloride.

These oxazoline derivatives, (XI), (XV), and (XIX), showed negative Beilstein test and reacted with methanol to give the corresponding methyl N-aroyl-3,4,6-tri-O-acetyl-β-D-glucosaminides. In their infrared spectra, instead of absorption bands for NH and secondary amide groups which were detected in the starting compounds, absorption of C=N double bond (1635~1650 cm^{-1}) was observed. On the other hand, each of the α-glycosyl chlorides, (XII), (XVI), and (XX), showed positive Beilstein test, reacted with methanol in the presence of silver carbonate as acid-acceptor to give the corresponding methyl N-aroyl-3,4,6-tri-O-acetyl-β-D-glucosaminides. Infrared spectra of these α-glycosyl chlorides revealed the presence of NH(near 3500 cm^{-1}) and secondary amide (1525~1540 cm^{-1}) groups.

When these chlorination reactions were conducted for a shorter period, the yield of oxazoline derivatives improved markedly. These results are listed in Table I.

It is found from Table I that in the chlorination reactions of N-aroyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines the yield of these oxazoline derivatives are in the descending order of N-anisoyl, N-benzoyl, and N-*p*-nitrobenzoyl derivatives.

The facts that shorter the period of chlorination reactions, the larger are the yields of oxazoline derivatives, and that α-glycosyl chlorides are formed from the oxazoline derivatives by treatment of the latter with hydrogen chloride in acetic anhydride may be explained by the assumption that these oxazoline derivatives are intermediate compounds in the reaction process of 1,2-*trans*-acetylated sugars to α-glycosyl chlorides.

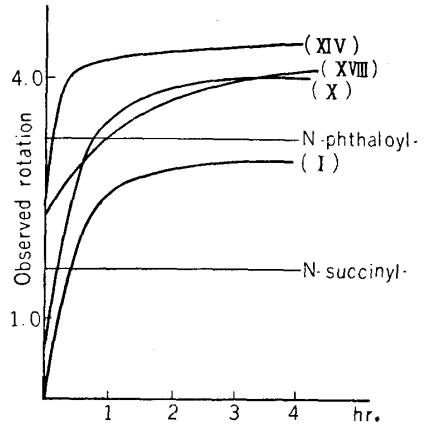


Fig. 3.

Reaction Rates (at 40.2°) of Equimolar Amounts of N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines and $TiCl_4$ (in $CHCl_3$)

In order to ascertain this assumption, kinetic studies of these chlorination reactions were made. At first, the reactions of (I), (X), (XIV), and (XVIII) with titanium tetrachloride in chloroform at 40° were followed by polarimetric method. The results are shown in Fig. 3. In the case of N,N-phthaloyl- and N,N-succinyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines, no increase of optical rotation was observed under this condition as shown in Fig. 3, but β-glycosyl chloride was obtained in good yield from the reaction mixture. It is therefore evident that in the reaction with titanium tetrachloride an acetoxyl group at C-1 of N-acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine dissociates rapidly to give β-glycosyl chloride or other intermediate and conversion of these intermediate into α-glycosyl chloride is a rate-controlling step. From Fig. 3, using the integrated polarimetric rate expression,

$$k=\frac{2.303}{t}\log\frac{\alpha_0-\alpha}{\alpha_t-\alpha},$$

the rate of the reactions of (I), (X), (XIV), and (XVIII) with titanium tetrachloride was found to be of the first order and the rate constants were calculated as shown in Table II.

Further, the decrease of oxazoline derivatives in the reactions of (X), (XIV), and (XVIII) with titanium tetrachloride in chloroform at 40° was followed by spectrophotometric method. The results are illustrated in Fig. 4. Thus, rate constants could be calculated as shown in Table II. As is seen from Table II, the rate constants of (X) and (XVIII) are

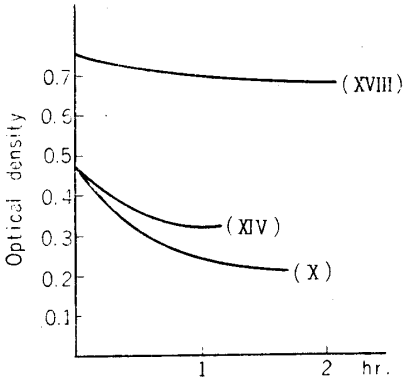


Fig. 4.

Reaction Rates (at 40.2°) of Equimolar Amounts of N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines and $TiCl_4$ (in $CHCl_3$)

Table II. Reaction Rate Constants (at 40.2°) of Equimolar Amounts of N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine and $TiCl_4$ in $CHCl_3$

	k, min^{-1}, (Mean value)	
	Polarimetric method	Spctrophotometric method
N-Acetyl (I)	0.034	
N-Anisoyl (XVIII)	0.014	0.014
N-Benzoyl (X)	0.029	0.026
N-p-NO_2-benzoyl (XIV)	0.069	0.045

very analogous with those obtained by the polarimetric method, but, in the case of (XIV), the rate constant obtained by the spectrophotometric method was somewhat smaller than that obtained by polarimetric method. This is assumed to be due to the rather small difference of optical density between (XV) and (XVI) at the wave length of maximum absorption of (XV).

Moreover, oxazoline derivatives (XI), (XV), and (XIX), were treated with hydrogen chloride in acetic anhydride and the reaction was followed by polarimetric method as shown in Fig. 5. The rate constants were calculated from Fig. 5 as shown in Table III.

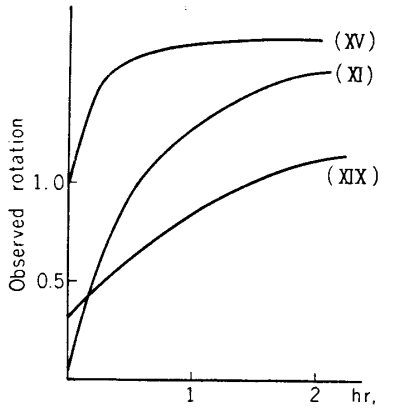


Fig. 5.

Reaction Rates (at 31.5°) of Oxazoline Derivatives obtained from N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines with HCl in Ac_2O (1.5 g. HCl in 10 cc.)

Table III. Reaction Rate Constant (at 31.5°) of Oxazoline Derivatives obtained from N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines with HCl in Ac_2O (1.5 g. HCl in 10 cc.)

	k (min^{-1}) (Mean value)
N-Anisoyl (XIX)	0.013
N-Benzoyl (XI)	0.027
N-*p*-NO_2-benzoyl (XV)	0.065

These rate constants agreed well with those obtained by polarimetric methods in the reaction of (X), (XIV), and (XVIII) with titanium tetrachloride at 40°.

Thus, it became apparent that the oxazoline derivatives are intermediate compounds during the chlorination of N-aroyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines. However, when hydrochloride of (XI) was dissolved in chloroform and shaken with water, free base of (XI) was obtained from the chloroform solution. Therefore, it seems reasonable to assume that hydrochlorides of oxazoline derivatives are intermediates in the chlorination reactions.

Further, the participation of acyloxyl groups at C-2 in the dissociation of acetoxyl groups at C-1 was examined. Treatment of N-trichloroacetyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XXII) with anhydrous aluminium chloride in cold chloroform resulted only in recovery of the starting material. In the case of N-benzoyl-1,3,4,6-tetra-O-acetyl-α-D-glucosamine[9] (XXIII), this compound was not affected by either anhydrous aluminium chloride in cold chloroform or titanium tetrachloride in chloroform at 40°. From these facts, it is evident that the participation of acyloxyl group at C-2 plays an important rôle in the dissociation of acetoxyl group at C-1.

From the foregoing series of experiments, the mechanism of chlorination at C-1 of N-acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine is summarized as follows. The acetoxyl group at C-1 dissociates rapidly with participation of acyloxyl group at C-2 to give the unstable β-glycosyl chloride. At this stage, in the cases of N-aroyl derivatives, unstable β-glycosyl chloride is stabilized through rapid rearrangement to the hydrochloride of corresponding oxazoline derivative in which C=N double bond conjugates with the phenyl ring. The process of transformation of β-glycosyl chloride or oxazoline derivatives to α-glycosyl chloride is a rate determining step in this chlorination reaction and greatly influenced by the character of a substituent at C-2. Thus, the faster the rate of formation of oxonium ion, a direct precursor of α-anomer, from unstable β-glycosyl chloride or oxazoline derivative, the more rapid would be the rate of the formation of α-glycosyl chloride. Therefore, N-acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamines, which have electronegative group on their N-substituent, such as in N-*p*-nitrobenzoyl- or N-chloroacetyl-

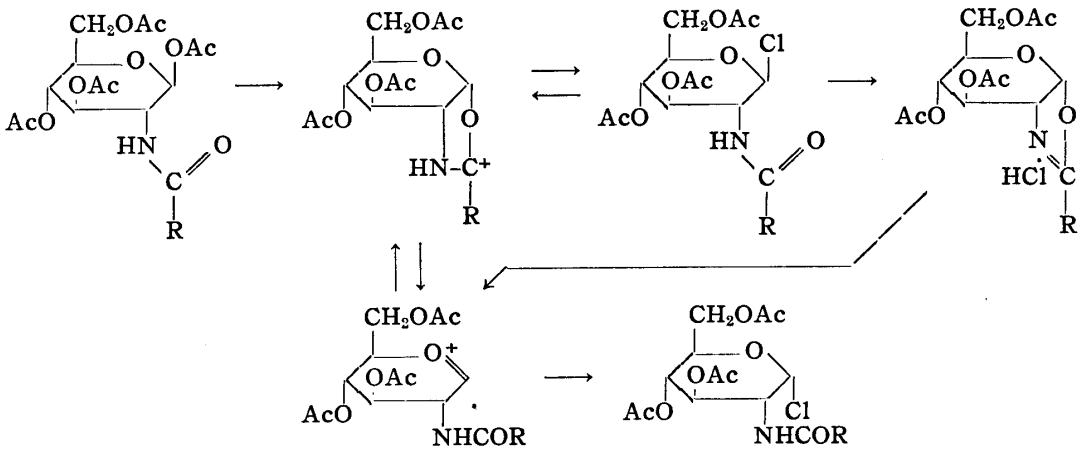


Chart 4.

1,3,4,6-tetra-O-acetyl-β-D-glucosamine, react rapidly with the chlorination agent to give α-glycosyl chloride.

Experimental

Reaction of (I) with Anhydrous $AlCl_3$—A mixture of 1.0 g. of (I) dissolved in 15 cc. of pure $CHCl_3$ and 1.0 g. of crushed anhyd. $AlCl_3$ was shaken vigorously for 40 min. at room temperature. The reaction mixture was poured into water and the separated aqueous layer was extracted with $CHCl_3$. The combined $CHCl_3$ solution was dried over $CaCl_2$ and evaporated *in vacuo* to a viscous syrup. This syrup was dissolved in dehyd. Et_2O, insoluble material was filtered off, and Et_2O was evaporated *in vacuo* to a syrup. Evaporation of Et_2O solution was repeated twice leaving 0.40 g. of a viscous syrup (III). No suitable solvent could be found for its crystallization. $[\alpha]_D^{20}$ +19.6° (c=0.92, $CHCl_3$). The optical rotational value increased on standing in $CHCl_3$ as follows: +0.18° (5 min.)→+0.26° (18 hr.)→+0.30° (24 hr.).

This syrup (III) was positive to the Beilstein test for halogen. Several reactions were tried on this syrup (III) as follows:

a) A solution of 0.40 g. of (III) dissolved in 10 cc. of pure $CHCl_3$, with 0.3 cc. of $TiCl_4$ added, was refluxed for 3 hr. When cooled, the reaction mixture was diluted with $CHCl_3$ and poured into ice water. The $CHCl_3$ solution was washed successively with water, cold $NaHCO_3$ solution, and water, dried over $CaCl_2$, and evaporated *in vacuo* to a syrup which crystallized on trituration with Et_2O. Recrystallization from AcOEt-petr. ether gave white needles, m.p. 135~136°, $[\alpha]_D^{22}$ +115.2° (c=1.37, $CHCl_3$). In admixture with authentic acetochloro-α-D-glucosamine[7] (II), no depression of m.p. was observed.

b) A solution of 0.30 g. of (III) dissolved in 10 cc. of anhyd. MeOH was kept standing overnight at room temperature. The reaction solution was evaporated *in vacuo* and the residue was recrystallized from AcOEt-petr. ether to white needles, m.p. 156°, $[\alpha]_D^{20}$ −23.1° (c=0.52, MeOH). Yield, 0.15 g. In admixture with authentic methyl N-acetyl-3,4,6-tri-O-acetyl-β-D-glucosaminide[10] (IV), no depression of m.p. was observed.

c) A solution of 0.35 g. of (III) dissolved in 10 cc. of water-saturated $CHCl_3$ was kept standing in a refrigerator. In a few hours, 0.27 g. of white needles, m.p. 182° (decomp.), $[\alpha]_D^{20}$ +132.0° (c=0.50, H_2O), was obtained (reported[9] m.p. 180°, $[\alpha]_D^{20}$ +130° (H_2O), for 1,3,4,6-tetra-O-acetyl-α-D-glucosamine hydrochloride). A solution of 0.25 g. of this product dissolved in 5 cc. of pyridine, with 0.15 g. of phthalic anhydride added, was heated for 30 min. at 90°. Then, 5 cc. of Ac_2O was added and heating was continued further for 1 hr. at 90°. The reaction mixture was poured into water and extracted with $CHCl_3$. The $CHCl_3$ solution was washed successively with water, 5% HCl, and water, dried over $CaCl_2$, and evaporated *in vacuo* to dryness. The residue was recrystallized from 30% EtOH to white needles, m.p. 124~126°, $[\alpha]_D^{20}$ +116.2° (c=1.57, $CHCl_3$). Yield, 0.16 g. In admixture with authentic N,N-phthaloyl-1,3,4,6-tetra-O-acetyl-α-D-glucosamine[5] (VI), no depression of m.p. was observed.

d) A solution of 0.3 g. of (III) dissolved in 10 cc. of benzene (dried over Na) was stirred with 0.3 g. of dry AgOAc and refluxed for 5 hr. After filtering through charcoal, the solution was evaporated *in vacuo* to dryness. The residue was recrystallized from EtOH to white needles, m.p. 184~185°, $[\alpha]_D^{20}$ −2.0° (c=1.00, $CHCl_3$). Yield, 0.2 g. In admixture with authentic penta-O-acetyl-β-D-glucosamine[8] (I), no depression of m.p. was observed.

Reaction of (I) with $TiCl_4$—A mixture of 1.0 g. of (I) dissolved in 10 cc. of $CHCl_3$, with 0.3 cc. of $TiCl_4$ added, was refluxed for 4 hr. The syrupy product, obtained on working up in the usual way, crystallized on trituration with Et_2O. Recrystallization from AcOEt-petr. ether gave white needles, m.p. 135~136°, $[\alpha]_D^{20}$ +115.2° (c=0.83, $CHCl_3$). Yield, 0.40 g. In admixture with authentic acetochloro-α-D-glucosamine,[7] no depression of m.p. was observed.

Brief treatment of (I) with $TiCl_4$—1.0 g. of (I) was treated with 0.3 cc. of $TiCl_4$ in 10 cc. of $CHCl_3$ for 5 min. at 40° and worked up in the usual way. The syrup obtained was dissolved in Et_2O, filtered, and Et_2O was evaporated *in vacuo* leaving 0.6 g. of a viscous syrup, $[\alpha]_D^{20}$ +20.0° (c=1.03, $CHCl_3$). The properties of this syrup were entirely the same with the syrup obtained in the reaction of (I) with $AlCl_3$.

Reaction of (VII) with Anhydrous $AlCl_3$—A solution of 1.0 g. of (VII) dissolved in 10 cc. of pure, dehyd. $CHCl_3$ was shaken with 0.7 g. of anhyd. $AlCl_3$ for 40 min. at room temperature. The product isolated in the usual way was syrupy and crystallized on dissolution in warm Et_2O. After standing in a refrigerator for a few hours, the crystals were collected and recrystallized from AcOEt-petr. ether to white needles, m.p. 143° (decomp.), $[\alpha]_D^{22}$ +115.4° (c=1.43, $CHCl_3$). Yield, 0.5 g. *Anal.* Calcd. for $C_{14}H_{19}O_8NCl_2$ (1-Chloro-N-chloroacetyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine (VIII)): C, 42.01;

10) W. O. Cutler, W. H. Haworth, S. Peat: J. Chem. Soc., **1937**, 1979.

H, 4.78; N, 3.50. Found : C, 41.87; H, 5.04; N, 3.49.

Reaction of (VII) with $TiCl_4$—A solution of 1.0 g. of (VII) dissolved in 10 cc. of pure $CHCl_3$, with 0.3 cc. of $TiCl_4$ added, was refluxed for 4 hr. The product was isolated in the usual way and the viscous syrup so obtained was crystallized from Et_2O to white needles, m.p. 143°(decomp.), $[\alpha]_D^{19}$ +115.6°(c=1.20, $CHCl_3$). Yield, 0.5 g. In admixture with (VIII) obtained in the reaction of (VII) with $AlCl_3$, no depression of m.p. was observed.

Reaction of (VII) with HCl in Ac_2O—A solution of 1.0 g. of (VII) dissolved in 15 cc. of Ac_2O saturated with HCl at 0° was kept standing for 18 hr. at room temperature. The reaction mixture was diluted with $CHCl_3$ and poured into ice-water. The $CHCl_3$ solution was washed successively with water, cold $NaHCO_3$ solution, and water, dried over $CaCl_2$, and evaporated *in vacuo*. The residue was recrystallized from AcOEt-petr. ether to white needles, m.p. 143°(decomp.), $[\alpha]_D^{22}$ +115.7°(c=1.85, $CHCl_3$). Yield, 0.5 g. In admixture with (VIII) obtained in the reaction of (VII) with $AlCl_3$, no depression of m.p. was observed.

Brief Treatment of (VII) with $TiCl_4$—A solution of 1.0 g. of (VII) dissolved in 10 cc. of pure $CHCl_3$, with 0.3 cc. of $TiCl_4$ added, was shaken for 5 min. at 40°. The reaction mixture was worked up in the usual way and the crude product was recrystallized from AcOEt-petr. ether to white needles, m.p. 143°(decomp.), $[\alpha]_D^{25}$ +116.0°(c=0.50, $CHCl_3$). Yield, 0.6 g. In admixture with (VIII) obtained in the reaction of (VII) with $AlCl_3$, no depression of m.p. was observed.

Methyl N-Chloroacetyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (IX)—A mixture of 0.50 g. of (VIII) in a suspension of 0.50 g. of Ag_2CO_3 in 20 cc. of MeOH was shaken for 2 hr. After filtration, the solution was evaporated *in vacuo* to dryness and the residue was recrystallized from AcOEt-petr. ether to white needles, m.p. 154~156°, $[\alpha]_D^{20}$ −6.67°(c=0.75, $CHCl_3$). Yield, 0.33 g. *Anal.* Calcd. for $C_{15}H_{22}O_9NCl$: C, 45.52; H, 5.60; N, 3.54. Found : C, 45.75; H, 5.87; N, 3.35.

Reaction of (X) with Anhydrous $AlCl_3$—1.0 g. of (X) was shaken with 0.7 g. of crushed anhyd. $AlCl_3$ in 10 cc. of pure $CHCl_3$ for 40 min. at room temperature and the reaction mixture was worked up in the usual way. The syrupy product obtained was dissolved in Et_2O, petr. ether was added to incipient turbidity, and placed in a refrigerator. The white plate crystals that deposited were collected and recrystallized from Et_2O-petr. ether, m.p. 56°, $[\alpha]_D^{20}$ +51.9°(c=1.58, $CHCl_3$), $[\alpha]_D^{20}$ +44.7°(c=1.41, pyridine-water=1:1). Yield, 0.6 g. [F. Micheel and Köchling[11] reported m.p. 56°, $[\alpha]_D^{23}$ +44.7°(pyridine-water=1:1)]. *Anal.* Calcd. for $C_{19}H_{21}O_8N$ (2-Phenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XI)) : C, 58.31; H, 5.41; N, 3.58. Found : C, 57.37; H, 5.78; N, 3.44.

Reaction of (X) with $TiCl_4$—A mixture of 1.0 g. of (X) dissolved in 10 cc. of pure $CHCl_3$ and 0.3 cc. of $TiCl_4$ added was refluxed for 4 hr. The syrupy product obtained on working up the reaction mixture in the usual way was dissolved in Et_2O, petr. ether was added to incipient turbidity, and placed in a refrigerator. The white crystals that deposited were composed of both needles and plates. Mechanical separation gave 0.30 g. of white needles which were recrystallized from AcOEt-petr. ether, m.p. 132~133°(decomp.), $[\alpha]_D^{20}$ +150.4°(c=1.21, $CHCl_3$). *Anal.* Calcd. for $C_{19}H_{22}O_8NCl$ (1-Chloro-N-benzoyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine (XII)) : C, 53.33; H, 5.17; N, 3.27. Found: C, 53.43; H, 5.44; N, 2,71.

The white plates (0.30 g.) obtained above were recrystallized from AcOEt-petr. ether, m.p. 56°, $[\alpha]_D^{21}$ +52.0°(c=1.55, $CHCl_3$). In admixture with (XI) obtained by the reaction of (X) with $AlCl_3$, no depression of m.p. was observed.

Reaction of (X) with HCl in Ac_2O—A solution of 1.0 g. of (X) dissolved in 15 cc. of Ac_2O saturated with HCl at 0° was kept standing for 18 hr. at room temperature. The reaction mixture was worked up in the usual way and the crude product was crystallized once from Et_2O-petr. ether. Recrystallization from AcOEt-petr. ether gave white needles, m.p. 132~133°(decomp.), $[\alpha]_D^{22}$ +150.4°(c=1.37, $CHCl_3$). Yield, 0.50 g. In admixture with (XII) obtained by the reaction of (X) with $TiCl_4$, no depression of m.p. was observed.

To the ethereal mother liquor, petr. ether was added further to incipient turbidity and white plates (0.15 g.) crystallized out. m.p. 56°, $[\alpha]_D^{20}$ +52.0°(c=1.24, $CHCl_3$). In admixture with (XI) obtained by the reaction of (X) with $AlCl_3$, no depression of m.p. was observed.

Methyl N-Benzoyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (XIII)—a) A solution of 0.20 g. of (XI) dissolved in 5 cc. of MeOH was refluxed for 1 min. and kept overnight at room temperature. The deposited crystals were collected and recrystallized from EtOH to long white needles, m.p. 221°, $[\alpha]_D^{20}$ +30.1°(c=1.30, $CHCl_3$). Yield, 0.10 g. In admixture with authentic (XIII),[9] no depression of m.p. was observed.

b) 0.12 g. of (XII) was shaken with a suspension of 0.5 g. of Ag_2CO_3 in 20 cc. of MeOH for 3 hr. After filtration, the solution was evaporated *in vacuo* to dryness. The residue was recrystallized from EtOH to long white needles, m.p. 221°, $[\alpha]_D^{20}$ +30.1°(c=1.51, $CHCl_3$). Yield, 0.10 g. In admixture with authentic (XIII), no depression of m.p. was observed.

11) F. Micheel, H. Köchling : Ber., **90**, 1597(1957).

N-*p*-Nitrobenzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XIV)—To a solution of 1.8 g. of 1,3,4,6-tetra-O-acetyl-β-D-glucosamine[8] dissolved in 15 cc. of anhyd. pyridine, 1.1 g. of *p*-nitrobenzoyl chloride dissolved in 10 cc. of benzene was added at 0° and kept standing for 3 hr. at room temperature. The reaction mixture was diluted with $CHCl_3$ and poured into water, $CHCl_3$ solution was washed successively with water, 5% HCl, and water, dried over $CaCl_2$, and evaporated *in vacuo* to dryness. The residue was recrystallized from EtOH to pale yellow needles, m.p. 211~212°, $[\alpha]_D^{25}$ +51.0° (c=2.61, $CHCl_3$). Yield, 1.4 g. *Anal.* Calcd. for $C_{21}H_{24}O_{12}N_2$: C, 50.81; H, 4.88; N, 5.64. Found: C, 50.68; H, 4.94; N, 5.47.

Reaction of (XIV) with Anhydrous $AlCl_3$—A solution of 1.5 g. of (XIV) dissolved in 23 cc. of pure $CHCl_3$, with 1.1 g. of anhyd. $AlCl_3$ added, was shaken vigorously for 40 min. at room temperature. The syrupy product obtained on working up in the usual way was dissolved in warm Et_2O and kept in a refrigerator. The deposited crystals were collected and recrystallized from toluene-petr. ether to pale yellow needles, m.p. 142~143°, $[\alpha]_D^{20}$ +72.2° (c=0.79, $CHCl_3$). Yield, 0.45 g. *Anal.* Calcd. for $C_{19}H_{20}O_{10}N_2$ (2-*p*-Nitrophenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XV)): C, 52.29; H, 4.63; N, 6.42. Found: C, 52.58; H, 4.58; N, 6.38.

To the ethereal mother liquor, petr. ether was added to incipient turbidity. On standing in a refrigerator, pale yellow needles, m.p. 105~107° (decomp.), $[\alpha]_D^{15}$ +152.0° (c=1.70, $CHCl_3$), crystallized out. Yield, 0.75 g. *Anal.* Calcd. for $C_{19}H_{21}O_{10}N_2Cl$ (1-Chloro-N-*p*-nitrobenzoyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine (XVI)): C, 48.27; H, 4.48; N, 5.92. Found: C, 48.99; H, 4.31; N, 6.40.

Reaction of (XIV) with $TiCl_4$—A solution of 1.0 g. of (XIV) dissolved in 10 cc. of pure $CHCl_3$, with 0.3 cc. of $TiCl_4$ added, was refluxed for 4 hr. The reaction mixture was worked up in the usual way and the syrupy product was dissolved in warm Et_2O. The pale yellow needle crystals that deposited were recrystallized from toluene-petr. ether. m.p. 142~143°, $[\alpha]_D^{20}$ +72.2° (c=0.75, $CHCl_3$). Yield, 0.05 g. In admixture with (XV) obtained by the reaction of (XIV) with $AlCl_3$, no depression of m.p. was observed.

To the ethereal mother liquor, petr. ether was added to incipient turbidity. The pale yellow needle crystals that deposited were recrystallized from Et_2O-petr. ether. m.p. 105~107°, $[\alpha]_D^{20}$ +151.6° (c=1.68, $CHCl_3$). Yield, 0.50 g. In admixture with (XVI) obtained by the reaction of (XIV) with $AlCl_3$, no depression of m.p. was observed.

Reaction of (XIV) with HCl in Ac_2O—A solution of 1.0 g. of (XIV) dissolved in 15 cc. of Ac_2O saturated with HCl at 0° was kept standing for 18 hr. at room temperature. After working up the reaction mixture in the usual way, the crude product was recrystallized from Et_2O-petr. ether to pale yellow needles, m.p. 105~107°, $[\alpha]_D^{15}$ +152.0° (c=2.04, $CHCl_3$). Yield, 0.8 g. In admixture with (XVI) obtained by the reaction of (XIV) with $AlCl_3$, no depression of m.p. was observed.

Methyl N-*p*-Nitrobenzoyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (XVII)—a) A solution of 0.20 g. of (XV) dissolved in 5 cc. of MeOH was refluxed for 1 min. and kept standing overnight at room temperature. The deposited crystals were collected and recrystallized from EtOH to pale yellow needles, m.p. 227~228°, $[\alpha]_D^{19}$ +35.1° (c=0.77, $CHCl_3$). Yield, 0.13 g. *Anal.* Calcd. for $C_{20}H_{24}O_{11}N_2$: C, 51.28; H, 5.17; N, 5.98. Found: C, 51.74; H, 4.38; N, 6.00.

b) 0.20 g. of (XVI) was shaken with a suspension of 0.3 g. of Ag_2CO_3 in 10 cc. of MeOH for 5 hr. After filtration, the solution was evaporated *in vacuo* to dryness and the residue was recrystallized from EtOH to pale yellow needles, m.p. 227~228°, $[\alpha]_D^{19}$ +35.1° (c=1.04, $CHCl_3$). Yield, 0.17 g. In admixture with the sample obtained by (a), no depression of m.p. was observed.

N-Anisoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XVIII)—To a solution of 4.0 g. of 1,3,4,6-tetraacetyl-β-D-glucosamine[8] dissolved in 30 cc. of pyridine, 2.2 g. of anisoyl chloride dissolved in 10 cc. of pyridine was added and the mixture was stood overnight in a refrigerator. The reaction mixture was poured into ice-water with stirring, the precipitate was collected and recrystallized from EtOH to white needles, m.p. 215°, $[\alpha]_D^{23}$ +48.6° (c=0.72, $CHCl_3$). Yield, 4.6 g. *Anal.* Calcd. for $C_{22}H_{27}O_{11}N$: C, 54.88; H, 5.65; N, 2.91. Found: C, 54.95; H, 5.48; N, 3.12.

Reaction of (XVIII) with Anhydrous $AlCl_3$—A mixture of 1.0 g. of (XVIII) dissolved in 10 cc. of pure $CHCl_3$ and 0.7 g. of crushed anhyd. $AlCl_3$ was shaken for 40 min. at room temperature. The syrupy product obtained on working up the reaction mixture in the usual way was dissolved in warm Et_2O and kept in a refrigerator, by which prismatic crystals began to form immediately. The deposited crystals were collected and recrystallized from Et_2O, m.p. 106~108°, $[\alpha]_D^{21}$ +66.7° (c=1.62, $CHCl_3$). Yield, 0.55 g. *Anal.* Calcd. for $C_{20}H_{23}O_9N$ (2-*p*-Methoxyphenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XIX)): C, 57.02; H, 5.50; N, 3.32. Found: C, 57.82; H, 5.35; N, 3.56. Further crop (0.10 g) of (XIX) was obtained when petr. ether was added to the mother liquor.

Reaction of (XVIII) with $TiCl_4$—A mixture of 1.0 g. of (XVIII) dissolved in 10 cc. of pure $CHCl_3$ and 0.3 cc. of $TiCl_4$ was refluxed for 4 hr. On working up in the usual way, the syrupy product was obtained. Upon solution of this syrup in warm Et_2O, prismatic crystals began to form immediately, a few hours later, needle crystals were seen to be forming. Mechanical separation gave 0.60 g. of prisamatic crystals, as recrystallized from Et_2O, m.p. 106~108°, $[\alpha]_D^{21}$ +66.7° (c=1.44,

$CHCl_3$). In admixture with (XIX) obtained by the reaction of (XVIII) with $AlCl_3$, no depression of m.p. was observed.

The needle crystals (0.07 g.) obtained as above were recrystallized from AcOEt-petr. ether. m.p. 137° (decomp.), $[\alpha]_D^{20}$ +152.6° (c=0.38, $CHCl_3$). *Anal.* Calcd. for $C_{20}H_{24}O_9NCl$ (1-chloro-N-anisoyl-3,4,6-tri-O-acetyl-1-deoxy-α-D-glucosamine (XX)) : C, 52.46; H, 5.29; N, 3.06. Found : C, 52.16; H, 5.16; N, 3.76.

Reaction of (XVIII) with HCl in Ac_2O—A solution of 2.0 g. of (XVIII) dissolved in 30 cc. of Ac_2O saturated with HCl at 0° was kept standing for 18 hr. at room temperature. The reaction mixture was worked up in the usual way and the syrupy product obtained was dissolved in warm Et_2O. The deposited crystals were composed of both white prisms and needles. Mechanical separation gave 1.2 g. of prismatic crystals, m.p. 106~108°, $[\alpha]_D^{20}$ +66.7° (c=1.39, $CHCl_3$). In admixtue with (XIX) obtained by the reaction of (XVIII) with $AlCl_3$, no depression of m.p. was observed.

The white needle crystals (0.20 g.) obtained as above were recrystallized from AcOEt-petr. ether. m.p. 137° (decomp.), $[\alpha]_D^{20}$ +152.6° (c=0.52, $CHCl_3$). In admixture with (XX) obtained by the reaction of (XVIII) with $TiCl_4$, no depression of m.p. was observed.

Methyl N-Anisoyl-3,4,6-tri-O-acetyl-β-D-glucosaminide (XXI)—a) A solution of 0.55 g. of (XIX) dissolved in 10 cc. of MeOH was refluxed for 1 min. and kept standing overnight at room temperature. The deposited crystals were recrystallized from MeOH to white needles, m.p. 233°, $[\alpha]_D^{23}$ +44.7° (c=0.76, $CHCl_3$). Yield, 0.53 g. *Anal.* Calcd. for $C_{21}H_{27}O_{10}N$: C, 55.62; H, 6.00; N, 3.09. Found : C, 54.80; H, 5.45; N, 3.33.

b) A mixture of 0.10 g. of (XX) in a suspension of 0.1 g. of Ag_2CO_3 in 20 cc. of MeOH was shaken for 2 hr. After filtration, the solution was evaporated *in vacuo* to dryness and the residue was recrystallized from MeOH to white needles, m.p. 233°, $[\alpha]_D^{25}$ +44.7° (c=1.02, $CHCl_3$). Yield, 0.06 g. In admixture with the sample obtained as in (a), no depression of m.p. was observed.

Brief Treatment of (XIV) with Anhydrous $AlCl_3$—A mixture of 1.0 g. of (XIV) dissolved in 10 cc. of pure $CHCl_3$ and 0.7 g. of crushed anhyd. $AlCl_3$ was shaken for 15 min. at room temperature. The syrupy product isolated in the usual way was dissolved in warm Et_2O, pale yellow needles crystallized out, and were recrystallized from toluene-petr. ether. m.p. 143°, $[\alpha]_D^{20}$ +72.2° (c=1.06, $CHCl_3$). Yield, 0.58 g. In admixture with authentic (XV), no depression of m.p. was observed.

To the ethereal mother liquor, petr. ether was added to incipient turbidity. Pale yellow needles, m.p. 105~107°, $[\alpha]_D^{20}$ +151.6° (c=1.23, $CHCl_3$), were obtained. Yield, 0.20 g. In admixture with authentic (XVI), no depression of m.p. was observed.

Brief Treatment of (X) and (XVI) with $TiCl_4$—A mixture of 1.0 g. of (X) dissolved in 10 cc. of pure $CHCl_3$ and 0.3 cc. of $TiCl_4$ was shaken for 5 min. at 40°. On working up in the usual way, a syrupy product obtained and was crystallized from Et_2O-petr. ether to white plates, m.p. 56°, $[\alpha]_D^{20}$ +52.0° (c=1.51, $CHCl_3$). Yield, 0.55 g. In admixture with authentic (XI), no depression of m.p. was observed.

By a similar treatment of 1.0 g. of (XIV), 0.67 g. of pale yellow needles, m.p. 143°, $[\alpha]_D^{20}$ +72.2° (c=0.71, $CHCl_3$), identical with (XV) by mixed m.p., and 0.07 g. of pale yellow needles, m.p. 105~107°, $[\alpha]_D^{20}$ +151.6° (c=1.35, $CHCl_3$), identical with (XVI) by mixed m.p., were obtained.

Brief Treatment of N,N-Phthaloyl- and N,N-Succinyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine with $TiCl_4$—A mixture of 1.0 g. of N,N-phthaloyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine dissolved in 10 cc. of pure $CHCl_3$ and 0.3 cc. of $TiCl_4$ was shaken for 5 min. at 40°. After working up in the usual way, crude crystals obtained were recrystallized from AcOEt-petr. ether to white needles, m.p. 149°, $[\alpha]_D^{20}$ +61.7° (c=0.79, $CHCl_3$). Yield, 0.55 g. In admixture with authentic 1-chloro-N-phthaloyl-3,4,6-tri-O-acetyl-1-deoxy-β-D-glucosamine,[5] no depression of m.p. was observed.

A similar treatment of N,N-succinyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine gave 0.60 g. of white needles, m.p. 132~134°, $[\alpha]_D^{20}$ +21.4° (c=1.03, $CHCl_3$), which were identical with 1-chloro-N-succinyl-3,4,6-tri-O-acetyl-1-deoxy-β-D-glucosamine[6] by mixed m.p. determination.

Brief Treatment of (X) and (XIV) with HCl in Ac_2O—A solution of 1.0 g. of (X) dissolved in 15 cc. of Ac_2O saturated with HCl at 0° was kept standing for 10 min. at room temperature. On working up in the usual way, 0.55 g. of white plates, m.p. 56°, $[\alpha]_D^{22}$ +52.0° (c=0.63, $CHCl_3$), identical with (XI) by mixed m.p. and 0.05 g. of white needles, m.p. 132~133°, $[\alpha]_D^{20}$ +150.4° (c=0.57, $CHCl_3$), identical with (XII) by mixed m.p., were obtained.

Similar treatment of 1.0 g. of (XIV) gave 0.30 g. of pale yellow needles, m.p. 143°, $[\alpha]_D^{20}$ +72.2° (c=1.02, $CHCl_3$), which were identified as (XV), and 0.40 g. of pale yellow needles, m.p. 105~107°, $[\alpha]_D^{20}$ +151.5° (c=1.17, $CHCl_3$), which were identified as (XVI).

Reaction of (XI), (XV), and (XIX) with HCl in Ac_2O—A solution of 1.0 g. of (XI) dissolved in 15 cc. of Ac_2O saturated with HCl at 0° was left standing for 18 hr. at room temperature. After working up in the usual way, syrupy product was crystallized from Et_2O-petr. ether to 0.65 g. of white needles, m.p. 132~133° (decomp.), $[\alpha]_D^{20}$ +150.4° (c=1.06, $CHCl_3$), which were identified as (XII), and 0.1 g. of the starting material (XI).

Treatment of 1.0 g. of (XV) in a similar fashion gave 0.8 g. of pale yellow needles, m.p. 105~107°,

$[\alpha]_D^{20}$ +151.6°(c=0.62, $CHCl_3$), which were identified as (XVI).

Similar treatment of 1.0 g. of (XIX) furnished 0.70 g. of recovered starting material (XIX) together with 0.10 g. of white needles, m.p. 137°(decomp.), $[\alpha]_D^{20}$ +152.6°(c=0.51, $CHCl_3$), which were identified as (XX).

2-Phenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline Hydrochloride—To a solution of (XI) in Et_2O, Et_2O containing equivalent amount of HCl was added and kept standing in a refrigerator. After a few hours, the deposited crystals were collected and washed thoroughly with Et_2O. m.p. 135° (decomp.), $[\alpha]_D^{25}$ +39.0°(c=0.77, pyridine-water=1:1). *Anal.* Calcd. for $C_{19}H_{22}O_8NCl$: C, 53.33; H, 5.19; N, 3.27. Found : C, 52.95; H, 5.73; N, 3.02.

A solution of 0.40 g. of this hydrochloride dissolved in $CHCl_3$ was washed with water, dried over $CaCl_2$, and evaporated *in vacuo* to a viscous syrup. This syrup was crystallized from Et_2O-petr. ether to white plates, m.p. 56°, $[\alpha]_D^{20}$ +52.0°(c=1.02, $CHCl_3$). Yield, 0.30 g. In admixture with authentic (XI), no depression of m.p. was observed.

N-Trichloroacetyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine (XXII)—A solution of 10 g. of 1,3,4,6-tetra-O-acetyl-β-D-glucosamine[8] dissolved in 50 cc. of $CHCl_3$, with 2.6 g. of trichloroacetyl chloride added at 0°, was kept standing in a refrigerator for 4 hr. The deposited 1,3,4,6-tetra-O-acetyl-β-D-glucosamine hydrochloride was collected and washed with $CHCl_3$. The filtrate and washing were combined, washed with water, dried over $CaCl_2$, and evaporated *in vacuo* to a small volume. (XXII) precipitated by the addition of petr. ether and recrystallized from Et_2O. m.p. 135~136°, $[\alpha]_D^{20}$ +2.7° (c=0.75,$CHCl_3$). Yield, 5.3 g. *Anal.* Calcd. for $C_{16}H_{20}O_{10}NCl_3$: C, 39.01; H, 4.10; N, 2.84. Found: C, 39.80; H, 4.91; N, 2.90.

Reaction of (XXII) with Anhydrous $AlCl_3$—A solution of 1.0 g. of (XXII) dissolved in 10 cc. of pure $CHCl_3$ and 0.7 g. of crushed anhyd. $AlCl_3$ was shaken for 40 min. at room temperature. On working up in the usual way, the starting material (XXII) was recovered quantitatively.

Reaction of N-Benzoyl-1,3,4,6-tetra-O-acetyl-α-D-glucosamine[9] (XXIII) with Anhydrous $AlCl_3$—A mixture of 1.0 g. of (XXIII) dissolved in 10 cc. of pure $CHCl_3$ and 0.7 g. of crushed anhyd. $AlCl_3$ was shaken for 40 min. at room temperature. On working up in the usual way, the starting material (XXIII) was recovered quantitatively.

Reaction of (XXIII) with $TiCl_4$ at 40°—A solution of 1.0 g. of (XXIII) dissolved in 10 cc. of pure $CHCl_3$ was shaken with 0.3 cc. of $TiCl_4$ for 5 min. at 40°. On working up in the usual way, the starting material (XXIII) was recovered quantitatitely.

Rate of the Reaction of N-Acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine with $TiCl_4$—a) Polarimetric method : The data plotted in Fig. 3 were obtained by dissolving 1 m.mole of dry N-acyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine in 20 cc. of a solution of 1 m.mole $TiCl_4$ in $CHCl_3$ with vigorous shaking at 40.2° and zero time. As soon as solution was complete, the mixture was transferred to an all-glass 2-dm. polarimeter tube kept at 40.2°±0.1°. The rotation at zero time was obtained by extrapolation.

(1) With Penta-O-acetyl-β-D-glucosamine

Time (min.)	0	7.5	14.5	24	35	45.5	55	65.5	76	86	222.5	256
Observed rotation	0.05° (calc.)	0.74°	1.24°	1.72°	2.08°	2.33°	2.48°	2.61°	2.69°	2.76°	2.95°	2.95°
k (min^{-1})		0.036	0.036	0.036	0.034	0.034	0.033	0.033	0.032	0.032		

(2) With N-Benzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	6	10	15	20	25	30	40	50	60	70	80	90	240	260
Observed rotation	0.70° (calc.)	1.15°	1.41°	1.75°	2.13°	2.45°	2.68°	3.05°	3.31°	3.48°	3.63°	3.70°	3.77°	4.04°	4.04°
k (min^{-1})		0.024	0.024	0.025	0.028	0.030	0.030	0.030	0.030	0.030	0.030	0.029	0.028		

(3) With N-p-Nitrobenzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	3	6	9	12	15	18	21	320	380
Observed rotation	2.50° (calc.)	2.89°	3.22°	3.55°	3.84°	3.97°	4.04°	4.09°	4.70°	4.70°
k (min^{-1})		0.065	0.066	0.072	0.078	0.074	0.067	0.061		

(4) With N-Anisoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	10	20	30	40	50	60	70	80	90	100	240	300
Observed rotation	2.30° (calc.)	2.51°	2.71°	2.91°	3.06°	3.21°	3.33°	3.44°	3.52°	3.61°	3.66°	4.08°	4.08°
k (min^{-1})		0.013	0.013	0.014	0.014	0.014	0.014	0.015	0.014	0.015	0.014		

b) Spectrophotometric method : The reaction solution was prepared as described in (a). At suitable times, 1 cc. of this solution was pipetted into 30 cc. of water, extracted with pure $CHCl_3$ (5 cc. × 2), dried over a few pieces of $CaCl_2$, filtered, and diluted exactly to 25 cc. with pure $CHCl_3$. Then, 0.5

cc. of this solution was diluted exactly to 25 cc. by the addition of pure $CHCl_3$ and the optical density was read in 1-cm. cell at the wave length of max. absorption of corresponding oxazoline derivative.

(1) With N-Benzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	10	20	30	40	50	60	240	300
$10\times$(Optical density at 247.5 mμ	4.70 (calc.)	4.08	3.54	3.14	2.80	2.56	2.40	1.80	1.80
k (min^{-1})		0.024	0.026	0.026	0.027	0.027	0.026		

(2) With N-*p*-Nitrobenzoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	7.5	9.5	14	20	25	30	40	100	160
$10\times$(Optical density at 282.5 mμ	4.70 (calc.)	4.30	4.20	4.00	3.80	3.64	3.50	3.32	3.15	3.20
k (min^{-1})		0.040	0.041	0.043	0.043	0.046	0.050	0.055		

(3) With N-Anisoyl-1,3,4,6-tetra-O-acetyl-β-D-glucosamine

Time (min.)	0	10	20	30	40	50	60	70	80	120	240
$10\times$(Optical density at 264.5 mμ	7.55 (calc.)	7.44	7.33	7.25	7.17	7.10	7.04	6.99	6.94	6.80	6.65
k (min^{-1})		0.013	0.014	0.014	0.014	0.014	0.014	0.014	0.014		

Rate of the Reactions of (XI), (XV), and (XIX) with HCl in Ac_2O—The data plotted in Fig. 5 were obtained by dissolving 0.5 m.mole of dry oxazoline derivatives in 10 cc. of Ac_2O containing 1.5 g. of HCl at 31.5° and zero time. The solution was transferred quickly to an all-glass 2-dm. polarimeter tube kept at 31.5°±0.1°. The rotation at zero time was obtained by extrapolation.

(1) With 2-Phenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XI)

Time (min.)	0	10	20	30	40	50	60	70	80	90	280	350
Observed rotation	0.03° (calc.)	0.47°	0.75°	0.94°	1.08°	1.19°	1.28°	1.35°	1.41°	1.46°	1.65°	1.65°
k (min^{-1})		0.032	0.029	0.028	0.026	0.025	0.024	0.024	0.024	0.024		

(2) With 2-*p*-Nitrophenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XV)

Time (min.)	0	4	8	12	16	20	24	28	32	125	180
Observed rotation	1.00° (calc.)	1.16°	1.30°	1.41°	1.48°	1.54°	1.60°	1.62°	1.65°	1.75°	1.75°
k (min^{-1})		0.060	0.064	0.066	0.064	0.067	0.062	0.063	0.063		

(3) With 2-*p*-Methoxyphenyl-4,5-(3,4,6-tri-O-acetyl-D-glucopyrano)-2-oxazoline (XIX)

Time (min.)	0	10	20	30	40	50	60	70	80	90	220	240
Observed rotation	0.33° (calc.)	0.45°	0.55°	0.64°	0.72°	0.79°	0.87°	0.92°	0.97°	1.02°	1.30°	1.30°
k (min^{-1})		0.013	0.013	0.013	0.013	0.013	0.014	0.013	0.014	0.014		

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Summary

Chlorination reactions of 1,3,4,6-tetra-O-acetyl-N-acyl-β-D-glucosamines at C-1 position were studied and it was found that these reactions suffered remarkable electronic effect of N-acyl groups. The mechanism of these reactions is discussed.

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