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.

Acknowledgment.—We are indebted to the staff of the Section on Microanalytical Services and Instrumentation of the National Institute of Arthritis and Metabolic Diseases for spectra and elementary analyses.

(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).

(3) Supported in part by Grant-in-Aid No. 170200 from The Ohio State University Development Fund. Funds for the 60-MHz nmr spectrometer were provided by the National Science Foundation, Washington, D. C.

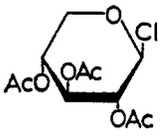
(4) To whom inquiries should be addressed.

(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.

stituents and a *syn*-diaxial interaction (of the acetoxy groups at C-2 and C-4) in determining the favored conformation.

In the present report, tri-*O*-acetyl-β-D-xylopyranosyl chloride (**1**), the thermodynamically less stable anomer, was prepared and its conformation was studied by nmr spectroscopy. Two chair conformations are possible for **1**, that having all four groups equatorial (*C1* conformation, **3**) and that having all four groups axial (*1C* conformation, **2**). The data show that, in chloroform solution, the all-axial *1C* conformation (**2**) is the favored form. It is, therefore, evident that the magnitude of the anomeric effect in this system exceeds the combined steric destabilizing influence of four axial groups and two *syn*-diaxial interactions.



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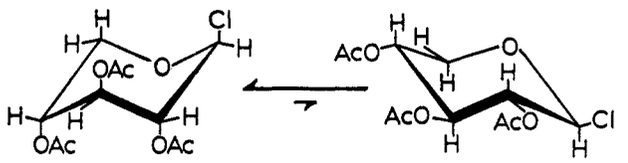

2 favored (1C) **3** not favored (C1)

Tri-*O*-acetyl-β-D-xylopyranosyl chloride (**1**) was first prepared by Schlubach and Gilbert,[7] who treated tri-*O*-acetyl-α-D-xylopyranosyl bromide with a specially prepared, active form of silver chloride. In our hands, this procedure gave erratic results, and most experiments gave mixtures from which the stable anomer, tri-*O*-acetyl-α-D-xylopyranosyl chloride, was the most readily isolated. However, treatment of tetra-*O*-acetyl-β-D-xylopyranose with aluminum chloride in cold chloroform, according to the general procedure of Korytnyk and Mills,[8] gave crystalline **1** in high yield, having a melting point and specific rotation in good agreement with literature values.[7,8] The substance was stable for several days at room temperature in the crystalline state or as a solution in pure chloroform or benzene, but traces of acid catalyzed the decomposition of **1**. The decomposition of **1** was rapid in acetone solution. Details of the nmr spectra of **1** and its anomer, tri-*O*-acetyl-α-D-xylopyranosyl chloride, are recorded in the Experimental Section.

The nmr spectrum of **1**, measured in chloroform-*d* (Figure 1) showed a narrow, one-proton triplet at τ 4.22, assigned to an equatorial hydrogen atom at C-1. If the favored conformation of **1** had been the *C1* chair form (**3**), the H-1 signal would have been observed as a wide doublet ($J_{1,2} \sim$ 8–10 Hz) because of 1,2-diaxial proton coupling. The fact that the H-1 signal is not observed as a simple doublet may be ascribed to the fact that possibilities exist for long-range[9] and virtual[10] coupling with H-3 because H-3 is equatorial and the difference in chemical shift between H-2 and H-3 is small. The signals of the protons on C-5 are observed as the typical eight-line pattern of the AB portion of an ABX multiplet, and the first-order $J_{4,5a}$ and $J_{4,5e}$ couplings are 3.0 and 3.7 Hz. The fact that both of these couplings are small indicates[2] that H-4 is not antiparallel to the axial proton at C-5, as would be required for the *C1* conformation (**3**), and the data are consistent with the *1C* conformation (**2**) where the C-4–hydrogen bond bisects the angle of the C-5–hydrogen bonds. The axial and equatorial H-5 signals were specifically assigned by considerations of relative deshielding and long-range couplings. Although axial hydrogen atoms tend, in general, to give signals at higher field than equatorial ones, the two polar groups *syn*-diaxial to H-5a may be expected to deshield H-5a strongly so that its signal appears at lower field than H-5e. The higher-field H-5 signal is broadened by long-range coupling with H-3, a feature characteristic[9] of the diequatorial arrangement of protons at C-3 and C-5 ("W" conformation), indicating that the higher field H-5 signal is H-5e. Irradiation of the H-2,3 signal at τ 4.97 caused the H-5e signal to collapse to a sharp quartet because of removal of the $J_{3,5e}$ coupling (0.6 Hz), and at the same time the H-1 signal was observed to collapse to a sharp singlet, through removal of all coupling with H-2 and H-3.

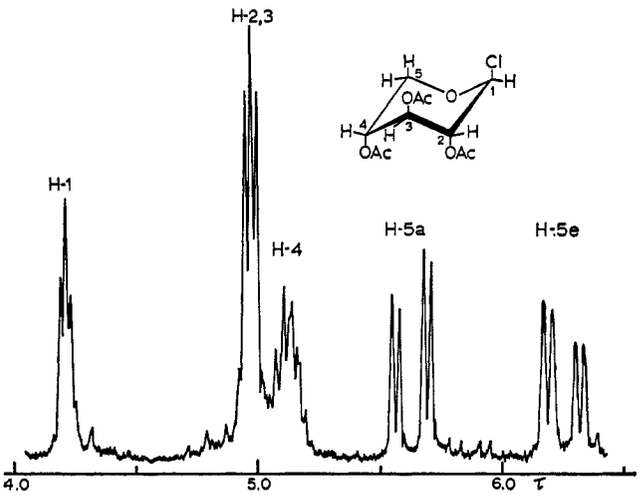

Figure 1.—The low-field portion of the 100-MHz nmr spectrum of tri-*O*-acetyl-β-D-xylopyranosyl chloride in chloroform-*d*.

The possibility that **1** adopts a conformation in the flexible cycle (*cf.* ref 2) was not considered probable because all possible structures of this type would be expected to give either one large $J_{4,5}$ coupling or a large $J_{1,2}$ coupling. It is, however, probable that the spectrum observed is the time-averaged spectrum of both conformers **2** and **3**, in rapid equilibrium, with **2** preponderating. A small proportion of the less favored conformer (**3**), in rapid equilibrium with **2**, would not greatly affect the magnitudes of the first-order couplings observed.

The nmr spectrum of **1**, measured immediately after dissolution in acetone-d_6, had the same general ap-

(7) H. H. Schlubach and R. Gilbert, *Ber.*, **63**, 2295 (1930).
(8) W. Korytnyk and J. A. Mills, *J. Chem. Soc.*, 636 (1959).
(9) L. D. Hall and L. Hough, *Proc. Chem. Soc.*, 382 (1962).
(10) J. I. Musher and E. J. Corey, *Tetrahedron*, **18**, 791 (1962); R. H. Bible, Jr., "Interpretation of NMR Spectra," Plenum Press, New York, N. Y., 1965, p 92.

pearance as the spectrum in chloroform-*d*, and the same conformational conclusions can be drawn. In benzene-d_6 the spectrum of **1** again showed small $J_{4,5a}$ and $J_{4,5e}$ couplings, indicating that the *1C* conformation is also strongly favored in this solvent. In benzene-d_6, the H-2 and H-3 signals were appreciably separated, with the result that the H-1 signal did not show virtual coupling[10] with H-3. The H-1 signal was observed as a narrow doublet ($J_{1,2}$ = 3.5 Hz) with broadening of each line indicative of the anticipated[9] long-range coupling ($J_{1,3}$ = 0.6 Hz) with H-3.

The signals for the acetyl groups in **1** were observed as three closely spaced three-proton singlets when the spectrum was measured in benzene-d_6. In acetone-d_6 two of the signals overlapped, and in chloroform-*d* a single, nine-proton line was observed. These data provide independent evidence against possible formulation of substance **1** as a 1,2-cyclic orthoacetyl chloride (*cf.* ref 8). In such a structure, the orthoacetyl methyl group would be expected to give a signal having a chemical shift considerably different from those of the acetyl methyl groups.[11]

In a related study, Hall has observed that the 1-fluoride analog of **1** likewise adopts the *1C* chair form as the favored conformation in chloroform-*d*.[12]

Experimental Section[13]

Nmr Measurements.—Spectra were obtained with Varian A-60 and HA-100 spectrometers, at probe temperatures of approximately 40° (60 MHz) or 32° (100 MHz). The freshly prepared compounds were examined as 10–20% solutions, with tetramethylsilane (τ 10.00) as the internal standard, and calibration (at 60 MHz) was made by the side-band technique. Chemical shifts are first-order, and were measured from spectra recorded at a sweep width of 500 Hz, and first-order couplings were measured from spectra recorded at a 100-Hz sweep width.

Preparation of Tri-*O*-acetyl-β-D-xylopyranosyl Chloride (1).—The procedure employed was a minor adaptation of the method of Korytnyk and Mills.[8] A solution of tetra-*O*-acetyl-β-D-xylopyranose[14] (2.0 g) in anhydrous chloroform[15] (20 ml) was stirred with anhydrous aluminum chloride (1.5 g) for 1.5 hr at room temperature. The mixture was then shaken quickly with ice and water (100 ml), the chloroform layer was separated, and the aqueous phase was extracted with two 20-ml portions of chloroform. The combined chloroform extract was dried (magnesium sulfate) without delay and evaporated, and the resultant syrup was crystallized from anhydrous ether: yield 1.7 g (90%); mp 112–113°; $[\alpha]^{19}D$ −130 ± 3° (*c* 1, chloroform); λ_{max}^{KBr} 5.73 (OAc), 12.01 μ (equatorial H at C-1 of pyranose ring);[16] X-ray powder diffraction data 9.51 w, 7.11 m, 6.58 m, 5.99 vw, 5.61 s (3, 3), 5.35 s (3, 3), 5.00 w, 4.78 vw, 4.56 w, 4.28 s (2), 4.11 vw, 3.96 vs (1), 3.62 m, 3.50 m, 3.30 m.

Anal. Calcd for $C_{11}H_{15}ClO_7$: C, 44.83; H, 5.13; Cl, 12.03. Found: C, 44.89; H, 4.80; Cl, 11.77.

For this compound, Schlubach and Gilbert[7] gave mp 112–113°, $[\alpha]^{23.5}D$ −131 ± 1° (*c* 1, carbon tetrachloride), and Korytnyk and Mills[8] gave mp 112–113°, $[\alpha]D$ −141° (*c* 1, chloroform).

Nmr Spectral Data for Tri-*O*-acetyl-β-D-xylopyranosyl Chloride (1). A. In Chloroform-*d* at 100 MHz.—The spectrum (Figure 1) showed τ 4.22 (one-proton narrow triplet, width = 4.0 Hz, H-1), 4.97 (two-proton apparent triplet, width = 4.7 Hz, H-2,3), 5.14 (one-proton multiplet, width = 11 Hz, H-4), 5.63 (one-proton quartet, $J_{4,5a}$ = 3.0 Hz, $J_{5e,5a}$ = 12.9 Hz, H-5a), 6.25 (one-proton broadened quartet, $J_{4,5e}$ = 3.7 Hz, $J_{3,5e}$ = 0.6 Hz, H-5e), and 7.90 (nine-proton singlet, OAc). The long-range coupling[9] of the equatorial protons at C-3 and C-5 was verified by spin decoupling. Irradiation at τ 4.97 (H-2,3 multiplet) caused the H-5e signal to collapse to a sharp quartet and the H-1 signal to collapse to a sharp singlet. The spectrum was unchanged after the solution had been kept for 24 hr at room temperature, but after 3–5 days, additional signals were detectable (τ 3.88, doublet, ~0.1 proton, *J* = 3.5 Hz) indicative of slow decomposition.

B. In Benzene-d_6 at 100 MHz.—The spectrum showed τ 4.35 (one-proton doublet of narrow doublets, $J_{1,2}$ = 3.5 Hz, $J_{1,3}$ = 0.6 Hz, H-1), 4.65–4.92 (two-proton multiplet, principal peaks 4.65, 4.70, 4.73, 4.78, 4.82, 4.92, H-2,3), 5.22 (one-proton broadened quartet, width 11.5 Hz, H-4), 5.90 (one-proton quartet, $J_{4,5a}$ = 3.1 Hz, $J_{5a,5e}$ = 12.9 Hz, H-5a), 6.60 (one-proton broadened quartet, $J_{4,5e}$ = 3.8 Hz, $J_{3,5e}$ = 0.6 Hz, H-5e), and 8.32, 8.35, and 8.40 (three-proton singlets, OAc).

C. In Acetone-d_6 at 60 MHz.—The spectrum, measured 5 min after dissolution showed τ 4.08 (one-proton narrow triplet, width at half-height = 5.6 Hz, separation of outer peaks = 4.6 Hz, H-1), 4.85–5.22 (three proton multiplet, H-2,3,4), 5.65 (one-proton quartet, $J_{4,5a}$ = 2.7 Hz, $J_{5a,5e}$ = 12.6 Hz, H-5a), 6.21 (one-proton quartet, peaks slightly broadened, $J_{4,5e}$ = 4.1 Hz, H-5e), and 7.91 and 7.93 (three and six protons, OAc). The spectrum showed changes after 30 min, and after 18 hr the H-1 signal had almost completely disappeared, and a narrow, one-proton doublet at τ 3.90 (*J* = 3.6 Hz) had appeared. After 48 hr the latter signal had disappeared. The possibility that the solvent contained traces of moisture absorbed from the atmosphere was not excluded (*cf.* ref 8).

The 60-MHz spectrum of **1** in acetonitrile was very closely similar to that measured in acetone-d_6.

Preparation of Tri-*O*-acetyl-α-D-xylopyranosyl Chloride.—This substance, prepared by the method of Hudson and Johnson,[14] had a melting point and specific rotation in good agreement with the values reported by Brauns[17] [mp 105°, $[\alpha]^{20}D$ +172.2° (chloroform)]. It showed λ_{max}^{KBr} 5.78 (OAc), 13.17, and no absorption near 12.0 μ (*cf.* ref 16). The same product was obtained, in low yield, after several recrystallizations of a product obtained by treatment of tri-*O*-acetyl-α-D-xylopyranosyl bromide[18] with freshly prepared silver chloride, according to the procedure of Schlubach and Gilbert[8] for preparation of the "unstable" chloride (**1**).

Nmr Spectral Data for Tri-*O*-acetyl-α-D-xylopyranosyl Chloride. A. In Chloroform-*d* at 100 MHz.—The spectrum showed τ 3.75 (one-proton doublet, $J_{1,2}$ = 3.9 Hz, H-1), 4.46 (one-proton triplet, $J_{3,4}$ = 9.4 Hz, H-3), 4.99 (one-proton multiplet, width 26 Hz, H-4), 5.05 (one-proton quartet, $J_{2,3}$ = 10.0 Hz, H-2), 5.98 (one-proton quartet, $J_{4,5e}$ = 6.4 Hz, $J_{5e,5a}$ = 11.4 Hz, H-5e), 6.13 (one-proton quartet, $J_{4,5a}$ = 10.1 Hz, H-5a), and 7.92 and 7.96 (three and six protons, OAc).

B. In Benzene-d_6 at 60 MHz.—The spectrum showed τ 3.82 (one-proton doublet, $J_{1,2}$ = 3.7 Hz, H-1), 4.25 (one-proton triplet, $J_{3,4}$ = ~9.5 Hz, H-3), ~4.94 (one-proton multiplet, H-4), ~5.03 (one-proton quartet, $J_{2,3}$ = ~10 Hz, H-2), 6.17 and 6.30 (broadened singlets, two protons, H-5e, H-5a), and 8.72 and 8.35 (three and six protons, OAc). The protons at C-5 were almost equivalent in this solvent.

C. In Acetone-d_6 at 60 MHz.—The spectrum showed τ 3.67 (one-proton doublet, $J_{1,2}$ = 3.4 Hz, H-1), 4.48 (one-proton triplet, $J_{3,4}$ = ~9 Hz, H-3), ~4.94 (one-proton multiplet, H-4), 4.97 (one-proton quartet, $J_{2,3}$ = ~10 Hz, H-2), 5.94 (one-proton quartet, H-5e), 6.17 (one-proton apparent triplet, $J_{4,5a}$ = ~10 Hz, H-5a), and 7.97, 8.00 (three and six protons, OAc). The couplings measured by first-order analysis of the H-5e and H-5a multiplet in this solvent may deviate considerably from the true *J* values because the chemical-shift difference between the H-5e and H-5a signals is small and large couplings

(11) A. S. Perlin, *Can. J. Chem.*, **41**, 555 (1963); K. Heyns, W. P. Trautwein, F. G. Espinosa, and H. Paulsen, *Ber.*, **99**, 1183 (1966).

(12) L. D. Hall, University of British Columbia, personal communication; L. D. Hall and J. F. Manville, *Carbohydrate Res.*, in press.

(13) Melting points were measured with a Thomas–Hoover Unimelt apparatus (Arthur H. Thomas Co., Philadelphia, Pa.). Infrared spectra were measured with a Perkin-Elmer Model 137 Infracord infrared spectrophotometer. Elemental analyses were made by W. N. Rond. X-Ray powder diffraction data give interplanar spacings (A) for Cu Kα radiation. The camera diameter was 114.59 mm. Relative intensities were estimated visually: s, strong; m, moderate; w, weak; v, very. The strongest lines are numbered (1, strongest); double numbers indicate approximately equal intensities.

(14) C. S. Hudson and J. M. Johnson, *J. Am. Chem. Soc.*, **37**, 2748 (1915).

(15) Prepared by passing U.S.P. chloroform through a column of Woelm alumina immediately prior to use.

(16) S. A. Barker, E. J. Bourne, and D. H. Whiffen, *Methods Biochem. Anal.*, **3**, 213 (1956); H. Spedding, *Methods Carbohydrate Chem.*, **1**, 539 (1962).

(17) D. H. Brauns, *J. Am. Chem. Soc.*, **47**, 1280 (1925).

(18) M. Bárczai-Martos and F. Kőrösy, *Nature*, **165**, 369 (1950).

are involved. The same reservation may be noted with regard to the H-5 and H-5a signals in the spectrum of tri-*O*-acetyl-α-D-xylopyranosyl bromide, measured in chloroform-*d* at 60 MHz.[2]

Registry No.—1, 10343-54-1; 2, 10300-18-2.

Acknowledgments.—The authors thank Mr. J. D. Wander for some of the 60-MHz nmr spectral measurements, and Mr. W. Jankowski (Varian Associates, Pittsburgh, Pa.) for 100-MHz spectral measurements.

Trichloroacetyl and Trifluoroacetyl as *N*-Blocking Groups in Nucleoside Synthesis with 2-Amino Sugars[1]

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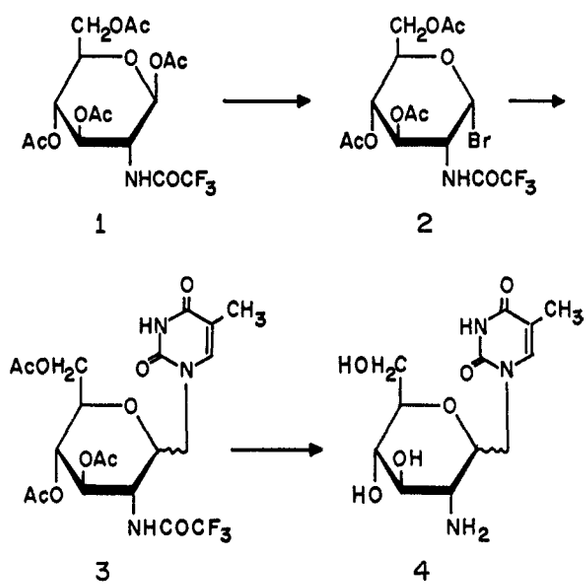
1,3,4,6-Tetra-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucose (1) was converted into the glycosyl halide and this in turn into a fully blocked pyrimidine nucleoside derivative on fusion with bis(trimethylsilyl)thymine. Complete deacylation was effected with methanolic hydrogen chloride or methanolic ammonia. Analogous experiments with the *N*-trichloroacetyl blocking group showed that the products were obtained in lower yield and the *N*-trichloroacetyl group required strong acid or hot barium hydroxide treatment for removal.

There has been a need for an easily removable and conveniently prepared *N*-blocking group in nucleoside synthesis utilizing 2-amino-2-deoxy sugars, especially for these with a *trans* configuration on C-2 and C-3.

In the present work, the trichloroacetyl group was initially tried as an *N*-blocking group. 1,3,4,6-Tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranose hydrochloride[2] was converted into its 2-trichloroacetamido derivative (1, F = Cl) and this in turn into a syrupy glycosyl chloride which on fusion[3] with bis(trimethylsilyl)thymine[4] yielded the crystalline 1-nucleoside derivative (3, F = Cl). Treatment of the latter with methanolic hydrogen chloride or methanolic ammonia then gave crystalline 1-(2-trichloroacetamido-2-deoxy-D-glucopyranosyl)thymine. Complete deblocking could be effected only by vigorous acid treatment or by hot barium hydroxide. In this manner the acid-stable pyrimidine nucleoside 4 was obtained in one anomeric form. (See Scheme I.) Since these conditions are too drastic to be employed for purine nucleosides, the use of the more labile *N*-trifluoroacetyl group was explored.

The trifluoroacetyl group had been used as an *N*-blocking group in the amino acid series[5] and Newman[6] had employed it in the synthesis of steroid glycosides with the glycosyl bromide of a 3,4,6-trideoxy-3-methylaminohexose. At the time our work was communicated,[1] Hirschmann and co-workers[7] reported the crystalline tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-α-D-glucopyranosyl bromide (2) and utilized it for the synthesis of ethyl 2-amino-2-deoxy-β-D-glucopyranoside. In the work herein reported we prepared the bromide 2 by a more convenient

SCHEME I



method starting from 1,3,4,6-tri-*O*-acetyl-2-deoxy-2-trifluoroacetamido-β-D-glucose prepared in turn from the 1,3,4,6-tetra-*O*-acetyl-2-amino-2-deoxy-β-D-glucose of Bergmann and Zervas.[2] When 2 was brought into reaction with bis(trimethylsilyl)thymine the crystalline acylated nucleoside 3 was obtained in high yield and this on deacylation with methanolic hydrogen chloride, gave crystalline 1-(2-amino-2-deoxy-D-glucopyranosyl)-thymine hydrochloride (4-HCl). The anomeric nature of this nucleoside is not herein established. The free base 4 is also reported. It was found possible to remove the *O*-acetyl and *N*-trifluoroacetyl groups by prolonged methanolysis and to so obtain the thymine nucleoside 4 in high yield. These alkaline conditions should be suitable for application to purine nucleosides.

A review of all *N*-blocking groups utilized so far in the sugar series has been made.[8] The thymine nucleoside was chosen in the present study as a model substance because of its ease of formation by the trimethylsilyl method and because the thymine nucleoside of 2-amino-2-deoxy-D-glucopyranose had not been synthesized. The trifluoroacetamido group should be

(1) Preliminary communication: M. L. Wolfrom and H. B. Bhat, *Chem. Commun.*, 146 (1966). The syrupy glycosyl chloride reported in the preliminary communication has been replaced herein by the crystalline bromide with better results. In addition, we now report the experiments with the trichloroacetyl *N*-blocking group as well as the removal of the *N*-trifluoroacetyl group under alkaline conditions.

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(8) M. L. Wolfrom, P. J. Conigliaro, and E. J. Soltes, *ibid.*, **32**, 653 (1967).