REACTIONS OF 2-ACETOXY-4,6-DI-*O*-ACETYL-3-*O*-(2,6-DICHLOROBENZOYL)-D-GLUCAL, TRI-*O*-ACETYL-3-DEOXY-α-D-*erythro*-HEX-2-ENOPYRANOSYL CHLORIDE, AND RELATED COMPOUNDS

R. U. LEMIEUX AND R. J. BOSE[1]

Department of Chemistry, University of Alberta, Edmonton, Alberta

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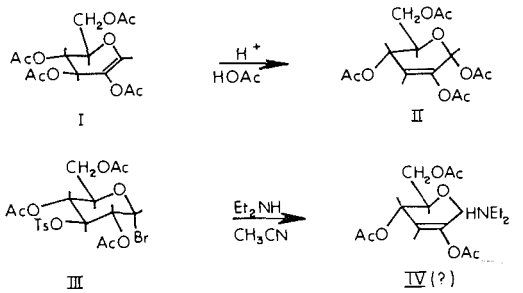
ABSTRACT

Attempts to dehydrobrominate tri-*O*-acetyl-3-*O*-tosyl-α-D-glucopyranosyl bromide with diethylamine led directly to products resulting from the replacement of the tosyloxy group by the diethylamine. It was readily possible to prepare 2-acetoxy-di-*O*-acetyl-3-(2,6-dichlorobenzoyl)-D-glucal (V). Acetolysis of this compound gave an equimolar mixture of the α- and β-anomers (II and VI, respectively) of 2-acetoxy-di-*O*-acetyl-pseudo-D-glucal as the first products of the reaction. Compound V reacted only reluctantly with methanol in pyridine to give a mixture of the anomeric methyl di-*O*-acetyl-3-deoxy-D-*erythro*-hex-2-enopyranosides. These glycosides were readily prepared by reaction of tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl chloride with methanol in the presence of pyridine. 2-Acetoxy-di-*O*-acetyl-3-*O*-mesitoyl-D-glucal was prepared from 3-*O*-mesitoyl-β-D-glucose. The anomerizations of compounds II and VI were examined with both sulfuric acid in 1:1 acetic acid – acetic anhydride and potassium acetate in acetic acid. The conformations of II and VI are discussed, as are a number of the mechanistic features of the reactions studied.

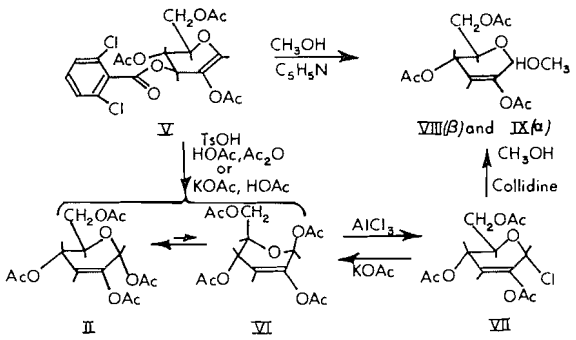
Lemieux *et al.* (1) have reported the acid-catalyzed isomerization of tetra-*O*-acetyl-1-deoxy-D-*arabino*-hex-1-enopyranose (I) (2-acetoxy-D-glucal triacetate) to tetra-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranose (II) (2-acetoxy-pseudo-D-glucal triacetate). The main objective of this research was to prepare a 3-*O*-derivative of 4,5-di-*O*-acetyl-2-acetoxy-D-glucal wherein the substituent at the 3-position was a sufficiently good leaving group for the compound to undergo solvolysis in the absence of acid, with attack of the entering group at the anomeric center. It was anticipated that if this could be accomplished the stereochemical route of the reaction could be established and compared with the S_N2' mechanism (2). Furthermore, the compound could conceivably be useful as a reagent for the synthesis of 2,3-unsaturated glycopyranosides, which could then presumably be converted into 2-ketoglycosides and so on.

In the first attempt, the tosyloxy group was chosen for the 3-substituent. Tri-*O*-acetyl-3-*O*-tosyl-α-D-glucopyranosyl bromide (III) was readily prepared by established procedures (3) from 1,2;5,6-di-*O*-isopropylidene-α-D-glucose. By use of the optimum conditions developed by Lemieux and Lineback (4) for dehydrobromination, the tosyloxy group was



[1]*Corn Industries Research Foundation Postdoctorate Fellow, 1964–1965. Present address: Fisheries Research Board of Canada, Technological Research Laboratory, Vancouver 8, British Columbia.*

removed and derivatives of the diethylamine were obtained in about 80% yield. Evidently, the initially formed 2-acetoxy-3-*O*-tosyl-D-glucal diacetate underwent extremely facile replacement of the tosyloxy group by the amine, most probably with migration of the double bond from the 1,2- to the 2,3-position. The nuclear magnetic resonance (n.m.r.) spectrum of the crude product showed the presence of at least two main components. As judged from the relative intensities of the signals, 1 mole of diethylamine had replaced the tosyloxy group. The product was very unstable and readily consumed about 2 moles of hydrogen when hydrogenated in the presence of palladium. These properties are consistent with those expected for an unsaturated glycosylamine (IV). The actual structures were not established, since the separation and purification of the compounds were not accomplished. Also, the product from the hydrogenation was found, by gas–liquid preparative chromatographic examination, to be a complex mixture.



The use of the mesyloxy rather than the tosyloxy group in the above sequence of reactions gave comparable results. This experience is analogous to that of Stork and White (2), who were unable to prepare *trans*-4-alkyl-3-tosyloxycyclohexene. Since these authors found the 2,6-dichlorobenzoyloxy group to be a useful leaving group in their research on the S_N2' reaction, 2-acetoxy-3-*O*-(2,6-dichlorobenzoyl)-D-glucal diacetate (V) was prepared by conventional methods. That the 2,6-dichlorobenzoyl group was, in fact, at the 3-position of V was demonstrated by conversion of the compound into the equilibrium mixture of the anomeric forms of 2-acetoxy-pseudo-D-glucal diacetate (II and IV) in a nearly quantitative yield (n.m.r.) by treatment with *p*-toluenesulfonic acid in a 1:5 acetic anhydride – acetic acid mixture under the conditions reported (1) for the isomerization of 2-acetoxy-D-glucal triacetate. Also, the n.m.r. spectrum of V was in complete agreement with that of a compound having the assigned structure.

Extensive reaction of compound V with methanol in the presence of pyridine occurred after 3 h at 100°. However, much decomposition to intractable material took place and the reaction showed no promise as a synthetic approach to glycosides. Nuclear magnetic resonance examination of the crude product indicated that the α- and β-methyl glycosides (IX and VIII, respectively) described below were present along with starting material (V).

Ferrier *et al.* (5) have recently reported the β-anomer (VI) of II. As was anticipated (1), the use of *p*-toluenesulfonic acid (0.05 *M*) in 1:5 acetic anhydride – acetic acid to isomerize I to II caused the equilibration of II and VI at a rate much faster than that of the isomerization. However, the equilibration reaction was followed with 0.00037 *M* sulfuric acid in 1:1 acetic acid – acetic anhydride. The half-life of the reaction was about 14 min at 23°. It is of interest to note that the half-life for the anomerization of the tetra-*O*-acetyl-2-deoxy-D-glucopyranoses under these conditions, but with 0.001 *M* acid,

is 4 min (6). Thus the increased opportunity for charge delocalization provided by the allylic double bond effectively cancels the effect of the 2-acetoxy group (7). The solvent itself did not cause equilibration at a measurable rate. The equilibrium constant was about 4.0 in favor of the α-anomer, both by n.m.r. analysis and from the optical rotation of the mixture. As indicated by Ferrier and his co-workers, the anomeric effect (8) may be mainly responsible for the greater stability of the α-form. In this regard, it is of interest to note the n.m.r. parameters for II and VI listed in Table I. In view of the differences in both $J_{3,4}$ and $J_{4,5}$, it is evident that the pyranose ring has different conformations for these compounds. From the value of $J_{4,5}$ for the α-anomer (9 c.p.s.), it follows that the 4-acetoxy and 4-acetoxymethyl groups are in an equatorial orientation and that the compound resides in the "regular" half-chair conformation, with the 1-acetoxy group in a quasi-axial orientation. Since these compounds have two trigonal carbons and an oxygen atom in the pyranose ring, the destabilizing interactions between opposing axial groups must be much less than in a chair conformation. Thus, it is reasonable to expect that the β-anomer may closely achieve a conformation which has the 4- and 5-substituents in a quasi-axial orientation to decrease the non-bonding interaction between these substituents. In fact, the n.m.r. data require that the 4- and 5-substituents be much further apart in the β- than in the α-anomer. Evidently, for the α-form, the anomeric effect is sufficiently great to overcome the gauche interaction between the 4- and 5-substituents.

TABLE I

Nuclear magnetic resonance parameters for derivatives of 2-acetoxy-pseudo-D-glucal

Compound	Chemical shifts (τ)			Coupling constants (c.p.s.)	
	H^1	H^3	H^4	$J_{3,4}$	$J_{4,5}$
α-Tri-*O*-acetyl (II) (1)	3.69	4.13	4.47	2.2	9
β-Tri-*O*-acetyl (VI)	3.63	4.04	4.69	5.5	~1
α-Di-*O*-acetyl-1-*O*-methyl (IX)	5.07	4.28	4.58	2	~9
β-Di-*O*-acetyl-1-*O*-methyl (VIII)	4.85	4.23	4.69	4.7	4.5
α-Di-*O*-acetyl-1-chloro-1-deoxy (VII)	3.72	4.19	4.4	2	~9

The anomeric compounds II and VI could also be equilibrated by heating them in acetic acid with potassium acetate, although substantial decomposition to other products occurred. The equilibrium constant was, within experimental error, the same as that observed under the acid conditions. The half-life of the reaction with *M* potassium acetate in acetic acid at 100° was about 100 min.

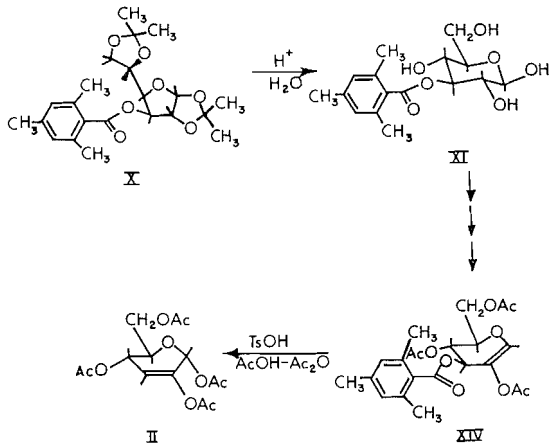
Di-*O*-acetyl-2-acetoxy-3-*O*-(2,6-dichlorobenzoyl)-D-glucal (V) also gave the anomeric tri-*O*-acetyl-2-acetoxy-pseudo-D-glucals (II and VI) on treatment with potassium acetate in acetic acid at 100°. The half-life of the reaction was about 10 min. Thus, this reaction is about 10 times faster than the anomerization of the products, and the stereochemistry of the reaction was readily established. In fact, compound V could be converted into an almost exactly equimolar mixture of the anomeric acetates (II and VI) in 27% yield by heating it for 5 min at 100° in *M* potassium acetate in acetic acid, conditions which left the products virtually unchanged. Thus, unlike the S_N2' reaction (2), this transformation was devoid of stereospecificity. This is not surprising since the ring oxygen must participate in the reaction to help delocalize the developing positive charge, and thus obviates the need for an attack by the entering nucleophile in *cis*-relationship to the leaving group to maximize the stability of the transition state. The molecularity of the reaction was not

established, and it is possible that the reaction proceeds by way of an ionic intermediate (S_N1).

Reaction of 2-acetoxy-pseudo-α-D-glucal triacetate (II) with aluminium chloride in chloroform under carefully controlled conditions gave the highly reactive tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl chloride (VII). The syrupy product appeared (n.m.r.) to be over 80% pure. The same product was obtained from 2-acetoxy-pseudo-β-D-glucal triacetate (VI).

The structure of the chloride (VII) was substantiated by reaction with sodium acetate in acetic acid to yield a mixture of II and VI in the ratio of 1:2, respectively. Thus, it was apparent that the compounds underwent replacement of the chlorine predominantly with inversion of the reacting center, as is normally found in these reactions (9).[2] The configuration of the chloride (VII) was established by the n.m.r. parameters listed in Table I.

At one point in this research, it was thought of interest to prepare 3-*O*-mesitoyl-2-acetoxy-D-glucal diacetate (XIV) to test the leaving power of the mesitoyloxy group. This preparation was readily possible by using the recently published method for preparing esters of hindered acids, which employs the use of trifluoroacetic anhydride as the activating reagent (10). It was remarkable to find that crystalline 1,2;5,6-di-*O*-isopropylidene-3-*O*-mesitoyl-α-D-glucose (X) was readily prepared in this way in 94% yield. The compound was hydrolyzed to crystalline 3-*O*-mesitoyl-β-D-glucose (XI), which was converted in the usual manner by way of the acetobromo derivative (XIII) into compound XIV. The compound seemed to be as stable as the tetraacetate (I), and underwent conversion into the 2-acetoxy-pseudo-D-glucal triacetates (II and VI) in 5:1 acetic acid – acetic anhydride 0.05 *M* in *p*-toluenesulfonic acid (1) at 0.34 times the rate of I and 6.7 times the rate of V.



Although this research failed to yield a 3-*O*-substituted-2-acetoxy-D-glucal diacetate of sufficient reactivity to serve as a useful reagent for the synthesis of 2,3-unsaturated glycosides, the tri-*O*-acetyl-3-deoxy-α-D-*erythro*-hex-2-enopyranosyl chloride (VII) described above shows considerable promise in this regard. The compound is extremely reactive, as shown by the fact that its reactions with methanol and ethanol to form glycosides were complete within minutes at room temperature in the presence of *sym*-collidine as buffer. The α- and β-anomers were formed in about equal amounts.

[2]*R. U. Lemieux and R. J. Bose, in preparation.*

EXPERIMENTAL

Unless otherwise stated, the optical rotations were measured in 1 dm tubes at the D-line of sodium and room temperature (23–24°). The n.m.r. spectra were determined in deuterated chloroform on the spectrometers previously described (4). The melting points were determined on a microstage and are uncorrected.

Attempts to Prepare a 3-O-Sulfonyl Derivative of 4,6-Di-O-acetyl-2-acetoxy-D-glucal

The 2,4,6-tri-*O*-acetyl-3-*O*-tosyl (3) and 2,4,6-tri-*O*-acetyl-3-*O*-mesyl (11) derivatives of α-D-glucosyl bromide were prepared as previously described. The physical constants were in close agreement with those published for these compounds. Furthermore, the n.m.r. spectra were in complete agreement with those of compounds having the assigned structures.

When the compounds were treated with diethylamine in acetonitrile according to the directions reported by Lemieux and Lineback (4) for the dehydrobromination of tetra-*O*-acetyl-α-D-glucopyranosyl bromide, a syrupy product was obtained which darkened rapidly when allowed to stand. The n.m.r. spectra showed the products to be devoid of the sulfonate ester grouping and to be virtually identical. Although integration showed the presence of one diethylamino group per tri-*O*-acetyl sugar residue, it was evident that the product was a mixture of at least two compounds. Attempts to obtain a pure compound failed. Hydrogenation in ethanol in the presence of 5% palladium on charcoal led to extensive hydrogenolysis as well as hydrogenation, as indicated by the rapid consumption of 2 moles of hydrogen. The product was deacetylated and converted into the trimethylsilyl derivative for analysis by gas–liquid preparative chromatography. Although a band corresponding to 80% of the mixture appeared to provide a single component, the n.m.r. spectrum required this fraction to be a mixture of several compounds.

Reaction of the crystalline 2,4,6-tri-*O*-acetyl-3-*O*-tosyl-α-D-glucosyl bromide with 1 mole equivalent of diethylamine and 3 moles of methanol in acetonitrile led to a reaction which was complete after 10 h. The observed decrease in rotation was 0.76°. When 2 more mole equivalents of diethylamine was added, the rotation decreased 0.89° in 10 h and then remained constant. The product of this reaction was identical with that described above, obtained in the absence of methanol and with a large excess of diethylamine. Increased concentrations of methanol had no effect on the course of the reaction.

1,2;5,6-Di-O-isopropylidene-3-O-(2,6-dichlorobenzoyl)-α-D-glucose

1,2;5,6-Di-O-isopropylidene-α-D-glucose (1.0 g, 3.00 mmoles) was dissolved in 3 ml dry pyridine containing 1 ml 2,6-dichlorobenzoyl chloride (2). The reaction mixture was heated for 2.5 h on the steam bath, cooled, and poured onto ice. The mixture was extracted with chloroform. Evaporation of the chloroform extract gave a deep-red syrup which was extracted with ether. The red ethereal solution was concentrated to a syrup (2.26 g) which was subsequently fractionated on a column of 30 g silicic acid (Mallinckrodt, 100 mesh, analytical reagent) with chloroform as the eluting solvent. A pale-yellow syrup (1.06 g) was obtained from the fast-moving zone; this syrup crystallized when allowed to stand and was recrystallized from ethanol as long needles, m.p. 122–123°, $[\alpha]_D$ −14.45° (*c*, 1.4 in chloroform).

Anal. Calcd. for $C_{19}H_{22}Cl_2O_7$: C, 52.67; H, 5.12. Found: C, 52.51; H, 5.11.

4,6-Di-O-acetyl-2-acetoxy-3-O-(2,6-dichlorobenzoyl)-D-glucal (V)

1,2;5,6-Di-*O*-isopropylidene-3-*O*-(2,6-dichlorobenzoyl)-D-glucose was heated on the steam bath under reflux for 2 h in 1:1 ethanol – 2 *N* sulfuric acid. Thin-layer chromatography of the resulting hydrolysate showed only one spot. The reaction mixture was diluted with water and neutralized with barium carbonate. The filtrate was concentrated to a syrup, $[\alpha]_D^{23}$ −29.1° (*c*, 2.6 in ethanol), which was directly acetylated in the usual manner with sodium acetate and acetic anhydride.

In a typical experiment, the syrupy 1,2,4,6-tetra-*O*-acetyl-3-*O*-(2,6-dichlorobenzoyl)-D-glucose (0.41 g, $[\alpha]_D$ +24.4° (*c*, 3 in chloroform)) was dissolved in an ice-cold mixture of 5 ml 32% hydrogen bromide in glacial acetic acid containing 1 ml of acetic anhydride. The reaction mixture remained overnight at room temperature and then was poured onto 100 g ice. The amorphous precipitate was recovered by filtration, washed with ice water, and dissolved in chloroform. The solution was washed with ice-cold sodium bicarbonate solution and then water, and finally dried over sodium sulfate. Evaporation gave a syrup, 0.28 g, $[\alpha]_D$ +120° (*c*, 2.8 in acetonitrile), which resisted crystallization. The n.m.r. spectrum in deuterated chloroform required the substance to be virtually pure 2,4,6-tri-*O*-acetyl-3-*O*-(2,6-dichlorobenzoyl)-α-D-glucopyranosyl bromide. The chemical shifts for H^1, H^2, H^3, and H^4 were τ 3.27, 5.07, 4.03, and 4.66, and the spacings in the closely first-order spectrum indicated $J_{1,2} = 4.0$, $J_{2,3} = J_{3,4} = 10.0$, and $J_{4,5} = 9.5$ c.p.s. The relative intensities of the signals in the spectrum were as expected. The three protons on the benzene ring gave a sharp singlet at τ 2.63.

2,4,6-Tri-*O*-acetyl-3-*O*-(2,6-dichlorobenzoyl)-α-D-glucopyranosyl bromide (0.282 g, 0.52 mmole) was dissolved in 10 ml dry acetonitrile. Dry diethylamine (0.4 ml, 3.9 mmoles) was added and the change in rotation observed. From an initial observed rotation of +3.39°, a final rotation of 1.11° was reached in 11 h. The reaction mixture was poured into 150 ml of ice-cold chloroform and washed successively with 100 ml 0.2 *N* hydrochloric acid (ice-cold) and ice-cold sodium bicarbonate solution. When the chloroform solution was concentrated a syrup (0.21 g) was obtained, $[\alpha]_D$ −11.35° (*c*, 3.13 in chloroform), which discolored when allowed to stand. In a separate experiment 4.24 g of the syrup was applied to a 30 g silicic acid column and

eluted with chloroform. A single, sharp band appeared on the column which was recovered as a single fraction (4.02 g). The pale-yellow syrup (V), $[\alpha]_D$ −9.32° (*c*, 2 in chloroform), was dried for 12 h at 100° and 0.5 mm pressure without appreciable darkening.

Anal. Calcd. for $C_{19}H_{18}O_9Cl_2$: C, 49.47; H, 3.93. Found: C, 48.99; H, 3.96.

Although the compound resisted crystallization, the n.m.r. spectrum in deuterated chloroform indicated a high degree of purity. Only the expected signals, having the proper relative intensities, were observed. The signals for H^1 (singlet), H^3 (doublet), and H^4 (triplet) were at τ 3.28, 4.06, and 4.58, respectively, with $J_{3,4} = J_{4,5} = 5$ c.p.s. The signals for the three acetyl groups were well separated, and the three protons on the benzene ring gave a sharp singlet at τ 2.67.

Tetra-O-acetyl-β-D-erythro-hex-2-enopyranose (VI)

The α-anomer (II) was prepared from 65 g of tri-*O*-acetyl-2-acetoxy-D-glucal according to the directions of Lemieux and his co-workers (1), with *p*-toluenesulfonic acid as catalyst. The reaction mixture was poured onto 2 l of crushed ice. The crude crystalline α-anomer was isolated by filtration and recrystallized from 600 ml of 1:1 ethanol–water to give 39.5 g of pure compound. The mother liquors from the above filtrations were combined and thoroughly extracted with chloroform. The neutralized and dried extract was concentrated to a syrup (23.2 g), which was a 1.6:1 mixture of VI and II, respectively. The β-anomer (VI) crystallized readily when the mixture was seeded with an authentic sample kindly provided by Dr. R. J. Ferrier, Birkbeck College. The compound, m.p. 81.5–83.5°, $[\alpha]_D$ +146° (*c*, 2.4 in chloroform), was purified by repeated recrystallizations from 95% ethanol. Ferrier and his co-workers (5) reported m.p. 81–83°, $[\alpha]_D$ +156° (*c*, 1 in chloroform). The n.m.r. parameters measured at 100 Mc.p.s. are reported in Table I.

Anomerization Reactions of Compounds II and VI

Acid-Catalyzed

When 0.2 g of II was dissolved at 25° in 3 ml of 1:1 acetic acid – acetic anhydride 0.37 *M* in sulfuric acid, the rotation fell from an initially observed value of +4.6° to 3.28° in 5 min and eventually to a nearly constant value of −3.12°. Since these observed rotational changes were in the direction opposite to that expected for anomerization, it was evident that these strongly acid conditions had caused rapid changes other than anomerization. Solutions of compounds II and VI in 1:1 acetic acid – acetic anhydride showed no change in rotation during 24 h at 25°. It was found that reactions limited to anomerization could be achieved by using 0.00037 *M* sulfuric acid. Under these conditions, the rotation increased from 3.2° after 3 min to a constant value of +4.02° in 30 min. The rate of change in rotation followed first-order kinetics ($k_\alpha + k_\beta = 5 \pm 1 \times 10^{-2}$ min^{-1}). After 80 min, 0.1 ml of collidine was added and the product isolated in the usual manner. The n.m.r. spectrum showed the product to be a 4:1 mixture of the α- and β-anomers, respectively. Based on the rotations at zero time obtained by plotting the rotational data for both II and VI, the equilibrium rotation for the 4:1 mixture is expected to be 4.10°.

Anomerization of compound VI under the above conditions gave a change in rotation from +8.40° at zero time to a nearly constant value of +4.05° in 60 min. The velocity of the reaction was, within experimental error, the same as that when the α-anomer was used.

Base-Catalyzed

Solutions (0.1 *M*) of II and VI were made up at room temperature in acetic acid 1 *M* in potassium acetate, and placed in sealed tubes. At zero time, the tubes were immersed in a boiling water bath. After various intervals of time, the solutions were added to cold chloroform and the mixtures immediately washed with water and then sodium bicarbonate solution, dried, and evaporated to the syrupy products. The compositions of the products were determined by n.m.r. The β-anomer (VI) was anomerized to a 2:1 mixture of the α- and β-forms, respectively, in 180 min. After 5 min, only 5% anomerization had occurred. The α-anomer (II) was isomerized to a 4:1 mixture of II and VI, respectively, after 16 h. The isolated yield of the product was 40%.

Conversions of 4,6-Di-O-acetyl-2-acetoxy-3-O-(2,6-dichlorobenzoyl)-D-glucal (V) into the Anomeric Tetra-O-acetyl-D-erythro-hex-2-enopyranoses (II and VI)

Acid Catalysis

Compound V (a 0.1 *M* solution in 1:5 acetic anhydride – acetic acid containing 0.05 *M* *p*-toluenesulfonic acid) was treated at 25° as described by Lemieux and his co-workers (1) for the isomerization of I. The rate of rotational change indicated a velocity constant of 2×10^{-2} h^{-1}. The product of reaction was a 4:1 equilibrium mixture of II and VI. The velocity constants for the conversions of compounds I and XIV were 40×10^{-2} and 13.5×10^{-2} h^{-1}, respectively.

Base Catalysis

Compound V was allowed to react in acetic acid 1 *M* in potassium acetate at 100° as described above for compounds II and VI. Products were isolated after reaction times of 5, 15, 30, and 180 min and contained 73, 29, 11, and 0% of the starting material, respectively, as indicated by the n.m.r. spectra. Compounds II and VI were the sole products of the reaction and were present in the products in ratios (α/β) of 1.08, 1.27, 1.54, and 2.70, respectively.

Tri-O-acetyl-3-deoxy-α-D-erythro-hex-2-enopyranosyl Chloride (VII)

Compound II (5.08 g, 15.4 mmoles) was dissolved in 100 ml of alcohol-free dry chloroform. Powdered aluminium chloride (2.1 g, 15.8 mmoles) was added and the mixture was vigorously shaken for 1 h at room temperature. The mixture was poured into 300 ml of dry benzene and filtered through a cotton plug. Evaporation of the solvents under reduced pressure left 3.07 g of a colorless syrup, $[\alpha]_D$ +53.4° (*c*, 2.5 in chloroform). The n.m.r. spectrum (see Table I) left no doubt that the product was virtually one compound. Characterization as VII is based on its n.m.r. spectrum and conversion into II and VI in high yield. Virtually the same product as described above was obtained when the β-anomer (VI) was treated with aluminium chloride.

The syrupy chloride (VII) (0.25 g) was dissolved in 5 ml of acetic acid containing 0.5 g of anhydrous sodium acetate and 1 ml of acetic anhydride. After 75 min at room temperature, 0.225 g of the product was isolated in the usual manner. Examination by n.m.r. showed the presence of a 2:1 mixture of VI and II, respectively, along with some impurity, giving rise to minor signals, particularly at τ 2.75.

Methyl Di-O-acetyl-3-deoxy-β-D-erythro-hex-2-enopyranoside (VIII)

Compound VII (3.07 g) was dissolved in a mixture of 5 ml of dry *sym*-collidine and 25 ml of anhydrous methanol. The observed rotation changed from an initial value of +7.74° to a constant value of +6.30° in 1 h. The solvents were largely removed by evaporation *in vacuo*, the residue was dissolved in ether, and the ethereal solution was washed with water, decolorized with charcoal, and evaporated to dryness in a high vacuum. The residue, 2.58 g (96% yield), had a n.m.r. spectrum consistent with that expected for an equimolar mixture of VIII and its α-anomer IX. A 0.91 g sample of the product was chromatographed on a 50 g column of silicic acid with chloroform as the eluting solvent. Although a clear separation was not obtained, a 0.07 g fraction had a n.m.r. spectrum (see Table I) consistent with that of a pure compound in the β-D-configuration. The specific rotation was +104° (*c*, 4 in chloroform) and showed a strongly plain, positive rotatory dispersion curve, as found by Ferrier and his co-workers (5) for the related β-anomer (VI).

1,2;5,6-Di-O-isopropylidene-3-O-mesitoyl-α-D-glucose (X)

Mesitoic acid (1.01 g, 0.1 mmole) (I) was dissolved in 5 ml trifluoroacetic anhydride and the mixture cooled in an ice bath. 1,2;5,6-Di-*O*-isopropylidene-α-D-glucose (1.82 g, 7.0 mmoles) was added and, after 30 min, the yellowish reaction mixture was diluted with 100 ml dry benzene. The solution was washed with ice-cold 10% aqueous sodium hydroxide and then with ice water. The benzene solution was dried over anhydrous sodium sulfate, filtered, and evaporated *in vacuo* to a pale-yellow, viscous syrup, 2.66 g, $[\alpha]_D$ −28.8° (*c*, 1.8 in chloroform). The n.m.r. spectrum was in complete agreement with that of a compound having the assigned structure.

3-O-Mesitoyl-β-D-glucose (XI)

1,2;5,6-Di-*O*-isopropylidene-3-*O*-mesitoyl-α-D-glucose (X) was dissolved in 20 ml of refluxing methanol, and 20 ml of 2 *N* sulfuric acid was added dropwise during 10 min. The mixture was refluxed for a further 60 min, cooled, and diluted with 50% aqueous methanol. The solution was shaken with Dowex 3 (OH^-) until neutral, filtered, and concentrated to a syrup, 1.615 g (98% yield). The compound was crystallized from water, and after two recrystallizations from this solvent melted at 153–154°, $[\alpha]_D$ +17.1° → +49.8° after 20 h (*c*, 1.55 in 95% ethanol 0.2% in pyridine).

Anal. Calcd. for $C_{16}H_{22}O_7$: C, 58.89; H, 6.79. Found: C, 58.95; H, 6.60.

1,2,4,6-Tetra-O-acetyl-3-O-mesitoyl-β-D-glucose (XII)

3-*O*-Mesitoyl-β-D-glucose (XI) (6.54 g) was heated for 2.5 h on the steam bath with 7 g of anhydrous sodium acetate and 70 ml of acetic anhydride. The mixture was poured onto 500 g of crushed ice, and the resulting solid product was washed with cold water. Recrystallization from 95% ethanol gave 5.36 g of fine needles, m.p. 170–171°, $[\alpha]_D$ +9.4° (*c*, 2.9 in chloroform). The n.m.r. spectrum was in complete agreement with that of a compound having the assigned structure.

Anal. Calcd. for $C_{24}H_{30}O_{11}$: C, 58.29; H, 6.12. Found: C, 58.21, H, 5.86.

2,4,6-Tri-O-acetyl-3-O-mesitoyl-α-D-glucosyl Bromide (XIII)

Compound XII was treated with 32% hydrogen bromide in glacial acetic acid in the usual manner to give a colorless syrup, in a nearly quantitative yield, which failed to crystallize. The high rotation ($[\alpha]_D$ +149° (*c*, 1.5 in acetonitrile)) and the n.m.r. spectrum were in complete agreement with those of a compound having the assigned structure.

4,6-Di-O-acetyl-2-acetoxy-3-O-mesitoyl-D-glucal (XIV)

Compound XIII was reacted with diethylamine in acetonitrile according to the directions described by Lemieux and his co-workers (1) for the preparation of I. The crude product was virtually pure XIV and was obtained in a nearly quantitative yield. The compound crystallized readily on trituration with methanol. Recrystallization from methanol gave pure material, m.p. 114–116°, $[\alpha]_D$ −39.6° (*c*, 1.2 in acetonitrile). The n.m.r. spectrum was in complete agreement with that of a compound having the assigned structure.

Anal. Calcd. for $C_{22}H_{26}O_9$: C, 60.82; H, 6.03. Found: C, 61.2; H, 6.04.

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