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Original Scientific Paper

The Behavior of 2-Acetamido-2-deoxy-D-galactose with Isopropenyl Acetate in the Presence of *p*-Toluenesulfonic Acid. Formation of an Unsaturated Aminosugar Derivative

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Treatment of 2-acetamido-2-deoxy-D-galactose (III) with isopropenyl acetate and *p*-toluenesulfonic acid gives 2-(D-*glycero*-1,2--diacetoxyethyl)-4-(*N*-acetylacetamido) furan (II), the anomeric 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-galactopyranoses (IV and V), a mixture of the anomeric 1,3,5,6-tetra-*O*-acetyl-2--(*N*-acetylacetamido)-2-deoxy-D-galactofuranoses (VII) and 1,4,6--tri-*O*-acetyl-2-(*N*-acetylacetamido)-2,3-dideoxy-D-*threo*-hex-2-enopyranose (X). The anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2--deoxy-D-galactopyranoses (VI) were also detected; they may be primary products or artifacts arising from IV and V by spontaneous de-*N*-acetylation in the course of the chromatography which was used.

On storage, VII loses an *N*-acetyl group to give a mixture of the anomeric 2-acetamido-1,3,5,6-tetra-*O*-acetyl-2-deoxy-D-galactofuranoses (VIII); the same mixture of anomers was also encountered in the fractionation of the original acetylation mixture and, like VI, may represent secondary products. Fusion of VII with phenol in the presence of *p*-toluenesulfonic acid, followed by deacetylation, gives phenyl 2-acetamido-2-deoxy-β-D-galactofuranoside (IX).

Deacetylation of the unsaturated derivative X gives crystalline 2-acetamido-2,3-dideoxy-D-*threo*-hex-2-enose (XI). The NMR spectra of X and XI, together with the fact that XI reduces Fehling solution, establish the structure of X which was obtained as a mixture of anomeric forms.

Mechanisms are proposed for the formation of II and X, and the behavior of III with isopropenyl acetate—*p*-toluenesulfonic acid is contrasted with that of 2-acetamido-2-deoxy-D-glucose and 2-acetamido-2-deoxy-D-mannose.

Although 2-acetamido-2-deoxy-D-glucose and 2-acetamido-2-deoxy-D-mannose differ only in the configuration of one carbon atom (C-2), their behavior when treated with isopropenyl acetate in the presence of a trace of *p*-toluenesulfonic acid forms a marked contrast. The former sugar simply undergoes complete acetylation to give a mixture of the anomeric 1,3,4,6-tetra-*O*-acetyl--2-(*N*-acetylacetamido)-2-deoxy-D-glucopyranoses.[1] The latter sugar, on the other hand, gives none of this type of product but, instead, the two unsaturated derivatives, 3,4,6-tri-*O*-acetyl-2-(*N*-acetylacetamido)-1,2-dideoxy-D-*arabino*-hex-1-

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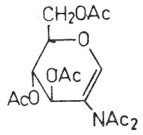
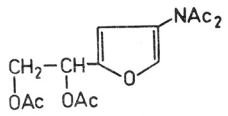
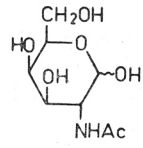


I

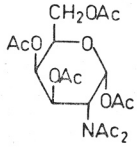


II

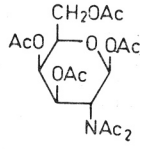
-enopyranose (I) and 2-D-*glycero*-1,2-diacetoxyethyl)-4-(*N*-acetylacetamido)furan (II), the acyclic derivative 1,1,3,4,5,6-hexa-*O*-acetyl-2-(*N*-acetylacetamido)-2--deoxy-D-mannose aldehydrol and the two anomeric 2-acetamido-1,3,4,6-tetra--*O*-acetyl-D-mannopyranoses.[2] In an earlier paper[3] we have presented evidence which suggests that the acetylation of 2-acetamido-2-deoxy-D-mannose with isopropenyl acetate most probably involves the formation of 1,3,4,6-tetra-*O*-acetyl--2-(*N*-acetylacetamido)-2-deoxy-α-D-mannopyranose as an unstable intermediate



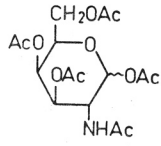
III



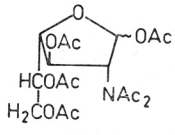
IV



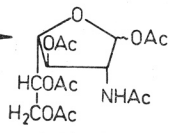
V



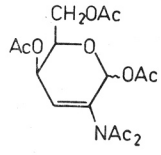
VI



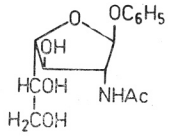
VII



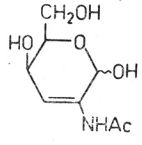
VIII



X



IX



XI

in which one of the acetyl groups in the axial diacetamido function at C-2 attacks C-1 with the expulsion of an axial acetoxy group, the formation of a cyclic ion and the expulsion of a proton at C-2 to yield I. The formation of II was rationalized by a similar mechanism involving the furanose form of the sugar. That neither I nor II appears to be formed in the acetylation of 2-acetamido--2-deoxy-D-glucose by isopropenyl acetate may be ascribed to the conformational stability of this sugar. On thermodynamic grounds, it is unlikely that the diacetamido group of 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy--β-D-glucopyranose would assume the axial position postulated as necessary for attack on C-1. Likewise, the conformational stability of the *gluco* configuration minimizes the proportion of the sugar present in the furanose form and thus the formation of II has not been observed.

With this background, we have now turned our attention to a third aminosugar, 2-acetamido-2-deoxy-D-galactose (III). The experimental results will be described first. Treatment of III with boiling isopropenyl acetate in the presence of a trace of *p*-toluenesulfonic acid for a period of 24 hours gave a complex mixture which was largely resolved by repeated chromatography on columns of silica gel. The furan derivative II[2] was isolated in 7.8% yield. Two crystalline esters were also encountered; their elemental composition and NMR spectra clearly identified them as the two anomeric 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-galactopyranoses (IV and V); the α anomer (IV) was isolated in 17% yield and the β anomer (V) in 0.34% yield. In addition, evidence for the presence of the two anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-galactopyranoses[4] (VI) was obtained; whether these vere primary reaction products or resulted from loss of *N*-acetyl groups from IV and V during the chromatography is uncertain.

A major product of the reaction (22% yield) was isolated as a chromatographically homogeneous syrup and proved to be isomeric with IV and V; deacetylation, followed by trimethylsilylation and VPC established the material as a derivative of 2-acetamido-2-deoxy-D-galactose (III). The VPC and NMR spectrum of the substance indicated that it is an anomeric mixture and, since it was not identical with either IV or V, it was tentatively assumed to be the anomeric 1,3,5,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-galactofuranoses (VII). On storage, the material spontaneously lost one *N*-acetyl group to give a mixture of the anomeric 2-acetamido-1,3,5,6-tetra-*O*-acetyl-2-deoxy-D--galactofuranoses (VIII); this material was also detected during the fractionation of the mixture from the acetylation of III where it probably arose through the spontaneous de-*N*-acetylation of VII. NMR spectroscopy and VPC suggest that the α anomer predominates in both VII and VIII. Fusion of VII with phenol in the presence of *p*-toluenesulfonic acid, followed by deacetylation, led to the isolation of crystalline phenyl 2-acetamido-2-deoxy-β-D-galactofuranoside (IX). Both anomeric phenyl 2-acetamido-2-deoxy-D-galactopyranosides are known[5] and the isomeric product obtained from VII was not identical with either of them; this evidence may be regarded as confirming the furanose structures of VII and VIII. Since IX was levorotatory ($[\alpha]_D^{20}$ — 75.7°), the β configuration was tentatively assigned to this glycoside.

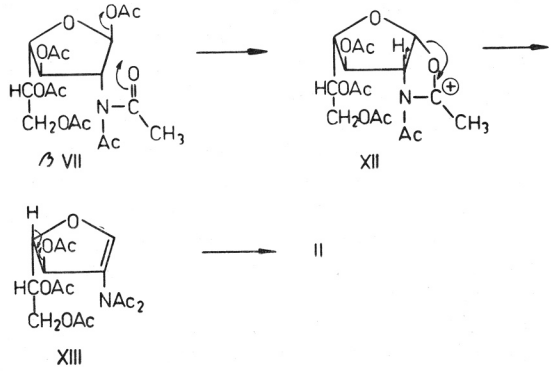
Of particular interest was the isolation (in 4.5% yield) of an optically active unsaturated compound (X) in the form of a chromatographically homogeneous syrup. Elemental analysis showed the substance to be an isomer of I; its IR and NMR spectra revealed the presence of three *O*-acetyl groups and two

N-acetyl groups. The same substance (but neither II nor VII) was also obtained by treatment of α VI with isopropenyl acetate (3.9% yield) although, in this case, the main product (84% yield) was IV. This evidence may be regarded as indicating that the unsaturated derivative has a pyranose ring. It remained to establish the position of the double bond. Treatment of the substance with methanolic sodium methoxide yielded a crystalline, unsaturated product (XI); elemental analysis and spectral evidence showed that one *N*-acetyl and three *O*-acetyl groups had been removed and that the remaining *N*-acetyl group was attached to a vinyl carbon atom, the NH signal in its NMR spectrum showing no coupling with a proton on an adjacent carbon atom. Assuming that no shift of the double bond had taken place during deacetylation, the evidence indicated that the double bond in X and XI spans C-1 and C-2 or C-2 and C-3. The deacetylated product, XI, reduced Fehling solution while the deacetylation product from I had been found[2] to be stable to this reagent. It may, therefore, be concluded that carbon one in the crystalline deacetylation product is unsubstituted, that the substance is 2-acetamido-2,3-dideoxy-D-*threo*--hex-2-enose (XI) and that the immediate product from the treatment of III with isopropenyl acetate is 1,4,6-tri-*O*-acetyl-2-(*N*-acetylacetamido)-2,3-dideoxy--D-*threo*-hex-2-enopyranose (X). Two low field singlets in the NMR spectrum of the substance (X) suggest that two anomers are present. The deacetylated product XI may, of course, exist in either anomeric form or, indeed, as a furanose; no evidence bearing on this point was obtained.

We shall now turn to a consideration of the mechanisms whereby some of these products may arise in the treatment of 2-acetamido-2-deoxy-D-galactose (III) with isopropenyl acetate.

Like 2-acetamido-2-deoxy-D-mannose, III bears an axial group, introducing an element of instability which is absent in 2-acetamido-2-deoxy-D-glucose. The formation of esters of the furanose form of III (*i. e.*, VII) is, therefore, not surprising, Indeed, the acetylation of D-galactose in boiling pyridine is a well-recognized method for the preparation of β-D-galactofuranose pentaacetate.[6]

In discussing the mechanism of the formation of II from 2-acetamido-2--deoxy-D-mannose, we earlier postulated[3] that a furanose ester of this sugar served as an intermediate. Evidence in support of this view has now been obtained in our studies of III. A crude mixture containing VIII (as well as VI) was subjected to the action of isopropenyl acetate—*p*-toluenesulfonic acid and II was isolated, though in low yield. It is not unreasonable, therefore, to assume

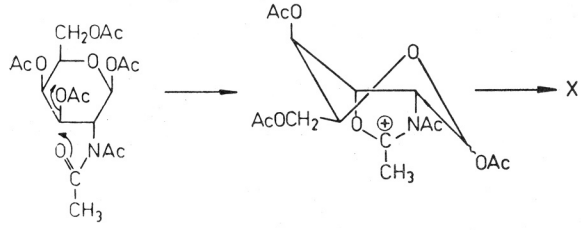


the following steps in the formation of II from VII. The reader is referred to an earlier paper[3] for a presentation of the evidence which suggests that a di-*N*-acetyl (rather than a mono-*N*-acetyl) derivative is the immediate precursor in eliminations of this type.

In contrast to the analogous case in the mannose series[3], the elimination of acetic acid from XIII to give II is, formally, a *cis* elimination. However, 3,5-di-*O*-benzoyl-1,2-dideoxy-D-*erythro*-pent-1-enofuranose undergoes with extreme ease a similar *cis* elimination of benzoic acid to give furfuryl benzoate[7] and in both cases it is probable that the acyloxy group on the allylic carbon 3 departs (to give a planar carbonium ion) prior to the loss of the proton at C-4.

Although evidence in the furanose series is lacking, we have earlier shown[3] that isopropenyl acetate—*p*-toluenesulfonic acid as used in our researches is a comparatively ineffective reagent for the anomerization of aldopyranose esters. Owing to the *cis* relationship of the groups at C-1 and C-2 in α VII, we should not expect this anomer to be converted to II and it may be significant that the VII isolated appeared to be predominantly the α anomer. Although II was isolated[2] subsequent to the treatment of 2-acetamido-2-deoxy-D-mannose with isopropenyl acetate and *p*-toluenesulfonic acid, no analogs of VII were detected although 1,3,5,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-α-D-mannofuranose (*trans* at C-1—C-2) was postulated[3] as an intermediate in the formation of II. Two explanations for this fact may be advanced. First, the *trans* product may be the dominant ester formed and it may undergo elimination (to give II) as rapidly as it is formed. Second, the corresponding *cis* ester may be formed but rapidly undergo anomerization under these conditions.

We shall now consider the mechanism of the formation of X. By analogy with the proposal made earlier for the formation of I[3], one can envisage an *N*-acetyl group in IV or V as attacking C-3, with an acetoxy group being eliminated to give the cyclic ion XIV which then loses a proton from C-2 to give X. Actually, the pure α anomer (IV) was treated with isopropenyl acetate



V XIV

and found not to give X; we must, therefore, assume that the β anomer (V) is the actual precursor of X. This assumption is supported by the fact that much more IV was isolated than V. The noteworthy fact that 2-acetamido-2--deoxy-D-glucose, configurationally identical at C-2 and C-3 with III, does not give an analog of X was reconfirmed in the course of the present research and it appears necessary to assume that the axial acetoxy group in V confers sufficient conformational instability on this molecule to permit the deformation of the ring which is required for the attack portrayed above. If, indeed, as the evidence indicates, V (rather than IV) is the precursor of X, we must, of course, assume that anomerization subsequently takes place since X, as isolated, was

a mixture of anomers. That IV and V were isolated here while neither 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-α-D-mannopyranose nor its anomer was detected after the acetylation of 2-acetamido-2-deoxy-D-mannose may probably be attributed to the fact that the groups at C-1 and C-2 in the mannose derivative are normally *trans* diaxial and hence the elimination (to form I) readily takes place. In addition, of course, the elimination of an acetoxy group from C-1 (as in the formation of I) is probably facilitated by electric and resonance factors which are not available to assist the departure of an acetoxy group from C-3 (as in the formation of X). All factors considered, it is not surprising that the yield of X (4.5%) from III is lower than that of I (14%) from 2-acetamido-2-deoxy-D-mannose.

EXPERIMENTAL

Melting points were taken on a Kofler hot stage. Thin layer chromatography was conducted on Silica Gel G (Merck, Darmstadt) using the solvent systems specified, components being detected by spraying with 10% sulfuric acid and heating to 100°. For the detection of unsaturated compounds, the plates were sprayed with aqueous fluorescein (0.04%, w./v.), dried without heating and then exposed to bromine vapors[8]. Column chromatography was conducted on silica gel (0.05—0.20 mm., Merck, Darmstadt), 15-ml. fractions being collected. The NMR spectra were obtained in $CDCl_3$ solution (unless otherwise specified) using a Varian A-60 spectrometer and tetramethylsilane as an internal standard. Infrared spectra were recorded using a Perkin-Elmer Model 21 or Model 137 spectrometer. An F & M Model 500 instrument, equipped with a flame ionization detector, was used for VPC; the column employed (0.25 in. × 6 ft.) was filled with 3% SE 52 on Gas-Chrom A (Applied Sci. Labs., Inc., State College, Pa.). The »Tri-Sil« reagent (Pierce Chem. Co., Rockford, Ill.) was used for the preparation of trimethylsilyl derivatives.

*Reaction of 2-Acetamido-2-deoxy-*D*-galactose* (III) *with Isopropenyl Acetate*

A solution of 2-acetamido-2-deoxy-D-galactose (Pfanstiehl Labs., Inc., Waukegan, Ill.) (5.0 g.) in isopropenyl acetate (100 ml.) containing *p*-toluenesulfonic acid monohydrate (*ca.* 50 mg.) was boiled under reflux for 24 hr., the progress of the reaction being followed by thin layer chromatography using ether. The first product to appear had a mobility identical to that of the anomeric 2-acetamido-1,3,4,6-tetra-*O*-acetyl-D-galactopyranoses (VI).[4] At the conclusion of the reaction, five components were detectable. The solvent was evaporated *in vacuo* and the dark residue, dissolved in ether, was passed through a small column of silica gel (60 ml.). Ether (300 ml.) eluted four components; the fifth was eluted with ether—methanol (9 : 1, v./v.).

The ethereal eluate was concentrated *in vacuo* and the yellow residue rechromatographed on a column of silica gel (450 ml.) using ether. Fractions 38 to 45 contained a yellowish oil (550 mg., 7.8%); the chromatographic behavior and NMR spectrum of the material were indistinguishable from those of 2-(D-*glycero*-1,2-diacetoxyethyl)-4-(*N*-acetylacetamido) furan (II)[2].

Fractions 46 and 47 contained a mixture. Fractions 48 to 54 were pooled and concentrated to yield a syrup (X, 380 mg., 4.5%).

Fractions 55 to 67 contained a mixture of three components (310 mg.). Fractions 68 to 90 were pooled and concentrated to give 1,3,4,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-α-D-galactopyranose (IV, 1.67 g., 17%).

Fractions 91 to 97 contained a mixture of IV and VII (520 mg.). Fractions 98 to 174 contained 1,3,5,6-tetra-*O*-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-galactofuranose (VII, 2.10 g., 22%), contaminated with traces of 4-acetamido-2-(D-*glycero*-1,2-diacetoxyethyl) furan[2].

The ether—methanol eluate from the first chromatography was concentrated *in vacuo* to yield a yellow syrup (2.4 g.) which was rechromatographed on silica gel using ether—methanol (12 : 1, v./v.). A material, which appeared to be chromatographically homogeneous in this and other solvent systems tried, was obtained as a semisolid: $[\alpha]_D^{20}$ + 64.4° (*c* 0.66, $CHCl_3$); the IR spectrum of the material showed the presence of an acetamido group. On VPC at 210°, the mixture was resolved into two components with retention times identical with those of the anomeric

2-acetamido-1,3,4,5-tetra-*O*-acetyl-2-deoxy-D-galactopyranoses (α VI and β VI[4]). The NMR spectrum of the mixture showed a complex pattern of signals, particularly in the region of *N*- and *O*-acetyl groups (τ 7.83, 7.86, 7.89, 7.95, 7.98, 8.03, and 8.06), confirming the presence of the two anomeric forms of VI and indicating the presence of the 2-acetamido-1,3,5,6-tetra-*O*-acetyl-2-deoxy-D-galactofuranoses (VIII). Confirmatory evidence for the presence of VIII in this mixture is presented in an experiment described later in this paper.

1,4,6-Tri-O-*acetyl-2-(*N-*acetylacetamido)-2,3-dideoxy*-D-threo-*hex-2-enopyranose* (X)

Fractions 48 to 54 contained material which gave a positive test for unsaturation; rechromatography on a column of silica gel (70 ml.), using ether, gave pure X as a colorless syrup: $[\alpha]_D^{20} + 16.0^0$ (*c* 0.90, $CHCl_3$).

Anal. $C_{16}H_{21}NO_9$ (371.36) calc'd.: C 51.75; H 5.70; N 3.77; Ac 57.96%
found: C 51.75; H 6.04; N 3.62; Ac 58.7 %

IR spectrum (neat): 1750 (OAc), 1700 (NAc), and 1600 cm.$^{-1}$(C=C). NMR spectrum: signals at τ 3.39 (doublet, $J_{3,4}$ 1.6 cps, H_3), 4.12 (singlet, α H_1), 4.21 (singlet, β H_1), 4.40 (quartet, $J_{3,4}$ 1.6 cps, $J_{4,5}$ 5.0 cps, H_4), 5.40 (multiplet, H_5), 7.61 (NAc), 7.88, 7.92, and 8.02 (OAc); the ratio of the intensities of the NAc signals to the OAc signals was 2 : 3.

1,3,4,6-Tetra-O-*acetyl-2-(*N-*acetylacetamido)-2-deoxy*-β-D-*galactopyranose* (V)

The heterogeneous material in fractions 55 to 67 was rechromatographed on a column of silica gel using ether and V was obtained in crystalline, chromatographically homogeneous form: 33 mg., 0.34%. Recrystallized from ethanol, the substance showed m. p. 169—171° and $[\alpha]_D^{20} + 5.8^0$ (*c* 0.51, $CHCl_3$).

Anal. $C_{18}H_{25}NO_{11}$ (431.41) calc'd.: C 50.11; H 5.84; N 3.25%
found: C 50.00; H 5.76; N 3.33%

IR spectrum ($CHCl_3$): 1750 (OAc) and 1690 cm.$^{-1}$ (NAc). NMR spectrum: signals at τ 3.48 (doublet, $J_{1,2}$ 8.5 cps, H_1), 4.09 (quartet, $J_{2,3}$ 11.0 cps, $J_{3,4}$ 3.6 cps, H_3), 4.54 (doublet, $J_{3,4}$ 3.6 cps, H_4), 5.84 (singlet, $H_5 + H_6 + H_{6'}$, 3 H), 5.88 (quartet, $J_{1,2}$ 8.5 cps, $J_{2,3}$ 11.0 cps, H_2), 7.63 (NAc, 6 H), 7.82, 7.90, 7.98, and 8.03 (OAc, 12 H).

1,3,4,6-Tetra-O-*acetyl-2-(*N-*acetylacetamido)-2-deoxy*-α-D-*galactopyranose* (IV)

The material obtained from fractions 68 to 90 was crystallized from ether: m. p. 118—119°, $[\alpha]_D^{22} + 53.4^0$ (*c* 0.80, $CHCl_3$).

Anal. $C_{18}H_{25}NO_{11}$ (431.41) calc'd: C 50.11; H 5.84; N 3.25%
found: C 50.16; H 5.68; N 3.13%

IR spectrum ($CHCl_3$): 1750 (OAc) and 1675 cm.$^{-1}$ (NAc). NMR spectrum: signals at τ 3.70 (doublet, $J_{1,2}$ 3.7 cps, H_1), 3.98 (quartet, $J_{2,3}$ 12.0 cps, $J_{3,4}$ 3.2 cps, H_3), 4.40 (quartet, $J_{3,4}$ 3.2 cps, $J_{4,5}$ 1.2 cps, H_4), 5.10 (quartet, $J_{1,2}$ 3.7 cps, $J_{2,3}$ 12.0 cps, H_2), 7.67 (NAc, 6 H), 7.84, 7.90, 7.98, and 8.06 (OAc, 12 H). The signal from H_1 lies at higher field than the corresponding signal from V. This reversal of the normal relationship of the signals from H_1 has also been reported for *N*-acylacylamino derivatives of the D-glucopyranose series[9].

1,3,5,6-Tetra-O-*acetyl-2-(*N-*acetylacetamido)-2-deoxy*-D-*galactofuranose* (VII)

The syrup (2.10 g.) from fractions 98 to 174 was rechromatographed on a column of silica gel (250 ml.) using ether—benzene—methanol (10 : 10 : 1, v./v.) and VII was obtained as a chromatographically homogeneous syrup (1.7 g.): $[\alpha]_D^{19} + 51.5^0$ (*c* 1.00, $CHCl_3$).

Anal. $C_{18}H_{25}NO_{11}$ (431.41) calc'd.: C 50.11; H 5.84; N 3.25%
found: C 50.22; H 5.85; N 3.10%

IR spectrum (neat): 1740 (OAc) and 1670 cm.$^{-1}$ (NAc). NMR spectrum: signals at τ 3.67 (doublet, $J_{1,2}$ 6.1 cps, H_1 of α anomer), 3.90 (quartet, $J_{2,3}$ 6.1 cps, $J_{3,4}$ 4.0 cps,

H_3), 4.42 (multiplet, H_4), 5.09 (triplet, $J_{1,2} = J_{2,3}$ 6.1 cps, H_2), 7.58 (NAc, 6H), 7.89, 7.94, and 7.97 (OAc, 12H).

On VPC at 210°, the material showed two components with retention times identical with IV and V.

A sample was deacetylated with sodium methoxide, converted to the trimethylsilyl derivative and then examined by VPC at 205°; the same pattern of peaks as shown by a trimethylsilylated sample of III was observed.

*2-Acetamido-1,3,5,6-tetra-*O*-acetyl-2-deoxy-*D*-galactofuranose* (VIII)

After storage at room temperature for 6—7 weeks, a sample of VII was found to have decomposed. It was rechromatographed on a column of silica gel using ether--methanol (15 : 1, v./v.) to give 2-acetamido-1,3,5,6-tetra-O-acetyl-2-deoxy-D-galactofuranose (VIII) as a nearly colorless syrup $[\alpha]_D^{20}$ + 43.0° (c 0.64, $CHCl_3$).

Anal. $C_{16}H_{23}NO_{10}$ (389.37) calc'd.: C 49.36; H 5.95; N 3.60%
found: C 49.34; H 5.95; N 3.57%

IR spectrum (Nujol): 3400 (NH), 1740 (OAc), 1660 (NAc), and 1530 cm.$^{-1}$ (amide II). NMR spectrum: signals at τ 3.71 (doublet, $J_{1,2}$ 4.7 cps, H_1 of α anomer), 7.86, 7.87, 7.95, and 8.01 (NAc and OAc).

The mobility of the substance in several different solvent systems differs only slightly from that of VI. Examination by VPC showed two components with the same retention times as the two corresponding galactopyranosides (VI); it appears, then, that the product is an anomeric mixture with the α anomer, clearly evident in the NMR spectrum, predominating. The α anomer of VI gives signals at τ 3.75 (doublet, $J_{1,2}$ 3.5 cps, H_1), 7.81, 7.97, and 8.05 (Nac and OAc)[9] which clearly distinguish this substance from VIII.

*2-Acetamido-2,3-dideoxy-*D*-*threo*-hex-2-enose* (XI)

A solution of X (450 mg.) in absolute methanol (10 ml.) containing sodium methoxide (3 ml., 0.1 *N*) was stored at room temperature for 3 hr. Amberlite IR-120 (H^+) was then added and the suspension stirred until neutral; it was then filtered and the filtrate was concentrated *in vacuo*. The crude crystalline product (210 mg., 85%) was twice recrystallized from 2-propanol—ether: m. p. 152—153°, $[\alpha]_D^{20}$ + 76.1° (c 1.00, H_2O).

Anal. $C_8H_{13}NO_5$ (203.20) calc'd.: C 47.29; H 6.45; N 6.89%
found: C 47.30; H 6.31; N 6.67%

IR spectrum (Nujol): 3480 (OH), 3250 (NH), 1640 (NAc), and 1545 cm.$^{-1}$ (amide II). NMR spectrum (dimethylsulfoxide-d_6): signals at τ 1.64 (singlet, disappearing after exchange with D_2O, NH*), 3.15 (singlet, vinyl, H_3), 5.29 (broad singlet, disappearing after exchange with D_2O, OH), and 8.10 (NAc).

The substance gave a positive Fehling test and a positive test with fluorescein--bromine on thin layer chromatography.

*Phenyl 2-Acetamido-2-deoxy-*β*-*D*-galactofuranoside* (IX)

The procedure which Weissmann[5] developed for the synthesis of phenyl 2-acetamido-2-deoxyglycopyranosides was adapted to the preparation of IX. A mixture of VII (3.0 g.), phenol (3.9 g.) and *p*-toluenesulfonic acid monohydrate (60 mg.) was heated at 100° (bath) *in vacuo* (ca. 20 mm. of Hg) for 40 min. The cooled mixture was dissolved in chloroform and the solution was washed thoroughly with cold 2 *N* sodium hydroxide and with water. Moisture was removed with sodium sulfate and the solvent was evaporated *in vacuo*, leaving a thick syrup (2.8 g., 95%). The IR spectrum of the substance (neat) showed absorption at 3450 (NH), 1750 (OAc), 1660 (NAc), 1540 (amide II), 1600 and 1500 (phenyl), as expected of the tri-*O*-acetyl derivative of IX. The crude product was dissolved in absolute methanol containing sodium methoxide and the solution was stored at room temperature for 3 hr.; it was then worked up in the usual manner to yield crystalline IX (1.8 g., 87%). Recrystallized twice from 2-propanol, the substance had m. p. 175—176° and $[\alpha]_D^{20}$ — 75.7° (c 1.00, H_2O).

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* See footnote 7 of reference 2.

Anal. $C_{14}H_{19}NO_6$ (297.31) calc'd.: C 56.56; H 6.44; N 4.71%
found: C 56.74; H 6.12; N 4.75%

NMR spectrum (dimethylsulfoxide-d_6): signals at τ 1.89 (doublet, disappearing after exchange with D_2O, NH), 2.70—3.05 (aromatic protons), 4.60 (doublet, J 2.6 cps, H_1), 4.66 (doublet, disappearing after D_2O exchange, secondary OH), 5.26 (doublet, disappearing after exchange with D_2O, secondary OH), 5.44 (triplet, disappearing after D_2O exchange, primary OH) and 8.15 (NAc).

Reaction of Material Eluted by Ether-Methanol with Isopropenyl Acetate

Rechromatographed syrup containing a mixture of VI and VII (1.8 g.) was treated with isopropenyl acetate (20 ml.) and *p*-toluenesulfonic acid monohydrate (*ca.* 20 mg.) and the mixture boiled under reflux for 48 hr. The solvent was evaporated *in vacuo* and the resulting syrup, dissolved in ether, was chromatographed on a column of silica gel (250 ml.), elution being made with ether.

Fractions 24 to 27 contained 30 mg. (2%) of material with chromatographic properties and IR spectrum indistinguishable from those of II as described earlier.[2]

Fractions 29 to 34 yielded X (120 mg., 7%) as shown by its chromatographic behavior and IR spectrum.

Fractions 43 to 53 yielded crystalline 1,3,4,6-tetra-O-acetyl-2-(*N*-acetylacetamido)-2-deoxy-α-D-galactopyranose (IV, 400 mg., 20%); a mixed m. p. with an analytical sample of IV was undepressed.

Fractions 59 to 83 contained 1,3,5,6-tetra-O-acetyl-2-(*N*-acetylacetamido)-2-deoxy-D-galactofuranose (VII, 700 mg., 35%); its chromatographic behavior and IR spectrum were identical with those described earlier in this paper.

Behavior of 2-Acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-α-D-galactopyranose (α VI) with Isopropenyl Acetate

2-Acetamido-1,3,4,6-tetra-O-acetyl-2-deoxy-α-D-galactopyranose (α VI, 5.0 g.) was treated with isopropenyl acetate (35 ml.) containing *p*-toluenesulfonic acid monohydrate (*ca.* 50 mg.) and the mixture was boiled under reflux for 48 hr. The solvent was evaporated *in vacuo* to give a dark residue which was treated with ether (*ca.* 30 ml.) to yield 1,3,4,6-tetra-O-acetyl-2-(*N*-acetylacetamido)-2-deoxy-α-D-galactopyranose (IV, 4.3 g., 78%); recrystallized from ethanol, the product had m. p. 116—117°.

The ethereal filtrate was concentrated and chromatographed on a column of silica gel (80 ml.) using ether for elution. Fractions 32 to 39 contained X (185 mg., 3.9%). From fractions 46 to 57 an additional quantity of IV (350 mg., m. p. 115—117°) was obtained, increasing the yield of this substance to 84%.

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IZVOD

Reakcija 2-acetamido-2-deoksi-D-galaktoze sa izopropenil acetatom u prisutnosti *p*-toluensulfonske kiseline. Stvaranje jednoga nezasićenog derivata iz reda amino-šećera

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U reakciji 2-acetamido-2-deoksi-D-galaktoze (III) s izopropenil acetatom i *p*-toluensulfonskom kiselinom nastaju: 2-(D-*glicero*-1,2-diacetoksietil)-4-(*N*-acetilacetamido) furan (II), dva anomera 1,3,4,6-tetra-*O*-acetil-2-(*N*-acetilacetamido)-2-deoksi-D-galaktopiranoze (IV i V), smjesa anomera 1,3,5,6-tetra-*O*-acetil-2-(*N*-acetilacetamido)-2-deoksi-D-galaktofuranoze (VII) i 1,4,6-tri-*O*-acetil-2-(*N*-acetilacetamido)-2,3-dideoksi-D-*treo*-heksen-2-piranoza (X). Izolirana su i dva anomera 2-acetamido-1,3,4,6-tetra-*O*-acetil-2-deoksi-D-galaktopiranoze (VI); oni su ili primarni produkti ili artifakti koji su mogli nastati od IV i V spontanim gubitkom jedne *N*-acetil skupine u toku kromatografske obrade.

Stajanjem VII gubi jednu *N*-acetil skupinu i prelazi u 2-acetamido-1,3,5,6-tetra-*O*-acetil-2-deoksi-D-galaktofuranozu (VIII); ista smjesa anomera nađena je i u toku frakcionacije originalne reakcione smjese. Taljenjem spoja VII s fenolom dobiven je produkt, koji je nakon deacetiliranja identificiran kao fenil 2-acetamido-2-deoksi-β-D-galaktofuranozid (IX).

Deacetiliranjem nezasićenoga derivata X dobivena je 2-acetamido-2,3-dideoksi-D-*treo*-heksen-2-oza (XI). Na temelju NMR spektara spojeva X i XI, kao i činjenice da XI reducira Fehling-ovu otopinu, utvrđena je struktura spoja X.

Predložen je mehanizam nastajanja II i X. Istaknuta je razlika u ponašanju 2-acetamido-2-deoksi-D-galaktoze s izopropenil acetatom i *p*-toluensulfonskom kiselinom prema ponašanju 2-acetamido-2-deoksi-D-glukoze i 2-acetamido-2-deoksi-D-manoze s istim reagensom.

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