Methyl 2-Deoxy-β-D-*arabino*-hexopyranoside 4,6-(Monophenyl phosphate) (III).—A mixture of 1 g. of sirupy methyl 2-deoxy-β-D-*arabino*-hexopyranoside 6-(diphenyl phosphate) (IIa) and (presumably) methyl 2-deoxy-β-D-*arabino*-hexopyranoside 4,6-bis(diphenyl phosphate) (9:1 by visual estimation) was dissolved in 100 ml. of chloroform. The chloroform was shaken for 10 min. at room temperature with 50 ml. of 10% sodium hydroxide solution. The chloroform solution was then washed with 50-ml. portions of saturated aqueous sodium sulfate until the washings were neutral (three times). The dried chloroform solution was concentrated under reduced pressure. Solid material recovered amounted to 0.26 g., which, when examined by thin layer chromatography (silica gel G and diethyl ether–ethyl acetate as above), indicated three zones (R_f 0.25, 0.49, and 0.95). The zones of R_f 0.25 and 0.49 were of nearly equal intensity while the zone with R_f 0.95 was much less intense. The starting material showed only a trace of material with R_f 0.49. An authentic sample of methyl 2-deoxy-β-D-*arabino*-hexopyranoside 4,6-(monophenyl phosphate) (III, see following) was also run: R_f 0.49. Crystallization was effected from ether–acetone–petroleum ether, yielding 0.078 g., m.p. 168–174°.

Methyl 2-deoxy-β-D-*arabino*-hexopyranoside (1 g., 5.6 mmoles) was dissolved in 20 ml. of dry pyridine. Benzene (10 ml.) was added and the solution was cooled to −10° in an ice–salt bath. Monophenyl phosphorodichloridate[15] (1.19 g., 6.6 mmoles) was added over a 45-min. period with care being taken to exclude extraneous moisture. After stirring an additional 45 min., the mixture was maintained at −10° overnight followed by several hours at 25°. Concentration under reduced pressure yielded a material which was dissolved in 150 ml. of ethylene dichloride. The ethylene dichloride solution was washed twice with 5% sulfuric acid, aqueous sodium bicarbonate, and with water, dried, and concentrated under reduced pressure to a solid. Crystallization from acetone–diethyl ether–petroleum ether gave fine needles, 0.425 g. (25%). Recrystallization, effected in the same manner, gave material: m.p. 182–183° dec.; $[\alpha]^{24}D$ −58° (*c* 1, chloroform); X-ray powder diffraction data,[16] 8.32 w, 8.13 w, 7.76 w, 7.38 vw, 6.78 m (2), 5.42 w, 5.26 w, 4.60 w, 4.43 m (3), 4.25 s (1), 4.05 w, 3.88 vw, 3.78 w, 3.58 w, and 3.40 w.

Anal. Calcd. for $C_{13}H_{17}O_7P$: C, 49.36; H, 5.38; P, 9.81. Found: C, 49.66; H, 5.43; P, 9.81.

Methyl 2-Deoxy-β-D-*arabino*-hexopyranoside 4,6-(Cyclohexylammonium phosphate) (IIIa).—Methyl 2-deoxy-β-D-*arabino*-hexopyranoside 4,6-(monophenyl phosphate) [(III), 0.5 g.] was refluxed for 10 min. in anhydrous methanol with about 0.5 g. of acid-washed carbon. The solution was suction-filtered and washed with another 10 ml. of methanol. Adams catalyst (0.1 g.) was added and the mixture was shaken with hydrogen (15 lb./in.²) for 16 hr. The catalyst was removed and cyclohexylamine was added to the solution pH 8–9. Concentration under reduced pressure gave a material which was crystallized from ethanol–ether, yielding 0.33 g. Recrystallization (ethanol–ether) gave pure material: m.p. 197–198° dec., $[\alpha]^{25}D$ −60.5 (*c* 2, ethanol).

Anal. Calcd. for $C_{13}H_{26}NO_7P$: C, 46.01; H, 7.67; N, 4.13. Found: C, 46.12; H, 7.65; N, 4.02.

3,4,5-Tri-O-benzoyl-2-deoxy-6-O-trityl-D-*arabino*-hexose Diethyl Dithioacetal.—2-Deoxy-D-*arabino*-hexose diethyl dithioacetal[19] (2 g.) was dissolved in dry pyridine and to this was added 2.1 g. of trityl chloride. After standing at room temperature for 40 hr., the solution was cooled to 0° and 4 g. of benzoyl chloride was added dropwise. The solution was then allowed to stand at room temperature for 2 days whereupon it was poured into 200 ml. of iced water. The separated gum was extracted with ethylene chloride and the extract was washed with aqueous sodium bicarbonate and water. Residual pyridine in the sirup obtained on solvent removal from the dried (decolorizing carbon) solution was removed by codistillation, under reduced pressure, with toluene. Crystallization was effected from ethanol, yielding 3.8 g., m.p. 123–124.5°. On allowing the product to stand at room temperature for some time, another melting point was taken. A slight softening was noted at 123° but the material then melted at 145–146°. In other preparations, only the higher melting form was obtained: $[\alpha]^{26}D$ +35.5° (*c* 2, chloroform).

Anal. Calcd. for $C_{50}H_{48}O_7S_2$: C, 72.81; H, 5.83; S, 7.76. Found: C, 72.76; H, 5.81; S, 7.91.

(19) I. W. Hughes, W. G. Overend, and M. Stacey, *J. Chem. Soc.*, 2846 (1949); H. R. Bollinger, *Helv. Chim. Acta*, **34**, 989 (1951).

Reaction of Ammonia with Some Acetylated and Benzoylated Monosaccharides. IX. The Migration of Benzoyl Groups in the Ammonolysis of 1,2,3,4,6-Penta-*O*-benzoyl-D-galactoses[1]

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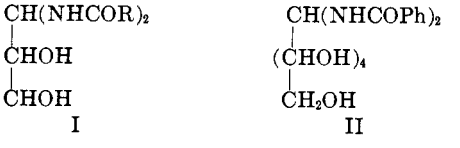
Received March 23, 1964

By ammonolysis of 1,2,3,4,6-penta-*O*-benzoyl-D-galactoses, having labeled benzoyl groups at different carbon atoms, the following contributions of each benzoyl group to the formation of 1,1-bis(benzamido)-1-deoxy-D-galactitol have been found: C-2, 0.13; C-3, 0.62; C-4, 1.02; C-6, 0.18 moles per mole. Compared with the penta-*O*-benzoyl-D-glucoses, the most interesting variation is the increase of the contribution of the benzoyl group at C-4, from 0.82 in the D-glucose series to total migration in the D-galactoses, that takes place at the expense of the contribution of the benzoyls in C-3 and C-6.

Ammonolysis, in methanolic solution, of acetylated and benzoylated pentoses,[2] L-rhamnose,[3] and hexoses[4] produces in various yields 1,1-bis(acylamido)-1-deoxyalditols (I, R = CH_3 or Ph). These products derive formally from the condensation of two molecules of acetamide or benzamide with the aldehyde group of one molecule of the sugar.



I II

The migration of the *O*-acyl groups from the different carbon atoms of monosaccharides to C-1, with the final production of the bisacylamido compounds (I), is an intramolecular reaction.[5] The formation of the acyclic 1,1-bis(acylamido)-1-deoxyalditols from the cyclic pyranose derivatives of the monosaccharides re-

(1) This work was supported, in part, by a grant from the Consejo Nacional de Investigaciones Científicas y Técnicas of Argentina.

(2) V. Deulofeu, J. O. Deferrari, and E. Recondo, *Anales Asoc. Quím. Arg.*, **46**, 137 (1958); J. O. Deferrari, M. A. Ondetti, and V. Deulofeu, *J. Org. Chem.*, **24**, 183 (1959).

(3) J. O. Deferrari and V. Deulofeu, *ibid.*, **22**, 807 (1957).

(4) (a) V. Deulofeu and J. O. Deferrari, *ibid.*, **17**, 1087 (1952); (b) *ibid.*, **17**, 1093 (1952); (c) *ibid.*, **17**, 1097 (1952).

(5) H. S. Isbell and H. L. Frush, *J. Am. Chem. Soc.*, **71**, 1579 (1949); R. C. Hockett, V. Deulofeu, and J. O. Deferrari, *ibid.*, **72**, 1840 (1950); V. Deulofeu and J. O. Deferrari, *Anales Asoc. Quím. Arg.*, **38**, 241 (1950).

TABLE I

APPARENT CONTRIBUTION[a] OF EACH BENZOYL GROUP TO THE MIGRATION WITH FORMATION OF 1,1-BIS(BENZAMIDO)-1-DEOXYHEXITOL

Ester	Location of benzoyl group C-2	C-3	C-4	C-6
1,2,3,4,6-Penta-*O*-benzoyl-D-glucose	0.12 ± 0.03	0.76 ± 0.02	0.82 ± 0.02	0.31 ± 0.02
2,3,4,6-Tetra-*O*-benzoyl-D-glucose	0.12 ± 0.03	0.80 ± 0.03	0.81 ± 0.02	0.27 ± 0.02
1,2,3,4,6-Penta-*O*-benzoyl-D-galactose	0.13 ± 0.01	0.62 ± 0.01	1.02 ± 0.02[b]	0.18 ± 0.01[b]
			1.03 ± 0.02[c]	0.17 ± 0.01[c]
			1.01 ± 0.02[d]	0.19 ± 0.04[d]

[a] In moles. [b] Calculated for a 6-*O*-benzoyl-carbonyl-C^{14}-1,2,3,4-tetra-*O*-benzoyl-α-D-galactose prepared from 1,2:3,4-di-*O*-benzylidene-D-galactose. [c] Calculated for a 6-*O*-benzoyl-carbonyl-C^{14}-1,2,3,4-tetra-*O*-benzoyl-α-D-galactose prepared from D-galactose dibutyl dithioacetal (see ref. 15). [d] Calculated for a 6-*O*-benzoyl-1,2,3,4-tetra-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose prepared from 1,2:3,4-di-*O*-benzylidene-D-galactose.

TABLE II

LABELED BENZOYL GROUPS IN 1,1-BIS(BENZAMIDO)-1-DEOXY-D-GALACTITOL (II, D-*galacto*) OBTAINED BY AMMONOLYSIS OF LABELED 1,2,3,4,6-PENTA-*O*-BENZOYL-D-GALACTOSES

Carbon atoms with labeled benzoyloxy groups in 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose	Activity, c.p.m./mmole	Activity/benzoyl group, c.p.m./mmole	Activity of II isolated, c.p.m./mmole	Labeled benzoyl groups in II, moles/mole
C-3	8266 ± 80	8266 ± 80	5145 ± 47	0.62 ± 0.01
C-6[a]	8290 ± 89	8290 ± 89	1509 ± 16	0.18 ± 0.01
C-6[b]	8196 ± 75	8196 ± 75	1431 ± 16	0.17 ± 0.01
C-4, C-6	16476 ± 50	8238 ± 75	9912 ± 110	1.20 ± 0.02
C-1, C-2, C-3	24429 ± 230	8143 ± 76	6136 ± 64	0.75 ± 0.01
C-1, C-2, C-3, C-4	33190 ± 308	8297 ± 77	15018 ± 137	1.81 ± 0.04

[a] Prepared from 1,2:3,4-di-*O*-benzylidene-D-galactose. [b] Prepared from D-galactose dibutyl dithioacetal (see ref. 15).

sults from a series of competitive reactions whose detailed mechanism is not known. It is a multistep process, and, as has been discussed in a previous article, more than one pathway can be devised to rationalize their formation.

It is important to note that the ammonolysis of the cyclic acetylated or benzoylated *N*-acylpyranosylamines does not produce compounds of type I, and that they cannot be considered as intermediates in the formation of I.[6] The migration of the *O*-acyl groups to C-1 has to take place through acyclic intermediates, as will be discussed when considering the differences found in the migration of benzoyl groups, in the ammonolysis of the related derivatives of D-glucose and D-galactose. For the ammonolysis of 1,2,3,4,6-penta-*O*-benzoyl-D-glucose and 2,3,4,6-tetra-*O*-benzoyl-D-glucose, it has been possible to determine the apparent contribution of each *O*-benzoyl group to the formation of the *N*-benzoyl groups present in 1,1-bis(benzamido)-1-deoxy-D-glucitol (II, D-*gluco*) isolated.[7]

The method employed required the preparation of several 1,2,3,4,6-penta-*O*-benzoyl-D-glucoses containing, at different carbon atoms, *O*-benzoyl groups labeled with C^{14} in such a way that, from the determination of the activity of the 1,1-bis(benzamido)-1-deoxy-D-glucitol (II, D-*gluco*), the migration of the benzoyl group could be evaluated. The final figures obtained are given in Table I, and they provide an indication of the intramolecular migration of each individual benzoyl group from the benzoyloxy groups originally present at atoms C-2, C-3, C-4, and C-5 to atom C-1 of the hexose, where they appear as benzamido groups, attached to the corresponding alditol.

It can be seen that the largest contribution comes from the benzoyloxy groups at C-3 and C-4, whereas the benzoyloxy group at C-6 makes only a moderate one and that at C-2 the smallest of all. It was also shown that the benzoyl group at C-1 does not participate in this reaction. With labeled 2,3,4,6-tetra-*O*-benzoyl-D-glucoses, there was no appreciable change in the results. A small increase in the contribution from the benzoyloxy group at C-3 was compensated by a small decrease from that at C-6.

It was then considered of interest to investigate the variation that a change in the configuration of the hexose would introduce into the contribution of the individual benzoyloxy groups to the migration. D-Galactose was selected because it has only one stereochemical difference from D-glucose at C-4, and also because it was expected that all of the needed 1,2,3,4,6-penta-*O*-benzoyl-D-galactoses could be prepared without difficulty.

This proved to be the case, and five labeled 1,2,3,4,6-penta-*O*-benzoyl-D-α-galactoses were prepared (Table II) and ammonolyzed, giving, in turn, labeled 1,1-bis(benzamido)deoxy-D-galactitol (II, D-*galacto*).

Following the method described in our earlier paper[6] the apparent contribution to the migration of each benzoyl group in 1,2,3,4,6-penta-*O*-benzoyl-D-galactose was then calculated. The figures obtained are included in Table I.

Discussion

The most interesting variation found in the contribution of the benzoyloxy groups to the formation of the 1,1-bis(benzamido)-1-deoxy-D-hexitol (II), in changing from D-glucose to D-galactose derivatives, is increased contribution of the benzoyloxy group at C-4; this

(6) A. Cerezo and S. Delpy, private communication. If the acyl group in an *N*-acylglycosylamine is mesyl or tosyl, which strongly attract electrons, then C-1 increases its positive charge, and ammonolysis of their acetylated derivatives can produce, in certain cases, bis(acylamido) compounds of type I. B. Helferich and A. Mitrowsky, *Ber.*, **85**, 1 (1952); B. Helferich, K. H. Schmidt, and D. Nachtheim, *Ann.*, **605**, 182 (1957).

(7) E. G. Gros, M. A. Ondetti, J. O. Sproviero, V. Deulofeu, and J. O. Deferrari, *J. Org. Chem.*, **27**, 924 (1962).

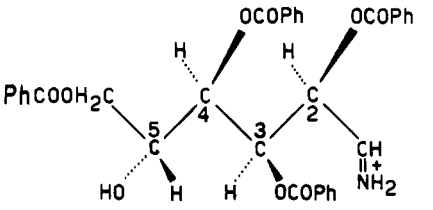
changed from a contribution of 0.82 mole/mole in the case of 1,2,3,4,6-penta-*O*-benzoyl-D-glucose, to 1.02 moles/mole for 1,2,3,4,6-penta-*O*-benzoyl-D-galactose, at the expense of the migration from the benzoyloxy groups at C-3 and C-6, which decreased their contribution.

The contribution of 1 mole/mole from the benzoyloxy group at C-4 means that this group is present in all of the molecules of the hypothetical acyclic derivative of D-galactose (IV, see also ref. 10), within which the migration of the benzoyl groups takes place. Otherwise it could never reach the level of 1 mole/mole.

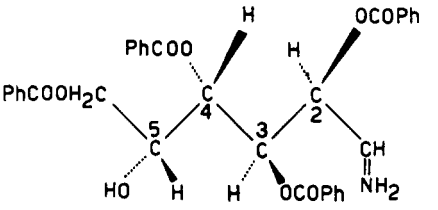
The benzoyl group at C-4 must also be present in almost all of the molecules of the similar intermediate III produced from 1,2,3,4,6-penta-*O*-benzoyl-D-glucose, because, whereas ammonolysis of the last compound gives a 21% yield of 1,1-bis(benzamido)-1-deoxy-D-glucitol (II, D-*gluco*), it could only be detected in traces (by paper chromatography) when 1,2,3,6-tetra-*O*-benzoyl-D-galactose, lacking the *O*-benzoyl group at C-4, was ammonolyzed.[6]

It is evident that the different extent of migration of the benzoyl group at C-4, when the ammonolysis of penta-*O*-benzoyl-D-glucose and penta-*O*-benzoyl-D-galactose is compared, is not due to large differences in benzoyloxy content at C-4 of the acyclic intermediates III and IV, but to the existence of more favorable conditions for that reaction to take place in the acyclic derivative of D-galactose IV. These conditions determine that in compound IV the intramolecular migration C-4 → C-1 is much faster than all other competitive reactions, such as the ammonolysis of the benzoyloxy group, with production of benzamide, or the methanolysis, with formation of methyl benzoate. For the derivative of D-glucose III almost 0.18 mole/mole of the benzoyl at C-4 participates in other reactions and not in the migration.

To explain some reactions of acyclic aldoses or aldose derivatives, such as the oxidation of certain hexitols[8] and a group of reactions involving C-1 in D-glucose,[9] a zig-zag conformation, where all the carbon atoms are in the same plane, has been postulated for those compounds. If we accept as a working hypothesis that one of the intermediates in the ammonolysis reaction is an acyclic derivative resulting from the condensation of 2,3,4,6-tetra-*O*-benzoyl-D-glucose and of 2,3,4,6-tetra-*O*-benzoyl-D-galactose with ammonia, the zig-zag conformation of the intermediate will be III for the first compound and IV for the second.[10] Neither conformation is the one with the smallest energy, and it seems reasonable to admit that in solution, as was previously pointed out,[6] other conformations can preponderate. Those conformations will result from the series of individual conformations of lowest energy adopted by



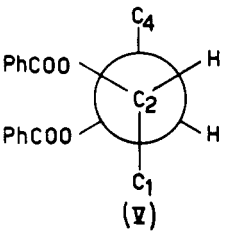
(III)



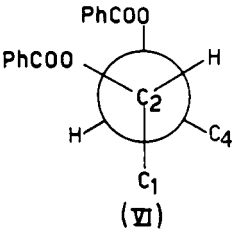
(IV)

each pair of successive carbon atoms that form the hexose.

If we consider that an important factor in determining the conformation between two successive carbon atoms in the molecule is the size of the substituents on the atoms involved and if we neglect ether interactions, the most stable conformation between C-2 and C-3 will *not* be V, which is present in the zig-zag conformations III and IV, but that in which all the bulky substituents are further separated in space. Conformation VI, in which all the carbon atoms of the hexose are not in the same plane, will be more stable.

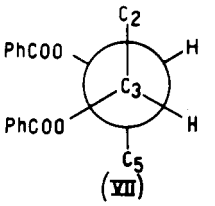


(V)

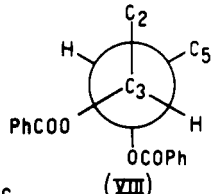


(VI)

By the same argument, the most stable conformation between C-3 and C-4, in the case of the acyclic D-glucose derivative will *not* be VII, which results from the coplanarity in III of C-3–C-5, but VIII, which is obtained by rotation around the axis C-3 to C-4. For the D-galactose derivative IV, the most stable conformation of C-3 to C-4 will be IX, which, in this particular case happens to be present in the zig-zag carbon chain of structure IV.



(VII)



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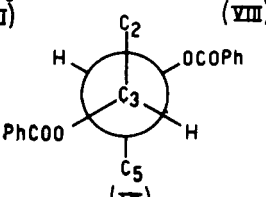


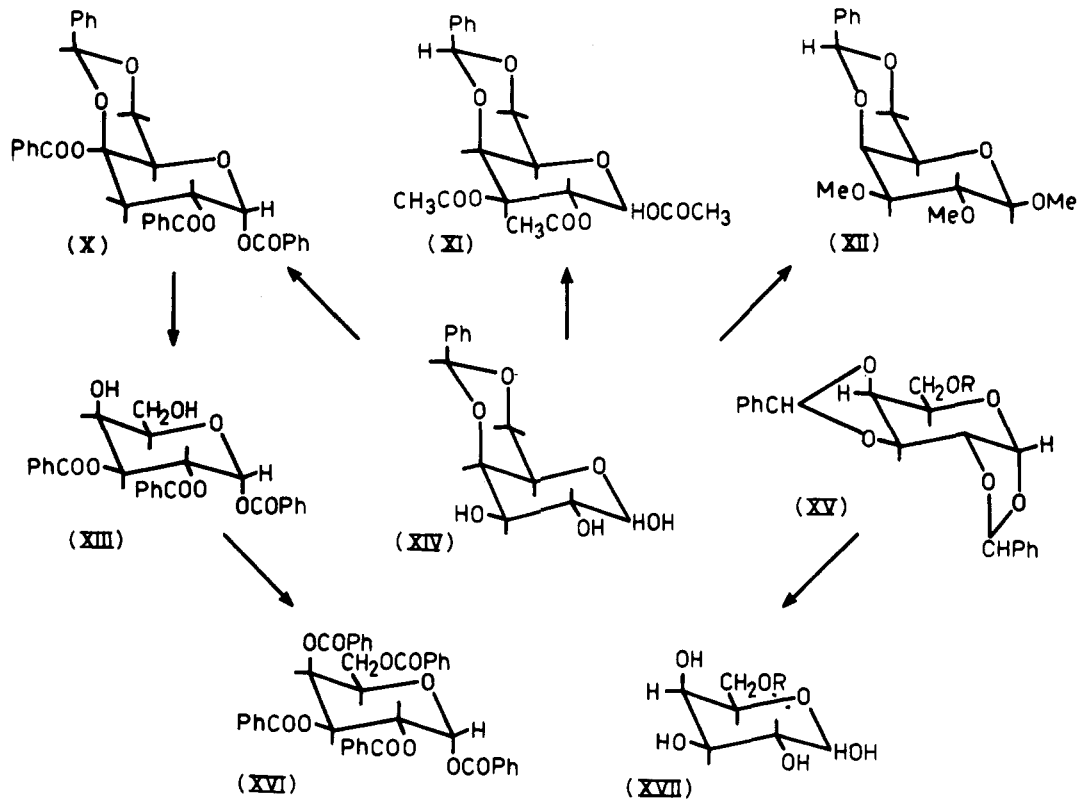
(IX)

(8) J. P. Schwartz, *J. Chem. Soc.*, 4276 (1947).

(9) P. D. Bragg and L. Hough, *ibid.*, 4347 (1957).

(10) The hypothetical fully acetylated derivatives III and IV are not necessarily the only ones within which the intramolecular migration of the benzoyl groups takes place. It is plausible to suppose that less fully benzoylated compounds also contribute to the reaction, and the mole migration found for each individual benzoyl group is the statistical average from all of the molecules participating, which are not all of them identical in number and in location of the benzoyl groups. For the ammonolysis of 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose, the migration of practically 1 mole of the benzoyl group at C-4 makes it necessary to accept that all the molecules of the acyclic derivatives which produce 1,1-bis(benzamido)-1-deoxy-D-galactitol must contain a benzoyloxy group at that carbon atom.

CHART I



If a model is built of the acyclic derivative of D-glucose III with conformation VI between C-2 and C-3 and VIII between C-3 and C-4, and if it is compared with a similar model for the D-galactose derivative IV with conformation VI between atoms C-2 and C-3 and IX between atoms C-3 and C-4, it can be seen that, for D-galactose, the benzoyloxy group at C-4 is nearer to C-1 than in the compound derived from D-glucose.

It happens that the most stable conformation for the acyclic D-galactose derivative is also the most favorable for direct migration from C-4 to C-1. In the similar benzoyl-D-glucose derivative, with the most stable partial conformations VI and VIII, migration is hindered, because the distances between C-1 and C-4 are larger. Direct migration of the benzoyl group from C-4 to C-1 is also possible in this case, provided that other conformations are adopted by this part of the molecule. They will have a higher energy content that the one which, in our hypothesis, is considered to be the most stable.

Although the differences in energy will obviously be small, this should in our opinion be one of the factors that determine, for D-galactose, that the entire benzoyl group at C-4 migrates to C-1, with formation of 1,1-bis(benzamido)-1-deoxy-D-galactitol (II, D-*galacto*), whereas for the similar 1,2,3,4,6-penta-*O*-benzoyl-D-glucose, only 0.82 mole (per mole) of the identically located benzoyl group is found in compound II (D-*gluco*).

Preparation of Labeled 1,2,3,4,6-Penta-*O*-benzoyl-D-galactoses.—The 1,2,3,4,6-penta-*O*-benzoyl-D-galactoses with labeled benzoyl groups at different carbon atoms were prepared, by alternative benzoylation, with normal and labeled benzoyl chloride, of partially benzoylated D-galactoses, as described below.

D-Galactose was condensed with benzaldehyde under the action of zinc chloride, giving 4,6-*O*-benzylidene-D-galactose (XIV) in rather good yield,[11] together with a small proportion of 1,2:3,4-di-*O*-benzylidene-D-galactose (XV, R = H), already described by Paćak and Černý.[12] The better yield of the monobenzylidene derivative is the result of the favorable position of the hydroxyl groups at C-4 and C-6 for such condensation. The new dioxane ring formed is condensed *cis* to the pyranose ring, and the 4,6-*O*-benzylidene-D-galactose presumably has a double ring, *O* inside, conformation, the phenyl group being in equatorial position. The structure of the 4,6-*O*-benzylidene-D-galactose was determined by methylation; the known methyl 4,6-*O*-benzylidene-2,3-di-*O*-methyl-β-D-galactoside (XII) was produced; confirmation was found in its periodate oxidation, when 2 moles of reagent was consumed per mole and no formaldehyde could be detected. On acetylation, 1,2,3-tri-*O*-acetyl-4,6-*O*-benzylidene-D-galactose (XI) was obtained. Benzoylation afforded the 1,2,3-tri-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactose (X), which, on acid hydrolysis, produced 1,2,3-tri-*O*-benzoyl-α-D-galactose (XIII). Benzoylation of the last compound yielded the known 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose (XVI).[4c,13] When benzoyl-carbonyl-C^{14} chloride was employed in the last benzoylation, the needed 1,2,3-tri-*O*-benzoyl-4,6-di-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose was obtained and, if the process were repeated, employing the labeled benzoyl chloride first, the 1,2,3-tri-*O*-benzoyl-carbonyl-C^{14}-4,6-

(11) E. G. Gros and V. Deulofeu, *Chem. Ind.* (London), 1502 (1962); J. Paćak and M. Černý, *Collection Czech. Chem. Commun.*, **28**, 541 (1963).

(12) J. Paćak and M. Černý, *ibid.*, **26**, 2212 (1961).

(13) M. L. Wolfrom and C. C. Christman, *J. Am. Chem. Soc.*, **58**, 39 (1936).

di-*O*-benzoyl-α-D-galactose became available. (See Chart I.)

These compounds permitted the evaluation of the migration of the benzoyl groups from the benzoyloxy groups present at the two pairs of carbon atoms, C-2–C-3 and C-4–C-5.

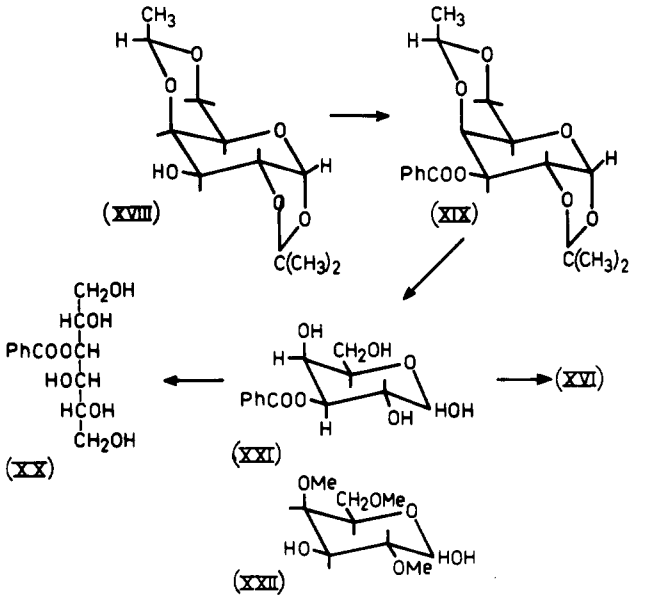
For the individual evaluation of the migration from C-4 and C-6 a 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose was prepared, starting from 1,2,3,4-di-*O*-benzylidene-D-galactose (XV, R = H). It was confirmed that this compound, already studied by Paćak and Černý, has a free hydroxyl group at C-6, because on methylation a mono-*O*-methyl derivative (XV, R = CH_3) was obtained which, on acid hydrolysis, produced the known 6-*O*-methyl-D-galactose (XVII, R = CH_3).[14] On benzoylation a 6-*O*-benzoyl-1,2:3,4-di-*O*-benzylidene-D-galactose (XV, R = COPh) was produced. By a similar hydrolysis the 6-*O*-benzoyl-D-galactose (XVII, R = COPh) of Zinner, *et al.*,[15] was obtained. When labeled benzoyl chloride was employed, 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose could be prepared, which on benzoylation gave 6-*O*-benzoyl-carbonyl-C^{14}-1,2,3,4-tetra-*O*-benzoyl-α-D-galactose. The same compound was prepared from a 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose obtained by way of D-galactose dibutyl dithioacetal.[15] By inversion of the order of the reagents, 6-*O*-benzoyl-1,2,3,4-tetra-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose was produced.

For the individual evaluation of the migration of the benzoyl group at C-2 and C-3 it was necessary to prepare a 1,2,3,4,6-penta-*O*-benzoyl-D-galactose with a labeled benzoyl group at C-2 or at C-3. The labeling at C-3 was considered to be easier than at C-2 and it was hoped that 4,6-*O*-benzylidene-D-galactose could be condensed with a second molecule of benzaldehyde or with another carbonyl compound to produce a substance having a free hydroxyl group at C-3, but the reaction failed, the original product being recovered.

This behavior can be explained by supposing that the 4,6-*O*-benzylidene-D-glucose, having two chair rings and having the phenyl group in an equatorial position, resists the deformations that must be introduced to allow the condensation of the hydroxyl groups at C-1 and C-2 with a carbonyl compound. Models show that the deformation has to take place, even in the case of the α-anomer, when the C-1 and C-2 hydroxyl groups are *cis*.

It was then decided to employ the 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (XVIII) of Ball and Jones,[16] the structure of which is well proved. Benzoylation of this compound yielded a crystalline monobenzoyl derivative XIX. After hydrolysis by acids, paper chromatography revealed the production of a small proportion of D-galactose and of another compound which was the main product of the reaction. The latter was separated by column chromatography and obtained pure as a reducing sirup which gave a crystalline 1-(2-methyl-2-phenylhydrazone) which from analysis contained one benzoyl group. Benzoylation of the sirup gave penta-*O*-benzoyl-α-D-galactose (XVI). When the sirup was reduced with potassium borohydride, a new crystalline compound, $C_{13}H_{18}O_7$, was obtained, which was a mono-*O*-benzoylgalactitol (XX). By its ammonolysis pure galactitol was obtained. The reducing sirup must then be a mono-*O*-benzoyl-D-galactose. (See Chart II.)

CHART II



That the benzoyl group in this mono-*O*-benzoyl-D-galactose (XIX) is at C-3 and has not migrated during the acid hydrolysis of 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (XVIII) was shown by transforming it first into a methyl mono-*O*-benzoyl-D-galactoside and further *O*-methylation of the glycoside. Elimination of the benzoyl group by ammonolysis, from the fully methylated product, and hydrolysis of the remaining D-galactoside gave a mixture which on paper chromatography revealed the presence of (a) 2,3,4,6-tetra-*O*-methyl-D-galactose, obviously resulting from the removal of the 3-*O*-benzoyl group during glycosidation, and (b) as a major compound, 2,4,6-tri-*O*-methyl-D-galactose (XXII), which was identified by crystallization and also by the transformation into the crystalline 2,4,6-tri-*O*-methyl-*N*-phenyl-D-galactosylamine.

That the benzoyl group in the mono-*O*-benzoyl-D-galactose can only be located at C-3 or C-4 resulted from sodium periodate oxidation of the crystalline mono-*O*-benzoyl-D-galactitol (XX) derived from it by reduction. In 1 hr. 3.06 moles/mole of the reagent was consumed and 2 moles of formaldehyde was produced.

The benzoyl group in 3-mono-*O*-benzoyl-D-galactose (XXI) seems also to be stable to mild alkaline conditions, like those used during methylation, because when the chromatographically pure compound was submitted to the pyridine stability test, as previously described,[6] it was recovered unchanged.

When, by these reactions, 3-*O*-benzoyl-carbonyl-C^{14}-4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose was prepared and the 3-*O*-benzoyl-carbonyl-C^{14}-D-galactose (XX) obtained was benzoylated with normal benzoyl chloride, the needed 3-*O*-benzoyl-carbonyl-C^{14}-1,2,4,6-tetra-*O*-benzoyl-α-D-galactose (XVI) was produced. It had a molar activity in agreement with the presence of only one labeled benzoyl group; this is im-

(14) K. Freudenberg and K. Smeykal, *Ber.*, **59**, 100 (1926); J. Munro and E. G. V. Percival, *J. Chem. Soc.*, 640 (1936); E. Pacsu and S. M. Trister, *J. Am. Chem. Soc.*, **62**, 2301 (1940); S. Peat, J. R. Turvey, and D. A. Rees, *J. Chem. Soc.*, 1590 (1961).

(15) H. Zinner, K. Wessely, W. Bock, K. Rieckhoff, F. Strandt, and W. Nimmich, *Chem. Ber.*, **90**, 500 (1957).

(16) D. H. Ball, and J. K. N. Jones, *J. Chem. Soc.*, 905 (1958).

portant because it shows that four normal benzoyl groups were introduced in the final benzoylation.

Experimental

All melting points are uncorrected. When not specified, optical rotations were determined in chloroform. Radioactive compounds were recrystallized to constant activity, which was determined by the method previously described.[6] All partially benzoylated D-galactoses were found stable when submitted to the stability test in pyridine.[6] When the hemiacetal group was hydroxyl free, the compound was fully benzoylated, without difficulty, by addition to a mixture of pyridine and benzoyl chloride diluted with chloroform.[4c] The α-anomer was always obtained.

Ammonolysis of the labeled 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactoses was done by suspending them, in the proportion of 1 g. to 35 ml., in methanolic ammonia (16% by volume) and shaking to dissolution. After standing for 18 hr. at room temperature, the solution was evaporated to dryness *in vacuo* and the residue crystallized from ethanol, when the labeled 1,1-bis(benzamido)-1-deoxy-D-galactitols were isolated. They were recrystallized with the results indicated in Table II. The yields obtained were 32–34% and their constants were in agreement with m.p. 207° and $[\alpha]^{25}D$ −6.2° given by Deferrari and Deulofeu for the original compound.[4c]

Two chromatographic descending systems were employed, using Whatman No. 1 paper: system 1, 1-butanol saturated with water; and system 2, 1-butanol–ethanol–water (3:1:1). As spot reagent, a mixture of 5% silver nitrate, 25% ammonia, and 2 *N* sodium hydroxide (1:1:2 by volume) was employed for the D-galactitols and nonreducing derivatives, and anisidine hydrochloride or aniline phthalate for the reducing substances.

4-6-*O*-Benzylidene-D-galactose (XIV).—To a mixture of 30 ml. of benzaldehyde and 13 g. of D-galactose was added 10 g. of fused zinc chloride, and the suspension was well shaken; in about 3 hr. it took on a solid consistency. More of benzaldehyde (30 ml.) was then added and shaking was resumed for 21 hr. when the mixture became a sirup, containing a small amount of undissolved zinc chloride. Water (30 ml.) was added and, on standing at 5°, the two phases slowly separated. The lower aqueous phase was collected and the upper phase was washed twice with 30 ml. of water and reserved for the preparation of 1,2:3,4-di-*O*-benzylidene-D-galactose. The united aqueous solutions were made alkaline with 10% sodium carbonate solution, giving a voluminous precipitate of zinc carbonate, which was removed by filtration, and the filtrate was extracted with petroleum ether (b.p. 40–60°) and evaporated to dryness *in vacuo*.

The solid residue was extracted three times with 250 ml. of boiling ethyl acetate; the extracts were united, concentrated to about 200 ml., and kept at 5°, giving needles, 8.3 g., m.p. 186–189°. On further concentration, a second crop (1.5 g.), m.p. 186–188°, was collected. Recrystallization several times from ethanol yielded 5.2 g. of the pure product: m.p. 190–191°, $[\alpha]^{18}D$ +118.5° (*c* 1.0, methanol).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.20; H, 6.01. Found: C, 58.42; H, 5.98.

4,6-*O*-Benzylidene-D-galactose is very soluble in water, much less soluble in cold ethanol, and has a low solubility in chloroform or acetone. On oxidation with periodic acid in water,[17] 2.0 moles of the reagent were consumed per mole in 4 hr., 1.81 moles of formic acid were titrated, and formaldehyde was not detected.

1,2:3,4-Di-*O*-benzylidene-D-galactose (XV, R = H).—The petroleum ether extract and the upper phase from the former preparation were combined and were evaporated *in vacuo*. The gummy residue was dried and dissolved in absolute warm ethanol, whereupon it crystallized on cooling. On filtration, 2 g. of a product, m.p. 160–165°, was collected which, after several recrystallizations from ethanol, gave needles (1.4 g.), m.p. 173–174°, $[\alpha]^{18}D$ −64.8° (*c* 1.2, Cl_3CH), $[\alpha]^{20}D$ −50.4° (methanol). Paćak and Černý[11] gave m.p. 179–180°, $[\alpha]^{18}D$ −49.2 (methanol).

Methyl 4,6-*O*-Benzylidene-2,3-di-O-methyl-β-D-galactoside (XII).—The 4,6-*O*-benzylidene-D-galactose (1.35 g.) was methylated by dissolving it in 10 ml. of water at 56–60° and treating with methyl sulfate and 40% sodium hydroxide. The mixture was then heated to 90–91° for 1 hr., water was added to dissolve the sodium sulfate, and the solution was neutralized with 6 *N* sulfuric acid and extracted with chloroform. The chloroformic extracts were dried and on evaporation left a gummy residue. It was dissolved in a small amount of benzene and chromatographed through a column of alumina, with benzene elution. The sirupy residue from the first fractions crystallized on treatment with ether. The crystalline fractions (65 mg.) were recrystallized from ether, when needles, m.p. 142–143°, $[\alpha]^{18}D$ +17.3° ($CHCl_3$), were obtained. Oldham and Bell[18] gave m.p. 148°, $[\alpha]D$ +18.0°.

1,2,3-Tri-*O*-acetyl-4,6-*O*-benzylidene-D-galactose (XI).—To a mixture of 8 ml. of pyridine and 4 ml. of acetic anhydride cooled to 0°, was added 1 g. of 4,6-*O*-benzylidene-D-galactose. The resulting suspension was kept at 5° for 24 hr. with occasional shaking, the sugar dissolving after 15 hr. The solution was then poured into ice–water, giving a sirup which crystallized readily on standing. After filtering, 1.17 g. of a product, m.p. 185–189°, was obtained; this was recrystallized several times from methanol and gave needles (1 g.), m.p. 192–193°, $[\alpha]^{21}D$ +176.8° (*c* 0.8).

Anal. Calcd. for $C_{19}H_{22}O_9$: C, 57.86; H, 5.62. Found: C, 57.95; H, 5.51.

This seems to be a different compound from the 1,2,3-tri-*O*-acetyl-4,6-*O*-benzylidene-D-galactose prepared by Paćak and Černý,[11] who gave m.p. 147–160°, $[\alpha]^{18}D$ +62°.

1,2,3-Tri-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactose (X).—To a mixture of 60 ml. of pyridine and 20 ml. of benzoyl chloride, cooled to 0°, was slowly added 6 g. of 4,6-*O*-benzylidene-D-galactose with constant agitation. The mixture was then kept for 1 hr. at 0° and for 24 hr. at room temperature, water (4 ml.) was then added, and the viscous mass was poured into 2 l. of ice–water, giving an insoluble sirup that solidified on stirring. It was filtered off, dried, and recrystallized several times from ethanol, yielding 9 g. of needles, m.p. 171–172°, $[\alpha]^{20}D$ +266.2° (*c* 0.95).

Anal. Calcd. for $C_{34}H_{28}O_9$: C, 70.34; H, 4.86. Found: C, 70.37; H, 4.97.

1,2,3-Tri-*O*-benzoyl-α-D-galactose (XIII).—To a solution of 2 g. of 1,2,3-tri-*O*-benzoyl-4,6-*O*-benzylidene-α-D-galactose in 15 ml. of acetone was added 2 ml. of 2 *N* hydrochloric acid. The solution was heated at 55–60° for 4 hr., with intermittent agitation. After cooling, barium carbonate was added in small excess and the suspension was evaporated *in vacuo* to an oily residue. Water was added (50 ml.) and the suspension was extracted with chloroform. On evaporation, the chloroform extracts gave a sirup which was dried and crystallized by dissolving in absolute ether and adding petroleum ether (b.p. 60–70°) to turbidity. After standing overnight at 5°, it was filtered, and 750 mg. of crystals, m.p. 72–78°, were obtained. Recrystallization from 70% ethanol gave needles, m.p. 75–78°, $[\alpha]^{25}D$ +237.1° (*c* 1.4, $CHCl_3$).

Anal. Calcd. for $C_{27}H_{24}O_9$: C, 65.85; H, 4.91. Found: C, 65.64; H, 4.93.

Benzoylation of the 1,2,3-tri-*O*-benzoyl-α-D-galactopyranose, dissolved in pyridine, with benzoyl chloride at 0° gave 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose (XVI), m.p. 158–159°, $[\alpha]^{20}D$ +186.6°.

1,2,3-Tri-*O*-benzoyl-4,6-di-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose.—Benzoylation of 1,2,3-tri-*O*-benzoyl-α-D-galactose, with benzoyl-carbonyl-C^{14} chloride of activity 8.190 ± 76 c.p.m., afforded the labeled penta-*O*-benzoyl-α-D-galactose, m.p. 158–159°, $[\alpha]^{25}D$ +185.5°, activity 16.076 ± 140 c.p.m.

1,2,3-Tri-*O*-benzoyl-carbonyl-C^{14}-4,6-di-*O*-benzoyl-α-D-galactose.—4,6-*O*-Benzylidene-D-galactose, on benzoylation with benzoyl-carbonyl-C^{14} chloride of 8.190 ± 76 c.p.m. activity, gave 1,2,3-tri-*O*-benzoyl-carbonyl-C^{14}-4,6-benzylidene-α-D-galactose, m.p. 170–171°, $[\alpha]^{25}D$ +265.3°, of 24.226 ± 235 c.p.m. activity. Elimination of the benzylidene group gave 1,2,3-tri-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose, m.p. 78–80°, $[\alpha]^{25}D$ +236.0°, 24.776 ± 238 c.p.m. activity. On benzoylation, 1,2,3-tri-*O*-benzoyl-carbonyl-C^{14}-4,6-di-*O*-benzoyl-α-D-galactose was obtained: m.p. 159–160°, $[\alpha]^{25}D$ +188.5°, 24.429 ± 230 c.p.m. activity.

1,2:3,4-Di-*O*-benzylidene-6-*O*-methyl-D-galactose (XV, R = CH_3).—To a solution of 160 mg. of 1,2:3,4-di-*O*-benzylidene-D-galactose, in 6 ml. of *N*,*N*-dimethylformamide and 2 ml. of methyl iodide was added 1.6 g. of freshly prepared silver oxide with constant shaking during 12 hr. The suspension was then filtered,

(17) L. Hough, T. J. Taylor, G. H. S. Thomas, and B. M. Woods, *J. Chem. Soc.*, 1212 (1958).

(18) J. W. H. Oldham and D. J. Bell, *J. Am. Chem. Soc.*, **60**, 323 (1938).

and the solid was washed with *N*,*N*-dimethylformamide and with 12 ml. of chloroform. The filtrate was treated with 10 ml. of a 10% solution of sodium cyanide, giving two phases. The lower phase was decanted, and the upper aqueous phase was extracted with chloroform. The collected chloroform extracts were united with the lower phase, washed with water, and evaporated *in vacuo*. The oily residue crystallized on standing in a desiccator, and was recrystallized from ethanol, giving 110 mg. of white needles, m.p. 130–131°, $[\alpha]^{20}D$ −81.4° (*c* 1.1).

6-*O*-Methyl-D-galactose (XVII, R = CH_3).—The 1,2:3,4-di-*O*-benzylidene-6-*O*-methyl-D-galactose (1.24 g.) was dissolved in 50 ml. of acetone, 10 ml. of 1 *N* hydrochloric acid was added, and the solution was refluxed for 9 hr. The acetone was removed by distillation *in vacuo;* this was continued (maintaining a constant volume by adding water) until all the benzaldehyde had distilled. The solution was then neutralized by passing it through a column of Amberlite IRA-400 bicarbonate and was evaporated *in vacuo*. The gummy residue was dissolved in methanol, an insoluble fraction was filtered off, and the clear methanolic solution was seeded with 6-*O*-methyl-D-galactose, whereupon needles appeared: after recrystallization from methanol, m.p. 128–130°, $[\alpha]^{18}D$ +127.5° (water, 10 min.) → +74.3° (6 hr.). The osazone had m.p. 197–198°, $[\alpha]^{20}D$ +134.1° → +98.0° (24 hr.) in pyridine, in agreement with the literature.[14]

6-*O*-Benzoyl-1,2:3,4-di-*O*-benzylidene-D-galactose (XV, R = COPh).—To a solution of 3 g. of 1,2:3,4-di-*O*-benzylidene-D-galactose in 45 ml. of pyridine, cooled to 5°, was slowly added 3 ml. of benzoyl chloride, any increase in temperature being avoided. The mixture was kept for 20 hr. at room temperature and then poured into a large volume of ice–water, giving an oil, which crystallized. It was filtered off, dried, and recrystallized from ethanol, yielding 3.17 g. of needles, m.p. 144–145°, $[\alpha]^{19}D$ −114.6° (*c* 1.0).

Anal. Calcd. for $C_{27}H_{24}O_7$: C, 70.58; H, 5.43. Found: C, 70.42; H, 5.25.

6-*O*-Benzoyl-D-galactose Monohydrate (XVII, R = COPh).—A solution of 3.2 g. of 6-*O*-benzoyl-1,2:3,4-di-*O*-benzylidene-D-galactose in 55 ml. of acetone and 15 ml. of 1 *N* hydrochloric acid was refluxed for 10 hr. The solution was then distilled *in vacuo*, with addition of water to keep a final volume of 15 ml., until the benzaldehyde had been eliminated. It was then neutralized by passage through a column of Amberlite IRA-400 bicarbonate and evaporated to dryness *in vacuo*.

The solid residue was dissolved in boiling ethyl acetate, a small insoluble fraction was filtered off, and the filtrate, on cooling, yielded 550 mg. of needles: m.p. 134–137°; after recrystallization from the same solvent, m.p. 136–138°, $[\alpha]^{21}D$ +100.1° (10 min.) → +79.8° (24 hr.) in pyridine, $[\alpha]^{28}D$ +59.3° (20 min.) → 48.2° (24 hr.) in methanol (*c* 0.78). It was the hydrate of 6-*O*-benzoyl-D-galactose and did not depress the melting point of an authentic sample prepared according to Zinner, *et al.*[15] For analysis, it was dried *in vacuo* until it became amorphous.

Anal. Calcd. for $C_{13}H_{16}O_7$: C, 54.92; H, 5.63. Found: C, 54.77; H, 5.84.

The *p*-nitrophenylhydrazone[15] had m.p. 203°, $[\alpha]^{19}D$ +47.4°. Condensation with benzaldehyde, using zinc chloride as catalyst, gave the original 6-*O*-benzoyl-1,2:3,4-di-*O*-benzylidene-D-galactose. On benzoylation 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose was produced.

When the 6-*O*-benzoyl-D-galactose was benzoylated with benzoyl-carbonyl-C^{14} chloride of 8.338 ± 78 c.p.m. activity, **1,2,-3,4-tetra-*O*-benzoyl-carbonyl-C^{14}-6-*O*-benzoyl-α-D-galactose**, m.p. 157–158°, $[\alpha]^{20}D$ +186.4°, 33.190 ± 308 c.p.m. activity, was obtained.

6-*O*-Benzoyl-carbonyl-C^{14}-α-D-galactose.—When the 1,2:3,4-di-*O*-benzylidene-D-galactose was treated with benzoyl-carbonyl-C^{14}-chloride of 8.338 ± 78 c.p.m. activity, it gave a 6-*O*-benzoyl-1,2:3,4-di-*O*-benzylidene-carbonyl-C^{14}-D-galactose, m.p. 144–146°, $[\alpha]^{20}D$ −115.1°, 8.405 ± 75 c.p.m. activity. By acid hydrolysis, 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose, m.p. 138–140°, $[\alpha]^{17}D$ +83.8° (pyridine, 24 hr.), was obtained with 8.368 ± 74 c.p.m. activity.

1,2,3,4-Tetra-*O*-benzoyl-6-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose was prepared by benzoylation of the above compound: m. p. 156–157°, $[\alpha]^{19}D$ +187.7°, 8.200 ± 89 c.p.m. activity.

6-*O*-Benzoyl-carbonyl-C^{14}-galactose Dibutyl Dithioacetal.—The following method, derived from the general one described by Zinner, *et al.*,[15] was employed. To a solution of 13.7 g. of D-galactose dibutyl dithioacetal in 100 ml. of pyridine, kept at −15°, a mixture of 4.6 ml. of benzoyl-carbonyl-C^{14} chloride, with activity of 8.190 ± 76 c.p.m., and 20 ml. of pyridine was very slowly added with good stirring. After addition, agitation was continued for 8 hr. at the same temperature, and the mixture was then kept for 18 hr. at 5° and 4 hr. at 25°. It was filtered, dried, dissolved in 250 ml. of cold acetone, filtered from a small insoluble residue, and diluted with water, when fine needles were precipitated. These were recrystallized from acetone–water, giving 13.5 g. of a product, m.p. 109–111°, $[\alpha]^{26}D$ +5.9°, in agreement with the constants given by Zinner,[15] with 8.120 ± 75 c.p.m. activity.

6-*O*-Benzoyl-carbonyl-C^{14}-D-galactose from 6-*O*-Benzoyl-carbonyl-C^{14}-D-galactose Dibutyl Dithioacetal.—The following adaptation of the method of Zinner, *et al.*,[15] was used. Nine grams of the 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose dibutyl dithioacetal, dissolved in 80 ml. of acetone and 12 ml. of water, was treated with 12 g. of yellow mercuric oxide. Mercuric dichloride (12 g.) in 40 ml. of acetone was added, and the suspension was shaken for 3 hr. at room temperature and for 2 hr. at 40°, and finally refluxed for 2 hr. The insoluble material was filtered off (Filter Aid); to the filtrate 1 g. of mercuric oxide was added and the mixture was evaporated to dryness *in vacuo*. The residue was extracted with two 200-ml. portions of boiling ethyl acetate; on cooling, the extract yielded 3.2 g. of needles, m.p. 140–142°. Recrystallized, they had m.p. 140–142°, $[\alpha]^{25}D$ +62.1° (24 hr.), 8.225 ± 75 c.p.m. activity. Zinner gave m.p. 140–141°, $[\alpha]^{25}D$ +62.5°; *p*-nitrophenylhydrazone, m.p. 204–205°, $[\alpha]^{25}D$ +47.3°.

On benzoylation this 6-*O*-benzoyl-carbonyl-C^{14}-D-galactose gave 1,2,3,4-tetra-*O*-benzoyl-6-*O*-benzoyl-carbonyl-C^{14}-α-D-galactose, m.p. 157–159°, $[\alpha]^{25}D$ +186.5°, 8.196 ± 75 c.p.m activity.

3-*O*-Benzoyl-4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (XIX).—To a solution of 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (XVIII)[16] (10.6 g.) in 35 ml. of pyridine, 5.3 ml. of benzoyl chloride was slowly added, keeping the mixture at room temperature. After standing for 24 hr., it was poured into ice–water, when the precipitate formed solidified easily. After several recrystallizations from ethanol, 5.7 g. were obtained of a product, m.p. 173–174°, $[\alpha]^{20}D$ +120.0° (*c* 1.0).

Anal. Calcd. for $C_{18}H_{22}O_7$: C, 61.70; H, 6.33. Found: C, 62.24; H, 6.29.

3-*O*-Benzoyl-D-galactose-1-(2-methyl-2-phenylhydrazone).—To a solution of 2.6 g. of the 3-*O*-benzoyl-4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose dissolved in 13 ml. of ethanol, 15 ml. of 1.2% hydrochloric acid was added, and the mixture was boiled for 2 hr. The ethanol was evaporated *in vacuo* and the acid was removed from the remaining aqueous solution by shaking with Amberlite IR-400 bicarbonate. Paper chromatography on Whatman No. 1 paper, using 1-butanol–ethanol–water (3:1:1) as the mobile phase, gave two spots, one with R_{TG} 0.14 corresponding to D-galactose and other with R_{TG} 0.79 (TG = 2,3,4,6-tetra-*O*-methyl-D-glucose).

Separation of the substance having R_{TG} 0.79 was performed with a column of cellulose powder (Whatman standard grade), the elution being done with 1-butanol saturated with water. All fractions giving the spot of R_{TG} 0.79 were collected and re-evaporated. A sirup (1.47 g.) was obtained. It was very soluble in water, the lower alcohols, or acetone, almost insoluble in ether or chloroform. The sirup (300 mg.) was dissolved in 6 ml. of water and 0.5 ml. of ethanol; 1 ml. of 1-methyl-1-phenylhydrazine was added, and then a few drops of acetic acid until a clear solution was obtained; and the solution was heated in a boiling water bath for 5 min. Needles were obtained on cooling: 197 mg., m.p. 152°; on recrystallization from benzene, m.p. 152–153°, $[\alpha]^{32}D$ +35.6° (*c* 0.56, ethanol).

Anal. Calcd. for $C_{20}H_{24}N_2O_6$: C, 61.83; H, 6.23; N, 7.21. Found: C, 61.99; H, 6.07; N, 7.35.

Electrophoresis of the sirup on Whatman No. 1 paper, with borate buffer at pH 10 for 3 hr. with 600 v., gave only one spot (G = D-glucose) with M_G 0.79, whereas D-galactose had M_G 0.93, and 6-*O*-benzoyl-D-galactose had M_G 0.85, indicating the better complexing of the last compound when compared with the 3-*O*-benzoyl isomer. On benzoylation, 1,2,3,4,6-penta-*O*-benzoyl-α-D-galactose, m.p. 156–158°, $[\alpha]^{20}D$ +184.70, was obtained.

3-*O*-Benzoyl-D-galactitol (XX).—The chromatographically pure 3-*O*-benzoyl-D-galactose (XXI, 360 mg.) was dissolved in 11 ml. of methanol, 70 mg. of potassium borohydride was slowly added, and the mixture was kept for 10 hr. at room temperature. The pH was 9.0, and Amberlite IR 120 H^+ was added until a pH 6.6–7.0 was obtained. The solution was evaporated *in vacuo*, and the boric acid was removed by repeated evaporations

with methanol; crude crystals were obtained in the last evaporation, 320 mg., m.p. 155–161°. Recrystallized from water, the needles had m.p. 160–162°; $[\alpha]^{22}D$ +2.6° (*c* 0.9, methanol); soluble in methanol or ethanol, insoluble in ether, chloroform, or benzene; R_f 0.08 (system 1) and 0.17 (system 2).

Anal. Calcd. for $C_{13}H_{18}O_7$: C, 54.53; H, 6.33. Found: C, 54.32; H, 6.19.

When the 3-*O*-benzoyl-D-galactitol was ammonolyzed in the usual way, evaporation of the solution gave a crystalline product which after recrystallization from water had m.p. 187–189°, did not depress the melting point of pure galactitol, m.p. 188–190°, and gave the same R_f with both systems on paper chromatograms.

Periodate oxidation of 3-*O*-benzoyl-D-galactitol was done according to Hough, *et al.*[17] D-Mannitol was used as the standard. After 1 hr., 1 mole of D-mannitol had consumed 4.90 moles of periodate, and 1 mole of 3-*O*-benzoyl-D-galactitol, 3.06 moles of periodate; after 4 hr., the values were 4.90 and 3.37 moles. The expected values were 5.0 moles for D-mannitol and 3.0 moles for 3-*O*-benzoyl-D-galactitol.

Determination of formaldehyde by the method of Reeves[19] (precipitation with dimedone) gave 2.16 moles; by the colorimetric method of O'Dea and Gibbons,[20] 1.91 moles (calcd., 2.0 moles).

2,4,6-Tri-*O*-methyl-D-galactose (XXII) from 3-*O*-Benzoyl-D-galactose.—To a solution of 300 mg. of 3-*O*-benzoyl-D-galactose in 10 ml. of methanol, 300 mg. of Amberlite IR 120 H^+ was added, and the suspension refluxed for 24 hr. It was then filtered, and the filtrate was evaporated to dryness.

Paper chromatography (system 1) of the resulting sirup revealed the presence of D-galactose (R_f 0.07), methyl D-galactoside (R_f 0.18), and of a nonreducing compound with R_f 0.89. This compound was isolated by paper chromatography on Whatman 3 MM, and elution of the band containing it. Evaporation of the eluate gave 95 mg. of the sirupy residue, which was dissolved in a mixture of 5 ml. of *N*,*N*-dimethylformamide and 1 ml. of methyl iodide, and stirred at room temperature for 12 hr. while 1 g. of silver iodide was slowly added. The insoluble part was then separated, washed with *N*,*N*-dimethylformamide and chloroform, and the washings were added to the original solution. The mixture was shaken with 5 ml. of 20% potassium cyanide solution, and the organic phase was separated, dried, and evaporated. The residue was dissolved in 10 ml. of methanolic ammonia and kept at room temperature for 24 hr., the solution was re-evaporated, and the new residue was treated with 5 ml. of 1 *N* hydrochloric acid and heated at 100° for 4 hr.

The acid was then neutralized with Amberlite IR 400 bicarbonate, the suspension was filtered, and the filtrate was evaporated to dryness, giving 35 mg. of a sirup. On paper chromatograms (system 2) it gave two main spots having R_{TG} 0.79 and 0.92. The substances responsible for these spots were separated by paper chromatography, eluted from the paper, and identified as 2,4,6-tri-*O*-methyl-D-galactose and 2,3,4,6-tetra-*O*-methyl-D-galactose, by running them with authentic samples.

On seeding, the 2,4,6-tri-*O*-methyl-D-galactose (R_{TG} 0.79) crystallized from ether, giving prisms, m.p. 103–104°, that did not depress the melting point of an authentic preparation melting at 104–105°. For further identification, it was transformed into the 2,4,6-tri-*O*-methyl-*N*-phenyl-D-galactosylamine as needles, m.p. 174–175°, in agreement with the data in the literature.[21]

3-*O*-Benzoyl-carbonyl-C^{14}-4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose, m.p. 172–174°, $[\alpha]^{16}D$ +118.1°, 8.290 ± 78 c.p.m. activity, was obtained by the method described above, by benzoylation of the 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose with benzoyl-carbonyl-C^{14} chloride with 8.296 ± 80 c.p.m. activity. On hydrolysis of the protecting groups, a chromatographically pure sirup of **3-*O*-benzoyl-carbonyl-C^{14}-D-galactose** was prepared, which, on reduction, gave **3-*O*-benzoyl-C^{14}-D-galactitol**, m.p. 161–163°, with an activity of 8.250 ± 79 c.p.m., and which on benzoylation produced the needed **3-*O*-carbonyl-C^{14}-1,2,4,6-tetra-*O*-benzoyl-α-D-galactose**, m.p. 156–157°, $[\alpha]^{21}D$ +185.4°, 8.266 ± 80 c.p.m. activity.

Acknowledgment.—We thank Professor J. K. N. Jones (Kingston, Ontario) for kindly supplying several samples, and Dr. A. Mitta for his help in the preparation of labeled compounds.

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Two Related Syntheses of 2-Amino-2,6-dideoxy-D-galactose (D-Fucosamine)[1]

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Received June 24, 1964

Two syntheses of 2-amino-2,6-dideoxy-D-galactose (D-fucosamine), an amino sugar present in bacterial polysaccharides, from derivatives of 2-amino-2-deoxy-D-galactose are described. In both syntheses, the primary 6-hydroxy group of the *galacto* derivative was removed by conversion into the 6-O-*p*-tolylsulfonyloxy compound, replacement of the *p*-tolylsulfonyloxy group by iodide, and hydrogenolysis of the iodo compound.

In 1958, Crumpton and Davies[3] reported the isolation of the crystalline hydrochloride of a new amino sugar from a lipopolysaccharide of *Chromobacterium violaceum*. From elementary analysis, deamination, and periodate oxidation studies, and examination of its phenylosazone, they concluded that the sugar could be either 2-amino-2,6-dideoxy-D-galactose or 2-amino-2,6-dideoxy-D-talose. The infrared spectrum of the amino sugar resembled that of fucose and was different from that of its epimer, 6-deoxytalose, and its molecular rotation was also consistent with a D-*galacto* configuration. Accordingly, the structure assigned to the newly isolated compound was that of 2-amino-2,6-dideoxy-D-galactose (D-fucosamine).

Synthesis of the enantiomorphic sugar, L-fucosamine, subsequently carried out by Kuhn and his co-workers,[4] did not provide unambiguous evidence for the configuration at C-2 of the product; these investigators had used 5-deoxy-L-lyxose as starting material, and a new asymmetric center was formed. More recently, 2-amino-2,6-dideoxy-L-galactose (L-fucosamine) has been isolated from type V *Pneumococcus* capsular polysaccharide,[5] in which it occurs together with 2-amino-2,6-dideoxy-L-talose.[6] The assignment of the *talo* configuration to the latter sugar was also based mainly on rotation data,

(1) Preliminary communications have appeared: U. Zehavi and N. Sharon, Abstracts, 145th Meeting of the American Chemical Society, New York, N. Y., Sept. 1963, p. 18D; *Israel J. Chem.*, **1**, 210 (1963).

(2) Part of a thesis to be submitted by U. Zehavi to the Hebrew University, Jerusalem, in partial fulfillment of the requirements for the Ph.D. degree.

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