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AMMONOLYSIS OF PENTA-*O*-BENZOYL-α-D-GLUCOPYRANOSE IN AN APROTIC MEDIUM. CHARACTERIZATION OF THE PRODUCTS ISOLATED, AND CONFORMATIONAL ANALYSIS OF ELEVEN *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES

AMELIA E. SALINAS, JORGE F. SPROVIERO, AND VENANCIO DEULOFEU*

Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón II, Ciudad Universitaria, 1428 Buenos Aires (Argentina)

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ABSTRACT

The reaction of penta-*O*-benzoyl-α-D-glucopyranose with chloroform–1,4-dioxane–liquid ammonia gave 1,1-bis(benzamido)-6-*O*-benzoyl-1-deoxy-D-glucitol (29.0%), three partially benzoylated derivatives of *N*-benzoyl-α-D-glucofuranosylamine (23.6%), a small proportion of *N*-benzoyl-di-*O*-benzoyl-β-D-glucofuranosylamine (0.2%), and four partially benzoylated derivatives of α-D-glucopyranose (9.9%). The structures of the hitherto-unknown products, and their anomeric configurations, were established by chemical and spectroscopic methods. The conformations in solution of both anomers of *N*-benzoyl-D-glucofuranosylamine, their partially benzoylated derivatives isolated from the ammonolysis reaction, and the per-*O*-acetyl derivatives of the various compounds were analyzed by ^{1}H-n.m.r. spectroscopy.

INTRODUCTION

The action of ammonia in protic solvents upon peracylated monosaccharides and disaccharides has been extensively studied. The reactions were conducted in aqueous or alcoholic ammonia solution. In most cases, 1,1-bis(acylamido)-1-deoxyalditols and *N*-acylglycosylamines were found to be formed simultaneously. The relative amounts of acyclic and cyclic nitrogenated products have been shown to depend on the substrate configuration, the acyl group, and the solvent. The subject has been reviewed[1].

The action of ammonia in aprotic media upon acylated sugars was earlier studied by Zechmeister and Tóth[2,3]. After heating a mixture of octa-*O*-acetylcellobiose and liquid ammonia in a sealed tube for 48 h at 55°, they could isolate an

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N-acetylcellobiosylamine (17%) and, by subsequent acetylation of the residue, the peracetate of 1,1-bis(acetamido)-1-deoxycellobiitol. For this compound, the authors proposed[3] alternative structures that were later[4] rejected. The *N*-acetylcellobiosylamine obtained was subsequently demonstrated to be the β anomer, as its peracetate was identical with the *N*-acetyl-hepta-*O*-acetyl-β-cellobiosylamine prepared by other workers[5]. The isolation of ammonium acetate from the reaction mixture was also reported[2,3].

The methanolic ammonolysis of penta-*O*-benzoyl-D-glucopyranose[6] afforded 1,1-bis(benzamido)-1-deoxy-D-glucitol. Application of chromatographic techniques[7] allowed the isolation of *N*-benzoyl-β-D-glucopyranosylamine as a minor product. On the other hand, when penta-*O*-benzoyl-D-glucopyranose was submitted to ammonolysis in 2-propanol or 2-butanol[8], 1,1-bis(benzamido)-6-*O*-benzoyl-1-deoxy-D-glucitol was produced.

The aim of the present work was to study the action of liquid ammonia upon the same compound. Aprotic conditions were chosen in order to avoid the competitive alcoholysis of benzoyloxy groups. The ammonolysis was conducted at $-60°$. Because the substrate is insoluble in liquid ammonia at this temperature, chloroform–1,4-dioxane was added to provide a homogeneous reaction medium. Under the conditions employed, a slow reaction took place. Nevertheless, these conditions proved to be advantageous because the lower rate of ammonolysis of benzoyloxy groups allowed the isolation of partially benzoylated cyclic and acyclic nitrogenated products. These compounds provided information as to which of the benzoyloxy groups of the substrate had been involved in the reaction. Moreover, the high yield of cyclic nitrogenated products obtained invalidated the earlier proposal[9] that the bulky benzoyloxy groups hinder the cyclization leading to *N*-benzoyl-D-glucofuranosylamines.

RESULTS AND DISCUSSION

The ammonolysis of penta-*O*-benzoyl-α-D-glucopyranose in 1:1:2 chloroform–1,4-dioxane–liquid amonia for 100 h at $-60°$ afforded a complex mixture of products, most of which were isolated by chromatographic techniques and characterized by chemical and spectroscopic procedures. The identified products and their respective yields are indicated in Table I.

From the reaction mixture, benzamide, ammonium benzoate, and benzoic acid were also isolated, in yields respectively corresponding to 1.047, 0.866, and 0.106 mol per mol of starting material. It was demonstrated that benzoic acid proceeded from the ammonium benzoate originally present in the reaction medium, so that the overall yield of the latter product should be considered to be 972 mmol per mol. The foregoing yields imply a substrate recovery of 62.7% and a benzoyl-group recovery of ~76% in the products isolated.

Compound **1**, the major product of the ammonolysis, was separated by spontaneous crystallization from the reaction mixture, after evaporation of ammonia. A

TABLE I

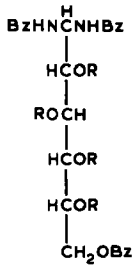
PRODUCTS FROM THE AMMONOLYSIS OF PENTA-*O*-BENZOYL-α-D-GLUCOPYRANOSE IN 1:1:2 CHLOROFORM–1,4-DIOXANE–LIQUID AMMONIA

Compound	*Yield (%)*
1,1-Bis(benzamido)-6-*O*-benzoyl-1-deoxy-D-glucitol (**1**)	29.0
N-Benzoyl-6-*O*-benzoyl-α-D-glucofuranosylamine (**3**)	11.9
N-Benzoyl-3,6-di-*O*-benzoyl-α-D-glucofuranosylamine (**4**)	9.6
N-Benzoyl-5,6-di-*O*-benzoyl-α-D-glucofuranosylamine (**5**)	2.1
N-Benzoyl-3,6-di-*O*-benzoyl-β-D-glucofuranosylamine (**6**)	0.2
2,6-Di-*O*-benzoyl-α-D-glucopyranose (**16**)	0.7
2,4,6-Tri-*O*-benzoyl-α-D-glucopyranose (**17**)	1.4
3,4,6-Tri-*O*-benzoyl-α-D-glucopyranose (**18**)	5.4
2,3,4,6-Tetra-*O*-benzoyl-α-D-glucopyranose (**19**)	2.4

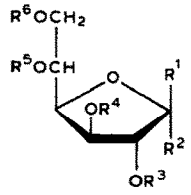
further amount of **1** was isolated by chromatography. This compound had already[8] been described, and was identified by comparison with an authentic sample. Its peracetate (**2**) was prepared.

When compounds **3**, **4**, and **5** were submitted to ammonolysis in methanol, *N*-benzoyl-α-D-glucofuranosylamine (**7**) was obtained. Under the same treatment, compound **6** afforded *N*-benzoyl-β-D-glucofuranosylamine (**8**).

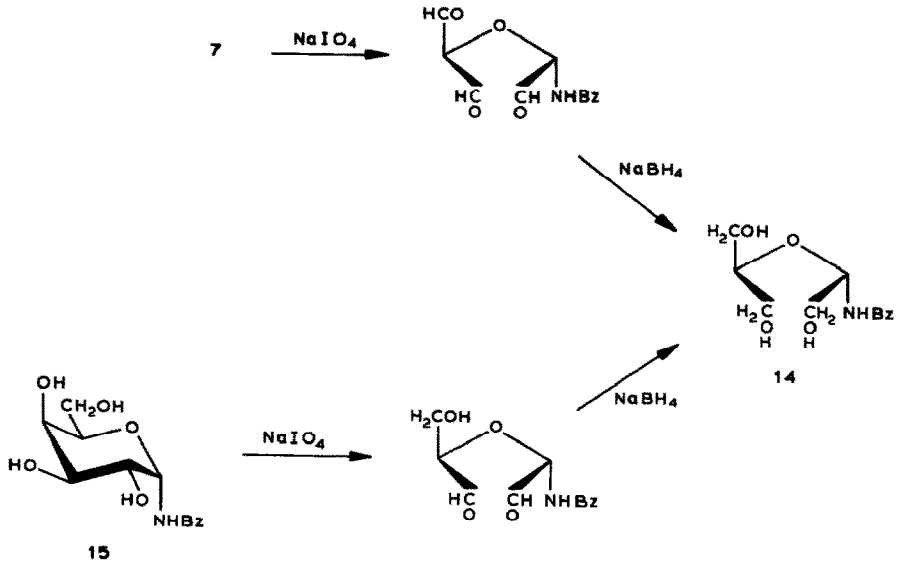
The furanose structure for compound **7** was established by oxidation with periodate, which produced 1.02 mol of formaldehyde per mol. The α-anomeric configuration was assigned by chemical methods[10] (see Scheme 1). By periodate oxidation, followed by borohydride reduction of the aldehyde groups produced, compound **7** yielded a new product in which all optically active centers were eliminated, except C-1 of the original monosaccharide. The optical rotation of the resulting polyalcohol (**14**) was compared with that obtained[11] by an analogous treatment of *N*-benzoyl-α-D-galactopyranosylamine (**15**). The similarity between the optical rotations of the polyalcohols produced from **7** (−4.3°) and **15** (−5.1°) demonstrated that both original compounds had the same configuration at C-1. The ^{1}H-n.m.r. spectrum, which is described later, provided further evidence for the α anomeric



1 R = H
2 R = Ac



3 $R^1 = H, R^2 = NHBz, R^3 = R^4 = R^5 = H, R^6 = Bz$
4 $R^1 = H, R^2 = NHBz, R^3 = R^5 = H, R^4 = R^6 = Bz$
5 $R^1 = H, R^2 = NHBz, R^3 = R^4 = H, R^5 = R^6 = Bz$
6 $R^1 = NHBz, R^2 = H, R^3 = R^5 = H, R^4 = R^6 = Bz$
7 $R^1 = H, R^2 = NHBz, R^3 = R^4 = R^5 = R^6 = H$
8 $R^1 = NHBz, R^2 = H, R^3 = R^4 = R^5 = R^6 = H$
9 $R^1 = H, R^2 = NHBz, R^3 = R^4 = R^5 = R^6 = Ac$
10 $R^1 = H, R^2 = NHBz, R^3 = R^4 = R^5 = Ac, R^6 = Bz$
11 $R^1 = H, R^2 = NHBz, R^3 = R^5 = Ac, R^4 = R^6 = Bz$
12 $R^1 = H, R^2 = NHBz, R^3 = R^4 = Ac, R^5 = R^6 = Bz$
13 $R^1 = NHBz, R^2 = H, R^3 = R^5 = Ac, R^4 = R^6 = Bz$



Scheme 1

configuration of compound **7**. Acetylation of **7** afforded the tetraacetate **9**.

For compound **3**, the furanose ring and α anomeric configuration were obvious, as, by methanolic ammonolysis, compound **7** was obtained (75.2%). Acetylation of **3** afforded the triacetate **10**. The benzoyloxy group was suspected from the beginning to be at C-6, because of the well-known resistance towards ammonolysis of the benzoyl group that esterifies the primary alcoholic hydroxyl

group of monosaccharides[8,12]. This suspicion was confirmed by the ^{1}H-n.m.r. spectrum of acetate **10**.

Compound **4** afforded compound **7** (74.6%) by methanolic ammonolysis, revealing a furanose structure and α-anomeric configuration. Acetylation of **4** produced the diacetate **11**. Ammonolysis of **4** in 2-propanol gave compound **3**; this fact revealed that one of the benzoyloxy groups of compound **4** was at C-6. The location of the other benzoyloxy group, at C-3, was shown by the ^{1}H-n.m.r. spectrum of **4**. Furthermore, the ^{1}H-n.m.r. spectrum of acetate **11** confirmed the position of the benzoyloxy groups at C-3 and C-6.

Compound **5** obviously had a furanose ring and α-anomeric configuration, because, by methanolic ammonolysis, compound **7** was produced (69.4%). Acetylation of **5** afforded the diacetate **12**. The position of benzoyloxy groups at C-5 and C-6 was revealed by the ^{1}H-n.m.r. spectrum of **5**. Further evidence was obtained from the ^{1}H-n.m.r. spectrum of acetate **12**.

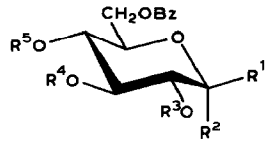
The furanose structure for compound **8** was established by periodate oxidation, which produced 0.98 mol of formaldehyde per mol. Owing to the scarcity of material, the β-anomeric configuration could not be ascertained by chemical methods, and was assigned on the basis of the ^{1}H-n.m.r. spectrum, as is later discussed.

Compound **6** showed infrared absorptions characteristic of the amide and benzoate carbonyl groups. When submitted to methanolic ammonolysis, compound **6** afforded compound **8** (57.8%), indicating a furanose structure and β-anomeric configuration. Acetylation of **6** produced the diacetate **13**, which could not be crystallized but was chromatographically homogeneous. The mass spectrum revealed the molecular ion at *m/z* 575, in accordance with the molecular weight of a di-*O*-acetyl-*N*-benzoyl-di-*O*-benzoyl-D-glucosylamine.

Concerning the position of benzoyloxy groups in compound **6**, one of them was expected to be at C-6, as all the monosaccharides isolated from the reaction mixture had the primary alcoholic hydroxyl group esterified. The location of the other benzoyloxy group, at C-3, was demonstrated by the ^{1}H-n.m.r. spectrum of **6**. In addition, a comparative analysis of the ^{1}H-n.m.r. spectra of both anomers of *N*-benzoyl-D-glucofuranosylamine (**7** and **8**), *N*-benzoyl-3,6-di-*O*-benzoyl-D-glucofuranosylamine (**4** and **6**), and 2,5-di-*O*-acetyl-*N*-benzoyl-3,6-di-*O*-benzoyl-D-glucofuranosylamine (**11** and **13**) showed that the components of each anomeric pair differ only in their configuration at C-1. The location of benzoyloxy groups at C-3 and C-6 of compound **6** was thus confirmed.

In regard to the partially benzoylated derivatives of α-D-glucopyranose isolated from the reaction mixture, compound **16** had earlier[13] been described, and so had[14,15] compound **19**. Our products were identified by comparison with authentic specimens.

Compound **16** was acetylated under two different conditions. By treatment at 0° with pyridine–acetic anhydride, the triacetate **20** was obtained, whereas heating at 100° with sodium acetate–acetic anhydride afforded the triacetate **21** already[13] described.

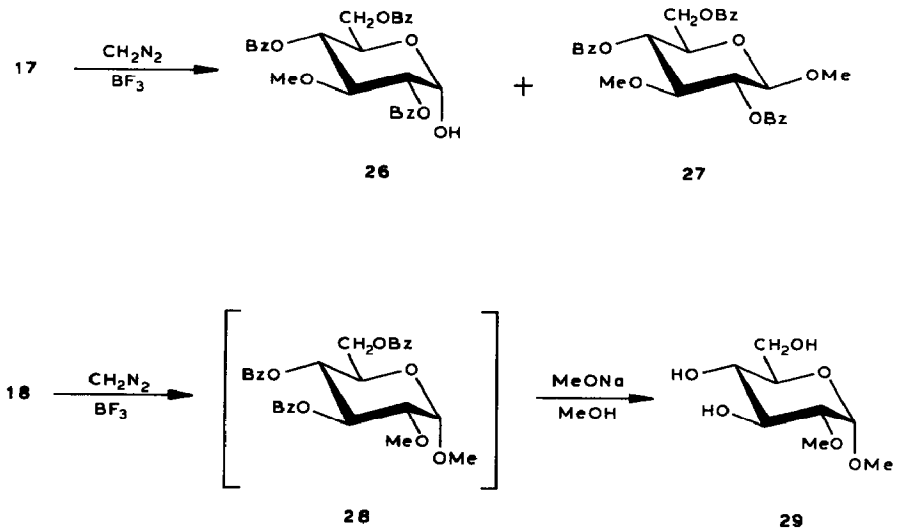


16 $R^1 = H, R^2 = OH, R^3 = Bz, R^4 = R^5 = H$
17 $R^1 = H, R^2 = OH, R^3 = R^5 = Bz, R^4 = H$
18 $R^1 = H, R^2 = OH, R^3 = H, R^4 = R^5 = Bz$
19 $R^1 = H, R^2 = OH, R^3 = R^4 = R^5 = Bz$
20 $R^1 = H, R^2 = OAc, R^3 = Bz, R^4 = R^5 = Ac$
21 $R^1 = OAc, R^2 = H, R^3 = Bz, R^4 = R^5 = Ac$
22 $R^1 = H, R^2 = OAc, R^3 = R^4 = R^5 = Bz$
23 $R^1 = OAc, R^2 = H, R^3 = R^4 = R^5 = Bz$
24 $R^1 = H, R^2 = OAc, R^3 = R^5 = Bz, R^4 = Ac$
25 $R^1 = H, R^2 = OAc, R^3 = Ac, R^4 = R^5 = Bz$

In the same way, compound **19** gave two different acetates when submitted to the two acetylation conditions; the first treatment produced the already[16] prepared acetate **22**, and by the second method the acetate **23** was obtained.

The structures of compounds **17** and **18** were chemically established by conversion into known derivatives, as shown in Scheme 2.

The characterization of compound **17** as 2,4,6-tri-*O*-benzoyl-α-D-glucopyranose was accomplished by methylation under conditions that avoid acyl migration, using diazomethane–boron trifluoride etherate[17]. The major product (76.5%) was the monomethyl derivative **26**, identified as 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-α-



Scheme 2

TABLE II

CHEMICAL SHIFTS (δ) AND MULTIPLICITIES IN THE ^{1}H-N.M.R. SPECTRA[a] OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES

Compound	*Solvent*	*H-1*	*H-3*	*H-2*	*H-4*	*H-5*	*H-6*	*H-6'*[b]	*OH*	*NH*	*Ar*	*OAc*
7	C_5D_5N	6.89dd	5.09q	4.79dd	4.98q	4.76m	4.43q	4.26q	5.26–5.70	8.54d	7.28–8.12	—
8	C_5D_5N	6.69dd	5.09q	4.95t	4.96q	4.86m	4.51q	4.33q	4.74–5.20	8.90d	7.29–8.13	—
3	C_5D_5N	7.00dd	←		4.66–5.24[c]			→	5.24–5.68	8.77d	7.26–8.24	—
4	C_5D_5N	6.88dd	6.35q	←		4.70–5.30[c]		→		8.90d	7.28–8.24	—
6	C_5D_5N	6.71dd	6.35q	←		4.72–5.26[c]		→		9.28d	7.26–8.26	—
5	C_5D_5N	7.02dd	5.25q	4.82q	5.29q	6.39sp	5.45q	5.03q	4.70–5.20	8.68d	7.26–8.24	—
9	$CDCl_3$	6.36q	5.52dd	5.20q	4.43q	5.19m	4.60q	4.12q	—	6.72d	7.44–7.82	1.99, 2.06, 2.11, 2.23
	C_5D_5N	6.92dd	5.90dd	5.67q	4.80q	5.50o	4.88q	4.31q	—	9.65d	7.30–8.20	1.98, 2.00 (×2), 2.04
10	$CDCl_3$	6.39q	5.56q	5.23q	4.50q	5.36o	4.76q	4.44q	—	6.69d	7.42–8.08	1.99, 2.14, 2.22
	C_5D_5N[d]	6.95dd	5.97q	5.69q	4.88q	5.68m	5.06q	4.59q	—	9.63d	7.34–8.28	2.01 (×2), 2.07
11	$CDCl_3$	6.48q	5.79dd	5.40dd	4.66q	5.42m	4.81q	4.48q	—	6.78d	7.38–8.11	1.90, 2.25
	C_5D_5N[d]	7.10q	6.30dd	5.93q	5.09q	5.83m	5.14q	4.68q	—	9.73d	7.27–8.28	1.88, 2.05
13	$CDCl_3$[d]	6.13dd	5.82dd	5.40t	4.67q	5.60m	4.96q	4.48q	—	7.07d	7.41–8.21	1.93, 2.20
12	$CDCl_3$	6.40q	5.55dd	5.28q	4.67q	5.69o	4.87q	4.59q	—	6.72d	7.38–8.03	2.08, 2.22
	C_5D_5N[d]	7.03q	6.10q	5.78q	5.18q	6.04m	5.23q	4.81q	—	9.63d	7.32–8.33	2.04 (×2)

[a]At 100 MHz. [b]The proton on C-6 that resonates at higher field is denoted H-6'. [c]Overlapping signals showing second-order behavior. [d]At 60 MHz.

TABLE III

COUPLING CONSTANTS[a] (Hz) IN THE ^{1}H-N.M.R. SPECTRA[b] OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES

Compound	*Solvent*	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$[c]	$J_{6,6'}$[c]	$J_{1,NH}$
7	C_5D_5N	3.5	1.0	3.0	7.5	3.5	5.5	−11.0	9.0
8	C_5D_5N	1.0	1.0	3.5	7.5	3.0	5.5	−11.3	9.0
3	C_5D_5N	3.5	[d]	[d]	[d]	[d]	[d]	[d]	9.0
4	C_5D_5N	3.7	0.8	2.8	[d]	[d]	[d]	[d]	9.1
6	C_5D_5N	2.0	1.0	4.0	[d]	[d]	[d]	[d]	8.7
5	C_5D_5N	3.5	1.0	3.2	8.2	2.5	5.7	−12.0	9.0
9	$CDCl_3$	3.7	0.9	3.5	9.6	2.7	4.9	−12.1	9.7
	C_5D_5N	4.0	1.4	3.6	9.0	2.7	5.5	−12.2	9.5
10	$CDCl_3$	3.7	0.9	3.6	9.6	2.8	5.0	−12.1	9.7
	C_5D_5N[e]	4.0	1.4	3.8	9.0	2.7	5.5	−12.2	9.5
11	$CDCl_3$	3.8	1.2	3.6	9.6	2.5	4.9	−12.2	9.7
	C_5D_5N[e]	4.5	1.7	3.8	9.0	2.5	5.2	−12.5	9.0
13	$CDCl_3$[e]	1.8	1.8	4.0	9.7	2.7	5.2	−12.5	9.0
12	$CDCl_3$	3.8	1.1	3.7	9.1	2.5	5.6	−12.1	9.7
	C_5D_5N[e]	4.5	1.7	4.0	9.2	2.5	6.0	−12.2	9.1

[a]Data obtained from spectra recorded at a sweep width of 250 Hz. [b]At 100 MHz. [c]The proton on C-6 that resonates at higher field is denoted H-6'. [d]Not determined because of second-order effects. [e]At 60 MHz.

D-glucopyranose[18] by comparison with an authentic specimen. The reaction also afforded minor amounts (9.5%) of a dimethyl derivative (**27**) whose physical properties agreed with those reported for methyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-β-D-glucopyranoside[19,20]. From compound **17**, the diacetate **24** was prepared.

A similar procedure was applied to establish the structure of compound **18** as 3,4,6-tri-*O*-benzoyl-α-D-glucopyranose. Methylation of **18** with diazomethane–boron trifluoride etherate afforded the syrupy dimethyl derivative **28**, which was homogeneous by thin-layer chromatography, and showed a clear ^{1}H-n.m.r. spectrum. Subsequent debenzoylation with sodium methoxide in methanol afforded a dimethyl derivative of D-glucose (**29**), identified as methyl 2-*O*-methyl-α-D-glucopyranoside[21,22] by comparison with an authentic sample. Acetylation of **18** produced the diacetate **25**.

The configuration at C-1 of the earlier prepared D-glucose benzoates **16** and **19**, and their peracetates **21** and **22**, had not been reported. These anomeric configurations, as well as those of the new derivatives **17, 18, 20, 23, 24,** and **25** described here, were assigned by ^{1}H-n.m.r. spectroscopy. It is known that, in the D-glucopyranose series, the value of $J_{1,2}$ is usually within the range of 3–4 Hz for α anomers (H-1, H-2 in the *cis* equatorial–axial relationship) and 7–9 Hz for β anomers (H-1, H-2 in the *trans* diaxial relationship)[23]. In the present study, the values of $J_{1,2}$ obtained demonstrated that compounds **16, 17, 18, 19, 20, 22, 24,** and **25** were α anomers ($J_{1,2}$ 3.5 Hz), and compounds **21** and **23** were β anomers ($J_{1,2}$ 8.0 Hz).

^{1}H-N.m.r. spectra of the N-*benzoyl*-D-*glucofuranosylamine derivatives.* — The spectra of compounds **7**, **8**, and **3–6** were measured in pentadeuteriopyridine, and those of compounds **9–13** in deuteriochloroform. For the sake of comparison, the spectra of compounds **9–12** were also recorded in deuteriopyridine. The chemical shifts and multiplicities observed are given in Table II, and the coupling constants in Table III.

The spectrum of *N*-benzoyl-α-D-glucofuranosylamine (**7**) is a representative example that illustrates the signals from the seven protons of the carbon chain. The H-1 signal appears clearly separated to low field, as a well defined pair of doublets, through coupling with H-2 and N–H. When H of N–H is exchanged for D by adding deuterium oxide, H-1 collapses to a doublet. The H-2 and H-3 resonances give rise to four-line patterns having similar coupling-constant values. The assignments of these signals were based on analogies[24]. The H-4 resonance appears as a rather distorted quartet between the H-2 and H-3 signals, owing to strong coupling with H-3. The signal for H-5 is a broad multiplet superimposed on the H-2 pair of doublets. The H-6 and H-6′ resonances display the typical eight-line pattern for the AB portion of an ABX system. The doublet corresponding to N–H is the lowest-field signal in the spectrum, and disappears on deuterium exchange, as well as the broad signal arising from hydroxyl protons.

The spectra of the acetyl derivatives **9–13** in deuteriochloroform and deuteriopyridine are all amenable to first-order analysis. As the N–H resonates in deuteriochloroform at higher field than in deuteriopyridine (see Table II), due to a higher degree of hydrogen bonding in the latter solvent[25], the H-1 quartet appears slightly distorted in the spectra recorded for solutions in chloroform, because of the proximity of the N–H signal. The assignments of H-2 and H-3 quartets, (that show similar coupling-constant values) were verified through spin-decoupling experi-

TABLE IV

PROTON CHEMICAL-SHIFT CHANGES IN THE ^{1}H-N.M.R. SPECTRA[a] OF BENZOYLATED FURANOSE DERIVATIVES WHEN BENZOYLOXY GROUPS ARE REPLACED BY HYDROXYL GROUPS

Compound	$\Delta\delta$[b] *(p.p.m.)*						
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6′*[c]
3[d,e]	+0.11	*f*	*f*	*f*	*f*	*f*	*f*
4[d,e]	−0.01	*f*	+1.26	*f*	*f*	*f*	*f*
5[d,e]	+0.13	+0.03	+0.16	+0.31	+1.63	+1.02	+0.77
6[e,g]	+0.02	*f*	+1.26	*f*	*f*	*f*	*f*
3,5,6-Tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucofuranose[h,i]	+0.10	+0.08	+1.17	+0.57	+1.51	+0.92	+0.66

[a]In C_5D_5N. [b]Difference between the proton chemical-shift value and that observed for the same proton in the compound resulting from replacing benzoyloxy groups by hydroxyl groups. [c]The proton at C-6 resonating at higher field is denoted H-6′. [d]Referred to compound **7**. [e]Chemical-shift values from Table II. [f]Chemical-shift values not determined. [g]Referred to compound **8**. [h]Chemical-shift values from ref. 26. [i]Referred to 1,2-*O*-benzylidene-α-D-glucofuranose[26].

TABLE V

PROTON CHEMICAL-SHIFT CHANGES IN THE ^{1}H-N.M.R. SPECTRA OF BENZOYLATED FURANOSE DERIVATIVES WHEN BENZOYLOXY GROUPS ARE REPLACED BY ACETOXY GROUPS

Compound	*Solvent*	$\Delta\delta^a$ *(p.p.m.)*						
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*[b]
10[c,d]	$CDCl_3$	+0.03	+0.03	+0.04	+0.07	+0.17	+0.16	+0.32
	C_5D_5N	+0.03	+0.02	+0.07	+0.08	+0.18	+0.18	+0.28
11[c,d]	$CDCl_3$	+0.12	+0.20	+0.27	+0.23	+0.23	+0.21	+0.36
	C_5D_5N	+0.18	+0.26	+0.40	+0.29	+0.33	+0.26	+0.37
12[c,d]	$CDCl_3$	+0.04	+0.08	+0.03	+0.24	+0.50	+0.27	+0.47
	C_5D_5N	+0.11	+0.11	+0.20	+0.38	+0.54	+0.35	+0.50
3,5,6-Tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucofuranose[e,f]	$CDCl_3$	+0.17	+0.19	+0.39	+0.37	+0.51	+0.33	+0.44

[a]Difference between the proton chemical-shift value and that observed for the same proton in the compound resulting from replacing benzoyloxy groups by acetoxy groups. [b]The proton at C-6 resonating at higher field is denoted H-6'. [c]Referred to compound **9**. [d]Chemical-shift values from Table II. [e]Referred to 3,5,6-tri-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose[27]. [f]Chemical-shift values from refs. 26 and 27.

ments. By irradiating, in turn, H-1, H-2, and H-3, the appropriate collapse of signals was observed. In all instances, the lower-field quartet corresponds to H-3.

The spectra of the β anomers **8, 6,** and **13** closely resemble those of the corresponding α anomers **7, 4,** and **11**, but display the H-1 signal shifted upfield, the N–H signal shifted downfield, and a considerably smaller $J_{1,2}$ value. In the spectra of **8** and **13**, the H-2 signal is an apparent triplet as a result of the similar magnitude of $J_{1,2}$ and $J_{2,3}$ values.

Structural analysis. — In order to ascertain the position of benzoyloxy groups in the partially benzoylated *N*-benzoyl-D-glucofuranosylamines **3, 4, 5,** and **6**, the spectra of these compounds were compared with the spectrum of the corresponding *O*-debenzoylated derivative (**7** or **8**, depending on the compound). The observed differences in chemical-shift values for the protons of the carbon chain are indicated in Table IV. The spectrum of a closely related compound, namely, 3,5,6-tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucofuranose[26], is also compared with the spectrum of its debenzoylated derivative[26]. The shifts to lower field of the signals from the protons reveal the presence of a benzoyloxy group at C-3 for compounds **4** and **6**, and demonstrate the location of benzoyloxy groups at C-5 and C-6 of compound **5**.

As the chemical-shift values for H-6 and H-6' could not be measured from the spectra of **3** and **4**, in order to demonstrate the presence of a benzoyloxy group at C-6 of these compounds, the spectra of the peracetates **10, 11,** and **12** were compared with the spectrum of the peracetyl derivative of *N*-benzoyl-α-D-gluco-

TABLE VI

H-1 AND N–H CHEMICAL-SHIFT CHANGES IN THE ^{1}H-N.M.R. SPECTRA OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES BY INVERTING THE ANOMERIC CONFIGURATION

Compound	*H-1, O-2 relationship*	*H-1*[a] *δ (p.p.m.)*	*Δδ*[b] *(p.p.m.)*	*NH, O-2 relationship*	*N–H*[a] *δ (p.p.m.)*	*Δδ*[c] *(p.p.m.)*
7[d]	*trans*	6.89	+0.20	*cis*	8.54	−0.36
8[d]	*cis*	6.69		*trans*	8.90	
4[d]	*trans*	6.88	+0.17	*cis*	8.90	−0.38
6[d]	*cis*	6.71		*trans*	9.28	
11[e]	*trans*	6.48	+0.35	*cis*	6.78	−0.29
13[e]	*cis*	6.13		*trans*	7.07	

[a]Values from Table II. [b]Difference between the H-1 chemical-shift values for α and β anomers. [c]Difference between the N–H chemical-shift values for α and β anomers. [d]In C_5D_5N. [e]In $CDCl_3$.

furanosylamine (**9**). The observed differences in chemical-shift values for the protons of the carbon chain, in chloroform and in pyridine, are recorded in Table V. The spectrum of 3,5,6-tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucofuranose[26] is also compared with the spectrum of 3,5,6-tri-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose[27]. The downfield shifts experienced by the signals from the protons demonstrate the presence of a benzoyloxy group at C-6 in compound **10**, confirm the location of benzoyloxy groups at C-3 and C-6 of compound **11**, and indicate that C-5 and C-6 bear benzoyloxy groups in compound **12**.

The anomeric configuration for the compounds studied could also be established or confirmed on the basis of the ^{1}H-n.m.r. spectra.

It is known that, in furanose derivatives, when the anomeric pair is available, the configuration at C-1 can be assigned unambiguously by comparison of the H-1 chemical shifts for the two anomers. When the substituents at C-1 and C-2 are in a *trans* relationship, H-1 resonates at higher field[28] than when they are in the *cis* orientation. The difference has been ascribed[29] to the shielding that an oxygenated group at C-2 exerts on H-1 when the two are situated on the same side of the ring. The H-1 chemical shifts for the anomeric pairs studied here, and the observed differences for each pair, are indicated in Table VI.

The shielding is also exerted on the N–H amidic proton when this group is in a *cis* relationship with the oxygenated substituent at C-2. This effect had been observed[30] in a study of *N*-acylglycopyranosylamines. The N–H chemical shifts for the anomeric pairs analyzed in the present work, and the differences obtained for each pair, are recorded in Table VI.

In furanose derivatives, when only one component of the anomeric pair is available, the configuration at C-1 can be assigned on the basis of the $J_{1,2}$ value. Although $J_{1,2}$ values can vary within the range of 3.5–8.0 Hz for *cis* protons and 0–8.0 Hz for *trans* protons[31], due to the flexible nature of the furanose ring, a systematic study of furanose derivatives[32] showed that H-1 and H-2 in a *trans* relationship usually give rise to $J_{1,2}$ values of 2 Hz or less. The $J_{1,2}$ values from Table

TABLE VII

DIHEDRAL ANGLES (DEGREES) BETWEEN VICINAL RING-PROTONS OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES, CALCULATED FROM THE OBSERVED COUPLING CONSTANTS

Compound	$\phi_{1,2}$	$\phi_{2,3}$	$\phi_{3,4}$
7	42	77 (98)	49
8	77 (101)	77 (98)	44
4	40	82 (93)	48
6	61 (113)	77 (98)	35
5	42	77 (98)	47
9	33	70 (104)	41
10	33	70 (104)	39
11	27	67 (108)	38
12	27	67 (108)	37

III are in agreement with these observations, as, in all instances, $J_{1,2} \geq 3.5$ Hz for α anomers (H-1, H-2 *cis*-oriented) and $J_{1,2} \leq 2.0$ Hz for β anomers (H-1, H-2 *trans*-oriented).

Conformational analysis. — The conformations of the *N*-benzoyl-D-glucofuranosylamine derivatives were analyzed from the ^{1}H-n.m.r.-spectral data for solutions in deuteriopyridine, in order to compare the hydroxylated compounds and their peracetylated analogs in the same solvent.

To perform the conformational analysis of the furanoid ring, various reported modifications of the Karplus equation were tested; the best approach to the experi-

TABLE VIII

ESTIMATED[a] DIHEDRAL ANGLES (DEGREES) IN DIFFERENT CONFORMATIONS OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINES

Conformation[b]	*Z*[c]	$\phi_{1,2}$[d]	$\phi_{2,3}$	$\phi_{3,4}$
E_2	0.28	43 (77)	77	26
	0.32	49 (71)	71	30
	0.36	54 (66)	66	33
	0.40	58 (62)	62	36
$^3T_2$	0.31	31 (89)	82	31
	0.36	36 (84)	77	36
	0.40	40 (80)	72	40
	0.43	44 (76)	68	44
	0.46	47 (73)	65	47
^3E	0.23	22 (98)	85	35
	0.28	26 (94)	77	43
	0.32	30 (90)	71	49

[a]From the model of Abraham and McLauchlan[38]. [b]For the nomenclature of conformations, see ref. 39. [c]Out-of-plane displacement (Å) of the atoms indicated in the conformational designation. [d]The first value corresponds to the α anomer, and that indicated in parentheses, to the β anomer.

mental data was given by the relation proposed by Streefkerk *et al.*[33], which takes into account the angular dependence of the vicinal coupling on the electronegativities of the substituents.

In the application of the modified Karplus equation, the following electronegativity values (X) were used: X_H 2.1 (ref. 34), X_{C-O} 2.5 (ref. 34), X_{-O-} 3.3 (ref. 35), X_{OH} 3.4 (ref. 35), X_{OAc} 3.7 (ref. 36), X_{OBz} 3.8, and X_{NHBz} 3.3. The last two values were calculated by the method of Cavanaugh and Dailey[35] from the ^{1}H-n.m.r. data for ethyl benzoate and *N*-ethylbenzamide, respectively. The dihedral angles between vicinal ring-protons, calculated from the observed coupling constants ($J_{1,2}$, $J_{2,3}$, and $J_{3,4}$) for the *N*-benzoyl-D-glucofuranosylamine derivatives are indicated in Table VII.

For vicinal ring-protons in a *cis* relationship, such as H-3, H-4 in all the compounds studied, and H-1, H-2 in the α anomers, only the values of ϕ smaller than 120° have physical significance. Moreover, as the puckering of the furanose ring preferably occurs in such a way that C-2, or C-3, or both, is (are) displaced from the mean plane of the ring[37], for the *N*-benzoyl-α-D-glucofuranosylamines **7**, **4**, **5**, and **9**–**12**, the larger $\phi_{2,3}$ values are not compatible with the values obtained for $\phi_{1,2}$ and $\phi_{3,4}$. Similarly, for the *N*-benzoyl-β-D-glucofuranosylamines **8** and **6**, the larger $\phi_{1,2}$ and $\phi_{2,3}$ values are incompatible with the corresponding values of $\phi_{3,4}$, as follows from inspection of molecular models. Therefore, the values indicated in parentheses in Table VII were discarded.

To deduce the favored conformation from the values of ϕ obtained, the model of Abraham and McLauchlan[38] was applied. The dihedral angles between vicinal ring-protons, estimated from that model for various symmetrical conformations of *N*-benzoyl-D-glucofuranosylamines, with different degrees of ring puckering, are shown in Table VIII.

On comparing the dihedral angles for compounds **7**, **4**, **5**, and **9**–**12** (see Table VII) with the values listed in Table VIII for the α anomers, the minimal deviations are observed for the $^3T_2$ conformation. However, as $\phi_{1,2}$ is smaller than $\phi_{3,4}$, a contribution of the ^3E conformation has to be considered. Thus, the "average" conformation for the *N*-benzoyl-α-D-glucofuranosylamine derivatives, resulting from the time-averaging of the various forms that are freely interconverted within a limited segment of the pseudorotational cycle[40,41], should be one that is intermediate between the $^3T_2$ and ^3E forms.

Similarly, a comparison of the dihedral angles for compounds **8** and **6** (see Table VII) with those listed in Table VIII for the β anomers, indicated that the $^3T_2$ conformation gives the best agreement. Nevertheless, the similar magnitude of $\phi_{1,2}$ and $\phi_{2,3}$ for compound **8** and the low value of $\phi_{3,4}$ for compound **6**, point to a contribution of the E_2 form in the conformational equilibrium.

The foregoing results are in accord with the criteria that predict the favored conformation of a furanose[41,42]. For *N*-benzoyl-D-glucofuranosylamines, the $^3T_2$ conformation permits maximum staggering of the substituents on C-1, C-2, C-3, and C-4, relieving *cis* 1,2-interactions, and allows the bulky side-chain to assume a

quasi-equatorial position. The contribution of the ^3E conformation observed for the α anomers probably arises from an attempt to lessen the destabilization produced by the electronegative substituent on C-1 (–NHBz) in a *quasi*-equatorial orientation in the $^3T_2$ form (unfavorable anomeric effect). On the other hand, the contribution of the E_2 conformation observed for the β anomers may be due to an attempt to alleviate the 1,3-parallel interaction between the –NHBz group on C-1 and the oxygen atom on C-3 in the $^3T_2$ form, even at the expense of lessening the staggering of the bulky substituents in the C-3–C-4 bond.

Because no significant changes in the conformation are observed when hydroxyl groups are replaced by acetoxy or benzoyloxy groups, it may be concluded that the size of the ring substituents in the *N*-benzoyl-D-glucofuranosylamines does not affect the conformational state of the ring.

The $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ values for the *N*-benzoyl-α-D-glucofuranosylamine derivatives (see Table III) are close to those reported for *N*-acetyl-α-D-glucofuranosylamine[24] and for esters of 1,2-*O*-isopropylidene-[27,43] and 1,2-*O*-benzylidene-α-D-glucofuranose[26]. In all instances, the coupling values indicate a $^3T_2$ "average" conformation, and preclude the contribution of the $^2T_3$ form to the conformational population. However, the coupling constants reported for methyl α-D-glucofuranoside[41] and penta-*O*-benzoyl-α-D-glucofuranose[44] reveal that these compounds exist as mixtures of $^3T_2$ and $^2T_3$ forms, with the former preponderating[41]. The significant changes produced in the conformational state of the furanoid ring when a benzamido group on C-1 is replaced by a benzoyloxy group suggest that, in the *N*-benzoyl-α-D-glucofuranosylamines, the –NH– of the benzamido group is responsible for the population of a single segment of the pseudorotational itinerary. The reasons for this behavior are not readily apparent.

For the corresponding β anomers, the conformational state of the furanoid ring is not altered when a benzamido group on C-1 is replaced by a methoxyl, acetoxy, or benzoyloxy group. The $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ values for the *N*-benzoyl-β-D-glucofuranosylamines **8** and **6** (see Table III), and those reported for methyl β-D-glucofuranoside[41] and for penta-*O*-acetyl- and penta-*O*-benzoyl-β-D-glucofuranose[44] indicate that a single segment of the pseudorotational cycle is populated by these compounds, $^3T_2$ being the "average" conformation.

The favored conformation in pyridine solution for the *N*-benzoyl-α-D-glucofuranosylamine derivatives agrees with that determined in the solid state for a related furanose compound, namely ethyl 1-thio-α-D-glucofuranoside. The calculation of the phase-angle of pseudorotation[45] (P) from the torsion angles reported for this compound in the crystal form[46], gave $P = -0.5°$. This value corresponds to an ideal $^3T_2$ conformation, according to a descriptor[47] applied in the carbohydrate field.

The orientation of the side chain for the *N*-benzoyl-D-glucofuranosylamine derivatives was determined by assuming that the energy barriers for rotation around the C-4–C-5 and C-5–C-6 bonds are low. From the various orientations that arise by rotation, only the staggered rotamers were considered: a_1, a_2, and a_3 of the

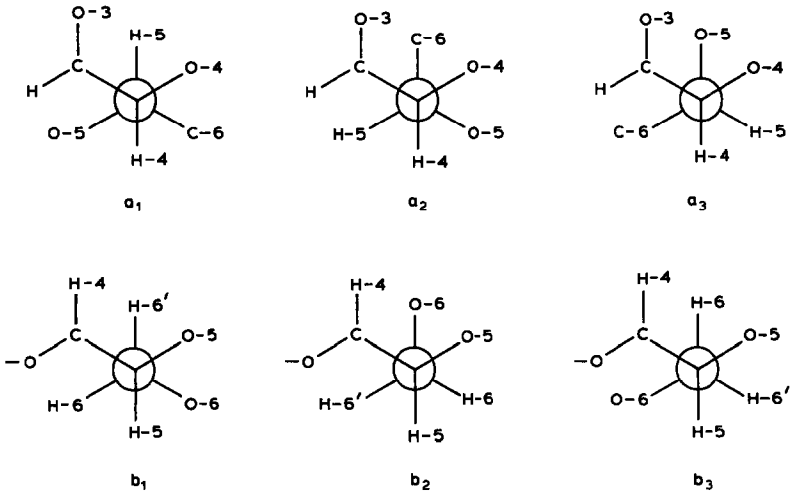


Fig. 1. The staggered rotamers of the C-4–C-5 fragment (a_1, a_2, and a_3) and of the C-5–C-6 fragment (b_1, b_2, and b_3) in *N*-benzoyl-D-glucofuranosylamines.

C-4–C-5 fragment, and b_1, b_2, and b_3 of the C-5–C-6 fragment (see Fig. 1). The mole fractions of these rotamers in the equilibrium were calculated from the $J_{4,5}$, $J_{5,6}$, and $J_{5,6'}$ values according to the method described by Streefkerk *et al.*[33].

In the C-4–C-5 fragment, rotamer a_3 was neglected, because of the unfavorable 1,3-parallel interaction between O-3 and O-5. On the basis of the theoretical values of $J_{4,5}$ for both of the remaining rotamers, calculated as had previously been proposed[33], the mole fractions of a_1 and a_2 for the *N*-benzoyl-D-glucofuranosylamine derivatives were derived from the observed $J_{4,5}$ values. The values obtained (see Table IX) reveal a considerable preponderance of rotamer a_1, having H-4 and H-5 in the *trans*-coplanar relationship. Rotamer a_2 is disfavored, because of the 1,3-parallel interaction between C-6 and O-3.

For the C-5–C-6 fragment, the mole fractions of rotamers b_1, b_2, and b_3 were deduced from the observed $J_{5,6}$ and $J_{5,6'}$ values, in combination with the theoretical values of $J_{5,6}$ and $J_{5,6'}$ for each of the three rotamers. The values obtained (see Table IX) indicated that the C-5–C-6 fragment of the *N*-benzoyl-D-glucofuranosylamine derivatives exists as a mixture of rotameric states with a substantial contribution of rotamers b_1 and b_2, having H-5 in a *trans*-coplanar relationship with H-6' and O-6, respectively. The lower contribution of rotamer b_3 to the conformational population results from the destabilizing, 1,3-parallel interaction between O-6 and the ring-oxygen atom.

The geminal coupling-constant $J_{6,6'}$ also indicates the orientational preference for the C-5–C-6 bond. Molecular orbital theory[48] predicts that, in rotamer b_3, where the O-5–C-5–C-6 plane bisects the axis between the geminal protons H-6 and H-6', an algebraic increase of $J_{6,6'}$ (smaller negative value) is expected. In such cases, values of $J_{6,6'}$ lying between -9.5 and -10 Hz were obtained[33,49]. On the other

TABLE IX

CALCULATED MOLE FRACTIONS (n) FOR THE ROTAMERS 1, 2, AND 3 OF (a) THE C-4–C-5 FRAGMENT AND (b) THE C-5–C-6 FRAGMENT OF *N*-BENZOYL-D-GLUCOFURANOSYLAMINE DERIVATIVES

Compound	*a*			*b*		
	n_1	n_2	n_3[a]	n_1	n_2	n_3
7	0.61	0.39	0.00	0.40	0.42	0.18
8	0.61	0.39	0.00	0.41	0.46	0.13
5	0.71	0.29	0.00	0.47	0.43	0.10
9	0.80	0.20	0.00	0.44	0.45	0.11
10	0.80	0.20	0.00	0.44	0.44	0.12
11	0.80	0.20	0.00	0.41	0.49	0.10
12	0.83	0.17	0.00	0.50	0.40	0.10

[a]Excluded, because of the unfavorable 1,3-parallel interaction between O-3 and O-5.

hand, in rotamers b_1 and b_2, where the O-5–C-5–C-6 plane and the axis between H-6 and H-6′ tend to the parallel arrangement, an algebraic decrease of the geminal coupling (larger negative value) is expected. In such cases, values of $J_{6,6'}$ between −11 and −12 Hz have been reported[33,49]. The $J_{6,6'}$ values for the *N*-benzoyl-D-glucofuranosylamine derivatives vary from −11 to −12.5 Hz (see Table III), revealing a great preponderance of rotamers b_1 and b_2 over b_3.

Our results concerning the preferred orientation of the side chain for the *N*-benzoyl-D-glucofuranosylamine derivatives are in reasonable agreement with those reported[50] for 1,2-*O*-isopropylidene-α-D-glucofuranose-6-^{13}C and its L-*ido* epimer. Considering the C-4–C-5 bond of these compounds, the values of H-4, H-5, and ^{13}C-6, H-4 vicinal couplings are consistent with the preponderance of a rotamer having H-4 and H-5 in a *trans* orientation[50]. In regard to the C-5–C-6 fragment, the magnitude of the H-5,H-6 and H-5,H-6′ vicinal couplings indicates a preference for the rotamer having H-5 *gauche* to H-6 and *trans* to H-6′. However, the small value of ^{13}C-6, H-5 geminal coupling suggests that the rotamer having H-5 *trans* to O-6 is the most highly favored[50].

With respect to the orientation of the C-1–NHBz fragment, the benzamido group is known as a stable, planar structure, with N–H and C-O in *trans* arrangement[51]. Concerning the C-1–NH bond of the *N*-benzoyl-D-glucofuranosylamines, the large values for $J_{1,NH}$, varying from 8.7 to 9.7 Hz (see Table III), suggest a *trans*-coplanar relationship between H-1 and N–H in a rotamer of restricted rotation. It has been pointed out[24,51,52] that the *trans* arrangement is energetically favorable, because of less steric hindrance with neighboring groups, as can be appreciated by inspection of molecular models.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns

apparatus, unless otherwise specified, and are uncorrected; mixed melting points were measured in capillary (cap.) tubes. Optical rotations were determined in 1-dm tubes with a Perkin–Elmer 141 polarimeter. Absorbances were measured with a Beckman D.U. spectrophotometer. Evaporations were conducted below 45°, under diminished pressure. Samples for analysis were dried over phosphorus pentaoxide at 60–100°/133 Pa. Column chromatography was performed on silica gel (Davison) grade 923 (100–200 mesh). Thin-layer chromatography (t.l.c.) was conducted on glass plates (10 × 20 cm) coated with silica gel G (Merck, 0.25-mm thickness). The following mixtures of benzene–2-propanol (v/v) were used as developing solvents: *A*, 97:3; *B*, 24:1; *C*, 9:1; *D*, 4:1; *E*, 3:2; and *F*, 1:1. Detection was effected with iodine vapor. Preparative t.l.c. was performed on glass plates (10 × 20 cm) coated with silica gel GF_{254} (Merck; 1-mm thickness); indication was effected by irradiation with u.v. light. Unless otherwise specified, identification of a known compound was made by comparison with an authentic sample, by mixed melting point, and by i.r. spectra. I.r. spectra were recorded for Nujol mulls with a Perkin–Elmer 137-B Infracord spectrophotometer, which was calibrated against a polystyrene standard. Unless otherwise stated, ^{1}H-n.m.r. spectra were recorded at 60 MHz with a Varian A-60 spectrometer. Spectra at 100 MHz were recorded with a Varian XL-100 spectrometer, operated in the continuous-wave mode. The concentration of each sample was ~10% (w/v). The spectra of compounds **6** and **8** were measured at 100 MHz, in the pulse, Fourier-transform mode, with a Varian XL-100-15 spectrometer coupled with a 620 L VFT computer; sample concentrations of ~2% (w/v) were used; both spectra were recorded after sufficient data-accumulation (100 scans). The probe temperature was 20–25°. Tetramethylsilane (~1%) was employed as the internal reference-standard. Hydroxyl and NH protons were exchanged for deuterium by adding deuterium oxide; deuteration of NH groups was complete only after 24 h. Spin-decoupling experiments were performed on solutions in chloroform-*d* with the XL-100 equipment operated in the continuous-wave mode. Spectra were analyzed on a first-order basis; the coupling constants reported (Hz) are the observed line-spacings. All vicinal coupling-constants were taken as positive, but the geminal coupling constant $J_{6,6'}$ was assumed to be negative, in analogy to the data on geminal coupling constants for other saturated carbohydrates[53]. Signal multiplicities are indicated by: bs, broad singlet; d, doublet; dd, double doublet; m, multiplet; o, octet; q, quartet; s, singlet; sp, septet; and t, triplet. Mass spectra were recorded with a Varian MAT CH 7-A spectrometer at 70 eV.

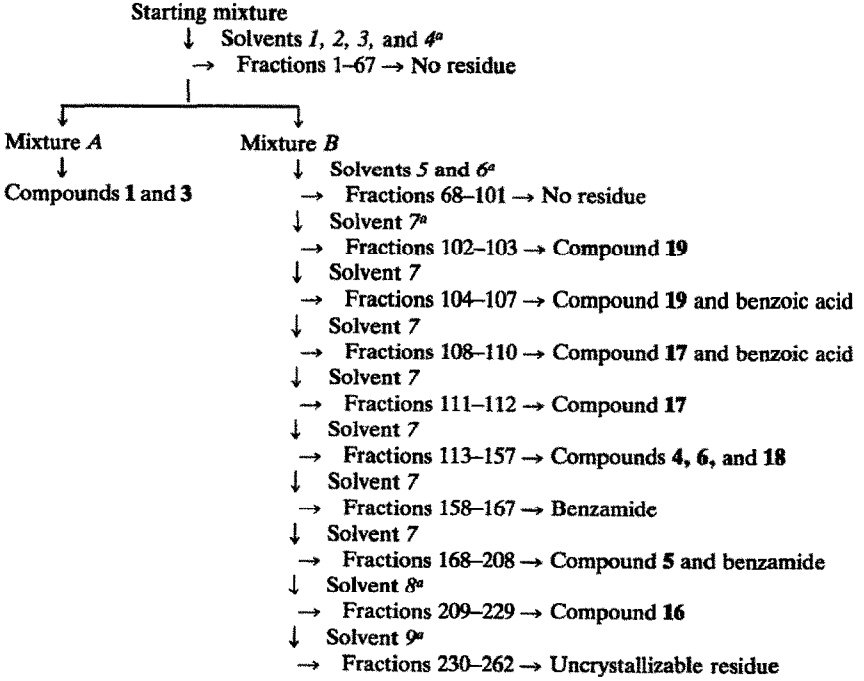
*1,2,3,4,6-Penta-*O*-benzoyl-α-*D*-glucopyranose.* — A solution of α-D-glucose (70 g) in dry pyridine (420 mL) was cooled to −20° and benzoyl chloride (365 mL) was slowly added. After standing for 1 h at 0°, the mixture was kept overnight in a refrigerator and then for 5 h at room temperature. It was now poured into ice–water (5 L); the solid deposited was pulverized, filtered off, washed with water, soaked in methanol, and dried. The crude product (270 g) was recrystallized from 3:1 methanol–acetone; after four recrystallizations, a pure product was obtained (129 g,

47%); m.p. 191–192°, $[\alpha]_D^{20}$ +138.4° (*c* 1, chloroform); lit. m.p. 187°, $[\alpha]_D$ +138.5° (chloroform)[54]; m.p. 190–191°, $[\alpha]_D$ +136.8° (chloroform)[55].

*1,1-Bis(benzamido)-6-*O*-benzoyl-1-deoxy-*D*-glucitol* (**1**). — To anhydrous liquid ammonia (700 mL), stirred at −60°, was added portionwise a solution of penta-*O*-benzoyl-α-D-glucopyranose (50 g) in 1:1 (v/v) chloroform–1,4-dioxane (700 mL) during 10 min. The homogeneous mixture was kept for 100 h at −60°, and a crystalline precipitate slowly formed. Ammonia was then evaporated by stirring the mixture, protected from moisture, at room temperature. The crystals deposited were filtered off (8.6 g); they had m.p. 188–192° (dec.). Two recrystallizations from ethanol afforded a product having m.p. 191–193° (cap.); it was identified as ammonium benzoate by comparison with an authentic sample; lit.[56] m.p. 190°.

The previous filtrate was kept for 24 h at room temperature; a crystalline precipitate (9 g) was formed, R_F 0.25 (t.l.c., solvent *D*). Recrystallization from ethanol gave **1**, m.p. 219–220° (dec.), m.p. 207–208° (dec.; cap.), $[\alpha]_D^{26}$ +3.0° (*c* 1, pyridine), identified by comparison with an authentic sample; lit.[8] m.p. 208–209°, $[\alpha]_D^{25}$ +6.3° (pyridine).

The filtrate was evaporated to dryness, and a solid (34.1 g) was obtained. T.l.c. of the residue (solvent *C*) showed nine spots, R_F 0.90, 0.80, 0.65, 0.50, 0.40, 0.35, 0.27, 0.20, and 0.15.



Scheme 3. The fractionation of the ammonolysis reaction mixture by column chromatography. [[a]Solvent systems used for development and elution: (*1*) benzene; benzene–chloroform (*2*) 7:3; (*3*) 2:3; (*4*) chloroform; chloroform–2-propanol (*5*) 99:1; (*6*) 49:1; (*7*) 97:3; (*8*) 19:1; (*9*) 9:1.]

The ammonolysis was repeated under the same conditions, with a further amount (50 g) of penta-*O*-benzoyl-α-D-glucopyranose; 8.6 g of ammonium benzoate and 8.8 g of compound **1** were isolated. Total yield of ammonium benzoate: 17.2 g. The remaining residue (33.6 g) was combined with that proceeding from the first ammonolysis reaction, and the mixture (67.7 g) was submitted to chromatography on a column (170 × 8 cm) of silica gel (4200 g) (see Scheme 3). The material was pulverized and placed on the top of the column, between two disks of filter paper. Fractions (500 mL each) were collected.

The development was performed with benzene, mixtures of benzene with increasing concentrations of chloroform, and then chloroform; 67 fractions that left no residue on evaporation were collected. At this stage, most of the unadsorbed material that still remained at the top of the column had turned crystalline. Therefore, it was removed to be studied separately (mixture *A*; 12.5 g). Meanwhile, the chromatographic separation of the remaining components adsorbed in the column (mixture *B*) was prosecuted.

T.l.c. of mixture *A* (solvent *D*) showed only two spots, R_F 0.60 and 0.25. The solid was dissolved in boiling ethanol; on cooling, white crystals (3.3 g) were obtained, R_F 0.25 (solvent *D*) and 0.15 (solvent *C*). Recrystallization from the same solvent afforded a further amount of **1**, m.p. 219–220° (dec.), $[\alpha]_D^{20}$ +3.8° (*c* 1, pyridine); total yield of compound **1**: 21.1 g (29.0%).

*2,3,4,5-Tetra-*O*-acetyl-1,1-bis(benzamido)-6-*O*-benzoyl-1-deoxy-*D*-glucitol* (**2**). — Compound **1** (500 mg) was dissolved in 1:1 pyridine–acetic anhydride (10 mL). The solution was kept for 24 h at room temperature and then poured into ice–water (100 mL). The resulting solid was filtered off, and recrystallized from ethanol, yielding 520 mg of **2**, m.p. 209–210° (sintering from 194–195°), $[\alpha]_D^{20}$ −44.0° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 5.78 (m, $J_{1,2}$ 9.0, $J_{1,NH}$ 7.0, $J_{1,NH'}$ 9.0 Hz, H-1; doublet on deuteration), 6.35 (q, $J_{2,3}$ 2.0 Hz, H-2), 5.70 (q, $J_{3,4}$ 7.5 Hz, H-3), 5.45 (t, $J_{4,5}$ 7.5 Hz, H-4), 5.23 (m, $J_{5,6}$ 3.0, $J_{5,6'}$ 5.0 Hz, H-5), 4.62 (q, $J_{6,6'}$ −12.0 Hz, H-6), 4.34 (q, H-6'), 8.23 (d, NH; disappeared on deuteration), 7.32–8.15 (16 H, Ar and NH'), and 1.97, 2.07, 2.10, and 2.16 (4 s, 12 H, 4 OAc).

Anal. Calc. for $C_{35}H_{36}N_2O_{12}$: C, 62.13; H, 5.32; N, 4.14. Found: C, 61.94; H, 5.48; N, 4.28.

N-*Benzoyl-6-*O*-benzoyl-α-D-glucofuranosylamine* (**3**). — The ethanolic mother liquor remaining after crystallization of **1** was concentrated to 1/10th of its original volume, and kept for 24 h at room temperature. A crystalline precipitate was formed (6.6 g, 11.9%); R_F 0.60 (solvent *D*) and 0.20 (solvent *C*). Recrystallization from ethanol gave **3**, m.p. 177–178°, m.p. 174–175° (cap.), $[\alpha]_D^{22}$ +30.2° (*c* 1, pyridine); for ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III.

Anal. Calc. for $C_{20}H_{21}NO_7$: C, 62.01; H, 5.46; N, 3.62. Found: C, 61.89; H, 5.43; N, 3.78.

*2,3,5-Tri-*O*-acetyl-*N*-benzoyl-6-*O*-benzoyl-α-D-glucofuranosylamine* (**10**). — Compound **3** (200 mg) was acetylated with 1:1 pyridine–acetic anhydride (4 mL) as described for **1**. Recrystallization of the crude product from ethanol gave **10** (228

mg), m.p. 151–152°, $[\alpha]_D^{21}$ +53.9° (*c* 0.5, chloroform); for the ^{1}H-n.m.r. data in pyridine-d_5 and $CDCl_3$, see Tables II and III.

Anal. Calc. for $C_{26}H_{27}NO_{10}$: C, 60.81; H, 5.30; N, 2.73. Found: C, 61.09; H, 5.42; N, 3.02.

N-*Benzoyl-α-*D-*glucofuranosylamine* (**7**). — Compound **3** (1 g) was dissolved in 16% (w/v) methanolic ammonia (40 mL); the solution was kept for 18 h at room temperature, and then evaporated to dryness. T.l.c. of the residue showed one spot, R_F 0.60 (solvent *E*); the solid crystallized (550 mg, 75.2%) from 2-propanol. Recrystallization from the same solvent gave **7**, m.p. 171–173°, $[\alpha]_D^{20}$ +45.0° (*c* 1, ethanol), $[\alpha]_D^{23}$ +41.6° (*c* 0.6, water); ^{1}H-n.m.r. (100 MHz, D_2O): δ 6.00 (d, $J_{1,2}$ 3.8 Hz, H-1), 4.30 (q, $J_{2,3}$ 0.6 Hz, H-2), 4.38 (q, $J_{3,4}$ 3.0 Hz, H-3), 4.15 (q, $J_{4,5}$ 8.6 Hz, H-4), 3.92 (m, $J_{5,6}$ 2.7, $J_{5,6'}$ 6.0 Hz, H-5), 3.84 (q, $J_{6,6'}$ −12.5 Hz, H-6), 3.62 (q, H-6'), and 7.49–7.81 (5 H, Ar); for the ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III.

Anal. Calc. for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05; N, 4.95. Found: C, 55.21; H, 6.25; N, 5.00.

Periodate oxidation of **7** — (*a*) *Determination of formaldehyde.* A solution of compound **7** (7.07 mg) in 15mM aqueous sodium metaperiodate (10 mL) was kept in the dark for 24 h at 35°. An aliquot (1 mL) was withdrawn, iodate and periodate were removed by addition of 0.5M sulfuric acid (1 mL) and M sodium arsenite (0.5 mL), and, after 10 min, the solution was diluted with water to 10 mL. On a sample (1 mL) of the resulting solution, the determination of formaldehyde was performed by the chromotropic acid method[57]. The absorbance (0.425) of the sample at 570 nm corresponded to a formaldehyde production of 1.02 mol per mol of **7**.

(*b*) *Determination of anomeric configuration.* To compound **7** (17.7 mg, 63 μmol) was added 75mM aqueous sodium metaperiodate (1.76 mL, 132 μmol), and the solution was kept in the dark at 4°. After 48 h, the optical rotation remained constant: $[\alpha]_D^{20}$ +21.3°. To the resulting solution were added sodium hydrogencarbonate (6 mg) and sodium borohydride (6 mg). The optical rotation remained constant after 24 h: $[\alpha]_D^{20}$ −4.3°, in agreement with the value reported[11] for *N*-benzoyl-α-D-galactopyranosylamine submitted to the same treatment. (The optical rotations were calculated on the basis of the weight of the original compound.)

*2,3,5,6-Tetra-*O*-acetyl-*N*-benzoyl-α-*D*-glucofuranosylamine* (**9**). — Compound **7** (100 mg) was acetylated with 1:1 pyridine–acetic anhydride (2 mL) as described for **1**. The resulting solid was recrystallized from 1:2 2-propanol–petroleum ether (b.p. 60–70°), yielding 125 mg of **9**, m.p. 136–137°, $[\alpha]_D^{22}$ +44.1° (*c* 0.6, chloroform); for ^{1}H-n.m.r. data in pyridine-d_5 and $CDCl_3$, see Tables II and III.

Anal. Calc. for $C_{21}H_{25}NO_{10}$: C, 55.87; H, 5.58; N, 3.10. Found: C, 56.10; H, 5.84; N, 3.15.

*2,3,4,6-Tetra-*O*-benzoyl-α-*D*-glucopyranose* (**19**). — After the removal of mixture *A* from the top of the column, the development of the chromatogram was continued using mixtures of chloroform with increasing concentrations of 2-

propanol (see Scheme 3). Employing 99:1 and 49:1 chloroform–2-propanol, 33 fractions that left no residue on evaporation were collected (fractions 68–101). The elution of the adsorbed products was initiated with 97:3 chloroform–2-propanol (fractions 102–208), continued with a 19:1 mixture of the same solvents (fractions 209–229), and finished with 9:1 chloroform–2-propanol (fractions 230–262). The fractions collected were monitored by t.l.c.

Fractions 102–107 contained a major product, R_F 0.70 (solvent *B*); fractions 104–107 showed, in addition, a white spot having an erratic R_F value (benzoic acid).

On evaporation, fractions 102–103 afforded a colorless, amorphous residue that crystallized *in vacuo*. Recrystallization from ligroin (b.p. 100–120°) gave **19** (1.7 g), R_F 0.70 (solvent *B*) and 0.90 (solvent *C*); m.p. 118–120°, $[\alpha]_D^{22}$ +72.2° (*c* 0.5, chloroform), $[\alpha]_D^{22}$ +70.2° (*c* 0.5, ethanol); ^{1}H-n.m.r. ($CDCl_3$): δ 5.74 (d, H-1, $J_{1,2}$ 3.5 Hz on deuteration), 5.30 (q, $J_{2,3}$ 9.5 Hz, H-2), 6.27 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.71 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.23–4.77 (3 H, H-5,6,6'), 7.17–8.12 (20 H, Ar), and 3.96 (bs, OH; disappeared on deuteration). It was identified by comparison with an authentic sample; lit. m.p. 119–120°, $[\alpha]_D^{21}$ +70.6° (ethanol)[14]; m.p. 117–120°, $[\alpha]_D$ +72.4° (chloroform)[15].

Evaporation of fractions 104–107 gave a residue (1.8 g), which was dissolved in chloroform (10 mL). The solution was extracted with 5% aqueous sodium hydrogencarbonate; on acidifying the aqueous extract with 2M hydrochloric acid, 0.84 g of benzoic acid were obtained, m.p. 121–122°, identical with an authentic sample. The chloroform layer was washed with water, dried (anhydrous sodium sulfate), and evaporated, yielding a syrup that crystallized on standing *in vacuo*. Recrystallization from ligroin (b.p. 100–120°) afforded a further amount of **19** (0.35 g); m.p. 118–120°, $[\alpha]_D^{22}$ +70.8° (ethanol); total yield of compound **19**: 2.05 g (2.4%).

1-O-Acetyl-2,3,4,6-tetra-O-benzoyl-α-D-glucopyranose (**22**). — Compound **19** (200 mg) was dissolved in pyridine (2 mL) and treated with acetic anhydride (2 mL) at 0°. The solution was kept for 24 h in a refrigerator and then evaporated *in vacuo* over sulfuric acid and potassium hydroxide. The resulting syrup crystallized from ethanol. Recrystallization from the same solvent gave 180 mg of **22**, m.p. 160–161.5°, $[\alpha]_D^{21}$ +90.2° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.65 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.55 (q, $J_{2,3}$ 9.5 Hz, H-2), 6.23 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.78 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.33–4.65 (3 H, H-5,6,6'), 7.18–8.17 (20 H, Ar), and 2.21 (s, 3 H, OAc). It was identified by comparison with an authentic sample; lit.[16] m.p. 160–161°, $[\alpha]_D$ +91.3° (chloroform).

1-O-Acetyl-2,3,4,6-tetra-O-benzoyl-β-D-glucopyranose (**23**). — Compound **19** (200 mg) was heated with acetic anhydride (2 mL) and freshly fused sodium acetate (120 mg) for 3 h at 100°. The solid material obtained on pouring the reaction mixture into ice–water crystallized from ethanol. On recrystallization from the same solvent, **23** (180 mg) was obtained; m.p. 189–190°, $[\alpha]_D^{20}$ +56.0° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.12 (d, $J_{1,2}$ 8.0 Hz, H-1), 5.46–6.02 (3 H, H-2,3,4), 4.28 (m, $J_{4,5}$ ~10.0, $J_{5,6}$ ~5.0, $J_{5,6'}$ ~3.5 Hz, H-5), 4.63 (q, H-6), 4.47 (q,

H-6'), 7.18–8.17 (20 H, Ar), and 2.02 (s, 3 H, OAc).

Anal. Calc. for $C_{36}H_{30}O_{11}$: C, 67.71; H, 4.70. Found: C, 67.86; H, 4.68.

2,4,6-Tri-O-benzoyl-α-D-glucopyranose (**17**). — T.l.c. of fractions 108–112 (solvent *B*) revealed the presence of a major component (R_F 0.50); fractions 108–110 contained, in addition, benzoic acid.

Evaporation of fractions 108–110 afforded a residue (2.1 g) that was dissolved in chloroform (10 mL), and the solution extracted with 5% aqueous sodium hydrogencarbonate. On acidification of the aqueous extract with 2M hydrochloric acid, a further amount (1.01 g) of benzoic acid separated; total yield of benzoic acid: 1.85 g. The chloroform solution was washed with water, dried, and evaporated; the syrupy residue obtained crystallized (0.85 g) from benzene; m.p. 115–119°; R_F 0.50 (solvent *B*) and 0.80 (solvent *C*).

On evaporation, fractions 111–112 gave a syrup (0.72 g) that crystallized from benzene; the crystals (0.60 g) had m.p. 115–118°; R_F 0.50 (solvent *B*). The two crops of crystals were combined (1.45 g), and purified by column chromatography using benzene containing increasing concentrations of chloroform. The fractions collected were monitored by t.l.c. (solvent *B*). The product having R_F 0.50 was eluted with 7:3 benzene–chloroform. Fractions showing only the spot with R_F 0.50 were combined and evaporated, to give crystals (1.0 g, 1.4%). Recrystallization from benzene afforded **17**; m.p. 124–126°, $[\alpha]_D^{28}$ +81.6° (*c* 0.5, ethanol); ^{1}H-n.m.r. ($CDCl_3$): δ 5.62 (d, H-1, $J_{1,2}$ 3.5 Hz on deuteration), 5.13 (q, $J_{2,3}$ 9.5 Hz, H-2), 5.42 (t, $J_{3,4}$ 9.5, $J_{4,5}$ 9.5 Hz, H-4), 4.30–4.75 (4 H, H-3,5,6,6'), 7.20–8.17 (15 H, Ar), and 2.03–2.97 (2 OH, disappeared on deuteration).

Anal. Calc. for $C_{27}H_{24}O_9$: C, 65.85; H, 4.91. Found: C, 65.68; H, 4.97.

1,3-Di-O-acetyl-2,4,6-tri-O-benzoyl-α-D-glucopyranose (**24**). — Compound **17** (60 mg) was acetylated with pyridine (0.8 mL) and acetic anhydride (0.8 mL) as described for **19**. The resulting syrup was dissolved in methanol, and the solvent evaporated at low temperature. On repeating this treatment several times, the product crystallized (50 mg). Recrystallization from the same solvent gave **24**; m.p. 129–131°, $[\alpha]_D^{23}$ +107.4° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.63 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.40 (q, $J_{2,3}$ 9.5 Hz, H-2), 5.99 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.61 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.30–4.65 (3 H, H-5,6,6'), 7.27–8.15 (15 H, Ar), and 1.88 and 2.19 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{31}H_{28}O_{11}$: C, 64.56; H, 4.90. Found: C, 64.34; H, 5.11.

2,4,6-Tri-O-benzoyl-3-O-methyl-α-D-glucopyranose (**26**). — Compound **17** (150 mg) was dissolved in dichloromethane (2 mL); the solution was cooled to 0° and 3% (v/v) boron trifluoride etherate in dichloromethane (0.2 mL) was added. Then, while the temperature was kept at 0°, a solution of diazomethane in dichloromethane was added portionwise, until a faint yellow color persisted in the reaction mixture for a short time. After 30 min at 0°, a white solid was filtered off; the filtrate was successively washed with 10% aqueous sodium hydrogencarbonate and water, dried (magnesium sulfate), and evaporated to a syrup that crystallized from 4:1 ethanol–water; the crystals (85 mg) had R_F 0.40 (solvent *A*). A further recrys-

tallization from the same solvent mixture gave **26**; m.p. 187–188°, m.p. 181–182° (cap.), $[\alpha]_D^{20}$ +96.0° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 5.59 (t, $J_{1,2}$ 3.5, $J_{1,OH}$ 3.5 Hz, H-1; doublet on deuteration); 5.08 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.12 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.45 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.22–4.69 (3 H, H-5,6,6'), 7.19–8.15 (15 H, Ar), 3.45 (s, 3 H, OMe), and 3.61 (d, OH, disappeared on deuteration). It was identified as the title compound by comparison with an authentic sample; lit.[18] m.p. 180–182°, $[\alpha]_D^{20}$ +93.6° (chloroform).

*Methyl 2,4,6-tri-*O*-benzoyl-3-*O*-methyl-β-*D*-glucopyranoside* (**27**). — The mother liquor from the first crystallization of **26** was evaporated to a syrup (63 mg). Examination by t.l.c. (solvent *A*) showed two spots, R_F 0.40 and 0.80. The syrup was chromatographed on a dry column (10 × 1.4 cm) of silica gel (6 g); elutions were performed by using benzene with increasing concentrations of ethyl acetate. Fractions (4 mL each) were collected, and monitored by t.l.c. (solvent *A*). Elution with 19:1 benzene–ethyl acetate afforded the product with R_F 0.80 (fractions 6–9), and a 9:1 mixture of the same solvents eluted the component having R_F 0.40 (fractions 11–18).

Evaporation of fractions 6–9 gave a residue that crystallized from ethanol. The crystals (15 mg, 9.5%) had m.p. 130–132° (sintering from 124°), $[\alpha]_D^{20}$ +16.3° (*c* 0.19, chloroform), in agreement with the values reported for **27**; lit. m.p. 125–126°, $[\alpha]_D$ +14.7° (chloroform)[19]; m.p. 132–134°, $[\alpha]_D^{25}$ +16° (chloroform)[20].

From fractions 11–18, on evaporation, and treatment of the residue with 4:1 ethanol–water, a further amount (33 mg) of **26** was obtained; total yield of **26**: 118 mg (76.5%).

N-*Benzoyl-3,6-di-*O*-benzoyl-α-*D*-glucofuranosylamine* (**4**). — When fractions 113–157 (see Scheme 3) were examined by t.l.c. (solvent *C*), two spots, having R_F 0.65 and 0.50, were detected. On evaporation, they afforded a partially crystalline residue (13.1 g) which was dissolved in boiling benzene. On cooling, crystals were obtained (6.7 g, 9.6%); R_F 0.65 (solvent *C*). Recrystallization from toluene gave **4**; m.p. 187–188°, m.p. 181–182° (cap.), $[\alpha]_D^{20}$ +45.5° (*c* 0.5, acetone), $[\alpha]_D^{20}$ +2.0° (*c* 1, pyridine), $[\alpha]_{365}^{20}$ −15.0° (*c* 1, pyridine); for ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III.

Anal. Calc. for $C_{27}H_{25}NO_8$: C, 65.98; H, 5.13; N, 2.85. Found: C, 65.89; H, 5.07; N, 2.98.

*2,5-Di-*O*-acetyl-*N*-benzoyl-3,6-di-*O*-benzoyl-α-*D*-glucofuranosylamine* (**11**). — Compound **4** (200 mg) was acetylated with 1:1 pyridine–acetic anhydride (4 mL) as described for **1**. The product was recrystallized from ethanol, giving **11** (215 mg); m.p. 121–123°, $[\alpha]_D^{20}$ +30.0° (*c* 1, chloroform); for the ^{1}H-n.m.r. data in pyridine-d_5 and $CDCl_3$, see Tables II and III.

Anal. Calc. for $C_{31}H_{29}NO_{10}$: C, 64.69; H, 5.04; N, 2.43. Found: C, 64.84; H, 5.05; N, 2.59.

Conversion of **4** *into* **3**. — Compound **4** (200 mg) was dissolved in 8% (w/v) 2-propanol–ammonia (10 mL), and the solution was kept for 18 h at room temperature. Examination by t.l.c. (solvent *C*) showed three spots, having R_F 0.65 (start-

ing material), 0.40, and 0.20. The solution was evaporated to a syrup that crystallized (65 mg) from ethanol; R_F 0.20 (solvent *C*). Recrystallization from the same solvent afforded **3**; m.p. 177–178°, $[\alpha]_D^{20}$ +30.5° (*c* 0.5, pyridine), identical with an authentic sample. On standing, the mother liquor from the first crystallization of **3** deposited 50 mg of compound **4**. The component having R_F 0.40 (solvent *C*) was later demonstrated to be *N*-benzoyl-5,6-di-*O*-benzoyl-α-D-glucofuranosylamine (**5**).

Conversion of **4** *into* **7**. — Compound **4** (200 mg) was dissolved in 16% (w/v) methanolic ammonia (8 mL), and the solution was kept at room temperature. After 5 min, t.l.c. of the reaction mixture (solvent *C*) revealed the presence of three components, having R_F 0.65 (starting material), 0.40 (compound **5**), and 0.20 (compound **3**). The examination by t.l.c. was repeated after 18 h; only one spot, having R_F 0.60 (solvent *E*), was then detected. The solution was evaporated to a solid residue; recrystallization from 2-propanol afforded 86 mg (74.6%) of compound **7**; m.p. 171–173°, $[\alpha]_D^{23}$ +45.5° (*c* 1, ethanol), identical with an authentic sample.

N-*Benzoyl-3,6-di*-O-*benzoyl*-β-D-*glucofuranosylamine* (**6**). — T.l.c. of the benzene mother-liquor remaining after crystallization of **4** showed one main spot, R_F 0.50 (solvent *C*). On standing for 24 h at room temperature, crystals (0.15 g, 0.2%) separated, R_F 0.50 (solvent *C*); m.p. 171–173°. Recrystallization from toluene afforded pure **6**, m.p. 173–174°, $[\alpha]_D^{20}$ −5.0° (*c* 0.6, acetone), $[\alpha]_D^{20}$ −9.5° (*c* 0.5, pyridine), $[\alpha]_{365}^{20}$ −42.5° (*c* 0.5, pyridine); ν_{max} 3520–3240 (OH and NH), 1700, 1680 (benzoate C=O), 1630 (Amide I), and 1520 cm^{-1} (Amide II); for the ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III.

Anal. Calc. for $C_{27}H_{25}NO_8$: C, 65.98; H, 5.13; N, 2.85. Found: C, 65.70; H, 5.42; N, 2.86.

2,5-Di-O-*acetyl*-N-*benzoyl-3,6-di*-O-*benzoyl*-β-D-*glucofuranosylamine* (**13**). — Compound **6** (30 mg) was dissolved in 1:1 pyridine–acetic anhydride (0.6 mL); the solution was kept for 24 h at room temperature and then evaporated *in vacuo* over sulfuric acid and potassium hydroxide. The syrupy residue, which could not be induced to crystallize by the usual procedures, was dried at room temperature/0.13 Pa, affording **13** as a colorless amorphous solid that showed a single spot in t.l.c., R_F 0.58 (solvent *B*); $[\alpha]_D^{25}$ −36.4° (*c* 0.5, chloroform); ν_{max} 3350 (NH), 1750–1680 (acetate and benzoate C=O), 1640 (Amide I), and 1510 cm^{-1} (Amide II); for ^{1}H-n.m.r. data in $CDCl_3$, see Tables II and III; mass spectrum (e.i.): *m/z* 575 ($M^{+\cdot}$) (Calc.: 575.18).

N-*Benzoyl*-β-D-*glucofuranosylamine* (**8**). — Compound **6** (30 mg) was dissolved in 16% (w/v) methanolic ammonia (1.2 mL), and the solution was kept for 18 h at room temperature. On evaporation, a crystalline residue was obtained; recrystallization from ethanol afforded **8** as colorless needles (10 mg, 57.8%); R_F 0.60 (t.l.c., solvent *E*). After being dried at 90°/0.13 Pa, it had m.p. 173–174°, $[\alpha]_D^{20}$ −84.9° (*c* 0.2, water), $[\alpha]_D^{20}$ −101.8° (*c* 0.2, ethanol); ν_{max} 3520–3200 (OH and NH), 1640 (Amide I), and 1510 cm^{-1} (Amide II); for ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III; mass spectrum (e.i.): *m/z* 283 ($M^{+\cdot}$) (Calc.: 283.11).

Anal. Calc. for $C_{13}H_{17}NO_6$: C, 55.12; H, 6.05. Found: C, 55.98; H, 6.26.

Periodate oxidation of **8**. *Determination of formaldehyde.* — Compound **8** (0.67 mg) was dissolved in 15mM aqueous sodium metaperiodate (1 mL), and the solution was kept in the dark for 24 h at 35°. The determination of formaldehyde in the periodate oxidation mixture was performed as described for **7**. The absorbance (0.395) of the sample at 570 nm corresponded to a formaldehyde production of 0.98 mol per mol of **8**.

*3,4,6-Tri-*O*-benzoyl-α-*D*-glucopyranose* (**18**). — The benzene mother-liquor remaining after the isolation of **6** was evaporated to a syrup (5.5 g). Examination by t.l.c. (solvent *C*) revealed the presence of a major component, R_F 0.50. The syrupy material was purified by dry-column chromatography using benzene with increasing concentrations of ethyl acetate. Fractions were collected and monitored by t.l.c. (solvent *C*). The product having R_F 0.50 was eluted with 7:3 benzene–ethyl acetate. The fractions that showed only the spot having R_F 0.50 were combined and evaporated, giving a colorless amorphous solid that crystallized from toluene (3.8 g, 5.4%). Recrystallization from the same solvent gave **18**; m.p. 164–165°, m.p. 162–163° (cap.), $[\alpha]_D^{20}$ +55.0° (*c* 0.5, ethanol); ^{1}H-n.m.r. ($CDCl_3$): δ 5.42 (d, H-1, $J_{1,2}$ 3.5 Hz on deuteration), 3.88 (c, H-2, $J_{2,3}$ 9.5 Hz on deuteration), 5.78 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.57 (H-4), 4.22–4.72 (3 H, H-5,6,6'), 7.17–8.12 (15 H, Ar), and 3.02 and 4.14 (2 bs, 2 OH, disappeared on deuteration).

Anal. Calc. for $C_{27}H_{24}O_9$: C, 65.85; H, 4.91. Found: C, 66.07; H, 5.22.

*1,2-Di-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α-*D*-glucopyranose* (**25**). — Compound **18** (100 mg) was acetylated with pyridine (1 mL) and acetic anhydride (1 mL) as described for **19**. The resulting syrup crystallized (75 mg) from methanol. Recrystallization from the same solvent gave **25**, m.p. 191–192°, m.p. 189–190° (cap.), $[\alpha]_D^{23}$ +42.0° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.46 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.35 (q, $J_{2,3}$ 9.5 Hz, H-2), 6.00 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.66 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.27–4.62 (3 H, H-5,6,6'), 7.17–8.15 (15 H, Ar), and 1.88 and 2.19 (2 s, 6 H, 2 OAc).

Anal. Calc. for $C_{31}H_{28}O_{11}$: C, 64.56; H, 4.90. Found: C, 64.36; H, 5.10.

*Methyl 2-*O*-methyl-α-*D*-glucopyranoside* (**29**). — Compound **18** (200 mg) was methylated under the conditions described for **17**. The syrup obtained, on examination by t.l.c. (solvent *A*), showed the presence of a major product having R_F 0.48. The syrup was submitted to dry-column chromatography using benzene containing increasing concentrations of ethyl acetate. The fractions collected were monitored by t.l.c. (solvent *A*). The product having R_F 0.48 was eluted with 19:1 benzene–ethyl acetate. Fractions showing only the spot having R_F 0.48 were combined and evaporated to a syrup (110 mg) that failed to crystallize. It was then dried at room temperature/0.13 Pa, to give methyl 3,4,6-tri-*O*-benzoyl-2-*O*-methyl-α-D-glucopyranoside (**28**) as a colorless, amorphous solid; $[\alpha]_D^{20}$ +57.0° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 5.03 (d, $J_{1,2}$ 3.5 Hz, H-1), 3.65 (q, $J_{2,3}$ 9.5 Hz, H-2), 5.95 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.51 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.22–4.70 (3 H, H-5,6,6'), 7.17–8.12 (15 H, Ar), and 3.42 and 3.50 (2 s, 6 H, 2 OMe).

Compound **28** (60 mg) was dissolved in methanol (1 mL), and the solution was treated with 2M methanolic sodium methoxide (0.05 mL). The mixture was kept for 6 h at room temperature, and the base neutralized with Dowex-50W ion-exchange resin. The suspension was filtered and the filtrate evaporated to dryness. The syrupy residue showed a single spot in t.l.c., R_F 0.50 (solvent *F*). It was purified by preparative t.l.c. using solvent *F*. The band having R_F 0.50 was removed from the plate and extracted with methanol. The suspension was filtered and the filtrate evaporated to a solid residue (20 mg) that crystallized from butanone. Colorless regular prisms were obtained, m.p. 146–148°, $[\alpha]_D^{25}$ +159.2° (*c* 0.2, water), identified as **29** by comparison with an authentic sample; lit. m.p. 147–148° (refs. 21 and 22), $[\alpha]_D^{19}$ +155.0° (water)[21], $[\alpha]_D^{24}$ +162.2° (water)[22].

N-*Benzoyl-5,6-di*-O-*benzoyl-α*-D-*glucofuranosylamine* (**5**). — T.l.c. (solvent *C*) of fractions 158–208 (see Scheme 3) revealed the presence of a major product having R_F 0.27; fractions 168–208 showed, in addition, a spot having R_F 0.40.

Evaporation of fractions 158–167 gave a crystalline residue (10.8 g); on recrystallization from benzene, benzamide (8.2 g) was obtained; m.p. 129–130°, R_F 0.27 (solvent *C*), identical with an authentic sample.

Evaporation of fractions 168–208 gave a partially crystalline residue (13.5 g), which was dissolved in boiling benzene. On cooling, a further amount of benzamide (9.9 g) was obtained; total yield of benzamide, 18.1 g. The mother liquor was evaporated to a residue that crystallized (1.5 g, 2.1%) from benzene, R_F 0.40 (solvent *C*). A further recrystallization from toluene, after decolorization of the solution with activated charcoal, gave **5**, m.p. 163–164°, m.p. 161–162° (cap.), $[\alpha]_D^{20}$ +49.0° (*c* 0.5, acetone), $[\alpha]_D^{20}$ −5.0° (*c* 1, pyridine), $[\alpha]_{365}^{20}$ −28.5° (*c* 1, pyridine); for ^{1}H-n.m.r. data in pyridine-d_5, see Tables II and III.

Anal. Calc. for $C_{27}H_{25}NO_8$: C, 65.98; H, 5.13; N, 2.85. Found: C, 65.83; H, 5.21; N, 3.02.

2,3-Di-O-*acetyl*-N-*benzoyl-5,6-di*-O-*benzoyl-α*-D-*glucofuranosylamine* (**12**). — Compound **5** (200 mg) was acetylated with 1:1 pyridine–acetic anhydride (4 mL) as described for **1**. The crude product was recrystallized from ethanol, giving **12** (190 mg); m.p. 81–83°, $[\alpha]_D^{20}$ +32.0° (*c* 1, chloroform); for the ^{1}H-n.m.r. data in pyridine-d_5 and $CDCl_3$, see Tables II and III.

Anal. Calc. for $C_{31}H_{29}NO_{10}$: C, 64.69; H, 5.04; N, 2.43. Found: C, 64.57; H, 5.28; N, 2.53.

Conversion of **5** *into* **7**. — Compound **5** (100 mg) was dissolved in 16% (w/v) methanolic ammonia (4 mL) and the solution was kept at room temperature. After 5 min, examination by t.l.c. (solvent *C*) showed three spots, having R_F 0.65 (compound **4**), 0.40 (starting material), and 0.20 (compound **3**). After 60 min, a product having R_F 0.60 (solvent *E*) was detected in the reaction mixture; this was the only component revealed by t.l.c. after a reaction period of 18 h. The solution was evaporated to a solid residue; on recrystallization from 2-propanol, **7** (40 mg; 69.4%) was obtained; m.p. 171–172°, $[\alpha]_D^{25}$ +44.6° (*c* 0.5, ethanol); it was identical to an authentic sample.

2,6-Di-O-benzoyl-α-D-glucopyranose (**16**). — Examination by t.l.c. (solvent *C*) of fractions 209–229 (see Scheme 3) showed the presence of a major component (R_F 0.35) and a minor one (R_F 0.40). Evaporation of the combined fractions afforded an amorphous solid (0.78 g) which was extracted with boiling benzene to remove the component having R_F 0.40. The insoluble material was dissolved in absolute ethanol (3 mL) and precipitated by adding hot petroleum ether (b.p. 60–70°) (6 mL); crystals were obtained (0.36 g, 0.7%); R_F 0.35 (solvent *C*). A further recrystallization from the same solvent mixture gave **16**; m.p. 187–188°, m.p. 181–182° (cap.), $[\alpha]_D^{23}$ +57.6° (*c* 0.5, ethanol); ^{1}H-n.m.r. (acetone-d_6): δ 5.50 (q, $J_{1,2}$ 3.5, $J_{1,OH}$ 4.0 Hz, H-1; doublet on deuteration), 4.93 (q, $J_{2,3}$ 9.5 Hz, H-2), 3.65–4.75 (5 H, H-3,4,5,6,6′), 7.33–8.22 (10 H, Ar), and 3.10 (2 OH; disappeared on deuteration). It was identified by comparison with an authentic sample; lit.[13] m.p. 182°, $[\alpha]_D^{19}$ +56.3° (ethanol).

1,3,4-Tri-O-acetyl-2,6-di-O-benzoyl-α-D-glucopyranose (**20**). — Compound **16** (100 mg) was acetylated with pyridine (1 mL) and acetic anhydride (1 mL) as described for **19**. The resulting syrup crystallized (110 mg) from methanol. Recrystallization from the same solvent gave **20**; m.p. 119–120°, $[\alpha]_D^{24}$ +150.0° (*c* 0.5, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 6.53 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.30 (q, $J_{2,3}$ 9.5 Hz, H-2), 5.77 (t, $J_{3,4}$ 9.5 Hz, H-3), 5.35 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.23–4.63 (3 H, H-5,6,6′), 7.33–8.17 (10 H, Ar), and 1.93, 2.02, and 2.12 (3 s, 9 H, 3 OAc).

Anal. Calc. for $C_{26}H_{26}O_{11}$: C, 60.70; H, 5.09. Found: C, 60.67; H, 5.38.

1,3,4-Tri-O-acetyl-2,6-di-O-benzoyl-β-D-glucopyranose (**21**). — Compound **16** (100 mg) was acetylated with acetic anhydride (1 mL) and sodium acetate (60 mg) as described for **19**. The resulting solid crystallized (94 mg) from methanol. Recrystallization from the same solvent afforded **21**; m.p. 181–182° (cap.), $[\alpha]_D^{20}$ +63.6° (*c* 0.5, acetone); ^{1}H-n.m.r. ($CDCl_3$): δ 5.93 (d, $J_{1,2}$ 8.0 Hz, H-1), 5.10–5.67 (3 H, H-2,3,4), 4.07 (m, $J_{4,5}$ ~10.0, $J_{5,6}$ ~5.0, $J_{5,6'}$ ~3.5 Hz, H-5), 4.57 (q, H-6), 4.36 (q, H-6′), 7.33–8.17 (10 H, Ar), 1.92, and 2.02 (×2) (2 s, 9 H, 3 OAc); lit.[13] m.p. 176°, $[\alpha]_D^{22}$ +64.7° (acetone).

Examination by t.l.c. (solvent *C*) of fractions 230–263 (see Scheme 3) showed four spots, R_F 0.40, 0.35, 0.27, and 0.20. On evaporation, they yielded an uncrystallizable residue (100 mg) that was not studied further.

Conversion of ammonium benzoate into benzoic acid. — Ammonium benzoate (100 mg) was shaken with a suspension of silica gel (10 g) in benzene (30 mL). After 24 h, the solvent was evaporated; the remaining solid material was placed in a glass column and the product adsorbed in the silica gel was eluted with 97:3 chloroform–2-propanol. Evaporation of the eluate gave crystals (83 mg, 95.4%) having m.p. 120–122°. On recrystallization from water, they had m.p. 122°, and were identified as benzoic acid by comparison with an authentic sample.

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