Carbohydrate Research, 111 (1982) 93–104
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

CHEMISTRY OF 1,1-BIS(ACYLAMIDO)-1-DEOXYALDITOLS. BASE-CATALYZED, INTRAMOLECULAR *O,N*-TRANSACYLATION OF PER-*O*-ACYL-1,1-BIS(BENZAMIDO)-1-DEOXY-D-GLUCITOLS IN APROTIC SOLVENTS

IRENE PALLARES, MARÍA E. GELPI, AND RAÚL A. CADENAS
Departamento de Química, Facultad de Agronomía, Universidad de Buenos Aires, 1417 Av. San Martín 4453, Buenos Aires (Argentina)
(Received June 8th, 1982; accepted for publication, July 1st, 1982)

ABSTRACT

Penta-*O*-acetyl and penta-*O*-propanoyl derivatives of 1,1-bis(benzamido)-1-deoxy-D-glucitol are transformed into 1-acetamido-1-benzamido-1-deoxy-D-glucitol and 1-benzamido-1-deoxy-1-propanamido-D-glucitol, respectively, by heating with a suspension of potassium cyanide in acetonitrile, and subsequently *O*-deacylating with sodium methoxide in methanol. The reaction was also studied in the presence of a crown ether. When other nucleophiles (HO^- and CH_3O^-) or other aprotic solvents (propanonitrile, benzene) were employed, the yields of transacylation products diminished noticeably; likewise, the use of sodium as the counter-ion significantly affected this reaction. These results are qualitatively discussed in terms of the solvent effects on the reactivity of the nucleophiles employed.

INTRODUCTION

The 1,1-bis(acylamido)-1-deoxyalditols are obtained by ammonolysis of aldose acyl esters or of acylated nitriles of aldonic acids, with yields varying between 20 and 80%, depending on the medium (aqueous or alcoholic) employed for the reaction, and on the nature of the starting ester[1].

Many studies have been conducted on the scope, mechanism and products of the reaction of ammonolysis in the field of mono- and di-saccharides[1], but little is known about the chemistry, reactivity, and possible chemical applications[2] of the substances obtained.

We describe here the behavior of the penta-*O*-acetyl (**2**) and penta-*O*-propanoyl (**3**) derivatives of 1,1-bis(benzamido)-1-deoxy-D-glucitol (**1**, obtained by ammonolysis of penta-*O*-benzoyl-β-D-glucopyranose) when treated with cyanide ion in such aprotic solvents as acetonitrile, propanonitrile, or benzene. Parallel reactions employing hydroxyl and methoxyl anions as nucleophiles were also studied. The behavior observed may be considered representative of that of 1,1-bis(acylamido)-1-deoxyalditols in general.

RESULTS AND DISCUSSION

The starting hypothesis was that the cyanide ion could attack C-1 of the sugar diamide, thus offering divers synthetic possibilities. To avoid competitive, cyclizing reactions involving the free hydroxyl groups of the sugar chain, the acyl esters, which, up to now, are the only protected derivatives of **1** known, were used; favored substitution by nucleophilic attack at C-1 being assumed, a 2:1 molar ratio of potassium cyanide to sugar, in acetonitrile, was employed. The nucleophile was insoluble in this solvent and was maintained in suspension while the mixture was boiled under reflux (80°) for ~46 h.

The result was that an acyl–nitrogen bond was cleaved, instead of a sugar–nitrogen bond, and transposition of an acyl group of the chain to one of the nitrogen atoms on C-1 took place, with concomitant displacement of the corresponding benzoyl group. Different acyl groups of the sugar backbone made their own contribution to this intramolecular transacylation, finally giving, as evidenced by t.l.c., a mixture of partially *O*-acylated 1-acylamido-1-benzamido-1-deoxy-D-glucitols. To avoid use of this complex mixture, the reaction products were routinely *O*-deacylated with sodium methoxide in methanol. In this way, the reaction of **2** with potassium cyanide showed, in paper chromatography, three clearly detectable compounds, namely, unreacted **1** (R_F 0.78), 1-acetamido-1-benzamido-1-deoxy-D-glucitol (**4**, R_F 0.62), and a third spot (R_F 0.23) coincident with D-glucose. The last compound could have originated, at least in part, by a secondary reaction of the mixed sugar diamide **4** with the sodium methoxide employed in the *O*-deacylation, which also explains the formation of a small amount of benzamide. In this treatment, the benzoyl leaving-group (and the remaining *O*-acyl substituents) were eliminated as volatile methyl esters. Prior to the *O*-deacylation stage, the suspended, insoluble solid (potassium cyanide) was separated, by filtration, from the acetonitrile solution. As some alkaline degradation occurred, variable amounts of a syrupy, uncrystallizable material were obtained as a final residue in the different experiments undertaken.

Compound **4** was produced in ~48% direct yield. Its acyclic structure was demonstrated by the uptake of four mol of sodium metaperiodate on oxidation, and the release of one mol of formaldehyde. The n.m.r. spectrum at 60 MHz of **4** in deuterium oxide showed one benzamido group as a multiplet at δ 7.40–7.85, and the acetyl-group singlet at δ 2.02; H-1 appeared as a doublet at δ 5.91 ($J_{1,2}$ 5.0 Hz), and the remaining six protons as a large multiplet at δ 3.63–4.15. By acetylation, **4** gave 1-acetamido-2,3,4,5,6-penta-*O*-acetyl-1-benzamido-1-deoxy-D-glucitol.

The stereochemistry at C-1 in compound **4** is not known. The available data do not indicate that **4** was a mixture of C-1 diastereoisomers. Its stereochemical purity, and the absence of the other diastereoisomeric, acyl-exchange product, constitute evidence of the stereocontrolled character of these transacylations. If each position of the acylated sugar backbone should contribute, in its own molar proportion, to the migration, some positions would be sterically more contributing than others, and it is also possible that some acyl groups were practically excluded

from this reaction. In this way, the different acylated bis(benzamido)-alditols from monosaccharides would show different stereochemical behavior.

Several modifications were introduced into the starting conditions, in order to improve the reaction and to ascertain qualitatively some mechanistic aspects, whose complexity does not appear to allow quantitative evaluations. The use of only the amount of potassium cyanide soluble in the volume of acetonitrile employed, so as to conduct the reaction in a homogeneous medium, afforded only traces of **4**. This showed that a reservoir of insoluble cyanide ion is needed, in order to provide a steady concentration of nucleophile in solution; but, when the amount of salt in suspension was lessened from 2 to 0.4 mol, even though the period of heating was increased to 72 h, the yield of **4** diminished (35.9%) and that of the unreacted, starting-material increased (61%), indicating some extent of heterogeneous catalysis, with the solid salt as a polar support.

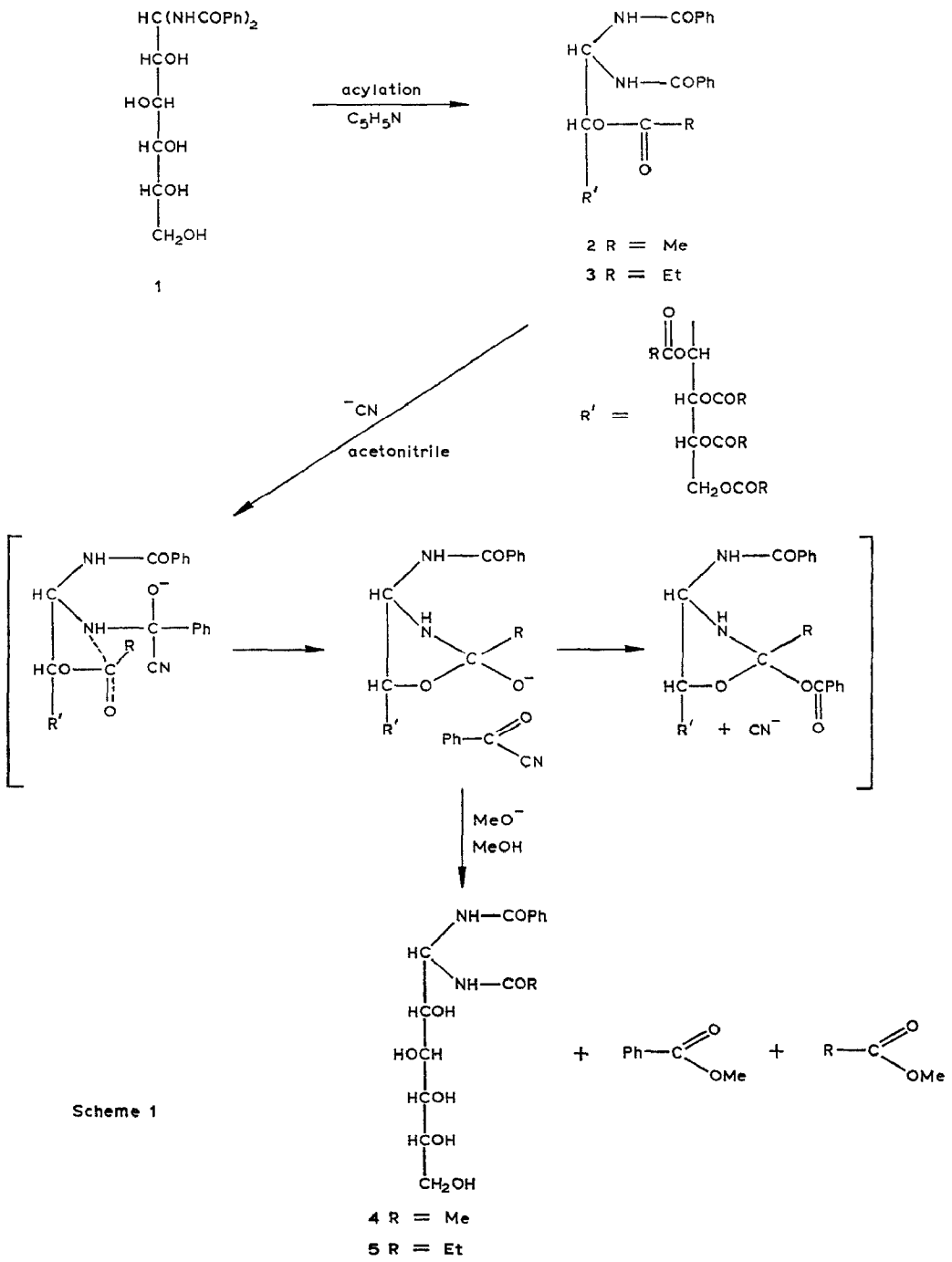
An increase of the temperature of reaction, using propanonitrile (b.p. 97°) as the solvent, led to recovery of unreacted **1** in ~51% yield, and to extensive browning. The colored mixtures of products did not crystallize, a rough estimate of the yield of **4** being ~10–15%. In benzene, the yield of **4** was very low (9.8%), with high recovery of unreacted material (62%).

The nucleophile was also changed, potassium hydroxide and potassium methoxide being employed instead of potassium cyanide, and, in both cases, the yields of **4** dropped to ~30%. The changing of the counter-ion, using the sodium salts of the three nucleophiles mentioned, was evidence of the importance of the alkali cation in the aprotic solvent employed, as will be discussed.

This reaction may be interpreted by a mechanism of substitution at the amide nitrogen atom, catalyzed by nucleophiles whose reactivity is markedly solvent-dependent. Scheme 1 shows a possible course of the reaction, whose first stage would be an enhancement of the basicity of the amide nitrogen atom through nucleophilic attack of the cyanide ion on one of the benzamido carbonyl-groups. The efficiency of this step would depend both on the assistance by a neighboring acyl-group and on the nucleophilicity of the anion.

With regard to the former factor, it is possible that, under the attack of the different nucleophiles (CN^-, HO^-, or CH_3O^-), many of the acyl groups of the sugar chain were eliminated prior to their migration (thus being excluded from the transacylation reaction), but, in the case of catalysis by cyanide ion, the very reactive acyl cyanide[3] was produced, and the chain deacylation was reversible. In the HO^-- and CH_3O^-promoted reactions, the sugar chain could, to a certain extent, be irreversibly deacylated (the acyl groups split leading to carboxylate anions or methyl esters, respectively) and the lower yields of **4** are attributable to a lower availability of migrating acyl groups.

However, the lack of assistance would make difficult, but not preclude, the unassisted splitting of one of the benzoyl groups (or, eventually, of both) which would afford, after the final treatment with methanol–sodium methoxide, a free amino group on C-1. Paper chromatography showed ninhydrin-positive substances


HC(NHCOPh)2
HCOH
HOCH
HCOH
HCOH
CH2OH
1
acylation
C5H5N
NH—COPh
HC
NH—COPh
HCO—C—R
O
R'
2 R = Me
3 R = Et
−CN
acetonitrile
R' =
O
RCOCH
HCOCOR
HCOCOR
CH2OCOR
NH—COPh
HC
O−
NH—C—Ph
HCO—C
R
CN
O
R'
NH—COPh
HC
H
N
R
C
HC—O
O−
R'
Ph—C
O
CN
NH—COPh
HC
H
N
R
C
HC—O
OCPh
O
R' + CN−
MeO−
MeOH
NH—COPh
HC
NH—COR
HCOH
HOCH
HCOH
HCOH
CH2OH
4 R = Me
5 R = Et
+
Ph—C
O
OMe
+
R—C
O
OMe

Scheme 1

that could have originated by this alternative. The mixed sugar-diamide **4** could also undergo this rupture, diminishing its yield. These amino derivatives were, in part, retained by the acid resin employed in the final neutralization of bases, in the alkaline medium, and also remained in the final, uncrystallizable syrup, which was not further investigated.

The fact that, in the reaction of **2** with the hydroxyl or methoxyl nucleophiles, compound **4** is also formed, supports a migration mechanism, instead of one of direct acylation, by acetyl cyanide, of the previously liberated amino group, as might be supposed on the basis of the cyanide-catalyzed reaction alone. This competitive alternative cannot, however, be excluded in the latter reaction.

With regard to the nucleophilicity of the anion, this is a complex aspect[4] that depends, among other factors, on its degree of solvation. As different, parallel, as well as concerted, reactions seem to operate, the situation appears too complex to permit speculation about the factors that can affect the transition state, the leaving-group ability, or the influence of the substrate upon the anions employed. On the other hand, the relation of nucleophile to solvent seems a factor that underlies the overall scheme in a way coherently explicable.

The reactivity of a nucleophile is lowered by an increase in solvation; such small anions as HO^-, CH_3O^-, or CN^- are poorly solvated by a dipolar, aprotic solvent such as acetonitrile, and are thus nucleophiles of high reactivity. However, their alkali salts, due to their insolubility, constitute a very limited anion-source that affects the adequate concentration of the reactive species, which explains the long periods of heating required in our experiments.

Studies conducted in the gas phase[5] indicated that, whereas the reactivity of the diverse anions appears enhanced, their relative order of nucleophilicity is close to that in dipolar, aprotic solvents[5,6]; for the anions employed here, it was in the sequence $HO^- > CH_3O^- \gg CN^-$. Consequently, HO^- and CH_3O^- having stronger nucleophilicities than CN^-, the lowering in yields of **4**, with concomitant increase in unreacted material, can be principally ascribable to the aforementioned, lessened supply of migrating acetyl groups.

It was also observed that acetonitrile has a leveling effect on the reactivity of diverse nucleophiles[6], provided that ion-pairing was avoided by crown-ether com-

TABLE I

APPROXIMATE YIELDS (%) OF COMPOUNDS **1** AND **4** OBTAINED FROM PENTA-*O*-ACETYL-1,1-BIS(BENZAMIDO)-1-DEOXY-D-GLUCITOL WITH DIFFERENT CATALYSTS IN ACETONITRILE

Compound	*Catalyst*					
	KCN	*KOH*	*KOMe*	*NaCN*	*NaOH*	*NaOMe*
4	48	32	29	23	12	14
1	41	52	62	64	70	70

plexation. It is known that the reactivity of a small nucleophile of high charge-density in a dipolar, aprotic solvent also depends on the behavior of the counter-ion in that solvent. The anions here employed, not being surrounded with tight solvation-shells tend to form "contact pairs", instead of "solvent separated pairs"[7] with the counter-ion, the anion in the former being a poor nucleophile, compared with that of the latter. We observed that catalysis with sodium as the counter-ion was less effective than that with the potassium cation (see Table I). Previously published, quantitative data[8] on the solvation of Na^+ and K^+ indicated that, in transfer from methanol (as the reference solvent) to acetonitrile, Na^+ loses, whereas K^+ gains, in solvation (which is quantitatively reflected in the opposed signs of the respective, solvent-transfer, activity coefficients[8]). This behavior shows, in acetonitrile, a different solvation capacity of both ions, which consequently affects the nucleophilicity of the anionic counterpart. Thus, Na^+, having a higher charge-density than K^+, forms more-stable ion-pairs possessing stronger attraction between the component ions, which implies a comparatively lowered nucleophilicity of the anion in its attack on the benzamido groups.

The deactivating effect provoked by ion association will be more pronounced the lower is the dielectric constant of the solvent, as in the case of benzene, whose weakly dissociating properties explain the low yield of transacylation product and the high yield of unreacted **1**.

When the reaction with potassium cyanide–acetonitrile was conducted in the presence of 10-crown-6 ether, the yields did not change much (46% of **4**, and 48% of **1**). This behavior, in a reaction that seemed clearly dependent on the nucleophilicity of the anion employed, was unexpected. As the heterogeneous character of the reaction persisted under the conditions employed, a restricted cation-complexing ability of the crown ether could be supposed. However, in this experiment was observed a better dispersion of the salt, of which only 50% was recovered by filtration of the acetonitrile suspension at the end of the heating period. Because, in the absence of the crown ether, the recovery was almost quantitative, the ether evidently helped to dissolve a substantial proportion of the catalyst, allowing a better interaction with the sugar.

The results obtained in this case show the role of factors independent of the nucleophilicity of the catalyst. One of them would be that the aforediscussed reacylation of the dibenzamido sugar backbone by the acyl cyanide has a limit to its efficiency in leading to compound **4**, imposed by the competitive presence of the previously transacylated molecules, whose chain reacylation does not lead to an improvement in the yield of **4**. Because benzoyl cyanide would also be present as a chain acylating agent, a double transacylation (dibenzamido-→mixed diamido-→ dibenzamido-alditol) cannot be excluded as a source of "unreacted **1**", the final yields of **1** and **4** being the result of a thermodynamic equilibrium. On this basis, the maximal yields obtainable were thus probably reached in the reaction without the crown ether, whose presence would, in consequence, be inutile.

On the other hand, if the polar, suspended solid plays an important role in the

catalysis, the proportionately lessened amount of heterogeneous phase in the presence of crown ether could also lower the foreseeable extent of the reaction.

The approximate yields of crystalline substances produced (compound **4** and unreacted **1**) with different bases and counter-ions are shown in Table I.

An alternative mechanism, similar to that proposed for intra-[9,14] and intermolecular[10] ester hydrolysis or transacylations in protic solvents, catalyzed by amide groups, could be envisaged, considering the liability of the amide proton, whose abstraction would enhance the basicity of the nitrogen atom. This would lead to the formation of 1-(*N*-acetylbenzamido)-1-benzamido-1-deoxy-D-glucitol, whose isolation would have been a valuable, mechanistic proof. The fact that this substance was not detected would not invalidate this alternative, as that compound could be only a transient intermediate to **4**. It is known that two acyl groups attached to a central atom are markedly labile[11] or, as was observed with some sugars[12], prone to *N*,*O*-migration in aprotic solvents, even at room temperature.

However, if the function of the cyanide ion were to generate the amide anion as the actual, reacting species, at the temperature of the reaction, a significant loss of hydrocyanic acid should have been observed. The quantitative recovery of potassium cyanide from the acetonitrile suspension indicated that, in our case, this pathway did not operate. In this context, the differences in efficiency observed with the different catalysts suggest that they function more as nucleophiles than merely as basic promoters of the amide-group ionization.

On the other hand, a similar role could be ascribed to the solvent, whose electron-donor capacity[13] is well known; but this view is invalidated by the poor results of the reaction conducted in homogeneous medium with potassium cyanide–acetonitrile, and that of the reaction in propanonitrile, a better electron-donor than acetonitrile[13]. The reaction in homogeneous medium also demonstrated that the amide group, by itself, is not a good, intramolecular nucleophile, in contrast to its behavior with some aromatic ester-amide systems, observed in neutral medium[14].

By similar reasoning, *i.e.*, involving the relative nucleophilicity of the solvent, could be postulated a competitive mechanism by attack of the nitrile group of the solvent upon C-1 of the sugar, with displacement of a benzamido group. The solvent–sugar adduct (nitrilium ion[15]) could afterwards undergo rearrangements and solvolysis (by the alcohol and water treatments) to afford an alkylamido group on C-1. This reaction would resemble known reactions of organic nitriles as nucleophiles in acidic and neutral media[15]. Although the low reactivity of C-1 and the basic medium employed were foreseeable drawbacks in our case, the activating effect of both benzamido groups, as well as the relatively drastic conditions employed, could probably promote such a reaction. This possibility was checked in the reaction of 1,1-bis(benzamido)-1-deoxy-penta-*O*-propanoyl-D-glucitol (**3**) with potassium cyanide–acetonitrile by n.m.r. spectroscopy of all of the syrupy and unresolved fractions obtained, which effectively failed to show the isolated methyl-peak that should appear by reaction with the solvent. Likewise, n.m.r.-spectral study of all of the fractions

obtained in the reaction of **2** in propanonitrile did not show the ethyl-group resonances predictable from an eventual, solvent insertion.

In the aforementioned reaction of **3**, an attempt was made, through an increased period of heating (66 h), to improve the yield of the transacylation reaction, but extensive browning took place, with lower yields of crystalline products. As a result of the more drastic conditions, a transacylation reaction with the second benzamido group occurred, and, after chromatography on a column of cellulose, not only compound **5** (25% yield), but also 1-deoxy-1,1-bis(propanonamido)-D-glucitol (4.6% yield) was isolated.

The ester–amide, acyl-exchange reactions so far described in the literature for aliphatic or aromatic amides are of the intermolecular type[10,16]. Related, intramolecular reactions mainly described the increased rate of hydrolysis of esters (especially in peptides) by the intermediate cooperation of neighboring amide functions, through cyclic imide intermediates[9], which did not imply acyl exchanges. The possibility of similar, intermolecular reactions in the studies described herein, employing a diversity of esters, opens perspectives to the chemistry of 1,1-bis(acylamido)alditols.

EXPERIMENTAL

General procedures. — Melting points (Kofler hot-stage) are not corrected. T.l.c. was conducted on plates of Silica Gel *G* (Merck) with the following eluants: (*A*) 97:3 (v/v) benzene–absolute ethanol, and (*B*) 17:3 (v/v) benzene–methanol. The spots were detected with (*C*) iodine vapor, (*D*) alkaline hydroxylamine–ferric nitrate for esters[17], and (*E*) 5% sulfuric acid in ethanol with subsequent heating at 140°. Paper chromatography was conducted on Whatman No. 1 paper by the descending technique, with (*F*) 5:2:2 (v/v/v) 1-butanol–ethanol–water as the developing solvent, which was also employed in column chromatography using Whatman CF-11 cellulose. The fractions from the column were evaporated at 60° and combined according to the results of paper chromatography and detection with (*G*) silver nitrate–sodium methoxide[18] or (*H*) aniline hydrogenphthalate[19]. Optical rotations were measured at 20–25° with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were recorded at 60 MHz and 20–25° with a Varian A-60 spectrometer, with sodium 4,4-dimethyl-4-silapentane-1-sulfonate as the internal, reference standard.

*Transacylation of penta-*O*-acetyl-1,1-bis(benzamido)-1-deoxy-*D*-glucitol in acetonitrile.* — Compound **2** (10 g, 16.3 mmol) was dissolved in acetonitrile (100 mL), and potassium cyanide (2.48 g; 38.2 mmol) was added; the mixture was maintained in suspension by magnetic stirring while it was heated at reflux temperature (80°) for 46 h. Then the solid in suspension was filtered off (2.28 g), and the filtrate was evaporated to dryness. The residue was dissolved in methanol (100 mL), and the solution was made alkaline (pH 10) with sodium methoxide. Compound **4** crystallized in several, successive crops contaminated with **1**. The final, mother liquors were evaporated to dryness, and treated with water (20 mL) affording almost pure,

crystalline **1**. The aqueous solution was evaporated to dryness, and the residue, taken up with isopropyl alcohol, gave a further crop of **4**. The several crops were collected, and recrystallized from ethanol, giving a total yield of 2.67 g (47.9%) of pure **4**, m.p. 195–196°, $[\alpha]_D$ −25.0° (*c* 1.5, pyridine). Paper chromatography (solvent *F*, reagent *G*) showed one spot, R_F 0.62; ν_{max}^{KBr} 1660 (CO), 1560, and 1540 cm^{-1} (N–H, C–N); n.m.r.: δ 7.40–7.85 (benzamido group), 5.90 (d, H-1, $J_{1,2}$ 5 Hz), 3.63–4.15 (m, H-2–H-6,6'), and 2.02 (acetyl group).

Anal. Calc. for $C_{15}H_{22}N_2O_7$: C, 52.63; H, 6.43; N, 8.28. Found: C, 52.31; H, 6.71; N, 8.26.

The total amount of unreacted compound **1** recovered was 2.66 g (41.2%), m.p. and mixed m.p. 201–203°, $[\alpha]_D$ +1.5° (*c* 1.6, pyridine), coincident with lit. data[20]. Evaporation of the final, 2-propanol solution gave a brown syrup that did not afford further crystalline substances from different solvents, and after column chromatography; it was a mixture of the aforedescribed products, plus ninhydrin-positive substances.

Periodate oxidation of compound **4**. — This compound (3.1 mg) was dissolved in a 15mM solution of sodium metaperiodate (3.42 mL), and was kept at 30°. Samples (0.1-mL) were taken at intervals, and diluted with water to 25 mL; the periodate consumed and the formaldehyde produced were determined according to spectrometric methods[21]. The following values were measured (mol of periodate/mol of substance): 3.40 (0.5), 3.47 (1), 3.51 (2), 3.81 (3), 3.81 (4), 3.96 (6), and 3.96 (24 h). The formaldehyde produced was 0.97 mol/mol at 6 h, and then remained constant.

1-Acetamido-2,3,4,5,6-penta-O-*acetyl-1-benzamido-1-deoxy*-D-*glucitol*. — A solution of compound **4** (270 mg) in 1:1 pyridine–acetic anhydride (10 mL) was kept for 24 h at room temperature, evaporated, and the residue macerated with water. The solid obtained (270 mg) was recrystallized from 2-propanol; m.p. 198–199°, $[\alpha]_D$ −17.0° (*c* 1.7, $CHCl_3$). T.l.c. showed one spot (solvent *B*, reagent *D*) of R_F 0.34. This acetate was *O*-deacetylated with methanolic ammonia almost quantitatively to compound **4**; n.m.r.: δ 7.30–7.90 (m, benzamido group), 5.99 (d, H-1, $J_{1,2}$ 7 Hz), 5.40 (m, 3 H, H-1–4), 4.96 (m, H-5), and 4.15 (H-6,6'); acetyl groups at δ 2.16, 2.11, 2.03, 1.97, 1.94, and 1.91.

Anal. Calc. for $C_{25}H_{32}N_2O_{12}$: C, 54.34; H, 5.79; N, 5.07. Found: C, 54.44; H, 5.92; N, 5.16.

1,1-Bis(benzamido)-1-deoxy-2,3,4,5,6-penta-O-*propanoyl*-D-*glucitol* (**3**). — Compound **1** (3.0 g; 7.5 mmol) was dissolved in pyridine (20 mL), and propanoic anhydride (20 mL, 151 mmol) was added. The mixture was kept for 24 h at room temperature, and then poured into ice–water; a solid (4.83 g, 94.8% yield) was obtained after several washings with water. Recrystallization from 1:1 methanol–water gave **3**, m.p. 112–114°, $[\alpha]_D$ −3.5° (*c* 1.6, ethanol); t.l.c. (solvent *B*, reagent *E*) showed one spot, R_F 0.69.

Anal. Calc. for $C_{35}H_{44}N_2O_{12}$: C, 61.40; H, 6.43; N, 4.09. Found: C, 61.52; H, 6.54; N, 4.12.

Transacylation of 1,1-bis(benzamido)-1-deoxy-2,3,4,5,6-penta-O-*propanoyl*-D-

glucitol. — Compound **3** (3.76 g, 5.4 mmol) was dissolved in acetonitrile (40 mL), and potassium cyanide (0.73 g, 11 mmol) was added. The suspension was refluxed for 66 h, and then the suspended solid was filtered off (0.82 g), and the filtrate evaporated to dryness. After the usual processing, 469 mg of 1,1-bis(benzamido)-1-deoxy-D-glucitol (**1**) precipitated from the methanol solution, which was then evaporated to a residue (968 mg) that, in paper chromatography (solvent *F*, reagent *G*), showed spots corresponding to compound **1** and to 1-benzamido-1-deoxy-1-propanamido-D-glucitol (**5**, R_F 0.72), 1-deoxy-1,1-bis(propanamido)-D-glucitol (R_F 0.60), and a spot (R_F 0.23) coincident with a standard of D-glucose. This mixture was chromatographed on a column (520 × 27 nm) of cellulose, but a satisfactory separation was not achieved; for several, crystalline fractions containing mixtures of two sugar diamides, the amount of each component was ascertained polarimetrically. From the column were isolated: (*a*) 1-deoxy-1,1-bis(propanamido)-D-glucitol (86.8 mg, 4.6% yield); m.p. 155°, $[\alpha]_D$ +6.0° (*c* 1.4, water); lit.[22] m.p. 155–156°, $[\alpha]_D$ +6.8°; n.m.r. (D_2O): δ 1.10 (t, 2 CH_3), 2.30 (q, 2 CH_2), 5.73 (d, H-1, $J_{1,2}$ 4.5 Hz), and 3.70–4.05 (m, H-2–H-6,6′).

(*b*) 1-Benzamido-1-deoxy-1-propanamido-D-glucitol (564 mg, 26% yield), m.p. 178–180°, $[\alpha]_D$ −37.5° (*c* 0.9, water); n.m.r. (D_2O): δ 7.40–7.90 (5 H, benzamido group), 5.92 (d, H-1, $J_{1,2}$ 5 Hz), 3.50–4.20 (m, H-2, H-6,6′), 2.30 (2 H, CH_2), and 1.10 (CH_3).

Anal. Calc. for $C_{16}H_{24}N_2O_7$: C, 53.93; H, 6.73; N, 7.86. Found: C, 53.40; H, 7.18; N, 7.64.

The total amount of 1,1-bis(benzamido)-1-deoxy-D-glucitol recovered was 617 mg (25% yield). The final fractions from the column were brown syrups that, in paper chromatography, showed reducing and ninhydrin-positive substances.

Potassium cyanide-catalyzed transacylation of compound **2** *in other solvents.* — (*a*) *In propanonitrile.* The reaction was conducted at 97° according to the technique already described, 50.6% of **1** being directly recovered by crystallization. The residual, brown syrup showed, in paper chromatography, the presence of **1**, compound **4**, and a reducing spot (of R_F 0.23). The n.m.r. spectrum of this syrup did not show peaks for a propanoyl group, thus excluding any reaction with the solvent. Attempts to separate further the components of this mixture, which did not crystallize despite several treatments, were not made.

(*b*) *In benzene.* Unreacted **1** recovered was in 61.9% yield; the compound **4** produced was 9.8%. The final syrup showed a diffuse sequence of many slow-moving substances on paper chromatograms.

(*c*) *In acetonitrile–crown ether.* Compound **2** (1 g) and 18-crown-6 (113 mg) were dissolved in acetonitrile (22 mL), and potassium cyanide (250 mg) was added. The suspension was magnetically stirred and refluxed for 46 h. The suspended solid then remaining was filtered off (120 mg), and the filtrate was percolated through a column containing 5 g of activated Silica Gel (to retain the ether). The solution was evaporated, the residue *O*-deacetylated, and the usual processing was used to separate

the crystalline components. The yields obtained were 46% of compound **4**, and 48% of compound **1**.

Transacylation of **2** *catalyzed by other bases.* — In all cases, the experiments were conducted with **2** (1 g) in acetonitrile at 80°, employing a 2:1 molar ratio of catalyst to sugar, and following the procedure already described. The proportion of each component in the mixtures of **1** and **4** was ascertained polarimetrically. The reaction with potassium cyanide was also repeated with 1 g of **2**, in order to compare the yields on the same basis; this small-scale experiment reproduced the results of the preparative one already described. The yields of starting, *O*-deacetylated **1** and of the mixed amide **4** obtained are shown in Table I.

Variations in the amount of catalyst. — (*a*) The molar ratio of suspended potassium cyanide to sugar was lowered to 0.4:1; the experiment was conducted as before, but the period of heating was extended to 72 h. The yields of unreacted **1** and **4** were 61 and 35.9%, respectively.

(*b*) Compound **2** (1 g) was dissolved in a saturated solution of potassium cyanide in boiling acetonitrile (10 mL). The clear solution was heated for 46 h, following the usual procedure. Compound **1** was recovered in 98.3% yield, and **4** was observed only as traces on paper chromatograms.

ACKNOWLEDGMENTS

The authors are indebted to UMYNFOR (CONICET-FCEN, Buenos Aires) for instrumental facilities and spectra, and to CONICET for partial financial support.

REFERENCES

1 M. E. GELPI AND R. A. CADENAS, *Adv. Carbohydr. Chem. Biochem.*, 31 (1975) 81–134.
2 M. E. GELPI AND R. A. CADENAS, *Carbohydr. Res.*, 28 (1973) 147–149; M. GALICIO, J. MOSETTIG, M. E. GELPI, AND R. A. CADENAS, *ibid.*, 108 (1982) 237–246.
3 A. DORNOW AND H. THEIDEL, *Angew. Chem.*, 66 (1954) 605.
4 J. F. BUNNETT, *Annu. Rev. Phys. Chem.*, 14 (1963) 271–290.
5 W. N. OLMSTEAD AND J. I. BRAUMAN, *J. Am. Chem. Soc.*, 99 (1977) 4219–4228.
6 C. L. LIOTTA, E. E. GRISDALE, AND H. P. HOPKINS, *Tetrahedron Lett.*, (1975) 4205–4208.
7 M. SZWARC, *Acc. Chem. Res.*, 2 (1969) 87–96.
8 R. ALEXANDER, E. C. F. KO, A. J. PARKER, AND T. J. BROXTON, *J. Am. Chem. Soc.*, 90 (1968) 5049–5069.
9 A. T. DE MOUILPIED AND A. RULE, *J. Chem. Soc.*, 91 (1907) 176–183; F. SALMON-LEGAGNEUR, *Bull. Soc. Chim. Fr.*, (1952) 580–585; A. R. BATTERSBY AND J. C. ROBINSON, *J. Chem. Soc.*, (1955) 259–269; E. SONDHEIMER AND R. W. HOLLEY, *J. Am. Chem. Soc.*, 76 (1954) 2467–2470; J. A. SHAFER AND H. MORAWETZ, *J. Org. Chem.*, 28 (1963) 1899–1901; S. A. BERNHARDT, A. BERGER, J. H. CARTER, E. KATCHALSKI, M. SELA, AND Y SHALITIN, *J. Am. Chem. Soc.*, 84 (1962) 2421–2434.
10 E. S. ROTHMAN, S. SEROTA, AND D. SWERN, *J. Org. Chem.*, 29 (1964) 646–650; E L. ALLRED AND M. D. HURWITZ, *ibid.*, 30 (1965) 2376–2381.
11 A. H. LAMBERTON AND A. E. STANDAGE, *J. Chem. Soc.*, (1960) 2957–2966; D. P. N. SATCHELL, *Q. Rev. (London)*, 17 (1963) 160–203.
12 T. D. INCH AND H. G. FLETCHER, JR., *J. Org. Chem.*, 31 (1966) 1821–1825.
13 C. REICHARDT, *Solvent Effects in Organic Chemistry*, Verlag Chemie, New York, 1979, p. 17.
14 M. T. BEHME AND E. H. CORDES, *J. Org. Chem.*, 29 (1964) 1255–1257.

15 J. J. RITTER AND P. P. MINIERI, *J. Am. Chem. Soc.*, 70 (1948) 4045–4048; J. E. GORDON AND G. C. TURRELL, *J. Org. Chem.*, 24 (1959) 269–271; Y. POCKER AND D. N. KEVILL, *J. Am. Chem. Soc.*, 87 (1965) 4771–4777; A. HASSNER, L. A. LEVY, AND R. GAULT, *Tetrahedron Lett.*, (1966) 3119–3123; J. R. POUGNY AND P. SINAŸ, *ibid.*, (1977) 4073–4076; R. R. SCHMIDT AND E. RÜCKER, *ibid.*, (1980) 1421–1424; A. A. PAVÍA, S. N. UNG-CHHUN, AND J. L. DURAND, *J. Org. Chem.*, 46 (1981) 3158–3160.
16 N. JOCHUM, K. RIEFSTAHL, AND A. TILLY, Ger. Pat. 1,164,397 (1964); *Chem. Abstr.*, 60 (1964) 15,742.
17 M. E. TATE AND C. T. BISHOP, *Can. J. Chem.*, 4 (1962) 1043–1048.
18 R. A. CADENAS AND J. O. DEFERRARI, *Analyst*, 86 (1961) 132–134.
19 S. M. PARTRIDGE, *Nature*, 164 (1949) 443.
20 P. BRIGL, H. MÜHLSCHLEGEL, AND R. SCHINLE, *Ber.*, 64 (1931) 2921–2934.
21 R. D. GUTHRIE, *Methods Carbohydr. Chem.*, 1 (1962) 435–441; J. C. SPECK JR., *ibid.*, 441–445.
22 A. S. CEREZO, J. F. SPROVIERO, V. DEULOFEU, AND S. DELPY, *Carbohydr. Res.*, 7 (1968) 395–404.