for 15 min at 25 °C. The alkaline solution was diluted with water and extracted with ethyl acetate. After drying, the solvent was evaporated to give 71 mg of crude hydroxy *tert*-butyl ether **12**: NMR δ 0.65 (s, 3 H, 18-CH_3), 0.85 (d, 3 H, J = 6 Hz, 27-CH_3), 0.89 (d, 3 h, J = 6 Hz, 21-CH_3), 0.98 (s, 3 H, 19-CH_3), 1.14 (s, 9 H, -CMe_3), 3.11 (m, 2 H, OCH_2), 5.32 (m, 1 H, 6-H).

To 20 mg of hydroxy *tert*-butyl ether **12** was added dropwise 0.6 mL of precooled trifluoroacetic acid in an ice bath and stirring was continued for 4 h; then the solution was concentrated in vacuo. To the residue was added 1 mL of 5% methanolic sodium hydroxide and the reaction was worked up in the same manner as described above. Purification by TLC (20% acetone in hexane) gave 4 mg of **13** and 3.7 mg of hydroxy ester **14** and some undetermined byproducts. The diol **13** had a smaller R_f value than that of the ester. **13**: mp 171-174 °C; NMR δ 0.66 (s, 3 H, 18-CH_3), 0.90 (d, 6 H, J = 6 Hz, 21,27-CH_3), 1.00 (s, 3 H, 19-CH_3), 3.54 (m, 3 H, 3,26-H), 5.32 (m, 1 H, 6-H); mass spectrum calcd for $C_{27}H_{46}O_2$ 402.349 78, found 402.349 65.

(25*S*)-3β-Acetoxy-26-[(*p*-bromobenzoyl)oxy]cholest-5-ene (18). A solution of 40 mg of crude **12** and 0.1 mL of acetic anhydride in 0.5 mL of pyridine was left standing overnight. The mixture was poured into water and extracted with methylene chloride. The combined extracts were washed with 2 N aqueous hydrochloric acid, saturated sodium bicarbonate, and water, then dried, and evaporated to give 41 mg of crude ester **15**: NMR δ 0.67 (s, 3 H, 18-CH_3), 0.91 (d, 6 H, J = 6 Hz, 21,27-CH_3), 1.01 (s, 3 H, 19-CH_3), 4.19 (m, 2 H, CH_2O).

To 40 mg of crude **15** was added dropwise 0.7 mL of precooled trifluoroacetic acid, and the mixture was stirred for 4 h in an ice bath and worked up in the same manner as described before. The crude mixture was purified on TLC (15% acetone in hexane) to give 4 mg of desired hydroxy ester **16** and diester **17**. NMR of **16**: δ 0.67 (s, 3 H, 18-CH_3), 0.91 (d, 6 H, J = 6 Hz, 21,27-CH_3), 1.01 (s, 3 H, 19-CH_3), 2.03 (s, 3 H, $COCH_3$), 3.45 (m, 2 H, CH_2O), 4.63 (m, 1 H, 3-H), 5.40 (m, 1 H, 6-H). NMR of **17**: δ 0.67 (s, 3 H, 18-CH_3), 0.91 (d, 6 H, J = 6 Hz, 21,27-CH_3), 1.01 (s, 3 H, 19-CH_3), 2.03 (s, 3 H, $COCH_3$), 4.19 (m, 2 H, CH_2O), 4.63 (m, 1 H, 3-H), 5.40 (m, 1 H, 6-H).

A solution of 4 mg of the alcohol **16** and 5 mg of *p*-bromobenzoyl chloride in 0.2 mL of pyridine was allowed to stand overnight and worked up as described above. The crude ester was purified on TLC (CH_2Cl_2 as eluant) to give 5 mg of *p*-bromobenzoate **18**: NMR δ 0.67 (s, 3 H, 18-CH_3), 0.91 (d, 3 H, J = 6 Hz, 21-CH_3), 1.00 (d, 3 H, J = 6 Hz, 27-CH_3), 1.01 (s, 3 H, 19-CH_3), 2.03 (s, 3 H, $COCH_3$), 4.17 (m, 2 H, CH_2O), 4.63 (m, 1 H, 3-H), 5.40 (m, 1 H, 6-H); mass spectrum, m/e 566 (M^+ - 60), 551 (M^+ - 75), 366 (M^+ - 260), 351 (M^+ - 275).

Acknowledgment. We are most grateful to Drs. Noal Cohen and Milan R. Uskokovič of Hoffmann-La Roche, Inc., Nutley, NJ, for helpful discussions and for the donation of a generous amount of (*S*)-(+)-3-hydroxy-2-methylpropanoic acid and to the Northeast Regional NSF-NMR Facility at Yale University for the registration of high-resolution NMR spectra.

Reverse Anomeric Effect of the Carbamoyl Group of 2,6-Anhydroheptonamides

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Received March 26, 1981

Photoaddition of formamide–acetone to 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol yields seven products; of these 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*ido*-heptonamide and 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*talo*-heptonamide, which can be converted into *C*-glycosyl compounds of α-D-gluco- and α-D-mannopyranoses, respectively, are of particular interest. In the same way, photoaddition of formamide–acetone to 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol gave six products, including 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*gluco*-heptonamide, a precursor of *C*-glycosyl compounds of α-D-galactopyranose. Analysis of the ^{1}H NMR spectral data of these formamide addition products revealed that all compounds in the "α-D" configuration existed predominantly in the $^2C_5$ conformation in $CDCl_3$ despite extensive 1,3-diaxial nonbonded interactions. However, when the more polar solvent Me_2SO-d_6 was used, these compounds existed only in the $^5C_2$ conformation. Anhydroheptonamides of the "β-D" configuration existed only in the $^5C_2$ conformation in either solvent. A polar effect that is a combination of a large reverse anomeric effect and other polar interactions is used to explain the shift in conformational equilibria.

Glycosides, oligosaccharides, and polysaccharides with the α-D configuration are important in nature, and their corresponding *C*-glycosyl analogues are of interest because of their potential as competitive inhibitors of glycohydrolases and glycosyltransferases. However, synthesis of *C*-glycosyl compounds of hexopyranoses (2,6-anhydroheptitols) in which the "glycosidic bond"[2] has the α-D configuration is more difficult than the synthesis of *C*-glycosyl compounds with the β-D configuration owing to two factors: (i) thermodynamic (the substituent group on the "anomeric"[2] carbon atom prefers the equatorial position over the axial position) and (ii) kinetic (participation of a 2-O-substitutent favors the relative trans configuration at the C-1 and C-2 carbon atoms, i.e., the β-D configuration in the case of those C-glycosyl compounds with the D-gluco and D-galacto configurations at C-3, -4, -5, and -6).[3] The purpose of this work was to find an efficient route to substituted 2,6-anhydroheptitols with the α-D configuration at C-1–C-2 which can then be transformed into a variety of *C*-glycosyl compounds.

Known methods based on displacement of the halogen atom of glycosyl halides by carbanions yield compounds with the β-D configuration of the anomeric carbon atom.[4]

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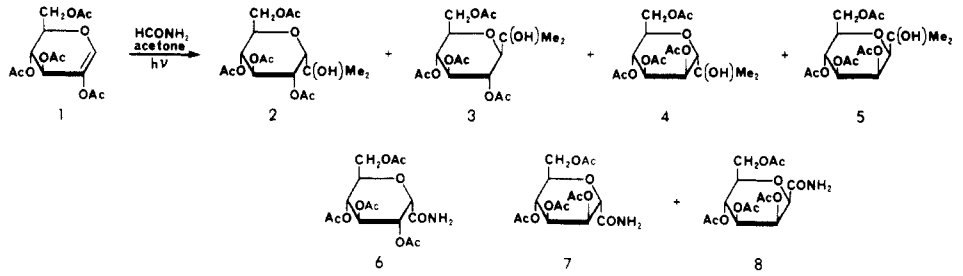
(2) The same nomenclature used with ordinary *O*-glycosides is used to describe the configuration of *C*-glycosyl compounds. Thus, a *C*-glycosyl compound with the α-D configuration is the compound with the same configuration as an α-D-hexopyranoside but with a methylene group in place of O-1, and what would be the central carbon atom in the O–C–O acetal linkage if the compound were an *O*-glycoside is still referred to as the anomeric carbon atom.

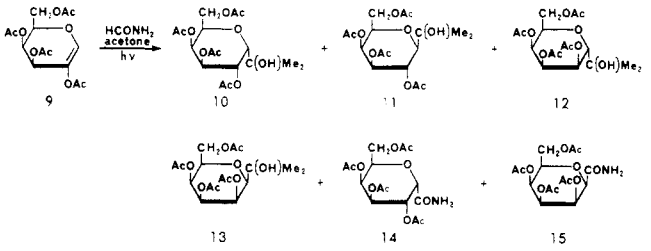
(3) Haynes, L. J. *Adv. Carbohydr. Chem.* **1963**, *18*, 227-258; **1965**, *20*, 357-369.

0022-3263/81/1946-3903$01.25/0

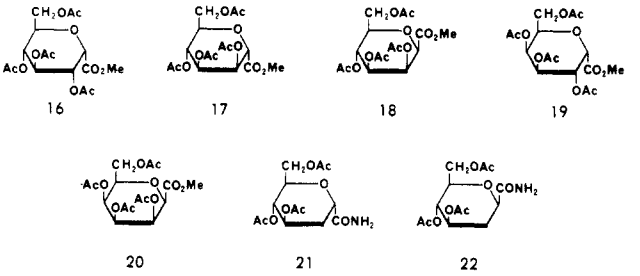
Scheme I



Scheme II



Scheme III



The same is true of *C*-glycosyl compounds obtained by Wittig reactions between free anomeric hemiacetal hydroxyl groups and phosphonium ylides.[5] The photochemical addition of 1,3-dioxolane to glycals proceeds with ease; however, again the majority of products have the β-D configuration.[6] Claisen rearrangement has been used to give a carbon–carbon bond in the α-D configuration at the anomeric carbon atom, but this reaction requires a difficultly available starting material, a derivative of D-allose.[7] Rosenthal and Ratcliffe[8] reported the carbamoylation of 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (**1**), the acetylated 2-hydroxyglycal derived from D-glucose. This photochemical addition of a carbonyl compound to the double bond of glycals thus offers an approach to the construction of *C*-glycosyl compounds with the α-D configuration. We have used this reaction with both **1** and 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (**9**), the acetylated 2-hydroxyglycal derived from D-galactose.

Results and Discussion

Irradiation of **1** in a formamide–acetone solution afforded a more complicated mixture than reported.[8] Four products from the addition of acetone (**2–5**) and three products from the addition of formamide (**6–8**) were obtained (See Scheme I). The less polar products (**2–5**) were easily separated from the amides (**6–8**). Further separation of both fractions was achieved by repeated chromatography. It was found, however, that the mixture of amides (**6–8**) could be used directly in the next steps. The ratio of compounds **2–5** was determined to be approximately 1:5:2:4 by chromatographic isolation. The ratio of amides **6–8** was determined to be 4:3:2 (total yield about 50%) from ^{13}C NMR spectral data of a chromatographically pure mixture.

Photoaddition of formamide–acetone to **9** furnished a similar mixture of four dimethylhydroxymethyl "*C*-glycosides" (**10–13**) in a ratio of 3:trace:1:2 (based on chromatographic isolation) but only two amides, **14** and **15**, in yields of 54% and 11%, respectively (see Scheme II). The amides (**14**, **15**) were separated from less polar products and easily purified by chromatography. An analytical sample of a mixture of **10**, **12**, and **13** was separated into pure components. The presence of traces of the β-D-galacto isomer (**11**) was observed in the ^1H NMR spectrum of its α-D anomer (**10**).

Carbamoylation of glycals **1** and **9** is regiospecific. The amide radical is added only to C-1; α attack is favored by electronic rather than steric effects (total yield of amides with the α-D configuration is similar for both starting materials). The next step, addition of a hydrogen radical, proceeds stereoselectively trans to the generated carbamoyl group, giving products with the α-D-gluco, α-D-galacto, β-D-manno, and β-D-talo configurations. Addition of the ketyl radical leading to dimethylhydroxymethyl compounds is less stereoselective.

Deduction of the configuration of the products was based on interpretation of their ^1H NMR spectra, analysis of which revealed interesting stereochemical properties of components **6–8**, **14**, and **15**. The coupling constants $J_{2,3}$, $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$ recorded in $CDCl_3$ (Table I) indicated that amides **6** and **14**, to which the α-D-gluco and α-D-galacto configurations were assigned, existed predominantly in the $^2C_5$ conformation (equivalent to the $^1C_4$ conformation in *O*-hexopyranosides). However, when Me_2SO-d_6 was used as the solvent, the equilibrium shifted significantly, and reversibly, toward the $^5C_2$ conformation (Figure 1). Roughly equal ring coupling constants $J_{3,4}$, $J_{4,5}$, and $J_{5,6}$ for **6** indicated that an equilibrium of two chair forms existed in $CDCl_3$.[9] Amides **8** and **15** do not display similar conformational properties; they existed only in the predicted $^5C_2$ conformation in either solvent. On this basis, the β-D-manno configuration was assigned to compound **8** and the β-D-talo configuration to **15**. Additional proof of configuration was obtained from the chemical shift of H-2 of **8** which was upfield compared to that of the α-D-

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(6) Ong, K.-S.; Whistler, R. L. *J. Org. Chem.* **1972**, *37*, 572–574.

(7) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1981**, *46*, 479–485.

(8) Rosenthal, A.; Ratcliffe, M. *Can. J. Chem.* **1976**, *54*, 91–96.

(9) It should be pointed out, however, that a boat conformation has been proposed for *N*-(tetra-*O*-acetyl-α-D-glucopyranosyl)-4-methylpyridinium bromide on the basis of $J_{4,5}$ = 5.7 Hz (larger than $J_{2,3}$ = 3.1 and $J_{3,4}$ = 3.2 Hz).[10]

(10) (a) Lemieux, R. U.; Morgan A. R. *Can. J. Chem.* **1965**, *43*, 2205–2213. (b) Lemieux, R. U. *Pure Appl. Chem.* **1971**, *27*, 527–547.

Table I. ^{1}H NMR Data, Specific Optical Rotation, and Percentage of $^5C_2$ Chair Conformation of Compounds 2-8, 10-22

compd	solvent	H-2	H-3	H-4	H-5	H-6	H-7	H-7′	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{6,7}$	$J_{6,7'}$	$J_{7,7'}$	$[\alpha]^{25}_D$	% $^5C_2$
2[b]	$CDCl_3$	3.77	5.16	5.33	4.91	4.34	4.39	*a*	3.7	5.8	5.0	6.0	6.7	2.7	−11.0		48
	Me_2SO-d_6	3.67	4.99	5.57	4.79	4.36	4.21	4.05	4.7	7.4	6.7	7.0	7.1	3.9	−12.0		67
3	$CDCl_3$	3.39	5.14	5.22	5.03	3.60	4.1-4.3		9.8	9.2	9.2	10.0	4.3	3.5	*a*	+14.4	
	Me_2SO-d_6	3.43	5.01	5.21	4.81	3.86	4.13	4.01	9.7	9.3	9.7	9.6	5.6	2.5	−12.2		
4	$CDCl_3$	3.62	5.56	5.63	5.17	4.14	4.3-4.5		3.2	3.8	8.7	7.1	*	*	*	−3.7	75
	Me_2SO-d_6	3.50	5.52	5.66	5.02	4.43	4.10	4.00	1.1	3.9	9.8	9.5	6.3	2.9	−11.8		99
5	$CDCl_3$	3.36	5.61	5.03	5.24	3.69	4.26	4.19	~1	3.4	10.3	9.8	5.7	3.1	−12.0	−14.0	
	Me_2SO-d_6	3.51	5.54	5.06	5.01	3.81	4.13	4.03	~1	3.2	10.4	9.8	6.0	2.6	−12.0		
6	$CDCl_3$	4.59	5.23	5.34	4.92	3.35	4.41	4.17	3.7	5.3	4.8	5.7	6.9	2.7	−11.0	+28.4	44
	Me_2SO-d_6	4.44	5.00	5.69	4.90	4.60	4.15	4.01	6.2	9.1	8.5	8.9	5.5	2.8	−12.5	+64.3	94
	$(CD_3)_2CO$	4.58	5.12	5.64	4.97	4.57	4.33	4.12	5.3	7.6	6.9	7.8	5.6	3.5	−12.2		76
7	$CDCl_3$	4.52	5.85	5.22	5.27	3.97	4.30	4.18	2.7	3.0	9.5	8.7	6.0	2.7	−12.5	+6.0	9
	Me_2SO-d_6	4.49	5.61	5.11	5.15	3.98	4.18	4.12	2.1	2.9	10.0	9.1	4.2	2.9	−12.7	+14.1	0
8	$CDCl_3$	4.19	5.82	4.12	5.25	3.74	4.31	4.23	1.5	3.5	10.0	9.5	5.6	3.0	−12.5	+3.0	
	Me_2SO-d_6	4.48	5.57	5.22	5.04	3.95	4.20	4.06	1.4	3.6	10.1	9.9	5.5	2.6	−12.2	−31.2	
	$(CD_3)_2CO$	4.45	5.75	5.25		4.02	4.25		1.5	*a*	*a*	*a*	*a*	*a*	*a*		
10	$CDCl_3$	3.79	5.25	5.34	5.42	4.45	4.73	4.12	2.3	5.2	3.5	5.8	9.6	3.2	−12.5	+42.0	22
	Me_2SO-d_6	3.69	5.16	5.46	5.23	4.02	4.40-4.56		3.5	6.8	3.7	9.4	*a*	*a*	*a*		44
11[b]	$CDCl_3$	3.39	*a*	5.06	*a*	*a*	*a*	*a*	9.6	10.0	3.6	*a*	*a*	*a*	*a*		
12	$CDCl_3$	3.71	5.21	5.62	5.24	4.48	4.59	4.12	6.8	3.8	3.3	4.5	9.0	3.1	−11.6	+43.6	34
	Me_2SO-d_6	3.55	5.29	5.55	5.13	4.52	4.20	3.98	2.2	4.4	3.5	2.1	8.2	4.5	−11.5		86
13[b]	$CDCl_3$	3.45	5.61	5.17	5.43	3.9	4.5		1.2	4.0	4.0	*a*	*a*	*a*	*a*		
14	$CDCl_3$	4.65	5.36	5.43	5.43	4.48	4.60	4.13	2.9	5.1	*a*	5.5	9.0	2.9	−12.0	+53.3	28
	Me_2SO-d_6	4.50	5.17	5.65	5.34	4.83	4.11	4.00	6.1	9.8	3.5	2.2	7.5	5.1	−11.7	+80.5	92
15	$CDCl_3$	4.21	5.72	5.16	5.33	3.99	4.32	4.17	1.5	3.4	4.1	1.4	7.4	5.5	−11.5	+14.0	
	Me_2SO-d_6	4.36	5.46	5.19	5.27	3.98	4.15	4.22	1.6	3.6	3.7	*a*	*a*	*a*	*a*	−7.0	
16[b]	$CDCl_3$	4.77	5.11	5.51	5.04	4.62	4.25	4.13	6.5	9.3	8.7	9.6	4.3	2.9	−12.0		
17[b]	$CDCl_3$	4.58	5.70	5.09	5.34	4.0	4.5		2.5	3.2	9.7	9.0	*a*	*a*	*a*		
18	$CDCl_3$	4.42	5.74	5.15	5.28	3.77	4.31	4.20	1.5	3.5	10.2	9.5	5.7	2.8	−12.5	−44.0	
19	$CDCl_3$	4.86	5.34	5.44	5.52	4.89	4.15	4.09	6.2	10.0	3.0	2.1	6.5	6.4	−11.5	+135.8	
20	$CDCl_3$	4.39	5.63	5.19	5.33	3.99	4.18-4.36		1.6	3.9	3.8	6.1	*a*	*a*	*a*	−24.0	
21[c]	$CDCl_3$	4.45	2.05 2.50	5.12	4.88	4.03	4.39	4.14	5.5 6.0	8.0 4.5	6.5	6.5				+16.0	
22[c]	$CDCl_3$	4.04	2.65 2.64	4.12	4.95	3.68	4.32	4.16	12.5 2.5							+31.0	

[a] Not resolved or too complex for analysis. [b] Compound was not obtained in pure form. [c] Data taken from ref 17.

Table II. ^{13}C NMR Chemical Shifts of Carbamoylated Compounds[a]

compd	C-2	C-3	C-4	C-5	C-6	C-7
6	72.85	67.97[b]	68.48[b]	67.08[b]	70.49	61.27
7	76.02	68.52[b]	69.17	66.13[b]	73.65	62.73
8	76.75	68.21[b]	71.75	65.72[b]	76.44	62.50
14	72.20	67.00	68.44	66.07	69.58	59.77
15	77.38	66.02	68.32	65.48	75.32	62.02

[a] $CDCl_3$, Me_4Si = 0 ppm. [b] Assignment uncertain.

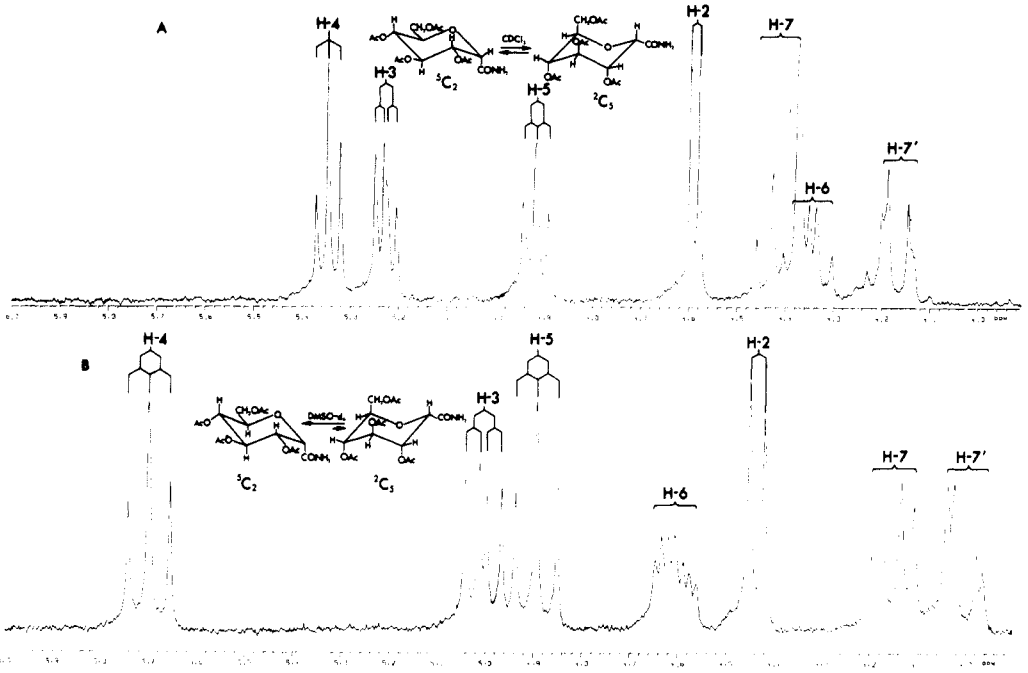

Figure 1. ^{1}H NMR spectra of **6** in $CDCl_3$ (A) and in Me_2SO-d_6 (B).

manno isomer **7** (axial proton signal shifted upfield compared to equatorial one) and from the specific optical rotations of amides **6–8**, **14**, and **15** and the methyl esters (**16–20**)[11] obtained from them (see Scheme III).

Amide **7**, to which the α-D-manno configuration was assigned, exhibited smaller diaxial coupling constants ($J_{4,5}$ and $J_{5,6}$) and a slightly larger diequatorial coupling constant ($J_{2,3}$) than expected for the $^5C_2$ conformation. Moreover, coupling constants between ring protons of **7** depended somewhat on the solvent used. Again these values can be explained, as for amides **6** and **14**, in terms of an equilibrium of the $^5C_2$ and $^2C_5$ forms. Taking into account $J_{2,3}$ = 1.5 Hz, Rosenthal and Ratcliffe[8] assigned the α-D-manno configuration to amide **8**; the same assignment was made by Matsuura et al.[12] for one of the products of the photoaddition of 1,3-dioxalone to **1**. However, a value of 1–1.5 Hz was found to be characteristic of the coupling between the axial H-5 and the equatorial H-4 protons in many hexopyranose derivatives bearing an axial OR group at C-4 and a terminal equatorial CH_2OAc, CH_3, or CO_2R group.[13] Thus, $J_{2,3}$ = 1.5 Hz, which is independent of the solvent used, could be assigned to the H-2 axial–H-3 equatorial coupling of amides with the β-D-manno (**8**) and β-D-talo (**15**) configurations. On the other hand, the diequatorial coupling constant $J_{1,2}$ found for many α-D-manno and α-L-rhamno hexopyranose derivatives with a pure $^4C_1$ conformation is 1.5–2.0 Hz.[14] This coupling constant is often larger in value than the $J_{1,2}$ (axial–equatorial) coupling found for β-D-manno anomers.[14] The value might be increased by conformational changes (see $J_{2,3}$ of compound **12**), but such a change should also affect other coupling constants between ring protons. What we conclude, therefore, is that $J_{2,3}$ = ~1.5 Hz is not proof of the α-D-manno configuration.

The shift of conformational equilibrium of compound **6** and **14** is also indicated by the optical rotation of both amides measured in $CHCl_3$ and Me_2SO (Table I) and by ^{13}C NMR data of **6–8**, **14**, and **15** (Table II). Although it is difficult to discuss the spectral data of a limited number of amides, a significant upfield shift of resonances owing to the ring carbon atoms of amides **6** and **14**, compared with appropriate data of other amides (**7**, **8**, and **15**), indicates a substantial population of $^2C_5$ conformers for amides with the α-D-gluco and α-D-galacto configurations.

The assignment of the configuration of dimethylhydroxymethyl compounds (**2–5** and **10–13**) is easier because spectra of eight possible isomers were recorded in $CDCl_3$ and Me_2SO-d_6 and compared. Compounds **2**, **4**, **10**, and **12** with trans positioned acetoxymethyl (C-8) and dimethylhydroxymethyl groups existed as an equilibrium of both $^5C_2$ and $^2C_5$ conformers, the position of the conformational equilibria depending on the sum of steric interactions in both forms.

By using $J_{2,3}$ = 6.5 Hz of ester **16** as characteristic for an equatorial–axial coupling constant (conformation $^5C_2$), $J_{2,3}$ = 1.5 Hz of amide **8** for an axial–equatorial coupling constant[15] (conformation $^2C_5$), $J_{2,3}$ = 9.8 Hz of compound **11** for a diaxial coupling constant, and $J_{2,3}$ = 2.0 Hz for a diequatorial coupling constant[15] (see $J_{2,3}$ of **7** in Me_2SO-d_6), the position of conformational equilibria of compounds **2–8** and **10–15** could be estimated (Table I). In this way it was found that, in $CDCl_3$ solution, compounds **2**, **6**, **7**, **10**, **12**, and **14** (α-D-gluco, α-D-galacto, and α-D-talo configurations were in the $^2C_5$ conformation, and compounds **3**, **5**, **8**, **11**, **13**, and **15** having the β-D configuration existed only in the $^5C_2$ conformation.

The position of the conformational equilibria of compounds **2–8** and **10–15** depends on the difference between

(11) For preparation of compounds **16–20**, intermediates in the synthesis of "*C*-glycosides" with the α-D configuration and phosphonate analogs of D-glucose and D-galactose 1-phosphates, see Chmielewski, M.; BeMiller, J. N.; Cerretti, D. P.; *Carbohydr. Res.*, in press.

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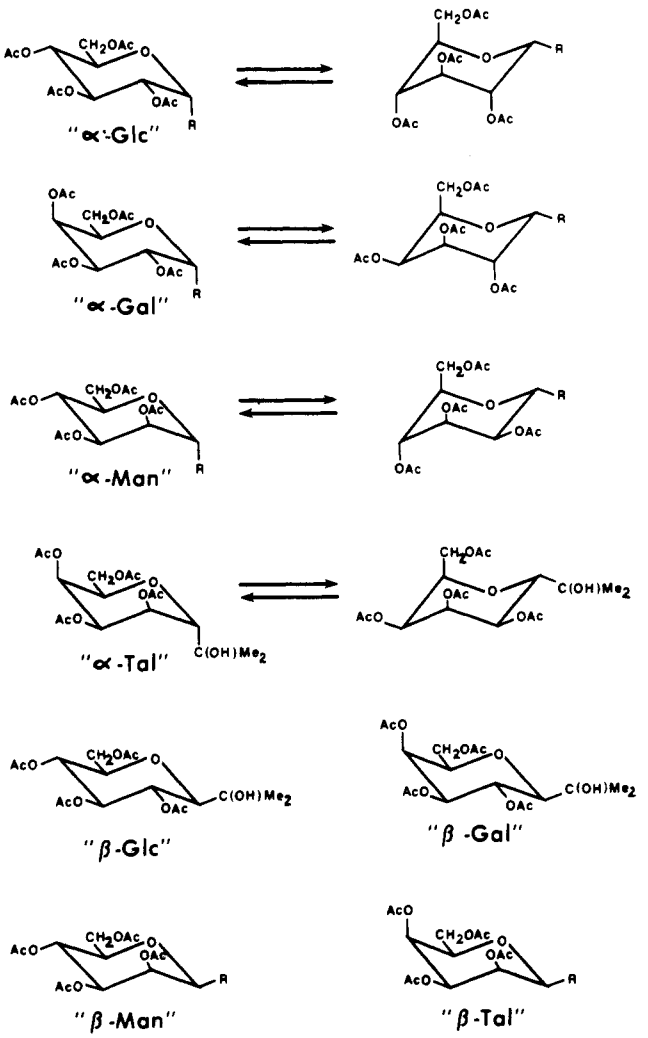
(15) For dimethylhydroxymethyl compounds **2**, **4**, **10**, and **12**, $J_{2,3}$ = 1.1 Hz was taken as a representative value of axial–equatorial coupling (see $J_{2,3}$ of **5** and **13**) and $J_{2,3}$ = 1.0 Hz as a representative value for diequatorial coupling (see $J_{2,3}$ of **4** in Me_2SO-d_6).

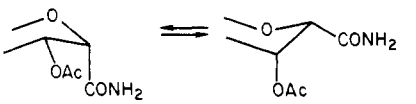
Scheme IV



the free-energy content of the components involved in the equilibrium, i.e., the $^5C_2$ and $^2C_5$ conformers. The free-energy content is the sum of all steric and polar interactions between substitutents and between substituents and the ring oxygen atom. Approximate interaction energies are known for a number of groups and atoms attached to the pyranose ring.[16] These values, however, do not explain the conformational behavior of compounds **2**, **4**, **6**, **7**, **10**, **12**, and **14**. It is clear that at least two effects play an important role in the conformational equilibrium: the free conformational energy of the R group (carbamoyl, dimethylhydroxymethyl or methoxycarbonyl) and the gauche interaction between the adjacent acetoxy group (on what was formerly C-2) and the R groups.[17] Although a similar position of the conformational equilibria of amides **6**, **7**, and **14** and the dimethylhydroxymethyl compounds **2**, **4**, and **10** with the same configurations suggests a similar basis for any shift, their nature is different. Steric interactions of the bulky dimethylhydroxymethyl group should be similar to that of the *tert*-butyl group. However, the position of the conformational equilibrium of **2**, **4**, **10**, and **12** depended on the solvent used (Table I), indicating that interactions of the dimethylhydroxymethyl group with neighboring substituents depends also on a polar factor or on specific solvation. On the other hand, the carbamoyl group is a small but polar group ($\mu \simeq 4$D).[19] Using known values of conformational interactions characteristic for hexopyranoses and the free-energy difference between both conformers found for compounds **2–8** and **10–15** from their ^{1}H NMR data (see above), we could estimate values of two new effects. The free conformational energy for a carbamoyl group at the anomeric carbon atom (of a hexopyranose peracetate in $CDCl_3$) is 3.6 ± 0.5 kcal·mol^{-1}, whereas for the dimethylhydroxymethyl group, the value[20] is 3.5 kcal·mol^{-1} (found for *tert*-butyl ~5 kcal·mol^{-1}).[21] The free energy of a gauche interaction of a carbamoyl group with an adjacent acetoxy group is about 2.7 ± 0.5 kcal·mol^{-1}, and that for a dimethylhydroxymethyl group with an adjacent acetoxy group[22] is 2.7 ± 0.5 kcal·mol^{-1}.

It is known that an alkoxycarbonyl group at C-2 of a tetrahydropyran ring has a larger free conformational energy than does cyclohexane (1.6 vs. 1.2 kcal·mol^{-1}). This difference was attributed to the reverse anomeric effect.[23] For the more polar carbamoyl group, the reverse anomeric effect should be larger in value. The reverse anomeric effect found for the *N*-(tetra-*O*-acetyl-α-D-*gluco*- and α-D-*manno*-pyranosyl)pyridinium and imidazolonium salts,[10,24] owing to the positive charge located on the glycosylamine nitrogen atom, was large enough to shift the equilibrium toward the $^1C_4$ form for both epimers.[10b] The carbamoyl group, having only a partial positive charge on the carbonyl carbon atom, has a similar effect.

The unexpected large gauche repulsion between the carbamoyl group and the adjacent acetoxy group found in amides **6–8**, **14**, and **15** could be assigned to a polar interaction between these groups. This interaction, however, was not found for imidazolonium salts, the conformational equilibrium of the α-D-manno salt being shifted only slightly toward $^1C_4$ compared to the equilibrium for the α-D-gluco epimer.[10b] The conformational properties of amides **6–8**, **14**, and **15** can be better explained in terms of an additional polar effect which is connected with the relative destabilization of arrangement A vs. arrangement



A ($^5C_2$) B ($^2C_5$)

B and is caused by a better compensation of partial dipole

(16) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Interscience: New York, 1966; pp 351–432 and references cited therein.

(17) ^{1}H NMR data published by Rosenthal and Zanlungo[18] for the 3-deoxy analogues (**20** and **21**) of compounds **6**(**7**) and **8** suggest a similar conformational behavior of compound **21** (Table I).

(18) Rosenthal, A.; Zanlungo, A. *Can. J. Chem.* **1972**, *50*, 1192–1198.

(19) Robin, M. B.; Bovey, F. A.; Basch, H. "The Chemistry of Amides"; Zabicky, J., Ed.; Interscience: New York, 1970; pp 1–72.

(20) For calculations, the following energies (in kcal·mol^{-1}) of interaction between substituents characteristic of the hexopyranose ring were used: gauche interactions OAc/CH_2OAc = 0.9, OAc/OAc = 0.35; 1:3 diaxial interactions OAc/H = 0.18, OAc/ring O = 0, OAc/OAc = 1.6, OAc/CH_2OAc = 2.2, CH_2OAc/H = 1.1. These values were obtained by modifying literature data[14] to give a better fit. Calculated values are approximations based upon these energies; errors are at least 0.5 kcal·mol^{-1}.

(21) Reference 14, p 44.

(22) These values are only approximations because available interaction increments are only approximate and calculations of the position of conformational equilibrium derived from ^{1}H NMR data are also approximate. The values found for the dimethylhydroxymethyl group seem to be reasonable. However, the appropriate increments found for the carbamoyl group are unusually large.

(23) Anderson, C. B.; Sepp, D. T. *J. Org. Chem.* **1968**, *33*, 3272–3276.

(24) Paulsen, H.; Gyorgydeak, Z.; Friedmann, M. *Chem. Ber.* **1974**, *107*, 1590–1613.

vectors in B of polar groups involved in this conformational equilibrium. This effect accompanies the reverse anomeric effect and 1,3-diaxial interaction of the carbamoyl group with protons at C-4 and C-6 in array A and is the force that moves the conformational equilibrium of **6** and **14** toward the $^2C_5$ form. The poorer compensation of dipole vectors in the $^2C_5$ conformation of the α-D-manno isomer **12** and the gauche interaction between the carbamoyl group and the neighboring acetoxy group cause **7** to exist predominantly in the $^5C_2$ form.

Experimental Section

Melting points were measured with a Thomas-Hoover Uni-melt melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained by using a Nicolet NT-200 spectrometer with Me_4Si as an internal standard. Infrared spectra were recorded with a Beckman IR-10 spectrometer. Optical rotations were determined with a Bendix ETL-NPL automatic polarimeter. Irradiations were done with a 450-W Hanovia, medium-pressure, mercury-vapor lamp fitted with a Pyrex filter in a 600-mL photolysis cell. Each reaction mixture was purged with argon for 2 h before irradiation was initiated. Thin-layer chromatography (TLC) was done on aluminum-backed silica gel 60 plates (E. Merck); components were detected by spraying the plates with an aqueous solution containing 20% H_2SO_4, 2.5% molybdic acid, and 1% ceric sulfate and heating them to ~120 °C. Column chromatography (silica gel 60, 230–400 mesh, E. Merck) was performed by gravity elution (40 g of silica gel/1 g of sample) or by the rapid chromatography method described by Still et al.[25] Compounds **1** and **9** were obtained according to the procedure of Lemieux and Lineback.[26]

Carbamoylation of 2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol (1).[8] A solution of **1** (14 g) in formamide (90 mL, redistilled) and acetone (30 mL, redistilled) was added dropwise to an irradiated solution of formamide (460 mL) and acetone (20 mL). The reaction was complete after 3–4 days (TLC; 5:5:1 v/v, hexane–EtOAc–EtOH). The reaction mixture was then diluted with 1 L of saturated aqueous NaCl solution and extracted with four portions of dichloromethane (total volume 1.5 L). The extract was reduced in volume to 700 mL, washed 3 times with saturated aqueous NaCl solution, dried with $MgSO_4$, filtered, and evaporated to a syrup. Rapid chromatography (250 cm^3 silica gel; 5:5:1 v/v, hexane–EtOAc–EtOH) resolved the products into two fractions, a less polar mixture of alcohols **2–5** (3.0 g) and a more polar mixture of amides **6–8** (8 g).

A sample (1 g) of the mixture of alcohols (**2–5**) was separated by repeated column chromatography using 100:100:3 v/v, petroleum ether–Et_2O–EtOH as eluant. The following three fractions were obtained. (1) 4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*talo*-octitol (**4**): 0.07 g; colorless syrup; IR (film) 3500 (OH), 1740, 1240 cm^{-1} (acetyl). Anal. Calcd for $C_{17}H_{26}O_{10}$: C, 52.30; H, 6.71. Found for a mixture of **2–5**: C, 52.57; H, 6.89. (2) 4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*gulo*- and D-*ido*-octitols: 0.42 g (**3**, 83%; **2**, 17%); colorless syrup; IR (film) 3500 (OH), 1750, 1230 cm^{-1} (acetyl). (3) 4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-D-*galacto*-octitol (**5**): 0.27 g; colorless crystals, mp 141–143 °C; IR (Nujol) 3500 (OH), 1750, 1230 cm^{-1} (acetyl).

A sample (2.0 g) of the mixture of amides (**6–8**) was separated by repeated gravity column chromatography using 50:50:3 v/v petroleum ether–EtOAc–EtOH as eluant. Two fractions were obtained. The first fraction (0.8 g) contained amides **6** and **7**. The second fraction (0.4 g) was 2,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*galacto*-heptonamide (**8**): colorless crystals, mp 151–153 °C; IR (Nujol) 3490, 3360, 1690, 1600 (amide), 1745, 1240 cm^{-1} (acetyl). Anal. Calcd for $C_{15}H_{21}NO_{10}$: C, 48.00; H, 5.64; N, 3.73. Found for the mixture of **6–8**: C, 47.99; H, 5.63; N, 3.68.

Amides **6** and **7** were separated by repeated gravity chromatography using 49:1 v/v $CHCl_3$–MeOH as eluant. 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*ido*-heptonamide (**6**): 0.4 g; colorless crystals, mp 159–161 °C; IR (Nujol) 3500, 3380, 1700, 1600 (amide), 1740, 1240 cm^{-1} (acetyl). 3,4,5,7-Tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*talo*-heptonamide (**7**): 0.1 g; colorless crystals, mp 187–189 °C; IR (Nujol) 3500, 3390, 1680, 1570 (amide), 1740, 1230 cm^{-1} (acetyl).

Carbamoylation of 2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-*lyxo*-hex-1-enitol (9). A solution of **9** (14.0 g) was reacted according to the procedure used for **1**. Rapid chromatography (250 mL of silica gel; 5:5:1 v/v, petroleum ether–EtOAc–EtOH) of a crude postreaction mixture afforded three fractions. The first fraction (2.5 g) contained a mixture of alcohols (**10–13**). The second fraction (8.5 g) contained 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*gluco*-heptonamide (**14**): mp 186–189 °C; IR (Nujol) 3490, 3330, 1680, 1590 (amide), 1740, 1230 cm^{-1} (acetyl). Anal. Calcd for $C_{15}H_{21}NO_{10}$: C, 48.00; H, 5.64; N, 3.73. Found: C, 48.09; H, 5.64; N, 3.68. The third fraction (1.7 g) was 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-*altro*-heptonamide: mp 186–187 °C; IR (Nujol) 3500, 3400, 1690, 1590 (amide), 1745, 1230 cm^{-1} (acetyl). Anal. Calcd for $C_{15}H_{21}NO_{10}$: C, 48.00; H, 5.64; N, 3.73. Found: C, 47.97; H, 5.67; N, 3.83. A sample of the mixture of **10–13** (1.0 g) was separated by using gravity column chromatography and 100:100:3 v/v petroleum ether–Et_2O–EtOH as eluant. The following fractions were obtained. 4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-L-*allo*-octitol (**12**): 0.20 g; colorless syrup; IR (film) 3500 (OH), 1750, 1240 cm^{-1} (acetyl). Anal. Calcd for $C_{17}H_{26}O_{10}$: C, 52.30; H, 6.71. Found for a mixture **12** and **10**: C, 52.39; H, 6.89. 4,5,6,8-Tetra-*O*-acetyl-3,7-anhydro-1-deoxy-2-*C*-methyl-D-*glycero*-L-*gluco*-octitol (**10**): 0.20 g; colorless syrup; IR (film) 3500 (OH), 1750, 1230 cm^{-1} (acetyl). The third fraction (0.06 g) contained **13** and traces of **11** and **10**.

Acknowledgment. This research was supported by a grant (R01 GM 26193) from the National Institutes of Health.

Registry No. **1**, 3366-47-0; **2**, 66807-63-4; **3**, 67844-47-7; **4**, 58825-12-0; **5**, 67844-48-8; **6**, 58825-10-8; **7**, 58825-11-9; **8**, 78393-34-7; **9**, 14125-78-1; **10**, 78420-07-2; **11**, 78477-96-0; **12**, 78420-08-3; **13**, 78420-09-4; **14**, 78393-35-8; **15**, 78393-36-9; **16**, 78477-97-1; **17**, 78477-98-2; **18**, 78477-99-3; **19**, 78478-00-9; **20**, 78478-01-0.

(25) Still W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

(26) Lemieux, R. U.; Lineback, D. R. *Can. J. Chem.* **1965**, *43*, 94–105.