The rearrangement which took place in the preparation of **2** is known.[4-6] The dibromide **2**, on treatment with triethyl phosphite, gave the phosphonate **3** in 70% yield based on the C_{20} diol. Selective reduction of **3** with Lindlar catalyst[7] resulted in retinyl phosphonate (**4**). The nmr spectra and the analytical data of **2–4** were compatible with the assigned structures.

The phosphonate **4** and vitamin A aldehyde **5** were stirred with sodium methoxide in pyridine at 0° to yield β-carotene. The reduction of an ethynyl function with Lindlar catalyst leads to the *cis* configuration. Since phosphonate reactions in general give *trans* couplings, the reaction of **4** and **5** was expected to lead to 11-*cis*-β-carotene. The uv spectrum of the product contained a "*cis* peak"[8] at 338 mμ; however, attempts to prepare an analytical sample of 11-*cis*-β-carotene by column chromatography or recrystallization led to a *cis–trans* mixture because of the mild condition at which isomerization took place.

Isomerization of the crude β-carotene by heating in heptane,[8] followed by recrystallization from methylene chloride, afforded *trans*-β-carotene (**6**) in 61% yield based on **5**.

Experimental Section[9]

1,8-Dibromo-3,7-dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,6-nonadien-4-yne (**2**).—3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,7-nonadien-4-yne-1,6-diol (**1**, 100 g) was placed in a 2-l. flask with ethyl ether (500 ml) and pyridine (1 ml). Phosphorous tribromide (32 ml) dissolved in hexane (200 ml) was added dropwise to the stirred solution at −5° in 3 hr. The reaction mixture was poured onto crushed ice in a separator and extracted with ethyl ether. The combined extracts were washed with water, saturated sodium bicarbonate solution, and, finally, water. The solvent was removed under vacuum after drying over anhydrous sodium sulfate. The dibromide **2** which was obtained as an orange syrup (125 g) and was used without further purification for the next step had uv max (EtOH) 285 mμ. The nmr spectrum showed signals for a *gem*-dimethyl group at δ 0.98 and 1.05 (singlets), a singlet at 1.65 (>C=C< CH_3), multiplet at 1.97 ($J \cong 1$ cps) (≡C(CH_3)C=), a doublet at 2.13 (J = 1.2 cps) (>CCH_3), a multiplet at 1.40 and 2.10 (-$CH_2CH_2CH_2$-), a signal at 2.78 (C=CCH_2-), a doublet at 4.20 (J = 8 cps) (CH_2Br), C*H*Br at 4.78, a singlet at 5.78 (=C*H*C≡C-), a triplet at 5.97 (J = 8 cps) (=C*H*-). *Anal.* Calcd for $C_{20}H_{28}Br_2$: Br, 37.32. Found: Br, 37.30.

3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,6,8-nonatrien-4-yn-1-ylphosphonic Acid Diethyl Ester (**3**).—The dibromide **2** (107 g), toluene (100 ml), and triethyl phosphite (83 g) were placed in a distillation flask and heated to 145° in 4 hr. The solvent was removed and the resulting residue was distilled through a centrifugal molecular still (Type CMS, Consolidated Vacuum Corp.) to yield 80.9 g (70%) of **3**, $n^{25}D$ 1.567, mp 28°, $E^{1\%}_{1\,cm}$ (318 mμ) 834 (in ethyl alcohol). *Anal.* Calcd for $C_{24}H_{37}O_3P$: C, 71.25; H, 9.22. Found: C, 71.23; H, 9.16.

3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8-nonatetraen-1-ylphosphonic Acid Diethyl Ester (**4**).—A solution of **3** (50 g) in toluene (1.5 l.) was hydrogenated in the presence of Lindlar catalyst.[7] The catalyst was filtered off and washed with toluene. On removal of the solvent under vacuum, **4** was obtained as a yellow syrup: 49 g (98%); $n^{25}D$ 1.555; nmr ($CDCl_3$), δ 5.15–6.70 (*m*, 6, olefin H), 4.10 (quintet, 4, OCH_2), 2.56 (*d* of *d* J = 7.5 and 21.5 cps, CH_2P), 1.96 (s, 6, two on-chain CH_3 groups), 1.78 (s, 3, terminal CH_3), 1.30 (t, 3, CH_3CH_2), 1.02 (s, 6, C(CH_3)$_2$). *Anal.* Calcd for $C_{24}H_{39}O_3P$: C, 70.70; H, 9.66. Found: C, 71.02; H, 9.84.

***trans*-β-Carotene** (**5**).—Retinyl phosphonate (**4**, 36 g) and vitamin A aldehyde (20 g) were dissolved in pyridine (280 ml) and the solution was cooled to 0°. Sodium methoxide (19 g) was added in portions to the stirred reaction over a period of 2 hr, while the temperature was maintained at 0–5°. After stirring for 3 hr, the reaction mixture was diluted with water and extracted with benzene. The combined extracts were washed with cold (5%) sulfuric acid and then with water until neutral. The solvent was removed under vacuum to yield 53 g of crude β-carotene: uv max (cyclohexane) 285, 338, 425, 448 ($E^{1\%}_{1\,cm}$ 834), and 475 mμ. A sample, after two recrystallizations from methylene chloride–methyl alcohol (methylene chloride washed with sodium bicarbonate) melted at 128°; uv max ($E^{1\%}_{1\,cm}$ 1300). Continued recrystallization resulted in a gradual increase in melting point with a loss of uv absorption at 338 mμ.

The crude β-carotene was isomerized by heating in heptane (100 ml) at reflux for 20 hr under an atmosphere of nitrogen. The reaction mixture was cooled to 20°, diluted with additional heptane (50 ml), and filtered. After two recrystallizations from methylene chloride, 23 g (61%) of *trans*-β-carotene was obtained (mp 181°), $E^{1\%}_{1cm}$ (454 mμ) 2500.

Registry No.—**2**, 18793-78-7; **3**, 18793-79-8; **4**, 18793-80-1; **6**, 116-32-5.

Acknowledgment.—We wish to thank Dr. A. Steyermark and his staff for the microanalyses, Dr. F. Forrester and Mr. J. Volpe for the ultraviolet spectra, and Dr. F. Vane and Dr. T. Williams for the nmr spectra.

(6) J. D. Surmatis, U. S. Patent 2,760,998 (1956).
(7) H. Lindlar, *Helv. Chim. Acta*, **35**, 446 (1952).
(8) J. D. Surmatis, J. Maricq, and A. Ofner, *J. Org. Chem.*, **23**, 157 (1958).
(9) Melting points were determined in vacuum capillaries and are uncorrected. The nuclear magnetic resonance (nmr) spectrum was obtained with a Varian A-60 spectrometer using deuteriochloroform as solvent and tetramethylsilane as the internal reference.

The Synthesis of Derivatives of 2,3-Diamino-2,3-dideoxy-D-galactose

HANS H. BAER AND K. S. ONG[1]

Department of Chemistry, University of Ottawa, Ottawa, Canada

Received August 26, 1968

Aminations of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*threo*-hex-2-enopyranoside (**2**) with aqueous ammonia or, better, with a molten mixture of dry ammonium acetate and acetamide furnished methyl 4,6-*O*-benzylidene-2-*N*-benzylideneamino-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**4**). In this reaction, one part of intermediate methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**3**) evidently was *N*-benzylidenated by benzaldehyde lost from another part. Acetic anhydride converted **4** into methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**5**) which by acidic de-*O*-benzylidenation yielded methyl 2-acetamido-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**6**) (4,6-diacetate, **7**). Catalytic hydrogenation of **6** followed by *N*-acetylation and *N,O*-acetylation, respectively, gave methyl 2-acetamido-3-amino-2,3-dideoxy-β-D-galactopyranoside hydrochloride (**8**), methyl 2,3-diacetamido-2,3-dideoxy-β-D-galactopyranoside (**9**), and methyl 2,3-diacetamido-4,6-di-*O*-acetyl-2,3-dideoxy-β-D-galactopyranoside (**10**).

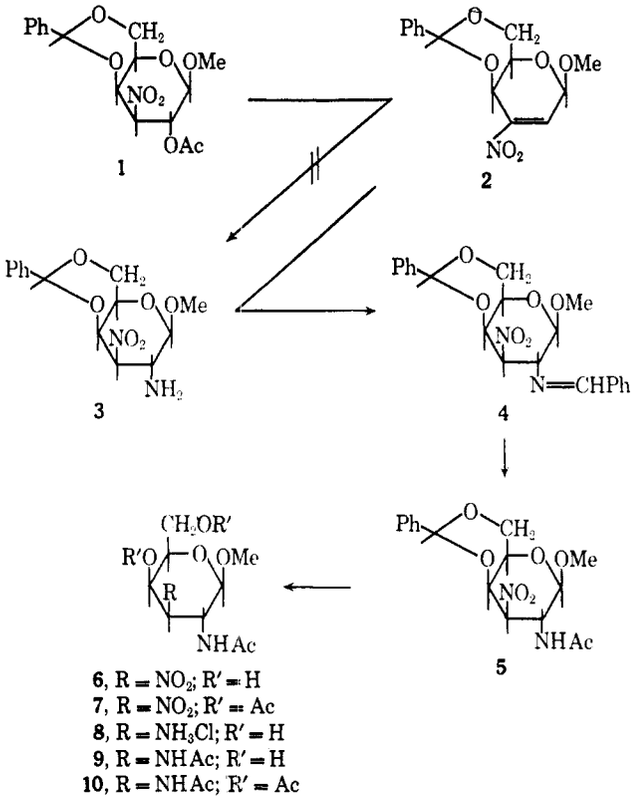
A recent paper from this laboratory commented upon the significance of diamino sugars in the chemistry of antibiotics and reported a new synthesis of 2,3-diamino-2,3-dideoxy-D-glucose.[2] The principle consisted of the

(1) Taken from the Ph.D. thesis of K. S. O., University of Ottawa, 1968.
(2) H. H. Baer and T. Neilson, *J. Org. Chem.*, **32**, 1068 (1967).

introduction of an amino function in position 2 of a suitable derivative of 3-deoxy-3-nitro-D-glucose, followed by reduction to the diamino stage. We have now employed the same method to synthesize derivatives of hitherto unknown 2,3-diamino-2,3-dideoxy-D-galactose.

Encouraged by success of the analogous procedure in the *gluco* series we at first tried to produce the *vic*-aminonitro glycoside **3**, methyl 2-amino-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside, by an elimination–addition reaction of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-galactopyranoside (**1**) with aqueous ammonia. However, the attempt failed inasmuch as the benzylidene blocking group evidently suffered far-reaching base-catalyzed fission, and no aminonitro sugar could be isolated. In concurrent work[3] a similar sensitivity of **1** was noticed in attempted Michael reactions with nitroalkanes in the presence of triethylamine, and this remarkable fact stood in contrast to the fair stability under the same conditions, in the *gluco* isomer of **1**. The present experience again emphasizes the role which steric factors appear to play in the alkaline, eliminative opening of acetal rings that are activated by a β-nitro group.[4]

SCHEME I



In the reaction from **1** to **3**, if it had been successful, nitro olefin **2**, methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-*threo*-hex-2-enopyranoside, would have been an intermediate (Scheme I). It was reasoned that olefin **2** itself was not liable to lose benzaldehyde but that such loss, which requires carbanion formation at the secondary nitro grouping, had occurred in **1** or/and in **3**. Therefore, we proceeded to examine the amination of **2**, to be used as a crystalline starting material in place of **1**, hoping that a fast formation of **3**, possibly under milder conditions and without its prolonged exposure to an alkaline medium, would afford an isolable amount of product. This approach appeared promising since **2** had served well as a Michael acceptor for nitroalkanes.[3]

Short heating of **2** in a mixture of tetrahydrofuran and aqueous ammonia produced a crystalline product whose structure, however, was not that of **3**. In the infrared spectrum it showed no N–H stretching vibrations for a primary amino group but a pronounced band at 1645 cm^{-1} which could be attributed to a C=N– grouping. A nitroalkane band (1550 cm^{-1}) was present, as were bands attributable to phenyl (690, 745 cm^{-1}). An nmr spectrum showed a singlet at τ 4.24 assignable to the benzylic proton of the 4,6-*O*-benzylidene group that was presumed to have survived, but the ratio of its intensity to that of the aromatic protons (τ 2.6 region) was 1:10 rather than 1:5 as expected for **3**. It was concluded that a second aromatic ring had entered the molecule, and this was corroborated by elemental analysis and mass spectroscopic molecular weight determination. The product was a Schiff base, methyl 4,6-*O*-benzylidene-2-*N*-benzylidenamino-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**4**), thought to have arisen from originally formed amine **3** and benzaldehyde engendered by a partial decomposition of the latter. The yield in **4** was 22% in terms of isolated sugar derivative (44% in terms of the stoichiometry 2 **2** → **4**).

$$2\ \mathbf{2} + 2NH_3 \longrightarrow 2\ \mathbf{3}$$

$$\mathbf{3} \longrightarrow PhCHO + \text{decomposition product(s)}$$

$$PhCHO + \mathbf{3} \longrightarrow \mathbf{4}$$

An improvement in the amination of **2** was achieved when a dry mixture of the nitro olefin, ammonium acetate, and acetamide in the weight ratio 4:5:10 was heated to melting for 3 min. A product was obtained which again seemed to consist largely of the Schiff base (**4**). Without purification it was treated with acetic anhydride in methanol whereby, in comparatively slow reaction, it furnished methyl 2-acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**5**) in a yield of 35–38% based on **2**. The same *N*-acetyl derivative was obtained, in an over-all yield of 15%, from (purified) **4** made in aqueous ammonia medium. Thus the advantage of employing the "dry" amination is obvious.

Acid-catalyzed de-*O*-benzylidenation of **5** afforded methyl 2-acetamido-2,3-dideoxy-3-nitro-β-D-galactopyranoside (**6**) which gave the 4,6-diacetate **7** on acetylation catalyzed by boron trifluoride.[5] Catalytic hydrogenation over platinum in the presence of 1 equiv of hydrochloric acid converted **6** into methyl 2-acetamido-3-amino-2,3-dideoxy-β-D-galactopyranoside hydrochloride (**8**), from which were subsequently obtained the 2,3-diacetamido derivative **9** and the fully acetylated derivative **10** by standard acetylation procedures.

The compounds in this series had been anticipated to possess the D-*galacto* configuration since in previous additions of a variety of nucleophiles to **2**[3] and its D-*erythro* isomer[2,3,6,7] all isolated products save one had

(3) H. H. Baer and K. S. Ong. *Can. J. Chem.*, **46**, 2511 (1968).

(4) Alkaline fissions of β-nitro acetals and ketals have been observed repeatedly [H. H. Baer and F. Kienzle, *Ann.* **695**, 192 (1966), and further literature cited there], but in only one case has attention been drawn to differential stabilities in a pair of diastereoisomers: H. O. L. Fisher and H. H. Baer, *ibid.*, **619**, 53 (1958).

(5) H. H. Baer, F. Kienzle, and F. Rajabalee, *Can. J. Chem.*, **46**, 80 (1968).

(6) H. H. Baer, T. Neilson, and W. Rank, *ibid.*, **45**, 991 (1967).

(7) H. H. Baer and F. Kienzle, *J. Org. Chem.*, **32**, 3169 (1967).

had 2,3-diequatorial substituent arrangement. The one exception happened to involve the ammonia addition to the D-*erythro* isomer,[2] and although the main product in that case, too, was the 2,3-diequatorial one, there was isolated a minor isomer later found[8] to have the D-*manno* configuration. In any event it was necessary to ascertain the steric course of the present amination, and this was possible through nmr spectra of compounds **7** and **10**.

A 100-MHz spectrum of **7** in deuteriochloroform exhibited at lowest field a broad one-proton doublet (splitting, 7 cps; τ ~3.85, variable with concentration) caused by the amide *N*–H. Centered at τ 4.2 was a two-proton multiplet attributable to overlapping signals of H-3 and H-4. The anomeric proton H-1 gave a sharp doublet at τ 4.85 with a splitting of 8 cps. The two protons at C-6 and that at C-5 gave partially overlapping signals in the region τ 5.8–6.1. A broad one-proton multiplet spaced over about 25 cps adjoining upfield could be assigned to H-2 since, upon its irradiation, the *N*–H doublet collapsed to a singlet. The glycosidic OCH_3 group gave its signal at τ 6.48, and three acetyl signals occurred in the τ 8 region. The large coupling of 8 cps between H-1 and H-2 conclusively proved diaxial orientation of these protons in accordance with the assumed β-D-*galacto* configuration. Axial orientation of H-3, the second feature requiring proof, could only be inferred from the width of the H-2 signal which suggested a large value for $J_{2,3}$. However, the spectrum in deuteriochloroform of the diacetamido-di-*O*-acetyl derivative **10** clearly supported the *galacto* configuration. While the ring proton signals were ill resolved, and were weak due to poor solubility of the compound, the substituent methyl resonances occurred as five sharp singlets of equal intensity. Signals at τ 6.53, 7.87, and 7.98 were assignable to the C-1 methoxyl, the axial C-4 acetoxyl, and the C-6 acetoxyl, respectively. The two acetamido groups gave signals at τ 8.09 and 8.16, and these shifts clearly indicated equatorial[9] rather than axial[10] substituent orientation at both C-2 and C-3.

Experimental Section[11]

Methyl 4,6-*O*-Benzylidene-2-*N*-benzylidenamino-2,3-dideoxy-3-nitro-β-D-galactopyranoside (4). A. Ammonia Procedure.—Nitroolefin **2**[12] (500 mg) was dissolved in tetrahydrofuran (7 ml), 15 *N* aqueous ammonium hydroxide (1 ml) was added, and the mixture was heated to reflux, with efficient stirring for 3 min. Upon cooling the mixture was evaporated with several additions of ethanol. The yellowish residue was dissolved in methanol (5 ml) from which crude **4** crystallized in the course of several hours at +4°. An additional, small crop of **4** was obtained by adding a few drops of water to the mother liquor (yield 150 mg, 22%). Two recrystallizations from methanol gave **4** as fine needles: mp 219° dec, $[\alpha]_D$ +43.1° (dimethylformamide); infrared bands (cm^{-1}) 1550 (NO_2), 1645 (C=N), 745, 690 (phenyl).

Anal. Calcd for $C_{21}H_{22}N_2O_6$: C, 63.31; H, 5.57; N, 7.03; mol wt, 398.4. Found: C, 63.74; H, 5.83; N, 7.63; mol wt, 398 (mass spectrum).

B. Ammonium Acetate Procedure.—A mixture of ammonium acetate (0.5 g) and acetamide (1.0 g) was allowed to melt on a steam bath, and nitroolefin **2**[12] (400 mg) was then introduced with stirring. A clear melt resulted but shortly began to resolidify in part. After 3 min of heating, the yellow mixture was cooled externally and then triturated well with about 100 ml of cold water. The water-insoluble material was filtered off with suction, washed with water, and dried in a desiccator. The dry material was heated in methanol (70 ml), and any undissolved matter was filtered off. The methanolic solution contained **4** and was used for preparing **5** as described below.

C. Attempted Amination of 2-*O*-Acetate 1.—A solution of methyl 2-*O*-acetyl-4,6-*O*-benzylidene-3-deoxy-3-nitro-β-D-galactopyranoside (**1**)[8] (100 mg) in warm tetrahydrofuran (15 ml) was cooled to room temperature and then vigorously stirred for 1 hr with 15 *N* aqueous ammonium hydroxide (4 ml). The mixture was then evaporated to give a syrup that smelled strongly of benzaldehyde. A thin layer chromatogram showed that all of **1** had been consumed, but at least four more slowly moving components were visible. Addition of water to the syrup did not cause separation of any crystallizable, water-insoluble sugar derivative.

Methyl 2-Acetamido-4,6-*O*-benzylidene-2,3-dideoxy-3-nitro-β-D-galactopyranoside (5).—Crystalline **4** (120 mg, from preceding section A) was dissolved with warming in methanol (30 ml). Upon cooling to room temperature, acetic anhydride (2 ml) was added regardless of partial recrystallization of **4**. The reaction mixture was stirred for 24 hr (during which period **5** began to separate) and was then evaporated to dryness by adding three consecutive portions of ethanol. The residue was suspended in a small amount of methanol, filtered, washed, and recrystallized from nitromethane to afford **5** (76 mg, 71.6%) that gradually decomposed without melting above 285°: $[\alpha]_D$ +26.9° (dimethylformamide); infrared bands (cm^{-1}) 3310 (NH), 1660 (amide I), 1555–1550 (amide II and NO_2), 750, 700 (phenyl).

Anal. Calcd for $C_{16}H_{20}N_2O_7$ (352.3): C, 54.54; H, 5.72; N, 7.95. Found: C, 54.68; H, 5.84; N, 8.03.

The methanol solution containing **4** (from section B) and acetic anhydride (3 ml) were stirred for 24 hr at room temperature. Work-up as described previously furnished 188 mg of **5** (178 mg after recrystallization from nitromethane). The yields based on **2** were 35–38% in several similar experiments.

Methyl 2-Acetamido-2,3-dideoxy-3-nitro-β-D-galactopyranoside (6).—Compound **5** (640 mg) and cation exchange resin (3.2 g of Rexyn 101, H^+) were refluxed with magnetic stirring for 6 hr in a mixture of methanol (52 ml) and water (13 ml). The filtrate was evaporated to give a residue which crystallized upon dehydration by ethanol. The material was dissolved in water, a trace of insoluble matter was filtered off, and the solution was brought to dryness again by several coevaporations with ethanol. The residue was recrystallized from methanol–ethyl acetate to yield 375 mg of **6**: mp 200° dec, raised to 208° (decomposition, darkening from 195°) by another recrystallization; $[\alpha]_D$ +16.6° (water); infrared bands (cm^{-1}) 3630, 3500 (OH), 3340 (NH), 1655 (amide I), 1540 (amide II), 1560 (NO_2).

Anal. Calcd for $C_9H_{16}N_2O_7$ (264.2): C, 40.90; H, 6.10; N, 10.60. Found: C, 40.76; H, 6.24; N, 10.77.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-dideoxy-3-nitro-β-D-galactopyranoside (7).—Two drops of boron trifluoride etherate was added to a suspension of **6** (150 mg) in acetic anhydride (2 ml). The glycoside dissolved, and after 20 min at ambient temperature the mixture was poured into methanol (20 ml) and evaporated with three subsequent additions of excess methanol and two additions of ethanol. The resulting syrup was chilled and triturated with ice-cold water (0.5 ml), which induced crystallization. The isolated and dried crystals, mp 162–165°, weighed 128 mg, and another 12 mg was obtained from the mother

(8) F. Kienzle, Ph.D. Thesis, University of Ottawa, 1968.

(9) Ample data recorded in the literature show that equatorial acetamido groups on pyranose rings resonate above τ 8.0 (in $CDCl_3$ solution): (a) D. Horton, J. B. Hughes, J. S. Jewell, K. D. Philips, and W. N. Turner, *J. Org. Chem.*, **32**, 1073 (1967); (b) S. Inouye, *Chem. Pharm. Bull. Jap.*, **14**, 1112, 1179 (1966); (c) H. Agahigian, G. D. Vickers, M. H. von Saltza, J. Reid, A. I. Cohen, and H. Gauthier, *J. Org. Chem.*, **30**, 1085 (1965); (d) H. H. Baer and T. Neilson, *Can. J. Chem.*, **43**, 840 (1965); (e) H. H. Baer, L. D. Hall, and F. Kienzle, *J. Org. Chem.*, **29**, 2014 (1964); (f) A. C. Richardson and K. A. McLauchlan, *J. Chem. Soc.*, 2499 (1962).

(10) Axial acetamido groups on pyranose rings have been found to resonate at τ 7.92–7.96; examples include derivatives of 2,3-diacetamido-2,3-dideoxy-D-mannose,[8] 2-acetamido-2-deoxy-D-mannose,[9e] and 4-acetamido-4,6-dideoxy-L-talose [S. W. Gunner, W. G. Overend, and N. R. Williams, *Carbohyd. Res.*, **4**, 498 (1967)].

(11) Melting points were taken in capillaries in an electric aluminum block apparatus. Evaporations were done *in vacuo* at a bath temperature of 35–40°. Optical rotations were measured at about 23° in a Perkin-Elmer automatic polarimeter, Model 141, with concentrations of approximately 1% unless otherwise specified. Infrared spectra were recorded on a Beckman IR-8 instrument using Nujol mulls.

(12) H. H. Baer, F. Kienzle, and T. Neilson, *Can. J. Chem.*, **43**, 1829 (1965).

liquor (yield, 71%). The product melted at 164–165° and had $[\alpha]_D$ +8.8° (chloroform), after one recrystallization from ethyl acetate–petroleum ether (bp 30–60°) (with the latter solvent being added cautiously so as to avoid gel formation); infrared bands (cm^{-1}) 3360 (NH), 1745 (NO_2), 1660 (amide I), 1540 (amide II), 1552 (NO_2).

Anal. Calcd for $C_{13}H_{20}N_2O_9$ (348.3): C, 44.83; H, 5.79; N, 8.05. Found: C, 44.66; H, 5.95; N, 8.14.

Methyl 2-Acetamido-3-amino-2,3-dideoxy-β-D-galactopyranoside Hydrochloride (8).—Compound **6** (320 mg) and 0.1 *N* hydrochloric acid (12.4 ml) in water (50 ml) were shaken under hydrogen, at 23° and atmospheric pressure, in the presence of prehydrogenated platinum catalyst (120 mg of PtO_2). Hydrogen consumption (86.5 ml) was complete within 3 hr (calcd for 3 mol at STP, 81.5 ml). Removal of the catalyst and evaporation (with several additions of ethanol) gave a residue which was recrystallized from methanol–ethyl acetate to yield **8** (304 mg, 92.5%), mp 210–215° dec. A further recrystallization gave **8** (269 mg): mp 222–223° dec; $[\alpha]_D$ +0.6° (water); infrared bands (cm^{-1}) 3400–3330 (NH, OH), 3000 (broad, NH_3^+), 1660 (amide I), 1535 (amide II), 1620, 1590 (NH_3^+ bending).

Anal. Calcd for $C_9H_{19}ClN_2O_5$ (270.7): C, 39.96; H, 7.07; N, 10.35. Found: C, 39.92; H, 7.20; N, 10.36.

Methyl 2,3-Diacetamido-2,3-dideoxy-β-D-galactopyranoside (9).—Amine hydrochloride **8** (320 mg) in water (10 ml) containing methanol (1 ml) was stirred in an ice bath for 90 min with acetic anhydride (0.2 ml) and 6 ml of Dowex 1-X8 (carbonate form). The filtrate from the anion exchange resin was briefly stirred with a small amount of cation exchange resin, Rexyn 101 (H^+), and then evaporated to give a colorless syrup that was dehydrated by evaporation with ethanol. For crystallization, the material was dissolved in boiling acetone (10 ml) containing several drops of water, and the hot solution was allowed to cool very slowly (to avoid gel formation) over a period of several hours. Compound **9** was so obtained as microscopic needles (200 mg, plus 54 mg by concentration of the mother liquor) that melted with decomposition at 265–267°. Recrystallized once in the same way, **9** (232 mg) decomposed at 269–270° upon very slow heating, or above 300° upon more rapid heating. The rotation was $[\alpha]_D$ −34.3 (water); infrared bands (cm^{-1}) 3580, 3420, 3340, 3300 (OH, NH), 1645 (amide I), 1565, 1555 (amide II). The product apparently contained water of crystallization, the analytical values corresponding to a hemihydrate after drying *in vacuo* at 56°.

Anal. Calcd for $C_{11}H_{20}N_2O_6 \cdot 0.5H_2O$ (285.3): C, 46.20; H, 7.42; N, 9.82. Found: C, 46.04; H, 7.37; N, 9.66.

Methyl 2,3-Diacetamido-4,6-di-*O*-acetyl-2,3-dideoxy-β-D-galactopyranoside (10).—Amine hydrochloride **8** (100 mg) was acetylated overnight at room temperature with acetic anhydride (0.75 ml) and pyridine (4 ml), the inhomogenous mixture being stirred magnetically. Exhaustive evaporation with ethanol, toluene, and again ethanol furnished a gel which was dried in a desiccator. Inspection by tlc revealed that the acetylation was incomplete, a more slowly moving product[13] being present in addition to the main product (**10**). The material was therefore subjected to a second, identical acetylation which yielded chromatographically homogeneous **10** as colorless needles [mp 258–260°, $[\alpha]_D$ −27.8° (*c* 0.5, chloroform)] upon crystallization from methanol and ethyl acetate; infrared bands (cm^{-1}) 3330, 3300 (NH), 1740 (ester carbonyl), 1665, 1650 (amide I), 1550, 1540 (amide II).

Anal. Calcd for $C_{15}H_{24}N_2O_8$ (360.4): C, 50.00; H, 6.71; N, 7.78. Found: C, 49.91; H, 6.60; N, 7.87.

Registry No.—**4**, 18888-65-8; **5**, 18888-66-9; **6**, 18907-05-6; **7**, 18888-67-0; **8**, 18888-68-1; **9**, 18888-69-2; **10**, 18888-10-5.

Acknowledgment.—Financial support by the National Research Council of Canada and the Life Insurance Medical Research Fund, Rosemont, Pa., is gratefully acknowledged.

(13) Part of this product crystallized from methanol-ethyl acetate; it melted at 265–267° dec and exhibited infrared absorption at 3480 (hydroxyl) and at 1730 cm^{-1} (ester carbonyl), the latter band being less intense relative to the corresponding band in **10**.

The Synthesis and Solvolysis of Some D-Glucopyranosyl Bromides Having a Benzyl Group at C-2

TOSHIO ISHIKAWA[1] AND HEWITT G. FLETCHER, JR.

National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Public Health Service, U. S. Department of Health, Education, and Welfare, Bethesda, Maryland 20014

Received June 10, 1968

The long-range effect of *p*-nitrobenzoyl *vs.* benzyl groups on the formation and solvolysis of various D-glucopyranosyl bromides, all having a benzyl group at C-2, has been studied. For this purpose, 2-*O*-benzyl-3,4,6-tri-*O*-*p*-nitrobenzoyl-α-D-glucopyranosyl bromide (α **3**), its anomer (β **3**), 2,3-di-*O*-benzyl-4,6-di-*O*-*p*-nitrobenzoyl-β-D-glucopyranosyl bromide (β **7**), 2,3,4-tri-*O*-benzyl-6-*O*-*p*-nitrobenzoyl-β-D-glucopyranosyl bromide (β **9**), and 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide (α **11**) have been synthesized through the action of hydrogen bromide on the corresponding 1-*O*-*p*-nitrobenzoyl esters in dichloromethane solution. In each case, and regardless of the anomeric configuration of the esters used, the β-D-glucopyranosyl bromide is formed first; equilibration with the more stable α-D-glucopyranosyl bromide then follows at a rate which is inversely related to the number of *p*-nitrobenzoyl groups present in the halide. The rates of methanolysis of the five D-glucopyranosyl bromides, with and without added bromide ion, have been measured and the ratio of methyl D-glucopyranosides has been determined in each case. In general, the β-D-glucopyranosyl bromides are more reactive than their α anomers and, with one exception, the α-D-glucopyranoside is the main product regardless of the anomeric configuration of the halide used. These and other facts suggest that the more rapid solvolysis of the equatorial bromides is probably the dominant feature of these reactions. Theoretical considerations aside, β **3** has been found to be an easily accessible substance and may prove valuable in the synthesis of α-D-glucopyranosides.

In an earlier paper[2] from this laboratory, a study of the methanolysis of 2-*O*-benzyl-3,5-di-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride, 2,3-di-*O*-benzyl-5-*O*-*p*-nitrobenzoyl-α-D-arabinofuranosyl chloride, and 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride was described and it was shown that acyl groups further removed from C-1 than C-2 (*i.e.*, either at C-5 or at C-3) in these glycofuranosyl halides exert a stabilizing effect upon the C-1–halogen bond. In this earlier study, all of the substrates had the same anomeric configuration and each was substituted at C-2 with the nonparticipating benzyl group to avoid the added complication of

(1) Associate in the Visiting Program of the National Institutes of Health, 1966–1967.

(2) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Amer. Chem. Soc.*, **87**, 4636 (1965).