(0.13 g) isolated in 7.5 and 6.5% total yield, respectively. The residue at distillation described above was crystallized from ether. Recrystallization from benzene–petroleum ether yielded the colorless needles (0.28 g, 7.5%). Recrystallizations afforded a pure analytical bicyclo[2.2.0]hexene derivative (**13**): mp 199–200°; uv max (95% C_2H_5OH) 207 mμ (log ε 4.56), 314 (4.46); and *ca.* 230 (sh) (4.14); ir (Nujol) 1730 (ester C=O), 1160 (ester C—O), 760, and 700 cm^{-1} (monosubstituted phenyl); nmr ($CDCl_3$) 2.70–3.10 (20) m, 4.28 (2) s, 6.58 (6) s, 7.50 (4) t (J = 7 Hz), and 7.90 (4) (J = 7 Hz).

Anal. Calcd for $C_{38}H_{38}O_4$: C, 81.98; H, 6.52; mol wt, 556. Found: C, 81.79; H, 6.54; mol wt, 556.

This compound **13** discolored the solutions of both potassium permanganate in acetone and bromine in carbon tetrachloride at room temperature. On the contrary, it could not be hydrogenated under the conditions in which *trans-trans*-1,4-diphenylbutadiene in ethanol was hydrogenated on platinum black at room temperature.

Hydrogenation of Methyl *trans*-2-Styryl 2-phenylcyclopropanecarboxylate (14a).—Methyl *trans*-2-styryl-2-phenylcyclopropanecarboxylate (0.078 g, 0.28 mmol) was hydrogenated in ethanol–ether (18:1, 90 ml) with palladium black catalyst (70 mg) at room temperature under atmospheric pressure. Hydrogen uptake (1 mol equiv) was complete after 1 hr. After the solvent was removed, the residual oil was subjected to an alumina column chromatography (7.8 g). Elution with ether gave methyl 2-(2′-phenylethyl)-2-phenylcyclopropanecarboxylate (**15a**, 0.058 g, 71%). Recrystallization from petroleum ether gave a pure analytical sample: mp 44–46°; nmr (CCl_4) 2.70–3.18 (10) m, 6.40 (3) s, 7.55–7.71 (2) m, 7.90–8.20 (3) m, and 8.46–8.82 (2) m.

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19. Found: C, 81.60; H, 7.17.

Hydrogenation of Methyl *cis*-2-Styryl-2-phenylcyclopropanecarboxylate (14b).—Methyl *cis*-2-styryl-2-phenylcyclopropanecarboxylate (**14b**, 0.233 g, 0.83 mmol) was hydrogenated in ethanol (40 ml) with palladium black catalyst (90 mg). Theoretical amount of hydrogen was absorbed after 1 hr. After the solvent was removed, the residual oil was chromatographed on alumina (30 g). Elution with petroleum ether gave colorless oil, methyl 2-(2′-phenylethyl)-2-phenylcyclopropanecarboxylate (**15b**, 0.166 g, 71%), which crystallized in an ice box. An analytical sample was obtained by preparative vpc (Apiezon L, 2 m, 264°) and recrystallized from petroleum ether: mp 10–12°; nmr (CCl_4) 2.80–3.11 (10) m, 6.69 (3) s 7.32–8.50 (6) m, and 8.82–9.10 (1) m.

Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.39; H, 7.19 Found: C, 81.53; H, 7.19.

Preparation of Authentic Materials.—To a stirred solution of 2,4-diphenylbut-1-ene[35] (7.0 g, 34 mmol) in dry ether (10 ml) containing cuprous chloride (2.5 g) was added a solution of methyl diazoacetate (6.2 g, 62 mmol) in dry ether (10 ml) for a period of 1 hr at 35° and the mixture was stirred for an additional 1 hr. After cuprous chloride was filtered off, the ether was evaporated, and residual oil was chromatographed on an alumina column (130 g). From a fraction eluted by petroleum ether (150 ml), colorless oily material was obtained, which was rechromatographed to give the starting olefin (4.8 g) and **15a** (0.52 g). Further elution with the same solvent (150 ml) gave the oily substance which was purified by rechromatography on alumina, yielding the starting olefin (0.2 g) and cyclopropanecarboxylate **15b** (0.58 g). Compounds **15a** and **15b** obtained in this reaction were identical in all respects with hydrogenated products of **14a** and **14b**, respectively.

Registry No.—**1** tosylhydrazone, 18793-81-2; **2** tosylhydrazone, 18793-82-3; **3**, 18793-83-4; 1,2,3-triphenylcyclopropene-3-carboxylic acid, 18793-84-5; **4**, 18076-30-7; **6**, 18793-86-7; **10**, 18793-87-8; 3,4-diphenyl-5-(2′-carboxyethyl)pyrazole, 18793-88-9; **13**, 18793-89-0; **14a**, 18793-91-4; **14b**, 18793-90-3; **15**, 18793-92-5.

(35) R. M. Parkhurst, J. O. Rodin, and R. M. Silverstein, *J. Org. Chem.*, **28**, 120 (1963).

Sugar Lactams. III. Synthesis of Five-, Six-, and Seven-Membered Analogs[1-3]

STEPHEN HANESSIAN[4]

Research Laboratories, Parke, Davis and Company, Ann Arbor, Michigan 48106

Received September 24, 1968

Sugar lactams having five-, six-, and seven-membered rings have been prepared by the reductive cyclization of appropriate azido lactones or carboxylic acids. The synthesis of sugar lactim ethers, a new group of sugars containing nitrogen in the ring, is described.

In earlier communications[5,6] we investigated newer methods for the synthesis of 5-amino-5-deoxypentopyranoses[7-9] by the reductive ring expansion of 5-azido-5-deoxypentofuranoses.[5,6] The reaction is an excellent preparative route to 3,4,5-trihydroxypiperidines[6,9] which are formed as sole products in the presence of excess catalyst. Anticipating that the reduction of certain azido aldonolactones would also proceed with ring enlargement of the intermediate amino aldonolactones, we synthesized sugar lactams of various ring sizes and studied their transformations.

Oxidation of 5-azido-2,3-*O*-benzylidene-5-deoxy-β-D-ribofuranose (**1**)[8] with pyridine–chromium trioxide proceeded very readily to give crystalline 5-azido-2,3-*O*-benzylidene-5-deoxy-D-ribonolactone (**2**)[3] (Scheme I). It should be noted that, whereas the oxidation of a secondary hydroxyl group in a furanose derivative with the pyridine–chromium trioxide reagent has been unsuccessful,[10] the anomeric hydroxyl group in **1** is readily oxidized. Hydrogenation of the azido lactone **2** afforded crystalline 5-amino-2,3-*O*-benzylidene-5-deoxy-D-ribo-

(1) Presented in part at the 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p 15C; and at the 159th National Meeting, Chicago, Ill. Sept 1967, p 16D.

(2) S. Hanessian and T. H. Haskell, *J. Heterocycl. Chem.*, **1**, 55 (1964).

(3) S. Hanessian and T. H. Haskell, *ibid.*, **1**, 57 (1964).

(4) Department of Chemistry, University of Montreal, Montreal, Quebec, Canada.

(5) S. Hanessian, *Chem. Ind.* (London), 1296 (1965).

(6) S. Hanessian, *ibid.*, 2126 (1966).

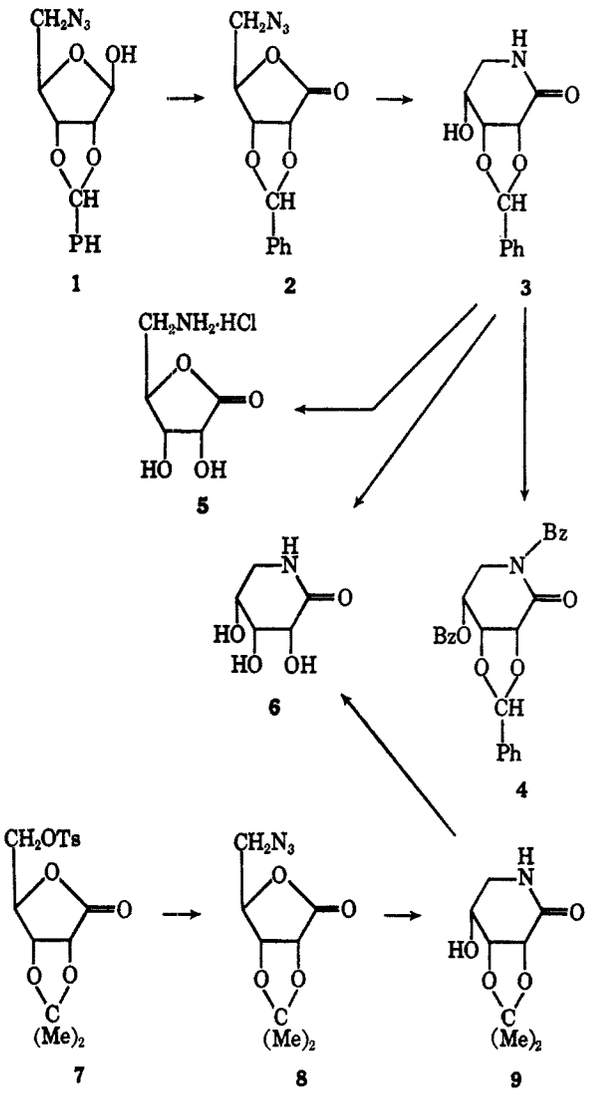
(7) T. H. Haskell and S. Hanessian, *J. Org. Chem.*, **28**, 2598 (1963).

(8) S. Hanessian and T. H. Haskell, *ibid.*, **28**, 2604 (1963).

(9) H. Paulsen, *Angew. Chem. Intern. Ed. Engl.*, **5**, 495 (1966).

(10) P. J. Beynon, P. M. Collins, P. T. Doganges, and W. G. Overend, *J. Chem. Soc.*, 1131 (1966), and references cited therein.

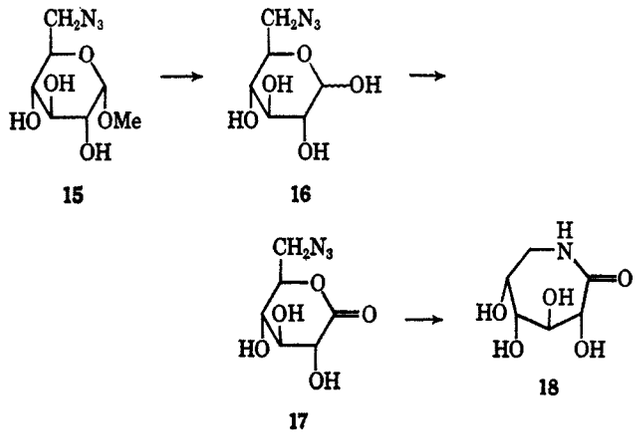
SCHEME I



nolactam (**3**)[3] in almost quantitative yield. This product could be readily identified by the characteristic carbonyl frequency at 1640 cm^{-1} (lactam) in its ir spectrum. As in the reductive ring enlargement of appropriately substituted 5-azido-5-deoxypentoses,[6] the product **3** contains an unsubstituted hydroxyl group at C-4 which originates from the ring oxygen by protonation and can be used advantageously for further selective transformations at that site. Benzoylation of **3** at elevated temperatures caused substitution at the hydroxyl and NH groups to give the crystalline dibenzoate **4**. Attempted removal of the acetal group from **3** in the presence of Amberlite IR-120 (H^+) afforded a negligible residue when the filtered solution was evaporated to dryness. Washing the resin with dilute hydrochloric acid and evaporation of the acidic effluent afforded a crystalline substance which proved to be 5-amino-5-deoxy-D-ribonolactone hydrochloride (**5**).[3] The structure of the latter product was evident from its ir spectrum and elemental analysis. Removal of the benzylidene group by hydrogenolysis over palladium on carbon in 95% ethanol, containing some acetic acid, afforded the desired product, 5-amino-5-deoxy-D-ribonolactam[3] (D-*ribo*-3,4,5-trihydroxy-2-piperidone, **6**) as a crystalline solid. It can be seen that the transformation **2** → **3** → **5** represents a case of ring enlargement and contraction; the latter process being favored under acidic conditions.

In another approach to the lactam **6** we started from the readily available 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-D-ribonolactone[11] (**7**) which was converted into the new 5-azido-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactone (**8**) by a displacement reaction with sodium azide. Hydrogenation of **8** afforded crystalline 5-amino-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactam (**9**) in good yield. Mild acidic hydrolysis of the ketal group in **9** afforded the crystalline lactam **6** in 90% yield. The ring expansion of amino lactones to lactams *via* an internal displacement of the lactone ring oxygen is a general reaction in the sugar series, provided that the potential amino group is favorably situated in the molecule. Thus, the direct synthesis of 5-amino-5-deoxypentonolactams from the 5-azido-5-deoxypentonolactones is possible.[1] The method is also applicable to the synthesis of seven-membered sugar lactams.[1,6] Methyl 6-azido-6-deoxy-α-D-glucopyranoside (**15**) (Scheme II)

SCHEME II



was prepared as a semicrystalline syrup from the corresponding 6-tosylate derivative,[12] by a displacement reaction with azide ion. The product **15** was characterized as the crystalline triacetate.[12] Acid hydrolysis of **15** in the presence of Amberlite IR-120 (H^+) afforded crystalline 6-azido-6-deoxy-D-glucopyranose (**16**) which was oxidized with bromine water to give crystalline 6-azido-6-deoxy-D-glucono-1,5-lactone[13] (**17**). The assignment of ring size to **17** is based on the carbonyl stretching frequency (1725 cm^{-1}) in its ir spectrum, which corresponds favorably to that exhibited by D-glucono-1,5-lactone (1732 cm^{-1}), but not with that of D-galactono-1,4-lactone (1749 cm^{-1}). Hydrogenation of **17** produced the desired 6-amino-6-deoxy-D-gluconolactam[6] (hexahydro-D-*gluco*-3,4,5,6-tetrahydroxy-2*H*-azepin-2-one, **18**) as a crystalline solid in good yield. The corresponding D-*galacto* isomer **22** was prepared in the same manner. Reaction of methyl 6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside[14] with sodium azide in

(11) L. Hough, J. K. N. Jones, and D. L. Mitchell, *Can. J. Chem.*, **36**, 1720 (1958).

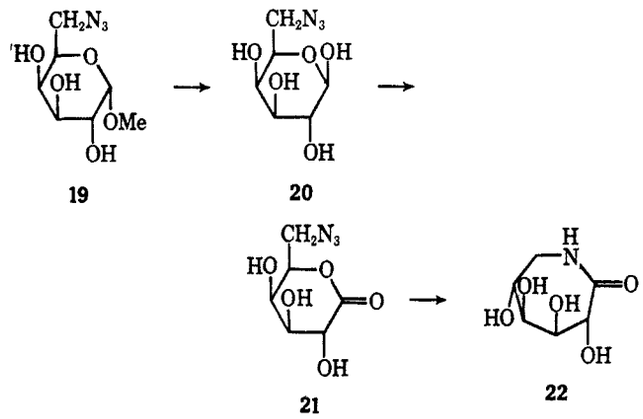
(12) F. Cramer, H. Otterbach, and H. Springmann, *Chem. Ber.*, **92**, 384 (1959).

(13) This product, mp 129–130°, was previously reported[6] having mp 138–140°.

(14) P. A. Rao and F. Smith, *J. Chem. Soc.*, 229 (1944).

N,N-dimethylformamide at 100°, afforded the corresponding 6-azido derivative[15] **19** (Scheme III) as a

SCHEME III



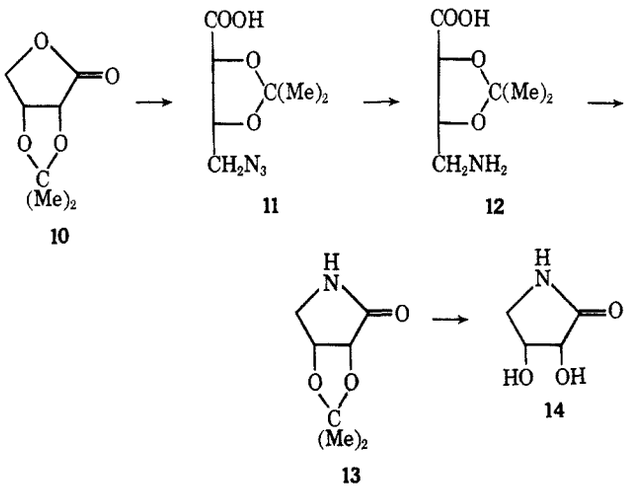
crystalline solid. Acid hydrolysis in the presence of a cation-exchange resin afforded the crystalline free sugar, 6-azido-6-deoxy-β-D-galactopyranose[6] (**20**), which was oxidized with bromine water to 6-azido-6-deoxy-D-galactono-1,5-lactone (**21**). The latter was obtained as a chromatographically homogeneous syrup and was directly hydrogenated to 6-amino-6-deoxy-D-galactonolactam (hexahydro-D-*galacto*-3,4,5,6-tetrahydroxy-2*H*-azepin-2-one, **22**). The synthesis of a seven-membered sugar lactam having the L-*gulo* configuration has been achieved[16] by the hydrogenation of the lactone of D-glucuronic acid oxime and subsequent rearrangement. It is also of interest to note that 5-amino-5-deoxy-D-gluconolactam was prepared in connection with the structure elucidation of the antibiotic nojirimycin[17] (5-amino-5-deoxy-D-glucopyranose).

The synthesis of a sugar containing a five-membered lactam ring was accomplished by the reductive cyclization of an azido carboxylic acid derivative. Reaction of 2,3-*O*-isopropylidene-D-erythronolactone[18] (**10**) with sodium azide in *N,N*-dimethylformamide at 100° in an atmosphere of nitrogen afforded crystalline 4-azido-4-deoxy-2,3-*O*-isopropylidene-D-erythronic acid[4] (**11**) (Scheme IV) in 70% yield. In effect, it is a nucleophilic displacement reaction by azide ion with the lactone ring oxygen acting as the leaving group. It represents a novel approach to the introduction of functional groups in sugar derivatives. While the reaction is of preparative significance, its applicability appears to be limited to lactones formed from primary alcohols, since efforts to extend the ring opening reaction to γ- and δ-lactones involving secondary hydroxyl groups have not been successful yet. To this end, we are investigating the possibilities of displacement reactions of activated lactones such as *O*-alkyllactonium salts,[19] which should be more susceptible to ring opening.

(15) D. C. DeJongh and S. Hanessian, *J. Amer. Chem. Soc.*, **87**, 3744 (1965).
(16) H. Weidmann and E. Fauland, *Ann.*, **679**, 192 (1964).
(17) S. Inouye, T. Tsuruoka, T. Ito, and T. Niida, *Tetrahedron*, **23**, 2125 (1968); *J. Antibiotics*, **A19**, 288 (1966).
(18) D. L. Mitchell, *Can. J. Chem.*, **41**, 214 (1963).
(19) In model experiments,[1] we have treated *O*-ethylbutyrolactonium fluoroborate [H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, **89**, 2060 (1956)] with sodium azide in acetonitrile and obtained 4-azibobutyric acid and some unreacted γ-butyrolactone. While the reaction still involves a primary lactone, the incorporation of azide with ring opening under mild conditions is indicative of the synthetic potentialities of such activated lactones.

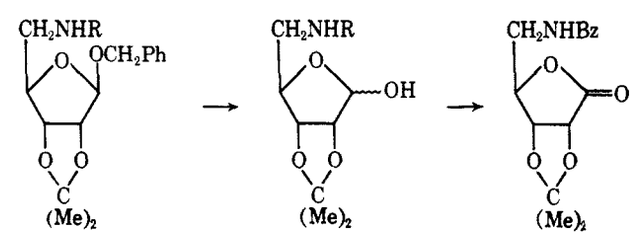
Catalytic hydrogenation of **11** afforded 4-amino-4-deoxy-2,3-*O*-isopropylidene-D-erythronic acid[4] (**12**) as a hygroscopic crystalline solid, which on sublimation at 150° was transformed into crystalline 4-amino-4-deoxy-2,3-*O*-isopropylidene-D-erythronolactam[4] (**13**). The ketal grouping was cleaved in a mixture of aqueous sulfuric acid and dioxane, to give the crystalline free lactam, 4-amino-4-deoxy-D-erythronolactam[4] (D-*erythro*-3,4-dihydroxy-2-pyrrolidinone, **14**).

SCHEME IV

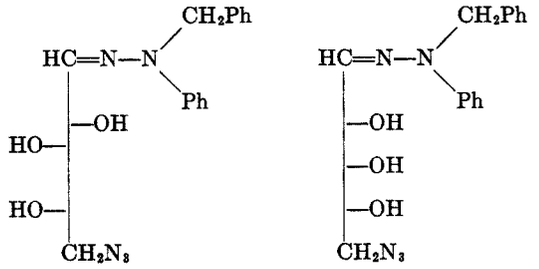


In the course of the present studies, we investigated the possibilities of effecting ring enlargements in certain sugar lactones which contained acylamido rather than amino groups. It was found that 5-benzamido-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactone (**25**) (Scheme V), which was prepared from benzyl 5-benzamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (**23**) in two steps, could be transformed into a sodium salt by treatment with dilute sodium hydroxide. Subsequent acidification of this solution afforded only 5-benzamido-5-deoxy-D-ribonolactone (tlc) and none of the corresponding lactam. A new crystalline precursor of 5-acetamido-5-deoxy-D-ribose[8] was also prepared during the present studies. Thus reductive debenzylation of benzyl 5-acetamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside[6] afforded crystalline 5-acetamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranose (**24a**) in 75% yield (Scheme V). We had shown[8] in a previous paper that among the 5-acetamido-5-deoxypentoses only the D-*ribo* analog exhibited a preference to remain in the furanose form, under acidic and neutral conditions. The synthesis of 5-acetamido-5-deoxy-D-ribopyranose[5] was effected through the reductive rearrange-

SCHEME V

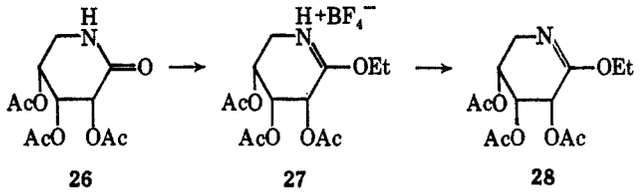


ment of 5-azido-5-deoxy-D-ribose in the presence of acetic anhydride. In this paper we describe the preparation of 5-azido-5-deoxy-L-arabinose and 5-azido-5-deoxy-D-ribose which have been characterized as the crystalline benzylphenylhydrazone derivatives **29** and **30**, respectively.



Inasmuch as sugar lactams are polyhydroxy derivatives of some of the well-known aliphatic analogs such as *N*-methylpyrrolidone, δ-valerolactam, and ε-caprolactam, they are subject to a variety of interesting transformations. Our interest in the reaction of carbohydrate derivatives with oxonium salts[20] prompted the synthesis of sugar lactim ethers and their protonated salts from appropriately substituted sugar lactams. Treatment of 5-amino-5-deoxy-D-ribonolactam (**6**) with acetic anhydride in pyridine effected selective *O*-acetylation to give 2,3,4-tri-*O*-acetyl-5-amino-5-deoxy-D-ribonolactam (**26**) (Scheme VI) as a homogeneous syrup.

SCHEME VI



The lactam derivative was treated in dichloromethane solution with triethyloxonium fluoroborate[21] at room temperature, whereupon the expected lactim ether derivative crystallized out of solution within 1–2 hr. This product formulated as 2-ethoxy-3,4,5,6-tetrahydro-3,4,5-tri-*O*-acetyl-D-*ribo*-pyridinetriol tetrafluoroborate (**27**). It is stable for prolonged periods when kept at 0° in a dry atmosphere and could be exposed to air for short periods of time, without appreciable alteration. Treatment of the salt with a mild base such as sodium azide or sodium acetate in acetonitrile effected a smooth transformation into the corresponding lactim ether, 2-ethoxy-3,4,5,6-tetrahydro-3,4,5-tri-*O*-acetyl-D-*ribo*-3,4,5-pyridinetriol (**28**). The latter was obtained as a chromatographically homogeneous colorless syrup which had the expected spectral properties. The product darkened on standing at room temperature for a few days, but it was stable when stored at 0°. The corresponding seven-membered lactim ether derived from 6-amino-6-deoxy-D-galactonolactam (**22**) was also prepared[1] by the same route and will be reported later.

(20) S. Hanessian, *Tetrahedron Lett.*, 1549 (1967).

(21) H. Meerwein, G. Hinz, P. Hofmann, E. Kroning, and E. Pfiel, *J. Prakt. Chem.*, **147**, 17 (1937).

Experimental Section

Melting points are uncorrected. Nmr spectra were obtained in chloroform-*d* unless otherwise stated, on a 60-MHz spectrometer using tetramethylsilane as reference. Optical rotations were measured with a Perkin-Elmer photoelectric polarimeter at 25°. Thin layer chromatography was performed on silica gel HF plates and the spots were detected with a spray containing 5% each of ammonium molybdate, sulfuric acid, and phosphoric acid after heating the plate for 10 min at 110° (for sugars), and with a 1% potassium permanganate solution in 0.1 *N* sulfuric acid (for lactams). Lactones were sprayed with the hydroxylamine spray. Processed solutions of chloroform and ether were dried over anhydrous sodium sulfate.

5-Azido-2,3-*O*-benzylidene-5-deoxy-D-ribonolactone (**2**).—A solution of **1**[8] (0.263 g) in 5 ml of pyridine was added dropwise with stirring to a slurry of the pyridine–chromium trioxide complex (prepared from 0.5 g of chromium trioxide and 6 ml of pyridine). The brown slurry was stirred overnight at room temperature in an atmosphere of nitrogen. The solvent was evaporated below 45°, and the residue was suspended in water and extracted several times with chloroform. The extracts were processed in the usual way and evaporated to dryness. The crystalline residue was triturated with ether–pentane and filtered to give 0.1 g of product, mp 140–142°. A further 0.11 g, mp 144–146° (total yield, 82%), was obtained from the mother liquors. Recrystallization of a portion from a mixture of ether and pentane containing a few drops of acetone gave pure material: mp 146–147°; $[\alpha]_D$ −13° (*c* 0.71, acetone); ir data (KBr), 1790 (lactone), 2120 cm^{-1} (azide). *Anal.* Calcd for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09. Found: C, 55.14; H, 4.26; N, 16.13.

5-Amino-2,3-*O*-benzylidene-5-deoxy-D-ribonolactam (**3**).—A solution of **2** (0.26 g) in 50 ml of ethyl acetate (or methanol) was hydrogenated at room temperature in the presence of platinum oxide (or palladium on carbon) during 1–2 hr. Filtration of the catalyst and evaporation of the filtrate gave a crystalline residue which was triturated with a mixture of methanol–ether and filtered; yield 0.24 g (92%), mp 202–203°. Recrystallization of 60 mg gave 55 mg of pure product: mp 203–204°; $[\alpha]_D$ 48.5° (*c* 0.7, methyl sulfoxide); ir data (KBr), 1640 cm^{-1} (lactam). *Anal.* Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.18; H, 5.66; N, 5.85.

5-Benzamido-4-*O*-benzoyl-2,3-*O*-benzylidene-5-deoxy-D-ribonolactam (**4**).—An amount of **3** (0.125 g) in 2 ml of pyridine was treated at 0° with 0.2 ml of benzoyl chloride. The solution was kept at room temperature for 4 hr, then heated at 60° for 1 hr. The precipitate which formed upon pouring the solution in ice–water was filtered and washed with ice–water, aqueous sodium bicarbonate, water, and finally with pentane, yield 0.27 g. A portion was recrystallized from ether–pentane containing some acetone to give an analytical sample: mp 199–200°; $[\alpha]_D$ −55° (*c* 1.01, chloroform); tlc (benzene–methanol, 10:2), fast. *Anal.* Calcd for $C_{26}H_{21}NO_6$: C, 70.42; H, 4.77; N, 3.16. Found: C, 70.27; H, 4.78; N, 3.20.

5-Amino-5-deoxy-D-ribonolactone Hydrochloride (**5**).—An aqueous solution of **3** (0.126 g) was heated at 90° for 2.5 hr in the presence of Amberlite IR-120 (H^+). Filtration and evaporation of the filtrate gave 10 mg of a crystalline starting material. The resin was transferred to a small column and eluted with 2 *N* hydrochloric acid. Evaporation of the eluate gave a syrup which crystallized upon trituration with methanol–ether, yield 30 mg. Recrystallization from methanol–ether gave the crystalline product with mp 185–187° dec; $[\alpha]_D$ 68° (*c* 0.35, methanol); ir data (KBr), 1775 (lactone), 1600 cm^{-1} (NH_2 twisting vibration). *Anal.* Calcd for $C_5H_{10}NO_4Cl$: N, 7.65; Cl, 19.2. Found: N, 7.19; Cl, 19.38.

5-Azido-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactone (**8**).—A solution of **7**[11] (1.4 g) in 50 ml of *N*,*N*-dimethylformamide containing 1.2 g of sodium azide was heated with stirring at 100° for 6 hr. The solvent was evaporated in the presence of butyl alcohol, and the residue was dissolved in water, extracted with ether, and processed in the usual way. Evaporation of the extracts afforded a colorless syrup in over 90% yield; tlc (benzene–methanol, 10:1), fast; ir data (liquid film), 1790 (lactone), 2120 cm^{-1} (azide). This was used as such in subsequent steps.

5-Amino-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactam[22] (**9**).—

(22) This intermediate was prepared by Mr. W. Regan of these laboratories.

An amount of **8** (0.5 g) in 100 ml of methanol was hydrogenated at atmospheric pressure in the presence of 0.2 g of palladium on carbon (6%). After 1 hr, the catalyst was filtered and the filtrate was evaporated to a syrup which crystallized. Trituration with acetone–ether and filtration gave the product, yield 0.3 g. A portion was recrystallized from the same solvent mixture to give an analytical sample: mp 139–140°; $[\alpha]_D$ 26.8° (*c* 1.02, chloroform); ir data (KBr), 1660 cm^{-1} (lactam); tlc (benzene–methanol, 10:1), medium. *Anal.* Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.0; N, 7.48. Found: C, 51.04; H, 7.15; N, 7.51.

5-Amino-5-deoxy-D-ribonolactam (6). A. From 3.—An amount of **3** (0.11 g) in 75 ml of 95% ethanol containing 5 ml of glacial acetic acid was hydrogenated at 50 psi in the presence of palladium on carbon. Filtration of the catalyst and evaporation of the solvent gave a crystalline residue which was triturated with methanol and filtered, yield 50 mg. Recrystallization was effected from hot methanol containing a little water; mp 240–242° dec (gradual browning after *ca.* 200°); $[\alpha]_D$ 33° (*c* 0.298, water); ir data (KBr), 1660 cm^{-1} (lactam). *Anal.* Calcd for $C_5H_9NO_4$: C, 40.81; H, 6.17; N, 9.52. Found: C, 40.77; H, 6.09; N, 9.61.

B. From 9.—A solution of **9** (0.5 g) in 25 ml of 0.1 *N* hydrochloric acid was heated at 50° for 2 hr. The solution was neutralized with Amberlite IR-45 (OH^-) and filtered, and the filtrate was evaporated to give a crystalline residue. Trituration with methanol and filtration gave the product (0.35 g, 89%) which was homogeneous on tlc (chloroform–methanol, 100:30; medium), mp 240–242° dec.

4-Azido-4-deoxy-2,3-*O*-isopropylidene-D-erythronic Acid (11).—To a solution of **10**[18] (3.5 g) in *N,N*-dimethylformamide (20 ml) was added sodium azide (5 g) and the suspension was heated at 100–110° for 16 hr in an atmosphere of nitrogen. The dark solution was filtered through a filter pad containing Celite and charcoal and the filtrate was diluted with 1 l. of ether. The precipitate was collected on a Celite pad and washed into a flask with water. The filtrate was acidified with 1 *N* sulfuric acid to pH 2 at 0° and the solution was extracted with ether. Drying and evaporation of the extracts afforded a syrup which crystallized at 0° to give, after trituration with pentane and filtration, 3.1 g (70%) of product. Recrystallization was effected from 2,2,4-trimethylpentane at 0°; mp 55–56°; $[\alpha]_D$ 72° (*c* 0.47, acetone); ir data (KBr), 1760 (COOH), 2100 cm^{-1} (azide). *Anal.* Calcd for $C_7H_{11}N_3O_4$: C, 42.80; H, 5.51; N, 20.90. Found: C, 42.20; H, 5.87; N, 21.08.

4-Amino-4-deoxy-2,3-*O*-isopropylidene-D-erythronic Acid (12).—An amount of **11** (0.50 g) in 100 ml of methanol was hydrogenated in the presence of 20% palladium on carbon, at room temperature and atmospheric pressure. After 1.5 hr, the catalyst was filtered, the filtrate was evaporated to a small volume, and ether was added to precipitate the product. The product was filtered and washed with ether to give 0.41 g (94%) of hygroscopic crystals, mp 150–160° (sublimation), $[\alpha]_D$ 92° (*c* 1.02, 60% aqueous acetone). *Anal.* Calcd for $C_7H_{13}NO_4 \cdot H_2O$: C, 43.51; H, 7.83; N, 7.25. Found: C, 43.51; H, 7.93; N, 7.16.

4-Amino-4-deoxy-2,3-*O*-isopropylidene-D-erythronolactam (13).—An amount of **12** (0.14 g) was gradually heated at 0.5 mm in a sublimation apparatus. The product which sublimed between 150 and 170°, as colorless crystals, was obtained as a hemihydrate: yield 0.1 g (80%); mp 147–148°; $[\alpha]_D$ −59° (*c* 0.78, methanol); ir data (KBr), 1680 (lactam; CCl_4), 3460 cm^{-1} (NH). *Anal.* Calcd for $C_7H_{11}NO_3 \cdot 0.5H_2O$: C, 50.59; H, 7.28; N, 8.43; H_2O, 6.00. Found: C, 49.77; H, 7.49; N, 8.24; H_2O, 6.06.

4-Amino-4-deoxy-D-erythronolactam (14).—A solution of **13** (0.12 g) in a mixture of dioxane (5 ml) and 0.1 *N* sulfuric acid (5 ml) was heated at 95° for 2.5 hr. The solution was neutralized with barium carbonate and filtered and the filtrate was evaporated to a semicrystalline residue. Crystallization was effected by dissolving the residue in methanol and evaporating the solution to a small volume; yield 40 mg; mp 153–154°; $[\alpha]_D$ −17° (*c* 0.2, water); ir data (KBr), 1700 cm^{-1} (lactam); tlc (2-propanol–water, 4:1), medium. *Anal.* Calcd for $C_4H_7NO_3$: N, 11.95. Found: N, 12.01.

Methyl 6-Azido-6-deoxy-α-D-glucopyranoside (15).—A solution containing 17.4 g of methyl 6-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside[12] and 13 g of sodium azide in 300 ml of 95% 2-methoxyethanol was refluxed with stirring for 20 hr. The solvent was evaporated and the residue was suspended in a mixture of acetone–ether and filtered. The process was repeated and the final filtrate was evaporated to a semicrystalline syrup (9 g) which was chromatographically homogeneous (tlc: chloroform–methanol, 100:10; medium) and exhibited the expected spectral characteristics. The product could also be prepared by heating the tosylate (10 g) in *N,N*-dimethylformamide containing sodium azide (10 g), for 6 hr at 105°. The product was used as such in further steps.

A portion of the syrup was acetylated with acetic anhydride in pyridine to give the crystalline triacetate derivative of **15**, mp 103°, lit.[12] mp 103°.

6-Azido-6-deoxy-D-glucopyranose (16).—A solution of **15** (4.1 g) in 50 ml of water was heated under reflux in the presence of excess Amberlite IR-120 (H^+) (120 ml, wet volume). After 7 hr most of the starting material had been hydrolyzed as evidenced by tlc of an aliquot. The resin was filtered, and the filtrate was evaporated to a syrup which was dissolved in ethanol and diluted with ether to the point of turbidity. The product crystallized upon cooling and scratching, yield 1.17 g. Recrystallization from a mixture of 2-propanol and ether gave the product as needles: mp 128–130°; $[\alpha]_D$ 62° (*c* 0.15, water); ir data (KBr), 2120 cm^{-1} (azide). *Anal.* Calcd for $C_6H_{11}N_3O_5$: C, 35.12; H, 5.40; N, 20.48. Found: C, 35.42; H, 5.10; N, 20.12.

6-Azido-6-deoxy-D-glucono-1,5-lactone (17).—A solution of **16** (0.3 g) in 10 ml of water was treated with bromine (0.5 ml). After stirring overnight, the solution was aerated and evaporated to dryness. The colorless crystalline residue was triturated with cold 2-propanol and filtered; yield 175 mg. Recrystallization was effected by dissolving in hot 2-propanol, evaporating the solution to a small volume, and adding some ether; mp 129–130°; $[\alpha]_D$ 82° (*c* 0.24, acetone); ir data (KBr), 1725 (lactone), 2095 cm^{-1} (azide). The carbonyl stretching bands in the ir spectra of D-glucono-1,5-lactone and D-galactono-1,4-lactone were 1732 and 1749 cm^{-1}, respectively. *Anal.* Calcd for $C_6H_9N_3O_5$: C, 35.47; H, 4.46; N, 20.65. Found: C, 35.83; H, 4.43; N, 20.49.

6-Amino-6-deoxy-D-gluconolactam (18).—A methanolic solution of **17** (0.16 g) was hydrogenated for 1 hr in the presence of 20% palladium on carbon (0.1 g). Filtration of the catalyst and evaporation afforded a crystalline residue which was suspended in ether–methanol and filtered, yield 0.12 g, mp 210–212° dec. Recrystallization was effected by dissolving in hot methanol containing a little water and evaporation of the solution to a small volume; mp 212–214° dec; $[\alpha]_D$ −71° (*c* 0.4, water); ir data (KBr), 1650, 1665 cm^{-1} (lactam). The product was homogeneous on tlc (chloroform–methanol, 100:30; medium). *Anal.* Calcd for $C_6H_{11}NO_5$: C, 40.67; H, 6.25; N, 7.90. Found: C, 40.85; H, 6.19; N, 7.88.

Methyl 6-Azido-6-deoxy-α-D-galactopyranoside (19).—Sodium azide (5 g) was added to a solution of methyl 6-*O*-*p*-tolylsulfonyl-α-D-galactopyranoside[14] (7 g) in 200 ml of *N,N*-dimethylformamide and the resulting suspension was heated at 100° overnight. The solvent was removed by codistillation with butyl alcohol on a rotatory evaporator at 60° and the residue was triturated with cold water to give the product in two crops; yield 2 g; tlc (chloroform–methanol, 100:3), medium. Recrystallization was effected from a mixture of acetone and ether; mp 172–173° dec. *Anal.* Calcd for $C_7H_{13}N_3O_5$: C, 38.31; H, 5.98; N, 19.19. Found: C, 38.11; H, 5.76; N, 18.90.

6-Azido-6-deoxy-β-D-galactopyranose (20).—To a solution of **19** (1.2 g) in 60 ml of water was added Amberlite IR-120 (H^+) (100 ml wet volume) and the mixture was refluxed with stirring for 6–7 hr, then left at room temperature overnight. The resin was filtered, the filtrate was evaporated to dryness, and the residue was triturated with cold methanol–acetone to give the product, 0.87 g. A portion of this product was recrystallized from a mixture of 2-propanol, ethyl acetate, and ether; mp 145–147°; $[\alpha]_D$ 25 → 48°, 10 min, constant (*c* 0.24, water). *Anal.* Calcd for $C_6H_{11}N_3O_5$: C, 35.12; H, 5.40; N, 20.48. Found: C, 35.32; H, 5.42; N, 20.53.

6-Azido-6-deoxy-D-galactono-1,5-lactone (21).—A solution of **20** (0.3 g) in 10 ml of water was treated with 0.6 ml of bromine and the mixture was stirred at room temperature overnight. The solution was aerated and evaporated to a syrup which was repeatedly evaporated from small volumes of water and finally from toluene. The resulting syrup (0.2 g) was homogeneous on tlc (chloroform–methanol, 100:20; medium) and gave a positive test with the hydroxylamine spray. This material was used as

such in subsequent steps; ir data (liquid film), 1735 (lactone), 2115 cm^{-1} (azide).

6-Amino-6-deoxy-D-galactonolactam (22).—A methanolic solution of **21** (0.15 g) was hydrogenated in the presence of 20% palladium on carbon. After 2 hr the catalyst was filtered and the filtrate was evaporated to dryness. The residue was dissolved in hot methanol and filtered, the filtrate was evaporated, and the crystalline solid which remained was triturated with methanol–ether and filtered; yield 0.1 g, mp 145–150° (softening). A portion was recrystallized by dissolving the sample in hot methanol and evaporating to a small volume; mp 175–177° (foaming); $[\alpha]_D$ −22° (*c* 0.13, water); ir data (KBr), 1655 cm^{-1} (lactam). *Anal.* Calcd for $C_6H_{11}NO_5$: C, 40.67; H, 6.25; N, 7.90. Found: C, 40.62; H, 5.03; N, 7.36.

Benzyl 5-Benzamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside (23).—A solution of benzyl 5-azido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside[8] (4 g) in 50 ml of ether was added dropwise to a stirring suspension of lithium aluminum hydride (1 g) in ether. The mixture was refluxed for 5 hr, excess reagent was cautiously decomposed with water, and the ethereal portion was processed as usual to give a syrup. The latter was dissolved in pyridine (30 ml), cooled to −30°, and treated with 2 ml of benzoyl chloride dropwise. After storing at room temperature overnight, the solution was poured into ice–water. Extraction with chloroform, followed by processing and evaporation gave a syrup which crystallized under pentane at 5° to give 3 g of product. Recrystallization was effected from a mixture of ether and pentane; mp 126°, $[\alpha]_D$ −124° (*c* 0.53, chloroform). *Anal.* Calcd for $C_{22}H_{25}NO_5$: C, 68.90; H, 6.57; N, 3.65. Found: C, 69.23; H, 6.76; N, 3.68.

5-Acetamido-5-deoxy-2,3-*O*-isopropylidene-D-ribofuranose (24a).—An amount of benzyl 5-acetamido-5-deoxy-2,3-*O*-isopropylidene-β-D-ribofuranoside[8] (1.6 g) in 125 ml of methanol was hydrogenated in the presence of 20% palladium on carbon (1.5 g) at 40 psi. After 22 hr the catalyst was filtered and the filtrate was evaporated to a syrup (1.25 g) which showed, in addition to the expected product, a trace of starting material (tlc: ethyl acetate–2,2,4-trimethylpentane, 3:2). The syrup was fractionated on a column containing silicic acid using the solvent mixture ethyl acetate–2,2,4-trimethylpentane–methanol (3:2:0.2). The fractions containing the product were combined and evaporated to a syrup which crystallized. The crystals were triturated with ethyl acetate containing some 2,2,4-trimethylpentane and filtered, yield 0.84 g (75%). Recrystallization was effected from the same solvent mixture; mp 100–101°; $[\alpha]_D$ −25° (*c* 0.4, chloroform); nmr data, τ 2.8–3 (NH proton, broad), 4.44 (C-1 proton, singlet), 5.7 (C-2, C-3 protons, singlet), 6.5 (center of a multiplet, C-4 proton), 3.45 (center of a multiplet, C-5 protons), 8.0 (N-acetyl protons, singlet), 8.55, 8.68 (ketal methyl protons). *Anal.* Calcd for $C_{10}H_{17}NO_5$: C, 51.93; H, 7.41; N, 6.05. Found: C, 51.62; H, 7.53; N, 5.81.

5-Benzamido-5-deoxy-2,3-*O*-isopropylidene-D-ribonolactone (25).—A solution of **23** (1 g) in 75 ml of methanol was hydrogenated in the presence of 20% palladium on carbon (1 g) at 40 psi. After 22 hr, the catalyst was filtered, the filtrate was evaporated to dryness, and the resulting syrup was fractionated on a column containing silicic acid using ethyl acetate–2,2,4-trimethylpentane (3:2) as developer. The fractions containing the product **24b** were combined and evaporated to a colorless syrup (0.45 g): tlc (ethyl acetate–2,2,4-trimethylpentane, 3:2), medium.

An amount of **24b** (0.15 g) was dissolved in 2 ml of pyridine and the solution was added to a slurry of the pyridine–chromium trioxide complex (prepared from 0.25 g of chromium trioxide and 3 ml of pyridine). After stirring at room temperature overnight in a nitrogen atmosphere, the solvent was evaporated and the residue was taken up in a small volume of water. Extraction with chloroform and processing in the usual way afforded after evaporation, a syrup which was dissolved in ether, filtered, and diluted with 2,2,4-trimethylpentane. The product crystallized upon evaporation of this solution to a small volume, yield 105 mg (70%). Recrystallization was effected from a mixture of acetone, ether, and pentane; mp 140–142°; $[\alpha]_D$ −51° (*c* 0.408, chloroform); ir data (KBr), 1645 (amide I), 1530 (amide II), 1815 cm^{-1} (lactone). *Anal.* Calcd for $C_{15}H_{17}NO_5$: C, 61.84; H, 5.88; N, 4.80. Found: C, 61.48; H, 5.86; N, 4.90.

A portion of **25** (10 mg) was dissolved in 2 ml of 0.05 *N* sodium hydroxide. After 10 min the solution was acidified with Amberlite IR-120 (H^+) and heated on the steam bath for 20 min. Examination of the product by tlc (benzene–methanol, 10:3) showed that the only product was the lactone (permanganate and hydroxylamine sprays).

2-Ethoxy-3,4,5,6-tetrahydro-3,4,5-tri-*O*-acetyl-D-*ribo*-pyridinetriol Tetrafluoroborate (27).—An amount of **6** (0.29 g) in 10 ml of pyridine was treated with 1.6 ml of acetic anhydride. After standing at room temperature overnight, the solution was poured into ice–water and processed in the usual way by extraction with chloroform. Evaporation of the organic extracts afforded the triacetate derivative **26** as a colorless syrup (0.6 g). This syrup (0.6 g) was dissolved in 4 ml of dry dichloromethane, and the solution was cooled to 0° and treated with 0.65 g of triethyloxonium fluoroborate.[21] After stirring the homogeneous solution at room temperature for 1.5 hr, a crystalline precipitate began to separate. After stirring for another 1 hr, the flask contents were transferred to a centrifuge tube, the supernatant solution was removed after centrifugation, and the residual precipitate was washed with small volumes of cold dichloromethane and dried in a vacuum desiccator, yield 0.45 g. Recrystallization was effected from dichloromethane–ether to give needles, mp 167–169°. *Anal.* Calcd for $C_{13}H_{20}NO_7BF_4$: C, 40.12; H, 5.18; N, 3.60. Found: C, 40.57; H, 5.13; N, 3.52.

2-Ethoxy-3,4,5,6-tetrahydro-3,4,5-tri-*O*-acetyl-D-*ribo*-3,4,5-pyridinetriol (28).—An amount of **27** (0.15 g) in 5 ml of dry acetonitrile was treated with 1 g of powdered sodium azide and the suspension was stirred at room temperature overnight. Filtration and evaporation gave a syrup which was dissolved in ether and filtered again, yield 0.1 g of a colorless syrup (tlc: benzene–methanol, 10:0.1; medium; permanganate spray); $[\alpha]_D$ 117° (*c* 2.5, chloroform); ir data ($CHCl_3$), 1755 (ester), 1680 cm^{-1} (C=N); nmr data (acetone-d_6), τ 4.3–4.9 (three-proton multiplets, C-3, C-4, C-5), 5.9 (center of a two-proton quartet, CH_2CH_3), 6.33 (center of a two-proton multiplet, C-6 protons), 7.94, 7.98, 8.02 (acetyl methyl protons), 8.80 (center of a three-proton triplet, CH_2CH_3). The sample darkened on standing at room temperature.

5-Azido-5-deoxy-L-arabinose Benzylphenylhydrazone[5] (29).—To a solution of 5-azido-5-deoxy-L-arabinose diethyl dithioacetal[8] (0.5 g) in 25 ml of water were added 1.62 g of mercuric chloride and 1.62 g of cadmium carbonate. The mixture was stirred at 75–80° for 1 hr, cooled, and filtered, and the insolubles were washed thoroughly with water. The filtrate and washings were cooled in ice and treated with hydrogen sulfide until precipitation of salts was complete. The mixture was filtered, and the filtrate was neutralized with Amberlite IR-45 (OH^-) and evaporated to a pale yellow syrup. The latter was dissolved in 95% ethanol, and the solution was filtered through a pad of Celite–charcoal and evaporated to a colorless syrup (0.3 g), homogeneous on paper chromatograms (butyl alcohol–ethanol–water, 3:1:1; silver nitrate; R_f 0.65) and reduced Fehling's solution; ir data (liquid film), 2120 cm^{-1} (azide).

To a portion of the above product (40 mg) in 1 ml of water were added 0.15 g of sodium acetate and 61 mg of 1-benzylphenylhydrazine hydrochloride. Ethanol was added to give a homogeneous solution and the latter was refluxed for 3 hr. The solution was filtered through charcoal, the filtrate was evaporated to dryness, and the residue was taken up in water and extracted with chloroform. Processing of the organic layer afforded a syrup which crystallized from a mixture of ether and petroleum ether (bp 30–60°); yield 40 mg. Recrystallization was effected from the same solvent mixture with the addition of a few drops of methanol; mp 76–78°, $[\alpha]_D$ −25° (*c* 0.86, methanol), lit.[5] mp 76–78° for the D enantiomer. *Anal.* Calcd for $C_{18}H_{21}N_5O_3$: C, 60.82; H, 5.95; N, 19.70. Found: C, 60.87; H, 6.04; N, 19.65.

5-Azido-5-deoxy-D-ribose Benzylphenylhydrazone[5] (30).—An amount of 5-azido-2,3-*O*-benzylidene-5-deoxy-β-D-ribofuranose[8] (0.25 g) was suspended in 15 ml of dilute sulfuric acid (pH 1.5). After stirring at room temperature overnight, the homogeneous solution was neutralized with barium carbonate and filtered and the filtrate was extracted with ether to remove benzaldehyde. Evaporation of the aqueous solution afforded a colorless syrup (0.11 g) which was homogeneous on paper chromatograms (butyl alcohol–ethanol–water, 3:1:1; R_f 0.61); ir data (liquid film), 2120 cm^{-1} (azide).

A portion of the above product (50 mg) was treated with 1-benzylphenylhydrazine hydrochloride as described above to

give the product **30** (53 mg). Recrystallization was effected from a mixture of ether and pentane; mp 99–100°, $[\alpha]_D$ −43° (*c* 0.38, methanol). *Anal.* Calcd for $C_{18}H_{21}N_5O_3$: C, 60.82; H, 5.95; N, 19.70. Found: C, 60.92; H, 5.85; N, 19.71.

Registry No.—**2**, 18908-30-0; **3**, 18908-31-1; **4**, 18908-32-2; **5**, 18908-33-3; **6**, 18908-35-5; **9**, 18908-34-4; **11**, 18908-36-6; **12**, 18908-37-7; **13**, 18908-38-8; **14**, 18908-39-9; **16**, 18908-40-2; **17**, 18908-41-3; **18**, 14199-62-3; **19**, 18908-43-5; **20**, 18908-44-6; **22**, 18908-45-7; **23**, 18908-46-8; **24a**, 18908-47-9; **25**, 18908-48-0; **27**, 18902-56-2; **28**, 18908-49-1; **29**, 18908-50-4; **30**, 18908-51-5.

Transalkylation of Phosphonates. Equilibrium Studies

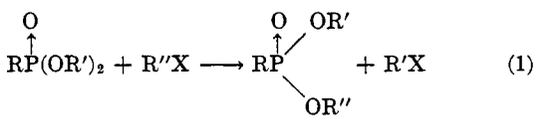
HAROLD M. BELL

Department of Chemistry, Virginia Polytechnic Institute, Blacksburg, Virginia 24061

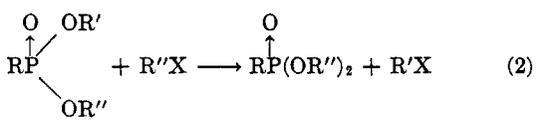
Received August 26, 1968

The reaction between alkylating agents and phosphonates (reactions 1 and 2) was found to proceed at a considerably lower temperature than previously reported. Use of a primary alkyl iodide as the alkylating agent results in a reasonably rapid and clean reaction at 130°, but a temperature as low as 70° can bring about slow interconversion; alkyl tosylates react somewhat faster than the corresponding iodides. Performing the reaction in a sealed tube results in establishment of equilibrium; equilibrium distributions agree closely with calculated values over a rather wide range of initial concentrations. The equilibrium data indicated that phosphonate exchange in the absence of external alkylating agent, reaction 3, should be a random, or entropy-controlled process; this was verified experimentally. The use of transalkylation equilibria as a means of obtaining free energy data for alkyl iodides and tosylates is discussed. Transalkylation can be used as a convenient means of synthesis of phosphonate esters, but the magnitude of the equilibrium constants for the reactions must be considered when planning such syntheses.

The reaction between alkylating agents and esters of pentavalent phosphorus acids (transalkylation) has been studied several times in this decade.[1–8] Reactions 1 and 2 illustrate the phosphonate case. There can be

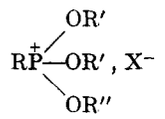


(1)



(2)

little doubt that these reactions proceed by nucleophilic attack by the phosphoryl oxygen,[1–5,7] producing alkoxyphosphonium salts as intermediates.[6,8] For reaction 1, the intermediate would be



Owing to the fact that the reported reaction conditions for transalkylation use high temperatures and long reaction times, it is easy to conclude that the reaction is of somewhat limited scope and utility.[9] It was therefore somewhat surprising to find phosphonate transalkylation at the temperature of refluxing propyl iodide (*ca.* 100°). Specifically, a mixed Michaelis–Arbuzov reaction between trimethyl phosphite and propyl iodide was attempted, with the hope of preparing dimethyl propylphosphonate. The phosphite was added slowly to a large excess of boiling propyl iodide contained in a distilling apparatus arranged in such a manner as to allow rapid removal of methyl iodide, minimizing formation of dimethyl methylphosphonate.[10] Analysis of the product by glpc and nmr indicated not only dimethyl propylphosphonate and dimethyl methylphosphonate, but also substantial amounts of the transalkylated materials, methyl propyl methylphosphonate, dipropyl methylphosphonate, methyl propyl propylphosphonate, and dipropyl propylphosphonate. This somewhat surprising result prompted additional studies on the generality and usefulness of the transalkylation reaction.

Results and Discussion

Generality of Phosphonate Transalkylation.—In order to establish the approximate lower temperature limit for transalkylation, various alkyl iodide–phosphonate mixtures were refluxed for 24 hr. The results are shown in Table I. The rather large reactivity difference as a function of alkylating agent must be almost

(1) H. J. Harwood and D. W. Grisley, Jr., *J. Amer. Chem. Soc.*, **82**, 423 (1960).

(2) A. N. Pudovik, A. A. Muratova, T. I. Konnova, T. Feoktistova, and L. N. Levkova, *Zh. Obshch. Khim.*, **30**, 2624 (1960); *Chem. Abstr.*, **55**, 15332a (1961).

(3) R. G. Laughlin, *J. Org. Chem.*, **27**, 1005 (1962).

(4) H. G. Henning, G. Hilgetag, and G. Busse, *J. Prakt. Chem.*, **33**, 188 (1966).

(5) J. I. G. Cadogan, R. K. Mackie, and J. A. Maynard, *J. Chem. Soc., C*, 1356 (1967).

(6) H. Teichmann, M. Jatkowski, and G. Hilgetag, *Angew. Chem. Intern. Ed. Engl.*, **6**, 372 (1967).

(7) H. J. Harwood, M. L. Becker, and R. R. Smith, *J. Org. Chem.*, **32**, 3882 (1967).

(8) L. V. Nesterov and R. I. Mutalapova, *Tetrahedron Lett.*, 51 (1968).

(9) Pudovik[2] uses 160–165° to realize the reaction of butyl iodide and diethyl ethylphosphonate; Laughlin[3] uses 170° for the reaction of dodecyl iodide and dimethyl ethylphosphonate. Henning[4] found that triphenylphosphine catalyzed the reaction such that somewhat lower temperatures and shorter reaction times could be used.

(10) G. M. Kosolapoff, "Organophosphorus Compounds," John Wiley & Sons, Inc., New York, N. Y., 1950, p 121.