Table II

Consistency and/or Viscosity (cp.) after Addition of

D.A.	Viscosity (cp.)	ZnCl₂ 0.25 g.	ZnCl₂ 0.50 g.	ZnCl₂ 0.75 g.	ZnCl₂ 1.00 g.	BaCl₂ 0.25 g.	BaCl₂ 0.50 g.	BaCl₂ 0.75 g.	BaCl₂ 1.00 g.	1 g. MnCl₂ or 1 g. MgCl₂
0.6	46	~1420, gel, lumps	~1150	500, thinning out	310	Heavy gel	Thinning out			31
0.7	39	~1180, gel, lumps	~1130	620	380	Heavy gel	Thinning out			
0.87	47	~600, thin gel	790	540	360	Heavy gel	Heavy gel	Thinning out		30
0.98	61	410	390	390	240	Gel, ~4850	~3300	~2400	1850	
1.21	45	99	133	107	89	Gel, ~3700	~2950	~2400	1630	24
1.39	70	117	134	121	107	Solution 1240	1160	1050	900	51
1.42	66	48	54	54	52	140–190	160–190	150	140	
1.47	55	32	31	32	31	31	30	29	29	

Experimental

Preparation of Ammonium Acetyl Alginate.—The acetyl alginates were prepared as described in the preceding paper.[4] The diacetate was obtained by washing 1000 g. of wet alginic acid (25% solids, 0.5% ash) three times with 800 cc. of glacial acetic acid. The liquid was filtered off on a Büchner funnel each time and then the material was reacted with a mixture of 1400 to 1500 cc. of acetic anhydride, 1000 cc. of acetic acid, and 2 cc. of perchloric acid. The perchloric acid was added at such a rate that the temperature of the reaction mixture did not exceed 45°. After a reaction time of about 3 hr. the material was pressed out, mixed and washed thoroughly with water until the wash water was neutral, then it was neutralized with ammonium hydroxide. The salt was precipitated in acetone and dried at 45° in the presence of an air stream.

The lower D.A. products were prepared by starting the reaction with 800 cc. of acetic anhydride. Then 300–400 cc. more of acetic anhydride was added during the reaction. At the desired D.A. the reaction was interrupted, the liquid removed by filtration and the material was washed with isopropyl alcohol until the odor of acetic acid had disappeared and then neutralized with ammonium hydroxide. Products with D.A. >1.3 were washed with water. The ammonium salt was precipitated in acetone and dried at 45° in the presence of an air stream.

Reactivity with Divalent Ions.—A 1-g. sample of ammonium acetyl alginate was dissolved in 100 cc. of distilled water, and its viscosity was measured with a Brookfield viscometer at 25° and 60 r.p.m. Then four 0.25-g. portions of calcium chloride as aqueous solutions were added successively while stirring vigorously. After each addition the consistency and, if possible, the viscosity were tested. The results are given in Table I.

The same measurements were made after adding barium chloride, zinc chloride, manganese dichloride, or magnesium chloride in place of the calcium chloride. Results are shown in Table II.

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[4] R. G. Schweiger, *J. Org. Chem.*, **27**, 1786 (1962).

The Addition of Sodium Methoxide to Carbohydrate α-Nitroolefins. Synthesis of 2-*O*-Methyl-D-mannose and 2-*O*-Methyl-D-ribose

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The reaction of D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene with sodium methoxide in methanol solution gives 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol. Hydrolysis of the nitro group (Nef reaction) then gives 2-*O*-methyl-D-mannose. Similarly, D-*erythro*-3,4,5-triacetoxy-1-nitro-1-pentene has been employed for the synthesis of 2-*O*-methyl-D-ribose.

The addition of sodium methoxide to simple, aliphatic α-nitroolefins, to yield alkyl nitroalkyl ethers, has long been known.[1] In the sugar series, Fischer and Baer[2] postulated such an addition of sodium methoxide to an intermediate α-nitroolefin to explain the monomethylated products arising from the action of the base on 6-deoxy-1,2:3,5-di-*O*-isopropylidene-6-nitro-D-glucose. We have now examined the action of sodium methoxide on two acetylated carbohydrate α-nitroolefins and find that the reaction leads to a useful method of preparation for the 2-*O*-methyl aldoses.

When a solution of D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene (I)[3] in methanol was treated at room temperature with slightly more than two equivalents of sodium methoxide, and the solution subsequently was acidified with acetic acid and

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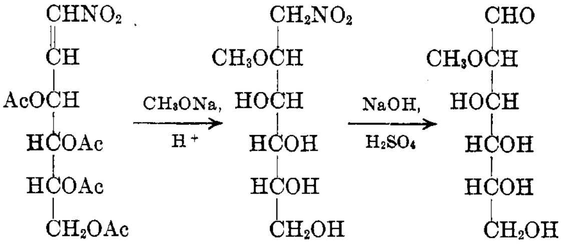
[1] J. Loevenich, J. Koch, and U. Pucknat, *Ber.*, **63**, 636 (1930); C. T. Bahner, U. S. Patent 2,391,815, Dec. 25, 1945; A. Lambert, C. W. Scaife, and A. E. Wilder-Smith, *J. Chem. Soc.*, 1474 (1947).

[2] H. O. L. Fischer and H. H. Baer, *Ann.*, **619**, 53 (1958).

[3] J. C. Sowden and H. O. L. Fischer, *J. Am. Chem. Soc.*, **69**, 1048 (1947).

concentrated, crystalline 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol (II) was obtained in 38% yield. Application of the Nef reaction[4] to this product then gave 2-*O*-methyl-D-mannose (III), which was isolated as the phenylhydrazone in 75% yield. Cleavage of the hydrazone with benzaldehyde gave the known crystalline 2-*O*-methyl-D-mannose.[5]



I II III

The action of sodium methoxide on D-*erythro*-3,4,5-triacetoxy-1-nitro-1-pentene failed to give a crystalline product directly. However, re-acetylation of the sirupy product yielded crystalline 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol triacetate which, on deacetylation, then gave crystalline 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol in 26% over-all yield. Application of the Nef reaction to the latter product gave sirupy 2-*O*-methyl-D-ribose, which was characterized as the *p*-toluenesulfonylhydrazone and the benzylphenylhydrazone.

The assignment of configuration to 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol was made through a comparison of its product of oxidation with periodate with that from 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol. The resulting solutions of the enantiomorphous 3-deoxy-2-*O*-methyl-3-nitroglyceraldehydes showed approximately equal specific optical rotations with opposite signs. For further confirmation, the 2-*O*-methyl-D-ribose was converted, by reduction to sirupy 2-*O*-methyl-D-ribitol and oxidation of the latter with periodate, to 2-*O*-methyl-L-glyceraldehyde, $[\alpha]^{25}D$ −2.2° ± 0.7°. The enantiomorphous 2-*O*-methyl-D-glyceraldehyde, prepared similarly from known 2-*O*-methyl-D-arabinose, gave $[\alpha]^{25}D$ +1.7° ± 0.6°.

Unexpected difficulty was encountered in the cleavage of 2-*O*-methyl-D-ribose benzylphenylhydrazone to the free sugar. Attempted cleavage with formaldehyde left the bulk of the hydrazone unchanged. Cleavage with benzaldehyde gave a somewhat colored sirup which showed a low methoxyl value and contained nitrogen (1.36%). Passage of this initial sirup over a cellulose column, however, provided a much purer product.

Experimental

1-Deoxy-2-*O*-methyl-1-nitro-D-mannitol.—A solution of 40 g. of D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene in 950 ml. of methanol was treated at room temperature with a solution of 5.4 g. of sodium in 450 ml. of methanol. After 30 min., 15 ml. of glacial acetic acid was added, and the solution was concentrated at reduced pressure to a thin sirup. This was dissolved in 200 ml. of water and the solution was freed of sodium ions by passage over a column of Dowex-50 resin. The effluent was decolorized with carbon and concentrated at reduced pressure to a crystalline mass. Two recrystallizations from ethanol then yielded 9.3 g. (38%) of 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol, m.p. 162–163° and $[\alpha]^{25}D$ −14.1° in water, *c* 1.1.

Anal. Calcd. for $C_7H_{15}O_7N$: C, 37.3; H, 6.71. Found: C, 37.8; H, 6.68.

Chromatography of the crude reaction product on Whatman No. 1 paper with the upper phase of *n*-butyl alcohol:ethanol:water (4:1:5) revealed, in addition to 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol (R_f 0.53), a second product (R_f 0.67) which presumably was the epimeric 1-deoxy-2-*O*-methyl-1-nitro-D-glucitol. This latter product was not investigated further.

2-*O*-Methyl-D-mannose Phenylhydrazone.—A solution of 10 g. of 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol in 26.2 ml. of 2 *N* sodium hydroxide was added dropwise at room temperature to a stirred solution of 13.2 ml. of sulfuric acid in 15.2 ml. of water. The resulting solution was deionized by successive passage over Dowex-50 and Duolite A-4 resins, and then concentrated at reduced pressure to a sirup. Further concentration of the latter from ethanol solution yielded 0.48 g. of unchanged starting material (m.p. 159–162°). After removal of the latter, the filtrate volume was adjusted to 25 ml. with ethanol, 7 ml. of phenylhydrazine was added, and the solution was heated on the water bath for 15 min. Cooling to 5° and filtration then yielded 8.8 g. (74%) of 2-*O*-methyl-D-mannose phenylhydrazone, m.p. 162–163° and $[\alpha]^{25}D$ −49.6° (5 min.) to −59.5° (23 hr.) in pyridine, *c* 1.1. Pacsu and Trister[5] report m.p. 163° and $[\alpha]D$ −49.1° (initial) to −60.7° (24 hr.) in pyridine for this compound.

2-*O*-Methyl-D-mannose.—Two grams of 2-*O*-methyl-D-mannose phenylhydrazone was refluxed for 135 min. with a solution consisting of 24 ml. of water, 5 ml. of ethanol, 2.4 ml. of benzaldehyde, and 0.15 g. of benzoic acid. The solution then was cooled to 5° and the benzaldehyde phenylhydrazone removed by filtration. The filtrate was extracted with four 15-ml. portions of chloroform, decolorized with carbon, and concentrated at reduced pressure to a colorless sirup (1.37 g., 100%). After several months, the sirup crystallized. Following recrystallization from ethanol, the resulting 2-*O*-methyl-D-mannose showed m.p. 135–137° and $[\alpha]^{25}D$ +4.5° (20 min.) to +2.6° (23 hr.) in water, *c* 7. For this substance, Pacsu and Trister[5] report m.p. 136–137° and $[\alpha]^{20}D$ +7.0° (initial) to +4.5° (24 hr.) in water, *c* 2.88.

1-Deoxy-2-*O*-methyl-1-nitro-D-ribitol Triacetate.—A solution of 25.8 g. of D-*erythro*-3,4,5-triacetoxy-1-nitro-1-pentene[6] in 1 l. of methanol was treated at room temperature with a solution of 4.35 g. of sodium in 400 ml. of methanol. After 30 min., 12 ml. of glacial acetic acid was added and the solution was concentrated at reduced pressure to a sirup. This was dissolved in water and freed of sodium ions by passage of the solution over Dowex-50 resin. After decolorization with carbon, the solution was again concentrated, evaporated several times with ethanol, and dried in high vacuum over potassium hydroxide and calcium chloride. The resulting pale yellow sirup (15 g.) was acetylated for 3 hr. at room temperature with 65 ml. of acetic anhydride containing 2 drops of sulfuric acid. The acetylation mixture was poured onto ice and water and, after 24 hr. at 0°, the resulting crystals were filtered to provide 11.5 g. of crude product, m.p. 92–94°. Recrystallization from ethanol gave 7.6 g. (26%) of pure 1-deoxy-2-*O*-methyl-1-nitro-D-

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[4] J. U. Nef, *Ann.*, **280**, 263 (1894); J. C. Sowden and H. O. L. Fischer, *J. Am. Chem. Soc.*, **66**, 1312 (1945).

[5] E. Pacsu and S. M. Trister, *J. Am. Chem. Soc.*, **63**, 925 (1941).

[6] J. C. Sowden, *J. Am. Chem. Soc.*, **71**, 1897 (1949); **72** 808 (1950).

ribitol triacetate, m.p. 99–100° and $[\alpha]^{25}\mathrm{D}$ $-10.7°$ in chloroform, c 2.1.

Anal. Calcd. for $C_{12}H_{19}O_9N$: C, 44.9; H, 5.96; N, 4.36. Found: C, 44.9; H, 5.89; N, 4.22.

1-Deoxy-2-*O*-methyl-1-nitro-D-ribitol.—A solution of 7 g. of the above triacetate in 400 ml. of methanol was treated at room temperature with a solution of 0.76 g. of sodium in 100 ml. of methanol. After 30 min., 2 ml. of glacial acetic acid was added and the solution was concentrated at reduced pressure to a sirup. This was dissolved in water and freed of sodium ions by passage over Dowex-50 resin. The effluent was filtered through carbon and concentrated at reduced pressure to a sirup. Several evaporations of the latter with ethanol, followed by drying in high vacuum over potassium hydroxide, yielded a crystalline residue. Recrystallization from ethanol–ether then gave 4.0 g. (93%) of 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol, m.p. 65–67° and $[\alpha]^{25}\mathrm{D}$ $-15.3°$ in water, c 1.5. The compound is hygroscopic.

Anal. Calcd. for $C_6H_{13}O_6N$: C, 36.9; H, 6.71; N, 7.18. Found: C, 37.0; H, 6.82; N, 7.38.

The oxidation of 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol with excess aqueous sodium metaperiodate was followed polarimetrically. The resulting solution of 3-deoxy-2-*O*-methyl-3-nitro-L-glyceraldehyde showed $[\alpha]^{25}\mathrm{D}$ $-12°$, c 1, 35 min., constant over 46 hr. Similar oxidation of 1-deoxy-2-*O*-methyl-1-nitro-D-mannitol gave a solution of 3-deoxy-2-*O*-methyl-3-nitro-D-glyceraldehyde, $[\alpha]^{25}\mathrm{D}$ $+13°$, c 0.9, 30 min., constant over 48 hr.

2-*O*-Methyl-D-ribose Benzylphenylhydrazone.—A solution of 3.0 g. of 1-deoxy-2-*O*-methyl-1-nitro-D-ribitol in 9.2 ml. of 2 *N* sodium hydroxide was added dropwise at room temperature to a stirred solution containing 4.5 ml. of sulfuric acid and 5.5 ml. of water. The resulting solution was deionized by passage over Dowex-50 and Duolite A-4 resins and concentrated at reduced pressure to a sirup. This was dissolved in 20 ml. of ethanol and 3.1 ml. of benzylphenylhydrazine was added. After 1 hr. at room temperature and 18 hr. at 5°, the solvent was blown off and the resulting sirup then slowly crystallized. Filtration with cold ether yielded a total of 4.4 g. (83%) of the crude hydrazone, m.p. 110–116°, in three crops. Recrystallization from ethanol–ether–petroleum ether gave pure 2-*O*-methyl-D-ribose benzylphenylhydrazone, m.p. 120–121° and $[\alpha]^{25}\mathrm{D}$ $+17.6°$ in chloroform, c 1.8.

Anal. Calcd. for $C_{19}H_{24}O_4N_2$: C, 66.2; H, 7.02; N, 8.13. Found: C, 65.8; H, 7.04; N, 8.17.

2-*O*-Methyl-D-ribose *p*-Toluenesulfonylhydrazone.—This hydrazone was obtained (66% crude yield) as described above for the benzylphenylhydrazone, except that the ethanolic solution of the sugar and *p*-toluenesulfonylhydrazine was refluxed for 45 min. Recrystallization from ethanol gave pure 2-*O*-methyl-D-ribose *p*-toluenesulfonylhydrazone, m.p. 145–146° dec. and $[\alpha]^{25}\mathrm{D}$ $+6°$ (20 min.) to $-8°$ (19 hr.) in water, c 1.

Anal. Calcd. for $C_{13}H_{20}O_6N_2S$: C, 47.0; H, 6.07; N, 8.43. Found: C, 47.1; H, 6.14; N, 8.22.

A mixed melting point of this hydrazone with 2-*O*-methyl-D-arabinose *p*-toluenesulfonylhydrazone[7] (m.p. 143–144°) showed m.p. 134–137°.

2-*O*-Methyl-D-ribose.—Regeneration of the sugar from its benzylphenylhydrazone was carried out as described above for 2-*O*-methyl-D-mannose phenylhydrazone. The sirup thus obtained (52%) was slightly colored, contained 14% OCH_3 and 1.36% *N*, and was shown by paper chromatography to contain a small amount of a contaminating impurity. The latter was largely removed by fractionation over a Chromax cellulose chromatographic column[8] using 90% *n*-butyl alcohol as developer. The 2-*O*-methyl-D-ribose thus recovered (77%) was very pale yellow in color and showed $[\alpha]^{25}\mathrm{D}$ $-22°$ in methanol, c 3.4. For 2-*O*-methyl-D-ribose prepared by a method based on partial methylation, a value of $[\alpha]^{20}\mathrm{D}$ $-32°$ in methanol, c 1.08, has been reported.[9]

Anal. Calcd. for $C_6H_{12}O_5$: OCH_3, 18.9; N, 0.0. Found: OCH_3, 18.1; N, 0.22.

Electrophoresis of the above 2-*O*-methyl-D-ribose along with D-ribose and 2-deoxy-D-ribose on Whatman 3MM paper in 0.1 *M* sodium tetraborate buffer (*p*H 9.2) at 1000 v. showed the following mobilities: D-ribose, 1; 2-deoxy-D-ribose, 0.40; 2-*O*-methyl-D-ribose, 0.40. Values with respect to D-ribose that have been reported previously are: 2-deoxy-D-ribose, 0.46; 2-*O*-methyl-D-ribose, 0.49,[10] and 2-deoxy-D-ribose, 0.42; 2-*O*-methyl-D-ribose, 0.44.[11]

2-*O*-Methyl-D-arabinitol and 2-*O*-Methyl-D-ribitol.—An aqueous solution of 2-*O*-methyl-D-arabinose, obtained by the method of Mitchell[12] from 3.0 g. of 3-*O*-methyl-D-glucose, was treated with 1.0 g. of sodium borohydride. After 3 hr. at room temperature, processing of the reaction mixture in the usual manner yielded 2.3 g. (92%) of 2-*O*-methyl-D-arabinitol, m.p. 97–99°. After recrystallization from ethanol–ether, the product showed m.p. 98–99° and $[\alpha]^{25}\mathrm{D}$ $-11°$ in methanol, c 2.7.

Anal. Calcd. for $C_6H_{14}O_5$: C, 43.4; H, 8.44. Found: C, 43.6; H, 8.42.

Similar reduction of the above, sirupy 2-*O*-methyl-D-ribose yielded 90% of a colorless, chromatographically homogeneous sirup with $[\alpha]^{25}\mathrm{D}$ $-5.4°$ in methanol, c 1.4.

The epimeric, monomethylated pentitols were oxidized with excess sodium metaperiodate and the oxidations were followed polarimetrically. The crystalline 2-*O*-methyl-D-arabinitol showed a final $[\alpha]^{25}\mathrm{D}$ $+1.7° \pm 0.6°$, calculated as 2-*O*-methyl-D-glyceraldehyde, in water, c 1.3. The sirupy 2-*O*-methyl-D-ribitol showed a final $[\alpha]^{25}\mathrm{D}$ $-2.3° \pm 0.7°$, calculated as 2-*O*-methyl-L-glyceraldehyde, in water, c 1.

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