Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.24; H, 8.04; N, 8.32.

Anilide from Bromocyclopentane.—The Grignard reagent was prepared by the action of 22.4 g. (0.15 mole) of bromocyclopentane on 3.6 g. (0.15 mole) of magnesium in a total of 225 ml. dry ether. To the solution was added 12.6 g. (0.12 mole) of phenyl isocyanate in 130 ml. of dry ether. The stirring of the reaction mixture was continued for 35 minutes after the addition was complete, and the product was then poured into an ice-water–hydrochloric acid mixture. A total of 18 g. of the anilide was isolated, representing a yield of 81%. The crude anilide was recrystallized once from methanol and subsequently from carbon tetrachloride to a constant melting point of 160.1–161.2° (cor.).

Anal. Calcd. for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.33; H, 7.99; N, 7.85.

α-Naphthalide from Bromocyclopentane.—The Grignard reagent was prepared as in the preparation of the anilide using 14.9 g. (0.10 mole) of bromocyclopentane and 1.9 g. (0.08 mole) of magnesium in 225 ml. of dry ether. To this reagent was added a solution of 19.1 g. (0.08 mole) of α-naphthyl isocyanate in 135 ml. of dry ether. Hydrolysis of the mixture was accomplished as in the previous experiment and a total of 13.5 g. of the naphthalide was isolated. The naphthalide was recrystallized once from ethanol and subsequently from carbon tetrachloride to a constant melting point of 174.2–175.0° (cor.).

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16, N, 5.85. Found: C, 79.45; H, 6.89; N, 6.07.

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Nitrate Esters of 2,2-Dimethylol-1-propanol Monoacetate and Diacetate[1]

BY N. S. MARANS AND R. F. PRECKEL

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In continuation of the investigation of nitrate esters of polyols[2] the mononitrate, dinitrate, acetate dinitrate and diacetate nitrate of 2,2-dimethylol-1-propanol, the alcohol commonly known as metriol, have been synthesized.

A mixture of metriol monoacetate and diacetate was prepared by equilibration of metriol and metriol triacetate in the presence of potassium carbonate.[3] Difficulty was encountered in the separation of the acetates but nitration of the reaction mixture gave the readily separable metriol acetate dinitrate. The metriol diacetate mononitrate was prepared by nitration of carefully fractionated metriol diacetate. Controlled saponification of metriol diacetate mononitrate and metriol acetate dinitrate gave metriol mononitrate and dinitrate, respectively. The preferential cleavage of the organic ester grouping in such compounds has been emphasized previously.[4]

Experimental

Materials.—Metriol, m.p. 198–200°, and metriol triacetate were obtained from Trojan Powder Company and were used without further purification.

Metriol Acetate Dinitrate.—A mixture of 106 g. of metriol and 123 g. of metriol triacetate in the presence of 2 g. of potassium carbonate was heated at 175–180° for 16 hours in a 500-ml. round-bottom flask equipped with a reflux condenser. Distillation of the crude product at 5 mm. gave the following fractions: (1) 122–130°, 101.5 g.; (2) 130–136°, 91 g.; and (3) residue, 16 g., m.p. 160–170°. Treatment of all three fractions with ethylene chloride gave a recovery of 65 g. of metriol as an insoluble precipitate.

After removal of the ethylene chloride by reduced pressure evaporation, a portion of fraction 2, 17 g., was nitrated at 0° using 90% water-white nitric acid and air agitation. The nitration solution was added to water and the organic layer separated and washed several times with water. The metriol acetate dinitrate was isolated by solution in ethanol and fractional precipitation with water. The first two fractions consisting of 16.5 g. (65.4%) gave similar nitrogen analyses and were metriol acetate dinitrate, d^{25} 1.302, $n^{25}\text{D}$ 1.4566.

Anal. Calcd. for $C_7H_{12}O_8N_2$: C, 33.33; H, 4.76; N, 11.11. Found: C, 34.24; H, 4.89; N, 10.78.

The ethanolic mother liquors contained a mixture of metriol acetate dinitrate and metriol diacetate nitrate. An 85–15 mixture of acetate and diacetate was obtained on nitration of fraction I.

Metriol Dinitrate.—A solution of 20 g. of metriol acetate dinitrate, 5.0 g. of sodium hydroxide and 150 ml. of 95% ethanol was allowed to stand for 20 minutes. The final solution was neutralized with 2.5 *N* HCl and then concentrated by evaporation under reduced pressure to remove the ethanol. Extraction of the mother liquors with ether and evaporation of the ethereal layer under reduced pressure gave 9.7 g. (57%) of metriol dinitrate, $n^{25}\text{D}$ 1.4692, d^{25} 1.362.

Anal. Calcd. for $C_5H_{10}O_7N_2$: C, 28.57; H, 4.81; N, 13.33. Found: C, 28.65; H, 4.87; N, 13.15.

Metriol Diacetate Nitrate.—A mixture of 60 g. of metriol and 260 g. of metriol triacetate in the presence of 4 g. of potassium carbonate was heated at 140° for five hours, then distilled collecting four fractions of equal weight. Fractionation of the initial distillate gave 55 g. of metriol diacetate, b.p. 107–108° (3 mm.), $n^{25}\text{D}$ 1.4409, d^{25} 1.109. The remaining distillates were mixtures of metriol acetate and diacetate.

Anal. Calcd. for $C_9H_{16}O_5$: C, 52.94; H, 7.84. Found: C, 52.39; H, 7.90.

Metriol diacetate, 18 g., was nitrated at 0° using water-white 90% nitric acid and air agitation. The nitration solution was added to ice and water and the solution ethereally extracted. The ethereal extracts were washed three times with water to remove residual nitric acid and then the ethereal layers concentrated by reduced pressure distillation at 2 mm. to give 16 g. (72.7%) of metriol diacetate nitrate, $n^{25}\text{D}$ 1.4455, d^{25} 1.213.

Anal. Calcd. for $C_9H_{15}O_7N$: C, 43.37; H, 6.02; N, 5.62. Found: C, 43.39; H, 5.99; N, 5.27.

Material prepared by nitration of a crude mixture of metriol diacetate and monoacetate and separated by differential solubility gave in two runs 5.95 and 6.05%, N.

Metriol Mononitrate.—Metriol diacetate mononitrate, 8.0 g., was dissolved in a solution containing 5.0 g. of sodium hydroxide, 30 ml. of ethanol and 10 ml. of water. After 20 minutes at 25° the solution was neutralized with 3 *N* HCl and the major portion of the ethanol removed under reduced pressure. The aqueous solution was saturated with sodium chloride and then ethereally extracted three times. Evaporation of the ethereal extracts yielded a semi-solid which was recrystallized from benzene to give 4.0 g. (75%) of metriol mononitrate, m.p. 76–77°.

Anal. Calcd. for $C_5H_9O_4N$: C, 36.37; H, 6.67; N, 8.48. Found: C, 36.56; H, 6.84; N, 8.08.

Metriol mononitrate was acylated in a 75% yield to metriol diacetate mononitrate using acetic anhydride and pyridine at 25°.

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(1) This work was performed at the Allegany Ballistics Laboratory, an establishment owned by the U. S. Navy and operated by Hercules Powder Company under Contract NOrd 10431.

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tory. The analyses reported were done by Micro-Tech Laboratories, Skokie, Illinois.

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Synthesis of Acetobromo Sugars

BY PAUL G. SCHEURER AND F. SMITH[1,2]

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Acetohalogen derivatives of sugars play an important role in synthetic carbohydrate chemistry and ease of preparation of these compounds is of considerable value. Formerly the classical procedure for preparing acetobromo sugars has involved treatment of the sugar acetate with a solution of hydrogen bromide in either glacial acetic acid or acetic anhydride.[3–5] Acetyl bromide has also been used.[6]

A simplified procedure for making acetobromoglucose has been described[7] in which the brominating agent (HBr) is generated *in situ* by adding water to a mixture of bromine and red phosphorus in glacial acetic acid.

We have been making use of a similar method except that no water was added to the brominating reagent (CH_3COBr). The reaction may be applied to either the free sugars or their acetates. Thus acetobromo derivatives have been prepared from the following: L-arabinose, D-xylose, D-glucose, β-D-glucose pentaacetate and β-cellobiose octaacetate (see Table I).

TABLE I

Compound	Yield, %	Acetobromo derivative M. p., ° C.	$[\alpha]^{24}D$ (CHCl$_3$)	Ref.
L-Arabinose	22	137	+284°	8
D-Xylose	63.5[a]	....	....	9
D-Glucose	66	87–89	+195	10
β-D-Glucose pentaacetate	84	88–89	+198	10
β-Cellobiose octaacetate	95–100	185	+ 94	11

[a] This value is based on the yield of methyl β-D-xylopyranosine triacetate (m. p. 112–113°, $[\alpha]^{24}D$ −60° ($CHCl_3$)) derived from the acetobromo compound.

Experimental

Generation of the Brominating Reagent.—Bromine (180 g.) is added dropwise to suspension of red phosphorus (30 g.) in glacial acetic acid (300 ml.) with cooling. After the reaction is complete the mixture is filtered (glass wool) and kept in the cold room if not required for immediate use.

Preparation of Acetobromo Sugars. (a) **From the Sugars,** *e.g.*, **D-Glucose.**—The sugar (10 g.) was added with shaking to the brominating reagent (100 ml.), the temperature being kept at or below 40°. After 2 hours at room temperature, the reaction mixture was diluted with chloroform (100 ml.) and poured with stirring into a mixture of ice and water (200 ml.). The chloroform layer was separated and the aqueous layer extracted with chloroform. The chloroform extracts were combined, washed with water then with an aqueous solution of sodium bicarbonate and dried ($CaCl_2$). Removal of solvent *in vacuo* gave α-acetobromo-D-glucose which was crystallized from ether. More material was obtained by adding petroleum ether to the ethereal mother liquors.

(b) **From the Sugar Acetates,** *e.g.*, **β-D-Glucose Pentaacetate.**—The acetate (216 g.) was added in portions with shaking to the brominating reagent prepared from bromine (180 g.). After 2 hours at room temperature the reaction mixture was diluted with chloroform (300 ml.) and poured into a mixture of ice and water (800 ml.). The α-acetobromo-D-glucose was isolated as in (a).

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Synthesis of Glycol Bis-(alkyl Sulfites)[1]

BY D. C. MORRISON

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Esters of sulfurous acid of various types are known, simple esters having been prepared long ago.[2] Richter[3] obtained diaryl sulfites while Carre and Libermann[4] prepared many mixed esters, including alkyl aryl sulfites. Some cyclic esters of glycols are known[5] and also the cyclic ester of catechol.[6]

However, no mixed diesters of glycols have been reported. It was the purpose of this work to attempt to prepare mixed glycol bis-(alkyl sulfites) of the type formula: $RO{\cdot}SO{\cdot}O{\cdot}(CH_2)_2{\cdot}X{\cdot}(CH_2)_2{\cdot}O\ SO{\cdot}OR$ where R is ethyl or β-chloroethyl and X is oxygen or sulfur. In addition diesters of tetramethylene glycol were studied.

The compounds were employed in tumor chemotherapy tests in mice. Structures of this type possess a formal analogy to the disulfonic esters of Timmis[7] who showed that the dimethanesulfonate of tetramethylene glycol has activity in causing tumor regression.

The glycol diesters were prepared by reaction of one mole of glycol in inert solvent medium with two moles of an ester chloride of sulfurous acid (alkyl chlorosulfites) in the presence of pyridine.[8] The syntheses were successful with tetramethylene glycol, diethylene glycol, thiodiglycol and butyne diol, when reacted with ethyl or β-chloroethyl chlorosulfites. The products, after appropriate purification, were high boiling oils of little or no odor. Several of the bis-(ethyl sulfites) were distilled but no attempt was made to distil the chloroethyl esters. None of these substances is steam volatile and they did not appear to decompose during short contact with boiling water.

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