Experimental[4]

1-Acetyl-3-*N*-piperidinomethylhydantoin (IIIa).—1,3-Diacetylhydantoin (5.0 g., 0.027 mole) was dissolved in piperidine (10.0 g., 0.12 mole). To the resulting solution aqueous formaldehyde (5 ml. 36.2% solution equivalent to 1.85 g. or 0.062 mole) was added in one portion. The product precipitated immediately as a white crystalline mass. After cooling to 10–15°, this product was collected by filtration and washed with petroleum ether (four 15-ml. portions). After air drying, the product (6.7 g., 0.026 mole, 98%) melted at 150–152°. A single recrystallization from ethyl acetate raised this melting point to 160–161°.

Anal. Calcd. for $C_{11}H_{17}O_3N_3$: C, 55.25; H, 7.13; N, 17.59. Found: C, 55.48; H, 7.12; N, 17.78.

1-Acetyl-3-*N*-morpholinomethylhydantoin (IIIb).—1,3-Diacetylhydantoin (5.0 g., 0.027 mole) was dissolved in morpholine (10.0 g., 0.12 mole). To this solution aqueous formaldehyde (5 ml. 36.2% solution equivalent to 1.85 g. or 0.062 mole) was added in one portion. The solution which resulted was cooled to 15–20° and stirred to induce crystallization. The product deposited as a mass of white crystals. It was collected by filtration and washed with dry ether (two 5-ml. portions). After air drying it amounted to 6.2 g. (0.025 mole, 91%) and melted at 139–141°. A single recrystallization from ethyl acetate yielded the compound in pure form, m.p. 154–155°.

Anal. Calcd. for $C_{10}H_{15}O_4N_3$: C, 49.87; H, 6.23; N, 17.42. Found: C, 50.17; H, 6.41; N, 17.08.

1-Acetyl-3-(3′-indolylmethyl)hydantoin (IV).—1-Acetyl-3-piperidinomethylhydantoin (7.6 g., 0.030 mole), indole (3.6 g., 0.031 mole), and sodium hydroxide (0.2 g., 0.005 mole) were placed in dry xylene (60 ml.) and heated at 135–145° for 24 hr. under nitrogen. Upon cooling a brown amorphous precipitate deposited and was collected by filtration. After washing with a small amount of petroleum ether, the product was air dried. It weighed 3.6 g. Extraction of this material with ethyl acetate in a Soxhlet apparatus yielded 2.5 g. (0.0097 mole, 32%) of a product which melted at 197–198°.

Anal. Calcd. for $C_{14}H_{13}O_3N_3$: C, 62.00; H, 4.80. Found: C, 61.61; H, 4.96.

The same derivative was obtained in somewhat lower yield by condensing 1-acetyl-3-morpholinomethylhydantoin with indole under the conditions described above.

The hydrolysis of 1-acetyl-3-(3′-indolylmethyl)hydantoin was accomplished by heating the compound with aqueous barium hydroxide. This hydrolysis yielded an appreciable quantity of glycine, identified by paper chromatography, and an insoluble resinous product, which was not characterized. The absence of tryptophan in the hydrolyzate was also established by paper chromatography.

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(4) All melting points are uncorrected.

S_N2 Reactions of Chloroacetals

WALTER E. CONRAD, LEONARD A. LEVASSEUR,
RAYMOND F. MURPHY, NANCY L. HARE,
AND HELEN M. CONRAD

Chemistry Department, Bradford Durfee College of Technology, Fall River, Mass.

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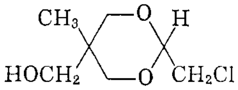
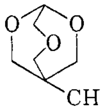
Nucleophilic substitutions of the chlorine atoms of bischloroethylidenepentaerythritol[1] (I) offer promise of producing several interesting difunctional compounds of possible interest in the synthesis of polymers and of fluids of high viscosity and low volatility. Because of the difficulty reported in effecting these reactions with sodium cyanide,[2] a study has been made of the nucleophilic substitution of the following cyclic acetals of chloroacetaldehyde: I; monochloroethylidenepentaerythritol (II); the acetal (III) of chloroacetaldehyde and 2-methyl-2-hydroxymethylpropanediol-1,3; two homologs of the latter (IV and V in Table I); and the chloroacetal of 2,2-dimethylpropanediol-1,3 (VI)[1] (see Table I).

The nucleophilic reagents chosen for study were ammonia and the anions of phenol and cyclohexanol. No difficulty was experienced in effecting S_N2 reactions with these reagents. In the reaction of ammonia with VI, the secondary amine was isolated, probably because the reaction was conducted in a two phase system. The product of the reaction of ammonia with I was a basic material, indicating that the reaction had taken place, but it was an intractable gum from which no pure product could be isolated.

Compounds III, IV, V, and their derivatives, are capable of existing in *cis* and *trans* forms. Distillation of III through a short packed fractionating column failed to effect a separation. If at least a part of III, IV, or V were present as the isomer in which the hydroxymethyl group is *cis* to the chloromethyl group (XVI for III),[3] it should be possible to effect cyclization to a bicyclic triether structure like XVII. However, treatment of III and IV with sodium cyclohexyloxide gave the cyclohexyl ethers, but no product of cyclization. The same results were obtained with II, even though in this case the chloromethyl group would necessarily be *cis* to a hydroxymethyl group. Also, an attempt to cyclize V by refluxing with a solution of sodium hydroxide in diethylene glycol produced no evidence of formation of a cyclic product.


XVI


XVII

Experimental[4]

Preparation of 2-*n*-Propyl-2-hydroxymethylpropanediol-1,3.[5]—To a stirred mixture of 86.1 g. (1 mole) of *n*-valeralde-

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[1] Correct systematic names for compounds I through VI are: I: 3,9-Bischloromethyl-2,4,8,10-tetraoxaspiro[5.5]undecane. II: 2-Chloromethyl-5,5-bishydroxymethyl-1,3-dioxane. III: 2-Chloromethyl-5-ethyl-5-hydroxymethyl-1,3-dioxane. V: 2-Chloromethyl-5-hydroxymethyl-5-propyl-1,3-dioxane. VI: 2-Chloromethyl-5,5-dimethyl-1,3-dioxane.

[2] J. B. Clements and L. M. Rice, *J. Org. Chem.*, **24**, 1958 (1959).

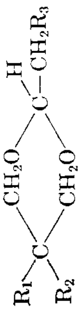
[3] The question whether this ring structure takes the chair, boat, or skew conformation is as yet unresolved.

[4] Microanalyses were performed by Weiler and Strauss Laboratories, Oxford, England; melting points and boiling points were uncorrected.

[5] An adaptation from the preparation of pentaerythritol. H. B. J. Schurink, *Org. Syntheses*, Coll. Vol. I, 425 (1941).

TABLE I

ACETALS OF POLYOLS



	R_1	R_2	R_3	M.P.	B.P.	Mm.	Yield, %	Formula	Calcd. C	Calcd. H	Calcd. Cl	Found C	Found H	Found Cl
IV	$HOCH_2$—	C_2H_5—	Cl	...	106–111	0.2	65	$C_8H_{15}O_3Cl$	49.36	7.76	18.21	49.53	7.92	18.28
V	$HOCH_2$—	n-C_3H_7	Cl	...	112–114	0.1	77	$C_9H_{17}O_3Cl$	51.78	8.21	16.99	52.01	8.18	17.10
VII	CH_3—	CH_3—	*O*-Phenyl	50.5–51		...	52	$C_{13}H_{18}O_3$	70.21	8.16		70.15	8.26	
VIII	CH_3—	CH_3—	*O*-Cyclohexyl-	...	78–80	0.05	29	$C_{13}H_{24}O_3$	68.38	10.59		68.84	11.11	
IX	$HOCH_2$—	CH_3—	*O*-Phenyl	98–99	...	...	30	$C_{13}H_{18}O_9$	65.50	7.61		65.56	8.02	
X	$HOCH_2$—	CH_3—	*O*-Cyclohexyl	...	130–132	0.1	25.6	$C_{13}H_{24}O_4$	63.90	9.90		64.65	10.14	
XI	$HOCH_2$—	C_2H_5—	*O*-Cyclohexyl	...	150–160	0.3	55	$C_{14}H_{26}O_4$	65.09	10.15		65.06	9.46	
XII	$HOCH_2$—	$HOCH_2$—	*O*-Phenyl	134–140	...	...	29	$C_{13}H_{18}O_5$	61.38	7.13		61.73	7.15	
XIII	$HOCH_2$	$HOCH_2$—	*O*-Cyclohexyl-	97–98	180–245	0.008	8.1	$C_{13}H_{24}O_5$	59.94	9.28		58.75	9.33	

hyde and 2060 g. of water, was added solid calcium hydroxide and 40% formaldehyde solution in small portions at a rate which kept the temperature of the reaction mixture between 50 and 55°. After 420 ml. of 40% formaldehyde (6 moles) and 44.5 g. (0.6 mole) of calcium hydroxide had been added, the mixture was kept at 50° with an infrared lamp and stirred for 3 hr. The *p*H at this time was 6.8. After filtering the mixture, removing the water by vacuum distillation and the resulting white inorganic precipitate by filtration, the remaining liquid was distilled at 1 mm. When the pot temperature reached 180°, distillation was stopped just as signs of darkening appeared. Attempts to distill beyond this point resulted in decomposition. On cooling, the pot contents (89.5 g.) solidified. On recrystallization from methanol, 43.0 g. (29.1 %) of 2-*n*-propyl-2-hydroxymethylpropanediol-1,3, m.p. 97–100°, was obtained; m.p. of an analytical sample was 100–101°.

Anal. Calcd. for $C_7H_{16}O_3$: C, 56.73; H, 10.88. Found: C, 56.10; H, 10.77.

Preparation of Chloroacetals.—The synthesis of II, III, and VI has been previously reported.[6] The other chloroacetals (I, IV, and V) were made by the same methods. I, which was made in 35% yield by reaction in aqueous solution, was found to have a m.p. 96.0–96.5°. The m.p. previously reported was 91.8°.[7]

Reaction of Chloroacetals with Sodium Phenoxide.—The following may be considered a model for all the reactions of this type which were conducted in this work. A solution of 12 g. (0.3 mole) of sodium hydroxide, 23.1 g. (0.3 mole) of phenol, and 36.82 g. (0.14 mole) of bischloroethylidenepentaerythritol in 200 ml. of ethylene glycol was refluxed for 26 hr. The reaction mixture solidified on cooling and was washed with water, yielding 38.5 g. of water-insoluble solid. On recrystallization from benzene, 20.1 g. (39%) of XIV, m.p. 203–205°, was obtained.

In the reaction of III with sodium phenoxide, the product was soluble in the reaction mixture, so that the solvent was removed by distillation and the sodium chloride was filtered as it precipitated. The product itself (IX) was distilled at 154–160° (0.14 mm.). It then solidified and was recrystallized from methanol and water to a m.p. of 98–99°.

Reactions of Chloroacetals with the Sodium Salt of Cyclohexanol.—The following is a general procedure for the preparation of the cyclohexyl ethers from the chloroacetals. To 250 ml. of cyclohexanol was added 6.9 g. (0.3 g.-atom) of metallic sodium, and the resulting mixture was refluxed until all the sodium dissolved. To this solution was added 58.4 g. (0.3 mole) of III. This mixture was refluxed for 1 hr., and the reaction mixture filtered hot to remove the salt (16.4 g.) formed during reaction. The filtrate was then distilled under reduced pressure.

In the reactions of the sodium salt of cyclohexanol with monochloroethylidenepentaerythritol and with bischloroethylidenepentaerythritol, the distillate solidified on cooling. The former was recrystallized to a constant melting point from benzene. The latter could not be recrystallized from any of the common solvents and was sent for analysis without recrystallization. In all of these reactions, no cyclization product was obtained in the boiling point range expected for these compounds.

Reaction of Chloroacetal of 1,1,1-Trimethylolbutane (V) and Sodium Hydroxide.—To a hot solution of 16.3 g. (0.41 mole) of sodium hydroxide in 300 ml. of diethylene glycol (b.p. 244°) was added dropwise 50 g. (0.24 mole) of V. A distillate was collected (7.1 g.) while the sodium hydroxide was being added (b.p. 98–110°). This, as well as another fraction (2.1 g., b.p. 110–135°) was almost entirely water. In the boiling point range expected for the cyclization product (135–210°) nothing was collected. The reaction

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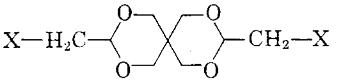
[6] W. E. Conrad, B. D. Gesner, L. A. Levasseur, R. F. Murphy, and H. M. Conrad, *J. Org. Chem.* **26**, 3571 (1961).

[7] V. G. Mkhitaryan, *J. Gen. Chem. U.S.S.R.*, **9**, 1923 (1939).

TABLE II
ACETALS OF PENTAERYTHRITOL



	X	M.P.	B.P.	Mm.	Yield, %	Formula	Calcd. C	Calcd. H	Calcd. Cl	Found C	Found H	Found Cl
XIV	O-Phenyl	203.5	...	...	39	$C_{21}H_{24}O_6$	67.73	6.45		66.93	6.66	
XV	O-Cyclohexyl	40–47	176–200	0.1	50	$C_{21}H_{36}O_6$	65.59	9.43		64.19	9.36	
I	Cl	96–96.5	...	...	35	$C_9H_{14}O_4Cl_2$	42.05	5.49	27.58	42.61	5.17	27.40

mixture was completely soluble in water. No further attempts were made to isolate a reaction product.

Reaction of VI with Ammonia.—A mixture of 82.3 g. (0.5 mole) of the chloroacetal of pentaglycol and 133.2 ml. (2 moles) of concd. ammonium hydroxide in 66.6 ml. of Cellosolve was placed in a sealed iron pipe and heated at 138° for 17 hr. The reaction mixture was then filtered and the filtrate formed two layers. The organic layer was separated and distilled. After a small forerun, a fraction (17.5 g.) was collected at 80–155° (1.3 mm.) which solidified on cooling. On recrystallization from benzene, 15.6 g. (23%) of bis[(5,5-dimethyl-*m*-dioxan-2-yl)methyl]amine, m.p. 60–65°, was obtained. Melting point of an analytical sample was 67–68°.

Anal. Calcd. for $C_{14}H_{27}O_4N$: C, 61.51; H, 9.95; N, 5.12. Found: C, 61.73; H, 10.12; N, 5.11.

Reaction of I with Ammonium Hydroxide.—Reaction of I with ammonia for 8.5 hr. at 140° in a procedure similar to the above, afforded a light-colored gummy material which was soluble in cold dilute hydrochloric acid. The gummy product could not be recrystallized. Attempts to form derivatives by benzoylation and by reaction with picric acid afforded only gummy materials again.

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Juglone 4-Monooxime, an Isomer of 8-Nitro-1-naphthol

D. C. MORRISON AND D. W. HEINRITZ

Hyman Laboratories, Inc., Berkeley, Calif.

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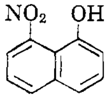
Meldola and Streatfeild[1] were the first to attempt to prepare 8-nitro-1-naphthol (I) by decomposition of the diazonium salt of 8-nitro-1-naphthylamine, but obtained only resinous material. Kozlov and Vorozhtzov[2] repeated this work and obtained a product of m.p. 212° dec., which they considered to be the compound in question. The reaction was later carried out by Luther and Gunzler,[3] and also by Anderson and co-workers[4] and by Bryson,[5] and the product accepted as 8-nitro-1-naphthol.



I

In the present work, the compound was prepared by the same method for comparison with other products which were suspected of containing this nitronaphthol. From Luther and Gunzler's infrared data, it was seen that the product obtained was identical to theirs. It eventually became apparent, however, that the substance did not have the infrared spectral characteristics nor the chemical properties of a nitronaphthol.

Thus, the spectrum was found to be quite similar to those of a number of naphthaquinone monooximes which had been prepared in this laboratory. Strong nitro bands were missing and three characteristic features of quinone oximes, as indicated by Hadzi,[6] were present: 1. Strong and broad absorption bands centered around 3100 cm.$^{-1}$, with one band appearing at 2830 cm.$^{-1}$. 2. A shoulder at 1655 cm.$^{-1}$, probably due to the C═O stretching mode of the 1,4-monooxime. 3. A strong band at 988 cm.$^{-1}$, ascribed to the N—O bending frequency in quinone oximes. No similar band was found in any of the isomeric nitronaphthols which were examined in this laboratory.

Among various possible structures considered for the compound was that of a 5-hydroxy-1,4-naphthaquinone 4-monooxime (8-hydroxynaphthaquinone 1-oxime) (III), isomeric with 8-nitro-1-naphthol. After further examination, this constitution proved to be compatible with the properties of the substance.

All three of the *ortho* substituted nitronaphthols (1,2- or 2,1- and 3,2-) have melting points below 130° and a peri (1,8-) isomer, with similar possibilities for chelation or H-bonding likewise might be expected to be less polar and therefore lower melting than other nitronaphthols. The m.p. of 212° dec. given by Kozlov and Vorozhtzov[2] is much higher than would be expected and, indeed, later work by Anderson *et al.*[4] and Bryson[5] give a decomp. point of 242° without melting.

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[1] R. Meldola and F. W. Streatfeild, *J. Chem. Soc.*, **63**, 1056 (1893).

[2] V. V. Kozlov and N. N. Vorozhtzov, *Ber.*, **69B**, 416 (1936).

[3] H. Luther and H. Gunzler, *Z. Naturfors.*, **10b**, 445 (1955).

[4] J. R. A. Anderson, A. J. Costoulas, and J. L. Garnett, *Anal. Chim. Acta.*, **20**, 236 (1959).

[5] A. Bryson, *Trans. Faraday Soc.*, in press (from ref. 4).

[6] D. Hadzi, *J. Chem. Soc.*, 2725 (1956).