Excess alcohol was distilled off (91% recovery) from the alkoxide prepared from 1.0 mole of *n*-hexyl alcohol and 0.3 mole of potassium. Two hundred ml. of *p*-cymene and 2.0 g. of U.O.P. nickel were added and the mixture was heated under reflux (173 to 175°) with stirring for 5.5 hours. No water collected in the trap. After the reaction mixture was worked up in the usual fashion distillation gave a 5-g. fraction at 90° to 102° (2.5 mm.) plus 5 g. of 2-*n*-butyloctanol-1, 18 g. of *n*-hexanoic acid and 2 g. of undistilled residue. The first 5-g. fraction gave a precipitate with 2,4-dinitrophenylhydrazine which upon recrystallization from ethanol formed golden plates which melted at 95–96°. They analyzed satisfactorily for the derivative of 2-*n*-butyloctanal. *Anal.* Calcd. for $C_{18}H_{28}N_4O_4$: C, 59.32; H, 7.75; N, 15.37. Found: C, 59.44; H, 7.89; N, 15.54. The corresponding derivative of authentic 2-*n*-butyl-2-octenal melted at 133–134°; a mixture of the two derivatives melted at 85° to 108°.

The ability of *n*-hexaldehyde to promote the formation of more than an equivalent amount of 2-*n*-butyloctanol-1 at a temperature below that at which it would otherwise be expected to occur in the absence of the nickel catalyst is shown by the following experiment. Two grams of pure *n*-hexaldehyde was added to a solution prepared from 1.0 mole of *n*-hexyl alcohol and 0.175 mole of potassium. After the reaction mixture was refluxed 22 hours (172°) in the standard apparatus only 0.02 ml. of water had collected. Eight grams more of the aldehyde was added and the solution was refluxed an additional 12 hours. The temperature rose from 171 to 180° as 2.9 ml. of water collected and no gas was evolved. It is to be noted that about four times as much water was evolved as would be produced by the conversion of only the added aldehyde to 2-*n*-butyl-2-octenal. In the usual manner there were obtained 62 g. of recovered *n*-hexyl alcohol, 22 g. of 2-*n*-butyloctanol-1 (b.p. 108 to 110° at 2.5 mm., n^{25}_{D} 1.4402), 2 g. of *n*-hexanoic acid and 20 g. of undistilled residue.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY AND KANSAS STATE COLLEGE]

Reactions of Alcohols and Phenols with Trimethylene Oxide[1]

BY S. SEARLES[2] AND C. F. BUTLER

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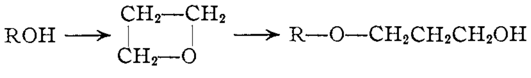
Trimethylene oxide reacts with alcohols in the presence of catalytic amounts of strong acids or bases or in the presence of water to give monoalkyl ethers of trimethylene glycol. The reactions with phenols are catalyzed by alkali but not by acids. There is great similarity to the analogous reactions of ethylene oxide; the products are also very similar to ethylene glycol monoethers. A much cheaper synthesis of trimethylene oxide is described, employing trimethylene chlorobromide as the starting material.

Although the reactions of alcohols and phenols with ethylene oxide have received a great deal of attention and give commercially important products, there appears to be nothing in the literature on similar reactions with trimethylene oxide. The reaction of thiols proceeds well with trimethylene oxide,[3] however, and the work has now been extended to alcohols and phenols.

It is found that trimethylene oxide reacts with alcohols in the presence of water or of a suitable acid or basic catalyst to give the expected 3-hydroxypropyl alkyl ethers in moderately good yields. Polyglycol ether by-products are also formed, as in the ethylene oxide reactions. The primary products were characterized by means of their allophanates, as the more common types of derivatives generally proved to be liquids or very difficult to crystallize.



$$ROH \longrightarrow \begin{array}{l}CH_2{-}CH_2\\ |\quad\;\;\; |\\ CH_2{-}O\end{array} \longrightarrow R{-}O{-}CH_2CH_2CH_2OH$$

Typical results are presented in Table I.[4] Primary alcohols reacted exothermically and easily at room temperature in the presence of catalytic amounts of sulfuric acid or *p*-toluenesulfonic acid, while isopropyl alcohol reacted much less readily and *t*-butyl alcohol still less so. This would indicate that the catalyst functions by coördination with the oxide rather than the alcohol in a manner similar to the analogous ethylene oxide reaction.[5] It is interesting that the reactivity of trimethylene oxide here is about the same as that of ethylene oxide, as also is the case in certain other reactions; a possible reason for this has been commented on previously.[3]

Alkoxide-catalyzed additions of alcohols to trimethylene oxide required considerably more vigorous conditions, but the yields were similar to those in the acid-catalyzed reactions. No reaction occurred when trimethylene oxide was heated with sodium methoxide in the absence of methanol, indicating the importance of hydrogen-bonding of alcohol to oxide as an intermediate stage of the reaction (Lowry mechanism[6]). Likewise there is no reaction when trimethylene oxide and absolute alcohol are heated, but on addition of water the expected glycol ether is formed.

Phenols react poorly with trimethylene oxide even in the presence of water or acid, but the phenoxide ion formed by addition of alkali cleaves the oxide ring to give the expected 3-hydroxypropyl aryl ether, as shown in Table II. The behavior of ethylene oxide toward phenols and phenoxides is very similar,[7] except that trimethylene oxide is somewhat less reactive.

Because of the many valuable uses of 2-alkoxyethanols and 1-alkoxy-2-propanols,[8] a few tests

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[1] Most of this material is taken from the M.S. Thesis of C. F. Butler, Northwestern University, May, 1952.

[2] Department of Chemistry, Kansas State College, Manhattan, Kansas.

[3] S. Searles, THIS JOURNAL, **73**, 4515 (1951).

[4] Most of the reaction times employed were much longer than necessary.

[5] S. Winstein and R. B. Henderson in "Heterocyclic Compounds," R. C. Elderfield, ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 29.

[6] W. C. J. Ross, *J. Chem. Soc.*, 2257 (1950).

[7] D. R. Boyd and E. R. Marle, *ibid.*, **105**, 2117 (1914).

[8] G. O. Curme, Jr., and F. Johnston, "Glycols," Reinhold Publ. Corp., New York, N. Y., 1952, Chapt. 6.

TABLE I

REACTION OF TRIMETHYLENE OXIDE WITH ALCOHOLS

Alcohol	Alcohol, moles	$(CH_2)_3O$, moles	Catalyst, moles	Time, hr.	Temp., °C.	Product, propanol	Yield, %	B.p. °C.	Mm.	$n^{20}D$	M.p., °C.	Allophanates Formula	% N Calcd.	% N Found
Methyl	1.32	0.14	0.005 H_2SO_4	1-16	25-45	3-Methoxy-1[a]	63-69	43-44	9	1.4116	129-129.5	$C_6H_{12}O_4N_2$	15.90	16.16
Ethyl	1.44	.15	.005 H_2SO_4	48	25	3-Ethoxy-1[b]	58.6	58-59	9	1.4149	118-118.5	$C_7H_{14}O_4N_2$	14.73	14.80
n-Propyl	1.33	.14	.005 H_2SO_4	18	25	3-(*n*-Propoxy)-1-[c]	55.4	66-67	10	1.4211	120.5-121	$C_8H_{16}O_4N_2$	13.72	13.76
n-Butyl	0.94	.15	.005 H_2SO_4	18	25	3-(*n*-Butoxy)-1-[d]	45.0	78-79	10	1.4243	110-111	$C_9H_{18}O_4N_2$	12.84	13.21
Isopropyl	1.29	.13	.005 H_2SO_4	2.5	83	3-(Isopropoxy)-1-[e]	43.2	59.5-60	9	1.4162	126	$C_8H_{16}O_4N_2$	13.72	13.89
t-Butyl	0.51	.09	.005 H_2SO_4	4	145	3-(*t*-Butoxy)-1-[f]	35.6	60-61	9	1.4185	149.5-150	$C_9H_{18}O_4N_2$	12.84	13.09
Benzyl	.50	.08	.006 TosOH	66	25	3-Benzoxy-1-[g]	23.2	111-114	2	1.5189(25°)	117-118[h]			
Hydrocinnamyl	.15	.05	.005 H_2SO_4	80	25	3-(3-Phenylpropoxy)-1-	25.9	153-156	18	1.5108(25°)	111-112[i]			
Methyl	1.00	.12	.05 $NaOCH_3$	16	145	3-Methoxy-1-	64.4	42-43	8	1.4110	129-129.5[j]			
n-Propyl	1.00	.11	.05 $NaOC_3H_7$	8	175	3-(*n*-Propoxy)-1-	45.0	61-62	8	1.4212	121			
Isopropyl	1.00	.12	.05 NaO-*i*-C_3H_7	8	175	3-(Isopropoxy)-1-	37.8	56-57	8	1.4158	126.5			

[a] R. Pummerer and M. Schonamsgruber, *Ber.*, **72**, 1838 (1939), reported b.p. 58-61° (14 mm.) $n^{20}D$ 1.4129, 1.4125. [b] E. P. Anderson, J. V. Crawford and M. L. Sherrill, THIS JOURNAL, **68**, 1294 (1946), reported b.p. 59-60° (12 mm.). [c] M. H. Palomaa, *Ann. Acad. Sci. Fennicae*, [A] **4**, 88 (1913), reported b.p. 170-172°, *Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.96; H, 11.94. Found: C, 61.09; H, 11.70. The following was obtained in this Laboratory. *Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.98; H, 11.94. Found: C, 61.07; H, 12.04. [d] E. M. Van Duzee and H. Adkins, THIS JOURNAL, **57**, 147 (1935), reported b.p. 81-85° (13 mm.), $n^{25}D$ 1.4238. [e] *Anal.* Calcd. for $C_6H_{14}O_2$: C, 60.98; H, 11.94. Found: C, 61.09; H, 11.89. [f] *Anal.* Calcd. for $C_7H_{16}O_2$: C, 63.59; H, 12.21. Found: C, 63.99; H, 12.34. [g] G. M. Bennett and A. L. Hock, *J. Chem. Soc.*, 472 (1927). B.p. 155° (23 mm.), $n^{20}D$ 1.5128. [h] L. Palfray, S. Sabetay and A. Halasz, *Compt. rend.*, **208**, 289 (1939), found b.p. 155-157° (20 mm.); $n^{20}D$ 1.5200; allophanate, m.p., 119°. [i] *Ibid.*, b.p. 160° (20 mm).; $n^{20}D$ 1.5123; allophanate, m.p. 113°. [j] Mixed m.p. with allophanate from H_2SO_4 cat. reaction showed no depression.

TABLE II

REACTION OF TRIMETHYLENE OXIDE WITH PHENOLS

Phenol	Phenol, moles	$(CH_2)_3O$, moles	Catalyst, moles	Time, hr.	Temp., °C.	Product, propanol	Yield, %	B.p. °C.	Mm.	$n^{20}D$	*p*-Nitrophenylurethans M.p., °C.	Formula	% N Calcd.	% N Found
Phenol	0.23	0.11	0.10 H_2O	4	150	3-Phenoxy-1-	2.4[a]	145-150	22	1.5229	104.5-105.5[b]			
Phenol	.12	.10	.2 NaOH	4	150	3-Phenoxy-1-[c]	43.3	148-149.5	21	1.5295	105-106	$C_{16}H_{16}O_5N_2$	8.86	9.14
1-Naphthol	.11	.10	.2 NaOH	4	150	3(1-Naphthoxy)-1-[d]	32.5	M.p. 66-67°			113.4-114.1	$C_{20}H_{18}O_5N_2$	7.65	7.66
2-Naphthol	.11	.10	.2 NaOH	4	150	3(2-Naphthoxy)-1-[e]	27.0	M.p. 99-100°			137.8-138.3	$C_{20}H_{18}O_5N_2$	7.65	7.78 7.88

[a] 88.5% of the phenol was recovered from this reaction. [b] *p*-Nitrophenylurethan when mixed with the *p*-nitrophenylurethan from the NaOH cat. reaction gave no m.p. depression. [c] R. E. Rindfusz, THIS JOURNAL, **41**, 665 (1919); b.p. 158-160 (125 mm.). [d] W. R. Kirner and G. H. Richter, *ibid.*, **51**, 3409 (1929), found m.p. 65.5-66.5°. [e] R. E. Rindfusz, P. M. Ginnings and V. L. Hornack, *ibid.*, **42**, 157 (1920), give m.p. 99-99.5°.

were made on 3-methoxy-1-propanol and 3-ethanoxy-1-propanol to explore their potentialities as solvents. With respect to the surface tension, the effect on the surface tension of water solutions and the solubility of resins there was close similarity to 2-ethoxyethanol. Further work might reveal novel properties, but we do not intend to pursue this aspect further.

Since it appears from this and other work that trimethylene oxide may have some value as a synthetic intermediate, it was of interest to examine other methods of preparation of its precursor, 3-chloropropyl acetate. The synthesis of this compound by the reaction of potassium acetate and 1-bromo-3-chloropropane, reported by Henry[9] in 1906 without any details, takes on interest because of the present commercial availability of the latter compound. This reaction is complicated by the facile subsequent formation of 3-bromopropyl acetate and trimethylene diacetate in the reaction mixture, but conditions were found which give 67% conversion to 3-chloropropyl acetate. This method has a great economic advantage over the acetylation of 3-chloro-1-propanol.[10]

The report that terminal epoxides yield mainly primary alcohols on reduction over Raney nickel[11] suggested reduction of epichlorohydrin as a possible synthesis of 3-chloro-1-propanol. However, the epoxide

[9] L. Henry, *Bull. acad. roy. Belg.*, 738 (1906).

[10] C. G. Derick and D. W. Bissell, THIS JOURNAL, **38**, 2478 (1916); C. F. H. Allen and F. W. Spangler, *Org. Syntheses*, **29**, 33 (1949).

[11] M. S. Newman, G. Underwood and M. Renoll, THIS JOURNAL, **71**, 3363 (1949).

ring cleaved predominantly to form 1-chloro-2-propanol and the 3-chloro-1-propanol that did form was difficult to purify.

Experimental[12]

3-Chloropropyl Acetate.—To a solution of 500 g. (3.17 moles) of trimethylene chlorobromide (Dow Chemical Co.) in 200 ml. of glacial acetic acid, stirred and heated under reflux, was added 310 g. (3.17 moles) of potassium acetate in 6 portions over a period of two hours. Stirring and refluxing was continued 3–4 hours longer. On cooling and standing the precipitate of inorganic salts settled, and the supernatant oil was decanted and washed with cold 10% sodium carbonate until carbon dioxide evolution ceased. The aqueous washings were used to dissolve the salt cake; the oily layer which separated was drawn off; and the aqueous solution was extracted with four 100-ml. portions of ether. The ether extracts were combined with the oil and dried over magnesium sulfate. After evaporation of the ether, the residue was distilled through a 40-cm. Stedman column with heated jacket and reflux still-head to give the following materials: 53 g. (10.6% recovery) of trimethylene chlorobromide, b.p. 48–53° (20 mm.), n^{20}D 1.4720 (lit. b.p. 138–140 (atm.), n^{25}D 1.4732)[13]; 8.5 g. (3% yield) of 3-chloro-1-propanol, b.p. 60–64° (20 mm.), n^{20}D 1.4465 (lit. b.p. 63–4 (16 mm.), n^{20}D 1.4469)[14]; 262 g. (60% conversion, 67% yield) of 3-chloropropyl acetate, b.p. 68–72° (20 mm.), n^{20}D 1.4325 (lit. b.p. 66° (14 mm.), n^{21}D 1.431)[14]; 6 g. (1% yield) of 3-bromopropyl acetate, b.p. 78–82° (20 mm.) (lit. 81–86 (20 mm.)),[15] n^{20}D 1.4473; and 81 g. (16% yield) of trimethylene diacetate, b.p. 97–102° (20 mm.) (lit. 91–2° (10 mm.))[16].

Trimethylene oxide was obtained by the procedure previously described[17] in yields of 39–49% (average, 44%) from pure 3-chloropropyl acetate. Alternatively, the crude ester from the acetate reaction may be treated with caustic directly. In this manner 12–15 g. (20–25% over-all yield) of trimethylene oxide, b.p. 47° (745 mm.) may be obtained from 160 g. of trimethylene chlorobromide.

Alkyl 3-Hydroxypropyl Ethers.—The following procedures are typical: (A) To a solution of 80 g. (1.33 moles) of *n*-propyl alcohol and 0.25 ml. of 95% sulfuric acid, cooled in an ice-bath, 8.0 g. (0.14 mole) of trimethylene oxide was added with stirring over a period of 20 minutes; the reaction mixture was then allowed to stand 18 hours at room temperature. After addition of 1.0 g. of sodium bicarbonate and filtration, the reaction mixture was distilled to give 10.5 g. (55.4%) of 3-propoxy-1-propanol, b.p. 66–67° (10 mm.) and 1.3 g. of a colorless liquid, b.p. 105–116° (8 mm.), which is probably a polyglycol ether. Substitution of the sulfuric acid by *p*-toluenesulfonic acid gave the same result; no reaction occurred, however, on substitution by zinc chloride (2.5 ml. of saturated solution) or 85% phosphoric acid (1 ml.), although presumably at a higher temperature the reaction would have gone.

(B) Trimethylene oxide (5.8 g., 0.1 mole) was added to a methanolic solution of sodium methoxide, prepared by dissolving 1.2 g. (0.05 g. atom) of sodium in 34 g. (1.0 mole) of methyl alcohol. The reaction mixture was heated in a sealed tube 16 hours at 175°, after which it was cooled and neutralized with concentrated hydrochloric acid. After drying with potassium carbonate, distillation yielded 5.8 g. (64%) of 3-methoxy-1-propanol, b.p. 47–48° (14 mm.) and 0.7 g. of a colorless liquid, b.p. 95–105° (12 mm.).

(C) A solution of 40 g. (0.87 mole) of ethyl alcohol, 10 g. (0.56 mole) of water and 5.8 g. (0.1 mole) of trimethylene oxide was heated in a sealed tube for 24 hours at 190°. After cooling, the reaction mixture was dried with potassium carbonate, filtered and distilled to yield 2.6 g. (25%) of 3-ethoxy-1-propanol, b.p. 57–60° (10 mm.) and 1.7 g. of a fraction, b.p. 97–106° (10 mm.).

Aryl 3-Hydroxypropyl Ethers.—An example of the procedure employed is as follows: A solution of 15.4 g. (0.11 mole) of 2-naphthol and 5.8 g. (0.10 mole) of trimethylene oxide in 50 ml. of 10% sodium hydroxide was heated in a sealed tube at 150° for 4 hours. After cooling, the reaction mixture was extracted with three 50-ml. portions of ether; evaporation of the ether left 5.6 g. (28%) of pale yellow needles of 3-(2-naphthoxy)-1-propanol, m.p. 95–98°; m.p. 99–100° after two recrystallizations from benzene.

Allophanate derivatives were prepared by the method of Béhal[18] and recrystallized from absolute alcohol.

Surface tension data were obtained with a Du Nouy tensiometer, following the procedure described by Harkins[19] and are summarized in Tables III and IV.

TABLE III

SURFACE TENSION OF GLYCOL MONOETHERS AT 28°, DYNES/CM.[2]

2-Methoxyethanol	33.0
2-Ethoxyethanol	29.5
3-Methoxy-1-propanol	30.8
3-Ethoxy-1-propanol	30.6

TABLE IV

SURFACE TENSION OF AQUEOUS SOLUTIONS AT 28°, DYNES/CM.[2]

Molarity	2-Ethoxyethanol soln.	3-Ethoxy-1-propanol soln.
0.00	74.1	74.1
.04	69.0	69.0
.20	63.4	62.5
1.02	54.1	51.0
5.13	38.2	38.0

Reduction of Epichlorohydrin.[20]—A solution of 79 g. (0.85 mole) of epichlorohydrin in 300 ml. of absolute alcohol was charged into a high pressure rocking autoclave with 15 g. of Mozingo nickel catalyst at an initial hydrogen pressure of 90 atmospheres and was heated two hours at 125°, a pressure drop corresponding to 0.8 mole of hydrogen having then occurred. The solution was distilled through a 40-cm. Stedman column to give 12.2 g. of 1-chloro-2-propanol, b.p. 125–130°, n^{20}D 1.4377 (lit. b.p. 126–127°, n^{20}D 1.4392)[21] and 15.3 g. of a fraction, b.p. 155–170°, n^{20}D 1.4665, which may be a mixture of 3-chloro-1-propanol and β-chloropropionaldehyde.

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[12] All melting points and boiling points are corrected. Microanalyses are by Misses J. Sorensen and C. Brauer.

[13] S. S. Rossander and C. S. Marvel, THIS JOURNAL, **50**, 1494 (1928).

[14] E. H. Huntress, "Organic Chlorine Compounds," John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 1135, 1146.

[15] J. S. Allen and H. Hibbert, THIS JOURNAL, **56**, 1399 (1934).

[16] M. Senkus, *ibid.*, **68**, 735 (1946).

[17] S. Searles, *ibid.*, **73**, 124 (1951).

[18] A. Béhal, *Bull. soc. chim.*, [4] **25**, 475 (1919).

[19] W. D. Harkins, "Physical Methods of Organic Chemistry," A. Weissberger, ed., Vol. I, 2nd ed., Interscience Publishers, Inc., New York, N. Y., 1945, p. 176.

[20] The assistance of Mr. H. M. Kash in this portion of the work is gratefully acknowledged.

[21] Reference 14, p. 1069.