[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MARYLAND]

Disproportionative Condensations. I. Modified Guerbet Reactions

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The procedure for carrying out Guerbet condensations has been modified to furnish a facile laboratory method for preparing a variety of alcohols. Normal primary alcohols are self-condensed with 60% conversions and 70% yields. Benzyl alcohol condenses quite satisfactorily with normal primary alcohols and especially well with α-methylbenzyl alcohol. Both benzyl and normal primary alcohols condense fairly well with cyclohexanol. Since with the improved procedure the amounts of the main product and chief by-products can be readily determined it has been possible to elucidate further the course of the reaction and to establish the optimum conditions.

In an attempted extension of the Diels and Rhodius[2] method of reducing anils a mixture of sodium *n*-hexylate, *n*-hexyl alcohol and benzalaniline was heated under reflux. An appreciable amount of 2-*n*-butyloctanol, the product of the Guerbet condensation[3] of one molecule of the hexyl alcohol with another was unexpectedly obtained.

$$2\,RCH_2CH_2OH \longrightarrow RCH_2CH_2CHRCH_2OH + H_2O \quad (1)$$

Since preliminary experiments with this method of carrying out Guerbet condensations indicated that the yields could be improved, the formation of undesirable by-product acid could be minimized and the need for an autoclave could be eliminated, it was decided to establish the optimum conditions for this modified method.

It was early found that the function of the benzalaniline in aiding the hydrogen interchange was advantageously accomplished by U.O.P. nickel[4] and that the isolation of the product was thereby greatly simplified. By collecting the by-product water in a Dean-Stark trap as it formed it was found possible to accelerate the reaction and to measure its extent.[5] The use of potassium in place of sodium to give more rapid alkoxide formation and, in certain cases, the attachment at the top of the condenser of a large volume gas buret to measure the by-product hydrogen evolved during the condensation completed the main modifications.

The facility with which the reaction could be carried out and the amounts of alcohol, water, acid and hydrogen produced could be determined made it desirable to study the scope of the condensation in more detail than had been done heretofore and to attempt to elucidate further the course of the reaction. It is felt that the value of the Guerbet reaction as a laboratory tool has in this way been significantly increased.

In Table I are shown the effects of varying the amount of potassium used to form the alkoxide. It is apparent that the maximum conversion to product alcohol and water and the minimum induction time resulted when 0.225 mole of potassium was used, but that both the reaction temperature and the amount of acid formed continued to increase with further increases in the amount of potassium.

TABLE I[a]

VARIATION OF THE AMOUNT OF POTASSIUM

K, mole	Induct. time, hr.[b]	Temp., °C.	Conversions, %			Alcohol yld., %[d]
			Water	Acid[c]	Alcohol	
0.100	2.2	163–168	12	..	19	67
.150	1.3	169–182	30	4	34	74
.175	1.0	173–188	34	8	38	69
.200	0.83	177–206	40	20	52	63
.225	.67	180–225	40	24	53	59
.250	.78	184–236	32	30	43	46
.275	.92	187–241	24	36	42	44

[a] Two grams of U.O.P. nickel and one mole of *n*-hexyl alcohol were used. As the reaction progresses the amount of potassium *n*-hexylate decreases as formation of the alkoxide of the product alcohol increases. [b] This is the time required for water to appear in the Dean–Stark trap. Refluxing was continued for 2 hours more. [c] These data are calculated on the arbitrary basis that one mole of acid is formed per mole of product alcohol. [d] These figures allow for the amount of *n*-hexyl alcohol recovered.

The decrease in amount of water and the increase in induction time with the higher amounts of alkoxide may well be due to increased hydrolysis of the alkoxide.[6] A rather high molecular elevation of the boiling point for *n*-hexyl alcohol appears to best explain the considerable increases in the initial reflux temperature as the amount of potassium was increased. The amount of high-boiling residues

TABLE II[a]

VARIATION OF THE AMOUNT OF U.O.P. NICKEL

U.O.P. nickel, g.	Induct. time, hr.[b]	Reaction time, hr.[b]	Product alcohol, %	
			Convers.	Yield
0.03	24.0	60.0	3	[c]
0.5	2.0	4.1	56	72
1.0	1.7	3.2	54	69
2.0	1.1	2.2	58	72
4.0	0.7	1.7	56	70

[a] One mole of *n*-hexyl alcohol and 0.175 mole of potassium were used. The temperature range, except for the first experiment for which the temperature did not exceed about 185°, was 173 ± 1° to 203 ± 1°. [b] The induction time is the time required for water to appear in the Dean–Stark trap. The reaction time is the additional time of heating under reflux. Heating was suspended when a 50% yield of water had collected (except for the first experiment in which water evolution stopped at 4%). [c] 96% of the starting alcohol was recovered.

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(1) From the Ph.D. thesis of D. G. Kubler, May, 1952.

(2) O. Diels and R. Rhodius, *Ber.*, **42**, 1072 (1909).

(3) M. Guerbet, *Compt. rend.*, **165**, 559 (1917), and earlier papers.

(4) Universal Oil Products Co., 310 S. Michigan Ave., Chicago 4, Ill.

(5) A patent which came to the attention of the authors after the experimental work was completed (C. A. Carter, U. S. Patent 2,457,866, Jan. 24, 1949) discloses the use of various dehydrogenation catalysts in the Guerbet condensation and the removal of the by-product water by distillation. Since the patent is directed toward the commercial application of the reaction while the present study is directed toward its laboratory application, the two investigations largely supplement rather than duplicate one another. Bolle (ref. 13) confirmed Carter's finding that Raney nickel was an effective catalyst.

(6) See last section of Experimental.

tended to increase from about 5 to about 16 g. with increasing amounts of potassium.

The best compromise with respect to high yield of alcohol, low yield of acid and convenient rate was reached with approximately 0.175 mole of potassium. This amount was, therefore, used for the experiments of Table II, the results of which adequately demonstrate the marked catalytic effect of U.O.P. nickel.

The generality of the modified method for self-condensation of alcohols of the series $CH_3(CH_2)_nCH_2OH$ is indicated by the data of Table III.

TABLE III[a]

VARIATION OF n IN $CH_3(CH_2)_nCH_2OH$

n	Temp., °C.	Total time, hr.[b]	Conversions, % H_2[c]	Acid[c]	Alcohol	Alcohol yld., %
		With 0.5 g. of U.O.P. nickel				
2[d]	136–155	26.0	32	5	42	75
3	155–180	17.5	18	3	46	74
4	174–204	6.1	30	8	56	72
5	195–238	2.3	42	17	59	66
6	205–250	1.6	44	20	62	72
7	222–276	1.3	60	24	61	66
8[e]	237–271	0.7	56	26	62	70
		Without U.O.P. nickel				
5	195–254	28.3	44	24	65	71
6	207–262	5.8	54	24	61	70
7	224–305	2.6	58	28	62	67
8	239–320	1.3	76	30	65	68

[a] One mole of alcohol and 0.175 mole of potassium were used unless noted otherwise. Refluxing was continued until a 50% yield of water had collected. [b] This includes the induction time. [c] To facilitate comparisons these data are calculated on the arbitrary basis of one mole of hydrogen or acid being formed per mole of product alcohol. [d] Four grams of U.O.P. nickel was used here to give a more convenient reaction time. [e] Two grams of U.O.P. nickel was used here and since the temperature was rising very rapidly refluxing was stopped when the yield of water was 39%.

Since the rate and course of the reaction for alcohols of this series would be expected to be largely independent of the value of n the primary influence of a change in n is the effect on the reaction temperature. A secondary influence, since no solvent was used, is the decrease in concentration of reactive centers as n increases. Satisfactory yields were obtained in all cases. The last four experiments of the table show that when the reflux temperature is sufficiently high a reasonable rate of reaction may be attained in the absence of nickel and the yields are equally good.

Since benzyl alcohol has no β-hydrogen for self-condensation it is not surprising that an excess of it condenses with a normal primary alcohol to give satisfactory conversions to the mixed product (Table IV).

On the average about 10% of the product of self-condensation of the normal primary alcohol was obtained. Benzyl alcohols also condense fairly satisfactorily with cyclohexanol. A considerable excess of cyclohexanol was used in these cases (Table IV) since, probably because of the unfavorable aldol equilibrium for ketones, self-condensation of the cyclohexanol was not as serious as further condensation of the 2-benzylcyclohexanols produced.

TABLE IV[a]

CONDENSATIONS OF BENZYL OR CYCLOHEXYL ALCOHOL WITH A SECOND ALCOHOL

Second alcohol	Temp., °C.	Total time, hr.[b]	Convers.,[c] %
2:1 ratio of benzyl to second alcohol			
n-Butyl[d]	143–187	3.7	55
n-Hexyl	177–207	2.0	59
n-Heptyl	184–211	1.4	58
3-Phenylpropyl[e]	225–241	1.8	62
3:1 ratio of cyclohexyl to second alcohol[f]			
Benzyl	172–186	2.0	61[g]
p-Methoxybenzyl	177–187	3.7	47
p-Chlorobenzyl	175–182	2.0	50
n-Octyl	175–190	2.5	61

[a] One mole of total alcohols, 0.175 mole of potassium and 2.0 g. of U.O.P. nickel used unless otherwise noted. [b] This includes the induction time. [c] Refluxing stopped at 75% yield of water for first four experiments and at 80% for last four. Further refluxing increased the amount of undistilled residue rather than the amount of desired product. [d] Four grams of U.O.P. nickel used here because of the low reflux temperature. [e] No nickel used here. [f] The conversion figures are for the mixture of *cis–trans* isomers where both were formed (see Experimental). [g] A 47% conversion was obtained when a 2:1 ratio of cyclohexyl to benzyl alcohols was used.

The last experiment of Table IV shows that normal primary alcohols also react satisfactorily with cyclohexanol. When heptanol-2 or 4-methylpentanol-2 replaced the cyclohexanol in condensations with *n*-octyl or benzyl alcohols only 25 to 35% yields of the analogous products were obtained. When, however, α-methylbenzyl alcohol replaced the cyclohexanol in the condensation with benzyl alcohol (Table IV) the reaction proceeded with unusual speed at 184° to 207° to give a 100% yield of water in eleven minutes and the 1,3-diphenylpropanol-1 was isolated in 84% yield.[7]

The allophanates proved to be of great value for characterizing the products.[8] Determination of the volume of by-product water formed upon etherification of several of the alcohols with triphenylcarbinol gave accurate values for the equivalent weights.[9]

Perhaps the most significant fact concerning the course of the reaction manifested by the foregoing data (Tables I and III) is that ordinarily less than half as much acid as product alcohol is formed. This is in marked contrast to Weizmann's proposal[10] that one molecule of acid is formed for each molecule of product alcohol. With larger amounts of potassium (Table I) the formation of acid increases at the expense of the alcohol. This is perhaps best ascribed to the occurrence of the Cannizzaro or Dumas–Stas[11] reactions to increasing extents. Since a mole of water (or of potassium hydroxide) is required by either of these reactions it may well

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(7) We wish to thank Mr. E. J. Frazza for carrying out the experiments with α-methylbenzyl alcohol.

(8) P. Mastagli, *Ann. chim.*, **10**, 281 (1938).

(9) E. F. Pratt and J. D. Draper, THIS JOURNAL, **71**, 2846 (1949).

(10) Ch. Weizmann, E. Bergmann and M. Sulzbacher, *J. Org. Chem.*, **15**, 54 (1950), and earlier papers.

(11) J. Dumas and J. S. Stas, *Ann.*, **35**, 129 (1840). See also E. E. Reid, H. Worthington and A. W. Larchar, THIS JOURNAL, **61**, 99 (1939). This reaction, $RCH_2CH_2OH + KOH \rightarrow RCH_2COOK + 2H_2$ may merely express the over-all result of a dehydrogenation (reaction 2) followed by a Cannizzaro reaction.

be that the continuous removal of water in the modified method is chiefly responsible for the decreased acid formation. In support of this it may be observed (Tables I and III) that the conversion to water plus the conversion to acid tends to approximate the conversion to alcohol.[12]

On the basis of reaction 2, below, two moles of hydrogen would be formed per mole of acid from the Cannizzaro reaction and this would also be true for the Dumas–Stas reaction. The data of Table III show that the hydrogen and acid are produced in approximately this ratio.

Our results, therefore, cannot be explained in terms of Weizmann's proposal,[10] but they do lend considerable support to the reaction course recently advanced by Bolle,[13] part of which is closely related to the earlier suggestions of Mastagli.[8]

$$2\,RCH_2CH_2OH \longrightarrow 2\,RCH_2CHO + 2\,H_2 \tag{2}$$

$$2\,RCH_2CHO \longrightarrow RCH_2CH{=}CRCHO + H_2O \tag{3}$$

$$RCH_2CH{=}CRCHO + RCH_2CH_2OH \longrightarrow RCH_2CH{=}CRCH_2OH + RCH_2CHO \tag{4}$$

$$RCH_2CH{=}CRCH_2OH \longrightarrow RCH_2CH_2CHRCHO \tag{5}$$

$$RCH_2CH_2CHRCHO + RCH_2CH_2OH \longrightarrow RCH_2CH_2CHRCH_2OH + RCH_2CHO \tag{6}$$

In place of the rearrangement 5 direct saturation of the olefinic bond by a disproportionation with RCH_2CH_2OH might occur, but because olefinic bonds are relatively stable to Meerwein–Ponndorf type reductions, because reaction 5 has been shown to be catalyzed by nickel[14] and because the saturated aldehyde, $RCH_2CH_2CHRCHO$, was isolated from one reaction mixture we prefer the route given. Mastagli[8] studied extensively the action of benzyl alcohol containing sodium or potassium hydroxides on aldehydes and ketones. By employing various reaction times and temperatures (from 100° to 200°) he was able to accomplish, in unspecified yield, all of the following conversions.

$$\begin{tikzcd}
RCH_2CHO \arrow[rr] \arrow[d] & & RCH_2CH_2CHRCH_2OH \\
RCH_2CH{=}CRCHO \arrow[r] \arrow[urr] & RCH_2CH{=}CRCH_2OH \arrow[ur] &
\end{tikzcd}$$

The two R groups were not identical in all cases.

Reaction 1 is the sum of reactions 3, 4, 5 and 6 and it is probable that reaction 2 serves primarily to initiate the process and thereafter the bulk of the RCH_2CHO is produced *via* reactions 4 and 6. In support of this view it was found that added RCH_2CHO promoted the formation of more than an equivalent amount of product alcohol in the absence of nickel and at relatively low temperatures. Bolle[13] found that added $RCH_2CH_2CHRCHO$ also gave product alcohol in considerable excess of the added aldehyde. From the data in Table III for the percentage conversion to hydrogen and to product alcohol it may be estimated that in the typical case of *n*-hexyl alcohol about one-fourth of the total aldehyde required was produced by reaction 2. For this estimation it is assumed that the above explanation of the source of the hydrogen is correct and that all the hydrogen escapes before it can saturate carbonyl or olefinic bonds.

It should be noted that the results of condensations of two different alcohols (Table IV) lend additional support to this interpretation of the reaction course.

Experimental[15,16]

General Procedure.—The alcohols were purified by standard methods until their refractive indices or melting points agreed closely with the literature values. The U.O.P. nickel catalyst, obtained as pellets,[4] was crushed to pass a 100-mesh sieve; a single batch sufficient for all of the experiments was prepared.

One mole of total alcohols was placed in a 500-ml. three-necked flask which was fitted with a stirrer, a thermometer and a Dean–Stark water trap surmounted by a reflux condenser. The trap was wrapped with asbestos cord for insulation. It was of interest to find that although the same reaction flask was used repeatedly no serious etching occurred. In several of the early experiments explosions occurred during the reaction of the potassium which ejected a solid glass stopper several feet. Explosions never occurred after the practice was adopted of sweeping out the system with nitrogen for several minutes and then adding the potassium in small portions with slow stirring. After formation of the alkoxide was complete the nickel catalyst was added, the stirrer was set at a more rapid rate and the mixture was heated to reflux with a hemispherical mantle. In order to make the stirring as reproducible as possible the same type of stirrer[17] was used throughout and the same voltage was applied to the induction type stirring motor. The temperature and the volume of water collected were read at frequent intervals. The amounts of nickel and potassium used and the volume of water collected are given in the first footnotes to each table.

After the specified volume of water had collected the reaction mixture was cooled below 100° and quenched with about 150 ml. of water. The catalyst was filtered off, the layers separated and the alcohol layer washed with 10% aqueous sodium hydroxide. The combined aqueous layers were extracted with ether and the combined non-aqueous layers were dried with sodium sulfate. After the ether was removed at the water aspirator the product was isolated by distillation at the oil-pump through an eight-inch Vigreux column. The by-product acid was recovered from the combined aqueous layers by acidification with dilute hydrochloric acid, extraction into benzene and distillation.

Hydrogen Evolution.—For the experiments of Table III the volume of gas evolved was determined by leading the gas from the top of the condenser through a Dry Ice–acetone trap and allowing it to displace water from an inverted 4-l. graduated cylinder. By means of a water overflow system the collected gas was maintained and measured at atmospheric pressure. Only a trace of material collected in the cold trap. The tabulated amounts of gas are corrected for the vapor pressure of the water and the temperature. Numerous determinations with the explosion pipet showed that the dry gas was 99.0 ± 1.0% hydrogen.

Identification of Known Products.—The refractive indices of the known product alcohols were found to agree closely with the literature values unless otherwise noted. These alcohols were converted to the allophanates by the method of Behal[18] and except for the cases noted below their melting points agreed closely with those reported by Mastagli.[8]

Since the allophanate of our **2-*n*-butyloctanol-1** from *n*-hexyl alcohol melted at 127° while the literature value is 119° our product was further characterized. It is felt that the detailed characterization of this compound also lends significant support to the structures assigned for other compounds made by the Guerbet condensation. The allophanate of 2-*n*-butyloctanol-1 from Carbide and Carbon Chemicals Corporation also melted at 126–127.5° both alone and

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[12] This approximation is closer if, for this particular purpose, the 5 to 16 g. of high-boiling residues is considered to be equivalent to product alcohol.

[13] J. Bolle, *Compt. rend.*, **233**, 1628 (1951).

[14] R. Paul, *Bull. soc. chim.*, [5] **8**, 507 (1941).

[15] We wish to thank Prof. Mary Aldridge and Mr. Byron Baer for the carbon, hydrogen and nitrogen determinations.

[16] All melting points are corrected.

[17] Ace Glass, Inc., Cat. no. 8242.

[18] A. Behal, *Bull. soc. chim.*, [4] **25**, 473 (1919). For an excellent review on allophanates which includes tables of melting points, see H. W. Blohm and E. I. Becker, *Chem. Revs.*, **51**, 471 (1952).

when mixed with the allophanate of our product. The results of carbon and hydrogen analyses on our **2-*n*-butyloctanol-1** (*n*²⁵D 1.4400) and its allophanate agreed closely with the calculated values. Our product was oxidized to 2-*n*-butyloctanoic acid (b.p. 114–116° at 2.5 mm., *n*²⁵D 1.4365) which gave a neutral equivalent of 200 which equals the calculated value. The corresponding amide was prepared by standard methods and recrystallized from aqueous acetone; m.p. 106–107.5°. *Anal.* Calcd. for $C_{12}H_{25}ON$: C, 72.30; H, 12.64; N, 7.04. Found: C, 72.51; H, 12.71; N, 7.01.

The equivalent weight of the 2-*n*-butyloctanol-1 was determined by measuring the volume of water evolved upon etherification with triphenylcarbinol[9]; good agreement of the experimental (189) and the calculated (186) values was obtained. A 50% yield of water was collected in 21 minutes as compared to 24 to 26 minutes for other primary alcohols under the same conditions; with secondary and tertiary alcohols water is evolved much more slowly.[19] The generality of this etherification method for determining equivalent weights of alcohols was demonstrated by applying it to the **2-*n*-amylnonanol-1**, **2-*n*-hexyldecanol-1** and 2-benzylbutanol-1 prepared in this investigation. The experimental values were 219, 246 and 163 as compared to the calculated values of 214, 242 and 164, respectively.

For **2-*n*-propylheptanol-1** the *n*²⁵D was 1.4356. Weizmann[10] reported this compound but gave no refractive index or analysis. *Anal.* Calcd. for $C_{10}H_{22}O$: C, 75.88; H, 14.10. Found: C, 76.38; H, 14.10. After one recrystallization from ethanol the allophanate, which has not been prepared previously, melted at 130–131°. *Anal.* Calcd. for $C_{12}H_{24}O_3N_2$: C, 59.01; H, 9.84. Found: C, 58.96; H, 9.96.

Although the refractive index and equivalent weight found for **2-benzylbutanol-1** agreed well with the literature or calculated values its allophanate was found to melt at 148° while the reported value is 134°.[8] Therefore the allophanate was analyzed. *Anal.* Calcd. for $C_{13}H_{18}O_3N_2$: C, 62.38; H, 7.25. Found: C, 62.43; H, 7.45.

Both isomers of **2-benzylcyclohexanol** were isolated although it is rather surprising that the less stable form was not isomerized to the more stable under the reaction conditions. A 75-g. portion of product which distilled at 156° to 165° (12 mm.) and which melted at 55° to 62° was recrystallized from 75 ml. of ligroin to give 39 g. of colorless needles which melted at 75.5–76.5°; the literature value is 76.5–77.5°.[20] The melting point of the 3,5-dinitrobenzoate of this isomer was 134.5–135.5° (lit. value 133–135°[20]). Since attempts to obtain a second solid isomer from the mother liquors from the 39 g. of needles were unsuccessful a portion of the liquid was treated with 3,5-dinitrobenzoyl chloride. Ivory colored needles were obtained which after three recrystallizations from ethanol melted at 126.5–127.5°. *Anal.* Calcd. for $C_{20}H_{20}O_6N_2$: C, 62.49; H, 5.24. Found: C, 62.37; H, 5.32. A mixture of this and the dinitrobenzoate which melted at 134.5–135.5° was found to melt at 110° to 125°. When a second portion of the mother liquors from the 39 g. of needles was oxidized with chromic anhydride in acetic acid 2-benzylcyclohexanone was obtained in 63% yield. The *n*²⁵D for the product was 1.5342 and its semicarbazone melted at 166–167° (lit. value 168–169°[20]).

The condensation of benzyl alcohol with 4-methylpentanol-2 gave a 31% conversion to **1-phenyl-5-methylhexanol-3**. Its allophanate after two recrystallizations from ethanol melted at 132–133.5°. *Anal.* Calcd. for $C_{15}H_{22}O_3N_2$: C, 64.72; H, 7.97. Found: C, 64.81; H, 8.02.

The **1,3-diphenylpropanol-1** (45 g.) prepared from 0.25 mole of benzyl alcohol and 0.75 mole of α-methylbenzyl alcohol had *n*²⁵D 1.5713 (lit. value *n*²¹D 1.5724[21]) and its phenylurethan melted at 83–84° (lit. value 82–83°[21]).

Isolation and Characterization of New Products.—The crude **2-anisylcyclohexanol** (26 g.) distilled at 195° to 207° (12 mm.). When this distillate which partly solidified on standing was recrystallized from ligroin 11 g. of colorless needles which melted at 52–55° were obtained. *Anal.* Calcd. for $C_{14}H_{20}O_2$: C, 76.50; H, 9.15. Found: C, 76.23; H, 9.02. The 3,5-dinitrobenzoate was prepared and found to melt at 122–123°. *Anal.* Calcd. for $C_{21}H_{22}O_7N_2$: C, 60.86; H, 5.35. Found: C, 60.85; H, 5.51. Attempts to isolate the alternate geometrical isomer from the mother liquors from which the solid alcohol was isolated were unsuccessful.

Thirty grams of crude **2-*p*-chlorobenzylcyclohexanol** distilled at 178° to 190° (12 mm.). The distillate solidified and remelted at 80° to 95°. Recrystallization from ligroin gave 13.5 g. of white needles which melted at 110–111°. *Anal.* Calcd. for $C_{13}H_{17}OCl$: C, 69.47; H, 7.63. Found: C, 69.90; H, 7.68. The 3,5-dinitrobenzoate obtained as tan needles after two recrystallizations from ethanol melted at 122–123.5°. *Anal.* Calcd. for $C_{20}H_{19}O_6N_2Cl$: C, 57.35; H, 4.57. Found: C, 57.63; H, 4.80.

The crude **2-*n*-octylcyclohexanol** (32 g.) distilled at 156° to 167° (14 mm.). Since it absorbed bromine with the evolution of hydrogen bromide it may have been contaminated with the corresponding ketone. For identification it was oxidized to the ketone in 57% yield with chromic anhydride in acetic acid. The ketone distilled at 155 to 159° (12 mm.) and had *n*²⁵D 1.4625. Its semicarbazone after recrystallization from aqueous ethanol melted at 108–109.5°. *Anal.* Calcd. for $C_{15}H_{29}ON_3$: C, 67.37; H, 10.93. Found: C, 67.18; H, 11.00.

Thirteen grams of **1-phenyloctanol-3** was isolated by distillation at 150° to 165° (13 mm.) from the condensation of benzyl alcohol and heptanol-2. Redistillation through a three-foot column packed with glass helices gave 9.0 g. of product which boiled at 165° (12 mm.), *n*²⁵D 1.4985. *Anal.* Calcd. for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.26; H, 11.01. After two recrystallizations from ethanol the allophanate melted at 95.7–96.5°. *Anal.* Calcd. for $C_{16}H_{24}O_3N_2$: C, 65.73; H, 8.27. Found: C, 65.56; H, 8.41.

The condensation of *n*-octyl alcohol with 4-methylpentanol-2 gave a 38% conversion to crude **2-methyltridecanol-4**. The distillation temperature was 147–148° (14 mm.) and *n*²⁵D was 1.4404. *Anal.* Calcd. for $C_{14}H_{30}O$: C, 78.43; H, 14.11. Found: C, 78.75; H, 14.15. The allophanate, after two recrystallizations from ethanol, melted at 90–91.5° when the bath was heated slowly from room temperature but if the compound was introduced at temperatures above 60° it melted almost instantaneously. It would appear that allotropic modifications are involved. *Anal.* Calcd. for $C_{16}H_{32}O_3N_2$: C, 63.96; H, 10.74. Found: C, 64.30; H, 10.70.

Supplementary Experiments.—Since in the early work water was observed to condense on the upper parts of the reaction vessel a Dean–Stark water trap was inserted between the reaction vessel and the condenser in all subsequent experiments. It was of interest to find, in agreement with Walker,[22] that the equilibrium $ROH + KOH \rightleftarrows ROK + H_2O$ could be forced practically completely to the right by the use of the water trap. In most cases, even though the temperature range might vary considerably a plot of the volume of water collected *versus* time gave curves of the same general shape.

Although Raney nickel proved to be an effective catalyst it was discarded in favor of U.O.P. nickel which gave much more closely reproducible results. Preliminary experiments showed that the use of potassium in place of sodium accelerated both the alkoxide formation and the condensation reaction and decreased the amount of high boiling residue formed.

It was found that a β-branched alcohol such as 2-ethylhexanol-1 condensed little if at all with a normal primary alcohol. This is consistent with the fact that β-branched primary alcohols are obtained in good yields from normal primary alcohols (Table III). Attempted self-condensation of heptanol-2 or octanol-2 gave only low yields of incompletely identified products.

A study of the effect of varying the reaction time on the amount of high-boiling residues formed in the self-condensation of *n*-hexyl alcohol showed that as the period of refluxing (after the water began to collect) was increased from 1.3 to 2.2 to 3.5 hours the amount of high-boiling residue, from one mole of alcohol, increased from 8 to 14 to 22 g. These residues absorbed bromine and boiled over a wide temperature range.

The saturated aldehyde, $RCH_2CH_2CHRCHO$, referred to in the last part of the Discussion was obtained as follows.

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(19) E. F. Pratt and P. W. Erickson, to be published.

(20) J. W. Cook, C. L. Hewett and C. A. Lawrence, *J. Chem. Soc.*, 71 (1936).

(21) P. Pfeiffer, E. Kalckbrenner, W. Kunze and K. Levin, *J. prakt. Chem.*, [2] **119**, 114 (1928).

(22) T. K. Walker, *J. Soc. Chem. Ind.*, **40**, 172T (1921).

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]

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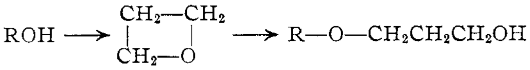
Trimethylene oxide reacts with alcohols in the presence of catalytic amounts of strong acids or bases or in the presence of water to give monoalkyl ethers of trimethylene glycol. The reactions with phenols are catalyzed by alkali but not by acids. There is great similarity to the analogous reactions 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.



$$\text{ROH} \longrightarrow \begin{array}{l} CH_2\text{—}CH_2 \\ |\qquad\ \ | \\ CH_2\text{—}O \end{array} \longrightarrow \text{R—O—}CH_2CH_2CH_2OH$$

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.

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