MODIFIED GUERBET CONDENSATIONS

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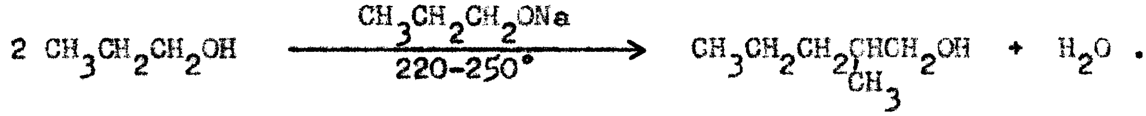
I. HISTORICAL INTRODUCTION

The literature of organic chemistry contains many examples of reactions which have been studied in only a cursory manner. The reasons for this are many but of chief importance among them are the drastic conditions required, the poor yields obtained, or the existence of better routes to the same products. As a consequence, a reaction may remain unused for many years until some worker in an entirely different corridor of research happens upon it and sees new ways of improving it. An excellent example of this is provided by the Guerbet reaction and its modification which is the subject of this thesis.

Guerbet,[1-6] in a series of papers beginning in 1899, demonstrated that an alcohol in the presence of the corresponding sodium alkoxide would self-condense when heated in a sealed tube. This may be represented for propanol-1 as follows:

(1) 

$$2\ CH_3CH_2CH_2OH \xrightarrow[220-250^\circ]{CH_3CH_2CH_2ONa} CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH + H_2O\ .$$

In addition, higher molecular weight alcohols and mixtures of acids were formed. Guerbet was able, in part, to show the scope of the reaction by self-condensing primary or secondary alcohols which contained a β-methylene or methyl group. In the case of mixed alcohol condensations, it was necessary that at least one of the alcohols contain such a methylene or methyl group.

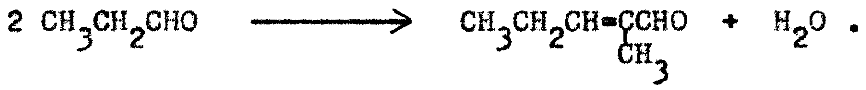
The fact that primary alcohols formed mainly acids when heated with potassium hydroxide,[3] while secondary alcohols formed only condensation products[4] and tertiary alcohols did not react,[5] led Guerbet to suggest this as a means of distinguishing alcohol types. This has not been adopted but it may prove of some value where the standard qualitative tests for alcohols fail.

Other workers[7,8] did little to improve the reaction until Weizmann and his co-workers reported their results in 1937.[9] This and subsequent papers put the Guerbet reaction on firmer synthetic grounds.[10,11]

The first proposal of a reaction mechanism[12] assumed that the alcohol was initially dehydrogenated to the aldehyde, i.e.,

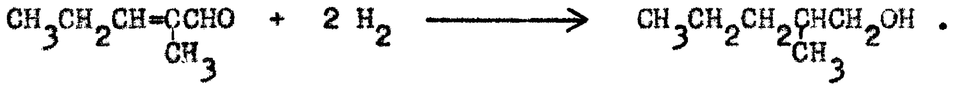
$$(2)\quad 2\ CH_3CH_2CH_2OH \longrightarrow 2\ CH_3CH_2CHO + 2\ H_2\ ,$$

which then underwent an aldol condensation in the alkaline medium with water elimination,

(3) 

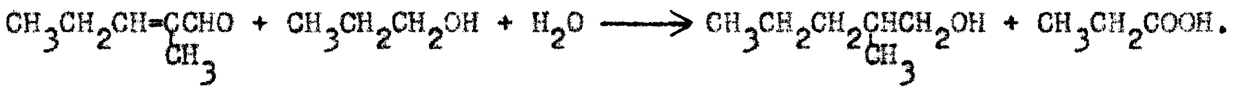
$$2\ CH_3CH_2CHO \longrightarrow CH_3CH_2CH{=}\underset{CH_3}{C}CHO + H_2O\ .$$

This product was then reduced to the saturated alcohol by molecular hydrogen,

(4) 

$$CH_3CH_2CH{=}\underset{CH_3}{C}CHO + 2\ H_2 \longrightarrow CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH\ .$$

Weizmann's group suggested a different route for the last step as follows:

(5) 

$$CH_3CH_2CH{=}\underset{CH_3}{C}CHO + CH_3CH_2CH_2OH + H_2O \longrightarrow CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH + CH_3CH_2COOH.$$

The reasons for this modification will be given in the discussion of the nature of the reaction.

The main modification of Weizmann's group was to use an autoclave instead of a sealed tube. The temperature at which the reaction began was indicated by the rapid rise in pressure due to hydrogen evolution. The temperatures varied from 220° to 310° depending, apparently, upon the temperature at which hydrogen evolution began and the reactions were continued for five to eighteen hours. The amount of sodium used to form the alkoxide was varied but apparently the best results were obtained when approximately 0.3 mole of sodium was used to 1.0 mole of starting alcohol. No solvent other than the alcohol itself was used.

The results were good for the self-condensation of primary alcohols having a methylene group adjacent to the methylol group. The alcohols used were propanol-1, butanol-1, 3-methylbutanol-1, pentanol-1, and octanol-1. The conversions to the condensed alcohols were 48, 61, 51, 48 and 35%, respectively. Approximately one mole of acid corresponding to the starting alcohol was also formed for each mole of condensed alcohol.

The reaction of 2-ethylhexanol-1 under the conditions favorable for the self-condensation of normal primary alcohols gave only 2-ethylhexanoic acid and bis-(2-ethylhexyl)ether.

Primary alcohols were found to condense with cyclohexanol in widely varying yields to form the corresponding β-substituted cyclohexanols. For example, butanol-1 gave a 61% yield of 2-butylcyclohexanol, benzyl alcohol gave a 33% yield of 2-benzylcyclohexanol and hexadecanol-1 gave only an 8% yield of 2-hexadecylcyclohexanol.

The yields were also erratic and poor for the condensation of <u>para</u> substituted benzyl alcohols with normal primary alcohols. Thus, benzyl alcohol condensed with propanol-1 to form 2-benzylpropanol-1 in 32% yield, while <u>p</u>-methoxybenzyl alcohol reacted with butanol-1 to form

2-(p-methoxybenzyl)butanol-1 in only 20% yield.

This work made the Guerbet reaction a practical process in some of its aspects. Analysis of the structures of the products formed with various types of alcohols not only gave a broader view of the reaction scope but, in addition, gave an improved picture of the sequence of steps involved in the over-all reaction.

There are three main weaknesses of Weizmann's procedure. These are: inefficient use of the starting alcohol due to its conversion in part to the corresponding acid, the need of high pressure equipment which is not always available in the organic laboratory and the absence of an indicator to show the extent of reaction.

In the sequence of steps given above for the Guerbet condensation, it appears reasonable to consider that the dehydrogenation of the alcohol to the aldehyde may control the over-all rate. In the work of Guerbet and Weizmann, discussed previously, it appears that the aldehyde is formed by the thermolytic dehydrogenation of the alcohol. The use of a carbonyl compound together with an alcohol might well facilitate the dehydrogenation since an Oppenauer oxidation would seem probable under these conditions. Such a system was used by Mastagli who studied the effect of potassium or sodium hydroxide in benzyl alcohol at the reflux temperature on carbonyl compounds and β,γ-unsaturated alcohols.[13] The concentration of the base varied from 0.50 to 2.0 normal.

The potassium hydroxide-benzyl alcohol reagent reacted with various substituted benzaldehydes to form substituted benzyl alcohols and benzoic acid in good yields. This may be represented by the following equations:

$$(6)\quad C_6H_5CH_2OH + p\text{-}XC_6H_4CHO \longrightarrow C_6H_5CHO + p\text{-}XC_6H_4CH_2OH$$

(7) $2\ C_6H_5CHO + KOH \longrightarrow C_6H_5CO_2K + C_6H_5CH_2OH$.

In typical examples, X was the methoxy or isopropyl group. The only acid isolated was benzoic acid, formed by a Cannizzaro reaction as by equation (7).

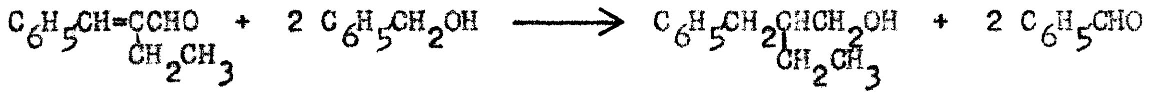
When the added aldehyde contained an α-methylene group, a more complicated reaction ensued. This phase of the work will be considered in detail only for butanal since the yields of the various products were not given. The same general situation existed for the eleven other aldehydes of this type which were studied.

An exchange of the hydrogen first occurred, as in every case in this study, but this was followed by aldol condensations and reductions. Thus, butanal with the potassium hydroxide-benzyl alcohol reagent formed 2-benzylbutanol-1, 2-ethylhexanol-1 and benzoic acid. Mastagli represented these results by the following group of equations but since the yields were not given, it is not possible to evaluate their relative importance.

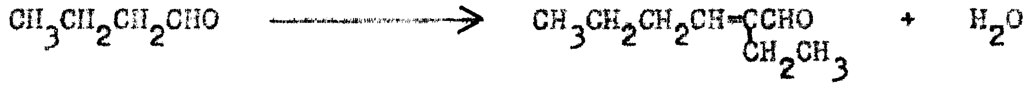
(8) $C_6H_5CH_2OH + CH_3CH_2CH_2CHO \longrightarrow C_6H_5CHO + CH_3CH_2CH_2CH_2OH$

(9) 

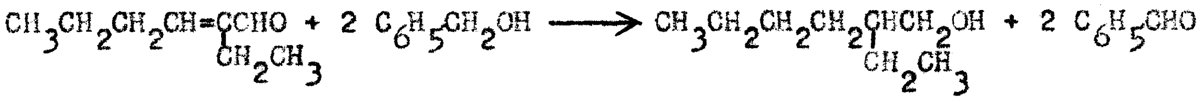
$$C_6H_5CHO + CH_3CH_2CH_2CHO \longrightarrow C_6H_5CH{=}\underset{CH_2CH_3}{C}CHO + H_2O$$

(10) 

$$C_6H_5CH{=}\underset{CH_2CH_3}{C}CHO + 2\ C_6H_5CH_2OH \longrightarrow C_6H_5CH_2\underset{CH_2CH_3}{C}HCH_2OH + 2\ C_6H_5CHO$$

(11) 

$$2\ CH_3CH_2CH_2CHO \longrightarrow CH_3CH_2CH_2CH{=}\underset{CH_2CH_3}{C}CHO + H_2O$$

(12) 

$$CH_3CH_2CH_2CH{=}\underset{CH_2CH_3}{C}CHO + 2\ C_6H_5CH_2OH \longrightarrow CH_3CH_2CH_2CH_2\underset{CH_2CH_3}{C}HCH_2OH + 2\ C_6H_5CHO$$

The benzaldehyde which was not consumed by condensation underwent a Cannizzaro reaction as shown by equation (7).

To show that equations (10) and (12) might represent the mode of obtaining the reduced alcohols, several 2-alkylcinnamaldehydes were treated with the same reagent. The expected products, the 2-alkyldihydrocinnamyl alcohols, were obtained.

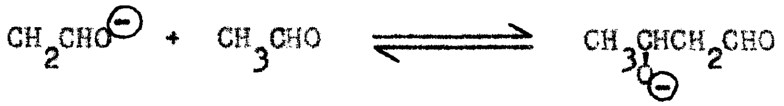
It was found that the reactions developed for aldehydes were also applicable to ketones. Several ketones were treated with the reagent and the products identified.

The chief importance of this work is not its synthetic applications, but rather in the use of its results to explain the Guerbet reaction. This will be discussed more fully in the section dealing with the nature of the reaction. Another valuable feature of this work was the proof of structure and the characterization of the products formed.

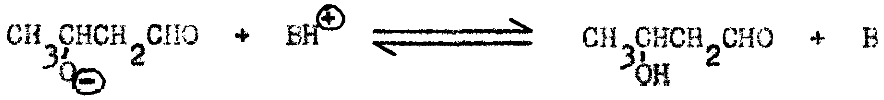
The hydrogenation of carbon monoxide in the presence of zinc and chromium oxides to form methanol and higher alcohols may be similar in some respects to the Guerbet reaction.[14] Some of the higher alcohols formed are ethanol, propanol-1, butanol-1, and 2-methylbutanol-1. All of these are believed to arise by successive aldolizations of the intermediate aldehydes. Indeed, the proportion of higher alcohols formed increased proportionally when the amount of alkali metal oxide in the catalyst was increased.

A wide variety of reactions may occur with carbonyl compounds in the presence of either acidic or basic catalysts. If an aldehyde or a ketone containing an α-methylene group is treated with aqueous or non-aqueous alkali, the primary reaction is the aldol condensation. This is believed to proceed by the following mechanism,[15] using acetaldehyde as an example:

(13) $$CH_3CHO + B \rightleftharpoons CH_2CHO^{\ominus} + BH^{\oplus}$$

(14) 

$$CH_2CHO^{\ominus} + CH_3CHO \rightleftharpoons CH_3\underset{O^{\ominus}}{CH}CH_2CHO$$

(15) 

$$CH_3\underset{O^{\ominus}}{CH}CH_2CHO + BH^{\oplus} \rightleftharpoons CH_3\underset{OH}{CH}CH_2CHO + B$$

The reaction is reversible throughout, as written, and if the temperature is raised much above room temperature, considerable dehydration normally occurs to give the α,β-unsaturated aldehyde. The dehydration is apparently also a reversible process.[16]

If the added catalyst is an acid a similar, but not identical, situation exists. The product in this case is the unsaturated aldehyde since the transformation of alcohols to olefins is normally acid catalyzed.[15]

The aldol equilibrium is most favorable for the condensation of aldehydes but it may be conveniently shifted to make it a practical process for ketones. A well-known example of this is the aldol condensation of acetone which forms diacetone alcohol in good yield if the acetone is allowed to distil onto barium hydroxide contained in a Soxhlet thimble.[17]

The conjugate base in equation (13) may be formed from a variety of active methylene compounds. The methylene compound may be another aldehyde, a ketone, an ester, an aliphatic nitro compound, or any compound having one or more electron attracting groups attached to a carbon having at least one hydrogen.

The general equation for conjugate base formation is:

$$(16)\quad H\text{-}CXYZ + B \rightleftharpoons {}^{\ominus}CXYZ + BH^{\oplus} ,$$

where at least one of the X, Y, or Z substituents is an electron attracting group. The greater the electron attracting nature of the attached group, the more acidic will be the compound and the weaker will be the base required for the formation of the conjugate base. This is strikingly demonstrated by the fact that aqueous sodium carbonate is sufficiently basic to give the conjugate base with aldehydes in the aldol condensation. However, the Claisen condensation of ethyl-2-methylpropionate to form the β-ketoester has not been effected with sodium ethoxide. A stronger base such as sodium triphenylmethide can give rise to the conjugate base and the reaction proceeds in fair yield.[18]

The conjugate base once formed, may then condense with the carbonyl compound, as by equations (14) and (15) above. The aldol,[15] Knoevenagel,[19,20] Perkin,[19,20] Stobbe,[21] Claisen[22] and Michael[23] reactions are all closely related. They are considered in detail in the references given and will not be discussed further here.

Aldehydes having not more than one α-hydrogen may undergo the Cannizzaro reaction. This is the disproportionation of an aldehyde to an alcohol and an acid. Equation (7) above is a typical example. If two aldehydes are used, it is called the "crossed" Cannizzaro reaction.

Other reagents, in addition to alkali hydroxides, which will effect the disproportionation include alkaline earth metal hydroxides, alkali metal amides in liquid ammonia, alkali metal alkoxides in alcohol, and magnesium or aluminum alkoxides in alcohol or in an inert solvent.[16] The last two types of reagents represent an interesting modification of the Cannizzaro reaction, which is referred to as the

Tischtschenko reaction. The product is the ester instead of the acid and the alcohol, i.e.,

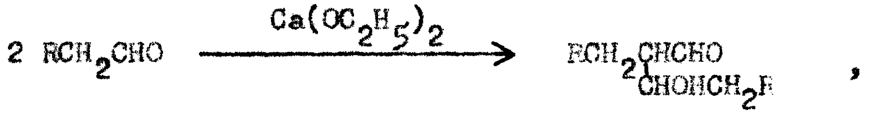
$$(16)\quad 2\ C_6H_5CHO \xrightarrow[\substack{\text{or}\\ \text{Al(OR)}_3}]{\text{NaOR}} C_6H_5CO_2CH_2C_6H_5\ .$$

This reaction is normally performed at about room temperature but in the presence of alkali metal alkoxides at 100°, considerable transformation of the ester occurs to give an ether and acid.[24,25]

$$(17)\quad C_6H_5CO_2CH_2C_6H_5 + RONa \longrightarrow C_6H_5CO_2Na + ROCH_2C_6H_5\ .$$

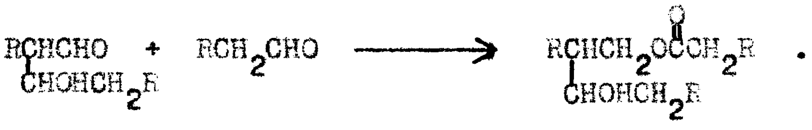
A completely satisfactory mechanism for the Cannizzaro reaction has not been proposed. It has not been possible to correlate all of the many factors which influence the reaction with any one of the existing postulates.[26]

Nord and co-workers have made an interesting study of the effect of different metal alkoxides on aldehydes.[27,28] Excellent yields of the dehydrated aldol were obtained when aldehydes containing an α-methylene group were treated with sodium alkoxides. Aluminum ethoxide gave the Tischtschenko reaction while calcium ethoxide, magnesium ethoxide, calcium aluminum ethoxide, and other complex alkoxides promoted the formation of the mono-ester of a 1,3-glycol. These glycol esters are believed to arise by the aldehyde first undergoing an aldol condensation,

(18) 

$$2\ RCH_2CHO \xrightarrow{Ca(OC_2H_5)_2} \begin{array}{l} RCH_2CHCHO \\ \quad\ \ |\ \ CHOHCH_2R \end{array} ,$$

followed by a "crossed" Tischtschenko reaction to give the product,

(19) 

$$\begin{array}{l} RCHCHO \\ \ \ |\ \ CHOHCH_2R \end{array} + RCH_2CHO \longrightarrow \begin{array}{l} RCHCH_2O\overset{O}{\overset{\|}{C}}CH_2R \\ \ \ |\ \ CHOHCH_2R \end{array}\ .$$

The results were somewhat different for aldehydes having only one α-hydrogen. When a strongly basic catalyst such as sodium ethoxide was used, the product was mainly the mono-ester of the glycol. All other types of catalysts were insufficiently basic to yield the aldol reaction and the chief product was the simple ester formed by a Tischtschenko reaction.

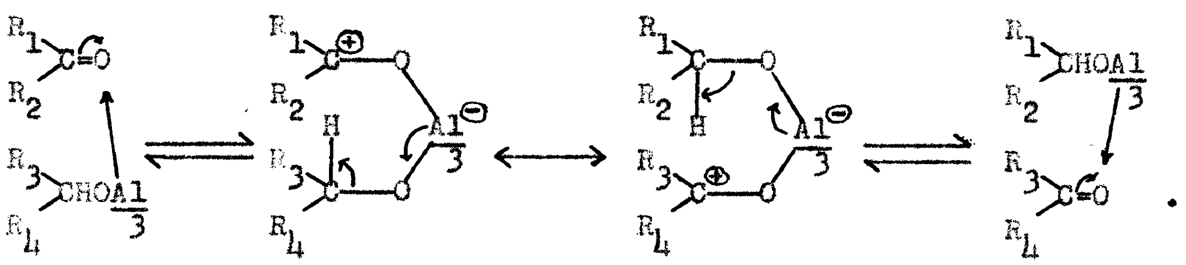
The Meerwein-Ponndorf-Verley reduction and the Oppenauer oxidation have become quite general and of increasing importance to the organic chemist. These reactions are equilibrium processes and they both may be represented by the following equation:

(20) 

$$R_1\overset{O}{\overset{\|}{C}}R_2 + R_3\overset{OH}{\overset{|}{C}}HR_4 \xrightleftharpoons{MOR} R_1\overset{OH}{\overset{|}{C}}HR_2 + R_3\overset{O}{\overset{\|}{C}}R_4 .$$

The reaction is named, then, according to the purpose. If it is desired to reduce $R_1\overset{O}{\overset{\|}{C}}R_2$, it is called the Meerwein-Ponndorf-Verley reduction and $R_3\overset{OH}{\overset{|}{C}}HR_4$ is isopropyl alcohol and MOR is aluminum isopropoxide.[29] Conversely, should it be the $R_3\overset{OH}{\overset{|}{C}}HR_4$ which is to be oxidized, the reaction is called the Oppenauer oxidation.[30] In this case $R_1\overset{O}{\overset{\|}{C}}R_2$ may be any one of a variety of aldehydes, ketones or quinones, although acetone and cyclohexanone are most commonly used. For the oxidation, MOR is ordinarily aluminum tertiary butoxide, isopropoxide, or phenoxide.

One possible mechanism for these reactions is,[30]

(21) 

This mechanism has been illustrated using an aluminum alkoxide but alkoxides of the metals of groups I, II, III, and IV have been used and as Woodward has pointed out, aluminum should have no unique function.[31] Aluminum alkoxides do give, in general, the most desirable results because they have little tendency to promote condensation reactions and they are soluble in both alcohols and hydrocarbons.

The proper choice of the hydrogen acceptor in the oxidation reaction or the hydrogen donor in the reduction reaction has been determined empirically for the most part. It should be noted, however, that Adkins and his co-workers have measured the oxidation potentials of a large number of carbonyl compounds equilibrated with their alcohols in the presence of aluminum alkoxides so that a wiser choice of the desired additive can be made.[32]

A large difference in oxidation potentials between two carbonyl compounds equilibrated with their alcohols does not, in itself, indicate that the reaction will be successful. Referring to equation (20); even though $R_1\overset{\overset{O}{\|}}{C}R_2$ may have a much higher oxidation potential than $R_3\overset{\overset{O}{\|}}{C}R_4$ the oxidation-reduction will not necessarily proceed satisfactorily to give a good yield of $R_3\overset{\overset{O}{\|}}{C}R_4$. The rate of attainment of equilibrium must also be considered and this factor cannot be predicted except by analogy. Adkins' group found, for example, that while 1,3-dimethoxyacetone had the highest oxidation potential of any compound measured, its rate of attainment of equilibrium was exceedingly slow. On the other hand, acetone and cyclohexanone have relatively low oxidation potentials but yet give very rapid attainment of equilibrium.

There are many other factors which must be considered in the application of these processes such as side reactions, ease of isolation of the products and methods of shifting the equilibrium. Thorough discussions of these factors are given in the references.[29,30]

It is possible that these redox reactions may not be limited to the carbon-oxygen system. For example, one worker reported the reduction of benzalaniline to benzylaniline, azobenzene to hydrazobenzene, cinnamic acid to dihydrocinnamic acid, benzophenone to benzhydrol and anthraquinone to anthrahydroquinone by the action of 3-methylbutanol-1 and its sodium alkoxide at the reflux temperature.[33] While the Guerbet reaction was also apparently involved (see Discussion), the actual reduction may well have been of the Meerwein-Ponndorf-Verley type. Indeed, it is possible that this is one of the first examples of this reaction. The same phenomenon may also be illustrated by the reduction of aromatic nitro and nitroso compounds by alkali alkoxides.[34,35] Relatively little work has been done on these types of reactions so that their similarity to the Meerwein-Ponndorf-Verley reduction-Oppenauer oxidation can only be estimated.

A very interesting modification of the carbon-oxygen redox equilibrium has been the use of Raney nickel instead of a metal alkoxide to effect the hydrogen exchange.[36] Thus, cholesterol, benzoin, benzhydrol and fluorenol were all oxidized to the corresponding ketones by the action of Raney nickel and cyclohexanone in a refluxing toluene solution. It was also found that the reverse procedure could be effected by using cyclohexanol or a variety of other alcohols as the hydrogen donors.

Apparently metal catalysts are able to promote a variety of reactions of compounds containing carbon-oxygen functional groups. A few examples will illustrate this adequately. Raney nickel and platinum have been used to catalyze the Cannizzaro reaction.[37,38] Metals such as magnesium and aluminum amalgum have been used to effect the benzoin condensation.[39] The aldol condensation and the Tischtschenko reaction apparently occur at high temperatures in the presence of a variety of metal oxides.[40,41,42] Raney nickel has been found to cause β,γ-unsaturated alcohols to rearrange to the corresponding saturated aldehydes or ketones.[43] The dehydrogenation of ethanol and propanol-1 over a nickel-thorium or a cobalt-thorium catalyst gave considerable amounts of acetals.[44] It might be anticipated, therefore, that as organic reactions become better understood and more important that as a sound theory of hetergeneous catalysis is evolved, metals will become one of the most important of all tools to the practicing organic chemist.

The above discussion has been given to explain the present status of the Guerbet reaction and to show, in part, the importance of catalytic influences upon reactions of alcohols, aldehydes and ketones. The remainder of this dissertation is devoted to a study of certain modifications of the Guerbet reaction and a proposal as to its nature. It will be seen that catalytic influences are of great importance.

II. DISCUSSION

A. Exploratory Experiments

The original objective of this research was to determine whether the important Meerwein-Ponndorf-Verley method for reducing carbonyl compounds to alcohols and the Oppenauer method for reversing this reaction could be extended to the nitrogen analogs of these compounds, which are the anils and the amines. In an experiment directed toward this end, the effect of sodium hexoxide in hexanol-1 on benzalaniline was studied. Benzylaniline was obtained as desired but it was of considerable interest to find that hexanoic acid and 2-butyloctanol-1 were also formed. Previous workers had used 3-methylbutanol-1 and its sodium alkoxide to reduce benzalaniline and obtained 3-methylbutanoic acid but did not report the formation of the ten carbon alcohol, although they referred to the Guerbet reaction as the most logical route for the reduction.[33]

The formation of 2-butyloctanol-1 and hexanoic acid from hexanol-1 strongly indicated that a Guerbet type of reaction had occurred. This could have proceeded by a hydrogen exchange between hexanol-1 and benzalaniline as given by equation (1):

$$(1)\quad CH_3(CH_2)_4CH_2OH + C_6H_5CH{=}NC_6H_5 \longrightarrow CH_3(CH_2)_4CHO + C_6H_5CH_2NHC_6H_5 .$$

The aldehyde so formed could then react as shown by equations (7), (11), and (12) in the Historical Introduction to yield the saturated condensed alcohol and the acid.

The Guerbet reaction as outlined in the Historical Introduction is not a satisfactory laboratory process because of the need of an autoclave, the undesirable formation of acid, the difficulty in determining when the reaction is complete and the frequently unsatisfactory yields. It would be desirable to develop this reaction so that it would become a generally useful laboratory process. Furthermore, since the work with sodium hexoxide suggested a promising method of doing this, the original objective of this work was abandoned in favor of the new goal. It is felt that the new objective has been reached in a satisfactory manner since as a result of this study, the Guerbet reaction may now be considered to be a facile laboratory process which proceeds in good yields. The scope of the reaction has been more completely defined and the course of the reaction has been further elucidated.

The attempt to evaluate the Guerbet reaction by using benzalaniline as a hydrogen acceptor was not successful because of the difficulty encountered in separating the benzylaniline from the 2-butyloctanol-1. A few typical experiments on this phase of the work are included in the Experimental.

It appeared that if the function of the benzalaniline was to provide aldehyde for promoting the Guerbet reaction, then a metal dehydrogenation catalyst might be substituted in its place. Such was found to be the case and the reaction system was not only considerably simplified but the reaction proceeded faster and in better yield.

The first metal dehydrogenation catalyst tried was Raney nickel.[44] This was added to a solution of sodium hexoxide in hexanol-1 and the solution was heated at reflux for 20 hours to obtain a fair yield of the twelve-carbon alcohol. It was observed during this reaction that water had formed and condensed on the upper parts of the reaction flask.

It seemed desirable to remove this by-product water and in the subsequent experiments a Dean-Stark water trap was used to accomplish this.

In the typical procedure using a dehydrogenation catalyst, the alkali metal was reacted with the alcohol contained in a three-necked flask equipped with a thermometer, an efficient mechanical stirrer and a Dean-Stark water trap surmounted by a reflux condenser. After all of the alkali metal had reacted, the dehydrogenation catalyst was added. Heat was applied with a "Glas-Col" mantle. The by-product water collected in the trap, as refluxing was continued, and the temperature was allowed to rise as high as required to maintain the refluxing. Not only did the removal of the water allow a much higher temperature to be attained, but it also allowed the reaction to be readily followed merely by noting the volume of water formed. It is also possible that removal of the water decreased the amount of acid formed (see below).

It was difficult to evaluate accurately the effect of Raney nickel on the Guerbet reaction since it could not be conveniently weighed with accuracy after it was prepared from the nickel-aluminum alloy. The alloy can be weighed to make up accurate weights of the catalyst but it is difficult to reproduce the catalyst activity from batch to batch. If a single large batch of catalyst is made for a number of experiments, its activity changes markedly with time.[46]

Three supposedly identical experiments were performed using 1.5 moles of hexanol-1, 0.30 mole of sodium and 3.54 g. of Raney nickel prepared separately for each experiment. This amount of nickel was contained in 6.25 g. of the nickel-aluminum alloy used, since it was 56.7% nickel as determined by gravimetric analysis. The temperature ranges during the reactions varied considerably as did the volumes of water produced in the reaction time of 5.2 hours after adding the catalyst. The yields of 2-butyloctanol-1 were fairly consistent, however, being 35%, 41% and 40%. Since it seemed desirable to be able to duplicate the temperature, the water volume and the reaction rate, it was felt that Raney nickel left much to be desired as a catalyst.

Universal Oil Products Hydrogenation Catalyst was tried as an alternate to Raney nickel.[47] This material is 50-55% nickel as the metal and metal oxides supported on kieselguhr and will be referred to hereafter as U.O.P. nickel. This catalyst is commercially available in pellet form and is activated for hydrogenations by heating it strongly in an atmosphere of hydrogen.[48] In this investigation the only treatment of the catalyst was to grind it with a mortar and pestle until it all passed a 100 mesh sieve. A single batch, sufficient for all of the work reported in this thesis, was prepared.

Table I shows the results of certain preliminary experiments with U.O.P. nickel. In each experiment 1.5 moles of hexanol-1, 0.30 mole of sodium and 2.5 g. of U.O.P. nickel were used, with a 3.5 hour reflux period after water began to distil from the reaction mixture.

Table I

Preliminary Studies with U.O.P. Nickel

Expt.	Induct. time, hrs.	Temp. range, °C	Moles of Products		
			Water	2-Butyl-octanol-1	Hexanoic Acid
A 11[a]	1.5	166-208°	0.31	0.39	0.13
A 12[a]	1.5	166-219°	0.27	0.35	0.17
A 13[b]	2.5	165-203°	0.27	0.37	0.13
A 14[c]	3.5	166-188°	0.20	0.34	0.14

[a] Catalyst powder added prior to reacting the sodium with the hexanol-1.
[b] Catalyst powder added after reacting the sodium with the hexanol-1.
[c] Catalyst pellets added after reacting the sodium with the hexanol-1.

It is evident from these results that U.O.P. nickel performs well. The yield of product alcohol and the reaction rate are seen to be fairly reproducible. If the catalyst is allowed access to hydrogen, (experiments A 11 and A 12 compared to experiment A 13), it is seen that the induction time is shortened but that the reaction goes at about the same rate once it starts. The induction time was taken to be the time which elapsed between the addition of the catalyst and the appearance of the first drop of water in the trap. While allowing the catalyst to have access to hydrogen decreases the total reaction time, it was felt that it would be undesirable to activate it since the extent of activation would vary with the amount of alkali metal and the rate at which the metal reacted. For this reason, in all subsequent experiments, the U.O.P. nickel was added after all of the alkali metal had reacted.

In experiment A 14 in Table I, the U.O.P. nickel pellets were used instead of the powder. When these results are compared with those of the other three experiments it is seen that powdering shortens the induction time and increases the reaction rate. This might be due to having the catalyst surface more readily available for reaction.

Copper chromite catalyst was tried in one experiment as a dehydrogenation catalyst for the Guerbet reaction.[49] Copper chromite was found to be effective but it produced a much larger amount of acid than either Raney nickel or U.O.P. nickel, under otherwise identical conditions. Since one catalyst that was used had been essentially pure metal, (however, see ref. 50), one a metal-metal oxide supported on kieselguhr and the other a combination of metal oxides, it was conceivable that a variety of catalytic surfaces could be used. In order to determine whether the catalyst support, kieselguhr, employed for U.O.P. nickel, could itself have any catalytic effect, an experiment with "Filter-Cel" was performed. The diatoms present a very large amount of surface and may be effective. However, under the conditions favorable for catalysis with U.O.P. nickel with hexanol-1 and its sodium alkoxide, no reaction was effected by "Filter-Cel" after five hours of refluxing.

It was stated above that the water of condensation was removed from the reaction mixture by distillation. It was rather surprising that this water could be removed from an alkoxide solution. Since it is common procedure to destroy alkoxides by treating them with water, it appeared that it might be feasible to reverse the process and make an alkoxide by treating an alcohol with an alkali metal hydroxide; e.g.,

$$(2) \quad ROH + NaOH \rightleftharpoons RONa + H_2O .$$

Possibly the equilibrium could be shifted in favor of the alkoxide by simply removing the water by distillation.

The results of three experiments to test this point are given in Table II. In the first experiment (A 17) with benzene as a solvent, 48 hours were required to obtain essentially all of the water, but 80% of it was obtained after 5 hours at reflux. The second experiment (A 18) did not go to completion after 48 hours of refluxing. The third experiment (A 19) gave 88% of the theoretical volume of water after 10 hours of refluxing and Raney nickel was then added, and a satisfactory Guerbet reaction was carried out.

Table II

The Formation of Sodium Hexoxide from Hexanol-1 and Sodium Hydroxide

Expt.	Hexanol-1, moles	Sodium Hydroxide, moles	Temp., °C	Ml. of Water	
				Found	Calcd.
A 17[a]	0.91	0.11	88°	2.02	1.94
A 18	1.5	0.30	156-178°	5.1	5.4
A 19	4.5	1.5	156-170°	23.7	27.0

[a] In this reaction, 250 ml. of benzene was used as a solvent.

The complete results of these experiments are included in the Experimental. While these results show that alkoxides can be prepared in this manner, it was deemed preferable to use the alkali metals in order to save time.

The literature contains relatively few references on this method of forming alkoxides although such an equilibrium is often alluded to.[51,52] One worker used pure sodium hydroxide and excess ethanol in benzene solution to form sodium ethoxide.[53] The water was removed by utilizing the ternary azeotrope of benzene, ethanol and water. The maximum reaction obtained was 68% as determined by an analysis of the distillate. The patent literature contains some references to the preparation of alkoxides by azeotropic distillation of water from a mixture of an alcohol and an alkali metal hydroxide.[54,55] An interesting variation reported in a patent was the addition of anhydrous acetone to a solution of sodium hydroxide in ethanol.[56] This precipitated the sodium ethoxide which could be filtered from the solution.

This displacement of this equilibrium makes it appear to be impractical to dry alcohols by treatment with an alkali metal followed by distillation.[*] While this is not a common procedure it has been recommended in at least one instance.[57] One might expect that the equilibrium between the alkali metal hydroxide and alcohol would shift to accommodate a minimum boiling azeotrope of alcohol and water since this represents the most volatile fraction of many water-alcohol systems.

In the Guerbet reaction as performed by other workers, the water of condensation could not be conveniently removed since a closed system was used in order to obtain a high temperature. It was of interest then to determine the effect of water removal on the reaction under the modified conditions which this thesis reports. An experiment

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[*] The author is indebted to Mr. J. H. Haslam, Pigments Department, E. I. du Pont de Nemours & Co., for this suggestion.

was performed with 1.5 moles of hexanol-1, 0.30 mole of potassium and 2.5 g. of U.O.P. nickel, with a total reflux period of 4.3 hours and the water was removed. The temperature continually increased until the reaction was stopped. In an identical experiment for a 4.3 hour reflux period without water removal, the temperature remained constant. With water removal the conversion of hexanol-1 to 2-butyloctanol-1 was 53%, while without water removal it was only 31%. In another identical experiment without water removal, except using a 7.0 hour reflux period, the temperature again remained constant and a 31% conversion to 2-butyloctanol-1 was obtained. The last experiment without water removal was allowed to reflux 60% longer than the first one so it appears that the reaction stopped after a certain amount of water had formed. This may be caused by a decrease in the alkoxide concentration as a consequence of hydrolysis. It is desirable, then, for the water to be removed from the reaction mixture as rapidly as possible in order to maintain the alkoxide concentration and to permit the temperature to reach higher values.

For the evaluation of the reaction variables, it would have been desirable to have had a constant reaction temperature. This was attempted with an inert solvent. Two experiments were performed with sodium hexoxide, hexanol-1 and Raney nickel in p-cymene. In one case the alkoxide was made by using sodium metal and in the other, sodium hydroxide was used. In these experiments the temperature varied only 10° and in spite of the fact that satisfactory yields were obtained, the use of a solvent has many disadvantages. The starting alcohol could not be satisfactorily recovered from the solvent and the use of a solvent requires considerably more work and time since it must be purified before use, it must be recovered from the reaction mixture and it decreases the reaction rate. For these reasons it was decided not to use a solvent to moderate the temperature changes.

A preliminary experiment with Raney nickel had indicated that potassium hexoxide might be superior to the sodium hexoxide. It appeared to be desirable to check this under the more reproducible conditions effected by U.O.P. nickel. The best experiment performed with sodium hexoxide in hexanol-1 and with U.O.P. nickel may be contrasted with two identical experiments in which equivalent quantities of potassium hexoxide were used. It was found that potassium hexoxide gave a shorter induction period and a more rapid reaction with less high-boiling residue than the sodium hexoxide. The conversions to 2-butyloctanol-1 were about 53% in all three experiments.

The potassium hexoxide gave a solution temperature about 10° higher than the sodium hexoxide at the start of reaction. If the temperature difference is due to the more complete dissociation of potassium hexoxide then this dissociation might favorably influence the Guerbet reaction aside from any temperature effect.

This information seemed to warrant the use of the more expensive potassium in preference to sodium. The use of potassium saved considerable time not only by giving a more rapid Guerbet reaction but also by greatly decreasing the time required to form the alkoxide.

A general procedure was devised for a systematic study of the reaction variables on the basis of the above exploratory work. Potassium metal was completely reacted with the alcohol prior to adding the U.O.P. nickel. The water of condensation was removed from the reaction mixture as rapidly as possible by distillation. In addition, it seemed expedient to stir the reaction mixture mechanically since U.O.P. nickel tended to adhere to the sides of the flask and towards the end of the reaction a small amount of solid, apparently the salt of the acid, separated out.

The results of the Guerbet condensation under these general conditions can be reproduced fairly satisfactorily. Even in those cases where there are variations in the rate, a reproducible yield of product is obtained.

After the work reported in this thesis was completed, a patent issued in 1949, describing related work came to the attention of the author.[58] In this patent the use of various dehydrogenation catalysts and the removal of water of condensation by distillation in the Guerbet reaction were disclosed. Since the information given in the patent was of value chiefly for the commercial application of the reaction while the information in this thesis is of value chiefly for a facile laboratory process, the results to a large extent supplement rather than duplicate one another. The conditions given in the patent provided good yields but a much longer time was required than was needed to obtain equal yields under the conditions of this investigation. The fact that the acid formation (without any ester formation) is a function of the alkoxide concentration has been corroborated.[59] Indeed, the long reaction times required for the experiments given in the patent result from the very low alkoxide concentrations which were used to prevent acid formation.

A very recent article based on the above patent is also of interest, chiefly because the water of condensation was removed by adding a large amount of calcium oxide to the reaction mixture.[60]

B. The Determination of Optimum Conditions

In the self-condensation of hexanol-1 and its homologs, there are three variables which seem to be most important. These are: the concentration of the alkoxide, the amount of dehydrogenation catalyst and the temperature. The temperature was varied primarily by changing the alcohol used, but it also varied greatly with the concentration of the alkoxide, as discussed below.

The effect of the alkoxide concentration was studied by varying the amounts of added potassium from zero to 0.325 mole with 1.0 mole of hexanol-1. These amounts were used in preference to 1.0 mole of alcohol in excess of the amount of potassium alkoxide since it seemed important to compare equivalent amounts of alcohol. This may be done since the condensed alcohol product and any acid formed can combine with the potassium ion, so that from this viewpoint the potassium hexoxide may be considered to be equivalent to hexanol-1. In all of these reactions, 2.0 g. of U.O.P. nickel and a reflux period of 2.0 hours after water began separating in the trap were used. The results are given in Table III.

A striking effect noticed as the alkoxide concentration is varied, is the direct variation of the solution temperature. These marked temperature elevations over the boiling point of hexanol-1 of 156° may seem a little unusual but it is not unlikely that they are due merely to the normal boiling point elevations for solutions. If it is assumed that the potassium hexoxide is completely dissociated (2 x m), then from the molalities used and the boiling point elevations

Table III

The Effect of Varying the Alkoxide Concentration

Expt.	ROK, moles	Induct. time, hrs.	Temp. range, °C	Moles of Product			Alcohol	
				Water	Alcohol	Acid	Conv., %	Yld., %
B 2	0.100	2.2	163-168°	0.061	0.097	-	19	67
B 3	0.150	1.3	169-182°	0.15	0.17	0.022	33	74
B 4	0.175	1.0	173-188°	0.17	0.19	0.043	38	69
B 5	0.200	0.83	177-206°	0.20	0.26	0.10	51	63
B 6	0.225	0.67	180-225°	0.20	0.26	0.12	53	59
B 7	0.250	0.78	184-236°	0.16	0.21	0.15	43	46
B 8	0.275	0.92	187-241°	0.12	0.21	0.18	42	44
B 9[a]	0.325	1.0	194°	0.00	0.16	0.16	31	54

[a] The reaction was stopped as soon as water started to form.

observed, a molal elevation constant for hexanol-1 can be calculated by,[61]

$$(3) \quad K_b = \frac{\Delta T}{m} \quad .$$

The values of K_b calculated for the solutions in Table III are given in Table IV. The average value of 4.6° is not unreasonable.

Table IV

A Qualitative K_b Calculation for Hexanol-1

Expt.	Molality	$\Delta T_{obs.}$	K_b
B 2	1.09	9°	4.1°
B 3	1.73	14°	4.0°
B 4	2.08	19°	4.6°
B 5	2.45	23°	4.7
B 6	2.85	28°	4.9°
B 7	3.27	32°	4.9°
B 8	3.72	36°	4.8°
B 9	4.72	43°	4.6°
		Avge. =	4.6°

Many compounds have molal elevation constants of this magnitude or greater. Thus, for acetic acid K_b is 3.07°, for bromobenzene it is 6.26° and for carbon tetrachloride it is 5.03°.[62] An approximate determination of K_b for hexanol-1 with triphenylcarbinol as a solute gave an average value of about 5°.

It is to be understood that this is not intended to represent an accurate calculation of the molal elevation constant for hexanol-1 since the concentrations of solute are far in excess of those at which equation (3) can be applied with precision. Furthermore, the degree of dissociation of potassium hexoxide is unknown so that the value obtained for K_b is probably a minimum value. It is also to be mentioned that the temperatures are not accurate to more than ± 0.5° and the potassium was probably not weighed more accurately than ± 0.25 g. The calculations do, however, show that the large increases in solution temperatures might be expected on this basis.

There are other points concerning Table III which are interesting. It is seen, for example, that the induction time at first decreases as the alkoxide concentration increases, but at the highest alkoxide concentrations, the induction time again slightly increases. It is believed that this may be caused by the increasing temperature at first increasing the reaction rate but that at the highest alkoxide concentration it is more difficult for the water to escape because of the mass action effect on the alkoxide-hydroxide equilibrium. This is partially verified by experiment B 9 in the table in which the reaction was stopped as soon as water began to separate in the trap. Since 0.16 mole of acid had formed by this time, it indicates that the alkoxide concentration had to decrease to about 0.17 mole before the water could escape. This does not mean that water cannot be distilled from an alkoxide solution of greater concentration than this, but that the water probably reacts with aldehyde to form acid before it can be removed under these conditions.

It is interesting to note that the moles of water and of 2-butyloctanol-1 are about equivalent at lower alkoxide concentrations. As the concentration is increased, this equality no longer holds and the amounts of each formed are seen to increase to maxima and then decrease. This is undoubtedly related to the fact that the amount of acid formed increases directly with increases in the alkoxide concentration. When no alkoxide was used, no reaction whatsoever was effected after four hours of refluxing hexanol-1 with U.O.P. nickel. These features of the table are also of importance in considering the details of the reaction course and will be examined more critically in that part of the Discussion.

The gas evolved throughout the reaction was shown to be essentially 100% hydrogen. It was checked several times during the course of three different experiments which varied greatly in the amount of evolved hydrogen.

As tentative values, 0.175 mole of potassium and 1.0 mole of alcohol were selected as the quantities to be used in studying the other variables. It is seen that these amounts give a convenient reaction rate to produce a good yield of condensed alcohol with a low yield of acid.

The effects of varying the amount of U.O.P. nickel from 0.031 to 4.0 g. while collecting a constant amount of water (0.26 mole) are shown in Table V. Except for the first experiment, the induction temperatures were the same (175 ± 0.5° to 173 ± 0.5°) as were the temperature ranges during reaction (173 ± 0.5° to 203 ± 1°). These results show very conclusively that U.O.P. nickel exerts a marked accelerating effect on the Guerbet reaction. Not only is the induction time decreased as the amount of U.O.P. nickel is increased but the required reaction time is also decreased. The yields and conversions to

Table V

The Effect of Varying the Amount of U.O.P. Nickel

Expt.	Am't. of nickel, g.	Induct. time, hrs.	Reaction time, hrs.[a]	Moles of Products[b]		Alcohol	
				Hydrogen	Alcohol	Conv., %	Yld., %
B 13[c]	0.031	24.0	60.0	-	0.013	-	-
B 14	0.50	2.0	4.1	0.15	0.28	55	72
B 15	1.0	1.7	3.2	0.16	0.27	54	69
B 16	2.0	1.1	2.2	0.18	0.29	57	72
B 17	3.0	0.92	1.9	0.20	0.27	54	68
B 18	4.0	0.67	1.7	0.21	0.28	56	70

[a] Zero time was taken as the time at which water first appeared.

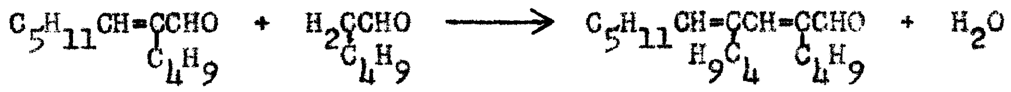
[b] There was approximately 0.04 mole of acid formed in each case.

[c] This experiment yielded only 0.019 mole of water.

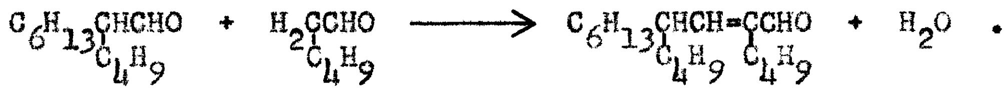
2-butyloctanol-1 are seen to be accurately reproducible even though the rate varied considerably. Experiment B 13 is included to show the limiting effect of the amount of U.O.P. nickel. Identical conditions, except that no nickel was used, failed to give any reaction after 21 hours of refluxing.

The only apparent effect caused by increasing the amount of U.O.P. nickel, aside from the rate effect, is the increase in the amount of hydrogen evolved. The yield of acid was about the same in the last five experiments (0.04 mole) and since the product was essentially saturated to bromine in carbon tetrachloride, it is felt that this increase in hydrogen evolution leads to more unsaturation in the high-boiling residues.

These high-boiling residues probably arise by advanced condensations. In a typical experiment, e.g., experiment B 4 of Table III, a residue was obtained which weighed about 8% as much as the amount of starting alcohol. The proposed intermediates, 2-butyl-2-octenal and 2-butyloctanal, could possibly condense with hexanal as shown by equations (4) and (5):

(4)


$$C_5H_{11}CH{=}\underset{C_4H_9}{C}CHO + H_2\underset{C_4H_9}{C}CHO \longrightarrow C_5H_{11}CH{=}\underset{H_9C_4}{C}CH{=}\underset{C_4H_9}{C}CHO + H_2O$$

(5)


$$C_6H_{13}\underset{C_4H_9}{C}HCHO + H_2\underset{C_4H_9}{C}CHO \longrightarrow C_6H_{13}\underset{C_4H_9}{C}HCH{=}\underset{C_4H_9}{C}CHO + H_2O\ .$$

These could be partially reduced to give a mixture of aldehydes and unsaturated alcohols. It is also possible that some glycols could be present. The high-boiling residues invariably showed unsaturation and boiled over a considerable temperature range. They were usually 50%

distillable or better, leaving a residue of thick tars.

It appeared that the approximate optimum conditions for the condensation of hexanol-1 were now established. In order to obtain a sufficiently rapid reaction and still obtain a good yield of product with little acid formation, it was decided to use 0.175 mole of potassium metal to 1.0 mole of alcohol with about 2.0 g. of U.O.P. nickel. The reactions were allowed to continue until they were about 50% complete as shown by the amount of water evolved. If the reaction is allowed to proceed much beyond this point, little is gained since the amount of high-boiling residue increases. This was indicated by a comparison of three experiments which were identical except for different reaction periods after water started to form. For these reactions 1.5 moles of hexanol-1, 0.30 mole of potassium and 2.5 g. of U.O.P. nickel were used. A 1.3 hour refluxing period after water started to form gave 0.30 mole of 2-butyloctanol-1 and 13 g. of residue. With a 2.2 hour refluxing period, 0.40 mole of 2-butyloctanol-1 and 20 g. of residue were formed and a 3.5 hour refluxing period yielded 0.40 mole of 2-butyloctanol-1 and 32 g. of residue.

The effects of changes in the reaction temperature were studied next. It was believed that this could be done satisfactorily by assuming that the straight-chain homologs of hexanol-1 would react about the same at the same temperature.

The results of varying n in $CH_3(CH_2)_nCH_2OH$ from 2 to 8 are given in Table VI. In these experiments, 1.0 mole of the alcohol, 0.175 mole of potassium and 0.5 g. of U.O.P. nickel were used, and 0.25 mole of water was collected except where noted. Only 0.5 g. of U.O.P. nickel instead of 2.0 g. was used because the reaction was found to be very

Table VI

The Effect of Varying n in $CH_3(CH_2)_nCH_2OH$

Expt.	n	Temp. range, °C	Reaction time, hrs.	Moles of Products			Alcohol/Acid	Alcohol	
				Hydrogen	Acid	Alcohol		Conv., %	Yld., %
B 20[a]	2	136-155°	26.0	0.16	0.024	0.21	8.1	42	75
B 21	3	155-180°	17.5	0.088	0.016	0.23	14.0	46	74
B 22[b]	4	174-204°	6.1	0.15	0.041	0.28	6.6	55	72
B 23[b]	5	195-238°	2.3	0.21	0.085	0.29	3.4	59	66
B 24	6	205-250°	1.6	0.22	0.10	0.31	3.1	62	72
B 25	7	222-276°	1.3	0.30	0.12	0.31	2.6	61	66
B 26[c]	8	237-271°	0.66	0.28	0.13	0.31	2.4	62	70

[a] In this experiment 4 g. of U.O.P. nickel was used to speed up the reaction and 3 ml. of o-xylene was added to the water trap to aid the water separation.

[b] In this experiment 0.26 instead of the standard 0.25 mole of water was collected.

[c] In this experiment 0.19 mole of water was collected and 2 g. of U.O.P. nickel was used.

fast with the higher alcohols.

The temperature is seen to affect the reaction rate in the expected manner. It is also seen that as the temperature is increased, the amounts of hydrogen and acid formed increase. It appears that the higher temperature favors acid production, even though from the standpoint previously considered, an increase in the rate of water removal might be expected to decrease the amount of acid formed.

The percent conversion of the reactant alcohol to the product alcohol is seen to increase as the temperature increases for the first four experiments tabulated. However, the ratio of product alcohol to acid decreases even though the percent yield of alcohol remains about constant. It would seem likely that with the higher boiling alcohols, a more efficient process would result if the alkoxide concentration was decreased since the amount of acid formed is a function of this (cf. Table III). It is seen, however, that good yields of the products are obtained with the 0.175 mole of potassium alkoxide.

In the experiments using octanol-1 and decanol-1, it was observed that the reaction began immediately upon heating the solutions to the reflux temperatures. This suggested that when the temperature is sufficiently high, as in a classical Guerbet reaction, the reaction could proceed without U.O.P. nickel being added. When the decanol-1 reaction was repeated without U.O.P. nickel, it was found to proceed rapidly, but not as rapidly as when nickel was used. It was of interest to find the approximate temperature at which reaction would proceed in the absence of U.O.P. nickel. It had been previously demonstrated that hexanol-1 does not react under these conditions without U.O.P. nickel at a temperature of 175° and so the series from heptanol-1 to decanol-1 was studied. An exploratory experiment during the benzalaniline work is of some interest since hexanol-1, in a solution containing only sodium hexoxide in the alcohol and at a solution temperature of about 186°, was converted to 2-butyloctanol-1 in 5% yield after 66 hours of refluxing.

For the experiments of this study, given in Table VII, 1.0 mole of alcohol and 0.175 mole of potassium were used. The solution was refluxed until 0.25 mole of water had been collected. It is evident that without U.O.P. nickel the reaction will proceed in good yield if the temperature is sufficiently high. From these results and from the results of the experiment referred to above with sodium hexoxide, it appears that at about 190° the reaction will begin and at above 200° it proceeds at a satisfactory rate. The conversions without nickel are as good or better than with nickel and the yields are about the same (cf. Tables VI and VII). The amounts of hydrogen are generally higher in the absence of nickel.

This study of the main reaction variables to establish the optimum conditions has resulted in a process which gives excellent yields for primary alcohols containing a β-methylene group. The required apparatus is available in most laboratories and the reaction can be conveniently followed by noting the volume of by-product water which has formed. It is to be emphasized that the reaction products are easily isolated in pure form.

It is not necessary to use potassium alkoxides since the sodium alkoxides will serve, but the latter require longer reaction periods. The alkoxides can be made from the alkali hydroxides if, for any reason, it is undesirable to use the alkali metals.

Table VII

The Effect of Varying n in $CH_3(CH_2)_nCH_2OH$ without U.O.P. Nickel

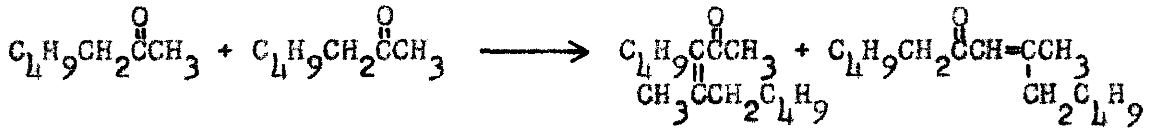
Expt.	n	Temp. range, °C	Reaction time, hrs.	Moles of Products			Alcohol	
				Hydrogen	Acid	Alcohol	Conv., %	Yld., %
B 28	4	175°	21.0	0.0	0.0	0.0	-	-
B 29[a]	5	195-254°	28.3	0.22	0.12	0.33	65	71
B 30	6	207-262°	5.8	0.27	0.12	0.31	61	70
B 31	7	224-305°	2.6	0.34	0.14	0.31	62	67
B 32[b]	8	239-320°	1.3	0.38	0.15	0.32	65	68

[a] This is an approximate value because a leak was found in the system.

[b] The reaction stopped after 0.24 mole of water had formed.

The self-condensation of secondary alcohols was studied briefly. The three secondary alcohols used were heptanol-2, octanol-2 and 5-methylnonanol-2. These reacted at reasonable rates under conditions favorable for the self-condensation of normal primary alcohols. The products were not obtained in good yields since considerable amounts of high-boiling residues were formed. In addition, the products were partially unsaturated and may have contained more than one condensation isomer. Two isomers may be formed here since the proposed intermediate ketone can condense at either of two positions with another molecule of ketone. Consider the equation for the condensation of heptanone-2:

(6)



$$C_4H_9CH_2\overset{O}{\overset{\|}{C}}CH_3 + C_4H_9CH_2\overset{O}{\overset{\|}{C}}CH_3 \longrightarrow C_4H_9\underset{CH_3CCH_2C_4H_9}{\underset{\|}{C}}\overset{O}{\overset{\|}{C}}CH_3 + C_4H_9CH_2\overset{O}{\overset{\|}{C}}CH{=}\underset{CH_2C_4H_9}{\underset{|}{C}}CH_3 .$$

Thus, the ketone can condense on the methyl group or the methylene group. This can be obviated by using symmetrical secondary alcohols but it restricts the process considerably. The condensation here probably occurred predominantly on the methyl group rather than on the methylene group. This is indicated by analogy to the reaction of benzaldehyde with butanone-2 in which the benzaldehyde condensed primarily on the methyl group of butanone-2 when base catalysis was used.[63] Acid catalysis gave the other isomer predominantly. This is also indicated by the distillation of the product after hydrogenation to remove the unsaturation. A more highly branched isomer would be expected to boil lower than a less highly branched compound. The compound which would be formed by condensation on the methylene group would be more highly branched and should boil at a lower temperature. It was found that a small amount of material distilled somewhat lower than the main fraction and may be the other isomer.

Since the secondary alcohol reactants gave poor yields of products difficult to purify, they were not further investigated. It may be that by altering the reaction conditions drastically the process could be improved. It would be of interest to do this since neither the reactants nor the products can be wasted in acid formation unless such drastic conditions are used that carbon-carbon cleavage occurs.

The products obtained from the self-condensations of normal primary alcohols in the Guerbet reaction are a rather unusual group of compounds. Apparently the branching on the carbon adjacent to the methylol group is responsible for their properties. All of them through the 24 carbon alcohol are colorless liquids with pleasant odors. Except for derivaties of 2-ethylhexanol-1, the only solid derivatives which have been reported are the allophanates.[13] It is possible to convert the alcohols to the aldehydes or some other type of compound and by this route obtain solid derivatives, but direct conversion to solid derivatives is difficult.

This failure to yield solid derivatives was interesting and oftentimes discouraging to the author. All of the standard types of alcohol derivatives were tried without success. The allophanates of these compounds are solids and their melting points, in general, checked the melting points given in the literature. For 2-butyloctanol-1, the allophanate melting point did not check the literature value, but the results of quantitative carbon and hydrogen analyses were satisfactory and sufficient additional evidence was obtained to characterize the compound.

Considerable effort has been expended to characterize

2-butyloctanol-1. Mastagli obtained this compound in the course of his work and proved its structure by synthesizing it by an alternate route.[13] He performed an aldol condensation with hexanal and subsequently reduced the α,β-unsaturated aldehyde.

Since the conversion of 2-butyloctanol-1 to the bromide gave a product which analyzed correctly for bromine but which reacted with alcoholic silver nitrate like a tertiary bromide rather than a primary bromide, further characterization was indicated. This tertiary bromide could have possibly formed by a carbonium ion rearrangement.[64]

The results of quantitative analyses for carbon and hydrogen were satisfactory. The alcohol was converted to the corresponding acid by oxidation in 46% yield. The neutralization equivalent of this acid was 191 as compared to the calculated value of 200. Neutralization equivalents of 202 and 199 were given by 2-butyloctanoic acid prepared by the Guerbet reaction starting with 2-butyloctanol-1. The acetate was made in excellent yield and it analyzed correctly for carbon and hydrogen, and had a saponification equivalent of 230 which may be compared to the calculated value of 228. The 2-butyloctanoic acid was converted to the solid amide and this substance analyzed correctly for carbon, hydrogen and nitrogen. This information, and that in the literature, adequately shows that the product obtained from hexanol-1 is 2-butyloctanol-1.

The etherification procedure of Pratt and Draper was adopted to obtain the equivalent weight of 2-butyloctanol-1.[65] This reaction is performed in a benzene solution using p-toluenesulfonic acid as a catalyst and triphenylcarbinol to etherify the alcohol, as shown by equation (7):

$$(7)\quad (C_6H_5)_3COH + ROH \longrightarrow (C_6H_5)_3COR + H_2O \; .$$

From the volume of water produced with a given weight of ROH, the equivalent weight of ROH may be calculated.

If the added alcohol is of the tertiary type it will probably be dehydrated rather than etherified but this will not alter the determination of the equivalent weight. The essential requirements are that every molecule of alcohol must yield a molecule of water either by dehydration or etherification and that no other reactions occur which yield water. The triphenylcarbinol cannot self-etherify and the trityl ether formed is stable at the low catalyst concentrations used. A value of 189 was obtained for 2-butyloctanol-1 as compared to the calculated value of 186. In addition, a half-reaction time of about 21 minutes was observed, which may be compared to half-reaction times of 23.8 to 25.6 minutes obtained for normal primary alcohols under the same conditions.[65] Secondary and tertiary alcohols etherify much more slowly.[66] This further supports the conclusion that the alcohol is a primary alcohol.

This method of equivalent weight determination was also used for 2-pentylnonanol-1, 2-hexyldecanol-1 and 2-benzylbutanol-1 for which the calculated equivalent weights are 214, 242 and 164, respectively. The experimental values were 219, 246 and 163. It appears that this is a satisfactory method of determining equivalent weights of primary alcohols.

The characterizations of the other compounds of this type were restricted to quantitative carbon and hydrogen analyses, and a comparison of their physical properties and the melting points of their allophanates in those cases for which the data are given in the literature. The compounds were analyzed for carbon and hydrogen since there has been some previous doubt as to the Guerbet reaction products.[2,13] This information supplemented by analogy to 2-ethylhexanol-1 and 2-butyloctanol-1 and certain structural proofs by synthesis in the literature serves to establish the structure of these compounds.

One feature of the identification work which should be emphasized is the use of allophanates as characterizing derivatives for alcohols. It is felt that they have not received adequate attention in light of the many advantages which they offer. Apparently all of them are readily purifiable solids which crystallize easily; they may be easily prepared even in the presence of water; they may be used for primary, secondary or tertiary alcohols, and the alcohols are easily regenerated and purified. This last feature represents a valuable procedure for the separation of alcohols from mixtures after the removal of any amines or phenols.

The allophanates are conveniently prepared by strongly heating cyanuric acid and passing the so formed cyanic acid into a liquid alcohol, or into a solution of the alcohol if it is a solid.[67] The equation for their formation, using ethanol as an example, is:

$$C_2H_5OH \ + \ 2\ HOCN \longrightarrow C_2H_5O\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NH_2 \quad . \tag{8}$$

The reason that allophanates have not been more widely used may be that so many alcohols form solids with cyanic acid that it is sometimes difficult to distinguish among some of them solely on the basis of the melting points of the allophanates. Another reason may be that such a high temperature is needed to decompose the cyanuric acid that a combustion tube is needed. This is not a serious disadvantage and the rest of the apparatus is available in every organic laboratory.

C. Mixed Guerbet Condensations

The possible use of two alcohols instead of permitting a single alcohol to self-condense in the Guerbet reaction is an important consideration. In choosing the ideal pair of alcohols many factors must be taken into account. The minimum requirements to permit condensation are that one of the alcohols must have a CH_3- or a $-CH_2$- group adjacent to the $>$CHOH group and the other alcohol may not be a tertiary alcohol, i.e., it must have a $>$CHOH group capable of being converted to the carbonyl group.

The preferred pair would appear to be a primary alcohol with no hydrogens on the carbon adjacent to the methylol group and a secondary alcohol with only one methylene or methyl group adjacent to the $>$CHOH group; a symmetrical secondary alcohol with two such methylene groups should also be satisfactory. With such a pair, the primary alcohol cannot self-condense and the secondary alcohol should show little tendency to do so by analogy with the unfavorable equilibrium for ketones in the aldol reaction. Thus, the mixed condensation should be the predominant reaction. Such a pair is represented by benzyl alcohol and 1-phenylethanol or 3-methylbutanol-2. Actually, few secondary alcohols of this type are readily available. Those which are readily available are of the 1-phenylethanol type which are not satisfactory to use in the Guerbet reaction because of the difficulties involved in obtaining and preserving the pure alcohols[68] and they have some tendency to dehydrate to the styrene compounds. It was necessary, therefore, to consider substitutes for this type of secondary alcohol.

An aliphatic β-branched primary alcohol and a normal primary alcohol represent an interesting pair. The β-branched primary alcohol cannot self-condense and even with equivalent quantities of each of the pair, the mixed reaction should be statistically preferred over the self-condensation of the normal primary alcohol. Furthermore, if the β-branched alcohol is used in excess, the mixed condensation will be even more favored. This, of course, ignores any difference in the relative tendencies of the two types of alcohols to be dehydrogenated or otherwise react. It was observed during the hexanol-1 evaluation, that prolonged reaction appeared to convert the product, 2-butyloctanol-1, to high-boiling residue by further condensations with hexanol-1. This indicated that the reaction discussed above might be feasible.

A reaction between 2-ethylhexanol-1 and hexanol-1 seemed to be a good choice. A 100% excess of 2-ethylhexanol-1 was used with 1.0 mole of total alcohols, 0.175 mole of potassium and 1.0 g. of U.O.P. nickel. The reaction stopped after 0.13 mole of water had formed. This reaction, very surprisingly, gave a 65% yield of 2-butyloctanol-1 by the self-condensation of hexanol-1 and practically no mixed reaction. A repeat of this, except using decanol-1 in place of hexanol-1, verified the result.

While this at first glance may appear to be strange in light of the large amounts of high-boiling residue formed in the self-condensation of hexanol-1 with long reaction times, it is on closer examination not unexpected. In the first place, the high yields of the self-condensed products in the Guerbet reaction must be ascribable to their less reactive nature as contrasted with the starting normal primary alcohols. Furthermore, advanced condensations can be just as logically explained on the basis that the intermediate condensed aldehydes react with an additional molecule of aldehyde before being reduced, rather than the reduced product being dehydrogenated to the aldehyde which then reacts. Certainly, the results of the above two experiments establish the fact that the normal primary alcohols self-condense much more rapidly than the aliphatic β-branched alcohols will react in a mixed condensation under these conditions.

It is not possible with the existing information to say definitely why the β-branched alcohols are so inert. This inertness may be due to steric factors but the process is too involved to analyze completely.

As an alternative to an aliphatic β-branched alcohol, benzyl alcohol might be satisfactory for condensation with a normal primary alcohol. This type of a reaction has been performed in a classical Guerbet reaction but in not too high yields.[2,9] The same structural features are involved here, as with 2-ethylhexanol-1, in that the only condensations which can occur are the mixed condensation and the self-condensation of the normal primary alcohol. The benzyl alcohol may, however, show a greater tendency to give a mixed reaction product than 2-ethylhexanol-1.

A preliminary experiment using equivalent amounts of benzyl alcohol and hexanol-1 gave a 31% yield of the mixed product, 2-benzylhexanol-1 and a 35% yield of 2-butyloctanol-1 on the basis of the amounts of alcohols used. However, in another experiment which is given in Table VIII, the use of 0.67 mole of benzyl alcohol and 0.33 mole of hexanol-1 gave a 59% yield of 2-benzylhexanol-1 and only a 14% yield of 2-butyloctanol-1. Thus, it was possible in this reaction merely by varying the ratio of the two alcohols to obtain

Table VIII

The Condensation of Benzyl Alcohol with Primary Alcohols Containing a β-Methylene Group

Expt.	Primary alcohol	U.O.P. nickel, g.	Temp. range, °C	Reaction time, hrs.	Moles of Products			Mixed alcohol, Yld., %
					Mixed alcohol	Self-cond. alcohol	Benzoic acid	
C 4[a]	Butanol-1	4.0	143-187°	3.7	0.18	0.026	0.037	55
C 5[a]	Hexanol-1	2.0	177-207°	2.0	0.20	0.024	0.049	59
C 6	Heptanol-1	2.0	184-211°	1.4	0.19	0.040	0.045	58
C 7[b]	3-Phenylpropanol-1	0.0	225-241°	1.8	0.21	-	0.065	62

[a] The amount of water collected was 0.27 mole.

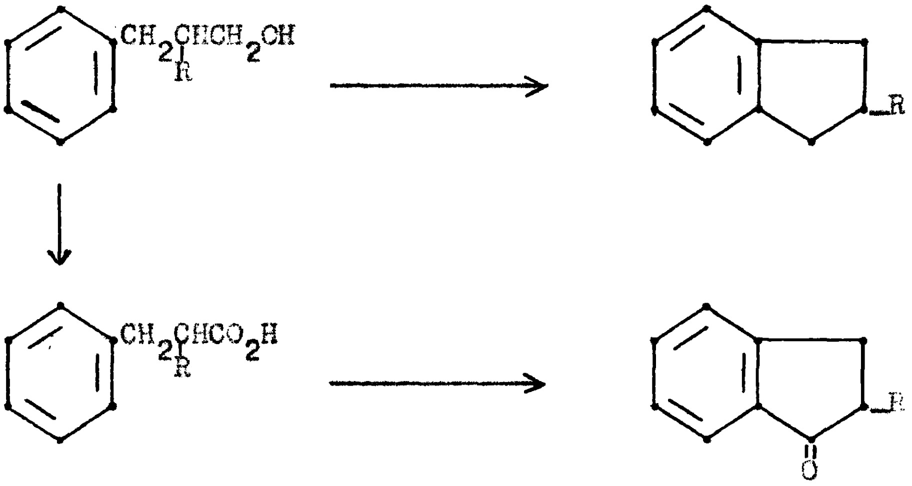
[b] The self-condensed alcohol was not isolated.

mainly the mixed condensation with little self-condensation.

The results of experiments in which benzyl alcohol was condensed with three additional primary alcohols containing a β-methylene group are given in Table VIII. In each of these reactions, 0.67 mole of benzyl alcohol, 0.33 mole of the primary alcohol and 0.175 mole of potassium metal were used and refluxing was maintained until 0.28 mole of water had been collected. It is seen that the reactions proceeded at reasonable rates to give the mixed products in good yields.

Since many valuable products may be obtained from this type of condensation, it is of some importance. For example, the products may be converted to the 2-alkylindanes or indanones by standard procedures:

(9)



There are, of course, many other possible uses for these compounds and by varying both the alkyl group and the substituents on the benzyl alcohol a variety of potentially valuable compounds may be made. It should be stressed in connection with application of the Guerbet reaction in synthesis, that it is probably not possible to use nitro compounds (or other easily reducible groups) because they readily react with alkali metal alkoxides to yield mixtures of reduction products.[34,35]

Indeed, this reduction of nitro compounds by alkoxides appears to merit further study.

It is significant to note here that all of the mixed condensations have been performed under conditions shown to be favorable to the self-condensation of normal primary alcohols. It may be possible by varying the alkoxide concentration, the amount of U.O.P. nickel or by the drop-wise addition of one of the reactants, that the mixed condensations could be still further improved. The yields obtained, however, are superior to those previously reported for the Guerbet reaction.[9] Alternate synthetic routes, such as the Perkin reaction followed by reduction, probably would not give better yields. The outstanding feature of this method is that it is a convenient one-step process to the products, while other methods involve two or more steps.

Another possible mixed condensation is that of benzyl alcohols or aliphatic β-branched primary alcohols with secondary alcohols. These represent, in some respects, an excellent choice since the primary alcohols of this type cannot self-condense and the secondary alcohols should preferentially give the mixed condensation products rather than the self-condensation products. One of the less desirable features of this system is that if the product formed is a straight chain alcohol, it will probably show a marked tendency to condense further. If the secondary alcohol is unsymmetrical and contains two methylene groups on which condensation can occur, then two products will probably be obtained. Such a mixture would be hard to separate and the usefulness of the process would decrease accordingly. The possibility of cis and trans isomers becomes an important consideration with cyclic secondary alcohols, such as cyclohexanol.

The reaction of benzyl alcohols with secondary alcohols was investigated. The secondary alcohols were used in excess to favor the mixed condensation but more importantly to decrease the opportunity of the products to undergo further condensations. It was assumed previous to carrying out the experiments that the self-condensation of the secondary alcohols was not important because of the unfavorable equilibria for the aldol condensations of the corresponding ketones. The presence of this type of a product was not detected.

A preliminary study was made with benzyl alcohol and cyclohexanol. In the first experiment, equivalent quantities of the reactants gave a 31% yield of the cis and trans 2-benzylcyclohexanols and considerable high-boiling residue. When the cyclohexanol was used in a 100% excess, the yield was 47% and the amount of residue was decreased by one-half. Finally, using the cyclohexanol in a 200% excess the yield was 61% and the residue was further decreased. This last experiment is included in Table IX as expt. C 12. These results indicate that a 200% excess of the secondary alcohol over the benzyl alcohol is desirable.

The results of using three different benzyl alcohols with certain secondary alcohols are given in Table IX. For these experiments 0.75 mole of the secondary alcohol, 0.25 mole of the benzyl alcohol, 0.175 mole of potassium and 2.0 g. of U.O.P. nickel were used.

It is seen that benzyl, p-methoxybenzyl and p-chlorobenzyl alcohols condense with cyclohexanol in a satisfactory manner. The products appear to be mixtures of the cis and trans isomers. This is, of course, an undesirable feature but oxidation of these stereoisomers converts them to a single valuable ketone. It was surprising to find that both the cis and the trans compounds were formed. The trans compound, which

Table IX

The Condensation of Benzyl Alcohols with Secondary Alcohols

Expt.	Benzyl alcohol	Secondary alcohol	Temp. range, °C	Reaction time, hrs.	Water, moles	Mixed product, moles	Yld.,[a] %
C 10	Benzyl	Heptanol-2	163-173°	4.5	0.15	0.061	24
C 11	Benzyl	4-Methylpentanol-2	143-152°	13.3	0.15	0.078	31
C 12	Benzyl	Cyclohexanol	172-186°	2.0	0.19	0.15	61
C 13	p-Methoxybenzyl	Cyclohexanol	177-187°	3.7	0.19	0.12	47
C 14	p-Chlorobenzyl	Cyclohexanol	175-182°	2.0	0.19	0.13	50

[a] The yield was calculated on the basis of the amount of the benzyl alcohol used.

is probably less hindered, should be favored, and the reaction was performed in an alkoxide solution under conditions which are commonly used to epimerize cis cyclic hydroxy compounds to the trans forms.[69]

The reactions of benzyl alcohol with heptanol-2 and 4-methylpentanol-2 did not give too satisfactory results. It is felt that these yields might be improved by a variation of the procedure such as a dropwise addition of the benzyl alcohol. Certainly it would be difficult to exceed these yields by using an alternate route such as the aldol condensation followed by reduction or the use of the Grignard reaction. The very desirable features of this process are the rapidity of the reaction, the easy isolation of the products and the availability of a wide range of these types of alcohols. It is a single step process, whereas, alternate procedures would probably involve two or more steps.

A primary alcohol containing a β-methylene group and a secondary alcohol is another possible reactant pair. This has the complicating factor that in addition to the self-condensation of the primary alcohol, considerable amounts of the product may condense. However, it seemed that by using the secondary alcohol in excess, both of these side reactions would be minimized. It is interesting to view the experimental results of this type of reaction.

In a reaction using equivalent quantities of octanol-1 and heptanol-2, only 17% of impure pentadecanol-6 was obtained along with a large amount of high-boiling residue. Furthermore, the use of the heptanol-2 in a 200% excess increased the yield of product to only 32% and the amount of residue did not decrease. Fortunately, practically no self-condensation of octanol-1 occurred even when the two alcohols were used in equivalent quantities. This shows that a primary alcohol has little tendency to self-condense if a secondary alcohol is available with which it can condense.

Octanol-1 was reacted with two additional secondary alcohols and the results are given in Table X. In the experiments, 0.25 mole of octanol-1, 0.75 mole of the secondary alcohol and 2 g. of U.O.P. nickel were used and 0.19 mole of water was collected.

Table X

The Condensation of Octanol-1 with Secondary Alcohols

Expt.	Secondary alcohol	Temp. range, °C	Reaction time, hrs.	Mixed product, moles	Yld.,[a] %
C 16	Heptanol-2	175-188°	4.5	0.079	32
C 17	Cyclohexanol	175-190°	2.5	0.15	61
C 18	4-Methylpentanol-2	151-165°	12.2	0.094	38

[a] The yield was calculated on the basis of the amount of octanol-1 used.

This type of mixed reaction was not too satisfactory. In the experiment with heptanol-2, the product contained some unsaturation and, in addition, probably a small amount of the isomer in which the octanol-1 had condensed on the methylene group of heptanol-2 rather than the methyl group. In the reaction between octanol-1 and cyclohexanol, the product was partially unsaturated and no doubt contained both the cis and trans isomers of 2-octylcyclohexanol. The reaction product from octanol-1 and 4-methylpentanol-2, in contrast to the above products, was completely saturated and boiled so sharply that it is doubtful if any octanol-1 condensed on the methylene group of the secondary alcohol. In all three cases a large amount of high-boiling residue was formed and this may be difficult to decrease by changing the conditions. These are the only instances of unsaturated compounds being formed in significant amounts, aside from the few cases of self-condensations of secondary alcohols.

The aliphatic β-branched primary alcohols were not tried with secondary alcohols. This is a more feasible reaction than that of the β-branched primary alcohols with normal primary alcohols and has been reported in a patent.[58] Still another possibility which was not tried is the mixed condensation of two normal primary alcohols. This is not believed to be of much value since four products would be formed and would, in most cases, be difficult to separate.[58]

Considerable effort was expended on the characterization of the products from the mixed Guerbet reactions. The products from the condensation of benzyl alcohol with primary alcohols having a β-methylene group were identified by their physical constants and the melting points of their allophanates which agreed with the literature values, except in one case. The exception was 2-benzylbutanol-1 but sufficient additional information was obtained to characterize it.

The results of quantitative carbon and hydrogen analyses for 2-benzylbutanol-1 and 2-benzylhexanol-1 agreed with the calculated values. The experimentally determined equivalent weight of 2-benzylbutanol-1 was 163, which agrees closely with the calculated value of 164. It appears that this information, along with the analogy to the products formed in the self-condensation of normal primary alcohols, adequately establishes these compounds as β-branched primary alcohols.

The products from the reactions of benzyl alcohols with cyclohexanol were more difficult to identify. This was due to the apparent formation of both cis and trans isomers in all three experiments. The situation with benzyl alcohol itself was somewhat more completely clarified than with the substituted benzyl alcohols. Elementary analyses for carbon and hydrogen of the mixture of cis and trans 2-benzylcyclohexanols gave exactly the calculated values. It was possible to separate only one of the isomers as a solid, although the mixture was solid. The melting point of this solid and of its 3,5-dinitrobenzoate agreed with the literature values.

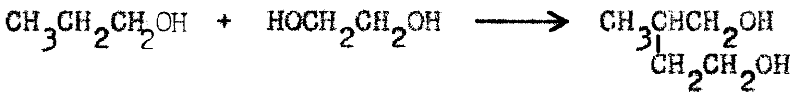
The liquid isomer or mixture yielded a 3,5-dinitrobenzoate having a different melting point and the melting point was markedly depressed when a mixture melting point determination with a sample of the 3,5-dinitrobenzoate of the solid alcohol was made. The liquid isomer or mixture was oxidized with chromic acid to form 2-benzylcyclohexanone and this ketone yielded a semicarbazone with the same melting point as that reported in the literature. The 3,5-dinitrobenzoate of the liquid isomer gave correct analytical results for carbon and hydrogen.

The 2-(p-methoxybenzyl)cyclohexanol and 2-(p-chlorobenzyl)cyclohexanol each yielded one pure solid isomer and a liquid which could not be crystallized. The solid isomers analyzed correctly for carbon and hydrogen as did their 3,5-dinitrobenzoates.

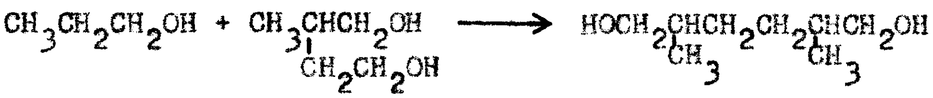
The products from the condensation of benzyl alcohol with heptanol-2 and with 4-methylpentanol-2, and the products from octanol-1 with secondary alcohols were identified in much the same manner as were the self-condensation products of normal primary alcohols. The details are given in the Experimental.

There are many other potential variations of the modified Guerbet reaction which were not investigated because of the lack of time. One of the more interesting possibilities is the substitution of an active methylene compound for one of the alcohols in a mixed condensation. Because of the large variety of active methylene compounds and of alcohols which are available, this may represent one of the most important uses of the Guerbet reaction.

Another potentially valuable class of reactants is the glycols. These compounds could possibly be used for self-condensations, for condensations with other alcohols or with active methylene compounds. Should their use be feasible, a wide range of bifunctional compounds would become conveniently available. To show this, consider a reaction with a normal primary alcohol, using propanol-1 and ethylene glycol as an example. Equations (10) and (11) represent one possibility.

(10)


$$CH_3CH_2CH_2OH + HOCH_2CH_2OH \longrightarrow CH_3\underset{\substack{| \\ CH_2CH_2OH}}{C}HCH_2OH$$

(11)


$$CH_3CH_2CH_2OH + CH_3\underset{\substack{| \\ CH_2CH_2OH}}{C}HCH_2OH \longrightarrow HOCH_2\underset{\substack{| \\ CH_3}}{C}HCH_2CH_2\underset{\substack{| \\ CH_3}}{C}HCH_2OH$$

This represents only one possible course of the reaction but it might well be the predominant one. This compound could be converted to all of the products for which alcohols are valuable precursors.

The use of aliphatic β-branched alcohols or benzyl alcohols to prepare ethers is worthy of consideration. This reaction was discussed in the Historical Introduction in connection with the Cannizzaro reaction.

Another variable is the type of metal alkoxide. Thus, by using aluminum alkoxides instead of alkali metal alkoxides, it might be possible to effect the Tischtschenko reaction to form the corresponding esters.

This discussion of possible Guerbet reaction variations has been given to show some of the broader aspects of the method. It is to be anticipated that the Guerbet reaction will become an important tool in the repertoire of the organic chemist.

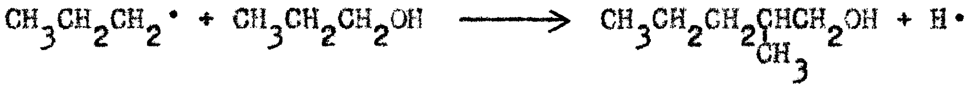
D. The Nature of the Reaction

The Guerbet reaction is a rather complex process which apparently involves several steps as described in the Historical Introduction. None of the previous workers have used a system sufficiently sensitive to show some of the more subtle features of the reaction. It is of importance to consider some of the courses by which the reaction could proceed.

It is conceivable that the Guerbet reaction is a free radical process. It has been observed, for example, that in most of these reactions an induction period occurs. This is oftentimes characteristic of a free radical process.[70] The fact that alkali metals have been used to make the alkoxides also suggests the possibility of a free radical reaction since it is difficult to prevent peroxide formation on the metal surfaces. One might expect that these would be reduced, however, by the hydrogen evolved as the metals react with the alcohols. The following might be written as a possibility for a free radical reaction:

$$(12)\quad CH_3CH_2CH_2OH \ + \ \text{peroxide} \longrightarrow CH_3CH_2CH_2\cdot$$

(13)



$$CH_3CH_2CH_2\cdot + CH_3CH_2CH_2OH \longrightarrow CH_3CH_2CH_2\underset{CH_3}{CH}CH_2OH + H\cdot$$

$$(14)\quad CH_3CH_2CH_2OH \ + \ H\cdot \longrightarrow CH_3CH_2CH_2\cdot \ + \ H_2O \quad .$$

A free radical reaction is merely one possibility out of several; there is little evidence for it and considerable evidence against it. One of the strongest points against this concept is that it predicts no difference in the reaction products with aliphatic β-branched alcohols as compared with normal primary alcohols. It should be expected that 2-ethylhexanol-1, for example, would give a condensation product with itself. Weizmann found, however, that 2-ethylhexanol-1 yielded only bis-(2-ethylhexyl)ether and 2-ethylhexanoic acid rather than a condensation product.[11] Tertiary alcohols do not give a Guerbet reaction, although a free radical process does not look unreasonable for them.[5] In the case of benzyl alcohol condensing with normal primary or secondary alcohols, one might expect considerable aromatic substitution by a free radical process. This has not been found and it is difficult to understand why the attack of a free radical would be almost exclusively on the carbon adjacent to the methylol group.

The process should not be particularly affected by the addition of a dehydrogenation catalyst if it is of the free radical type. The fact that an induction period is often observed is as satisfactorily interpreted on the basis that it is required for the production of sufficient aldehyde to promote the reaction, as it is on the basis of a free radical process. If the alcohol boils sufficiently high, as does decanol-1, no induction period is observed.

One might still suppose that the peroxides on the alkali metal could oxidize the alcohol to aldehyde to start the reaction, e.g.,

$$(15) \quad CH_3CH_2CH_2OH + Na_2O_2 \longrightarrow CH_3CH_2CHO + 2\ NaOH \quad .$$

As previously mentioned, the peroxides may not be capable of existing in the presence of hydrogen and, in addition, the alkoxides can be made from the hydroxides as satisfactorily as from the metals to perform the reaction. It should not be expected that the hydroxides would contain any peroxides. While these facts do not completely invalidate the concept of a free radical reaction, they do cast considerable doubt upon it.

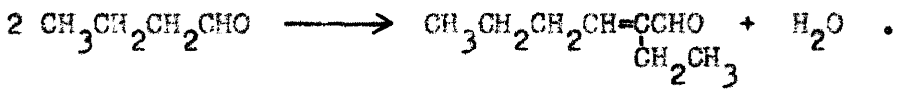
Guerbet not only did a good job of showing the scope of the reaction but he also identified some of the reaction products.[1-6] At the time he performed this work, however, the details of the courses of organic reactions were not understood as well as they are today. As a consequence, Guerbet indicates a reaction in which the alkali metal alkoxide can attack the alcohol at the β or the γ-position to give the condensed alcohol and alkali metal hydroxide. It is not believe that this is very likely in the light of later studies which have been made.

Weizmann and his co-workers have proposed a reaction course which is based primarily upon the amounts and types of products formed.[9] With butanol-1, for example, 2-ethylhexanol-1 and butanoic acid were formed in approximately equivalent amounts. To account for the formation of the β-branched alcohol it was assumed that thermolytic dehydrogenation first occurred,

$$(16) \quad 2\ CH_3CH_2CH_2CH_2OH \longrightarrow 2\ CH_3CH_2CH_2CHO + 2\ H_2\ ,$$

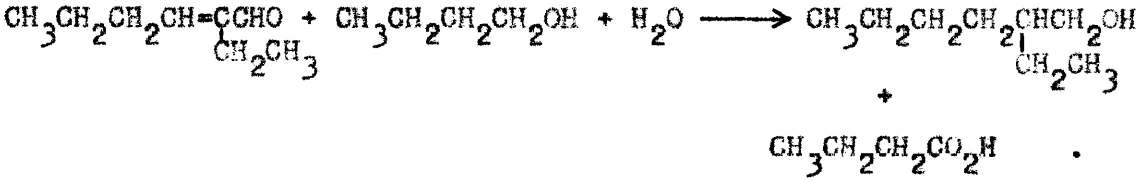
followed by an aldol condensation with water elimination,

(17)



$$2\ CH_3CH_2CH_2CHO \longrightarrow CH_3CH_2CH_2CH{=}\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}CHO + H_2O\ .$$

Hueckel and Naab, as mentioned in the Historical Introduction, first proposed these same reaction stages but they assumed that the molecular hydrogen as evolved by equation (16) was responsible for the reduction of the unsaturated aldehyde to the saturated alcohol.[12] According to Weizmann, however, this did not account for the acid production. He proposed the following reaction:

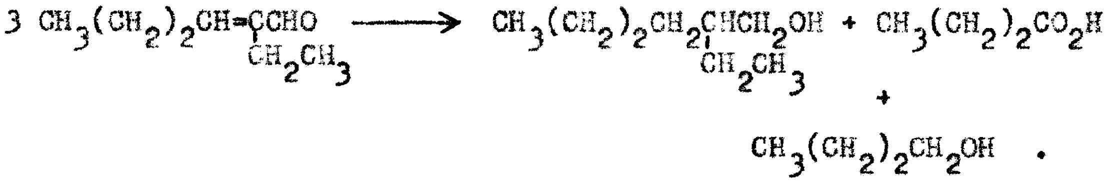
(18) 

$$CH_3CH_2CH_2CH{=}\underset{CH_2CH_3}{C}CHO + CH_3CH_2CH_2CH_2OH + H_2O \longrightarrow CH_3CH_2CH_2CH_2\underset{CH_2CH_3}{CH}CH_2OH + CH_3CH_2CH_2CO_2H \quad .$$

This accounted for the reduction of the aldehyde to the alcohol and explained the fact that acid was obtained in amounts equivalent to the condensed alcohol.

Weizmann's contention that a mole of acid must be formed for every mole of product alcohol is not borne out by the results of this thesis since, as reported above, very little acid need be formed. The amount of acid formed under the modified conditions has been found to be a function of the alkoxide concentration and to a lesser extent of the reaction temperature. This is very clearly illustrated in Table VI and the results are corroborated by another worker.[59] Weizmann has used mainly one alkoxide concentration, namely, 0.3 mole of sodium alkoxide to 0.7 mole of free alcohol. It is at about this concentration of alkoxide under the modified conditions that equivalent production of alcohol and acid occur, even if water is removed from the system. It follows that if equation (18) is valid, then an alternate explanation must be formulated to account for the appearance of condensed alcohol in excess of the amount of acid. It is felt that Weizmann's equation is without precedent and that the formation of acid can be explained as discussed below in terms of well-established reactions.

In a later article, Weizmann gives a different equation in place of equation (18).[11] This does not explain the reaction any better since the meaning of this new equation is very obscure. It is:

(19)


$$3\ CH_3(CH_2)_2CH{=}\underset{CH_2CH_3}{C}CHO \longrightarrow CH_3(CH_2)_2CH_2\underset{CH_2CH_3}{C}HCH_2OH + CH_3(CH_2)_2CO_2H + CH_3(CH_2)_2CH_2OH\ .$$

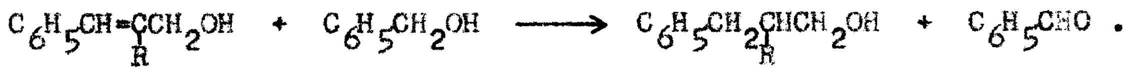
This equation as given is not balanced and in order to do so hydrogen and water must be added as reactants. In this same article it has been stated, in contradiction to equations (18) and (19), that the presence of copper bronze aids in the production of the condensed alcohol and represses the production of the undesirable acid. While the acid is undesirable since it wastes the starting alcohol, it is necessary if either of his equations is correct. The acid formation according to the modified Guerbet reaction, as reported in this thesis, is both undesirable and unnecessary. It will be seen that the acid formation can be adequately explained as a side reaction and not as a process indigenous to the Guerbet reaction.

Before proceeding to a discussion of the reaction course in the light of this work, it would be well to consider first some of the finer points of Mastagli's research, which was discussed partially in the Introduction.[13] It is of importance to the following statements to recall the main features here since certain of his basic concepts have been applied to explain the course of the Guerbet reaction.

His reagent was sodium or potassium hydroxide in benzyl alcohol and this was reacted with various aldehydes, ketones and β,γ-unsaturated alcohols. He showed that benzyl alcohol could undergo a hydrogen exchange with an aldehyde. If the added aldehyde contained only one or no α-hydrogens, then the only products obtained were the alcohols corresponding to the aldehydes and benzoic acid formed by a Cannizzaro reaction with benzaldehyde. When, however, the added aldehyde contained an α-methylene group it could self-condense as well as condense with benzaldehyde formed by a hydrogen exchange between the aldehyde and benzyl alcohol. The two α,β-unsaturated aldehydes formed could then be reduced by hydrogen exchanges with benzyl alcohol.

To demonstrate that the benzyl alcohol could reduce an α,β-unsaturated aldehyde, a series of compounds of the type, $C_6H_5CH{=}\underset{R}{C}CHO$, were prepared and treated with the reagent by Mastagli. The products were the corresponding saturated alcohols and twice the amount of benzoic acid (from benzaldehyde) was formed as would result from a single hydrogen exchange. The above results were obtained with the potassium hydroxide solution at 100° or 200° and with the sodium hydroxide solution at 200°. When the sodium hydroxide solution was used for the same compounds at 100°, the products were the corresponding β,γ-unsaturated alcohols and only half of the amount of benzoic acid as formed at 200° was obtained.

This information very clearly indicates that the exchange of hydrogen between the methylol and carbonyl groups occurs as in a typical Meerwein-Ponndorf-Verley reduction-Oppenauer oxidation system. It also shows that the benzyl alcohol reduces the ethylenic double bond of the aldehydes but Mastagli does not explain this other than to give the equation:

(20) 

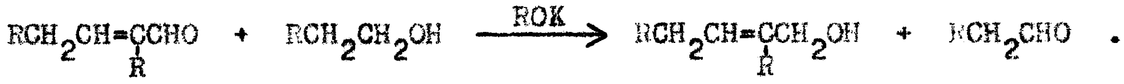
$$C_6H_5CH{=}\underset{R}{C}CH_2OH + C_6H_5CH_2OH \longrightarrow C_6H_5CH_2\underset{R}{C}HCH_2OH + C_6H_5CHO\ .$$

He did demonstrate, however, that the potassium hydroxide-benzyl alcohol reagent could reduce the double bond of the unsaturated alcohols with the corresponding production of benzoic acid.

To show that the intermediate α,β-unsaturated aldehydes could form in the reaction, he heated heptaldehyde with the reagent at the reflux temperature for 5 minutes. The dehydrated aldol product, 2-pentyl-2-nonenal, was obtained. With a 40 minute reflux period, he obtained 2-benzylheptanol-1, 2-pentylnonanol-1 and small amounts of the corresponding unsaturated alcohols. Thus, all of the proposed intermediates, except benzaldehyde, were not only isolated but these intermediates performed in the reaction as postulated. Mastagli further demonstrated that the aldehyde did not condense directly with the alcohol. When he treated benzaldehyde with potassium hydroxide in heptanol-1 at the reflux temperature for 5 minutes, the product was 2-benzalheptanal and not 2-benzalheptanol-1. There is at least one report in the literature which indicates that direct condensation of the aldehyde with the alcohol might occur.[71] This is a German patent and only meager details were available. For example, butanal was heated with butanol-1 and sodium butoxide at the reflux temperature. The product was 2-ethyl-2-hexenol-1 but this can be adequately explained by assuming a process such as Mastagli's resulting from the action of sodium hydroxide in benzyl alcohol at 100° on α,β-unsaturated aldehydes. It is also pertinent that under Mastagli's conditions the potassium hydroxide-benzyl alcohol reagent gave no reaction with heptanol-1.

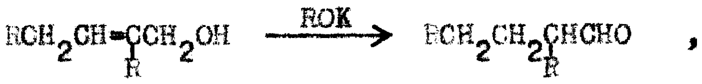
Mastagli then rejected Guerbet's idea that the alkoxide directly attacks the alcohol.[2] Indeed, he claims the Guerbet reaction is different on the basis that Guerbet proposed that with heptanol-1 the product was 3-butyldecanol-1 and not the 2-pentylnonanol-1 which he obtained. It cannot be agreed that Guerbet gave the correct structure for this product because in the modified Guerbet reaction, the use of heptanol-1 gave a product identical with that which Mastagli obtained. It is, therefore, concluded that the Guerbet reaction may involve the same reaction course that Mastagli gives, once sufficient aldehyde has been obtained by dehydrogenation. The following discussion gives the proposed reaction course for the Guerbet reaction and the evidence for it.

It is proposed that the primary process which must occur to start the Guerbet reaction is dehydrogenation of the alcohol to the aldehyde as given by equation (16). The aldehyde, so formed, may condense in the basic medium with water elimination to form the unsaturated aldehyde as given by equation (17). It is further proposed that this unsaturated aldehyde undergoes a three stage reduction, the starting alcohol being oxidized to aldehyde in two of these stages. First, the carbonyl group is reduced by a hydrogen exchange with the starting alcohol,

(21) 

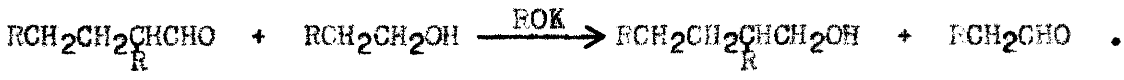
$$RCH_2CH{=}\underset{R}{C}CHO + RCH_2CH_2OH \xrightarrow{ROK} RCH_2CH{=}\underset{R}{C}CH_2OH + RCH_2CHO \; .$$

The unsaturated alcohol rearranges to the saturated aldehyde,

(22) 

$$RCH_2CH{=}\underset{R}{C}CH_2OH \xrightarrow{ROK} RCH_2CH_2\underset{R}{C}HCHO \; ,$$

which is then reduced by another hydrogen exchange with the starting alcohol,

(23) 

$$RCH_2CH_2\underset{R}{C}HCHO + RCH_2CH_2OH \xrightarrow{ROK} RCH_2CH_2\underset{R}{C}HCH_2OH + RCH_2CHO \; .$$

These equations, with equation (17), show that for every two molecules of aldehyde which are condensed and reduced, one molecule of water is formed and two more molecules of aldehyde are formed from the starting alcohol. This means that the reaction could be self-sustaining in aldehyde production, once some aldehyde had formed. This reaction course adequately explains the formation of the saturated condensed alcohol but it does not consider acid formation. Since it appears that the latter is an undesirable side reaction of the intermediate aldehyde, it will be treated separately.

In the Guerbet reaction, the same products are obtained with normal primary alcohols as would result if the corresponding aldehydes were aldolized, dehydrated and reduced. Furthermore, only those alcohols can be used for the reaction which can be dehydrogenated to carbonyl compounds and if it is a self-condensation reaction, the alcohol must contain a β-methyl or methylene group. In mixed condensations both of the alcohols must be convertible to carbonyl compounds but only one need contain a β-methyl or methylene group. Thus, β-branched primary alcohols cannot self-condense but they can react with normal primary alcohols or secondary alcohols. Tertiary alcohols cannot give a Guerbet condensation reaction under any conditions.[5] This evidence, together with the fact that water is eliminated and the facts that the reaction mixture contains base and that the reaction is markedly aided by dehydrogenation catalysts, is strong support for intermediate aldehyde formation and the aldol condensation. Since the reaction would then depend on the presence of aldehyde, this must be obtained by thermolytic or catalytic dehydrogenation at the beginning of the reaction. Once some aldehyde has formed, the reaction might be self-sustaining as indicated by equations (21), (22) and (23).

If this is the case, then the addition of a small quantity of aldehyde to an alcohol solution of alkoxide should give the reaction. This was verified by dissolving 0.175 mole of potassium in 1.0 mole of hexanol-1 and adding 0.10 mole of hexanal. The solution was heated at reflux for 12 hours, during which time 0.16 mole of water was collected. The temperature did not rise sufficiently (180° maximum) to give the standard Guerbet reaction without added U.O.P. nickel and hydrogen was not evolved. It was found that 0.12 mole of 2-butyl-octanol-1 had formed along with a considerable amount of high-boiling residue. A small amount of hexanoic acid was also isolated.

Since the product isolated was the saturated condensed alcohol and the amount of water formed was far in excess of the amount which would be obtained (0.05 mole) from the aldol condensation of the added aldehyde, then the process here must be of the same type as Mastagli's. The reaction had sufficient added aldehyde to promote a rapid reaction if the dehydrogenation catalyst has as its main function the initiation of reaction. Since most reactions with hexanol-1 were completed in three to four hours when catalyzed by U.O.P. nickel, the nickel must have at least the added function of continuing to supply aldehyde throughout the reaction. The dehydrogenation process, whether it be thermolytic or catalytic, can perhaps provide an optimum amount of aldehyde for the condensation reaction along with that aldehyde formed by hydrogen exchanges. These results also suggest, as does the demonstration that nickel catalyzes the reaction, that the formation of the first portion of the aldehyde is the highest energy step involved.

It might be proposed that the U.O.P. nickel not only aids dehydrogenation of the alcohol but that it serves the additional function of catalyzing the reduction of the α,β-unsaturated aldehyde. This may not be involved to any great extent since the same reaction can be performed without nickel if the solution of alkoxide in alcohol boils sufficiently high. As discussed previously, heptanol-1, octanol-1, nonanol-1 and decanol-1 gave as good or better yields without U.O.P. nickel as with it. In addition, it does not seem very likely that at the high temperatures used and in an open system that the hydrogen tending to be evolved by dehydrogenation could be responsible for any appreciable amounts of reduction.

The moles of water formed should equal the moles of condensed alcohol if the process involves only the formation of these substances. The major side reaction product is the acid. It was found that the moles of water plus the moles of acid were approximately equal to the moles of condensed alcohol. It is believed that these quantities should be equal since the acid formation will utilize an equivalent amount of water whether it involves the Cannizzaro reaction or the Dumas-Stas reaction,[72] which is,

$$(24) \quad RCH_2OH + KOH \longrightarrow RCO_2K + 2\,H_2 \quad .$$

The potassium hydroxide may be formed by hydrolysis of the potassium alkoxide. These data from Table VI are given in Table XI to show that there is an approximate equivalence.

Table XI

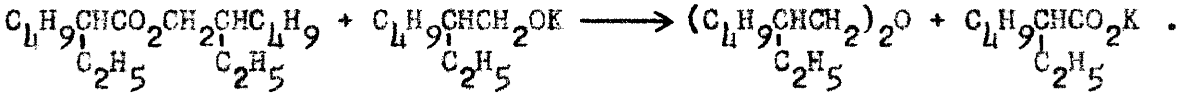
A Correlation of the Yields of Products for the Variation of n in $CH_3(CH_2)_nCH_2OH$

n	Product alcohol, moles	Water + Acid, moles
2	0.21	0.27
3	0.23	0.27
4	0.28	0.30
5	0.29	0.35
6	0.31	0.35
7	0.30	0.37
8	0.31	0.38

While this relationship is not exact, it is approximately correct. It is to be noted that in every case the moles of acid and water exceed the moles of condensed alcohol. High-boiling residues were always formed and their presence could easily account for the lack of equality since they are the products of advanced condensations, at least in part. In many cases better equivalences were obtained but these were selected as being fairly typical.

It was proposed that in the reduction of the β,γ-unsaturated alcohol, a rearrangement to the saturated aldehyde occurred (equation 22) which was, in turn, reduced to the saturated alcohol. In a typical Meerwein-Ponndorf-Verley reduction of α,β-unsaturated aldehydes or ketones, catalyzed with aluminum alkoxides, the carbon-carbon double bond is not reduced.[29] These reactions are performed at much lower temperatures than the Guerbet reaction and the aluminum alkoxides are of different nature than the alkali metal alkoxides. The aluminum alkoxides probably have more of an acid function than a base function.[73] It should be recalled that there is even a difference between the sodium and potassium hydroxides in benzyl alcohol in their ability to reduce the ethylenic double bond of α,β-unsaturated aldehydes at 100°.[13]

It is known that this rearrangement of unsaturated alcohols to saturated carbonyl compounds is catalyzed by Raney nickel.[43] In addition, it may not be unrelated to the migration of the double bond in olefins under the influence of catalysts.[74] To test this idea, 2-ethyl-2-hexenol-1 was prepared and treated with 2-ethylhexanol-1 and its potassium alkoxide at 150-160° for 7 hours. If the rearrangement occurred, it should be possible to isolate the saturated aldehyde or its reaction products. Under the conditions used, no dehydrogenation would be expected to occur and the most probable reaction available to 2-ethylhexanal would be the Tischtschenko reaction to form the corresponding ester. The ester might, in turn, react with the potassium alkoxide to form bis-(2-ethylhexyl)ether and 2-ethylhexanoic acid as discussed in the Introduction, and given by,

(25) 

$$C_4H_9\underset{\substack{|\\ C_2H_5}}{C}HCO_2CH_2\underset{\substack{|\\ C_2H_5}}{C}HC_4H_9 + C_4H_9\underset{\substack{|\\ C_2H_5}}{C}HCH_2OK \longrightarrow (C_4H_9\underset{\substack{|\\ C_2H_5}}{C}HCH_2)_2O + C_4H_9\underset{\substack{|\\ C_2H_5}}{C}HCO_2K \quad .$$

Although it was hoped that the saturated aldehyde might be isolated, none was detected. The acid, 2-ethylhexanoic acid, was isolated and identified by its boiling point, its neutralization equivalent and by the melting point of its amide. The bis-(2-ethylhexyl)ether was also isolated but insufficient amounts were obtained to allow purification for satisfactory carbon and hydrogen analyses. The proposed intermediate 2-ethylhexanal probably formed by rearrangement since the most reasonable way that 2-ethylhexanoic acid could form is by the reaction given in equation (25). In the hexanol-1 work, the saturated condensed aldehyde was isolated on one occasion and shown not to be 2-butyl-2-octenal but rather 2-butyloctanal. Thus, there are experimental evidence and analogies for this proposed rearrangement.

An alternate explanation would be that the carbon-carbon double bond is directly reduced by a Meerwein-Ponndorf-Verley reduction with the starting alcohol. There is little existing evidence which shows that the carbon-carbon double bond can participate in a reaction of this type. Should this be true, it would be an interesting extension of the carbon-oxygen redox system.

The route for the formation of 2-ethylhexanoic acid given above might be suggested as the route of acid formation in a typical Guerbet reaction. This would necessitate the occurrence of ether and ester or ester alone. Neither of these have been detected in any of the Guerbet reactions performed. The presence of ester was not detected, even in an experiment with high acid yield, when the products were carefully isolated to prevent ester hydrolysis.

There are two ways in which acid formation can be explained. One is the Cannizzaro reaction and the other is the Dumas-Stas reaction. The Cannizzaro reaction may seem to be an improbable route since aldehydes with an α-methylene group give predominantly the aldol condensation under typical Cannizzaro reaction conditions.[75] This does not mean, however, that this type of aldehyde cannot give a to allow purification for satisfactory carbon and hydrogen analyses. The proposed intermediate 2-ethylhexanal probably formed by rearrangement since the most reasonable way that 2-ethylhexanoic acid could form is by the reaction given in equation (25). In the hexanol-1 work, the saturated condensed aldehyde was isolated on one occasion and shown not to be 2-butyl-2-octenal but rather 2-butyloctanal. Thus, there are experimental evidence and analogies for this proposed rearrangement.

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Cannizzaro reaction, but rather that the aldol process is the preferred reaction. The results of the experiments reported in this thesis also indicate this, but show that acid formation becomes more important in alkoxide solutions with small amounts of water present as the alkoxide concentration is increased. The isolation of benzoic acid from the mixed reactions involving benzyl alcohol is interesting because the intermediate benzaldehyde can undergo a Cannizzaro reaction. The reaction discussed above, involving added aldehyde to promote the Guerbet reaction, yielded a small amount of acid without any hydrogen evolution.

There is some evidence that a Cannizzaro reaction can occur with aldehydes containing an α-methylene group but it is not conclusive at present.[16] A recent publication indirectly indicates a Cannizzaro reaction for this type of aldehyde.[76] This paper reported the treatment of 2-ethyl-2-hexenal with 50% aqueous sodium hydroxide solution in an autoclave at 200°. From the reaction mixture butanol-1, butanoic acid, 2-ethylhexanol-1, 2-ethyl-2-hexenoic acid and some high-boiling neutral materials were isolated. It is significant to note that the amount of butanoic acid increased as the amount of sodium hydroxide was increased. It has also been reported that with a less basic catalyst, such as an aluminum alkoxide, this type of aldehyde gives an excellent Tischtschenko reaction, which may be closely related to the Cannizzaro reaction.[27,28]

The alternate course, the Dumas-Stas reaction, (equation 24) might be responsible for acid production but it is not possible with the existing information to choose between the two processes. The Cannizzaro reaction requires two moles of aldehyde for each mole of acid formed and, hence, two moles of hydrogen from the dehydrogenation stage should be evolved in the Guerbet reaction. The Dumas-Stas reaction also produces two moles of hydrogen per mole of acid formed. In practically all experiments there has been obtained two moles of hydrogen per mole of acid. While this relationship is not exact, the ratio is always 2:1 or greater (see Tables V and VI).

The Dumas-Stas reaction was first reported in 1840.[72] Since that time some work has been done on the reaction but as yet no one has correlated the results sufficiently to evaluate the reaction course.[77,78,79] The process is generally performed under about the same conditions as the classical Guerbet reaction except that the alkali metal hydroxides are used instead of the alkali metals. An alcohol is treated with about an equal molar quantity of sodium or potassium hydroxide in an autoclave and heated to 300-400°.[78] It has been found that the addition of water prevents the Guerbet condensation and excellent yields of the acid are obtained.[78] It has also been observed that the addition of a mixture of cadmium and cadmium oxide permits the reaction to proceed about 75° lower than normally.[79] It appears that dehydrogenation of the alcohol to the aldehyde occurs in both the Guerbet reaction and the Dumas-Stas reaction. It is not possible to attribute the acid formation in the Guerbet reaction definitely to either a Cannizzaro or a Dumas-Stas reaction, but the Dumas-Stas may be merely a dehydrogenation plus a Cannizzaro. Once aldehyde has formed by dehydrogenation, it may undergo a Cannizzaro reaction to form acid and alcohol. The regenerated alcohol may then be dehydrogenated again and so on until all of the alcohol has been converted to acid. This is, however, merely a proposal but if it is correct, it would show the similar nature of the Guerbet reaction and the Dumas-Stas reaction in that both require aldehyde from the alcohol but then take alternate paths to their respective products.

III. EXPERIMENTAL*

A. Exploratory Experiments

1. Purification of the Reactants

The alcohols used in this work are commercially available except for p-chlorobenzyl alcohol. Purification was relatively easy and was accomplished by distillation at atmospheric pressure or under reduced pressure if the alcohol boiled above 200°.

Three different distillation apparatuses were used. One was a 12 in. Vigreaux column which was used for some of the distillations at atmospheric pressure and all of the distillations at reduced pressure. A 24 in. by 1 in. glass helices-packed, total reflux column and a 36 in. glass helices-packed Todd column[80] were also used. The Todd column was 25 mm. in diameter.

The p-chlorobenzyl alcohol was prepared by Mr. H. J. E. Segrave in this laboratory by the hydrolysis of the corresponding p-chlorobenzyl chloride.[81] This substance melted at 71-71.5° (lit.[81] m.p. 70.5-73°). The physical constants for the other alcohols are given in Table XII. In the experiments to follow, the properties of the starting alcohols are not given and if it was necessary to purify an alcohol on more than one occasion, the values obtained for the physical constants were as good or better than those recorded.

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*The author wishes to thank Professor Mary Aldridge and Mr. Byron Baer for the microanalyses reported in this thesis.

Table XII

Alcohol Purification

	Physical Constants			
	Observed		Literature[a]	
Alcohol	b.p.(mm.)	n_D^{25}	b.p.(mm.)	n_D(T)
Butanol-1[b]	116-117°	1.3950	116-117°	1.3974(25°)
Pentanol-1[d]	138-138.7°	1.4096	137.9°	1.4101(20°)
Hexanol-1[c]	156-157°	1.4160	157.2°	1.4162(25°)
Heptanol-1[c]	175-175.8°	1.4220	175°	1.4224(25°)
Octanol-1[d]	194.5-195°	1.4272	194-195°	1.4292(20°)
Nonanol-1[e]	-	1.4320	-	1.4311(20°)
Decanol-1[b]	115-116°(14)	1.4350	120°(12)	1.4368(20°)
3-Methylbutanol-1[c]	130-130.5°	1.4063	130°	1.4085(20°)
2-Ethylhexanol-1[b]	182.5-183°	1.4290	184-185°	1.4300(20°)
3-Phenylpropanol-1[b,f]	118-120°(12)	1.5245	119°(12)	1.5357(20°)
Heptanol-2[d]	159-160°	1.4188	158-160°	1.4190(25°)
Octanol-2[b]	178-179°	1.4225	179.5°	1.4240(25°)
4-Methylpentanol-2[b]	131-132°	1.4092	131-132°	1.4100(25°)
5-Ethylnonanol-2[b,g]	114-115°(14)	1.4382	225°	1.4362(30°)[82]
Cyclohexanol[c]	160°	1.4641	161°	1.4656(22.6°)
Benzyl alcohol[b]	94-95°(12)	1.5378	93°(10)	1.5396(20°)
p-Methoxybenzyl alcohol[b]	136-137°(12)	1.5441	127-130°(8)	1.5438(25°)

a. These values are from standard handbooks.
b. The 12 in. Vigreaux column was used.
c. The 24 in. glass helices-packed column was used.
d. The Todd column was used.
e. This compound was used as obtained from Halogen Chemicals, Inc.
f. The compound was obtained from The Matheson Co., Inc., and was used in spite of the refractive index being different from the lit. value.
g. This alcohol has been reported only as a commercial product of Carbide and Carbon Chemicals Company.

2. The Effect of Benzalaniline

A few typical experiments that were performed with benzalaniline are included here. These emphasize the difficulties involved in trying to evaluate the Guerbet reaction with benzalaniline.

Preparation of Benzalaniline. - This compound was prepared by the procedure given in "Organic Snytheses", using twice the quantities listed.[83] The product was obtained in 85% yield and melted at 51-52°.

Expt. A 1. - This experiment is essentially a repeat of Diels and Rhodius' reaction.[33] In a 500 ml., three-necked flask equipped with a reflux condenser was placed 350 ml. (3.2 moles) of 3-methylbutanol-1. To this alcohol 36 g. (1.5 moles) of clean sodium was added portionwise and the solution containing unreacted sodium was heated at reflux by means of a "Glas-Col" mantle until all of the sodium had reacted. To the resulting solution, 18 g. (0.10 mole) of benzalaniline was added and the deep yellow solution was refluxed for 42 hrs. At the end of this time the solution, which was clear and colorless, was poured onto ice. The water layer was removed and the organic layer was washed once with water, dried over "Drierite" and distilled. After the 3-methylbutanol-1 was removed, a fraction was obtained which distilled at 110° to 145° (2 mm.). This fraction was treated with 10% hydrochloric acid and the solid which formed was filtered off and washed with ether to give 15 g. (69%) of benzylaniline hydrochloride which melted from 198° to 205° (lit. m.p. 215-216°).

The combined water layers from this experiment were acidified with concentrated hydrochloric acid and extracted three times with 125 ml. portions of ether. The ether extracts were combined and distilled through a 6 in. Vigreaux column to give 10 g. of

3-methylbutanoic acid; b.p. 174-177°.

Expt. A 2. - A one l., three-necked flask equipped with a reflux condenser was used for this experiment. Into it were placed 800 ml. (6.4 moles) of hexanol-1 and 55 g. (2.4 moles) of clean sodium and the solution was heated at reflux for 12 hrs. to react all of the sodium. This solution was clear and colorless when 24 g. (0.133 mole) of benzalaniline was added. The resulting solution was deep yellow and a small amount of a solid was present but after 58 hrs. of heating at reflux, the solution was clear and only a faint yellow. The mixture was cooled and poured into water and after removing the water layer, the alcoholic layer was washed once with water, dried and distilled. Distillation afforded 75 g. (13%) of crude 2-butyloctanol-1 which boiled from 100° to 111° (2.5 mm.) and 10 g. (44%) of benzylaniline which boiled at 140° to 150° (2.5 mm.). The 2-butyloctanol-1 was redistilled through an 8 in. Vigreaux column and collected in twenty-two approximately equal small fractions. The middle fifteen fractions (54.5 g.) distilled at 104-105° (2.5 mm.) and the refractive indices at 27° varied from 1.4458 to 1.4475 (lit.[13] b.p. 132° (15 mm.), n_D^{16} 1.4435) This compound prepared by the use of a dehydrogenation catalyst distilled at 108-110° (2.5 mm.) and had a refractive index at 25° of 1.4400. It appears that the benzylaniline forms a minimum boiling azeotrope with the 2-butyloctanol-1. This probably contains only a small percentage of the amine ($n_D^{24.8}$ 1.6118).

Acidification of the water layer followed by extraction with benzene and distillation of the extracts yielded 53 g. of hexanoic acid; b.p. 200-203°.

Expt. A 3. - To 200 ml. (1.6 moles) of hexanol-1 in a 500 ml., three-necked flask equipped with a reflux condenser was added 11.5 g. (0.50 mole) of clean sodium and the solution was heated at reflux until all of the sodium had reacted. There was then added 22.5 g. (0.125 mole) of benzalaniline and the solution was heated at reflux for 10 hrs. more. The mixture was cooled, poured into water and the organic layer was washed once more with water and dried. The bulk of the hexanol-1 was removed by distillation and the residual liquid was dissolved in 150 ml. of benzene and exhaustively extracted with 25 ml. portions of 30% sulfuric acid. It was necessary to use thirty-five extractions before the acid layer failed to become cloudy upon making it basic. The benzene layer was distilled to give 18 g. (12%) of 2-butyloctanol-1, which boiled at 104-105° (2.0 mm.); n_D^{25} 1.4450.

The combined acid layers were made basic with sodium hydroxide, extracted with benzene and the extracts distilled to give 14 g. (0.077 mole, 61%) of benzylaniline which boiled at 140° to 145° (2.5 mm.).

The water layer containing the sodium salt of the acid was acidified, extracted with benzene and the extracts distilled to give 10 g. of hexanoic acid; b.p. 201-205°.

Expt. A 4. - In the apparatus used in the preceding experiment, there were placed 200 ml. (1.6 moles) of hexanol-1 and 11.5 g. (0.50 mole) of clean sodium. Benzalaniline (45 g., 0.25 mole) was added after all of the sodium had reacted. This caused considerable precipitation and 100 ml. (0.80 mole) of hexanol-1 was added in an unsuccessful attempt to effect solution. The reaction remained heterogeneous throughout the 20 hrs. at reflux. The mixture was cooled, poured into water and after the water layer was removed, the alcoholic layer was washed once with water, dried and distilled. The hexanol-1 was removed and the material boiling between 105° and 190° (20 mm.) was collected. This was dissolved in 400 ml. of anhydrous ether and dry hydrogen chloride was introduced to precipitate the amine hydrochloride. After filtration the ether was removed from the filtrate and the residue distilled to give 22 g. of very impure 2-butyloctanol-1; b.p. 104-105° (2.5 mm.), n_D^{25} 1.4502. Further distillation did not alter the refractive index, which suggests that some 1-chloro-2-butyloctane may have formed by reaction with the hydrogen chloride.

It should be mentioned that the 2-butyloctanol-1 could not be purified by steam distillation from aqueous acid in a satisfactory manner since the substance is relatively non-volative with steam.

These experiments showed that evaluation of the reaction using benzalaniline was difficult. The use of dehydrogenation catalysts was, therefore, tried and they proved to be of great help.

3. General Procedure

The following procedure was used throughout the rest of the work unless otherwise specified.

The reactant alcohol was placed in a 500 ml., three-necked flask equipped with a half-moon paddle stirrer, a glass stopper and a 5 ml., asbestos-wrapped Dean-Stark water trap surmounted by a condenser. The stirrer was supported through a rubber sealed, glass sleeve and driven by a "Barber-Coleman" motor. The system was swept with nitrogen for several minutes before adding the alkali metal. The metals were cut and weighed under petroleum ether and dried with filter paper before weighing, and again before adding them in portions to the alcohol with slow stirring.

In experiments with potassium, failure to stir or sweep the flask with nitrogen resulted in explosions on several occasions which were violent enough to blow the solid glass stopper several feet. With the above procedure no explosions resulted at any time in using potassium. After all of the alkali metal had reacted, the dehydrogenation catalyst was added and the stopper replaced by a 360° thermometer supported by rubber through a glass sleeve. The flask was heated with a "Glas-Col" mantle and maximum voltage (110) was applied to the stirrer motor. A rubber tube was attached to the top of the condenser after refluxing began and connected with a dry ice-acetone trap which, in turn, was connected to an inverted 4 liter graduated cylinder. The gas evolved during the reaction was collected over water and maintained at atmospheric pressure by means of a water overflow system whose level was adjusted to that in the graduated cylinder. The volumes of hydrogen trapped were corrected for the vapor pressure of water and converted to moles by the ideal gas equation. The gas was not collected in the exploratory work or in some of the experiments in which the alkoxide concentration was varied. It was collected and its volume recorded in all other work.

Except for the Raney nickel experiments, the amount of material collected in the dry ice-acetone trap was insignificant except for its effect on the volume of gas. Because of this, the trap was routinely used to give more accurate hydrogen volumes.

The solutions were maintained at rapid reflux, for the most part, by applying a standard 90 v. to the mantle. It was necessary in some cases to use less heat in order that the vapors would not go beyond the condenser tip because stronger heating gave poor water separation. This situation occurred with butanol-1 and pentanol-1 in the self-condensation work, and in some of the mixed condensations. The reactions in which it was necessary to maintain the minima refluxing rates so that the water could be removed, are indicated in the individual experiments.

Prior to the initiation of the reaction, as indicated by water distillation, the hydrogen would slowly start to evolve. The volume of hydrogen, the solution temperature and the volume of water were noted at intervals throughout the reaction. The volume of water was used to indicate the proper time to stop the reaction. With alcohol self-condensations this was at about 4.5 ml. (50%) for 1.0 mole of the alcohol. In the mixed condensations the reactions could be continued until a 60% to 80% yield of water was obtained.

The mixture was cooled below 100°, and 100 ml. to 150 ml. of water was added through the condenser. The resulting two layers were filtered with suction through a Buechner funnel to remove the dehydrogenation catalyst and the catalyst was washed with 50 ml. to 100 ml. of ether. The water layer was removed and the alcoholic layer was washed once with a small volume of 10% sodium hydroxide and once more with water. The aqueous layers were combined and extracted twice with 25 ml. to 50 ml. portions of ether, and these extracts were added to the organic layer which was then dried over anhydrous sodium sulfate or magnesium sulfate and distilled.

Distillation was effected through an 8 in. Vigreaux column and an oil bath was used for heating in all cases. The ether was removed by means of a water aspirator allowing the pressure to drop as concentration occurred. The residual liquid was then distilled at reduced pressures. In most cases, a single distillation through the Vigreaux column gave products which were analytically pure. In instances where distillation ranges were observed, further purification was effected, usually by distillation through the Todd column.

The combined water layers were acidified with 1:1 hydrochloric acid and extracted twice with 50 ml. portions of benzene. The benzene extracts were distilled at atmospheric pressure through a 6 in. Vigreaux column to recover the acid formed in the reaction.

The boiling points given in this thesis are not corrected but all melting points are corrected. The literature values for physical constants are from standard handbooks unless otherwise indicated.

4. The Effect of Dehydrogenation Catalysts

This section includes the experiments performed in the exploratory work with Raney nickel, U.O.P. nickel and copper chromite. The general procedure was used except where indicated and the gas was not collected.

<u>Expt. A 5</u>. - Raney nickel prepared by a standard procedure was the first dehydrogenation catalyst tried.[45] In the standard flask equipped only with a condenser and a thermometer, there were placed 200 ml. (1.6 moles) of hexanol-1 and 11.5 g. (0.50 mole) of clean sodium. To the resulting solution 5 g. of Raney nickel was added. Since there was considerable solid present, 100 ml. (0.80 mole) of hexanol-1 was added to effect complete solution. The solution temperature was 156° throughout a 20 hr. reflux period. It was observed that water had condensed on the upper portion of the flask

during the reaction and that the catalyst tended to settle against the sides of the flask.

Upon purifying the reaction mixture there were obtained 37 g. of recovered hexanol-1 and 68 g. (30%) of 2-butyloctanol-1 distilling at 106-108° (2 mm.); n_D^{25} 1.4410. There were also 29 g. of a high-boiling residue and 32 g. of hexanoic acid which distilled at 200° to 208°; n_D^{25} 1.4140 (lit. b.p. 205°, n_D^{20} 1.4145).

Expt. A 6. - Since it was observed in the above experiment that water had formed, this reaction was performed with a Dean-Stark water trap in the system. A stirrer was used to prevent the catalyst from settling on the sides of the flask. There were utilized in this reaction 153 g. (1.5 moles) of hexanol-1, 7.0 g. (0.30 mole) of sodium and 7 g. of Raney nickel. The temperature rose from 165° to 240° and 2.1 ml. of water was collected. Isolation of the products yielded 9 g. of recovered hexanol-1, and 40 g. (29%) of 2-butyloctanol-1 which distilled at 108-111° (3 mm.); n_D^{25} 1.4408. There were also obtained 33 g. of distillation residue and 18 g. of hexanoic acid distilling at 200° to 210°.

Expt. A 7. - In a repeat of experiment A 6 but using only 2 g. of Raney nickel for a 20 hr. reflux period, 5.0 ml. of water was collected and the temperature varied from 172° to 243°.

There were obtained from this reaction 10 g. of recovered hexanol-1 and 59 g. (42%) of 2-butyloctanol-1 which distilled at 108-111° (3.0 mm.); n_D^{25} 1.4410. There remained from the distillation 42 g. of residue and the water layer yielded 22 g. of hexanoic acid distilling at 200-210°.

The dry ice-acetone trap was used in this experiment and 6 g. of a material condensed; b.p. 35-37°, n_D^{25} 1.3601. This may be pentane which boils at 35-36° and has a refractive index at 20° of 1.3570. The material obtained here contained very little unsaturation as indicated by the bromine in carbon tetrachloride test. This product could have formed by decarbonylation of the intermediate hexaldehyde,[43] or by decarboxylation of the sodium salt of the acid. This material was not further investigated since it was formed in appreciable amounts only with the Raney nickel experiments. The maximum amount obtained in the U.O.P. nickel experiments was 2 g. from 1.0 mole of alcohol and this was at a very high alkoxide concentration.

It would have been desirable to use accurately reproducible amounts of Raney nickel in each experiment to evaluate the reaction variables. In the three experiments above, the catalyst was weighed by removing a portion from a tared bottle containing the catalyst under hexanol-1. It is obvious that the weights given are inaccurate since all of the hexanol-1 could not be drained from the catalyst. To obtain an accurate weight of the catalyst, 6.25 g. of the nickel-aluminum alloy (56.69% nickel, determined gravimetrically by the dimethylglyoxime procedure) was used to make the catalyst for three duplicate experiments. At the time it was considered that this would give 3.54 g. of the catalyst if all of the aluminum reacted with the sodium hydroxide. A recent article reports that Raney nickel prepared in this way is only 77% nickel and 21% aluminum oxide.[50] This is not significant, however, since a reproducible weight of catalyst was probably obtained.

These three experiments are included in Table XIII. For these reactions, 153 g. (1.5 moles) of hexanol-1 and 7.0 g. (0.30 mole) of sodium were used together with the catalyst prepared from 6.25 g. of the alloy. After the catalyst was prepared the final ethanol wash was decanted and the nickel was washed twice more by decantation with 10 ml. portions of hexanol-1.

Table XIII

Typical Experiments using Raney Nickel[a]

Expt.	Temp. range, °C	Moles of Products Water	 Alcohol	 Acid	Residue, g.	Hexanol-1 recovered, g.
A 8	160-179°	0.16	0.26	0.13	30	46
A 9	160-203°	0.28	0.30	0.16	35	21
A 10	158-185°	0.23	0.30	0.14	32	37

[a] A 5.2 hr. refluxing period was used in each experiment after the nickel was added.

The lower yield of alcohol in expt. A 8 is probably due to a difference in the preparation of the catalyst. In this experiment the temperature was not held strictly within the prescribed limits of 50 ± 2° during the preparation.

It is seen that Raney nickel fails to give a reproducible reaction. In place of this material U.O.P. nickel was used.[48] A total of 1150 g. of U.O.P. nickel powder was prepared by crushing the pellets with a mortar and pestle until it all passed a 100 mesh sieve.

The results of four experiments with 153 g. (1.5 moles) of hexanol-1, 7.0 g. (0.30 mole) of sodium and 2.5 g. of U.O.P. nickel are given in Table I of the Discussion. Additional information is given in the Supplement to Table I.

Supplement to Table I

Expt.	Reaction time, hrs.	Induct. temp., °C	Hexanol-1 recovered, g.	Distillation residue, g.
A 11	5.0	169-166°	15	34
A 12	5.0	170-166°	11	37
A 13	6.0	169-165°	17	33
A 14	7.0	170-166°	32	31

Expt. A 15. - It was of interest to see if copper chromite would aid the reaction. To the standard flask containing 153 g. (1.5 moles) of hexanol-1 which had reacted with 7.0 g. (0.30 mole) of sodium, there was added 2.5 g. of copper chromite catalyst.[49] The mixture soon turned red-brown and as the reaction proceeded it became quite viscous. A total reflux period of 3.5 hrs. was used, during which time the temperature rose from 165° to 194° and 2.0 ml. of water was collected. Separation of the products by the standard procedure afforded 29 g. of recovered hexanol-1, 57 g. (41%) of 2-butyloctanol-1 (n_D^{25} 1.4411), 21 g. of distillation residue and 31 g. of hexanoic acid which distilled at 200-210°.

Expt. A 16. - To determine any catalytic effect of "Filter-Cel", the standard apparatus was used with 153 g. (1.5 moles) of hexanol-1, 7.0 g. (0.30 mole) of sodium and 2.5 g. of "Filter-Cel". The mixture was heated at reflux for 5.0 hrs. with stirring, during which time the temperature remained constant at 170° and no water was evolved.

After pouring the reaction mixture into water, filtering and separating the layers, acidification of the water layer gave only a faint cloudiness. The alcohol layer was not distilled since no reaction apparently occurred.

5. Other Exploratory Experiments

The fact that water had been removed from alkoxide solutions by distillation in many of the above experiments was very interesting. To ascertain if alkali metal alkoxides could be made by treating an alcohol with alkali metal hydroxides and removing the water by distillation, three experiments were performed with hexanol-1 and sodium hydroxide. The results of these experiments are given in Table II of the Discussion and further details are recorded here.

Expt. A 17. - In a 500 ml., three-necked flask were placed 4.3 g. (0.11 mole) of C.P. sodium hydroxide and 250 ml. of dry benzene. The flask was fitted with a thermometer and a 14 in. glass helices-packed column surmounted by a 5 ml. water trap and a condenser. The system was protected from atmospheric moisture by a calcium chloride tube. The reaction mixture was heated at reflux to remove any water and then 93 g. (0.91 mole) of hexanol-1 was added. After 5.0 hrs. at reflux, 1.55 ml. (80%) of the water had distilled and 48 hrs. were required to obtain 2.02 ml. (104%). The temperature remained constant at 88°.

Expt. A 18. - For this reaction 153 g. (1.5 moles) of hexanol-1 and 12.0 g. (0.30 mole) of sodium hydroxide were heated at reflux in a 500 ml., three-necked flask equipped with a thermometer and a 5 ml. water trap surmounted by a condenser and a calcium chloride tube.

After 24 hrs., the solution temperature was 169° and 4.40 ml. (81%) of water had collected. Since the water had stopped distilling, a 9 in. column packed with porcelain saddles was placed in the system. Water began to distil immediately upon heating the solution to refluxing and after 24 additional hrs. 5.10 ml. (95%) of the water had been removed. The final solution temperature was 178°.

<u>Expt. A 19</u>. - The standard equipment was used in this experiment, except that a one l., three-necked flask was used with a 20.0 ml. water trap having a stopcock at the bottom. A 9 in. column packed with porcelain saddles was inserted in the system. In the flask there were placed 460 g. (4.5 moles) of hexanol-1 and 60 g. (1.5 moles) of sodium hydroxide. Ten hrs. of refluxing yielded 23.7 ml. (88%) of water and the solution temperature was 176°. To this solution was added 7 g. of Raney nickel and the mixture was heated at reflux for 4 hrs. The final solution temperature was 225° and 7.6 ml. of water collected.

From the reaction mixture there were obtained 61 g. of recovered hexanol-1 and 150 g. (35%) of 2-butyloctanol-1 (n_I^{25} 1.4408) leaving 21 g. of residue. The water layer yielded 80 g. of hexanoic acid distilling from 200° to 210° and 75 g. of acid residue.

The effect of water removal under the modified conditions was studied by comparing two reactions in which the water was not removed to one in which it was removed.

<u>Expt. A 20</u>. - This experiment has been used for showing the effect of removing the water, the effect of varying the type of alkoxide and the effect of varying the time. In the standard apparatus was placed 153 g. (1.5 moles) of hexanol-1 and 11.7 g.

(0.30 mole) of potassium was added in the prescribed manner. When all of the potassium had reacted, 2.5 g. of U.O.P. nickel was added and the solution was heated to refluxing. The reaction did not start until after 50 min. of refluxing and the temperature dropped during this period from 178° to 176°. The solution was heated for 3.5 hrs. after the water began to distil and the temperature reached 227° as 6.4 ml. of water collected. This reaction afforded 11 g. of recovered hexanol-1, and 74 g. (53%) of 2-butyloctanol-1; n_D^{25} 1.4410. There was 32 g. of distillation residue and the water layer gave 16 g. of hexanoic acid which distilled at 200-210°.

Expt. A 21. - With the same conditions as for expt. A 20 except that a water trap was not used, the solution was heated at reflux for 4.3 hrs. The temperature remained constant at 176 ± 1° after water began to appear in the condenser. There were obtained 86 g. of recovered hexanol-1, 44 g. (31%) of 2-butyloctanol-1 (n_D^{25} 1.4412), 10.0 g. of distillation residue and 7 g. of hexanoic acid, which distilled at 200° to 210°.

Expt. A 22. - This experiment is a repeat of expt. A 21 except that a 7.0 hr. reflux period was used. Water appeared in the condenser after 1.0 hr. at reflux and the temperature remained constant at 176 ± 1° after this time. This reaction yielded 68 g. of recovered hexanol-1, 44 g. (31%) of 2-butyloctanol-1 (n_D^{25} 1.4410) and 11 g. of residue. The hexanoic acid distilled at 200° to 210° (7 g.).

In an attempt to moderate the reaction temperature, and to determine the effect of a solvent on the reaction, two experiments were performed. Since benzene has been used as a solvent for Oppenauer oxidations with potassium tertiary butoxide, it seemed likely that p-cymene could serve as a solvent to give a sufficiently high temperature to permit the Guerbet reaction to proceed.[31]

Expt. A 23. - One-half l. of p-cymene, purified by distillation, was placed in a one l., three-necked flask with the standard apparatus attached except that a 10 ml. water trap was used. To the p-cymene were added 102 g. (1.0 mole) of hexanol-1 and 4.6 g. (0.20 mole) of sodium. The mixture was heated at reflux and vigorously stirred until all sodium had reacted and then 2 g. of Raney nickel was added. A reaction period of 20 hrs. was used and 2.9 ml. of water was collected as the solution temperature varied from 167° to 178°.

It was not possible to obtain a satisfactory separation of hexanol-1 and p-cymene but the 2-butyloctanol-1 (41 g., 43%) distilled at 108-111° (3 mm.) and there was 14 g. of residue. The hexanoic acid boiled at 200° to 210° (15 g.)

Expt. A 24. - The same apparatus was used as in expt. A 23 except that a 9 in. column packed with porcelain saddles was placed in the system. There were placed in the flask 600 ml. of p-cymene, 153 g. (1.5 moles) of hexanol-1 and 8.4 g. (0.21 mole) of sodium hydroxide. The mixture was heated at reflux for 24 hrs. during which time 2.8 ml. (88%) of the water was collected. To this solution, 2 g. of Raney nickel was added and the reaction was continued for 20 hrs. The temperature varied from 166° to 176° and 7.5 ml. of water collected. Again the hexanol-1 could not be recovered from the p-cymene and the 2-butyloctanol-1 was distilled to yield 56 g. (40%); n_D^{25} 1.4410. There was 22 g. of residue and the water layer afforded 10 g. of hexanoic acid which distilled at 200° to 210°.

In an attempt to evaluate the relative effectiveness of potassium hexoxide and sodium hexoxide, three experiments were performed and the results compared. One of the experiments using potassium hexoxide was A 20, given above, and the others are given below as A 25 and A 26.

Expt. A 25. - This experiment is a repeat of expt. A 20 except that a reaction time of only 2.2 hrs. was used after water started to distil. The temperature dropped from 179° to 176° during a 45 min. induction period. Six ml. of water collected during the reaction and the temperature increased to 206°. This experiment gave 28 g. of recovered hexanol-1, 74 g. (53%) of 2-butyloctanol-1 (n_D^{25} 1.4402) and 20 g. of high-boiling residue. There was also obtained 16 g. of hexanoic acid which boiled at 200° to 209°.

Expt. A 26. - In this reaction the same apparatus and quantities of reactants were used as in expts. A 20 and A 25 except that sodium was used in place of the potassium. The reaction had a 1.5 hr. induction period during which time the temperature dropped from 169° to 166°. A 3.5 hr. refluxing period was used after the water began to distil to obtain 5.5 ml. of water and the final solution temperature was 208°. From the distillation, 15 g. of hexanol-1 was recovered followed by 73 g. (52%) of the 2-butyloctanol-1 (n_D^{25} 1.4410) leaving 34 g. of residue. The water layer yielded 15 g. of hexanoic acid distilling from 200° to 207°.

On the basis of the foregoing results, it was decided to use potassium metal because of the time which could be saved and to remove the water as fast as possible from the reaction mixture. The standard apparatus and procedure were used for all of the subsequent experiments except where indicated.

B. The Determination of Optimum Conditions

1. The Effect of Varying the Alkoxide Concentration

This variable was studied by altering the amount of potassium from zero to 0.325 mole with 1.0 mole of hexanol-1 and using 2.0 g. of U.O.P. nickel as a catalyst. A 2.0 hr. reflux period was used after water started to distil. The hydrogen evolved was not collected for all of the reactions included in this section but it was in all of the subsequent reactions. The results of these experiments are included in Table III of the Discussion. Additional information is given in the Supplement to Table III. The moles of product alcohol are re-tabulated with the moles of acid plus the moles of water to show their correspondence.

The reaction products were isolated in the standard fashion. The 2-butyloctanol-1 distilled within the range 108-111° (3 mm.) and the hexanoic acid in the range from 200° to 210°. No fractions intermediate to the reactant alcohol and the product alcohol fractions were observed in the work given in this thesis except where indicated.

Experiment B 9 was stopped as soon as water began to appear in the trap. The gas evolved was analyzed at three different times during the reaction. When one l. of gas had been collected, a 19.2 ml. portion was transferred to an explosion pipet directly from the reaction mixture. Then 73.4 ml. of oxygen was admitted and after standing 10 min. the mixture was exploded and a contraction in volume of 28.6 ml. observed. Since each volume of oxygen reacts with two volumes of hydrogen, the volume of hydrogen must be two-thirds of the decrease in volume. The

Supplement to Table III

Expt.	Potassium, moles	Induct. temp., °C	Hydrogen,[a] moles	Hexanol-1 recovered, moles	Alcohol residue, g.	Product alcohol, moles	Acid + Water, moles
B 1	0.00	158°	0.00	0.97	2	0.00	0.00
B 2	0.100	165-163°	-	0.71	5	0.097	0.061
B 3	0.150	170-169°	-	0.55	6	0.17	0.17
B 4	0.175	174-173°	-	0.44	8	0.19	0.21
B 5	0.200	179-177°	-	0.19	7	0.26	0.30
B 6	0.225	184-180°	-	0.10	17	0.26	0.33
B 7	0.250	188-184°	0.50	0.073	15	0.21	0.31
B 8	0.275	192-187°	0.53	0.049	16	0.21	0.30
B 9	0.325	199-194°	0.33	0.42	2	0.16	0.16

[a] The hydrogen was not collected in expts. B 2 through B 6.

percentage hydrogen then must be,

$$\% H_2 = \frac{2 \times 28.6}{3 \times 19.2} = 99.5$$

In a similar manner a sample of the gas taken at 3.5 liters and 8.3 liters of evolution was analyzed. The respective results were 100.0% and 100.3% hydrogen. Work previous to this experiment had indicated that the gas evolved was essentially pure hydrogen. It failed to be absorbed in 50% potassium hydroxide (carbon dioxide), alkaline pyrogallol (oxygen), ammoniacal cuprous chloride (carbon monoxide), or in 50% potassium hydroxide after exhaustive combustion over cupric oxide at 275° (hydrocarbons).

Expt. B 10. - To check the hydrogen analyses, this experiment was performed as a repeat of expt. B 4 except that the reaction was continued until 4.5 ml. (50%) of water had been collected. The temperature varied from 172° to 201° during the 4.0 hrs. after water commenced to distil. The gas evolved was analyzed at six different times during the reaction and found to be 99.0 ± 1.0% hydrogen. A total of 0.18 mole of hydrogen was collected. The reaction yielded 30 g. of recovered hexanol-1, 49 g. (53%) of 2-butyloctanol-1, 9 g. of distillation residue and 5 g. of hexanoic acid.

Expt. B 11. - This experiment was performed as a repeat of expt. B 8 to again check the gas analyses. For the 2.0 hr. refluxing period after water began to distil, the temperature range was 187° to 243° as 2.7 ml. (30%) of water, and 0.44 mole of hydrogen were collected. The gas was found to be 100.1 ± 0.1% hydrogen as determined with samples taken at five different times during the reaction.

Isolation of the products yielded 5 g. of recovered hexanol-1, 47 g. (50%) of 2-butyloctanol-1, 9 g. of non-distilled material and 19 g. of hexanoic acid.

An Approximate Kb Determination for Hexanol-1. - The marked temperature elevations observed in the alkoxide variation work has been interpreted in terms of the molal elevation constant for hexanol-1. To obtain a check of this, the constant for hexanol-1 was approximately determined with triphenylcarbinol as a solute.

Into a 500 ml., three-necked flask equipped with a 360° thermometer and a condenser, was placed 100.0 g. of hexanol-1. Boiling chips were added and the hexanol-1 was heated at reflux for 2 hrs. before reading the temperature to 0.1° with a magnifying meniscus reader. The triphenylcarbinol was added in increments of 0.010 mole, 0.010 mole, 0.020 mole and 0.040 mole, allowing 2 hrs. or more between the additions and the temperatures were recorded for each concentration. A constant voltage (70) was applied to the "Gas-Col" mantle.

Table XIV

K_b for Hexanol-1

Molality	$T_{obs.}$	ΔT	K_b
0.00	159.0°	-	-
0.10	159.5°	0.5°	5.0°
0.20	159.9°	0.9°	4.5°
0.40	161.5°	2.5°	6.2°
		Avge. =	5.2°

The values of K_b in Table XIV were calculated by equation (3) given in the Discussion. The value for the 0.80 molal solution is not included in the table since considerable water formed in the solution after refluxing overnight. A 5 ml. water trap filled with hexanol-1 was placed in the system and the water removed by distillation. A total of 0.65 ml. of water was collected and the temperature did not vary from 162.9° during an 18 hr. refluxing period while the water was being removed.

2. The Effect of Varying the Amount of U.O.P. Nickel

This variable was studied using 1.0 mole of hexanol-1 in the standard apparatus with 0.175 mole of potassium and varying the amount of U.O.P. nickel from zero to 4.0 g. A constant amount of water, 4.7 ml. (52%), was collected and the major results are included in Table V in the Discussion; additional data are listed in the Supplement to Table V. The moles of product alcohol are re-tabulated with the moles of acid plus the moles of water to show their correspondence.

Supplement to Table V

Expt.	U.O.P. nickel, g.	Hexanol-1 recovered, moles	Alcohol residue, g.	Product alcohol, moles	Acid + Water, moles
B 12	0.0	0.96	2	-	-
B 13	0.031	0.90	1	0.013	0.019
B 14	0.50	0.24	10	0.28	0.30
B 15	1.0	0.23	9	0.27	0.30
B 16	2.0	0.21	12	0.29	0.30
B 17	3.0	0.22	13	0.27	0.30
B 18	4.0	0.20	13	0.28	0.30

It was mentioned in the Discussion that if the reaction was permitted to proceed too long, considerable high-boiling residue formed. Three experiments were performed which show this. Two of them, expts. A 20 and A 25, have been given previously and the third is recorded here.

Expt. B 19. - In this reaction using 1.5 moles of hexanol-1, 0.30 mole of potassium and 2.5 g. of U.O.P. nickel, a refluxing period of only 1.3 hrs. was used after water began to distil. An induction period of 50 min. was observed and the temperature dropped from 179° to 175° during this time. The temperature range during the reaction was 175° to 186° and 3.6 ml. of water collected. Purification of the reaction mixture yielded 72 g. of recovered hexanol-1, 56 g. (40%) of 2-butyloctanol-1, only 13 g. of distillation residue and 7 g. of hexanoic acid.

3. The Characterization of 2-Butyloctanol-1

This has been included as a separate section since the work was rather extensive. All derivatives made in this thesis were by the procedures given in Shriner and Fuson, unless otherwise specified.[84] Where ethanol was used as a solvent this material was 95% ethanol.

The following physical properties were obtained: b.p. 131-132° (15 mm.), 108-110° (2.5 mm.); n_D^{25} 1.4400. The literature values for this compound are:[13] b.p. 132° (15 mm.); n_D^{16} 1.4435.

<u>Anal</u>. Calcd. for $C_{12}H_{26}O$: C 77.34%, H 14.07%. Found: C 77.36%, H 13.81%.

The quantitative carbon and hydrogen analyses for this compound and most of the other compounds in this work were obtained since many of them were liquids which were made by modified procedures. There has also been some doubt as to the structure of the products obtained in a standard Guerbet reaction.[13] The solid products or their derivatives were not analyzed unless they were new compounds or a discrepancy existed between the melting points obtained and those reported in the literature.

The 2-butyloctanol-1 gave negative results with 2,4-dinitrophenylhydrazine and bromine in carbon tetrachloride; it was insoluble in the Lucas reagent and did not give the hydroxamic acid test for esters. It gave positive tests with sodium metal, acetyl chloride and ceric nitrate solution, and a positive Ferrox test.

The following derivatives were attempted without success: the phenylurethane (diphenylurea obtained), the α-naphthylurethane (di-α-naphthylurea obtained), the 3,5-dinitrobenzoate, the xanthate,[85] the benzoate, the 3-nitrophthalic acid ester, the tetrachlorophthalic acid ester[86] and the phthalimidomethylene ether.[87]

The allophanate of this compound has been reported by Mastagli[13] and since efforts to obtain a more common derivative were not successful, this derivative was made.

The procedure of Behal was used, which involves the decomposition of cyanuric acid in a combustion tube with a furnace and passing the evolved cyanic acid into the chilled alcohol.[67] The cyanuric acid may be conveniently prepared by a standard procedure.[88] In place of the furnace, a Meeker burner was used at the front end of a combustion tube (14 x 250 mm.) sealed at one end and a Bunsen burner was used to heat the cyanuric acid. The Bunsen flame was moved from the front to the back of the tube over a period of about 15 min. for 3 g. of cynuric acid. The outlet tube from the combustion tube was immersed in about 2 g. of the alcohol placed in an 18 x 150 mm. test tube. A hood is recommended for this work. As the cyanic acid was passed into the alcohol, the latter became milky and quite hot. The tube was removed from the alcohol as soon as the cynuric acid was decomposed and the material allowed to stand until solid (1 to 4 hrs.). The solid cake was broken up and triturated with ether to remove unreacted alcohol and the urethane. In some cases the allophanates were soluble in ether and had to be chilled in an ice bath to precipitate them. The solid was filtered from the ether and dissolved in hot ethanol and passed through a fluted filter to remove any residue. Then upon chilling the alcoholic solution in an ice bath, the allophanate crystallized. After filtering and drying the solid, a melting point was taken and then the compound was recrystallized to constant melting point. In many cases one recrystallization was sufficient and never more than three were required.

The allophanate of 2-butyloctanol-1, after two recrystallizations from ethanol, melted at 126-127°. Mastagli reports a melting point of 119°. Because of this discrepancy, the allophanate of the commercial 2-butyloctanol-1 was made and this melted at 126-127.5°. A mixture melting point determination of the two allophanates gave a melting point of 126-127.5°.

Anal. Calcd. for $C_{14}H_{28}O_3N_2$: C 61.73%, H 10.36%. Found: C 61.91% 61.78%; H 10.49%, 10.55%.

Preparation of 1-Bromo-2-Butyloctane. - In a 50 ml. flask was placed 20.0 g. (0.11 mole) of 2-butyloctanol-1 and 28.7 g. (0.11 mole) of phosphorus tribromide was added in small portions while swirling the flask. A condenser supporting a calcium chloride tube was attached to the flask and then warmed on a steam bath for 1 hr. The mixture was poured onto ice and 50 ml. of carbon tetrachloride was added. The water layer was removed and the organic layer washed successively with a small portion of concentrated sulfuric acid, twice with water, once with 5% sodium hydroxide and once more with water; it was then dried over calcium chloride and distilled. The product distilled at 100-102° (2.5 mm.); n_D^{25} 1.4557. There was obtained 13.5 g. (51%).

Anal. Calcd. for $C_{12}H_{25}Br$: Br 32.13%. Found: Br 32.26%, 32.46%.

As mentioned in the Discussion, some rearrangement may have occurred to a tertiary bromide since the product gave an immediate and copious precipitate with alcoholic silver nitrate. It is also possible that a small amount of the unsaturated bromide was present.

Preparation of 2-Butyloctanoic Acid. - This compound was prepared by a standard oxidation procedure with potassium dichromate and sulfuric acid. The 2-butyloctanol-1 (12.0 g., 0.065 mole) with 60 ml. of water, 30 g. of potassium dichromate and 40 ml. of concentrated sulfuric acid yielded 6 g. (46%) of 2-butyloctanoic acid. This substance boiled at 114-116° (0.5 mm.) and had a refractive index of n_D^{25} 1.4350. The experimental values for the neutralization equivalent were 191 and 190; the calculated value is 200. The acid was derivatized as its amide and recrystallized from acetone-water; m.p. 106.2-107.5°.

Anal. Calcd. for $C_{12}H_{25}ON$: C 72.30%, H 12.64%, N 7.04%. Found: C 72.34%, 72.68%; H 12.71%, 12.71%; N 7.14%, 6.87%.

This acid was also prepared by treating 93 g. (0.5 mole) of 2-butyloctanol-1 with 3.9 g. (0.1 mole) of potassium and 0.8 g. of U.O.P. nickel. A 250 ml., three-necked flask equipped with a condenser and a stirrer was used. The solution was heated at 200° for 1.5 hrs. and then at reflux (258° to 268°) for 1.5 hrs. After cooling and pouring into water, the water layer was treated in the standard manner to yield 14 g. (14%) of 2-butyloctanoic acid which distilled at 115-117° (0.5 mm.); n_D^{25} 1.4367. The acid prepared in this manner gave neutralization equivalents of 202 and 199.

Preparation of 2-Butyloctyl Acetate. - In a 500 ml., one-necked flask there were placed 300 ml. of benzene, 18.6 g. (0.10 mole) of 2-butyloctanol-1, 12.0 g. (0.20 mole) of glacial acetic acid and 0.5 g. of p-toluenesulfonic acid. A water trap surmounted by a condenser was attached to the flask and the solution held at reflux until the water stopped distilling. A total of 2.3 ml. (128%; probably contained acetic acid) of aqueous layer was collected. The benzene solution was washed with water, twice with saturated sodium bicarbonate solution and twice more with water. The benzene was removed by distillation and the product distilled under reduced pressure to give 20 g. (88%) of the 2-butyloctyl acetate. This product was a very mobile, colorless liquid which distilled at 112-113° (2 mm.); n_D^{25} 1.4308. The diethylene glycol method was used to determine the saponification equivalent of this compound.

Anal. Calcd. for $C_{14}H_{28}O_2$: C 73.63%, H 12.36%, S.E. 228. Found: C 73.84%, 73.90%; H 12.16%, 12.11%; S.E. 230.

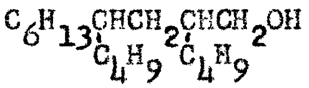
Preparation of 2-Butyloctyl p-Chlorobenzoate. - In a one l. flask equipped with a water trap surmounted by a condenser were placed 18.6 g. (0.10 mole) of 2-butyloctanol-1, 31.3 g. (0.20 mole) of p-chlorobenzoic acid, 500 ml. of benzene and 1.0 g. of p-toluenesulfonic acid. After 1.8 ml. of water had been collected, the reaction mixture was treated as for the 2-butyloctyl acetate to yield 23 g. (71%) of 2-butyloctyl p-chlorobenzoate which distilled at 152-155° (0.1 mm.); n_D^{25} 1.4946. This substance did not solidify after standing for a year and a half and was a light yellow, viscous liquid.

The Equivalent Weight of 2-Butyloctanol-1. - This reaction was considered in the Discussion. One-half l. of benzene, 32.4 g. (0.125 mole) of triphenylcarbinol and 23.2 g. (0.125 mole) of 2-butyloctanol-1 were placed in a one l., one-necked flask equipped with a water trap surmounted by a condenser and a calcium chloride tube. To this mixture, 0.047 g. of p-toluenesulfonic acid was added and the solution was held at reflux for 24 hrs. After 21 min., 1.10 ml. (49%) of water had collected and after 1.5 hrs., 2.02 ml. (90%). For the 2-butyloctanol-1 this gives a value of 189 for the molecular weight, which compares favorably to the calculated value of 186. The reaction mixture was purified as above for the 2-butyloctyl acetate. The triphenylmethyl 2-butyloctyl ether distilled at 202-203° (0.2 mm.); n_D^{25} 1.5460. The yield was 37.5 g. (70%).

Characterization of the High-Boiling Residues. - The residues from several exploratory experiments were collected and distilled through an 8 in. Vigreaux column under reduced pressure. A total of 260 g. was used to obtain 35 g., distilling at 95° to 100° (0.2 mm.). The temperature rapidly rose to 125° and 75 g. was obtained in the range of 125° to 135° (0.2 mm.); n_D^{25} 1.4575. A final fraction of 61 g. in the range of 145° to 165° (1.2 mm.) was obtained (n_D^{25} 1.4595) and 89 g. of a tar remained. The second and third fractions were analyzed for carbon and hydrogen. Fraction 2: C 80.31%, H 13.62%. Fraction 3: C 79.38%, H 13.14%.

All of the fractions were unsaturated to bromine in carbon tetrachloride so the first fraction may be mainly the 2-butyl-2-octenol-1 since this probably boils higher than the 2-butyloctanol-1.

If the analyzed fractions contained alcohol(s) of the triply condensed structure, e.g., a product from the condensation of 2-butyloctanol-1 and hexanol-1, they might be mixtures of the saturated and the unsaturated alcohols. Two possible structures and calculated values for carbon and hydrogen are:



$C_6H_{13}\underset{C_4H_9}{CH}CH_2\underset{C_4H_9}{CH}CH_2OH$ C 79.92%, H 14.16%

$C_6H_{13}\underset{C_4H_9}{CH}CH{=}\underset{C_4H_9}{C}CH_2OH$ C 80.52%, H 13.52%.

The calculated values for the last structure are seen to agree fairly well with analyses obtained for fraction 2 above. This may be the correct structure for the compound but the evidence is insufficiently definite to classify it. No further work was done on these compounds.

4. The Effect of Varying n in $CH_3(CH_2)_nCH_2OH$

The above work was sufficiently consistent to indicate the optimum conditions for a conveniently rapid reaction with hexanol-1. It was felt that these conditions could be generally applied to the homologs of hexanol-1. It is significant to note that plots of the volume of water against time for hexanol-1, heptanol-1 and octanol-1 had the same general shape. This was in spite of large temperature differences and rates of temperature changes during the reactions.

The following reactions of this section are in two series; one utilizing U.O.P. nickel and one without U.O.P. nickel. The major results of the first series are given in Table VI and those of the second series in Table VII of the Discussion. Other pertinent information on the reactions and properties of the products are given here under each experiment. For these reactions, 1.0 mole of the alcohol and 0.175 mole of potassium were used. For the first series 0.5 g. of U.O.P. nickel was used except where indicated and none was used in the second series. The standard apparatus and procedure were used in all cases.

<u>Expt. B 20</u>. - Butanol-1 was used in this experiment with 4.0 g. of U.O.P. nickel to give a faster reaction. In addition, 3.0 ml. of <u>o</u>-xylene was added to the water trap to aid in the water separation. The reaction started soon after the reflux temperature (136°) was reached and before hydrogen began to be evolved, 0.3 ml. of water collected. This may have been due to a small amount of aldehyde or water in the butanol-1. It was necessary to use the minimum heating which allowed water separation. After 12.5 hrs. of refluxing, 1.2 ml. (13%) of water had distilled and the temperature increased from 136° to

140°. The reaction was stopped by cooling to room temperature and the mixture allowed to stand overnight under an atmosphere of nitrogen. The next day the reaction was continued for 8.5 hrs. and the total water volume reached 3.1 ml. (34%) and the temperature increased to 146°. The reaction mixture was again allowed to stand overnight as above and on continuing for 5.0 hrs. longer (26.0 hrs. total), 4.5 ml. (50%) of water had collected and a final temperature of 155° was achieved. A total of 0.16 mole of hydrogen was evolved.

This reaction afforded 32 g. of recovered butanol-1 distilling at 115-118°. The 2-ethylhexanol-1 distilled at 106-108° (55 mm.); n_D^{25} 1.4309 (lit. n_D^{20} 1.4300). The yield was 27 g. (42%). Three g. of distillation residue and 2 g. of butanoic acid were also obtained. The acid distilled at 160° to 166° (lit. b.p. 163°).

The allophanate of 2-ethylhexanol-1 was prepared as described above and after one recrystallization from ethanol melted at 124.7-125° (lit.[13] m.p. 125°).

Expt. E 21. - Pentanol-1 required 18.5 hrs. for reaction using 0.5 g. of U.O.P. nickel and was twice permitted to stand overnight during this time. As for butanol-1, the minimum heating was used which allowed water separation. A temperature range of 155° to 180° was observed while collecting 4.5 ml. (50%) of water and 0.088 mole of hydrogen.

There were obtained 34 g. of recovered pentanol-1 distilling at 60-63° (25 mm.) and 36 g. (46%) of 2-propylheptanol-1 in the distillation range of 106° to 114° (14 mm.) with most of it coming over at 106-108°. There was also 7 g. of distillation residue. Insufficient acid was obtained for distillation but after isolation from the water, it was titrated to a phenolphthalein end point with standard sodium hydroxide. This procedure indicated that 1.6 g. of pentanoic acid was obtained.

The refractive index of the product, 2-propylheptanol-1, at 25° was 1.4356. Weizmann reported this compound but he only gave a boiling point of 112-115° (14 mm.).[11] He did not give a refractive index or the analytical results for carbon and hydrogen.

Anal. Calcd. for $C_{10}H_{22}O$: C 75.88%, H 14.10%. Found: C 76.40%, 76.37%; H 14.15%, 14.06%.

The allophanate was made and after one recrystallization from ethanol melted at 130-131°.

Anal. Calcd. for $C_{12}H_{24}O_3N_2$: C 59.01%, H 9.84%. Found: C 59.04%, 58.79%; H 9.98%, 9.92%.

Expt. B 22. - This experiment with hexanol-1 has been previously given in the U.O.P. variation work as expt. B 14.

Expt. B 23. - Heptanol-1 gave a fairly rapid reaction with only 0.5 g. of U.O.P. nickel. An induction time of 0.5 hr. was observed with practically no temperature drop. A total reaction time of 2.2 hrs. was required to give 4.7 ml. (52%) of water and 0.20 mole of hydrogen, during which the temperature increased from 195° to 238°.

Isolation of the products gave 15 g. of recovered heptanol-1, distilling at 60-62° (2.5 mm.) and 63 g. (59%) of 2-pentylnonanol-1 which distilled at 128-129° (2 mm.); n_D^{25} 1.4441 (lit.[13] b.p. 154° (13 mm.), n_D^{21} 1.4460). There remained from the distillation 10 g. of high-boiling residue. The water layer yielded 11 g. of heptanoic acid which distilled at 220° to 228°; n_D^{25} 1.4215. (lit. b.p. 221-222°, n_D^{20} 1.4216).

Anal. Calcd. for $C_{14}H_{30}O$: C 78.43%, H 14.11%. Found: C 78.73%, H 14.13%.

The 2-pentylnonanol-1 (26.75 g.) without further purification gave 2.20 ml. of water in an equivalent weight determination as described for 2-butyloctanol-1. This gives a value of 219 as compared to the calculated value of 214. The trityl ether was not isolated.

The allophanate was made and after one recrystallization from ethanol melted at 121-122° (lit.[13] m.p. 120°). This compound has the correct structure as shown by an independent synthesis by Mastagli.[13] He reports many liquid derivatives of this compound.

Expt. B 24. - In the same manner as for the previous experiments, the use of octanol-1 gave an excellent reaction. No induction period was observed and only a 1.5 hr. refluxing period was required to give 4.5 ml. (50%) of water and 0.22 mole of hydrogen. The temperature increased from 205° to 250° during this period.

There were obtained from this reaction 18 g. of recovered octanol-1 which boiled at 90-95° (13 mm.) and 75 g. (62%) of 2-hexyldecanol-1 distilling at 128-130° (0.8 mm.); n_D^{25} 1.4472. A high-boiling residue of 7 g. and 15 g. of octanoic acid were obtained. The latter distilled over the range of 233° to 240°; n_D^{25} 1.4268 (lit. b.p. 237.5°, n_D^{21} 1.4268).

Anal. Calcd. for $C_{16}H_{34}O$: C 79.27%, H 14.14%. Found: C 79.53%, 79.46%; H 14.01%, 13.91%.

The product was used as distilled above for the carbon and hydrogen analyses and an equivalent weight determination. The equivalent weight obtained with 30.25 g. of the alcohol was 246 (2.21 ml. of water) which may be compared to the calculated value of 242. The trityl ether formed in this determination was not isolated.

The allophanate was made and recrystallized once from ethanol; m.p. 92-93° (lit.[13] m.p. 90°). The 2-hexyldecanol-1 had the following boiling points: 182-184° (16 mm.), 144-146° (2 mm.), 128-130° (0.8 mm.). The literature values are 177° (15 mm.)[13] and 181-183° (15 mm.).[89] The value of the refractive index was n_D^{25} 1.4472, while it has been previously reported as being $n_D^{16.5}$ 1.4520[13] and n_D^{25} 1.4470.[89] The last value for the refractive index compares very well with the value obtained in this work and it is of interest since the compound was obtained by reducing ethyl-2-hexyldecanoate with sodium and ethanol. The ester was prepared by the malonic ester synthesis.

Expt. B 25. - This reaction with nonanol-1 required 1.3 hrs. to yield 4.5 ml. (50%) of water and 0.30 mole of hydrogen with a temperature range of 222° to 277°. The recovered nonanol-1 (12 g.) distilled at 102-106° (15 mm.) followed by a fraction of 82 g. (60%) of 2-heptylundecanol-1 which distilled at 135-138° (0.8 mm.); n_D^{25} 1.4506 (lit.[13] n_D^{15} 1.4550). There were 9 g. of distillation residue and 19 g. of nonanoic acid which distilled at 250-255°; n_D^{25} 1.4300 (lit. b.p. 253-254°, n_D^{20} 1.4306).

Anal. Calcd. for $C_{18}H_{38}O$: C 79.92%, H 14.16%. Found: C 80.08%, H 14.14%.

The allophanate was made and after two recrystallizations from ethanol-water melted at 78-79.5° (lit.[13] m.p. 80°).

Expt. B 26. - Decanol-1 was used with 2.0 g. of U.O.P. nickel under otherwise standard conditions. This amount of nickel instead of 0.5 g. was used by mistake but it was not considered necessary to repeat the reaction. This merely gave a slightly faster reaction than 0.5 g. would have probably given (cf. expt. B 32). The reaction began immediately on taking the solution to the reflux temperature and was stopped after 3.5 ml. (39%) of water had collected (40 min.) since the temperature was rising very rapidly (about 2° per min.) the last ten min. of reaction. The temperature range was 237° to 271° and 0.28 mole of hydrogen was collected.

There were obtained from the reaction 18 g. of recovered decanol-1, distilling at 120-125° (14 mm.) and 92 g. (62%) of 2-octyldodecanol-1 which distilled at 168-170° (0.8 mm.), n_D^{25} 1.4526 (lit.[13] b.p. 215° (15 mm.), n_D^{19} 1.4545). There were also obtained 8 g. of distillation residue and 23 g. of decanoic acid; b.p. 268-272°, m.p. 28-31° (lit. b.p. 268-270°, m.p. 31.5°).

Anal. Calcd. for $C_{20}H_{42}O$: C 80.46%, H 14.18%. Found: C 80.28%, 80.26%; H 13.61%, 13.86%.

The presence of nonanoic acid in the preceding experiment and of decanoic acid in this experiment caused the formation of emulsions in working up the mixtures. Long standing periods were required to effect separation of the water layers even in the presence of ether to aid in breaking the emulsion.

The allophanate was made for the 2-octyldodecanol-1 and after three recrystallizations from ethanol melted at 67-69° (lit.[13] m.p. 69°).

For the second series of experiments included here, U.O.P. nickel was not utilized. The first one was performed with sodium hexoxide and different quantities of it were used as compared to the succeeding potassium alkoxide experiments. The same general procedure was used, however.

Expt. B 27. - In a one l., one-necked flask equipped with a condenser were placed 800 ml. (6.4 moles) of hexanol-1 and 55.0 g.

(2.4 moles) of sodium. The mixture was heated at reflux overnight (12 hrs.) to react the sodium and then for 54 hrs. longer. The temperature was not recorded but in another experiment a solution of this same concentration of sodium hexoxide was observed to have a solution temperature of 186°. The products were isolated in the standard fashion to yield 29 g. (5%) of 2-butyloctanol-1, which distilled at 93-95° (0.8 mm.), (n_D^{25} 1.4415) and 13 g. of hexanoic acid distilling at 200° to 210°.

Expt. B 28. - This experiment, included in Table VII, for hexanol-1 has been given in the U.O.P. nickel variation study as expt. B 12.

Expt. B 29. - Heptanol-1 was very slow to start to react without U.O.P. nickel in the presence of potassium heptoxide. It required 28 hrs. for reaction and it is interesting to note that only 2.5 ml. (27%) of the water had been collected (temperature was 211°) after 22 hrs. and the balance, 2.0 ml., was obtained in the next 6 hrs. The temperature range during the reaction was 195° to 254°. There was 0.22 mole of hydrogen collected but this is not an accurate value since a leak was found during the reaction.

Purification of the reaction mixture yielded 9 g. of recovered heptanol-1, 70 g. (65%) of 2-pentylnonanol-1 (n_D^{25} 1.4449), 11 g. of distillation residue and 15 g. of heptanoic acid (n_D^{25} 1.4215).

Expt. B 30. - The reaction with octanol-1 without U.O.P. nickel required 5.8 hrs. to yield 4.5 ml. (50%) of water and 0.27 mole of hydrogen, with a temperature range of 207° to 262°.

The reaction mixture yielded 16 g. of recovered octanol-1 and 74 g. (62%) of 2-hexyldecanol-1 which distilled at 182-184° (16 mm.); n_D^{25} 1.4471. There were also obtained 10 g. of high-boiling residue and 17 g. of octanoic acid; n_D^{25} 1.4268.

Expt. B 31. - Nonanol-1 gave a good reaction without U.O.P. nickel but the water stopped distilling after 4.4 ml. (49%) had been collected. For the 2.6 hr. reaction time, 0.34 mole of hydrogen was collected and the temperature range was 224° to 305°.

The isolation procedure yielded 12 g. of recovered nonanol-1, 84 g. (62%) of 2-heptylundecanol-1 (n_D^{25} 1.4505), which distilled at 134-137° (0.4 mm.) and 10 g. of high-boiling residue. There was 21 g. of nonanoic acid; n_D^{25} 1.4300.

Expt. B 32. - The reaction of decanol-1 without U.O.P. nickel required only 1.3 hrs. to give 4.5 ml. (50%) of water and 0.38 mole of hydrogen. The temperature range during this time was 239° to 320°.

The reaction afforded 7 g. of recovered decanol-1 and 96 g. (65%) of 2-octyldodecanol-1 (n_D^{25} 1.4528). The product distilled at 164-165° (0.4 mm.) and there were 12 g. of distillation residue and 25 g. of decanoic acid; b.p. 265-272°.

5. The Self-Condensation of Secondary Alcohols

These reactions were performed with 1.0 mole of the secondary alcohol, 0.175 mole of potassium and 2.0 g. of U.O.P. nickel in the standard apparatus. The usual isolation procedure was used but no acid was formed.

Expt. B 33. - Heptanol-2 (116 g., 1.0 mole) reacted with the potassium to give a yellow-brown solution. After the addition of the U.O.P. nickel, the reaction required 9.0 hrs. to give 4.5 ml. (50%) of water with the solution temperature increasing from 174° to 195°. Hydrogen evolution was rather vigorous during the first hour of reaction but thereafter tapered off to yield only 0.097 mole of hydrogen.

Purification of the reaction mixture provided 63 g. of recovered heptanol-2 which boiled at 69-70° (15 mm.) and 27 g. of the product(s) distilled from 135° to 158° (15 mm.). There was 15 g. of non-distilled material and the water layer became only faintly cloudy upon acidification.

The product(s) showed considerable unsaturation to bromine in carbon tetrachloride with some hydrogen bromide evolution. The material was dissolved in 100 ml. of 95% ethanol and hydrogenated over Raney nickel at 150° and 2300 p.s.i. for 1 hr. in a 300 ml. rocker-type bomb. Distillation of the hydrogenated material gave 6 g. distilling from 122° to 138° (14 mm.) having a refractive index of n_D^{25} 1.4328 and 17 g. distilling from 138° to 148° (14 mm.) but mainly at 141-142°; n_D^{25} 1.4408. There was 2 g. not distilled and both fractions were saturated to bromine in carbon tetrachloride. The main fraction was assumed to be 8-methyltridecanol-6, formed by the condensation of a molecule of heptanol-2 on the methyl group of another molecule of heptanol-2.

Anal. Calcd. for $C_{14}H_{30}O$: C 78.43%, H 14.11%. Found: C 78.69%, H 14.13%.

Expt. B 34. - This reaction with octanol-2 required 4.1 hrs. to yield 5.4 ml. (60%) of water and the temperature rose from 190° to 216°. A total of 0.10 mole of hydrogen was evolved.

Purification of the reaction mixture gave 58 g. of recovered octanol-2, 32 g. of product(s) in the distillation range of 128° to 142° (2.5 mm.) and there was 25 g. of high-boiling residue.

Expt. B 35. - The use of 5-ethylnonanol-2 is interesting in that no U.O.P. nickel was needed to effect the reaction and only 0.10 mole of potassium was used for 1.0 mole of the alcohol. The reaction required 40 min. to give 4.6 ml. (51%) of water and the temperature varied from

228° to 237° as 0.10 mole of hydrogen was evolved.

The mixture was purified to give 93 g. of recovered 5-ethylnonanol-2, 49 g. of a fraction distilling from 152° to 162° (15 mm.) and there was 17 g. of distillation residue.

The product(s) obtained in this reaction and from the preceding reaction were unsaturated and evolved hydrogen bromide when treated with bromine in carbon tetrachloride. No further work was done on the identification of these products.

C. Mixed Guerbet Condensations

1. General Considerations

The mixed reactions are described in somewhat greater detail than previous reactions because more careful purifications were required in most instances. For these reactions 1.0 mole of total alcohols, 0.175 mole of potassium and in most cases, 2.0 g. of U.O.P. nickel were used.

The first distillations were performed with an 8 in. Vigreaux column and any redistillations with the 12.5 mm. diameter Todd column. In general, for the fractions previous to the product, the oil bath was maintained at the temperature at which the succeeding fraction would distil. This was slow in many cases but it allowed a good separation of the recovered reactants and of the products. The same general methods were used here as with the other Guerbet reactions.

2. The Condensation of 2-Ethylhexanol-1 with Normal Primary Alcohols

Expt. C 1. - In this reaction, 2-ethylhexanol-1 (86.6 g., 0.67 mole), hexanol-1 (34.0 g., 0.33 mole) and only 1.0 g. of U.O.P. nickel were used. A reaction period of 6.7 hrs. was required to give 2.3 ml. of water after which the water ceased to distil. The temperature increased from 188° to 205° and 0.12 mole of hydrogen collected.

The mixture afforded 1 g. of recovered hexanol-1 distilling at 67-70° (14 mm.) and 74 g. of 2-ethylhexanol-1 distilling at 79-84° (14 mm.). When these substances were removed 26 g. (83%) of 2-butyloctanol-1 was obtained in the distillation range of 136° to 144° (18 mm.); n_I^{25} 1.4410. There remained from the distillation 6 g. of high-boiling residue. The product was redistilled through the Todd column at atmospheric pressure.

Twenty g. (65%) of the 2-butyloctanol-1, which distilled at 250-251°, had a refractive index at 25° of 1.4400. There was 5 g. of material held in the column.

The water layer yielded some acid upon acidification but it was not a sufficient amount to distil. Titration with standard base to a phenolphthalein end point indicated 0.036 mole of total acid.

Expt. C 2. - This experiment was an exact repeat of expt. C 1 except that 52.6 g. (0.33 mole) of decanol-1 was used in place of the hexanol-1. This reaction required only 4.0 hrs. to yield 2.0 ml. of water and the temperature varied from 205° to 208°, while 0.12 mole of hydrogen was evolved.

The reaction mixture was purified in the standard manner to give 77 g. of recovered 2-ethylhexanol-1 and 3 g. of decanol-1. Further distillation yielded 10 g. of material which came over between 140° to 160° (0.8 mm.) and 27 g. at 159-161° (0.5 mm.), leaving 6 g. of residue. The combined acids were distilled to yield 2 g. of 2-ethylhexanoic acid which boiled at 220° to 228° and 5 g. of decanoic acid at 263° to 274°.

The two alcohol product fractions and the residue were combined and distilled through the Todd column. There was obtained 6 g. of material that was probably the mixed product, 2-hexyl-4-ethyloctanol-1, and which distilled at 146-151° (1.0 mm.); n_D^{25} 1.4515. This was followed by 30 g. (60%) of 2-octyldodecanol-1 distilling at 172-173° (1.0 mm.); n_D^{25} 1.4523. There was 6 g. of material held in the column.

3. The Condensations of Benzyl Alcohol with Primary Alcohols Containing a β-Methylene Group

The major results of these experiments are included in Table VIII in the Discussion. Further information on the reactions and properties of the products are given here.

Expt. C 3. - This was a preliminary experiment designed with expt. C 5 to ascertain the effect of the reactant alcohol ratio for benzyl alcohol and hexanol-1. Hexanol-1 (51 g., 0.50 mole) and benzyl alcohol (54 g., 0.50 mole) were mixed in the standard apparatus and the potassium added. After the potassium had reacted, 2.0 g. of U.O.P. nickel was added and the mixture taken to the reflux temperature. The reaction required 2.2 hrs. to yield 4.7 ml. (52% for the mixed reaction) of water and the temperature varied from 172° to 204° as 0.11 mole of hydrogen was collected.

From the reaction there was obtained 10 g. of hexanol-1 distilling from 56° to 69° (2.5 mm.) but very little was collected from 60° to 69°. The benzyl alcohol fraction (24 g.) was obtained at 69° to 95° (2.5 mm.). The crude 2-butyloctanol-1 (15 g.) distilled at 95° to 115° (2.5 mm.), followed by the 2-benzylhexanol-1 fraction (33 g.) from 113° to 124° (2 mm.) and there was 6 g. of distillation residue. The water layer gave 4 g. of benzoic acid; m.p. 112-116° (lit. mp. 121-122°).

Since the distillation through the standard column afforded poor separation, the benzyl alcohol, the 2-butyloctanol-1 and the 2-benzylhexanol-1 fractions were recombined and distilled through the Todd column at 15 mm. pressure. This yielded 21 g. of recovered benzyl alcohol, which distilled at 103-104° (n_D^{25} 1.5350) and 16 g. (35%) of 2-butyloctanol-1, which distilled at 132-133°; n_D^{25} 1.4420. The 2-benzylhexanol-1 came over at 156-157° (n_D^{25} 1.5100), leaving 2 g. of material in the column; n_D^{25} 1.5000. The yield of 2-benzylhexanol-1 was 30 g. (31%) and the literature physical constants are:[13] b.p. 155° (15 mm.), n_D^{20} 1.5138.

Expt. C 4. - In this reaction, 72.0 g. (0.67 mole) of benzyl alcohol, 24.6 g. (0.33 mole) of butanol-1 and 4.0 g. of U.O.P. nickel were used. In addition, 1.5 g. butanol-1 and 3.0 g. of benzyl alcohol were added to the water trap to aid in water separation and these amounts are not included in the recovery data. It was necessary to use the minimum heating which would give water separation and the reaction required 3.7 hrs. to yield 4.8 ml. (80%) of water with a temperature range of 143° to 187° and 0.18 mole of hydrogen was evolved.

There were recovered 3 g. of butanol-1 which boiled at 115-118° and 46 g. of a fraction of mainly benzyl alcohol which boiled at 90° to 110° (14 mm.). The next fraction (27 g.) was the impure 2-benzylbutanol-1, distilling at 110° to 134° (14 mm.), and there was 3 g. of residue. The water layer yielded 5 g. of benzoic acid which melted at 114° to 120°.

The benzyl alcohol and 2-benzylbutanol-1 fractions were recombined along with 10 g. of 2-pentylnonanol-1 and fractionated through the Todd column. The 2-pentylnonanol-1 was used as a "pusher" to get the maximum recovery of the 2-benzylbutanol-1. This distillation gave 3 g. (16%) of 2-ethylhexanol-1 boiling at 184-185°, n_D^{25} 1.4300, and 38 g. of recovered benzyl alcohol which boiled at 102-103° (15 mm.); n_D^{25} 1.5312. The product, 2-benzylbutanol-1, (30 g., 55%) distilled at 138-139° (15 mm.); n_D^{25} 1.5155. The literature physical constants are: b.p. 134-135° (15 mm.), n_D^{16} 1.5180;[13] b.p. 136° (12 mm.);[9] b.p. 105-107° (4 mm.).[90]

Anal. Calcd. for $C_{11}H_{16}O$: C 80.44%, H 9.82%. Found: C 80.64%, 80.67%; H 9.95%, 10.00%.

The allophanate was made and recrystallized once from ethanol; m.p. 148-149° (lit.[13] m.p. 134°).

Anal. Calcd. for $C_{13}H_{18}O_3N_2$: C 62.38%, H 7.25%. Found: C 62.52%, 62.35%; H 7.31%, 7.59%.

The 2-benzylbutanol-1 (10.25 g.) gave an excellent equivalent weight. A total of 1.13 ml. of water was obtained which gives a value of 163. The calculated value of the molecular weight is 164.

Expt. C 5. - This reaction was a repeat of expt. C 3 except that 72.0 g. (0.67 mole) of benzyl alcohol and 34.0 g. (0.33 mole) of hexanol-1 were used. This reaction required 2.0 hrs. to yield 4.8 ml. (80%) of water with a temperature range of 176° to 207° as 0.11 mole of hydrogen was collected.

Isolation of the reaction components yielded less than 1 g. of recovered hexanol-1 and 41 g. of benzyl alcohol, which distilled at 92-95° (14 mm.). There was no fraction at the 2-butyloctanol-1 distillation temperature (132°) but there was obtained 42 g. of impure 2-benzylhexanol-1 distilling from 149° to 159° (14 mm.). There were 4 g. of distillation residue and 6 g. of benzoic acid; m.p. 115-119°.

The product fraction and the residue were recombined and distilled through the Todd column at 15 mm. pressure. This gave 4 g. (14%) of 2-butyloctanol-1, which distilled at 131-133°, and 38 g. (59%) of 2-benzylhexanol-1, which distilled at 156-157°; n_I^{25} 1.5098.

Anal. Calcd. for $C_{13}H_{20}O$: C 81.20%, H 10.48%. Found: C 81.28%, 81.07%; H 10.43%, 10.20%.

The allophanate was made and after one recrystallization from ethanol melted at 144-145° (lit.[13] m.p. 144°).

Expt. C 6. - In this reaction there were used 72.0 g. (0.67 mole) of benzyl alcohol and 38.6 g. (0.33 mole) of heptanol-1. There was 2 g. of heptanol-1 added to the water trap which was not counted with the recovered alcohol. The reaction required 1.4 hrs. to yield 5.0 ml.

(83%) of water and 0.11 mole of hydrogen. The temperature range was 184° to 211°.

There was no heptanol-1 recovered but there was 38 g. of benzyl alcohol, which distilled at 95° to 105°; n_D^{25} 1.5305. This was followed by 49 g. of impure 2-benzylheptanol-1 which boiled at 155° to 164° (13 mm.); n_D^{25} 1.4912. There was 4.0 g. of high-boiling residue and the water layer yielded 6 g. of benzoic acid which melted at 111° to 116°.

Since the product was impure, it was recombined with the residue and distilled through the Todd column at 15 mm. There were obtained 9 g. (24%) of rather impure 2-pentylnonanol-1, which distilled at 160° to 169° (n_D^{25} 1.4640) and 40 g. (58%) of 2-benzylheptanol-1. This latter substance distilled at 169-170°; n_D^{25} 1.5016. The literature physical constants are: b.p. 162° (13 mm.), n_D^{18} 1.5039;[13] b.p. 119-120° (2.5 mm.).[90] It has also been reported that the 3,5-dinitrobenzoate of this alcohol is a liquid.[90]

The allophanate of this compound was made and recrystallized three times from ethanol; m.p. 124.5-126° (lit.[13] m.p. 125°).

Expt. C 7. - There were utilized for this reaction 72.0 g. (0.67 mole) of benzyl alcohol, 45.2 g. (0.33 mole) of 3-phenylpropanol-1 and no U.O.P. nickel. The potassium reacted very rapidly with the mixture of alcohols giving off white fumes and the solution turned a dark brown. A 12.5 ml. water trap for liquids heavier than water was used but as the reaction progressed the water went to the bottom (1.0 ml.). The reaction was stopped, a 5 ml. water trap was inserted and the organic layer was transferred to the reaction mixture with the water being discarded. After a total reaction time of 1.8 hrs., 5.0 ml. (83%) of water had been collected. The temperature varied from 227° to 241° and 0.11 mole of hydrogen was collected.

The reaction mixture yielded 38 g. of benzyl alcohol distilling from 94° to 105° (12 mm.); n_D^{25} 1.5358. One g. of substance distilled at 105° to 192° (12 mm.) and the product (47 g., 62%), which was 2,2-dibenzylethanol, distilled at 145° to 155° (0.5 mm.) with the bulk coming over at 145-147°; n_D^{25} 1.5662. There was 12 g. of non-distilled residue and the water layer gave 8 g. of acid which melted at 90° to 112°. The latter is probably mainly benzoic acid since 3-phenylpropionic acid melts at 48°.

The product has been reported as having a boiling point of 202° (15 mm.), n_D^{18} 1.5693, and its allophanate as melting at 140°.[13] The allophanate of the compound obtained in this work after three recrystallizations from ethanol melted at 139-140°.

4. The Condensation of Benzyl Alcohols with Secondary Alcohols

There are included here three preliminary experiments which were performed with benzyl alcohol and cyclohexanol. One of these, expt. C 12, is included in Table IX of the Discussion. These experiments show the effect on the yield of product of varying the ratio of the reactant alcohols.

Expt. C 8. - In the standard manner, 54.0 g. (0.50 mole) of benzyl alcohol and 50.0 g. (0.50 mole) of cyclohexanol were reacted. Two g. of cyclohexanol was added to the water trap and this amount was not counted with the recovered alcohol. This reaction required 2.5 hrs. to give 5.5 ml. (61%) of water and 0.089 mole of hydrogen as the temperature increased from 172° to 197°.

Purification of the reaction mixture yielded 22 g. of recovered cyclohexanol which distilled at 67-68° (12 mm.), n_D^{25} 1.4645, and 11 g. of benzyl alcohol which distilled at 94-96° (12 mm.). These fractions were followed by 29 g. (31%) of impure 2-benzylcyclohexanol which boiled at 158° to 165° (12 mm.) and which crystallized to an oily solid in the receiver. There were 23 g. of distillation residue and 2 g. of benzoic acid; m.p. 115-118°.

Expt. C 9. - This experiment was a repeat of expt. C 8 except that 36.0 g. (0.33 mole) of benzyl alcohol and 66.7 g. (0.67 mole) of cyclohexanol were used. The reaction required 2.1 hrs. to yield 4.4 ml. (73%) of water and 0.056 mole of hydrogen. The reaction temperature varied from 172° to 194° during this time.

There were recovered 42 g. of cyclohexanol and 5 g. of benzyl alcohol. The 2-benzylcyclohexanol (30 g., 47%) distilled at 159° to 165° (13 mm.) and there was 12 g. of high-boiling residue. The benzoic acid obtained (1.5 g.) melted at 110° to 115°.

The other experiment of this series is included below as expt. C 12. The experiments which follow all utilize 0.25 mole of benzyl alcohol and 0.75 mole of the secondary alcohol and are included in Table IX of the Discussion.

Expt. C 10. - For this reaction, 27.0 g. of benzyl alcohol and 87.0 g. of heptanol-2 were used with 2 g. of additional heptanol-2 in the water trap. The reaction proceeded for 4.5 hrs. during which time the temperature varied from 163° to 173° as 2.8 ml. (62%) of water and 0.054 mole of hydrogen were collected. The reaction gave only 0.05 ml. of water during the last hour at reflux.

The mixture was separated to yield 66 g. of recovered heptanol-2, which distilled at 67-69° (13 mm.), n_D^{25} 1.4200, and 9 g. of benzyl alcohol which distilled at 94° to 105° (13 mm.); n_D^{25} 1.5302. There were 13 g. (24%) of 1-phenyloctanol-3 which distilled at 158° to 165° (13 mm.), n_D^{25} 1.4996, and 11.5 g. of distillation residue. The water layer yielded 0.8 g. of benzoic acid; m.p. 118-120°.

The product was redistilled through the Todd column to yield 0.5 g. of a forerun up to 165° (12 mm.) and the 1-phenyloctanol-3 (9 g.) distilled at a constant 165° (12 mm.); n_D^{25} 1.4985.

Anal. Calcd. for $C_{14}H_{22}O$: C 81.50%, H 10.75%. Found: C 81.26%, H 11.01%.

The allophanate was made and after two recrystallizations from ethanol 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%.

Expt. C 11. - Benzyl alcohol (27.0 g.) and 4-methylpentanol-1 (76.5 g.) were used in this experiment and 4 g. of the secondary alcohol was added to the water trap. This reaction was allowed to proceed until 2.7 ml. (60%) of water had distilled (13.3 hrs.) and 0.016 mole of hydrogen was collected. The temperature range during the reaction was 143° to 152° and the heating was kept at the minimum amount necessary to effect water separation.

Purification afforded 60 g. of recovered 4-methylpentanol-1, which boiled at 59-60° (28 mm.) and 11 g. of benzyl alcohol at 95-98° (11 mm.). The product, 1-phenyl-5-methylhexanol-3, distilled at 146-150° (11 mm.); n_D^{25} 1.5023. The yield was 15 g. (31%) and there was 6 g. of distillation residue. The water layer did not yield any acid upon acidification.

Anal. Calcd. for $C_{13}H_{20}O$: C 81.20%, H 10.48%. Found: C 81.31%, 81.00%; H 10.45%, 10.38%.

This compound has been reported by Mastagli and he independently synthesized it for a structure proof by an aldol condensation of benzaldehyde and 4-methylpentanone-2, followed by reduction.[91] He reports the physical constants: b.p. 151° (15 mm.), n_D^{24} 1.5010.

The allophanate was made and recrystallized twice from ethanol; m.p. 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%.

Expt. C 12. - This experiment was compared to expts. C 8 and C 9 and is included in Table IX of the Discussion. For the reaction, 27.0 g. of benzyl alcohol and 75.0 g. of cyclohexanol were used with 2 g. of additional cyclohexanol in the water trap. The reaction required 2.0 hrs. as 3.4 ml. (75%) of water and 0.045 mole of hydrogen were collected over the temperature range of 172° to 186°.

From this reaction there were obtained 54 g. of recovered cyclohexanol and 1 g. of benzyl alcohol. The 2-benzylcyclohexanol distilled at 156° to 165° (12 mm.), there being 29 g. (61%) and 8 g. of distillation residue. The water layer yielded only 1 g. of benzoic acid; m.p. 115-118°.

The combined yields of the product from expts. C 8, C 9, and C 12 were used for further identification.

Anal. Calcd. for $C_{13}H_{18}O$: C 82.20%, H 9.53%. Found: C 82.30%, 81.90%; H 9.47%, 9.45%.

This substance melted over the range of 55° to 62° and was saturated to bromine in carbon tetrachloride solution. It was dissolved (75 g.) in 75 ml. of 90-100° petroleum ether with warming. The solution was chilled in an ice bath and the white crystalline precipitate was filtered off to yield 34 g.; m.p. 75.5-76.5°. The petroleum ether was evaporated to leave an oily solid which was distilled to give 25 g. boiling at 154-157° (13 mm.), 13 g. boiling at 157-159° (13 mm.) and there was 3 g. not distilled. These fractions partially solidified and they were recrystallized from petroleum ether. The 25 g. portion yielded 3 g. of solid melting at 73-76° and the 13 g. portion yielded 2 g. of solid melting at 73-75°. The total pure 2-benzylcyclohexanol isomer melting at about 76° weighed 39 g. (52% of the mixture). The literature values for this solid are: m.p. 75°,[9] 76.5-77.5°.[92] This solid was converted to its 3,5-dinitrobenzoate and after two recrystallizations from ethanol melted at 134.5-135.5° (lit. m.p. 134-135°,[9] 133-135°[92]).

A 1 g. sample of the 25 g. fraction above, after removing the petroleum ether, was converted to a 3,5-dinitrobenzoate to give faintly yellow needles after three recrystallizations from ethanol; m.p. 126.5-127.5°. When a mixture melting point determination was made with this compound and the 3,5-dinitrobenzoate obtained above (m.p. 135°), a melting range of 110° to 125° was observed.

Anal. Calcd. for $C_{20}H_{20}O_6N_2$: C 62.49%, H 5.24%. Found: C 62.48%, 62.27%; H 5.29%, 5.36%.

The liquid isomer or mixture remaining after the removal of solid alcohol could not be crystallized on allowing to stand or from ethanol, ethanol-water, petroleum ether, carbon tetrachloride, benzene, ether or dioxane. This compound has not been reported in the literature but it may be that since the isomer melting at 76° was always obtained from petroleum ether, that the mother liquors have never been investigated for the other isomer.

To show that these two compounds might be cis and trans isomers, the liquid isomer or mixture was converted to 2-benzylcyclohexanone, which has been previously obtained from the solid isomer.[92,93] A portion (3.5 g.) of the 25 g. fraction from above, after removal of the solid isomer, was dissolved in 25 ml. of glacial acetic acid and 1 g. of chromic acid in 3 ml. of 80% acetic acid was slowly added. The mixture was allowed to stand for three days and then poured into 100 ml. of water. The water was extracted twice with 50 ml. portions of benzene and the combined extracts dried and distilled. After the benzene had been removed, the residual liquid distilled to give 2.2 g. (63%) of 2-benzylcyclohexanone, which boiled at 154-156° (14 mm.), n_D^{25} 1.5342 (lit.[93] b.p. 119-121° at 0.1 mm.). The semicarbazone was made and recrystallized three times from ethanol-water; m.p. 166-167° (lit.[92,93] m.p. 168-169°).

The liquid residue after recrystallization of the 13 g. distillation fraction did not show further purification by distillation since 4.3 g. of five small fractions of constant refractive index gave a mixture of 3,5-dinitrobenzoates melting over the range of 108° to 116° after one recrystallization from ethanol-water.

Expt. C 13. - For this reaction, the potassium was reacted with 75.0 g. of cyclohexanol and then 34.5 g. of p-methoxybenzyl alcohol was added to prevent any ether cleavage by the potassium. There was 2 g. of cyclohexanol added to the water trap and the minimum heating was applied to the mantle which would effect water separation. The reaction was continued for 3.7 hrs. during which time the temperature increased from 177° to 187° as 3.4 ml. (75%) of water and 0.045 mole of hydrogen collected.

From the reaction mixture there were obtained 54 g. of cyclohexanol which distilled at 67-68° (12 mm.) and 4 g. of material which distilled at 120° to 152° (12 mm.) and which is probably impure p-methoxybenzyl alcohol; n_D^{25} 1.5250. The product, 2-(p-methoxybenzyl)cyclohexanol (26 g., 47%), distilled at 195° to 207° (12 mm.); n_D^{25} 1.5419. There was 11 g. of residue not distilled and the water layer yielded 2 g. of a gummy, brown solid which was not purified.

The product partially solidified after standing for two days and was dissolved in 25 ml. of 60-80° petroleum ether and chilled in an ice bath to yield 11 g. of white needles; m.p. 52-55°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C 76.50%, H 9.15%. Found: C 76.23%, H 9.02%.

This solid was converted to its 3,5-dinitrobenzoate which was obtained as yellow needles after three recrystallizations from ethanol; m.p. 122-123°.

Anal. Calcd. for $C_{21}H_{22}O_7N_2$: C 60.86%, H 5.35%. Found: C 60.97%, 60.73%; H 5.51%, 5.51%.

The mother liquor from the recrystallization of the 2-(p-methoxybenzyl)cyclohexanol was evaporated to remove the petroleum ether. The residue could not be crystallized by allowing it to stand or from any of the solvents given above for 2-benzylcyclohexanol. No further work was performed on these compounds.

Expt. C 14. - This experiment is a repeat of expt. C 13 using p-chlorobenzyl alcohol in place of p-methoxybenzyl alcohol.

The reaction was allowed to proceed until 3.4 ml. (75%) of water had been obtained (2.0 hrs.). The temperature increased from 175° to 182° and only 0.015 mole of hydrogen was collected.

The purification yielded 52 g. of recovered cyclohexanol, which distilled at 66-69° (12 mm.) and 3.5 g. of material distilling from 100° to 170° (12 mm.). There was 28 g. (50%) of product distilling from 178° to 190° (12 mm.), n_D^{25} 1.5487, leaving 14 g. of residue. The water layer yielded 0.5 g. of p-chlorobenzoic acid, melting at 210° to 218° and which after one recrystallization from ethanol-water, melted at 240-241.5° (lit. m.p. 243°).

The product, 2-(p-chlorobenzyl)cyclohexanol, solidified after an hour at room temperature and melted over the range of 80° to 95°. It was dissolved in 25 ml. of 90-100° petroleum ether and recrystallized to yield 13.5 g. of white needles, which melted at 109.8-111°.

Anal. Calcd. for $C_{13}H_{17}OCl$: C 69.47%, H 7.63%. Found: C 69.86%, 69.94%; H 7.88%, 7.51%.

The petroleum ether was evaporated but the residue failed to yield a different solid on standing or on attempted crystallization from the solvents given above for 2-benzylcyclohexanol.

The pure product obtained was converted to its 3,5-dinitrobenzoate which, after two recrystallizations from ethanol, gave tan needles melting 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%.

5. The Condensation of Octanol-1 with Secondary Alcohols

In these experiments, except for the first one given (C 15), there were utilized 0.75 mole of the secondary alcohol, 0.25 mole of octanol-1, 0.75 mole of potassium and 2.0 g. of U.O.P. nickel. It was found to be necessary to use the minimum amount of heat from the mantle which would permit water separation. The standard apparatus and purification procedure were used except that the octanoic acid was not isolated since so little of it formed in each case. The amounts of alcohols added to the water trap were not included in the recovery data.

Expt. C 15. - This reaction was between octanol-1 (65 g., 0.50 mole) and heptanol-2 (58 g., 0.50 mole) and 2 g. of each of the starting alcohols was placed in the water trap. The reaction yielded 3.6 ml. (40%) of water after 2.1 hrs. of refluxing with a temperature range of 183° to 202°. There was 0.11 mole of hydrogen collected.

Purification yielded 27 g. of recovered heptanol-2 which boiled at 67-69° (12 mm.) and 32 g. of octanol-1 at 90-95° (12 mm.). The product (20 g., 17%) was impure and distilled at 156° to 164° (12 mm.); n_D^{25} 1.4452. This substance, pentadecanol-6, solidified in the receiver at room temperature (21°) but completely melted on warming with the hand. There was 3 g. of material which distilled at 178° to 185° (12 mm.); n_D^{25} 1.4507. The experimentally determined values for 2-hexyldecanol-1 are: b.p. 182-184° (16 mm.), n_D^{25} 1.4472. There remained from the distillation 18 g. of high-boiling residue.

Expt. C 16. - The standard quantities of octanol-1 (32.5 g.) and heptanol-2 (87.0 g.) were used in this experiment. In addition, 1 g. of octanol-1 and 3 g. of heptanol-2 were placed in the water trap. In 4.5 hrs. there were obtained 3.4 ml. (75%) of water and 0.079 mole of hydrogen over a temperature range of 175° to 188°.

The reaction mixture afforded 63 g. of recovered heptanol-2 and

13 g. of octanol-1. The impure pentadecanol-6 distilled at 150° to 164° (12 mm.), n_D^{25} 1.4446. The yield of product was 18 g. (31%) and there was 18 g. of distillation residue.

The product obtained in the above two reactions was unsaturated to bromine in carbon tetrachloride and evolved hydrogen bromide. The combined product (30 g.) was dissolved in 100 ml. of 95% ethanol and hydrogenated over Raney nickel for one hr. at 150° and 2300 p.s.i. A pressure drop of 150 p.s.i. was observed at room temperature. The hydrogenated material was distilled to give 4 g. of product boiling at 156° to 162° (12 mm.), n_D^{25} 1.4417, and 23 g. boiling at 162-164° (12 mm.); n_D^{25} 1.4430. Both of these fractions were saturated to bromine in carbon tetrachloride. The forerun may have contained some of the condensation isomer wherein the octanol-1 had condensed on the β-methylene group of heptanol-2. The main fraction was a solid which melted at 31-33°, and after one recrystallization from 30-60° petroleum ether melted at 34-35°.

The pentadecanol-6 was converted to its α-naphthylurethane which, after three recrystallizations from 20-40° petroleum ether, melted at 50.5-52°.

This compound, pentadecanol-6, has been made by passing a mixture of hexanoic and decanoic acids over a thorium oxide catalyst at 400° and subsequently reducing the pentadecanone-6 to the alcohol.[94] The following properties were reported: b.p. 159° (10 mm.) and m.p. 36°. The α-naphthylurethane melted at 54°.

<u>Expt. C 17</u>. - Cyclohexanol (75.0 g.) and octanol-1 (32.5 g.) were used in this experiment. One g. of octanol-1 and 3 g. of cyclohexanol were used in the water trap. The reaction required 2.5 hrs. to yield

3.4 ml. (75%) of water as the temperature ranged from 175° to 190° and 0.044 mole of hydrogen was collected.

Distillation of the reaction mixture yielded 55 g. of recovered cyclohexanol which distilled at 67-69° (13 mm.) and 3 g. of octanol-1 at 92-95° (13 mm.). There were also obtained 32 g. (61%) of crude 2-octylcyclohexanol, which distilled at 156° to 167° (14 mm.), n_D^{25} 1.4656, and 10 g. of high-boiling residue.

The product was unsaturated to bromine in carbon tetrachloride and gave rather poor analyses for carbon and hydrogen.

Anal. Calcd. for $C_{14}H_{28}O$: C 79.18%, H 13.29%. Found: C 79.58%, 79.40%; H 12.22%, 12.90%.

In order to get a better quality substance for analysis, the compound (5.3 g.) was oxidized to the ketone with chromic acid as previously given for 2-benzylcyclohexanol. There was obtained 3.0 g. (57%) of 2-octylcyclohexanone; b.p. 155-159° (12 mm.), n_D^{25} 1.4625.

The semicarbazone was made and recrystallized three times from ethanol-water; m.p. 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%.

The crude 2-octylcyclohexanol was reacted with 3,5-dinitrobenzoyl chloride in pyridine but no solid derivative was obtained.

Expt. C 18. - This is the final mixed reaction that was studied and for it, 76.5 g. of 4-methylpentanol-2 and 32.5 g. of octanol-1 were used. In the water trap were placed 1 g. of octanol-1 and 3 g. of the secondary alcohol. The reaction temperature varied from 151° to 165° during a 12.2 hr. reflux period while collecting 3.4 ml. (75%) of water and 0.095 mole of hydrogen.

The reaction components were isolated to yield 53 g. of recovered 4-methylpentanol-2 which distilled at 60-63° (30 mm.) and 11 g. of octanol-1 which distilled at 90-93° (14 mm.). The product, 20 g. (38%), which was 2-methyltridecanol-4, distilled at 147-148° (14 mm.); n_D^{25} 1.4404. There remained 15 g. of non-distilled material.

Anal. Calcd. for $C_{14}H_{30}O$: C 78.43%, H 14.11%. Found: C 78.78%, 78.73%; H 14.10%, 14.20%.

The compound was converted to its allophanate and recrystallized twice from ethanol. It melted at 90-91.5° with slow heating (2° to 5° per min.) but it was noticed that if the compound was placed in the melting point bath above 60° it melted. When the temperature was rapidly raised from room temperature, the substance melted at about 55° to 60° but remained cloudy and then cleared at about 89°. This peculiarity in the melting point may be due to allotropic modifications.

Anal. Calcd. for $C_{16}H_{32}O_3N_2$: C 63.96%, H 10.74%. Found: C 64.35%, 64.26%; H 10.69%, 10.70%.

An equivalent weight determination for this compound (13.37 g.) was unsatisfactory since a large excess of p-toluenesulfonic acid was needed to catalyze the reaction. This apparently caused a side reaction which formed water because a 125% yield of water was obtained. It is necessary that further work be performed on this method before it becomes satisfactory for secondary alcohols.

D. The Nature of the Reaction

There are five experiments included here which were designed to show specific features of the reaction. All distillations were through an 8 in. Vigreaux column.

Expt. D 1. - Into the standard apparatus was placed 102 g. (1.0 mole) of hexanol-1 and 6.8 g. (0.175 mole) of potassium was reacted with it in the prescribed manner. To the resulting solution there was added 2.0 g. of hexanal which had been purified by a sodium carbonate wash followed by drying and distillation. After 22.5 hrs. at the reflux temperature (172°), the original yellow solution was colorless but only 0.02 ml. of water had collected. There was then added 8.0 g. (0.08 mole) of hexanal and the solution refluxed for 12 hrs. longer. This gave 2.9 ml. of water as the temperature increased from 171° to 180° and there was no gas evolved.

There were obtained 62 g. of recovered hexanol (with no odor of hexanal), 22 g. (21%) of 2-butyloctanol-1, which distilled at 108-110° (2.5 mm.); n_D^{25} 1.4402. There were also 20 g. of non-distilled residue and 2 g. of hexanoic acid.

Expt. D 2. - This reaction was performed to determine the effect on the Guerbet reaction of having mainly alkoxide with little alcohol present. The isolation of a product is of interest. One mole (102 g.) of hexanol-1 was placed in the standard apparatus and 0.3 mole (11.7 g.) of potassium was added as previously described. The excess hexanol-1 was distilled off with stirring to leave the solid white potassium hexoxide. A total of 65 g. (91%) of the free hexanol-1 was recovered. The cake was broken up and 200 ml. of p-cymene was added with vigorous stirring. The exposure of the potassium hexoxide to the air caused it to turn brown which was probably due to air oxidation. To the solution was added 2.0 g. of U.O.P. nickel and it was heated to reflux for 5.5 hrs. during which time the temperature varied from 173° to 175°. No water distilled and only 0.029 mole of hydrogen was collected.

Purification of the reaction mixture gave 5 g. of a colorless liquid distilling from 90° to 102° (2.5 mm.) and 5 g. of a colorless product from 102° to 108° (2.5 mm.); n_D^{25} 1.4412. There were 2 g. of distillation residue and 18 g. of hexanoic acid.

The second fraction above is apparently 2-butyloctanol-1 but the first fraction contained an aldehyde. It gave positive tests with the 2,4-dinitrophenylhydrazine and fuchsin-aldehyde reagents. It was converted to its 2,4-dinitrophenylhydrazone and recrystallized twice from ethanol to give golden plates; m.p. 95-96°.

Anal. Calcd. for $C_{18}H_{28}N_4O_4$: C 59.32%, H 7.75%, N 15.37%. Found: C 59.41%, 59.48%; H 7.83%, 7.95%; N 15.61%, 15.47%.

From these results and because of the starting alcohol used, it would appear that this compound is 2-butyloctanal. To show that it was not 2-butyl-2-octenal, this latter compound was prepared in a small amount by an aldol condensation. This material, a pale yellow oil, distilled at 103-104° (3 mm.); n_D^{25} 1.4551. Its 2,4-dinitrophenylhydrazone was made which, when recrystallized twice from ethanol, yielded brillant red needles melting at 133-134°.

Anal. Calcd. for $C_{18}H_{26}N_4O_4$: C 59.65%, H 7.23%, N 15.46%. Found: C 59.73%, 60.00%; H 6.99%, 6.99%; N 15.47%, 15.42%. A mixture melting point determination with the above 2,4-dinitrophenylhydrazone gave a melting point range of 85° to 108°.

Expt. D 3. - This experiment represents an attempt to rearrange 2-ethyl-2-hexenol-1 to 2-ethylhexanal. Into a 500 ml., three-necked flask equipped with a condenser, a half-moon mechanical stirrer and a thermometer was placed 74 g. (1.0 mole) of t-butyl alcohol (b.p. 81-82°). The flask was swept with nitrogen for a few minutes and then 3.9 g. (0.1 mole) of potassium was added in small pieces while stirring the alcohol. The solution was protected from atmospheric moisture by a calcium chloride tube and after all of the potassium had reacted, 22.0 g. (0.17 mole) of 2-ethyl-2-hexenol-1 was added. (The preparation of this compound is given below.) The solution was held at reflux (87°) for twenty min. and then poured into 100 ml. of cold water. The organic layer was washed once with 50 ml. of water and the combined water layers were extracted twice with 50 ml. portions of ether which were added to the organic layer, dried over anhydrous magnesium sulfate and distilled. There was recovered 19.7 g. (90%) of the 2-ethyl-2-hexenol-1, which distilled at 86-86.4° (18 mm.); n_D^{25} 1.4493.

Expt. D 4. - In the same apparatus as used in expt. D 3 was placed 65 g. (0.5 mole) of 2-ethylhexanol-1 and 3.9 g. (0.1 mole) of potassium was reacted with it. The solution was heated to 150° and 19.7 g. (0.15 mole) of 2-ethyl-2-hexenol-1 was added in one portion. The temperature was maintained at 150° to 160° for 7.0 hrs. with the reaction mixture under an atmosphere of nitrogen.

The mixture was poured into 100 ml. of water and the layers were separated. The water layer was extracted twice with 50 ml. portions of ether which were combined with the organic layer, dried and distilled. This gave 67 g. of material, distilling at 81-86° (15 mm.), which was mainly 2-ethylhexanol-1 and may have contained some of the unreacted alcohol. Further distillation gave a fraction (3.5 g.) from 122° to 143° (15 mm.); n_D^{25} 1.4494. The next fraction (2.3 g.) distilled at 144-148° (15 mm.); n_D^{25} 14526. This latter fraction is believed to be bis-(2-ethylhexyl)ether (lit.[11] b.p. 144-146° at 14 mm.). Several carbon and hydrogen analyses were performed for this substance but it gave erratic results. Since only a small amount of material was obtained, it was not further purified.

The water layer, by the standard purification procedure, yielded 3 g. of 2-ethylhexanoic acid, distilling at 120-122° (15 mm.), n_D^{25} 1.4271, leaving 2 g. of distillation residue. The calculated neutral equivalent is 144 and the values obtained experimentally were 149 and 148. The amide was made and after two recrystallizations from water, melted at 100-101° (lit.[27] 101-102°). The literature physical constants for this acid are:[95] b.p. 119-121° (14 mm.), n_D^{25} 1.4255.

Preparation of 2-Ethyl-2-hexenal.* - This compound was prepared according to Haeusermann.[76] Eighty-five g. (1.18 mole) of butanal yielded 64 g. (86%) of 2-ethyl-2-hexenal; b.p. 65-65.2° (15 mm.), n_D^{25} 1.4493. Haeusermann gives: yield 86%, b.p. 59.5-60° (10 mm.), n_D^{18} 1.4556.

Preparation of 2-Ethyl-2-hexenol-1.* - This compound was prepared by the procedure of Nystrom and Brown.[96] In a 500 ml., three-necked flask equipped with a half-moon mechanical stirrer, a dropping funnel and a Friedrichs condenser, which supported a calcium chloride tube, was placed 100 ml. of an ether solution containing 4.0 g. (0.11 mole) of lithium aluminum hydride. A solution of 25.2 g. (0.20 mole) of 2-ethyl-2-hexenal in 75 ml. of ether was added through the dropping funnel at a rate

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*The author is indebted to Mr. R. G. Rice for this preparation.

(45 min. for complete addition) such as to maintain gentle refluxing. The mixture was stirred for 10 min. longer and then 5 ml. of water was cautiously added dropwise to decompose the excess lithium aluminum hydride. The contents of the flask were poured into 100 ml. of water and 10% sulfuric acid (200 ml.) was added until all of the solid material dissolved. The layers were separated and the water layer was extracted with two 50 ml. portions of ether which were added to the organic layer, dried over anhydrous magnesium sulfate and distilled. The product distilled at 86-86.8° (18 mm.); n_D^{25} 1.4493. The yield was 22 g. (86%). The literature physical constants for this compound are:[97] b.p. 68-71° (12 mm.), n_D^{22} 1.4418.

<u>Expt. D 5</u>. - This experiment was performed to determine if any ester could be present in the Guerbet reaction mixture. A high concentration of alkoxide was used since this gives a high yield of acid and the acid may form by hydrolysis of the ester during the isolation.

One-third mole (13 g.) of potassium was reacted with 1.0 mole of hexanol-1 in the standard apparatus. Two g. of U.O.P. nickel was added to the solution and 5 ml. of hexanol-1 was placed in the water trap which was not included in the recovered alcohol. The solution temperature at the beginning of refluxing was 201° and hydrogen was being evolved. During a 1.1 hr. induction period, the temperature decreased to 197° and 0.39 mole of hydrogen collected. Upon continuing the reaction for 35 min. longer, 0.47 ml. of water and 0.58 mole of total hydrogen collected. The final solution temperature was 225°.

The mixture was cooled to 15° and 30% acetic acid (90 ml.) was added with stirring until the aqueous layer was neutral. The nickel was removed by filtration and the neutral water layer was separated.

The organic layer was exhaustively extracted with saturated sodium bicarbonate solution until no further acid was obtained. The remaining organic layer was placed in a 500 ml. Erlenmeyer flask with 75 ml. of 10% sodium hydroxide. A condenser was attached and the flask was heated on a steam bath for 2 hrs. The mixture was cooled and the basic water layer was separated and acidified, but this did not yield any acidic material.

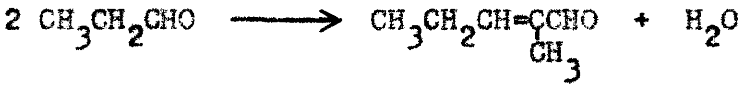
The sodium bicarbonate extracts were acidified and the organic acid removed. The remaining water layer was extracted twice with 50 ml. portions of benzene and these were added to the acid material. Distillation of the benzene solution yielded 27 g. of hexanoic acid, which boiled at 200° to 210°.

The organic layer from the attempted ester hydrolysis was dried over sodium sulfate and then distilled. This yielded 7 g. of recovered hexanol-1 and 38 g. (41%) of 2-butyloctanol-1 which boiled at 108-111° (3 mm.) and there remained 13 g. of non-distilled material.

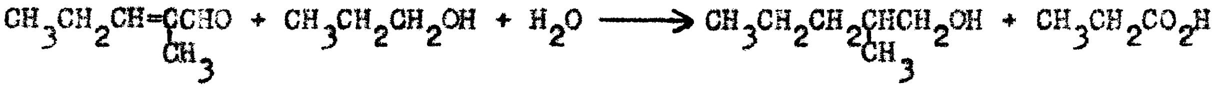
IV. SUMMARY

According to the recent work of Weizmann,[11] the Guerbet condensation proceeds as follows:

$$2\ \mathrm{CH_3CH_2CH_2OH} \xrightarrow{\mathrm{ROK}} 2\ \mathrm{CH_3CH_2CHO} + 2\ \mathrm{H_2} \tag{a}$$

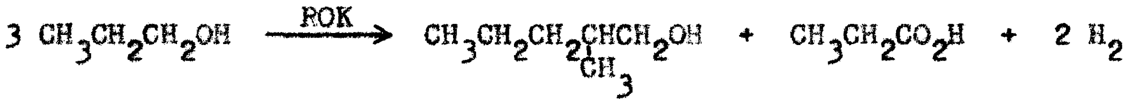


$$2\ \mathrm{CH_3CH_2CHO} \longrightarrow \mathrm{CH_3CH_2CH{=}\underset{CH_3}{C}CHO} + \mathrm{H_2O} \tag{b}$$



$$\mathrm{CH_3CH_2CH{=}\underset{CH_3}{C}CHO} + \mathrm{CH_3CH_2CH_2OH} + \mathrm{H_2O} \longrightarrow \mathrm{CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH} + \mathrm{CH_3CH_2CO_2H} \tag{c}$$

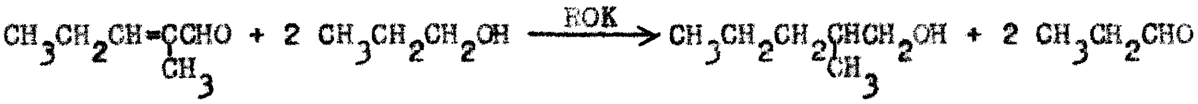
The sum of these equations is:



$$3\ \mathrm{CH_3CH_2CH_2OH} \xrightarrow{\mathrm{ROK}} \mathrm{CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH} + \mathrm{CH_3CH_2CO_2H} + 2\ \mathrm{H_2} \tag{d}$$

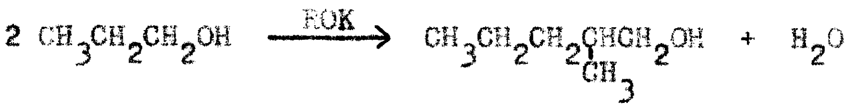
An autoclave was required for his work and the yields were only moderate, partly because of the undesirable side reaction which formed the acid.

In the present study, certain modifications were introduced and as a result an open reflux system could be used. With this system, the amounts of product alcohol, acid, water and hydrogen could be determined under a variety of conditions. The results of these and certain other studies suggested that, at least under the modified conditions, the reduction proceeds according to (e) rather than (c).



$$\mathrm{CH_3CH_2CH{=}\underset{CH_3}{C}CHO} + 2\ \mathrm{CH_3CH_2CH_2OH} \xrightarrow{\mathrm{ROK}} \mathrm{CH_3CH_2CH_2\underset{CH_3}{C}HCH_2OH} + 2\ \mathrm{CH_3CH_2CHO} \tag{e}$$

The major features of the reaction are given by (b) and (e), which upon addition give (f) as the primary over-all process:



$$2\ CH_3CH_2CH_2OH \xrightarrow{ROK} CH_3CH_2CH_2\underset{CH_3}{CH}CH_2OH + H_2O \qquad (f)$$

A detailed sequence of steps for (e) is proposed.

In corroboration of a recent patent which came to the author's attention after the laboratory work had been completed, it was found that the reaction was catalyzed by nickel and that it was advantageous to remove the by-product water as rapidly as possible by distillation into a water trap.

A careful study was made to determine the optimum time and temperature and the optimum amounts of nickel catalyst and alkoxide. The reaction is readily carried out by dissolving the potassium in the reactant alcohol, adding the nickel and refluxing with stirring for one to five hours in most cases. Since the temperature depends upon the alkoxide concentration and the boiling points of the reactant and product alcohols, the effect of varying the temperature was determined by studying the series of normal primary alcohols with four to ten carbons. The desired products were obtained with conversions of 42% to 62% and in yields of about 70%. It was found that at the higher reflux temperatures, equally good yields of the product alcohols were formed rapidly in the absence of the catalyst. Under optimum conditions, the amount of acid formed was approximately 5% by weight of the starting alcohol. The amount of acid increased and the amount of water decreased with increasing alkoxide concentration.

A variety of pairs of alcohols were studied in an attempt to determine which mixed condensation products could be prepared satisfactorily.

It was found that the benzyl alcohols condensed in good yields with normal primary alcohols and with certain secondary alcohols, including cyclohexanol. Normal primary alcohols also condensed satisfactorily with these secondary alcohols.

The product alcohols were characterized by conversion to the solid allophanates and in certain cases by measuring the volume of water evolved upon etherification with triphenylcarbinol.

It is felt that as a result of this study the Guerbet reaction has been developed into a facile laboratory process suitable for making a variety of alcohols in good yield.

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