one new phenoxymethyl aryl ketone have been prepared. Phenoxymethyl methyl and ethyl ketones, previously reported in the literature, have been resynthesized in a higher degree of purity and more adequately characterized.

2. The method of Blaise and Picard was shown to be unsatisfactory for the production of these phenoxymethyl alkyl ketones and a better procedure was developed.

3. Determinations of vapor pressures were made for phenoxyacetonitrile and the phenoxymethyl alkyl ketones at selected temperatures. These data have been recorded in both graphic and tabular form and used to determine the values *A* and *B* in Young's vapor pressure equation. These constants were then employed to calculate the latent heat of vaporization of the respective compounds.

4. Eight 5,5-disubstituted hydantoins of the new aryloxy-alkyl type have been prepared.

5. N-Methylation of one of these hydantoins, to form 1,3,5-trimethyl-5-phenoxymethylhydantoin, was effected.

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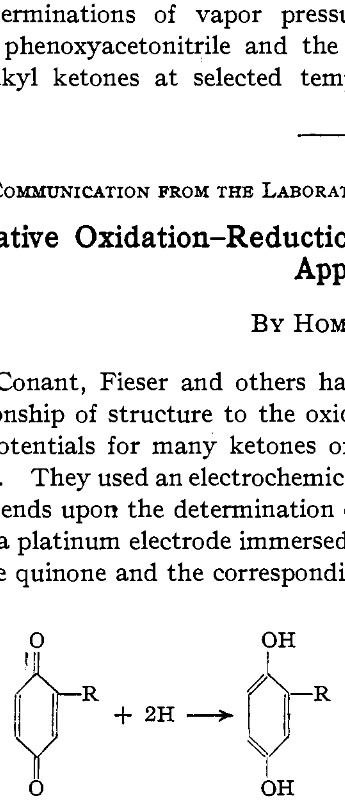
[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Relative Oxidation–Reduction Reactivities of Ketones and Aldehydes and Applications in Synthesis[1]

BY HOMER ADKINS AND FRED W. COX

Clark, Conant, Fieser and others have shown the relationship of structure to the oxidation–reduction potentials for many ketones of the quinone type. They used an electrochemical method which depends upon the determination of the potential at a platinum electrode immersed in a mixture of the quinone and the corresponding hydroquinone.



Since this procedure is not applicable to the common ketones, a method has been sought in this Laboratory whereby the relative reducing power of various alcohols and the oxidizing power of the corresponding ketones could be determined. Because the ordinary ketones cannot be measured against their alcohols by the electrochemical method, it seemed necessary to equilibrate one ketone against another and thus secure a measure of their relative oxidation–reduction reactivities. Several years ago attempts were made to set up equilibrium in the systems of the type

$$R_2CO + R'_2CHOH \longleftrightarrow R_2CHOH + R'_2C{=}O$$

but reaction could be attained only at relatively high temperatures over such catalysts as nickel or copper–chromium oxide and under conditions where side reactions occurred.

Recently it has been found possible to establish equilibrium at 40 to 100° without side reactions through the use of aluminum *t*-butoxide. At the same time the usefulness of the polarograph as a means of determining the concentrations of ketones in a mixture has become evident[2] so that it has been used in the analysis of the equilibrium mixtures. Incidentally the polarograph enables independent measurements to be made of the reduction potential of a number of ketones and aldehydes.

Our experimental results will be discussed in four sections: first, the use of a polarograph as a means of determining directly the reduction potential of a ketone or aldehyde; second, the use of the polarograph as a means of determining the concentrations of two ketones in a mixture; third, the determination of relative oxidation–reduction reactivities by direct equilibration of two ketones; and, fourth, some practical applications of these methods to synthetic organic chemistry.

Reduction Potentials as Determined with a Polarograph.—A discussion of reduction potentials determined with a polarograph requires first a consideration of the method of determination. When a polarogram is made upon a solution of certain aldehydes and ketones a "break" in the curve is shown, which is characteristic of the compound.

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[1] This investigation was supported in part by the Wisconsin Alumni Research Foundation.

[2] Borcherdt, Meloche and Adkins, THIS JOURNAL, **59**, 2171 (1937).

Figure 1 shows a section of a typical polarogram. It may be seen that as the voltage increases, the curve departs from a straight line at A, which is the lowest voltage at which the compound in question *shows* reduction. The curve then becomes more nearly parallel with the horizontal axis and then after a time turns upward so that at E it again becomes a straight line, more or less perpendicular to the x-axis. Now for a typical ketone, acetophenone, dissolved in an isopropyl alcohol–water solution containing ammonium chloride, the value at A was 1.31 v., while at E it was 1.73 v. Heyrovsky[3] recommends that the reduction potential be calculated as follows: tangents are drawn at A and E, and a line drawn through the horizontal portion of the curve intersecting the tangents at B and D. The values of the voltage at B and D are then taken, and their average, C, is considered to be the reduction potential. For a typical experiment the values at B, D and C were 1.43, 1.69 and 1.56 v., respectively.

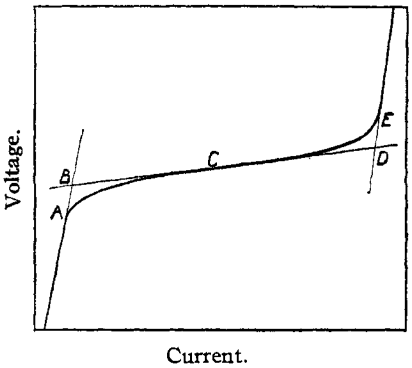

Fig. 1.—Method of measuring reduction potentials on a polarogram.

The reduction of the ketone occurs at the interface between the dropping mercury cathode and the solution so that the significant potential is at this boundary. The figure for the polarographic reduction potential given above represents the algebraic sum of the two potentials at the cathode and at the anode of the cell. The potential at the anode is of the order of 0.05 v. and is constant for a given concentration of an electrolyte, so that the discussion for the present will be based upon the potential across the cell.

The effect of variation in the electrolyte on the polarographic reduction potential of a given compound is apparently small. For example, in the case of ten ketones whose potential was determined both in an ammonium chloride and in a tetramethylammonium hydroxide solution the greatest deviation was 0.07 v. while the average difference was 0.04 v. In five of the cases the higher potential was in the acid and in five cases in the alkaline solution.

The effect of variation in the electrolyte on the organic compound present in the solution undergoing test may be very considerable. If the compound is enolizable it may show quite a different reduction potential in the alkaline as compared to the acid solution. Vanillin, *p*-hydroxybenzaldehyde, salicylaldehyde, dibenzoylmethane, flavone, γ-pyrone and flavanone show reduction potentials as much as 0.3 v. lower in the acid as compared with the alkaline solution.

The presence of another reducible compound in the cell may affect the reduction potential of a given compound. For example, the reduction potentials of benzophenone and of propyl phenyl ketone were about 0.03 v. higher when the other ketone was present. Acetophenone showed a reduction potential 0.08 v. higher in the presence of benzophenone than in its absence.

It will be apparent from the above description of the method of measurement that a reduction potential of a ketone determined on a polarograph is a rather arbitrary figure which is the average of rather widely different values, and is usually as much as 0.2 v. higher than the lowest potential at which reduction takes place. The values are readily reproducible with an accuracy of 0.01 or 0.02 v., yet for the present variations of much less than 0.1 v. should not be considered as significant.

It should be pointed out that a compound may have two different reduction potentials which may be so close together that the break between them is hardly perceptible. For example, benzalacetone in tetramethylammonium hydroxide apparently showed a reduction potential of 1.24 v. When the same compound was studied in ammonium chloride it was found to have two reduction potentials, one at 1.12 and one at 1.36 v. A reexamination of the first polarogram showed that it also gave a hint of two breaks, so that the value of 1.24 was really the average of two reduction potentials.

One further limitation on the determination of reduction potentials with a polarograph is that the cations of the electrolytes, ammonium chloride and tetramethylammonium hydroxide, begin to be re-

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[3] Heyrovsky and Ilkovic, *Coll. Czech. Chem. Comm.*, 7, 198 (1935).

duced at about 1.8 and 2.1 v., respectively. Thus acetone, acetylacetone, cyclopentanone, triacetoneamine and presumably other saturated aliphatic ketones do not show a reduction potential, since it is higher than 2.1 v.[4]

TABLE I

POLAROGRAPHIC REDUCTION POTENTIALS OF VARIOUS COMPOUNDS

	Reduction potentials		
Compounds	1st	2nd	Reported
Aldehydes			
CH_3CHO	−1.87		−1.60* S., W.
C_2H_5CHO	1.92		1.60* S., W.
n-C_3H_7CHO	1.90		
i-C_3H_7CHO	1.91		
n-C_4H_9CHO	1.90		
n-$C_5H_{11}CHO$	1.98		
n-$C_6H_{13}CHO$	1.90		
C_6H_5CHO	1.34		1.25* S., W.
$CH_3CH{=}CHCHO$	1.37 1.36*	1.80 1.64*	
p-$CH_3OC_6H_4CHO$	1.46 1.50*		1.33* W.
p-HOC_6H_4CHO	1.75 1.50*		1.38* W.
o-HOC_6H_4CHO	1.61 1.43*		1.28* W.
4-OH-3-$CH_3OC_6H_3CHO$	1.73 1.46*		1.33* W.
3,4-$(CH_2O_2)C_6H_3CHO$	1.39 1.43*		1.30* W.
Alkyl aryl ketones			
o-$HOC_6H_4COCH_3$	1.64^{B} 1.61^{*B}		
i-$C_3H_7COC_6H_5$	1.61 1.58*		
n-$C_3H_7COC_6H_5$	1.60 1.55*		
$CH_2BrCH_2COC_6H_5$	1.60		
$(CH_3)_2CBrCOC_6H_5$	1.55		
$C_6H_5CH_2CH_2COC_6H_5$	1.54		
$CH_3COC_6H_5$	1.52 1.56*		1.32* S., 1.44* W.
p-$BrC_6H_5COCH_3$	1.52 1.48*		
$C_6H_5CH_2COC_4H_5$	1.48 1.47*		
Diaryl ketones			
$C_6H_5COC_6H_5$	1.35 1.30*		1.23* W., 0.89* S.
p-$ClC_6H_4COC_6H_5$	1.28 1.21*		
o-$C_2H_5O_2CC_6H_4COC_6H_5$	1.50		
Unsaturated ketones			
$CH_3COCH{=}CHC_6H_5$	1.12* 1.24	1.36*	
$CH_3COCH{=}C(CH_3)_2$	1.64 1.61*		
$CH_3COCH{=}CHCH{=}CHCH_3$	1.25		
$CH_3COCH{=}CHC_4H_3O$	1.14 1.14^{*B}	1.40	
$C_6H_5COCH{=}CHCH{=}CHC_6H_5$	0.93	1.11	
$C_6H_5CH{=}CHCOCH{=}CHC_6H_5$	1.22		
$C_6H_5CH{=}CHCOCH_2C_4H_9$-$t$	1.26		
1,3-Diketones			
$CH_3COCH_2COC_6H_5$	....	1.80	
$CH_3COCH(C_2H_5)COC_6H_5$	1.52	1.79	
$CH_3COCH(C_4H_9)COC_6H_5$	1.55	1.81	
$CH_3COCH(CH_2C_6H_5)COC_6H_5$	1.49	1.77	
$C_6H_5COCH_2COC_6H_5$	1.60^{B} 1.30^{*B}	...	
$C_6H_5COC(C_2H_5)_2COC_6H_5$	1.45	...	
o-HO—$C_6H_4COCH_2COC_6H_5$	1.51^{B} 1.42^{*B}	1.79	
$C_6H_5COCH_2COC_4H_3O$	1.53	1.88	
$(CH_3)_3CCOCH_2COC_6H_5$	....	1.89	
$CH_3COCH_2COC_4H_3O$	....	1.79	
Miscellaneous compounds			
9,10-Anthraquinone	0.6		
9,10-Phenanthraquinone	.4		
p-Benzoquinone	.1*		
Benzil	.7	1.4	0.58* W.
Benzoin	.7	1.4	1.22* W., 1.18 S.
Diacetyl	.93*	1.68*	
Pyruvic acid	1.14^{*B}		
Cholestenone	1.30*		
Quinoline	1.27* 1.54		
Flavone	1.43^{B} 1.26^{*B}		
γ-Pyrone	1.91^{B} 1.69^{*B}		
Flavanone	1.12 1.47^{*B}	1.89B	
2-Ethylchromone	1.66^{B} 1.53^{*B}		

* The starred numerals were determined in an ammonium chloride, the others in a tetramethylammonium hydroxide solution. The potentials marked B were determined by R. H. Baker upon materials supplied by Ralph Mozingo. W. and S. refer to measurements made by Winkle and Proske,[5] and Shikata and Tachi,[6] respectively.

The aliphatic aldehydes show reduction potentials in the vicinity of 1.9 v. (Table I). The phenyl alkyl ketones show a lower reduction potential of the order of 1.5 to 1.6 v. Benzophenone and benzaldehyde are still lower at about 1.3 v. Certain hydroxy- and methoxybenzaldehydes show higher reduction potentials than the parent compound. Still lower are the unsaturated ketones such as benzalacetone, furfuralacetone and dibenzalacetone, which show a reduction potential of the order of 1.1 to 1.2 v. Pyruvic acid is in the same range. The highly unsaturated ketones such as the quinones and benzil have the lowest reduction potentials of the compounds measured, p-benzoquinone being reduced at 0.1 v. or less. Diacetyl showed a reduction potential (0.93) somewhat higher than benzil but lower than any of the unsaturated monoketones. A number of compounds show two reduction potentials, *e. g.*, benzoin at 0.7 and 1.4 v., while several 1,3-diketones show one break at about 1.5 and another at about 1.8.

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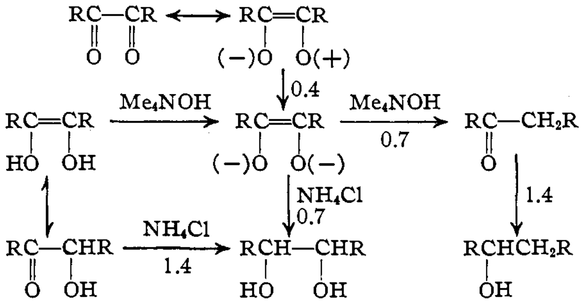
(4) The reduction potential of dialkyl ketones cannot be measured directly but if the relationship between crotonaldehyde and butyraldehyde holds for the relationship of mesityl oxide to methyl isobutyl ketone, then the latter type of compound has a reduction potential of about 2.2 v.

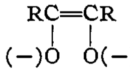
(5) Winkle and Proske, *Ber.*, **69**, 693, 1917 (1936).

(6) Shikata and Tachi, *Mikrochemie*, **12**, 62 (1933).

One general tendency is quite marked, *i. e.*, increase in unsaturation decreases the reduction potential. The aromatic aldehydes and crotonaldehyde are much lower than the saturated aldehydes, the alkyl aryl ketones and mesityl oxide are lower than the saturated ketones, while the diaryl ketones are lower than the alkyl aryl ketones. The unsaturated aliphatic aryl ketones are much lower than the saturated alkyl aryl ketones. Lowest of all in reduction potentials are the quinones and the α-diketones. The effectiveness of an alkene linkage in lowering the reduction potential is only a little less than that of an aryl group.

The behavior of benzil and benzoin in a polarographic cell is of considerable interest. Both compounds give a break at 0.7 and at 1.4 v. in alkali, while in an acid solution benzil gives breaks at 0.4 and 0.7 v. Benzoin in an ammonium chloride solution gives a break at 1.4 v. These facts may be rationalized by the following scheme where R is phenyl.



This scheme involves three assumptions, *i. e.*, that benzoin enolizes in an alkaline solution, that the ion  $\underset{(-)O\ \ O(-)}{RC{=}CR}$ in an alkaline solution is first reduced to benzyl phenyl ketone, while in a slightly acid solution it is reduced to a glycol. There can be no question about the validity of the first assumption, while the second is well justified by the fact that the polarograms show that benzoin is reduced in two steps in tetramethylammonium hydroxide solution. The highest break is at 1.4 v., which is only 0.08 v. below that found for pure benzyl phenyl ketone which is postulated as the intermediate compound in the two step alkaline reduction. The glycol cannot be an intermediate compound because it shows no reduction potential on a polarograph. There is no justification for the third assumption except that it offers a reasonable rationalization of the facts.

The polarographic reduction potentials of a number of the compounds listed in the tables have been previously reported. In a general or qualitative sense our values are in agreement with those previously published. However, exact comparisons are impossible since the same method of measuring the polarograms has not been used by all investigators. We have used the method of the "half wave potentials" now recommended by Heyrovsky, but which he did not use in his earlier work. Winkle and Proske use the voltage at A in Fig. 1, while Shikata and Tachi use the "45° tangent method," *i. e.*, the point at which an increase of 0.01 v. produces an increase of 10^{-8} amperes in the current. In the case of acetone, pyridine and acetylacetone we have been unable to detect any break below 1.9 v., although Shikaga reports 1.28, 1.30 and 1.23 for these compounds.

The Determination of the Ratio and Concentration of Ketones with a Polarograph.—The method previously described[2] for the polarographic determination of ketones has proved very satisfactory and further study has only served to confirm the validity of the procedure. For purposes of analysis we regard the polarograph as we would a colorimeter, *i. e.*, as a means of comparing solutions of unknown concentration with those of known concentration. One cannot *expect* to obtain accurate and dependable analytical results unless the solution of unknown concentration contains the same components (and no others) in approximately the same amounts as the solution of known concentration. While it is true, as will be illustrated below, that in some cases the concentration of the ketone is precisely proportional to the wave height and independent of the concentration of other reducible compounds in the cell, yet it is not safe to assume that this is true in a given case without objective evidence. The truth of these statements is shown by the behavior of mixtures of acetophenone and benzophenone summarized in line A of Fig. 2.

Figure 2 serves four purposes: first, it shows that the wave height for a given ketone is sometimes but not always proportional to its concentration in the cell; second, it shows that the relation of the wave height to concentration may be a function of the nature and concentration of a second ketone in the cell; third, it illustrates the simplest way, through the use of two standard solutions, of converting the ratio of wave heights to the ratio of ketones; and, fourth, it illustrates the accuracy of the polarographic method of analysis for ketones.

The standard solutions referred to in line A of Fig. 2 were prepared so that the 5 ml. of solution in the polarographic cell contained in one case (S_1) 0.153 mg. of benzophenone and 0.505 mg. of acetophenone, *i. e.*, moles B/moles A = 0.2. The other standard solution (S_2) contained 1.225 mg. of benzophenone and 0.505 mg. of acetophenone, *i. e.*, moles B/moles A = 1.6. The ratio of the wave heights in the polarograms were for S_1, 3.44 cm./6.68 cm. = 0.51 and for S_2, 17.29 cm./4.81 cm. = 3.59. The actual ratios of ketones in S_1 and S_2 (0.2 and 1.6) were plotted against the observed ratio of the wave heights 0.51 and 3.59, respectively, for these two solutions. A line drawn through the two points should represent the actual ratio of ketones corresponding to any observed ratio of wave heights.

The validity of the method of correction is shown by the fact that when it was applied to the polarograms made upon six solutions which contained 0.505 mg. of acetophenone and from 0.306 to 1.072 mg. of benzophenone the calculated ratio of ketones in no case varied by more than 3.4%, and on the average only 1% from the ratio of ketones known to be present in the solution. The agreement between the calculated values (represented by the line) and the actual ratio of ketones (represented by the dots) will be apparent from an inspection of Fig. 2.

The marked effect of benzalacetone upon the wave height of acetophenone is evidenced by the following data. A cell which contained 0.31 mg. of acetophenone gave a wave 5.66 cm. in height, while cells containing 0.31 mg. of acetophenone and in addition 0.15, 0.30 or 0.45 mg. of benzalacetone showed wave heights for acetophenone of 3.94, 2.50 and 1.68 cm., respectively. A cell containing 0.62 mg. of acetophenone to which had been added 0.00, 0.15, 0.30 or 0.45 mg. of benzalacetone gave wave heights for acetophenone of 9.61, 7.80, 6.23 and 4.96 cm., respectively. These data show that benzalacetone is very effective in lowering the height of the acetophenone wave. The concentration of acetophenone has very little effect in modifying the wave height of the benzalacetone wave. For example, increasing the concentration of acetophenone in the cell from 0.31 to 0.62 mg. did not decrease the wave height of benzalacetone by more than a few per cent. This illustrates an important consideration in preparing standard solutions for polarographic analysis. Variations in the concentration of B have a much larger effect upon the wave height of A, than variations in the concentrations of A have on the wave height of B, where B is the substance with the lower reduction potential. Therefore in making up standard solutions of A and B, the concentration of B should be constant, the necessary variations in ratio being obtained by varying the concentration of A.

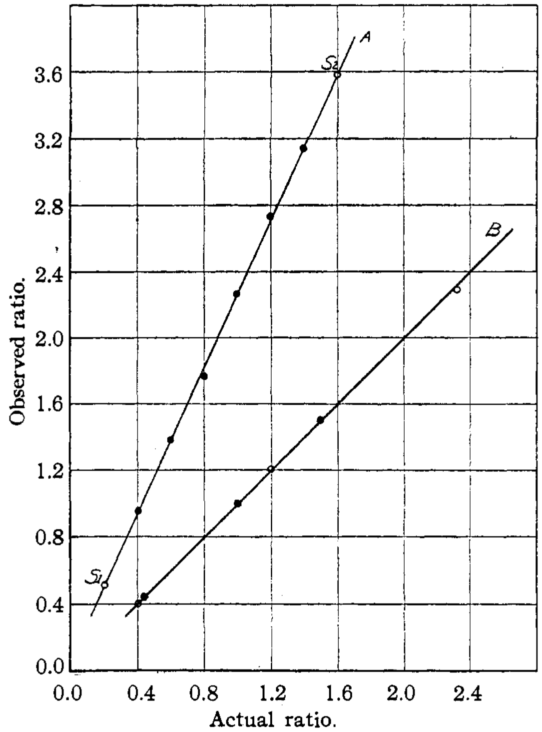


Fig. 2.—Relation of ratio of ketones to ratio of wave heights. The upper line A is for mixtures of acetophenone and benzophenone, while the lower line B is for benzophenone with *n*-propyl or isopropyl phenyl ketone. The "b" method[2] was used in measuring the polarograms.

In contrast to the cases considered above, the wave heights of polarograms made upon mixtures of *n*-propyl phenyl ketone and benzophenone, and of isopropyl phenyl ketone and benzophenone were quantitatively proportional to the concentration of the ketones and independent of the second ketone present in the mixture. This is shown by the fact that the ratios of the wave heights for three mixtures of each of the two pairs of ketones are within 0.3 to 3.0% of a line drawn at an angle of 45° with the coördinates. The data are plotted in line B of Fig. 2. In these solutions the amount of benzophenone in the cell varied from 1 to 2.5 mg., while the amounts of the propyl and isopropyl ketones varied from 0.9 to 2.0 mg. The wave heights varied from 3.44 to 17.26 cm.

Determination of Relative Oxidation–Reduction Reactivities of Ketones from Concentrations at Equilibrium.—The reduction potential of a ketone as determined with a polarograph apparently enables one to predict at least qualitatively its tendency to be reduced by an alcohol. That is to say, of two ketones the one with the higher reduction potential will be found in the larger concentration in an equilibrium of the type[7]

$$R_2CO + R'_2CHOH \longleftrightarrow R_2CHOH + R'_2CO$$

For example, if diphenylcarbinol is equilibrated with acetone there are only a few per cent. of benzophenone formed, because the reduction potential of acetone is so much higher than is that of benzophenone. Similarly, if crotonaldehyde is equilibrated with isopropyl alcohol the concentration of the aldehyde at equilibrium is less than 10%. Mixtures of benzil and benzyl alcohol, and of phenanthraquinone and methylphenylcarbinol show a predominance at equilibrium of the carbonyl compound having the higher reduction potential. None of these systems are very well suited for quantitative study because of the relatively large difference in the reduction potentials and therefore the relatively large difference in the concentrations of the carbonyl compounds at equilibrium. Acetophenone and benzophenone differ from each other by less than 0.2 v. so that attempts were made to determine the concentrations at equilibrium in the system

$$(C_6H_5)_2C{=}O + C_6H_5CHOHCH_3 \longleftrightarrow (C_6H_5)_2CHOH + C_6H_5C(O)CH_3$$

It was found as expected that the concentration of acetophenone at equilibrium was much higher than that of benzophenone, but dypnone was also formed by the condensation of acetophenone under the influence of the aluminum *t*-butoxide. This made it impractical to follow the reaction, since dypnone would itself be reduced and thus a complicated set of equilibria would be set up. A similar difficulty was encountered in attempting to equilibrate acetophenone with furfural- or benzalacetone.

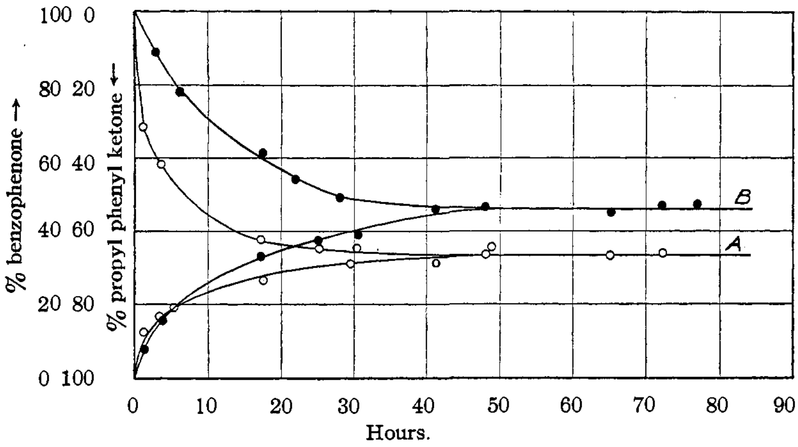


Fig. 3.—The rate of approach to equilibrium $(C_6H_5)_2C{=}O + RCHOHC_6H_5 \rightleftarrows (C_6H_5)_2CHOH + RCOC_6H_5$, where R is *n*-propyl (A) at 80° or isopropyl (B) at 100°.

The reactions of benzophenone with *n*-propyl or isopropyl phenyl ketone went to equilibrium without side reactions

$$(C_6H_5)_2CO + C_6H_5CHOHC_3H_7 \longleftrightarrow (C_6H_5)_2CHOH + C_6H_5C(O)C_3H_7$$

Equilibrium was established from both directions and the polarographic method of analysis used to determine the ratio of the ketones at equilibrium. The data are plotted in Fig. 3. The *n*-propyl differed markedly from the isopropyl ketone. The former reacted much more rapidly with benzophenone and was half way to equilibrium after about three hours at 80°. The isopropyl ketone could not be equilibrated conveniently with benzophenone at 80° because of the slowness of reaction. The reaction had gone half way to equilibrium after about eight hours at 100°. The two ketones also differed in the concentrations at equilibrium. The equilibrium mixtures in the case of the *n*-propyl phenyl ketone contained 67 parts of that ketone as compared to 33 parts of benzophenone. There were 54 parts of isopropyl phenyl ketone and 46 parts of benzophenone at equilibrium. Thus it is seen that there is a marked difference on this basis between the oxidation–reduction potential of the isopropyl as compared to the *n*-propyl ketone, while the two ketones have practically the same reduction potential as determined on the polarograph. The reduction of a ketone in the determination of a reduction potential on a polarograph is

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(7) It must be remembered that while the reactions are formulated as above for simplicity's sake, yet actually there is aluminum *t*-butoxide present so that the alcohols are at least in part present as their alkoxides and the ketones presumably form addition products.

presumably an irreversible process.[8] The new method described herewith for the determination of relative reduction potentials involves a reversible process just as does the classical method for quinones referred to in the introduction of this paper. The new method also makes it possible to compare the rates of oxidation–reduction, which cannot be accomplished readily by the older method.

Sufficient data are not at hand to justify assigning numerical values to the relative oxidation–reduction potentials of the few ketones studied. However, it seems probable that by comparing ketones and aldehydes with others differing from them by a few tenths of a volt, numerical values expressing their oxidizing power can be assigned to carbonyl compounds over the range from the quinones to the dialkyl ketones.

Practical Application of Relative Oxidation–Reduction Reactivities, Polarographic Analysis, and Aluminum *t*-Butoxide.—The alcohols R_2-CHOH whose ketones have a high reduction potential are the most effective reducing agents, since at equilibrium there will be a high concentration of R_2CO and of the desired alcohol. The dialkyl ketones have the highest reduction potentials among aldehydes and ketones, therefore, isopropyl alcohol is perhaps the best reducing agent. There is, therefore, no reason to believe that the well-known aluminum isopropoxide can be replaced by a more effective alkoxide. Polarographic analysis is, however, of advantage in ascertaining the conditions under which a given reduction can be most advantageously made. For example, polarographic analyses made on reaction mixtures of crotonaldehyde and aluminum isopropoxide showed that the reaction was complete after three to four hours at 40° and that there was little advantage in distilling out the acetone since the equilibrium was so favorable to the formation of crotyl alcohol. Upon the basis of these and other observations a method is described in the experimental part which we believe is an improvement over that described by Young, Hartung and Crossley.[9]

The choice of a ketone (X) to be used as an oxidizing agent is by no means so clearly indicated as is the choice of an alcohol to be used as a reducing agent. In order that there may be favorable concentrations at equilibrium, the ketone (X) must have a considerably lower reduction potential than the aldehyde or ketone (Y) to be formed. It would be advantageous to remove (Y) as rapidly as possible from the reaction mixture in order to drive the reaction in that direction. Suitable ketones (X) to be used as oxidizing agents appear to be the quinones and the α-hydroxy ketones, and α-diketones which have reduction potentials of considerably less than 1 v. on the polarograph.

The alcohol to be oxidized must be present in the reaction mixture as an alkoxide. The formation of the alkoxide directly from the alcohol and aluminum is in most cases inconvenient and in many cases not feasible. It is preferable to prepare the alkoxide of the alcohol to be oxidized through reaction with another alkoxide which can be kept in stock. The alcohol from which this stock alkoxide is to be derived must be a tertiary alcohol, otherwise it would be oxidized in the reaction mixture. Attempts to prepare aluminum *t*-butoxide, which is the most obvious choice for a stock alkoxide, have until recently been unsuccessful.[10] In 1936 R. V. Oppenauer[11] at Amsterdam and E. E. Bowden in this Laboratory prepared the compound which is now readily obtained in any desired quantity. Oppenauer made the first application of the *t*-butoxide in the oxidation in an acetone solution of unsaturated steroids to the corresponding ketones. Upon the basis of the facts here presented acetone is not the best oxidizing agent from the standpoint of the concentrations at equilibrium in a homogeneous solution. We are inclined to suspect that the real oxidizing agent in Oppenauer's preparations is not acetone but one of its condensation products. These substituted ketones have lower reduction potentials and would therefore be better oxidizing agents than acetone. Such condensation products are formed from acetone under the conditions used by Oppenauer for the preparation of stereneones.

Another useful application of aluminum *t*-butoxide was discovered in attempting to equilibrate acetophenone and benzophenone in the presence of the alkoxide. Polarograms made upon the reaction mixture showed the presence

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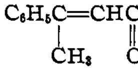
[8] In order that the reader may not lose contact with reality, it may be well to point out that a polarographic reduction potential involves the reaction occurring at the surface of an electrically charged droplet of mercury as it falls through an alcohol–water solution containing about 0.2 g. of ketone per liter.

[9] Young, Hartung and Crossley, THIS JOURNAL, **58**, 100 (1936).

[10] Adkins, *ibid.*, **44**, 2179 (1922).

[11] Oppenauer, *Rec. trav. chim.*, **56**, 137 (1937).

of a compound having a reduction potential corresponding to an unsaturated ketone such as benzal acetone. Therefore a sample of acetophenone was refluxed in dioxane with aluminum *t*-butoxide. From the reaction mixture dypnone  $C_6H_5\underset{CH_3}{\underset{|}{C}}{=}CH\underset{O}{\underset{\|}{C}}C_6H_5$ was isolated in a yield of about 30%. This suggests a method whereby compounds of the mesityl oxide type might be made from a number of ketones which do not readily undergo this reaction. Winston Wayne in this Laboratory has developed this method so that yields of the order of 80% have been obtained from several ketones.

Determination of Reduction Potentials on a Polarograph.—The potentials were determined with a Leeds and Northrup polarograph using the type of cell listed as "1" by Heyrovsky.[12] The cell contained 0.000005 mole of the carbonyl compound, dissolved in 5 ml. of a 50% (by volume) ethanol–water solution which was 0.1 *N* in ammonium chloride or 0.2 *N* in tetramethylammonium hydroxide. Nitrogen was used as the inert gas for flushing out the cell. Isopropyl is more satisfactory than ethyl alcohol as a solvent in polarographic analysis, and has been used in the more recent work. Both alcohols oxidize in air, to give acetone or acetaldehyde, respectively, but on account of its lower reduction potential the acetaldehyde interferes much more than does acetone.

Equilibration of Ketones.—Equimolecular amounts (0.083 mole) of a ketone and an alcohol were mixed with 44 ml. of dioxane. The mixture was contained in a 100-ml. three-necked round-bottomed flask held in an electrically heated oil-bath. The flask was fitted with a reflux condenser, a mechanical stirrer, and a pipet so designed that samples could be taken out without removing the pipet from the flask. Twenty-one grams of *t*-aluminum butoxide was added when the mixture had reached the temperature of 80 or 100°. Samples (1 ml.) were removed at intervals and hydrolyzed in 25 ml. of a 92.5% isopropyl alcohol–water solution. Polarograms were then made in a cell which contained 0.5 ml. of this hydrolysate, and 1 ml. of a *N* solution of tetramethylammonium hydroxide, made up to 5 ml. with 92.5% isopropyl alcohol. The measurements of volume given above need not be exact since the analysis depends upon the ratio, not the amounts, of ketones in the cell.

Crotyl Alcohol.—Aluminum isopropoxide was prepared by the reaction of 47 g. of aluminum, 500 ml. of dry isopropyl alcohol and 2.5 g. of mercuric chloride in a 2-liter round-bottomed flask provided with a reflux condenser. The mixture was heated on a steam-bath until reaction began and then the flask was cooled with cold water. After reaction was complete and the product was cold, a liter of dry isopropyl alcohol and 257 ml. (218 g.) of crotonaldehyde were added. The flask was provided with a mechanical stirrer, placed in an electrically heated oil-bath and maintained for four hours at approximately 50°. The excess solvent was then removed under 50–150 mm. pressure, care being taken to keep the oil-bath below 60°. A liter of water was then added to the residue in the flask. The oily top layer was then removed by means of a pipet attached to a suction flask which was in turn connected to a water pump. The aqueous layer was then treated with solid sodium carbonate until no more oil separated. The oily upper layer was removed as before and combined with the oily layer previously obtained. The crude product was then treated with potassium carbonate, the aqueous layer which separated after a time was discarded, the product dried with potassium carbonate, and distilled below 125° (50 mm.). The crude product was again dried over potassium carbonate and fractionated through a Widmer column. The yield (125 g.) of crotyl alcohol, b. p. 120–121°, was 55% of the theoretical amount.

Aluminum *t*-Butoxide.—*t*-Butyl alcohol is less reactive toward aluminum than are the lower primary and secondary alcohols and the product must be separated by crystallization rather than by distillation. Amalgamated aluminum,[10] aluminum plus mercuric chloride and aluminum plus a few grams of an aluminum alkoxide have been used successfully in this Laboratory in securing reaction with the alcohol. Amalgamated aluminum probably gives the most satisfactory results for the first preparation. Subsequent runs are carried out readily in the flask containing the sludge from an earlier preparation. The sheet aluminum or aluminum wire ordinarily available is not sufficiently pure to be entirely satisfactory for the reaction with *t*-butyl alcohol although they may be used. Apparently the most satisfactory aluminum is in the form of turnings made in a lathe from "fast cutting rods." This grade of aluminum is available from metal supply houses in rods 5 cm. in diameter. Ordinarily, the commercial grade of *t*-butyl alcohol available in this country does not need purification, but in case it does, it should be dried over lime or an aluminum alkoxide.

t-Butyl alcohol (50 to 75 ml.) was added to amalgamated aluminum turnings (27 g.), contained in a liter flask provided with a reflux condenser, protected with a drying tube. The alcohol was refluxed until the reaction began to slow up, as evidenced by a decrease in the rate of evolution of hydrogen through the condenser, or solid alkoxide began to separate out. Additional alcohol was then added until the total amount in the flask was 180 ml. When solid alkoxide again began to separate out, dry benzene (up to 600 ml.) was added as needed to keep the alkoxide in solution. Refluxing was continued (twelve to eighteen hours) until hydrogen was no longer evolved. The warm solution was then centrifuged until clear and colorless. The solution was decanted and the residue extracted with 200 ml. of hot benzene and centrifuged. The solutions were then combined and evaporated to dryness, the last of the benzene being removed at 30 to 50 mm. pressure. The product was white and weighed 110 to 135 g., which represents a yield of 65 to 80% based upon the alcohol used.

If the reaction does not start within a few minutes after refluxing begins, the reaction may be accelerated by the addition of 3 to 4 g. of an aluminum alkoxide or a small amount of the reaction mixture from a previous preparation. If a clear and colorless solution is not obtained after centrifuging for an hour or two, the addition of a little moist benzene or ether to the reaction mixture

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[12] Heyrovsky, *Mikrochemie*, **12**, 26 (1932).

will facilitate the separation although it may somewhat reduce the yield. Pure white aluminum *t*-butoxide may also be obtained by allowing it to crystallize from a benzene solution even though the latter is colored.

Summary

A method has been described whereby the rate of approach to, and the concentrations at, equilibrium may be determined in reactions of the type $R_2CO + R'_2CHOH \longleftrightarrow R_2CHOH + R'_2CO$. The relative reducing power of various alcohols and the oxidizing power of the corresponding ketones have been estimated in several cases.

The usefulness and the limitations of the polarograph as an instrument in the determination of the reduction potential and of the concentrations of aldehydes and ketones has been illustrated and discussed. The reduction potentials of forty-three representative aldehydes and ketones have been determined through the use of a polarograph. Significant relations of structure and electrolyte to the reduction potential have been pointed out. In particular, the effectiveness of unsaturation in decreasing the polarographic reduction potential has been illustrated.

The preparation and uses of aluminum *t*-butoxide and the choice of a ketone to be used in a new method for the oxidation of alcohols has been considered.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Desaturation Products from 1,3,3-Trimethoxybutane[1]

BY R. O. NORRIS, J. J. VERBANC AND G. F. HENNION

Introduction

The numerous desaturation products of 1,3,3-trimethoxybutane are of considerable interest. The latter compound is readily prepared directly from vinylacetylene by catalytic addition of methanol.[2] It has not been found possible to isolate intermediate addition products from this reaction since three molecules of methanol add exclusively. The mono- and dimethoxy compounds are obtainable only[3] by desaturation[4] of the trimethoxy compound.

The purpose of the present investigation was threefold: (1) to obtain each desaturation product in maximum yield; (2) to determine the mechanism of progressive desaturation; and (3) to study the readdition of methanol to the desaturation products.

The results of our studies are summarized in Fig. 1. Compounds IV, V, VI and VII are interconvertible in various ways as shown. Thermal desaturation of IV at 300–320° yields VI. The same result may be accomplished at 140–150° by employing a small amount of boric acid as a catalyst. Desaturation of VI with sodium acid sulfate as a catalyst yields V and VII. Compound V is probably not a primary desaturation product but originates rather by readdition of methanol to VII. The sequence of desaturation is therefore likely IV $\longrightarrow$ VI $\longrightarrow$ VII. Compounds I, II and III react catalytically with methanol to yield IV but the reactions cannot be reversed.

The unsaturated ethers V, VI and VII react vigorously with anhydrous methanol when a trace of acid is added. In fact it was found essential, in the preparation of these compounds, to collect the crude desaturation products over dilute sodium carbonate solution and to remove the methanol formed by thorough washing with water. Otherwise, upon distillation recombination took place as evidenced by the fact that the distillation temperature fluctuated considerably and the distillate was always very warm. The six unsaturated compounds listed manifest a strong orientation influence with respect to addition of methanol. Isomers of IV have not been isolated from any reaction studied. There is probably no other instance on record (except in cases of hydrogenation) where six unsaturated compounds have been saturated to yield the same addition product.

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[1] Paper XXV on the chemistry of substituted acetylenes and their addition products; previous paper, THIS JOURNAL, **60**, 718 (1938).

[2] Killian, Hennion and Nieuwland, *ibid.*, **56**, 1786 (1934).

[3] A possible exception is 1-methoxy-2-butyne which may be obtained from vinylacetylene by heating with methanol and sodium methylate in a bomb tube. Jacobson, Dykstra and Carothers, *ibid.*, **56**, 1169 (1934).

[4] Dykstra, *ibid.*, **57**, 2255 (1935).