[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Mechanism of the Hydrolytic Cleavage of Carbon–Carbon Bonds. II. Alcoholysis of Acetylacetone and Some 2-Ketoalkylpyridinium Salts

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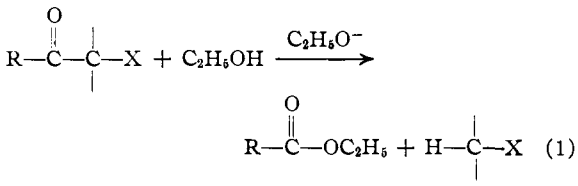
The rates of alkaline alcoholysis of acetylacetone and some 2-ketoalkylpyridinium salts in ethanol have been measured over a range of catalyst concentrations. The reaction involves one ethoxide ion and one neutral diketone molecule or one quaternary cation. The reaction, analogous to alkaline hydrolysis, involving two ethoxide ions is not observed.

In the first paper of this series[1] it was shown that the base-catalyzed hydrolysis of β-diketones involved in part reaction between two hydroxide ions and a molecule of diketone. The base-catalyzed cleavage of 2-ketoalkylpyridinium salts[2] also appears to occur only by a reaction between the quaternary cation and two hydroxide ions. To see how general this is, the base-catalyzed alcoholysis of acetylacetone and some phenacylpyridinium salts has been studied kinetically. The results presented here indicate that there is no reaction involving two ethoxide ions but that the cleavage in every case involves one ethoxide ion and one molecule of diketone or quaternary cation. The results are believed to be typical for the reaction



where X is a suitable activating group.

The alkaline alcoholysis of acetylacetone has been previously studied in a semi-quantitative way of Kutz and Adkins[3] who determined the amount of ester formed as a function of time for a number of diketones and ketoesters. For ratios of acetylacetone to sodium ethoxide of 5:1, 2:1 and 1:1 the relative rates were found to be 1, 2 and somewhat less than 2. The concentration of diketone was constant at 0.25 *M* in these experiments and the sodium ethoxide was varied. For a 1:1 ratio about 40% of the ester was formed in thirty hours at 60°. As pointed out by Kutz and Adkins their data are not very accurate because of the difficulties of isolating the ester product. Hence their values for the amounts formed at various times are minimum values.

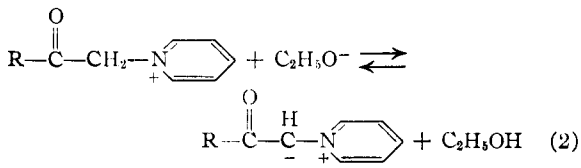
Experimental

Acetylacetone, phenacylpyridinium iodide, *p*-methoxyphenacylpyridinium iodide and *p*-bromophenacylpyridinium iodide were purified as previously described.[1,2] Stock solutions were prepared in ethyl alcohol which had been dried by the method of Manske.[4] It was found desirable to bubble dried nitrogen through the solvent to remove dissolved oxygen. Solutions of sodium ethoxide were made by dissolving freshly cut sodium metal and analyzing by titration. Such solutions were stable for several days but were restandardized before each run.

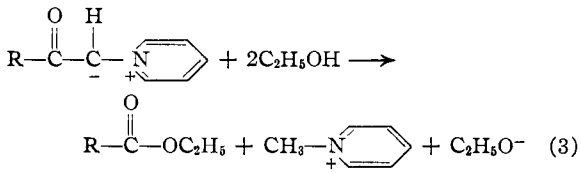
The reactants were thermostated before mixing though the long reaction times for acetylacetone (5–8 days) made this superfluous. Temperature control over the longest reaction times was good to ±0.1°. For acetylacetone the course of the reaction was followed by a bromine titration of the remaining diketone as a function of time. Samples were withdrawn from the reaction mixture and added to an excess of 0.1 *N* aqueous acid solution which stopped the reaction. A slight excess of bromine water was then added to the sample. After 4 minutes reaction time the excess bromine was removed by adding phenol. Potassium iodide was then added and after 5 or 10 minutes the liberated iodine was titrated with 0.1 *N* thiosulfate.

Theoretically four moles of thiosulfate should be required for each mole of acetylacetone. Tests with known samples showed that this was not achieved, but by following the above procedure 3.77 moles of thiosulfate per mole of diketone were required. This corresponds to 94% of the theoretical value. Allowing the bromine to be in contact with the diketone for longer or shorter times than 4 minutes reduced the ratio appreciably. It was later found that allowing the potassium iodide to be in contact with the brominated diketone for 30 or 40 minutes before titrating increased the ratio to 3.87 moles to 1 or 97%. This was not done in most of the runs but since a ratio determined from knowns was used for each procedure, no error is introduced. The absorption of bromine by acetone or ethyl acetate during an analysis is not detectable.

For the 2-ketoalkylpyridinium salts the change in electrical resistance as the reaction proceeds was used to follow the kinetics. The first reaction of the quaternary cation with a strong base such as ethoxide ion is to form the non-conducting enol-betaine[5]



This reaction goes to completion essentially. The net result of the cleavage is then to produce methylpyridinium ethoxide, or two ions, from a non-conductor.



Consequently the conductance of the solution increases about 50% if equivalent quantities of base and quaternary salt are used. (Sodium iodide is also present.)

The procedure used for measuring the resistance has been described before.[6] Some difficulty was experienced in getting the equilibrium value of the resistance which fell to a minimum and then very slowly increased. The minimum value which was constant for about an hour was taken as the equilibrium resistance and the increase attributed to secondary reactions such as the hydrolysis of the ester. The rate of increase in resistance was at most only $^1/_{30}$ of the lowest measured decrease.

Calculations and Results

Acetylacetone is an acid of sufficient strength ($K_a = 10^{-9}$ in water) so that it will completely neutralize an equivalent quantity of ethoxide ion.

(1) Pearson and Mayerle, THIS JOURNAL, **73**, 926 (1951).
(2) Pearson and Dillon, *ibid.*, **70**, 1933 (1949).
(3) Kutz and Adkins, *ibid.*, **52**, 4391 (1930).
(4) Manske, *ibid.*, **53**, 1106 (1931).
(5) Kröhnke, *Ber.*, **66B**, 604 (1933); **68B**, 1177 (1935).
(6) Pearson, THIS JOURNAL, **71**, 2212 (1949).

$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-CH_3 + C_2H_5O^- \rightleftharpoons CH_3-\overset{O}{\overset{\|}{C}}-\underset{H}{\underset{|}{C}}-\overset{O}{\overset{\|}{C}}-CH_3 + C_2H_5OH \quad (4)$$

If we let HA be the neutral diketone and A^- the carbanion we have

$$[A^-]/[HA][C_2H_5O^-] = K_{eq} \quad (5)$$

where K_{eq} is large. If we let a be the initial concentration of diketone or sodium ethoxide, whichever is present in least amount, and if x is the concentration of ester formed by alcoholysis then $[A^-]$ will be equal to a whenever the diketone is in excess and equal to $(a - x)$ whenever sodium ethoxide is in excess. Now if the mechanism of the alcoholysis is such that one ethoxide ion reacts with one neutral diketone molecule the rate expression will be

$$dx/dt = k[HA][C_2H_5O^-] \quad (6)$$

but because of the equilibrium shown in (4) and (5) this becomes

$$\frac{dx}{dt} = \frac{k}{K_{eq}}[A^-] = k'[A^-] \quad (7)$$

This is kinetically indistinguishable from the rate expression which would hold if the reaction involved the spontaneous cleavage of the carbanion. Reference 1 cites reasons for believing that the carbanion is not involved.

From (7) it is clear that two experimental orders of reaction will be observed. Solutions containing excess diketone will be pseudo-zero order with a zero order rate constant equal to $k'a$, where a is the concentration of sodium ethoxide. Solutions containing excess base will be pseudo-first order with a first order rate constant equal to k'. Since in no case is sodium ethoxide used up as reaction occurs, a solution initially having diketone in excess will always become a solution with sodium ethoxide in excess. At some point then the kinetics will switch from zero order to first order. Figure 1 shows the result of plotting log $(a - x)$ in the form of log (ml. $Na_2S_2O_3$/5 ml. sample) against the time for solutions containing excess base. Figure 2 shows a plot of the remaining diketone concentration in the form of (ml. $Na_2S_2O_3$/5 ml. sample) against the time for solutions containing excess diketone initially. The expected orders of reaction are observed. Also Fig. 2 shows the change from zero order to first order kinetics at the points where the base begins to exceed the diketone.

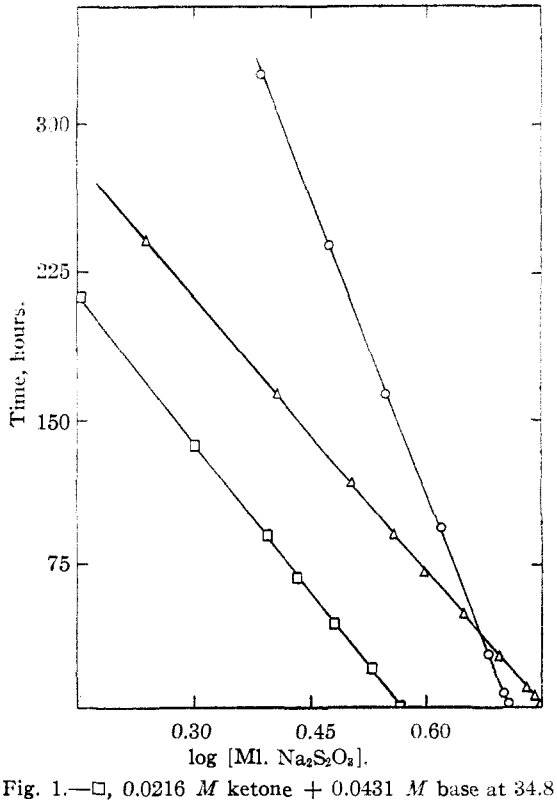


Fig. 1.—□, 0.0216 *M* ketone + 0.0431 *M* base at 34.8°; △, 0.0321 *M* ketone + 0.0321 *M* base at 34.8°; ○, 0.0277 *M* ketone + 0.0275 *M* base at 25.4°.

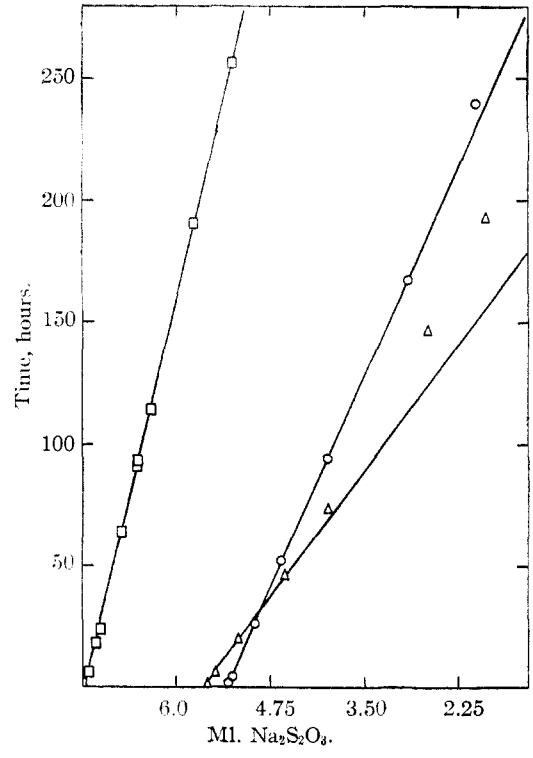


Fig. 2.—□, 0.0403 *M* ketone + 0.0081 *M* base at 34.8°; △, 0.0292 *M* ketone + 0.0234 *M* base at 34.0°; ○, 0.0275 *M* ketone + 0.0143 *M* base at 34.8°.

From the slopes of the graphs the observed rate constant, k', was calculated by multiplying by 2.3 for the first order runs and by using the relationship

$$k' = (\text{slope})\left(\frac{\text{normality of } Na_2S_2O_3}{5}\right)\left(\frac{1}{3.77}\right)\left(\frac{1}{a}\right) \quad (8)$$

for the zero order runs. Table I presents the data. Runs were made at three temperatures and the activation energy calculated as 19.1 kcal. Since the value of K_{eq} is not known no attempt was made to calculate the true rate constant or true heat of activation. To check whether the presence of water affected the kinetics several runs were made with 1 or 2% of water added. The order was not affected but the rate constants were slightly reduced.

For the 2-ketoalkylpyridinium salts the same arguments as above hold true in that the quaternary

TABLE I

ACETYLACETONE + SODIUM ETHOXIDE

Diketone, mole/l.	Base mole/l.	Temp., °C.	k', min.$^{-1}$
0.0615[a]	0.0775	34.8	7.0×10^{-5}
.0216	.0431	34.8	7.5×10^{-5}
.0258	.0388	34.8	8.0×10^{-5}
.0321	.0321	34.8	8.3×10^{-5}
.0292	.0234	34.8	9.0×10^{-5}
.0275	.0143	34.8	8.9×10^{-5}
.0403	.0081	34.8	8.8×10^{-5}
.0239[b,c]	.0239	34.8	8.1×10^{-5}
.0277[c]	.0275	43.9	2.25×10^{-4}
.0277[c]	.0275	43.9	2.32×10^{-4}
.0277[c]	.0275	25.4	3.33×10^{-5}

[a] Containing 2% water. [b] Containing 0.0313 M sodium bromide. [c] Plotted as first order.

cation is a strong enough acid to neutralize an equivalent of ethoxide ion. Only solutions containing excess ethoxide ion could be studied because if the quaternary salt is in excess the net change in conductivity is due to replacement of a phenacylpyridinium ion with a methylpyridinium ion. This change is too small to be useful. Accordingly the log $(a-x)$ in the form of log $(R/(R-Re))$ was plotted against the time. Some results are shown in Fig. 3. From the slopes the first order rate constants were calculated and the values are given in Table II. Only one temperature was used and the effect of water was not investigated.

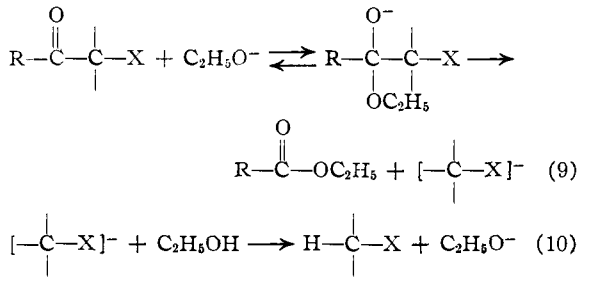
TABLE II

SOME PHENACYLPYRIDINIUM SALTS + SODIUM ETHOXIDE AT 34.8°

Pyridinium iodide	Concn., mole/l.	Base, mole/l.	k', min.$^{-1}$ $\times 10^{-2}$
Phenacyl-	0.00517	0.0086	1.09
	.00426	.0106	1.09
	.00258	.0086	1.02
p-Bromo-	.00229	.0033	1.08
	.00208	.0038	1.08
p-Methoxy-	.0114	.0117	1.11

Discussion

The constancy of the rate constant k' for wide variations in the ethoxide ion concentration is consistent with a reaction between one ethoxide ion and a molecule of neutral diketone or quaternary cation. Presumably the mechanism is similar to that of ester hydrolysis or alcoholysis



It is noted from Table I that the observed rate constant, k', diminishes somewhat as the concentration of base goes up. This is attributed to the effect of increasing ionic strength. The addition of sufficient sodium bromide to bring the ionic strength

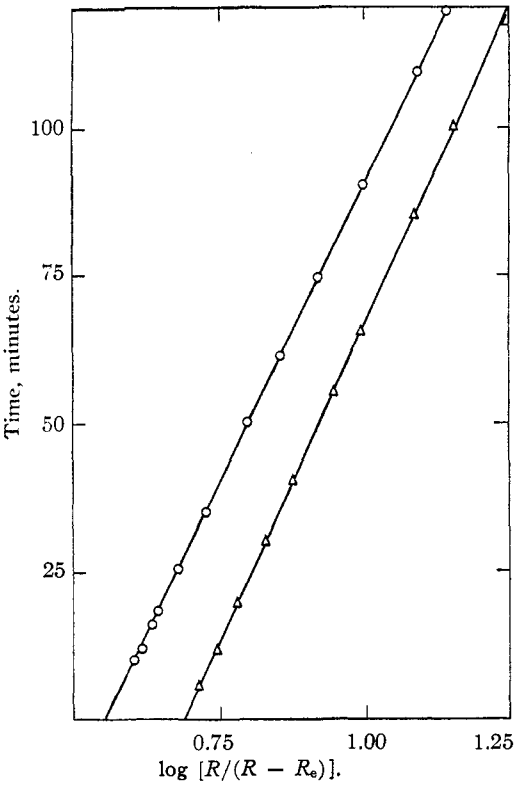


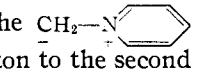
Fig. 3.—O, 0.00517 M phenacylpyridinium iodide + 0.0855 M base; △, 0.00208 M *p*-bromophenacylpyridinium iodide + 0.00381 M base.

up to 0.055 did reduce the rate constant but not quite as much as an equivalent increase in the concentration of base (see Table I).

The ethoxide ion is continuously regenerated and serves as a true catalyst for the cleavage. Neglecting the effect of ionic strength the theoretical ratio of the rates for the solutions studied by Kutz and Adkins (5:1, 2:1 and 1:1 diketone to base) would be 1 to 2.5 to 3.58 compared to the observed values of 1 to 2 to less than 2. The difference is attributed to the greater loss of ester product due to hydrolysis in working up the more alkaline solutions and to the decrease in rate constant for the solutions of higher ionic strength. Using the activation energy of 19 kcal. obtained here it can be calculated that in 30 hours at 60° the diketone should be cleaved to the extent of about 70% for a 1 to 1 ratio. The observed *ca.* 40% of ester indicates again a considerable loss due to hydrolysis.

As Table II brings out, the rate constants for the three quaternary salts studied is very nearly the same. This is in contrast to the results for the hydrolysis of these same salts where the *p*-bromo derivative cleaves twice as fast as the unsubstituted and the *p*-methoxy cleaves two-thirds as fast as the unsubstituted.[7] The difference in mechanism can explain these results. The alcoholysis involves addition of an ethoxide ion to the carbonyl and displacement of the CH_2-N^+ group. The first of these processes is favored by an electron attracting substituent such as a bromine atom and the second is hindered. The two effects might well

(7) Kröhnke, *Ber.*, **70B**, 864 (1937).

cancel. In the hydrolysis two hydroxide ions are involved and besides the addition of one to the carbonyl and the displacement of the $CH_2—N$  there is an additional loss of a proton to the second hydroxyl (see reference 1 for the complete mechanism). The effect of a substituent may again cancel for the first two processes but the loss of the proton will be aided by a bromine substituent and hindered by the electron donating methoxyl. Consequently the observed changes in the rate will occur.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, GEORGIA INSTITUTE OF TECHNOLOGY]

Some Azeotropes of Bromine

BY WILLIAM M. SPICER AND LEON H. MEYER

Vapor-liquid equilibria were investigated at 1 atm. pressure for four systems involving bromine and suitable solvents. Homogeneous azeotropes were observed to exist in three of the systems studied—Br_2–$CF_2ClCFCl_2$, Br_2–CCl_3CClF_2, Br_2–$C_6H_5CF_3$. A two-phase azeotope was found to exist in the system composed of the partially miscible liquids bromine and $CF_3CCl_2CF_2Cl$. Liquid-liquid equilibrium data were also obtained for this system between 0° and the azeotropic boiling point. The investigation of another system, Br_2–CS_2, was not carried to completion due to evidence of a reaction occurring between the components. No evidence of reaction between the components of the other systems could be detected. As a further indication of the deviations of the systems from ideality, volume changes occurring on mixing the two components of each system were determined.

I. Introduction

As a continuation of an investigation to prepare binary azeotropes consisting of one colored and one colorless component,[1] it was decided to study further possibilities in systems of bromine and colorless bromine solvents. Azeotropes of this general type are valuable in the study of the methods employed to separate azeotropic mixtures, since separation can be observed visually.

Due to the inert character and the availability of certain of the completely halogenated saturated hydrocarbons, it was felt that certain of these compounds would be suitable as second components of the systems to be studied. Spicer and Kruger[1] proved the existence of an azeotrope in the system bromine–carbon tetrachloride. To go higher in this series, however, it was necessary to use fluorine containing compounds in order that the boiling point of the second component should not be excessively high, a condition which would be unfavorable for azeotrope formation. Three systems involving bromine solvents of this general type were studied—Br_2–$CF_2ClCFCl_2$, Br_2–CCl_3CClF_2 and Br_2–$CF_3CCl_2CF_2Cl$.

Two other systems were investigated. One of these employed benzotrifluoride ($C_6H_5CF_3$) as the bromine solvent, for it was deemed probable that no reaction would occur between the components in the absence of a catalyst, due to the inhibiting effect of the trifluoromethyl group.[2,3] The final system studied involved bromine and carbon disulfide, a commonly employed bromine solvent.

II. Experimental

Merck and Co., Inc., analyzed C.P. bromine was used in all investigations without further purification. One of the solvents—CCl_3CClF_2, a low melting solid at room temperature (m.p. 40.6°)—was furnished pure by the General Chemical Division of the Allied Chemical and Dye Corporation. The $CF_2ClCFCl_2$ was obtained from Kinetics Chemicals, Inc., and purified by fractionation in a five-foot glass helix packed column. A middle cut was taken, boiling point range 46.6–46.8° at 739.6 mm. pressure. The carbon disulfide was purified by the method of Chenevier,[4] fractionation being performed in the same column. A middle cut, boiling point range 45.2–45.4° at 740 mm., was retained.

It was not possible to purify further the $CF_3CCl_2CF_2Cl$ and the $C_6H_5CF_3$, since they were obtained in insufficient quantity to permit this. These compounds were furnished by Halogen Chemicals, Inc., and by the Hooker Electrochemical Company, respectively. Purity of both was listed as approximately 98%. This impurity was tolerated since it was felt probable that it was of similar chemical constitution.

Vapor-liquid equilibrium data were obtained using an equilibrium still similar to that described by Jones, Schoenborn and Colburn.[5] A constant pressure control maintained pressure at 760 mm. It consisted of a large (approximately 25 l.) air reservoir, equipped with a 1/6 horsepower compressor, to which the system was open. The pressure in the reservoir was set by manual operation and checked approximately every 20 minutes during a run (estimated accuracy of pressure control ± 1 mm.). Equilibrium temperatures, which were measured by means of a calibrated copper-constantan thermocouple using a potentiometer reading to one microvolt, were accurate to approximately 0.1°. Composition of equilibrium liquid and vapor phases were determined in all cases, except for a few runs made on the system Br_2–$CF_3CCl_2CF_2Cl$, by titrating samples, withdrawn from the still into concentrated potassium iodide solutions, with standardized sodium thiosulfate solution to a starch indicator end-point. This followed, of course, determination of the weight of each sample. The liquids bromine and $CF_3CCl_2CF_2Cl$ were found to be only partially miscible and to complete the phase diagram above 0° the liquid-liquid equilibria were determined for the two layers. These determinations were carried out by allowing the system to equilibrate in a water-bath equipped with an automatic temperature control capable of maintaining regulation within approximately ±0.1°, and then analyzing samples from each layer in the usual manner. Not before this information was available, was it possible to obtain complete vapor-liquid equilibria data from the equilibrium still, since the composition of the vapor phase in the region in which the condensed vapor separated into two liquid layers could not be determined by the usual method. To perform the analyses within this region, the following method was used. The entire vapor condensate was withdrawn into a separatory

(1) W. M. Spicer and J. Kruger, THIS JOURNAL, **72**, 1855 (1950).
(2) J. H. Simons and E. O. Rambler, *ibid.*, **65**, 391 (1943).
(3) J. H. Simons, *Ind. Eng. Chem.*, **39**, 240 (1947).
(4) A. Weissberger and E. Proskauer, "Organic Solvents," Oxford University Press, London, 1935, p. 170.
(5) C. A. Jones, E. M. Schoenborn and A. P. Colburn, *Ind. Eng. Chem.*, **35**, 666 (1943).