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

Alcoholysis of 1,3-Diketones

BY LELAND J. BECKHAM AND HOMER ADKINS

This paper is the report of a continuation of the study of alcoholysis of 1,3-diketones, at 150–250° under approximately 100 atmospheres of hydrogen.[1] The primary objective of the study has been to ascertain the relation of structure to the mode of cleavage of diketones under conditions complicated as little as possible by secondary or side reactions such as occur in alcoholysis using hydrogen chloride or sodium ethoxide as catalysts. The preparation of the diketones,[2] the general procedure,[3] and the method of analysis[4] have been described.

A long series of experiments was carried out with the objective of ascertaining whether the temperature of reaction or the extent to which alcoholysis had occurred, or the ratio of ethanol to diketone, modified the proportion of acetyl cleavage. It was found that at temperatures from 150 to 250°, with alcoholysis from 6 to 100% complete and with ratios of diketone to ethanol varying from 1 to 1.3 to 1 to 5 that the proportion of acetyl cleavage was constant to within about the limit of experimental error. The acetyl cleavage was also independent of whether the gas over the reaction mixture was hydrogen or nitrogen or the pressure was 100 or 200 atmospheres. These experiments were also valuable as indicating the reliability of the experimental method in ascertaining the ratio of cleavage products. For example, in eight experiments under widely varying conditions the percentage acetyl cleavage from *n*-valerylacetylmethane was 52, 52, 55, 53, 53, 54, 54 and 54, and from trimethylacetylacetylmethane it was 84% under five sets of conditions. Isovalerylacetylmethane gave 62, 60 and 62% acetyl cleavage under three different conditions.

However, the proportion of cleavage products is within certain limits a function of the catalysts present. The proportion of acetyl cleavage was higher in very dry alcohol than in alcohol containing 0.1 to 0.2% of water (see Table I). The addition of aluminum ethoxide to the alcoholysis mixture also decreased the proportion of acetyl cleavage. The proportion of acetyl cleavage was higher in a glass than in a copper vessel while in both cases the acetyl cleavage was higher than in brass or iron containers. Presumably the zinc or iron in the brass and iron containers formed metallic alkoxides which functioned as did aluminum ethoxide since soluble compounds of iron or zinc were found in the reaction mixtures.

TABLE I

EFFECT OF CATALYSTS UPON % OF ACETYL CLEAVAGE IN ALCOHOLYSIS OF 1,3-DIKETONES $CH_3C(O)CH_2C(O)R$

Container	R....*n*-Pr	*n*-Bu	*i*-Bu	*s*-Bu	*t*-Bu	Ph
Glass[a]			65		90	100
Glass[b]	50	59	62	67	84	80
Brass[b]	52	54	59	63	75	
Steel[b]			60		76	
Glass[c]		53	58		75	
Glass[d]			60		75	
Copper[b]					84	

[a] Ethanol dried with aluminum ethoxide. [b] Ethanol dried twice over lime. [c] Ethanol containing 1 to 2% aluminum ethoxide. [d] 56% Ethanol, 44% water.

An apparently significant fact emerges from these data, *i. e.*, the addition of any of several catalysts reduced the acetyl cleavage to a certain minimum value characteristic of the diketone.[5] This fact is considered significant because it is in accord with the mechanism for "high temperature" alcoholysis suggested in our first paper[1] and developed in detail below. At temperatures of 150–250° it is presumed that in the absence of a catalyst the reaction may take place in either of the two manners previously described. On this consideration the velocity of cleavage of unsubstituted and monosubstituted diketones occurring according to the basic mechanism is $\alpha(k_1k_8/k_2)$ (B) (OEt^-), and the velocity of cleavage according to the acidic mechanism is $\alpha'(k'_8k'_5/k_6)$ (B) (H^+) (EtOH), where the symbols refer to the corresponding velocity constants and compounds

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(1) For references see Beckham and Adkins, THIS JOURNAL, **56**, 1119 (1934).

(2) Sprague, Beckham and Adkins, *ibid.*, **55**, 2665 (1934).

(3) Connor and Adkins, *ibid.*, **54**, 4320 (1932).

(4) Kutz and Adkins, *ibid.*, **52**, 4036 (1930). In addition to the data on the partition of acids given in the last paper, the distributions of isobutyric and propionic acids between benzene and water were needed. The ratios under similar conditions were found to be: millimoles of isobutyric acid per liter (benzene/water) 11.7/35.2, 79.2/102, 38.2/67.4; propionic acid 4.1/35.5, 5.2/47.

(5) This minimum value is easily reproducible under a wide variety of conditions as has been indicated above, while it is difficult to reproduce precisely the higher values for acetyl cleavage since it is exceedingly difficult if not impossible to eliminate traces of catalysts.

given in the previous paper.[1] Consequently the total velocity of cleavage will be the sum of these two terms

$$\text{vel.} = \alpha \frac{k_1 k_8}{k_2} (\text{B}) (\text{OEt}^-) + \alpha' \frac{k_8' k_5'}{k_6'} (\text{B})(\text{H}^+) (\text{HOEt})$$

k_2 and k_6' are influenced by same factors, $k_2 = c'k_6'$

k_8 and k_8' are influenced by same factors, $k_8 = c''k_8'$

$$= \frac{k_8}{k_2} (\text{B}) \left(\alpha k_1 (\text{OEt}^-) + \alpha' \frac{c'}{c''} \text{H}^+ k_5' \text{ HOEt} \right)$$

set $(\alpha' c'/c'')$ HOEt = a constant = β

B $\cong$ concentration of all enolized forms present in solution

$$= (k_8/k_2)(\alpha k_1 \text{ OEt}^- + \beta k_1' \text{ H}^+) (\% \text{ Enol})$$

The high temperature cleavage of the disubstituted diketones can only occur through the basic mechanism. Therefore the same factors control it as with sodium ethoxide at 60°.[6]

Thus we have an expression for the rate of cleavage of a diketone under the high temperature conditions. It is evident that an addition of acid will make the second term predominant and the results will follow the acidic mechanism, whereas an excess of base will make the first term predominant and the results will follow the basic mechanism. The question then arises as to which term of the expression predominates in the absence of a base or acid, or whether they are approximately equal. Upon the basis of the experimental results with the different catalysts given above and the fact of a definite limiting value for the ratio of cleavage in the case of all of these materials, it seems justifiable to postulate that the presence of these catalysts enhances the basic cleavage with respect to the acidic cleavage, and that in the practical absence of any catalyst both the acidic and basic terms have appreciable magnitudes. Upon this basis the factors determining the ratio of cleavage products in "high temperature" alcoholysis in the presence of small amounts of catalysts are the same as those for alcoholysis by sodium ethoxide at 60° *except* that the extent of enolization becomes an important consideration.

The data upon the ratio of cleavage products of various diketones produced by alcoholysis in a brass reaction vessel are given in Table II. The more important facts there presented are as follows (Table I).

TABLE II

PROPORTION OF CLEAVAGE PRODUCTS IN ALCOHOLYSIS OF DIKETONES

$CH_3C(O)CHRC(O)R'$ R	R'	%, Enol	%, Acetyl cleavage[a]
Et	*t*-Bu	7	75
n-Bu	*t*-Bu	3	82
Benzyl	*t*-Bu	2	80
H	*t*-Bu	60	75
H	Ph	100	80[b]
H	Et	67	51
H	Me	80	50
H	*n*-Pr	84	52
H	*i*-Pr	85	38
H	*n*-Bu	73	54
H	*i*-Bu	86	59
H	*s*-Bu	..	63
Et	Ph	3	34
n-Bu	Ph	9	34
Benzyl	Ph	0	16
n-Heptyl	Ph	..	43
(Benzyl)$_2$	*t*-Bu	..	43

[a] Alcoholysis at 200° in brass liner under 100 atm. of hydrogen with ethanol twice dried over lime. The figures are the average of 2 to 10 analyses. [b] The diketone having three Me groups substituted in the acetyl (*i. e.*, trimethylacetylbenzoylmethane)[7] gave 79% "acetyl" cleavage.

In an unsymmetrical diketone $CH_3C(O)$. . .(a) . . .CHR. . .(b). . .C(O)R' cleavage occurred more at (a) than at (b) where R' was phenyl or any one of several primary, secondary or iso alkyl radicals, the only exception being isopropyl. Among the alkyl groups the longer the chain and especially the more branched the chain among the butyl groups, the greater the proportion of acetyl or (a) cleavage.

In the diketone where R' was *t*-butyl the substitution of an ethyl, *n*-butyl or benzyl group at R had little effect upon the ratio of cleavage as compared with that in the parent diketone. In the diketone where R' was phenyl the substitution of an ethyl, *n*-butyl, or benzyl group brought about an enormous lowering of acetyl cleavage, (a) the effect being especially marked with the benzyl group, which showed only 16% acetyl cleavage as compared with the 80% of the parent diketone. The substitution of two benzyl groups on the central carbon atom of the diketone also lowered the acetyl cleavage but not so markedly as did one substituent.

The rate of alcoholysis of various diketones was also measured by interrupting the reaction before completion and determining the amount and ratio of products formed. The velocity constants were calculated upon the basis of a first order reaction since ethanol was present in excess and experiment showed that the rates so calculated

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[6] The various velocity constants mentioned above have the same significance and are influenced by the same factors as in the corresponding basic and acidic mechanisms.[1]

[7] Prepared as by Kohler and Barnes, THIS JOURNAL, **55**, 692 (1933).

were fairly constant. Some of these results are summarized in Table III, the rate of alcoholysis of acetylvalerylmethane being used as the basis of comparison. It should be noted that these reactions occurred in glass containers so designed that the reactants did not come in contact with the steel of the surrounding bomb. The rates of reaction are slower and the proportion of acetyl cleavage higher in glass than in brass vessels. The magnitude of this difference may be obtained by a comparison of the proportion of acetyl cleavage as given for the same diketones in Tables III and II as well as in Table I. These rate studies show that lengthening of the chain from methyl to butyl (R′) increased the rate of alcoholysis as well as of acetyl cleavage. Branching of the chain in the butyl groups decreased the rate of alcoholysis, particularly at the adjacent (b) linkage. Isopropyl is again an exception.

TABLE III

RATES OF CLEAVAGE OF 1,3-DIKETONES

$CH_3C(O)..(a)..CH(R)..(b)..C(O)R'$

		Cleavage		Comparison of rates of reaction		
R	R′	Total %	at (a), %	Total	at (a)	at (b)
H	*n*-Bu[a]	14	59	100	59	41
H	*i*-Bu[a]	11	62	74	46	28
H	*s*-Bu[a]	7	67	51	34	17
H	*t*-Bu[a]	7	84	48	40	8
H	*n*-Pr[a]	11	50	79	40	39
H	*i*-Pr	27	10	92	9	83
H	Et[a]	11	50	77	39	38
H	Me[a]	8	50	55	28	27
H	*t*-Bu	15	84	48	40	8
Et	*t*-Bu	10	78	31	24	7
n-Bu	*t*-Bu	11	75	34	26	8
Benzyl	*t*-Bu	10	66	30	20	10
(Benzyl)$_2$	*t*-Bu	2	..	5	..	..
H	Ph	60	100	268	268	0
Et	Ph	83	24	519	124	395
n-Bu	Ph	71	24	363	87	276
Benzyl	Ph	59	29	261	76	145

[a] These diketones reacted for eight hours at 150°, the others for 16 hrs. at 180°. The two sets of data were calculated to the same basis by using the rates for the diketone where R is *t*-butyl, which was run under both conditions. All reactions were in glass using ethanol twice dried over lime.

The substitution of ethyl, *n*-butyl or benzyl groups on the central carbon atom where R′ was *t*-butyl also decreased cleavage, particularly at the bond adjacent to the *t*-butyl. Two benzyl groups almost prevented alcoholysis under the conditions used for comparison. In acetylbenzoylmethane (where R′ is phenyl) the substitution of an ethyl or *n*-butyl group (R) also decreased the rate of cleavage at (a) but enormously increased the cleavage at (b) so that the net effect was an increase rather than a decrease in the rate of cleavage.

While it is true that a number of the facts reported above apparently cannot at this time be rationalized in terms of the polarity and polarizability of the substituents, yet many of the facts may be so explained.

For example, acetylbenzoylmethane cleaved faster than diacetylmethane in the higher temperature alcoholysis, but at about the same rate at 60° in the presence of a base. As acetylbenzoylmethane is more enolized than diacetylmethane, and as the extent of enolization becomes one of the factors for the rate of cleavage of a diketone at high temperatures (traces of catalyst), it is in accord with prediction that the acetylbenzoylmethane should cleave faster under these conditions as compared to diacetylmethane than in the basic mechanism where the extent of enolization does not enter.

The amount of acetyl cleavage was lower in the case of acetylbenzoylmethane in the presence of aluminum ethoxide as compared to the runs without any catalyst in a glass liner. According to the statement of the high temperature mechanism the term αk_1 OEt enters the expression for the rate with aluminum ethoxide almost exclusively, while in the other case the term $\beta k_5'$ H$^+$ also enters. Now the phenyl group has a depressing effect on k_5' and not much influence on k_1. From this it is evident that if we change the conditions so that k_1 predominates greatly over k_5' we reduce the retarding effect of the phenyl group, and thus increase the amount of cleavage on the benzoyl end of the molecule, *i. e.*, lower the acetyl cleavage.

The presence of traces of aluminum ethoxide lowered the percentage of acetyl cleavage of the compounds of the formula CH_3COCH_2COR where R is an alkyl group (*e. g.*, *n*-butyl, *i*-butyl, *s*-butyl, *t*-butyl) in the high temperature alcoholysis. The retarding effect of the +I of these groups is more important in the acid than in the basic cleavage (Table I of earlier paper). Therefore, in the presence of aluminum ethoxide, these groups will not have as great a retarding effect as in the case of the mixed mechanism (glass containers). Therefore there should be more cleavage on the (b) bond in the case of aluminum ethoxide and consequently lower acetyl cleavage in actual accord with the experimental evidence.

In the series of compounds RCOCH$_2$COCH$_3$ (R equals *n*-butyl, *i*-butyl, *s*-butyl or *t*-butyl) the effect of branching was to lower greatly the cleavage at the branched end of the molecule, but also to affect the cleavage at the acetyl bond slightly. Thus is demonstrated the weak retarding effect of groups exhibiting $+$I effects on carbon 3 (Table I of earlier paper).

The dibenzylacetyltrimethylacetylmethane was only very slightly cleaved in glass apparatus. This is in accord with the lack of appreciable cleavage of the unenolized form in the high temperature cleavage without addition of the catalyst. However, the diketone was readily cleaved in the presence of traces of catalyst.

Summary

The relation of the structure of a number of unsymmetrical 1,3-diketones to the proportion of cleavage products under a variety of conditions has been studied. The results have been tabulated and summarized above. A number of these experimental observations have been correlated with the I and T effects of the substituent groups and the mechanism outlined in an earlier paper.

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The 2,3,5-Triphenylfurans and the Related Saturated and Unsaturated 1,4-Diketones

BY ROBERT E. LUTZ, W. R. TYSON,[1] AGNES G. SANDERS AND C. K. FINK

This paper deals with some further studies on the reactions between phosphorus pentahalides and saturated and unsaturated 1,4-diketones and related furans, and on the nitric–acetic acid oxidation of the furans to unsaturated 1,4-diketones.[2]

Dibenzoylphenylethylene (I), dibenzoylphenylethane V, 2,3,5-triphenylfuran III, and 2,3,5-triphenyl-4-acetoxyfuran II, react readily with phosphorus pentachloride to give in each case the known 2,3,5-triphenyl-4-chlorofuran IV[3] which is prepared also by the action of alcoholic hydrogen chloride[3] or acetyl chloride and sulfuric acid on dibenzoylphenylethylene. Phosphorus pentabromide reacts similarly with all of these compounds (excepting dibenzoylphenylethane) yielding however 2,5-di-(*p*-bromophenyl)-3-phenyl-4-bromofuran VI, a substance which is identical with that prepared by Japp and Klingemann by the direct bromination of dibenzoylphenylethylene.[3] In these reactions both of the α- (but not the β-) phenyl groups are brominated in the para positions. The greater reactivity of the α-phenyl groups as compared with the β-phenyls is doubtless due to the influence of the adjacent furan oxygen.

Phosphorus pentabromide reacts with 2,3,5-triphenylfuran III, when the temperature is controlled, brominating only the unoccupied β-position of the furan nucleus to give 2,3,5-triphenyl-4-bromofuran VII (known);[3,4] the latter compound (VII) is brominated further in a second stage under more drastic conditions, giving the 2,5-di-(*p*-bromophenyl) derivative VI. These facts show that the furan nucleus in triphenylfuran III is considerably more reactive than any of the phenyl groups; this is consistent with the so-called superaromatic character of the furan nucleus.[5] These relationships are outlined in diagram 1.

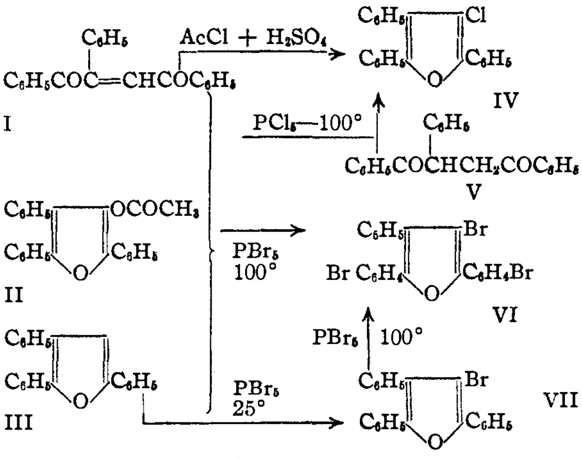

DIAGRAM 1.

The oxidation of triphenylfuran III by the nitric–acetic acid method is described by Japp

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[1] The larger part of this work was presented by Mr. W. R. Tyson in a thesis for a Master's Degree, University of Virginia, 1933.

[2] *Cf.* Lutz and Wilder, THIS JOURNAL, **56**, (a) 2145, (b) 978 (1934).

[3] Japp and Klingemann, *J. Chem. Soc.*, **57**, 674 (1890).

[4] Allen, THIS JOURNAL, **49**, 2110 (1927); **51**, 3591 (1929).

[5] Gilman and Calloway, *ibid.*, **55**, 4197 (1933).