

[CONTRIBUTION FROM THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

Chemistry of Enolates. III. Cation and Solvent Effects in the Alkylation of Butyrophenone¹BY H. D. ZOOK AND W. L. GUMBY²

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The rates of alkylation of ethereal solutions of butyrophenone anion increase by more than three powers of ten as the accompanying cation is varied from lithium to potassium. Tetraalkylammonium salts are powerful catalysts. The reaction exhibits autocatalysis by the ketonic product. Ebulliometric studies of sodiobutyrophenone indicate an average association of three ion pairs in ether solution. Alkylation within a coordination complex is suggested by a reaction order greater than unity for alkyl halide, although no appreciable concentration of complex is evident from vapor pressure measurements of the system methyl bromide-etheral sodiobutyrophenone.

The "carbanion" nature of metallic derivatives of organic compounds is frequently overemphasized in substitution and condensation mechanisms. Recently, Brändström³ has stressed the importance of chelation of anion and coordination of reagent with alkali metal in the alkylation and acylation of alcoholic solutions of malonic ester and related compounds. Similar coordination of reagents should be even more pronounced in the alkylation of enolates in less polar solvents. Although reasonable pseudo-first-order kinetics were observed throughout the first half-lives for the alkylations of a variety of phenyl alkyl ketones, increases in specific rates were observed during subsequent half-lives. These complications, as well as the results of ebulliometric measurements, suggested that the enolate was more complex than a single ion or ion pair.⁴

Variation of Cation.—In this study the rates of alkylation of ethereal solutions of lithio-, sodio- and potassio-derivatives of butyrophenone are compared. Half-lives for thirteen alkylations are listed in Table I. The importance of the metallic cation

is varied from lithium to potassium. Alkylations of potassio-butyrophenone by iodides are too rapid for convenient measurement.

Attempts to prepare quaternary ammonium enolates have thus far been unsuccessful. However, the addition of a catalytic amount of tetra-*n*-butylammonium perchlorate to a sodium enolate increases the rate of ethylation by a factor of three. That this effect is due to the cation is shown by similar catalysis by tetrabutylammonium iodide and no catalysis by sodium iodide.

These comparisons were made in terms of half-lives taken from curves of enolate concentration *versus* time. Meaningful rate constants were not obtained in all cases.

Complexity of the Alkylation Reaction.—Although pseudo-first-order constants for alkylation by ethyl bromide deviate less than 5% from the mean during the first half-life,⁴ the constants for ethylations by ethyl iodide increase as much as 20% over this period. This increase is not due to a more rapid dialkylation to triethylacetophenone⁵ nor to concentration of the solution by loss of

TABLE I

HALF-LIVES FOR ALKYLATIONS OF BUTYROPHENONE			
Enolate	Halide ^c	E^0 ^a	$t^{1/2}$, sec. $\times 10^{-6}$
K	EtBr	0.07	0.0045
Na	EtBr	.09	0.39
Li	EtBr	.07	31
K	<i>n</i> -PrBr	.04	0.0096
Na	<i>n</i> -PrBr	.09	.98
K	<i>i</i> -PrBr	.05	.25
Na	<i>i</i> -PrBr	.09	~23
Na	EtI	.08	0.031
Li	EtI	.08	1.5
Na	MeI	.10	0.00054
Li	MeI	.10	.035
Na (R ₄ N ⁺ ClO ₄ ⁻) ^b	EtI	.08	.009
Na (R ₄ N ⁺ I ⁻) ^b	EtI	.08	.013

^a Initial molar concentration of enolate. ^b Tetra-*n*-butylammonium salt, 0.3 g., added to 200 ml. of ethereal sodiobutyrophenone. ^c 1.72 *M*.

in the transition state is evident from these data. For example, the rate of ethylation by ethyl bromide increases more than 6000-fold as the metal

TABLE II

ETHYLATION OF SODIOPHENOLATE BY ETHYL IODIDE				
Run	EtI, <i>M</i>	Enolate, <i>M</i>	Ketone, ^a <i>M</i>	Initial rate ^b
1	1.86	0.388	0.005	35.9
2	1.86	.171	.003	20.8
3	1.86	.150		20.0
4	1.86	.120	.002	15.3
5	1.86	.080	.002	13.2
6	1.86	.050		8.1
7	0.506	.100		2.9
8	.568	.100	.004	3.4
9	.845	.100	.004	5.1
10	.994	.100		5.1
11	1.50	.100		10.1
1-6	1.86	(.100) ^c	.002	(14.2) ^e
12	2.01	.100		12.2
13	2.51	.100		21.2
14	1.86	.176 ^d	.003	21.0
15	1.86	.110	.50	100
16	1.86	.104	.40 ^e	43.7
17	1.86	.108	.50 ^f	38.4

^a Free ketone present; butyrophenone unless otherwise stated. ^b Decrease in enolate concentration over the first 10-25% of the reaction in moles/l./sec. $\times 10^7$. ^c Initial rate at 0.100 *M* enolate taken from curve in Fig. 1. ^d Initially contained 13.1 g. of powdered sodium iodide. ^e Initial molar concentration of α -ethylbutyrophenone. ^f Hexamethylacetone.

(1) The authors gratefully acknowledge support from the National Science Foundation (NSF-G4475) which made this work possible.

(2) Taken in part from the M.S. thesis of W. L. Gumby, The Pennsylvania State University, August, 1959.

(3) A. Brändström, *Arkiv Kemi*, **6**, 155 (1954); **7**, 81 (1954).

(4) H. D. Zook and W. L. Rellahan, *This Journal*, **79**, 881 (1957).

(5) W. L. Rellahan and H. D. Zook, *J. Org. Chem.*, **24**, 709 (1959).

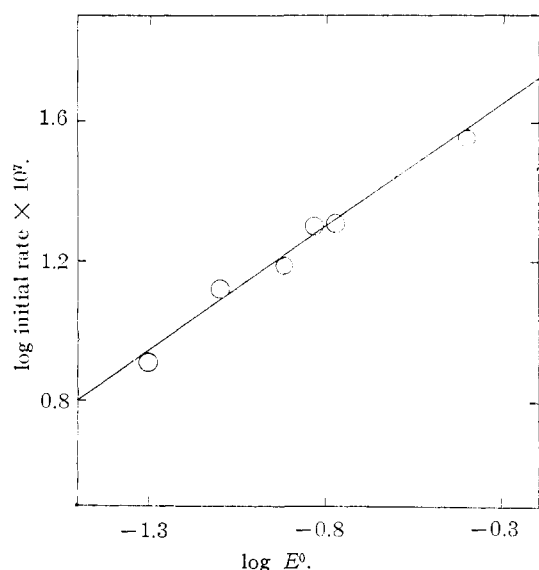


Fig. 1.—Ethylation of sodiobutyphenone; order in enolate.

ether. Evaporation of solvent during transfers is easily held to less than 3%.

At least two factors are responsible for the increase in specific rate. These factors have been separated by the method of initial rates in which the concentrations of the several reactants were varied independently.⁶ The results are presented in Table II.

The most obvious reason for the increase in specific rate is catalysis by products. In this case, one product, sodium iodide, begins to precipitate within the first 5% of the reaction. Kornblum recently described remarkable effects of surface catalysis in the alkylation of phenoxide ions.⁷ A comparison of runs 2 and 14 shows that a large amount of powdered sodium iodide, when rapidly stirred with the enolate, has no effect on the initial rate. However, the rate is tripled when the other product of the reaction, α -ethylbutyphenone, is added in initial concentration of 0.40 *M* (run 16). An even more effective catalyst is butyphenone. Catalysis is not dependent upon the presence of α -hydrogen atoms in the ketone, for hexamethylacetone is almost equivalent to α -ethylbutyphenone in activity.

Because the data for any single run did not conform to an expression for a first-order autocatalytic reaction, other factors contributing to the complexity were sought. For this work, enolate solutions which contained negligible amounts of free ketone were prepared. The maximum amounts of ketone listed in Table II were determined by infrared analysis of the enolate solutions. Runs 1–6 at constant concentration of alkyl halide were used to determine the order of the reaction in enolate. A plot of $\log dE/dt$ versus $\log E$ (Fig. 1) gives a slope of approximately 0.7. Although the precision is not as great as might be desired, the order in enolate is surely far from unity.

(6) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 44.

(7) N. Kornblum and A. P. Lurie, Abstracts of Papers, 133rd Meeting of the American Chemical Society, San Francisco, Calif., April, 1958, p. 14-N.

The alkylations so far described in this and a former study⁴ were carried out in 10- to 25-fold excess of alkyl halide. In runs 7–13 the rates of ethylation of 0.1 *M* solutions of sodiobutyphenone by excess ethyl iodide were measured at eight concentrations of ethyl iodide in the range 0.5–2.5 *M*. The order in alkyl halide determined from the slope of a plot of $\log dE/dt$ versus $\log [Et I]$ (Fig. 2) is unity within experimental error at concentrations of halide less than 1 *M*, but increases to a value as great as 3/2 at higher halide concentrations.

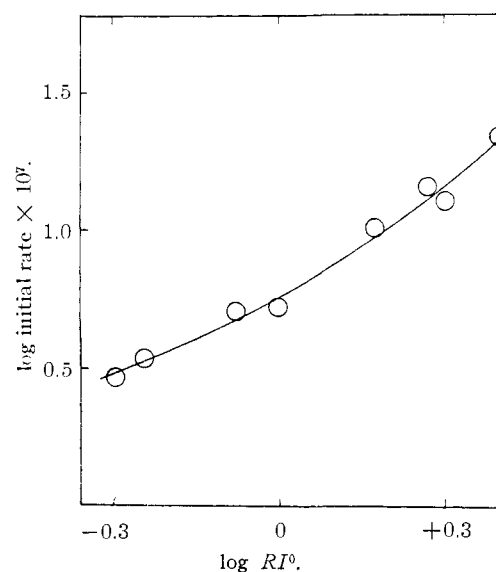


Fig. 2.—Ethylation of sodiobutyphenone; order in ethyl iodide.

Association of Sodiobutyphenone.—Ebulliometric measurements on ethereal solutions of this enolate have been made over a range of concentration from 0.13 to 0.63 molal (Table III). The

TABLE III
BOILING POINT ELEVATIONS AND AGGREGATION NUMBERS OF SODIOBUTYPHENONE SOLUTIONS

Enolate, molality	Free ketone molality	ΔT , °C.	α
0.630	0.008	0.421	3.0
.490	.029	.363	2.8
.404	.004	.237	3.4
.397	.011	.273	2.9
.304	.005	.196	3.1
.200	.010	.150	3.2
.152	.003	.105	2.9
.134	.003	.084	3.2
			Average 3.1

solutions contained insignificant amounts of free butyphenone (see Experimental). An average aggregation of three ion pairs is indicated by the boiling-point elevation.⁸ The constancy of the

(8) A value of two was reported earlier⁴ for a solution of enolate prepared from sodium triphenylmethide. It is now known that such solutions contain more than an equivalent amount of triphenylmethane, which, because of its relatively low molecular weight compared with that of the aggregated enolate, greatly reduces the precision of this determination.

ammonia. Ammonia was distilled, and the mixture was refluxed for three days, filtered and refluxed for another three days under a column to remove last traces of ammonia.

Alkylation Studies.—The apparatus and procedure for the kinetic studies have been described.⁴ All reactions were carried out at $30.00 \pm 0.02^\circ$. Nitrogen gas for the sampling operation was bubbled through ethereal sodium triphenylmethide solution to remove traces of oxygen and water vapor and to saturate the gas with ether vapor. At all other times the system was closed and contained a small positive pressure. Evaporation throughout an entire run amounted to less than 3%, most of which occurred during the initial addition of the enolate solution to the nitrogen-filled flask. In order to eliminate this error, as well as any error due to possible non-additivity of volumes of halide and enolate solutions, a "zero-time" aliquot was titrated soon after mixing. The results of thirty alkylations are listed in Tables I and II.

Vapor Pressure of Methyl Bromide-Enolate System.—A 55-ml. flask immersed in a constant-temperature bath at $25.30 \pm 0.05^\circ$ was attached to a manometer, gas buret and vacuum line. The flask was filled with anhydrous ether freshly distilled from lithium aluminum hydride. The system was evacuated intermittently until a constant vapor pressure of 545 mm. was obtained. The vapor pressure of ethyl ether at 25.3° is 544 mm.¹⁴ The volume of liquid at this time was 52 ml. Five portions of about 100 ml. each of methyl bromide (Dow Chemical Co., purified by isothermal distillation) were accurately measured and added through a capillary at the bottom of the flask. After each addition, air pressure was applied to the open end of the manometer in order to fill the other leg with mercury and thereby force the vapor back into the flask. After circulating the mercury in this way several times, a constant value of the vapor pressure was obtained. The vapor pressures are plotted against mole fraction of methyl bromide in Fig. 3.

The procedure was repeated with a 0.42 *M* solution of sodiobutyrophenone. The five portions of methyl bromide were added over a period of one hour. The slope of the vapor

(14) "International Critical Tables," Vol. 3, McGraw-Hill Book Co., Inc., New York, N. Y., 1928, p. 19.

pressure curve was the same as that for the system ether-methyl bromide. The amount of alkylation in this time is negligible. A titration after 17 hours indicated that the reaction was then only 48% complete.

Ebulliometric Studies.—A differential ebulliometer of the type described by Swietoslowski and Anderson¹⁵ was employed. The exit led to a 2-ml. receiver and thence through Drierite to a T-tube over which was passed a very slow stream of nitrogen. Temperatures were measured to 0.001° with micro-Beckmann thermometers. In order to obtain constant reproducible temperature differences, it was necessary to drain the water from the condenser for several minutes and distil up to 2 ml. of ether.

The enolate solutions were freshly prepared in 2-3-liter batches and forced by nitrogen pressure directly from the sodium hydride into the boiler. The apparatus was flushed several times with the solution and filled to a 40.0-ml. calibration mark. After the boiling point determination, a 25.0-ml. aliquot was drained into a volumetric flask, weighed and titrated. The remainder of the solution was transferred to a 0.16-mm. infrared cell for estimation of ketone at 5.88μ . The results for eight separate preparations are listed in Table III. The concentrations of free ketone represent maximum amounts that could be present. They are calculated on the unlikely assumptions that the pure enolate has no absorption in the carbonyl region and that no moisture was adsorbed on the surfaces of the infrared cell. The aggregation numbers listed in Table III have been calculated without correction for free ketone. When corrections are applied, the average aggregation number is 3.35, an increase of about 8%.

The molal boiling point constant for ethyl ether in the instrument used, 2.00, was determined by measuring boiling point elevations of 0.1-0.4 molal solutions of triphenylmethane, m.p. $92-93^\circ$.

(15) A. Weissberger, "Physical Methods of Organic Chemistry," Vol. 1, 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1949, p. 121.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

Studies of the Mechanisms of the Reactions of Benzoyl Peroxide with Secondary Amines and Phenols

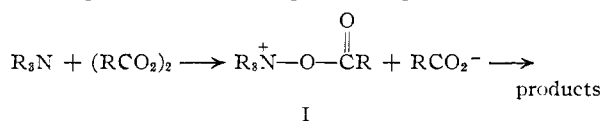
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The reactions of dibenzylamine, diphenylamine and *p*-cresol with benzoyl peroxide, labeled with oxygen-18 in the carbonyl positions, have been studied. Dibenzylamine reacts by nucleophilic displacement on an oxygen of the peroxide link to give ultimately benzoic acid and *O*-benzoyl-*N,N*-dibenzylhydroxylamine which contains all of the excess oxygen-18 in the carbonyl oxygen. Diphenylamine reacts by the same process to give *O*-benzoyl-*N,N*-diphenylhydroxylamine which is unstable under these conditions and rearranges to give *N*-phenyl-*N*-*o*-hydroxyphenylbenzamide. The amide contains 55% of the excess oxygen-18 in the carbonyl group and 45% in the phenolic hydroxyl group. Similarly *p*-cresol reacts to give 2-hydroxy-4-methylphenyl benzoate which contains 87% of the excess oxygen-18 in the carbonyl group and 13% in the phenolic hydroxyl group. Mechanisms for these reactions are proposed and discussed.

Amine Reactions.—The reactions of amines with peroxides, in particular benzoyl peroxide, have been studied by a large number of investigators.¹

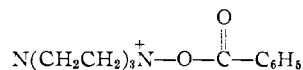
The reaction of tertiary amines with diacyl peroxides is thought to proceed by an initial polar displacement, as shown below, to give I which then decomposes by a radical path into products.²



(1) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 590-595.

Secondary aliphatic amines react quite simply with benzoyl peroxide to give *N,N*-dialkyl-*O*-benzoylhydroxylamines and benzoic acid. There has

(2) W. B. Geiger, *J. Org. Chem.*, **23**, 298 (1958), has prepared *N*-acetoxytrimethylammonium bromide by treatment of trimethylamine with acetyl peroxide and then with concentrated hydrobromic acid. Thus it has been demonstrated that 1 is formed by the initial reaction of a tertiary amine with an acyl peroxide. D. Buckley, S. Dunstan and H. B. Henbest, *J. Chem. Soc.*, 4901 (1957), also have suggested this mechanism for these reactions and have spectral evidence for the



ion obtained from the reaction of triethylenediamine with benzoyl peroxide.