TABLE I

INFLUENCE OF TEMPERATURE ON THE OBSERVED ROTATION OF OPTICALLY ACTIVE α-PHENYLETHYL CHLORIDE

T, °C.	αD	T, °C.	αD
30.1	77.1	24.7	78.7
27.5	77.8	23.6	79.2
26.8	78.0	22.7	79.3
26.3	78.2	22.0	79.6
25.7	78.4	20.5	80.1
25.0	78.6	18.8	80.6

active alcohol had a boiling point of 80–80.5° at 5.6 mm., $n^{25}D$ 1.5264. The rotational value for optically pure α-phenylethyl alcohol is taken as $\alpha^{25}D$ 43.7°.[6]

Optically Active α-Phenylethyl Chloride (I).—This compound was prepared by a modification of an earlier procedure.[6]

In a 500-ml. three-necked flask equipped with a sealed stirrer, a low temperature thermometer, a drying tube and an addition funnel was placed 47.5 g. (0.6 mole) of dry pyridine, 24.3 g. (0.2 mole) of optically active α-phenylethyl alcohol ($\alpha^{25}D$ −38.24°, 1 dm., neat) and 200 ml. of dry chloroform. The mixture was cooled to −13° in a Dry Ice–methanol-bath, and 30.7 g. (0.2 mole) of phosphorus oxychloride was added as rapidly as possible with stirring, keeping the temperature of the reaction mixture below −9°. The resulting mixture was stirred for 5 min. at −9 to −13°, and a solution of 0.8 mole of dry pyridine hydrochloride in approximately 150 ml. of dry chloroform was added, maintaining the same temperature range. After warming for 3 hr. at 40 ± 3° the reaction mixture was decomposed by shaking with crushed ice for 5 min. and the two layers then separated. The chloroform layer (with which was combined two 25-ml. chloroform extracts of the aqueous layer) was washed with two 25-ml. portions of 85% phosphoric acid, followed by ice-water, and dried over anhydrous sodium sulfate at 0° for 30 min., then overnight with Drierite at 0°. The solvent was removed *in vacuo* at approximately 27°, and the residue fractionally distilled to give 17.5 g. (62%) of L(+)-α-phenylethyl chloride, b.p. 53–54° at 4.3 mm., $n^{25}D$ 1.5247, $\alpha^{24.6}D$ +84.31° (1 dm., neat); corrected to optically pure alcohol, $\alpha^{24.6}D$ +96.4°.

α-Phenylethylation of Phenylacetonitrile with I.—To a stirred solution of 0.101 mole of potassium amide in 600 ml. of liquid ammonia was added 12.0 g. (0.102 mole) of phenylacetonitrile in 15 ml. of anhydrous ether, followed after 5 min. by 14.1 g. (0.1 mole) of α-phenylethyl chloride ($\alpha^{26}D$ +90.21°) in 15 ml. of anhydrous ether (added during 15 min.). After one hour, the liquid ammonia was replaced by ether, and 100 ml. of 1.5 *N* hydrochloric acid added to the reaction mixture. The ether was removed by distillation and the solid collected on a funnel. The solid was washed with water and then dissolved in acetone. Ethanol was added, and most of the acetone distilled. After cooling the solution overnight in the refrigerator there was precipitated 15.2 g. (88%) of *erythro*-D(−)-2,3-diphenylbutyronitrile (II), $[\alpha]^{26}D$ −24° (*c* 2 in benzene). The product melted at 134.5–135°; reported m.p. for the racemate is 132.5–133.5°.[2]

α-Phenylethylation of Phenylacetic Acid with I.—To a stirred solution of 0.11 mole of potassium amide[14] in 400 ml. of liquid ammonia was added 7.5 g. (0.055 mole) of phenylacetic acid, followed by 7.0 g. (0.05 mole) of α-phenylethyl chloride ($\alpha^{25}D$ +84.31°) in 10 ml. of anhydrous ether. The reaction mixture was stirred for 1 hr. The liquid ammonia was evaporated on the steam-bath and ether added. The ethereal mixture was filtered, and the solid dissolved in water. After filtering, the aqueous solution was acidified to precipitate 10.3 g. (86%) of *erythro*-D(+)-2,3-diphenylbutyric acid (III), m.p. 170–180°. After one recrystallization from a mixture of ether and petroleum ether the acid melted at 185–186°, $[\alpha]^{26}D$ +25.5° (*c* 4 in absolute ethanol); reported[4] m.p. for the racemate 187–187.5°.

Influence of Temperature on the Observed Rotation of Optically Active α-Phenylethyl Chloride.—A water-jacketed 1-dm. polarimeter tube was filled with optically active α-phenylethyl chloride ($\alpha^{25}D$ +78.6°). The desired temperature for each reading was obtained by changing the temperature of the water in a large bath which was connected to the polarimeter tube jacket through a circulating pump. The results are given in Table I.

(14) See R. S. Yost and C. R. Hauser, THIS JOURNAL, **69**, 2325 (1947).

DURHAM, NORTH CAROLINA

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

Chemistry of Enolates. I. The Kinetics and Mechanism of Alkylation of Alkyl Phenyl Ketones[1]

BY HARRY D. ZOOK AND WILLIAM L. RELLAHAN[2]

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Alkylations of sodium enolates prepared from eight primary and secondary alkyl phenyl ketones have been measured kinetically. Homogeneous solutions of the enolates in ether were obtained quantitatively from the ketones and sodium triphenylmethide. By varying the length of the alkyl chain from methyl to octyl, a maximum rate of ethylation was found with propiophenone. A marked decrease in rate accompanied branching on the α-carbon atom of the ketone. Alkylation of butyrophenone by various alkyl bromides gave the following rate sequences: methyl > ethyl > *n*-propyl > isobutyl >> neopentyl and ethyl > isopropyl < *t*-butyl. The rate of alkylation was a function of the concentration of sodium enolate for all alkylations, including alkylations by *t*-butyl bromide and benzyl chloride. The mechanism of the reaction involves a transition state which has both SN1 and SN2 character. Association of two molecules of the sodium enolate of butyrophenone in 0.07–0.13 *M* ethereal solutions is indicated by ebulliometric measurements.

The two-stage alkylation of ketones by a strong base such as sodamide[3] or sodium alkoxide[4] and an alkyl halide is a well known synthetic process. The ketones first are converted to the corresponding sodium enolates, and the latter compounds react metathetically with the alkylating agents. The reaction mechanism is generally considered to involve carbanions, although there is no evidence that the intermediate sodium enolates are dissociated under the conditions employed. These studies were undertaken to investigate the nature of the enolate and the mechanism of its alkylation.

Phenyl alkyl ketones were converted to sodium

(1) Taken in part from a Ph.D. thesis submitted by William L. Rellahan to the Graduate School of The Pennsylvania State University, August, 1956.

(2) Du Pont Postgraduate Teaching Assistant, 1955–1956.

(3) F. W. Bergstrom and W. C. Fernelius, *Chem. Revs.*, **12**, 106 (1933); A. Haller, *Bull. soc. chim.*, [4] **31**, 1073 (1922).

(4) G. Vavon and J. M. Conia, *Compt. rend.*, **223**, 157, 245 (1946); J. M. Conia, *Ann. chim.*, **8**, 709 (1953).

enolates by an ethereal solution of sodium triphenylmethide.

$$C_6H_5COCHR_2 + Na^+ C(C_6H_5)_3^- \longrightarrow HC(C_6H_5)_3 + (C_6H_5COCR_2)^-Na^+$$

The quantitative nature of this reaction in ether solution was demonstrated over a range in concentration from 0.06 to 0.14 *M*. The characteristic deep red color of the base vanishes at the stoichiometric end-point, and the resulting homogeneous solutions of sodium enolates contain no excess ketone or base.

The alkylation reaction is a nucleophilic substitution; the enolate ion displaces a halide ion at a saturated carbon atom in the halide.

$$RCH_2X + (C_6H_5COCR_2)^-Na^+ \longrightarrow C_6H_5COCR_2CH_2R + Na^+X^-$$

Sodium halide precipitates as the reaction proceeds. The alkylations were followed by measuring the decrease in enolate concentration and also by measuring the amount of sodium halide produced. Frequently, both analytical procedures were employed. The amount of halide formed always equalled the amount of enolate consumed. Rates of alkylation were determined at 30° for a variety of enolates and alkyl halides. The rate constants are listed in Tables I and II. It will be shown that the experimental findings support a bimolecular mechanism in which the transition state has a little SN1 character for alkylations by certain halides.

TABLE I

ALKYLATION OF BUTYROPHENONE BY RX[a] AT 30°

R	X	E_0[b]	k_2[c]
	(α-Substituted)		
CH_3CH_2–	I	0.096	13
CH_3CH_2–	Br	.094	1.0
$(CH_3)_2CH$–	Br	.091	0.015
$(CH_3)_3C$–	Br	.086	0.072
$C_6H_5CH_2$–	Cl	.126	8.8[d]
	(β-Substituted)		
CH_3CH_2–	Br	0.094	1.0
$CH_3CH_2CH_2$–	Br	.090	0.34
$(CH_3)_2CHCH_2$–	Br	.089	.043
$(CH_3)_3CCH_2$–	Br	.087	.0000

[a] 1.72 *M* in ether solution. [b] Initial molar concentration of sodium enolate. [c] Liter mole^{-1} sec.$^{-1}$ × 10^6. [d] Calculated from the first 25% of the reaction.

Variation in the Structure of the Alkylating Agent.—The alkylation of butyrophenone was studied in some detail (Table I). Ethylation of a 0.1 *M* solution of the enolate in 1.72 *M* ethereal ethyl bromide at 30° had a half-life of 117 hr. Ethylation by ethyl iodide was much more rapid; the half-life for reaction under these conditions was 9 hr. When the number of alkyl groups on the β-carbon atom of the halide was increased, the rate of alkylation decreased markedly. The effect of methyl substitution is shown by the following series of reaction rates: ethyl > *n*-propyl > isobutyl >> neopentyl. No evidence of alkylation by neopentyl bromide could be detected after four months at 30°.

This series strongly suggests a bimolecular mechanism (SN2) in which rearward attack by the enolate on the halide is hindered by substituents in the β-position. This same series of relative rates is observed when the substituting entity is an ion in polar media, provided that the concentration of the ion appears in the rate equation; *i.e.* the rate is not controlled by slow initial ionization of the halide.[5] Since the tendency for ionization of the halide should be slight in ether–halide solvent, these results were not unexpected. The fact that the rate of alkylation varied with the enolate concentration in each case is in line with this argument and eliminates a pure SN1 mechanism.

Substitution of methyl groups on the α-carbon atom of the halide gives the following series of reaction rates: methyl > ethyl > isopropyl < *t*-butyl. Except for the tertiary halide, this series also is indicative of bimolecular substitution. The higher rate for the tertiary halide suggests an SN1 or E_1 mechanism for this halide. However, when an SN1 mechanism is observed, as in the hydrolysis and alcoholysis of halides in polar media,[6] the ratio of the rates of *t*-butyl to isopropyl halides is of the order of 10^3 to 10^6. In the alkylations reported here, the rate for *t*-butyl bromide was only five times that for isopropyl bromide, and in both alkylations, the rate was dependent upon the enolate concentration.

Benzyl chloride is another halide which undergoes SN1 reactions in polar media. Dehydrohalogenation is not possible with this halide. Benzyl chloride is more than eight times faster than ethyl bromide in the alkylation of the sodium enolate of butyrophenone. But again, the rate is dependent upon enolate concentration. Furthermore, benzyl chloride reacts more than twice as fast with the enolate of propiophenone than with the enolate of butyrophenone, an additional fact which eliminates a prior ionization of the halide as the rate-determining step.

These findings are best interpreted by a combination SN1–SN2 mechanism. A consideration of the effects of β-substitution in the halide, together with the fact that the rate of alkylation is dependent upon the concentration of enolate for all alkylations studied, confirms the SN2 character of the transition state. The relatively high rates of alkylation by tertiary and benzyl halides is indicative of some SN1 contribution to this state. Borderline mechanisms have been advanced by Winstein[7] and by Swain[8] to correlate many substitution reactions. Recently, much evidence for this mechanism as applied to alkylations of the nitrite and other ambident ions has been presented by Kornblum.[9] SN2 character for the alkylation of silver nitrite was demonstrated by decrease in rate with increased substitution on the β-carbon atom of the halide. However, SN1 character was indicated by the series of rates: *t*-butyl > *s*-butyl > *n*-butyl in the ratio 1500:4:1. The transition state for the

(5) I. Dostrovsky and E. D. Hughes, *J. Chem. Soc.*, 157 (1946).

(6) L. C. Bateman, K. A. Cooper, E. D. Hughes and C. K. Ingold, *ibid.*, 925 (1940); L. C. Bateman and E. D. Hughes, *ibid.*, 945 (1940).

(7) S. Winstein, E. Grunwald and H. W. Jones, THIS JOURNAL, **73**, 2700 (1951).

(8) C. G. Swain and C. B. Scott, *ibid.*, **75**, 141 (1953).

(9) N. Kornblum, R. A. Smiley, R. K. Blackwood and D. C. Iffland, *ibid.*, **77**, 6269 (1955).

alkylation of butyrophenone must possess considerably less SN1 character, for the rates of alkylation by the secondary and tertiary halides are more nearly of the same magnitude. This result is not surprising because the sodium ion should aid less in the polarization of the halide than the more electrophilic silver ion.[9]

TABLE II

ALKYLATION OF ENOLATES $(C_6H_5C{:::}CR_1R_2)^-Na^+$ (with O)

R_1	R_2	RX[a]	E_0[b]	k_2[c]
H	H	C_2H_5Br	0.095	1.0[d]
H	CH_3	C_2H_5Br	.138	1.6
H	C_2H_5	C_2H_5Br	.094	1.0
H	n-C_3H_7	C_2H_5Br	.135	0.9
H	n-C_4H_9	C_2H_5Br	.135	.8
H	n-C_7H_{13}	C_2H_5Br	.136	.8
CH_3	CH_3	CH_3I	.109	460
CH_3	CH_3	C_2H_5Br	.130	1.0
C_2H_5	C_2H_5	C_2H_5I	.069	3.7
H	C_2H_5	C_2H_5I	.096	13
H	CH_3	$C_6H_5CH_2Cl$	.127	20[d]
H	C_2H_5	$C_6H_5CH_2Cl$	.126	8.8[d]

[a] 1.72 M in ether solution. [b] Initial molar concentration of sodium enolate. [c] Liter mole^{-1} sec.$^{-1}$ $\times$ 10^6. [d] Calculated from the first 25% of the reaction.

Variation in the Structure of the Enolate.—Rate constants for the alkylation of eight alkyl phenyl ketones are given in Table II. The ethylation of the enolate of acetophenone is complicated by a subsequent acid–base equilibrium and further alkylation of the product. However, the initial rate determined over the first 25% of the reaction was found to be only 60% of that for the ethylation of the next higher homolog, propiophenone. The rate then decreased again in going from propiophenone to butyrophenone. Further increase in the length of the alkyl chain did not affect the rate appreciably. These results may be explained by an increase in the nucleophilic character of propiophenone enolate over acetophenone enolate owing to a positive inductive effect of the methyl group. Thereafter, the rate of alkylation is decreased because of steric hindrance by the ethyl and larger groups. Similar variations in reactivity with chain length have been observed in the hydrogenation,[10] bromination[11] and base-catalyzed enolization[12] of these ketones. Usually the anomalous member of the series is butyrophenone which, here in a comparison of the enolates rather than the ketones, appears quite regular.

Branching on the α-carbon atom of the ketone hinders further alkylation at this position. α-Ethylbutyrophenone is alkylated by ethyl iodide at less than one-third the rate of alkylation of butyrophenone. Half-lives for other alkylations of normal and secondary alkyl phenyl ketones are compared in Table III. The hindrance to further alkylation produced by two alkyl groups already present on the carbon atom more than overcomes any enhanced activity due to the polar effects of these groups. The ethyl group in butyrophenone is equivalent to the two methyl groups in isobutyrophenone.

(10) V. N. Ipatieff and V. Haensel, THIS JOURNAL, **64**, 520 (1942).
(11) D. P. Evans, *J. Chem. Soc.*, 785 (1936).
(12) D. P. Evans and J. J. Gordon, *ibid.*, 1434 (1938).

TABLE III

HALF-LIVES OF SOME ALKYLATION REACTIONS

Ketone	Halide	$t^1/_2$, hours
Butyrophenone	EtBr	117
Isobutyrophenone	EtBr	115
Propiophenone	EtBr	70
Isobutyrophenone	EtBr	115
Butyrophenone	EtI	9
α-Ethylbutyrophenone	EtI	30

Kinetic and Product Studies.—The alkylations were carried out as pseudo-first-order processes in ether solution containing 13–18-fold excess alkyl halide. This excess was desirable because the rates were very slow even at 40° in sealed tubes. The rate of alkylation varied directly with the concentration of the enolate. By plotting the log of the enolate concentration, E, against time, straight lines were obtained over the first half-life for most alkylations. Good reproducibility of the results is indicated by runs 14, 15 and 22 (Fig. 1). These

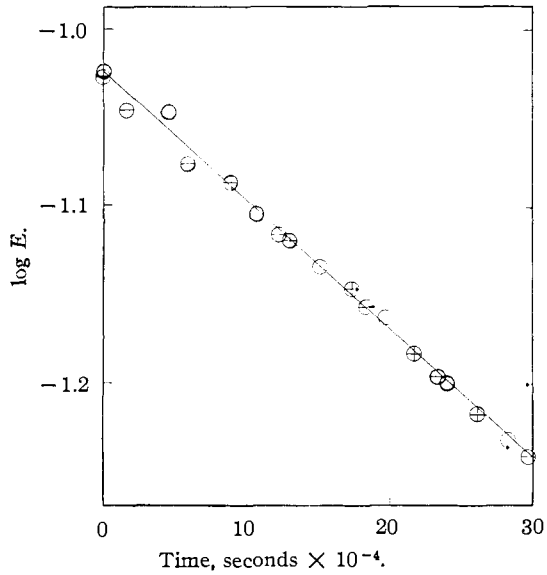

Fig. 1.—Ethylation of butyrophenone, log E *vs.* time: ○, run 14; ⊕, run 15; ⊖, run 22.

experiments gave the same rate constant for the ethylation of butyrophenone even though the alkylations were carried out at different times with different samples of ketone and different batches of sodium triphenylmethide. Especially good fits to a pseudo-first-order rate equation were obtained for the alkylation of enolates with branching on the α-carbon atom. The rate constant for the ethylation of α-ethylbutyrophenone showed no deviation over 80% of the reaction.

For enolates of ketones with no branching on the α-carbon atom, the pseudo-first-order rate constants increased about 50% during the second half-life. The constants for benzylations were particularly poor. In fact, the data for any one run could better be fit to a pseudo-zero-order reaction. However, when the initial concentration of enolate was decreased from 0.127 to 0.061 M, the rate con-

stant determined over the first 25% of the reaction, as well as the half-life of the reaction, varied less than 10%. That the rate of benzylation is not independent of enolate is shown also by the widely different rates of benzylation of propiophenone and butyrophenone. Several possible explanations for the increase in rate constant were considered. Since at least one hydrogen atom remains on the α-carbon atom of these enolates, consecutive reactions involving acid–base equilibrium and further alkylation are possible (equations 3 and 4). An

$$C_6H_5COCHR_2 + (C_6H_5COCHR)^-Na^+ \rightleftharpoons C_6H_5COCH_2R + (C_6H_5COCR_2)^-Na^+ \quad (3)$$

$$(C_6H_5COCR_2)^-Na^+ + RX \longrightarrow C_6H_5COCR_3 + NaX \quad (4)$$

increase in the rate constant corresponds to an increase in the rate of disappearance of base. However, base is not consumed in equation 3. The position of this equilibrium would be expected to lie to the left. By comparing the inductive effects of one *versus* two alkyl groups on the acidity of the α-hydrogen atom, it is expected that the enolate with the more alkyl groups would be the more basic. Maron and La Mer[13] have shown that the introduction of an alkyl group on the α-carbon atom of a nitroalkane lowers the velocity constant in the reaction with hydroxyl ion by a factor of 10. Pearson has estimated a 50–100-fold decrease in acidity by the substitution of an ethyl group into the α-position of malonic ester.[13] The extent of equation 3 in 26 hr. at 30° has been measured by quenching equimolar amounts of α-ethylbutyrophenone and the enolate of butyrophenone in deuterium oxide.[14] If equilibrium is obtained in this time, the equilibrium constant is approximately 0.1. Equations 3 and 4 are important in the alkylation of acetophenone as shown by a product study of this reaction. However, no α,α-diethylbutyrophenone could be detected in the products of a large-scale alkylation of butyrophenone.

The rate of disappearance of base by subsequent alkylation (equation 4) has been measured independently for α-ethylbutyrophenone enolate and found to be only 30% as fast as the alkylation of butyrophenone. Complications due to equations 3 and 4 should give a decrease in rate constant as this alkylation proceeds, whereas just the reverse was observed.

Another possible reason for the increase in pseudo-first-order constant would be a change in the amount of aggregation of the ion pairs representing the sodium enolate in ether solution. Ion-pair aggregation has been demonstrated in solutions of tetra-alkylammonium salts in benzene solution.[15] The association of halomagnesium salts of carbanions in ether has been demonstrated by boiling-point elevation[16] and that of lithium perchlorate in ether by vapor pressure, conductivity and viscosity measurements.[17] Aggregation would reduce the total enolate concentration by a factor, α, which may be called the aggregation number. Then, rate $= k_1'E/\alpha$, where $\alpha = 1$ at infinite dilution. The rates of reaction at various values of E were obtained from the slopes of the curves of plots of E *vs.* t, and the quantity k_1'/α was plotted against E. A value of k_1' was obtained by extrapolation to infinite dilution. The calculated values of α required to give a straight line over 95% of the reaction varied from 1.4 at $E = 0.006$ M to 6.5 at $E = 0.1$ M. However, no change in the average molecular weight with concentration could be detected by ebulliometric studies of ethereal solutions of butyrophenone enolate. The boiling point elevations corresponded to an association of two molecules of the sodium enolate ($\alpha = 2.0 \pm 0.2$) over a range of enolate concentration from 0.07 to 0.12 M. Possibly the activity of the enolate is influenced by other enolate ion pairs by forces too weak to produce stable aggregates.

The products from a large-scale ethylation of butyrophenone were investigated. After four half-lives, α-ethylbutyrophenone was obtained in 90% yield along with a small amount of recovered butyrophenone. No α,α-diethylbutyrophenone could be detected. A similar study of the ethylation of acetophenone after two half-lives gave recovered acetophenone (25%), butyrophenone (45%), α-ethylbutyrophenone (7%), but no α,α-diethylbutyrophenone. The pseudo-first-order rate constant for this run was fairly good over the first 36 hr. but gradually increased as the more rapid alkylation of the enolate of butyrophenone became appreciable. These results are in accord with numerous syntheses in which only C-alkylation occurs. Although both O- and C-alkylation have been observed when steric considerations become serious, *e.g.*, in the alkylation of diphenylacetophenone by β-chloroethyldimethylamine,[18] the product is exclusively the one obtained by C-alkylation when the halide is small. Propiophenone undergoes C-alkylation even with β-chloroethyldimethylamine.[19]

Experimental

Materials.—Anhydrous ether was Mallinckrodt analytical reagent distilled from sodium triphenylmethide solution and stored under a slight positive pressure of nitrogen. Isobutyrophenone, methyl iodide, *n*-propyl bromide, isopropyl bromide and isobutyl bromide were Eastman Kodak Co. white-label products refractionated through a 12-plate column. Ethyl bromide was Matheson, Coleman, Bell Co. practical grade refractionated from phosphorus pentoxide. *t*-Butyl bromide, b.p. 33° at 177 mm. (12-plate column), $n^{25}D$ 1.4255, was prepared in 77% yield.[20] Neopentyl bromide, b.p. 103° at 733 mm., $n^{25}D$ 1.4349, was prepared in 72% yield.[21]

Preparation of *n*-Alkyl Phenyl Ketones.—Four of these ketones were prepared by the action of Grignard reagents on benzonitrile. This method has not been used previously for the preparation of phenyl alkyl ketones, although several have been made from aliphatic nitriles and phenylmagnesium bromide.[22] The preparation of valerophenone is typical.

(13) (a) S. H. Maron and V. K. La Mer, THIS JOURNAL, **60**, 2588 (1938); (b) R. G. Pearson, *ibid.*, **71**, 2212 (1949).

(14) Unpublished work of W. L. Rellahan, The Pennsylvania State University.

(15) D. T. Copenhafer and C. A. Kraus, THIS JOURNAL, **73**, 4557 (1951); C. G. Swain and M. M. Kreevoy, *ibid.*, **77**, 1122 (1955).

(16) J. Meisenheimer and W. Schlichenmaier, *Ber.*, **61**, 720 (1928).

(17) K. Ekelin and L. G. Sillen, *Acta Chem. Scand.*, **7**, 987 (1953).

(18) H. Rinderknecht, THIS JOURNAL, **73**, 5770 (1951).

(19) N. Sperber, R. Fricano and D. Papa, *ibid.*, **72**, 3068 (1950).

(20) L. Henry, *Rec. trav. chim.*, **23**, 327 (1904), footnote 1.

(21) L. H. Sommer, H. D. Blankman and P. C. Miller, THIS JOURNAL, **76**, 803 (1954).

(22) C. R. Hauser, W. J. Humphlett and M. J. Weiss, *ibid.*, **70**, 426 (1948); R. L. Shriner and T. A. Turner, *ibid.*, **52**, 1267 (1930).

To the Grignard reagent prepared from 37.9 g. (1.56 atoms) of magnesium, 211 g. (1.54 moles) of *n*-butyl bromide and 550 ml. of dry ether was added with stirring a solution of 120 g. (1.17 moles) of benzonitrile in 125 ml. of dry ether.[23] After refluxing for 16 hr., the solution containing the precipitated yellow ketimine salt was poured onto a mixture of ice and concentrated hydrochloric acid. The product was extracted into ether and fractionated through a 12-plate column. Valerophenone was obtained in ten fractions boiling at 108–109° at 6.5 mm., $n^{25}D$ 1.5122. The yield was 83% based on the benzonitrile.

The physical constants of the *n*-alkyl phenyl ketones used in this study are listed in Table IV. The freezing points were determined from cooling curves on 10-ml. samples in a cryostat equipped with a mechanical stirrer and a calibrated 0.1° thermometer.

TABLE IV

PHYSICAL CONSTANTS OF *n*-ALKYL PHENYL KETONES

Ketone	B.p. °C.	B.p. Mm.	F.p., °C.	$n^{25}D$
Propiophenone[a]	76	5	17.7	1.5242[e]
Butyrophenone[b]	61	2	12.5	1.5170[f]
Valerophenone	109	6.5	−9.4	1.5122[g]
Caprophenone	102	3	21.7	1.5080[h]
Enanthophenone	98	1	16.7[c]	1.5049
Pelarogonophenone	120	2	14.9[d]	1.5000

[a] Eastman Kodak Co. refractionated through a 12-plate column. [b] Prepared by Friedel-Crafts acylation and fractionated through a 12-plate column. [c] V. Auger, *Bull. soc. chim. France*, [2] **47**, 50 (1887), gives 17°. [d] The m.p. of 46° reported by P. Sabatier and A. Mailhe, *Compt. rend.*, **158**, 834 (1914), is probably that of benzophenone. [e] $n^{20}D$ 1.5270, ref. 22. [f] $n^{20}D$ 1.5203, ref. 22. [g] $n^{20}D$ 1.5146, ref. 22. [h] $n^{20}D$ 1.5116, ref. 22.

Preparation of α-Ethylbutyrophenone.—This preparation also served as a product study of the alkylation reaction. All operations were carried out in a nitrogen atmosphere. Butyrophenone, 33.0 g., 0.22 mole, was converted to its sodium enolate by adding an ethereal solution of sodium triphenylmethide until a permanent red end-point was obtained. Ethyl bromide, 343 g., was then added to give a total volume of 1840 ml. of solution, 0.12 *M* in enolate and 1.7 *M* in alkyl halide. This is the same ratio of reagents used in the alkylation studies. The solution was refluxed, while the progress of the reaction was followed by titrating 10-ml. aliquots. The temperature of the refluxing liquid was 35.5°. When the concentration of enolate had decreased to 0.002 *M* (360 hr.), the reaction was stopped by the addition of 500 ml. of water. Distillation through an 8-plate column gave eight fractions, 23.9 g. (62%) of α-ethylbutyrophenone,[24] b.p. 68° at 2 mm., $n^{26}D$ 1.5085, and five lower-boiling fractions, 12.3 g. (32%), which contained a small amount of butyrophenone. Solid triphenylmethane distilled immediately following the pure α-ethylbutyrophenone. No α,α-diethylbutyrophenone could be detected.

Sodium Triphenylmethide.—Triphenylcarbinol was prepared in 5-mole batches from ethyl benzoate and phenylmagnesium bromide.[25] The reactions were carried out in 12-liter flasks cooled by ice in 20-gal. drums. The steam distillations were continued for six days. The yields of carbinol, m.p. 161–163°, were 67–70%. Triphenylchloromethane was prepared from the carbinol and acetyl chloride.[26] Solutions of sodium triphenylmethide were made in 1.5-l. quantities by a modification of a procedure previously described.[27] A 2-liter round-bottom flask set in an empty metal trough was fitted with a T-tube and mercury-sealed stainless steel crescent-blade stirrer driven by a Gast air motor. An atmosphere of nitrogen was maintained by passing a slow stream of the gas through the T-tube into a bubbler containing mineral oil. In a typical preparation, 70 g. (0.25 mole) of triphenylchloromethane in 1.5-l. of dry ether was stirred with 1144 g. of 1.3% sodium amalgam (0.51 atom of sodium). Heat was evolved and a red color developed within a few minutes. Cooling was effected by squirting ether or acetone from a plastic bottle onto the exterior of the flask in amounts determined by the rate of bubbling of the nitrogen stream. Actually, little cooling is required, and the deep red solution is stirred for several hours without further attention. After standing overnight, the clear red solution was siphoned by nitrogen pressure into the storage system described below. Yields of eight preparations were in the range of 75 to 80%. Best results were obtained when the ether was freshly distilled from ethylmagnesium bromide or sodium triphenylmethide solutions. Amalgams with concentrations higher than 1.3% were difficult to transfer and stir.

Apparatus and Procedure for Alkylation Reactions.—The apparatus consisted of three parts: a storage and measuring system for sodium triphenylmethide, a reaction vessel for the preparation of sodium enolates and for the study of rapid alkylations and a sampling system to remove aliquots from the alkylations performed in the reaction vessel or to fill tubes for the studies of slower alkylations. Initially, the entire apparatus was part of a vacuum system and was pumped at 10^{-5} mm. for 24 hr. prior to each run. Later it was found that equally good results could be obtained by rinsing the apparatus with anhydrous ether and drying with a stream of purified nitrogen. All transfers were made under a slight positive pressure of nitrogen.

The storage system consisted of a 2-liter flask equipped with a manometer, nitrogen inlet and siphon leading to the top of a 100-ml. buret. A three-way stopcock in a shunt between the flask and buret permitted nitrogen to be expelled from the buret to start the siphon or pressure in the flask and buret to be equalized, thus stopping the siphon.

The reaction vessel was a 500-ml. flask with four long narrow inlets to permit it to rest deep in the constant-temperature bath. One inlet was attached directly to the bottom of the buret on the storage system. The others carried a mercury-sealed stirrer, nitrogen inlet, reagent buret and sample buret.

The sample buret was of the self-leveling type and delivered 36.1 ml. at 28.8°. The upper and lower sections of the buret were connected by a three-way stopcock to permit equalization of pressure or to bleed nitrogen from the upper section in order to start the siphon. Alkylations were followed by periodic removal and titration of 36.1-ml. aliquots through this part of the system. When the alkylations were relatively slow, all reagents were mixed in the reaction flask, and the 36.1-ml. portions were sealed in glass tubes under nitrogen. Each tube, in turn, was attached to the outlet of the sample buret, evacuated and filled with nitrogen by an auxiliary line, cooled to −70°, filled with the aliquot and sealed. The tubes were 1.9 × 19 cm. with narrow necks 1.0 × 16 cm. A long thin dripper ring-sealed into the buret outlet extended into the necks of the tubes to prevent the enolate solution from wetting the walls before the sealing operation.

Alkylation of *n*-Alkyl Phenyl Ketones.—The ethylation of butyrophenone is typical. Run 15 is described here in some detail. Approximately 220 ml. of 0.11 *M* sodium triphenylmethide solution was transferred from the storage system to the reaction flask. Butyrophenone, 3.691 g., 0.0249 mole, was added through the reagent buret. Three ml. of anhydrous ether was then added to wash the ketone from the walls of the buret. The red color of the sodium triphenylmethide disappeared instantaneously. More of the solution was added to give a permanent orange end-point. The total volume used was 230 ml. (0.0253 mole). The solution was made 1.72 *M* in alkyl halide by the addition of 35.1 ml. of ethyl bromide through the reagent buret. Six 36.1-ml. aliquots were sealed in tubes during the next 42 minutes. The tubes were numbered consecutively and stored at −70° until all had been filled. Timing was begun when the tubes were placed in the constant-temperature bath at 30.00 ± 0.03°.

The tubes were opened at selected intervals in the order filled, so that the error involved in neglecting the reaction time during the filling process was less than 1%. The contents of each tube was rinsed into a separatory funnel. The ether layer was washed with three portions of distilled water. The combined aqueous solution was titrated first

(23) Benzonitrile, b.p. 73–74° at 14 mm., $n^{20}D$ 1.5282, was obtained in 65% yield from benzamide; A. Vogel, "Practical Organic Chemistry," Longmans Green and Co., New York, N. Y., 1948, pp. 755, 761.

(24) D. Bardan, *Bull. soc. chim. France*, [4] **49**, 1875 (1931).

(25) W. E. Bachmann and H. P. Hetzner, *Org. Syntheses*, **23**, 98 (1943).

(26) W. E. Bachmann, *ibid.*, **23**, 100 (1943).

(27) C. R. Hauser and B. E. Hudson, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 286.

to a phenolphthalein end-point with 0.1 M nitric acid and then, by the Volhard method, for bromide ion. The initial concentration of enolate, E_0, calculated from the weight of ketone and volume of reagents was 0.092 M. The sum of the enolate concentration, E, and the halide ion concentration for each tube was 0.094 ± 0.02 M. The Volhard titration of an infinity sample gave the same value. Log E was plotted against time (Fig. 1), and a pseudo-first-order rate constant, $k_1 = 1.67 \times 10^{-6}$ sec.$^{-1}$, was determined from the slope of the curve. A second-order constant, $k_2 = 0.97 \times 10^{-6}$ liter mole^{-1} sec.$^{-1}$, was obtained by dividing k_1 by the concentration of ethyl bromide. A plot of log E *vs.* time (Fig. 1) is shown for three independent ethylations of butyrophenone, two of which were made with different solutions of sodium triphenylmethide. The common slope is indicative of the reproducibility of these alkylations.

Second-order rate constants for eighteen alkylations of eight ketones are listed in Tables I and II. The rapid hydrolysis of *t*-butyl bromide made necessary a modification of the analytical procedure for alkylations by this compound. Only the sealed-tube technique could be used. Sodium bromide was filtered on sintered glass, washed with anhydrous ether in an atmosphere of nitrogen and determined by the Volhard procedure.

Ebulliometric Measurements.—Relative boiling points of ethereal solutions of the sodium enolate of butyrophenone were determined with a Beckmann thermometer in a modified Cottrell ebullioscope.[28] The molal elevation of the boiling point of ethyl ether is 2.01°.[29] Several determinations of the molecular weights of naphthalene and triphenylmethane were made to a precision of ±5%. Solutions of the enolate of butyrophenone containing equimolar amounts of triphenylmethane were prepared from the ketone and sodium triphenylmethide. The average molecular weight of the two species in these solutions is 207 provided that no molecular association is present. The average molecular weight determined from boiling-point elevation was 302 ± 20 for enolate concentrations ranging from 0.0705 to 0.1263 M. No regular variation was observed: at enolate concentrations of 0.0705, 0.0882 and 0.1263 M, the average molecular weight was 294, 298 and 295, respectively. From the equation, ave. mol. wt. = (244 + 170 α)/2, the association number, α, for the sodium enolate at these concentrations is constant and equal to 2.0.

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(28) Weissberger, "Physical Methods of Organic Chemistry," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1949, pp. 113, 133.

(29) C. S. Hoyt and C. K. Fink, *J. Phys. Chem.*, **41**, 453 (1937).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STATE UNIVERSITY OF IOWA]

The Kinetics of the Reactions of Quaternary Ammonium Tribromides with Crotonic Acid in Ethylene Chloride[1]

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The kinetic results obtained for the addition reaction of quaternary ammonium tribromide with crotonic acid in ethylene chloride are best explained by a combination of three reactions. The first involves both quaternary ammonium tribromide and bromine attacking the double bond. It was the predominant process when mixtures of bromine and tribromide were used with crotonic acid. The second reaction is that of quaternary ammonium tribromide or the kinetically equivalent equilibrium combination of quaternary ammonium bromide and bromine with crotonic acid. This reaction predominated in the early stages of the addition when tetrabutylammonium tribromide was used with crotonic acid. The third reaction appeared to involve a salt catalysis of the reaction of tribromide with crotonic acid. Tetrabutylammonium bromide was more effective than the nitrate, but the extent of catalysis was diminished by the presence of a large excess of the salt. The catalysis was also observed in the later stages of the reaction of tetrabutylammonium tribromide with crotonic acid. When tetramethylammonium tribromide was used without added bromine, the concentration of bromide was kept at a low, constant value by the relatively low solubility of tetramethylammonium bromide in ethylene chloride. Under these conditions, both the reaction of bromine and tribromide with crotonic acid and that of tribromide with crotonic acid took place to an appreciable extent. Rate constants for the reaction of crotonic acid with quaternary ammonium tribromide and bromine and that with quaternary ammonium tribromide alone were determined at 10, 20, 30 and 40°. They are listed in Table IV along with the heats of activation and the entropies of activation.

In an earlier investigation[3] it was found that the reaction of crotonic acid with a mixture of bromine and tetramethylammonium tribromide was faster than the corresponding reaction with tribromide alone which in turn was faster than that with bromine alone. It was shown that the presence of the solid tetramethylammonium bromide, which precipitated during the reaction of tetramethylammonium tribromide with crotonic acid, had no effect on the reaction rate. It was believed desirable, however, to test the effect of bromide in solution on the reaction. To this end the present investigation is concerned with the kinetics of the reaction of tetrabutylammonium tribromide with crotonic acid since tetrabutylammonium bromide is reasonably soluble in ethylene chloride.

Experimental Part

Materials.—Ethylene chloride was purified as described for earlier investigations.[3,4] Each batch of purified solvent was tested with bromine to ensure that the solvent was not reactive. Bromine, crotonic acid, tetramethylammonium bromide and tetramethylammonium tribromide were purified as described for an earlier investigation.[3]

Tetra-*n*-butylammonium Bromide.—A solution of 185 g. (1.0 mole) of tri-*n*-butylamine and 137 g. (1.0 mole) of *n*-butyl bromide in 300 ml. of butyl acetate was boiled under reflux for 24 hr. Cooling yielded 125 g. (39%) of crude tetra-*n*-butylammonium bromide. Crystallization from benzene gave 92 g. (29%) of salt of m.p. 115.5–116° (sealed tube), 102–102.5° (open tube). Other acetate esters were found to be much less satisfactory as reaction solvents. Although the use of ethyl acetate as a solvent has been reported[5] to give rise to a product contaminated by tetrabutylammonium acetate, the product used in this investigation was reasonably pure.

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(2) Eastman Kodak Fellow, 1954–1955.

(3) R. E. Buckles and J. P. Yuk, THIS JOURNAL, **75**, 5048 (1953).

(4) R. E. Buckles and J. F. Mills, *ibid.*, **75**, 552 (1953).

(5) H. Sadek and R. M. Fuoss, *ibid.*, **72**, 301 (1950).