ride in 150 ml. of ether at a rate such as to produce gentle reflux. Then after 30 minutes an addition of 100 ml. of water and 100 ml. of 6 N sulfuric acid was made. The clear solution was transferred to a separatory funnel and, after removing the ether layer, the aqueous layer was continuously extracted with ether for 48 hours. From the combined ether extracts the crude product was obtained, after drying the solution over Drierite and removal of ether. This material was purified by fractional distillation through a Nester–Faust 18″ micro spinning band column under reduced pressure and there was secured an 86% yield of 3-bromo-1-propanol, b.p. 70–72° (10 mm.). The α-naphthylurethan derivative was prepared and melted at 73°.

Reduction of Methyl 3-Bromopropionate to 3-Bromo-1-propanol by Lithium Aluminum Hydride–Aluminum Chloride—Normal Addition at −75°.—The mixed hydride was prepared as described above. Through the dropping funnel, a solution of 16.7 g. (0.1 mole) of methyl 3-bromopropionate in 150 ml. of ether was added to 0.1 mole of the lithium aluminum hydride–aluminum chloride reagent which was cooled at −75°. Thirty minutes after the last addition of ester, a solution containing 20 ml. of methanol and 20 ml. of ether was added dropwise to destroy the excess hydride. After allowing the mixture to warm to room temperature, 100 ml. of water and 100 ml. of 6 N sulfuric acid were added. The reaction mixture was treated as described in the previous example. There was obtained a 90% yield of 3-bromo-1-propanol, b.p. 71–72° (10 mm.). The α-naphthylurethan derivative was prepared and melted at 73°.

Reduction of 3-Bromopropionyl Chloride to 3-Bromo-1-propanol by Lithium Aluminum Hydride—Normal Addition at −75°.—A solution of 17.1 g. (0.1 mole) of 3-bromopropionyl chloride in 150 ml. of ether was added dropwise to 0.1 mole of lithium aluminum hydride in 200 ml. of ether at −75°. Thirty minutes after the last addition of acid chloride, the excess hydride was destroyed with methanol and the product isolated as described above. An 87% yield of 3-bromo-1-propanol was obtained, b.p. 71–72° (10 mm.). The α-naphthylurethan derivative was prepared and melted at 73°.

URBANA, ILL.

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, VANDERBILT UNIVERSITY]

The Beckman Rearrangement. VIII. The Influence of Alkyl Groups on the Rates of Rearrangement of Acetophenone Oximes[1]

BY PATRICK J. MCNULTY[2] AND D. E. PEARSON[3]

RECEIVED JULY 9, 1958

Several rather unusual observations were made in comparing rates of rearrangement of alkyl-substituted acetophenone oximes. The most remarkable observation was that *p*-alkyl substituents show less electron-release ability (relative to hydrogen) than they do in nucleophilic reactions, a fact hardly compatible with present-day theory of alkyl group behavior. The second observation was that σ-constants of alkyl groups occupying positions *ortho* to each other were not additive in predicting rate. A third observation was that the rate of rearrangement of propiophenone oxime was much faster than anticipated, suggesting a considerable influence of the non-migrating group on the rate. A fourth observation was that the log rate of rearrangement of acetophenone oxime was correlative with H_0(slope = −0.72). These observations were made possible by the development of a new spectrophotometric method of analysis of ketone concentration.

In our opinion knowledge concerning the electronic behavior of alkyl groups is in an advanced state of confusion. Theoretically, as surmised from the resultant dipole of several carbon–hydrogen bonds, the sequence of electron release for alkyl groups should be in the order: *t*-butyl>isopropyl>ethyl>methyl. This order is found in many nucleophilic reactions for which the Hammett equation[4] has been found applicable. Thus, the σ-constant for the *p*-*t*-butyl group is −0.20 and for the *p*-methyl group is −0.17, the ethyl and isopropyl group constants probably falling in between these values.[5] In other words, alkyl groups have considerable electron-release ability compared with a hydrogen atom, but only small differences compared with each other. In certain reactions, and it is impossible to always predict when, the order of electron release of alkyl groups is methyl>ethyl>isopropyl>*t*-butyl>>hydrogen, often called the hyperconjugative order.[6,7] The question then arises as to what happens to the σ-constants of alkyl groups in the hyperconjugative order. We studied this problem several years ago[8,9] in connection with the observation of the influence of substituents on the rates of the Beckmann rearrangement of substituted acetophenone oximes. One tentative conclusion was that atoms or groups with unshared electrons, such as the amino, hydroxyl, alkoxyl, vinyl, aryl and halogens attached in either the *o*- or *p*-positions of the aromatic ring showed greater electron-release ability in influencing the rates of rearrangement of aromatic oximes than they did in nucleophilic reactions as represented by the Hammett σ-constants. On the basis of this conclusion, more negative σ-constants, called σ_e constants, were proposed for these groups in electrophilic reactions. Another tentative conclusion was that alkyl groups retained the same electrical influence and that the hyperconjugative order of these groups was caused by some type of solvation inhibition in the stabilization of the transition complex,[8,10] the *t*-butyl grouping having the

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(1) Paper VII, Frances Greer and D. E. Pearson, THIS JOURNAL, **77**, 6649 (1955).

(2) National Science Foundation Research Grant Fellow throughout graduate work. Ph.D. thesis to be microfilmed, University Microfilm Service, Ann Arbor, Mich.

(3) To whom correspondence should be sent.

(4) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

(5) The σ-value for the *p*-ethyl group is given as −0.15.[4] This value is based on one set of experimental data and therefore is open to question.

(6) J. W. Baker, "Hyperconjugation," Oxford at the Clarendon Press, 1952.

(7) The term hyperconjugation implies the contribution to the hybrid of a canonical form which has double-bonded character between the alkyl group and the aromatic ring. We believe that the term has been used much too loosely to explain simple inductive or inductomeric effects. The inductomeric effect, if existent, would be merely a distortion toward the benzene ring of the sp^3-hybridized orbital of the electrons bewteen the alkyl group and the ring. Nevertheless, until otherwise proved, we will use the word hyperconjugative order whenever this particular sequence is met.

(8) D. E. Pearson, J. F. Baxter and J. C. Martin, *J. Org. Chem.*, **17**, 1511 (1952).

(9) D. E. Pearson and J. D. Bruton, *ibid.*, **19**, 957 (1954).

(10) C. C. Price and D. C. Lincoln, THIS JOURNAL, **73**, 5836 (1951).

greatest inhibition, the methyl the least. Thus, the σ-value of the *p*-methyl group was retained ($\sigma = -0.17$) and that of the *p*-*t*-butyl group was reduced from -0.2 to -0.13. The hyperconjugative sequence now applied, but, in our interpretation, not because the methyl group has an abnormally large electron-release ability but because the branched chain alkyl groups are less able to stabilize the transition complex. Brown and co-workers[11-13] have taken the opposite viewpoint, and others have accepted it,[14,15] namely that the *p*-methyl group has abnormally great electron release powers in electrophilic reactions and this effect falls off slightly as the alkyl group becomes branched. Thus, the σ-constants, called σ^+, were given large negative values with methyl having the greatest alteration, as

p-group	$\sigma^{+,12}$	$\sigma_e^{8,9}$	σ
CH_3	−0.29	−0.17	−0.17
t-C_4H_9	−0.25	−0.13	−0.20
H	0	0	0
Cl	+0.11	+0.11	+0.23
CH_3O	−0.76	−0.6[16]	−0.27

The implications of the discrepancies in interpretation of behavior of alkyl groups in electrophilic reactions are important in general concepts of reaction mechanism. To state it briefly in the form of a question: does the *p*-methyl group and even the *p*-*t*-butyl group have greatly increased electron-release influence in electrophilic reactions or does the *p*-methyl group retain its same influence and the more highly branched chain alkyl groups have less effect on accelerating reaction rates because of decreased ability to stabilize the transition complex?[17a,b] We decided that the question was important enough to put to test in the Beckmann rearrangement of substituted acetophenone oximes, starting anew by developing a more accurate method for following the rates of rearrangement, by bringing evidence to bear on the electrophilic nature of the rearrangement, and by extending the work to include the ethyl group.

Kinetic Method and Application.—Previous methods of analysis in the study of the rates of rearrangement of acetophenone oximes in concentrated sulfuric acid involved the gravimetric determination of the unreacted oxime in an aliquot sample as the 2,4-dinitrophenylhydrazone of the ketone.[8,9] The main criticism of the method was that too great a concentration of oxime in sulfuric acid was needed to obtain accurate results. The development of a colorimetric analysis of the 2,4-dinitrophenylhydrazones in following rates of rearrangement of aliphatic oximes suggested its application to study of the rates of acetophenone oximes.[18] The 2,4-dinitrophenylhydrazones of aromatic ketones, however, were too insoluble to extract quantitatively into a solvent which was immiscible with the aqueous hydrolysis layer. A method was therefore developed which involved direct measurement of the concentration of the ketone.[19] An aliquot of the oxime in sulfuric acid was diluted and hydrolyzed. The ketone was extracted into isöoctane and its concentration determined from the optical density at the wave length of maximum absorption in the ultraviolet region. The method obviously made it possible to study rates at extremely high dilution, and the results in comparison with previous data are interesting as shown in Table I.

TABLE I

HALF-LIVES OF ACETOPHENONE OXIMES IN SULFURIC ACID AT 50.77°

	$t_{1/2}$, min., at concentrations of:	
Acetophenone oxime	1/27[a,8]	1/10,000[a]
Unsubstituted	630	510
p-Methyl	330	280
m-Methyl	390[b]	360
p-*t*-Butyl	345	290
p-Nitro	22,400	19,000

[a] Grams of oxime/g. of sulfuric acid. [b] Concn.:[9] 1/135.

In the greater dilution all oximes were rearranged at faster rates apparently because of greater ideality of solution and because of smaller decrease in H_0 of the sulfuric acid in the more dilute solution. Fortunately, the increments of increase were about the same for each oxime so that all conclusions based on earlier data are still valid. Further discussion of these data is made in the section on the Hammett equation.

In order to show that the Beckmann rearrangement is of an electrophilic nature, the dependency of rates on the concentration of sulfuric acid was studied with acetophenone oxime. The results are shown in Table II.

TABLE II

VARIATION IN RATE OF REARRANGEMENT OF ACETOPHENONE OXIME WITH CONCENTRATION OF SULFURIC ACID AT 50.77°

H_2SO_4,[a] %	$k \times 10^4$,[b]	H_0[c] + log k	J_0[d] + log k
95.8	13.6	−11.74	−16.77
92.8	6.79	−11.67	−15.52
90.8	4.33	−11.63	−15.24
87.5	2.40	−11.40	−14.67
84.8	1.43	−11.36	−14.20
80.0	0.044	−11.20	−13.46
75.3	Hydrolysis of oxime occurs		

[a] Concentration determined by titration of aliquot with base. [b] In reciprocal minutes. [c] The Hammett acidity constant[12]; slope of the straight line by the method of least squares is −0.72. [d] Gold-Hawes acidity constant. See Discussion.

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[11] H. C. Brown and Y. Okamoto, THIS JOURNAL, **79**, 1913 (1957).

[12] Y. Okamoto and H. C. Brown, *J. Org. Chem.*, **22**, 485 (1957).

[13] H. C. Brown, J. D. Brady, M. Grayson and W. H. Bonner, THIS JOURNAL, **79**, 1897 (1957).

[14] N. C. Deno and W. L. Evans, *ibid.*, **79**, 5804 (1957).

[15] R. W. Taft, Jr., and I. C. Lewis, *ibid.*, **80**, 2436 (1958). These authors have gone so far as to attribute over two-thirds of the electron release powers of alkyl groups to resonance interaction.

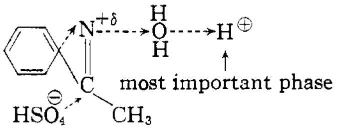
[16] Minimum value as shown by abnormal entropy of activation, indicative of partial protonation of the methoxyl group in *p*-methoxyacetophenone oxime dissolved in sulfuric acid.[8]

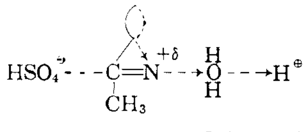
[17] (a) For a similar statement of the problem with a different conclusion than that to be offered later in this paper, see E. Berliner and M. M. Chen, THIS JOURNAL, **80**, 343 (1958). (b) Another question which will be discussed in a later paper is: are σ_e (or σ^+) values variable depending on the nature of the attacking reagent? See references 8, 14 and 15 for recorded discussion of this question.

[18] P. T. Scott, D. E. Pearson and L. J. Bircher, *J. Org. Chem.*, **19**, 1815 (1954).

[19] Initial phases of the development of the analytical procedure were done by Dr. Harold F. Smith in work to be described in a later publication.

Table II shows that the log rate of rearrangement of the oxime is linear (except for a very slight trend) with respect to the Hammett acidity constant, H_0,[20] and non-linear with respect to the Gold–Hawes acidity constant J_0,[21] and to the Deno constant, C_0.[22,23] At first thought these facts were disturbing: J_0 and C_0 would be expected to apply if the rearrangement were dependent upon the loss of water in the rate-determining step, and the presently proposed mechanism does show the loss of water in this step. However, J_0 and C_0 probably are applicable to processes involving the loss of water by a reversible mechanism. The loss of water in the Beckmann rearrangement is an irreversible reaction. The log rate of the pinacol rearrangement, another irreversible reaction, has been shown also to be correlative with H_0.[24] Two other facts need explanation. Hammett[20] limits the use of H_0 to protonation of neutral bases while the presently proposed mechanism suggests that a positively charged ion is further protonated. Bonner and Lockhart[25] have shown recently that the log of the equilibrium constant for the further protonation of a positively charged base ($BH^+ \xrightarrow{H^+} BH_2^{++}$) is linear with respect to H_0.[26] Provided that the oxime is completely in the monoprotonated form, there is no reason to believe that the log rate of rearrangement of such an ion should not be linear with respect to H_+. Since acetophenone has been shown to be protonated completely in 86% sulfuric acid,[27] acetophenone oxime, a more basic substance, should be protonated completely in 95% aqueous sulfuric acid. Finally the unusual slope of −0.72 for log k *vs.* H_+, in contrast to the usual slope of −1 for H_0 relationships must be explained. The neutralization of an indicator base by a strong acid is a simple, stoichiometric combination. The loss of water from the oxime salt through the influence of acid is more complex just as it is in the pinacol rearrangement in which the slope of the line of log rate *vs.* H_0 (or H_+) approximates that of the Beckmann rearrangement.[24] This study of the dependency of rate on acid strength suggests that the transition complex formerly proposed[28] should now be revised to include the effect of acid as shown. This complex accounts for all the most important characteristics of the rearrangement of oximes: the dependency of rate on acid concentration and on the electron-release properties of groups attached, *trans* migration, the retention of configuration in the migrating group,[28] and the fact that the oxygen atom in benzophenone oxime is not the same as in the rearrangement product, benzanilide.[29] The dependency of rate on acid strength establishes more firmly the classification of the Beckmann rearrangement as electrophilic in character. Moreover the mechanism of the rearrangement is reminiscent of that of aromatic substitution. Just as a positive ion attacks the π-electron cloud above the plane of the aromatic ring, so must the nitrogen atom, partially charged as shown in transition complex, attack the π-orbital electron cloud.[30] The transition complex is reillustrated below to emphasize the position of the atoms relative to the ring





Hammett Equation and Discussion of Substituent Effect.—The logs of the relative rates (k/k_0) for the Beckmann rearrangement are plotted *vs.* σ_e in Fig. 1. The slope of the line (−2.0) was established from the positions of the points which most chemists, including Brown, agree are most likely to be invariant: the *p*-nitro, the unsubstituted, 3-ethyl, 3-methyl and 3,5-dimethyl. By no stretch of the imagniation could the σ^+-values of Brown for *p*-ethyl and *p*-methyl groups be shown to fall on this line. Indeed, most remarkably, the *p*-alkyl groups fall below the line thus showing less electron-release ability relative to hydrogen in the Beckmann rearrangement than in nucleophilic reactions. This comparison can best be brought out by observance of the σ_p/σ_m ratios in Table III.

TABLE III

	σ_p/σ_m		
	CH_3	CH_3CH_2-	$(CH_3)_2C-$
Hammett[12]	2.46	3.5[a]	1.64
Brown[4,5]	4.43	4.65	4.31
Present work	1.73[b]	1.56[b]	..

[a] Probably in error because of uncertain σ-constant for *m*-ethyl group (−0.043). [b] Calculated from log $k/k_0 = -2.0 \times \sigma$.

These results constitute an exception to the Brown hypothesis that *p*-alkyl groups have unusually large electron-release influence in all electrophilic reactions.[31] The Beckmann rearrangement is an electrophilic reaction as shown in this paper; the rearrangement brings out the latent

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(20) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

(21) V. Gold and B. W. V. Hawes, *J. Chem. Soc.*, 2102 (1951).

(22) N. C. Deno, J. J. Jaruzelski and A. Schriesheim, THIS JOURNAL, **77**, 3044 (1955). Above 82% sulfuric acid J_0 and C_0 have a constant difference so that a conclusion based on one constant holds for the other above this concentration.

(23) Y. Ogata, M. Okano and K. Matsumoto, *ibid.*, **77**, 4643 (1955), have studied the rates of rearrangement of cyclohexanone oxime in various concentrations of sulfuric acid and found that the log rates were only approximately linear with respect both to H_0 and J_0. A higher accuracy of analytical determination and more dilute solutions than used in their rate study are required to demonstrate the dependence of log rate on H_0.

(24) C. A. Bunton, T. Hadwick, D. R. Llewellyn and Y. Pocker, *Chemistry & Industry*, 547 (1956).

(25) T. G. Bonner and J. C. Lockhart, *J. Chem. Soc.*, 364 (1957).

(26) The acidity constant is called H_+ under these circumstances and will be described as such in further references to the Beckmann rearrangement.

(27) L. A. Flexser, L. P. Hammett and A. Dingwall, THIS JOURNAL, **57**, 2103 (1935).

(28) D. E. Pearson and F. Ball, *J. Org. Chem.*, **14**, 118 (1949).

(29) A. I. Brodskii, *Izvest. Akad. Nauk, S.S.S.R., Otdel, Khim. Nauk*, 3 (1949); *C. A.*, **43**, 5011 (1949).

(30) D. E. Pearson and W. E. Cole, *J. Org. Chem.*, **20**, 488 (1955).

(31) For the same reasons, the results all constitute a strong argument against the reality of hyperconjugation as defined in footnote 7. For other references see W. M. Schubert, J. Robins and J. L. Haun, THIS JOURNAL, **79**, 910 (1957); E. Spinner, *J. Chem. Soc.*, 1590 (1956); M. I. Batuev, *J. Gen. Chem., U.S.S.R.*, **26**, 1888 (1956).

electron-release powers of other groups such as *p*-halogen and *p*-methoxyl as shown previously[8,9]; yet, it fails to show any such effect with either the *p*-methyl or the *p*-ethyl group. Substantiation of the Beckmann data is to be found in other papers dealing with the kinetic behavior of the rearrangement of the picryl ethers of acetophenone oximes in inert solvents, the *p*-methyl/*m*-methyl ratio being 2.0.[32]

Brown further argued in support of his theory that σ^+ for *p*-alkyl groups showed better correlation of data (log k/k_0 *vs.* σ^+) for twenty-four selected electrophilic reactions than σ- or σ_e-values.[12] Our study of these same reactions, using the σ_e-constants for alkyl groups in Table IV, revealed just as good a correlation.

TABLE IV

p-Group	σ_e	*m*-Group	σ_e
CH_3	−0.17	CH_3	$-0.07^{a,c}$
C_2H_5	− .16	C_2H_5	$-\ .07^{b,c}$
t-C_4H_9	− .13		

[a] Rounded off. [b] Estimated on basis of present kinetic work. [c] These figures do not differ appreciably from σ except for the hyperconjugative order for the *p*-substituents.

Sufficient space is not available to discuss each reaction but the important differences will be summarized: (1) The slopes of the lines using σ_e are usually greater, in some cases great enough to decide decisively between the use of σ_e or σ^+ if more invariant groups, particularly the *m*- and *p*-nitro groups, would be included in future studies. These reactions are: Protonolysis of trimethylsilanes[33]: $\rho^+ = -4.59$[12]; $\rho_e = -8.$ (ρ^+ for use with σ^+ and ρ_e for use with σ_e.) Thermal rearrangement of α-phenylethylcarbonates in dioxane[34]: $\rho^+ = -3.08$; $\rho_e = -5.6$. Migration aptitudes in acid-catalyzed decomposition of diphenylmethylcarbinyl azides[35]: $\rho^+ = -2.77$; $\rho_e = -3.5$.

(2) In the following reactions, the points for *p*-alkyl substituents fall above the line thus showing the supposedly abnormal electron-release ability for these groups which Brown proposes is shown for all electrophilic reactions: the solvolysis of phenyldimethylcarbinyl chlorides,[11] equilibrium constants for carbonium ions from triphenylcarbinols and benzhydrols in sulfuric acid,[22] chlorination of cinnamic acids[36] and ethanolysis of triphenylmethyl chlorides.[37] Perhaps it is more than fortuitous that all these reactions are reversible ones and involve the formation of a benzyl-type carbonium ion. Perhaps the so-called unusual electron-release powers of alkyl groups are restricted to reactions of the above nature.

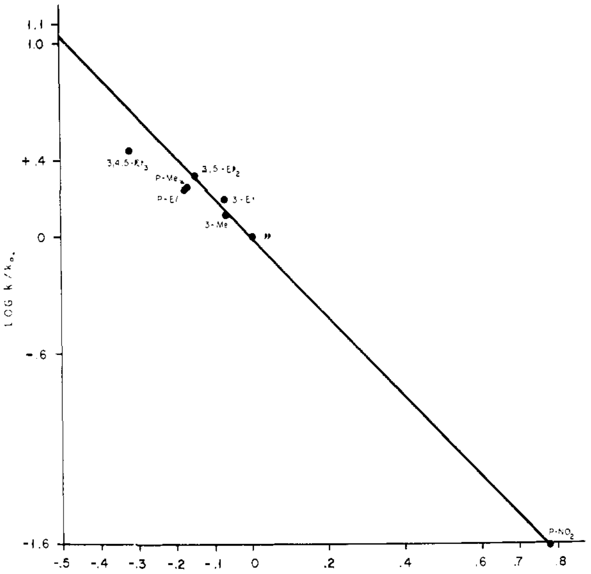
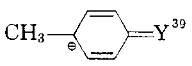


Fig. 1.—log k/k_0 for the rates of rearrangement of acetophenone oximes in concentrated sulfuric acid *vs.* σ; see Table IV for σ-constants used.

Apparently at this time no coherent theory of σ_e or σ^+ effects of alkyl groups can be formed, particularly to explain the unusual σ_p/σ_m ratio in the Beckmann rearrangement. One implausible theory is that the electronically deficient nitrogen atom in the rearrangement intermediate is so reactive that differences between group effects are lessened.[38] But the same theory must also explain the fact that the *p*-methoxyl and *p*-halogen groups show about the same electromeric response in the Beckmann rearrangement as in all other electrophilic reactions. A second tentative theory would suggest that the σ_p/σ_m ratio in the Beckmann rearrangement was the least complex comparison of electrical effects of alkyl groups so far observed. For example less solvation contributions may be involved or less contribution of the following canonical form to the transition complex hybrid



In most other electrophilic reactions, this canonical form may contribute to the hybrid to a greater extent. In reversible electrophilic reactions involving the formation of benzyl-type carbonium ions, the canonical form illustrated may have its greatest contribution to the hybrid. In any event our opinion, based mostly on the results of this paper and to a lesser extent on correlation of the results of other workers, is that *p*-alkyl groups do not have latent electron-release powers brought out by electrophilic reagents and that the hyperconjugative sequence, particularly that found in the solvolysis of benzyl-type halides, is a consequence of solvent effects as just discussed, and is not the result of an intrinsic electronic property. Indeed,

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(32) R. Huisgen, J. Witte, H. Walz and W. Jira, *Ann.*, **604**, 191 (1957).

(33) C. Eaborn, *J. Chem. Soc.*, 4858 (1956).

(34) K. B. Wiberg and T. M. Shryne, THIS JOURNAL, **77**, 2774 (1955).

(35) S. N. Ege and K. W. Shirk, *ibid.*, **75**, 354 (1953).

(36) H. P. Rothbaum, I. Ting and P. W. Robertson, *J. Chem. Soc.*, 980 (1948).

(37) A. C. Nixon and G. E. K. Branch, THIS JOURNAL, **58**, 492 (1936).

(38) See H. C. Brown and C. W. McGary, Jr., *ibid.*, **77**, 2300 (1955) for correlation of isomer distribution in aromatic substitution with the activity of the reagent.

(39) Y is any functional group mentioned in above discussion. The canonical form is written in the above manner to avoid the use of the term hyperconjugation, which would involve a form such as

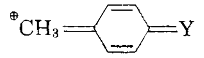

TABLE V

PHYSICAL CONSTANTS AND DERIVATIVES OF ETHYL-SUBSTITUTED ACETOPHENONES

Acetophenone	Yield, %	B.p. at 20 mm.	n^{25}_D	d^{25}_{25}	Oxime, m.p., °C.	Semicarb. m.p., °C.	2,4-DNPH m.p., °C.	Benzoic acid m.p., °C.	Acetanilide m.p., °C.
4-Ethyl	82	127	1.5270[b]	0.994	83–84[c]	188–191[d]	205.5–207[e]		
3 Ethyl	25[a]	123	1.5230[f]		56–57	170.5–172[g]	185–187.5[h]		
2,4-Diethyl	91	138	1.5215	.977	B.p. 145(20) n^{25}_D 1.5364	136–136.5	125–126[i] 100.5–101.5	85.5–86.5	113–113.5[j]
2,5-Diethyl	94	137	1.5171	.975	B.p. 145(20)[k] n^{25}_D 1.5348	106–106.5	104–105.5[l]	36-37.5	156–156.5[m]
3,5-Diethyl	18[a]	147	1.5186	.970	86–87	151.5–152.5[n]	184–186[o]	129–129.5[p]	116.116.5
3,4-Diethyl	6[a]	151	1.5281	.987	29.5–31	178–179[q]	158–160[r]	107–109	
3,4,5-Triethyl	9[a]	171	1.5289	.985	85–86[s]	180.5–182	194.5–195[t]	142–143[u]	104–105

[a] Made by ethylation of acetophenone and separation of mixture by fractionation. The yields are approximate. [b] S. F. Birch, *et al.*, THIS JOURNAL, **71**, 1362 (1949), give 1.5273. [c] A. Klages, *Ber.*, **35**, 2250 (1902), gives 82–83°. [d] G. Baddeley, *J. Chem. Soc.*, 232 (1944), gives 191°. [e] Brilliant red plates; ref. *d* and 44 give 202–203°; H. Pines and A. W. Shaw, *J. Org. Chem.*, **20**, 373 (1955), give 208–209°. [f] Second reference of *e* gives 1.5233. [g] References *f* and *d* give 175–176°. [h] Dark-red plates. Calcd. for $C_{16}H_{16}N_4O_4$: N, 17.07. Found: N, 16.77. [i] See Experimental for description. [j] J. E. Copenhaver and E. Emmet Reid, THIS JOURNAL, 49, 3157 (1927), report 112–113.5°. [k] Reference *d* and A. Klages and R. Keil, *Ber.*, **36**, 1632 (1903), report an oil. [l] Bright orange needles; ref. *d* reports 105°. [m] W. J. Gaudion, W. H. Hook and S. G. P. Plant, *J. Chem. Soc.*, 1631 (1947), report 154°. [n] Reference *d* reports 149°, and D. T. Mowry, THIS JOURNAL, **67**, 1050 (1945), misreports 125°. [o] Orange-red, large crystals; ref. *d* reports 185°. [p] Mowry, ref. *n*, reports 128–129°, and H. R. Snyder, R. R. Adams and A. V. McIntosh, THIS JOURNAL, **63**, 3280 (1941), report 129.5–130°. [q] Reference *d* reports 180°. [r] Purple red spars. Calcd. for $C_{18}H_{20}N_4O_4$: N, 15.72. Found: N, 15.61. [s] $C_{14}H_{21}NO$: N, 6.39. Found: N, 6.56. [t] Extremely fine, bright red needles. Calcd. for $C_{20}H_{24}N_4O_4$: N, 14.57. Found: N, 14.24. [u] Neut. equiv. calcd. 206, found 205.

when we find that the influence even of *m*-alkyl groups in solvolysis reactions is attributed to the intrinsic property, hyperconjugation,[13,17a,40] we believe that there is some basis for considering knowledge of the behavior of alkyl groups to be in a state of confusion.

Further Conclusions.—Further conclusions can also be made concerning the influence of alkyl groups on the rates of the Beckmann rearrangement. Jaffé[4] has stated that the effects of multiple substituents on rate (or equilibrium) constants can be expressed by the sum of the σ-constants for each substituent. This statement does not hold for the results of the Beckmann rearrangement. The rates of rearrangement of 3,4-diethyl- (see Table VII) and 3,4,5-triethylacetophenone oximes (see Fig. 1) were much slower than predicted on the basis of additivity of σ-constants. However, σ-constants were additive in predicting the wave length of maximum absorption of oximes from the crude formula (see Table VI)[41]

$$\lambda_{\max} \text{ in isoöctane} = 20 \times \sigma + 244 \text{ m}\mu$$

However, again, adjacent alkyl σ-constants were not additive in predicting $\lambda_{\max}$ of oximes in sulfuric acid from the formula (see Table VI)

$$\lambda_{\max} \text{ in sulfuric acid} = 100 \times \sigma + 271 \text{ m}\mu$$

The Rate of Rearrangement of Propiophenone Oxime.—In pursuit of the long range objective of being able to predict the rate of rearrangement of any oxime in any concentration of sulfuric acid, attention was next focused on the non-migrating group. The work of Chapman and Fidler[42] suggested that the non-migrating group in substituted benzophenone oximes had only a small effect on the rates of rearrangement. It was quite surprising therefore to find that the change of an ethyl group for the methyl group of acetophenone oxime had a very considerable effect on the rate

$$k(\text{propiophenone oxime})/k(\text{acetophenone oxime}) = 8.3$$

TABLE VI

ULTRAVIOLET ABSORPTION SPECTRA OF KETOXIMES

Oxime	In isoöctane $\lambda_{\max}$, mμ[a]	In isoöctane $\epsilon \times 10^{-3}$	In concentrated sulfuric acid $\lambda_{\max}$, mμ[b]	In concentrated sulfuric acid $\epsilon \times 10^{-3}$
Propiophenone oxime	243	11.98	273	13.30
Acetophenone oxime	244	10.98	271	11.72
3-Ethyl-	245	11.00	278	12.42
4-Ethyl-	248	14.37	290	16.10
3,4-Diethyl-	250	13.71	295	14.57
3,5-Diethyl-	247	10.33	285	12.33
3,4,5-Triethyl-	253	13.05	303	14.84
2,4-Diethyl-	Less than 215 mμ		254	12.41
2,5-Diethyl-	Less than 215 mμ		246	7.89

[a] $\lambda_{\max}$ can be calculated from formula: $20 \times \sigma + 244$.
[b] $\lambda_{\max}$ can be calculated from formula: $100 \times \sigma + 271$.

Futher study is needed before an explanation of the large effect can be made. An application of this fact, however, is apparent: the preparation of anilines by the Beckmann rearrangement could be done more easily with propiophenone oximes than with the customary acetophenone oximes.

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Experimental

All m.p.'s are corrected. Microanalyses are by Galbraith Laboratories. All b.p.'s are uncorrected. The yield of any liquid refers to the total weight of a series of collected fractions, the refractive indices of which do not vary from each other by more than ±0.0001.

Synthetic Work.—Table V collects and summarizes the properties of the ethyl-substituted acetophenones and their derivatives. It is particularly useful in filling out gaps in the literature and in reporting constants of compounds that

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(40) V. J. Shiner, Jr., and C. J. Verbanic, THIS JOURNAL, **79**, 369 (1957).

(41) σ-Constants were additive also in predicting the dissociation constants of substituted benzoic acids. This work will be published later.

(42) A. W. Chapman and F. A. Fidler, *J. Chem. Soc.*, 448 (1936).

TABLE VII

RATE CHARACTERISTICS OF THE BECKMANN REARRANGEMENT OF SOME KETOXIMES IN 95.9% SULFURIC ACID

Oxime	Temp., °C.	$k \times 10^3$ min.$^{-1}$	Half-life,[c] min.	ΔE[a]	ΔS[b,e]
Propiophenone oxime	31.30	0.897	775	25.3	+0.5
	41.23	3.37	205		
	50.77	11.30	60		
Acetophenone oxime	41.23	0.386	1795	26.0	−1.6
	50.77	1.36	510		
	51.37	1.47	470		
	61.30	4.75	145		
3-Methyl-	41.23	0.542	1280	25.4	−2.6
	50.77	1.92	360		
	61.30	6.31	110		
3-Ethyl-	41.23	0.601	1155	25.4	−2.8
	51.37	2.14	324(326)		
	61.30	6.98	100		
4-Ethyl-[d]	41.23	0.682	1015	26.3	+0.4
	51.37	2.60	264(270)		
	61.30	8.67	80		
3,5-Diethyl	41.23	0.837	830	26.0	−0.2
	51.37	3.08	226(224)		
	61.30	10.27	70		
3,4-Diethyl	41.23	0.858	810	26.1	−0.02
	51.37	2.96	235(233)		
	61.30	10.65	65		
3,4,5-Triethyl	51.37	4.10	170	24.3	−4.8
	61.80	13.26	50		

[a] Calculated from $k = Ae^{-E/RT}$, The plots of log k *vs.* reciprocal temperature for all oximes were linear; units are kilocalories. [b] Calculated from $k = kT/h \times e^{\Delta S/R} \times e^{-E/RT}$. [c] Duplicate run given in parentheses; k is average of two runs. [d] $k_{p-CH_3}/k_{p-C_2H_5}$ at 51.37° = 1.03. [e] Calories per degree per mole at 51.37° except 3-methyl (50.77°) and propiophenone oxime (41.23°).

have been prepared and purified with more than ordinary care. Some additional comments on methods and facts not communicable in the table are made below.

Ketones.—4-Ethylacetophenone was made by the Perrier modification of the Friedel–Crafts reaction. The reverse type of addition (acid chloride to hydrocarbon and catalyst) at 10° led to a nearly quantitative yield of 2,4-diethylacetophenone separated by fractional distillation from acetophenone, a by-product of the disproportionation reaction. This experiment illustrates the great mobility of the ethyl compared to the methyl group in Friedel–Crafts reactions and extends similar experiences of other workers.[43] 2,4-and 2,5-Diethylacetophenones were also made by the Perrier modification of the Friedel–Crafts reaction. The respective hydrocarbons used in the acylation reaction were obtained by the Wolff–Kishner reduction of 3- and 4-ethylacetophenones, which in turn were first purified by synthesis and crystallization of the respective oximes to constant m.p., followed by hydrolysis. *m*-Diethylbenzene, so obtained, had b.p. 179°, n^{25}D 1.4930, (reported[44] 185° (760 mm.), n^{25}D 1.4936), while *p*-diethylbenzene had b.p. 181°, n^{25}D 1.4923 (reported[44] 184° (760 mm.), n^{25}D 1.4933). The interesting fact concerned with the preparation of 3-, 3,5-, 3,4- and 3,4,5-ethyl substituted ketones is that they were all made by a single reaction, the ethylation of acetophenone following the directions of Baddeley.[45] Since crude isolates from a number of runs were combined, the yields given in Table IV are only approximate. Furthermore, ratios of reactants (acetophenone, 3 moles; $AlCl_3$, 6 moles; ethyl ether, 2 moles) were selected to give a spread of products favoring the formation of the less alkylated members. The yield of 3,4,5-triethylacetophenone could be increased greatly by increasing the molar ratio of ether and aluminum chloride. The alkylation reaction of Baddeley was found also to give less tar when run at 112° for 7 hours rather than 180–190° for several hours. The purification of crude 3-ethylacetophenone and 3,4,5-triethylacetophenone isolates was accomplished by fractional distillation of each with a 35-cm. Podbielniak Heli-Pak filled column at a reflux ratio of 15 to 1. The separation of 3,4- and 3,5-diethylacetophenone mixtures was brought about by fractional distillation with a 70-cm., Heli-Pak filled column at a reflux ratio of 40 to 1. The structure of the 3,4,5-triethylacetophenone is indicated by analysis of oxime and 2,4-dinitrophenylhydrazone, by neutral equivalent of the corresponding acid, and by the fact that the absorption spectrum of the oxime shows no ethyl group *ortho* to the oximino grouping.

Derivatives.—The oximes were made by the procedure of Pearson and Bruton,[9] the semicarbazones in a similar manner. Some of the oximes were stable indefinitely, and others, particularly 4-ethyl- and 3,4,5-triethylacetophenone oximes, tended to decompose in several weeks. All oximes were stored in individual desiccators containing Drierite. The oximes not reported in Table V, but used in this work, were comparable in purity and in physical properties to those of Pearson, Baxter and Martin.[8] Propiophenone oxime, m.p. 54.5–55.5°, was made from the ketone which first was fractionally distilled to constant refractive index, n^{25}D 1.5246. The ethyl-substituted benzoic acids of Table V were synthesized by hypobromite oxidation of the corresponding ketones according to the procedure of Taylor and Watts[46] except that an emulsifying agent was used to facilitate the oxidation of the heterogeneous mixture. The anilides were made by rearrangement of the oximes in concentrated sulfuric acid; 2,4- and 2,5-diethylacetophenone oximes did not yield the respective acetanilides by the sulfuric acid treatment but did so by polyphosphoric acid rearrangement. The 2,4-dinitrophenylhydrazones (2,4-DNPH) were made by the procedure of Pearson and Greer.[47] Both *syn* and *anti* isomers of 2,4-diethylacetophenone were separated by differences in solubility in butyl acetate. The more soluble isomer was isolated in the form of massive, deep red plates, m.p. 125–126°, the less soluble in the form of bright yellow needles, m.p. 85.5–86.5°.

Anal. Calcd. for $C_{18}H_{20}N_4O_4$: N, 15.72. Found: N, 15.42.

The yellow isomer was converted to the ketone by the method of Robinson[48] and reconverted to the mixture of 2,4-dinitrophenylhydrazone isomers. From this mixture the red form was isolated and shown to be identical to that previously isolated on the basis of mixture m.p. This experiment established that one compound was a *syn* or *anti* isomer of the other.

Ultraviolet Absorption Spectra of Ketoximes.—The absorption spectra of the oximes each in a concentration of 5.5 × 10^{-5} mole/liter, were determined by means of a Beckman spectrophotometer, model DU. The results which extend those of Pearson and Watts[49] are presented in Table VI.

Rate Data. General Procedure.—A 125-ml., glass-stoppered erlenmeyer flask containing approximately 50 ml. of concentrated sulfuric acid (Merck, 95.9%) was placed in a constant temperature oil-bath (Sargent Thermonitor; temperature recorded by certified thermometers, Chicago Apparatus Co.). When the temperature of the acid had reached that of the bath, approximately 10 mg. of oxime was added and well-mixed by swirling. The flask was stoppered and returned to the bath. The first aliquot was removed after 30 minutes by means of a 2-ml. graduated pipet, previously heated to the temperature of the bath. Care was exercised to avoid contact of the pipet tip with the walls of the flask. The pipet was wiped quickly with a Kleenex, brought to mark, and discharged over a 90-second period into a two-ounce, French square-type bottle containing 23.00 ml. of distilled water at ice temperature. The bottle was swirled during the addition so that local heating was minimized. A Teflon-lined screw cap was placed on the bottle and the contents gently rolled inside to assure complete dilution of acid. The sample was labeled and allowed to stand until all samples were collected. Generally seven samples

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(43) W. J. Heintzelman and B. B. Corson, *J. Org. Chem.*, **22**, 25 (1957).

(44) E. D. Bergmann and C. Resnik, *ibid.*, **17**, 1291 (1952).

(45) G. Baddeley, *J. Chem. Soc.*, S229 (1949).

(46) E. P. Taylor and G. E. Watts, *ibid.*, 1123 (1952).

(47) D. E. Pearson and Frances Greer, THIS JOURNAL, **77**, 1294 (1955).

(48) R. Robinson, *Nature*, **173**, 541 (1954).

(49) D. E. Pearson and Exum D. Watts, *J. Org. Chem.*, **20**, 494 (1955).

were drawn during a period of time equal to two half-lives. The samples were then hydrolyzed by immersing the tightly sealed bottles in an oil-bath at 60° to the water level within the bottles. After 24 hours, the bottles were removed from the bath and cooled to room temperature. Isoöctane (25.00 ml.) added from a buret was mixed with the contents of each bottle. The caps were again placed securely on the bottles, the contents shaken thoroughly for several minutes and allowed to stand 24 hours. (The time of standing could be shortened probably by more frequent shaking.) At this point, the ketone was dissolved in the isoöctane layer, and the substituted aniline salt and acetic acid in the aqueous layer. The samples were then analyzed by measuring the optical density of the isoöctane layer relative to a blank of pure isoöctane at the wave length of maximum absorption of the ketone. The log of the optical density plotted *vs.* time gave a straight line indicative of a pseudo first-order rate. The slope of the straight line was obtained by the method of least squares which, multiplied by 2.303, gave *k*. These results are summarized in Table VII.

Further Comments on Kinetic Work.—All analytical operations were conducted in an air-conditioned room. Any rate given is highly precise (standard deviation 10^{-3} to 10^{-4}) but probably is reproducible only to the extent of ±1% among different operators. A better idea of the reproducibility in this paper can be obtained by comparison of duplicate rates given in the half-life column of Table VII. A more thorough check of kinetic data was made with acetophenone oxime using different sources of oxime for each run: the half-lives found at 50.77° were 509, 509 and 516 minutes and at 51.37° were 475, 465, 474 and 479 minutes. The above method of analysis did not succeed in determination of the rate of rearrangement of 3,4,5-triethylacetophenone oxime. The abnormality was detected by the non-linearity of the log concentration *vs.* time curve, and its cause was found to be loss of carbonyl concentration in the hydrolysis step—possibly by rearrangement of oxime undergoing hydrolysis. The abnormality was remedied by hydrolyzing the samples at 50° for at least 36 hours rather than at 60° for 24 hours. Lesser periods of time showed incomplete hydrolysis of the anilide. The length of time of hydrolysis did not affect the concentration of ketone. Greater detail of any experiment is recorded in the thesis of P. J. M.[2]

NASHVILLE 5, TENN.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA]

Carbonyl Reactions. VII. The Effect of Substituents upon the Rate of Condensation of Substituted Benzaldehydes with Acetophenone[1]

BY DONALD S. NOYCE AND WILLIAM A. PRYOR[2]

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The rates of condensation of anisaldehyde, *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde with acetophenone have been measured in acetic acid with sulfuric acid as the catalyst. The modest effect of the substituent upon the rate of condensation is interpreted as the result of two nearly counterbalancing factors, the change in basicity of the aldehyde and the change in the ease of condensation of the protonic salt of the aldehyde with the enol of acetophenone. Comparison with the corresponding base-catalyzed reaction is made.

Introduction

In continuation of studies of the acid-catalyzed condensation of benzaldehyde with acetophenone as typical of the acid-catalyzed aldol condensation[3] we have examined the effect of substituents upon the rate of condensation. The number of reactions of aromatic aldehydes for which $\rho-\sigma$ correlations have been reported[4] is somewhat limited, but there are examples of both positive and negative ρ-values. We have previously reported on the situation prevailing in the formation of semicarbazones[5] and have commented upon possible reasons for the failure to obtain a linear $\rho-\sigma$ correlation.

The condensation reaction of substituted benzaldehydes with acetophenone is additionally valuable, since Coombs and Evans[6] have measured the rates of the corresponding base-catalyzed reaction in 90% ethanol. It is thus possible to compare the rates of acid- and base-catalyzed reactions of the same compounds.

Results and Discussion

The kinetic measurements were carried out under conditions which were known from the results with benzaldehyde and acetophenone to give simple kinetic behavior. These conditions obtain when the concentrations of both benzaldehyde and acetophenone are reasonably low, so that the unimolecular dehydration step following the bimolecular condensation step is fast. For the compounds studied here, the plotted data of any individual kinetic run revealed no evidence of an induction period in the formation of the final unsaturated ketone.

The kinetic results obtained are summarized in Table I.

The effect of the substituent upon the rate of condensation is quite small. The change from *p*-nitrobenzaldehyde to anisaldehyde results in a rate change of only a factor of two. This undoubtedly results from two opposing factors. One is the effect of the substituent on the basicity of the aldehyde. Anisaldehyde is distinctly more basic than *p*-nitrobenzaldehyde, and the concentration of the aldehydic oxonium salt will, therefore, be higher for anisaldehyde than for *p*-nitrobenzaldehyde at a given acidity. Such a contributing factor would be expected for anisaldehyde to increase the rate of the condensation step, which we have previously[3] described as involving the oxonium salt of the aldehyde and the enol of acetophenone. The second, opposing factor is the change in the resonance system as carbon–carbon bond formation takes place. This process is unfavorably influenced by the methoxyl substituent, since the resonance interaction between the methoxyl group and the aldehyde group is partly lost at the transition state.

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(2) Union Carbide and Carbon Fellow, 1952–1953; U. S. Rubber Co. Fellow, 1953–1954.

(3) D. S. Noyce and W. A. Pryor, THIS JOURNAL, **77**, 1397 (1955).

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(6) E. Coombs and D. P. Evans, *J. Chem. Soc.*, 1295 (1940).