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The Michael Reaction in Non-alkaline Media. II. The Kinetics of the Reaction of Barbituric Acid with β-Nitrostyrene[1]

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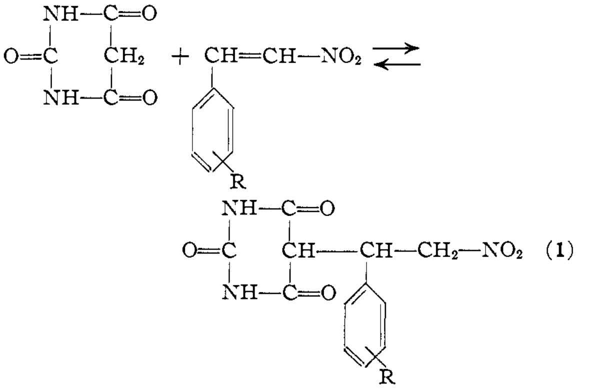
The reaction of β-nitrostyrene with barbituric acid in slightly acidic media follows a second-order rate law, the rate depending on the concentrations of β-nitrostyrene and the barbiturate anion. The effects of solvent composition, *p*H and substituents on rates and equilibria are discussed. A linear relationship between log $k_{\rm spec}$ and the dielectric constant was observed.

1. Introduction

Although no kinetic investigation of the Michael addition has been reported, Ingold[2] has suggested that this reaction follows the pattern of the addition of hydrogen cyanide to α,β-double bonds[3] and that the rate-determining step involves the attack of the anion of the pseudo-acidic active methylene compound at the β-carbon atom of the α,β-unsaturated molecule. In an earlier paper the addition of barbituric acid to a series of β-nitrostyrenes to yield the 5-(2-nitro-1-arylethyl)-barbituric acids was described.[4]



R = H, *p*-$(CH_3)_2N$, *p*-CH_3O, *p*-Cl, 3,4-CH_2O, *m*-NO_2

Although seemingly atypical in that these reactions took place in neutral or even acidic media, it was postulated that Ingold's mechanism applied, a sufficient quantity of the anion of the active methylene compound being furnished without recourse to alkaline catalysts as a result of the comparatively high dissociation constant of barbituric acid. The present study was undertaken in order to obtain evidence concerning the mechanism and deals with the kinetics of these reactions as carried out in buffered media under various conditions of temperature and dielectric constant.

2. Experimental Procedures and Results

2.1 Materials.—The preparation and purification of the nitrostyrenes was described in an earlier paper.[4] Eastman Kodak Co. "White Label" barbituric acid was recrystallized twice from water, then dried two days at 100°. Eastman primary standard potassium acid phthalate, "White Label" phthalic acid, succinic acid, acetic acid and methanol and Matheson, Coleman and Bell reagent grade potassium acetate were used without further purification. Fisher "purified" dioxane was further purified by the method of Fieser,[5] the periods of refluxing with concentrated hydrochloric acid and with metallic sodium each being extended from 12 hours to three days.

2.2 Spectrophotometric Methods.—The reactions were followed by measuring spectrophotometrically the rate of decrease in the concentrations of the nitrostyrenes. Since these concentrations ranged from 4×10^{-3} to 4×10^{-5} molar it was necessary to carry out at least one volumetric dilution to get solutions about 2×10^{-5} molar with corresponding optical densities of 0.2 to 0.6. Carrying out these dilutions in methanol which contained a slight amount of hydrochloric acid served the further functions of quenching the reaction and depressing the concentration of potassium acid phthalate which absorbed slightly at the $\lambda_{\max}$ of most of the nitrostyrenes. Measurements were made at the $\lambda_{\max}$ of the nitrostyrene except in the case of *m*,β-dinitrostyrene ($\lambda_{\max}$ 271 mμ) where the phthalic acid (ϵ_{271} *ca.* 1000) interfered. In this case the measurements were made at 310 mμ at which wave length the molar absorptivity of *m*,β-dinitrostyrene was 10,800. The absorption maxima and molar absorptivities of the nitrostyrenes were given in a previous paper.[6] In the typical case of β-nitrostyrene (ϵ_{310} 16,500), the molar absorptivities of the other components of the reaction mixture were as follows: barbituric acid, 47.5; 5-(2-nitro-1-phenylethyl)-barbituric acid, 16; potassium acid phthalate, 22.5; phthalic acid, 2; water, dioxane and methanol, nil. Measurements were made on a Beckman Model DU spectrophotometer using 1 cm. quartz cells.

2.3 Apparatus.—All volumetric glassware was calibrated. Reactions and dilution operations were carried out in "low actinic" glassware and light was excluded wherever possible to preclude a light-catalyzed reaction of the nitrostyrene which otherwise led to fading absorbances at the $\lambda_{\max}$.[6] Thermostats were controlled to within 0.1° at all temperatures.

2.4 Stock Solutions.—Dioxane-distilled water solutions were prepared by weight. The composition of the solutions was considered known to ±0.05%. For a typical reaction series the following stock solutions were prepared: (a) 0.2564 g. of barbituric acid and (b) 0.2985 g. of β-nitrostyrene each in 250.0 ml. of 66-²/₃% dioxane-distilled water to give solutions $8.00 \pm 0.04 \times 10^{-3}$ molar; (c) 4.0849 g. of potassium acid phthalate and (d) 3.3225 g. of phthalic acid each in 250.0 ml. of 66-²/₃% dioxane-water to give solutions $8.00 \pm 0.04 \times 10^{-2}$ molar. Solutions were made up at 30.0° or at the temperature at which they were to be used and periodically analyzed spectrophotometrically or titrimetrically to confirm the concentrations. Solutions were used within one week of the time at which they were prepared.

2.5 Kinetic Methods.—For a typical kinetic measurement involving 0.001 *M* β-nitrostyrene, 0.002 *M* barbituric acid and 0.02 *M* phthalic acid and potassium acid phthalate in 66-²/₃% dioxane-water at 30.0°, 25.0 ml. of solution (b) was pipetted into a 50.0-ml. volumetric flask and diluted to the mark at 30.0° with 66-²/₃% dioxane-water to give solution (e) $4.00 \pm 0.02 \times 10^{-3}$ molar in β-nitrostyrene. Twenty-five milliliters each of solutions (a), (c) and (d) were then pipetted into a 250-ml. erlenmeyer flask and mixed by swirling followed by 25.0 ml. of solution (e). The flask was swirled again vigorously and set into the thermostated bath at 30.0°. The time at which the pipet containing

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[1] Presented in part before the Division of Organic Chemistry, 127th national meeting of the American Chemical Society, Cincinnati, March, 1955.

[2] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 692–695.

[3] W. J. Jones, *J. Chem. Soc.*, 1547 (1914).

[4] M. J. Kamlet, THIS JOURNAL, **77**, 4896 (1955).

[5] L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1941, pp. 368–369.

[6] M. J. Kamlet and D. J. Glover, THIS JOURNAL, **77**, 5696 (1955).

solution (e) started draining into the reaction flask was taken as t_0. Measurements of nitrostyrene concentration were made periodically, at least one and preferably two or three readings being taken during every 10% interval in the range 15 to 75% completion. Depending on the anticipated concentration of nitrostyrene, 2-, 5- or 10-ml. aliquots were withdrawn, diluted with methanol as described above, and read within one minute on the spectrophotometer. The time at which the aliquot-containing pipet started draining into the diluent-containing volumetric flask was taken as t. Two readings were taken on every sample and if they did not agree to within 1% a third reading was taken.

2.6 Calculations, Apparent Rate Constants.—Early experiments showed the reaction rate to conform with the general relationship

$$-\mathrm{d(NS)}/\mathrm{d}t = k_{\mathrm{apparent}}\,(\mathrm{NS})(\mathrm{HBarb}_{\mathrm{formal}}) \qquad (2)$$

where (NS) represents the nitrostyrene concentration and ($\mathrm{HBarb}_{\mathrm{formal}}$) the total concentration of barbituric acid, both ionized (Barb^-) and un-ionized (HBarb). Apparent rate constants were calculated from the integrated second-order equations

$$k_{\mathrm{app}} = \frac{X}{A(A-X)t} \qquad (3)$$

$$k_{\mathrm{app}} = \frac{1}{(A-B)t}\ln\frac{B(A-X)}{A(B-X)} \qquad (4)$$

$$k_{\mathrm{app}} = \frac{X_{\mathrm{e}}}{(A^2-X_{\mathrm{e}}^2)t}\ln\frac{X_{\mathrm{e}}(A^2-XX_{\mathrm{e}})}{A^2(X_{\mathrm{e}}-X)} \qquad (5)$$

where A represents the initial formal concentration of the reactants present in equal amounts, B the concentration of the second reactant in the case of unequal amounts and X the concentration of the product. A_{e} and X_{e} represent these concentrations at equilibrium.

Between ten and twenty readings were taken during each run. The mean of the values within each 10% interval was then determined and the resulting six values for the range 15 to 75% completion were averaged to give the rate constant. Most of the constants tabulated below represent the average of at least two runs. Duplicate runs generally checked within 3%.

Data for a typical run in Table I show that equation 3 gave reasonably consistent apparent second-order rate constants to about 70% completion. Beyond this range there was a pronounced downward drift and the reaction seemingly reached equilibrium at about 92% completion.[7]

When the same data were fitted to equation 5 which is the integrated expression for a reaction involving a second-order forward step and a first-order reverse step,[8,9] the range over which the apparent second-order rate constants showed average deviations of less than 3% was extended to 85% completion.

In Table II are listed the k values for a series of experiments in which the reactant concentrations were each varied over a fourfold range. The apparent rate constants are in fair agreement with one another, confirming a true second-order reaction over the concentration range studied.

TABLE I

APPARENT RATE CONSTANTS FOR THE REACTION OF BARBITURIC ACID (0.002 M) WITH β-NITROSTYRENE (0.002 M) IN 66-2/3% DIOXANE-WATER AT 30.0° (EQUILIBRIUM AT 92% COMPLETION)

(Phthalic acid) = (KHPhthalate) = 0.02 M

Completion, %	k_{app}, l. mole^{-1} min.$^{-1}$ eq. 3	eq. 5
20	8.42	8.42
30	8.70	8.71
40	8.58	8.61
50	8.49	8.55
60	8.52	8.62
70	8.16	8.36
80	(7.55)	8.05
85	(7.18)	8.18
Av.	8.48 ± 0.15[a]	8.42 ± 0.19

[a] Average based only on values up to 70% completion.

TABLE II

APPARENT RATE CONSTANTS FOR THE REACTION OF BARBITURIC ACID WITH β-NITROSTYRENE IN 66-2/3% DIOXANE-WATER AT 30.0°

(Phthalic acid) = (KHPhthalate) = 0.02 M

Concn., mole l.$^{-1}$ Barbituric acid	β-Nitrostyrene	k_{app}, l. mole^{-1} min.$^{-1}$
0.002	0.002	8.48 ± 0.15
.002	.001	8.88 ± .18
.002	.004	8.18 ± .11
.001	.002	8.52 ± .10
.001	.001	8.57 ± .13
.004	.002	8.12 ± .07
.004	.004	8.07 ± .14
	Av.	8.45 ± 0.24

2.7 Apparent Equilibrium Constants.—The determination of exact equilibrium constants was complicated by a slow side reaction of unknown nature which led to a by-product absorbing in the same region of the ultraviolet as β-nitrostyrene. Thus a typical plot of apparent nitrostyrene concentration as a function of time had the shape of Fig. 1. Although the approximations involved in choosing the minimum in such a curve as the equilibrium concentration of nitrostyrene severely limited the

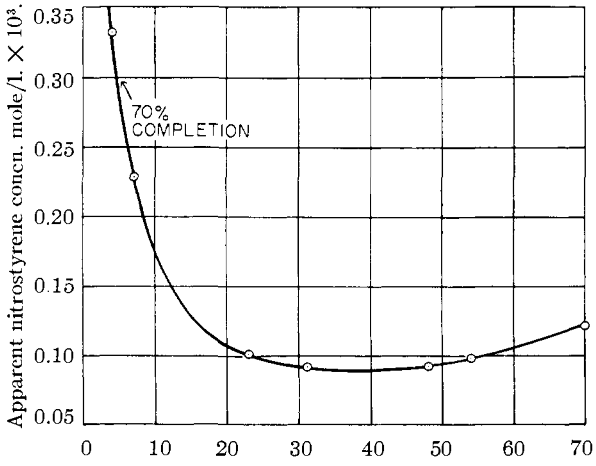

Fig. 1.—Apparent nitrostyrene concentration as a function of time; initial (NS) = (HBarb) = 1.00×10^{-3} mole/l.; 66-2/3% dioxane-water at 30.0°.

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[7] The slow reappearance of the nitrostyrene band in the ultraviolet when the purified product, 5-(2-nitro-1-phenylethyl)-barbituric acid, was subjected to similar reaction conditions furnished further evidence for the equilibrium nature of the reaction.

[8] K. J. Laidler, "Chemical Kinetics," McGraw-Hill Book Co., New York, N. Y., 1950, p. 21.

[9] The difficulties involved in the determination of X_{e} are described below.

accuracy of the determinations, rough experimental equilibrium constants were calculated from the relationship

$$K_{\text{equil}} = \frac{(\text{NS}_{\text{initial}}) - (\text{NS}_{\text{equil}})}{(\text{NS}_{\text{equil}})^2} \qquad (6)^{10}$$

at a series of concentrations and in the presence of various buffers and are given in Table III.

TABLE III

EQUILIBRIUM CONSTANTS IN REACTION OF EQUIMOLAR BARBITURIC ACID AND β-NITROSTYRENE IN 66-$^2/_3$% DIOXANE–WATER AT 30.0°

Buffer	Nitrostyrene concn., mole l.$^{-1}$ × 10^5 Initial	Nitrostyrene concn., mole l.$^{-1}$ × 10^5 Equilibrium	K_{equil}, l. mole^{-1} × 10^{-4}
KHP-PA[a] 1:1	200	15.8	7.4
	400	21.5	8.2
	100	9.2	10.8
KHS-SA[b] 1:1	50	6.1	11.8
KOAc-HOAc[c] 4:1	50	6.2	11.4

[a] Potassium acid phthalate–phthalic acid. [b] Potassium acid succinate–succinic acid. [c] Potassium acetate–acetic acid.

2.8 Calculations, Specific Rate Constants.—If the reaction conformed with the scheme postulated by Ingold,[2] the rate-determining step should involve barbiturate anion and the rate would be given by the expression

$$-\text{d(NS)}/\text{d}t = k_{\text{specific}}(\text{NS})(\text{Barb}^-) \qquad (7)$$

Defining by α the quantity $(\text{Barb}^-)/(\text{HBarb}_{\text{formal}})$ which is the proportion of total barbituric acid in the ionized form, it follows from equations 2 and 7 that

$$k_{\text{spec}} = k_{\text{app}}/\alpha \qquad (8)$$

In a solution of sufficient buffer capacity α is independent of the total barbituric acid concentration and can be determined as shown

$$\frac{(\text{Barb}^-)}{(\text{HBarb})} = \frac{(\text{buffer base})}{(\text{buffer acid})} \times \frac{K_{\text{Barb}}}{K_{\text{Buffer}}} \qquad (9)$$

$$\alpha = \frac{(\text{Barb}^-)/(\text{HBarb})}{1 + (\text{Barb}^-)/(\text{HBarb})} \qquad (10)$$

The only quantity required for the determination of α and for the conversion of apparent to specific rate constants in a given buffer system is $K_{\text{Barb}}/K_{\text{Buffer}}$, the ratio of the ionization constants of these two acids in the dioxane–water media being considered.

2.9 Ionization Constant Ratios in Aqueous Dioxane.—Van Uitert and Haas[11] have experimentally substantiated the assumption that the activity coefficients of electrolytic solutes in partially non-aqueous solvents are independent of the nature of the solutes and are determined by the solvent composition and the total ionic concentration. Van Uitert and Fernelius[12] have presented a useful method based on this assumption whereby the thermodynamic ionization constant of a weak acid in a dioxane–water mixture may be determined from the pH meter reading, B, at half neutralization

$$pK_{\text{D}} = B + \log U_{\text{H}}^{\circ} + 1/\gamma \qquad (11)$$

Log U_{H}° is a conversion factor for the particular solvent mixture at the given temperature and is independent of ionic concentration, and $1/\gamma$ is the negative log of the mean stoichiometric activity coefficient for hydrochloric acid at the same mean molality in this same solvent mixture.

In converting experimental to specific rate constants, the quantity $K_{\text{Barb}}/K_{\text{Buffer}}$ was required at each temperature and in each solvent composition studied. While it was possible to calculate the individual thermodynamic ionization constants at 30° from the pH meter readings and from the values given by Van Uitert and Fernelius[12,13] for log U_{H}° and $1/\gamma$, the determination of the individual ionization constants at the other temperatures would require the determination of new values of log U_{H}°.

However, since in each case we were primarily interested in the *ratio* of the ionization constants of barbituric acid and the buffer acid it was possible to avoid this further complication. Thus both log U_{H}° and $1/\gamma$ are independent of the nature of the solute and it follows from (11) that at the same ionic concentration

$$(pK)_{\text{Barb}} - (pK_{\text{D}})_{\text{Buffer}} = B_{\text{Barb}} - B_{\text{Buffer}} \qquad (12)$$

and that the ratio of the thermodynamic ionization constants of the two acids in any mixed solvent and at any temperature is the same as the ratio of the apparent ionization constants as determined directly from pH meter readings of half-neutralized solutions in this same system. These pH meter readings and the calculated ratios $K_{\text{Barb}}/K_{\text{Phthal}}$ are given in Table IV.

TABLE IV

pH METER READINGS ON HALF-NEUTRALIZED SOLUTIONS OF BARBITURIC ACID (BA) AND PHTHALIC ACID (PA)

(Acid) = (Salt) = 0.002 M, (KNO_3) = 0.02 M

Dioxane, %	Temp., °C.	PA	BA	$\frac{K_{\text{Barb}}}{K_{\text{Phthal}}}$
33-$^1/_3$	30.0	3.68	4.28	0.251
41-$^2/_3$	30.0	3.87	4.48	.246
50	30.0	4.01	4.72	.195
58-$^1/_3$	30.0	4.20	5.00	.159
66-$^2/_3$	0.0	4.67	5.53	.138
	17.0	4.54	5.43	.129
	30.0	4.44	5.35	.123
	40.0	4.33	5.25	.118
	50.0	4.25	5.20	.112
	70.0	4.25	5.25	.100
75	30.0	4.65	5.63	.105

2.10 Effects of Varying the Parameters.—Data illustrating the effects on the rate of changing buffer ratio, solvent composition, reaction temperature and the nature of the substituent on the nitrostyrene molecule are given in Table V. The effect on the apparent equilibrium constant of changing the solvent composition is shown in Table VI.

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(10) This equation corresponds to

$$K_{\text{equil}} = (\text{adduct})/(\text{NS})(\text{HBarb}_{\text{formal}})$$

and represents an apparent rather than specific equilibrium constant in that the total concentrations of barbituric acid and adduct are involved rather than the concentrations of the corresponding anions which probably enter into the rate-determining steps of both the forward and reverse reactions.

(11) L. G. Van Uitert and C. G. Haas, THIS JOURNAL, **75**, 451 (1953).

(12) L. G. Van Uitert and W. C. Fernelius, *ibid.*, **76**, 5887 (1954).

(13) The values of $1/\gamma$ at other temperatures may be determined by interpolation of the data of H. S. Harned and B. B. Owen, ref. 20, pp. 548–549.

TABLE V

EFFECT OF BUFFER RATIO, SOLVENT COMPOSITION, TEMPERATURE AND SUBSTITUENTS ON THE RATE OF REACTION OF BARBITURIC ACID WITH β-NITROSTYRENE IN DIOXANE–WATER

(Barbituric acid) = (β-Nitrostyrene) = 0.002 *M*, (KHPhthalate) = 0.02 *M*.

Nitrostyrene Substituent	Temp., °C.	Dioxane, %	Dielectric constant	$\frac{(\text{Phthalate}^-)}{(\text{Phthalic Acid})}$	k_{app}, l./mole min.	α	k_{spec}, l./mole min.
Unsubst.	30.0	66-2/3	19.5	1.000	8.48 ± 0.15	0.1095	77.4 ± 1.3
Unsubst.	30.0	66-2/3	19.5	0.200	1.86 ± 0.04	.0240	77.4 ± 1.7
	30.0	66-2/3	19.5	.400	3.76 ± .10	.0468	80.3 ± 2.1
	30.0	66-2/3	19.5	.667	5.93 ± .10	.0758	78.2 ± 1.3
	30.0	66-2/3	19.5	1.428	11.58 ± .22	.1495	78.1 ± 1.4
Unsubst.	30.0	75	13.4	1.000	5.26 ± 0.10	.0950	55.5 ± 1.1
	30.0	58-1/3	26.4	1.000	16.2 ± .33	.1370	118.5 ± 2.4
	30.0	50	33.3	1.000	24.9 ± .43	.1629	152.9 ± 2.6
	30.0	41-2/3	40.3	1.000	47.9 ± .70	.1970	243 ± 3.5
	30.0	33-1/3	47.4	1.000	66.0 ± 1.09	.2009	329 ± 5.4
Unsubst.	0.0	66-2/3	23.1	1.000	1.70 ± 0.02	.1210	14.0 ± 0.2
	17.0	66-2/3	21.0	1.000	4.31 ± .10	.1140	39.4 ± 0.9
	40.0	66-2/3	18.4	1.000	12.9 ± .23	.1063	122.1 ± 2.1
	50.0	66-2/4	17.4	1.000	18.5 ± .39	.1008	183.5 ± 3.6
	70.0	66-2/3	15.6	1.000	34.4 ± .63	.0914	378 ± 5.8
4-$(CH_3)_2N$	30.0	66-2/3	19.5	1.000	1.52 ± 0.07	.1095	13.9 ± 0.6
4-CH_3O	30.0	66-2/3	19.5	1.000	4.60 ± .20	.1095	42.0 ± 1.8
3,4-CH_2O_2	30.0	66-2/3	19.5	1.000	4.86 ± .09	.1095	44.4 ± 0.8
4-Cl	30.0	66-2/3	19.5	1.000	11.63 ± .21	.1095	106.2 ± 1.9
3-NO_2	30.0	66-2/3	19.5	1.000	20.7 ± .42	.1095	188.5 ± 3.8
4-NO_2	30.0	66-2/3	19.5	1.000	30.5 ± .71	.1095	279.0 ± 6.4

TABLE VI

EFFECT OF SOLVENT COMPOSITION ON EQUILIBRIUM IN THE REACTION OF BARBITURIC ACID WITH β-NITROSTYRENE IN DIOXANE-WATER AT 30.0°

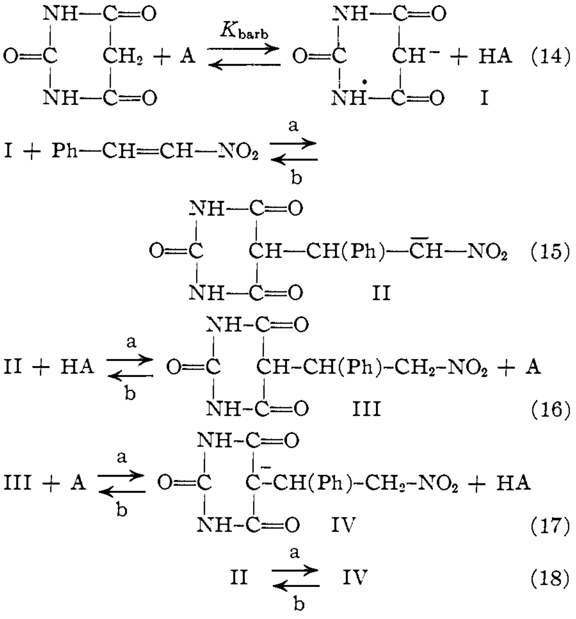
(Phthalic acid) = (KNPhthalate) = 0.02 *M*

Dioxane, %	Nitrostyrene, mole $l.^{-1} \times 10^5$ Initial	Equil.	K_{equil}, l. mole$^{-1} \times 10^{-4}$
75	200	16.1	7.1
66-2/3	av. of 3 expts. (Table III)		8.8
58-1/3	100	7.7	15.6
50	200	6.5	46
41-2/3	100	3.7	70
33-1/3	200	3.9	129

3. Discussion

3.1 Mechanism.—The constancy of k_{spec} over a wide range of buffer ratios is shown in the first set of data in Table V. As a further test the reaction was carried out under identical conditions but in the presence of a 1:1 succinic acid–potassium acid succinate buffer (α = 0.850) and a 4:1 acetic acid–potassium acetate buffer (α = 0.980). The apparent rate constants were 63.5 ± 1.2 and 76.1 ± 1.4 l. mole^{-1} min.$^{-1}$; the derived specific rate constants were 74.8 ± 1.4 and 77.6 ± 1.4 l. mole^{-1} min.$^{-1}$, substantially the same as with the phthalate buffer. Thus the rate depends on the concentration of barbiturate anion and the kinetics are consistent with a mechanism similar to Ingold's[2] and according to which rates and equilibria are governed by the following complex series of transformations.[14]

$$\text{HBuffer} + \text{A} \overset{K_{\text{buffer}}}{\rightleftarrows} \text{Buffer}^- + \text{HA} \qquad (13)$$



According to this scheme, the barbiturate anion, the concentration of which is governed by the total concentration of barbituric acid and by the ionization constants K_{13} and K_{14}, would react in the rate-determining step (15a) with β-nitrostyrene to give II, the adduct ionized at the position alpha to the nitro group. A subsequent step in this preferred mechanism would involve a rapid protonation by HA to give the un-ionized 5-(2-nitro-1-phenylethyl)-barbituric acid (III) *via* (16a) or a rapid internal proton transfer to give the more stable adduct anion IV *via* (18a). If this mechanism applies, the specific rate constants listed in Table V are identical with k_{15a}.

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[14] HA represents oxonium ion, water or other proton donor, while A represents the corresponding conjugate base.

An alternative mechanism, not completely eliminated by the kinetics, would involve a rapid equilibrium in step (15) followed by a rate-determining proton transfer in (16a).[15] If the requirement that k_{15a} and $k_{15b} >> k_{16a}$ were fulfilled, the kinetics would reduce to

$$-\mathrm{d(NS)}/\mathrm{d}t = \frac{k_{15a}k_{16a}}{k_{15b}}(\mathrm{barb}^-)(\mathrm{NS})(\mathrm{HA}) \qquad (19)$$

and

$$k_{\mathrm{spec}}\,(\text{Table V}) = k_{15a}k_{16a}\,(\mathrm{HA})/k_{15b} \qquad (20)$$

To explain the constancy of k_{spec} (Table V) over the wide acidity range, this mechanism would further demand that HA be H_2O rather than H_3O^+ or H Buffer.

Little evidence is available concerning the retrograde process but some conclusions may be deduced from the equilibrium studies given in Table III. The constancy, within experimental limits, of the apparent equilibrium constant in changing from the phthalate to the succinate to the acetate buffer would require that at equilibrium the concentration of the species (II in the preferred mechanism) entering into the rate determining step of the reverse reaction varied to about the same extent, *i.e.*, ninefold, with the several hundred-fold change in oxonium ion concentration as did the concentration of I, the reactive species in the forward reaction.

While a hydrogen atom alpha to an isolated nitro group dissociates to a substantially lesser degree than the methylene hydrogen in barbituric acid (*cf.* barbituric acid, $pK = 3.96$ in water at 25°; nitroethane, $pK = 8.60$[16]), the concentration of II, the conjugate base of a much weaker acid, is connected by the *p*H independent equilibrium (18) or by the equilibria (16) and (17) to that of IV, the conjugate base of an acid of about the same strength as barbituric acid. Since the concentration of IV and therefore II would vary with changing acidity to the same degree as I the constancy of the equilibrium constants with changing *p*H is clearly consistent with the principle of microscopic reversibility if the preferred mechanism applies.

3.2 Effect of Substituents.—On the basis of the preferred mechanism it might be predicted that electron withdrawing substituents on the nitrostyrene ring would, by decreasing the electron density at the carbon atom at which barbiturate anion attacks, cause an increase in k_{15a}, the specific rate constant for the forward reaction. The last set of data in Table V confirms this expectation. A fourfold increase in rate was observed in going from the unsubstituted compound to *p*,β-dinitrostyrene and a sixfold decrease in going to *p*-dimethylamino-β-nitrostyrene.

While electron withdrawing substituents would be expected to decrease k_{16a}, the rate constant for the slowest step in the alternative mechanism, the anticipated increase in the ratio k_{15a}/k_{15b} might offset this effect with a resulting over-all increase in rate. Thus, the effect of substituents is not inconsistant with the alternative mechanism.

A Hammett plot of these data[17,18] shows five of the points falling in line. For *p*-dimethylamino-β-nitro- and *m*,β-dinitrostyrene to fit this line would require a σ-constant for *p*-dimethylamino of −0.80 and for *m*-nitro of +0.52. If all seven points are included, the reaction constant, ρ, is 0.844 and the correlation coefficient, *r*, is 0.972.[19] If the point for the *p*-dimethylamino group (the σ-constant for which is the most questionable) is ignored, ρ becomes 0.739 and *r* is 0.989.

3.3 Isocomposition Activation Energy.—Data required for calculation of the isocomposition activation energy in the reaction of barbituric acid with the unsubstituted nitrostyrene are given in the third series of Table V. From an Arrhenius plot of these data[18] $\Delta E^*_{\mathrm{I.C.}}$ (66-²/₃% dioxane) was determined to be 8700 ± 300 cal. per mole. The Arrhenius frequency factor, log *A*, was 8.17 at 30°.

3.4 Effect of Solvent Composition on Rates.—The second series of data in Table V shows the effect of variation in solvent composition on k_{spec}. The over-all result was a sixfold increase in going from 75% dioxane–water (dielectric constant = 13.4) to 33-¹/₃% dioxane–water (D.C. = 47.4).[20,21] A plot of log k_{spec} against the first power of the dielectric constant was very close to linear over the entire range studied (Fig. 2).

3.5 Isodielectric Activation Energies.—From the above plot and the data discussed in 3.3, the following new method was developed for the calculation of isodielectric activation energies and frequency factors.[22] The logarithm of the specific rate constant in 66-²/₃% dioxane–water at 0.0° is 1.146. The dielectric constant of the solvent is 23.1.[20] At this D.C. and at 30.0°, log k_{spec}, determined graphically from Fig. 2, is 1.976. Using these values of log k_{spec} in the integrated Arrhenius expression, $\Delta E^*_{\mathrm{I.D.}}$ (D.C. = 23.1) was determined to be 10450 cal./mole and log $A_{\mathrm{I.D.}}$ was 9.50. Isodielectric activation energies and frequency factors at other dielectric constants were similarly calculated and are given in Table VII. It can be seen that both activation energy and frequency factor increase with increasing dielectric constant.

3.6 Comparison with Theory.—Hughes and Ingold have suggested that the activation energies of ion–molecule reactions should increase, and that rates should decrease with increasing ionizing power of the medium as a consequence of the charge dispersal in going from the reacting ion to the transition state and the resulting increased dif-

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[15] This possibility was suggested by Dr. Jack Hine of Georgia Institute of Technology.

[16] R. G. Pearson and R. L. Dillon, THIS JOURNAL, **75**, 2439 (1953).

[17] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 184.

[18] Plot available on request.

[19] H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953).

[20] Dielectric constants were obtained by interpolation from the data of H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publ. Corp., New York, N. Y., 1950, p. 118.

[21] If the alternative mechanism discussed in Section 3.1 applies and $k_{\mathrm{spec}} = k_{15a}k_{16a}(H_2O)/k_{15b}$, a portion of this increment in rate may be due to the increase in (H_2O). However, since (H_2O) increases only two and one half-fold over the range studied, some other factor must also be operative.

[22] For a discussion of the significance of activation energies as determined in solutions of fixed dielectric constant as compared with fixed composition, see W. J. Svirbely and J. C. Warner, THIS JOURNAL, **57**, 1883 (1935).

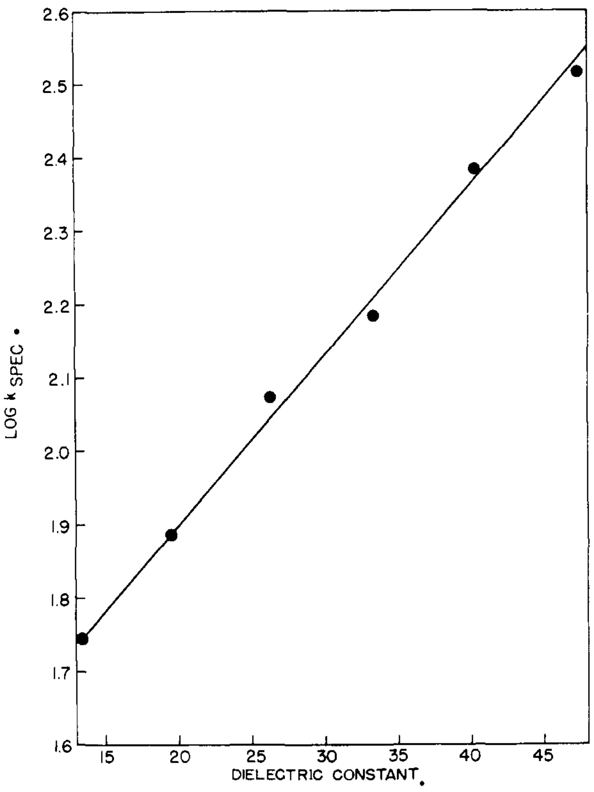

Fig. 2.—Specific rate constant as function of dielectric constant at 30.0°.

TABLE VII

ISODIELECTRIC ACTIVATION ENERGIES IN THE REACTION OF BARBITURIC ACID WITH β-NITROSTYRENE IN DIOXANE–WATER

Temp., °C.	D.C. of $66\text{-}^2/_3\%$ dioxane–water	Log k_{spec} at this D.C. At this temp.	At 30.0°	$\Delta E^*_{I.D.}$, cal./mole	Log A (30.0°)
0.0	23.1	1.146	1.976	10,450	9.50
17.0	21.0	1.596	1.925	10,200	9.27
40.0	18.4	2.087	1.861	9,800	8.91
50.0	17.4	2.264	1.839	9,540	8.75
70.0	15.6	2.578	1.799	9,280	8.47

ference in solvation energy.[23,24] The Laidler–Eyring equation[25] represented an attempt to give quantitative measure to this decrease in rate. Alternative expressions proposed by Amis[26] and by Amis, Jaffe and Overman[27] require that in more ionizing media the rates decrease in the case of positive ion–molecule reactions, but increase in the case of negative ion–molecule reactions.

An assumption implicit in the Hughes–Ingold theory and in the derivation of the equations mentioned above was that variation in rate was primarily due to changes in activation energy (which in the derivations was assumed equal to free energy of activation).[28] Changes in the Arrhenius frequency factor (which is directly related to the entropy of activation) were assumed to be nil or, at most, slight. This assumption, however, was not borne out by the findings of Leffler,[29] who has recently presented a wealth of evidence to show that in varying a number of parameters (including the composition of the medium) a linear relationship of positive slope exists between entropy of activation and enthalpy of activation for reactions of many types. Indeed, in a majority of the cases considered, the effect on rate of the change in log A was of the same magnitude as the effect due to changes in ΔE^*. In only very few cases was the change in log A (or ΔS^*) comparatively negligible.

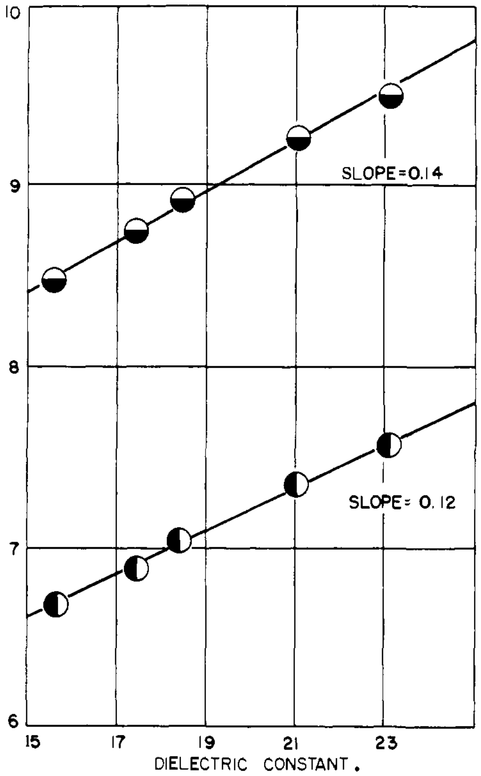

Fig. 3.—Log $A_{I.D.}$ ◒ and $\Delta E^*_{I.D.}/2.303\ RT$ ◐ as a function of dielectric constant.

To evaluate the effect of these competing influences on the over-all velocity in the reaction of barbiturate ion with β-nitrostyrene, the following treatment is presented. It follows from the Arrhenius expression that

$$(\mathrm{d}\log k_{spec}/\mathrm{d}D)_T = (\mathrm{d}\log A/\mathrm{d}D)_T - (\mathrm{d}\Delta E^*/\mathrm{d}D)/2.303RT \quad (21)$$

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(23) E. D. Hughes and C. K. Ingold, *Trans. Faraday Soc.*, **37**, 665 (1942); E. D. Hughes, *ibid.*, **37**, 609 (1942).

(24) The referee has suggested that since the charge in barbiturate ion is certainly well distributed to start with, and since the activated complex may in this case partake more of the nature of the product than of the reactants, there may actually be concentration of charge in going from the reactants to the transition state. If this be the case, the example here discussed is indeed theoretically ambiguous.

(25) K. J. Laidler and H. Eyring, *Ann. N. Y. Acad. Sci.*, **39**, 303 (1940).

(26) E. S. Amis, *J. Chem. Educ.*, **30**, 353 (1953).

(27) E. S. Amis, G. Jaffe and R. T. Overman, THIS JOURNAL, **66**, 1823 (1944).

(28) Amis states, "In deriving this equation, free energy and energy of activation were assumed to be equivalent. This assumption can be verified since, for reaction in solution, both $p\Delta V$ and the change of entropy of activation due to coulombic effects for rate processes carried out in solvents of constant dielectric constant are each equal to zero."[26]

(29) J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955); see also W. R. Gilkerson, G. A. Gallup and M. M. Jones, *Trans. Kansas Acad. Sci.*, **57**, 391 (1954).

The quantities on the right side of equation 21, determined from the slopes of plots of log A and $\Delta E^*/2.303RT$ as functions of the dielectric constant (Fig. 3) are 0.14 and 0.12, respectively. The difference between these values agrees well with the value of 0.023 for d log $k/\mathrm{d}D$ as determined from the slope in Fig. 2.

It can thus be seen that to the extent that the arguments presented by Hughes and Ingold apply to activation energies, the reaction here discussed fits the theory. The activation energy increases with increasing dielectric constant as predicted for ion–molecule reactions in general. The effect on the rate, however, is offset by the even greater effect of the change in log A.

The results discussed above agree neither quantitatively nor qualitatively with the Amis theory which would require a decrease in activation energy with increasing ionizing power of the solvent for an anion–molecule reaction. In addition, the Amis equations as well as the Laidler–Eyring equation predict a linear relationship between the logarithm of the rate constant and the *reciprocal* of the dielectric constant of the medium. Figure 2 shows that while a good linear relationship existed, it was with the *first power* of the dielectric constant, and from Fig. 3 it can be seen that a similar relationship (albeit over a short range) existed between the latter function, the isodielectric activation energy and the Arrhenius frequency factor.

That this linear dependence of log k, log A and ΔE^* on the dielectric constant is not unusual for ion–molecule reactions in general will be the subject of a forthcoming publication.

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Electronic Correlation in Molecules. I. Hydrogen in the Triplet State[1]

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For H_2 in the triplet state the London energy corresponding to dipole–dipole interaction is the dominant term at distances near or greater than the potential minimum. Other terms arising from hybridization are shown to be small at these distances but become important as the atoms come closer together. Since the interaction between closed electron shells is similar in essential features to that in triplet H_2, we conclude that the London energy term should be considered in binding energy calculations of complex systems.

The correlation of electronic motions has been recognized as very important in bond energy calculations and as extremely difficult to treat adequately. We are developing a scheme to estimate the contribution of correlation to the bond energy of molecules which is based on the treatment of London for intermolecular interactions. It has been recognized that the attractive force between polarizable electron clouds, first elucidated by London,[2] arises from the correlation of electron motion in the combined electron system. Born and Mayer[3] considered these forces in their treatment of ionic crystals and Davydov[4] and Simpson[5] have considered these effects in conjugated π electron systems. Also one of us[6] has published preliminary results on the halogen series. However, we are not aware of any previous general treatment of this type.

Our present paper includes an examination of the triplet state of hydrogen for the relative magnitude of various terms. Paper II contains a critical review of several formulas for the London energy together with the development of an improved formula for further calculations; while Paper III gives calculations for the paraffin hydrocarbons through the pentanes.

While several treatments[7,8] have been published for the H–H interaction in the triplet state and for the closely related problem of the interaction of two helium atoms, there remain unanswered important questions about the effect of certain terms in the wave function. These types of terms are of interest in discussions of closed shell interactions between heavier atoms.

Recently there have been suggestions[6,9,10] that interactions between closed electron subshells may contribute appreciably to chemical bonding. For example in Cl_2 the $3p\pi$ subshell in each chlorine atom is filled with four electrons yet it is suggested that interactions with the vacant $3d\pi$ orbitals may be such that these electrons contribute substantially to the Cl–Cl bond energy. Two different proposals have been made.

Mulliken[9] suggested that the $3p\pi$ atomic orbitals should be hybridized by linear combination with

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(1) This research was assisted by the American Petroleum Institute through Research Project 50.

(2) F. London, *Z. physik. Chem.*, **B11**, 222 (1930); *Z. Physik*, **63**, 245 (1930).

(3) M. Born and J. E. Mayer, *ibid.*, **75**, 1 (1932).

(4) A. S. Davydov, *Zhur. Eksptl. Teoret. Fiz.*, **18**, 201 (1948).

(5) W. T. Simpson, THIS JOURNAL, **73**, 5363 (1951).

(6) K. S. Pitzer, *J. Chem. Phys.*, **23**, 1735 (1955).

(7) J. O. Hirschfelder and J. W. Linnett, *ibid.*, **18**, 130 (1951).

(8) James, Coolidge and Present, *ibid.*, **4**, 187, 193 (1936).

(9) R. S. Mulliken, THIS JOURNAL, **77**, 884 (1955).

(10) K. S. Pitzer, *ibid.*, **70**, 2140 (1948).