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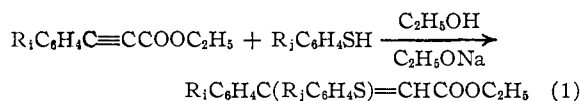
Kinetics of the Ethoxide-catalyzed Addition of Aryl Thiols to Ethyl Phenylpropiolates
Structure-Reactivity Correlations^{1,2}

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Kinetic data are reported for the addition of aryl thiols, $R_1C_6H_4SH$, to ethyl phenylpropiolates, $R_1C_6H_4C\equiv CCOOC_2H_5$, in sodium ethoxide-ethanol in the range -30° to $+35^\circ$. Activation parameters for ten pairs of R_1 , R_2 and single rate constant for four other pairs were determined. These data provide another example of the greater reactivity of alkynes over alkenes with nucleophiles. The variation of $\log k$ with Hammett σ_1 or σ_2 and with $1/T$ was adequately linear; but two- and threefold correlations of $\log k$ with these variables were inadequate and serve to emphasize the empirical and approximate nature of the Hammett and/or Arrhenius equations. Ultraviolet spectral and polarographic data were not simply related to the electrophilicity of the acetylenic esters. The $E_{1/2}$'s of aryl thiolates but not their infrared and ultraviolet data were simply related to their nucleophilicity.

In this paper we report kinetic data for the system



By combining these data with spectral and polarographic data for the reactants, we hoped to gain insight into the problem of nucleophilicity and electrophilicity.

It was anticipated that the Arrhenius and Hammett⁵ equations would apply to the rate data, that is, $\log k$ would be linear in $1/T$ or σ_1 or σ_2 . A more interesting test of the linear equations involves an appropriate form of

$$\log k = f(\sigma_1, \sigma_2, 1/T) \quad (2)$$

If in fact the linear equations are applicable, it can be shown that eq. 2 must take the form^{6,7}

$$\log k = a + b_1\sigma_1 + b_2\sigma_2 + b_3/T + c_1\sigma_1\sigma_2 + c_2\sigma_1/T + c_3\sigma_2/T + q\sigma_1\sigma_2/T \quad (3)$$

Obedience to such a simultaneous variation is obviously a more stringent test of the individual linear "laws."

For the purposes of this paper, the synthetic and mechanistic aspects of eq. 1 are well understood. Ruhemann and Stapleton first prepared ethyl β -thiophenylcinnamate in this way⁸ and later workers have used similar syntheses. Recently it has been shown that nucleophilic additions to acetylenes almost always are in the *trans* sense.⁹ Moreover, the available kinetic evidence requires that the thiolate and the acetylene are involved in the rate-determining process.

(1) (a) Supported by the Office of Ordnance Research, U. S. Army; (b) Abstracted in part from the Ph.D. thesis of G. S. Krishnamurthy, Illinois Institute of Technology, June, 1960.

(2) This is one of several studies^{3,4} concerned with physical properties and reactivity in the system $C\equiv C + RSH \rightarrow -RSC=CH-$.

(3) Spectral data on substituted benzenethiols.

(4) Polarographic data on substituted benzenethiols and on substituted ethyl phenylpropiolates.

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

(6) S. I. Miller, *J. Am. Chem. Soc.*, **81**, 101 (1959).

(7) S. I. Miller, unpublished results.

(8) S. Ruhemann and H. E. Stapleton, *J. Chem. Soc.*, **77**, 1179 (1900).

(9) (a) S. I. Miller, *et al.*, *J. Am. Chem. Soc.*, **77**, 5038 (1955); **78**, 5091 (1956); (b) W. E. Truce, *et al.*, *ibid.*, **78**, 695, 2746, 2756 (1956); **82**, 3799 (1960); (c) F. Montanari and A. Negrini, *Boll. sci. fac. chim. Ind. Bologna*, **15**, 27 (1957); *Tetrahedron Letters*, **4**, 18 (1960).

Experimental¹⁰

Materials.—The solvent was commercially available "absolute" ethanol. Since the sodium ethoxide solutions which were used to convert the thiols to thiolates deteriorated in *ca.* 4 weeks, fresh solutions were prepared as needed from clean sodium and absolute ethanol. The aryl thiols used in this work have been described elsewhere.^{1b,3}

The dehydrobromination of ethyl cinnamate dibromide with sodium hydride in benzene yielded ethyl phenylpropiolate,¹¹ b.p. $89-90^\circ$ (1 mm.), n_D^{25} 1.5499 (lit.¹¹ n_D^{25} 1.5490).

Ethyl *p*-nitrophenylpropiolate was prepared by dehydrobromination of the corresponding cinnamic ester dibromide with sodium ethoxide. Ethyl *p*-nitrophenylpropiolate had m.p. $123-124^\circ$ (lit.¹¹ $123-123.8^\circ$); a mixed m.p. with an authentic sample was undepressed.

Professor M. S. Newman sent us small samples of the ethyl *p*-chloro- and *m*-chlorophenylpropiolate. The *p*-chloro isomer was shown to be impure by elemental analysis. There was not enough of the *m*-chloro compound for a purity check.

Ethyl *p*-methoxyphenylpropiolate was prepared from *p*-anisaldehyde and malonic acid in a series of steps.¹² It was found that dehydrobromination of the ethyl *p*-methoxycinnamate dibromide, m.p. $112-113^\circ$ (lit.¹² m.p. $111-112^\circ$), gave the preferred intermediate *trans-p*-methoxy- α -bromocinnamic acid, m.p. $188-189^\circ$ (lit.¹¹ $188-189^\circ$). On the other hand, dehydrobromination of *p*-methoxycinnamic acid dibromide gave 85% of the *cis*-acid, m.p. $102-103^\circ$ (lit.¹² m.p. 103°). The *trans*-acid was treated with alcoholic potassium hydroxide to yield *p*-methoxyphenylpropiolic acid, m.p. $142-143^\circ$ (lit.¹¹ m.p. $144-144.4^\circ$). This was esterified and the ester distilled at 110° (0.1 mm.), n_D^{25} 1.5670 (lit.¹¹ n_D^{25} 1.5675).

In order to verify the stoichiometry given by eq. 1, thiophenol (0.12 g., 0.001 mole), 5 ml. of 0.2 *M* sodium ethoxide and ethyl phenylpropiolate (1.74 g., 0.01 mole) were dissolved in 25 ml. of ethanol. After 2 hours the reaction was stopped: 0.29 g. of white crystalline ethyl β -thiophenyl cinnamate was isolated in 90% yield, m.p. $94-94.5^\circ$ (lit.⁸ m.p. $95-96^\circ$).

Kinetic Runs.—We describe a novel "kinetics" flask in some detail (see Fig. 1). It made possible three important operations of a batch kinetic run without atmospheric contact: (1) thermostating of reactants, (2) mixing of reactants and (3) dispensing of aliquots.

A reaction flask *a* has *ca.* 200-ml. capacity and a standard ground glass joint ($\text{F } 60/71$); *b* is calibrated bulb of *ca.* 50-ml. capacity fitted with a standard ground glass joint ($\text{F } 10/14$) so that it can be conveniently detached from a delivery tube leading to the bottom of *a*. Two stopcocks, one at the top and the other at the bottom, can be manipulated to control the flow of the liquid from the bulb into the flask. The lower stopcock can be operated from above by means of a pulley and chain arrangement. *c* is a calibrated bulb of approximately 10-ml. capacity, one end of

(10) Detailed information may be found in G. Krishnamurthy's doctoral thesis.^{1b}

(11) M. S. Newman and S. H. Merrill, *J. Am. Chem. Soc.*, **77**, 5549 (1955).

(12) K. V. Hariharan and J. J. Sudborough, *J. Indian Inst. Sci.*, **8A**, 189 (1925).

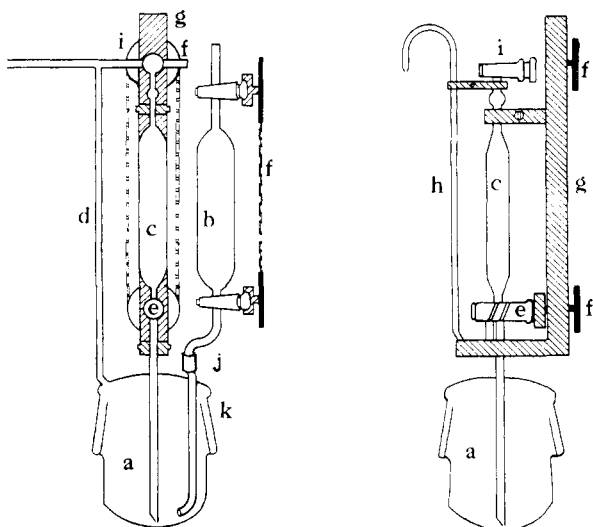


Fig. 1.—"Kinetics" flask: a, flask, ca. 200-ml. capacity; b, calibrated bulb 50 ml.; c, calibrated bulb 10 ml.; d, vent for nitrogen; e, three-way stopcock; f, pulley and chain unit; g, aluminum frame; h, capillary tube for delivering aliquots; i, three-way stopcock; j, joint, $\frac{10}{30}$; k, joint, $\frac{71}{60}$.

which is connected through a three-way stopcock e to a capillary tube which goes all the way to the bottom of the flask a. By operating this stopcock, the bulb c can be connected either to the flask a or to a capillary delivery tube h for delivering the aliquots. g is an aluminum frame which provides mechanical support to the upper portion of the kinetic flask and contains a pulley and chain unit f which is used for operating the three-way stopcock e from above. Dow Corning high vacuum Silicone grease was found suitable as a lubricant for the stopcocks at temperatures down to -30° .

Solutions of both the reactants, namely, ethyl phenylpropionate and the thiol, were made. The ester solution could be kept standing indefinitely without loss of concentration. The thiol solution contained an excess of sodium ethoxide. As such solutions decompose gradually on contact with air, *i.e.*



it was desirable to prepare the thiol solution and check its concentration just before the start of each run.

The bulb b was completely filled with the thiol solution while 48.0 ml. of the ester solution was pipetted into the flask a. The upper portion of the kinetic flask then was fitted to the flask a, the bulb b was put in place and the whole unit was immersed to stopcock i in a thermostat bath and equilibrated for several hours. This bath was an insulated 33-l. jar containing 60% Prestone antifreeze.¹³ Temperatures, determined on calibrated thermometers, were maintained at $\pm 0.05^{\circ}$ by a suitable refrigeration coil and/or heater.

The reaction was started by opening the bottom stopcock of bulb b and forcing the solution into a with nitrogen gas which was admitted through the top stopcock. Thorough mixing was achieved in about 5 sec. The nitrogen escaped through the vent d. With light suction at stopcock i, aliquots were drawn into bulb c from a through stopcock e. After c was filled, stopcock e was turned to connect it to the delivery tube h and the aliquot was rapidly delivered under nitrogen pressure into a 150-ml. beaker containing 15 ml. of methanol and 5 ml. of glacial acetic acid. The uncertainty in any time interval was ± 0.10 min.

The extent of reaction was followed by amperometric titration of the remaining thiol with standard silver nitrate.¹⁴ A Sargent Ampot was used to measure the current between

(13) This bath was kindly loaned to us by Dr. T. J. Neubert. Details of its construction may be found in G. J. Nichols' Ph.D. thesis, Illinois Institute of Technology, 1957.

(14) I. M. Kolthoff and W. E. Harris, *Anal. Chem.*, **18**, 161 (1946); **21**, 963 (1949).

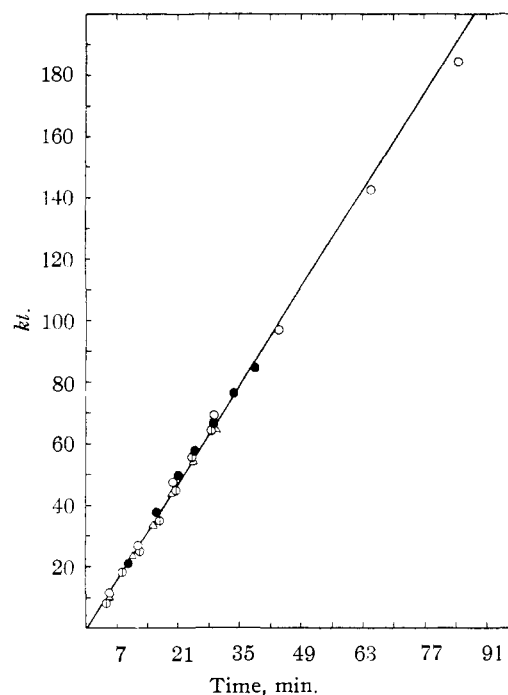
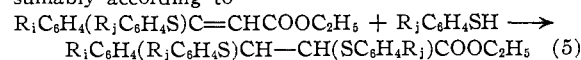


Fig. 2.—Nucleophilic addition of *p*-thiocresol to ethyl phenylpropionate at 0° in ethanol-sodium ethoxide (4 runs).

a rotating platinum electrode and a mercury-mercuric iodide electrode.

As the solutions were made up at room temperature, it was necessary to correct for the expansion or contraction of the solvent (ethanol) at the temperature of the reaction. For this purpose these various multiplication factors were used: $35^{\circ}(0.989)$, $25^{\circ}(1.000)$, $15^{\circ}(1.011)$, $0^{\circ}(1.026)$, $-15^{\circ}(1.048)$, $-30^{\circ}(1.059)$.¹⁵ In this way, the initial concentrations of the reactants were corrected to the bath temperature. Since sample aliquots are taken at the temperature of the reaction, no further correction was necessary. The correction factors are in the reverse order to the usual situation in which aliquots are delivered at room temperature and brought to reaction temperature.

Preliminary runs with ethyl phenylpropionate and thiophenol each at ca. 0.05 *M* gave falling rate constants. It was shown that more than one thiolate was consumed, presumably according to



Fortunately the second step was always slower than the first: for $\text{R}_1 = \text{R}_j = \text{H}$, $k_1/k_2 \approx 13$ at 0° . Kinetically this becomes the standard but difficult problem of two consecutive competitive second-order reactions.¹⁶ Elsewhere¹⁰ it is shown in detail how both rate constants for this system can be evaluated. Here we were interested only in k_1 . The use of a high ester to thiol ratio, ca. $>10/1$, minimized the importance of 5. Of course, practical considerations of high rates or analytical limitations did restrict the choice of absolute and relative concentrations of the reactants¹⁰; for example, the following pairs of concentrations in mole/liter were used for the reactants ethyl phenylpropionate-*p*-nitrothiophenol in four runs at 0° : 0.05980, 0.005827; 0.07804, 0.005583; 0.03887, 0.003736; 0.02163, 0.001623.

The rate constants for 1 were calculated according to

$$kt = \frac{2.303}{a-b} \log \frac{b(a-x)}{a(b-x)} \quad (6)$$

where a = initial concentration of the ester in mole liter⁻¹, b = initial concentration of the thiolate in mole liter⁻¹, and $b-x$ = concentration of thiolate, mole liter⁻¹, at time, t . The results for two typical runs are given in Table I and those for another system are shown in Fig. 2. All of

(15) N. S. Osborne, *J. Research Natl. Bur. Standards*, **9**, 371 (1913).

(16) A. A. Frost and R. G. Pearson, "Kinetics and Mechanisms," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 136.

TABLE I
REACTION OF $C_6H_5C\equiv CCOOC_2H_5$ AND $p\text{-ClC}_6H_4SH$ AT -30°

$a = 0.08724, b = 0.004155$			$a = 0.10480, b = 0.002164$		
t	x	k	t	x	k
0	0	...	0	0	...
31.26	0.000677	0.0654	35.30	0.000448	0.0629
60.58	.001122	.0599	50.10	.000557	.0569
90.71	.001474	.0559	65.29	.000692	.0565
120.62	.001832	.0559	80.30	.000792	.0544
150.54	.002122	.0552	95.82	.000929	.0561
181.58	.002407	.0555	110.49	.001036	.0565
210.36	.002623	.0553	126.05	.001137	.0567
241.02	.002796	.0542	141.11	.001197	.0548
270.89	.002988	.0544	157.30	.001278	.0545
k (mean) 0.0569 ± 0.003			k (mean) 0.0566 ± 0.002		

Hammett plots for the kinetic data are given in Figs. 3-5. The data fit the equation within the usual precision, ca. 15%.⁸ The parameters for these lines are collected in Table IV. The temperature dependence of ρ is given in Fig. 6; here the necessary relation is^{6,7}

$$\Delta\rho = q\Delta(1/T) \quad (8)$$

when 1 has the form $\log k = f(\sigma, 1/T)$. A similar relation holds for $\log k = f(\sigma_i, \sigma_j)$, i.e., $\Delta\rho_i = q\sigma_j$.

Calculations.—Where possible, a statistical analysis by computer was made of the multiple variation according to eq. 3.²¹ The analysis yielded the error variance and the square of Students' t for parameters b to q . The variance is roughly equivalent to the square of the standard deviation in $\log k$; t measures the confidence level of the calculated parameter.²² The following information will be listed: the variables; N , the number of experimental points; the calculated form of 1; the variance; t^2 followed by a figure in parentheses which translates it into a level of significance given as a per cent.²²

TABLE II
RATE CONSTANTS IN LITER MOLE⁻¹ MIN.⁻¹ FOR THE REACTION

$$R_1C_6H_4C\equiv CCOOC_2H_5 + R_1C_6H_4SH \xrightarrow[\text{HO}C_2H_5]{\text{NaOC}_2\text{H}_5} R_1C_6H_4C(SC_6H_4R_1)=CHCOOC_2H_5$$

R_1	R_1	Temperature $\pm 0.05^\circ$					
		-30.20°	-15°	0°	15°	24.84°	35.45°
H	$p\text{-CH}_3$	0.124	0.575	2.26			
H	$p\text{-Cl}$.0586	.254	1.09			
H	H	.0671	.308	1.31			
H	$m\text{-CH}_3$.104	.465	1.95			
H	$p\text{-t-C}_4\text{H}_9$			2.06			
H	$m\text{-COOC}_2\text{H}_5$			0.707			
H	$p\text{-NO}_2$.10		0.819	1.755
$p\text{-Cl}$	$p\text{-NO}_2$.388			
$p\text{-NO}_2$	$p\text{-NO}_2$			8.26			
$p\text{-CH}_3\text{O}$	$p\text{-CH}_3$		0.109	0.500	2.04		
$p\text{-CH}_3\text{O}$	$p\text{-Cl}$.0492	.225	0.945		
$p\text{-CH}_3\text{O}$	H		.0782 ^a	.303	1.06		
$p\text{-CH}_3\text{O}$	$m\text{-CH}_3$.106	.361	1.43		
$p\text{-CH}_3\text{O}$	$p\text{-NO}_2$				0.0766	0.183	0.422

^a When 1% water, ca. 0.5 mole liter⁻¹, is added, the rate constant becomes 0.088.

TABLE III
ACTIVATION PARAMETERS FOR THE REACTION
 $R_1C_6H_4C\equiv CCOOC_2H_5 + R_1C_6H_4SH \xrightarrow[\text{HO}C_2H_5]{\text{NaOC}_2\text{H}_5} R_1C_6H_4C(SC_6H_4R_1)=CHCOOC_2H_5$

R_1	R_1	ΔH^* , kcal. mole ⁻¹	ΔS^* , cal. deg. ⁻¹ mole ⁻¹
H	$p\text{-CH}_3$	12.2	-12
H	$p\text{-Cl}$	12.2	-13.5
H	H	12.5	-12
H	$m\text{-CH}_3$	12.3	-12
H	$p\text{-NO}_2$	13.1	-15
$p\text{-CH}_3\text{O}$	$p\text{-CH}_3$	13.9	-9
$p\text{-CH}_3\text{O}$	$p\text{-Cl}$	14.0	-10
$p\text{-CH}_3\text{O}$	H	12.3	-16
$p\text{-CH}_3\text{O}$	$m\text{-CH}_3$	12.1	-16
$p\text{-CH}_3\text{O}$	$p\text{-NO}_2$	14.2	-14

the rate constants are listed in Table II. For reactions whose activation parameters were sought, three to five runs were made at each temperature and the rate constants were averaged. These k 's agreed with those calculated from k vs. t plots such as Fig. 2. The average deviation in k is less than 5% and usually less than 3%.

The activation parameters for system 1 were calculated using a least squares fit of the expression¹⁷

$$2.303 \log k = KT/h - \Delta H^*/RT + \Delta S^*/R \quad (7)$$

These quantities are given in Table III and were checked against conventional Arrhenius plots.

(17) Reference 16, p. 96.

$\log k$ vs. σ_i, σ_j ; $N = 13, t = 0^\circ$

$$\log k = 0.1841 - 0.7214\sigma_i - 0.2681\sigma_j + 0.0268\sigma_i\sigma_j \quad (9)$$

variance 0.0224, $t_1^2 = 46.84(99)$, $t_2^2 = 61.59(99)$, $t_3^2 = 0.6456(55)$

$\log k$ vs. $\sigma_j, 1/T$; $N = 17, \sigma_i = 0$

$$\log k = 10.33 - 0.5719\sigma_j - 2774.4/T - 91.987\sigma_j/T \quad (10)$$

variance 0.002914, $t_1^2 = 1.591(80)$, $t_2^2 = 1322(99)$, $t_3^2 = 0.5177(50)$

$\log k$ vs. $\sigma_i, \sigma_j, 1/T$; $N = 34$

$$\log k = 10.36 - 0.1297\sigma_i - 0.5829\sigma_j - 2782/T + 1.445\sigma_i\sigma_j - 90.12\sigma_j/T + 695.6\sigma_i/T - 388.9\sigma_i\sigma_j/T \quad (11)$$

variance 0.00263, $t_1^2 = 0.00652(10)$, $t_2^2 = 2.16(84)$, $t_3^2 = 1470(99)$, $t_4^2 = 0.518(53)$, $t_5^2 = 0.675(58)$, $t_6^2 = 2.63(87)$, $t_7^2 = 0.503(51)$

Discussion

Qualitatively the kinetic data of Tables II-IV exhibit these various trends: Electron-withdrawing groups, R_i , on the electrophile increase the rate of thiolate addition: ρ is strongly positive. Electron-withdrawing groups, R_j , decrease the charge density at the sulfur and lower the nucleophilicity: ρ is negative. However, the activation parameters show small variations but no definite

(18) For related data see ref. 5 and (a) M. S. Newman and S. H. Merrill, *J. Am. Chem. Soc.*, **77**, 5554 (1955); (b) J. D. Roberts and R. A. Carboni, *ibid.*, **77**, 5554 (1955).

(19) Y. Schaafsma, A. F. Bickel and E. C. Kooyman, *Recueil*, **76**, 180 (1957).

(20) I. Benhiet and E. I. Becker, *J. Org. Chem.*, **23**, 885 (1958).

(21) 650 Program Library, File Number 6.0.018 kindly supplied by

TABLE IV
HAMMETT CORRELATIONS INVOLVING ARYL THIOLS AND ALKYNES¹⁸

Reaction	Solvent	T, °C.	ρ	$\log k_0^a$
$C_6H_5C\equiv CCOOC_2H_5 + ArSH \rightarrow C_6H_5(ArS)C=CHCOOC_2H_5$	Ethanol	-30	-0.83	-1.06
		-15	-.87	-0.408
		0	-.92	0.194
$p-CH_3OC_6H_4C\equiv CCOOC_2H_5 + ArSH \rightarrow p-CH_3OC_6H_4(ArS)C=CHCOOC_2H_5$	Ethanol	-15	-.87	-1.089
		0	-.90	-0.473
		15	-.95	0.162
ArSH + R· + → ArS· + RH	Toluene	110	-.4 ¹⁹	
$E_{1/2}$'s (RPE), 2ArSH → ArSSAr	20% ethanol	25	3.00 ^b	0.240 ^c
$ArC\equiv CCOOC_2H_5 + p-O_2NC_6H_4S^- \rightarrow Ar(p-O_2NC_6H_4S)C=CHCOOC_2H_5$	Ethanol	0	2.58	0.105
$ArC\equiv CCOOCH_3 + \text{tetracyclone} \rightarrow \text{Diels-Alder adduct}$	50% ethanol	175.6	1.10 ²⁰	

^a k_0 is in l. mole⁻¹ min.⁻¹. ^b In log units converted from 0.180 volt by the factor 1/0.0591. ^c $E_{1/2}$, volts at the rotating platinum electrode.⁴

pattern. The spread in enthalpies is 2 kcal.; the spread in the entropies is 7 e.u.

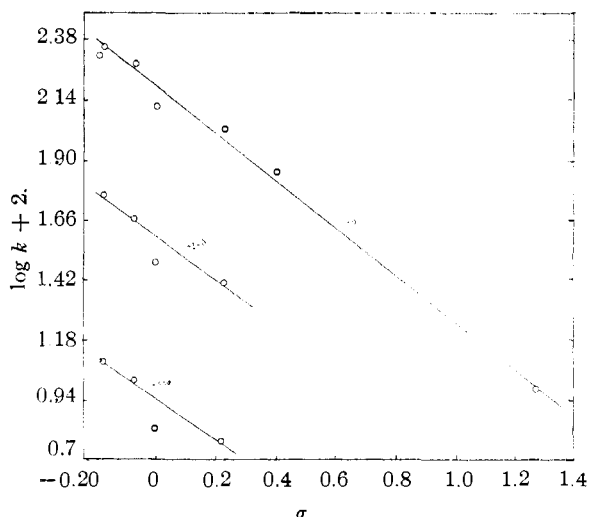


Fig. 3.—Hammett plots for the addition of thiophenols to ethyl phenylpropiolate.

The entropies of activation are negative—the pre-exponential factors of the Arrhenius equation are below “normal” by 10^2 to 10^3 for ion-neutral molecule reactions. Analogous additions of negative ions to other unsaturated systems, e.g., methoxide-phenylacetylene,^{21a} iodide-*p*-nitro- ω -bromostyrene,²³ *p*-toluenethiolate-phenylacetylene²⁴ and iodide-iodine-acetylene,²⁵ also have low entropies of activation. Unfortunately, it does not seem possible to correlate these entropy effects with kinetic order and thereby specify the role of the protonic solvent in these additions.

Were there more of them, the reactions in Table IV could be used to place system 1 in a more general context. Strictly speaking there appears to be only one thiol reaction and one acetylene reaction with which our data can be classed. It is true that there are other interesting data for the aryl propiolates,

International Business Machines Corp., 590 Madison Ave., N. Y. 22, N. Y.

(22) C. A. Bennett and N. L. Franklin, "Statistical Analysis in Chemistry and Chemical Industry," John Wiley and Sons, Inc., New York, N. Y., 1954; R. A. Fisher and F. Yates, "Statistical Tables," Hafner Publishing Co., New York, N. Y., 1949, p. 32.

(23) S. I. Miller and P. K. Yonan, *J. Am. Chem. Soc.*, **79**, 5931 (1957).

(24) W. E. Truce and R. F. Heine, *ibid.*, **81**, 592 (1959).

(25) S. I. Miller and R. M. Noyes, *ibid.*, **74**, 3403 (1952).

but these involve reactions at the carbonyl^{15,18}; these data indicate that the triple bond transmits electronic effects relatively poorly to the benzene nucleus.

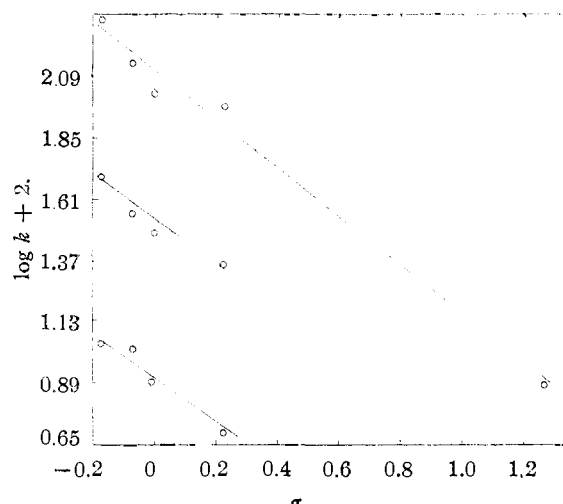


Fig. 4.—Hammett plots for the addition of thiophenols to ethyl *p*-methoxyphenylpropiolate.

System 1 does provide a specific example of the greater reactivity of a nucleophile in addition to an alkyne as compared with addition to an alkene.²⁶ Just as the pK 's of substituted phenylpropionic acids are greater than those of corresponding cinnamic acids, just as the rates of basic hydrolysis of the acetylenic esters are greater than those of corresponding cinnamic esters,^{5,18,20} so too the rates of nucleophilic addition of thiolate and the ease of reduction favor the ethyl phenylpropiolates over the ethyl cinnamates. These relative reactivities are consistent with the greater electron affinity of acetylenes, e.g., their ionization potentials. (The lower reactivities of alkynes toward electrophiles can be rationalized on the same basis.²⁶)

Up to this point, the kinetic data for 1 have been discussed from a “linear” point of view. The statistical analysis suggests that in 9, the cross-term is of negligible importance and that the data essentially lie on a plane. The same conclusion can be obtained qualitatively from Table IV by

(26) (a) S. I. Miller, *J. Org. Chem.*, **21**, 247 (1956); (b) F. Bohlmann, *Angew. Chem.*, **69**, 82 (1957); (c) R. Daniels and L. Bauer, *J. Chem. Educ.*, **35**, 444 (1958).

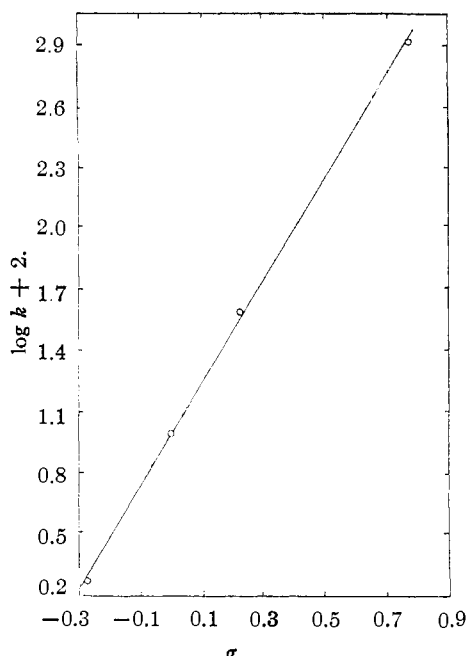


Fig. 5.—Hammett plot for the addition of *p*-nitrothiophenol to substituted ethyl phenylpropiolates at 0°.

noting that $q = \Delta\rho/(\sigma_H - \sigma_p - \text{OCH}_3)$ is close to zero. From the few systems that have been examined in this way it appears that some have statistically significant cross-terms and others do not.^{6,7,27} Further discussion of the "interaction" term q must be postponed until more precise data become available.

On the basis of the statistical analysis, we can have little confidence in eq. 10 and 11 describing two- and threefold variations of $\log k$. The confidence level in the parameters is rarely above 90% and too often below 50%. (It is conceded that the data are few and the tests of eq. 3 are not as extensive as they might be.) Yet acceptable Arrhenius and Hammett plots were obtained (see Figs. 3–5), the necessary linearity of ρ in $1/T$ was found (Fig. 6) and correlation 9 appeared adequate. Equation 8 also provides an index of the striking discrepancy between the two- and three-dimensional approach. Thus, a best fit of all of the points in 10 gives $q = -92$ while a best fit to individual lines as in Fig. 6 and subsequent insertion in 8 gives $q \approx 200$. A study of multiple variation has revealed weaknesses in the linear "laws"!

(27) See ref. 5, Table 2: reactions 171–174, $q \approx 0$; reactions 119 and 120, $q \approx 6$; reactions 114a and 115, $q \approx 1.14$. These last two examples were brought to my attention by Mr. V. Story.

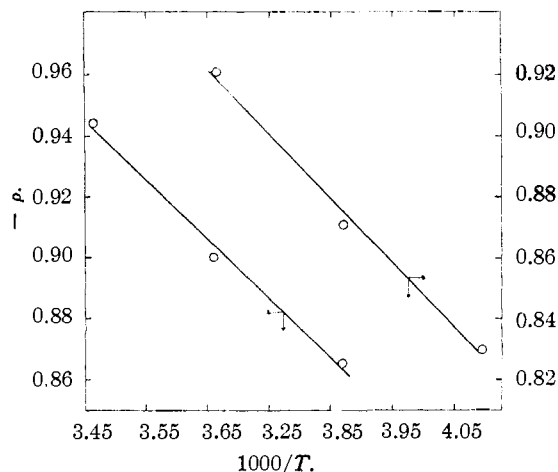


Fig. 6.—Reaction of aryl thiols with ethyl phenylpropiolate (upper right line) and ethyl *p*-methoxyphenylpropiolate (lower left line).

At this stage, it would appear that either the Hammett or the Arrhenius equations, or both, are only poorly applicable to system 1—the more taxing requirements of simultaneous fit or multiple correlation underline the empirical and approximate nature of these relations. What is novel here is not the conclusion but the analytical approach in obtaining it. Again, it is accepted that structure–reactivity comparisons based on large changes in Hammett ρ are fairly safe, while those based on the fine distinctions in ρ are not. Where possible, multiple correlation can make for a more definitive statement. Indeed, a satisfactory multiple correlation gives the exact dependence of ρ on the other variables.

Nucleophilicity and Electrophilicity.—System 1 also has been used to test the notion that polarographic and spectral data might be used as measures of reactivity. It was soon evident that ultraviolet data of the phenylpropiolic esters¹¹ or the aryl thiols³ do not relate simply to various σ constants.⁴ Contrary to a recent report,²⁸ infrared S–H stretching frequencies do not relate simply to σ or σ^+ constants.³ Polarographic $E_{1/2}$'s (DME) for the propiolates varied unsystematically with σ .⁴ Only the $E_{1/2}$'s (RPE) for the thiols correlated adequately with σ .⁴ Such findings are necessary and useful in establishing both the limitations and the direction of broad structure–reactivity correlations.

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(28) J. Jan, D. Hadzi and G. Modena, *Ricerca Sci.*, **30**, 1065 (1960).