

and α'' represents halogen acid absorption (reaction 13). Values of α' are 0.94, 3.6 and 3.4 for chloride, bromide and iodide, respectively; α'' is obtained by subtracting α' from the values of α in Table IV.

The effect of chloride on acetol formation is similar to that of perchlorates and nitrates, and appears to be a true kinetic salt effect. The values for bromide and iodide are so large as to suggest a specific catalysis by these ions; this might result if the intermediate complex of reaction (13) partly reacts with water to form acetol instead of decomposing to haloacetone.

Olson and Tong¹² found potassium bromide and iodide to have much larger effects than the chloride on the rate of hydrolysis of dipropylformal in dilute hydrochloric acid. This is not an effect on the activity of the neutral molecules, which is expected to go in the opposite direction.

There is no explanation for the selective absorption of certain acids. It might be thought that other acids would catalyze reaction (1) by entering the product temporarily, then being replaced by water. This process is excluded by the demonstration that salt effects are normal.

3. **Temperature Coefficients.**—Table I gives measurements from which activation energies and entropy can be calculated. While the temperature range is small, great care was taken to be sure that the accuracy was sufficient for the present purpose. Rates at the three temperatures are represented within less than 1% by the equation

$$k_2 = 6.79 \times 10^{12} e^{-19800/RT} \text{ liters mole}^{-1} \text{ sec.}^{-1} \quad (15)$$

where k_2 is the specific second-order rate constant.

The entropy, enthalpy and free energy of activation have been calculated²⁴ and are compared in Table VI with corresponding values for diazoacetic ester²⁵ and azodicarbonate ion.²⁶ No data for other diazo compounds are available. The maximum error in E for diazoacetone is estimated as 400 cal., corresponding to 1.3 units in ΔS .*

TABLE VI
ENERGIES AND ENTROPY OF ACTIVATION

Substrate	E , kcal.	ΔS^* , e.u.	ΔH^*	ΔF^*
Diazoacetone	19.8	- 2.1	19.2	19.8
Diazoacetic ester	17.5	- 2.7	16.9	17.7
Azodicarbonate	10.2	+12.9	9.6	5.7

There is strong indication in the values of Table VI that the reactions of diazoacetone and diazoacetic ester are similar in mechanism. The ester is more sensitive to hydronium ion catalysis, and since the entropies are similar most of the difference is due to the smaller enthalpy and free energy of activation. These energies include the effect of temperature on equilibrium (11). The greater sensitivity of the ester probably indicates that it is more basic than diazoacetone and a higher concentration of the acid ion is available for the rate-determining reaction.

(24) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, pp. 197-199.

(25) W. Fraenkel, *Z. physik. Chem.*, **60**, 202 (1907).

(26) C. V. King and J. J. Josephs, *THIS JOURNAL*, **66**, 767 (1944).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

Formation and Kinetics of Formation of Substituted Mercaptopyrylium Salts¹

BY FRANCIS J. OZOG, VIVIANE COMTE AND L. CARROLL KING

RECEIVED JULY 17, 1952

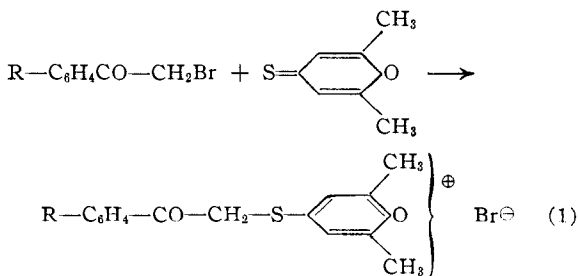
Substituted phenacyl bromides react with 2,6-dimethyl-4-thiopyrone to give pyrylium salts. In benzene or in acetone solution the reaction is first order with respect to each of the reacting species. The effect on the reaction rate of meta and para substituents in the phenacyl bromide was determined. These results can be described by the Hammett equation where ρ has the value 1.0 at 14.8° and 0.98 at 25.4°.

A recent paper from this Laboratory reported the reaction of 2,6-dimethyl-4-thiopyrone with active alkylating agents to give substituted mercaptopyrylium salts.² In the present paper the reactions of a number of substituted phenacyl bromides with 3,6-dimethyl-4-thiopyrone are reported. The results of the preparative experiments are summarized in Table I. The structures of the pyrylium salts described in Table I will be evident from a consideration of the method of preparation (equation 1). In each case the structure of the expected pyrylium salt was verified by analytical data.³

(1) Paper No. 102, Division of Organic Chemistry of the American Chemical Society, Chicago Meeting, September, 1950.

(2) L. C. King, F. J. Ozog and J. Moffat, *THIS JOURNAL*, **73**, 300 (1951).

(3) A further discussion of the structural assignment is given in reference 2.



The kinetics of the reaction between phenacyl bromide and 2,6-dimethyl-4-thiopyrone (DMTP) was studied in detail. Some typical results are given in Table II and in Figs. 1 and 2. The reaction is a second-order process. In benzene solution the second-order rate constants show a drift, becoming significantly smaller when the reaction is

TABLE I
PYRYLIUM SALT

Halide	Reaction time, hr.	Yield, %	M. p., °C. dec.	Formula	Carbon, %		Hydrogen, %	
					Calcd.	Found	Calcd.	Found
<i>p</i> -CH ₃ OC ₆ H ₄ COCH ₂ Br	1	92	195-196	C ₁₆ H ₁₇ BrO ₃ S	52.04	51.60	4.64	4.67
<i>p</i> -CH ₃ C ₆ H ₄ COCH ₂ Br	1	93	193-194	C ₁₆ H ₁₇ BrO ₂ S	54.40	53.76	4.85	4.78
β -C ₁₀ H ₇ COCH ₂ Br	1	97	210-211	C ₁₉ H ₁₇ BrO ₂ S	58.62	57.28	4.40	4.46
<i>p</i> -C ₆ H ₅ C ₆ H ₄ COCH ₂ Br	1	95	174-175	C ₂₁ H ₁₉ BrO ₂ S	60.72	61.97	4.61	5.06
<i>p</i> -BrC ₆ H ₄ COCH ₂ Br	1	99	198	C ₁₅ H ₁₄ Br ₂ O ₃ S	43.08	43.27	3.37	3.40
<i>p</i> -Cl-C ₆ H ₄ COCH ₂ Br	1	96	208-209	C ₁₅ H ₁₄ ClBrO ₃ S	48.21	48.69	3.78	4.09
<i>m</i> -Br-C ₆ H ₄ COCH ₂ Br	1	94	192-193	C ₁₅ H ₁₄ Br ₂ O ₃ S	43.08	43.01	3.37	3.26
<i>m</i> -NO ₂ C ₆ H ₄ COCH ₂ Br	1	96	149-150	C ₁₅ H ₁₄ BrNO ₄ S	46.89	46.57	3.67	4.15
<i>p</i> -NO ₂ C ₆ H ₄ COCH ₂ Br	1	96	171-172	C ₁₅ H ₁₄ BrNO ₄ S	46.89	47.43	3.67	3.98

TABLE II
T = 25.4°; solvent, benzene

<i>t</i> , sec.	Salt, g.	$k \times 10^4$ l mole ⁻¹ sec. ⁻¹
A. 25 cc. of 0.200 <i>M</i> 2,6-dimethyl-4-thiopyrone and 25 cc. of 0.200 <i>M</i> phenacyl bromide		
315	0.1038	20.7
990	.2777	19.8
3600	.6950	19.3
5280	.8413	18.7
7200	.9635	18.3
8100	1.0110	18.2
14400	1.2004	16.8
		Av. 18.8
B. 25 cc. of 0.100 <i>M</i> 2,6-dimethyl-4-thiopyrone and 25 cc. of 0.200 <i>M</i> phenacyl bromide		
610	0.0851	18.0
1815	.2198	17.8
3600	.3619	17.7
5400	.4562	17.0
10800	.6273	16.3
		Av. 17.4
C. 25 cc. of 0.200 <i>M</i> 2,6-dimethyl-4-thiopyrone and 25 cc. of 0.100 <i>M</i> phenacyl bromide		
300	0.0473	19.3
945	.1286	18.2
1830	.2361	19.3
3600	.3779	19.7
5400	.4732	18.2
		Av. 18.3

over 80% complete. This drift was less noticeable when excess DMTP was present in the reaction mixture. In acetone solution the deviation of the observed rate constants from the mean value was random.

The reaction between DMTP and a number of meta and para substituted phenacyl bromides was studied in benzene solution. In these cases the specific rate constants were determined by observing the rate at the half-reaction time assuming in each case that the reaction was second order. The rate constants obtained in this study are listed in Table III. The order of effectiveness of substituents in increasing the reaction rate is *p*-NO₂ > *m*-NO₂ > *m*-Br > *p*-Br > *p*-C₆H₅ > H > *p*-CH₃ > *p*-CH₃O-. This sequence shows that the reaction is favored by substituents in the benzene ring which tend to withdraw electrons from the ring, and it is in general agreement with the observations of

Baker⁴ in his study of the reaction of pyridine on substituted phenacyl bromides in acetone solution.

When the log of the rate constants obtained in this study are plotted against the σ function as listed by Hammett⁵ it is seen (Fig. 3) that essentially a straight line relationship exists. The reaction can then be described by means of the Hammett equation taking ρ as 1.00 for the measurements at 14.8° and 0.984 at 25.4°.

The kinetics of the reactions were studied at two temperatures, 25.4 and 14.8°, and the Arrhenius activation energy for each reaction was determined. Values for E_a are recorded in Table III. The entropy of activation was calculated using the Eyring equation⁶ and taking $\Delta H^\ddagger = E_a - RT$. The results of these calculations are given in Table III.

TABLE III				
R	$10^4 \times k^{25^\circ}$	$10^4 \times k^{15^\circ}$	ΔE_a	ΔS^\ddagger
a.—Solvent, benzene				
<i>p</i> -Anisyl	13.5	6.78	11.1	-36.4
<i>p</i> -Tolyl	16.3	7.80	11.8	-33.4
Phenyl	18.7	9.05	11.7	-33.8
β -Naphthyl	21.3	10.0	12.1	-32.2
4-Biphenyl	22.7	11.3	11.2	-35.1
<i>p</i> -Bromophenyl	30.8	15.2	11.3	-34.2
<i>p</i> -Chlorophenyl	31.6	15.8	11.1	-34.7
<i>m</i> -Bromophenyl	34.0	16.8	11.3	-34.0
<i>m</i> -Nitrophenyl	93.5	46.5	11.2	-32.3
<i>p</i> -Nitrophenyl	107	54.5	10.8	-33.4
b.—Solvent, acetone				
Phenyl	118	56.9	11.7	-30.3

The mean value of the activation energy E_a as calculated from Table III is 11.5 ± 0.4 kcal./mole. Since the deviation of any one value from the mean is probably within the limits of experi-

(4) J. W. Baker, *J. Chem. Soc.*, 445 (1948).(5) L. P. Hammett, *This Journal*, 59, 96 (1937); "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 186.(6) H. Eyring, *J. Chem. Phys.*, 3, 498 (1935).

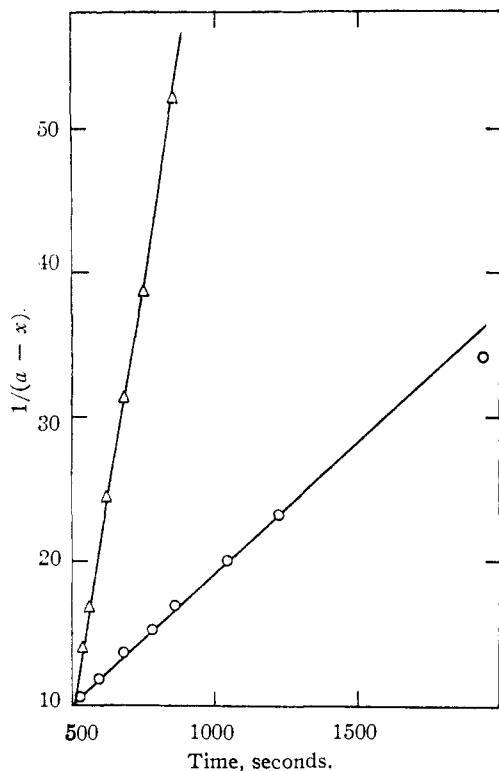


Fig. 1.—Upper curve, reaction of 0.100 *M* DMTP with 0.100 *M* phenacyl bromide at 25.4° in acetone solution; lower curve, reaction of 0.100 *M* DMTP with 0.100 *M* phenacyl bromide at 25.4° in benzene solution.

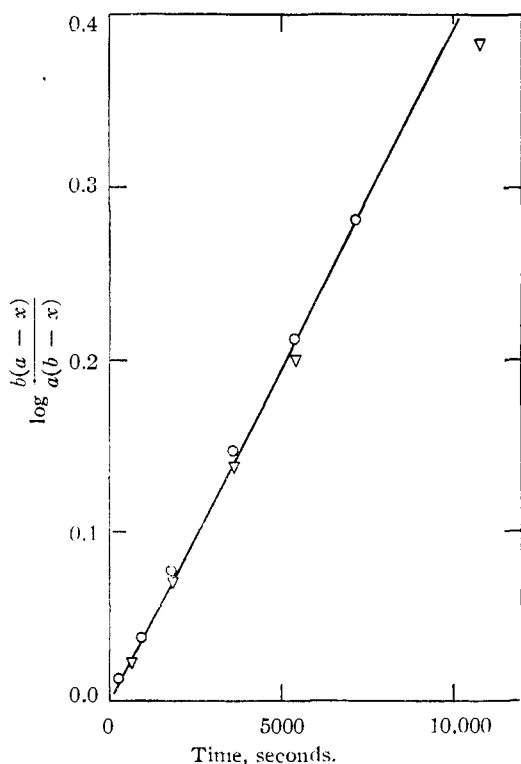


Fig. 2.—Circles, reaction of 0.05 *M* DMTP and 0.1 *M* phenacyl bromide at 25.4° in benzene solution; triangles ∇ , reaction of 0.1 *M* DMTP and 0.05 *M* phenacyl bromide at 25.4° in benzene solution.

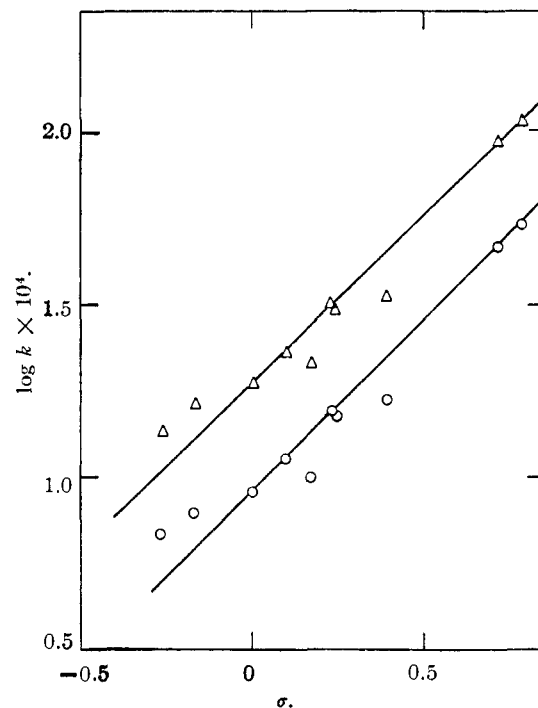


Fig. 3.—Upper line, reactions at 25.4°; lower line, reactions at 14.8°.

mental error, no conclusion can be drawn from a consideration of activation energy other than that the magnitude of the activation energy is the same general order as that for the reaction of phenacyl-type bromides with various nucleophilic reagents. Thus the activation energy for the reaction of pyridine with various types of phenacyl bromides in acetone was shown to be 11.6 ± 0.1 kcal./mole.⁴ The reaction of phenacyl bromide with thiourea in methanol is 10.5 kcal.⁷ The reaction of phenacyl bromide with aniline was measured in 12 different solvents by Cox,⁸ and the activation energy of these reactions calculated from the original data is 12 kcal.

The activation energy of the reaction between phenacyl bromide and DMTP in both benzene and acetone solution is 11.7 kcal./mole. The marked difference in the rate constants is due entirely to the entropy of activation.

Experimental

Reagents.—The phenacyl bromides were prepared by bromination of the corresponding ketone according to procedures in the literature. They were recrystallized from ethyl acetate-Skellysolve B and dried under vacuum prior to use.

Acetone was purified by means of the sodium iodide addition product.⁹ 2,6-Dimethyl-4-thiopyrone was prepared and purified as described in reference 2.

Preparation of Pirylium Salts.—These reactions all were carried out by refluxing a benzene solution of the appropriate phenacyl halide and DMTP for one hour in benzene solution. See Table I for results.

Kinetic Studies.—Stock solutions of the 2,6-dimethyl-4-thiopyrone (DMTP) and phenacyl bromide were made up 0.2000 molar by weight in the appropriate dry solvent at the operating temperature. At zero time 25.0 cc. of phenacyl bromide was pipetted to 25.0 cc. of DMTP in a glass-

(7) W. J. McGuire, M.S. Thesis, Northwestern University, 1949.

(8) H. E. Cox, *J. Chem. Soc.*, **119**, 149 (1921).

(9) K. Shipsey and E. A. Werner, *ibid.*, **103**, 1255 (1913).

stoppered 125-ml. erlenmeyer flask and the flask thoroughly swirled. Precipitation began within a minute. After the appropriate time elapsed, the mixture was filtered through a tared sintered glass funnel containing a layer of glass wool to aid in rapid filtration. The reaction flask and the precipitate were washed with 50 cc. of anhydrous benzene and 25 cc. of anhydrous ether, the last traces of the precipitate being removed from the flask during this operation. The funnel and salt were then dried at 50° under vacuum to constant weight and the amount of salt determined by weighing. Direct determination of the solubility of the salt in

each of the reactants showed it to be negligible in comparison to the total weight, when benzene was used. In acetone, however, the weight of the salt was corrected for the solubility (0.027 g./50 cc.).

In order to compare the rates of reaction of various substituted phenacyl bromides under approximately equivalent conditions three determinations at the half-reaction time were carried out for each substituent in benzene solution, assuming the reaction to be second order in each case.

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[CONTRIBUTION OF THE DEPARTMENT OF CHEMISTRY, CLARK UNIVERSITY]

Stability of Metal Chelates. IV. N,N'-Ethylenediaminediacetic Acid and N,N'-Ethylenediaminediacetic-N,N'-dipropionic Acid

BY S. CHABEREK, JR.,¹ AND A. E. MARTELL

RECEIVED MAY 28, 1952

Acid dissociation constants and chelate stability constants of N,N'-ethylenediaminediacetic acid and of ethylenediamine-N,N'-diacetic-N,N'-dipropionic acid are reported for Cu⁺², Ni⁺², Co⁺², Zn⁺², Pb⁺², Cd⁺² and Mg⁺² ions. The results are compared with the stabilities of the corresponding ethylenediaminetetraacetate chelates, and the relative values for these three chelating agents are interpreted in the light of the corresponding structural differences.

The sequestering properties of ethylenediaminetetraacetic acid have been well known for some time. Extensive equilibrium studies of this complexing agent with both alkaline earth and transition metal ions have been made by Schwarzenbach and co-workers,^{2,3} who found that this α -amino acid formed unusually strong complexes with these metal ions. Although there has been considerable speculation regarding the reasons for this unusually strong metal ion affinity, especially with the alkaline earth metals, very few additional quantitative data have been obtained. The ethylenediaminetetraacetate anion has been considered to supply from four to six donor groups to the metal ion, and various workers in this field have disagreed as to the probable structures of the corresponding chelates, the proposed formulas varying from tetradentate to hexadentate in nature. There is no doubt but that in the case of copper at least, the ligand possesses more coordinating groups than are actually required for complete chelation of the metal. This is not true of other first-row transition metals, however. No definite information is available regarding the function of the acetate groups and their effect upon the stability of the chelate.

In order to obtain additional information on the relation between ligand structure and chelation, metal stability constants of two amino acids related structurally to ethylenediaminetetraacetic acid have been measured. These are N,N'-ethylenediaminediacetic acid and N,N'-ethylenediaminediacetic-N,N'-dipropionic acid.

Both compounds retain at least a portion of the basic structure necessary for chelation, namely, two nitrogen atoms and two acetic acid groups, but differ in the additional substituents on the nitrogen atoms. It is interesting to note, also, that while

complex formation involving ethylenediaminetetraacetic acid results in the formation of five-membered chelate rings, chelation with the corresponding dipropionic-diacetic acid derivative can involve the formation of five-membered rings with the acetic acid groups or six-membered rings with the propionic acid groups. The effect of these substituents upon complex formation has not been determined previously.

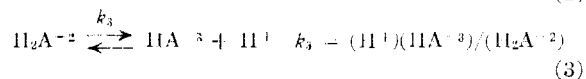
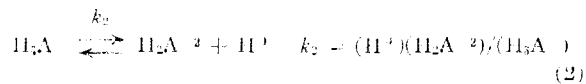
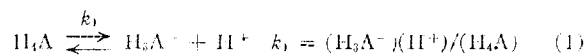
Experimental

The experimental method used in this investigation is the same as that described in detail in the first paper of this series.⁴ The N,N'-ethylenediaminediacetic-N,N'-dipropionic acid and N,N'-ethylenediaminediacetic acid were synthesized by a method to be described in a subsequent publication.⁵

Calculations.—The potentiometric titration data for N,N'-ethylenediaminediacetic acid and N,N'-ethylenediaminediacetic-N,N'-dipropionic acid in the presence and in the absence of an equivalent concentration of metal ion are given in graphic form in Figs. 1 and 2. It is apparent from these curves that both reagents produce 1:1 metal chelates, as in the case of ethylenediaminetetraacetic acid.

The acid dissociation constants of the symmetrical diacetic acid were calculated both by the algebraic and modified Bjerrum methods described previously.⁴ The stability constants were calculated by the algebraic method, only. The acid dissociation constants of N,N'-ethylenediaminediacetic-N,N'-dipropionic acid were calculated by the method of Schwarzenbach and Ackermann.^{2b}

The calculation of the metal stability constants for the ethylenediaminediaceticdipropionic acid was accomplished in the following way: The acid dissociation equilibria may be described by the relations.



(1) Bersworth Postdoctoral Fellow, Clark University.

(2) (a) G. Schwarzenbach and H. Ackermann, *Helv. Chim. Acta*, **30**, 1798 (1947); (b) G. Schwarzenbach and H. Ackermann, *ibid.*, **31**, 1029 (1948).

(3) G. Schwarzenbach and E. Freitag, *ibid.*, **34**, 1503 (1951).

(4) S. Chaberek, Jr., and A. E. Martell, *THIS JOURNAL*, **74**, 3052 (1952).

(5) S. Chaberek, Jr., F. C. Bersworth and A. E. Martell, unpublished results.