are involved. This is reasonable, since the positively charged dye ion would attract the negatively charged developer ion. The concentration of hydroquinone and catechol ion at *p*H 8 would be relatively low, since the *pK* values are 9.9 and 9.1, respectively, and it would be even lower at *p*H 6. However, ionization may be strongly promoted in the vicinity of positively charged adsorbed dye layer. Resorcinol, although its *pK* value is the same as that of catechol, shows much less mordanting effect at a given *p*H, which may be associated with a weaker adsorption.

The present results do not demonstrate unequivocally that hydroquinone and catechol are adsorbed by silver bromide in the absence of adsorbed dye, although such adsorption seems highly probable. The results are of special interest, however, in view of the accelerating effect which the dyes have on photographic development by hydroquinone and, to a smaller extent, catechol.

Other negatively charged ions which are adsorbed by silver bromide mordant the dyes. Thus, no dye is eluted by 0.001 *M* bromide solution. The mordanting effect of the thiosulfate and sulfite ions may stem from the same cause. It is probable that these ions are adsorbed by silver halide because of the complexes which they form with silver ions. Sulfate, which does not form a complex and which is not adsorbed by silver bromide to any significant extent, has little effect upon the rate of elution of the dyes. On the other hand, the positively charged silver ion promotes elution of the dyes.

The quaternary salt, lauryl pyridinium *p*-toluenesulfonate, shows unusual behavior in two ways. Its effectiveness in displacing the dyes increases with increasing *p*H, and the dependence of rate of displacement on the concentration of the solution is slight. It is possible that the latter effect is associated with the tendency of the quaternary salts to form colloidal micelles in more concentrated solution. The solvent action of the quaternary salt on the silver bromide apparently increases with *p*H, and this may be responsible for the more effective displacement of the dyes at the higher *p*H.

The comparison between benzimidazole and 6-nitrobenzimidazole given in Table VIII is of interest because benzimidazole is relatively ineffective as an antifoggant, while 6-nitrobenzimidazole is a good antifoggant in photographic developing solutions. At a given *p*H, the 6-nitro derivative is much more effective in displacing the dyes than is the parent substance. This indicates that 6-nitrobenzimidazole is more strongly adsorbed by the silver bromide than is benzimidazole itself. Solov'ev and Smirnova[3] reached the same conclusion on the basis of experiments carried out on simultaneous adsorption of 2-methylbenzimidazole and 3,3′-diethyl-9-methylthiacarbocyanine iodide by silver bromide and of 6-nitro-2-methylbenzimidazole and the dye by silver bromide. Their results indicate that the 6-nitro compound expelled the dye from the surface or prevented its adsorption, whereas the 2-methylbenzimidazole did not. They conclude that the stronger adsorption of the 6-nitro compound is an important factor in determining its antifogging activity.

The *p*H dependence of the displacement of dyes by benzimidazole contrasts sharply with that of the 6-nitro derivative. The effectiveness of the benzimidazole is much greater at *p*H 6 than at *p*H 3.5, whereas the effectiveness of the 6-nitro derivative is about the same at the two *p*H values. Both agents show some loss of effectiveness in going from *p*H 6 to *p*H 8.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Determination of Rho and Sigma Constants for Quinoline Carboxylic Acids and Their Methyl Esters[1]

BY ROBERT C. ELDERFIELD AND MALCOLM SIEGEL

The relative pK_a values for the seven quinoline monocarboxylic acids in 50% methanol have been determined. Alkaline hydrolysis rate constants for the methyl esters of the acids have been determined. From these data tentative values of ρ and σ for the quinoline compounds have been calculated.

A considerable fund of information concerning the effects of substituents on reactions of given groups in the benzene series is available.[2] On the basis of these data, it is possible to correlate such effects by a simple mathematical treatment, and to express the magnitude of such effects by unique constants. Thus a constant, σ, measures a change in electron density produced by a substituent, and a second constant, ρ, measures the susceptibility of the reaction in question to changes in electron density. In contrast to this situation in the benzene series, little or no information on similar effects in heterocyclic systems is at hand. In many of the heterocyclic nuclei, the problem is further complicated by the presence of hetero atoms which themselves are capable of producing changes in electron density. As a start on the major problem of providing such information for various heterocyclic systems, the quinoline carboxylic acids and their esters have been chosen for study with the hope that the results obtained might be of use in explaining and predicting the chemistry of the quinoline compounds. The present investigation has been confined to the determina-

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[1] The material presented herein is taken from a dissertation submitted by Malcolm Siegel in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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

tion of the acid dissociation constants of the acids and the hydrolysis rate constants of their esters in alkaline solution.

Dissociation constants for quinaldinic and cinchoninic acid were reported as long ago as 1889 by Ostwald.[3] Kindler[4] has measured the hydrolysis rates of the 2-, 3- and 4-carbethoxyquinolines. Steck and Ewing[5,6] have pointed out the similarities between amino- and hydroxypyridines and quinolines and the corresponding benzene and naphthalene derivatives. Albert[7] has measured the basicity of the aminoquinolines; Felsing and Biggs,[8] that of the methylquinolines; and Irvin and Irvin,[9] some substituted 4-aminoquinolines. Phillips and Merritt[10] have measured the acidity of some 8-hydroxyquinolines, as have Stone and Friedman.[11]

Discussion of Methods.—The very limited water solubility of the esters and of some of the quinoline carboxylic acids made necessary the use of a mixed alcohol–water solvent. Attempts to measure hydrolysis rates in aqueous ethanol solutions resulted in rate constants which diminished with time, indicating an ester interchange followed by the slower hydrolysis of the ethyl esters.[12] This difficulty was avoided by the use of an aqueous methanol solvent.

The bimolecular rate constants were then calculated from the equation

$$\frac{(a-b)}{2.303}kt = \log\frac{b}{a} - \log\left(\frac{b-a}{a-x}+1\right)$$

in which k is the rate constant, t is time in seconds, a is the initial concentration of alkali, b is the initial concentration of ester and x is the concentration of alkali and ester that have reacted at time, t. By plotting

$$-\log\left[\frac{(b-a)\times\text{vol. of the withdrawn aliquot}}{\text{milliequivs. of sodium hydroxide}}+1\right]$$

against time a linear curve of slope $k(a-b)/2.303$ was obtained from which k can be calculated. The t_0 value was neglected and the slopes of the curves were determined from nine experimental points by the method of least squares.

Because of the limited solubilities of the acids and the presence of a basic nitrogen atom, the relative dissociation constants of the quinoline acids were determined potentiometrically in 50% by volume methanol–water. An expression for the dissociation constant can be written

$$K_a = \frac{[\text{QCOO}^-][\text{HSH}^+]}{[\text{QCOOH}]} \times \frac{f_{\text{QCOO}^-}f_{\text{HSH}^+}}{f_{\text{QCOOH}}}$$

in which K_a is the thermodynamic acid dissociation constant, $[\text{HSH}^+]$ is the molar concentration of lyonium ion, $[\text{QCOO}^-]$ is the concentration of quinoline carboxylate ion, [QCOOH] the molar concentration of undissociated quinolinecarboxylic acid, and f the corresponding activity coefficient. The above equation may be rewritten as

$$pH = pK_a + \log\frac{[\text{QCOO}^-]}{[\text{QCOOH}]} + \log\frac{f_{\text{QCOO}^-}}{f_{\text{QCOOH}}}$$

Since all the acids at the same temperature, concentration, and in the same solvent would be expected to have very nearly the same ionic interaction term, the last term in the above equation may reasonably be neglected.

By neglecting the activity coefficient term, the above equation can be rewritten as

$$pK_a = pH - \log\frac{[\text{QCOO}^-]}{[\text{QCOOH}]}$$

$[\text{QCOO}^-]$ is determined by the number of moles of sodium hydroxide added. [QCOOH] is equal to the initial concentration of acid minus $[\text{QCOO}^-]$. In the calculation of pK_a it is unnecessary to correct for the volume of the added alkali since this correction will not alter the ratio $[\text{QCOO}^-]/[\text{COOH}]$. The pK_a values were determined by averaging the values of pK_a determined at 30, 40, 50, 60 and 70% neutralization.

Results.—In Table I there are sample data for the determination of the alkaline hydrolysis rate of one of the esters in 50% methanol at 25°.

TABLE I

SAMPLE DATA FOR ALKALINE HYDROLYSIS OF 6-CARBOMETHOXYQUINOLINE AT 25°

Initial concentration of ester 0.01014 M; initial concentration of sodium hydroxide 0.01778 M; 3 ml. of 0.03925 M HCl added to each aliquot

Time, sec.	Sodium hydroxide titer, 0.03703 M	$-\log\left[\frac{(b-a)\text{ volume of aliquot}}{\text{milliequiv. of NaOH in aliquot}}+1\right]$
94	1.19	0.256
330	1.39	.272
642	1.66	.296
1090	1.97	.332
1660	2.28	.379
2350	2.54	.429
3186	2.82	.503
4210	3.06	.595
5450	3.24	.692

In Table II are shown the average of two determinations of reaction rate constants for each ester, the per cent. of the reaction over which the plot was linear, and the fraction of the hydrolysis over which the reaction was observed.

TABLE II

ALKALINE HYDROLYSIS RATE CONSTANTS OF QUINOLINE ESTERS AT 25° IN 50% METHANOL

Ester	$k \times 10^3$, liters/mole/sec.	Completion of reaction, % At end of linear portion	Completion of reaction, % At removal of last aliquot
2-Carbomethoxyquinoline	298 ± 2	81	98
3-Carbomethoxyquinoline	74.7 ± 0.7	70	96
4-Carbomethoxyquinoline	177 ± 1	76	88
5-Carbomethoxyquinoline	18.6 ± 0.2	68	83
6-Carbomethoxyquinoline	24.2 ± 0.2	81	81
7-Carbomethoxyquinoline	28.0 ± 0.1	81	88
8-Carbomethoxyquinoline	3.90 ± 0.03	51	51
Methyl benzoate	4.63 ± 0.03	59	59

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(3) W. Ostwald, *Z. physik. Chem.*, **3**, 395 (1889).

(4) K. Kindler, *Ber.*, **69**, 2792 (1936).

(5) E. A. Steck and G. W. Ewing, THIS JOURNAL, **70**, 3397 (1948).

(6) G. W. Ewing and E. A. Steck, *ibid.*, **68**, 2181 (1946).

(7) A. Albert, *Nature*, **153**, 467 (1944).

(8) W. A. Felsing and B. S. Biggs, THIS JOURNAL, **55**, 3624 (1933).

(9) J. L. Irvin and E. M. Irvin, *ibid.*, **69**, 1091 (1947).

(10) J. P. Phillips and L. L. Merritt, Jr., *ibid.*, **70**, 410 (1948).

(11) K. G. Stone and L. Friedman, *ibid.*, **69**, 209 (1947).

(12) E. Anderson and H. B. Pierce, *J. Phys. Chem.*, **22**, 44 (1918).

In some runs the rate constants began to increase after 70–80% reaction. This may be due to absorption of atmospheric carbon dioxide while the earlier points were being taken.

Table III summarizes the pK_a data for the various acids.

TABLE III

RELATIVE pK_a VALUES OF THE QUINOLINE ACIDS IN 50% METHANOL AT 25°

Acid	Concn. in moles/liter $\times 10^3$	pK_a
Quinoline-2-carboxylic	2.158	4.96 ± 0.01
Quinoline-3-carboxylic	2.090	4.62 ± .02
Quinoline-4-carboxylic	2.115	4.53 ± .02
Quinoline-5-carboxylic	2.125	4.81 ± .02
Quinoline-6-carboxylic	2.062	4.98 ± .02
Quinoline-7-carboxylic	2.120	4.97 ± .02
Quinoline-8-carboxylic	2.109	7.20 ± .01
Benzoic	2.057	5.27 ± .01

It was noted in every titration that the pK_a calculated at 30% neutralization was 0.01 to 0.06 pK unit higher than pK_a calculated at 70% neutralization. This effect may be due to the increase in ionic strength as more ions are formed, to the error in neglecting the contribution of the inherent dissociation of QCOOH on [QCOO$^-$] at low percentages neutralization, or to the effect of hydrolysis of the salt on [QCOOH] as neutralization nears completion.

Discussion of Results.—Inspection of the values for the hydrolysis rate constants of the esters and of those for the relative ionization constants for the acids shows that the expected qualitative relationship between the two exists. Methyl esters of the strong acids hydrolyze more readily than do the methyl esters of the weak acids. That a quantitative relationship between these values should exist is not so obvious. Quinoline-5-, 6-, 7- and 8-carboxylic acids may be regarded as substituted benzoic acids in which the fused pyridine ring is considered as a substituent. In the quinoline-2-, 3- and 4-carboxylic acids, the fused benzene ring may be considered as one substituent, and the electron-attracting ring nitrogen as a second substituent. Hammett[2] has shown that linear relationships exist between equilibrium and rate constants for practically all side-chain reactions of benzene derivatives containing meta or para substituents. It should be emphasized that a condition for such linear relationships is that there be no significant change in entropy of activation. In the reactions presently under discussion available data do not permit a decision on this point. However, pending further information, accumulation of which is currently underway, it appears to be profitable to proceed on the assumption of such constancy of entropy. Likewise it should be pointed out that the assumption that the second fused ring involves no ortho effect may be subject to revision in the light of later data, particularly since no information is available on the analogous α-naphthyl compounds.

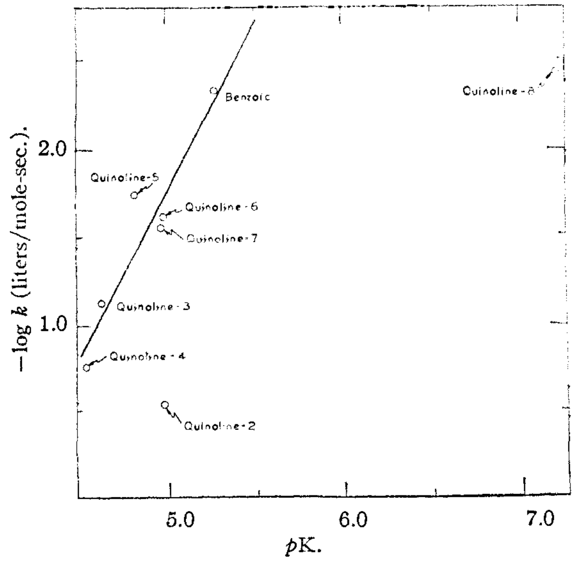

Fig. 1.—Relationship between pK of the quinolinecarboxylic acids and hydrolysis rate constants of their methyl esters at 25° in 50% methanol.

Despite the above assumptions, it is interesting that such a linear relationship exists between the ionization constants of the acids and the hydrolysis rate constants of the corresponding esters as shown in Fig. 1. In this plot of the negative logarithm of the ester hydrolysis rate against the pK_a of the corresponding acid, benzoic and the 3-, 4-, 6- and 7-quinolinecarboxylic acids lie well on the line determined by the method of least squares. The point corresponding to the 5-acid is slightly displaced and those representing the 2- and 8-acids are greatly displaced from this line. The slope of the line is 1.94 ± 0.09.

Subject to the above restrictions, the following expression may therefore be written relating the reaction constant, ρ, for the ester hydrolysis reaction and the ρ for the acid dissociation for those esters and acids the values for which fall reasonably well on the straight line of Fig. 4.

$$1.94 = \frac{\rho_{\text{ester hydrolysis}}}{\rho_{\text{acid dissociation}}}$$

A tentative value for $\rho_{\text{acid dissociation}}$ in 50% methanol of 1.25 may be assigned.[13] Substitution of this ρ value in the above equation gives a value for $\rho_{\text{ester hydrolysis}}$ of 2.42 ± 0.09.

It then becomes possible to calculate tentative substituent constant values, σ, for the quinoline series by use of the equation

$$\log k - \log k^0 = \rho\sigma$$

in which k is either an equilibrium or rate constant for the substituted benzene derivative and k^0 that for the unsubstituted benzene derivative. The value of ρ used was 1.25. The values of σ thus obtained are given in Table IV. For comparison the σ values for several benzene derivatives[14] are also given.

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[13] This value is based on data reported by Kilpatrick and Mears (THIS JOURNAL, **62**, 3051 (1940)) and by Roberts, McElhill and Armstrong, (*ibid.*, **71**, 2923 (1949)) and has been estimated by Dr. Ernest Grunwald of these laboratories. We are deeply indebted to Dr. Grunwald for permission to use his calculations which led to this value for ρ.

[14] Ref. 2, p. 188.

TABLE IV

σ FOR QUINOLINE DERIVATIVES AND SELECTED BENZENE DERIVATIVES

Position of the reacting group in quinoline	σ
2	0.74 ± 0.09
3	.52 ± .03
4	.59 ± .03
5	.37 ± .03
6	.23 ± .03
7	.24 ± .03
8	− .06 ± .09
Substituent in benzene	
m-NO_2	+0.71 ± 0.07
p-NO_2	+ .78 ± .08
p-Cl	+ .23 ± .05
m-Cl	+ .37 ± .05

The σ-value for quinoline-2-carboxylic acid was arrived at by introduction of a correction of the observed *pK* of this acid sufficient to bring the point corresponding to this acid in Fig. 1 onto the straight line, the slope of which is determined by six experimentally observed points. Similar treatment furnished the σ for the 8-acid. This is essentially Hammett's method for calculating σ's from a series of reactions for substituents for which *pK* is unknown.

The positive sign for $\rho_{\text{ester hydrolysis}}$ implies that the reaction is favored by low electron density. This is expected for a reaction the rate of which is determined by the approach of the negative hydroxyl ion. Unfortunately there are no data available for the alkaline hydrolysis rates under comparable conditions for the monosubstituted meta and para derivatives of benzoic acid. However, in Fig. 2 data from the literature[4] for the alkaline hydrolysis at 30° in ethanol of some meta and para derivatives of ethyl benzoate and the 2-, 3- and 4-carbethoxy derivatives of quinoline and pyridine has been plotted against σ. The σ values for the substituents of the monosubstituted benzene derivatives were obtained from Hammett,[15] the σ for the 3,5-dinitrobenzene derivative was obtained from the ionization constant reported by Kendall,[16] the σ for the quinolinecarboxylic acids from Table IV, and the σ for the pyridinecarboxylic acids from their reported dissociation constants in water.[17] The straight line so obtained has a slope of 2.55 ± 0.19 (by least squares) which compares favorably with the ρ of 2.50 ± 0.07 found by Hammett for the alkaline hydrolysis at 30° of benzoic esters in 87.83% ethanol. Two points are shown for quinoline-2-carboxylic acid methyl ester. The point which does not lie on the straight line uses a value for σ obtained from the *pK* data of Table III. The corrected point uses the σ of Table IV obtained as indicated above.

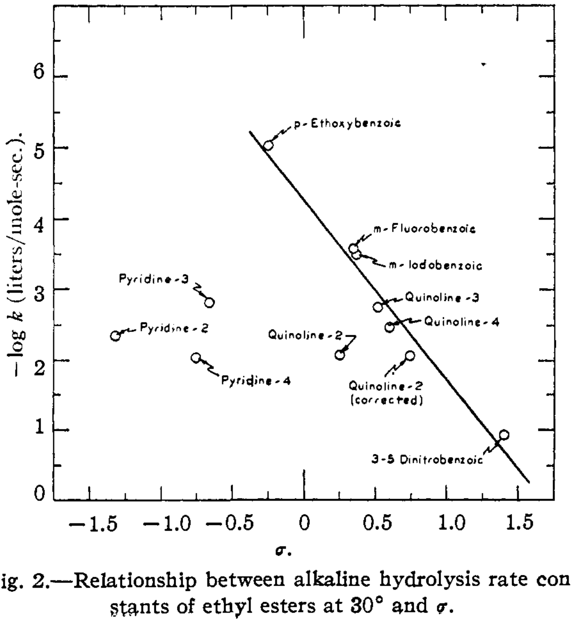
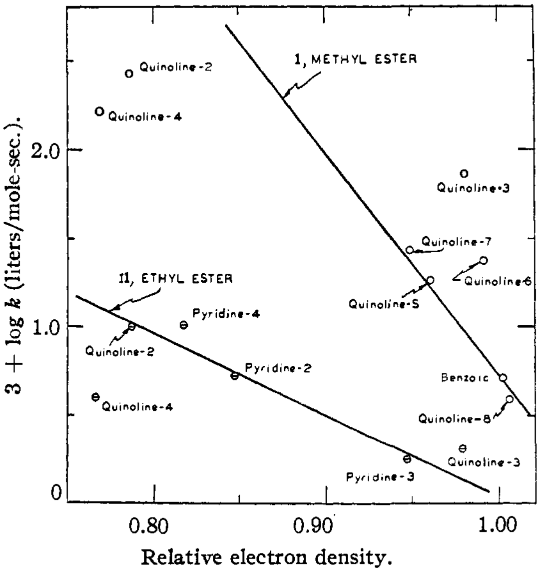


Fig. 2.—Relationship between alkaline hydrolysis rate constants of ethyl esters at 30° and σ.

The failure of picolinic, nicotinic and isonicotinic esters to fall on the straight line of Fig. 2 may be attributed to misleading apparent pK_a values obtained for the parent acids in aqueous solution. In such a solution with its high dielectric constant which is favorable to dipolar ion formation, these acids exist at least to a certain extent as zwitterions. The apparent weak acid dissociation results from the binding of the proton liberated by the carboxyl group to the basic ring nitrogen. The masking of the true acid strength, therefore, makes these pyridine acids appear weaker than benzoic acid and gives the substituent (the ring nitrogen) a negative value for σ. This is not in keeping with the electron attracting ability of the nitrogen which should make these acids stronger than benzoic acid. If, in Fig. 2, the positive values for σ obtained for the closely related quinoline-3- and quinoline-4-carboxylic acids are used for the pyridine compounds, then the points for nicotinic and isonicotinic acid fall on the straight line. Likewise, in Fig. 3 the pyridinecarboxylic esters fall on the linear plot of log of the hydrolysis rate



Relative electron density.

Fig. 3.—Relationship between hydrolysis rates of esters and relative electron density.

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[15] Ref. 2, p. 204.

[16] J. Kendall, *Medd. Vetenskapsakad. Nobelinst.*, **2**, No. 38 (1913).

[17] A. Kailan, *Monatsh.*, **28**, 705 (1907).

against calculated electron density. Therefore, we believe that the failure of the pyridine esters to fall on the straight line of Fig. 2 may be attributed to misleading apparent values for pK_a, rather than to a fallacy in treating the ring nitrogen as a substituent.

The fact that five of the quinolinecarboxylic acids lie on the linear plot of Fig. 1 suggests that measurement of the pK's in the solvent of lower dielectric constant (50% methanol) gives a true value for the acid dissociation constants. It is not surprising that the points representing the 2- and the 8-acids lie off this linear plot. It would be surprising if the same explanation which applied to the pyridine acids in water should also be applicable only to these two quinoline acids in 50% methanol. It appears more reasonable to explain the deviation of the observed points on the basis of hydrogen bonding between the carboxyl groups and the ring nitrogen. The 8-acid almost certainly would contain a strong hydrogen bond, whereas with the 2-acid such a hydrogen bond would be weaker. This is in accordance with the observed data which show a relatively greater deviation from the straight line of Fig. 1 for the 8-acid than for the 2-acid.

In Fig. 3 a plot of the log of the hydrolysis rates of the various esters against the π-electron density at the carbon atom bearing the substituent as calculated from molecular orbitals[18] by Longuet-Higgins and Coulson[19] is shown. In curve I the alkaline hydrolysis data of the methyl esters in 50% methanol, and in curve II the alkaline hydrolysis data of the ethyl esters in ethanol at 30° have been plotted. In view of the approximations involved in the calculation of the relative π-electron densities the extent of the agreement is surprising. In the case of quinoline-8-carboxylic acid, which fits the curve of Fig. 1 so poorly, the agreement is remarkable. The hydrogen bond, to which the weakness of the acid is due, is no longer present in the ester, and the rate of hydrolysis of the ester should depend on the electron density at the 8 carbon atom. This calculated density, 1.003, is very near the density on carbon in benzene, 1.00. Assuming that the carbomethoxy group in both quinoline and benzene exerts similar electron attracting effects, the hydrolysis rate of the quinoline-8 ester should be nearly identical with that of methyl benzoate if any ortho effect is neglected. This was observed experimentally. The low calculated electron densities at the 2- and 4-positions may result from the assumption of too large a resonance contribution in the calculations, and the high value at the 3-position from an underestimation of the inductive effect.

The high electron density at the 3-position is not in accord with the frequently observed failure of the usual electrophilic reagents to attack the quinoline ring at this position. Likewise, the high value for the 6-position (higher than that for 5) is not in accord with the commonly observed attack by electrophilic reagents at positions 5 and 8. However it must be emphasized that the values for electron density used above will be valid only in neutral or basic solution. Since reactions with electrophilic reagents are commonly carried out in acid media, the quinoline will exist as quinolinium ion with a resultant shift in the electron distribution about the molecule.

It can be seen from the data of Table IV that the azomethine linkage of quinoline exerts about 75% of the effect on a reacting group in the 3- or 4-position as is exerted by a nitro group meta or para, respectively, to the same reacting group in benzene. A group in the 5- or 6-position in quinoline is subject to electronic effects comparable to that produced by a chlorine meta to a reacting group in benzene.

Experimental[20,21]

I. **Preparation of the Quinoline Acids. A. Quinaldic Acid.**—Quinaldic acid (Eastman Kodak Company) was recrystallized from benzene to a constant m.p. of 156–157°; reported m.p. 156°.[22]

B. **Quinoline-3-carboxylic Acid.**—3-Bromoquinoline[23] was converted to 3-cyanoquinoline with cuprous cyanide,[24] and the cyanoquinoline was hydrolyzed to the acid.[24] The acid melted at 280–281° after recrystallization from 67% aqueous ethanol; reported m.p. 275°.[25]

C. **Quinoline-4-carboxylic Acid (Cinchoninic Acid).**—4-Styrylquinoline[26] was oxidized to cinchoninic acid with permanganate in acetone according to Campbell, *et al.*,[27] in 93% yield. Recrystallization from water gave the acid melting constantly at 256–257°; reported 253–254° (uncor.).[28]

D. **Quinoline-5-carboxylic Acid.**—This was prepared by the Skraup reaction from *m*-aminobenzoic acid according to Bradford, Elliott and Rowe.[29] The acid was recrystallized from acetic acid to a constant m.p. of 346–347° (uncor.); reported 342°.[29] No quinoline-7-carboxylic acid was isolated from this reaction.

E. **Quinoline-6-carboxylic Acid.**—6-Methylquinoline, prepared by the Skraup reaction from *p*-toluidine, was oxidized to quinoline-6-aldehyde with selenium dioxide according to the method of Rodionov and Berkengein[30] in 45% yield. Recrystallization from water gave material, m.p. 52–54°; reported 55°.[30]

An aqueous solution of 8.1 g. of quinoline-6-aldehyde in a 3-necked flask equipped with stirrer, thermometer and dropping funnel was heated to 70°. A solution of 11.4 g. of potassium permanganate in 120 ml. of water was added dropwise over 45 minutes. The temperature was maintained at 70–80° for an additional hour. After making the mixture alkaline with potassium hydroxide, it was filtered and the manganese dioxide was washed thoroughly with hot water. The combined filtrate and washings were acidified with acetic acid. The precipitated crude acid (6.9 g. or 78%) was recrystallized from ethanol to a constant m.p. of 294–296°; reported 290–291°.[31]

F. **Quinoline-7-carboxylic Acid.**—7-Methylquinoline, prepared according to Bradford, Elliott and Rowe,[29] was oxidized to quinoline-7-carboxylic acid with chromium trioxide by the method of Seibert, Norton, Benson and Bergstrom.[32] The acid was recrystallized from ethanol and then

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[18] C. A. Coulson, *Quarterly Revs.*, **1**, 144 (1947).

[19] H. C. Longuet-Higgins and C. A. Coulson, *Trans. Faraday Soc.*, **43**, 87 (1947).

[20] All melting points are corrected unless otherwise noted.

[21] Microanalyses by the Clark Microanalytical Laboratories, Urbana, Illinois.

[22] O. Doebner and W. von Miller, *Ber.*, **16**, 2472 (1883).

[23] Edinger, *J. prakt. Chem.*, [2] **54**, 357 (1896).

[24] Gilman and Spatz, THIS JOURNAL, **63**, 1553 (1941).

[25] W. H. Mills and W. H. Watson, *J. Chem. Soc.*, **97**, 745 (1910).

[26] A. D. Ainley and H. King, *Proc. Roy. Soc.* (*London*), **B125**, 60 (1938).

[27] K. N. Campbell, *et al.*, *J. Org. Chem.*, **11**, 803 (1946).

[28] Z. D. Skraup, *Ann.*, **201**, 302 (1880).

[29] L. Bradford, T. J. Elliott and F. M. Rowe, *J. Chem. Soc.*, 437 (1947).

[30] V. M. Rodionov and M. A. Berkengein, *J. Gen. Chem.* (*U. S. S. R.*), **14**, 330 (1944) [*C. A.*, **39**, 4076 (1945)].

[31] A. Schlosser and Z. D. Skraup, *Monatsh.*, **2**, 526 (1881).

[32] R. A. Seibert, T. B. Norton, A. A. Benson and F. W. Bergstrom, THIS JOURNAL, **68**, 2721 (1946),

TABLE V

QUINOLINE CARBOXYLIC ACID METHYL ESTERS

Position of $COOCH_3$	M.p., °C.	Lit. m.p., °C.	Solvent for crystallization	Refractive index ±0.0001	B.p.,	
					°C.	Mm.
2	86–87	85[a]	Hexane			
3	73.5–74.5	73–74[b]	Hexane			
4	25	24[c]		$n^{27.5}D$ 1.6025	88–94	0.1
5	52–53	[d]	Water		105–110	.2
6	86–87	[e]	Alcohol–water			
7	73.5–74.5	[f]	Water			
8		[g]		$n^{25}D$ 1.6019	128–132	0.2[h]

[a] E. Besthorn and J. Ibele, *Ber.*, **39**, 2332 (1906). [b] F. C. Uhle and W. A. Jacobs, *J. Org. Chem.*, 10, 76 (1945). [c] H. Meyer, *Monatsh.*, **22**, 115 (1901). [d] New compound. *Anal.* Calcd. for $C_{11}H_9NO_2$: C, 70.6; H, 4.8; N, 7.5. Found: C, 70.5; H, 4.5; N, 7.7. The picrate from ethanol melted at 198–199°. *Anal.* Calcd. for $C_{17}H_{12}N_4O_9$: C, 49.0; H, 2.9. Found: C, 48.7; H, 3.0. [e] New compound. *Anal.* Found: C, 70.5; H, 4.6; N, 7.5. The picrate from ethyl acetate melted at 217–218°. *Anal.* Found: C, 48.9; H, 2.7. [f] New compound. *Anal.* Found: C, 70.6; H, 4.7; N, 7.6. The picrate from ethanol melted at 214–215°. *Anal.* Found: C, 49.0; H, 2.9. [g] New compound. *Anal.* C, 70.6; H, 5.0; N, 7.9. The picrate from ethanol melted at 166–167°. *Anal.* Found: C, 48.9; H, 2.8. [h] When distilled at 0.2 mm. the refractive index varied irregularly on redistillation. The ester was therefore distilled in a molecular still to constant refractive index.

from water to a constant m.p. of 256–257°; reported 252–254°.[32]

G. Quinoline-8-carboxylic Acid.—8-Methylquinoline was prepared by a modification of the method of Bradford, Elliott and Rowe.[29] A mixture of 60 g. of *o*-toluidine, 100 g. of glycerol, 154 g. of sodium *m*-nitrobenzenesulfonate and 400 ml. of 80% sulfuric acid was refluxed for three hours with stirring. The dark solution was diluted with 400 ml. of water and 50 g. of sodium nitrite was added. The solution was made alkaline with saturated sodium hydroxide solution and steam distilled. The distillate was extracted with ether and, after removal of the ether, yielded 56.5 g. (71%) of 8-methylquinoline, b.p. 131–137° (25 mm.).

8-Methylquinoline was oxidized to the aldehyde as was done in the case of quinoline-6-aldehyde. Quinoline-8-aldehyde melted at 95–96° after recrystallization from water; reported m.p. 94–95°.[30]

Quinoline-8-carboxylic acid, prepared in 72% yield by oxidation of the aldehyde as with quinoline-6-carboxylic acid melted at 187° after recrystallization from water; reported 187°.[33]

II. Preparation of the Quinoline Methyl Esters.—The methyl esters were prepared by adding 10% excess of a redistilled ethereal solution of diazomethane to a suspension of the appropriate acid in ether at 0 to −10°. With the exception of quinaldic acid the methylation proceeded so slowly that it was necessary to allow the reactants to stand overnight for completion of the reaction. Distillation of the ether left a dark or highly colored residue in every case. The crude esters were purified by recrystallization with Norite in the cases of the solid ones and by distillation to constant refractive index in the cases of the liquid ones. The properties of the esters thus obtained are summarized in Table V.

Solvents and Solutions.—The solvent used in all measurements was prepared by mixing at 25° equal volumes of methanol (distilled over potassium hydroxide) and carbon dioxide free water. Aqueous and methyl alcoholic sodium hydroxide solutions were prepared by dilution of a clear saturated sodium hydroxide solution with the appropriate solvent. The alkaline solutions were standardized against Bureau of Standards potassium acid phthalate.

Dissociation Constants.—All measurements were made in a water-bath maintained at 25.00 ± 0.02°. The titrations of 100-ml. solutions approximately 0.002 *M* in quinoline carboxylic acid were carried out in open beakers immersed in the water-bath. Standardized alcoholic alkali solution was added in small increments from a 5-ml. microburet (graduated in 0.01 ml.) suspended over the bath. Agitation was provided by a motor-driven paddle stirrer. The *p*H was measured with an external glass electrode connected to a model G Beckman *p*H meter. Before each potentiometric titration the *p*H meter was balanced against a standard buffer, *p*H 7.00, then checked against a 0.0500 *M* solution of potassium acid phthalate, *p*H 4.00.[34] In no case did the *p*H measurement of the standard phthalate buffer shift by more than 0.02 unit during the time required for titration.

In the measurements up to 70% neutralization the acidity of the solution was great enough and the titration rapid enough to avoid the pick-up of sufficient carbon dioxide from the air to cause drifting in the *p*H.

In the case of the quinoline-5-carboxylic acid, solution of sufficient acid to prepare a 0.002 *M* solution could not be effected. However, solution of the acid in a calculated amount of sodium hydroxide followed by titration with hydrochloric acid provided a satisfactorily reproducible method for determining pK_a. It is not believed that this titration was performed under non-equilibrium conditions since no visible precipitate nor turbidity was observed in any partially acidified solution of the sodium salt of quinoline-5-carboxylic acid at 25°.

Hydrolysis Rates.—The reaction flasks were 250-ml. guttered iodine flasks. Rapidly draining calibrated pipets were used for the addition of solvents or solutions of reactants and for the removal of aliquots.

A 50-ml. freshly prepared solution (approximately 0.02 *M*) of the ester was placed in the reaction flask and brought to temperature equilibrium with the bath. An equal volume of approximately 0.04 *M* sodium hydroxide was added rapidly and with swirling to the reaction flask. The time at half-addition of the alcoholic alkali was taken as t_0. At varying time, depending on the rate of reaction as determined by preliminary runs, 10-ml. aliquots were removed and placed in a flask containing a sufficient and known amount of acid to neutralize all the alkali and effectively stop the hydrolysis. Excess acid was titrated with standard alkali to the phenolphthalein end-point.

That no significant acid hydrolysis of the esters occurred during the short time the samples awaited back titration in acid solution was shown with the ester of quinoline-4-carboxylic acid. The extent of acid hydrolysis was negligible in 30 minutes which is the maximum time any ester stood in acid solution awaiting back titration. It is safe to assume from this that the same will hold with the other esters since this reaction is relatively insensitive to the nature of the substituent[35] and must therefore exhibit a low value for ρ.[36]

Errors.—There is a constant error in each *p*H measurement which is due to the junction potential between the saturated calomel electrode and the aqueous methanol solvent.[37] No effort has been made to correct the *pK* for this potential since σ is the difference between two *pK* values each containing the same constant error. The precision of measurement of the *pK* is 0.02, and that of σ is therefore 0.03. The precision of measurement of ρ is the medium deviation of the points from the best straight line and is 0.09 for Fig. 4 and 0.19 for Fig. 5. The deviations for σ in the quinoline series of Table IV are precision measurements

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[33] E. Lellman and H. Reusch, *Ber.*, **22**, 1391 (1889).

[34] D. A. MacInnes, D. Belcher and T. Shedlovsky, THIS JOURNAL, **60**, 1094 (1938).

[35] E. Tommila and C. N. Hinshelwood, *J. Chem. Soc.*, 1801 (1938).

[36] Ref. 2, p. 189.

[37] J. C. Speakman, *J. Chem. Soc.*, 270 (1943).

for one reaction only, whereas the benzene data in Table V represent the median value of σ calculated from a number of different reactions.

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

Application of Absolute Reaction Rate Theory to the Racemization of Certain Sterically Hindered Compounds[1]

BY F. WM. CAGLE, JR., AND HENRY EYRING

The racemization of certain sterically hindered biphenyls and related compounds has been investigated by the use of the absolute reaction rate theory. It is possible to correlate structure and the observed values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ calculated from rate data. An approximate calculation of the resonance energy of biphenyl due to π bonding between the rings gives 5,000 cal./g. mole.

Introduction

The optical activity which may arise from steric hindrance introduced by the substitution of the O–O′-positions in biphenyls and related compounds was discovered by Christie and Kenner in 1922.[2] Since that date, the kinetics involved in the racemization of these compounds have received considerable study especially by Adams and his students. These studies have been made by the use of the familiar Arrhenius equation

$$\ln k' = \ln A - \frac{E}{RT}$$

The purpose of this paper is the application of the Absolute Reaction Rate Theory to the investigation of available data. This is done to permit an examination of the nature of the activated complex in the process of racemization. In this way, it is possible to study the relation between structure and reaction rate. These unimolecular racemizations provide information which may be interpreted in terms of a relatively very simple activated complex.

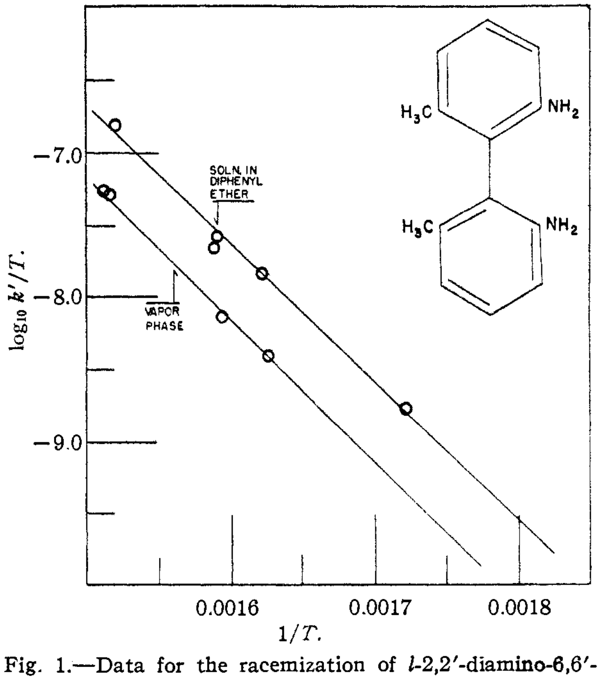

Fig. 1.—Data for the racemization of *l*-2,2′-diamino-6,6′-dimethyldiphenyl.

Theoretical Treatment

Consider the racemization of an optical antipode

$$d \underset{k'}{\overset{k'}{\rightleftarrows}} l$$

This is a reversible first order reaction with the same rate constant, k', in both directions. This constant may be expressed in terms of the measured optical rotation of a solution, α_t, at time, t, as

$$k' = \frac{1}{2t} \ln \alpha_0/\alpha_t$$

The theory of absolute reaction rates may be expressed as[3]

$$k' = \frac{\kappa k T}{h} \exp\left(-\frac{\Delta H^{\ddagger}}{RT}\right) \exp\left(\frac{\Delta S^{\ddagger}}{R}\right)$$

In the equation, k' is the rate constant; k, Boltzmann's constant; h, Planck's constant; T, absolute temperature; κ, the transmission coefficient; $\Delta H^{\ddagger}$ the enthalpy of activation; $\Delta S,^{\ddagger}$ the entropy of activation; and R, the gas constant. If one makes the usual assumption that the transmission coefficient is unity, the absolute rate equation may be written

$$\log_{10} \frac{k'}{T} = 10.319 - \frac{1}{T}\left(\frac{\Delta H^{\ddagger}}{4.574}\right) - \left(\frac{\Delta S^{\ddagger}}{4.574}\right)$$

From this it is seen that the linear plot of $\log_{10} k'/T$ *versus* $1/T$ will have as its slope $-\Delta H^{\ddagger}/4.574$ and that $\Delta S^{\ddagger}$ may be evaluated from the same data.

The Gibb's free energy of activation may be calculated since $\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$.

Discussion

Figure 1 is a plot of the experimental data of Kistiakowsky and Smith[4] for the racemization of the *l*-antipode of 2,2′-diamino-6,6′-dimethyldiphenyl both in the vapor phase and in solution in diphenyl ether. From this graph $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ may be determined.

In Table I values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the racemization of optically active antipodes of various compounds are given. The sources of the experimental

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(1) This paper was presented before the Physical and Inorganic Division of The American Chemical Society, Cleveland, Ohio, March, 1951.

(2) G. H. Christie and J. Kenner, *J. Chem. Soc.*, 614 (1922).

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

(4) G. B. Kistiakowsky and W. R. Smith, THIS JOURNAL, **58**, 1043 (1936).