In discussing these results let us first consider the proton transfer rate constants found in Table I (k_{34} and k_{43}). It is evident that the faster rate constant for a given system is identical for ATP and ADP within experimental error. At first glance, this appears to be somewhat unexpected since the charges on ATP, ADP and the indicators are such that proton transfers involving ADP should be faster than those for ATP. However, the ionic strength effect partially cancels out the difference in charge between ATP and ADP.[6]

It now appears that proton transfer reactions, although fast,[7,8] are not always diffusion controlled even if the equilibrium favors the transfer in that direction. From these studies the difference between the donor and acceptor pK's (log k_{43}/k_{34}) seems to be important.

As expected, the metal ions react faster with ATP than ADP. The magnitude of the differences found is just about what would be estimated from elementary electrostatic considerations. The ionic strength effect of KNO_3 would not be of great importance here since the doubly positive Mg^{++} or Ca^{++} would undoubtedly dislodge any weakly bound potassium ion upon reaching the vicinity of the ATP molecule. Since the rate controlling step of complete complex formation is the substitution of a water molecule from the complex initially formed by the metal and ligand,[8] the charge of the partners after formation of the initial complex should be decisive.

From these studies of ATP and ADP, it is clear that although the equilibrium constants for Ca^{++} and Mg^{++} complex formation (k_{31}/k_{13} and k_{42}/k_{24}) do not differ greatly, the kinetics of the two ions differ by at least two orders of magnitude. This is a general property of the two metal ions[8] and may be of significance in explaining why the two metals differ greatly as enzymatic activators (*cf.* also ref. 1). This problem will be discussed in more detail in a forthcoming publication.[9]

We are indebted to the National Science Foundation for granting a postdoctoral Fellowship to G.G.H. during the tenure of which this work was done.

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(7) A. Weller, *Z. Elektrochem.*, **64**, 55 (1960).

(8) M. Eigen, *ibid.*, **64**, 115 (1960).

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THE INFLUENCE OF STERIC FACTORS IN FAST PROTOLYTIC REACTIONS AS STUDIED WITH HF, H_2S AND SUBSTITUTED PHENOLS

Sir:

The development of relaxation spectrometry has led to the study of a wide variety of diffusion controlled protolytic reactions. The rate constants associated with these very rapid recombinations which are of the order of 10^{10} to 10^{11} M^{-1} sec.$^{-1}$ can be represented by a formula derived by Debye[1]

$$k_R = \frac{4\pi N_A\,(z_+ z_- e_0^2)(u_+ + u_-)}{\epsilon[\exp(z_+ z_- e_0^2/\epsilon a k T) - 1]} \tag{1}$$

where N_A is Avogadro's number, $z_\pm$ the ionic valence, e_0 the elementary charge, $u_\pm$ the ionic mobilities ($u_i = D_i/kT$; D_i = diffusion coefficient of ion i) ϵ the dielectric constant, "a" an effective reaction distance, k Boltzmann's constant, and T the absolute temperature. At ionic concentrations less than $\sim 10^{-3}$ M the applicability of this equation is limited only by the fact that the dielectric constant depends upon the effective reaction distance a, and that steric factors may restrict the total number of possible approaches for successful encounters. It has been shown previously[2] that for most of these reactions the effective reaction distance is large enough (two to three hydrogen bonds, *i.e.*, approximately 7.5 Å.) to permit the use of the macroscopic dielectric constant. This investigation has been undertaken to demonstrate the influence of steric factors on the rate of diffusion controlled reactions. HF and H_2S have been chosen because of the simple structure of the anions.

The experiments were performed by using the dissociation field method.[3] The principle of this method is the perturbation of a system at chemical equilibrium by rapidly changing the electric field density (up to 10^5 kv./cm.). The measured increase in conductance under the application of high fields (and Wien effect) is a (known) function of the impulse duration due to relaxation. From the dispersion of the amplitude of the conductivity change in sinusoidal pulses the relaxation time necessary for the reattainment of equilibrium can be determined and related to the rate constants of the chemical reactions of the system.[4] Detailed descriptions of the 2nd Wien effect[5,6] and experimental procedures[3,4] may be found elsewhere.

For these investigations the H_2S was prepared from reagent grade FeS and HCl.[7] Similarly, reagent grade HF was used, and measurements were carried out in a glass vessel lined with pure paraffin wax. All measurements were done at 25° and at essentially zero ionic strength.

The reactions studied are

$$H^+ + HS^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} H_2S \tag{I}$$

$$H^+ + F^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} HF \tag{II}$$

where k_R has the same meaning as in equation (1), and k_D is the dissociation rate constant. The relaxation time is given by[3]

$$\tau = [k_D + k_R(C_+ + C_-)]^{-1} \tag{2}$$

Since the equilibrium constants are known,[8,9] both rate constants may be determined. The rate constants obtained are:

(1) P. Debye, *Trans. Electrochem. Soc.*, **82**, 265 (1942).

(2) M. Eigen and L. De Maeyer, *Proc. Roy. Soc.*, **A247**, 505 (1958).

(3) M. Eigen and J. Schoen, *Z. Elektrochem.*, **59**, 483 (1955).

(4) (a) M. Eigen, *ibid.*, **64**, 115 (1960); (b) L. De Maeyer, *ibid.*, **64** 65 (1960).

(5) M. Wien and J. Schiele, *Z. Physik*, **32**, 545 (1931).

(6) L. Onsager, *J. Chem. Phys.*, **2**, 599 (1934).

(7) "Handbuch der Praeparativen Anorganischen Chemie," Georg Bauer, Ferdinand Enke Verlag, Stuttgart, 1960, p. 313.

(8) Lange's "Handbook of Chemistry," Ninth Edition, p. 1198.

(9) H. H. Broene and T. De Vries, *J. Am. Chem. Soc.*, **69**, 1644 (1947).

	k_R (M^{-1} sec.$^{-1}$)	k_D (sec.$^{-1}$)
H_2S	7.5×10^{10}	4.3×10^{3} (±15%)
HF	$\sim 1.0 \times 10^{11}$	$\sim 6.7 \times 10^{7}$

For HF no essential dispersion was found. As a result, the value given above represents a lower limit, which is, however, almost identical with the upper limit required by equation (1).

To examine these rate constants in the light of steric effects we make a comparison with the rate constant of the neutralization reaction

$$H^+ + OH^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} H_2O \qquad \text{(III)}$$

for which $k_R = 1.3 \times 10^{11}$ M^{-1} sec.$^{-1}$.[10] This value of k_R may be calculated from equation (1) with the macroscopic dielectric constant of 78.5 and an effective reaction distance a of 7.5 Å.[2]

Because of the uniquely high mobility of hydrogen and hydroxyl ions, $[k_R]_{H_2O}$ may be considered an upper limit for diffusion controlled bimolecular rate constants of this charge type. The steric factor is unity, since the hydrogen and hydroxyl ions are always correctly oriented when diffusing toward each other. For the spherical fluoride ion the ratio of rate constants for reactions (II) and (III) is given by the ratio of the ionic mobilities provided the effective reaction distance remains the same. A value of $[k_R]_{HF} = 9.6 \times 10^{10}$ M^{-1} sec.$^{-1}$ results. Since the dissociation field effect showed essentially no dispersion, we find that a value of about 1.0×10^{11} M^{-1} sec.$^{-1}$, with an effective reaction distance of 2–3 hydrogen bonds, represents a reasonable rate constant for this system.

The bisulfide ion, in contrast to the fluoride ion, should show a steric effect. When the hydrated proton and bisulfide ion approach with the hydrogen end of the bisulfide ion directed toward the $(H_9O_4)^+$ complex an unfavorable orientation occurs. From a consideration of the molecular structure of the bisulfide ion it is estimated that the solid angle corresponding to unreactive collision paths decreases the number of successful encounters by about 25%. Thus, we may estimate $[k_R]_{H_2S} = 7.5 \times 10^{10}$ k^{-1} sec.$^{-1}$, which is in excellent agreement with the measured value.

Steric restrictions are still more pronounced when the reacting group represents only a small residue of a larger molecule as is often the case for organic anions. Two examples will be discussed in the following, namely, *p*- and *m*-nitrophenol, which in addition seem to show another small restrictive influence resulting from charge delocalization in a structure exhibiting resonance.

The measurements were carried out using Riedel De Haen *p*-nitrophenol (m.p. 114°) and E. Merck *m*-nitrophenol. The latter was washed repeatedly and recrystallized from water until the m.p. was 96°. All measurements were made at 25° and essentially zero ionic strength. The reactions studied are:

$$H^+ + O_2NC_6H_4O^- \underset{k_D}{\overset{k_R}{\rightleftarrows}} O_2NC_6H_4OH \qquad \text{(IV)}$$

for the *meta* and *para* isomers. Since the equilibrium constants are known[11] both rate constants may be determined. The results are:

	k_R (M^{-1} sec.$^{-1}$)	k_D (sec.$^{-1}$)
m-Nitrophenol	4.2×10^{10}	1.9×10^{2} (±15%)
p-Nitrophenol	3.6×10^{10}	2.6×10^{3} (±15%)

A comparison of k_R with equation (1) yields a steric factor of about 0.5 for both phenols. Weller[12] found a similar value for the corresponding reaction of β-naphthol (in the excited state) from fluorescence transformation measurements ($k_R = 4.8 \times 10^{10}$ M^{-1} sec.$^{-1}$). The greater localization of charge on the *m*-phenolate oxygen may enhance somewhat the diffusion controlled rate of recombination with respect to the *para*-isomer. The same effect also is expressed in the entropy of ionization,[13] where it indicates that water molecules are more effectively oriented by the *m*-phenolate oxygen. However, the present accuracy of the measurements is not yet great enough to permit one to draw such detailed conclusions with safety.

We are indebted to the National Cancer Institute, United States Public Health Service, for granting a Postdoctoral Fellowship to K. K. during the tenure of which this work was done.

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[10] M. Eigen and L. De Maeyer, *Z. Elektrochem.*, **59**, 986 (1955).

[11] C. M. Judson and M. K. Kilpatrick, *J. Am. Chem. Soc.*, **71**, 3110 (1949).

[12] A. Weller, *Z. physik. Chem.*, NF., **17**, 224 (1958).

[13] L. P. Fernandez and L. G. Hepler, *J. Am. Chem. Soc.*, **81**, 1783 (1959). We are indebted to Prof. H. Morawetz for calling our attention to this article.

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OPTICAL ROTATORY DISPERSION STUDIES. XLIV.[1] ANOMALOUS ROTATORY DISPERSION CURVES OF OLEFIN DERIVATIVES. OSMATE ESTERS[2]

Sir:

We have pointed out already[1,3] that the most effective way of extending the scope of anomalous rotatory dispersion applications—which have proved so useful[3] with optically active chromophores such as the carbonyl group—is to convert a "non-chromophoric" functional group into a "chromophoric" derivative. Some successful approaches in converting amino, hydroxyl, and carboxylic acid functions into such derivatives have already been recorded,[1,3,4] but one of the most severe challenges, namely, how to secure Cotton effect curves among mono-unsaturated olefins, has not yet been met. Indeed, the spectroscopic properties of such olefins preclude with the presently available instruments direct measurement of any Cotton effect that may be associated with their absorption maximum below 200 mμ. Nevertheless,

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[1] Paper XLIII, C. Djerassi and K. Undheim, THIS JOURNAL, **82**, 5755 (1960).

[2] Supported by grant No. CRTY-5061 from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service, and by the National Science Foundation.

[3] C. Djerassi, *Rec. Chem. Progress*, **20**, 140 (1959); C. Djerassi, "Optical Rotatory Dispersion: Applications to Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1960, Chapter 15.

[4] B. Sjöberg, A. Fredga and C. Djerassi, THIS JOURNAL, **81**, 5002 (1959).