$1/T_1$ is the weighted average of $1/T_1$ in the coordination shell and in bulk water.[30] If we assume that $1/T_{1,\text{bulk}}$ in bulk water varies as η/η_0, then $1/T_{1,\text{cs}}$ in the coordination shell can be deduced from

$$\eta_0/\eta T_1 = (1 - p)/T_{1.\text{bulk}} + p/T_{1.\text{cs}} \qquad (34)$$

The fit of eq 34 is satisfactory, and $1/T_{1.\text{cs}} = 6.0 \pm 0.3 \text{ sec}^{-1}$.

$1/T_{1.\text{cs}}$ can provide a rough measure of the radius of the rotating

hydrated aluminum ion, on the following basis. In diffusion, the radius of hydrated aluminum ion is larger than that of $Al(OH_2)_6{}^{3+}$. If we assume, therefore, that water molecules adjacent to $Al(OH_2)_6{}^{3+}$ are "irrotationally" bound,[23] then proton spin relaxation in $Al(OH_2)_6{}^{3+}$ is due to fluctuations of the magnetic field resulting from rotation of the hydrated ion. On applying the model of a sphere in a viscous fluid, proposed by Bloembergen, Purcell, and Pound,[31] we calculate the radius of the rotating sphere to be 5.05 Å.

(30) Z. Luz and S. Meiboom, *J. Chem. Phys.*, 40, 2686 (1964).
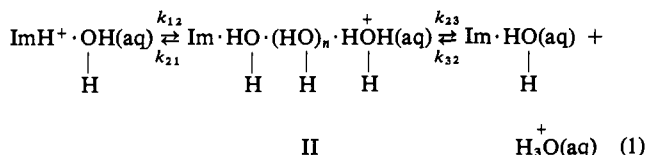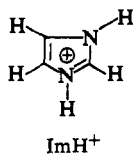
(31) Reference 8, p 202.

Kinetics of Proton Exchange in the Ionization and Acid Dissociation of Imidazole in Aqueous Acid[1]

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Abstract: Rates of proton exchange of imidazolium ion (ImH$^+$) have been measured in aqueous acid by the nmr method over a wide range of conditions. The rate law is unusually complex. A comparison of rates of proton exchange with rates of relaxation subsequent to temperature jump shows that acid dissociation of the imidazolium ion occurs in two distinct steps, ionization and dissociation. The immediate product of ionization (II, see text) makes a contribution to the rate of proton exchange by the breaking of the Im·HOH hydrogen bond. Dissociation of this ionized intermediate appears to be distinctly slower than 10^{11} sec^{-1}. Criteria for the general detection of ionized intermediates are discussed.

The acid dissociation of a Brønsted acid is usefully discussed as involving two distinct steps, ionization and dissociation, as illustrated for imidazolium ion (ImH$^+$) in water in eq 1. The current view is that for a weak acid the rate constant for the reversal of the ionization step (k_{21} in eq 1) is extremely high, while the rate of dissociation is limited by the rate of diffusion.[2-4]

ImH$^+$

$$\text{ImH}^+ \cdot \text{OH(aq)} \underset{k_{21}}{\overset{k_{12}}{\rightleftarrows}} \text{Im} \cdot \text{HO} \cdot (\text{HO})_n \cdot \overset{+}{\text{HOH(aq)}} \underset{k_{32}}{\overset{k_{23}}{\rightleftarrows}} \text{Im} \cdot \text{HO(aq)} +$$

II $\overset{+}{\text{H}_3\text{O}}$(aq) (1)

We wish to report a kinetic study of proton exchange between imidazolium ion and water in aqueous solution over a wide range of pH, in which the ionized state, II, is

detected as a reactive intermediate. Detection is possible because the N·HOH hydrogen bond is broken at a rate, $k_{H}{}'$, that is comparable to k_{23}. A possible mechanism is shown in eq 2.

$$\text{Im} \cdot \text{HO} \cdot (\text{HO})_n \cdot \overset{+}{\text{HOH(aq)}} \overset{k_{H}{}'}{\rightarrow} \text{Im} \cdot \text{HO} \cdot (\text{HO})_n \cdot \overset{+}{\text{HOH(aq)}} \quad (2)$$

II

Our data also evaluate the rate constant for the over-all process of acid dissociation. The result is in good agreement with a value determined by the temperature-jump method.[5] Moreover, our data evaluate the rate constant for breaking the N·HOH hydrogen bond in the product, Im·HOH(aq).

Experimental Section

Materials. Imidazole (Eastman) was recrystallized from benzene, equiv wt 68.28 (calcd 68.08). Solutions of imidazole in aqueous HCl were prepared by standard analytical techniques.

Nmr Measurements. The exchange broadening of the dominant water resonance was determined in air-saturated solutions by spin-echo measurements[6] of the transverse (T_2) and longitudinal (T_1) relaxation times at 56.4 MHz. Exchange broadening was equal to $(1/T_2) - (1/T_1)$.

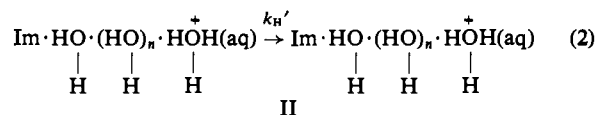Three parameters are needed to convert the experimental ex-

(1) Work supported in part by the National Science Foundation and by the Petroleum Research Fund of the American Chemical Society. Grateful acknowledgment is made to that foundation and to the donors of that fund.

(2) M. Eigen, W. Kruse, H. Maas, and L. DeMaeyer, *Progr. Reaction Kinetics*, 2, 285 (1964).

(3) M. M. Kreevoy and C. A. Mead, *Discussions Faraday Soc.*, 39, 166 (1965).

(4) E. Grunwald, *Progr. Phys. Org. Chem.*, 3, 317 (1965).

(5) (a) M. Eigen, G. G. Hammes, and K. Kustin, *J. Amer. Chem. Soc.*, 82, 3482 (1960); (b) G. G. Hammes, private communication to the authors, Aug 29, 1967.

(6) E. Grunwald and E. Price, *J. Amer. Chem. Soc.*, 86, 2965, 2970 (1964).

change broadening to the rate of proton exchange:[6] the NH-to-HOH proton chemical shift (δ), the longitudinal relaxation time of the ^{14}N nucleus (T^1), and the N–H coupling constant (J) in ImH^+. The chemical shift was determined from the maximum exchange broadening,[6] and T^1 and J were calculated from the slow-passage line shape[7] of the ImH^+ protons in concentrated HCl at 25°. T^1's were obtained at other temperatures by assuming that T^1 is proportional to T_1 of water protons. The parameters used in the kinetic analysis (temperature, δ, J_{NH}, T^1) are 30°, 9.99 ppm, 72 Hz, 6.8 msec; 25°, 9.00 ppm, 72 Hz, 5.7 msec; −0.4°, 11.12 ppm (?), 72 Hz, 3.6 msec. The anomalously large value of δ at −0.4° is the result of a single series of experiments. It was not redetermined, however, because the rates of proton exchange of interest at that temperature are in the region of lifetime broadening[6] and therefore quite independent of δ.

Independent measurements of the NH to OH chemical shift in an aqueous solution containing 1 M ImHCl and 6 M HCl by slow-passage nmr have failed to show a minimum between 0 and 40°. We are indebted to Mr. James A. Bell for these measurements.

pK_a Measurements. The pK_a of imidazolium chloride was determined at 25° by the differential potentiometric method[8] as a function of $[ImH^+]$, the imidazolium concentration. Results are described by the equation, pK_a = 6.976 + 0.185 $[ImH^+]$. A Beckman Research pH meter and a Model 39030 glass–Ag|AgCl "combination electrode" was used in all measurements of pH. The pK_a's at other temperatures were obtained using $\Delta H° = 7.97$ kcal, which was calculated from the mean temperature coefficient of pK_A obtained in four independent investigations.[9-12] The standard deviation of that mean is about ±1%.

Kinetic Analysis

Temperature-Jump Method. The rate constant for acid dissociation of imidazolium ion was measured at 13° by the temperature-jump method.[5] Discussion of these early results with two of their authors, Drs. Hammes and Kustin, led to the conclusion that the experimental relaxation times are quite accurate, but that the rate constants derived from them should be recalculated on the basis of a more accurate, modern value of K_A. The recalculation was undertaken by Dr. Hammes, who used 6.1 × 10^{-8} M for K_a of imidazolium ion at 13°, a value consistent with our measurements. On that basis, the following rate constants appear to fit the data best: for acid dissociation of imidazolium ion, $k_a = (1.1 \pm 0.4) \times 10^3$ sec^{-1}; for the reverse reaction, $k_{-a} = (1.8 \pm 0.5) \times 10^{10}$ M^{-1} sec^{-1}.[5b]

Nmr Method. In the temperature-jump method one disturbs the dynamic equilibrium by a sudden change of temperature and measures the rate of relaxation to equilibrium at the new temperature. In the nmr method one measures proton exchange at dynamic equilibrium at a fixed temperature. The nmr method will detect *all* processes giving rise to proton exchange, including symmetrical processes in which there is no net chemical reaction.

Rates (R_{NH}) of exchange of NH protons of imidazolium ion with OH protons of water in the pH range 6–3.5 are represented by the simple rate law[13]

$$R_{NH} = k_2[ImH^+][Im] + k_1[ImH^+] \quad (pH\,6-3.5) \quad (3)$$

(7) J. A. Pople, *Mol. Phys.*, **1**, 168 (1958).

(8) A. L. Bacarella, E. Grunwald, H. P. Marshall, and E. L. Purlee, *J. Org. Chem.*, **20**, 747 (1955).

(9) R. Mathur and H. Lal, *J. Phys. Chem.*, **63**, 439 (1959).

(10) B. L. Mickel and A. C. Andrews, *J. Amer. Chem. Soc.*, **77**, 5291 (1955).

(11) J. T. Edsall, G. Felsenfeld, D. S. Goodman, and F. R. N. Gurd, *ibid.*, **76**, 3054 (1954).

(12) C. Tanford and C. Wagner, *ibid.*, **75**, 434 (1953).

(13) E. K. Ralph and E. Grunwald, *ibid.*, **90**, 517 (1968).

The second-order rate constant, k_2, refers to a process involving ImH^+, Im, and an average of 1.4 water molecules.[13] The first-order rate constant, k_1, is significantly greater than the rate constant k_a for acid dissociation, as measured by temperature jump. At 13°, $k_1 = (2.7 \pm 0.3) \times 10^3$ sec^{-1}, while $k_a = (1.1 \pm 0.4) \times 10^3$ sec^{-1}.

In what follows, we shall show that k_1 is the sum of two rate constants: one of them has a magnitude which is in good agreement with the value of k_a; the other refers to a closely related process having the same activation energy as k_a and involving, probably, the ionized state II as a reaction intermediate. The complete kinetic scheme is shown in eq 4.

$$\text{(4)}$$
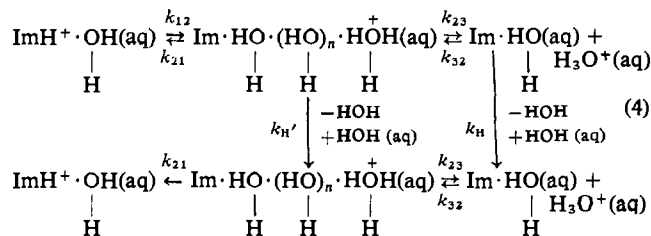
A proton exchange requires the breaking of the Im·HOH hydrogen bond, either in the ionized intermediate, II, or in Im·HOH. Because of the small ionization constant and low pH, both the ionized and dissociated states of imidazole may be treated kinetically as reactive intermediates of low concentration in the steady state. The resulting rate law is given in eq 5. It is

$$R_{NH} = \frac{k_H'k_{12}(k_H + k_{32}[H^+])[ImH^+]}{(k_H' + k_{21})(k_H + k_{32}[H^+]) + k_H k_{23}} +$$

$$\frac{k_H k_{12} k_{23}[ImH^+]}{(k_H' + k_{21})(k_H + k_{32}[H^+]) + k_H k_{23}} \quad (5)$$

probable that $k_{21} \gg k_H'$, k_H, and k_{23}.[2-4] It then follows that

$$R_{NH}/[ImH^+] = k_H'k_{12}/k_{21} +$$

$$k_H k_{23} k_{12}/\{k_{21}(k_H + k_{32}[H^+])\} \quad (6)$$

On the same basis ($k_{21} \gg k_{23}$) the rate constant measured by temperature jump is

$$k_a = k_{23} k_{12}/k_{21} \quad (7)$$

If we let $k_{cyclic} = k_H'k_{12}/k_{21}$ and $Q = k_{32}/k_H$, eq 6 may be rewritten in the form

$$R_{NH}/[ImH^+] = k_{cyclic} + k_a/(1 + Q[H^+]) \quad (8)$$

According to eq 8, there are two limiting values of $R_{NH}/[ImH^+]$, depending on the magnitude of $Q[H^+]$. At high pH, $R_{NH}/[ImH^+] = k_{cyclic} + k_a$. This limiting case is realized in the pH range 6–3.5; hence in eq 3, $k_1 = k_{cyclic} + k_a$. At very low pH, $R_{NH}/[ImH^+]$ is equal to k_{cyclic}, since $Q[H^+]$ is now very large. Representative data are shown in Figure 1 for the high pH region. The intercept yields k_1. The data at low pH are shown in Figure 2, where the solid curve is plotted according to eq 8 with $k_a = 2.44 \times 10^3$ sec^{-1} and $Q = 13$. The dotted line represents k_{cyclic}, which appears to vary somewhat with the ionic strength. The appropriate relationship is given in eq 9 and was obtained by least-squares fitting of experimental points between 1.1 and 4.3 M HCl.
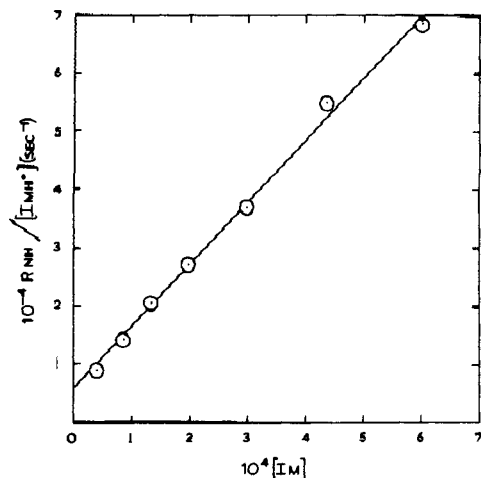
Figure 1. Kinetic plot of $R_{NH}/[ImH^+]$ vs. [Im] in the pH range 3.5–6 at 25°. The intercept and slope give k_1 and k_2 according to eq 3.
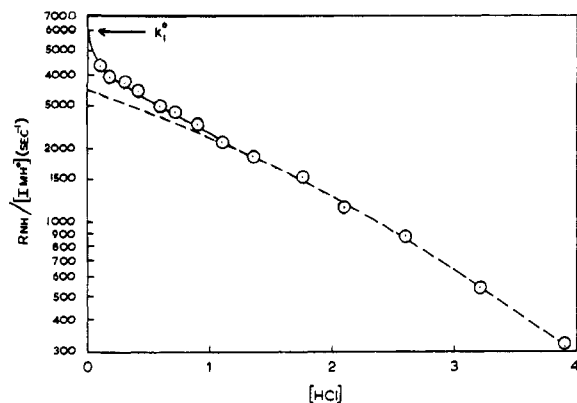

Figure 2. Plot of log $R_{NH}/[ImH^+]$ vs. [HCl] at 25°. Dotted line represents k_{cyclic} (eq 9); solid line represents eq 8. $Q = 13$; $k_a = 2.44 \times 10^3 \text{ sec}^{-1}$.

$$\log (k_{cyclic}) = 3.539 - $$
$$0.1663[HCl] - 0.02584[HCl]^2 \quad (9)$$

Linear or slightly curved relationships between log k and the salt concentration are characteristic of kinetic "neutral" salt effects.[14] The magnitude of the salt effect is comparable to that found previously on rate constants for acid dissociation of amines.[15]

Results are summarized in Table I. Measurements were made at −0.4, 25, and 30°. The fit of eq 8 is excellent, as illustrated in Table II. In view of the number of parameters involved in the kinetic analysis, we did a large number of experiments to secure the rate law. For example, at 30° the rate constants are based upon more than 80 experiments between pH 6 and 4.4 M HCl, in which [ImH$^+$] ranges from 0.02 to 0.2 M. The interpolation of k_a to 13° gives the value $(1.0 \pm 0.15) \times 10^3$ sec^{-1}, in good agreement with the value, $(1.1 \pm 0.4) \times 10^3$ sec^{-1}, obtained by temperature jump.[5b]

(14) F. A. Long and W. F. McDevit, Chem. Rev., 51, 119 (1952).
(15) E. Grunwald, J. Phys. Chem., 67, 2208 (1963).

Table I. Summary of Kinetic Results

Parameter	Temperature, °C				E_{act}, kcal
	−0.4	13[a]	25	30	
$10^{-3}k°_1$, sec^{-1}	1.14	...	5.90	6.65	...
$10^{-3}k°_a$, sec^{-1}	0.41	1.0	2.4$_4$	2.2$_4$	9.9
$10^{-3}k°_{cyclic}$, sec^{-1}	0.73[b]	...	3.4$_6$[b]	4.4$_1$[b]	9.8
Q, M^{-1}	15	...	13	...	
$10^{-10}k°_{32}$, M^{-1} sec^{-1}	1.4	...	2.3	...	
$10^{-9}k_H$, sec^{-1}	0.9	...	1.8	...	
$10^{-8}k°_2$, M^{-1} sec^{-1}	0.86	...	1.07	1.20	

[a] Interpolated. [b] Log $k_{cyclic} = \log k°_{cyclic} + A[HCl] + B[HCl]^2$. Temperature, A, B: −0.4°, −0.209, 0.00; 25°, −0.1663, −0.0258; 30°, −0.1982, −0.0123.

Table II. Test of the Rate Law (Eq 8) at 25°

HCl, M	$10^{-3}R_{NH}/[ImH^+]$ (obsd)	$10^{-3}k_{cyclic}$,[a] sec^{-1}	Q,[b] M^{-1}
0.108	4.22 ± 0.16	3.32	16
0.175	3.88 ± 0.02	3.23	16
0.255	3.32 ± 0.4	3.13	(46)[c]
0.303	3.72 ± 0.1	3.06	9
0.424	3.44 ± 0.1	2.91	9
0.579	3.00 ± 0.1	2.72	13
0.718	2.84 ± 0.1	2.55	10
0.890	2.50 ± 0.1	2.35	17
		Av	(13 ± 3)

[a] Calculated from eq 9. [b] Calculated from eq 8, using $k_a = 2.44 \times 10^3$ sec^{-1} and data listed in this table. $k_2[Im]$ is negligible compared to $R_{NH}/[ImH^+]$ at these [HCl]. [c] Omitted from average.

Discussion

The agreement between the rate constant, k_a, for proton exchange and that measured by temperature jump leaves little doubt that the process is acid dissociation. The kinetic form of the term involving k_a in eq 8 shows that the product of acid dissociation is the imidazole hydrate.[16] The rate constant k_H for the dissociation of Im·HOH is smaller than any other known k_H value for an amine hydrate[16,17] and suggests that the hydrogen bond is relatively strong.

The process associated with k_{cyclic} has been of great interest to us. The fact that this process is not detected by temperature jump suggests that it is symmetrical; i.e., the equilibrium constant is unity. The fact that the activation energy for k_{cyclic} is nearly equal to that for k_a (Table I) suggests a close similarity of reaction mechanisms. Indeed, we believe that k_{cyclic} involves the ionized state as a reaction intermediate. An alternative explanation is rejected in the Appendix.

If this be granted, then the kinetics of proton exchange is represented by the scheme shown in eq 4. According to that scheme, $k_{cyclic}/k_a = k_H'/k_{23}$. k_H' is the rate constant for breaking the N·HOH hydrogen bond in the

(16) E. Grunwald and E. K. Ralph, J. Amer. Chem. Soc., 89, 4405 (1967). The evidence presented in that paper, that k_a as measured by temperature jump is equal to k_a as measured by nmr, is updated and strengthened in the present work.
(17) M. Cocivera, J. Phys. Chem., 72, 2520 (1968).

ionized state, a necessary process for proton exchange to be observed.

As far as we know, this is the first case in which k_H'/k_{23} in the acid dissociation of an ammonium salt has been measurable. The fact that the ratio can be evaluated implies that k_H' is abnormally high or that k_{23} is abnormally small. In view of the relatively strong hydrogen bond between imidazole and water, as reflected by the value of k_H, we favor the interpretation that k_{23} is small.

Let us predict some numbers. If k_{23} were of normal magnitude for a diffusion-controlled mechanism of dissociation, then, according to the theory of Eigen,[18] $k_{23} = 3(D_{Im} + D_{H^+})/\sigma^2$, where D is the diffusion coefficient and σ is the distance of separation in the encounter complex, in this instance the ionized state. This model predicts that k_{23} is on the order of 10^{11} sec^{-1}. Since $k_H' \approx k_{23}$, k_H' would also have to be about 10^{11} sec^{-1}. We reject this calculation, finding it hard to believe that k_H' for a process such as (2) should be much greater than k_H for the dissociation of Im·HOH, which is on the order of 10^9 sec^{-1}.

Our results further strengthen the evidence that in acid dissociation the ionized state is a genuine intermediate. It will be interesting to study the properties of such intermediates in other systems, and our work suggests the following experimental methods: (1) comparison of proton exchange rates with rates of chemical relaxation; (2) kinetic analysis of proton exchange and search for rate laws of the form of eq 8. Method 2 will be feasible only when Q is relatively large.

Appendix

We wish to consider the theory that the kinetic term, $k_{cyclic}[ImH^+]$, results from a symmetrical reaction involving H_3O^+, Im, and water, such as that shown in (10).
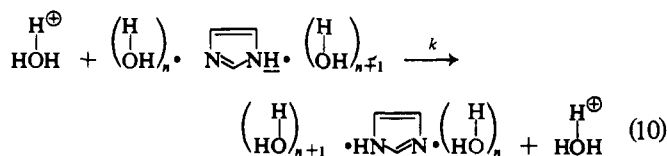
Analogous reactions involving the carboxyl group (O=C—OH rather than N=C—NH) are known. For

(18) M. Eigen, Z. Physik. Chem. (Frankfurt), 1, 176 (1954).

example, hydrogen ion-catalyzed proton exchange of benzoic acid in methanol involves such a mechanism and proceeds with a rate constant of 2.5×10^8 M^{-1} sec^{-1} at 24.8°.[19]

Such a theory must be rejected for the following reasons. If $n > 1$, (10) will lead to proton exchange only if the N·HOH hydrogen bond in the product breaks during the lifetime of the imidazole hydrate. The latter process must occur with the same rate constant, k_H, that appears in the rate law for proton exchange by reversible acid dissociation. The rate law (11) was derived for the case that acid dissociation and reaction 10 with $n > 1$ are parallel processes. In (11), k_a is the rate constant for acid

$$\frac{R_{NH}}{[ImH^+]} = \frac{k_a k_H}{k_H + k_{-a}[H^+]} \times \left(1 + \frac{k_H \alpha}{k_H + k_{-a}[H^+] + k(1 - \alpha)}\right) \quad (11)$$

dissociation, k_{-a} that for the reverse reaction ($k_a/k_{-a} = K_A$), and k that for reaction 10. The parameter $\alpha = k/(k + k_{-a})$. According to (11) the entire first-order rate, $R_{NH}/[ImH^+]$, should become small when $k_{-a}[H^+] \gg k_H$, whereas in fact only about half of the first-order rate disappears under these conditions. Thus the rate law (11) is inconsistent with the experimental results.

If we postulate that $n = 0$, we generate a theoretical monstrosity. Assuming the validity of reaction 10, the rate constant $k = k_{cyclic}/K_A = 3.3 \times 10^{10}$ sec^{-1} M^{-1} at 25°. At the same temperature, the rate constant for the reversal of acid dissociation, $k_{-a} = k_a/K_A$, is 2.3×10^{10} sec^{-1} M^{-1}. One would be forced to conclude that both reactions are diffusion controlled. For reversal of acid dissociation, the reactive encounter complex is known to be Im·(HOH)$_n$·HOH$_2^+$, with $n \geq 1$. If in addition we postulate diffusion-controlled reaction with $n = 0$, we are saying in effect that diffusion can take place efficiently in very large jumps, so that H_3O^+ ion can become a nearest neighbor to the imidazole molecule without having first to be a next-nearest neighbor. We regard this as unlikely, particularly since the displacement of a water molecule from the appropriate site adjacent to the imidazole molecule is known to be relatively difficult; k_H is relatively small.

(19) E. Grunwald and C. F. Jumper, J. Amer. Chem. Soc., 85, 2051 (1963).