Kinetics and Mechanism of the Metal Ion Catalyzed Hydrolysis of 8-Acetoxyquinoline

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Abstract: The influence of metal ions on the rate of hydrolysis of 8-acetoxyquinoline has been investigated in water at 25° and ionic strength 0.1. The pseudo-first-order rate constant conforms to the equation

$$k_e = \frac{1}{[H^+] + K_a}\{k_1[H^+]^2 + K_a(k_2[H^+] + k_3 + k_4[OH^-] + k_m[M^{+2}][OH])\}$$

where K_a is the acid dissociation constant of the 8-acetoxyquinolinium ion and the rate constants k_1, k_2, k_3, k_4, and k_m characterize various reaction paths of the ester. The relative order and magnitude of the k_m values of the metal ions investigated is somewhat surprising. Below pH 3, only copper(II) and indium(III) catalyze the reaction. Aluminum(III), gallium(III), and lanthanum(III) do not affect the rate below pH 3. At pH 5, zinc(II) is catalytically active and lead(II) shows a slight catalytic effect. Nickel(II), cadmium(II), cobalt(II), manganese(II), and calcium(II) do not affect the rate at pH 5. Exploratory studies of the cadmium(II) and nickel(II) systems at pH 7.1 showed that both metals catalyze the reaction with cadmium(II) being superior to nickel(II). A mechanism is suggested which attributes the relative order of the k_m's of divalent metal ions to the selective nature of a seven-membered chelated activated complex. The possibility that k_m is influenced by the kinetic lability of the aquated metal ion as well as by thermodynamic stability factors is considered.

The study of the hydrolysis of 8-acetoxyquinoline in the absence and presence of metal ions is of a dual interest. First, in view of the considerable recent interest in the use of the hydrolysis reaction to precipitate very pure metal oxinates from homogeneous solution,[1] a knowledge of factors influencing the rate is of obvious importance. Second, the study would have bearing on a more general problem of interest in coordination chemistry, namely the study of changes in ligand reactivity which arise on coordination. There has been considerable recent interest in the metal ion catalysis of nucleophilic organic reactions.[2,3] This interest is based in part on the possible relationship of these reactions to analogous enzymatic processes.[4]

In an earlier paper,[5] it was observed that the predominant reaction path for the hydrolysis of 8-acetoxyquinoline probably involved intramolecular catalysis by the quinoline nitrogen. Copper(II), an ion capable of forming a complex with 8-quinolinol, was observed to radily catalyze the reaction, even in solutions of pH less than 3. In view of the large number of metal ions that form stable complexes with 8-quinolinol, an investigation of the hydrolysis reaction in the presence of other metal ions seemed promising.

Experimental Section

Apparatus. Absorption spectra were obtained with a Cary Model 14 recording spectrophotometer. A Beckman Model DU quartz spectrophotometer with suitably matched 1- and 10-cm cells was used for rate measurements. A Beckman Model GS pH meter with a glass and saturated calomel electrode pair was used for pH measurements. For measurements above pH 3.2 the meter was standardized with Beckman pH 4.01, 7.00, and 9.18 buffers. For measurements below pH 3.2 the meter was calibrated with standard solutions of perchloric acid.

Reagents. 8-Acetoxyquinoline, PFHS grade, mp 56.5–57.0° (Burdick and Jackson Laboratories), was stored over phosphorus pentoxide and used without further purification. Metal perchlorate solutions were prepared from the reagent grade compounds manufactured by G. Frederick Smith Co. Copper perchlorate solutions were standardized by iodometric titration.[6] The other metal perchlorate solutions were standardized by EDTA titration.[6,7] Solutions studied at pH below 3.2 were prepared in unbuffered perchloric acid medium. Above pH 3.2, formate, acetate, phosphate, and borate buffers were used for pH control. All other chemicals used were of reagent grade quality.

Measurement of the pK_A of 8-Acetoxyquinoline. The pK_A was measured spectrophotometrically at 25 ± 0.5° and ionic strength 0.1. The absorbancy at 313.5 mμ of solutions of known ester concentration was measured over the pH range of 2.50–3.40. At 313.5 mμ both the conjugate acid and conjugate base forms of 8-acetoxyquinoline have absorption maxima. The molar absorbancy index of the conjugate acid is 5775 and that of the conjugate base is 2600. All measurements were recorded before any significant hydrolysis of the ester occurred. Measurement of six solutions yielded an average pK_A of 3.08 ± 0.01 (previously reported[5] pK_a = 3.14) in an ethanolic-water (5:95) medium.

Kinetic Measurement of the Rate of Hydrolysis. Kinetic experiments were carried out at 25.0 ± 0.03°, ionic strength 0.1, in a 5% ethanol–95% water medium. All solutions were made up to ionic strength 0.1 with sodium perchlorate. Initial ester concentrations were in the range of 1.7×10^{-5} to 2.2×10^{-4} *M*. The total concentration of the buffer component was generally 5×10^{-3} to 1×10^{-2} *M*. Experiments were sometimes run at a higher buffer concentration and at variable metal ion/buffer concentration ratios in order to establish that the buffer was not affecting the kinetics. Other observations, including the effect of varying the buffer system at a given pH, indicated that the buffers were not interfering in the concentration ranges employed.

In a typical experiment, a 100-ml volumetric flask containing the desired volumes of water, ethanol, sodium perchlorate solution, metal perchlorate solution, and buffer or perchloric acid solution was placed in a constant-temperature bath. An aliquot of a freshly prepared solution of 8-acetoxyquinoline in ethanol was added and the resulting solution diluted to the mark, mixed, and returned to the thermostat. At appropriate time intervals, aliquots were with-

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[1] F. N. Firsching, *Advan. Anal. Chem. Instr.*, 4, 1, (1965).

[2] M. Bender, Advances in Chemistry Series, No. 37, American Chemical Society, Washington, D. C., 1963, p 2.

[3] M. Jones, Advances in Chemistry Series, No. 49, American Chemical Society, Washington, D. C., 1965, p 153.

[4] G. Eichhorn, ref 2, p 37.

[5] C. R. Wasmuth and H. Freiser, *Talanta*, 9, 1059, (1962).

[6] A. Vogel "Quantitative Inorganic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1961.

[7] F. Welcher, "The Analytical Uses of Ethylenediaminetetraacetic Acid," D. Van Nostrand Co., Inc., Princeton, N. J., 1958.

drawn and their absorbancies measured. The choice of wavelengths at which the various reactions were followed was dictated by the absorption spectra of the reactant and product. A suitable wavelength is one at which the reactant or product has an absorption maximum and at which the ratio of molar absorbancy indexes of reactant and product is large. In solutions of pH less than 4 the reaction was followed at 313.5 mμ. Other rate measurements were made at 285 mμ. In each experiment the pH was constant and the concentration of metal ion was 35–1900 times greater than the concentration of ester. Rate constants were therefore obtained as pseudo-first-order rate constants from the slope of plots of log $(A_{+} - A_{\infty})$ *vs.* time. A_{+} is the absorbancy at time *t*, and A_{∞} is the absorbancy after a time long enough for the system to reach equilibrium. Rate constants were reproducible to ±3%.

Results and Discussion

Kinetic analysis of the hydrolysis of 8-acetoxyquinoline reveals the reaction involves a number of reaction paths including the H^+-catalyzed hydrolysis of both the protonated $[HE^+]$ and neutral [E] ester species, the OH^--catalyzed hydrolysis of the neutral ester, and one that involves neither H^+ or OH^- ions. The general rate expression

$$-\frac{d[E]_T}{dt} = k_1[H^+][HE^+] + k_2[H^+][E] + k_3[E] + k_4[OH][E]$$

can be transformed with the help of the acid dissociation equilibrium expression of the ester (characterized by K_A) to $-d[E]_T/dt = k_e[E]_T$, where

$$k_e = \frac{1}{[H^+] + K_a}\{k_1[H^+]^2 + K_a(k_2[H^+] + k_3 + k_4[OH^-])\} \tag{1}$$

The values of $k_1 \cdots k_4$ obtained in this study (see Table I) are listed below and compared with the values reported by Wasmuth and Freiser.[5]

k_1, M^{-1} sec^{-1}	2.55×10^{-5}	2.84×10^{-5}
k_2, M^{-1} sec^{-1}	3.7×10^{-3}	4.6×10^{-3}
k_3, sec^{-1}	4.7×10^{-5}	4.5×10^{-5}
k_4, M^{-1} sec^{-1}	1.14	1.13

Table I. Kinetic Data for the Hydrolysis of 8-Acetoxyquinoline at 25° and Ionic Strength 0.1

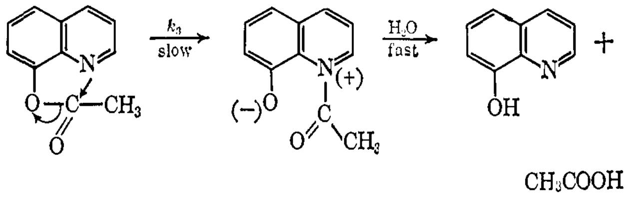
pH	10^5k_e, sec^{-1} Found	10^5k_e, sec^{-1} Calcd[a]
1.00	0.59	0.60
1.50	0.50	0.50
2.00	0.68	0.67
2.20	0.83	0.82
2.80	1.78	1.83
3.00	2.32	2.32
4.83	4.6	4.6
7.03	4.7	4.8
7.21	4.8	4.8
8.62	5.6	5.5
8.78	5.7	5.9
9.03	6.7	6.7
9.12	7.1	7.2

[a] Calculated from eq 1.

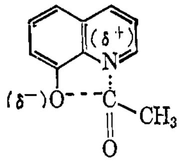
As can be seen from Table I, a comparison of experimentally obtained k_e values with those calculated on the basis of eq 1 is satisfactory. The $k_1 \cdots k_4$ values obtained here are seen to be in satisfactory general agreement with those observed by Wasmuth and Freiser. Inasmuch as Wasmuth and Freiser employed a different value for pK_A, the values of k_1 and k_2, which depend on the K_a, differ somewhat.

The course of 8-acetoxyquinoline hydrolysis is similar in many respects to that observed in most esters which are known to follow both H^+- and OH^--catalyzed paths.[8,9] Two features distinguish the hydrolysis of 8-acetoxyquinoline from that of most simple esters: the reactions paths characterized by k_1 and k_3. The first of these represents the H^+-catalyzed hydrolysis of the protonated ester. It is interesting to note that the corresponding reaction in protonated ethyl glycinate is three orders of magnitude faster although the OH^--catalyzed rates of both neutral esters are approximately the same.[10] The electron-withdrawing effect of the positively charged nitrogen in the glycine ester may be more effective because it is two atoms less removed from the reaction site than it is in 8-acetoxyquinoline. Alternatively, stronger hydrogen bonding between the protonated nitrogen and the carbonyl oxygen in the 8-acetoxyquinoline could result in a decrease in the ability of this oxygen to be protonated to form the intermediate associated with acid-catalyzed hydrolysis of esters.

The most interesting aspect of 8-acetoxyquinoline hydrolysis is the so-called "spontaneous" or water reaction path, characterized by k_3, which has been attributed to intramolecular catalysis.[5,9] By analogy to the carefully established mechanism of the corresponding path in the hydrolysis of aspirin, and other acyl salicylates,[9] as well as that of the imidazole, pyridine, and other N-containing nucleophilic catalyses of simple esters, the following mechanism for the k_3 path can be proposed.



The absence of general nucleophilic catalysis by the buffer components is consistent with an intramolecular mechanism.[9] The mechanism proposed is further supported by the observation that the k_3 value of 2-methyl-8-acetoxyquinoline, in which the nucleophilic character of the N atom is increased, is about four times greater than the value for 8-acetoxyquinoline.[11] Rate data for the hydrolysis of 7-acetoxyquinoline[12] indicate that the path corresponding to k_3 is much smaller than observed with 8-acetoxyquinoline. Hence, acyl group migration in intramolecular catalysis would seem to be favored by the possibility of the formation of a cyclic activated complex, *i.e.*



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[8] L. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940.

[9] M. Bender, *Chem. Rev.*, 60, 53 (1960).

[10] W. Connor, M. Jones, and P. Tulleen, *Inorg. Chem.*, 4, 1129, (1964).

[11] R. H. Barca and H. Freiser, unpublished results.

[12] D. Elliott, L. Howick, B. Hudson, and W. Noyce, *Talanta*, 9, 723 (1962).

Effect of Metal Ions on the Hydrolysis. (a) Copper(II). The presence of copper(II) results in an increase in the rate of hydrolysis of 8-acetoxyquinoline. The contribution of the copper reaction path is appreciable and can be readily measured at pH 3 and 0.03 *M* copper(II). In the presence of copper(II), eq 1 can be modified as follows

$$k_e = \frac{1}{[H^+] + K_a}\{k_1[H^+]^2 + K_a(k_2[H^+] + k_3 + k_4[OH^-] + k_m[M^{+2}][OH^-])\} \quad (2)$$

The value of k_m (9.1×10^7 M^{-2} sec^{-1}) was obtained from the slope of a plot of k_e *vs.* copper(II) concentration at a constant pH of 3.15. The value of k_e obtained from the intercept of this plot was in good agreement with the value calculated from eq 1. In Table II, experimental rate constants are compared with values calculated from eq 2. These finding are in accord with those previously reported.[5]

Table II. Kinetic Data for the Hydrolysis of 8-Acetoxyquinoline in the Presence of Copper(II) at 25° and Ionic Strength 0.1

pH	[Cu^{+2}], *M*	10^5k_e, sec^{-1} Found	Calcd[a]
2.76	0.0330	2.72	2.65
2.93	0.0330	3.9	3.9
3.03	0.0330	5.0	4.9
3.15	0.0330	6.6	6.4
3.15	0.0198	4.9	4.9
3.15	0.0132	4.2	4.2
3.15	0	2.70	2.70

[a] Calculated from eq 2 with $k_m = 9.1 \times 10^7$ M^{-2} sec^{-1}.

(b) Zinc(II). In solutions of pH less than 4 and ionic strength 0.1, the magnitude of the zinc(II)-catalyzed reaction path is too small to be measured. Measurement of the rate of hydrolysis over a zinc(II) concentration range of 0.01–0.03 *M* and a pH range of 4.3–5.0, however, showed that the reaction is analogous to that observed with copper(II) and that k_e is described by eq 2. The value of k_m (2.97×10^5 M^{-2} sec^{-1}) was obtained from rate data at pH 5 and 0.031 *M* zinc(II) concentration. Under these conditions, the zinc(II)-catalyzed reaction path is responsible for 24% of the value of k_e. The system was not investigated above pH 5 in order to avoid the presence of hydroxide complexes of zinc(II). In Table III, experimental rate constants are compared with those calculated from eq 2.

Table III. Kinetic Data for the Hydrolysis of 8-Acetoxyquinoline in the Presence of Zinc(II) at 25° and Ionic Strength 0.1

pH	[Zn^{+2}], *M*	10^5k_e, sec^{-1} Found	Calcd[a]
4.99	0.0309	6.1	6.1
4.80	0.0155	5.0	5.1
4.78	0.0206	5.1	5.2
4.73	0.0258	5.2	5.3
4.60	0.0144	4.9	4.9
4.59	0.0309	5.2	5.2
4.59	0.0180	5.0	4.9
4.58	0.0120	4.8	4.8
4.54	0.0240	5.0	5.0
4.47	0.0240	5.0	4.9
4.27	0.0309	4.7	4.7

[a] Calculated from eq 2 with $k_m = 2.97 \times 10^5$ M^{-2} sec^{-1}.

(c) Effect of Other Divalent Metal Ions. From the data in Table IV, it can be seen that nickel(II), cadmium(II), cobalt(II), manganese(II), and calcium(II) do not affect the rate of hydrolysis at pH 5 and 0.03 *M* metal ion concentration. Lead(II) exhibits slight catalytic ability, but the magnitude of the catalysis is too small to warrant quantitative evaluation. Mercury(II), an ion subject to extensive hydrolysis, was not investigated since 0.03 *M* solutions developed a yellow turbidity.

Table IV. Effect of Various Metal Ions on the Rate of Hydrolysis of 8-Acetoxyquinoline at 25° and Ionic Strength 0.1

Metal ion	[M^{+2}], *M*	pH	10^5k_e, sec^{-1} Found	Calcd[a]
Ni(II)	0.0312	4.83	4.6	4.6
	0.0204	4.88	4.6	4.7
Cd(II)	0.0315	4.44	4.6	4.6
	0.0262	4.90	4.6	4.7
Co(II)	0.0204	5.10	4.6	4.7
	0.0294	5.10	4.6	4.7
Mn(II)	0.03	5.16	4.8	4.7
Ca(II)	0.03	5.22	4.8	4.7
Pb(II)	0.025	4.90	4.9	4.7
	0.030	4.72	5.0	4.6

[a] Calculated from eq 1.

From eq 2 it can be seen that if $k_m \leq 5.2 \times 10^4$ M^{-2} sec^{-1} the contribution of the metal-catalyzed path will be a maximum of 5% at pH 5 and 0.03 *M* metal ion. If, however, the k_m for an "inactive" metal ion is not more than 100-fold smaller than the value for zinc(II), significant catalysis should be observed at pH 7, provided the metal-catalyzed path is first order in hydroxide ion concentration. Detailed studies were not attempted at pH values above 5 since, as recently pointed out by Jones,[3] the formation of metal hydroxide complexes complicates the interpretation of results. It is nevertheless of interest to explore metal ions such as nickel(II) and cadmium(II) at higher pH in an attempt to assess their catalytic ability. At pH 7.13 and 0.03 *M* metal ion, both nickel(II) and cadmium(II) rapidly catalyze the reaction. The approximate k_m values are 1.5×10^4 M^{-2} sec^{-1} for nickel(II) and 4.5×10^4 M^{-2} sec^{-1} for cadmium(II). These values explain why catalysis by these metal ions could not be observed at pH 5.

(d) Tervalent Metal Ions. It is often observed that the ability of a metal ion to accelerate an organic reaction increases with increasing charge of the ion. The quantitative study of trivalent metal ions is, however, hampered by their extensive hydrolysis, even at pH 3. Nevertheless, it is of interest to compare the catalytic ability of trivalent metal ions with copper(II), which is catalytically active below pH 3. Therefore, the effect of approximately 0.03 *M* aluminum(III), gallium(III), lanthanum(III), and indium(III) was investigated at pH 2.5–2.9. All of the above trivalent ions were inactive with the exception of indium(III), which increased k_e by a factor of 2 at pH 2.70. Thallium(III), the last member of group(III), was not investigated since it forms a colloidal oxide even at pH 1–2.5.

Since the exploratory experiment indicated that the catalytic ability of indium(III) was comparable to that of copper(II), a more detailed study of the indium(III) system was undertaken. In solutions of pH 2.3 and indium(III) concentrations not exceeding 0.01 M, it can be calculated from Biedermann's[13] data that less than 1% of the indium is present as $InOH^{+2}$.

In a solution of pH 2.3 and 0.01 M indium(III), k_e is 14% greater than the value calculated from eq 1. Because of the restricted range of pH and indium(III) concentration that can be studied, it was not possible to positively conclude that the indium(III) system obeys a rate law analogous to that of the copper(II) and zinc(II) systems. Under the experimental conditions employed, however, the behavior of k_e is compatable with a linear equation having the theoretical intercept given by eq 1 and having a term that is first order in indium(III) concentration. In evaluating k_m (2.64×10^8 M^{-2} sec^{-1}) it was also assumed that the indium(III)-catalyzed reaction path is first order in hydroxide ion concentration. In Table V, experimental rate constants are compared with calculated values.

Table V. Kinetic Data for the Rate of Hydrolysis of 8-Acetoxyquinoline in the Presence of Indium(III) at 25° and Ionic Strength 0.1

pH	$[In^{3+}]$, M	10^5k_e, sec^{-1} Found	Calcd[a]
2.30	0	0.94	0.94
2.30	0.0103	1.07	1.07
2.30	0.00931	1.03	1.05
2.30	0.00915	1.07	1.05
2.30	0.00828	1.03	1.03
2.30	0.00725	1.02	1.02
2.30	0.00621	1.02	1.02
2.30	0.00518	0.98	1.00
2.30	0.00458	0.98	0.98
2.23	0.00946	0.92	0.93

[a] Calculation from eq 2 with $k_m = 2.64 \times 10^8$ M^{-2} sec^{-1}.

Effect of Temperature Variation. The effect of temperature variation was studied in the hope that the value of rate and equilibrium constants in eq 2 might be altered in a manner that would increase the relative contribution of the k_m term and therefore permit the "inactive" metal ions to be studied under the conditions employed for copper(II) and zinc(II). For this reason, the rate of hydrolysis of 8-acetoxyquinoline was studied at 35 and 15° both in the absence and presence of nickel(II), cadmium(II), and cobalt(II). At neither temperature did the presence of these metal ions affect the rate of hydrolysis when conditions similar to those of Table IV were used. Lead(II) indicated some catalytic activity but, as at 25°, not enough to warrant quantitative evaluation.

The rate of hydrolysis of 8-acetoxyquinoline in a solution of pH 4.90 at which k_3 is the predominant rate component was measured at 25, 35, and 45° (Table VI). A plot of log k_e *vs.* $1/T$ is linear over this temperature range. An apparent activation energy of 14.5 kcal/mole was calculated from the slope of this line.

Table VI. Effect of Temperature Variation on the Rate of Hydrolysis of 8-Acetoxyquinoline at pH 4.90 and Ionic Strength 0.1

Temp, °C	10^5k_e, sec^{-1}
25	4.7
35	10.4
45	23.2

Mechanism of the Metal-Catalyzed Reaction. The kinetic order of the metal ion catalyzed reaction path can be explained on the following basis: a rapid[14,15] formation of a 1:1 metal ion-ester complex which must involve metal nitrogen coordination since the resulting species requires OH^- catalysis in place of the intramolecular catalyzed path possible with the free ester. Thus

$$M^{n+} + E \underset{}{\overset{K_f}{\rightleftharpoons}} (ME)^{n+}$$

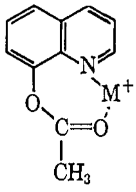
$$(ME)^{n+} + OH^- \xrightarrow[\text{slow}]{k_5} MOx^{(n-1)+} + CH_3COOH$$

from which k_m may be written

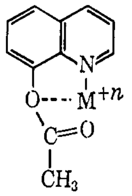
$$k_m = K_f k_5$$

A small k_m could, therefore, be attributed either to the failure of the metal–ester complex to form (low K_f) or for it to be less susceptible to hydrolysis than the uncomplexed ester (k_5 small relative to k_3).

In order to understand the factors influencing the values of K_f and k_5, it is necessary to consider the likely structures of the intermediate metal–ester complex and the activated complex for the k_5 step. The structure of the 1:1 intermediate complex would involve metal–nitrogen bonding and possibly weak interaction of the metal with oxygen of the acetyl group. The magnitude of K_f would, therefore, primarily reflect the stability of the metal–nitrogen bond. It is possible that the lack of reactivity of aluminum, gallium, and lanthanum, compared with indium, arises from the low coordination tendency of these metal ions with nitrogen. For effective metal ion catalysis, the activated complex of the k_5 step may involve chelation.[2,16] In addition to metal–nitrogen bonding, the metal may be bound to either the carbonyl oxygen (structure A) or to the ether oxygen (structure B).



A



B

Structure A is electrostatically more favorable since the partially negative carbonyl oxygen could be stabilized to a greater extent than the essentially neutral ether oxygen in structure B. Further, infrared studies of solid metal–ester complexes[17] as well as a study in D_2O solution[16] have indicated metal–carbonyl oxygen bonding. If the activated complex can be visualized as the interaction of hydroxide ion and structure A, k_5 values would be influenced by (a) the ability of the metal ion to withdraw electron density from the carbonyl and thereby render the carbon undergoing attack by OH^- more electropositive, and (b) the stability of the N–O seven-membered chelate structure relative to the struc-

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[13] G. Biedermann, *Arkiv Kemi*, **9**, 277 (1956).

[14] R. Holger, C. Hubbard, S. Kettle, and R. Wilkins, *Inorg. Chem.*, **4**, 929 (1965).

[15] R. Wilkins and M. Eigen, ref 3, p 55.

[16] D. Alexander and D. Busch, *J. Am. Chem. Soc.*, **88**, 1130 (1966).

[17] M. P. Springer and C. Curran, *Inorg. Chem.*, **2**, 1270 (1963).

ture of the ground-state intermediate. Factors a and b cannot, of course, be separated. It is probable that the surprising catalytic ability of indium(III) is connected with factor a above.

The order of catalytic ability observed for the divalent metal ions, Cu(II) > Zn(II) > Pb(II) > Cd(II) > Ni(II), is not the order expected if either the stability of a metal–nitrogen complex (K_f) or the stability of a normal N–O chelate such as 8-quinolinol were the dominating factor. The "stability-dominated" catalytic order would be Cu(II) > Ni(II) > Co(II) > Zn(II) > Cd(II).

One possible explanation for the observed k_m order is that the unusual order could be associated with the selectivity of the seven-membered ring structure discussed above. Observations indicate that the selectivity of large chelate rings causes changes in the usual stability sequence. For example, nickel(II) is known to be more susceptible to steric hindrance influences than zinc(II).[18] The seven-membered O–O ring of phthalic acid exhibits the stability order Cu(II) > Cd(II) > Zn(II) > Ni(II) > Co(II).[19]

Another possible explanation for the unusual order lies in the assumption of a more active role of the complexed metal ion in the rate-determining step. If the metal ion, complexed either to nitrogen alone or as shown in structure A, were to bond to the phenoxy oxygen at the same time OH^- attacks the complex, k_5 would reflect the rate of substitution of metal ions.[20] The composite dependence of k_m upon stability factors as well as the kinetic lability of the metal ion could result in the observed order.

Under current investigation is the extension of this study of the role of metal ion catalysis of the hydrolysis of 8-acetoxyquinoline and other related compounds in the hope of resolving some of the questions discussed.

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(20) B. E. McClelland and H. Freiser, *Anal. Chem.*, **36**, 2262 (1964).