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Structure and Behavior of Organic Analytical Reagents. III. Stability of Chelates of 8-Hydroxyquinoline and Analogous Reagents[1]

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Stabilities of chelates of 8-hydroxyquinoline and several analogous reagents have been determined for a representative group of common divalent metals in order to determine the effect of certain structural changes on chelate stability. Stability measurements made on a series of chelates of 8-hydroxyquinaldine show that significant steric hindrance, considered responsible for the non-reaction of this reagent with Al(III), is also encountered in the case of Ni(II). A study of the stabilities of chelates of 2-(*o*-hydroxyphenyl)-quinoline and 1-(*o*-hydroxyphenyl)-isoquinoline was undertaken in order to evaluate the effect of ring size on chelate stability. The lack of reactivity of 2-(*o*-hydroxyphenyl)-quinoline with divalent metals and the relatively low stability of chelates of 1-(*o*-hydroxyphenyl)-isoquinoline indicate that for this type of reagent five-membered ring chelates are more stable than chelates having six membered rings. The divalent metal stability sequence of 8-hydroxyquinoline chelates is in agreement with reported metal orders for other chelating reagents. This order for the transition metals shows an increase in chelate stability as the transition electron shell becomes more completely filled. A similar effect has been noted in the case of La(III) and Ce(III) of the inner transition metals.

Since 8-hydroxyquinoline is a most useful and versatile analytical reagent, it was thought desirable to subject it and compounds of similar structure to a study of the stability of their metallic chelates. As steric factors have been considered responsible for several cases of abnormal reagent behavior,[2,3] we have included in this study the determination of stabilities of typical metal chelates of 8-hydroxyquinaldine in order to learn whether the inactivity of this reagent toward aluminum would also be reflected in the stability of the chelates of divalent metals. The compounds, 2-(*o*-hydroxyphenyl)-quinoline and 1-(*o*-hydroxyphenyl)-isoquinoline, were included in an attempt to compare 8-hydroxyquinoline with 6-membered ring analogs. Both of these proved surprisingly inactive chelating agents.

Experimental

Materials.—B. L. Lemke Co. pure 8-hydroxyquinoline was recrystallized several times from water and alcohol to give a compound that melted at 74–76° which is in agreement with reported values.[4] 8-Hydroxyquinaldine was prepared by a modified Skraup synthesis.[2] After several recrystallizations from alcohol and water it melted at 72–74° (reported[5] 74°). 2-(*o*-Hydroxyphenyl)-quinoline and 1-(*o*-hydroxyphenyl)-isoquinoline were made by the method of Geissman and co-workers.[6] The melting points obtained after several recrystallizations from alcohol and water are in agreement with those reported by Geissman.

Anal. Calcd. for $C_{15}H_{11}NO$: C, 81.42; H, 5.01. Found[7] for 2-(*o*-hydroxyphenyl)-isoquinoline: C, 80.84; H, 5.11. Found for 1-(*o*-hydroxyphenyl)-isoquinoline: C, 81.05; H, 4.76.

The method of purification of dioxane and the procedures used in standardizing metal perchlorate solutions have been previously described.[6]

Apparatus and Procedure.—The titration apparatus and procedure have been previously described.[8]

Results

The results of representative titrations of metals with the various compounds are given in Table I, where $\bar{n}$ is the average number of bound reagent anions per metal ion and pR is the negative logarithm of the concentration of reagent anion. Included in Table I are the acid dissociation constants of the reagents studied. Table II summarizes the chelate formation constants calculated from the titration data. It has been previously pointed out that incorrect stability values may result if measurements are carried out in a pH range in which the metal ion will undergo appreciable hydrolysis. The measurements listed in Table I were

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[1] Paper II, THIS JOURNAL, **74**, 1385 (1952).

[2] L. L. Merritt and J. K. Walker, *Ind. Eng. Chem., Anal. Ed.*, **16**, 387 (1944), found that 8-hydroxyquinaldine formed well-defined compounds with all of the metals that reacted with 8-hydroxyquinoline, except with aluminum which gave no precipitate at all.

[3] H. Irving, E. J. Butler and M. F. Ring, *J. Chem. Soc.*, 1489 (1949), extending the study of Merritt and Walker, found that other 2-substituted 8-hydroxyquinolines failed to react with aluminum as did 1-hydroxyacridine and 9-hydroxy-1,2,3,4-tetrahydroacridine. With all other metals these reagents behaved similarly to 8-hydroxyquinoline.

[4] K. Bedall and O. Fischer, *Ber.*, **14**, 442 (1881).

[5] O. Doebner and W. v. Miller, *ibid.*, **17**, 1698 (1884).

[6] T. A. Geissman, M. J. Schlatter, I. D. Webb and J. D. Roberts, *J. Org. Chem.*, **11**, 741 (1946).

[7] All microanalyses by Mr. G. L. Stragand.

[8] H. Freiser, R. G. Charles and W. D. Johnston, THIS JOURNAL, **74**, 1383 (1952).

Table I

Acid Dissociation Constants in 50% Dioxane at 25°

	pK_{NH}	pK_{OH}
8-Hydroxyquinoline	3.97	11.54
8-Hydroxyquinaldine	4.51	11.69
1-(*o*-Hydroxyphenyl)-isoquinoline	4.31	11.59
2-(*o*-Hydroxyphenyl)-quinoline	*ca.* 2	12.77

Representative Titrations of Solutions of Metal Perchlorates and Chelating Agents in 50% Dioxane–Water Solutions with Sodium Hydroxide at 25°

Cu(II) and 8-hydroxyquinoline: 0.0002981 mole organic reagent, 0.00005274 mole metal ion, 0.0005403 mole perchloric acid, original volume 100 ml., concentration NaOH 0.01424 *M*.

NaOH, ml.	*p*H	n	*p*R
0.00	2.47	0.84	13.18
1.00	2.49	.90	13.16
4.00	2.55	1.05	13.07
5.00	2.57	1.11	13.05
10.00	2.68	1.33	12.89
14.00	2.78	1.48	12.74
15.00	2.80	1.55	12.72
20.00	2.95	1.75	12.50

Ce(III) and 8-hydroxyquinoline: 0.0003275 mole organic reagent, 0.00004645 mole metal ion, 0.0004880 mole perchloric acid, original volume 110 ml., concentration NaOH 0.0980 *M*.

NaOH, ml.	*p*H	$\bar{n}$	*p*R
4.75	4.74	0.38	9.45
5.00	5.05	.56	9.13
5.10	5.23	.61	8.94
5.20	5.41	.71	8.76
5.40	5.78	.99	8.40
5.50	5.96	1.17	8.23
5.60	6.14	1.34	8.07
5.70	6.27	1.55	7.95

Cu(II) and 8-hydroxyquinaldine: 0.0003365 mole organic reagent, 0.00004790 mole metal ion, 0.0005370 mole perchloric acid, original volume 110 ml., concentration NaOH 0.01959 *M*.

NaOH, ml.	*p*H	$\bar{n}$	*p*R
10.00	3.14	0.81	12.58
12.00	3.26	.97	12.37
13.00	3.33	1.04	12.24
15.00	3.47	1.23	12.00
17.00	3.62	1.41	11.74
18.00	3.70	1.52	11.61
20.00	3.88	1.69	11.30
25.00	4.41	1.96	10.45

Ce(III) and 8-hydroxyquinaldine: 0.0003365 mole organic reagent, 0.00004645 mole metal ion, 0.0004880 mole perchloric acid, original volume, 110 ml., concentration NaOH, 0.0980 *M*.

NaOH, ml.	*p*H	$\bar{n}$	*p*R
5.00	5.99	0.26	8.60
5.10	6.48	.32	8.10
5.25	6.91	.59	7.68

Cu(II) and 1-(*o*-hydroxyphenyl)-isoquinoline: 0.0003319 mole organic reagent, 0.00001916 mole metal ion, 0.0005370 mole perchloric acid, original volume 104 ml., concentration NaOH 0.01959 *M*.

NaOH, ml.	*p*H	$\bar{n}$	*p*R
14.00	3.79	0.42	11.05
15.00	3.89	.47	10.88
16.00	3.99	.48	10.72
17.00	4.07	.62	10.60
18.00	4.17	.59	10.44
20.00	4.34	.78	10.19
21.00	4.43	.84	10.07

Table II

Formation Constants in 50% Dioxane–Water Solutions at 25°

8-Hydroxyquinoline	log K_1	log K_2	log K_{av}
Cu(II)	13.49 (calcd.)	12.73	13.11
Ni(II)	11.44	9.94	10.80
Co(II)	10.55	9.11	9.83
Zn(II)	9.96	8.90	9.36
Pb(II)	10.61	8.09	9.30
Mn(II)	8.28	7.17	7.67
Cd(II)	9.43	7.68	8.50
Mg(II)	6.38	5.43	5.93
La(III)[a]	8.66	7.74	...
Ce(III)[a]	9.15	7.98	...
8-Hydroxyquinaldine			
Cu(II)	13.00 (calcd.)	11.64	12.32
Ni(II)	9.50	8.50	8.98
Co(II)[b]	9.68	8.92	9.27
Zn(II)	10.10	9.07	9.54
Pb(II)	10.35	8.25 (calcd.)	9.30
Mn(II)	7.72	6.84 (extrap.)	7.29
Ce(III)	7.71	...	...
1-(*o*-Hydroxyphenyl)-isoquinoline			
Cu(II)	10.72	9.02 (calcd.)	9.87 (extrap.)

[a] K_3 not determined. [b] The original manuscript contained higher values for the stability constants of cobalt 8-hydroxyquinaldinate. Subsequent work in this Laboratory on temperature dependence of stability constants indicated these values were in error. Repetition of the determination with more time allowed for the attainment of equilibrium yielded the results reported here. The need for correction of the original values was also pointed out by Dr. Harry Irving of Oxford University on the basis of studies conducted in his Laboratory.

all made in regions which had been shown to be free from metal hydrolysis. In the case of Ce(III) and Mn(II) it was impossible to determine the hydrolysis region because of oxidation of the metallic ion. Hence, the limiting *p*Hs were assigned to be 7 and 8, respectively, according to Britton's *p*H of partial hydroxide precipitation.[9] However, no oxidation of these metals occurred during chelation titrations. This was shown from the titration data since only two and three moles of hydrogen per mole of Mn(II) and Ce(III), respectively, were released during chelation. Apparently the Mn(II) and Ce(III) oxidation states were stabilized by the chelating reagents used.

Due to chelation occurring in regions of hydrolysis it was impossible to calculate any constants for Co(II), Ni(II) and Zn(II) chelates of 1-(*o*-hydroxyphenyl)-isoquinoline, Al(III) with 8-hydroxyquinoline, and La(III) with 8-hydroxyquinaldine. For the same reason it was impossible to calculate K_2 and K_3 for the Ce(III) chelate of 8-hydroxyquinaldine. Because of rapid oxidation of Fe(II) in the presence of either 8-hydroxyquinoline or 8-hydroxyquinaldine the stability could not be calculated. Precipitation interfered with calculation of K_3 for the La(III) and Ce(III) chelates of 8-hydroxyquinoline.

Reaction of 2-(*o*-Hydroxyphenyl)-quinoline with Metals.—2-(*o*-Hydroxyphenyl)-quinoline was unusual in that it would not react with any of the divalent metals tested. A similar, effect has been noted in the case of a group of quinaldyl ketones.[10] In this case chelation with Cu(II) was attempted as a means of isolation of the synthesis product. Hoste[11] reports that no chelation with divalent metals occurs in 6,6′-dimethyl-2,2′-dipyridyl, 2-pyridyl-2′-quinolyl, 2,2′-diquinolyl and 2-quinolyl-2′-isoquinolyl. However, specific reactions for copper were observed by first reducing Cu(II) to Cu(I) by means of hydroxylamine hydrochloride and then testing with any of the reagents listed. However, no similar reaction appeared to occur in the case of 2-(*o*-hydroxyphenyl)-quinoline and Cu(I). It is probable that the specific activity of this structurally related group of re-

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(9) H. T. S. Britton, *J. Chem. Soc.*, **127**, 2100, 2142 (1925).

(10) N. N. Goldberg and R. Levine, unpublished data.

(11) J. Hoste, *Anal. Chem. Acta*, **4**, 23 (1950).

agents is due to a steric blocking effect of the benzene portion of the quinolyl compounds and the 6-methyl groups of the pyridyl compounds. The typical red phenol test with Fe(III) constitutes the only reaction between a metal ion and this reagent. Further study is planned in this very interesting group of compounds.

Reaction of 1-(*o*-Hydroxyphenyl)-isoquinoline with Metals.—In an acetate–acetic acid medium this reagent gave a yellow-green precipitate with Cu(II), a white precipitate with Cr(III), and a red color with Fe(III). In an ammoniacal tartrate solution the same precipitations and colorations as noted in the acetic acid medium were observed. Additional precipitations in this medium include Ni(II), yellow-green; Co(II), brown; Zn(II), yellow; and white precipitates of Al(III), La(III) and Ce(III). In sodium hydroxide and tartrate a yellow green precipitate with Hg(II) was obtained. Analysis of the Cu(II) and Ni(II) chelates of this reagent indicated the expected composition of two reagent molecules per metal. The Cu(II) chelate was dried under vacuum while the Ni(II) chelate was dried at 130°.

Anal. Calcd. for $Cu(C_{15}H_{10}ON)_2$: Cu, 12.61; Found: Cu, 12.53. Calcd. for $Ni(C_{15}H_{10}ON)_2 \cdot {}^1/_2H_2O$: C, 70.90; H, 4.17. Found: C, 71.24; H, 4.35.

The Co(II) and Zn(II) chelates of this reagent could not be brought to constant weight either at 110° or 130°. Vacuum desiccation at room temperature was also unsatisfactory.

Reaction of 8-Hydroxyquinaldine with Metals.—While the qualitative reactions of 8-hydroxyquinaldine are well known only the Cu(II), Zn(II), Mg(II) and Fe(III) chelates have been previously analyzed.[2] The analysis of the Pb(II), Co(II) and Ni(II) chelates were attempted in this work. The Ni(II) chelate appeared to be an indefinite hydrate and did not yield good analytical data. The Pb(II) and Co(II) chelates came to constant weight after drying at 130°.

Anal. Calcd. for $Pb(C_{10}H_8ON)_2$: N, 5.35. Found: N, 5.14. Calcd. for $Co(C_{10}H_8ON)_2 \cdot {}^1/_2H_2O$: C, 62.51; H, 4.56; N, 7.29. Found: C, 61.77; H, 4.52; N, 7.81.

Reaction of 8-Hydroxyquinoline with Metals.—Exhaustive qualitative and quantitative studies of chelates of 8-hydroxyquinoline appear in the literature.

Discussion of Results

A comparison of the acid dissociation constants of the chelating reagents is important to an evaluation of chelate stability. A comparison of 8-hydroxyquinaldine with oxine reveals a slightly more basic nitrogen in the quinaldine compound while the phenols are of virtually equal acidity. The increase in nitrogen basicity may be attributed to the inductive and hyperconjugative effects of the 2-methyl group of 8-hydroxyquinaldine. The nitrogen of 1-(*o*-hydroxyphenyl)-isoquinoline is slightly more basic than that of oxine due to resonance interaction with the *o*-hydroxyphenyl substituent. In this connection, it should also be noted that isoquinoline itself is more basic than quinoline.[12] The phenols of 1-(*o*-hydroxyphenyl)-isoquinoline and oxine are of about equal acidity. The very strange values of the acid dissociation constants exhibited by 2-(*o*-hydroxyphenyl)-quinoline have not been satisfactorily explained. In connection with the almost negligible basicity of the nitrogen of this compound, it is interesting to note that *o*-phenanthroline though having two nitrogens acts as a monoacid base, possibly due to steric requirements.[13] The fact that steric requirements may also be responsible for low nitrogen basicity in 2-(*o*-hydroxyphenyl)-quinoline is substantiated by the general lack of reactivity of this compound with metal ions.

The constants listed in Table II indicate a very high order of stability for chelates of 8-hydroxyquinoline. The stabilities of these chelates are greater (by a factor of 4–9 log $K_{\text{av.}}$ units) than those of β-diketones and substituted salicylaldehydes.[14] This greater stability may be attributed to the fact that the basic character of the 8-hydroxyquinoline nitrogen is greater than that of the carbonyl oxygens of the β-diketones and substituted salicylaldehydes. Also, the phenolic group of 8-hydroxyquinoline is a weaker acid than the phenolic groups of the diketones and hydroxyaldehydes. Since, according to Calvin and Wilson,[14] the forces holding a hydrogen ion to a molecule are similar to those forces that will hold a metal ion to the same molecule, the extreme stability of chelates of 8-hydroxyquinoline can be explained by the high basicity of its functional groups. *o*-Aminophenol which has the same reactive grouping and virtually the same basicity as 8-hydroxyquinoline forms chelates with metals which are much less stable than the oxinates.[1] This might be attributed in part to the hydrogen atoms in the amino group of *o*-aminophenol which could exert a steric blocking influence on coördination with metals. Also, in accord with Calvin and Wilson, the greater possibilities for resonance interaction in the 8-hydroxyquinoline chelates than those of *o*-aminophenol, would account for their greater stability.

The stability sequence for various divalent metals with a given reagent has been shown to be rather inflexible regardless of the reagent used. The metal order for oxine is seen to be Cu > Ni > Co > Zn > Pb > Cd > Mn > Mg. This order is in perfect agreement with metal orders given for sodium 5-salicylaldehyde sulfonate[15] and ethylenediamine.[16] The order reported for *o*-aminophenol is the same with the exception of an inversion of the order of Zn and Co.[1] It is also in agreement with the salicylaldehyde order[17] with the exception of the position of the Pb chelates. Data for the *p*H of precipitation[18] of oxine chelates also give this metal order. In this case also the lead chelate is out of order. The apparent discrepancy in the case of lead may be partially explained by observing that the K_1 values for 8-hydroxyquinoline chelates are in the same order as the stability sequence for salicylaldehyde, even in the case of lead. Thus the distortion of the K_{av} series for oxine is obviously due to an abnormally small K_2 of the lead oxinate chelate indicating difficulty in introduction of a second chelate anion to the lead complex. An abnormally low K_2 value has also been noted in the lead chelate of *o*-aminophenol.[1]

Merritt[18] has used the *p*H values at which metallic 8-hydroxyquinolinates begin to precipitate to obtain information about the relative stabilities of these complexes. In general, his results are compatible with those reported here. In obtaining theoretical information from *p*H of precipitation

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[12] E. Jantzen, *Dechema Monographien*, **5**, 117 (1932).

[13] T. S. Lee, I. M. Kolthoff and D. L. Leussing, THIS JOURNAL, **70**, 2348 (1948).

[14] M. Calvin and K. W. Wilson, *ibid.*, **67**, 2003 (1945).

[15] M. Calvin and N. C. Melchior, *ibid.*, **70**, 3270 (1948).

[16] L. E. Maley and D. P. Mellor, *Nature*, **161**, 436 (1948).

[17] L. E. Maley and D. P. Mellor, *Australian J. Sci. Research*, **2**, 92 (1949).

[18] L. L. Merritt, *Record Chem. Progress* (*Kresge-Hooker Sci. Lib.*), **10**, 59 (1949).

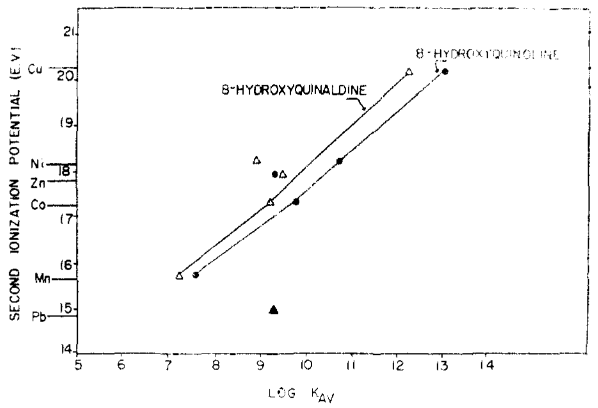

Fig. 1.

data it must be either assumed that the stability constant of a chelate is proportional to its insolubility or that the chelates are of infinite insolubility. These assumptions seriously limit the general applicability of this technique. Moreover, Charles and Freiser in a study of the chelates of dimethylglyoxime[19] found that the least soluble chelate, that of nickel, was not the most stable.

A potentiometric study of the stability of chelates of 8-hydroxyquinoline carried out in a 70% dioxane solution by Maley and Mellor[17] has yielded a somewhat different stability order. The fact that no correction was made for the change in the behavior of the glass–calomel electrode pair in this medium casts serious doubt on the validity of their results. It has been found that while a 50% v./v. aqueous dioxane solution permits determination of hydrogen ion concentration with an accuracy equal to that obtained in aqueous medium,[14] the results in 70% dioxane deviate by a factor of 1.7.[20] It can be shown mathematically that $^1/_2(\log K_1 + \log K_2) = p\text{R}$ at $n = 1$. In other words at $\bar{n} = 1$, pR should equal the average of the two formation constants. The almost hyperbolic curves obtained by Maley and Mellor do not fulfill this qualification, further indicating the questionable validity of their results.

Merritt and Walker[2] found that a methyl group in the 2 position of 8-hydroxyquinoline would prevent the reagent from reacting with Al(III). In order to determine more subtle manifestations of this supposed blocking effect, it was decided to determine the stabilities of 8-hydroxyquinaldine chelates of a series of metals and compare them with the stabilities of the corresponding chelates of 8-hydroxyquinoline. On the basis of the greater basicity of the functional groups of 8-hydroxyquinaldine than those of oxine, correspondingly greater chelate stabilities might be expected. If, however, the methyl group exerts the type of hindrance to chelate formation for the divalent metals, as was encountered with Al(III), the oxinates might be found to be more stable. As can be seen from Table II the Cu(II), Co(II), Zn(II), Mn(II) and Pb(II) chelates of the two reagents have stabilities of the same order of magnitude. However the Ni(II) chelate of 8-hydroxyquinaldine is significantly less stable than the corresponding oxinate. This unusual behavior of the Ni(II) chelate of 8-hydroxyquinaldine is clearly illustrated in the graph of log K_{av} *vs.* the second ionization potential of the gaseous metal atom (Fig. 1). This graph shows a high degree of linearity in the case of oxine for the metals of the first transition. The linearity of log K_{av} *vs.* the second ionization potential of the metal involved was first pointed out by Calvin and Melchior[15] in the case of the chelates of 5-salicylaldehydesulfonic acid. The lack of complete linearity in the 8-hydroxyquinaldinates is immediately seen to be caused by the Ni(II) chelate. It is apparent that some type of steric hindrance due to the 2-methyl group is operative in the Ni(II) chelate of 8-hydroxyquinaldine. It is reasonable to suppose that the steric hindrance shown here is similar in nature to that which has been found to prevent the precipitation of Al(III) with 8-hydroxyquinaldine.

In order to evaluate the effect of ring size on chelate stability, the chelating tendencies of 2-(*o*-hydroxyphenyl)-quinoline and 1-(*o*-hydroxyphenyl)-isoquinoline were studied. The lack of reactivity of 2-(*o*-hydroxyphenyl)-quinoline has been previously discussed. Only in the case of Cu(II) was it possible to determine the stability for a 1-(*o*-hydroxyphenyl)-isoquinoline chelate. In all other cases most of the chelation occurred in a region of metal hydrolysis and hence were not completely calculable. However, sufficient data were obtained to permit reliable determination of part of the $\bar{n}$ *vs.* pR curve and thereby to permit designation of the metal stability sequence as Cu > Co > Zn > Ni. This order suggests the presence of a steric effect similar to that which was found in the 8-hydroxyquinaldinates. The greater basicity of this reagent as compared with oxine should lead to comparatively greater chelate stability. Actually the chelates of this reagent are far less stable than the oxinates. This would seem to show that at least for reagents analogous to 8-hydroxyquinoline 5-membered ring chelates are more stable than 6-membered ring chelates.

Of the trivalent metal ions, those of the rare earths are least susceptible to hydrolysis. For this reason, La(III) and Ce(III) were chosen for study. K_1 values for the Ce(III) chelates of oxine and 8-hydroxyquinaldine illustrate the very pronounced blocking effect of the 2-methyl group. Qualitatively, it has been observed that the same tendency is also present in the La(III) chelates of these reagents. For the transition metals it has been shown that there is an increase in chelate stability as the transition electron shell becomes more completely filled. The stability constants for La(III) and Ce(III) chelates of oxine indicate that a similar sequence is probable in the inner transition series. This tendency might also be expected from the absorption sequence of rare earth citrate complexes on an ion exchange column where the stability of the complex is assumed to be inversely related to the absorption on the exchange column.[21]

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(19) R. G. Charles and H. Freiser, in press.

(20) L. Van Uitert, Ph.D. Thesis, Pennsylvania State College, 1951.

(21) B. H. Ketelle and G. E. Boyd, THIS JOURNAL, **69**, 2800 (1947).