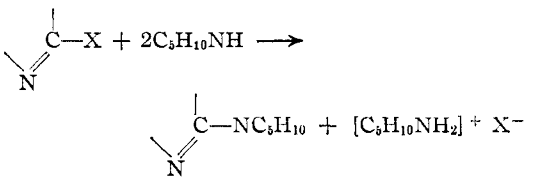
basic than the 2-piperidinoheterocyclic product, the proton is exchanged from one base to the other. The over-all reaction is therefore


(2)

Since the main electrical effect activating the α-carbon to nucleophilic attack is the +E effect of imine nitrogen, all of the compounds (I to VI) would be expected to behave similarly, the extent to which halogen activation occurs in any particular case depending on the amount of imine character of the C=N bond, and on the electrical effects of the halogen substituent and of the other ring atoms.

It is clear that the reactivity of the halogen in replacement with piperidine is proportional to the magnitude of the positive charge which can be generated on the substituted ring carbon at the moment of attack. This implies, of course, that the slow, rate-determining step is the coördination of the piperidine nitrogen to the acid carbon and the establishment of the activated complex. Hence, any factors which increase this positive charge would be expected to increase the rate of reaction. This implies that the reaction should be of the S_N2 type, which is entirely reasonable. The same conclusion is also indicated by the "aromatic nature" of the nuclear bound halogen.[18]

While we wish to postpone a thorough discussion of the present results until data on further related structures can be included, we think it is interesting to point out that halogen attached to the 2-position of quinoline is more easily replaced by nucleophilic reagents than that attached to the 2-position of pyridine. One might expect therefore that hydrogen situated on the 2-position of pyridine would more easily be replaced by electrophilic reagents than the 2-hydrogen of quinoline. So far as is known, the above conclusion cannot be proved nor disproved empirically because typical electrophilic reagents never substitute either of those positions preferentially under comparable conditions. It is interesting to discover, however, that qualitatively the same result has been calculated by Longuet-Higgins and Coulson[19] by the method of molecular orbitals. In the same way we might conclude that the effective electron density at the 2-position of thiazole is greater than that at the 2-position of benzothiazole. This conclusion is consistent with the calculated relative electron densities at those positions as published by Pullman and Metzger.[20]

[18] That there is basis for an alternative conception is proposed by Berliner, Quinn and Edgarton (ref. 4).

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

[20] Pullman and Metzger, *Bull. soc. chim. France*, 1021 (1948).

BETHLEHEM, PA. RECEIVED MARCH 21, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF RADIATION BIOLOGY, SCHOOL OF MEDICINE AND DENTISTRY, UNIVERSITY OF ROCHESTER]

The Beryllium: Citrate System. I. Dialysis Studies in Alkaline Solution[1]

BY ISAAC FELDMAN, W. F. NEUMAN, ROBERT A. DANLEY AND JEAN R. HAVILL

Dialysis–equilibrium studies of the beryllium:citrate system in bicarbonate buffer showed that the maximum molar ratio in which beryllium and citrate ions combine to form a stable, soluble complex at *p*H 8.25 μ equaling 0.1, and at about 10^{-3} *M* derylium is two. The effect of *p*H and of the order in which citrate and bicarbonate are added to beryllium is discussed.

To aid in the elucidation of the toxicology of beryllium,[2] it is desirable to study the reaction of beryllium with biologically important substances in aqueous medium, particularly in slightly alkaline solution. It has been shown[3,4] that the reaction of beryllium with citrate ions may be of prime importance.

Information in the literature concerning the complexing of beryllium by citrate is of a qualitative nature only. Thomas and Miller,[5] by investigating the effect of various potassium salts on the *p*H and conductance of beryllium hydrosols, concluded that citrate ions have a greater tendency to coördinate with beryllium than do the conjugate bases of dicarboxylic acids, of monocarboxylic acids, or of mineral acids other than phosphoric. This conclusion was confirmed by Kosel and Neuman[4] who carried out potentiometric titrations of equimolar mixtures of beryllium sulfate and various organic acids.

In this paper we have applied the method of continuous variations[6,7] to the dialysis–equilibrium technique of Klotz[8] to show that in alkaline solution the maximum molar ratio in which beryllium and citrate ions combine to form a slightly dissociated, soluble complex ion is two.

Experimental

Materials.—The beryllium chloride stock solution was prepared from pure beryllium metal and standardized according to the directions of Underwood and Neuman[9] with

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[1] This paper is based on work performed under contract with the United States Atomic Energy Commission at the University of Rochester Atomic Energy Project, Rochester, New York. Presented before the Division of Physical and Inorganic Chemistry of the American Chemical Society at Chicago, September, 1950.

[2] J. K. Scott, W. F. Neuman and R. Allen, *J. Biol. Chem.*, **182**, 291 (1950).

[3] I. Feldman, W. F. Neuman, R. A. Danley and J. R. Havill, Univ. of Rochester Atomic Energy Project Report No. UR-59 (1949).

[4] G. E. Kosel and W. F. Neuman, *ibid.*, Report No. UR-106 (1950).

[5] A. W. Thomas and H. S. Miller, THIS JOURNAL, **58**, 2526 (1936).

[6] P. Job, *Ann. Chim.*, **11**, 97 (1936).

[7] W. C. Vosburgh and G. R. Cooper, THIS JOURNAL, **63**, 436 (1941).

[8] I. M. Klotz, F. M. Walker and R. B. Pivan, *ibid.*, **68**, 1486 (1946).

[9] A. L. Underwood and W. F. Neuman, *Anal. Chem.*, **21**, 1345 (1949).

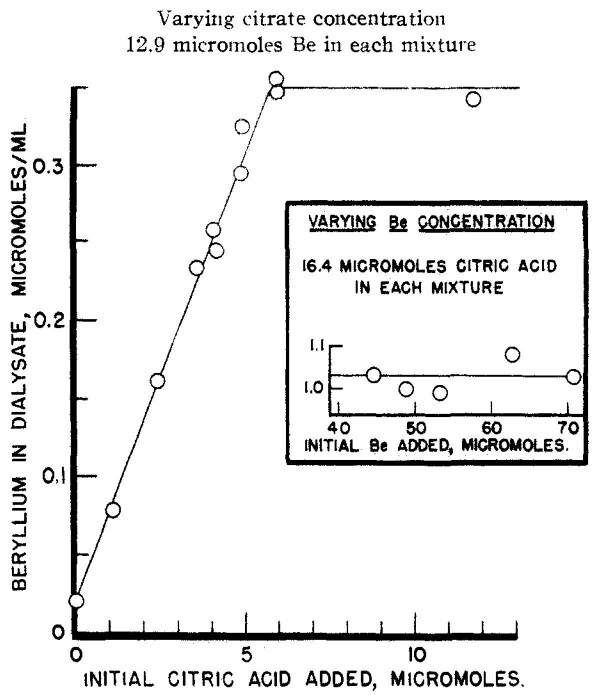

Fig. 1.—Dialysis of beryllium citrate-bicarbonate-hydroxide system. After dialysis for four days at room temperature, equilibrium *p*H was 8.4 ± 0.1. Total volume of system was 35 ml. Sodium bicarbonate buffer concentration was 0.025 *M*.

the modification that the final solution contained only about 2% excess hydrochloric acid. All other chemicals were Baker C.P. Analyzed grade. The citric acid stock solution was checked by titration with sodium hydroxide.

Analysis for Beryllium.—Beryllium was determined by the alkannin method.[9] Preliminary experiments, however, demonstrated that the presence of citrate decreased the color intensity. To minimize this error, standards were prepared containing an amount of citrate equal to that in the unknown being analyzed.

***p*H Adjustment.**—In the preliminary experiments, 0.5% potassium hydroxide was added to each mixture until the *p*H was raised to 8.1, as measured by a Beckman model G *p*H meter. During the course of dialysis, the *p*H rose to 8.3–8.5. Later, CO_2-free sodium hydroxide was used for *p*H adjustment and the solutions were kept in glass-stoppered cylinders sealed with paraffin. In these cases, the *p*H was constant within the range 8.22 to 8.28 throughout the experiment.

Examination of the two sets of data indicated that *p*H variation within the range 8–8.5 and the variation in carbon dioxide did not significantly affect the results.

Dialysis–Equilibrium Technique.—Dialysis bags were prepared from Visking seamless cellophane tubing, 19 mm. in diameter. These cellophane bags containing 10 ml. of the sodium bicarbonate buffer at the proper *p*H were suspended in cylinders containing 25 ml. of solution prepared by mixing the appropriate amounts of beryllium chloride, citric acid and bicarbonate buffer and raising the *p*H to the values reported below. The dialysis was allowed to proceed, with occasional shaking by hand, for the time indicated. Preliminary experiments showed that four days was sufficient time for the attainment of equilibrium. The *p*H and beryllium concentration of each dialysate were then determined.

Method of Continuous Variations.—A series of beryllium chloride–citric acid mixtures was prepared in such a way that the molar ratio Be/Be + citric acid varied from zero to one but the sum of the molar concentrations (Be + citric acid) remained constant. Five milliliters of 1.0 *M* sodium chloride to assure constant ionic strength and 10 ml. of 0.06 *M* sodium bicarbonate to serve as a buffer were added. These mixtures were adjusted to *p*H 8.25 ± 0.03 with 0.3% CO_2-free sodium hydroxide and diluted to a volume of 30 ml., the *p*H being rechecked after dilution. Each mixture was then dialyzed against 10 ml. of 0.02 *M* sodium bicarbonate for four or for five days at 30°. The sum of the molar concentrations of beryllium chloride and citric acid of the entire system was then 1.0×10^{-3} *M* for each mixture.

Results and Discussion

The results of the preliminary experiments may be summarized: (1) In the absence of solubilizing ions (bicarbonate or citrate) beryllium could not be detected in the dialyzate. This suggests that the beryllium precipitated in an undialyzable form near *p*H 8. (2) In the presence of 0.025 *M* bicarbonate and at a *p*H of at least 8.0 but not greater than 8.5, regardless of the initial beryllium concentration, the concentration of dialyzable beryllium was 0.02 micromole/ml. (3) A series of mixtures in 0.025 *M* sodium bicarbonate at *p*H 8.3–8.5 was prepared in which the initial beryllium concentration was kept constant but the initial citric acid concentration was varied. With increasing citrate the amount of dialyzable beryllium increased linearly, as is seen in Fig. 1. At a Be/Citrate molar ratio of 2.2, almost all of the beryllium was dialyzable. When the reverse experiment was performed, *i.e.*, increasing amounts of beryllium were added to a constant amount of citrate, the ratio of Be/citrate in the dialyzate remained constant at about 2.2 (see inset, Fig. 1).

It was evident from these studies that in a 0.025 *M* bicarbonate buffer containing citrate ions within the *p*H range 8.0–8.5, if the soluble beryllium concentration is large compared to 0.02 micromole/ml., the concentration of dialyzable beryllium is a measure of the concentration of complexed beryllium.

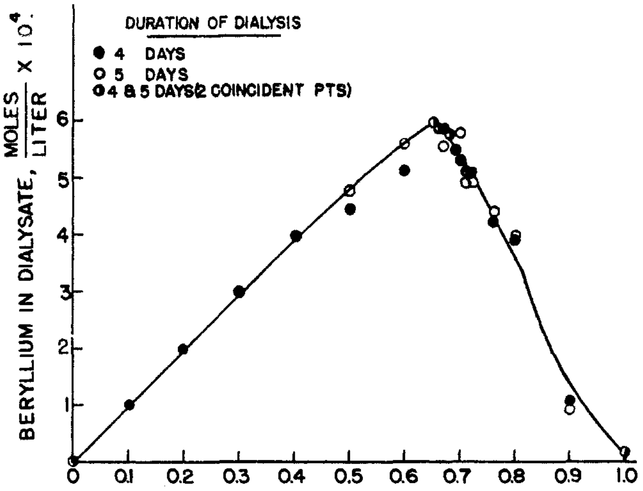

Fig. 2.—Application of method of continuous variations: *p*H 8.25 ± 0.03; temp., 30.0°; total (Be + citrate) concentration in each mixture, 1.0×10^{-3} *M*; total volume of each system, 40.0 ml.; ionic strength, 0.1; $NaHCO_3$ concentration, 0.02 *M*.

The results of the application of the method of continuous variations to the dialysis–equilibrium data at *p*H 8.25 ± 0.03 are presented in Fig. 2. It is clear that the maximum concentration of complexed beryllium was obtained when the initial molar ratio Be/Be + citric acid was 0.65, which is sufficiently close to the theoretical value of 0.67 to establish the existence of a stable, soluble beryllium–citrate complex at *p*H 8.25 having a beryllium to citrate combining ratio of two. Undoubtedly, none of the beryllium in this complex is ionic since any ionic beryllium would precipitate at this *p*H.

It should be noted that this method gives no information concerning the existence of a complex having a Be/citrate ratio less than two, but only establishes the maximum number of beryllium atoms bound by one citrate ion, since only the total concentration of dialyzable beryllium, rather than a physical property of one particular complex, is measured.

The stability of the 2:1 complex decreases rapidly above *p*H 8.5. This *p*H effect is shown by Fig. 3. The increased diffusibility of beryllium at *p*H 11 is probably due to the formation of beryllate ions.[10]

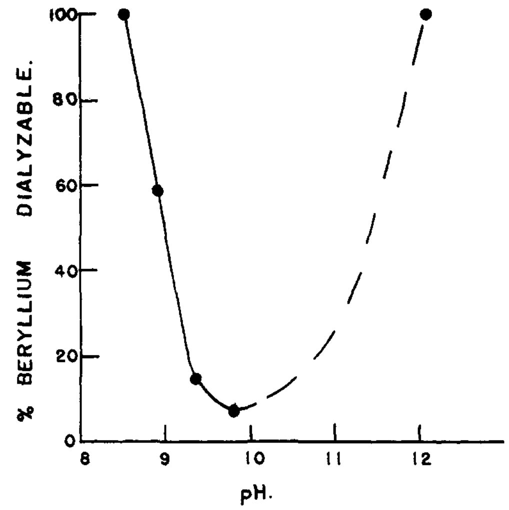

Fig. 3.—Effect of *p*H on diffusibility of beryllium in mixture containing beryllium and citrate in molar ratio of two: total Be concentration, 1.9 × 10^{-4} *M;* ionic strength ($NaHCO_3$ concentration), 0.025 *M;* room temperature; duration of dialysis, 4 days.

The complexing action of citrate ions on beryllium in the system beryllium chloride–citrate–bicarbonate at *p*H 8 is dependent on the order of mixing the constituents. The maximum concentration of dialyzable beryllium reported above, 94 ± 4%, was obtained only when the beryllium chloride and citric acid were mixed *before* the solution was made alkaline. When sodium citrate was added to beryllium chloride in the molar ratio of Be_2R and the *p*H was raised to 8.3, duplicate experiments showed that only 82 ± 3% of the beryllium was dialyzable after four days. It seems, therefore, that even though the citrate is a very strong complexer for beryllium and even though the citrate/hydroxyl ratio in these mixtures was 10^5, beryllium reacts more rapidly with hydroxyl ions than with citrate ions but that in the presence of sufficient citrate the beryllium hydroxide is solubilized in time. As was to be expected, then, when citric acid was added to a mixture of beryllium chloride in 0.025 *M* bicarbonate and the *p*H was raised to 8.3, slightly less beryllium was dialyzable, 77 ± 5%.

ROCHESTER, N. Y. RECEIVED MARCH 15, 1951

[10] N. V. Sidgwick, "Chemical Elements and Their Compounds," Oxford University Press, London, 1950, p. 202.

[CONTRIBUTION FROM THE INSTITUTE FOR ATOMIC RESEARCH AND THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

The Structure of Thorium Dicarbide by X-Ray and Neutron Diffraction[1]

BY ELTON B. HUNT AND R. E. RUNDLE

Good-X-ray powder diagrams show that ThC_2 is not tetragonal, as previously reported. Single crystals have been obtained, and the lattice has been established as C-centered monoclinic with $a_0 = 6.53$, $b_0 = 4.24$, $c_0 = 6.56$ Å., $\beta = 104°$, $Z = 4$. The space group is C2/*c* or C*c*. Thorium positions, determined by X-ray diffraction, are the same in either group, and satisfactory carbon positions have been found in C2/*c* by neutron diffraction.

The structure contains C_2 groups, but the C–C distance is about 1.5 Å., so that acetylene ions are eliminated. The arrangement of thoriums about the C_2 group combines ethane-like, ethylene-like and acetylene-like character, and considerable covalent character for the Th–C bonds is indicated.

Introduction

The tetragonal structure proposed for ThC_2 by von Stackelberg[2] on the basis of powder diffraction data has been one of the classical type structures for the dicarbides for 20 years. In suggesting carbon positions for ThC_2, von Stackelberg assumed $C_2^=$ ions were involved, and it has generally been supposed that these were acetylene ions, such as those found in CaC_2.

Good powder data show that the correct structure for ThC_2 cannot be based on a tetragonal lattice.[3] Recently, with the help of Mr. F. J. Modic and Dr. Premo Chiotti we have been able to secure single crystals, and have found the true lattice and thorium positions by X-ray diffraction. In addition, rough carbon parameters have been determined by neutron diffraction.

Preparation of Single Crystals.—Thorium dicarbide single crystals were prepared by the extended heating of thorium metal surrounded by graphite at 2000–2500°. A ThC_2 diffusion band forms in such samples, and in favorable cases crystals as large as a mm. in cross section were found. Most crystals were highly twinned, but upon polishing and optical observation of lumps from these

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[1] Contribution No. 111 from the Institute for Atomic Research and Department of Chemistry, Iowa State College, Ames, Iowa. Work performed in the Ames Laboratory of the Atomic Energy Commission.

[2] von Stackelberg, *Z. physik. Chem.*, [B] 9, 487 (1930).

[3] N. C. Baenziger, unpublished research, Ames Laboratory of the A.E.C.