curve for this substance, so attempts were made to determine the curve potentiometrically. However, the species PH_4^{++} is a sufficiently strong acid that the complete titration curve could not be observed in water, aqueous methanol, or aqueous dioxane. The anhydrous solvents could not be used because the LiCl required to maintain a constant high ionic strength for the accurate determination of curve shape was not sufficiently soluble in them.

Discussion

Although acid–base and oxidation–reduction systems have traditionally been considered from different viewpoints, the exact analogy in principle between the two classes has been discussed by various authors.[9,10] For both systems, the titration curves (potential or *p*H plotted against per cent. reaction) form a family in which the individual members can be identified by their midpoint slopes. Michaelis demonstrated the existence of this family of curves both experimentally and theoretically in his studies of the semiquinones.[11] He showed that the titration curves of lowest midpoint slope, for reactions in which two electrons are transferred simultaneously, are replaced by curves whose midpoint slope increases as conditions are chosen which increase the stability of the semiquinone intermediate in the reaction. The extreme case is the two-step titration curve (with very steep midpoint slope) observed for very stable semiquinone systems.

In the case of the dibasic acids, successive stages of proton transfer almost always occur with increasing difficulty because of the accompanying ionic charge accumulation. As a result, the intermediate stage of ionization is stable and reaches a maximum concentration exceeding 50% that of the total acid–base system at the titration midpoint, and $K_1 >> K_2$. Only in the limiting case of dibasic acids in which the functional groups are separated by long carbon chains do the protons dissociate independently. The intermediate then has the same stability as the completely ionized or completely un-ionized forms, and reaches a maximum concentration of 50% that of the total acid–base system at the midpoint of the titration.[6,10] The acid–base reactions given by equations (1) and (2) *cannot* be of this type, with $K_1 = 4K_2$, since the concentration of intermediate has been shown to be too small to detect, and certainly less than the 50% maximum expected in such a reaction. (If $K_1 = K_2$, as has been assumed previously for the porphyrins, the concentration of PH_3^+ would still reach a maximum equal to 33% that of the total acid–base system.) Thus the intermediate PH_3^+ is less stable than PH_4^{++} or PH_2, and in consequence the second proton is transferred more readily than the first. (The transfer is simultaneous if the concentration of PH_3^+ is zero.) In this case, $K_1 << K_2$, and the individual constants have little meaning. The significant constant is that for the overall reaction, equation (5), given by $K = K_1K_2$.

One previous example has been reported of proton transfer leading to an intermediate of lower stability, so that the second proton is transferred more readily than the first. Schwarzenbach[10] described a dibasic acid in which the maximum concentration of intermediate was only 22% at the titration midpoint, but his system was too unstable for complete reversibility.

Consideration of the oxidation–reduction analogy has led to the expectation that the intermediate PH_3^+ will be less stable than either PH_4^{++} or PH_2. This is confirmed by consideration of the structures which might reasonably contribute to resonance in the porphyrin system. Assuming fixed N–H bonds, two uncharged and four separated charge structures have been proposed for PH_2, and twelve with no charge separation for PH_4^{++}.[12] The number of such structures depends upon the twofold axis of symmetry in PH_2, and the fourfold axis in PH_4^{++}. Loss of these symmetry elements in PH_3^+ reduces the number of structures contributing to its resonance, and results in its relatively lower stability.

The argument can be repeated for the ionization of PH_2 to give $P^=$, and one would expect in this case also a smaller stability for PH^- than for the other species. (The very close similarity of the absorption spectra of PH_4^{++} and $P^=$ in the case of etioporphyrin[12] indicates that they must be similar electronically.) The ionization of PH_2 could not, however, be studied conveniently by the method of continuous variations, because the *pK* value reported by McEwen[5] would require that the solutions of both porphyrin and hydrogen ion be of the order of 10^{-16} *M* concentration, too low for spectrophotometric work.

Although variation of substituents on the porphyrin ring will alter the magnitude of the acid dissociation constants, their distribution would not be greatly changed. It thus seems probable that the simultaneous dissociation reported here is general for the porphyrin ring system (but not necessarily for reduced ring systems such as the chlorins).

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[9] M. Schubert, *Ann. N. Y. Acad. Sci.*, **40**, 111 (1940).

[10] G. Schwarzenbach and R. Sulzberger, *Helv. Chim. Acta*, **26**, 453 (1943).

[11] L. Michaelis and M. P. Schubert, *Chem. Revs.*, **22**, 437 (1938).

[12] J. G. Erdman and A. H. Corwin, THIS JOURNAL, **68**, 1885 (1946).

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Studies on Coördination Compounds. VIII. Some Factors Concerning the Effect of the Terminal Groups on the Chelating Abilities of β-Diketones

BY LEGRAND G. VAN UITERT[1] AND W. CONARD FERNELIUS

RECEIVED FEBRUARY 13, 1953

The general relationships between the stability constants of the β-diketones and their terminal groups have been discussed in a previous paper.[2] Additional constants are given herein which enable a further clarification of the relationships involved to be made.

Experimental

The β-diketones, other than those mentioned previously,

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[1] Union Carbide and Carbon Corporation Fellow, 1951–1952; Bell Telephone Laboratories, Murray Hill, New Jersey.

[2] L. G. Van Uitert, W. C. Fernelius and B. E. Douglas, THIS JOURNAL, **75**, 457 (1953).

were prepared in this Laboratory by Mrs. Lillian Berg. The $NiCl_2$ and $Ce(ClO_4)_3$ employed were reagent grade.

The experimental procedures were those previously employed with the exception that the chelate compound formation constants for cerium were measured using 1×10^{-4} mole of $Ce(ClO_4)_3$ and 6×10^{-4} mole of chelating agent in 100 ml. of solution. Measurements were made in 75 volume per cent. dioxane–25 volume per cent. water (mole fraction of dioxane, n_2, = 0.380) at 30°.

Discussion

Previously it has been observed[2] that within certain groups of β-diketones there exists a linear relationship between the negative logarithms of the acid dissociation constants (pK_D values) of the β-diketones and their formation constants (log K_f values) with a given metal ion. These principal groups consist of a series of β-diketones with aromatic rings as terminal groups (containing combinations of the groups: 2-thienyl, 2-furyl and phenyl) and a series having one methyl group. The values plotted in Figs. 1 and 2 for Ni^{++} and Ce^{+++}, respectively, show that each of these groups may be subdivided.

The chelation constants for the β-diketones containing methyl groups with nickel(II), as shown in Fig. 1 (refer Table I), resolve into two subgroups; one consisting of those having one aromatic group and the other having the terminal group series: CH_3, C_2H_5, $CH(CH_3)_2$, $CH_2CH_2Si(CH_3)_3$ and $C(CH_3)_3$ where log $K_{f_{av}}$ and pK_D increase in that order. 2-Methyl-3,5-heptanedione falls on the latter line. Within the limits that the above series of β-diketones have equivalent keto–enol ratios (50% enol or better),[3] the observed inductive effects are in the order to be expected from the group electronegativities.[4]

TABLE I

CHELATION DATA FOR NICKEL(II) EMPLOYING 0.01 *M* $NiCl_2$ SOLUTION

Symbol in Fig. 1	Chelating agent	pK_D	log K_{f_1}	log K_{f_2}
⦶	2,4-Pentanedione	12.70	9.37	8.03
⊖	2,4-Hexanedione	13.20	9.60	8.30
⦸	2-Methyl-3,5-hexanedione	13.40	9.55	8.60
⊘	2,2-Dimethyl-2-sila-5,7-octanedione	13.50	9.65	8.70
●	2-Methyl-3,5-heptanedione	13.95	9.86	9.03
⊕	2,2-Dimethyl-3,5-hexanedione	14.20	9.94	9.19

◔2, ⊙3, ◒4, ◕6, ◓7, ◑8, ◐9 (see Table II).

TABLE II

CHELATION DATA FOR CERIUM(III) EMPLOYING 0.001 *M* $Ce(ClO_4)_3$ SOLUTION

No. in Fig. 2		pK_D	log K_{f_1}	log K_{f_2}	log K_{f_o}
1	Di-2-furoylmethane	12.10	10.61	9.59	7.87
2	2-Thenoyl-2-furoylmethane	12.30	10.60	9.81	8.17
3	2-Thenoylacetone	12.35	10.05	9.40	7.74
4	Di-2-thenoylmethane	12.63	10.65	10.20	8.87
5	2,4-Pentanedione	12.70	9.86	8.53	6.91
6	Benzoylacetone	12.85	10.09	9.33	7.62
7	2-Furoylbenzoylmethane	12.95	10.82	10.21	8.40
8	2-Thenoylbenzoylmethane	13.30	11.02	10.57	9.07
9	Dibenzoylmethane	13.75	10.99	10.54	8.85
10	2,2-Dimethyl-3,5-hexanedione	14.20	10.60	10.20	8.50

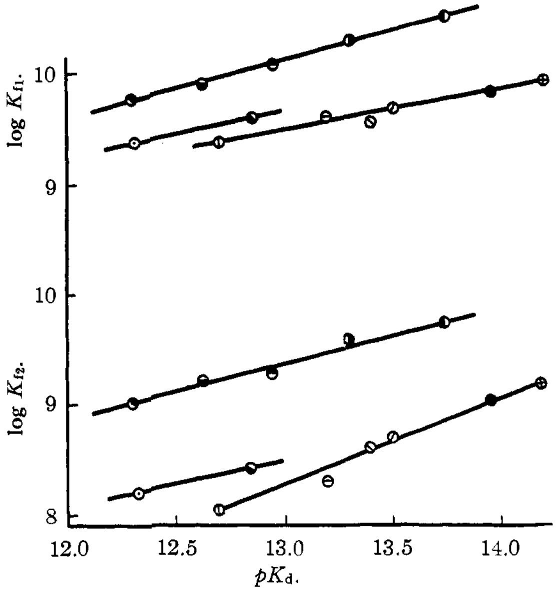

Fig. 1.—Nickel(II) chelation constants *vs.* β-diketone pK_d values. (See Table I).

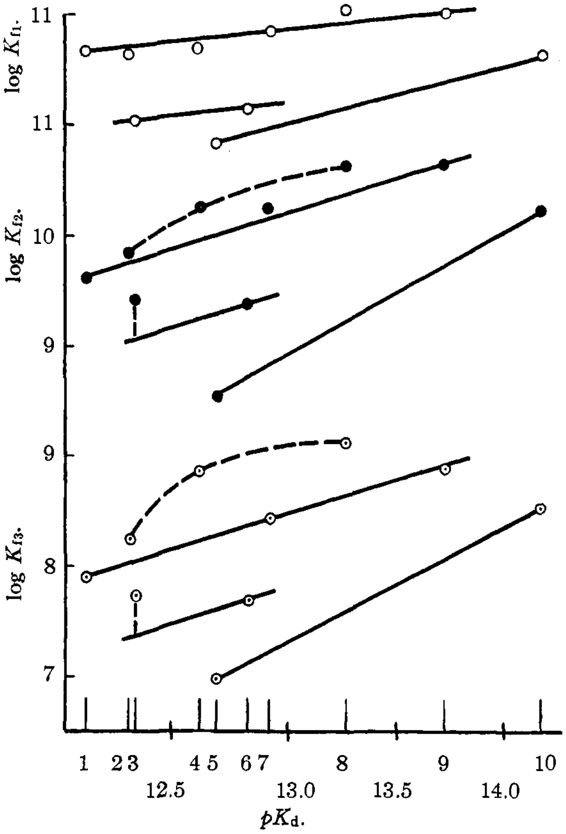

Fig. 2.—Cerium(III) chelation constants *vs.* β-diketone pK_d values. Numbers refer to compounds listed in Table II: O, first constant; ●, second constant; ⊙, third constant.

Data for the points in Fig. 1 that are not given in Table I have been given previously.[2] However,

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[3] L. G. Van Uitert, with C. G. Haas, Jr., W. C. Fernelius and B. E. Douglas, THIS JOURNAL, **75**, 455 (1953).

[4] D. Walsh, *J. Chem. Soc.*, 401 (1948).

the β-diketones employed in obtaining the previous data have been used again in obtaining the data for Ce(III) given in Table II. So, for convenience of comparison of the points in Fig. 1, the symbols for the points representing the previously reported data are given at the bottom of Table I along with the Table II guide numbers for the β-diketones involved.

In Fig. 2, it is seen that there is essentially a linear relationship between pK_{D} and $\log K_{f_1}$, the first chelate compound formation constant, for the series of β-diketones containing two aromatic rings with cerium(III). However, upon the addition of a second chelating group to cerium(III), those β-diketones which contain a thienyl group have slightly higher stability constants than would be expected from the positions of the other β-diketones. The same relationship, but of greater magnitude, is noted for the third constants. Since the effect is most pronounced for the third constants, in which case the cerium is probably surrounded by the six oxygen atoms of the three attached β-diketones in an octahedral fashion, it would appear that the close proximity of the bulky sulfur atoms to the central metal ion aids in shielding the coördination centers from interaction with the solvent.

Acknowledgment.—The authors gratefully acknowledge financial support furnished for this work by the United States Atomic Energy Commission through Contract AT(30-1)-907.

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COMMUNICATIONS TO THE EDITOR

ACHROMYCIN.[1] SYNTHETIC STUDIES. III. SYNTHESIS OF 3-AMINO-D-RIBOSE, A HYDROLYTIC PRODUCT

Sir:

One of the hydrolysis products of Achromycin is a 3-aminopentose, either 3-aminoribose or 3-aminoxylose. This is the first known 3-amino sugar and first known aminopentose to exist in a natural source.[2] The structure has now been proven to be 3-amino-D-ribose by synthesis from L-arabinose via β-methyl 2,3-anhydro-L-ribopyranoside (I).[3]

Treatment of I with ammonium hydroxide at 100° under pressure afforded a 65% yield of β-methyl-3-amino-L-xylopyranoside, m.p. 191–192° dec., $[\alpha]^{34}\mathrm{D}$ +61.4° (1% in H_2O). *Anal.* Calcd. for $C_6H_{13}NO_4$: C, 44.2; H, 8.03; N, 8.60. Found: C, 44.2; H, 8.07; N, 8.93. Acetylation with aqueous acetic anhydride formed 98% of β-methyl 3-acetamino-L-xylopyranoside (II), m.p. 194–195°, $[\alpha]^{24}\mathrm{D}$ +64.4° (2% in H_2O). *Anal.* Calcd. for $C_8H_{15}NO_5$: C, 46.8; H, 7.36; N, 6.83. Found: C, 46.4; H, 7.53; N, 6.74. Since II failed to consume periodate, the alternate structure, β-methyl-2-amino-L-arabinopyranoside, which could be formed on ring opening of I, was eliminated.[4]

When II was treated with methanesulfonyl chloride in pyridine, an 83% yield of β-methyl-2,5-dimesyl-3-acetamino-L-xylopyranoside (III), m.p. 150°, $[\alpha]^{24}\mathrm{D}$ +18.8° (2% in pyridine), was obtained. *Anal.* Calcd. for $C_{10}H_{19}NO_9S_2$: C, 33.2; H, 5.30; N, 3.88. Found: C, 33.7; H, 5.43; N, 4.06. Reaction of III with sodium acetate in boiling 95% alcohol caused elimination of one mesyl group with inversion via an oxazoline.[5] Work-up by acetylation gave a 66% yield of β-methyl 2-acetyl-3-acetamino-4-mesyl-L-lyxopyranoside, m.p. 171–172°, $[\alpha]^{24}\mathrm{D}$ −11.0° (1.4% in pyridine). *Anal.* Calcd. for $C_{11}H_{19}NO_8S$: C, 40.6; H, 5.89; N, 4.31. Found: C, 40.9; H, 5.78; N, 4.22. Further treatment with sodium acetate in 95% boiling Methyl Cellosolve eliminated the second mesyl group with inversion to an all *cis*-configuration. Acetylation then afforded 70% of α-methyl-2,4-diacetyl-3-acetamino-D-ribopyranoside, IV, m.p. 116–117°, $[\alpha]^{24}\mathrm{D}$ +93.7° (1.6% in $CHCl_3$). *Anal.* Calcd. for $C_{12}H_{19}NO_7$: C, 49.8; H, 6.62; N, 4.85. Found: C, 49.8; H, 6.84; N, 4.73. Direct treatment of III with sodium acetate in 95% Methyl Cellosolve caused elimination of both mesyl groups with inversion. Acetylation afforded 70% yield of IV. Hydrolysis of IV with boiling 1% hydrochloric acid gave 83% of 3-amino-D-ribose hydrochloride, m.p. 160° dec., $[\alpha]\mathrm{D}$ −25.0° (2% in H_2O). *Anal.* Calcd. for $C_5H_{11}NO_4{\cdot}HCl$: C, 32.4; H, 6.52; N, 7.55. Found: C, 32.6; H, 6.82; N, 7.79. Comparative I.R. spectra showed this compound to be identical with the 3-aminopentose obtained on hydrolysis of Achromycin.[2]

It is interesting to note that this synthesis proceeds through all four pentose configurations. Derivatives of 3-amino-D-allose also have been

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[1] Achromycin is the American Cyanamid Co. trademark for the antibiotic, Puromycin.

[2] C. W. Waller, P. W. Fryth, B. L. Hutchings and J. H. Williams, THIS JOURNAL, **75**, 2025 (1953).

[3] S. Mukherjee and A. R. Todd, *J. Chem. Soc.*, 971 (1947).

[4] It should be noted that a *trans* configuration of amine and hydroxyl is obtained by Walden inversion. Opening of the oxide ring of α-methyl-2,3-anhydro-4,6-benzylidene-D-mannopyranoside with ammonia has been shown by W. H. Myers and G. J. Robertson [THIS JOURNAL, **65**, 8 (1943)] to give α-methyl-3-amino-4,6-benzylidene-D-altropyranoside and α-methyl-2-amino-4,6-benzylidene-D-glucopyranoside.

[5] Although this is the first known example of this reaction in the carbohydrate field, the reaction has been described with *trans*-acetaminocyclohexanol-2-tosylate by G. E. McCasland, R. K. Clark and H. E. Carter in THIS JOURNAL, **71**, 641 (1949).