

Figure 1.—Differential thermal analysis and thermogravimetric analysis of $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$, sample a; testing rate $5^\circ/\text{minute}$.

sufficient drying) and the relationship between these two materials seemed worthy of reexamination. The material usually designated $\text{Cu}(\text{IO}_3)_2 \cdot \text{H}_2\text{O}$ was indeed found to be identical with bellingerite, $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$, the structure of which has symmetry $P\bar{1}$ (triclinic) with unit cell $a = 7.228 \text{ \AA}$, $b = 7.829 \text{ \AA}$, $c = 7.940 \text{ \AA}$, $\alpha = 105.039^\circ$, $\beta = 96.985^\circ$, and $\gamma = 92.942^\circ$.^{12,18}

Experimental Section

Precipitations were carried out by mixing 0.1 mol of CuSO_4 in 100 ml of H_2O with 0.2 mol of HIO_3 or KIO_3 in 100 ml of H_2O with continuous agitation at 3° , at room temperature, or at the boiling point. After 0.5 hr the product was filtered, washed with water at the same temperature, and air-dried. Some preparations were also dried at 110° .

Crystal growth was carried out by the use of the HIO_3 -boiling-point-precipitated compounds. Saturated solutions (~ 2 l.) were prepared in water at 47° and at the boiling point and in concentrated nitric acid at its boiling point (about 120°) and permitted to evaporate slowly over a 2-week period. In the case of the boiling mixtures evaporation was permitted under reflux conditions at a controlled¹⁴ rate of about 100 ml/day until about 200 ml remained and several grams of ~ 1 -mm crystals was harvested. These crystals were used as seeds in repeat runs and crystals up to 10 mm resulted. A very fine crystalline powder was obtained from water at 47° .

A Du Pont 900 differential thermal analyzer (dta) and the thermogravimetric analyzer (tga) attachment were used with flowing nitrogen or air atmospheres (no differences) and a heating rate of $20^\circ/\text{min}$ or $5^\circ/\text{min}$ (no significant difference). X-Ray powder diffraction patterns were taken with vanadium-filtered $\text{Cr K}\alpha$ radiation in a 114.6-mm diameter Straumanis-type Norelco camera. Copper analyses were performed by dissolving the samples in HCl and using atomic absorption spectrometry determinations with reference standards.

Results and Discussion

All samples made, which cover essentially all of the preparative techniques used previously, gave powder X-ray diffraction patterns identical with that of each other and with that of the mineral bellingerite, $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$.¹²

The dta and tga results shown in Figure 1 were typical of the high-temperature crystal growth for which the water loss occurred at 290 – 300° and the weight loss at that temperature corresponded to 2.7–2.9 wt % H_2O , i.e., to 1.92–2.06 H_2O on the bellingerite

TABLE I

	% Cu^a	% H_2O^b
Precipitate using HIO_3 and boiling		
H_2O	15.45	2.9
Crystals grown from boiling H_2O	15.10	2.7
Crystals grown from boiling HNO_3	14.97	2.85
Calculated for $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$	14.94	2.82

^a Estimated accuracy ± 0.10 . ^b Estimated accuracy ± 0.1 .

formulation. Decomposition of the iodate began at about 450° .

A sample of natural bellingerite from the type locality Chuquicamata, Chile, from the Harvard University collection gave a dta pattern essentially identical with that of Figure 1. Another sample from the same location from the Smithsonian Institution showed an additional endotherm at about 380° ; the presence of an extra phase in the Smithsonian specimen has been previously noted by Kaplan.¹⁸ There was an insufficient amount of this material for further investigation.

Precipitations ranged in water content from 2.9 to 3.6% and main water loss temperature from 135 to 295° ; some water was, however, lost below 100° in these specimens. It was found that incomplete washing, and in particular the presence of free iodic acid, had the effect of lowering the main water evolution temperature. The addition of 5% HIO_3 lowered the water evolution temperature from 295 to 230° .

Analytical results on three high-temperature preparations are given in Table I. These are considered to be the best conditions for the preparation of $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$.

In view of the identity of the X-ray powder diffraction patterns and the excellent analysis results on the slowly grown crystals, the identity of " $\text{Cu}(\text{IO}_3)_2 \cdot \text{H}_2\text{O}$ " with bellingerite, $3\text{Cu}(\text{IO}_3)_2 \cdot 2\text{H}_2\text{O}$, can be considered to be established.

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Synthesis of Tautomeric Schiff Base Complexes and Ketimine \rightarrow Aldimine Conversion Rates of Copper(II) Complexes

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Transamination is one of the key reactions catalyzed by pyridoxal-dependent enzymes.^{2,8} It and other nonoxidative transformations of amino acids effected

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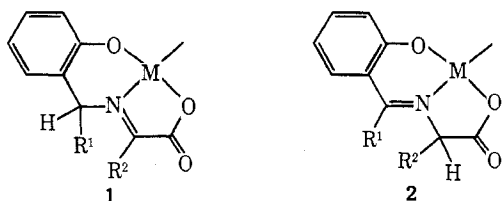
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by these enzymes may be reproduced in model systems containing amino acids, pyridoxal, and metal ions such as Al(III), Cu(II), and Zn(II).³⁻⁶ In the generally accepted mechanism for transamination,⁵⁻⁷ represented by the overall reaction $RCH(NH_2)COOH + R'CO-COOH \rightleftharpoons R'CH(NH_2)COOH + RCOCOOH$, a step of prime importance is the conversion of an initially formed *N*-pyridoxylideneaminoacidato (aldimine) complex, $M(\text{pyr-aa})$, into its 2-pyridoxyliminoacidato (ketimine) form, $M(\text{pym-ka})$. Hydrolysis of the latter affords pyridoxamine and an α -keto acid and completes the first step in the transamination sequence. Reversal of this process, involving formation of $M(\text{pym-ka}')$ from the initially present ketoacid followed by tautomerization and hydrolysis, accomplishes the overall reaction. Studies of the tautomerization process have been approached from the ketimine side, *i.e.*, $M(\text{pym-ka}) \rightarrow M(\text{pyr-aa})$, due to the appreciably greater stability of the aldimine form under ordinary conditions. Tautomerization of ketimine complexes generated in solution has been observed by electronic spectral measurements^{8,9} and by pmr.¹⁰ In view of the importance of ketimine species and their tautomerization reactions in mechanisms for transamination and other transformations in model systems,⁸ we report here the preparation and characterization of the complexes $M(\text{hba-ka})$ (1, $R_1 = H, R_2 = CH_3, CH(CH_3)_2$)



and $M(\text{mhba-ka})$ (1, $R_1 = CH_3, R_2 = CH_3, CH(CH_3)_2$), and several rate determinations of the base-catalyzed process $Cu(\text{hba-ka}) \rightarrow Cu(\text{sal-aa})$ (2, $R_1 = H, R_2 = CH_3, CH(CH_3)_2$) in 95% ethanol. This work is part of our recent studies¹⁰⁻¹³ of Schiff base complexes related to vitamin B₆ catalysis. Complexes of types 1 and 2, rather than those derived from pyridoxamine and pyridoxal, have been employed due to their greater ease of isolation and their higher hydrolytic stability.

Experimental Section

Preparation of Compounds.—*o*-Hydroxybenzylamine (mp 126–127°) and α -methyl-*o*-hydroxybenzylamine (mp 86–87°) were prepared from the corresponding oximes by reduction with sodium in liquid ammonia.¹⁴ In the following preparations of new complexes the quoted water contents were inferred from best fits of the analytical data; independent determinations by weight loss studies were not carried out.

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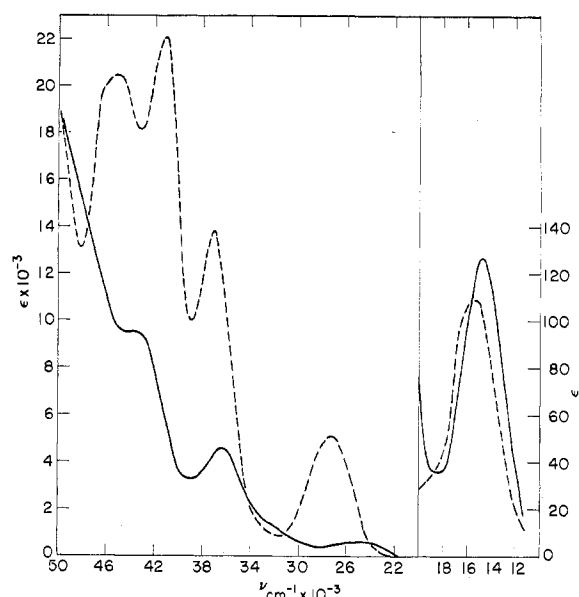


Figure 1.—Electronic spectra of $Cu(\text{sal-L-val}) \cdot \frac{3}{2}H_2O$ (---) and $Cu(\text{hba-ival})$ (—) in 95% ethanol solution.

2-*o*-Hydroxybenzyliminopropionatocopper(II) Monohydrate, $Cu(\text{hba-prop}) \cdot H_2O$.¹⁵—*o*-Hydroxybenzylamine (3.3 mmol) was added to 3.3 mmol of pyruvic acid in 5 ml of water and the solution stirred at 5° for 5 min. At this temperature 20 ml of an aqueous solution containing an equimolar amount of cupric acetate was added dropwise. After an additional 10 min of stirring the light green microcrystalline product was collected and washed with 5 ml of ether; mp 225–226°. *Anal.* Calcd for $C_{10}H_{11}NO_4 \cdot Cu$: C, 44.04; H, 4.04; N, 5.17. Found: C, 44.27; H, 3.85; N, 5.26.

2-*o*-Hydroxybenzyliminopropionatozinc(II) Hemihydrate, $Zn(\text{hba-prop}) \cdot \frac{1}{2}H_2O$.—The Schiff base was prepared by allowing *o*-hydroxybenzylamine (10 mmol) and sodium pyruvate (10 mmol) to react with stirring in 15 ml of anhydrous methanol for 15 min at 25°. The crude base was collected and dried under vacuum at 25°; mp 178–180°. Zinc acetate dihydrate (2.5 mmol) dissolved in 40 ml of methanol was added to a solution of 2.5 mmol of the Schiff base in 75 ml of methanol. After stirring for 2.5 hr, the product was collected and dried at 25° (0.05 mm); mp >300°. *Anal.* Calcd for $C_{10}H_{10}NO_4 \cdot Zn$: C, 45.23; H, 3.77; N, 5.28. Found: C, 45.78; H, 3.61; N, 5.37.

2-*o*-Hydroxybenzyliminoisovaleratocopper(II), $Cu(\text{hba-ival})$.—A procedure analogous to that for $Zn(\text{hba-prop}) \cdot \frac{1}{2}H_2O$ using α -ketoisovaleric acid was employed except that the ligand was not isolated and was reacted with cupric acetate for 30 min. The complex was obtained as bright green microcrystals, mp 229–230°. *Anal.* Calcd for $C_{12}H_{13}NO_4 \cdot Cu$: C, 50.79; H, 4.60; N, 4.96. Found: C, 50.40; H, 4.70; N, 5.02.

***N*-*o*-Hydroxyacetophenoneimino-L-alaninatocopper(II) Monohydrate, $Cu(\text{hac-L-ala}) \cdot H_2O$.**—Potassium hydroxide (1 mmol) in 25 ml of methanol was added to a solution of 1 mmol of L-alanine in 5 ml of methanol. The solution was warmed until all the alanine dissolved, a solution of 1 mmol of *o*-hydroxyacetophenone in 5 ml of methanol was added, and the mixture stirred at 5° for 10 min. Ether (20 ml) was added to precipitate any unreacted alanine and the solution was filtered. To the filtrate was added a solution of 0.9 mmol of cupric acetate in 100 ml of methanol; the reaction mixture was stirred for 2 hr and filtered to remove a small amount of bis(L-alaninato)copper(II). Reduction of the filtrate volume to 5 ml followed by the addition of 10 ml of acetone afforded the crude complex as a deep blue solid. This material was recrystallized from water and dried at 25°, yielding a deep green powdery product, mp 271–273°. *Anal.* Calcd for $C_{11}H_{13}NO_4 \cdot Cu$: C, 46.07; H, 4.54; N, 4.89. Found: C, 45.70; H, 4.44; N, 4.80.

2-(α -Methyl-*o*-hydroxybenzylimino)propionatocopper(II) monohydrate, $Cu(\text{mhba-prop}) \cdot H_2O$.—A procedure analogous to

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TABLE I
 MAGNETIC AND SPECTRAL DATA FOR TAUTOMERIC Cu(II) COMPLEXES

Pair	Complex	μ_{eff} , BM ^a	λ_{max} , cm ⁻¹ (ϵ) ^b
I	Cu(sal-L-ala)·3H ₂ O	1.72	15,500 (111), 27,300 (4,890), 37,310 (12,500), 41,150 (21,100), 45,050 (19,900)
	Cu(hba-prop)·H ₂ O	1.57	14,790 (153), 25,640 (563), 36,230 (4,700), 43,500 (sh) (8,600)
II	Cu(sal-L-val)· ³ / ₂ H ₂ O ^c	1.65	15,600 (109), 27,320 (5,030), 37,040 (13,800), 41,150 (21,900), 45,040 (20,500)
	Cu(hba-ival)	1.39	14,820 (128), 24,880 (597), 36,360 (4,540), 43,480 (9,450)
III	Cu(hac-L-ala)·H ₂ O	1.70	15,820 (101), 27,860 (4,590), 37,590 (11,600), 43,860 (23,400)
	Cu(mhba-prop)·H ₂ O	1.58	14,930 (127), 24,040 (574), 35,970 (4,460), 42,900 (8,500)
	Cu(mhba-ival)· ¹ / ₂ H ₂ O	1.46	15,390 (104), 24,630 (610), 35,970 (5,410), 42,920 (sh) (9,200)

^a Solid state, ~25°. ^b 95% ethanol solution. ^c Data from ref 13.

that for Zn(hba-prop)·¹/₂H₂O was used, except that the complex was precipitated from methanol solution by the addition of isobutyl alcohol and *n*-pentane. The complex was obtained as a green solid after recrystallization from chloroform, mp >350°. Anal. Calcd for C₁₁H₁₃NO₄Cu: C, 46.07; H, 4.54; N, 4.89. Found: C, 45.76; H, 4.44; N, 4.73.

2-(α -Methyl-*o*-hydroxybenzylimino)isovaleratocopper(II) Hemihydrate, Cu(mhba-ival)·¹/₂H₂O.—A preparation analogous to that for the preceding complex was used. The product was recrystallized from ether and dried at 25°; it was obtained as a light green powder, mp 212–215°. Anal. Calcd for C₁₃H₁₆NO_{3.5}Cu: C, 51.06; H, 5.24; N, 4.58. Found: C, 50.60; H, 5.51; N, 4.84.

Physical Measurements.—Electronic spectra were obtained on a Cary Model 14 spectrophotometer, magnetic moments were measured by the Faraday method (HgCo(NCS)₄ calibrant), pmr spectra were determined on a Varian T-60 instrument (TMS reference), and a Varian V-4502 spectrometer was employed for epr measurements. All quantities dependent upon formula weights were calculated using those including the water contents specified above.

Rates of Ketimine \rightarrow Aldimine Conversion.—Rates of base-catalyzed tautomerization of Cu(hba-prop)·H₂O and Cu(hba-ival) were measured spectrophotometrically in 95% ethanol solutions at 30.0 \pm 0.1° and 50.0 \pm 0.1°. Sample solutions (50 ml) were prepared by dissolving the isolated complex in degassed 95% ethanol and adding a sufficient volume of standardized¹³ degassed stock solution of sodium hydroxide in 95% ethanol to achieve an apparent base concentration equal to within \pm 5% of that of the complex (usually 1.5–2.0 \times 10⁻⁴ M). The reaction was followed by monitoring the increase in absorption of the ca. 27,320-cm⁻¹ band of the aldimine forms (cf. Figure and Table I). Kinetic runs were carried out for at least two half-lives and the complete electronic spectra at the end of each run showed that most of the ketimine had transaminated with no apparent decomposition. The following control experiments were also performed. Solutions identical with those used in kinetic runs, except for the presence of base, were maintained at 50° for times longer than two half-lives of the transamination reaction in basic solutions. In all cases the energies and intensities of the band maxima in the ultraviolet and visible regions were unchanged. Plots of log(*A*_{aldimine} - *A*) vs. time in all cases gave straight lines from which pseudo-first-order rate constants *k*_{t(obsd)} (min⁻¹) were obtained by least-squares treatment of the data. Tautomerization (transamination) rate constants were obtained from *k*_t (M⁻¹ min⁻¹) = *k*_{t(obsd)} / (OH⁻).

Results and Discussion

Numerous aldimine complexes of the type M(sal-aa)·*n*H₂O, principally containing Cu(II), have been prepared.^{11,13,15–18} Their structures (2) follow from the method of synthesis, and that of Cu(sal-gly)·³/₂H₂O¹⁹ has been confirmed by X-ray methods. The

only previous example of a ketimine complex 1 has been the report¹⁵ of the synthesis of Cu(hba-prop)·H₂O and its tautomer Cu(sal-L-ala)·2H₂O (Pair I). Limited spectral and polarographic data were presented in order to show that the complexes did in fact possess different ligand structures. We have confirmed the synthesis of the Pair I complexes. This and previous work^{11,13} has resulted in the preparation of two other pairs of tautomeric Cu(II) complexes, Cu(sal-L-val)·³/₂H₂O-Cu(hba-ival) (Pair II), and Cu(hac-L-ala)·H₂O-Cu(mhba-prop)·H₂O (Pair III). The members of each pair may be readily distinguished by their electronic spectra (cf. Table I and Figure 1). In particular, complexes with structure 2 possess an intense feature at ~27,500 cm⁻¹ whereas the complexes 1 do not have a maximum at this energy, their closest band (~24,000–25,600 cm⁻¹) being considerably less intense. The d-d band in the visible region of the type 1 complexes was consistently found to be at slightly lower energies than the corresponding feature of the complexes of structure 2. A fourth type 1 complex, Cu(mhba-ival)·¹/₂H₂O, has also been prepared. Its tautomer, derived from *o*-hydroxyacetophenone and L-valine, could not be obtained. Other physical data (magnetic moments, infrared frequencies, epr parameters) have not proven satisfactorily characteristic of the members of Pairs I–III. Magnetic moments are somewhat dependent on the extent of hydration,⁶ and evidence is accumulating that anhydrous Cu(sal-aa) complexes are antiferromagnetic dimers or polymers in the solid or in noncoordinating solvents.²⁰ The epr spectra of the Pair II complexes were determined in fluid and frozen (77°K) methanol solution. The following parameters, which afford little differentiation between the two structures, were obtained: Cu(hba-ival) $\langle g \rangle$ = 2.127, $\langle a \rangle$ = 0.00636 cm⁻¹, *g*_{||} = 2.269, *g*_⊥ = 2.057, *a*_{||} = 0.0180 cm⁻¹; Cu(sal-L-val)·³/₂H₂O $\langle g \rangle$ = 2.125, $\langle a \rangle$ = 0.00693 cm⁻¹, *g*_{||} = 2.257, *g*_⊥ = 2.059, *a*_{||} = 0.0188 cm⁻¹. Values of *a* refer to ^{63,65}Cu hyperfine splitting; superhyperfine splittings due to nitrogen could not be resolved in either case.

In addition to the Cu(II) complexes Zn(hba-prop)·¹/₂H₂O has been prepared. It together with Zn(sal-L-ala)·H₂O¹¹ form an analogous Pair I whose members are readily differentiated by the following pmr data: Zn(hba-prop)·¹/₂H₂O (pyridine-*d*₆) 2.49 (3, CH₂), 4.67

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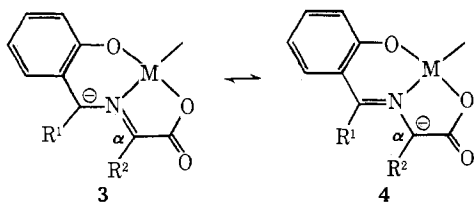
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(2, CH₂), ~7.1 ppm (4, phenyl); Zn(sal-L-ala)·H₂O (methanol-d₄) 1.35 (3, doublet ($J = 7$ Hz), CH₃), 3.97 (1, quartet, CH), ~7.1 (4, phenyl), 8.33 ppm (1, azomethine).

The tautomerization kinetics of Cu(hba-prop)·H₂O and Cu(hba-ival) were determined in 95% ethanol solutions containing equimolar sodium hydroxide under conditions closely similar to those employed in the study of the racemization kinetics of Cu(II) Schiff base complexes.¹³ No reaction was observed in water, ethanol, or methanol solutions at 50° for 24 hr unless base was present. Tautomerization rate constants k_t , which are averages of at least three kinetic runs, were found to be 2.29 ± 0.21 (30°) and 7.16 ± 0.64 M⁻¹ min⁻¹ (50°) for Cu(hba-prop)·H₂O and 0.87 ± 0.11 (30°) and 3.70 ± 0.30 M⁻¹ min⁻¹ (50°) for Cu(hba-ival). The lower rates for the latter presumably reflect the greater degree of steric hindrance of the isopropyl group with regard to base attack on the methylene protons. The value of k_t (50°) for the latter complex is directly comparable with the rate of racemization of its tautomer Cu(sal-L-val)·³/₂H₂O at the same temperature. The ratio k_t/k_r , ~150 provides a quantitative demonstration that ketimine → aldimine tautomerization (transamination), presumably preceding through the anion **3** ↔ **4** which preferentially protonates at the



α -carbon, is a faster process than racemization of the aldimine when determined under similar experimental conditions. The rate of aldimine → ketimine tautomerization, although not yet measured for the complexes **2**, is clearly much less than that of aldimine racemization since no spectral features now known to be associated with M(hba-ka) were observed at any point during the racemization reactions of M(sal-aa).¹³ Consequently, the scheme proposed for α -deuteration of amino acids by heating with Cu(II) and salicylaldehyde in D₂O,²¹ which involves the rapid interconversion of **1** and **2** and hydrolysis of the latter, is considered less likely than racemization and concomitant H-D exchange *via* the anion **4** followed by hydrolysis. It is also observed that the tautomerization rates of Cu(hba-ka) are qualitatively slower than those of M(pym-ival) (M = Cu(II), Zn(II)) in neutral methanol solution.⁸ As discussed previously,^{5,6,13} this situation arises at least in part from resonance stabilization of the anionic intermediate similar to **4** which is effected by an electron-withdrawing group ortho or para to the R₁CNCR₂ unit.

Lastly, two complexes of structure **1** (R₁ = CH₃), Cu(mhba-prop)·H₂O and Cu(mhba-ival)·¹/₂H₂O, were prepared from the potentially resolvable α -methyl-*o*-hydroxybenzylamine with the eventual goal of ascertaining if base-assisted proton transfer from an asymmetric center to the α -carbon necessarily resulted in a racemic product **2**. Unexpectedly, these complexes

did not tautomerize when heated in methanol or 95% ethanol with equimolar base at 50–60° for 24 hr or in a pH 10 aqueous solution at 50° for several hours. Therefore, no attempt was made to obtain them in an optically active form.

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Ion-Pair Dissociation of Periodic Group Ia Acetates in Anhydrous Acetic Acid

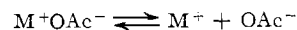
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Trends in the ion-pair association constants for alkali metal salts with variation of the cation have been established in water and in a number of aqueous-organic binary solvents. Conductometric methods for the measurement of these constants have been applied to mixed solvents in the dielectric constant (D) range of 9–30 (at 25°). In aqueous and other hydrogen-bonding media the order of increasing association for salts with an anion in common parallels that of increasing cationic radius.¹

It is important to test this conclusion with non-aqueous solvents having still lower dielectric constants, and we are reporting new results for periodic group Ia acetates in anhydrous acetic acid ($D = 6.2$). Although values for the ion-pair dissociation constants of several acetates (as concentration constants) have been published, the data derived from different techniques are conflicting and the sequence for increasing association is unclear.^{2–4}

Our potentiometric method for the determination of the ion-pair dissociation constant (K_B) of the defined equilibrium



is based upon eq 1 and 2 which were derived earlier.⁵

$$E_B = (E^\circ_{GC} + E_i) + \frac{RT}{F} \ln K_s - \frac{RT}{2F} \ln K_B - \frac{RT}{2F} \ln C_B \quad (1)$$

$$pK_{B1} = pK_{B2} + \frac{2F}{RT}(E_{B1} - E_{B2}) \quad (2)$$

The cell potential (E_B) developed by the glass-saturated calomel electrode pair when immersed in a solution of MOAc in anhydrous acetic acid is dependent upon the constant terms: standard cell potential, E°_{GC} ; the liquid junction potential, E_i ; and the solvent

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