

CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY,
MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASSACHUSETTS 02139

Preparation, Properties, and Racemization Kinetics of Copper(II)–Schiff Base–Amino Acid Complexes Related to Vitamin B₆ Catalysis

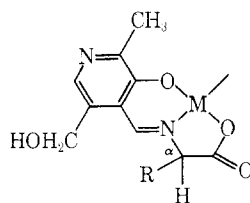
By G. N. WEINSTEIN,¹ M. J. O'CONNOR, AND R. H. HOLM

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Series of tridentate aldimine complexes of types 1, 2, and 3 (X = H, 4-, 6-NO₂) of copper(II) and zinc(II) and protonated copper(II) complexes of type 2, obtained as bromide salts, have been prepared from L-amino acids. Synthetic methods and characterization data are given. Also prepared were the bis-chelate amino acid ester complexes of copper(II), 7 and 8. The inertness of these two complexes to H–D exchange at the asymmetric carbons under basic conditions contrasts with the ready exchange of 4 in the absence of base. This result shows that facile exchange and racemization properties of 4 derive principally from the direct attachment of the electron-withdrawing HC=N and COOC₂H₅ groups to the asymmetric center. The base-catalyzed racemization rates of four copper(II)–aldimine complexes in 95% ethanol at 50° were found to increase in the order Cu(sal-L-val) (3, X = H) < Cu(pyr-L-val) (1) < Cu(3,2-hpy-L-val) (2) < Cu(4-NO₂sal-L-val) (3, X = 4-NO₂). This order is essentially the same as that of qualitative catalytic effectiveness of the constituent *o*-hydroxyarylcarbonyl compounds in nonenzymatic transamination and reinforces in semiquantitative fashion the prevailing model of ligand electronic features requisite to catalytic activity of these compounds. ORD and CD spectra are presented which further establish the correlation between a negative Cotton effect or CD feature associated with an ultraviolet absorption band and the L configuration of the condensed amino acid in the copper(II) complexes 1–3.

Introduction

Aldimine–Schiff base complexes of general type 1 and their ring-protonated forms are key intermediates in

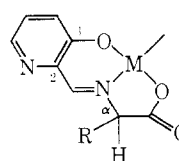


1, M(pyr-aa)

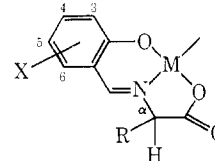
metal ion containing model systems which reproduce non-oxidative transformations of α -amino acids effected by pyridoxal-dependent enzymes.^{2–6} These transformations include, among others, racemization and transamination. Both depend upon enhanced activation or weakening of the α C–H bond of the condensed amino acid in the complex. Loss of the α proton yields a highly reactive entity capable of charge delocalization and susceptible to electrophilic attack. Reprotonation at the α carbon or azomethine carbon, followed by hydrolysis, results in the formation of racemic amino acid and pyridoxal, or α -keto acid and pyridoxamine (transamination).

Of particular significance are the structural and electronic properties of pyridoxal and other *o*-hydroxyarylcarbonyl compounds requisite to their catalytic activity in model systems. The work of Snell, *et al.*,^{3,4,7} has demonstrated that the minimal features of pyri-

doxal which are essential for nonenzymatic catalysis of transamination are provided by 3-hydroxypyridine-2- and -4-carboxaldehydes. 4-Nitro- and 6-nitrosalicylaldehydes have also been found to be catalytically active whereas salicylaldehyde itself is not.⁷ Despite the importance of Schiff base chelates derived from these compounds, relatively little attention has been given to their isolation and detailed characterization and to their reactions under conditions where their basic stoichiometries and structures are retained and thus are known. A number of 1:1 and 2:1 complexes⁸ of types 1,^{9–12} 2,¹³ and 3 (X = H),^{14–17} including some with the pyridine ring protonated,^{11–13} have been isolated but in a number of instances characterization has been incomplete, particularly for 1:1 complexes. X-Ray struc-



2, M(3,2-hpy-aa)



3, M(X-sal-aa)

(8) The following ligand designations are employed throughout: pyr-aa, N-pyridoxylideneamino acidato anion; Hpyr-aa, ring-protonated form of pyr-aa; X-sal-aa, ring-substituted N-salicylideneamino acidato anion (X = H not stated); 3,2-hpy-aa, N-(3-hydroxypyridyl-2-methylene)amino acidato anion; H-3,2-hpy-aa, ring-protonated form of 3,2-hpy-aa; aa (condensed amino acid) = gly (glycine), ala (alanine), Phgly (α -phenylglycine), Phala (phenylalanine), tyr (tyrosine), ab (3-aminobutyric acid), aib (3-aminoisobutyric acid); R-sal, R (condensed acid ester) = Etab (3-aminoethylbutyrate), Etiab (3-aminoethylisobutyrate).

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TABLE I
 CHARACTERIZATION DATA FOR SCHIFF BASE-AMINO ACID COMPLEXES

| Complex | X | R ^a | n | Mp, °C | % calcd | | | % found | | |
|--|-------------------|--|-----|---------|---------|------|------|---------|------|------|
| | | | | | C | H | N | C | H | N |
| Cu(X-sal-aa)·nH ₂ O (3) | 6-NO ₂ | CH ₃ | 2 | >300 | 35.77 | 3.60 | 8.34 | 36.31 | 3.66 | 8.27 |
| | 4-NO ₂ | CH ₂ C ₆ H ₅ | 2 | >300 | 46.66 | 3.92 | 6.80 | 46.92 | 4.18 | 6.71 |
| | 6-NO ₂ | CH ₂ C ₆ H ₅ | 1 | >300 | 48.79 | 3.58 | 7.11 | 48.66 | 3.64 | 7.00 |
| | H | CH(CH ₃) ₂ ^c | 1.5 | 229–231 | 46.52 | 5.21 | 4.52 | 46.59 | 5.61 | 4.47 |
| | 4-NO ₂ | CH(CH ₃) ₂ | 1 | >300 | 41.68 | 4.08 | 8.10 | 41.73 | 4.13 | 7.90 |
| | H | C ₆ H ₅ ^b | 2 | 191–192 | 51.06 | 4.29 | 3.97 | 50.96 | 4.25 | 3.89 |
| | H | CH ₂ C ₆ H ₄ -4-OH ^d | 0 | >300 | 55.41 | 3.78 | 4.04 | 55.15 | 3.89 | 3.70 |
| Zn(X-sal-aa)·nH ₂ O (3) | H | H | 0 | >360 | 44.57 | 2.89 | 5.78 | 44.67 | 2.84 | 5.70 |
| | H | H | 1 | >360 | 41.49 | 3.46 | 5.38 | 41.18 | 3.44 | 5.29 |
| | H | CH(CH ₃) ₂ | 0.5 | >360 | 49.10 | 4.77 | 4.77 | 48.92 | 4.98 | 5.23 |
| | H | CH(CH ₃) ₂ | 1 | >360 | 47.63 | 4.96 | 4.63 | 47.54 | 4.94 | 4.64 |
| Cu(H-3,2-hpy-aa)Br·nH ₂ O (2 ^h) | ... | CH ₃ ^e | 0.5 | 189 | 31.27 | 2.92 | 8.10 | 31.24 | 3.28 | 8.17 |
| | | CH ₂ C ₆ H ₅ ^f | 0 | 190 | 43.65 | 3.15 | 6.79 | 43.54 | 3.33 | 6.70 |
| | | CH(CH ₃) ₂ ^g | 0 | 189–190 | 36.23 | 3.59 | 7.68 | 36.33 | 3.87 | 7.57 |

^a All complexes prepared from L-amino acids unless otherwise noted. ^b Prepared from D-α-phenylglycine. ^c Recrystallized from ethanol–water. ^d Recrystallized from absolute ethanol. ^e Br: calcd, 23.12%; found, 23.40%. ^f Br: calcd, 19.36%; found, 19.50%. ^g Br: calcd, 21.91%; found, 21.65%. ^h Pyridine nitrogen protonated.

tural studies have established the chelate ring structure shown in 1–3 for [Cu(sal-gly)(H₂O)]·0.5H₂O,¹⁸ Cu(pyr-DL-val),¹⁹ and [Cu(pyrphosphate-DL-Phala)(H₂O)].²⁰

Of the reactions dependent upon activation of the α C–H bond in Schiff base complexes, transamination has been by far the most thoroughly investigated.^{2,3,5,6} Recent work in this laboratory has dealt with definition of structures and solution equilibria of Schiff base complexes formed by pyridoxal and pyridoxamine²¹ and investigation of the ketimine → aldimine conversion essential to nonenzymatic transamination.^{21c} Racemization of L-amino acids in systems containing metal ions and pyridoxal,^{22,23} salicylaldehyde,^{24,25b} or substituted salicylaldehydes²⁵ has been detected, but only recently have any reaction rates been determined.²⁵ Because racemization is a mechanistically simpler reaction than transamination, measurement of its kinetics affords an opportunity to assess activation of the α C–H bond as a function of ligand structure. We report here measurement of the rates of base-catalyzed racemization of a series of 1:1 copper(II)–Schiff base complexes derived from pyridoxal, 3-hydroxypyridine-2-aldehyde, 4-nitrosalicylaldehyde, salicylaldehyde, and L-valine (1–3 (X = H, 4-NO₂), R = CH(CH₃)₂). The use of preformed characterized complexes and 95% ethanol as the reaction medium reduces uncertainty as to the identity of the species undergoing reaction. Synthetic methods for these and other 1:1 Schiff base-amino acid complexes of Cu(II) and Zn(II) are described and certain physical properties are also reported.

Related to the matter of racemization of the condensed

amino acid in complexes 1–3 is the extraordinary proton lability and consequent ease of racemization of the asymmetric centers in bis-chelate metal(II) complexes obtained from the condensates of salicylaldehyde and α-amino acid esters. These complexes, of general formulation M(R''O₂CCHR'-sal)₂, have been the subject of a recent investigation,¹⁶ and further information pertinent to their optical instability is presented here.

Experimental Section

Preparation of Compounds. (a) Ligand Components.—4-Nitrosalicylaldehyde was prepared by the reaction of N,N-dimethyl-*p*-nitrosoaniline with 2-hydroxy-4-nitrobenzylpyridinium bromide in 95% ethanol in the presence of sodium hydroxide.²⁶ The resulting mixture was treated with 5 *N* hydrochloric acid to afford, after recrystallization from ethanol–water, a brick-red crystalline product; mp 134° (lit.²⁶ mp 134°).

6-Nitrosalicylaldehyde was prepared by the reaction of *m*-nitrophenol with sodium hydroxide in refluxing chloroform.²⁷ The reaction mixture was steam distilled and the aldehyde separated from the unreacted starting material in the distillate through precipitation as its copper complex by addition of saturated aqueous copper acetate. The green solid was treated with dilute sulfuric acid and the liberated product was extracted into diethyl ether. The solvent was removed and the resultant solid was recrystallized from ethanol to give yellow crystals; mp 53° (lit. mp 50–51°, ²⁷ 54–55°²⁸).

3-Hydroxypyridine-2- and -4-carboxaldehyde were synthesized by published methods.^{29,30} The penultimate step in the preparation of the 4-carboxaldehyde was a modification³¹ of the original synthesis. The compounds were purified by vacuum sublimation at 70–80° immediately before use.

(b) Complexes.—The following groups of complexes were prepared by the indicated procedures. Analytical data are collected in Table I. The degrees of hydration *n* indicated in this table and in the preparations described below were obtained from best fits of the analytical data; independent determinations by weight loss studies were not carried out. All quantities de-

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pendent upon formula weights were calculated using these n values. N-Salicylidene-L-alaninatocopper(II) trihydrate and N-salicylidene-L-phenylalaninatocopper(II) monohydrate were prepared previously.¹⁶

(N-(Salicylidene)amino acidato)copper(II) Complexes, Cu(sal-aa) (3, X = H).—Salicylaldehyde (0.020 mol) was added to the amino acid (0.022 mol) in 30 ml of water and the mixture was warmed to 50°. Solid cupric acetate monohydrate (0.020 mol) was introduced and the mixture was stirred vigorously at 40–60° for *ca.* 90 min. After cooling to room temperature the crude complex was collected by filtration. Purification was effected by recrystallization from 1:1 v/v dioxane–water at 50–70° (unless otherwise noted in Table I) to afford a blue-green crystalline solid in 70–85% yield. Several additional preparations of the complex derived from phenylalanine were also carried out and are probably generally applicable. The Schiff base was isolated as its potassium salt³² and treated with an equivalent of cupric acetate in dioxane at 50°. The solution was filtered and the filtrate taken to dryness *in vacuo*. The resultant solid was recrystallized from aqueous dioxane to give the pure complex. Reaction of bis(L-phenylalaninato)copper(II) and bis(salicylaldehydato)copper(II) in aqueous dioxane at 50° also afforded the pure complex.

(N-(Salicylidene)amino acidato)zinc(II) Complexes, Zn(sal-aa) (3, X = H).—These complexes were obtained by the same procedure used for the analogous copper(II) complexes. The initially isolated species obtained from the reaction with glycine was boiled five times with 100 ml of 95% ethanol and 15 ml of water and twice with 100 ml of absolute ethanol. Drying at 80° (10^{−2} mm) gave the anhydrous complex. The monohydrate was obtained by combining the preceding aqueous ethanol solutions and reducing the volume until white crystals separated. This solution was allowed to stand for 2 weeks; the crystalline complex was collected by filtration and then dried at 80°. The initially isolated valinato complex was recrystallized three times from 5:1 v/v ethanol–water and dried to constant weight at 80° (10^{−2} mm). The white product obtained was found to be the hemihydrate. The monohydrate was isolated as white crystals by volume reduction of the combined aqueous ethanol filtrates.

(N-(Nitrosalicylidene)amino acidato)copper(II) Complexes, Cu(4-, 6-NO₂-sal-aa) (3).—To a solution of 0.011 mol of the amino acid in 1:1 v/v dioxane–water (40 ml) maintained at 50° under nitrogen 0.01 mol of 4- or 6-nitrosalicylaldehyde was added. The resultant orange slurry was stirred for 15 min. Solid cupric acetate monohydrate (0.010 mol) was added and the mixture was vigorously stirred at 50° for an additional 30 min. After cooling, the complexes were collected by filtration and purified by recrystallization from 1:1 v/v ethanol–water.

(N-(3-Hydroxypyridyl-2-methylene)amino acidato)copper(II) Hydrobromide Salts, Cu(H-3,2-hpy-aa)Br.—The amino acid (0.010 mol) was dissolved in 50 ml of anhydrous methanol containing 0.010 mol of potassium hydroxide under nitrogen at 10°. A methanol solution (20 ml) containing 3-hydroxypyridine-2-carboxaldehyde (0.010 mol) was added and the solution was stirred at 10° for 15 min. Solid anhydrous cupric bromide (0.010 mol) was added and after 1 hr the green microcrystalline product was collected, washed with anhydrous methanol (200 ml) and anhydrous ether (150 ml), and then dried at 25° (0.05 mm). Yields of *ca.* 80% were obtained.

N-(3-Hydroxypyridyl-2-methylene)alaninatozinc(II) Monohydrate, Zn(3,2-hpy-L-ala)·H₂O (2, R = CH₃).—Hydrated lithium hydroxide (0.01 mol) was dissolved in 25 ml of anhydrous methanol under nitrogen. L-Alanine (0.0050 mol) was added and the mixture was stirred vigorously at 5° for 15 min. 3-Hydroxypyridine-2-carboxaldehyde (0.0050 mol) was added and then finely powdered zinc nitrate hexahydrate (0.0050 mol) was added to the yellow solution over the course of 15 min, producing a pale yellow microcrystalline solid. Stirring was continued under nitrogen for 1 hr at 5°; the product was col-

lected by filtration, washed with 20 ml of cold methanol and 50 ml of ether, dried at 25° (0.05 mm), and obtained in *ca.* 80% yield. It was found to be light sensitive and was stored in the dark; mp >300°. *Anal.* Calcd for C₉H₁₀N₂O₄Zn: C, 39.23; H, 3.66; N, 10.17. Found: C, 38.90; H, 3.79; N, 10.07.

N-(3-Hydroxypyridyl-4-methylene)alaninatozinc(II) Sesquihydrate, Zn(3,4-hpy-L-ala)·1.5H₂O.—The compound was prepared by the same procedure used for the 2-pyridinal analog and was obtained as light-sensitive, pale yellow microcrystals; mp >300°. *Anal.* Calcd for C₉H₁₁N₂O_{4.5}Zn: C, 37.98; H, 3.90; N, 9.84. Found: C, 37.53; H, 3.93; N, 9.67.

N-(Pyridoxylidene)valinatocopper(II) Monohydrate, Cu(pyr-L-val)·H₂O (1, R = CH(CH₃)₂).—Pyridoxal was obtained from its hydrochloride (Calbiochem) by treatment with aqueous potassium hydroxide. Hydrated lithium hydroxide (9.50 mmol) was added to a solution of 4.75 mmol of L-valine in 20 ml of degassed methanol at 5° under nitrogen and allowed to react for 1 hr. Pyridoxal (4.75 mmol) was then added and the mixture was stirred for 15 min at 5°. An equivalent amount of aqueous cupric nitrate solution was added dropwise, producing almost immediate crystallization of the product. Methanol (*ca.* 5 ml) was added and after additional stirring for 1 hr the complex was collected by filtration. It was obtained as a dark green solid after washing with ice-cold methanol (three 10-ml portions) and ether (five 10-ml portions) and drying at 25° (10^{−2} mm) for 24 hr; mp >360° with decomposition beginning at 235°. *Anal.* Calcd for C₁₈H₁₉N₃O₅Cu: C, 45.15; H, 5.21; N, 8.10. Found: C, 45.16; H, 4.70; N, 7.90.

N-(3-Hydroxypyridyl-2-methylene)valinatocopper(II) Hemihydrate, Cu(3,2-hpy-L-val)·0.5H₂O (2, R = CH(CH₃)₂).—This compound was prepared by the procedure for the related pyridoxylidene complex. Analytically pure samples were obtained either by washing the precipitated product with methanol and ether or by recrystallizing it from a chloroform–methanol–2-butanol solvent mixture. Dark green crystals were obtained; mp 258–260°. *Anal.* Calcd for C₁₁H₁₃N₂O_{3.5}Cu: C, 45.13; H, 4.44; N, 9.57. Found: C, 45.13; H, 4.08; N, 9.52.

Bis[N-(2-ethoxycarbonyl-1-propyl)salicylaldiminato]copper(II), Cu(Etaib-sal)₂ (7).—The ethyl ester hydrochloride of the amino acid was prepared by dissolving 0.010 mol of β-aminoisobutyric acid³³ in 30 ml of absolute ethanol and passing dry hydrogen chloride gas through the solution for 3 hr. Removal of the solvent gave the crude hydrochloride as an oil. The free ester was obtained by dissolving the oil in 50 ml of dichloromethane and passing dry ammonia gas through the solution for 15 min. Ammonium chloride was filtered off, the dichloromethane was evaporated, and 30 ml of absolute ethanol was added to the residue. This solution was heated just to the boiling point and bis(salicylaldehydato)copper(II) (0.0050 mol) was added. The reaction was allowed to proceed for 30 sec, the solution was filtered, and the brownish green filtrate was evaporated until crystallization began. The solution was maintained at 40° for 1 hr and the product was filtered off. It was recrystallized twice from absolute ethanol and dried *in vacuo* for 3 hr at room temperature. The pure product was obtained as greenish brown crystals, mp 122–123°. *Anal.* Calcd for C₂₆H₃₂N₂O₆Cu: C, 58.70; H, 6.02; N, 5.27. Found: C, 58.38; H, 6.27; N, 5.10.

Bis[N-(3-ethoxycarbonyl-2-propyl)salicylaldiminato]copper(II), Cu(Etab-sal)₂ (8).—Crude ethyl 3-aminobutyrate was obtained on a 0.030-mol scale from commercial 3-aminobutyric acid using the method in the preceding preparation. It was treated with 0.030 mol of salicylaldehyde in 15 ml of dichloromethane for 15 min at room temperature. Removal of solvent gave the Schiff base as a yellow oil which was distilled at 140° (10^{−2} mm). The Schiff base (0.021 mol) was dissolved in 60 ml of dry *t*-butyl alcohol containing 0.025 mol of potassium *t*-butoxide under a nitrogen atmosphere. Tetraethylammonium tetrabromocuprate(II) (0.013 mol) was added and the reaction was allowed to proceed for 3 hr at 50°. Removal of the *t*-butyl alcohol yielded

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a brown tar which was extracted with warm, dry *n*-heptane. The solvent was removed *in vacuo* and the resultant brown oil was subjected to pumping at 30–50° for 2 hr. The complex obtained in this way was found to be of adequate purity. Despite repeated attempts it could not be recrystallized to yield a solid. It could not be prepared in solid form by a method similar to that employed for complex 7. *Anal.* Calcd for $C_{26}H_{32}N_2O_6$: Cu, 58.70; H, 6.02; N, 5.27. Found: C, 58.65; H, 6.17; N, 5.16.

N-(Salicylidene)-3-aminoisobutyratecopper(II), Cu(sal-aib) (9, R = H, R' = CH₃).—3-Aminoisobutyric acid (0.015 mol) was dissolved in 15 ml of water and 0.015 mol of salicylaldehyde was added. The yellow solution was heated for 30 min at 60–70° and then 0.015 mol of cupric acetate monohydrate in 20 ml of hot water was added dropwise. The green complex precipitated as the addition was completed. Reaction was allowed to proceed for 1 hr at 60–70° and the solution was filtered when hot to yield *ca.* 3.0 g of product. This material was recrystallized from 300 ml of absolute ethanol and dried to constant weight at 80° (10^{−2} mm). An anhydrous dark green solid was obtained; mp 281–283°. *Anal.* Calcd for $C_{11}H_{11}NO_3Cu$: C, 49.12; H, 4.08; N, 5.21. Found: C, 49.28; H, 4.15; N, 5.08.

N-(Salicylidene)-3-aminobutyratecopper(II) Hemihydrate, Cu(sal-ab)·0.5H₂O (9, R = CH₃, R' = H).—This compound was obtained using the preceding method. It was recrystallized twice from 90% ethanol and obtained as a light green solid after drying at 80° (10^{−2} mm) to constant weight; mp 258–260°. *Anal.* Calcd for $C_{11}H_{12}NO_{3.5}Cu$: C, 47.42; H, 4.31; N, 5.03. Found: C, 47.68; H, 4.73; N, 5.26.

ORD and CD Spectra.—Measurements were made on a Cary Model 60 spectrometer at *ca.* 28° using 1-cm cells. The following results were obtained in methanol solutions from measurements in the 280–650-mμ range and serve to characterize the important features of the ORD spectra.

Cu(sal-L-ala)·3H₂O.—(*c* 0.318): $[M]_{650} + 320$, $[M]_{589} + 515$, $[M]_{550} + 583$; (*c* 0.032): $[M]_{390} - 3980$, $[M]_{335} + 6020$, $[M]_{290} + 2430$.

Cu(sal-L-val)·1.5H₂O.—(*c* 0.330): $[M]_{650} + 314$, $[M]_{615} + 357$, $[M]_{589} + 263$; (*c* 0.033): $[M]_{404} - 6470$; $[M]_{342} + 13,400$, $[M]_{290} + 5080$.

Cu(sal-L-Phala)·H₂O.—(*c* 0.246): $[M]_{650} 0$, $[M]_{616} + 170$, $[M]_{589} + 28$; (*c* 0.025): $[M]_{397} - 18,300$, $[M]_{336} + 25,800$, $[M]_{290} + 14,200$, $[M]_{285} + 16,600$.

Cu(sal-D-Phgly)·2H₂O.—(*c* 0.260): $[M]_{650} - 80$, $[M]_{600} - 336$, $[M]_{589} - 311$; (*c* 0.026): $[M]_{403} + 17,900$, $[M]_{335} - 27,200$, $[M]_{297} - 22,100$, $[M]_{290} - 26,300$.

Cu(sal-L-tyr).—(*c* 0.260): $[M]_{650} 0$, $[M]_{589} - 163$; (*c* 0.026): $[M]_{396} - 20,600$, $[M]_{340} + 29,900$, $[M]_{297} + 20,400$, $[M]_{290} + 24,400$.

Cu(4-NO₂sal-L-val)·1.5H₂O.—(*c* 0.250): $[M]_{650} + 535$, $[M]_{589} + 349$; (*c* 0.025): $[M]_{456} - 4810$, $[M]_{387} + 8930$, $[M]_{310} - 2750$.

Cu(4-NO₂sal-L-Phala)·2H₂O.—(*c* 0.220): $[M]_{650} - 19$, $[M]_{589} - 547$; (*c* 0.022): $[M]_{450} - 10,930$, $[M]_{380} + 12,890$, $[M]_{310} - 7540$.

Cu(6-NO₂sal-L-ala)·2H₂O.—(*c* 0.280): $[M]_{650} + 336$, $[M]_{589} + 585$, $[M]_{547} + 767$; (*c* 0.028): $[M]_{413} - 2200$, $[M]_{387} + 839$, $[M]_{350} + 683$, $[M]_{310} + 9590$.

Cu(6-NO₂sal-L-Phala)·H₂O.—(*c* 0.210): $[M]_{650} + 783$, $[M]_{589} + 363$; (*c* 0.021): $[M]_{427} - 9970$, $[M]_{343} + 18,830$, $[M]_{305} + 26,070$, $[M]_{290} + 21,390$.

Cu(H-3,2-hpy-L-ala)Br·1.5H₂O.—(*c* 0.102): $[M]_{650} + 235$, $[M]_{589} + 490$, $[M]_{545} + 637$; (*c* 0.010): $[M]_{389} - 5600$, $[M]_{280} 0$.

Cu(H-3,2-hpy-L-val)Br.—(*c* 0.104): $[M]_{650} + 1400$, $[M]_{589} + 1860$, $[M]_{535} + 2000$; (*c* 0.010): $[M]_{390} - 4030$, $[M]_{335} + 4130$, $[M]_{325} + 3990$, $[M]_{290} + 8060$, $[M]_{280} + 6660$.

Cu(H-3,2-hpy-L-Phala)Br.—(*c* 0.184): $[M]_{650} + 404$, $[M]_{506} + 764$, $[M]_{589} + 755$; (*c* 0.018): $[M]_{394} - 15,800$, $[M]_{305} + 18,600$, $[M]_{295} + 18,100$, $[M]_{280} + 19,400$.

Magnetic Measurements.—Magnetic moments of representative Cu(II) complexes at 25° were measured by the Faraday or Gouy method using HgCo(NCS)₄ as a calibrant. Moments for five complexes are given in Table II. Additional values are: Cu(sal-ab)·0.5H₂O, 1.76 BM; Cu(sal-aib), 1.78 BM.

TABLE II
MAGNETIC MOMENTS AND ELECTRONIC SPECTRA OF
Cu(II)-SCHIFF BASE-AMINO ACID COMPLEXES

| Complex | $\mu_{\text{eff}},^a$ BM | $\lambda_{\text{max}}, \text{cm}^{-1}$ (ϵ) ^b |
|--|--------------------------|--|
| Cu(sal-L-val)·1.5H ₂ O | 1.65 | 45,040 (20,500), 41,150 (21,900), 37,040 (13,800), 27,320 (5030), 15,600 (109) |
| Cu(4-NO ₂ sal-L-val)·H ₂ O | 1.75 | 46,730 (17,700), 40,000 (19,900), 34,970 (14,000), 23,920 (4420), 14,900 (118) |
| Cu(3,2-hpy-L-val)·0.5H ₂ O | 1.96 | 46,300 (26,300), 41,150 (13,900), 35,700 sh (2860), 27,470 (7960), 15,000 (104) |
| Cu(H-3,2-hpy-L-val)Br | 1.73 | 46,300 (24,300), 41,150 (13,200), 35,700 sh (3100), 27,860 (7490), 14,800 (108) |
| Cu(pyr-val)·H ₂ O | 1.72 | 43,480 (21,100), 36,760 (9300), 25,640 (5720), 15,200 (120) |

^a Solid. ^b 95% ethanol solution.

Acidity Measurements.—Measurements of apparent hydrogen ion concentrations in 95% or other aqueous ethanol solutions were made with a Radiometer 26 pH meter equipped with a Radiometer combined glass-calomel electrode, which was equilibrated in the particular solvent medium prior to measurement.

Deuterium-Exchange Studies of Bis(N-ethoxycarbonylpropylsalicylaldiminato)copper(II) Complexes.—The deuterium-exchange properties of the proton attached to the asymmetric carbon in Cu(Etaib-sal)₂ and Cu(Etab-sal)₂ were investigated under neutral and basic conditions in ethanol-1-*d* solutions. After the treatments described below, the complexes were reisolated and dissolved in carbon tetrachloride, and the Schiff bases were freed by passing hydrogen sulfide through the solutions. The precipitated sulfide was removed by filtration, the volume of the solution was reduced to *ca.* 2–3 ml, and the pmr spectrum of the free ligand was recorded. A 0.09 *M* solution of Cu(Etaib-sal)₂ was refluxed for 30 min and a 0.08 *M* solution containing equimolar sodium ethoxide was refluxed for 17 hr in ethanol-1-*d*. Solutions of Cu(Etab-sal)₂ 0.08 *M* in complex and sodium ethoxide were refluxed for periods up to 17 hr and a similar solution containing a 1:5 mole ratio of complex to base was refluxed for 30 min. In all cases the pmr spectra revealed no deuterium exchange of the proton in question or of any other protons and were the same as those of the separately prepared Schiff bases. The following chemical shift data (Hz, CCl₄ solution, TMS reference) were obtained: H(Etaib-sal), −73 (both CH₃'s, triplet + doublet), −168 (β-H, quartet), −222 (NCH₂, doublet), −247 (ester CH₃, quartet), −420 (ring protons), −500 (HC=N); H(Etab-sal), −69 (ester CH₃, triplet), −74 (CHCH₃, doublet), −148 (CHCH₂, doublet), −240 (ester CH₂ + α-H, multiplet), −420 (ring protons), −499 (HC=N). All coupling constants are 6–7 Hz. Spectra were recorded at 60 MHz.

Measurement of Racemization Rates.—Rates of racemization of Cu(sal-L-val)·1.5H₂O, Cu(4-NO₂sal-L-val)·H₂O, Cu(3,2-hpy-L-val)·1.5H₂O, and Cu(pyr-L-val)·H₂O were measured polarimetrically in basic 95% ethanol solutions at 50.0 ± 0.1°. A Perkin-Elmer Model 141 spectropolarimeter and a 10-cm jacketed cell attached to a circulating constant-temperature bath were employed. Sample solutions (50 ml) were prepared by dissolving the complex in degassed 95% ethanol and adding a sufficient volume of standardized, degassed stock solution of sodium hydroxide in 95% ethanol to achieve an apparent base concentration equal to within ±2% of that of the complex (usually (1–1.5) × 10^{−3} *M*). The *ca.* 0.05 *M* stock solution was standardized by pH titration with a 95% ethanol solution of benzoic acid. Measurements of optical rotations of the four complexes were

made at 589 $m\mu$ and in several cases at 578 and 436 $m\mu$ also. At the concentrations employed (*cf.* Table III) initial rotations ranged from 0.150 to 0.350°. Kinetic runs were carried out for at least 2 half-lives and some were continued to zero rotation. The average number of measurements per run was 25, and as many as 50 measurements were made for the longer runs. The following control experiments were also performed. Solutions identical with those used in the kinetic runs, except for the presence of base, were maintained at 50° for times longer than 2 half-lives of the racemization reaction in basic solutions. In all cases the values of $[\alpha]_{589}$ and the wavelengths and intensities of absorption band maxima in the 210–450- $m\mu$ region were unchanged. Spectral data are given in Table II. As a check on possible decomposition of the complexes during the kinetic runs, spectra in the 210–800- $m\mu$ range were recorded at the beginning and end of these runs using solutions maintained at 50° and having the same concentrations as those employed in rate measurements. In the 210–450- $m\mu$ range no new absorption features were observed, and

TABLE III
KINETIC DATA FOR THE BASE-CATALYZED RACEMIZATION OF
Cu(II)-SCHIFF BASE-AMINO ACID COMPLEXES IN 95%
ETHANOL SOLUTION AT 50°

| Complex | Concn $\times 10^3$, M | $k_r(\text{obsd})^a$, min^{-1} | $k_r =$ | |
|--|-------------------------------|---|---|---|
| | | | $k_r(\text{obsd})/$ (OH^-) , $M^{-1} \text{ min}^{-1}$ | $k_r(\text{av})$, $M^{-1} \text{ min}^{-1}$ |
| Cu(sal-L-val) · 1.5H ₂ O | 1.67 | 0.394 | 0.0236 | 0.0246 |
| | 1.56 | 0.361 | 0.0231 | |
| | 1.06 | 0.278 | 0.0262 | |
| | 1.04 | 0.266 | 0.0256 | |
| Cu(4-NO ₂ sal-L-val) · H ₂ O | 1.58 | 9.25 ^b | 0.585 | 0.558 |
| | 1.54 | 8.40 | 0.546 | |
| | 1.08 | 5.94 | 0.550 | |
| | 0.87 | 4.90 | 0.563 | |
| | 0.74 | 4.04 | 0.547 | |
| Cu(3,2-hpy-L-val) · 0.5H ₂ O | 1.54 | 5.17 | 0.336 | 0.309 |
| | 1.53 | 4.95 | 0.324 | |
| | 1.09 | 3.01 | 0.276 | |
| | 1.00 | 2.99 | 0.299 | |
| Cu(pyr-L-val) · H ₂ O | 1.57 | 3.53 | 0.225 | 0.236 |
| | 1.56 | 3.56 | 0.228 | |
| | 1.06 | 2.53 | 0.238 | |
| | 1.03 | 2.55 | 0.248 | |
| | 0.77 | 1.84 | 0.239 | |

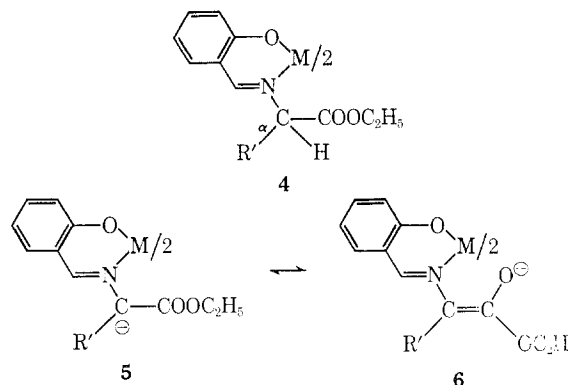
^a Determined from α_{589} data; concentrations of complex and sodium hydroxide are equal. ^b Determined from α_{578} data.

band intensities changed by $\leq 6\%$ with changes of $<4\%$ observed in most cases. In addition, the absorption, ORD, and/or CD spectra of fresh solutions without base and in the presence of equimolar base were compared (*cf.* Figures 1 and 2). Only slight changes were found in the ultraviolet absorption spectra and in the visible a weak shoulder was detectable on the trailing edge of the ultraviolet absorption at 490–525 $m\mu$ in basic solutions of the four complexes. Band maxima at 640–670 $m\mu$ in neutral solutions were shifted by 10–20 $m\mu$ to higher energies in the basic solutions. Intensities of these features changed by $<10\%$ during kinetic runs except for Cu(3,2-hpy-val) · 0.5H₂O, whose bands at 650 and 500 $m\mu$ (sh) increased considerably in intensity. Possible sources of spectral differences between neutral and basic solutions are mentioned in the text. To establish that the added base acted as a catalyst and was not consumed during loss of optical activity, glass electrode measurements were made on portions of solutions used in the kinetic runs. Prior to each run solutions were diluted under nitrogen to 50% aqueous ethanol composition using degassed distilled water and the apparent pH was determined; the same procedure was followed at the end of each run. A 0.01 M succinic acid buffer in 50% ethanol was employed as a standard.³⁴ Changes of less than 10% in initial and final readings were found except for solutions of Cu(3,2-hpy-L-val) · 0.5H₂O where differences of

10–15% were observed. Plots of $\log \alpha_{589}$ vs. time in all cases gave excellent straight lines for at least 2 half-lives from which pseudo-first-order rate constants $k_r(\text{obsd})$ (min^{-1}) were obtained by least-squares fits of the data. Racemization rate constants were obtained from the relation $k_r (M^{-1} \text{ min}^{-1}) = k_r(\text{obsd})/(\text{OH}^-)$. Kinetic data are set out in Table III.

Results and Discussion

Racemization of Bis[N-(ethoxycarbonylalkyl)salicylaldiminato]metal(II) Complexes.—In recent work¹⁶ we have verified the earlier observation by Pfeiffer, *et al.*,³⁵ that reaction of bis(salicylaldehydato)copper(II) with optically active amino acid ethyl esters yields optically inactive bis chelates of type 4. Preparation of Cu(II) and other metal(II) complexes under extremely mild conditions in no case gave a product with measurable optical rotation.³⁶ Consistent with the optical instability of these complexes are their exchange properties. When prepared in ethanol-1-*d* solutions or when dissolved in this solvent after isolation, Cu(II) and Zn(II) complexes underwent ready H-D exchange at the α carbon. Added base was not required to effect this exchange. Labeling experiments revealed no incorporation of deuterium at the azomethine carbon, thereby excluding as a significant intermediate in exchange a neutral ketimine complex formed by protonation of this carbon. The racemization-exchange mechanism considered most likely for 4 is that involving formation of the anionic intermediate 5 \leftrightarrow 6 stabilized by enolate resonance.¹⁶

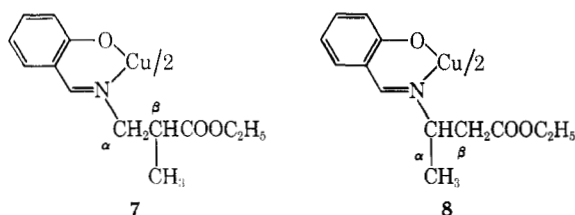


Activation of the α C-H bond in 4 is particularly evident from the finding that racemization of the free base N-(ethoxycarbonylbenzyl)salicylaldehyde in ethanol is nearly complete only after 160 hr.³⁵ The source of α -proton lability would appear to rest in the electron-withdrawing properties of the metal-azomethine and carboethoxy groups and from resonance stabilization of the intermediate. In order to investigate this matter, two new complexes, Cu(Etaib-sal)₂ (7) and Cu(Etab-sal)₂ (8), were prepared. These differ from 4 in that the asymmetric center is proximal to either the carboethoxy

(35) P. Pfeiffer, W. Offermann, and H. Werner, *J. Prakt. Chem.*, **159**, 313 (1942).

(36) Samples of Cu(Etala-sal)₂, Cu(EtPhala-sal)₂, and Cu(MePhala-sal)₂ derived from the L-amino acid esters and possessing some optical activity have been isolated in unpublished work and were observed to racemize upon standing overnight in ethanol solution or upon recrystallization: K. R. Turnbull, Ph.D. Thesis, Australian National University, 1965.

(34) R. G. Bates, "Determination of pH, Theory and Practice," Wiley, New York, N. Y., 1964, Chapter 8.



(7) or the metal-azomethine group (8) but not both. Further, only in 7 is resonance stabilization of the type $5 \leftrightarrow 6$ possible for an anionic intermediate. Because of the labor involved in the synthesis of the derivative amino acids in optically active form and in resolution of the racemic acids,³⁷ the complexes were prepared as mixtures of diastereoisomers from the racemic ethyl esters. Exchange propensities of the protons at the

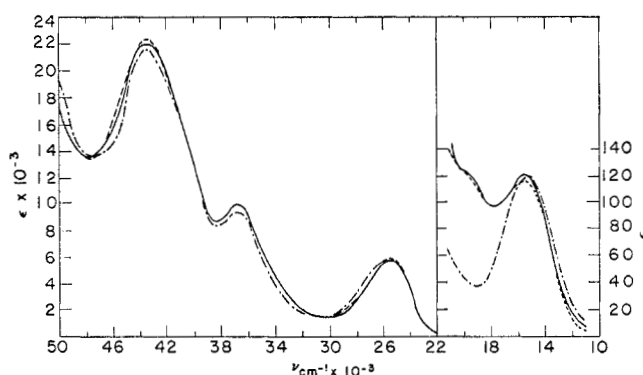


Figure 1.—Absorption spectrum of $\text{Cu}(\text{pyr-L-val}) \cdot \text{H}_2\text{O}$ in 95% ethanol solution: ---, no base; —, in presence of equimolar sodium hydroxide at start of kinetic run; - - - -, in presence of equimolar sodium hydroxide at end of kinetic run.

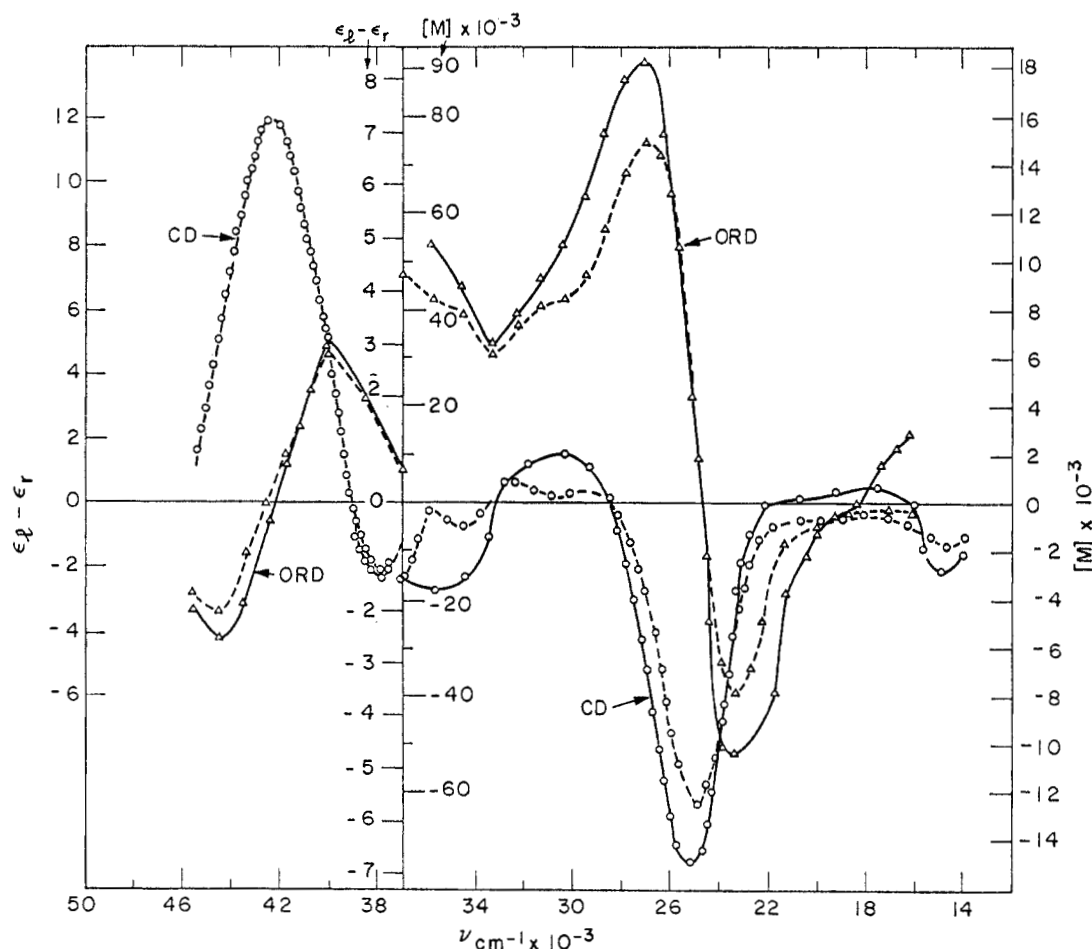


Figure 2.—ORD and CD spectra of $\text{Cu}(\text{pyr-L-val}) \cdot \text{H}_2\text{O}$ in 95% ethanol in the presence of equimolar sodium hydroxide at the beginning of a kinetic run and in the absence of base. CD: $\circ-\circ-\circ$, no base; $\circ-\circ-\circ$, with base; ORD: $\triangle-\triangle-\triangle$, no base; $\triangle-\triangle-\triangle$, with base.

asymmetric centers were investigated by refluxing solutions of these complexes in ethanol- $1-d$ in the presence and absence of base (sodium ethoxide), followed by their decomposition with hydrogen sulfide. Pmr spectra of the free Schiff bases revealed no H-D exchange at the asymmetric carbon or any other position. This same procedure was used to demonstrate exchange

at the α carbon only in the type 4 complexes $\text{Cu}(\text{Etgly-sal})_2$,³⁸ and $\text{Cu}(\text{Etala-sal})_2$, $\text{Cu}(\text{EtPhala-sal})_2$, and $\text{Zn}(\text{Etala-sal})_2$.¹⁶

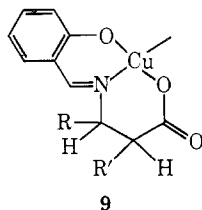
The striking lack of lability of the protons attached to the asymmetric carbons in 7 and 8 in refluxing, basic ethanol- $1-d$, compared to the facile exchange of 4 in the same solvent at *ca.* 25° without added base, affords evidence of the source of α C-H bond activation in the

(37) E. Fischer and H. Scheibler, *Justus Liebig's Ann. Chem.*, **383**, 337 (1911); K. Balenović, D. Cerar, and Z. Fuks, *J. Chem. Soc.*, 3316 (1952); K. Balenović and N. Bregant, *Tetrahedron*, **5**, 44 (1959).

(38) G. A. Auld and A. Davison, *Inorg. Chem.*, **7**, 306 (1968).

latter. Direct attachment of *one or the other* of the electron-withdrawing groups COOC_2H_5 and $\text{HC}=\text{NM}$ to the asymmetric carbon is insufficient to activate the CH bonds toward exchange. Therefore, it appears justifiable to conclude that the facile exchange and racemization properties of **4** are produced primarily by the concerted effects of *both* of these groups and, presumably, resonance stabilization of the anionic intermediate.

Schiff Base-Amino Acid-Metal(II) Complexes.—Although 1:1 complexes of types **1–3** containing Cu(II) and other metal ions have been prepared previously,^{9–11,13–16} their composition and properties and methods of preparation were in some cases not adequately described. Here detailed preparations are given for Cu(II) and Zn(II) complexes of these types and for the ring-protonated forms of Cu(3,2-hpy-aa) (**2**), which were isolated as bromide salts. Complexes derived from 4- and 6-nitrosalicylaldehyde have not been prepared in earlier work. Two members of a new class of Schiff base-amino acid complexes having two six-membered chelate rings have also been synthesized. These are of general structure **9** and are formed from 3-aminobutyric acid ($\text{R} = \text{CH}_3$, $\text{R}' = \text{H}$) and 3-amino-



isobutyric acid ($\text{R} = \text{H}$, $\text{R}' = \text{CH}_3$). Of principal interest are the four complexes $\text{Cu}(\text{sal-L-val}) \cdot 1.5\text{H}_2\text{O}$, $\text{Cu}(4\text{-NO}_2\text{sal-L-val}) \cdot \text{H}_2\text{O}$, $\text{Cu}(3,2\text{-hpy-L-val}) \cdot 0.5\text{H}_2\text{O}$, and $\text{Cu}(\text{pyr-L-val}) \cdot \text{H}_2\text{O}$, all of which were isolated as crystalline solids. Magnetic and spectral data for these complexes are compiled in Table II. They are simple spin-doublet species and the spectral data are consistent with those reported for Cu(II)-Schiff base complexes obtained from valine or other simple amino acids.^{11,14,39} The composite ligand field absorptions in the visible region fall in the narrow range $14,900\text{--}15,600\text{ cm}^{-1}$, a result strongly suggestive of a common Cu(II) chromophore composed of the O_2N donor group from the Schiff base and two^{18–20} or three additional ligands, which must be ethanol or water molecules. Data for a typical protonated complex of **2**, $\text{Cu}(\text{H-3,2-hpy-L-val})\text{-Br}$, are included in the table.

Racemization Kinetics.—The purpose of the kinetics measurements has been to obtain a quantitative indication of the activation of the α C–H bond in a series of 1:1 Schiff base complexes derived from the same amino acid and metal ion but variant in the *o*-hydroxyaryl-carbonyl ligand component. The latter has been selected according to its reported catalytic activity (pyridoxal, 3-hydroxypyridine-2-carboxaldehyde, and

4-nitrosalicylaldehyde⁴⁰) or lack of same (salicylaldehyde) in glutamate \rightarrow α -ketoglutarate transamination carried out at $\text{pH} \sim 5$ in the presence of Al(III).^{3,4,7} Copper(II) and L-valine have been employed as the other constituents since they afford rather stable complexes which racemize at rates conveniently followed by polarimetry. The solvent used was 95% ethanol in order to suppress hydrolytic decomposition.

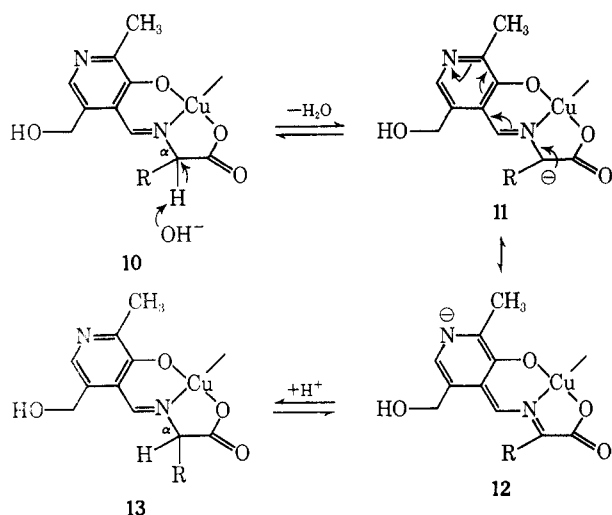
The control experiments described in the Experimental Section reveal that (i) racemization does not occur at 50° in the absence of base, (ii) decomposition of the complexes during kinetic runs is slight, and (iii) the apparent concentration of sodium hydroxide is not significantly altered during the runs. The only exception to these statements is for (ii) with $\text{Cu}(3,2\text{-hpy-L-val}) \cdot 1.5\text{H}_2\text{O}$. Although the ultraviolet spectrum of this complex did not reveal significant changes at the beginning and end of kinetic measurements, such changes were observed in the visible region. Accordingly, the rate constants for this complex are considered the least reliable. The largest spectral changes were found for neutral solutions compared to solutions with equimolar base and complex at the start of kinetic runs and are illustrated by the absorption, ORD, and CD spectra of $\text{Cu}(\text{pyr-L-val}) \cdot \text{H}_2\text{O}$ in Figures 1 and 2. The origin of these changes is obscure but may be due to the formation of a species such as, *e.g.*, $\text{Cu}(\text{pyr-L-val})\text{OH}^-$ in a labile preequilibrium step prior to the onset of the racemization process. No new features or significant intensity alterations of ultraviolet bands which might arise from carbinolamine complexes or hydrolysis products were found in the presence of base.

In order to obtain rate data suitable for comparison, racemization kinetics of the four complexes were determined over the same or nearly the same concentration range of complex and base; the two solutes were maintained at equimolar concentrations in all runs. Pseudo-first-order rate constants $k_{r(\text{obsd})}$ and racemization rate constants k_r corresponding to the relation $\text{rate} = k_r(\text{complex})(\text{OH}^-)$ are given in Table III. In the range of *ca.* $(0.7\text{--}1.7) \times 10^{-3}\text{ M}$ k_r values are reasonably independent of concentration. The apparent order of racemization rates under these experimental conditions is $\text{Cu}(4\text{-NO}_2\text{sal-L-val}) > \text{Cu}(3,2\text{-hpy-L-val}) \gtrsim \text{Cu}(\text{pyr-L-val}) \gg \text{Cu}(\text{sal-L-val})$.

The most significant feature of the order of rates is the relatively slow racemization of $\text{Cu}(\text{sal-L-val})$ and may be accommodated by the following mechanism illustrated with $\text{Cu}(\text{pyr-L-val})$. Removal of the α proton by base in the slow step affords an anionic intermediate stabilized by resonance (**11** \leftrightarrow **12**), the protonation of which affords the starting complex or its enantiomer (**13**). The same scheme may be applied to $\text{Cu}(3,2\text{-hpy-L-val})$ and also to $\text{Cu}(4\text{-NO}_2\text{sal-L-val})$, since an analogous stabilization of its intermediate is possible

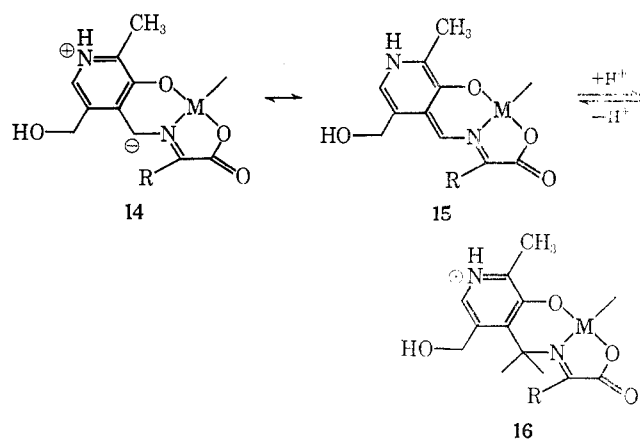
(39) (a) Y. Matsuo, *J. Amer. Chem. Soc.*, **79**, 2011 (1957); (b) Yu. M. Torchinskii, *Biochemistry (USSR)*, **31**, 909 (1966); (c) Y. Matsushima and A. E. Martell, *J. Amer. Chem. Soc.*, **89**, 1322 (1967); (d) Y. Matsushima, *Chem. Pharm. Bull.*, **16**, 2143 (1968).

(40) The strictly catalytic function of this compound in transamination is questionable since the observed reduction of the nitro group⁷ could result in oxidative deamination of the amino acid.² It has been included in this work, for like pyridoxal and 3-hydroxypyridine-2-carboxaldehyde, it possesses an electron-withdrawing function *para* to the azomethine group in the Schiff base complex.



due to the presence of the electron-withdrawing 4-NO₂ group. While resonance structures in addition to 11 and 12 are possible, that of type 12 differentiates Cu(sal-L-val) from the other complexes. Resonance stabilization of its anionic intermediate must be relatively less because this species lacks an electron-withdrawing group *ortho* or *para* to the azomethine function. Consequently, formation of the intermediate requires a somewhat higher activation energy, resulting in a slower rate provided preexponential factors for the four racemization reactions are of comparable magnitude.

Transamination and racemization of amino acids in model systems containing pyridoxal and metal ions are competitive and distinct processes²³ but appear to have the common requirement of intermediates produced by loss of the α proton.²⁻⁴ The two reactions differ in the site of protonation of the intermediate(s), the occurrence of which at the azomethine and α carbon results in transamination and racemization, respectively. This is in turn affected by the pH because the latter reaction tends to predominate in alkaline solutions having pH's well above the pK_a values of the pyridinium protons of aldimine complexes.⁴¹ The results of this study emphasize two important aspects of the electronic factors proposed to be operative in transamination and racemization.^{3,4} First, the high degree of retention of aldimine structure 1 (and to a lesser extent, 2) upon completion or near-completion of racemization further indicates that absence of the protonated pyridine unit enhances the rate of this reaction compared to transamination. For the latter the stabilized intermediate 14 \leftrightarrow 15 is of prime importance; its protonation affords the ketimine complex 16.⁴² Under acidic conditions racemization is considered to occur mainly by reversal



of transamination.³ Second, the qualitative order of effectiveness of the various *o*-hydroxyarylcarbonyl compounds as transamination catalysts in acid solution²⁻⁴ (salicylaldehyde \ll 4-nitrosalicylaldehyde⁴⁰ \sim 3-hydroxypyridine-2-carboxaldehyde \sim pyridoxal) is essentially the same as that of increasing base-catalyzed racemization rates of complexes derived from them. This relationship supports the contention that appreciable reaction rates for transamination in acid solution and racemization in basic solution derive from resonance stabilization of the appropriate intermediates (14 \leftrightarrow 15, 11 \leftrightarrow 12), for which an electron-withdrawing group ($-N=$, $-N^+H=$, $-NO_2$) *ortho* or *para* to the azomethine portion is required.

ORD and CD Spectra.—Torchinskii^{39b,43} has reported the ORD and CD spectra of a number of Cu(pyr-L-aa) and Cu(sal-L-aa) complexes and has observed a negative Cotton effect or negative CD band associated with strong absorption bands at 25,000–28,000 cm⁻¹. We have further investigated this correlation and the results are summarized in Figure 2 for a typical complex and by the ORD data given in the Experimental Section. Without exception Cu(II) complexes of types 1–3 derived from L-amino acids give negative Cotton effects. Thus they constitute one of the larger groups of metal chelates in which there is a general relation between ORD and CD features and the absolute configuration of a ligand asymmetric center. Torchinskii^{39b} also observed that at pH 8.5 and 65–90° aqueous solutions of pyridoxal, Cu(II), and several amino acids suffered a first-order loss of CD intensity. This effect was ascribed without proof to aldimine \rightarrow ketimine conversion. Because these observations were made under basic conditions, the kinetics might well be a composite of first-order rates of tautomerization and racemization *via* the intermediate 11 \leftrightarrow 12 or simply represent the rates of the latter process. These systems clearly require further investigation.

Finally, we are unable to offer any convincing rationale for the great difference in optical stabilities of the Cu(sal-aa) and Cu(C₂H₅OOCHR-sal)₂ complexes.

(41) D. L. Leussing and N. Huq, *Anal. Chem.*, **38**, 1388 (1966).

(42) Unprotonated forms related to 14 could also contribute to the resonance stabilization of intermediates in racemization. Such forms, having substantial negative charge on the azomethine carbon, seemingly do not accurately represent the electrophilic reactivity of intermediates since no appreciable amounts of ketimine complex could have been formed unless it converted rapidly and essentially completely to its aldimine tautomer. The total lack of involvement of species such as 16 in racemization cannot be established from the data at hand, however. For a discussion of electrophilic reactivities of protonated and unprotonated (metal-free) aldimine intermediates, cf. A.-M. Perault, B. Pullman, and C. Valdemoro, *Biochim. Biophys. Acta*, **46**, 555 (1961).

(43) Yu. M. Torchinskii and L. G. Koreneva, *Dokl. Biochem.*, **155**, 110 (1964); *Biochemistry (USSR)*, **30**, 31 (1965).

Possibly the energy required to deform even slightly the five-membered chelate ring in **3** upon formation of its anionic intermediate is responsible inasmuch as the ester oxygens in $\text{Cu}(\text{Etala-sal})_2$ are coordinated weakly or not at all.¹⁶

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CONTRIBUTION FROM THE MATERIALS SCIENCE LABORATORIES, DEPARTMENT OF CHEMICAL ENGINEERING, UNIVERSITY OF TEXAS AT AUSTIN, AUSTIN, TEXAS 78712, AND THE REACTOR CHEMISTRY DIVISION, OAK RIDGE NATIONAL LABORATORY, OAK RIDGE, TENNESSEE 37830

The Crystal Structure of Erbium Oxalate Trihydrate¹

By H. STEINFINK AND G. D. BRUNTON

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The compound $\text{Er}(\text{C}_2\text{O}_4)(\text{HC}_2\text{O}_4) \cdot 3\text{H}_2\text{O}$ crystallizes in space group $P4/n$ with $a_0 = 8.6664(3) \text{ \AA}$ and $c_0 = 6.4209(8) \text{ \AA}$ at 24° . The measured density is $2.8(1) \text{ g/cm}^3$ and the calculated density is 2.742 g/cm^3 so that there are two formula weights in the unit cell. Molybdenum radiation was used to measure the integrated intensities of 1641 independent reflections with a scintillation counter and a four-circle diffractometer. The parameters were refined by least squares to $R = 0.072$ using anisotropic temperature factors for all atoms except for the water molecules. The erbium atom is coordinated to eight oxygen atoms at distances of $2.362(5)$ – $2.418(5) \text{ \AA}$ and they form a distorted square antiprism around the cation. A water molecule forms the ninth near neighbor at $2.441(9) \text{ \AA}$ above the larger square face of the antiprism. The acid oxalate and oxalate anions occupy crystallographic sites at random. The "statistically averaged" oxalate group is centrosymmetric and planar with $\text{C}=\text{C} = 1.529(11) \text{ \AA}$, $\text{C}-\text{O}$ equivalent to $\text{C}=\text{O}$ equals $1.254(7) \text{ \AA}$; the values of the angles are $\text{O}(1)-\text{C}-\text{O}(2) = 125.9(5)^\circ$, $\text{O}(1)-\text{C}-\text{C} = 116.8(7)^\circ$, and $\text{O}(2)-\text{C}-\text{C} = 117.3(6)^\circ$. Hydrogen bonding exists between $\text{H}_2\text{O}(1)$ and the oxygen atoms of the acid groups at distances of $2.73(7) \text{ \AA}$. A very short hydrogen bond, $2.43(4) \text{ \AA}$, is observed between two $\text{H}_2\text{O}(2)$ molecules but the physical significance is difficult to assess because $\text{H}_2\text{O}(2)$ is disordered in this structure. This compound occurs also for dysprosium, ytterbium, and yttrium analogs but could not be prepared for neodymium.

Introduction

The rare earth oxalate hydrates $\text{Ln}_2(\text{C}_2\text{O}_4)_3 \cdot 10\text{H}_2\text{O}$ ($\text{Ln} = \text{La}, \text{Nd}, \text{Gd}$) have been prepared and characterized optically² and by X-ray diffraction powder data^{2,3} which show that they are isomorphous. Some of the transuranic elements also form these oxalate hydrates and are isomorphous with the rare earth compounds.³ No comparable oxalate hydrates for the heavy rare earth elements have been reported. Dr. R. H. Karraker of Eastern Illinois University undertook the preparation of oxalates of the heavy rare earths. It was observed that the powder X-ray diffraction diagrams of his oxalate preparations were different from the previously reported patterns for the lanthanide oxalate decahydrates and an analysis of the erbium compound indicated that the material has the formula $\text{Er}(\text{HC}_2\text{O}_4)(\text{C}_2\text{O}_4) \cdot 3\text{H}_2\text{O}$. The complete crystal structure analysis of this compound was undertaken because no structural investigation of a rare earth oxalate has been reported and because these materials contain both the acid monoanion and the dianion in the same structure. The presence of a dicarboxylic acid molecule together with its doubly charged ion has recently been reported for potassium hydrogen malonate.^{4,5} Oxalic

acid has different bond lengths for $\text{C}=\text{O}$ and $\text{C}-\text{OH}^{6-8}$ and we planned to identify the bonding that exists between the cation and the two different anions. Also, the oxalate ion is not always planar⁹ and the conformation of the oxalate ion in this compound is therefore also of interest.

Experimental Section

Erbium oxalate trihydrate, $\text{Er}(\text{HC}_2\text{O}_4)(\text{C}_2\text{O}_4) \cdot 3\text{H}_2\text{O}$, was prepared by precipitating erbium oxalate from an aqueous solution of erbium chloride and oxalic acid. The erbium oxalate precipitate was redissolved in concentrated HCl and pink crystals were grown by evaporating the HCl slowly at room temperature. After about 1 week good crystals were obtained. A similar technique was used to prepare the Dy, Yb, and Y analogs of the erbium compound but the Nd isomorph could not be prepared. Results of a wet chemical analysis of the crystals follow (as weight per cent). *Anal.* Calcd for $\text{Er}(\text{HC}_2\text{O}_4)(\text{C}_2\text{O}_4) \cdot 3\text{H}_2\text{O}$: Er, 41.99; oxalate, 44.45; H_2O , 13.56. Found: Er, 40.8; oxalate, 43.6; H_2O , 15.4.

Precession photographs of a crystal show the diffraction symmetry $4/m$ and the only observed systematic absences were $h00$ with $h + k = 2n + 1$. These absences are characteristic solely of space group $P4/n$ (C_{4h} , no. 85).

Most of the crystals are bounded by the forms $\{110\}$ and $\{001\}$. A crystal bounded by these forms and with dimensions $0.312 \times 0.390 \times 0.299 \pm 0.005 \text{ mm}$ was mounted on a Picker four-circle automatic single-crystal diffractometer. The takeoff angle was reduced to 1.2° and 32 reflection maxima between

(1) Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corp.

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