

Complexes of Nicotinamide, Isonicotinamide, and Picolinamide with Copper(II) Perchlorate in Acetonitrile and in Propylene Carbonate

Kuang-Ling H. Chen and Reynold T. Iwamoto

Received December 27, 1968

The complexes of nicotinamide, isonicotinamide, and picolinamide with copper(II) ion in acetonitrile and in propylene carbonate have been investigated by electrochemical, infrared, and visible spectral techniques. Picolinamide forms in these solvents a 2:1 chelated complex species in which the pyridine nitrogen and carbonyl oxygen are involved in coordination and which in solutions with picolinamide/copper(II) ratio greater than two takes on at least one additional ligand molecule. The latter picolinamide is mono-coordinated to copper(II) through the carbonyl oxygen of the amide group. In acetonitrile, nicotinamide and isonicotinamide appear to form the respective hexacoordinated complex species with the ligands mono-coordinated to copper(II) ion through the pyridine nitrogen.

Introduction

Nicotinamide is the form in which the vitamin niacin is found in its physiological active combination. It is an integral part of three different coenzymes which act as the prosthetic group of a variety of metabolic enzymes. The main function of these enzymes lies in the area of biological oxidation-reduction. In order to understand better the interaction of metal ions with nicotinamide in its biological environment, the nature of the complexes of copper(II) and nicotinamide (NA), and its isomers isonicotinamide (INA) and picolinamide (PA) in acetonitrile and in propylene carbonate has been investigated by infrared and visible spectral techniques and by voltammetry.

Experimental

Acetonitrile (Matheson Coleman and Bell) was refluxed over calcium hydride for several hours, then distilled. The distillate was treated with phosphorus(V) oxide, refluxed, and distilled. The fraction distilling at 81° was collected. Propylene carbonate (Aldrich Chemical Co.) was purified by passage through a column (1.8 cm (i.d.) × 45 cm) of Woelm, activity grade 1, neutral alumina, followed by vacuum distillation.

Nicotinamide (U.S.P. grade), isonicotinamide (Aldrich Chemical Co.), and picolinamide (Reilley Tar

and Chemical Corp.) were recrystallized two to three times from water, and dried at 90°. The melting points were 128, 155, and 106°, respectively. The literature values are: nicotinamide, 129°; isonicotinamide, 159°; and picolinamide, 107°.¹

Hexaaquocopper(II) perchlorate was dried in a vacuum oven at 75° for one day and stored over anhydrous magnesium perchlorate. The water content of the salt was determined indirectly by analyzing the salt for copper by EDTA titration with murexide as indicator² or by iodometry, and assuming two perchlorate ions per copper(II) ion in the salt. The analyses indicated a mole of the copper salt contained from 3.0-3.5 moles of water. Tetraethylammonium perchlorate was prepared by mixing equal molar quantities of tetraethylammonium chloride or bromide and sodium perchlorate in water. The salt was fractionally crystallized several times from water. When the addition of silver nitrate to a solution of a small portion of the salt gave no silver halide, the product was dried at 110°. Current-voltage curves at the dropping mercury electrode of 0.10 *F* solutions of the purified tetraethylammonium perchlorate in acetonitrile showed no waves indicative of halide ion or any reducible species.

Infrared absorption spectra were obtained with a Perkin Elmer Model 421 spectrophotometer using a 0.1-mm BaF₂ cell. The Cary Model 14 recording spectrophotometer and the Beckman DU spectrophotometer were used to obtain the visible spectra.

Current-voltage curves were recorded with a controlled potential polarograph of the type designed by Kelley, Fisher, and Jones.^{3,4} An H-type polarographic cell with a glass frit of medium porosity was used, with either a dropping mercury electrode or a rotating platinum electrode in one side arm and a saturated calomel electrode and a platinum foil electrode, to function as the auxiliary electrode in a three-electrode system, in the other arm. The rotating platinum electrode was a ca. 1-mm length of 22-gauge platinum wire extending from the tip of a soft glass tubing rotated at ca. 600 rpm with a Sargent rotator. One tenth for-

(1) H. Negoro, T. Miki, and S. Ueda, *J. Pharm. Soc. Japan*, **80**, 665 (1960).

(2) H. Flaschka, *EDTA Titrations*, Pergamon Press, New York, 1959, p. 78.

(3) M. T. Kelley, H. C. Jones, and D. J. Fisher, *Anal. Chem.*, **31**, 1475 (1959).

(4) M. T. Kelley, D. J. Fisher, and H. C. Jones, *ibid.*, **32**, 1262 (1960).

mal tetraethylammonium perchlorate solutions *ca.* $5 \times 10^{-4} F$ or less in copper(II) perchlorate were used in the electrochemical study. The solutions were deoxygenated with purified nitrogen and protected from atmospheric oxygen during the course of measurement by passing nitrogen over the surface. All solutions were examined at room temperature.

Results and Discussion

Acetonitrile Solutions. Infrared Study. The site of coordination of copper(II) ion to pyridine carboxylic acid amides can be determined from shifts of the bands of the carbonyl stretching and ring C—C and C—N stretching vibrations of the complexes from those for similar vibrations of the free ligands. Gill *et al.*,⁵ Greenwood and Wade,⁶ and Mitchell⁷ have pointed out that the infrared spectrum of coordinated pyridine shows some fairly major differences in the position of some of the bands when compared with that of the free base. These investigators observed blue shifts of the four principal bands of pyridine between 1430 and 1600 cm^{-1} , which are ring C—C and C—N stretching frequencies, with the highest frequency showing the largest shift, and of the ring breathing and C—H in-plane deformation frequencies, which occur in the 985 to 1250 cm^{-1} region.

When the carbonyl oxygen of an amide is involved in coordination, the stretching frequency of the carbonyl group is shifted to a lower value.⁸ On the other hand, when the pyridine nitrogen of these ligands is involved in coordination, the electron density in the ligand is shifted toward the pyridine nitrogen. This shift results from either an inductive effect or a combination of inductive effect and resonance, depending on the amide, and leads to an increase in the double bond character of the carbonyl group and a shift of the stretching frequency to a higher value.⁹ The carbonyl stretching frequency along with the highest ring stretching frequency of free and coordinated ligands can, therefore, provide valuable information concerning whether pyridine nitrogen or carbonyl oxygen of these amides are involved in coordination. Pertinent infrared spectral data on the free ligands and their copper(II) complexes for solutions 1:1 and 2:1 in ligand to copper(II) concentrations are summarized in Table I.

For the NA and INA complexes, the blue shift of the band for the carbonyl stretching vibration and the shift of the band at 1585 cm^{-1} , the highest ring stretching vibration, to 1600-1610 cm^{-1} indicate that in both of these complexes it is the ring nitrogen which is involved in coordination. The infrared data on the coordination of PA to copper(II) ion, on the other hand, indicate both carbonyl and pyridine nitrogen coordination of copper(II) ion. The carbonyl stretching frequency is shifted red, and the highest ring

Table I. Infrared Data for Solutions 1:1 and 2:1 in Pyridine Carboxylic Acid Amide to Copper(II) in Acetonitrile (cm^{-1})^a

Compound	Carbonyl stretching	Highest ring stretching
Nicotinamide Cu(NA) _n (ClO ₄) ₂	1685 1693	<i>ca.</i> 1585 1602
Isonicotinamide Cu(INA) _n (ClO ₄) ₂	1689 1693	1585 1605
Picolinamide Cu(PA) _n (ClO ₄) ₂	1691 <i>ca.</i> 1677	<i>ca.</i> 1578 1582

^a Acetonitrile solutions: $5 \times 10^{-2} F$ in Cu(ClO₄)₂ and $5 \times 10^{-2} F$ and $1.0 \times 10^{-1} F$ in pyridine carboxylic acid amides.

Table II. Visible Spectral Data, λ_{max} Values (m μ). ($1.0 \times 10^{-2} F$ Cu(ClO₄)₂ in Acetonitrile)

Ligand: Copper(II)	Nicotinamide	Isonicotinamide	Picolinamide
1:2	—	—	730
1:1	690	690	710
2:1	650	650	670
3:1	620	620	680
4:1	610	610	685
5:1	600	600	690
6:1	600	600	690-700
7:1	595-600	595-600	695-700
8:1	590-595	590-595	700
> 10:1	—	—	<i>ca.</i> 720

stretching frequency is shifted blue. The smaller blue shift of the ring stretching frequency of PA than those of NA and INA and the smaller red shift of the carbonyl stretching frequency of PA than those observed for benzamide and acetophenone on coordination of these two carbonyl containing compounds to copper(II) ion, 20-30 cm^{-1} , are due to the two coordination acts in PA working against each other in drawing the electron density in the ligand to the two coordination sites.

Visible Spectral Study. Acetonitrile solutions of copper(II) perchlorate containing varying concentrations of nicotinamide, isonicotinamide, and picolinamide have broad absorption bands of low absorptivity spanning the 550-800 m μ region. Values for λ_{max} of solutions with different ligand to copper(II) ion ratios are listed in Table II.

The higher λ_{max} values for the picolinamide-copper(II) complexes than for the nicotinamide and isonicotinamide-copper(II) complexes are not surprising in view of the fact that in the case of picolinamide complexes there is carbonyl oxygen coordination of copper(II) ion along with pyridine nitrogen coordination while in the cases of nicotinamide and isonicotinamide there is only pyridine nitrogen coordination and ligands which coordinate through an oxygen atom are below pyridine in the spectrochemical series.¹⁰

A study of the picolinamide-copper(II) complex-formation system by the molar ratio method, in which the copper(II) perchlorate concentration was kept con-

(5) N. S. Gill, R. H. Nuttal, D. E. Scaife, and D. W. A. Sharp, *J. Inorg. Nucl. Chem.*, **18**, 79 (1961).

(6) N. N. Greenwood and K. Wade, *J. Chem. Soc.*, 1130 (1960).

(7) P. C. H. Mitchell, *J. Inorg. Nucl. Chem.*, **21**, 382 (1961).

(8) L. J. Andrews and R. M. Keefter, *Molecular Complexes in Organic Chemistry*, Holden-Day, San Francisco, 1964, p. 36.

(9) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, Methuen and Co., Ltd, London, 1958, p. 139.

(10) C. K. Jørgensen, *Absorption Spectra and Chemical Bonding in Complexes*, Pergamon Press, London, 1962, p. 109.

stant at $1.0 \times 10^{-2} F$ and the ligand concentration was gradually increased, indicated, from absorbances at several wavelengths between 600 and 680 $m\mu$, the formation of a stable complex of 2:1 picolinamide to copper(II) stoichiometry. As the ligand to metal ratio was increased beyond two, the absorbance decreased—initially at about one-third of the rate with which it increased—indicating formation of a higher complex or complexes. At the same time, the absorption maximum shifted to higher wavelengths, in a manner similar to the pentammine effect.¹¹ The absence of an infrared band at *ca.* 1600 cm^{-1} , a coordinated pyridine band, for solutions with PA to copper(II) ratios greater than two is taken as indication of monocoordination of the third and fourth, if there is formation of a 4:1 complex, PA to copper(II) through the carbonyl oxygen.

From the infrared and visible spectral studies, it can be concluded that the first two PA molecules coordinate to copper(II) ion by chelation. The two ligand molecules undoubtedly lie in a plane with acetonitrile molecules occupying the two apex positions in a distorted octahedral configuration. In the PA-copper(II) complexes with ligand to metal ion ratio greater than two, there is replacement of one or two of the acetonitrile molecules in the apex positions by PA. Monocoordination of the additional PA molecule(s) to copper(II) ion through the carbonyl oxygen rather than pyridine nitrogen is the result of steric hindrance of the amide group of the PA molecules taking up the apex positions in preventing close approach of the 2:1 complex to the pyridine nitrogen coordination site.

The visible spectra of the NA and INA complexes of copper(II) are essentially identical. For both series of complexes, the maximum wavelength of absorption

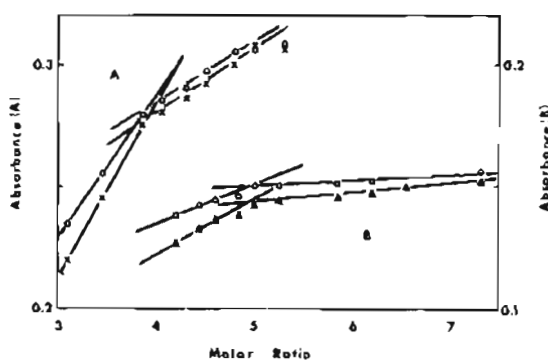


Figure 1. (A) Absorbance of solutions of acetonitrile containing $4 \times 10^{-2} F$ copper(II) perchlorate and nicotinamide versus the ratio of total concentrations of nicotinamide to copper(II) ion, 1-mm cell. Above molar ratio of 5.3, precipitation of perchlorate salt of complexed copper(II) ion occurred.

○ 600 $m\mu$ × 590 $m\mu$

(B) Absorbance of solutions of acetonitrile containing $2 \times 10^{-2} F$ copper(II) perchlorate and nicotinamide versus the ratio of total concentrations of nicotinamide to copper(II) ion, 1-mm cell.

○ 600 $m\mu$ Δ 580 $m\mu$

(11) J. Bjerrum, C. J. Balhausen, C. K. Jørgensen, *Acta Chem. Scand.* 8, 1275 (1954).

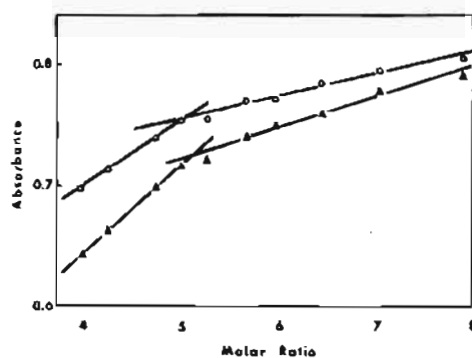


Figure 2. Absorbance of solutions of acetonitrile containing $1 \times 10^{-2} F$ copper(II) perchlorate and isonicotinamide versus the ratio of total concentrations of isonicotinamide to copper(II) ion, 1.0-cm cell.

○ 600 $m\mu$ Δ 580 $m\mu$

shifts from 700 $m\mu$ for ligand to copper(II) ratio of one to *ca.* 590 $m\mu$ for ratios greater than 6. Unlike the PA case, there is no shift of λ_{max} back toward the red. Similar observations have been reported with pyridine in aqueous medium.^{12,13} It is noteworthy that in aqueous medium, the shift of λ_{max} with high pyridine concentration also reaches a limiting value of *ca.* 590 $m\mu$. Analysis of the spectral data of 2×10^{-2} and $4 \times 10^{-2} F$ copper(II) solutions containing varying amounts of NA and $1.0 \times 10^{-2} F$ copper(II) solutions containing varying amounts of INA by the molar ratio method (Figures 1 and 2) indicates that with both ligands, complexes with up to six ligand molecules can be obtained. Formation of the 6:1 complex species is based on the slow continuous increase in absorption beyond molar ratio of 5, following essentially quantitative formation of the 5:1 complexes. In the infrared spectra of solutions with 8:1 ratio of the amides to copper(II), there is no new absorption band (for coordinated carbonyl) on the lower frequency side of the band for the carbonyl stretching vibration of the free ligands. It, therefore, appears that all six NA and INA ligand molecules in the 6:1 complexes are monocoordinated to copper(II) through the pyridine nitrogen.

Electrochemical Study. Current-voltage studies at the rotating platinum electrode of solutions of copper(II) perchlorate and excess picolinamide in acetonitrile yielded voltammetric curves with two steps. The first step involving reduction of copper(II) to copper(I) is reversible. From the slopes of the plots of the shift in half-wave potential for the copper(II)/copper(I) step vs. the logarithm of excess PA concentration, a value of two was obtained for the ratio of PA to copper(II) for the highest complex obtained in the acetonitrile solutions.¹⁴ From the electrochemical data, an overall formation constant of $10^{14.4}$ was obtained for $Cu(PA)_2^{2+}$. Voltammetric detection of the formation of the 3:1 complex in acetonitrile does not appear to be possible because of the weak character of the complex. Information on the nature of the

(12) J. Bjerrum and E. J. Nielsen, *Acta Chem. Scand.*, 2, 297 (1948).

(13) D. L. Leussing and R. C. Hansen, *J. Am. Chem. Soc.*, 79, 4270 (1957).

(14) I. M. Kolthoff and J. J. Lingane, *Polarography*, 2nd ed., Interscience Publisher, Inc., New York, N. Y., Vol. 1, Chapter 12.

NA and INA complexes of copper(II) in acetonitrile could not be established by this voltammetric technique owing to the irreversibility of the copper(II)/copper(I) reduction step at the rotating platinum electrode. The strong solvation of copper(I) ion by acetonitrile prevents the formation of any copper(I)-pyridine carboxylic acid amide complexes, as indicated by no change in the half-wave potential for the copper(I)/copper(0) reduction step on the addition of the amides to solutions of copper(II) perchlorate of the same concentration in acetonitrile.

Propylene Carbonate Solution. A similar electrochemical study of the pyridine carboxylic acid amide complexes of copper(II) in propylene carbonate with the dropping mercury electrode revealed that picolinamide formed a 2:1 complex with copper(I) ion and a 3:1 complex with the divalent ion. The slopes of the plots of the half-wave potentials of the copper(II), copper(I) and copper(I), copper(Hg) steps vs. $\log PA$ were 0.8×0.059 and 2.0×0.059 , respectively. The irreversible character of the first reduction step of copper(II) in the presence of NA and of INA also prevented any information on these pyridine carboxylic acid amide-copper(II) complexes in this solvent from being obtained by electrochemical methods. The unexpected formation of tetracoordinated copper(I) complexes of NA and INA in propylene carbonate has been communicated earlier.¹⁵

(15) K. L. Chen and R. T. Iwamoto, *Inorg. Nucl. Chem. Letters*, 4, 499 (1968).

The presence of an isosbestic point at 683 m μ in the visible spectra of copper(II) perchlorate solutions in propylene carbonate containing varying amounts of PA (from 2:1 to 7:1 ligand to metal ratio) supports the results of the electrochemical study that PA forms a 3:1 complex with copper(II). A molar ratio study of this complex-formation system at several different wavelengths between 570 and 650 m μ likewise indicates the formation of a 3:1 copper(II) complex; the absorbance of the solutions increased sharply to a maximum value at PA to copper(II) ratio of two, then decreased, at first rapidly then gradually, with increasing amount of ligand.

In summary, picolinamide forms in acetonitrile and propylene carbonate, a 2:1 chelated complex species in which the pyridine nitrogen and carbonyl oxygen groups are involved in coordination and which in solutions with picolinamide/copper(II) ratio greater than two takes on at least one additional ligand molecule. The latter picolinamide is monocoordinated to copper(II) through the carbonyl oxygen of the amide group. In acetonitrile, nicotinamide and isonicotinamide form the respective hexacoordinated complex species with the ligands monocoordinated to copper(II) ion through the pyridine nitrogen.

Acknowledgment. The authors gratefully acknowledge the support of the National Science Foundation and the General Research Fund of the University of Kansas.