[Chem. Pharm. Bull.]
[25(7) 1694—1700 (1977)]

UDC 547.857.7.02.08 : 543.422.4.06

Infrared Spectrum and Electron Paramagnetic Resonance Studies on Copper-(adeninato)(diethylenetriamine) Monohydrate

TADAO FUJITA and TAKEICHI SAKAGUCHI

Faculty of Pharmaceutical Sciences, Chiba University¹⁾

(Received October 27, 1976)

A mixed ligand complex, copper-(adeninato)(diethylenetriamine)monohydrate, was prepared and the coordination site of the compound was suggested from infrared spectroscopic analysis. Assignments of infrared bands of this compound are discussed in some detail.

Electron paramagnetic resonance (EPR) spectra of this compound were recorded at room temperature and the EPR spectral line shape and *g*-values were compared with those of other mixed ligand complexes containing the adenine ligand. It was assumed that the coordination sphere of Cu²⁺ was a square-based pyramidal and the nitrogen atom N9 of adenine monoanion coordinated with Cu²⁺.

Keywords—mixed ligand complex of adenine; IR spectra; EPR spectra; coordination site; stereochemistry; complex of biological importance

The ligand adenine (denoted by adeH) has been found to form a variety of complexes with bivalent copper.²⁻⁶⁾ Recently mixed ligand complexes containing the constituents of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), for example adenine, have been prepared and the structures of the compounds have been investigated by means of infrared spectroscopic analysis⁷⁾ and X-ray methods.⁸⁻¹⁰⁾

We have reported the preparation of (Glycylglycinato)Cu²⁺ (adeH) monohydrate and its examination by infrared (IR) spectrometry.⁷⁾ Tomita, *et al.*⁸⁾ determined the crystal structure of the compound and concluded that the nitrogen atom N9 coordinated to copper.²⁺

Fig. 1. Structure of Adenine (Denoted by adeH)

Sletten²⁾ demonstrated by X-ray methods that the complex Cu(ade)₂·4H₂O is a dimeric form, and it was established that the neutral adenine functions as a *syn-syn* bidentate bridge (*via* N3 and N9) in the compound [Cu₂(adeH)₄(H₂O)₂](ClO₄)₄·2H₂O.³⁾

The electron paramagnetic resonance (EPR) spectra of the mixed ligand complexes containing adenine have not so far been reported. In this paper the EPR spectra and *g*-values of the complex Cu²⁺(ade)₂-(dien) monohydrate will be reported, and compared with those of other mixed ligand complexes containing adenine.

- 1) Location: Yayoi-cho, Chiba, 280, Japan.
- 2) E. Sletten, *Chem. Commun.*, **1967**, 1119; *idem*, *Acta Crystallogr., Sect. B*, **25**, 1480 (1969).
- 3) A. Terzis, A.N. Beauchamp, and R. Rivest, *Inorg. Chem.*, **12**, 1166 (1973).
- 4) P. de Meester, D.M.L. Goodgame, K.A. Price, and A.C. Skapski, *Nature* (London), **229**, 191 (1971); P. de Meester and A.C. Skapski, *J. Chem. Soc. A*, **1971**, 2167.
- 5) P. de Meester and A.C. Skapski, *J. Chem. Soc. A*, **1972**, 2400.
- 6) P. de Meester and A.C. Skapski, *J. Chem. Soc. A*, **1973**, 424.
- 7) T. Sakaguchi and M. Tanno, *Nippon Kagaku Kaishi*, **1974**, 1637.
- 8) K. Tomita, T. Izuno, and T. Fujiwara, *Biochem. Biophys. Res. Commun.*, **54**, 96 (1974).
- 9) D.J. Szalda, T.J. Kistenmacher, and L.G. Marzilli, *Inorg. Chem.*, **14**, 2623 (1975).
- 10) T.J. Kistenmacher, L.G. Marzilli, and D.J. Szalda, *Acta Crystallogr. Sect. B*, **32**, 186 (1976).

Results and Discussion

IR Spectra

The infrared spectra of adenine and its metal complexes have been reported in some detail and band assignments have been proposed,⁷⁾ but IR spectra of mixed ligand complexes of biological importance has little been investigated.

The frequencies and relative intensities of infrared absorption bands for $\text{Cu}^{2+}(\text{ade})_2(\text{dien}) \cdot \text{H}_2\text{O}$ complex are listed in Table I. The assignment of the bands to the fundamental modes of vibrations will be discussed in detail below. A tentative band assignment for metal complexes with diethylenetriamine as a ligand has been investigated by Schmidtke and Garthoff.¹¹⁾ A band assignment is made, using the deuterated complex in this paper.

(1) $\text{NH}_2(\text{NH})$ and CH_2 Stretching Vibrations

The band at 3325 cm^{-1} in the mixed ligand complex was assigned to NH_2 stretching due to adenine,⁷⁾ which shifted to higher wave numbers by complex formation. Four bands are found in the NH_2 and NH stretching region from 3088 to 3325 cm^{-1} . The CH_2 stretching vibrations have a low intensity compared with the NH_2 stretching mode and are hardly recognizable in the mixed ligand complex.¹¹⁾ The bands at 1901 , 1805 , and 1765 cm^{-1} were unassigned.

(2) $\text{NH}_2(\text{NH})$ Deformations

The assignment of NH_2 and CH_2 deformations follows the frequency sequence proposed for ethylenediamine complexes,^{11,12)} according to which these vibrational modes decrease in the energetic order of deformation, wagging, twisting, and rocking.

(2a) NH_2 Deformation—The band at 1670 cm^{-1} was assigned to NH_2 deformation of adenine ligand in the mixed ligand complex.⁷⁾ This band disappeared in the spectrum of the deuterated complex and did not shift on complexation. This may indicate that Cu^{2+} does not bind to NH_2 of adenine ligand. The vibrational mode is found at 1548 cm^{-1} in the mixed ligand complex. In this region the band does not appear in adenine and it is concluded that this band at 1548 cm^{-1} is due to diethylenetriamine.

(2b) NH_2 Wagging and Twisting—The bands at 1375 and 1342 cm^{-1} were assigned to CH_2 wagging deformation and ring vibration, which appeared at the same frequencies in both adenine and the mixed ligand complex.^{11,13)}

The band at 1321 cm^{-1} in the mixed ligand complex assigned to NH_2 wagging deformation did not show a marked shift but the bands at 1160 and 1132 cm^{-1} due to adenine, which were assigned to NH_2 wagging and twisting deformations, shifted to lower wave numbers in the mixed ligand complex.

The band at 1242 cm^{-1} has only a very weak intensity and is possibly due to CH_2 twisting deformation, which is expected to appear in this region also as NH wagging deformation.

(2c) NH_2 Rocking—The bands in the region of 635 to 878 cm^{-1} were assigned to CH_2 , NH_2 , and NH rocking and C-N stretching.

(3) CH_2 Deformation

The CH_2 deformation is expected to appear in the region of 1500 to 1400 cm^{-1} for all 1,2-disubstituted ethanes.¹⁴⁾ For the mixed ligand complex three absorption bands are found in this region accompanied by another weak absorption which is possibly due to the purine ring vibration.

11) H.H. Schmidtke and D. Garthoff, *Inorg. Chim. Acta*, **1968**, 357.

12) G.W. Watt and D.S. Klett, *Inorg. Chem.*, **5**, 1278 (1966).

13) G.W. Watt and W.A. Cude, *J. Am. Chem. Soc.*, **90**, 6382 (1968).

14) S. Mizushima, I. Ichishima, I. Nakagawa, and J.V. Quagliano, *J. Phys. Chem.*, **59**, 293 (1955).

(4) C-C and C-N Skeletal Vibration

The weak and medium intensity bands at 1040–1080 cm^{-1} are assigned to C-C and C-N ring vibrations. Five bands are found in this region. The high intensity band at 1602 cm^{-1} is assigned to the C=C and C=N ring vibration, which shifts to lower wave numbers on complexation.

(5) Cu-N and NCCN Skeletal Vibrations

Metal-nitrogen stretching occurs in the region of 600–450 cm^{-1} .¹⁵⁾ The band at 545 cm^{-1} was assigned to NCCN skeletal vibrations of adenine ligand, which shifted little on complexation. This band does not vary much with change in the geometry of the compounds in general and the band at 545 cm^{-1} in this complex was unchanged compared with adenine ligand.

Fig. 2. IR Spectra of $\text{Cu(ade)}_2\text{dien} \cdot \text{H}_2\text{O}$ (top) and Its N-Deutrated Complex from 3500 to 2000 cm^{-1} in KBr Disk

Fig. 3. IR Spectra of Adenine (top), $\text{Cu(ade)}_2\text{dien} \cdot \text{H}_2\text{O}$ (center), and Its N-Deutrated Complex (bottom) from 1700 to 1500 cm^{-1} in KBr Disk

EPR Spectra

The EPR spectra of the compounds are illustrated in Figs. 4, 5, and 6. By the methods of Sands¹⁶⁾ and Kneubuhl,¹⁷⁾ g -values were determined and the values of $(g_{\parallel} - 2)/(g_{\perp} - 2)$ (hereafter referred to as G) have been calculated.¹⁸⁾

Hathaway and Billing discussed some typical polycrystalline EPR spectral line-shape, with use of approximate g -values.¹⁹⁾ They reported that an isotropic spectrum would suggest the presence of Cu^{2+} ion in a complex containing grossly misaligned tetragonal axes, as in $\text{Cu}^{2+}\text{-dien}_2(\text{NO}_3)_2$ ²⁰⁾ most commonly. Recently, synthesis, and crystal and molecular structures of the complex (bistheophyllinato) (diethylenetriamine)-copper²⁺ were reported by Sorrell,

15) M.N. Hughes and W.R. McWhinnie, *J. Chem. Soc. A*, **1967**, 592.

16) R.H. Sands, *Phys. Rev.*, **99**, 1222 (1955).

17) F.K. Kneubuhl, *J. Chem. Phys.*, **33**, 1074 (1960).

18) I.M. Procter, B.J. Hathaway, and P. Nicholls, *J. Chem. Soc. A*, **1968**, 1678.

19) B.H. Hathaway and D.H. Billing, *Coord. Chem. Rev.*, **5**, 143 (1970).

20) F.S. Stephens, *J. Chem. Soc. A*, **1969**, 883.

TABLE I. IR Data of $\text{Cu}(\text{ade})_2(\text{dien}) \cdot \text{H}_2\text{O}$ compared with Adenine

Tentative assignment	Adenine	$\text{Cu}(\text{de})_2(\text{dien}) \cdot \text{H}_2\text{O}$
NH_2 and NH str.		3325 s
	3290m	3250 s
		3175m
	3110 s	3088 s
NH (due to adenine) and CH_2 (due to dien) str.	2975 w	2962 w
	2790 w	2925 w
	2690 w	2688 w
	2600 w	
		1901 w
		1805 w
		1765 w
NH_2 in-plane sym. def.	1670 s	1670 s
C=C, C=N str.	1610 s	1602 s
NH_2 def.		1548m
CH_2 def. and purine ring vib.	1510 w	1488 w
	1458 w	1470 m
	1426 m	1395 m
CH_2 wagging def. and ring vib.	1375 m	1375 w
	1342 m	1341 m
NH_2 wagging def.	1318 m	1321 m
CH_2 twisting def.		1290 w
NH_2 out-plane sym. def.	1260 w	1264 m
NH wagging		1242 sh
		1228 w
		1212 s
NH_2 wagging and NH_2 twisting def.	1160 w	1143 m
	1132 m	1110 m
C-C, C-N str.		1080 w
		1070 m
		1062 w
		1050 m
		1042 w
NH	1028 m	1030 m
C-C, C-N str.		1023 m
NH_2 out-plane def.	945 m	974 m
	918 m	910 w
CH_2 , NH_2 , NH rocking and C-N str.	875 w	878 w
	850 w	875 w
		825 w
	801 m	810 m
		760 w
	728 m	728 w
		708 w
		699 w
	644 w	660 m
	625 w	635 w
CuN str.		570 w
		555 w
C-N str.	546 m	545 m
ring def.		494 w
		475 w
N-Cu-N def.		410 w

TABLE II. g -Values and G -Values of the Mixed Ligand Complexes Containing Adenine

Compound	g	$g_{\perp}$ or g_1	$g_{\parallel}$ or g_2	g_3	G
Cu(ade) ₂ (dien)·H ₂ O	2.11				
Cu(adeH)GlyCl·H ₂ O		2.06	2.10	2.13	1.67
Cu(adeH)GlyGly·H ₂ O		2.05	2.10	2.11	2.00

Marzilli, and Kistenmacher.²¹⁾ They concluded that the primary coordination sphere about the Cu²⁺ center was approximately a square pyramidal, and that N(7) of strongly bound theophylline monoanion defined the equatorial plane, and a second theophylline monoanion, bound to an axial position through N(7) of its purine ring system, completed the coordination sphere. The complex represented the first report of a metal-purine system where two purine ligands occupied a widely divergent coordination site.

The EPR spectrum of Cu(ade)₂(dien) monohydrate appears to be isotropic. Therefore, the compound probably contains tetragonal axes as in Cu-dien(NO₃)₂²⁰⁾ and Cu-dien₂Br₂·H₂O.^{22,23)} Tomlinson and Hathaway²⁴⁾ reported the g -values of the compounds whose molecular symmetry probably approximated more closely that of a square-based pyramidal rather than a trigonal bipyramidal configuration.²⁴⁾ It appears that the g -values of Cu(ade)₂dien·H₂O approximate the values described by Tomlinson and Hathaway.²⁴⁾

Infrared spectroscopic and elementary analyses reveal that Cu(ade)₂dien·H₂O contains two adenine anions and one diethylenetriamine molecule as in (bistheophyllinato) (diethylene-

Fig. 4. EPR Spectra of Cu(ade)₂dien·H₂O at Room Temperature

triamine)-copper²⁺.²¹⁾ The tridentate chelate diethylenetriamine, with its terminal amine nitrogen atoms in the commonly observed *trans* positioning,^{23,25-27)} occupies three of the four equatorial coordination sites. Therefore, it is assumed that the primary coordination sphere about the copper center in Cu(ade)₂dien·H₂O is approximately square-based pyramidal, and the coordination sphere is assumed to be complicated by a strongly bound, equatorial adenine anion, and loosely bound, axial adenine anion. The conformation features of the compound is in good agreement with those in [(thyminato)(aquo)(dien)-copper²⁺] bromide, where a water molecule occupies the axial position.²⁵⁾

In Cu(ade)₂(dien)·H₂O the axial Cu-N (of adenine anion) bond distance is assumed to be typically long in order to limit steric hindrance between the two adenine anions, and it is likely that the presence of an axially bound and on equatorially bound adenine anion is sterically feasible for Cu²⁺. Tomita, *et al.* reported that the complex Cu(adeH)GlyGly·H₂O

- 21) T. Sorrell, L.G. Marzilli, and T.J. Kistenmacher, *J. Am. Chem. Soc.*, **98**, 2181 (1976).
- 22) B.J. Hathaway, M.J. Bew, D.E. Billing, R.J. Dudley, and P. Nicholls, *J. Chem. Soc. A*, **1969**, 2312.
- 23) F.S. Stephens, *J. Chem. Soc. A.*, **1969**, 2233.
- 24) A.A.G. Tomlinson and B.J. Hathaway, *J. Chem. Soc. A.*, **1968**, 1685.
- 25) T.J. Kistenmacher, T. Sorrell, and L.G. Marzilli, *Inorg. Chem.*, **14**, 2479 (1975).
- 26) F.S. Stephens, *J. Chem. Soc. A*, **1969**, 2493.
- 27) G. Davey and F.S. Stephens, *J. Chem. Soc. A*, **1971**, 103.

showed a square-based pyramidal coordination geometry with an axial ligand of loosely bound water molecule as in [(thyminato)(aquo)(dien)cooper²⁺] bromide.²⁵⁾

The EPR spectra of Cu(adeH)GlyGly·H₂O and Cu(adeH)GlyCl·H₂O⁷⁾ show axial spectra and three *g*-values. Because of similarity of the *g*-values the latter is assumed to show a square-based pyramidal coordination geometry as the former although the crystal structure of the latter has not so far been determined by X-ray methods. Furthermore, the *g*-values of Cu(ade)₂(dien)·H₂O approximate the values of other mixed ligand complexes containing adenine ligand and in this respect the coordination sphere of Cu(ade)₂(dien)·H₂O is close to that of Cu(adeH)GlyGly·H₂O. Consequently it is revealed that the three complexes containing adenine have similar *g*-values, whenever the second ligand is glycine, glycyglycine, or diethylenetriamine.

Fig. 5. EPR Spectra of Cu(adeH)GlyGly·H₂O at Room Temperature

Fig. 6. EPR Spectra of Cu(adeH)GlyCl·H₂O at Room Temperature

Cu(ade)₂(dien)·H₂O containing the axial ligand of adenine monoanion showed an isotropic spectrum, but the other complexes showed axial spectra, which contained the axial ligand of a water molecule. In general, adenine monoanions are the more grossly misaligned axes than a water molecule because of the steric hindrance. Therefore, an isotropic spectrum would suggest the presence of a Cu²⁺ ion in a complex containing grossly tetragonal axes as Hathaway and Billing have reported.¹⁹⁾ It is also probable that two adenine anions are bound equatorially and an NH₂ of diethylenetriamine axially. The structure is now studied by X-ray methods by H. Sakaguchi, *et al.*

Experimental

Apparatus—IR spectra were taken as KBr pellets on a Hitachi Infrared spectrometer, Model G3. EPR spectra were taken on a JES-ME-IX EPR spectrometer, and the spectra were recorded on polycrystalline samples at room temperature.

Reagents—Diethylenetriamine was purchased from Tokyo Kasei Co., Tokyo. Other reagents were obtained from Wako Pure Chemical Ind. Ltd., Tokyo. They were of reagent grade and were used without further purification.

Preparation—The complexes Cu(ade)·4H₂O, Cu(adeH)Cl₂, Cu(adeH)GlyCl·H₂O, and Cu(adeH)GlyGly·H₂O were synthesized according to methods described in literature,^{2,7)} and their purity was checked by elementary analysis.

The deuterated sample of Cu(ade)₂(dien)·H₂O was prepared by dissolving a nondeuterated samples in hot heavy water and successive lyophilization of the solution.

Cu(ade)₂(dien)·H₂O: Method I: A mixture of Cu(OH)₂, freshly prepared from 2.4 g Cu(NO₃)₂·3H₂O and 2 g of NaOH in 40 ml of H₂O, 1.04 g of diethylenetriamine, and 0.270 g of adenine in 200 ml of hot water was heated on a water-bath until no more Cu(OH)₂ dissolved. After filtration of the solution, the filtrate

was evaporated and blue fine crystals were obtained. These were collected by filtration and recrystallized from water and dried under a reduced pressure.

Method II: To a solution of 0.4 g of $\text{Cu}(\text{ade})_2 \cdot 4\text{H}_2\text{O}$ or $\text{Cu}(\text{adeH})\text{Cl}_2$ dissolved in 50% MeOH, 0.21 g of diethylenetriamine was added. The solution was evaporated, and blue crystals were obtained. They were recrystallized from H_2O and dried under a reduced pressure. *Anal.* Calcd. for $\text{C}_{14}\text{H}_{23}\text{CuN}_{13}\text{O}$: C, 37.10; H, 5.13; N, 40.20. Found: C, 36.91; H, 5.11; N, 40.20.

Acknowledgement Thanks are due to Miss H. Oida for elementary analysis.