

## An approach to the structure and spectra of copper barbiturate trihydrate

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### Abstract

In the neutral title complex  $[\text{Cu}(\text{C}_4\text{N}_2\text{H}_3)_2(\text{H}_2\text{O})_3]$  or  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  ( $\text{BBR}^- = \text{Barbiturate}$ ), the  $\text{Cu}^{\text{II}}$  ion, in the slightly distorted square-pyramidal geometry, is coordinated by two O atoms of the two monodentate barbiturates and three O atoms of three water ligands. The average bond length of  $\text{Cu}-\text{O}(\text{BBR}^-)$  is 1.981(5) Å and the average bond length of  $\text{Cu}-\text{O}(\text{H}_2\text{O})$  at the basal sites is 1.94(5) Å, *i.e.* much shorter than that of  $\text{Cu}-\text{O}(\text{H}_2\text{O})$  [2.175(11) Å]. The crystal structure is characterized by an extensive network of hydrogen bonds in which each  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  entity links to six adjacent  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  by  $\text{O}(\text{C}=\text{O}) \cdots \text{H}-\text{O}(\text{H}_2\text{O})$  bonds. Tautomerism in the coordination process for  $\text{BBR}^-$  was found from the crystal structure and i.r. spectral analysis. The interaction of  $\text{Cu}^{\text{II}}$  and  $\text{BBR}^-$  in aqueous solution was also investigated by electronic spectra and electrochemical method. It was observed that the copper ion could not only form the  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  complex in aqueous but also catalyze the decomposition of  $\text{BBR}^-$  at pH 1.1.

### Introduction

Barbiturates (abbreviated as  $\text{BBR}^-$ s) and derivatives thereof are widely used as sedative hypnotic drugs under a variety of conditions and are also employed for anesthesia [1]. For example, phenytoin, one of the cyclic ureides related in structure to the Barbiturate, was reported to be the least hypnotic, most strongly anti-convulsant and most effective against grand mal [1]. Due to its importance in medicine, this type of compound has been investigated frequently by various methods including crystal structure determination [2–6]. Recently these complexes have often been used as building blocks in ordered organic supramolecular assemblies with the desired hydrogen network [7–11]. However, investigations on the related crystal structures were mainly focused on  $\text{BBR}^-$  and its substitutes. The crystal structure of the complexes of  $\text{BBR}^-$  with metal ions has been the subject of few reports. Berking [12] determined the crystal structure of Ca 5,5-diethylbarbiturate trihydrate.

Considering that copper is a common ion existing in the body, an approach to the interaction of copper ions with  $\text{BBR}^-$  should be beneficial in our better understanding of the medical mechanism of drugs and the effects of copper ion on drug activity. Therefore, we have prepared and crystallized the title compound. The main aim of this paper is devoted to probing the coordination modes of copper ion and  $\text{BBR}^-$  in the solid

state by X-ray crystal structure analysis and to investigating the interaction of copper ion with  $\text{BBR}^-$  in aqueous solution by u.v. spectra and cyclic voltammetry.

### Experimental

#### $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$

To an aqueous solution of sodium  $\text{BBR}$  ( $200 \text{ cm}^{-3}$ ,  $1.0 \text{ mmol l}^{-1}$ ), a  $\text{CuSO}_4$  solution ( $100 \text{ cm}^{-3}$ ,  $1.0 \text{ mmol l}^{-1}$ ) was added. The mixture was stirred for 15 min at room temperature. Green polyhedral crystals (85% yield) appeared within 2 days.

#### Measurements

Cyclic voltammetry measurements were carried out in the CHI650A electrochemical system (P.R. China) with two Si-base Pt film electrodes as working and counter electrodes, respectively, and a saturated calomel reference electrode (s.c.e.). Electronic and i.r. spectra were recorded on a Shimadzu UV 2501 PC and on a Bruker Equinox 55 IR spectrophotometer, respectively.

#### Determination and refinement of the structure

The crystal data and data collection parameters of the complex are summarized in Table 1. The X-ray data for the complex were collected on a Siemens P4

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Table 1. Summary of crystallographic data and data collection parameters for  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$

Empirical formula	$\text{C}_8\text{H}_{12}\text{CuN}_4\text{O}_9$
Formula weight	371.76
Temperature (K)	293(2)
Wavelength (Å)	0.71073
Crystal system	Orthorhombic
Space group	Fdd2
<i>a</i> (Å)	11.755(3)
<i>b</i> (Å)	30.332(12)
<i>c</i> (Å)	7.220(2)
Volume (Å <sup>3</sup> )	2574.3(14)
<i>Z</i>	8
$\rho_{\text{calc}}$ (g cm <sup>-3</sup> )	1.918
$\mu$ (mm)	1.756
<i>F</i> (0 0 0)	1512
Crystal size (mm)	0.42 × 0.40 × 0.36
$\theta$ range (deg)	2.69–28.02
Index ranges	0 ≤ <i>h</i> ≤ 15, −1 ≤ <i>k</i> ≤ 40, 0 ≤ <i>l</i> ≤ 8
Reflections collected	819
Independent reflections	792 ( $R_{\text{int}} = 0.0232$ )
Absorption correction	Semi-empirical
Max. and min. transmission	0.862 and 0.649
Refinement method	Full-matrix least-squares on $F^2$
Data/restraints/parameters	792/1/102
Goodness-of-fit on $F^2$	1.126
Flack parameter	0.01(5)
Extinction coefficient	0.0022(5)
Final <i>R</i> -indices [ $I > 2\sigma(I)$ ]	$R_1 = 0.0490$ , $wR_2 = 0.1241$
<i>R</i> -indices (all data)	$R_1 = 0.590$ , $wR_2 = 0.1331$
$\Delta\rho_{\text{max}}/\Delta\rho_{\text{min}}$ (e Å <sup>-3</sup> )	0.767 and −0.828

diffractometer using  $\text{MoK}_\alpha$  radiation ( $\lambda = 0.71073$  Å). The structure was solved by the direct method and refined anisotropically on  $F^2$  by full matrix least-squares techniques using the SHELXTL 97 program [13].

All hydrogen atoms were generated geometrically. Selected bond lengths and bond angles for the complex are given in Table 2. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center no 176865.

Table 2. Bond lengths (Å) and angles (deg) for  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$

Bond lengths			
Cu(1)—O(2w)	1.941(5)	O(3)—C(3)	1.239(10)
Cu(1)—O(2w)	1.941(5)	C(1)—C(2)	1.384(11)
Cu(1)—O(1)	1.981(5)	C(1)—N(1)	1.393(9)
Cu(1)—O(1a)	1.981(5)	C(2)—C(3)	1.411(12)
Cu(1)—O(1w)	2.175(11)	N(1)—C(4)	1.369(10)
O(1)—C(1)	1.285(9)	N(2)—C(4)	1.349(11)
O(2)—C(4)	1.253(9)	N(2)—C(3)	1.418(10)
Bond angles			
O(2wa)—Cu(1)—O(2w)	176.2(8)	O(1)—C(1)—N(1)	115.0(6)
O(2wa)—Cu(1)—O(1)	93.0(2)	C(2)—C(1)—N(1)	118.9(7)
O(2w)—Cu(1)—O(1)	86.6(2)	C(1)—C(2)—C(3)	120.4(7)
O(2wa)—Cu(1)—O(1a)	86.6(2)	C(4)—N(1)—C(1)	123.2(7)
O(2w)—Cu(1)—O(1a)	93.0(2)	C(4)—N(2)—C(3)	124.7(7)
O(1)—Cu(1)—O(1a)	168.6(4)	O(3)—C(3)—C(2)	126.3(7)
O(2wa)—Cu(1)—O(1w)	91.9(4)	O(3)—C(3)—N(2)	117.5(7)
O(2w)—Cu(1)—O(1w)	91.9(4)	C(2)—C(3)—N(2)	116.1(7)
O(1)—Cu(1)—O(1w)	95.69(19)	O(2)—C(4)—N(2)	122.4(8)
O(1a)—Cu(1)—O(1w)	95.69(19)	O(2)—C(4)—N(1)	120.9(8)
C(1)—O(1)—Cu(1)	126.3(5)	N(2)—C(4)—N(1)	116.7(6)
O(1)—C(1)—C(2)	126.1(6)		

Symmetry code: (a)  $-x, -y, z$ .

## Results and discussion

### Crystal structure

The molecular structure of the title complex, together with the atom-numbering scheme, is shown in Figure 1. It is a neutral complex consisting of one copper, two monodentate barbiturates and three-coordinated  $\text{H}_2\text{O}$  molecules. The geometry of the five-coordination  $\text{CuO}_5$  core is a slightly distorted square pyramid. The basal sites are occupied by the two O atoms at C(1) of  $\text{BBR}^-$  and the two O atoms in coordinated  $\text{H}_2\text{O}$ . The average bond lengths of Cu—O ( $\text{BBR}^-$ ) and Cu—O (2W, 2Wa) are 1.981(5) Å and 1.94(5) Å. The apical position is occupied by a relatively weakly coordinated water molecule (1W). The bond length of Cu—O (1W) is 2.175(11) Å, much longer than that of Cu—O (2W or 2Wa) at the basal sites.

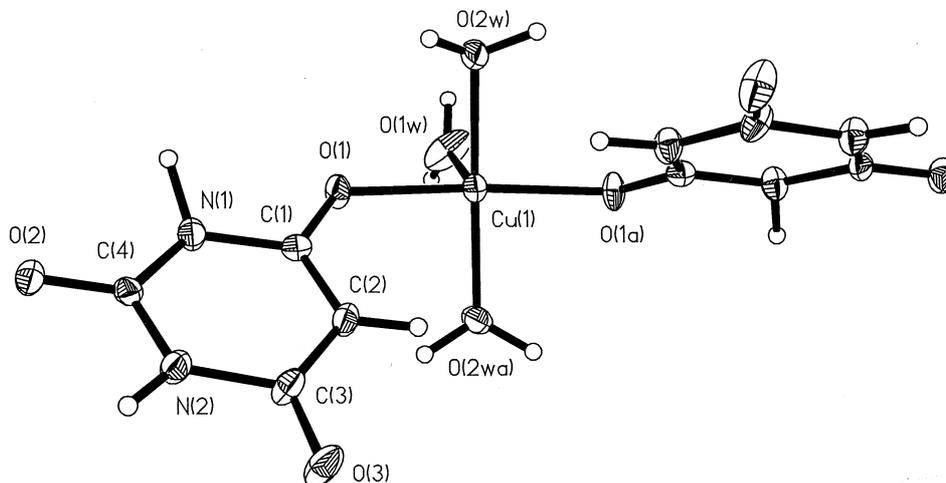


Fig. 1. An ORTEP view of  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$ .

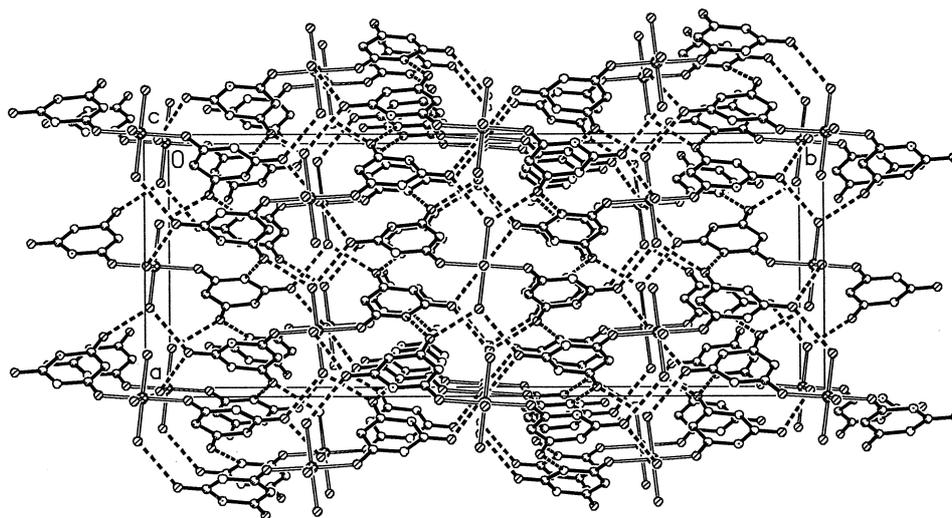
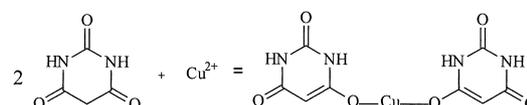


Fig. 2.  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  packing diagram.

The packing diagram of the complex is shown in Figure 2, from which it can be seen that, due to existing rich proton acceptors and donors in the complex,  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  molecules are hydrogen-bonded to each other to form an extensive layer network of hydrogen bonds. In this network each  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  links six adjacent  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  molecules by the  $\text{O}(\text{C}=\text{O}) \cdots \text{H}-\text{O}(\text{H}_2\text{O})$  bond, as shown in Figure 3, in addition to intermolecular  $\text{N}-\text{H}(\text{BBR}) \cdots \text{H}-\text{O}(\text{H}_2\text{O})$ . This extensive network of hydrogen bonds contributes much to the stabilization of the lattice.

The two  $\text{BBR}^-$  ligands are located *trans* with respect to each other in the basal plane in an antisymmetrical mode. The planes of the two  $\text{BBR}^-$  rings form

dihedral angles of  $60.4^\circ$  with respect to the basal plane. It has been noticed that the structure of coordinated  $\text{BBR}^-$  is somewhat different from that of free  $\text{BBR}^-$ . The negative charge of free  $\text{BBR}^-$  was mainly located at C(2) [14], while that of the present coordinated  $\text{BBR}^-$  was mainly centered on O(1), as shown in Figure 1. This indicated that, in the process of coordination, copper ions induce migration of the negative charge from C(2) to O(1); in other words, the C(1) carbonyl group become a hydroxyl anion as follows



Although similar tautomerism has been founded in the crystal structure of a derivative of  $\text{BBR}^-$ , 5-nitrobarbiturate, in which the hydrogen atom nominally at C(2) has migrated to form the 1-hydroxy tautomer, this tautomerism is first deserved example for a metal complex of  $\text{BBR}^-$ .

#### *I.r. evidence for tautomerism*

It cannot be said for certain if similar tautomerism for O(2) or O(3) has not occurred purely by X-ray determination of the crystal structure, since the C(1)–O(1) bond lengths, C(3)–O(3) and C(4)–O(2) are located in the range of typical single and double C–O bond lengths, although the C(1)–O(1) bond length is somewhat longer than other two C–O bonds. As a result, the i.r. spectra of  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  and sodium barbiturate were recorded. As shown in Figure 4, the spectrum of  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  shows two strong absorption at  $1675.8$  and  $1595.4 \text{ cm}^{-1}$ , suggesting the presence of two types of carbonyl groups. The former is the C(3) carbonyl stretching vibration absorption, while the latter is that of the C(4) carbonyl groups. Free  $\text{BBR}^-$  exists in the

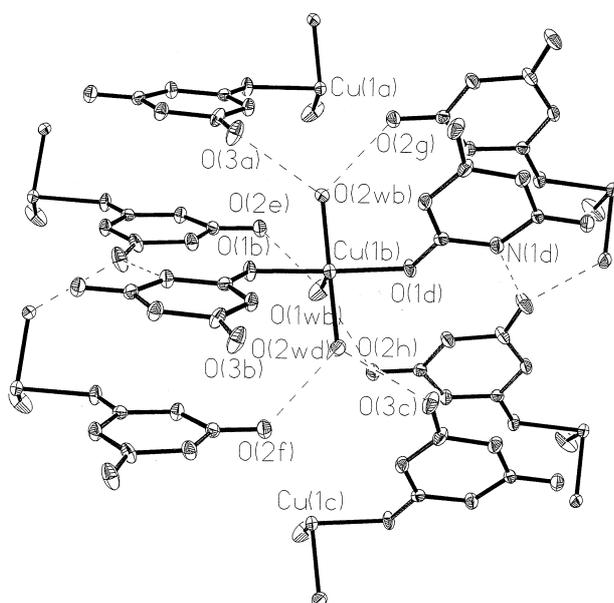


Fig. 3. A view of the intermolecular hydrogen bond in  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$  with adjacent molecules.

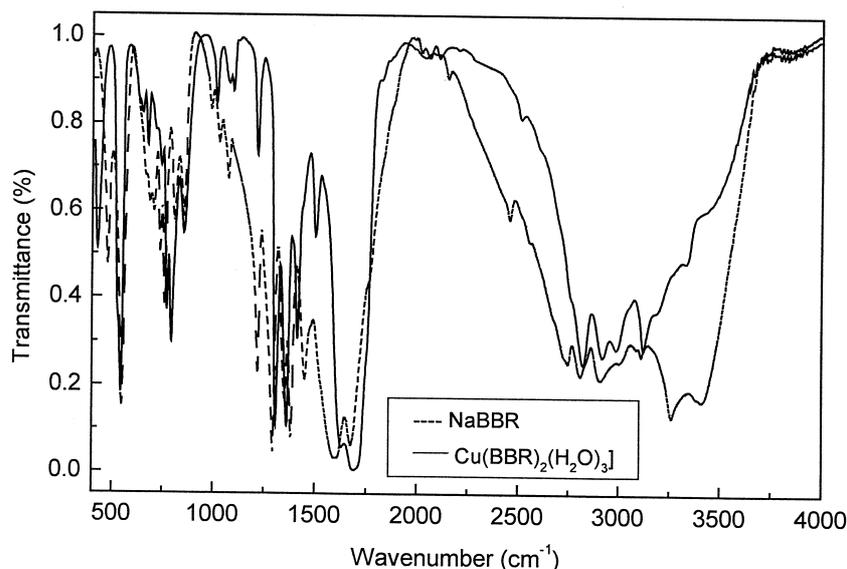


Fig. 4. I.r. spectra of NaBBR and  $[\text{Cu}(\text{BBR})_2(\text{H}_2\text{O})_3]$ .

triketo form [15, 16] in which the two carbonyl groups at C(1) and C(3) are structurally identical. Therefore only two types of carbonyl group absorption peaks were observed, at  $1690.6$  and  $1629.0 \text{ cm}^{-1}$  for free  $\text{BBR}^-$ . The wider and stronger absorption peaks at  $1690.9 \text{ cm}^{-1}$  can be attributed to the overlapping peaks of two carbonyl groups at C(1) and C(3).

Compared with the i.r. spectrum of free and coordinated  $\text{BBR}^-$ , carbonyl group peaks have a marked change in shape except for the apparent red-shifts. The carbonyl group absorption peak at high wave number for free  $\text{BBR}^-$  is obviously stronger than that at the lower wave number. For the complex, the strength and width orders of carbonyl peaks are the very reverse. In other words, the overlapping peak of two carbonyl group at C(1) and C(3) of  $\text{BBR}^-$  become weak during the process of the coordination. This weakening may be evidence for the disappearance of the carbonyl group at C(1) due to the above-mentioned tautomerism.

#### Interaction of copper ion and $\text{BBR}^-$ in aqueous solution

The above experiments were carried out with respect to characterizing the behavior of the solid complex. The investigations were focused on probing the interaction of  $\text{Cu}^{2+}$  and  $\text{BBR}^-$  in aqueous solution by cyclic voltammetry and electronic spectra.

The electronic spectra of a  $\text{Cu}^{2+}$ - $\text{BBR}^-$  solution for various mole ratios are shown in Figure 5. It can be seen from this figure that there are two absorption peaks, at  $325.4$  and  $800.4 \text{ nm}$ , respectively. The former is attributed to the  $\text{BBR}^- \pi-\pi^*$  transition, while the latter originates from the  $d-d^*$  transition of the copper ion. A well-defined isobestic point was observed at  $616.6 \text{ nm}$ , suggesting that the copper ion and  $\text{BBR}^-$  also exist as a metal complex in aqueous solution. The reduction potential of copper in the copper- $\text{BBR}^-$

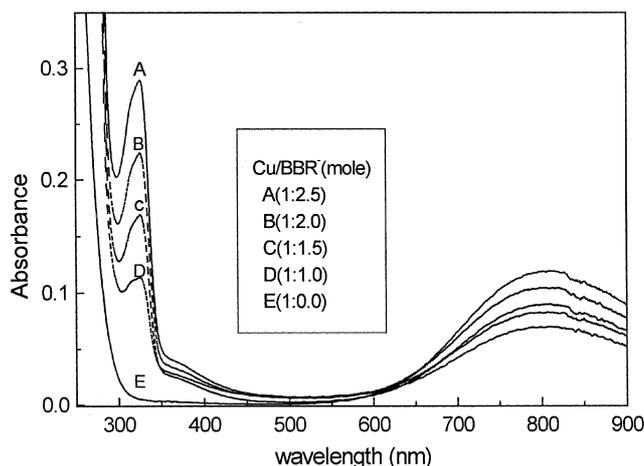


Fig. 5. Electronic spectra of  $\text{Cu}^{2+}$ - $\text{BBR}^-$  aqueous solution.

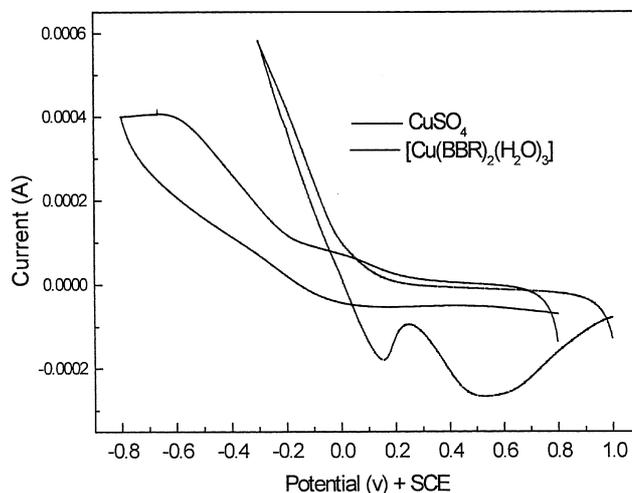


Fig. 6. Cyclic voltammetry of  $\text{CuSO}_4$  and the  $\text{Cu}^{2+}$ - $\text{BBR}^-$  system.

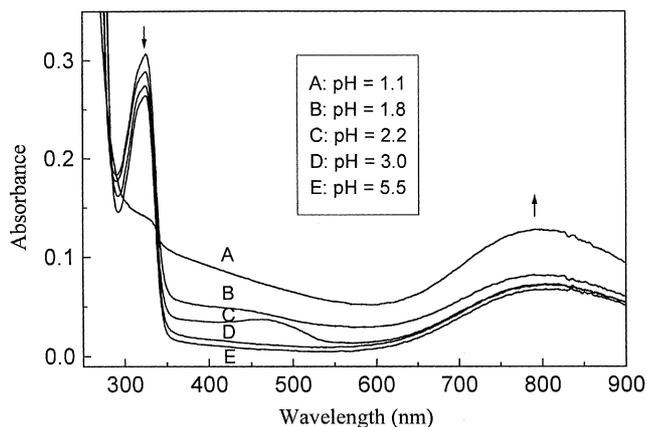


Fig. 7. pH-dependent electronic spectra of the  $\text{Cu}^{2+}$ - $\text{BBR}^-$  system.

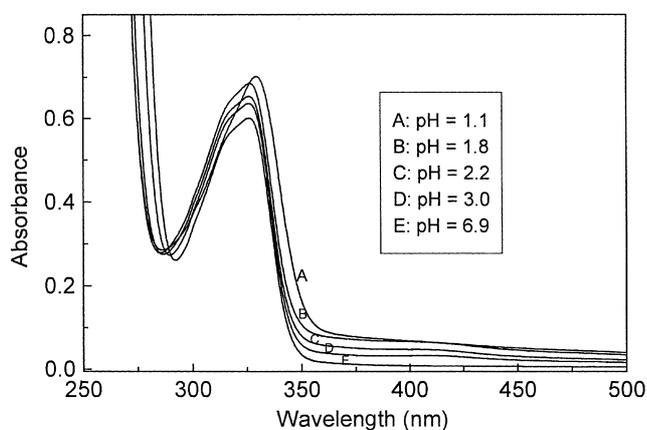


Fig. 8. pH-dependent electronic spectra of free  $\text{BBR}^-$ .

system is *ca.*  $-0.1$  V (s.c.e.), obviously lower than that of the free copper ion, *i.e.* *ca.*  $0.17$  V (s.c.e.) for  $\text{Cu}^{2+}/\text{Cu}^+$  and *ca.*  $0.51$  V (s.c.e.) for  $\text{Cu}^{2+}/\text{Cu}$ , as shown in Figure 6. The decrease in reduction potential can be considered to be electrochemical evidence for the formation of the  $\text{Cu}^{2+}$ - $\text{BBR}^-$  complex in aqueous solution.

The pH-dependent electronic spectra of free  $\text{BBR}^-$  and  $\text{Cu}^{2+}$ - $\text{BBR}^-$  systems are presented in Figures 7 and 8. Comparing the two spectra, an opposite change tendency of absorption peaks at *ca.*  $325$  nm with the change of pH was observed. For free  $\text{BBR}^-$  the peak exhibits hyperchromicity with increasing acidity of the solution, while the peak for the complex exhibits hypochromicity with increasing acidity of the solution. In particular, when the pH value changes from 1.8 to 1.1, the absorption peak of free  $\text{BBR}^-$  exhibits a 3.4-nm red-shift while the absorption peak for the complex abruptly disappears completely. Moreover when the final spectra at pH = 1.1 is returned to the original by adding base, the spectral changes for free  $\text{BBR}^-$  are fully

reversible, while the peaks at *ca.*  $325$  nm for the complex no longer appear, denoting that the coordinated  $\text{BBR}^-$  has possibly been decomposed. It is reasonable that the decomposition is believed to be due to the catalytic role of the coordinated copper ion although the catalysis mechanism remains unknown.

In conclusion, the above observations collectively indicate that the copper ion can strongly bind to  $\text{BBR}^-$ , not only in solid but also in aqueous solution. Moreover the copper ion still can catalyze the decomposition of  $\text{BBR}^-$  at pH 1.1. It is expected that copper ion also will affect the medical activity of barbiturate and its derivatives according to the above observations.

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