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# Charge-Transfer Interactions between Metal Ions and Some Uracil Derivatives

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*Abstract.* The interaction between $Cu^{2+}$ and a few uracil derivatives has been investigated by means of electron spin resonance and optical absorption studies. It could be shown that a charge transfer interaction occurs. Its strength depends upon the electron attracting or releasing properties of the substituents of the nucleobase.

*Key words:* CT-Interactions — Metal Ions — Uracil Derivatives — ESR — Optical Absorption.

## Introduction

Recently we have shown that $Cu^{2+}$ added to a uracil solution using dimethylsulfoxide (DMSO) as a solvent causes a splitting of the N-H nuclear magnetic resonance peak (Lohmann and Penka, 1973). This as well as the H-6 and H-5 line broadenings occuring concomitantly was explained by a charge-transfer (CT) interaction between the metal ions and the solvent molecules DMSO bound to N-1 of uracil via hydrogen bond. In this way, $Cu^{2+}$ exhibits an indirect influence on the nucleobase without being attached directly to it. In a few cases, however, a direct interaction seems to occur: when $Cu^{2+}$ was added to 6-methyluracil, 6-methyl-2-thiouracil or to 2-thiouracil, a colorization of the solution was observed, a fact, which indicates the formation of a CT complex between $Cu^{2+}$ and the uracil derivatives. Further support of this conclusion is given by the observation that a splitting of the N-H peak did not appear. In order to elucidate the mechanism of interaction, electron spin resonance and optical absorption studies have been conducted.

## Material and Methods

6-methyluracil (6-$CH_3$-Ura), 6-methyl-2-thiouracil (6-$CH_3$-2-S-Ura), and 2-thiouracil (2-S-Ura) were purchased from Fluka AG., Buchs, Switzerland, and Schwarz Bioresearch Inc., Orangeburg, New York, USA, respectively. $Cu(NO_3)_2$ as well as dimethylsulfoxide (DMSO) were obtained from Merck AG., Darmstadt, Germany. All substances used were of reagent-grade quality and were used without further purification. All measurements were conducted at room temperature.

Different concentrations of these substances were prepared by dissolving them in either 5.0 mM (for ESR experiments) or 3.0 mM $Cu(NO_3)_2$ (for optical studies) solutions using DMSO as a solvent. For the difference spectra recorded in the near UV region a concentration of 0.25 mM $Cu(NO_3)_2$ was used.

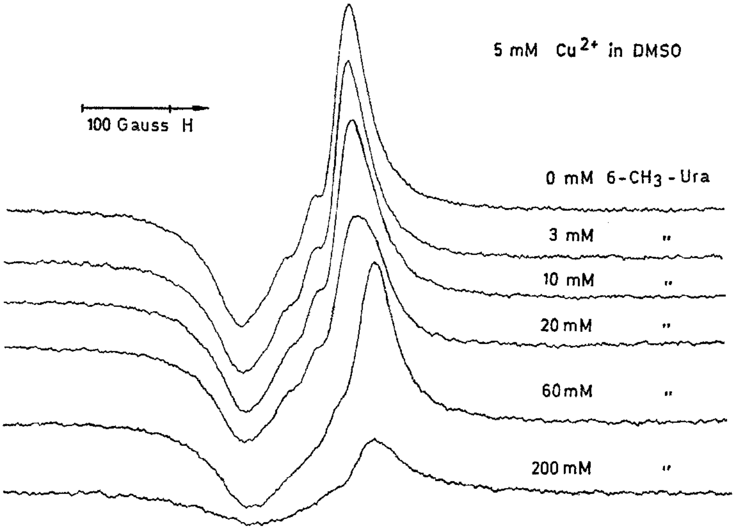

Fig. 1. The effect of varying concentrations of 6-methyluracil on a 5 mM $Cu^{2+}$ ESR spectrum using dimethylsulfoxide as a solvent

The electron spin resonance (ESR) spectra were determined with a Varian E9 100-kc ESR spectrometer using a liquid sample accessory. A Wang 600 computer was used for the integration of the spectra yielding the spin concentration. The optical absorption studies were carried out with a Cary 14 spectrometer. The spectra were recorded 4 min after preparing the samples in the wavelength region between 600 and 1400 nm (as rel. difference spectra: $Cu^{2+}$ and Ura-derivative vs. Ura-derivative) and 300 and 450 nm (as absolute difference spectra).

## Results and Discussion

The partly resolved hf structure of $Cu^{2+}$ in DMSO (see Fig. 1) has been pointed out previously (Lohmann *et al.*, 1966). Such an hf splitting of $Cu^{2+}$ in certain other solvents has been originally observed by McGarvey (1956) and described theoretically by McConnell (1956).

The influence of increasing concentrations of 6-$CH_3$-Ura (up to 200 mM) on the $Cu^{2+}$ ESR spectrum is also shown in Fig. 1. As can be seen, 6-$CH_3$-Ura addition results in a reduction in spin concentration and the formation of a new peak at a higher field. In the case of 6-$CH_3$-2-S-Ura and 2-S-Ura a new peak appeared at a still higher field; the reduction in spin concentration is considerably less than with 6-$CH_3$-Ura (see Fig. 2). Since the peak at the upper field cannot be observed with the other derivatives, is should be associated with the sulfur. This peak increases with increasing concentration while the $Cu^{2+}$ signal decreases.

It should be pointed out that the complexes are rather stable since the spectra do not change with time except in the case when S-containing substances are used. In this case, the spin concentration is nihil after about one day when e.g. 800 mM 2-S-Ura had been added to 5 mM $Cu(NO_3)_2$. The "S" peak at upper

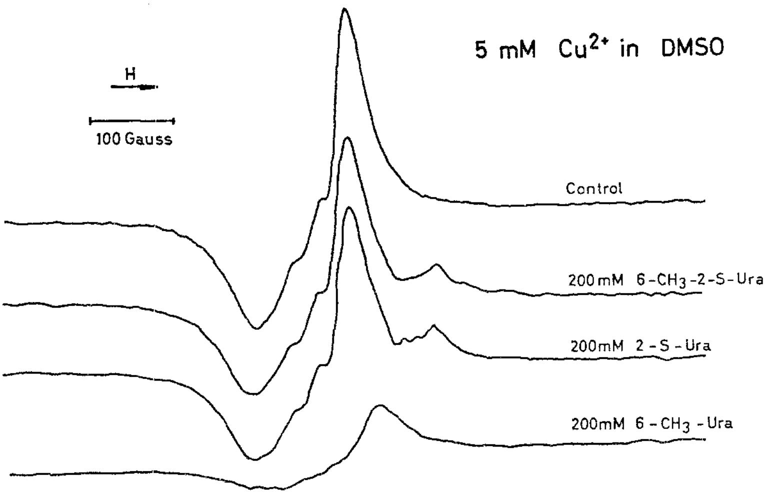

Fig. 2. Influence of different uracil derivatives (200 mM each) on a 5 mM $Cu^{2+}$ ESR spectrum. Explanation of the abbreviations used see text

field is also diminished, its disappearance is probably due to dimerization. Furthermore, the rate of decrease in spin concentration is affected by the electron donor/acceptor property of the substituent. As expected, the rate is considerably slower in the case of 6-$CH_3$-2-S-Ura if compared to 2-S-Ura. For these reasons, all spectra were recorded 4 min after preparing the solutions.

From the change of the $Cu^{2+}$ spectrum and the decrease in spin concentration obtained with the 3 derivatives shown in Fig. 2 it can be concluded, therefore, that a charge transfer complex is formed between the metal ion and the derivative resulting in a reduction of $Cu^{2+}$ to $Cu^{1+}$.

Further support of this assumption was obtained by optical absorption studies. In Fig. 3 the visible-IR difference spectra of $Cu^{2+}$ with the 3 uracil derivatives are shown. As can be seen all three substances affect, to a varying extent, the copper absorption band which can be associated with a *d-d* transition (Ilse and Hartmann, 1951a, b). As expected, the absorption band of the complex formed with 6-methyluracil is located at the longest wavelength. The electron releasing entity $CH_3$ causes a decrease in ionisation potential and, thus, according to the CT theory an increase in wavelength. S, an electron attracting entity, causes an opposite effect. The red shift exerted by $CH_3$ was also observed in the case of 6-$CH_3$-2-S-uracil if compared with 2-S-uracil.

The optical studies also indicate the existence of a CT complex and, thus, confirm the ESR results. Since the $\pi$ orbitals of the uracil derivatives investigated do not posses the axial symmetry of the wave function of the $Cu^{2+}$ acceptor, $d_{x^2-y^2}$, it is very unlikely for the uracil derivatives to act as $\pi$ donors. It seems to be more likely that the two ring nitrogens with their lone electron pairs act as donors since the largest negative charge density of the molecule is located at this position (B. and A. Pullman, 1963). The two oxygen atoms do not need to be considered since the electrostatic potential in the plane of the molecule exhibits a

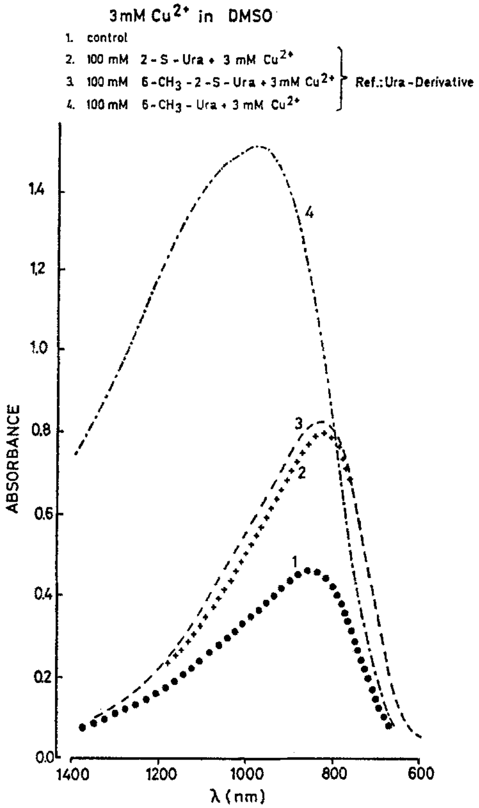

Fig. 3. Difference spectra of 3 mM $Cu^{2+}$ and some uracil derivatives (100 mM each) using DMSO as a solvent

strong minimum near these atoms (Bonaccorsi *et al.*, 1972). There seems to be, however, some influence of the sulfur atom substituted at C-2. The slowly developing reaction observed with 2-S-Ura indicates that either sulfur influences the interaction between the metal ions and the nitrogen atoms or that, to a certain probability, the molecule is present in its SH configuration and the SH entity is acting directly with $Cu^{2+}$. The present data rather suggest, however, that the main interaction takes place at the nitrogen atoms. If this should be the case, then, of course, the strength of the hydrogen bonds occurring between the N-1 protons of the uracil derivative and the solvent DMSO (Lohmann and Penka, 1973) should be modified. Concomitantly with this, the CT complex formed between $Cu^{2+}$ and the solvent molecules (DMSO) should be influenced, too. This CT complex absorbs in the near UV region, e.g. at 289 nm for $Cu(NO_3)_2$ and DMSO (Basolo and Pearson, 1973).

Based on the experimental results obtained the following mechanism might be proposed: The uracil derivatives form hydrogen bonds with the solvent DMSO via the N-1 proton. The hydrogen bonds are the stronger the less electronegative the N-1 is (Lohmann and Penka, 1973). This is influenced by electron releasing

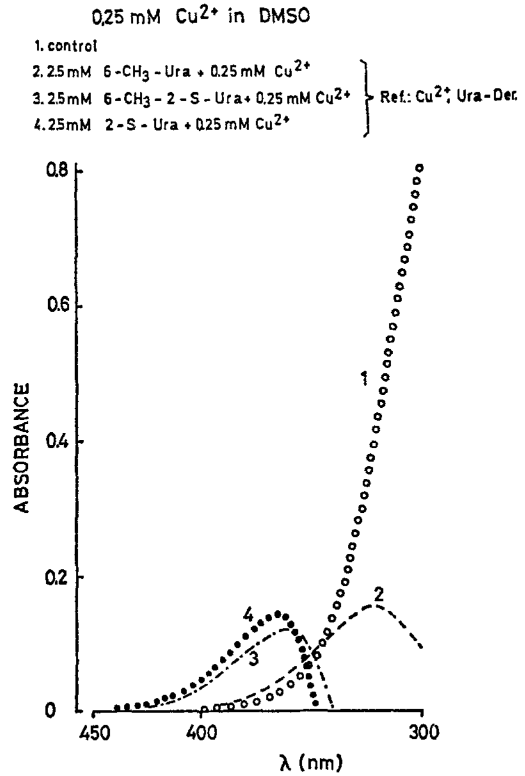

Fig. 4. Difference spectra of 0.25 mM Cu$^{2+}$ and some uracil derivatives (2.5 mM each) using DMSO as a solvent

and/or attracting substituents. Thus, the strength of the hydrogen bond is the strongest in the case of 2-S-Ura and the weakest for 6-$CH_3$-Ura. Addition of Cu$^{2+}$ to a DMSO solution containing one of the three uracil derivatives investigated results in a complex formation between the metal ion and uracil derivative and DMSO as well. In the case of interaction between Cu$^{2+}$ and N-1, this interaction should be the largest the larger the electron density at N-1, that is the weaker the hydrogen bond. In agreement with this, the experimental results shown in Fig. 3 exhibit the following order in wavelength of the absorption bands: 6-$CH_3$ > 6-$CH_3$-2-S > 2-S which according to the CT theory also expresses the strength of the complex formed between the metal ion and the nucleobase.

If this idea is correct, then, the Cu$^{2+}$ interaction with the S = O entity of the DMSO molecule should be the smallest the weaker the hydrogen bond between N-1 and DMSO. The experimental results shown in Fig. 4 confirm this prediction. The absorption bands originating from the Cu$^{2+}$-DMSO CT interaction and being influenced by the uracil derivatives exhibit, as expected, the inverse order in wavelength response to the one obtained with the direct Cu$^{2+}$-uracil derivative CT interaction: 2-S > 6-$CH_3$-2-S > 6-$CH_3$.

In the case of a lower electron density at N-1, that is a stronger hydrogen bond, produced by electron attracting substituents such as S, the $Cu^{2+}$ interaction with N-1 of the nucleobase should be less and with S (of DMSO) more pronounced than in the case when $CH_3$ is substituted at C-6. Again, this is in agreement with the experimental results.

It is interesting to note that the total energy, that is the sum of the two CT absorption frequencies of e.g. 6-$CH_3$-Ura, is about 4.9 eV. The same value is obtained for all of the other derivatives investigated. This, again, seems to be an excellent confirmation of the model proposed.

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