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# One-Electron Redox Processes of the $\mathrm{Cu^{II}}$ Chelate of 3,8,12,17-Tetraethyl-2,7,13,18-tetramethylbilin-1,19-dione

**Maria Carme Anglada, Joan-Anton Farrera, and Josep M. Ribó***

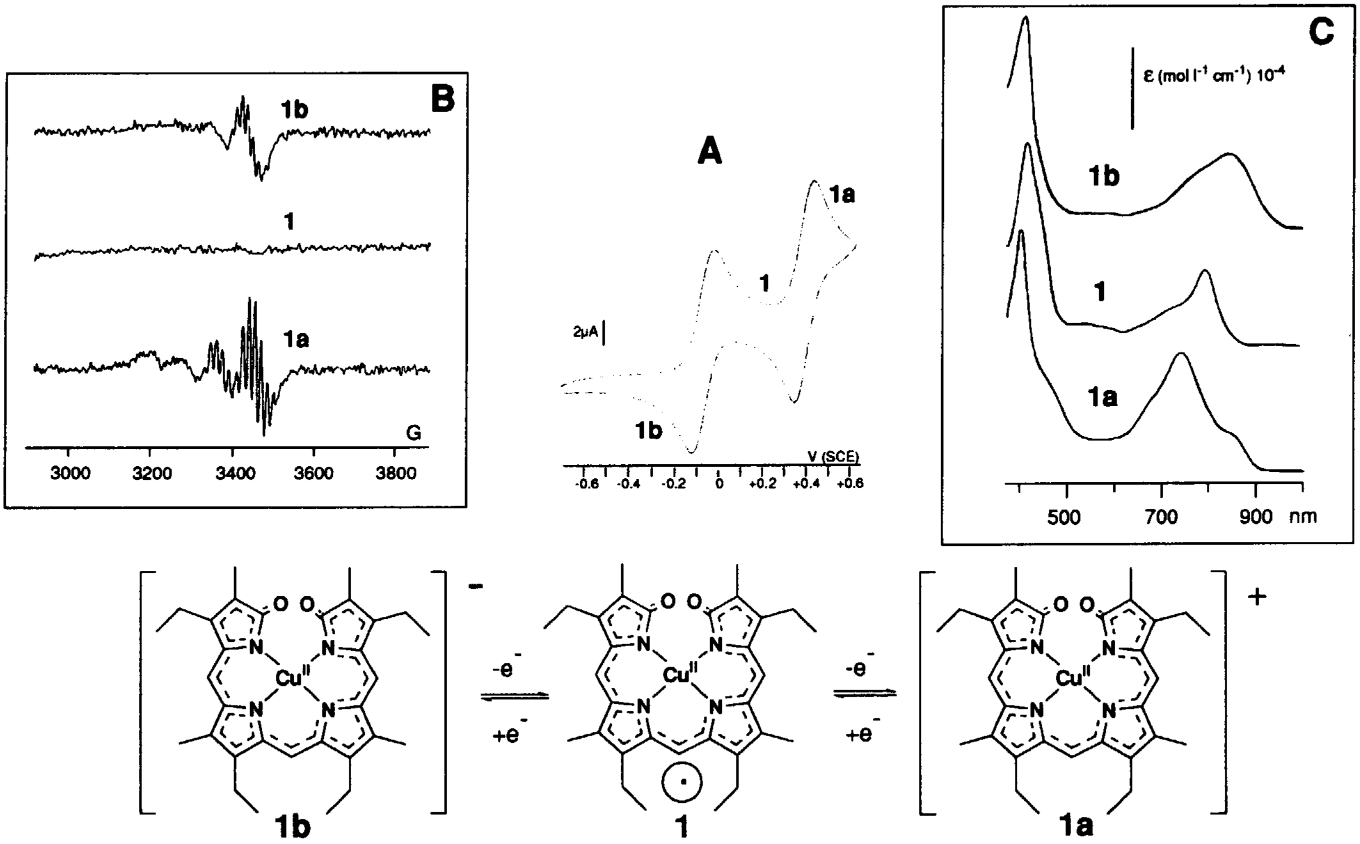
*Department of Organic Chemistry, University of Barcelona.*
*c/ Martí i Franquès 1, E-08028, Barcelona, Catalonia, Spain*

***Abstract.*** In solution ($CH_2Cl_2$) one-electron redox process can be performed electrochemically on the ligand of the $\mathrm{Cu^{II}}$ chelate (**1**) of the title biliverdin. **1** shows an electronic triplet state configuration with one of the unpaired electrons in the ligand $\pi$ system. The one-electron oxidation product (**1a**) and the one electron reduction product (**1b**) correspond to the $\mathrm{Cu^{II}}$ chelates of the electron paired cation and anion respectively.

We report on the redox and magnetic behaviour of the $\mathrm{Cu^{II}}$ chelate of bilin-1,19-diones (biliverdins).[1] Porphyrins act, under dideprotonation of their two NH groups, as tetracoordinating ligands. By NH di- or trideprotonation octaalkylbilin-1,19-diones become tetracoordinating ligands, with a helicoidal structure.[2] In the case of dideprotonation the non-deprotonated end lactam ring tautomerizes to the hydroxyimino form. Our results show that the transition metal chelates of biliverdins, in spite of being acyclic and capable of containing a three negatively charged ligand, show likenesses with the corresponding metalloporphyrins.[3]

The structures of $\mathrm{Fe^{III}}$, $\mathrm{Mn^{III}}$ and $\mathrm{Zn^{II}}$ chelates of bilin-1,19-diones are already established.[2a,c,e,4] The Co, Ni and Cu chelates are coordinated by a trideprotonated biliverdin ligand.[5] However, their magnetic properties do not agree with the transition metal formal oxidation state (III) or (II).[6]

Recently, it has been shown that the structure of the $\mathrm{Cu^{II}}$ biliverdin chelates,[2d,f] such as **1**, corresponds to the free neutral radical of the organic ligand.[2f] These $\mathrm{Cu^{II}}$ biliverdinates are stable as solids and in solution in non-nucleophilic solvents (*e.g.* $CH_2Cl_2$). **1** in dilute solutions is an EPR-silent paramagnetic species. The values of the magnetic susceptibility in the solution of $\mathrm{Cu^{II}}$ biliverdinates[2d,f] suggest that there is a ferromagnetic coupling giving a triplet state with large zero splitting. The detection for dilute solutions of **1**[8] of a small half-field peak at 4 K confirms the triplet state character of $\mathrm{Cu^{II}}$ biliverdinates in dilute solutions. Such ferromagnetic coupling is also described for planar $\mathrm{Cu^{II}}$ porphyrinato cation radicals.[3] However, **1** is non-planar, but its $C_2$ symmetry produces a zero overlap between the unpaired electron of the $\pi$ ligand system and the unpaired electron of the, roughly speaking, $d_{x^2-y^2}$ system of $\mathrm{Cu^{II}}$. This simple model is confirmed by density funcional LSDA/VMN (DN basis) calculations.[9] **1** shows in the solid state a weak antiferromagnetic $\pi$-Cu coupling and a moderate antiferromagnetic intermolecular $\pi$-$\pi$ coupling.[2f] In this respect **1** shows, as solid, similar behaviour to that of the non-planar porphyrins.[10]



Cyclic voltammetry (A) of **1** in a $CH_2Cl_2$ solution (1.5 $10^{-3}$ mol $l^{-1}$; 0.1 mol $l^{-1}$ tetrabutylammonium perchlorate; sweep rate 50 $mVs^{-1}$). EPR (B) and UV/Vis (C) spectra of **1**, **1a** and **1b**.

The spectra were obtained *in situ* by electrolysis of **1** in three electrode cells (EPR and thin layer UV/Vis).

The electronic configuration of **1** suggests a chemical reactivity based on one-electron redox processes. The already described oxidation of the $Cu^{II}$ chelates of biliverdins probably occurs through the $Cu^{II}$ biliverdinate cation intermediate obtained by one-electron oxidation.[11] In respect to one-electron reduction processes, two different pathways can be expected, affecting the transition metal ($Cu^{II}/Cu^{I}$) or the biliverdin ligand (neutral free radical/ anion).

Cyclic voltammetry confirms that **1** is stable only in a narrow range of potentials since it undergoes a one-electron redox process both in the anodic and in the cathodic sweep (see Fig. A). The electroactive redox products obtained from **1** are stable in solution. The CV shows only quasi-reversible electrochemical processes. The decrease in the sweep rate, from 200 mV $s^{-1}$ to 2 mV $s^{-1}$, produces a decrease in $\Delta E_p$ from $\approx$ 115 mV to $\approx$ 85 mV. This discrepancy in respect to the 60 mV expected for a reversible process may be attributed to homo- or hetero-association of the electroactive species near the electrode.[10]

Electrolysis experiments in an EPR cell show that both the oxidized (**1a**) and the reduced (**1b**) species correspond to $Cu^{II}$ chelates (see Fig. B);[12] from the EPR-silent initial compound the characteristic spectra were obtained of two different $Cu^{II}$ species coordinated to a ligand with four nitrogens. The cation **1a** shows a very similar EPR spectrum to those of neutral non-planar $Cu^{II}$ porphyrins.[3e] The differences between the EPR spectra of **1a** and **1b** can be explained by the different spin-polarization due to a positively or negatively charged ligand.

The electrolysis of **1** to **1a** or **1b** can also be followed through the UV/Vis spectra (See Fig. C).

These results could be of significance for the understanding of the biological differences between bilirubin and biliverdin.[11] The $Cu^{II}$ chelates of biliverdin, and also perhaps the Co and Ni chelates, could act as one-electron reaction promotors without change of the $Cu^{II}$ oxidation state. This behaviour is similar to those of the corresponding metalloporphyrins and could be of significance in understanding the behaviour of the bilindione Fe chelates obtained in the oxidative degradation of the prosthetic group of hemoproteins (*e.g.* catalases).

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## References and Notes

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2. For Mn, Fe, Co, Ni, Cu and Zn chelates see (a) Falk, H.; Schlederer, T. *Liebigs Ann. Chem.* **1979**, 1560-1570. (b) Bonfiglio, J. V.; Bonnett, R.; Buckley, D. G.; Hamzetash, D.; Hursthouse, M. B.; Abdul Malik, K. M. *Tetrahedron* **1983**, *39*, 1865-1874. (c) Balch, A.; Latos-Grazinsky, L.; Noll, B. C.; Olmstead, M. M.; Safari, N. *J. Am. Chem. Soc.* **1993**, *115*, 9056-9061. (d) Balch, A.; Mazzanti, M.; Noll, B. C.; Olmstead, M. M. *J. Am. Chem. Soc.* **1993**, *115*, 12206-12207. (e) Balch, A.; Mazzanti, M.; Noll, B. C.; Olmstead, M. M. *J. Am. Chem. Soc.* **1994**, *116*, 9114-9122; f) Jaumà, A.; Escuer, A.; Farrera, J.-A.; Ribó, J. M. Monatsh. Chem. **1996**, in press.

3. In respect to the magnetic behaviour of metalloporphyrins and metalloporphyrinato cation radicals see *e. g.* (a) Scholtz, W. Z.; Reed, C. A.; Lee, Y. A.; Scheidt, R.; Lang, G. *J. Am. Chem. Soc.* **1982**, *104*, 6791-793. (b) Godziela, G. M.; Goff, H. M. *J. Am. Chem. Soc.* **1986**, *108*, 2237-2243. (c) Erler, B. S.; Scholtz, W. F.; Lee, Y. A.; Scheidt, R.; Reed, C. A. *J. Am. Chem. Soc.* **1987**, *109*, 2644-2652. (d) Song, H.; Reed, C. A.; Scheidt, W. R. *J. Am. Chem. Soc.* **1989**, *111*, 6865-6866. (e) Renner, M. W.; Barkigia, K. M.; Zhang, Y.; Medforth, C. J.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1994**, *116*, 8582-8592.

4. The structure of the $Fe^{III}$ and $Mn^{III}$ chelates of bilin-1,19-diones corresponds to a trideprotonated bilin-1,19-dione ligand coordinating the metal ion[2c,e]. These $Fe^{III}$ and $Mn^{III}$ chelates are pentacoordinated; in the presence of a good axial ligand, *e.g.* pyridine, they are monomers, but they can also be isolated as dimers; one of the oxygens of one half acts as the axial ligand of the other half of the dimer. The structure of the

$Zn^{II}$ chelates corresponds to a dideprotonated ligand, with one of the end lactam rings tautomerized to the hydroxyimino form.

5. The structure of the Co and Cu chelates of biliverdins has been established from X-ray diffraction analysis.[2d,e] In the case of the Ni chelate the available X-ray crystallographic data[2b] do not allow to distinguish between a dideprotonated and a trideprotonated ligand. However, its chemical and magnetical behaviour, and the fact that it is isostructural with the corresponding Co, and Cu chelates,[2e] also points towards a trideprotonated ligand.

6. The magnetic behaviour of the Co and Ni biliverdin chelates does not agree with the formal oxidation states either (III) or (II).[2b,c] To clarify this point a detailed study of the magnetic behaviour in dilute solutions, concentrated solutions and solid state, such as has been performed for the Cu chelate, should be undertaken. For Co and Ni the presence of an equilibrium between two different electronic configurations corresponding to the oxidation states (II) and (III) $[BV(^{\cdot 2-})M^{2+} = (BV^{3-})M^{3+}]$ cannot be ruled out, since some of the published experimental results point in this direction. Valence tautomerism has already been observed for some $Cu^{II}$ hydroquinone chelates, which are in equilibrium with the $Cu^{I}$ semiquinone chelates; $Cu^{I}(Q^{\cdot -})(L) = Cu^{II}(Q^{2-})(L)$.[7] For the biliverdin ligand, which can oscillate between two or three negative charges, there could be valence tautomerism between the oxidation states (II) and (III). For Cu the redox potential for the transition $Cu^{III}/Cu^{II}$ is generally very high and consequently the Cu biliverdinate is present as the $Cu^{II}$ chelate of the radical of the ligand. However, the lower redox potentials corresponding to Co and Ni could allow the presence of valence tautomerism between the states (III) and (II).

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8. **1** was obtained as described in ref.[2f] : UV/Vis ($CH_2Cl_2$): $\lambda_{max}$ (relative intensities); 796 (8800), 415 (23000) nm; EPR ($CH_2Cl_2/CH_3OH$, 1:1): No bands were detected at 77 K or 4 K, only a low intensity band could be detected at half-field at 4 K.

9. Density functional calculations were performed using Spartan v.4.1.1 (Wavefunction Inc., Irvine, CA, USA) in a SG R8000 work station.

10. Planar $Cu^{II}$ porphyrinato cation radicals are diamagnetic as solids, since they undergo dimerization. Non-planar porphyrins, as solids, only show an intermolecular antiferromagnetic coupling because of the steric hindrance to the establishment of a strong-bonded diamagmetic dimer. The helical structure of the $Cu^{II}$ chelates of biliverdins probably prevents the formation of a diamagnetic dimer. Furthermore, for **1** in the solid state, most of the expected geometries for a weak intermolecular interaction would result in the loss of the ligand $C_2$ symmetry and in consequence in antiferromagnetic coupling; *e.g.* the centrosymmetric association, through one of the end lactam rings, of two helices of different sign.

11. The oxidative degradation of $Cu^{II}$ biliverdinates in nucleophilic solvents[2f] shows the well known pathway of bilin-1,19-diones to give bilipurpurins and biliviolins, which has been proposed to occur through such cations; Acero, C.; Ribó, J. M.; Solé, R.; Trull, F. R. *Monatsh. Chem.* **1993**, *124*, 401-417.

12. EPR experiments were performed on a Bruker EST 300E instrument (9.77 GHz, X band). EPR and UV/Vis electrolysis measurements were performed *in situ* on three-electrode cells (Cu wire as pseudo-reference electrode). The UV/Vis spectra of **1a** and **1b** were obtained by *in situ* electrolysis of **1** in a sandwich type cell with two compartments and a transparent mesh of Au as work electrode. **1a**: UV/Vis ($CH_2Cl_2$): $\lambda_{max}$ (relative intensities); 853 sh, 740 (13800), 400 (28000) nm; EPR ($CH_2Cl_2$): $g_{\parallel} = 2.098$, $g_{\perp} = 2.020$, $a_{Cu} = 90$ G, $a_N = 14$ G. **1b**: UV/Vis ($CH_2Cl_2$): $\lambda_{max}$ (relative intensities); 840 (8500), 409 (24000) nm. EPR ($CH_2Cl_2$) $g_{\parallel} = 2.123$, $g_{\perp} = 2.031$, $a_{Cu} = 84$ G, $a_N = 13$ G.

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