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EVIDENCES FOR THE FORMATION OF COMPLEXES OF D,L-DIHYDROTHIOCTIC ACID (REDUCED LIPOIC ACID) WITH Ni^{II} , Co^{II} AND Fe^{III} SALTS

We wish to report here very preliminar evidences about the complexing ability of D,L-dihydrothioctic acid (D,L-dihydrolipoate, DHL) towards some metallic ions. The occurrence of the Fe^{III} -DHL complex was first noticed in studies dealing with the enzymatic synthesis of iron-sulfur structures [1,3], and DHL was found able to remove ferritin-bound iron to an extent which compares more than favourably with the figures obtained by using other iron-chelators [4]. The possibility of using complexes of DHL with Ni^{II} and Co^{II} in the enzymic biosynthesis of hetero-metallic, sulfur-coordinated clusters, such as those known to occur in some bacterial hydrogenases [5] and nitrogenases [6], suggested the present preliminary investigation.

All experimental operations were performed anaerobically. DHL was prepared by NaBH_4 reduction of an aqueous solution of D,L-thioctic acid brought to pH 9.0 with NaOH. After acidification to destroy the excess reductant, DHL was extracted with chloroform, dried with sodium sulphate, and its concentration determined by sulfhydryl titration [7]. The same procedure was used for the synthesis of D,L-dihydrothioctamide, starting with an ethanolic solution of D,L-thioctamide.

Fig. 1 shows the electronic spectra of mixtures of DHL and of halides of the investigated metals.

All the spectra show two major charge-transfer absorption bands, and the Fe^{III} -DHL complex gave, on a metal-content basis, the most intense absorption. The iron complex can be reduced with dithionite to give an almost colorless solution. Careful air-oxidation of this dithionite-reduced

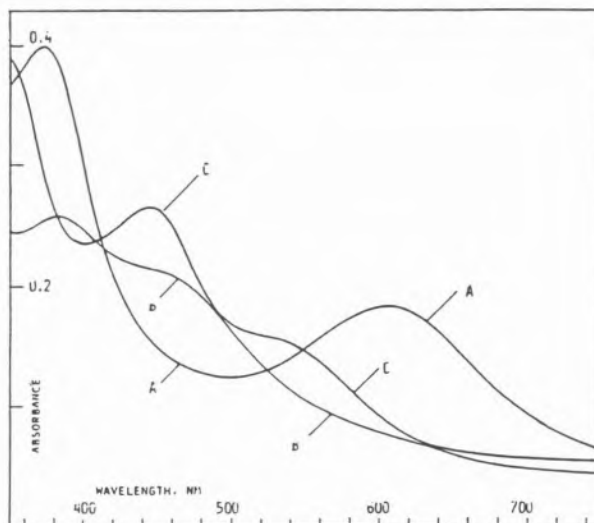


Fig. 1

Electronic spectra of buffered solutions of DHL in the presence of different metal ions. Spectra were recorded in 0.05 cm cuvettes and in 0.2 M Tris/sulfate pH 9.00. A — 20 mM DHL and 1 mM FeCl_3 ; B — 1 mM DHL and 2.2 mM CoCl_2 ; C — 1 mM DHL and 1.8 mM NiCl_2

sample allows recovery of the spectral features of the starting mixture (not shown). This and other evidences (3) suggest that iron is bound to DHL in the ferric form. When aqueous-detergent micellar solutions of D,L-dihydrothioctamide replaced DHL in the reaction with Fe^{III} , the same results were obtained, whereas D,L-thioctic acid and its amide did not display any chelating ability. These observations rule out the possible involvement of the carboxylate moiety of DHL as a ligand. Fig. 2 shows that, whatever the ion used, complexes are formed at an approximate 1/1 molar ratio between DHL and the metal. On the basis of the diamagnetic behaviour of the $\text{Fe}^{\text{II,III}}$ -DHL complexes, and of the strong resemblance of the electronic spectra of Fe^{III} -DHL to those of $\text{Fe}_2(\text{ethanedithiolate})_4^{2-}$, we are inclined to assign to the Fe-DHL complex the structure $\text{Fe}_2(\text{DHL})_4^{6-}$. The apparent 1/1 stoichiometry observed in the titration experiments could be explained by the reduction of some of the iron with concomitant oxidation of the thiol groups of DHL.

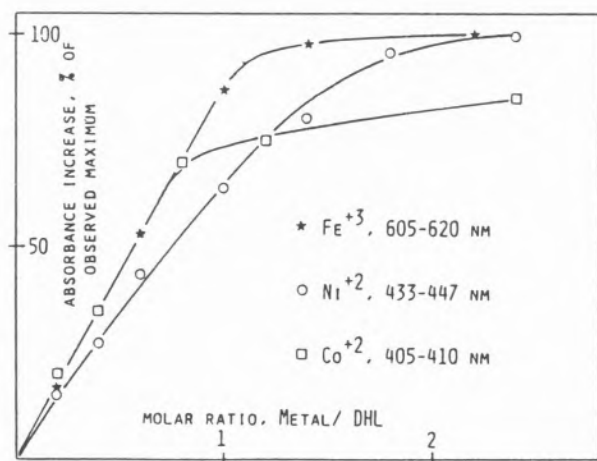


Fig. 2

Spectrophotometric titrations of DHL with increasing concentrations of different metal ions. To 50-100 ml of an anaerobic solution of DHL in 0.2 M Tris/sulfate pH 9.00, small volumes of concentrated aqueous solutions of the metal chlorides were added in the given molar ratios. Samples were anaerobically withdrawn for measuring the absorbance spectra 5 minutes after each addition

Work is in progress in order to crystallize and isolate all these compounds, to determine their structure and their electrochemical properties and to test their ability as substrates in the biosynthesis of naturally-occurring structures.

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PS4.7 — MO

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A UNIFIED CONCEPT OF ELECTRONIC PERTURBATIONS OF PORPHYRINS

This communication addresses the problem whether different observables on porphyrins, or hemes, are understandable within a unified model or whether each experimental technique expresses itself in its own language. Does a pattern exist such that an observed quantity of one parameter immediately predicts a quantity of another?

The effects of 2,4-substitutions on a number of observables are collected in Table 1. For most of them a working model based upon delocalized electron density suffices to give a unified view. Removing electron density from the annular structure weakens the N-H bond, increases its H-donor capacity (E_H), and lowers its pK_3 . It also diminishes its Soret band energy (increases λ_{Soret}) and reduces the electron availability at the iron atom. The latter effect, which is observed as a more positive FeIII/II reduction potential (ΔE_m), will also increase ν_{CO} and decrease ν_{FeC} of liganded CO. The trend of these observables persists in the succession R=CHO, COCH₃, CHCH₂, H, and C₂H₅ but for a 0,5 nm shift of the Soret band upon H for C₂H₅ substitution. The trend holds also for another two observables, the melting point T_m of the esters and the 1-CH₃ proton chemical shift δ_1 . In these cases, however, the mechanism is less obvious.

On the assumption that T_m reflects the strength of intermolecular attraction certain classes of tunable forces are plausible [1]. The basicity of the pyrrolic nitrogen atoms could modulate the strength of