1-ALKYL-4-ETHOXYTHIOCARBONYL-5-HYDROXY-3-METHYLPYRAZOLE : SYNTHESIS , COPPER COMPLEXES AND SOLVENT EXTRACTION STUDIES

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Abstract: 1-Alkyl-4-ethoxythiocarbonyl-5-hydroxy-3-methylpyrazole, HETCP, (alkyl = n-octyl ; n-dodecyl) were prepared in high yield by the reaction of 1-alkyl-3-methyl-2-pyrazolin-5-one with bis (ethoxythiocarbonyl)sulfide and sodium acetate in dimethylformamide. These reagents act as O, S bidentate ligands in solvent extraction/reextraction studies of Cu (II) from acid aqueous solutions and the extracted specie resulted to be $Cu(ETCP)_2$.

Keywords: 5- Pyrazolone, ethoxythiocarbonyl, bidentate ligand, copper complex, solvent extraction

Introduction

It is known that β-diketones like acetylacetone, dibenzoylmethane, thenoyltrifluoroacetone, 4-acyl-5-pyrazolones or 4-acyl-5-isoxazolones are chelating ligands with a wide use in the solvent extraction of transition metal, actinides, lanthanides and others ions [1-11]; analogous compounds containing sulfure like monothiodibenzoylmethane and dithiocarboxylate derivatives also have been employed [12,13]. We have reported several studies on this matter, concerning to synthetic methods, chelating and extractive properties of pyrazolyl-4-alkyldithiocarboxylate derivatives synthesized from 5-pyrazolones [14-21]. More recently, we have described the application of these dithiocarboxylates as inhibitors of copper corrosion in aggressive aqueous saline media [22]. Continuing with these studies, in this paper we describe a straightforward method to synthesize pyrazolyl derivatives 1 (HETCP) in high yield, where the chelating alkyldithiocarboxylate moiety has been replaced by the ethoxythiocarbonyl group (Fig 1). Also, we describe the synthesis of complexes 2 and the solvent extraction behavior of aqueous Cu (II) solutions with these ligands in chloroform or Escaid 103 (an industrial solvent).

1a , 2a: R = n-C_8H_{17} **1b, 2b** : R = n-$C_{12}H_{25}$

Fig. 1 General structure of the ligands 1-alkyl-4-ethoxythiocarbonyl-3-methyl-5-hydroxypyrazole 1 and copper complexes 2

Experimental

All reagents used in the synthetic procedures as well as in the solvent extraction studies were of analytical grade Elemental. analysis of carbon, hydrogen, nitrogen and sulfur were obtained with a Perkin Elmer 2400 Serie II Analyser. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrophotometer, using KBr discs. NMR spectra of ligands were recorded in the Centro de Resonancia Magnética Nuclear V Region, located at the Universidad Técnica Federico Santa María, on a Avance 400 Digital NMR Bruker spectrometer at 400.132 MHz for ^{1}H and 100.623 MHz for ^{13}C in deuterochloroform with internal TMS as reference. UV-VIS spectra were recorded on a Perkin Elmer UV/VIS Lambda EZ 201 spectrophotometer, with chloroform as solvent. Melting points were measured in a Kofler Bristol apparatus and are uncorrected. Individual stock solutions 0.01 M in Cu(II) and 0.1 M in potassium nitrate at fixed pH, were prepared from cupric nitrate and standardized by iodometric titration with $Na_2S_2O_3$ 0.01 M. The pH of these Cu (II) solutions was adjusted in the range 1-5 by the addition of hydrochloric acid solutions of variable concentration. Acetic acid-sodium acetate buffer was used in the extraction studies as a function of the ligand concentration at constant pH. Freshly distilled chloroform and Escaid 103 were used as solvent and all extraction experiments were achieved by the batch method with a variable-speed vortex mixer (Orbital Shaker).

Synthetic Procedures
Synthesis of bis(ethoxythiocarbonyl)disulfide.

To a stirred solution of 28.05 g (0.5 moles) of KOH in 120 mL of ethanol, 38.00 g (0.5 moles) of CS_2 were dropwise added from a dropping funnel. The solid potassium ethylxantate obtained was filtered, washed with cold ethyl alcohol and then dissolved in the minimal amount of water. The aqueous solution was cooled with an ice/water bath and then 18.50 g (0.17 moles) of ethyl chloroformiate were slowly dropwise added. The oily organic phase formed was separate and keep overnight at the freezer. The solid disulfide obtained was recrystallized from 1:3 ethyl alcohol/water. 21.00 g (60% yield), yellow solid, m.p 53°C. IR (cm^{-1}): 2988 (CH); 1372 (C=S); 1150 (C-O);^{1}H RMN (CDCl$_3$, TMS, δ ppm): 1.48 (t, 6H, CH$_2$CH$_3$. J = 7.6 Hz) ; 4.67 (c, 4H, CH$_2$CH$_3$, J = 7.6 Hz); ^{13}C RMN (CDCl$_3$, TMS, δ ppm): 13.5 (OCH$_2$CH$_3$): 70.9 (OCH$_2$CH$_3$); 205.0 (C=S). Anal. calcd for $C_6H_{10}O_2S_3$: C, 34.26; H, 4.79; S, 45.73. Found C, 34.16; H, 4.70; S, 45.65.

Synthesis of 1-alkyl-4-ethoxythiocarbonyl-5-hydroxy-3-methylpyrazole   1a-b.
General Procedure.

A mixture of 10.0 mmoles of the corresponding 1-alkyl-5-pyrazolone, 0.90 g (11 mmole) of sodium acetate, 2.31 g (11 mmole) of bis(ethoxythiocarbonyl)sulfide and 30 mL of DMF were stirred at 40°C for 14 h. The cold reaction mixture was poured over 100 mL HCl 2M mixed with crushed ice, stirred 30 min and then extracted with CH$_2$Cl$_2$ (2x 100 mL). The organic phase was washed with water until liquid which was purified by column chromatography (CC) with hexane/ethyl acetate as eluent.

4-Ethoxythiocarbonyl-5-hydroxy-3-methyl-1-octylpyrazole 1a.

Purified by CC with hexane/ethyl acetate 3:1; 2.22 g (75% yield), red oil liquid. IR (cm^{-1}): 3300-2500 (associated OH-thiocarbonyl; 1540 (pyrazole ring); 1379 (C=S). UV-Visible (λ, nm, CHCl$_3$): log ꓱ 4.25, λmáx 31. ^{1}HMR (CDCl$_3$,TMS, δ ppm): 0.85 (t, 3H, NCH$_2$CH$_2$(CH$_2$)$_5$CH$_3$. J=6.7 Hz); 1.26(m, 10H, NCH$_2$CH$_2$(CH$_2$)$_5$CH$_3$): 1.46 (t, 3H, OCH$_2$CH$_3$, J = 7.7 Hz); 1.77 (t, 2H, NCH$_2$CH$_2$(CH$_2$)$_5$CH$_3$): 2.35 (s, 3H, CH$_3$, pyrazole); 3.90 (t, 2H, NCH$_2$(CH$_2$)$_6$CH$_3$, J = 7.4 Hz); 4.64 (c, 2H, OCH$_2$CH$_3$, J = 7.7

Hz); 11.76 (s, 1H, -OH). ^{13}C NMR (CDCl$_3$, TMS, δ ppm): 13.8 (NCH$_2$(CH$_2$)$_6$CH$_3$); 14.0 (OCH$_2$CH$_3$); 66.0 (OCH$_2$CH$_3$); 145.6 (C5-OH); 159.0 (C3-pirazol); 204.1 (C=S). Anal calcd for C$_{15}$H$_{26}$N$_2$O$_2$S: C 60.37, H 8.72, N 9.39, S 10.74; Found C 60.48, H 8.78, N 9.35, S 10.80.

4-Ethoxythiocarbonyl-1-dodecyl-5-hydroxy-3-methylpyrazole 1b.
Purified by CC with hexane/ethyl acetate 5:1; 2.80g (80% yield), pale yellow solid, m.p 35°C. IR (cm^{-1}): 3300-2500 (associated OH-thiocarbonyl; 1540 (pyrazole ring); 1380 (C=S). UV-Visible (λ, nm, CHCl$_3$): log □ 4.28, λ max 312. ^{1}H NMR (CDCl$_3$, TMS, δ ppm,): 0.88 (t, 3H, NCH$_2$CH$_2$(CH$_2$)$_9$CH$_3$ J= 6.8 Hz); 1.26 (m, 18H, NCH$_2$CH$_2$(CH$_2$)$_9$CH$_3$): 1.47 (t, 3H, OCH$_2$CH$_3$ J= 8.8 Hz); 2.35 (s, 3H, CH$_3$-pyirazole); 3.90 (t, 2H, NCH$_2$(CH$_2$)$_{10}$CH$_3$ J= 7.4 Hz); 4.63 (c, 2H, OCH$_2$CH$_3$ J= 8.8 Hz); 11.76(s, 1H, -OH). ^{13}C NMR (CDCl$_3$, TMS, δ ppm,): 13.8 (NCH$_2$(CH$_2$)$_6$CH$_3$); 14.0 (OCH$_2$CH$_3$); 66.0 (OCH$_2$CH$_3$); 145.6 (C5-OH); 159.0 (C3-pirazol); 205.1 (C=S). Anal calcd for C$_{19}$H$_{34}$N$_2$O$_2$S: C 64.36, H 9.67, N 7.90, S 9.04; Found C 64.48, H 9.51, N 7.96, S 8.95.

Synthesis of the copper complexes. General Procedure
0.20 g (1 mmol) of Cu(OAc)$_2$.H$_2$O in 15 mL of methanol were mixed with 2 mmole of the corresponding   5-hydroxypyrazole (HETCP) dissolved in 10 mL of chloroform and stirred at 40°C overnight. The solid complex was filtered and washed several times with cold methanol.

Copper complex of 4-ethoxythiocarbonyl-5-hydroxy-3-methyl-1-octylpyrazole 2a.
0.65g (96% yield), green solid, m.p 98°C. UV-Visible (λ, nm, CHCl$_3$): log □ 4.27, λ max 295. IR (cm^{-1}): 2980-2853 (aliphatic CH); 1580 (pyrazole ring). Anal calcd for C$_{30}$H$_{50}$N$_4$O$_4$S$_2$Cu : C 54.73, H 7.65, N 8.51, S 9.74, Cu 9.65; found: C 54.62, H 7.65, N 8.63, S 9.64, Cu 9.70.

Copper complex of 4-ethoxythiocarbonyl-1-dodecyl-5-hydroxy-3-methylpyrazole 2b.
0.64g (83% yield) green solid, m.p 112°C. UV-Visible (λ, nm, CHCl$_3$): log □ 4.27, λ max 295. IR (cm^{-1}): 2932-2850 (aliphatic CH); 1580 (pyrazole ring). Anal calcd for C$_{38}$H$_{66}$N$_4$O$_4$ S$_2$Cu: C 60.00, H 8.75, N 7.37, S 8.43, Cu, 8.35; found C 59.85, H 8.69, N 7.30, S 8.48, Cu 8.42.

Extraction and Analytical Procedures
Extraction of Cu(II) from 0.01 M Stock Solutions as a function of pH.
15.00 mL of the copper(II) stock solution adjusted to the desire initial pH in the range of 0-5.5 with HCl were shaken for 30 min with an equal volume of a 0.02 M chloroform or Escaid 103 solution of HETCP ligand in a separatory funnel. The aqueous phase was saved and the organic one was shaken 30 min with 15.00 mL of 2M H$_2$SO$_4$ solution. The resulting organic phase was added to the saved aqueous solution and shaken again during 30 min. After phase separation, the concentration of Cu(II) left in the aqueous phase was evaluated either by titration with 0.01 M EDTA solution or by atomic absorption technique. The concentration of the metal ion as complex in the organic phases was then deduced from a material balance.

Stoichiometry of the Extracted Complex.
15.00 mL of the copper (II) stock solution at constant fixed pH with acetic acid-sodium acetate buffer, was treated with 15.00 mL of chloroform solutions of each ligand at variable concentrations. Both phases were separated and the content of

Cu(II) in the aqueous phase was evaluated as before and the concentration of the metal ion as complex in the organic phases was then deduced from a material balance. Kd was taken as the ratio of the equilibrium concentration of Cu(II) as complex in the organic phase to that present in the aqueous phase.

Reextraction of Cu (II) with 2M H_2SO_4 solution.

Each loaded organic phase obtained from the extraction process at pH = 0-5.5 and containing the extracted copper complex was shaken with 15.00 mL of 2M H_2SO_4 solution during 30 min. The content of metal ion in the resulting aqueous phase was evaluated as before.

Results and discussion
Chemistry

The chemistry employed in the synthesis of 4-ethoxythiocarbonyl-5-hydroxy-3-methyl-1-octylpyrazole **1a** and 4-ethoxythiocarbonyl-1-dodecyl-5-hydroxy-3-methylpyrazole **1b** is shown in the Scheme 1. Potassium ethylxantate was prepared from the reaction of an ethanolic solution of potassium hydroxide with carbon disulfide and converted to bis(ethoxythiocarbonyl)sulfide by treatment with ethyl chloroformiate. This sulfide was then used as the ethoxythiocarbonylating reagent after the treatment of 1-octyl or 1-dodecyl-3-methyl-2-pyrazolin-5-one with sodium acetate in DMF.
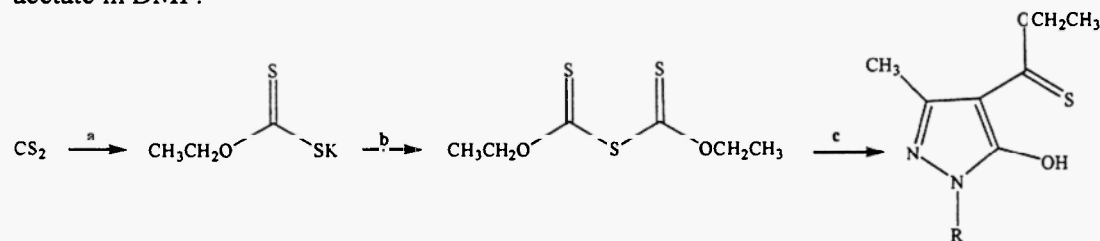
Scheme 1. (a) KOH, CH_3CH_2OH ; (b) H_2O, Ethyl chloroformiate ; (c) 1-Alkyl-2-pyrazolin-5-one, CH_3CO_2Na, DMF.

The spectroscopic data of both ligands is in agreement with the proposed thiocarbonyl enolic structure, where the hydrogen bonding associated singlet signal of OH proton was observed at 11.76 ppm in the ^1H NMR spectra, while the carbon signal of the thiocarbonyl group appeared at 204-205 ppm in the ^{13}C spectra. Main ^1H and ^{13}C NMR data, IR absorptions and other physical data are given in the experimental section.

To characterize the copper complexes **2a-b** of both ligands, they were prepared by the reaction of copper acetate in methanol with each ligand dissolved in chloroform at 40°C. Elemental analysis of carbon, hydrogen, nitrogen and sulfur is in agreement with a molecular formula of $C_{30}H_{50}N_4O_4S_2Cu$ and $C_{38}H_{66}N_4O_4S_2Cu$ for the complexes **2a** and **2b**, respectively, meaning that the ligands are bidentate and form complexes of the type $Cu(ETCP)_2$. According to previously reported results with analog dithiocarboxylate derivatives [14-21], oxygen attached to carbon 2 of pyrazole and sulfur of the methoxythiocarbonyl group are responsible for the Cu (II) chelation.

Extraction and Reextraction Studies

Extraction of Cu(II) as Function of Initial pH.

In a first approach, stock solutions of Cu(II) 0.01 M at fixed pH (0-5.5) were extracted with 0.02 M organic solutions (CHCl$_3$, Escaid 103) of **1a** or **1b** in a single loading extraction step. Under these conditions it was observed that the extraction extent varied from 17-65% , the metal ion as complex in the loaded organic phase can be stripped with 2M H$_2$SO$_4$ aqueous solution and that the ligand in the organic phase is not decomposed during the stripping step. Taking into account these results, the extraction studies as function of pH were achieved with two loading extractions and one stripping step. To do this, the stock solution of Cu(II) was extracted with the 0.02 M organic solution of the ligand and after separation, the loaded organic phase with the copper complex was stripped with the 2M H$_2$SO$_4$ solution; the resulting organic phase, containing the recovered ligand, was shaken again with the aqueous phase from the first step to complete the extraction of Cu (II), followed by the evaluation of the copper content in the overall final aqueous layer either by complexometry or atomic absorption. The concentration of the metal ion as complex in the loaded organic phase was then deduced from a material balance. The results of the extraction process under these conditions are shown in Fig.2 and the following general observations can be made: a) The global extraction extent change from 59 to 98% with the ligand **1a** in CHCl$_3$ or Escaid 103 as solvent at pH 0-5.5. b) Using **1a** there is not a great difference in the Cu(II) extraction with CHCl$_3$ or Escaid 103 and with both solvents it is almost quantitative at pH 5.0-5.5. c) The global extraction extent change from 51 to 87% with **1b** in CHCl$_3$ as solvent at pH 0-5.5. d) The extractive properties of ligand **1a** in CHCl$_3$ are higher than **1b** in all the pH range considered in this study, probably due to a better arrangement of the complexing moiety in the water/organic interface by the ligand containing the shorter octyl chain [1,2]. Back extraction of Cu (II) from the organic phase was efficiently achieved with 2M aqueous H$_2$SO$_4$ solution. Taking into account only the stripping step, the back-extraction extent was 93-100% and 55-98% if the two loading and stripping steps were considered.

Effect of Ligand Concentration on the Cu (II) extraction. Stoichiometry of the Extracted Complex.

Both stoichiometric and equilibrium constant information about the extraction process were deduced by studying the effect of the ligand concentration at constant ion metal concentration and constant pH on the Cu (II) extraction process. Plot of log Kd vs log[HETCP]$_{equil.}$ at constant pH (Fig. 3) gave straight lines with slopes near to two for both ligands. These results are in agreement with a Cu(ETCP)$_2$ composition of the extracted complex and with the release of two hydrogen ions during the complex formation. Table 1 contains the extraction constant values (log Kex) calculated from the slope analysis for each ligand **1a** and **1b**, confirming the higher extractives properties of the octyl ligand **1a**
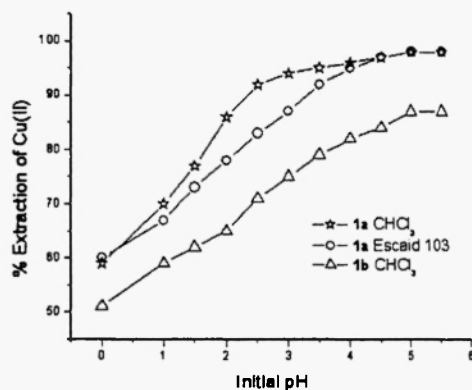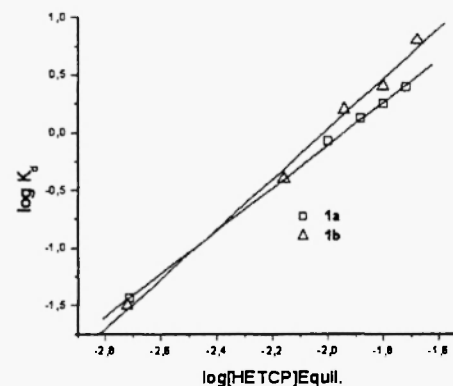
Fig 2 Plot of % Extraction of Cu (II) vs initial pH

Fig 3 Plot of log Kd vs log   HETCP concentration

Table 1. Data of parameters obtained from slope analysis in the extraction studies

Ligand	pH	Slope	Intercept	Log Kex
1a	4.65	1.9	4.4	-4.90
1b	4.65	2.2	3.6	- 5.70

Conclusions

From the results of this investigation, it is possible to establish the following conclusions : a) 1-alkyl-4-   ethoxythiocarbonyl-5-hydroxy-3-methylpyrazole are prepared in good yield by the reaction of 1-alkyl-3-methyl-2-pyrazolin-5-one, bis(etoxythiocarbonyl)sulfide and sodium acetate, in DMF. b) These ligands behave as O, S bidentate extractant reagent of Cu (II) in chloroform or Escaid 103 at pH 0-5.5. c) The Cu (II) is extracted as a $Cu(ETCP)_2$ complex to the organic phase. d) The Cu (II) is back-extracted from the organic layer with diluted aqueous H_2SO_4, recovering the ligand in the organic layer without decomposition and is available to be used again in the extraction process. e) The extraction/back-extraction steps are almost quantitative at pH 5.5.

Acknowledgement

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