1,5-Bis(4- dithiocarboxylate-5-hydroxypyrazolyl)pentane Derivatives of 5-Pyrazolones

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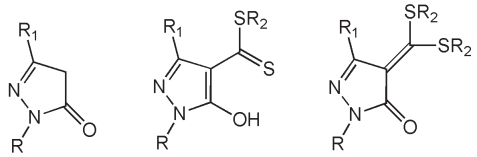
Received October 26, 2004

3-Methyl-1-phenyl-2-pyrazolin-5-one **1b** and 1-dodecyl-3-methyl-2-pyrazolin-5-one **1c** react with carbon disulfide and 1,5-dibromopentane in the presence of sodium acetate in dimethylformamide or *n*-butyllithium in tetrahydrofuran to afford 1,5-bis(4-dithiocarboxylate-5-hydroy-pyrazolyl)pentane derivatives **6b-c**.

J. Heterocyclic Chem., **42**, 595 (2005).

It is known that the reaction of active methylene compounds with carbon disulfide and alkyl halides affords alkyldithiocarboxylate or ketene dithioacetal derivatives, depending on the stoichiometry of the reaction or on the nature of the base employed [1-3]. With 5-pyrazolones **1**, the pyrazolyl-4-alkyldithiocarboxylates **2** or the ketene dithioacetals **3** are obtained and reactions can be achieved in *n*-butyllithium-THF, sodium acetate-DMF [4-7] or under phase-transfer catalysis (PTC) conditions [8-10].

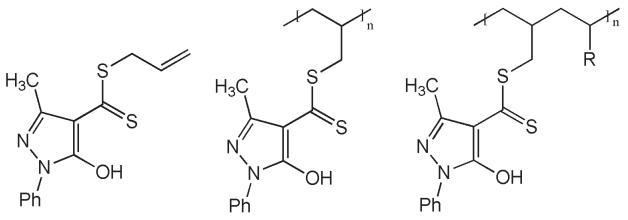


1 **2** **3**

R = Alkyl, Phenyl; R_1 = Methyl, Hydroxyl; R_2 = Alkyl

Figure 1

When R_2 in the general structure **2** is an allylic substituent, it is possible to carry out vinylic polymerization and recently we have reported the synthesis of vinyl polymers **4** and **5a-b**, containing the methylene-5-hydroxy-3-methyl-1-phenylpyrazolyl-4-dithiocarboxylate group. These polymers were obtained by homopolymerization of the allylic derivative **2a** (R = Phenyl; R_1 = Methyl; R_2 = Allyl) or by its copolymerization with styrene or acrylamide, in the presence of benzoyl peroxide or aluminum trichloride catalyst [11].

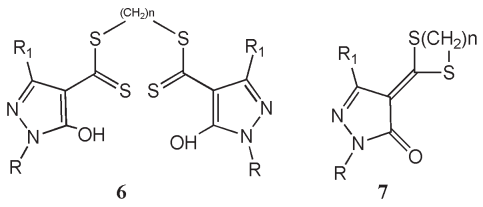


2a **4** **5a**: R = Ph
5b: R = $CONH_2$

Figure 2

The pyrazolyldithiocarboxylates **2** are heterocyclic bidentate chelating ligands with interesting solvent-extraction properties, where the dithiocarboxylate and the hydroxy substituents are responsible of these properties. They allow the extraction of several divalent transition metal ions [12,13], including the separation of Cu(II) from Fe(III) in acidic lixiviation solutions of a copper mineral with a high content of iron [14]. Also they extract toxic mercury, lead and cadmium ions and some of them can be used to separate Hg(II) from Pb(II) and/or Cd(II) at pH 1 in a single step [15].

Because of our interest on the chelating and extractive properties of the pyrazolyldithiocarboxylates **2**, we have studied the reaction of 5-pyrazolones with 1,2-dibromoethane and 1,3-dibromopropane in order to get bis-pyrazolyl derivatives **6** with tetradentate complexing properties. However, independant of stoichiometry conditions of the reaction, the only isolated compounds were the cyclic ketene dithioacetals **7**, probably due to the stability of the five member dithiolane and six member dithiane cycle [4,8,9].



6 **7**

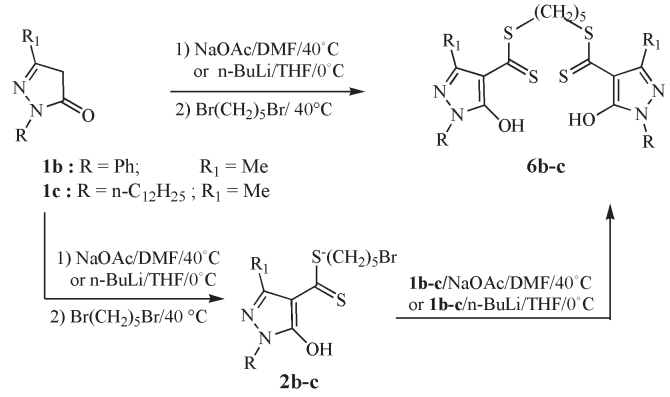
Figure 3

According to these results we decided to analyze the reaction of 5-pyrazolones **1** with longer linear alkyl chain dibromides. Molecular model analysis shows that a linear alkyl chain of five carbon atoms allows for a better conformation to both pyrazolyl groups in adopting a planar tetradentate structure to chelate metal ions, and in this paper we wish to report the succesfully preparation of

1,5-bis(4-dithiocarboxylate-5-hydroxypyrazolyl) pentane derivatives **6b-c** (n=5) with potential tetradentate characteristics.

The synthesis was achieved by reaction of 5-pyrazolones **1b-c** (**1b**: R = Ph, R_1 = Me; **1c**: R = *n*-dodecyl, R_1 = Me) with carbon disulfide, followed by the addition of 1,5-dibromopentane (2:1 molar ratio), using sodium acetate in DMF at 40 ºC or *n*-butyllithium in THF at 0 ºC. Also, the reaction was performed in two steps, by reacting **1b-c**, carbon disulfide and 1,5-dibromopentane (1:1 molar ratio), isolating the intermediate bromopentyl derivative **2b-c** and then adding this intermediate to the dithiocarboxylate prepared as before (Scheme 1).

Scheme 1



The enolic 5-hydroxypyrazolyl-4-dithiocarboxylate structure of compounds **2b-c** and **6b-c** was assigned on the basis of the ^{1}H and ^{13}C nmr data. The ^{1}H nmr spectra shows a downfield singlet at 12.30-13.74 ppm due to the enolic proton of the 5-hydroxy group, while in the ^{13}C nmr spectra the thiocarbonyl, the C-3, C-4 and C-5 signals of the pyrazole ring are observed around 213, 146, 111 and 158 ppm respectively, in agreement with previously reported values [4-10,16]. Preliminary studies on the chelating and extractives properties of **6b-c** with Cu(II) confirm the tetradentate character of the synthesized compounds by formation of a 1:1 metal/ligand complex. Studies on this matter are in progress.

EXPERIMENTAL

All nmr spectra were recorded in the Centro de Resonancia Magnética Nuclear V Región located at the Universidad Técnica Federico Santa María, Valparaíso, Chile on a Avance 400 Digital NMR Bruker spectrometer operating at 400.132 MHz for ^{1}H and 100.623 MHz for ^{13}C in deuterochloroform with internal TMS as reference. Chemical shifts are expressed in ppm, followed by multiplicity and coupling constant (J) in Hertz. IR spectra were recorded on a Perkin Elmer FT IR 1600 spectrophotometer, as KBr discs. Elemental analysis of carbon, hydrgen and nitrogen were obtained with a Perkin Elmer 2400 Serie II CHN Elemental Analyser. Melting points were measured in a Kofler Bristole apparatus and are uncorrected. The reactions were conducted in previously dried apparatus, under a nitrogen atmosphere.

Synthesis of 1,5-Bis(4-dithiocarboxylate-5-hydroxypyrazolyl)-pentane Derivatives. **6b-c**.

General Procedure.

A solution of 10.0 mmoles of **1b** or **1c**, anhydrous sodium acetate (0.90 g , 11.0 mmoles) in 30.0 mL DMF was stirred at 40 ºC during 2 h. After the addition of carbon disulfide (0.83 g, 11.0 mmoles), the solution was stirred another 2 h at the same temperature and then, 1,5-dibromopentane (1.15 g, 5.0 mmoles) was added. Stirring of the resulting red to orange solution was maintained overnight at 40 ºC and then, the pale yellow solid that formed was collected by filtration, washed with hexane and water, dried and recrystallized with ethyl acetate or hexane.

By an analogous procedure, the synthesis was carried out at 0 ºC in dry THF and 1.6 *M n*-butyllithium in hexane. After stirring the colored organic solution overnight at r.t., it was washed with saturated sodium chloride solution and dried over anhydrous sodium sulphate. Solvents were removed under vacuum and from the residue and the product was isolated by crystallization with ethyl acetate or hexane. These procedures were also applied to the two-step preparation of **6b-c**, isolating the intermediate bromopentyl derivatives **2b-c**.

4-(5-Bromopentyldithiocarboxylate)-5-hydroxy-3-methyl-1-phenylpyrazole (**2b**).

This compound was prepared with 68% yield, as an amorphous yellow to orange solid, mp 53-54 ºC (ethyl acetate); ir (cm^{-1}, potassium bromide): ν enolic OH 3300-2490, pyrazole ring 1560; ^{1}H nmr (deuteriochloroform): δ 1.65 (m, 2H, -$CH_2C\underline{H}_2CH_2$-), 1.81 (m, 2H, C$\underline{H}_2CH_2$Br), 1.94 (m, 2H, -C$\underline{H}_2CH_2$S-), 2.67 (s, 3H, CH_3 pyrazole), 3.40 (t, 2H, J= 7.4, CH_2Br), 3.44 (t, 2H, J= 7.3, CH_2S), 7.31 (m, 1H, Ph), 7.46 (m, 2H, Ph), 7.81 (m, 2H, Ph), 13.74 (s, 1H, HO); ^{13}C nmr (deuteriochloroform): δ 18.1 (CH_3 pyrazole), 27.0 (-$\underline{C}H_2CH_2$Br, -$\underline{C}H_2CH_2$S-), 27.5 (-$CH_2\underline{C}H_2CH_2$-), 33.3 (CH_2Br), 33.4 (CH_2S), 111.3 (C-4 pyrazole), 121.6 (Ph), 127.0 (Ph), 129.0 (Ph), 137.1 (Ph), 146.8 (C-3 pyrazole), 157.6 (C-5 pyrazole), 213.3 (C=S).

Anal. Calcd. for $C_{16}H_{19}BrN_2OS_2$: C, 48.10; H, 4.80; N, 7.02. Found: C, 48.23; H, 4.75; N, 6.94.

4-(5-Bromopentyldithiocarboxylate)-1-dodecyl-5-hydroxy-3-methyl-1-phenylpyrazole (**2c**).

This compound was prepared with 80% yield, as orange viscous oil; ir (cm^{-1}, potassium bromide): ν enolic OH 3300-2510, pyrazole ring 1565; ^{1}H nmr (deuteriochloroform): δ 0.87 (t, 3H, J = 6.6, CH_3 dodecyl), 1.24 (bs, 16H, CH_2 dodecyl) 1.63 (m, 4H, -C$\underline{H}_2CH_2CH_2$S-, -C$\underline{H}_2CH_2CH_2$N-), 1.80 (m, 4H, C$\underline{H}_2CH_2$Br, -C$\underline{H}_2CH_2$N-), 1.93 (qn, 2H, J = 6.9, -C$\underline{H}_2CH_2$S-), 2.56 (s, 3H, CH_3 pyrazole), 3.38 (t, 2H, J = 7.3, CH_2Br), 3.43 (t, 2H, J = 7.8, -CH_2S-), 3.91 (t, 2H, J = 7.7, -CH_2N-), 13.00 (s, 1H, OH). ; ^{13}C nmr (deuteriochloroform) : δ 14.1 (CH_3 dodecyl), 18.0 (CH_3 pyrazole), 22.7, 26.5, 28.7, 29.1, 29.3, 29.4, 29.5, 29.6,31.9, 32.1 (CH_2 dodecyl), 27.1 (-$\underline{C}H_2CH_2$Br, -$\underline{C}H_2CH_2$S-), 27.5 (-$\underline{C}H_2CH_2CH_2$S-), 33.2 (-CH_2Br), 33.4 (-CH_2S-), 46.3 –CH_2N-),

110.8 (C-4 pyrazole), 145.5 (C-3 pyrazole), 157.7 (C-5 pyrazole), 212.8 (C=S).

Anal. Calcd. for $C_{22}H_{39}BrN_2OS_2$: C, 53.73; H, 8.00; N, 5.70. Found: C, 54.18; H, 7.73; N, 5.93.

1,5-Bis(4-dithiocarboxylate-5-hydroxy-3-methyl-1-phenylpyrazolyl)pentane (**6b**).

This compound was obtained with 71% yield as an amorphous pale yellow solid, mp 172-173 ºC (ethyl acetate); ir (cm^{-1}, potassium bromide): ν enolic OH 3300-2490, pyrazole ring 1565 ; ^{1}H nmr (deuteriochloroform) : δ 1.68 (m, 2H, -C$\underline{H}_2$CH$_2$CH$_2$S-), 1.88 (m, 4H, -CH$_2$C$\underline{H}_2$CH$_2$S-), 2.68 (s, 6H, CH$_3$ pyrazole), 3.44 (t, 4H, J= 7.4, -CH$_2$S), 7.31 (m, 2H, Ph), 7.47 (m, 4H, Ph), 7.81 (m, 4H, Ph), 13.74 (s, 2H, HO) ; ^{13}C nmr (deuteriochloroform) : δ 18.2 (CH$_3$), 27.4 (-CH$_2$$\underline{C}H_2CH_2$S-), 28.4 (-$\underline{C}H_2CH_2CH_2$S-), 33.4 (-CH$_2CH_2$$\underline{C}H_2$S-), 111.4 (C-4 pyrazole), 121.1 (Ph), 127.1 (Ph), 129.1 (Ph), 137.1 (Ph), 146.8 (C-3 pyrazole), 157.7 (C-5 pyrazole), 213.4 (C=S).

Anal. Calcd. for $C_{27}H_{28}N_4O_2S_4$: C, 56.99; H, 4.96; N, 9.86. Found: C, 59.61; H, 4.70; N, 9.92.

1,5-Bis(4-dithiocarboxylate-1-dodecyl-5-hydroxy-3-methyl pyrazolyl)pentane (**6c**).

This compound was prepared with 77% yield as an amorphous yellow solid, mp 79-80 ºC (hexane); ir (cm^{-1}, potassium bromide): ν enolic OH 3300-2500, pyrazole ring 1560; ^{1}H nmr (deuteriochloroform): δ 0.86 (t, 6H, J= 6.6, CH$_3$ dodecyl), 1,29 (bs, 36 H, CH_2 dodecyl), 1.66 (m, 2H, -C$\underline{H}_2$CH$_2$CH$_2$S-), 1.83 (m, 8H, -CH$_2$C$\underline{H}_2$CH$_2$S-, -C$\underline{H}_2$CH$_2$N-), 2.58 (s, 6H, CH$_3$ pyrazole), 3.41 (t, 4H, J= 7.4, -CH$_2$S), 3.92 (t, 4H, J= 7.2, CH$_2$N), 12.11 (s, 2H, HO); ^{13}C nmr (deuteriochloroform): δ 14.1 (CH$_3$ dodecyl), 18.0 (CH$_3$ pyrazole), 22.7, 26.5, 29.3, 29.5, 29.6, 31.9 (CH$_2$ dodecyl), 27.5 (-CH$_2$$\underline{C}H_2CH_2$S-), 28.7 (-$\underline{C}H_2CH_2CH_2$S-), 33.2 (-CH$_2CH_2$$\underline{C}H_2$S-), 46.3 (CH$_2$N dodecyl), 110.8 (C-4 pyrazole), 145.5 (C-3 pyrazole), 157.7 (C-5 pyrazole), 212.8 (C=S).

Anal. Calcd. for $C_{39}H_{68}N_4O_2S_4$: C, 62.17 ; H, 9.10 ; N, 7.44. Found: C, 62.35; H, 9.45; N, 7.60.

Acknowledgements.

The authors wish to thank financial support from the Dirección de Investigación (Projet 125.773/2004) of the Pontificia Universidad Católica de Valparaíso, Chile.

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