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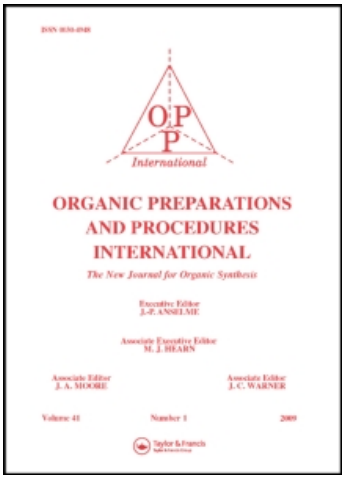

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AN IMPROVED SYNTHESIS OF ALKYL 1-ALKYL-3-METHYL-2-PYRAZOLINE-5-ONE-4-DITHIOCARBOXYLATES

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AN IMPROVED SYNTHESIS OF ALKYL 1-ALKYL-3-METHYL-2-PYRAZOLINE-5-ONE-4-DITHIOCARBOXYLATES

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There are two known preparations of methyl and ethyl esters of 3-methyl-1-phenyl-2-pyrazoline-5-one-4-dithiocarboxylic acid. The reaction of 3-methyl-1-phenyl-2-pyrazoline-5-one with carbon disulfide and ethyl chloroformate (or ethyl bromide) in the presence of anhydrous aluminum chloride,[1] is unsatisfactory, giving at best a 20-30% yield. Our experience with the two-step synthesis involving initial conversion of 3-methyl-2-pyrazoline - 5-one to the 4-dithiocarboxylic acid followed by alkylation with dimethyl or diethyl sulfate,[2] shows that the isolation of the dithiocarboxylic acid is less than routine. We have reported the synthesis of alkyl 3-dimethylhydrazonoalkanedithioate by the reaction of N,N-dimethylhydrazones with n-butyllithium, carbon disulfide and alkyl halides,[3] and we decided to apply this synthetic scheme to 1-alkyl-3-methyl-2-pyrazoline-5-ones (1), in order to obtain alkyl esters of 1-alkyl-3-methyl-2-pyrazoline-5-one-4-dithiocarboxylic acids (2).

1 2

i) n-BuLi, THF, 0° ii) CS_2, THF, 0° iii) R_1X, THF, 20°

a) R = C_2H_5, R_1 = n-$C_{12}H_{25}$; b) R = n-$C_{10}H_{21}$, R_1 = C_2H_5; c) R = n-$C_{12}H_{25}$, R_1 = C_2H_5
d) R = n-$C_{12}H_{25}$, R_1 = n-C_6H_{13}; e) R = R_1 = n-$C_{12}H_{25}$

The reaction is carried out by deprotonation of 1 with n-butyllithium at 0°, condensation of the carbanion with carbon disulfide, followed by the addition of the alkyl halide to afford 2 in 50-78% yield. The reaction works well with short, medium or long chain primary alkyl halides and since the length of the N-alkyl group can be also controlled, these factors allow the variation of the solubility of 2 in hydrocarbon solvents. This is an important aspect for the use of these compounds as transition metal extractants.

The enolic structure (2) was assigned on the basis of a signal at δ 13.00-13.05 (enolic OH) in the ^1H NMR (Table 3), which also shows signals at δ 3.86-3.90 (CH_2N) and at δ 3.33-3.36 (CH_2S). In the ^{13}C NMR spectra, the C5-OH signal appears at δ 157.5-157.9 and the C=S at δ 213.2-213.5.[4] The IR spectra show strong absorptions at 1560 cm^{-1} due to the pyrazole ring.[5]

TABLE 1. Physical Data of Pyrazoles 2

Cmpd	Yield (%)	mp.[a] (°C)	Color[b]	IR (KBr,cm^{-1}) OH	Pyr	UV[c] (nm)
2a	66	39-40	Yellow	3300-2650	1560	314, 349
2b	50	28-29	Yellow	3300-2700	1560	310, 349
2c	58	36-37	Yellow	3250-2700	1560	310, 349
2d	72	20-21	Yellow-orange	3250-2700	1565	312, 358
2e	78	46-47	Orange	3300-2650	1565	312, 356

a) Uncorrected. b) Needles. c) Methanol.

TABLE 2. Analytical Data of Pyrazoles 2

Cmpd	MW[a] Found (Calcd)	Elemental Analysis Found (Calcd) C	H	N	S
2a	370.2110 (370.2115)	61.47 (61.58)	9.30 (9.25)	7.48 (7.56)	17.18 (17.30)
2b	342.1801 (342.1802)	59.40 (59.61)	8.71 (8.83)	8.10 (8.18)	18.32 (18.72)
2c	370.2112 (370.2115)	61.52 (61.58)	9.32 (9.25)	7.50 (7.56)	17.23 (17.30)
2d	426.2738 (426.2742)	64.70 (64.74)	9.75 (9.92)	6.48 (6.56)	14.97 (15.03)
2e	510.3663 (510.3681)	68.07 (68.18)	10.75 (10.65)	5.53 (5.84)	12.38 (12.55)

a) High resolution mass spectra.

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EXPERIMENTAL SECTION

All reactions were performed under a nitrogen atmosphere in flame-dried glassware. THF was distilled from sodium benzophenone ketyl. Commercial reagents were purchased from Merck Química Chilena and were used without further purification. Compounds 1 were prepared by known procedures.[6] ^{1}H NMR spectra were recorded at 60 MHz using a Varian 360 A instrument and ^{13}C on a Jeol FX90Q; chemical shifts are reported in δ units relative to internal tetramethylsilane. IR spectra were recorded on a Perkin Elmer 599 spectrophotometer in KBr discs. High resolution mass spectra were obtained on a KRATOS-AEI MS 50 instrument.

Alkyl 1-Alkyl-3-methyl-2-pyrazoline-5-one-4-dithiocarboxylates. General Procedure.- n-Butyllithium (1.45 M in hexane, 4 mmol) was added dropwise to a solution of 1-alkyl-3-methyl-2-pyrazoline-5-one (1) (4 mmol) in 10 ml THF at 0°. The mixture was stirred 1.5 hr, followed by the addition of a solution of carbon disulfide (4 mmol) in 10 ml THF. After 15 min at 0° and 1 hr at 20°, the alkyl halide (4 mmol)[7] in 10 ml THF was added and the reaction mixture was stirred overnight. Dilution with 20 ml hexane was followed by hydrolysis with a saturated aqueous solution of potassium chloride. The organic layer was dried over anhydrous sodium sulfate and after removal of solvents in vacuo, the products 2 were isolated as yellow to orange solids and recrystallized from ethanol-water (90%) as shown in Tables 1 and 2.

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TABLE 3. Selected NMR Data of Pyrazoles 2

Cmpd	^{1}H NMR ($CDCl_3$, δ)	^{13}C NMR ($CDCl_3$, δ)
2a	2.53 (s, 3H, C3-CH_3); 3.33 (t,2H, J = 7.2Hz, CH_2S); 3.90 (q, 2H, J = 7.2Hz, CH_2N) 13.05 (s, 1H, OH)	33.8 (CH_2S); 41.3 (CH_2N); 157.5 (C5-OH); 213.5 (C = S)
2b	2.53 (s, 3H, C3-CH_3); 3.33 (q, 2H, J = 7.1Hz, CH_2S); 3.87 (t, 2H, J = 7.1Hz, CH_2N); 13.00 (s, 1H, OH)	33.9 (CH_2S); 46.4 (CH_2N); 157.8 (C5-OH); 213.5 (C = S)
2c	2.53 (s, 3H, C3-CH_3); 3.33 (q, 2H, J = 7.1Hz, CH_2S); 3.87 (t, 2H, J = 7.1Hz, CH_2N); 13.00 (s, 1H, OH)	33.9 (CH_2S); 46.4 (CH_2N); 157.9 (C5-OH); 213.2 (C = S)
2d	2.55 (s, 3H, C3-CH_3); 3.36 (t, 2H, J = 7.0Hz, CH_2S); 3.90 (t, 2H, J = 7.0Hz, CH_2N); 13.03 (s, 1H, OH)	33.8 (CH_2S); 46.3 (CH_2N); 157.8 (C5-OH); 213.2 (C = S)
2e	2.54 (s, 3H, C3-CH_3); 3.34 (t, 2H, J = 7.2Hz, CH_2S); 3.90 (t, 2H, J = 7.2Hz, CH_2N); 13.03 (s, 1H, OH).	33.8 (CH_2S); 46.4 (CH_2N); 157.8 (C5-OH); 213.4 (C = S)

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7. Although the yields reported were for alkyl bromides, the reaction works well with alkyl chlorides. Alkyl iodides give the best yields.

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A SIMPLE ROUTE TO SOME SPIROIMIDAZOLONES

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Although the synthesis of imidazoles is relatively well-known reaction,[1] the yields are low. One such approach for the preparation of spiroimidazoles (4) involves reactions of aminocarboxamides (3) with ethyl orthoformate at reflux for several days;[2] often the non-cyclic intermediate (5) was obtained in the mixture together with the desired spiroimidazolone. In this context, we have developed a simple method for synthesis of spiroimidazolones using gaseous formaldehyde in the cyclization. Under these conditions and working at room temperature, the reaction time was shortened. Treatment of the aminocarboxamides (3)[3,4] (from the aminonitriles 2)[5] with a high concentration of formaldehyde made extraction of the product unnecessary since the products (4) precipitated as solids by addition of water and basification with ammonium hydroxide. Recrystallization provided pure products as white or yellow needles. A maximun yield (by IR) was obtained after 20-30 min. in all reactions, irrespective of the aminocarboxamide employed. Unfortunately, preliminary experiments indicated that non-cyclic aminocarboxamides derived from diisopropyl ketone 3g (R = R_1 = $CHMe_2$), benzophenone 3h (R = R_1 = Ph) and acetophenone 3i (R = Me, R_1 = Ph) did not undergo the desired reaction, with gaseous