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3-Hydroxy-1-phenyl-2-pyrazolin-5-one **1** reacts with primary, secondary and allylic alcohols under catalytic acidic conditions and in the presence of 3 Å molecular sieves, to afford 3-alkoxy-1-phenyl-2–pyrazolin-5-ones **3**.

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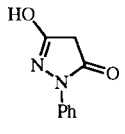
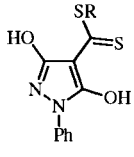
A few years ago, we initiated a program on the synthesis of 4–alkyldithiocarboxylate derivatives of 5–pyrazolones with chelating and extractive properties of metal ions, especially copper [1-4]. As a part of this program, recently we have synthesized alkyl 3,5-dihydroxy-1-phenylpyrazole-4-dithiocarboxylates **2** by the reaction of 3-hydroxy-1-phenyl-2-pyrazolin-5-one **1** with carbon disulfide and alkyl bromides in the presence of sodium acetate.



1

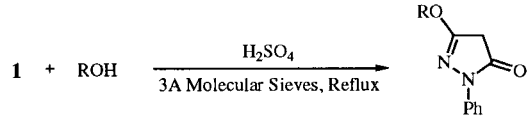


2

Compounds **2** in chloroform are very good extractants of copper(II) under strong acidic conditions (*p*H 0-3) and they are capable of the separation of the copper(II) cation from iron(III) when both are present in acid lixiviation solution of copper sulfide minerals.

Continuing these studies, we were interested in the replacement of the 3-hydroxy group of **1** with an alkoxyl in order to improve the solubility of the corresponding 4-alkyl dithiocarboxylates in cheap industrial solvents. The information about the synthesis of 3-alkoxy-5-pyrazolones is very limited in the literature and some of the information are in patents. The reported methods involve the condensation of hydrazines with ethyl β,β-dialkoxyacrylate [5], ethyl β-alkoxy-β-iminopropionate [6,7] or β-alkoxy-β-chloroacryloyl chloride [8]. Another approach is the direct alkylation of 4-substituted-1-phenyl-3,5-dioxopyrazolidines and related compounds by nucleophilic substitution with diazomethane, methyl iodide or diethyl sulphate, but under these conditions a mixture of *N*, *O* and *C*-alkylation is observed [9,10].

To our knowledge, the preparation of 3-alkoxy-5-pyrazolones **3** by the direct reaction of **1** with alcohols have not been previously reported. Usually the dehydration of alcohols to afford ethers can be achieved with concentrated sulfuric or phosphoric acids at 100-200° and it works well with primary alcohols. Taking in account this information together with the fact that 3 Å molecular sieves have been succesfully used to trap water and improve the yield in the esterification of ferulic acid [11], we wish to propose a new method to synthesize 3-alkoxy-5-pyrazolones **3** by direct reaction of **1** with alcohols. The synthesis is achieved by refluxing **1** with the alcohol and few drops of sulfuric acid in a Soxhlet extractor charged with activated 3 Å molecular sieves, and after aqueous work-up the 3-alkoxy-1-phenyl-2-pyrazolin-5-one **3** is isolated in variable yields.



3a, R = Me
3b, R = Et
3c, R = *n*-Pr
3d, R = *i*-Pr
3e, R = *n*-Bu
3f, R = *sec*-Bu
3g, R = Allyl

3a-g

The reported yield in the synthesis of **3a** and **3b** by other methods [5-8] is similar to that observed in our reaction, but this new approach presents some advantages over previous methods. First, the reaction is straightforward with primary, secondary and allylic alcohols and this allows the introduction of secondary and allylic groups as substituents. Secondly, the only isolated product is the 3–alkoxy derivative **3** and there is no evidence of the *N* or *C*-alkylation observed when **1** is reacted with diazomethane or methyl iodide [9].

The product of the reaction can exist in three tautomeric forms and the keto form proposed is supported on the basis of the ir and nmr spectroscopic data. In the ir the stretching carbonyl vibration is observed at 1703-1714 cm^{-1} and in the ^1H nmr spectra (deuteriochloroform) the methylene group of the ring displays a singlet at 3.47-3.52 ppm.

In conclusion, we have developed a simple alternative method to synthesize 3-alkoxy-1-phenyl-2-pyrazolin-5-ones **3** from readily available 3-hydroxy-1-phenyl-2-pyrazolin-5-one **1** and alcohols.

EXPERIMENTAL

Melting points are uncorrected. The ^1H nmr (200 MHz) and ^{13}C nmr (50 MHz) were recorded on a Bruker AC-200 spectrometer in deuteriochloroform solutions with internal TMS and the chemical shifts are quoted in ppm. The ir spectra were recorded on a Perkin Elmer FT IR 1600 spectrophotometer in sodium chloride discs, and the absorption frequencies are quoted in reciprocal centimeters. Compound **1** was synthesized by a previously reported procedure [12].

General Procedure for the Sythesis of 3-Alkoxy-1-phenyl-2-pyrazolin-5-ones, **3a-g**.

A mixture of 1.0 g (5.7 mmoles) of **1**, 50 ml of the anhydrous alcohol and five drops of concentrated sulfuric acid is refluxed overnight in a Soxhlet extractor charged with 5.0 g of 3 Å molecular sieves. The resulting solution is poured over ice-water to precipitate **3a-g** which are purified by silica gel column chromatography with hexane-ethyl acetate (4:1) or by recrystallization from ethyl alcohol.

3-Methoxy-1-phenyl-2-pyrazolin-5-one (**3a**).

This compound was obtained in 46% yield as a yellow granular solid (ethyl alcohol), mp 92-93°; ir: ν C=O 1703; ^1H nmr (deuteriochloroform): δ 3.50 (s, 2H, C-4), 3.97 (s, 3H, CH_3O), 7.11-7.90 (m, 5H, Ph); ^{13}C nmr (dueteriochloroform): δ 37.6 (C-4), 55.6 (CH_3O), 118.7, 124.6, 128.8, 138.4 (Ph), 162.3 (C=N), 167.1 (C=O).

3-Ethoxy-1-phenyl-2-pyrazolin-5-one (**3b**).

This compound was obtained in 90% yield as a pale yellow granular solid (ethyl alcohol), mp 115-116°C; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 1.41 (t, 3H, CH_3), 3.47 (s, 2H, C-4), 4.34 (q, 2H, CH_2O), 7.04-7.84 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 14.2 (CH_3), 37.8 (C-4), 64.6 (CH_2O), 118.7, 124.5, 128.8, 138.5 (Ph), 161.8 (C=N), 167.1 (C=O).

3-Propoxy-1-phenyl-2-pyrazolin-5-one (**3c**).

This compound was obtained in 50% yield as orange plates (ethyl alcohol), mp 68-69°; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 1.02 (t, 3H, CH_3), 1.75-1.89 (m, 2H, CH_2-CH_3), 3.49 (s, 2H, C-4), 4.25 (t, 2H, CH_2O), 7.10-7.98 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 10.4 (CH_3), 21.9 (CH_2-CH_3), 37.7 (C-4), 70.2 (CH_2O), 118.7, 124.5, 128.7, 138.4 (Ph), 161.8 (C=N), 167.1 (C=O).

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.08; H, 6.46; N, 12.82. Found: C, 65.96; H, 6.62; N, 12.73.

3-Isopropoxy-1-phenyl-2-pyrazolin-5-one (**3d**).

This compound was obtained in 51% yield as a yellow granular solid (ethyl alcohol), mp 64-65°; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 1.40 (d, 6H, CH_3), 3.46 (s, 2H, C-4), 5.06-5.18 (m, 1H, OCH), 7.00-7.89 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 21.7 (CH_3), 38.2 (C-4), 72.3 (CH), 118.7, 124.5, 128.8, 138.5 (Ph), 161.1 (C=N), 167.1 (C=O).

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.08; H, 6.46; N, 12.82. Found: C, 66.36; H, 6.51; N, 12.60.

3-Butoxy-1-phenyl-2-pyrazolin-5-one (**3e**).

This compound was obtained in 41% yield as a pale brown granular solid (ethyl alcohol), mp 54-55°; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 0.98 (t, 3H, CH_3), 1.41-1.52 (m, 2H, CH_2-CH_3), 1.73-1.79 (m, 2H, CH_2-CH_2O), 3.48 (s, 2H, C-4), 4.29 (t, 2H, CH_2O), 7.10-7.88 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 13.7 (CH_3), 19.1 (CH_2-CH_3), 30.6 (CH_2-CH_2O), 37.4 (C-4), 68.4 (CH_2O), 118.7, 124.5, 128.7, 138.4 (Ph), 161.8 (C=N), 167.0 (C=O).

Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.01; H, 6.90; N, 11.80.

3-(sec-Butoxy)-1-phenyl-2-pyrazolin-5-one (**3f**).

This compound was obtained in 38% yield as a pale orange granular solid (ethyl alcohol), mp 52-53°; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 0.98 (t, 3H, CH_3-CH_2), 1.38 (d, 3H, CH_3-CH), 1.56-1.85 (m, 2H, CH_2), 3.46 (s, 2H, C-4), 4.87-5.03 (m, 1H, OCH), 7.05-7.88 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 9.7 (CH_3-CH_2), 19.0 (CH_3-CH), 28.8 (CH_2), 38.1 (C-4), 77.0 (OCH), 118.8, 124.6, 128.8, 138.6 (Ph), 161.1 (C=N), 167.1 (C=O).

Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.56; H, 6.80; N, 12.20.

3-Allyloxy-1-phenyl-2-pyrazolin-5-one (**3g**).

This compound was obtained in 24% yield as a yellow granular solid (ethyl alcohol), mp 69-70°; ir: ν C=O 1714; ^1H nmr (deuteriochloroform): δ 3.52 (s, 2H, C-4), 4.80 (d, 2H, CH_2O), 5.32-5.49 (m, 2H, CH=CH_2), 5.94-6.16 (m, 1H, CH=CH_2), 7.11-7.88 (m, 5H, Ph); ^{13}C nmr (deuteriochloroform): δ 37.7 (C-4), 69.1 (CH_2O), 119.6 (CH=CH_2), 131.4 (CH=CH_2), 118.6, 124.6. 128.8, 138.4 (Ph), 161.4 (C=N), 167.0 (C=O).

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.68; H, 5.59; N, 12.94. Found: C, 66.23; H, 5.41; N, 13.04.

Acknowledgements.

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