Synthesis and Prototropic Tautomerism of 1-*n*-Alkyl-3-methyl-4-Nitroso-5-pyrazolones

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Nitrosation at C-4 of 1-*n*-alkyl-3-methyl-5-pyrazolones is achieved in about 50% yield with sodium nitrite in hydrochloric acid medium. A tautomeric equilibrium in solution with a proton moving from the OH at C-5 to N-2 in the nitrosated pyrazolones is proposed.

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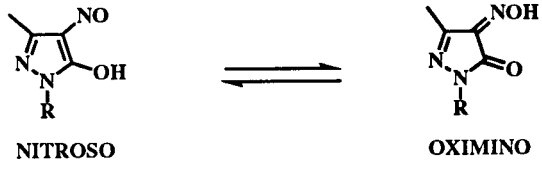
Prototropic tautomerism in 5-pyrazolones has been widely studied [1,5]. Most of the works deal with 1-phenylpyrazolones while 1-*n*-alkyl-derivatives are almost unknown. 4-Nitrosopyrazolones [6] are supposed to exist as oximino tautomers (Figure 1). Pyrazolones can be nitrosated with sodium nitrite in hydrochloric acid medium. This method remains unchanged since the early synthesis of 1-phenyl-3-methyl-4-nitroso-5-pyrazolone was achieved [7]. In a previous paper [8] the synthesis of 1-*n*-alkyl-3-methyl-5-pyrazolones was reported, now the 4-nitroso derivatives and the prototropic tautomerism involved are reported. The nitrosation of 1-*n*-alkyl-3-methyl-5-pyrazolones was achieved in about 50% yield and takes place at C-4 (Figure 2). The pmr spectrum of **2b** shows a singlet at 8.96 ppm (1H) corresponding to the OH that forms a bridging hydrogen bond with the nitroso group. The methylene α to N-1 can be seen as a triplet at 3.78 ppm, the other four methylenes exhibit a multiplet at 1.50 ppm. There also are signals at 0.89 ppm corresponding to the methyl of the alkyl chain and two singlets having time depending intensities that after a period of several hours remain constant. From this fact an equilibrium between two tautomers can be followed. Several spectra of **2b** were recorded at different times and using three different solvents (Table 1).



NITROSO OXIMINO

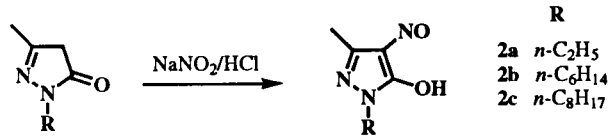
Figure 1. Nitroso and Oximino tautomers of 4-nitrosopyrazolones.

The ^{15}N spectrum of **2c** in deuteriochloroform shows six signals that can be assigned as follows [9-10]: 428.3 and 423.5 ppm to N=O, 322.6 and 311.5 ppm to N-2, the signals at 185.6 and 185.0 ppm to N-1. These results can not be explained with the above mentioned nitroso-oximinio equilibrium (Figure 1). An equilibrium between NH and OH tautomers (Figure 3) is in better agreement with the information obtained.

Table 1

Time and Solvent Dependence of Tautomer Absorbance in Solution of 1-*n*-Hexyl-3-methyl-4-nitroso-5-pyrazolone (**2b**)

Time [h]	δ (ppm)	Tautomer abundance [%] $CDCl_3$	Pyridine-d_6	CD_3CO_2D
0	2.41	61	92	74
	2.21	39	8	26
6	2.41	36	71	62
	2.21	64	29	38
24	2.41	33	66	60
	2.21	67	34	40



1 **2**

R	
2a	*n*-C_2H_5
2b	*n*-C_6H_{14}
2c	*n*-C_8H_{17}

Figure 2. Preparation of 1-*n*-alkyl-3-methyl-4-nitroso-5-pyrazolones.

NH OH

Figure 3. NH ⇌ tautomeric equilibrium in 1-*n*-alkyl-3-methyl-4-nitroso-5-pyrazolones.

The ir spectra of the nitroso compounds in the solid phase show a band corresponding to the carbonyl stretching about 1679 cm^{-1}. This fact supports the existence of the NH tautomer in the solid state although the presence in low concentrations of the other one (OH) can not be excluded. The dissolution of the compounds shifts the equilibrium towards the formation of the OH tautomer to an extent that depends on the polarity of the solvent. The more polar the solvent, the higher the concentration of the NH form. Now it can be stated that in the pmr spectrum, the methyl group at C-3 will be shifted downfield in the NH form with respect to that of the OH tautomer.

The cmr spectra of these compounds show six downfield signals. Again the number of signals at agrees with an equilibrium between the two tautomers. The cmr spectra exhibit also two signals at about 40 ppm corresponding to the methylene α to N-1. The lowfield signal was assigned to the OH tautomer. To assign the cmr signals sequence in each tautomer, the multiplicity, the approximate coupling constant obtained from the off-resonance spectra, the chemical shifts and electronic distribution were considered. At low fields the approximate ^2J, ^3J and ^4J between the methyl carbon at C-3 with each carbon of the ring are 8.0, 2.5 and 1.44 Hz, though approximate these constant must diminish with the distance. This information is summarized in Table 2.

Table 2

^{13}C Chemical Shifts for Carbon in the Rings of Tautomers NH and OH ($CDCl_3$)

	NH tautomer		OH tautomer	
Carbon	Compound **2a**	Compound **2c**	Compound **2a**	Compound **2c**
C-3	139.3	140.9	145.6	147.8
C-4	143.6	144.6	143.2	144.0
C-5	160.1	161.8	152.1	154.2
N-CH_2	37.7	44.0	37.9	44.3

EXPERIMENTAL

Elemental analyses were performed at Laboratorio de Microanálisis, Department of Organic Chemistry, Universidad de Concepción. Melting points were determined on a Kofler microscope and are uncorrected. The nmr spectra were recorded with Varian T60-A (^1H) and CFT-20 (^{13}C) and Jeol FX 100 (^1H, ^{13}C and ^{15}N) spectrometers using tetramethylsilane as the reference for proton and carbon spectra, nitromethane was used for nitrogen. Chemical shifts are quoted in parts per million (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). The signals corresponding, to the OH tautomers are designated with ' when it is possible to establish the difference. The ir spectra were measured with a Perkin-Elmer 577 spectrophotometer. Absorption frequencies are quoted in reciprocal centimeters.

Synthesis of 1-*n*-Alkyl-3-methyl-4-nitroso-5-pyrazolones **2**.

To a magnetically stirred ethanolic solution of **1** (0.5 mole) and concentrated hydrochloric acid (0.55 mole, 46 ml) a solution containing 37.95 g (0.55 mole) in water is added dropwise. The container is surrounded with an ice-salt bath to keep the reaction temperature at 0°. After the addition, stirring is continued an hour. Then the solvent is removed in a rotary evaporator and the crude crystallized, yield 50-55%.

Synthesis of 1-Ethyl-3-methyl-4-nitroso-5-pyrazolone (**2a**).

Dark orange crystals are obtained from *n*-hexane, mp 112-113; ir (potassium bromide): ν N-H 3300-3100, ν C-H 2990, ν C=O 1670, ν C=C 1605; pmr (deuteriochloroform): 12.07 (s, 1H, N-H), 3.79 (q, CH_2 α to N-1), 2.40, 2.25 (s, s, 3H, Me at C-3 and C'-3 respectively), 1.28 (t, 3H, Me, alkyl chain); cmr (deuteriochloroform): 160.1 (C-5, C=O), 152.0 (C'-5, C-OH), 145.6 (C'-3), 1436 (C-4), 143.2 (C'-4), 139.3 (C-3), 37.9 (CH_2 α to N'-l), 37.7 (CH α to N-l), 16.1 (Me at C-3), 12.4 (Me at C'-3), 11.23 (Me, alkyl chain;, ^{15}N nmr (deuteriochloroform): 422.4, 422.2 (N=O), 322.8, 322.3 (N-2), 185.9, 185.4 (N-l).

Anal. Calcd. for $C_6H_9N_3O_2$: C, 46.44; H, 5.84. Found: C, 46.14; H, 5.89.

Synthesis of 1-*n*-Hexyl-3-methyl-4-nitroso-5-pyrazolone (**2b**).

Dark orange crystals are obtained from *n*-hexane, mp 89-90; ir (potassium bromide): ν N-H 3350-3100, ν C-H 2960, ν C=O 1675, ν C=C 1620; pmr (deuteriochloroform): 8.96 (s, 1H, OH), 3.78 (t, 2H, CH_2 α to N-1), 2.45, 2.26 (s, s, 3H, Me at C-3 and C'-3 respectively), 1.50 (m, 8H, $4CH_2$, alkyl chain), 0.89 (t, 3H, Me, alkyl chain); cmr (perdeuteriobenzene): 162.4 (C-5, C=O), 154.8 (C'-5, C-OH), 145.0 (C-4), 147.9 (C'-3), 144.5 (C-4), 141.0 (C-3), 44.6 (CH_2 α to N'-1), 44.2 (CH_2 α to N-1), 31.5, 28.1, 26.4, 22.7 (4 CH_2, alkyl chain), 17.6 (Me at C-3), 14.1 (Me at C'-3), 12.1 (Me, alkyl chain).

Anal. Calcd. for $C_{10}H_{17}N_3O_2$: C, 56.85; H, 8.11. Found: C, 56.68; H, 8.19

Synthesis of 1-*n*-Octyl-4-nitroso-5-pyrazolone (**2c**).

Dark orange crystals are obtained from *n*-hexane, mp 83-84°; ir (potassium bromide): ν N-H 3315-3080, ν C-H 2890, ν C=O 1680, ν C=C 1620; pmr (deuteriochloroform): 8.16 (s, 1H, OH), 3.55 (t, 2H, CH_2 α to N-l), 2.33, 2.19 (s, s, 3H, Me at C-3 and C'-3 respectively); 1.50 (m, 12H, 6 CH_2, alkyl chain), 0.83 (t, 3H, Me, alkyl chain); cmr (deuteriochloroform): 161.8 (C-5, C=O), 154.2 (C'-5, C-OH), 144.6 (C-4), 144.0 (C'-4), 140.9 (C-3), 44.3 (CH_2 α to N'-l), 44.0 (CH_2 α to N-l), 31.5, 30.9, 28.9, 27.7, 26.3, 22.3 (6 CH_2, alkyl chain); ^{15}N nmr (deuteriochloroform): 428.3, 423.5 (N=O), 322.3, 312.5 (N-2), 185.6, 185.0 (N-l).

Anal. Calcd. for $C_{12}H_{21}N_3O_2$: C, 60.22; H, 8.84. Found C, 60.42; H, 8.56.

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