SYNTHESIS OF PYRAZOLO[4,3-d]OXAZOLES FROM 1-(2,4-DINITROPHENYL)-3-METHYL-5-PYRAZOLON-4-OXIME

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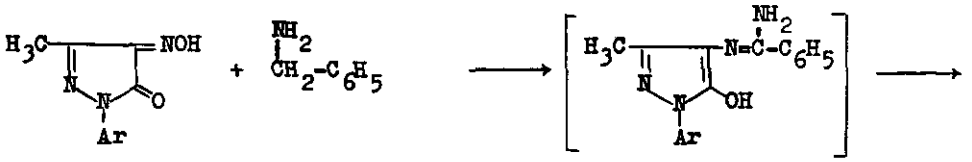
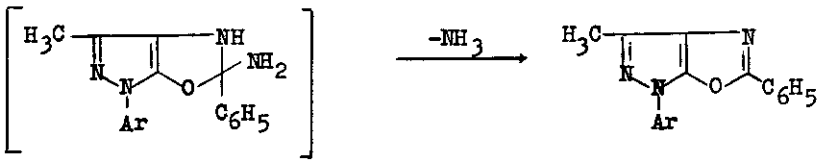
Abstract — 1-(2,4-Dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime (I) reacts with benzylamine to give 1-(2,4-dinitrophenyl)-3-methyl-5-phenyl-1H-pyrazolo[4,3-d]oxazole (II). Its structure has been established by another route involving reaction of I with benzyl cyanide in the presence of sodium ethoxide. 1-(2,4-Dinitrophenyl)-3-methyl-1H-pyrazolo[4,3-d]oxazole (III) has been prepared by the interaction of I with methyl iodide in the presence of K_2CO_3. Its structure has been elucidated by an unambiguous synthesis involving reaction of diazomethane with I.

Literature shows that no work on the synthesis of pyrazolooxazoles has been done, but isoxazolopyrazole and oxazolinopyrazole were prepared previously[1,2]. In continuation of our work on condensed oxazoles[3,4], we now report the synthesis of pyrazolooxazoles from 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime (I). The action of benzylamine and benzyl cyanide on nitroso compounds has been studied before[5,6], and hence we were interested to test such reactions with I which is tautomeric with 5-hydroxy-4-nitrosopyrazole. It was found that benzylamine reacted readily with I in absolute ethanol to give yellow compound which was identified as 1-(2,4-dinitrophenyl)-3-methyl-5-phenyl-1H-pyrazolo[4,3-d]oxazole (II). The mechanism[5] of formation of II can be explained as follows (Scheme 1).

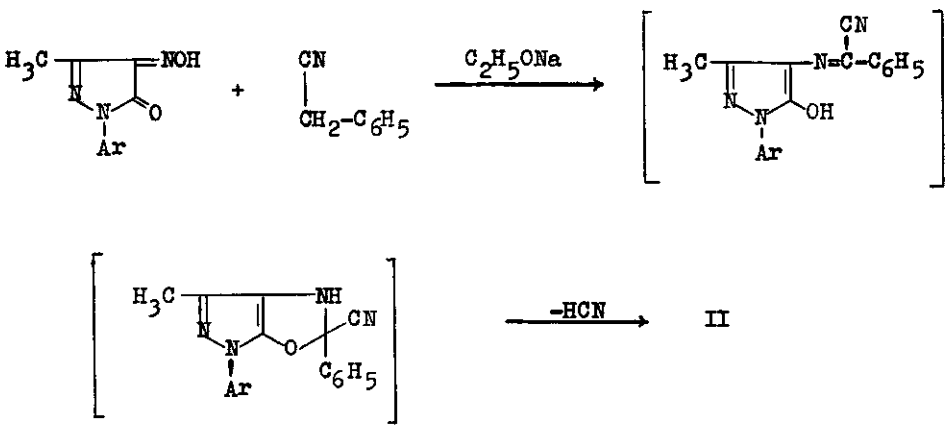


I, Ar = $2,4(NO_2)_2C_6H_3$-



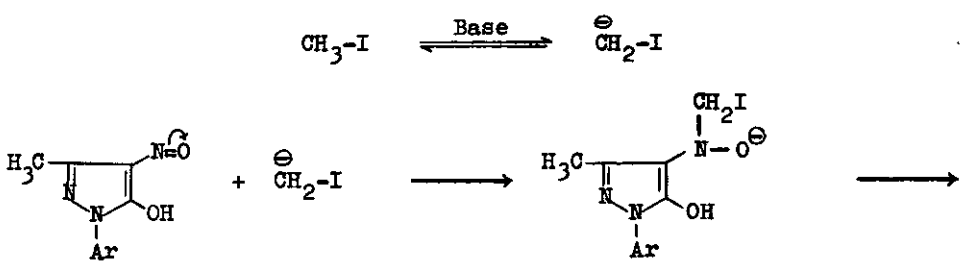
Scheme 1

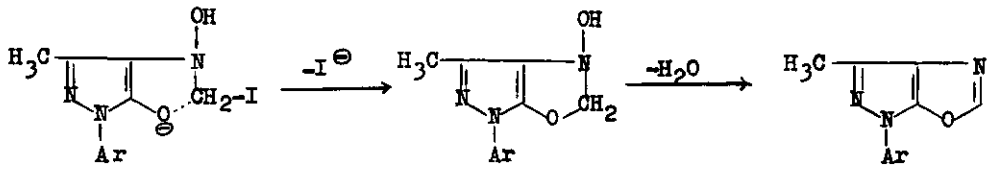
The structural assignment of II was based on elemental analysis and ir spectrum. The pyrazolooxazole II was also prepared by refluxing 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime with benzyl cyanide in the presence of sodium ethoxide as basic catalyst. It was identical (elemental analysis, mp, mmp, ir) with an authentic sample prepared by the above method. The reaction[6] is believed to proceed as in Scheme 2.



Scheme 2

Interaction of methyl iodide with 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime in dry acetone in the presence of anhydrous K_2CO_3 as basic catalyst led to the formation of 1-(2,4-dinitrophenyl)-3-methyl-1H-pyrazolo[4,3-d]oxazole(III). The sequence[7,8] of reaction is shown in Scheme 3.

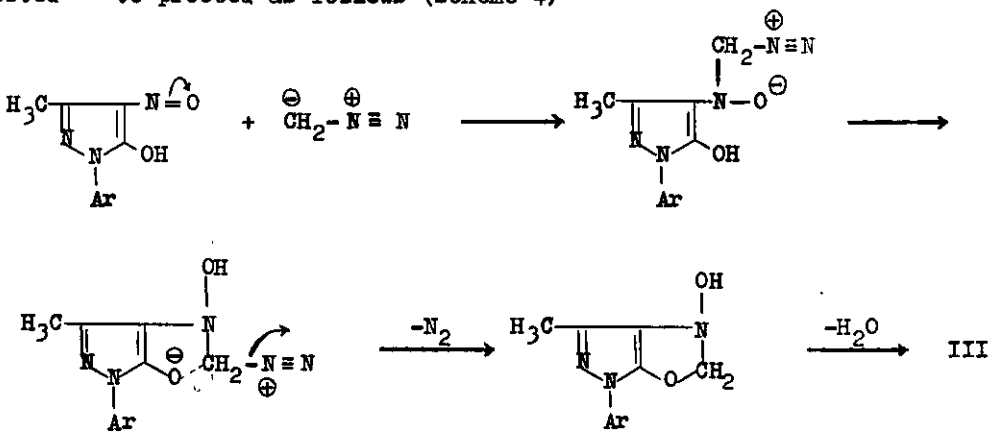




III

Scheme 3

The pyrazolooxazole III was also prepared by another route involving the reaction of I with diazomethane. It was identical (elemental analysis, mp, mmp and ir) with an authentic sample obtained by the above method. The reaction can be suggested[7,8] to proceed as follows (Scheme 4)



Scheme 4

EXPERIMENTAL PROCEDURE

All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 599 B spectrophotometer using KBr wafer technique (ν_{max} in cm^{-1}).

1-(2,4-Dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime (I). 1-(2,4-Dinitrophenyl)-3-methyl-5-pyrazolone[9] (2.64 g; 0.01 mol) was dissolved in a mixture of HCl (3 ml) and ethanol (1 ml), a solution of which was then kept in an ice bath at zero degree. A cold solution of sodium nitrite (8.28 g; 0.12 mol) was added dropwise. The precipitate was formed immediately but the reaction mixture was kept in ice bath with stirring for 1 h and then allowed to stand in refrigerator overnight. This was then filtered and washed with water. The product was recrystallized from ether-pet. ether (bp 60-80°C) as greenish yellow crystals, mp 160-161°C, in 70 % yield, ir: 3500 (OH), 1720 (C=O), 1590 (cyclic C=N) and 1520(NO_2)

(Found: C, 41.25; H, 2.50; N, 24.01. $C_{10}H_7N_5O_6$ requires C, 40.96; H, 2.41; N, 23.89).

Reaction of 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime(I) with benzylamine. Formation of 1-(2,4-dinitrophenyl-3-methyl-5-phenyl-1H-pyrazolo[4,3-d]-oxazole (II). A solution of I (0.001 mol) in 30 ml of abs. ethanol was refluxed with benzylamine (0.001 mol) on a water bath for 5 h. The reaction mixture was concentrated, cooled and the precipitated brownish yellow product was collected and washed with few drops of ethanol. It was crystallized from ethanol to give yellow crystals, mp 210-211°C, in 54 % yield, ir: 1600 (cyclic C=N of pyrazole ring), 1640, 1130, 1090 (heterocyclic oxazole system[10]) and 1500 (NO_2) (Found: C, 56.0; H, 3.13; N, 19.21. $C_{17}H_{11}N_5O_5$ requires C, 55.89; H, 3.04; N, 19.17).

Reaction of 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime(I) with benzyl cyanide. Formation of II. A mixture of purified I (0.001 mol) and benzyl cyanide (0.001 mol) was refluxed on a water bath in abs. ethanol in the presence of few drops of sodium ethoxide for 6 h. The reaction mixture was concentrated and cooled. The brownish yellow product precipitated was collected, dried and recrystallized from ethanol as yellow crystals, mp 209-210°C in 50 % yield. It was found to be identical in all aspects with the product obtained by the reaction of I with benzylamine.

Reaction of 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime (I) with methyl iodide. Formation of 1-(2,4-dinitrophenyl)-3-methyl-1H-pyrazolo[4,3-d]oxazole (III). A mixture of I, anhydrous potassium carbonate and methyl iodide in a molar ratio of 1:1.5:1.5 was refluxed in dry acetone on a water bath for 5 h. The reaction mixture was filtered and acetone removed. The remaining residue was extracted several times with toluene and the extract was concentrated and cooled. Pet. ether (bp 60-80°C) was added to the extract whereby a yellow product precipitated out. It was collected and recrystallized from toluene-pet. ether (bp 60-80°C) as yellow compound, mp 94-96°C,in 20 % yield, ir: 1600 (cyclic C=N of pyrazole ring), 1630, 1130, 1090 (heterocyclic oxazole system) and 1520 (NO_2) (Found: C, 45.88; H, 2.61; N, 24.33. $C_{11}H_7N_5O_5$ requires C, 45.68; H, 2.44; N, 24.22).

Reaction of 1-(2,4-dinitrophenyl)-3-methyl-5-pyrazolon-4-oxime (I) with diazomethane. Formation of III. Excess ethereal solution of diazomethane (30 ml) (obtained from 3 g of nitrosomethylurea) was added to a cold ethereal solution of

I (0.001 mol) and the reaction mixture was left in a refrigerator for 7 days. The solid was collected by filtration and a further crop of the product was obtained by removing the solvent. The solid was extracted several times with toluene, and pet. ether (bp 60-80°C) was added to the extract whereby III precipitated out. It was collected and recrystallized from toluene-pet. ether (bp 60-80°C) as yellow product, mp 94-96°C, in 24% yield, identical in all aspects with the compound obtained by the above method.

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