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VICARIOUS C-AMINATION OF 1-METHYL-4-NITROPYRAZOLE

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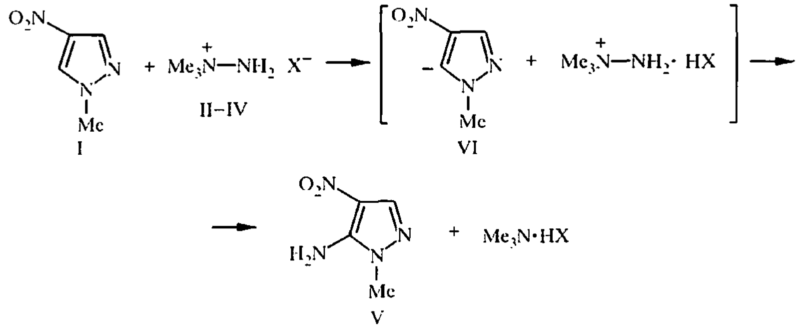
Aminonitropyrazoles are widely used in organic chemistry because of their high reactivity. Several methods are known for preparation of these compounds. 3-Amino-4-nitropyrazole was obtained in 87% yield by the Hofmann rearrangement of 4-nitropyrazole-3-carboxamide at 50-55°C [1] or by treatment of 3(5)-acetamino-4-nitropyrazole with 20% HCl [2]. 5-Amino-3-nitropyrazole is formed on reduction of 3,5-dinitropyrazole with hydrazine in the presence of $FeCl_3$ [3]. 5-Amino-1-methyl-4-nitropyrazole was obtained by heating of 5-bromo-1-methyl-4-nitropyrazole with aqueous ammonia in an autoclave at 190°C [4] or by nitration of 5-amino-1-methylpyrazole with a mixture of sulfuric and nitric acids [5]. N-Amination of substituted 3-, 4-, and 5-nitropyrazoles with hydroxylamino-O-sulfonic acid in aqueous alkaline solution is also known [6].

There is no information of the vicarious nucleophilic substitution of hydrogen atoms attached to carbon atoms of the pyrazole ring in the literature.

We have established that treatment of 1-methyl-4-nitropyrazole (I) with 1,1,1-trimethylhydrazinium halides (II-IV) under mild conditions (DMSO, 20°C) in the presence of dry sodium methoxide or potassium *tert*-butoxide gives 5-amino-1-methyl-4-nitropyrazole (V) in 15-20% yield. A similar reaction has been previously used successfully to prepare aminonitrobenzenes [7].



II X = Cl; III X = Br; IV X = I

The reaction of 1-methyl-4-nitropyrazole with 1,1,1-trimethylhydrazinium halides (II-IV) probably includes the intermediate formation of the pyrazolyl anion VI as a result of deprotonation at $C_{(5)}$ of the pyrazole ring. 1-Methyl-3-nitropyrazole does not react with iodide IV under the same conditions and starting 1-methyl-3-nitropyrazole is recovered from the reaction mixture.

The selectivity of the vicarious amination of 1-methyl-4-nitropyrazole I (substitution of the hydrogen atom at position 5 of the pyrazole ring) may be explained by the charge distribution on the carbon atoms of the pyrazole ring. The *ab initio* calculations using the 6-31* G basis set have shown that in 1-methyl-4-nitropyrazole the positive

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charge (+0.159) is the highest at position 5 and considerably smaller (+0.095) at position 3. Calculation has shown that atom $C_{(4)}$ in 1-methyl-3-nitropyrazole has a negative charge (-0.316) while atom $C_{(5)}$ has a positive charge (+0.081), but considerably smaller than at $C_{(5)}$ in 1-methyl-4-nitropyrazole I. This is probably the reason for the inactivity of 1-methyl-3-nitropyrazole in the vicarious amination reaction.

5-Amino-1-methyl-4-nitropyrazole (V). Trimethylhydrazinium iodide IV (8.28 g, 0.041 mol) was added slowly with stirring to solution of 1-methyl-4-nitropyrazole (5 g, 0.039 mol) in absolute DMSO (60 ml). The mixture was stirred at 20°C until solution was complete, and dry sodium methoxide (4.43 g, 0.082 mol) was then added. The solution became intensely red after 5-7 min. It was stirred for 40 h at 20°C, then poured onto ice and acidified to pH 3.0 with 10% HCl solution. The precipitate of pyrazole V was filtered off and the filtrate extracted three times with ethyl acetate. The ethyl acetate solution was treated with ammonium chloride solution and water, and dried over $MgSO_4$. The ethyl acetate was removed in vacuum, the residue combined with the previously obtained pyrazole V and recrystallized from methanol and then from hot water to give V (1.1 g, 20%); mp 264-266°C (lit. mp 265°C [5]).

The yield of V was not changed when potassium *tert*-butoxide was used.

IR spectrum (KBr): 3420 (ν_{NH_2}), 3152 ($\nu_{CH\ ring}$), 1640 (δ_{NH_2}), 1580 ($\nu_{C=N\ ring}$), 1520 (ν_{NO_2}), 1210 ($\delta_{CH\ ring}$). ^1H NMR spectrum (DMSO-d_6): 3.56 (3H, s, Me); 7.38 (2H, s, NH_2); 7.84 ppm (1H, s, $C_{(3)}H$). ^{13}C NMR spectrum (DMSO-d_6): 35.04 (CH_3); 117.84 ($C_{(4)}$); 134.37 ($C_{(3)}$); 146.01 ppm ($C_{(5)}$). Mass spectrum, *m/z*: 142 $[M]^+$. Found, %: C 33.76; H 4.30; N 39.29. Calculated %: C 33.80; H 4.22; N 39.43.

The reactions of pyrazole I with 1,1,1-trimethylhydrazinium chloride (II) and bromide (III) were carried out analogously to give 12 and 13% yields of 5-aminopyrazole, respectively. Strong resinification of the reaction mixture prevented isolation of unreacted 1-methyl-4-nitropyrazole or any other reaction products.

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