

THE REACTION OF 3,5-DIMETHYL-1,4-DINITROPYRAZOLE WITH AMINES.

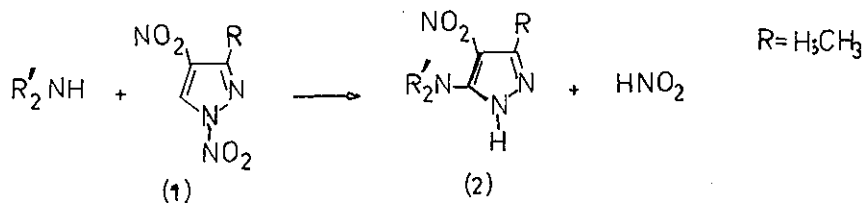
A NOVEL REACTION OF A N-NITROPYRAZOLE.¹

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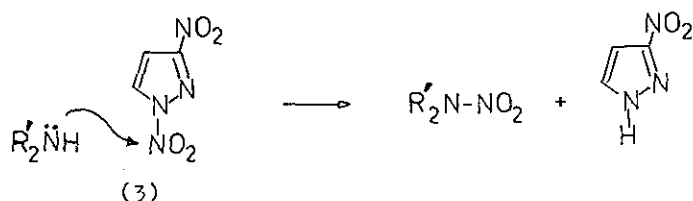
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The reaction in alcohol solution of 3,5-dimethyl-1,4-dinitropyrazole (4) with the secondary amines (5a-b) and with triethylamine (10) afford 3(5)-hydroxymethyl-5(3)-methyl-4-nitropyrazole (7) and the 3(5)-alkoxymethyl-5(3)-methyl-4-nitropyrazoles (8a-c) presumably formed via an elimination-addition mechanism involving a diazafulvene intermediate (9).

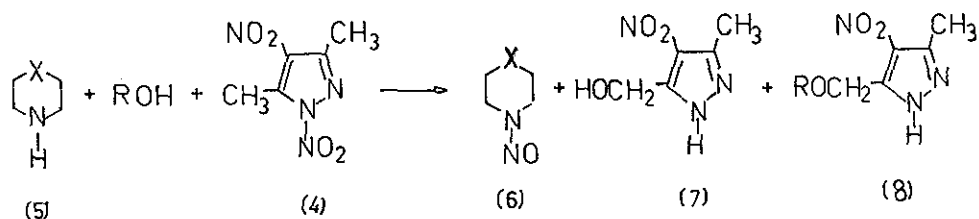
Virtually N-nitroazoles are unique chemical compounds². In a previous paper³ we reported that 3- and 4-substituted N-nitropyrazoles react with secondary amines as nucleophiles in two ways. First, a 'cine' substitution reaction on the 5-position in the ring for the 1,4-dinitropyrazoles (1) with the nucleophile coming in ortho to the leaving group affording 3(5)-N,N-disubstituted amino pyrazoles (2). And secondly, a nucleophilic



substitution on the nitrogen of the N-nitro group of 1,3-dinitropyrazole (3) affording N-nitroamines besides 3(5)-nitropyrazole.



Expecting to divert the nucleophilic attack from the ring to the nitrogen of the N-nitro group in 1,4-dinitropyrazole by blocking the 5-position in the pyrazole ring, we reacted 3,5-dimethyl-1,4-dinitropyrazole (4) (0,01-0,05 mole) with secondary amines (1-2 equivalents) while maintaining the temperature below 30°C. However, the products obtained from the reaction with morpholine (5a) in ethanol solution were N-nitrosomorpholine (6a), 3(5)-hydroxymethyl-5(3)-methyl-4-nitropyrazole (7) and 3(5)-ethoxymethyl-5(3)-methyl-4-nitropyrazole (8a). Similarly, from the reaction



(5a, 6a) X=O

(5b, 6b) X=CH₂

(8a) R=Et

(8b) R=iPr

(8c) R=Me

of (4) with piperidine (5b) in ethanol solution N-nitrosopiperidine (6b), (7) and (8a) were obtained.

The nitrosamines (6a-b) were identified by comparison of their mass and

nmr spectral data with those reported in the literature^{4,5}. The hydroxymethylpyrazole (7), mp 155°C, was independently synthesized by nitration according to the procedure of Morgan and Ackerman⁶ of 3(5)-hydroxymethyl-5(3)-methylpyrazole. The structure assignment of (8a), mp 137°C, was based particularly on its ¹³C-nmr spectrum showing signals for two separate CH₂ carbons and for two separate CH₃ groups in addition to the signals for the aromatic carbon atoms⁷.

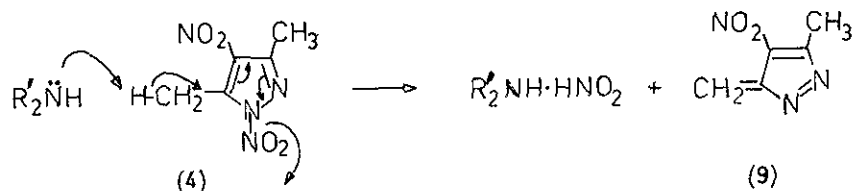
Performing the reaction of (4) with (5a) in isopropanol solution afforded 3(5)-isopropoxymethyl-5(3)-methyl-4-nitropyrazole (8b)⁷, mp 101-102°C, besides (6a) and (7). On the other hand, the reaction of (4) with (5a)

Reaction of (4) with amines in various solvents

amine	solvent	yields in % based on (4)		
(5a)	EtOH	(6a) 74	(7) 81	(8a) 18
(5a)	EtOH	(6b) 50	(7) 75	(8a) 24
(5a)	CH ₃ CN	(6a) 45	(7) 81	-
(5a)	iPrOH [†]	(6a) 80	(7) 71	(8b) 16
(10)	iPrOH	-	(7) 67	(8b) 15
(10)	EtOH [*]	-	(7) 57	(8a) 37
(10)	MeOH [*]	-	(7) 44	(8c) 40

[†] reflux for two hours; ^{*} anhydrous conditions

performed in acetonitrile as solvent only afforded (6a) and (7) (see table). From these results we assumed that we were not dealing with a nucleophilic attack on the nitro group but with an elimination-addition reaction with the diazafulvene (9) as an intermediate. Recently Freeman⁸ and Burgess⁹ et al reported on other diazafulvenes as intermediates in eliminati-



on-addition reactions. To test this assumption we treated (4) with triethylamine (10) in isopropanol solution and we obtained indeed both (7) and (8b) in the same ratio as in the reaction with (5a).

All these reactions were performed in reagent grade solvents under non-anhydrous conditions therefore resulting in the formation of both (7) and (8a-c). Anticipating only formation of (8) by performing the reaction with (10) under anhydrous conditions, (4) was treated accordingly in ethanol and in methanol solution. However, after workup, in both cases (7) was also obtained besides the expected products (8a) and 3(5)-methoxymethyl-5(3)-methyl-4-nitropyrazole (8c), mp $103^\circ C$, albeit in much smaller ratio than in the former reactions (see table). Presumably (7) is also formed from (9) in the workup procedure i.e. the separation of the reaction mixture by column chromatography over silica¹⁰. The fact that the reaction mixtures are bright orange colored solutions whereas both (4) and the reaction products (7) and (8a-c) are colorless or light yellow colored compounds might support the assumption of a diazafulvene as an intermediate.

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