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REACTION OF m-NITROBENZYLIDENEACETYLACETONE WITH PHENYL- AND METHYLHYDRAZINES

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Reaction of m-nitrobenzylideneacetylacetone with phenyl- and methylhydrazine in aqueous acetonitrile, methanol, and glacial acetic acid afforded 4-(α-hydroxy-, methoxy-, and acetoxy-m-nitrobenzyl)-3,5-dimethyl-1-phenylpyrazoles(Va-VIIa) and the corresponding 1-methyl derivatives(Vb-VIIb), presumably *via* the pseudo-bases(III), in excellent yields.

In the course of our studies on the behaviors of hydrazine dihydrochloride toward substituted benzylideneacetylacetones(1, 2), the reaction between m-nitrobenzylideneacetylacetone and phenyl- or methylhydrazines was carried out in three solvent systems.

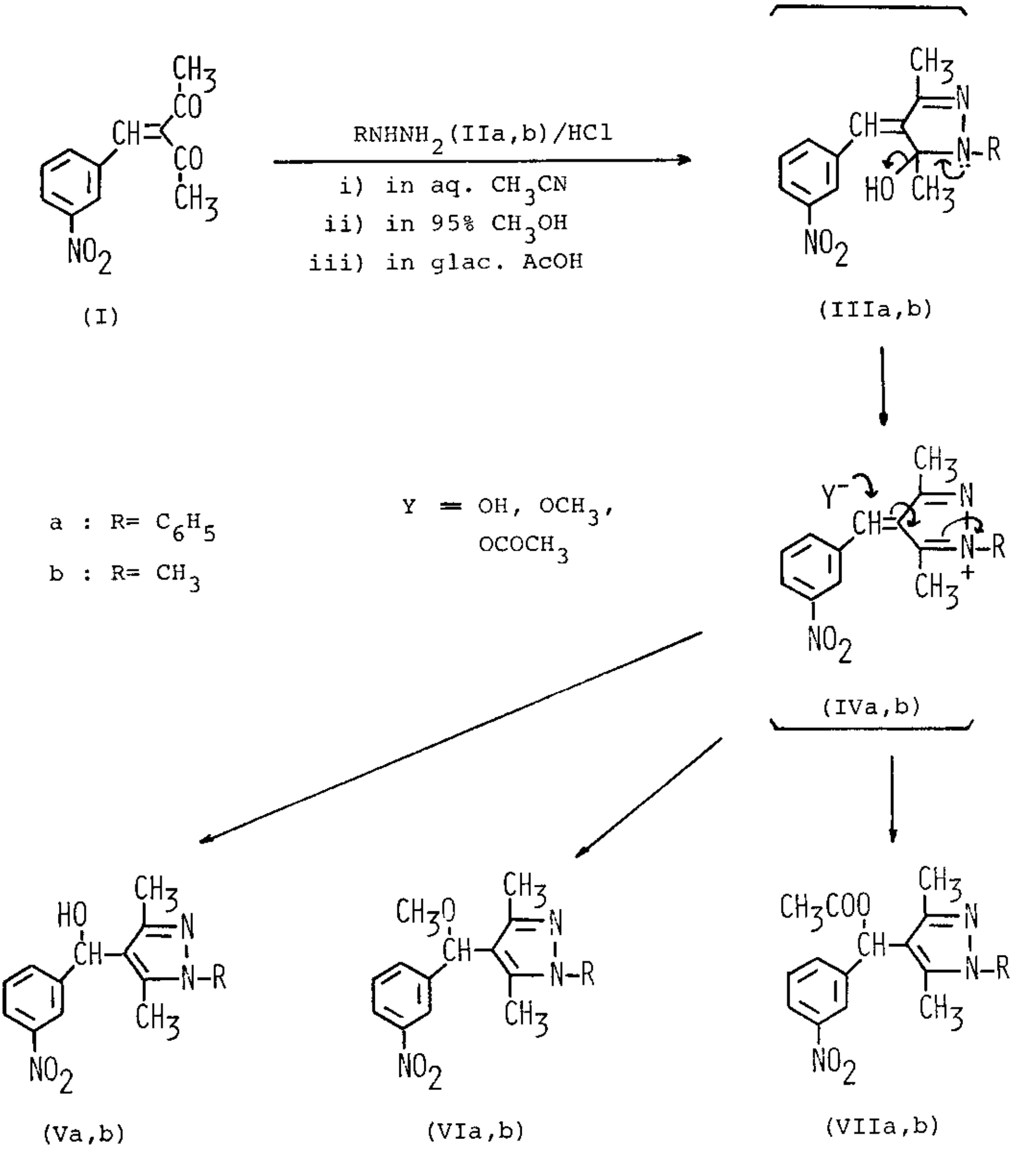
Treatment of the diketone(I) in acetonitrile containing a small amount of water with phenylhydrazine hydrochloride(IIa) at room temperature for 10 hr gave a 88% yield of 4-(α-hydroxy-m-nitrobenzyl)-3,5-dimethyl-1-phenylpyrazole(Va) [ν_{max}^{KBr} 3240, 1540 and 1360 cm^{-1}; δ(DMSO-d_6) 2.06 and 2.28(each 3H, each s), 5.90(1H, s), 7.45-8.30 (10H, m)].

The diketone(I) was treated with IIa in 95% methanol or glac. acetic acid at 60° for 10 hr to give a 90% yield of 4-(α-methoxy-m-nitrobenzyl)-3,5-dimethyl-1-phenylpyrazole(VIa)[$\delta(CDCl_3)$ 2.19 and 2.23(each 3H, each s), 3.43(3H, s), 5.43(1H, s), 7.40-8.30 (9H, m)] and a 72% yield of 4-(α-acetoxy-m-nitrobenzyl)-3,5-dimethyl-1-phenylpyrazole(VIIa)[$\delta(CDCl_3)$ 2.17, 2.24 and 2.30(each 3H, each s), 7.00(1H, s), 7.25-8.20(9H, m)].

On the other hand, heating the acetonitrile solution of I and methylhydrazine(IIb) containing an equivalent amount of hydrochloric acid (3) gave a 78% yield of the hydrochloride salt of 4-(α-hydroxy-m-nitrobenzyl)-1,3,5-trimethylpyrazole(Vb), which was converted to free base[ν_{max}^{KBr} 3220, 1540 and 1380 cm^{-1}; $\delta(DMSO\text{-}d_6)$ 1.95, 2.15 and 3.61(each 3H, each s), 5.80(2H, bs changed to s with D_2O)].

Treatment of I with IIb in 95% methanol in the presence of hydrochloric acid(3), followed by neutralization, gave the known methoxy derivative(VIb)(2) in good yield. Similarly reaction of I with IIb in glac. acetic acid afforded the acetate(VIIb) in good yield. The results are summerized in the Table.

The mechanism of the formation of these pyrazoles can reasonably be rationalized as follow. It is well known that N-alkylpyridinium hydroxides are in equilibrium with N-alkyl-2-hydroxy-1,2-dihydropyridines, known as pseudo-bases or carbinol-bases(4), and the acridine or phenanthridine pseudo-bases can readily be isolated in a pure form(5). Condensation of I with IIa,b to form the intermediate pseudo-bases(III) followed by the attack of


(I)
RNHNH$_2$(IIa,b)/HCl
i) in aq. CH$_3$CN
ii) in 95% CH$_3$OH
iii) in glac. AcOH
(IIIa,b)
a : R= C$_6$H$_5$
b : R= CH$_3$
Y = OH, OCH$_3$, OCOCH$_3$
(IVa,b)
(Va,b)
(VIa,b)
(VIIa,b)

nucleophiles at benzal position of 1-substituted 4-(m-nitrobenzylidene)-3,5-dimethylisopyrazolium ion(IV) gave the pyrazole derivatives. Decker reported(6) when the 10-methylacridine pseudobase was crystallized from ethanol or even on treatment with cold ethanol formed the O-ethyl ether. The hydroxypyrazoles(Va,b), however, did not give the methyl ether even on refluxing in methanol, but the hydrochloride salt of Va,b gave the methyl ether (VIa,b) at room temperature.

Table

Product	Mp (°C)[a]	Yield (%)
Va	179-180	88
Vb·HCl	159-160	78
Vb	185-186	
VIa	oil	90
VIb	124-125	95
VIIa	oil	72
VIIb	114-116	98

[a] Melting points are uncorrected.

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3 It is essential for increase the yield of products to add the diketone(I) to the previously mixed solution of methylhydrazine and hydrochloric acid in acetonitrile under ice cooling.

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