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Synthesis of Some Pyrazolines and its Derivatives

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Chalcones **(IIIa–b)** were treated with hydrazine hydrate in ethanol to give pyrazoline **(IVa–b)**. Pyrazolines **(IVa–b)** reacted with acetic acid to form 1-acetyl pyrazoline **(Va–b)**. Pyrazolines **(IVa–b)** were condensed with benzoyl chloride in pyridine medium to give 1-benzoyl pyrazoline **(VIa–b)**. Pyrazolines **(IVa–b)** were reacted with acetic anhydride and a pinch of fused sodium acetate to give 1-acetyl-3-(2-acetoxy)-3-nitro-5-methyl)phenyl-5-substituted Δ^2-pyrazoline **(VIIa–b)**.

Key Words: Synthesis, Pyrazolines, Derivatives.

INTRODUCTION

Pyrazolines are known to have bacterial[1], fugicidal[2] and insecticidal properties. Some pyrazolines are also reported to have antiinflammatory, antidiabetic, anaesthetic and analgesic properties[3–5]. Pyrazolines and their derivatives have been reported to contain biological[6–8] activities. Recently, Ali *et al.*[9] have reported the synthesis of isomeric Δ^2-pyrazolines and their derivatives.

Chalcones reacted with hydrazine hydrate in ethanol to give 1-H pyrazolines[10–14]. It was thought of interest to prepare some pyrazolines and their derivatives from 2-hydroxy-3-nitro-5-methyl-4-methoxy chalcones **(Scheme-1).**

EXPERIMENTAL

Melting points were taken in a silicon oil bath (Precision) in open capillary tubes and are uncorrected. Purity of compounds was checked by TLC on silica gel-G. IR spectra were recorded on Perkin-Elmer-577 spectrophotometer, PMR spectra were recorded on DRX AC 300 F spectrophotometer (300 HZ) using TMS as an internal standard and UV on Varian-Cary 2390 UV spectrophotometer.

Synthesis of 2-hydroxy-3-nitro-5-methyl-4-substituted chalcones (IIIa–b): 2-Hydroxy-3-nitro-5-methyl acetophenone (0.01 M) was dissolved in ethanol. Benzaldehyde (0.01 M)/4-methoxy benzaldehyde (0.01 M) was added and the solution was heated to boiling. To this hot solution 40% NaOH was added with

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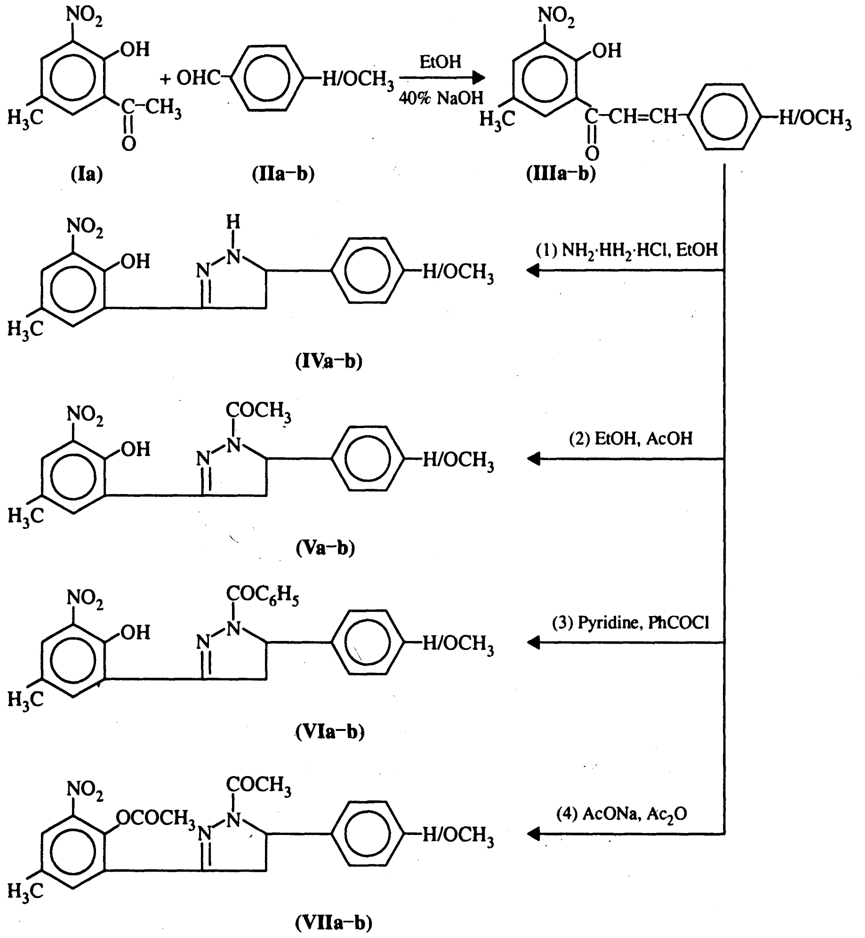

Scheme-1

constant stirring. A yellow-orange coloured solid mass was obtained which was kept overnight and acidified by 10% HCl, washed with 10% $NaHCO_3$ followed by water and crystallized from ethanol to give chalcone **(IIIb)**, m.p. 210°C (literature m.p. 210°C), yield 75%, m.f. $C_{17}H_{15}O_5N$ and m.w. 313. IR (nujol, cm^{-1}): 3640 ν(O—H stretching), 1660 ν(>C═O stretching in *o*-hydroxy aryl ketones), 1543 ν(asymmetric stretching in —CO—CH═CH—), 1140 ν(Ar—O stretching in aromatic ethers), 1275 ν(C—N str.), 1570 ν(Ar—NO_2 sym. str.), 1350 ν(Ar—NO_2 asym. str.), 985 ν(*trans* —CH—CH— wagging). The PMR ($CDCl_3$): 1.6 δ (S, 3H, Ar—CH_3), 3.0 δ (S, 3H, Ar—O—CH_3), 5.9–7.1 δ (d, 2H —CH═CH—) and (m, 6H, Ar—H), 10.9 δ (S, 1H, Ar—OH).

Synthesis of 1-H-3-(2′-hydroxy-3′-nitro-5′-methyl)-phenyl-5-anisyl-Δ^2-pyrazoline (IVa–b): 2-Hydroxy-3-nitro-5-methyl-4-methoxy chalcone **(IIIb)** dissolved in ethanol (25 mL) and hydrazine hydrate (0.02 mol) was added to it.

The reaction mixture was refluxed for 2 h, cooled concentrate and allowed to stand overnight. The resulting solid which separated out was crystallized from ethanol to get 1-H-3-(2′-hydroxy-3′-nitro-5-methyl)-phenyl-5-anisyl-Δ^2-pyrazoline with m.p. 189°C and yield 80%. IR (nujol, cm^{-1}) 3400–3350 ν(N—H), 3300 ν(O—H), 1620 ν(C═N of pyrazoline), 1300 ν(N—H), 1260 ν(C—O); 1530 ν($C—NO_2$), 1330 ν($C—NO_2$) and 850 ν(*p*-substituted benzene). UV (MeOH) λ_{max}: 290 and 350 nm corresponding to π-π* and n-π* transition. PMR ($CDCl_3$): 2.3 δ (s, 3H, $Ar—CH_3$), 3.7 δ (S, 3H, $O—CH_3$), 3.05 δ (dd, 1H, $—CHH_A$, $J_{AB} = 18$ Hz, $J_{Ax} = 4$ Hz), 3.5 δ (dd, 1H—CHBH, $J_{AB} = 18$ Hz, $J_{BX} = 11$ Hz), 4.8 δ (dd, 1H, $—CH_x$, $J_{Ax} = 4$ Hz, $J_{Bx} = 11$ Hz), 6.6δ-8δ (m, 7H, Ar—H).

Synthesis of 1-acetyl-3-(2′-hydroxy-3′-nitro-5′-methyl)phenyl-5-anisyl Δ^2-pyrazoline (Va–b): 1H-3-(2′-hydroxy-3′-nitro-5′-methyl)phenyl-5-anisyl-Δ^2-pyrazoline and acetic acid (10 mL) were reflured for 2 h. The reaction mixture was then concentrated, allowed to cool, the solid product filtered, washed with water and recrystallized from ethonol to get 1-acetyl-3-(2′-hydroxy-3′-nitro-5′-methyl-phenyl-5-anisyl-Δ^2-pyrazoline (m.p. 242°C and yield 80%). IR spectrum (nujol, cm^{-1}) 3400 ν(OH), 1670 ν($N—COCH_3$), 1620 ν(C═N of pyrazoline), 1530 ν($C—NO_2$ sym. str.), 1330 ν($C—NO_2$), 1260 ν(C—O), 1190 ν(C—N). UV (MeOH) λ_{max}: 290 and 345 nm.

Synthesis of 1-benzoyl-3-(2′-hydroxy-3′-nitro-5′-methyl)phenyl-5-anisyl-Δ^2-pyrazoline (VIa–b): 1H-3-(2′-hydroxy-3′-nitro-5′-methyl) phenyl-5 anisyl-2-pyrazoline and benzoyl chloride was dissolved in pyridine and stirred at rom temperature for 1 h after which the reaction mixture was treated with cold dilute HCl. The resulting solid was filtered, washed successively with water, cold NaOH (2%) and water and finally crystallized from glacial acetic acid to obtain 1-benzoyl-3-(2′-hydroxy-3′-nitro-5′-methyl)phenyl-5-anisyl-Δ^2-pyrazoline (yield 85% and m.p. 210°C). UV (MeOH) λ_{max}: 242 and 316 nm. IR (nujol, cm^{-1}): 3000–3200 ν(OH), 1640 ν(C═N of pyrazoline), 1700 ν(N—C═O), 1540 ν($C—NO_2$), 1350 ν($C—NO_2$), 1210 ν(C—H).

Synthesis of 1-acetyl-3-(2′-acetoxy-3′-nitro-5′-methyl) phenyl-5-anisyl-Δ^2-pyrazoline (VIIa–b): To a mixture of 1H-3-(2′-hydroxy-3′-nitro-5′-methyl)-phenyl-5-anisyl-2-pyrazoline and acetic anhytride, a pinch of fused sodium acetate was added and the reaction mixture was heated under reflux for 45 min and diluted with water. The solid thus obtained was crystallized from ethanol to obtain 1-acetyl-3-(2′-acetoxy-3′-nitro-5′-methyl)phenyl-5 anisyl-Δ^2-pyrazoline (yield 72% and m.p. 134°C). UV-MeOH λ_{max}: 280 and 380 nm. IR (nujol, cm^{-1}): 1630 ν($OCOCH_3$), 1700 ν($N—COCH_3$), 1580 ν(C═N of pyraoline), 1550 ν($C—NO_2$); 1360 ν($C—NO_2$), 1270 ν(C—N). PMR ($CDCl_3$): 2.2 δ (s, 3H, $Ar—CH_3$), 2.3 δ (s, 6H, $2COCH_3$), 3.08 δ (dd, $1H > CHH_A$, $J_{AB} = 18$ Hz, $J_{AX} = 5$ Hz), 3.64 δ (dd, 1H > CHBH, $J_{AB} = 18$ Hz, $J_{BX} = 11$ Hz), 3.7 δ (s, 3H, OCH_3), 5.37 (dd, $1H > CH_X$, $J_{Ax} = 5$ Hz, $J_{Bx} = 11$ Hz), 6.67–7.4 δ (m, 6H, Ar—H).

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF SYNTHESIZED COMPOUNDS

Compound	m.f.	m.p. (°C)	Yield (%)
IIIa	$C_{16}H_{13}O_4N$	158	70
IIIb	$C_{17}H_{15}O_5N$	210	70
IVa	$C_{16}H_{15}O_3N_3$	137	75
IVb	$C_{17}H_{17}O_4N_3$	189	80
Va	$C_{18}H_{17}O_4N_3$	192	78
Vb	$C_{19}H_{19}O_5N_3$	242	80
VIa	$C_{23}H_{19}O_4N_3$	168	78
VIb	$C_{24}H_{21}O_5N_3$	210	85
VIIa	$C_{20}H_{19}O_5N_3$	183	75
VIIb	$C_{21}H_{21}O_6N_3$	134	72

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