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Synthesis and Reactions of 3-Formyl-1-Phenyl-5-[(2̄-Thiazolo) Monoazamethine] Pyrazole

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3-Formyl-1-phenyl-5-[(2̄-thiazolo) monoazamethine] pyrazole was condensed with acetophenone and acetophenone derivatives. The resulting α,β-unsaturated ketonic system was condensed with hydrazines, hydroxylamine, urea and thiourea affording isolated pyrazolines, isoxazolines, pyrimidines and/or pyrimidine-thione derivatives.

INTRODUCTION

In continuation of our efforts for the synthesis of new compounds of isolated or fused systems of pyrazolines, oxazolines, isoxazolines and pyrimidine derivatives[1–4] and because of their wide uses in many biological processes as herbicides[5], as a plant growth regulators[6] and as synthetic drugs[7,8] I was prompted to explore the possibility of utilizing 3-methyl-1-phenyl pyrazolidin-5-one as substrate for the synthesis of the newly isolated pyrazolines, isoxazolines and pyrimidine compound derivatives.

RESULTS AND DISCUSSIONS

3-methyl-1-phenyl pyrazolidin-5-one was condensed easily with 2-amino thiazole in absolute ethanol and 3-methyl-1-phenyl-5[(2̄-thiazolo) monoazamethine] pyrazole(I) was prepared in almost quantitative yield in alkaline medium. Oxidation of (I) with selenium dioxide gave the corresponding 3-formyl compound (II). The ^{1}H-NMR shows absorption at 9.5 ppm as an indication to the presence of the aldehydic group. The active aldehydic group in position 3 of the pyrazolidene ring in (II) was subjected to condensation with acetophenone and its derivatives in absolute ethanol to yield 3-chalcone-1-phenyl-5-[(2̄-thiazolo) monoazamethine] pyrazole derivatives (III_{a-c}). The ^{1}H-NMR shows absorption at δ 6–6.3 due to the presence of α,β-unsaturated ketonic system. The activation exerted by the carbonyl group on the exocyclic double bond renders these chalcones more available to condense with hydrazine derivatives. Interaction of (III_{a-c}) with hydrazine hydrate in ethanol in presence of acetic acid, phenyl-

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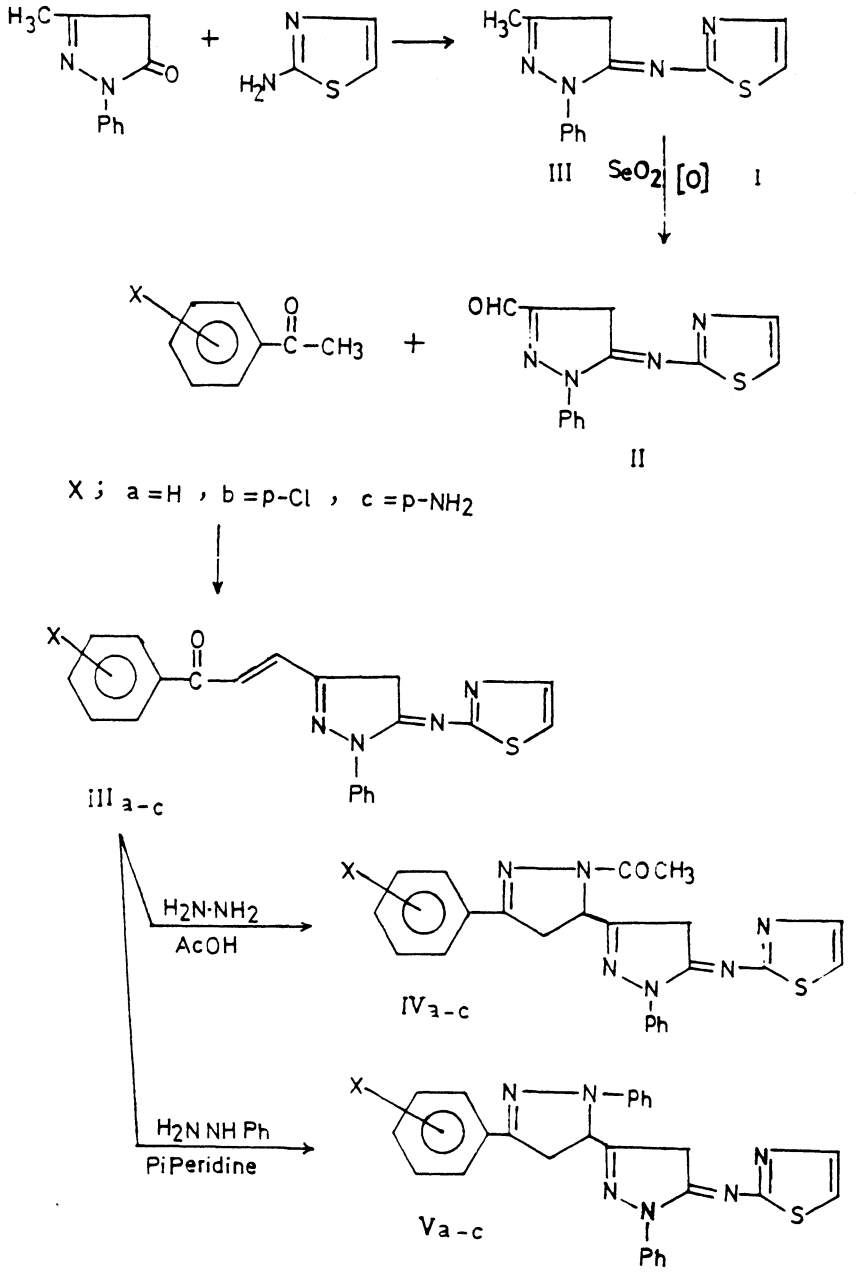
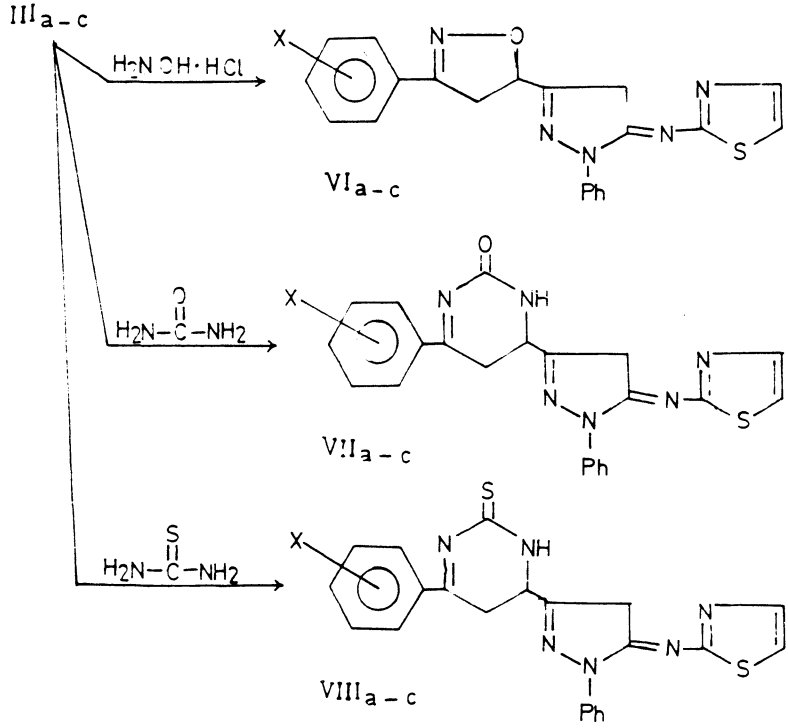
hydrazine in presence of piperidine, hydroxylamine hydrochloride in presence of ethanolic sodium hydroxide and urea or thiourea in presence of hydrochloric acid afforded the corresponding isolated 1-phenyl-5-[(2-thiazolo) monoazamethine]



pyrazole derivatives of N-acetyl and/or N-phenyl pyrazolidene, isoxazolines, pyrimidinones and pyrimidine thione derivatives (IV_{a-c}), (V_{a-c}), (VI_{a-c}), (VII_{a-c}) respectively. The structure of these compounds was established through elemental analysis, IR, and ^{1}H-NMR spectra.



III_{a-c}, IV_{a-c}, V_{a-c}, VI_{a-c}, VII_{a-c}, $VIII_{a-c}$, (a, X = H; b, X = *P*-Cl; X = *p*-NH_2)

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded on a Perkin-Elmer 127B spectrophotometer and PMR spectra on a EM 390 (90 MHz) spectrometer.

3-Methyl-1-phenyl-5-[(2-thiazolo) monoazamethine] pyrazole derivatives (I)

3-Methyl-1-phenyl pyrazoline-5-one and 2-amino thiazole in equimolar ratio were dissolved in absolute ethanol and few drops of piperidine as catalyst were added, and the mixture was refluxed for about 20 h. The reaction mixture was then evaporated under vacuum, and the resulting precipitate filtered off, washed and crystallised from the proper solvent. ^{1}H NMR δ (DMSO): at δ 2.0 (s, 3H, CH_3) and at 8.5–6.5 ppm (m, 7H, aromatic and thiazolo nuclei), at 0.9–1.5 (s, 2H, —CH_2 of pyrazole ring). IR (KBr): at 2995 cm^{-1} ν(CH), at 1600 cm^{-1} ν(—C=N), 1575 cm^{-1} (—N=) and at 1100–1000 cm^{-1} (aromatic ring). The chemical analysis and some of the physical properties are recorded in Table-1.

TABLE-1
PHYSICAL DATA OF COMPOUNDS I–VIII

Compound	Molecular Formula	m.p. (°C)	Yield (%)	Solvent of Cryst.
I	$C_{13}H_{12}N_4S$	170	85	Ethanol
II	$C_{13}H_{10}N_4OS$	145	60	Ethanol
III_a	$C_{21}H_{16}N_4OS$	115	70	Ethanol
III_b	$C_{21}H_{15}N_4OSCl$	150	57	Ethanol
III_c	$C_{21}H_{17}N_5OS$	130	72	Methanol
IV_a	$C_{23}H_{20}N_6OS$	175	80	Methanol
IV_b	$C_{23}H_{19}N_6OSCl$	150	60	Ethanol
IV_c	$C_{23}H_{21}N_7OS$	160	72	Methanol
V_a	$C_{27}H_{22}N_6S$	>300	40	Ethanol
V_b	$C_{27}H_{21}N_6SCl$	255	35	Ethanol
V_c	$C_{27}H_{23}N_7S$	270	53	Methanol
VI_a	$C_{21}H_{17}N_5OS$	130	60	Methanol
VI_b	$C_{21}H_{16}N_6OSCl$	160	40	Methanol
VI_c	$C_{21}H_{18}N_6OS$	145	50	Methanol
VII_a	$C_{22}H_{18}N_6OS$	200	60	Ethanol
VII_b	$C_{22}H_{17}N_7OSCl$	170	35	Ethanol
VII_c	$C_{22}H_{19}N_7OS$	190	55	Methanol
$VIII_a$	$C_{22}H_{18}N_6S_2$	245	50	Ethanol
$VIII_b$	$C_{22}H_{17}N_6S_2Cl$	190	35	Methanol
$VIII_c$	$C_{22}H_{19}N_7S_2$	210	45	Ethanol

All compounds gave satisfactory C, H and N analysis

3-Formyl-1-phenyl-5-[($\bar{2}$-thiazolo)monoazamethine]pyrazole (II)

3-Methyl-1-phenyl-5-([$\bar{2}$-thiazolo) monoazamethine] pyrazole derivatives (II) and selenium dioxide were dissolved in absolute ethanol, and the mixture was refluxed for about 8 h. The reaction mixture was filtered and the filtrate was refluxed for about 4 h. The reaction mixture was then evaporated under vacuum, and the resulting precipitate filtered off, washed and recrystallised from the proper solvent. ^{1}H NMR δ (DMSO): at δ 9.5 ppm (s, 1H, CHO). IR (KBr): at 1730 cm^{-1} due to the presence of —CHO group. The physical data and the chemical analysis are given in Table-1.

3-Chalcones-1-phenyl-5-[($\bar{2}$-thiazolo) monoazamethine] pyrazole derivatives (III_{a-c})

3-Formyl-1-phenyl-5-[($\bar{2}$-thiazolo) monoazamethine] pyrazole derivatives and substituted acetophenone in equimolar ratio were dissolved in ethanol and the mixture was refluxed for about 23 h. The reaction mixture was then evaporated under vacuum, and the resulting precipitate filtered off and crystallised from the

proper solvent. ^{1}H NMR δ (DMSO): at δ 6, 6.5 ppm (d, 2H, CH=Ch). IR (KBr): at 1700 cm^{-1} ν(—C=O) and at 1600 cm^{-1} ν(C=C). The chemical analysis and the physical data are recorded in Table-1.

3-[3-Substituted phenyl, N-acetyl pyrazolino]-1-phenyl-5-[(2-thiazolo) monoazamethine] pyrazole (IV_{a-c})

To a solution of chalcones (III_{a-c}) in ethanol, hydrazine hydrate (50%, 8 mL) was added followed by glacial acetic acid (9 mL) and the reaction mixture refluxed for 5–20 h. The reaction mixture was then filtered while hot concentrated to one-third of its volume and poured in ice-water mixture with stirring; the resulting solid was filtered, washed several times with water, dried and crystallised from proper solvent. ^{1}H NMR δ (DMSO): at δ 2.2 ppm, (s, 3H

CH_3—C—), at δ 6.5–8.0 ppm, (12H, aromatic and thiazolo ring), at 0.9–1.9 ppm (m, 5H, heterocyclic nuclei). IR (KBr): at 1670 cm^{-1} ν(C=O), at 2290 cm^{-1} ν(C—H). The chemical analysis and the physical data are recorded in Table-1.

3-[3-Substituted phenyl, N-phenylpyrazolino]-1-phenyl-5-[(2-thiazolo) monoazamethine] pyrazole (V_{a-c})

A mixture of (III_{a-c}) (0.01 mol) and phenylhydrazine (0.01 mol) was dissolved in ethanol (30 mL) containing piperidine (1 mL) and refluxed for 15–30 h. The reaction mixture was then filtered while hot, concentrated, poured in ice-water mixture with stirring and left overnight at room temperature. The resulting solid was washed several times with water, dried and crystallised from proper solvent. ^{1}H NMR δ (DMSO): at δ 6.5–8 ppm (m, 17H, aromatic and thiazole ring), at 0.9–1.9 (m, 5H, heterocyclic nuclei). IR (KBr): at 1100–800 cm^{-1} (aromatic and heterocuclic rings). The chemical analysis and physical data are recorded in Table-1.

3-[3-Substituted phenyl, Ioxazolino]-1-phenyl-5-[(2-thiazolo) monoazamethine] pyrazole (VI_{a-c})

A mixture of (III_{a-c}) (0.01 mol) and hydroxylamine hydrochloride was dissolved in ethanol in presence of sodium hydroxide for 5–20 h. The reaction mixture was then evaporated and triturated with 20 mL petroleum ether where a resinous material deposited. The latter was triturated with water; the separated product was filtered, washed with water and crystallised from proper solvent ^{1}H NMR δ (DMSO): at δ 6.5–8 ppm (m, 12H, aromatic and thiazole ring), at δ 0.9–1.9 ppm (m, 5H, heterocyclic nuclei), IR(KBr): at 1100–800 cm^{-1} (aromatic and heterocyclic ring). The chemical analysis and the physical data are recorded in Table-1.

3-[3-Substituted phenyl, pyrimidino and/or pyrimidine thiono]-1-phenyl-5-[(2-thiazolo) monoazamethine] pyrazole (VII_{a-c})

A mixture of an ethanolic solution (III_{a-c}) (0.02 mol), urea and/or thiourea

(4 g) and concentrated hydrochloric acid (20 mL) was refluxed for 12–20 h. The reaction mixture was then filtered while hot, allowed to cool and neutralised with 5 N-sodium hydroxide. The resulting solid was washed several times with water, dried and crystallised from the proper solvent. ^{1}H NMR δ (DMSO) for (VII_{a-c}): at δ 8.5–6 ppm (m, 12H, aromatic and thiazole ring), at δ 3.2 ppm (s, 1H, NH), at δ 0.9–1.5 ppm (m, 5H, heterocyclic nuclei). IR (KBr): at 1100–800 cm^{-1} (aromatic and heterocyclic ring), at 3450–3390 cm^{-1} (NH), 1450 cm^{-1} (C=N), and at 1720 cm^{-1} (C=O for pyrimidine). ^{1}H NMR δ (DMSO) for ($VIII_{a-c}$): at δ 8.3–6 ppm (m, 12H, aromatic and thiazolo ring), δ 0.7–2.2 ppm (m, 5H) and δ 3.5 ppm (n, 4H, pyrimidine protons)[9]. IR (KBr): at 1350 cm^{-1} (C=S for pyrimidine thione)[10].

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