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Synthesis of Chlorosubstituted 3,5-Diaryl-1-substituted Pyrazolines

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Pyrazoline derivatives have been extensively studied because of their ready accessibility through synthesis, diverse chemical reactivity, various biological activities and variety of industrial applications. New chlorosubstituted 3,5-diaryl-1-substituted pyrazolines (**3a-i**), (**4a-i**) and (**5a-i**), were synthesized from 1,3-diaryl-prop-2-ene-1-ones (**2a-i**) on condensation with nucleophiles like thiosemicarbazide, isonicotinicacid-hydrazide and semicarbazide hydrochloride in ethanol/DMF medium. The synthesized compounds have been characterized by IR and ^{1}H NMR spectroscopic studies.

Key Words: Synthesis, Substituted pyrazolines.

INTRODUCTION

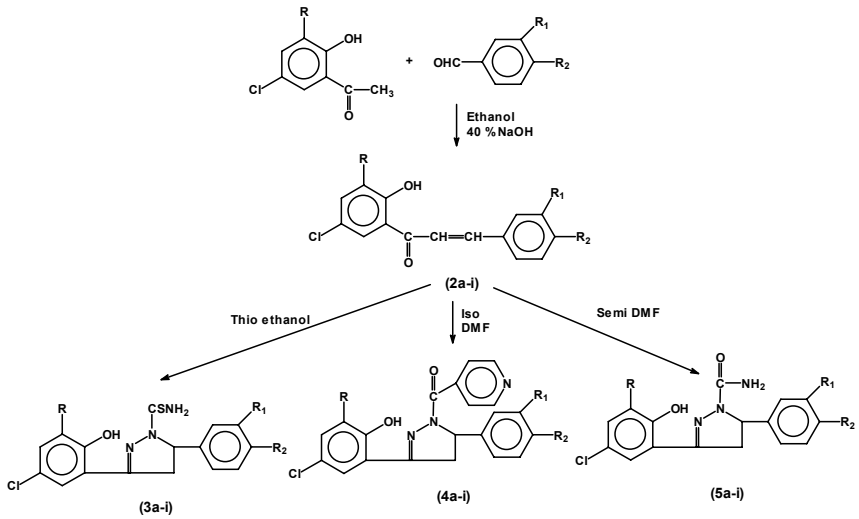
Pyrazolines have been reported to show a broad spectrum of biological activities including antibacterial[1], antifungal[2], antiinflammatory[3] and antidepressant activities[4]. The pyrazoline function is quite stable and has inspired chemists to utilize this stable fragment in bioactive moieties to synthesize new compounds possessing biological activities. Pyrazolines are important heterocycles because they furnish substituted products which are used in medicines[5]. The literature survey reveals the importance of pyrazolines as an intermediate in dye industry[6]. They are also useful as biodegradable agrochemicals[7].

The reaction between substituted hydrazines and 2-hydroxy chalcones or flavanones leads to the formation of pyrazolines. Pyridine[8] as reaction medium has been widely used. The use of DMF[9], ethylenediamine[10], DMSO[11] and acetic acid-ethanol[12] mixture as reaction media in the synthesis of pyrazolines have also been reported.

Ferfra *et al.*[13] reported the synthesis of pyrazolines and pyrazoles. Rajvaidya *et al.*[14] reported the formation of pyrazolines by the condensation of chalcones with hydrazine hydrate and malononitrile and ammonium acetate. Kumar *et al.*[15] also reported the synthesis of antiinflammatory, analgesic and COX-II inhibitory activities of indolyl pyrazolines.

The present work reported the synthesis of chlorosubstituted 3,5-diaryl-1-substituted pyrazolines by treatment of 1,3-diaryl-prop-2-ene-1-ones with thiosemicarbazide/isonicotinicacidhydrazide/semicarbazide hydrochloride in ethanol/DMF solvent.

The structures of all the synthesized compounds were assigned on the basis of their IR, ^{1}H NMR spectra.



Scheme

EXPERIMENTAL

The melting points were taken in silicon oil bath instrument in open capillary and are uncorrected. Purity of the compounds was checked by TLC on silica Gel-G plates. IR spectra were recorded on a Perkin-Elmer spectrophotometer. ^{1}H NMR spectra were recorded on a Brucker AC 300 FTNMR spectrometer (300 MHz), using ($CDCl_3$ + DMSO) as an internal standard.

Preparation of 1,3-diaryl-prop-2-ene-1-ones: 2-Hydroxy-5-chloro acetophenone (0.01 mol) was dissolved in ethanol (20 mL). The aromatic aldehyde (0.01 mol) was added to it. The mixture was heated to boiling. Aqueous NaOH solution (40 %) was added dropwise with constant stirring to the reaction mixture. Orange coloured cake was formed. The reaction mixture was kept overnight. The salt was decomposed by adding HCl (50 %). The product was crystallized from ethanol-acetic acid mixture to obtain 1,3-diaryl-prop-2-ene-1-ones (**2a-i**). The identity of the products was confirmed by their IR and ^{1}H NMR spectroscpic data studies.

Spectral data: 2a: IR (KBr, ν_{max}, cm^{-1}): 3698 (-OH *str.*), 1638 (-C=O *str.*), 1566 (HC=CH *str.*), 752 (C-Cl *str.*),. NMR ($CDCl_3$ + DMSO) (δ ppm): 3.7-3.9 (s, 3H, $-OCH_3$), 6.8-7.6 (m, 7H, Ar-H), 7.9-8.0 (d, 1H, -CH), 7.7-7.8 (d, 1H, -CH), 12.9 (s, 1H, -OH).

Synthesis of chlorosubstituted 3,5-diaryl-1-substituted pyrazolines: 1,3-Diaryl-prop-2-ene-1-ones (0.01 mol) (**2a-i**) was refluxed with thiosemicarbazide/isonicotinicacidhydrazide/semicarbazide hydrochloride (0.02 mol) for 6-7 h in ethanol/DMF solvent. Water containing a little HCl was added to decompose DMF. The product obtained was filtered, washed with sufficient water and crystallized from ethanol to obtain pyrazolines (**3a-i**), (**4a-i**) and (**5a-i**).

Spectral data: 3a: IR (KBr, ν_{max}, cm^{-1}): 3427 (-OH *str.*), 2930 (C-H *str.*), 1605 (C=N *str.*), 1243 (C-N *str.*), 717 (C-Cl *str.*). NMR ($CDCl_3$ + DMSO) δ ppm: 3.7 (s, 3H, $-OCH_3$), 3.1-3.4 (dd, $1H_a$, -CH), 3.8-4.0 (dd, $1H_b$, -CH), 5.9-6.0 (dd, $1H_c$, -CH), 6.8 (s, 2H, $-NH_2$), 6.9-7.4 (m, 7H, Ar-H), 9.6 (s, 1H, -OH).

4a: IR (KBr, ν_{max}, cm^{-1}): 3450 (-OH *str.*), 2927 (C-H *str.*), 1611 (C=N *str.*), 1653 (C=O *str.*), 1254 (C-N *str.*). NMR ($CDCl_3$ + DMSO) δ ppm: 3.8 (s, 3H $-OCH_3$), 3.4 (s, $1H_a$, -OH), 3.9 (dd, $1H_b$, -CH), 5.7 (dd, $1H_c$, -CH), 7.8 (dd, 1H, -CH), 6.9-7.6 (m, 11H, Ar-H).

TABLE-1
PHYSICAL DATA OF THE PYRAZOLINES

Compd.	R	R_1	R_2	m.f.	m.p. (ºC)	Yield (%)	R_f value
3a	H	H	$-OCH_3$	$C_{17}H_{16}N_3O_2SCl$	176	60	0.52
3b	H	H	H	$C_{16}H_{14}N_3OSCl$	215	65	0.58
3c	H	Cl	H	$C_{16}H_{13}N_3OSCl$	208	60	0.71
3d	Br	H	$-OCH_3$	$C_{17}H_{15}N_3O_2SBrCl$	185	65	0.53
3e	Br	H	H	$C_{16}H_{13}N_3OSBrCl$	200	65	0.69
3f	Br	Cl	H	$C_{16}H_{12}N_3OSBrCl_2$	240	60	0.66
3g	NO_2	H	$-OCH_3$	$C_{17}H_{15}N_4O_4SCl$	225	60	0.51
3h	NO_2	H	H	$C_{16}H_{13}N_4O_3SCl$	212	65	0.61
3i	NO_2	Cl	H	$C_{16}H_{12}N_4O_3SCl_2$	244	65	0.60
4a	H	H	$-OCH_3$	$C_{22}H_{18}N_3O_3Cl$	147	60	0.61
4b	H	H	H	$C_{21}H_{16}N_3O_2Cl$	145	55	0.57
4c	H	Cl	H	$C_{21}H_{15}N_3O_2Cl_2$	177	50	0.65
4d	Br	H	$-OCH_3$	$C_{22}H_{17}N_3O_3BrCl$	160	60	0.63
4e	Br	H	H	$C_{21}H_{15}N_3O_2BrCl$	152	60	0.62
4f	Br	Cl	H	$C_{21}H_{14}N_3O_3BrCl_2$	202	55	0.63
4g	NO_2	H	$-OCH_3$	$C_{22}H_{18}N_4O_5Cl$	210	60	0.55
4h	NO_2	H	H	$C_{21}H_{16}N_4O_4Cl$	189	60	0.67
4i	NO_2	Cl	H	$C_{21}H_{15}N_4O_4Cl_2$	229	50	0.57
5a	H	H	$-OCH_3$	$C_{17}H_{16}N_3O_3Cl$	153	65	0.57
5b	H	H	H	$C_{16}H_{14}N_3O_2Cl$	151	60	0.55
5c	H	Cl	H	$C_{16}H_{13}N_3O_2Cl_2$	156	50	0.74
5d	Br	H	$-OCH_3$	$C_{17}H_{15}N_3O_3BrCl$	189	60	0.47
5e	Br	H	H	$C_{16}H_{13}N_3O_2BrCl$	194	60	0.50
5f	Br	Cl	H	$C_{16}H_{13}N_3O_2BrCl_2$	216	55	0.59
5g	NO_2	H	$-OCH_3$	$C_{17}H_{15}N_4O_5Cl$	215	60	0.62
5h	NO_2	H	H	$C_{16}H_{13}N_4O_4Cl$	193	50	0.47
5i	NO_2	Cl	H	$C_{16}H_{12}N_4O_4Cl_2$	221	50	0.75

5a: IR (KBr, ν_{max}, cm^{-1}): 3478 (-OH *str.*), 2966 (C-H *str.*), 1675 (-C=O *str.*), 756 (C-Cl *str.*), 1254 (C-N *str.*), 1613 (-C=N *str.*). NMR ($CDCl_3$ + DMSO) δ ppm: 3.8 (s, 3H $-OCH_3$), 3.3 (dd, $1H_a$, -CH), 5.4-5.5 (dd, $1H_b$, -CH), 7.4 (dd, $1H_c$, -CH), 6.9-7.6 (m, 7H, Ar-H), 8.9 (s, 1H, -OH), 6.7 (s, 2H, $-NH_2$).

Similarly compounds (**3b-i**), (**4b-i**) and (**5b-i**) of the series were prepared. The physical data of the synthesized heterocycles is recorded in Table-1.

RESULTS AND DISCUSSION

Structures of the synthesized compounds have been elucidated by IR and ^1H NMR analysis. IR spectra showed absorption bands areound 1650-1550 cm^{-1}, which is a characteristic of C=N *str.* of pyrazoline. In ^1H NMR, the protons of aromatic ring and methoxy group were observed at 6.9-7.6 and 3.7-3.8 ppm, respectively. H_a, H_b and H_c of pyrazoline ring were seen as double doublet at 3.1-3.4, 3.8-4.0 and 5.4-5.5, 5.8-6.0 and 7.4 ppm, respectively.

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