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NOTE

A Novel Method for Synthesis of 3,5-Diaryl Isoxazolines and 3,5-Diaryl Isoxazoles

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Some new 3,5-diaryl isoxazolines and 3,5-diaryl isoxazoles have been synthesized by a novel method and by short route. 3,5-Diaryl 1-phenyl isoxazolines (3) were synthesized by the reaction of 2-hydroxy acetophenones (1) with hydroxylamine hydrochloride in alcohol medium containing a little piperidine. 2-aroyl acetophenones (2) with hydroxylamine hydrochloride in alcohol medium containing a little piperidine produces 3,5-diaryl-1-phenyl isoxazoles (4). Structures of these compounds have been established by spectral analysis (IR, UV and NMR).

2-Hydroxychalcones and flavanones form flavanone oxime which can be converted into isoxazolines.[1] 3,5-Diaryl isoxazolines are reported to be synthesized[2] directly from 2-hydroxy chalcones and flavanones. Isoxazolines and their isomers have been reported to form from furochalcones and $NH_2OH{\cdot}HCl$[3]. 3,5-Diaryl isoxazoles are usually synthesized[4] by the action of $NH_2OH{\cdot}HCl$ on 1,3-dicarbonyl compounds. 3,5-Diaryl-isoxazoles are reported to be formed from flavones,[5] chromones,[6] chalcone dibromides or α-bromochalcones.[7–11] Reaction of $NH_2OH{\cdot}HCl$ on β-diketone, flavone, 3-bromoflavanone[2] is a method for synthesis of 3,5-diaryl isoxazole. From the literature survey we have not found the method for the synthesis of 3,5-diaryl isoxazolines directly from 2-hydroxy acetophenones and synthesis of 3,5-diaryl isoxazole from 2-aroyloxy acetophenones. It was therefore thought of interest to use such economical short routes for the synthesis of the titled compounds which saved laborious work and time. Antimicrobial activity of isoxazolines has been reported.[12] Isoxazolines are not only used in textile and cinematographic films but they have also shown widely differing bacteriological activity. Isoxazole derivatives have been reported to possess antitubercular,[13] antiviral[14] and antibacterial[15] activity. Recently more antimycotic formulations[16] have been prepared containing isoxazoles. Isozazoles[17] has been found to have antiviral properties against Herpes type 2 virus.

Present work deals with the synthesis of 3,5-diaryl isoxazolines (3) from 2-hydroxy acetophenones (1) and 3,5-diaryl isoxazooles (4) from 2-Aroyloxy acetophenones (2) in alcohol medium containing a little piperidine.

Melting points are uncorrected. IR spectra was recorded on Perkin-Elmer 577 (4000–200 cm^{-1}). NMR spectra was recorded on Bruker AC300 NMR spectrom-

meter at 300 MHz in $CDCl_3$. UV-VIS spectra were recorded on Hitachi 320 UV-VIS spectrometer.

1. Preparation of 3,5-diaryl-1-phenyl isoxazolines (3a–3j)

2-Hydroxy acetophenones (1) (0.01 M) was refluxed in alcohol (15 mL) containing a little piperidine for about 2 h. Then to it hydroxylamine hydrochloride (0.02 M) was added and the mixture was further refluxed for about 2 h. Reaction mixture was cooled, diluted with water and acidified with dil. HCl. The solid product obtained was filtered and crystallised from ethanol-acetic acid mixture.

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF SYNTHESISED COMPOUNDS
(3a–3j) and (4a–4j)

Compound	R	R_1	R_2	R_3	Yield (%)	m.p. (°C)	Molecular formula	N%, Found (Calcd.)
3a	H	H	CH_3	H	67	182	$C_{16}H_{15}O_2N$	5.2 (5.5)
3b	H	H	CH_3	OCH_3	72	204	$C_{17}H_{17}O_3N$	4.6 (4.9)
3c	Br	H	CH_3	H	65	162	$C_{16}H_{14}O_2NBr$	4.0 (4.2)
3d	Br	H	CH_3	OCH_3	62	182	$C_{17}H_{16}O_3NBr$	3.5 (3.8)
3e	H	CH_3	H	H	71	180	$C_{16}H_{15}O_2N$	5.2 (5.5)
3f	H	CH_3	H	OCH_3	73	245	$C_{17}H_{17}O_3N$	4.3 (4.9)
3g	CH_3	H	H	H	67	120	$C_{16}H_{15}O_2N$	5.1 (5.5)
3h	CH_3	H	H	OCH_3	63	130	$C_{17}H_{17}O_3N$	4.5 (4.9)
3i	H	H	H	H	76	165	$C_{15}H_{13}O_2N$	5.3 (5.8)
3j	H	H	H	OCH_3	82	179	$C_{16}H_{15}O_3N$	5.0 (5.2)
4a	H	H	CH_3	H	68	210	$C_{16}H_{15}O_2N$	5.2 (5.5)
4b	H	H	CH_3	OCH_3	74	228	$C_{17}H_{17}O_3N$	5.0 (5.2)
4c	Br	H	CH_3	H	69	192	$C_{16}H_{12}O_2NBr$	4.0 (4.2)
4d	Br	H	CH_3	OCH_3	64	156	$C_{17}H_{14}O_3NBr$	3.5 (3.8)
4e	H	CH_3	H	H	80	210	$C_{16}H_{13}O_2N$	5.1 (5.5)
4f	H	CH_3	H	OCH_3	75	130	$C_{17}H_{15}O_3N$	4.9 (5.2)
4g	CH_3	H	H	H	81	175	$C_{16}H_{13}O_2N$	5.0 (5.5)
4h	CH_3	H	H	OCH_3	73	235	$C_{17}H_{14}O_3N$	5.0 (5.2)
4i	H	H	H	H	82	205	$C_{15}H_{11}O_2N$	5.4 (5.9)
4j	H	H	H	OCH_3	78	131	$C_{16}H_{13}O_3N$	4.9 (5.2)

Spectral interpretation ν of 3b (Table-1)

IR (ν_{max}): 1580 cm^{-1} ν(C=N—O); 1124 cm^{-1} ν(C—O), 1440 cm^{-1} ν(—CH_2)).

NMR: δ 2.3 (S, 3H, —CH_3); 3.4 (d, 2H, —CH_2); 3.8 (S, 3H, —OCH_3); 5.0 (t, 1H, —CH); 6.7–8.0 (m, 7H, Ar–H); 11.0 (S, 1H, —OH).

UV (λ_{max}): 320 nm.

2. Preparation of 3,5-diaryl-1-phenyl isoxazoles (4a–4j)

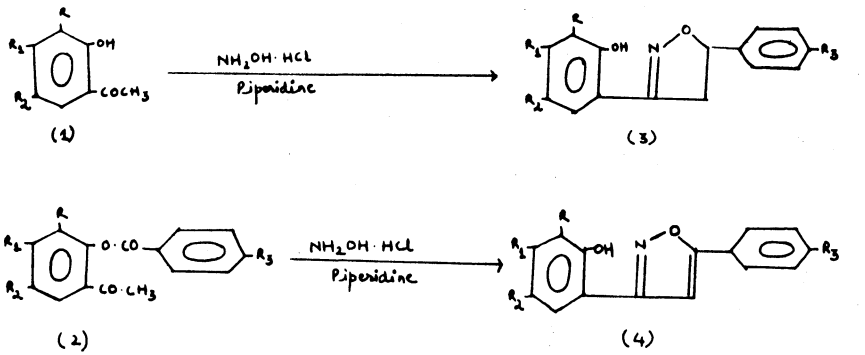
2-Aroyloxy acetophenone (2) (0.01 M) was refluxed in alcohol (15 mL) containing a little piperidine for about 2 h. Then to it hydroxylamine hydrochloride (0.02 M) was added and the mixture was further refluxed for about 2 h. The reaction mixture was cooled, diluted with water and acidified with dil HCl. The solid product obtained was filtered and crystallised from ethanol-acetic acid mixture.

Spectral interpretation of 4b (Table-1):

IR (ν_{max}): 1590 cm^{-1} ν(C=N), 1370 cm^{-1} ν(C—O), 1440 cm^{-1} ν(Ar—H).

NMR: δ 2.5 (S, 3H, —CH_3); 3.7 (S, 3H, —OCH_3); 4.1 (S, 1H, —CH); 7.0–8.0 (m, 7H, ·ArH); 8.8 (S, 1H, —OH). UV. (λ_{max}): 320, 350 nm.

Physical data of all the series were recorded in Table-1.



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