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NOTE

Synthesis and Antibacterial Activity of Some New Chlorosubstituted-4-Aroyl Isoxazoles

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4-Aroyl isoxazoles (**2a–d**) have been synthesized by the condensation of 3-aroyl flavones (**1a–d**) with hydroxylaminehydrochloride in DMSO containing a few drops of piperidine. Structural clucidation has been done on the basis of elemental analysis, chemical properties and spectral data. Antibacterial activities of these compounds were screened against *E. coli, S. aureus, B. subtilis* and *P. vulgaris* by disc diffusion method. These compounds showed appreciable activity towards microorganisms.

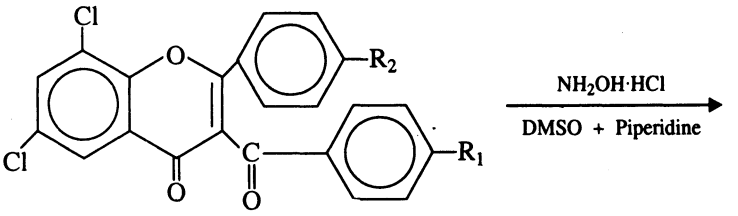
Key Words: Chlorosubstituted-4-aroyl isoxazoles, Synthesis, Antibacterial activity.

Among a wide variety of heterocycles that have been explored for developing biologically active molecules, isoxazoles[1-4] have played an important role in medicinal chemistry. Some of them have received considerable attention as potential antimicrobial agents. Keeping in view the biological importance of isoxazoles, we herein report the synthesis and antibacterial activities of some new chlorosubstituted 4-aroyl isoxazoles.

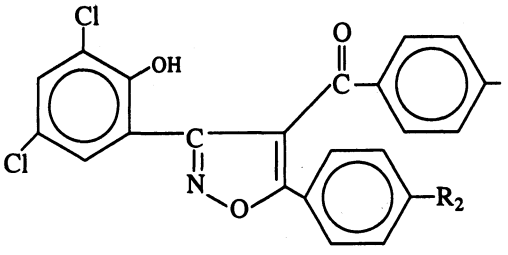
In the present work new chlorosubstituted 3-aroylflavone **(1a–d)** were allowed to reflux separately with hydroxylamine hydrochloride in DMSO containing a few drops of piperidine to get 3,5-diaryl-4-aroyl-isoxazoles **(2a–d).**

Structures of all the synthesized products have been established by elemental analysis, chemical propeties and spectral data. The compounds were screened for their antibacterial activity against different stains of bacteria.

A mixture of 3-aroylflavone (0.01 mol) and hydroxylaminehydrochloride (0.02 mol) in DMSO (20 mL) containing a few drops of piperidine was refluxed for 1.5 h. After cooling the reaction mixture was acidified with dil. HCl (1 : 1). The solid product thus obtained was recrystallized from ethanol-acetic acid mixture to get 4-aroyl isoxazole. It gives a dark brown colouration with neutral ferric chloride solution and dissolving in NaOH, thereby confirming the presence of free phenolic —OH group.



(1a-d)



(2a-d)

The spectral analysis of compound **(2c)** is as under:

IR (cm^{-1}) (nujol) show absorption bands at 3076 ν(OH), 1047 ν(>C=O), 1602 ν(>C=N), 1354 ν(C—O) and 827 ν(C—Cl). UV-Vis ($CHCl_3$) showed λ_{max} 370 nm corresponding to $n \rightarrow \pi^*$ transition. PMR ($CDCl_3$) showed 3.9 (s, 3H, Ar—OCH_3), 6.77–8.09 (m, 11H, Ar—H), 12.08 (s, Ar—OH).

Melting points were determined in open capillaries and are uncorrected. Purity of the synthesized compounds was checked by TLC on glass coated plates in the laboratory with silica gel G in benzene and CCl_4.

Similarly the other compounds **(2a–d)** were prepared.

Analytical and physical data of 3,5-diaryl-4-aroylisoxazoles **(2a–d)** is given in Table-1.

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF COMPOUNDS **(2a–2d)**

S. No.	R_1	R_2	m.f.	Yield (%)	m.p. (°C)	Nitrogen (%)	
						Found	Calculated
2a	—OCH_3	—OCH_3	$C_{30}H_{19}NO_5Cl_2$	75	180	3.00	3.05
2b	—H	—H	$C_{28}H_{15}NO_3Cl_2$	80	190	3.37	3.41
2c	—OCH_3	—H	$C_{29}H_{17}NO_4Cl_2$	70	197	3.10	3.18
2d	—H	—OCH_3	$C_{29}H_{17}NO_4Cl_2$	85	193	3.06	3.18

Antibacterial activity

All the newly synthesized compounds **(2a–d)** were screened for their antibacterial activity *in vitro* against *E. coli, S: aureus, B. subtilis* and *P. vulgaris* in dioxane medium at a concentration of 100 μg/mL using disc diffusion method[5] in nutrient agar-agar culture media.

The compounds (**2a** and **2d**) are found remarkably active against all the organisms. It may be due to the presence of —OCH_3 (methoxy) group in the nucleus.

However, the compounds (**2b** and **2c**) showed moderate activity against the organism *E. coli, S. aureus, P. vulgaris* but weak against *B. subtilis.*

The zones of inhibition of compounds (**2a–d**) are shown in Table-2.

TABLE-2
ANTIBACTERIAL ACTIVITIES OF COMPOUNDS (**2a–2d**)

Compound	*E. coli*	*B. subtilis*	*S. aureus*	*P. vulgaris*
2a	+++	++	+++	+++
2b	++	+	++	++
2c	++	+	+	+
2d	+++	++	+++	+++

+ = weak, ++ = moderate, +++ = strongly active.

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