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NOTE

Synthesis and Antimicrobial Activity of 3, 5-Diarylpyrazoles

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3,5-diarylpyrazoles having substituents on the aryl group were synthesized from diaryl-β-diketones by reaction with hydrazine hydrate and characterized by spectral studies. All the four synthesized compounds synthesized have been tested for their antimicrobial activity.

Key Words: Synthesis, Antimicrobial activity, 3,5-Diarylpyrazoles.

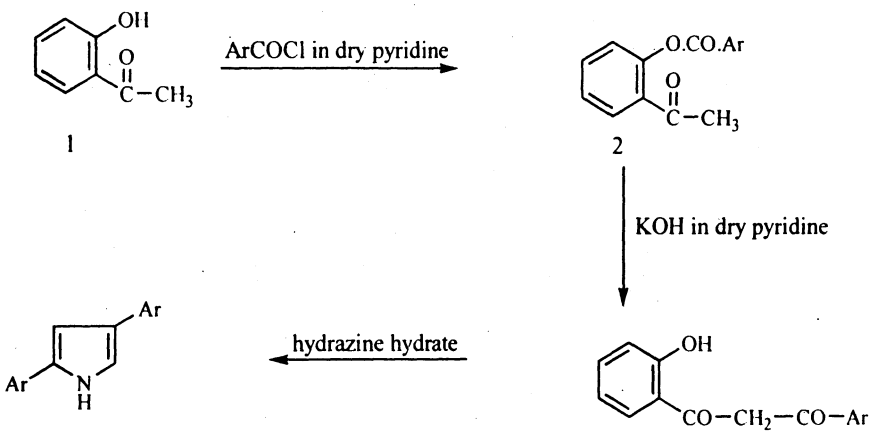
Pyarazole derivatives have attracted much attention during recent years because of their wide use in therapeutics[1-3]. They are used as anticancer agents[4] and certain alkyl pyrazoles have shown significant bacteriostatic, bactericidal and fungicidal activities[5, 6]. Pyrazoles having sulfanilamide moiety attached at different positions have been synthesized and reported to be active against *Staphylococcus aureus* and *Escherichia coli*[7]. The synthesis of pyrazoles having aryl-azo-grouping at position four have been reported[8] and found to exhibit antibacterial activity. Alkyl and aryl pyrazoles have pronounced sedative action on the central nervous system[9]. In view of these reports, it was considered worthwhile to synthesize some 3,5-diarylpyrazoles and screen them for their antimicrobial activity.

Melting points were determined on a Boietus micromelting point apparatus and are uncorrected. UV spectra were recorded using Shimadzu UV 1201. The IR spectra were recorded on a Perkin-Elmer FTIR 881. The ^{1}H-NMR spectra were taken in $CDCl_3$/DMSO-d_6 on a Bruker DRX 300 MHz. TMS was used as an internal standard and chemical shifts are reported in δ (ppm). Microanalysis values were obtained from CDRI, Lucknow.

The general scheme of preparation of these substituted pyrazoles involving O-aroylation of *o*-hydroxyacetophenones and subsequent Baker-Venkataraman rearrangement[10] followed by condensation of the resulting β-diketones with hydrazine hydrate **(Scheme-1).**

General method of preparation of diarylpyrazoles: A mixture of diaryl-β-diketone (0.01 M) and hydrazine hydrate (0.015 M) was refluxed in alcohol (15 mL) and acetic acid (3 mL) on a water bath for 4 h. After cooling the reaction mixture it was diluted and again refluxed for 1 h. The crystalline product obtained after keeping the reaction mixture for one day was filtered and crystallized from alcohol.

The compounds were purified either by simple crystallization or in some cases by column chromatography using silica gel (finer than 200 mesh). Silica gel-G coated plates were used for TLC. Iodine chamber and UV light were used for detection of spots on TLC plates.

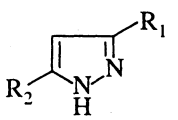


1 2

Scheme 1. Formation of 3,5-diarylpyrazoles from *o*-hydroxyacetophenone

The pyrazole derivatives synthesized were identified (Table-1) by elemental analysis and spectral data (UV, IR, ^{1}H-NMR, MS). The UV spectra for the compounds showed absorption maxima around 220 and 258 nm characteristic of pyrazole nucleus[11]. The IR spectra (KBr disc) of theses compounds showed absorption around 1600, 1555, 1470 and 1010 cm^{-1} which are characteristic of pyrazole ring stretching modes[12] (C=N and C=C). Absorption bands around 3200 cm^{-1} were observed for compounds which are characteristic of ν(N—H) stretching. The IR spectra also revealed absorption bands characteristic of ν(OH) and ν(NO_2) (symmetric and asymmetric) stretchings. In the ^{1}H-NMR spectra of all these compounds the pyrazole proton at C-4 was observed at δ 7.11 and the NH proton appeared at 9.07. The aromatic protons of the two-aryl groups substituted at 3 and 5 position of the pyrazole nucleus were observed in between 6.3–6.8 as multiplet integrating for the required 8 protons. The mass spectra of these compounds showed expected molecular ions and fragment ions[13]. The major fragmentation was found to occur by loss of HCN and N_2 + H as reported for pyrazoles[13]. Rearrangement of the fragment ions leads to the formation of the corresponding flourenyl cation, which characterizes the pyrazole derivatives[14].

TABLE-1
PYRAZOLE DERIVATIVES



Compounds	Substituents		m.f.	m.p. (°C)
	R_1	R_2		
I	C_6H_5	2,5-$C_6H_3(OH)_2$	$C_{15}H_{12}N_2O_2$	130
II	C_6H_5	2,4-$C_6H_3(OH)_2$	$C_{15}H_{12}N_2O_2$	122
III	3,5-$C_6H_3(NO_2)_2$	2,5-$C_6H_3(OH)_2$	$C_{15}H_{10}N_4O_6$	95
IV	3,5-$C_6H_3(NO_2)_2$	2,4-$C_6H_3(OH)_2$	$C_{15}H_{10}N_4O_6$	125

Antimicrobial activity: The antimicrobial activity of all the four compounds was tested by agar-cup plate method[15] at 0.05% concentration and compared with that of neomycin. Methanol was used as solvent to prepare the test solutions. From the results (Table-2) it may be seen that all the compounds were strongly active against the test organism *S. aureus*.

TABLE-2
ANTIMICROBIAL ACTIVITY (INHIBITION OF ZONE DIAMETER IN MM) OF PYRAZOLE DERIVATIVES **I–IV**

Compounds	*B. pumilis*	*B. subtilis*	*S. aureus*	*E. coli*	*Pseudomonas* species	*C. albicans*
I	14	12	18	16	15	16
II	15	12	17	15	15	14
III	15	15	19	16	14	16
IV	16	14	19	15	14	15
Neomycin	20	21	24	17	18	16

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