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NOTE

Synthesis of Some Substituted Pyrazoles and Isoxazoles as Antibacterial Agents

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A variety of novel substituted pyrazoles and isoxazoles have been synthesized by the reaction of 3-acetylchromone with various reagents: hydrazine hydrate, phenylhydrazine and hydroxylamine hydrochloride in different media and their antibacterial activity were screened.

Key Words: Substituted pyrazoles, Isoxazoles, Antibacterial activity.

A substituted azole unit is an essential pharmacophore of a number of antifungual[1], antibacterial[2] and various biological activities[3–5]. These observations have prompted us to synthesize some substituted pyrazoles and isoxazoles and screen them for their antibacterial activity.

Minimum inhibitory concentration of the compounds synthesized was determined against gram positive bacteria *S. aureus* and gram negative *P. aerugenosa* using disc diffusion method (Table-1).

Melting points were measured in open capillary and are uncorrected. IR absorptions were recorded on Perkin-Elmer R-32 and Varian XL-100, high resolution spectrophotometer. TLC was run on silica gel-G plate.

3-Acetyl-2-methylchromones **(IIa–c)** have been synthesized from a mixture of substituted 1,3-propanediones **(Ia–c)** (1 g) acetic anhydride (10 mL) and fused sodium acetate (2 g) on an oil both at 160°C for 30 min. After cooling, the mixture was poured in cold water. The structures were assigned on the basis of elemental and spectral analyses.

5-(2-Hydroxyphenyl)-4-acetyl-3-methyl-1-phenylpyrazole (IIIa–c)

A mixture of 3-acetyl-2-methylchromone **(IIa–c)** (0.01 mol) and phenylhydrazine (0.02 mol) in methanol (20 mL) or pyridine (20 mL) was refluxed separately for 3 h. After cooling the reaction mixture was diluted with water acidified with HCl. The solid product thus obtained was crystallized from ethanol (60–70% yield). IR (cm^{-1}): 3400–3060 ν(OH), 1680 ν(C=O), 1530 ν(C=N); besides these some other stretching and bending vibrations were observed. NMR in δ (ppm) 2.15 (s, 3H, heteroaromatic), 2.24 (s, 3H, Ar—CH_3), 2.58 (s, 3H, —$COCH_3$), 6.65–7.50 (m, 8H, Ar—H), UV λ_{max} 376 nm **(IIIa)**.

5-(2-Hydroxyphenyl-4-acetyl-3-methylpyrazoles (IVa–c)

A mixture of compound **(IVa–c)** (0.01 mol) and hydrazine hydrate (0.02 mol) in ethanol (20 mL) was refluxed separately for 1 h. On cooling, the reaction mixture was diluted with water to get products **(IVa–c)** with 55–60% yield. IR (cm^{-1}): 3360 ν(OH), 3040–3000 ν(NH), 1720 ν(C=O), 1590–1570 ν(C=N), PMR in δ (ppm)

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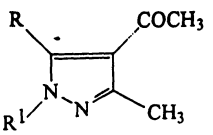
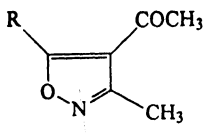
2.15 (s, H, Ar—CH_3), 2.16 (s, 3H, hetero Ar—CH_3), 2.10 (s, 3H, $COCH_3$), 6.85–7.25 (m, Ar—H), 9.5–11.5 (S, br, 1H, OH), 5.35 (s, br, 1H, N—H) **(IVa).**

5-(2-Hydroxyphenyl)-4-acetyl-3-methylisoxazoles (Va–c)

A mixture of compound **(IIa–c)** (0.01 mol) hydroxylamine hydrochloride (0.02 mol, 2 mL water) and NaOH in methanol (20 mL) or pyridine was refluxed separately for 3 h. It was then cooled and acidified with dilute HCl. An off white product thus obtained was crystallized in ethanol, with 70–75% yield. IR (cm^{-1}): 3300–3180 ν(br, OH), 1640 ν($COCH_3$), 1530 ν(C=N). The peak observed in PMR spectrum in δ (ppm): 1.62 (s, 3H, Ar—CH_3), 2.26 (s, 3H, hetroaromatic CH_3), 2.23 (s, 3H, $COCH_3$), 6.80–7.40 (m, 4H, Ar—H), UV λ_{max} 370 nm **(Va).**



III & IV a-c



V a-c

Compound	R	R′	
a	2-Hydroxy-5-methylphenyl	**IIIa–c**	Ph
b	2-Hydroxyphenyl	**IVa–c**	H
c	2-Hydroxy-4-methylphenyl		

TABLE-1

PHYSICAL DATA & ANTIBACTERIAL ACTIVITY OF SYNTHESIZED COMPOUNDS

S.No.	Compound	m.p. (°C)	*S. aureus*	*C. aerugenosa*
1.	**IIa**	113	10	12
2.	**IIb**	78	12	11
3.	**IIc**	92	9	10
4.	**IIIa**	180	11	11
5.	**IIIb**	180	11	10
6.	**IIIc**	103	12	12
7.	**IVa**	160	9	9
8.	**IVb**	85	11	10
9.	**IVc**	128	10	12
10.	**Va**	190	11	11
11.	**Vb**	212	10	10
12.	**Vc**	210	9	10

(Zone of inhibition in mm.)

REFERENCES

1. L.S. Goodman and A. Gillman, The Pharmacological Basis of Therapeutics, MacMillan, New York (1980).
2. P. Descaca, A. Nuhrich, M. Capdepuy and G. Devaux, *Eur. J. Chem.*, **25**, 285 (1990).
3. V.K. Ahluwalia and B. Mittal, *Indian J. Chem.*, **28B**, 150 (1989).
4. H.G. Garg and C. Prakash, *J. Med. Chem.*, **14**, 175 (1971).
5. A. Kabra, G.S. Saharia and N.R. Sharma, *J. Indian Chem. Soc.*, **54**, 508 (1977).

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