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NOTE

Synthesis and Antifungal Activity of Substituted 5- and 6-Hydroxy 3-Methyl-1,2-Benzisoxazoles

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In the present work authors report the synthesis and antifungal activity of substituted 5- and 6-hydroxy-3-methyl-1,2-benzisoxazoles.

Benzisoxazole derivatives are known to possess antiinflammatory[1], tuberculostatic[2], antibacterial and antifungal[3] activity. Some nitro and amino 1,2-benzisoxazoles have been found to show antitubercular activity[4]. Substituted 5-hydroxy-1,2-benzisoxazole (**1**) are not reported in literature so far. Therefore, a series of substituted 5/6-hydroxy-1,2-benzisoxazole have been synthesised.

5-Hydroxy-3-methyl-1,2-benzisoxazole (**1**) and 6-hydroxy-3-methyl-1,2-benzisoxazole (6) have been prepared from 2,5-dihydroxy acetophenone and 2,6-dihydroxy acetophenone respectively. Some bromo[5]-nitro[6]- and amino substituted 5- and 6-hydroxy-1,2-benzisoxazoles have been prepared following the known methods to study their biological activity.

Compound (**1**) is obtained from 2,5-dihydroxy acetophenone oxime which on treatment with acetic anhydride affords oxime acetate[7]. Cyclization of the latter gave 5-hydroxy-1,2-benzisoxazole. Some new benzisoxazoles have been synthesized by following this method (Table-1). Similarly 6-hydroxy-1,2-benzisoxazoles have been prepared from 2,6-dihydroxy acetophenone oxime acetate.

Melting points were taken in open capillaries and are uncorrected. The IR spectra (KBr) were recorded on a magna 550 series II, Nicolet, USA and NMR Bruker DR x-300 spectrometer.

General proceudre for the synthesis of compound (1)

2,5-Dihydroxy acetophenone oxime acetate (0.01 M) was refluxed with dry pyridine (15 mL) for about 4 h; excess pyridine was removed by distillation. The residue was poured over crushed ice containing dil. HCl. The compound obtained was washed with water and recrystallized in ethanol, m.p. 146°C (yield 68%). [Found (%): C, 64.10; H, 4.52; N, 9.24. $C_8H_7NO_2$ required (%): C, 64.42; H, 4.69; N, 9.39].

UV-VIS : λ_{max} 248 and 276 nm

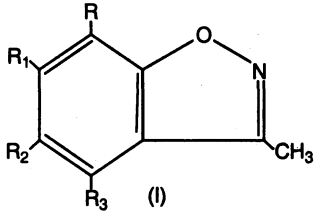
IR ν_{max} (cm^{-1}) : 3450 ν(OH), 1625–1640 ν(C=N), 1567–1600 (C=C), 800–830 cm^{-1} isoxazole ring Str.

NMR : δ 2.70 (S, 3H, —CH_3), 10.82 (S, 1H, —OH), 6–8 (S, 3H, aromatic proton)

TABLE-1
PHYSICAL DATA OF COMPOUND (1)

Compound No.	R	R_1	R_2	R_3	Yield (%)	m.p. (°C)
1.	H	H	OH	H	68	146
2.	H	H	OH	NO_2	48	201
3.	H	H	OH	NH_2	47	214
4.	H	H	OH	Br	72	198
5.	H	NO_2	OH	NO_2	49	239
6.	H	OH	H	H	67	164
7.	H	OH	NO_2	H	48	198
8.	H	OH	NH_2	H	49	222
9.	H	OH	Br	H	75	181
10.	NO_2	OH	NO_2	H	52	134

*C,H,N analysis is found to be satisfactory



(I)

Antifungal Activity

The synthesized compounds have been tested for their antifungal activity against *Sporotrichum polverolentun*, *Phenerochaete chirysosporium* and *Paecilomyces fusisporous* by liquid medium method[8, 9]. The compounds were tested at a concentration of 100 ppm against three organisms. Nystatin was used as standard: a known commercially available fungicide. 0.1 mL of solution containing compound is added to 9.9 mL of potato dextrose broth (sterilized by autoclaving). To all the tubes including standard and control the inoculum was added to concentration of 10%. After incubating all tubes at 25°C for 48 h, their absorbance was measured at 660 nm along with nystatin. Concentration of the micro-organism was determined and % inhibition was determined by comparing with control which was not containing any compound and was inoculated with organism. The results are recorded in Table-2.

TABLE-2
% INHIBITION DATA FOR ANTIFUNGAL ACTIVITY

Compound No.	*S. polverolentum*	*P. chirysosporium*	*P. fusisporous*
1.	50	45	45
2.	60	65	60
3.	70	75	70
4.	65	60	55
5.	45	45	50
6.	40	45	50
7.	70	50	70
8.	60	60	65
9.	50	70	55
10.	70	75	50
Standard	60	55	65

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