Asian Journal of Chemistry Vol. 5, No. 2 (1993), 352–357

Studies on Synthesis and Antimicrobial Activity of Some Flavonols

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Flavonols are synthesised from 1-(2'-hydroxy-simple/substituted phenyl)-3- (simple/substituted-1-naphthyl)-2-propene-1-ones by oxidation with alkaline hydrogen peroxide solution (Algar-Flynn-Oyamada reaction). These flavonols are characterised by elemental analysis and spectral study. All these compounds were screened for their antimicrobial activity against bacteria (*E. coli* and *S. aureus*) and fungi (*C. lunata* and *H. oryzae*). In few compounds the results are found to be encouraging.

INTRODUCTION

Chalcones have bactericidal[1–3], fungicidal[4], germicidal[5–8] activities. Flavonols are also found to possess some pharmacological properties. Some flavonols[9] are used as Lipoxygenase inhibitors, some are useful in the inhibition of ethoxy- and pentoxyresorfin dealkylases of rat liver[10]. Recently flavonols[11] like cataechins are found to be useful in the enhancement of sweetness and flavour of food drinks. By mixing the catechins to the chewing gum, it was found that above properties were enhanced.

As flavonols are the derivatives of chalcones having hydroxyl group, it is expected that these compounds may be active against some micro-organism like bacteria and fungi. Even the literature survey reveals that very little work is done on flavonols, which are having 1-naphthyl moiety at 2-position. Considering these facts few flavonols are synthesised expecting enhanced antimicrobial activity.

2'-Hydroxy chalcones on oxidation with alkaline hydrogen peroxide give flavonols[12–18]. This reaction is known as Algar-Flynn-Oyamada (AFO) reaction. Flavonols were prepared from 2'-hydroxy chalcones by treating their solutions in methanol with sodium hydroxide solution in ice-bath followed by hydrogen peroxide (20 vol.). The reaction mixture was kept in freezing mixture for 4–5 hrs, then at room temperature for overnight. On acidification of the reaction mixture, flavonols were isolated. These compounds give characteristic greenish yellow fluorescence in ethanolic solution as well as with conc. H_2SO_4 and brown colouration with ethanolic ferric chloride.

The purity of all these compounds was checked by TLC. The IR spectra of these compounds in nujol mulls showed a band in the region 1620–1650 cm^{-1}

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due to carbonyl group and a band in the region 3310–3480 cm^{-1} due to hydroxyl group.

The reaction scheme for the synthesis of flavonols is represented as in Fig. 1: where in flavonols,

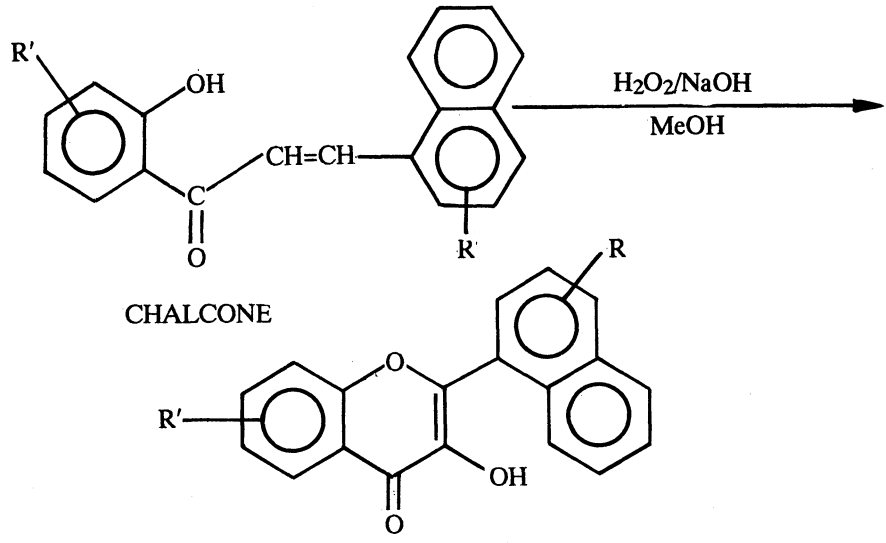

Fig. 1

R = H, 2′–OCH_3;

R′ = H, 6-Cl, 6-Br, 8Cl, 6,8-diCl_2, 6,8-diI_2

TABLE 1
CHARACTERISATION DATA OF 2-(SUBSTITUTED ARYL) FLAVONOL (Fig. 1).

Sl. No.	R′	R	M.pt.* C	Yield %	Mol. Formula	Elemental Analysis (%) Found/(Calcd.)		
						C	H	X
I	H	H	217	70	$C_{19}H_{12}O_3$	79.10 (79.17)	4.15 (4.17)	—
II	H	2′-OCH_3	239	66	$C_{20}H_{14}O_4$	75.50 (75.45)	4.45 (4.40)	—
III	6-Cl	H	204	68	$C_{19}H_{11}O_3Cl$	68.17 (68.09)	3.75 (3.96)	11.14 (11.01)
IV	6-Cl	2′-OCH_3	247	65	$C_{20}H_{13}O_4Cl$	—	—	10.12 (10.07)
V	8-Cl	H	202	65	$C_{19}H_{11}O_3Cl$	—	—	11.03 (11.01)
VI	8-Cl	2′-OCH_3	285	68	$C_{20}H_{13}O_4Cl$	—	—	10.03 (10.07)

TABLE 1 (Contd.)

Sl. No.	R′	R	M.pt.* C	Yield %	Mol. Formula	Elemental Analysis (%) Found/(Calcd.)		
						C	H	X
VII	6-Br	H	200	70	$C_{19}H_{11}O_3Br$	—	—	21.78 (21.80)
VIII	6-Br	2′-OCH_3	250	68	$C_{20}H_{13}O_4Br$	60.39 (60.45)	3.34 (3.27)	20.12 (20.15)
IX	6,8-diCl_2	H	250	60	$C_{19}H_{10}O_3Cl_2$	—	—	19.85 (19.89)
X	6,8-diCl_2	2′-OCH_3	210	58	$C_{20}H_{12}O_4Cl_2$	61.95 (62.02)	3.18 (3.10)	18.31 (18.35)
XI	6,8–diI_2	H	277	65	$C_{19}H_{10}O_3I_2$	–	–	47.45 (47.50)
XII	6,8–diI_2	2′-OCH_3	225	60	$C_{20}H_{12}O_4I_2$	–	–	44.50 (44.55)

*M.pt. uncorrected. All above compounds are recrystallised from ethanol.

Antimicrobial activity

All the synthesised compounds were studied for their antimicrobial (i.e. antibacterial and antifungal) activity.

For antibacterial activity the disc diffusion method[19] was employed against two organisms namely *Escherichia coli* and *Staphylococcus aureus*. The filter paper discs were soaked in the solutions of above compounds at a concentration of 150 ppm. in 10% ethyl alcohol and placed at the centre of the bacteria seeded agar plates (petri dishes). The petri dishes were incubated at 30 ± 1°C for 24 hrs. The strength is reported by measuring the diameter of zone of inhibition of mm. and the results are standardized against chloromycetin.

Similarly for antifungal activity two phytopathogens, e.g. *Curvularia lunata* and *Helminthosporium oryzae* were studied. The spore suspensions, prepared from five day old culture of *Curvularia lunata* and *Helminthosporium oryzae,* were used in germination studies by hanging drop method. Solutions of above synthesised compounds in 10% ethanol and their concentrations (150 ppm.) were adjusted in spore suspensions. Percentage germination and germ tube length with effect of these compounds after a period of 12 hrs. were recorded. Aqueous ethanol (90 : 10, v/v) served as control. From the observations it is found that halogen substituted flavonols were found more active compounds. Compound nos. IX and X and compound no. IX, X, XI & XII were found to be more inhibitory in action with bacteria and fungi respectively. The results of antimicrobial activity are presented in Table 2.

EXPERIMENTAL

Melting points are taken in open capillaries and are uncorrected. IR spectra

TABLE 2
ANTIMICROBIAL ACTIVITY OF 2-(SUBSTITUTED ARYL) FLAVONOLS (Fig. 1).

Sr. No.	R′	R	Antifungal activity: Germination (%) after 12 hrs.				Antibacterial activity (zone of inhibition in mm)	
			C. lunata		*H. oryzae*			
			% germination	length of germ tube (μ)	% germination	length of germ tube (μ)	*E. Coli*	*S. aureus*
I	H	H	100	450	100	490	Nil	Nil
II	H	2′-OCH_3	100	300	100	460	Nil	Nil
III	6-Cl	H	35	260	50	375	08	Nil
IV	6 -Cl	2′-OCH_3	95	250	90	300	13	07
V	8-Cl	H	85	310	95	480	18	13
VI	8-Cl	2′-OCH_3	90	320	100	500	22	14
VII	6-Br	H	80	300	70	325	10	Nil
VIII	6-Br	2′-OCH_3	100	400	100	450	12	Nil
IX	6,8-diCl_2	H	30	80	100	240	45	40
X	6,8- diCl_2	2′-OCH_3	20	90	35	130	46	38
XI	6,8-diI_2	H	40	90	95	250	15	10
XII	6,8-diI_2	2′-OCH_3	25	190	40	160	19	11
Control:			95.0	320	95.0	400		
Chloromycetin:							48	25

of these compounds were scanned by using Perkin-Elmer spectrophotometer in nujol mull (ν_{max} in cm^{-1}).

6,8-Dichloro-2-(2'-methoxy-1'-naphthyl) flavonol (X)

1-(2'-Hydroxy-3',5'-dichlorophenyl)-3-(2-methoxy-1-naphthyl)-2-propen-1-one (3.73 g, 0.01 mole) in methanol (25 ml) was treated with sodium hydroxide (10 ml, 5 per cent and the reaction mixture was kept in ice-bath. Then hydrogen peroxide (15 ml, 20 vol.) was added and the reaction mixture kept in ice-salt freezing mixture for about 4 hrs. and then at room temperature for overnight. The colour of the reaction mixture changed from dark red to deep yellow. It was then poured into ice-cold water and then acidified a light yellow coloured product was obtained. The crude product is recrystallized from ethanol, m.pt. 210, yield 58%; IR (nujol): 1620 cm^{-1} (C=O), 3320 cm^{-1} ν(OH), 1560–1675 cm^{-1} ν(C=C).

A similar method was used for the preparation of other members of the series. The characterisation data of these compounds is given in Table 1 (Fig. 1).

ACKNOWLEDGEMENTS

The authors are thankful to Shri N.C. Vardacharyulu, Principal, Yeshwant Mahavidyalaya, Nanded for providing necessary facilities. They are also thankful to Dr. M.S. Shingare, Deptt. of Chemistry, M.U., Aurangabad for spectral analysis and Dr. S.S. Wadje, Department of Botany, Yeshwant Mahavidyalaya, Nanded for biological testing of the compounds. One of the authors (GRS) is grateful to U.G.C., New Delhi for the award of the Teacher fellowship, to Shri K.S.P. Mandal of Udgir and Dr. P.G. Jadhav, Principal, Shivaji Mahavidyalaya, Udgir for deputation for research work.

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(*Received*: 1 October 1991; *Accepted*: 1 July 1992) AJC-444