Int. J. Chem. Sci. : 2 (1), 2004, 96–100

STUDIES ON SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW IODOCHALCONES, FLAVONES AND FLAVONOLS

S. S. MOKLE*, M. A. SAYYED, KOTHAWAR AND CHOPDE

P. G. Department of Chemistry, Yeshwant Mahavidyalaya, NANDED–431602 (M.S.) INDIA
E–mail: mokless@rediffmial.com

ABSTRACT

New iodo chalcones, flavones and flavonols were prepared and tested for their antimicrobial activity in vivo. Some of the compounds were found more active than tetracycline.

Key word : Antimicrobial activity, Flavone, Flavonol, Iodochalcone.

INTRODUCTION

Chalcones, flavones and flovonoids have been reported to possess various biological activities such as antibacterial[1-4], antifungal[5-7], antiviral[8-9], antifedent[10], anticancer[11] and antitumor[12]. The present communication reports the synthesis of some new iodochalcones, flavones and flavonols expecting their enhanced antimicrobial activities.

Different substituted–2'–hydroxyacetophenones on condensation with substituted aldehyde in ethanolic potassium hydroxide yielded the corresponding chalcones (**Ia–h**). The purity of all chalkones was checked by TLC. All the chalcones give pink colouration with concentrated sulphuric acid, positive Wilson test[13] and violet colouration with alcoholic ferric chloride solution. IR spectra of these chalcones showed bands at 1665–1610 (C=C conjugated) and 1630–1640 cm^{-1} (C=O).

Further chalcones (**Ia–h**) on heating with traces of iodine in dimethyl sulphoxide (DMSO) for 2 hrs gave the corresponding flavones (**IIa–h**). All these flavones didn't gave violet colouration with ferric chloride solution and pink colouration with concentrated sulphuric acid. The IR spectra showed a band near 1645 cm^{-1} (C=O).

Chalcones (**Ia–h**) were converted to the corresponding flavonols (**IIIe–h**) by their oxidation using hydrogen peroxide in methanolic sodium hydroxide solution. These flavonols gave characteristic greenish yellow fluorescence in ethanolic solution as well as with concentrated sulphuric acid. IR spectra of these flavonols showed bands at 1635–1655 cm^{-1} (C=O) and 3450 cm^{-1} (OH). Further structure of compounds have been supported by halogen analysis, and by PMR spectra of chalcone (**I**), flavone (**II**) and flavonol (**III**) as the representative cases.

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. The IR spectra (nujol) were recorded on a Perkin–Elmer spectrophotometer and PMR spectra ($CDCl_3$) on a Varian – 200 MHz spectrometer using TMS as internal standard.

1– (2'– hydroxy–5'– chloro–3'– iodophenyl)–3–(2–hydroxy–3, 5–diiodophenyl)–2–propen–1–one (Ia): In the solution of 2'–hydroxy–5'–chloro–3'–iodo acetophenone (0.01 mol) and 2–hydroxy–3, 5– diiodobenzaldehyde (0.01 mol) dissolved in ethanol (20–25 mL), aqueous potassium hydroxide solution 10% was added (10 mL) and reaction mixture was kept at 55°C for 14 hr. It was then diluted with water and acidified with concentrated HCl. The separated yellow solid was washed with cold water, dried and crystllised from glacial acetic acid; I.R. ν_{max} 1627 (C=O) and 1610 cm^{-1} (C=C); δ ($CDCl_3$) 10.2 (s, 1H, OH) and 6.8–8.4 (m, Ar–H & CH=CH). Similarly other compounds of the series were prepared.

6–chloro–8, 3',5'–triiodo–2'–hydroxy flavone (IIa): To the solution of chalcone **(Ia)**, in dimethylsulfoxide (10 mL) 2–3 crystals of iodine were added. Reaction mixture was refluxed for 2.30 hr. on wire guage. Then it was cooled and diluted with water. The separated solid was filtered, washed with cold water, dried and crystallised from dioxane. I.R. ν_{max} 1645 cm^{-1} (C=O) and 1325 cm^{-1} (γ – pyrone ring); PMR δ ($CDCl_3$) 6.63 (s, 1H, 3H), 7.6–8.4 (m, 4H, Ar H.). Similarly the compounds of the series were prepared.

6–chloro–3–hydroxy–8–iodo–4'–methoxy flavone (IIIa): To the solution of chalcone **(Ib)** 0.01 mol in methanol (15–20 mL) was treated with sodium hydroxide (5–10 mL; 5%) and the reaction mixture was cooled in ice bath. H_2O_2 (5–7 mL; 20 vol) was then added and the reaction mixture was kept in ice salt freezing mixture for 3 hr. and the kept for overnight at room temp. It was then diluted with cold water and acidified with HCl (1: 1). The resulting yellowish solid was washed with water, dried and recrystallised from dioxane I.R. ν_{max} 1630 cm^{-1} (C=O) and 3370 cm^{-1} (OH), PMR δ ($CDCl_3$) 5.85 (s, 1H, 3–OH) 3.95 (s, 3H, $COCH_3$) 6.95–8.12 (m, 6H, Ar H). Similarly other compounds of the series prepared (Table 1).

Antimicrobial activity

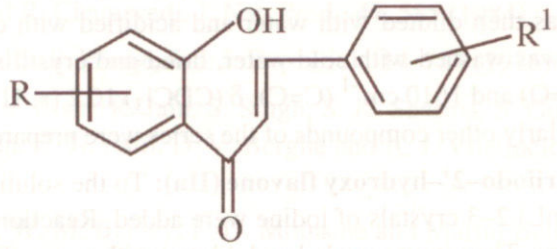
All the compounds were tested for their antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus* following disc diffusion method[14]. The compounds were tested at 150 ppm concentration using solvent DMSO and 5 mm filter paper discs. Under similar conditions, control experiment was carried out using tetracycline as standard for comparison. The area of inhibition zone was measured in mm. Some of the chalcones were found to be more active than tetracycline where as flavone and flavonols were less active than tetracycline (Table 1).

RESULTS

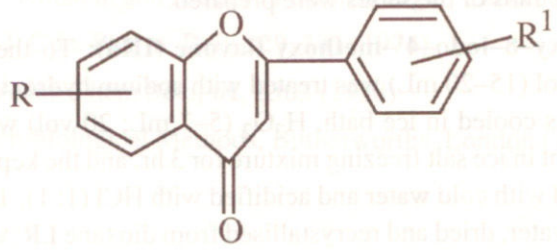
Table 1 shows that all the chalcones are having lower M.P. than respective flavone and flavonol. Further it shows that flavonols are having higher M.P. than respective flavones.

ACKNOWLEDGEMENT

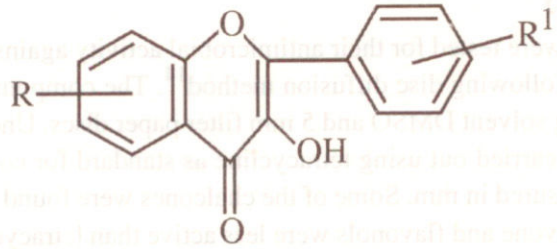
The authors are thankful to Dr. Y. B. Vibhuate for his keen interest and Principal, Yeshwant Mahavidyalaya, Nanded for providing necessary facilities.



(I)



(II)



(III)

Table 1. Physical and biological activity data of compounds I–III.

Compound No.	R	R^1	M.P. (°C)	Molecular Formula	Halogen analysis % found	(required)	Antimicrobial activity zone of Inhibition in mm	
							E. coli	S. aureus
Ia	2'–OH, 5'–Cl 3'–I	2–OH,3,5–I	200	$C_{15}H_8O_3I_3Cl$	63.83	(63.43)	30	19
Ib	2'–OH, 3'–I, 5'–CH_3	2–OH,3,5–I	210	$C_{16}H_{11}O_3I_3$	60.28	(59.80)	20	11
Ic	3'–I, 4'–CH_3 2'–OH, 5'–Cl	2–OH,3,5–I	205	$C_{16}H_{10}O_3I_3Cl$	62.49	(62.09)	15	12
Id	2'–OH, 3', 5'–I	2–OH,3,5–I	220	$C_{15}H_8O_3I_4$	68.27	(67.87)	18	16
Ie	2'–OH, 3'–I, 5'–CI	4–OCH_3	150	$C_{16}H_{12}O_3ClI$	39.20	(38.80)	33	24
If	2'–OH, 3'–I 5'–CH_3	4–OCH_3	155	$C_{17}H_{15}O_3I$	32.23	(31.83)	29	19
Ig	2'–OH, 3'–I, 4'–CH_3,,5'–Cl	4–OCH_3	170	$C_{17}H_{14}O_3ClI$	37.92	(37.52)	32	23
Ih	2'–OH, 3', 5'–I	4–OCH_3	190	$C_{16}H_{12}O_3I_2$	50.19	(49.79)	19	15
IIa	6'–Cl,8–I	2'–OH,3', 5'–I	220	$C_{15}H_6O_3I_3Cl$	64.02	(63.62)	16	11
IIb	8–I, 6–CH_3	2'–OH,3', 5'–I	260	$C_{16}H_9I_3O_3$	60.47	(60.07)	20	15
IIc	8–I, 7–CH_3, 6–Cl	2'–OH,3', 5'–I	231	$C_{16}H_8O_3I_3Cl$	62.67	(62.27)	21	14
IId	6,8–I	2'–OH,3', 5'–I	276	$C_{15}H_6O_3I_4$	68.46	(68.06)	17	12
IIe	8–I, 6–Cl	4'–OCH_3	165	$C_{16}H_{10}O_3ICl$	39.39	(38.99)	19	13
IIf	8–I, 6–CH_3	4'–OCH_3	171	$C_{17}H_{13}O_3I$	32.39	(31.99)	21	15
IIg	8–I, 7–CH_3, 5–Cl	4'–OCH_3	160	$C_{17}H_{12}O_3ICl$	38.10	(37.70)	22	12
IIh	6,8–I	4'–OCH_3	220	$C_{16}H_{10}O_3I_2$	50.39	(49.99)	15	14
IIIe	3–OH, 8–I, 6–Cl	4'–OCH_3	245	$C_{16}H_{10}O_4ICl$	37.92	(37.52)	23	13
IIIf	3–OH, 8–I, 6–CH_3	4'–OCH_3	203	$C_{17}H_{13}O_4I$	31.12	(30.72)	20	06
IIIg	3–OH, 8–I, 7–CH_3, 6–Cl	4'–OCH_3	180	$C_{17}H_{12}O_4ClI$	36.72	(36.32)	18	16
IIIh	3–OH, 6, 8–I	4'–OCH_3	210	$C_{16}H_{10}O_4I_2$	48.84	(48.44)	17	10
	Tetracycline	———	———	———	———	———	27	18

REFERENCES

1. Hung–Wen–Lin, Takenorl Kusnmi and Kolnishi K., J. Chem. Soc. Chem. Commun. 1271 (1981)
2. V. K. Ahluwalia, N. Kalia and S. Bala, Indian J. Chem., **25B**, 663 (1986).
3. V. K. Ahluwalia, R. R. Mann and S. Bala, Indian J. Chem, **28B**, 608 (1989).
4. J. Mathew, A. V. Subbrao and S. Rambhav, Curr. Sci., **53**, 576 (1984).
5. Mizabuchis and Satoy, Agric. Biol. Chem., **48**, 2771 (1984).
6. D. S. Bhakuni and R. Chaturvedi, J. Nat. Prod., **47**, 585 (1984).
7. Y. B. Vibhute and S. S. Wadje, Ind. J. Exp. Biol., **14**, 724 (1976).
8. V. S. Parmat, K. S. Bisht, R. Jain, S. Singh, S. K. Sharma, S. Gupta, S. Malhotra, O. D. Tyagi, A. Vardhan, H. N. Patil, D. V. Berghe and A. J. Vlietincic, Indian J. Chem., **35B**, 220 (1996).
9. M. S. Simmonds, W. M. Blaney, F. D. Monache and Marini Bettolo, J. Chem. Ecol., **16** 365 (1996).
10. Middleton (Jr.) and H. Drezewiecki, Biochem. Pharma. Col., **33**, 3333 (1984).
11. M. Schwenolt; W. Kittstein and Murk F. Fuerslenberger, Cancer Lett. **25**, 177 (1984).
12. J. C. Dore and C. J. Cile, Pharm. Belg., **29**, 341 (1974).
13. C. W. Wilson, J. Asian Chem Soc., **61**, 2303 (1938).
14. C. H. Collins, Microbiological Methods, Butherworths, London (1967), p. 364.

Accepted : 10.11.2003