Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Der Pharmacia Lettre, 2013, 5 (2):101-104
(http://scholarsresearchlibrary.com/archive.html)

Der Pharmacia Lettre
Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Synthesis and antimicrobial activity of some new chalcones of pyridine/pyrrole carboxaldehyde

Seema I. Habib* and Praffullkumar A. Kulkarni

P.G. Department of Chemistry and Organic Research Laboratory, Yeshwant Mahavidyalaya, Nanded

---

ABSTRACT

A series of 1, 3-diaryl-2-propene-1-ones have been synthesized by using Claisen-Schmidt condensation method in alkaline solution. The structures of the products were confirmed by spectral analysis (IR, ^1H NMR and Mass). All the newly synthesized compounds were screened for their antibacterial and antifungal activity.

Keywords: Chalcone, spectral analysis, antimicrobial activity

---

INTRODUCTION

1,3-Diaryl-2-propenones (chalcones) belong to flavanoid family, have displayed an impressive array of biological activities, among which anti-malarial[1], anti-cancer[2,3], anti-tuberculosis[4], cardiovascular[5], anti-leishmanial[6], anti-mitotic[7], anti-hyperglycemic[8], nitric oxide inhibition[9,10], anti-inflammatory[11], tyrosinase inhibition[12], activities have been reported. Chalcones are also key precursors in the synthesis of many biologically important heterocycles such as benzothiazepine[13], pyrazolines[14], 1, 4-diketones[15], and flavones[16] . Thus the synthesis of chalcones has generated vast interest to organic as well as for medicinal chemist. The presence of a reactive α-β unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic rings In view of these observations it was thought to synthesize some new series of chalcone derivatives.

MATERIALS AND METHODS

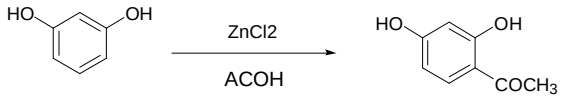
All the melting points were determined in an open capillary tube and are uncorrected. Completion of the reaction was monitored by thin layer chromatography on pre-coated sheets of silica gel-G. IR spectra were recorded on FTIR Shimadzu (in KBr cm^{-1}) spectrometer. PMR spectra were recorded in DMSO-d^6 on Avanve-300 MHz spectrometer using TMS as an internal standard. The mass were recorded on EI-Shimadzu-GC-MS spectrometer.

Synthesis of 2, 4-dihydroxy Acetophenone

Freshly prepared anhydrous Zinc chloride 100 gm was dissolved by refluxing in 50 ml of glacial acetic acid. Hot solution of Zinc chloride was added in 50 gm of resorcinol taken in 1000 ml beaker.

Reaction mixture was heated on sand bath till solution become wine red. Reaction beaker was removed and kept on asbestos pad for 10-15 minutes and to this solution 1:1 hydrochloric acid 50ml was added with stirring and beaker kept overnight. Orange crystals separate out. It is crystallized from 10% HCl.

Scheme-1



2, 4-dihydroxy Acetophenone
(Res-Acetophenone)

General procedure for the synthesis of 2'-hydroxychalcone derivatives (3a-f)

A mixture of substituted acetophenone (0.01mol), aromatic carboxaldehyde (0.01mol) and NaOH (0.02mol) were dissolved in methanol solution. The reaction mixture was heated for 2-3 hr. The progress of the reaction was monitored by TLC. After completion of the reaction the contents were poured in ice water and then acidified by dil. HCl. The solid obtained was filtered, washed with cold water. Then crude product was crystallized from ethanol to give the corresponding product.

Scheme-2

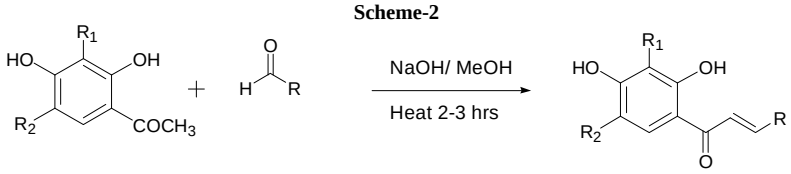
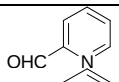
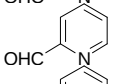
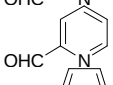
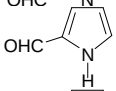
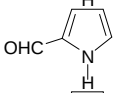
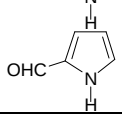


Table-1: Physico-chemical data of chalcones containing pyridine and pyrrole moiety.

Sr.no.	Product	R_1	R_2	R	Molecular Formula	Yield %	M.P ºC
1	Ia	H	H		$C_{13}H_{11}O_3N$	84	143
2	Ib	Br	Br		$C_{13}H_9O_3Br_2N$	66	137
3	Ic	I	I		$C_{13}H_9O_3I_2N$	82	188
4	IIa	H	H		$C_{14}H_{12}O_3N$	74	160
5	IIb	Br	Br		$C_{14}H_{10}O_3Br_2N$	80	156
6	IIc	I	I		$C_{14}H_{10}O_3I_2N$	78	192

Spectral data of some selected compounds:

(Ia): IR (KBr): 3136 (-OH), 1648 (>C=O), 1596 (C=C) cm^{-1}; ^1H NMR (DMSO-d^6): δ 6.91-8.68 (m, 9H, Ar-H +CH=CH), δ 12.62 (s, 1H, OH) ppm; M.S (m/z): 230 (M+).

(Ib): IR (KBr): 3088 (-OH), 1652 (>C=O), 1620 (C=C) cm^{-1}; ^1H NMR (DMSO-d^6): δ 7.31-8.65 (m, 8H, Ar-H +CH=CH), δ 13.22 (s, 1H, OH) ppm; M.S (m/z): 390 (M+).

(Ic): IR (KBr): 3067 (-OH), 1656 (>C=O), 1624 (C=C) cm^{-1}; ^1H NMR (DMSO-d^6): δ 7.28-8.68 (m, 8H, Ar-H +CH=CH), δ 13.45 (s, 1H, OH) ppm; M.S (m/z): 484 (M+).

(IIa): IR (KBr): 3156 (-OH), 1650 (>C=O), 1608 (C=C) cm^{-1}; ^1H NMR (DMSO-d^6): δ 7.35–7.55 (m, 8H, Ar-H +CH=CH), δ 12.38 (s, 1H, OH) ppm; M.S (m/z): 242 (M+).

Antimicrobial activity:

The antibacterial activity of the compounds was determined by agar diffusion method against various bacteria like *E.coli, S. typhi, S. aureus, and B. subtilis* at various concentrations such as 20, 50and 100 µg /ml. The zone of

inhibition was measured in mm and DMSO was used as solvent. Sterile nutrient agar was seeded with test organism and layered in sterile petri plate. After solidification, agar cups were borered with cork borer 0.1 ml of the compound solution was added to the cup with the help of micropipettes, one cup in the plates was filled with solvent. Standard penicillin (10v/ml) was used as reference drug. The plates were kept at low temperature (4°C) for 20 minutes to allow diffusion of the compound. Then the plates were incubated at 37 °C for 24 hr. After proper incubation the plates were observed for zone of no growth (zone of inhibition of growth) around the cup. Similarly the same compounds were screened for the antifungal activity against different organisms like *P.chrysogenum*, *A. niger*, *F. moniliformae*, and *C.albicans* by using poison plate method. The compound was mixed with sterile potato dextrose agar medium so as to get final concentration 2%. It was then poured in sterile petri plate and allowed to solidify. Spots of test organisms were placed on the agar surface. A plate without compound was prepared for control. The plates were incubated at room temperature for 48 hr. After proper incubation plates were observed for growth of the test organisms. The growth indicates that the compound is not antifungal while inhibition of growth of test organism indicates antifungal activity. The antifungal activities of the compounds were compared with standard grysofulvin.

Table 2 Antimicrobial activity of synthesized compounds

Product	Bacterial strain				Fungal Strain			
	Ec	St	Sa	Bs	An	Pc	Fm	Ca
Ia	19	12	32	30	-ve	-ve	-ve	-ve
Ib	17	22	20	17	+ve	-ve	-ve	+ve
Ic	--	17	22	15	+ve	RG	-ve	+ve
IIa	15	18	25	11	-ve	-ve	-ve	+ve
IIb	16	13	30	--	-ve	-ve	RG	-ve
IIc	--	11	18	21	-ve	+ve	+ve	-ve
Penicillin	18	20	32	28	NA	NA	NA	NA
Grysofulvin	NA	NA	NA	NA	-ve	-ve	-ve	-ve

Ec-E.coli, St-S.typhi, Sa- S.aureus, Bs-B.subtilis; An-A.niger, Pc-P.chrysogenum, Fm-F.moneliformae, Ca-C.albicans; -ve: No growth of fungi,+ve: Growth of fungi, RG-Reduced growth, NA-Not Applicable, Zone of inhibition was measured in mm.

RESULTS AND DISCUSSION

In this present paper, a series of various substituted chalcones were synthesized by the condensation of substituted acetophenones with pyridine-2-carboxaldehyde/pyrrole-2-carboxaldehyde in alkaline (NaOH) methanolic solution (Scheme-1 and Table-1). The products were confirmed by their spectral analysis. Appearance of IR bands at 3136-3156 (-OH) and 1648-1656 cm^{-1} (>C=O) supported the structure. ^1H NMR spectra, the multiplate around the δ 6.91-8.68 ppm assigned to the aromatic protons. The phenolic proton appeared as singlet at δ 12.62-13.45 ppm, while other aliphatic protons are appeared at expected regions. The mass spectra of the compounds were showed corresponding molecular ion peak which was correlated with their molecular weight of that respected compound. The results of antimicrobial data are given in Table-2. The data revealed that all the compounds were found to be active against S. aureus and S. typhi. Only Compounds Ia compound showed inhibition of growth against all the tested fungi. Compound Ic and IIb showed reduced growth against one or more pathogens.

CONCLUSION

In summary, we have synthesized some novel hetero chalcones having pyridine/pyrrole moiety. All the synthesized compounds gave satisfactory spectral and analytical data. The screening of antimicrobial data revealed that compounds with pyridine nucleus showed much activity than pyrrole.

Acknowledgement
The authors are thankful to Principal, Yeshwant Mahavidyalaya, Nanded for providing laboratory facilities and also to the Director, IICT, Hyderabad for providing the instrumentation facilities.

REFERENCES

[1] M. Liu , P. Wilairat P., M. L. Go, *J. Med. Chem*., **2001**, 44, 4433.
[2] M. L. Edwards, D. M. Stemerick, P. S. Sunkara, *J. Med. Chem*., **1990**, 33, 1948.
[3] F. Bois, C. Beney, A. Boumendjel, A. M. Mariotte, G. Conseil, A. Di. Pietro , *J. Med. Chem*., **1998**, 41,4161.
[4] Y.-M. Lin, Y. Zhou, M. T. Flavin, L.-M. Zhou, W. Nie, F.- C. Chen, *Bioorg. Med. Chem*., **2002** 10, 2795.

[5] C. Furman, J. Lebeau, J.-C. Fruchart, J. -L. Duriez, P. N. Cotelle, E. J. Teissier, *Biochem. Mol. Toxicol*., **2001**, 15,270.
[6] S. F. Nielsen, S. B. Christensen, G. Cruciani, A. Kharazmi, T. Liljefors, *J. Med. Chem.* **1998**, 41,4819.
[7] S. Ducki, R. Forrest, J. A. Hadfield, A. Kendall, N. J. Lawrence, A. T. McGown, D. Rennison, *Bioorg. Med. Chem. Lett*.,**1998**, 8,1051.
[8] M. Satyanarayana, P. Tiwari, B. K. Tripathi, A. K. Srivastava, R. Pratap, *Bioorg. Med. Chem*., **2004**, 12, 883.
[9] F. Herencia, M. L. Ferrandiz, A. Ubeda, I. Guillen, J. N. Dominguez, J. E. Charris, G. M. Lobo, M. J. Alcaraz, *Free Rad. Biol. Med*., **2001**, 30, 43.
[10] J. Rojas, M. Paya, J. N. Dominguez, M. Luisa Ferrandiz, *Bioorg. Med.Chem. Lett*., **2002**, 12,1951 .
[11] F. Herencia, M. L. Ferrfandiz, A. Ubeda, J. N. Dominguez, J. E. Charris, G. M. Lobo, M. J. Alcaraz, *Bioorg. Med. Chem. Lett*., **1998**, 8, 1169.
[12] E. B. Yang, Y. J. Guo, K. Zhang, Y. Z. Chen, P. Mack, *Biochim. Biophys. Acta*, **2001**, 144–152,1550.
[13] O. Prakash, A. Kumar, A. Sadana, R. Prakash, P. S. Singh, M. R. Claramunt, D. Sanz, I. Alkortac, Elgueroc *J*., *Tetrahedron*., **2005**, 61, 6642.
[14] R. Y. Prasad, L. A. Rao, L. Prasoona, K. Murali, R. P. Kumar, *Bioorg. Med.Chem. Lett*., **2005**, 15, 5030.
[15] S. Raghavan, K. Anuradha, *Tetrahedron Lett*., **2002**, 43, 5181.
[16] B. A. Bohm, Introduction to Flavonoids, *Harwood Academic, Amsterdam*, (**1998)**.