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Synthesis, Characterization and Microbial Activities of Novel Acetylthiophene Chalcone Derivatives

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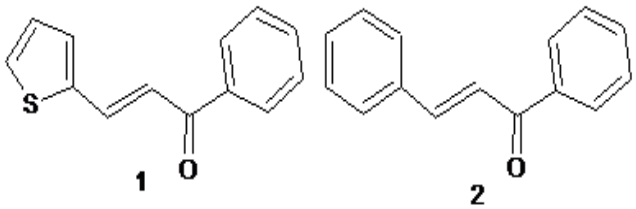
Abstract: ***Synthesis of Chalcones from acetylthiophene with substituted aromatic aldehyde in dilute ethonolic sodium hydroxide at cool condition reaction followed by Claisen – Schmidt condensation method. The resulting compounds were characterised by IR, ^{1}HNMR, ^{13}CNMR spectral studies and elemental analysis. The synthesized compounds were screened for their antibacterial and antifungal activities by disc diffusion method. The antibacterial and antifungal activity was evaluated against Klebsiella aerogenes, Proteus Vulgaris, Mucor racemosus, Aspergillus flavous and Aspergillus fumigatous(fungal strain) using Ciprofloxacin and Nystatin as the standard drug for bacteria and fungus respectively. The preliminary in antibacterial and antifungal screening of the chalcone derivatives PI – PV compounds showed potent activity.***

Keywords: Chalcones, Acetylthiophene, Disc diffusion.

1. Introduction

Chalcones are synthesized by Claisen – Schmidt condensation of aldehyde and ketone by base catalyzed followed by dehydration to yield chalcones [1]. The synthesis of chalcone compounds incorporating with heterocyclic become the great importance in medicinal chemistry (2, 3). The hetero atom products variety of application in the biological engineering and in other field of their specific structure(4). To the best of our knowledge acetylthiophene involving different substituted aldehyde under basic condition reaction is unprecented. In continuation of our interest to developing novel synthetic methodologies and use of chalcones for organic synthesis.

The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial [5], anti-inflammatory [6], analgesic [7], antiulcerative [8], antimalarial [9], anticancer [10], antiviral [11] and antioxidant[12] activities. Antifungal activity of chalcones has been investigated by a number of researchers [13]. Elemental sulfur has long been known to act as an antibacterial agent[14]. Sulfur is present in antifungal agents of natural origin, e.g., *Allium sativum* (garlic), which is known to inhibit *Candida albicans*. The present work indicates that, when a thiophene ring was incorporated into a chalcone structure, the molecule exhibited antifungal activity [15].



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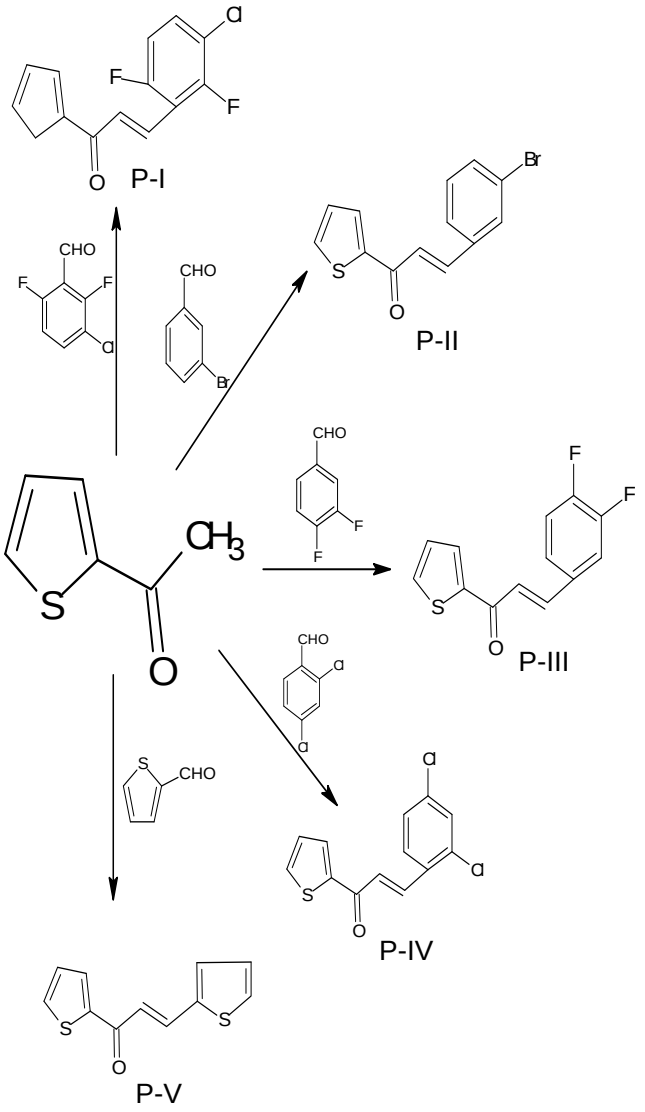
The compound(1) was found to have activity against *Candida albicans* at concentration of 25 mg/ml while the compound(2) was inactive at 400mg/ml.

2. Materials and Methods

The melting point of the compounds was determined in open capillaries, using Eligo digital melting point apparatus and expressed in degree Celsius and the values were uncorrected. IR spectra of the compounds were recorded on Shimadzu 8201 spectrophotometer using KBr and the values are expressed in 4000-400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV 400 MHz Spectrophotometer using TMS as an internal standard and the values are expressed in δ ppm. All the solvents used were analytical grade. The purity of the compound was checked by TLC using silica gel plates.

2.1 General procedure for synthesis of Chalcones:

Equimolar quantity of 2-Acetylthiophene (0.01 mol) and substituted aromatic aldehyde (0.01 mol) were dissolved in 20 ml of ethanol was cooled to 5-10^{0}C in an ice bath. The reaction mixture was magnetically stirred for 3h.In the cold solution, 10 ml of 10% Sodium hydroxide solution was added drop wise. A flocculants precipitate was formed. The precipitate was filtered and washed with cold water and recrystallise from ethanol.



2.2 Antibacterial Activity

The purified products were screened for their antibacterial activity by using disc diffusion method. The nutrient agar broth prepared by the usual method, was inoculated aseptically with 0.5 ml of 24 hr old subculture of *Staphylococcus aureus* and *Escherichia coli* in separate conical flask at 40^0-50^0C and mixed well by gentle shaking. About 25 ml of the contents of the flask were poured and evenly spread in Petridis (90 mm in diameter) and allowed to set for two hrs. The cups (8mm in diameter) were formed by the help of borer in agar medium and filled with 0.1 ml (1 mg/ml) solution of sample in acetone.

2.3 Antifungal Activity

Aspergillus niger was employed for testing antifungal activity by disc diffusion method. The culture was maintained on Sabouraud dextrose agar slants. Sterilized Sabouraud dextrose agar medium was inoculated with 72 hr old 0.5 ml suspension of fungal spores in a separate flask. About 25 ml of the inoculated medium was evenly spreader in a sterilized Petridis and allowed to set for 2 hr. The cups (8 mm in diameter) were punched in Petridis and loaded with 0.1 ml (2 mg/ml) of solution of sample in acetone. The plates were incubated at 20 – 250^0C for 72 hr. After the completion of incubation period, the zones of inhibition growth is in the form of diameter in mm was measured. Along the test solution in each Petridis one cup was filled up with solvent which acts as control.

3. Results and Discussion

The results are obtained using various spectral data. The results discussed are given below.

PI - (2*E*)-3-(3-chloro-2,6-difluorophenyl)-1-(cyclopenta-1,3-dien-1-yl)prop-2-en-1-one:

Mp: 176^0C. IR (KBr) cm^{-1}: 3527 (ArC-H_{str}), 2924 (C-H_{str} thiophene), 2854(C-H_{str} alkene), 1743 (C=O_{str}), 1651 (C=C_{str}), 1321 (C-F_{str}), 802 (C-H_{def}) and 677 (C-Cl_{str}). ^{1}H NMR (DMSO) ppm; 7.1-7.6 (Ar), 7.7 (H_β =CH-Ar), 6.6 (H_α –CO-C=). ^{13}C NMR ($CDCl_3$)ppm: 181 (-CO-), 128-134 (Ar), 145 (C_β), 112 (C_α).

PII - (2*E*)-3-(3-bromophenyl)-1-(thiophen-2-yl)prop-2-en-1-one

Mp: 157^0C. IR (KBr) cm^{-1}: 3446 (ArC-H_{str}), 2924 (C-H_{str} thiophene), 2854(C-H_{str} alkene), 1745 (C=O_{str}), 1649 (C=C_{str}), 671 (C-Br_{str}) and 889 (C-H_{def}). ^{1}H NMR (DMSO) ppm; 7.0-7.6 (Ar), 7.7 (H_β =CH-Ar), 6.8 (H_α –CO-C=). ^{13}CNMR ($CDCl_3$) ppm: 127-142 (Ar), 181 (-CO-), 145(C_β), 122 (C_α).

PIII – (2*E*)-3-(3,4-difluorophenyl)-1-(thiophen-2-yl)prop-2-en-1-one

Mp: 168^0C. IR (KBr) cm^{-1}: 3516 (ArC-H_{str}), 2924 (C-H_{str} thiophene), 2856(C-H_{str} alkene), 1805 (C=O_{str}), 1651 (C=C_{str}), 1473 (C-F_{str}) and 835 (C-H_{def}). ^{1}H NMR (DMSO) ppm; 7.4-7.7 (Ar), 7.3 (H_β =CH-Ar), 6.9 (H_α –CO-C=). ^{13}C NMR; ($CDCl_3$)ppm: 181 (-CO-),126-140 (Ar), 145 (C_β) 124 (C_α),

PIV - (2*E*)-3-(2,4-dichlorophenyl)-1-(thiophen-2-yl)prop-2-en-1-one

Mp: 172^0C. IR (KBr) cm^{-1}: 3454 (ArC-H_{str}), 2922 (C-H_{str} thiophene), 2854(C-H_{str} alkene), 1743 (C=O_{str}), 1649 (C=C_{str}), 979 (C-S_{str}), 734 (C-H_{def}), and 675 (C-Cl_{str}). ^{1}H NMR (DMSO) ppm; 8 (H_β =CH-Ar), 7.3-7.7 (Ar), 7.2 (H_α – CO-C=). ^{13}C NMR; ($CDCl_3$)ppm: 129-138 (Ar), 192 (-CO-), 143 (C_β),128 (C_α).

PV – (2*E*)-1,3-di(thiophen-2-yl)prop-2-en-1-one

Mp: 167^0C. IR (KBr) cm^{-1}: 2924 (C-H_{str} thiophene), 2854(C-H_{str} alkene), 1743 (C=O_{str}), 1635 (C=C_{str}), 974 (C-S_{str}), 889 (C-H_{def}) and 731(C-H_{def}). ^{1}H NMR (DMSO) ppm; 7.8 (H_β =CH-Ar), 7.0-7.7 (Ar), 6.9 (H_α –CO-C=). ^{13}C NMR; ($CDCl_3$) ppm: 181 (-CO-), 145 (C_β), 128-134 (Ar), 120 (C_α).

4. Antimicrobial Screening

In antibacterial activity of chalcone derivatives (PI – PV) were carried out using culture of *Klebsiella aerogenes* and *Proteus Vulgaris* by the disc diffusion method and the minimum inhibitory concentration (MIC) of these compounds were determined. Ciprofloxacin was used as the standard drug, where as dimethyl sulphoxide (DMSO) as solvent. The minimum inhibitory concentration (MIC) was evaluated by the micro dilution method of test compounds. The bacterial studies showed that the compounds PIII was

more active against *Klebsiella aerogenes*. Compound PV was better antibacterial activity against *klebsiella aerogenes*.

In antifungal activity of chalcone derivatives (PI – PV) were carried out using the culture of *Mucor racemosus*, *A. flavous* and *A. fumigatous* by the disc diffusion method and the MIC of these compounds were determined. *Nystatin* used as the standard drug. The compound PV shows high(35mm) antifungal activity against aspergillus fumigatous than other compounds (PI – PV)

Table 1: Antimicrobial activity of the synthesized compounds PI – PV

S. No	*Name of the Microorganisms*	*Zone of inhibition in mm*						
		P I	*P II*	*P III*	*P IV*	*P V*	*Solvent control*	*Std*
1.	*Klebsiella aerogenes* (NCIM 2098)	12	10	16	14	15	-	30
2.	*Proteus Vulgaris* (NCIM 2027)	10	10	16	11	14	-	26
3.	*Mucor racemosus* (NCIM 108)	15	16	16	22	26	-	30
4.	*Aspergillus flavous* (ATCC 204304)	12	22	20	30	32	-	32
5.	*Aspergillus fumigatous* (ATCC 204305)	23	28	30	32	35	-	32

Standard – Ciprofloxacin 5µg /dics for bacteria; Nystatin 100 units /disc for fungi.

5. Conclusion

The present study of an efficient protocol for the Chalcones can be synthesized in good yields from aromatic aldehyde and ketone using the catalytic system of NaOH/ EtOH. The synthesized compounds were characterized by TLC, melting point, IR, NMR spectroscopy and elemental analysis. The results obtained from this study confirmed that the product has formed. The synthesized compounds PI and PII show significant antibacterial activity against *Klebsiella aerogenes* and *Proteus vulgaris*. Compounds PIII – PV shows significant antifungal activity against *Mucor rcemosus*, *A. flavous* and *A. fumigatous*. Hence, it is concluded that there is ample scope for further study in developing these as good lead compounds.

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References

[1] Christian Ruzie Michael Krayer and Jonathan S. Lindsey, *Org. letter*., 2009. 11(8), 1761.
[2] Padhy AK, Bardham M and Danda CS. *Indian J Chem*., 2003. 42B(4), 910.
[3] Nakum KH and Shah VH, Indian *J Het Chem*., 2002. 12(1), 37.
[4] Nagham MA. Preparation & Bio-Chemical identification of series organic compounds, *J Chem & Chemi Sci*., 2013. 3(2), 70
[5] S. S. Mokle, M. A. Sayeed, Kothawar and Chopde, *Int.J.Chem. Sci.*, 2004, 2(1), 96.
[6] H. K. Hsieh, L. T. Tsao and J. P. Wang, *J. Pharm. Pharmacol.*, 2000, 52, 163.
[7] G. S. Viana, M. A. Bandeira and F. Matos, *J. Phytomedicine*, 2003, 10, 189.
[8] S. Mukarami, M. Muramatsu, H. Aihara and S. Otomo, *Biochem. Pharmacol*, 1991, 42, 1447.
[9] M. Liu, P. Wilairat and L. M. Go, *J. Med. Chem*, 2001, 44, 4443.
[10] E. Francesco, G. Salvatore, M. Luigi, C. Massimo, *Phytochem*, 2007**,** 68, 939; J.A. Beutler, J., H. II Cardellina, G. N. Gray, T.R.Prather, R. H.Shoemaker, M. R. Boyd, C. M. Lin, E. Hamel, G., M. Cragg, *J. Nat. Prod.*, 1993**,** 56, 1718**;** L. W. Wattenberg, J. B. Coccia, A. R. Galbraith, *Cancer Lett.*, 1994**,** 83, 165**;** C. C. Yit, and N. P. Das, , *Cancer Lett.*, 1994**,** 82, 65**;** R., Ramanthan, , C. H. Tan, N. P. Das, *Cancer Lett.*, 1992**,** 62, 217**;** Y. Satoni, *Int. J. Cancer*, 1993**,** 55, 506.
[11] J. C. Onyilagna, B. Malhotra, M. Elder and G. H. N. Towers, *Can. J. Plant Pathol*, 1997, 19,133.
[12] C. L. Miranda, G. L. M. Aponso, J. F. Stevens, M. L. Deinzer and D. R. Buhler, *J Agric. Food Chem*, **2000,** 48, 3876.
[13] Shaita Sabir, Maghmana Rashid, Sidra Naz and Bilal Masood, *Int. J. Phar & Pharmacetical Science* 2013, 5(3), 177.
[14] Thanh-Dao Tran, Thi-Thao-Nhu Nguyen, Tuong-Ha Do, Thi-Ngoc-Phuong Huynh, Cat-Dong Tran and Khac-Minh Thai, *Molecules*, 2012, 17, 6684.
[15] Bag S, Ramar S and Degani MS, *Medicinal Chemistry Research*, 2009 18:309-316.

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