DAV International Journal of Science

Synthesis and characterization of novel 5-(3,4-dichlorophenyl)-2-furanyl chalcones

R. G. Gawali[1,2], S. Y. Jadhav[2] and R. B. Bhosale[1*]

[1]Organic Chemistry Research Laboratory, School of Chemical Sciences, Solapur University, Solapur-413255, Maharashtra, India.

[2]Department of Chemistry, D.B.F. Dayanand College of Arts and Science, Solapur-413002, Maharashtra, India

E-mail:*rggjknk@gmail.com*

ABSTRACT

A series four new 5-(3,4-dichlorophenyl)-2-furanyl chalcones were designed and synthesized from 5-(3,4-dichlorophenyl) furan-2-carbaldehyde and substituted acetophenones with good yields. All the synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR and Mass Spectroscopy.The synthesized chalcones would lead the promising pharmacological properties in the future.

KEYWORDS: Furan-2- carbaldehyde, Chalcone.

INTRODUCTION

A series four new chalcones were designed by considering the importance of biologically active pharmacophores and prepared successfully.The heterocycle, furan found in many naturally occurring compounds originated from plants and marine organisms. It is a key component, in a number of biologically significant natural products. Various substituted furans are used as commercial pharmaceutical agents, flavor and fragrance compounds. Medicinal properties of Furan include anticancer[Burris *et al.*, 2004], antidepressant[Viola *et al.*, 2004], anti-inflammatory[Munro *et al.*, 2008], muscle relaxant[Krause *et al.*, 2004], antimicrobial [Tripathy *et al.*, 2009 a], anti-ulcer[Tripathy *et al.*, 2009 b],anti-parkinsonism [Hodgson *et al.*, 2009], antidiuretic[Rossi *et al.*, 2004]. Polysubstituted furans can also be employed as building blocks for the total synthesis of complicated naturally occurring metabolites and as versatile starting materials for the preparation of a variety of heterocyclic and acyclic compounds. The biologically active pharmacophore chalcone is one of the major classes of natural product with wide spread distribution in fruit, vegetables, spices, tea and soya based foodstuff has been recently subjects of great interest for their interesting pharmacological activities [Mathew *et al.*, 2014]. Majority of synthesized chalcones and chalcones isolated from the natural product are flavonoid and isoflavonoid precursors which are abundant in edible plants and display a wide spectrum of biological activities including antioxidant, anti-inflammatory [Bandgar *et al.*, 2010], antimicrobial [Fang *et al.*, 2014], antileishmanial [Aponte *et al.*, 2010], anticancer activities[Syam *et al.*, 2012]. The growing interest in these compounds and their potential use in medicinal applications are proved by the growing number of publications concerning the synthesis and biological evaluation of chalcones analogues. The

significant biological activity and great utility of both the heterocvclic scaffolds have encouraged us to synthesize furan substituted chalcone derivatives.

EXPERIMENTAL SECTION

All the compounds and reagents were commercially available without pretreatment. All solvents and reagents are analytically pure and no further purification was needed. Melting points were recorded in open capillary tubes and were found uncorrected. Reaction courses and product mixtures were routinely monitored by TLC on Silica gel precoated plates GF-254. IR spectra were recorded on Thermo Scientific Spectrometer,. ^{1}H NMR, ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer using TMS as internal standard.

General procedure for the synthesis of 5-aryl furan-2-carbaldehydes

The substituted aniline (0.01 mole) was dissolved in a mixture of 5 ml conc. hydrochloric acid and 20 mL of water under stirring and cooled in an ice bath at 0 -5 ºC. A solution of sodium nitrite (0.012 mole) in water was added portion wise, keeping the temperature below 7-8 ºC. The reaction mixture was left for 1 h for the completion of diazotization, filtered with the help of glass wool (if any turbidity observed). Then, to the solution of furan-2-carbaldehyde (0.01 mole), the diazonium salt solution was added drop wise followed by a solution of copper chloride (0.003 mole in 5 ml of water). The temperature was raised to 30 ºC by heating (if necessary) and stirred for 4-6 h. The completion of reaction was monitored by TLC. Then, the reaction mixture was left for 24 h at room temperature. The precipitate obtained was diluted and washed with water. Then the crude product was filtered, dried and recrystallized from ethanol to afford 5-aryl furan-2-carbaldehydes

General procedure for the synthesis of chalcones

The equimolar mixture of 5-aryl furan-2-carbaldehydes (3 mmole) and substituted aromatic ketones (3 mmole) was dissolved in minimum amount of ethanol. To this mixture sodium hydroxide (20%, 3 ml) was added slowly and the reaction mixture was stirred at room temperature for 1-4 h using magnetic stirrer. The completion of reaction was monitored by TLC. Then, the reaction mixture was poured slowly into ice-cold water with constant stirring, the product was precipitated out. The precipitate obtained was filtered, washed and dried. The crude product was recrystallised from ethanol to give pure chalcones.

CHARACTERISATION

(E)-3-(5-(3,4-dichlorophenyl)furan-2-yl)-1-(3,4,5-trimethoxyphenyl)prop-2-en-1-one (4a):

Yellow solid, yield 95%, mp 193 ºC IR (cm^{-1}): 2988, 2832, 1660, 1606, 1579, 1066; ^{1}H NMR (400 MH$_z$, $CDCl_3$) δ: 6.832 (d, 1H Furan), 6.853 (d, 1H Furan), 7.327 (s, 2H), 7.502 (d, 1H), 7.53-7.64 (m, 3H), 7.864 (d, 1H).

(E)-3-(5-(3,4-dichlorophenyl)furan-2-yl)-1-(4-hydroxyphenyl)prop-2-en-1-one (4b):

Dark yellow solid, yield 82%, mp 227 ºC IR (cm^{-1}): 3450, 2961, 2848, 1661, 1604, 1573, 1059; ^1H NMR (400 MH_z, $CDCl_3$) δ: 5.035 (s, 1H, –OH gr.), 6.828(d,1H Furan), 6.850 (d, 1H Furan), 6.924 (d, 2H),7.291 (d, 1H), 7.435-7.638 (m, 3H), 7.695 (d, 2H), 7.837 (d, 1H).

(E)-3-(5-(3,4-dichlorophenyl)furan-2-yl)-1-(2,4-difluorophenyl)prop-2-en-1-one (4c):

Faint yellow solid, yield 85%, mp 210 ºC IR (cm^{-1}): 2930, 2853, 1658, 1601, 1568, 1071; ^1H NMR (400 MH_z, $CDCl_3$) δ: 6.832 (d,1H Furan), 6.849 (d, 1H Furan), 6.862-6.981 (m, 2H), 7.468-7.749 (m, 3H), 7.770-7.783 (m, 3H).

(E)-3-(5-(3,4-dichlorophenyl)furan-2-yl)-1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (4d):

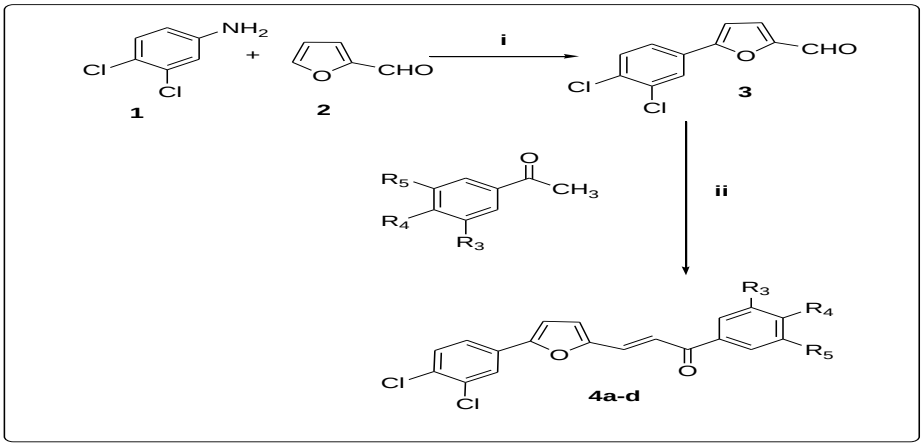
Yellow solid, yield 90%, mp 235 ºC IR (cm^{-1}): 2922, 2852, 1659, 1601, 1563, 1067; ^1H NMR (400 MH_z, $CDCl_3$) δ: 6.845 (d, 1H Furan), 6.885 (d, 1H Furan), 7.370 (d, 1H), 7.478-7.745 (m, 3H), 7.785 (d, 2H), 7.804 (d, 1H), 8.153 (d, 2H).

RESULT AND DISCUSSION

CHEMISTRY

In the present investigation, the 5-aryl furan-2-carbaldehyde was synthesized through Meerwein-arylation[Obushak *et al*, 2009], in which the substituted anilines after diazotisation using HCl and $NaNO_2$. The diazonnium salt when treated with the furan-2-carbaldehyde in presence of $CuCl_2$ as catalyst in aqueous media on stirring at room temperature gave 5-aryl furan-2-carbaldehyde. This intermediate was confirmed by TLC and characterized by IR, ^1H NMR and Mass Spectroscopy.

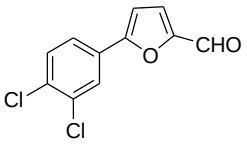
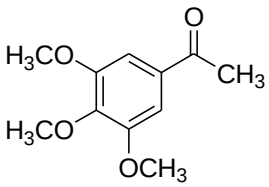
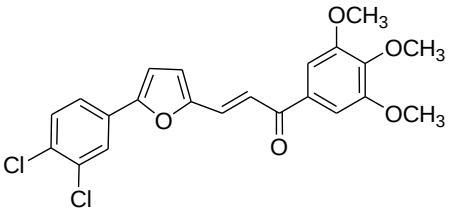
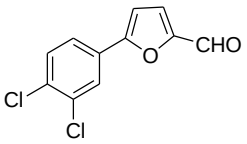
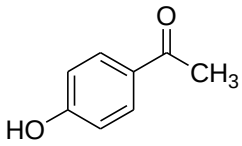
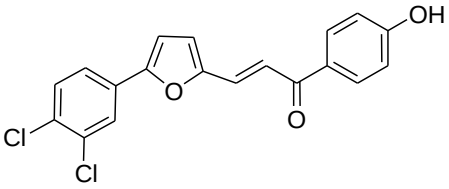
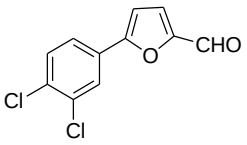
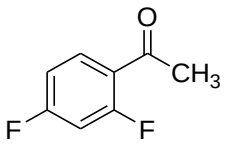
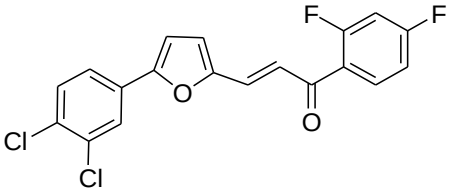
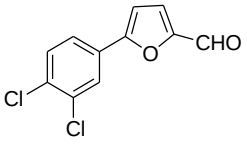
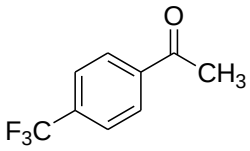
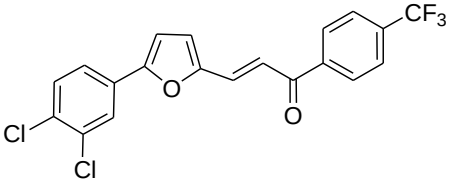
The title compounds were synthesized from equimolar amount of substituted 5-aryl furan-2-carbaldehydes and substituted acetophenones using NaOH in ethanol at room temperature by Claisen-Schmidt condensation.All the synthesized compounds were characterized by IR, ^1H NMR, ^{13}C NMR and Mass Spectroscopy.



Reagents and conditions: (i) Conc. HCl, 0 ºC, $NaNO_2/H_2O$, $CuCl_2$, stirr at rt, 4-6 h.;

(ii) NaOH, ethanol, Stirr at R. T. for 2-3 h

Table 1: Synthesized Furanyl chalcones

Sr. No.	Entry	Reactants		Product (Chalcone)
		Aromatic aldehyde	Aromatic ketone	
1	4a			
2	4b			
3	4c			
4	4d			

In the IR spectrum of titled compounds, the absorption band observed at 2988-2830 cm^{-1} due to C-H stretching of furan and olefinic C-H stretching, whereas the absorption band at 1655-1660 cm^{-1} and 1601-1606 cm^{-1} are observed due to the presence of >C=O stretching of α,β-unsaturated carbonyl group and stretching of >C=C< respectively. The furan ring is also confirmed by characteristic absorption band at 1059-1071 cm^{-1}due to presence of C-O-C ether stretching. ^{1}H NMR (400 MHz in $CDCl_3$) spectra of titled compounds reveals that, the two furan proton showed doublet at δ ~ 6.832-6.885 ppm, whereas two olefinic trans protons showed doublet to each other in the region δ ~ 7.291-7.864 ppm. The three protons of 3,4-dichloro aromatic ring showed multiplet at δ ~ 7.435-7.640 ppm.

CONCLUSION

We have efficiently designed and synthesized four 5-(3,4-dichlorophenyl)-2-furanyl chalcones from 5-(3,4-dichlorophenyl) furan-2-carbaldehyde and substituted acetophenones with excellent yields without formation of any side products. The synthesized chalcones would lead the promising pharmacological properties in the future.

REFERENCES

Burris H.A.(2004).Dual kinase inhibition in the treatment of breast cancer: initial experience with the EGFR/ErbB-2 inhibitor lapatinib. *Oncologist*.9 (3), 10–15.

Viola G., Vedaldi D.and dall'Acqua F. (2004). Synthesis, cytotoxicity, and apoptosis induction in human tumor cells by geiparvarin analogues. *Chem Biodivers.* 1(9)

Munro T.A., Duncan K.K., Xu W., Wang Y., Liu-Chen L.Y., Carlezon W.A., Cohen B.M.and Béguin C.(2008). Standard protecting groups create potent and selective kappa opio-ids: salvinorin B alkoxymethyl ethers. *Bioorg.& Med. Chem*. 16 (3), 1279–1286.

Krause T., Gerbershagen M.U., Fiege M., Weisshorn R.and Wappler F.(2004). Dantrolene – a review of its pharmacology, therapeutic use and new developments. *Anaesthesia.* 59 (4), 364–373.

KD Tripathy,(2009). Essentials of medicaL pharmacology, Jay-pee Brothers Medical Publishers (P) Limited, New Delhi. 6th Ed. (a) 862; (b) 630.

Hodgson R.A., Bertorelli R., Varty G.B., Lachowicz J.E., Forlani A., Fredduzzi S., Cohen-Williams M.E., Higgins G.A., Impagnatiello F., Nicolussi E., Parra L.E., Foster C., Zhai Y., Neustadt B.R., Stamford A.W., Parker E.M., Reggiani A.and Hunter J.C. (2009). Characterization of the Potent and Highly Selective A2A Receptor Antagonists Preladenant and SCH 412348 in Rodent Models of Movement Disord-ers and Depression. *The Journal of Pharmacology and Experimental Therapeutics*. 330 (1), 294–303.

Rossi S. (2004). Australian Medicines Handbook (5th ed.). Ade-laide, S.A.: Australian Medicines Handbook Pvt. Ltd..

Mathew B., Suresh J., Anbazghagan S., Paulraj J. and Krishnan G.K. (2014). Heteroaryl chalcones: Mini review about their therapeutic voyage. *Biomedicine & Preventive Nutrition*.4, 451-458.

Bandgar B.P., Patil S.A., Gacche R.N., Korbad B.L., Hote B.S., Kinkar S.N. and Jalde S.S.(2010). Synthesisand biological evaluation of nitrogen-containing chalcones as possible anti-inflammatoryand antioxidant agents. *Bioorg.& Med. Chem. Lett*.20, 730-33.

Fang X., Yang B., Cheng Z., Zhang P. and Yang M. (2014). Synthesis and antimicrobial activity of novel chalcone derivatives. *Research on Chemical Intermediates*.40, 1715-1725.

Mohammad F., Rahaman S.A. and Moinuddin M. (2012). Synthesis and antimicrobial activity of 1-(2",4"-dichlorophenyl)-3-(substituted aryl)-2-propene-1-ones.*International Journal of LifeScience and Pharma Research*. 2(3), 82-87.

Aponte J.C., Castillo D., Estevez Y., Gonzalez G. and Arevalo J. (2010). In vitro and in vivo antileishmania activity of polysubstituted synthetic chalcones. *Bioorg.& med.Chem. lett.*20: 100-103.

Obushak N.D., Lesyuk A.I., Gorak Yu.I. and Matiichuk V.S.(2009). Mechanism of Meerwein arylation of furan derivatives.Russian Journal of Organic Chemistry, September, 45, 1375