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Synthesis and antimicrobial activity of chalcones of naphtho[2,1-b]furan condensed with barbituric acid

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ABSTRACT

Barbitones were synthesized by the condensation of chalcones with barbituric acid. The stuctures of the synthesized compounds assigned on the basis of elemental analysis, IR, [1]H NMR and mass spectral studies. All the products were evaluated for their in vitro antimicrobial activity against various strains of bacteria and fungi.

Keywords: Barbitones, chalcones, Naphtho[2,1-*b*]furan, antimicrobial activity.

INTRODUCTION

Nitrogen containing heterocyclic compounds, such as barbitones, are known to posses a wide range of activities, such as hypnotics,[1] cadiovascular,[2] analgesics,[3] antiviral,[4]anticancer[5] etc. Moreover, Furan moieties are common substructures in numerous natural products[6]. Naphthofuran derivatives have been isolated from various natural sources like Fusarium oxy-sporum[7], Gossypium barbadense[8], etc and are well known for various biological activities like antitumour[9], antifertility[10], mutagenic[11], growth inhibitory[12] and oestrogenic[13]. Many of the condensed heterocycles and biheterocycles enclosing naphthofuran have been reported processes wide spectrum of activities[14-19].The starting compound, 2-acetyl naphthofuran was condensed with different aryl aldehydes to yield chalcones. These on condensation with barbituric acid in glacial acetic acid furnished the target molecules (scheme-1). The constitution of all the products were characterized using elemental analysis and IR, ^{1}H NMR and mass spectroscopy. All the compounds were screened for their in vitro antimicrobial activity against different strains of bacteria and fungi.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and are uncorrected. Purity of the compounds were checked by TLC, FT-IR spectra were taken in a Perkin Elmer 157 infrared spectrophotometer. ^{1}H NMR spectra (300 MHz) were recorded on a Brucker supercon FT-NMR instrument using TMS as internal standard (chemical shifts in ppm).

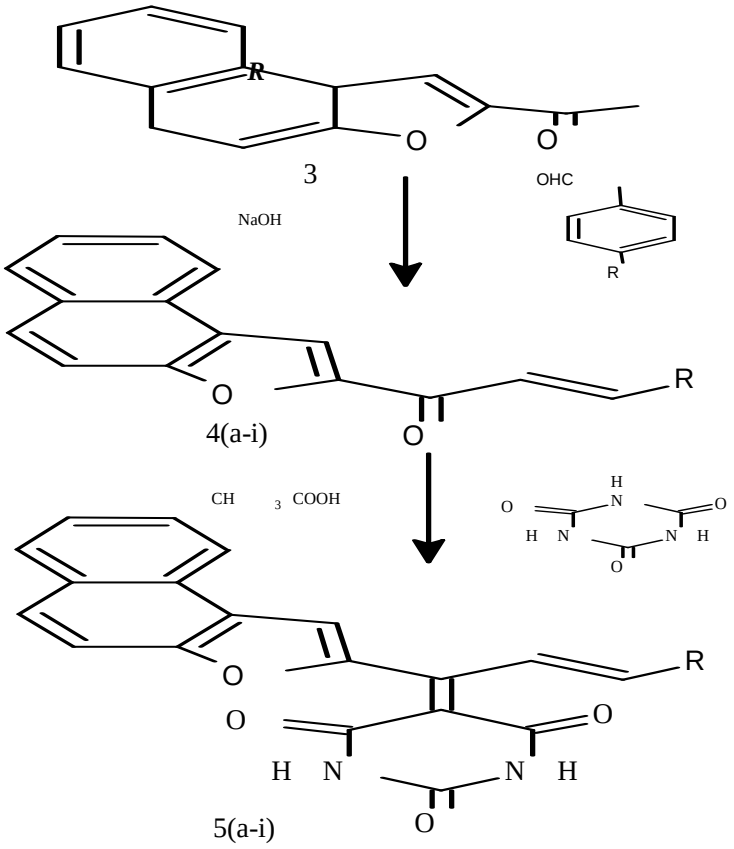
2-Amino-4-(4-hydroxyphenyl)-6-naphtho[2,1-*b*]furan-2-ylnicotinonitrile 4d

A mixture of 1-(4-metoxyphenyl)-3-(1,3-diphenyl-4-pyrazolyl)-2-propen-l-one (3.8 g, 0.01mol), barbituric acid (1.28 g, 0.01 mol) in glacial acetic acid was refluxed for 12 h in an oil bath. The contents were poured into ice and the product was isolated and crystallized from DMF.Similarly, the compounds **4** (b-g) were synthesized from **3** by reacting with appropriate aromatic aldehydes.

RESULTS AND DISCUSSION

The required starting material 2-acetylnaphtho[2,1-*b*]furan **3** was synthesised from 2-hydroxy-1-naphthaldehyde and chloroacetone in presence of anhydrous K_2CO_3 and dry acetone by well established method in our laboratory. The synthesis of key intermediate 2-amino-4-(substituted phenyl)-6-naphtho[2,1-*b*]furan-2-yl-nicotinonitriles **4**(a-g) was accomplished by reacting 2-acetylnaphtho[2,1-*b*]furan **3** with appropriate aromatic aldehydes, with dilute NaOH. The structure of 2-amino-4-naphtho[2,1-*b*]furan-2-yl-6(4-hydroxyphenyl)nicotinonitrile **4**a was established by IR, ^{1}H NMR and mass spectral studies. The IR spectrum exhibited broad absorption band at 3444 cm^{-1} due to -NH_2 stretching frequency and a sharp absorption peak at 2202 cm^{-1} corresponds to -CN stretching frequency. The formation of **4**d was confirmed by its the ^{1}H NMR spectrum. The presence of broad singlet (D_2O exchangeable) at δ-6.8 indicated the two protons of -NH_2 , a multiplet between δ 7.5 - 8.5 were due to eleven aromatic protons and a peak at δ 9.8 was asindicasigned to -OH group. The mass spectra showed the molecular ion peak at m/z 377,which is consistant to its molecular weight.

SCHEME-1



a) 3-NO_2 C_6H_4 , b) 4-Cl C_6H_4 , c) C_6H_5 , d) 4-OH C_6H_4, e) 3-OCH_3 C_6H_4, f) 4-$OCH_3C_6H_4$, g) 4-OH 3-OCH_3 C_6H_3

Table – 1: Antibacterial activity of the compounds

Compound	Diameter of zone of inhibition (mm*)			
	Staphylococcus aureus	***Escherichia coli***	***Psedomona auregenosa***	***Bacillus subtilis***
5a	12	00	00	16
5b	00	00	00	15
5c	00	00	09	14
5d	00	00	00	00
5e	10	11	09	00
5f	13	08	08	15
5g	00	09	11	13
5h	00	00	00	00
5i	00	00	00	13
5j	00	10	00	15
DMF	00	00	00	00
Ciproflaxacin	25	40	43	44

Antibacterial activity

All the synthesized compounds were screened for their antibacterial activity against *Staphylococcus aureus, Escherichia coli, Psedomona auregenosa* and *Bacillus subtilis*. The activity was carried out using cup plate method[24]. The zone of inhibition was measured in mm. DMF was used as a vehicle and Ciproflaxacin as standard drug for comparison. The compounds were tested at 10 mg/mL concentration and each well was loaded with 50 µg/mL. All the synthesized compounds were found to exhibit moderate activity against all bacteria. The zones of inhibition are presented in Table -1.

Antifungal activity

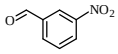
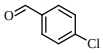
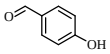
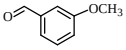
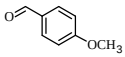
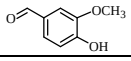
The synthesized compounds were evaluated *invitro* for antifungal activity by using standard agar disc diffusion method[24] against *Curvularia*, *Aspergillus niger* and *Candida albicans*. DMF was used as a vehicle. The compounds were tested at 10 mg/mL concentration and each well was loaded with 50 µg/mL of the sample. Clotrimazole was used standard drug. The zones of inhibition are presented in Table-2. All synthesized compounds were found to be febly active against fungi.

Antifungal activity of the compounds

Table – 2

Compound	**Diameter of zone of inhibition (mm*)**		
	Curvularia	***Aspergillus niger***	***Candida albicans***
5a	00	00	00
5b	15	00	00
5c	18	00	00
5d	00	00	00
5e	10	00	00
5f	13	00	00
5g	00	00	00
5h	00	00	00
5i	00	00	00
5j	13	00	00
DMF	00	00	00
Clotrimazole	48	38	27

Table-3 Physical data of the compounds: 5a-j

Compound	R	Mol. Formula	Yield (%)	M.P (^{o}C)	Elemental Analysis Calcd (Found)%		
					C	H	N
5a		$C_{24}H_{14}N_4O_3$	62	168	70.90 (70.93)	3.45 (3.47)	13.77 (13.79)
5b		$C_{24}H_{14}ClN_3O$	68	175	72.80 (72.82)	3.53 (3.56)	10.60 (10.62)
5c		$C_{24}H_{15}N_3O$	70	189	79.73 (79.76)	4.15 (4.18)	11.60 (11.63)
5d		$C_{24}H_{15}N_3O_2$	65	183	76.34 (76.38)	3.99 (4.01)	11.11 (11.13)
5e		$C_{25}H_{17}N_3O_2$	70	173	76.69 (76.71)	4.36 (4.38)	10.72 (10.74)
5f		$C_{25}H_{17}N_3O_2$	65	195	76.69 (76.71)	4.35 (4.38)	10.70 (10.74)
5g		$C_{25}H_{17}N_3O_3$	67	168	73.68 (73.70)	4.19 (4.21)	10.29 (10.31)

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