

SOME NEWLY DEVELOPED NAPHTHOFURAN DERIVATIVES CONTAINING QUINOLINE MOIETY AS BIOLOGICAL ACTIVE COMPOUNDS

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ABSTRACT

The starting materials 2-acetylnaphtho [2,1-b]furan (**1**) have been synthesized by literature(Stoermer and Schaffer's) method. It converts to series of substituted Chalcones (**2a-e**) prepared by Claisen-Schmidt condensation with substituted aromatic aldehydes. These chalcones on reaction with 2-[(quinoline-8yl) oxy] acetohydrazide (**3**) in presence of glacial acetic acid gives the title compounds. (**4a-e**).The structures of the synthesized compounds have been established on the basis of elemental analysis and spectral data. The newly synthesized compounds are characterized for biological activity.

Keywords: Naphthofuran, chalcone, quinoline, synthesis, biological activity.

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INTRODUCTION

Survey of literature revealed the importance of naphthofuran derivatives as biologically, pharmacologically and industrially important molecules^{1,2}. Their derivatives have been isolated from various natural sources like *Fusarium oxysporum*, *Gossypium barbadense* etc^{3,4}. And are well known for various types of biological activities like antifertility, growth inhibitory, antitumour⁵⁻⁷.The heterocycles containing quinoline moieties also maintains a wide range of biological activities⁸⁻¹⁰. Hence, with these observation we examine the feasibility and efficiency of an approach to synthesis naphthofuran coupled with quinoline nucleus and to get cyclized pyrazoline ring. Pyrazole and pyrazoline derivatives have been reported to posses antinociceptive effect in mice, antimicrobial, insecticidal and local anesthetic activities¹¹⁻¹⁵.The biheterocyclic compounds in which pyrazole moiety is coupled with furan or benzofuran nucleus exhibit antimicrobial and anti-inflammatory activities^{16,17}. However there are no reports in literature concerning of pyrazole ring with another biologically active naphtho [2,1-b] furan nucleus, either directly or through carbon bridge.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded in KBr on Bruker FT-IR(Alpha-P). ¹H NMR spectra on Bruker "AVANCE400" MHz Spectrometer using TMS as a standard. (chemical shift in δ ppm) and mass spectrum on Shimadzu GCMS QP5050A, Japan Mode-DI Mass Spectrometer operating at 70eV. 2-acetylnaphtho[2,1-b]furan and 2(quinolin-8-yloxy) acetohydrazide were synthesized by literature method^{18,19}. Progress of reaction was monitored by TLC, p-substituted aromatic aldehydes, 8-hydroxyquinoline, hydrazine hydrate and silica gel were purchased from merck, India.

Synthesis of 3-(4-hydroxyphenyl)-1-(naphtho [2, 1-b] furan – 2yl) prop-2-en-1-one. (2c)

A mixture of 2-acetylnaphtho [2,1-b] furan (0.02mole) and p-hydroxy benzaldehyde (0.022 mole) was stirred in ethanol (50mL) and then aqueous solution of potassium hydroxide (50%) (10mL) was added to it portionwise, keeping the temperature below 10°C throughout the addition. The mixture was kept for 36 hr and it was acidified with conc.HCl. The reaction mixture was poured into crushed ice and the solid obtained was filtered under vacuum. It was washed firstly with sodium carbonate solution and

then with water, dried and the product was recrystallized from ethanol **2c**. Same procedure is extended for other compounds of this series **2a-e** by using appropriate aromatic aldehydes.

IR : (KBr, $\nu_{\max}$, cm^{-1}) 3310 (Ar-O-H), 3058 (-C-H str. of Ar), 1644 (C=O str. in ketone), 1586 (C = C str.), 1515 (C = C str. in Ar), 1443 and 1359 (-CH₃ def.), 1153 and 1167 (C-O-C str.) 830 (-CH str.) 747 (Ar-H opb.).

¹H NMR: (CDCl_3 in δ ppm): 6.35 (d, 1H, -CO-CH), 6.95 (d, 1H, -C=CH), 7.21 – 8.24 (complex m, 11H, Ar-protons) and 10.32(s, 1H, phenolic -OH) proton. Mass: (m/z) 314 [M]⁺, 221, 195, 147, 119, 118, 91, 69, 65, 43.

Synthesis of 2[(quinoline-8-yloxy] acetohydrazide (**3**)

A mixture of ethyl 2-(quinolin-8-yloxy) acetate (0.05mole) and hydrazine hydrate 99% (0.07mole) in ethanol was refluxed for 9 hr. The excess of solvent is distilled off and it was cooled and poured on crushed ice, solid obtains, the separated product was recrystallized from ethanol.

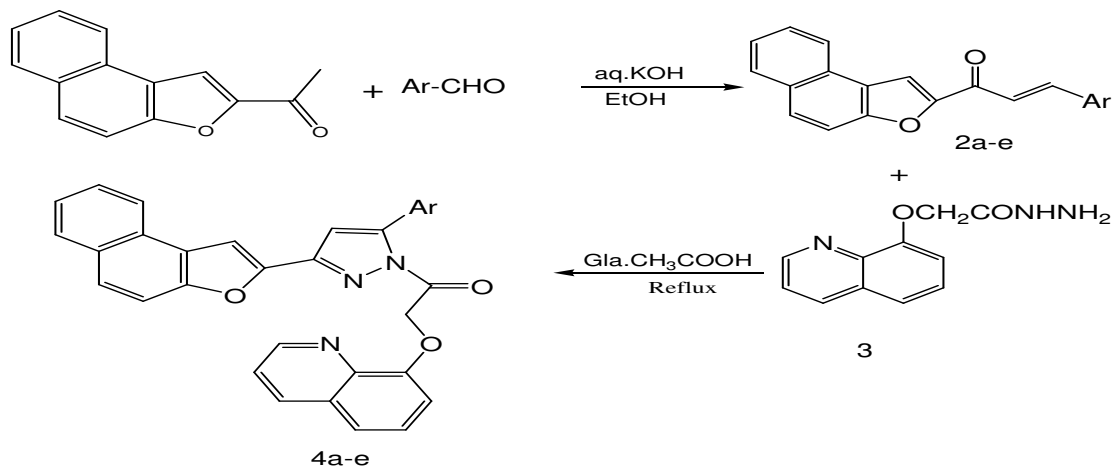
IR : (KBr, $\nu_{\max}$, cm^{-1}): 3365 (N-H), 3070 (C-H), 1660 (C=O amide), 1430 (C-N).

¹H NMR: (CDCl_3 in δ ppm): 10.71(s, 1H, -NH), 8.05-7.15 (m, 5H, Ar Protons), 4.80(s, 2H, -OCH₂), 3.75 (s, 2H, NH₂). Mass: (m/z) 314 [M]⁺, 217, 188, 186, 172, 158, 77.

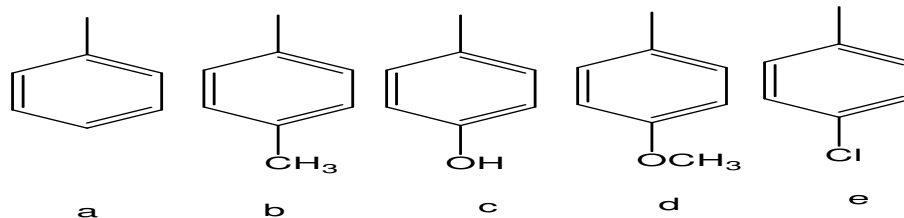
Synthesis of 1-(4, 5-dihydro-5-(4-hydroxyphenyl)-3-(naphtho[2,1-b]fura-2y1)pyrazol-1-y1)-2-(quinolin-8-yloxy) ethanone. (**4c**)

A mixture of 3-(4-hydroxyphenyl)-1-(naphtho[2,1-b]furan-2yl) prop-2-en-1-one. **2c** (Chalcone) (0.02mole) in 25mL glacial acetic acid and 2-(quinolin-8-yloxy) acetohydrazide (0.02mole) **3** was added. The mixture was refluxed for 10 hr. and left overnight. The reaction mixture was poured into crushed ice and the solid obtained was filtered under vacuum washed with cold ethanol, dried and recrystallized from Pet. ether. Same procedure is extended for other compound of this series **4a-e**.

IR : (KBr, $\nu_{\max}$, cm^{-1}): 2970 (C-H), 1679 (C=O), 1593 (C=C), 1514 (N-N). ¹H NMR: (CDCl_3 in δ ppm): 6.40(d, 1H, -CO-CH=), 7.01(d, 1H, C=CH), 7.26-8.31 (Complex m, 11H, Ar protons), 10.37(s, 1H, Phenolic -OH), 6.10-6.80(m, 6H, Ar Protons of quinolines). Mass: (m/z) 513[M]⁺, 346, 327, 186, 167, 94.



Where, Ar =



Scheme-1

Biological activity

The antimicrobial activity was assayed by cup plate at the concentration of 500 µg/ml. All the synthesized compounds were tested in vitro for their antibacterial activity against various microbes such as *S. typhi* and *S. aureus*. The inhibition zone of the tested compounds was measured in mm. Antifungal activity against *A. niger* and *C. albicans*. Plate was incubated for 24hr for bacterial activity and 48 hr. for fungicidal activities. Penicillin and Griseofulvin were used as standard. (Table I).

RESULTS AND DISCUSSION

It has shows all prepared compounds have significant effect. It can be concluded from the Table I that compound **4c**, **4d** and **4b** were active against both microbes such as *S. typhi* and *S. aureus*. Compound **4a**, **4b**, **4c** and **4d** were found active against *A. niger*, *C. albicans*.

Table-1: Antimicrobial activity of the compounds

Compound	Antibacterial activity Zone of inhibition (in mm)		Antifungal activity	
	<i>Salmonila typhi</i>	<i>Staphylocus aureus</i>	<i>Aspergillus nigar</i>	<i>Candida albicans</i>
4a	14	26	+ ve	+ve
4b	15	28	+ ve	+ve
4c	18	32	+ve	+ve
4d	16	30	+ ve	+ve
4e	12	20	-ve	+ve
Penicillin	20	32	-	—
Griseofulvin	—	—	+ ve	+ ve

Control (DMSO), (– ve) – No activity

Table-2: Physical and analytical data of synthesized compounds

Comp.	Molecular formula	Molecular weight	Yield %	M.P. °C	Element % cal (found)			
					C	H	N	Cl
2a	C ₂₁ H ₁₄ O ₂	298.10	60	132	84.53	4.69	-	-
					(84.55)	(4.70)	-	-
2b	C ₂₂ H ₁₆ O ₂	312.13	66	151	84.58	5.12	-	-
					(84.57)	(5.10)	-	-
2c	C ₂₁ H ₁₄ O ₃	314.00	65	172	80.25	4.45	-	-
					(80.24)	(4.44)	-	-
2d	C ₂₃ H ₁₆ O ₃	340.20	72	135	81.17	4.70	-	-
					(81.11)	(4.69)	-	-
2e	C ₂₁ H ₁₃ ClO ₂	332.70	55	143	75.74	3.90	-	10.67
					(75.73)	(4.00)	-	(10.61)
4a	C ₃₂ H ₂₃ N ₃ O ₃	497.54	58	234	77.25	4.66	8.45	-
					(77.23)	(4.67)	(8.43)	-
4b	C ₃₃ H ₂₅ N ₃ O ₃	511.57	56	240	77.48	4.92	8.21	-
					(77.50)	(4.93)	(8.18)	-
4c	C ₃₂ H ₂₃ N ₃ O ₄	513.54	54	264	74.84	4.50	8.16	-
					(74.86)	(4.52)	(8.18)	-
4d	C ₃₃ H ₂₅ N ₃ O ₄	527.50	58	245	75.13	4.79	7.95	-
					(75.12)	(4.80)	(7.97)	-
4e	C ₃₂ H ₂₂ ClN ₃ O ₃	532.00	51	240	72.25	4.16	7.91	6.66
					(72.26)	(4.15)	(7.89)	(6.68)

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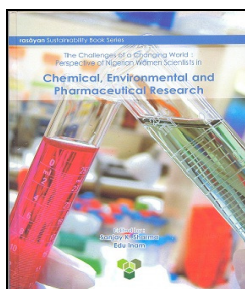
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