FACILE SYNTHESIS OF 2-CINNAMOYL-4-METHYL/4,6 DIMETHYL 3-PHENYL-FURO [3,2-C] QUINOLINES AS MARKED ANTI MICROBIAL AGENTS

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Abstract

In a continuing programme on therapeutic activity of quinolines a series of novel cinnamoyl furano quinolines is described. These compounds were evaluated for their anti microbial activity. The starting materials 2-Methyl-3-benzoyl-4-hydroxy-2,8-dimethyl-3-benzoyl-4-hydroxy quinolines are prepared in above 80-90% yields under Microwave irradiation with in 3 minutes at power level 300 watts in 800T (BPL model) domestic oven.

Introduction

The Chemistry of Quinoline derivatives has received particular attention over the last few years and a large variety of quinolines has been synthesized and arrived as anti malarial (1) anti allergic (2), anti microbial (3), anti tumor and other therapeutic activity(4) .

From our laboratories, we have reported marked anti inflammatory activity of 2-Aroyl-4-methyl-4,6-dimethyl-3-phenyl furo [3,2-C]Quinolines(5), Chalcones displayed significant toxicity towards murine P 388 and L1210 Leukemia cells as well as number of human tumor cell lines (6). We also reported 8-Cinnamoyl-2,3-dimethyl-9-phenyl-4H-furo[2,3-h]-1-benzo pyran-4-ones as potent anti bacterial agents (7). Hence the purpose of present study was on facile synthesis of 2-cinnamoyl-4-methyl/4,6 Dimethyl-3-phenyl-Furo[3,2-C] quinolines as marked Anti microbial Agents.

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Experimental

All melting points reported were determined in open capillaries using silicon oil bath, the purity of all the compounds is checked by TLC over silica gel. IR spectra were recorded on Shimadzu FTIR model 8010 Spectrophotometer and are given in Cm^{-1} in KBr. The H^1 NMR spectra in $CDCl_3$ were recorded on C17-20-ZM-390-200 MHz NMR Spectrophotometer and are reported in δ units (PPM) relative to TMS as internal standard. The mass spectra of the compounds described are recorded on Jeol TMS-D300 at 70ev. Elemental analysis are indicated by the symbols of the elements and were within ±0.3% of the theoretical values.

In our previous communications, we have reported 54.3% yield of 3-Benzoyl-4-hydroxy 2-methyl / 2,8-dimethyl quinoline using anhydrous $AlCl_3$ (conventional method), but in the present communication we wish to report 80% yield of 3-Benzoyl-4-hydroxy-2-methyl / 2,8-dimethyl quinoline using anhydrous $AlCl_3$ in 800 T BPL Model Microwave oven. The reaction time was comparatively very less. And all the reactions were carried at 300-Watt power level. It was depicted in **Scheme I**. The products were compared with authentic samples by TLC and super imposable IR spectrum. All cinnamoyl compounds gave Halochromic colours in H_2SO_4. The results were given in **Table-I**.

General experimental procedure for the synthesis of 2-Methyl-3-benzoyl-4-Hydroxy Quinoline (1a-b) under Microwave irradiation.

A mixture of 2-Methyl-4-hydroxy quinoline (0.01mole, 1.59gr) and distilled Benzoyl chloride (0.01mole, 1.41ml) were taken in a beaker. To this, anhydrous $AlCl_3$(5gms) is added and irradiated in a domestic microwave oven at 300-watt power level for about 3-4 minutes, it was cooled and decomposed in ice and Conc. HCl (1:1). The crude product obtained is re crystallized from ethanol. M.P.: 265^{O}C; Yield : 2.11gr (80%)

Similarly 2,8- Dimethyl-3-benzoyl-4-hydroxy quinoline also synthesized as above.

M.P.: 298^{O}C; Yield: 2.50gr (90%)

Synthesis of 2-Acetyl-3-phenyl-4-methyl furo [3,2-C] quinoline (2a-b):-

2-Methyl-3-benzoyl-4-hydroxy quinoline 1a (0.01mole, 2.63gms) is treated with chloroacetone (0.01mol, 0.93ml) in dry acetone (100ml) and baked K_2CO_3 (6 gms) refluxed up to 16-18 hrs, the solvent was removed under reduced pressure. The crude product was re crystallized from ethanol.. M.P.: 219^{O}C; Yield: 2.11gr (70%)

Similarly, 2-Acetyl-3-phenyl-4,6-dimethyl furo [3,2-C] quinoline (2b) also synthesized as above. M.P.: 158^{O}C; Yield: 2.37gr (75%)

Synthesis of 2-Cinnamoyl-4-methyl-3-phenyl furo [3,2-C] quinoline(3a-i) :-

2-Acetyl-3-phenyl-4-methyl furo [3,2-C] quinoline 2a (0.01mole, 3.01gms) is taken in ethanol (20ml) and aromatic aldehyde (0.01mole), 40 % KOH (10ml) solution is added with constant stirring for 6 hrs. at room temparature. The reaction mixture is kept aside over night and treated with crushed Ice. It is extracted with ether to remove the un reacted aldehyde. The aqueous layer is neutralized with dil HCl. The solid obtained is filtered and washed, dried, re crystallized from dioxan. Similarly 2-Cinnamoyl-4,6-dimethyl-3-phenyl furo [3,2-C] quinolines 3 (a-i) and 2-cinnamoyl-4,8-Dimethyl-3-phenyl furo [3,2-C] Quinolines 3 (j-r) were synthesized similarly.

Anti Microbial Activity

2-Cinnamoyl-4-Methyl / 4,6-Dimethyl-3-Phenyl Furo [3,2-c] Quinolines synthesized were screened in vitro against bacteria *Escherichia Coli* and *Staphylococcus aureus* at 10μg /ml and 20μg /ml concentrations using cup-plate agar diffusion method(8) .The compounds 3i and 3r were active against *E.Coli* and *S.Aureus*. Compounds were also screened for their anti fungal activity against *fusarium moniforme* at 120μg/ml, 360μg/ml,600μg/ml,840μg/ml concentration using the glass slide humid chamber technique(9). Compounds 3b(99.9%), 3d(91.7%), 3e(97.4%), 3i(99.2%) and 3r(99.6%) showed maximum spore germination inhibition at higher concentrations. The results were depicted in **Table 1**.

Acknowledgement

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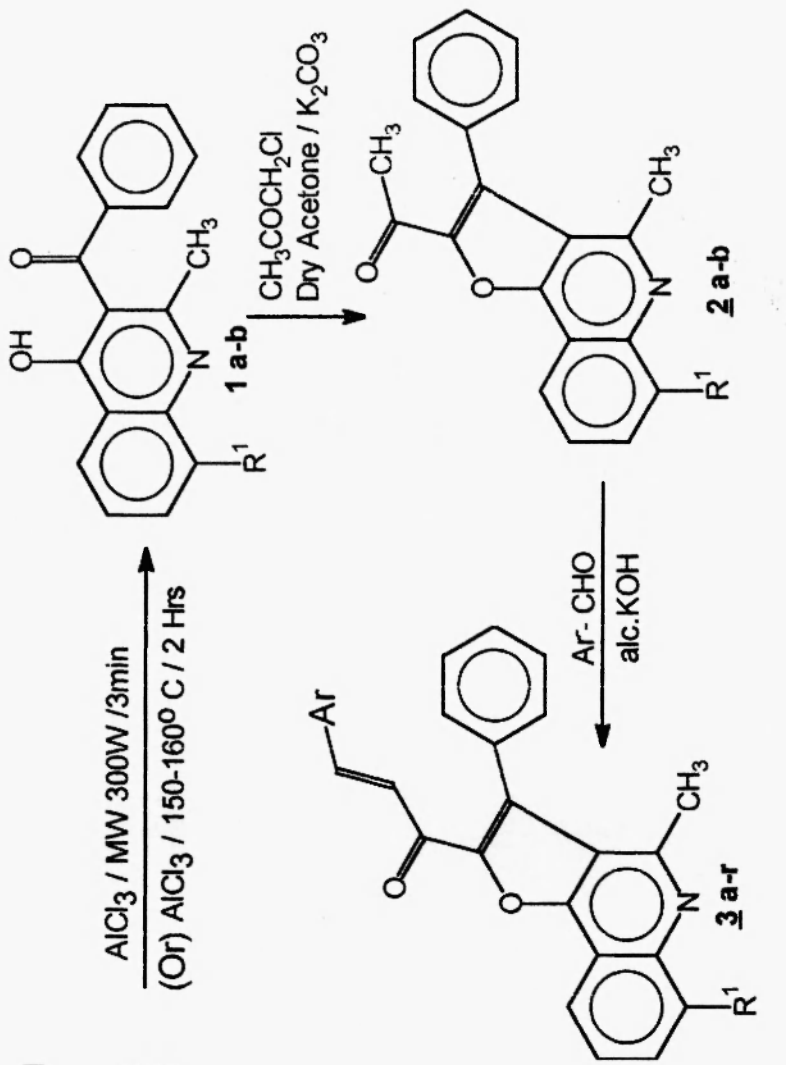

	R1	Ar
3a	H	- Phenyl
3b	H	- 2-Cl-Phenyl
3c	H	- 2-OH-Phenyl
3d	H	- 4-OH-Phenyl
3e	H	- 4-OMe-Phenyl
3f	H	- 4-Me-Phenyl
3g	H	- 3,5-Di-t-Bu-4-OH-Phenyl
3h	H	- 4-OH-3-Coumarinyl
3i	H	- 2(p-OMe-Naphthyl)-Propyl
3j	CH_3	- Phenyl
3k	CH_3	- 2-Cl-Phenyl
3l	CH_3	- 2-OH-Phenyl
3m	CH_3	- 4-OH-Phenyl
3n	CH_3	- 4-OMe-Phenyl
3o	CH_3	- 4-Me-Phenyl
3p	CH_3	- 3,5-Di-t-Bu-4-OH-Phenyl
3q	CH_3	- 4-OH-3-Coumarinyl
3r	CH_3	- 2(p-OMe-Naphthyl)-Propyl

Scheme 1

Table 1: Reactivity, Halochromic effects, spectral data & anti fungal activity (Spore inhibition %) of Compounds **3 a-r**

Entry	Halochromism	M.P (°C)	Yield (%)	I.R (cm^{-1})	^1H NMR ($CDCl_3$)	Concentration (µg / ml)			
						120	360	600	840
3a	Orange	248	65	1661, 1640, 1595, 1170, 840	δ 2.4(s, 3H, 4-CH_3), 7.2(d, Cα-H, J=9 Hz), 7.3 (s, 5H, 3-Ph); 7.4-7.6(m, 9H, Ar-H); 8.2(d, 1H, C_8, J=16 Hz); 8.5(d, Cβ-H, J=9 Hz)	---	---	---	---
3b	Red	188	55	1689, 1640, 1595, 1170, 820	---	25.2	35.7	99.8	99.9
3c	Orange Red	235	70	3230, 1670, 1640, 1595, 1175, 840	---	---	---	---	---
3d	Pink	243	85	3300, 1681, 1640, 1595, 1175, 841	---	Nil	Nil	24.9	91.7
3e	Permanganate	130	60	1658, 1600, 1595, 1170, 833	---	1.2	7.1	10.2	97.4
3f	Pink	158	55	1681, 1640, 1595, 1175, 840	δ 2.35(s, 6H, Two-CH_3), 7.1(d, Cα-H, J=9 Hz); 7.25(s, 5H, 3-Ph); 7.5(m, 7H, Ar-H), 8.1(d, 1H, J=16 Hz); 8.4(d, Cβ-H, J=9 Hz)	---	---	---	---
3g	Pink	176	65	3325, 2872, 1668, 1640, 1595, 1197, 891	---	---	---	---	---
3h	Green	230	70	3230, 1670, 1640, 1595, 1170, 860	---	3.25	6.6	34.1	56.8
3i	Green	196	75	1680, 1640, 1595, 1170, 840	---	9.2	10.0	98.3	99.2
3j	Orange	258	65	1680, 1640, 1595, 1170, 840	---	Nil	Nil	50.8	75.2
3k	Scarlet Red	178	65	1660, 1625, 1595, 1175, 840	---	---	---	---	---
3l	Permanganate	220	65	3240, 1681, 1640, 1175, 840	---	---	---	---	---
3m	Pink	233	80	3200, 1660, 1640, 1595, 1175, 890	---	Nil	Nil	1.6	34.5
3n	Violet	165	70	1670, 1640, 1595, 1175, 840	δ 2.3(s, 3H, 6-CH_3); 2.8(s, 3H, 4-CH_3), 3.9(s, 3H, OCH_3); 7.2(s, 5H, 3-Ph); 7.4(d, Cα-H, J=9 Hz); 7.5(m, 7H, aromatic & Cβ-H merged	---	---	---	---
3o	Pink	122	55	1660, 1625, 1595, 1190, 840	---	---	---	---	---
3p	Green	138	70	3300, 2920, 1676, 1640, 1175, 840	---	---	---	---	---
3q	Pale Green	145	65	3230, 1670, 1640, 1170, 840	---	---	---	---	---
3r	Blue	180	75	1680, 1640, 1200, 1170, 840	δ 2.4(s, 6H, Two-CH_3); 2.8(s, 3H, 4-CH_3); 3.9(s, 3H, OCH_3); 7.1(d, 1H, Cα-H); 7.3(s, 5H, 3-Ph); 7.5(m, 6H, aromatic); 7.8(d, 2H, J= 9 Hz); 8.2(d, 1H, J=9 Hz); 8.4(d, 1H, Cβ-H, J=9 Hz)	---	---	---	---

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