Fast synthesis of some pyrimidines under microwave irradiation

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Abstract: - Under microwave irradiation furfuraldehye reacts with substituted acetophenones in the presence of sodium hydroxide solution, chalcones have been synthesised. These chalcones were allowed to react with urea in the presence of aqueous sodium hydroxide under microwave irradiation giving rise to corresponding hydroxy pyrimidines. In few minutes, syntheses of chalcones have been achieved rather than 24 hours of shaking. Again syntheses of hydroxyl pyrimidines have been achieved in few minutes rather than 16-22 hours of heating[1]. To diminish the cost of target use of ethanol[1] as solvent has been ignored.

Keywords: - Chalcones, hydroxy pyrimidines, microwave irradiation, solvent free condition.

INTRODUCTION

Among various classes of organic compounds owing to their diverse biological activities, heterocyclic compounds, especially five and six membered ring compounds, have got the top position. The biological significance of pyrimidine derivatives[1] has also been reported. As pyrimidine is a basic nucleus in DNA and RNA, it has been found to be associated with diverse biological activities[2]. Several important sulfa drugs are pyrimidine derivatives namely sulfadiazine, sulfamerazine and sulfadimidine. A variety of natural products such as alkaloids also contain the pyrimidine ring system. These include hypoxanthine and xanthine, which occur in tea, caffeine and theophylline. The pyrimidine compounds show interesting activities like antimicrobial[3], antitumor[4], antifungal[5], anti-inflamatory[6] and anthelmentic[7].

The chalcones are α, β-unsaturated ketones containing the reactive ketoethylenic group, -CO-CH = CH - . Presence of α, β-unsaturated carbonyl system in chalcone makes it biologically active. Some substituted chalcones and their derivatives have been reported to possess some interesting biological and pharmacological properties.

Inspired by the varied biological and pharmacological activities of chalcones and pyrimidines, it was invisaged to synthesise a few of them starting from furfural. The same has been achieved under microwave irradiation in solvent free condition. The purpose is to save the time and to lower the cost of the products, as they have medicinal value. Microwave irradiation is an efficient and environmentally benign method to activate various organic transformations to afford products in higher yields and in shorter reaction periods. It also results in an increase in the purity of the products and involves very small amount of solvent or no solvent. In the present work, use of solvent (ethanol) has been discarded. The synthetic sequences leading to the formation of the target has been depicted in Scheme-1.

EXPERIMENTAL

In open capillary tubes all melting points were determined and are uncorrected. For monitoring the reaction and to chek the purity, TLC was used. Reactions were carried out under microwave irradiation in a Kenstar OM-20ESP (800W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table-1 and 2.

To synthesise 3-(furan-2-yl)-1-phenylprop-2-en-1-one (3a), a mixture of 0.01 mol (0.840 g) of furfural, 0.01 mol (1.200 g) of acetophenone and 10ml of 40% NaOH was irradiated by microwaves at 20% (160W) level in a Kenstar OM-20ESP (800W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table-1. On cooling, crushed ice was added and then the reaction mixture was rendered acidic with hydrochloric acid. The product was filtered off, washed with water and recrystallised from aqueous ethanol. The remaining chalcones were synthesised in similar fashion.

To synthesise 4-(furan - 2 - yl) - 6 - phenylpyrimidine-2-ol (4a), a mixture of 0.01 mol of chalcone (3a), 0.01 mole of urea and 10 ml of 40% NaOH was irradiated by microwaves at 40% (320 W) level in a Kenstar OM-20ESP (800W), unmodified domestic oven operating at 2450 MHz for the time indicated in Table-2. On cooling, ice cold water (250 ml) was added. The precipitate so formed was filtered off, washed with cold water and then recrystallised from aqueous ethanol.

3-(Furan-2-yl)-1-phenylprop-2-en-1-one (3a) :

IR (KBr, υ_{max} , cm^{-1}) :	3120, 2915	(C-H)
1667	(C=O)	
1581	(C = C)	
1077	(C-O-C)	

^{1}H NMR (TMS, δ ppm) :7.5 - 7.7		(m, Ar-H, 5H)
7.9 - 8.14	(m, furan, 3H)	
6.8	(d, = C.H, 1H)	
6.5	(d, = C.H, 1H)	

3-(Furan-2-yl)-1-(2-hydroxyphenyl) prop-2-en-1-one (3b) :

IR (KBr, υ_{max} , cm^{-1}) :	3120, 2915	(C-H)
1668	(C=O)	
1580	(C = C)	
1075	(C-O-C)	
3600	(O-H)	

^{1}H NMR (TMS, δ ppm) : 7.5 - 7.7		(m, Ar-H, 5H)
7.9 - 8.14	(m, furan, 3H)	
6.8	(d, = C.H., 1H)	
6.5	(d, = C.H., 1H)	
10.8	(s, OH)	

4-(Furan-2-yl)-6-phenylpyrimidine-2-ol (4a) :

IR (KBr, υ_{max} , cm^{-1}) :	3125	(C-H)
1582	(C=C)	
1553	(C = N)	
1159	(C-O-C)	

^{1}H NMR (TMS, δ ppm) :12.83	(s, OH, 1H)
6.58 - 7.93	(m, Ar-H, 9H)

4-(Furan-2-yl)-6-(2-hydroxphenyl) Pyrimidine-2-01 (4b) :

IR (KBr, υ_{max} , cm^{-1}) :	3125	(C-H)
1581	(C=O)	
1554	(C = N)	
1158	(C-O-C)	

^{1}H NMR (TMS, δ ppm) :12.83 (s, OH, 1H)
10.58 (s, OH, 1H)
6.58 - 7.93 (m, Ar-H, 8H)

RESULT AND DISCUSSION

In first step, chalcones (3a - k) were prepared under microwave irradiation at 20% (160W) level in Kenstar OM-20 ESP (800W) for 4-5 minutes rather than 24 hours of shaking. In second step pyrimidines (4a-k) have been synthesised under microwave irradiation at 40% (320 W) level in the household microwave oven (800W) for 3-4 minutes rather than 16-22 hours of traditional heating. In both the steps, use of ethanol as solvent has been ignored to diminish the cost of the products.

Reactions were carried out under atmospheric pressure in an open vessel adopted to a microwave oven. Purity of the compounds were checked by TLC. Melting points were taken in an open glass capillary using Elico Melting Point apparatus and are uncorrected. The compounds synthesised are all known compounds and have been characterised on the basis of their melting points, IR and NMR.

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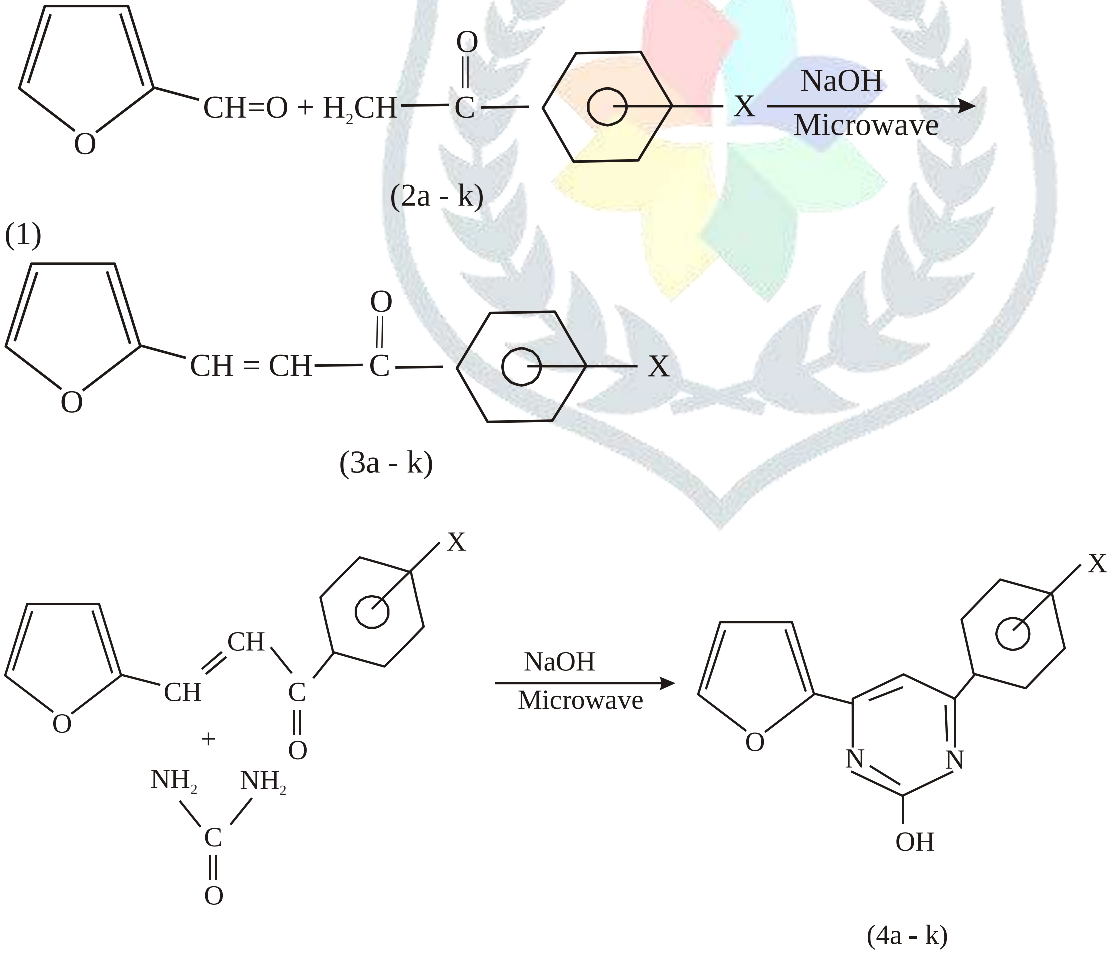

(Scheme - 1)

Table - 1

Results of synthesis of chalcones under microwave irradiation

Compound	X	Time (min.)	M.P. (^{0}C)	Yield (%)
3a	H	5		79
3b	o-OH	5	148-150	85
3c	p-OH	5	158-160	88
3d	p-Cl	5	171-173	78
3e	p-OCH_3	5	162-164	82
3f	p-CH_3	5	150-152	77
3g	m-NO_2	4	140-143	80
3h	p-NO_2	4	155-157	75
3i	p-NH_2	5	144-146	83
3j	p-Br	5	136-138	80
3k	o-NO_2	4	154-156	85

Table - 2

Results of synthesis of pyrimidines under microwave irradiation

Compound	X	Time (min.)	M.P. (^{0}C)	Yield (%)
4a	H	4		75
4b	o-OH	4	132-135	85
4c	p-OH	4	171-173	80
4d	p-Cl	4	108-110	79
4e	p-OCH_3	4	142-144	70
4f	p-CH_3	4	136-138	80
4g	m-NO_2	3	114-116	76
4h	p-NO_2	3	186-188	75
4i	p-NH_2	4	118-120	79
4j	p-Br	4	98-100	72
4k	o-NO_2	3	181-183	87

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