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AN EFFICIENT ONE POT SYNTHESIS OF 3-PHENYL AND 3-NAPHTHYLCOUMARINS USING MICROWAVE IRRADIATIONS

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ABSTRACT
A simple, one pot, fast and high yielding method with simple workup procedure for the synthesis of 3-phenyl and 3-naphthylcoumarins is reported by modification of Perkin method using activated $Ba(OH)_2$ / DMSO medium under microwave irradiation.

KEYWORDS
3-phenylcoumarin, 3-naphthylcoumarin, modified Perkin reaction, microwave irradiation, activated $Ba(OH)_2$, 2-hydroxybenzaldehyde, DMSO.

INTRODUCTION

Coumarin, an important class of oxygen heterocyclic compounds, occupies a special place in the realm of natural and synthetic organic chemistry because of their diverse and potent biological activities[1]. The very long association of plant coumarins with various animal species and other organism throughout evolution may account for the extraordinary range of biochemical and pharmacological activities of these compounds in mammalian and other biological system[2]. The coumarins have long been recognized to possess anticoagulant, antimicrobial, antioxidant, cytotoxic and anti-HIV activities[1,3].

Among these 3-phenylcoumarins have attracted a special interest because they play a vital role in electrographic and electroluminescent devices[4] and also show fungicidal[5] and anti-HIV[6] activities. Recently they have also been found as potent inhibitor of aromatase[7], horseradish peroxidase[8] catalytic activities and do inhibition of thromboplastin induced disseminated intravascular coagulation[9].

Synthesis of 3-phenylcoumarins has been affected in several ways. Perkin method[10] which involves condensation of phenyl acetic acid with appropriate *o*-hydroxy benzaldehyde in acetic anhydride is the standard method which is even used today. But Perkin method suffers drawback of using excess of acetic anhydride, harsh conditions, tedious workup and unsatisfactory low yields. So, other modifications of Perkin method have been reported in which phenylacetic acid or acetic anhydride is replaced by more reactive and milder species such as Perkin Oglialoro reaction[11]. In another modifications use of Phenylacetyl chloride/K_2CO_3 in acetone[12], N,N,-Dimethyldichloro phosphoryl oxomethylene ammonium chloride/phenylacetic

acid in Et_3N[13], phenylacetic anhydride/ K_2CO_3 in phase transfer catalysed condition[14] has been reported. Synthesis of 3-phenyl coumarin has also been reported by Meerwin reaction[15], by reduction of 4- hydroxy-3-phenylcoumarin[16], by Wittig reaction[17], from Isoflavylium salts[18], by photochemical coupling reaction[19], from 2-methoxychalcones[20], by Mukaiyama esterification conditions[21] and intramolecular cyclisation of the esters of salicylaldehyde[22].

But the modifications of Perkin method and other methods which are reported so far, suffer one or more limitations, such as multiple steps, hazardous and non economical conditions, corrosive condensing agent, tedious and unhygienic workup, lengthy reaction time, and low yields. So methods for synthesis of these compounds are still demanding further improvement.

In these days organic reactions using microwave irradiations have gained enormous importance as it accelerates the variety of organic transformations[23]. Another important feature of this technique is that many of the reactions can be carried out in solvent free conditions and also minimize the side products[24].

RESULTS AND DISCUSSION

Herein we report an efficient modification of the Perkin method for the synthesis of 3-phenycoumarins (scheme1) by reacting 2-hydroxy benzaldehydes with phenylacetic anhydride in activated $Ba(OH)_2$/DMSO medium under microwave irradiations, which give 3-phenylcoumarin in improved yield, directly in one step on simple acidification of the reaction mixture in cold. For model reaction, a mixture of salicyldehyde and phenylacetic anhydride in DMSO was taken in 20 ml loosely stoppard Pyrex bottle and was irradiated using activated barium hydroxide as base in domestic microwave oven for 10 seconds. The progress and completion of the reaction was checked on TLC which showed a blue fluorescent spot in ultraviolet light where as starting material exhibited themselves as purple non fluorescent spots. The compound obtained after working up was identified as 3- phenylcoumarin by its ^1H NMR, CO-IR and on direct comparison with authentic sample. Using this procedure variously substituted 3-phenylcoumarins were synthesized by reacting differently substituted 2-hydroxybenzaldehydes with phenylacetic anhydride and 4- methoxy phenylacetic anhydride (Table1).

3-(1-Naphthyl)coumarins though are not of natural occurrence but like 3-phenyl coumarins they are reported to exhibit anticoagulant properties[25]. So application of the present method was further successfully extended for the synthesis of 3-(1-naphthyl) coumarin by reaction of differently substituted 2-hydroxybenzaldehydes with 1-naphthyl acetic anhydride.

Table 1. Synthesis of 3-phenyl and 3-naphthyl coumarins[a]

Entry	R	R^1	Time (sec.)	Yield (%)[b]	mp °C Obs.(Lit)	References
1	C_6H_5	H	10	96	140-141(141)	12
2	C_6H_5	Cl	8	95	195-196 (194)	26
3	C_6H_5	Br	8	96	194-196 (197)	26
4	C_6H_5	CH_3	10	92	144-145 (146-147)	14
5	*p*-MeO C_6H_4	H	12	90	143-144 (142-144)	14
6	*p*-MeO C_6H_4	Cl	10	92	190-192	-
7	*p*-MeO C_6H_4	Br	10	91	201-202	-
8	*p*-MeO C_6H_4	CH_3	10	92	142-143 (143)	14
9	1-Naphthyl	H	12	94	155-156 (155-156)	27
10	1-Naphthyl	Cl	10	92	152-153 (154-155)	27
11	1-Naphthyl	Br	10	94	127-128 (126-127)	27
12	1-Naphthyl	CH_3	10	91	133-134 (133-134)	27

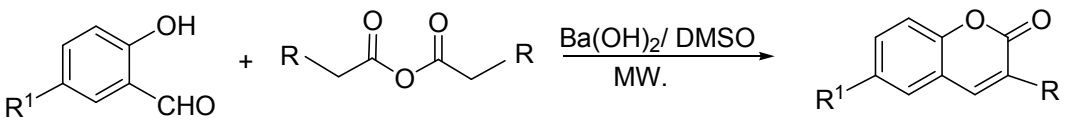
[a]The products were characterised from their ^{1}H NMR , IR and on comparison with the authentic samples. [b]isolated yields.

EXPERIMENTAL

The reaction was carried out in a domestic microwave oven (Samsung output energy 900W, frequency 2450MHz, with temperature control arrangement No. CE 118KF) Using 30% power for all the experiments and maintaining the oven temperature at 40 ^{0}C in 20 ml loosely stoppered Pyrex bottle. The ^{1}H NMR spectra were recorded on Bruker Avance II 400 spectrometer at 400 MHz in $CDCl_3$ using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constant in Hz. The IR spectra were recorded using Perkin Elmer spectrometer (KBr plates).

General experimental procedure

A mixture of 2-hydroxybenzaldehyde (0.004 mole), phenylacetic anhydride (0.005 mole) and activated $Ba(OH)_2$ (C-200; 0.5 g) in DMSO (5.0 ml) was taken in 20 ml loosely stoppard Pyrex bottle and was irradiated in domestic microwave oven for the time period as shown in the table. Completion of the reaction was checked on TLC. Crushed ice was added to the reaction mixture and acidified with conc. HCl, solid product thus obtained was filtered and recrystallized from diethyl ether/pet.ether.



Scheme 1

Spectral data of compounds (6-7)

6. IR (KBr) 1718 cm^{-1} ($\nu_{C=O}$)
^1H NMR ($CDCl_3$) δ 3.86, (3H, OCH_3) δ 6.97-7.68 (m, 8H,7 Ar-H and H-4).

7. IR (KBr) 1720 cm^{-1} ($\nu_{C=O}$)
^1H NMR ($CDCl_3$) δ 3.86, (3H, OCH_3) δ 6.97-7.67 (m, 8H,7 Ar-H and H-4)

Conclusion

In conclusion it can be stated that present method is highly efficient, microwave assisted, one step protocol for the synthesis of 3-phenyl and 3-naphthylcoumarin. It provides the title compounds very rapidly by the use of safe chemicals, easy workup procedure, in highly improved yields.

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