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Solvent Free Microwave Assisted O – Alkylation and Acylation of 4 – Hydroxy Coumarin

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ABSTRACT

Under microwave irradiation 4-Hydroxy coumarin reacts remarkably fast with a number of alkyl and acyl halides to give O-alkyl and acyl derivatives of coumarin. The reaction was carried out under solvent free conditions in the presence of sodium hydroxide and copper/ copper chloride reagent. The short reaction time (60 to 240 sec.), cleaner reaction and easy work up make this protocol practically and economically attractive.

Keywords: *Coumarin, Sodium hydroxide, copper/copper chloride, alkyl halide, acyl halide and Microwave.*

INTRODUCTION

Microwaves are a powerful reliable energy source that may be adapted to many applications. It has been reported that microwaves will provide the organic chemist with the right tools and knowledge to be able to effectively apply microwave energy to any synthetic route [1].

Microwave heating and its application in organic chemistry for the reactions in 'dry' media is currently developed successfully and in the past few years there has been a tremendous interest in this area [2]. Remarkable decrease in reaction times and in some cases cleaner reaction and better yields have been reported with microwave irradiation. Reactions under dry conditions (i.e., in the absence of a solvent, on solid support with or without catalysts) were originally developed in last eighties. Synthesis without solvents under microwave irradiation offers several advantages. The absence of solvent reduces the risk of hazardous explosions when the reaction takes place in a closed vessel in an oven. During microwave induction of reactions under dry conditions the reactants adsorbed on the surface of alumina, silica gel and clay absorb the microwaves where as the support does not. Consequently, such supported reagents efficiently induce reactions under safe and simple conditions with domestic microwave ovens instead of specialized commercial microwave systems that require sealed Teflon bombs [3].

Coumarin derivatives have been of great interest because of their role in natural and synthetic organic chemistry. Many products which contain a coumarin subunit exhibit biological activity such as anthelmintic, hypnotic, insecticidal activity and some are serving as anticoagulant agents and fluorescent brighteners. Coumarins containing a Schiff base are expected to have enhanced antitumor and other biological activities [4].

A large number of structurally novel coumarin derivatives have ultimately been reported to show substantial cytotoxic and anti-HIV activity in vitro and in vivo [5]. Coumarin derivatives are also used as drug and pesticide intermediates. Several natural products with a coumarin moiety have been reported to have multiple biological activities. The compounds derived from natural coumarin, scopoletin, showed insect antifeedants activity [6]. 4-Hydroxycoumarins have evoked a great deal of interest due to their biological properties and characteristic conjugated molecular architecture. Many of them display important pharmacological effects, including analgesic [7], anti-arthritis [8], anti-inflammatory [9], anti-pyretic [10], anti-bacterial [11, anti-viral [12], anti-cancer [13] and also show antifungal action [14] properties.

MATERIALS AND METHODS

General procedure for synthesis of ethers and esters

In a typical experiment of coumarin (2·5 mmol) in aqueous sodium hydroxide (NaOH 3 mmol, H_2O cm^3) was irradiated in 600 W for 60 seconds in order to obtain solid coumarin salt. Then organic halide (3·0 mmol) was mixed with the resulting solid and few drops of water were added. The reaction mixture was irradiated in the specified power for the specified time. After cooling down at room temperature, the product formed was washed with water to remove the unreacted salt and the excess sodium hydroxide. Finally it was purified by recrystlisation.

In another experiment, coumarin (3 mmol), alkyl halide (2 mmol) and copper (1·1 mmol) were irradiated in microwave oven. The product was washed with water (20 cm^3) and dried over anhydrous sodium sulphate. The crude product was purified by using ethanol.

The melting points were taken in open capillaries in paraffin bath and are uncorrected. IR spectra were recorded in KBr discs on a Perkin Elmer spectrometer for all products ^{1}H NMR spectra were recorded on EM – 360 60 MHz NMR spectrometer in $CDCl_3$ using DMSO as internal standard. The mass spectra were recorded on GCMS-QP 2010 mass spectrometer. All the reagents used were of AR grade and were used without further purification. The reactions were carried out in microwave oven. (CE 2977 Samsung). All compounds were characterized by modern spectral and elemental techniques.

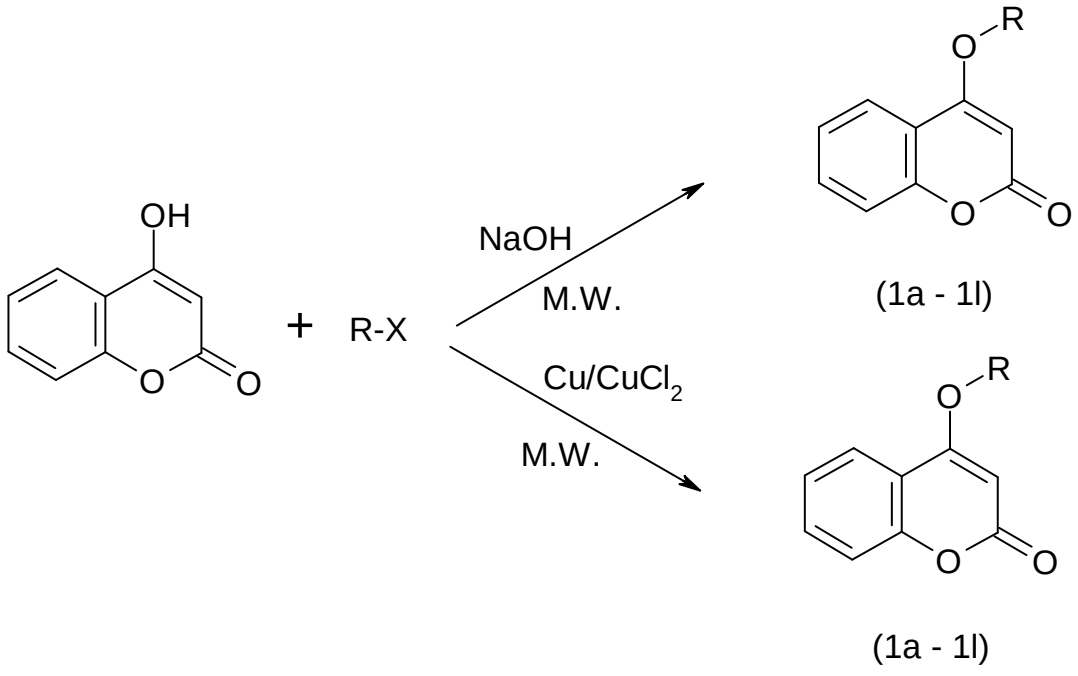
1f. ***4-(benzyloxy)-2H-chromen-2-one***

FT-IR (KBr, ν cm^{-1}): 3067 (C-H aromatic), 2892 (C-H aliphatic), 1605 (C=O), 1296, 1326 (C-O ether), 1397 (C -H bending), 1199 (C-O aliphatic).

^{1}H NMR: ($CDCl_3$, δ ppm) : - 7.860-7.285 (m, 9H,Arom), 5.740 (s, 1H) , 3.362 (s, 2H), Mass (ES/MS): m/z 253 (M - H).

RESULT AND DISCUSSION

Under microwave irradiation, number of alkyl and acyl halides reacts remarkably fast with coumarin to give aromatic ethers and esters. The results are summarized in Table- I.



R-X = Acyl / alkyl halide

Table:-I Alkylation and Acylation of Coumarin under Microwave irradiation

Compd	R	W and T required for reaction* NaOH method W	Sec.	Cu/CuCl2 method W	Sec.	M.P. (^{0}C)	Yield (%) NaOH Method	Cu/$CuCl_2$ Method
1a	C_2H_5--	600	90	600	120	208	48	60
1b	CH_2=CH-CH_2-	600	120	600	90	280	62	62
1c	Cl-CH_2-	600	90	600	120	210	58	68
1d	Cl-CH_2-CH_2 -	600	90	600	120	212	49	66
1e	COOH-CH_2-	600	98	600	120	209	69	78
1f	PhCH_2-	600	90	600	120	210	60	54
1g	ClPhCOCH_2-	600	60	600	120	155	54	85
1h	CH_3CO-	600	60	600	238	198	66	64
1i	C_2H_5CO-	600	60	600	240	175	70	68
1j	C_4H_9CO-	600	60	600	240	209	62	60
1k	PhCO-	600	90	600	120	187	60	71
1l	ClPhCO-	600	60	600	120	200	49	73

* Where W and T indicate watts and time, respectively.

It has been observed that the presence of a few drops of water is very important for NaOH method presumably, the major effect was that water could couple efficiently with microwave or could make the reaction subjects homogenization. “Water was so crucial that its absence decrease the yield”.

CONCLUSION

The present investigation has been developed by simple and economical one step Procedure for ethers and esters of coumarin that occurs under mild conditions using Inexpensive reagents and microwave oven as the irradiation source. Moreover, our Method of ether and ester synthesis is superior to other methods. We use coumarin, Alkyl and acyl halides as starting materials instead of Inorganic carriers and organic Solvents. This makes the procedure simple, convenient and safe. On the other hand, this Study leads to a better understanding of O-alkylation and acylation of coumarin derivatives.

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REFERENCES

1. Brittany L. Hayes. (2002) "Microwave Synthesis" © CEM Publishing U.S.A. P. 14.
2. Caddick S. (1995).Tetrahedron, 51, 10403.
3. Bram G., Loupy A., Villemin D. (1992). In Solid supports and catalysts in organic chemistry Ellis Harwood London.
4. Jin L., Chen J., Song B., Chen Z., Yang S., Li Q., Hu D., Xu R. (2006). *Bioorg. Med.Chem. Lett*., 16, 5036.
5. Spino **C.**, Dodier M., Sotheeswaran S. B. (1998). *Med. Chem. Lett.,* 8, 3475.
6. Nagaiah K., Krupadanam G. L., David S. G. (2002). *Indian J. Chem*., 41B (4), 858.
7. Adami E., Marazzi-Uberti E., Turba C. (1959). *Ital. Sci. Farmacol*., 9, 61.
8. Chiarino D., Grancini G. C., Frigeni V., Carenzi A. (1988).Eur. Pat. Appl. EP. 284017.
9. Luchini A. C., Rodrigues-Orsi P., Cestari S. H., Seito L. N., Witaicenis A., Pellizzon C. H. (2008). *Biol. Pharm. Bull*., 31, 1343.
10. Stern P., Dezelic M., Kosak R. (1957). *Arch. Exp. Pathol. Pharmakol*., 232, 356.
11. Chohan Z.H., Shaikh A.U., Rauf A., Supuran C. T. (2006*). J. Enz. Inhib. Med. Chem*., 21, 741.
12. Kirkiacharian B.S., Clercq E., Kurkjian R., Pannecouque C. (2008*). J. Pharm. Chem.,* 42, 265–270.
13. Velasco-Velázquez M. A., Agramonte-Hevia J., Barrera D., Jiménez-Orozco A. M.,García - Mondragón J., Mendoza-Patiño N., Landa A., Mandoki (2003). *J.Cancer Lett.,* 198, 179.
14. Nagaiah K., Krupadanam G. L., David S. G. (2002). *Indian J. Chem.,* 41B (**4**), 858.