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Microwave assisted synthesis of 1,4-benzothiazine esters

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ABSTRACT

A series of phenyl 2-(3,4-dihydro-3-oxo-2H-benzo[b][1,4]thiazin-2-yl)acetate have been synthesized by using microwave technique. This method requires very short period of time, better yield with high purity as compared to conventional method.

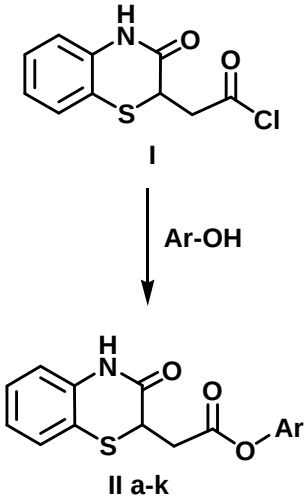
KEYWORDS

1,4-benzothiazine;
Ester;
Microwave irradiation.

INTRODUCTION

Heterocyclic moieties can be found in a large number of compounds which display biological activity. The biological activity of the compounds is mainly dependent on their molecular structures[1]. In recent years sulphur and nitrogen containing compounds have gained unique importance due to broad spectrum of pharmacological activities[2,3] which are reflected by their use as analgesic[4], antifungal[5], antiinflamatory[6,7] and anti HIV activity[8]. 1, 4-benzothiazine and it's derivatives plays an important role in biochemical processes[9]. Clinical and pharmacological properties of 10H-phenothiazines and 4H-1,4-benzothiazines have been widely studied since a long time which appears in numerous biologically active natural products[10]. The biological activities of the compound containing this basic moiety wieldy used as antihistaminics[11], antipsychotics[12], antiemetics[13], neuroleptics[14], tranquilizers[15] esterification is an important reaction in organic synthesis; and ester have a wide applicability in peptide synthesis[16], medicinal chemistry[17,18], as chiral sources[19-22] and polymer materials[23,24].

The use of microwaves in organic synthesis has increased dramatically in the last years, receiving widespread acceptance and becoming an indispensable tool[25]. Microwave technology has become a powerful tool in organic synthesis, since by employing this technique it is generally possible to prepare organic compounds very fast, with high purity and better yields compared to other more conventional methods[26-28]. In the search for economic and environmentally friendly synthetic methods, syntheses of esters of 1,4- Benzothiazine acid with phenols by using microwave offer a significant rout for green method.



Scheme 1

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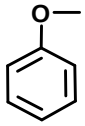
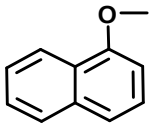
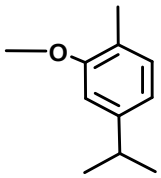
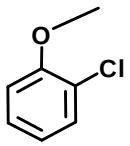
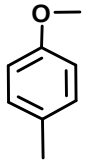
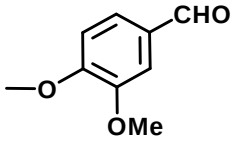
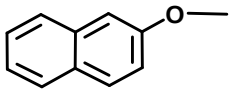
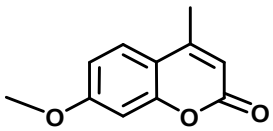
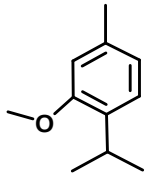
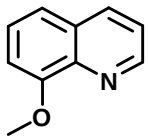
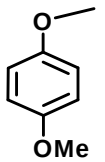
TABLE 1 : Physical constants and time requirement of compounds (II a-k)

Comp.	Ar	Obs. M. P. (°C) (Lit[29].M.P.)	Time in Min. (Time for Conventional in Hrs.)	M.W. Yield (%) (conventional yield %)	Molecular Formula
II a		269-270 (267-268)	6 (6)	93 (82)	$C_{16}H_{13}O_3NS$
II b		237-238 (239)	8 (7)	88 (75)	$C_{20}H_{15}O_3NS$
IIc		274-275 (276-278)	8 (7)	81 (77)	$C_{20}H_{21}O_3NS$
II d		280-281 (278-279)	9 (7)	83 (76)	$C_{16}H_{12}O_2NSCl$
II e		206-208 (204-205)	7 (8)	79 (73)	$C_{17}H_{12}O_3NS$
II f		291-292 (292)	12 (8)	89 (78)	$C_{18}H_{15}O_5NS$
II g		282-283 (281-282)	9 (7)	88 (75)	$C_{20}H_{15}O_3NS$
II h		247-248 (245-246)	10 (7)	86 (77)	$C_{20}H_{15}O_5NS$
II i		277-278 (279-280)	8 (7)	87 (76)	$C_{20}H_{21}O_3NS$
II j		256-257 (255-256)	7 (8)	88 (79)	$C_{19}H_{14}O_3N_2S$
II k		189-190 (188)	8 (8)	89 (80)	$C_{17}H_{16}O_3NS$

EXPERIMENTAL

Melting points of all the synthesized compounds were determined by open capillary method and are uncorrected. The purity of synthesized compounds was checked by thin layer chromatography. The homogeneity of the compounds was monitored by ascending TLC on silica gel (Merck) glass plates, visualized by iodine-vapour. Developing solvents were hexane-ethyl acetate (8:2). All the chemicals and solvents used were of synthetic grade (S. d. Fine, chemicals, Mumbai, India).

phenyl 2-(3,4-dihydro-3-oxo-2H-enzo[b][1,4]-thiazin-2-yl)acetate (Va)

A mixture of phenol (10mmol) in DMF (30mL) containing K_2CO_3 (20mmol) were irradiated for 2 min and then compound I (10mmol) was added slowly over the period of 2 min. The reaction mixture was again irradiated in microwave at power 60 for 4 min. with intervals of 1 min. The progress of reaction was monitored by TLC. After completeion of reaction, the reaction mixture was cooled, poured in ice and neutralized with dilute HCl. The separated solid was filtered, washed with water. Crude compound was recrystallised from ethanol. Yield 93 %, m.p. 269-270^{0}C. A Kenstar, (OM30DCF), (2450W) domestic monomode microwave with facility to change the power level was used to carryout the reaction.

RESULT AND DISCUSSION

In contribution of our works on synthesis of heterocyclic compound[29], ester of 1,4-benzothiazines were synthesized by conventional method. The conventional method requires 6-8 hrs. with moderate yield. Phenol, p- cresol requires less time while vanillin, 4-Me-7-hydroxy coumarin requires more time and remaining requires moderate time.Further increase in microwave irradiation period resulted no improvements of results.

CONCLUSION

The 1,4-benzothiazine esters were synthesized by conventional as well as microwave irradiation technique. The microwave irradiation technique was found to be more convinent dueto short reaction time, small quantity of reactants and solvent are required. Moreover the product obtained were of high purity with greater yield than conventional methode.

In conclusion, we have developed simple, rapid and greener methodology for the synthesis of esters of 1,4-benzothiazine.

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