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A Microwave – assisted : Synthesis and Characterization of Thiazines or 2-Mercapto-4,6-Diaryl-5,6-Dihydropyrimidines and their Antimicrobial activity

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Abstract : The reaction time needed to synthesize differently substituted 2-mercapto-4,6-diaryl-5,6-dihydropyrimidine and their antimicrobial activity was substantially reduced from hours to minutes by means of microwave irradiation MORE chemistry techniques have many advantages i.e. very rapid reactions, low electrical energy consumption and safe operation high yield less time.
Key words: Microwave irradiation, thiazines of derivatives and antimicrobial activity.

INTRODUCTION:

The earlier workers have studied the reaction of chalcones with thirourea and reported the products either as 2-mercaptopyrimidines or thiazines[1-3].

This prompted US to study the reactions of substituted chalcones with thiourea using different reaction solvent media conditions such as ethanol (S_1), DMF (S_2) and DMSO (S_3) the reactions were carried out for 6 min to 3 hrs for getting the maximum yields of the products (S)[4-5].

In recent years, microwave irradiation using commercial domestic ovens has been rapidly increased for optimization and acceleration of organic synthesis under solvent free conditions[6-12]. It has been reported for the variety of reactions such synthesis of heterocyclic[13] and more recently for synthesis of polymers[14] because of advantages such as reduction in reaction time, improved energy utilization, potential for lower processing temperature and improved product uniformity.

In connection with our interest in the use of microwave, we report herein the synthesis of several 2-mercaptopyrimidines in minimum solvent and minimum time under microwave irradiation (Scheme I).

In conventional method for the synthesis of several 2-mercaptopyrimidines thiazine derivatives. The molar ration of chalcone with thiourea using different solvent media condition such as ethanol, DMF and DMSO with KOH and refluxed for 3 hrs for effective condensations. In contrast under microwave irradiation, the reaction are completed within 6-8 min in equimolar proportion and almost in all cases afford the product in high yield.

The products were characterised on the basis of their M.P., TLC, IR, ^{1}HNMR.

In conclusion, we have described a novel and highly efficient rapid microwave induced modification of the synthesis of 2-mercaptopyrimidines or thiazine. MORE chemistry reactions are highly accelerated, they are cleaner than conventional reactions and lead to higher atom economy (less chemical waste) and follow the environmental friendly protocol include a reaction set up not requiring specialized equipment, high product yields, short reactions times and the

elimination of usage of excess of solvents in some reactions.[15-22]

EXPERIMENTAL SECTION

All the synthesized compounds were purified by recrystallization by using ethanol. The melting points were recorded on melting point apparatus in open capillaries and are uncorrected. All melting points were composed with the authentic samples and are found to be same. The purity of compounds was checked by TLC using silica gel. All reactions were carried out in a commercially available IFB domestic microwave oven having a maximum power output of 110W operating at 2450 H_2, IR spectra were obtained on a Perkin Elmer 1800 spectrophotometer using KBr discs, ^{1}HNMR spectra were recorded using AC Bruker 300 F.

Synthesis of thiazines or 2-mercapto-4,6-diaryl-5,6dihydropyrimidine(4) under different two methods

Method-A (Conventional)

Benzalacetophenone (chalcone) (3) (0.01 mole; 2.08 g) thiourea (0.02 mole; 1.52 g) and KOH (0.02 mole; 1.12 g) were taken in a 100 ml round bottom flask. To the above reaction mixture ethanol (30ml) was added. Reaction mixture was refluxed for 3 hrs using water condenser. It was then cooled and poured in cold water. Acidified with dill HCl filtered washed with water and dried. The product was recrystalization from ethanol to get the product.

Yield 70% **M.P.** 179ºC

Method-B (Microwave Irradiation)

Benzalacetophenone (chalcone) (3) (0.01 mole; 2.08 g) thiourea (0.02 mole; 1.52 g) and KOH (0.02 mole; 1.12 g) were dissolved in 10 mother-in-law ethanol. The contents were thoroughly mixed. The reaction mixture was subjected to microwave irradiation in a commercially available IFB domestic microwave oven having a maximum power output of 110W operating at 2450Hz intermittently at 30 seconds intervals for 6-8 min on a completion of reaction as monitored by TLC. It was then cooled and poured in cold water acidified with dill HCl. Filtered, washed and dried. The product was recrystallized from ethanol to get product. The purify of the compound was checked with TLC.

Yield 90% **M.P.** 180ºC

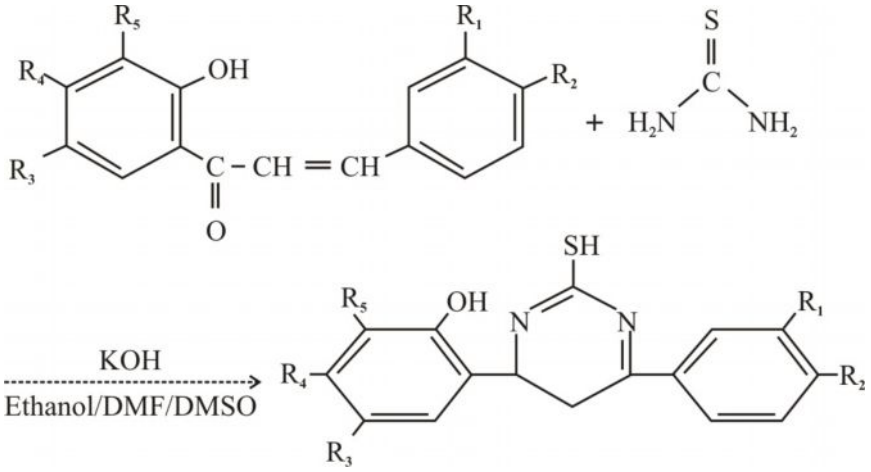
RESULTS AND DISCUSSIONS

2-mercapto-4,6-diaryl-5,6-dihydropyrimidines, prepared by the cyclic condensation of 2-hydroxy chalcone with thiourea in ethanol, dimethyl formamide and dimethyl sulphoxide.

In conventional method for the synthesis of several 2-mercaptopyrimidines thiazine derivatives. The molar ration of chalcone with thiourea using different solvent media condition such as ethanol, DMF and DMSO with KOH and refluxed for 3 hrs for effective condensations. In contrast under microwave irradiation, the reactions are completed within 6-8 min in equimolar proportion and almost in all cases afford the product in high yield.

The products were characterised on the basis of their M.P., TLC, IR, ^{1}HNMR and their antimicrobial activity of dihydropyrimidines with their zone of inhibition (in mm) 4a to 4n.

SCHEME – I



Characterization data of Method – A (conventional) in time and yield of compounds synthesized (4-4^n)

Compounds	R_1	R_2	R_3	R_4	R_5	Molecular formula	MP°C	Method-A Yield/Time %/hr
4a	H	H	H	OH	H	$C_{16}H_{14}N_2OS$	185	60/3
4b	H	H	CH_3	H	H	$C_{17}H_{16}N_2OS$	205	70/3
4c	H	H	Cl	H	H	$C_{16}H_{13}N_2CloS$	215	75/3
4d	H	H	CH_3	H	NO_2	$C_{17}H_{15}N_3O_3S$	210	70/3
4e	H	H	Cl	H	NO_2	$C_{16}H_{12}N_3O_3ClS$	205	70/3
4f	H	H	Cl	H	Br	$C_{16}H_{12}N_2ClBrOS$	207	60/3
4g	H	OCH_3	H	H	H	$C_{17}H_{15}N_2O_2ClS$	195	70/3
4h	H	OCH_3	H	OH	H	$C_{17}H_{15}N_2O_2ClS$	165	67/3
4i	H	OCH_3	CH_3	H	H	$C_{18}H_{18}N_2O_2S$	185	65/3
4j	H	OCH_3	Cl	H	H	$C_{17}H_{15}N_2O_2ClS$	210	80/3
4k	H	OCH_3	CH_3	H	NO_2	$C_{18}H_{17}N_3O_4S$	195	65/3
4l	H	OCH_3	Cl	H	NO_2	$C_{17}H_{14}N_3O_4ClS$	195	63/3
4m	H	OCH_3	Cl	H	H	$C_{17}H_{14}N_2O_2ClBrS$	161	60/3
4n	NO_2	H	Cl	H	H	$C_{16}H_{12}N_3O_3ClS$	160	70/3

Characterization data of Method – B (microwave irradiation) in time and yield of compounds synthesized (4-4^n)

Compounds	R_1	R_2	R_3	R_4	R_5	Molecular formula	MP°C	Method-B Yield/Time %/min
4a	H	H	H	OH	H	$C_{16}H_{14}N_2OS$	185	89/6
4b	H	H	CH_3	H	H	$C_{17}H_{16}N_2OS$	205	90/6
4c	H	H	Cl	H	H	$C_{16}H_{13}N_2CloS$	215	91/6
4d	H	H	CH_3	H	NO_2	$C_{17}H_{15}N_3O_3S$	210	84/6
4e	H	H	Cl	H	NO_2	$C_{16}H_{12}N_3O_3ClS$	205	90/6
4f	H	H	Cl	H	Br	$C_{16}H_{12}N_2ClBrOS$	207	80/6
4g	H	OCH_3	H	H	H	$C_{17}H_{15}N_2O_2ClS$	195	90/6
4h	H	OCH_3	H	OH	H	$C_{17}H_{15}N_2O_2ClS$	165	84/6
4i	H	OCH_3	CH_3	H	H	$C_{18}H_{18}N_2O_2S$	185	81/6
4j	H	OCH_3	Cl	H	H	$C_{17}H_{15}N_2O_2ClS$	210	95/6
4k	H	OCH_3	CH_3	H	NO_2	$C_{18}H_{17}N_3O_4S$	195	80/6
4l	H	OCH_3	Cl	H	NO_2	$C_{17}H_{14}N_3O_4ClS$	195	76/6
4m	H	OCH_3	Cl	H	H	$C_{17}H_{14}N_2O_2ClBrS$	161	82/6
4n	NO_2	H	Cl	H	H	$C_{16}H_{12}N_3O_3ClS$	160	92/6

The products obtained in different solvent i.e. S_1, S_2 and S_3, were identical (M.P., M.F. and Yield)

(a) IR : (KBr) δ_{cm}^{-1} : 3330 (NH), 3112 (OH), 1490 (-S=C-N), 1200 (>C=S)

(b) ^{1}HNMR : δ 2.2 (S,3H,Ar-CH_3), 3.3(S,3H,Ar-CH_3), 3.3 (S,1H,Ar-SH), 5.1=5.2 (d,2H,CH_2), 6.8-7.3 (m,8H,ArH), 8.6 (S,1H,NH), 8.7(S,1H,CH), 9.7 (S,1H,OH).

ANTI-MICROBIAL ACTIVITY

The synthesized dihydropyrimidines were tested for anti-microbial activity by the filter paper disc sensitivity technique95 using DMF as a solvent at a concentration of 100 µg/ml. Dihydropyrimidines were tested against S.aureus, E.coli, B.subtilis, Pr. Mirabilis.

The antimicrobial activity of the dihydropyrimidines with their zone of inhibition (in mm) are shown

Compound	E.coli	Pr.mirabilis	S.aureus	B.subtilis
4a	n.i	2	4	n.i
4b	1	n.i	6	4
4c	5	n.i	5	n.i
4d	n.i	n.i	5	4
4e	n.i	n.i	9	7
4f	6	n.i	n.i	n.i
4g	n.i	n.i	n.i	n.i
4h	n.i	n.i	3	I
4i	n.i.	3	n.i.	1
4J	n.i.	1	n.i.	n.i.
Std (penicillin)	15	15	15	20

n.i.=not inhibited

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REFERENCES

1. At Kinson Shaw, Schaffner and Warrener, Chem. Soc., 1956, 3847.
2. Shaw and Warrner, J. Chem. Soc., 1959, 5088.
3. Shaw and Nayler, J. Chem. Soc., 1959, 1169.
4. Ghiya B. J., Ind. Hetero. Chem., 1996, 5, 323.
5. Amine M. S. and Nassar S. A., Ind. J. Chem., 1996, 35B, 388.
6. Reimlinger H., Linger W.R.F. andVandewalle J. J. M., Synthesis, 1970, 2, 433.
7. Prabhu V. S. and Sheshadri S., Ind. J. Chem., 1985, 24B, 137.
8. Rashod N., El Massry A. M., El Ashry, El-Sayed H., Amer A and I Zimmer H, J. Hetero. Chem., 1990, 27, 691.
9. Potts K. T. and Burtor H. R., J. Org. Chem., 1996, 31, 251.
10. Moghilaioh K, Rama Sudhakar G. and Reddy N. V., Ind. J. Chem., 1985, 42B, 1753.
11. R. S. Verma, Pure Appl. Chem., 2001, 73, No.1, 193-198.
12. Rahatgaonkar A. and Rathod, A., Asian J. Chem., 2006 Vol.18, No.2, 1039-1042.
13. Moghilaioh K. and Reddy N. V., Synth. Commun., 2003, 33, 1067.
14. Rani H. S., Moghilaiah K. and Sreenivasulu B., Ind. J. Chem., 1996, 35B, 106.
15. K. Darrell Berlin and Melvin D. Hard, Proc. Okla. Acad. Sci., 1991, 71, 29-32.
16. Manoj P. and Ghiya, B. J., Ind. J.Hetero. Chem., 1998, Vol.7., 311-312, April-June .
17. Heda, P. B. and Ghiya, B. J., Asian J. Chem., 1999, Vol.11, No.2, 591-594.
18. Rahatgaonkar A. M. and Ghiya, B. J., Ind. J. Hetero. Chem., 1996, Vol.5, 323-324, April-June.
19. Melagraki G., Afntitis A., Sarimveeis H., Igglessi-Markopoulou O., Supuran, C. T. Bio-organic and Med. Chem., 2006, 14, 1108.
20. Mandloi D., Khadikar P. V., et. Al. Bio-organic and medicinal chemistry letters, 2005, 15, 405-411.
21. Antreas Afantitis et. Al. Bio-organic and Med. Chem., 2006, 14, 6686-6694.
22. Balasubramanian Narasimhan et. al. Arkivok (I), 2007, 189-204.

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