Int. J. Chem. Sci.: 6(4), 2008, 2214-2223

MICROWAVE ASSISTED SOLID-SUPPORT SYNTHESIS OF HETEROCYCLIC SYSTEMS CONTAINING BRIDGEHEAD NITROGEN ATOMS

V. PEESAPATI* and APPA RAO THOOMU

Industrial Chemistry Lab., Centre for Environment, IST, J. N. T. Uiniversity
HYDERABAD - 500 085 (A. P.) INDIA

ABSTRACT

2-Arylidene-7-methyl-3,4-dihydro-H-naphthalen-1-one **(2a-l**) was obtained by the condensation of 7-methyl-3,4-dihydro-2H-naphthalen-1-ones **(1A)**, with aromatic aldehydes in ethanolic KOH. Compounds **(2a-l)** on reaction with thiourea in alkaline medium under conventional method yielded thiones **(3a-l)**. In microwave method **(2a-l)** was obtained by the condensation of **(1a)**, with aromatic aldehydes, 2-3 drops of alc. KOH and basic alumina. Compounds **(2a-l)** on reaction with thiourea and basic alumina for yielded thiones **(3a-l)**. A considerable increase in the reaction rate has been observed with better yields.

Key words: Tetralones, Aromatic aldehydes, Alc. KOH, Thiourea, Basic alumina.

INTRODUCTION

During the past decades, the environmental consciousness has compelled the chemist to make a new theme[1]. In this endeavor, solid support reagents[1,2] have made a landmark and made significant contribution to preserve the green environment by reducing the waste/effluent. With the development of microwave assisted reactions[3,4] as a part of on going research towards the non-traditional approach to the experimental set-up of organic reactions, the concept of "Microwave induced Organic Reaction Enhancement" (MORE) chemistry[5] has been utilized for rapid and efficient synthesis of 4-aryl-8-9-dimtheyl-3,4,5,6-tetrahydro-1-H-benzo [h] quinazoline-2-thiones **(3a-l)**.

In recent years, the use of microwave techniques have developed rapidly in organic synthesis due to shorter reaction times, higher yields, easy work-up and environmentally friendliness. We have already prepared a number of polycyclic heterocyclic molecules

* Author for correspondence

starting from the key intermediates[6,7]. Preliminary studies on 6-arylidene derivatives have shown antibacterial, antifungal and anti-inflammatory in them.

EXEPERIMENTAL

2-Arylidene-7-dimethyl-3, 4-dihydro-2H-naphthalen-1-one (2a-l)

Conventional method

General procedure: A mixture of 7-methyl-3,4-dihydro-2H-naphthalen-1-one (**1a**) (0.35g, 2 mmol), benzaldehyde (0.22 g, 2 mmol) in ethanolic potassium hydroxide (0.08 g in 2 mL) was stirred at room temperature for ½ hour. The reaction mixture was neutralized with dilute acetic acid. The solid thus obtained was filtered and washed thoroughly with water and dried. Recrystallised from methanol gave the product **2a**.

Solid phase microwave irradiation method

General procedure: Basic alumina (0.5 g) was added to the solution of 7-dimethyl-3,4-dihydro-2H-naphthalen-1-one **(1a)** (0.1 g, 0.6 mmol) and benzaldehyde (0.06 g, 0.6 mmol) in 2-3 drops 4% ethanolic potassium hydroxide (0.02 g, 5 mL) at room temperature. The reaction mixture was mixed and the adsorbed material was dried, placed inside the microwave oven, and then irradiated for 1-2 minutes with and interval of 30 seconds. The reaction was followed by TLC. The mixture was cooled and product was extracted into CH_2Cl_2. The product was collected by evaporating the solvent. Recrystallisation from methanol gave the product **(2a)**.

Compound 2a: IR (KBr): 1659 (C=O) cm^{-1}; 1586 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.35 (3H, s, 7-CH_3), δ 2.25-2.28 (2H, t, 3-CH_2), δ 2.55-2.60 (2H, t, 4-CH_2), δ 7.00-7.50 (8H, m, Ar-CH) δ 7.80 (1H, s, -C=CH), MS : m/z 248 (M^+).

Compound 2b: IR (KBr): 1661 (C=O) cm^{-1}; 1601 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.29-2.31 (6H, s, 6 & 7-CH_3), δ 2.26-2.29 (2H, t, 3-CH_2), δ 2.60 (2H, t, 4-CH_2), δ 7.00-7.60 (7H, m, Ar-CH), δ 7.75 (1H, s, -C=CH).

Compound 2c: IR (KBr): 1650 (C=O) cm^{-1}; 1580 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.30-2.32 (3H, s, 7-CH_3), δ 2.25-2.28 (2H, t, 3-CH_2), δ 2.57-2.59 (2H, t, 4-CH_2), δ 7.00-7.55 (7H, m, Ar-CH) δ 7.75 (1H, s, -C=CH), 3.73 (3H, s, O-CH_3).

Compound 2d: IR (KBr): 1663 (C=O) cm^{-1}; 1588 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.31-2.33 (6H, s, 6 & 7-CH_3), δ 2.26-2.28 (2H, t, 3-CH_2), δ 2.65-2.69 (2H, t, 4-CH_2), δ 7.00-7.50 (7H, m, Ar-CH) δ 7.65 (1H, s, -C=CH).

Compound 2e: IR (KBr): 1653 (C=O) cm^{-1}; 1582 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.35 (6H, s, 4 & 7-CH_3), δ 2.24-2.27 (2H, t, 3-CH_2), δ 2.58-2.61 (2H, t, 4-CH_2), δ 7.00-7.60 (8H, m, Ar-CH) δ 7.75 (1H, s, -C=CH).

Compound 2f: IR (KBr): 1660 (C=O) cm^{-1}; 1580 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.26-2.29 (9H, s, 4,6 & 7-CH_3), δ 2.23-2.25 (2H, t, 3-CH_2), δ 2.65-2.68 (2H, t, 4-CH_2), δ 7.00-7.62 (7H, m, Ar-CH), δ 7.70 (1H, s, -C=CH).

Compound 2g: IR (KBr): 1650 (C=O) cm^{-1}; 1595 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.28(3H, s, 7-CH_3), δ 2.22-2.27 (2H, t, 3-CH_2), δ 2.67-2.70 (2H, t, 4-CH_2), δ 7.20-7.55 (7H, m, Ar-CH) δ 7.70 (1H, s, -C=CH).

Compound 2h: IR (KBr): 1665 (C=O) cm^{-1}; 1580 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.27-2.30 (6H, s, 6 & 7-CH_3), δ 2.25-2.28 (2H, t, 3-CH_2), δ 2.58-2.61 (2H, t, 4-CH_2), δ 6.90-7.50 (7H, m, Ar-CH), δ 7.75 (1H, s, -C=CH). MS : m/z 341 (M^+).

Compound 2i: IR (KBr): 1663 (C=O) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.27-2.29 (2H, t, 3-CH_2) δ 2.31 (3H, s, 7-CH_3), δ 2.58-2.61 (2H, t, 4-CH_2), δ 6.60-7.80 (6H, m, Ar-CH).

Compound 2j: IR (KBr): 1651 (C=O). ^1H NMR ($CDCl_3$): δ 2.28-2.30 (2H, t, 3-CH_2) δ 2.30-2.33 (6H, s, 6 & 7-CH_3), δ 2.45-2.48 (2H, t, 4-CH_2) δ 7.00-7.80 (5H, m, Ar-CH).

Compound 2k: IR (KBr): 1659 (C=O) cm^{-1}; 1582 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): 2.30-2.31 (6H, s, 7-CH_3), δ 2.25-2.28 (2H, t, 3-CH_2), δ 2.75-2.78 (2H, t, 4-CH_2) δ 6.90-7.70 (5H, m, Ar-CH), δ 7.08 (1H, s, -C=CH).

Compound 2l: IR (KBr): 1659 (C=O) cm^{-1}; 1582 (C=C) cm^{-1} ^1H NMR ($CDCl_3$):

δ 2.30-2.31 (6H, s, 6 & 7-CH_3), δ 2.93-2.97 (2H, t, 3-CH_2), δ 3.15-3.19.(2H, t, 4-CH_2) δ 7.20-7.77 (5H, m, Ar-CH), δ 8.01 (1H, s, C=CH).

4-Aryl-8-9dimtheyl-3,4,5,6-tetrahydro-1-H-benzo [h] quinazoline-2-thione(3a-l)

Conventional method

General method: A mixture of 2-arylidene-7-dimetheyl-3,4-dihydro-2H-naphthalen-1-one (**2a**) 0.262 g, and thiourea (0.15g, 2 mmole) in 4% ethnolic potassium hydroxide (0.08g in mL) was heated under reflux for 11/2 hours. At the end of the reaction, the reaction mixture was poured into ice-cooled water and neutralized with dil. HCl. The solid thus obtained was filtered and washed thoroughly with water and dried. Purification by preparative TLC using 15% ethyl acetate and hexane solution gave the product **3a.**

Solid phase microwave irradiation method

General procedure: Basic alumina (0.5 g) was added to the solution of 2-arylidene-7-methyl-3,4-dihydro-2H-naphthalen-1-one (**2a**) 0.262 g, and thiourea (0.15g, 2 mmol) in 4% ethanolic potassium hydroxide (0.02g in 0.5 mL) at room temperature. The reaction mixture was mixed and the adsorbed material was dried, placed inside the microwave oven; and the irradiated for 1-2 min, with an interval of 30 seconds. The reaction was followed by TLC. The mixture was cooled and product was extracted into CH_2Cl_2. The product was collected by evaporating the solvent. Purification by preparative TLC using 15% ethyl acetate and hexane gave the product **3a**.

Compound 3a: IR (KBr): 3350 (NH), 1250 (C=S) cm^{-1}; 1659 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.01 (NH, br) δ 2.27 (3H, s, 9-CH_3), δ 2.30-2.33 (2H, t, 5-CH_2), δ 2.56-2.58 (2H, t, 6-CH_2), δ 5.05 (1H, s, Ha), δ 7.00-7.20 (8H, m, Ar-CH) MS : m/z 306 (M^+).

Compound 3b: IR (KBr): 3443 (NH), 1280 (C=S) cm^{-1}, 1605 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03 (NH, br) δ 2.31-2.33 (6H, s, 8 & 9-CH_3), δ 2.26-2.29 (2H, t, 5-CH_2), 2.48-2.50 (2H, t, 6-CH_2), δ 5.05 (1H, s, Ha), δ 6.80-7.20 (7H, m, Ar-CH) MS : m/z 320 (M^+).

Compound 3c: IR (KBr): 3400 (NH), 1245 (C=S) cm^{-1}; 1610 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.04 (NH, br) δ 2.26-2.29 (3H, s, 9-CH_3), δ 2.32-2.34 (2H, t, 5-CH_2), δ 2.58-2.60 (2H, t, 6-CH_2), 3.69 (3H, s, O-CH_3) δ 5.25 (1H, s, Ha), δ 6.80-7.20 (7H, m, Ar-

CH).

Compound 3d: IR (KBr): 3401 (NH), 1253 (C=S) cm^{-1}, 1609 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03 (NH, br) 2.25-2.27 (6H, s, 8 & 9-CH_3), δ 2.29-2.31 (2H, t, 5-CH_2), δ 2.55-2.57 (2H, t, 6-CH_2), δ 5.10 (1H, s, Ha), δ 6.80-7.10 (6H, m, Ar-CH).

Compound 3e: IR (KBr): 3390 (NH), 1295 (C=S) cm^{-1}; 1659 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.01 (NH, br) δ 2.31-2.35 (6H, s, 4 & 9-CH_3), δ 2.25-2.28 (2H, t, 5-CH_2), δ 2.54-2.58 (2H, t, 6-CH_2), δ 5.05 (1H, s, Ha), δ 7.00-7.20 (8H, m, Ar-CH).

Compound 3f: IR (KBr): 3443 (NH), 1280 (C=S) cm^{-1}, 1605 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03 (NH, br) δ 2.31-2.33 (3H, s, 8 & 9-CH_3), δ 2.26-2.29 (2H, t, 5-CH_2), δ 2.48-2.50 (2H, t, 6-CH_2), δ 5.05 (1H, s, Ha), δ 6.80-7.20 (7H, m, Ar-CH).

Compound 3g: IR (KBr): 3210 (NH), 1195 (C=S) cm^{-1}; 1659 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.05 (NH, br) δ 2.34-2.36 (3H, s, 9-CH_3), δ 2.24-2.27 (2H, t, 5-CH_2), δ 2.28-2.30 (2H, t, 6-CH_2), δ 4.90 (1H, s, Ha), δ 6.80-7.30 (7H, m Ar-CH).

Compound 3h: IR (KBr): 3365 (NH), 1265 (C=S) cm^{-1}, 1583 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03 (NH, br) δ 2.32-2.34 (6H, s, 8 & 9-CH_3), δ 2.25-2.27 (2H, t, 5-CH_2), 2.48-2.51 (2H, t, 6-CH_2), δ 5.05 (1H, s, Ha), δ 6.90-7.45 (7H, m, Ar-CH) MS;m/z 399 (M^+).

Compound 3i: IR (KBr): 3400 (NH), 1185 (C=S) cm^{-1}; 1605 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.01 (NH, br) δ 2.33 (3H, s, 9-CH_3), δ 2.25-2.27 (2H, t, 5-CH_2), δ 2.48-2.51 (2H, t, 6-CH_2), δ 4.85 (1H, s, Ha), δ 6.85-7.30 (6H, m, Ar-CH).

Compound 3j: IR (KBr): 3383 (NH), 1191 (C=S) cm^{-1}; 1600 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.29-2.31 (2H, t, 5-CH_2), δ 2.26 (6H, s, 8 & 9-CH_3), δ 2.58-2.60 (2H, t, 6-CH_2), 4.1-4.3 (NH, br) 5.30 (1H, s, Ha) δ 6.01-7.30 (6H, m, Ar-CH). MS;m/z 310 (M^+).

Compound 3k: IR (KBr): 3401 (NH), 1261 (C=S) cm^{-1}; 1610 (C=C) cm^{-1}. ^1H

NMR ($CDCl_3$): δ 2.27-2.30 (2H, t, 5-CH_2), δ 2.25 (3H, s, 9-CH_3), δ 2.65-2.78 (2H, t, 6-CH_2), 4.1-4.3 (NH, br) 5.32 (1H,s,Ha) δ 6.60-7.10 (6H, m, Ar-CH).

Compound 3l: IR (KBr): 3449 (NH), 1245 (C=S) cm^{-1}; 1610 (C=C) cm^{-1}. ^1H NMR ($CDCl_3$): δ 2.03-2.10 (2H, t, 5-CH_2), δ 2.25 (6H, s, 8 & 9-CH_3), δ 2.65-2.78 (2H, t, 6-CH_2), 4.1-4.3 (NH, br) 5.37 (1H,s,Ha) δ 6.90-7.75 (6H, m, Ar-CH)

RESULTS AND DISCUSSION

The basic skeleton of arylidene is widely figured in natural products[7] and are known to have multipronged activity. Some of them are useful as drugs and agrochemicals. A further study on the efficient synthesis of arylidenes is of current interest because of their wide range of applications. 2-Arylidene-7-methyl-3, 4-dihydro-H-naphthalen-1-one **(2a-l)** was obtained by the condensation of 7-methyl-3,4-dihydro-2H-naphthalen-1-one with aromatic aldehydes in ethanolic KOH. Compounds **(2a-l)** on reaction with thiourea in alkaline medium under conventional method yielded thiones **(3a-l) (Scheme-I).** In microwave method 2-arylidene-7-methyl-3,4-dihydro-H-naphthalen-1-one **(2a-l**) was obtained by the condensation of 7-methyl-3,4-dihydro-2H-naphthalen-1-one with aromatic aldehydes, 2-3 drops of alc. KOH and basic alumina. Similarly compounds **(2a-l)** on reaction with thiourea and basic alumina gave thiones **(3a-l).** The rate of reaction is faster in microwave condition than the conventional method. The structures of compounds were confirmed at ^1H NMR spectra and IR spectra. ^1H NMR spectrum of **(2a)** displayed a signal at δ 7.80 characteristic peak of -C=CH. The IR spectrum contained a C=C peak at 1586 cm^{-1} and C=O peak at 1659 cm^{-1}. ^1H NMR spectrum of **(3a)** displayed a signal at δ 5.05 the characteristic peak of Ha. The IR spectrum contained a C=S peak at 1250 cm^{-1} and C=C peak at 1609 cm^{-1}. Elemental analysis also confirmed the structures.

Table 1. Physical data of arylidenes

Comp.	Molecular formula	MP (°C)	Yield (%)		MW irradiation time (min)	Found / Calcd. (%)	
			Conv	MW		C	H
2a	$C_{18}H_{16}O$	128-130	72	83	2	81.03	6.01
						82.04	6.04

Cont…

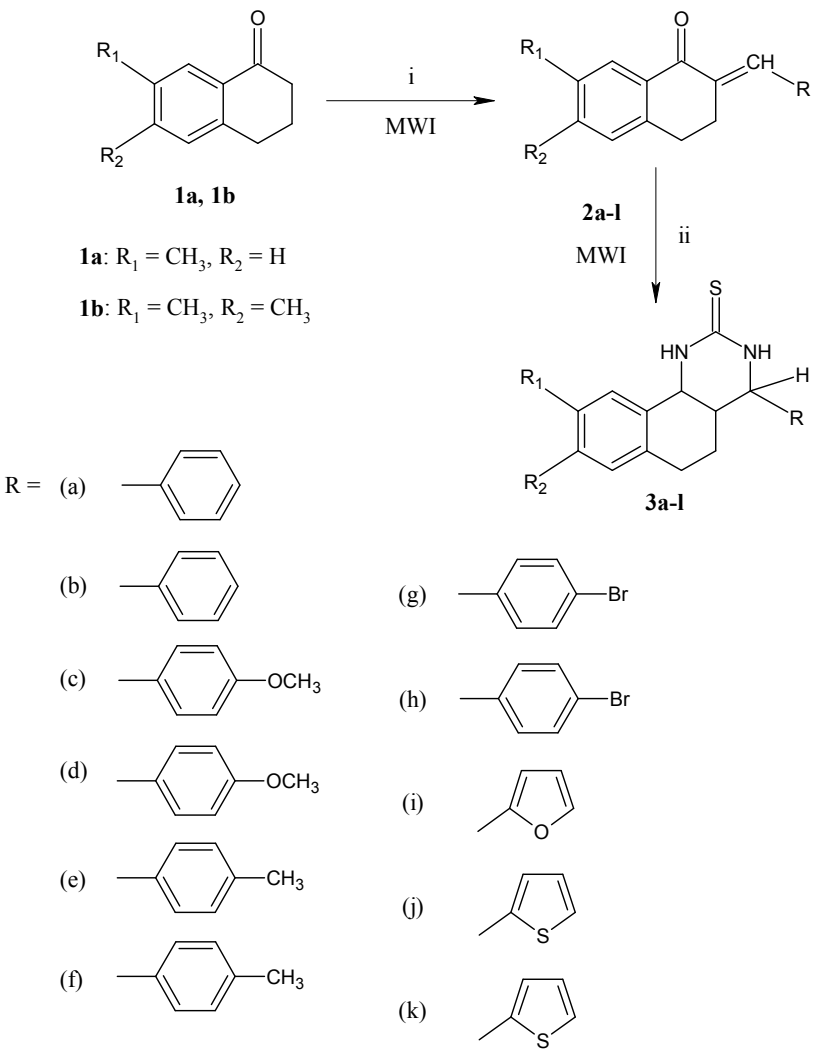
Comp.	Molecular formula	MP (°C)	Yield (%)		MW irradiation time (min)	Found / Calcd. (%)	
			Conv	MW		C	H
2b	$C_{19}H_{18}O$	125-127	80	93	2	87.00	6.80
						87.02	6.87
2c	$C_{19}H_{18}O_2$	155-156	75	98	2	87.09	5.88
						88.01	6.79
2d	$C_{20}H_{20}O_2$	144-146	89	73	1.5	82.00	6.87
						82.19	6.85
2e	$C_{19}H_{18}O$	120-121	76	85	2	87.02	7.75
						88.12	7.98
2f	$C_{20}H_{20}O$	160-161	73	89	1.5	96.90	7.20
						96.95	7.24
2g	$C_{18}H_{15}BrO$	170-172	75	85	2	68.13	5.64
						69.20	5.84
2h	$C_{19}H_{17}BrO$	196-197	75	78	1.5	66.83	4.95
						66.86	4.98
2i	$C_{16}H_{14}O_2$	80-82	78	81	2	80.67	5.85
						81.12	6.76
2j	$C_{17}H_{16}O_2$	115-117	76	91	2	80.92	6.37
						80.95	6.34
2k	$C_{16}H_{14}SO$	88-90	78	81	2	74.38	5.78
						74.46	6.68
2l	$C_{17}H_{16}OS$	155-156	80	85	2	76.10	5.97
						76.11	5.99

Table 2. Physical data of thiones

Comp.	Molecular formula	MP (°C)	Yield (%)		MW irradia-tion time (min)	Found / calcd.(%)		
			Conv.	MW		C	H	N
3a	$C_{19}H_{18}N_2S$	95-97	85	90	2	70.40	5.35	8.25
						70.80	5.59	8.69
3b	$C_{20}H_{20}N_2S$	122-124	71	82	5	74.98	6.22	8.72
						75.00	6.25	8.75
3c	$C_{20}H_{20}N_2OS$	80-82	86	88	3	71.01	5.65	8.01
						71.42	5.95	8.33
3d	$C_{21}H_{22}N_2OS$	225-227	72	75	4	71.96	6.27	7.99
						75.44	6.58	8.10
3e	$C_{20}H_{20}N_2S$	125-127	85	90	2	74.80	6.01	8.60
						75.00	6.25	8.75
3f	$C_{21}H_{22}N_2S$	125-126	83	90	4	75.96	6.55	8.35
						75.44	6.58	7.38
3g	$C_{19}H_{17}BrN_2S$	130-132	95	90	3	60.01	4.10	6.90
						61.25	4.30	7.08
3h	$C_{20}H_{19}BrN_2S$	128-130	77	78	4	60.14	4.74	7.00
						60.15	4.76	7.20
3i	$C_{17}H_{16}N_2OS$	107-109	88	90	5	65.01	5.01	8.70
						65.38	5.12	8.97
3j	$C_{18}H_{18}N_2OS$	200-202	72	71	6	69.30	5.45	9.01
						69.61	5.80	9.30
3k	$C_{17}H_{16}N_2S_2$	106-108	75	83	2	65.10	5.25	8.15
						65.85	5.48	8.53
3l	$C_{18}H_{18}N_2S_2$	115-117	80	79	6	68.90	5.40	9.45
						69.8	5.55	9.98

Likewise other compounds **3b**, **3d**, **3f**, **3h**, **3j**, and **3l** were prepared starting

from **(1b)**. Characterization data of the synthesized compounds are reported in Tables1 and 2.



Reagents

Conventional method:	(i) alc KOH, aromatic aldehyde
	(ii) alc KOH, thiourea
Microwave method:	(i) alc KOH, aromatic aldehyde, basic alumina
	(ii) alc KOH, thiourea, basic alumina

Scheme 1

REFERENCES:

1. A. Oussaid, L. N. Thach and A. Loupy, Tetrahedron Lett., **38**, 2451 (1997).
2. A. Cornellis and P. Laszlo, Synthesis (1985) p. 909
3. S. Caddick, Tetrahedron, **51**, 10403 (1995).
4. A. K. Bose, N. Lavlinskaia, M. Jayaraman and M. S. Manhas, Chem. Tech., **27**, 18 (1997)
5. A. K. Bose, M. S. Mahhns, M. Ghosh, M. Shah, S. Bari and A. G. Coudhary, J. Org. Chem., **56**, 199, (1968).
6. V. Peesapati and Nageswara Rao Vasireddy, Indian J. Chem., **44B**, 783 (2005).
7. V. Peesapati and Sreelakshmi Ponnuru, Indian J. Chem., **42B,** 1978 (1975).
8. G. Venkat Reddy, D. Maitraie, B. Narsaiah, V. Rambabu and P. Shanthan Rao, Syn. Commun., 2881-2884 (2001)
9. V. Peesapati and Anuradha, Syn. Commun., **29(24)**, 4381 (1999)
10. M. Kidwai, P. Spra, P. P. Misra, R. K. Sexana and M. Singh. Bioorg. Medicinal Chem., **9**, 217 (2001).

Accepted : 13.06.2008