

## Effect of Solvents in Synthesis of New 4-(2-hydroxy-5-methylphenyl)-5-aryl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines

S.R. DIGHADE\* and M.M. CHINCHOLKAR†

*Department of Chemistry  
R.D.I.K. College, Badnera-444 701, India*

Seven different 3-arylflavanones and 3-arylchromanones were synthesised from 1,3-propanedione by literature method. They were subjected to react with different compounds such as (i) thiourea in pyridine, (ii) pyridine-KOH and (iii) ethanol-KOH medium to give respective 4-(2-hydroxy-5-methylphenyl)-5-aryl-6-aryl-2-imino-6H-2,3-dihydro 1,3-thiazines. The yield is better in case of pyridine-KOH.

### INTRODUCTION

1,3-Thiazines and their derivatives are reported to have antibacterial and antitumour activity. These are also used as drugs, drug intermediates, pesticides<sup>1-4</sup> etc. In the present work we have synthesised 4-(2-hydroxy-5-methylphenyl)-5-aryl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 3-arylflavanones and 3-arylchromanones in pyridine, in pyridine-KOH and in ethanol-KOH by the action of thiourea. Early workers<sup>5-9</sup> have synthesized various substituted 1,3-thiazines in different media.

From literature survey, it is revealed that no systematic study has been reported on use of pyridine or pyridine-KOH for synthesis of 4-(2-hydroxy-5-methylphenyl)-5-aryl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines. It was therefore thought interesting to synthesise above mentioned 1,3-thiazines in various media as (1) in pyridine (2) in pyridine-KOH, (3) in ethanol-KOH and compare the yield, reflux time in these three media.

An attempt was made to prepare various 3-arylflavanones and 3-arylchromanones by literature method<sup>10</sup> by condensing 1,3-propanediones with aromatic aldehydes. Thus five 3-arylflavanones and two 3-arylchromanones were synthesised which were reacted with thiourea to give seven different 1,3-thiazines in pyridine, in pyridine-KOH and in ethanolic-KOH.

### EXPERIMENTAL

Melting points of all the compounds were determined on Tempo melting point apparatus and are uncorrected. IR and NMR spectra were obtained from R.S.I.C.

†Department of Chemistry, Vidarbha Mahavidyalaya, Amravati-444 604, India.

and C.I.L. Chandigarh. Purity of the compounds prepared was checked by TLC on Silica gel-G plates.

**1. Synthesis of 3-benzoylflavanones and 3-benzoyl chromanones (5a–g) (Table-1):** A mixture of 1-(2-hydroxy-5-methylphenyl)-3-phenyl-1,3-propanedione (**4**) (0.02 mol) and an aromatic aldehyde (0.02 M) was refluxed in 30 mL ethanol containing 0.05 mL piperidine for 30 min and processing by literature method gave compounds (**5a–g**).

**2. Synthesis of 4-(2-hydroxy-5-methylphenyl)-5-aryoyl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines in pyridine (6a–g):** A mixture of 3-aryoylflavanones and 3-aryoylchromanones (**5**) (0.01 mol) and thiourea (0.01 mol) in 20 mL pyridine was refluxed for 3 to 3.5 h and cooled. The reaction mixture was diluted with water and acidified with conc. HCl. The product obtained was washed with water and crystallized in ethanol to give compounds (**6a–g**).

**3. Synthesis of 4-(2-hydroxy-5-methylphenyl)-5-aryoyl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines (in pyridine-KOH):** A mixture of 3-aryoylflavanones and 3-aryoylchromanones (**5**) (0.01 mol) and thiourea (0.01 mol) in 20 mL pyridine containing 0.25 g of KOH solution was refluxed for 2.5–3 h and processed as described above to give compounds (**7a–g**).

**4. Synthesis of 4-(2-hydroxy-5-methylphenyl)-5-aryoyl-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazine (in ethanol-KOH):** A mixture of 3-aryoylflavanone and 3-aryoylchromanones (**5a–g**) and thiourea (0.01 mol) in 20 mL ethanol containing 0.25 g of KOH solution was refluxed for 3.5 to 4 h and processed as above to give (**8a–g**).

The compounds **6a–g**, **7a–g** and **8a–g** were found to be same on the basis of mixed melting points determination. The structures of these compounds were established on the basis of chemical properties, elemental analysis and spectral analysis. The melting points, per cent yield, reflux time is shown in Table-2.

TABLE-1  
3-AROYLFLAVANONES AND 3-AROYLCHROMANONES

Compd. No.	Compound	m.p. (°C)
<b>5a</b>	3-Benzoyl-6-methylflavanone	148
<b>5b</b>	3-Benzoyl-6-methyl-4'-methoxyflavanone	155.8
<b>5c</b>	3-Benzoyl-2-(2'-furyl)-6-methylchromanone	125
<b>5d</b>	3-Benzoyl-6-methyl-2-(2-phenylethenyl)-chromanone	116
<b>5e</b>	3-Benzoyl-6-methyl-3'-nitroflavanone	120
<b>5f</b>	3-Benzoyl-2'-hydroxy-6-methylflavanone	148
<b>5g</b>	3-Benzoyl-3',4'-methylenedioxy-6-methyl flavanone	136

TABLE-2  
 PHYSICAL DATA OF COMPOUNDS 6a-6g, 7a-7g and 8a-8g

Compound	m.p.(°C) durating	m.f.	Yields % and duration of reaction		
			in pyridine (3 h)	in pyridine- KOH (2.5-3 h)	in ethanol- KOH (3.5-4 h)
6a, 7a, 8a	83	C <sub>22</sub> H <sub>18</sub> O <sub>3</sub> N <sub>2</sub> S	68	72	66
6b, 7b, 8b	197	C <sub>24</sub> H <sub>20</sub> O <sub>2</sub> N <sub>2</sub> S	61	68	63
6c, 7c, 8c	246	C <sub>25</sub> H <sub>22</sub> O <sub>3</sub> N <sub>2</sub> S	67	72	68
6d, 7d, 8d	182	C <sub>26</sub> H <sub>22</sub> O <sub>2</sub> N <sub>2</sub> S	59.4	63	60
6e, 7e, 8e	143	C <sub>25</sub> H <sub>20</sub> O <sub>4</sub> N <sub>2</sub> S	57.4	61	56
6f, 7f, 8f	183	C <sub>24</sub> H <sub>20</sub> O <sub>3</sub> N <sub>2</sub> S	56	59	61
6g, 7g, 8g	58	C <sub>24</sub> H <sub>19</sub> O <sub>4</sub> N <sub>3</sub> S	65	70	62

All compounds gave satisfactory elemental analysis.

#### IR Absorption observed (cm<sup>-1</sup>) for 5a

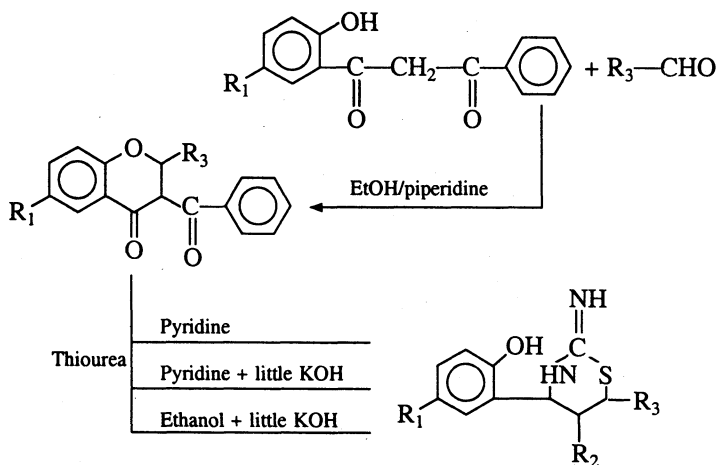
1596-1568-, C=O stretching of aroyl group 1348 cm<sup>-1</sup> pyrone,  
 1290-1173 Ar-O, 1492 stretching vibration in aryl C=C bond.

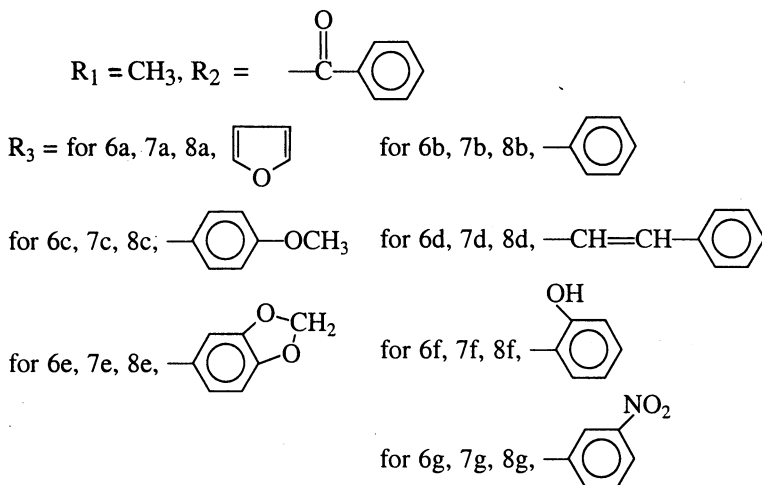
#### PMR, (peaks in δ) for 5a

2.35 (s) 3H AR-CH<sub>3</sub>, 5.05 (d) 1H C<sub>3</sub>H, J<sub>AB</sub> = 12 Hz, 6.05-6.13 (d) 1H  
 C<sub>2</sub>-H, J<sub>AB</sub> = 12 Hz, 6.7-7.85 (m) 13H-Ar-H.

#### IR Absorption Bands (cm<sup>-1</sup>) for compounds 6a, 7a, 8a

3755-3680 (w, b) O-H stretching, 3436-3000 w, b -C-N-H stretching,  
 2930(s) C-N-H stretching, 2854(m) C-H stretching due to CH<sub>3</sub>, 1597  
 -C=O of aroyl group, 1483(s) C=N stretching and C=C stretching vibration  
 of aryl group, 1294 (d) C-N stretching.





### NMR for compounds 6a, 7a, 8a, (Chemical shift in $\delta$ )

2.30–2.40 (s) 3H Ar—CH<sub>3</sub>, 3.10 (d) 1H 1HH<sub>B</sub>, 3.7 (d) 1H 1HH<sub>A</sub>, 5.20 (d) 1H HC, 5.90 (d) 1H N—H, 6.20 (d) =N—H, 6.37–7.90 (m) 9H Ar—H, 11.9 (s) 1H Ar—OH.

## RESULTS AND DISCUSSION

Flavanones on treatment with thiourea in pyridine, pyridine-KOH and ethanol-KOH gave corresponding 1,3-thiazines (**6**, **7**, **8**). In these reactions  $\gamma$ -pyrone ring of flavanone may open in basic medium and gives formation of corresponding chalcones. On addition of thiourea carbonyl group is involved in nucleophilic attack by nitrogen.

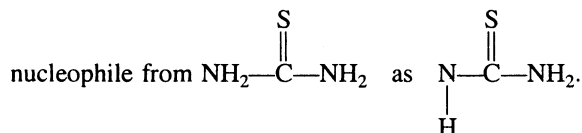
Here there is formation of in :N—C—NH<sub>2</sub> nucleophile which attacks carbonyl carbon and follows 1,2-addition type of mechanism. This results in formation of adduct which then loses water molecules. The cyclization and rearrangement leads to the formation of 4-(2-hydroxy-5-methylphenyl)-5-aryl-6-aryl-2-imino-6-H-2,3-dihydro-1,3-thiazine.

From Table-2 it is observed that in solvent pyridine-KOH the percentage yield of product was increased and the time required for completion of reaction was comparatively less by 2.5 to 3 h.

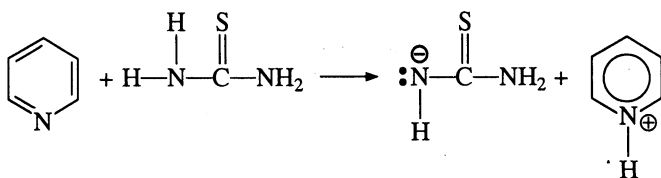
Hence use of pyridine-KOH is better in the synthesis of 1,3-thiazines.

### In ethanol-KOH

KOH may ionise as K<sup>+</sup> and OH<sup>-</sup>; OH<sup>-</sup> ions activate the formation of



In pyridine, formation of nucleophile is as given below:



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### REFERENCES

1. H.S. Patel and Nilesh P. Patel, *Orient. J. Chem.* **13**, 69 (1997).
2. H.I. El-Subbagh, A.H. Abadi, I.E. Al-Khawad and K.A. Al-Rashood, *Arch. Pharm.*, **332**, 19 (1999)
3. K. Mogilaiah, P. Reddy, Raghatham Rao and R. Balu, *Indian J. Chem.*, **38B**, 495 (1999).
4. P.B. Raghuvanshi and A.G. Doshi, *Asian J. Chem.*, **6**, 291 (1994).
5. G. Aziz, M.H. Mosseir, N.L. Doss and A.S. Rizk, *Indian J. Chem.*, **14(B)**, 286 (1976).
6. M.M. Chincholkar, B.S. Kakade and V.S. Jamode, *Indian J. Chem.*, **17B**, 629 (1979).
7. M.A. Ramekar and M.M. Chincholkar, *J. Indian Chem. Soc.*, **71**, 199 (1994).
8. B.S. Kakade, Ph.D. Thesis, Nagpur University (1982).
9. S.K. Gudadhe, Ph.D. Thesis, Amravati University (1992).
10. M.M. Chincholkar and V.S. Jamode, *Indian J. Chem.*, **17B**, 510 (1979).

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