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Effect of Solvents in Synthesis of New 4-(2-Hydroxy-5-Methylphenyl)-6-Aryl-2-Imino-6H-2,3-Dihydro-1,3-Thiazines

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Seven different chalcones were synthesised from 2-hydroxy-5-methyl acetophenone using two ketones and five aldehydes in alkaline medium. These chalcones **I(a)–I(g)** on treatment with thiourea in pyridine gave seven 1,3-thiazines **II(a)–II(g)**. It is also reported that pyridine-KOH gives better yield and shorter duration for reaction completion than pyridine or ethanol-KOH. The structures of these compounds were confirmed on the basis of chemical and spectral analysis.

INTRODUCTION

Chalcones show amebicidal and antimicrobial activity[1]. These chalcones are synthesised by condensation of 2-hydroxyacetophenone with aromatic aldehydes in presence of acidic[2] or basic[3] media. The 1,3-thiazines and their derivatives are reported to have antibacterial[4], antitumor[5] and antimicrobial[6] activities.

From literature it is observed that the above reported titled compounds are not synthesised by using pyridine or pyridine-KOH as solvents. Chincholkar *et al*[7] reported the synthesis of 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 2′-hydroxy chalcones with thiourea in alkaline medium. Kakade[8] reported the use of DMSO as solvent containing sodium methoxide in the synthesis of 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 2′-hydroxychalcones. Rajput *et al*[9] synthesised 1,3-thiazines from β-(2′-furyl)-acrylophenone. Parate *et al.*[10] have reported 1,3-thiazines from nitrochalcones. Gudadhe[11] synthesised iodosubstituted-4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from 2′-hydroxy chalcones in ethanol containing piperidine and sodium-methoxide from 2′-hydroxychalcones. Doifode[12] synthesised 4,6-diaryl-2-imino-6H-2,3-dihydro-1,3-thiazines from aurones by the action of thiourea in presence of aqueous KOH and ethanol. Raghuwanshi *et al.*[13] has synthesised 1,3-thiazines from nitrochalcones in DMSO in presence of sodium methoxide.

Thus it was thought interesting to synthesise 4-(2-hydroxy-5-methylphenyl)-6-aryl-2-imino-6H-2,3-dihydro-1,3-thiazines in pyridine/pyridine-KOH/ethanol-KOH and to study the effect of solvents in their synthesis.

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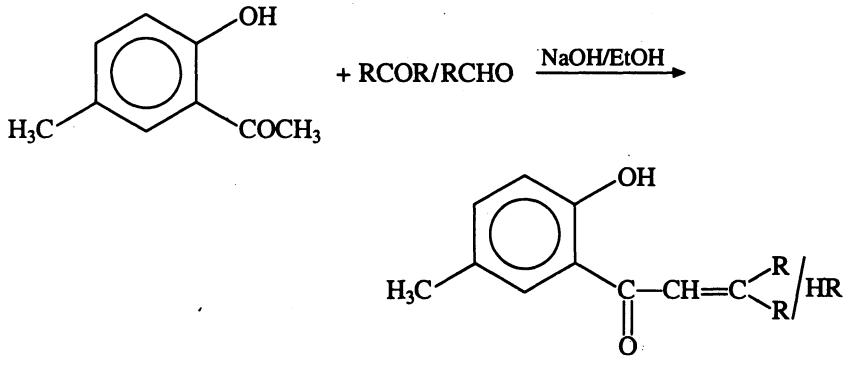
EXPERIMENTAL

Melting points of all compounds were determined on Tempo melting point apparatus and are uncorrected. Compounds **I, II, III, IV** were prepared in the laboratory by known method; m.p., purity of the compounds were checked by TLC on silica gel-G plates. The structures of compounds **I(f), I(b), II(c), III(c), IV(c)** were confirmed by chemical analysis, IR and NMR spectra.

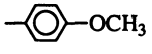
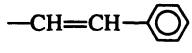
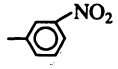
Synthesis of compounds I(a)–I(g): 2-Hydroxy-5-methylacetophenone (0.1 mol) and appropriate aldehyde (or ketone) (0.1 mol) were taken in alcoholic KOH solution and heated to boiling. The reaction mixture was kept overnight and decomposed by 1 : 1 HCl, filtered and crystallized from ethanol to get seven chalcones. Physical data are given in Table-1.



I(a)–I(g)

R = as shown in Table-1.

TABLE-1
PHYSICAL DATA OF COMPOUNDS *I(a)–I(g)

Compd. No.	R	m.f.	m.p. °C	Yield (%)
I(a)		$C_{22}H_{18}O_2$	90	72
I(b)		$C_{16}H_{14}O_2$	98.5	76
I(c)		$C_{17}H_{16}O_3$	100.5	81
I(d)		$C_{18}H_{16}O_2$	133	68
I(e)		$C_{16}H_{13}NO_4$	114	72
I(f)		$C_{12}H_{14}O_2$	138	70
I(g)		$C_{14}H_{12}O_3$	86	69

*All compounds I(a)–I(g) gave satisfactory elemental analysis.

IR for I(f) (cm^{-1}): 3306 —H bonded —OH, 2917 C—H, 1600 C=CH=C stretching, 1495 —C=C— in aryl, 1700 —C=O stretching, 1250 stretching in phenol, 1036 $=C(CH_3)_2$.

NMR for I(f): (2.25–2.35 s, 9H, Ar—CH_3 and $=C(CH_3)_2$, (6.8–7.3 m, 3H, Ar—H), (7.85 d, 1H, C—H), (11.25 Ar—OH).

IR for I(b): 3032(s) strongly hydrogen bonded —OH stretching, 1639(s) C=O stretching, 1569(s) C—CH=CH stretching, 1267(d) Ar—O stretching,

1184 (C—O) stretching in phenol.

NMR for I(b): (2.35 s, 3H, Ar—CH_3), (6.9–7.0 dd, 1H, CH_A), (7.33 dd, 1H, $=CH_B$), (7.35–7.95 m, 8H, Ar—H), (12.61, s, 1H, OH phenolic).

Synthesis of compounds II(a)–II(g)

Chalcones (0.01 mol) **I(a)–I(g)** and thiourea (0.01 mol) were refluxed in pyridine (20 mL) for 3 to 3.5 h and cooled. On further processing as per literature method gave seven 1,3-thiazines **II(a)–II(g)**. Physical data of compounds **II(a)–II(g)** are given in Table-2.

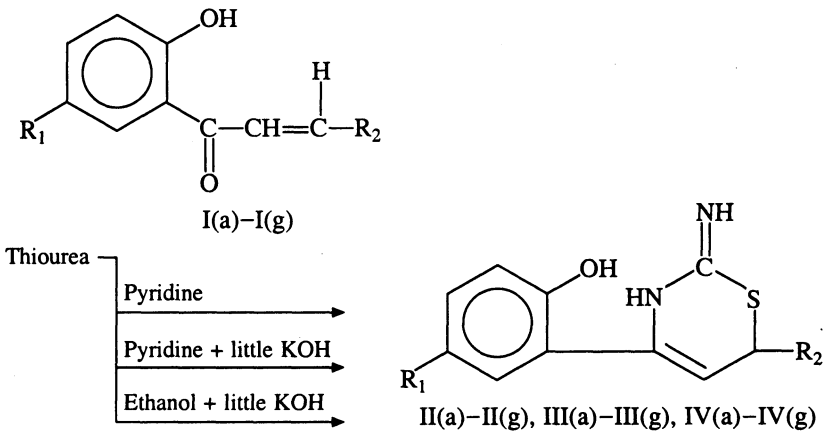
Synthesis of compounds III(a)–III(g)

Chalcones (0.01 mol), thiourea (0.01 mol) and 0.25 g of KOH in pyridine (20 mL) were refluxed for 2.5–3 h. On further processing as per literature method, gave seven 1,3-thiazines **III(a)–III(g)**. Physical data for compounds **III(a)–III(g)** are given in Table-2.

Synthesis of compounds IV(a)–IV(g)

Chalcones (0.01 mol) **I(a)–I(g)**, thiourea (0.01 M) and 0.25 g of KOH in ethanol (20 mL) were refluxed for 3.5–4 h to give seven different 1,3-thiazines **IV(a)–IV(g)**. The physical data of compounds **IV(a)–IV(g)** are given in Table-2.

Reaction:

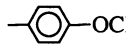
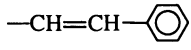
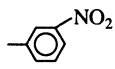


Where $R_1 = CH_3$, R_2 = as shown in Table-2.

IR for compounds II(c), III(c): 3760–3300 (broad) —OH, 3374(s) C—N—H stretching, 3014 C=NH stretching, 1690–1638 >C=N stretching, 1485 >C=C stretching vibration in aryl group, 1421(s) CH_3, 1288–1223 C—N stretching, 1175(m) Ar—O stretching.

NMR for compounds II(c), III(c), IV(c): (2.35–2.40s, 3H, Ar—CH_3), (2.8 d, 1H, CH_A), (3.2 dd, 1H, CH_B), (3.7–3.9s, 3H, Ar—OCH_3), (4.05 d, 1H, =N—H), (5.4 d, 1H, N—H), (6.9–7.9 m, 7H, Ar—H), 12.75 s, 1H, Ar—OH.

TABLE-2
PHYSICAL DATA OF COMPOUNDS *II(a)–II(g), III(a)–III(g), IV(a)–IV(g)

Compd. No.	R_2	m.f.	m.p. (°C)	Yield (%)		
				Pyridine (3.0–3.5 h)	Pyridine + KOH (2.5–3 h)	Ethanol + KOH (3.5–4.0 h)
II(a), III(a), IV(a)		$C_{23}H_{20}N_2OS$	146	65	69	62
II(b), III(b), IV(b)		$C_{17}H_{16}N_2OS$	84	68	70	67
II(c), III(c), IV(c)		$C_{18}H_{18}N_2O_2S$	78	73	78	70
II(d), III(d), IV(d)		$C_{19}H_{18}N_2OS$	189	60	68	57
II(e), III(e), IV(e)		$C_{17}H_{15}N_3O_3S$	120	72	74	70
II(f), III(f), IV(f)		$C_{13}H_{16}N_2OS$	Gummy products	Gummy products	Gummy products	Gummy products
II(g), III(g), IV(g)		$C_{15}H_{14}N_2O_2S$	160	64	68	61

*All compounds gave satisfactory elemental analysis.

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