

Note

Synthesis of thiazines using an unusual means-sonication

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A trouble free & swift method have been established for synthesis of thiazines from carbostyryl **CAB**¹ and dimidone **DIM**² using sulphur powder and iodine as a catalyst in presence of THF solvent. The structures of the compounds have been elucidated on the basis of spectral analysis.

Keywords: Carbostyryl, dimidone, thiazine

Thiazines are known to exhibit various kinds of biological activities such as Ca²⁺ antagonist, blood platelet aggregation inhibitors³ and antipsychotic⁴, antiviral⁵, antimicrobial⁶ and antihypertensive⁷ agents. In the view of this observation and extension of earlier work, thiazine derivatives have been prepared by sonication as well as by conventional method. The synthesis of novel thiazines^{8,9} have been reported using aminothiophenols and the synthesis of thiazine using an alternative route by reacting substituted amines using sulphur powder and iodine as a catalyst in presence of THF as a solvent is reported.

However in the earlier method expensive chemicals were used and the method was time consuming. In order to overcome these limitations and in vision of the requirement of green chemistry for energy saving, high efficiency and environment benevolence, we carried out series of reactions under sonication in addition to conventional method. The recent process gives excellent yield and time saving. Ultrasound method has been used to prepare thiazines (**Scheme I**). These derivatives have been also obtained by conventional method.

Experimental Section

Melting points of all synthesized compounds were determined in open capillary tubes on an electrothermal apparatus and are uncorrected. The purity of the compounds was monitored by TLC on silica gel

coated aluminium plates (Merck) as adsorbent and UV light as visualizing agent. IR spectra (KBr in cm⁻¹) were recorded on a Perkin-Elmer spectrophotometer in the range of 4000-400 cm⁻¹. ¹H NMR spectra were recorded on a Varian 500 MHz NMR spectrometer using CDCl₃/DMSO-*d*₆ as solvent and TMS as an internal standard (chemical shifts in δppm). Experiment under ultrasound irradiation was carried out in probe sonicator manufactured by Dakshin.

2,3-(substituted)benzo-1,4-thiazino[5,6-*b*]-4*H*-9*H*-5/7-substituted-10-oxoquinolines **4** Method A (ultrasound method): General procedure

The mixture of carbostyryls (**CAB**) **2** (0.05 mole), substituted amines **1** (0.05 mole) and sulphur powder (1 g) in THF 5 mL was irradiated on a sonicator in presence of iodine (0.15 g) as catalyst for 25 minutes. After completion of the reaction (monitored on TLC), the content was cooled, solid formed was filtered washed with dil. HCl, warm water followed by CS₂ and recrystallized from acetic acid to yield **4**.

Method B (Conventional method): General procedure

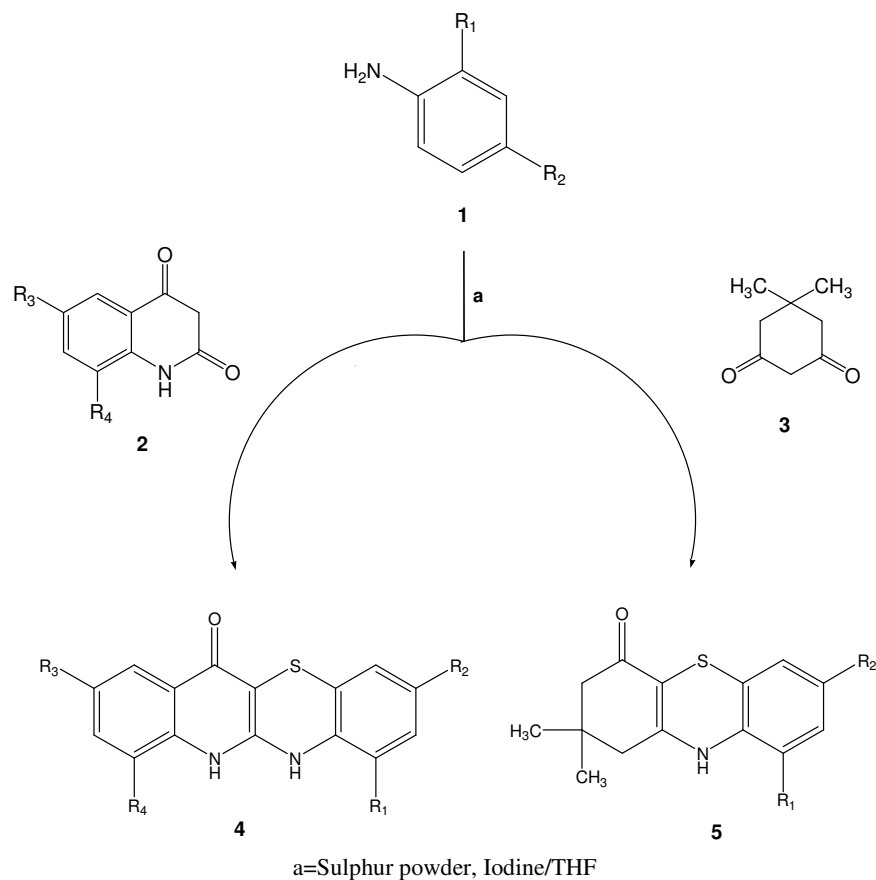
An equimolar mixture of carbostyryls (**CAB**) **2** (0.05 mole), substituted amines **1** (0.05 mole) and sulphur powder (1 g) in THF 5 mL was refluxed in presence of iodine (0.15 g) as catalyst for 3 hr at 180°C. On completion of reaction (monitored by TLC), the content was brought to RT, the solid formed was filtered washed with dil. HCl followed by carbon disulphide and recrystallized from acetic acid to obtain **4**.

The compound **4** obtained by both the routes showed undepressed mix m.p and similar spectral data.

7/9-Substituted-2,2-dimethyl-2,3-dihydro-1*H*,10*H*-phenothiazin-4-one **5**

Method A (ultrasound method): General procedure

Mixture of 5,5-dimethylcyclohexanon-1,2-dione (**DIM**) **3** (0.05 mole), substituted amines **1** (0.05 mole), sulphur powder (1 g), iodine solid (0.15 g) and THF 5 mL as a solvent was taken in 100 mL round



Scheme I

Table I — Characterization of synthesized compounds

Compd	R ₁	R ₂	R ₃	R ₄	m.p (°C) lit/obs	Yield (%)		Spectral data IR (KBr cm ⁻¹)/ ¹ H NMR (ppm) in DMSO- <i>d</i> ₆
						Ults	Conv	
4a	H	H	CH ₃	H	200/205	84	69	IR: 3248 (NH), 1620 (C=O) ¹ H NMR: 2.4 (s, 3H, CH ₃), 6.9- 8.2 (m, 7H, ArH), 10.98 (s, 1H, ring NH), 12.48 (s, 1H, ring NH),
4b	H	H	H	CH ₃	189/192	82	65	-
4c	H	H	OCH ₃	H	189/190	81	68	-
4d	H	CH ₃	OCH ₃	H	200/204	80	64	IR: 3248 (NH), 1657 (C=O) ¹ H NMR: 2.27 (s, 3H, CH ₃), 3.8 (s, 3H, OCH ₃), 6.7-8.2 (m, 6H, ArH), 10.8 (s, 1H, ring NH), 11.1 (s, 1H, ring NH).
4e	H	CH ₃	Cl	H	178/182	89	62	-
4f	H	OCH ₃	CH ₃	H	180/183	78	54	IR: 3184.9 (NH), 1622 (C=O) ¹ H NMR: 2.41 (s, 3H, CH ₃), 3.85 (s, 3H, OCH ₃), 7.00-7.7 (m, 6H, ArH), 10.32 (s, 1H, ring NH), 11.3 (s, 1H, ring NH).
4g	H	OCH ₃	Cl	H	190/193	81	54	-
4h	H	Cl	CH ₃	H	140/138	84	65	IR: 3300 (NH), 1653 (C=O) ¹ H NMR: 2.3 (s, 3H, CH ₃), 7.1-7.7 (m, 6H, ArH), 11.5 (s, 1H, ring NH), 12.15 (s, 1H, ring NH).
4i	H	Cl	H	CH ₃	135/139	76	64	-
4j	H	Cl	OCH ₃	H	150/154	89	63	-
4k	H	Cl	Cl	H	130/126	91	72	-
4l	H	Br	H	H	140/138	82	67	IR: 3248 (NH), 1620 (C=O) ¹ H NMR: 6.6-7.8 (m, 7H, ArH), 11.67 (s, 1H, ring NH), 11.77 (s, 1H, ring NH).
4m	H	Br	CH ₃	H	150/148	80	68	-
4n	H	Br	H	CH ₃	180/176	82	58	-

Method A: Ultrasound Time: 25 min

Method B: Conventional Time: 3hr

Table II — Characterization of synthesized compound

Compd	R ₁	R ₂	m.p (°C) lit/obs	Yield(%)		Spectral data IR (KBr cm ⁻¹)/ ¹ H NMR (ppm) in CDCl ₃
				Ults	Conv	
5a	H	H	264/260	86	64	IR: 3248 (NH), 1620 (C=O) ¹ H NMR: 1.10 (s, 6H, 2xCH ₃), 2.17 (s, 2H, CH ₂), 2.30 (s, 2H, CH ₂), 6.2-7.2 (m, 4H, ArH), 8.96 (s, 1H, NH).
5b	CH ₃	H	---/185	82	60	-
5c	H	CH ₃	194/190	88	59	IR: 3275 (NH), 1608 (C=O) ¹ H NMR: 1.08 (s, 6H, 2xCH ₃), 2.2 (s, 2H, CH ₂), 2.3 (s, 2H, CH ₂), 2.35 (s, 3H, CH ₃), 7.05-7.35 (m, 3H, ArH), 9.42 (s, 1H, NH).
5d	H	OCH ₃	246/242	80	67	IR: 3275 (NH), 1610 (C=O) ¹ H NMR: 1.08 (s, 6H, 2xCH ₃), 2.08 (s, 2H, CH ₂), 2.15 (s, 2H, CH ₂), 3.9 (s, 3H, OCH ₃), 7.05-7.35 (m, 3H, ArH), 11.6 (s, 1H, NH)
5e	Cl	H	---/198	78	65	-
5f	H	Cl	215/218	84	62	IR: 3244 (NH), 1620 (C=O) ¹ H NMR: 0.97 (s, 6H, 2xCH ₃), 2.13 (s, 2H, CH ₂), 2.17 (s, 2H, CH ₂), 6.4-7.0 (m, 3H, ArH), 8.94 (s, 1H, NH).

Method A: Ultrasound Time: 15 min

Method B: Conventional Time: 3hr

C H N S analysis was found satisfactory.

bottom flask and subjected to ultrasound for 15 minutes. After monitoring the reaction on TLC, the reaction- mixture was cooled at RT to obtained **5** which was filtered, washed with dil. HCl, warm water and then with CS₂ and recrystallised from ethanol.

Method B (Conventional method):

General procedure

Mixture of 5,5-dimethylcyclohexanon-1,2-dione (**DIM**) **3** (0.05 mole), substituted amines **1** (0.05 mole), sulphur powder (1 g), iodine soild (0.15 g) and THF 5 mL as a solvent was taken in 100 mL round bottom flask and the mixture was heated at 180°C for three hr. After monitoring the reaction on TLC, the reaction- mixture was worked-up in a same manner as discussed above to yield **5**.

Compound **5** obtained by both the routes showed underpressed mix m.p and similar spectral data.

The schematic data of the compound **4** and **5** are listed in the **Tables I** and **II**.

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