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Uncatalyzed Condensation Reactions between Aromatic Aldehydes and Thiobarbituric Acid in Water

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Abstract: A series of 5-arylidene thiobarbituric acids were prepared from aromatic aldehydes and thiobarbituric acid in water without catalyst conditions in good yields. The structures were characterized by elemental analysis, IR and ^{1}H NMR spectra.

Keywords: 5-Arylidene thiobarbituric acid, uncatalyzed reaction, environmentally benign synthesis.

Eco-benign version of organic reactions is potential candidates for the synthesis of biologically active compounds[1]. Recently, microwave assisted synthesis, sonication, solid-phase methods and other environmentally friendly reaction in organic synthesis have been paid considerable attention and are becoming an increasingly popular technology[2]. The use of water as solvent in organic chemistry under uncatalyzed conditions was particularly eco-friendly because of cheap, uninflammable and not toxic. This technique was discovered by Breslow[3] in the 1980s. 5-Arylidene thiobarbituric acids are widely used as precursors for the synthesis of bioactive derivatives[4] and its derivatives are also very important intermediates in organic reactions[5]. Cross aldol-type condensation of thiobarbituric acid with aromatic aldehydes using acetic acid as a catalyst is available for the preparation[6]. In this paper, we describe a rapid and convenient method for the synthesis of 5-arylidene thiobarbituric acids under uncatalyzed conditions using water as the solvent (**Scheme 1**). All the reactions were carried out at 95-100 ℃ for 45 min in water and the results were summarized in **Table 1**.

Scheme 1

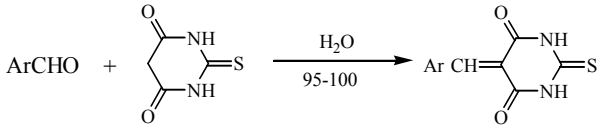

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Table 1 Synthesis of 5-arylidene thiobarbituric acids

Entry	Ar	Yields** (%)
3a	4-$(CH_3)_2NC_6H_4$	87.3
3b	C_6H_5	66.8
3c	4-ClC_6H_4	82.4
3d	4-HOC_6H_4	88.6
3e	3,4-$(CH_2O_2)C_6H_3$	61.6
3f	4-$CH_3OC_6H_4$	95.4
3g	2,4-$Cl_2C_6H_3$	83.0
3h	2-HOC_6H_4	50.4
3i	(η^5-C_5H_5)Fe(η^5-C_5H_4)	85.4

** isolated yields.

It is interesting that the reaction easily occurs in water although the mechanism involves a net dehydration to the alcoholic intermediate obtained by nucleophilic attack of the active methylene neighbouring to the carbonyl groups. We propose that water helps the thiobarbituric acid dissociation, due to its high ε value, that generates the nucleophilic species able to attack the carbonium of the aldehyde. It also makes the product easily to be isolated and this method can be employed in many kinds of aromatic aldehydes in liquid or solid forms.

Experimental

Thiobarbituric acid was prepared according to the literture[7].

Synthesis of 5-arylidene thiobarbituric acids

A mixture of 4-dimethylaminobenzaldehyde (10 mmol) and thiobarbituric acid (10 mmol) in water (40 mL) was stirred at 95-100℃ for 45 min. Then the solid was filtered and washed subsequently with boiling water, ether. After drying in vacuum, the 5-benzylidene thiobarbituric acid **3a** was obtained in 87.3% yield, mp>250℃; ^{1}H NMR （DMSO-d_6, 400 MHz, δ ppm:）3.16 (s, 6H), 6.83 (d, 2H, J = 9.2 Hz), 8.16 (s, 1H), 8.47 (d, 2H, J = 9.2 Hz,), 12.03 (s, 1H), 12.13 (s, 1H); IR (KBr) υ: 3455, 3114, 1646, 1493, 1233 cm^{-1}. Anal. Calcd. for $C_{13}H_{13}N_3O_2S$: C 56.73, H 4.73, N 15.27; found C 56.96, H 4.46, N 15.20. All products **3a-i** were characterized by IR, ^{1}H NMR and elemental analysis.

In conclusion, a simple synthetic route for 5-arylidene thiobarbituric acids by the condensation reaction of aromatic aldehydes with thiobarbituric acid in water without catalyst is described. This new method is a simple, good-yielding and environmentally friendly process.

Acknowledgments

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