One-pot Syntheses of 5-Oxo-1,4,5,6,7,8-hexahydroquinolines and Pyrimido[4,5-*b*]quinolines using Microwave Irradiation and Ultrasound

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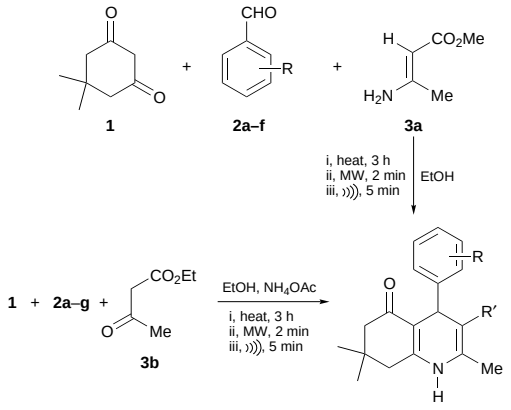
A rapid and efficient method for the synthesis of alkyl 4-aryl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylates by the condensation of 5,5-dimethylcyclohexane-1,3-dione and aromatic aldehydes with methyl 3-aminocrotonate or ethyl acetoacetate in the presence of ammonium acetate and of pyrimido[4,5-*b*]quinolines by the condensation of *N*-methylaniline with an aromatic aldehyde and 1,3-diaryl-2-thiobarbituric acid using microwave- and ultrasound-induced methods is reported.

We report a convenient, inexpensive and efficient method for the synthesis of methyl 4-aryl-1,4,5,6,7,8-hexahydro-2,7,7-trimethyl-5-oxoquinoline-3-carboxylates (**4a–f**) and the corresponding ethyl esters (**5a–g**) using microwave- and ultrasound-induced[17,18] methods. A one-pot synthesis of pyrimido[4,5-*b*]quinolines (**9a–i**) under microwave-induced conditions is also reported.

The synthesis of **4a–f** and **5a–g** involves the condensation of 5,5-dimethylcyclohexane-1,3-dione (**1**), aromatic aldehydes (**2a–g**) and either methyl 3-aminocrotonate[19] (**3a**) or ethyl acetoacetate (**3b**) in the presence of ammonium acetate, respectively, at ambient temperature on exposure either to ultrasound or microwave irradiation. Classical synthesis of these compounds requires refluxing for 3 h in the presence of ethanol on a sand-bath. However, when the reaction is carried out in a sonicator bath at ambient temperature or with microwave irradiation, the products are obtained in nearly quantitative yields and in very short time (2–5 min) (Scheme 1).



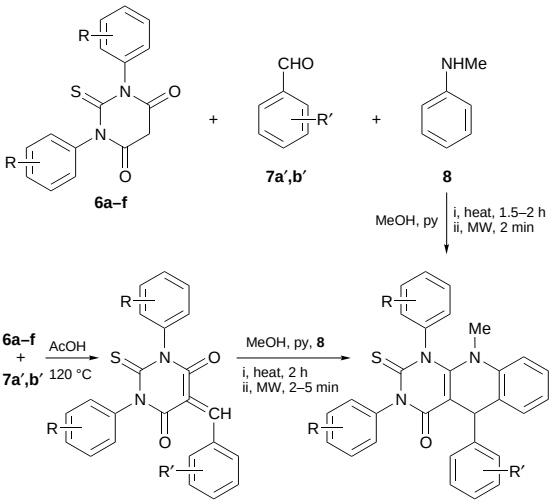
2,4,5	R
a	4-Cl
b	2-NO_2
c	H
d	4-Me
e	4-OMe
f	4-OEt
g	4-NMe_2

	R′
4a–f	CO_2Me
5a–g	CO_2Et

Scheme 1

The one-pot synthesis of pyrimido[4,5-*b*]quinolines (**9a–i**) under microwave-induced conditions involves the reaction of 1,3-diaryl-2-thiobarbituric acids[20] (**6a–f**), the appropriate aldehyde (**7a′**–b′) and *N*-methylaniline (**8**). Yields are 72–88% and the reaction is complete in 2 min, compared to 1.5–2 h under thermal conditions (Scheme 2).

Our method is noteworthy owing to the easy availability of the starting materials, the experimental simplicity of the one-pot procedure and the very high yield of products in very short time. Also, it provides a new entry into a variety of pyrimido[4,5-*b*]quinolines substituted at the 5,10-positions.



6,9,10	R
a	2-OMe
b	H
c	2-Me
d	3-Me
e	4-Me
f	3-OMe
g	2-OMe
h	H
i	2-Me

	R′
7a′	4-Me
7b′	2-NO_2
9,10a–f	4-Me
9,10g–i	2-NO_2

Scheme 2

Techniques used: ^{1}H NMR, IR, mass spectrometry

References: 20

Schemes: 2

Tables 1, 2: Physical and spectral data for **4a–f** and **5a–g**

Table 3: Comparison of reaction times and yields for the reactions **6a–f**→**9a–i** and **10a–i**→**9a–i**

Tables 4, 5: Physical and spectral data for **9a–i** and **10a–i**

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