A Novel Method for the Synthesis of Disubstituted Ureas and Thioureas Under Microwave Irradiaton†

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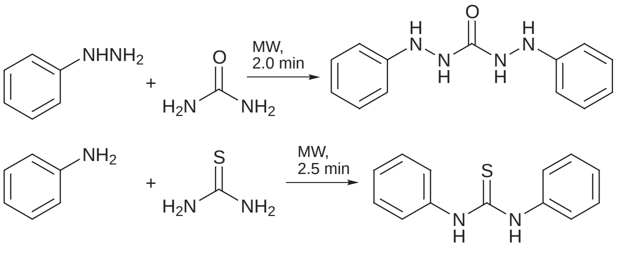
Several symmetrically disubstituted ureas and thioureas are synthesized by heating of urea or thiourea with aromatic amines or phenylhydrazine under environmentally benign conditions without any solvent in a conventional microwave oven.

The synthesis of substituted ureas and thioureas are important reactions in organic owing chemistry to their applications in agriculture, medicinal chemistry and chemical transformations.[1–3] Although the synthesis of mono- and di-substituted ureas have been extensively documented by a variety of methods, many of these have limitations in their general applications.[4–7] Recently the preparation of symmetrically substituted ureas and thioureas were reported by reductive alkylation of aromatic aldehydes,[8] from amines and CS_2,[9] and from aliphatic amines with acetoacetanilide.[10]

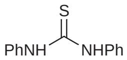
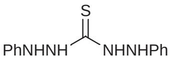
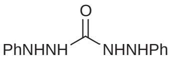
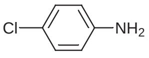
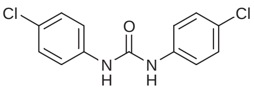
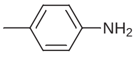
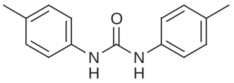
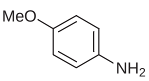
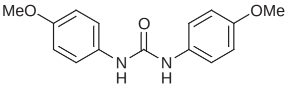
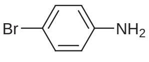
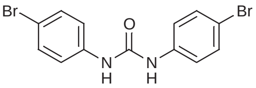
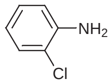
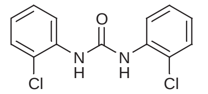
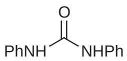
Microwave irradiation has opened new perspectives in synthetic organic chemistry, not only in terms of yield and selectivity, but also ease of the reaction conditions.[11] In view of the above, and in conjunction with our recent work on microwave-assisted reactions under solvent-free conditions,[12] we sought to develop a new method for the preparation of symmetrically disubstituted ureas and thioureas under environmentally benign conditions, using a microwave oven, without any solvent.



Scheme 1

Here, we report a new method for the synthesis of symmetrically disubstituted ureas and thioureas from aromatic amines or phenylhydrazine under microwave irradiation without any solvent or solid support. The reaction of an aromatic amine or phenylhydrazine (2 mmol) with urea or thiourea (1 mmol) in a conventional microwave oven produced symmetrically disubstituted ureas or thioureas in good to excellent yields, Scheme 1. The product is formed by loss of ammonia after 1–10 min (Table 1). Disubstituted ureas and thioureas were easily recovered by adding water to the final reaction mixture, removing the solid product by filtration, and recrystallizing the product from ethanol–water. Moreover, in comparison with reported procedures,[9,10] there is no need for the use of any heterogeneous catalysts or CS_2 in this procedure.

Table 1 Preparation of disubstituted ureas from aromatic amines or phenylhydrazine under microwave irradiation

Entry	Amine	Product	Yield[a] (%)	*t* / min
1	$PhNH_2$	 $PhNHC(=S)NHPh$	65	2.5
2	$PhNHNH_2$	 $PhNHNHC(=S)NHNHPh$	40	1.0
3	$PhNHNH_2$	 $PhNHNHC(=O)NHNHPh$	90	2.0
4			70	4.0
5			83	4.0
6			85	4.0
7			40	4.0
8			45	5.0
9	$PhNH_2$	 $PhNHC(=O)NHPh$	66	2.0

[a] Yields refer to isolated and chromatographically pure products. All products exhibited spectral data consistent with their structures.

In conclusion, we have shown that direct heating of aromatic amines or phenylhydrazine with urea or thiourea leads to an efficient synthesis of symmetric N,N-disubstituted ureas or thioureas from aromatic amines or phenylhydrazine.

Experimental

^1H NMR spectra were recorded in $CDCl_3$ on a Bruker AC 80 spectrometer, using $SiMe_4$, as internal standard. IR spectra were obtained on Matt Son 1000 Unicam FTIR spectrophotometer. Mass spectra were recorded on Fisons 800 Trio instrument.

General Procedure for the Preparation of Disubstituted Ureas.—An aromatic amine or phenylhydrazine (2 mmol) was mixed thoroughly with urea (1 mmol, 0.06 g) in a 5 ml beaker. Then the beaker was placed in conventional microwave oven until the mixture became liquid. The time required for each reaction is indicated in Table 1. To remove the unreacted urea, water (10 mL) was added to the

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

reaction mixture which was filtered. The recovered solid material was recrystallized from water–ethanol. The structure of the products were confirmed by IR, ^{1}H, ^{13}C NMR, and MS, and comparison of their melting points with those reported in the literature.[1,3,13]

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