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Solvent-free Synthesis of *N,N′*-Diarylureas Using Microwave Technology

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A simple and rapid solvent-free synthesis of *N,N′*-diarylureas in a microwave oven has been reported for the first time. Nine compounds were synthesized. The reaction time is short (2~5 min) and gives excellent yield (80-95%).

Keywords: Solvent-free synthesis; Microwave technology; *N,N′*-diarylureas.

INTRODUCTION

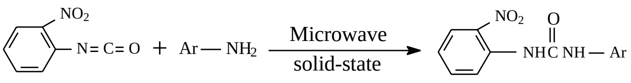
The *N,N′*-diarylurea derivatives are very interesting reagents due to their useful properties and important medical[1-3] and biological applications.[4,5] It has been reported that *N,N′*-diarylurea derivatives can be synthesized from corresponding isocyanate with aromatic amine in organic solvent.[6,7] But most of the cases mentioned above suffer from drawbacks such as extended reaction time, tedious purification and toxic solution. Consequently, a simple, rapid, convenient and environmentally benign method for synthesis of *N,N′*-diarylureas is required.

Recently, the microwave technique assisted organic reaction has gained considerable attention. This method has a number of advantages such as short reaction time, high yield and simple experimental procedure. Most of the reactions under microwave irradiation using solvent were practically limited because high vapour pressure sometimes leads to explosions. Solvent-free organic synthesis under microwave irradiation has great applied value and expansive prospects because of energy saving, high efficiency and environment acceptability. It has been applied to several organic reactions.[8,9] The solvent-free synthesis *N,N′*-diarylureas using microwaves has not been reported so far.

RESULTS AND DISCUSSION

Nine *N,N′*-diarylureas were prepared from 2-nitrophenylisocyanate with corresponding aromatic amine in satisfying yields (80-95%) (Scheme I). The results are summarized in Table 1.

Scheme I



1 2

Ar:

a) 4-methylphenyl
b) 4-methoxyphenyl
c) 3,4-dimethylphenyl
d) 4-chlorophenyl
e) 4-bromophenyl
f) 4-iodophenyl
g) 2-nitrophenyl
h) 3-nitrophenyl
i) 4-nitrophenyl

It was found that the aromatic amines with electron-donating substituents needed lower power or shorter time than those with electron-attracting substituents. Among the three nitroanilines, the reaction of 3-nitroaniline has the rapidest reaction rate and needs the lowest microwave power. The reaction of 4-iodoaniline is easier to complete than that of 4-bromoaniline and 4-chloroaniline.

The structure of the products were confirmed by IR, Elemental analysis, ^{1}H NMR, and MS spectroscopy.

EXPERIMENTAL SECTION

Melting points were determined with a Kolfer micro melting point apparatus and were uncorrected. The reactions were carried out in a Galanz Cambi-Grill microwave oven (the power output 750 W). IR spectra were recorded on a Bio-Rad Win-IR spectrophotometer in KBr. ^{1}H NMR spectra were measured on a Mercury 300 spectrophotometer using TMS as internal standard and d_6-DMSO as solvent. Elemental analyses were performed on a Elementar Vario EL. Mass spectra were recorded on a KYKY QP-1000A.

Table 1. The Solvent-free Synthesis of *N,N′*-diarylureas under Microwave Irradiation

Entry	Ar	Reaction time/min	Microwave Power/w	Yields/%
2a	4-MeC_6H_4	2.5	80%	93
2b	4-$MeOC_6H_4$	2.5	80%	90
2c	3,4-$(Me)_2C_6H_3$	2	80%	95
2d	4-ClC_6H_4	3	80%	89
2e	4-BrC_6H_4	3	100%	86
2f	4-IC_6H_4	2.5	80%	90
2g	2-$NO_2C_6H_4$	5	100%	80
2h	3-$NO_2C_6H_4$	5	80%	88
2i	4-$NO_2C_6H_4$	5	100%	90

General Procedure for the Preparation of *N,N′*-diarylureas (2a-2i)

2-Nitroisocyanate (1 mmol) and substituted aniline (1 mmol) were milled respectively and mixed thoroughly in an agate mortar. Then the mixture was placed in a beaker and irradiated by microwave for 2-5 min. in a household microwave oven. The procedure of the reaction was monitored by thin-layer chromatography. The crude products were recrystallized with ethanol or acetone and dried under vacuum to yield the pure products.

N-(2-nitrophenyl)-N′-(4-methylphenyl)urea (2a)

Yellow needles. mp (°C): 192-193 (lit.:[10] 191-193). yield: 93%. IR (ν, cm^{-1}): 3326, 3302 (NH), 1652 (C= O).

N-(2-nitrophenyl)-N′-(4-methyoxyphenyl)urea (2b)

Pale yellow sticks. mp (°C): 176-179 (no lit. mp reported). yield: 90%. IR (ν, cm^{-1}): 3296 (NH), 1642 (C=O). MS: 287 (M^+), 138, 122, 91. ^1H NMR (δ, ppm): 9.56-9.69 (2H, NH), 6.88-7.41 (8H, Ar-H), 3.72 (3H, OCH_3-H). Anal. Calc.: C, 58.54; H, 4.53; N, 14.63. Found: C, 58.51; H, 4.72; N, 14.63.

N-(2-nitrophenyl)-N′-(3,4-dimethylphenyl)urea (2c)

Pale yellow silk needles. mp (°C): 190-192 (no lit. mp reported). yield: 95%. IR (ν, cm^{-1}): 3296 (NH), 1648 (C=O). MS: 285 (M^+), 147, 138, 121. ^1H NMR (δ, ppm): 9.56-9.68 (2H, NH), 7.04-8.32 (7H, Ar-H), 2.16-2.19 (6H, CH_3-H). Anal. Calc.: C, 63.16; H, 5.26; N, 14.74. Found: C, 63.07; H, 5.44; N, 14.84.

N-(2-nitrophenyl)-N′-(4-chlorophenyl)urea (2d)

Yellow needles. mp (°C): 205-207 (lit.:[7] 208-209.6). yield: 89%. IR (ν, cm^{-1}): 3335 (NH), 1668 (C=O).

N-(2-nitrophenyl)-N′-(4-bromophenyl)urea (2e)

Yellow needles. mp (°C): 215-217 (lit.:[11] 207-208). yield: 86%. IR (ν, cm^{-1}): 3336 (N-H), 1666 (C=O). MS: 335 (M^+), 170, 155, 138. ^1H NMR (δ, ppm): 9.58-9.94 (2H, NH), 7.17-8.25 (8H, Ar-H). Anal. Calc.: C, 46.57; H, 2.99; N, 12.54. Found: C, 46.55; H, 3.13; N, 12.64.

N-(2-nitrophenyl)-N′-(4-iodophenyl)urea (2f)

Pale yellow needles. mp (°C): 220-222 (lit.:[12] 223-224). yield: 90%. IR (ν, cm^{-1}): 3328, 3286 (NH), 1651(C=O).

N-(2-nitrophenyl)-N′-(2-nitrophenyl)urea (2g)

Pale yellow needles. mp (°C): 226-228 (lit.:[13] 225). yield: 80%. IR (ν, cm^{-1}): 3298 (NH), 1659 (C=O).

N-(2-nitrophenyl)-N′-(3-nitrophenyl)urea (2h)

Orange sticks. mp (°C): 240-243 (lit.:[7] 246-247) yield: 88%. IR (ν, cm^{-1}): 3381 (NH), 1729 (C=O).

N-(2-nitrophenyl)-N′-(4-nitrophenyl)urea (2i)

Yellow needles. mp (°C): 270 (dec.) [lit.:[13] 270-275 (dec.)]. yield: 90%. IR (ν, cm^{-1}): 3375 (NH), 1611(C=O).

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REFERENCES

1. Beaver, D. J.; Roman, D. P.; Stoffel, P. T. *J. Am. Chem. Soc.* **1957**, *79,*1236.
2. Peng, C.-T.; Daniels, T. C. *J. Am. Chem. Soc.* **1956**, *78,* 3703.
3. Pavia, M. R.; Lobbestael, S. J.; Tayol, C. P. *J. Med. Chem.* **1990**, *33*, 845-861.
4. Bruce, M. I.; Zwar, J. A. *Proc . Roy. Soc.* (London), *SerB* **1966**, *165*, 245.
5. Qiao, L.-X.; Li, Z.-M.; Yang, H.-Z. *Chem. Res. Chin. Univ.* **1995**, *11,* 291.
6. Etter, M. C.; Zofia Urbaňczyk-Lipkowska; Zia, M. *J. Am. Chem. Soc.* **1990**, *112,* 8415.

7. Beaver, D. J.; Roman, D. P.; Stoffel, P. J. *J. Org. Chem.* **1959**, *24*, 1676.
8. Li, J. P.; Luo, Q. F.; Wang, Y. L. *J. Chin. Chem. Soc.* **2001**, *48*, 73.
9. Jin, J.; Wen, Z.; Long, J. *Synth. Commun.* **2000**, *30*, 829.
10. Grammaticakis, I. P. *Bull. Sec. Chim. France* **1959**, 1559.
11. Sah, Peter P. T.; Kao, C.-H.; Wang, S.-M. *J. Chin. Chem. Soc.* **1936**, *4*, 193.
12. Sah, P. T.; Wang, Y.-K. *Rec. Trav. Chim.* **1940**, *59*, 364.
13. Heilborn, I.; Bunbary, H. M. etc. *Dictionary of Organic Compounds*, 4th, Eyre and Spottiswoode Publishers Ltd, London, 1965.