Indian Journal of Chemistry
Vol. 45B, February 2006, pp. 546-547

## Note

# A rapid microwave assisted synthesis of N, N'-diarylureas under solvent-free condition

S Sarveswari & T K Raja*

Department of Chemistry, Vellore Institute of Technology, Deemed University, Vellore 632 014, India

Email: professor_raja@yahoo.co.uk

*Received 6 October 2004; accepted (revised) 16 August 2005*

A novel microwave assisted phosgene-free synthesis of N,N'-diarylureas under solvent-free conditions has been described.

**Keywords**: N,N'-diarylureas, microwave assisted synthesis

**IPC**: **Int.Cl.**[7] **C 07 C**

The microwave induced organic reactions are becoming popular because of their simplicity and operational convenience[1,2]. The synthesis of bis-arylureas has received considerable attention of the organic chemists due to their wide range of biological applications[3,4]. They act as potential Raf kinase inhibitors[3] and antagonists of human vanilloid receptor1 (VR 1)[4]. Phenyl thiazolylurea derivatives have been reported as inhibitors of Murine receptor A and Murine receptor B[5]. Some substituted ureas are used as antidiabetic and tranquilizing drugs, antioxidants in gasoline, corrosion inhibitor and herbicides[6].

The conventional methods reported for the synthesis of arylureas are essentially based on phosgene and isocyanates[6], phosgene substitutes[6], carbonates, carbamates[6], carboxylic acid derivatives[6] and aniline and urea[7]. Phosgene and isocyanates are expensive, hazardous and toxic chemicals to handle. There is a continuing interest in the simple phosgene-free rapid synthesis of diarylureas.

In view of the above, we report a hitherto unknown microwave assisted synthesis of N,N'-diarylureas from aryl primary amines and ethylacetoacetate. The conventional method involves five hours of reflux using zeolite HSZ-360 catalyst, whereas in our method of microwave irradiation the product is formed in 4-16 min without the need for any supporting agents or catalysts. The synthesis of compounds (**3a**-**3j**) is attributed to the initial formation of acetoacetanilides followed by their subsequent reactions with a second molecule of arylamines to give diarylureas and acetone (**Scheme I**). The $^1$H NMR data of the synthesized diarylureas are **3b**: δ 7-7.8 (m, 8H, ArH), 9 (br, 2H, NH) **3c**: δ 3.5 (s, 6H, -$OCH_3$), 6.5-7.1 (m, 8H, ArH), 8.8 (br, 2H, NH) and **3d**: δ 2.3 (s, 6H, -$CH_3$), δ 6.8-7.9 (m, 8H, ArH), 8.2 (br, 2H, NH).

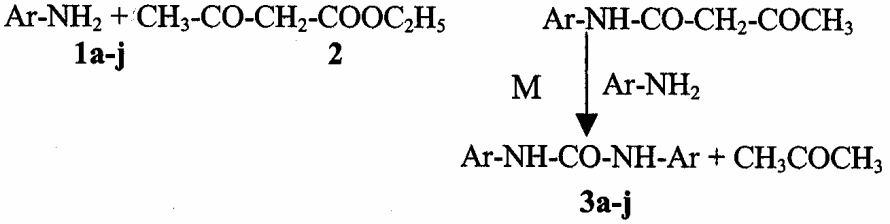
### Experimental Section

All melting points are uncorrected. IR spectra of all the compounds were recorded on AVATAR330 FT-IR spectrometer, $^1$H NMR spectra were recorded on AMX400. The reactions were carried out in SAMSUNG and LG domestic microwave ovens. The product formation was confirmed by NMR, mass and X-ray single crystal structural studies.

### General procedure for the synthesis of N,N'-diphenylurea 3a

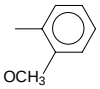
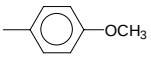
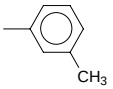
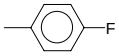
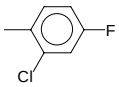
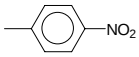
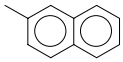
A mixture of aniline **1a (**4.6 mL, 0.05 *M*) and ethylacetoacetate **2 (**6.5 mL, 0.05 *M*) was taken in a conical flask and irradiated with microwave at 450W for 15 min. The reaction mixture was cooled and poured onto ethanol. The resulting crystals of diphenylurea **3a** were filtered, dried and recrystallized from ethanol.

The above synthetic methodology was extended to other aromatic primary amines to get the corresponding diarylurea derivatives (**3b**-**3j**) and thereby to prove the generality of the reaction. The




**Scheme I**

**Table I —** Physical and spectroscopic data of **3a-3j**

| Compound | Ar | mp (°C) | Time(min) and power | Yield (%) | IR Data | Mass ($M^+$) |
|---|---|---|---|---|---|---|
| **3a**[6] |  | 236 | 15 (450W) | 62 | 3320 (N-H), 3068 (C-H), 1647 (C=O) | 212 |
| **3b** |  | 234 | 6 (450W) | 61 | 3291 (N-H), 1635 (C=O), 872 (C-Cl) | 280 |
| **3c** |  | 220 | 16 (450W) | 60 | 3319 (N-H), 2829 (C-H), 1647 (C=O) | 272 |
| **3d** |  | 224 | 16 (450W) | 62 | 3309 (N-H), 2829 (C-H), 1642 (C=O) | 272 |
| **3e** |  | 235 | 11 (450W) | 69 | 3304 (N-H), 2922 (C-H), 1641 (C=O) | 238 |
| **3f** |  | 236 | 11 (450W) | 70 | 3298 (N-H), 2913 C-H ($CH_3$), 1635 (C=O) | 238 |
| **3g** |  | 246 | 4 (360W) | 56 | 3293 (N-H), 1632 (C=O), 1209 (C-F) | 248 |
| **3h** |  | 228 | 4 (360W) | 42 | 3321(N-H), 1657 (C=O), 1212(C- F), 884 (C-Cl) | 316 |
| **3i** |  | 238 | 7 (360W) | 60 | 3344 (N-H), 1324 (N=O), 1650 (C=O) | 302 |
| **3j** |  | 264 | 3 (360W) | 63 | 3279 (N-H), 3050 (C-H), 1634 (C=O) | 312 |

irradiation time, power levels, IR and mass spectral data are given in **Table I**. The shorter irradiation time and lesser power levels led to reduction in yields, while the longer irradiation time and higher power levels led to decomposition.

## Acknowledgement

The authors are thankful to Dr. R. Vijayaraghavan, Asst. Professor, Department of Chemistry, Vellore Institute of Technology, Vellore, Prof. T. N. Guru Row, SSCU, IISc, Bangalore and to RSIF, IISc, Bangalore and Shasun Chemicals, Chennai for providing X-ray crystallographic, $^1$H NMR and mass spectral data.

## References

1 Patel V M & Desai K R, *Indian J Chem*, 43B, **2004**, 199.

2 Longe J H M, Verveer P. C, Osnabrug S J M & Visser G M, *Tetrehedran Lett*, 42, **2001**,1367.

3 Khire U R, Bankston D, Barbosa J, Brittelli D R, Caringal Y, Carlson R, Dumass J, Gane T, Heald S L, Hibner B, Johnson J S, Katz M E, Kennure N, Wood K J, Lee W, Liu X G, Lowinger T B, McAlexander I, Monahan M K, Natero R, Renick J, Riedl B, Rong H, Silbley R N, Smith R A & Wolanin D, *Bio Org & Med Chem Lett*, 14, **2004**, 783.

4 McDonnell M E, Zhang S P, Nasser N, Dubin A E & Dax S L, *Bio Org & Med Chem Lett*, 14, **2004**, 531.

5 Francisco G D, Li Z, Albright J D, Eudy N H, Katz A H, Petersen P J, Labthavikul P, Singh G, Yang Y, Rasmussen B A, Lin Y I & Mansour T S, *Bio Org & Med Chem Lett*, 14, **2004**, 235.

6 Bigi F, Maggi R, Sartori G & Zambonin E, *Chem Commun*, 4, **1998**, 513 and the references cited therein.

7 Davis T L & Blanchard K C, *Organic Synthesis*, Coll Vol 1, 453.