

Synthesis of symmetrical 1,3-diarylureas by sulfur-catalyzed carbonylation in ionic liquids

Xiaofang Wang, Peng Li, Xiaohua Yuan, Shiwei Lu*

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 161 ZhongShan Road, Dalian, Liaoning, 116011, PR China

Received 10 January 2006; received in revised form 17 March 2006; accepted 23 March 2006

Available online 3 May 2006

Abstract

A relatively efficient catalytic system containing elemental sulfur–ionic liquid was developed for the carbonylation of nitroaromatics and corresponding aromatic amines with carbon monoxide to give symmetric diarylureas in yields up to 96%. Additionally, unsymmetrical urea *N*-phenyl-*N'*-(piperidine) urea was obtained in 70% yield in this catalytic system.

© 2006 Elsevier B.V. All rights reserved.

Keywords: Elemental sulfur; Ionic liquids; Carbonylation; 1,3-Diarylureas

1. Introduction

Non-phosgene processes for the synthesis of carbamates and/or ureas have attracted increasing interest in recent years, particularly in the area of green chemistry because of the environmental concerns regarding the use of highly toxic phosgene [1]. Many strategies for nonphosgene routes including reductive carbonylation [2] and oxidative carbonylation [3] catalyzed by expensive transition metals such as Ru, Rh and Pd have been extensively studied. Furthermore, main-group elements such as selenium [4,5] or sulfur [6–8] have also been reported to catalyze these reactions. Sulfur is cheap, readily available and less toxic, but in most cases, the reactions were performed in the presence of excess or stoichiometric amounts of sulfur [6,8]. Macho et al. have reported the carbonylation of nitrobenzene using elemental sulfur as catalyst in methanol with 13 MPa CO in the presence of sodium metavanadate gives methyl-*N*-phenyl carbamate (MPC) predominantly [7]. Recently, we have found that selenium exhibited excellent catalytic performance in polar and hydrophilic solvents such as DMF and DMSO [9,10]. With this in mind, we hypothesized that sulfur combined with polar solvents, i.e., ionic liquids might provide a new platform for the sulfur catalytic system.

2. Experimental

The organic solvents were all reagent grade and were used without further purification. Ionic liquids were synthesized according to the literature [11]. Sulfur (99.5%) and carbon monoxide (99.9%), nitroaromatics, anilines and triethylamine (Et₃N) were all used as purchased. Melting points were determined on a Taikex X-4 apparatus (Beijing, China) and are uncorrected. ¹H and ¹³C NMR spectra were obtained on a Bruker DRX 400 spectrometer. Chemical shifts were reported in parts per million relative to tetramethylsilane (δ units), and dimethylsulfoxide (DMSO)-*d*₆ as solvents.

2.1. Procedure for the synthesis of diphenylurea

Elemental sulfur (0.048 mg, 1.5 mmol), aniline (0.47 g, 5 mmol), nitrobenzene (0.62 g, 5 mmol), Et₃N (0.50 g, 5 mmol), BMImBF₄ (BMIm = 1-butyl-3-methylimidazolium) (1.5 g) were successively introduced into a 100 ml stainless-steel autoclave. The reactor was sealed, flushed with 1.0 MPa of carbon monoxide three times, pressured with 3 MPa carbon monoxide, and then placed in an oil bath preheated to 150 °C. After the reaction was finished in 8 h, the apparatus was cooled to ambient temperature, and the remaining carbon monoxide was evacuated. Water (15 ml) was poured into the mixture to precipitate the crude product. Purification by column chromatography on silica gel using Et₂O–AcOEt (20:1–10:1) as the

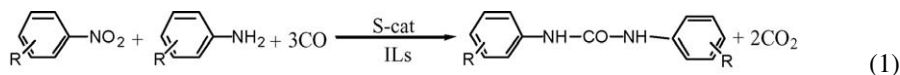
* Corresponding author. Fax: +86 411 83698749.
E-mail address: lusw@dicp.ac.cn (S. Lu).

eluent afforded the urea product (1.02 g, 96%). Products were identified by NMR and/or comparison with authentic samples.

3. Results and discussion

3.1. Solvent, amount of Et_3N and sulfur on sulfur-catalyzed carbonylation

Symmetric diarylureas are synthesized from the sulfur-catalyzed carbonylation of nitroarenes and corresponding anilines in ionic liquids.



The carbonylation of nitroarenes and corresponding anilines was carried out under pressurized carbon monoxide in the presence of triethylamine (Et_3N) as accelerant and a catalytic amount of sulfur in ionic liquids at 150°C (Eq. (1)) [12]. To determine the optimized reaction conditions nitrobenzene and aniline were treated with carbon monoxide under various reaction conditions and these results are shown in Table 1. Although the preparation of diphenylurea (DPU) by the reaction of nitrobenzene and aniline with carbon monoxide in the presence of the sulfur catalyst can occur even in DMF, toluene, THF and methanol, the yields obtained were only from 8% to 29% (Table 1, entries 4–7). Higher yields (75%) were achieved in ionic liquids (Table 1, entry 1). On the other hand, the type of cations and anions of the ionic liquids also have a strong impact on the formation of DPU. With BMIm^+ as cation, the effect of anions, e.g., BF_4^- , PF_6^- , Cl^- , on the carbonylation was examined (Table 1, entries 2, 3, 9). Higher yield of DPU was achieved in BMImBF_4 .

Base, Et_3N , employed plays a critical role. The reaction afforded the product in 10% yield in the absence of Et_3N (Table 1, entry 8). However, the yield of DPU was improved by the addition of 5 mmol Et_3N (96%) and then decreased with any further increase in the amount of Et_3N (87% yield) (Table 1, entries 9, 10). The reaction performed using 0.5 mmol sulfur in

Table 1
Carbonylation of nitrobenzene and aniline to 1,3-diphenylurea

Entry	Solvent (1.5 g)	Et_3N (mmol)	Sulfur (mmol)	Yield (%) ^a
1	BMImBF_4	5	1.5	75 ^b
2	BMImCl	5	1.5	57
3	BMImPF_6	5	1.5	86
4	DMF	5	1.5	8 ^b
5	THF	5	1.5	29 ^b
6	Toluene	5	1.5	10 ^b
7	Methanol	5	1.5	29
8	BMImBF_4	0	1.5	10
9	BMImBF_4	5	1.5	96
10	BMImBF_4	10	1.5	87
11	BMImBF_4	5	0.5	41
12	BMImBF_4	5	1.0	87

Nitrobenzene, 5.0 mmol; aniline, 5.0 mmol; $P_{\text{CO}} = 3.0 \text{ MPa}$; $T = 150^\circ\text{C}$, isolated yields.

^a $t = 8 \text{ h}$.

^b $t = 5 \text{ h}$.

Table 2
The effect of the pressure of carbon monoxide on sulfur-catalyzed carbonylation

Run	P_{CO} (MPa)	Yield (%)
1	3.0	96
2	2.0	68
3	1.0	51
4	1.0 ^a	59

S, 1.5 mmol; nitrobenzene, 5.0 mmol; aniline, 5.0 mmol; Et_3N , 5 mmol; $\text{BMIm}[\text{BF}_4]$, 1.5 g; $T = 150^\circ\text{C}$; $t = 8 \text{ h}$.

^a $P_{\text{CO}} = 1.0 \text{ MPa}$; $P_{\text{N}_2} = 2.0 \text{ MPa}$.

$[\text{BMIm}]\text{BF}_4$ afforded the product with the yield of 41% (Table 1, entry 11). Meanwhile, the best result was obtained in the presence of 1.5 mmol sulfur (Table 1, entry 9).

3.2. Effect of pressure of carbon monoxide on sulfur-catalyzed carbonylation

As shown in Table 2, DPU was produced in the yield of 51% in the presence of 1 MPa CO (Table 2, run 3). When was added 2 MPa nitrogen to 1 MPa CO (Table 2, run 4), DPU was obtained with 59% yield, which suggested that pressure of gas slightly affected the yield of the desired product. While the pressure of CO was increased from 1.0 to 3.0 MPa, the yield of DPU was increased from 51% to 96% (Table 2, runs 1–3).

3.3. Carbonylation of substituted nitroarenes and corresponding amines

The present DPU synthetic methodology can be applied to substituted nitroarenes and corresponding amines, and symmetrical substituted 1,3-diarylureas were also obtained.

As revealed in Table 3, when 4-isopropyl-, 4-methyl-, 3-methyl-, 2-methyl-, 3-chloro, and 3-bromonitrobenzenes, and

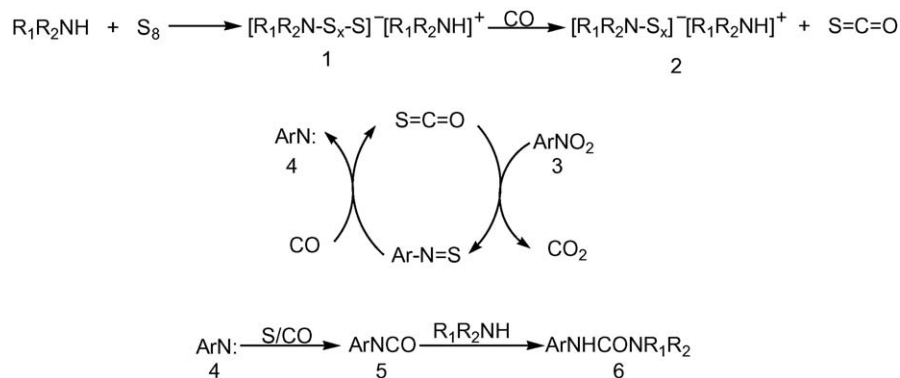
Table 3
Carbonylation of substituted nitroarenes and corresponding anilines

Entry	R	Yield (%) ^a
1	H	96
2	4- <i>i</i> -Pr	74
3	4- CH_3	92
4	3- CH_3	78
5	2- CH_3	78
6	3-Cl	93 ^b
7	3-Br	92
8	3- CF_3	20
9	3-Cl, 4- CH_3	45
10	4- CH_3CO	74

S, 1.5 mmol; nitroarene, 5.0 mmol; aromatic amine, 5.0 mmol; Et_3N , 5.0 mmol; $\text{Bmim}[\text{BF}_4]$, 1.5 g; $P_{\text{CO}} = 3.0 \text{ MPa}$; $T = 150^\circ\text{C}$; $t = 8 \text{ h}$.

^a Isolated yields.

^b $t = 5 \text{ h}$.

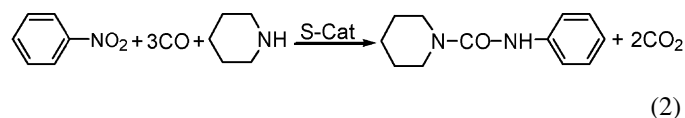


Scheme 1. Proposed reaction pathway of sulfur-catalyzed carbonylation of nitrobenzene and aniline.

4-nitroacetophenone and corresponding anilines were allowed to react with carbon monoxide in ionic liquid [BMIm]BF₄ in the presence of a catalytic amount of sulfur, the 1,3-diarylureas were produced in 74–93% yield. However, *N,N'*-bis-(3-chloro-4-methylphenyl)urea was obtained with the yield of 45%. It is unclear why no obvious reaction occurred with 3-trifluoromethylnitrobenzene under the same reaction conditions (Table 3, entry 8).

3.4. Carbonylation of piperidine and nitrobenzene

The catalytic system was widened to synthesize the unsymmetrical urea *N*-phenyl-*N'*-(piperidine) urea from nitrobenzene and piperidine (Eq. (2)).



When the ratio of nitrobenzene to piperidine is unity, 35% unsymmetrical urea was given. As seen in Table 4, the yields of *N*-phenyl-*N'*-(piperidine) urea increased as the amount of piperidine was increased to 1.5-folds, and then decreased with any further increase in the amount of piperidine. Additionally, longer reaction time did not result in a higher yield (Table 4, runs 2, 4).

3.5. A plausible reaction pathway

Although a detailed study of the reaction mechanism has not been undertaken, we found that higher yields were obtained when elemental sulfur was firstly mixed with aniline than when

aniline was lastly introduced. The present reaction can be proposed in Scheme 1. Salts of thiolates 1 from elemental sulfur and amine react with carbon monoxide to produce carbonyl sulfide (SCO) [13,14]. Deoxygenation of nitroarene with SCO results in the reactive intermediate nitrene 4 [15]. Nitrene 4 reacts with aniline in the presence of sulfur and carbon monoxide to afford urea 6.

4. Conclusions

In conclusion, we have developed a relative efficient protocol for the production of symmetrically substituted urea by elemental sulfur-catalyzed oxidative-reductive carbonylation of nitroaromatics and corresponding aromatic amines with carbon monoxide in ionic liquids. Unsymmetrical urea *N*-phenyl-*N'*-(piperidine) urea was obtained in 70% yield in this catalytic system. The methodology reported herein offers a useful alternative to the existing methodology due to using less toxic catalysis system.

References

- [1] H.J. Knölker, J. Braxmeier, G. Schlechtingen, *Angew. Chem. Int. Ed.* 34 (1995) 2497.
- [2] M. Gasperini, F. Ragaini, C. Cazzaniga, S. Cenini, *Adv. Synth. Catal.* 347 (2005) 105, and references therein.
- [3] B. Gabriele, G. Salerno, R. Mancuso, M. Costa, *J. Org. Chem.* 69 (2004) 4741, and references therein.
- [4] N. Sonoda, T. Yasuhara, K. Kondo, T. Ikeda, S. Tsutsumi, *J. Am. Chem. Soc.* 93 (1971) 6344.
- [5] Y. Yang, S.W. Lu, *Tetrahedron Lett.* 40 (1999) 4845.
- [6] R.A. Franz, F. Applegath, F.V. Morriss, F. Baiocchi, *J. Org. Chem.* 26 (1961) 3304.
- [7] V. Macho, M. Králik, F. Halmo, *J. Mol. Catal. A: Chem.* 109 (1996) 119.
- [8] T. Mizuno, J. Takahashi, A. Ogawa, *Tetrahedron* 58 (2002) 7805.
- [9] X.F. Wang, S.W. Lu, Z.K. Yu, *Adv. Synth. Catal.* 346 (2004) 929.
- [10] X.F. Wang, S.W. Lu, *Eur. J. Org. Chem.* (2005) 1675.
- [11] S. Park, R.J. Kazlauskas, *J. Org. Chem.* 66 (2001) 8395.
- [12] The ionic liquid was reused 3rd times, the yield still can be up to 94%.
- [13] W.G. Hodgson, S.A. Buckler, G. Peters, *J. Am. Chem. Soc.* 85 (1963) 543.
- [14] T. Mizuno, T. Iwai, T. Ito, *Tetrahedron* 60 (2004) 2869.
- [15] V. Macho, M. Králik, J. Hudec, J. Cingelova, *J. Mol. Catal. A: Chem.* 209 (2004) 69.

Table 4

The ratio of nitrobenzene to piperidine

Run	Benzene:piperidine	Yield (%)
1	1:1	35
2	1:1.5	70
3	1:2	41
4	1:1.5 ^a	66

S, 1.5 mmol; nitrobenzene, 5.0 mmol; Et₃N, 5 mmol; [BMIm][BF₄], 1.5 g; P_{CO} = 3.0 MPa; T = 150 °C; t = 6 h.

^a t = 11 h.