

Selenium-catalyzed carbonylation of nitroarenes to symmetrical 1,3-diarylureas under solvent-free conditions

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Abstract

An efficient synthetic system without solvent was developed for the selenium-catalyzed carbonylation of nitroarenes with CO to afford symmetrical 1,3-diarylureas in high yields. Additionally, three herbicides were readily obtained from diarylureas and dimethyl-amine.

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1. Introduction

The development of cleaner technologies is a major emphasis in green chemistry. Among the several aspects of green chemistry, solvents are high on the list of damaging chemicals for two simple reasons: (1) they are used in huge amounts and (2) they are usually volatile liquids, so the reduction [1]/replacement [2–6] of the damaging organic solvent from the reaction medium is of utmost importance. Here, we report results of our study concerning the synthesis of symmetrical diphenylureas under solvent-free conditions from nitroarenes, carbon monoxide and water. Substituted ureas have found widespread use as agricultural chemicals, pharmaceuticals, resin precursors, dyes, and additives to petroleum compounds and polymers [7]. Furthermore, 1,3-disubstituted ureas are important intermediates in the production of carbamates. Conventional methods for preparing ureas have been essentially based on use of phosgene, which is toxic, corrosive, expensive, and difficult to handle [8]. It is thus natural that a great deal of recent research has been directed toward alternative routes to ureas without using phosgene. Carbonylation of nitroarenes has been an attractive area with high academic and industrial interests. Transition metal-catalyzed carbonylation of nitroarenes with CO and water can afford ureas as the major product and CO₂ as the co-product [9–13], avoiding the danger of mixing CO with O₂ [14–18]. However, carbonylation reactions of nitroarenes to

ureas with expensive transition metals such as Ru or Rh are usually carried out under harsh condition [9–13]. Sonoda et al. [19,20] and our group [21–26] found that non-transition metal selenium also catalyzed the carbonylation of nitroaromatics and/or amines or alcohol to produce urea derivatives. Zhang et al. [27,28] reported the synthesis of symmetrical urea from nitroarenes, water and 4.5–5.0 MPa carbon monoxide catalyzed by Se in THF, and moderate and good yields were produced.

2. Experimental

The organic solvents were all reagent grade and were used without further purification. Ionic liquids were synthesized according to the literature [29–31]. Selenium (99.5%) and carbon monoxide (99.9%), nitroaromatics and triethylamine (Et₃N) were all used as purchased. Water involved the reaction without further purification. Melting points were determined on a Taike 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.

Typical procedures for the synthesis of diphenylurea (DPU) and unsymmetrical ureas are as follows.

2.1. Synthesis of diphenylurea

Selenium, nitrobenzene, Et₃N, H₂O were successively introduced into a 100 ml stainless-steel autoclave. The reactor was

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sealed, flushed with 1.0 MPa of carbon monoxide three times, pressured with 2.0 MPa carbon monoxide, and then placed in an oil bath preheated to 80 °C. After the reaction was finished in 7 h, the apparatus was cooled to ambient temperature, and the remaining carbon monoxide was evacuated. DPU was collected and further purified by recrystallization from DMF–H₂O, and then the pure product was obtained.

2.1.1. 1,3-Bis(3-isopropylphenyl)urea (6)

White solid; mp: 169–171 °C. ¹H NMR (400 MHz, *d*₆-DMSO, 23 °C): δ = 8.60 (s, 1H, NH), δ = 7.39 (s, 1H), δ = 7.30 (d, *J* = 7.6 Hz, 1H), δ = 7.18 (t, *J* = 8.0 Hz, 1H), δ = 6.84 (d, *J* = 7.2 Hz, 1H), δ = 2.84 (m, *J* = 6.8 Hz, 1H), δ = 1.20 (d, *J* = 6.8 Hz, 6H). ¹³C NMR: δ = 152.8, 149.3, 140.0, 129, 120.0, 116.4, 116.1, 33.8, 24.1.

2.1.2. 1,3-Bis(3-chloro, 4-methyl-phenyl)urea (13)

White solid; mp: 259 °C. ¹H NMR (400 MHz, *d*₆-DMSO, 40 °C): δ = 8.64 (s, 1H, NH), δ = 7.66 (d, 1H), δ = 7.19 (m, 2H), δ = 2.24 (s, 3H), ¹³C NMR: δ = 152.1, 138.4, 133.0, 130.7, 128.23, 118.3, 116.9, 18.4.

2.2. Synthesis of unsymmetric phenylurea

Diphenyl urea, aqueous dimethyl-amine (33%) solution, toluene were charged into the 100 ml stainless-steel autoclave, sealed and put into an oil bath maintained at 150 °C with magnetic stirring for 3 h. 1,1-Dimethyl-3-phenylurea was collected and purified by column chromatography on silica gel using CHCl₃–AcOEt (20:1–5:3) as the eluent.

3. Results and discussion

We have recently reported that selenium-catalyzed the reductive carbonylation of nitroarenes produced symmetrical 1,3-diarylureas with moderate to good yields under atmospheric pressure of CO in DMF [32]. In the reaction, a reaction pathway including the formation of nitrene intermediate [32,33], which was generated by the reductive deoxygenating of the nitro group by carbon monoxide and selenium in the presence of base, was suggested. The reaction has subsequently been more thoroughly explored. It was found that selenium-catalyzed the carbonylation of nitroarenes proceeded efficiently to afford the symmetrical ureas with high yields under solvent-less condition. The results were shown in Tables 1–3.

3.1. Effect of amount of H₂O or Et₃N

As revealed in Table 1, solvent is not essential to the reaction. Though polar and hydrophilic reaction media such as BMImBF₄, DMF, are helpful to the reaction (Table 1, Entries 1

Table 1
Effect of solvent on the carbonylation of nitrobenzene (R = H)

Entry	Solvent	Yield (%)
1	BMImBF ₄ ^a	96
2	BMImPF ₆	66
3	THF	77
4	Toluene	12
5	DMF	90
6	–	92

Reaction condition: Se (0.38 mmol), nitrobenzene (8.0 mmol), CO (2.0 MPa), Et₃N (3.0 mmol), H₂O (5.0 mmol), at 80 °C for 3.5 h.

^a BMIm = 1-butyl-3-methylimidazolium.

Table 2
Effect of the amount of Et₃N or H₂O on the carbonylation of nitrobenzene (R = H)

Entry	H ₂ O (mmol)	Et ₃ N (mmol)	Yield (%)
1	7.7	0	8
2	7.7	2.5	92
3	7.7	5	91
4	7.7	10	94
5	77	10	92

Reaction conditions: nitrobenzene (10 mmol), Se (0.2 mmol), CO (2.0 MPa), at 80 °C for 7 h.

Table 3
Carbonylation of nitroarenes to 1,3-diarylureas under solvent-free conditions

Entry	R	Products MP (°C) (Reference)	Yield (%) ^a
1	H	239–240 (234–236) [34], 1	94 ^b
2	4-Me	273 (270–271) [35], 2	94
3	3-Me	220 (221) [36], 3	98
4	2-Me	266 (263–265) [37], 4	92
5	4- <i>i</i> -Pr	241 (206–208) [38], 5	74/91 ^b
6	3- <i>i</i> -Pr	169–171, 6	95
7	2- <i>i</i> -Pr	238–239 (220–222) [39], 7	81
8	4-OEt	237–238 (225–226) [40], 8	97
9	4-OMe	243–246 (242) [41], 9	85
10	2-OMe	189–190 (190–191) [34], 10	74
11	3-Cl	247 (245–246) [42], 11	95
12	3-CF ₃	198 (199) [34], 12	98
13	3-Cl, 4-Me	259, 13	52/98 ^b
14	2-Me, 3-Cl	263–265 (310) [43], 14	93
15	2-OMe ^c	232–233 (228–231) [24], 15	20

Reaction conditions: nitroaromatic (10 mmol), Se (0.2 mmol), CO (2.0 MPa), Et₃N (10 mmol), H₂O (5.0 mmol) at 80 °C for 7 h.

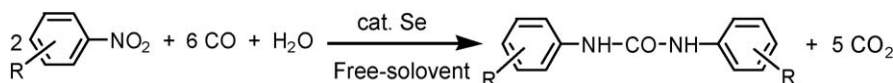
^a Isolated yield.

^b H₂O (7.7 mmol).

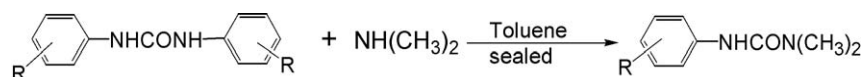
^c Nitroaromatic: 2-methoxy-5-nitropyridine.

and 5), DPU was also obtained with 92% yield without solvent (Table 1, Entry 6).

The base plays an important role in the reaction (Tables 1–3). The reaction proceeded very slowly in the absence of base (Table 2, Entry 1). DPU in the yield of 92% was achieved in



Scheme 1.



Scheme 2.

the presence of Et₃N 2.5 mmol, but continuously enhancing the amount of Et₃N only slightly affected the yields of DPU (Table 2, Entries 2, 3, and 4).

Judging from Scheme 1 and reaction conditions shown in Tables 2 and 3, 5.0 mmol water is indispensable to the reaction. Furthermore, excess amounts of water did not lead to evident change of the yield of DPU. Increasing amount of water from 7.7 to 77 mmol, the yields of DPU slightly altered from 94 to 92% (Table 2, Entries 4 and 5). However, 4-isopropyl-nitrobenzene and 4-methyl-3-chloronitrobenzene are susceptible to water. Slightly excess amounts of water (7.7 mmol) resulted in higher yields of their desired products and/or fast rate of the reaction (Table 3, Runs 5, 13). The predominant by-products from the reactions are aniline and some unidentified colloidal compounds.

3.2. Carbonylation of nitroarenes

The yields of symmetrically substituted 1,3-diarylureas slightly varied depending on the substituent alkyls on the phenyl rings. The electron-donating property of 3-positioned large alkyl on the phenyl rings made the nitro group more reactive than those of 4 and 2-substituted analogues, resulting in higher yields of products (Table 3, Entries, 5-7), which is different from the results under atmospheric pressure [32]. The steric effects of 2-positioned alkyl or alkoxy on phenyl rings may be attributed to the lower yield (Table 3, Entries 3, 4, 6, 7 and 9, 10). It is noteworthy that 2-methoxynitrobenzene afforded the desired symmetrical urea which was not obtained under the atmospheric pressure reaction system (Table 3, Entry 10) [32]. Nitroarenes with electron-withdrawing substituents such as 3-chloronitrobenzene, 4-methyl-3-chloronitrobenzene, and 2-methyl-3-chloronitrobenzene as well as 3-trifluoromethylnitrobenzene also gave the respective ureas in high yields. Heteroaromatic nitro compound such

as 2-methoxy-5-nitropyridine was found not to be equally tolerated in the employed reaction condition and afforded the desired product only in 20% yields (Table 3, Entry 15).

3.3. Substitution reaction of symmetrical ureas with dimethyl-amine

Unsymmetric phenylureas are known to be useful agrochemicals and pharmaceuticals. Here, several important unsymmetric phenylureas such as fenuron, fluometuron and isoproturon were produced from symmetrical diarylureas and dimethyl amine with high yields [44] (Scheme 2, Table 4).

4. Conclusions

In summary, we succeed in the synthesis of 1,3-diarylureas from the nitroarenes using selenium as catalyst avoiding using of any solvent. The methodology reported herein offers a useful alternative to the existing methodologies due to its efficiency, simplicity and high yields. In addition, three important herbicides were synthesized by substitution reaction of diarylureas with amine.

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Table 4
Unsymmetrical phenylureas from diphenylureas and dimethyl amine

Entry	R	Product	Yield (%)
1	H		91
2	3-CF ₃		96
3	4- <i>i</i> -Pr		92

Reaction conditions: diphenylurea (1 mmol), dimethyl amine (5 mmol), toluene (5 g), at 150 °C for 3 h.

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