



A novel $\text{ZrO}_2\text{--SO}_4^{2-}$ supported palladium catalyst for syntheses of disubstituted ureas from amines by oxidative carbonylation

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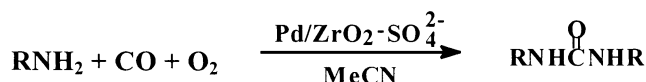
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Abstract—The syntheses of disubstituted ureas by carbonylation of a series of amines in the presence of a sulfate modified zirconia supported palladium catalyst was investigated at an initial total pressure of 4.0 MPa and 135°C. High conversions and yields were achieved for the synthesis of symmetric dialkylureas. This supported catalyst could also be easily separated and recovered after reaction. © 2001 Elsevier Science Ltd. All rights reserved.

The disubstituted ureas are very useful intermediates for the production of pharmaceuticals and agricultural chemicals.^{1–3} The traditional syntheses for symmetric dialkylureas include reactions of amines with carbamyl halides, isocyanates or phosgene.^{4,5} Highly toxic and corrosive phosgene or hydrogen chloride were inevitably involved in these processes, which caused serious problems of environmental pollution and equipment corrosion. Recently, a process for preparing 1,3-disubstituted ureas through reacting a cyclic carbonic acid ester with an amine over a proper catalyst was disclosed.⁶ This method, however, was expensive to use on a large scale. The transformation of amines through catalytic carbonylation to produce disubstituted ureas provides an alternative environmental benign method and has been investigated over many years. Homogeneous Pd,^{7–9} Ru,¹⁰ Co,¹¹ Mn,¹² Se,^{13–15} and more recently, W^{16,17} catalysts were used for the oxidative carbonylation of amines into the ureas, and the yields were usually good to excellent. One of the problems associated with the previously reported catalyst system was the isolation of catalysts from the products and their reusability, and a stoichiometric oxidizing reagent such as I_2 may be used.

In this work, the syntheses of dialkylureas by oxidative carbonylation of a series of amines catalyzed by a sulfate modified dioxide zirconium supported palladium catalyst were investigated. It was found that excellent performance for the synthesis of symmetric aliphatic dialkylureas was achieved:



$\text{Pd/ZrO}_2\text{--SO}_4^{2-}$ was prepared as follows: PdCl_2 (0.18 g) was mixed with zirconyl chloride solution (12 ml, 0.62 M), and under stirring, a 25% $\text{NH}_3\text{--H}_2\text{O}$ solution was added dropwise into the solution until the pH reached 8–9. The resulting precipitate was filtered, washed several times with distilled water, and dried at 120°C for 10 h, and then crushed and screened. The resulting powder was further impregnated with H_2SO_4 (15 ml, 1 M) for 25–30 min, and then it was calcined in air at 600°C for 2 h. The XPS analysis (VG ESC ALAB 210) showed that S^{6+} and Pd^{2+} were detected and the Pd and sulfate contents on the catalyst surface were ca. 6.3 and 4.6 wt%, respectively. For the purpose of comparison, $\text{Ru/ZrO}_2\text{--SO}_4^{2-}$ was also prepared with the same procedure as $\text{Pd/ZrO}_2\text{--SO}_4^{2-}$.

The results of catalytic carbonylation of *n*-butylamine for the synthesis of the corresponding symmetric dialkylureas showed that only low and moderate activities were observed when using $\text{ZrO}_2\text{--SO}_4^{2-}$ or PdCl_2 as the catalysts, respectively (Table 1, entries 1 and 2). Much better results, however, were obtained if the $\text{Pd/ZrO}_2\text{--SO}_4^{2-}$ catalyst was employed and almost 100% conversion and 98% selectivity were achieved (entry 3). This indicated that there might exist synergism between Pd^{2+} and $\text{ZrO}_2\text{--SO}_4^{2-}$, which could significantly enhance the catalyst performance. Since the resulting dialkylureas were not dissolved in CH_3CN , crystallized product was formed and the catalyst and the desired product could be separated by simple filtration. The pure product could be easily obtained by

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sieving the resulting solid mixture, for example, 79% of the directly isolated yield was obtained for the dibutyl-urea (Table 1, entry 3), since the catalyst particles and the crystallized product did not adhere to each other and the size of the catalyst particles was much smaller than that of the crystallized product.

Other primary aliphatic amines, including hexylamine, cyclohexylamine, and dodecylamine were also tested with $\text{Pd/ZrO}_2\text{-SO}_4^{2-}$ catalyst (entries 4–6). The results suggested that the directly isolated yield would be increased remarkably with the increasing of the C number or the chain length of the attached alkyl, e.g. almost 99% of directly isolated yield could be achieved when using dodecylamine as the substrate. This may be partially due to even further lower solubility of those amines due to the higher C number or the longer chain length of the attached alkyl. These results also suggested that better yield could be obtained with proper choice of solvent.

Only a moderate conversion and poor selectivity were obtained when aniline was used as substrate (entry 7). The main by-products were quinazoline (32%), benzene isocyanato (25%), and *N*-phenyl formamide (2%). Since the conversion and selectivity for the desired product was so low, no crystallized product could be separated out directly. Such low reactivity of aniline towards the oxidative carbonylation may be related to the weak nucleophilicity of aniline.

In order to examine the scope and the limitation of this catalyst system, iso-butyl amine and two secondary amines as substrates were also tested. As for iso-butyl amine (entry 8), the selectivity for desired di-isobutyl urea was moderately reduced in comparison with that of *n*-butylamine. Only 80% conversion and 37% selectivity were achieved when using dibutylamine as substrate (entry 9). Even poor results were obtained for the benzyl methylamine (entry 10). The main by-products were corresponding formamides for the secondary amines. The results suggested that the catalytic performance could be remarkably inhibited by the steric hindrance of the substrate molecules.

Under same reaction conditions, $\text{Ru/ZrO}_2\text{-SO}_4^{2-}$ was used as catalyst (entries 11–14) and it can be seen that $\text{Ru/ZrO}_2\text{-SO}_4^{2-}$ was relatively less effective for the carbonylation of amines to afford the corresponding ureas in comparison with $\text{Pd/ZrO}_2\text{-SO}_4^{2-}$. The fact that higher conversion and selectivity for aliphatic amines but poor conversion and selectivity for aromatic amine could also be achieved over the $\text{Ru/ZrO}_2\text{-SO}_4^{2-}$ catalyst indicated that the reaction mechanism of carbonylation over these two catalysts were similar.

Using $\text{Pd/ZrO}_2\text{-SO}_4^{2-}$ as catalyst, an attempt for the syntheses of asymmetric disubstituted ureas by oxidative carbonylation of an aliphatic amine with aniline (Table 2) was also made, in which aniline was also worked as solvent. Since aniline was excessive, the conversion of other aliphatic amine was higher than

Table 1. Results of syntheses of symmetric urea by oxidative carbonylation of amines^a

Ent.	Substrate	Catalyst	Con.(%)	Sel.(%)	TOF ^c	Yields, isolated directly (%)		Main byproduct, Sel.(%)	
1		$\text{ZrO}_2\text{-SO}_4^{2-}$	26	40	-----		----		35
2		PdCl_2	82	79	595		46		8
3		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	100	98	718		79		Trace
4		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	92	93	440		62		3
5		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	100	96	622		96		4
6	$\text{C}_{12}\text{H}_{25}\text{NH}_2$	$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	100	100	190	$\text{C}_{12}\text{H}_{25}\text{NHCNHHC}_{12}\text{H}_{25}$	99	 RCO_2H	Trace
7		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	64.8	25	493		----		32
8		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	99.5	70	718		63		28
9		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	80	37	334		12		43
10		$\text{Pd/ZrO}_2\text{-SO}_4^{2-}$	12	20	77.2		----		72
11		$\text{Ru/ZrO}_2\text{-SO}_4^{2-}$	66	95	476		34		Trace
12		$\text{Ru/ZrO}_2\text{-SO}_4^{2-}$	34	18	235		----		47
13	$\text{C}_{12}\text{H}_{25}\text{NH}_2$	$\text{Ru/ZrO}_2\text{-SO}_4^{2-}$	86	84	606	$\text{C}_{12}\text{H}_{25}\text{NHCNHHC}_{12}\text{H}_{25}$	38	RCO_2H	8
14		$\text{Ru/ZrO}_2\text{-SO}_4^{2-}$	42	73	320		----		35

^a The reactions were conducted in a stainless steel autoclave with a glass tube inside. Cat.: 35 mg; substrate: 2 ml (liquid substrate) or 1.5 g (solid substrate); solvent: CH_3CN , 15 ml; $\text{P}(\text{CO})=3.5$ MPa; $\text{P}(\text{O}_2)=0.5$ MPa; $T=135^\circ\text{C}$; $t=1$ h. After reaction, the reacted mixture was directly analyzed with a HP 6890/5793 GC-MS instrument equipped with a HP-5MS column (30 cm in length). The qualitative and quantitative data of the substrate and products were directly given by the system of GC-MS chemstation according to the area of each chromatograph peak.

Table 2. Results of synthesis of asymmetric ureas by oxidative carbonylation of amines^a

Ent.	Substrate	Catalyst	Con.(%)	TOF	Products, Sel.(%)			
					1-phenyl, 3-alkyl urea		Dialkylurea	
1		Pd/ZrO ₂ -SO ₄ ²⁻	97	696		30		62
2		Pd/ZrO ₂ -SO ₄ ²⁻	99 ⁱ	473		88		8
3		Pd/ZrO ₂ -SO ₄ ²⁻	90	560		31		69

^a Same conditions as in Table 1 but the solvent was 15 ml aniline.

90%, and two kinds of ureas were produced, i.e. symmetric and unsymmetric disubstituted ureas. This suggested that competition reactions exist between similar and different amines. Since the resulting ureas were well soluble in the aniline, no crystallized product could be separated out directly. It could be seen that the best result was obtained in the synthesis of 1-phenyl, 3-hexyl urea, with conversion and selectivity of 99 and 88%, respectively (Table 2, entry 2). As to *n*-butylamine and cyclohexylamine, the formation of symmetric disubstituted ureas was more favourable.

In summary, the syntheses of disubstituted ureas by oxidative carbonylation of a series of aliphatic amines in the presence of a sulfate modified zirconia supported palladium catalyst could be performed with excellent conversion and selectivity. This supported catalyst could also be easily separated and recovered from the reaction medium after carbonylation. The reaction conditions could still be further optimized. To the best of our knowledge this is the first reported study of a Pd(Ru)/ZrO₂-SO₄²⁻ catalyst for the oxidative carbonylation of amines to afford corresponding disubstituted ureas.

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