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Selenium-catalyzed Reductive Carbonylation of Nitrobenzene with Amines as Coreagents to Give Unsymmetric Phenylureas

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Abstract: The reductive carbonylation of nitrobenzene catalyzed by selenium to yield unsymmetric phenylureas has been studied. When secondary amines were used as coreagents, a single product, $PhNHCONR_2$, was formed; when primary amines were chosen as coreagents, mixed products, including RNHCONHR, RNHCONHPh and PhNHCONHPh, were obtained.

Keywords: Selenium; Carbonylation; Nitrobenzene; Amines; Unsymmetrical phenylureas.

Unsymmetric phenylureas are known to be useful agrochemicals and pharmaceuticals. Methods for their industrial synthesis include the reaction of amines with carbamyl halides and the addition of amines to isocyanates. Both reactions use the highly toxic compound-phosgene. A very promising nonphosgenation process for the synthesis of unsymmetric phenylureas is the reductive carbonylation of nitro compounds catalyzed by noble metals, including palladium, ruthenium and rhodium. In addition, non-transition elements such as selenium[1,2] and sulfur[3] have also been found to catalyze the reaction. In this paper the reductive carbonylation of nitrobenzene catalyzed by selenium with amines as coreagents, in which unsymmetric phenylureas are formed, is described. For different starting materials, i.e., primary or secondary amines, different product distributions were discovered.

Nitrobenzene and the amine react with carbon monoxide in the presence of selenium according to the following equation:

$$R_2NH + PhNO_2 + 3CO \xrightarrow{Se} R_2NCONHPh + 2CO_2$$

Several secondary amines were investigated and the results are summarized in Table 1. As Table 1 shows, the reductive carbonylation of $PhNO_2$ with secondary amines as coreagent gave

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unsymmetric phenylureas. Both cyclic amines, including piperidine, pyrrolidine and morpholine, and non-cyclic amines, including Me_2NH, Et_2NH, *n*-Pr_2NH and *n*-Bu_2NH react well and the yields are from moderate to good. However, the reaction of *i*-Pr_2NH gave none of the expected product, while that of *i*-Bu_2NH gave poor yield, perhaps due to steric hindrance.

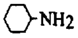
Table 1. Carbonylation of $PhNO_2$ with secondary amines as coreagents

Substrate	Product	m.p. (℃)		Yield (%)	Recry. solvent
		Found	Lit.		
		162~163	161.5~162[4]	70	CH_3CH_2OH
		168~170	171~172[4]	80	CH_3CH_2OH
		130~132	133~134[4]	65	CH_3CH_2OH
Me_2NH	$Me_2NCONHPh$	129~131	127.5~128[5]	50	$CHCl_3$
Et_2NH	$Et_2NCONHPh$	85~87	84~85[5]	76	$CHCl_3$
n-Pr_2NH	*n*-$Pr_2NCONHPh$	68~70	/	72	$CHCl_3$
i-Pr_2NH	*i*-$Pr_2NCONHPh$	/	/	0	/
n-Bu_2NH	*n*-$Bu_2NCONHPh$	83~84	/	75	$CHCl_3$
i-Bu_2NH	*i*-$Bu_2NCONHPh$	105~107	/	20	$CHCl_3$

Conditions: Substrate, 10mmol; $PhNO_2$, 10mmol; Se, 0.5mmol; Et_3N, 10mmol; CO, 3.0MPa; PhMe, 10g; 150~160℃, 1.5h.

When primary amines were used as coreagents, in contrast with the good selectivity of secondary amines, a mixture of RNHCONHR, RNHCONHPh and PhNHCONHPh was obtained from the reaction (Table 2). The results show that both aliphatic and aryl amines give mixed products of three components, although the total yields are good.

Table 2. Carbonylation of $PhNO_2$ with primary amines as coreagents

Substrate	Yield of Product (%)		
RNH_2	RNHCONHR	RNHCONHPh	PhNHCONHPh
i-$PrNH_2$	34.2	32.1	24.7
	18.0	57.7	3.3
$PhCH_2NH_2$	35.7	14.4	27.2
p-$ClC_6H_4NH_2$	25.1	39.5	28.4
m-$ClC_6H_4NH_2$	23.0	38.4	26.7

Reaction conditions are the same as Table 1.

The reaction uses nitrobenzene reduction and amine selenocarbonylation in one pot, which can generate unsymmetric ureas $PhNHCONR_2$ efficiently.

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