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SHORT COMMUNICATIONS

A MECHANISTIC STUDY OF THE SELENIUM-CATALYSED CARBONYLATION OF SECONDARY AMINES WITH CARBON MONOXIDE

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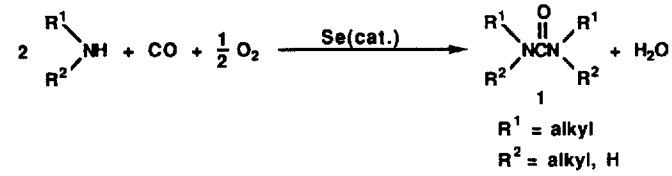
ABSTRACT

The reaction pathway of urea formation by selenium-catalysed carbonylation of secondary amines with carbon monoxide in the presence of oxygen was studied using piperidine as a secondary amine. It was established that selenium reacts with carbon monoxide and piperidine to give carbamoselenoate as an intermediate, which affords biscarbamoyl diselenide by the oxidation with molecular oxygen. Aminolysis of biscarbamoyl diselenide gives the urea derivative, accompanying the regeneration of selenium catalyst.

We have found that selenium has excellent catalytic activity for the carbonylation of amines with carbon monoxide in the presence of oxygen.[1] This reaction proceeds under mild conditions, where primary amines and relatively less hindered secondary amines are carbonylated to give corresponding urea derivatives (**1**) quantitatively [equation (1)].



(1)

Since this finding, efforts have been directed toward expanding the scope and synthetic utility of this reaction.[2] As for the reaction pathway, the intermediacy of ammonium carbamoselenoates (**2**) was strongly supported by the successful isolation of *Se*-alkyl carbamoselenoates by treatment of the reaction mixture of selenium, secondary amine and carbon monoxide with alkyl halides.[3] Further mechanistic details proposed so far have been deduced from indirect chemical evidence. In this paper we report the results of controlled experiments using piperidine, in order to shed light on the reaction pathway of the selenium-catalysed carbonylation of secondary amines.

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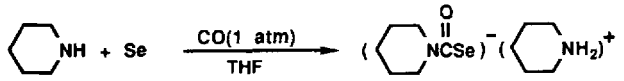
The treatment of selenium with 2 equivalents of piperidine in THF at 25 °C under a carbon monoxide atmosphere resulted in a colourless homogeneous solution. NMR spectra of the solution showed a peak of carbonyl carbon at 178.4 ppm from TMS and a ^{77}Se peak at 172 ppm from dimethyl selenide (0 ppm), which can be assigned to carbamoselenoate (**2**) [equation (2)]. This ^{77}Se NMR chemical shift is reasonable for **2**, since those of several alkyl- and arylselenoate anions were reported to appear in the range of about −500 to 200 ppm.[4] No formation of the corresponding urea derivative (**1**) was observed at this stage.

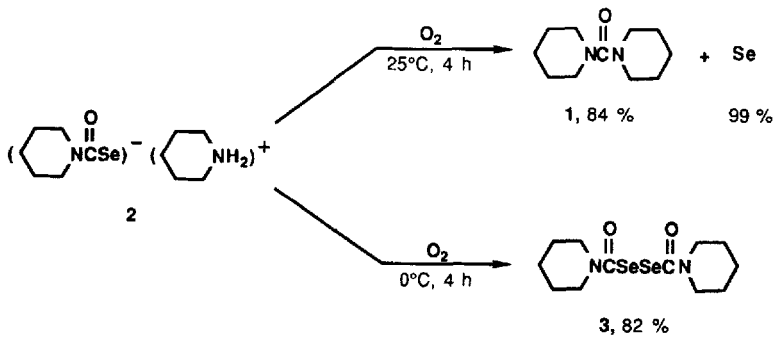


(2)

2

^{13}C NMR 178.4 ppm (C=O)
^{77}Se NMR 172 ppm

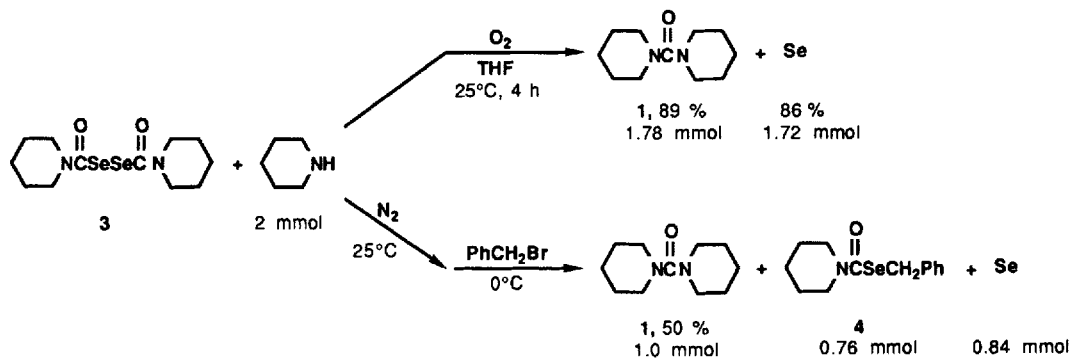
In order to elucidate the reaction pathway from the intermediate **2** to the product **1**, the following controlled experiments were performed. When a homogeneous solution of **2** was stirred in the presence of molecular oxygen at 25 °C for 4 h, a urea (**1**) was isolated in 84% yield (recrystallization from ethanol) based on the amine used, and selenium (99%) was recovered. In marked contrast, the similar reaction conducted at 0 °C gave bis(*N*, *N*-pentamethylenecarbamoyl) diselenide (**3**) in 82% yield (recrystallization from diethyl ether), together with a trace amount of the corresponding urea (**1**) [equation (3)]. This result coincides with the fact that selenols are easily oxidized with molecular oxygen to corresponding diselenides.[5]



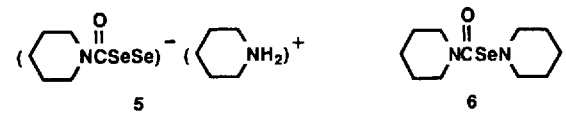
(3)

In order to confirm diselenide **3** as the precursor of urea **1**, aminolysis of **3** was undertaken. Diselenide **3** was allowed to react with 2 equivalents of piperidine at 25 °C in the presence of oxygen to produce urea **1** in 89% yield, with recovery of selenium (86%). However, a similar reaction of **3** (1 mmol) with piperidine (2 mmol) under nitrogen, without oxygen, gave carbamoselenoate **2**, which was confirmed as *Se*-benzyl carbamoselenoate (**4**, 0·76 mmol) by treatment of the reaction mixture with benzyl bromide, as well as urea **1** in 50% yield and elemental selenium (0·84 mmol) [equation (4)].

From these results, we can postulate the following reactions as plausible pathways for this step: (a) nucleophilic attack of piperidine at the carbamoyl carbon of **3** gives equimolar amounts of **1** and an intermediate (**5**), which then undergoes deselenation to regenerate elemental selenium and **2**; (b) nucleophilic attack of piperidine occurs at selenium atom of **3** to give equimolar amounts of **2** and an intermediate (**6**), which then undergoes inter- or intramolecular aminolysis to give urea **1** and selenium. Our trials to confirm the intermediacy

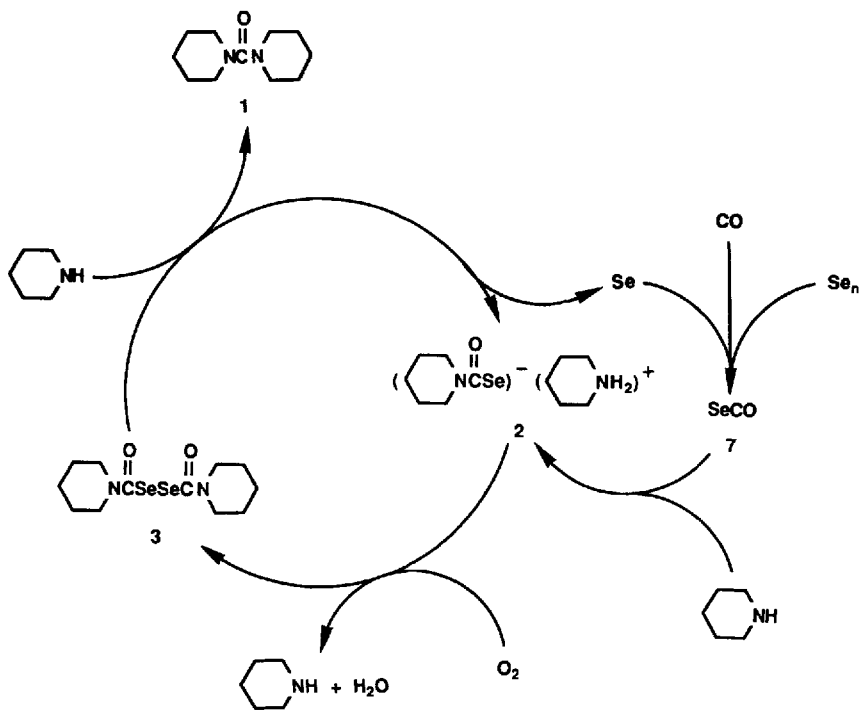


of **5** or **6** failed, presumably owing to instability of such an intermediate. In the presence of oxygen, the thus formed carbamoselenoate **2** may be oxidized to regenerate biscarbamoyl diselenide **3**.



5 **6**

The selenium catalysis for the carbonylation from these results may be presented as shown in Scheme 1. Selenium reacts with carbon monoxide and amine to give carbamoselenoate **2** as an intermediate, probably via nucleophilic attack of amine to carbonyl selenide (**7**) formed from selenium and carbon monoxide. Subsequent oxidation of **2** with molecular oxygen affords diselenide **3** accompanied by the liberation of free amine. Finally, the urea derivative **1** is



Scheme 1

formed by the aminolysis of **3** and at this stage **2** and selenium are re-produced. This catalytic cycle is pertinent to the carbonylation of secondary amines, and further investigation is now underway on the mechanism of the carbonylation of primary amines, where alternative pathways may be possible.

ACKNOWLEDGEMENT

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