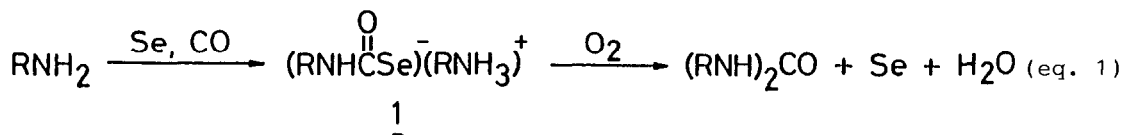


A NEW SYNTHESIS OF CYCLIC UREAS FROM AROMATIC DIAMINES BY SELENIUM-  
 ASSISTED CARBONYLATION WITH CARBON MONOXIDE

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**Summary:** Aromatic cyclic ureas have been synthesized in good yields from o-amino or o-aminoalkyl substituted aromatic amines by the reaction with carbon monoxide using selenium.

During the course of our study on selenium-assisted carbonylation, we have developed a convenient method for the synthesis of symmetrical ureas from the corresponding amines, carbon monoxide, and oxygen in the presence of catalytic amounts of selenium under mild conditions.<sup>1,2)</sup> This catalytic reaction has been postulated to proceed via selenocarbamate ammonium salt 1 as an intermediate which undergoes aminolysis by the nucleophilic attack of a second amine molecule at the carbonyl carbon to form a urea derivative in the presence of oxygen<sup>3)</sup> (eq. 1).

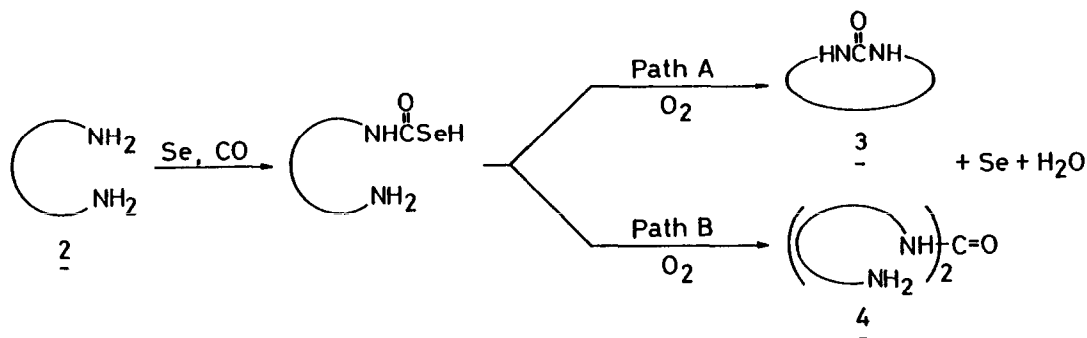


When bifunctional compounds 2 were applied to this catalytic reaction system, intra- and intermolecular reactions took place often competitively to give a mixture of cyclic urea 3 and acyclic one 4, respectively<sup>4)</sup> (Scheme 1). For instance, β-(o-aminophenyl)ethylamine 5 was treated with carbon monoxide and a catalytic amount of selenium in the presence of oxygen at 100°C to afford cyclic urea 7 together with acyclic urea 8 in 61% and 29% yields, respectively<sup>5)</sup> (eq. 2).

We report here the results obtained in the study aimed at the selective formation of cyclic urea derivatives. We have found that the perfect selectivity could be attained by the use of stoichiometric amount of selenium.

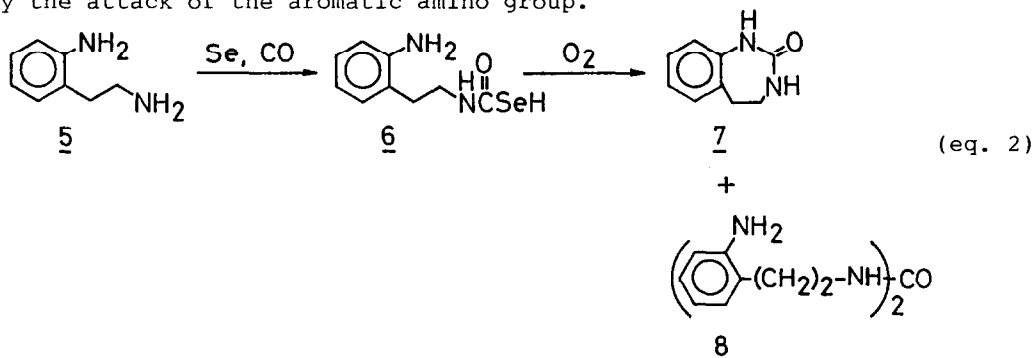
Aniline and naphthylamine derivatives bearing an o-amino or an o-aminoalkyl substituent underwent carbonylation under CO atmosphere using stoichiometric amount of selenium and gave the corresponding cyclic urea derivatives

exclusively. The results are given in Table 1. Acyclic ureas were not detected in any cases examined.



Scheme 1

These results may be interpreted as follows. The aliphatic amino group is more nucleophilic than the aromatic amino group and may react faster with selenium and carbon monoxide to form selenocarbamate 6, so that in the stoichiometric reaction all of the aliphatic amino group might be converted rapidly to selenocarbamate moiety which then undergoes intramolecular cyclization by the attack of the aromatic amino group.



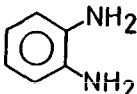
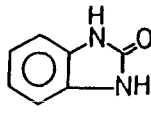
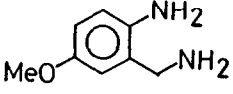
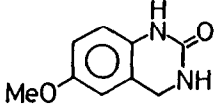
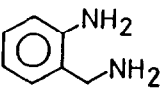
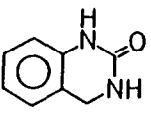
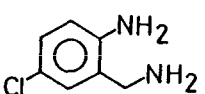
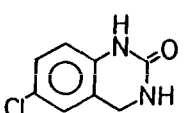
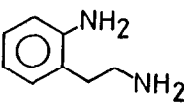
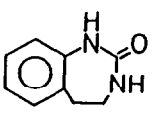
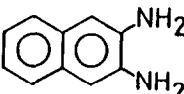
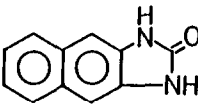
On the other hand, in the catalytic reaction, there remains most of the starting material possessing the aliphatic amino group which can attack the carbamoyl carbon of the selenocarbamate 6 intermolecularly to form the acyclic urea. Thus, both reactions via path A and path B take place competitively (Scheme 1).

Typical experimental procedure is as follows. In a stainless-steel autoclave, were placed  $\beta$ -(o-aminophenyl)ethylamine (340 mg, 2.5 mmol), selenium (591 mg, 7.5 mmol), N-methylpyrrolidine<sup>7)</sup> (0.79 mL, 7.5 mmol), and THF (10 mL). The reaction mixture was heated at 100°C for 20 h under the pressure of CO (30 Kg/cm<sup>2</sup>) with stirring. After evacuation of carbon monoxide, the resulting mixture was stirred under the atmosphere of air for 1 h in order to oxidize the resulting hydrogen selenide. Then, the deposited

selenium was filtered off, and the solvent was evaporated *in vacuo*. The residual solid was recrystallized from THF/n-hexane to give 298 mg (74%) of 1,3,4,5-tetrahydro-2H-benzo-diazepin-2-one **7**.

Cyclic ureas and these derivatives have been widely used as the starting materials for pigments, resins,<sup>8,9)</sup> and some of these have bio-activities.<sup>10-12)</sup> Several synthetic approaches to these compounds have already been reported which can be classified to the following two types of reactions: a) amination of *in situ* formed isocyanates *via* Hoffmann, Curtius, or Lossen<sup>13)</sup> rearrangements; b) carbonylation of amines using carbonylating

Table 1. Selective Formation of Cyclic Urea Derivatives.<sup>a</sup>

entry	substrate	product	yield(%)	mp(°C)
1			99	299-300 <sup>b</sup>
2			96	230-231
3			86	243-244 <sup>c</sup>
4			85	285-286
5			74	170.5-171 <sup>d</sup>
6			97	>300

(a) All compounds show spectral (IR, <sup>1</sup>H-NMR, MS) data in complete accord with the assigned structures. (b) Literature (ref. 14) mp 300°C. (c) Literature (ref. 6) mp 229-231°C. (d) Literature (ref. 13) mp 169-171°C.

reagents such as phosgene, carbonyldiimidazole, and disuccinimido-carbonate.<sup>14-16)</sup> Yields of products in the former cases are not consistently high and phosgene is highly toxic in the latter.

The present method is simple and convenient, and provides the high yields of the products.

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