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A NEW SYNTHESIS OF HETEROCYCLES BY THE REACTION OF AMINO ALCOHOLS OR AMINO THIOLS WITH CARBON MONOXIDE IN THE PRESENCE OF SELENIUM

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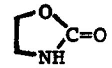
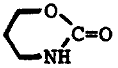
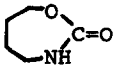
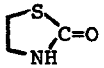
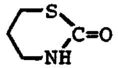
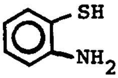
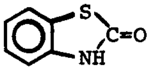
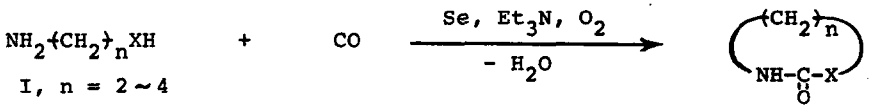
As a part of our continuing studies on the organic selenium chemistry, we reported that ureas can be synthesized by the reaction of carbon monoxide with ammonia or amines in the presence of selenium catalyst and oxygen.[1,2] The formation of ureas in such cases was interpreted as involving the reaction of carbonyl selenide (formed *in situ*) with amine to give selenocarbamate followed by nucleophilic attack by the amine molecule to the carbonyl carbon of the selenocarbamate. The similar method was also successful for the synthesis of carbamate by adding alcohol as the nucleophile.[3] Very recently Koch and Perrotti have reported the formation of some heterocycles from α,β-bifunctional compounds by our method.[4] This has prompted us to disclose our results[5] on the synthesis of heterocyclic compounds by the reaction of a variety of amino alcohol or amino thiol with carbon monoxide in the presence of selenium. Most outstanding feature of the present synthesis is that the procedure is quite simple, and the reaction involved proceeds under mild conditions with high selectivity and has wide applicability to the synthesis of various heterocycles containing carbamoyl moiety.

When amino alcohols I (n = 2 ~ 4) were reacted with carbon monoxide in the presence of equimolar amount of selenium at room temperature under atmospheric pressure (method A), corresponding cyclic urethanes were obtained (eq. 1) in good yields (Table I).

Table I. Stoichiometric Synthesis* of Various Heterocycles.

Reactant	(mmol)	Cyclic Product	(Yield %)	Urea Derivative	(Yield %)
$NH_2(CH_2)_2OH$	(20)		(94 %)	-----	
$NH_2(CH_2)_3OH$	(20)		(85 %)	$(HO(CH_2)_3NH)_2CO$	trace
	(40)		(29 %)		(63 %)
$NH_2(CH_2)_4OH$	(20)		(68 %)	$(HO(CH_2)_4NH)_2CO$	(17 %)
	(40)		trace		(98 %)
$NH_2(CH_2)_2SH$	(20)		(77 %)		
$NH_2(CH_2)_3SH$	(20)		(76 %)		
	(20)		(64 %)		

* Se (20 mmol) was used.



$$NH_2(CH_2)_nXH + CO \xrightarrow[- H_2O]{Se,\ Et_3N,\ O_2} \text{II} \quad \text{(eq. 1)}$$

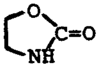
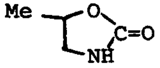
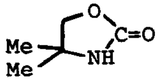
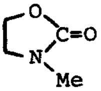
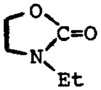
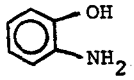
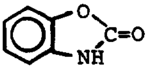
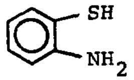
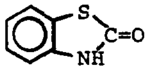
I, n = 2~4
X = O, S

II

For instance, 20 mmol of 3-aminopropan-1-ol and 100 mmol of triethylamine were dissolved in 70 ml of DMF to which was added 20 mmol. of metallic selenium, and carbon monoxide was blown through the solution at a rate of 60 ml/min for 2 hr with stirring. To the homogeneous solution thus obtained was bubbled oxygen to precipitate the selenium. Removal of recovered selenium and the solvent gave tetrahydro-2H-1,3-oxazine-2-one in an 85 % yield. Method A is also usable for the synthesis of heterocycles from various bifunctional amines including amino thiols or aromatic amine as shown in the Table I.

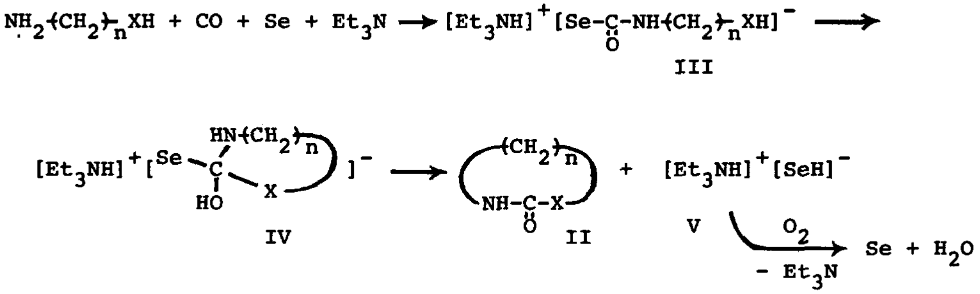
Then, five membered heterocyclic compounds such as oxazolidones and tetrahydro-1,3-thiazole-2-one were synthesized from corresponding substituted amines by the procedure using *catalytic amount* of selenium (method B). In a typical example of method B, 100 mmol of 2-aminoethan-1-ol and 100 mmol of triethylamine

Table II. Catalytic Synthesis of 2-Oxazolidones and 2-Thiazolidone.

Reactant	Cyclic Product (Yield %)	
$NH_2-CH_2CH_2-OH$		(95 %)
$NH_2-CH_2CH(Me)OH$		(99 %)
$NH_2-C(Me)_2CH_2-OH$		(90 %)
$Me-NH-CH_2CH_2-OH$		(90 %)
$Et-NH-CH_2CH_2-OH$		(90 %)
		(84 %)
		(64 %)

were dissolved in 70 ml of DMF to which was added 5 mmol of selenium, and carbon monoxide was blown into the solution for about ten minutes at room temperature until the selenium catalyst dissolved completely. Thereafter oxygen (15 % volume of carbon monoxide) was passed through the solution together with carbon monoxide stream for 6 hr. Finally the flow of carbon monoxide was stopped and only oxygen flow was continued to precipitate the selenium. Removal of solvent and selenium catalyst gave 2-oxazolidone in 95 % yield. This catalytic method was also applicable successfully for the synthesis of 2-benzoxazolone and 2-benzothiazolone from corresponding o-substituted aromatic amines, and furthermore for the synthesis of 5-membered cyclic carbamate from secondary ethanolamines such as 2-hydroxyethyl methylamine (Table II). The success of the synthesis of heterocycles from bifunctional secondary amines is in marked contrast to the earlier results obtained from the carbonylation of aliphatic secondary amines in which corresponding carbamoyl diselenides have been obtained selectively.[6)] Application of method B to the amines (n = 3, 4) produced corresponding ureas as the main products whereas the formation of heterocyclic compounds was markedly suppressed.

The reaction process may be described by the following scheme, which involves intramolecular nucleophilic addition of -OH or -SH group to the carbonyl group of the selenocarbamate salt (III) to form an intermediate (IV) which dissociate to yield heterocycles (II) and salt of hydrogen selenide (V). Reaction of hydrogen selenide with oxygen gave selenium. In the process of method B, the selenium regenerated may be circulated in the reaction system.



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