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<td>Ogawa, Akiya</td>
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Osaka University
STUDIES ON CARBON MONOXIDE-SELENIUM REACTION SYSTEM

AKIYA OGAWA

1985
STUDIES ON CARBON MONOXIDE-SELENIUM REACTION SYSTEM

(AKIYA OGAWA)

OSAKA UNIVERSITY

1985
Preface

This thesis deals with the studies completed by the author under the guidance of Professor Noboru Sonoda at Department of Applied Chemistry, Faculty of Engineering, Osaka University.

The author wishes to express his sincerest gratitude to Professor Noboru Sonoda for his constant guidance, helpful suggestions and hearty encouragement throughout this work. The author also wishes to make a grateful acknowledgement to Associate Professor Shinji Murai for his continuous advices and stimulating discussions. The author acknowledges the continuing encouragement of Dr. Noritaka Miyoshi, Dr. Kiyoshi Kondo, Dr. Ilhyong Ryu, and Dr. Nobuaki Kambe.

Furthermore he wishes to thank Mr. Jun-ichi Miyake, Mr. Yutaka Nishiyama, and Mr. Yuji Karasaki, for their collaborations. His gratitude is expended to Dr. Naoto Chatani, Mr. Toshiaki Murai, and all the members of the research group of Professor Noboru Sonoda for their occasional discussions and hearty cooperation with him.

Finally the author would like to express his thanks to his parents for their perpetual support.

Suita, Osaka
January 1985

Akiya Ogawa
List of Publications

The contents of this thesis are composed of the following papers.

(1) Selenium-assisted Carbonylation of o-Hydroxyacetophenone with Carbon Monoxide
   A. Ogawa, K. Kondo, S. Murai, and N. Sonoda

(2) Selenium Assisted Carbonylation of Alkyl Aryl Ketones with Carbon Monoxide
   A. Ogawa, N. Kambe, S. Murai, and N. Sonoda
   Tetrahedron, in press.

(3) Synthesis Utilizing Reducing Ability of Carbon Monoxide. A New Method for Synthesis of Selenocarboxamides: Reaction of Nitriles with Selenium, Carbon Monoxide, and Water
   A. Ogawa, J. Miyake, Y. Karasaki, S. Murai, and N. Sonoda

(4) Synthesis Utilizing Reducing Ability of Carbon Monoxide. New Methods for Synthesis of N-Substituted Selenocarboxamides
   A. Ogawa, J. Miyake, N. Kambe, S. Murai, and N. Sonoda
(5) Selenocarboxamides as New Reagents for Stereospecific Deoxygenation of Epoxides under Mild Conditions
A. Ogawa, J. Miyake, S. Murai, and N. Sonoda
Tetrahedron Lett. in press.

(6) Synthesis Utilizing Reducing Ability of Carbon Monoxide. In Situ Formation and Michael Addition of Benzeneselenol
A. Ogawa, Y. Nishiyama, N. Kambe, S. Murai, and N. Sonoda
to be submitted for publication.

Supplementary Papers

(1) A β-Metal Ketone Strategy. Reactions of Siloxycyclopropanes with Silver (I) Tetrafluoroborate and Copper (II) Tetrafluoroborate Leading to 1,6-Diketones
I. Ryu, M. Ando, A. Ogawa, S. Murai, and N. Sonoda

(2) Ring Cleavage Reaction of a Siloxycyclopropane with Copper Halides Affording α-Methyleneketone
I. Ryu, A. Ogawa, and N. Sonoda
Nippon Kagaku Kaishi. in press.
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General Introduction

Development of new synthetic reactions using carbon monoxide has been one of the main subjects in organic synthesis and in industry.\(^1\) Furthermore, recent numerous works\(^2\) on transition metal complexes or catalysts have come to suggest a variety of novel possibilities concerning utilization of carbon monoxide.

Recently it has been found in our laboratory that selenium, a non-transition element, assists carbonylation of amines with carbon monoxide,\(^3\) and special interest has been focused on the reaction system using carbon monoxide and selenium.

The main object of the present research is to develop new synthetic reactions using carbon monoxide-selenium reaction system.

This thesis consists of three chapters. Chapter 1 deals with the use of carbon monoxide as a carbonylating reagent, while Chapters 2 and 3 are concerned with that as a reducing reagent.

In Chapter 1 is dealt with the selenium assisted carbonylation of alkyl aryl ketones with carbon monoxide. Novel non-transition metal catalyzed C-carbonylation with carbon monoxide will be described. A plausible reaction path is also described.

Chapter 2 refers to the new selenium catalyzed reduction of diphenyl diselenide with carbon monoxide and water. This chapter also involves Michael addition of in situ formation of benzene-selenol with various unsaturated compounds.

In chapter 3, a new method for synthesis of selenocarboxamides
by the reaction of nitriles with carbon monoxide, selenium, and water will be described. As applications of selenoamides obtained to organic synthesis, the stereospecific deoxygenation of epoxides with selenocarboxamides and the method for synthesis of a new selenium-nitrogen heterocycle by the reaction of selenoamides with aliphatic aldehydes are also revealed.

References


Chapter 1  Selenium Assisted Carbonylation of Alkyl Aryl Ketones with Carbon Monoxide

1-1 Introduction

A large number of works concerning transition metal catalyzed carbonylation of various organic compounds with carbon monoxide have been reported, and have shown that carbon monoxide is particularly useful as a source of carbon in organic synthesis.

Whereas, there have been few reports of carbonylations with carbon monoxide in which non-transition metals act as catalysts. Known examples of non-transition metal catalysis are concentrated in the following three types of reactions: (1) alkaline base-catalyzed O-carbonylation of alcohols to formates and N-carbonylation of amines to formamides; (2) acid-catalyzed C-carbonylation of olefins or alcohols to carboxylic acids (Koch reaction); (3) free radical initiated copolymerization of olefins and carbon monoxide to polyketones.

Recently it has been found in our laboratory that selenium, a non-transition element, effectively catalyzed the carbonylation of various amines (or alcohols) with carbon monoxide and oxygen to give urea (or carbonate) derivatives in excellent yields, respectively (eq 1-1).

$$2RNH_2 + CO + \frac{1}{2}O_2 \xrightarrow{Se} (RNH)_2CO + H_2O \quad (1-1)$$
Successful isolation of the amine salts 1 of selenocarbamic acid from the reaction system and formation of the salts 1 by the reaction of amines with carbonyl selenide isolated suggested that the reaction process involved formation of 1 by a nucleophilic attack of amines at the carbon of carbonyl selenide (2), generated in situ from carbon monoxide and selenium under basic conditions (Scheme 1-1). Amine salts 1 were converted to the corresponding ureas following nucleophilic attack of another amine molecule.

From the studies of selenium catalyzed carbonylation described above, the use of a C-nucleophile instead of N- or O-nucleophile would be of special interest since a novel C-carbonylation with carbon monoxide assisted by selenium might be expected. A variety of C-nucleophiles were examined, and several ketone enolates were found to be carbonylated by carbon monoxide and selenium.

This chapter describes the first example of a selenium assisted
carbonylation with carbon monoxide leading to the formation of a C-
carbonylated products.

1-2 Carbonylation of Acetophenone with Carbon Monoxide in the
Presence of Selenium

The reaction of acetophenone with carbon monoxide and selenium
in tetrahydrofuran (THF) at 100°C for 72 h using 1,5-diazabicyclo-
[5.4.0]undec-5-ene (DBU) as a base, followed by quenching with n-
butylamine gave the amide 3 in 28 % yield (eq 1-2).

\[
\text{Ph} + \text{CO} + \text{Se} \underset{\text{DBU}}{\xrightarrow{\text{THF}}} \text{Ph} + \text{CO} \underset{n-\text{BuNH}_2}{\xrightarrow{\text{H} \cdot \text{DBU}^+}} \text{NHBu}^n
\] (1-2)

The product 3 may be derived from aminolysis of the intermediate
seleno-acid 4 generated by the reaction of the enolate anion of
acetophenone with carbonyl selenide 2 (eq 1-3).

\[
\text{Ph} + [\text{SeCO}] \underset{\text{DBU}}{\xrightarrow{[\text{H} \cdot \text{DBU}^+]}} \text{Ph} + \text{OH} \underset{n-\text{BuNH}_2}{\xrightarrow{[\text{H} \cdot \text{DBU}^+]}} \text{NHBu}^n
\] (1-3)
The low yield may be due to the decomposition of seleno-acid 4 into acetophenone and 2 through the equilibrium of eq 1-3 before the quenching of 4 with n-butylamine.

Then we examined intramolecular capture of the carbonylated intermediate 4.

1-3 Carbonylation of o-Hydroxyacetophenones with Carbon Monoxide in the Presence of Stoichiometric Amount of Selenium

The carbonylation of o-hydroxyacetophenone (5a) to 4-hydroxy-coumarin (6a) with carbon monoxide and equimolar amount of selenium (eq 1-4) was examined varying bases and temperatures: The results are summarized in Table 1.

\[
\text{O} \begin{array}{c} \text{CH}_3 \\ \text{OH} \end{array} + \text{CO} + \text{Se} \xrightarrow{\text{base}} \begin{array}{c} \text{OH} \\ \text{O} \end{array} + \text{H}_2\text{Se} \quad (1-4)
\]

The nature of the base has a marked effect on this reaction: strongly basic conjugated diaza compounds such as DBU and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) were most effective for the carbonylation of 5a (entries 6, 8, and 9 of Table 1), but the carbonylation did not take place in reactions using tertiary amines such as triethylamine, N-methylpyrrolidine, or 1,4-diazabicyclo[2.2.2]octane (DABCO) (entries
It has been reported that DBU is the base of choice in the carboxylation of active methylene compounds with carbon dioxide, where CO$_2$-DBU complex (7) formed from carbon dioxide and DBU has been considered to be an active species for carboxylation.  

Furthermore it was found that carbonyl sulfide (S=O=C) when blown into the N$_2$N-dimethylformamide (DMF) solution of DBU at room temperature afforded white solids, which were thermally unstable and regenerated carbonyl sulfide on warming to 45°C. These solids were assumed to

---

**Table 1.**

<table>
<thead>
<tr>
<th>entry</th>
<th>base (mmol)</th>
<th>temp ($^\circ$C)</th>
<th>yield (%)</th>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
<td>N=CH$_3$</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>DABCO</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>DBU</td>
<td>100</td>
<td>26</td>
</tr>
<tr>
<td>5</td>
<td>DBU</td>
<td>40</td>
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<td>DBU</td>
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</tr>
<tr>
<td>9</td>
<td>DBN</td>
<td>100</td>
<td>40</td>
</tr>
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Reaction conditions: 5a(20 mmol), THF(10 mL), CO(30 kg/cm$^2$), 30 h.
be a SCO-DBU complex.

In spite of my efforts confirming a SeCO-DBU complex, both isolation from the present reaction system and spectroscopical detection of the complex were unsuccessful, probably because the complex would be much more susceptible to air and thermal instability, compared with 7. It is not understood why DBU is effective in the present carbonylation while other tertiary amines are not. However it is assumed from analogy with the carboxylation with carbon dioxide in the presence of DBU that DBU would react with carbonyl selenide 2, a key intermediate in the present carbonylation, to form a DBU-SeCO complex, which might act as an active SeCO-transfer species. 10

The molar ratio of DBU/5a is also important, and the reaction proceeded smoothly when four molar equivalents of DBU to substrate 5a was employed (entry 8 of Table 1). 11 The best reaction temperature for the carbonylation was 100°C (entries 4, 5, 6, and 7 of Table 1). The present carbonylation also proceeded in benzene, dioxane, or DMF as the solvent, although the yields were slightly lower. The best reaction conditions leading to the quantitative formation of 4-hydroxycoumarin (6a) were as follows: a stirred mixture of 5a (20 mmol), selenium (20 mmol), carbon monoxide (30 kg/cm²; initial pressure at 25°C), DBU (80 mmol), and THF (10 mL) in a stainless steel autoclave were heated at 25°C for 30 h to give 6a (100 %) with concomitant formation of hydrogen selenide (8). 12

Similar reaction occurred under the same reaction conditions with 5-methyl-2-hydroxyacetophenone (5b) and 4-methoxy-2-hydroxyacetо-
phenone (5c) to give 6-methyl-4-hydroxycoumarin (6b) and 7-methoxy-4-hydroxyacetophenone (6c), respectively, in about 40% yields (entries 2 and 4 in Table 2). In order to increase the yields of 6b and 6c, greater excesses of base were required (entries 3 and 5 in Table 2). When this reaction was applied to o-hydroxypropiophenone (5d), whose enolate (9d) possessed a secondary carbanion at the reaction site, the expected 3-methyl-4-hydroxycoumarin (6d) was not formed in the reaction at 100°C for 30 h in spite of appreciable uptake of carbon monoxide (entry 6 in Table 2). However a 42% yield of 6d was obtained with slightly elevated temperature (at 130°C) (entry 7 in Table 2).

Table 2.

<table>
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<tr>
<th>entry</th>
<th>Substrate</th>
<th>DBU (mmol)</th>
<th>THF (mL)</th>
<th>temp. (°C)</th>
<th>product</th>
<th>yield (%)</th>
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<td>5</td>
<td>130</td>
<td><img src="image" alt="Structure" /></td>
<td>42</td>
</tr>
</tbody>
</table>

*Reactions were run on 5 mmol of substrate in tetrahydrofuran with 1.0 equiv. of selenium and carbon monoxide (30 Kg/cm² at 25°C) in the presence of DBU for 30 h. bIsolated yields.*
1-4 Catalytic Carbonylation of o-Hydroxyacetophenone with Carbon Monoxide.

In the study of carbonylation of o-hydroxyacetophenones (5) using stoichiometric amount of selenium, it was revealed that hydrogen selenide (8) was formed in equimolar amount with the carbonylated products. If the hydrogen selenide formed in situ could be oxidized to selenium by an appropriate oxidizing agent, it would be expected that the carbonylation could proceed with a catalytic amount of selenium (Scheme 1-2).

Scheme 1-2.

Various types of oxidizing agents including p-quinone, manganese dioxide, and molecular oxygen were examined for this purpose in vain. Finally, however, the carbonylation of 5 with carbon monoxide was found to proceed catalytically in the presence of nitrobenzene as the oxidizing agent. For instance the reaction of 10 mmol of 5a with 0.2 equivalent of selenium and carbon monoxide (30 kg/cm² at 25°C) in the presence of DBU (40 mmol) and nitrobenzene (5 mmol) in THF (5 ml) at 90°C for 2 days afforded 6.8 mmol of carbonylated product 6a in which the turnover number of selenium catalyst was about 3.5.
Nitrobenzene was reduced concomitantly to aniline during the reaction. The proposed catalytic cycle is given in Scheme 1-3.

\[ \text{Scheme 1-3.} \]

\[
\text{Nitrobenzene} \xrightarrow{\text{base}} \text{aniline} \quad \text{[SeCO]} \quad \text{Se}^2- \quad \text{PhNO}_2 \quad \text{PhNH}_2 + \text{H}_2\text{O}
\]

1-5 A Plausible Reaction Path

The exact course of the carbonylation of 5 with carbon monoxide and selenium has not been elucidated yet. The two plausible reaction paths as illustrated in Scheme 1-4.

\[ \text{Scheme 1-4.} \]

The first possibility is that the reaction involves selenoic acid 10a, formed by nucleophilic attack of the enolate site of 9a to the carbon atom of 2, followed by intramolecular cyclization with elimination of
hydrogen selenide to give 6a (Path A: C-carbonylation). The second possibility is that the phenolate site of 9a attacks 2 to form selenocarbonate 11a (Path B: O-carbonylation). The trapping of an intermediate anion by alklylation would be desirable. It has already been described that carbonylation of 5d to 6d did not proceed at 100°C for 30 h in spite of appreciable absorption of CO. Here, the resulting reaction mixture was yellow homogeneous solution, and metallic selenium had disappeared. On exposure to air, the yellow solution gradually changed to dark brown solution with deposition of metallic selenium. When the brown solution was worked up in the usual way, no carbonylated product was obtained: starting 5d was recovered in almost quantitative yield. These observations suggested that the yellow solution might include a transient carbonylated intermediate, which gave the starting compounds 5d and metallic selenium on exposure to air. A slight excess of allyl bromide relative to 5d was added dropwise to the yellow solution to yield 3-allyl-3-methyl-2,4-chromandione 12 (44 % yield based on 5d) with concomitant formation of diallyl selenide, however, the desired alkylated intermediate were not obtained at all. This experimental result would suggest the following (see Scheme 1-5). (1) Carbonylation of 5d might occur even at 100°C to form intermediate 10d or 11d. The cyclization of 10d or 11d proceeded at 130°C to give 6d (Table 2, entry 7); (2) Treatment of the yellow solution with allyl bromide might afford Se-allylated intermediate 13d or 14d, which might easily cyclize at room temperature to give 6d, since
RSe\(^{-}\) is a much better leaving group than Se\(^{2-}\). Formation of 12 might be due to further alkylation of thus formed 6d; (3) When air was introduced into the yellow solution, 10d or 11d would decompose to 6d, metallic selenium, and CO. As shown above, it seems difficult to trap the carbonylated intermediate from the carbonylation of 6d.

Scheme 1-5.

However the carbonylation of acetophenone with carbon monoxide and selenium leading to a C-carbonylated product suggests that the C-carbonylation path seems to be more plausible for the present carbonylation of 5 to 6.

1-6 Experimental

General
The instruments used were as follows: $^1$H-NMR, Hitachi R-24B; IR, Shimadzu IR-400; MS, Hitachi RMU-6A; melting points, Yanagimoto micro melting point apparatus.

Tetrahydrofuran (THF), dioxane, and benzene used were dried over sodium wire and/or lithium aluminum hydride, and distilled before use. N,N-dimethylformamide (DMF) was purified by distillation. Metallic selenium (99.99 %) from Nakarai Chem. Co. and carbon monoxide (99.999 %) from Seitetsu Chem. Co. were used as purchased. Tertiary amines (1,5-diazabicyclo[5.4.0]undec-5-ene (DBU), triethylamine, 1,4-diazabicyclo[2.2.2]octane (DABCO), and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN)), aryl alkyl ketones (o-hydroxyacetophone, o-hydroxypropiophenone, 2-hydroxy-5-methylacetophenone, and 2-hydroxy-4-methoxyacetophenone), and other reagents (nitrobenzene, p-quinone, manganese dioxide, molecular oxygen, and allyl bromide) were all purchased from commercial sources, and purified by distillation or recrystallization.

**Synthesis of 4-Hydroxycoumarin (6a): Carbonylation of o-Hydroxyacetophenone (5a) Using Stoichiometric Amount of Selenium**

In a 50 mL stainless steel autoclave were placed 5a (1.36 g, 10 mmol), selenium (0.79 g, 10 mmol), DBU (6.08 g, 40 mmol), THF (5 mL), and a magnetic stirring bar. The apparatus was flushed several times with carbon monoxide and charged with carbon monoxide at 30 kg/cm$^2$. The mixture was heated with stirring at 90°C for 30 hr. After the reaction was complete, carbon monoxide was purged...
and air was blown into the resulting solution to oxidize hydrogen selenide to selenium and water. Water (10 mL) was added to the mixture, which was then neutralized with aqueous hydrochloric acid (35 %). The deposited selenium was filtered off and the filtrate was poured into 50 ml of water. The product was extracted with diethyl ether (100 mL x 3), dried over anhydrous magnesium sulfate, concentrated on a rotary evaporator and recrystallized from benzene-ethyl acetate (1:1) solvent, affording 1.62 g (100 %) of 6a: m.p. 206.7-207.2°C (lit., 206°C); IR (KBr) 3600-2000 (OH), 1680 (C=O, conj), 1605 cm⁻¹ (C=C); ¹H-NMR (d₆-DMSO) δ 5.60 (s, 1H), 7.20-7.86 (m, 4H); MS 162 (M⁺).

**Carbonylation of 2-Hydroxy-5-methylacetophenone (5b) into 4-Hydroxy-6-Methylcoumarin (6b)**

A mixture of 5b (0.75 g, 5 mmol), selenium (0.40 g, 5 mmol), DBU (6.08 g, 40 mmol) and THF (15 mL) was stirred at 95°C for 30 hr under 30 Kg/cm² of carbon monoxide (initial pressure at 25°C). The resulting mixture was worked up in the same manner as described in the synthesis of 6a to yield 0.68 g (77 %) of 6b: m.p. 255-257°C (recrystallized from MeOH, lit., 258°C); IR (KBr) 3600-2200 (OH), 1680 (C=O, conj), 1600 cm⁻¹ (C=C); ¹H-NMR (d₆-DMSO) δ 2.40 (s, 3H), 5.60 (s, 1H), 7.10-7.60 (m, 3H); MS 176 (M⁺).

**Carbonylation of 2-Hydroxy-4-methoxyacetophenone (5c) into 4-Hydroxy-7-methoxycoumarin (6c)**
Reaction of 5c (0.83 g, 5 mmol) and the following workups were performed as described above, resulting in the formation of 6c in 36% yield (0.35 g); m.p. 255-256°C, (recrystallized from MeOH, lit., 15 256°C); IR (KBr) 3600-2000 (OH), 1685 (C=O), 1600 cm\(^{-1}\) (C=C); \(^1\)H-NMR (d\(_6\)-DMSO) \(\delta\) 3.81 (s, 3H), 5.35 (s, 1H), 6.70-7.70 (m, 3H); MS 192 (M\(^+\)).

Carbonylation of o-Hydroxypropiophenone (5d) into 4-Hydroxy-3-methylcoumarin (6d)

A mixture of 5d (0.75 g, 5 mmol), selenium (5 mmol), DBU (20 mmol), and THF (5 mL) was stirred at 130°C for 30 hr under carbon monoxide (30 Kg/cm\(^{-1}\): initial pressure at 25°C). The crude product obtained in the same manner as described in the synthesis of 6a was subjected to column chromatography on silica gel (n-hexane-MeOH) to afford 0.74 g (42%) of 6d; m.p. 228-230°C (lit., 16 230-231 °C); IR (KBr) 3500-2000 (OH), 1675 (C=O, conj), 1615 cm\(^{-1}\) (C=C); \(^1\)H-NMR (d\(_6\)-DMSO) \(\delta\) 2.00 (s, 3H), 6.55-7.95 (m, 4H); MS 176 (M\(^+\)).

Catalytic carbonylation of o-hydroxyacetophenone (5a)

A mixture of 5a (1.36 g, 10 mmol), selenium (0.16 g, 2 mmol), DBU (6.08 g, 40 mmol), nitrobenzene (5 mmol), and THF (5 mL) was heated with stirring under a pressure of carbon monoxide (30 Kg/cm\(^{-1}\): initial pressure at 25°C) at 90°C for 30 hr. The resulting mixture was worked up in the same manner as described in the synthesis of 6a using stoichiometric amount of selenium, and
1.10 g of 6a was obtained (6.8 mmol, 68 %).

Carbonylation of Acetophenone

A stirred mixture of acetophenone (2.9 mL, 25 mmol), selenium (0.395 g, 5 mmol), DBU (6.0 mL, 40 mmol), and THF (5 mL) was heated at 100°C for 72 hr under the pressure of CO (30 kg/cm²). After the reaction was complete, CO was purged in the well ventilated hood. n-Butylamine (5 mL, 50 mmol) was added to the mixture at 0°C, and then the reaction was continued at 15°C for 12 h. Extraction of the product with diethyl ether (100 mL x 3), followed by column chromatography on silica gel (n-hexane - Et₂O) gave N-(n-butyl)-benzoylacetamide (3) (28 % yield): IR (NaCl) 3350 (N-H), 1695 (C=O), 1645 (C=C), 1565 cm⁻¹ (C-N); ¹H-NMR (CCl₄) δ 0.87 (t, 3H), 1.35 (m, 4H), 3.08 (t-d, 2H), 5.50 (s, 1H), 7.00-8.05 (m, 5H); MS 219 (M⁺).

An Attempt for the Trapping of the Intermediate

In a 50 mL stainless steel autoclave with a glass insert were placed 5d (1.50 g, 10 mmol), selenium (0.79 g, 10 mmol), DBU (6.08 mL, 40 mmol), and THF (5 mL). The mixture was stirred at 90°C for 24 h under the pressure of carbon monoxide (30 Kg/cm⁻¹: initial pressure at 25°C). The final pressure after cooling to 25°C was 23 Kg/cm⁻¹. After releasing the pressure, the glass
insert was taken out, into which allyl bromide (0.95 mL, 11 mmol) was added at 0°C under nitrogen. The mixture was stirred at room temperature for additional 10 h. The resulting mixture was worked up in the same manner as described in the carbonylation of aceto-phenone to give 3-allyl-3-methyl-2,4-chromandione (12) (44 % yield): m.p. 62.0°C (lit.,17 65-65.5°C); IR (NaCl) 1780 (C=O), 1700 (C=O), 1620 cm⁻¹ (C=C); ¹H-NMR (CDCl₃) δ 1.55 (s, 3H), 2.65 (d, 2H), 4.80-5.95 (m, 3H), 6.95-7.90 (m, 4H); MS 216 (M⁺).

1-7 References and Notes


(9) Unpublished data.

(10) Alternative explanation, which does not involve the formation of SeCO, can be also offered in the present carbonylation: (1) reaction of nucleophile with CO gave rise to a CO-nucleophile addition product, which was rapidly trapped by selenium to afford Nu-C(O)-Se\(^-\), or (2) reaction of nucleophile with selenium occurred at first, followed by insertion of CO between nucleophile and selenium which gave Nu-C(O)-Se\(^2-\). At present, we do not have enough evidence to rule out the possibility of the above explanation.

(11) Similar observations were reported in the carboxylation\(^8\) of 5a with carbon dioxide, where 3-4 molar equivalents of DBU to 5a were required. It may be assumed that DBU was consumed for both generation of dianion (9a) from 5a and formation of a SeCO-DBU complex. Furthermore DBU may also react with hydrogen selenide (8) formed in situ to give a H\(_2\)Se-DBU salt ([DBU·H]\(^+\) [SeH\(^-\)].

(12) Hydrogen selenide 8 was isolated from the present reaction system by acidification of the system with conc. sulfuric acid.


(15) A. Sonn, Ber., 50, 1292 (1917).


Chapter 2 Selenium Catalyzed Reduction with Carbon Monoxide and Water. In Situ Formation and Michael Addition of Benzeneselenol

2-1 Introduction

Development of novel synthetic reactions using carbon monoxide and water as a reducing agent has been one of the subject of current interest. Several metal hydrides, which are well known to be key intermediates in the water gas shift reaction, have been reported to be effective catalysts for reduction or reductive carbonylation of nitrobenzenes and carbonylation of olefins.1c,4

Recently a convenient method for preparation of hydrogen selenide (8) by the reduction of metallic selenium with carbon monoxide and water has been found in our laboratory (eq 2-1).5

\[ \text{Se} + \text{CO} + \text{H}_2\text{O} \xrightarrow{\text{base}} \text{H}_2\text{Se} + \text{CO}_2 \] (2-1)

Hydrogen selenide has not only been recognized to be an important reagent in the syntheses of various organic selenium compounds but also has been proved to have a potent reducing ability toward organic compounds.7

It has been also shown that the successful combination of these of two reactions, preparation of H₂Se and application of
that, along our strategy, made a novel reduction system by use of the reducing ability of carbon monoxide catalyzed by elemental selenium, in which aromatic nitro compounds were reduced to aromatic amines quantitatively with carbon monoxide in the presence of water and a catalytic amount of selenium.\textsuperscript{7}

This chapter describes a new selenium assisted reduction of diphenyl diselenide with carbon monoxide and water to benzeneselenol (15), which gave Michael adducts with a variety of activated olefins in good yields.

2-2 Reduction of Diphenyl Diselenide with Carbon Monoxide, Selenium, and Water Leading to Benzeneselenol

The reduction of diphenyl diselenide took place under the pressure of carbon monoxide (20 kg/cm\textsuperscript{2}: initial pressure at 25°C) at 50°C by use of N-methylpyrrolidine as a base, and benzeneselenol (15) was isolated by distillation in 21 % yield (eq 2-2).

\[
\text{PhSeSePh + CO + H}_2\text{O} \xrightarrow{\text{Se base}} 2\text{PhSeH + CO}_2 \quad (2-2)
\]

The observed low yield may be due to oxidation of once formed selenol to diphenyl diselenide during workup, because air-oxidation of 15 was much faster under basic condition.
Benzeneselenol is the most general reagent for the phenylselenenylation\textsuperscript{8} or reduction\textsuperscript{9} of various organic compounds, but is highly susceptible to air-oxidation so that special care is required in its manipulation, and in some cases in situ generated 15 was used without isolation. In order to avoid such trouble in the isolation of 15 and to enable the use of selenol formed in situ directly for phenylselenenylation, we examined the reduction of diphenyl diselenide in the presence of Michael acceptors. The reduction of diphenyl diselenide with carbon monoxide (5 Kg/cm\textsuperscript{2}), water, and one equivalent of selenium using of N-methylpyrrolidine carried out in the presence of excess methyl vinyl ketone at 50°C, and Michael adduct, 4-(phenylselenenyl)butan-2-one (16a) was successfully obtained in 78 % yield (eq 2-3).

\[
\text{PhSeSePh} + \xrightarrow{\text{Se-CO-H}_2\text{O}} \text{base} \quad \xrightarrow{\text{SePh}} 4\text{-(phenylselenenyl)butan-2-one (16a)}
\]

The reaction was accompanied by the concomitant formation of bis(3-oxo-buthy)selenide (17a), which might be produced by the reaction of hydrogen selenide with methyl vinyl ketone.

The reaction also proceeded at atmospheric pressure of carbon monoxide, and 16a was obtained in 72 % yield by introduction of
CO into the the reaction mixture. The synthesis of 16a using stoichiometric amount of methyl vinyl ketone was also achieved successfully as follows. After the reduction of diphenyl diselenide was complete, the resulting mixture was acidified with acetic acid. The subsequent addition of methyl vinyl ketone to the mixture gave 16a in 78 % yield.

A variety of Michael acceptors were examined, and in every case benzeneselenol formed in situ underwent smooth conjugate addition (Table 3).

Table 3.

<table>
<thead>
<tr>
<th>run</th>
<th>substrate</th>
<th>product</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>2</td>
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<td>58</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td>76</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>55</td>
</tr>
<tr>
<td>5a)</td>
<td></td>
<td></td>
<td>60b)</td>
</tr>
</tbody>
</table>

a) 80°C  b) Z-isomer
Since the reduction of diphenyl diselenide is expected to proceed with a catalytic amount of selenium, the selenium-catalyzed reduction was examined using 0.1 equivalent of selenium at 50°C for 24 h, resulted in the formation of adduct 16a in 56 % yield based on diphenyl diselenide used (the turnover number: 5.6) together with a trace amount of 17a.

Although the details of the reaction mechanism are not clear yet, it seems likely that the present reaction may involve the nucleophilic attack of HSe⁻ at the selenium atom of diphenyl diselenide deduced from an analogy of the similar reductions, in which disulfides were reduced to thiols with some nucleophiles such as cyanide ion, phosphines, thiolates, and sodium hydrogen selenide. A plausible path for the catalytic reaction is shown in Scheme 2-1.

Scheme 2-1.
2-4 Experimental

General.

Tertiary amine (N-methylpyrrolidine), Michael acceptors (methyl vinyl ketone, cyclohexenone, methyl acrylate, acrylonitrile, and phenyl acetylene), and tetrahydrofuran were all purchased from commercial sources, and purified by distillation. Diphenyl diselenide was prepared as described in the literature, purified by recrystallization from n-hexane, and dried under reduced pressure.


In a 50 mL stainless steel autoclave were placed diphenyl diselenide (0.79 g, 2.5 mmol), selenium (0.20 g, 2.5 mmol), water (0.5 mL, 28 mmol), N-methylpyrrolidine (1.0 mL, 9.0 mmol), methyl vinyl ketone (2 mL, 24 mmol), THF (7 mL), and a magnetic stirring bar. The apparatus was flushed several times with carbon monoxide and charged at 5 Kg/cm². The mixture was heated in an oil bath maintained at 50°C with magnetic stirring for 5 h. After the reaction, carbon monoxide was purged in a well-ventilated hood, and the resulting mixture was slightly acidified with aqueous hydrochloric acid (2 N), and extracted with diethyl ether (100 mL x 3). The organic layer was dried (MgSO₄), and evaporation of the solvent gave a yellow residue, which was chromatographed on silica gel (n-hexane-Et₂O) to give 0.89 g (3.9 mmol, 78%) of
4-(phenylselenenyI)butan-2-one (16a): IR (NaCl) 1720 (C=O), 735, and 680 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\)) \(\delta\) 2.04 (s, 3H), 2.60-3.10 (m, 4H), and 7.10 (m, 5H); mass m/e 228 (M\(^+\)); Anal. Calcd for C\(_{10}\)H\(_{12}\)OSe: C, 52.87; H, 5.32. Found: C, 52.74; H, 5.46.

**Catalytic Reduction of Diphenyl Diselenide in the Presence of Methyl Vinyl Ketone.**

Reaction using 2.5 mmol of diphenyl diselenide, 0.1 equivalent of selenium (0.25 mmol), water (0.5 mL), and methyl vinyl ketone (24 mmol) in the presence of N-methylpyrrolidine (5 mL) in THF (7 mL) at 50°C for 24 h, and the subsequent workup as described above were performed to give 2.8 mmol (56 % based on diphenyl diselenide) of 16a.

**Alternative Procedure for Synthesis of 16a Using Stoichiometric Amount of Methyl Vinyl Ketone.**

In the autoclave were placed diphenyl diselenide (0.94 g, 3.0 mmol), selenium (0.24 g, 3.0 mmol), carbon monoxide (5 Kg/cm\(^2\)), water (0.5 mL, 28 mmol), N-methylpyrrolidine (1.2 mL, 11.0 mmol) and THF (7 mL). The mixture was heated at 50°C with magnetic stirring for 5 h. After the reaction was complete, the resulting mixture was slightly acidified with acetic acid (ca. 4.5 mL) under the atmosphere of nitrogen, followed by the addition of methyl vinyl ketone (0.41 mL, 5 mmol) to the mixture. The reaction was continued at room temperature for 3 h under nitrogen. By the
similar workup of the resulting mixture, 0.89 g (3.9 mmol, 78 %) of 16a was obtained.

**Isolation of Benzeneselenol (15) from the Present Reaction System.**

A mixture of diphenyl diselenide (3.14 g, 10 mmol), selenium (0.78 g, 10 mmol), water (2 mL, 112 mmol), N-methylpyrrolidone (2 mL, 14 mmol), and THF (7 mL) were stirred at 50°C for 24 h under 20 Kg/cm$^2$ of CO (initial pressure at 25°C). The resulting mixture was slightly acidified with aqueous hydrochloric acid (2 N), and extracted with Et$_2$O (50 mL x 2). The extracts were dried under nitrogen (CaSO$_4$), and filtered. Evaporation of the filtrate, followed by distillation (47-52°C/5 mmHg; lit.,$^{16}$ bp 73-74°C/20 mmHg) gave 0.64 g (20 %) of 15: $^1$H-NMR (CCl$_4$) δ 1.37 (s, 1H), 6.85-7.50 (m, 5H).

2-5 References and Notes


(10) It was confirmed by using kinetic technique that reduction of disulfides to thiols involved the nucleophilic attack of cyanide ion, phosphines, thiolates or sodium hydrogen selenide to the sulfur atom of disulfides.


3-1 A New Method for Synthesis of Selenocarboxamides: Reaction of Nitriles with Selenium, Carbon Monoxide, and Water

3-1-1 Introduction

Selenocarboxamides, which are well-known to be useful reagents for the synthesis of selenium-nitrogen heterocycles such as 1,3-selenazoles, have been prepared by the addition of hydrogen selenide (H₂Se) to the corresponding nitriles. In earlier investigations, poisonous hydrogen selenide was directly bubbled into the reaction vessel; however, the yields were generally very low. Better yields have been reported by Cohen using excess amounts of aluminum selenide (Al₂Se₃) and water as the source of H₂Se.

As shown in chapter 2, CO-Se-H₂O reaction system is exceedingly convenient, in terms of manipulation without isolation of air-sensitive and highly toxic hydrogen selenide. Then the reaction of in situ formed H₂Se with nitriles was examined to synthesize selenocarboxamides (eq 3-1).

\[
\text{RCN} + \text{Se} + \text{CO} + \text{H}_2\text{O} \xrightarrow{\text{base}} \text{R-C-NH}_2 + \text{CO}_2 + \text{Se} \quad (3-1)
\]
This section describes a new synthesis of various kinds of selenoamides by using CO-Se-H$_2$O reaction system.

3-1-2 Synthesis of N-Unsubstituted Selenocarboxamides

Treatment of benzonitrile with selenium, carbon monoxide, and water in the presence of triethylamine at 100°C for 5 h gave rise to the corresponding selenocarboxamide 18a (76 % yield).

In a similar manner a number of aromatic and heterocyclic selenocarboxamides were successfully synthesized from the corresponding nitriles as shown in Table 4. Structural assignments of selenocarboxamides were based on spectral analyses (IR, $^1$H-NMR, and Mass spectrum) after isolation of the products (see Table 4). The elemental analyses of new amides (18b, 18f, 18h, 18j, and 18k) were also in good agreement with the calculated values. The yields of selenocarboxamides were high except for some cases of sterically hindered amides such as 18b and 18j.

The aromatic selenoamides obtained are all yellow solids and are stable enough under nitrogen at ordinary temperature to be kept for several weeks with high purity. On exposure to air, they gradually decomposed into the starting nitriles, selenium, and water at room temperature or lower temperature. These observations may show that the selenoamides are in equilibrium with the corresponding nitriles and hydrogen selenide (eq 3-2), and that the
Table 4.

<table>
<thead>
<tr>
<th>entry</th>
<th>formula</th>
<th>yield, %</th>
<th>mp, °C (Lit.)</th>
<th>TR, cm⁻¹ (KBr)</th>
<th>¹H-NMR (Me₂SO-d₆)</th>
<th>MS (m/e H⁺)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="attachment" alt="formula" /> 18a</td>
<td>76</td>
<td>126.0-126.5</td>
<td>3325, 3265, (125²f) 1622</td>
<td>7.20-7.70(m,3H), 7.70-8.10(m,2H), 185</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td><img src="attachment" alt="formula" /> 18b</td>
<td>22</td>
<td>104.0-106.0</td>
<td>3390, 3270, 1615</td>
<td>2.26(s,3H), 7.70(s,4H), 199</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td><img src="attachment" alt="formula" /> 18c</td>
<td>78</td>
<td>72.0-73.0</td>
<td>3280, 1610, (74²f)</td>
<td>2.27(s,3H), 7.15-7.47(m,4H), 199</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td><img src="attachment" alt="formula" /> 18d</td>
<td>100</td>
<td>165.0-167.0</td>
<td>3370, 3270, (186²f, 161²b) 1620</td>
<td>2.30(s,3H), 7.02-7.15(d,2H), 7.69-7.93(d,2H), 199</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td><img src="attachment" alt="formula" /> 18e</td>
<td>99</td>
<td>127.5-128.5</td>
<td>3320, 3280, (129²f) 1630</td>
<td>7.33-7.47(d,2H), 7.79-7.93(d,2H), 219</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td><img src="attachment" alt="formula" /> 18f</td>
<td>61</td>
<td>125.5-126.5</td>
<td>3330, 3285, 1620</td>
<td>10.15(brs,1H), 10.75(brs,1H), 219</td>
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<tr>
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<td><img src="attachment" alt="formula" /> 18g</td>
<td>91</td>
<td>155.0-156.5</td>
<td>3360, 3270, (157²f) 1598</td>
<td>3.80(s,3H), 6.81-6.95(d,2H), 7.85-8.05(d,2H), 215</td>
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<tr>
<td>8</td>
<td><img src="attachment" alt="formula" /> 18h</td>
<td>82</td>
<td>221.0-222.5</td>
<td>3370, 3270, 1605</td>
<td>2.94(s,6H), 6.46-6.62(d,2H), 7.78-7.93(d,2H), 228</td>
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</tr>
<tr>
<td>9</td>
<td><img src="attachment" alt="formula" /> 18i</td>
<td>74</td>
<td>142.0-143.5</td>
<td>3320, 3250, (142²f) 1500</td>
<td>7.36-8.57(m,4H), 10.70(brs,2H), 186</td>
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<tr>
<td>10</td>
<td><img src="attachment" alt="formula" /> 18j</td>
<td>21</td>
<td>131.0-132.0</td>
<td>3370, 3260, 1615</td>
<td>7.30-8.20(m,7H), 10.30(brs,1H), 235</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td><img src="attachment" alt="formula" /> 18k</td>
<td>82</td>
<td>138.0-140.0</td>
<td>3355, 3280, 1620</td>
<td>10.90(brs,1H), 10.67(brs,1H), 235</td>
<td></td>
</tr>
</tbody>
</table>
equilibrium lies so far to the selenoamide products at room temperature under nitrogen, however, in the atmosphere of air hydrogen selenide is easily consumed by oxidation to water and selenium, so that the equilibrium may be shifted to the left of equation 3-2.

\[
\text{Se} \quad \overset{\text{R-C-NH}_2}{\rightleftharpoons} \quad \text{RCN + H}_2\text{Se} \quad (3-2)
\]

In contrast to aromatic selenoamides, little is known about the isolation of N-unsubstituted aliphatic selenoamides. Phenyl-selenoacetamide has been prepared by Kindler\textsuperscript{2c} and shown to be thermally unstable and susceptible to air. Another example is a carbohydrate possessing the selenoamide group.\textsuperscript{3} Aliphatic selenoamides are assumed to be less stable owing to the lack of conjugation between the aromatic ring and the selenocarbonyl group observed in aromatic ones. The synthesis of aliphatic selenoamides was attempted using aliphatic nitriles in a similar fashion to that described above, and the corresponding selenoamides were successfully isolated as shown in Table 5. These selenoamides isolated were thermally unstable and highly sensitive to air and, even under nitrogen, gradually dissociated at room temperature into the starting nitriles and hydrogen selenide, which deposited elemental selenium on exposure to air: The position of the equilibrium of aliphatic selenoamides was slightly shifted to left compared with that of aromatic ones. This is the cause of the
lower yields of the aliphatic selenoamides. Owing to such instability of aliphatic selenoamides, confirmation of their structures by mass spectrom and elemental analyses was unsuccessful and therefore the assignments of selenoamides (18l, 18m, and 18n) were performed only on the basis of spectral analyses (IR and 1H-NMR spectrum).

Table 5.

| entry | formula            | yield, %
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₃CH₂CH₂CNH₂</td>
<td>18₁</td>
</tr>
<tr>
<td>2</td>
<td>PhCH₂CNH₂</td>
<td>18m</td>
</tr>
<tr>
<td>3</td>
<td>CH₃OCH₂CNH₂</td>
<td>18n</td>
</tr>
</tbody>
</table>

3-1-3 Synthesis of N-Substituted Selenocarboxamides

The hitherto known procedures for synthesis of N-substituted selenocarboxamides (19) were limited to the following three methods: (i) the reaction of amides with phosphorus pentaselenide,⁴ (ii) the substitution reaction of selenoesters with amines,⁵ and
(iii) the addition of secondary amines to alkynyl selenols.\textsuperscript{6} However these methods are not general, and in some cases the yields are very low.

Our strategy for the synthesis of 19 is the amino-group exchange reaction of 18 formed in situ from the reaction of equation 3-1 with primary or secondary amines (eq 3-3).

\[
\text{RCN + Se + CO + H}_2\text{O } \xrightarrow{\text{base}} \text{R}$\text{-C-NHR'} \quad \text{18} \quad \xrightarrow{\text{Se}} \text{R-C-NHR'} \quad \text{19}
\]

Reaction of benzonitrile with selenium, carbon monoxide, and water in the presence of triethylamine in THF at 100°C for 5 h, followed by treatment of the resulting mixture with n-butylamine at 100°C for 3 h successfully afforded N-(n-butyl)benzeneselenocarboxamide (19b) (81\%) [Method A].

The representative results were shown in Table 6. The reaction appears general with respect to the substituents of selenoamides: both aromatic and aliphatic, and both N-monosubstituted and N,N-disubstituted selenoamides were all easily synthesized in moderate to high yields. But the yields of aromatic selenoamides (19a-19g) differed depending on the bulkiness of the alkyl groups of amines (R = primary alkyl group: >80\%; secondary: 30-50\%; tertiary: 0\%). In the cases of N-(sec-alkyl) derivatives (19a, 19c, and 19f), the yields could be improved by prolonged reaction time in the
Table 6.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Selenocarboxamide</th>
<th>Yield, %</th>
<th>IR, cm⁻¹</th>
<th>H-NMR δ (CCl₄)</th>
<th>Mass (H) mp, °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_2 )</td>
<td>19a</td>
<td>41 (74)</td>
<td>3180, 1.42 (d, 6H), 4.05 (m, 1H), 7.00-7.70</td>
<td>227 60</td>
</tr>
<tr>
<td></td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19b</td>
<td>81</td>
<td>3180, 0.84 (t, 3H), 1.00-1.90 (m, 4H), 3.53</td>
<td>241 011</td>
</tr>
<tr>
<td>2</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19c</td>
<td>34 (77)</td>
<td>3180, 0.98 (t, 3H), 1.28 (d, 3H), 1.70 (m, 2H), 4.64</td>
<td>241 011</td>
</tr>
<tr>
<td>3</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19d</td>
<td>(0)</td>
<td>(0)</td>
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</tr>
<tr>
<td>4</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19e</td>
<td>67</td>
<td>3155, 4.04 (d, 2H), 7.00-7.80 (m, 1H),</td>
<td>275 76-78</td>
</tr>
<tr>
<td>5</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19f</td>
<td>47 (75)</td>
<td>3155, 8.20 (brs, 1H),</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19g</td>
<td>88</td>
<td>3135, 6.50-2.50 (m, 1H), 4.52 (m, 1H),</td>
<td>267 95</td>
</tr>
<tr>
<td>7</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19h</td>
<td>46</td>
<td>3150, 7.00-7.80 (m, 5H), 7.95 (brs, 1H),</td>
<td>297 011</td>
</tr>
<tr>
<td>8</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19i</td>
<td>45</td>
<td>3150, 2.90 (s, 3H), 3.52 (s, 3H), 7.14 (s, 5H)</td>
<td>213 46-46.5</td>
</tr>
<tr>
<td>9</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19j</td>
<td>54</td>
<td>3150, 1.74 (m, 6H), 3.46 (m, 2H), 4.38 (m, 2H), 7.18 (m, 5H),</td>
<td>253 89-89.5</td>
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<tr>
<td>10</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19k</td>
<td>74</td>
<td>3150, 2.66 (t, 2H), 3.62 (q, 2H), 0.70 (brs, 1H),</td>
<td>207 011</td>
</tr>
<tr>
<td>11</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19l</td>
<td>48</td>
<td>3150, 0.93 (t, 3H), 1.00 (t-2H), 2.62 (t, 2H),</td>
<td>213 80-89</td>
</tr>
<tr>
<td>12</td>
<td>( \text{Se} \quad \text{Ph-C-HIC}_4 \text{H}_9 )</td>
<td>19m</td>
<td>71</td>
<td>3145, 4.13 (s, 2H), 4.81 (m, 1H), 7.20 (s, 5H),</td>
<td>289 94.5-95.5</td>
</tr>
</tbody>
</table>

The yields in the parentheses refer to that obtained by prolonged reaction periods in the amino-group exchange reaction (20 h).
amino-group exchange reaction (20 h). On the other hand, the amino-group exchange reaction with aromatic amines did not take place under these reaction conditions.

Structural assignments of selenoamides were based on spectral analyses (IR, $^1$H-NMR, and Mass spectrum: see Table 6) and elemental analyses after purification of the products by column chromatography on silica gel.

N-Substituted selenoamides are yellow crystalline or red oil, and are generally stable enough to be kept for several weeks under the atmosphere of nitrogen at about 0°C without degradation. On exposure to air, however, they gradually decomposed with deposition of elemental selenium.

In addition to Method A, for the preparation of N-mono-substituted selenoamides a more facile procedure became available (Method B, eq 3-4). For example, N-benzylbenzeneselenoamide (19e) was obtained in 94 % yield by heating the mixture of benzonitrile, selenium, and benzylamine under CO pressure in THF.

$$\text{RCN} + \text{Se} + \text{CO} + 3\text{R'}\text{NH}_2 \rightarrow \text{R-C-NHR'} + (\text{R'}\text{NH})_2\text{CO} + \text{NH}_3 \quad (3-4)$$

As shown in eq 3-4, Method B affords the corresponding urea derivative as the by-product concomitantly, which is easily separable from 19. A suggested reaction path is illustrated in equation 3-5.
This method is inapplicable to synthesis of N,N-disubstituted selenoamides probably because the reaction of secondary amines with carbon monoxide and selenium does not give hydrogen selenide but the amine salts of selenol carbamic acids.\(^7\)

In summary, general and convenient methods for synthesis of selenoamides using carbon monoxide and selenium has been developed. Present methods offers several advantages against hitherto known methods: (i) a wide range of applicability to a variety of selenoamides (aromatic and aliphatic; N-unsubstituted, N-monosubstituted, and N-disubstituted); (ii) high yields of selenoamides; (iii) one-pot syntheses with simple operation without troublesome handling of hydrogen selenide.

3-1-4 Experimental

General

All reactions were carried out using a 50 mL stainless steel autoclave (SUS-304) purchased from Taiatsu Glass Kogyo. Nitriles (benzonitrile, n-butyronitrile, acetonitrile, and phenylacetonitrile), amines (i-propylamine, n-butylamine, sec-butylamine,
t-butylamine, benzylamine, cyclohexylamine, n-octylamine, dimethyl-
amine, piperidine, and triethylamine), and solvent (tetrahydrofuran) were all purchased from commercial sources, and purified by distil-
lution or recrystallization. CO pressures mentioned in the paper refer to those at 25°C.

**General Procedures for Synthesis of N-Unsubstituted Selenoamide**

In a typical reaction, a stirred mixture of benzonitrile (0.52 g, 5 mmol), selenium (0.43 g, 5.5 mmol), water (1 mL, 56 mmol), triethylamine (1 mL, 7 mmol), and tetrahydrofuran (5 mL) in a 50 mL stainless steel autoclave was heated under the pressure of carbon monoxide (5 atm: initial pressure) at 100°C for 5 h. After the reaction carbon monoxide was purged in the well-ventilated hood, and the reaction mixture was slightly acidified with aqueous hydrochloric acid (2 N) and extracted with diethyl ether (50 mL x 3). The combined extracts were dried (MgSO₄) under nitrogen, filtered, and evaporated. The crude material was chromatographed on silica gel, affording 0.69 g (76 %) of benzeneselenocarboxamide (18a). Anal. Calcd for C₇H₇NSe: C, 45.67; H, 3.83; N, 7.61. Found: C, 45.78; H, 3.91; N, 7.48.

**o-Methylbenzeneselenoamide (18b)**

Found: C, 48.68; H, 4.74; N, 6.95 %. Calcd for C₈H₉NSe: C, 48.50; H, 4.58; N, 7.07 %.
p-Methylbenzeneselenoamide (18d)

Found: C, 48.80; H, 4.79; N, 6.90 %. Calcd for C₈H₉NSe:
C, 48.50; H, 4.58; N, 7.07 %.

m-Chlorobenzeneselenoamide (18f)

Found: C, 38.43; H, 2.93; N, 6.16 %. Calcd for C₇H₆ClNSe:
C, 38.47; H, 2.77; N, 6.41 %.

α-Naphthylselenoamide (18j)

Found: C, 56.55; H, 3.95; N, 5.76 %. Calcd for C₁₁H₉NSe:
C, 56.42; H, 3.87; N, 5.98 %.

β-Naphthylselenoamide (18k)

Found: C, 56.71; H, 3.97; N, 5.90 %. Calcd for C₁₁H₉NSe:
C, 56.42; H, 3.87; N, 5.98 %.

n-Propylselenoamide (18l)

IR (KBr) 3280, 1630 cm⁻¹; ¹H-NMR (Me₂SO-d₆) δ 0.87 (t, 3H),
1.62 (t-q, 2H), 2.52 (t, 2H), 9.80 (br s, 1H), 10.00 (br s, 1H).

Phenylselenoacetamide (18m)

IR (Nujol) 3280, 1635 cm⁻¹; ¹H-NMR (Me₂SO-d₆) δ 3.09
(s, 2H), 7.31 (m, 5H), 9.90 (br s, 2H).

Methoxyselenoacetamide (18n)
IR (Nujol) 3260, 1635 cm\(^{-1}\); \(^1\)H-NMR (Me\(_2\)SO-d\(_6\)) \(\delta\) 3.41 (s, 3H), 4.04 (s, 2H), 9.40 (br s, 1H), 10.60 (br s, 1H).

4-(N, N-Dimethylamino)-benzeneselenocarboxamide (18h)

The reaction was carried out in the same manner described above for the general procedure of selenoamide synthesis. After the reaction, the reaction mixture was neutralized. A yellow precipitate deposited, was filtered off, and washed with water, n-hexane, and benzene successively. The remaining solid, containing metallic selenium, was dissolved in acetone and metallic selenium was removed by filtration. The filtrate was dried and evaporated to give 0.92 g of selenoamide 18h (82 % yield). Anal. Calcd for C\(_9\)H\(_{12}\)N\(_2\)Se: C, 47.56; H, 5.33; N, 12.34. Found: C, 47.74; H, 5.58; N, 12.51.

General Experimental Procedure for Synthesis of 19b (Method A)

In an autoclave were placed benzonitrile (0.52 g, 5 mmol), selenium (0.43 g, 5.5 mmol), water (1 mL, 56 mmol), triethylamine (1 mL), THF (5 mL), and a magnetic stirring bar. The autoclave was flushed with carbon monoxide for three times, charged at 5 Kg/cm\(^2\), and set in an oil bath maintained at 100°C. The reaction was carried out for 5 h with magnetic stirring. Then the autoclave was cooled to room temperature, and carbon monoxide was purged in a well-ventilated hood. n-Butylamine (1.0 mL, 10 mmol) was immediately added to the reaction mixture under an atmosphere of
nitrogen, and the reaction was continued at 100°C for 3 h under nitrogen. After the reaction was complete, the resulting mixture was transferred into a 100 mL flask, dried overnight (MgSO₄), and then filtered. Evaporation of the filtrate, followed by purification by the column chromatography on silica gel (n-hexane - Et₂O) gave 0.97 g (4.0 mmol, 81%) of 19b: Found: C, 55.39; H, 6.58; N, 5.85. Calcd for C₁₁H₁₅NSe: C, 55.00; H, 6.29; N, 5.83.

Similarly prepared were the followings.

19a: Found: C, 53.38; H, 5.85; N, 6.18%. Calcd for C₁₀H₁₃NSe: C, 53.10; H, 5.79; N, 6.19.

19c: Found: C, 55.38; H, 6.51; N, 5.72. Calcd for C₁₁H₁₅NSe: C, 55.00; H, 6.29; N, 5.83.

19e: Found: C, 61.36; H, 4.76; N, 5.01. Calcd for C₁₄H₁₃NSe: C, 61.32; H, 4.78; N, 5.11.


19g: Found: C, 60.97; H, 8.05; N, 4.87. Calcd for C₁₅H₂₃NSe: C, 60.80; H, 7.82; N, 4.73.

19h: Found: C, 50.98; H, 5.34; N, 6.57. Calcd for C₉H₁₁NSe: C, 50.95; H, 5.23; N, 6.60.

19i: Found: C, 57.21; H, 6.08; N, 5.50. Calcd for C₁₂H₁₅NSe: C, 57.15; H, 5.99; N, 5.55.

19j: Found: C, 47.09; H, 8.71; N, 6.81. Calcd for C₈H₁₇NSe: C, 46.60; H, 8.31; N, 6.79.
19k: Found: C, 55.13; H, 6.34; N, 5.72. Calcd for C_{11}H_{15}NSe: C, 55.00; H, 6.29; N, 5.83.

19l: Found: C, 51.18; H, 5.18; N, 6.55. Calcd for C_{9}H_{11}NSe: C, 50.95; H, 5.23; N, 6.60.

19m: Found: C, 62.60; H, 5.24; N, 4.82. Calcd for C_{15}H_{15}NSe: C, 62.50; H, 5.25; N, 4.86.

Method B

Benzonitrile (0.52 g, 5 mmol), selenium (0.43 g, 5.5 mmol), n-butylamine (2.0 mL, 20 mmol), and THF (5 mL) were placed in the autoclave with a magnetic stirring bar. The reaction was carried out under the pressure of CO (5 Kg/cm²) at 80°C for 5 h in the similar manner to that described in Method A. After the reaction was complete, the autoclave was cooled to room temperature, and carbon monoxide was purged. The reaction mixture was transferred into a 100 mL flask and left overnight under the atmosphere of air in order to decompose benzeneselenoamide (18a) and the remaining hydrogen selenide. The deposited metallic selenium was filtered off, and the solvent was removed from the filtrate under reduced pressure. The resulting residue was chromatographed on silica gel to give 1.12 g (4.7 mmol, 93 %) of 19b and 0.86 g (5.0 mmol) of di(n-butyl)urea.


(8) A larger scale reaction is also possible: benzenenitrile (5.1 mL, 50 mmol), Se (3.95 g, 50 mmol), water (2 mL, 112 mmol), carbon monoxide (40 atm), Et₃N (5 mmol, 35 mmol), THF (7 mL).

(9) The remaining hydrogen selenide, which generated upon the acidification of the reaction system, could be captured entirely by introducing into aqueous KOH solution. Elemental selenium was easily recovered on exposure of the solution to air.
3-2 Selenocarboxamides as New Reagents for Stereospecific Deoxygenation of Epoxides under Mild Conditions

3-2-1 Introduction

The preceding section has dealt with a general and convenient method for synthesis of selenocarboxamides by using CO-Se reaction system.

On the other hand little has been known about the chemistry of selenoamides, because general procedures for synthesis of selenoamides had been lacking. However selenoamides are synthetically promising and expected to react with various organic or inorganic reagents owing to high reactivity of their carbon-selenium double bond.

In the course of investigations of reactivities of selenoamides against electrophiles, it has been found that selenoamides are efficient reagents for converting epoxides into olefins stereospecifically in high yields under mild conditions.

Deoxygenation of epoxides is one of the important methodologies for control of olefin stereochemistry\(^1\) and for synthesis\(^2\) and structural analysis\(^3\) of natural products. For this purpose, high yields, mild conditions, and high stereospecificity are essential. A variety of methods\(^4\) have been devised to accomplish the transformation, and in some cases, the deoxygenation was found to proceed stereospecifically: for example, inversion with Me\(_3\)SiK,\(^{1g}\)
This section describes stereospecific deoxygenation of epoxides using selenoamides.

3-2-2 Stereospecific Deoxygenation of Epoxides

The reaction of cyclohexene oxide with benzeneselenoamide (18a) in the presence of trifluoroacetic acid in dichloromethane at 0°C gave cyclohexene in 84% yield (eq 3-6).

![Reaction equation](image)

Similar deoxygenation of some other epoxides was examined, and the results were shown in Table 7. 1- and 2-octene oxides, cyclohexene oxide, and 1-methylcyclohexene oxide underwent smooth deoxygenation at 0°C. Cyclopentene oxide and cyclooctadecene oxide were sluggish under the same conditions. But slightly higher temperatures and longer reaction times enabled these reactions to complete successfully. On the other hand, sterically hindered epoxides such as norbornene oxide did not give any olefinic products. Reaction of cis- and trans-2-octene oxides and trans-dodecene oxide afforded
olefins having the same geometry as the epoxides. All reactions in Table 7 were accompanied by the concomitant formation of metallic selenium and benzamide.

Table 7.

<table>
<thead>
<tr>
<th>entry</th>
<th>epoxide</th>
<th>temp, °C</th>
<th>time</th>
<th>product</th>
<th>yield, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="epoxide" /></td>
<td>0</td>
<td>5 min</td>
<td><img src="image2" alt="product" /></td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="epoxide" /></td>
<td>0</td>
<td>10 min</td>
<td><img src="image4" alt="product" /></td>
<td>74&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="epoxide" /></td>
<td>0</td>
<td>10 min</td>
<td><img src="image6" alt="product" /></td>
<td>75&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="epoxide" /></td>
<td>0</td>
<td>30 min</td>
<td><img src="image8" alt="product" /></td>
<td>54</td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="epoxide" /></td>
<td>20</td>
<td>30 h</td>
<td><img src="image10" alt="product" /></td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="epoxide" /></td>
<td>0</td>
<td>5 min</td>
<td><img src="image12" alt="product" /></td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td><img src="image13" alt="epoxide" /></td>
<td>0</td>
<td>5 min</td>
<td><img src="image14" alt="product" /></td>
<td>51</td>
</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="epoxide" /></td>
<td>40</td>
<td>21 h</td>
<td><img src="image16" alt="product" /></td>
<td>82&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Single isomer was formed stereospecifically.

Some other selenoamides (19e, 19f, 19h, 19l, and 19m) were examined and found to be effective for the deoxygenation. For example, cyclohexene oxide was converted into cyclohexene in ca. 80 % yield in every case.

A suggested reaction path<sup>5</sup> for the present deoxygenation of acyclic epoxides is illustrated in Scheme 3-1 from an analogy of the deoxygenation using KSeCN.<sup>1m</sup>
3-2-3 Experimental

General

Trifluoroacetic acid, some epoxides (cyclohexene oxide and styrene oxide), olefins (1- and 2-octene, cyclopentene, methylcyclohexene, cyclododecene, and norbornene), and m-chloroperbenzoic acid (80 %) were all purchased from commercial sources.

Gas chromatographic results were obtained on either a Shimadzu GC-3BF (analytical gas chromatography) or a Hitachi K-53 (preparative gas chromatography).

General Procedure for Synthesis of Epoxides
In a 50 mL three necked flask with a cooler were placed m-chloroperbenzoic acid (m-CPBA: 4.31 g, 20 mmol) and dichloromethane (40 mL), and olefin (20 mmol) was added dropwise at 0°C under nitrogen, and then the mixture was stirred overnight. After the reaction was complete, aqueous sodium sulfite (10%) was added in order to decompose excess m-CPBA. The depositing m-chlorobenzoic acid was filtered off, and then the filtrate was extracted with diethyl ether. The extracts were dried (MgSO₄), and evaporation of the solvent gave the crude product, of which distillation afforded the desired epoxides.

**Cis- and Trans-2-Octene Oxides**

Epoxidation of 2-octene oxides (cis and trans mixture) was carried out in the similar fashion to that described above. The purification of cis- or trans-2-octene oxide was performed by preparative gas chromatography.

**General Procedure for Deoxygenation of Epoxides**

In a typical reaction, to the stirred mixture of cyclohexene oxide (0.098 g, 1 mmol) and benzeneselenoamide (18a) (0.276 g, 1.5 mmol) in 7 mL of dry dichloromethane under nitrogen at 0°C was added dropwise trifluoroacetic acid (0.11 g, 1 mmol). Elemental selenium precipitated almost instantly. After stirring for 5 minutes, GLC analysis indicated the formation of cyclohexene in 84% yield.
3-2-4 References and Notes


(5) In the case of cyclic epoxides, absence of C-C free rotation indicates that the mechanism of Scheme 3-1 is unlikely. The deoxygenation of cyclic epoxides may be explained by the following scheme:

Scheme 3-2.

(6) Deoxygenation using 0.03 equivalent of trifluoroacetic acid relative to cyclohexene oxide also proceeded at 25°C for 24 h to give the corresponding olefin in 87 % yield.
3-3 A New Selenium-Containing Heterocycle. Acid Catalyzed Reaction of Benzeneselenocarboxamide with Aliphatic Aldehyde

3-3-1 Introduction

Selenocarboxamides would be expected to be employable as reagents for synthesis of new selenium-nitrogen heterocycles, because they have a Se-C-N bond as their structural feature.¹

This section describes the reaction of benzeneselenoamide (18a) with some aliphatic aldehydes under acidic conditions leading to the formation of a new six-membered heterocycle containing selenium, nitrogen, and oxygen.²

3-3-2 Reaction of Selenoamide with Aliphatic Aldehydes under Acidic Condition

Reaction of benzeneselenoamide (18a) with acetaldehyde in the presence of sulfuric acid gave 2,6-dimethyl-4-phenyl-6H-1,3,5-oxaselenazine (20a) as a major product (eq 3-7) with concomitant formation of a condensation product (21a) of 20a with acetaldehyde.

\[
\begin{align*}
\text{Ph-C-NH}_2 + 2 \text{RCHO} & \xrightarrow{\text{H}_2\text{SO}_4} \text{R} \text{Se}=\text{N} \text{R} + \text{H}_2\text{O} \\
\text{Se} & \\
\text{Ph-C-NH}_2 & + 2 \text{RCHO} & \xrightarrow{\text{H}_2\text{SO}_4} & \text{R} \text{Se}=\text{N} \text{R} + \text{H}_2\text{O} & \text{(3-7)}
\end{align*}
\]
In the same manner, the reaction using some other aliphatic aldehydes was examined, and every reaction afforded the corresponding oxaselenazines (20b-20e) (Table 8).

Table 8.

<table>
<thead>
<tr>
<th>aldehyde</th>
<th>yield, %</th>
<th>20</th>
<th>21</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CHO</td>
<td></td>
<td>42</td>
<td>6</td>
</tr>
<tr>
<td>n-PrCHO</td>
<td></td>
<td>24</td>
<td>11</td>
</tr>
<tr>
<td>i-PrCHO</td>
<td></td>
<td>34</td>
<td>15</td>
</tr>
<tr>
<td>t-BuCHO</td>
<td></td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>CHO</td>
<td></td>
<td>15</td>
<td>12</td>
</tr>
</tbody>
</table>

This reaction was also proceeded by using Lewis acid such as boron trifluoride etherate complex instead of sulfuric acid.

Further work is in progress to extend the scope of the reaction and to clarify the reaction mechanism. A plausible reaction path was shown in Scheme 3-3.

Scheme 3-3.

\[
\begin{align*}
\text{Se}^\|_{\text{Ph-C-NH}_2} + \text{RCHO} \\
\text{H}^+ \text{ cat.} \\
\text{Se}^\|_{\text{Ph-C-NH-CH}_R} \rightarrow \text{Se}^\|_{\text{Ph-C-N=CH}_R}
\end{align*}
\]
Experimental

General

Aldehydes (n- and iso-butyraldehydes, pivalaldehyde, and cyclohexanecarboxaldehyde), chloroform, acetic acid, sulfuric acid, and boron trifluoride etherate complex were all purchased from commercial sources. Acetaldehyde was obtained by treatment of paraldehyde with p-toluenesulfonic acid.³

General Procedure for Synthesis of 6H-1,3,5-Oxaselenazine Derivative

In a typical reaction, sulfuric acid (0.28 mL, 5 mmol) in acetic acid (3 mL) was added to the mixture of benzeneselenocarboxamide (0.92 g, 5 mmol), acetaldehyde (0.67 mL, 12 mmol), and acetic acid (10 mL) at 18°C, and the solution was kept at 18°C for 24h with magnetic stirring. The resulted mixture was extracted with diethyl ether after neutralization with aqueous sodium carbonate, and followed by purification by column chromatography on silica gel, affording 0.53 g (42 %) of 2,6-dimethyl-4-phenyl-6H-1,3,5-oxaselenazine (20a): IR (NaCl) 1620 cm⁻¹; ¹H-NMR (CCl₄) δ 1.55 (d, 3H, J=6.0 Hz), 1.70 (d, 3H, J=6.0 Hz), 5.01 (q, 1H), 5.45 (q, 1H), and 7.10-7.80 (m, 5H); ¹³C-NMR (CDCl₃) 23.085, 23.918, 73.378, 89.582, 126.536, 128.440, 128.765, 140.298, and 157.841.
Procedure for Synthesis of 20a using Lewis Acid

The reaction of selenoamide 18a (0.92 g, 5 mmol) with actaldehyde (1.5 mL, 27 mmol) in the presence of boron trifluoride etherate complex (1.26 mL, 10 mmol) in chloroform (20 mL) at 18°C for 15 h and similar workups described above gave oxaselenazaine 20a in 55 % yield.

3-3-4 References and Notes


(2) Sulfur analog see: C. Giordano and A. Belli, Synthesis, 789 (1975).

Conclusion

The aim of this research was to develop new synthetic reactions using carbon monoxide-selenium reaction system.

The important results mentioned in each chapter of this thesis are summarized as follows.

In chapter 1, a new selenium assisted carbonylation of alkyl aryl ketones with carbon monoxide leading to formation of 1,3-dicarbonyl compounds as C-carbonylated products has been described. o-Hydroxyacetophenone and its derivatives have been converted to the corresponding 4-hydroxycoumarins in moderate to quantitative yields by treatment with an equivalent of selenium and carbon monoxide with concomitant formation of hydrogen selenide. It has been further revealed that oxidation of in situ formed hydrogen selenide to selenium with an appropriate oxidizing agent such as nitrobenzene permitted catalytic use of selenium for the present carbonylation.

In chapter 2, a new selenium catalyzed reduction with carbon monoxide and water has been described. Reduction of diphenyl diselenide with carbon monoxide and water in the presence of selenium gave benzeneselenol, which was treated in situ Michael acceptors such as methyl vinyl ketone to afford the corresponding adducts in high yields.

In chapter 3, a new method for synthesis of selenocarboxamides by using carbon monoxide-selenium reaction system has been
described. A variety of N-unsubstituted selenoamides have been prepared in moderate to high yields by the reaction of nitriles with hydrogen selenide, generated in situ from elemental selenium, carbon monoxide, and water in the presence of triethylamine. Furthermore, convenient one-pot synthesis of N-substituted selenoamides has been developed on the basis of amino-group exchange reaction of N-unsubstituted selenoamides formed in situ with primary or secondary amines. Chapter 3 has also referred to applications of selenoamides to organic synthesis. Selenoamides have been found to be efficient reagents for converting epoxides into olefins stereospecifically in high yields under mild conditions. In addition, acid-catalyzed synthesis of a new heterocyclic compound containing selenium, nitrogen, and oxygen using selenoamides has been described.

Characteristic feature of carbon monoxide-selenium reaction system are summarized as follows.

Carbon monoxide-selenium reaction system may involve several key intermediates such as carbonyl selenide, selenocarboxylic acid, and hydrogen selenide (or HSe\textsuperscript{-}), and synthetic reactions utilizing the reaction system are principally classified into two types of reactions:

(i) carboylation reaction where carbonyl selenide acts as a key carbonylating species

(ii) synthetic reactions using hydrogen selenide (or HSe\textsuperscript{-}), that is, reduction by the use of reducing ability of HSe\textsuperscript{-}
and synthesis of various selenium-containing compounds employing hydrogen selenide as a source of selenium.

Several important knowledges obtained through the present investigations on carbon monoxide-selenium reaction system would open a new area of synthetic utilization of carbon monoxide.