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SELENIUM, CARBON MONOXIDE, AND WATER AS A NEW REDUCTION SYSTEM: REDUCTIVE CLEAVAGE OF DISULFIDES AND DISELENIDES TO THIOLS AND SELENOLS

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Summary: Disulfides and diselenides were effectively reduced to the corresponding thiols and selenols with carbon monoxide and water using selenium.

Development of synthetic reactions using carbon monoxide and water as reducing agents has been one of the subjects of current interest. In this context, several metal hydrides generated in the water gas shift reaction[1] have been reported to be effective catalysts for reduction[2] or reductive carbonylation[3] of nitrobenzenes and reduction of olefins.[1c,4]

We have recently developed a new reduction system using carbon monoxide and water, in which hydrogen selenide (or HSe^-), produced in situ from elemental selenium, carbon monoxide, and water, acts as the active reducing species,[5] and we have successfully used it to reduce a number of aromatic nitro compounds into the corresponding amines in high yields.[6]

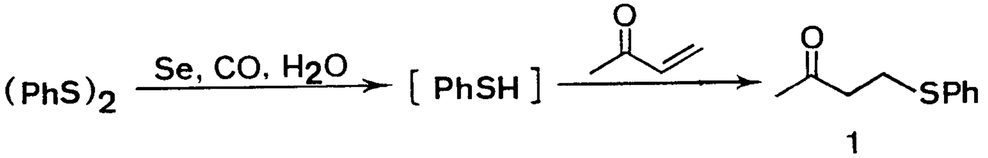
In the course of our studies to elucidate characteristic features of the reducing ability of thus generated hydrogen selenide[7] toward various functional groups, we have found that disulfides and diselenides are easily reduced to the corresponding thiols and selenols, which are well-known to be the most general reagents for thiolation,[8] selenation,[9] or reduction[9c] of various organic compounds. The reduction of diphenyl disulfide took place under the pressure of CO at 70°C by use of equimolar amount of selenium and N-methylpyrrolidine as a base, and benzenethiol, the reduction product, was successfully isolated by distillation in 72 % yield (eq. 1).[10] In the same manner, diphenyl diselenide was also reduced to benzeneselenol in 62 % yield (eq. 1).

$$(PhS)_2 + CO + H_2O \xrightarrow{Se} 2PhSH + CO_2$$

(eq. 1)

$$(PhSe)_2 + CO + H_2O \xrightarrow{Se} 2PhSeH + CO_2$$

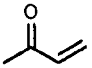
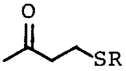
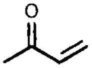
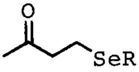
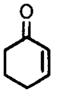
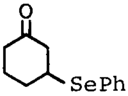
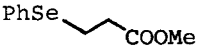
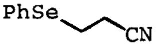
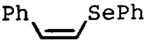
Thiol and selenol are generally ill-smelling and highly susceptible to air-oxidation, and therefore in some cases in situ generated thiol and selenol were used without isolation.[11] In order to enable the use of thiol and selenol formed in the present reaction system directly for thiolation and selenation, we examined the reduction of several disulfides and diselenides in the presence of various activated olefins (eq. 2). The reduction of thiols and selenols proceeded successfully even in the presence of olefins, and thiolation and selenation products[8,12] were obtained in a single stage. Representative results are summarized in Table 1.



1

(eq. 2)

Table 1. Reduction of Disulfides and Diselenides with Se - CO - H_2O in the Presence of Michael Acceptors[a)]

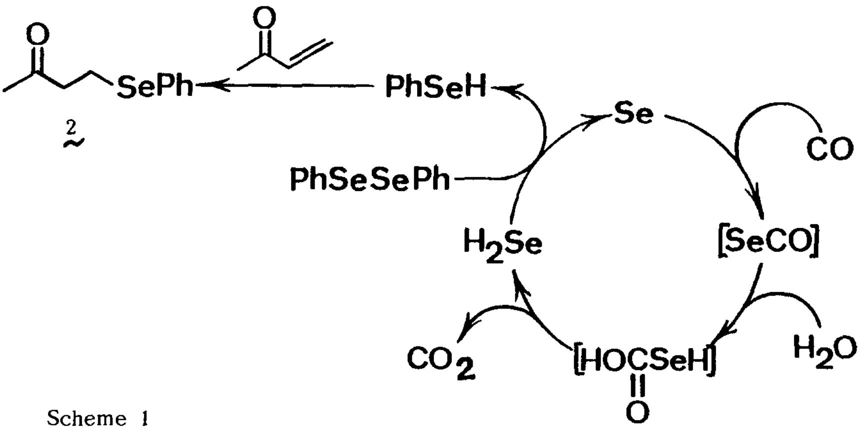
substrate	olefin	product
$(RS)_2$		
R = Ph		85 %$^{b), c)}$
= n-Bu		83 %$^{b)}$
= sec-Bu		79 %$^{b)}$
= $PhCH_2$		71 %$^{b)}$
$(RSe)_2$		
R = Ph		78 %
= CH_3		83 %
= n-Bu		75 %
$(PhSe)_2$		 58 %
		 76 %
		 55 %
	PhC≡CH	 60 %$^{d)}$

a) Reaction conditions described in the text. b) CO (20 atm), N-methylpyrrolidine (5 mL), 80°C, 24 h. c) 50°C. d) Phenylacetylene was added after the reduction of diselenide was complete, and then the reaction was continued at 80°C for 20 h.

A typical procedure is as follows: 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), methyl vinyl ketone (2 mL, 24 mmol), THF (7 mL), and a mangnetic stirring bar. The apparatus was flushed several times with carbon monoxide and charged at 5 atm. 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 acidified (to a slightly acidic end) with aqueous hydrochloric acid (2 N), and extracted with diethyl ether (100 mL x 3). The organic layer was dried ($MgSO_4$), and evaporation of the solvent gave a yellow residue, which was chromatographed on silica gel (n-hexane/Et_2O) to give 0.89 g (3.9 mmol, 78 %) of 4-(phenylselenenyl)butan-2-one (**2**)[13]: IR (NaCl) 1720 (C=O), 735, and 680 cm^{-1}; ^{1}H-NMR (CCl_4) δ 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.

It is anticipated that the present reduction proceeds with a catalytic amount of selenium. A selenium-catalyzed reduction was exemplified by the reaction using diphenyl disulfide as a substrate and 0.1 equivalent of selenium at 100°C for 24 h, which resulted in the formation of the adduct **1** in 69 % yield based on diphenyl disulfide. Diphenyl diselenide was also reduced in a similar catalytic manner to give adduct **2** in 56 % yield (temperature: 50°C).

Although the details of the mechanism of the reduction are not clear, it seems likely that the present reaction involves the nucleophilic attack of HSe^- at the selenium atom of diphenyl diselenide from an analogy of the reductions[14] of disulfides into thiols with some nucleophiles such as cyanide ion,[15] phosphines,[16] thiolates,[17] and sodium hydrogen selenide.[18] A possible catalytic cycle for the present reduction is shown in Scheme 1.



Scheme 1

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(1) See, for example: (a) W. Reppe and H. Vetter, Justus Liebigs Ann. Chem., **582**, 133

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(7) For the reactions of H_2Se obtained from different routes, see for example: (a) V. I. Cohen, *Synthesis*, 668 (1978); (b) V. I. Cohen, *J. Org. Chem.*, **42**, 2510 (1977); (c) D. L. Klayman and T. S. Griffin, *J. Am. Chem. Soc.*, **95**, 197 (1973).

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(9) For reviews, see: (a) D. L. Klayman and W. H. H. Günther (Eds), "*Organic Selenium Compounds: Their Chemistry and Biology*", Wiley, New York, 80 (1973); (b) D. Liotta, *Acc. Chem. Res.*, **17**, 28 (1984); (c) N. Sonoda and A. Ogawa, in "*The Chemistry of Organic Selenium and Tellurium Compounds*", Vol. 1, S. Patai and Z. Rappoport (Eds), Wiley, pp 619 (1986).

(10) A typical procedure for isolation of thiol and selenol is as follows: A mixture of disulfide or diselenide (10 mmol), selenium (0.78 g, 10 mmol), water (2 mL, 112 mmol), N-methylpyrrolidine (2 mL), and THF (7 mL) was stirred at 70°C for 15 h under 20 atm of carbon monoxide. The resulting mixture was acidified under nitrogen. Extraction with ether and distillation gave thiol (56-57°C/15 mmHg) or selenol (45-45.5°C/4.5 mmHg).

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(13) The reaction was accompanied by the concomitant formation of bis(3-oxo-butyl) selenide, which might have been produced by the reaction of hydrogen selenide with methyl vinyl ketone.

(14) It was suggested by using kinetic technique that reduction of disulfides to thiols involved the nucleophilic attack of cyanide ion,[15] phosphines,[16] thiolates,[17] or sodium hydrogen selenide,[18] to the sulfur atom of disulfides.

(15) D. A. R. Happer, J. W. Mitchell, and G. J. Wright, *Aust. J. Chem.*, **26**, 121 (1973).

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