Selective Reduction of α,β-Unsaturated Carbonyl Compounds with Carbon Monoxide and Water Assisted by Selenium

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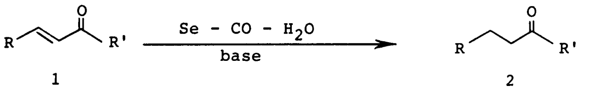
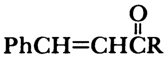
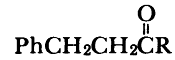
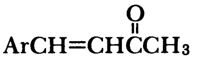
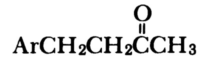
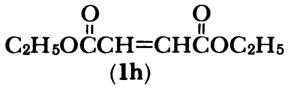
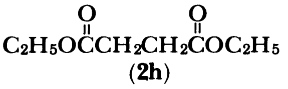
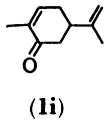
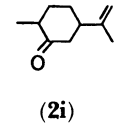
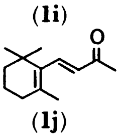
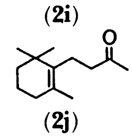
Synopsis. Carbon–carbon double bond of α,β-unsaturated carbonyl compounds can be reduced selectively with hydrogen selenide, generated in situ by the reaction of elemental selenium with carbon monoxide and water in the presence of strongly basic tertiary amine.

Recently we have developed a new reduction system, in which hydrogen selenide or its amine salt, formed in situ by the reaction of selenium with carbon monoxide and water, acts as an active reducing species.[1] The advantage of the utilization of this reduction system is to use strongly toxic hydrogen selenide[2] safely for reduction of organic compounds.[3] Now we have found that the Se–CO–H_2O reaction system is successfully usable for the selective reduction of the olefinic linkage of various α,β-unsaturated carbonyl compounds (Eq. 1).

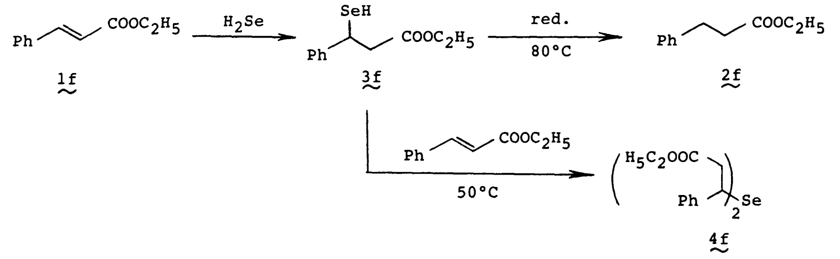

(1)

When benzylideneacetone (**1a**) was treated with carbon monoxide, water, and an equivalent amount of selenium in the presence of 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU)[4] at 50 °C, reduction of the carbon–carbon double bond took place selectively to give 4-phenyl-2-butanone (**2a**) in 82% yield. It was confirmed that similar reduction was widely applicable for the reduction of various α,β-unsaturated carbonyl compounds, and the results are summarized in Table 1. Enones having furyl or thienyl group undergo selective reduction without affecting the furyl or thienyl group (Runs 3 and 4). Reduction of α,β-unsaturated carboxylic acid (Run 5), ester (Run 6), and nitrile (Run 7) also proceeds at somewhat higher temperatures (80—100 °C). In the case of α,β-unsaturated aldehydes such as cinnamaldehyde, the similar reduction did not take place under the conditions employed.[5] Interestingly, enone (**1i**), which has no aromatic ring at the β position, underwent reduction of only conjugated C–C double (Run 9).[6] β-Ionone was reduced to 4-(2,6,6-trimethyl-

Table 1. Selective Reduction of α,β-Unsaturated Carbonyl Compounds[a]

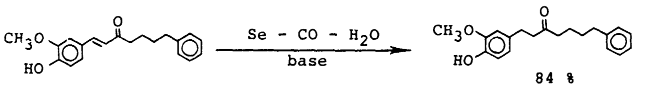
Run	Substrate		Product	Yield/%[b]
	 $\mathrm{PhCH{=}CH\overset{O}{\overset{\|}{C}}R}$		 $\mathrm{PhCH_2CH_2\overset{O}{\overset{\|}{C}}R}$	
1	R=CH_3	(**1a**)	(**2a**)	82 (84)[c]
2	R=Ph	(**1b**)	(**2b**)	87
	 $\mathrm{ArCH{=}CH\overset{O}{\overset{\|}{C}}CH_3}$		 $\mathrm{ArCH_2CH_2\overset{O}{\overset{\|}{C}}CH_3}$	
3	Ar= 	(**1c**)	(**2c**)	75 (74)[c]
4	Ar= 	(**1d**)	(**2d**)	71
	PhCH=CH-X		$PhCH_2CH_2X$	
5[d]	X=COOH	(**1e**)	(**2e**)	93
6[e]	X=$COOC_2H_5$	(**1f**)	(**2f**)	89
7[f]	X=CN	(**1g**)	(**2g**)	72
8	 $\mathrm{C_2H_5O\overset{O}{\overset{\|}{C}}CH{=}CH\overset{O}{\overset{\|}{C}}OC_2H_5}$ (**1h**)		 $\mathrm{C_2H_5O\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OC_2H_5}$ (**2h**)	86
9	 (**1i**)		 (**2i**)	85
10	 (**1j**)		 (**2j**)	83

a) Reaction conditions described in the text was used. b) Isolated yield. c) The yields in the parentheses obtained by the reaction using *N*-methylpyrrolidine (20 mmol) at 80 °C for 24 h. d) DBU (10 mmol), 100 °C. e) H_2O (10 mmol), 80 °C. f) 80 °C.



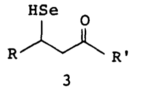
Scheme 1.

1-cyclohexenyl)-2-butanone (**2j**) in good yield (Run 10). This method is effective for the conversion of yakuchinone B (**1k**) to yakuchinone A (**2k**), both of which are linear diarly heptanoids with high pungency (Eq. 2).



(1k) (2k) (2)

Although the mechanism of the reduction is not fully clarified, the reaction proceeds most probably through the Michael adduct **3** formed in situ by the



3

addition of hydrogen selenide to α,β-unsaturated carbonyl compound **1**. The formation of **3** is supported by the following observation: when the reaction of ethyl cinnamate (**1f**) with carbon monoxide, water, and selenium was carried out under controlled conditions (see Experimental section), the selenide **4f** was mainly formed probably through the Michael adduct **3f** (Scheme 1).

A number of methods have been reported for selective reduction of α,β-unsaturated carbonyl compounds: for example, catalytic hydrogenation using metal catalysts,[7] reduction with metal hydrides,[8] and reduction with metal or metal alloy.[9] However, high functional selectivity demonstrated in the text makes the present method more attractive.

Experimental

Instruments. The Instruments Used Were as Follows: ^{1}H NMR JEOL JNM-PS-100 and JEOL JNM-GXS-400; ^{13}C NMR Hitachi R-90H; IR, JASCO A-202; MS, Hitachi RMU-6A and JEOL JMS-QH100; melting points, Yanagimoto micro melting point apparatus.

Materials. Metallic selenium (99%) of Wako Chem. Co. and carbon monoxide (99.9%) of Seitetsu Chem. Co. were used. α,β-Unsaturated ketones (**1b**,[10] **1c**,[11] and **1k**[12]) were prepared according to the literatures. Preparation of **1d** was described below. Tetrahydrofuran (THF), amines, and other α,β-unsaturated carbonyl compounds were all purchased from commercial sources and purified by distillation or recrystallization.

4-(2-Thienyl)-3-buten-2-one (1d). To a mixture of 2-thiophenecarbaldehyde (22.4 g, 200 mmol), acetone (26.3 g, 453 mmol), and water (150 mL) was added 33% sodium hydroxide solution (3.8 mL) at 0 °C, and the mixture was stirred for 4 h at room temperature. The reaction mixture was neutralized with dilute sulfuric acid (10%). The organic layer was separated and dried over $MgSO_4$. The solvent was evaporated and the resulting liquid was distilled to give 24.1 g (79%) of 4-(2-thienyl)-3-buten-2-one (**1d**): bp 103—104 °C/6 mmHg (1 mmHg≈133.322 Pa). IR (NaCl) 1660, 1610, 960, 700 cm^{-1}; ^{1}H NMR δ=2.24 (s, 3H), 6.40 (d, *J*=16 Hz,1H), 6.84—7.40 (c, 3H), 7.53 (d, *J*=16 Hz,1H); MS (*m/z*) 152 (M$^+$).

Typical Procedure for Reduction of α,β-Unsaturated Carbonyl Compounds. A stirred mixture of benzylideneacetone (1.46 g, 10 mmol), selenium (0.79 g, 10 mmol), water (1.8 mL, 100 mmol), DBU (3.0 mL, 20 mmol), and THF (5 mL) sealed in a 50 mL stainless steel autoclave was heated under the pressure of carbon monoxide (30 atm; initial pressure at 25 °C) at 50 °C for 24 h. After the reaction was complete, carbon monoxide was purged in a well-ventilated hood, and air was blown into the solution for 10 min in order to oxidize the remaining hydrogen selenide to elemental selenium. Selenium deposited was filtered off and the filtrate was acidified with aqueous hydrochloric acid (2 M; 1 M=1 mol dm^{-3}) to pH 1—2, followed by extracted with diethyl ether (4×50 mL) and benzene (50 mL). The combined extracts were dried over $MgSO_4$. After the filtration, the solvent was evaporated in vacuo to leave yellow oil of crude material, which was chromatographed on silica gel (benzene/Et_2O=1:1) to give 1.22 g (82%) of 4-phenyl-2-butanone (**2a**): IR (neat) 1700, 740, 700 cm^{-1}; ^{1}H NMR δ=1.96, (s, 3H), 2.62 (t, *J*=7 Hz, 2H), 2.68 (t, *J*=7 Hz, 2H), 6.96—7.10 (m, 5H); MS (*m/z*) 148 (M$^+$).

Reduction of other α,β-unsaturated carbonyl compounds (**1b**—**1k**) and the following isolation were performed with the similar procedure described above, and the spectral data of the reduced products (**2b**—**2k**) were shown below. All products were identified by comparison of their ^{1}H NMR, IR, and mass spectra with those of samples commercially available or synthesized independently.

1,3-Diphenyl-1-propanone (2b). IR (neat) 1675, 740, 690 cm^{-1}; ^{1}H NMR (CCl_4) δ=2.76—3.17 (c, 4H), 6.90—7.40 (c, 8H), 7.78 (dd, *J*=8 and 2 Hz, 2H); MS (*m/z*) 210 (M$^+$); mp 71.5—73 °C (lit,[7a] 72—73 °C).

4-(2-Furyl)-2-butanone (2c). IR (neat) 1715, 730 cm^{-1}; ^{1}H NMR (CCl_4) δ=2.03 (s, 3H), 2.72 (t, *J*=8 Hz, 2H), 2.79 (t, *J*=8 Hz, 2H), 5.85—5.98 (m, 1H), 6.10—6.24 (m, 1H), 7.15—7.29 (m, 1H); MS (*m/z*) 138 (M$^+$).

4-(2-Thienyl)-2-butanone (2d). IR (neat) 1710, 695 cm^{-1}; ^{1}H NMR (CCl_4) δ=2.10 (s, 3H), 2.62 (t, *J*=8 Hz, 2H), 2.94 (t, *J*=8 Hz, 2H), 6.60—7.00 (c, 3H); MS (*m/z*) 154 (M$^+$).

3-Phenylpropionic Acid (2e). IR (KBr) 3500—2800, 1710, 735, 695 cm^{-1}; ^{1}H NMR (CCl_4) δ=2.50 (t, *J*=7 Hz, 2H), 2.82 (t, *J*=7 Hz, 2H), 7.02—7.24 (m, 5H), 11.68 (s, broad, 1H); MS (*m/z*) 150 (M$^+$); mp 47—48.5 °C (lit,[13] 47—49 °C).

Ethyl 3-Phenylpropionate (2f). IR (neat) 1720, 1180, 740, 695 cm^{-1}; ^{1}H NMR (CCl_4) δ=1.12 (t, *J*=8 Hz, 3H), 2.45 (t, *J*= 8 Hz, 2H), 2.82 (t, *J*= 8 Hz, 2H), 3.99 (q, *J*=8Hz, 2H), 7.00—7.35 (m, 5H); MS (*m/z*) 178 (M$^+$).

3-Phenylpropiononitrile (2g). IR (neat) 2240, 745, 695 cm^{-1}; ^{1}H NMR (CCl$_2$) δ=2.30 (t, J=8 Hz, 2H), 2.68 (t, J=8 Hz, 2H), 6.94—7.26 (m, 5H); MS (m/z) 131 (M$^+$).

Diethyl Succinate (2h). IR (neat) 1720, 1150 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=1.34 (t, J=12 Hz, 6H), 2.54 (s, 4H), 4.18 (q, J=12 Hz, 4H); MS (m/z) 174 (M$^+$).

Dihydrocarvone (2i). IR (neat) 1710, 1650 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=1.00—1.20 (m, 3H), 1.35—2.10 (c, 8H), 2.15—2.85 (m, 3H), 4.80—4.95 (m, 2H); MS (m/z) 152 (M$^+$).

4-(2,6,6-Trimethyl-1-cyclohexenyl)-2-butanone (2j). IR (neat) 1720, 1365, 1165 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=1.00 (s, 6H), 1.40—2.15 (c, 8H), 1.57 (s, 3H), 2.15 (s, 3H), 2.25—2.55 (m, 2H); MS (m/z) 194 (M$^+$).

1-(3-Hydroxy-4-methoxyphenyl)-7-phenyl-3-heptanone (Yakuchinone A) (2k). IR (neat) 3560, 1710, 1275 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.51—1.62 (m, 4H), 2.38 (t, J=8 Hz, 2H), 2.58 (t, J=8 Hz, 2H), 2.60—2.90 (m, 4H), 3.82 (s, 3H), 5.50 (s, broad, 1H), 6.61 (dd, J=2,8 Hz, 1H), 6.73 (d, J=2 Hz, 1H), 6.78 (d, J=8 Hz, 1H), 7.00—7.40 (m, 5H); MS (m/z) 312 (M$^+$).

Isolation of Monoselenide (4f). A stirred mixture of ethyl cinnamate (**1f**) (1.76 g, 10 mmol), selenium (10 mmol), water (10 mmol), *N*-methylpyrrolidine[14] (20 mmol), and THF (5 mL) was heated under CO (30 atm) at 50 °C for 24 h. By a similar workup and purification as described above, the selenide (**4f**) was obtained in 84% yield as a mixture of its diastereoisomers whose IR, ^{1}H NMR, ^{13}C NMR, and mass spectrum are listed. Owing to thermal instability of the selenide, confirmation of their structures by elemental analyses was unsuccessful. IR (neat) 1730 (C=O), 1250, 1180 cm^{-1}; ^{1}H NMR (CCl$_4$) δ=1.10 (t, J=7.1 Hz, 3.6H), 1.15 (t, J=7.1 Hz, 2.4H), 2.76—2.98 (m, 2H), 3.94—4.07 (m, 4H), 4.18 (dd, J=7.3 and 8.4 Hz, 1.2H), 4.43 (dd, J=7.8 and 8.1 Hz, 0.8H), 7.11—7.29 (m, 10H); ^{13}C NMR (CDCl$_3$) δ=13.9 ($\underline{\mathrm{C}}\mathrm{H_3CH_2}$–), 39.3 and 39.5 ($\underline{\mathrm{C}}$–C=O), 41.5 and 41.8 ($\underline{\mathrm{C}}$–Se), 60.2 (O–$\underline{\mathrm{C}}$). 126.8, 127.0, 127.3, 127.6, 128.2, 141.6 (Ph), 170.1 and 170.2 ($\underline{\mathrm{C}}$=O); MS (m/z) 434 (M$^+$,^{80}Se).

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2) Hydrogen selenide is regarded to be high toxic and unstable against air. To overcome these inconvenience, in situ formation and utilization without isolation are available. Cf. V. I. Cohen, *Synthesis*, **1978**, 668. D. L. Klayman and T. G. Griffin, *J. Am. Chem. Soc.*, **95**, 197 (1973). T. S. Woods and D. L. Klayman, *J. Org. Chem.*, **39**, 3716 (1974). A. Ogawa, J. Miyake, Y. Karasaki, S. Murai, and N. Sonoda, *ibid.*, **50**, 384 (1985). A. Ogawa, J. Miyake, N. Kambe, S. Murai, and N. Sonoda, *Bull. Chem. Soc. Jpn.*, **58**, 1448 (1985).

3) Y. Nishiyama, H. Hamanaka, A. Ogawa, S. Murai, and N. Sonoda, *Synthetic Commun.*, **16**, 1059 (1986). Y. Nishiyama, S. Hamanaka, A. Ogawa, N. Kambe, and N. Sonoda, *J. Org. Chem.*, **53**, 1326 (1988). A. Ogawa, Y. Nishiyama, N. Kambe, S. Murai, and N. Sonoda, *Tetrahedron Lett.*, **28**, 3271 (1987).

4) The reduction also proceeded in the presence of tertiary amine such as *N*-methylpyrrolidine.

5) When the reduction of cinnamaldehyde was carried out under the similar conditions as described in the text, side reactions took place to afford a complex mixture.

6) In the case of methyl vinyl ketone, the Michael adduct [bis(3-oxo-butyl) selenide] was formed as a main product.

7) See for example: R. Adams, J. W. Kern, and R. L. Shriner, *Org. Synth.*, Coll. Vol. 1, 101 (1956). H. Adkins and R. Connor, *J. Am. Chem. Soc.*, **53**, 1091 (1931). C. Djerassi and J. Gutzwiller, *ibid.*, **88**, 4537 (1966). R. E. Harmon, J. L. Parsons, D. W. Cooke, S. K. Gupta, and J. Schoolenberg, *J. Org. Chem.*, **34**, 3684 (1969). R. L. Augustine, D. C. Migliorine, R. E. Foscante, C. S. Sodano, and M. J. Sisbarro, *ibid.*, **34**, 1075 (1969).

8) See for example: R. W. Goetz and M. Orchin, *J. Am. Chem. Soc.*, **85**, 2782 (1963). J. P. Collman, R. G. Finke, P. L. Matlock, R. G. Wahren, and J. I. Brauman, *ibid.*, **100**, 1119 (1978). R. Noyori, I. Umeda, and T. Ishigami, *J. Org. Chem.*, **37**, 1542 (1972). M. F. Semmelhack and R. D. Stauffer, *ibid.*, **40**, 3619 (1975). M. Yamashita, Y. Kato, and R. Suemitsu, *Chem. Lett.*, **1980**, 847.

9) See for example: M. Contento, D. Saroia, C. Trombini, and A. Umani-Ronochi, *Synthesis*, **1979**, 30. N. A. Cortese and R. F. Heck, *J. Org. Chem.*, **43**, 3985 (1978). G. A. Page and D. S. Tarbell, *Org. Synth.*, Coll. Vol. 4, 136 (1963).

10) S. Wattanasin and W. S. Murphy, *Synthesis*, **1980**, 647.

11) G. J. Leuck and L. Cejka, *Org. Synth.*, Coll. Vol. 1, 283 (1956).

12) H. Itokawa, R. Aiyama, and A. Ikuta, *Chem. Pharm. Bull.*, **31**, 2491 (1983).

13) Catalog Handbook of Fine Chemicals, Aldrich; Aldrich Chemical Company: 1986—1987; p. 739.

14) Monoselenide was also formed in the case using DBU as a base.