Supporting Information for

Carbonylation of Lithium Enolates with Carbon Monoxide Mediated by Selenium

Shin-ichi Fujiwara,^{*,†} Akira Nishiyama,[‡] Tsutomu Shin-ike,[†]
Nobuaki Kambe,[‡] and Noboru Sonoda^{*,§}

[†]*Department of Chemistry, Osaka Dental University
Hirakata, Osaka 573-1121, Japan*

[‡]*Department of Molecular Chemistry, Graduate School of Engineering
Osaka University, Suita, Osaka 565-0871, Japan*

[§]*Department of Applied Chemistry, Faculty of Engineering
Kansai University, Suita, Osaka 564-8680, Japan*

General.

THF was distilled from sodium benzophenone ketyl. HMPA and hexamethyldisilazane were fractionally distilled and dried over calcium hydride. Ketones and MeI were distilled from P₂O₅. BuLi, MeLi, and selenium are commercially available and were used as received. Trimethylsilyl enol ethers were prepared according to the method of House.^{s1}

¹H and ¹³C NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz and 68 MHz, respectively) spectrometer using Me₄Si as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Column chromatography and preparative TLC were conducted by using Fuji Silysia silica gel WB-300 (100-250 mesh) and Wakogel B-5F silica gel (325 mesh), respectively. HPLC separations were performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using CHCl₃ as eluent. Mass spectra (CI) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus.

***Se*-Methyl 2-benzoylselenopropanoate (2a):** Typical procedure for carbonylation of lithium enolates of ketones. Selenium (2.4 mmol) was added to a THF (15 mL) solution of LHMDs, prepared from BuLi (1.60 M in hexane, 1.5 mL, 2.4 mmol) and hexamethyldisilazane (2.6 mmol), at -78 °C under argon. After 5 min, dry ice-EtOH bath was removed. A black suspension was obtained within 10 min and the suspension was cooled again to -78 °C. To the suspension was added dropwise propiophenone (**1a**, 2.0 mmol) in THF (10 mL) over 10 min, and the stirring was continued for additional 20 min. The reaction mixture was then warmed to -23 °C and argon was replaced with CO. After 2 h, MeI (4.0 mmol) was added at the same temperature, and the mixture was warmed to room temperature. Aqueous saturated NH₄Cl solution (100 mL) was added and the product was extracted with Et₂O (50 mL). After the organic layer was dried over MgSO₄, evaporation of the solvent gave a yellow residue. Purification by bulb-to-bulb distillation (Kugelrohr, 160-165 °C/2 mmHg) yielded 390 mg (76%) of **2a** as a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.55 (d, *J* = 6.8 Hz, 3 H), 2.22 (s, 3 H), 4.72 (q, *J* = 6.8 Hz, 1 H), 7.48 (dd, *J* = 7.3, 7.8 Hz, 2 H), 7.60 (t, *J* = 7.3 Hz, 1 H), 8.01 (d, *J* = 7.8 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.5, 14.8, 56.7, 128.8, 128.9, 133.7, 135.9, 194.7, 199.3; IR (neat) 1698, 1676 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 257 (*M*⁺+1, 100), 161 (49), 105 (18). Anal. Calcd for C₁₁H₁₂O₂Se: C, 51.78; H, 4.74. Found: C, 51.84; H, 4.87.

***Se*-Methyl 2-benzoyl-2-methylselenopropanoate (2b).** The residue was purified by column chromatography on silica gel using *n*-hexane-Et₂O (20:1, v/v) to give **2b** (467 mg, 87 %) as a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.60 (s, 6 H), 2.27 (s, 3 H), 7.43 (dd, *J* = 7.3, 7.8 Hz, 2 H), 7.53 (t, *J* = 7.3 Hz, 1 H), 7.86 (d, *J* = 7.8 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.1, 24.3, 64.2, 128.4, 129.2, 132.7, 134.8, 197.8, 205.1; IR (neat) 1694, 1674 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 271 (*M*⁺+1, 40), 175 (100), 105 (11). Anal. Calcd for C₁₂H₁₄O₂Se: C, 53.54; H, 5.24. Found: C, 53.56; H, 5.40.

Se-Methyl 2,2,4-trimethyl-3-oxoselenopentanoate (2c). The residue was purified by bulb-to-bulb distillation (Kugelrohr, 110-115 °C/2.5 mmHg) to give **2c** (397 mg, 85 %) as a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.06 (d, *J* = 6.8 Hz, 6 H), 1.44 (s, 6 H), 2.23 (s, 3 H), 2.95 (sept, *J* = 6.8 Hz, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.0, 20.4, 22.0, 36.8, 66.3, 204.5, 211.7; IR (neat) 1719, 1682 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 237 (M⁺+1, 91), 141 (100), 71 (14). Anal. Calcd for C₉H₁₆O₂Se: C, 45.96; H, 6.86. Found: C, 46.05; H, 6.97.

Se-Methyl 2-methyl-3-oxoselenopentanoate (2d). The residue was purified by bulb-to-bulb distillation (Kugelrohr, 85-95 °C/2.5 mmHg) to give **2d** (209 mg, 50 %) as a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.06 (t, *J* = 7.3 Hz, 3 H), 1.39 (d, *J* = 7.3 Hz, 3 H), 2.26 (s, 3 H), 2.42-2.72 (m, 2 H), 3.85 (q, *J* = 7.3 Hz, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.5, 7.7, 13.6, 35.1, 64.5, 199.5, 204.8; IR (neat) 1725, 1690 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 209 (M⁺+1, 74), 113 (100). Anal. Calcd for C₇H₁₂O₂Se: C, 40.59; H, 5.84. Found: C, 40.71; H, 6.08.

Se-Methyl 2-oxocyclohexaneselenocarboxylate (2e). The residue was purified by column chromatography on silica gel using *n*-hexane-Et₂O (20:1, v/v) to give **2e** (180 mg, 41%) as a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.60-1.75 (m, 4 H), 2.22 (s, 3 H), 2.26 (brs, 2 H), 2.35 (brs, 2 H), 12.78 (s, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 4.4, 21.2, 22.5, 23.1, 29.2, 109.2, 169.4, 199.5; IR (neat) 1618 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 221 (M⁺+1, 57), 125 (100). Anal. Calcd for C₈H₁₂O₂Se: C, 43.84; H, 5.52. Found: C, 43.69; H, 5.54.

Carbonylation of lithium enolate 3a of cyclohexanecarboxaldehyde starting from trimethylsiloxymethynecyclohexane at -23 °C. MeLi (1.10 M in Et₂O, 2.0 mL, 2.2 mmol) was added to a THF (25 mL) solution of trimethylsiloxymethynecyclohexane (2.0 mmol) at 20 °C under Ar. After 30 min, the solution was cooled to -23 °C and selenium (2.4 mmol) and HMPA (6.0 mmol) was added. The stirring was continued for additional 30 min, and then the reaction vessel was purged with CO. After CO absorption ceased (60 min), MeI (4.0 mmol) was added at the same temperature, and the mixture was warmed up to room temperature. Aqueous saturated

NH₄Cl solution (100 mL) was added and the product was extracted with Et₂O (50 mL). After the organic layer was dried over MgSO₄, evaporation of the solvent gave a yellow residue. Purification by PTLC using *n*-hexane-Et₂O (10:1, v/v) yielded *Se*-methyl 1-formylcyclohexaneselenocarboxylate (**4a**, 78 mg, 16%) and *Se*-methyl *O*-methyne-cyclohexaneselenocarbonate (**5a**, 319 mg, 64%). **Data for 4a**: a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.39-1.65 (m, 6 H), 1.96-2.08 (m, 4 H), 2.24 (s, 3 H), 9.51 (s, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.1, 22.3, 25.0, 29.2, 69.3, 198.4, 201.9; IR (neat) 1731, 1678 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 235 (M⁺+1, 42), 217 (17), 139 (100), 111 (29). Anal. Calcd for C₉H₁₄O₂Se: C, 46.36; H, 6.05. Found: C, 46.23; H, 6.14. **Data for 5a**: a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 1.54 (br, 6 H), 2.03 (brs, 2 H), 2.22 (brs, 2 H), 2.28 (s, 3 H), 6.86 (s, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 6.5, 26.1, 26.4, 26.7, 27.8, 30.3, 126.9, 128.9, 165.8; IR (neat) 1721 cm⁻¹; MS (CI), *m/z* (relative intensity, %) 235 (M⁺+1, 84). Anal. Calcd for C₉H₁₄O₂Se: C, 46.36; H, 6.05. Found: C, 46.17; H, 6.19.

Carbonylation of lithium enolate 3b of isobutyraldehyde starting from 1-trimethylsiloxy-2-methylpropene at -23 °C. MeLi (1.10 M in Et₂O, 2.0 mL, 2.2 mmol) was added to a THF (25 mL) solution of 1-trimethylsiloxy-2-methylpropene (2.0 mmol) at 20 °C under Ar. After 30 min, the solution was cooled to -23 °C and selenium (2.4 mmol) and HMPA (6.0 mmol) was added. The stirring was continued for additional 30 min, and then the reaction vessel was purged with CO. After CO absorption ceased (30 min), BuI (4.0 mmol) was added at the same temperature, and the mixture was warmed up to room temperature. Aqueous saturated NH₄Cl solution (100 mL) was added and the product was extracted with Et₂O (50 mL). After the organic layer was dried over MgSO₄, evaporation of the solvent gave a yellow residue. Purification by PTLC using *n*-hexane-Et₂O (10:1, v/v) yielded *Se*-butyl 2,2-dimethyl-3-oxoselenopropionate (**4b**, 183 mg, 38%) and *Se*-butyl *O*-(2-methylpropene) selenocarbonate (**5b**, 141 mg, 29%). **Data for 4b**: a pale yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.30-1.50 (m, 8 H, including singlet at δ 1.40 (6 H)), 1.65 (q, *J* = 7.3 Hz, 2 H), 2.95 (t, *J* = 7.3 Hz, 2 H), 9.64 (s, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 13.5, 20.0, 23.1, 25.6, 32.3, 64.4, 198.5, 203.6; IR (NaCl) 1735,

1678 cm^{-1} ; MS (CI), m/z (relative intensity, %) 237 ($M^+ + 1$, 100), 209 (61). Anal. Calcd for $\text{C}_9\text{H}_{16}\text{O}_2\text{Se}$: C, 45.96; H, 6.86. Found: C, 45.83; H, 7.02. **Data for 5b**: a pale yellow oil; ^1H NMR (270 MHz, CDCl_3) δ 0.93 (t, $J = 7.4$ Hz, 3 H), 1.42 (sext, $J = 7.4$ Hz, 2 H), 1.64 (s, 3 H), 1.68 (s, 3 H), 1.72 (quint, $J = 7.4$ Hz, 2 H), 2.93 (t, $J = 7.4$ Hz, 2 H), 6.86 (s, 1 H); ^{13}C NMR (68 MHz, CDCl_3) δ 13.5, 15.7, 19.4, 22.9, 27.1, 32.5, 119.2, 130.8, 165.7; IR (neat) 1721 cm^{-1} ; MS (CI), m/z (relative intensity, %) 237 ($M^+ + 1$, 100). HRMS (CI) calcd for $\text{C}_9\text{H}_{17}\text{O}_2\text{Se}$: 237.0394. Found: 237.0375.

Carbonylation of lithium enolate of cyclohexyl methyl ketone 1f starting from trimethylsiloxyethylidenecyclohexane. MeLi (1.10 M in Et_2O , 2.0 mL, 2.2 mmol) was added to a THF (25 mL) solution of trimethylsiloxyethylidenecyclohexane (2.0 mmol) at 20 $^\circ\text{C}$ under Ar. After 30 min, the solution was cooled to -23 $^\circ\text{C}$ and selenium (2.4 mmol) and HMPA (6.0 mmol) was added. The stirring was continued for additional 30 min, and then the reaction vessel was purged with CO. After CO absorption ceased (60 min), MeI (4.0 mmol) was added at the same temperature, and the mixture was warmed up to room temperature. Aqueous saturated NH_4Cl solution (100 mL) was added and the product was extracted with Et_2O (50 mL). After the organic layer was dried over MgSO_4 , evaporation of the solvent gave a yellow residue. Purification by preparative HPLC yielded *Se*-methyl 1-acetylcyclohexanecarboxoselenoate (**2f**, 303 mg, 63%) as a pale yellow oil; ^1H NMR (270 MHz, CDCl_3) δ 1.35-1.45 (m, 3 H), 1.45-1.58 (m, 4 H), 2.00-2.09 (m, 4 H), 2.13 (s, 3 H), 2.22 (s, 3 H); ^{13}C NMR (68 MHz, CDCl_3) δ 5.0, 22.8, 25.2, 26.0, 31.2, 71.4, 203.8, 204.5; IR (neat) 1714, 1681 cm^{-1} ; MS (CI), m/z (relative intensity, %) 249 ($M^+ + 1$, 16), 153 (100), 125 (23). Anal. Calcd for $\text{C}_{10}\text{H}_{16}\text{O}_2\text{Se}$: C, 48.59; H, 6.53. Found: C, 48.58; H, 6.73.

Reference

- (1) (a) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324. (b) Ito, Y.; Fujii, S.; Nakatsuka, M.; Kawamoto, F.; Saegusa, T. *Organic Syntheses*; Wiley: New York, 1988; Coll. Vol. 6, pp 327-333.