

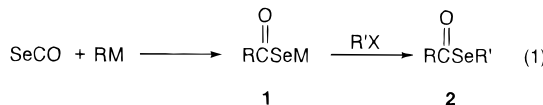
A New Synthesis of Selenol Esters via Carbophilic Addition of Organocopper Reagents to Carbonyl Selenide

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Carbonyl sulfide (SCO) reacts with Grignard reagents exclusively at the carbonyl carbon¹ and has been used for introduction of a thiocarboxyl unit into organic molecules.^{2,3} Although carbonyl selenide (SeCO)⁴ has potential synthetic utility as the most straightforward selenocarboxylation reagent, practical use of SeCO has been limited only to the synthesis of ureas and carbamates by the reaction with amines and amino alcohols, respectively.⁵ This is mostly because, in contrast to the thiocarbonyl compounds,^{6–16} selenocarbonyl compounds are prone to undergo selenophilic addition when treated with organolithiums or Grignard reagents.^{17–23} Here we report the selenocarboxylation with SeCO via carbophilic addition of organocopper reagents (eq 1).



It is reported, for example, that PhLi attacks only at the selenium atom of 1,1,3,3-tetramethylindane-2-selone^{18a} and 2,6-xylyl isoselenocyanate²¹ even though the corresponding thio analogues predominantly or exclusively give carbophilic products. This is also the case for SeCO, *i.e.*, the simple carbophilic addition of organometallic reagents (RM) to SeCO expressed by eq 1 hardly proceeds when organolithiums or Grignard reagents are used.

Indeed, the reaction of SeCO with an equimolar amount of PhLi at –78 °C resulted in selenophilic attack with concomitant elimination of CO giving rise to PhSeBn

(10) (a) Beak, P.; Yamamoto, J.; Upton, C. J. *J. Org. Chem.* **1975**, *40*, 305. (b) Walter, W.; Lüke, H.-W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 535. (c) Karakasa, T.; Hanzawa, T.; Motoki, S. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3469. (d) Tominaga, Y.; Kohra, S.; Hosomi, A. *Tetrahedron Lett.* **1987**, *28*, 1529.

(11) (a) Walter, W.; Bode, K.-D. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 447. (b) Entenmann, G. *Chem. Ztg.* **1977**, *101*, 508. (c) Gosselin, P.; Masson, S.; Thuillier, A. *Tetrahedron Lett.* **1978**, 2715. (d) Ito, Y.; Kobayashi, K.; Saegusa, T. *Tetrahedron Lett.* **1979**, 1039. (e) Krapcho, A. P.; Stephens, W. P. *J. Org. Chem.* **1980**, *45*, 1106. (f) Kelly, T. R.; Echavarren, A.; Chandrakumar, N. S.; Köksal, Y. *Tetrahedron Lett.* **1984**, *25*, 1217. (g) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 5251. (h) Ares, J. J. *Synth. Commun.* **1991**, *21*, 625.

(12) (a) Jensen, K. A.; Henriksen, L. *Acta Chem. Scand.* **1968**, *22*, 1107. (b) Meijer, J.; Ruitenberg, K.; Westmijze, H.; Vermeer, P. *Synthesis* **1981**, 551. (c) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 2623. (d) Verkruisje, H. D.; Brandsma, L. *J. Organomet. Chem.* **1987**, *332*, 95. (e) Ali, S. M.; Tanimoto, S. *J. Org. Chem.* **1989**, *54*, 5603. Only one example of thiophilic attack: (f) Okazaki, R.; Fujii, T.; Inamoto, N. *J. Chem. Soc., Chem. Commun.* **1984**, 1010.

(13) (a) Narasimhan, L.; Sanitra, R.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1978**, 719. (b) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Veale, C. A.; Furst, G. T. *J. Am. Chem. Soc.* **1987**, *109*, 2504.

(14) (a) Seebach, D. *Chem. Ber.* **1972**, *105*, 487. (b) Nilsson, N. H.; Senning, A. *Chem. Ber.* **1974**, *107*, 2345. (c) Saquet, M. C. R. *Acad. Sci., Ser. C* **1976**, *283*, 641.

(15) Schumann, E.; Walter, W. *Chem. Ber.* **1974**, *107*, 3562.

(16) (a) Barbaro, G.; Battaglia, A.; Giorgianni, P.; Maccagnani, G.; Macciantelli, D. *J. Chem. Soc., Perkin Trans. I* **1986**, 381. (b) Bonini, B. F.; Maccagnani, G.; Masiero, S.; Mazzanti, G.; Zani, P. *Tetrahedron Lett.* **1989**, *30*, 2677.

(17) Selenoketones,¹⁸ selenoaldehydes,¹⁹ selenoformates,²⁰ and isoselenocyanates²¹ react with organolithiums and Grignard reagents at both the carbon and selenium atoms depending on the nature of the nucleophile used. Only examples of the carbophilic attack are known for selenoamides²² and CSe₂.²³

(18) (a) Okazaki, R.; Ishii, A.; Inamoto, N. *Tetrahedron Lett.* **1984**, *25*, 5147. (b) Guzic, F. S., Jr.; SanFilippo, L. J.; Murphy, C. J.; Moustakis, C. A.; Cullen, E. R. *Tetrahedron* **1985**, *41*, 4843. (c) Ishii, A.; Okazaki, R.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 861.

(19) Okazaki, R.; Kumon, N.; Inamoto, N. *J. Am. Chem. Soc.* **1989**, *111*, 5949.

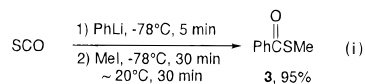
(20) (a) Okazaki, R.; Ishii, A.; Inamoto, N. *J. Chem. Soc., Chem. Commun.* **1986**, 71. (b) Ishii, A.; Okazaki, R.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2529.

(21) Maeda, H.; Kambe, N.; Sonoda, N.; Fujiwara, S.; Shin-ike, T. *Tetrahedron* **1996**, *52*, 12165.

(22) Sekiguchi, M.; Ogawa, A.; Fujiwara, S.; Ryu, I.; Kambe, N.; Sonoda, N. *Chem. Lett.* **1990**, 2053.

(23) Jensen, K. A.; Henriksen, L. *Acta Chem. Scand.* **1970**, *24*, 3213.

(24) The reaction of SCO with PhLi was examined in detail in order to compare the reactivities of SeCO and SCO. Thus, SCO was treated with PhLi under identical conditions as in run 1 of Table 1 by using MeI instead of BzBr; the corresponding thiol ester **3** was obtained in 95% yield via carbophilic attack without any thiophilic products (eq 1).



[†] Osaka University.

[‡] Current address: Department of Applied Chemistry, Faculty of Engineering, Kansai University, Suita, Osaka 564-8680, Japan.

(1) Weigert, F. *Chem. Ber.* **1903**, *36*, 1007.

(2) Thiocarboxylation towards carbon nucleophiles such as enolates (a, b), phosphorus ylides (c), and an acyllithium (d). (a) Demuynek, C.; Thuillier, A. *Bull. Soc. Chim. Fr.* **1969**, 2434. (b) Vedejs, E.; Nader, B. *J. Org. Chem.* **1982**, *47*, 3193. (c) Bestmann, H. J.; Saalbaum, H. *Bull. Soc. Chim. Belg.* **1979**, *88*, 951. (d) Seyferth, D.; Hui, R. C. *Tetrahedron Lett.* **1984**, *25*, 2623.

(3) Thiocarboxylation towards heteroatom nucleophiles such as alcoholates (a), phenolates (b), and amines (a). (a) Fém, R. *J. Chem. Rev.* **1957**, *57*, 621. (b) Chanyshv, N. T.; Kalaschnikov, S. M.; Kuramshin, E. M.; Naimushin, A. I.; Imashev, U. B. *Zh. Obshch. Khim.* **1990**, *60*, 2568; *Chem. Abstr.* **1991**, *115*, 28833r.

(4) For a high-yield synthesis of SeCO under mild conditions, see: Kondo, K.; Yokoyama, S.; Miyoshi, N.; Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 691.

(5) Kondo, K.; Yokoyama, S.; Miyoshi, N.; Murai, S.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 692.

(6) As for thiocarbonyl compounds, thioketones,⁷ thioaldehydes,⁸ and dithioesters^{7b,9} react with nucleophiles at both the carbon and sulfur atoms. Thioamides,¹⁰ isothiocyanates,¹¹ and CS₂¹² react at the carbon atom, but thioesters,¹³ trithiocarbonates,^{7b,14} thioketenes,¹⁵ and silyl thioketenes¹⁶ react at the sulfur atom.

(7) (a) Beak, P.; Worley, J. W. *J. Am. Chem. Soc.* **1970**, *92*, 4142. (b) Beak, P.; Worley, J. W. *J. Am. Chem. Soc.* **1972**, *94*, 597. (c) Dagonneau, M.; Vialle, J. *Tetrahedron* **1974**, *30*, 415. (d) Dagonneau, M.; Vialle, J. *Tetrahedron* **1974**, *30*, 3119. (e) Ohno, A.; Nakamura, K.; Shizume, Y.; Oka, S. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1003. (f) Masson, J.; Metzner, P.; Vialle, J. *Tetrahedron* **1977**, *33*, 3089. (g) Paquer, D.; Vazeux, M. *J. Organomet. Chem.* **1977**, *140*, 257.

(8) (a) Vedejs, E.; Perry, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 1683. (b) Okazaki, R.; Fukuda, N.; Oyama, H.; Inamoto, N. *Chem. Lett.* **1984**, 101. (c) Vedejs, E.; Perry, D. A.; Wilde, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 2985.

(9) Reactions of dithioesters with organolithium and Grignard reagents proceed in a thiophilic manner: (a) Léger, L.; Saquet, M. *Bull. Soc. Chim. Fr.* **1975**, 657. (b) Burgot, J.-L.; Masson, J.; Vialle, J. *Tetrahedron Lett.* **1976**, 4775. (c) Olsson, L.-I. *Acta Chem. Scand.* **1977**, *B31*, 639. (d) Meyers, A. I.; Tait, T. A.; Comins, D. L. *Tetrahedron Lett.* **1978**, 4657. (e) Metzner, P. *J. Chem. Soc., Chem. Commun.* **1982**, 335. (f) Bulpin, A. B.; Masson, S.; Sene, A. *Tetrahedron Lett.* **1989**, *30*, 3415. Reactions of dithioesters with allyl, benzyl, propargyl, and vinyl Grignard reagents proceed in a carbophilic manner: (g) Masson, S.; Saquet, M.; Thuillier, A. *Tetrahedron* **1977**, *33*, 2949. (h) Gosselin, P.; Masson, S.; Thuillier, A. *J. Org. Chem.* **1979**, *44*, 2807. Diorganocuprates react with dithioesters at the carbon atom: (i) Bertz, S. H.; Dabbagh, G.; Williams, L. M. *J. Org. Chem.* **1985**, *50*, 4414.

Table 1. Reaction of SeCO with Organometallic Reagents^a

run	RM	R'	2 (yield, %) ^b	others (yield, %) ^b
1	PhLi	Bn	(0)	PhSeBn (69) ^c
2	PhMgBr	Bn	(0)	PhSeBn (50) ^c
3	PhCu	Me	2a (55)	
4	Ph ₂ CuLi	Me	2a (37)	Ph ₂ CO (48)
5	Ph ₂ CuLi (0.5 equiv)	Me	2a (67)	Ph ₂ CO (<1)
6	PhCu(CN)Li	Me	2a (86)	
7	<i>p</i> -MeOC ₆ H ₄ Cu(CN)Li	Me	2b (80)	
8	<i>p</i> -MeC ₆ H ₄ Cu(CN)Li	Me	2c (65)	
9	<i>p</i> -ClC ₆ H ₄ Cu(CN)Li	Me	2d (84)	
10	<i>p</i> -CF ₃ C ₆ H ₄ Cu(CN)Li	Me	2e (77)	
11	1-naphthylCu(CN)Li	Me	2f (70)	
12	<i>t</i> -BuCu(CN)Li	Bu	2g (22)	
13	<i>t</i> -Bu ₂ CuLi	Bu	2g (54)	
14	Bu ₂ CuLi	Bu	2h (26)	
15	<i>s</i> -Bu ₂ CuLi	Bu	2i (11)	

^a Conditions: organometallic reagent (2.0 mmol), SeCO (2.0 mmol), THF (10 mL), -78 °C, 5 min; R'X (4.0 mmol), -78 °C, 30 min, approximately +20 °C, 30 min. ^b Isolated yields based on SeCO. ^c NMR yields.

after trapping with BnBr (Table 1, run 1).²⁴ A similar result was also obtained with PhMgBr (Table 1, run 2). In marked contrast with these results, when PhCu was used, carbophilic attack took place successfully to give **2a** in 55% yield after trapping with MeI (Table 1, run 3). The corresponding lithium cuprate, Ph₂CuLi, afforded benzophenone in 48% yield as the major product together with 37% of the desired product **2a** (Table 1, run 4). These results and the evidence that the use of 0.5 equiv of Ph₂CuLi improved the yield of **2a** up to 67% (Table 1, run 5) indicate that the intermediate **1a** (M = Cu or Cu(Ph)Li) and/or the product **2a** can undergo arylation with Ph₂CuLi (and/or with the resulting PhCu), though it is slower than the reaction with SeCO. Indeed, diorganocuprates and alkenylcoppers were known to react with selenol esters to give the corresponding ketones in high yields.²⁵ In the reaction of dithioesters with organometallic reagents, it is also reported that lithium diorganocuprates favor carbophilic addition over thiophilic attack.⁹¹ When cyanocuprate, PhCu(CN)Li, was employed, selenol ester **2a** was obtained in 86% yield (Table 1, run 6). In a similar manner, selenol esters **2b–e** were obtained in high yields from cyanoarylcuprates having an electron-releasing or -withdrawing substituent at the *para* position (Table 1, runs 7–10). Cyano-1-naphthylcuprate also gave selenol ester **2f** in 70% yield (Table 1, run 11). Although *t*-BuCu(CN)Li gave a low yield of **2g** under identical conditions, use of *t*-Bu₂CuLi instead of *t*-BuCu(CN)Li improved the yield of **2g** to 54% (Table 1, runs 12 and 13). Similarly, Bu₂CuLi and *s*-Bu₂CuLi afforded the corresponding selenol esters **2h** and **2i**, respectively, albeit in lower yields (Table 1, runs 14 and 15).

Selenol esters have now attracted much attention for their role as important intermediates in organic synthesis.²⁷ Although we have recently revealed that selenol esters were prepared in good to high yields by carbonylation of thermodynamically stable organolithiums de-

rived from acidic hydrocarbons such as fluorene, triphenylmethane, and the related compounds with selenium and CO,²⁸ this method is not applicable to carbonylation of aryllithiums. Since SeCO in THF solution is easily available,⁴ the present selenocarboxylation provides not only a complementary method to the selenium-mediated carbonylation but also a useful addition to the hitherto known methods for the synthesis of selenol esters.²⁹

Experimental Section

General Procedure for the Reaction of SeCO with Cyanocuprates. A 30-mL, two-necked flask containing a slurry of CuCN (2.0 mmol) and THF (20 mL) under argon was cooled to -78 °C, and ArLi³⁰ (2.0 mmol) in THF (5 mL) was added dropwise. The mixture was warmed until a bright yellow homogeneous solution was obtained, and it was recooled to -78 °C. The solution was then transferred via a cannula under argon to another flask containing SeCO (2 mmol) in THF (5 mL) at -78 °C. After the mixture was stirred for 5 min, methyl iodide (4.0 mmol) was added, stirring was continued for an additional 30 min, and then the mixture was warmed to 20 °C. After the mixture was filtered through Celite using Et₂O (80 mL), the filtrate was washed with aqueous saturated NH₄Cl solution (80 mL), dried, and concentrated. The crude product was purified by preparative TLC (PTLC, hexane–Et₂O 50:1), giving the corresponding selenol esters **2**. Selenol esters **2a**,³¹ **2b**,³² **2c**,³² **2f**,³² and **2g**³³ are known compounds, and the spectral data of these compounds that we obtained agreed with those in the literature. Analytical instruments used were the same as reported previously.²⁸

Se-Methyl 4-(chloroseleno)benzoate (2d): white solid; mp 48.2–48.5 °C; ¹H NMR (270 MHz, CDCl₃) δ 2.40 (s, 3 H, ²J_{Se–H} = 10.7 Hz), 7.43 (d, *J* = 8.3 Hz, 2 H), 7.85 (d, *J* = 8.3 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.35, 128.37, 129.10, 137.35, 139.93, 193.67; IR (KBr) 1669, 1585, 1396, 1203, 1082, 883, 830 cm⁻¹; MS (CI) *m/z* 235 (M⁺ + 1, 61), 139 (100). Anal. Calcd for C₈H₇ClOSe: C, 41.14; H, 3.02. Found: C, 40.83; H, 2.99.

Se-Methyl 4-[(trifluoromethyl)seleno]benzoate (2e) was purified by a recycling preparative HPLC using CHCl₃ as eluent under PTLT: white solid; mp < 30 °C; ¹H NMR (270 MHz, CDCl₃) δ 2.44 (s, 3 H, ²J_{Se–H} = 10.7 Hz), 7.73 (d, *J* = 8.3 Hz, 2 H), 8.01 (d, *J* = 8.3 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 5.59 (¹J_{Se–C} = 59.2 Hz), 123.55 (¹J_{F–C} = 272.6 Hz), 125.94 (³J_{F–C} = 4.2 Hz), 127.34, 134.82 (²J_{F–C} = 33.2 Hz), 141.74, 194.24; IR (KBr) 1678, 1407, 1324, 1131, 1111, 1066, 888, 846 cm⁻¹; MS (EI) *m/z* 268 (M⁺, 15), 145 (16), 95 (100); HRMS calcd for C₉H₇F₃OSe 267.9608, found: 267.9623.

Se-Butyl butanecarbosenoate (2h): yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 0.91 (t, *J* = 7.3 Hz, 6 H), 1.30–1.71 (m, 4 H), 1.65 (quint, *J* = 7.3 Hz, 4 H), 2.62 (t, *J* = 7.3 Hz, 2 H), 2.90 (t, *J* = 7.3 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 13.55, 13.72, 22.03, 23.07, 25.23, 27.58, 32.65, 48.03, 202.23; IR (NaCl) 2958, 2931, 1707, 1465, 1008 cm⁻¹; MS (EI) *m/e* 222 (M⁺, 5), 85 (83), 57 (100). Anal. Calcd for C₉H₁₈OSe: C, 48.87; H, 8.20. Found: C, 48.88; H, 8.35.

Se-Butyl 1-methylpropanecarbosenoate (2i): yellow oil; ¹H NMR (270 MHz, CDCl₃) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 0.94 (t, *J* = 7.3 Hz, 3 H), 1.16 (d, *J* = 6.8 Hz, 3 H), 1.32–1.53 (m, 3 H), 1.59–1.80 (m, 3 H), 2.61 (sext, *J* = 6.8 Hz, 1 H), 2.89 (t, *J* = 7.3 Hz, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 11.49, 13.57, 16.51,

(28) (a) Maeda, H.; Fujiwara, S.; Shin-ike, T.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1996**, *118*, 8160. (b) Maeda, H.; Nishiyama, A.; Kambe, N.; Sonoda, N.; Fujiwara, S.; Shin-ike, T. *Synthesis* **1997**, 342.

(29) As for the hitherto known synthetic methods of selenol esters, see the literature cited in ref 28b.

(30) Aryllithiums except PhLi were prepared according to the literature procedure: Schlosser, M.; Ladenberger, V. *J. Organomet. Chem.* **1967**, *8*, 193.

(31) Nishiyama, Y.; Katsuura, A.; Negoro, A.; Hamanaka, S.; Miyoshi, N.; Yamana, Y.; Ogawa, A.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 3776.

(32) Kojima, Y.; Ibi, K.; Kanda, T.; Ishihara, H.; Murai, T.; Kato, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 990.

(33) Inoue, T.; Takeda, T.; Kambe, N.; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 5824.

(25) Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Kochetkov, N. K. *Tetrahedron Lett.* **1983**, *24*, 4355 and 4359.

(26) It is not clear yet why organocopper reagents prefer carbophilic attack to selenophilic attack.

(27) For recent reviews, see: (a) Ogawa, A.; Sonoda, N. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds; Pergamon Press: Oxford, 1991; Vol. 6, pp 461–484. (b) Ogawa, A.; Sonoda, N. In *Comprehensive Organic Functional Group Transformations*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds; Pergamon Press: Oxford, 1995; Vol. 5, pp 231–255.

23.10, 24.84, 26.95, 32.73, 53.94, 206.79; IR (NaCl) 2962, 2932, 1703, 1460, 937 cm^{-1} ; MS (EI) m/e 222 (M^+ , 1), 85 (30), 57 (100). Anal. Calcd for $\text{C}_9\text{H}_{18}\text{OSe}$: C, 48.87; H, 8.20. Found: C, 48.95; H, 7.93.

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Instrumental Analysis Center, Faculty of Engineering, Osaka University.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra for new compounds **2d**, **2e**, **2h**, and **2i** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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