Selenonthiolesters: Isolation and Characterization

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Received August 31, 1992

There are formally 15 kinds of chalcogeno esters in which one or two oxygen atoms of carboxylic acid esters are displaced by sulfur, selenium, or tellurium. In contrast to the sulfur isologues such as thio- and dithiocarboxylic acid esters,[1] the selenium and tellurium isologues have been studied much less extensively.[2] To date, the synthesis and isolation of six chalcogeno esters (RCSeSR, RCSeSeR′, RCTeSR′, RCSeTeR′, RCTeSeR′ and RCTeTeR′) have remained elusive because of their extreme instability. Concerning *S*-organyl thioselenocarboxylates **2** (RCSeSR′) (hereafter called selenonthiolesters) containing both sulfur and selenium atoms,[3] only a cyclic selenothiophthalide has been prepared from the reaction of imidoylphthalide with hydrogen selenide.[4] No acyclic selenonthiolesters have yet been described due to the difficulty of synthesis,[5] though they are of considerable interest synthetically, spectroscopically, and biologically.[6] We now report the first isolation and characterization of acyclic selenonthiolesters **2**.

The synthesis of selenonthiolesters **2** was achieved by the reaction of *Se*-alkynyl selenoacetates **1**[7] with thiols in the presence of an acid catalyst. The reaction conditions shown in Scheme I appear to be preferred. Thus, *Se*-phenylethynyl selenoacetate (**1**, R = phenyl) and 2 equiv of alkanethiols[8] were refluxed in tetrahydrofuran in the presence of a catalytic amount of trifluoroacetic acid for 48 h (the color gradually changed from pale yellow to violet). Washing with water, removal of the solvent, and vacuum distillation or silica gel column chromatography (hexane) of the residue afforded *S*-alkyl benzeneethaneselenothioates **2a–d** in 30–70% yields[9] as a blue-violet liquid.[10] The synthesis of the simplest acetyl derivative **2e** was realized by

Scheme I

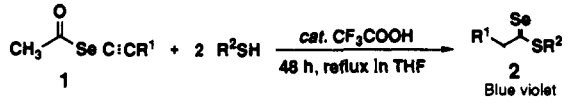


Table I. Yields and Spectra of Selenonthiolesters **2** and **2′**

compd no.	R^1	R^2	yield[a] (%)	bp (°C/Torr)	vis[b] (nm)	NMR[c] (δ) $^{13}C{=}Se$	NMR[c] (δ) ^{77}Se[d]
2a	C_6H_5	C_2H_5	48	41/0.2	575	240.0	1538.8
2b	C_6H_5	*n*-C_3H_7	70	128/3	577	240.0	1555.5
2c	C_6H_5	*i*-C_3H_7	54[e]	46/0.2	580	239.2	1552.1
2d	C_6H_5	*t*-C_4H_9	33[e]	59/0.2	591	238.4	2294.8
2e	H	*n*-C_3H_7	30[f]	liq[g]	571	237.5	1569.7
2′[h]	C_6H_5	*n*-C_3H_7	80	liq[i]	567	245.3	1570.2

[a] Isolated yield. [b] *cyclo*-C_6H_{12}. [c] $CDCl_3$. [d] Relative to Me_2Se. [e] Reaction time, 72 h. [f] Using $CH_3COSeC{\equiv}CSi(CH_3)_3$ as a starting compound. [g] Purified on silica gel column (hexane). Too unstable to distill. [h] See **2′** (R^3 = H) in Scheme II. [i] Purified on silica gel column (CH_2Cl_2/hexane = 1:1).

using *Se*-(trimethylsilyl)ethynyl acetate[11] as the starting compound (Table I). Presumably, **2** would be formed via a selenoketene intermediate.[12] As mentioned below, we have also found another route to α-allylated selenonthiolesters **2′** via a Seleno-Claisen rearrangement of ketene-*Se*-allyl-*S*-organyl acetals derived from **2**. Significantly, the obtained esters are stable toward heat and moisture. Under argon, **2a–d** can be stored at 20 °C for at least 7 days without any appreciable change. However, they are extremely sensitive toward oxygen and quickly decompose in air with liberation of red selenium.

Functionalized selenonthiolesters in solution are observable by visible and ^{13}C and ^{77}Se NMR spectroscopy (Table I). The n–π^* transitions (565∼590 nm) of the selenocarbonyl groups shift to longer-wavelength regions in the sequence from R^2 = ethyl to isopropyl and tert-butyl groups. On the other hand, the selenocarbonyl carbon and selenium chemical shifts show upfield and downfield shifts, respectively, suggesting a correlation with the n–π^* transitions.

The reactions of **2** are shown in Scheme II.[9] So far the preparation of selenoacylating agents such as selenoacyl chlorides has not been described in the literature because of their extreme instability. We have found that **2** readily reacted with primary and secondary amines in tetrahydrofuran (THF) to give the corresponding selenoamides **4** in moderate to good yields. This is the first example of selenoacylation to give the isolable selenocarbonyl compounds. Treatment of **2** in THF with bases such as triethylamine and lithium diisopropylamide below −20 °C led exclusively to the formation of eneselenolate anions **3** [$R^1CH{=}C(SR^2)Se^-$]. Moreover, trapping with various electrophiles such as alkyl halides, acyl chlorides, etc. afforded good yields of the corresponding ketene *Se*,*S*-acetals **5–10**.[9] The (*E*)/(*Z*) ratios of these products are between 40:60 and 10:90.[13] When alkylations of **3** were extended to allyl bromides, the resulting

(1) (a) Scheithauer, S.; Mayer, R. In *Topics in Sulfur Chemistry*; Seening, A., Ed.; Georg Thieme Publishers: Stuttgart, 1979; Vol. 4. (b) Voss, J. In *Supplement B: The Chemistry of Carboxylic Acid Derivatives*; Patai, S., Ed.; John Wiley & Sons: New York, 1979; pp 1021–1062. (c) Reid, D. H. *Organic Sulphur, Selenium and Tellurium*; Royal Society of Chemistry: London, 1970–81; Vols. 1–6. (d) Mayer, R.; Scheithauer, S. In *Methoden der Organischen chemie*; Falbe, J., Ed.; Georg Thieme Publishers: Stuttgart, 1985; Band 5, Teil 2, pp 891–930. (e) Kato, S.; Ishida, M. *Sulfur Rep.* **1988**, *8*, 155–323. (f) Kato, S.; Murai, T. In *Supplement B: The Chemistry of Acid Derivatives*; Patai, S., Ed.; John Wiley & Sons: New York, 1992; Vol. 2, pp 803–847.

(2) (a) Jensen, K. A.; Mygind, H.; Nielsen, P. H. In *Organic Selenium Compounds: Their Chemistry and Biology*; Klayman, D. L., Günther, W. H. H., Eds.; Wiley-Interscience: New York, 1973; pp 263–271. (b) Kato, S.; Murai, T.; Ishida, M. *Org. Prep. Proced. Int.* **1986**, *18*, 369–427. (c) Guziec, F. S., Jr. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; John Wiley & Sons: New York, 1987; Vol. 2, pp 215–273. (d) Guziec, F. S., Jr. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley-Interscience: New York, 1987; pp 277–324.

(3) RCSSeR′: Kato, S.; Yasui, E.; Terashima, K.; Ishihara, H.; Murai, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3931 and references therein.

(4) Wallmark, I.; Krakov, M. H.; Chu, S. H.; Mautner, H. G. *J. Am. Chem. Soc.* **1970**, *92*, 4447.

(5) A number of attempts to synthesize and isolate acyclic selenonthiolesters **2** by the reaction of imidoyl chlorides with hydrogen selenide and 1,2,3-selanadiazole (selenoketene precursor)[2c] with thiols resulted in the formation of an intractable dark brown oil which included red selenium.

(6) Chu, S. H.; Mautner, H. G. *J. Med. Chem.* **1976**, *11*, 446.

(7) **1** was prepared from $RC{\equiv}CSeLi$ and CH_3COCl: Ishihara, H.; Yoshimi, M.; Hara, N.; Ando, H.; Kato, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 835.

(8) When arenethiols instead of alkanethiols were used, the color of the reaction mixture changed from pale yellow to green-violet which quickly disappeared, indicating the formation of *S*-aryl selenonthiolesters (**2**, R^2 = aryl). However, they appeared to be too unstable to isolate.

(9) Isolated yields are shown. All new compounds show satisfactory spectral and analytical data.

(10) A typical procedure, forming *S*-propyl benzeneethaneselenothioate (**2b**): to a solution of *Se*-phenylethynyl selenoacetate (**1**) (2.24 g, 10 mmol) in tetrahydrofuran (5 mL) were added propanethiol (1.52 g, 20 mmol) and trifluoroacetic acid (80%) (0.142 g, 1 mmol) under an argon atmosphere, and the mixture was refluxed for 48 h. Ether (50 mL) was added, and the mixture was washed with water (3 × 50 mL), followed by drying with anhydrous sodium sulfate. The solvent was removed under reduced pressure, and vacuum distillation of the residue afforded 1.81 g (70%) of **2b** as a blue-violet liquid.

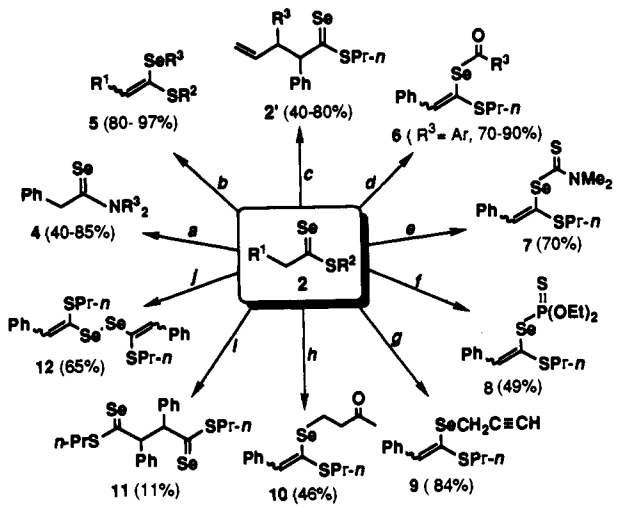
(11) The cleave of the Si–C bond of silylacetylene under acidic conditions is well known: Fleming, I.; Dunogues, J.; Smither, R. *Org. React.* **1989**, *37*, 57.

(12) The STO-3G level molecular orbital calculations predict that selenoketene is more favorable than ethynselenol: $H_2C{=}C{=}Se$, E = −2449.431 au; $HC{=}CSeH$, E = −2449.423 au.

(13) The NOE analysis indicates that the δ values for Hb of *Z*-isomers $Ph(Hb)C{=}C(SR)(SeR^2)$ appear higher upfield than Ha of *E*-isomers [$Ph(Ha)C{=}C(SR)(SeR^2)$]. The *E*/*Z* ratios were determined on the basis of the integral ratio of the vinylic protons Ha and Hb.

0002-7863/93/1515-3000$04.00/0

Scheme II [a]



[a] (a) **2b**/R^3_2NH (1:2), THF, reflux, 1 h; (b) **2b**/Et_3N/R^3I (1:1:2), THF, −25 °C, 2 h; (c) **2b**/Et_3N/CHR^3=$CHCH_2Br$ (1:1:2), THF, −25 °C, 2 h; (d)–(f) **2c**/*i*-Pr_2NLi/R^3COCl or $Me_2NC(S)Cl$ or $(EtO)_2P(S)Cl$ (1:1:2), THF, −25 °C, 2 h; (g) **2b**/Et_3N/R^3C≡CCH_2Br (1:1:2), THF, −25 °C, 2 h; (h) **2b**/Et_3N/CH_2=$CHCOCH_3$ (1:1:2), THF, −25 °C, 2 h, and then 23 °C, 3 h; (i) **2b**/*m*-CPBA (1:1), xylene, 100 °C, 2 h; (j) **2b**/*m*-CPBA (1:1), CH_2Cl_2 −25 °C, 10 min.

ketene-*Se*-allyl-*S*-alkyl acetals **5** (R^3 = allyl) underwent [3,3]-sigmatropic rearrangement to give selenonthiolesters **2'** in good yields. The Thio-Claisen rearrangement is well known;[14] however, there has been no precedent for such a Seleno-Claisen rearrangement. It is noted that lithium eneselenolate (**3**, R^1 = Ph, R^2 = *n*-Pr) readily added to methyl vinyl ketone to give Michael adduct **10** in 46% yield. Oxidation of **2** by *m*-chloroperbenzoic acid (*m*-MCPBA) under refluxing xylene afforded the novel bis(selenonthiolester) **11** in low yield, while the reaction below −20 °C led to a 65% yield of diselenide **12**.[15] Similar oxidation of thionselenolesters (RCSSeR') led to the formation of sulfine [RC(=S=O)SeR'] and acyl areneselenenyl sulfides (RCOSSeR').[3]

In summary, we have succeeded in isolating the first acyclic selenonthiolester. This development has opened up the possibility of preparing a large variety of new functional organoselenium compounds.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research on Priority Area of Organic Unusual Valency and partially by a Grand-in-Aid (No. 04650768) for Scientific research provided by the Ministry of Education, Science and Culture, Japan. We greatly appreciate additional support of our program by Lock Paint Research Fund.

Supplementary Material Available: Listing of spectral and analytical data for compounds **2**, **2'** and **4**–**12** (5 pages). Ordering information is given on any current masthead page.

(14) (a) Schoufs, M.; Meijer, J.; Vermeer, P.; Brandsma, L. *Synthesis* **1978**, 439. (b) Schuijl, P. J. W.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 929. (c) Apparo, S.; Bhattacharjee, S. S.; Ila, H.; Junjappa, H. *J. Chem. Soc., Perkin Trans. I* **1985**, 641. (d) Leger, L.; Saquet, M.; Thuillier, A.; Julia, S. *J. Organomet. Chem.* **1975**, *96*, 313.

(15) Bis(selenonthiolester) **11** appears to be formed via [3,3]-sigmatropic rearrangement of **12**, because heating of **12** in xylene above 100 °C led to **11**.