Diselenoic Acid Esters: Stability and Reactivity

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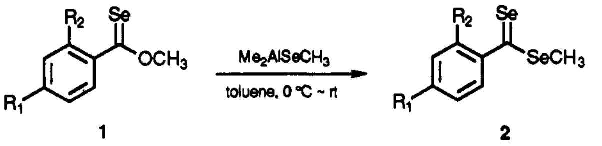
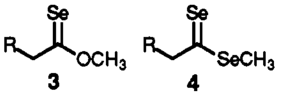
The chemistry of dithioic acid esters has been the subject of intense investigation for over 50 years.[1] In contrast, and despite recent advances in the rich chemistry of carbon–heteroatom multiple bonds,[2,3] the chemistry of their seleno counterparts, i.e., diselenoic acid esters (hereafter called diselenoesters) is all but unknown.[2–4] Our recent studies in the area of chalcogenoesters[5] have now prompted us to tackle the synthesis of diselenoesters, and we report here the first successful isolation and characterization of diselenoic acid methyl esters.

After several disappointing results, application of the Kozikowski reaction[6] to selenoester **1a**[7] allowed for the synthesis of diselenoester **2a** (eq 1, Table I). In particular, it was found that mixing **1a** with $Me_2AlSeCH_3$ at 0–20 °C for 1 h gave a solution that gradually turned from red to green. Followed by the usual workup involving washing and column chromatography on silica, this gave the desired ester **2a** in 91% yield. Interestingly, *no appreciable change of ester* ***2a*** *occurred during the purification!*[8,9] This suggested remarkable stability for this product. Indeed, the selenocarbonyl groups of esters **1a** and **2a** survived under the reaction conditions, and selective substitution of the OCH_3 group by $SeCH_3$ had proceeded according to plan. However, product **2a** was clearly more reactive than the initial substrate **1a** as described later. Nonetheless, the isolated ester **2a** is easily soluble in hexane and stable at room temperature unless it is exposed to air.



(1)

Chart I



R =			
n-C_4H_9	(a)	4-$MeOC_6H_4$	(e)
$Cl(CH_2)_3$	(b)	4-ClC_6H_4	(f)
C_6H_5	(c)	1-naphthyl	(g)
4-MeC_6H_4	(d)		

Table I. Yields[a] and Spectroscopic Properties of Diselenoic Acid Methyl Esters **2**

product	R¹	R²	yield,[b] %	δ(C=Se),[c] ppm	UV–vis,[d] nm	
2a	H	H	91	236.2	382	616
2b	Me	H	64	235.6	383	618
2c[e]	H	Me	37	240.5	367	615
2d[f]	MeO	H	73	233.5	356	616
2e	Br	H	51	233.3	383	619
2f	CF_3	H	64	233.6	381	615

[a] The reaction of selenoester **1** was carried out with $Me_2AlSeCH_3$ (1.5 equiv) in toluene (45 mL) at 0–20 °C for 1 h unless otherwise noted. [b] Isolated yields. [c] In $CDCl_3$. [d] In cyclohexane. [e] For 5 h. [f] For 2 h.

As shown in Table I, a variety of aromatic selenoesters **1** were converted smoothly to the corresponding diselenoesters **2**[10,11] except for the ortho-substituted ester **1c**. The reaction of **1c** needed longer reaction times and gave **2c** in lower yield. Esters having electron-donating groups such as **2b–d** can be stored at −10 °C for at least 1 month, whereas red selenium was seen under these conditions to be deposited slowly in the case of esters with electron-withdrawing groups, such as **2e** and **2f**. Aliphatic selenoesters **3a-g**[5b] could also be employed as starting materials (Chart I). In analogy to the above, similar workup of the mixture prepared from $Me_2AlSeCH_3$ and esters **3a** or **3b** gave a deep purple oil. However, in this case ester **4a** or **4b** as well as an unidentified product[12] was involved. In an effort to enhance the stability of aliphatic diselenoesters, a bulky group was attached to the α-carbon of the selenocarbonyl group. As a result, while esters **4c-f** were not stable enough to be obtained as single products, ester **4g** could be isolated in pure form as a deep purple oil in 61% yield. Attempts to obtain a phenyl ester from i-$Bu_2AlSePh$[13] and **1a** also failed and resulted in the recovery of PhSeSePh.

The ^{13}C NMR spectra of esters of type **2** generally displayed signals at ca. 235 ppm corresponding to the *C*=Se moiety. As compared with the values for these peaks seen for esters **1**, those of esters **2** were shifted to lower field by 12 ± 0.5 ppm regardless of the substituents on the aromatic ring. Furthermore, the *C*=Se signal of ester **2a** appeared at the lowest field among those of the

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(1) For reviews of dithioic acid esters, see: (a) Scheithauer, S.; Mayer, R. In *Topics in Sulfur Chemistry*; Senning, A., Ed.; George Thieme Publishers: Stuttgart, 1979; Vol. 4. (b) Ramadas, S. R.; Srinivasan, P. S.; Ramachandran, J.; Sastry, V. V. S. K. *Synthesis* **1983**, 605. (c) Kato, S.; Ishida, M. *Sulfur Rep.* **1988**, *8*, 155. (d) Kato, S.; Murai T. In *Supplement B*: *The Chemistry of Acid Derivatives Volume 2*; Patai, S., Ed.; John Wiley & Sons: New York, 1992; pp 803–847.

(2) For reviews of carbon –chalcogen double bonds, see: (a) Jensen, K. A. *Q. Rep. Sulfur Chem.* **1970**, *5*, 45. (b) Jensen, K. In *Organic Selenium Compounds*: *Their Chemistry and Biology*; Klayman, D. L., Günther, W. H. H., Eds.; Wiley-Interscience: New York, 1973, pp 263–272. (c) Kato, S.; Murai, T.; Ishida, M. *Org. Prep. Proced. Int.* **1986**, *18*, 369. (d) Guziec, F. S., Jr. In *The Chemistry of Organic Selenium and Tellurium Compounds Volume 2*; Patai, S., Ed.; John Wiley & Sons: New York, 1987; pp 215–273. (e) Guziec, F. S., Jr. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley-Interscience: New York, 1987; pp 277–324.

(3) (a) *Organic Compounds of Sulphur, Selenium and Tellurium*; Specialist Periodical Reports; The Chemical Society: London, 1970–1981; Vols. 1–6. (b) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis*; Baldwin, J. E., Ed.; Pergamon Press: 1986; pp 58–83. (c) Okazaki, R. *J. Synth. Org. Chem. Jpn.* **1988**, *46*, 1149.

(4) Jensen has noted that some esters can be obtained by the treatment of selenoacylammonium salts with hydrogen selenide but are very unstable.[2a,b] No details, however, are available at present. Very recently, Nakayama et al. have presented the formation of carbenium diselenoesters: Akiyama, I.; Nakayama, J.; Nishio, T. 20th Symposium on Heteroatom Chemistry, Hachioji, January 1993; Abstract, p 173.

(5) (a) RCSSeR′: Kato, S.; Yasui, E.; Terashima, K.; Ishihara, H.; Murai, T. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3931. (b) RCSeOR′: Ishihara, H.; Yoshimi, M.; Hara, N. Ando, H.; Kato, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 835. (c) $RCSeOSiR'_3$: Kato, S.; Kageyama, H.; Murai, T.; Ishihara, H. *Chem. Ber.* **1992**, *125*, 417. (d) RCSeSR′: Kato, S.; Komuro, T.; Kanda, T.; Ishihara, H.; Murai, T. *J. Am. Chem. Soc.* **1993**, *115*, 3000.

(6) (a) Kozikowski, A. P.; Ame, A. J. *J. Org. Chem.* **1978**, *43*, 2735. (b) Sviridov, A. F.; Ermolenko, M. S.; Yashunsky; D. V.; Kochetokov, N. K. *Tetrahedron Lett.* **1983**, *24*, 4355. (c) Khalid, M.; Ripoll, J.-L.; Vallée, Y. *J. Chem. Soc., Chem. Commun.* **1991**, 964.

(7) Segi, M.; Takahashi, T.; Ichinose, H.; Li, G. M.; Nakajima, T. *Tetrahedron Lett.* **1992**, *33*, 7865.

(8) Even cyclic diselenophthalide, which was believed to be more stable than **1a**, was reported to be unstable.[9]

(9) Wallmark, I.; Krackov, M. H.; Chu, S.-H.; Mauntner, H. G. *J. Am. Chem. Soc.* **1970**, *92*, 4447.

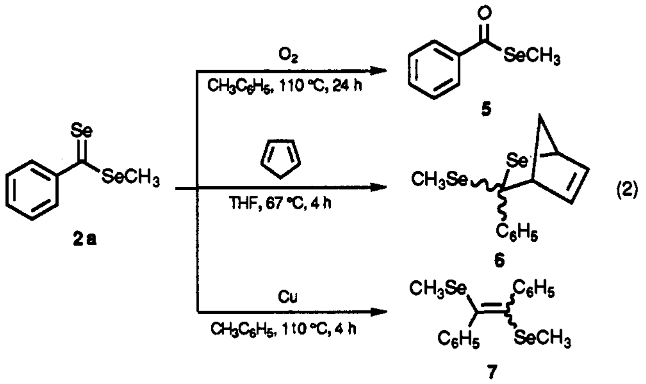
(10) A typical experimental procedure is as follows: Into a 100-mL three-necked flask was placed selenium powder (0.46 g, 4.5 mmol). It was then heated in vacuo until the selenium began to melt and was then cooled. To the resulting selenium were added toluene (45 mL) and trimethylaluminum in hexane (4.6 mL, 4.5 mmol) at 20 °C, and the mixture was stirred at 110 °C. After 3 h, selenobenzoic acid *O*-methyl ester (**1a**) (0.6 g, 3.0 mmol) was added, and the mixture was stirred for 30 min at 0 °C. The reaction mixture was allowed to warm to 20 °C, and the stirring was continued for an additional 30 min. The resulting mixture was poured onto ice/water and extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated, and the residue was chromatographed through a silica gel column using hexane as an eluent to give 0.72 g (91%) of **2a** as a green oil.

(11) All new compounds were isolated in >95% purity as measured by ^1H NMR and were characterized by ^1H and ^{13}C NMR, IR, UV, and microanalysis or HRMS; see supplementary material.

(12) On the basis of ^1H and ^{13}C NMR and mass spectra, this material was tentatively assigned as a cyclodimer of **4a** or **4b** having a 1,3-diselenacyclobutane skeleton.

(13) Maruoka, K.; Miyazaki, T.; Ando, M.; Matsumoto, Y.; Sakane, S.; Hattori, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1983**, *105*, 2831.

0002-7863/93/1515-5823$04.00/0



generalized C$_6$H$_5$CEE′CH$_3$ (E, E′ = O, S, Se) series.[14] The C═*Se* signal in the ^{77}Se NMR spectrum (1786.5 ppm in CDCl$_3$) also showed a low-field shift by 876.5 ppm compared with that of **1a**. These results imply that the lone pair electrons of selenium attached to C═Se are not effectively delocalized on C═Se, presumably because of the longer single-bond length between carbon and selenium.

As would be expected for selenium isologues of benzoic acid esters, the UV–visible spectrum of **2a** bears some resemblance to those of dithioester[1a] and selenoester.[15] However, both π–π^* and n–π^* transitions (382 (ϵ 5990), 616 (ϵ 704)) are substantially red-shifted. In particular, the n–π^* transitions of **2** were shifted to longer wavelengths by ca. 105 nm compared with that of **1**.

The results of the reactivity tests carried out with ester **2a** are shown in eq 2. Upon exposure of **2a** to air for 2 h at room temperature, the formal exchange of oxygen for selenium of the C═Se group took place to give ester **5** in 65% yield along with red selenium. A similar exchange was observed in the case of the selenoaldehyde.[16] Unlike the case of selenobenzophenone,[17] no cyclodimer of **2a** could be detected. Heating ester **2a** in toluene under O$_2$ at 110 °C gave **5** quantitatively. The sensitivity of **2a** toward O$_2$ is in sharp contrast to that of **1a**, which did not change under the same reaction conditions. The fact that the reactivity of ester **2** is similar to that of selenoaldehydes is further reflected in the reactions with cyclopentadiene. In the case of **2a**, for instance, cycloaddition proceeded smoothly at 67 °C to produce **6** as a stereoisomeric mixture in 67% yield.[18] Similar reactions are known for selenoaldehydes.[19] On the other hand, Diels–Alder reactions are rare for carbon–chalcogen double bonds of esters, with only a few examples known in the case of dithioesters bearing electron-withdrawing groups.[20] Finally, the copper-mediated reductive coupling reaction known for selenoamides[21] was carried out using ester **2a** in toluene to afford **7** in 39% yield.

In summary, we have documented that aromatic diselenoic acid methyl esters are stable in spite of the previously noted instability. In fact, they may be isolated as green oils under simple laboratory conditions. Appropriate modification of the substituents can also be used to prepare stabilized aliphatic diselenoesters. Preliminary reactivity results further serve to reveal that ester **2a** behaves in a manner similar to the better-known selenoaldehydes, although they are more reactive. The lability and optical properties of the diselenoesters thus make them attractive candidates for synthetic and material-related studies. Work along these lines is currently in progress.

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Supplementary Material Available: Listings of spectral and analytical data for products **2a–f** and **4g** (2 pages). Ordering information is given on any current masthead page.

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(14) The signals of carbonyl carbon of chalcogeno isologues of benzoic acid methyl ester are as follows: C$_6$H$_5$CS$_2$CH$_3$, 226.7 ppm; C$_6$H$_5$CSSeCH$_3$, 233.2 ppm; C$_6$H$_5$CSeSCH$_3$, 233.7 ppm.

(15) Barton, D. H. R.; Hansen, P.-E.; Picker, K. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1723.

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

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(18) Diels –Alder reaction of **2a** with pentamethylcyclopentadiene also proceeded in a similar manner to give the adduct in 24% yield with low stereoselectivity, whereas in the reaction of ester **4g** the decomposition of **4g** became competitive to give the adduct in 9% yield.

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(21) Sekiguchi, M.; Ogawa, A.; Kambe, N.; Sonoda, N. *Chem. Lett.* **1991**, 315.