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A Convenient Preparation of O-Alkyl Selenoesters from Esters

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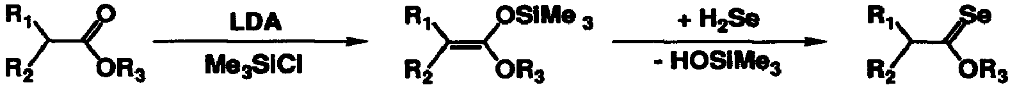
Abstract: A new methodology is described for the synthesis of O-alkyl selenoesters from esters. The ester is converted to the silyl ketene acetal with LDA and Me_3SiCl, which is then treated with H_2Se generated in situ from aluminum selenide and dilute HCl.

The chemistry of selenocarbonyl compounds has attracted considerable attention in recent years.[1] The preparation of selenoesters, selenoaldehydes, selenoketones, and selenoamides have all been reported. Of more interest are those preparative methods in which the readily available oxygen compounds are converted to their selenocarbonyl isosteres. Reagents that have been used for this purpose include bis(trimethylsilyl) selenide[2a] and dichlorophenylphosphine selenide ($PhP(=Se)Cl_2$).[2b] Fewer methods have been reported for the synthesis of selenoesters.[3] Of these, the most generally useful method proceeds from a tertiary carboxamide by conversion to the imidoyl chloride with phosgene, followed by sequential treatment with an appropriate alcohol and sodium hydrogen selenide.[4] This method is of course limited to those carboxamides and alcohols that are sufficiently robust to survive the strongly acidic conditions of this method.

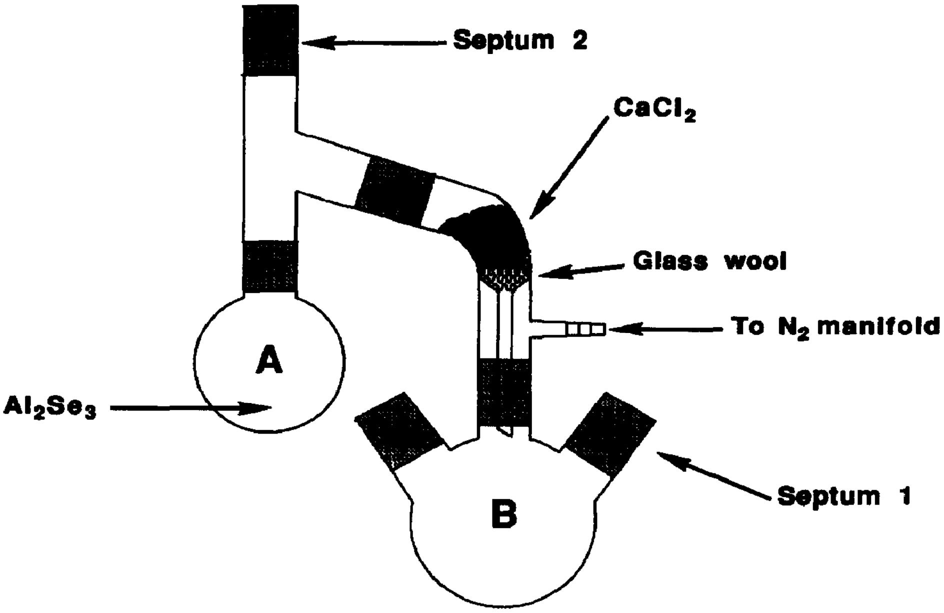
We anticipated that esters might be convertible directly to the corresponding selenoesters by the reaction of their trimethylsilyl ketene acetals with hydrogen selenide (Scheme 1). As H_2Se is an expensive and unstable gas, we sought to employ H_2Se generated *in situ* by the hydrolysis of inexpensive and easily prepared aluminum selenide.[5]

Scheme 1



Indeed, we found that monosubstituted ketene acetals (R_2 = H) underwent immediate reaction at -78 °C to give the desired selenoester in good yields (Table 1), while disubstituted ketene acetals ($R_1,R_2 \neq H$) required approximately 10 minutes at 0 °C for complete reaction.

In as much as H_2Se is readily decomposed by rubber and other materials, we designed an all-glass apparatus, using common pieces of glassware, in which to conduct this transformation. The reaction apparatus consists of a 50 mL flask (A) in which hydrogen selenide is generated by the action of 3 M HCl upon Al_2Se_3. This is connected to a 100 mL 3-neck reaction flask (B) by means of a 3-way distilling adapter and a vacuum adapter. The bend in the vacuum adapter is charged with a few grams of granular anhydrous $CaCl_2$ held in place with a little glass wool, which serves to dry the H_2Se prior to its contact with the silyl ketene acetal in flask B.

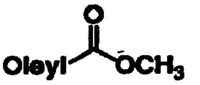
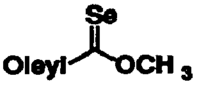
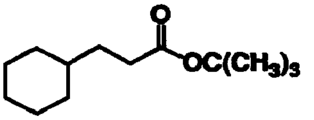
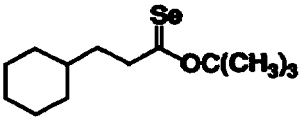
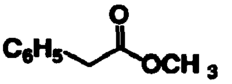
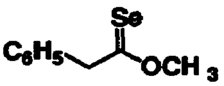
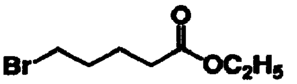
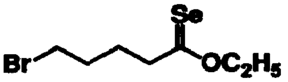
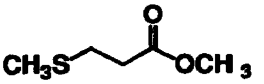
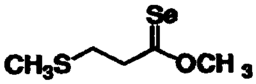
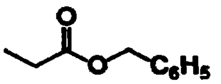
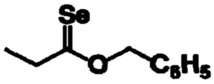
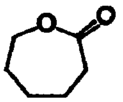
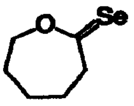


In a typical experiment, the apparatus is assembled as shown and flask A is charged with aluminium selenide (1.60 g, 5.5 mmol). The apparatus is then evacuated and flushed with dry nitrogen three times. A solution of LDA is prepared in flask B from 0.242 g (2.4 mmol) of diisopropylamine and 0.90 mL (2.44 M, 2.2 mmol) of n-butyllithium) in 10 mL of THF. The LDA solution is cooled to -78 °C, and chlorotrimethylsilane (0.261 g, 2.4 mmol) is added, followed after 5 min by a solution of methyl oleate (0.593 g, 2 mmol) in 5 mL of THF added dropwise by cannula at -78 °C via septum 1. Following addition, the mixture was stirred for 10 min at -78 °C, then 1 mL of 3 M hydrochloric acid was added to the Al_2Se_3 in flask A via septum 2. The reaction mixture was maintained at -78 °C until hydrogen selenide evolution was complete and for 10 min longer.[6] The cooling bath was then removed and the mixture was allowed to warm to 20 °C and was kept at 20 °C for not longer than 15 minutes.[7] Hexanes (16 mL) and ether (8 mL) were added, followed by 20 mL of 1 M sodium bicarbonate. The organic solution was washed with 2 more portions of 1 M sodium bicarbonate, then with brine (1 x 20 mL), dried and evaporated. Flash chromatography of the residue on silica eluting with hexanes gave 0.647 g (90%) of O-methyl selenooleate as a yellow oil.[8] ^1H NMR ($CDCl_3$): $\delta = 5.37$ (m, 2 H, 9- and 10-CH); 4.21 (s, 3 H, $-OCH_3$); 2.67 (t, 2 H, $2-CH_2$); 2.03 (m, 4 H, 8- and $11-CH_2$); 1.77 (m, 2 H, $3-CH_2$); 1.25 (m, 20 H, 4- through 7-, 12- through $17-CH_2$); 0.88 (t, 3 H, $-CH_3$). IR (neat): 1435 (C=Se) cm^{-1}. UV (EtOH): λ_{max} = 270 nM. MS (NH_3 CI): 360 ($M + H^+$). TLC (9:1 hexane - ether): $R_f = 0.7$ (methyl oleate, 0.4).

The selenoesters were isolated as brilliant yellow oils or solids with a peculiar "skunky" odor. They were stable to silica gel chromatography, and were much more mobile on silica gel than the starting esters.

Characteristic features of the spectra were infrared absorbances at 1190 and 1435 cm^{-1} and an ultraviolet absorbance maximum at 275 nM. The alkoxyl protons were deshielded relative to those of the starting ester by 0.4 to 0.5 ppm, and those α to the selenocarbonyl were deshielded by about 0.3 ppm. Results for a variety of substrates are presented in Table 1.

Table 1

Example	Starting Ester	Selenoester Product	Yield[a]
1			90%[b]
2			72%
3			74%
4			62%[c]
5			87%
6			83%
7			80%
8			85%

[a] All products gave satisfactory ^1H NMR, IR, UV, and mass spectral data. [b] Oleyl = Z-$(CH_2)_7CH{=}CH(CH_2)_7CH_3$. [c] mp 150 - 152 °C (lit. mp 151 - 153 °C).[4b]

It is interesting to note that the primary bromide (Example 5) does not undergo displacement by selenium under these conditions, despite the powerful nucleophilic character of the selenide anion. The reaction is also successful with a *t*-butyl ester (Example 2), a benzyl ester (Example 7), and a ε-lactone (Example 8), all of which are inaccessible by the imidate-alcohol-NaHSe method. The reaction could not be successfully applied to vinyl esters or δ-lactones. In these cases the formation of the trimethylsilyl ketene acetal was found to occur normally, but the ketene acetals suffered extensive decomposition upon exposure to H_2Se to give a complex mixture of seleniferous products. Not surprisingly, attempts to extend this methodology to the preparation of O-alkyl telluroesters by the use of Al_2Te_3 in place of Al_2Se_3 were unsuccessful.[9]

In summary, we have found that a variety of alkyl esters and certain lactones may be conveniently transformed in good yields to the corresponding selenocarbonyl analogs by reaction of their trimethylsilyl ketene acetals with hydrogen selenide generated *in situ* by the hydrolysis of aluminum selenide.

References and Notes

1. See, for example: (a) Jensen, K. A.; Kjaer, A. *The Chemistry of Organic Selenium and Tellurium Compounds;* Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1986; Vol. 1, Chapter 1; (b) Krafft, G. A.; Meinke, P. T. *J. Am. Chem. Soc.* **1988**, *110*, 8671 - 8678; (c) Okazaki, R.; Kumon, N.; Inamoto, N. *J. Am. Chem. Soc.*, **1989**, *111*, 5949 - 5951; (d) Abelman, M. M. *Tetrahedron Letters*, **1991**, *32*, 7389 - 7392.
2. Segi, M.; Nakajima, T.; Suga, S.; Murai, S.; Ryu, I.; Ogawa, A.; Sonoda, N. *J. Am. Chem. Soc.*, **1988**, *110*, 1976 - 1978; (b) Michael, J. P.; Reid, D. H.; Rose, B. G.; Speirs, R. A. *J. Chem. Soc., Chem. Commun.* 1988, 1494 - 1496. Interestingly, the known selenium analog of Lawesson's reagent (Woolins, J. D.; Williams, D. J.; Parkin, I. P.; Pilkington, M. J.; Slawin, A. M. Z. *Polyhedron*, **1990**, *9*, 987 - 990) has apparently not been used for this purpose.
3. (a) Collard-Charon, C.; Renson, M. *Bull. Soc. Chim. Belg.*, **1962**, *71*, 563 - 578; (b) Mayer, R.; Scheithauer, S.; Kunz, D. *Chem. Ber.*, **1966**, *99*, 1393 - 1413.
4. (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. I*, **1975**, 1574-1585; (b) Barton, D. H. R.; Hansen, P.-E.; Picker, K. *J. Chem. Soc., Perkin Trans. I*, **1977**, 1723-1730.
5. Aluminum selenide is commercially available; however, its reactivity with acid to generate H_2Se can vary considerably. Aluminum selenide prepared in the laboratory by the direct pyrothermal combination of the elements is inexpensive (\$ 0.10 gm^{-1}) and has been found to always hydrolyze immediately to afford H_2Se.
6. The mixture is kept at -78 °C to facilitate the condensation of H_2Se (bp -41 °C) in the reaction mixture.
7. Prolonged contact (> 30 min) of the reaction mixture with H_2Se at 0 °C or higher temperatures results in the eventual precipitation of red selenium and the decomposition of the product to a complex mixture of seleniferous products. H_2Se is known to be a reducing agent for carbonyl compounds (Sonoda, N.; Murai, S.; Kondo, K.; Kambe, N. *Angew. Chem. Int. Ed. Engl.*, **1980**, *19*, 1008-1009); it is not unreasonable to expect that it may reduce selenocarbonyl compounds with the formation of (poly)selenide products.
8. The crude product is homogeneous by TLC and ^1H NMR; it may contain some amorphous red selenium.
9. O-alkyl telluroesters that lack a hydrogen α to the C=Te group have been reported: (a) Barton, D. H. R.; Barrett, A. G. M.; Read, R. W. *J. Chem. Soc. Chem. Commun.* **1979**, 645-647; (b) Barton, D. H. R.; Barrett, A. G. M.; Read, R. W. *J. Chem. Soc. Perkin Trans. I*, **1980**, 2191-2195. Telluroesters with a hydrogen α to the C=Te group are unstable and decompose presumably via radical pathways. In the present work, the reaction of the TMS ketene acetal with H_2Te at -78 °C afforded a purple solution characteristic of a telluroester; however the putative telluroester could not be isolated by conventional workup techniques.

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