Reductive cyclization of γ,δ-unsaturated selenothioic acid *S*-esters leading to tetrahydroselenophenes

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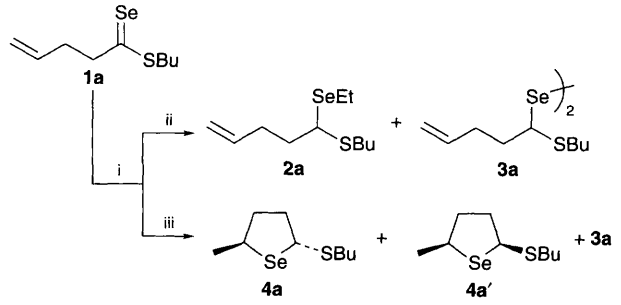
Reductive cyclization of γ,δ-unsaturated selenothioic acid *S*-esters with $NaBH_4$ or $LiAlH_4$ proceeds *via* δ,ε-unsaturated selenols to afford tetrahydroselenophenes in good to high yields.

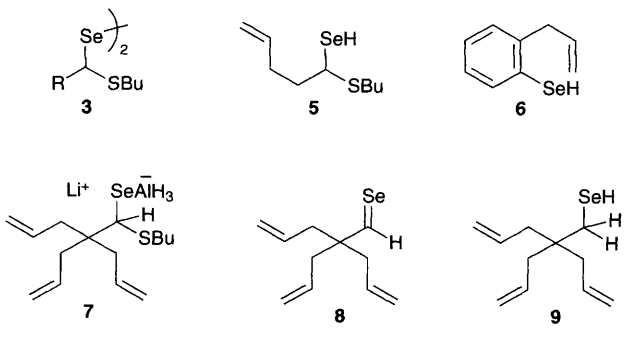
Organoselenium compounds have attracted considerable attention because of their unique chemical properties and versatility as synthetic reagents.[1] Although various kinds of synthetic methods have been developed for some selenium containing heterocycles such as selenophenes and diselenafulvenes,[2] the synthesis and properties of tetrahydroselenophenes have been studied to lesser extent, which is partly due to the lack of general synthetic routes.[3] Although synthetic efforts to produce a variety of selenocarbonyl compounds have also been reported, there have been few studies on their reactivities and applications.[4] Recently we have established facile syntheses of selenothioic acid *S*-esters [RC(Se)SR'].[5] Here we report the first reductive cyclization of γ,δ-unsaturated selenothioic acid *S*-esters leading to tetrahydroselenophenes with high stereoselectivity.

The reduction of γ,δ-unsaturated selenothioic acid *S*-ester **1a** with $NaBH_4$ in MeOH took place in a similar manner to that of selenoketones[6] and selenoesters [RC(Se)OR'].[7] The deep purple reaction mixture of **1a** and $NaBH_4$ turned red at 50 °C after 5 h (Scheme 1).

Trapping of the mixture with ethyl iodide gave the selenothioacetal **2a** in 48% yield.[8] Acidic aqueous work-up of the mixture gave the tetrahydroselenophene **4a** and **4a'** in 30% combined yield and diselenide **3a** in 27% yield.†,‡.

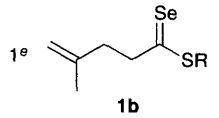
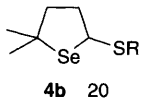
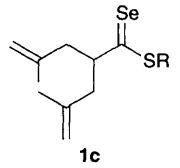
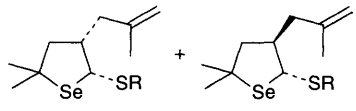
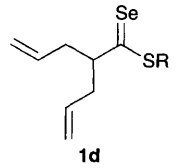
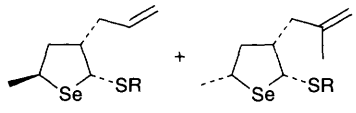
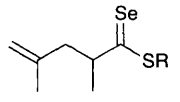
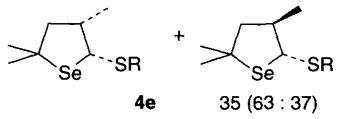
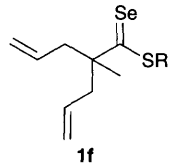
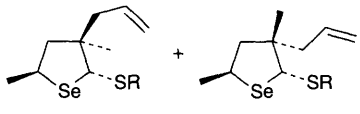
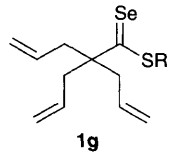
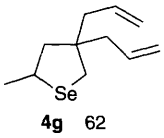


Scheme 1 *Reagents and conditions*: i, $NaBH_4$, 50 °C, 5 h, ii, EtI, **2a**: 48%, **3a**: 3%, iii, 10% HCl, **4a**: 22%, **4a'**: 7%, **3a**: 27%



The results of the reductive cyclization of a variety of γ,δ-unsaturated selenothioic acid *S*-esters **1b–g** are summarized in Table 1.§ Reduction of di- and tri-substituted esters **1c–g** with $NaBH_4$ did not take place. Reaction at higher temperatures gave complex mixtures. Attempts to reduce them with DIBAL-H, $LiBH_4$ and $LiEt_3BH$ also failed and gave mixtures containing unreacted starting materials. In contrast, the reduction of **1c–g** with $LiAlH_4$ in Et_2O was successful and gave tetrahydroselenophenes with high stereoselectivity in moderate to high yields along with less than 30% yields of the corresponding

Table 1 Reductive cyclization of γ,δ-unsaturated selenothioic acid *S*-esters[a]

Entry	Ester[b]	Product yield (%)[c], (ratio)[d]
1[e]	 **1b**	 **4b** 20
2	 **1c**	 **4c** 93 (92 : 8)
3	 **1d**	 **4d** 65 (91 : 9)
4	 **1e**	 **4e** 35 (63 : 37)
5[f]	 **1f**	 **4f** 58 (69 : 31)
6[g]	 **1g**	 **4g** 62

[a] Conditions: ester (1 mmol), $LiAlH_4$ (1 mmol), Et_2O (5 ml), 20 °C, 0.5 h, then, 10% HCl. [b] R = Bu. [c] Isolated yield. [d] The ratio was determined by ^1H NMR spectra. [e] Conditions: ester (2 mmol), $NaBH_4$ (2 mmol), MeOH (5 ml), 50 °C, 3 h. [f] THF (5 ml), −20 °C, 3 h. [g] 20 °C, 3 h.

diselenides **3**. The cyclization may take place *via in situ* generated δ,ε-unsaturated selenols **5**.

Although the similar reaction of 2-allylbenzeneselenol **6** was reported to give both five- and six-membered cyclic products,[9] the products derived from *endo*-cyclization were not observed in the present reaction. Noteworthy is that only one isomer **4d** was obtained as a major product out of the four possible stereoisomers (entry 3). The relative stereochemistry of the products was estimated on the basis of the difference NOE spectra and comparison of the chemical shifts and coupling constants of **4a**, **c–f**¶ in the ^{1}H NMR spectra. As for **4d**, **f**, Me and SBu groups attached to the carbons adjacent to selenium atom are *trans* (entries 3 and 5). The allylic and SBu groups of **4c**, **d** are *cis* (entries 2 and 3).

In the reaction of the triallylic ester **1g**, the SBu group was also reduced to give **4g** in good yield (entry 6). Ester **1g** reacted with $LiAlH_4$ to lead to the intermediate **7** because of the high reactivity of the selenocarbonyl group. The steric congestion around the carbon atom bearing the selenium and sulfur groups may induce the elimination of lithium thiolate to generate the selenoaldehyde intermediate **8** which may be reduced quickly resulting in the formation of **4g** *via* the intermediate **9**.

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Footnotes

† *Typical experimental procedure* for the reductive cyclization of γ,δ-unsaturated selenothioic acid *S*-esters: To a solution of Et_2O (5 ml) and $LiAlH_4$ (0.076 g, 1 mmol) was added γ,δ-unsaturated selenothioic acid *S*-ester **1** (1 mmol) at −20 °C. The mixture was stirred for 0.5 h, 10% HCl (5 ml) was added at room temp. and the mixture was poured into iced water and extracted with Et_2O three times. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography with hexane–CH_2Cl_2 as eluent to give the corresponding tetrahydroselenophene **4**.

‡ *Selected spectroscopic data* for **4a**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (3 H, t, *J* 7.3 Hz), 1.42 (2 H, sextet, *J* 7.3 Hz), 1.45 (3 H, d, *J* 5.7 Hz), 1.56 (2 H, quintet, *J* 7.3 Hz), 1.73 (1 H, q, *J* 5.6 Hz), 2.05 (1 H, q, *J* 7.3 Hz), 2.24 (1 H, q, *J* 5.6 Hz), 2.41 (1 H, q, *J* 6.8 Hz), 2.60 (2 H, t, *J* 7.3 Hz), 3.89 (1 H, sextet, *J* 5.7 Hz) and 4.79 (1 H, sextet, *J* 6.0 Hz).

§ All new compounds gave satisfactory spectral and microanalytical data.

¶ *Selected spectroscopic data* for *cis*-**4c**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (3 H, t, *J* 7.3 Hz), 1.40 (2 H, m), 1.56 (2 H, m), 1.58 (3 H, s), 1.64 (3 H, s), 1.75 (3 H, s), 1.83 (1 H, dd *J* 13.0, 4.0 Hz), 2.07 (1 H, t, *J* 13.0 Hz), 2.25 (1 H, dd, *J* 14.3, 6.6 Hz), 2.29 (1 H, dd, *J* 14.3, 8.3 Hz), 2.58 (2 H, t, *J* 7.2 Hz), 2.96 (1 H, m), 4.74 (1 H, d, *J* 5.1 Hz) and 4.78 (2 H, s). For **4e**: ^{1}H NMR (400 MHz, $CDCl_3$) δ for *cis*-**4e**: 0.92 (3 H, t, *J* 7.3 Hz), 1.18 (3 H, d, *J* 6.8 Hz), 1.40 (2 H, m), 1.57 (3 H, s), 1.59 (2 H, m), 1.62 (3 H, s), 1.79 (1 H, dd, *J* 12.8, 3.8 Hz), 2.11 (1 H, t, *J* 12.8 Hz), 2.59 (1 H, t, *J* 7.4 Hz), 2.84 (2 H, m) and 4.70 (1 H, d, *J* 5.4 Hz); for *trans* **4e**: 0.91 (3 H, *J* 7.3 Hz), 1.17 (3 H, d, *J* 6.6 Hz), 1.40 (2 H, m), 1.56 (3 H, s), 1.57 (2 H, m), 1.64 (3 H, s), 1.75 (1 H, *J* 12.8 Hz), 2.04 (1 H, dd, *J* 12.8, 4.6 Hz), 2.43 (1 H, m), 2.58 (2 H, t, *J* 7.3 Hz), 4.37 (1 H, d, *J* 10.2 Hz).

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