Chemoselective Synthesis of Functionalized Diselenides.
Part 2: A Mild Preparation of Keto-Diselenides *via* Samarium Diiodide Reduction of Selenocyanates[1,2]

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Abstract: The action of samarium diiodide on various keto-selenocyanates led to the chemoselective formation of the diselenide bond under very mild conditions. The flexibility of this method also allowed one to get either dialdehyde-diselenides or dicyanohydrin-dialdehydes from the same parent oxo-selenocyanates. © 1998 Elsevier Science Ltd. All rights reserved.

Despite being an already thoroughly investigated field, dichalcogenide bond formation is still receiving attention. For instance, peroxides,[3] disulfides[4] and diselenides[5] are regularly the aim of significant synthetic advancements. New natural occurrences[6], developing biological activity[7] and emerging role in asymmetric synthesis[8] of diselenides led us to recently propose a systematic access to functionalized diselenides along with excellent yields.[1] Although aralkyl ketones gave good results with dibutylaluminum hydride at -78°C, the main limitation of this method was related to the over-reduction of purely aliphatic carbonyls. For example, reduction of 4-oxo-octane-selenocyanate (**1**) led to a mixture of diketo- (**2**), dihydroxy- (**3**), and hydroxy-keto-(**4**) diselenides, even at -105°C. (see scheme 1)
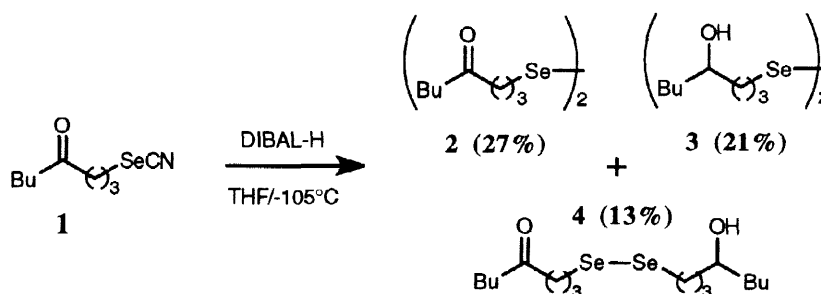
Scheme 1

We now wish to report that this limitation was circumvented by using samarium diiodide - instead of hydrides[1] - in order to carry out the selenocyanate[9] reduction (see equation 1), thus broadening the scope of this methodology to different types of carbonyl groups.

$$\textbf{Eq. 1} \qquad \textbf{RSeCN} \xrightarrow[\textbf{THF/-105°C}]{\textbf{SmI}_2} \textbf{1/2 RSeSeR}$$
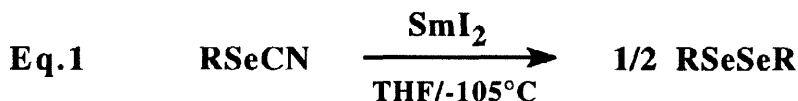
A typical experiment is as follows: To a solution of selenocyanate (**6**) (240 mg, 1 mmole) in dry THF (15 mL) maintained at -105°C under nitrogen was added dropwise the samarium (II) diiodide® (Aldrich Chem. Co. Inc.) (2.4 mL of 0.1M solution in THF, 2.4 mmoles). The flask was maintained at -105°C for 30 minutes, then opened and the medium was allowed to reach room temperature. The yellow

solution was concentrated *in vacuo* and the resulting residue filtered through a pad of silica (ethyl acetate/hexane : 2/8). The filtrate was then concentrated under high vacuum to afford the corresponding pure diselenide (**11**) as a yellow oil (193 mg, 90%).[10]
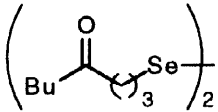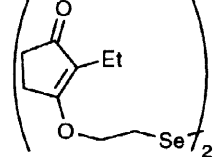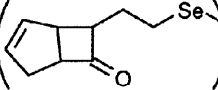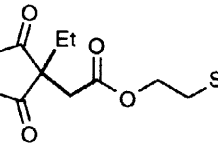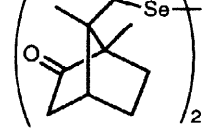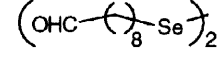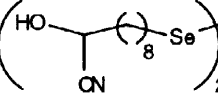
Selenocyanates	Diselenides		Isolated yields
1		2	92%
5		10	89%
6		11	90%
7		12	76%
8		13	85%
9		14	82%
		15	85%

Table 1

As displayed in table 1, this methodology clearly allows one to treat acyclic ketones (see entry 1 which compares very favorably with scheme 1), Michael systems[11] (entry 5), strained ketones (entry 6[12] and 8[13]), and diketones (entry 7)[11] without any reaction at the carbonyl site. Noteworthy is the case of aldehydes (entry 9), whose flexibility further underlines the functional usefulness of our methodology. Indeed, when the reaction vessel was opened at -105°C, only the expected dialdehyde-diselenide was obtained (compound **14**). However, when the reaction was allowed to warm up to room temperature and only then opened, the sole dicyanohydrin-diselenide was formed (compound **15**). To explain this

observation, it could be suggested that in the first case, the "SmI$_2$CN" formed during the selenocyanate reduction would be hydrolized by the condensed water, *forming HCN. The latter would possibly evolve*, thus leaving the aldehyde untouched. In the second case, the now available "SmI$_2$CN" would perform a nucleophilic addition on the aldehyde, prior to the quench of the resulting samarium alcoholate.

Although samarium diiodide has already been used in an analogous reaction with thiocyanates to produce disulfides,[14] only unfunctionalized thiocyanates were tested, leaving the chemoselective aspect unaddressed. Some aspects of these reactions (SmI$_2$/RSCN vs SmI$_2$/RSeCN) present differences. For instance, in the case of thiocyanates the reaction was carried out at room temperature, while for selenocyanates very mild low temperature conditions were used. Also, the stoichiometry used (1/1 ratio substrate/reagent)[14] could be reproduced in our study only in the case of unfunctionalized selenocyanates; for example, when one mmole of benzyl selenocyanate was reacted at -105°C with one mmole of SmI$_2$, benzyl diselenide was instantaneously formed with a 94% isolated yield. However, when keto-selenocyanates were reacted under the same conditions, yields of only about 45% were obtained. To get the results reported in table 1, a minimum of 2 equivalents must be used.

Consequently, samarium diiodide reduction of selenocyanates[2] represents an easy, mild and versatile complement of our first method[1] by broadening the access of functionalized diselenides to the key-function in organic chemistry, *i.e.* the carbonyl group.

ACKNOWLEDGEMENT

REFERENCES AND NOTES

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2. Part of the results described in the present letter was presented as a preliminary communication at the VIIth International Conference on the Chemistry of Selenium and Tellurium. Vaalsbroeck Castle, Netherlands, July 20-25th 1997.

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10. Diselenides spectra were taken on an AC 200 Bruker NMR machine (200 MHz), in $CDCl_3$ (except **5** and **10** in acetone-d6), and the chemical shifts are expressed as δ ppm. **2:** [1]H: 2.90 (4H, t, J=7Hz), 2.55 (4H, t, J=7Hz), 2.41 (4H, t, J=7Hz), 2.02 (4H, quint., J=7Hz), 1.56 (4H, quint., J=7Hz), 1.33 (4H, sextet, J=7Hz), 0.90 (6H, t, J=7Hz); [13]C: 210.35, 42.69, 41.78, 29.07, 25.96, 24.65, 22.35, 13.85. **3:** [1]H: 3.63 (2H, m), 2.94 (4H, t, J=7Hz), 1.93-1.25 (22H, m), 0.91 (6H, t, J=7Hz); [13]C: 71.45, 37.32, 37.06, 30.02, 27.83, 27.15, 22.73, 14.08. **4:** [1]H: 3.65 (1H, m), 2.94 (4H, quad., J=7Hz), 2.57 (2H, t, J=7Hz) 2.45-1.23 (19H, m), 0.91 (6H, t, J=7Hz); [13]C: 210.54, 71.45, 42.72, 41.83, 37.30, 37.09, 30.14, 28.98, 27.83, 27.10, 25.96, 24.75, 22.73, 22.36, 14.06, 13.84. **10:** [1]H: 4.39 (4H, t, J=6Hz), 3.14 (4H, t, J=7Hz), 2.76 (4H, m), 2.33-2.23 (8H, m), 1.53 (6H, t, J=2Hz); [13]C: 204.31, 184.60, 115.86, 69.00, 33.99, 31.72, 26.01, 25.51, 6.25. **11:** [1]H: 5.92 (2H, d, J= 6Hz), 5.77 (2H, m), 3.83 (2H, m), 3.63 (4H, m), 2.95 (4H, t, J=7Hz), 2.70 (2H, d, J=17Hz), 2.46-1.75 (6H, m); [13]C: 214.63, 135.26, 129.31, 64.02, 59.59, 42.00, 34.08, 27.35, 26.51. **12:** [1]H: 4.21 (4H, t, J=7Hz), 2.97 (4H, t, J=7Hz), 2.90 (4H, s), 2.84-2.73 (8H, m), 1.52 (4H, quad., J=7Hz), 0.83 (6H, t, J=7Hz); [13]C: 216.13, 171.46, 64.91, 57.17, 38.73, 35.65, 28.10, 26.81, 8.37. **13:** [1]H: 3.27 (2H, d, J=12Hz), 2.98 (2H, d, J=12Hz), 2.43 (2H, t, J=4Hz), 2.32 (2H, dt, J1=4Hz, J2=18Hz), 2.25-1.39 (10H, m), 0.93 (6H, s), 0.92 (6H, s); [13]C: 217.71, 58.97, 51.39, 42.69, 40.72, 38.45, 29.48, 26.77, 17.42, 9.40. **14:** [1]H: 9.77 (2H, t, J=2Hz), 2.90 (4H, t, J=7Hz), 2.43 (4H, dt, J1=7Hz, J2=2Hz), 1.76-1.26 (24H, m); [13]C: 202.82, 43.88, 30.91, 30.15, 29.40, 29.22, 29.08, 28.87, 22.03. **15:** [1]H: 4.48 (2H, t, J= 7Hz), 3.19 (2H, broad), 2.91 (4H, t, J=7Hz), 1.90-1.23 (28H, m); [13]C: 120.07, 61.27, 35.14, 30.87, 30.18, 29.37, 29.19, 28.90, 28.85, 24.50; IR (neat, ν cm^{-1}): 3115-3620 (OH). All compounds displayed good MS-EI data for diselenated structures.

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