JOC*Note*

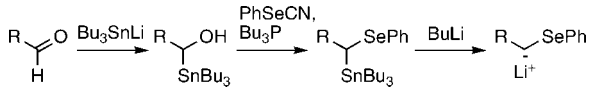
[1-(Phenylseleno)alkyl]stannanes−Mixed Selenium/Tin Analogs of Acetals: Preparation from α-Hydroxystannanes and Use for Generating Selenium-Stabilized Carbanions

Shimal C. Fernandopulle, Derrick L. J. Clive,* and Maolin Yu

Chemistry Department, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

derrick.clive@ualberta.ca

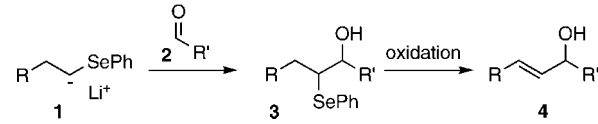
Received February 22, 2008



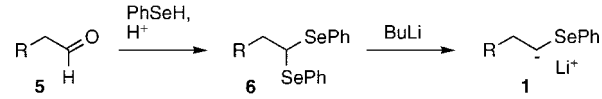
Selenium-stabilized carbanions are available by a route that does not involve acid-catalyzed formation of selenoacetals. Aldehydes are converted first into α-hydroxystannanes and then into α-(phenylseleno)stannanes. Treatment with BuLi affords selenium-stabilized carbanions by preferential Sn/Li exchange.

In connection with work aimed at the synthesis of the complex natural product halichlorine,[1] a need arose in this laboratory to generate a selenium-stabilized carbanion that could be condensed[2] with an aldehyde in order to form an allylic alcohol[3] by selenoxide fragmentation (Scheme 1). The standard route to selenium-stabilized carbanions is by the action of BuLi on selenoacetals (**6** → **1**, Scheme 2).[2,4] In turn, the selenoacetals are normally made[5] by reaction of an aldehyde with PhSeH in the presence of a protic or Lewis acid. In the particular case that prompted the present investigation, such acidic conditions were deemed unacceptable, and so we considered a route to selenium-stabilized carbanions that involves the use of nucleophilic reagents (Bu_3SnLi and $PhSe^-$) along the lines summarized in Scheme 3. Several 1-[(phenylseleno)alkyl]stannanes of type **8** had been reported,[6] and it was known that they react in the desired manner with BuLi, the rate of attack of BuLi on tin evidently being higher than on selenium. A similar preference

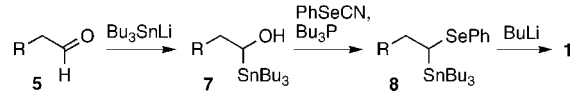
SCHEME 1. Formation of Allylic Alcohols by Selenoxide Fragmentation



SCHEME 2. Conversion of Selenoacetals into Selenium-Stabilized Carbanions



SCHEME 3. Formation of α-(Phenylseleno)stannanes



for Sn/Li exchange is observed with α-halostannanes.[7] However, the compounds of type **8** had previously been made from (phenylseleno)acetals **6** by conversion into the corresponding selenium-stabilized carbanions **1** and quenching with Bu_3SnCl.[6] Our proposed route (Scheme 3) avoids the acid-catalyzed formation of (phenylseleno)acetals and proceeds instead by way of α-stannyl alcohols **7**. These compounds are well-known, but although they can be trapped by acylation[8] or as ethers,[8a,d,9,10] they have the reputation[7,10,11] of being quite labile, and it was not clear if they could be converted into the selenides **8**.

In our first experiment, isovaleraldehyde was used as a test substrate (Table 1, entry i). Reaction with Bu_3SnLi was accomplished by generating the tin reagent at 0 °C from Bu_3SnH and LDA.[10,12] We also examined the effect of generating a suitable tin reagent by other methods such as reaction of Li with Bu_3SnCl,[13] reaction of $(Bu_3Sn)_2$ with BuLi,[14] treatment of Bu_3SnH with *i*-PrMgCl,[15] or the generation of what we assume (from the stoichiometry used) to be $Bu_3SnCeCl_2$. However, in none of these experiments was there any obvious improvement in the yield of (phenylseleno)stannane obtained from the crude α-stannyl alcohol (see later), and so we settled

(1) Clive, D. L. J.; Yu, M.; Wang, J.; Yeh, V. S. C.; Kang, S. *Chem. Rev.* **2005**, *105*, 4483–4514.

(2) Review on selenium-stabilized carbanions: Clive, D. L. J. *Organic Compounds of Sulphur, Selenium, and Tellurium*; Royal Society of Chemistry: London, 1981; Vol. 6, Specialist Periodical Reports, pp 112−126.

(3) (a) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697–2699. Review:(b) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049–1132.

(4) Hoffmann, R. W.; Bewersdorf, M. *Liebigs Ann. Chem.* **1992**, 643–653.

(5) Review on the chemistry of selenoacetals: Krief, A.; Hevesi, L. *Janssen Chim. Acta* **1984**, *2*, 3–14.

(6) Hoffmann, R. W.; Julius, M.; Oltmann, K. *Tetrahedron Lett.* **1990**, *31*, 7419–7422.

(7) Torisawa, Y.; Shibasaki, M.; Ikegami, S. *Tetrahedron Lett.* **1981**, *22*, 2397–2400.

(8) E.g (a) Dussault, P. H.; Eary, C. T.; Lee, R. J.; Zope, U. R. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2189–2204. (b) Tsai, Y.-M.; Chang, S.-Y. *J. Chem. Soc., Chem. Commun.* **1995**, 981–982. (c) Ritter, K. *Tetrahedron Lett.* **1990**, *31*, 869–872. (d) Ye, J.; Bhatt, R. K.; Falck, J. R. *J. Am. Chem. Soc.* **1994**, *116*, 1–5.

(9) For example: (a) Linderman, R. J.; Godfrey, A.; Horne, K. *Tetrahedron* **1989**, *45*, 495–506. (b) Chan, P.C.-M.; Chong, J. M. *J. Org. Chem.* **1988**, *53*, 5584–5586. (c) Pratt, A. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1115–1117. (d) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392–2398. (e) Candela Lena, J. I.; Rico Ferreira, M. del R.; Martin Hernando, J. I.; Arseniyadis, S. *Tetrahedron: Asymmetry* **2001**, *12*, 3281–3291. (f) Katsumura, S.; Fujiwara, S.; Isoe, S. *Tetrahedron Lett.* **1985**, *26*, 5827–5830. (g) Marshall, J. A.; Gung, W. Y. *Tetrahedron Lett.* **1989**, *30*, 309–312. (h) Crimmins, M. T.; Thomas, J. B. *Tetrahedron Lett.* **1989**, *30*, 5997–6000.

(10) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481–1487.

(11) Mohapatra, S.; Bandyopadhyay, A.; Barma, D. K.; Capdevilla, J. H.; Falck, J. R. *Org. Lett.* **2003**, *5*, 4759–4762.

(12) Marshall, J. A.; Garofalo, A. W.; Hinkle, K. W. *Organic Syntheses*; Wiley: New York, 2004; Collect. Vol *10*, pp 496−500.

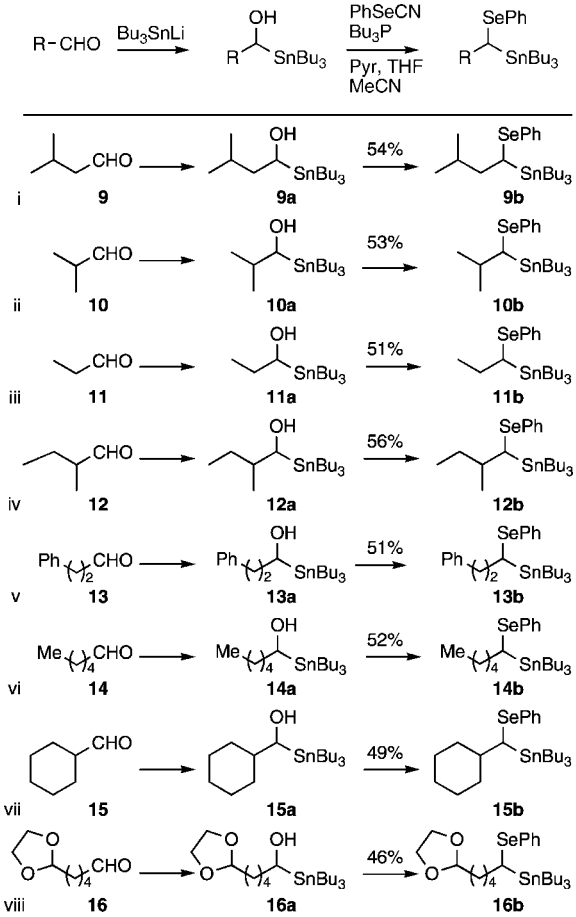
(13) Mochida, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3299–3306.

(14) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836–4838.

(15) Pearson, W. H.; Lindbeck, A. C.; Kampf, J. W. *J. Am. Chem. Soc.* **1993**, *115*, 2622–2636.

10.1021/jo8004292 CCC: $40.75 © 2008 American Chemical Society
Published on Web 07/02/2008

TABLE 1. Conversion of Aldehydes into α-(Phenylseleno)stannanes[a]



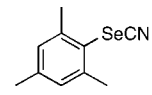
[a] Yields refer to two steps from the aldehyde and are based on the aldehyde as the limiting component.

on the LDA/Bu_3SnH procedure.[10,12,16] The crude α-hydroxystannane **9a** was then treated with PhSeCN-Bu_3P[17] under a variety of conditions in attempts to optimize the yield of the desired α-(phenylseleno)stannane **9b**. Compound **9b** was easily handled and could be chromatographed over silica gel without decomposition, unlike its precursor **9a**. Attempts to chromatograph **9a** over silica gel always resulted in significant loss (at least 20%) of material, and TLC analysis using a plate developed in two orthogonal directions confirmed that extensive decomposition occurs. The alcohol → selenide conversion for **9a** → **9b** was tried in THF−MeCN mixtures with and without pyridine, the yields being 33% (THF), 30% (1:3 THF−MeCN), 21% (1:0.13 THF−pyridine), and 54% (1:3:0.4 THF−MeCN−pyridine).

Attempts were also made (using **9a**) to introduce the PhSe group via displacement of the corresponding tosylate, mesylate, or iodide, but these experiments did not give improved yields over the PhSeCN/Bu_3P method. Instead of PhSeCN we tried *N*-(phenylseleno)phthalimide-Bu_3P[18] (with **9a**); again no improvement was found. When we made the selenides in THF, with neither pyridine nor MeCN, we usually isolated some alkyl selenide corresponding to the desired (phenylseleno)stannane but having the Bu_3Sn unit replaced by H; however, under the optimum conditions (THF−MeCN−pyridine), formation of this byproduct was usually insignificant.

The (phenylseleno)stannanes are nonpolar, and the nonpolar byproduct, PhSeSePh, was most conveniently removed by reaction with $NaBH_4$ and capture of the resulting phenylselenide anion with $BrCH_2CO_2H$. As shown in Table 1, yields of (phenylseleno)stannanes over the two steps from the aldehyde are usually a little above 50%; this represents our optimum conditions. The (phenylseleno)stannane **12b** was a 3:2 mixture of diastereoisomers. Since a few examples are known in which an aldehyde is converted in well over 70% yield via its α-hydroxystannane into the corresponding *O*-acyl derivative,[8a,b,d] bromide,[19] or MOM ether[8a,9a,c,e,f,h] it is probable that in our sequence the alcohol → selenide conversion is inefficient.

Generation of selenium-stabilized carbanions from compounds **9b**−**16b** proceeded without incident, and only a few experiments were needed to establish satisfactory conditions.[6] These involve treatment of the α-(phenylseleno)stannane with an excess of BuLi (2 equiv) in THF at −78 °C, usually for no longer than 15 min (except for example x of Table 2), followed by addition of the aldehyde (3 equiv). Yields are generally well above 70% based on the α-(phenylseleno)stannane. In one case (Table 2, entry xi) the intermediate carbanion was quenched with D_2O to afford the expected monodeuterated product **30** in 90% yield, indicating that selective cleavage of the C−Sn bond occurs efficiently, at least in this case. However, a few of the condensation yields were below 70%, and so the possibility was considered of blocking attack of BuLi at selenium by making the ArSe unit more hindered. To this end the known selenocyanate **33** was prepared,[20] but attempts to use it in place of PhSeCN under the standard conditions[17] for replacement of an OH group gave low yields; hence the matter was not pursued.



33

As expected, the hydroxyselenides shown in Table 2 were generally obtained as mixtures of *syn* and *anti* diastereoisomers; in three cases the isolated hydroxyselenides (Table 2, compounds **25**, **26**, and **28**) appeared (^1H and ^{13}C NMR) to be single isomers.

Once we had gained some experience in making (phenylseleno)stannanes, we attempted to prepare the germanium analogs. Deprotonation of Bu_3GeH with LDA and addition to isovaleraldehyde did afford the desired α-germyl alcohol, which could be converted into the α-germyl selenide **34**,[21] although the overall yield was very low (17%). A few examples have been reported of the formation of germyl alcohols by addition of trialkylgermyl alkali metals to carbonyl compounds, although

(16) For preparation of α-hydroxystannanes by use of silyl stannanes, see: (a) Bhatt, R. K.; Ye, J.; Falck, J. R. *Tetrahedron Lett.* **1994**, *35*, 4081–4084. (b) Busch-Petersen, J.; Bo, Y.; Corey, E. J. *Tetrahedron Lett.* **1999**, *40*, 2065–2068.

(17) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485–1486.

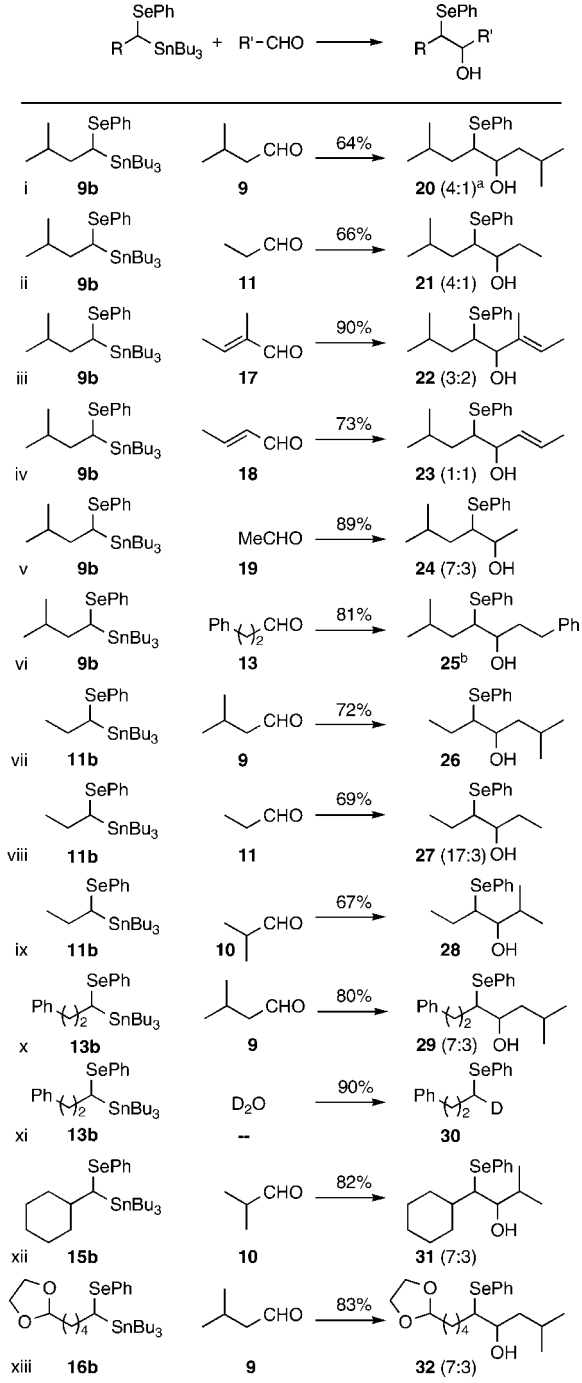
(18) Grieco, P. A.; Jaw, J. Y.; Claremon, D. A.; Nicolaou, K. C. *J. Org. Chem.* **1981**, *46*, 1215–1217.

(19) Jeanjean, F.; Fournet, G.; Le Bars, D.; Goré, J. *Eur. J. Org. Chem.* **2000**, 1297–1305.

(20) (a) Klapötke, T. M.; Krumm, B.; Mayer, P.; Piotrowski, H.; Vogt, M. Z. *Anorg. Allg. Chem.* **2003**, *629*, 1117–1123. (b) We made the selenocyanate from the aryl iodide: Suzuki, H. *Synthesis* **1977**, 640–641.

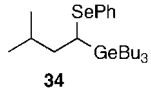
(21) For rare examples of systems with germanium and selenium attached to the same carbon, see:(a) Ryazantsev, V. A.; Stadnichuk, M. D.; Petrov, A. A. *J. Gen. Chem. USSR* **1980**, *50*, 1053–1059. (b) Wieber, M.; Schwarzmann, G. *Monatsh. Chem.* **1969**, *100*, 74–78.

TABLE 2. Conversion of α-(Phenylseleno)stannanes into *β*-Hydroxyselenides



[a] Ratio of diastereoisomers is given in parentheses. [b] Contains slight impurities.

the process can be problematic.[22] This step was not investigated, however, because germanium/lithium exchange under our usual conditions did not appear to take place, as judged by trapping experiments with D_2O or isovaleraldehyde.



34

Formation of allylic alcohols from *β*-hydroxyselenides is a well-established reaction,[3] and so the present route provides access to these alcohols in a way that bypasses the need to generate (phenylseleno)acetals.

Experimental Section

Tributyl[3-methyl-1-(phenylseleno)butyl]stannane (9b). BuLi (1.6 M in hexane, 0.63 mL, 1.00 mmol) was added to a stirred and cooled (−78 °C) solution of *i*-Pr_2NH (0.15 mL, 1.1 mmol) in THF (3 mL). Stirring was continued at −78 °C for 30 min, and the flask was transferred to an ice bath. Bu_3SnH (0.30 mL, 1.1 mmol) was added, and stirring was continued for 15 min. The flask was then transferred back to a cold bath at −78 °C and aldehyde **9** (0.055 mL, 0.50 mmol) was added dropwise. Stirring was continued at −78 °C for 30 min, and the mixture was quenched with saturated aqueous NH_4Cl. The cold bath was removed, and the mixture was allowed to reach room temperature (ca. 30 min). The aqueous phase was extracted with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. The crude product (**9a**) was left under oilpump vacuum for 15 min and used directly in the next step.

The above crude hydroxystannane was dissolved in 3:1 MeCN−THF (4 mL), and pyridine (0.4 mL, 5.0 mmol) was added. The mixture was cooled to 0 °C, and PhSeCN (0.12 mL, 1.0 mmol) and Bu_3P (0.25 mL, 1.0 mmol) were added successively at a fast dropwise rate. The ice bath was removed, and stirring was continued for 4 h. The solvent was evaporated, and the residue was dissolved in 4:1 THF−MeOH (5 mL). The stirred solution was cooled to 0 °C, and an excess of $NaBH_4$ (100 mg) was added. Stirring was continued for 20 min, an excess of $BrCH_2CO_2H$ (400 mg) was added, and the ice bath was removed. Stirring was continued for 30 min, the mixture was diluted with EtOAc, and saturated aqueous $NaHCO_3$ was added. The mixture was extracted with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (1 × 25 cm), using hexane, gave **9b** (138 mg, 54%) as a colorless oil: FTIR (CH_2Cl_2, cast) 3071, 2956, 2926, 2870, 2854 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.76−1.07 (m, 21 H), 1.25−1.40 (sextet, J = 7.1 Hz, 6 H), 1.45−1.68 (m, 7 H), 1.77−1.83 (m, 2 H), 3.05 (dd, J = 8.4, 7.5 Hz, 1 H), 7.2−7.29 (m, 3 H), 7.5 (dd, J = 8.1, 1.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.9 (t), 13.7 (q), 22.0 (q), 22.7 (q), 23.0 (d), 27.4 (t), 28.8 (d), 29.2 (t), 45.6 (t), 126.4 (d), 128.8 (d), 132.3 (d), 132.6 (s); exact mass *m/z* calcd for $C_{23}H_{42}{}^{80}Se^{118}Sn$ 516.14679, found 516.14617.

2,7-Dimethyl-5-(phenylseleno)octan-4-ol (20). BuLi (1.6 M in hexane, 0.12 mL, 0.19 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of **9b** (49 mg, 0.095 mmol) in THF (3 mL) (Ar atmosphere). Stirring was continued for 15 min at −78 °C, and a solution of isovaleraldehyde (0.03 mL, 0.29 mmol) in THF (1 mL) was added dropwise (ca. 1 min). Stirring was continued for 30 min and the mixture was quenched with saturated aqueous NH_4Cl. The cooling bath was removed and stirring was continued for 30 min. The aqueous phase was extracted with EtOAc, and the combined organic extracts were dried (Na_2SO_4) and evaporated. Flash chromatography of the residue over silica gel (0.5 × 10 cm), using 5:95 *t*-BuOMe−CH_2Cl_2, gave **20** (19 mg, 64%) as a colorless oil: FTIR (CH_2Cl_2, cast) 3455, 3072, 2956, 2931, 2869 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) (4:1 mixture of stereoisomers) δ 0.81−0.98 (m, 12 H), 1.17−1.25 (m, 1 H), 1.33−1.53 (m, 2 H), 1.54−1.65 (m, 1 H), 1.70−1.82 (m, 1 H), 1.85−1.96 (m, 0.8 H), 1.98−2.08 (m, 0.2 H), 2.24 (d, J = 5.6 Hz, 0.8 H), 2.30 (d, J = 5.3 Hz, 0.2 H), 3.13−3.20 (m, 0.2 H), 3.32−3.39 (m, 0.8 H), 3.55−3.63 (m, 0.2 H), 3.67−3.75 (m, 0.8), 7.25−7.30 (m, 3 H), 7.56−7.60 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4 (q), 21.6 (q), 21.8 (q), 21.9 (q), 23.1 (q), 23.3 (q), 23.3 (q), 23.5 (q), 24.8 (d), 24.9 (d), 26.2 (d), 26.3 (d), 39.0 (t), 41.2 (t), 42.5 (t), 44.0 (t),

(22) (a) Kruglaya, O. A.; Bravo-Zhivotovskii, D. A.; Vyazankin, N. S. *J. Gen. Chem. USSR* **1979**, *46*, 1847. (b) Bulten, E. J.; Noltes, J. G. *J. Organomet. Chem.* **1971**, *29*, 409–417.

54.7 (d), 70.7 (d), 71.5 (d), 127.5 (d), 127.6 (d), 128.7 (s), 128.9 (d), 129.0 (d), 129.3 (s), 134.5 (d), 134.9 (d); exact mass *m*/*z* calcd for $C_{16}H_{26}O^{80}Se$ 314.11490, found 314.11466.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

Supporting Information Available: NMR spectra for **9b**−**16b**, **21**−**32**, and **34** and experimental procedures for **10b**−**16b**, **21**−**32**, and **34** This material is available free of charge via the Internet at http://pubs.acs.org.

JO8004292