Synthesis of 2-(Phenylselanyl)tetrahydrofurans from γ-Lactones and of γ-Hydroxydiselenoacetals from γ-Lactols

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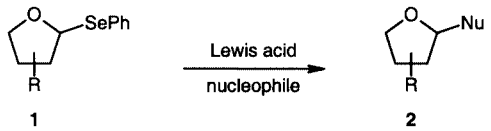
Received 12 December 2000; revised 1 February 2001

Abstract: A known one-pot procedure for the synthesis of 2-(phenylselanyl)tetrahydrofurans could be applied to the transformation of γ-lactones **3a-c** into 2-(phenylselanyl)tetrahydrofurans **1a-c**. Surprisingly, formation of γ-hydroxydiselenoacetals **5b** and **5c** was observed when γ-lactols **4b** and **4c** were treated with selenophenol and boron trifluoride etherate.

Key words: furans, lactones, reductions, selenium, selenoacetal

In a series of publications, we reported that γ-lactols are converted into 2-substituted tetrahydrofuran derivatives by treatment with silylated nucleophiles[1] or organometallic compounds[2] in the presence of a suitable Lewis acid. The stereoselectivity of this transformation was systematically studied and found to be particularly high for 4-substituted γ-lactols. In these investigations, we also wanted to vary the leaving group at the tetrahydrofuran core and therefore became interested in the synthesis of 2-(phenylselanyl)tetrahydrofurans **1**. These cyclic selenoacetals should not only be of importance for the nucleophilic substitution given in Scheme 1, but they might also be precursors for the generation of tetrahydrofuryl radicals[3] or 2-lithiotetrahydrofurans.[4]

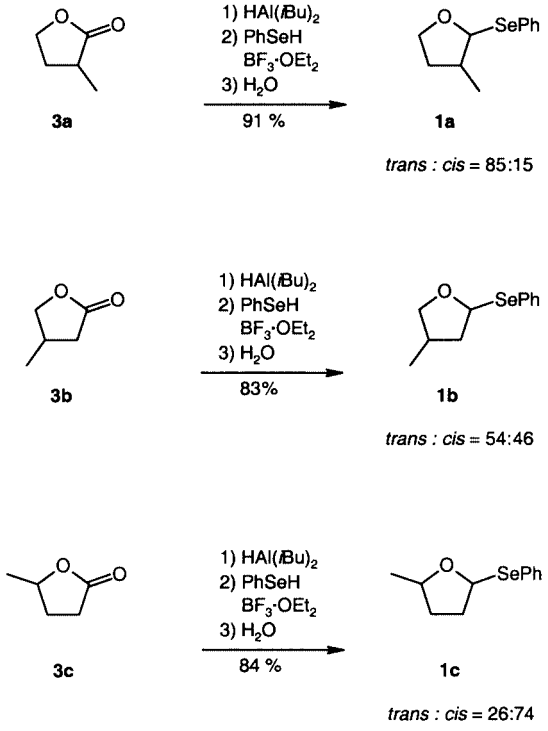


1 2

Scheme 1

We here report that the required 2-(phenylselanyl)tetrahydrofurans **1a–c** can be easily prepared in a one-pot procedure using the γ-lactones **3a–c** as starting material. This method has been described by Goldsmith, Liotta et al.[5] for γ-lactone **3c** and two δ-lactones and consists of the subsequent treatment of lactones with diisobutylaluminium hydride, selenophenol, and boron trifluoride followed by aqueous workup. When applied to γ-lactones **3a–c,** this procedure furnished the desired (phenylselanyl)tetrahydrofurans **1a–c** in high yields and good purity (Scheme 2).

The *trans:cis* ratios range from 85:15 to 26:74 and are probably the result of thermodynamic rather than kinetic



Scheme 2

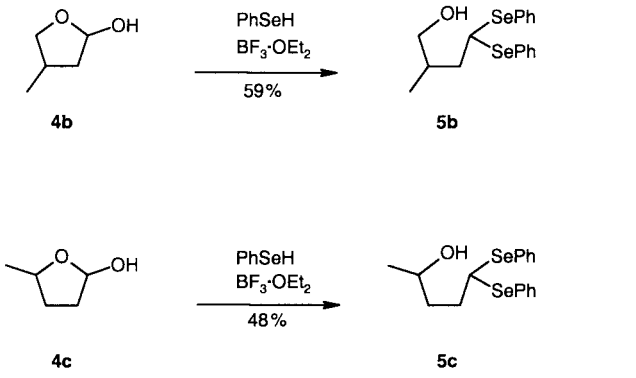
control. Goldsmith, Liotta et al.[5] also obtained a diastereomeric mixture (3:1) of **1c** and assigned *trans*-configuration to the major isomer. Contrarily, we assume that this major component should have a *cis*-configuration.[6]

We were rather surprised that our first attempt to prepare **1** the γ-lactols **4** did not provide the desired cyclic O,Se-acetals but the acyclic γ-hydroxydiselenoacetals **5** (Scheme 3). Treatment of γ-lactols **4b** and **4c** with selenophenol and boron trifluoride afforded compounds **5b** and **5c** as crude products in high yield and reasonable purity, containing only diphenyldiselenide as side product. Column chromatography furnished pure **5b** and **5c** in good yield.[7]

The formation of the cyclic selenoacetals **1** in the one-pot procedure must occur by nucleophilic attack of selenophenol to the cyclic oxocarbenium ion **7** derived from the intermediate reduction product **6** and boron trifluoride (Scheme 4). In contrast, γ-lactols **4** apparently react with selenophenol via the γ-hydroxyaldehydes **8**, thus giving the acyclic products **5**. The Lewis acid added to the mix-

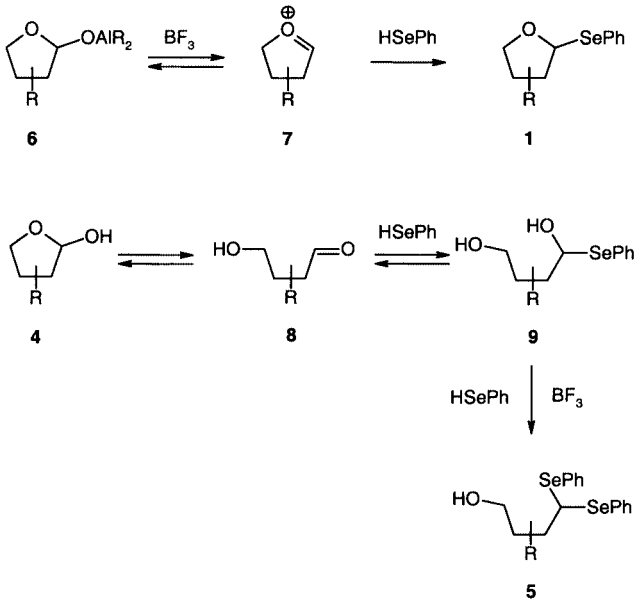
Synthesis 2001, No. 6, 04 05 2001. Article Identifier:
1437-210X,E;2001,0,06,0867,0870,ftx,en;T04400SS.pdf.

ISSN 0039-7881



Scheme 3

ture of γ-lactol and selenophenol may only be involved after formation of semiacetal **9**, which, after dissociation and reaction with the second equivalent of selenophenol, gives the isolated diselenoacetals **5** (Scheme 4). A similar dichotomy of γ-lactols has been reported by Paquette et al.[8] for reactions with thiols which strongly depend on the Lewis acid used.



Scheme 4

All reactions were performed under argon atmosphere in flame-dried flasks and the components were added by means of syringes. All solvents were dried by standard methods. For other general information and synthesis of γ-lactols **4b** and **4c** see ref. 2. Starting material γ-lactones **3b**,[9] **3c**,[10] and selenophenol[11] were prepared according to literature procedures. Compound **3a** was purchased from Lancaster.

Synthesis of 2-(Phenylselanyl)tetrahydrofurans 1 Starting from γ-Lactones 3; General One-pot Procedure

γ-Lactone **3** was dissolved in toluene (2 mL/mmol of **3**) and cooled to –80 °C to –90 ºC. Then, 1.2 equivalents of diisobutylaluminium hydride (1 M solution in toluene) were added within 30 min. The resulting solution was stirred for 30 min at –78 ºC, 3 equivalents of BF_3•OEt_2 and, after 15 min, 2 equivalents of selenophenol were added. The mixture was warmed to –30 ºC within 2 h, then hydrolysed with 10 mL of H_2O and warmed to r.t. After precipitation of the aluminium hydroxides the mixture was filtered through a Celite pad and the filtrate was extracted with *tert*-butyl methyl ether. The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was purified by Kugelrohr distillation.

3-Methyl-2-(phenylselanyl)tetrahydrofuran (**1a**)
According to the general procedure, a solution of γ-lactone **3a** (2.00 g, 20.0 mmol) in toluene was treated with diisobutylaluminium hydride, then with BF_3•OEt_2 and finally with selenophenol. After workup the residue was purified by distillation (110 °C/0.01 torr). Yield: 4.41 g (91%) as a *trans*:*cis*-mixture of **1a** (85:15). The NMR data are given in Tables 1 and 2.

IR (neat): ν = 3080–3020 (=CH), 2980–2840 (CH), 1570 (C=C), 1070–1000 cm^{-1} (O-C-Se).

Anal. Calcd for $C_{11}H_{14}OSe$ (241.2): C, 54.78; H, 5.85. Found: C, 54.98; H, 6.08.

4-Methyl-2-(phenylselanyl)tetrahydrofuran (**1b**)
According to the general procedure, a solution of γ-lactone **3b** (1.50 g, 15.0 mmol) in toluene was treated with diisobutylaluminium hydride, then with BF_3•OEt_2 and finally with selenophenol. After workup the residue was purified by distillation (110 °C/0.01 torr). Yield: 3.00 g (83%) as a *trans*:*cis*-mixture of **1b** (54:46). The NMR data are given in Tables 1 and 2.

IR (neat): ν = 3090–3030 (=CH), 2980–2830 (CH), 1580 (C=C), 1100–990 cm^{-1} (O-C-Se).

Anal. Calcd for $C_{11}H_{14}OSe$ (241.2): C, 54.78; H, 5.85. Found: C, 55.16; H, 6.03.

5-Methyl-2-(phenylselanyl)tetrahydrofuran (**1c**)
According to the general procedure, a solution of γ-lactone **3c** (1.50 g, 15.0 mmol) in toluene was treated with diisobutylaluminium hydride, then with BF_3•OEt_2 and finally with selenophenol. After workup the residue was purified by distillation (110 °C/0.01 torr). Yield: 3.04 g (84%) as a *trans*:*cis*-mixture of **1c** (26:74). The NMR data are given in Tables 1 and 2.

IR (neat): ν = 3090–3040 (=CH), 3000–2840 (CH), 1575 (C=C), 1090–1030 cm^{-1} (O-C-Se).

Anal. Calcd for $C_{11}H_{14}OSe$ (241.2): C, 54.78; H, 5.85. Found: C, 54.91; H, 5.80.

2-Methyl-4,4-bis(phenylselanyl)-1-butanol (5b)
A solution of γ-lactol **4b** (500 mg, 4.90 mmol) and selenophenol (1.15 g, 7.37 mmol) in diethyl ether (20 mL) was slowly treated with BF_3•OEt_2 (0.8 mL). The mixture was stirred at room temperature for 3 h, quenched with water (7.5 mL) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to dryness. Yield: 1.30 g (89%) of **5b** containing traces of diphenyldiselenide. Analytically pure **5b** (872 mg, 59%) was obtained by thin layer chromatography (silicagel, pentane–diethyl ether, 1:1).

IR (film): ν = 3600–3100 (O-H), 3040, 3030 (=C-H), 2980–2800 (C-H), 1570 (C=C), 1470, 1430 (C-H), 1100–1000 cm^{-1} [$C(SePh)_2$].

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.54–7.02 (m, 10 H, Ph), 4.55 (dd, *J* = 8.5 Hz, *J* = 6.5 Hz, 1 H, 4-H), 3.36 (d, *J* = 5.5 Hz, 2 H, 1-H), 2.15–1.95 (m, 2 H, 3-H), 1.80–1.68 (m, 1 H, 2-H), 1.70–1.50 (br s, 1 H, OH), 0.83 (d, *J* = 6.5 Hz, 3 H, 2-Me).

^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 134.8, 129.0, 128.1 (3 d, Ph), 130.2 (s, Ph), 67.5 (t, C-1), 41.5 (d, $J_{^{13}C\text{-}^{77}Se}$ = 75 Hz C-4), 41.1 (t, C-3) 34.8 (d, C-2), 16.3 (q, 2-Me).

Table 1 ^{1}H NMR (300 MHz, $CDCl_3$), Data of Compounds **1a–c**[a]; δ, *J* (Hz)

Product	2-H	3-H	3-H	4-H	4-H	5-H	5-H	3/4/5-Me	2-SePh
trans-**1a**	5.41 (d, *J* = 5)	2.39 (sext. d, *J* = 7, 5)	-	2.12 (ddt, *J* = 12, 7, 5)	1.52 (dtd, *J* = 12, 8.5, 7)	3.98 (dd, *J* = 8.5, 5)	3.98 (dd, *J* = 8.5, 5)	1.13 (d, *J* = 7)	7.70–7.58, 7.30–7.20 (2 m)
cis-**1a**	5.93 (d, *J* = 5.5)	2.58–2.44 (m)	-	2.18–2.00 (m)	1.72 (dtd, *J* = 12, 9, 8)	4.15 (td, *J* = 9, 4.5)	3.89 (q, *J* = 9)	1.18 (d, *J* = 7)	7.70–7.58, 7.30–7.20 (2 m)
trans-**1b**	5.94 (dd, *J* = 7, 3)	2.22 (ddd, *J* = 13.5, 7.5, 3)	1.95 (dt, *J* = 13.5, 7)	2.25–2.15 (m)	-	4.11 (dd, *J* = 8.5, 7)	3.43 (dd, *J* = 8.5, 5)	0.99 (d, *J* = 7)	7.70–7.45, 7.32–7.10 (2 m)
cis-**1b**	5.85 (dd, *J* = 7, 6)	2.58 (ddd, *J* = 13.5, 9, 7)	1.57 (ddd, *J* = 13.5, 8.5, 6)	2.42 (br sext., *J* = 8)	-	3.93 (dd, *J* = 8, 7)	3.50 (dd, *J* = 9, 8)	1.02 (d, *J* = 6.5)	7.70–7.45, 7.32–7.10 (2 m)
trans-**1c**	5.87 (dd, *J* = 7, 3)	2.45–1.85 (m)	2.45–1.85 (m)	1.65–1.48 (m)	1.65–1.48 (m)	4.22 (br sext., *J* = 6.5)	-	1.18 (d, *J* = 6)	7.55–7.45, 7.20–7.10 (2 m)
cis-**1c**	5.67 (dd, *J* = 6.5, 3)	2.45–1.85 (m)	2.45–1.85 (m)	1.65–1.48 (m)	1.65–1.48 (m)	4.09 (br sext., *J* = 6.5)	-	1.24 (d, *J* = 6)	7.55–7.45, 7.20–7.10 (2 m)

[a] The integrals have the expected intensities.

Table 2 ^{13}C NMR (75.5 MHz, $CDCl_3$), Data of Compounds **1a–c**; δ

Product	C-2[a]	C-3	C-4	C-5	3/4/5-Me	2-SePh
trans-**1a**	91.2 (d)	41.5 (d)	33.4 (t)	67.7 (t)	18.6 (q)	133.7, 128.9, 127.2 (3 d), 130.6 (s)
cis-**1a**	92.3 (d)	39.9 (d)	32.6 (t)	67.1 (t)	16.2 (q)	134.3 (d)[b]
trans-**1b**	84.3 (d)	42.1 (t)	33.2 (d)	74.3 (d)	16.5 (q)	133.3, 128.6, 127.0 (3 d), 130.7 (s)
cis-**1b**	84.6 (d)	41.7 (t)	32.5 (d)	73.5 (t)	16.4 (q)	133.7 (d)[b]
trans-**1c**	84.3 (d)	33.8 (t)[c]	31.7 (t)[c]	74.6 (d)	19.8 (q)	133.3, 128.9, 127.0 (3 d), 130.7 (s)
cis-**1c**	83.4 (d)	34.8 (t)[c]	32.3 (t)[c]	77.9 (d)	21.7 (q)	134.4, 127.1 (2 d)[b]

[a] J = 75 Hz.
[b] The other signals of SePh are overlapping with signals of the major diastereomer and cannot be assigned unambiguously.
[c] Assignment interchangeable.

Anal. Calcd for $C_{17}H_{20}OSe_2$ (398.3): C, 51.27; H, 5.06. Found: C, 51.42; H, 5.17.

5,5-Bis(phenylselanyl)-2-pentanol (5c)
Analogously to the synthesis of **5b**, γ-lactol **4c** (450 mg, 4.41 mmol) and selenophenol (942 mg, 6.03 mmol) in diethyl ether (10 mL) were treated with BF_3•OEt_2 (0.7 mL). Yield: 1.37 g of crude **5c** containing traces of diphenyldiselenide. Analytically pure **5c** (580 mg, 48%) was obtained by thin layer chromatography (silicagel, pentane–diethyl ether, 1:1).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.59–7.31 (m, 10 H, Ph), 4.50 (t, *J* = 6.5 Hz, 1 H, 5-H), 3.82 (sext., *J* = 6.0 Hz, 1 H, 2-H), 2.12–1.89, 1.75–1.65 (2 m, 5 H, 4-H, 3-H, OH), 1.10 (d, *J* = 6.0 Hz, 3 H, 1-H).

^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 134.6, 129.2, 128.0 (3 d, Ph), 130.2 (s, Ph), 67.2 (d, $J_{^{13}C\text{-}^{77}Se}$ = 75 Hz, C-5), 43.8 (d, C-2), 37.7, 33.3 (2 t, C-4, C-3), 23.5 (q, C-1).

MS (70 eV, EI): *m/z* = 405, 404, 403, 402, 401, 400, 399, 398, 397, 396, 395, 394, 393, 392, 390 (M^+), 159, 157, 155, 153 ($SePh^+$), 85 [M^+-(2 SePh + H)], 77 ($C_6H_5^+$).

Acknowlegdement

Generous support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is most gratefully acknowledged.

References

(1) (a) Schmitt, A.; Reissig, H.-U. *Eur. J. Org. Chem.* **2000**, 3893. (b) Schmitt, A.; Reissig, H.-U. *Eur. J. Org. Chem.* **2001**, 1169. (c) For a preliminary communication of our results see: Schmitt, A.; Reissig, H.-U. *Synlett* **1990**, 40. (d) For earlier work with highly substituted γ-lactols see: Brückner, C.; Lorey, H.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 556. (e) Brückner, C.; Holzinger, H.; Reissig, H.-U. *J. Org. Chem.* **1988**, *53*, 2450. (f) Reissig, H.-U.; Holzinger, H.; Glomsda, G. *Tetrahedron* **1989**, *45*, 3139. (g) For recent contributions of other groups see: Alonso, E.; Ramón, D. J.; Yus, M. *Tetrahedron* **1997**, *53*, 2641. (h) Nishiyama, Y.; Katoh, T.; Deguchi, K.; Morimoto, Y.; Itoh, K. *J. Org. Chem.* **1997**, *62*, 9339. (i) Pilli, R. A.; Riatto, V. B. *Tetrahedron: Asymmetry* **2000**, *11*, 3675.

(2) Schmitt, A.; Reissig, H.-U. *Chem. Ber.* **1995**, *128*, 871.

(3) Review: Renaud, P. *Top. Curr. Chem.* **2000**, *208*, 81.

(4) Review: Ponthieux, S.; Paulmier, C. *Top. Curr. Chem.* **2000**, *208*, 113.

(5) Goldsmith, D. J.; Liotta, D. C.; Volmer, M.; Hoekstra, W.; Waykole, L. *Tetrahedron* **1985**, *41*, 4873.

(6) In ref. 7 only a 90 MHz ^{1}H NMR spectrum of **1c** was reported. We present data resulting from a 300 MHz spectrum and a ^{13}C NMR spectrum. Comparing our data with many other 1,5-disubstituted tetrahydrofuran derivatives, a cis-configuration of the major isomer is very likely.

(7) Reviews about synthesis and reactions of selenoacetals see: (a) Clarembeau, M.; Cravador, A.; Dumont, W.; Hevesi, L.; Krief, A.; Lucchetti, J.; VanEnde, D. *Tetrahedron* **1985**, *41*, 4793. (b) Paulmier, C. *Selenium Reagents and Intermediates in Organic Synthesis* Pergamon Press: Oxford, **1986**.

(8) Bulman-Page, P. C.; Roberts, R. A.; Paquette, L. A. *Tetrahedron Lett.* **1983**, *24*, 3555.

(9) Grimm, E.; Reissig, H.-U. *J. Org. Chem.* **1985**, *50*, 242.

(10) Hünig, S.; Märkl, G.; Sauer, J. *Integriertes organisches Praktikum* Verlag Chemie: Weinheim, **1979**, 538.

(11) Foster, D. C. *Org. Synth. Coll.* Vol. III, John Wiley & Sons: London, **1995**, 771.