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

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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 nucleophiles1 or organometallic compounds2 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 radicals3 or 2-lithiotetrahydrofurans.4

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 disobutylaluminium 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 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-hydroxylaldehydes 8, thus giving the acyclic products 5. The Lewis acid added to the mix-
Scheme 3

ture of γ-lactol and selenophenol may only be involved after formation of semiacetals 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. 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-lactones 4b and 4c see ref. 2. Starting material γ-lactones 3b, 3c, and selenophenol 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 °C. Then, 1.2 equivalents of disobutylaluminium hydride (1 M solution in toluene) were added within 30 min. The resulting solution was stirred for 30 min at −78 °C. 2 equivalents of BF3·OEt2 and, after 15 min, 2 equivalents of selenophenol were added. The mixture was warmed to 30–35 °C within 2 h, then hydrolysed with 10 mL of H2O 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 (MgSO4) 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 disobutylaluminium hydride, then with BF3·OEt2 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 (≈C–H), 2980–2840 (CH), 1570 (C=C), 1070–1000 cm−1 (O–C–Se).


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 disobutylaluminium hydride, then with BF3·OEt2 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 (≈C–H), 2980–2830 (CH), 1580 (C=C), 1100–990 cm−1 (O–C–Se).


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 disobutylaluminium hydride, then with BF3·OEt2 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 (≈C–H), 3000–2840 (CH), 1575 (C=C), 1090–1030 cm−1 (O–C–Se).


2-Methyl-4,4-bis(phenylselanyl)-1-butanol (5b)

A solution of γ-lactone 4b (500 mg, 4.90 mmol) and selenophenol (1.15 g, 7.37 mmol) in diethyl ether (20 mL) was slowly treated with BF3·OEt2 (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 (Na2SO4) 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 (CH), 1570 (C=C), 1470, 1430 (C–H), 1100–1000 cm−1 [C(SePh)3].

1H NMR (CDCl3, 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).

13C NMR (CDCl3, 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 = 13C–77Se = 75 Hz C–4), 41.1 (t, C–3) 34.8 (d, C–2), 16.3 (g, 2-Me).

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1.75 were treated with BF₃ and selenophenol (942 mg, 6.03 mmol) in diethyl ether (10 mL).

**1H NMR (CDCl₃, 300 MHz):**
- δ 7.70–7.58, 7.30–7.20 (2 m)
- δ 7.10–7.00, 6.50–6.40 (2 m)
- δ 4.50–4.40, 3.50–3.40 (2 m)
- δ 2.50–2.40, 1.50–1.40 (2 m)
- δ 1.00–0.90, 0.80–0.70 (2 m)

**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 (C₆H₆⁺).

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References


(6) In ref. 7 only a 90 MHz 1H NMR spectrum of 1c was reported. We present data resulting from a 300 MHz spectrum and a 13C 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:  