# Synthesis of Carbohydrate-based Vinyl Selenides via Wittig-type Reactions

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## Abstract

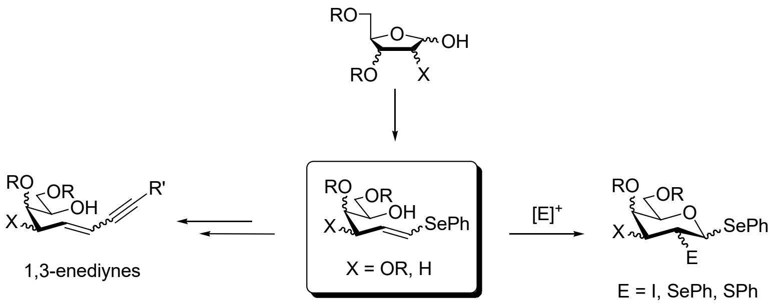
Carbohydrate-based vinyl selenides of *arabino*, *ribo,* and 2-deoxy-*ribo* configurations have been prepared by Wittig-type reactions of various protected furanoses. Moderate yields were always obtained due to nature and reactivity of both carbohydrate lactols and selenium-based olefinating reagents under the conditions tested. A detailed study of the olefination reaction and the behaviour of vinyl selenides towards the electrophilic-induced cyclization will be discussed.

## 1. Introduction

Organic chalcogenides are compounds of increasing importance in organic synthesis because of their particular reactivity[1] and their attractive biological properties.[2] Selenium chemistry has been shown to provide highly efficient and selective transformations, and therefore has been widely used in the synthesis of natural products.[3,4]. Among various organoselenium compounds, vinyl selenides have been found particularly useful intermediates in the stereoselective preparation of functionalized alkenes[5], carbonyl compounds[6], as well as suitable substrates in carbon-carbon bond formation[7].

A wide variety of methods have been developed for synthesizing vinyl selenides involving reactions of organoselenium compounds with alkynes[8], vinyl halides[9] or boranes[10], and Wittig-type reactions[11]. Surprisingly, no paper dealing with the synthesis of carbohydrate-based vinyl selenides has been issued to date despite the fact that these products are good candidates for the preparation of complex 1,6-, and 1,3-enediynes[12], enantiomerically pure 1,2-diol derivatives[13], and commonly occurring fragments in natural products[14].

Recently, we have reported a new procedure for the synthesis of 2-deoxy-2-iodo-1-thio-glycosides from pentoses through a short synthetic route that involves olefination and iodonium-ion-mediated *6-endo* cyclization, and discussed the use of these glycosides as glycosyl donors for the stereocontrolled synthesis of 2-deoxy-2-iodo-disaccharides[15]. As part of our ongoing projects on the chemistry of natural and synthetic 2-deoxy- and 2,6-dideoxy glycosides, we became interested in the development of useful glycosyl donors such as 2-deoxy-2-iodo-1-seleno-glycosides[16], and exploit their high reactivity in developing milder stereoselective glycosylation protocols by using this methodology (Scheme1).

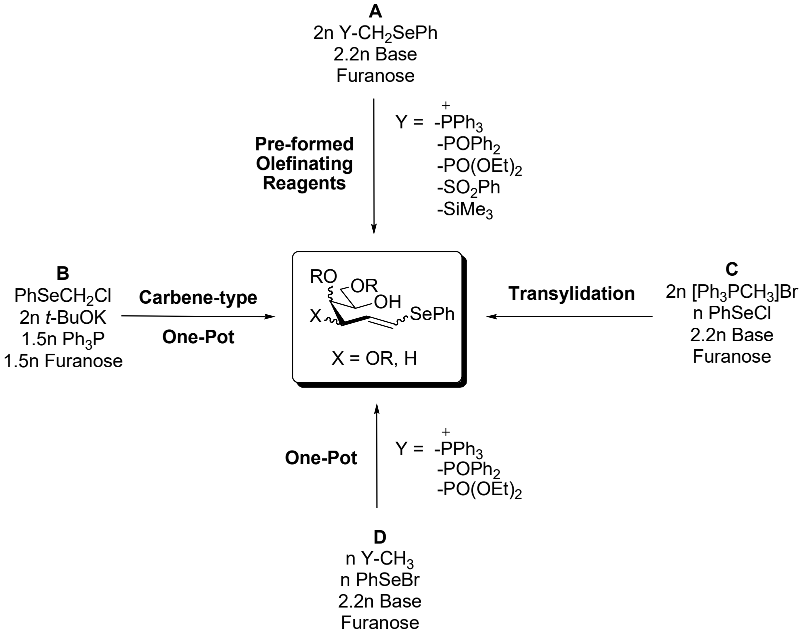


**Scheme 1.** Possible applications of carbohydrate-based vinyl selenides.

Encouraged by the previous results[15], we postulated that the presence of a selenium atom would provide milder glycosylation conditions in order to improve the yield and stereoselectivity. Therefore, it was deemed interesting to investigate the synthesis of carbohydrate-based vinyl selenides and explore their reactivity with electrophiles.

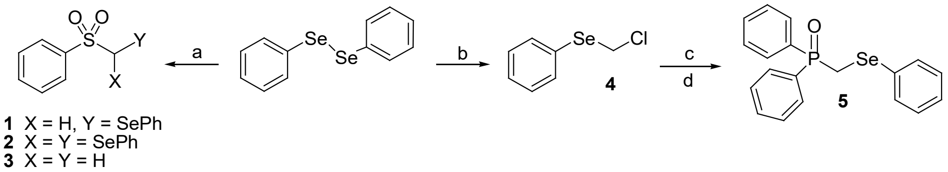
## 2. Results and Discussion

Among the methods developed for synthesizing vinyl selenides[8-11], Wittig-type reactions seem to be the best strategy as this would avoid complex manipulation on the carbohydrate scaffold (Scheme 2).



**Scheme 2.** Wittig-type olefination strategies towards the synthesis of carbohydrate-based vinyl selenides.

We initially decided to focus on the classical Wittig-type methodology (Scheme 2, A). The appropriate α-seleno pre-formed phosphorus reagents are the obvious starting materials for these reactions. Thus, chloromethyl phenylselenide **4** was readily obtained from diphenyl diselenide according to the method reported in the literature by Huang and co-workers[17] (Scheme 3). The preparation of the corresponding α-selenophosphine oxide **5** was accomplished starting from derivative **4** under Michaelis-Arbuzov reaction conditions[18]. Next we tried the synthesis of the selenosulfone derivative **1**[19] (Julia-Lythgoe olefinating reagent), which was obtained from bromomethyl phenyl sulfone, diphenyl diselenide and sodium hydride[20] in 54 % yield together with small amounts of products **2** and **3**[21] which were separated by standard chromatographic procedures.



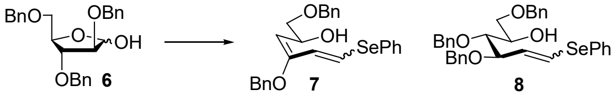
**Scheme 3.** Reagents and conditions: (a) $PhSO_2CH_2Br$, NaH, THF, reflux, 3 h, **1** (54 %), **2** (9 %), and **3** (27 %); (b) $KBH_4$, EtOH, $CH_2Cl_2$, reflux, 3 h, 51 %; (c) $Ph_2POEt$, 150 ºC, 3 h, 31 %; (d) $Ph_2POEt$, TBAI, 150 ºC, 4.5 h, 39 %.

The reaction conditions for olefination[11,22] were optimized by starting from the commercially available arabinose derivative **6**. The reactions of **6** with $Me_3SiCH_2SePh$ (Peterson) (Table 1, entry 7), with **5** (Wittig-Horner) (Table 1, entry 8), and **1** (Julia-Lythgoe) (Table 1, entry 9) were unsuccessful even though different bases were used.[23] Three one-pot procedures were considered (Scheme 2, B, C, and D). Vinyl selenides have been previously prepared[11a] by addition of *t*-BuOK to a solution of chloromethyl phenyl selenide **4** and triphenylphosphine in THF, followed by addition of an aldehyde (Scheme 2, B). Unfortunately, no reaction product was detected using arabinose derivative **6** (Table 1, entry 1).

The second method (Scheme 2, C) consists of the transylidation reaction between alkylidene triphenylphosphorane ($Ph_3P=CH_2$) and phenylselenenyl chloride. In this case, the subsequent reaction with the carbohydrate derivative **6** furnished vinyl selenide **8** in moderate yield and *Z*/*E* ratio of up to 1:12 (Table 1, entry 3). Forcing the reaction conditions by refluxing the mixture for prolonged reaction time did not afford the desired compound; rather it led to the formation of diene **7** in 55 % yield and 3:2 3*Z*,5*E*/3*Z*,5*Z* ratio (Table 1, entry 2) as a result of benzyl alcohol elimination in the open-ring sugar followed by Wittig reaction of the resulting enal as previously reported.[24] The same group has described the use of $Bu_3SnCl$ to avoid the benzylic elimination. Under these conditions, when *n*-BuLi was used at room temperature **8** was obtained in moderated yield as a 1:9 *Z*/*E* mixture (Table 1, entries 4, 5). It is worthy to note that while increasing the equivalents of olefinating reagent and base the yield is increased, an enitol impurity ($R\text{-}CH{=}CH_2$) appears as result of alkylidene triphenylphosphorane ($Ph_3P{=}CH_2$) formation[25] followed by reaction with the carbohydrate lactol moiety (Table 1, entries 3, 4, and 6). Furthermore, the presence of the $Bu_3SnCl$ has no influence either in the yield or in the enitol impurity formation, but affects the stereochemical outcome of the reaction.

Finally, the third method (Scheme 2, D) consists of the generation of α-seleno triphenylphosphonium reagent by the reaction of equimolar amounts of arylselenenyl bromides and phosphonium salts. In this case, the use of double equivalents of base with respect to the olefinating reagent is crucial for obtaining the corresponding vinyl selenide instead of the undesired 1,1-bis-selenides[11b]. Thus, under these conditions, vinyl selenide **8** was obtained in 30 % yield as a 1:7 *Z*/*E* mixture (Table 1, entry 6). The behaviour observed was similar to that found using more equivalents of olefinating reagent and base (Table 1, entries 3-5). Thus, this protocol provided the best result due to the use of less equivalents of base which is important to avoid not only the observed degradation of the α-seleno olefinating reagent due to C-Se bond lithiation, but also to prevent any epimerization at C-2 during the Wittig reaction[26]. In order to confirm the degradation of these compounds, stability tests of the *in situ* generated α-seleno olefinating reagents were performed following the procedure reported in the experimental section without adding any carbonyl compound. After 12 h stirring at room temperature the reaction mixture was quenched. Further GC-EI-MS, $^1H$, $^{13}C$, and $^{31}P$ NMR analysis of the crude showed signals corresponding to degradation products such as PhSeBu, $PhSeCH_2SePh$, and PhSeSePh due to C-Se cleavage occurred in highly basic media.

**Table 1.** Olefination of *Arabino*-furanose **6** to Obtain Alkenyl Selenides **7** and **8** Containing Reagents.

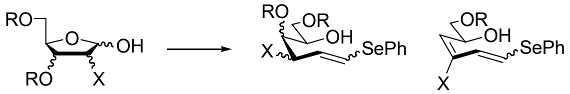


| Entry | Olefination conditions[a] (eq) | Olefination product | Yield (%) | *Z*/*E* ratio[b] |
|---|---|---|---|---|
| 1[c] | $PhSeCH_2Cl$ (1)<br>$Ph_3P$ (1.5)<br>*t*-BuOK (2)<br>rt to reflux, 14h | mixture | - | - |
| 2 | $[Ph_3PCH_3]Br$ (2)<br>PhSeCl (1)<br>*n*-BuLi (2.2)<br>reflux, 17h | **7** | 55 | 3:2[d] |
| 3 | $[Ph_3PCH_3]Br$ (6)<br>PhSeCl (3)<br>*n*-BuLi (6.6)<br>rt, 14h | **8** | 29[e] | 1:12 |
| 4 | $[Ph_3PCH_3]Br$ (6)<br>PhSeCl (3)<br>*n*-BuLi (6.6)<br>$Bu_3SnCl$ (0.5)<br>rt, 14h | **8** | 30[e] | 1:9 |
| 5 | $[Ph_3PCH_3]Br$ (4)<br>PhSeCl (2)<br>*n*-BuLi (4.4)<br>$Bu_3SnCl$ (0.5)<br>rt, 14h | **8** | 19 | 1:9 |
| 6 | $[Ph_3PCH_3]Br$ (2)<br>PhSeBr (2)<br>*n*-BuLi (4.4)<br>-78 ºC to rt, 14h | **8** | 30[e] | 1:7 |
| 7 | $Me_3SiCH_2SePh$ (2)<br>*n*-BuLi or LDA or KHMDS (3.3)<br>-78 ºC to rt, 14h | mixture | - | - |
| 8 | $Ph_2P(O)CH_2SePh$ (4)<br>*n*-BuLi (4.4)<br>-78 ºC to reflux, 20h | mixture | - | - |
| 9 | $PhSO_2CH_2SePh$ (2)<br>*n*-BuLi (4.4)<br>-78 ºC to rt, 14h | **6** | - | - |

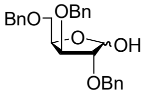
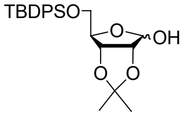
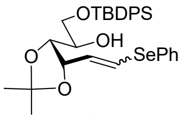
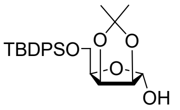
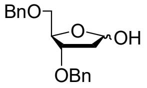
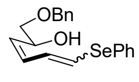
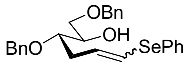
[a] Solvent = THF. [b] Determined by integration of the olefinic proton signals in the $^1H$ NMR spectrum of the crude reaction mixture. [c] Starting Material (1.5 eq) was used. [d] 3*Z*,5*E*/3*Z*,5*Z* ratio. [e] Trace amounts of the corresponding enitol ($R\text{-}CH=CH_2$).

This protocol was extended to different protected furanoses in order to determine the generality of the reaction and the influence of the stereochemistry at position 2. In the case of xylose derivative **9** all the reaction conditions tested were unsuccessful and only starting material was recovered (Table 2, entry 1). Reaction of ribose derivative **10** under Wittig conditions led to the formation of the desired alkene **13** in low yield (74 % starting material was also recovered and could be further reused) regardless of the base used as already observed for the reaction of isopropylidene and silyl-protected *lyxo*-furanoses with Li-bases[15b]. The *Z*-isomer was detected as the major component in the mixture, in accordance with the known stereochemical course of Wittig olefinations under lithium salt free conditions[11a] (Table 2, entry 2). In contrast, when the same reaction was carried out using lyxose derivative **11** only 25 % of starting material was recovered together with some other minor side products (Table 2, entry 3). Despite the use of 2-deoxyribose derivative **12** which has less steric hindrance at C-2, diene **14** was obtained under Wittig and Horner-Wadsworth-Emmons conditions (Table 2, entry 4). Fortunately, the expected alkene **15** was obtained in 34 % yield as a 1:1 *Z*/*E* mixture under Wittig-Horner conditions (Table 2, entry 5).

**Table 2.** Olefination of furanoses **9-12** to Obtain Alkenyl Selenides **13-15** Containing Reagents.



X = OR
X = H

| Entry | Starting material | Olefination conditions[a] (eq) | Olefination product | Yield (%) | $Z/E$ ratio[b] |
|---|---|---|---|---|---|
| 1 |  **9** | $Me_3SiCH_2SePh$ (2) or<br>$[Ph_3PCH_3]Br$ (2) or<br>$Ph_2P(O)CH_3$ (2) or<br>$(EtO)_2P(O)CH_3$ (2)<br>PhSeBr (2)<br>*n*-BuLi or LDA or KHMDS (4.4)<br>-78 °C to rt, 14-48h | **9** | - | - |
| 2 |  **10** | $[Ph_3PCH_3]Br$ (2)<br>PhSeBr (2)<br>KHMDS (4.4)<br>-78 °C to rt, 6 days |  **13** | 15[c] | 11:1 |
| 3 |  **11** | $[Ph_3PCH_3]Br$ (2)<br>PhSeBr (2)<br>KHMDS (4.4)<br>-78 °C to rt, 6 days | mixture[d] | - | - |
| 4 |  **12** | $[Ph_3PCH_3]Br$ (2) or<br>$(EtO)_2P(O)CH_3$ (2)<br>PhSeBr (2)<br>*n*-BuLi (4.4)<br>-78 °C to rt, 32h |  **14** | 13 | 1:1[e] |
| 5 | **12** | $Ph_2P(O)CH_3$ (2)<br>PhSeBr (2)<br>*n*-BuLi (4.4)<br>-78 °C to rt, 31h |  **15** | 34[f] | 1:1 |

[a] Solvent = THF. [b] Determined by integration of the olefinic proton signals in the $^1H$ NMR spectrum of the crude reaction mixture. [c] 74% starting material was recovered. [d] 25% starting material was recovered. [e] *3E,5E/3E,5Z* ratio. [f] Trace amounts of the corresponding diene.

At this point, having synthesized different protected vinyl selenides from carbohydrate precursors and demonstrated how the C-2 substitution affects the reaction course, we next turned our attention to study their reactivity with electrophiles. In all the cases the *Z*/*E* mixtures of alkenes proved to be inseparable; hence, the cyclization reactions were assayed directly on the mixture of diastereomers.

Electrophile-induced cyclization was studied for derivative **8**. Initial attempts using iodine electrophiles such as $I_2$, IDCP, NIS, and $IPy_2BF_4$ gave an inseparable mixture of products. Since selenoglycosides are activated in milder conditions than thioglycosides, we assumed that if any electrophilic cyclization occurred, the excess of electrophile would promote the activation of the phenylselenenyl moiety. In order to trap any oxocarbenium ion formed, the reaction mixture was quenched by addition of a few drops of methanol. However, no reaction product was detected by TLC analysis. Electrophilic cyclization using other electrophiles, such as Selectfluor®, *p*-TsOH, and PhSeCl has also been examined, but complex mixtures were always obtained.

## 3. Conclusions

This paper describes a new method for the preparation of carbohydrate-based vinyl selenides under Wittig-type reaction conditions from protected furanoses. The proposed method allows synthesizing vinyl selenides in *arabino*, *ribo,* and 2-deoxy-*ribo* series. The modest yield observed with the vinyl selenides reported herein is potentially related to the nature and reactivity of both carbohydrate lactols and selenium based olefinating reagents under the conditions tested. Reaction with electrophiles proved to be challenging but no cyclization products were obtained. The preparation of vinyl selenides proved to be much more difficult than the related vinyl sulfides, which can be prepared in good yields using Wittig-Horner reaction.

## 4. Experimental

### 4.1. General procedures

$^1$H, $^{13}$C, $^{19}$F and $^{31}$P NMR spectra were recorded using Varian Gemini Varian Mercury 400 MHz spectrometers. In all the $^1$H NMR spectra TMS was used as an internal reference, in the $^{13}$C NMR spectra the residual solvent signal was used as an internal reference ($CDCl_3$, triplet at 77.23 ppm) unless otherwise stated. All the $^{31}$P and $^{19}$F NMR spectra were referenced to 85 % $H_3PO_4$, and $CFCl_3$, respectively as external standards. Elemental analysis (C, H, N, S) were performed with Carlo Erba EA 1108 Analyser in the Servei de Recursos Científics (URV). Optical rotations were recorded on a Perkin-Elmer 241 MC polarimeter in a 1 dm cell at 20 ºC. Melting points were determined on a Tottoli Büchi 510 apparatus and are uncorrected. FT-IR was obtained with a Bruker Equinox 55 spectrophotometer. GC-EI-MS spectrometry was performed on a HP 5890 (Ti 75 ºC (2) and 20 ºC/min. to 250 ºC) chromatograph with a quadrupolar detector HP 5989A (45-600, 70 eV) in the Servei de Recursos Científics (URV). Flash column chromatography was performed with silica gel 60 (E. Merck, 40-63 μm). Medium-pressure liquid chromatography (MPLC) was performed using silica gel 60 ACC (SDS, 6-35 μm). Radial chromatography was performed on 1, 2, or 4 mm plates of Kieselgel 60 $PF_{254}$ silica gel (E. Merck), depending on the amount of product. Solvents were purified using standard procedures. Thin layer chromatography (TLC) was performed on aluminium sheets coated with silica gel 60 $F_{254}$ (E. Merck). Compounds were visualized by UV (254 nm), and also by spraying the TLC plates with 6 % $H_2SO_4$ in EtOH, or 2 % $PdCl_2$ and 15 % $H_2SO_4$ in water, followed by charring at 150 ºC for a few minutes. Starting materials **1**, **4**, **6**, **9**, **11**, and **12** were prepared as described in the literature[17,19,27]. Iodonium dicollidine perchlorate (IDCP) was prepared following the method reported by Lemieux and co-workers[28]. All other reagents were used as received from commercial suppliers.

### 4.2. Diphenyl phenylselenenylmethyl phosphine oxide (5)

Ethyl diphenylphosphinite (330 μl, 1.5 mmol), chloromethyl phenyl selenide **4** (257 mg, 1.25 mmol), and TBAI (470 mg, 1.25 mmol) were heated together under argon at 150 ºC for 4.5 h. The crude was purified by radial chromatography (from 1: 1 EtOAc/hexane to EtOAc) to afford **5** (182 mg, 39 %) as a white crystalline solid; mp: 121-123 ºC; $R_f$ (EtOAc): 0.36; FT-IR (KBr): ν 3048, 2971, 2916, 1573, 1475, 1435, 1190 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.78-7.17 (m, 15H, Ar), 3.60 (s, 2H, $J_{H,P}$ 7.6 Hz, $CH_2$); $^{13}C$ NMR

($CDCl_3$, 100.6 MHz): δ 133.6-127.9 (C, CH, Ar), 25.6 (d, $J_{C,P}$ 69 Hz, $CH_2$); $^{31}P$ NMR ($CDCl_3$, 162 MHz): δ 28.8 (s, P=O); Anal. Calcd for $C_{19}H_{17}OPSe$: C, 61.47; H, 4.62. Found: C, 61.23; H, 4.60.

### 4.3. General Wittig olefination of furanoses via transylidation reaction

To a dispersion of methyltriphenylphosphonium bromide (2n mmol) (n = 1, 2, or 3. i.e. if n = 2 then 2n mmol = 4 mmol) in dry THF (7n mL) at -78 ºC was added the corresponding base (2.2n mmol) under an atmosphere of argon. PhSeCl (n mmol) in dry THF (3.5n mL) was added and the mixture was left to stir at low temperature for 30 min. A solution of the corresponding furanose (1 mmol) in dry THF (2 mL) was then added dropwise. The mixture was allowed to warm to room temperature overnight. The crude was filtered through Celite® 545, diluted with petroleum ether and washed with saturated aqueous $NH_4Cl$ and brine. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude was purified by chromatographic techniques.

### 4.4. General Wittig-type olefination of furanoses in a one-pot reaction

To a dispersion of the corresponding methyl phosphonium salt, phosphine oxide, or phosphonate (2 mmol) in dry THF (4 mL) at -78 ºC was added the corresponding base (4.4 mmol) under an atmosphere of argon. PhSeBr (2 mmol) in dry THF (4 mL) was added and the mixture was left to stir at low temperature for 30 min. A solution of the corresponding furanose (1 mmol) in dry THF (2 mL) was then added dropwise. The mixture was allowed to warm to room temperature overnight. A saturated aqueous solution of $NH_4Cl$ was then added and the mixture was extracted with $Et_2O$. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The crude was purified by chromatographic techniques.

### 4.5. (3*Z*,5*E*,2*S*/3*Z*,5*Z*,2*S*)-1,4-Di-*O*-benzyl-6-phenylselenenyl-hexa-3,5-dien-2-ol (7)

As described in the general procedure for the Wittig olefination of furanoses-Transylidation reaction, a solution of 2,3,5-tri-*O*-benzyl-β-D-*arabino*-furanose **6** (2.20 g, 5.2 mmol) in dry THF (10.5 mL) was olefinated by reaction with methyltriphenylphosphonium bromide (3.81 g, 10.5 mmol) in dry THF (73 mL), PhSeCl (1 g, 5.2 mmol) in dry THF (18 mL), and 1.6 M *n*-BuLi in hexane (7.2 mL, 11.5 mmol) for 17 h under refluxing conditions. The crude was purified by flash chromatography (1: 3 EtOAc/hexane) to afford diene **7** (1.33 g, 55 %) as an inseparable 3:2 3*Z*,5*Z*/3*Z*,5*E* mixture as an orange syrup; Data obtained from the mixture; $R_f$ (1:3 EtOAc/hexane): 0.18; FT-IR (neat): ν 3383, 3063, 3030, 2862, 1952, 1687, 1578, 1438 $cm^{-1}$; Anal. Calcd for $C_{26}H_{26}O_3Se$: C, 67.09; H, 5.63. Found: C, 67.34; H, 5.65. **7***E*: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.58-7.28 (m, 15H, Ar), 6.99 (d, 1H, $J_{5,6}$ 15.6 Hz, H-6), 6.16 (d, 1H, $J_{5,6}$ 15.6 Hz, H-5), 4.96 (d, 1H, $J_{2,3}$ 8.4 Hz, H-3), 4.89-4.82 (m, 2H, $CH_2Ph$), 4.78-4.69 (m, 1H, H-2), 4.51 (s, 2H, $CH_2Ph$), 3.39-3.28 (m, 2H, H-1a,b), 2.22 (bs, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 154.3-126.9 (C, CH, Ar, C-4,6), 123.1 (C-5), 115.6 (C-3), 74.0-73.1 (2$CH_2Ph$, C-1), 65.8 (C-2). **7***Z*: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.58-7.28 (m, 15H, Ar), 6.79 (d, 1H, $J_{5,6}$ 10 Hz, H-6), 6.37 (d, 1H, $J_{5,6}$ 10 Hz, H-5), 5.04 (d, 1H, $J_{2,3}$ 8.4 Hz, H-3), 4.89-4.82 (m, 2H, $CH_2Ph$), 4.78-4.69 (m, 1H, H-2), 4.66 (s, 2H, $CH_2Ph$), 3.39-3.28 (m, 2H, H-1a,b), 2.22 (bs, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 154.3-126.9 (C, CH, Ar, C-4,6), 133.7 (C-5), 116.2 (C-3), 74.0-73.1 (2$CH_2Ph$, C-1), 65.1 (C-2).

### 4.6. (*Z*/*E*)-3,4,6-Tri-*O*-benzyl-1,2-dideoxy-1-phenylselenenyl-D-*arabino*-hex-1-enitol (8)

As described in the general procedure for the Wittig-type olefination of furanoses-One-pot reaction, a solution of 2,3,5-tri-*O*-benzyl-β-D-*arabino*-furanose **6** (3.5 g, 8.3 mmol) in dry THF (16.6 mL) was olefinated by reaction with methyltriphenylphosphonium bromide (6 g, 16.5 mmol) in dry THF (33 mL), PhSeBr (3.96 g, 16.8 mmol) in dry THF (33.6 mL), and

1.6 M *n*-BuLi in hexane (23 mL, 36.8 mmol). After 14 h stirring at room temperature the reaction mixture was quenched and the crude was purified by flash chromatography (1: 3 EtOAc/hexane) to afford **8** (1.43 g, 30 %) as an inseparable 1:7 *Z*/*E* mixture as a yellowish syrup; Data obtained from the mixture; $R_f$ (1:3 EtOAc/hexane): 0.29; FT-IR (neat): ν 3472, 3061, 3029, 2864, 1951, 1875, 1809, 1606, 1558 $cm^{-1}$; Anal. Calcd for $C_{33}H_{34}O_4Se$: C, 69.10; H, 5.97. Found: C, 69.38; H, 5.99. **8***E*: $^1H$ NMR ($CDCl_3$, 400 MHz): δ 7.49-7.19 (m, 20H, Ar), 6.69 (d, 1H, $J_{1,2}$ 15.6 Hz, H-1), 5.98 (dd, 1H, $J_{1,2}$ 15.6 Hz, $J_{2,3}$ 7.6 Hz, H-2), 4.64 (d, 1H, $J_{AB}$ 12 Hz, $CH_2Ph$), 4.53 (d, 2H, $J_{AB}$ 8 Hz, $CH_2Ph$), 4.49 (s, 2H, $CH_2Ph$), 4.37 (d, 1H, $J_{AB}$ 12 Hz, $CH_2Ph$), 4.14 (dd, 1H, $J_{2,3}$ 7.6 Hz, $J_{3,4}$ 3.6 Hz, H-3), 3.99 (m, 1H, H-5), 3.58 (m, 3H, H-4, H-6a,b), 2.71 (d, 1H, $J_{5,OH}$ 5.6 Hz, OH); $^{13}C$ NMR ($CDCl_3$, 100.6 MHz): δ 138.1-137.8 (C, Ar), 133.2-127.8 (CH, Ar), 132.0 (C-1), 123.6 (C-2), 80.6 (C-4), 80.1 (C-3), 74.4, 73.5 ($2CH_2Ph$), 70.9 (C-6, $CH_2Ph$), 70.3 (C-5). Selected signals for **8***Z*: $^1H$ NMR ($CDCl_3$, 400 MHz): δ 6.79 (d, 1H, $J_{1,2}$ 9.2 Hz, H-1), 6.22 (dd, 1H, $J_{1,2} = J_{2,3}$ 9.2 Hz, H-2), 2.89 (d, 1H, $J_{5,OH}$ 4.4 Hz, OH).

### 4.7. (*Z*/*E*)-6-*O*-(*tert*-Butyldiphenylsilyl)-3,4-*O*-isopropylidene-1,2-dideoxy-1-phenylselenenyl-D-*ribo*-hex-1-enitol (13)

As described in the general procedure for the Wittig-type olefination of furanoses-One-pot reaction, a solution of 5-*O*-(*tert*-Butyldiphenylsilyl)-2,3-*O*-isopropylidene-α,β-D-*ribo*-furanose **10** (100 mg, 0.233 mmol) in dry THF (0.5 mL) was olefinated by reaction with methyltriphenylphosphonium bromide (170.1 mg, 0.467 mmol) in dry THF (1 mL), PhSeBr (113.5 mg, 0.467 mmol) in dry THF (1 mL), and KHMDS (209 mg, 1.03 mmol). After 6 days stirring at room temperature the reaction mixture was quenched and the crude was purified by radial chromatography (from hexane to 1:3 EtOAc/hexane) to afford **13** (20 mg, 15 %) as an inseparable 11:1 *Z*/*E* mixture as a colourless syrup; Data obtained from the mixture; $R_f$ (1:3 EtOAc/hexane): 0.45; Anal. Calcd for $C_{31}H_{38}O_4SeSi$: C, 64.01; H, 6.58.

Found: C, 64.00; H, 6.60. **13*E***: $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.71-7.26 (m, 15H, Ar), 6.80 (dd, 1H, $J_{1,2}$ 15.2 Hz, $J_{1,3}$ 1.2 Hz, H-1), 6.11 (dd, 1H, $J_{1,2}$ 15.2 Hz, $J_{2,3}$ 7.2 Hz, H-2), 4.75 (m, 1H, H-3), 4.13 (dd, 1H, $J_{3,4}$ 9.2 Hz, $J_{4,5}$ 6 Hz, H-4), 3.88-3.80 (m, 2H, H-6a,b), 3.67 (m, 1H, H-5), 2.51 (d, 1H, $J_{5,OH}$ 5.6 Hz, OH), 1.36, 1.33 (s, 6H, 2CH$_3$), 1.07 (s, 9H, *t*-Bu); $^{13}$C NMR (CDCl$_3$, 100.6 MHz): δ 136.0-127.6 (C, CH, Ar, C-1,2), 109.3 (C$_{\text{ketal}}$), 79.3 (C-3), 77.7 (C-4), 70.2 (C-5), 65.7 (C-6), 28.2, 25.8 (2CH$_3$), 27.2 (CH$_3$, *t*-Bu), 19.7 (C, *t*-Bu). **13*Z***: $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.71-7.26 (m, 15H, Ar), 6.77 (dd, 1H, $J_{1,2}$ 9.6 Hz, $J_{1,3}$ 0.8 Hz, H-1), 6.15 (dd, 1H, $J_{1,2}$ 9.6 Hz, $J_{2,3}$ 8.4 Hz, H-2), 5.09 (m, 1H, H-3), 4.21 (dd, 1H, $J_{3,4}$ 8.8 Hz, $J_{4,5}$ 6.4 Hz, H-4), 3.88-3.80 (m, 2H, H-6a,b), 3.72 (m, 1H, H-5), 2.61 (d, 1H, $J_{5,OH}$ 5.2 Hz, OH), 1.42, 1.37 (s, 6H, 2CH$_3$), 1.07 (s, 9H, *t*-Bu); $^{13}$C NMR (CDCl$_3$, 100.6 MHz): δ 136.0-127.6 (C, CH, Ar), 129.6 (C-2), 126.1 (C-1), 109.5 (C$_{\text{ketal}}$), 77.8 (C-4), 77.2 (C-3), 70.7 (C-5), 65.5 (C-6), 28.2, 25.8 (2CH$_3$), 27.2 (CH$_3$, *t*-Bu), 19.7 (C, *t*-Bu).

### 4.8. (3*E*,5*E*,2*S*/3*E*,5*Z*,2*S*)-1-*O*-Benzyl-6-phenylselenenyl-hexa-3,5-dien-2-ol (14)

As described in the general procedure for the Wittig-type olefination of furanoses-One-pot reaction, a solution of 3,5-di-*O*-benzyl-2-deoxy-α,β-D-*ribo*-furanose **12** (80 mg, 0.25 mmol) in dry THF (0.5 mL) was olefinated by reaction with methyltriphenylphosphonium bromide (186 mg, 0.51 mmol) in dry THF (1 mL), PhSeBr (124 mg, 0.51 mmol) in dry THF (1 mL), and 1.6 M *n*-BuLi in hexane (0.7 mL, 1.12 mmol). After 32 h stirring at room temperature the reaction mixture was quenched and the crude was purified by radial chromatography (from hexane to 1:3 EtOAc/hexane) to afford **14** (12 mg, 13 %) as an inseparable 1:1 3*E*,5*E*/3*E*,5*Z* mixture as an orange syrup; Data obtained from the mixture; R$_f$ (1:3 EtOAc/hexane): 0.21; **14*E***: $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.50-7.26 (m, 10H, Ar), 6.71-6.31 (m, 3H, H-4,5,6), 5.57 (dd, 1H, $J_{3,4}$ 15 Hz, $J_{2,3}$ 6 Hz, H-3), 4.59 (m, 2H, CH$_2$Ph), 4.42 (m, 1H, H-2), 3.56, 3.39 (m, 2H, H-1a,b), 2.47 (bs, 1H, OH); $^{13}$C NMR (CDCl$_3$, 100.6 MHz): δ 134.6-123.8 (C, CH, Ar, C-3,4,5,6), 74.0 (CH$_2$Ph), 71.3 (C-2), 70.3 (C-1). **14*Z***: $^1$H

NMR ($CDCl_3$, 400 MHz): δ 7.50-7.26 (m, 10H, Ar), 6.71-6.31 (m, 3H, H-4,5,6), 5.79 (dd, 1H, $J_{3,4}$ 14 Hz, $J_{2,3}$ 6 Hz, H-3), 4.57 (m, 2H, $CH_2Ph$), 4.38 (m, 1H, H-2), 3.56, 3.39 (m, 2H, H-1a,b), 2.51 (bs, 1H, OH); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 134.6-123.8 (C, CH, Ar, C-3,4,5,6), 74.1 ($CH_2Ph$), 71.0 (C-2), 70.3 (C-1).

### 4.9. (*Z*/*E*)-4,6-Di-*O*-benzyl-1,2,3-trideoxy-1-phenylselenenyl-D-*ribo*-hex-1-enitol (15)

As described in the general procedure for the Wittig-type olefination of furanoses-One-pot reaction, a solution of 3,5-di-*O*-benzyl-2-deoxy-α,β-D-*ribo*-furanose **12** (80 mg, 0.25 mmol) in dry THF (0.5 mL) was olefinated by reaction with diphenyl methyl phosphine oxide (112 mg, 0.51 mmol) in dry THF (1 mL), PhSeBr (124 mg, 0.51 mmol) in dry THF (1 mL), and 1.6 M *n*-BuLi in hexane (0.7 mL, 1.12 mmol). After 31 h stirring at room temperature the reaction mixture was quenched and the crude was purified by radial chromatography (from hexane to 1:3 EtOAc/hexane) to afford **15** (40 mg, 34 %) as an inseparable 1:1 *Z*/*E* mixture as a yellowish syrup; Data obtained from the mixture; $R_f$ (1:3 EtOAc/hexane): 0.26; **15***E*: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.50-7.22 (m, 15H, Ar), 6.51 (d, 1H, $J_{1,2}$ 15 Hz, H-1), 6.13 (ddd, 1H, $J_{1,2}$ 15 Hz, $J_{2,3a} = J_{2,3b}$ 8.4 Hz, H-2), 4.67-4.48 (m, 4H, $2CH_2Ph$), 3.86 (m, 1H, H-4), 3.70-3.51 (m, 3H, H-5,6a,b), 2.61-2.48 (m, 2H, H-3a,b), 2.41 (d, 1H, $J_{5,OH}$ 5 Hz, OH); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 135.0 (C-2), 134.6-127.1 (C, CH, Ar), 119.6 (C-1), 78.9 (C-5), 73.7 ($2CH_2Ph$), 71.6 (C-4), 71.1 (C-6), 35.4 (C-3). **15***Z*: $^1$H NMR ($CDCl_3$, 400 MHz): δ 7.50-7.22 (m, 15H, Ar), 6.57 (d, 1H, $J_{1,2}$ 9 Hz, H-1), 6.16 (ddd, 1H, $J_{1,2}$ 15 Hz, $J_{2,3a} = J_{2,3b}$ 8.8 Hz, H-2), 4.67-4.48 (m, 4H, $2CH_2Ph$), 3.86 (m, 1H, H-4), 3.70-3.51 (m, 3H, H-5,6a,b), 2.61-2.48 (m, 2H, H-3a,b), 2.45 (d, 1H, $J_{5,OH}$ 5.6 Hz, OH); $^{13}$C NMR ($CDCl_3$, 100.6 MHz): δ 135.0 (C-2), 134.6-127.1 (C, CH, Ar, C-1), 78.7 (C-5), 72.6, 72.4 ($2CH_2Ph$), 71.6 (C-4), 71.2 (C-6), 32.1 (C-3).

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## References

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1. (a) Patai, S. Rappoport, Z. In *The Chemistry of Organic Selenium and Tellurium Compounds*, Vol. 2; John Wiley & sons, Inc., Chichester, 1987. (b) Paulmier, C. In *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon Press, Oxford, 1986.

2. Mugesh, G.; du Mont, W-W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125.

3. (a) Pérez-Balado, C.; Markó, I. E. *Tetrahedron* **2006**, *62*, 2331. (b) Denis, J. N.; Krief, A. *Tetrahedron Lett.* **1982**, 3411.

4. Several references centered on selenium also concern tellurium chemistry. For recent reviews in organic tellurium chemistry, see: (a) Zeni, G.; Lüdtke, D. S.; Panatieri, R. B.; Braga, A. L. *Chem. Rev.* **2006**, *106*, 1032. (b) Petragnani, N.; Stefani, H. A. *Tetrahedron* **2005**, *61*, 1613. (c) Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731. (d) Comasseto, J. V.; Barrientos-Astigarraga, R. E. *Aldrichimica Acta* **2000**, *33*, 66.

5. (a) Comasseto, J. V.; Ling, L. W.; Petragnani, N.; Stefani, H. A. *Synthesis* **1997**, 373. (b) Comasseto, J. V.; Petragnani, N. *J. Organomet. Chem.* **1983**, *253*, 131.

6. Comasseto, J. V.; Petragnani, N. *J. Organomet. Chem.* **1978**, *152*, 295.

7. (a) Hevesi, L.; Hermans, B.; Allard, C. *Tetrahedron Lett.* **1994**, *35*, 6729. (b) Okamura, H.; Miura, M.; Kosugi, K.; Takei, H. *Tetrahedron Lett*. **1980**, *21*, 87.

8. For some nucleophilic or electrophilic organoselenium addition to alkynes, see: (a) Moro, A. V.; Nogueira, C. W.; Barbosa, N. B. V.; Menezes, P. H.; Teixeira da Roca, J. B.;

---

Zeni, G. *J. Org. Chem.* **2005**, *70*, 5257. (b) Zeni, G.; Stracke, M. P.; Nogueira, C. W.; Braga, A. L.; Menezes, P. H.; Stefani, H. A. *Org. Lett*. **2004**, *6*, 1135. (c) Barros, O. S. D.; Lang, E. S.; de Oliveira, C. A. F.; Peppe, C.; Zeni, G. *Tetrahedron Lett.* **2002**, *43*, 7921.

9. (a) Ranu, B. C.; Chattopadhyay, K.; Banerjee, S. *J. Org. Chem.* **2006**, *71*, 423. (b) Zue, L. S.; Huang, Z. Z.; Huang, X. *Tetrahedron* **1996**, *52*, 9819. (c) Comasseto, J. V.; Menezes, P. H.; Stefani, H. A.; Zeni, G.; Braga, A. L. *Tetrahedron* **1996**, *52*, 9687. (d) Cristau, H. J.; Chabaud, B.; Labaudiniere, R.; Christol, H. *J. Org. Chem*. **1986**, *51*, 875.

10. Rarcher, S.; Hansen, M. R.; Colter, M. A. *J. Org. Chem.* **1978**, *43*, 4885.

11. (a) Silveira, C. C.; Begnini, M. L.; Boeck, P.; Braga, A. L. *Synthesis* **1997**, 221.(b) Shin, W. S.; Lee, K.; Oh, D.Y. *Bull. Korean Chem. Soc.* **1996**, *17*, 981. (c) Shin, W. S.; Lee, K.; Oh, D.Y. *Tetrahedron Lett.* **1992**, *33*, 5375. (d) Petragnani, N.; Comasseto, J. V.; Rodrigues, R. Brocksom, T. J. *J. Organomet. Chem.* **1977**, *124*, 1. (e) Petragnani, N.; Rodrigues, R.; Comasseto, J. V. *J. Organomet. Chem.* **1976**, *114*, 281.

12. (a) Moslin, R. M.; Jamison, T. F. *Org. lett.* **2006**, *8*, 455. (b) Galm, U.; Hager, M. H.; Van Lanen, S. G.; Ju, J.; Thorson, J. S.; Shen, B. *Chem. Re*v. **2005**, *105*, 739. (c) Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. (d) Nicolaou, K. C.; Smith, A. L. *Acc. Chem. Res.* **1992**, *25*, 497. (e) Nicolaou, K. C.; Dai, W.-M. *Angew. Chem. Int. Ed.* **1991**, *30*, 1387. (f) Lee, M. D.; Ellestad, G. A.; Borders, D. B. *Acc. Chem. Res.* **1991**, *24*, 235. (g) Goldberg, I. H. *Acc. Chem. Res.* **1991**, *24*, 191.

13. (a) Enders, D.; Voith, M.; Lenzen, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 1304. (b) Luanphaisarnnont, T.; Ndubaku, C. O.; Jamison, T. F. *Org. Lett.* **2005**, *7*, 2937. (c) Georges, Y.; Allenbach, Y.; Ariza, X.; Campagne, J.-M.; Garcia, J. *J. Org. Chem.* **2004**, *69*, 7387.

14. (a) Ruiz, P.; Murga, J.; Carda, M.; Marco, J. A. *J. Org. Chem.* **2005**, *70*, 713. (b) Trost, B. M.; Frederiksen, M. U.; Rudd, M. T. *Angew. Chem. Int. Ed.* **2005**, *44*, 6630. (c) López,

---

S.; Fernández-Trillo, F.; Castedo, L.; Saá, C. *Org. Lett.* **2003**, *5*, 3725. (d) Crimmins, M. T.; Emmitte, K. A. *Org. Lett.* **1999**, *1*, 2029. (e) Pearson, W. H.; Hines, J. V. *Org. Chem.* **2000**, *65*, 5785. (f) Wiesler, W. T.; Nakanishi, K. *J. Am. Chem. Soc.* **1989**, *111*, 3446.

15. (a) Boutureira, O.; Rodríguez, M. A.; Matheu, M. I.; Díaz, Y.; Castillón, S. *Org. Lett.* **2006**, *8*, 673. (b) Rodríguez, M. A.; Boutureira, O.; Arnés, X.; Díaz, Y.; Matheu, M. I.; Castillón, S. *J. Org. Chem.* **2005**, *70*, 10297. (c) Arnés, X.; Díaz, Y. Castillón, S. *Synlett* **2003**, 2143.

16. For some synthesis and application of selenoglycosides, see: (a) Kawai, Y.; Ando, H.; Ozeki, H.; Koketsu, M.; Ishihara, H. *Org. Lett.* **2005**, *7*, 4653. (b) Yamago, S.; Yamada, T.; Hara, O.; Ito, H.; Mino, Y.; Yoshida, J.-I. *Org. Lett.* **2001**, *3*, 3867. (c) Horne, G.; Mackie, W. *Tetrahedron Lett.* **1999**, *40*, 8697. (d) Czernecki, S.; Ayadi, E.; Xie, J. *Tetrahedron Lett.* **1996**, *37*, 9193. (e) Mehta, S.; Pinto, M. *J. Org. Chem.* **1993**, *58*, 3269. (f) Czernecki, S.; Randriamandimby, D. *Tetrahedron Lett.* **1993**, *34*, 7915. (g) Sato, T.; Fujita, Y.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1992**, 33, 239.

17. Huang, X.; Duan, D.-H. *Synlett* **1998**, 1191.

18. Bhattacharya, A. K.; Thyagarajan, G. *Chem. Rev.* **1981**, *81*, 415.

19. Simpkins, N. S. *Tetrahedron* **1991**, *47*, 323.

20. Dowd, P.; Kennedy, P. *Synth. Commun.* **1981**, *11*, 935.

21. Sometimes selenols act as reducing agents of the C-halogen bond, see: a) Seshadri, R.; Pegg, W. J.; Israel, M. *J. Org. Chem.* **1981**, *46*, 2596. (b) Hevesi, L. *Tetrahedron Lett.* **1979**, *32*, 3.

22. Similar protocols are used for the synthesis of vinyl selenides and vinyl sulfides because the phenylselenenyl substituent largely behaves like the phenylsulfanyl with respect to different manipulations. For some Wittig-type synthesis of vinyl sulfides, see: (a) Aucagne, V.; Tatibouët, A.; Rollin, P. *Tetrahedron* **2004**, *60*, 1817. (b) van Staden, L.

---

F.; Gravestock, D. Ager, D. J. *J. Chem. Soc., Chem. Soc. Rev.* **2002**, *31*, 195. (c) Stephan, E.; Olaru, A.; Jaouen, G. *Tetrahedron Lett.* **1999**, *40*, 8571. (d) Clayden, J.; Warren, S. *Angew. Chem., Int. Ed. Eng*. **1996**, *35*, 241. (e) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (f) Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1986**, 183. (g) Earnshaw, C. E.; Wallis, C. J.; Waren, S. *J. Chem. Soc., Perkin Trans. 1* **1979**, 3099. (h) Grayson, J. I.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1977**, 2263. (i) Carey, F.; Cour, A. S. *J. Org. Chem.* **1972**, *37*, 939. (j) Corey, E. J.; Shulman, J. I. *J. Org. Chem.* **1970**, *35*, 777.

23. In the Peterson olefination, the C-Se bond is cleaved by alkyllithiums to afford trialkylsilyl carbanions instead of the expected deprotonation, see: Dumont, W.; Krief, A. *Angew. Chem. Int. Ed.* **1976**, *15*, 161.

24. Costantino, V.; Imperatore, C.; Fattorusso, E.; Mangoni, A. *Tetrahedron Lett.* **2001**, *42*, 8185.

25. Galli, R. *J. Org. Chem.* **1987**, *52*, 5349.

26. Freeman, F.; Robarge, K. D. *Carbohydr. Res.* **1986**, *154*, 270.

27. (a) Barbat, J.; Gelas, J.; Horton, D. *Carbohydr. Res.* **1991**, *219*, 115. (b) van Boom, J. H.; Veeneman, G. H.; Gomes, L. J. F. *Tetrahedron* **1989**, *45*, 7433. (c) Provelenghiou, C.; Czernecki, S.; Georgoulis, C. *Tetrahedron Lett.* **1976**, *39*, 3535. (d) Bishop, C. T.; Cooper, F. P. *Can. J. Chem.* **1963**, *41*, 2743.

28. Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190.