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STEREOSELECTIVE SYNTHESIS OF SUBSTITUTED TETRAHYDROPYRAN RINGS *VIA* 6-*EXO* AND 6-*ENDO* SELENOETHERIFICATION

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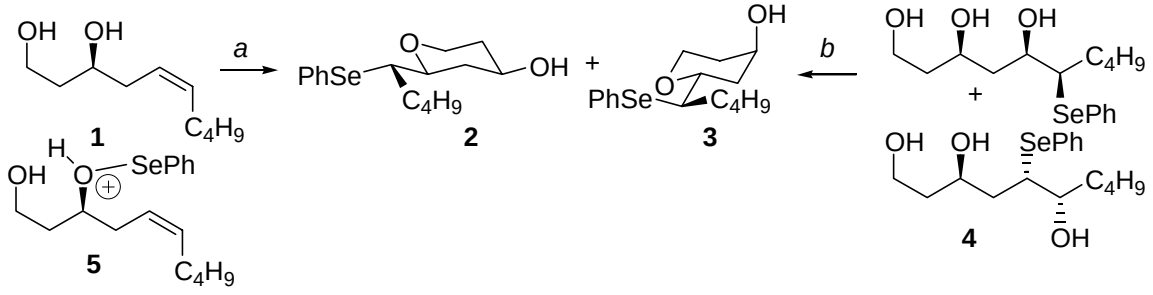
Abstract - Eight unsaturated alcohols were cyclized by selenoetherification in 6-*exo* or 6-*endo* manner to give substituted tetrahydropyran rings. Yields, regio- and stereoselectivities were discussed in terms of steric and electronic effects such as Se-O interaction. For the first time examples of the use of silica gel in selenoetherification and the effect of the X^- counter ion of $PhSe^+$ on the reaction course are discussed. These effects are related to the occurrence of Se-O interaction.

INTRODUCTION

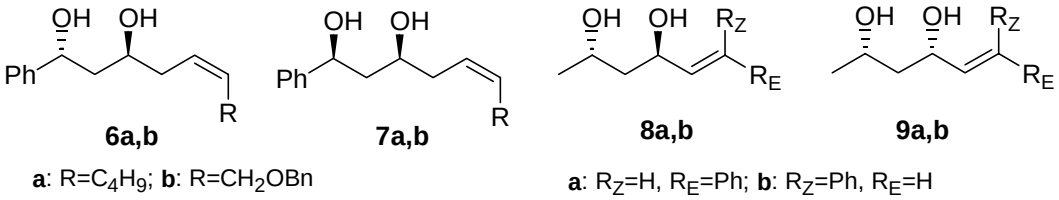
The stereoselective synthesis of substituted tetrahydropyran rings is of great interest due to their presence in many natural products. In recent years we have been interested in the stereoselective synthesis of oxygenated heterocyclic rings *via* the intermediate formation of a seleniranium ion.[1-6] It is well established that when an electrophilic seleno species, such as $PhSe^+$, attacks a C-C double bond carrying a tethered nucleophile, such as a hydroxyl group, the seleniranium ion formed undergoes an intramolecular attack leading to the oxygenated heterocyclic ring. In the case of tetrahydropyran synthesis two strategies can be employed: 6-*exo* and 6-*endo* cyclization. In order to explain the observed stereoselectivities in the intramolecular selenoetherification several factors could be taken in account such as: *i*) selectivity of seleniranium ions formation; *ii*) stereoelectronic effects during the course of the cyclization; *iii*) steric hindrances during cyclization; *iv*) equilibration of intermediate protonated heterocyclic rings. Point *i* usually plays a role in the intermolecular addition, moreover, reported experiments revealed stereoselectivity in intermolecular additions opposite to that seen in intramolecular cyclizations.[7] Point *iv* is important when the reaction is carried out under thermodynamic control.[3]



Scheme 1

We reported that the 6-*exo* cyclization of compound (**1**) gave a 33:67 ratio of tetrahydropyrans (**2**) and (**3**) when the reaction was carried out under kinetic control (*via* a; Scheme 1). This small preference for the tetrahydropyran ring having the hydroxyl group

in axial position could be due to a stabilizing Se--O interaction during the cyclization process. When we treated the mixture of hydroxy selenides (**4**) with a catalytic amount of perchloric acid in dichloromethane (*via* b), we found a 75:25 mixture of tetrahydropyrans (**2**) and (**3**). We proposed that the epimerization takes place through the intermediate oxonium ion (**5**).[3] The same ratio was found when above conditions were directly applied to **2** and/or **3**. The stereoselectivity depended on the equilibration of the protonated tetrahydropyran rings through the intermediate ion (**5**). It has been reported that selenium can interact with nearby heteroatoms.[10-14] In some cases, the existence of this intramolecular interaction is supported by theoretical calculations and it has been demonstrated both by crystal structure and by NMR spectroscopy determinations.[15-16] In order to get more insight on the steric and electronic effects, such as Se--O interaction, we considered the stereoselective 6-*exo* synthesis of 2,4,6-trisubstituted tetrahydropyran derivatives, investigating the behavior of four unsaturated alcohols (**6a,b**;**7a,b**) with PhSeCl, and the stereoselective 6-*endo* synthesis of 2,3,4,6-tetrasubstituted tetrahydropyran ring investigating the behavior of four hex-5-en-6-phenyl-2,4-diols (**8a,b**;**9a,b**) (Scheme 2).

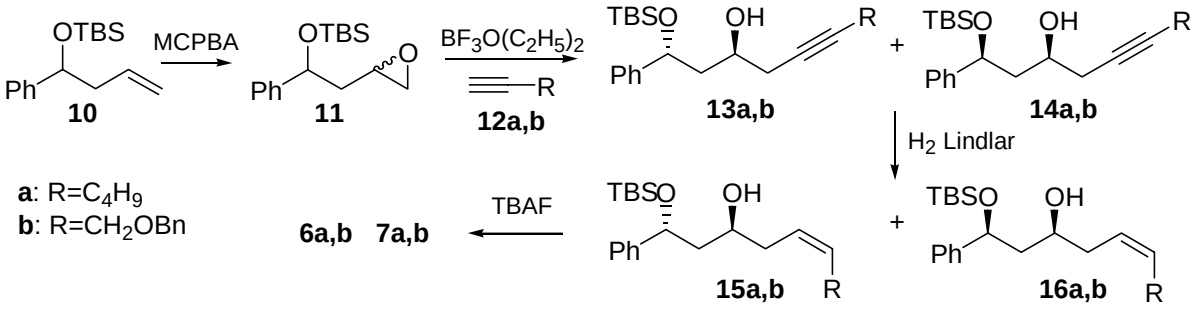


Scheme 2

RESULTS AND DISCUSSION

A: 6-*exo* cyclization

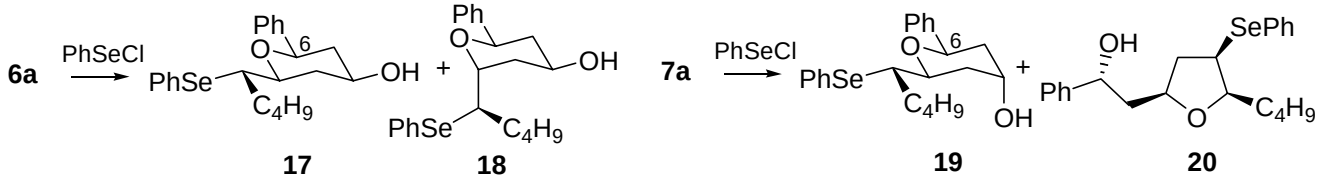
Compounds (**6a,b**) and (**7a,b**) were prepared as outlined in Scheme 3.



Scheme 3

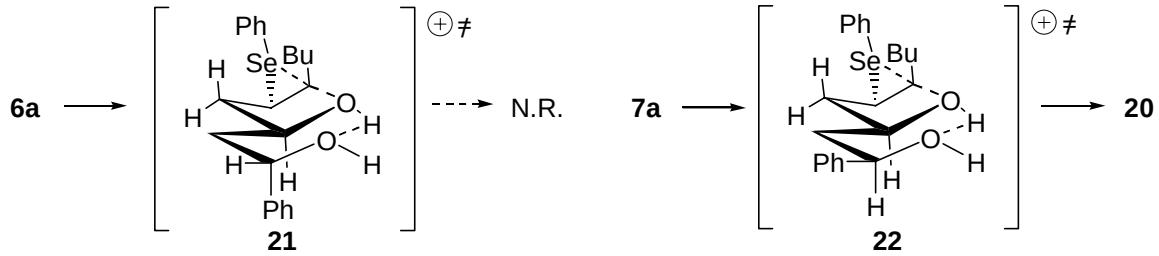
Epoxidation of protected homoallylic alcohol (**10**), prepared by reaction of benzaldehyde with allylmagnesium bromide, gave the diastereomeric mixture of **11**. Treatment of the proper lithioacetylide in tetrahydrofuran at –78 °C with $BF_3O(C_2H_5)_2$ gave epoxide ring opening. Separation with column chromatography gave pure *anti* and *syn* diols (**13a**) and (**14a**). The relative stereochemistry was ascertained by ^{13}C-NMR spectrum. The two carbinol carbons of the less polar stereoisomer resonate at 69.7 and 75.7 ppm, while in the more polar stereoisomer they resonate at 67.0 and 72.9 ppm. Since it is well known[17] that the carbinol carbons in 1,3-*anti* diols always resonate more upfield than those in 1,3-*syn* diols we assigned the relative stereochemistry. Compounds (**13b** and **14b**) were not separated at this stage and used as mixture. They were separated after the deprotection step to give pure *anti* and *syn* diols (**6b**) and (**7b**). Similarly, we assigned the stereochemistry for compound 1,3-*anti* (68.1 and 71.6 ppm) and *syn* (72.3 and 71.6 ppm). Although two carbon atoms have the same chemical shift in the *anti* and *syn* isomers, this attribution is consistent with the stereochemistry of the cyclized products. Hydrogenation over Lindlar catalyst followed by deprotection gave the diols (**6a,b**) and (**7a,b**). Reaction of **6a** under kinetic control (PhSeCl, K_2CO_3, -78 °C) afforded a 93:7 mixture of **17** and **18** in 65% yield.

The reaction was carried out at -78 °C for 2 h then at 25 °C for 22 h. The stereochemical assignment was based on coupling constants. The axial position of H-6 in compound (**17**) was ascertained by the large coupling constant H-6-H-5_{ax} (11.6 Hz); H-2 position was based on the large coupling constant (11.9 Hz) between H-2 and H-3_{ax}, while H-4 gave a large multiplet. Compound (**18**) showed H-2 proton more deshielded with a large coupling constant with H-1' (11.8 Hz) and small coupling constants between H-2 and H-3 (2.4 and 2.4 Hz).



Scheme 4

Compound (**7a**) gave, after 2 h at -78 °C then 22 h at 25 °C, a 5:1 ratio of tetrahydropyran (**19**) and tetrahydrofuran (**20**) in 60% yield plus several unidentified products. Again the stereochemical assignment of compound (**19**) was based on coupling constants (11.6 Hz H-6-H-5_{ax}, narrow multiplet for H-4, 11.7 Hz H-2-H-3_{ax}). The tetrahydrofuran structure (**20**) was established by ^{1}H-NMR, COSY and HETCOR spectra. In particular, the methylene of the butyl group coupled with H-2 (multiplet at 3.92 ppm) which coupled with H-3 (multiplet at 3.25 ppm). Proton H-3 was found to be bonded to the same carbon atom carrying the PhSe group. The presence of compound (**20**) can be explained by assuming the intermediacy of a partial chair-like transition state (**22**) in which the $PhCH(OH)CH_2$ group lies in equatorial position. The intramolecular hydrogen bond may assist the cyclization process. This transition state shows the most favorable 1,3-interaction between the hydrogen atoms. Starting from the *anti* diol (**6a**) the corresponding transition state (**21**) should display the less favorable 1,3-interaction between the hydrogen atom and phenyl group. The 2,5-*cis* stereochemistry was not ascertained, however, it is consistent with mode of preparation and literature reports.[18-19] In order to overcome the problem of the presence of **20** we studied the cyclization of compound (**7b**). The presence of the CH_2OBn group should avoid the formation of the *endo* product.[1]

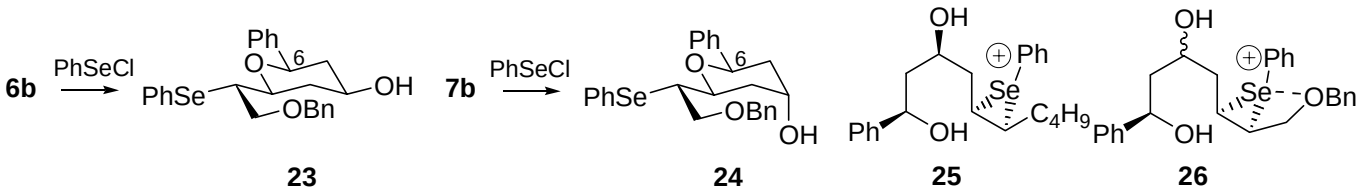


Scheme 5

However, compound (**7b**) behaved differently; indeed, carrying out the reaction as above we isolated only a 3% of **24** and we recovered **7b** (89%), although, at -78 °C, the TLC showed a big spot as compound (**24**). When the reaction mixture was promptly chromatographed after 2 h at -78 °C, we isolated **24** and **7b** in 35 and 40% yield respectively.[20] In order to obtain a higher yield in **24** we used phenylselenenyl sulfate in dry acetonitrile for 30 h at room temperature.[21] In this way we obtained **24** in 57% yield and starting material (5%). Similarly **6b** gave **23** (5%) and starting material (63%) when treated with $PhSeCl/K_2CO_3$ from -78 to 25 °C for 24 h whereas we obtained **23** in 64% yield together a 9% of starting material, when we used the phenylselenenyl sulfate. Compound (**6b**) was also treated with $PhSeCl/K_2CO_3$ in dry acetonitrile; after 24 h at 25 °C we isolated **23** in 15% yield and starting material.

On the basis of these observations we suggest that at -78 °C the tetrahydropyran ring is not present but we have an appreciable concentration of a sufficiently stable seleniranium ion (**26**) that on contact with silica gel is transformed into the final

tetrahydropyran compounds (**23,24)**. The higher stabilities of the seleniranium ion (**26**) could be attributed to the Se--OBn interaction, absent in **25**. Then **25** should be more reactive. Actually **25** could be stabilized by the interaction between the selenium atom and the hydroxyl group, but we have evidence that this interaction plays a more important role when the oxygen atom is closer to the seleniranium ring.[1,22] Seleniranium ion (**26)** may be stable at -78 °C, but when the solution is allowed to warm at room temperature, instead of the ring closure to **23** and **24**, we observed the formation of **6b** and **7b** probably because, as **26** are more stable, they survive sufficiently to undergo the intermolecular attack of the chloride ion on the seleniranium ring.

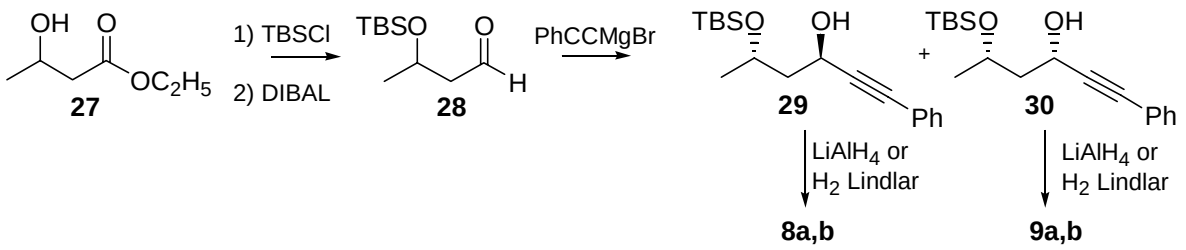


Scheme 6

The use of phenylselenenyl sulfate in acetonitrile gave good yields of the cyclized products probably because being the sulfate ion a harder nucleophilic species than chloride ion, it does not react with the soft electrophilic selenium atom. The solvent plays a minor role, indeed in acetonitrile the Se--OBn interaction is still operative as demonstrated by the poor yield of the cyclization of **6b**. Considering our hypothesis that at -78 °C we have the intermediate seleniranium ion that is probably transformed into the tetrahydropyran by silica gel, we quenched the reaction, performed on **6b** with PhSeCl and K_2CO_3, after 0.5 h at -78 °C, by adding silica gel to the reaction mixture. The mixture was allowed to warm to room temperature and stirred for 20 min then evaporated under reduced pressure. Column chromatography gave **23** in 68% yield with several minor unidentified products; no starting material was found. The reaction was also realised by adding the PhSeCl solution to a suspension of silica gel, K_2CO_3 and **6b** at -78 °C. The reaction was stirred at this temperature for 20 min then allowed to warm to room temperature. Column chromatography gave again the final product with the same yield. In the same way compound (**7b**) gave the tetrahydropyran (**24**) in 61% yield. Tetrahydrofuran derivative was not found in appreciable amount. The reactions with silica gel are in agreement with our hypothesis; the hydroxyl groups of the silica gel are able to destroy the Se--OBn interaction as a consequence of the coordination of the ethereal oxygen atom, destabilizing in this way **26** and then allowing their closure to **23** and **24**.

B: 6-*endo* cyclization

Anti and *syn*, *trans* and *cis* stereoisomers (**8-9a,b**) were considered. These compounds were prepared as outlined in Scheme 7. The β-hydroxy aldehyde (**28**) was allowed to react with phenylethynylmagnesium bromide to give the mixture of *anti* and *syn* diols (**29**) and (**30**).

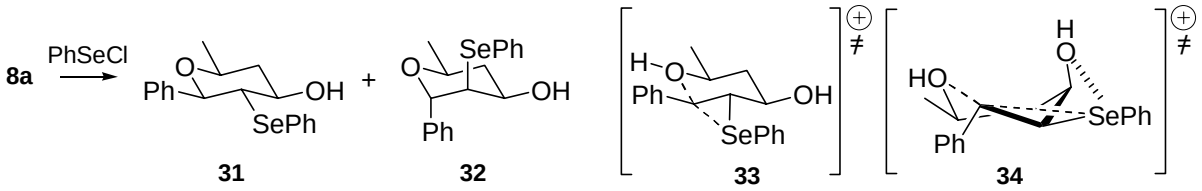


Scheme 7

These products were separated by column chromatography. The relative stereochemistry was ascertained by ^{13}C-NMR spectrum. The two carbinol carbons of the less polar stereoisomer resonate at 60.7 and 67.1 ppm (1,3-*anti*), while in the more polar

stereoisomer they resonate at 61.8 and 67.7 ppm (1,3-*syn*). This stereochemistry was also confirmed in compounds (**8-9a,b**). Reduction with $LiAlH_4$ afforded directly the deprotected *trans*- diols (**8-9a**). Hydrogenation with H_2/Lindlar catalyst followed by deprotection with TBAF afforded the *cis*- diols (**8-9b**).

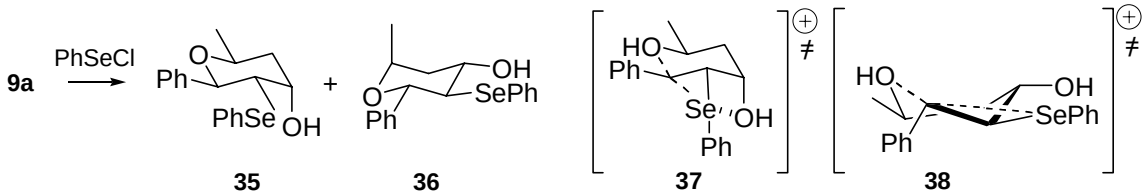
Recently unexpected results have been reported for 6-*endo* cyclization of diols with PhSeCl.[8] In the cyclization of a series of pent-4-en-1,3-diols with phenylselenenyl chloride the reactions gave as major products (diastereoselectivity: 4/1) the tetrahydropyrans in which the oxygen substituent at the 4-position occupies an axial site. This preference was explained by means of stereoelectronic effects. The authors claimed a $CO\sigma^*$-$C{=}C\pi$ overlap when the C_4 oxygen is equatorially disposed, then exerting a deactivating electron-withdrawing effect. In our opinion, the stereoelectronic effect could be related to the Se--O interaction not only in the starting seleniranium ion, but during the course of the cyclization and through the transition state leading to the final tetrahydropyran ring. Axial hydroxyl group is closer than equatorial hydroxyl group towards the equatorial Se atom and this could be the reason for the observed stereoselectivity. First we considered compound (**8a**). The reaction performed with phenylselenenyl chloride, in the presence of K_2CO_3, from –78 °C to room temperature gave the products (**31**) and (**32**) in 82 and 5% yields respectively. The stereochemical assignment of cyclized products was based on coupling constants (see EXPERIMENTAL).



31 **32** **33** **34**

Scheme 8

The stereochemistry of the major compound is based on the expectation that the lowest energy cyclization transition state would lead to a chair conformation in which steric interactions were minimized. However, in our opinion, no stabilizing Se--O interaction can takes place during the cyclization process (see **33**). By contrast, compound (**32**) is disfavored by steric reasons but, probably, the stabilizing Se--O interaction can takes place. Indeed, this product could come from a crowded transition state that displays the methyl and hydroxyl groups in axial position or, more probably, through the twisted transition state (**34**) that does not have the methyl group in axial position avoiding in such a way the strong 1,3-diaxial repulsion. This transition state could preserve the Se--O interaction. The cyclization of compound (**9a**) gave almost exclusively the 2,6-*cis*-tetrahydropyran ring (**35**) in 93% yield. Less than 1% of compound (**36**) was detected (Scheme 9).



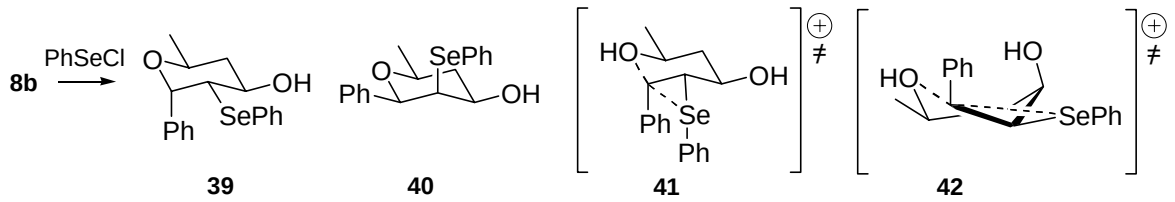
35 **36** **37** **38**

Scheme 9

The excellent selectivity could be ascribed to the fact that compound (**35**) is favored both by steric and electronic reasons (see **37**). By converse, compound (**36**) is disfavored both by steric and electronic reasons (see **38**).

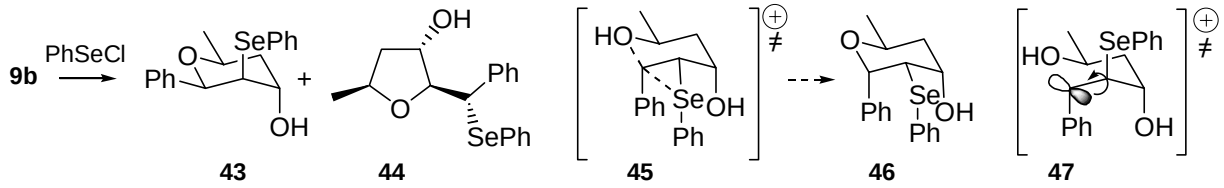
We then examined the *cis*-alkenes (**8b**) and (**9b**). Compound (**8b**) gave only the 2,6-*trans*-tetrahydropyran (**39**) (Scheme 10). The 2,6-*cis*-product (**40**) was not observed. This result is probably due to the *cis* geometry of the C-C double bond. Indeed, the Ph group must lie in axial position (see **41**). Since the Se--O interaction can takes place when the hydroxyl group is axially disposed, it can not be preserved during the cyclization process because of the strong steric repulsion (see **42**). A reaction *via* an

allylic carbenium ion was observed starting from a similar cyclic *anti* diol to give an all equatorial tetrahydropyran such as **31**.[23] In our case this reaction did not take place.



Scheme 10

Finally, diol (**9b**) gave tetrahydropyran (**43**) in 9% yield, tetrahydrofuran (**44**) in 14% yield, starting material (56%) plus several not identified minor products (Scheme 11). The ^{1}H NMR spectrum of compound (**43**) showed a 2,6-diequatorial-3,4-diaxial substitution instead of the expected structure (**46**). The absence of compound (**46**) could be related to the steric repulsion between phenyl and hydroxyl groups in **45**. The poor yield of compound (**43**) can be ascribed to the severe steric interactions in the transition state leading to the tetrahydropyran ring. This product could come *via* a crowded transition state in which methyl and phenyl groups lie in axial position or, in order to minimize such strong interactions, *via* the benzylic carbenium ion (**47**). Being the tetrahydropyran formation very unfavorable the tetrahydrofuran ring (**44**) was obtained as major product, but still in low yield.



Scheme 11

Table. Yields and stereochemistry of cyclic products.

entry	Compd	THP major (yield%) stereochemistry[a]	THP minor (yield%) stereochemistry	THF (yield%)
1	**6a**	**17** (60) 2e4e6e	**18** (5) 2a4e6e	
2	**7a**	**19** (50) 2e4a6e		**20** (10)
3	**6b**	**23** (68)[b] 2e4e6e		
4	**7b**	**24** (61)[b] 2e4a6e		
5	**6b**	**23** (64)[c]		
6	**7b**	**24** (57)[c]		
7	**6b**	**23** (5)[d]		
8	**7b**	**24** (3)[d]		
9	**8a**	**31** (82) 2e3e4e6e	**32** (5) 2a3a4e6e	
10	**9a**	**35** (93) 2e3e4a6e	**36** (<1) 2e3e4e6a	
11	**8b**	**39** (74) 2a3e4e6e		
12	**9b**	**43** (9) 2e3a4a6e		**44** (14)

[a]) e=equatorial; a=axial. [b]) Reaction with PhSeCl/silica gel.

[c]) Reaction with $PhSeOSO_3^-$. [d]) Reaction with PhSeCl.

CONCLUSION

Data collected in this work seem to show that, for the studied substrates, independently from mode of cyclization (6-*exo* or 6-*endo*) steric interactions are the major factors determining the stereoselectivity and also the regioselectivity (Table, entries 2 and 12) of reaction. However, electronic interactions, such as Se-O interaction, though less important, sometimes play a role in determining reaction yields (Table, entries 7, 8), diastereoselectivity (Table, entries 9, 10) and regioselectivity (Table, entries 3-6). Finally, the nature of the X^- counter ion of the electrophilic species $PhSe^+$ as well as the use of silica gel can influence the studied reactions (Table, entries 5, 6 and 7, 8). These effects, at the best of our knowledge, are shown operative in selenoetherification for the first time.[24]

EXPERIMENTAL

Anhydrous solvents were distilled as follow: tetrahydrofuran was distilled under argon from sodium benzophenone. Dichloromethane and toluene were distilled under argon from calcium hydride and used immediately. Acetonitrile was treated with potassium carbonate then distilled under argon from phosphorus pentoxide. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-C series 250 MHz spectrometer in $CDCl_3$ solution. Flash chromatography was carried out using Macherey-Nagel silica gel (0.04-0.063 mm). Light petroleum ether refers to the fraction boiling in the range 40-60 °C. Melting points were determined after column chromatography with a Kofler hot stage and are uncorrected.

Epoxide (**11**). - A solution of compound (**10**) (3.88 g, 14.77 mmol) and MCPBA (70%, 3.82 g, 14.77 mmol) in anhydrous dichloromethane (58 mL) under argon was stirred at rt for 18 h. The mixture was filtered through Celite and the filtrate washed with sat. aq. $NaHCO_3$, brine, dried (Na_2SO_4) and the solvent evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-Et_2O 10-1) gave epoxide (**11**) as a diastereomeric mixture (3.66 g, 89%); oil. IR (liquid film) 1490, 1470, 1460, 1450 cm^{-1}; ^1H NMR δ -0.12 (s, 3H), 0.08 (s, 3H), 0.91 (s, 9H), 1.61-1.82 (m, 1H), 1.90-2.15 (m, 1H), 2.43-2.46 (m, 1H), 2.70 (dd, J=5.0 and 4.6 Hz, 1H, minor diastereoisomer), 2.79 (dd, J=5.0 and 4.3 Hz, 1H, major diastereoisomer), 2.82-2.91 (m, 1H, minor diastereoisomer), 3.12-3.20 (m, 1H, major diastereoisomer), 4.84-4.94 (m, 1H), 7.22-7.35 (m, 5H); ^{13}C NMR δ -5.1, -4.6, 18.2, 25.8, 43.8, 44.4, 46.9, 47.7, 49.5, 49.7, 72.7, 73.1, 125.6, 125.9, 127.2, 127.3, 128.2, 144.4, 145.1. *Anal.* Calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41. Found: C, 69.10; H, 9.43.

Procedure for the preparation of compounds (**13-14a,b**). – Butyllithium (1.60 M in hexane, 12.3 mL, 19.7 mmol) was added dropwise to a solution of 1-hexyne (2.26 mL, 19.7 mmol) in anhydrous tetrahydrofuran (43 mL) at –78 °C. After 20 min, BF_3-$(C_2H_5)_2O$ (2.5 mL, 19.7 mmol) was added followed, after 5 min, by a solution of the epoxide (**11**) (3.66 g, 13.1 mmol) in anhydrous tetrahydrofuran (6 mL). After 2 h at –78 °C, sat. aq. $NaHCO_3$ (15 mL) was added, the mixture allowed to warm to rt and added to water. The mixture was extracted with ether and the combined organic extracts were washed with brine, dried (Na_2SO_4) and the solvent evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-Et_2O 30-1) gave **13a** and **14a** (3.66 g, 46 and 31% yield respectively) as oils. Compound (**13a**). IR (liquid film) 3420, 1485, 1455 cm^{-1}; ^1H NMR δ -0.10 (s, 3H), 0.09 (s, 3H), 0.87-0.93 (m, 12H), 1.33-1.48 (m, 4H), 1.86-1.95 (m, 2H), 2.10-2.18 (m, 2H), 2.29-2.34 (m, 2H), 3.22 (s, 1H, OH), 3.84-3.94 (m, 1H), 5.09 (dd, J=6.5 and 3.9 Hz, 1H), 7.22-7.34 (m, 5H); ^{13}C NMR δ -5.3, -4.7, 13.5, 18.0, 18.3, 21.8, 25.7, 27.7, 30.9, 45.5, 67.0, 72.9, 76.0, 82.5, 125.5, 127.0, 128.0, 144.3. *Anal.* Calcd for $C_{22}H_{36}O_2Si$: C, 73.28; H, 10.06. Found: C, 73.35; H, 10.07.

Compound (**14a**). IR (liquid film) 3450, 1490, 1455 cm^{-1}; ^1H NMR δ -0.22 (s, 3H), 0.06 (s, 3H), 0.86-0.92 (m, 12H), 1.36-1.48 (m, 4H), 1.90-1.97 (m, 2H), 2.10-2.19 (m, 2H), 2.30-2.38 (m, 2H), 3.42 (d, J=2.0 Hz, 1H, OH), 3.79-3.90 (m, 1H), 4.91 (dd,

J=7.9 and 5.7 Hz, 1H), 7.25-7.35 (m, 5H); ^{13}C NMR δ -5.1, -4.5, 13.6, 18.0, 18.4, 21.9, 25.8, 27.5, 31.0, 46.1, 69.7, 75.7, 76.1, 82.6, 126.0, 127.4, 128.2, 144.6. *Anal.* Calcd for $C_{22}H_{36}O_2Si$: C, 73.28; H, 10.06. Found: C, 73.21; H, 10.05.

Compounds (**13b**) and (**14b**) were isolated as mixture by flash chromatography (light petroleum ether-Et_2O 10-1 then 5-1) (65%) as oil. IR (liquid film) 3430, 1490, 1465, 1457, 1450 cm^{-1}; ^{1}H NMR δ -0.20 (s, 3H, minor diastereoisomer), -0.08 (s, 3H, major diastereoisomer), 0.09 (s, 3H, minor diastereoisomer), 0.11 (s, 3H, major diastereoisomer), 0.13 (s, 9H, minor diastereoisomer), 0.95 (s, 9H, major diastereoisomer), 1.93-2.01 (m, 1H), 2.40-2.45 (m, 1H), 3.45 (br s, 1H, OH, major diastereoisomer), 3.55 (br s, 1H, OH, minor diastereoisomer), 3.92-4.01 (m, 1H), 4.16-4.19 (m, 2H), 4.57-4.59 (m, 2H), 4.94 (dd, J=7.0 and 7.0 Hz, 1H, major diastereoisomer), 5.12 (dd, J=5.2 and 5.2 Hz, 1H, minor diastereoisomer), 7.27-7.37 (m, 1H); ^{13}C NMR δ -5.3, -4.7, -4.4, 18.0, 18.1, 25.8, 27.5, 27.8, 45.4, 46.1, 57.6, 57.7, 66.9, 69.7, 71.4, 73.2, 76.0, 78.1, 83.4, 125.7, 126.0, 127.2, 127.8, 128.1, 128.4, 137.5, 144.1, 144.4. *Anal.* Calcd for $C_{26}H_{36}O_3Si$: C, 73.54; H, 8.54. Found: C, 73.60; H, 8.56.

Procedure for the preparation of compounds (**15-16a,b).** – A suspension of Lindlar catalyst (180 mg) in a solution of the alkyne (**13a**) (1.2 g, 3.33 mmol) in ethanol (27 mL) was stirred vigorously under hydrogen until disappearance of the alkyne (reaction monitored by ^{1}H-NMR). The mixture was filtered through Celite and the filtrate was evaporated *in vacuo*. The product was characterized and used without further purification.

Compound (**15a**). (96%), oil. IR (liquid film) 3450, 1490, 1455 cm^{-1}; ^{1}H NMR δ -0.10 (s, 3H), 0.10 (s, 3H), 0.88-0.94 (m, 12H), 1.25-1.32 (m, 4H), 1.79-1.85 (m, 2H), 1.96-2.08 (m, 2H), 2.12-2.26 (m, 2H), 3.06 (br s, 1H, OH), 3.72-3.86 (m, 1H), 5.09 (dd, J=10.0 and 4.8 Hz, 1H), 5.31-5.53 (m, 2H), 7.21-7.55 (m, 5H); ^{13}C NMR δ -5.3, -4.8, 13.9, 18.0, 22.2, 25.7, 27.1, 31.7, 35.4, 45.8, 68.0, 73.3, 125.0, 125.6, 126.9, 128.1, 132.7, 144.4. *Anal.* Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.89; H, 10.54.

Compound (**16a**). (97%), oil. IR (liquid film) 3450, 1490, 1465, 1458 cm^{-1}; ^{1}H NMR δ -0.23 (s, 3H), 0.07 (s, 3H), 0.80-0.91 (m, 12H), 1.25-1.35 (m, 4H), 1.72-2.32 (m, 6H), 3.75-3.85 (m, 1H), 4.89 (dd, J=9.1 and 4.5 Hz, 1H), 5.35-5.53 (m, 2H), 7.22-7.33 (m, 5H); ^{13}C NMR δ -5.1, -4.5, 13.9, 17.9, 22.3, 25.8, 27.0, 31.7, 35.2, 46.5, 71.0, 76.3, 124.9, 125.9, 127.3, 128.2, 132.6, 144.7. *Anal.* Calcd for $C_{22}H_{38}O_2Si$: C, 72.87; H, 10.56. Found: C, 72.91; H, 10.58.

Compounds (**15b-16b**). (97%), oil. IR (liquid film) 3440, 1490, 1465, 1455 cm^{-1}; ^{1}H NMR δ -0.23 (s, 3H, minor diastereoisomer), -0.10 (s, 3H, major diastereoisomer), 0.05 (s, 3H, minor diastereoisomer), 0.08 (s, 3H, major diastereoisomer), 0.90 (s, 9H, minor diastereoisomer), 0.92 (s, 9H, major diastereoisomer), 1.76-1.86 (m, 1H), 2.16-2.26 (m, 1H), 3.26 (d, J=2.0 Hz, 1H, OH, major diastereoisomer), 3.59 (s, 1H, OH, minor diastereoisomer), 4.02-4.07 (m, 2H), 4.50 (s, 2H), 4.88 (dd, J=9.1 and 4.2 Hz, 1H, minor diastereoisomer), 5.08 (dd, J=5.0 and 5.0 Hz, 1H, major diastereoisomer), 5.58-5.80 (m, 2H), 7.24-7.37 (m, 10H); ^{13}C NMR δ -5.3, -5.1, -4.8, -4.5, 17.9, 18.1, 25.8, 35.6, 35.8, 45.9, 46.6, 65.6, 67.6, 70.5, 72.2, 73.3, 76.1, 125.6, 125.9, 127.0, 127.4, 127.5, 127.7, 127.8, 128.1, 128.3, 128.4, 128.5, 129.3, 129.5, 138.2, 144.3, 144.6. *Anal.* Calcd for $C_{26}H_{38}O_3Si$: C, 73.19; H, 8.98. Found: C, 73.26; H, 8.91.

Procedure for the deprotection with TBAF - A solution of tetrabutylammonium fluoride (1.01 g, 3.2 mmol) in tetrahydrofuran (5 mL) was added dropwise to a solution of compound (**13a**) (580 mg, 1.6 mmol) in tetrahydrofuran (10 mL) at 0 °C, and the mixture allowed to warm to rt and stirred for 15 h. The solution was concentrated under reduced pressure then dissolved in ethyl acetate and extracted with water. The organic phase was washed with brine, dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-ethyl acetate 4-1) gave **6a** (88%) as oil. IR (liquid film) 3350 1495, 1450 cm^{-1}; ^{1}H NMR δ 0.89 (t, J=7.1 Hz, 3H), 1.25-1.36 (m, 4H), 1.75-1.88 (m, 2H), 1.97-2.09 (m, 2H), 2.15-2.31 (m, 2H), 3.30 (d, J=3.0 Hz, 1H, OH), 3.80-3.94 (m, 1H), 4.07 (d, J=4.0 Hz, 1H, OH), 4.99 (dd, J=7.5 and 3.7 Hz,

1H), 5.28-5.39 (m, 1H), 5.45-5.54 (m, 1H), 7.23-7.35 (m, 5H); ^{13}C NMR δ 13.8, 22.2, 27.0, 31.6, 35.0, 43.9, 68.5, 71.2, 124.6, 125.4, 126.9, 128.1, 132.9, 144.5. *Anal.* Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.34; H, 9.76.

Compound (**7a**) (90%) oil (light petroleum ether-ethyl acetate 2-1). IR (liquid film) 3345, 1495, 1455 cm^{-1}; ^{1}H NMR δ 0.91 (t, J=7.1 Hz, 3H), 1.30-1.40 (m, 4H), 1.75-1.83 (m, 2H), 2.00-2.10 (m, 2H), 2.12-2.30 (m, 2H), 3.84-4.00 (m, 1H, overlapped with s, 1H, OH), 4.49 (d, J=1.3 Hz, 1H, OH), 4.84 (dd, J=6.3 and 6.3 Hz, 1H), 5.31-5.42 (m, 1H), 5.48-5.59 (m, 1H), 7.23-7.36 (m, 5H); ^{13}C NMR δ 13.8, 22.2, 26.9, 31.6, 35.6, 44.4, 72.1, 74.7, 124.4, 125.6, 127.2, 128.2, 133.3, 144.3. *Anal.* Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.41; H, 9.75.

Compound (**6b**) (45%) oil (ethyl acetate-ether 2-1). IR (liquid film) 3350, 1495, 1454 cm^{-1}; ^{1}H NMR δ 1.84-1.89 (m, 2H), 2.15-2.38 (m, 2H), 3.06 (br s, 2H, OH), 3.83-3.91 (m, 1H), 4.04 (dd, J=6.5 and 3.7 Hz, 1H), 4.51 (s, 2H), 5.02 (dd, J=6.8 and 4.9 Hz, 1H), 5.59-5.69 (m, 1H), 5.75-5.85 (m, 1H), 7.24-7.38 (m, 10H); ^{13}C NMR δ 35.7, 44.3, 65.3, 68.1, 71.6, 72.5, 125.5, 127.2, 127.9, 128.3, 128.4, 128.8, 129.8, 137.9, 144.5. *Anal.* Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.92; H, 7.77.

Compound (**7b)** (42%) oil (ethyl acetate-ether 2-1). IR (liquid film) 3380, 1490, 1450 cm^{-1}; ^{1}H NMR δ 1.71-1.89 (m, 2H), 2.20-2.32 (m, 2H), 3.89-4.00 (m, 1H), 4.02 (d, J=6.1 Hz, 2H, overlapped with br s, 2H, OH), 4.50 (s, 2H), 4.89 (dd, J=8.6 and 4.5 Hz, 1H), 5.64-5.83 (m, 2H), 7.23-7.36 (m, 10H); ^{13}C NMR δ 36.0, 44.9, 65.3, 71.5, 72.3, 74.8, 125.6, 127.6, 127.8, 128.3, 128.6, 129.5, 136.2, 137.8, 144.5. *Anal.* Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.89; H, 7.77.

Compound (**8b**) (55% over two steps: hydrogenation over Lindlar catalyst and deprotection) pale yellow oil. IR (liquid film) 3340 1490 cm^{-1}; ^{1}H NMR δ 1.15 (d, J=6.3 Hz, 3H), 1.62-1.77 (m, 2H), 3.59 (br s, 1H, OH), 3.78 (br s, 1H, OH), 4.06-4.13 (m, 1H), 4.84-4.95 (m, 1H), 5.71 (dd, J=10.7 and 9.4 Hz, 1H), 6.44 (d, J=10.7 Hz, 1H), 7.19-7.35 (m, 5H); ^{13}C NMR δ 23.2, 44.2, 65.1, 65.3, 127.1, 128.2, 128.6, 129.9, 134.0, 136.4. *Anal.* Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.01; H, 8.41.

Compound (**9b**) (62% over two steps: hydrogenation over Lindlar catalyst and deprotection) pale yellow oil. IR (liquid film) 3330 1490 cm^{-1}; ^{1}H NMR δ 1.19 (d, J=6.2 Hz, 3H), 1.59-1.81 (m, 2H), 3.79 (br s, 2H, OH), 4.00-4.08 (m, 1H), 4.77-4.86 (m, 1H), 5.65 (dd, J=11.6 and 9.1 Hz, 1H), 6.49 (d, J=11.6 Hz, 1H), 7.23-7.38 (m, 5H); ^{13}C NMR δ 23.9, 44.7, 68.2, 68.5, 127.1, 128.2, 128.6, 130.3, 133.9, 136.4. *Anal.* Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C,75.08; H, 8.41.

Synthesis of compounds (**29**) and (**30**) – To a solution of compound (**28**) (1.66 g, 8.22 mmol) in anhydrous tetrahydrofuran (9 mL) at 0 °C a solution of phenylethynylmagnesium bromide (1.0 M in tetrahydrofuran, 11 mL, 11 mmol) was added dropwise. The reaction was allowed to warm to rt and stirred for 90 min. After this period the mixture was cooled at 0 °C then quenched with sat. aq. NH_4Cl. The mixture was extracted with ether and the combined organic extracts were washed with brine, dried (Na_2SO_4) and the solvent was evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-ethyl acetate 20-1) gave **29** (526 mg, 21%) and **30** (640 mg, 26%) as oils. Compound (**29**): IR (liquid film) 3421, 2360, 1599, 1490 cm^{-1}; ^{1}H NMR δ 0.13 (s, 3H), 0.16 (s, 3H), 0.92 (s, 9H), 1.26 (d, J=6.3 Hz, 3H), 1.92-1.97 (m, 2H), 3.64 (d, J=5.8 Hz, 1H, OH), 4.35-4.43 (m, 1H), 4.81-4.89 (m, 1H), 7.27-7.34 (m, 3H), 7.42-7.46 (m, 2H); ^{13}C NMR δ -4.8, -4.2, 17.9, 23.5, 25.8, 45.1, 60.7, 67.1, 84.5, 90.1, 122.9, 128.1, 128.2, 131.6. *Anal.* Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 71.09; H, 9.28.

Compound (**30**): IR (liquid film) 3356, 2360, 1599, 1489 cm^{-1}; ^{1}H NMR δ 0.11 (s, 3H), 0.13 (s, 3H), 0.91 (s, 9H), 1.24 (d, J=6.1 Hz, 3H), 1.83-2.09 (m, 2H), 2.91 (d, J=3.6 Hz, 1H, OH), 4.11-4.19 (m, 1H), 4.75-4.82 (m, 1H), 7.27-7.36 (m, 3H), 7.40-7.46 (m, 2H); ^{13}C NMR δ -4.8, -4.1, 17.9, 24.3, 25.8, 46.9, 61.8, 67.7, 84.9, 89.9, 122.8, 128.2, 128.3, 131.6. *Anal.* Calcd for $C_{18}H_{28}O_2Si$: C, 71.00; H, 9.27. Found: C, 70.90; H, 9.29.

Synthesis of compounds (**8a**) and (**9a**) – Lithium aluminum hydride-bis(tetrahydrofuran) complex (1.0 M in toluene, 6.00 mL, 6.00 mmol) was added dropwise to a stirred solution of compound (**29**) (700 mg, 2.31 mmol) in anhydrous tetrahydrofuran (30 mL) and anhydrous toluene (30 mL) at rt and the resulting mixture stirred at reflux for 3 h. The cooled, stirred mixture was treated cautiously with ethyl acetate (16 mL) and water (16 mL). After 10 min, the two layers separated and the aqueous layer extracted with ethyl acetate. The combined organic solutions were dried (Na_2SO_4) and the solvent evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-ethyl acetate 1-1 then 1-2) gave **8a** (264 mg, 60%) as oil. IR (liquid film) 3330, 1595, 1490 cm^{-1}; ^1H NMR δ 1.26 (d, J=6.3 Hz, 3H), 1.74-1.83 (m, 2H), 2.55 (br s, 1H, OH), 2.89 (br s, 1H, OH), 4.17-4.24 (m, 1H), 4.62-4.68 (m, 1H), 6.29 (dd, J=15.9 and 6.0 Hz, 1H), 6.64 (dd, J=15.9 and 1.1 Hz, 1H), 7.20-7.41 (m, 5H); ^{13}C NMR δ 23.3, 44.3, 64.9, 69.8, 126.3, 127.3, 128.4, 129.4, 131.9, 136.6. *Anal.* Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.66; H, 11.16.

Compound (**9a**) (68%), oil, mp 56-57 °C; IR (nujol) 3240, 3310, 1490 cm^{-1}; ^1H NMR δ 1.23 (d, J=6.2 Hz, 3H), 1.64-1.80 (m, 2H), 3.74 (br s, 2H, OH), 4.02-4.17 (m, 1H), 4.49-4.57 (m, 1H), 6.21 (dd, J=15.9 and 6.5 Hz, 1H), 6.59 (15.9 Hz, 1H), 7.21-7.40 (m, 5H); *Anal.* Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.70; 11.20.

Procedure for the cyclization with PhSeCl. Synthesis of compounds (**17, 18, 19, 20, 31, 32, 35, 36, 39, 43, 44**) – To a solution of compound (**6a**) (714 mg, 2.87 mmol) in anhydrous dichloromethane (14 mL) was added K_2CO_3 (793 mg, 5.74 mmol). The mixture was cooled at –78 °C then a solution of PhSeCl (659 mg, 3.44 mmol) in anhydrous dichloromethane (9 mL) was added. The mixture was stirred at –78 °C for 1 h then at rt for 22 h. After this period water was added, the organic extracts were washed with brine, dried (Na_2SO_4) and the solvent evaporated *in vacuo*. Purification of the crude product by flash chromatography (light petroleum ether-ethyl acetate 4-1) gave **18** (54 mg, 5%) as yellow oil and **17** (696 mg, 60%) as white solid. Compound (**17**). mp 68-69 °C; IR (nujol) 3340, 1575, 1490, 1470, 1450 cm^{-1}; ^1H NMR δ 0.92 (t, J=7.3 Hz, 3H), 1.28-1.83 (m, 7H), 1.93-2.10 (m, 1H), 2.15-2.30 (m, 2H, overlapped with 1H, OH), 3.28-3.35 (m, 1H, C*H*SePh), 3.70 (ddd, J=11.9, 2.6 and 2.6 Hz, 1H, H-2), 3.91-4.04 (m, 1H, H-4), 4.38 (dd, J=11.6 and 1.8 Hz, 1H, H-6), 7.23-7.40 (m, 8H), 7.57-7.63 (m, 2H); ^{13}C NMR δ 13.9, 22.4, 30.4, 32.0, 37.5, 43.3, 51.2, 68.3, 77.4, 77.9, 125.6, 127.0, 127.3, 128.2, 128.9, 130.5, 133.8, 142.1. *Anal.* Calcd for $C_{22}H_{28}O_2Se$: C, 65.50; H, 7.00. Found: C, 65.55; H, 7.01.

Compound (**18**). IR (liquid film) 3420, 1577, 1495, 1477 cm^{-1}; ^1H NMR δ 0.87 (t, J=7.3 Hz, 3H), 1.25-2.20 (m, 10H), 3.18-3.26 (m, 1H), 4.18 (ddd, J=11.8, 2.4 and 2.4 Hz, 1H, H-2), 4.37-4.52 (m, 1H, H-4, overlapped with 1H, OH), 4.87 (dd, J=11.7 and 3.7 Hz, 1H, H-6), 7.23-7.45 (m, 8H), 7.55-7.61 (m, 2H); ^{13}C NMR δ 13.9, 22.5, 30.5, 32.7, 35.6, 41.0, 52.1, 65.1, 73.5, 125.6, 126.9, 127.1, 128.1, 128.9, 133.8, 143.1. *Anal.* Calcd for $C_{22}H_{28}O_2Se$: C, 65.50; H, 7.00. Found: C, 65.58; H, 6.98

Compound (**19**) (50%) pale yellow oil (light petroleum ether-ethyl acetate 5-1). IR (liquid film) 3400, 1575, 1490, 1470 cm^{-1}; ^1H NMR δ 0.94 (t, J=7.1 Hz, 3H), 1.29-2.25 (m, 10H, overlapped with 1H, OH), 3.24-3.31 (m, 1H, C*H*SePh), 4.25 (ddd, J=11.7, 2.5 and 2.5 Hz, 1H, H-2), 4.43-4.47 (m, 1H, H-4), 4.94 (dd, J=11.6 and 2.3 Hz, 1H, H-6), 7.29-7.44 (m, 8H), 7.63-7.67 (m, 2H); ^{13}C NMR δ 13.9, 22.4, 26.7, 30.4, 32.6, 35.5, 40.8, 52.0, 64.9, 73.4, 73.7, 125.5, 126.8, 127.0, 128.2, 128.8, 130.8, 133.7, 143.0. *Anal.* Calcd for $C_{22}H_{28}O_2Se$: C, 65.50; H, 7.00. Found: C, 65.50; H, 7.02.

Compound (**20**) (10%) pale yellow oil (light petroleum ether-ethyl acetate 5-1). IR (liquid film) 3445, 1577, 1495, 1475 cm^{-1}; ^1H NMR δ 0.89 (t, J=7.1 Hz, 3H), 1.26-1.93 (m, 9H), 2.48-2.59 (m, 1H, H-4), 3.19-3.30 (m, 1H, H-3), 3.87-3.97 (m, 1H, H-2), 4.08 (s, 1H, OH), 4.18-4.29 (m, 1H, H-5), 4.90 (dd, J=12.4 and 7.1 Hz, 1H, Ph C*H*OH), 7.24-7.36 (m, 8H), 7.55-7.64 (m, 2H); ^{13}C NMR δ 14.0, 22.6, 28.3, 33.5, 41.3, 43.5, 45.0, 74.2, 78.1, 84.2, 125.7, 127.3, 128.1, 128.3, 129.1, 134.7, 135.2, 144.2. *Anal.* Calcd for $C_{22}H_{28}O_2Se$: C, 65.50; H, 7.00. Found: C, 65.60; H, 7.03.

Compound (**31**) (82%) white solid mp 76 °C (light petroleum ether-ethyl acetate 6-1). IR (nujol) 3400, 1455, 1375 cm^{-1}; ^1H

NMR δ 1.26 (d, J=6.2 Hz, 3H), 1.58 (ddd, J=11.1, 11.1 and 11.1 Hz, H-5_{ax}), 2.22 (ddd, 11.1, 4.8 and 1.9 Hz, H-5_{eq}), 3.01 (dd, J=10.5 and 10.5 Hz, H-3), 3.17 (br s, 1H, OH), 3.64-3.78 (m, 2H), 4.32 (d, J=10.5 Hz, H-2), 7.09-7.32 (m, 10H); ^{13}C NMR δ 21.5, 41.4, 58.8, 70.1, 72.0, 82.8, 128.1, 128.7, 135.6, 139.4. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.30; H, 5.82.

Compound (**32**) (5%) white solid mp 109 °C (light petroleum ether-ethyl acetate 6-1). IR (nujol) 3440, 1580, 1490, 1475 cm^{-1}; ^{1}H NMR δ 1.32 (d, J=6.4 Hz, 3H), 1.55 (ddd, J=13.1, 9.4 and 9.4 Hz, H-5_{ax}), 1.87 (ddd, J=13.1, 4.2 and 1.1 Hz, H-5_{eq}), 2.52 (br s, 1H, OH), 3.73-3.81 (m, 1H, H-4), 3.89-4.00 (m, 1H, H-6), 4.10 (ddd, 3.7, 3.7 and 1.1 Hz, H-3), 5.53 (d, J=3.7 Hz, H-2), 7.22-7.40 (m, 8H), 7.57-7.62 (m, 2H); ^{13}C NMR δ 21.1, 39.9, 56.8, 65.5, 66.8, 78.1, 126.5, 127.6, 127.8, 128.7, 129.3, 134.2, 139.2. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.26, 5.78.

Compound (**35**) (93%) white solid mp 162-163 °C (light petroleum ether-ethyl acetate 5-1). IR (nujol) 3430, 1455, 1375 cm^{-1}; ^{1}H NMR δ 1.21 (d, J=6.2 Hz, 3H), 1.68 (ddd, J=13.9, 11.4 and 2.8 Hz, H-5_{ax}), 2.05 (ddd, J=13.9, 3.2 and 2.1 Hz, H-5_{eq}), 2.72 (br s, 1H, OH), 3.50 (dd, J=11.1 and 2.5 Hz, H-3), 4.04-4.07 (m, 1H, H-4), 4.12-4.23 (m, 1H, H-6), 4.78 (d, J=11.1 Hz, H-2), 7.15-7.40 (m, 5H); ^{13}C NMR δ 21.5, 40.2, 55.9, 66.1, 68.2, 77.9, 127.4, 127.9, 128.2, 129.0, 135.0, 140.3. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.25, 5.81.

Compound (**36)** (<1%) recovered in mixture with compound (**35)** (light petroleum ether-ethyl acetate 5-1). ^{1}H NMR δ 1.42 (d, J=7.0 Hz, 3H), 2.07-2.27 (m, 2H), 2.80 (br s, 1H, OH), 3.16 (dd, J=10.6 and 10.6 Hz, H-3), 4.00-4.15 (m, 1H, H-4), 4.53-4.60 (m, 1H, H-6), 4.74 (d, J=10.6 Hz, H-2), 7.21-7.49 (m, 10H); ^{13}C NMR δ 17.6, 37.8, 59.4, 66.0, 69.5, 75.6, 127.4, 127.9, 128.0, 128.1, 128.2, 128.8, 129.0, 135.7, 139.6. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.31; H, 5.82.

Compound (**39)** (74%) white solid mp 92 °C (light petroleum ether-ethyl acetate 6-1). IR (nujol) 3430, 1455, 1375 cm^{-1}; ^{1}H NMR δ 1.22 (d, J=6.3 Hz, 3H), 1.52 (ddd, 13.1, 9.2 and 9.2 Hz, H-5_{ax}), 2.27 (ddd, J=13.1, 4.4 and 3.5 Hz, H-5_{eq}), 2.80 (s, 1H, OH), 3.53 (dd, J=9.4 and 5.2 Hz, H-3), 3.70-3.78 (m, 1H, H-6), 4.41-4.51 (m, 1H, H-4), 5.48 (d, J=5.2 Hz, H-2), 7.20-7.56 (m, 10H); ^{13}C NMR δ 21.2, 40.3, 55.3, 66.3, 68.6, 76.6, 127.6, 127.7, 128.2, 128.4, 129.2, 131.1, 133.5, 138.8. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.20; H, 5.78.

Compound (**43**) (9%) pale yellow oil (light petroleum ether-ethyl acetate 4-1). IR (liquid film) 3400, 1575, 1490 1470 cm^{-1}; ^{1}H NMR δ 1.33 (d, J=6.3 Hz, 3H), 1.68 (dddd, J=14.5, 1.9, 1.9 and 1.9 Hz, H-5_{eq}), 1.99 (br s, 1H, OH), 2.12 (ddd, J=14.5, 11.8 and 2.8 Hz, H-5_{ax}), 3.32 (ddd, J=3.6, 1.9 and 1.9 Hz, H-3), 4.07-4.16 (m, 1H, H-6), 4.47-4.50 (m, 1H, H-4), 5.28 (d, J=1.9 Hz, H-2), 7.10-7.41 (m, 10H); ^{13}C NMR δ 21.7, 36.0, 55.2, 69.3, 69.8, 74.9, 125.7, 127.0, 127.3, 127.9, 128.8, 130.1, 134.1, 141.3. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.29; H, 5.83.

Compound (**44)** (14%) pale yellow oil (light petroleum ether-ethyl acetate 4-1). IR (liquid film) 3390, 1490 1450 cm^{-1}; ^{1}H NMR δ 1.23 (d, J=5.9 Hz, 3H), 1.69 (m, 1H, H-4, overlapped with 1H, OH), 1.99 (ddd, J=13.2, 5.3 and 1.8 Hz, H-4), 4.17 (dd, J=7.2 and 2.8 Hz, H-2), 4.21-4.32 (m, 1H, H-5), 4.50-4.55 (m, 1H, H-3), 4.80 (d, J=7.2 Hz, C*H*SePh), 7.29-7.46 (m, 10H); ^{13}C NMR δ 20.5, 42.4, 63.5, 75.1, 75.2, 90.0, 127.8, 128.0, 128.4, 130.5, 138.2. *Anal.* Calcd for $C_{18}H_{20}O_2Se$: C, 62.25; H, 5.80. Found: C, 62.30; H, 5.80.

Procedure for the cyclization with $PhSeOSO_3^-$. A mixture of compound (**7b**) (110 mg, 0.35 mmol), diphenyl diselenide (55 mg, 0.17 mmol) and ammonium peroxydisulfate (48 mg, 0.21 mmol) in anhydrous acetonitrile (3 mL) was stirred for 30 h. After this period the solvent was evaporated *in vacuo* and the residue was purified by flash chromatography (light petroleum ether-ethyl acetate 3-1) to give **24** (57%).

Procedure for the cyclization with PhSeCl in the presence of silica gel. Synthesis of compounds **(23, 24)**. – To a solution of

compound (**6b**) (173 mg, 0.55 mmol) in anhydrous dichloromethane (3.9 mL) was added K_2CO_3 (153 mg, 1.11 mmol). The mixture was cooled at –78 °C then a solution of PhSeCl (127 mg, 0.66 mmol) in anhydrous dichloromethane (3.9 mL) was added. The mixture was stirred at –78 °C for 2 h then silica gel (2 g, 0.040-0.063 mm) was added. After stirring for 5 min, the mixture was warmed at rt and stirred for 20 min. The solvent was evaporated *in vacuo*, then flash chromatography (light petroleum ether-ethyl acetate 3-1) gave **23** (68%) as colorless oil. IR (liquid film) 3380, 1604, 1577, 1494, 1477 cm^{-1}; ^1H NMR δ 1.85 (br s, 1H, OH), 2.00-2.11 (m, 2H, H-5), 2.17-2.25 (m, 1H, H-3_{eq}), 3.38 (ddd, J=9.7, 4.4 and 1.8 Hz, 1H, C*H*SePh), 3.78 (dd, J=9.7 and 4.4 Hz, 1H, C*H*HOBn), 3.97-4.10 (m, 3H, CH*H*OBn, H-4 and H-6), 4.40 (dd, J=12.1 and 1.5 Hz, 1H, H-2), 4.50 (s, 2H, OCH_2Ph), 7.26-7.40 (m, 13H), 7.56-7.62 (m, 2H); ^{13}C NMR δ 39.0, 43.3, 50.7, 68.2, 70.8, 72.9, 74.0, 77.2, 125.6, 126.1, 127.2, 127.3, 127.6, 128.2, 128.3, 129.0, 130.2, 133.8, 134.7, 138.1, 142.1. *Anal.* Calcd for $C_{26}H_{28}O_3Se$: C, 66.80; H, 6.04. Found: C, 66.88; H, 6.06.

Compound (**24**) (61%) colorless oil (light petroleum ether-ethyl acetate 3-1). IR (liquid film) 3430, 1577, 1494, 1477, 1452 cm^{-1}; ^1H NMR δ 1.62 (br s, 1H, OH), 1.68-1.79 (m, 2H, H-3 and H-5), 1.90-1.99 (m, 1H, H-3), 2.30-2.42 (m, 1H, H-5), 3.33 (ddd, J=9.7, 4.8 and 2.2 Hz, 1H, C*H*SePh), 3.76 (dd, J=9.7 and 4.8 Hz, 1H, C*H*HOBn), 4.00 (dd, J=9.7 and 9.7 Hz, 1H, CH*H*OBn), 4.39-4.44 (m, 1H, H-4), 4.46-4.55 (m, 1H, H-6, overlapped with 4.49 s, 2H, OCH_2Ph), 4.90 (dd, J=11.7 and 2.3 Hz, 1H, H-2), 7.22-7.37 (m, 13H), 7.53-7.58 (m, 2H); ^{13}C NMR δ 36.6, 40.7, 51.2, 64.9, 70.2, 70.9, 72.9, 73.2, 125.5, 127.0, 127.5, 127.6, 128.1, 128.3, 129.0, 130.4, 133.5, 138.2, 143.1. *Anal.* Calcd for $C_{26}H_{28}O_3Se$: C, 66.80; H, 6.04. Found: C, 66.77; H, 6.02.

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