Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 7365–7376

TETRAHEDRON

Electrophilic selenocyclization in 2-ene-1,5-diol systems: unexpected oxetane vs. tetrahydrofuran formation

Pierre Van de Weghe, Stéphane Bourg and Jacques Eustache*

Laboratoire de Chimie Organique et Bioorganique associé au CNRS, Université de Haute-Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse 3, rue Alfred Werner, F-68093 Mulhouse Cedex, France

Received 11 April 2003; revised 3 July 2003; accepted 22 July 2003

Abstract—Electrophile-induced cyclization of (*E*)- and (*Z*)-2-ene-1,5-diols to tetrahydrofurans and oxetanes is described. Significant differences between the present report and previous work have been noted. A tentative model is proposed.

1. Introduction

The allylic/homoallylic system found in 2-ene-1,5-diols offers many possibilities for chemical conversion. For example, we recently described the use of (*Z*)-2-ene-1,5-diols as key intermediates in the synthesis of spiroketals.[1] Another synthetically useful possibility would be their conversion into tetrahydrofurans (Fig. 1). Combined with the mildness of the silicon-tethered RCM approach, which allows the facile preparation of highly functionalized allylic homoallylic diols, this conversion potentially provides a new entry toward complex tetrahydrofurans as found in e.g. acetogenins.

To test the feasibility of this approach, we chose tetrahydrofuran **A**, a potential intermediate in acetogenin synthesis,[2] as a target molecule. The planned conversion implies an electrophile-induced cyclization, following a 5-*endo* mode, to afford a tetrahydrofuran, as shown in Figure 2.

Besides this desired process, however, two other possibilities exist, leading to the formation of oxetanes or oxiranes. The latter (3-*exo* cyclization), in turn, could suffer nucleophilic opening by the homoallylic hydroxyl leading again to the desired tetrahydrofurans. Thus, several competing pathways leading to different products potentially exist in 2-ene-1,5-diols making difficult to predict the overall regio- and stereochemical outcome of the reaction.

Over the last 15 years, numerous research efforts have been devoted to the study of intramolecular halogeno (seleno) etherifications.[3] In simple homoallylic alcohols, the 5-*endo* and 4-*exo* modes compete.[4] However, although the former process (leading to tetrahydrofurans) is in principle disfavoured,[5] in almost all reported studies, using (*Z*)- or (*E*)-1,2-disubstituted olefinic double bonds, the tetrahydrofuran is the only product of the reaction,[6] while we are aware of only one instance where oxetane formation was observed.[7] This apparent deviation from Baldwin's rules has been explained by considering that the transition state in such reactions is pyramidalized, therefore not corresponding to a 'true' 5-*endo*-trig process.[6d,e] Fewer examples deal with allylic alcohols and we could find only one example of iodoetherification in a 2-ene-1,5-dihydroxy system related to ours. In this case, formation of a single tetrahydrofuran was also observed.[8] Representative examples of such studies are shown in Figure 3. Although no example exactly matching our case had been published, the abundant data available in related systems led us to be confident in the validity of our approach.

2. Results and discussion

For the preparation of the required allylic homoallylic precursor **7** (Scheme 1), we used the silicon-tethered RCM approach recently developed by us[1] and others (Scheme 1).[9,10]

Allylic alcohol **3** was prepared in 45% overall yield from tridecanal by treatment with $Ph_3P{=}CH{-}COOMe$, reduction of the resulting α,β-unsaturated ester to the corresponding allylic alcohol with DIBAL-H, asymmetric Katsuki–Sharpless epoxidation using (−)-diisopropyltartrate and deoxygenation by Cp_2TiCl.[11] Homoallylic alcohol **4** was obtained from D-glyceraldehyde acetonide as described by Roush.[12] The two alcohols were coupled as follows: **4** was silylated using excess dimethyldichlorosilane and after evaporation of the volatile material the

Keywords: electrophilic; cyclization; oxetane; tetrahydrofuran.
* Corresponding author. Tel.: +33-3-89-33-68-58; fax: +33-3-89-33-68-60; e-mail: j.eustache@uha.fr

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4020(03)01134-7

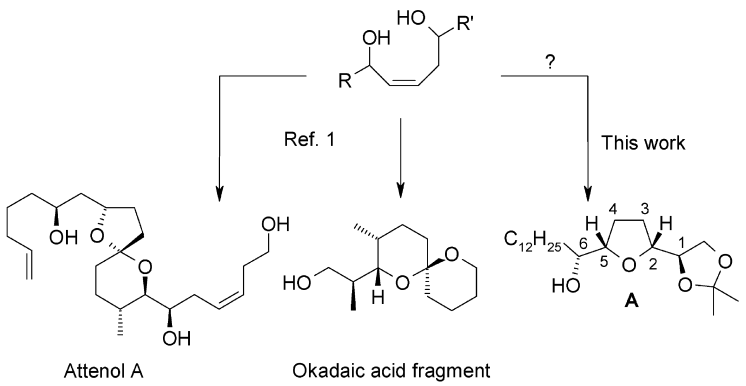


Figure 1. (*Z*)-2-ene-1,5-diols as versatile synthetic intermediates.

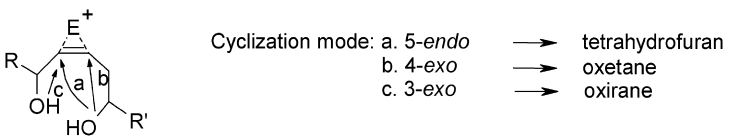


Figure 2. Possible cyclization modes in (*Z*)-2-ene-1,5-diols.

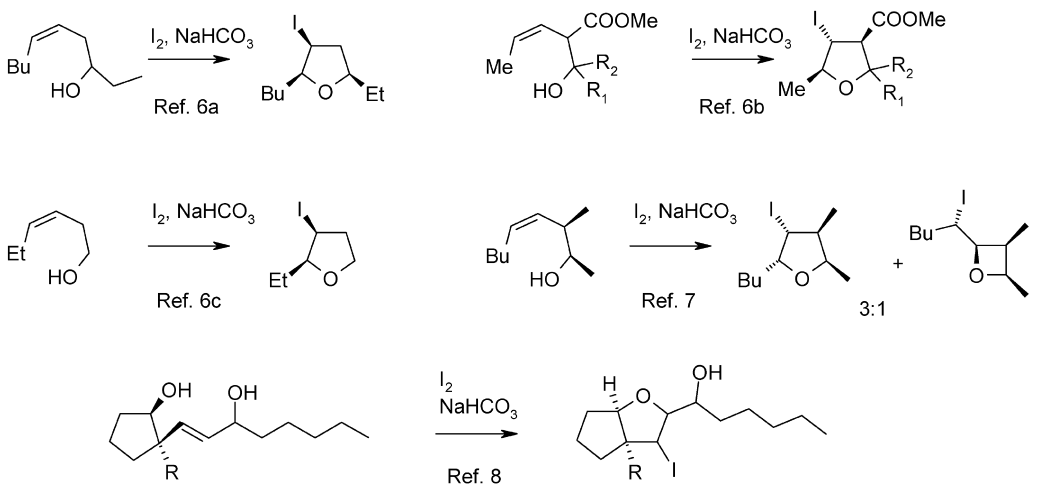
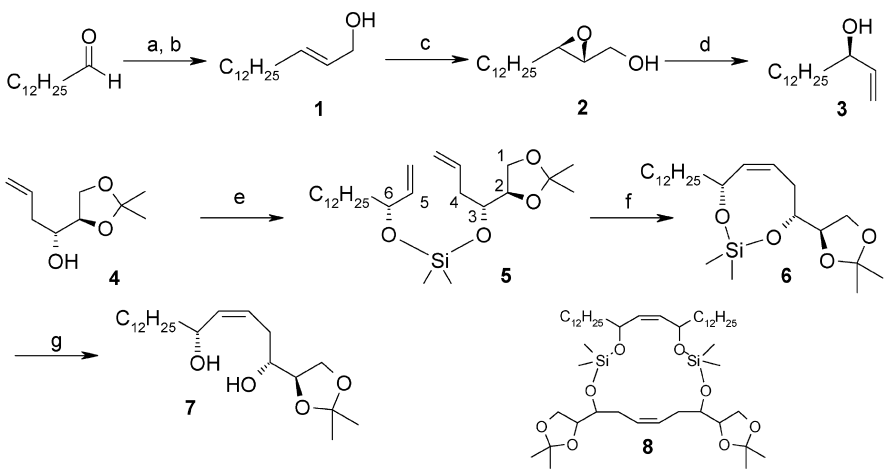
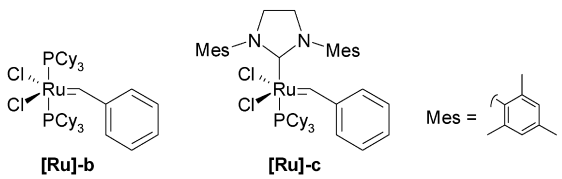


Figure 3. Electrophile-induced cyclization of homoallylic alcohols.



Scheme 1. *Reagents and conditions.* (a) $Ph_3P{=}CHCO_2Me$ (1.5 equiv.), THF, 0°C to rt, 16 h, 78%. (b) DIBAH (3 equiv.), toluene, −78°C, 2 h, 85%. (c) $Ti(OiPr)_4$, *t*BuOOH, (−)-DIPT, 16 h. (d) Cp_2TiCl_2 (5 equiv.), Zn (5 equiv.), $ZnCl_2$ (2 equiv.), THF, 15 min, 67% (2 steps). (e) (i) BuLi (1.1 equiv.), THF, −78°C, 10 min then Me_2SiCl_2 (5 equiv.), −78°C to rt, 1 h; (ii) volatiles removal; (iii) **3**, imidazole (3 equiv.), THF, rt, 16 h, 92%; (f) [**Ru**]-**b** (20 mol%), C_6H_6, reflux, 48 h, 68%; (g) TBAF, THF, rt, 30 min, 80%.

crude chlorodimethylsilyl ether was allowed to react with **3** to afford acyclic silalketal **5**. The RCM conditions were examined next: using the 'first generation' Grubbs's catalyst [**Ru**]-**b**, and low concentrations of the reagents (0.01 M), **5** was smoothly converted to cyclic silalketal **6**.



Raising the concentration to 0.1 M led to the formation of significant amounts of macrocycle **8**, (the result of a cross coupling metathesis followed by RCM).[13] The same side-reaction occurred when using the more active 'second generation' Grubbs's catalyst [**Ru**]-**c**, regardless of the concentration of the reagents. Removal of the silicon tether by fluoride ion provided the desired (*Z*)-2-ene-1,5-diol (**7**) in 50% overall yield (from alcohol **4**).

With precursor **4** in hand, we proceeded to the key electrophilic cyclization shown in Scheme 2. Our initial attempts using a variety of halogen-based electrophiles (NBS, NIS, I_2-collidine) were unsuccessful. In contrast, selenoetherification, using *N*-phenylselenenylphthalimide (*N*-PSP) proceeded smoothly but afforded, instead of the expected tetrahydrofuran(s), or oxirane(s) the two oxetanes **9** and **10** in 45 and 30% yields, respectively. **10** was quantitatively converted back to **9** by treatment with 2,2-dimethoxypropane (DMP). Finally, Bu_3SnH removal of the selenium in **9** gave oxetane **11** in 70% yield.

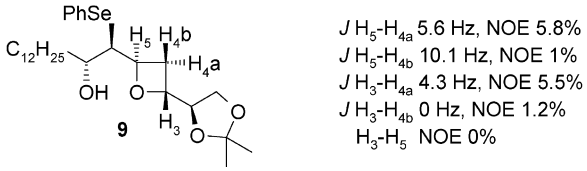


Figure 4. Structure determination of oxetane **9**.

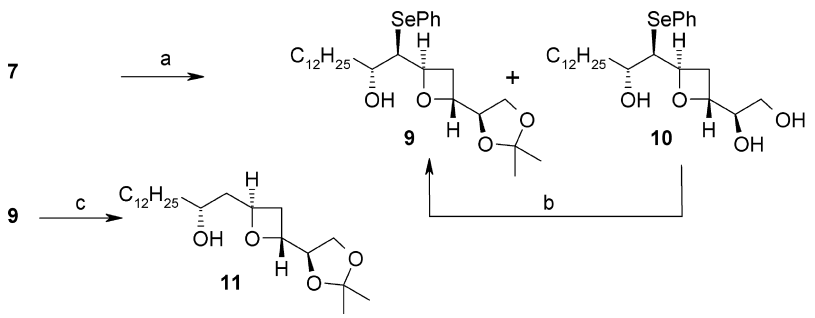
The structure of **9** (then **11**) was established by proton and ^{13}C NMR (Figure 4) and confirmed by synthesis (see Ref. 14). Relevant features of the NMR data include:

- The absence of signals in the region 3.5–3 ppm, which rules out the presence of an epoxide.
- The high δ values for protons H3 and H5, (4.45 and 4.75 ppm, respectively) consistent with an oxetane and making a tetrahydrofuran structure unlikely.
- The two H4 protons couple only with the two low field protons H3 and H5 and not with the proton adjacent to Se, which rules out both the oxirane and tetrahydrofuran possibilities.

Noteworthy is the absence of a NOE effect between H3 and H5, indicative of a *trans* relationship between these protons. This is confirmed by the strong NOE effects between H5 and H4a and H3 and H4b. The strong coupling between H5 and H4b is characteristic of a *trans* diaxial relationship while the two weak couplings between H4 and H3 define an equatorial position for the latter. Thus, although well supported by many hints from the literature, the assumption we made at the onset of this work that electrophile-induced cyclization of diol **7** should preferably lead to tetrahydrofurans **1** proved to be wrong.

Faced with this unexpected result, we felt that a more detailed study of (*Z*)- and (*E*)-2-ene-1,5-diols, *N*-PSP-induced cyclization, was warranted. The aim of this study was twofold: beside gaining interesting information on the almost unprecedented electrophile-induced cyclization of 2-ene-1,5-diols, we were hoping that (*E*)-2-ene-1,5-diols might behave differently from the (*Z*)-isomers, perhaps leading to preferential tetrahydrofurans formation. Then, the approach could still be viable for accessing isomers of **A**. These would also be interesting in connection to acetogenin synthesis.[15] For that purpose, systematic variation of the structural elements thought to play an important role for the outcome of the cyclization, i.e. the configuration of the olefinic double bond and the relative stereochemistries at the homoallylic and allylic carbon atoms was undertaken (Fig. 5).[16]

The 1-(*R*)-*trans*-ene **12** was easily obtained, albeit only in modest yield, by photoisomerization of **7**[17] (Scheme 3), and the 1-(*S*)-*cis*-isomer **13** was prepared as shown in Scheme 4. Thus, ynone **16** was obtained by acylation of *bis*-trimethylsilylacetylene with tridecanoyl chloride.[18] Enantioselective reduction according to Brown[19] then treatment with $LiAlH_4$ afforded cleanly the (*S*)-allylic alcohol **19** in >90% ee as determined from the ^1H NMR spectrum of the corresponding Mosher's ester.



Scheme 2. *Reagents and conditions*. (a) *N*-PSP (1.7 equiv.), CSA (0.1 equiv.), CH_2Cl_2, −78°C to rt, 16 h, **9** (45%) and **10** (30%); (b) DMP, CSA (0.2 equiv.), rt, 16 h, quantitative; (c) Bu_3SnH (3.0 equiv.), AIBN (cat.), toluene, reflux, 16 h, 70%.

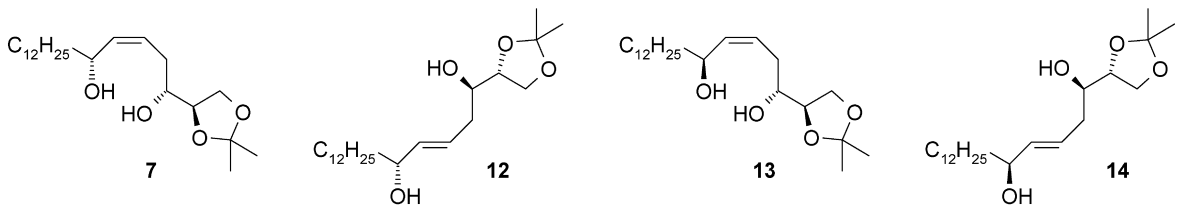
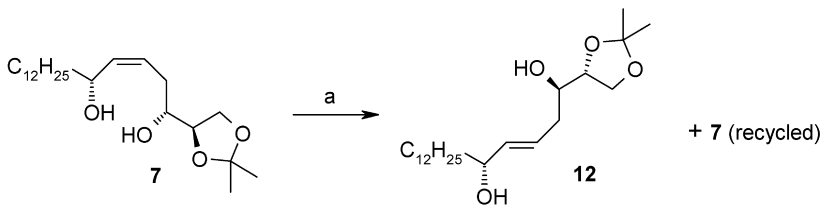
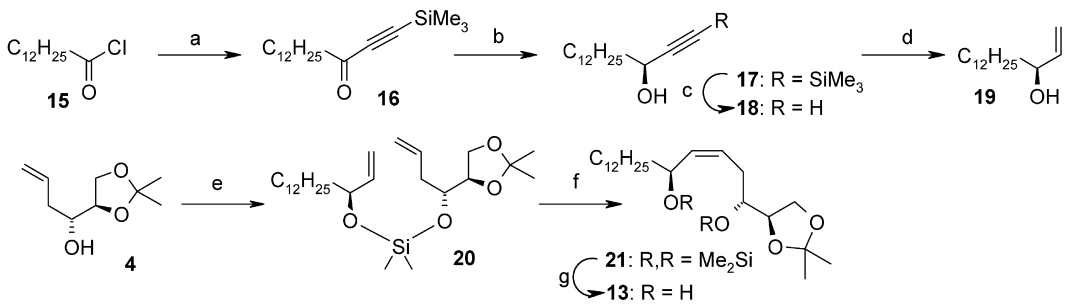


Figure 5. *N*-PSP-induced cyclization: the four possible 5-(*R*)-2-ene-1,5-diols.



Scheme 3. *Reagents and conditions*. (a) $h\nu$, $(PhS)_2$ (cat.), dioxane/hexane, rt. 2 h, 47% (two cycles).



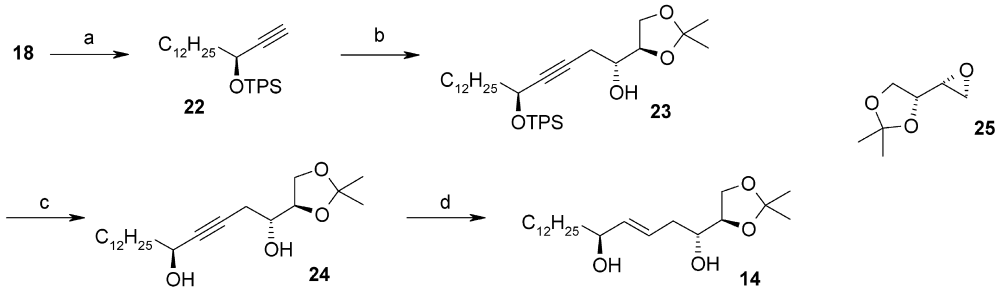
Scheme 4. *Reagents and conditions*. (a) $Me_3Si-C\equiv C-SiMe_3$ (1 equiv.), $AlCl_3$ (1 equiv.), CH_2Cl_2, 0°C, 2 h, 86%; (b) (*S*)-alpineborane, 0°C to rt, neat, 16 h; (c) TBAF, THF, rt, 30 min, 75% (two steps); (d) $LiAlH_4$ (4.0 equiv.), THF, 0°C to rt, 72 h, 74%; (e) (i) BuLi (1.1 equiv.), THF, −78°C, 10 min then Me_2SiCl_2 (4 equiv.), −78°C to rt, 1 h; (ii) volatiles removal; (iii) **19**, imidazole (3 equiv.), THF, rt, 16 h, 97%; (f) [**Ru**]-**b** (20 mol%), toluene, reflux, 48 h; (g) TBAF, THF, rt, 30 min, 51% (two steps).

Coupling with homoallylic alcohol **4** through a silicon bridge was performed as described earlier. The resulting silalketal was cyclized to **21** using [**Ru**]-**b**. Removal of the silicon tether by fluoride ion afforded **13** in 51% overall yield.

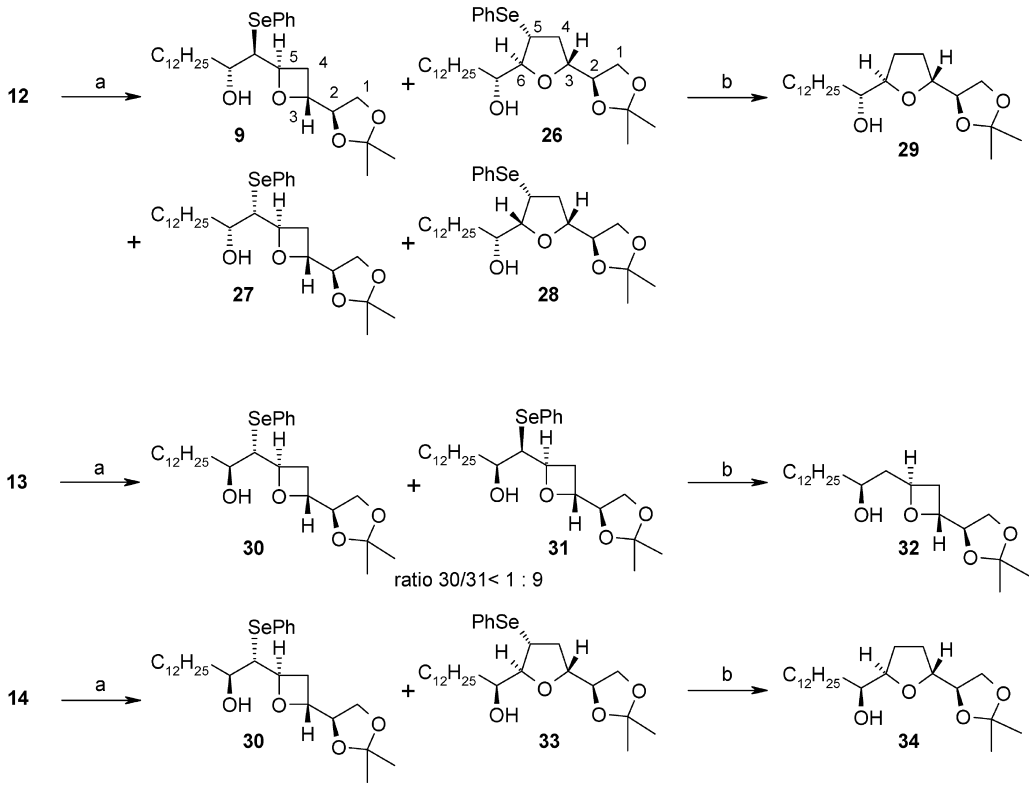
The last required (*E*,1*S*)-2-ene-1,5-diol was prepared as shown in Scheme 5: propargylic alcohol **18** was converted to the *tert*-butyldiphenylsilyl (TPS) ether **22** which was deprotonated and allowed to react with the known epoxide **25**[20] in presence of $BF_3{\cdot}OEt_2$. Removal of the TPS group gave yne-diol **24** in excellent (85%) overall yield. Finally, **24** was reduced to ene-diol **14** by treatment with lithium aluminium hydride. **14** was obtained in 60% yield along with 18% recovered unreacted **24**.

With the three ene-diols **12**, **13** and **14** in hand[21] we proceeded to the electrophilic cyclization (Scheme 6). The conditions were the same as those used for **7** (treatment with *N*-PSP, for 16 h) except that, after completion of the reaction and removal of most phthalimide by filtration, excess DMP was added to the reaction mixture in order to convert the deprotected diol back to the corresponding isopropylidene.

Some trends are clearly apparent:



Scheme 5. *Reagents and conditions*. (a) TPSCl, Et_3N, 4-DMAP, CH_2Cl_2, reflux, 16 h, quantitative; (b) (i) BuLi, THF, −78°C, 30 min; (ii) BF_3OEt_2, THF, −78°C, 30 min; (iii) **25**, THF, −78°C, 3 h, 88%; (c) TBAF, THF, 20°C, 16 h, 97%; (d) $LiAlH_4$ (4 equiv.), THF, 0–20°C, 16 h, **14** (60%) and **24** (18%).



Scheme 6. *Reagents and conditions*. (a) (i) *N*-PSP (1.5 equiv.), CSA (0.1 equiv.), CH_2Cl_2, −78°C to rt, 16 h; (ii) DMP, CSA (0.2 equiv.), rt, 16 h, **9**+**26**+**27**+**28** (53%) **9**:**26**:**27**:**28**=2:55:8:27 or **30**+**31** (20%) ratio **30**:**31** <1:9 or **30**+**33** (40%) **30**:**33**=2:8; (b) Bu_3SnH (3.0 equiv.), AIBN (cat.), toluene, reflux, 10 h, **29** (85%), **32** (80%) or **34** (65%).

- The (*Z*)-ene-diols (**7** and **13**) lead to the exclusive formation of (3*R*,5*R*)-*trans*-oxetanes.
- The (*E*)-ene-diols (**12** and **14**) lead to mixtures of tetrahydrofurans/oxetanes in which tetrahydrofurans predominate.
- Starting from the (*E*,1*R*,5*R*)-2-ene-1,5-diol **12**, one observes a strong preference for tetrahydrofuran over oxetane formation but a poor selectivity 6-(*R*) vs. 6-(*S*) tetrahydrofurans. In contrast, **14** leads to the exclusive formation of a single tetrahydrofuran and a single oxetane.

The *trans* relationship between H3 and H5 in all oxetane derivatives was established from NMR data, as described for **9** (no NOE between H3 and H5, strong NOE between H5 and one of the H4, coupling pattern within the H3, H4, H5 system similar to that observed in **9**). The absolute configurations of the selenium-bearing carbon atoms are tentatively assigned and correspond to those expected in such cyclizations. Upon treatment with Bu_3SnH the mixture **30**+**31** furnished **32**. Regarding tetrahydrofuran formation from the (*E*)-ene-diols, the results are similar to those previously reported and the model proposed by Knight et al.[6e] correctly predicts the observed configurations. Obviously, the stereochemistry at C7 is responsible for the difference between the strong stereoselectivity observed when cyclizing **14**, and **12** but the reason for this dramatic effect is difficult to explain and the lack of precedent in the literature makes any conclusion derived from the present, non mechanistic, study risky. A tentative explanation is shown Figure 6: according to Knight's model, the more stable transition state is the one which places the large (L) substituent in equatorial position. Inspection of the model suggests an unfavourable electrostatic interaction between the incoming OH and OH-7 in the cyclisation of **12** (but not of **14**).

When compared to previous related work, the main difference in our case is the increased steric bulk at position 7 of the ene-diol system which, in the case of **7** and **13** is probably responsible for the exclusive formation of oxetanes. The easier formation of *trans* (relative to *cis*) oxetanes has some precedent in the literature and can be explained by a disfavoured transition state when substituents are on the same side of the forming ring.[14]

3. Conclusion

While attempting to prepare a synthetic intermediate for acetogenin synthesis, involving electrophilic selenocyclization of a (*Z*)-2-ene-1,5-diol as a key step, we observed the exclusive formation of oxetanes, instead of the expected tetrahydrofurans. This led us to extend our studies to three other ene-diols, varying the configuration of the olefinic double bond and the relative configuration of the two hydroxyl groups (*Z* and *E*, *syn* and *anti*). From this work, the following conclusions can be drawn: (*E*)-2-ene-1,5-diols afford tetrahydrofurans as expected but, unlike previously

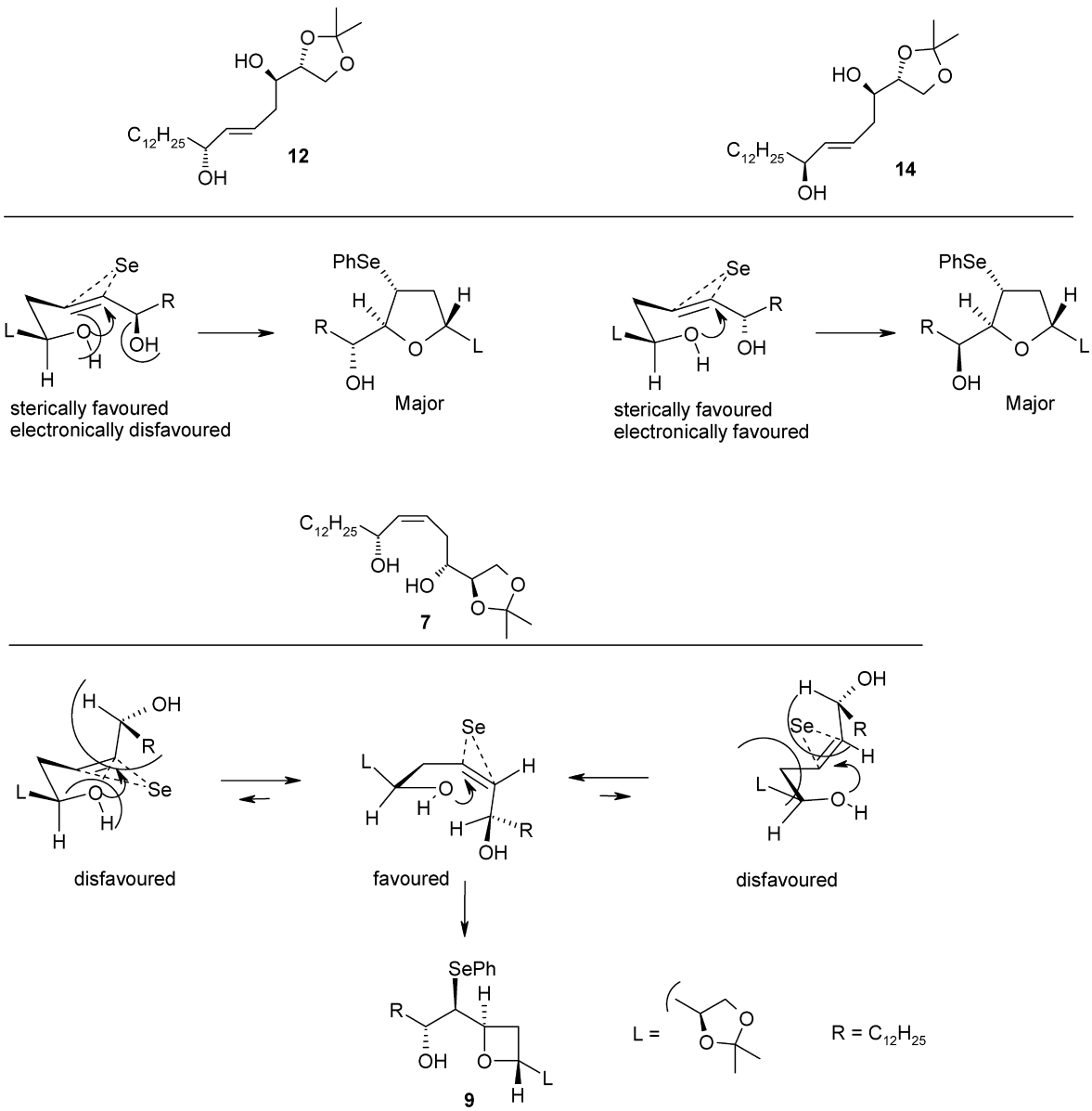


Figure 6. Tentative model for electrophilic cyclization of (*E*)- and (*Z*)-2-ene-1,5-diols.

reported examples of electrophile-induced homoallylic alcohol cyclizations, the (*Z*)-2-ene-1,5-diols used in the study furnished oxetanes only. We believe that steric effect considerations can explain this preferential oxetane formation and suggest that electronic effects may influence the differing stereochemical course of the cyclization of *syn*- and *anti*-(*E*)-2-ene-1,5-diols. Obviously, these conclusions should be taken with caution. Beside the major products which were considered in the study, many impurities were formed during the cyclization which could be neither isolated nor characterized. Clearly, more stable substrates (without functions other than those directly involved in the cyclisation) should be used for 'real' mechanistic studies. The present work, however, indicates that subtle factors, which remain to be precisely defined, govern the oxetane/tetrahydrofuran ratio in electrophile-induced homoallylic alcohols cyclizations. Given the synthetic potential of the selenocyclization reaction, further studies along this line are warranted.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Melting points were taken on a capillary melting point apparatus and are not corrected. Optical rotations were measured using a Perkin–Elmer 341 LC polarimeter. All reactions were carried-out under argon atmosphere with standard techniques for the exclusion of air and moisture. All solvents were dried before use (CH_2Cl_2, toluene and benzene were distilled over CaH_2, THF was distilled from sodium benzophenone ketyl). TLC was performed using fluorescent $60F_{254}$ Merck coated plates. Column chromatography was performed on Macherey–Nagel silica gel 60 (70–230 mesh) with the mixture of solvents indicated in each case.

4.1.1. (2*R*,3*R*)-(3-Dodecyl-oxiranyl)-methanol (2). To a suspension of 4 Å molecular sieves (1.50 g) in CH_2Cl_2

(30 mL) kept at −25°C was added a solution of $Ti(OiPr)_4$ (400 μL, 0.20 equiv., 1.34 mmol) in CH_2Cl_2, (3 mL), and (*S*,*S*)-DIPT (360 μL, 1.68 mmol, 0.25 equiv.) in 3 mL CH_2Cl_2. After 15 min, a solution of allylic alcohol **1** (1.52 g, 1.0 equiv., 6.72 mmol) in CH_2Cl_2 (5 mL) was added dropwise and the reaction mixture was stirred at −25°C for 30 min. Then excess TBHP (5.0–6.0 M in decanes, 8 mmol, 1.60 mL) was slowly added. After 14 h at −25°C, the temperature was raised to −15°C and the reaction was quenched with a solution of tartaric acid (30%). The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were dried over $MgSO_4$. After purification by chromatography over silica gel (cyclohexane/ethyl acetate, 8:2), epoxide **2** (1.20 g, 74%) was obtained: mp 68–70°C; $[\alpha]_D^{20}$=+26.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.87 (3H, broad t, *J*=6.0 Hz, CH_3), 1.18–1.55 (22H, m, 11×CH_2), 1.82 (1H, broad t, *J*=5.9 Hz, OH), 2.95 (2H, m, CH_2O), 3.60 (1H, m, CHO oxirane), 3.90 (1H, m, CHO oxirane); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) 14.1, 22.7, 25.2, 29.3–29.6, 31.5, 31.9, 56.0, 58.4, 61.7; Anal. calcd for $C_{15}H_{30}O_2$: C, 74.38; H, 12.40. Found: C, 74.11; H, 12.41.

4.1.2. (*R*)-Pentadec-1-en-3-ol (3). To a red solution of Cp_2TiCl_2 (6.22 g, 25.0 mmol, 5.0 equiv.) and $ZnCl_2$ (1.36 g, 10.0 mmol, 2.0 equiv.) in THF (90 mL), was added 1.63 g (5.0 equiv., 25.0 mmol), of powdered Zn. The reaction mixture was stirred for 1 h at room temperature at which time the colour had turned to green. Epoxide **2** (1.0 equiv., 5.01 mmol) in 10 mL THF was added and stirring was continued for 15 min. Aqueous HCl (1.0 M, 20 mL) was added and the mixture was extracted with ether. The organic layer was successively washed with water, 10% aqueous $NaHCO_3$, water, brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was chromatographed over silica gel (cyclohexane/ethyl acetate, 8:2), to afford **3** (1.05 g, 67%, two steps): mp 28–30°C; $[\alpha]_D^{20}$=−6.2 (*c* 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.87 (3H, broad t, *J*=6.0 Hz, CH_3), 1.14–1.54 (22H+1H, m, 11×CH_2 and OH), 4.07 (1H, q, *J*=6.2 Hz, CHOH), 5.17 (2H, m, CH_2=), 5.86 (1H, m, CH=); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) 14.1, 22.7, 25.3, 29.3–29.6, 31.9, 37.0, 73.3, 114.5, 141.3; Anal. calcd for $C_{15}H_{30}O$: C, 79.65; H, 13.27. Found: C, 79.67; H, 13.31.

4.1.3. Silalketal (5). A cold (−78°C) solution of homoallylic alcohol **4** (0.466 g, 2.70 mmol) in THF (7 mL) was placed under argon atmosphere. BuLi (1.6 M in hexanes, 1.85 mL, 2.97 mmol) was added dropwise and the solution was stirred for 15 min. Freshly distilled Me_2SiCl_2 (1.60 mL, 5.0 equiv., 13.55 mmol) was added and the reaction mixture was allowed to warm to room temperature. The solvents and Me_2SiCl_2 were removed under reduced pressure and a solution of allylic alcohol **3** (660 mg, 2.90 mmol, 1.07 equiv.) and imidazole (610 mg, 9 mmol, 3 equiv.) in THF (7 mL) was added. The resulting suspension was stirred at room temperature for 16 h, hydrolyzed and extracted with ethyl acetate. The organic layer was washed with brine and dried over $MgSO_4$. After chromatography silica gel (cyclohexane/ethyl acetate, 95:5), silalketal **5** (1.10 g, 92%) was obtained as a colorless oil: $[\alpha]_D^{20}$=+4.2 (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.12 (6H, s, CH_3SiCH_3), 0.87 (3H, broad t, *J*=6.3 Hz, CH_3), 1.20–1.52 (22H, m, 11×CH_2), 1.33 (3H, s, CH_3), 1.44 (3H, s, CH_3), 2.10–2.35 (2H, m, CH_2, H-4), 3.73 (1H, t, *J*=7.6 Hz, CH, H-1), 3.85 (1H, m, CH, H-3), 3.97 (1H, t, *J*=7.6 Hz, CH, H-1), 4.09 (1H, m, CH, H-2), 4.21 (1H, m, CH, H-9), 5.00–5.16 (4H, m, 2×CH_2, H-6 and H-7), 5.73–5.93 (2H, 2×CH, H-5 and H-8); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) −1.6, −1.5, 14.1, 22.7, 25.2, 25.3, 26.4, 29.3–29.6, 31.9, 37.5, 37.8, 65.5, 72.8, 73.7, 78.3, 109.0, 113.7, 117.1, 134.9, 141.4.

4.1.4. Cyclic silalketal (6). A solution of **5** (1.10 g, 2.4 mmol) and Grubbs's catalyst [**Ru**]-**b** (0.20 g, 0.25 mmol, 0.1 equiv.) in benzene (240 mL) was stirred at reflux for 16 h. Then more catalyst (0.20 g, 0.25 mmol, 0.1 equiv.), was added and stirring was continued for 48 h. The solvent was removed under reduced pressure and the residue was chromatographed (cyclohexane/ethyl acetate, 97:3) to give 0.60 g of **5** (68%). $[\alpha]_D^{20}$=−29.3 (*c* 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.16 (6H, s, CH_3SiCH_3), 0.90 (3H, broad t, *J*=6.8 Hz, CH_3), 1.26–1.60 (22H, m, 11×CH_2), 1.36 (3H, s, CH_3), 1.44 (3H, s, CH_3), 2.22 and 2.68 (2H, m, CH_2, H-4), 3.73 (1H, t, *J*=7.8 Hz, CH, H-1), 3.98 (2H, m, 2×CH, H-1 and H-3), 4.10 (1H, q, *J*=6.6 Hz, CH, H-2), 4.36 (1H, q, *J*=6.0 Hz, CH, H-7), 5.59 (1H, m, CH, H-5), 5.76 (1H, dd, *J*=11.2, 5.9 Hz, CH, H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) −2.5, 0.0, 14.1, 22.7, 25.4, 25.8, 26.6, 29.3, 29.5, 29.6, 29.6, 29.7, 31.4, 31.9, 37.9, 65.9, 70.8, 74.5, 79.2, 109.4, 126.5, 137.0.

4.1.5. (*Z*,1*R*,5*R*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol (7). To a solution of **6** (30 mg, 0.08 mmol) in THF (0.2 mL) at room temperature was added 60 μL of TBAF (1.0 M in THF, 0.60 mmol, 2.2 equiv.). After 30 min, the solvent was removed and the residue chromatographed (cyclohexane/ethyl acetate, 7:3) to yield **7**, (8 mg, 80%), a colorless oil. $[\alpha]_D^{20}$=+10.0 (*c* 0.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, broad t, *J*=6.8 Hz, CH_3), 1.18–1.68 (22H, m, 11×CH_2), 1.36 (3H, s, CH_3), 1.45 (3H, s, CH_3), 2.22–2.55 (4H, m, 2×OH and CH_2, H-4), 3.60 (1H, q, *J*=5.8 Hz, CH, H-3), 3.80 (1H, broad t, *J*=7.7 Hz, CH, H-1), 4.0 (1H, t, *J*=7.7 Hz, CH H-1), 4.10 (1H, q, *J*=6.5 Hz, CH, H-2), 4.40 (1H, q, *J*=6.9 Hz, CH, H-7), 5.47–5.65 (2H, m, 2×CH, H-5 and H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.1, 22.7, 25.2, 25.4, 26.5, 29.4, 29.61, 29.63, 29.66, 29.68, 31.9, 32.1, 37.0, 65.9 (*C1*), 67.1, 71.3, 77.6, 109.6, 126.4, 136.5; Anal. calcd for $C_{22}H_{42}O_4$: C, 71.35; H, 11.35. Found: C, 70.71; H, 11.38.

4.1.6. Cyclization of (*Z*,1*R*,5*R*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol 7: oxetanes 9 and 10. To a cold (−78°C) solution of diol **7** (50 mg, 0.13 mmol) in CH_2Cl_2 (2 mL), under argon, was added CSA (3 mg, 0.1 equiv.) and *N*-PSP (70 mg, 0.23 mmol, 1.7 equiv.). The temperature was slowly allowed to reach 20°C and the reaction mixture was stirred for 16 h. After solvent removal, the residue was chromatographed (cyclohexane/ethyl acetate, 1:1) to give **9** (32 mg, 45%) and **10** (20 mg, 30%).

Oxetane **9**. $[\alpha]_D^{20}$=−8.2 (*c* 1.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.88 (3H, t, *J*=6.6 Hz, CH_3), 1.20–1.30 (20H, m, 10×CH_2), 1.38 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.74 (2H, m, CH_2, H-8), 2.05 (1H, dd, *J*=13.0, 5.6 Hz, CH,

H-4), 2.45 (1H, ddd, J=13.0, 10.1, 4.3 Hz, CH, H-4), 3.19 (1H, d, J=2.2 Hz, OH), 3.25 (1H, dd, J=2.6, 1.7 Hz, CH, H-6), 3.90–4.10 (4H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.45 (1H, dd, J=4.3, 2.8 Hz, CH, H-3), 4.75 (1H, ddd, J=10.1, 5.6, 1.6 Hz, CH, H-5), 7.20 and 7.50 (5H, m, SePh); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) 14.1, 19.4, 22.7, 25.8, 28.6, 29.38, 29.59, 29.66, 31.9, 35.4, 39.0, 60.7, 61.0, 70.6, 75.0, 75.4, 82.4, 97.4, 127.0, 129.2, 131.1, 133.1.

Oxetane **10**. ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.88 (3H, t, J=6.6 Hz, CH_3), 1.20–1.30 (20H, m, 10×CH_2), 1.75 (2H, m, CH_2, H-8), 2.10 (1H, dd, J=12.9, 5.6 Hz, CH, H-4), 2.45 (1H, ddd, J=12.9, 10.0, 4.3 Hz, CH, H-4), 2.45 (1H, broad s, OH), 3.10 (1H, d, J=2.7 Hz, OH), 3.30 (1H, m, CH, H-6), 3.43 (1H, d, J=3.6 Hz, OH), 3.90–4.15 (4H, CH_2 and 2×CH, H-1, H-2 and H-7), 4.60 (1H, m, CH, H-3), 4.70 (1H, m, CH, H-5), 7.20 and 7.50 (5H, m, SePh); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) 14.1, 22.7, 25.9, 29.37, 29.58, 29.66, 29.68, 31.9, 35.6, 41.1, 60.6, 61.8, 74.1, 75.2, 81.9, 82.3, 127.2, 128.2, 130.7, 133.4.

4.1.7. Deselenylation of oxetane 9: oxetane 11. To a solution of 20 mg (0.038 mmol) of **9** in toluene (1 mL), under argon, was added a crystal of AIBN and 30 μL (3 equiv., 0.114 mmol) of Bu_3SnH. After 10 h at reflux, the solvent was removed and the residue chromatographed (cyclohexane/ethyl acetate, 1:1) to yield **11** (10 mg, 70%). $[\alpha]_D^{20}$=−9.7 (c 0.35, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm) 0.88 (3H, t, J=6.6 Hz, CH_3), 1.15–1.60 (24H, m, 12×CH_2 and CH, H-6 and H-4), 1.38 (3H, s, CH_3), 1.44 (3H, s, CH_3), 2.17 (1H, dd, J=13.1, 5.6 Hz, CH, H-4), 3.58 (1H, d, J=0.8 Hz, OH), 3.80–4.10 (4H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.40 (1H, t; J=3.6 Hz, CH, H-3), 4.55 (1H, tdd, J=10.1, 5.5, 2.7 Hz, CH, H-5); ^{13}C NMR ($CDCl_3$, 62.9 MHz) δ (ppm) 14.1, 19.8, 22.7, 25.4, 28.3, 29.38, 29.66, 29.70, 31.9, 37.4, 41.0, 42.7, 60.9, 70.4, 71.7, 74.0, 79.5, 97.6; EIMS m/z (rel. int.) 355 (3), 201 (19), 197 (16), 157 (9), 143 (25), 125 (12), 114 (9), 99 (24), 81 (35), 68 (100), 59 (46), 43 (36); Anal. calcd for $C_{22}H_{42}O_4$: C, 71.35; H, 11.35. Found: C, 70.25; H, 11.28.

4.1.8. (*E*,1*R*,5*R*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol (12). Argon was bubbled for 30 min through a solution of **7** (0.195 g, 0.53 mmol) in hexane (40 mL) and dioxane (13 mL) (molarity of solution 0.01 M). Diphenyl disulphide (35 mg, 0.16 mmol, 0.3 equiv.) was added. The reaction mixture was irradiated with a light source (mercury lamp, 450 W, medium pressure, quartz) for 1.5 h to provide a mixture of diols **7** and **12**. The reaction mixture was treated by addition of Et_3N (4 mL), then the solvents were removed under reduced pressure and the two stereoisomers were separated by flash chromatography (cyclohexane/ethyl acetate, 7:3) to give **12** (91 mg, 47%) and **7** (50 mg, 25%) which was recycled. Data for **12**: mp 47–48°C; $[\alpha]_D^{20}$=+3.7 (c 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, t, J=6.7 Hz, CH_3), 1.10–1.70 (22H, m, 11×CH_2), 1.36 (3H, s, CH_3), 1.43 (3H, s, CH_3), 2.17 (1H, t, J=6.4 Hz, CH_2, H-4), 2.28 (1H, broad s, OH), 2.78 (1H, broad s, OH), *3*.57 (1H, broad s, CH, H-3), 3.57, 4.00 (2H, m, CH_2, H-1), 4.10 (2H, m, 2×CH, H-2 and H-7), 5.60 (2H, m, 2×CH, H-5 and H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.10, 22.69, 25.37, 25.46, 26.61, 29.35, 29.62, 29.08, 31.92, 36.52, 37.12, 66.06, 71.85, 72.87, 78.74, 109.48, 126.72, 136.80; Anal. calcd for $C_{22}H_{42}O_4$: C, 71.35; H, 11.35. Found: C, 70.97; H, 11.67.

4.1.9. (*Z*,1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol (13). Prepared as **7**: from **21** (0.240 g), 0.190 g of **13** (91%) were obtained as a white solid: mp 31–32°C; $[\alpha]_D^{20}$=−24.5 (c 1.9, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.86 (3H, broad t, J=6.8 Hz, CH_3), 1.24 (18H, broad s, 9×CH_2), 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.40 and 1.83 (2H, m, CH_2, H-8), 2.05 (1H, m, CH_2, H-4), 2.39 (1H, m, CH_2, H-4), 3.05 (2H, broad s, 2×OH), 3.50 (1H, m, CH, H-3), 3.70 (1H, m, CH_2, H-1), 4.02 (2H, m, CH_2 and CH, H-1 and H-2), 4.35 (1H, broad q, J=7.0 Hz, CH, H-7), 5.57 (2H, m, 2×CH═, H-5 and H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.10, 20.80, 22.68, 25.26, 25.44, 26.65, 29.03, 29.34, 29.61, 29.64, 31.68, 31.91, 36.85, 53.83, 65.97, 66.52, 71.44, 78.80, 109.61, 127.43, 136.53; Anal. calcd for $C_{22}H_{42}O_4$: C, 71.35; H, 11.35. Found: C, 71.31; H, 11.42.

4.1.10. (*E*,1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol (14). To a cold (0°C) solution of **24** (0.330 g, 0.90 mmol) in THF (5 mL) was added $LiAlH_4$ (0.140 g, 3.60 mmol, 4.0 equiv.). The reaction mixture was stirred overnight at 20°C. After usual work-up, and extraction with ether and evaporation of the solvent, the crude product was purified by chromatography (cyclohexane/ethyl acetate, 6:4) to give **14** as a white solid (0.200 g, 60%) and recovered **24** (60 mg, 18%) which was recycled: mp 41–42°C; $[\alpha]_D^{20}$=+8.5 (c 1.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.86 (3H, broad t, J=6.8 Hz, CH_3), 1.25 (20H, broad s, 10×CH_2), 1.36 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.52 (2H, m, CH_2, H-8), 1.77 (1H, broad s, OH), 2.19 (2H, broad t, J=6.5 Hz, CH_2, H-4), 2.40 (1H, d, J=4.5 Hz, OH), 3.57 (1H, m, CH, H-3), 3.73 (1H, m, CH, H-2), 4.05 (3H, m, CH_2 and CH, H-1 and H-7), 5.57 (1H, dd, J=15.5, 6.5 Hz, ═CH, H-5), 5.67 (1H, m, ═CH, H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.11, 22.69, 25.34, 25.49, 26.42, 29.35, 29.58, 29.61, 29.66, 31.92, 36.58, 37.29, 66.04, 71.80, 72.71, 78.51, 109.46, 126.41, 136.56; Anal. calcd for $C_{22}H_{42}O_4$: C, 71.35; H, 11.35. Found: C, 71.11; H, 11.22.

4.1.11. 1-Trimethylsilanyl-pentadec-1-yn-3-one (16). To a solution of tridecanoic acid (4.30 g, 20 mmol) in toluene (30 mL) kept under argon at 20°C, was slowly added oxalyl chloride (2.10 mL, 1.2 equiv., 24 mmol). After 45 min, the volatile material was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (30 mL) and cooled to 0°C under argon. Bis-trimethylsilylacetylene (4.55 mL, 20 mmol) then $AlCl_3$ (2.66 g, 20 mmol) were added. The reaction mixture was stirred for 2 h at 0°C then poured on ice/H_2O and extracted with hexane. The organic layers were washed successively with a saturated solution of Na_2CO_3 then brine. After chromatography (cyclohexane/ethyl acetate, 97:3) **16** was obtained as a colorless oil (5.10 g, 86%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.24 (9H, s, $SiMe_3$), 0.87 (3H, broad t, J=6.8 Hz, CH_3), 1.28 (18H, s, 9×CH_2), 1.65 (2H, m, CH_2, H-5), 2.54 (2H, t, J=7.3 Hz, CH_2, H-4); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) −0.74, 14.12, 22.70, 23.80, 23.97, 28.92, 29.33, 29.35, 29.44, 29.60, 29.64, 31.93, 45.33, 97.56, 102.10; Anal. calcd for $C_{18}H_{34}OSi$: C, 73.47; H, 11.56. Found: C, 73.36; H, 11.67.

4.1.12. (*S*)-1-Trimethylsilanyl-pentadec-1-yn-3-ol (17). To a cold (0°C) solution of (*S*)-Alpine borane (0.5 M in THF, 14 mL, 7 mmol, 2.0 equiv.) **16** (1.036 g, 3.52 mmol) was added. The THF was removed under reduced pressure at 0°C and the reaction mixture was stirred overnight at room temperature then cooled to 0°C. Et_2O (5 mL) was added followed by acetaldehyde and diethanolamine (1 mL each). The precipitate which formed was filtered-off and the filtrate partitioned in water/HCl 1 M (9:1) and Et_2O. Chromatography (cyclohexane to cyclohexane/ethyl acetate, 95:5) afforded **17** as a colorless oil (0.899 g, 86%) which was used as such for the next step. $[\alpha]_D^{20}=+1.03$ (*c* 1.85, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.10 (9H, s, $SiMe_3$), 0.81 (3H, broad t, *J*=6.8 Hz, CH_3), 1.15 (18H, s, 9×CH_2), 1.30 (2H, m, CH_2, H-5), 1.60 (2H, m, CH_2, H-4), 1.78 (1H, d, *J*=5.6 Hz, OH), 4.28 (1H, broad q, *J*=5.7 Hz, CH, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 0.00, 14.12, 22.71, 25.14, 29.25, 29.38, 29.53, 29.57, 29.67, 29.71, 32.00, 37.76, 62.95, 89.29, 107.04. HMRS *m*/*z* found 319.2415, calcd for $C_{18}H_{36}ONaSi$ *m*/*z* 319.2433.

4.1.13. (*S*)-Pentadec-1-yn-3-ol (18). To a solution of **17** in 4 mL THF was added TBAF (1.0 M in THF, 4 mL, 4 mmol). The solution was stirred 30 min at rt. The solvent was removed under reduced pressure and the residue was purified by chromatography (cyclohexane/ethyl acetate, 7:3) to yield **18** as a white solid (0.590 g, 75%): mp 34–35°C; $[\alpha]_D^{20}=-1.9$ (*c* 1.15, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, broad t, *J*=6.6 Hz, CH_3), 1.20 (18H, s, 9×CH_2), 1.42 (2H, m, CH_2, H-5), 1.70 (2H, m, CH_2, H-4), 2.13 (1H, d, *J*=5.2 Hz, OH), 2.44 (1H, d, *J*=2 Hz, CH, H-1), 4.36 (1H, m, CH, H-3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.10, 22.68, 25.03, 29.25, 29.35, 29.52, 29.54, 29.64, 29.67, 31.92, 37.65, 62.31, 72.77, 85.09; Anal. calcd for $C_{15}H_{28}O$: C, 80.36; H, 12.50. Found: C, 80.11; H, 12.56.

4.1.14. (*S*)-Pentadec-1-en-3-ol (19). The propargylic alcohol **18** (0.400 g, 1.77 mmol) was added to a suspension of $LiAlH_4$ (0.270 g, 7.10 mmol, 4.0 equiv.) in cold (0°C) THF. The reaction mixture was stirred for 3 days at 20°C, then slowly hydrolyzed. After extraction with ethyl acetate, the combined organic layers were dried over $MgSO_4$ and the solvents evaporated. The crude product was chromatographed (cyclohexane/ethyl acetate, 95:5) to give **19** as a white solid (300 mg, 74%): mp 28–30°C; $[\alpha]_D^{20}=+6.0$ (*c* 0.7, $CHCl_3$); spectroscopic data as for **3**.

4.1.15. Silalketal (20). Prepared as **5**: from 0.200 g of homoallylic alcohol **4** and 0.300 g of allylic alcohol **19**, 0.510 g (97%) of silaketal **20** were isolated. $[\alpha]_D^{20}=+11.9$ (*c* 1.6, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.13 (6H, broad s, Me_2Si), 0.87 (3H, broad t, *J*=6.6 Hz, CH_3), 1.25 (20H, broad s, 10×CH_2), 1.34 (3H, s, CH_3), 1.41 (3H, s, CH_3), 1.50 (2H, m, CH_2, H-10), 2.30 (2H, m, CH_2, H-4), 3.73 (1H, broad t, *J*=7.7 Hz, CH_2, H-1), 3.85 (1H, m, CH, H-3), 3.95 (1H, m, CH_2, H-1), 4.08 (1H, m, CH, H-2), 4.20 (1H, m, CH, H-9), 5.10 (4H, m, 2×CH_2=, H-6 and H-7), 5.80 (2H, m, 2×CH=, H-5 and H-8); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) −1.68, −1.34, 14.12 22.71, 25.27, 25.37, 26.45, 29.38, 29.67, 31.94, 37.60, 37.87, 65.56, 72.86, 73.72, 78.42, 109.14, 113.82, 117.15, 134.90, 141.36.

4.1.16. Cyclic silalketal (21). Prepared as **6**: from **20** (0.460 g), **21** (0.240 g, 55%) was obtained. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.09 and 0.12 (6H, s, Me_2Si), 0.87 (3H, broad t, *J*=6.8 Hz, CH_3), 1.40 (20H, broad s, 10×CH_2), 1.45 and 1.55 (2H, CH_2, H-8), 2.34 (2H, m, CH_2, H-4), 3.72 (1H, m, CH, H-3), 3.86 (1H, dd, *J*=8.30, 6.8 Hz, CH_2, H-1), 4.02 (1H, dd, *J*=8.3, 6.5 Hz, CH_2, H-1), 4.15 (1H, m, CH, H-2), 4.45 (1H, m, CH, H-7), 5.68 (2H, m, 2×CH=, H-5 and H-6); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) −1.31, −1.21, 14.11, 22.70, 25.35, 25.54, 26.37, 29.37, 29.55, 29.61, 29.64, 29.67, 30.67, 31.94, 37.32, 65.50, 67.91, 73.36, 78.64, 109.41, 128.93, 137.38.

4.1.17. (*S*)-Pentadec-1-yn-3-ol, *tert*-butyldimethylsilyl ether (22). To a solution of **18** (0.700 g, 3.125 mmol) in CH_2Cl_2 (6 mL) under argon were successively added Et_3N (525 μL, 3.75 mmol, 1.2 equiv.), DMAP (0.190 g, 1.56 mmol, 0.5 equiv.) then TPSCl (895 μL, 3.44 mmol, 1.1 equiv.). The reaction mixture was refluxed for 16 h, quenched with water and extracted with CH_2Cl_2. After chromatography (cyclohexane/ethyl acetate, 95:5) **22** was isolated as a white solid (1.44 g, quantitative): mp 34–35°C; $[\alpha]_D^{20}=-21.2$ (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.80 (3H, broad t, *J*=6.8 Hz, CH_3), 1.05 (9H, s, *t*BuSi), 1.10 (18H, s, 9×CH_2), 1.25 (2H, m, CH_2, H-5), 1.60 (2H, m, CH_2, H-4), 2.24 (1H, broad s, CH, H-1), 4.27 (1H, m, CH, H-3), 7.37 and 7.70 (10H, m, 2×PhSi); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.16, 19.32, 22.73, 24.69, 26.59, 26.90, 26.95, 29.21, 29.40, 29.50, 29.57, 29.67, 29.69, 29.72, 31.97, 38.27, 63.78, 72.51, 85.20, 127.42, 127.60, 129.52, 129.65, 133.60, 133.73, 135.57, 135.88.

4.1.18. (1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-5-trimethylsilanyloxy-heptadec-3-yn-1-ol (23). To a cold (−78°C) solution of silyl ether **22** (0.770 g, 1.66 mmol, 1.2 equiv.) in THF (10 mL) was added dropwise BuLi (1.6 M in hexanes, 1.15 mL, 1.81 mmol, 1.3 equiv.). Stirring was continued for 30 min and $BF_3{\cdot}OEt_2$ (230 μL, 1.81 mmol, 1.3 equiv.) was added. After a further 30 min **25** (0.200 g, 1.39 mmol) dissolved in THF (5 mL) was transferred to the solution and stirring was continued for 2 h at which time the reaction was stopped by addition of a saturated solution of NH_4Cl. The mixture was allowed to warm to 20°C and was extracted by ethyl acetate. After usual work-up and solvent removal under reduced pressure. The crude product was purified by chromatography (cyclohexane/ethyl acetate, 8:2) to give **23** as a colorless oil (0.740 g, 88%). $[\alpha]_D^{20}=-37.3$ (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.90 (3H, broad t, *J*=6.8 Hz, CH_3), 1.08 (9H, s, *t*BuSi), 1.15–1.40 (20H, m, 10×CH_2), 1.35 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.67 (2H, m, CH_2, H-8), 2.16 (1H, d, *J*=6 Hz, OH), 2.27 (2H, m, CH_2, H-4), 3.43 (1H, m, CH, H-3), 3.74 and 3.92 (2H, m, CH_2, H-1), 4.02 (1H, m, CH, H-2), 4.37 (1H, m, CH, H-7), 7.40 and 7.70 (10H, m, 2×PhSi); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.12, 19.29, 22.70, 24.12, 24.99, 25.22, 26.48, 26.89, 29.24, 29.37, 29.55, 29.59, 29.66, 29.70, 31.94, 38.54, 64.03, 65.97, 70.31, 77.43, 80.47, 84.17, 109.35, 127.32, 127.55, 129.53, 129.68, 133.80, 134.13, 135.81, 135.99. HMRS *m*/*z* found 629.4019, calcd for $C_{38}H_{58}O_4NaSi$ *m*/*z* 629.4002.

4.1.19. (1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-yne-1,5-diol (24). A solution of **23** (0.580 g, 0.96 mmol) in THF (3 mL) was treated by TBAF (1.0 M in THF, 1.7 mL, 1.7 mmol, 1.5 equiv.) for 16 h at rt. The solvent was removed under reduced pressure and the residue chromatographed (cyclohexane/ethyl acetate, 1:1) to give **24** as a white solid (0.350 g, 97%): mp 34–35°C; $[\alpha]_D^{20}=-2.4$ (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm): 0.87 (3H, broad t, 6.8 Hz, CH_3), 1.25 (18H, broad s, 9×CH_2), 1.37 (3H, s, CH_3), 1.39 (2H, m, CH_2, H-9),1.43 (3H, s, CH_3), 1.67 (2H, m, CH_2, *H8*), 2.29 (1H, broad s, OH), 2.48 (2H, m, CH_2, H-4), 2.67 (1H, d, *J*=5.5 Hz, OH), 3.70 (1H, m, CH, H-3), 3.83 and 4.05 (2H, m, CH_2, H-1), 4.15 (1H, m, CH, H-2), 4.34 (1H, m, CH, H-7); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm): 14.12, 22.70, 24.11, 25.21, 25.25, 26.52, 29.31, 29.36, 29.58, 29.60, 29.66, 29.68, 31.93, 38.00, 62.57, 66.02, 70.51, 77.59, 80.57, 83.93, 109.57; Anal. calcd for $C_{22}H_{40}O_4$: C, 71.74; H, 10.87. Found: C, 71.76; H, 11.03.

4.1.20. Cyclization of (*E*,1*R*,5*R*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol 12: oxetanes 9 and 27, tetrahydrofurans 26 and 28. The same procedure as for the cyclization of **7** was used. From 180 mg (0.486 mmol) of **12** were obtained **9**+**27** (21 mg), **28** (38 mg) and (**26**) 75 mg (combined yield: 53%—cyclohexane/ethyl acetate, 1:1).

Tetrahydrofuran **26**. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.83 (3H, t, *J*=6.8 Hz, CH_3), 1.25–1.60 (22H, m, 11×CH_2), 1.33 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.80 (1H, broad s, OH), 1.90 (1H, m, CH_2, H-4), 2.37 (1H, m, CH_2, H-4), 3.50 (1H, m, CH, H-7), 3.60 (2H, m, CH_2 and CH, H-1 and H-5), 3.75 (1H, m, CH, H-6), 3.90 (2H, m, CH_2 and CH, H-1 and H-3), 4.05 (1H, m, CH, H-2), 7.20 and 7.50 (5H, m, PhSe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 22.70, 25.58, 25.89, 26.38, 29.37, 29.50, 29.62, 29.67, 29.70, 31.95, 35.03, 36.68, 39.79, 65.73, 70.44, 78.17, 79.31, 86.74, 109.84, 128.11, 129.21, 135.16; Anal. calcd for $C_{28}H_{46}O_4Se$: C, 64.00; H, 8.76. Found: C, 64.09; H, 8.85.

Oxetane **27**. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, t, *J*=6.8 Hz, CH_3), 1.05–1.60 (22H, m, 11×CH_2), 1.42 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.70 (1H, m, CH_2, H-4), 2.45 (1H, m, CH_2, H-4), 3.10 (1H, d, *J*=5.5 Hz, OH), 3.25 (1H, m, CH, H-6), 4.00 (4H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.35 (1H, m, CH, H-3), 4.72 (1H, m, CH, H-5), 7.28 and 7.55 (5H, m, SePh); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 19.62, 22.70, 25.72, 28.43, 29.37, 29.58, 29.65, 29.67, 29.70, 31.94, 35.04, 40.95, 59.54, 60.91, 70.42, 72.99, 74.41, 80.75, 97.56, 127.68, 129.34, 134.48, 134.79.

Tetrahydrofuran **28**. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, t, *J*=6.8 Hz, CH_3), 1.15–1.50 (22H, m, 11×CH_2), 1.37 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.80 (1H, broad s, OH), 2.00 (1H, m, CH_2, H-4), 2.35 (1H, m, CH_2, H-4), 3.75 (1H, m, CH, H-7), 3.84 (1H, m, CH_2, H-1), 3.93 (1H, m, CH, H-5), 4.00 (2H, m, CH_2 and CH, H-1 and H-6), 4.12 (1H, m, CH, H-2), 4.20 (1H, m, CH, H-3), 7.20 and 7.50 (5H, m, PhSe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.14, 22.72, 25.73, 26.05, 29.39, 29.50, 29.62, 29.68, 29.71, 30.95, 31.95, 32.39, 37.36, 39.65, 66.29, 73.41, 77.13, 77.50, 88.77, 109.74, 127.97, 129.25, 134.70. HMRS *m*/*z* found 549.2518, calcd for $C_{28}H_{46}O_4NaSe$ *m*/*z* 549.2459.

4.1.21. Deselenylation of tetrahydrofuran 26: tetrahydrofuran 29. The same procedure as for the deselenylation of **9** was used. From 140 mg (0.27 mmol) of **26** were isolated 83 mg of **29** (85% yield, cyclohexane/ethyl acetate, 1:1). $[\alpha]_D^{20}=+13.3$ (*c* 0.75, $CHCl_3$).[22] ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, t, *J*=6.8 Hz, CH_3), 1.15–1.60 (22H, m, 11×CH_2), 1.38 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.65 and 2.05 (4H, m, 2×CH_2, H-4 and H-5), 2.38 (1H, s, OH), 3.40 (1H, m, CH, H-7), 3.70 (1H, t, *J*=7.8 Hz, CH_2, H-1), 3.85 (1H, m, CH, H-6), 4.00 (2H, m, CH_2 and CH, H-1 and H-3), 4.10 (1H, m, CH, H-2); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 22.71, 25.60, 25.67, 26.49, 28.25, 28.49, 29.37, 29.62, 29.64, 29.67, 29.67, 29.69, 29.74, 31.94, 33.49, 65.96, 74.05, 78.62, 79.62, 83.40, 109.80; EIMS *m*/*z* (rel. int.) 355 (6), 269 (38), 171 (31), 113 (100), 101 (49), 83 (51), 69 (38), 57 (57), 43 (87).

4.1.22. Cyclization of (*Z*,1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol 13: oxetanes 30 and 31. The same procedure as for the cyclization of **7** was used. From **13** (40 mg) were obtained: 10 mg (20%) of a 1:9 mixture of **30** and **31** from which pure **31** could be isolated by chromatography (cyclohexane/ethyl acetate, 1:1), $[\alpha]_D^{20}=-8.9$ (*c* 0.95, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, t, *J*=6.7 Hz, CH_3), 1.20 (18H, s, 9×CH_2), 1.36 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.40 and 1.70 (2H, m, CH_2, H-8), 2.10 (1H, dd, *J*=13.1, 5.5 Hz, CH_2, H-4), 2.38 (1H, ddd, *J*=13.1, 10.3, 4.3 Hz, CH_2, H-4), 2.83 (1H, broad d, *J*=6.8 Hz, OH), 3.30 (1H, d, *J*=3.0 Hz, CH, H-6), 3.95 (4H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.46 (1H, m, CH, H-3), 4.82 (1H, ddd, *J*=10.3, 5.6, 1.5 Hz, CH, H-5), 7.25 and 7.60 (5H, m, SePh); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 19.70, 22.70, 25.47, 26.14, 28.38, 29.37, 29.53, 29.62, 29.66, 29.69, 31.94, 35.67, 39.19, 58.92, 60.95, 70.64, 74.69, 75.44, 78.03, 97.53, 127.27, 129.19, 130.56, 133.52.

4.1.23. Deselenylation of the mixture of oxetanes 30 and 31: oxetane 32. The same procedure as for the deselenylation of **9** was used. From 15 mg of **31** were isolated 8 mg of **32** (80% yield, cyclohexane/ethyl acetate, 1:1). White solid: mp 53–54°C; $[\alpha]_D^{20}=-7.5$ (*c*=0.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.86 (3H, t, *J*=6.8 Hz, CH_3), 1.20 (20H, s, 10×CH_2), 1.33 (3H, s, CH_3),1.40 (2H, m, CH_2, H-9),1.41 (3H, s, CH_3), 1.60 and 1.80 (5H, m, 3×CH_2, H-4, H-6 and H-8), 2.10 (1H, dd, *J*=13.1, 5.3 Hz, CH_2, H-4), 2.69 (1H, broad s, OH), 3.80 (3H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.05 (1H, dd, *J*=12.3, 3.3 Hz, CH_2, H-1), 4.45 (1H, broad t, *J*=3.5 Hz, CH, H-3), 4.60 (1H, m, CH, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 20.13, 22.70, 25.80, 28.03, 29.37, 29.63, 29.65, 29.69, 31.94, 37.48, 39.98, 41.40, 60.87, 69.34, 70.95, 74.09, 76.58, 97.70. HMRS *m*/*z* found 393.2956, calcd for $C_{22}H_{42}O_4Na$ *m*/*z* 393.2981.

4.1.24. Cyclization of (*E*,1*R*,5*S*)-1-(4(*S*)-2,2-Dimethyl-[1,3]dioxolan-4-yl)-heptadec-3-ene-1,5-diol 14: oxetanes 30 and tetrahydrofuran 33. The same procedure as for the cyclization of **7** was used. From 43 mg (0.48 mmol) of **14**

were obtained oxetane **30** (5 mg) and tetrahydrofuran **33** (20 mg) (combined yield: 41%—cyclohexane/ethyl acetate, 1:1).

Oxetane **30**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.88 (3H, t, J=6.8 Hz, CH_3), 1.25 (20H, s, 10×CH_2), 1.36 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.45 and 1.68 (2H, m, CH_2, H-8), 1.76 (1H, ddd, J=13.6, 9.8, 3.0 Hz, CH_2, H-4), 2.32 (1H, dd, J=13.6, 5.6 Hz, CH_2, H-4), 2.70 (1H, broad s, OH), 3.30 (1H, dd, J=8.3, 2.5 Hz, CH, H-6), 3.86–4.00 (4H, m, CH_2 and 2×CH, H-1, H-2 and H-7), 4.37 (1H, broad t, J=3.2 Hz, CH, H-3), 4.72 (1H, ddd, J=9.85, 8.6, 5.6 Hz, CH, H-5), 7.25 and 7.60 (5H, m, SePh); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 19.73, 22.71, 25.63, 26.91, 29.38, 29.54, 29.63, 29.67, 29.70, 31.95, 34.71, 40.35, 58.65, 60.90, 67.99, 70.58, 72.85, 74.45, 80.69, 97.62, 127.49, 129.16, 129.99, 133.85, 134.26.

Tetrahydrofuran **33**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, broad t, J=6.8 Hz, CH_3), 1.25 (20H, broad s, 10×CH_2), 1.36 (3H, s, CH_3), 1.42 (3H, s, CH_3), 1.50 (2H, m, CH_2, H-8), 1.83 (1H, m, CH_2, H-4), 2.05 (1H, broad s, OH), 2.42 (1H, m, CH_2, H-4), 3.55 (1H, dd, J=7.9, 7.0 Hz, CH, H-2), 3.74 (1H, m, CH, H-7), 3.95–4.10 (4H, m, CH_2 and 2×CH, H-1, H-3 and H-6), 7.28 and 7.55 (5H, m, PhSe); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 22.71, 25.44, 26.20, 26.57, 29.38, 29.54, 29.56, 29.63, 29.67, 29.70, 31.94, 32.53, 37.45, 38.01, 65.79, 78.12, 80.33, 86.87, 110.01, 123.63, 128.10, 128.52, 129.23, 134.34, 135.05. HMRS m/z found 549.2470, calcd for $C_{28}H_{46}O_4NaSe$ m/z 549.2459.

4.1.25. Deselenylation of tetrahydrofuran 33: tetrahydrofuran 34. The same procedure as for the deselenylation of **9** was used. From 25 mg of **33** were isolated 11 mg of **34** (65% yield, cyclohexane/ethyl acetate, 1:1). $[\alpha]_D^{20}$=+8.0 (c 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 0.87 (3H, broad t, J=6.8 Hz, CH_3), 1.20 (20H, broad s, 10×CH_2), 1.32 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.40–1.55 (2H, m, CH_2, H-8), 1.55–1.95 (4H, m, 2×CH_2, H-4 and H-5), 2.10 (1H, broad s, OH), 3.62 (1H, t, J=7.3 Hz, CH_2, H-1), 3.85–4.05 (5H, m, CH_2, 4×CH, H-1, H-2, H-3, H-6 and H-7); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 14.13, 22.70, 24.42, 25.56, 26.04, 26.57, 28.38, 29.37, 29.56, 29.62, 29.66, 29.68, 31.94, 32.48, 65.91, 71.17, 79.00, 80.51, 82.86, 109.87. HMRS m/z found 393.2976, calcd for $C_{22}H_{42}O_4Na$ m/z 393.2981.

References

1. (a) Boiteau, J.-G.; Van de Weghe, P.; Eustache, J. *Tetrahedron Lett.* **2001**, *42*, 239–242. (b) Van de Weghe, P.; Aoun, D.; Boiteau, J.-G.; Eustache, J. *Org. Lett.* **2002**, *4*, 4105–4108.
2. **A** would give rise to rare 2(*R*), 5(*S*) acetogenins (see Figure 1 for numbering). The corresponding 2(*R*), 5(*R*) isomer has been used as synthetic intermediate in the synthesis of corossolins: Yu, Q.; Yao, Z. J.; Chen, X. G.; Wu, Y. L. *J. Org. Chem.* **1999**, *64*, 2440–2445.
3. (a) Bravo, F.; Castillón, S. *Eur. J. Org. Chem.* **2001**, 507–516, and references therein. (b) Bew, S. P.; Barks, J.; Knight, D. W.; Middleton, R. J. *Tetrahedron Lett.* **2000**, *41*, 4447–4451, and references therein. For a recent review see: (c) Robin, S.; Rousseau, G. *Eur. J. Org. Chem.* **2002**, 3099–3114.
4. See for example: Evans, R. D.; Magee, J. W.; Schauble, J. H. *Synthesis* **1988**, 862–868.
5. Baldwin, J. E.; Cutting, J.; Dupont, W.; Kruse, L.; Silberman, L.; Thomas, R. C. *J. Chem. Soc., Chem. Commun.* **1976**, 736–738.
6. (a) Bedford, S. B.; Bell, K. E.; Fenton, G.; Hayes, C. J.; Knight, D. W.; Shaw, D. E. *Tetrahedron Lett.* **1992**, *33*, 6511–6514. (b) Galatsis, P.; Millan, S. D.; Nechala, P.; Ferguson, G. *J. Org. Chem.* **1994**, *59*, 6643–6651. (c) Jung, M. E.; Nichols, C. J. *Tetrahedron Lett.* **1996**, *37*, 7667–7670. (d) Galatsis, P.; Millan, S. D.; Ferguson, G. *J. Org. Chem.* **1997**, *62*, 5048–5056. (e) Fujita, K.-I.; Murata, K.; Iwaoka, M.; Tomoda, S. *Tetrahedron* **1997**, *53*, 2029–2048. (f) Andrey, O.; Ducry, L.; Landais, Y.; Planchenault, D.; Weber, V. *Tetrahedron* **1997**, *53*, 4339–4352. (g) Bedford, S. B.; Bell, K. E.; Bennet, F.; Hayes, C. J.; Knight, D. W.; Shaw, D. E. *J. Chem. Soc., Perkin Trans 1* **1999**, 2143–2153.
7. (a) Barks, J. M.; Knight, D. W.; Seaman, C. J.; Weingarten, G. G. *Tetrahedron Lett.* **1994**, *35*, 7259–7262. (b) In contrast, exclusive oxetane formation is observed for homoallylic alcohols in which a silicon atom is attached to the olefinic carbon atom distal from the hydroxyl group: Rofoo, M.; Roux, M.-C.; Rousseau, G. *Tetrahedron Lett.* **2001**, *42*, 2481–2484.
8. Temesvari-Major, E.; Gruber, L.; Toemoeskoezi, I.; Kovacs, G.; Cseh, Gy. *Tetrahedron Lett.* **1980**, *21*, 4035–4038.
9. For previous examples of tethered ring-closing metathesis using silalketals see: (a) Evans, P. A.; Murthy, V. S. *J. Org. Chem.* **1998**, *63*, 6768–6769. (b) Hoye, T. R.; Promo, M. A. *Tetrahedron Lett.* **1999**, *40*, 1429–1432. (c) Briot, A.; Bujard, M.; Gouverneur, V.; Nolan, S. P.; Mioskowski, C. *Org. Lett.* **2000**, *2*, 1517–1519. (d) Gierash, T. M.; Chytil, M.; Didiuk, M. T.; Park, J. Y.; Urban, J. J.; Nolan, S. P.; Verdine, G. L. *Org. Lett.* **2000**, *2*, 3999–4000. (e) Lobbel, M.; Köll, P. *Tetrahedron: Asymmetry* **2000**, *11*, 393–396. (f) Harrison, B. A.; Verdine, G. L. *Org. Lett.* **2001**, *3*, 2157–2159. (g) Harrison, B. A.; Gierash, T. M.; Neilan, C.; Pasternak, G. W.; Verdine, G. L. *J. Am. Chem. Soc* **2002**, *124*, 13352–13353.
10. For previous examples of tethered ring-closing metathesis using silylethers see: (a) Chang, S.; Grubbs, R. H. *Tetrahedron Lett.* **1997**, *38*, 4757–4760. (b) Meyer, C.; Cossy, J. *Tetrahedron Lett.* **1997**, *38*, 7861–7864. (c) Cassidy, J. H.; Marsden, S. P.; Stemp, G. *Synlett* **1997**, 1411–1413. (d) Ahmed, M.; Barrett, A. G. M.; Beall, J. C.; Braddock, D. C.; Flack, K.; Gibson, V. C.; Procopiou, P. A.; Salter, M. M. *Tetrahedron* **1999**, *55*, 3219–3232. (e) Hoshi, T.; Yasuda, H.; Sanji, T.; Sakurai, H. *Bull. Chem. Soc. Jpn* **1999**, *72*, 821–827. (f) Taylor, R. E.; Engelhardt, F. C.; Yuan, H. *Org. Lett.* **1999**, *1*, 1257–1260. (g) Denmark, S. E.; Yang, S.-M. *Org. Lett.* **2001**, *3*, 1749–1752. (h) Yao, Q. *Org. Lett.* **2001**, *3*, 2069–2072. (i) Denmark, S. E.; Yang, S.-M. *J. Am. Chem. Soc* **2002**, *124*, 15196–15197.
11. Yadav, J. S.; Valli, M. H.; Prasad, A. R. *Tetrahedron* **1998**, *54*, 7551–7562.
12. Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109–4117.
13. This behaviour is not surprising and has already been observed for difficult RCMs. See for example: (a) Joe, D.; Overman, L. E. *Tetrahedron Lett.* **1997**, *38*, 8635–8638. (b) Nevalainen, M.; Koskinen, A. M. P. *Angew. Chem. Int. Ed.* **2001**, *40*, 4060–4062.
14. In *cis*-2,4-disubstituted oxetanes, there is a strong NOE effect

between H2 and H4 see: Aftab, T.; Carter, C.; Chrstlieb, M.; Hart, J.; Nelson, A. *J. Chem. Soc., Perkin Trans 1* **2000**, 711–722. To further ascertain the presence of an oxetane (and not of an oxirane), **7** was treated with isopropyldimethylsilyl chloride which led to selective silylation of the allylic alcohol (determined by COSY NMR). *N*-PSP-induced cyclization afforded two compounds: **9** and the corresponding silyl ether (which was identical to the compound obtained by silylation of **9**).

15. Most of mono-THF-acetogenins shared as a common moiety a 2,5-disubsituted THF flanked by two a-hydroxyls. The relative position of these structural elements defines a variety of subfamilies featuring *threo-trans-threo*, *threo-cis-threo*, *erythro-trans-threo*, *threo-trans-erythro*, etc. α,α-bis-hydroxy-THF system. For reviews on acetogenins, see: (a) Alali, F. Q.; Liu, X.-X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62*, 504–540. (b) Figadere, B. *Acc. Chem. Res.* **1995**, *28*, 359–365.
16. For a recent approach to the various types of THF cores in acetogenins, see: Maezaki, N.; Kojima, N.; Asai, M.; Tominaga, H.; Tanaka, T. *Org. Lett.* **2002**, *4*, 2977–2980.
17. Nugent, T. C.; Hudlicky, T. J. *Org. Chem.* **1998**, *63*, 510–520.
18. Schwab, J. M.; Lin, D. C. T. *J. Am. Chem. Soc* **1985**, *107*, 6046–6052.
19. Oestreich, M.; Frohlich, R.; Hoppe, D. *J. Org. Chem.* **1999**, *64*, 8616–8626.
20. Vargese, C.; Abushanab, E. *J. Org. Chem.* **1990**, *55*, 4400–4403.
21. An efficient synthesis of both (*E*) and (*Z*)-2-ene-1,5-diols has recently been reported: Flamme, E. M.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 13644–13645.
22. Tetrahydrofuran **29** has NMR data identical to those reported in the literature,[2] except for optical rotation ($[\alpha]_D^{20}=+3.3$ (*c* 0.9, $CHCl_3$). In order to make sure that **29** had the correct structure, it was converted to the corresponding MOM ether which had a value similar ($[\alpha]_D^{20}=+29.0$ (*c* 0.3, $CHCl_3$) to that reported in Ref. 2: $[\alpha]_D^{20}=+30.1$ (*c* 0.17, $CHCl_3$)).