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1-Iodo-1-selenoalkenes as versatile alkene 1,1-dianion equivalents. Novel connective approach towards the tetrahydropyran subunit of polycavernoside A

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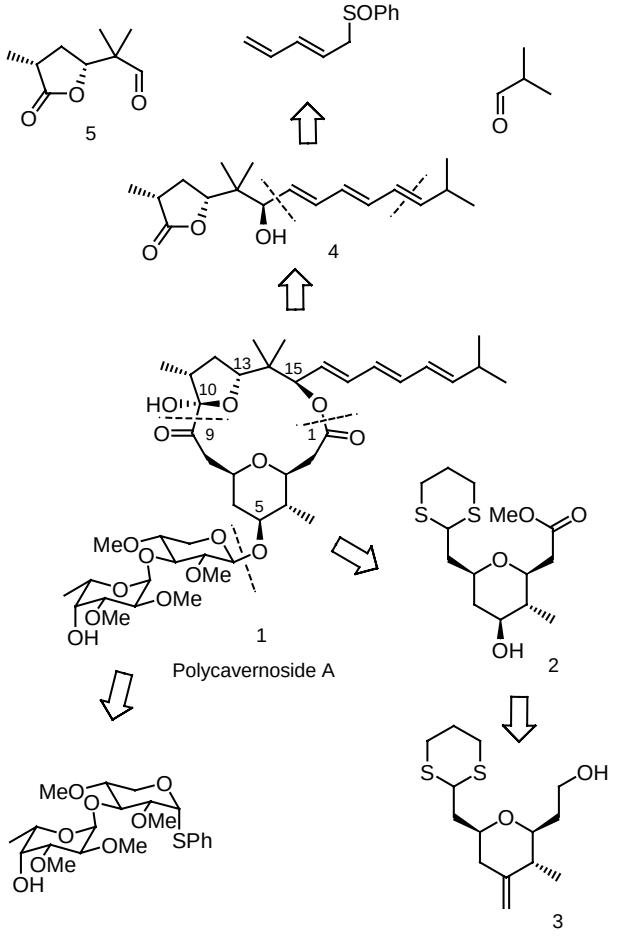
Abstract—*syn*-Hydroalumination of 2,4,6-triisopropylphenylselanyl-1-alkynes with DIBAL-H followed by Al/I exchange with I_2 afforded exclusively (*E*)-1-iodo-1-selenoalkenes in good yields. 1-Iodo-1-selenopropene **10** proved to be a convenient 1,1 dianion equivalent, leading to the stereodivergent synthesis of allylsilanes (*Z*)-**6** and (*E*)-**6**. Adduct **3**, an intermediate in the synthesis of the tetrahydropyran subunit of polycavernoside A, was efficiently synthesised from allylsilane (*Z*)-**6** and aldehyde **7** via an intramolecular Sakurai cyclisation.

1. Introduction

In April 1991, the ingestion of the red alga *gracilaria tsudae* caused a severe human intoxication in the island of Guam. Thirteen people were affected; three of them died.[1] This alga, documented only from the west coast of Guam, is a local gastronomic speciality that develops seasonal toxic properties for still unknown reasons. In 1993, Yasumoto and co-workers reported the isolation, from the causative alga, of polycavernosides A and B, which were identified as the responsible toxins for fatal poisoning.[2] Three other analogs (A2, A3, B2) were reported by Yasumoto in 1995.[3] Polycavernoside A **1** is the main member of a growing family of polycavernoside congeners. Since the elucidation of its planar structure, **1** has attracted the attention of several synthetic groups, undoubtedly due to its challenging architectural features and its biological activities. Polycavernoside A possesses an unusual 13-membered keto-lactone ring and an interesting five-membered hemiketal function connected to the C_9 ketone group. Moreover, a labile triene moiety is linked to C_{15} (Scheme 1). The first total synthesis of **1** was reported by Murai and co-workers in 1998. They established at the same time its absolute stereochemistry.[4] Two other total synthesis have been reported so far.[5]

Our retrosynthetic analysis of **1** is depicted in Scheme 1. Disconnection of the C_1–O and C_9–C_{10} bonds leads to three fragments of approximately the same molecular complexity.



Scheme 1. Retrosynthetic analysis of polycavernoside A.

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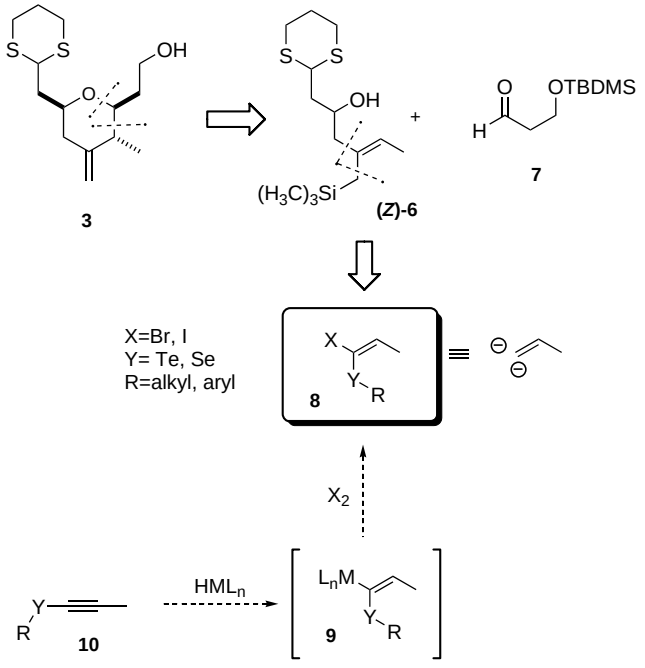
The northern subunit consists of the five-membered lactone **4**, bearing the trienyl side chain, and the southern moiety **2** embodies a tetrasubstituted tetrahydropyran core. The disaccharide residue has already been efficiently prepared by Murai et al.[6] Our laboratory has previously disclosed an expedient synthesis of **4** from the readily available γ-butyrolactone subunit **5**.[7] Recently, we have reported our preliminary results on a stereocontrolled approach to the tetrahydropyran subunit **2**, via an intramolecular Sakurai cyclisation (IMSC).[8] In this article, we wish to present a full account of our investigations directed towards a connective and efficient synthesis of the tetrahydropyran subunit of polycavernoside A, using as a key intermediate, a novel alkene 1,1-dianion equivalent.

According to our strategy, the southern subunit **2** could be derived from the tetrahydropyran **3** by a few functional group transformations. Thus, the stereocontrolled preparation of **3** became our prime objective. Our antithetic analysis of **3** is shown in Scheme 2. Application of the IMSC retron to **3** leads to the generation of two simple fragments: the allylsilane **6** and the β-hydroxy aldehyde **7**. The condensation of these two fragments should afford stereoselectively the requisite *exo*-methylene tetrahydropyran **3**. The intramolecular Sakurai cyclisation is believed to proceed via a two-step mechanism. The coupling between an allylsilane such as **6** and an aldehyde such as **7**, in the presence of a Lewis acid, generates initially an oxocarbenium cation intermediate, which undergoes subsequent ring closure by intramolecular nucleophilic addition of the pendant allylsilane function, to give a tetrahydropyran ring possessing an exocyclic C–C double bond. The relative configuration of the three stereogenic centres in the final product is governed by the preference of the substituents to occupy pseudoequatorial positions in the chair-like transition-state during the ring closure step.[9] An important parameter in the control of the relative orientation of the substituents in the final adduct is the geometry of the C–C double bond of the allylsilane. According to this model, the (*Z*)-allylsilane **6** is required to obtain the tetrahydropyran possessing the correct stereochemistry present in polycavernoside A.



Scheme 2. Strategy for the synthesis of tetrahydropyran **3**.

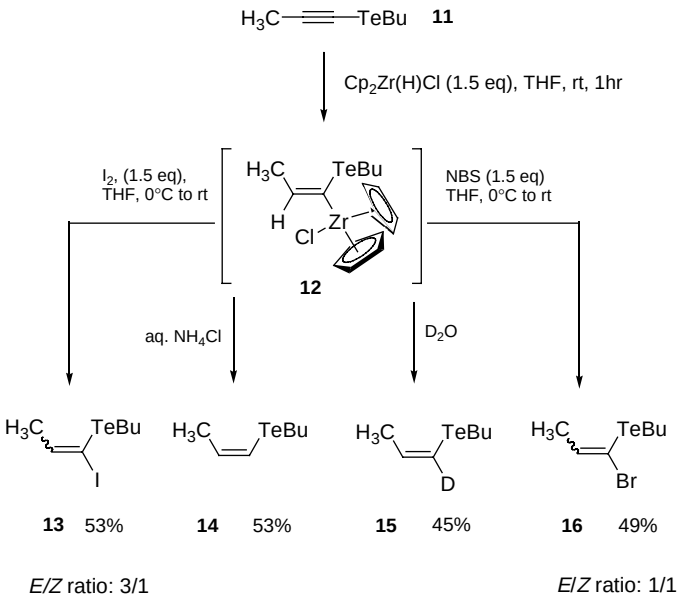
Despite the number of procedures described in the literature for the synthesis of alkenes, there are few, simple and general methodologies that lead to the preparation of trisubstituted allylsilanes with good stereocontrol of the olefin geometry.[10] In order to explore new strategies in this field, we decided to prepare allylsilane **6** from a synthetic equivalent of an alkene 1,1-dianion. Several reports describe the synthesis of alkene 1,1-bismetallic species.[11] Unfortunately, most of these reagents were found to suffer from serious shortcomings, such as lack of reactivity, difficulty in handling and, often, tedious preparation. Therefore, it was deemed interesting to investigate the reactivity of 1-halo-1-chalcogeno-alkenes **8** as equivalents of alkene 1,1-dianions. Compounds such as **8** can be handled without special precautions and can be transformed easily into a variety of di- and tri-substituted olefins via a sequential functionalisation of both hetereoatom positions. Interestingly, by inverting the sequence, the same precursor **8** should afford the opposite *E*/*Z* isomer of **6**.

The stereoselective synthesis of 1-halo-1-chalcogeno-alkenes **8** was envisaged to be accomplished by the hydrometallation of the C–C triple bond of 1-alkynyl chalcogenides **10**, followed by metal/halogen exchange of the in situ generated 1-metallo-1-chalcogeno alkene species **9**. Hydrometallation of hetero-substituted alkynes is usually a highly regio- and stereoselective reaction and, in most cases, the addition can be controlled to take place in a *syn* manner. The C–C triple bond of 1-alkynyl chalcogenides is polarized in such a way that the metal residue is typically positioned on the carbon bearing the chalcogen substituent. The most common hydrometallating agents are boron, aluminium and zirconium mono hydrides. Among these, $Cp_2Zr(H)Cl$ is the most tolerant with regard to other functional groups.

2. Results and discussion

2.1. Synthesis of 1-halogeno-1-chalcogeno-alkenes

2.1.1. 1-Telluro-1-halogeno propenes. Attracted by the broad range of interesting potential transformations that organotellurides can undergo,[12] we began our investigations by the preparation of 1-halo-1-telluro propenes, according to the procedure described by Dabdoud et al.[13] Hydrozirconation of 1-butyltellanyl-propyne **11** with $Cp_2Zr(H)Cl$ generated in situ the 1-telluro-1-zircono alkene species **12**,[14,15] which was subsequently trapped with different electrophiles giving the corresponding 1-alkenyl tellurides **13**–**16** (Scheme 3). In our hands, hydrozirconation of **11** afforded the 1-alkenyl tellurides in only moderate yields. Besides the desired products, and in all cases, a considerable amount of dibutyl ditelluride was formed. It has been reported that 1-butyltellanyl alkynes undergo easy tellurium–spC bond cleavage by treatment with hydrides, such as DIBAL-H, $LiAlH_4$ or $NaBH_4$, affording the tellurium free alkyne and dibutyl ditelluride. It is believed that hydride addition on the tellurium moiety generates

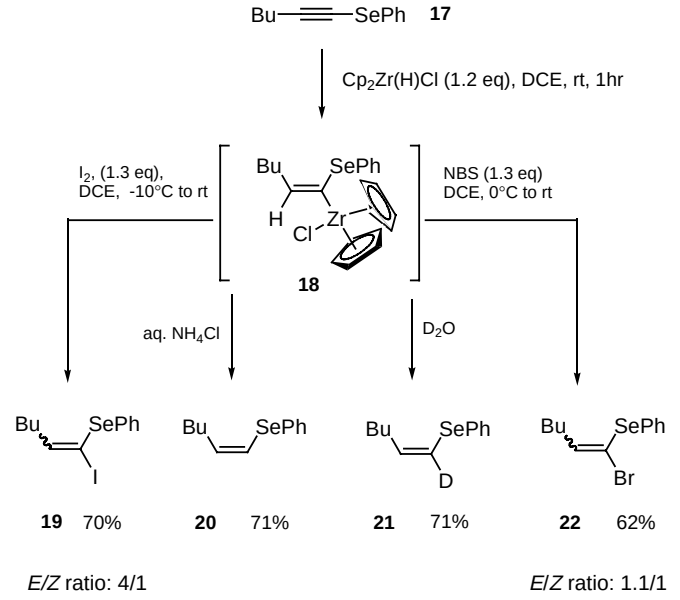


Scheme 3. Hydrozirconation–halogenation of telluroalkyne **11**.

butyltellurol and an acetylide anion. Butyltellurol is deprotonated by the hydride to give butyltellurate, which rapidly oxidises to dibutyl ditelluride in the presence of oxygen, during the work-up.[15] Our results indicate that the hydrozirconation of **11** leads to the competitive formation of dibutyl ditelluride via an analogous pathway.

In our case, the optimised conditions for the hydrozirconation of **11** were found to require 1.5 equiv of freshly prepared $Cp_2Zr(H)Cl$. However, other groups reported the use of 1.1[13b] and 2.0[13a] equiv as the optimal number of $Cp_2Zr(H)Cl$ equivalents. The isolated yields of 1-alkenyl tellurides also differ significantly from one group to another, indicating that the hydrozirconation of 1-alkynyl tellurides is highly dependent upon the quality and the mode of preparation of $Cp_2Zr(H)Cl$.[16] These results are thus difficult to reproduce and it was decided to investigate the hydrozirconation of other, more ameanable precursors. Moreover, 1-iodo-1-butyltellanyl-propene **13** and 1-bromo-1-butyltellanyl propene **16** were always obtained as an inseparable mixture of *E*/*Z* isomers.

2.1.2. 1-Seleno-1-halogeno alkenes. Searching for substrates less prone to undergo heteroatom-spC cleavage during the hydrozirconation step, and aware that the C–Se bond is stronger than the C–Te bond, we elected to study the hydrometallation of the corresponding alkynyl selenides. As a model compound, hex-1-ynylselanyl-benzene **17** was hydrozirconated with $Cp_2Zr(H)Cl$ and the in situ generated 1-seleno-1-zircono-alkene intermediate **18** was quenched with various electrophiles (Scheme 4).[17,18] As expected, the corresponding 1-alkenyl selenides **19**–**22** were obtained in better yields (around 70%) as compared to the 1-alkenyl tellurides. However, diphenyl diselenide was formed as

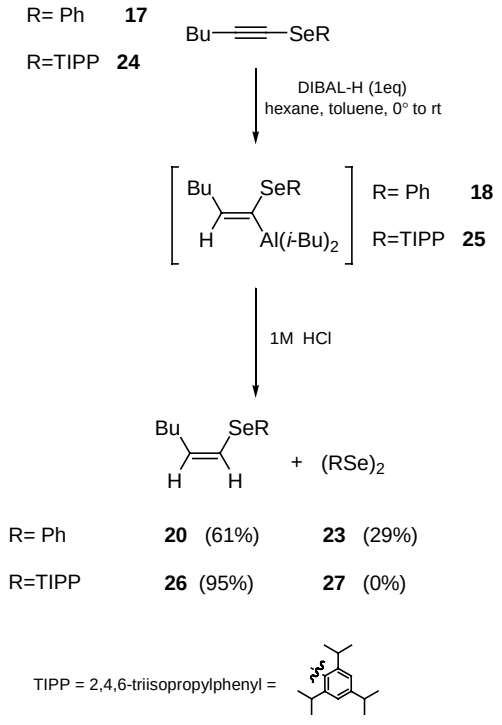


Scheme 4. Hydrozirconation–halogenation of selenoalkyne **17**.

the main by-product, indicating that the competitive Se–spC cleavage could not be completely prevented. Trapping **18** with I_2 or NBS, at low temperature, provided an inseparable mixture of (*E*)- and (*Z*)-isomers of the corresponding 1-halo-1-selenoalkenes **19** and **22**. Though the iodoalkene **19** was obtained in a fairly good yield, and a reasonable *E*/*Z* ratio of 4:1, such a selectivity is clearly not adequate for synthetic purposes.

In order for our methodology to embrace broad synthetic interest, it proved imperative to overcome three main drawbacks; (i) to prevent completely the competitive Se–spC bond cleavage; (ii) to avoid the isomerisation during the metal/halogen exchange and (iii) if possible, to replace the expensive and sensitive $Cp_2Zr(H)Cl$ by another, cheaper and easier to handle, hydrometallating agent.

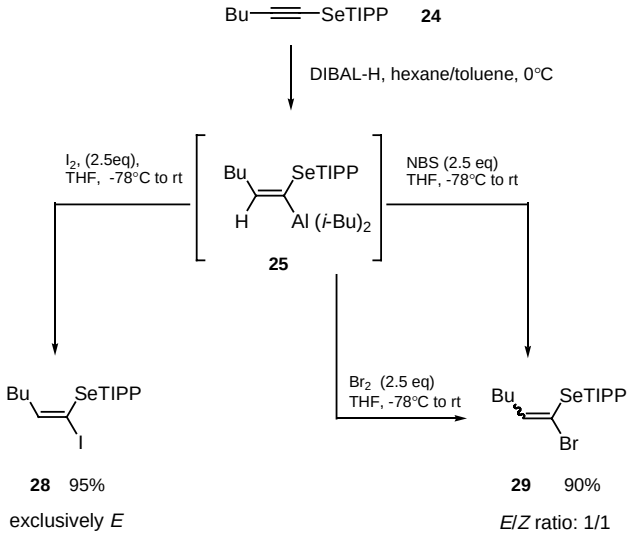
Hydroalumination of hex-1-ynylselanyl-benzene **17** with DIBAL-H,[19] followed by quenching with dilute HCl, provided a mixture of 1-hexenyl selenide **20** (61% yield) and diphenyl diselenide **23** (39% yield, Scheme 5). Although DIBAL-H produced more diphenyl diselenide than $Cp_2Zr(H)Cl$, it was envisioned that the competitive spC–Se bond cleavage could probably be suppressed by selectively hindering the selenium atom, thereby impeding the coordination between the selenium substituent and the aluminium reagent and hence, thwarting the delivery of hydride on selenium. In order to verify our hypothesis, 1-(2,4,6)-triisopropylphenyl-selenyl-hex-1-yne **24**, bearing the voluminous 2,4,6-triisopropylphenyl (TIPP) substituent instead of the phenyl group, was prepared.[20] When **24** was treated with DIBAL-H, followed by quenching of the intermediate vinyl alane **25** with dilute HCl (under the same conditions than **18**), we were delighted to observe the exclusive formation of the (*Z*)-alkenyl selenide **26**, which



Scheme 5. Effect of the TIPP group on the hydroalumination of selenoalkynes.

was isolated in 95% yield. Diselenide **27** could not be detected in the crude reaction mixture (Scheme 5). It thus transpires that the steric hindrance of the TIPP group dramatically influences the selectivity of the hydroalumination reaction by suppressing the competitive C–Se bond cleavage. The formation of the diselenide by-product **27** is prevented and the hydrometallation of the C–C triple bond becomes essentially quantitative.

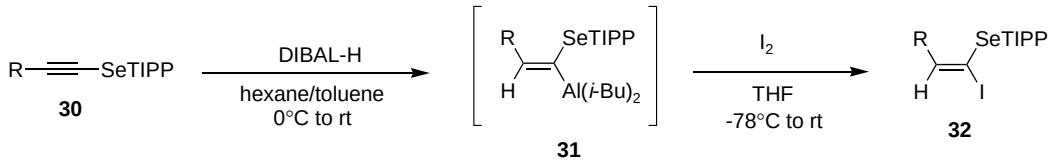
Having discovered that the use of the TIPP group enabled the efficient hydroalumination of **24**, we next turned our attention to the metal/halogen exchange reaction. To our delight, trapping of **25** with I_2, at low temperature, afforded the corresponding 1-iodo-1-selenoalkene **28** in 95% yield. Even more gratifyingly, only the (*E*)-isomer was isolated, indicating that the replacement of Al by I took place with retention of configuration of the C–C double bond (Scheme 6). In sharp contrast, bromination of **25**, either with Br_2 or NBS, afforded a 1/1 mixture of (*E*)- and (*Z*)-1-bromo-1-selenoalkenes **29**. Although the yields were good, the replacement of Al by Br occurred with complete scrambling of the configuration of the C–C double bond, even under carefully controlled reaction conditions. These observations suggest that bromination and iodination of **25** might follow different mechanistic pathways.

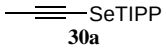
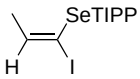
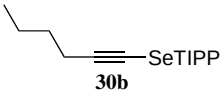
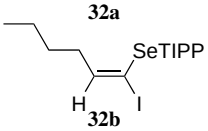
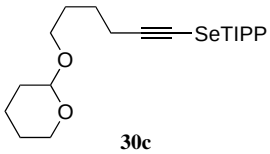
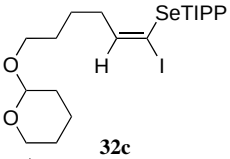
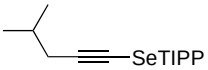
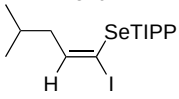
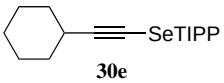
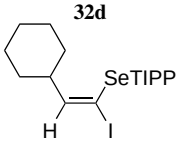
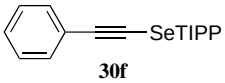


Scheme 6. Hydroalumination–halogenation of selenoalkyne **24**.

In order to verify that this sequence could constitute a new method for the synthesis of (*E*)-1-iodo-1-selenoalkenes, this procedure was applied to other 1-alkynyl selenides bearing the TIPP group. The results of our investigations are shown in Table 1. In all cases, the corresponding (*E*)-1-iodo-1-selenoalkenes **32** were obtained in good to excellent yields and as a single isomer. Only the phenyl acetylene derivative **30f** refused to react (entry 6). In this case, the addition of DIBAL-H to the triple bond did not occur, even when the reaction was attempted in hexane at reflux. This lack of reactivity could be due to prohibitive steric repulsions that gradually build up between the phenyl and the SeTIPP groups during the addition of the aluminium hydride.

Table 1. Synthesis of (*E*)-1-iodo-1-selenoalkenes via hydroalumination–iodination



Entry	Substrate	Product	Yield (%)[a]
1	 **30a**	 **32a**	92
2	 **30b**	 **32b**	95
3	 **30c**	 **32c**	96
4	 **30d**	 **32d**	82
5	 **30e**	 **32e**	91
6	 **30f**	—	0

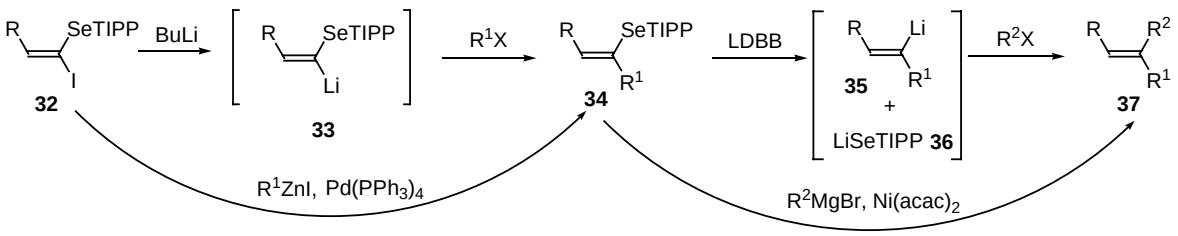
[a] Isolated yield after purification by column chromatography.

The Al/I exchange requires a careful control of the reaction conditions in order for the iodination to be complete. If the reaction mixture is stirred longer than 1 h at room temperature, some degradation occur, accompanied by the appearance of the (*Z*)-isomer.

It did not escape us that the 1-alumino-1-seleno-alkene intermediate **25** (Scheme 6) could be an interesting precursor for the stereodefined synthesis of alkenes, since it is readily accessible from **24** via a simple and selective hydroalumination. Unfortunately, **25** proved to be rather unreactive towards various carbon electrophiles.

2.1.3. Functionalisation of 1-iodo-1-selenoalkenes. With an efficient access to (*E*)-1-iodo-1-selenoalkenes in hand, we turned our attention to the sequential functionalisation of both heteroatom positions (Scheme 7). Initially, the more labile C–I bond was selectively replaced by a C–C bond, either via the intermediacy of the 1-seleno-1-lithio-alkene species **33** or via a palladium-catalysed cross-coupling with organozinc derivatives. Subsequently, the selenium substituent was replaced by a second C–C bond, either via the generation of the disubstituted 1-alkenyl lithium species **35** or via nickel-catalysed cross-coupling with Grignard reagents. No loss of the C–C double bond integrity was observed in this overall process, indicating that 1-iodo-1-selenoalkenes **32** are convenient 1,1-dianion equivalents for the stereoselective synthesis of trisubstituted alkenes.

2.1.4. Functionalisation of the iodo position. 1-Iodo-1-selenoalkene **32a** underwent smooth I/Li exchange when reacted with *n*-BuLi or *t*-BuLi, to give the 1-seleno-1-alkenyllithium intermediate **33a**.[21] Subsequent treatment with various electrophiles, including acylating agents,



Scheme 7. Functionalisation of 1-iodo-1-selenoalkenes.

aldehydes, epoxides or alkyl halides, afforded the corresponding functionalised 1-alkenyl selenides **34** in good yields (Table 2). The I/Li exchange was carried out with 1 equiv of *n*-BuLi, either in THF at −78 °C or in hexane at room temperature. The choice of the best conditions depends strongly upon the electrophile. In the case of valeraldehyde (entry 7), better yields were obtained when the I/Li exchange was performed in hexane, at room temperature.[22] On the contrary, benzoyl chloride (entry 4) gave better results when the metallation was performed in THF, at −78 °C. In order to prevent the formation of butylated by-products, when alkyl halides (entries 10 and 11) were used as electrophiles, the exchange was performed with 2 equiv of *t*-BuLi in THF, at −78 °C. In the case of the allysilane **34k** (entry 11), an interesting improvement was observed when the alkenyl lithium intermediate **33a** was generated by reverse addition, that is, by adding 1-iodo-1-selenoalkene **32a** to a solution of *t*-BuLi in THF, cooled at −78 °C. Subsequent treatment of **33a** with iodomethyltrimethylsilane afforded **34k** in 78% yield. Normal addition (*t*-BuLi added to a THF solution of **33a** at −78 °C) gave **34k** in only 41% yield.

Treatment of **32a** with 2 equiv of isopropylmagnesium chloride, in THF, at room temperature led to the I/Mg exchange.[23] However, the resulting 1-seleno-1-alkenyl magnesium chloride intermediate did not react with carbon electrophiles. This Grignard reagent only underwent protonolysis and deuterolysis.

The palladium-catalysed cross coupling of 1-iodo-1-selenoalkene **32b** with organozinc species (Scheme 8) enabled the direct formation of a C–C bond from the C–I bond. However, only moderate yields were obtained so far.

2.1.5. Functionalisation of the seleno position. The vinylic C–Se bond of several functionalised 1-alkenyl selenides was reductively cleaved in the presence of 2 equiv of LDBB (lithium 4,4′-di-*tert*-butylbiphenyl),[24] generating in situ lithium 2,4,6-triisopropylphenylselenoate **36** and the corresponding 1-alkenyl lithium **35** (Scheme 7).[25] Trapping of the 1-alkenyl lithium derivatives with various electrophiles, at low temperature, afforded the expected trisubstituted alkenes **37–42** in good yields and with complete retention of the C–C double bond geometry (Table 3). The selenoate **36**, generated as a by-product, proved to be a better nucleophile than the 1-alkenyl lithium species. In the reactions of **35** with alkylating agents, the selective quenching of selenoate **36** with 1 equiv of MeI (to give 1 equiv of 2,4,6-triisopropylphenyl methyl selenide), was routinely performed prior to the addition of the electrophile.

It has been described that the vinyl C–Se bond of 1-alkenyl selenides undergoes cross-coupling with organomagnesium derivatives in the presence of nickel complexes as catalyst.[26] This coupling led to a straightforward construction of tri- and tetrasubstituted allylsilanes.[27] In our case, probably due to the steric hindrance of the TIPPSe group, only methylmagnesium bromide could be coupled to **34** (Table 3, entries 5 and 6) using $Ni(acac)_2$ as catalyst. When nickel complexes bearing phosphino ligands were employed, only the starting material was recovered. This observation indicates that only ligandless Ni(0) species are able to insert into the sterically hindered C–Se bond. More encumbered organomagnesium derivatives, such as phenylmagnesium bromide or (trimethylsilylmethyl)magnesium chloride, in the presence of $Ni(acac)_2$, did not afford the expected products.

2.1.6. Synthesis of the (*Z*)- and (*E*)-allylsilanes 6. As previously discussed, the construction of the tetrahydropyran core of polycavernoside A was envisioned from the (*Z*)-allylsilane **6** and the aldehyde **7**, via an IMSC condensation. The (*Z*)-allylsilane **6** was readily assembled from the (*E*)-1-iodo-propenyl selenide **32a** by sequential replacement of the heteroatom substituents (Scheme 9).

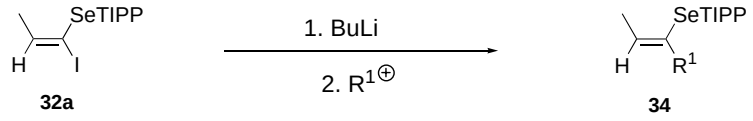
Opening of the dithianylmethyl oxirane **43**, by the vinylic anion derived from **32a** by I/Li exchange with *n*-BuLi, in the presence of $BF_3{\cdot}OEt_2$, resulted in the formation of the homoallylic alcohol **34i** in 50% yield based upon **32a** (100% based upon oxirane **43**). In the absence of the Lewis acid, this vinyl lithium species proved to be rather unreactive towards oxirane **43**. The moderate yield in the presence of $BF_3{\cdot}OEt_2$ is due to the concomitant formation of an unreactive vinyl fluoroborate intermediate,[28] which consumes 50% of the vinyl lithium reagent. By employing two equivalents of vinylselenide **32a**, a quantitative yield of adduct **34i** was obtained.

After treatment of **34i** with methylmagnesium bromide, in order to deprotonate the homoallylic hydroxy function, the alkenyl C–Se bond was reductively cleaved with LDBB, generating the carbanion **45** and lithium selenoate **36** (Scheme 7). Whilst it is reasonable to assume that the lithium salt **45** is initially formed under these reductive conditions, it is quite plausible that metal exchange might take place under the reaction conditions, leading either to **46** or an equilibrating mixture of **45** and **46**, with the latter reagent being the active species in the subsequent coupling step. In this regard, using *n*-BuLi to perform the deprotonation of alcohol **34i**, followed by LDBB treatment, led to significant erosion in the yields of **44** (Scheme 10).

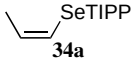
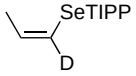
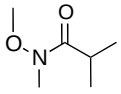
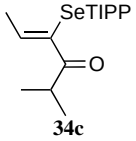
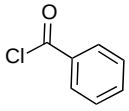
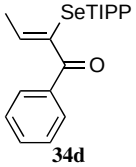
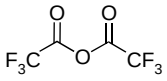
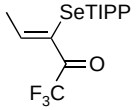
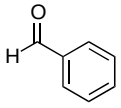
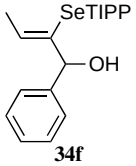
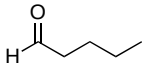
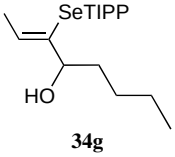
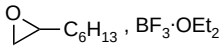
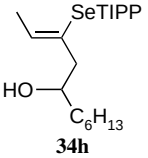
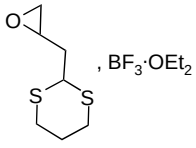
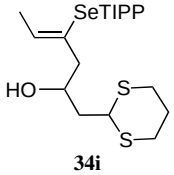
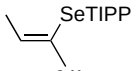
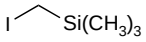
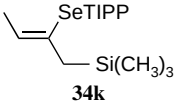
Attempts to react the organometallic derivatives **45/46** with various alkylating agents, in order to introduce directly the CH_2TMS moiety failed, probably owing to the lack of reactivity of these silyl-containing electrophiles. Quenching of **45/46** with I_2 led to the vinyl iodide **44** in excellent yield. It is noteworthy that 1 equiv of MeI has to be added to the lithiated species **45/46**, before the iodine quench, in order to obtain good yields of **44**. Cross-coupling of **44** with trimethylsilylmethyl magnesium chloride, catalysed by $Pd(PPh_3)_4$, ultimately generated the requisite (*Z*)-allylsilane **6** in 55% overall yield from **34i** (Scheme 6). The (*Z*)-configuration of the C–C double bond was established by NOE experiments and subsequently confirmed by the independent synthesis of the (*E*)-isomer, indicating that the transformation of **32a** to (*Z*)-**6** took place with retention of configuration.

To demonstrate the versatility of our methodology, the opposite (*E*)-allylsilane **6** was synthesised from the same precursor **32a** by simply inverting the heteroatom exchange/alkylation sequence. Thus, vinyl selenide **34k** was obtained in 78% yield by alkylation of the vinyl anion, derived from

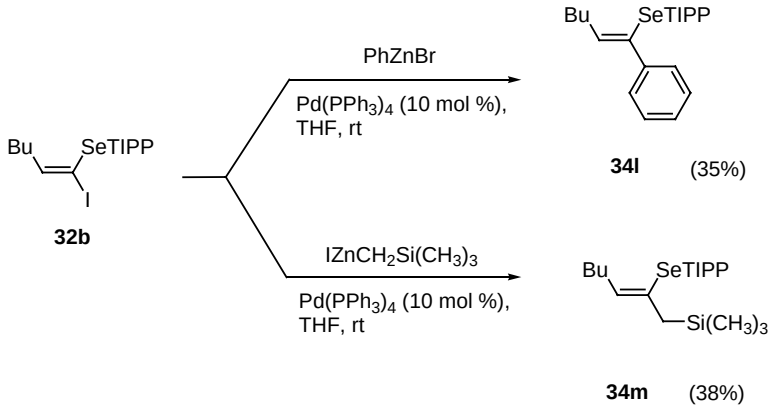
Table 2. Stereocontrolled iodine replacement in **32a**



32a **34**

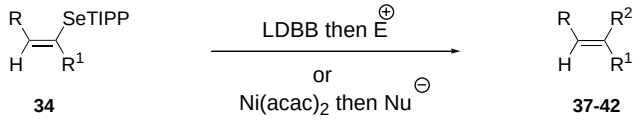
Entry	Conditions	Electrophile	Product	Yield (%)[a]
1	*n*-BuLi (1 equiv), THF, −78 °C	H_2O	 **34a**	91
2	*n*-BuLi (1 equiv), hexane, rt	D_2O	 **34b**	92
3	*n*-BuLi (1 equiv), THF, −78 °C		 **34c**	67
4	*n*-BuLi (1 equiv), THF, −78 °C		 **34d**	72
5	*n*-BuLi (1 equiv), THF, −78 °C		 **34e**	78
6	*t*-BuLi (2 equiv), THF, −78 °C		 **34f**	82
7	*n*-BuLi (1 equiv), hexane, rt		 **34g**	65
8	*n*-BuLi (1 equiv), THF, −78 °C		 **34h**	50
9	*n*-BuLi (1 equiv), THF, −78 °C		 **34i**	50
10	*t*-BuLi (2 equiv), THF, −78 °C	MeI	 **34j**	93
11	*t*-BuLi (2 equiv), THF, −78 °C, reverse addition		 **34k**	78

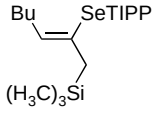
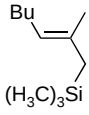
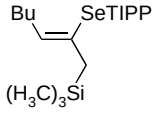
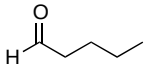
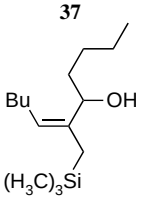
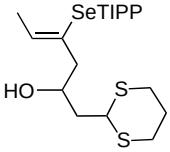
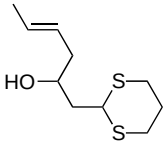
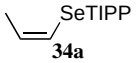
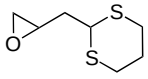
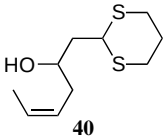
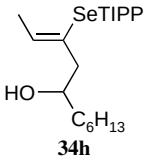
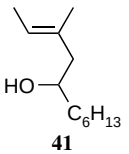
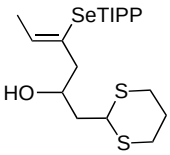
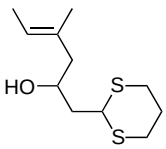
[a] Isolated yield after purification by column chromatography.



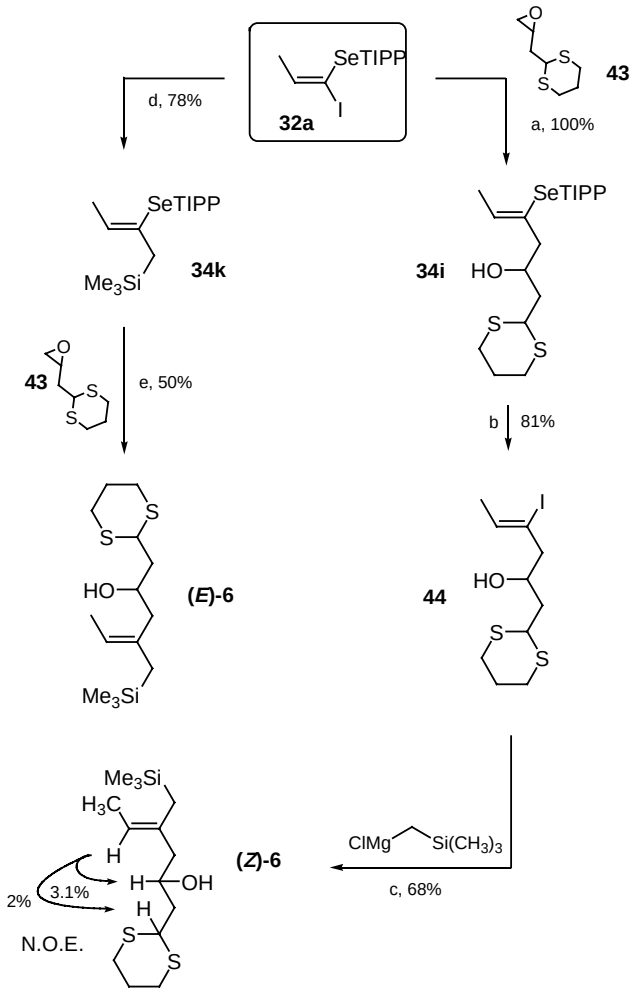
Scheme 8. Negishi coupling of **32b**.

Table 3. Stereocontrolled selenium substitution in **34**

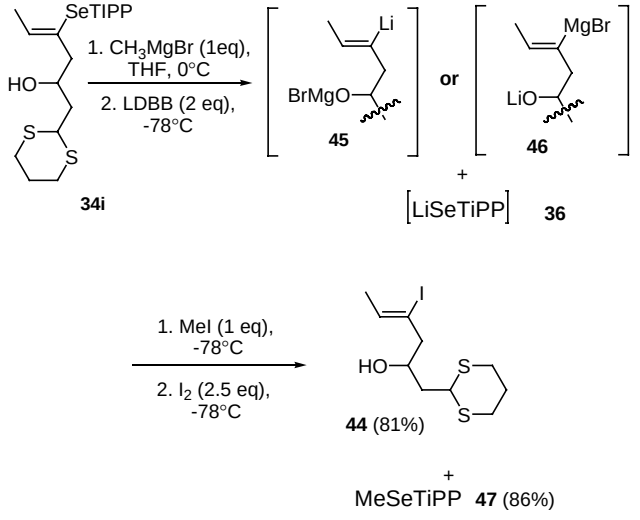


Entry	Sustrate	Conditions	Electrophile/ nucleophile	Product	Yield (%)[a]
1	 **34m**	LDBB (2 equiv), THF, −78 °C	MeI	 **37**	67
2	 **34m**	LDBB (2 equiv), THF, −78 °C		 **38**	62
3	 **34i**	(1) *n*-BuLi (1 equiv), THF, −78 °C (2) LDBB (2 equiv)	H_2O	 **39**	92
4	 **34a**	LDBB (2 equiv), THF, −78 °C	 $BF_3 \cdot OEt_2$	 **40**	85
5	 **34h**	$Ni(acac)_2$ (1 mol%), THF, room temperature	MeMgBr	 **41**	60
6	 **34i**	$Ni(acac)_2$ (1 mol%), THF, room temperature	MeMgBr	 **42**	64

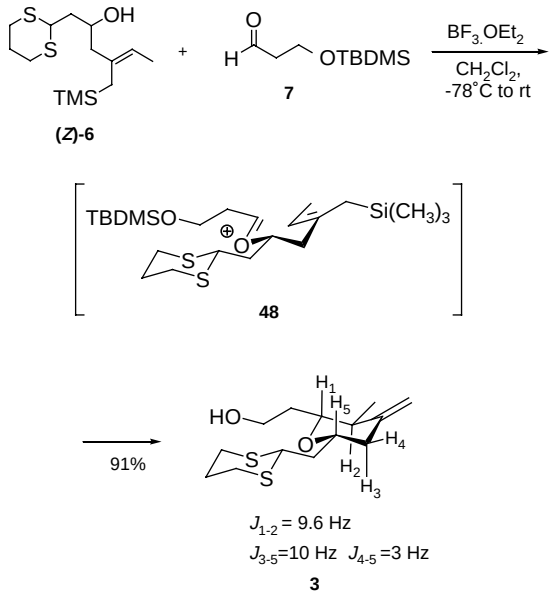
[a] Isolated yield after purification by column chromatography.



Scheme 9. Preparation of (*Z*)- and (*E*)-allysilanes **6**. Conditions: (a) *n*-BuLi, THF, −78 °C, 30 min, $BF_3\cdot OEt_2$, then (±)-**43**, THF, −78 °C, 1 h; (b) CH_3MgBr, THF, 0 °C, 15 min, LDBB (2 equiv), −78 °C, 30 min, MeI, −78 °C, 15 min, then I_2, −78 °C, 1 h; (c) $ClMgCH_2Si(CH_3)_3$, $Pd(PPh_3)_4$, THF, rt, 9 h; (d) *t*-BuLi (2 equiv), THF, −78 °C, 10 min, then iodomethyltrimethylsilane, THF, −78 °C to rt; (e) LDBB (2 equiv), THF, −78 °C, 30 min, MeI, −78 °C, 15 min, $BF_3\cdot OEt_2$ then (±)-**43**, THF, −78 °C, 1 h.



Scheme 10. Selenium replacement in **34i**.



Scheme 11. The IMSC condensation.

32a by I/Li exchange with *t*-BuLi, with iodomethyltrimethylsilane. Reductive lithiation of **34k** with LDBB generated in situ the corresponding 1-alkenyl lithium species, which opened oxirane **43** in the presence of $BF_3\cdot OEt_2$, to give the (*E*)-allylsilane **6** in 39% overall yield from **32a**.

2.1.7. Intramolecular Sakurai cyclisation. With a ready supply of allylsilane (*Z*)-**6** in hand, we next turned our attention to the crucial intramolecular Sakurai cyclisation. We were delighted to observe that the tetrahydropyran **3** could be readily obtained, in a 91% yield, when (*Z*)-**6** and aldehyde **7** were treated with 1 equiv of $BF_3\cdot OEt_2$, at low temperature. Interestingly, it was found that smooth deprotection of the TBDMS group occurred concomitantly, when the reaction mixture was allowed to warm up to room temperature, affording in a single operation the free alcohol **3**. The relative stereochemistry of **3** was unambiguously established by careful analysis of its ^1H NMR spectrum. The coupling constant values of 9.6 and 10 Hz for the H^1–H^2 and H^5–H^3 hydrogen pairs clearly indicate that the three substituents occupy equatorial positions on the tetrahydropyran ring system (Scheme 11).

The relative stereochemistry of adduct **3** can be easily rationalised by examining the transition state invoked in the final cyclisation of the allylsilane residue onto the oxocarbenium cation **48**. In order to minimise steric interactions, the substituents occupy pseudoequatorial positions. The geometry of the allylsilane double bond controls the C_2 configuration.

3. Conclusions

In summary, we have shown that racemic tetrahydropyran **3** could be efficiently synthesised from allylsilane (*Z*)-**6** and aldehyde **7**, using the IMSC condensation as a key step. By the judicious control of the allylsilane C–C double bond, the relative stereochemistry of three stereogenic centres could be

established in a single operation. We have also developed a simple and efficient procedure for the stereocontrolled preparation of a range of 1-iodo-1-selenoalkenes and demonstrated that they are useful precursors for the synthesis of stereodefined di- and tri-substituted alkenes, including the important allylsilane **6**. These interesting vinylselenides can be considered as alkene-1,1-dianion equivalents.

4. Experimental

4.1. Generalities

Unless otherwise stated all the reactions were carried out using anhydrous conditions and under an atmosphere of argon. ^{1}H and ^{13}C NMR spectra were recorded on Varian Gemini 200 and 300 instruments. Chemical shifts are expressed as parts per million (ppm) downfield from tetramethylsilane or calibrated from $CDCl_3$. Mass spectra were obtained using Varian MAT-44 and Finnigan MAT-TSQ 70 spectrometers with electron impact (70 eV) and chemical ionization (100 eV, ionization gas, isobutene). IR spectra were taken with a BIO-RAD FTS 135 spectrometer. Microanalysis were performed in Professor V. Jäger's analytical laboratory (Institut für Organishe Chemie, Universität Stuttgart, Germany). High resolution mass spectra were recorded in Professor R. Flamant's laboratory (Université de Mons, Belgium).

4.1.1. 1-Butyltellanyl-propyne (11). Methylacetylene was bubbled through a stirred solution of *n*-BuLi (6.25 mL, 10 mmol, 1.6 M in hexanes) in THF (7 mL) cooled at 0 °C, until the initial yellow solution becomes a milky suspension. Tellurium (1.3 g, 10 mmol) was added and the suspension heated for 1 h at reflux. The heat source was removed, 1-iodobutane (1.1 mL, 10 mmol) was added and the mixture was stirred overnight at room temperature. The reaction mixture was diluted with petroleum ether (30 mL), washed with brine (30 mL), dried over $MgSO_4$ and the solvents were removed under reduced pressure. The crude material was purified by flash chromatography (petroleum ether) affording 1.63 g (73%) of the title compound as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=2.79$ (t, $J=7.4$ Hz, 2H), 2.16 (s, 3H), 1.85 (m, 2H), 1.42 (d, $J=6.9$ Hz, 2H), 0.94 (t, $J=7.3$ Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=$ 189.3, 125.7, 33.7, 24.7, 13.3, 8.6, 5.8 ppm. IR (neat, NaCl): $\nu=3027$, 2936, 2197, 1423, 1030, 1011 cm^{-1}. MS (EI): *m/z* (%): 224 [$M^{+\cdot}$] (76), 168 [$M^{+\cdot}-C_4H_9$] (41). Elemental analysis calcd for $C_7H_{12}Te$ (223.77): C, 37.57; H, 5.41. Found C, 38.02; H, 5.63.

4.1.2. (*Z*/*E*)-1-Butyltellanyl-1-iodo-propene (13). To a suspension of $Cp_2Zr(H)Cl$ (348 mg, 1.35 mmol) in THF (1.5 mL) under argon was added a solution of 1-butyltellanyl-propyne **11** (201 mg, 0.9 mmol) in THF (2 mL). The mixture was stirred at room temperature until a red solution was obtained (ca. 15 min). The solution was cooled to 0 °C and a solution of I_2 (343 mg, 1.35 mmol) in THF (0.5 mL) was added. The mixture was stirred for 1 h at 0 °C and was then allowed to slowly reach room temperature. It was diluted with hexane (10 mL), washed with a saturated aqueous solution of $Na_2S_2O_3$ (10 mL) and then with brine (8 mL). The organic layer was dried over Na_2SO_4 and the solvents were removed under reduced pressure. The crude material was purified by flash chromatography (hexane as eluent) affording 168 mg (53% yield) of the title compound as an inseparable mixture of isomers (*E*/*Z*:3/1; brown oil). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=7.08$ (q, $J=6.8$ Hz, 1H), 6.70 (q, $J=6.4$ Hz, 1H), 2.92 (t, $J=7.4$ Hz, 2H), 2.88 (t, $J=$ 7.4 Hz, 2H), 1.90–1.72 (m, 4H), 1.75 (d, $J=6.3$ Hz, 3H), 1.67 (d, $J=7.4$ Hz, 3H), 1.50–1.33 (m, 4H), 0.94 (t, $J=$ 7.2 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=150.6$, 149.2, 78.6, 74.6, 34.0, 24.8, 20.8, 14.9, 14.1, 13.5, 6.9 ppm.

4.1.3. (*Z*)-1-Butyltellanyl-propene (14). To a suspension of $Cp_2Zr(H)Cl$ (198 mg, 0.76 mmol, 1.2 equiv) under argon in THF (1.5 mL) was added a solution of 1-butyltellanyl-propyne **11** (143 mg, 0.64 mmol) in THF (2 mL). The yellow suspension was stirred at room temperature for 20 min until a clear red solution was obtained. H_2O (2 μL) was added and the mixture was stirred for a further 15 min. Hexane was added until a white precipitate was formed. It was filtered through a short path of silica and the solvents were removed under reduced pressure. The crude material was purified by column chromatography (hexane as eluent) affording 56 mg (53% yield) of the title compound as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=6.58$ (dd, $J=$ 9.3, 1.2 Hz, 1H), 6.24 (dq, $J=9.3$, 6.4 Hz, 1H), 2.68 (t, $J=$ 7.4 Hz, 2H), 1.84–1.68 (m, 2H), 1.71 (dd, $J=6.4$, 1.2 Hz, 2H), 1.45–1.30 (m, 2H), 0.92 (t, $J=7.3$ Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=142.4$, 100.2, 34.1, 24.9, 13.9, 13.6, 9.9 ppm. IR (neat, NaCl): $\nu=3025$, 2940, 2923, 2201, 1424, 1031, 1011 cm^{-1}. MS (EI): *m/z* (%): 226 [$M^{+\cdot}$] (85). Elemental analysis calcd for $C_7H_{14}Te$ (225.78): C, 37.24; H, 6.25. Found C, 37.69; H, 6.47.

4.1.4. (*Z*/*E*)-1-Bromo-1-butyltellanyl-propene (16). To a suspension of $Cp_2Zr(H)Cl$ (240 mg, 0.93 mmol) in THF (1 mL) under argon was added a solution of 1-butyltellanyl-propyne **11** (137 mg, 0.62 mmol) in THF (1.5 mL). The mixture was stirred at room temperature until a red solution was obtained (ca. 15 min). The solution was cooled to −40 °C and neat NBS (166 mg, 0.93 mmol) was added. The mixture was stirred for 1 h at −40 °C and then it was allowed to slowly reach −10 °C. Hexane (6 mL) was added in order to precipitate the zirconium salts. The solids were removed by filtration through a path of silica and the solvents were removed under reduced pressure. The crude material was purified by flash chromatography (hexane as eluent) affording 92 mg (49% yield) of the title compound as an inseparable mixture of isomers (*Z*/*E*:1/1; brownish oil). ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=6.74$ (q, $J=6.5$ Hz, 1H), 6.59 (q, $J=6.9$ Hz, 1H), 2.95 (t, $J=7.5$ Hz, 4H), 1.94–1.76 (m, 4H), 1.81 (d, $J=6.5$ Hz, 3H), 1.72 (d, $J=6.9$ Hz, 3H), 1.51–1.32 (m, 4H), 0.94 (t, $J=7.2$ Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): $\delta=144.5$, 138.2, 109.2, 106.5, 33.9, 24.7, 13.3, 12.5, 12.0, 7.0 ppm.

4.1.5. Hex-1-ynylselanyl-benzene (17). To a solution of 1-hexyne (2.3 g, 27.5 mmol) in dry THF (35 mL) at 0 °C was added dropwise *n*-BuLi (12.1 mL, 30.3 mmol, 2.5 M in hexanes), and the mixture was stirred for 10 min at 0 °C. A solution of phenyl selenyl bromide (6.5 g, 27.5 mmol) in THF (16 mL) was added dropwise over a 5 min period. The reaction mixture was then allowed to reach slowly room temperature and was stirred overnight. It was poured into

a saturated NH_4Cl solution (100 mL) and extracted with petroleum ether (3×75 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (petroleum ether as eluent) affording 6.3 g (92% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.55–7.45 (m, 2H), 7.35–7.15 (m, 3H), 2.45 (t, J=7.0 Hz, 2H), 1.65–1.40 (m, 4H), 0.93 (t, J=7.1 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ= 129.3, 128.6, 126.6, 104.6, 67.4, 30.8, 21.9, 20.2, 13.6 ppm. IR (neat, NaCl): ν=3059, 2957, 2931, 2871, 2180, 1578, 1477, 1439, 1325 cm^{-1}. MS (EI): m/z (%): 238 [$M^{+\cdot}$] (94), 194[$M^{+\cdot}-C_3H_8$] (24). Elemental analysis calcd for $C_{12}H_{14}Se$ (237.19): C, 60.76; H, 5.95. Found C, 61.23; H, 6.03.

4.1.6. (*Z*/*E*)-(1-Iodo-hex-1-enylselanyl)-benzene (19). To a flask containing $Cp_2Zr(H)Cl$ (274 mg, 1.06 mmol) under argon was added 1,2-dichloroethane (2 mL). To this suspension was added a solution of hex-1-ynylselanyl-benzene **17** (210 mg, 0.88 mmol) in 1,2-dichloroethane (1.5 mL) via syringe. The suspension was stirred for 20 min until a clear red solution was obtained. The solution was cooled to −10 °C and a solution of I_2 (290 mg, 1.14 mmol) in 1,2-dichloroethane (1.5 mL) was added dropwise. The reaction mixture was stirred at −10 °C for 30 min and then it was allowed to slowly reach room temperature. It was diluted with petroleum ether (15 mL), washed with a saturated $Na_2S_2O_3$ solution (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (petroleum ether as eluent) affording 225 mg (70% yield) of the title compound as an inseparable mixture of isomers (*E*/*Z*:4/1; brownish oil). ^1H NMR (300 MHz, $CDCl_3$): δ=7.60–7.30 (m, 10H), 7.03 (t, J= 7.4 Hz, 1H), 6.40 (t, J=6.9 Hz, 1H), 2.30–2.10 (m, 4H), 1.50–1.30 (m, 8H), 0.95 (t, J=7.1 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=153.3, 148.5, 132.6, 132.4, 129.3, 129.2, 128.8, 127.6, 79.4, 74.5, 38.2, 35.1, 35.0, 30.6, 22.2, 13.9 ppm. IR (neat, NaCl): ν=3030, 2936, 1480, 1427, 1027, 1010 cm^{-1}. MS (EI): m/z (%): 366 [$M^{+\cdot}$] (26), 239 [$M^{+\cdot}-I$] (5).

4.1.7. (*Z*)-Hex-1-enylselanybenzene (20). To a 10 mL round bottomed flask, containing $Cp_2Zr(H)Cl$ (286 mg, 1.1 mmol) under argon, was added freshly distilled 1,2-dichloroethane (1.5 mL). To this suspension was added via cannula a solution of hex-1-ynylselanyl-benzene **17** (219 mg, 0.92 mmol) in 1,2-dichloroethane (1.5 mL). The mixture was stirred for 20 min at room temperature and quenched by the addition of a saturated NH_4Cl solution (0.5 mL). Petroleum ether was added dropwise until a white precipitate was formed. The precipitate was removed by filtration over florisil and washed with petroleum ether. The crude material was purified by column chromatography (petroleum ether as eluent) affording 157 mg (71% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.55–7.40 (m, 2H), 7.35–7.20 (m, 3H), 6.43 (dt, J=8.9, 1.2 Hz, 1H), 6.05 (dt, J=8.9, 7.1 Hz, 1H), 2.19 (qd, J=7.2, 7.1 Hz, 2H), 1.50–1.25 (m, 4H), 0.92 (t, J=7.1 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=135.4, 131.7, 129.2, 126.8, 120.1, 31.1, 22.3, 13.9 ppm. IR (neat, NaCl): ν=3043, 2960, 2870, 2850, 1579, 1456 cm^{-1}. MS (EI): m/z (%): 240 [$M^{+\cdot}$] (100), 197 [$M^{+\cdot}-C_3H_8$] (18). Elemental analysis calcd for $C_{12}H_{16}Se$ (239.22): C, 60.25; H, 6.74. Found C, 60.41; H, 6.87.

4.1.8. (*Z*/*E*)-(1-Bromo-hex-1-enylselanyl)-benzene (22). To a 10 mL round bottomed flask containing $Cp_2Zr(H)Cl$ (304 mg, 1.17 mmol) under argon was added 1,2-dichloroethane (2 mL). To this suspension was added a solution of hex-1-ynylselanyl-benzene **17** (233 mg, 0.98 mmol) in 1,2-dichloroethane (1.5 mL) via syringe. The suspension was stirred for 20 min until a clear red solution was obtained. This solution was transferred via cannula to a flask containing a suspension of NBS (227 mg, 1.27 mmol) in 1,2-dichloroethane (2 mL) cooled to 0 °C. The reaction mixture was stirred at 0 °C for 1 h and then it was allowed to slowly reach room temperature. Petroleum ether was added until a white precipitate was formed. The precipitate was removed by filtration through a short path of florisil and the filtrate was concentrated in vacuo. The crude material was purified by flash chromatography (petroleum ether as eluent) affording 189 mg (61% yield) of the title compound as an inseparable mixture of isomers (*E*/*Z*:1.1/1; colourless oil). ^1H NMR (300 MHz, $CDCl_3$): δ=7.54–7.47 (m, 4H), 7.36–7.28 (m, 6H), 6.61 (t, J=7.2 Hz, 1H), 6.52 (t, J=7.1 Hz, 1H), 2.28 (q, J=7.2 Hz, 2H), 2.23 (q, J=7.1 Hz, 2H), 1.50–1.28 (m, 8H), 0.92 (t, J=7.0 Hz, 3H), 0.91 (t, J=7.1 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=145.7, 143.8, 132.4, 132.3, 129.3, 127.8, 127.6, 107.1, 105.8, 33.5, 33.1, 30.8, 30.1, 22.2, 22.1, 13.8 ppm. IR (neat, NaCl): ν=3023, 2957, 2871, 2858, 1578, 1477, 1439, 1022 cm^{-1}. MS (EI): m/z (%): 318 [$M^{+\cdot}$] (14), 81 [Bu–C≡$C^{+\cdot}$] (100). HRMS (EI+, M+) calcd for $C_{12}H_{15}BrSe$, 317.9522; found 317.9699.

4.1.9. 2,4,6-Ditriisopropylphenyl diselenide. To a solution of 1-bromo-2,4,6-triisopropylbenzene (11.67 g, 41.23 mmol) in THF (134 mL) cooled at −78 °C was added *t*-butyllithium (48 mL, 82.47 mmol, 1.7 M in pentane) dropwise. The mixture was stirred for 15 min at −78 °C until a yellow milky solution was formed. Selenium (3.58 g, 45.35 mmol) was added. The reaction mixture was allowed to reach room temperature slowly and was stirred overnight. A saturated aqueous NH_4Cl solution (40 mL) was added and the whole was stirred in the presence of atmospheric oxygen for 15 min. The reaction mixture was extracted with Et_2O (3×75 mL). The combined organic layers were washed with brine (75 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was recrystalized from ethanol/petroleum ether to yield 9.76 g (84%) of the title compound as an orange crystalline solid. ^1H NMR (300 MHz, $CDCl_3$): δ=6.89 (s, 4H), 3.53 (hep, J=6.9 Hz, 4H), 2.82 (hep, J=6.9 Hz, 2H), 1.19 (d, J= 6.9 Hz, 12H), 0.99 (d, J=6.9 Hz, 24H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ_C=153.6, 150.3, 129.0, 121.6, 34.4, 34.0, 23.9, 23.8 ppm. IR (neat, NaCl): ν=3043, 2958, 2926, 2866, 1594, 1382, 1361, 1166, 1154 cm^{-1}. MS (EI): m/z (%): 564 [$M^{+\cdot}$] (100), 282 [SeTIPP$^+$] (16). Elemental analysis calcd for $C_{30}H_{46}Se_2$ (564.61): C, 63.82; H, 8.21. Found C, 63.96; H, 8.16.

4.2. General procedure for the preparation of 1-(2,4,6)-triisopropylphenyl-1-alkynyl selenides

To a solution of di-2,4,6-triisopropyldiselenide (23.7 mmol) in THF (400 mL) at 0 °C was added a solution of Br_2

(24.9 mmol) in benzene (23 mL) over a period of 15 min, using an addition funnel. The dark brown solution was allowed to reach room temperature and was stirred for a further 30 min. In parallel, to a solution of the corresponding terminal alkyne (49.8 mmol) in THF (60 mL) at 0 °C was added *n*-BuLi (49.7 mmol, 1.6 M in hexanes). This solution was transferred via cannula to the solution of selenyl bromide cooled to 0 °C. The clear solution obtained was stirred for 2 h at room temperature. The reaction mixture was diluted with petroleum ether (300 mL) and washed with H_2O (300 mL) and brine (300 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by column chromatography to give pure 1-TIPP-1-alkynyl selenides.

4.2.1. (1,3,5)-Triisopropyl-2-prop-1-ynylselanyl-benzene (30a). The title compound was obtained as a light yellow oil in 87% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.04 (s, 2H), 3.88 (hep, J=6.9 Hz, 2H), 2.89 (hep, J=6.9 Hz, 1H), 1.90 (s, 3H), 1.27 (d, J=6.9 Hz, 12H), 1.25 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=152.2, 150.3, 125.7, 122.1, 92.8, 60.1, 34.3, 34.2, 24.2, 23.9, 5.2 ppm. IR (neat, NaCl): ν=3043, 2960, 2926, 2867, 2243, 1594, 1383, 1314, 1168 cm^{-1}. MS (EI): *m*/*z* (%): 322 [$M^{+\cdot}$] (100), 280 [$M^{+\cdot}-C_3H_7$] (16). Elemental analysis calcd for $C_{18}H_{26}Se$ (321.36): C, 67.36; H, 8.11. Found C, 67.28; H, 8.16.

4.2.2. 2-Hex-1-ynylselanyl-(1,3,5)-triisopropyl-benzene (30b). The title compound was obtained as a colourless oil in 93% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.03 (s, 2H), 3.88 (hep, J=6.9 Hz, 2H), 2.88 (hep, J=6.9 Hz, 1H), 2.24 (t, J=7.0 Hz, 2H), 1.50–1.30 (m, 4H), 1.26 (d, J=6.9 Hz, 12H), 1.25 (d, J=6.9 Hz, 6H), 0.85 (t, J=7.1 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=152.2, 150.4, 126.0, 122.2, 97.8, 61.1, 34.6, 34.5, 31.0, 24.5, 24.2, 22.2, 20.4, 13.9 ppm. IR (neat, NaCl): ν=2960, 2931, 2869, 2346, 1653, 1560, 1472, 1104 cm^{-1}. MS (EI): *m*/*z* (%): 364 [$M^{+\cdot}$] (34), 349 [$M^{+\cdot}-CH_3$] (13). Elemental analysis calcd for $C_{21}H_{32}Se$ (363.44): C, 69.51; H, 8.89. Found C, 69.32; H, 8.86.

4.2.3. 2-[6-(2,4,6-Triisopropyl-phenylselanyl)-hex-5-ynyloxyl]-tetrahydro-pyrane (30c). The title compound was obtained as a light yellow oil in 76% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.03 (s, 2H), 4.55 (t, J=3.4 Hz, 1H), 3.89 (hep, J=6.6 Hz, 2H), 3.87–3.79 (m, 1H), 3.71 (dt, J=10.0, 6.0 Hz, 1H), 3.52–3.44 (m, 1H), 3.36 (dt, J=10.0, 6.0 Hz, 1H), 2.89 (hep, J=6.6 Hz, 1H), 2.29 (t, J=7.0 Hz, 2H), 1.85–1.46 (m, 10H), 1.26 (d, J=6.6 Hz, 12H), 1.25 (d, J=6.6 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.3, 150.4, 125.9, 122.3, 98.9, 97.4, 67.1, 62.4, 61.6, 34.6, 34.5, 30.9, 29.1, 25.8, 25.7, 24.5, 24.2, 20.5, 19.8 ppm. IR (neat, NaCl): ν=3043, 2959, 2867, 2655, 1593, 1463, 1382, 1361 cm^{-1}. MS (EI): *m*/*z* (%): 464 [$M^{+\cdot}$] (2), 384 [$M^{+\cdot}-$THP] (2). Elemental analysis calcd for $C_{26}H_{40}O_2Se$ (463.55): C, 67.37; H, 8.70. Found C, 66.64; H, 8.47.

4.2.4. 1,3,5-Triisopropyl-2-(4-methyl-pent-1-ynylselanyl)-benzene (30d). The title compound was obtained as a light yellow oil in 91% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.05 (s, 2H), 3.92 (hep, J=6.9 Hz, 2H), 2.89 (hep, J=6.9 Hz, 1H), 2.15 (d, J=6.9 Hz, 2H), 1.76 (non, J=6.9 Hz, 1H), 1.28 (d, J=6.9 Hz, 6H), 1.27 (d, J=6.9 Hz, 12H), 0.93 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.5, 150.2, 126.2, 122.4, 107. 3, 62.2, 34.9, 34.7, 30.1, 28.7, 24.8, 24.5, 22.5 ppm. IR (neat, NaCl): ν=2999, 2943, 2860, 2246, 1657, 1562, 1471, 1112 cm^{-1}. MS (EI): *m*/*z* (%): 364 [$M^{+\cdot}$] (34), 349 [$M^{+\cdot}-CH_3$] (13), 321 [$M^{+\cdot}-C_3H_7$] (12). Elemental analysis calcd for $C_{21}H_{32}Se$ (363.44): C, 69.40; H, 8.87. Found C, 69.52; H, 8.63.

4.2.5. 2-Cyclohexylethynylselanyl-1,3,5-triisopropyl-benzene (30e). The title compound was obtained as a yellow oil in 86% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.02 (s, 2H), 3.90 (hep, J=6.6 Hz, 2H), 2.88 (hep, J=6.6 Hz, 1H), 2.90–2.79 (m, 1H), 1.80–1.23 (m, 10H), 1.26 (d, J=6.6 Hz, 6H), 1.25 (d, J=6.6 Hz, 12H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.1, 150.1, 125.9, 122.0, 101. 5, 61.0, 34.3, 34.2, 32.7, 30.7, 25.9, 24.9, 24.3, 24.0 ppm. IR (neat, NaCl): ν=2997, 2953, 2898, 2546, 1653, 1565, 1476 cm^{-1}. MS (APCI): *m*/*z* (%): 390 [$M^{+\cdot}$] (97). Elemental analysis calcd for $C_{23}H_{34}Se$ (389.48): C, 70.93; H, 8.80. Found C, 70.99; H, 8.54.

4.2.6. 1-(2,4,6)-Triisopropylphenylselenyl-1-phenyl-acetylene (30f). The title compound was obtained as a yellow crystalline solid in 95% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.41–7.31 (m, 2H), 7.27–7.23 (m, 5H), 7.06 (s, 2H), 3.89 (hep, J=6.6 Hz, 2H), 3.87–3.79 (m, 1H), 3.95 (hep, J=6.6 Hz, 2H), 2.88 (hep, J=7.2 Hz, 1H), 1.30 (d, J=6.6 Hz, 12H), 1.26 (d, J=7.2 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=152.6, 150.9, 131.7, 128.4, 128.4, 125.6, 123.8, 122.5, 96.7, 73.3, 34.7, 34.4, 24.5, 24.1 ppm. IR (neat, NaCl): ν=3057, 2963, 2932, 2866, 2240, 1567, 1383, 1321, 1163 cm^{-1}. MS (EI): *m*/*z* (%): molecular peak not observed, 204 [$TIPP^+$]. Elemental analysis calcd for $C_{23}H_{28}Se$ (383.43): C, 71.92; H, 7.35. Found C, 71.80; H, 7.36.

4.3. General procedure for the preparation of (*E*)-1-iodo-1-selenoalkenes

To a solution of the corresponding 1-alkynyl selenide (37.8 mmol) in hexane (80 mL) at 0 °C was added dropwise DIBAL-H (39.6 mmol, 1.5 M in toluene). The colourless solution was stirred at 0 °C for 1 h and then for 3 h at room temperature. The mixture was cooled to −78 °C and a solution of I_2 (94.5 mmol) in THF (45 mL) was added dropwise via cannula. The reaction was stirred at −78 °C for 30 min, then it was allowed to slowly reach 0 °C and finally it was stirred during 45 min at room temperature. It was poured in a mixture of EtOH (215 mL)/EtOAc (215 mL)/H_2O (108 mL) and treated with $NaBH_4$ until the solution became colourless or slightly yellow. The resulting solution was washed with aqueous 1 M HCl (120 mL), a saturated aqueous $Na_2S_2O_3$ solution (100 mL), brine (130 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography to give pure 1-iodo-1-selenoalkenes.

4.3.1. (*E*)-2-(Iodo-propenylselanyl)-1,3,5-triisopropyl-benzene (32a). The title compound was obtained as a red-brown oil in 92% yield following the general procedure. ^{1}H

NMR (300 MHz, $CDCl_3$): δ=7.04 (s, 2H), 6.83 (q, J=6.9 Hz, 1H), 3.67 (hep, J=6.9 Hz, 2H), 2.91 (hep, J=7.0 Hz, 1H), 2.75 (d, J=6.9 Hz, 3H), 1.27 (d, J=7.0 Hz, 6H), 1.25 (d, J=6.9 Hz, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=153.0, 150.7, 140.7, 125.8, 121.9, 82.1, 34.2, 33.9, 24.2, 23.8, 20.2 ppm. IR (neat, NaCl): ν=3041, 2959, 2926, 1701, 1462, 1382, 1361, 1168, 1069 cm^{-1}. MS (EI): m/z (%): 450 [$M^{+\cdot}$] (62), 324 [$M^{+\cdot}-I$] (73). Elemental analysis calcd for $C_{18}H_{27}ISe$ (449.27): C, 48.12; H, 6.06. Found C, 49.45; H, 6.23.

4.3.2. (*E*)-2-(1-Iodo-hex-1-enylselanyl)-1,3,5-triisopropyl-benzene (32b). The title compound was obtained as a brown oil in 95% yield following the general procedure. ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.03 (s, 2H), 6.78 (t, J=6.9 Hz, 1H), 3.68 (hep, J=6.9 Hz, 2H), 2.91 (hep, J=7.0 Hz, 1H), 2.27 (m, 2H), 1.50–1.32 (m, 4H), 1.27 (d, J=7.3 Hz, 6H), 1.23 (d, J=7.3 Hz, 12H), 0.94 (t, J=7.0 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.9, 150.8, 146.7, 125.8, 122.0, 81.2, 34.6, 34.3, 33.9, 30.7, 24.3, 23.9, 22.2, 13.9 ppm. IR (neat, NaCl): ν=3043, 2960, 2927, 1701, 1594, 1382, 1361, 1154 cm^{-1}. MS (EI): m/z (%): 492 [$M^{+\cdot}$] (100), 365 [$M^{+\cdot}-I$] (55). Elemental analysis calcd for $C_{21}H_{33}ISe$ (491.35): C, 51.33; H, 6.77. Found C, 52.17; H, 6.71.

4.3.3. 2-[6-Iodo-6-(2,4,6)-triisopropyl-phenylselanyl)-hex-5-enyloxy]-tetrahydropyran (32c). The title compound was obtained as a yellow oil in 96% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.03 (s, 2H), 6.78 (t, J=7.2 Hz, 1H), 4.60 (dd, J=6.0, 2.7 Hz, 1H), 3.94–3.81 (m, 1H), 3.77 (dt, J=9.4, 6.0 Hz, 1H), 3.66 (hep, J=6.7 Hz, 2H), 3.58–3.42 (m, 1H), 3.42 (dt, J=9.4, 6.0 Hz, 1H), 2.91 (hep, J=6.6 Hz, 1H), 2.30 (q, J=7.2 Hz, 2H), 1.90–1.45 (m, 10H), 1.26 (d, J=6.7 Hz, 6H), 1.22 (d, J=6.6 Hz, 12H), 0.94 (t, J=7.0 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=153.0, 150.8, 146.3, 125.7, 122.1, 98.9, 81.9, 67.4, 62.5, 34.9, 34.5, 34.1, 31.0, 29.5, 25.7, 25.5, 24.5, 24.2, 19.9 ppm. IR (neat, NaCl): ν=3043, 2960, 2868, 2667, 1708, 1576, 1364, 1361, 1154 cm^{-1}. MS (EI): m/z (%): 592 [$M^{+\cdot}$] (100), 465 [$M^{+\cdot}-I$] (61). HRMS (EI+, M+) calcd for C_{26} $H_{41}IO_2Se$, 592.1316; found 592.1319.

4.3.4. 2-(1-Iodo-4-methyl-pent-1-enylselanyl)-1,3,5-triisopropyl-benzene (32d). The title compound was obtained as a yellow oil in 82% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.02 (s, 2H), 6.79 (t, J=6.9 Hz, 1H), 3.66 (hep, J=6.6 Hz, 2H), 2.90 (hep, J=6.9 Hz, 1H), 2.16 (t, J=6.6 Hz, 2H), 1.76 (non, J=6.9 Hz, 1H), 1.26 (d, J=6.9 Hz, 6H), 1.22 (d, J=6.6 Hz, 6H), 0.96 (d, J=6.6 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=153.3, 151.1, 145.9, 130.6, 122.4, 82.5, 44.4, 34.8, 34.4, 28.8, 24.9, 24.5, 22.9 ppm. IR (neat, NaCl): ν=2958, 2959, 2920, 1594, 1463, 1382, 1168, 1061 cm^{-1}. MS (APCI): m/z (%): 492 [$M^{+\cdot}$] (76), 365 [$M^{+\cdot}-I$] (100). HRMS (CI+, M+) calcd for $C_{21}H_{33}ISe$, 492.0792; found 492.0799.

4.3.5. 2-(2-Cyclohexyl-1-iodo-vinylselanyl)-1,3,5-triisopropyl-benzene (32e). The title compound was obtained as a yellow oil in 91% yield following the general procedure. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.02 (s, 2H), 6.79 (t, J=6.9 Hz, 1H), 3.66 (hep, J=6.6 Hz, 2H), 2.90 (hep, J=6.9 Hz, 1H), 2.16 (t, J=6.6 Hz, 2H), 1.76 (non, J=6.9 Hz, 1H), 1.26 (d, J=6.9 Hz, 6H), 1.22 (d, J=6.6 Hz, 6H), 0.96 (d, J=6.6 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=152.8, 152.0, 150.6, 130.3, 121.9, 79.5, 44.4, 34.3, 33.9, 32.1, 25.9, 25.7, 24.4, 24.0 ppm. IR (neat, NaCl): ν=2958, 2959, 2920, 1594, 1463, 1382, 1168, 1061 cm^{-1}. MS (APCI): m/z (%): 518 [$M^{+\cdot}$] (34), 391 [$M^{+\cdot}-I$] (100). HRMS (CI+, M+) calcd for $C_{23}H_{35}ISe$, 518.0949; found 518.0943.

4.3.6. (*Z*)-1,3,5-Triisopropyl-2-propenylselanyl-benzene (34a). To a solution of the vinyl iodide **32a** (325 mg, 0.72 mmol) in THF (10 mL) at −78 °C was added *n*-BuLi (470 μL, 0.75 mmol, 1.6 M in hexanes) dropwise. The solution was stirred for 20 min at −78 °C and then it was poured into a saturated aqueous solution of NH_4Cl (8 mL) and extracted with petroleum ether (3×10 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE) to afford 212 mg (91% yield) of the title compound as a slightly yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$): δ=7.04 (s, 2H), 6.09 (dd, J=8.8, 1.3 Hz, 1H), 5.90 (dq, J=8.8, 6.6 Hz, 1H), 3.82 (hep, J=6.9 Hz, 2H), 2.90 (hep, J=6.9 Hz, 1H), 1.80 (dd, J=6.6, 1.3 Hz, 3H), 1.25 (d, J=6.9 Hz, 6H), 1.23 (d, J=6.9 Hz, 12H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=152.8, 149.3, 127.5, 125.3, 121.8, 121.6, 34.2, 34.1, 24.3, 23.9, 16.2 ppm. IR (neat, NaCl): ν=3041, 2962, 2860, 1685, 1762, 1595, 1381 cm^{-1}. MS (EI): m/z (%): 324 [$M^{+\cdot}$] (100), 309 (27). Elemental analysis calcd for $C_{18}H_{28}Se$ (323.37): C, 66.86; H, 8.73. Found C, 66.89; H, 8.79.

4.3.7. (*E*)-4-(2,4,6 Triisopropylphenyl)seleno-2-methyl hex-4-en-3-one (34c). To a solution of the vinyl iodide **32a** (195 mg, 0.43 mmol) in THF (5 mL) at −78 °C was added *n*-BuLi (282 μL, 0.45 mmol, 1.6 M in hexanes) dropwise. The solution was stirred for 20 min at −78 °C and then neat *N*-methoxy-*N*-methylamide (56 mg, 0.48 mmol) was added at once. The reaction mixture was allowed to reach slowly room temperature. It was poured into a saturated aqueous solution of NH_4Cl (5 mL) and extracted with petroleum ether (3×10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:30/1 as eluent) to afford 110 mg (67% yield) of the title compound as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.88 (s, 2H), 6.69 (q, J=6.6 Hz, 1H), 3.64 (hep, J=6.9 Hz, 2H), 2.98 (hep, J=6.9 Hz, 1H), 2.76 (hep, J=6.9 Hz, 1H), 1.66 (d, J=6.9 Hz, 3H), 1.13 (d, J=6.9 Hz, 6H), 1.11 (d, J=6.9 Hz, 12H), 0.77 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=202.8, 153.7, 150.6, 139.8, 137.7, 127.1, 122.5, 36.6, 34.9, 34.8, 24.9, 24.5, 19.4, 17.6 ppm. IR (neat, NaCl): ν=3045, 2962, 2869, 1685, 1595, 1463, 1361 cm^{-1}. MS (EI): m/z (%): 394 [$M^{+\cdot}$] (45), 323 [$M^{+\cdot}-COC_3H_7$] (12). Elemental analysis calcd for $C_{22}H_{34}OSe$ (393.46): C, 67.16; H, 8.71. Found C, 67.19; H, 8.65.

4.3.8. (*Z*)-1-Phenyl-2-(2,4,6-triisopropyl-phenylselanyl)-but-2-en-1-one (34d). To a solution of the vinyl iodide **32a** (250 mg, 0.55 mmol) in THF (6 mL) at −78 °C was added

n-BuLi (362 μL, 0.58 mmol, 1.6 M in hexanes) dropwise. The solution was stirred for 20 min at −78 °C and then a solution of benzoyl chloride (67 μL, 0.58 mmol) in THF (2 mL) was added dropwise. The reaction mixture was allowed to slowly reach room temperature. It was poured into a saturated aqueous solution of $NaHCO_3$ (5 mL) and extracted with petroleum ether (3×10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:25/1 as eluent) to afford 169 mg (72% yield) of the title compound as a yellowish oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.70–7.65 (m, 2H), 7.03 (s, 2H), 7.01–6.90 (m, 3H), 6.15 (q, J=6.8 Hz, 3H), 3.97 (hep, J=6.9 Hz, 2H), 2.68 (hep, J=6.9 Hz, 1H), 1.73 (d, J=6.8 Hz, 3H), 1.28 (d, J=6.9 Hz, 12H), 1.11 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=194.0, 153.5, 152.7, 149.7, 137.3, 136.9, 132.1, 129.2, 128.4, 127.8, 121.5, 34.1, 33.9, 24.3, 24.0, 17.2 ppm. IR (neat, NaCl): ν=3045, 2961, 2869, 1722, 1662, 1596, 1382 cm^{-1}. MS (EI): *m*/*z* (%): 428 [$M^{+\cdot}$] (12). HRMS (EI+, M+) calcd for $C_{25}H_{32}OSe$, 428.1618; found 428.1614.

4.3.9. (*Z*)-1,1,1-Trifluoro-3-(2,4,6-triisopropyl-phenylselanyl)-pent-3en-2one (34e). To a solution of the vinyl iodide **32a** (200 mg, 0.45 mmol) in THF (5 mL) at −78 °C was added *n*-BuLi (292 μL, 0.47 mmol, 1.6 M in hexanes) dropwise. The solution was stirred for 20 min at −78 °C and then a solution of trifluoroacetic anhydride (103 mg, 0.49 mmol) in THF (1 mL) was added. The reaction mixture was allowed to slowly reach room temperature. It was poured into a saturated aqueous solution of $NaHCO_3$ (4 mL) and extracted with petroleum ether (3×10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography (pure PE as eluent) to afford 147 mg (78% yield) of the title compound as a colourless oil. ^1H NMR (200 MHz, $CDCl_3$): δ=7.12 (s, 2H), 6.87 (qq, J=6.9, 1.3 Hz, 1H), 4.01 (hep, J=6.9 Hz, 2H), 2.70 (hep, J=6.9 Hz, 1H), 1.58 (d, J=6.9 Hz, 3H), 1.28 (d, J=6.9 Hz, 12H), 1.12 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=200.8, 154.2, 151.1, 139.8, 137.7, 132.5, 127.1, 122.5, 34.9, 34.8, 24.8, 24.3, 19.4 ppm. IR (neat, NaCl): ν=3043, 2962, 2871, 1716, 1594, 1463, 1383 cm^{-1}. MS (EI): *m*/*z* (%): 420 [$M^{+\cdot}$] (100), 377 [$M^{+\cdot}-C_3H_7$] (25). Elemental analysis calcd for $C_{20}H_{27}F_3OSe$ (419.38): C, 57.28; H, 6.49. Found C, 57.74; H, 6.61.

4.3.10. (*E*)-2-(2,4,6-Triisopropylphenyl)seleno-1-phenyl-but-2-ene-1-ol (34f). To a solution of the vinyl iodide **32a** (490 mg, 1.1 mmol) in THF (15 mL) at −78 °C was added *t*-BuLi (750 μL, 2.3 mmol, 1.5 M in pentane). The solution was stirred at −78 °C for 15 min and neat benzaldehyde (122 μL, 1.2 mmol) was added. The mixture was stirred for 1 h at −78 °C and then it was allowed to slowly room temperature. The reaction was quenched by the addition of deuterated methanol (500 μL) and stirred for further 15 min. It was diluted with petroleum ether (15 mL) and then poured into a saturated aqueous solution of NH_4Cl (20 mL). It was extracted with petroleum ether (3×15 mL) and the combined organic layers were washed with brine (40 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:4/1 as eluent) to afford 335 mg (82% yield) of the allylic alcohol as a yellowish oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.37–7.15– (m, 5H), 7.00 (s, 2H), 5.92 (qt, J=6.6, 0.9 Hz, 1H), 4.87 (s, 1H), 3.62 (hep, J=6.9 Hz, 2H), 2.88 (hep, J=6.9 Hz, 1H), 1.88 (dd, J=6.6, 0.9 Hz, 3H), 1.26 (d, J=6.9 Hz, 6H), 1.18 (d, J=6.9 Hz, 6H), 1.16 (d, J=6.9 Hz, 6H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=153.4, 150.1, 141.7, 138.3, 128.3, 127.7, 127.1, 126.9, 125.1, 122.0, 76.2, 34.4, 33.9, 24.6, 24.3, 24.1, 16.8 ppm. IR (neat, NaCl): ν=3414, 3030, 3031, 2960, 1632, 1595, 1462, 1312 cm^{-1}. MS (EI): *m*/*z* (%): 430 [$M^{+\cdot}$] (100), 323 [$M^{+\cdot}-CH(OH)Ph$] (89). Elemental analysis calcd for $C_{25}H_{34}OSe$ (429.50): C, 70.07; H, 8.04. Found C, 70.00; H, 7.99.

4.3.11. (*Z*)-3-(2,4,6-Triisopropyl-phenylselanyl-oct-2-en-4-ol (34g). To a solution of the vinyl iodide **32a** (325 mg, 0.72 mmol) in hexane (10 mL) at room temperature was added *n*-BuLi (470 μL, 0.75 mmol, 1.6 M in hexanes) dropwise. The solution was stirred at room temperature for 10 min and neat valeraldehyde (92 μL, 0.86 mmol) was added. The mixture was stirred for 1.5 h at room temperature and then poured into a saturated aqueous solution of NH_4Cl (8 mL). It was extracted with petroleum ether (3×10 mL) and the combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1 as eluent) to afford 191 mg (65% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.00 (s, 2H), 6.05 (qd, J=6.6, 0.9 Hz, 1H), 3.78 (hep, J=6.9 Hz, 2H), 3.84–3.70 (m, 1H), 2.87 (hep, J=6.9 Hz, 1H) 1.89 (dd, J=6.6, 0.9 Hz, 3H), 1.60–1.10 (m, 6H), 1.24 (d, J=6.9 Hz, 12H), 1.20 (d, J=6.9 Hz, 6H), 0.87 (t, J=6.9 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.1, 149.9, 139.2, 125.5, 124.8, 122.0, 75.2, 36.5, 34.5, 34.2, 28.3, 24.7, 24.2, 22.8, 16.8, 14.3 ppm. IR (neat, NaCl): ν=3396, 3042, 2960, 2929, 1632, 1595, 1462, 1362 cm^{-1}. MS (EI): *m*/*z* (%): 409 [$M^{+\cdot}$] (35). Elemental analysis calcd for $C_{23}H_{38}OSe$ (409.50): C, 67.46; H, 9.35. Found C, 67.17; H, 9.04.

4.3.12. (*Z*)-3-(2,4,6-Triisopropyl-phenylselanyl)-undec-2-en-5-ol (34h). To a solution of the vinyl iodide **32a** (660 mg, 1.47 mmol) in THF (15 mL) at −78 °C was added *n*-BuLi (920 μL, 1.47 mmol, 1.6 M in hexanes) dropwise. The solution was stirred for 20 min at −78 °C and neat epoxide (225 μL, 1.47 mmol) and then neat $BF_3\cdot OEt_2$ (144 μL, 1.47 mmol) were added. The solution was stirred at −78 °C for 30 min and then it was allowed to slowly reach 0 °C. At this temperature a saturated aqueous solution of $NaHCO_3$ (8 mL) was added and the mixture was allowed to warm up to room temperature. It was extracted with EtOAc (3×10 mL), the combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1 as eluent) to afford 332 mg (50% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.00 (s, 2H), 5.79 (q, J=6.6 Hz, 1H), 3.70 (hep, J=6.9 Hz, 2H), 3.46 (m, 1H), 2.88 (hep, J=6.9 Hz, 1H), 2.05 (d, J=14.1 Hz, 1H), 1.94 (dd, J=14.1, 9.0 Hz, 1H), 1.90 (d, J=6.6 Hz, 3H), 1.70 (m, 1H), 1.24 (d, J=6.9 Hz, 6H), 1.22 (d, J=6.9 Hz, 6H), 1.17

(d, J=6.9 Hz, 3H), 1.39–098 (m, 10H), 0.85 (t, J=6.9 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.1, 149.9, 133.4, 126.5, 125.7, 121.9, 69.2, 46.0, 36.6, 34.4, 34.2, 32.0, 29.6, 25.7, 24.8, 24.2, 23.0, 17.1, 14.3 ppm. IR (neat, NaCl): ν=3410, 3043, 2960, 2868, 1630, 1595, 1462, 1361 cm^{-1}. MS (EI): *m/z* (%): 452 [$M^{+\cdot}$] (100), 323 (11). Elemental analysis calcd for $C_{26}H_{44}OSe$ (451.59): C, 69.15; H, 9.82. Found C, 69.05; H, 9.88.

4.3.13. (*Z*)-1,3,5-Triisopropyl-2-(1-methyl-propenyl-selanyl)-benzene (34j). To a solution of vinyl iodide **32a** (355 mg, 0.79 mmol) in THF (4 mL) at −78 °C was added *t*-BuLi (1.0 mL, 1.5 M in pentane, 1.58 mmol) dropwise. It was stirred at −78 °C for 15 min and neat methyl iodide (74 μL, 1.2 mmol) was added in three portions. The mixture was stirred at −78 °C for 1 h, then it was allowed to slowly reach room temperature It was diluted with petroleum ether (10 mL), washed with H_2O, dried over $MgSO_4$ and the solvents were evaporated under reduced pressure. The crude material was purified by flash chromatography (pure petroleum ether as eluent) to afford 251 mg of the title compound (93% yield) as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.01 (s, 2H), 5.65 (qq, J=6.6, 1.5 Hz, 1H), 3.79 (hep, J=6.9 Hz, 2H), 2.88 (hep, J=6.9 Hz, 1H), 1.82 (dq, J=6.6, 1.5 Hz, 3H), 1.67 (m, 3H), 1.25 (d, J=6.9 Hz, 6H), 1.20 (d, J=6.9 Hz, 12H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.5, 149.8, 131.2, 125.3, 122.3, 121.7, 34.4, 34.3, 25.2, 24.4, 24.2, 16.8 ppm. IR (neat, NaCl): ν=2960, 2868, 1640, 1595, 1461, 1424, 1143 cm^{-1}. MS (EI): *m/z* (%): 338 [$M^{+\cdot}$] (100), 323 [$M^{+\cdot}-CH_3$] (28). Elemental analysis calcd for $C_{19}H_{30}Se$ (337.40): C, 67.64; H, 8.96. Found C, 68.08; H, 9.20.

4.3.14. (*Z*)-Trimethyl-[2-(2,4,6-triisopropyl-phenylselanyl)-but-2-enyl]-silane (34k). To a 25 mL round bottomed flask, containing THF (2 mL) at −78 °C were added *t*-BuLi (1.0 mL, 1.77 mmol, 1.7 M in pentane) and immediately after, a solution of vinyl iodide **32a** (361 mg, 0.8 mmol) in THF (1 mL). The mixture was stirred for 5 min at −78 °C, meanwhile the formation of a white precipitate was observed. Neat iodomethyltrimethylsilane (275 μL, 1.9 mmol) was added and the mixture was stirred for 1 h at −78 °C and then allowed to slowly reach room temperature. It was poured into a mixture of PE (10 mL)/H_2O (10 mL) and extracted with petroleum ether (3× 8 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography (pure PE as eluent) to afford 256 mg (78% yield) of the title compound as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.18 (s, 2H), 5.45 (q, J=6.6 Hz, 1H), 4.12 (hep, J=6.9 Hz, 2H), 2.76 (hep, J=6.9 Hz, 1H), 1.93 (d, J=6.6 Hz, 3H), 1.61 (m, 2H), 1.32 (d, J=6.9 Hz, 12H), 1.18 (d, J=6.9 Hz, 6H), 0.05 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.6, 149.6, 133.1, 127.2, 123.0, 122.0, 34.6, 34.3, 27.8, 24.8, 24.6, 17.7, −0.8 ppm. IR (neat, NaCl): ν=3043, 2961, 2929, 2870, 1624, 1595, 1562, 1462, 1422, 1382, 1248 cm^{-1}. MS (EI): *m/z* (%): 410 [$M^{+\cdot}$] (37), 395 [$M^{+\cdot}-CH_3$] (12). Elemental analysis calcd for $C_{22}H_{38}SeSi$ (409.58): C, 64.51; H, 9.35. Found C, 64.03; H, 9.25.

4.3.15. (*Z*)-Trimethyl-[2-(2,4,6-triisopropyl-phenylselanyl)-hept-2-enyl]-silane (34m). To a solution of vinyl iodide **32a** (225 mg, 0.46 mmol) and $Pd(PPh_3)_4$ (53 mg, 0.046 mmol) in THF (4 mL) at room temperature was added trimethylsilylzinc iodide[29] (500 μL, 0.55 mmol, 1.0 M in THF). The yellow solution thus obtained was stirred at reflux for 10 h. It was diluted with petroleum ether (10 mL), washed with aqueous 0.5 M HCl (8 mL) and extracted several times with PE. The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography (PE) affording 79 mg (38% yield) of the title compound as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.99 (s, 2H), 5.42 (t, J=7.0 Hz, 1H), 3.79 (hep, J=6.9 Hz, 2H), 2.88 (hep, J=6.9 Hz, 1H), 2.32 (dd, J=7.0, 7.0 Hz, 2H), 1.49 (s, 2H), 1.45–1.30 (m, 4H), 1.26 (d, J=6.9 Hz, 6H), 1.18 (d, J=6.9 Hz, 12H), 0.93 (t, J=7.0 Hz, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.2, 149.3, 131.7, 128.8, 126.0, 121.6, 34.1, 33.6, 32.0, 31.5, 27.2, 24.2, 23.9, 22.4, 14.0, −1.4 ppm. IR (neat, NaCl): ν=3042, 2959, 2927, 2870, 1762, 1595, 1562, 1462, 1422, 1382, 1247 cm^{-1}. MS (EI): *m/z* (%): 452 [$M^{+\cdot}$] (92), 437 [$M^{+\cdot}-CH_3$] (19), 379 [$M^{+\cdot}-Si(CH_3)_3$] (20). Elemental analysis calcd for $C_{25}H_{44}SeSi$ (451.66): C, 66.48; H, 9.82. Found C, 66.73; H, 9.64.

4.4. Preparation of Lithium 4,4′-di-*tert*-butyl biphenylide (LDBB)

To a flame-dried two necked flask, equipped with a glass-coated stirring bar, rubber septum and Ar inlet, were added 4,4′-di-*tert*-butyl-biphenyl (DBB) (1.6 g, 6.02 mmol) and THF (20 mL). Lithium ribbon was prepared by scraping the dark oxide coating off the surface while it was immersed in mineral oil. The shiny metal was dipped in hexane in order to remove the oil and then weighed (50 mg, 7.13 mmol) in a tared beaker containing mineral oil. The metal was sliced into small pieces while it was still immersed in mineral oil. The lithium pieces were dipped again in hexane prior to addition to the solution of DBB in THF, while the flask was rapidly being purged with Ar. The reaction mixture was stirred at room temperature for 5 min until a dark green colour appeared on the lithium surface, then it was cooled down to 0 °C and stirred for 4–5 h. The resulting dark green LDBB solution (6.02 mmol, 0.3 M in THF) was ready for use in reductive lithiation. The actual amount of LDBB is usually less than indicated due to impurities on the lithium ribbon and decomposition of LDBB. The real concentration can be calculated by titration with $PhSCH_2Si(CH_3)_3$. A solution of this phenylthio ether in THF was added dropwise to a known volume of solution of LDBB at −78 °C until the colour of the solution changed from dark green to yellow-red. The concentration of the LDBB solution was calculated from the amount of phenylthio ether added.

4.4.1. (*E*)-Trimethyl-(2-methyl-hept-2-enyl)-silane (35). To a freshly prepared solution of LDBB (4.3 mL, 1.3 mmol, 0.3 M in THF) at −78 °C was added a solution of selenide **34m** (275 mg, 0.6 mmol) in THF (10 mL) dropwise. At the end of the addition the dark green solution changed to pale red. It was stirred for further 10 min at −78 °C and neat methyl iodide (50 μL, 1.3 mmol) was added. The reaction mixture was stirred for 30 min at −78 °C and then was allowed to reach slowly 0 °C. It was diluted with petroleum ether (10 mL), washed with aqueous 1 M HCl (10 mL)

and extracted with PE (3×10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (pure PE as eluent) to afford 74 mg (67% yield) of the title compound as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.16 (tt, J=7.0, 1.0 Hz, 1H), 2.32 (d, J=1.0 Hz, 2H), 2.07 (q, J=7.0 Hz, 2H), 1.35 (s, 3H), 1.40–1.20 (m, 4H), 0.90 (t, J=7.0 Hz, 3H), 0.08 (s, 9H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=132.6, 102.5, 36.8, 36.7, 30.8, 24.1, 22.3, 13.9, −1.3 ppm. IR (neat, NaCl): ν=3417, 2959, 2985, 2870, 1595, 1562, 1462, 1422, 1382, 1247 cm^{-1}. MS (EI): m/z (%): 184 [$M^{+\cdot}$] (63). HRMS (EI+, M+) calcd for $C_{11}H_{24}Si$, 184.1647; found 184.1642.

4.4.2. (*E*)-6-Trimethylsilanylmethyl-undec-6-en-5-ol (36). To a freshly prepared solution of LDBB (1.1 mL, 0.32 mmol, 0.3 M in THF) at −78 °C was added a solution of selenide **34m** (71 mg, 0.16 mmol) in THF (2.5 mL) dropwise. At the end of the addition the dark green solution changed to pale red. It was stirred for a further 10 min at −78 °C and neat valeraldehyde (50 μL, 0.47 mmol) was added. The reaction mixture was stirred for 30 min at −78 °C and then was allowed to slowly reach 0 °C. It was diluted with petroleum ether (10 mL), washed with aqueous 1 M HCl (10 mL) and extracted with PE (3×8 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/EtOAc:30/1) to afford 25 mg (62% yield) of the title compound as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.08 (t, J=7.4 Hz, 1H), 4.49 (t, J=6.9 Hz, 1H), 2.15–1.90 (m, 4H), 1.63–1.15 (m, 10H), 0.90 (t, J=6.9 Hz, 3H), 0.89 (t, J=6.9 Hz, 3H), 0.03 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=138.5, 126.0, 70.5, 35.3, 32.7, 28.2, 27.2, 22.7, 22.3, 19.9, 14.0, 13.9, −0.7 ppm. IR (neat, NaCl): ν=3415, 2960, 2920, 2860, 1638, 1457, 1379, 1248 cm^{-1}. MS (EI): m/z (%): 256 [$M^{+\cdot}$] (41). HRMS (EI+, M+) calcd for $C_{15}H_{32}OSi$, 256.2222; found 256.2223.

4.4.3. (*E*)-1-[1,3]Dithian-2-yl-1-hex-4-en-2-ol (37). To a solution of selenide **34i** (275 mg, 0.55 mmol) in THF (6 mL) at −78 °C was added *n*-BuLi (343 μL, 0.55 mmol, 1.6 M in hexanes) dropwise and then the solution was allowed to warm up slowly to 0 °C. This solution was added via cannula to a freshly prepared solution of LDBB (4.3 mL, 1.3 mmol, 0.3 M in THF). At the end of the addition the dark green solution changed to pale red. It was stirred for a further 10 min at −78 °C and neat methanol (1.5 mL) was added. The reaction mixture was allowed to slowly reach room temperature. It was diluted with petroleum ether (15 mL), washed with aqueous 1 N HCl (10 mL) and extracted with PE (3×10 mL). The combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:1/1 as eluent) to afford 110 mg (92% yield) of the title compound as a coulorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.53 (dqt, J=15.2, 6.2, 1.1 Hz, 1H), 5.39 (dqt, J=15.2, 7.5, 1.2 Hz, 1H), 4.25 (dd, J=6.8, 6.7 Hz, 1H), 3.89 (m, 1H), 2.94–2.75 (m, 4H), 2.30–2.08 (m, 3H), 1.96–1.81 (m, 4H), 1.67 (dd, J=6.2, 1.2 Hz, 3H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ=129.3, 126.3, 67.7, 44.2, 42.0, 40.7, 30.3, 29.9, 25.9, 17.9 ppm. IR (neat, NaCl): ν=3416, 3021, 2933, 2903, 2858, 1635, 1423, 1275 cm^{-1}. MS (EI): m/z (%): 219 [$M^{+\cdot}$] (25). Elemental analysis calcd for $C_{10}H_{18}OS_2$ (218.38): C, 55.00; H, 8.31, S, 29.36. Found C, 55.00; H, 8.29; S, 29.36.

4.4.4. (*Z*)-1-[1,3]Dithian-2-yl-1-hex-4-en-2-ol (38). To a freshly prepared solution of LDBB (32 mL, 9.52 mmol, 0.3 M in THF) at −78 °C was added a solution of selenide **34a** (1.53 g, 4.76 mmol) in THF (3 mL) dropwise. At the end of the addition the dark green solution changed to pale red. It was stirred for a further 10 min at −78 °C and neat methyl iodide (100 μL, 4.76 mmol) was added. The reaction mixture was stirred for 30 min at −78 °C and then a solution of oxirane **41** (418 mg, 2.38 mmol) in THF (1.5 mL) and neat $BF_3\cdot OEt_2$ (150 μL, 2.38 mmol) were added. The reaction mixture was stirred for 2 h at −78 °C and then quenched by addition of a saturated aqueous solution of $NaHCO_3$ (2 mL). The mixture was allowed to reach room temperature and poured into a mixture PE (40 mL)/H_2O (40 mL). It was extracted with petroleum ether (2×40 mL) and the combined organic layers were washed with brine (60 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1 as eluent) to afford 441 mg (85% yield) of the title compound as a crystalline white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.22 (dq, J=9.1, 1.4 Hz, 1H), 5.99 (m, 1H), 4.25 (dd, J=6.8, 6.7 Hz, 1H), 3.89 (m, 1H), 4.05 (m, 1H), 3.10–2.79 (m, 5H), 2.53 (dd, J=12.9, 5.1 Hz, 1H), 2.30–2.02 (m, 4H), 1.72 (dd, J=6.2, 1.4 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=129.3, 106.6, 67.5, 44.2, 42.1, 34.9, 30.5, 30.2, 26.1, 18.5 ppm. IR (neat, NaCl): ν=3410, 3021, 2936, 2858, 1636, 1423, 1275 cm^{-1}. MS (EI): m/z (%): 219 [$M^{+\cdot}$] (25). Elemental analysis calcd for $C_{10}H_{18}OS_2$ (218.38): C, 55.00; H, 8.31, S, 29.36. Found C, 54.98; H, 8.34; S, 29.36.

4.4.5. (*E*)-Methyl-undec-2-en-5-ol (39). To a round bottomed flask containing $Ni(acac)_2$ (10 mg, 0.03 mmol), under argon, was added a solution of alcohol **34h** (250 mg, 0.55 mmol) in THF (9 mL). The suspension was cooled down to 0 °C and methylmagnesium bromide (424 μL, 1.28 mmol, 3.0 M in ether) was added dropwise. At the end of the addition, the solution changed from green to red. The reaction mixture was stirred 16 h at room temperature. It was diluted with EtOAc (5 mL) and poured into a saturated aqueous solution of NH_4Cl (10 mL). The aqueous phase was extracted with EtOAc (3×8 mL) and the combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/EtOAc:10/1 as eluent) to afford 61 mg (60% yield) of the title compound as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.32 (q, J=6.9 Hz, 1H), 3.74–3.60 (m, 1H), 2.19 (d, J=13.2 Hz, 1H), 1.98 (dd, J=13.2, 9.6 Hz, 1H), 1.67 (s, 1H), 1.63 (s, 3H), 1.61 (d, J=6.9 Hz, 3H), 1.52–1.14 (m, 10H), 0.88 (t, J=6.6 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=133.5, 122.6, 68.7, 48.3, 37.3, 32.1, 29.7, 26.0, 22.9, 16.0, 14.4, 13.8 ppm. IR (neat, NaCl): ν=3411, 2958, 2928, 2858, 1638, 1457, 1379, 1125 cm^{-1}. MS (EI): m/z (%): 184 [$M^{+\cdot}$] (4), 96 [$M^{+\cdot}-C_6H_{15}$] (24). HRMS (EI+, M+) calcd for $C_{12}H_{24}O$, 184.1827; found 184.1830.

4.4.6. (*E*)-1-[1,3]Dithian-2-yl-4-methyl-hex-4-en-2-ol (40). To a round bottomed flask containing $Ni(acac)_2$ (2 mg, 0.008 mmol), under argon, was added a solution of alcohol **34i** (134 mg, 0.27 mmol) in THF (2.5 mL). The suspension was cooled down to 0 °C and methylmagnesium bromide (270 μL, 0.8 mmol, 3.0 M in ether) was added dropwise. At the end of the addition, the solution changed from green to red. The reaction mixture was stirred 20 h at room temperature. It was diluted with EtOAc (5 mL) and poured into a saturated aqueous solution of NH_4Cl (8 mL). The aqueous phase was extracted with EtOAc (3×10 mL) and the combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/EtOAc:10/1 as eluent) to afford 40 mg (64% yield) of the title compound as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.33 (qq, J=6.6, 1.2 Hz, 1H), 4.30 (dd, J=8.6, 6.9 Hz, 1H), 4.01 (m, 1H), 3.00–2.78 (m, 4H), 2.18 (dd, J=13.2, 4.5 Hz, 1H), 2.08 (dd, J=13.2, 8.7 Hz, 1H), 2.20–2.08 (m, 1H), 1.96–1.81 (m, 4H), 1.63 (s, 3H), 1.61 (d, J=6.6 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=132.5, 123.1, 65.5, 48.2, 44.5, 42.6, 30.6, 30.3, 26.2, 15.9, 13.7 ppm. IR (neat, NaCl): ν=3413, 2929, 2905, 2858, 1668, 1497, 1382, 1275 cm^{-1}. MS (EI): *m*/*z* (%): 232 [$M^{+\cdot}$] (29), 161 [$M^{+\cdot}-C_5H_9S_2$] (19). Elemental analysis calcd for $C_{11}H_{20}OS_2$ (232.40): C, 56.85; H, 8.67, S, 27.59. Found C, 56.89; H, 8.44; S, 28.36.

4.4.7. (*rac*)-2-[1,3]Dithian-2-ylmethyl-oxirane (41). To a solution of 1,3 dithiane (5.0 g, 41.6 mmol) in THF (100 mL) at −78 °C was added *n*-BuLi (30 mL, 41.6 mmol, 1.6 M in hexanes) dropwise via syringe. The reaction mixture was warmed to −20 °C and stirred at that temperature for 2 h. It was then cooled down to −78 °C and neat (±)-epichlorohydrin (3.3 mL, 41.6 mmol) was added. The mixture was allowed to slowly reach room temperature and was stirred overnight at that temperature. The solution was concentrated under reduced pressure to 75 mL, then washed with H_2O and extracted with petroleum ether (4×40 mL). The combined organic layers were washed with brine (150 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1) to afford 6.68 g (92% yield) of the title compound as a yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=4.26 (t, J=7.0 Hz, 1H), 3.20–3.12 (m, 1H), 3.10–2.80 (m, 5H), 2.55 (dd, J=5.1, 2.7 Hz, 1H), 2.20–2.08 (m, 1H), 1.97 (dd, J=6.9, 6.0 Hz, 2H), 1.94–1.80 (m, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=49.9, 47.3, 45.0, 38.9, 30.8, 30.6, 26.0 ppm. IR (neat, NaCl): ν=3348, 2992, 2901, 2827, 1687, 1480, 1277, 1258 cm^{-1}. MS (EI): *m*/*z* (%): 176 [$M^{+\cdot}$] (84). Elemental analysis calcd for $C_7H_{12}OS_2$ (176.30): C, 47.69; H, 6.86, S, 36.37. Found C, 47.61; H, 6.88; S, 36.07.

4.4.8. (*Z*)-1-[1,3]Dithian-2-yl-4-(2,4,6-triisopropyl-phenylselanyl)-hex-4-en-2-ol (34i). To a solution of iodide **32a** (23.2 g, 51.6 mmol) in THF (500 mL) at −78 °C was added *n*-BuLi (34 mL, 51.6 mmol, 1.6 M in hexanes) dropwise and the mixture was stirred for 15 min at −78 °C. Neat $BF_3\cdot OEt_2$ (3.27 mL, 25.8 mmol) was added and immediately after, a solution of the oxirane **41** (4.5 g, 28.5 mmol) in THF (10 mL) was added all at once. The reaction mixture was stirred at −78 °C for 1 h and then quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (15 mL). The mixture was allowed to slowly reach room temperature. It was diluted with petroleum ether (300 mL), washed with H_2O and extracted several times with petroleum ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1 as eluent) to afford 6.45 g (100% yield, based upon oxirane) of the title compound as a white crystalline solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.99 (s, 2H), 5.81 (q, J=6.6 Hz, 1H), 4.26 (dd, J=9.4, 4.8 Hz, 1H), 3.95–3.80 (m, 1H), 3.70 (hep, J=6.8 Hz, 2H), 2.90–2.78 (m, 5H), 2.05 (d, J=6.5 Hz, 2H), 1.91 (d, J=6.6 Hz, 3H), 2.15–1.72 (m, 2H), 1.70–1.55 (m, 2H), 1.25 (d, J=6.8 Hz, 6H), 1.22 (d, J=6.8 Hz, 6H), 1.17 (d, J=6.8 Hz, 6H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.9, 149.4, 132.1, 127.2, 125.0, 121.5, 65.8, 45.6, 43.8, 41.7, 33.9, 33.7, 30.2, 29.7, 25.7, 24.3, 24.1, 23.8, 16.4 ppm. IR (neat, NaCl): ν=3347, 3042, 2959, 2907, 2867, 1594, 1560, 1462, 1382 cm^{-1}. MS (EI): *m*/*z* (%): 499 [$M^{+\cdot}$] (10), 217 [$M^{+\cdot}-$SeTIPP] (100). Elemental analysis calcd for $C_{25}H_{40}OS_2Se$ (499.68): C, 60.10; H, 8.07; S, 12.83. Found C, 59.97; H, 8.04; S, 13.59.

4.4.9. 1-[1,3]Dithian-2-yl-4-iodo-hex-4-en-2-ol (42). To a solution of selenide **34i** (130 mg, 0.26 mmol) in THF at 0 °C under argon was added dropwise CH_3MgBr (130 μL, 0.39 mmol, 3.0 M in Et_2O). The reaction mixture was stirred for 15 min at 0 °C. This solution was added to a LDBB solution (2.5 mL, 0.3 M in THF) at −78 °C via syringe. At the end of the addition, the solution colour changed from dark green to clear red. It was stirred for 30 min at −78 °C, neat MeI (16 μL, 0.26 mmol) was added and the mixture was stirred for a further 10 min. After the addition, the solution became colourless. A solution of I_2 (165 mg, 0.65 mmol) in THF (2 mL) was added dropwise and the reaction mixture was stirred for 1 h to −78 °C. It was quenched by the addition of ethanol (2 mL) at −78 °C and then it was allowed to reach room temperature. It was diluted with petroleum ether (5 mL), washed with a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) and the aqueous layer extracted several times with petroleum ether. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:1/1 as eluent) to afford 73 mg (81% yield) of the title compound as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.73 (qt, J=6.3, 1.1 Hz, 1H), 4.28 (dd, J=8.4, 6.0 Hz, 1H), 4.35–4.20 (m, 1H), 2.99–2.80 (m, 4H), 2.62 (d, J=6.5 Hz, 2H), 2.25–1.80 (m, 4H), 1.77 (d, J=6.3 Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ=128.4, 106.3, 67.3, 53.3, 44.7, 42.4, 30.6, 30.2, 26.4, 22.5 ppm. IR (neat, NaCl): ν=3348, 2938, 2900, 2827, 1647, 1422, 1275, 1164, 1072 cm^{-1}. MS (EI): *m*/*z* (%): 219 [$M^{+\cdot}-$I] (15), 205 (29), 188 (22), 145 (24). HRMS (CI+, M+) calcd for $C_{10}H_{17}IOS_2$, 344.9765; found 344.9769.

4.4.10. (*Z*)-1-[1,3]Dithian-2-yl-trimethylsilanylmethyl-hex-4-en-2-ol ((*Z*)-6). To a solution of vinyl iodide **42** (462 mg, 1.35 mmol) and $Pd(PPh_3)_4$ (80 mg, 0.07 mmol) in THF (5 mL) was added trimethylsilylmagnesium chloride (1.7 mL, 4.05 mmol, 2.3 M in THF) dropwise. The mixture was stirred overnight at room temperature. It was then poured into a saturated aqueous solution of NH_4Cl (10 mL) and the aqueous layer extracted with EtOAc (4×10 mL).

The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:1.5/1 as eluent) to afford 279 mg (68% yield) of the title compound as a colourless oil. ^1H NMR (500 MHz, $CDCl_3$): $\delta=5.20$ (q, $J=7.0$ Hz, 1H), 4.29 (dd, $J=9.2$, 5.2 Hz, 1H), 3.98 (m, 1H), 2.86 (m, 4H), 2.11 (m, 2H), 2.01 (d, $J=2.4$ Hz, 1H), 1.97 (dd, $J=13.1$, 9.2 Hz, 1H), 1.88 (m, 1H), 1.82 (m, 2H), 1.62 (d, $J=14.4$ Hz, 1H), 1.54 (d, $J=7.0$ Hz, 3H), 1.40 (d, $J=14.4$ Hz, 1H), 0.02 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=134.3$, 119.3, 65.1, 47.3, 44.2, 42.3, 30.3, 30.0, 25.9, 20.8, 13.9, −0.8 ppm. IR (neat, NaCl): $\nu=3321$, 2958, 2931, 2902, 1637, 1561, 1461, 1422, 1382, 1056 cm^{-1}. MS (EI): *m/z* (%): 304 [$M^{+\cdot}$] (25), 233 [$M^{+\cdot}-Si(CH_3)_3$] (39). Elemental analysis calcd for $C_{14}H_{28}OS_2Si$ (304.59): C, 55.31; H, 9.28, S, 21.09. Found C, 55.59; H, 9.10; S, 21.14.

4.4.11. (*E*)-1-[1,3]Dithian-2-yl-trimethylsilanylmethyl-hex-4-en-2-ol ((*E*)-6). To a freshly prepared solution of LDBB (11.2 mL, 3.15 mmol, 0.28 M in THF) at −78 °C was added a solution of allylsilane **34k** (645 mg, 1.58 mmol) in THF (1 mL) dropwise. At the end of the addition the dark green solution turned to pale red. It was stirred for a further 10 min at −78 °C and neat methyl iodide (98 μL, 1.58 mmol) was added. The reaction mixture was stirred for 30 min at −78 °C and then a solution of oxirane **41** (280 mg, 1.58 mmol) in THF (1 mL) and neat $BF_3\cdot OEt_2$ (198 μL, 1.58 mmol) were added. The reaction mixture was stirred for 2 h at −78 °C and then quenched by the addition of a saturated $NaHCO_3$ aqueous solution (2 mL). It was allowed to reach room temperarture and was poured into a mixture of PE (40 mL)/H_2O (40 mL). The aqueous layer was extracted with petroleum ether (2×40 mL) and the combined organic layers were washed with brine (60 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by HPLC using a reverse phase column (hexane/isopropanol:99/1) affording 240 mg (50% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): $\delta=5.54$ (q, $J=6.6$ Hz, 1H), 4.27 (t, $J=7.0$ Hz, 1H), 3.95 (m, 1H), 2.86 (m, 4H), 2.56 (d, $J=3.3$ Hz, 1H), 2.11 (m, 2H), 2.18–2.05 (m, 2H), 1.96–1.85 (m, 2H), 1.88 (s, 2H), 1.81 (d, $J=6.6$ Hz, 3H), 0.05 (s, 9H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=132.3$, 126.7, 67.5, 59.31, 44.3, 42.2, 33.3, 30.3, 29.4, 26.2, 17.9, 0.9 ppm. IR (neat, NaCl): $\nu=3321$, 2957, 2929, 2902, 1640, 1459, 1422, 1164, 1072 cm^{-1}. MS (EI): *m/z* (%): 304 [$M^{+\cdot}-I$] (15), 233 ($M^{+\cdot}-Si(CH_3)_3$, 53), 214 (63). Elemental analysis calcd for $C_{14}H_{28}OS_2Si$ (304.59): C, 55.31; H, 9.28, S, 21.09. Found C, 55.49; H, 9.18; S, 21.06.

4.4.12. 2-(6-[1,3]Dithian-2-ylmethyl-3-methyl-4-methylene)-tetrahydro-pyran-2-yl-ethanol (3). To a solution of (*Z*)-allylsilane **6** (65 mg, 0.21 mmol) and aldehyde **7** (60 μL, 0.32 mmol) in CH_2Cl_2 (2 mL), at −78 °C, was added neat $BF_3\cdot OEt_2$ (41 μL, 0.32 mmol) dropwise. The reaction mixture was allowed to warm up slowly to −30 °C and the disappearance of the starting material was monitored by TLC. The solution was then allowed to slowly reach room temperature. It was poured into a saturated aqueous solution of $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (4×5 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude material was purified by flash chromatography (PE/Et_2O:2/1) affording 55 mg (91% yield) of the title compound as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$): $\delta=4.80$ (d, $J=1.5$ Hz, 1H), 4.73 (d, $J=1.5$ Hz, 1H), 4.23 (dd, $J=9.3$, 4.8 Hz, 1H), 3.92–3.82 (m, 2H), 3.62 (tt, $J=10.0$, 3.0 Hz, 1H), 3.18 (td, $J=9.6$, 3.0 Hz, 1H), 3.00–2.66 (m, 4H), 2.30–1.60 (m, 9H), 1.99 (d, $J=6.9$ Hz, 3H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 148.3, 107.3, 83.2, 75.2, 60.9, 44.4, 42.5, 41.5, 41.4, 35.6, 30.8, 30.5, 26.1, 12.7 ppm. IR (neat, NaCl): $\nu=3332$, 3084, 2935, 2899, 2859, 1647, 1423, 1364, 1324, 1191 cm^{-1}. MS (EI): *m/z* (%): 288 [$M^{+\cdot}$] (89). Elemental analysis calcd for $C_{14}H_{24}O_2S_2$ (288.47): C, 58.29; H, 8.39. Found C, 57.54; H, 8.35.

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