Tetrahedron: *Asymmetry* 20 (2009) 2871–2879

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Syntheses and reactions of terpene β-hydroxyselenides and β-hydroxydiselenides

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ARTICLE INFO

Article history:
Received 12 November 2009
Accepted 1 December 2009
Available online 6 January 2010

ABSTRACT

A convenient method for the synthesis of optically active *trans*-hydroxyselenides and *trans*-hydroxydiselenides from the bicyclic terpene group based on the reactions of sodium selenide or sodium diselenide with *cis*- and *trans*-(+)-3-carane, *trans*-(+)-2-carane and (−)-β-pinane epoxides is described. The corresponding *cis*-hydroxy and *cis*-methoxydiselenides were obtained in the reaction of sodium diselenide with β-hydroxy- and β-methoxytosylates. The influence of a hydroxy group at the β-position on the diastereomeric ratio of the products of the asymmetric methoxyselenenylation of styrene has been established by composition of the products, crystal structure analyses, and theoretical calculations using a DFT method on the B3LYP level (6-311G(d)).

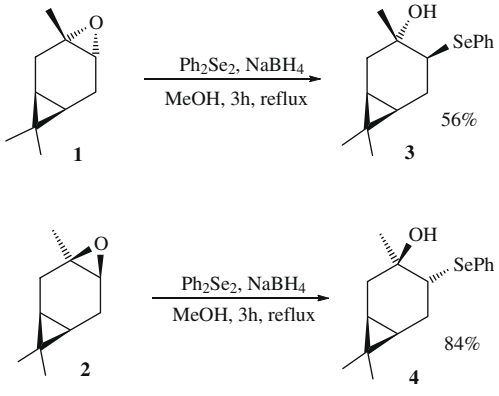
1. Introduction

Optically active diselenides are a very important class of organic compounds. They were frequently used as chiral auxiliaries and ligands in asymmetric syntheses.[1,2] For example, the optically active electrophilic reagents obtained from diselenides have been used for the formation of new asymmetric carbon–oxygen, carbon–nitrogen, and carbon–carbon bonds in addition reactions to the double bonds or in cyclization reactions.[3–6] Another important example is the use of chiral diselenides as the precursors of nucleophilic reagents for epoxide ring openings.[7] An essential advantage of the use of organoselenium reagents in synthesis is the fact that the products might easily be transformed by elimination or substitution of a selenide group.[4,8–10]

Recently we have reported a convenient method for the synthesis of optically active non-functionalized and functionalized diselenides from mono- and bicyclic terpene group, based on the reaction of alkyl tosylates and chlorides with sodium diselenide.[11,12] We have demonstrated that the terpene diselenides can be used successfully for asymmetric methoxyselenenylation and selenocyclization reactions.[12–16]

The main goal of the currently presented investigations was to develop a new convenient methodology for the synthesis of *trans*-hydroxydiselenides based on the reaction of sodium diselenide with the epoxides derived from the carane and pinane groups. Another aim was to establish the regio- and stereoselectivity of the epoxide ring opening in the reaction with sodium diselenide.

During our earlier investigations, we had established that β-pinane and (+)-2- and (+)-3-carane epoxides react easily with a selenium anion. For example, in the reactions of the (+)-3-carene *cis*-epoxide **1** and *trans*-epoxide **2** with sodium benzenoselenolate, we obtained the corresponding hydroxyphenylselenides **3** and **4**[17] (Scheme 1).



Scheme 1. Synthesis of hydroxyphenylselenides.

There are only two literature reports on the synthesis of hydroxydiselenides from epoxides. One paper reported the reaction of selenium hydride with ethylene oxide[18,19] and the second one described the reaction of propylene oxide with lithium diselenide.[20]

To explore other possibilities, we decided to obtain the corresponding *cis*-hydroxy- and *cis*-methoxydiselenides in the reaction

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doi:10.1016/j.tetasy.2009.12.001

of *trans*-hydroxy- and *trans*-methoxytosylates with sodium diselenide.

The final goal was to use the hydroxy- and methoxydiselenides for the methoxyselenenylation reaction of styrene to establish the influence of hydroxy and methoxy groups at the β-position relative to the diselenide group on the diastereomeric ratio of the reaction products and to compare them with the results obtained for other alkyl diselenides.

2. Results and discussion

The initial investigations on epoxide ring opening with sodium diselenide were conducted with the use of cyclohexane epoxide **5**. Using the methodology of sodium diselenide generation (Se, NaOH, $N_2H_4{\cdot}H_2O$, DMF 15 min 100 °C—method 1) described by us earlier,[12] we obtained a mixture of three products. The ^{77}Se NMR analysis revealed their identity as selenide **6**, diselenide **7,** and triselenide **8** (Scheme 2). The composition of the products depended on the temperature and time of the reaction. The best yield was obtained for the reaction conducted at room temperature for 24 h (Table 1).

Using a two-step methodology for the synthesis of sodium diselenide described by Krief,[21] we obtained a mixture of the two products, selenide **6** and diselenide **7** in a 22:88 ratio (20 °C, 24 h—method 2). The problems caused by the separation of the reaction mixture led us to further modify sodium diselenide synthesis. The best result for the synthesis was observed using a two-step method. In the first step, we obtained sodium selenide (Se, $NaBH_4$, DMF/EtOH 1:1, 65 °C, 15 min.), then a further equivalent of selenium was added (1 h, rt)—method 3. From the reaction with oxide **5**, we obtained a mixture of diselenide **7** and triselenide **8** in a ratio 72:28. We did not observe the formation of selenide **6**. Purification of the crude reaction mixture, based on a reduction with $NaBH_4$ and subsequent air oxidation, selectively gave diselenide **7** (Scheme 3). The purification procedure of diselenides via reduction and subsequent air oxidation has also been described by Wirth et al.[22,23]

As a result of the sodium selenide reaction with cyclohexane oxide we obtained selenide **6** (Scheme 4).

The above methodology for the preparation of sodium selenide and sodium diselenide was used for the synthesis of selenides **14–17** and diselenides **18–21** derived from (+)-3-carene, (+)-2-carene, and (−)-β-pinene (Scheme 5). These reactions were conducted at 75 °C for 9 h. The synthesis of selenide **16** from epoxide **12** was unsuccessful, probably because of steric effects. The epoxides **10**, **12,** and **13** were prepared in the reaction of (+)-3-carene, (+)-2-carene, and (−)-β-pinene with peracetic acid.[24] *cis*-(+)-3-Carene epoxide **11** was obtained by the Chabudzyński method.[25]

The structures of diselenides **18** and **19** were confirmed by X-ray structural analysis (Figs. 1 and 2).[26–28]

Structure **18** contains two diselenide molecules in the asymmetric unit. The selenium atoms are bound to C3, while the C–Se distances vary between 1.968(5) and 1.985(5) Å and are similar to those reported for other terpene diselenides.[12,13] The Se–Se distances of 2.2995(7) and 2.2979(7) Å for Se1–Se2 and Se3–Se4, respectively, are slightly shorter than that of 2.3182(11) Å reported for dineomenthyl diselenide.[12] The conformation of the diselenide bridges in two molecules is almost identical with the C–Se–Se–C torsion angles being 80.25(18)° and 80.19(19)° for C3–Se1–Se2–C13 and C23–Se3–Se4–C33, respectively, with the absolute values significantly lower than that of −112.1(4)°, reported for dineomenthyl diselenide.[12]

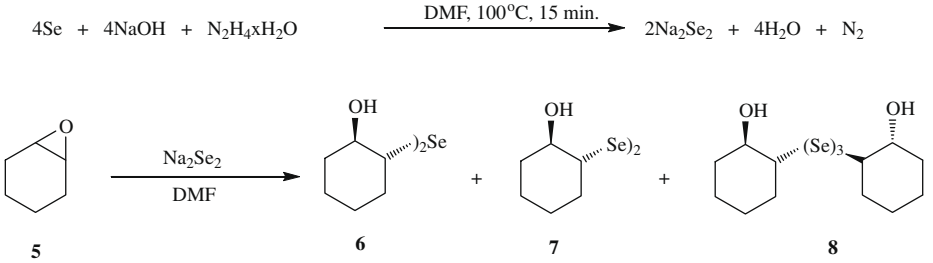
Table 1
Yields and the products of the reaction of the epoxide ring opening with sodium diselenide—method 1

Temp (°C)	Time (h)	Yield (%)	Composition of products[a] (%)		
			6	**7**	**8**
100	2	66	67	26	7
50	3	73	49	35	16
20	24	99	49	51	—

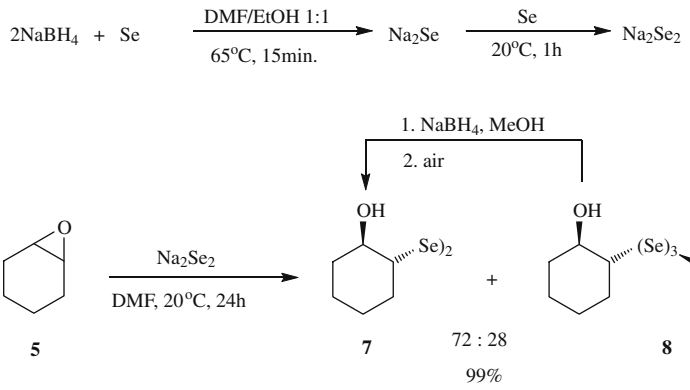
[a] Established on the basis of ^{77}Se NMR of the crude products.

In compound **18**, the hydroxy groups bound to C4 or its equivalents occupy the positions resulting in the (4*S*)-configuration in all carane moieties. The (3*S*,4*S*)-configuration observed for all carane moieties results in the Se–C3–C4–O torsion angles being slightly different for the two halves of each molecule. These values are Se1–C3–C4–O1 99.5(4)° and Se2–C13–C14–O2 80.4(4)° in molecule 1, while the corresponding values in molecule 2 are Se4–C33–C34–O4 95.7(4)° and Se3–C23–C24–O3 85.6(4)°. Such a geometry results in the intramolecular Se···O contacts varying between 3.459(3) Å for Se2–O2 to 3.690(3) Å for Se1–O1, the distances almost equal to the sum of the van der Waals radii of these atoms. This indicates the intramolecular interactions between these heteroatoms. On the other hand, the positions of the H atoms on the hydroxy groups do not suggest any OH···Se hydrogen bond.

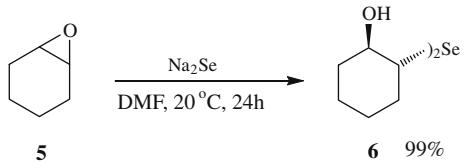
The asymmetric part of compound **19** contains a single diselenide molecule. The hydroxy group and selenide atom are bound to the ring system to give a (3*R*,4*R*)-absolute configuration, which is opposite to that found for **18**. The selenium atoms are bound to C3, while the C–Se distances of 2.001(5) and 1.996(6) Å are slightly longer that those reported for **18**. The spatial arrangement of Se and hydroxy group in **19** results in the torsion angles Se1–C3–C4–O1 −55.4(6) and Se2–C13–C14–O2 −55.1(5)°, with their absolute values being much smaller than those of 80.4(4)° to 99.5(4)° found for **18**. This indicates an increased steric hindrance in **19** when compared to its (3*S*,4*S*)-counterpart and explains the larger C–Se distances observed in **19**. Such a position of both the substituents in **19** results in the Se–O distances being 3.141(4) and 3.145(4) Å for Se1···O1 and Se2···O2, respectively. These distances are more that 0.4 Å shorter than those calculated for **18**, and this confirms that intramolecular interactions between the heteroatoms, are much stronger for the (3*R*,4*R*)-diastereoisomer. On the other



Scheme 2. The epoxide ring opening with sodium diselenide—method 1.



Scheme 3. The epoxide ring opening with sodium diselenide—method 3.

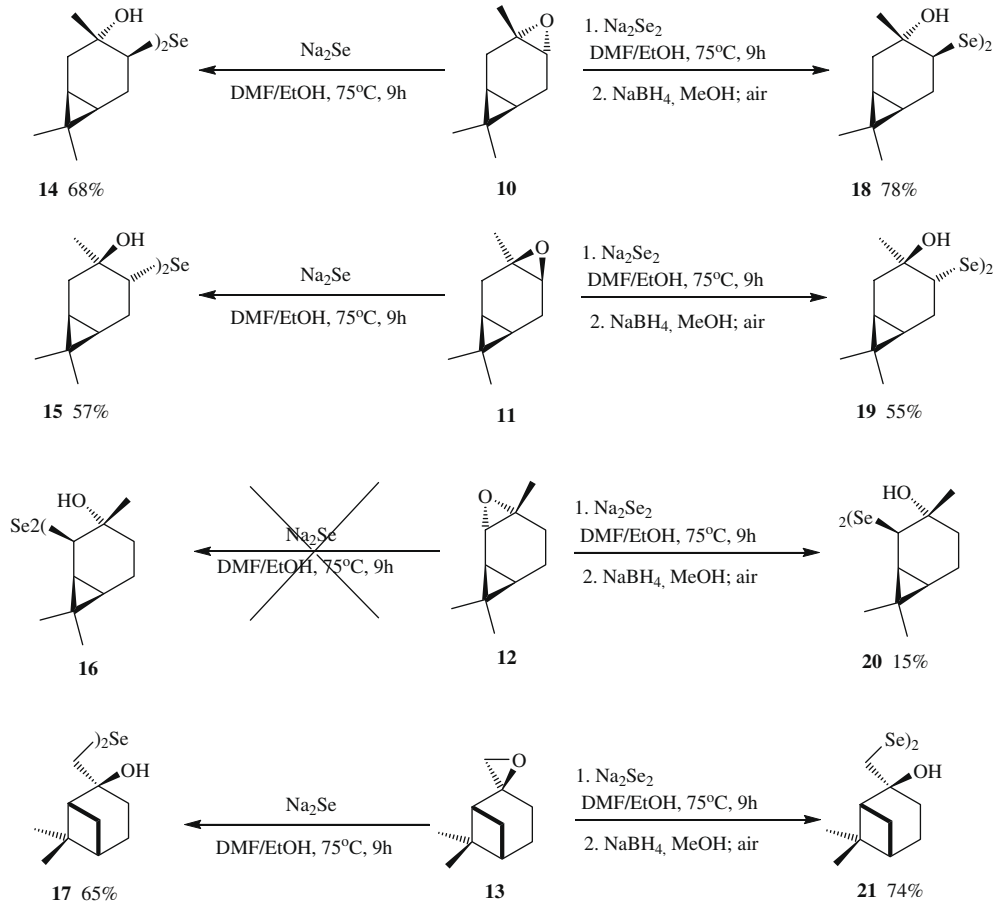


Scheme 4. Synthesis of *trans*-hydroxyselenide **6**.

hand, the Se1···C10 and Se2···C20 distances of 3.401(7) and 3.442(7) Å, are similar to those reported for **18**.

The conformation of the diselenide bridge in **19** as described with the torsion angle C3–Se1–Se2–C13 of −107.9(2)° is opposite to that found for **18**, but is similar to that of −112.1(4)°, found for dineomenthyl diselenide.[12] The Se–Se distance Se1–Se2 of 2.3136(9) Å is significantly longer than that found in both molecules of the (3*S*,4*S*)-diastereoisomer **18**, but is almost identical to that found for dineomenthyl diselenide.[12]

The syntheses of *cis*-hydoxydiselenide **24** and *cis*-methoxydiselenide **27** were conducted by the reaction of *trans*-hydroxytosylate **23** and *trans*-methoxytosylate **26** with sodium diselenide (Scheme 6). Tosylates **23** and **26** were obtained from oxide **10** and a 1% aqueous or methanolic solution of sulfuric acid. Then the reaction was carried with tosyl chloride in pyridine.



Scheme 5. Synthesis of *trans*-hydroxyselenides **14**–**17** and *trans*-hydroxydiselenides **18**–**21**.

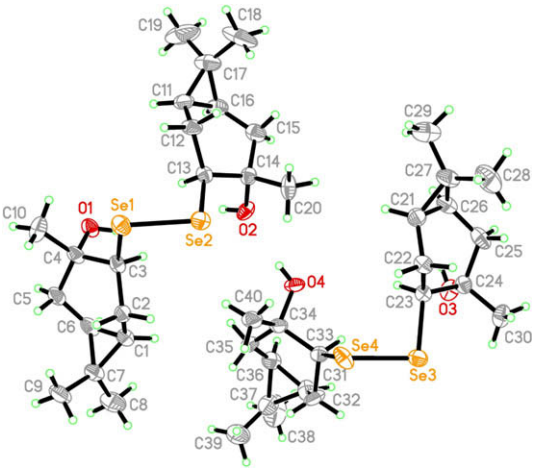


Figure 1. Asymmetric unit of the structure of diselenide **18**.

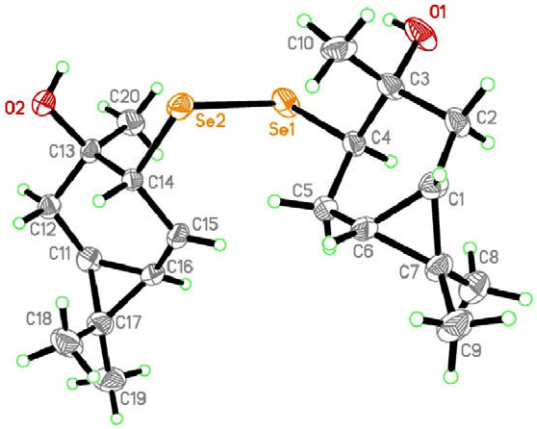
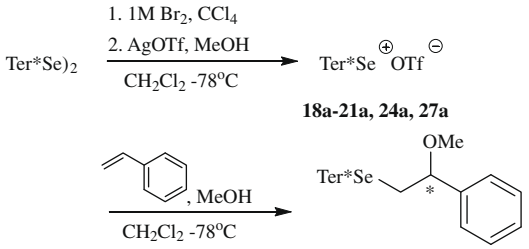


Figure 2. Asymmetric part of the structure of diselenide **19**.

Hydroxydiselenides **18**–**21**, and **24** and methoxydiselenide **27** were used for the asymmetric methoxyselenenylation of styrene. The first step of the methoxyselenenylation reaction involved the generation of triflate salts **18a**–**21a**, **24a,** and **27a** as a result of a reaction of diselenides with bromine and silver triflate, then the reaction with styrene was carried out(Table 2). The isolation of the methoxyselenenylation products from diselenides **20** and **21** was unsuccessful.



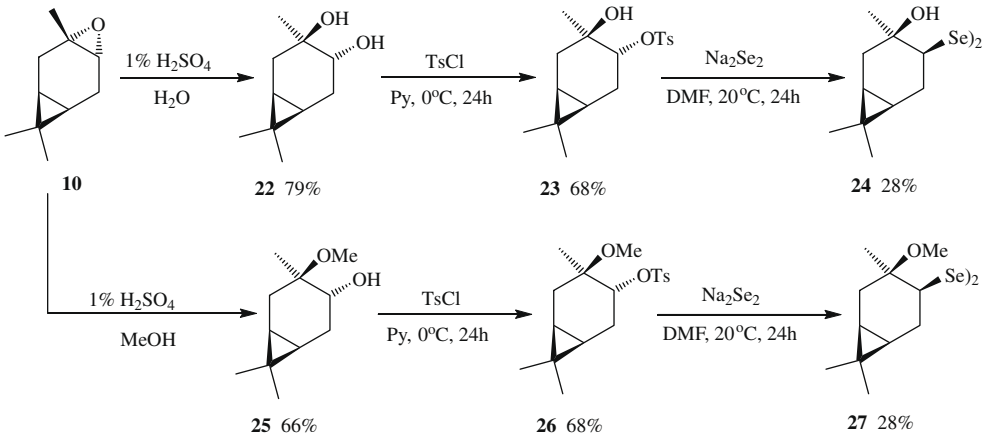
The highest diastereoselectivity of a methoxyselenenylation reaction was obtained for electrophile **19a** (dr 90:10). We assume, that the significant increase in diastereoselectivity for electrophile **19a** is the result of an equatorial–equatorial arrangement of a hydroxy and selenide group in the carane system, for which the effective interaction between the oxygen and selenium atom is possible ($n - \sigma^*$). The possibility of heteroatom–selenium interactions and their influence on the reactivity has been discussed earlier.[29,30]

On the basis of molecular modeling by a DFT method (B3LYP 6-311G(d))[31–33] we have optimized a geometry for selenium electrophiles **32**–**34** derived from hydroxydiselenides **18**, **19,** and **24** (Fig. 3). To simplify the calculations, triflate anions have been replaced with bromine anions.

The DFT calculations for electrophile **32** proved that the axial–axial arrangement of the hydroxy and selenide groups made the interaction of oxygen with an antibonding orbital of a selenium–bromine bond impossible. Also, the axial Se–Br group and the equatorial OH group for an electrophile **34** did not permit the Se···O interaction. Despite the fact that the sum of the van der Walls radii (vdw(Se) + vdw(O) = 1.90 + 1.52 = 3.42 Å)[34] is greater than the calculated distance between selenium and oxygen ($r_{Se\cdots O}$ = 3.09 Å), an efficient overlap of orbitals was not possible because of the 76.5° angle value ($\theta_{O\cdots Se-Br}$). For electrophile **33** in which the hydroxy and selenium groups occupy an equatorial–equatorial position, the interatomic distance Se···O ($r_{Se\cdots O}$ = 2.84 Å) and nearly linear arrangement of the O···Se–Br atoms ($\theta_{X\cdots Se-Br}$ = 155.8°) created a possibility of interactions between oxygen and selenium atoms. It seems that the observed increase of diastereoselection of a methoxyselenenylation reaction for an electrophile **19a** results from the possibility of such interaction.

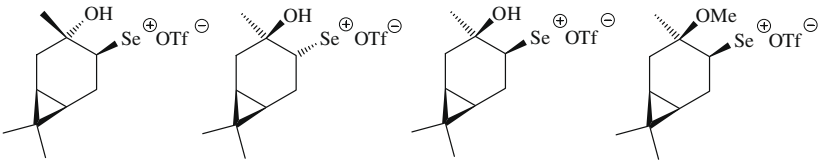
3. Conclusions

A convenient method for the *trans*-hydroxyselenides and *trans*-hydroxydiselenides synthesis from the pinane and carane groups

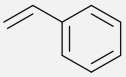
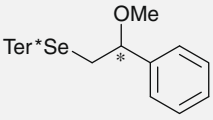


Scheme 6. Synthesis of *cis*-hydroxydiselenide **24** and *cis*-methoxydiselenide **27**.

Table 2
Methoxyselenenylation of styrene with triflate salts obtained from hydroxydiselenides



18a **19a** **24a** **27a**

Alcene	Electophile	Product		dr[a]	Yield (%)
	**18a**		**28**	74:26	58
	19a		**29**	90:10	54
	24a		**30**	61:39	60
	27a		**31**	64:36	69

[a] dr established on the basis of ^{1}H and ^{77}Se NMR.

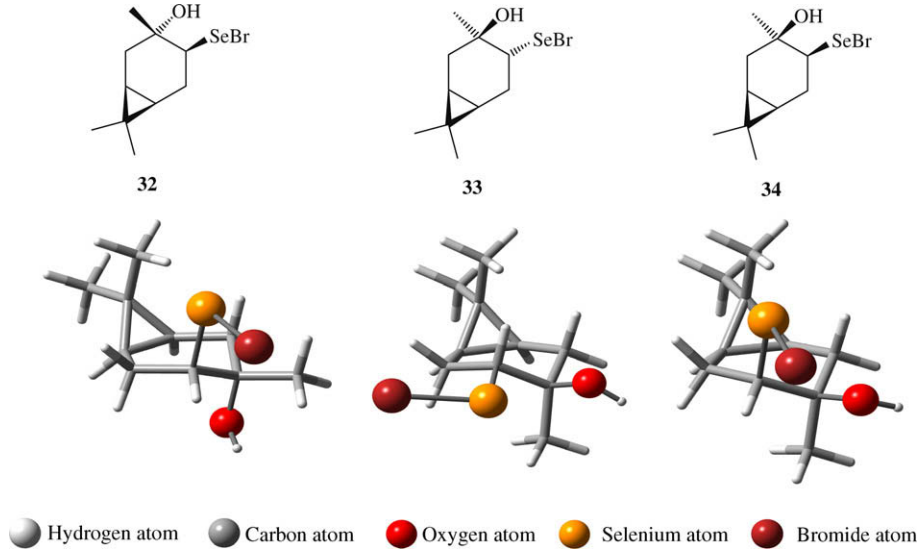


Figure 3. The DFT-optimized structures of selenium electrophiles **32**–**34**.

based on the reaction of epoxides with sodium selenide and sodium diselenide has been described. It has been shown that the method used for the synthesis of sodium diselenide influences the composition of the products of the epoxide ring opening. Convenient conditions have also been established for the sodium diselenide synthesis leading to the epoxide ring opening products, which do not contain selenides. It has been shown that the respective *cis*-hydroxy and *cis*-methoxydiselenides can be obtained as a result of a reaction of sodium diselenide with *trans*-hydroxy and *trans*-methoxytosylates.

The hydroxy- and methoxydiselenides have been used for the asymmetric methoxyselenenylation of styrene. Analysis of the reaction products, crystal structures, and DFT calculations showed that the structure of the electrophile and the intramolecular oxygen–selenium interactions seem to be an important factor resulting in a high diastereomeric ratio of the products. Diselenide **19** revealed the best diastereomeric ratio for the products of methoxyselenenylation reactions of styrene among different alkyl diselenides derived from the *p*-menthane, pinane, and carane systems. No significant increase in the diastereoselectivity after the change of a hydroxy for a methoxy group was observed.

4. Experimental

Melting points were measured with a Büchi Tottoli SPM-20 heating unit and are uncorrected. NMR spectra were recorded on Bruker AM-300 at 300 MHz or Varian 200 at 200 MHz for ^{1}H and 75.5 MHz or 50.3 MHz for ^{13}C. Chemical shifts are expressed in parts per million (ppm) relative to TMS. ^{77}Se NMR spectra were recorded on Varian 200 with diphenyl diselenide as an external standard. Elemental analyses were performed on a Vario MACRO CHN analyzer. TLC was conducted on precoated silica gel plates (Merck $60F_{254}$) and the spots were visualized under UV light. Column chromatography was carried out on column using Silica Gel 60 Merck (70–230 mesh). Methanol was distilled from magnesium turning. Dichloromethane was distilled from calcium hydride and restored under molecular sieves 4 Å. All reactions requiring anhydrous conditions were conducted in flame-dried apparatus.

4.1. General procedure for the preparation of dialkyl selenides

To a mixture of sodium tetrahydroborate (0.38 g, 10.0 mmol) and selenium (0.40 g, 5.0 mmol), anhydrous ethanol (10 mL) was carefully added at ambient temperature under an argon atmosphere. Dry DMF (10 mL) was added and the mixture was warmed up to 60 °C for 10 min. The dark brownish solution was decolorized. The reaction mixture was then allowed to cool to ca. 20 °C and epoxide (10 mmol) was added all at once. The reaction mixture was stirred and kept at constant temperature (for terpene oxides, 75 °C) for 9–20 h. The solution was poured into water (50 mL) and extracted with diethyl ether (3 × 50 mL). The combined ethereal layers were washed with water (50 mL), brine (50 mL), dried with anhydrous $MgSO_4$, and the solvent was evaporated. A crude product was purified by column chromatography, eluting with CH_2Cl_2/EtOAc, 95:5→90:10 to give the pure dialkyl selenide.

4.1.1. *rac*-Bis(*trans*-2-hydroxycyclohexyl) selenide 6

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 95:5. Yield 99%; colorless solid; mp 73–75 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.15–1.39 (m, 6H), 1.40–1.97 (m, 6H), 2.02–2.30 (m, 4H), 2.60–3.08 (m, 4H), 3.30–3.61 (m, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.3 (4 × CH_2), 26.6 (2 × CH_2), 26.7 (2 × CH_2), 34.3 (2 × CH_2), 33.5 (2 × CH_2), 34.6 (2 × CH_2), 34.7 (2 × CH_2), 47.4 (2 × CH), 49.3 (2 × CH), 72.8 (2 × CH), 74.8 (2 × CH) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 272.6 (Se), 294.3 (Se) ppm. Elemental Anal. Calcd for $C_{12}H_{22}O_2Se$ (277.26): C, 51.98; H, 8.00. Found: C, 52.07; H, 8.09.

4.1.2. (1*S*,3*S*,1′*S*,3′*S*)-(+)-Bis(3-hydroxy-4-caranyl) selenide 14

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 90:10. Yield 68%; yellow solid; mp 97–98 °C; $[\alpha]_D^{20} = +117.3$ (*c* 5.00, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.68–0.88 (m, 4H), 0.96 (s, 6H, CH_3), 0.99 (s, 6H, CH_3), 1.23 (s, 6H, CH_3), 1.25–1.35 (m, 4H), 2.02 (dd, *J* = 15.6, 9.0 Hz, 2H), 2.29–2.45 (m, 4H), 2.91 (dd, *J* = 10.8, 4.8 Hz, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.4 (2 × CH_3), 18.4 (2 × CH), 18.8 (2 × C), 23.7 (2 × CH), 27.6 (2 × CH_2), 28.3 (2 × CH_3), 28.6 (2 × CH_3), 33.2 (2 × CH_2), 55.0 (2 × CH), 72.4 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 247.7 (Se) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se$ (385.44): C, 62.32; H, 8.89. Found: C, 62.41; H 8.96.

4.1.3. (1*S*,3*R*,1′*S*,3′*R*)-(−)-Bis(3-hydroxy-4-isocaranyl) selenide 15

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 90:10. Yield 57%; yellow solid; mp 99–101 °C; $[\alpha]_D^{20} = -129.4$ (*c* 4.80, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.48–0.81 (m, 4H), 0.95 (s, 6H, CH_3), 0.97 (s, 6H, CH_3), 1.21 (s, 6H, CH_3), 1.24–1.32 (m, 2H), 1.95–2.13 (m, 4H), 2.32 (dd, *J* = 15.0, 7.2 Hz, 2H), 2.46 (s, 2H, OH), 2.71 (dd, *J* = 12.9, 7.2 Hz, 2H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.3 (2 × CH_3), 17.7 (2 × C), 20.4 (2 × CH), 20.5 (2 × CH), 23.1 (2 × CH_3), 28.7 (2 × CH_3), 30.3 (2 × CH_2), 33.4 (2 × CH_2), 55.2 (2 × CH), 71.4 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 206.8 (Se) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se$ (385.44): C, 62.32; H, 8.89. Found: C, 62.44; H, 8.79.

4.1.4. (1*R*,2*S*,1′*R*,2′*S*)-(−)-Bis(2-hydroxymyrtanyl) selenide 17

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 95:5. Yield 65%; yellow solid; mp 71–73 °C; $[\alpha]_D^{20} = -70.0$ (*c* 5.20, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.92 (s, 6H, CH_3), 1.22 (s, 6H, CH_3), 1.49 (d, *J* = 10.0 Hz, 2H), 1.75–1.95 (m, 10H), 1.97–2.05 (m, 2H), 2.12–2.25 (m, 2H), 2.85 (br s, 2H, OH), 2.95 (s, 4H, CH_2) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.5 (2 × CH_3), 24.8 (2 × CH_2), 27.4 (2 × CH_2), 27.5 (2 × CH_3), 30.9 (2 × CH_2), 38.1 (2 × C), 40.8 (2 × CH), 42.3 (2 × CH_2), 52.1 (2 × CH), 75.8 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 21.1 (Se) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se$ (385.44): C, 62.32; H, 8.89. Found: C, 62.40; H, 8.96.

4.2. General procedure for the preparation of dialkyl diselenides

To a mixture of sodium tetrahydroborate (0.38 g, 10.0 mmol) and selenium (0.40 g, 5.0 mmol), anhydrous ethanol (10 mL) was carefully added at ambient temperature under an argon atmosphere. Then dry DMF (10 mL) was added and the mixture was warmed up to 60 °C for 10 min. The dark brownish solution was decolorized. The reaction mixture was then allowed to cool to ca. 20 °C and another portion of selenium (0.40 g, 5.0 mmol) was added. The reaction mixture was stirred at this temperature for an additional 1 h, and the respective epoxide (10.0 mmol) was added with vigorous stirring. Temperature was kept constant (for terpene oxides, 75 °C) for 9–20 h. The solution was poured into water (50 mL), and extracted with diethyl ether (3 × 50 mL). The combined ethereal layers were washed with water (50 mL), brine (50 mL), dried with anhydrous $MgSO_4$, and the solvent was evaporated. A crude product was purified by column chromatography, eluting with CH_2Cl_2/EtOAc, 95:5→90:10 to give the pure dialkyl diselenide.

4.2.1. *rac*-Bis(*trans*-2-hydroxycyclohexyl) diselenide 7

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 95:5. Yield 91%; yellow crystalline solid; mp 76–78 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.28–1.48 (m, 6H), 1.50–1.85 (m, 6H), 2.05–2.25 (m, 2H), 2.64 (br s, 2H, OH), 2.71 (br s, 2H, OH), 2.80–2.95 (m, 2H), 3.40–3.55 (m, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.1 (2 × CH_2), 24.2 (2 × CH_2), 26.3 (4 × CH_2), 33.3 (2 × CH_2), 33.4 (2 × CH_2), 34.3 (4 × CH_2), 51.2 (2 × CH), 51.6 (2 × CH), 73.0 (2 × CH), 73.1 (2 × CH) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 304.9 (Se_2), 309.0 (Se_2) ppm. Elemental Anal. Calcd for $C_{12}H_{22}O_2Se_2$ (356.22): C, 40.46; H, 6.22. Found: C, 40.49; H, 6.20.

4.2.2. (1*S*,3*S*,1′*S*,3′*S*)-(+)-Bis(3-hydroxy-4-caranyl) diselenide 18

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 90:10. Yield 78%; yellow crystalline solid; mp 63–65 °C; $[\alpha]_D^{20} = +230.7$ (*c* 5.50, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.69–0.92 (m, 4H), 0.98 (s, 6H, CH_3), 1.00 (s, 6H, CH_3), 1.30 (s, 6H, CH_3), 1.33 (m, 4H), 1.97 (dd, *J* = 15.3, 8.4 Hz, 2H), 2.31 (s, 2H, OH), 2.93 (ddd, *J* = 14.7, 7.8, 5.7 Hz, 2H), 3.37 (dd, *J* = 10.5, 5.7 Hz, 2H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.3 (2 × CH_3), 18.0 (2 × C), 18.7 (2 × CH), 22.8 (2 × CH), 26.9 (2 × CH_2), 28.1 (2 × CH_3), 28.3 (2 × CH_3), 33.4 (2 × CH_2), 55.3 (2 × CH), 73.0 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 360.8 (Se_2) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se_2$ (464.40): C, 51.73; H 7.38. Found: C, 51.65; H, 7.36.

4.2.3. (1*S*,3*R*,1′*S*,3′*R*)-(−)-Bis(3-hydroxy-4-isocaranyl) 19

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 90:10. Yield 55%; yellow crystalline solid; mp 102–104 °C; $[\alpha]_D^{20} = -219.5$ (*c* 5.10, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.61 (t, *J* = 8.4 Hz, 2H), 0.78 (dt, *J* = 9.4, 5.0 Hz, 2H) 0.99 (s, 6H, CH_3), 1.03 (s, 6H, CH_3), 1.22 (s, 6H, CH_3), 1.23–1.37 (m, 2H), 1.97–2.16 (m, 4H), 2.30 (dd, *J* = 15.0, 8.4 Hz, 2H), 2.39 (s, 2H, OH), 3.07 (dd, *J* = 12.6, 7.4 Hz, 2H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.2 (2 × CH_3), 17.8 (2 × C), 20.4 (2 × CH), 20.6 (2 × CH), 22.4 (2 × CH_3), 28.6 (2 × CH_3), 29.3 (2 × CH_2), 34.7 (2 × CH_2), 58.5 (2 × CH), 72.4 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 352.1 (Se_2) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se_2$ (464.40): C, 51.73; H, 7.38. Found: C, 51.70; H, 7.40.

4.2.4. (1*S*,3*R*,1′*S*,3′*R*)-(−)-Bis(3-hydroxy-2-caranyl) 20

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 90:10. Yield 15%; yellow oil;

$[\alpha]_D^{20} = -174.9$ (*c* 4.86, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.81–1.00 (m, 2H), 1.06 (s, 6H, CH_3), 1.17 (s, 6H, CH_3), 1.19–1.45 (m, 4H), 1.45 (s, 6H, CH_3), 1.50–1.68 (m, 4H), 1.84–2.08 (m, 2H), 2.33 (s, 2H, OH), 4.25 (d, *J* = 10.6 Hz, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 16.1 (2 × CH_2), 17.4 (2 × CH_3), 22.2 (2 × C), 22.3 (2 × CH), 26.6 (2 × CH), 28.3 (2 × CH_3), 30.1 (2 × CH_3), 33.1 (2 × CH_2), 55.6 (2 × CH), 72.6 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 431.1 (Se_2) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se_2$ (464.40): C, 51.73; H, 7.38. Found: C, 51.92; H, 7.57.

4.2.5. (1*R*,3*S*,1′*R*,3′*S*)-(−)-Bis(2-hydroxymyrtanyl) diselenide 21

Purification by column chromatography on silica gel with methylene chloride/ethyl acetate, 95:5. Yield 74%; yellow solid; mp 87–90 °C; $[\alpha]_D^{20} = -99.7$ (*c* 5.40, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.95 (s, 6H, CH_3), 1.24 (s, 6H, CH_3), 1.51 (d, *J* = 10.2 Hz, 2H), 1.75–2.10 (m, 8H), 2.12–2.32 (m, 2H), 2.35 (br s, 2H, OH), 3.44 (s, 4H, CH_2), 2.55 (s, 2H), 3.08 (dd, *J* = 12.3, 7.2 Hz, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 23.5 (2 × CH_3), 24.8 (2 × CH_2), 27.2 (2 × CH_2), 27.4 (2 × CH_3), 30.8 (2 × CH_2), 38.2 (2 × C), 40.8 (2 × CH), 47.7 (2 × CH_2), 51.8 (2 × CH), 76.4 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 278.0 (Se_2) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se_2$ (464.40): C, 51.73; H, 7.38. Found: C, 51.89; H, 7.55.

4.3. (1*S*,3*R*)-(−)-3-Hydroxy-4-isocaranol 22

(1*S*,3*S*)-3,4-Epoxycarane **10** (80.0 g, 0.53 mol) was shaken with 1% aqueous solution of H_2SO_4 (480 mL) and crumbled ice (160 g) for 5 h for a decline of the smell of the oxide. Acid was neutralized with 5% aqueous solution of sodium hydroxide, and the precipitate formed was filtered off and dried under vacuum. The resulting (1*S*,3*R*)-(−)-3-hydroxy-4-isocaranol hydrate (89.5 g) was crystallized from hexane to afford the desired anhydrous diol 67.2 g, 79%; mp 84–86 °C; $[\alpha]_D^{23} = -0.6$ (*c* 8.12, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.68–0.75 (m, 2H), 0.97 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 1.22 (d, *J* = 1.0 Hz, 3H, CH_3), 1.24 (m, 1H), 1.57–1.74 (m, 1H), 1.81 (br s, 1H, OH), 1.82–2.18 (m, 3H), 3.38 (dd, *J* = 10.0, 7.1 Hz, 1H, CH) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 15.7 (CH_3), 17.6 (C), 19.0 (CH), 20.0 (CH_3), 21.0 (CH), 27.8 (CH_2), 28.6 (CH_3), 33.7 (CH_2), 73.3 (C), 74.4 (CH) ppm. Elemental Anal. Calcd for $C_{10}H_{18}O_2$ (170.25): C, 70.55; H, 10.66. Found: C, 70.61; H, 10.68.

4.4. (1*S*,3*R*)-(+)-3-Hydroxy-4-isocaranyl tosylate 23

To a stirred solution of a (1*S*,3*R*)-(−)-3-hydroxy-4-isocaranol **22** (2.0 g, 11.75 mmol) in dry pyridine (12 mL) chilled below 5 °C (ice bath) tosyl chloride (2.5 g, 13.0 mmol) was added in one portion. The reaction mixture was stirred at this temperature for an additional 1 h, the cooling bath was removed and stirring was continued at ambient temperature for 20 h. It was then poured into water and extracted with chloroform. The combined organic phases were washed with water and brine and dried over anhydrous $MgSO_4$. A crude product left after solvent removal was purified on silica gel column chromatography using chloroform/ethyl acetate, 50:50. Yield 68%, colorless oil; $[\alpha]_D^{19} = +12.5$ (*c* 3.28, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.66–0.75 (m, 2H), 0.91 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.31 (m, 1H), 1.77–2.11 (m, 4H), 2.45 (s, 3H, CH_3), 4.26 (dd, *J* = 10.0, 8.0 Hz, 1H, CH), 7.38 (d, *J* = 8.4 Hz, 2H, 2 × CH), 7.80 (d, *J* = 8.4 Hz, 2H, 2 × CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.7 (CH_3), 17.8 (C), 19.2 (CH), 20.4 (CH_3), 21.0 (CH), 21.6 (CH_3), 26.5 (CH_2), 28.2 (CH_3), 33.5 (CH_2), 70.9 (C), 87.2 (CH), 127.7 (2 × CH), 129.8 (2 × CH), 134.0 (C), 144.8 (C) ppm. Elemental Anal. Calcd for $C_{17}H_{24}O_4S$ (324.44): C, 62.93; H, 7.46. Found: C, 63.92; H, 7.79.

4.5. (1*S*,3*R*,1′*S*,3′*R*)-(+)-Bis(3-hydroxy-4-caranyl) diselenide 24

The compound was prepared according to the literature.[12] The crude product was purified on silica gel column chromatography using chloroform. Yield 28%, yellow oil; $[\alpha]_D^{22} = +190.0$ (*c* 10.70, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.55–0.85 (m, 4H), 0.98 (s, 6H, CH_3), 1.02 (s, 6H, CH_3), 1.20 (s, 6H, CH_3), 1.25–1.35 (m, 2H), 2.00–2.10 (m, 4H), 2.29 (dd, *J* = 15.0, 7.5 Hz, 2H), 2.55 (s, 2H, OH), 3.08 (dd, *J* = 12.3, 7.2 Hz, 2H) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.3 (2 × CH_3), 17.9 (2 × C), 20.5 (2 × CH), 20.7 (2 × CH), 22.4 (2 × CH_3), 28.6 (2 × CH_3), 29.4 (2 × CH_2), 34.7 (C2 × H_2), 58.7 (2 × CH), 72.5 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 343.4 (Se_2) ppm. Elemental Anal. Calcd for $C_{20}H_{34}O_2Se_2$ (464.40): C, 51.73; H, 7.38. Found: C, 51.84; H, 7.52.

4.6. (1*S*,3*R*)-(−)-3-Methoxy-4-isocaranol 25

(1*S*,3*S*)-3,4-Epoxycarane **10** (80.0 g, 0.53 mol) was shaken with 1% methanolic solution of H_2SO_4 (480 mL) at ambient temperature for 20 h. The residue was quenched with 5% aqueous solution of sodium hydroxide and the solvent was removed in vacuo. The oily residue was extracted with diethyl ether, washed with water and with brine, dried over anhydrous magnesium sulfate, and concentrated. The crude product was purified by the distillation under reduced pressure 65–67 °C/0.5 mmHg. Yield 66%; colorless oil; $[\alpha]_D^{20} = -9.5$ (*c* 4.44, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.63–0.69 (m, 2H), 0.95 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 1.11 (m, 1H), 1.15 (s, 3H, CH_3), 2.03–2.16 (m, 2H), 2.27 (br s, 1H, OH), 3.20 (s, 3H, OCH_3), 3.39 (dd, *J* = 10.2, 7.4 Hz, 1H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 13.6 (CH_3), 15.8 (CH_3), 17.6 (C), 19.5 (CH), 20.4 (CH), 26.5 (CH_2), 28.1 (CH_2), 28.7 (CH_3), 48.6 (OCH_3), 72.9 (CH), 77.4 (C) ppm. Elemental Anal. Calcd for $C_{11}H_{20}O_2$ (184.28): C, 71.70; H, 10.94. Found: C, 71.76; H, 10.83.

4.7. (1*S*,3*R*)-(−)-3-Methoxy-4-isocaranyl tosylate 26

To a stirred solution of (1*S*,3*R*)-(−)-3-methoxy-4-isocaranol **25** (5.0 g, 27.13 mmol) in dry pyridine (27 mL) chilled below 5 °C (ice bath), tosyl chloride (5.7 g, 30.0 mmol) was added in one portion. The reaction mixture was stirred at this temperature for an additional 1 h, after which the cooling bath was removed and stirring was continued at ambient temperature for 20 h. It was then poured into water and extracted with chloroform. The combined organic phases were washed with water and brine and dried over anhydrous $MgSO_4$. A crude product left after solvent removal was purified on silica gel column chromatography using chloroform. Yield 68%, colorless oil; $[\alpha]_D^{21} = -21.6$ (*c* 7.63, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ = 0.63–0.73 (m, 2H), 0.93 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.88–2.07 (m, 4H), 2.43 (s, 3H, CH_3), 3.00 (s, 3H, OCH_3), 4.36 (dd, *J* = 8.8, 7.4 Hz, 1H, CH), 7.28 (d, *J* = 8.4 Hz, 2H, 2 × CH), 7.78 (d, *J* = 8.4 Hz, 2H, 2 × CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.6 (CH_3), 16.1 (CH_3), 17.9 (C), 18.8 (CH), 20.3 (CH), 21.5 (CH_3), 26.3 (CH_2), 28.2 (CH_3), 29.6 (CH_2), 48.9 (OCH_3), 74.8 (C), 84.7 (CH), 127.7 (2 × CH), 129.3 (2 × CH), 135.0 (C), 144.0 (C) ppm. Elemental Anal. Calcd for $C_{18}H_{26}O_4S$ (338.46): C, 63.88; H, 7.74. Found: C, 63.92; H, 7.79.

4.8. (1*S*,3*R*,1′*S*,3′*R*)-(+)-Bis(3-methoxy-4-caranyl) diselenide 27

The compound was prepared according to the literature.[12] The crude product was purified on silica gel column chromatography using petroleum ether/ethyl acetate, 95:5. Yield 28%, yellow solid; mp 91–94 °C, $[\alpha]_D^{22} = +257.9$ (*c* 4.28, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.49 (dt, *J* = 8.4, 6.0 Hz, 2H), 0.70 (dt, *J* = 8.4, 7.5 Hz, 2H), 1.00 (s, 6H, CH_3), 1.04 (s, 6H, CH_3), 1.38 (s, 6H, CH_3), 1.48–1.60 (m, 4H), 1.82 (dd, *J* = 15.0, 8.4 Hz, 2H), 2.42 (ddd, *J* = 14.4,

13.5, 4.8 Hz, 2H), 2.93 (dd, J = 12.6, 4.8 Hz, 2H), 3.15 (s, 6H, OCH_3) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 15.0 (2 × CH_3), 18.7 (2 × C), 18.8 (2 × CH), 24.0 (2 × CH), 25.7 (2 × CH_3), 26.2 (2 × CH_2), 28.5 (2 × CH_3), 28.6 (2 × CH_2), 49.2 (2 × OCH_3), 56.5 (2 × CH), 75.3 (2 × C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): δ = 341.2 (Se_2) ppm. Elemental Anal. Calcd for $C_{22}H_{38}O_2Se_2$ (492.46): C, 53.66; H, 7.78. Found: C, 53.65; H, 7.80.

4.9. [(1*S*,3*S*)-3-Hydroxy-4-caranyl]-(2-methoxy-2-phenylethyl) selenide 28

Purification by column chromatography on silica gel with chloroform. Yield 58%; colorless oil; dr 74:26; ^1H NMR (300 MHz, $CDCl_3$): major diastereomer δ = 0.62–0.93 (m, 2H), 0.97 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.06–1.22 (m, 2H), 1.25 (s, 3H, CH_3), 2.03 (dd, J = 15.2, 8.4 Hz, 1H), 2.19–2.34 (m, 1H), 2.82–3.07 (m, 4H), 3.24 (s, 3H, OCH_3), 4.36 (dd, J = 8.4, 5.6 Hz, 1H, CH), 7.26–7.41 (m, 5H, 5 × CH) ppm; minor diastereomer—only separated signals: 1.23 (s, 3H, CH_3), 4.38 (dd, J = 8.4, 5.6 Hz, 1H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): major diastereomer δ = 15.3 (CH_3), 18.4 (CH), 18.7 (C), 24.0 (CH), 27.6 (CH_2), 28.3 (CH_3), 28.5 (CH_3), 33.0 (CH_2), 33.2 (CH_2), 52.6 (CH), 56.8 (OCH_3), 72.7 (C), 84.9 (CH), 126.5 (2 × CH), 128.1 (CH), 128.6 (2 × CH), 141.1 (C) ppm; minor diastereomer—only separated signals: 23.6 (CH), 27.3 (CH_2), 32.3 (CH_2), 51.2 (CH), 72.6 (C), 84.1 (CH), 126.7 (2 × CH), 128.5 (2 × CH) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): major diastereomer δ = 195.7 (Se) ppm; minor diastereomer: 191.1 (Se) ppm. Elemental Anal. Calcd for $C_{19}H_{28}O_2Se$ (367.38): C, 62.12; H, 7.68. Found: C, 62.05; H, 7.63.

4.10. [(1*S*,3*R*)-3-Hydroxy-4-isocaranyl]-(2-methoxy-2-phenylethyl) selenide 29

Purification by column chromatography on silica gel with chloroform. Yield 54%; colorless oil; dr 90:10; ^1H NMR (300 MHz, $CDCl_3$): major diastereomer δ = 0.53 (t, J = 8.1 Hz, 1H), 0.79 (dt, J = 9.9, 5.1 Hz, 1H), 0.97 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.27 (m, 1H), 1.28 (s, 3H, CH_3), 1.88 (ddd, J = 15.0, 12.9, 8.1 Hz, 1H), 2.10 (dd, J = 14.7, 10.2 Hz, 1H), 2.25 (dd, J = 15.0, 7.5 Hz, 1H), 2.69 (dd, J = 13.2, 6.0 Hz, 1H), 2.93 (d, J = 6.9 Hz, 2H, CH_2), 3.27 (s, 3H, OCH_3), 3.80 (s, 1H), 4.24 (t, J = 6.9 Hz, 1H, CH), 7.26–7.39 (m, 5H, 5 × CH) ppm; minor diastereomer—only separated signals: 1.00 (s, 3H, CH_3), 3.25 (s, 3H, OCH_3) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): major diastereomer δ = 15.3 (CH_3), 17.6 (C), 20.2 (CH), 20.3 (CH), 22.7 (CH_3), 28.6 (CH_3), 28.9 (CH_2), 33.0 (CH_2), 33.4 (CH_2), 53.9 (CH), 56.9 (OCH_3), 71.6 (C), 84.6 (CH), 126.4 (2 × CH), 128.0 (CH), 128.5 (2 × CH), 140.7 (C) ppm; minor diastereomer—only separated signals: 15.2 (CH_3), 20.4 (CH), 22.8 (CH_3), 28.7 (CH_3), 32.8 (CH_2), 56.7 (OCH_3), 71.5 (C), 84.1 (CH), 126.6 (2 × CH), 140.8 (C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): major diastereomer δ = 171.9 (Se) ppm; minor diastereomer: 165.0 (Se) ppm. Elemental Anal. Calcd for $C_{19}H_{28}O_2Se$ (367.38): C, 62.12; H, 7.68. Found: C, 62.18; H, 7.75.

4.11. [(1*S*,3*R*)-3-Hydroxy-4-caranyl]-(2-methoxy-2-phenylethyl) selenide 30

Purification by column chromatography on silica gel with chloroform. Yield 60%; colorless oil; dr 61:39; ^1H NMR (200 MHz, $CDCl_3$): major diastereomer δ = 0.59 (t, J = 8.4 Hz, 1H), 0.73–0.86 (m, 1H), 0.99 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.22 (s, 3H, CH_3), 1.25–1.35 (m, 1H), 1.91–2.05 (m, 2H), 2.16 (dd, J = 15.0, 7.5 Hz, 1H), 2.36 (s, 1H, OH), 2.61 (dd, J = 12.3, 7.2 Hz, 1H), 2.68 (dd, J = 12.6, 5.4 Hz, 1H, CH*H*), 2.93 (dd, J = 12.6, 8.0 Hz, 1H, CH*H*), 3.22 (s, 3H, CH_3), 4.28 (dd, J = 8.0, 5.4 Hz, 1H, CH), 7.22–7.38 (m, 5H, 5 × CH) ppm; minor diastereomer—only separated signals: 2.70 (dd, J = 12.6, 5.4 Hz, 1H, CH*H*), 2.91 (dd, J = 12.6, 8.0 Hz, 1H, CH*H*), 3.24 (s, 3H, CH_3), 4.29 (dd, J = 8.0, 5.4 Hz, 1H, CH) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): major diastereomer δ = 15.3 (CH_3), 17.9 (C), 20.5 (CH), 20.3 (CH), 20.8 (CH_2), 22.5 (CH_3), 28.5 (CH_3), 29.3 (CH_2), 31.2 (CH_2), 53.9 (CH), 56.9 (OCH_3), 71.6 (C), 84.5 (CH), 126.4 (2 × CH), 128.1 (CH), 128.5 (2 × CH), 140.9 (C) ppm; minor diastereomer—only separated signals: 28.3 (CH_3), 32.0 (CH_2), 56.7 (OCH_3), 71.5 (C), 84.3 (CH), 126.6 (2 × CH), 140.8 (C) ppm; ^{77}Se NMR (38.1 MHz, $CDCl_3$): major diastereomer δ = 146.7 (Se) ppm; minor diastereomer: 147.2 (Se) ppm. Elemental Anal. Calcd for $C_{19}H_{28}O_2Se$ (367.38): C, 62.12; H, 7.68. Found: C, 62.18; H, 7.75.

4.12. [(1*S*,3*R*)-3-Methoxy-4-caranyl]-(2-methoxy-2-phenylethyl) selenide 31

Purification by column chromatography on silica gel with petroleum ether/ethyl acetate, 90:10. Yield 69%; light yellow oil; dr 64:36; ^1H NMR (300 MHz, $CDCl_3$): major diastereomer δ = 0.38–0.50 (m, 1H), 0.59 (dt, J = 8.4, 7.5 Hz, 1H), 0.96 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 1.42–1.61 (m, 2H), 1.71 (dd, J = 15.0, 8.1 Hz, 1H), 2.01–2.12 (m, 1H), 2.47 (dd, J = 12.3, 4.2 Hz, 1H), 2.71 (dd, J = 12.3, 6.3 Hz, 1H, CH*H*), 2.90 (dd, J = 12.3, 7.5 Hz, 1H, CH*H*), 3.10 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3), 4.32 (dd, J = 7.5, 6.3 Hz, 1H, CHSe), 7.34 (m, 5H, 5 × CH) ppm; minor diastereomer—only separated signals: 0.67 (dt, J = 8.4, 7.5 Hz, 1H), 0.98 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.78 (dd, J = 15.0, 8.1 Hz, 1H), 2.69 (dd, J = 12.3, 6.3 Hz, 1H, CH*H*), 2.94 (dd, J = 12.3, 7.5 Hz, 1H, CH*H*), 3.11 (s, 3H, OCH_3), 3.24 (s, 3H, OCH_3), 4.32 (dd, J = 7.5, 6.3 Hz, 1H, CHSe) ppm; ^{13}C NMR (50.3 MHz, $CDCl_3$): major diastereomer δ = 14.8 (CH_3), 18.4 (C), 18.5 (CH), 23.5 (CH), 25.7 (CH_3), 25.8 (CH_2), 28.1 (CH_2), 28.4 (CH_3), 29.7 (CH_2), 48.8 (OCH_3), 50.1 (CH), 56.6 (OCH_3), 74.5 (C), 84.6 (CH), 126.7 (2 × CH), 127.6 (CH), 128.2 (2 × CH), 141.4 (C) ppm; minor diastereomer—only separated signals: 25.9 (CH_3), 29.9 (CH_2), 50.2 (CH), 56.7 (OCH_3), 74.6 (C), 85.0 (CH), 126.4 (2 × CH), 141.6 (C). ^{77}Se NMR (38.1 MHz, $CDCl_3$): major diastereomer δ = 205.3 (Se) ppm; minor diastereomer: 212.2 (Se) ppm. Elemental Anal. Calcd for $C_{20}H_{30}O_2Se$ (381.41): C, 62.98; H, 7.93. Found: C, 62.90; H, 8.01.

4.13. Computational methods

All theoretical calculations were carried out by using the GAUSSIAN03 program.[31] The hybrid Berke 3-Lee-Yang-Parr (B3LYP) exchange—correlation functional[32,33] was applied for DFT calculations. Geometries were fully optimized at the B3LYP/6-311G(d) level of theory. For all stable conformers a minimum of potential energy was established at the B3LYP/6-311G(d) level by verifying that all vibration frequencies were real.

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