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Regio- and Stereocontrolled Synthesis of (*Z*)-α-(Phenylseleno)sulfinyl and -sulfonyl Alkenes via Sulfenic Acids, and a Study of their Reactivity

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Dedicated to Professor Gianfranco Scorrano on the occasion of his 72nd birthday

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A general procedure for the synthesis of α-(phenylseleno)-sulfinyl and -sulfonyl alkenes has been described. 1-(Phenylseleno)ethenyl sulfoxides were prepared by the *syn*-addition of in situ-generated sulfenic acids on to the triple bond of suitably substituted (phenylseleno)acetylenes. 1-(Phenylseleninyl)ethenyl sulfones were obtained by further oxidation of their sulfinyl analogues. The mild conditions of the sulfenic acid/(phenylseleno)alkyne *syn*-addition and its stereospecificity and regioselectivity allowed us to obtain electron-poor alkenes with a well defined stereochemistry and sensitive substituents at the double bond. Chiral (*Z*)-1-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-1-(phenylseleno)-1-hexene was also obtained via the enantiopure 2,3,4,6-tetra-*O*-acetylglucosulfenic acid. The reactivity of α-(phenylseleninyl)sulfinyl and -sulfonyl alkenes has been evaluated in nucleophilic additions to the electron-poor double bond, conducted with hard nucleophiles such as piperidine and phenol.

Introduction

The stereocontrolled synthesis of electron-poor alkenes has always represented an interesting topic in organic synthesis because of the potential of the reactive double bond in nucleophilic additions, 1,3-dipolar and Diels–Alder cycloadditions, because of the nature of the electron-withdrawing (EW) groups present on the unsaturated system, which can control the stereoselectivity of such reactions. In particular, α,β-unsaturated sulfoxides[1] as well as electron-deficient vinylic selenides[2] show many types of reactivity for the ability of these heteroatoms to stabilize both negative and positive charges, because they are good leaving groups and can be subjected to a number of transformations. Furthermore, the sulfinyl group has been shown to be one of the most efficient chiral auxiliaries for accessing optically active vinyl sulfoxides in stereocontrolled syntheses.[3] Vinylic selenides, on the other hand, represent interesting substrates with which cross-coupling reactions with various organometallic reactions can be carried out.[4]

The idea of localizing two heteroatoms, such as selenium and sulfur, in different oxidation states on a double bond has been already exploited and described in few papers, and these substrates act as good nucleophilic acceptors for amines[5] or enamines[6] affording, in the latter case, the corresponding ketones. A radical cyclization route to pyrrolidines has been recently described, based on Michael-type addition of allyl or propargylamines to α-(phenylseleno)-sulfonyl alkenes.[7] A general procedure for the synthesis of 2-alkynylcyclopropanes has also been described, using α-(phenylseleno)sulfonyl enynes as starting materials.[8]

Not many synthetic approaches to seleno- and sulfur-substituted alkenes are reported in the literature. In particular, α-(phenylseleno)sulfinyl and -sulfonyl alkenes are usually obtained following three main procedures, two of which are comparable. They are based on the addition of a phenylselenenyl halide to a vinyl sulfone or sulfoxide in the presence[7] or absence[9] of zinc chloride. Subsequent dehydrohalogenation with a base affords the desired compounds. In a recent methodology, the *cis*-carbocupration of acetylenic sulfoxides, followed by electrophilic reaction with phenylselenenyl bromide, led to α-(phenylseleno)-*p*-tolylsulfinyl alkenes in good yields.[10]

In this paper we present a new approach to the synthesis of α-(phenylseleno)sulfinyl and -sulfonyl alkenes by the *syn*-addition of transient sulfenic acids to the triple bond of variously substituted (phenylseleno)acetylenes.[11] The *syn*-addition of sulfenic acids to the triple bond constitutes a general stereocontrolled methodology to obtain vinyl sulfoxides.[12] Enantiopure sulfenic acids can be generated from suitable enantiopure sulfinyl precursors and their addition to unsaturated bonds produces diastereomeric mixtures of sulfoxides that can usually be separated by simple column

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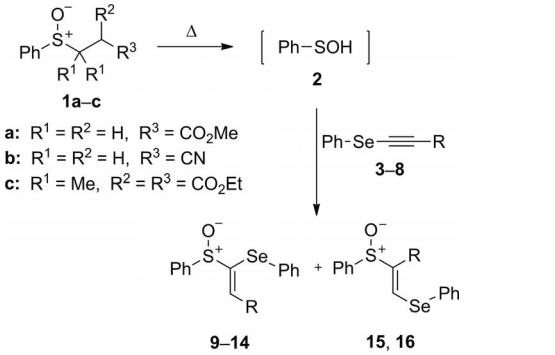
chromatography.[13] We have used this route to obtain optically pure active derivatives. Furthermore, the reactivity of such electron-poor alkenes has been exploited and discussed with regard to accessing substituted vinyl sulfoxides with controlled stereochemistry at the double bond.

Results and Discussion

Synthesis

A general procedure for the synthesis of (phenylseleno)-sulfinyl alkenes is shown in Scheme 1. The key step of the pathway is the in situ generation of sulfenic acid **2** from a suitable sulfinyl precursor, and its *syn*-addition to the triple bond of variously substituted (phenylseleno)acetylenes **3**–**8**, which were prepared according to literature procedures.[11,14] In sulfoxides **1a**–**c**[15] the different alkyl moieties linked to the sulfur atom, with at least one EW group on the β-carbon atom, allow the generation of the transient sulfenic acid **2** by thermal β-*syn*-elimination at different temperatures.[16] We thermolyzed each of the three sulfoxides **1**, in the presence of the same sulfenic acid acceptor **3**, to find the best sulfenic acid precursor to obtain (phenylseleno)sulfinyl alkenes **9**–**16**. Sulfoxide **1c** and 1-(phenylseleno)-1-hexyne (**3**), in 1:3 molar ratio, reacted at 40 °C (CH_2Cl_2) for 14 h to afford **9** in only 40% yield. The use of precursor **1b** led to **9** after 6 h in $ClCH_2CH_2Cl$ (83 °C) in 75% yield. The best sulfenic acid precursor was **1a**, which afforded **9** under the same reaction conditions as those of **1b** but in 85% yield. The use of tetrahydrofuran (THF, 65 °C, 12 h) as the solvent in the reaction of **1a** with **3** was less effective, and **9** was obtained in 70% yield. In all these experiments excess **3** was recovered (75% yield) from column chromatography performed on the reaction mixture.



Scheme 1. General procedure for the synthesis of (phenylseleno)-ethenyl sulfoxides.

Once we had chosen **1a** as the best sulfinyl precursor for sulfenic acid **2**, we decided to test the general validity of the procedure with differently substituted (phenylseleno)acetylenes **3**–**8**, and the results are reported in Table 1. (Phenylseleno)sulfinyl alkenes **9**–**16** were obtained in very good overall yields under mild conditions, allowing the presence of acid/base sensitive substituents such as $SiMe_3$, phthalimido or ester groups (Entries 4–6) in the final products. The *syn*-addition of a sulfenic acid to an unsaturated bond is a stereospecific reaction,[17] which, in these cases, generally led to the exclusive formation of (*Z*)-alkenes. It is also a regioselective addition when substituents are present on the unsaturated bond; it usually follows the Markovnikov rule[15b,18] that the sulfinyl group adds on to the most electrophilic unsaturated carbon atom. The regiochemistry of this addition was determined on the basis of NOESY experiments on **9**: a positive cross peak was observed between the H-2 and H_2-3 resonances (Figure 1). The (*Z*)-configuration in **9** comes from the stereospecificity of the sulfenic acid *syn*-addition. Analogously, the structures of **12**–**14** were unequivocally attributed. The geminal or vicinal spin–spin coupling of the olefinic protons distinguishes **10** from **15** (Experimental Section). Finally, the carbon resonance of SCSe in **11** (142.8 or 142.1 ppm) was in the range 143.8–142.3 ppm, characterizing the corresponding nucleus in strictly related **9**, **13** and **14**.

Table 1. Synthesis of **9**–**16** from **1a** in $ClCH_2CH_2Cl$.

Entry	Ph–Se≡R	Products (ratio)	Reaction time [h]	% Yield[a]
1	**3** R = Bu	**9**	6	85
2	**4** R = H	**10/15** (25 : 75)	6	85
3	**5** R = Ph	**11/16** (98 : 2)	6.5	85
4	**6** R = $SiMe_3$	**12**	6.5	80
5	**7** R = $(CH_2)_3$-NPht	**13**	6	70
6	**8** R = $(CH_2)_3$-OBz	**14**	6	72

[a] Calculated with respect to **1a**. Excess **3**–**8** was always recovered (75% yield).

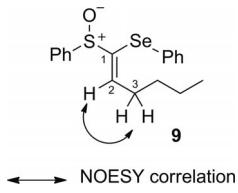


Figure 1. NOESY correlations in **9**.

Compounds **9** and **12**–**14** were obtained with complete and expected regioselectivity (Entries 1 and 4–6, respectively). High regioselectivity was also observed in the reaction of **2** with the unsaturated acceptor **5**. Alkenes **11** and **16** were obtained in a 98:2 ratio (Entry 3), confirming that electronic effects govern the regioselectivity of the reaction in this case. The result obtained when **2** was treated with (ethynylseleno)benzene (**4**, Entry 2) can be ascribed to the absence of substituents other than the seleno group on the triple bond of **4** and to the consequent preferred addition

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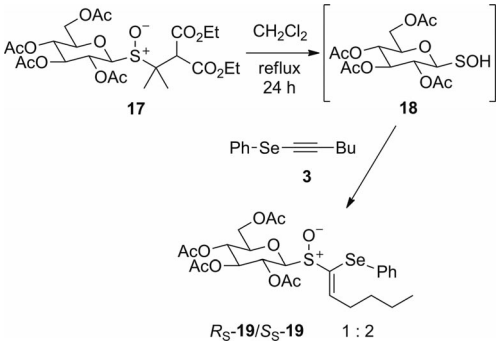
of the sulfur group to the less hindered carbon atom of the unsaturated skeleton.[15b]

Furthermore, we decided to generate enantiopure glucosulfenic acid **18** from the sulfinyl precursor **17** (sulfur epimeric mixture) in the presence of a (phenylseleno)acetylene to synthesize α-(phenylseleno)sulfinyl alkenes with controlled stereochemistry at the sulfur atom of the sulfinyl moiety (Scheme 2).[19] In our experience a 1,1-diethoxycarbonyl-2-methylprop-2-yl residue linked to the anomeric sulfur atom in glucosyl sulfoxide **17** allows us to overcome the problem of regioselectivity in the generation of sulfenic acid **18**, due to the presence of two different *syn*-β-hydrogen atoms with respect to the SO group.[19b] The thermolysis was conducted at 40 °C (CH_2Cl_2) in the presence of alkyne acceptor **3**, leading to a mixture of the two sulfinyl epimers **19**. Stereoselectivity was observed in this reaction, and epimers **19** were obtained in a 1:2 ratio. Our attribution of the sulfur configuration in the two sulfur epimers **19** comes from the well-known influence that an anomeric configuration exerts on the sulfoxide configuration in sulfinyl glycosides owing to the *exo*-anomeric effect.[20] We have previously reported[19a] that the *syn*-addition to a triple bond by a α-D-glucosulfenic acid affords a glucosyl vinyl sulfoxide mixture with a major amount of (R_S)-configured product stereoselectively, whereas the contrary is found when the same reaction involves β-D-glucosulfenic acid **18**.[19b] The generation of the transient glucosulfenic acid **18** and its addition to **3** provide a significant model for the development of a stereocontrolled synthesis of 1-(phenylseleno)-1-sulfinylalkenes.

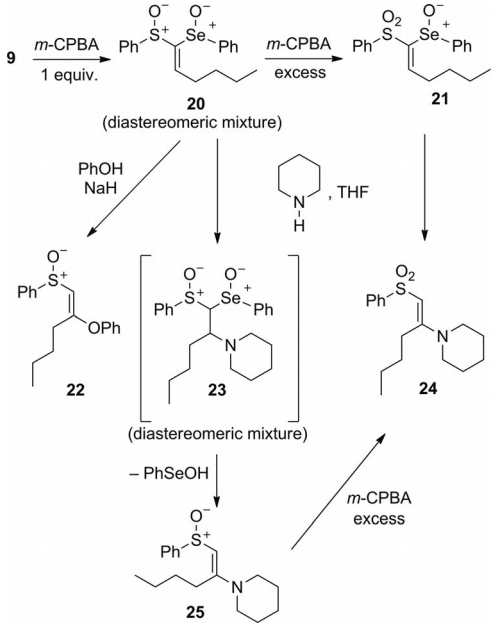


Scheme 2. Stereoselective synthesis of glucopyranosyl (*Z*)-1-(phenylseleno)alkenyl sulfoxides.

The controlled oxidation of (*Z*)-[{1-(phenylseleno)-1-hexen-1-yl}sulfinyl]benzene (**9**) with *m*-chloroperoxybenzoic acid (*m*-CPBA) led to a diastereomeric mixture of racemic α-(phenylseleninyl)sulfinyl alkenes **20**, which gave α-phenylseleninyl sulfonyl alkene **21** when treated with an excess of oxidant (Scheme 2).

Reactivity

The three alkenes **9**, **20** and **21** were subjected to conjugate addition with nucleophiles, such as piperidine and phenol. Compound **9** proved to be a poorly reactive substrate, giving insignificant results when it was involved in the reaction with piperidine. Sulfoxide **20** and sulfone **21** reacted with the cyclic amine to afford **25** and **24**, respectively, in good yields as shown in Scheme 3. Vinyl sulfoxide **22** comes from phenate addition/phenylselenenyl loss. A positive NOESY cross peak observed between the olefinic proton and CH_2NCH_2 moiety supports the structure of sulfoxide **25**. Similarly, **22** shows a positive NOESY cross peak between the $CH_2C=$ and the *ortho* protons of the phenylsulfinyl moiety.



Scheme 3. Nucleophilic additions to α-(phenylseleninyl)sulfinyl and -sulfonyl alkenes.

α-(Phenylseleno)sulfonyl and β-(phenylseleninyl)sulfonyl alkenes have been subjected to nucleophilic additions with cyclic and linear amines[5,7] or enamines[6] previously. This confirmed our finding for reactive substrate **21**, which gave vinyl sulfone **24** as a unique reaction product in good yield after the spontaneous loss of PhSeOH. To the best of our knowledge, α-(phenylseleninyl)sulfinyl alkenes, such as **20**, have not been prepared in the past possibly because of their poor stability. However, we found that **20** remained unaltered on the bench for a few days. This observation confirms the (*Z*)-configuration of alkene **9**. Otherwise, if **20**, and consequently its precursor **9**, was (*E*)-configured the PhSeOH *syn*-elimination would occur even at low temperature and **20** would not have been isolated.

Results obtained from the piperidine addition to **20** appear significant and deserve comment. The reaction may occur through a first addition step leading to the unstable diastereomeric mixture of α-(phenylseleninyl)sulfinyl alkanes **23**, that spontaneously loses PhSeOH to afford **25**. The exclusive formation of **25** from this elimination suggests an interesting stereocontrol of the overall synthetic process under study. An analysis of Newman projections that allow the stereospecific *syn*-elimination of PhSeOH from the intermediates **23** indicates that the diastereomeric

mixture **23** must have the two new stereogenic carbon atoms in the relative configuration (*R*,*S*), which requires an *anti*-approach in the nucleophilic addition.[21] This can include the stereoinfluence exerted by the two chiral heteroatoms in **20** (Scheme 3). Similar considerations could support the (*E*)-stereochemistry found in product **22**. Moreover, the analogous stereochemistry observed in α,β-unsaturated sulfone **24** was confirmed by oxidation of the sulfinyl group of **25** and seems to suggest that the stereogenic selenoxide group is remarkably effective in inducing asymmetry, outweighing the influence of the sulfinyl group.

Conclusions

α-(Phenylseleno)sulfinyl alkenes **9**–**14** and **19** can be easily prepared by the *syn*-addition of in situ generated sulfenic acids to the triple bond of suitably substituted selenoacetylenes. The stereospecificity and the regioselectivity of this reaction contribute to the formation of electron-poor alkenes with a well defined stereochemistry at the double bond. Moreover, the mild conditions adopted for the reaction, without the use of a basic or acidic environment, allows the presence of sensitive substituents on the final α-(phenylseleno)sulfinyl alkenes. α-(Phenylseleninyl)sulfonyl alkenes, such as **21**, can be easily obtained by oxidation of the sulfinyl analogues with complete chemoselectivity. Most importantly, this synthetic pathway involving transient sulfenic acids offers easy access to enantiopure α-(phenylseleno)sulfinyl alkenes via enantiopure sulfenic acids. In this paper we have reported the synthesis of (*Z*)-1-(phenylseleno)-1-[(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-sulfinyl]-1-hexene (**19**) as a diastereomeric mixture (Scheme 2), and other interesting substrates can be prepared starting from suitable precursors of enantiopure sulfenic acids. Initial studies on the reactivity of the unsaturated acceptors **20** or **21** with hard nucleophiles disclose some interesting features: it occurs with a significant stereocontrol, with the opportunity to obtain β-heterosubstituted α,β-unsaturated sulfoxides, such as **22** and **25**, and sulfones, such as **24**. These two classes of compounds are potentially interesting as starting materials for further transformations, for instance the alkylation/hydrolysis of the enamines **24** and **25** to obtain β-sulfonyl and -sulfinyl ketones, respectively. Moreover, the suitable transformation of α-(phenylseleno)sulfinyl alkenes, such as enantiopure sulfoxide (S_S)-**19**, once separated by column chromatography from its sulfur epimer, can be regarded as a new methodology for the synthesis of enantiopure α,β-unsaturated sulfoxides.[22] Following the rationale depicted in Scheme 3, (S_S)-**19** could be oxidized to an epimeric mixture of selenoxides, however, the final product will be enantiopure, owing to the loss of selenium functionality.

Experimental Section

General: Reactions were monitored by TLC on commercially available precoated plates Aldrich silica gel 60 F 254 or Macherey–Nagel Alugram Alox N/UV_{254}. Products were visualized by UV or with vanillin [1 g dissolved in MeOH (60 mL) and conc. H_2SO_4 (0.6 mL)]. Column chromatography was performed on Aldrich 60 silica gel or Fluka aluminum oxide Brockmann activity I. Melting points were determined with a Kofler hotstage apparatus. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions with $SiMe_4$ as the internal standard at 500 (or 300) and 125 (or 75) MHz respectively, unless otherwise stated. *J* values are given in Hz. ^1H NMR peak assignments follow from COSY experiments. ^{13}C NMR spectra were acquired by the APT technique. Heteronuclear single quantum coherence and NOESY experiments were also performed for several compounds. The starting products **1a**–**c**,[15] **3**–**7**[11,14] and **17**[15c] have been reported previously. Benzoate **8** was prepared following the procedure previously described.[11]

General Procedure for the Synthesis of [{(Phenylseleno)-ethenyl}sulfinyl]benzenes 9–16: A solution of methyl-3-(phenylsulfinyl)propanoate (**1a**) (212 mg, 1.00 mmol) and [(phenylseleno)ethynyl]benzenes **3**–**8** (3.00 mmol) in $ClCH_2CH_2Cl$ (9 mL) was heated to reflux until complete sulfoxide disappearance as verified by TLC (EtOAc/hexane). The solvent was removed under reduced pressure, and the crude reaction mixture was purified by column chromatography (silica gel, EtOAc/hexane) to give the expected [{(phenylseleno)ethenyl}sulfinyl]benzene. Reaction times and yields are shown in Table 1.

5-(Phenylseleno)-4-pentyn-1-yl Benzoate (8): Oil; yield 84%. ^1H NMR (200 MHz): δ = 7.9–8.0 (m, 2 H, CH_{Ph}), 7.3–7.5 (m, 5 H, CH_{Ph}), 7.1–7.3 (m, 3 H, CH_{Ph}), 4.25 (t, J_{vic} = 6.2 Hz, 2 H, CH_2O), 2.54 (t, J_{vic} = 6.9 Hz, 2 H, $CH_2C{\equiv}$), 1.97 (tt, 2 H, $CH_2CH_2CH_2$) ppm. ^{13}C NMR (50 MHz): δ = 166.5 (C=O), 135.3, 133.7 (2 C), 132.7, 130.3, 129.6 (2 C), 129.5 (2 C), 128.3 (2 C), 128.1, 107.2, 63.8, 62.9, 31.5, 26.8 ppm. $C_{18}H_{16}O_2Se$ (343.28): calcd. C 62.98, H 4.70; found C 62.84, H 4.91.

(*Z*)-[{1-(Phenylseleno)-1-hexen-1-yl}sulfinyl]benzene (9): Racemic mixture; colourless oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.74. ^1H NMR: δ = 7.6–7.3 (m, 10 H, CH_{Ph}), 7.57 (s, 1 H, $CH_2CH{=}$), 2.2–2.1 (m, 2 H, $CH_2CH{=}$), 1.2 (m, 4 H, $CH_3CH_2CH_2$), 0.80 (t, J_{vic} = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 143.8 and 142.9 (CSC), 133.0, 131.2, 129.6, 129.2, 128.2, and 125.3 (CH_{Ph}), 129.3 (SeC_{Ph}), 128.7 ($CH_2CH{=}$), 29.8 ($CH_2CH_2CH_2$), 27.6 ($CH_2CH{=}$), 22.5 (CH_2CH_3), 13.6 (CH_3) ppm. NOESY correlation: CH_2CH =/$CH_2CH{=}$. $C_{18}H_{20}OSSe$ (363.38): calcd. C 59.50, H 5.55; found C 59.74, H 5.63.

[{1-(Phenylseleno)ethenyl}sulfinyl]benzene (10):[9] Racemic mixture; yellow oil; m.p. 35 °C.[9] TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.54. ^1H NMR: δ = 7.7–7.2 (m, 10 H, CH_{Ph}), 6.92 (d, J_{gem} = 1.5 Hz, 1 H) and 6.16 (d, 1 H, $CH_2{=}$) ppm. ^{13}C NMR: δ = 146.6 (SCSe), 142.3 (SC_{Ph}), 133.2, 129.4, 129.0, 128.2, 126.3, and 126.0 (CH_{Ph}), 131.6 (SeC_{Ph}), 126.3 ($CH_2{=}$) ppm. $C_{14}H_{12}OSSe$ (307.27): calcd. C 54.72, H 3.94; found C 54.67, H 4.27.

(*Z*)-[{2-Phenyl-1-(phenylseleno)ethenyl}sulfinyl]benzene (11): Racemic mixture; white crystals; m.p. 58 °C. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.70. ^1H NMR: δ = 7.75 (s, 1 H, CH=), 7.6–7.1 (m, 15 H, CH_{Ph}) ppm. ^{13}C NMR: δ = 142.8 and 142.1 (CSC), 133.0, 130.9, 129.5, 129.0, 128.9, 128.8, 128.6, 128.2, and 124.8 (CH_{Ph} and $=CHC_{Ph}$), 132.2 ($=CHC_{Ph}$), 129.2 (SeC_{Ph}) ppm. $C_{20}H_{16}OSSe$ (383.37): calcd. C 62.66, H 4.21; found C 62.57, H 4.46.

(*Z*)-[{2-(Trimethylsilyl)-1-(phenylseleno)ethenyl}sulfinyl]benzene (12): Racemic mixture. Yellow oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.65. ^1H NMR: δ = 7.92 (s, 1 H, SiCH=), 7.7–7.2 (m, 10 H, CH_{Ph}), 0.23 (s, 9 H, CH_3) ppm. ^{13}C NMR: δ = 148.0

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(SCSe), 143.2 (SiCH=), 143.0 (SC_{Ph}), 131.4, 130.3, 129.3, 128.8, 127.1, and 126.4 (CH_{Ph}), 129.7 (SeC_{Ph}), –0.49 (CH_3) ppm. NOESY correlation: SiCH =/CH_3. $C_{17}H_{20}OSSeSi$ (379.45): calcd. C 53.81, H 5.31; found C 53.82, H 5.64.

(*Z*)-2-[2-(Phenylseleno)-2-(phenylsulfinyl)ethenyl]-1*H*-isoindole-1,3(2*H*)-dione (13): Racemic mixture; yellow oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.46. ^{1}H NMR: δ = 7.9–7.3 (m, 14 H, CH_{Ar}), 7.59 (s, 1 H, CH_2CH=), 3.58 (t, J_{vic} = 7.1 Hz, 2 H, NCH_2), 2.22 (m, 2 H, CH_2CH=), 1.56 (m, 2 H, $CH_2CH_2CH_2$) ppm. ^{13}C NMR: δ = 168.1 (C=O), 142.4 and 142.3 (CSC), 134.0, 133.2, 131.3, 130.2, 129.6, 129.3, 128.3, 125.1, and 123.2 (CH_{Ar} and CH=), 132.0 (*C*C=O), 128.9 (SeC_{Ph}), 37.4 (NCH_2), 26.6 (CH_2CH=), 25.2 ($CH_2CH_2CH_2$) ppm. NOESY correlation: CH_2CH=/CH_2CH=. $C_{25}H_{21}NO_3SSe$ (494.46): calcd. C 60.73, H 4.28, N 2.83; found C 60.49, H 4.56, N 2.92.

(*Z*)-[{5-(Benzoyloxy)-1-(phenylseleno)-1-penten-1-yl}sulfinyl]benzene (14): Racemic mixture; colourless oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.63. ^{1}H NMR: δ = 8.0–7.3 (m, 15 H, CH_{Ph}), 7.64 (s, 1 H, CH_2CH=), 4.21 (t, J_{vic} = 5.9 Hz, 2 H, OCH_2), 2.34 (m, 2 H, CH_2CH=), 1.71 (m, 2 H, $CH_2CH_2CH_2$) ppm. ^{13}C NMR: δ = 166.2 (C=O), 142.5 and 142.4 (CSC), 133.1, 132.9, 131.2, 130.7, 129.6, 129.5, 129.2, 128.3, 128.2, and 125.0 (CH_{Ph} and CH=), 130.0 (*C*C=O), 128.7 (SeC_{Ph}), 63.8 (OCH_2), 26.8 (CH_2CH=), 24.5 ($CH_2CH_2CH_2$) ppm. NOESY correlation: CH_2CH=/CH_2CH=. $C_{24}H_{22}O_3SSe$ (469.45): calcd. C 61.40, H 4.72; found C 61.39, H 4.97.

(*E*)-[{2-(Phenylseleno)ethenyl}sulfinyl]benzene (15): Racemic mixture; brown oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.50. ^{1}H NMR: δ = 7.71 and 6.28 (AB system, J_{AB} = 11.3 Hz, 2 H, SCH=CHSe), 7.6–7.3 (m, 10 H, CH_{Ph}) ppm. ^{13}C NMR: δ = 143.6 (SC_{Ph}), 134.6, 131.0, 129.8, 129.3, 129.0, and 124.5 (CH_{Ph}), 133.0 and 132.6 (SCH=CHSe), 126.6 (SeC_{Ph}) ppm. $C_{14}H_{12}OSSe$ (307.27): calcd. C 54.72, H 3.94; found C 54.75, H 4.25.

(*E*)-[{1-Phenyl-2-(phenylseleno)ethenyl}sulfinyl]benzene (16): Compound **16** was detected during the chromatographic purification of its isomer **11** by observation of a typical ^{1}H NMR olefinic singlet at δ = 8.23 ppm and comparison with the spectroscopic data of sulfoxide **15**.

(*Z*)-1-[(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)sulfinyl]-1-(phenylseleno)-1-hexene (19): A solution of **3** (712 mg, 3.00 mmol) and **17** (581 mg, 1.00 mmol) in CH_2Cl_2 (13 mL) was heated to reflux overnight. The solvent was removed under vacuum, and **19** isolated by column chromatography (silica gel, EtOAc/hexane, 1:9 up to 4:6); yield 50%, sulfur epimeric mixture; colourless oil. TLC (silica gel plate, EtOAc/hexane, 5:5): R_f = 0.40. ^{1}H NMR: δ = 7.6–7.3 (m, 6 H, CH_{Ph} and CH_2CH=), 5.4–5.0 (m, 3 H, glucose 2–4-H), 4.37 (d, $J_{1,2}$ = 9.4 Hz, 1 H, glucose 1-H), 4.18 (m, 2 H, glucose 6-H_2), 3.76 (m, 1 H, glucose 5-H), 2.5–2.2 (m, 2 H, CH_2CH=), 2.09, 2.04, 2.02, and 2.01 (four s, 12 H, CH_3C=O), 1.7–1.3 (m, 4 H, $CH_3CH_2CH_2$), 0.98 (t, J_{vic} = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR: δ = 170.3, 170.0, 169.13, and 169.09 (C=O), 137.8 (SC), 132.7, 129.4, 129.3, and 128.1 (CH_{Ph} and CH_2CH=), 128.7 (SeC_{Ph}), 90.1 (glucose C-1), 76.3, 73.5, 67.3, and 66.8 (glucose C-2–5), 61.6 (glucose C-6), 29.4 ($CH_2CH_2CH_2$), 28.5 (CH_2CH=), 22.5 (CH_2CH_3), 20.6, 20.5, 20.4, and 20.3 (CH_3C=O), 13.6 (CH_2CH_3) ppm. $C_{26}H_{34}O_{10}SSe$ (617.57): calcd. C 50.57, H 5.55; found C 50.54, H 5.92.

(*Z*)-[{1-(Phenylseleninyl)-1-hexen-1-yl}sulfinyl]benzene (20): A solution of *m*-CPBA (80 wt.-%, 149 mg, 0.69 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a solution of **9** (251 mg, 0.69 mmol) in CH_2Cl_2 (5 mL) at room temperature. After 2 h the disappearance of **9** was verified by TLC, and the reaction was quenched by adding a 10% aq. solution of $Na_2S_2O_3$ (10 mL). The organic layer was then separated and washed with $NaHCO_3$ (saturated aq. solution, 2 × 10 mL) and NaCl (saturated aq. solution, 2 × 10 mL). The organic phase was dried with Na_2SO_4 and, after evaporation of the solvent at reduced pressure, **20** was quantitatively obtained as a 1:1 diasteromeric mixture; colourless oil. TLC (silica gel plate, EtOAc/hexane, 8:2): R_f = 0.20. ^{1}H NMR: δ = 7.8–7.5 (m, 11 H, CH_{Ph} and CH_2CH=), 2.8–2.1 (m, 2 H, CH_2CH=), 1.6–1.3 (m, 4 H, $CH_3CH_2CH_2$), 0.90 (t, J_{vic} = 7.2 Hz), 0.85 (t, J_{vic} = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 159.7, 159.5, 141.6, 141.3, and 140.3 (quaternary carbons), 133.7, 132.9, 132.5, 132.2, 131.8, 131.7, 130.3, 130.0, 129.7, 129.6, 126.1, 126.0, and 125.6 (CH_{Ph} and CH_2CH=), 32.0, 31.8, 28.1, 27.0, 22.6, and 22.5 ($CH_2CH_2CH_2$), 13.6 and 13.5 (CH_3) ppm. $C_{18}H_{20}O_2SSe$ (379.38): calcd. C 56.99, H 5.31; found C 57.06, H 5.62.

(*Z*)-[{1-(Phenylseleninyl)-1-hexen-1-yl}sulfonyl]benzene (21): A solution of *m*-CPBA (80 wt.-%, 89 mg, 0.41 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a solution of **20** (155 mg, 0.41 mmol) in CH_2Cl_2 (5 mL) at room temperature. After 2 h the disappearance of **20** was verified by TLC (silica gel plate, CH_2Cl_2/EtOAc, 6:4), and the reaction was quenched with 10% aq. solution of $Na_2S_2O_3$ (10 mL). The organic layer was then separated and washed with $NaHCO_3$ (saturated aq. solution, 2 × 10 mL) and NaCl (saturated aq. solution, 2 × 10 mL). After drying the solution over Na_2SO_4 and removing the solvent under reduced pressure, **21** was obtained quantitatively as racemic mixture; colourless oil. TLC (silica gel plate, acetone/hexane, 9:1): R_f = 0.60. ^{1}H NMR: δ = 7.8–7.4 (m, 11 H, CH_{Ph} and CH_2CH=), 2.7–2.4 (m, 2 H, CH_2CH=), 1.7–1.3 (m, 4 H, $CH_3CH_2CH_2$), 0.83 (t, J_{vic} = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 153.0 (SC_{Ph}), 142.4 (CH_2CH=), 139.5 and 137.6 (CSeC), 134.3, 132.2, 130.2, 129.5, 128.6, and 126.2 (CH_{Ph}), 32.3 ($CH_2CH_2CH_2$), 29.0 (CH_2CH=), 22.6 (CH_2CH_3), 13.5 (CH_3) ppm. $C_{18}H_{20}O_3SSe$ (395.37): calcd. C 54.68, H 5.10; found C 54.42, H 5.39.

(*E*)-[(2-Phenoxy-1-hexen-1-yl)sulfinyl]benzene (22): To a solution of NaH (60% dispersion in mineral oil, 5 mg, 0.13 mmol) in anhydrous THF (2 mL) was added a solution of phenol (149 mg, 1.58 mmol) in anhydrous THF (2.5 mL) under argon at room temperature. After about 10 min, a solution of **20** (100 mg, 0.26 mmol) in anhydrous THF (10 mL) was added. The reaction was followed by TLC (alumina plate, EtOAc/hexane, 5:5) and stopped after 4 h by washing the crude mixture with saturated aq. NaCl solution (10 mL) and extracting the organic phase into Et_2O (2 × 10 mL). The organic layer was dried with Na_2SO_4. After evaporation of the solvent under reduced pressure, column chromatography (alumina, EtOAc/hexane, 5:95) afforded **22** (49 mg, 0.16 mmol, yield 62%) as a racemic mixture; colourless oil. TLC (alumina plate, EtOAc/hexane, 5:5): R_f = 0.60. ^{1}H NMR: δ = 7.7–7.6 [m, 2 H, S(O)CH_{Ph}(*ortho*)], 7.5–7.0 (m, 9 H, CH_{Ph} and CH_2C=C*H*), 2.17 (m, 2 H, CH_2C=), 1.4–1.0 (m, 4 H, $CH_3CH_2CH_2$), 0.76 (t, J_{vic} = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 156.6 (OC_{Ph}), 148.1 (SCH=), 142.8 (SC_{Ph}), 129.0 (CH_2C=), 130.6, 129.9, 129.0, 124.9, 124.4, and 117.1 (CH_{Ph}), 30.6 ($CH_2CH_2CH_2$), 22.5 (CH_2CH_3), 22.0 (CH_2C=), 13.6 (CH_3) ppm. NOESY correlation: CH_2C=/S(O)CH_{Ph}(*ortho*). $C_{18}H_{20}O_2S$ (300.42): calcd. C 71.96, H 6.71; found C 72.01, H 6.92.

(*E*)-[{2-(1-Piperidinyl)-1-hexen-1-yl}sulfonyl]benzene (24): To **21** (100 mg, 0.25 mmol) dissolved in anhydrous THF (1 mL) was added piperidine (150 μL, 1.52 mmol) under argon. After 4 h the total disappearance of **21** was verified by TLC (alumina plate, EtOAc/hexane, 3:7). After removal of the solvent under reduced pressure, **24** was purified by column chromatography (alumina,

EtOAc/hexane, 1:9) and obtained in 60% yield (46 mg, 0.15 mmol). Yellow oil. TLC (alumina plate, EtOAc/hexane, 8:2): R_f = 0.80. ^{1}H NMR: δ = 7.8–7.4 (m, 6 H, CH_{Ph} and NC=CH), 3.32 (m, 4 H, CH_2NCH_2), 2.15 (m, 2 H, CH_2C=), 1.6–1.2 (m, 10 H, $CH_3CH_2CH_2$ and $NCH_2CH_2CH_2CH_2$), 0.78 (t, J_{vic} = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 145.4 (=CHS), 143.2 (SC_{Ph}), 131.5, 128.6, and 127.1 (CH_{Ph}), 102.8 (NC), 51.6 (NCH_2), 32.6, 26.1, 25.5, 24.0, and 22.5 (butyl CH_2 and $NCH_2CH_2CH_2CH_2$), 13.6 (CH_3) ppm. $C_{17}H_{25}NO_2S$ (307.45): calcd. C 66.41, H 8.20, N 4.56; found C 66.03, H 8.59, N 4.52. Sulfone **24** was obtained quantitatively by *m*-CPBA oxidation of **25**.

(*E*)-[{2-(1-Piperidinyl)-1-hexen-1-yl}sulfinyl]benzene (25): To **20** (80 mg, 0.21 mmol) dissolved in anhydrous THF (0.8 mL) was added piperidine (122 μL, 1.23 mmol). The reaction was performed under argon at room temperature in the presence of 3 Å molecular sieves. After 24 h, **20** was completely transformed, as verified by TLC (alumina plate, acetone/hexane, 6:4). After evaporation of the solvent under reduced pressure, the crude reaction mixture was purified by column chromatography (alumina, acetone/hexane, 0.5:9.5), and **25** was obtained (40 mg, 0.14 mmol, yield 65%) as a racemic mixture; yellow oil. TLC (alumina plate, acetone/hexane, 9:1): R_f = 0.80. ^{1}H NMR: δ = 7.6–7.5 [m, 2H CH_{Ph}(*ortho*)] 7.4–7.3 (m, 3 H, CH_{Ph}), 6.70 (s, 1 H, NC=CH), 3.3 (m, 4 H, CH_2NCH_2), 2.2–1.9 (m, 2 H, CH_2CH=), 1.6–0.8 (m, 10 H, $CH_3CH_2CH_2$ and $NCH_2CH_2CH_2CH_2$), 0.70 (t, J_{vic} = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR: δ = 145.5 (=CHS), 145.2 (SC_{Ph}), 129.4, 128.4, and 125.1 (CH_{Ph}), 110.8 (NC), 51.3 (NCH_2), 25.9, 24.1, 22.9, 22.5, and 22.4 (butyl CH_2 and $NCH_2CH_2CH_2CH_2$), 13.5 (CH_3) ppm. NOESY correlation: NC=C*H*/CH_2NCH_2. $C_{17}H_{25}NOS$ (291.45): calcd. C 70.06, H 8.65, N 4.81; found C 69.91, H, 8.97, N 4.79.

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