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Sulfur dioxide mediated one-pot, four-component synthesis of polyfunctional sulfones and sulfonamides, including medium-ring cyclic derivatives

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Abstract—In previous papers (*Synthesis* **2002**, 232 and *J. Org. Chem.* **2004**, *69*, 6413), we have shown that the hetero-Diels–Alder addition of sulfur dioxide to 1-oxy or 1,3-dioxy-1,3-dienes generates zwitterions that add to enoxysilanes or allylsilanes giving silyl sulfinates that can be converted in the same pot into polyfunctional sulfones, sulfonamides or sulfonic esters. We are presenting further applications of this method, including the synthesis of new medium-size heterocyclic systems of the type tetrahydro-2*H*-thiocines and hexahydro-1,2-thiazonine.

1. Introduction

Organosulfones are important compounds[1] because of their chemical properties[2] and biological properties.[3] They are important synthetic targets and are widely used synthons.[4] The sulfone functional group is found in various drugs, including the recently selective COX-2 inhibitor Vioxx.[5] Sulfones have been shown also to inhibit HIV-1 reverse transcriptase.[6] Their preparation involves oxidation of the corresponding sulfides and sulfoxides[7a–d] or displacement reaction of sodium arenesulfinate with an appropriate alkyl halides.[7e,f] Diaryl sulfones are prepared also through the classical Friedel–Crafts sulfonylation using of arenesulfonyl chlorides and arenes, and Lewis acids catalysts.[7g,h] Recently, biaryl sulfones were derived from sulfinic acid salts and aryl iodides using copper[8] and palladium catalyst.[9] In 2004, we[10a] and Bandgar[1n] have reported that diaryl sulfones can be prepared through palladium-catalyzed cross-coupling reactions between areneboronic acids and arenesulfonyl chlorides.

The sulfonamides constitute an important class of drugs (the sulfa drugs), with several types of pharmacological agents possessing antibacterial, anticarbonic anhydrase, diuretic hypoglycemic anti-thyroid, anti-hypertensive, anti-inflammatory, and antiviral properties.[11,12] Recently, structurally novel sulfonamide derivatives have shown substantial antitumor activities,[13,14] or are caspase-1[15] inhibitors.[16] The majority of sulfonamides are prepared from the reaction of sulfonyl chlorides with ammonia, primary or secondary amines.[17] Arenesulfonyl chlorides are prepared from arenes by electrophilic substitution with $ClSO_3H$ or from arenesulfonic acids by reaction with PCl_5,[18] $POCl_3$[19] or $COCl_2$.[20] Other methods imply the reactions of arenediazonium salts with $SO_2/CuCl_2$,[21] the oxidation of thioesters[22] or sulfenyl chlorides,[23] or the reaction of organolithium[24] or organomagnesium[25] reagents with SO_2Cl_2 or SO_2+Cl_2. Alkanesulfonyl chlorides can be obtained by reaction of the corresponding alkane with SO_2 and Cl_2 under radical conditions.[26] All these methods[27] are relatively harsh (acidic, basic) and cannot be applied to polyfunctional substrates. Recently, the direct synthesis of sulfonamides and sulfonic esters from sulfonic acids[28] and a one-pot synthesis of sulfonamides from Grignard reagents and SO_2[28,29] has been reported. Both procedures are amenable to aromatic and heteroaromatic sulfonamides.

Enoxysilanes **1**,[30] allylsilanes **2**,[30] and allylstannanes **3**[31] undergo ene-reactions with sulfur dioxide giving the corresponding silyl or stannyl sulfinate intermediates **4** that react with Bu_4NF and carbon electrophiles R^3Y to produce the corresponding sulfones **5** in one-pot operations (Scheme 1).[30] Chlorination (Cl_2 or NCS) or bromination

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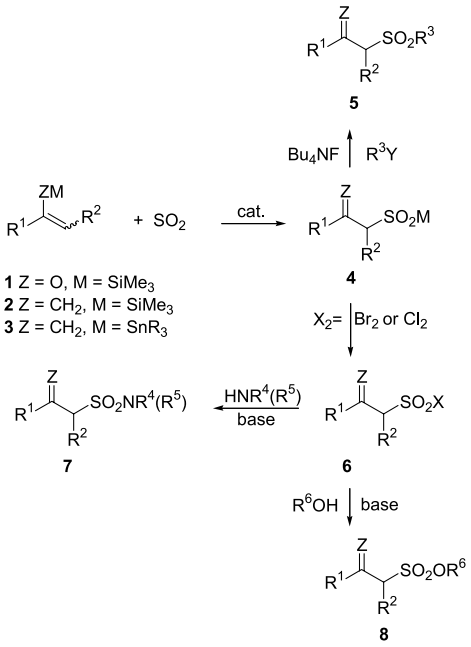
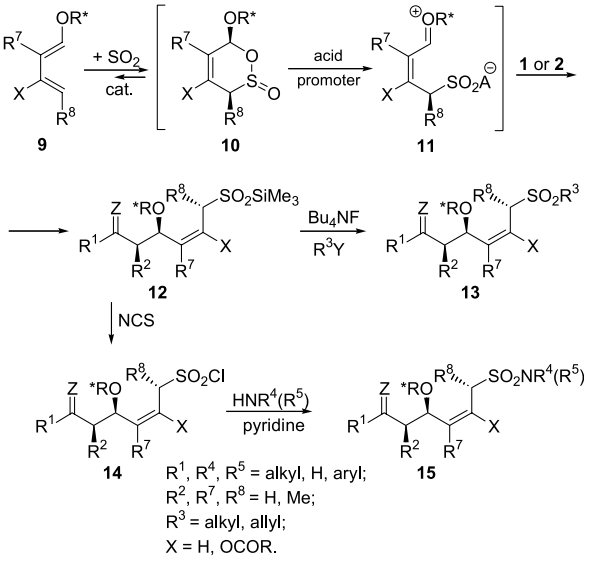


Scheme 1. One-pot, three-component synthesis of polyfunctional sulfones **5**, sulfonamides **7** and sulfonic esters **8**.

(Br_2 or NBS) of silyl sulfinates **4** generate the corresponding sulfonyl halides **6** that react in situ with primary or secondary amines to produce the corresponding sulfonamides **7**, or with alcohols to generate the corresponding sulfonic esters **8** (Scheme 1).[32]

We have found a new C–C bond forming reaction (Scheme 2),[33–38] involving a cascade of reactions starting with the hetero-Diels–Alder addition of sulfur dioxide to 1,3-dienyl ethers **9**. This generates unstable sultines **10** that are ionized in the presence of an acid promoter giving zwitterionic species **11**. In the presence of enoxysilanes **1** or allylsilanes **2**, the latter are quenched forming the corresponding silyl sulfinates **12** with high diastereoselectivity. Desilylation of **12** with Bu_4NF followed by



Scheme 2. One-pot, four-component synthesis of polyfunctional sulfones **13** and sulfonamides **15**.

addition of electrophile R^3Y generates the corresponding sulfones **13**, thus, realizing a one-pot, four-component method for the synthesis of polyfunctional sulfones.[34,39] Chlorination or bromination of silyl sulfinates **12** provides the corresponding sulfonyl chlorides or bromides that react with primary or secondary amines in pyridine to produce the corresponding polyfunctional sulfonamides **15**.[32,40] Using enantiomerically enriched dienes **9** (R*=1-arylethyl), enantiomerically enriched sulfones **13** and sulfonamides **15** are obtained.

We present here new applications of our one-pot, four-component synthesis of sulfones and sulfonamides.[41] New β,γ-unsaturated sulfones have been obtained, including cyclic derivatives resulting from intramolecular sulfinates allylation. Furthermore, we have found that not only (*Z*)-β,γ-unsatured sulfones can be formed. Depending on the nature of the enoxysilanes and 1-oxydienes and upon the nature of the acid catalyst, the (*E*)-isomeric sulfones can also be obtained. For the first time, intramolecular allylation of sulfonamides have allowed to prepare hexahydro-1,2-thiazonine derivatives, a new kind of medium-size heterocyclic compounds.[42]

2. Results and discussion

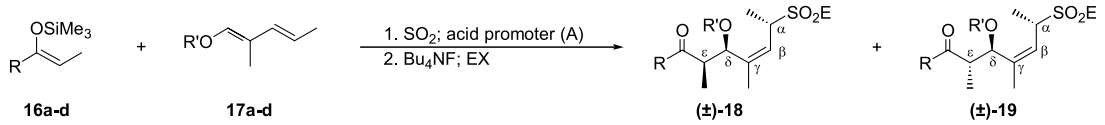
2.1. Diastereoselectivity of the oxyallylations of enoxysilanes

In our previous work[34,38] we found that the δ,ε-*syn* versus *anti* diastereoselectivity of the oxyallylations of (*Z*)-enoxysilane **16a** using (*E*,*E*)-1-oxy-2-methylpenta-1,3-dienes never surpass 3:1 (product ratio **18**/**19**, Scheme 3). As we shall see, the diasteroselectivity varies with the nature of the enoxysilane **16** and of the diene **17** and that it can be increased to 9:1.

For instance, when a 2:1 mixture of enoxysilane **16b** (R=*p*-$MeOC_6H_4$) and diene **17b** (R=Bn) was reacted with an excess of SO_2 premixed with 0.2 equiv of Tf_2NH (Tf=trifluoromethanesulfonyl) or $TfOSiR_3$ (R=Me, *t*-Bu) at −78 °C for 12 h, a mixture of silyl sulfinates was obtained that was quenched with 1 equiv of Bu_4NF and 2.5 equiv of methallyl bromide to give a 5:1 mixture of sulfonylketones (±)-**18b** and (±)-**19b** from which the major isomer (±)-**18b** was isolated pure in 76% yield (Table 1). Its structure was not established unambigiously but it is proposed to be similar (δ,ε-*syn*, α,δ-unlike) to those of similar compounds obtained under similar conditions.[34,38]

Under the same conditions, enoxysilane **16c**+ diene **17b** gave a 6:1 mixture of sulfonylketones (±)-**18c** and (±)-**19c** from which (±)-**18c** could be isolated pure in 70% yield. With enoxysilane **16d** [(*Z*)-1,2-bis(trimethyl-silyloxy)but-1-ene][43] and racemic diene (±)-**17c** a 3:1 mixture of (±)-**18d** and (±)-**19d** (electrophile, EX=MeI) was obtained. Pure (±)-**19d** could be isolated by flash column chromatography on silica gel. The combination of more sterically bulky diene **17d** (R′=$SiMe_2t$-Bu) with enoxysilane **16c** (R=2,4,6-$(MeO)_3$–C_6H_2) resulted in enhanced 9:1 δ,ε-*syn* versus *anti* diastereoselectivity (Table 1, entry 6).

Table 1. Synthesis of (*Z*)-β,γ-unsaturated sulfones



Entry	Reactants				Products	
	16	**17**	EX	A	Ratio	Total yield (%)
1	**16a**: R = Me	**17a**: R′ = $SiMe_3$	MeI	Tf_2NTMS, 45%	**18a**:**19a** = 1:1[a]	72 [Ref. 38]
2	**16b**: R = *p*-$MeOC_6H_4$	**17b**: R′ = Bn		Tf_2NH, 20%	**18b**:**19b** = 5:1	91
3	**16c**: R = 2,4,6-$(MeO)_3C_6H_2$	**17b**: R′ = Bn		Tf_2NH, 20%	**18c**:**19c** = 6:1	90
4	**16d**: R = CH_2OSiMe_3	**17c**: R′ = (*RS*)-2,4,6-(*i*-$Pr)_3C_6H_2$(Me)CH	MeI	Tf_2NH, 20%	**18d**:**19d** = 3:1	29
5	**16c**: R = 2,4,6-$(MeO)_3C_6H_2$	**17a**: R′ = $SiMe_3$		Tf_2NH, 20%	**18e**:**19e** = 6:1[a]	82
6	**16c**: R = 2,4,6-$(MeO)_3C_6H_2$	**17d**: R′ = $SiMe_2t$-Bu		Tf_2NH, 20%	**18f**:**19f** = 9:1[b]	60

[a] Products **18a/19a** and **18e/19e** are obtained in their desilylated form where R′ = H.
[b] This represents the yield and ratio of **18f/19f** after additional silylation of the crude reaction mixture. For more details see Section 4.

On increasing the amount of the protic acid promoter the oxyallylation reaction produced mixtures of (*Z*)- and (*E*)-β,γ-unsatured sulfinates.[38] For instance, when using 0.5 equiv (instead of 0.1–0.2 equiv) of Tf_2NH, the reaction of enoxysilane **16a** with diene **17a** led to a mixture of (*E*)-β,γ-unsatured silyl sulfinates that reacted with Bu_4NF and Me_2CHCH_2I giving a 1:1 mixture of (*E*)-β,γ-unsatured sulfones (±)-**20a** and (±)-**21a**. When treated with TfOH in THF, this mixture generated a single (*E*,*E*)-dienone (±)-**22** demonstrating that the relating configuration for (±)-**20a** and (±)-**21a** are δ,ε-*syn*, α,δ-unlike and δ,ε-*anti*, α,δ-unlike, respectively, (Table 2).

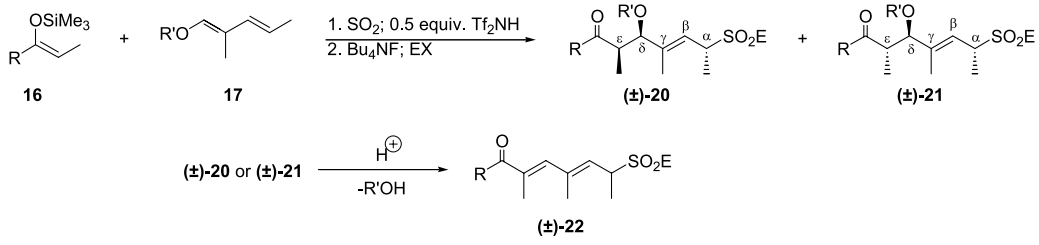
Similarly, when enoxysilane **16c** and diene **17d** were treated as above with 0.5 equiv of Tf_2NH in an excess of SO_2 at −78 °C, a mixture of (*E*)-β,γ-unsaturated sulfones (±)-**20b** and (±)-**21b** was obtained. Flash chromatography of this mixture allowed the obtainment of a 9:1 mixture of (±)-**20b** and (±)-**21b** in 60% yield. The relative configuration of these compounds was not established unambiguously, it is proposed to be the same as that of related compounds prepared under similar conditions.[38] However, the (*E*)- or (*Z*)-configurations of the alkene units were confirmed by NOESY ^1H NMR experiments.

2.2. Oxyallylation of allylsilanes

We had shown[35] that the oxyallylation of allylsilanes **23** fails when reacting them with 1-oxy-1,3-dienes such as **17** and SO_2 activated by a Lewis or protic acid. Nevertheless, successful oxyallylation of allylsilanes could be realized using 1,3-dioxy-1,3-dienes of type **24**. As a new illustration of the reaction, we report here that 2:1 mixture of allylsilane **23a** with the enantiomerically enriched diene (−)-**24a** (97% ee, derived from the inexpensive (1*S*)-1-phenylethanol)[35] produces a single silyl sulfinate **25a**, when treated in anhyd CH_2Cl_2/SO_2 premixed with 0.3 equiv of Tf_2NSiMe_3 (Scheme 3). After evaporation of SO_2 and CH_2Cl_2 at −50–20 °C, the residue was treated with *N*-chlorosuccinimide (NCS) in acetonitrile at −30 °C. This produced the corresponding sulfonyl chloride that was not isolated but mixed with benzylamine (10 equiv) in pyridine at −40 °C.

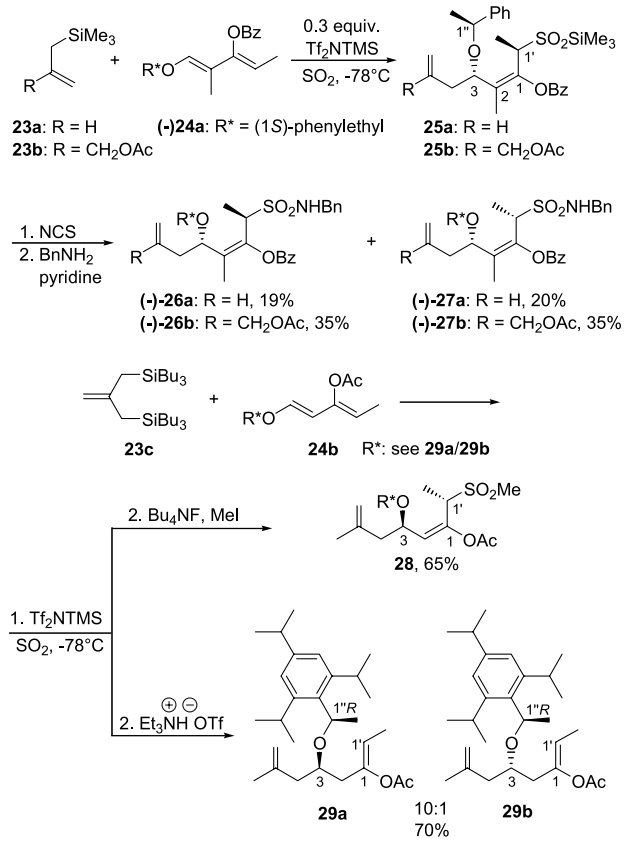
After 4 h at −20 °C, the formation of sulfonamides was

Table 2. Synthesis of (*E*)-β,γ-unsaturated sulfones



Entry	Reactants			Products	
	16	**17**	EX	Ratio	Total yield (%)
1	**16a**: R = Me	**17a**: R′ = $SiMe_3$		**20a**:**21a** = 1:1[a]	82
2	**16c**: R = 2,4,6-$(MeO)_3C_6H_2$	**17d**: R′ = $SiMe_2t$-Bu		**20b**:**21b** = 9:1[b]	60

[a] Products **20a/21a** are obtained in their desilylated form where R′ = H.
[b] This represents the yield and ratio of **20b/21b** after additional silylation of the crude reaction mixture. For more details see Section 4.



Scheme 3. Oxyallylation of allysilanes and synthesis of sulfonamides and sulfones.

over and, after flash column chromatography on silica gel, isomeric *N*-benzylsulfonamides (−)-**26a** and (−)-**27a** were isolated in 19 and 20% yield, respectively. Although the sulfonamide formation reaction was carried out low temperature, these results demonstrated that basicity of the medium is sufficient to promote a complete epimerization (−)-**26a**↔(−)-**27a**. The structure of sulfonamide (−)-**27a** was established by X-ray diffraction studies (Fig. 1). That of (−)-**26a** was deduced from its spectral data and by comparison with those collected for (−)-**27a**.

With the hope to carry out two successive oxyallylations on disilyl system **23c**[45] we reacted it with the enantiomerically pure diene **24b** (derived from (1*R*)-1(2,4,6-tri(isopropyl))-phenylethanol: the Greene's chiral auxiliary)[46] in the presence of SO_2 and an acid promoter. For 2:1–1:3 mixtures of **23c** and **24b** as major product only sulfone **28** (10:1 epimers at C(3)) was isolated in 65% yield, when the reaction mixture was methylated with MeI/Bu_4NF. Under the conditions used, only one oxyallylation occurred and the second allylsilane moiety in intermediate underwent desilylation with Bu_4NF. The relative configuration in **28** was not established unambiguously, but it is proposed to be similar to that observed in related product proposed under similar conditions.[35] When the reaction mixture **23c**+**24b** was submitted to desilylation and desulfitation by retro-ene reaction (triethylamonium trifluoromethanesulfonate buffer, see Scheme 3), a 10:1 mixture of diastereomeric dienes **29a** and **29b** was obtained. As the analogous retro-ene eliminations have all shown high stereoselectivity in the chirality transfer between centers C(1′) and C(2) in the corresponding diene, the 10:1 mixture of diastereomers **29a**+**29b** is proposed to correspond to the like (1″*R*, 3*R*) for the major isomer **29a**, and unlike (1″*R*, 3*S*) for the minor product **29b**.

The reaction of a 2:1 mixture of allylsilane **23b** and enantiomerically enriched (ee 97%) diene (−)-**24a** in SO_2/toluene premixed with 0.3 equiv of Tf_2NSiMe_3 (−78 °C, 36 h) gave a single silyl sulfinate **25b** (by ^1H NMR of the crude) that was oxidized with NCS to the corresponding sulfonyl chloride that was not isolated but treated with an excess of benzylamine in pyridine. Flash column chromatography provided pure sulfonamides (−)-**26b** and (−)-**27b** each in 35% yield (Scheme 3). Both compounds were treated with 1 equiv of Cs_2CO_3 in anhyd DMF in the presence of 0.1 equiv of $(Ph_3P)_4Pd$. After heating to 100 °C for 40 min., the 1,2-thiazonin-8-yl benzoates (−)-**30** (81%) and (−)-**31** (79%) were obtained. They resulted from intramolecular *N*-allylation[47] of the *N*-benzylsulfonamides (Scheme 4). Except for the relative configuration between the (1*S*)-phenylethyl group and the stereogenic centers C(6), which was assumed to be the same as that observed for other related systems obtained under similar conditions,[35] the

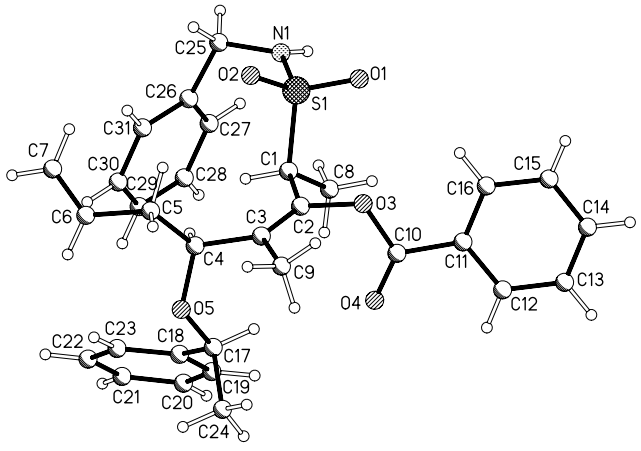
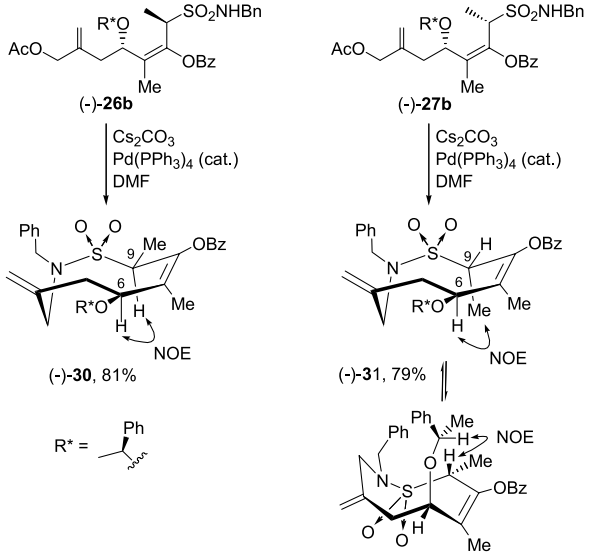
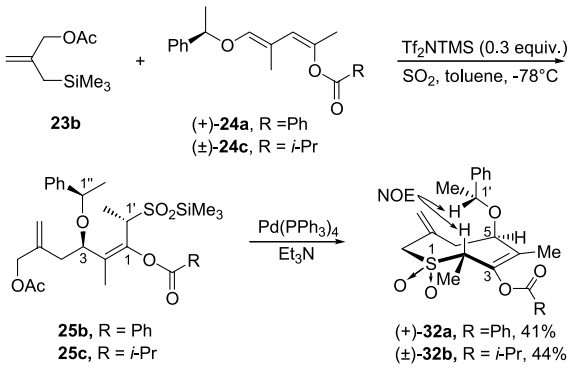


Figure 1. Representation of the X-ray molecular structure of (−)-**27a**.[44]



Scheme 4. Synthesis of 1,2-thiazonin-8-yl derivatives.



Scheme 5. Synthesis of a 5,6,7,8-tetrahydro-2*H*-thiocines.

relative configuration 6,9-*cis* in (−)-**30** and 6,9-*trans* in (−)-**31** was established by the 2D-^{1}H NMR spectra and especially by the NOESY spectra. Compounds (−)-**30** and (−)-**31** are the first members of the 2,3,4,5,6,9-hexahydro-1,2-thiazonine class of heterocycles.[42]

We have also explored the possibility to generate 5,6,7,8-tetrahydro-2*H*-thiocine derivatives by intramolecular electrophilic quenching of our intermediate silyl sulfinates. An example is given (Scheme 5) by the reaction of the racemic silyl sulfinate **25c** obtained by oxyallylation of allylsilane **23b** with diene (±)-**24c**. Its treatment with 2 equiv of Et_3N and 0.1 equiv of $(Ph_3P)_4Pd$ in THF provided the cyclic sulfone (±)-**32b**, which was purified by column chromatography on silica gel and isolated in 44% yield. Its structure has been established by single crystal X-ray diffraction studies (Fig. 2). The same reaction sequence has been applied to the enantiomerically enriched (97% ee) diene (+)-**24a**[35,37] (Scheme 5), which produced (+)-**32a** through **25b** in 41% overall yield. As for other related systems obtained under similar conditions[35] the relative configuration between C(1″) of the 1-phenylethyl group (chiral auxiliary) and the adjacent stereogenic center C(3) in the open chain system **25b** is assumed to be like. Moreover, NMR data proved the unlike relative configuration between C(5) and C(2) in the thiocine structure (+)-**32a**.

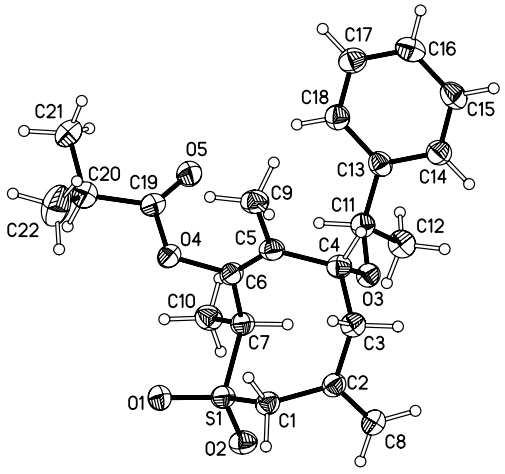


Figure 2. Molecular structure of (±)-**32b** by single crystal X-ray diffraction.[48]

3. Conclusion

Our one-pot, four-component syntheses of polyfunctional sulfones and sulfonamides have been extended to a large variety of 1,3-dienes, enoxysilanes and allylsilanes. In the case of sulfonamide formation, epimerization of the stereogenic α-center of the β,γ-unsaturated sulfonamides cannot be avoided in several instances. For the first time new heterocyclic synthesis such as 2,3,4,5,6,9-hexahydro-1,2-thiazonine derivatives have been obtained. This was possible by intramolecular Pd-catalyzed *N*-allylation reactions. In a similar way, intramolecular S-allylation of intermediate silyl sulfinate has allowed the preparation of a new tetrahydro-2*H*-thiocine derivatives. Using enantiomerically enriched 1-oxy- or 1,3-dioxy-1,3-dienes enantiomerically enriched polyfunctional sulfones and sulfonamides are prepared readily.

4. Experimental

4.1. General remarks

Reagents were purchased from Acros, Fluka, Senn, Aldrich or Merk and used without further purification. All solvents for extraction and chromatography were distilled prior to use. Anhyd THF, Et_2O and toluene were distilled from sodium benzophenone, CH_2Cl_2 from CaH_2, and methanol from magnesium. Reactions were monitored by TLC (Merk Kiesegel $60F_{254}$) silica gel plates; detection with UV (254 nm) light or molybdic reagent (21 g of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1 g of $Ce(SO_4)_2$, 31 mL H_2SO_4 and 470 mL of H_2O). Flash chromatography (FC) used 230–400 mesh silica gel (Merk no.9385). Melting points were measured with a Mettler FP52 and were uncorrected. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. UV spectra were recorded on a Kontron Uvikon 810 CW spectrophotometer. IR spectra were recorded on Perkin Elmer Paragon 1000 FT-IR spectrometer. Mass spectra were recorded on a Nermag R 10-10C in chemical ionisation mode. Electron spray mass analyses were recorded on a Finnigan MAT SSQ 710C spectrometer in positive ionisation mode. ^{1}H NMR spectra were recorded on Bruker DPX-400 FT, Bruker ARX-400 FT spectrometers. ^{13}C NMR spectra were recorded on Bruker DPX-400 FT (100.61 MHz), Bruker ARX-400 FT (100.61 MHz) machines; all ^{13}C signal assignments were confirmed by HMQC spectra. Chemical shifts in ppm, relative to internal standard such as residual signals of solvents, coupling constants in hertz. All structures and signal assignments were confirmed by 2D-NOESY ^{1}H NMR and 2D-COSY ^{1}H NMR spectra. Microanalyses were performed by the Ilse Beetz Laboratory, Kronach (Germany).

Starting materials **16a**[49] (risk of explosion in the preparation of this compound!), **16b**,[50] **16c**,[51] **16d**,[43] **17a**,[33b,51] **17b**,[32,52] **17c**,[34,39b] **17d**,[53] **24a**,[35–37] and **24c**,[35–37] were prepared according to the literature procedures.

4.2. General procedure for the preparation of oxo-(*Z*)-β, γ-unsaturated sulfones 18, 19 using enoxysilanes

Tf_2NH (0.5 M in CH_2Cl_2, 1.35 mL, 0.68 mmol, 0.2 equiv) in anhyd CH_2Cl_2 (2 mL) was degassed by freeze-thaw cycles on the vacuum line. SO_2 (5 mL, 114.0 mmol, 34 equiv), dried through a column packed with basic alumina and phosphorus pentoxide, was transferred on the vacuum line to the CH_2Cl_2 solution frozen at −196 °C. The mixture was allowed to melt and to warm to −78 °C. After 1 h at this temperature a solution of 1,3-diene **17** (1 equiv) and the enoxysilane **16** (2–5 equiv) in CH_2Cl_2 (3 mL) was added slowly. The mixture was stirred at −78 °C for 12 h. Excess of SO_2 and solvent were evaporated under reduced pressure (10^{-1} Torr) to dryness, while temperature was rising to 25 °C in ca. 1 h. A 1 M solution of Bu_4NF in THF (1 equiv) and electrophile **EX** (2.5–7 equiv) were added under Ar atmosphere. The mixture was stirred at −40 °C for 1 h, then allowed to reach 20 °C in about 10 h. After the addition of H_2O (40 mL) and neutralization with satd aq soln of $NaHCO_3$ (10 mL), the mixture was extracted with CH_2Cl_2 (30 mL, three times). The combined organic extracts were washed with brine (30 mL, two times), dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (FC).

4.2.1. (±)-(2*RS*,3*RS*,4*Z*,6*SR*)-3-benzyloxy-1-(4-methoxyphenyl)-2,4-dimethyl-6-((2-methylprop-2-enyl)sulfonyl-(-1-phenylhept-4-en-1-one ((±)-18b). This preparation followed the above procedure and used (*Z*)-1-(4-methoxyphenyl)-1-trimethylsilyloxypropylene (**16b**)[50] (2.09 g, 8.8 mmol) and (*E*,*E*)-1-benzyloxy-2-methyl-penta-1,3-diene **17b**[32] (870 mg, 4.41 mmol) and 3-bromo-2-methylpropene (1.11 mL, 11.01 mmol). A 5:1 mixture of (±)-**18b** and (±)-**19b** was obtained. FC (light petroleum ether/EtOAc 8:2, R_f=0.30), gave 1.04 g (76%) of pure (±)-**18b** as a colorless oil. IR (film): *ν* 2975, 2935, 1670, 1405, 1375, 1305, 1210, 1120, 1070, 970, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.92 (d, 2H, ^3J=8.9 Hz, H–C(ar)), 7.51 (t, 2H, ^3J=8.8 Hz, H–C(ar)), 7.41 (d, 2H, ^3J=8.0 Hz, H–C(ar)), 7.38 (t, 2H, ^3J=7.1 Hz, H–C(ar)), 7.30 (d, 1H, ^3J=7.5 Hz, H–C(ar)), 5.32 (br s, 1H, H–C(3′)), 5.29 (d, 1H, $^3J(H_5,H_6)$=10.7 Hz, H–C(5)), 5.18 (br s, 1H, H–C(3′)), 4.63 (d, 1H, ^2J=11.8 Hz, H–CH_2Bn), 4.54 (d, 1H, $^3J(H_3,H_2)$=9.8 Hz, H–C(3)), 4.49 (d, 1H, ^2J=11.8 Hz, CH_2Bn), 4.34 (dq, 2H, $^3J(H_6,H_5)$=10.7 Hz, $^3J(H_6,H_7)$=6.6 Hz, H–C(2)) 3.89 (m, 1H, H–C(6)), 3.89 (s, 3H, O*Me*), 3.79 (d, 1H, ^2J=13.2 Hz, Hb–C(1′)), 3.59 (d, 1H, ^2J=13.2 Hz, Ha–C(1′)), 2.03 (s, 3H, *Me*-C(2′)), 1.79 (s, 3H, *Me*-C(4)), 1.39 (d, 6H, ^3J=6.6 Hz, *Me*-C(2) and *Me*-C(6)). ^{13}C NMR (100.6 MHz, $CDCl_3$): *δ* 164.0 (s, CO), 133.2 (s, C(2′)), 129.8 (m, C(ar)), 126.3 (s, C(4)), 122.3 (t, ^1J(C,H)=152 Hz, C(3′)), 114.1 (d, ^1J(C,H)=160 Hz, C(5)), 78.7 (d, ^1J(C,H)=167 Hz, C(6)), 70.9 (t, ^1J(C,H)=158 Hz, *C*H_2–Bn), 58.1 (t, ^1J(C,H)=157 Hz, C(1′)), 56.6 (q, ^1J(C,H)=125 Hz, O*Me*), 55.5 (d, ^1J(C,H)=168 Hz, C(3)), 43.5 (d, ^1J(C,H)=138 Hz, C(2)), 23.1 (q, ^1J(C,H)=126 Hz, *Me*-C(4)), 18.6 (q, ^1J(C,H)=132 Hz, *Me*-C(6)), 16.3 (q, ^1J(C,H)=126 Hz, *Me*-C(2′)), 15.5 (q, ^1J(C,H)=132 Hz, *Me*-C(2)). CI-MS (NH_3): *m/z* 392 (100, $[M+18]^+$), 375 (57, $[M+1]^+$). MALDI-HRMS: calcd for $C_{27}H_{34}SO_4+Na^+$: 493.2025; found: 493.2019.

4.2.2. (±)-(2*RS*,3*RS*,4*Z*,6*SR*)-3-benzyloxy-6-[(2-methylprop-2-en-yl)sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one ((±)-18c). This preparation followed the above general procedure using trimethyl{[(1*E*)-1-(2,4,6,-trimethoxyphenyl)prop-1-enyl]-oxy}silane[51] (**16c**, 3.5 g, 11.8 mmol, 2.8 equiv), (*E*,*E*)-1-benzyloxy-penta-1,3-diene[32] (**17b**, 800 mg, 4.2 mmol, 1 equiv) and 3-bromo-2-methylpropene (1.72 g, 1.3 mL, 12.8 mmol, 3 equiv). A 6:1 mixture of (±)-**18c** and (±)-**19c** was obtained. FC (light petroleum ether/EtOAc 4:1, R_f=0.27), gave 1.63 g (77%) of pure (±)-**18c** and 0.27 g (13%) of (±)-**19c**, both yellowish oils. Data of **18c**: UV (CH_3CN): λ_{max}=214 nm (*ε*=19600). IR (film): *ν* 2973, 2842, 1693, 1645, 1587, 1455, 1414, 1305, 1229, 1207, 1158, 1130, 1068, 1029, 968, 914, 856 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.39 (d, 2H, ^3J=7.7 Hz, H–C(ar)), 7.34 (t, 2H, ^3J=7.7 Hz, H–C(ar)), 7.28 (t, 1H, ^3J=7.7 Hz, H–C(ar)), 6.10 (s, 2H, H–C(ar)), 5.42 (d, 1H, $^3J(H_5–H_6)$=9.6 Hz, H–C(5)), 5.27 (br s, 1H, H–C(3′)), 5.15 (br s, 1H, H–C(3′)), 4.58 (d, 1H, ^2J=11.8 Hz, H–*C*H_2–Bn), 4.55 (d, 1H, $^3J(H_3,H_2)$=8.6 Hz, H–C(3)), 4.47 (dq, 1H, $^3J(H_6,H_5)$=9.6 Hz, $^3J(H_6,H_7)$=6.7 Hz, H–C(6)), 4.42 (d, 1H, ^2J=11.8 Hz, *C*H_2–Bn), 3.84 (s, 3H, H–O*Me*), 3.76 (s, 6H, H–O*Me*), 3.73 (d, 1H, ^2J=13.4 Hz, Ha–C(1′)), 3.64 (d, 1H, ^2J=13.4 Hz, Hb–C(1′)), 3.43 (dq, 1H, $^3J(H_2–H_3)$=8.6 Hz, $^3J(H_2–Me_2)$=7.1 Hz, H–C(2)), 2.02 (s, 3H, *Me*-C(4)), 1.85 (s, 3H, *Me*-C(2′)), 1.49 (d, 3H, $^3J(H_7,H_6)$=6.7 Hz, H–C(7)), 1.29 (d, 3H, ^3J(Me, 2H)=7.1 Hz, *Me*-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$): *δ* 206.2 (s, CO), 163.1–158.9 and 139.3 (s, 5C(ar)), 143.1 (s, C(2′)), 133.6 (s, C(4)), 128.1–128.06 (d, 7C, ^1J(C,H)=149 Hz, C(ar)), 122.1 (t, ^1J(C,H)=159 Hz, C(3′)), 120.7 (d, ^1J(C,H)=152 Hz, C(5)), 79.9 (t, ^1J(C,H)=156 Hz, *C*H_2–Bn), 71.1 (t,^1J(C,H)=148 Hz, C(1′)), 58.5 (d, ^1J(C,H)=132 Hz, C(3)), 57.4 (d, ^1J(C,H)=140 Hz, C(6)), 55.5 (q, ^1J(C,H)=138 Hz, C(O*Me*)), 51.4 (d, ^1J(C,H)=128 Hz, C(2)), 23.5 (q, ^1J(C,H)=125 Hz, *Me*-C(2′)), 19.4 (q, ^1J(C,H)=129 Hz, *Me*-C(4)), 15.8 (q, ^1J(C,H)=134 Hz, C(7)), 14.6 (q, ^1J(C,H)=130 Hz, *Me*-C(2)). CI-MS (NH_3): $C_{29}H_{38}SO_7$, *m/z* 548 (12, $[M+18]^+$), 531 (100, $[M+1]^+$), 225 (69). MALDI-HRMS: calcd for $C_{29}H_{38}SO_7+Na^+$: 553.2236; found: 553.2229.

4.2.3. (±)-(3*RS*,4*RS*,5*Z*,8*SR*)-1-hydroxy-3,5-dimethyl-7-(methylsulfonyl)-4-{1-(*RS*)-[2,4,6-tris(isopropyl)phenyl]-ethoxy}octa-5-en-2-one ((±)-18d). This compound was prepared applying the above general procedure using (*Z*)-1,2-bis(trimethylsilyloxy)but-1-ene (**16d**)[43] (0.3 g, 1.28 mmol, 1.2 equiv), (±)-1,3,5-triisopropyl-2-{(*R*,*S*)-1-[(*E*,*E*)-2-methylpenta-1,3-dien-1-yloxy]ethyl}benzene (**17c**)[34,39c] (0.2 g, 0.64 mmol) and MeI (0.3 mL, 4.8 mmol). A 3:1 mixture of (±)-**18d** and (±)-**19d** was obtained. FC (light petroleum ether/AcOEt 2:1) gave 66 mg (23%) of pure (±)-**18d**, colorless oil. Data for (±)-**18d**: ^1H NMR ($CDCl_3$, 400 MHz): *δ* 7.0–6.9 (m, 2H arom); 5.45 (d, 1H, $^3J(H_6,H_7)$=11 Hz, H–C(6)); 4.98 (q, 1H, $^3J(H_{1'}–H_{2'})$=6.7 Hz, H–C(1′)); 4.43 (d, 1H, $^3J(H_4,H_3)$=9.9 Hz, H–C(4)); 4.35 (s, 1H, H_1); 4.21 (dq, 1H, $^3J(H_7,H_6)$=11 Hz, $^3J(H_7,H_8)$=6.7 Hz, H–C(7)); 3.7, 3.09 (2 sept. 2H, $^3J((CH_3)_2CH$-Ar, $(CH_3)_2CH$-Ar)=6.7 Hz, 2 $(CH_3)_2CH$-Ar); 2.9 (s, 3H, $–SO_2CH_3$); 2.87 (m, 1H, $(CH_3)_2CH$-Ar); 2.87 (m, 1H, H–C(3)); 1.91 (d, 3H, $^4J(Me_5–H_6)$=1.3 Hz, Me-C(5)); 1.52 (d, 3H, $^3J(Me_{2'}–H_{1'})$=6.7 Hz, Me(2′)); 1.43

(d, 3H, $^3J(Me_8,H_7)=6.7$ Hz, Me-C(8)); 1.27–1.19 (m, 3H, 3 $(CH_3)_2CH$-Ar); 1.15 (d, 3H, $^3J(Me_3,H_3)=6.7$ Hz, Me-C(3)). ^{13}C NMR ($CDCl_3$, 100.61 MHz): δ 211.9 148.0, 147.5, 145.8, 141.6, 135.0, 123.1, 120.4, 121.8, 84.6, 73.7, 68.0, 58.2, 46.7, 36.8, 34.0, 29.6, 29.2, 24.99, 24.56, 24.05, 23.9, 21.4, 14.5, 14.2, 10.46. CI-MS (NH_3): 512 (36, $[M+18]^+$), 479 (6), 231 (100), 189 (3), 167 (8.29), 141 (17), 84 (26).

4.2.4. 6:1 Mixture of (±)-(2*RS*,3*RS*,4*Z*,6*SR*)-3-hydroxy-6-[(3-hydroxy-2-methylpropen-2-yl)sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one (±)-18e and (±)-(2*RS*,3*SR*,4*Z*,6*RS*)-3-hydroxy-6-[(3-hydroxy-2-methylpropen-2-yl)sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one (±)-19e. This preparation followed the above general procedure using (*E*,*E*)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene (580 mg, 3.41 mmol, 1 equiv) and trimethyl{[(1*E*)-1-(2,4,6,-trimethoxyphenyl)prop-1-enyl]oxy}silane (1.7 g, 5.8 mmol, 1.7 equiv). The reaction mixture was quenched with a 1 M solution of Bu_4NF in THF (3.41 mL, 3.41 mmol, 1 equiv) and 3-bromo-2-methylpropene (1.15 g, 0.86 mL, 8.52 mmol, 2.5 equiv) in CH_2Cl_2 (5 mL). Crude reaction mixture contains (±)-**18e** and (±)-**19e** with the ratio 6:1. FC (light petroleum ether/EtOAc 1:1, $R_f=0.33$) gives 0.95 g (82%) of 6:1 mixture of (±)-**18e** and (±)-**19e** as a yellowish oil. Only (±)-**18e** can be analyzed from the spectra of the mixture. UV (CH_3CN): $\lambda_{max}=224$ nm ($\varepsilon=13737$), 200.6 (9177). IR (film): ν 3410, 2980, 2940, 2840, 1670, 1605, 1455, 1415, 1300, 1205, 1160, 1000, 900, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) of (±)-**18e**: δ 6.12 (s, 2H, H–C(ar)), 5.26 (br s, 1H, H–C(3′)), 5.18 (d, 1H, $^3J(H_5–H_6)=9.6$ Hz, H–C(5)), 5.11 (br s, 1H, H–C(3′)), 4.80 (d, 1H, $^3J(H_3–H_2)=7.0$ Hz, H–C(3)), 4.43 (dq, 1H, $^3J(H_6–H_5)=9.6$ Hz, $^3J(H_6–H_7)=7.0$ Hz, H–C(6)), 3.83 (s, 3H, H–OMe), 3.79 (s, 6H, H–OMe), 3.71 (d, 1H, $^2J=13.4$ Hz, Ha–C(1′)), 3.64 (d, 1H, $^2J=13.4$ Hz, Hb–C(1′)), 3.28 (qd, 1H, $^3J(H_2–Me_2)=(H_2–H_3)=7.0$ Hz, H–C(2)), 2.73 (br s, 1H, H–OH)), 1.98 (s, 3H, Me-C(4)), 1.84 (s, 3H, Me-C(2′)), 1.49 (d, 3H, $^3J(H_7–H_6)=7.0$ Hz, H–C(7)), 1.23 (d, 3H, $^3J(Me_2–H_2)=7.1$ Hz, Me-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$) of (±)-**18e**: δ 206.0 (s, CO), 162.6–158.4 (s, 4Car), 145.4 (s, C(2′)), 133.2 (s, C(4)), 122.8 (t, $^1J(C,H)=162$ Hz, C(3′)), 119.4 (d, $^1J(C,H)=159$ Hz, C(5)), 90.8 and 90.6 (d, 2C, $^1J(C,H)=159$ Hz, C(ar)), 70.8 (t, $^1J(C,H)=144$ Hz, C(1′)), 58.1 (d, $^1J(C,H)=134$ Hz, C(3)), 55.9 (d, $^1J(C,H)=140$, Hz C(6)), 55.6 (q, $^1J(C,H)=145$ Hz, C(OMe)), 51.1 (d, $^1J(C,H)=131$ Hz, C(2)), 23.1 (q, $^1J(C,H)=129$ Hz, Me-C(2′)), 19.2 (q, $^1J(C,H)=130$ Hz, Me-C(4)), 14.7 (q, $^1J(C,H)=131$ Hz, C(7)), 12.4 (q, $^1J(C,H)=130$ Hz, Me-C(2)). CI-MS (NH_3): $C_{22}H_{32}O_7S$: *m*/*z* 441 (62, $[M+1]^+$), 225 (100). Anal. Calcd for $C_{28}H_{50}O_3Si_2$ (440.19): C, 59.98; H, 7.32. Found: C, 59.83; H, 7.29.

4.2.5. 9:1 Mixture of (±)-(2*RS*,3*RS*,4*E*,6*RS*)-3-{[(*tert*-butyl)dimethylsilyl]oxy}-6-[(2-methylprop-2-enyl) sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one ((±)-18f) and (±)-(2*RS*,3*RS*,4*E*,6*SR*)-3-{[(*tert*-butyl)dimethylsilyl]oxy}-6-[(2-methylprop-2-enyl) sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one ((±)-19f). This preparation followed the above general procedure using from (*E*,*E*)-2-methyl-1-trimethylsilyloxy-1,3-pentadiene (580 mg, 3.41 mmol, 1 equiv) and trimethyl{[(1*E*)-1-(2,4,6,-trimethoxyphenyl)prop-1-enyl]oxy}silane (1.7 g, 5.8 mmol, 1.7 equiv) in CH_2Cl_2 (3 mL). The reaction mixture was quenched with a 1 M solution of Bu_4NF in THF (3.41 mL, 3.41 mmol, 1 equiv) and 3-bromo-2-methylpropene (1.15 g, 0.86 mL, 8.52 mmol, 2.5 equiv) in CH_2Cl_2 (5 mL). Then 2,6-lutidine (1.82 g, 1.97 mL, 17.05 mmol, 5 equiv) followed by TBSOTf (2.69 g, 2.35 mL, 10.23 mmol, 3 equiv) were added to the resulting residue stirred at −78 °C (1.49 g, 3.41 mmol, 1 equiv) in anhyd CH_2Cl_2 (10 mL). After 2 h at −78 °C, the crude reaction mixture was allowed to warm to room temperature within 1 h. The mixture was then treated with 2 M aqueous solution of NaOH (2 mL) and extracted with CH_2Cl_2 (40 mL, three times). The combined organic extracts were washed with 1 M HCl (20 mL) and with brine (40 mL, twice), dried (Na_2SO_4) and the solvent eliminated under reduced pressure. Crude reaction mixture contains (±)-**18f** and (±)-**19f** with the ratio 9:1. FC (light petroleum ether/EtOAc 4:2, $R_f=0.30$) gives 1.14 g (60%) of a 9:1 mixture of (±)-**18f** and (±)-**19f** as a yellow oil. Both diastereoisomers can be analyzed from the specta of the mixture. UV (CH_3CN): $\lambda_{max}=209$ nm ($\varepsilon=7924$). IR (film): ν 2987, 1694, 1606, 1456, 1421, 1305, 1266, 1157, 1132, 898, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) of (±)-**18f**: δ 6.09 (s, 2H, Har), 5.54 (d, 1H, $^3J(H_5–H_6)=10.5$ Hz, H–C(5)), 5.26 (br s, 1H, H–C(3′)), 5.05 (br s, 1H, H–C(3′)), 4.58 (d, 1H, $^3J(H_3–H_2)=6.2$ Hz, H–C(3)), 3.92 (dq, 1H, $^3J(H_6–H_5)=10.5$ Hz, $^3J(H_6–H_7)=7.1$ Hz, H–C(6)), 3.82 (s, 3H, H–O*Me*), 3.77 (s, 6H, H–O*Me*), 3.59 (d, 1H, $^2J=12.1$ Hz, Ha–C(1′)), 3.57 (d, 1H, $^2J=12.1$ Hz, Hb–C(1′)), 3.2 (qd, 1H, $^3J(H_2–Me_2)=7.4$ Hz, $^3J(H_2–H_3)=6.2$ Hz, H–C(2)), 1.97 (s, 3H, *Me*-C(4)), 1.73 (s, 3H, *Me*-C(2′)), 1.42 (d, 3H, $^3J(H_7–H_6)=7.1$ Hz, H–C(7)), 1.11 (d, 3H, $^3J(Me_2–H_2)=7.4$ Hz, *Me*-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$) of (±)-**18f**: δ 209.2 (s, CO), 162.3–158.4 (s, 4C, C(ar)), 144.4 (s, C(2′)), 133.1 (s, C(4)), 120.4 (t, $^1J(C,H)=149$ Hz, C(3′)), 117.9 (d, $^1J(C,H)=161$ Hz, C(5)), 90.6 and 90.5 (d, 2C, $^1J(C,H)=161$ Hz, C(ar)), 70.4 (t, $^1J(C,H)=154$ Hz, C(1′)), 58.1 (d, $^1J(C,H)=148$ Hz, C(3)), 56.9 (d, $^1J(C,H)=133$ Hz, C(6)), 55.6 (q, $^1J(C,H)=151$ Hz, C(O*Me*)), 51.6 (d, $^1J(C,H)=146$ Hz, C(2)), 25.8 (q, $^1J(C,H)=142$ Hz, *t*-Bu), 23.1 (q, $^1J(C,H)=133$ Hz, *Me*-C(2′)), 18.3 (q, $^1J(C,H)=132$ Hz, *Me*-C(4)), 15.1 (s, Cquat-*t*Bu)), 14.6 (q, $^1J(C,H)=131$ Hz, *Me*-C(6)), 12.6 (q, $^1J(C,H)=139$ Hz, *Me*-C(2)), −4.2 (q, $^1J(C,H)=127$ Hz, Me_2Si–C(3)), −5.0 (q, $^1J(C,H)=129$ Hz, Me_2Si–C(3)). ^1H NMR (400 MHz, $CDCl_3$) of (±)-**19f**: δ 6.09 (s, 2H, H–C(ar)), 5.54 (d, 1H, $^3J(H_5–H_6)=10.5$ Hz, H–C(5)), 5.21 (br s, 1H, H–C(3′)), 5.14 (br s, 1H, H–C(3′)), 4.80 (d, 1H, $^3J(H_3–H_2)=7.6$ Hz, H–C(3)), 4.4 (qd, 1H, $^3J(H_6–H_5)=10.5$ Hz, $^3J(H_6–H_7)=6.5$ Hz, H–C(6)), 3.82 (s, 3H, H–O*Me*), 3.77 (s, 6H, H–O*Me*), 3.56 (d, 1H, $^2J=12.7$ Hz, H–C(1′)), 3.54 (d, 1H, $^2J=12.7$ Hz, H–C(1′)), 3.2 (dq, 1H, $^3J(H_2–Me_2)=7.4$ Hz, $^3J(H_2–H_3)=6.5$ Hz, H–C(2)), 2.01 (s, 3H, *Me*-C(4)), 1.82 (s, 3H, *Me*-C(2′)), 1.37 (d, 3H, $^3J(H_7–H_6)=6.5$ Hz, H–C(7)), 1.11 (d, 3H, $^3J(Me_2–H_2)=7.4$ Hz, *Me*-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$) of (±)-**19f**: δ 209.1 (s, CO), 162.3–158.4 (s, 4C, C(ar)), 145.6 (s, C(2′)), 133.3 (s, C(4)) 120.6 (t, $^1J(C,H)=146$ Hz, C(3′)), 117.9 (d, $^1J(C,H)=161$ Hz, C(5)), 90.6 and 90.5 (d, 2C, $^1J(C,H)=161$ Hz, C(ar)), 70.4 (t, $^1J(C,H)=154$ Hz, C(2′)), 57.6 (d, $^1J(C,H)=143$ Hz, C(3)), 56.7 (d, $^1J(C,H)=131$ Hz, C(6)), 55.6 (q, $^1J(C,H)=151$ Hz, C(O*Me*)), 53.4 (d,

^1J(C,H)=139 Hz, C(2)), 25.8 (q, ^1J(C,H)=142 Hz, *t*-Bu), 23.2 (q, ^1J(C,H)=130 Hz, *Me*-C(2′)), 18.2 (q, ^1J(C,H)=129 Hz, *Me*-C(4)), 15.4 (q, ^1J(C,H)=128 Hz, *Me*-C(6)), 15.0 (s, Cquat-*t*Bu), 13.8 (q, ^1J(C,H)=132 Hz, *Me*-C(2)), −4.7 (q, ^1J(C,H)=126 Hz, *Me*Si–C(3)), −5.3 (q, ^1J(C,H)=129 Hz, *Me*Si–C(3)). CI-MS (NH_3): $C_{28}H_{46}SSiO_7$, *m/z* 555 (25, $[M+1]^+$), 108 (100). Anal. Calcd for $C_{28}H_{46}O_7SSi$ (554.27): C, 60.62; H, 8.36. Found: C, 60.80; H, 8.49.

4.3. General procedure for the preparation of oxo-(*E*)-β,γ-unsaturated sulfones (20,21) using enoxysilanes

Same procedure for the preparation of **18**, **19**, but using 0.5 equiv of Tf_2NH introduced to the $SO_2+CH_2Cl_2$ solution as a 0.5 M solution in anhyd CH_2Cl_2.

4.3.1. 1:1 Mixture of (±)-(3*RS*,4*RS*,5*E*,7*RS*)-4-hydroxy-7-(2-methyl-propyl-1-sulfonyl)-3,5-dimethyloct-5-en-2-one and ((±)-20a) (±)-(3*RS*,4*SR*,5*E*,7*SR*)-4-hydroxy-7-(2-methyl-propyl-1-sulfonyl)-3,5-dimethyloct-5-en-2-one ((±)-21a). This preparation applies the above procedure using a 1:1 mixture of (*E*) and (*Z*)- 2-triethylsilyloxybut-2-ene (7.92 g, 43 mmol, 2 equiv), (*E*,*E*)-2-methyl-1-trimethylsilyloxypenta-1,3-diene (4 g, 21.25 mmol, 1 equiv) and 1-iodo-2-methylpropane (4.84 g, 26.3 mmol, 5 equiv) in CH_3CN (15 mL) DMF (55 mL). FC (light petroleum ether/EtOAc 7:3, R_f=0.31) gave 6.7 g (82%), colorless oil. UV (CH_3CN): λ=219 nm (ε=5800). IR (film, cm^{-1}): ν 3470, 2970, 2930, 2855, 1710, 1650, 1460, 1340, 1285, 1195, 1135, 1040, 740. ^{1}H NMR (400 MHz, $CDCl_3$, 283 K) of (±)-**20a**: δ 5.58 (d, 1H, $^3J(H_6,H_7)$=10.3 Hz, H–C(6)), 4.46 (m, 2H, H–C(4)), 3.87 (dq, 1H, $^3J(H_7,H_6)$=10.3 Hz, $^3J(H_7,H_8)$=7.1 Hz, H–C(7)), 3.15 (d, 1H, $^3J(H_4,OH)$=2.6 Hz, H–OH), 2.77 (m, 3H, H–C(1′), H–C(3)), 2.41 (tqq, 1H, $^3J(H_{2'},H_{1'})$=6.4 Hz, $^3J(H_{2'},H_{3'a})$=6.4 Hz, $^3J(H_{2'},H_{3'b})$=6.4 Hz, H–C(2′)), 2.26 (s, 3H, H–C(1)), 1.87 (s, 3H, *Me*-C(5)), 1.50 (d, 3H, $^3J(H_8,H_7)$=7.1 Hz, H–C(8)), 1.16 (d, 3H, $^3J(Me_3,H_3)$=6.4 Hz, *Me*-C(3)), 1.15 (d, 3H, $^3J(H_{3'},H_{2'})$=6.4 Hz, H–C(3′)), 1.13 (d, 3H, $^3J(H_{3'},H_{2'})$=6.4 Hz, H–C(3′)). ^{13}C NMR (100 MHz, $CDCl_3$, 283K) of (±)-**20a**: δ 211.2 (s, C(2)), 142.7 (s, C(5)), 121.1 (d, ^1J(C,H)=155 Hz, C(6)), 75.2 (d, ^1J(C,H)=140 Hz, C(7)), 64.1 (d, ^1J(C,H)=130 Hz, C(3)), 58.9 (d, ^1J(C,H)=142 Hz, C(4)), 56.9 (t, ^1J(C,H)=136 Hz, C(1′)), 49.5 (d, ^1J(C,H)=135 Hz, C(2′)), 29.4 (q, ^1J(C,H)=129 Hz, C(1)), 23.5 (q, ^1J(C,H)=140 Hz, *Me*-C(5)), 23.3 (q, ^1J(C,H)=134 Hz, C(8)), 15.3 (q, ^1J(C,H)=131 Hz, *Me*-C(3)), 14.2 (q, ^1J(C,H)=132 Hz, C(3′)), 14.1 (q, ^1J(C,H)=133 Hz, C(3′)). ^{1}H NMR (400 MHz, $CDCl_3$, 283 K) of (±)-**21a**: δ 5.57 (d, 1H, $^3J(H_6,H_7)$=10.3 Hz, H–C(6)), 4.46 (m, 2H, H–C(4)), 3.86 (dq, 1H, $^3J(H_7,H_6)$=10.3 Hz, $^3J(H_7,H_8)$=7.1 Hz, H–C(7)), 3.08 (d, 1H, $^3J(H_4,OH)$=2.6 Hz, H–OH), 2.77 (m, 3H, H–C(1′), H–C(3)), 2.41 (tqq, 1H, $^3J(H_{2'},H_{1'})$=6.4 Hz, $^3J(H_{2'},H_{3'a})$=6.4 Hz, $^3J(H_{2'},H_{3'b})$=6.4 Hz, H–C(2′)), 2.24 (s, 3H, H–C(1)), 1.86 (s, 3H, *Me*-C(5)), 1.48 (d, 3H, $^3J(H_8,H_7)$=7.1 Hz, H–C(8)), 1.16 (d, 3H, $^3J(Me,H_3)$=6.4 Hz, *Me*-C(3)), 1.15 (d, 3H, $^3J(H_{3'},H_{2'})$=6.4 Hz, H–C(3′)), 1.13 (d, 3H, $^3J(H_{3'},H_{2'})$=6.4 Hz, H–C(3′)). ^{13}C NMR (100 MHz, $CDCl_3$, 283K) of (±)-**21a**: δ 211.1 (s, C(2)), 142.2 (s, C(5)), 119.5 (d, ^1J(C,H)=150 Hz, C(6)), 74.3 (d, ^1J(C,H)=148 Hz, C(7)), 63.9 (d, ^1J(C,H)=130 Hz, C(3)), 58.5 (d, ^1J(C,H)=141 Hz, C(4)), 56.7 (t, ^1J(C,H)=132 Hz, C(1′)), 49.1 (d, ^1J(C,H)=140 Hz, C(2′)), 29.3 (q, ^1J(C,H)=133 Hz, C(1)), 23.4 (q, ^1J(C,H)=133 Hz, *Me*-C(5)), 23.2 (q, ^1J(C,H)=136 Hz, C(8)), 14.9 (q, ^1J(C,H)=132 Hz, *Me*-C(3)), 10.7 (q, ^1J(C,H)=129 Hz, C(3′)), 9.8 (q, ^1J(C,H)=130 Hz, C(3′)). MALDI-HRMS: calcd for $C_{14}H_{26}O_4S+K^+$: 329.1189 and $C_{14}H_{26}O_4S+Na^+$: 313.1449, found: 313.2285. Anal. Calcd for $C_{14}H_{26}O_4S$ (290.16): C, 57.90; H, 9.02. Found: C, 57.86; H, 9.02.

4.3.2. 9:1 Mixture of (±)-(2*RS*,3*RS*,4*E*,6*RS*)-3-{[(*tert*-butyl)dimethylsilyl]oxy}-6-[(2-methylprop-2-enyl) sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one ((±)-20b) and (±)-(2*RS*,3*RS*,4*E*,6*SR*)-3-{[(*tert*-butyl)dimethylsilyl]oxy}-6-[(2-methylprop-2-enyl) sulfonyl]-2,4-dimethyl-1-(2,4,6-trimethoxyphenyl)hept-4-en-1-one ((±)-21b). This preparation followed the above general procedure and used **16c**[49] (1.7 g, 5.8 mmol, 1.7 equiv), (*E*,*E*)-2-methyl-1-[(*tert*-butyl)dimethylsilyl]-oxy-penta-1,3-diene **17d**[33b,51] (580 mg, 3.41 mmol, 1 equiv) and 3-bromo-2-methylpropene (1.15 g, 0.86 mL, 8.52 mmol, 2.5 equiv) in CH_2Cl_2 (5 mL). This provided a mixture of alcohols that was treated with 2,6-lutidine (1.82 g, 1.97 mL, 17.05 mmol, 5 equiv) and by TBSOTf (2.7 g, 2.35 mL, 10.23 mmol, 3 equiv) at −78 °C (1.49 g, 3.41 mmol, 1 equiv) in anhyd CH_2Cl_2 (10 mL). for 1 h. The mixture was then treated with 2 M aq soln of NaOH (2 mL) and extracted with CH_2Cl_2 (40 mL, three times). The combined organic extracts were washed with 1 M HCl (20 mL) and with brine (40 mL, twice), dried (Na_2SO_4) and the solvent was eliminated under reduced pressure. The residue contained α,β-*syn* and α,β-*anti* diastereoisomers (±)-**20c** and (±)-**21c** with the ratio 9:1. FC (light petroleum ether/EtOAc 4:2, R_f=0.30) gave 1.14 g (60%) of a 9:1 mixture of (±)-**20c** and (±)-**21c**, yellow oil. UV (CH_3CN): λ_{max}=209 nm (ε=7924). IR (film): ν 2987, 1694, 1606, 1456, 1421, 1305, 1265, 1155, 1130, 900, 740 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) of (±)-**20c**: δ 6.09 (s, 2H, Har), 5.54 (d, 1H, $^3J(H_5,H_6)$=10.5 Hz, H–C(5)), 5.26 (br s, 1H, H–C(3′)), 5.05 (br s, 1H, H–C(3′)), 4.58 (d, 1H, $^3J(H_3,H_2)$=6.2 Hz, H–C(3)), 3.92 (dq, 1H, $^3J(H_6,H_5)$=10.5 Hz, $^3J(H_6,H_7)$=7.1 Hz, H–C(6)), 3.82 (s, 3H, H–O*Me*), 3.77 (s, 6H, H–O*Me*), 3.59 (d, 1H, ^2J=12.1 Hz, Ha–C(1′)), 3.57 (d, 1H, ^2J=12.1 Hz, Hb–C(1′)), 3.2 (qd, 1H, $^3J(H_2,Me_2)$=7.4 Hz, $^3J(H_2,H_3)$=6.2 Hz, H–C(2)), 1.97 (s, 3H, *Me*-C(4)), 1.73 (s, 3H, *Me*-C(2′)), 1.42 (d, 3H, $^3J(H_7,H_6)$=7.1 Hz, H–C(7)), 1.11 (d, 3H, $^3J(Me_2,H_2)$=7.4 Hz, *Me*-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$) of (±)-**20c**: δ 209.2 (s, CO), 162.3–158.4 (s, 4C, C(ar)), 144.4 (s, C(2′)), 133.1 (s, C(4)), 120.4 (t, ^1J(C,H)=149 Hz, C(3′)), 117.9 (d, ^1J(C,H)=161 Hz, C(5)), 90.6 and 90.5 (d, 2C, ^1J(C,H)=161 Hz, C(ar)), 70.4 (t, ^1J(C,H)=154 Hz, C(1′)), 58.1 (d, ^1J(C,H)=148 Hz, C(3)), 56.9 (d, ^1J(C,H)=133 Hz, C(6)), 55.6 (q, ^1J(C,H)=151 Hz, C(O*Me*)), 51.6 (d, ^1J(C,H)=146 Hz, C(2)), 25.8 (q, ^1J(C,H)=142 Hz, *t*-Bu), 23.1 (q, ^1J(C,H)=133 Hz, *Me*-C(2′)), 18.3 (q, ^1J(C,H)=132 Hz, *Me*-C(4)), 15.1 (s, Cquat-*t*Bu)), 14.6 (q, ^1J(C,H)=131 Hz, *Me*-C(6)), 12.6 (q, ^1J(C,H)=139 Hz, *Me*-C(2)), −4.2 (q, ^1J(C,H)=127 Hz, *Me*$_2$Si–C(3)), −5.0 (q, ^1J(C,H)=129 Hz, *Me*$_2$Si–C(3)). ^{1}H NMR (400 MHz, $CDCl_3$) of (±)-**21c**: δ 6.09 (s, 2H, H–C(ar)), 5.54 (d, 1H, $^3J(H_5,H_6)$=10.5 Hz, H–C(5)), 5.21 (br s, 1H, H–C(3′)), 5.14 (br s, 1H, H–C(3′)), 4.80 (d, 1H, $^3J(H_3,H_2)$=7.6 Hz,

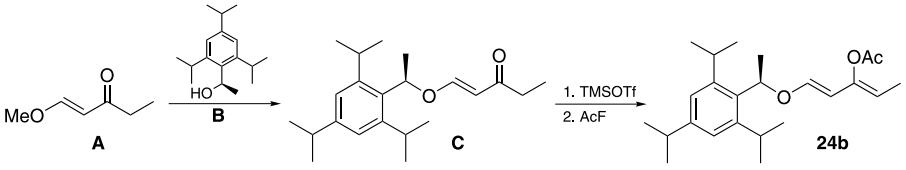
H–C(3)), 4.4 (qd, 1H, $^3J(H_6,H_5)=10.5$ Hz, $^3J(H_6,H_7)=6.5$ Hz, H–C(6)), 3.82 (s, 3H, H–O*Me*), 3.77 (s, 6H, H–O*Me*), 3.56 (d, 1H, $^2J=12.7$ Hz, H–C(1′)), 3.54 (d, 1H, $^2J=12.7$ Hz, H–C(1′)), 3.2 (dq, 1H, $^3J(H_2,Me_2)=7.4$ Hz, $^3J(H_2,H_3)=6.5$ Hz, H–C(2)), 2.01 (s, 3H, *Me*-C(4)), 1.82 (s, 3H, *Me*-C(2′)), 1.37 (d, 3H, $^3J(H_7,H_6)=6.5$ Hz, H–C(7)), 1.11 (d, 3H, $^3J(Me_2,H_2)=7.4$ Hz, *Me*-C(2)). ^{13}C NMR (100.6 MHz, $CDCl_3$) of (±)-**21c**: δ 209.1 (s, CO), 162.3–158.4 (4s, C(ar)), 145.6 (s, C(2′)), 133.3 (s, C(4)) 120.6 (t, $^1J(C,H)=146$ Hz, C(3′)), 117.9 (d, $^1J(C,H)=161$ Hz, C(5)), 90.6 and 90.5 (d, 2C, $^1J(C,H)=161$ Hz, C(ar)), 70.4 (t, $^1J(C,H)=154$ Hz, C(2′)), 57.6 (d, $^1J(C,H)=143$ Hz, C(3)), 56.7 (d, $^1J(C,H)=131$ Hz, C(6)), 55.6 (q, $^1J(C,H)=151$ Hz, C(O*Me*)), 53.4 (d, $^1J(C,H)=139$ Hz, C(2)), 25.8 (q, $^1J(C,H)=142$ Hz, *t*-Bu), 23.2 (q, $^1J(C,H)=130$ Hz, *Me*-C(2′)), 18.2 (q, $^1J(C,H)=129$ Hz, *Me*-C(4)), 15.4 (q, $^1J(C,H)=128$ Hz, *Me*-C(6)), 15.0 (s, Cquat-*t*Bu), 13.8 (q, $^1J(C,H)=132$ Hz, *Me*-C(2)), −4.7 (q, $^1J(C,H)=126$ Hz, *Me*Si–C(3)), −5.3 (q, $^1J(C,H)=129$ Hz, *Me*Si–C(3)). CI-MS (NH_3): $C_{28}H_{46}SSiO_7$, *m/z* 555 (25, $[M+1]^+$), 108 (100). Anal. Calcd for $C_{28}H_{46}O_7SSi$ (554.27): C, 60.62; H, 8.36. Found: C, 60.80; H, 8.49.

4.3.3. Tributyl{2-[(tributylsilyl)methyl]prop-2-enyl}-silane (23c). A mixture of 3-chloro-2-(chloromethyl)prop-1-ene (0.84 mL, 7.93 mmol) and tributylsilyl chloride (4.30 mL, 16.00 mmol, 2 equiv) in anhyd THF (16 mL) was added dropwise (cannulated) to a stirred mixture of anhyd THF (16 mL), naphthalene (104 mg, 0.81 mmol, 0.1 equiv) and lithium shots (0.420 g, 60.51 mmol, 7.6 equiv) at −78 °C. The mixture was stirred overnight after removal of the cooling bath. The mixture was then treated with water (10 mL), extracted with ether (15 mL, three times), the organic phase dried ($MgSO_4$). The crude yellow liquid was distilled over CaH_2 under reduced pressure (0.2 mbar, $T=170$ °C) to yield 2.0 g (4.43 mmol, 56%) of a colorless oil. UV (CH_3CN): $\lambda_{max}=274$ ($\varepsilon=225$), 217 (5160), 200 (3990), 186 (330). IR (neat): 2955, 2920, 2870, 2860, 1620, 1465, 1410, 1375, 1340, 1295, 1275, 1195, 1160, 1080, 1030, 1000, 965, 885, 850, 790, 760, 730. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.37 (s, 2H, H–C(1)), 1.48 (s, 4H, H–C(3)), 1.35–1.24 (m, 24H, H–C(2′), H–C(3′)), 0.89 (t, 18H, $^3J=7.0$ Hz, H–C(4′)), 0.57–0.53 (m, 12H, H–C(1′)). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 145.4 (C(2)), 105.3 (C(1)), 26.8 (C(2′) or C(3′)), 26.1 (C(2′) or C(3′)), 17.8 (C(4′)), 12.2 (C(1′)). MS-CI (NH_3): 453 (1, [M+1]), 425 (1), 397 (2), 374 (4), 340 (4), 199 (49), 143 (100), 87 (29). Anal. Calcd for $C_{28}H_{60}Si_2$ (452.42): C, 74.25; H, 13.65; Si, 12.40. Found: C, 74.36; H, 13.26.

Diene **24b** was prepared according to the synthetic sequence shown below (Scheme 6).

4.3.4. (+)-(1*E*)-1-[1(*R*)-(2,4,6-triisopropylphenyl) ethoxy]pent-1-en-3-one (C). In a 25 mL round bottom flask were added successively (*E*)-1-methoxypent-1-en-3-one (**A**) (1.02 g, 8.93 mmol, 1.03 equiv), (*R*)-(+)-Greene's alcohol (**B**) (2.15 g, 8.65 mmol), pyridinium *p*-toluenesulfonic acid (0.024 g, 0.095 mmol, 1.1%) and toluene (0.5 mL). The flask was placed under vacuum (20 mbar, 30 °C) for 15 h. The mixture was purified by column chromatography (light petroleum ether/ether 4:1) to give 2.664 g (90%) of **C**, colorless solid. $[\alpha]_{589}^{25}+32$; $[\alpha]_{577}^{25}+37$; $[\alpha]_{546}^{25}+40$; $[\alpha]_{435}^{25}+98$; $[\alpha]_{405}^{25}+130$ (*c* 1.0, $CHCl_3$). $R_f=0.24$ (light petroleum ether/ether 4:1). UV (CH_3CN): $\lambda_{max}=261$ ($\varepsilon=7605$), 249 (8300), 225 (7060), 218 (6770), 203 (5400), 188 (1170). IR (KBr): ν 2960, 2930, 2870, 1680, 1660, 1635, 1610, 1590, 1460, 1380, 1360, 1225, 1190, 1110, 1060, 1030, 1000, 945, 880, 650. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, 1H, $^3J=12.1$ Hz, H–C(1)), 7.02 (s, 2 arom CH), 5.67 (d, 1H, $^3J=12.1$ Hz, H–C(2)), 5.64 (q, 1H, $^3J=7.0$ Hz, H–C(1′)), 2.88 (sept, 1H, $^3J=6.8$ Hz, Me_2CH), 2.39 (q, 2H, $^3J=7.7$ Hz, H–C(4)), 1.71 (d, 3H, $^3J=7.0$ Hz, H–C(2′)), 1.31–1.22 (m, 20H, Me_2CH, Me_2CH), 1.06 (t, 3H, $^3J=7.7$ Hz, H–C(5)). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 200.3 (C(3)), 161.0 (C(1)), 148.5 (arom C), 131.3 (arom C), 122.2 (arom C), 106.7 (C(2)), 77.6 (C(1′)), 34.0 (Me_2CH), 29.3 (Me_2CH), 24.6, 24.4, 23.9, 23.8, 22.4, 8.5 (C(5)). MS-CI (NH_3): 331 (4, [M+1]), 231 (100), 215 (20), 189 (12), 147 (28), 131 (15), 91 (9). Anal. Calcd for $C_{22}H_{34}O_2$ (330.51): C, 79.95; H, 10.37; O, 9.68. Found: C, 79.80; H, 10.34.

4.3.5. 3:1 Mixture of (+)-(1*E*,3*E* and 1*E*,3*Z*,1*R*′)-1-[1′-(2,4,6-triisopropylphenylethoxy)]penta-1,3-dien-3-yl acetate (24b). To a solution of (+)-(1*E*)-1-[1-(1*R*)-(2,4,6-triisopropylphenyl)ethoxy]pent-1-en-3-one (**C**) (1.995 g, 6.04 mmol), in 22 mL of anhyd ether were added at −20 °C triethylamine (1.90 mL, 13.63 mmol, 2.25 equiv) and trimethylsilyl triflate (1.22 mL, 6.75 mmol, 1.11 equiv). The mixture was stirred at −20 °C for 2 h and 50 mL of precooled (−78 °C) pentane were added. The organic phase was extracted with a satd soln of aq $NaHCO_3$ (50 mL, three times), $CuSO_4$ (50 mL), brine (50 mL) and dried over Na_2SO_4 and concentrated under vacuum. To the crude mixture were added 4.6 mL of anhyd THF and acetyl fluoride (0.8 mL, 12.89 mmol) was transferred on the vacuum line to the THF frozen solution at −196 °C. The solution was warmed up to −20 °C and TBAF (1 M solution in THF, 0.1 mL) was added dropwise. The temperature was then rised to −15 °C and the reaction mixture was stirred overnight. THF was evaporated under vacuum. FC (light petroleum ether/ether 4:1): 1.35 g (3.62 mmol, 60%), unseparable 3:1 mixture of 1*E*,3*E* and 1*E*,3*ZE* geometric isomers of **24b**. $R_f=0.44$ (light petroleum ether/ether 9:1). UV (CH_3CN): $\lambda_{max}=250$ ($\varepsilon=8345$), 198 (4510), 189 (1100). IR (KBr): ν 2960, 2930, 2870, 1760, 1675, 1635, 1610, 1575, 1460, 1375, 1210,



Scheme 6.

1165, 1125, 1100, 1065, 1020, 910, 880, 840, 780, 650. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (s, 2 arom CH), 6.35 (d, 1H, ^3J=12.3 Hz, H–C(1) *E*,*Z*), 6.30 (d, 1H, ^3J=12.3 Hz, H–C(2) *E*,*E*), 5.67 (d, 1H, ^3J=12.3 Hz, H–C(1) *E*,*E*), 5.47 (d, 1H, ^3J=12.3 Hz, H–C(2) *E*,*Z*), 5.42 (q, 3H, ^3J=6.8 Hz, H–C(1′) *E*,*E*+*E*,*Z*), 5.04 (q, 1H, ^3J=7.4 Hz, H–C(4) *E*,*Z*), 4.94 (q, 1H, ^3J=7.4 Hz, H–C(4) *E*,*E*), 2.85 (sept, 2H, ^3J=6.8 Hz, Me_2CH *E*,*Z*+*E*,*E*), 2.08 (s, 3H, MeCO *E*,*Z*), 2.08 (s, 3H, MeCO *E*,*E*), 1.64 (d, 3H, ^3J=6.8 Hz, H–C(5) *E*,*E*), 1.62 (d, 3H, ^3J=6.8 Hz, H–C(5) *E*,*Z*), 1.53 (d, 3H, ^3J=6.8 Hz, H–C(2′) *E*,*E*), 1.49 (d, 3H, ^3J=6.8 Hz, H–C(2′) *E*,*Z*), 1.26–1.20 (m, 20H, Me_2CH, Me_2CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 169.1 (CO), 148.1–147.8 (C(3), *E*,*Z*+*E*,*E*), 146.3 (C(1)), 144.8 (arom C), 144.0 (arom C), 132.2 (arom C), 122.2 (arom C), 110.4 (C(4)), 103.0 (C(2)), 75.6 (C(1′)), 34.0 (Me_2CH), 29.0 (Me_2CH), 24.5 (Me_2CH), 23.9, 23.8, 22.4 (C(2′)), 20.2 (MeCO)), 11.0 (C(5)). MS (EI): 372 (11, M), 305 (15), 245 (3), 231 (100), 215 (7), 147 (10), 91 (3). MS (EI): calcd for $C_{24}H_{36}O_3$: 372.2664; found: 372.2679.

4.4. General procedure for the preparation of methylidene (*Z*)-β,γ-unsaturated sulfonamides 26, 27 using allysilanes

A mixture of allyltrimethylsilane (0.12 mL, 0.61 mmol, 0.3 equiv) and 0.5 M bistrifluoromethanesulfonimide Tf_2NH in CH_2Cl_2 (1.21 mL, 0.61 mmol, 0.3 equiv) were mixed and stirred at 20 °C for 30 min. The mixture frozen at −196 °C (vacuum line, freeze/thaw cycles for degassing) and SO_2 (through a column of P_2O_5 and alumina) was transferred (9 mL). The mixture was allowed to melt at −78 °C. After 30 min at this temperature a mixture of allylsilane (**23a** or **23b**) (4 mmol, 2 equiv) and diene **24a** (2 mmol, 1.0 equiv) in anhyd CH_2Cl_2 (5 mL) was added. After stirring at −78 °C 16 h, the solvents were evaporated under vacuum to dryness (−78–20 °C, 1.5 h). The residue was taken in CH_3CN (10 mL) and a solution of *N*-chlorosuccinimide (1.35 g, 10.1 mmol, 5 equiv) in CH_3CN (10 mL) was added slowly under stirring at −40 °C. The mixture was stirred at −40 °C for 15 min, then for more 15 min at −30 °C. It was cannulated into a solution of $BnNH_2$ (2.16 g, 20.2 mmol) in pyridine (10 mL) under stirring at −30 °C. The mixture was stirred for 4 h at −20 °C, then 1 h at 0 °C, and 1.5 h at 20 °C. EtOAc (600 mL) was added and the solution washed with a satd aq soln of $CuSO_4$. The aq phase was separated and extracted with EtOAc (100 mL). The combined organic extracts were washed with satd aq soln of $NaHCO_3$ (100 mL), then with brine (100 mL), dried (Na_2SO_4). After solvent evaporation under vacuum, the residue was purifed by FC.

4.4.1. (−)-(1*E*,3*S*)-1-((1*S*)-1-((benzylamino)sulfonyl)ethyl)-2-methyl-3-((1*S*)-1-phenylethoxy)hexa-1,5-dien-1-yl benzoate ((−)-26a) and (−)-(1*E*,3*S*)-1-((1*R*)-1-((benzylamino)sulfonyl)ethyl)-2methyl-3-((1*S*)-1-phenylethoxy)hexa-1,5-dien-1-yl benzoate ((−)-27a).

A 1:1 mixture of (−)-**26a** and (−)-**27a** was prepared following the above procedure. FC (toluene/EtOAc 97:3) gave 0.202 g (19% of (−)-**26a**, R_f=0.37, toluene/EtOAc 9:1) and 0.208 g (20%) of (−)-**27a** (R_f=0.45, toluene/EtOAc 9:1). Compound (−)-**27a** was recrystallized from light petroleum ether and submitted to X-ray diffraction studies (Fig. 1). Data of (−)-**26a**: yellowish oil; $[\alpha]_{589}^{25}$−111; $[\alpha]_{577}^{25}$−94; $[\alpha]_{435}^{25}$−192; $[\alpha]_{405}^{25}$−247 (*c* 0.25, $CHCl_3$). IR (film): ν 3295, 3060, 2970, 2930, 2355, 1735, 1640, 1600, 1490, 1450, 1375, 1315, 1275, 1230, 1155, 1080, 1070. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.17 (d, 2H, ^3J=7.7 Hz), 7.64 (t, 1H, ^3J=7.7 Hz), 7.50 ((t, 2H, ^3J=7.7 Hz), 7.39–7.35, 7.33–7.31, 7.28–7.24, 7.23–7.19, 7.05–7.03 (5m, 10H, H–C(Ar)), 5.68 (ddt, 1H, ^3J=17.3 Hz, 9.6, 7.4, H–C(5)), 5.05 (d, 1H, ^3J=17.3 Hz, Ha–C(6)), 5.03 (d, 1H, ^3J=9.6 Hz, Hb–C(6)), 4.71 (q, 1H, ^3J=6.4 Hz, H–C(1″)), 4.55 (m, 1H, H–N), 4.20 (dd, 1H, AB syst, ^2J=14.71, 5.8 Hz, Ha-PhCH_2), 4.10 (dd, 1H, AB syst, ^2J=14.7, 6.4 Hz, Hb-PhCH_2), 3.98 (q, 1H, ^3J=7.0 Hz, H–C(1′)), 3.98 (t, 1H, ^3J=7.0 Hz, H–C(3)), 2.47 (dt, 1H, ^2J=14.1 Hz, ^3J=7.0 Hz, Ha–C(4)), 2.35 (dt, 1H, ^2J=14.08 Hz, ^3J=7.0 Hz, Hb–C(4)), 1.69 (s, 3H, CH_3–C(2)), 1.41 (d, 3H, ^3J=6.4 Hz, H–C(2′)), 1.35 (d, 3H, ^3J=7.0 Hz, H–C(2″)). ^{13}C NMR (C_6D_6, 100.6 MHz): δ 164.9, 144.7, 138.8, 137.9, 137.3, 134.1, 132.3, 130.7, 129.3, 128.9, 128.7, 127.9, 118.3, 75.8, 75.2, 59.2, 47.7, 39.5, 30.11, 25.6, 13.7. MALDI-HRMS: calcd for $C_{31}H_{35}NO_5SK^+$ 572.1873; found: 572.1870. Anal. Calcd for $C_{31}H_{35}NO_5S$ (533.22): C, 69.77; H, 6.61; N, 2.62; O, 14.99; S, 6.01. Found: C, 69.69; H, 6.69; N, 2.75; O, 14.90; S, 5.97. Data of (−)-**27a**: white crystals, mp 97–99 °C. $[\alpha]_{589}^{25}$−56; $[\alpha]_{577}^{25}$−57; $[\alpha]_{435}^{25}$−106; $[\alpha]_{405}^{25}$−125 (*c* 0.5, $CHCl_3$). IR (KBr): ν 3295, 3060, 2970, 2930, 2355, 1735, 1640, 1600, 1490, 1450, 1375, 1315, 1275, 1230, 1155, 1080, 1070. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.14 (d, 2H, ^3J=7.7 Hz), 7.66 (t, 1H, ^3J=7.7 Hz), 7.52 ((t, 2H, ^3J=7.7 Hz), 7.42–7.34, 7.35–7.33, 7.31–7.28, 7.23–7.24, 7.22–7.21 (5m, 10H, H–C(Ar)), 5.91 (ddt, 1H, ^3J=17.3, 10.2, 7.0 Hz, H–C(5)), 5.13 (dd, 1H, ^3J=17.3 Hz, ^2J=3.5 Hz, Ha–C(6)), 5.10 (dd, 1H, ^3J=10.3 Hz, ^2J=3.5 Hz, Hb–C(6)), 4.51 (m, 1H, H–C(1″)), 4.51 (d, 1H, ^3J=5.8 Hz, H–N), 4.16 (dd, 1H, AB syst, ^2J=14.1, 5.8 Hz, Ha-PhCH_2), 4.05 (dd, 1H, AB syst, ^2J=14.1, 5.8 Hz, Hb-PhCH_2), 4.06 (dd, 1H, ^3J=7.0, 2.9 Hz, H–C(3)), 3.69 (q, 1H, ^3J=6.4 Hz, H–C(1′)), 2.54 (ddd, 1H, ^2J=14.4 Hz, ^3J=9.9, 7.0 Hz, Ha–C(4)), 2.41 (ddd, 1H, ^2J=14.4 Hz, ^3J=7.0, 2.9 Hz, Hb–C(4)), 1.69 (s, 3H, CH_3–C(2)), 1.45 (d, 3H, ^3J=6.4 Hz, H–C(2′)), 1.44 (d, 3H, ^3J=5.1 Hz, H–C(2″)). ^{13}C NMR (C_6D_6, 100.6 MHz): δ 164.9, 144.6, 139.2, 137.9, 136.3, 133.9, 132.7, 130.8, 129.1, 129.0, 128.9, 127.1, 117.3, 74.6, 74.5, 58.7, 47.8, 38.6, 25.5, 13.0, 11.5. MALDI-HRMS: calcd for $C_{31}H_{35}NO_5SK^+$ 572.1873; found: 572.1879. Anal. Calcd for $C_{31}H_{35}NO_5S$ (533.22): C, 69.77; H, 6.61; N, 2.62; O, 14.99; S, 6.01. Found: C, 69.75; H, 6.61; N, 2.59; O, 14.99; S, 6.06.

4.4.2. (−)-(1*E*,3*S*)-5-((acetyloxy)methyl)-1-((1*S*)-1-((benzylamino)sulfonyl)ethyl)-2-methyl-3-((1*S*)-1-phenylethoxy)hexa-1,5-dien-1-yl benzoate ((−)-26b) and (−)-(1*E*,3*S*)-5-((acetyloxy)methyl)-1-((1*R*)-1-((benzylamino)sulfonyl)ethyl)-2-methyl-3-((1*S*)-1-phenylethoxy)hexa-1,5-dien-1-yl benzoate ((−)-27b).

A 1:1 mixture of a (−)-**26b** and (−)-**27b** was obtained applying the above procedure and using (2-acetoxy)allyltrimethylsilane[54] (**23b**, 5 g, 26.8 mmol, 2 equiv) and diene (−)-**24a** (4.3 g, 13.4 mmol). FC (toluene/EtOAc 95:5) gave (−)-**26b**, R_f=0.29 (2.85 g, 35%) and (−)-**27b**, R_f=0.38 (toluene/EtOAc 9:1) (2.85 g, 35%). Their structures were established by their transformation into the cyclic derivatives (−)-**30** and (−)-**31** (see below). Data of (−)-**26b**: colorless oil. $[\alpha]_{589}^{25}$−32; $[\alpha]_{577}^{25}$−34; $[\alpha]_{435}^{25}$−64;

$[\alpha]_{405}^{25}$ −77 (*c* 1.0, $CHCl_3$). IR (film): *ν* 3060, 3030, 2970, 2925, 1735, 1730, 1600, 1490, 1450, 1375, 1325, 1275, 1235, 1150, 1085, 1065. ^{1}H NMR ($DMSO_{d\text{-}6}$, 400 MHz, +80 °C): *δ* 8.12 (dm, 2H, ^3J=8.0 Hz, H–C(Bz)), 7.72 (t, 1H, ^3J=7.5 Hz, H–C(Bz)), 7.58 (t, 2H, ^3J=7.5 Hz, H–C(Bz)), 7.39–7.22 (5m, 10H, H–C(Ar)), 5.08, 5.03 (2 br s, 2H, H–C(6)), 4.60, 4.53 (2d, 2H, AB syst, ^2J=13.7 Hz, AcOCH_2–C(5)), 4.50 (q, 1H, ^3J=6.5 Hz, H–C(1″)), 4.15 (t, 1H, ^3J=6.1 Hz, H–C(3)), 4.04, 3.95 (2dd, 2H, AB syst, ^2J=15.1 Hz, ^3J=6.2 Hz, PhCH_2–N), 3.66 (q, 1H, ^3J=6.9 Hz, H–C(1′)), 3.61–3.39 (br s, 1H, NH), 2.41 (d, 2H, ^3J=6.5 Hz, H–C(4)), 2.02 (s, 3H, CH_3COOCH_2–C(5)), 1.64 (s, 3H, CH_3–C(2)), 1.38 (d, 3H, ^3J=6.5 Hz, H–C(2″)), 1.31 (d, 3H, ^3J=6.9 Hz, CH_3–C(2′)). ^{13}C NMR ($DMSO_{d\text{-}6}$, 100.6 MHz, +80 °C): *δ* 169.1, 163.1, 142.6, 141.0, 138.2, 137.8, 133.2, 130.3, 129.2, 128.2, 127.7, 127.6, 127.0, 126.8, 126.5, 125.8, 113.0, 110.7, 73.3, 73.1, 65.8, 57.3, 46.0, 36.2, 23.6, 19.8, 11.6, 10.3. MALDI-HRMS: calcd for $C_{34}H_{39}NO_7SNa^+$ 628.2345; found: 628.2349. Anal. Calcd for $C_{34}H_{39}NO_7S$ (605.74): C, 67.42; H, 6.49; N, 2.31; S, 5.29. Found: C, 67.35; H, 6.63; N, 2.33; S, 5.33. Data of (−)-**27b**: colorless oil. $[\alpha]_{589}^{25}$ −114; $[\alpha]_{577}^{25}$ −123; $[\alpha]_{435}^{25}$ −246; $[\alpha]_{405}^{25}$ −301 (*c* 0.5, $CHCl_3$). IR (film): *ν* 3060, 3030, 2970, 2925, 1735, 1600, 1490, 1450, 1375, 1325, 1275, 1235, 1150, 1085, 1065. ^{1}H NMR (C_6D_6, 400 MHz, +70 °C): *δ* 8.23 (dm, 2H, ^3J=7.7 Hz, H–C(Bz)), 7.52 (d, 2H, ^3J=6.8 Hz, H–C(Ar)), 7.21–7.02 (m, 11H, H–C(Ar)), 5.06, 5.03 (2 br s, 2H, H–C(6)), 4.86 (q, 1H, ^3J=6.5 Hz, H–C(1′)), 4.54, 4.45 (2d, 2H, AB syst, ^2J=13.6 Hz, AcOCH_2–C(5)), 4.45 (q, 1H, ^3J=6.5 Hz, H–C(1″)), 4.36 (t, 1H, ^3J=6.5 Hz, H–C(3)), 4.14 (br t, 1H, ^3J=5.9 Hz, NH), 4.05 (m, 2H, PhCH_2–N), 2.56 (dd, 1H, AB syst, ^2J=13.6 Hz, ^2J=7.4 Hz, Ha–C(4)), 2.40 (dd, 1H, AB syst, ^2J=13.6 Hz, ^2J=6.2 Hz, Ha–C(4)), 1.74 (s, 3H, CH_3COOCH_2–C(5)), 1.68 (s, 3H, CH_3–C(2)), 1.45 (d, 3H, ^3J=6.8 Hz, H–C(2″)), 1.40 (d, 3H, ^3J=6.5 Hz, CH_3–C(2′)). ^{13}C NMR (C_6D_6, 100.6 MHz, +70 °C): *δ* 169.7, 164.4, 144.7, 140.8, 139.9, 138.8, 133.4, 132.3, 130.7, 130.2, 128.9, 128.8, 128.6, 127.9, 127.2, 116.5, 115.3, 75.8, 75.6, 67.1, 59.7, 47.7, 39.5, 24.8, 20.3, 13.7, 12.5. MALDI-HRMS: calcd for $C_{34}H_{39}NO_7SNa^+$ 628.2345; found: 628.2346. Anal. Calcd for $C_{34}H_{39}NO_7S$ (605.74): C, 67.42; H, 6.49; N, 2.31; S, 5.29. Found: C, 67.37; H, 6.40; N, 2.24; S, 5.30.

4.4.3. (2*S*,3*E*,5*R*)-5-[(1*R*)-(2,4,6-triisopropylphenyl)-ethyloxy]-7-methylsulfonylocta-3,7-dien-3-yl acetate (28). Allyltrimethylsilane (0.03 mL, 0.188 mmol, 0.28 equiv) and Tf_2NH (0.5 M in CH_2Cl_2) (0.27 mL, 0.35 mmol, 0.20 equiv) were stirred at 20 °C for 20 min. Anhyd CH_2Cl_2 (1.4 mL) was added. SO_2 (0.5 mL, 11.18 mmol) dried by passing through a column of P_2O_5 and alumina was transfered on the vaccum line to the CH_2Cl_2 solution frozen at −196 °C. The mixture was allowed to melt and to warm to −78 °C. After 30 min at this temperature a mixture of **24b** (247.0 mg, 0.663 mmol) and **23c** (607 mg, 13.4 mmol) in anhyd CH_2Cl_2 (0.8 mL) was added dropwise at −80 °C After stirring at −78 °C overnight, SO_2 was evaporated at −78 °C for 1 h. Then MeI (0.41 mL, 6.58 mmol, 10 equiv) followed by TBAF (1 M in THF, 3.40 mmol, 5.13 equiv) were added. The reaction mixture was allowed to reach slowly 0 °C. After 2 h at this temperature an aqueous solution of $NaHCO_3$ (5%) was added (10 mL). The reaction mixture was warmed to room temperature and CH_2Cl_2 (10 mL) was added. The organic phase was washed with a satd aq solution of $NaHCO_3$, dried (Na_2SO_4) and concentrated under vacuum. FC (light petroleum ether/EtOAc 3:2) 220 mg (65%) of a 10:1 mixture of diastereoisomers **28** and 3-epi-**28**. Only the isomer **28** can be analyzed from the spectra of the mixture UV (CH_3CN): λ_{max}=265 (*ε*=488), 225 (5565), 189 (660). IR (neat): *ν* 3075, 2960, 2930, 2870, 1760, 1700, 1645, 1460, 1370, 1220, 1180, 1075, 1020, 890, 880, 780. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.03–6.94 (2s, 2 arom CH), 5.55 (d, 1H, ^3J=6.9 Hz, H–C(2)), 5.18 (q, 1H, ^3J=6.6 Hz, H–C(1″)), 4.78–4.68 (2s, 2H, H–C(6)), 4.38 (q, 1H, ^3J=7.0 Hz, H–C(1′)), 4.19 (m, 1H, H–C(3)), 3.85–3.25 (2 br s, 2H, Me_2–CH)), 3.06 (s, 3H, SO_2Me), 2.85 (sept, ^3J=6.5 Hz, Me_2–CH), 2.40 (br d, 1H, H–C(4)), 2.23 (s+m, 4H, MeCO+H–C(4)), 1.63 (s, 3H, Me-C(5)), 1.57 (2d, 6H, ^3J=7.0 Hz, H–C(2′), ^3J=6.6 Hz, H–C(2″)), 1.26–1.22 (m, 18H, Me_2–CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): *δ* 168.8 (CO), 147.5–147.1–140.9–140.7–133.9–129.0 (4 arom C+C(5)+C(1)), 128.2 (C(2)), 123.2–120.5 (2 arom C.), 114.2 (C(6)), 74.4 (C(3)), 73.0 (C(1″)), 59.9 (C(1′)), 44.3 (C(4)), 38.6 (SO_2Me), 34.0 (Me_2C), 29.1–28.6 (Me_2–C), 24.8–24.3–23.9–23.3 (2Me_2–C+Me-C(7)+C(2″)), 20.9 (MeCO), 14.2 (Me_2–C)), 11.2 (C(1)). HRMS (MALDI): calcd for $C_{29}H_{46}O_5SNa^+$ 529.2963 [M+Na^+]; found: 529.2912.

4.4.4. (1*Z*)-1-ethylidene-5-methyl-3-[1-(2,4,6-triisopropyl-phenyl)ethoxy]hex-5-enyl acetate (29a). Allyltrimethylsilane (0.03 mL, 0.19 mmol, 0.20 equiv) and Tf_2NH (0.5 M in CH_2Cl_2) (0.33 mL, 0.17 mmol, 0.20 equiv) were mixed and stirred for 20 min at room temperature. Anhyd CH_2Cl_2 (1.8 mL) was added. SO_2 (0.5 mL, 11.18 mmol, 13.8 equiv) dried over a column of P_2O_5 and alumina was transferred on the vacuum line to the CH_2Cl_2 solution frozen at −196 °C. The mixture was allowed to melt and to warm at −78 °C. After 30 min at this temperature a mixture of diene **24b** (304.0 mg, 0.81 mmol) and **23c** (477 mg, 1.67 mmol, 2.06 equiv) in anhyd CH_2Cl_2 (1.8 mL) was added dropwise at −80 °C. The resulting reaction mixture was stirred at −78 °C for 16 h. SO_2 was then evaporated at −78 °C for 1 h. A solution of triethylamine (0.14 mL, 1.00 mmol, 1.22 equiv), trimethylsilyl trifluoromethanesulfonate (0.18 mL, 0.99 mmol, 1.22 equiv) in anhyd MeOH (0.20 mL) was added. The temperature was kept at −78 °C for 3 h and a satd aq solution of $NaHCO_3$ (10 mL) was added. The reaction mixture was warmed to room temperature and diluted with CH_2Cl_2 (10 mL). The organic phase was washed with saturated $NaHCO_3$, dried (Na_2SO_4) and concentrated. The crude was purified on chromatographic column (petroleum ether 95/Ethyl acetate 5) to yield 237 mg (70%) as a 10:1 mixture of diastereoisomers **29a/29b**. R_f=0.51 (petrol ether/ether 85:15). Only **29a** can be analyzed from the spectra of the mixture. UV (CH_3CN): 265 (490), 225 (5560), 189 (660). IR (neat): 30745 2960, 2930, 2870, 1760, 1700, 1645, 1460, 1370, 1220, 1180, 1080, 1020, 890, 880, 780 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): 7.03–6.94 (2s, 2 arom CH), 5.20 (q, 1H, ^3J=6.9 Hz, H–C(1′)), 5.10 (q, 1H, ^3J=6.6 Hz, H–C(1″)), 4.71–4.60 (2s, 2H, H–C(6)), 3.91 (br s, 1H, Me_2–C*H*)), 3.67 (m, 1H, H–C(3)), 3.91 (br s, 1H, Me_2–C*H*)), 2.85 (sept, ^3J=6.5 Hz, Me_2–C*H*), 2.49 (br d, 1H, H–C(4)), 2.45 (s, 3H, H–C(2′)), 2.44–2.42 (m, 2H,

H–C(2)), 2.11–2.05 (m, 2H, H–C(4)), 1.58 (s, 3H, Me-C(5)), 1.55 (d, 3H, ^3J=6.9 Hz, H–C(2″)), 1.50 (d, 3H, ^3J=6.6 Hz, H–C(2′)), 1.26–1.22 (m, 17H, *Me*$_2$–CH). ^{13}C NMR (100.6 MHz, $CDCl_3$): 168.7 (C(1′)), 147.2 (C(1)), 147.1–146.6–142.3–134.6, 123.1–120.3 (arom C+C(5)), 113.4 (C(1″)), 112.9 (C(6)), 73.7 (C(3)), 71.6 (C(1‴)), 43.3 (C(2)), 38.6 (C(4)), 34.0 (Me$_2$–*C*H), 25.2–24.8–24.2–23.9–23.8 (Me$_2$–*C*H+*Me*$_2$–CH), 22.7 (Me-C(5)), 22.3 (C(Ac)), 20.7 (C(2″)), 10.8 (C(2′)). MS-CI (NH_3): 446 (1, [M+18]), 429 (1, [M+1]$^+$), 344 (1), 231 (100). El. Anal. Calcd $C_{28}H_{44}O_3$ (428.66): C, 78.46; H, 10.35; O, 11.20. Found: C, 78.40; H, 10.33.

4.4.5. (−)-(6*S*,7*E*,9*R*)-2-benzyl-7,9-dimethyl-4-methylene-1,1-dioxido-6-((1*S*)-1 phenylethoxy)-2,3,4,5,6,9-hexahydro-1,2-thiazonin-8-yl benzoate ((−)-30). A mixture of (−)-**26b** (0.40 g, 0.66 mmol), Cs_2CO_3 (0.215 g, 0.66 mmol) and Pd(PPh$_3$)$_4$ (76 mg, 0.07 mmol) in anhyd DMF (20 mL) was heated to 100 °C for 40 min (control by TLC). The resulting black solution was evaporated under vacuum to dryness. The residue was purified by FC (toluene/EtOAc 9:1, R_f=0.62), 0.291 g (81%), $[\alpha]^{25}_{589}$ −93; $[\alpha]^{25}_{577}$ −99; $[\alpha]^{25}_{435}$ −176; $[\alpha]^{25}_{405}$ −211 (*c* 0.3, $CHCl_3$). IR (film): *ν* 3065, 2975, 2925, 1735, 1730, 1715, 1605, 1595, 1500, 1470, 1455, 1330, 1265, 1240, 1170, 1145, 1085, 1065, 1025. ^{1}H NMR (DMSO$_{d\text{-}6}$, 400 MHz, +80 °C): *δ* 8.08 (dm, 2H, ^3J=7.4 Hz, H–C(Bz)), 7.73 (t, 1H, ^3J=7.4 Hz, H–C(Bz)), 7.60 (t, 2H, ^3J=7.4 Hz, H–C(Bz)), 7.48–7.42, 7.39–7.33, 7.30–7.26, 7.17–7.13, 6.79–6.74 (5m, 10H, H–C(Ar)), 4.96, 4.82 (2s, 2H, CH_2=C(4)), 4.50 (q, 1H, ^3J=6.6 Hz, H–C(1′)), 4.30 (dd, 1H, ^3J=9.6, 5.5 Hz, H–C(6)), 4.07, 3.99 (2d, 2H, AB syst, ^2J=15.8 Hz, PhC*H*$_2$–N(2)), 3.81 (d, 1H, AB syst, ^2J=15.8 Hz, Ha–C(3)), 3.62 (q, 1H, ^3J=7.0 Hz, H–C(9)), 3.50 (d, 1H, AB syst, ^2J=15.8 Hz, Hb–C(3)), 2.69–2.58 (m, 2H, H–C(5)), 1.64 (s, 3H, CH_3–C(7)), 1.43 (d, 3H, ^3J=6.6 Hz, H–C(2′)), 1.31 (d, 3H, ^3J=7.0 Hz, CH_3–C(9)). ^{13}C NMR (DMSO$_{d\text{-}6}$, 100.6 MHz, +80 °C): *δ* 163.1, 142.9, 140.1, 138.0, 135.6, 133.3, 130.8, 129.1, 128.6, 128.4, 128.0, 127.8, 127.2, 126.9, 125.9, 118.2, 118.0, 114.9, 74.0, 71.9, 57.6, 50.8, 50.6, 38.4, 23.3, 10.5, 9.8. MALDI-HRMS: calcd for $C_{32}H_{35}NO_5SNa^+$ 584.1873; found: 584.1879. Anal. Calcd for $C_{32}H_{35}NO_5S$ (545.69): C, 70.43; H, 6.46; N, 2.57; S, 5.88. Found: C, 70.52; H, 6.46; N, 2.58; S, 5.86.

4.4.6. (−)-(6*S*,7*E*,9*R*)-2-benzyl-7,9-dimethyl-4-methylene-1,1-dioxido-6-((1*S*)-1-phenylethoxy)-2,3,4,5,6,9-hexahydro-1,2-thiazonin-8-yl benzoate ((−)-31). Same procedure as that applied for the preparation of (−)-**30**, using (−)-**27b** (0.40 g, 0.66 mmol). Yield 0.285 g (79%). R_f=0.72, toluene/EtOAc 9:1), colorless oil. $[\alpha]^{25}_{589}$ −108; $[\alpha]^{25}_{577}$ −113; $[\alpha]^{25}_{435}$ −257; $[\alpha]^{25}_{405}$ −320 (*c* 0.2, $CHCl_3$). IR (film): *ν* 3060, 3030, 2970, 2925, 1735, 1730, 1680, 1600, 1495, 1455, 1330, 1270, 1225, 1210, 1140, 1085, 1065, 1025. ^{1}H NMR ($CDCl_3$, 400 MHz): *δ* 8.21 (d, 2H, ^3J=7.4 Hz, H–C(Bz)), 7.63 (t, 1H, ^3J=7.7 Hz, H–C(Bz)), 7.70 (t, 2H, ^3J=7.4 Hz, H–C(Bz)), 7.43–7.28 (m, 10H, H–C(Ar)), 5.23 (s, 2H, CH_2=C(4)), 5.21 (q, 1H, ^3J=7.1 Hz, H–C(9)), 4.89 (d, 1H, AB syst, ^2J=15.1 Hz, Ha-(PhC*H*$_2$–N(2))), 4.86 (q, 1H, ^3J=6.5 Hz, H–C(1′)), 4.07 (d, 1H, AB syst, ^2J=15.1 Hz, Ha–C(3)), 4.02 (d, 1H, AB syst, ^2J=15.1 Hz, Hb-(PhC*H*$_2$–N(2))), 3.89 (dd, 1H, ^3J=8.6, 4.9 Hz, H–C(6)), 3.41 (d, 1H, AB syst, ^2J=15.1 Hz, Hb–C(3)), 2.68 (dd, 1H, AB syst, ^2J=15.2 Hz, ^3J=8.6 Hz, Ha–C(5)), 2.54 (dd, 1H, AB syst, ^2J=15.2 Hz, ^3J=5.0 Hz, Hb–C(5)), 1.58 (s, 3H, CH_3–C(7)), 1.57 (d, 3H, ^3J=6.5 Hz, CH_3–C(9)), 1.43 (d, 3H, ^3J=6.5 Hz, H–C(2′)). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 164.1, 143.4, 140.6, 137.2, 136.9, 133.9, 132.4, 130.4, 128.9, 128.8, 128.7, 128.6, 128.3, 127.8, 126.6, 122.8, 75.0, 74.8, 61.8, 54.2, 52.9, 38.7, 24.9, 20.2, 11.4. MALDI-HRMS: calcd for $C_{32}H_{35}NO_5SK^+$ 568.2134; found: 568.2104. Anal. Calcd for $C_{32}H_{35}NO_5S$ (545.69): C, 70.43; H, 6.46; N, 2.57; S, 5.88. Found: C, 70.47; H, 6.50; N, 2.42; S, 5.77.

4.4.7. (±)-(2*RS*,5*SR*)-2,4-dimethyl-7-methylene-1,1-dioxido-5-((1*SR*)-1-phenylethoxy)-5,6,7,8-tetrahydro-2*H*-thiocin-3-yl isobutyrate ((±)-32b). Allyltrimethylsilane (0.194 mL, 1.22 mmol) was added to Tf_2NH (0.5 M in CH_2Cl_2) (2.44 mL, 1.22 mmol) diluted with toluene (6 mL). The mixture was stirred at 20 °C for 20 min. SO_2 (7 mL, 157 mmol, 51 equiv) dried over a column of P_2O_5 and alumina was transferred on the vacuum line to the toluene solution frozen at −196 °C. The mixture was allowed to melt and to warm at −78 °C. After 30 min at −78 °C a mixture of (±)-**24c**[37] (0.88 g, 3.05 mmol, 1 equiv) and 2-acetoxymethyl allyltrimethylsilane **23b** (0.68 g, 3.66 mmol, 1.2 equiv) in anhyd toluene (2 mL) was added dropwise under stirring at −78 °C. The mixture was stirred overnight. SO_2 was then evaporated at −78 °C for 2 h, followed by evaporation to dryness at 20 °C. The residue (crude **25c**) was taken in THF (15 mL) and added at 20 °C to a mixture of (Ph$_3$P)$_4$Pd (0.35 g, 0.30 mmol, 0.1 equiv) and NEt_3 (0.85 mL, 6.10 mmol, 2 equiv) in THF (15 mL) and stirred at 20 °C for 3 h. The mixture was then poured in brine, extracted by EtOAc. The collected organic layers were washed with brine, dried (Na_2SO_4) and evaporated under vacuum. FC (light petroleum ether/EtOAc 7:3): 0.55 g (44%) of (±)-**32b**, that was recrystallized from pentane/CH_2Cl_2 to yield a sample suitable for X-ray crystallography (Fig. 2). White solid, mp 90 °C, R_f=0.63 (light petroleum ether/EtOAc 7:3). IR (KBr): *ν* 2950, 2880, 1745, 1680, 1455, 1380, 1295, 1315, 1240, 1190, 1140, 1125, 1115, 1080, 1045. ^{1}H NMR ($CDCl_3$, 400 MHz, +60 °C): *δ* 7.38–7.27 (m, 5H, H–C(Ph)), 5.64, 5.45 (2s, 2H, CH_2=C(7)), 5.37 (br s, 1H, H–C(2)), 4.55 (q, 1H, ^3J=6.2 Hz, H–C(1′)), 4.03 (d, 1H, ^2J=14.2 Hz, Ha–C(8)), 3.77 (br s, 1H, H–C(5)), 3.67 (d, 1H, ^2J=14.2 Hz, Hb–C(8)), 2.77 (sept, 1H, ^3J=6.8 Hz, $(CH_3)_2$C*H*COO–C(3)), 2.60 (dd, 1H, ^2J=14.2 Hz, ^3J=5.6 Hz, Ha–C(6)), 2.24 (br d, 1H, ^2J=14.2 Hz, Hb–C(6)), 1.48 (d, 3H, ^3J=6.8 Hz, CH_3–C(2)), 1.46 (s, 3H, CH_3–C(4)), 1.40 (d, 3H, ^3J=6.8 Hz, H–C(2′)), 1.31 (2d, 6H, ^3J=7.4 Hz, (C*H*$_3$)$_2$CHCOO–C(3))). ^{13}C NMR ($CDCl_3$, 100.6 MHz, +60 °C): *δ* 174.1, 143.0, 139.5, 131.3, 130.0, 128.8, 128.0, 127.1, 126.5, 75.6, 75.4, 57.3, 54.9, 41.5, 34.2, 24.2, 19.0, 19.1, 18.4, 6.3. MALDI-HRMS: calcd for $C_{22}H_{30}O_5SNa^+$ 429.1712; found: 429.1712. Anal. Calcd for $C_{22}H_{30}O_5S$ (406.54): C, 65.00; H, 7.44; S, 7.89. Found: C, 65.05; H, 7.46; S 7.99.

4.4.8. (+)-(2*S*,5*S*)-2,4-dimethyl-7-methylene-1,1-dioxido-5-((1*R*)-1-phenylethoxy)-5,6,7,8-tetrahydro-2*H*-thiocin-3-yl benzoate ((+)-32a). Same procedure as that applied for the preparation of (±)-**32b** using (+)-**24a** (0.82 g, 2.54 mmol). Yield 0.45 g (41%). R_f=0.52, light petroleum ether/EtOAc 7:3), colorless oil. IR (film): *ν* 2970,

1735, 1450, 1315, 1270, 1220, 1140, 1120, 1080, 1020, 705, 620. ^{1}H NMR (C_6D_6, 400 MHz, +70 °C): δ 8.21 (d, 2H, ^3J=7.7 Hz, H–C(Bz)), 7.23 (d, 2H, ^3J=7.4 Hz, H–C(Ar)), 7.16–7.06 (m, 6H, H–C(Ar)), 5.56, 5.22 (2s, 2H, CH_2=C(7)), 5.39 (br s, 1H,((H–C(2)), 4.60 (q, 1H, ^3J= 6.2 Hz, H–C(1′)), 3.76 (d, 1H, AB syst, ^2J=14.2 Hz, Ha–C(8)), 3.61 (br s, 1H, H–C(5)), 3.45 (d, 1H, ^2J=14.2 Hz, AB syst, Hb–C(8)), 2.30 (dd, 1H, ^2J=14.2 Hz, ^3J=5.6 Hz, AB syst, Ha–C(6)), 1.82 (br d, 1H, ^2J=14.2 Hz, AB syst, Hb–C(6)), 1.51 (d, 3H, ^3J=6.8 Hz, CH_3–C(2)), 1.27 (s, 3H, CH_3–C(4)), 1.25 (d, 3H, ^3J=6.8 Hz, H–C(2′). ^{13}C NMR (C_6D_6, 400 MHz, +70 °C): δ 164.2, 143.4, 140.6, 133.6, 132.2, 130.6, 129.9, 129.7, 128.9, 128.8, 128.2, 126.8, 126.3, 76.7 (2C), 57.6, 55.6, 41.4, 24.1, 18.1, 6.5. MALDI-HRMS: calcd for $C_{25}H_{28}O_5SNa^+$ 463.1555; found: 463.1558. $[\alpha]_{589}^{25}$+76 (*c* 1.0 $CHCl_3$).

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