Metallated 2-Alkenyl Sulfoximines in Asymmetric Synthesis: Regio- and Stereoselective Synthesis of Highly Substituted Oxabicyclic Ethers and Studies Towards the Total Syntheses of the Euglobals G1 and G2 and Arenaran A

Michael Reggelin,*[a] Matthias Gerlach,[a] and Melanie Vogt[a]

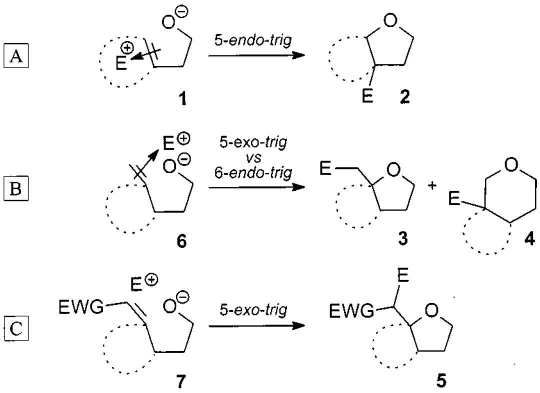
Keywords: Sulfoximines / Oxabicyclic ethers / Asymmetric synthesis / Euglobal / Arenaran

2-Cyclopentenyl- and 2-cyclohexenylmethyl sulfoximines can be converted into angular carbon-functionalised, highly substituted, isomerically pure (*ds* ≥ 98%) 2-oxabicyclo[3.3.0]octanes and 2-oxabicyclo[3.4.0]nonanes in high yields by a convenient one-pot sequence. Molecular frameworks such as these can be found in many biologically active natural products. In addition to the methodological work, we report on studies towards the total synthesis of the euglobals G1 and G2 and arenaran A.

Introduction

The angular carbon-substituted 2-oxabicyclic moiety is an important structural element in terrestrial as well as marine natural products.[1] Since many of them are biologically active, it is of interest to develop efficient methods for their stereoselective synthesis.

In the majority of reactions allowing access to oxamono- and -bicyclic systems **2**−**5** the key step is a nucleophilic attack of an oxygen atom onto an activated double bond (Scheme 1).



Scheme 1. Strategies for the synthesis of oxacyclic and oxabicyclic compounds: **A**: homoallylic alcohols with electrophilically activated double bonds react regioselectively in a 5-*endo-trig* process yielding tetrahydrofurans or 2-oxabicyclic heterocycles; **B**: bishomoallylic alcohols often furnish mixtures of products resulting from regio-unselective cyclisations yielding the corresponding heterocycles **3** and **4**; **C**: in bishomoallylic alcohols bearing electron-withdrawing groups the ambiguity in the ring-closing mode (5-*exo-trig* versus 6-*endo-trig*) is absent

The regio- and stereochemical outcome of these reactions depends strongly on a variety of structural and external parameters. Thus, the successful application of strategies such as these in natural product synthesis is possible only in those cases where the substrate-controlled attack onto the double bond by the oxygen atom is perfect. Some examples are epoxide activation in the total synthesis of nargenicin A_1,[2] I_2 activation in the total synthesis of brevetoxins,[3] acid-induced cyclisation in the total synthesis of (+)-pyripyropene A,[4] and $Hg(OAc)_2$ activation in the total synthesis of nodusmicin.[5]

To date no general techniques have been revealed which could be used to build up the required structural motive independently of other substituents in a stereocontrolled manner. Encouraged by the successful application of metallated 2-alkenyl sulfoximines in the diastereoselective synthesis of highly substituted THF derivatives[6] we started to consider more robust solutions to the synthetic problem outlined above.

Titanated 2-alkenyl sulfoximines are efficient solutions for asymmetric d^3 synthons.[7] A recent application is their γ-hydroxyalkylation with α-silyloxypropanals to yield 5-silyloxy-substituted vinyl sulfoximines **8,** which, after fluoride-ion-induced deprotection, undergo cyclisation reactions to form the previously mentioned THF derivatives **9** (Scheme 2).[6] This reaction takes place due to the electron deficiency in the sulfonimidoyl moiety, which activates the vinylic double bond towards nucleophilic attack (C in Scheme 1).[7]

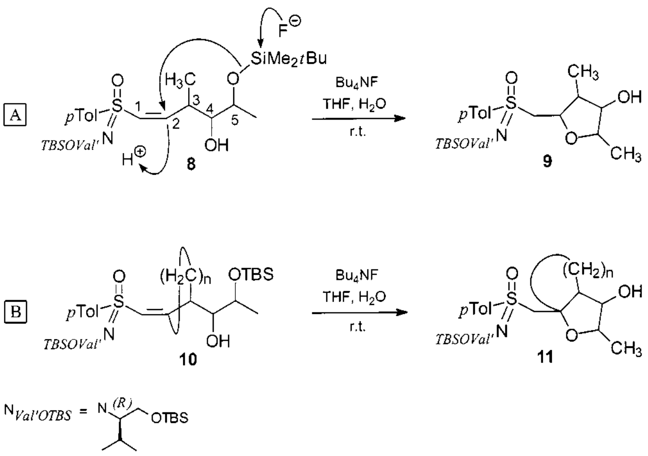
Similar to the *cyclic* primary γ-hydroxyalkylation addition products **10**, the fluoride-ion-induced desilylation of the oxygen atom at C-5 reveals an oxygen nucleophile, which should attack on the activated double bond forming the bicyclic ethers **11**. Four relevant examples of natural products and the target molecular framework **12**, that they have in common, are shown in Scheme 3.

Structure **12** can be disconnected retrosynthetically adjacent to the bridgehead atoms, leaving an oxy-func-

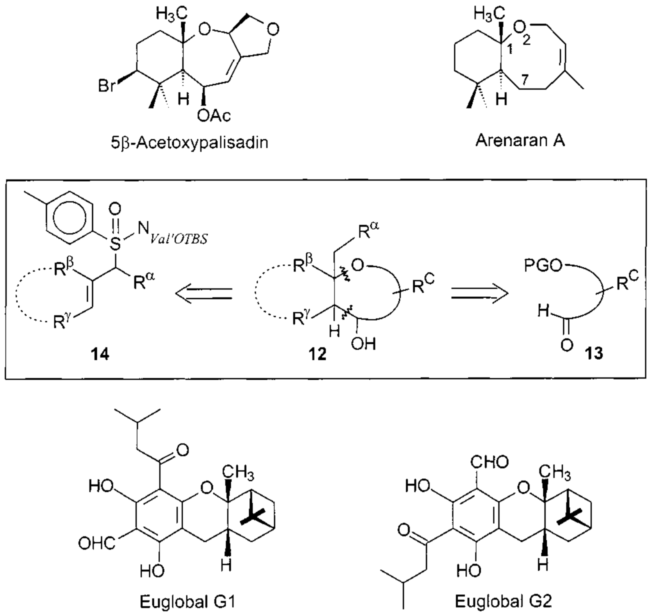
---

[a] Institut für Organische Chemie der Johann Wolfgang Goethe Universität,
Marie-Curie-Straße 11, D-60439 Frankfurt a.M., Germany
Fax: (internat.) + 49(0)69/79829128
E-mail: re@krypton.org.chemie.uni-frankfurt.de
re@cortex.chemie.uni-mainz.de

1434−193X/99/0505−1011 $ 17.50+.50/0



Scheme 2. Fluoride-ion-induced cyclisations of 5-silyloxy-substituted vinyl sulfoximines



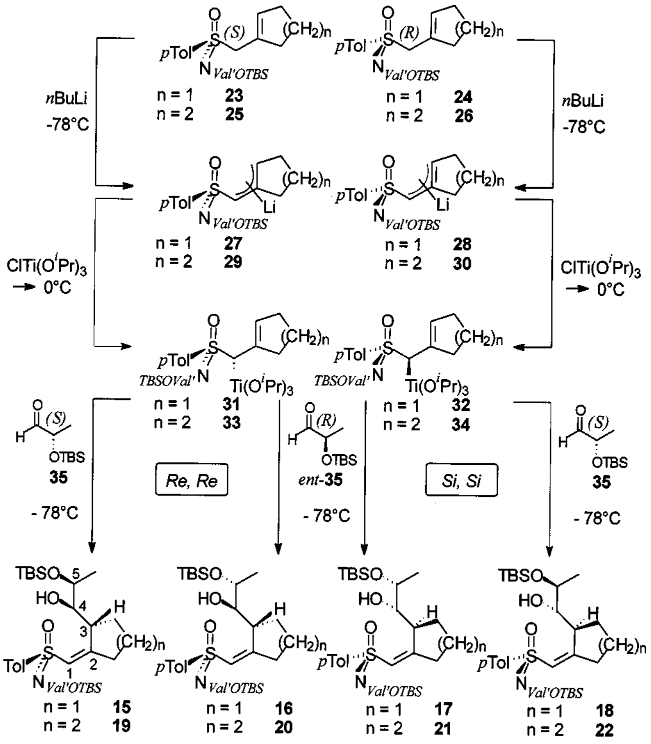
Scheme 3. Structural target motif **12** and potential total synthesis targets

tionalised aldehyde **13** and an allylic sulfoximine **14** as synthons.

In the case the dotted line connecting R^{β} and R^{γ} represents a carbon chain, structure **12** matches for the angular carbon-substituted 2-oxabicyclic framework found in many natural products such as the oxygenated terpenes depicted in Scheme 3. 5β-Acetoxypalisadin,[9] extracted from the marine alga *Laurencia* cf. *palisada*, exposes the acetyl-protected oxygen functionality derived from the aldehyde fragment and *trans*-fused six- and seven-membered rings. In addition, the latter is true for arenaran A, which is also isolated from a marine sponge.[10] Here, however, the eight-membered ring lacks the oxygen functionality in the 7-position. The terrestrial natural products euglobals G1 and G2 also lack the oxygen functionality. The 6,6-ring connection is *cis*. The aldehyde fragment can be derived from a known aromatic aldehyde (see below).

Results and Discussion

We report here on the fluoride-ion-induced cyclisation of the isomerically pure 5-silyloxy-substituted cycloalkenylvinyl sulfoximines **15**−**22** (Scheme 4) yielding the 2-oxabicyclic heterocycles **36**−**43** (Scheme 5).



Scheme 4. The γ-hydroxyalkylation reaction of cyclic 2-alkenyl sulfoximines

The cyclic vinyl sulfoximines needed for the preparation of the above-mentioned bicyclic systems are accessible in enantiomerically pure form by the diastereoselective γ-hydroxyalkylation of the titanated 2-cyclopentenylmethyl sulfoximines **31**, **32** and 2-cyclohexenylmethyl sulfoximines **33**, **34** with TBS-protected lactaldehydes **35**, *ent*-**35** as we have reported earlier.[7]

In accordance with the results we achieved previously with open-chain sulfoximines,[11] metallated 2-cycloalkenylmethyl sulfoximines transfer their allylic fragment with perfect regio- and stereoselectivity to achiral, as well as chiral, nonracemic aldehydes. Irrespective of the chiral induction by the substrate, S_S reagents[12] add to aldehydes exclusively from the *Re* face and R_S reagents attack from the *Si* face.[7,11]

Cycloalkenylmethyl sulfoximines **23**−**26**[7,8,13] are lithiated to the configurationally labile allylic anions **27**−**30** which can be titanated in a diastereomer-differentiating transmetallation to form the organotitanium compounds **31**−**34**.[14] In the subsequent γ-hydroxyalkylation reaction one new C−C bond is formed. The stereochemical outcome at the two new stereogenic centres at C-3 and C-4 is perfectly controlled by the stereogenic sulfur atom. Only with the cyclohexenylmethyl sulfoximines **25**, **26** does the relative configuration of the stereogenic centres of the auxiliary (at

Table 1. Synthesis of 2-Oxabicyclo[*n*.3.0]alkanes **36**−**39** and **41**−**43**

Bicyclic compound	*y* [%][a]	*ds* [%][b]	$[\alpha]_D^{20}$[c]	m.p. [°C]	$\delta_{C-3'}$	δ_{C-4}
36	49	≥ 98	+25.0 (0.73)	oil	11.82	72.14
37[d]	**60**	**≥ 98**	**+74.2 (0.97)**	**124.5**	**16.63**	**76.31**
38	52	≥ 98	−15.6 (0.93)	153.7	18.31	77.96
39	28	≥ 98	−19.3 (0.86)	oil	12.91	75.44
41[d]	**43**	**≥ 98**	**+90.2 (0.47)**	**47.6**	**19.84**	**79.72**
42	72	≥ 98	−62.2 (0.82)	53.9	20.08	79.81
43	72	≥ 98	−18.3 (0.87)	50.5	14.92	77.11

[a] Overall yield starting from the sulfoximines **23**−**26**. − [b] Determined from the crude cyclisation products by ^{1}H-NMR spectroscopy. − [c] All values of optical rotation have been determined in CH_2Cl_2. Values in brackets denote a concentration in g/100 mL. − [d] These substances have been characterised by X-ray structural analysis

the sulfur atom and in the valine moiety) have a recognisable influence on the stereochemical uniformity of the products **19**−**22**. If the interaction is synergistic (mutual enhancement) the relative configuration is called intramolecular matched (^{i}m). This is attained when the configuration at the sulfur and the side-chain stereogenic centres is alike (R_S, R_C or S_S, S_C). This second-order effect does not affect the generality of the method, since the ^{i}m configuration can always be obtained by choosing the appropriate valine enantiomer when preparing the chiral auxilliary.[7,8]

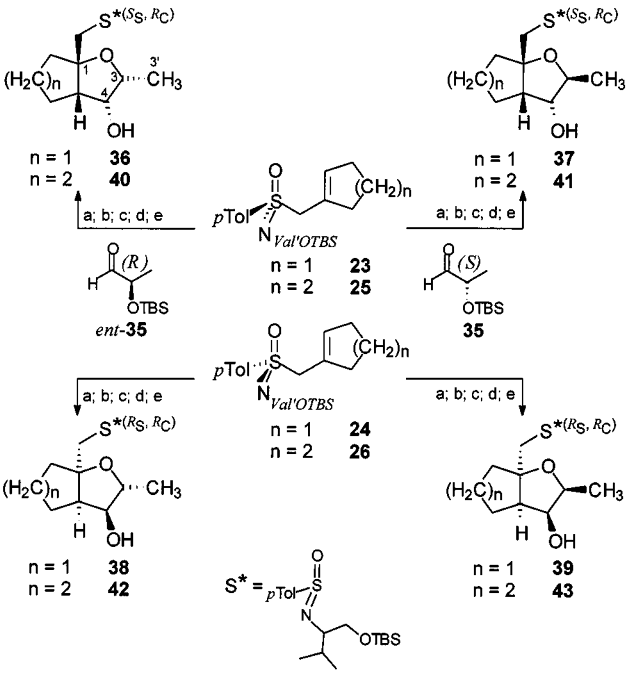
2-Oxabicyco[*n*.3.0]alkanes

When 5.2 equivalents of tetrabutylammonium fluoride (TBAF) were added to the γ-hydroxyalkylation adducts **15**−**22** (Scheme 4) after workup 2-oxabicyclo[3.3.0]octanes **36**−**39** and 2-oxabicyclo[4.3.0]nonanes **40**−**43** were obtained in a one-pot sequence starting from the corresponding cycloalkenylmethyl sulfoximines **23**−**26** (no isolation of the homoallylic alcohols **15**−**22**, Scheme 4, was needed) (Scheme 5, Table 1). ^{1}H-NMR spectra of the crude products showed the bicyclic ethers **36**−**43** to be diastereomerically pure (*ds* ≥ 98%).

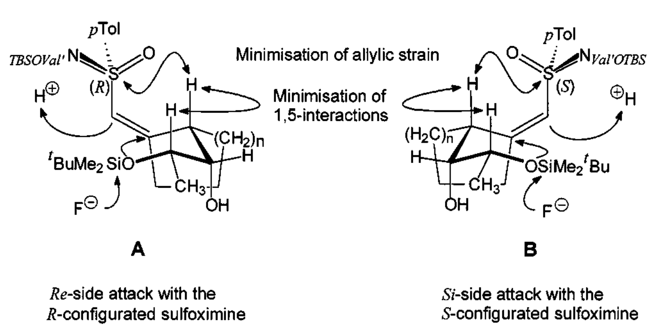
By analogy to the THF derivatives, *cis* arrangement of the methyl substituent at C-3 and the hydroxy substituent at C-4 is reflected in a high-field shift of the ^{13}C-NMR signals from the 3-methyl group and the carbinol centre C-4 of about 5 ppm compared to the respective *trans* arrangement.[15]

The absolute configuration of the stereogenic centres was established by anomalous X-ray scattering in the course of the crystal-structural analysis of **37** and **41**.[16a] As expected in both cases the rings are *cis*-fused. Furthermore, from the absolute configuration of the bridgehead C-1, it can be deduced that for the S_S-sulfoximines the double bond has been attacked from the *Si* face while in the R_S systems the double bond has been attacked from the *Re* face. We can explain this stereochemical outcome by a preferred conformation of the vinyl sulfoximine in the course of the cyclisation reaction (Scheme 6).[6]

To allow a bonding interaction between the oxygen atom and the double bond the former has to be positioned close to the π* orbital of the latter. While obeying these demands the system tries to avoid additional increase of internal energy due to allylic strain or 1,5 interactions. Following these lines the structures **A** and **B** shown in Scheme 6 represent reasonable conformations of the cyclising vinyl sulfoximines for both absolute configurations at the sulfur atom. Within this model the stereochemistry of the cyclisation step is controlled exclusively by the absolute configuration of the sul-



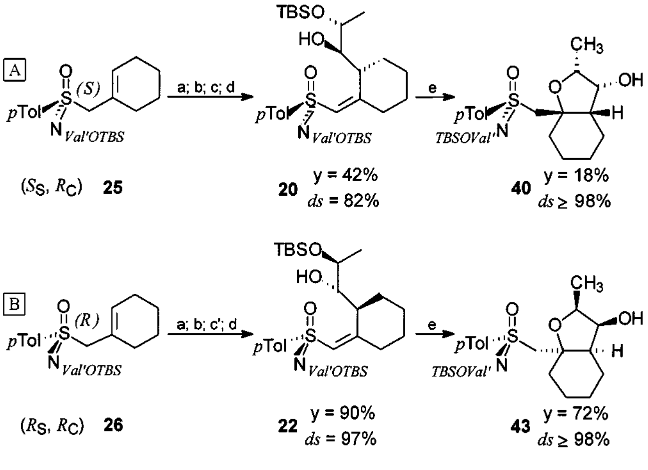
Scheme 5. Synthesis of 2-oxabicyclo[*n*.3.0]alkanes: a: *n*BuLi, −78°C; b: $ClTi(OiPr)_3$, → 0°C; c: −78°C, aldehyde; d: $(NH_4)_2CO_3$; e: TBAF, THF, H_2O



Scheme 6. Preferred conformations of the vinyl sulfoximines in the course of the cyclisation

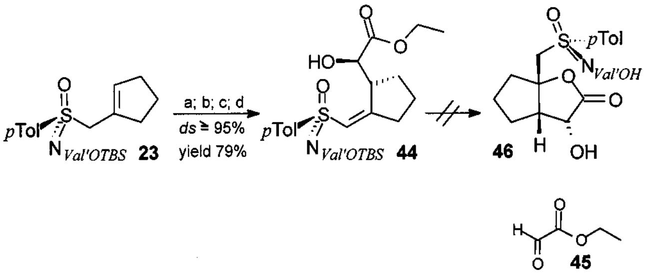
fonimidoyl group, which is strongly supported by experimental data (Table 1). In short, the stereogenic sulfur atom allows control of the absolute configuration at C-4, C-5 and C-1 of the bicyclic system.

Table 1 lacks an entry for compound **40** (Scheme 5). The diastereomeric cyclohexenylmethyl sulfoximines **25** and **26** differ merely in their absolute configuration at the sulfur atoms, not in the valine-derived side chain. While in **25** the relative configuration in the auxiliary is *unlike* (S_S,R_C), sulfoximine **26** displays the like situation (R_S,R_C). Since the γ-hydroxyalkylation reaction and the cyclisation are both stereochemically controlled by the stereogenic sulfur atom the reaction pathways **A** and **B** lead to enantiomorphous bicyclic moieties within **40** and **43**. However, due to the different relative configuration in the auxilliary the reaction pathways are diastereomorphous: In **A** the γ-adduct **20** was isolated with only 82% *ds* and 42% yield while the oxabicyclic compound **40** was found to be diastereomerically pure (*ds* ≥ 98%, 18% yield). This effect clearly demonstrates that a diastereomer-discriminating cyclisation takes place. As expected, the increase in diastereomeric excess of the product entails a diminished yield since the "wrong" diastereomer cyclises only very slowly. The low-yield pathway to the stereotriade in the cyclic moiety in **40** can be avoided by simply altering the absolute configuration in the valine-derived side chain to form the intramolecular matched (^{i}m) pair in the auxiliary (see above). Following the reaction cascade **B** the enantiomorphous bicyclic moiety can be synthesised in 72% overall yield and *ds* ≥ 98%. The same should of course be true for the *N*(1*S*) epimer of **25** (S_S,S_C) furnishing *ent*-**43** (by the enantiomorphous reaction route forming **43**). The corresponding reaction sequence is shown in Scheme 7.



Scheme 7. Influence of the relative configuration in the chiral auxiliary (X_S, X_C) on the formation of the bicyclic compounds **40** and **43**: **A**: the yield of the bicyclic compound **40** is found to be diminished due to a diastereomer-differentiating cyclisation reaction; **B**: the enantiomorphous stereotriade in the bicyclic moiety of compound **43** can be obtained in high yield and excellent stereoselectivity by employing the *like*-configurated alkenyl sulfoximine **26**; a: *n*BuLi, −78°C; b: ClTi(O*i*Pr)$_3$, → 0°C; c: −78°C, *ent*-**35**; c′: −78°C, **35**; d: (NH$_4$)$_2$CO$_3$; e: TBAF, THF, H$_2$O

To evaluate the electrophilicity of the vinylic double bond we changed the electronic state of the cyclising oxygen functionality. As anticipated, we found carboxylate functionalities to be poor nucleophiles in the cyclisation reaction (Scheme 8).



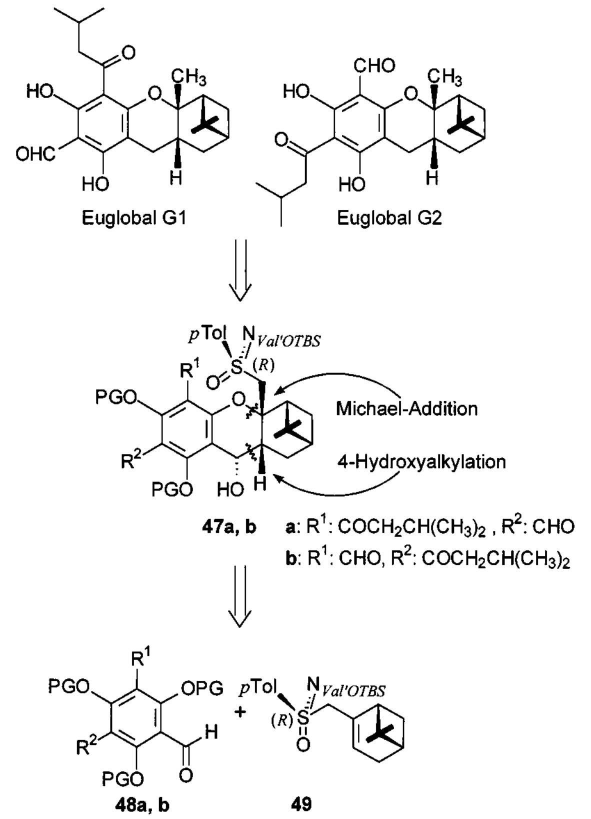
Scheme 8. Studies towards the synthesis of bicyclic γ-lactones; a: *n*BuLi, −78°C; b: ClTi(O*i*Pr)$_3$, → 0°C; c: −78°C, **45**; d: (NH$_4$)$_2$CO$_3$

Although the γ-hydroxyalkylation adduct **44** from cyclopentenylmethyl sulfoximine **23** and ethylglyoxylate **45**[17] could be isolated in 79% yield (*ds* ≥ 95%) no conditions have been found to cyclise it yielding the bicyclic γ-lactone **46**. Under various basic and Lewis acidic conditions reactions other than deprotection of the carboxylic acid were not achieved.

Summarising the results reported so far, 2-cyclopentenyl- and 2-cyclohexenylmethyl sulfoximines can be converted to angular carbon-functionalised, highly substituted, isomerically pure (*ds* ≥ 98%) 2-oxabicyclo[3.3.0]octanes **36**−**39** and 2-oxabicyclo[3.4.0]nonanes **40**−**43** by a convenient one-pot sequence (Scheme 5). These bicyclic ethers can be obtained in 28−60 (oxabicyclo[3.3.0] systems) and 72% yield (oxabicyclo[4.3.0] systems), respectively. The method introduced in this paper opens up the opportunity for the synthesis of four out of eight possible isomers, since the relative configuration of the stereogenic centres formed in the γ-hydroxyalkylation reaction (at C-4 and C-5) is necessarily *cis* due to the reaction mechanism. The fusion of rings is *cis*, while the absolute configuration at C-3 and C-4 can individually be controlled completely. The method introduced above can be considered as a possible way to implement the structural motif **12** found in many polycyclic ethers of marine origin (e.g. brevetoxin,[18] maitotoxine[19]) and other natural products (Scheme 3). We were therefore keen to apply the method outlined above on a natural product target, which would also help to evaluate the scope and limitations of the method.

Euglobals G1 and G2

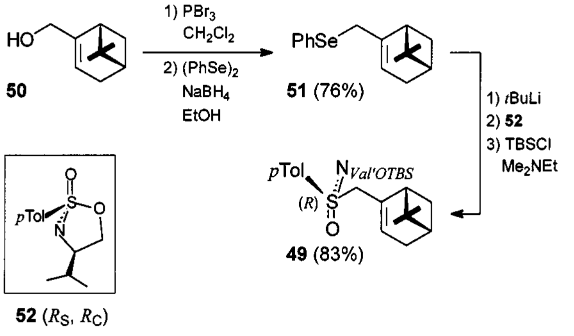
The euglobals G1 and G2 are terrestrial natural products which have been isolated from *Eucalyptus grandis* (Scheme 9).[20] The constitution and the relative configuration have been determined by 2D-NMR spectroscopy. In both compounds an aromatic moiety, structurally related to grandinole,[21] and an α-pinene-like terpene fragment are found. The euglobales G1 and G2 merely differ in the substitution pattern of the aromatic ring. Due to their biological properties (especially inhibition of the Epstein−Barr virus[22]) they are regarded as substances exhibiting anticarcinogenic effects and could be considered as potential precursors of anti-tumour



Scheme 9. Retrosynthetic analysis of euglobales G1 and G2

drugs.[23–25] To our knowledge they have not yet been synthesised.

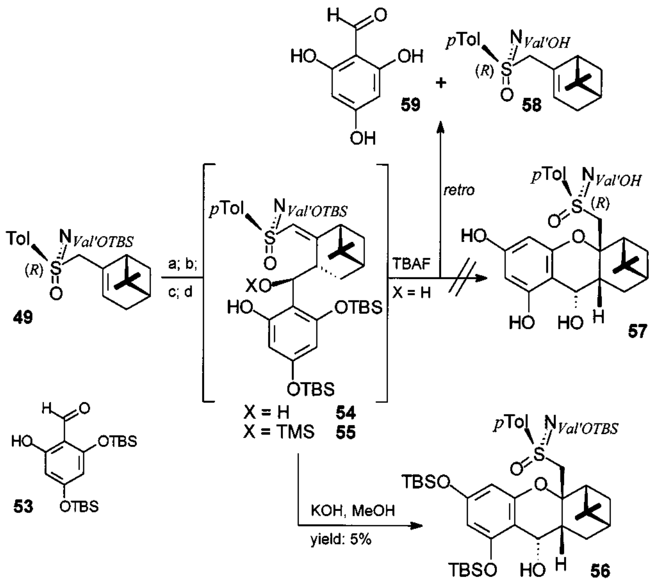
Retrosynthetic analysis via sulfoximines **47a**, **b** following the retro 4-hydroxyalkylation reaction and retro-Michael-like addition shows the grandinol-related aldehydes **48a**, **b** and the (1*R*)-myrthenol-derived sulfoximine **49** to be the first synthetic targets. Starting from (1*R*)-myrthenol (**50**) the sulfoximine **49** has been obtained in 61% overall yield via the selenide **51** (Scheme 10).



Scheme 10. Synthesis of the bicyclic sulfoximine **49** via selenide **51**

The titanium compound derived from sulfoximine **49** was brought to reaction with the partially silylated trihydroxybenzaldehyde **53**[26] under the conditions outlined above (Scheme 11).

This aldehyde offers the opportunity for fluoride-ion-induced, as well as base-induced, cyclisation and was therefore attractive in a test system. While the base-induced pathway should open up a route to the partially silylated tetracyclic compound **56** the fluoride-ion-induced cleavage of all protecting groups should lead to the fully deprotected tetracyclic compound **57**. It was hoped that both may be converted to euglobales G1 and G2 by appropriate manipulations of the aromatic ring.

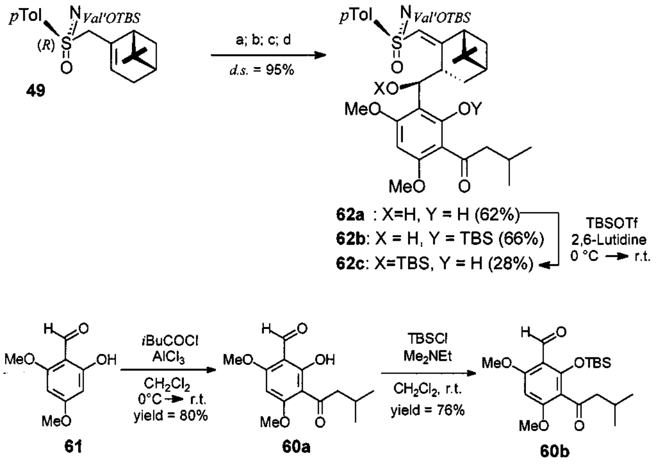


Scheme 11. Synthesis of the tetracyclic euglobal precursor **56**; a: *n*BuLi, −78°C; b: ClTi(O*i*Pr)$_3$, → 0°C; c: −78°C, **53**; d: (NH$_4$)$_2$CO$_3$

In order to isolate the expected 4-hydroxyvinyl sulfoximine the crude product **54** (X = H) was silylated yielding the protected sulfoximine **55** (X = TMS) isomerically pure ($ds \geq 98\%$) in 31% yield. This successful γ-hydroxyalkylation reaction with the sterically highly demanding aldehyde **53** highlights two important features of the system. The titanated species derived from sulfoximine **49** acts only as a nucleophile and not as a base. The acidic phenolic proton does not interfere in the C−C bond-forming process. Furthermore, the system is susceptible to retro addition. As a consequence, chromatographic purification is always accompanied by varying degrees of bond cleavage. Therefore, all cyclisation attempts have to be performed with the crude products and reaction conditions have to be adjusted carefully. In fact, experiments to induce cyclisation of the γ-hydroxyalkylation adduct **54** in situ with TBAF lead to complete retro addition, only fully desilylated starting materials **58** and **59** have been isolated (Scheme 11). However, after considerable experimentation we finally found that basic unravelling of the oxygen functionality made it possible to isolate the desired tetracyclic compound **56** diastereomerically pure but in only 5% yield.

In spite of major efforts to improve the yield, because of the retro addition we were unable to optimise the reaction to an acceptable extent. We therefore switched to the sterically far less demanding methyl-protected aldehyde **60a** (Scheme 12). This electrophile was easily accessible by Friedel−Crafts acylation of the commercially available benzaldehyde derivative **61** in 80% yield. A further advantage of **60** is that the acyl side chain is already installed and that it should be possible to use both *ortho* positions for the cyclisation reaction. This opens up the opportunity of synthesising both euglobales G1 and G2 from the same precursor **62**.

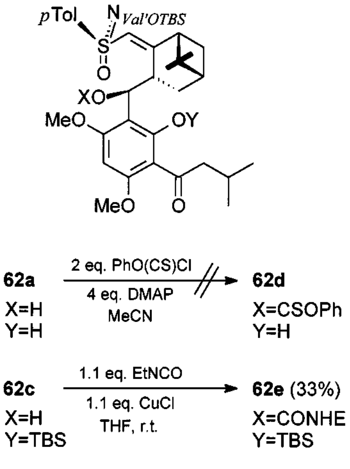
The product **62a** of the corresponding γ-hydroxyalkylation reaction was isolated in 62% yield without protection of the phenolic hydroxy functionality, thus confirming our expectations concerning the increased stability towards retro reaction and again demonstrating the insensitivity of the system towards steric bulk. Unfortunately, efficient cyclisation conditions could be found neither for **62a** nor for the protected vinyl sulfoximine **62c**. Again retro addition is the major reaction pathway. Under basic conditions mi-



Scheme 12. Synthesis of trihydroxybenzaldehyde derivatives **60a−b** and their application in γ-hydroxyalkylation reactions with sulfoximine **49**; a: *n*BuLi, −78 °C; b: ClTi(O*i*Pr)$_3$, → 0 °C; c: −78 °C, **60a** or **b**; d: $(NH_4)_2CO_3$

gration of the silyl protecting group of **62b** from the benzylic to the phenolic oxygen atom is believed to initiate retro addition.

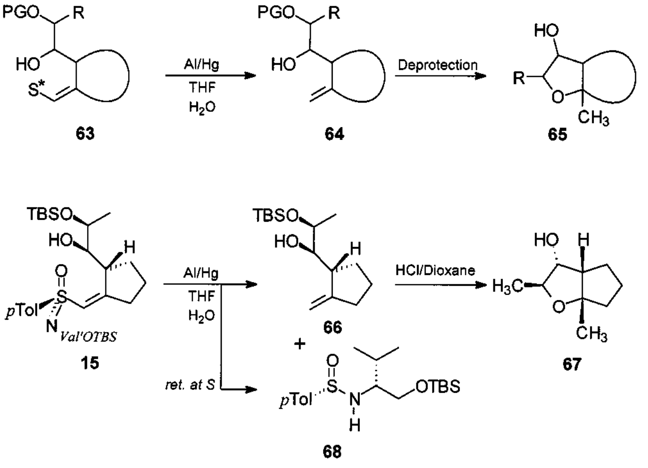
It was therefore obvious that the protecting group strategy at the benzylic position had to be changed. Envisaging the necessary deoxygenation in the central ring of the synthetic targets euglobals G1 and G2, a xanthogenate-masking of the benzylic hydroxy function could firstly serve as a protecting group with negligible migration tendency and secondly prepare the position for the required derivatisation. Unfortunately, the xanthogenate **62d** could not be obtained (no conversion under basic conditions[27]) (Scheme 13).



Scheme 13. Protection of the benzylic hydroxy function

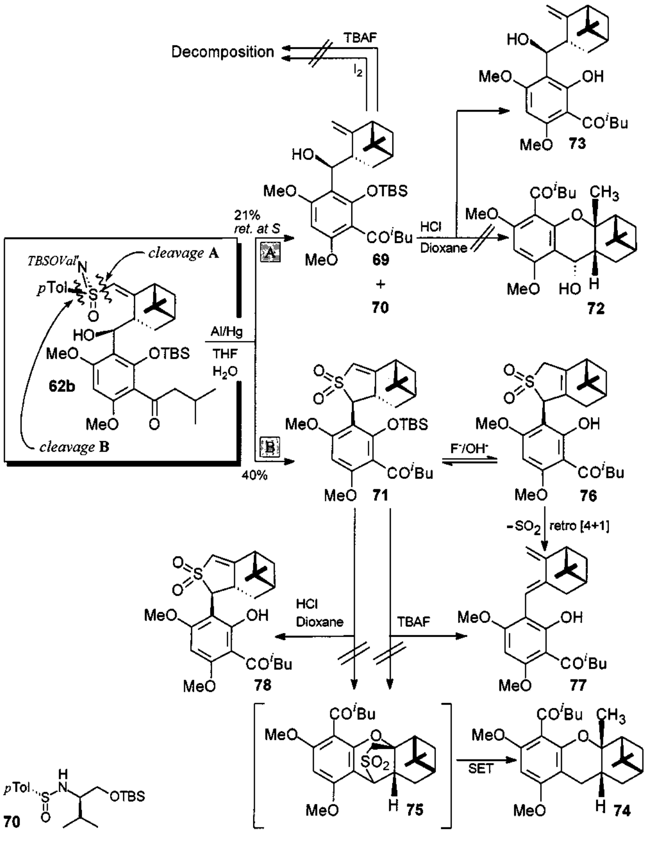
Finally, we were able to protect the benzylic position as an ethyl urethane. Starting from **62b** which was obtained in a γ-hydroxyalkylation reaction employing aldehyde **60b** (Scheme 12) a CuCl-catalysed process[28] yielded **62e** in 33% yield. To our disappointment, however, this substance again failed to cyclise under fluoridic conditions (3 equivalents TBAF, room temp.).

After careful consideration of the results reported so far, we felt it necessary to change the strategy in a radical way. The susceptibility of the system to retro addition had to be further reduced. Therefore we decided to eliminate the sulfoximine moiety which stabilises the negative charge at C-1 evolving during retro addition. It is known that under acidic conditions homoallylic alcohols such as **64** can cyclise to give angular methyl-substituted ethers **65** (Scheme 14 and Scheme 1a).



Scheme 14. Acid-induced cyclisation after removal of the sulfoximine auxiliary

From our own work we know that reductive cleavage of the C−S bond in **15** yields the olefin **66** which undergoes facile cyclisation in HCl/dioxane to yield the oxabicyclic compound **67** in 54% yield.[29] Transferring these results to the system under study, vinyl sulfoximine **62b** was treated with freshly prepared aluminium amalgam[30] in aqueous THF (Scheme 15).[29b,31,32]



Scheme 15. Cyclisation studies with the products of reductive C−S bond cleavage

Chromatographic purification delivered the desired olefin **69** in 21% yield (Pathway **A**) along with a second more polar substance

(40% yield, pathway **B**) which we were able to identify using X-ray structural analysis as tricyclic sulfone **71**![16b] Furthermore it was rather disappointing to discover that olefin **69** failed to cyclise under acidic conditions. Only the desilylated olefin **73** was obtained. TBAF deprotection of the oxygen nucleophile as well as I_2 activation of the electrophilic double bond both lead to the decomposition of **69**.

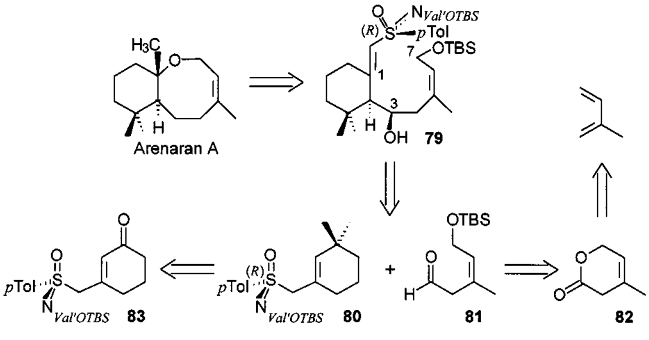
To our great surprise the single-electron transfer ability of aluminium amalgam and homolytic cleavage of the S−C bond at site B (and not at the desired site A) had set off a complicated reaction sequence forming the completely unexpected cyclic vinyl sulfone **71**.[33] We therefore recognised that it should be possible to transform **71** into the euglobal G1 precursor **74** by nucleophilic attack on the double bond followed by a reductive desulfuration (Scheme 15). Compared to tetracyclic compound **72** this structure already lacks the hydroxy function in the middle ring and is therefore an attractive synthetic target. However, while fluoride-ion-induced desilylation led to SO_2 extrusion (probably via the isomerised sulfone **76**) and formation of the diene **77**, acidic conditions led to desilylation forming **78** only.

Summarising, the high susceptibility of the vinyl sulfoximine to undergo retro addition was, once again, the major synthetic problem. This feature, which among others prohibited the cyclisation to the desired four-ring framework, is very pronounced with aromatic aldehydes i.e. benzylic hydroxy functionalities. Also, the nucleophilicity of a phenolic oxygen atom is rather low compared to the alkoxide anions employed in the successful cyclisations as in the case of the carboxylate anion (Scheme 5 and Scheme 8).

In general, three variables influence the cyclisation reaction: (a) electrophilicity of the double bond, (b) nucleophilicity of the attacking heteroatom and (c) susceptibility towards retro addition. Although it is possible to enhance the electrophilicity of the vinylic double bond by *N*-methylation[34] we did not pursue this option. Options (b) and (c) cannot be further influenced without losing synthetic efficiency. Although our method is therefore not suitable for the synthesis of the euglobals G1 and G2, the experiments gave us the opportunity to discover much more about the method than from the usual set of artificial examples. We therefore chose the marine natural product arenaran A as a more promising total synthesis target.

Arenaran A

Arenaran A[10] is a marine terpenoid which had been isolated from Dysidea arenaria in 1995 (Scheme 16).

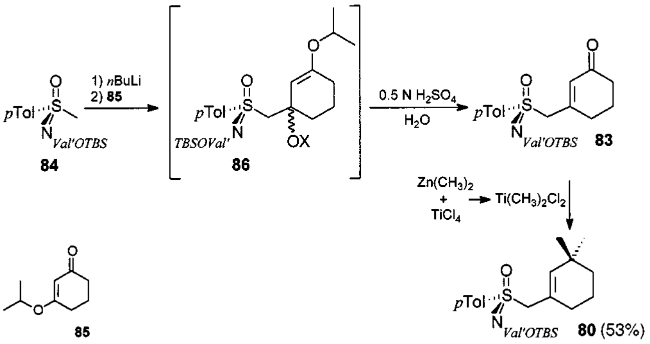


Scheme 16. Retrosynthetic analysis of arenaran A

Although we anticipated problems due to cyclisation of an eight-membered ring, we proceeded on the basis that the masked aliphatic alkoxide anion in the corresponding arenaran precursor **79** should be of higher nucleophilicity than a phenolic oxygen atom and at the same time the oxygen functionality at C-3 (in structure **79**) derived from an aliphatic aldehyde should render the molecule less sensitive towards retro addition. The constitution and relative configuration of arenaran A were elucidated by NMR spectroscopy but the absolute configuration is still unknown.[10] Besides the required confirmation of the absolute configuration, by comparing the natural product with a synthetic sample, in vitro cytotoxic activity against various cancer cell lines shows arenaran to be also of pharmacological interest.[10]

The bicyclic structure formed by condensation of a six- and an eight-membered ring is noticeable. The six-membered ring is geminally dimethylated in the 9-position. Except for the double bond (which could help with ring closure by reducing transanular interactions) and the eight-membered ring, arenaran A is very closely related, both structurally and electronically, to the 2-oxabicyclo[3.4.0]nonane compounds **40** to **43** (Scheme 5) which we have been able to obtain in high yields. Retrosynthetic analysis of the cyclisation precursor **79** reveals sulfoximine **80** and aldehyde **81** to be synthons (Scheme 16). The characteristic feature of the electrophilic synthon, 5-hydroxy aldehyde **81**, is the non-conjugated (*Z*) double bond. In our synthetic strategy we employed the cyclic intermediate **82** to solve this structural problem.

As a precursor for the sulfoximine **80** we envisaged the ketone **83**. Although the preferred position of the double bond in this multifunctionalised molecule was not clear from the beginning, we were fortunate to prepare it successfully in 72% yield starting from methyl sulfoximine **84**[7,8,13] (Scheme 17).

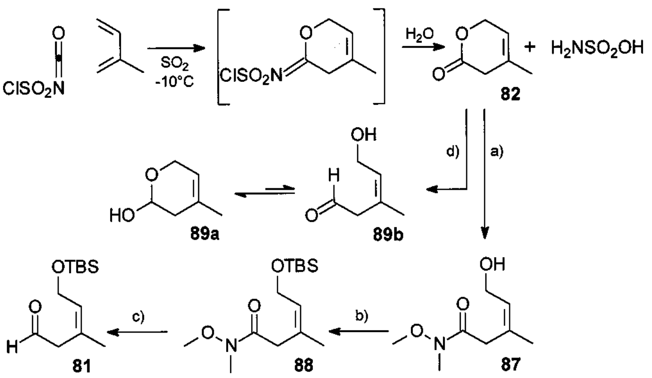


Scheme 17. Preparation of the target sulfoximine **80** via ketone **83**

Geminal disubstitution was achieved by altering a procedure described by Reetz et al.[35] in which the methylating agent is formed in situ from $Zn(CH_3)_2$ and $TiCl_4$. Precise control of reaction time (1.5 to 2 h), temperature (−25 to −20°C) and workup conditions [cooling to −78°C, dilution with CH_2Cl_2, slow addition to vigorously stirred saturated aqueous $(NH_4)_2CO_3$] allowed us to isolate up to 53% of the desired sulfoximine **80** (see Experimental Section for further details). Thus, under these altered reaction conditions we exclusively obtained the geminal dimethylated alkene **80**, thereby extending the Reetz procedure to conjugated enones.

The Δ^3-lactone **82** was obtained in a Diels−Alder reaction of chlorosulfonyl isocyanate and isoprene in liquid SO_2 after aqueous workup in one step (Scheme 18).[36]

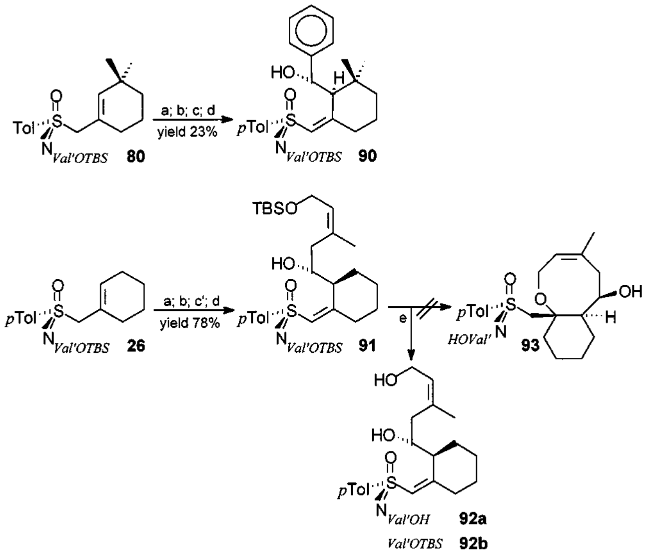
The lactone **82** was opened to the Weinreb amide **87** following standard procedures (condition a).[37] After silyl protection of the hydroxy group the amide **88** was purified by flash chromatography. It was isolated in over 50% overall yield starting from isoprene. DIBALH reduction delivered the projected aldehyde **81** (92−96% yield) which could be utilised in γ-hydroxyalkylation reactions without further purification. [Due to the negligible aldehyde reac-



Scheme 18. Synthesis of the target aldehyde **81** via lactone **82**; a: Me(Cl)AlN(OMe)Me; b: TBSCl, Me_2NEt, DMAP, CH_2Cl_2; c: DIBALH, THF/hexane, −78 °C; then 0.5 M tartaric acid; d: DIBALH, THF/hexane, −78 °C

tivity of the reduction product **89** (conditions d) the obvious route to the desired electrophile failed.[38]]

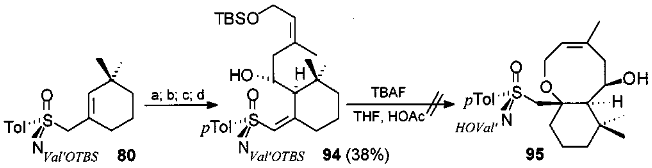
Both the sulfoximine **80** and the aldehyde **81** have been studied in model reactions (Scheme 19, see also Scheme 4) to learn more about their respective reactivities.



Scheme 19. Application of the key building blocks of arenaran A in γ-hydroxyalkylation reactions with model substances. Studies towards cyclisation of model adduct **91**; a: *n*BuLi, −78 °C; b: $ClTi(OiPr)_3$, → 0 °C; c: −78 °C, PhCHO; c′: −78 °C, **81**; d: $(NH_4)_2CO_3$; e: TBAF, HOAc, THF, H_2O

From the reactions of **80** with benzaldehyde and **81** with cyclohexenylmethyl sulfoximine **26** the γ-hydroxyalkylation adducts **90** and **91**, respectively, have been isolated by flash chromatography diastereomerically pure (*ds* ≥ 98%) in 23 and 78% yield, respectively, showing the sterically highly demanding sulfoximine **80** to offer the desired reactivity and the aldehyde **81** to be a very potent electrophile.

In the light of these model studies we were not surprised but nevertheless very pleased to recognise that the coupling of the sulfoximine **80** and the aldehyde **81** delivered the advanced intermediate **94** with perfect uniformity at all stereogenic centres and the prostereogenic double bond in about 38% yield (Scheme 20). Since the vinyl sulfoximine **94** could not be purified completely by flash chromatography (mainly due to retro addition) its identification was unequivocally achieved using NMR techniques (^{1}H and ^{13}C, HSQC and DQF-COSY).



Scheme 20. Addition of the relevant alkenyl sulfoximine **80** to the aldehyde **81** and cyclisation attempts; a: *n*BuLi, −78 °C; b: $ClTi(OiPr)_3$, → 0 °C; c: −78 °C, **81**; d: $(NH_4)_2CO_3$

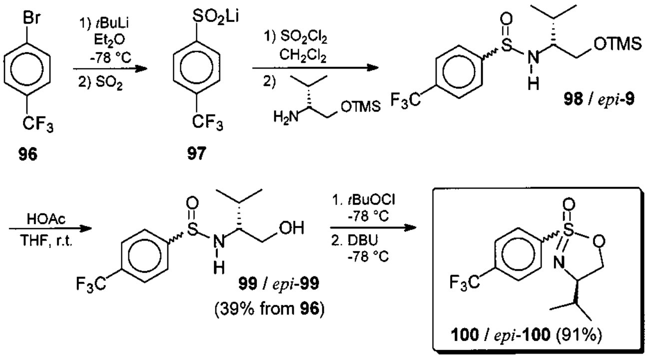
As a model for the cyclisation reaction we tried to cyclise the cyclohexenylmethyl sulfoximine derived γ-adduct **91** (Scheme 19). Although more drastic reaction conditions (compared to the ones applicable in the euglobale chemistry) can be applied (temperature: 40 °C, high concentration of TBAF in THF) without any risk of retro addition when the TBAF solution has been neutralised with glacial acetic acid before use, fluoride-ion-induced deprotection of the oxygen nucleophile allowed isolation merely of the desilylated starting compounds **92** and no cyclisation adduct **93** was obtained (Scheme 19). Unfortunately, but not unexpectedly, the same was true for the complete precursor **94** (Scheme 20).

To summarise, we obtained the desired sulfoximine **80** and aldehyde **81** in high overall yields presenting the correct configurations of their respective stereogenic elements. We were also able to connect these key fragments forming the 4-hydroxyvinyl sulfoximine **94** with all structural features of arenaran A except for its bicyclic structure being set up (Scheme 20). To our disappointment deprotection of the oxygen atom again does not uncover a nucleophile strong enough to initiate a Michael-like attack on the sulfonimidoyl-activated double bond.

Scope and Limitations

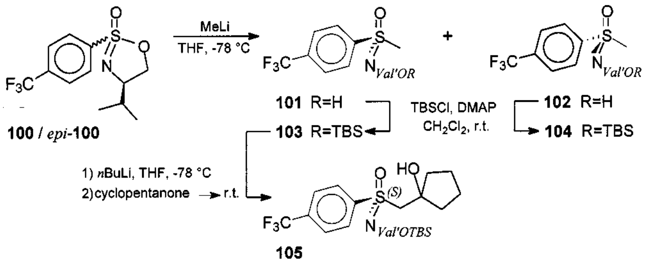
The results obtained so far led us to consider a categorical change to the system. There are two possibilities for altering the method in order to facilitate the crucial cyclisation reactions. The Michael activity of the double bond can be increased by enhancing the electron-withdrawing capacity of the sulfonimidoyl moiety (no restriction of constitutional scope). Alternatively, the nucleophilicity of the cyclising heteroatom can be increased by changing the heteroatom (restriction of constitutional scope). Although the first alternative seems to be rather simple, replacing the *p*-tolyl group with a more electron-withdrawing group might have a major impact on the stereochemical control mechanism of the method, mostly in the γ-hydroxyalkylation reaction step. Gais et al.[39] have demonstrated that in lithiated trifluoromethyl sulfones (triflones) rotation around the $S-C_{aliphatic}$ bond was greatly hindered due to a strong $n_C-\sigma^*_{S-C}$ interaction. This could, of course, dramatically change the pathway to diastereomerically pure titanated sulfoximines (Scheme 4). It is to be expected that the electron-withdrawing group may render the configuration of the lithiosulfoximine stable which would change the stereodifferentiating step from a diastereomer-differentiating transmetallation to a diastereotopos-differentiating deprotonation of unknown efficiency.

The first strategy for facilitating the cyclisation does not entail any restriction to the constitutional scope of the reaction and should therefore be helpful in the synthesis of the three natural products envisaged. In order to establish a more electron-deficient auxilliary we switched from a *p*-tolyl to a *p*-trifluoromethylphenyl group (Scheme 21).



Scheme 21. Synthesis of the CF_3-substituted cyclic sulfonimidates **100**, *epi*-**100**

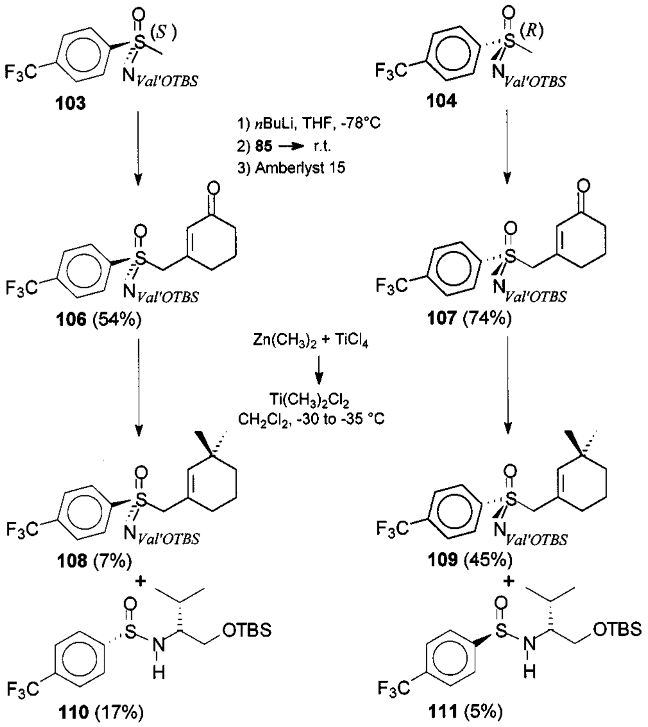
Starting from commercially available 1-bromo-4-(trifluoromethyl)benzene (**96**), sulfinate **97** was obtained as an off-white solid by halogen/lithium exchange followed by electrophilic substitution with SO_2. Chlorination and amidation yielded the diastereomeric sulfinamides **98** and *epi*-**98** (1:1, NMR-spectroscopically determined) which could be desilylated under acidic conditions. Due to our experience with *p*-nitro-substituted derivatives we did not attempt to desilylate the sulfinamides **98**, *epi*-**98** with MeOH/K_2CO_3.[40] The former were found to form the corresponding sulfinic acid esters, thus giving a hint as to the expected enhanced electrophilicity of the sulfinamide. The mixture of epimeric hydroxy sulfinamides **99** and *epi*-**99** was isolated by chromatography in 39% yield starting from bromide **96**. The sulfinamides could be cyclised following the standard procedure.[8] The mixture of diastereomeric sulfonimidates **100** and *epi*-**100** was isolated in 91% yield. Their reaction with methyllithium furnished the corresponding hydroxymethyl sulfoximines **101** and **102** which were separated chromatographically (**101** in 70%, **102** in 89% yield, Scheme 22).



Scheme 22. Alkylative ring opening and addition to cyclopentanone

The TBS-protected (S_S)- and (R_S)-methyl sulfoximines **103** and **104** were isolated in 78 and 85% yield, respectively. Their absolute configuration was ascertained by X-ray structural analysis (anomalous X-ray scattering) of the derived alcohol **105**.[16a]

To our delight the protected (S_S)- and (R_S)-methyl sulfoximines **103** and **104** could be converted into the corresponding ketones **106** and **107** in a one-pot reaction applying conditions related to the *p*-tolyl-substituted auxiliary when Amberlyst 15 was employed instead of 0.5 N H_2SO_4 (Scheme 23, compare with Scheme 17). The ketones **106** and **107** were obtained in 54 and 74% yield, respectively, as colourless solids.



Scheme 23. Synthesis of the dimethylated cyclohexenylmethyl sulfoximines **108** and **109**

Conditions for the geminal dimethylation were again optimised. The temperature range of maximum product formation and minimum reduction was found to be −35 to −30°C. While the (R_S)-epimeric product **109** could be isolated in 45% yield the (S_S)-epimeric ketone **106** is very susceptible to reduction. Only 7% of the desired dimethylated cyclohexenylmethyl sulfoximine **108** needed to proceed in the synthesis were isolated, besides 17% of the corresponding (S_S)-TBS-sulfinamide **110**.

To summarise, we found a convenient way to access the CF_3-modified sulfonimidates **100**, *epi*-**100**. Furthermore, we again established the building blocks needed for the synthesis of arenaran A diastereomerically pure by synthesising the CF_3-derived sulfoximine **108** (S_S,R_C). Unfortunately, but not unexpectedly of course, we found the susceptibility of sulfur towards reduction to be increased in the *p*-(trifluoromethyl)phenyl sulfoximines compared to the *p*-tolyl derivatives. Since the required arenaran A precursor, dimethylated cyclohexenylmethyl sulfoximine **108** could only be isolated in 7% yield no further investigations have been undertaken to use the new building blocks for the synthesis of arenaran A.

Conclusion

We have found a method for the synthesis of 2-oxabicyclic compounds with general structure **12** (Scheme 3). This method is broad in constitutional scope if both rings of the bicyclic system are five- or six-membered and the oxygen nucleophile is not derived from a phenol.

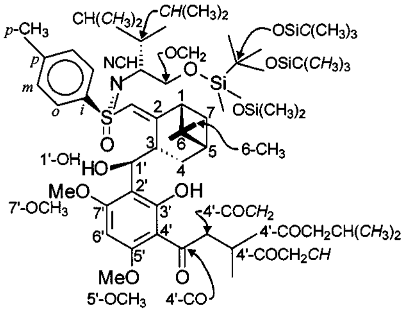
2-cyclopentenyl- and 2-cyclohexenylmethyl sulfoximines can be converted to angular carbon-functionalised, highly substituted, isomerically pure (*ds* $\geq$ 98%) 2-oxabicyclo[3.3.0]octanes **36**−**39** and 2-oxabicyclo[3.4.0]nonanes **40**−**43** by a convenient one-pot sequence (Scheme 5). The corresponding bicyclic ethers can be obtained in 28−60 (oxabicyclo[3.3.0] systems) and 72% yield (oxabicyclo[4.3.0] systems), respectively.

For the total synthesis of euglobals G1 and G2 and arenaran A the method has both merits and limitations. The titanated sulfoximine which acts as a nucleophile in the γ-hydroxyalkylation reaction was proven not to react as a base. The partly silylated trihydroxybenzaldehyde **53** was employed in such a reaction without protection of the phenolic OH group ($pK_a \approx 9$, Scheme 11). In addition, the γ-hydroxyalkylation reaction is barely susceptible to steric hindrance. With the *o,o*-disubstituted aldehydes **60a** and **60b** the expected products **62a** and **62b** have been obtained in 62 and 66% yield, respectively (Scheme 12). Even the sterically crowded geminal dimethylated nucleophile **80** reacted with various aldehydes (PhCHO and **81**) in reasonable yields (23 and 38% respectively, Schemes 19 and 20). For the synthesis of cyclic 2-alkenyl sulfoximines miscellaneous approaches exist. While the nonsubstituted derivatives (**23**−**26**, Scheme 4) have been obtained from (lithiated) methyl sulfoximines (e.g. **84**) and the corresponding ketones after elimination and equilibration of the double bond,[7] other entries have been utilised in the attempted natural-product syntheses. Ketone **83** was prepared from lithiated methyl sulfoximine **84** and the vinylogous ester **85** (Scheme 17). Conjugation with the carbonyl group stabilised the double bond at the desired position in such a way as to render the isomerisation of the double bond an unfavourable process. The related euglobal fragment **49** was prepared by opening the cyclic sulfonimidate **52** with the organolithium compound derived from selenide **51** (Scheme 10).

Replacement of the oxygen atom by a more nucleophilic nitrogen atom as the cyclising atom was found to facilitate the cyclisation step and we developed a new enantioselective pyrrolidine synthesis based on the γ-hydroxyalkylation reaction of 2-alkenyl sulfoximines with FMOC-protected α-amino aldehydes.[41] Further developments directed towards an extremely versatile set of reactions to highly substituted aza(poly)cyclic compounds as potent β-turn mimetics are of current interest in our laboratories. The results achieved so far are extremely promising[42] and will be published in due course.

Experimental Section

General: All manipulations except workup and chromatographic purification were performed under dry oxygen-free argon using Schlenk and syringe techniques. $MgSO_4$ was applied to dry organic layers. Solvents were purified and dried prior to use by distillation from an appropriate drying agent. Diethyl ether (ether) and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Starting materials were obtained from commercial sources and used without further purification unless otherwise stated. The assay from *n*BuLi was obtained by titration with menthol in THF in the presence of 1,10-phenanthroline.[43] Chlorotris(isopropoxy)titanium (ClTIPT) was prepared by literature procedures,[44] distilled at 8 mbar with exclusion of moisture and stored at 4 °C as a hexane solution (1.0 mmol/g). − Analytical thin layer chromatography (TLC): Macherey−Nagel precoated TLC plates (SilG/UV 254). − Flash chromatography: E. Merck silica gel 60 (15−40 μm). − Melting points (m.p.): Gallenkamp apparatus, uncorrected values. − Optical rotations: Perkin Elmer 241 polarimeter. − IR spectra: Perkin Elmer 1310. − ^{1}H- and ^{13}C-NMR spectra: Bruker AMX 400, WH 270 and AC 250. ^{1}H-NMR and ^{13}C-NMR spectra are reported in ppm relative to tetramethylsilane or to [D$_6$]DMSO as solvent ($\delta_H = 2.50$ and $\delta_C = 39.5$). For the sake of convenience, atom numbering does not strictly follow IUPAC rules (Scheme 24). The naming of the auxiliary part is based on connectivities (e.g. NCH for the α position next to the sulfoximine nitrogen atom), the cyclic structures directly connected to the auxiliary are numbered according to IUPAC (1, 2, 3,···) and all structural moieties attached to these structures are given primed numbers starting from the connecting bond (1′, 2′, 3′,···). Primed atoms (C′, H′) stand for the low-field-shifted of two diastereotopic nuclei. Diastereoselectivities of the γ-hydroxyalkylation products were determined from the ^{1}H-NMR spectra of the crude products (integration of the olefin proton of the vinyl sulfoximine).



Scheme 24. A relevant example for the atom numbering applied in the experimental section of this paper

γ-Hydroxyalkylation of the Sulfoximines. − General Procedure (GP1): To a well-stirred solution of the 2-alkenyl sulfoximine (1.0 equiv.) in dry THF (3 mL/mmol) under argon at −78 °C was added dropwise via syringe *n*BuLi (1.1 equiv., 1.6 M in hexane). After 15 min at −78 °C, ClTIPT (1.5 equiv., 1.0 M in hexane) was introduced to the resultant orange reaction mixture and stirring was continued for another 5 min. The mixture was then allowed to warm to 0 °C, stirred for 60 min, and finally cooled again to −78 °C at which point the aldehyde (2.0 equiv.) was added. The reaction mixture was stirred for an appropriate time (about 2 h, TLC control) and quenched by pouring it into a rapidly stirred solution of sat. aqueous $(NH_4)_2CO_3$ (20 mL/mmol). After 30 min of violent stirring, the mixture was extracted with ether (3 × 10 mL), the combined extracts were dried, concentrated and the residue purified by flash chromatography (eluent: e.g. ether/hexane, 1:1).

Synthesis of the Bicyclic Ethers. − General Procedure (GP2): The crude product from the γ-hydroxyalkylation (GP1) was dissolved in THF (3 mL/mmol) and nBu$_4$NF (5.2 equiv., 1.0 M in THF) was added dropwise at 0°C. The reaction mixture was kept at room temp. for an appropriate amount of time (48−72 h, TLC control), poured into water (5 mL/mmol) and extracted with ethyl acetate (3 × 10 mL). The combined extracts were dried, concentrated and the residue purified by flash chromatography (eluent: ethyl acetate/hexane, 10:1).

Bicyclic Compound 36: From 465 mg (1.07 mmol) of sulfoximine **23** and 402 mg (2.13 mmol) of aldehyde *ent*-**35**, 204 mg (49%) of **36** was isolated as a colourless solid, m.p. 136.9°C. − R_f = 0.25 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = 25.00 (c = 0.73, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3406 cm^{-1} (OH), 1220, 1130 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.75 [d, J(3,3-CH_3) = 6.2 Hz, 3-CH_3], 0.85 [d, J(CH,CH_3) = 6.8 Hz, $CHCH_3$], 0.85 [d, J(CH,CH'_3) = 6.9 Hz, $CHCH'_3$], 1.52−2.04 [m; 6-H_2, 7-H_2, 8-H_2, $(CH_3)_2CH$], 2.42 (s, p-CH_3), 2.56 (m, 5-H), 2.69 (ddd, NCH), 3.40 (m; SCH, 3-H, OCH_2), 3.65 (dd, CH_2OH), 3.79 (d, $J_{SCH,SCH'}$ = 14.8 Hz, SCH′), 3.87 (ddd, $J_{4,OH}$ = 5.7 Hz, 4-H), 4.08 (d, $J_{4,OH}$ = 5.7 Hz, 4-OH), 7.32 (d, m-H_2), 7.71 (d, o-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = 11.82 (3-CH_3), 16.33 ($CHCH_3$), 17.95 ($CHC'H_3$), 21.21 (p-CH_3), 21.98 (C-6), 24.07 (C-7), 29.21 [$(CH_3)_2CH$], 36.34 (C-8), 53.47 (C-5), 60.33 (SCH), 60.89 (NCH), 63.29 (OCH_2), 72.14 (C-4), 76.22 (C-3), 89.34 (C-2), 127.45 (o-C), 127.57 (m-C), 137.52 (i-C), 140.85 (p-C). − $C_{21}H_{33}NO_4S$ (395.55): calcd. C 63.77, H 8.41, N 3.54; found C 63.40, H 8.71, N 3.24.

Bicyclic Compound 37: From 235 mg (0.539 mmol) of sulfoximine **23** and 203 mg (1.078 mmol) of aldehyde **35**, 128 mg (60%) of **37** was isolated as a colourless solid, m.p. 124.5°C. − R_f = 0.27 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = 74.20 (c = 0.97, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3250 cm^{-1} (OH), 1250, 1090 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.76 [d, J(3,3-CH_3) = 6.4 Hz, 3-CH_3], 0.80 [d, J(CH,CH_3) = 6.6 Hz, CH_3], 0.81 [d, J(CH,CH'_3) = 6.7 Hz, $CHCH'_3$], 1.30−1.99 [m; 5-H, 6-H_2, 7-H_2, 8-H_2, $(CH_3)_2CH$], 2.38 (s, p-CH_3), 2.66 (m; 4-OH, NCH), 3.31 (m; OCH_2, CH_2OH), 3.55−3.72 (m, SCH_2, 3-H), 3.96 (m, 4-H), 4.79 (d, $J_{4,OH}$ = 4.9 Hz, 4-OH), 7.36 (d, m-H_2), 7.70 (d, o-H_2). − ^{13}C NMR (100 MHz, 320 K, [D$_6$]DMSO): δ = 16.63 (3-CH_3), 17.96 ($CHCH_3$), 19.98 ($CHC'H_3$), 20.59 (p-CH_3), 23.82 (C-6), 25.28 (C-7), 28.77 (C-8), 29.22 [$(CH_3)_2CH$], 51.12 (C-5), 61.25 (SCH), 63.93 (NCH), 64.03 (OCH_2), 76.31 (C-4), 78.04 (C-2), 89.56 (C-3), 128.56 (o-C), 128.75 (m-C), 137.24 (i-C), 141.94 (p-C). − $C_{21}H_{33}NO_4S$ (395.55): calcd. C 63.77, H 8.41, N 3.54; found C 63.55, H 8.28 N 3.30.

Bicyclic Compound 38: From 425 mg (1.00 mmol) of sulfoximine **24** and 377 mg (2.00 mmol) of aldehyde *ent*-**35**, 205 mg (52%) of **38** was isolated as a colourless solid, m.p. 153.7°C. − R_f = 0.17 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = −15.60 (c = 0.93, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3370 cm^{-1} (OH), 1284, 1048 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.95 (m; 4-OH, 3-CH_3, $CHCH_3$, $CHCH'_3$), 1.57−2.04 [m; 6-H_2, 7-H_2, 8-H_2, $(CH_3)_2CH$], 2.42 (s, p-CH_3), 2.76 (m, 5-H), 3.02 (ddd, NCH), 3.40 (d, $J_{SCH,SCH'}$ = 14.6 Hz, SCH), 3.52 (m; 3-H, CH_2OH, OCH_2), 3.62 (d, $J_{SCH,SCH'}$ = 14.6 Hz, SCH′), 3.87 (m, 4-H), 7.30 (d, m-H_2), 7.79 (d, o-H_2). − ^{13}C NMR (100 MHz, 300 K $CDCl_3$): δ = 18.31 (3-CH_3), 19.11 ($CHCH_3$), 19.37 ($CHC'H_3$), 21.46 (p-CH_3), 24.51 (C-6), 26.06 (C-7), 32.00 [$(CH_3)_2CH$], 40.06 (C-8), 51.70 (C-5), 62.81 (SCH), 63.83 (NCH), 64.40 (OCH_2), 77.96 (C-4), 78.80 (C-3), 86.76 (C-1), 128.96 (o-C), 129.52 (m-C), 137.69 (i-C), 143.32 (p-C). − $C_{21}H_{33}NO_4S$ (395.55): calcd. C 63.77, H 8.41, N 3.54; found C 63.53, H 8.37, N 3.28.

Bicyclic Compound 39: From 208 mg (0.477 mmol) of sulfoximine **24** and 180 mg (0.955 mmol) of aldehyde **35**, 52 mg (28%) of **39** was isolated as a colourless liquid. − R_f = 0.16 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = −19.30 (c = 0.86, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 3445 cm^{-1} (OH), 1229, 1126 (N=S=O). − ^{1}H NMR (400 MHz, 300K, $CDCl_3$): δ = 0.81 [d, J(3,3-CH_3) = 6.3 Hz, 3-CH_3], 0.94 [d, J(CH,CH_3) = 6.8 Hz, $CHCH_3$], 0.97 [d, J(CH,CH'_3) = 6.7 Hz, $CHCH'_3$], 1.47−2.17 [m; 6-H_2, 7-H_2, 8-H_2, $(CH_3)_2CH$], 2.43 (s, p-CH_3), 2.56 (pseudo t, 5-H), 3.02 (ddd, NCH), 3.36−3.60 (m; SCH_2, 3-H, 4-OH, CH_2OH, OCH_2), 3.91 (dd, 4-H), 7.32 (d, m-H_2), 7.82 (d, o-H_2). − ^{13}C NMR (100 MHz, 300K, $CDCl_3$): δ = 12.91 (3-CH_3), 19.11 ($CHCH_3$), 19.45 ($CHC'H_3$), 21.45 (p-CH_3), 25.72 (C-6), 27.46 (C-7), 32.00 [$(CH_3)_2CH$], 37.94 (C-8), 55.62 (C-5), 60.12 (SCH), 62.87 (NCH), 64.51 (OCH_2), 75.44 (C-4), 77.67 (C-3), 91.53 (C-1), 129.01 (o-C), 129.46 (m-C), 137.42 (i-C), 143.25 (p-C). − $C_{21}H_{33}NO_4S$ (395.55): calcd. C 63.77, H 8.41, N 3.54; found C 63.82, H 8.35, N 3.24.

Bicyclic Compound 40: From 307 mg (0.68 mmol) of sulfoximine **25** and 257 mg (1.36 mmol) of aldehyde *ent*-**35**, 50 mg (18%) of **40** was isolated as a colourless solid, m.p. 106.2°C. − R_f = 0.37 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = 78.92 (c = 0.62, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3346 cm^{-1} (OH), 1218, 1069 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.89 [pseudo t; J(CH,CH_3) = 6.8 Hz, J(CH,CH'_3) = 6.9 Hz; $CHCH_3$, $CHCH'_3$], 1.09 [d, J(3,3-CH_3) = 6.5 Hz, 3-CH_3], 1.21−2.17 [m; 6-H_2, 7-H_2, 8-H_2, 9-H_2, $(CH_3)_2CH$, 4-OH], 2.43 (s, p-CH_3), 2.66 (ddd, $J_{4,5}$ = 7.1 Hz, 5-H), 2.73 (ddd, NCH), 3.42 (d, $J_{SCH,SCH'}$ = 14.7 Hz, SCH), 3.51 (m; OCH_2, CH_2OH), 3.56 (d, $J_{SCH,SCH'}$ = 14.7 Hz, SCH′), 3.94 [dq; J(3,3-CH_3) = 6.5 Hz, $J_{3,4}$ = 3.4 Hz; 3-H], 4.19 (ddd; $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ = 7.1 Hz; 4-H), 7.32 (d, m-H_2), 7.73 (d, o-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = 14.95 (3-CH_3), 15.24, 21.38, 22.30 (C-7 or C-8 or C-9), 18.95 ($CHCH_3$), 19.67 ($CHC'H_3$), 21.38 (p-CH_3), 32.19 [$(CH_3)_2CH$], 35.75 (C-6), 45.79 (C-5), 63.07 (SCH), 63.90 (NCH), 65.46 (OCH_2), 65.82 (C-1), 76.35 (C-3), 81.07 (C-4), 129.00 (o-C), 129.66 (m-C), 136.99 (i-C), 143.22 (p-C). − $C_{22}H_{35}NO_4S$ (409.58): calcd. C 64.52, H 8.61, N 3.42; found C 64.55, H 8.35, N 3.18.

Bicyclic Compound 41: From 217 mg (0.482 mmol) of sulfoximine **25** and 182 mg (0.965 mmol) of aldehyde **35**, 85 mg (43%) of **41** was isolated as a colourless solid, m.p. 47.6°C. − R_f = 0.37 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = 90.21 (c = 0.47, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3385 (OH), 1250, 1073 (N=S=O) cm^{-1}. − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.89 [pseudo t; J(CH,CH_3) = 6.8 Hz, J(CH,CH'_3) = 6.7 Hz; $CHCH_3$, $CHCH'_3$], 1.13 [d, J(3,3-CH_3) = 6.2 Hz, 3-CH_3], 1.26−1.76 [m; 6-H_2, 8-H_2, 9-H_2, $(CH_3)_2CH$], 2.10 (m, 7-H_2), 2.43 (s, p-CH_3), 2.69 (ddd, NCH), 2.76 (ddd, $J_{4,5}$ = 6.4 Hz, 5-H), 3.28 (d, $J_{SCH,SCH'}$ = 14.5 Hz, SCH), 3.45 (m; 4-OH, OCH_2, CH_2OH), 3.62 (d, $J_{SCH,SCH'}$ = 14.5 Hz, SCH′), 3.91 [dq; J(3,3-CH_3) = 6.2 Hz, $J_{3,4}$ = 3.6 Hz; 3-H], 4.21 (pseudo t; $J_{3,4}$ = 3.6 Hz, $J_{4,5}$ = 6.4 Hz; 4-H), 7.32 (d, m-H_2), 7.70 (d, o-H_2). −^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = 18.83 ($CHCH_3$), 19.84 (3-CH_3), 20.12 ($CHC'H_3$), 21.47 (p-CH_3), 22.49, 22.66, 22.78 (C-6 or C-8 or C-9), 32.09 [$(CH_3)_2CH$], 33.45 (C-7), 44.24 (C-5), 63.99 (NCH), 65.27 (SCH), 65.59 (OCH_2), 78.82 (C-3), 79.72 (C-4), 82.32 (C-1), 129.04 (o-C), 129.78 (m-C), 136.67 (i-C), 143.42 (p-C). − $C_{22}H_{35}NO_4S$ (409.58): calcd. C 64.52, H 8.61, N 3.42; found C 64.41, H 8.51, N 3.40.

Bicyclic Compound 42: From 268 mg (0.596 mmol) of sulfoximine **24** and 244 mg (1.192 mmol) of aldehyde *ent*-**35**, 175 mg (72%) of **42** was isolated as a colourless solid, m.p. 53.9°C. − R_f = 0.25 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = −62.20 (c = 0.82, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 3409 cm^{-1} (OH), 1260, 1078 (N=S=O). − ^{1}H

NMR (400 MHz, 300 K, CDCl$_3$): δ = 0.94 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$], 0.97 [d, *J*(CH,CH$'_3$) = 6.9 Hz, CHC*H*$_3$'], 1.08 (d, $J_{3,3'}$ = 6.3 Hz, 3'-H$_3$), 1.11−1.20 [m; 6-H$_2$, 7-H$_2$, 8-H$_2$, 9-H$_2$, (CH$_3$)$_2$C*H*, 4-OH], 2.43 (s, *p*-CH$_3$), 2.65 (ddd, $J_{4,5}$ = 4.8 Hz, 5-H), 2.75 (br. s, CH$_2$O*H*), 2.99 (ddd, NCH), 3.15 (d, $J_{\mathrm{SCH,SCH'}}$ = 14.6 Hz, SCH), 3.47 (m, OCH$_2$), 3.67 (d, $J_{\mathrm{SCH,SCH'}}$ = 14.6 Hz, SCH'), 3.89 [dq; *J*(3,3-CH$_3$) = 6.3 Hz, $J_{3,4}$ = 3.2 Hz; 3-H), 4.17 (pseudo t, $J_{4,5}$ = 4.8 Hz, 4-H), 7.35 (d, *m*-H$_2$), 7.78 (d, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = 19.03 (CHC*H*$_3$), 19.34 (CHC*H'*$_3$), 20.08 (3-CH$_3$), 21.45 (*p*-CH$_3$), 21.47, 22.49, 22.75 (C-6 or C-8 or C-9), 31.99 [(CH$_3$)$_2$CH], 33.18 (C-7), 44.24 (C-5), 62.60 (NCH), 63.78 (SCH), 64.24 (OCH$_2$), 78.73 (C-3), 79.81 (C-4), 82.25 (C-1), 128.82 (*o*-C), 129.69 (*m*-C), 138.01 (*i*-C), 143.44 (*p*-C). − C$_{22}$H$_{35}$NO$_4$S (409.58): calcd. C 64.52, H 8.61, N 3.42; found C 64.25, H 8.52, N 3.28.

Bicyclic Compound 43: From 151 mg (0.336 mmol) of sulfoximine **26** and 127 mg (0.672 mmol) of aldehyde **35**, 99 mg (72%) of **43** was isolated as a colourless solid, m.p. 50.5°C. − R_f = 0.25 (ethyl acetate/hexane, 10:1). − $[\alpha]_D^{20}$ = −18.27 (*c* = 0.87, CH$_2$Cl$_2$). − IR (KBr): ṽ = 3406 (OH), 1231, 1120 (N=S=O) cm^{-1}. − ^{1}H NMR (400 MHz, 300 K, CDCl$_3$): δ = 0.93 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.95 [d, *J*(CH,CH$'_3$) = 6.9 Hz, CHC*H'*$_3$], 1.07 [d, *J*(3,3-CH$_3$) = 6.4 Hz, 3-CH$_3$], 1.10−2.07 [m; 6-H$_2$, 7-H$_2$, 8-H$_2$, 9-H$_2$, (CH$_3$)$_2$C*H*, 4-OH, CH$_2$O*H*], 2.43 (s, *p*-CH$_3$), 2.61 (dt, $J_{4,5}$ = 4.6 Hz, 5-H), 3.05 (ddd, NCH), 3.36 (d, $J_{\mathrm{SCH,SCH'}}$ = 14.6 Hz, SCH), 3.48 (m, OCH$_2$), 3.60 (d, $J_{\mathrm{SCH,SCH'}}$ = 14.6 Hz, SCH'), 3.90 [dq; *J*(3,3-CH$_3$) = 6.4 Hz, $J_{3,4}$ = 3.2 Hz; 3-H], 4.15 (t; $J_{3,4}$ = 3.2 Hz, $J_{4,5}$ = 4.6 Hz; 4-H), 7.32 (d, *m*-H$_2$), 7.81 (d, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = 14.92 (3-CH$_3$), 19.06 (CH*C*H$_3$), 19.26 (CH*C'*H$_3$), 21.42 (*p*-CH$_3$), 21.46, 22.30, 22.35 (C-6 or C-8 or C-9), 32.01 [(CH$_3$)$_2$*C*H], 35.73 (C-7), 45.84 (C-5), 62.00 (SCH), 62.75 (NCH), 64.32 (OCH$_2$), 76.33 (C-3), 77.11 (C-4), 80.99 (C-1), 128.79 (*o*-C), 129.60 (*m*-C), 137.81 (*i*-C), 143.23 (*p*-C). − C$_{22}$H$_{35}$NO$_4$S (409.58): calcd. C 64.52, H 8.61, N 3.42; found C 64.32, H 8.61, N 3.19.

γ-Hydroxyalkylation Adduct 44: Following GP1 we employed 1.098 g (2.520 mmol) of **23**, 1.249 g (2.772 mmol) of *n*BuLi (2.22 mmol/g in hexane), 3.78 mL (3.780 mmol) of ClTIPT (1.0 M in hexane) and 513 mg (5.040 mmol) of **45** to obtain 1.066 g (79%, *ds* = 95%) of **44** as a colourless solid, m.p. 96.5°C, after chromatographic purification (eluent: ether/hexane = 1:7). − R_f = 0.13 (ether/hexane, 1:2). − $[\alpha]_D^{20}$ = −50.30 (*c* = 1.10, CH$_2$Cl$_2$). − IR (KBr): ṽ = 3160 cm^{-1} (OH), 1230, 1110 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, CDCl$_3$): δ = 0.05, 0.06 [2 × s, Si(CH$_3$)$_2$], 0.79, 0.90 [2 × d, CH(C*H*$_3$)$_2$], 0.88 [s, SiC(C*H*$_3$)$_3$], 1.33 (t, $J_{4',5'}$ = 7.1 Hz, 5'-H$_3$), 1.63−1.89 [m; 3-H$_2$, 4-H$_2$, C*H*(CH$_3$)$_2$], 2.38, 2.66 (2 × m, 5-H$_2$), 2.42 (s, *p*-CH$_3$), 3.03 (ddd, NCH), 3.72 (dd, OCH$_2$), 3.97 (m; 2-H, 1'-H), 4.25 (q, $J_{4',5'}$ = 7.1 Hz, 4'-H$_2$), 6.29 (br. s, 1'-OH), 6.45 (s, SCH), 7.27 (d, *m*-H$_2$), 7.84 (d, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −5.33, −5.21 [Si(CH$_3$)$_2$], 14.25 (C-5'), 17.20 [CH(*C*H$_3$)(CH$_3$)], 18.45 [Si*C*(CH$_3$)$_3$], 20.30 [CH(CH$_3$)(*C*H$_3$)], 21.15 (C-3), 21.49 (*p*-CH$_3$), 25.99 [SiC(*C*H$_3$)$_3$], 28.77 (C-4), 29.74 [*C*H(CH$_3$)$_2$], 33.63 (C-5), 45.46 (C-2), 60.96 (C-4'), 62.01 (NCH), 66.51 (OCH$_2$), 72.96 (C-1'), 126.40 (SCH), 128.72 (*o*-C), 129.52 (*m*-C), 138.41 (*i*-C), 143.24 (*p*-C), 160.79 (C-1), 172.68 (C-2'). − C$_{28}$H$_{47}$NO$_5$SSi (537.82): calcd. C 62.53, H 8.81, N 2.61; found C 62.80, H 8.87, N 2.47.

Sulfoximine 49: According to our previously published procedure,[7] we obtained 2.746 g (83%) of **49** from 1.622 g (6.769 mmol) of **52**, 3.943 g (13.538 mmol) of **51** and 1.530 g (10.154 mmol) of *tert*-butyldimethylsilyl chloride as a colourless solid, m.p. 42.3°C. − R_f = 0.47 (ether/hexane, 1:3). − $[\alpha]_D^{20}$ = 3.20 (*c* = 0.50, CH$_2$Cl$_2$). − IR (KBr): ṽ = 1252 cm^{-1}, 1130 (N=S=O). − ^{1}H NMR (400 MHz, 300K, CDCl$_3$): δ = −0.01, 0.00 [2 × s, Si(CH$_3$)$_2$], 0.80, 0.88 (2 × s; 6-CH$_3$, 6-CH$'_3$), 0.88 [s, SiC(C*H*$_3$)$_3$], 0.93, 1.014 [2 × d; *J*(CH,CH$_3$) = 6.8 Hz, *J*(CH,CH$'_3$) = 6.9 Hz; (C*H*$_3$)$_2$], 1.13 (d, 7-H), 2.03 [m, C*H*(CH$_3$)$_2$], 2.14−2.44 (m; 1-H, 4-H$_2$, 5-H, 7-H'), 2.46 (s, *p*-CH$_3$), 3.09 (ddd, $J_{\mathrm{NCH,CH}}$ = 5.3 Hz, NCH), 3.52 (m, OCH$_2$), 3.77, 3.95 (2 × d, $J_{\mathrm{SCH,SCH'}}$ = 13.5 Hz. SCH$_2$), 5.15 (m, 3-H), 7.31 (d, *m*-H$_2$), 7.79 (d, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −5.44, −5.35 [Si(CH$_3$)$_2$], 16.50, 20.13 (6-CH$_3$, 6-C'H$_3$), 17.68, 20.33 [CH(*C*H$_3$)$_2$], 18.66 (C-6), 21.46 (*p*-CH$_3$), 20.97, 31.81, 37.78, 39.92 (C-1 or C-4 or C-5 or C-7), 25.97 [SiC(*C*H$_3$)$_3$], 26.50 [Si*C*(CH$_3$)$_3$], 29.64 [*C*H(CH$_3$)$_2$], 61.07 (SCH), 63.85 (NCH), 65.69 (OCH$_2$), 127.52 (C-3), 129.16 (*o*-C), 129.57 (*m*-C), 136.33 (C-2), 136.93 (*i*-C), 142.91 (*p*-C). − C$_{28}$H$_{47}$NO$_2$SSi (489.83): calcd. C 68.66, H 9.67, N 2.86; found C 68.70, H 9.78, N 2.93.

Selenide 51: According to our previously published procedure[7] we converted 12.0 g (55.78 mmol) of (−)-(1*R*,5*S*)-myrthenyl bromide[45] to 13.03 g (80%) of **51**. Purification was achieved by distillation in vacuo [yellowish liquid, b.p. 153−155°C (0.1 Torr)]. − R_f = 0.63 (ether/hexane, 1:3). − $[\alpha]_D^{20}$ = 5.22 (*c* = 1.91, CH$_2$Cl$_2$). − IR (film): ṽ = 1579 cm^{-1} (C=C aromatic). − ^{1}H NMR (270 MHz, 300 K, CDCl$_3$): δ = 0.79, 1.27 (2 × s; 6-CH$_3$, 6-CH$'_3$), 1.08 (d, 7-H), 1.20−2.24 (m; 1-H, 5-H, 4-H$_2$), 2.37 (m, 7-H'), 3.53 (m, SeCH$_2$), 5.33 (t, 3-H), 7.23 (m; *m*-H$_2$, *p*-H), 7.47 (m, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = 21.22, 26.13, 31.25, 31.65, 34.87, 38.04, 40.35, 45.71 (C-1 or C-4 or C-5 or C-6 or 6-CH$_3$ or 6-C'H$_3$ or C-7 or C-8), 119.93, 126.60, 128.74, 131.02, 132.75, 143.69 (C-2 or C-3 or *i*-C or *o*-C or *m*-C or *p*-C). − C$_{16}$H$_{20}$Se (291.29): calcd. C 65.97, H 6.92; found C 65.74, H 7.05.

2,4-Di-(*tert*-butyldimethylsilyloxy)-6-hydroxybenzaldehyde (53): 5.00 g (32.43 mmol) of 2,4,6-trihydroxybenzaldehyde (**59**) was dissolved in 100 mL of dry CH$_2$Cl$_2$ and treated with 19.55 g (129.70 mmol) of TBSCl, 14.23 g (194.55 mmol) of ethyldimethylamine and 3.96 g (32.43 mmol) of DMAP at ambient temperature for 75 h. The reaction mixture was poured into 200 mL of ice/water, the organic layer was extracted (3 × 50 mL CH$_2$Cl$_2$), the combined organic layers were dried and concentrated in vacuo. The residue was purified by flash chromatography (eluent: ethyl acetate/hexane, 1:7) yielding 3.75 g (30%) of the product as an orange oil. − R_f = 0.75 (ethyl acetate/hexane, 1:3). − IR (film): ṽ = 3217 cm^{-1} (OH), 1639 (C=O). − ^{1}H NMR (270 MHz, 300 K, CDCl$_3$): δ = 0.25, 0.28 [2 × s, Si(CH$_3$)$_2$], 0.97, 1.00 [2 × s, SiC(CH$_3$)$_3$], 5.79 (s, 3-H), 5.99 (s, 5-H), 10.10 (s, CHO), 12.12 (s, 6-OH). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −4.43, −4.39 [Si(CH$_3$)$_2$], 18.17, 18.25 [Si*C*(CH$_3$)$_3$], 25.43, 25.55 [SiC(*C*H$_3$)$_3$], 101.23, 102.23 (C-3 or C-5), 109.00 (C-1), 160.67 (C-6), 164.70, 165.41 (C-2 or C-4), 192.34 (CHO). − C$_{19}$H$_{34}$O$_4$Si$_2$ (382.65): calcd. C 59.64, H 8.96; found C 59.59, H 8.93.

4-Hydroxyalkylation Adduct 55: The crude product **54** from the γ-hydroxyalkylation reaction (GP1), employing 503 mg (1.027 mmol) of sulfoximine **49** and 472 mg (1.232 mmol) of aldehyde **53**, was dissolved in CH$_2$Cl$_2$. 167 mg (1.541 mmol) of trimethylsilyl chloride and 150 mg (2.054 mmol) ethyldimethylamine were added. Following the usual workup we obtained 296 mg (31%, *ds* ≥ 98%) of **55** being a colourless solid, m.p. 54.8°C, after chromatographic purification (eluent: ether/hexane, 1:12). − R_f = 0.43 (ether/hexane, 1:5). − $[\alpha]_D^{20}$ = 75.12 (*c* = 0.62, CH$_2$Cl$_2$). − IR (KBr): ṽ = 3376 cm^{-1} (OH), 1253, 1102 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, CDCl$_3$): δ = −0.11, −0.10, −0.07, 0.19, 0.25, 0.27 [6 × s; 3 × Si(CH$_3$)$_2$], 0.04 [s, Si(CH$_3$)$_3$], 0.82, 0.96 [2 × s, SiC(CH$_3$)$_3$], 0.83 (s, 6-CH$_3$), 0.90, 0.99 [2 × d, CH(C*H*$_3$)$_2$], 1.13 (s, 6-CH$'_3$), 1.29−2.35 [m; 1-H, 4-H$_2$, 5-H, 7-H, C*H*(CH$_3$)$_2$], 2.44 (s, *p*-CH$_3$), 2.45 (pseudo t; $J_{1,7\text{-H}}$ = 5.3 Hz, $J_{5,7}$ = 5.2 Hz, 5.1 Hz, $J_{7\text{-H},7\text{-H}'}$ = 5.2 Hz; 7-H′), 2.98 (ddd, NCH), 3.44, 3.55 (2 × d, OCH_2), 3.74 (pseudo t; $J_{1',3}$ = 9.7 Hz, $J_{3,4}$ = 9.1 Hz; 3-H), 5.24 (d, $J_{1',3}$ = 9.7 Hz, 1′-H), 5.85, 6.13 (2 × s; 4′-H, 6′-H), 6.31 (s, SCH), 7.20 (d, *m*-H_2), 7.85 (d, *o*-H_2), 8.71 (s, 7′-OH). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −5.48, −5.38, −4.44, −3.81, −0.07, 17.04, 18.18, 18.28, 19.83, 20.60, 24.86, 25.10, 21.31, 25.63, 25.96, 26.05, 27.36, 27.88, 29.90, 37.78, 40.91, 46.03, 54.08, 60.51, 65.58, 70.85, 101.13, 102.79, 106.65, 124.85, 127.72, 129.19, 136.48, 141.06, 142.03, 155.92, 160.26. − $C_{50}H_{89}NO_6SSi_4$ (944.66): calcd. C 63.57, H 9.50, N 1.48; found C 63.50, H 9.42, N 1.26.

Tetracyclic Compound 56: The crude product **54** from the γ-hydroxyalkylation (GP1, reaction time 90 min), employing 527 mg (1.076 mmol) of sulfoximine **49** and 618 mg (1.614 mmol) of aldehyde **53**, was dissolved in 3 mL of dry methanol and 91 mg (1.61 mmol) of KOH was added. After stirring at ambient temp. for 18 h, the reaction was quenched by addition of 10 mL of water and 10 mL of ether. The aqueous layer was extracted with ether (3 × 10 mL), the combined extracts were dried and concentrated in vacuo. Purification was achieved by flash chromatography (eluent: ethyl acetate/hexane, 1:10) yielding 50 mg (5%) of **56** as a colourless solid, besides 248 mg of reisolated compound **49**. − R_f = 0.25 (ethyl acetate/hexane, 1:3). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.06, 0.04, 0.12, 0.13 [4 × s, 3 × $Si(CH_3)_2$], 0.86, 0.91 [2 × d, $CH(CH_3)_3$], 0.83, 0.91, 0.93 [3 × s, 3 × $SiC(CH_3)_3$], 1.07, 1.26 (2 × s; 10-CH_3, 10-CH'_3), 1.75 (m, 8-H), 1.80−1.99 [m; 1-H, 11-H, 9-H, 8′-H, $CH(CH_3)_3$], 2.37 (s, *p*-CH_3), 2.73 (pseudo t; $J_{11\text{-H},11\text{-H}'}$ = 5.6 Hz, $J_{11\text{-H}',9}$ = 5.6 Hz; 11-H′), 2.99 (m, 7-H, NCH), 3.47 (dd; $J_{\text{NCH, OCH}}$ = 6.4 Hz, $J_{\text{OCH, OCH}'}$ = 10.2 Hz; OCH), 3.56 (m; SCH_2, OCH′), 5.47, 5.91 [2 × d; J(4-CH,5-C($OSiR_3$)CH) = 2.2 Hz; 4-CH, 5-C($OSiR_3$)C*H*], 5.55 (d, $J_{6,7}$ = 5.7 Hz, 6-H), 7.22 (d, *m*-H_2), 7.77 (d, *o*-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ −5.37, −4.54, 17.65, 18.15, 18.41,19.06, 21.45, 22.59, 25.44, 25.64, 25.96, 27.32, 28.23, 30.78, 37.27, 39.35, 39.89, 40.44, 52.23, 61.52, 65.52, 66.32, 69.02, 83.49, 100.39, 101.51, 102.46, 106.91, 124.96, 129.26, 129.33, 135.70, 137.74, 142.95, 155.91, 156.22, 157.53, 172.22. − $C_{47}H_{81}NO_6SSi_3$ (872.48): calcd. C 64.70, H 9.36, N 1.61; found C 64.60, H 9.07, N 1.45.

Aldehyde 60a:[47] 5.00 g (41.20 mmol) of isovaleryl chloride was added dropwise to an ice-cold solution of 5.50 g (41.20 mmol) of $AlCl_3$ in 40 mL of dry CH_2Cl_2 within 15 min. The reaction mixture was stirred for another 30 min at which point a solution of 5.00 g (27.40 mmol) of 2,4-dimethoxy-6-hydroxybenzaldehyde in 30 mL of dry CH_2Cl_2 was added at once. After stirring for 20 h at ambient temp., the reaction was quenched by pouring the mixture into 50 mL of ice/water. After 30 min of rapid stirring, the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL), the organic layers were dried and concentrated in vacuo. Purification by flash chromatography (ethyl acetate/hexane, 1:3) yielded 5.80 g (80%) of the product **60a** as a colourless solid (melting point 91.0°C). − R_f = 0.27 (ethyl acetate/hexane, 1:1). − IR (KBr): ṽ = 3450 cm^{-1}(OH), 1694 (C=O, ketone), 1633 (C=O, aldehyde). − ^1H NMR (270 MHz, 300 K, $CDCl_3$): δ = 0.96 [d; 3-$COCH_2CH(CH_3)_2$], 2.21 [m, 3-$COCH_2CH$], 2.70 (d, 3-$COCH_2$), 3.91, 3.94 (2 × s; 6-OCH_3, 4-OCH_3), 5.94 (s, 5-H), 10.16 (s, CHO), 12.98 (br. s, 2-OH). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = 22.70 [3-$COCH_2CH(CH_3)_2$], 25.00 [3-$COCH_2CH$], 53.80 (3-$COCH_2$), 55.90 (6-OCH_3, 4-OCH_3), 86.00 (C-5), 105.90 (C-1), 111.40 (C-3), 163.30 (C-2), 165.30 (C-4, C-6), 191.50 (CHO), 202.60 (3-CO). − $C_{14}H_{18}O_5$ (266.30): calcd. C 63.15, H 6.81; found C 63.25, H 6.79.

Aldehyde 60b: 1.671 g (11.085 mmol) of TBSCl, 1.70 mL (14.780 mmol) of ethyldimethylamine and 271 mg (2.217 mmol) of DMAP were added to a solution of 1.968 g (7.390 mmol) of **60a** in 15 mL of dry CH_2Cl_2. Stirring was continued for 20 h at ambient temp. The solvent was evaporated in vacuo and the residue purified by flash chromatography (ethyl acetate/hexane, 1:5) yielding 2.138 g (76%) of **60b** as colourless solid of melting point 105.8°C. − R_f = 0.48 (ethyl acetate/hexane, 1:1). − IR (KBr): ṽ = 1678 (C=O) cm^{-1}. − ^1H NMR (270 MHz, 300 K, $CDCl_3$): δ = 0.00 [s, $Si(CH_3)_2$], 0.86 [d; 3-$COCH_2CH(CH_3)_2$], 0.90 [s, $SiC(CH_3)_3$], 2.02 (m, 3-$COCH_2CH$), 2.55 (d, 3-$COCH_2$), 3.77, 3.84 (2 × s; 4-OCH_3, 6-OCH_3), 6.06 (s, 5-H), 10.13 (s, 7-H). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −3.95 [$Si(CH_3)_2$], 18.31 [$SiC(CH_3)_3$], 22.55 [3-$COCH_2CH(CH_3)_2$], 24.57 (3-$COCH_2CH$), 25.86 [$SiC(CH_3)_3$], 53.98 (3-$COCH_2$), 55.73, 55.95 (4-OCH_3 or 6- OCH_3), 89.05 (C-5), 111.74, 117.46 (C-1 or C-3), 156.96 (C-2), 162.11, 163.34 (C-4 or C-6), 187.41 (CHO), 202.79 (4-CO). − $C_{20}H_{32}O_5Si$ (380.56): calcd. C 63.09, H 8.47; found C 62.89, H 8.42.

4-Hydroxyalkylation Adduct 62a: From 503 mg (1.027 mmol) of **49** and 547 mg (2.154 mmol) of **60a** we obtained 482 mg (62%, *ds* = 95%, GP1) of **62a** as a colourless solid after chromatographic purification (ether/hexane, 1:5), m.p. 140.3°C. − R_f = 0.25 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 71.18 (*c* = 0.85, CH_2Cl_2). − IR (KBr): ṽ = 3430 (OH), 1222, 1128 (N=S=O) cm^{-1}. − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = −0.034, −0.017 [$Si(CH_3)_2$], 0.23 (s, 6-CH_3), 0.85 [s, $SiC(CH_3)_3$], 1.00 [m; 4′-$COCH_2CH(CH_3)_2$, $CH(CH_3)_2$], 1.18 (s, 6-CH'_3), 1.45−2.33 [m; 4-H_2, 5-H, 7-H_2, 4′-$COCH_2CH$, $CH(CH_3)_2$], 2.42 (s, *p*-CH_3), 2.53 (pseudo t; $J_{1,7\text{-H}}$ = 5.3, $J_{1,7\text{-H}}$ = 5.4 Hz; 1-H), 2.88 (dd, 4′-$COCH_2$), 3.27 (ddd, NCH), 3.57 (dd, OCH_2), 3.91, 4.00 (2 × s; 5′-OCH_3, 7′-OCH_3), 4.31 (pseudo t; $J_{1',3}$ = 11.2 Hz, $J_{3,4}$ = 9.6 Hz; 3-H), 5.30 (d, $J_{1',3}$ = 11.2 Hz, 1′-H), 5.53 (br. s, 1′-OH), 6.01 (s, 6′-H), 6.12 (s, SCH), 7.29 (d, *m*-H_2), 7.94 (d, *o*-H_2), 14.26 (s, 3-OH). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −5.46, −5.35, 16.64, 17.98, 21.09, 22.61, 18.16, 18.30, 21.39, 25.25, 25.31, 25.39, 27.29, 29.54, 36.38, 40.78, 45.06, 53.34, 54.62, 55.29, 55.39, 60.58, 65.84, 69.89, 86.21, 105.81, 125.83, 162.14, 163.74, 164.39, 111.29, 128.60, 129.30, 140.52, 142.39, 162.50, 205.87. − $C_{42}H_{65}NO_7SSi$ (756.13): calcd. C 66.72, H 8.66, N 1.85; found C 66.58, H 8.63, N 1.87.

4-Hydroxyalkylation Adduct 62b: With 1.500 g (3.062 mmol) of **49** and 2.330 g (6.125 mmol) of **60b**, 1.753 g [66%, *ds* ≥ 98%, *GP1*)] of **62b** was obtained after chromatographic purification (ether/hexane, 1:5) as a colourless solid, m.p. 73.2°C. − R_f = 0.43 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 79.32 (*c* = 0.88, CH_2Cl_2). − IR (KBr): ṽ = 1702 cm^{-1} (C=O), 1258, 1119 (N=S=O). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = −0.06, −0.04 [2 × s, $CH_2OSi(CH_3)_2$], 0.07 (s, 6-CH_3), 0.23, 0.26 [2 × s, Ar-$OSi(CH_3)_2$], 0.83, 0.93 [2 × s, 2 × $SiC(CH_3)_3$], 0.87, 0.88 [2 × d; J(4′-$COCH_2CH$, 4′-$COCH_2CHCH_3$) = 6.7 Hz, J(4′-$COCH_2CH$,4′-$COCH_2CHCH'_3$) = 6.8 Hz; 4′-$COCH_2CH(CH_3)_2$], 0.95, 1.01 [2 × d, $CH(CH_3)_2$], 1.15 (s, 6-CH'_3), 1.32 (d, $J_{3,4\text{-H}}$ = 9.7 Hz, 4-H), 1.55 (d, $J_{3,4\text{-H}'}$ = 9.7 Hz, 4-H′), 1.74 (d, $J_{1,7}$ = 6.5 Hz, 1-H), 1.81 (d, $J_{5,7}$ = 6.6 Hz, 5-H), 1.97 [ddqq; J(4′-$COCH_2CH$, 4′-$COCH_2CHCH_3$) = 6.7, J(4′-$COCH_2CH$,4′-$COCH_2CHCH'_3$) = 6.8 Hz; 4′-$COCH_2CH$], 2.08 [dqq, $CH(CH_3)_2$], 2.26 (m, 7-H), 2.40 (s, *p*-CH_3), 2.46 (m; 4′-COC*H*H′, 7-H′), 2.66 (dd, 4′-COCH*H*′), 3.34 (ddd, NCH), 3.55 (dd, OCH_2), 3.80, 3.99 (2 × s; 5′-OCH_3, 7′-OCH_3), 4.23 (pseudo t; $J_{1',3}$ = 10.0 Hz, $J_{3,4}$ = 9.7 Hz; 3-H), 4.93 (dd; $J_{1',3}$ = 10.0 Hz, $J_{1',\text{OH}}$ = 10.5 Hz; 1′-H), 5.20 (d, $J_{1',\text{OH}}$ = 10.5 Hz, 1′-OH), 5.97 (s, SCH), 6.22 (s, 6′-H), 7.25 (d, *m*-H_2), 7.91 (d, *o*-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −5.47, −5.31, −4.26, −3.47, 16.48, 21.18, 22.56, 22.95, 18.29, 21.41, 25.38, 25.38, 25.77, 25.93, 25.98, 26.30, 27.84, 29.39, 36.94, 40.54, 54.45, 54.52, 55.29, 55.78, 60.62, 65.81, 70.90, 113.58, 125.72, 116.03, 116.94, 151.76, 156.74, 160.73, 128.54, 129.28, 140.66, 142.40, 162.03, 203.70. − $C_{48}H_{79}NO_7SSi$ (870.38): calcd. C 66.24, H 9.15, N 1.61; found C 66.41, H 9.14, N 1.52.

4-Hydroxyalkylation Adduct 62c: 367 mg (1.389 mmol) of TBS triflate and 202 mg (1.852 mmol) of 2,6-lutidine were added to an ice-cold solution of 700 mg (0.926 mmol) of **62a** in 4 mL of dry CH_2Cl_2 by hypodermic syringe. After 3.5 h, the reaction mixture was poured into 20 mL of ice/water, the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), the combined organic layers were dried and concentrated in vacuo. Purification by flash chromatography (eluent: ether/hexane, 1:6) of the oily residue yielded 223 mg (28%) of **62c** being a colourles solid, m.p. 69.3°C. − R_f = 0.34 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 112.90 (*c* = 0.62, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1696 cm^{-1}(C=O), 1251, 1114 (N=S=O). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = −0.13, −0.11, −0.09, −0.03 [4 × s, 2 × $Si(CH_3)_2$], 0.12 (s, 6-CH_3), 0.80, 0.85 [2 × s, 2 × $SiC(CH_3)_3$], 0.98 [m; 4′-$COCH_2CH(CH_3)_2$, $CH(CH_3)_2$], 1.13 (s, 6-CH'_3), 1.22 (m, 4-H_2), 1.55−2.24 [m; 5-H, 7-H_2, 4′-$COCH_2CH$, $CH(CH_3)_2$], 2.35 (s, *p*-CH_3), 2.43 (pseudo t; $J_{1,7}$ = 5.2, $J_{1,7}$ = 5.3 Hz; 1-H), 2.70, 2.82 (2 × dd, 4′-$COCH_2$), 2.98 (ddd, NCH), 3.38 (dd, OCH_2), 3.50 (m; 3-H, OCH_2), 3.78, 3.79 (2 × s; 5′-OCH_3 or 7′-OCH_3), 5.60 (d, $J_{1',3}$ = 9.6 Hz, 1′-H), 5.95 (s, 6′-H), 6.32 (s, SCH), 7.19 (d, *m*-H_2), 7.83 (d, *o*-H_2), 9.24 (s, 3′-OH). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −5.47, −5.38, −5.28, −4.34, 16.97, 18.43, 19.64, 21.12, 18.33, 21.41, 22.76, 22.96, 25.09, 25.26, 25.89, 25.98, 26.14, 26.87, 29.86, 38.84, 40.55, 46.69, 54.02, 54.10, 55.60, 59.92, 65.26, 71.86, 86.29, 109.20, 127.93, 155.99, 157.59, 158.15, 113.62, 128.65, 129.72, 141.10, 142.29, 160.73, 205.38. − $C_{48}H_{79}NO_7SSi_2$ (870.38): calcd. C 66.24, H 9.15, N 1.61; found C 66.32, H 9.30, N 1.65.

Carbamate 62e: 300 mg (0.345 mmol) of **62b** was dissolved in 3 mL of dry THF and treated with 30 μL (0.379 mmol) of ethyl isocyanate and 38 mg (0.379 mmol) of CuCl. After being stirred for 24 h at ambient temp., the greenish suspension was diluted with 10 mL of ether and poured into 10 mL of water. The aqueous layer was extracted with ether (3 × 20 mL), the combined organic layers were dried and concentrated in vacuo. Purification by flash chromatography (eluent: ether/hexane, 1:5) yielded 108 mg (33%) of **62e** as a colourless solid, m.p. 53.6°C. − R_f = 0.45 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 57.30 (*c* = 0.86, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3430 cm^{-1} (NH), 1717 (C=O, carbamate), 1258, 1118 (N=S=O), 830 (SiO). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = −0.01, 0.02, 0.10, 0.15 [4 × s, 2 × $Si(CH_3)_2$], 0.82, −1.43 [m; 6-CH_3, 6-CH_3', 4′-$COCH_2CH(CH_3)_2$, 1′-$OC(O)NHCH_2CH_3$, $CH(CH_3)_2$, 2 × $SiC(CH_3)_3$], 1.49 (dd, $J_{3,4}$ = 9.2 Hz, 4-H_2), 1.90 (m; 5-H, 4′-$COCH_2CH$), 1.92 [m; 7-H, $CH(CH_3)_2$], 2.05−2.48 (m; 1-H, 7-H′, 4′-COC*H*H′, *p*-CH_3), 2.74 [dd; *J*(4′-COCH′*H*,4′-COCH*H*′) = 8.4 Hz, *J*(4′-COCH*H*′,4′-$COCH_2CH$) = 6.2 Hz; 4′-COCH*H*′], 3.04 [m, 1′-OC(O)NHC*H*H′], 3.19 [m, 1′-OC(O)NHCH*H*′], 3.32 (m, NCH), 3.61 (dd, OCH), 3.79 (m; 5′-OCH_3, OCH′), 4.00 (s, 7′-OCH_3), 4.57 (pseudo t; $J_{1',3}$ = 9.4 Hz, $J_{3,4}$ = 9.2 Hz; 3-H), 5.70 (s, 6′-H), 6.23 (s, SCH), 6.25 (d, $J_{1',3}$ = 9.4 Hz, 1′-H), 6.67 (br. s, 1′-OC(O)N*H*], 7.22 (d, *m*-H_2), 7.84 (d, *o*-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −5.49, −5.36, −3.69, −2.86, 15.37, 16.62, 18.34, 19.95, 21.40, 22.51, 22.93, 25.34, 25.63, 25.82, 26.09, 26.53, 25.90, 26.62, 29.76, 35.51, 35.62, 40.78, 46.09, 54.34, 55.60, 55.73, 61.07, 65.78, 72.38, 90.50, 112.02, 116.12, 125.09, 128.98, 129.25, 140.24, 142.26, 153.30, 157.44, 157.55, 162.10, 169.00, 203.40. − $C_{48}H_{79}NO_7SSi$ (870.38): calcd. C 66.24, H 9.15, N 1.61; found C 66.41, H 9.14, N 1.52.

Desulfuration of 62b by Aluminium Amalgam. − Alkene 69 and Sulfone 71: 336 mg (0.386 mmol) of **62b** was dissolved in a mixture of 6 mL of dry THF and 1 mL of water. Aluminium amalgam [freshly prepared from 760 mg (28.120 mmol) of aluminium shot] was added to this solution and the reaction was monitored by TLC. After 15 h, the excess amalgam was separated by filtration. The filtrate was concentrated in vacuo and the residue was taken up in 10 mL of ether/water, 1:1. The aqueous layer was extracted with ether (3 × 10 mL), the combined organic phases were dried and concentrated in vacuo. The oily product was purified by flash chromatography yielding 42 mg (21%) of **69** and 85 mg (40%) of **71**, both being colourless solids having m.p. 127.5°C and 67−69°C, respectively. − **69**: R_f = 0.27 (ethyl acetate/hexane, 5:3). − $[\alpha]_D^{20}$ = −31.33 (*c* = 0.30, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 3360 cm^{-1} (OH), 1710 (C=O). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.07, 0.21 [2 × s, $Si(CH_3)_2$], 0.72 (s, 6-CH_3), 0.89, 0.90 [2 × d; 4′-$COCH_2CH(CH_3)_2$], 0.96 [s, $SiC(CH_3)_3$], 1.24 (s, 6-CH'_3), 1.36−1.72 (m; 1-H, 4-H_2,), 1.92 (ddd, 5-H), 2.01 [ddqq; *J*(4′-COCH′*H*,4′-$COCH_2CH$) = 6.6, *J*(4′-COCH*H*′,4′-$COCH_2CH$ = 6.7 Hz, 4′-$COCH_2CH$], 2.31 (m, 7-H), 2.50 (m; 7-H′, 4′-COC*H*H′), 2.69 [dd; *J*(4′-COCH*H*′,4′-$COCH_2CH$) = 6.7, *J*(4′-COCH′*H*,4′-COCH′*H*) = 6.6 Hz; 4′-COCH*H*′], 2.98 (pseudo t; $J_{1',3}$ = 9.6 Hz, $J_{3,4}$ = 7.6 Hz; 3-H), 3.16 (d, $J_{1',OH}$ = 9.5 Hz, 1′-OH), 3.79, 3.92 (2 × s; 5′-OCH_3, 7′-OCH_3), 4.71 (pseudo t; $J_{1',OH}$ = 9.5 Hz, $J_{1',3}$ = 9.6 Hz; 1′-H), 4.87 (s, 2-C*H*H′), 4.97 (s, 2-CH*H*′), 6.21 (s, 6′-H). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −3.93 [$Si(CH_3)_2$], 18.24 (C-6), 21.74 (6-CH_3), 22.60, 22.89 [4′-$COCH_2CH(CH_3)_2$], 25.23 (4′-$COCH_2CH$), 25.77 [$SiC(CH_3)_3$], 26.14 [$SiC(CH_3)_3$], 26.89 (C-1), 27.51 (C-4), 29.69 (6-$C'H_3$), 40.65 (C-5), 41.11 (C-3), 52.38 (C-7), 54.23 (4′-$COCH_2$), 55.57, 55.80 (5′-OCH_3 or 7′-OCH_3), 72.09 (C-1′), 90.42 (C-6′), 111.09 (2-CH_2), 116.03 (C-2′), 151.21, 152.29 (C-2 or C4′), 156.66, 160.06, 160.13 (C-3′ or C-4′ or C-5′ or C-7′), 203.74 (CHO). − $C_{30}H_{48}O_5Si$ (516.79): calcd. C 69.72, H 9.36; found C 69.45, H 9.40. − **71**: R_f = 0.18 (ethyl acetate/hexane, 1:3). − $[\alpha]_D^{20}$ = 70.41 (*c* = 0.85, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1707 cm^{-1} (C=O), 1333, 1152 (O=S=O). − ^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.13, 0.20 [2 × s, $Si(CH_3)_2$], 0.92 {pseudo t; *J*[3′-$COCH_2CH$,3′-$COCH_2CH(CH_3)_2$] = 7.1, 7.3 Hz; 3′-$COCH_2CH(CH_3)_2$}, 1.02 [s, $SiC(CH_3)_3$], 1.09 (s, 9-CH_3), 1.10 (dd; $J_{8,10}$ = 11.7 Hz, $J_{10\text{-}H,1}$ = 5.4; 10-H), 1.37 (s, 9-CH'_3), 1.76 (m, 7-H), 2.10 [ddqq; *J*(3′-COCH′*H*,3′-$COCH_2CH$) = 6.0, *J*(3′-COCH*H*′,3′-$COCH_2CH$) = 7.3 Hz, *J*(3′-$COCH_2CH$,3′-$COCH_2CHCH_3$) = 7.1, *J*(3′-$COCH_2CH$,3′-$COCH_2CHCH'_3$) = 7.3 Hz; 4′-$COCH_2CH$], 2.21 (m; 7-H′, 8-H), 2.58 [dd; *J*(3′-COCH′*H*,3′-COCH*H*′) = 10.8 Hz, *J*(3′-COCH′*H*,3′-$COCH_2CH$) = 6.0; 3′-COC*H*H′], 2.68 [dd; *J*(3′-COCH′*H*,3′-COCH*H*′) = 10.8 Hz, *J*(3′-COCH*H*′,3′-$COCH_2CH$) = 7.3 Hz; 3′-COCH*H*′), 2.79 (m, 10-H′), 2.92 (pseudo t; $J_{10\text{-}H,1}$ = 5.4, $J_{10\text{-}H',1}$ = 5.6 Hz; 1-H), 3.80, 3.88 (2 × s; 4′-OCH_3, 6′-OCH_3), 4.80 (d, $J_{5,6}$ = 10.0 Hz, 5-H), 4.92 (m, 6-H), 6.25 (s, 5′-H), 6.29 (d, 3-H). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = −3.13, −2.89 [$Si(CH_3)_2$], 18.87 [$SiC(CH_3)_3$], 22.63, 22.66 [3′-$COCH_2CH(CH_3)_2$], 22.89, 26.95 (9-CH_3, 9-$C'H_3$), 24.49 (3′-$COCH_2CH$), 25.77 [$SiC(CH_3)_3$], 26.35 [$SiC(CH_3)_3$], 29.86 (C-7), 27.51 (C-9), 35.22 (C-10), 35.78 (C-6), 42.18 (C-8), 48.32 (C-1), 54.13 (3′-$COCH_2$), 55.66, 56.39 (4′-OCH_3 or 4′-OCH_3), 68.65 (C-5), 91.12 (C-5′), 101.83 (C-2), 117.61 (C-3′), 120.54 (C-3), 153.73 (C-1′), 158.00 (C-2′), 162.81 (C-6′), 164.14 (C-4′), 203.99 (3′-CO). − $C_{30}H_{46}O_6SSi$ (562.83): calcd. C 64.00, H 8.30; found C 63.88, H 8.32.

Hydroxy Diene 77: 92 mg (0.163 mmol) of **71** was dissolved in 2 mL of dry THF and treated with 327 μL (0.327 mmol, 1.0 M in THF) of TBAF at ambient temp. for 2 h. The reaction mixture was diluted with 10 mL of ether and poured into 10 mL of water. After stirring for 15 min, the aqueous layer was extracted with ether (3 × 10 mL), dried and concentrated in vacuo. The oily residue was purified by flash chromatography (eluent: ether/hexane, 1:5) yielding 37 mg (59%) of **77** as a colourless solid. − R_f = 0.40 (ether/hexane, 1:1). − IR (KBr): $\tilde{\nu}$ = 1690 cm^{-1} (C=O), 1604 (C=C). − ^{1}H NMR (400 MHz, 300 K, CDCl$_3$): δ = 0.84, 1.26 (2 × s; 6-CH$_3$, 6-CH′$_3$), 0.97 {d; J[4′-COCH$_2$CH,4′-COCH$_2$CH(CH_3)$_2$] = 6.7 Hz; 4′-COCH$_2$CH(CH_3)$_2$}, 1.24 (d, $J_{5,7}$ = 9.6 Hz, 7-H), 1.94 (m, 5-H), 2.23 (m; 4-H, 4′-COCH$_2$CH), 2.37 (m, 7-H′), 2.50 (pseudo t, $J_{1,7}$ = 5.6 Hz, 1-H), 2.58 (dd, $J_{1',4}$ = 2.0 Hz, 4-H′), 2.87 (d, 4′-COCH$_2$), 3.88, 3.93 (2 × s; 5′-OCH$_3$, 7′-OCH$_3$), 4.59 (d, $J_{\text{2-CH,2-CH'}}$ = 1.2 Hz, 2-CHH′), 5.36 (d, $J_{\text{2-CH,2-CH}}$ = 1.2 Hz, 2-CHH'), 5.97 (s, 6′-H), 6.73 (d, $J_{1',4}$ = 2.0 Hz, 1′-H), 14.22 (s, 3′-OH). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = 21.27 (6-CH$_3$), 22.81 [s, 4′-COCH$_2$CH(CH$_3$)$_2$], 25.35 (4′-COCH$_2$$C$H), 26.27 (6-C′H$_3$), 30.14 (C-7), 31.60 (C-4), 39.39 (C-5), 40.76 (C-6), 50.64 (C-1), 53.31 (4′-COCH$_2$), 55.37, 55.48 (5′-OCH$_3$ or 7′-OCH$_3$), 85.95 (C-6′), 104.38 (2-CH$_2$), 115.43 (C-1′), 137.23 (C-4′), 151.93 (C-2′), 162.31 (C-3′), 162.88 (C-7′), 163.95 (C-5′), 205.83 (4′-CO). − $C_{24}H_{32}O_4$ (384.51): calcd. C 74.97, H 8.39; found C 74.71, H 8.48.

Dimethylated Sulfoximine 80: In a 25-mL Schlenk flask 1.88 mL (17.12 mmol) of titanium tetrachloride was mixed with 8.56 mL (17.12 mmol) of dimethylzinc (2 M in toluene) in 20 mL of dry CH$_2$Cl$_2$ at −30°C for 20 min whereupon the colour of the solution turned from orange to dark green. 3.308 g (7.133 mmol) of ketone **83**, dissolved in 7.8 mL of CH$_2$Cl$_2$, was added at −40°C (colour changed to dark red). The temperature was kept at −20°C and the reaction was monitored by TLC (target R_f = 0.37, ether/hexane, 1:3, 1.5−2 h). The mixture was further diluted at −50°C with 10 mL of dry CH$_2$Cl$_2$ and poured into a vigorously stirred ice-cold sat. aqueous solution of (NH$_4$)$_2$CO$_3$ and the two-phase system was allowed to warm to ambient temp. within 30 min. The aqueous layer was washed with ether (3 × 40 mL), the combined organic layers were dried, concentrated in vacuo and purified by flash chromatography yielding 1.82 g (53%) of the dimethylated sulfoximine **80** as white solid, m.p. 40.5°C. − R_f = 0.37 (ether/hexane, 1:3). − $[\alpha]_D^{20}$ = −14.03 (c = 1.0, CH$_2$Cl$_2$). − IR (film): $\tilde{\nu}$ = 1242 cm^{-1}, 1134 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.48, −0.04 [2 × s, Si(CH$_3$)$_2$], 0.65 (s, 3-CH$_3$), 0.85 (s, 3-CH′$_3$), 0.84 [s, SiC(CH$_3$)$_3$], 0.90 [d, J(CH,CH$_3$) = 6.8 Hz, CHCH_3], 0.98 [d, J(CH,CH′$_3$) = 7.0 Hz, CHCH'_3], 1.24 (m, 4-H$_2$), 1.49 (m, 5-H$_2$), 1.82 (dt, $J_{\text{5,6-H}}$ = 6.1 Hz, 6-H), 2.00 [dqq; $J_{\text{NCH,CH}}$ = 3.2 Hz, J(CH,CH$_3$) = 6.8 Hz, J(CH,CH′$_3$) = 7.0 Hz; CH(CH$_3$)$_2$], 2.19 (dt; $J_{\text{5,6-H'}}$ = 6.1 Hz, $J_{\text{6-H,6-H'}}$ = 17.5 Hz; 6-H′), 2.40, (s, p-CH$_3$), 3.08 (dt; $J_{\text{OCH,NCH}}$ = 5.9 Hz, $J_{\text{OCH',NCH}}$ = 7.8 Hz, $J_{\text{CH,NCH}}$ = 3.2 Hz; NCH), 3.48 (dd; $J_{\text{OCH,OCH'}}$ = 10.0 Hz, $J_{\text{OCH,NCH}}$ = 5.9 Hz; OCH) 3.54 (dd; $J_{\text{OCH,OCH'}}$ = 10.0 Hz, $J_{\text{OCH',NCH}}$ = 7.8 Hz; OCH′), 3.62 (d, $J_{\text{SCH,SCH'}}$ = 13.6 Hz, SCH), 3.80 (d, $J_{\text{SCH,SCH'}}$ = 13.6 Hz, SCH′), 4.91 (s, 2-H), 7.26 (d, m-H$_2$), 7.74 (d, o-H$_2$). − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.56, −5.47 [Si(CH$_3$)$_2$], 16.53 (CHCH$_3$), 18.20 [SiC(CH$_3$)$_3$], 19.60 (C-5), 19.91 (CHC'H$_3$), 21.27 (p-CH$_3$), 25.84 [SiC(CH$_3$)$_3$], 28.67 (C-6), 29.05 (4-CH$_3$), 29.17 (4-C′H$_3$), 29.71 [CH(CH$_3$)$_2$], 31.97 (C-3), 36.16 (C-4), 60.86 (NCH), 64.66 (SCH$_2$), 65.56 (OCH$_2$), 124.87 (C-1), 129.02 (m-C), 129.69 (o-C), 135.73 (i-C), 142.24 (C-2), 142.84 (p-C). − $C_{27}H_{47}NO_2SSi$ (477.84): calcd. C 68.09, H 9.91, N 2.93; found C 68.08, H 9.87, N 2.82.

Aldehyde 81: 431 mg (1.5 mmol) of the TBS-protected amide **88** was dissolved in 10 mL of dry THF and 4.5 mL (4.5 mmol) of DIBALH (1 M in hexane) was added at −78°C. After 15 min, the reaction was found to be complete (TLC, eluent: ethyl acetate/hexane, 3:1), and quenched with 15 mL of 0.5 M tartaric acid. After the mixture had reached room temp., the aqueous phase was extracted with ether (3 × 20 mL), the combined organic layers were washed with sat. aqueous NaHCO$_3$ and afterwards with brine, dried and concentrated in vacuo and used without further delay. − R_f = 0.76 (ethyl acetate/hexane, 3:1). − IR (film): $\tilde{\nu}$ = 1728 (HC=O) cm^{-1}. − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.06 [s, Si(CH$_3$)$_2$], 0.89 [s, SiC(CH$_3$)$_3$], 1.79 [d, J(3-CH$_3$,4) = 1.3 Hz, 3-CH$_3$], 3.17 (d, $J_{1,2}$ = 2.4 Hz, 2-H$_2$), 4.15 (d, $J_{4,5}$ = 6.5 Hz, 5-H$_2$), 5.65 [t; J(4,3-CH$_3$) = 1.3 Hz, $J_{4,5}$ = 6.5 Hz; 4-H], 9.58 (t, $J_{1,2}$ = 2.4 Hz, 1-H). − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.34 [Si(CH$_3$)$_2$], 18.20 [SiC(CH$_3$)$_3$], 24.37 (3-CH$_3$), 25.79 [SiC(CH$_3$)$_3$], 47.46 (C-2), 59.34 (C-5), 128.41 (C-4), 129.36 (C-3), 198.81 (C-1).

Lactone 82: 100 mL of SO$_2$ was condensed into a 500-mL three-necked flask (cooling CCl$_4$/CO$_2$, −22°C) and taken as solvent for 42.9 g (375 mmol) of freshly distilled chlorosulfonyl isocyanate. 25.5 g (375 mmol) of freshly distilled isoprene was added dropwise keeping the reaction mixture boiling slightly. The mixture was stirred for another 6 h at −10°C (refluxing SO$_2$) and then poured onto 100 mL of ice and 100 mL of ether. The diphasic system was stirred for an additional 90 min whereupon a yellowish solid precipitated. After filtration, the aqueous layer was extracted with ether (4 × 100 mL) and the combined organic layers were dried and concentrated in vacuo yielding 31.9 g (79%) of lactone **82** as an orange oil which could be used for further reactions without purification. It is not recommended to purify the crude product by distillation in vacuo because of partial double-bond migration to ***iso*-82**. − **82**: R_f = 0.17 (ether/hexane, 1:1). − B.p. 57°C (0.8 mbar; 40−41°C, 0.01 mbar). − IR (film): $\tilde{\nu}$ = 1738 cm^{-1} (C=O) (1737[36]) − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 1.79 (m, 3-CH$_3$), 2.98 (m, 2-H$_2$), 4.83 (m, 5-H$_2$), 5.59 [ttq; $J_{2,4}$ = 1.5 Hz, J(4,3-CH$_3$) = 1.5 Hz, $J_{4,5}$ = 1.5 Hz; 4-H]. − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = 21.14 (3-CH$_3$), 34.64 (C-2), 68.43 (C-5), 115.91 (C-4), 130.39 (C-3), 169.47 (C-1). − $C_6H_8O_2$ (112.12): calcd. C 64.22, H 7.19; found C 64.01, H 7.23. − ***iso*-82: R$_f$** = 0.29 (ether/hexane, 1:1). − B.p. 70°C (0.8 mbar). − IR (film): $\tilde{\nu}$ = 1724 cm^{-1} (C=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 1.99 (m, 3-CH$_3$), 2.37 (t, $J_{4,5}$ = 6.4 Hz, 4-H$_2$), 4.37 (t, $J_{4,5}$ = 6.4 Hz, 5-H$_2$), 5.80 (m, 2-H). − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = 22.66 (3-CH$_3$), 28.84 (C-4), 65.71 (C-5), 116.14 (C-2), 158.17 (C-3), 164.36 (C-1). − $C_6H_8O_2$ (112.12): calcd. C 64.22, H 7.19; found C 64.02, H 7.19.

Ketone 83: In a 25-mL Schlenk flask 1.45 g (3.92 mmol) of **84** was dissolved in 12 mL of dry THF. At −78°C 2.16 g of nBuLi (2.18 mmol/g in hexane) was added via hypodermic syringe, while the solution turned yellow. 10 min later, 0.97 g (6.28 mmol) of the vinylogous ester **85**[46] was added dropwise. After 5 min, the temperature was allowed to increase to room temp. over a period of 80 min. Thereupon the colour deepened to orange. The reaction was monitored by TLC (about 2.5 h, eluent: ether/hexane, 3:1). Elimination was induced by adding 4 mL of 0.5 N sulfuric acid at ambient temp. After about 1.5 h, the reaction mixture was diluted with water and ether (50 mL each). The aqueous phase was extracted with ether (3 × 30 mL), the combined organic layers were washed with 50 mL of sat. aqueous NaHCO$_3$, dried and concentrated in vacuo. Purification by flash chromatography yielded 1.3 g (72%) of ketone **83** as a white solid, m.p. 95.7°C. − R_f = 0.26 (ether/hexane, 3:1). − $[\alpha]_D^{20}$ = 1.2 (c = 1.0, CH$_2$Cl$_2$). − IR (KBr): $\tilde{\nu}$ = 1659 cm^{-1} (C=O); 1255, 1136 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.01, 0.00 [2 × s, Si(CH$_3$)$_2$], 0.86 [s, SiC(CH$_3$)$_3$], 0.91 [d, J(CH,CH$_3$) = 7.0 Hz, CHCH_3], 0.98 [d, J(CH,CH′$_3$) = 7.0 Hz, CHCH'_3], 1.94 (m, 5-H$_2$), 2.00 [ddd; $J_{\text{NCH,CH}}$ = 3.4 Hz, J(CH,CH$_3$) = J(CH,CH′$_3$) = 7.0 Hz; (CH$_3$)$_2$CH], 2.30 (m, 6-H$_2$), 2.39 (br. d, $J_{\text{4-H,4-H'}}$ = 18.5 Hz, 4-H), 2.42 (s, p-CH$_3$), 2.65 (ddd, $J_{\text{4-H,4-H'}}$ = 18.5 Hz, 4-H′), 3.14 (ddd; $J_{\text{OCH',NCH}}$ = 6.1 Hz, $J_{\text{OCH,NCH}}$ = 7.5 Hz, $J_{\text{CH,NCH}}$ = 3.4 Hz; NCH), 3.52 (dd; $J_{\text{OCH,NCH}}$ = 7.5 Hz, $J_{\text{OCH,OCH'}}$ = 10.0 Hz; OCH), 3.56 (dd; $J_{\text{OCH',NCH}}$ = 6.1 Hz, $J_{\text{OCH,OCH'}}$ = 10.0 Hz; OCH′), 3.82 (d, $J_{\text{SCH,SCH'}}$ = 11.8 Hz, SCH), 4.11 (d, $J_{\text{SCH,SCH'}}$ = 11.8 Hz, SCH′) 5.50 (s, 2-H), 7.29 (d, J = 8.1 Hz, *m*-H$_2$), 7.76 (d, J = 8.1 Hz, *o*-H$_2$). – ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.54, −5.46 [Si(CH$_3$)$_2$], 16.51 (CH*C*H$_3$), 18.22 [Si*C*(CH$_3$)$_3$], 19.99 (C-5), 21.40 (CH*C′*H$_3$), 22.46 (*p*-CH$_3$), 25.83 [SiC(*C*H$_3$)$_3$], 29.89 [*C*H(CH$_3$)$_2$], 36.95 (C-4), 61.54 (NCH), 64.31 (SCH$_2$), 65.59 (OCH$_2$), 129.19 (*m*-C), 129.53 (*o*-C), 131.90 (C-2), 135.05 (*i*-C), 143.95 (*p*-C), 152.86 (C-3), 198.63 (C-1). – $C_{25}H_{41}NO_3SSi$ (463.75): calcd. C 64.75, H 8.91, N 3.02; found C 64.49, H 8.83, N 2.94.

Weinreb Amides 87 and 88: According to a literature procedure[37] 1.951 g (20 mmol) of *N,O*-dimethylhydroxylamine hydrochloride, 10 mL (20 mmol) of trimethylaluminium (2 M in hexane) and 1.212 g (10 mmol) of lactone **82** were converted into 1.31 g of crude hydroxy amide **87**. – R_f = 0.12 (ethyl acetate/hexane, 3:1). – IR (film): ṽ = 3446 cm^{-1} (O-H), 1655 (NC=O). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 1.79 [d, J(4,3-CH$_3$) = 0.7 Hz, 3-CH$_3$], 3.21 (s, NCH$_3$), 3.28 (s, 2-H$_2$), 3.72 (s, OCH$_3$), 4.04 (d, $J_{4,5}$ = 7.6 Hz, 5-H$_2$), 5.81 [dt; J(4,3-CH$_3$) = 0.7 Hz, $J_{4,5}$ = 7.6 Hz; 4-H]. – The crude product was dissolved in 20 mL of dry CH$_2$Cl$_2$, 2.2 mL (20 mmol) of ethyldimethylamine, 0.37 g (3 mmol) of DMAP and 2.41 g (16 mmol) of TBSCl was added and the mixture was stirred for 12 h at ambient temp. Standard aqueous workup and purification by flash chromatography yielded 1.59 g (55%, corresponding to isoprene) of the TBS-protected amide **88** as a colourless oil. – R_f = 0.65 (ethyl acetate/hexane, 3:1). – IR (film): ṽ = 1668 cm^{-1} (NC=O). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.06 [s, Si(CH$_3$)$_2$], 0.89 [s, SiC(CH$_3$)$_3$], 1.79 [d, J(4,3-CH$_3$) = 0.9 Hz, 3-CH$_3$], 3.18 (s, NCH$_3$), 3.21 (s, 2-H$_2$), 3.69 (s, OCH$_3$), 4.20 (d, $J_{4,5}$ = 6.6 Hz, 5-H$_2$), 5.53 [dt; J(4,3-CH$_3$) = 0.9 Hz, $J_{4,5}$ = 6.6 Hz; 4-H]. – ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.28 [Si(CH$_3$)$_2$], 18.25 [Si*C*(CH$_3$)$_3$], 23.87 (3-CH$_3$), 25.84 [SiC(*C*H$_3$)$_3$], 32.38 (NCH$_3$), 35.56 (C-2), 59.94 (C-5), 61.54 (OCH$_3$), 128.21 (C-3), 130.57 (C-4), 191.10 (C-1). – $C_{14}H_{29}NO_3Si$ (287.47): calcd. C 58.49, H 10.17; N 4.87; found C 58.58, H 10.10, N 4.93.

Lactol 89: In a Schlenk flask a solution of 0.854 g (7.53 mmol) of lactone **82** in 11 mL of ether was cooled to −78°C and 11.3 mL (11.30 mmol, 1 M in hexane) of diisobutylaluminium hydride was added dropwise. The reaction mixture was stirred for an additional 90 min and then 7.2 mL of water was added for workup. The mixture was allowed to reach room temp. and stirring was continued overnight. Decanting (3 × 20 mL of ether) and concentration in vacuo afforded 804 mg (93%) of the lactol **89** as a colourless liquid. – R_f = 0.31 (ether/hexane, 2:1). – IR (film): ṽ = 3403 cm^{-1} (OH). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 1.71 (m, 3-CH$_3$), 2.02 (br. d, $J_{2\text{-H},2\text{-H}'}$ = 17.3 Hz, 2-H), 2.28 (br. d, $J_{2\text{-H},2\text{-H}'}$ = 17.3 Hz, 2-H′), 3.11 (br. d, $J_{1,\text{OH}}$ = 2.5 Hz, OH),4.12 (d, $J_{4,5\text{-H}}$ = 7.4 Hz, 5-H), 4.31 (d, $J_{4,5\text{-H}'}$ = 7.1 Hz, 5-H′), 5.17 (d, $J_{1,\text{OH}}$ = 2.5 Hz, 1-H) 5.43 [dq; J(4,3-CH$_3$) = 1.6 Hz, $J_{4,5\text{-H}}$ = 7.4 Hz; 4-H]. – ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = 22.62 (3-CH$_3$), 35.91 (C-2), 61.62 (C-5), 91.53 (C-1), 118.42 (C-4), 129.38 (C-3). – $C_6H_{10}O_2$ (114.14): calcd. C 63.14, H 8.83; found C 63.21, H 8.95.

Vinyl Sulfoximine 90: Following GP1, 478 mg (1 mmol) of sulfoximine **80**, 579 mg (1.2 mmol) of *n*BuLi (2.07 mmol/g in hexane), 600 mg (1.5 mmol) of ClTIPT (2.50 mmol/g in hexane) and 244 mg (2.3 mmol) of freshly distilled benzaldehyde were afforded 134 mg (23%, *ds* > 98%) of **90** after workup and chromatographical purification (eluent: ether/hexane, 1:8) as a colourless glass. – R_f = 0.13 (ether/hexane, 1:3). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.14, −0.10 [2 × s, Si(CH$_3$)$_2$], 0.21 [s; 3-(CH$_3$)$_2$], 0.78 [s, SiC(CH$_3$)$_3$], 0.90 [d, J(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.96 [d, J(CH,CH′$_3$) = 6.9 Hz, CHC*H′*$_3$], 1.50–1.80 (m; 4-H$_2$, 5-H$_2$), 1.98 [dqq; $J_{\text{NCH,CH}}$ = 3.3 Hz, J(CH,CH$_3$) = J(CH,CH′$_3$) = 6.9 Hz; C*H*(CH$_3$)$_2$], 2.21 (br. d, $J_{6\text{-H},6\text{-H}'}$ = 14.3 Hz, 6-H), 2.42 (s, *p*-CH$_3$), 2.50 (d, $J_{6\text{-H},6\text{-H}'}$ = 14.3 Hz, 6-H′), 2.96 (ddd; $J_{\text{OCH,NCH}}$ = 5.6 Hz, $J_{\text{OCH}',\text{NCH}}$ = 8.4 Hz, $J_{\text{NCH,CH}}$ = 3.3 Hz; 9-H), 3.31 (dd; $J_{\text{OCH,OCH}'}$ = 10.0 Hz, $J_{\text{OCH,NCH}}$ = 5.6 Hz; OCH), 3.48 (dd; $J_{\text{OCH,OCH}'}$ = 10.0 Hz, $J_{\text{OCH}',\text{NCH}}$ = 8.4 Hz; OCH′), 3.80 (dd; $J_{\text{SCH},2}$ = 1.8 Hz, $J_{\text{SCH}',2}$ = 10.3 Hz; 2-H), 3.99 (br. d, $J_{1',\text{OH}}$ = 9.5 Hz, OH), 4.62 (br. pseudo d; $J_{1',2}$ = 10.3 Hz, $J_{1',\text{OH}}$ = 9.5 Hz; 1′-H), 6.55 (d, $J_{\text{SCH}',2}$ = 1.8 Hz, SCH′), 7.28–7.40 (m; 1′-*o*-H$_2$, 1′-*m*-H$_2$, 1′-*p*-H), 7.56 (d, J = 8.4 Hz, *m*-H$_2$), 7.89 (d, J = 8.4 Hz, *o*-H$_2$). – ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −5.52, −5.45 [Si(*C*H$_3$)$_2$], 16.96 (CH*C*H$_3$), 18.26 [Si*C*(CH$_3$)$_3$], 19.95 (CH*C′*H$_3$), 21.43 (*p*-CH$_3$), 22.60 (C-4 or C-5), 25.90 [SiC(*C*H$_3$)$_3$], 27.37 (3-C′H$_3$), 29.71 [*C*H(CH$_3$)$_2$], 30.57 (3-CH$_3$), 32.71 (C-6), 34.19 (C-4 or C-5), 34.83 (C-3), 52.10 (C-2), 60.84 (NCH), 65.45 (OCH$_2$), 73.17 (C-1′), 127.40 (SCH), 127.72, 128.53, 143.05 (1′-*o*-C or 1′-*m*-C or 1′-*p*-C), 128.80 (1′-*i*-C$_2$), 129.02 (*m*-C), 129.56 (*o*-C), 139.20 (*i*-C), 145.88 (*p*-C), 159.86 (C-1).

Vinyl Sulfoximine 91: Following GP1, 250 mg (0.56 mmol) of cyclohexenylmethyl sulfoximine **26**, 303 mg (0.67 mmol) of *n*BuLi (2.21 mmol/g hexane), 334 mg (0.84 mmol) of ClTIPT (2.50 mmol/g in hexane) and 292 mg (1.28 mmol) of aldehyde **81** afforded 294 mg (78%, *ds* ≥ 98%) of the 4-hydroxy-substituted vinyl sulfoximine **91** after aqueous workup and purification by flash chromatography (eluent: ether/hexane, 1:8, 1:6) as a colourless oil. – R_f = 0.15 (ether/hexane, 1:3). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.15, −0.11 [2 × s, NCHCH$_2$OSi(C*H*$_3$)$_2$], 0.08 [s, 5′-OSi(CH$_3$)$_2$], 0.78 [s, NCHCH$_2$OSiC(C*H*$_3$)$_3$], 0.91 [s, 5′-OSiC(CH$_3$)$_3$], 0.94 [d, J(CH,CH$_3$) = 7.0 Hz, CHC*H*$_3$], 0.99 [d, J(CH,CH′$_3$) = 7.0 Hz, CHC*H′*$_3$], 1.27 (m, 4-H$_2$), 1.45–1.60 (m; 5-H$_2$, 2′-H$_2$), 1.76 (m, 6-H), 1.84 [d, J(3′-CH$_3$,4′) = 1.1 Hz, 3′-CH$_3$], 1.85–2.10 [m, C*H*(CH$_3$)$_2$], 2.11 (br. d, $J_{6\text{-H},6\text{-H}'}$ = 13.7 Hz, 6-H′), 2.44 (s, *p*-CH$_3$), 2.84 (br. s, 1′-H), 3.27 (ddd; $J_{\text{OCH,NCH}}$ = 5.7 Hz, $J_{\text{OCH}',\text{NCH}}$ = 9.9 Hz; NCH), 3.48, 3.61 (2 × m, OCH$_2$), 3.87 (ddd, 2-H), 4.22 (m, 5′-H$_2$), 4.38 (br. s, OH), 5.48 [dt; J(4′,3′-CH$_3$) = 1.1 Hz, $J_{4',5'}$ = 5.5 Hz; 4′-H], 6.39 (br. s, SCH), 7.33 (br. d, *m*-H$_2$), 7.82 (br. d, *o*-H$_2$).

Deprotected Vinyl Sulfoximines 92 and 92b. – Reaction with TBAF at Room Temp.: 315 mg (1.00 mmol) of TBAF trihydrate was dissolved in 1 mL of THF and neutralised with acetic acid (98%, 5 drops). The resulting mixture was added to 130 mg (0.19 mmol) of **91** in 0.5 mL of THF. The reaction mixture changed colour to orange. After stirring for 12 h at room temp. and aqueous workup, the aqueous phase was extracted with ethyl acetate (2 × 20 mL) and ether (1 × 20 mL), the combined organic layers were dried, concentrated in vacuo and purified by flash chromatography (eluent: ethyl acetate/hexane, 5:1–10:1) yielding 67 mg (78%) of the fully deprotected compound **92a** accompanied by 22 mg (11%) of the partially (in the aldehyde fragment) deprotected derivative **92b** (characterised only by ^{1}H NMR). – **92a**: R_f = 0.13 (ethyl acetate/hexane, 10:1). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.96 [d, J(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.98 [d, J(CH,CH′$_3$) = 6.9 Hz, CHC*H′*$_3$], 1.45–1.55 (m, 4-H$_2$; 5-H$_2$), 1.82 [d, J(4′,3′-CH$_3$) = 1.2 Hz, 3′-CH$_3$], 1.89 [m; 2′-H$_2$, C*H*(CH$_3$)$_2$], 2.08 (br. d, $J_{1',\text{OH}}$ = 10.3 Hz, 1′-OH), 2.25 (dd; $J_{5,6}$ = 2.0 Hz, $J_{6\text{-H},6\text{-H}'}$ = 13.6 Hz; 6-H), 2.43 (s, *p*-CH$_3$), 2.46 (dd; $J_{5,6\text{-H}}$ = 9.3 Hz, $J_{6\text{-H},6\text{-H}'}$ = 13.6 Hz; 6-H′), 3.09 (ddd; $J_{\text{OCH,NCH}}$ = 5.0 Hz, $J_{\text{OCH}',\text{NCH}}$ = 5.2 Hz, $J_{\text{NCH,CH}}$ = 4.3 Hz; NCH), 3.52 (ddd; $J_{\text{OCH,OCH}'}$ = 10.2 Hz, $J_{\text{OCH,NCH}}$ = 5.0 Hz, $J_{\text{OCH}',\text{NCH}}$ = 5.2 Hz; OCH$_2$), 3.90 (m; 5′-H; 2-H), 4.04 (br. d, $J_{1',\text{OH}}$ = 10.3 Hz, 1′-H), 4.19 (dd; $J_{4',5'\text{-H}}$ = 8.6 Hz, $J_{5'\text{-H},5'\text{-H}'}$ = 11.9 Hz; 5′-H′), 5.75 [ddd; J(4′,3′-CH$_3$) = 1.2 Hz, $J_{4',5'\text{-H}}$ = 6.3 Hz, $J_{4',5'\text{-H}'}$ = 8.6 Hz; 4′-H], 6.02 (d, $J_{\text{SCH},2}$ = 1.6 Hz, SCH), 7.34 (d, J = 8.3 Hz, *m*-H$_2$), 7.86 (d, J = 8.3 Hz, *o*-H$_2$). – **92b**: R_f = 0.68 (ethyl acetate/hexane, 10:1). – ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.10, −0.07 [s, Si(CH$_3$)$_2$], 0.80 [s, SiC(CH$_3$)$_3$], 0.95 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.99 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*′$_3$], 1.45−1.60 (m; 3-H$_2$, 4-H$_2$ and 5-H$_2$), 1.81 [d, *J*(4′,3′-CH$_3$) = 1.2 Hz, 3′-CH$_3$], 1.88 (m, 2′-H$_2$), 1.98 [dqq; $J_{\text{NCH,CH}}$ = 3.2 Hz, *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 6.9 Hz; C*H*(CH$_3$)$_2$], 2.09 (br. d, OH), 2.21 (br. d, $J_{\text{6-H,6-H}'}$ = 13.6 Hz, 6-H), 2.44 (s, *p*-CH$_3$), 2.52 (m, 6-H′), 2.82 (ddd; $J_{\text{OCH,NCH}}$ = 6.1 Hz, $J_{\text{NCH,CH}}$ = 3.2 Hz; NCH), 3.34 (d, $J_{\text{OCH,NCH}}$ = 6.1 Hz, OCH), 3.54 (d, $J_{\text{OCH}',\text{NCH}}$ = 7.9 Hz, OCH′), 3.86 (d, $J_{4',5'\text{-H}}$ = 6.9 Hz, 5′-H), 4.15 (d, 5′-H′), 5.49 (br. s, OH), 5.78 [dt; *J*(4′,3′-CH$_3$) = 1.2 Hz, $J_{4',5'\text{-H}}$ = 6.9 Hz; 4′-H], 6.40 (br. s, SCH), 7.33 (d, *m*-H$_2$), 7.82 (d, *o*-H$_2$).

TBAF at 40°C: To 282 mg (0.42 mmol) of **91** a solution of 2.0 mL (2.00 mmol) of TBAF (1 M in THF) and 9 drops of acetic acid (98%) were added dropwise. After stirring for 10 min at room temp., the homogeneous reaction mixture was kept at 40°C for 3 d. Aqueous workup was followed by extraction of the aqueous phase with ether (3 × 20 mL), removal of all volatiles in vacuo and purification by flash chromatography yielded 167 mg (89%) of the fully deprotected product **92a** with complete conservation of the optical purity.

Vinyl Sulfoximine 94: Following GP1, 111 mg (0.23 mmol) of sulfoximine **80**, 125 mg (0.28 mmol) of *n*BuLi (2.23 mmol/g in hexane), 140 mg (0.35 mmol) of ClTIPT (2.50 mmol/g in hexane) and 133 mg (0.58 mmol) of aldehyde **81** yielded 203 mg (*ds* > 98%, traces of impurity, not any other isomer) of the 4-hydroxy-substituted vinyl sulfoximine **94** after workup and purification by chromatography (eluent: ether/hexane, 1:8) being a colourless oil. − R_f = 0.53 (ether/hexane, 1:3). − ^{1}H NMR (270 MHz, 300 K, CDCl$_3$): δ = −0.09, −0.07 [2 × s, NCHCH$_2$OSi(C*H*$_3$)$_2$], 0.05 [s, 5′-OSi(CH$_3$)$_2$], 0.80 [s, NCHCH$_2$OSiC(C*H*$_3$)$_3$], 0.84 (s, 3-CH$_3$), 0.85 (s, 3-CH′$_3$), 0.85 [d, *J*(CH,CH$_3$) = 7.0 Hz, CHC*H*$_3$)], 0.89 [s, 5′-OSiC(CH$_3$)$_3$], 0.95 [d, *J*(CH,CH′$_3$) = 7.0 Hz, CHC*H*′$_3$], 1.10−1.50 (m; 4-H, 2′-H$_2$), 1.58 (d, $J_{\text{5-H}',\text{4-H}'}$ = 5.6 Hz, 4-H′), 1.79 (dd; $J_{\text{5-H,5-H}'}$ = 13.6 Hz, $J_{\text{5-H,6-H}}$ = 10.6 Hz; 5-H), 1.82 (m, 3′-CH$_3$), 1.95 [dqq; $J_{\text{NCH,CH}}$ = 3.1 Hz, *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 7.0 Hz; C*H*(CH$_3$)$_2$], 2.01 (dd, $J_{\text{5-H,6-H}}$ = 10.6 Hz, 6-H), 2.21 (dd; $J_{\text{4-H}',\text{5-H}'}$ = 5.6 Hz, $J_{\text{5-H,5-H}'}$ = 13.6 Hz; 5-H′), 2.37 (m, 6-H′), 2.42 (s, *p*-CH$_3$), 2.92 (ddd; $J_{\text{OCH,NCH}}$ = 6.1 Hz, $J_{\text{OCH}',\text{NCH}}$ = 7.4 Hz, $J_{\text{NCH,CH}}$ = 3.1 Hz; NCH), 3.37 (dd; $J_{\text{OCH,OCH}'}$ = 10.0 Hz, $J_{\text{OCH,NCH}}$ = 6.1 Hz; OCH), 3.49 (dd; $J_{\text{OCH,OCH}'}$ = 10.0 Hz, $J_{\text{OCH}',\text{NCH}}$ = 7.4 Hz; OCH′), 3.56 (br. d, $J_{1',2}$ = 10.0 Hz, 2-H), 4.15 (dd; $J_{4',5'}$ = 7.7 Hz, $J_{\text{5}'\text{-H,5}'\text{-H}'}$ = 12.8 Hz; 5′-H), 4.30 (dd, $J_{\text{5}'\text{-H,5}'\text{-H}'}$ = 12.8 Hz, 5′-H′), 4.63 (br. t, $J_{1',2}$ = 10.0 Hz, 1′-H), 4.93 (br. s, OH), 5.50 (pseudo t; $J_{4',5'\text{-H}}$ = 5.7 Hz, $J_{4',5'\text{-H}'}$ = 7.7 Hz; 4′-H), 6.87 (s, SCH), 7.28 (d, *J* = 8.2 Hz, *m*-H$_2$), 7.73 (d, *J* = 8.2 Hz, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −5.51, −5.40 [Si(CH$_3$)$_2$], 17.08 (CH*C*H$_3$), 17.21 (C-3), 18.31 (3-CH$_3$), 18.39 (3′-CH$_3$), 19.57, 19.71 [2 × Si*C*(CH$_3$)$_3$], 21.45 (*p*-CH$_3$), 23.81 (3-C′H$_3$), 25.94, 26.03 [2 × SiC(*C*H$_3$)$_3$], 29.01 (CH*C*′H$_3$), 29.88 [*C*H(CH$_3$)$_2$], 32.13 (C-4), 36.40 (C-6), 37.05 (C-1′), 37.71 (C-5), 60.05 (C-5′), 60.80 (C-2), 61.74 (C-6), 64.91 (C-2′), 65.16 (OCH$_2$), 125.35 (C-3′), 127.83 (C-4′) 129.31 (*m*-C), 129.42 (SCH), 130.23 (*o*-C), 134.10 (*i*-C), 143.66 (*p*-C), 144.29 (C-1).

Lithium Sulfinate 97: In a 250-mL three-necked flask 4.14 mL (30.0 mmol) of **96** was dissolved in 30 mL of dry THF and 12.5 g (33 mmol) of *t*BuLi (2.64 mmol/g in hexane) was added dropwise at −78°C. The turbid and greenish solution was stirred for another 5 min at which point SO$_2$ was added in portions maintaining the temperature around −78°C until no further reactive uptake of SO$_2$ occurred. The colour of the solution became light yellow while precipitation was observed. The reaction mixture was stirred for another hour, then all volatiles were evaporated in vacuo at room temp. The light yellow residue (powder) was dried in vacuo and could be used without further purification. − IR (film): ṽ = 1336 cm^{-1} (C−F), 1242, 1134 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, D$_2$O): δ = 7.64 (d, *J* = 8.3 Hz, aromatic *H*$_2$), 7.58 (d, *J* = 8.3 Hz, aromatic *H*$_2$).

TMS−Sulfinamides 98, *epi*-98 and Hydroxy Sulfinamides 99, *epi*-99: A solution of 3.26 mL (5.35 g, 45 mmol) of thionyl chloride in 10 mL of dry CH$_2$Cl$_2$ was added dropwise to an ice-cold suspension of freshly prepared sulfinate **97** (30 mmol) in 30 mL of dry CH$_2$Cl$_2$. After 2 h, the excess thionyl chloride was evaporated in vacuo at room temp. and the remaining thionyl chloride was removed by co-evaporation with CH$_2$Cl$_2$ (3 × 20 mL). Without further delay the resulting sulfinyl chloride was suspended in 60 mL of dry CH$_2$Cl$_2$ and added dropwise to a −78°C cold solution of 5.26 g (30.0 mmol) of TMS−valinol and 4.39 g of ethyldimethylamine in 100 mL of dry CH$_2$Cl$_2$. The reaction was monitored by TLC (about 2.5 h, eluent: ether/hexane, 1:2). Aqueous workup, extraction of the aqueous phase with CH$_2$Cl$_2$ (1 × 100 mL) and ether (3 × 80 mL), drying of the combined organic layers and concentration in vacuo yielded the diastereomeric sulfinamides **98** and *epi*-**98**. − R_f = 0.25 (ether/hexane, 1:2). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.08 [s, Si(CH$_3$)$_2$], 0.98 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.99 [d, *J*(CH,CH′$_3$) = 6.9 Hz, CHC*H*$_3$′], 2.03 [dqq; *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 6.9 Hz, $J_{\text{NCH,CH}}$ = 6.2 Hz; C*H*(CH$_3$)$_2$], 3.16 (ddd; $J_{\text{OCH,CH}}$ = 4.8 Hz, $J_{\text{OCH}',\text{CH}}$ = 4.3 Hz, $J_{\text{NCH,CH}}$ = 6.2 Hz; NCH), 3.63 (dd; $J_{\text{OCH,NCH}}$ = 4.8 Hz, $J_{\text{OCH,OCH}'}$ = 10.4 Hz; OCH), 3.70 (dd; $J_{\text{OCH}',\text{NCH}}$ = 4.3 Hz, $J_{\text{OCH,OCH}'}$ = 10.4 Hz; OCH′), 4.29 (d, $J_{\text{NH,NCH}}$ = 8.2 Hz, NH), 7.76 (d, *J* = 8.4 Hz, *m*-H$_2$), 7.88 (d, *J* = 8.4 Hz, *o*-H$_2$). − R_f = 0.19 (ether/hexane, 1:2). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.13 [s, Si(CH$_3$)$_2$], 0.75 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.78 [d, *J*(CH,CH′$_3$) = 6.9 Hz, CHC*H*$_3$′], 1.79 [dqq; *J*(CH,CH′$_3$) = *J*(CH,CH$_3$) = 6.9 Hz, $J_{\text{NCH,CH}}$ = 6.3 Hz; C*H*(CH$_3$)$_2$] 2.96 [ddd; *J*(CH,OCH$_2$) = 4.6 Hz, $J_{\text{NCH,CH}}$ = 6.3 Hz; NCH], 3.72 [d, *J*(NCH,OCH$_2$) = 4.6 Hz, OCH$_2$], 4.52 (d, $J_{\text{NH,NCH}}$ = 8.9 Hz, NH), 7.75 (d, *J* = 8.3 Hz, *m*-H$_2$), 7.87 (d, *J* = 8.3 Hz, *o*-H$_2$). − The crude oily product was dissolved in 10 mL of THF/H$_2$O, 1:1 and 3 mL of acetic acid (98%) was added dropwise at 0°C. Desilylation proceeded at room temp. and was monitored by TLC (ethyl acetate/hexane, 1:1). After approximately 1.5 h, the reaction mixture was poured into 200 mL of ether/H$_2$O, 1:1 and the aqueous layer was extracted with ether (3 × 80 mL). The combined organic layers were neutralised with sat. aqueous NaHCO$_3$, washed with brine, dried and concentrated in vacuo. The oily residue was purified by flash chromatography yielding 3.41 g (39% with respect to **96**) of the hydroxy sulfinamides **99** and *epi*-**99** (diastereomeric ratio 1:1). − R_f = 0.17 (ethyl acetate/hexane, 1:1). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.75 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$], 0.82 [d, *J*(CH,CH′$_3$) = 6.9 Hz, CHC*H*$_3$′], 0.97 [d, *J*(CH,CH′$_3$) = 6.9 Hz, CHC*H*$_3$], 1.03 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.71 [dqq; *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 6.9 Hz, $J_{\text{NCH,CH}}$ = 5.3 Hz; C*H*(CH$_3$)$_2$], 1.89 [dqq; *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 6.8 Hz, $J_{\text{NCH,CH}}$ = 5.8 Hz; C*H*(CH$_3$)$_2$], 2.74 (ddd; $J_{\text{OCH,NCH}}$ = 8.3 Hz, $J_{\text{NCH,CH}}$ = 5.3 Hz, $J_{\text{NH,NCH}}$ = 9.8 Hz; NCH), 3.26 (ddd; $J_{\text{OCH,NCH}}$ = 7.6 Hz, $J_{\text{OCH,NCH}}$ = 3.3 Hz, $J_{\text{NCH,CH}}$ = 5.8 Hz; NCH), 3.40 (dd; $J_{\text{OCH,NCH}}$ = 8.3 Hz, $J_{\text{OCH,OCH}'}$ = 12.0 Hz; OCH), 3.57 (m, 2 × OCH), 3.79 (dd; $J_{\text{OCH,NCH}}$ = 3.3 Hz, $J_{\text{OCH,OCH}'}$ = 12.0 Hz; OCH), 4.09 (m, NH), 4.33 (br. s, 2 × OH), 4.61 (d, $J_{\text{NH,NCH}}$ = 9.8 Hz, NH), 7.83 (m; 2 × *m*-H$_2$, 2 × *o*-H$_2$). − $C_{12}H_{16}F_2NO_2S$ (295.31): calcd. C 48.81, H 5.46, N 4.74; found C 48.62, H 5.50, N 4.61.

Cyclic Sulfonimidates 100, *epi*-100: According to our DBU-based protocol[8] 2.600 g (8.804 mmol) of the epimeric sulfinamides **94**

and *epi*-**94** were cyclised employing 1.089 g (10.037 mmol) of *tert*-butyl hypochlorite and 2.788 g (18.314 mmol) of DBU. Workup after 1.5 h of reaction time yielded 2.790 g (91%) of the epimeric sulfonimidates **100** and *epi*-**100** (1:1, ^{1}H-NMR-spectroscopically determined) melting at 35.2−36.2°C, which could be partially separated by flash chromatography. − R_f = 0.38 (ether/hexane, 1:2). − ^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 0.99 [d, $J(\mathrm{CH,CH_3})$ = 6.7 Hz, $\mathrm{CHC}H_3$], 0.94 [d, $J(\mathrm{CH,CH'_3})$ = 6.7 Hz, $\mathrm{CHC}H_3{}'$], 1.93 [dqq, $J(\mathrm{CH,CH_3}) = J(\mathrm{CH,CH'_3})$ = 6.7 Hz, $\mathrm{C}H(\mathrm{CH_3})_2$] 3.88 (dd; $J_{\mathrm{OCH,CH}}$ = 7.5 Hz, $J_{\mathrm{OCH',CH}}$ = 7.0 Hz; NCH), 4.02 (dd; $J_{\mathrm{OCH,NCH}}$ = 7.6 Hz, $J_{\mathrm{OCH,OCH'}}$ = 7.6 Hz; OCH), 4.45 (dd; $J_{\mathrm{OCH',NCH}}$ = 7.0 Hz, $J_{\mathrm{OCH,OCH'}}$ = 7.6 Hz; OCH′), 7.79 (d, J = 8.1 Hz, *m*-H_2), 7.98 (d, J = 8.1 Hz, *o*-H_2). − ^{13}C NMR (100 MHz, 300 K, $CDCl_3$): δ = 18.34 ($\mathrm{CH}C\mathrm{H_3}$), 20.16 ($\mathrm{CH}C\mathrm{H_3}$), 34.20 [$C\mathrm{H(CH_3)_2}$], 71.11 (NCH), 76.00 (OCH_2), 123.14 (q, $J_{\mathrm{C,F}}$ = 273.6 Hz, CF_3), 126.23 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 129.13 (*m*-C), 135.11 (q, $J_{\mathrm{C,F}}$ = 33.0 Hz, *p*-C), 142.28 (*i*-C). − R_f = 0.34 (ether/hexane, 1:2). − ^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 1.13 [d, $J(\mathrm{CH,CH_3})$ = 6.7 Hz, $\mathrm{CHC}H_3$], 1.16 [d, $J(\mathrm{CH,CH'_3})$ = 6.7 Hz, $\mathrm{CHC}H_3{}'$], 1.76 [dqq; $J(\mathrm{CH,CH_3}) = J(\mathrm{CH,CH'_3})$ = 6.7 Hz, $J_{\mathrm{CH,NCH}}$ = 8.2 Hz; $\mathrm{C}H(\mathrm{CH_3})_2$], 3.90 (ddd; $J_{\mathrm{OCH,CH}}$ = 8.4 Hz, $J_{\mathrm{OCH',CH}}$ = 7.6 Hz; NCH), 4.05 (dd; $J_{\mathrm{OCH,NCH}}$ = 8.4 Hz, $J_{\mathrm{OCH,OCH'}}$ = 6.0 Hz, OCH), 4.73 (dd; $J_{\mathrm{OCH',NCH}}$ = 7.6 Hz, $J_{\mathrm{OCH,OCH'}}$ = 6.0 Hz; OCH′), 7.77 (d, J = 8.2 Hz, *m*-H_2), 8.09 (d, J = 8.2 Hz, *o*-H_2). − ^{13}C NMR (62.5 MHz, 300 K, $CDCl_3$): δ = 18.55 ($\mathrm{CH}C\mathrm{H_3}$), 19.37 ($\mathrm{CH}C'\mathrm{H_3}$), 33.45 [$C\mathrm{H(CH_3)_2}$], 72.47 (NCH), 73.81 ($OCH_2$), 122.97 (q, $J_{\mathrm{C,F}}$ = 273.1 Hz, CF_3), 126.12 (q, $J_{\mathrm{C,F}}$ = 3.8 Hz, *o*-C), 127.73 (*m*-C), 134.62 (q, $J_{\mathrm{C,F}}$ = 32.8 Hz, *p*-C), 143.32 (*i*-C). − Mixture: $C_{12}H_{14}NO_2F_3S$ (293.30): calcd. C 49.14, H 4.81, N 4.78; found C 49.37, H 4.97, N 4.81.

TBS−Methyl Sulfoximines 103, 104: In a 10-mL flask 0.119 g (0.406 mmol) of **100**/*epi*-**100** (1:1) was dissolved in 1.2 mL of dry THF and cooled to −78°C when 0.38 mL (0.607 mmol) of methyllithium (1.6 M in ether) was added dropwise. The reaction was monitored by TLC (eluents: ether/hexane, 1:2 and ethyl acetate/hexane, 3:1). After 25 min, the reaction mixture was poured onto ice-cold sat. aqueous $(NH_4)_2CO_3$. The aqueous layer was extracted with ether (3 × 20 mL), the combined organic layers were dried and concentrated in vacuo. Purification by flash chromatography yielded 44 mg (70%) and 56 mg (89%) of the epimeric (S_S)- and (R_S)-hydroxy sulfoximines **101** and **102**, respectively.

(*S*$_S$) Epimer 101: R_f = 0.23 (ethyl acetate/hexane, 3:1). − $[\alpha]_D^{20}$ = 123.6 (*c* = 1.0, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 1322 cm^{-1} (C−F), 1244, 1136 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 0.86 [d, $J(\mathrm{CH,CH_3})$ = 6.5 Hz, $\mathrm{CHC}H_3$], 0.89 [d, $J(\mathrm{CH,CH'_3})$ = 6.5 Hz, $\mathrm{CHC}H_3{}'$], 1.69 [dqq; $J(\mathrm{CH,CH_3}) = J(\mathrm{CH,CH'_3})$ = 6.7 Hz, $J_{\mathrm{CH,NCH}}$ = 5.4 Hz; $\mathrm{C}H(\mathrm{CH_3})_2$], 2.68 (ddd; $J_{\mathrm{OCH,CH}}$ = 7.9 Hz, $J_{\mathrm{OCH',CH}}$ = 2.8 Hz; NCH), 3.15 (br. s, OH), 3.21 (s, SCH_3), 3.46 (dd; $J_{\mathrm{OCH,NCH}}$ = 7.9 Hz, $J_{\mathrm{OCH,OCH'}}$ = 11.4 Hz; OCH), 3.55 (dd; $J_{\mathrm{OCH',NCH}}$ = 2.8 Hz, $J_{\mathrm{OCH,OCH'}}$ = 11.4 Hz; OCH′), 7.81 (d, J = 8.3 Hz, *m*-H_2), 8.02 (d, J = 8.3 Hz, *o*-H_2). − ^{13}C NMR (62.5 MHz, 300 K, $CDCl_3$): δ = 18.61 ($\mathrm{CH}C\mathrm{H_3}$), 19.45 ($\mathrm{CH}C'\mathrm{H_3}$), 31.58 [$C\mathrm{H(CH_3)_2}$], 45.30 ($SCH_3$), 64.36 (NCH), 65.21 ($OCH_2$), 123.21 (q, $J_{\mathrm{C,F}}$ = 273.4 Hz, CF_3), 126.42 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 129.04 (*m*-C), 134.71 (q, $J_{\mathrm{C,F}}$ = 33.2 Hz, *p*-C), 142.76 (*i*-C). − $C_{13}H_{18}F_3NO_2S$ (309.34): calcd. C 50.48, H 5.86, N 4.53; found C 50.75, H 5.88, N 4.34.

(*R*$_S$) Epimer 102: R_f = 0.18 (ethyl acetate/hexane, 3:1). − $[\alpha]_D^{20}$ = −38.9 (*c* = 1.0, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 1323 (C−F), 1244, 1140 (N=S=O) cm^{-1}. − ^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 0.96 [d, $J(\mathrm{CH,CH_3})$ = 6.7 Hz, $\mathrm{CHC}H_3$], 0.99 [d, $J(\mathrm{CH,CH'_3})$ = 7.0 Hz, $\mathrm{CHC}H_3{}'$], 1.89 [dqq; $J(\mathrm{CH,CH_3})$ = 6.7 Hz, $J(\mathrm{CH,CH'_3})$ = 7.0 Hz, $J_{\mathrm{CH,NCH}}$ = 5.4 Hz; $\mathrm{C}H(\mathrm{CH_3})_2$], 2.53 (br. s, OH), 3.08 (m, NCH), 3.15 (s, SCH_3), 3.49 (dd; $J_{\mathrm{OCH,NCH}}$ = 7.5 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.8 Hz; OCH), 3.76 (dd; $J_{\mathrm{OCH',NCH}}$ = 3.9 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.8 Hz; OCH′), 7.82 (d, J = 8.3 Hz, *m*-H_2), 8.16 (d, J = 8.3 Hz, *o*-H_2). − ^{13}C NMR (62.5 MHz, 300 K, $CDCl_3$): δ = 18.59 ($\mathrm{CH}C\mathrm{H_3}$), 19.46 ($\mathrm{CH}C'\mathrm{H_3}$), 31.55 [$C\mathrm{H(CH_3)_2}$], 43.15 ($SCH_3$), 63.25 (NCH), 64.57 ($OCH_2$), 123.23 (q, $J_{\mathrm{C,F}}$ = 272.8 Hz, CF_3), 126.37 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 128.74 (*m*-C), 134.77 (q, $J_{\mathrm{C,F}}$ = 33.7 Hz, *p*-C), 144.05 (*i*-C). − $C_{13}H_{18}F_3NO_2S$ (309.34): calcd. C 50.48, H 5.86, N 4.53; found C 50.54, H 5.88, N 4.81. − 367 mg (1.25 mmol) of the (S_S) epimer was TBS-protected applying 282 mg (1.88 mmol) of TBS chloride, 46 mg (0.37 mmol) of DMAP and 183 mg (2.5 mmol) of ethyldimethylamine yielding 412 mg (78%) of the expected product **103** melting at 49.6°C. − R_f = 0.36 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 92.8 (*c* = 1.0, CH_2Cl_2). − IR (KBr): $\tilde{\nu}$ = 1323 cm^{-1} (C−F), 1256, 1140 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 0.03, 0.05 [$\mathrm{Si(CH_3)_2}$], 0.87 [$\mathrm{SiC(CH_3)_3}$], 0.87 [d, $J(\mathrm{CH,CH_3})$ = 6.9 Hz, $\mathrm{CHC}H_3$], 0.90 [d, $J(\mathrm{CH,CH'_3})$ = 6.9 Hz, $\mathrm{CHC}H_3{}'$], 1.89 [dqq; $J(\mathrm{CH,CH_3}) = J(\mathrm{CH,CH'_3})$ = 6.9 Hz, $J_{\mathrm{CH,NCH}}$ = 4.2 Hz; $\mathrm{C}H(\mathrm{CH_3})_2$], 2.98 (ddd; $J_{\mathrm{CH,NCH}}$ = 4.2 Hz, $J_{\mathrm{OCH,NCH}} = J_{\mathrm{OCH',NCH}}$ = 6.5 Hz; NCH), 3.17 (s, SCH_3), 3.65 (d, $J_{\mathrm{OCH,NCH}}$ = 6.5 Hz, OCH_2), 7.81 (d, J = 8.3 Hz, *m*-H_2), 8.12 (d, J = 8.3 Hz, *o*-H_2). − ^{13}C NMR (67.5 MHz, 300 K, $CDCl_3$): δ = −5.38, −5.28 [$\mathrm{Si(CH_3)_2}$], 16.96 ($\mathrm{CH}C\mathrm{H_3}$), 18.34, [$\mathrm{Si}C\mathrm{(CH_3)_3}$], 20.04 ($\mathrm{CH}C'\mathrm{H_3}$), 25.98 [$\mathrm{SiC(}C\mathrm{H_3)_3}$], 29.81 [$C\mathrm{H(CH_3)_2}$], 44.83 ($SCH_3$), 62.26 (NCH), 66.30 ($OCH_2$), 123.39 (q, $J_{\mathrm{C,F}}$ = 273.4 Hz, CF_3), 126.13 (q, $J_{\mathrm{C,F}}$ = 3.7 Hz, *o*-C), 129.02 (*m*-C), 134.32 (q, $J_{\mathrm{C,F}}$ = 33.3 Hz, *p*-C), 144.60 (*i*-C). − $C_{19}H_{32}F_3NO_2SSi$ (423.60): calcd. C 53.87, H 7.61, N 3.31; found C 53.96, H 7.50, N 3.19. − 389 mg (1.326 mmol) of the (R_S) epimer was TBS-protected applying and 300 mg (1.99 mmol) of TBS chloride, 49 mg (0.40 mmol) of DMAP and 196 mg (2.65 mmol) of ethyldimethylamine yielding 498 mg (88%) of **104** melting at 55.7°C. − R_f = 0.29 (ethyl acetate/hexane, 3:1). − $[\alpha]_D^{20}$ = −49.4 (*c* = 1.0, CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 1322 cm^{-1} (C−F), 1250, 1134 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 0.01 [s, $\mathrm{Si(CH_3)_2}$], 0.87 [s, $\mathrm{SiC(CH_3)_3}$], 0.96 [d, $J(\mathrm{CH,CH_3})$ = 6.9 Hz, $\mathrm{CHC}H_3$], 1.03 [d, $J(\mathrm{CH,CH'_3})$ = 6.9 Hz, $\mathrm{CHC}H_3{}'$], 2.02 [dqq; $J(\mathrm{CH,CH_3}) = J(\mathrm{CH,CH'_3})$ = 6.9 Hz, $J_{\mathrm{CH,NCH}}$ = 3.6 Hz; $\mathrm{C}H(\mathrm{CH_3})_2$], 3.08 (ddd; $J_{\mathrm{CH,NCH}}$ = 3.6 Hz, $J_{\mathrm{OCH,NCH}}$ = 6.5 Hz, $J_{\mathrm{OCH',NCH}}$ = 6.8 Hz; NCH), 3.16 (s, SCH_3), 3.49 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.5 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.1 Hz; OCH), 3.60 (dd; $J_{\mathrm{OCH',NCH}}$ = 6.8 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.1 Hz; OCH′), 7.83 (d, J = 8.3 Hz, *m*-H_2), 8.20 (d, J = 8.3 Hz, *o*-H_2). − ^{13}C NMR (62.5 MHz, 300 K, $CDCl_3$): δ = −5.43, −5.33 [$\mathrm{Si(CH_3)_2}$], 17.00 ($\mathrm{CH}C\mathrm{H_3}$), 18.41, [$\mathrm{Si}C\mathrm{(CH_3)_3}$], 19.87 ($\mathrm{CH}C'\mathrm{H_3}$), 25.97 [$\mathrm{SiC(}C\mathrm{H_3)_3}$], 30.26 [$C\mathrm{H(CH_3)_2}$], 44.88 ($SCH_3$), 61.72 (NCH), 65.72 ($OCH_2$), 123.44 (q, $J_{\mathrm{C,F}}$ = 272.4 Hz, CF_3), 126.19 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 129.19 (m-C), 134.43 (q, $J_{\mathrm{C,F}}$ = 39.9 Hz, *p*-C), 145.19 (*i*-C). − $C_{19}H_{32}F_3NO_2SSi$ (423.60): calcd. C 53.87, H 7.61, N 3.31; found C 53.84, H 7.57, N 3.27.

Alcohol 105: 407 mg (0.981 mmol) of (S_S)-methyl sulfoximine **103** was dissolved in 3 mL of dry THF and 1 mL of toluene; then 522 mg (1.153 mmol) of *n*BuLi (2.207 mmol/g in hexane) was added at −78°C. The solution changed colour to green and lightened up when after 15 min 129 mg (1.54 mmol) of cyclopentanone was added. After 5 min, all the starting material had been consumed (TLC, eluent: ether/hxane, 1:1) and the reaction was quenched by pouring the mixture into sat. aqueous NH_4Cl. The aqueous phase was extracted with ether (3 × 30 mL), the combined organic layers were dried and concentrated in vacuo. Purification by chromatography (ether/hexane) yielded 426 mg (87%) of **105** as a white solid, m.p. 98.9°C. Recrystallisaton from ethyl acetate/hexane yielded crystals suitable for X-ray crystallographic analysis. − R_f = 0.55 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 103.6 (*c* = 1.0, CH_2Cl_2). − IR

(KBr): $\tilde{\nu}$ = 3327 cm^{-1} (OH), 1323 (C−F), 1264, 1136 (N=S=O). − ^{1}H NMR (400 MHz, 300 K, CDCl$_3$): δ = −0.01, 0.02 [2 × s, Si(CH$_3$)$_2$], 0.84 [SiC(C*H*$_3$)$_3$], 0.87 [d, *J*(CH,CH$_3$) = 6.9 Hz, CHC*H*$_3$], 0.89 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.34−2.10 [m; 2-H$_2$, 3-H$_2$, 4-H$_2$, 5-H$_2$, C*H*(CH$_3$)$_2$], 2.82 (ddd; $J_{\mathrm{CH,NCH}}$ = 3.5 Hz, $J_{\mathrm{OCH,NCH}}$ = 8.2 Hz, $J_{\mathrm{OCH',NCH}}$ = 5.0 Hz; NCH), 3.07 (d, $J_{1,1'}$ = 13.6 Hz, SCH), 3.58 (dd; $J_{\mathrm{OCH,NCH}}$ = 8.2 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.1 Hz; OCH), 3.72 (dd; $J_{\mathrm{OCH',NCH}}$ = 5.1 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.1 Hz; OCH′), 3.88 (br. d, $J_{1,1'}$ = 13.6 Hz, SCH′), 7.83 (d, *J* = 8.2 Hz, *m*-H$_2$), 8.09 (d, *J* = 8.2 Hz, *o*-H$_2$). − ^{13}C NMR (100 MHz, 300 K, CDCl$_3$): δ = −5.49, −5.37 [Si(CH$_3$)$_2$], 16.26 (CH*C*H$_3$), 18.21 [Si*C*(CH$_3$)$_3$], 20.67 (CH*C*′H$_3$), 22.82, 24.03 (C-3 or C-4), 25.89 [SiC(*C*H$_3$)$_3$], 28.75 [*C*H(CH$_3$)$_2$], 38.68, 41.59 (C-2 or C-5), 62.18 (NCH), 65.12, 65.17 (SCH$_2$ or OCH$_2$), 79.79 (COH), 123.25 (q, $J_{\mathrm{C,F}}$ = 273.6 Hz, CF$_3$), 126.38 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 129.71 (*m*-C), 134.88 (q, $J_{\mathrm{C,F}}$ = 33.6 Hz, *p*-C), 143.47 (*i*-C). − $C_{24}H_{40}F_3NO_3SSi_2$ (507.72): calcd. C 56.78, H 7.94, N 2.76; found C 56.85, H 7.89, N 2.73.

Ketones 106, 107: In a 10-mL flask 185 mg (0.44 mmol) of (S_S)-sulfoximine **103** was dissolved in 1.1 mL of dry THF. At −78°C 240 mg of *n*BuLi (2.19 mmol/g in hexane) was added via hypodermic syringe, while the solution turned red. After 20 min, 109 mg (0.704 mmol) of the vinylogous ester **85**[46] was added dropwise. After 5 min, the temperature was allowed to increase to room temp. over a period of 80 min while the color changed via green to yellow. The reaction was monitored by TLC (eluent: ether/hexane, 1:1). Elimination was induced by adding 185 mg of Amberlyst 15 and two drops of water at room temp. After 15 min, the resin was separated by filtration, the crude product was concentrated and purified by flash chromatography yielding 122 mg (54%) of the desired ketone **106**, being a colourless solid, m.p. 105.8°C. − R_f = 0.15 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 33.2 (*c* = 1.0, CH$_2$Cl$_2$). − IR (KBr): $\tilde{\nu}$ = 1669 cm^{-1} (C=O), 1322 (C−F), 1258, 1141 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.03, 0.05 [2 × s, Si(CH$_3$)$_2$], 0.87 [s, SiC(C*H*$_3$)$_3$], 0.91 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$], 0.92 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.94 [m; C*H*(CH$_3$)$_2$, 5-H$_2$], 2.33 (m, 6-H$_2$), 2.40 (br. dt; $J_{\mathrm{4\text{-}H,4\text{-}H'}}$ = 18.7 Hz, $J_{\mathrm{5,4\text{-}H}}$ = 5.9 Hz; 4-H), 2.62 (br. dt; $J_{\mathrm{4\text{-}H,4\text{-}H'}}$ = 18.7 Hz, $J_{\mathrm{5,4\text{-}H'}}$ = 5.8 Hz; 4-H′), 3.11 [ddd; $J_{\mathrm{CH,NCH}}$ = 4.0 Hz, *J*(NCH,OCH$_2$) = 6.4 Hz; NCH], 3.65 [d, *J*(NCH,OCH$_2$) = 6.4 Hz, OCH$_2$], 3.98 (d, $J_{\mathrm{SCH,SCH'}}$ = 13.4 Hz, SCH), 4.25 (d, $J_{\mathrm{SCH,SCH'}}$ = 13.4 Hz, SCH′), 5.56 (s, 2-H), 7.80 (d, *J* = 8.3 Hz, *m*-H$_2$), 8.03 (d, *J* = 8.3 Hz, *o*-H$_2$). − ^{13}C NMR (67.5 MHz, 300 K, CDCl$_3$): δ = −5.38, −5.29 [Si(CH$_3$)$_2$], 16.86 (CH*C*H$_3$), 18.35, [Si*C*(CH$_3$)$_3$], 20.51 (CH*C*H$_3$), 22.59 (C-5), 25.96 [SiC(*C*H$_3$)$_3$], 30.06 [*C*H(CH$_3$)$_2$], 30.09, 37.05 (C-6 or C-4), 62.44 (NCH), 63.32, 66.34 (SCH$_2$ or OCH$_2$), 123.13 (q, $J_{\mathrm{C,F}}$ = 273.1 Hz, CF$_3$), 126.09 (q, $J_{\mathrm{C,F}}$ = 3.8 Hz, *o*-C), 129.69 (*m*-C), 132.02 (C-2), 134.80 (q, $J_{\mathrm{C,F}}$ = 33.0 Hz, *p*-C), 142.08 (*i*-C) 152.48 (C-3), 198.45 (C-1). − $C_{25}H_{38}F_3NO_3SSi$ (517.72): calcd. C 58.00, H 7.40, N 2.71; found C 58.22, H 7.57, N 2.95. − Following the same procedure 242 mg (0.57 mmol) of the (R_S) epimer **104** was converted to 220 mg (74%) of the corresponding ketone **107** by applying 303 mg (0.685 mmol) of *n*BuLi, 141 mg (0.914 mmol) of **85**,[46] 2.5 mL of dry THF, 4 drops of water and 242 mg of Amberlyst 15. The product was found to be a colourless solid, m.p. 108.2°C. − R_f = 0.09 (ether/hexane, 1:1). − $[\alpha]_D^{20}$ = 20.0 (*c* = 1.0, CH$_2$Cl$_2$). − IR (film): $\tilde{\nu}$ = 1670 cm^{-1} (C=O), 1322 (C−F), 1264, 1137 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.04 [s, Si(CH$_3$)$_2$], 0.83 [s, SiC(CH$_3$)$_3$], 0.91 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$], 0.97 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.96 [m; C*H*(CH$_3$)$_2$, 5-H$_2$], 2.33 (m, 6-H$_2$), 2.44 (br. dt; $J_{\mathrm{4\text{-}H,4\text{-}H'}}$ = 18.8 Hz, $J_{\mathrm{5,4\text{-}H}}$ = 6.0 Hz; 4-H), 2.64 (br. dt; $J_{\mathrm{4\text{-}H,4\text{-}H'}}$ = 18.8 Hz, $J_{\mathrm{5,4\text{-}H'}}$ = 6.0 Hz; 4′-H), 3.13 (ddd; $J_{\mathrm{CH,NCH}}$ = 3.6 Hz, $J_{\mathrm{OCH,NCH}}$ = 6.7 Hz, $J_{\mathrm{OCH',NCH}}$ = 6.2 Hz; NCH), 3.48 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.7 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.0 Hz; OCH), 3.56 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.2 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.0 Hz; OCH′), 3.86 (d, $J_{\mathrm{SCH,SCH'}}$ = 13.3 Hz, SCH), 4.12 (d, $J_{\mathrm{SCH,SCH'}}$ = 13.3 Hz, SCH′), 5.63 (s, 2-H), 7.77 (d, *J* = 8.2 Hz, *m*-H$_2$), 8.07 (d, *J* = 8.2 Hz, *o*-H$_2$). − ^{13}C NMR (67.5 MHz, 300 K, CDCl$_3$): d = −5.58 [Si(CH$_3$)$_2$], 16.86 (CH*C*H$_3$), 18.22 [Si*C*(CH$_3$)$_3$], 19.70 (CH*C*H$_3$), 22.40 (5-C), 25.75 [SiC(*C*H$_3$)$_3$], 30.02 [*C*H(CH$_3$)$_2$], 30.39, 36.88 (C-4 or C-6), 61.92 (NCH), 64.71, 65.64 (SCH$_2$ or OCH$_2$), 123.21 (q, $J_{\mathrm{C,F}}$ = 273.5 Hz, CF$_3$), 126.08 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 129.63 (*m*-C), 132.53 (C-3), 134.78 (q, $J_{\mathrm{C,F}}$ = 33.2 Hz, *p*-C), 143.25 (*i*-C) 151.71 (C-2), 198.36 (C-1). − $C_{25}H_{38}F_3NO_3SSi$ (517.72): calcd. C 58.00, H 7.40, N 2.71; found C 57.96, H 7.45, N 2.78.

Alkenyl Sulfoximines 108, 109: In a 25-mL Schlenk flask 0.105 mL (0.181 g, 0.955 mmol) of titanium tetrachloride was mixed with 0.477 mL (0.955 mmol) of dimethylzinc (2 M in toluene) in 0.5 mL of dry CH$_2$Cl$_2$ and stirred at −30°C for 10 min whereupon the colour of the solution turned from orange to dark green. 215 mg (0.415 mmol) of (R_S)-ketone **107**, dissolved in 1 mL of CH$_2$Cl$_2$, was added at −60°C (colour changed to dark red). The reaction was kept exactly at −30°C and monitored by TLC (ether/hexane, 1:3, 1.5−2.0 h). At −78°C the mixture was diluted with 10 mL of dry CH$_2$Cl$_2$ and poured into an ice-cold sat. aqueous (NH$_4$)$_2$CO$_3$. The two-phase system was vigorously stirred for another 30 min after which the mixture had reached room temp. The aqueous layer was extracted with ether (3 × 20 mL). The combined organic layers were dried and concentrated in vacuo. Purification by flash chromatography yielded 99 mg (45%) of the dimethylated (R_S)-sulfoximine **109** being a white solid, m.p. 84.6°C and 9 mg of the corresponding reduction product **111** (R_S). − Following the same procedure 291 mg (0.245 g, 0.56 mmol) of the (S_S)-enone **106** was converted to the corresponding sulfoximine (S_S)-**108** by employing 0.142 mL (1.293 mmol) of titanium tetrachloride, 0.646 mL (1.296 mmol) of dimethylzinc (2 M in toluene), 0.65 mL and 1.5 mL of dry CH$_2$Cl$_2$ (for Lewis acid/dimethylzinc and ketone, respectively) at −30°C. Purification by flash chromatography yielded two colourless solids, found to be 38 mg (7.1%) of the desired product **108** as a colourless solid and 40 mg (17%) of the corresponding sulfinamide **110** (S_S) melting at 92.7°C.

(S_S) Epimer 108: R_f = 0.50 (ether/hexane, 1:3). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.02, 0.01 [2 × s, Si(CH$_3$)$_2$], 0.63 (s, 3-CH$_3$), 0.80 (s, 3-CH$_3$′), 0.85 [s, SiC(C*H*$_3$)$_3$], 0.91 [d, *J*(CH,CH$_3$) = 6.7 Hz, CHC*H*$_3$], 0.92 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.25, 1.52 (2 × m; 4-H$_2$, 5-H$_2$), 1.96 [m; C*H*(CH$_3$)$_2$, 6-CH], 2.16 [br. dt; $J_{\mathrm{4\text{-}H,4\text{-}H'}}$ = 17.7 Hz, *J*(4-H,CH$_2$) = 6.2 Hz; 4-H′], 2.99 (ddd; $J_{\mathrm{CH,NCH}}$ = 3.6 Hz, $J_{\mathrm{OCH,NCH}}$ = 6.0 Hz, $J_{\mathrm{OCH',NCH}}$ = 7.6 Hz; NCH), 3.60 (dd; $J_{\mathrm{OCH,NCH}}$ = 7.6 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.0 Hz; OCH), 3.68 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.0 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.0 Hz; OCH′), 3.78 (br. s, SCH$_2$), 4.86 (s, 2-H), 7.75 (d, *J* = 8.2 Hz, *m*-H$_2$), 7.97 (d, *J* = 8.2 Hz, *o*-H$_2$). − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.02, −4.93 [Si(CH$_3$)$_2$], 16.82 (CH*C*H$_3$), 18.65 [Si*C*(CH$_3$)$_3$], 20.06 (CH*C*′H$_3$), 21.09 (C-5), 26.33 [SiC(*C*H$_3$)$_3$], 29.07 [*C*H(CH$_3$)$_2$], 29.51, 29.55 (3-CH$_3$ or 3-C′H$_3$), 29.88 (C-6), 32.50 (C-3), 36.61 (C-4), 62.55 (NCH), 65.91, 66.43 (SCH$_2$ or OCH$_2$), 124.41 (q, $J_{\mathrm{C,F}}$ = 273.7 Hz, CF$_3$), 125.48 (C-1), 125.90 (q, $J_{\mathrm{C,F}}$ = 3.4 Hz, *o*-C), 130.83 (*m*-C), 134.51 (q, $J_{\mathrm{C,F}}$ = 32.8 Hz, *p*-C), 142.48 (C-2), 143.22 (*i*-C).

(R_S) Epimer 109: R_f = 0.40 (ether/hexane, 1:3). − $[\alpha]_D^{20}$ = −23.6 (*c* = 1.0, CH$_2$Cl$_2$). − IR (film): $\tilde{\nu}$ = 1323 cm^{-1} (C−F), 1252, 1140 (N=S=O). − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = −0.05 [s, 2 × Si(C*H*$_3$)$_2$], 0.63 (s, 3-CH$_3$), 0.80 (s, 3-CH′$_3$), 0.83 [s, SiC(CH$_3$)$_3$], 0.91 [d, *J*(CH,CH$_3$) = 6.7 Hz, CHC*H*$_3$], 0.98 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 1.26, 1.53 (2 × m; 4-H$_2$, 5-H$_2$), 1.91 [m;

C*H*(CH$_3$)$_2$, 6-CH], 2.22 [br. dt; $J_{4\text{-H},4\text{-H}'}$ = 17.7 Hz, *J*(4-H′,CH$_2$) = 6.4 Hz; 4-H′], 3.51 (ddd; $J_{\mathrm{CH,NCH}}$ = 3.7 Hz, $J_{\mathrm{OCH,NCH}}$ = 6.5 Hz, $J_{\mathrm{OCH',NCH}}$ = 6.8 Hz; NCH), 3.45 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.5 Hz, $J_{\mathrm{OCH,OCH'}}$ = 9.8 Hz; OCH), 3.55 (dd; $J_{\mathrm{OCH,NCH}}$ = 6.8 Hz, $J_{\mathrm{OCH,OCH'}}$ = 9.8 Hz; OCH′), 3.68 (br. d, $J_{\mathrm{SCH,SCH'}}$ = 13.5 Hz, SCH),3.82 (br. d, $J_{\mathrm{SCH,SCH'}}$ = 13.5 Hz, SCH′), 4.89 (s, 2-H), 7.73 (d, *J* = 8.1 Hz, *m*-H$_2$), 8.03 (d, *J* = 8.1 Hz, *o*-H$_2$). − ^{13}C NMR (62.5 MHz, 300 K, CDCl$_3$): δ = −5.07, −5.01 [Si(CH$_3$)$_2$], 17.38 (CH*C*H$_3$), 18.74 [Si*C*(CH$_3$)$_3$], 20.06 (CH*C*′H$_3$), 20.20 (C-5), 26.30 [SiC(*C*H$_3$)$_3$], 29.12 [C*H*(CH$_3$)$_2$], 29.46, 29.56 (3-CH$_3$ or 3-C′H$_3$), 30.77 (C-6), 32.51 (C-3), 36.59 (C-4), 61.88 (NCH), 65.64, 66.18 (SCH$_2$ or OCH$_2$), 121.62 (CF$_3$), 125.12 (C-1), 125.89 (q, $J_{\mathrm{C,F}}$ = 3.8 Hz, *o*-C), 130.67 (*m*-C), 134.41 (q, $J_{\mathrm{C,F}}$ = 32.7 Hz, *p*-C), 143.45 (C-2), 143.8 (*i*-C). − $C_{27}H_{44}F_3NO_2SSi$ (531.79): calcd. C 60.98, H 8.32, N 2.63; found C 61.00, H 8.35, N 2.88.

(S_S) Sulfinamide 110: R_f = 0.37 (ether/hexane, 1:3). − $[\alpha]_\mathrm{D}^{20}$ = 106.8 (*c* = 0.5, CH$_2$Cl$_2$). − IR (film): ṽ = 1323 (C−F), 1060 (S=O) cm^{-1}. − ^{1}H NMR (250 MHz, 300 K, CDCl$_3$): δ = 0.04, 0.05 [2 × s, Si(C*H*$_3$)$_2$], 0.76 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$], 0.79 [d, *J*(CH,CH′$_3$) = 6.9 Hz, CHC*H*$_3$′], 0.90 [s, SiC(C*H*$_3$)$_3$], 1.79 [ddd; *J*(CH,CH$_3$) = 6.8, *J*(CH,CH′$_3$) = 6.9 Hz, $J_{\mathrm{CH,NCH}}$ = 6.3; C*H*(CH$_3$)$_2$], 2.96 [ddt; $J_{\mathrm{CH,NCH}}$ = 6.3 Hz, *J*(NCH,OCH$_2$) = 4.2 Hz, $J_{\mathrm{NH,NCH}}$ = 9.2 Hz; NCH], 3.77 [d, *J*(NCH,OCH$_2$) = 4.2 Hz, OCH$_2$], 4.52 (br. d, $J_{\mathrm{NH,NCH}}$ = 9.2 Hz, NH), 7.75 (d, *J* = 8.2 Hz, *m*-H$_2$), 7.87 (d, *J* = 8.2 Hz, *o*-H$_2$). − ^{13}C NMR (250 MHz, 300 K, CDCl$_3$): δ −5.46, −5.42 [Si(CH$_3$)$_2$], 18.22 [Si*C*(CH$_3$)$_3$], 18.58 (CH*C*H$_3$), 19.27 (CH*C*′H$_3$), 25.86 [SiC(*C*H$_3$)$_3$], 29.39 [*C*H(CH$_3$)$_2$], 60.36 (NCH), 64.77 (OCH$_2$), 123.64 (q, $J_{\mathrm{C,F}}$ = 273.3 Hz, CF$_3$), 125.60 (q, $J_{\mathrm{C,F}}$ = 3.6 Hz, *o*-C), 126.79 (*m*-C), 132.86 (q, $J_{\mathrm{C,F}}$ = 33.0 Hz, *p*-C), 149.37 (*i*-C). − $C_{18}H_{30}F_3NO_2SSi_2$ (407.51): calcd. C 52.78, H 7.38, N 3.42; found C 52.66, H 7.44, N 3.14.

(R_S)-Sulfinamide 111: R_f = 0.15 (ether/hexane, 1:3). − ^{1}H NMR (250 MHz 300 K, CDCl$_3$): δ = 0.03, 0.04 [2 × s, Si(CH$_3$)$_2$], 0.85 [s, SiC(CH$_3$)$_3$], 0.98 [d, *J*(CH,CH$_3$) = 6.8 Hz, CHC*H*$_3$), 1.00 [d, *J*(CH,CH′$_3$) = 6.8 Hz, CHC*H*$_3$′], 2.02 [ddd; *J*(CH,CH$_3$) = *J*(CH,CH′$_3$) = 6.8 Hz, $J_{\mathrm{CH,NCH}}$ = 6.0; C*H*(CH$_3$)$_2$], 3.16 (dddd; $J_{\mathrm{CH,NCH}}$ = 6.0 Hz, $J_{\mathrm{OCH,NCH}}$ = 5.0 Hz, $J_{\mathrm{OCH',NCH}}$ = 4.1 Hz, $J_{\mathrm{NH,NCH}}$ = 8.5 Hz; NCH), 3.66 (dd; $J_{\mathrm{OCH,NCH}}$ = 5.0 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.2 Hz; OCH), 3.73 (dd; $J_{\mathrm{OCH,NCH}}$ = 4.1 Hz, $J_{\mathrm{OCH,OCH'}}$ = 10.2 Hz; OCH′), 4.26 (br. d, $J_{\mathrm{NH,NCH}}$ = 8.5 Hz, NH), 7.76 (d, *J* = 8.5 Hz, *m*-H$_2$), 7.88 (d, *J* = 8.5 Hz, *o*-H$_2$).

Acknowledgments

This work was supported by the Fonds der Chemischen Industrie. M. R. acknowledges support by the Deutsche Forschungsgemeinschaft under grant Re 1007/1-3 and 1-4, M. V. and M. G. thank the Graduiertenkolleg "Chemische und Biologische Synthese von Wirkstoffen" for fellowships. Furthermore we are indebted to Dr. J. W. Bats for his careful work on the X-ray structural analysis of **37**, **41** and **105**. Dr. B. Berger solved the X-ray structure of **71**. Continuous support from Prof. Dr. C. Griesinger is gratefully acknowledged.

---

[1] J. Buckingham, *Dictionary of Natural Products*, Chapman & Hall Electronic Publishing Division, London, UK, **1994**.

[2] J. Kallmerten, *Tetrahedron Lett.* **1984**, *25*, 2843−2846.

[3] P. A. Bartlett, P. C. Ting, *J. Org. Chem.* **1986**, *51*, 2230−2240.

[4] T. Nagamitsu, T. Sunazuka, R. Obata, H. Tomoda, H. Tanaka, Y. Harigaya, S. Omura, *J. Org. Chem.* **1995**, *60*, 8126−8127.

[5] E. Gössinger, M. Graupe, C. Kratky, K. Zimmermann, *Tetrahedron* **1997**, *53*, 3083−3100.

[6] M. Reggelin, H. Weinberger, T. Heinrich, *Liebigs Ann.* **1997**, 1881−1886.

[7] [7a] M. Reggelin, H. Weinberger, M. Gerlach, R. Welcker, *J. Am. Chem. Soc.* **1996**, *118*, 4765−4777. − [7b] J. Bund, H.-J. Gais, E. Schmitz, I. Erdelmeier, G. Raabe, *Eur. J. Org. Chem.* **1998**, *7*, 1319−1335. − [7c] S. Boßhammer, H.-J. Gais, *Synlett* **1998**, 99−101. − [7d] H.-J. Gais, H. Müller, J. Decker, R. Hainz, *Tetrahedron Lett.* **1995**, *36*, 7433−7436. − [7e] R. Hainz, H.-J. Gais, G. Raabe, *Tetrahedron: Asymmetry* **1996**, *7*, 2505−2508.

[8] M. Reggelin, R. Welcker, *Tetrahedron Lett.* **1995**, *35*, 5885−5886.

[9] [9a] V. J. Paul, W. Fenical, *Tetrahedron Lett.* **1980**, *21*, 2787−2790. − [9b] R. de Nys, A. D. Wright, G. M. König, O. Sticher, *J. Nat. Prod.* **1993**, *56*, 877−883.

[10] P. A. Horton, P. Crews, *J. Nat. Prod.* **1995**, *58*, 44−50.

[11] M. Reggelin, H. Weinberger *Angew. Chem.* **1994**, *106*, 489−491; *Angew. Chem. Int. Ed.* **1994**, *33*, 444−446.

[12] The terms (S_X) and (R_X) are descriptors used to describe the sense of chirality (*S*) or (*R*) at heteroatom positions (X). This nomenclature was introduced by: D. J. Cram, J. Day, D. R. Rayner, D. M. von Schriltz, D. J. Duchamp, D. C. Garwood, *J. Am. Chem. Soc.* **1970**, *92*, 7369−7384.

[13] M. Reggelin, H. Weinberger, *Tetrahedron Lett.* **1992**, *33*, 6959−6962.

[14] Although until now we were not able to isolate the transmetallation products and identify them unambiguously as the proposed titanium compounds **31**−**34**, their existence is strongly supported by experiments employing α-methylated sulfoximines.[11] Furthermore, very recently Gais et al. (H. J. Gais, personal communication; H. J. Gais, R. Hainz, G. Raabe, J. Runsink, *Angew. Chem.* **1998**, accepted) succeeded in the isolation and X-ray structural characterisation of a bis(sulfonimidoylallyl)titanium complex. This complex, which has been synthesised in a very similar way to our method, is characterised by Ti−C bonds as assumed for **31**−**34**.

[15] [15a] H. Weinberger, PhD Thesis, Frankfurt/M., **1994**. − [15b] D. W. Knight, D. Shaw, G. Fenton *Synlett* **1994**, 295−296. − [15c] M. De Amici, C. De Micheli, G. Molteni, D. Pitrè, G. Carrea, S. Riva, S. Spezia, L. Zetta, *J. Org. Chem.* **1991**, *56*, 67−72.

[16] [16a] J. W. Bats, M. Gerlach, M. Reggelin, **1998** (compounds **37**, **41**); J. W. Bats, M. Vogt, M. Reggelin, **1999** (compound **105**): X-ray crystallographic data (excluding structure factors) for the structures of these compounds have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-104998 (**37**), -112150 (**41**), -113894 (**105**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code + 44-1223/336-033; E-mail: deposit@ccdc.com.ac.uk]. − [16b] J. W. Bats, B. Berger, M. Gerlach, M. Reggelin, *Acta Crystallogr., Sect. C: Cryst. Struc. Commun.* **1999**, *C55*, IUC9900002.

[17] J. M. Hook, *Synth. Commun.* **1984**, *14*, 83−87.

[18] K. C. Nicolaou, *Angew. Chem.* **1996**, *108*, 120−136; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 589−607.

[19] [19a] T. Nakata, S. Nomura, H. Matsukura, *Chem. Pharm. Bull.* **1996**, *44*, 627−629. − [19b] D. Xi, D. T. Kurz, J. S. Ransdell, *Biochem. Pharmacol.* **1996**, *51*, 759−769. − [19c] M. Satake, S. Ishida, T. Yasumoto, M. Murata, *J. Am. Chem. Soc.* **1995**, *117*, 7019−7020.

[20] M. Takasaki, T. Konoshima, M. Kozuka, M. Haruna, K. Ito, T. Shingu, *Chem. Pharm. Bull.* **1994**, *58*, 2591−2597.

[21] R. Nakayama, M. Murata, S. Homma, K. Aida, *Agric. Biol. Chem.* **1990**, *54*, 231−232.

[22] G. A. Olah, *Friedel Crafts and Related Reactions*, Wiley, New York, **1963**−**1964**, vol. 1 and 2.

[23] M. Takasaki, T. Konoshima, K. Fujitami, S. Yoshida, H. Nishimura, H. Tokuda, H. Nishino, A. Iwashima, M. Kozuka, *Chem. Pharm. Bull.* **1990**, *38*, 2737−2739.

[24] M. Takasaki, T. Konoshima, T. Shingu, M. Tokuda, H. Nishino, A. Iwashima, M. Kozuka, *Chem. Pharm. Bull.* **1990**, *38*, 1444−1446.

[25] M. Ohigashi, *Cancer Lett.* **1986**, *30*, 143.

[26] Aldehyde **53** was prepared from trihydroxybenzaldehyde in 30% yield using TBSCl/DMAP/EtNMe$_2$ as silylating agent.

[27] [27a] V.R. Khazanchi, P. L. Yu, F. Johnson, *J. Org. Chem.* **1993**, *58*, 2552−2556. − [27b] V. Samano, M. J. Robins, *Can. J. Chem.* **1993**, *71*, 186−191. − [27c] M. J. Robins, J. S. Wilson, F. Hanske, *J. Am. Chem. Soc.* **1983**, *105*, 4059−4065. − [27d] M. Miyazaki, K. Nakanishi, *Jpn. Tokyo Koho* **1957**, 1322.

[28] M. E. Duggan, J. S. Imagire, *Synthesis* **1989**, 131−132

[29] B. Junker, Diploma Thesis, Frankfurt/M., **1997**.

[30] E. J. Corey, M. Chaykovsky, *J. Am. Chem. Soc.* **1964**, *86*, 1639−1640.

[31] C. R. Johnson, J. R. Shanklin, R. A. Kirchhoff, *J. Am. Chem. Soc.* **1973**, *95*, 6462−6463.

[32] M. Julia, J.-M. Paris, *Tetrahedron Lett.* **1973**, *49*, 4833−4836.

[33] Matthias Gerlach, PhD Thesis, Frankfurt/M., **1997**.

[34] Attempts to use this enhancement in intermolecular conjugate addition reactions were not very encouraging: Heinz Weinberger, PhD Thesis, Frankfurt/M., **1994**.

[35] M. T. Reetz, J. Westermann, R. Steinbach, *J. Chem. Soc., Chem. Commun.* **1981**, 257.

[36] P. Goebel, K. Clauß, *Justus Liebigs Ann. Chem.* **1969**, *722*, 122−131.

[37] T. K. Jones, R. A. Reamer, R. Desmond, S. G. Mills, *J. Am. Chem. Soc.* **1990**, *112*, 2998−3017.

[38] M. Vogt, Diploma Thesis, Frankfurt/M., **1997**.

[39] H.-J. Gais, G. Hellmann, H. Günther, F. Lopez, H. J. Lindner, S. Braun, *Angew. Chem.* **1989**, *101*, 1061−1063.

[40] Unpublished results from these laboratories.

[41] [41a] M. Reggelin, T. Heinrich, *Angew. Chem.* **1998**, *110*, 3005−3008; *Angew. Chem. Int. Ed.* **1998**, *37*, 2883−2886. For FMOC-protected amino aldehydes see also ref. [41b,41c]. − [41b] J. A. Fehrentz, C. Pothion, J. C. Califano, A. Loffet, J. Martinez, *Tetrahedron Lett.* **1994**, *35*, 9031−9034. − [41c] M. Soucek, J. Urban, *Collect. Czech. Chem. Com.* **1995**, *60*, 693−696.

[42] M. Reggelin, T. Heinrich, B. Junker, J. Antel, U. Preuschoff, German Patent, München, DE 19821418.9, 13.05.**1998**.

[43] E. Vedejs, *J. Org. Chem.* **1978**, *43*, 188−190.

[44] M. T. Reetz, *Organotitanium Reagents in Organic Synthesis*, Springer, Berlin, **1986**.

[45] [45a] G. Wilke, *Justus Liebigs Ann. Chem.* **1974**, 1820−1830. − [45b] G. Ohloff, H. Farnow, G. Schade, *Chem. Ber.* **1956**, *89*, 1549−1559

[46] J. E. McMurry, V. Farina, W. J. Scott, A. H. Davidson, D. R. Summers, A. Shenvi, *J. Org. Chem.* **1984**, *49*, 3803−3812.

[47] M. Köck, B. Reif, M. Gerlach, M. Reggelin, *Molecules* **1996**, *1*, 41−45.

Received August 13, 1998
[O98381]