# A Practical Route to Enantiopure, Highly Functionalized Seven-Membered Carbocycles and Tetrahydrofurans: Concise Synthesis of (+)-Nemorensic Acid

**Fernando López, Luis Castedo, and José L. Mascareñas*[a]**

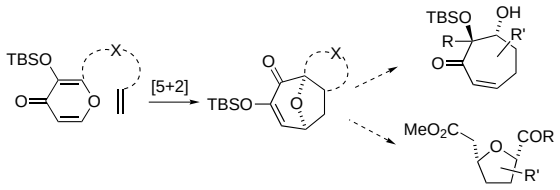
**Abstract:** Highly diastereoselective thermal [5C+2C] intramolecular pyrone–alkene cycloadditions can be achieved by introducing a homochiral *p*-tolylsulfinyl group at a suitable position of the alkene. The resulting adducts can be readily desulfinylated to give optically active 8-oxabicyclo[3.2.1]octane derivatives. Interestingly, switching from a sulfinyl to a sulfonimidoyl group allows one to reverse the direction of the diastereofacial selectivity and thereby produces oxa-bridged carbocyclic systems enantiomeric to those obtained from the sulfinyl precursors. Cleavage of the oxa-bridge on the desulfurated adducts yields highly functionalized seven-membered carbocyclic derivatives in enantiopure form. Alternative cleavage of the seven-membered carbocycle provides enantiomerically enriched tetrahydrofurans. We have exploited this reaction pathway for the synthesis of the naturally occurring enantiomer of nemorensic acid.

**Keywords:** asymmetric synthesis · cycloaddition · polycycles · sulfoxides · sulfoximines

## Introduction

Modern organic synthesis is increasingly demanding the development of methods that allow a rapid and efficient increase in target-relevant molecular complexity while minimizing waste.[1] Among the different alternatives to meet this challenge, cycloaddition reactions, involving the regio- and stereoselective construction of new rings by simple addition of two or more molecules, gain a leading position.[2] Until recently most of the synthetic applications of cycloadditions have been limited to the construction of six-membered rings by means of Diels–Alder-type reactions.[3] The growing number of bioactive natural products containing larger rings, and in particular seven-membered carbocycles,[4] makes the development of cycloaddition routes to assemble these types of cycles a highly appealing goal. A number of interesting thermal and metal-catalyzed cycloaddition routes to carbocycles of this size have already been developed.[5] Among them those that lead to oxa-bridged systems are particularly attractive since this type of frameworks offers unique opportunities for the stereoselective introduction of new functionality into the carbocycle.[6]

Our work in recent years has shown that the intramolecular thermal [5C+2C] cycloaddition of $\beta$-silyloxy-$\gamma$-pyrones to alkenes is a very practical method to rapidly assemble highly functionalized 8-oxabicyclo[3.2.1]octane skeletons from simple, readily available precursors (Scheme 1).[7] We have already shown that the high functionalization of these adducts coupled to the stereochemical framework posed by the oxabicyclic system allows for their divergent and stereoselective elaboration into a variety of valuable multifunctional skeletons, from highly substituted cycloheptanes[8] to tetrahydrofurans.[9]




Scheme 1. Pyrone–alkene [5C+2C] cycloaddition and possibilities for elaboration of the resulting oxa-bridged adducts.

A major goal in this area consists of the development of asymmetric versions of the cycloaddition that could allow the synthesis of the oxabicyclic adducts as single enantiomers. Recently, several methods to prepare optically active 8-oxabicyclo[3.2.1]octane skeletons have been described, the most

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author. Procedures for transforming sulfinyl cycloadducts into their sulfide derivatives, for the desulfinylation of **24**, and for the synthesis of racemic adducts **11** and **20**.



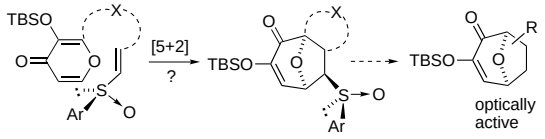
0947-6539/02/0804-0884 $ 17.50+.50/0

effective of which are based on the desymmetrization of *meso* derivatives[10] and on asymmetric versions of allyl cation–furan [4+3] cycloadditions.[11] Asymmetric versions of [5+2] cycloaddition of a carbonyl ylide to activated alkynes,[12] and [5+2] cycloadditions of pyranylmolybdenum π-complexes to electron deficient alkenes[13] have also been reported.

We have previously communicated that attaching a *p*-tolylsulfinyl or a *p*-tolylsulfonimidoyl chiral auxiliary at the *trans*-terminal position of an alkene accelerates its thermal [5C+2C] intramolecular cycloaddition to β-silyloxy-γ-pyrones and leads to excellent levels of stereodifferentiation.[14, 15] Herein we describe more details of this research and demonstrate the utility of the approach to obtain enantioenriched, highly functionalized seven-membered carbocycles. We also illustrate how the methodology can be used for the synthesis of enantiopure tetrahydrofurans by reporting a concise synthesis of (+)-nemorensic acid.

## Results and Discussion

Although our initial attempts to induce asymmetry in [5+2] pyrone–alkene cycloadditions used the incorporation of a chiral sulfoxide unit as part of the tether connecting the reacting partners, we found that this strategy leads to moderate levels of diastereofacial selectivity.[16] This result coupled with the likely difficulty in the preparation of these type of precursors in enantioselective form led us to investigate an alternative strategy based on the introduction of a homochiral sulfoxide unit at the *trans*-terminal position of the alkene (Scheme 2). Although vinylsulfoxides have been

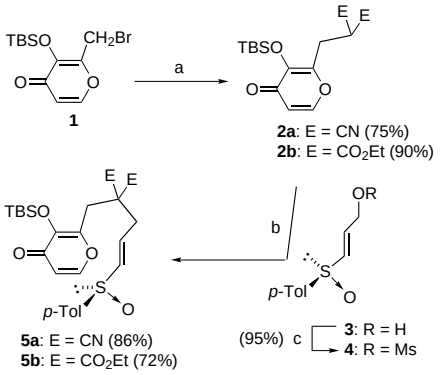



Scheme 2. Sulfinyl-based strategy proposed for asymmetric induction in [5+2] pyrone–alkene cycloadditions.

**Abstract in Spanish:** *La introducción de un grupo p-tolilsulfinilo en una posición adecuada de un alqueno permite llevar a cabo su cicloadición intramolecular [5C+2C] a una β-sililoxi-γ-pirona con una diastereoselectividad elevada. Los cicloaductos resultantes pueden desulfinilarse fácilmente para dar sistemas 8-oxabiciclo[3.2.1]octánicos. Si se transforma el grupo sulfinilo en uno sulfonimidoilo es posible invertir la diastereoselectividad facial de la reacción y como consecuencia obtener sistemas oxabicíclicos enantioméricos de los obtenidos a partir de los precursores sulfinílicos. Las rotura del puente de oxígeno en los aductos desulfurados produce carbociclos de siete miembros enantiomericamente puros. Si lo que se fragmenta es el sistema carbocíclico de los aductos se obtienen tetrahidrofuranos enantiomericamente enriquecidos. Esta última posibilidad ha permitido sintetizar el enantiómero natural del ácido nemorénsico.*

previously used as two carbon partners in intermolecular cycloadditions to 3-oxidopyridinium ylides they lead to modest yields and low stereoselectivities.[17] We reasoned that the intramolecularity of our process and the mandatory *endo* approach of the chiral sulfinyl group to the planar pyrone might induce good levels of dissimilar facial interference. The assembly of the required precursors in enantiomerically enriched form was anticipated to be not especially difficult as a variety of methods for the synthesis of optically pure alkenylsulfoxides have been described.[18]

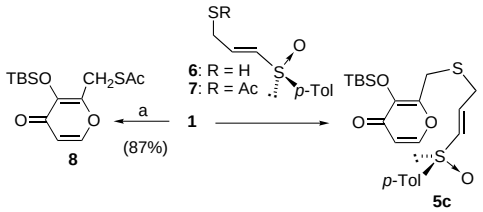
We projected the preparation and evaluation of two types of precursors, one having the alkene and the pyrone connected through a carbon tether and another bearing a removable linker, such as a sulfide. Compounds **5a** and **5b** were easily synthesized by coupling pyrones **2a** or **2b** with the enantiopure mesylate **4** (Scheme 3), a compound which was




Scheme 3. Synthesis of cycloaddition precursors **5a** and **5b**. a) $(CO_2Et)_2CH_2$, NaH, THF, 0 °C → RT; b) NaH, THF, 0 °C → RT; c) MsCl, $Et_3N$, 0 °C.

obtained by mesylation of the corresponding alcohol **3**. This alcohol was readily synthesized from (+)-methyl *p*-tolyl sulfoxide in three steps (43% overall yield).[19] It is pertinent to comment that all attempts to transform alcohol **3** into the corresponding bromide using standard procedures failed or gave very poor yields.

The synthesis of the mixed sulfide **5c** was more problematic and required a number of trials. Although it could be prepared by coupling bromide **1** with thiol **6** (THF, $Et_3N$, 75% yield, Scheme 4), this thiol was difficult to obtain. The

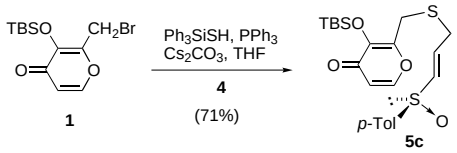



Scheme 4. Attempts to prepare **5c**. a) HSAc, $Et_3N$, THF.

best procedure we found consisted of the coupling of mesylate **4** with NaSH in DMF, which provided **6** in a low 25% yield. Attempts to obtain sulfide **5c** from thioacetate **7** by reductive cleavage and in situ coupling with the bromide **1** led to

complex reaction mixtures. On the other hand, although the thiopyrone **8** could be efficiently prepared by treatment of bromide **1** with thioacetic acid and $Et_3N$, we were not able to induce its coupling with mesylate **4** under a variety of conditions.[20]

A recent publication describing a method for the formation of mixed sulfides from epoxides based on the use of triphenylsilanethiol as sulfur-transfer reagent,[21] led us to test its applicability in our system. Using the described experimental conditions [1) i) **4**, $Ph_3SiSH$, $Et_3N$; ii) TBAF, AcOH, MeOH; 2) $Et_3N$, **1**] we obtained low yields of the desired sulfide **5c** (Scheme 5). However, we found that stirring




Scheme 5. Synthesis of cycloaddition precursor **5c**.

$Ph_3SiSH$ with mesylate **4**, $PPh_3$ and $Cs_2CO_3$ in THF at $-5\,^{\circ}C$ for 15 min followed by addition of a solution of bromide **1** in THF provides the desired sulfide **5c** in a satisfactory 71% yield. This one-step procedure is very simple and seems to provide a mild, practical alternative to other current methods of synthesizing mixed sulfides.[21, 22]

With the precursors at hand the first cycloaddition assays were carried out by heating toluene solutions of the pyrone **5a** in a sealed tube for 160 °C, conditions that were previously used for inducing the cycloaddition of the alkene-unsubstituted homologue.[7d] Remarkably, while in this last case complete conversion required heating for more than 12 h, the cycloaddition of **5a** was over in less than 5 h. Indeed, we found that the reaction could be efficiently carried out by simple heating in toluene under reflux for 10 h (Table 1). This was also the case for the diester **5b**, where the cycloaddition required just 3.5 h in refluxing toluene for its completion. These results indicate that the presence of the sulfinyl substituent considerably accelerates the process, most probably by exerting a moderate electron-activating effect.[23] Most importantly, the diastereoselectivity of the reaction was good for the case of **5a** and excellent for **5b**, which fulfilled our expectations about the facial-differentiating effect of the *endo*-placed sulfinyl group. The cycloaddition of sulfide **5c** could also be achieved in refluxing toluene albeit required prolonged heating than that of **5a** or **5b**, and proceeded as well with high facial diastereoselectivity. It can be noted that the cycloaddition of the sulfinyl-unsubstituted homologue of **5c** requires more stringent conditions (160 °C, more than 40 h), which further confirms the accelerating role of the sulfinyl substituent.

The stereochemical identity of the adducts obtained in the above cycloadditions was established by comparing their $^1H$ NMR spectra with those of their reduced sulfide derivatives, compounds which were obtained in good yields by treatment of the sulfoxides with $PBr_3$ in DMF. As shown in the Table 2, the signals corresponding to the hydrogens of position 4 for both diastereoisomers appear at higher field than the homologous signals in the sulfide. On the other hand, there is a clear deshielding for H-7 in the major diastereoisomer and of the hydrogens of position 5 in the minor. These data are consistent with the structure **9** for the major diastereoisomers and **10** for the minor, and with conformations close to those depicted in Figure 1. The shielding is caused by the anisotropic effect of the phenyl substituent while the deshielding is induced by the well-known *syn*-axial effect of the sulfinylic oxygen on the 1,3-parallel hydrogen.[24]

Table 2. $\Delta\delta = \delta$ (sulfoxide) $- \delta$ (sulfide).

| | H's | **9a** | **9b** | **9c** | **10a** | **10b** | **10c** |
|---|---|---|---|---|---|---|---|
| 1 | H-4 | −0.57 | −0.61 | −0.70 | −0.31 | −0.37 | −0.20 |
| | | −0.97 | −0.79 | −0.89 | −0.81 | −0.60 | −0.55 |
| 2 | H-7 | +0.32 | +0.30 | +0.32 | +0.05 | +0.00 | −0.07 |
| 3 | H-5 | −0.16 | −0.17 | −0.16 | +0.60 | +0.60 | +0.60 |

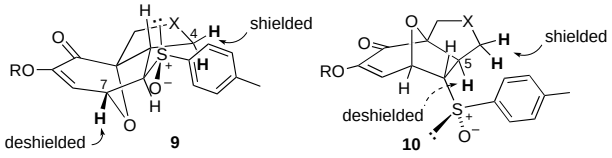
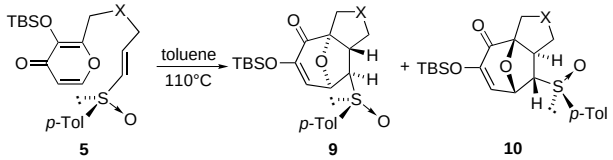



Figure 1. Conformations of **9** and **10** consistent with the NMR data.

Table 1. Cycloaddition of pyrones **5a–c**.




| | Pyrone | X | Yield[a] | 4:5[b] | *t* |
|---|---|---|---|---|---|
| 1 | **5a** | $C(CN)_2$ | 98% | **9a**:**10a** (91:9) | 10 h |
| 2 | **5b** | $C(CO_2Et)_2$ | 99% | **9b**:**10b** (97:3) | 3.5 h |
| 3 | **5c** | S | 95% | **9c**:**10c** (93:7) | 46 h |

[a] Combined isolated yield after chromatography. [b] Ratio determined by $^1H$ NMR of the crude reaction mixture. In all cases both diastereoisomers could be readily separated by simple flash chromatography.

The stereochemical outcome of the above reactions could be rationalized by assuming that the alkenylsulfoxide unit prefers to adopt an *S*-trans-type of conformation in order to avoid repulsive dipole–dipole interactions with the pyrone. The approach from the less hindered face of the sulfoxide, which is that displaying the lone pair, is hence favored (Figure 2).[25]

That the above cycloadditions occurred without racemization at the sulfur was confirmed by checking the optical purity of the desulfinylated oxabicycles. Although the dinitrile derivative **9a** could not be cleanly desulfurated upon treatment with Raney nickel under different conditions, probably because there are lateral reductions of the nitriles, treatment



0947-6539/02/0804-0886 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

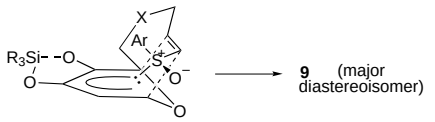
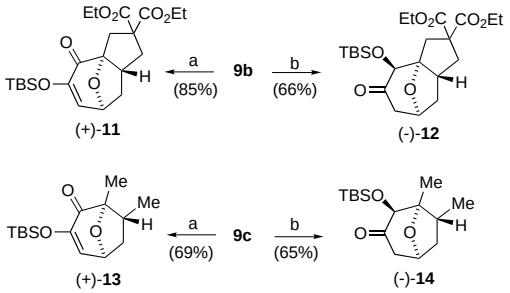



Figure 2. Qualitative representation of the more favored transition state for the cycloaddition.

of **9b** with Raney nickel in refluxing THF for 4 h led to the expected oxabicycle **11** in a 85% yield (Scheme 6). Prolonging the reaction time or carrying out the reduction with $H_2$ induced the concomitant reduction of the enone leading to the $\alpha$-silyloxyketone **12** in 66% yield. Analysis of the $^1$H NMR spectrum in the presence of Eu(hfc)$_3$ using racemic mixtures



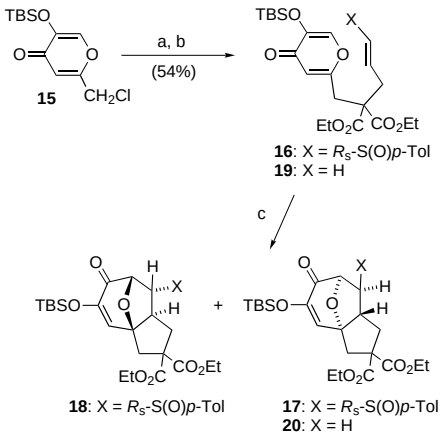

Scheme 6. Desulfuration of the cycloadducts. a) Raney Ni, THF, 60 °C; b) Raney Ni, THF, $H_2$, 60 °C.

as reference confirmed that products **11** ($[\alpha]_D^{20} = +42.6$, $c = 1$ in $CHCl_3$) and **12** ($[\alpha]_D^{20} = -19.0$, $c = 1$ in $CHCl_3$) are enantiomerically pure (97% *ee*).[26] On the other hand, treatment of sulfoxide **9c** with Raney Ni gave **13** in a 69% yield ($[\alpha]_D^{20} = +103$, $c = 1$ in $CHCl_3$, 97% *ee*). If the reaction is carried out under an atmosphere of hydrogen the optically active oxabicycle **14** is obtained in a 65% yield ($[\alpha]_D^{20} = -44.0$, $c = 0.25$ in $CHCl_3$, 97% *ee*).

The feasibility of using the above asymmetric strategies to obtain enantiomerically enriched cycloadducts with complementary regiochemistry, and therefore of expanding the range of attainable ring substitution patterns, was also investigated. As could have been anticipated owing to the existence of a mismatched electronic arrangement, the cycloaddition of pyrone **16**, readily assembled from the known chloride **15**,[7b] required much more harsh conditions (toluene 160 °C, 50 h, Scheme 7) than those needed for the reaction of its regioisomer **5b**, and even than those for completing the cycloaddition of its unsubstituted derivative **19** (160 °C, 27 h). In any event the expected cycloadducts **17** and **18** could be isolated in a modest 51% combined yield and a diastereoisomeric ratio of 89:11.

The structural assignment of the diastereoisomers was made by comparison of their $^1$H NMR spectra with those of the sulfide homologues following the same reasoning as that used above for the identification of the regioisomeric adducts (Figure 3).

Reductive removal of the sulfoxide moiety from **17** by treatment with Raney Ni in refluxing THF gave the expected tricycle **20** in enantiomerically pure form, as determined by $^1$H NMR in the presence of Eu(hfc)$_3$ (68% yield, 97% *ee*,




Scheme 7. Cycloaddition of regioisomeric precursors. a) $(EtO_2C)CH_2$, NaH, THF, 0 °C → RT; b) NaH, THF, **4**, 0 °C → RT; c) toluene, 160 °C.

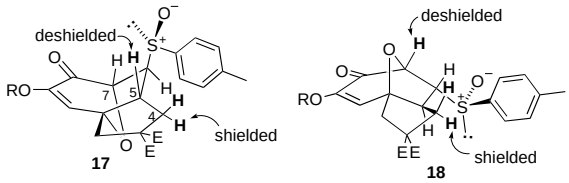



Figure 3. Conformations of **17** and **18** consistent with the NMR data. Key hydrogens for the assignment are marked in bold.

$[\alpha]_D^{20} = +64$, $c = 0.5$ in $CHCl_3$). The formation of **17** as major product in the cycloaddition of **16** can be explained by assuming that, in this case, the alkenylsulfoxide prefers to adopt an *S*-cis conformation when approaching the pyrone, most probably to avoid interactions with the *tert*-butylsilyloxy group (Figure 4).

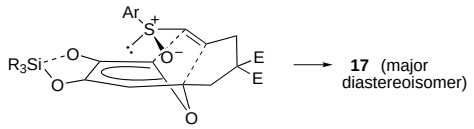
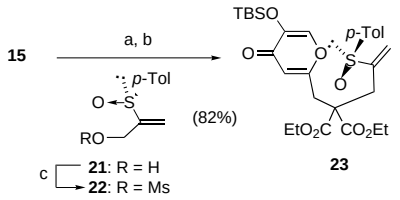



Figure 4. Qualitative representation of the more favored transition state for the cycloaddition.

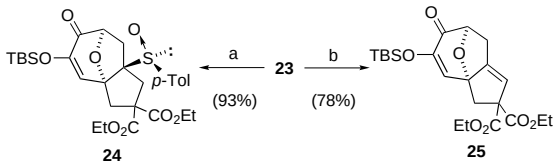
The low yield of the cycloaddition of **16** restricts the applicability of the above sulfinyl-directed asymmetric cycloaddition to obtain enantiomerically enriched adducts with substitution patterns such as in **20**. We envisaged that this drawback could be overcome if the sulfoxide unit is introduced at the internal instead of the terminal side of the alkene, so that the alkene might present a favorable electronic orientation for the cycloaddition. To test this possibility we prepared the precursor **23** using as alkenylsulfinyl coupling unit the mesylate **22**, itself obtained from the known sulfinyl alcohol **21** (Scheme 8).[27]

Gratifyingly, the [5+2] cycloaddition of **23** could be accomplished by simple refluxing in toluene for 4 h to give the adduct **24** in 93% yield as the only observed diastereoisomer (Scheme 9). The structural assignment of this cycloadduct was accomplished after removal of the sulfinyl moiety, a process which was best carried out by sequential reduction



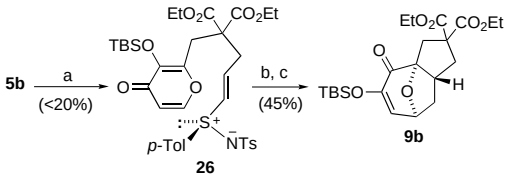

Scheme 8. Synthesis of cycloaddition precursor **23**. a) $(EtO_2C)CH_2$, NaH, THF, 0 °C; b) NaH, THF, **22**, 0 °C; c) MsCl, $Et_3N$, 0 °C.

to the sulfide with $PBr_3$ and $Et_3N$ followed by desulfurization with Raney Ni in refluxing THF (55% yield). The spectral properties and optical rotation of the resulting product ($[\alpha]_D^{20} = +63.5$, $c = 1$ in $CHCl_3$) are identical to those of compound **20** that we had previously obtained by desulfinylation of **17** (see Scheme 7). Noteworthy is the fact that heating of **23** for a longer time induced an in situ pyrolytic $\beta$-elimination of the *p*-tolylsulfinyl group in the initially formed cycloadduct (**24**) to directly provide the optically active alkene **25**, which could be isolated in a 38% yield after 52 h of heating. This low yield seemed to be caused by side reactions of the oxatricycle with the *p*-tolylsulfenic acid formed in the elimination process. We later found that adding a small amount of $(EtO)_3P$ to the reaction medium, just after the cycloaddition was complete (approx. 4 h), and keeping the heat for additional 48 h leads to the alkene **25** in a rather good yield (78%) and excellent enantioselectivity (97% *ee*), as determined by $^1H$ NMR in the presence of $Pr(hfc)_3$ ($[\alpha]_D^{20} = +60.0$, $c = 0.5$ in $CHCl_3$). Therefore, simple heating of a readily available pyronic precursor (three steps from commercially available kojic acid) affords a much more complex and synthetically valuable product (**25**) in enantiomerically pure form (Scheme 9).




Scheme 9. Cycloaddition of **23**. a) Toluene, 110 °C, 4 h; b) toluene, 110 °C, $(EtO)_3P$, 52 h.

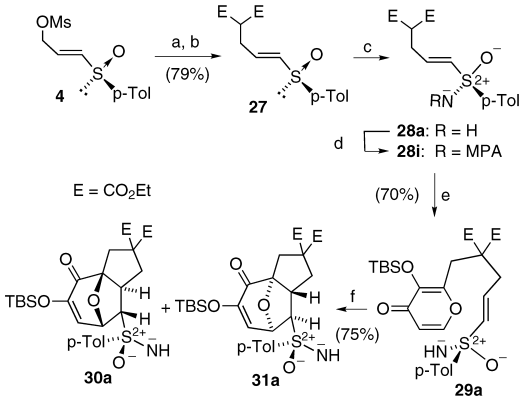
The cycloadditions described above provide a practical route to a variety of optically pure oxa-bridged polycyclic systems. However, just like most of chiral auxiliary-based asymmetric synthesis, obtaining the enantiomeric series of adducts requires the assembly of precursors bearing the enantiomeric partner of the chiral auxiliary. We thought that this drawback could be overcome if we were able to formally invert the stereochemical configuration of the sulfoxide in the cycloaddition precursor such that the facial diastereoselectivity of the cycloaddition could be reversed. We initially examined the conversion of the sulfoxide into a sulfimide, a reaction that has been shown to take place in most of the cases with inversion of configuration.[28] All attempts to transform the alkenylsulfoxide **5b** into the *N*-tosylsulfimide **26** gave low yields (less than 20% in the best case), albeit we could isolate a small amount of the product (Scheme 10). The cycloaddition




Scheme 10. Preparation and cycloaddition of the sulfimide **26**. a) $Et_3N$, $P_2O_5$, *p*-$TsNH_2$, $CH_2Cl_2$, RT; b) toluene, 110 °C; c) Raney Ni, THF, 60 °C (**9b**: $[\alpha]_D^{20} \approx 0$).

of this sulfimide could be readily achieved by heating in refluxing toluene for 3 h, and led to a 9:1 diastereoisomeric ratio of cycloadducts. Unfortunately, the optical rotation of the tricycle obtained after desulfuration was nearly zero, indicating that an almost complete racemization took place at some point of the process (Scheme 7), most probably during the thermolysis.[29]

Instead of studying this process further we preferred to turn our attention to the configurationally more robust sulfoximines, a type of chiral functional group that has not received much attention in asymmetric synthesis despite its particular modulability characteristics owing to the presence of a nitrogen substituent on the sulfur.[30] Most of the procedures that have been described for the synthesis of 1-alkenylsulfoximines are based on the elaboration of the methyl group of *N*-alkylarylmethylsulfoximines.[31] The direct transformation of dialkylsulfoxides into N-unsubstituted sulfoximines using *O*-mesitylsulfonylhydroxylamine (MSH) as aminating agent, which takes place with retention of configuration at the sulfur, has also been reported.[32] Although to our knowledge this last procedure has not been previously used for the preparation of vinylic sulfoximines we still considered it worthy to assess its applicability for transforming the alkenylsulfoxide **5b** into the corresponding sulfoximine. Unfortunately, all attempts to directly aminate this compound by reaction with MSH in different solvents failed, apparently because there was a concomitant desilylation of the pyrone hydroxyl group. In any event, the amination reaction could be efficiently achieved on the diethylmalonate **27**, an immediate precursor of the cycloaddition substrate, which was readily prepared by reaction of mesylate **4** with the sodium anion of diethylmalonate (Scheme 11). We found that the use of




Scheme 11. Preparation and cycloaddition of the sulfoximine **29a**. a) KI, acetone; b) $(EtO_2C)CH_2$, NaH, THF, 0 °C → RT; c) MSH, $CH_3CN$; d) MPA, EDC, DMAP, $CH_2Cl_2$; e) NaH, **1**, THF, 0 °C → RT; f) toluene, 110 °C.



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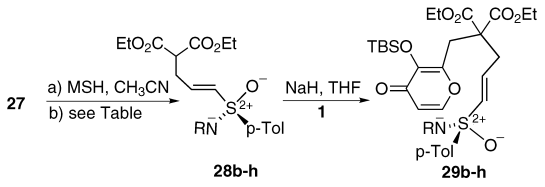
$CH_3CN$ as solvent is critical for the success of the amination; other solvents previously used for this type of reaction, such as $CH_2Cl_2$,[32c] gave much poorer yields of the product. To our knowledge this is the first case reported of the formation of an optically active *N*-unsubstituted alkenylsulfoximine from $\alpha,\beta$-unsaturated sulfoxides.

The optical purity of the sulfoximine **28a** was confirmed to be at least 97% by analysis and comparison of the $^1$H NMR spectra of the *N*-methoxyphenylacetyl [(+)-MPA and (+/−)-MPA] sulfoximines **28i**.[32b] The coupling between the alkenylsulfoximine **28a** and the bromopyrone **1** proceeded cleanly to give the expected cycloaddition precursor **29a** in 70% yield. The cycloaddition of this compound took place by simple heating in toluene under reflux for 2 h, being therefore over two times faster than that of its sulfinyl analogue. This acceleration may be related to the stronger electron-withdrawing character of the sulfonimidoyl group. Although the yield of the reaction was good (75%), its diastereoselectivity was almost negligible, a result that was not too surprising owing to the relatively similar electronic and steric characteristics of the oxygen and "free" nitrogen sulfur substituents.

We envisaged that introducing suitable substituents at the nitrogen could induce conformational preferences in the alkenylsulfoximine that might eventually lead to a diastereofacial selection complementary to that obtained from the sulfoxide. To prove this point we prepared a variety of N-substituted pyrone-alkenyl sulfoximines **29b–h** by derivatizing the amine **28a** and coupling the resulting sulfoximines with the bromopyrone **1** (Table 3).[33]

Table 3. Preparation of N-substituted sulfonimidoyl cycloaddition precursors.

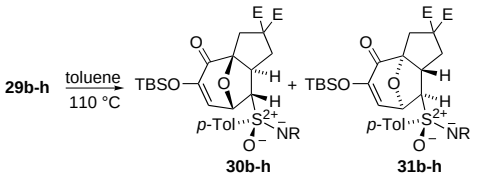



| | Conditions (step b)[a] | R | **29** (Yield[b]) |
|---|---|---|---|
| 1 | $CH_3COCl$, $Et_3N$, 0 °C | $COCH_3$ | **29b** (63%) |
| 2 | $(CF_3CO)_2O$, $Et_3N$, RT | $COCF_3$ | **29c** (67%) |
| 3 | PhCOCl, $Et_3N$, DMAP, RT | COPh | **29d** (47%) |
| 4 | $pNO_2C_6H_5COOH$, EDC,DMAP | $CO pNO_2Ph$ | **29e** (63%) |
| 5 | $CH_3SO_2Cl$, $Et_3N$, 0 °C | $SO_2CH_3$ | **29f** (60%) |
| 6 | $(CF_3SO_2)_2O$, Py, 0 °C | $SO_2CF_3$ | **29g** (51%) |
| 7 | $p$TolSO$_2$Cl, Py, 0 °C | $SO_2 p$Tol | **29h** (65%) |

[a] All these reactions were carried out in $CH_2Cl_2$, except entry 7. [b] Overall yield for the three steps.

As illustrated in Table 4, cycloadditions of the acyl or sulfonylsulfoximines **29b–h** gave a reasonable degree of facial diastereoselectivity which ranged from a modest 58:42 for the *p*-nitrobenzoyl derivative **29e** to a notable 90:10 for the case of the *N*-tosyl derivative **29h**. In all cases, except those of the *N*-tosyl, *N*-mesyl and *N*-acetyl derivatives, it was possible to separate the two diastereoisomeric cycloadducts by flash chromatography. Most importantly the facial selectivity of the cycloaddition was opposite to that of the

Table 4. Intramolecular [5+2] thermal cycloadditions.

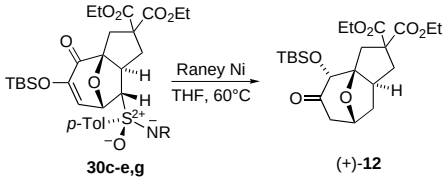



| Entry | Pyrone | R | **30**:**31**[a] | Yield[b] |
|---|---|---|---|---|
| 1 | **29b** | $COCH_3$ | 65:35 | 86% |
| 2 | **29c** | $COCF_3$ | 86:14 | 85% |
| 3 | **29d** | COPh | 76:24 | 95% |
| 4 | **29e** | $CO pNO_2Ph$ | 58:42 | 91% |
| 5 | **29f** | $SO_2CH_3$ | 77:23 | 88% |
| 6 | **29g** | $SO_2CF_3$ | 87:13 | 80% |
| 7 | **29h** | $SO_2 p$Tol | 90:10 | 88% |

[a] Diastereoisomeric ratio determined by $^1$H NMR of the crude reaction mixture. [b] Combined isolated yield after chromatography.

precursor sulfoxides, which confirmed our expectations of switching the diastereofacial selection of the cycloaddition.

The structures of the major diastereoisomers were unequivocally established as the oxabicycles **30b–h** on the basis of the optical rotation of their desulfinimidoylated derivative **12** which was of opposite sign to that of the same compound obtained from the desulfuration of stereochemically fully characterized sulfoxide **9b** (Scheme 6). The desulfurization reaction was achieved with Raney nickel in refluxing THF (71–83% yields), although it required the use of more excess of reagent than in the case of the sulfoxide (Scheme 12).




Scheme 12. Desulfuration of sulfoximinyl cycloadducts; (+)-**12**: $[\alpha]_D^{20} = +19$, $c = 1$ in $CHCl_3$.

The formation of **30** as major product in the cycloaddition of **29** can be explained by assuming that the alkenylsulfoximine prefers to set the nitrogen substituent in an *S-trans* arrangement with respect to the alkene (Figure 5).

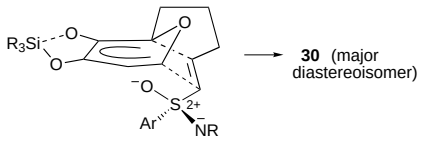
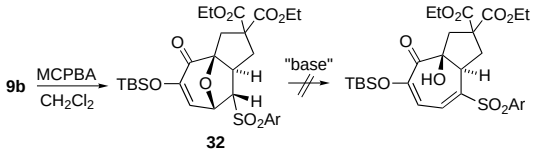



Figure 5. Qualitative representation of the favored transition state for the cycloaddition of sulfoximines **29b–h**.

The sulfoxide to sulfoximine switch described above represents a very practical tactic to invert the diastereofacial selectivity in [5+2] pyrone–alkene cycloadditions and hence provides a straightforward access to oxa-bridged carbocycles

enantiomeric to those coming from the sulfoxides. The tactic avoids the lengthier but otherwise mandatory synthesis of cycloaddition precursors bearing sulfoxide units of both configurations, and might be useful in other sulfinyl-mediated asymmetric processes.

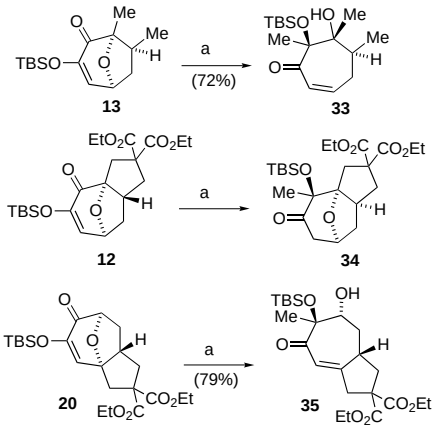
Having developed a practical route to a variety of enantiomerically pure oxa-bridged carbocyclic systems it was pertinent to demonstrate that these adducts can indeed be elaborated into compounds of more immediate synthetic value such as highly functionalized seven-membered carbocycles. The presence of the sulfinyl substituent in cycloadducts such as **9** led us first to test whether it might be possible to induce the opening of the oxa-bridge by generating a carbanion in $\alpha$ to the bridgehead carbon in the sulfone **32**,[34] compound readily obtained by oxidation of **9b** with MCPBA (Scheme 13). However, all assays carried out using




Scheme 13. Initial attempts to open the oxygen bridge.

LDA or *n*BuLi as bases in different solvents led to the recovery of the starting material or formation of mixtures of unwanted products.

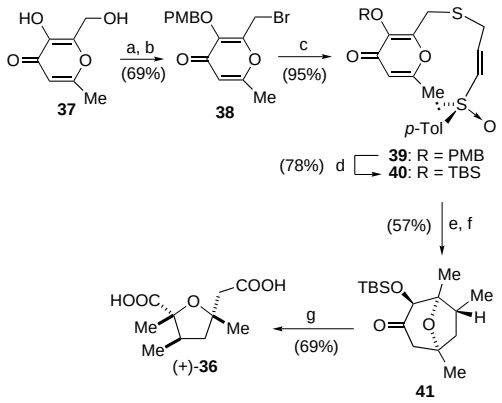
We therefore moved to our recently developed tandem "push–pull" procedure for opening the oxa-bridge of this type of oxabicyclic pyrone–alkene adducts, based on the combined action of an electron-donating enolate and a strong Lewis acid.[8] As expected, treatment of enone **13** with MeLi at $-78\,^{\circ}C$ followed by addition of $BF_3\cdot OEt_2$ led to the methylated ring-opened product **33** in a 72% yield ($[\alpha]_D = -14$, $c = 1$ in $CHCl_3$), an optically active seven-membered carbocycle susceptible of further manipulation (Scheme 14).




Scheme 14. Addition-bridge opening process. a) i) MeLi, THF, $-78\,^{\circ}C$; ii) $BF_3\cdot OEt_2$ $-78\,^{\circ}C$.

Curiously, the attempts to apply this methylation opening protocol to cleave the oxa-bridge of tricycle **12** failed, with the only product isolated being the methylated bridged system **34**. Since the bridge-opening of similar tricyclic systems is feasible,[8] this failure appears to be due to the presence of the ester groups at that particular position of the five-membered cycle which are most probably interfering with the required pulling action of the Lewis acid. Remarkably, opening of the corresponding regioisomer **20** was successfully achieved using this method to provide the interesting highly functionalized bicarbocyclic system **35** in 79% yield and optically active form ($[\alpha]_D^{20} = +35.3$, $c = 0.3$ in $CHCl_3$). These types of 5,7-fused ring systems are found in many natural products,[4f] and therefore there is a great interest in developing practical routes for their assembly in enantiomerically pure form.

Finally, we also wanted to demonstrate the utility of our methodology for preparing optically active tetrahydrofurans, synthesizing enantiomerically pure nemorensic acid (**36**),[35] the diacid portion of the naturally occurring pyrrolizidine alkaloid nemorensine.[36] The synthesis was carried out following a slightly improved route with respect to that previously used for obtaining the racemic product.[9b] As illustrated in the Scheme 15 attaching the chiral vinylsulfinyl




Scheme 15. Synthesis of (+)-nemorensic acid. a) KOH, then PMBCl, KI, acetone; b) $CBr_4$, $PPh_3$, THF, RT; c) i) **4**, $Ph_3SiSH$, $Cs_2CO_3$, $PPh_3$, THF; ii) TFA, $CH_2Cl_2$; d) imidazole, TBSCl, $CH_2Cl_2$; e) toluene, $160\,^{\circ}C$; f) Raney Ni, THF, $60\,^{\circ}C$; g) two steps, ref. [9].

unit to the pyrone was best achieved on the PMB-protected derivative **38**. The formation of the thioether and the change from PMB to TBS was carried out in a 74% yield without intermediate purifications. As expected, the presence of the methyl group in the pyrone slowed down the cycloaddition reaction, which was carried out best by heating a solution of **40** in toluene in a sealed tube for 12 h. The reaction gave the expected cycloadducts in an 82% yield and a diastereoisomeric ratio of 93:7. Treatment of the major diastereoisomer with excess of Raney nickel (new bottle) allowed its complete desulfuration as well as the reduction of the enone system to give the optically active oxabicycle **41** in a 71% yield, ($[\alpha]_D^{20} = -50.4$, $c = 0.17$ in $CHCl_3$). The transformation of this compound in natural nemorensic acid was accomplished in two steps as previously described.[9b] The final product obtained had spectroscopic and optical properties identical to those previously reported for the natural product [($[\alpha]_D^{20} = +87$, $c = 0.35$ in EtOH), lit.: $[\alpha] = +87$, $c = 0.35$ in EtOH)].



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Overall the synthesis consisted of eleven steps from commercially available kojic acid and provided the target in a 16% yield, thereby comparing positively with recently published asymmetric syntheses of this product, which are appreciably more linear.[35]

## Conclusion

In summary, attaching a *p*-tolylsulfinyl group at an appropriate position in the alkene allows one to accelerate its thermal [5C+2C] intramolecular cycloaddition to $\beta$-silyloxy-$\gamma$-pyrones and, most importantly, leads to excellent levels of diastereodifferentiation. Switching from the sulfinyl to a *N*-sulfonylsulfoximine provides a practical tactic to invert the diastereofacial selectivity of the cycloaddition and thereby of obtaining enantiomeric adducts. The resulting oxabicyclic adducts, by virtue of their high functionalization can be readily converted into stereochemically enriched seven-membered carbocycles and/or tetrahydrofurans. In particular we have demonstrated the utility of the methodology by its application to a concise synthesis of (+)-nemorensic acid.

## Experimental Section

**General**: All dry solvents were freshly distilled under argon from the appropriate drying agent before use. Toluene and THF were distilled from sodium/benzophenone. $CH_2Cl_2$ was distilled from $P_2O_5$. MeOH was distilled from $Mg/I_2$. All reactions were conducted in dry solvents under argon atmosphere unless otherwise stated. Thin-layer chromatography (TLC) was performed on silica gel aluminium plates and components were visualized by observation under UV light, or by treating the plates with a phosphomolybdic reagent followed by heating. Flash chromatography was performed on silica gel (230–400 mesh), unless stated otherwise. The organic phases were dried with anhydrous $Na_2SO_4$. Concentrations were carried out in a rotary evaporator. $^1H$ and $^{13}C$ NMR spectra were recorded in $CDCl_3$, at 250 MHz and 62.9 MHz, respectively, and in some cases at 300 or 500 MHz (75.4 or 125.7 for $^{13}C$ NMR). Carbon types were determined from DEPT $^{13}C$ NMR experiments. The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. $[\alpha]_D$ were measured at 20 °C in $CHCl_3$. The diastereoisomeric ratio of the cycloadducts was determined by integration of the signals of the vinylic hydrogen of the two isomers in the $^1H$ NMR spectrum of the crude reaction mixture, unless stated otherwise. Eu(hfc)$_3$ refers to tris[heptafluoropropylhydroxymethylene)-(−)camphorate]europium (III). Pr(hfc)$_3$ refers to tris[heptafluoropropylhydroxymethylene)-(−) camphorate]praseodymium (III).

**(2*E*,$R_S$)-3-*p*-Tolylsulfinyl-2-propenylmethanesulfonate (4)**: Methanesulfonyl chloride (116 mg, 1.02 mmol) was added dropwise to an ice-water cooled solution of the alcohol **3**[19] [100 mg, 0.50 mmol, 97% *ee* $[\alpha]_D = +234$ ($c = 1$); lit.: $[\alpha]_D^{20} = +233$ ($c = 1$, *ee* = 97%] and $Et_3N$ (0.14 mL, 1.02 mmol) in $CH_2Cl_2$ (10 mL). The reaction mixture was warmed to RT and stirred for 1 h. The resulting solution was poured into water, extracted with $CH_2Cl_2$, dried, filtered, and concentrated. The crude residue was purified by flash chromatography (50–100% EtOAc/hexanes) to afford **4** as a white solid (133 mg, 95%). $R_f = 0.50$ (EtOAc); m.p. 58–60 °C; $[\alpha]_D = +249$ ($c = 1.1$); $^1H$ NMR: $\delta = 7.51$ (d, $J = 7.9$ Hz, 2H), 7.33 (d, $J = 7.9$ Hz, 2H), 6.62 (s, 2H), 4.90 (s, 2H), 3.03 (s, 3H), 2.41 (s, 3H); $^{13}C$ NMR: $\delta = 142.3$ (CH), 139.3 (C), 138.3 (C), 130.2 (CH), 128.3 (CH), 124.8 (CH), 67.0 ($CH_2$), 37.8 ($CH_3$), 21.3 ($CH_3$); LRMS: *m*/*z*: 274 (0.04) $[M]^+$, 226 (44), 139 (41), 131 (100), 91 (54), 65 (38); HRMS: calcd for $C_{11}H_{14}O_4S_2$: 274.0333, found: 274.0334.

**2-[(3-*tert*-Butyldimethylsilyloxy-4-oxo-4*H*-2-pyranyl)methyl]-2-[(2*E*,$R_S$)-3-*p*-tolylsulfinyl-2-propenyl]malononitrile (5a)**: Malononitrile (0.83 g, 12.5 mmol) was added to a −78 °C cooled suspension of NaH (0.5 g, 60% mineral oil, 12.5 mmol) in THF (20 mL). After stirring for 15 min at RT, the reaction mixture was cooled at −78 °C, and bromide **1** (2 g, 6.27 mmol) was added. The reaction mixture was stirred for 1 h at that temperature poured into brine, extracted with $Et_2O$, dried, filtered, and concentrated. The residue was purified by flash chromatography (90% $CH_2Cl_2$/hexanes) to afford **2a** as a colorless viscous oil (2.2 g, 75%). $R_f =$ 0.15 (90% $CH_2Cl_2$/hexanes); $^1H$ NMR: $\delta = 7.67$ (d, $J = 5.5$ Hz, 1H), 6.35 (d, $J = 5.5$ Hz, 1H), 4.26 (t, $J = 7.2$ Hz, 1H), 3.40 (d, $J = 7.2$ Hz, 2H), 0.93 (s, 9H), 0.26 (s, 6H); $^{13}C$ NMR: $\delta = 173.6$ (C), 153.7 (CH), 147.6 (C), 144.5 (C), 115.8 (CH), 111.4 (CN), 29.3 ($CH_2$), 26.0 ($CH_3$), 20.1 (CH), 18.6 (C), −3.9 ($CH_3$); LRMS: *m*/*z*: 289 (3) $[M - CH_3]^+$, 247 (79), 182 (100), 154 (12), 111 (18); HRMS: calcd for $C_{15}H_{20}O_3N_2Si - CH_3$: 289.1008, found 289.1015.

A solution of compound **2a** (200 mg, 0.66 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (26 mg, 0.60 mmol) in THF (10 mL). After stirring for 15 min at RT a solution of mesylate **4** (163 mg, 0.60 mmol) in THF (2 mL) was added. The reaction mixture was stirred for 12 h and the reaction quenched by adding water (3 mL). The solvent was evaporated and the residue diluted with $Et_2O$, washed with brine, dried, filtered, and concentrated. The crude was purified by flash chromatography (35% EtOAc/hexanes) to afford **5a** as a brown solid (244 mg, 86%). $R_f = 0.30$ (50% EtOAc/hexanes); m.p. 147–149 °C; $[\alpha]_D = +160$ ($c = 0.42$); $^1H$ NMR: $\delta = 7.71$ (d, $J = 5.5$ Hz, 1H), 7.53 (d, $J = 8.1$ Hz, 2H), 7.32 (d, $J = 8.1$ Hz, 2H), 6.65 (m, 2H), 6.39 (d, $J = 5.5$ Hz, 1H), 3.41 (s, 2H), 2.95 (d, $J = 3.6$ Hz, 2H), 2.40 (s, 3H), 0.95 (s, 9H), 0.30 (s, 6H); $^{13}C$ NMR: $\delta = 173.6$ (C), 153.6 (CH), 147.0 (C), 145.3 (C), 143.6 (CH),142.4 (C), 139.1(C), 130.3 CH), 125.7 (CH), 125.0 (CH), 115.9 (CH), 113.5 (CN), 39.3 ($CH_2$), 35.3 (C), 34.7 ($CH_2$), 26.1 ($CH_3$), 21.4 ($CH_3$), 18.8 (C), −3.5 ($CH_3$); LRMS: *m*/*z*: 425 (42) $[M - C_4H_9]^+$, 245 (31), 182 (100), 139 (24), 73 (25); HRMS: calcd for $C_{25}H_{30}O_4SiSN_2 - C_4H_9$: 425.0991, found 425.0986.

**Diethyl 2-[(3-*tert*-butyldimethylsilyloxy-4-oxo-4*H*-2-pyranyl)methyl]-2-[(2*E*,$R_S$)-3-*p*-tolylsulfinyl-2-propenyl]malonate (5b)**: Diethylmalonate (2 g, 12.5 mmol) was added to a −78 °C cooled suspension of NaH (0.5 g, 60% mineral oil, 12.5 mmol) in THF (20 mL). After being stirred for 20 min at RT, the reaction mixture was cooled at −78 °C, and bromide **1** (2 g, 6.27 mmol) was added. After being stirred for 2 h the mixture was poured into brine, extracted with $Et_2O$, dried, filtered, and concentrated. The crude was purified by flash chromatography (10–25% EtOAc/hexanes) to afford **2b** as a colorless viscous oil (2.2 g, 90%). $R_f = 0.15$ (10% EtOAc/hexanes); $^1H$ NMR: $\delta = 7.57$ (d, $J = 5.5$ Hz, 1H), 6.3 (d, $J =$ 5.5 Hz, 1H), 4.20 (q, $J = 7.1$ Hz, 4H), 3.77 (t, $J = 7.7$ Hz, 1H), 3.31 (d, $J =$ 7.7 Hz, 2H), 1.24 (t, $J = 7.1$ Hz, 6H), 0.95 (s, 9H), 0.27 (s, 6H); $^{13}C$ NMR: $\delta = 174.5$ (C), 168.1 (C), 153.3 (C), 152.8 (CH), 143.0 (C), 115.6 (CH), 61.8 ($CH_2$), 48.9 (CH), 27.6 ($CH_2$), 26.0 ($CH_3$), 18.7 (C), 14.0 ($CH_3$), −3.7 ($CH_3$); LRMS: *m*/*z*: 341 (100) $[M - C_4H_9]^+$, 267 (9), 239 (9), 195 (39), 165 (4); HRMS: calcd for $C_{19}H_{30}O_7Si - C_4H_9$: 341.1056, found 341.1054.

A solution of compound **2b** (240 mg, 0.60 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (24 mg, 0.60 mmol) in THF (10 mL). After stirring for 15 min at RT a solution of mesylate **4** (150 mg, 0.55 mmol) in THF (2 mL) was added. The reaction mixture was stirred at rt for 12 h and the reaction quenched by adding water (3 mL). The solvent was evaporated and the residue diluted with $Et_2O$, washed with brine, dried, filtered, and concentrated. The crude was purified by flash chromatography (35% EtOAc/hexanes) to afford **5b** as a colorless oil (221 mg, 72%). $R_f =$ 0.38 (50% EtOAc/hexanes); $[\alpha]_D = +39$ ($c = 0.72$); $^1H$ NMR: $\delta = 7.50$ (d, $J = 4.4$ Hz, 1H), 7.41 (d, $J = 6.6$ Hz, 2H), 7.25 (d, $J = 6.6$ Hz, 2H), 6.49 (m, 1H), 6.26 (d, $J = 5.1$ Hz, 1H), 6.20 (d, $J = 15.1$ Hz, 1H), 4.10 (m, 4H), 3.45 (s, 2H), 2.70 (m, 2H), 2.34 (s, 3H), 1.15 (m, 6H), 0.94 (s, 9H), 0.21 (s, 6H); $^{13}C$ NMR: $\delta = 173.8$ (C), 169.3(C), 169.2 (C), 152.9 (CH), 152.4 (C), 144.1 (C), 141.4 (C), 140.3 (C), 139.5 (CH), 133.2 (CH), 129.9 (CH), 124.5 (CH) 115.5 (CH), 61.9 ($CH_2$), 56.3 (C), 35.9 ($CH_2$), 31.0 ($CH_2$), 25.9 ($CH_3$), 21.2 ($CH_3$), 18.6 (C), 14.8 ($CH_3$), −3.8 ($CH_3$); LRMS/FAB: *m*/*z*: 577 (16) $[M+H]^+$, 519 (8), 249 (27), 239 (19), 182 (100), 179 (41), 173 (74); HRMS: calcd for $C_{29}H_{41}O_8SiS$: 577.2291, found: 577.2277.

**3-*tert*-Butyldimethylsilyloxy-2-[((2*E*,$R_S$)-3-*p*-tolylsulfinyl-2-propenyl)sulfanylmethyl]-4*H*-4-pyranone (5c)**: Triphenylsilanethiol (187 mg, 0.64 mmol) was added to a solution of mesylate **4** (175 mg, 0.639 mmol), $PPh_3$ (168 mg, 0.64 mmol) and $Cs_2CO_3$ (416 mg, 1.28 mmol) in THF (7 mL), cooled at −5 °C. After stirring for 15 min, a solution of bromide **1** (510 mg, 1.6 mmol) in THF (2 mL) was added and the reaction mixture stirred for an additional 10 h at RT. The resulting solution was poured into brine, extracted with $Et_2O$, dried, filtered, and concentrated. The crude residue was purified by flash chromatography (30–60% EtOAc/hexanes) to afford **5c** as an orange-pale solid (201 mg, 71%). $R_f = 0.33$ (50% EtOAc/

hexanes); m.p. 83–86 °C; $[\alpha]_D = +112$ ($c = 1.8$); $^1$H NMR: $\delta = 7.60$ (d, $J =$ 5.6 Hz, 1H), 7.50 (d, $J = 7.9$ Hz, 2H), 7.32 (d, $J = 7.9$ Hz, 2H), 6.45 (m, 1H), 6.30 (d, $J = 14.9$ Hz, 1H), 6.17 (d, $J = 5.6$ Hz, 1H), 3.6 (s, 2H), 3.28 (d, $J =$ 6.85 Hz, 2H), 2.30 (s, 3H), 0.9 (s, 9H), 0.05 (s, 6H); $^{13}$C NMR: $\delta = 173.5$ (C), 153.2 (CH), 149.9 (CH), 142.4 (C), 141.4 (C), 140.0 (C), 137.4 (CH), 132.9 (CH), 129.8 (CH), 124.2 (CH), 115.2 (CH), 32.7 ($CH_2$), 27.6 ($CH_2$), 25.7 ($CH_3$), 21.1 ($CH_3$), 18.4 (C), −3.9 ($CH_3$); LRMS/FAB: *m/z*: 451 (77) $[M+H]^+$, 392 (11), 240 (32), 212 (35), 182 (33), 163 (50); HRMS: calcd for $C_{22}H_{31}O_4S_2Si$: 451.1433, found: 451.1429.

**Procedure for the thermal cycloadditions**

Compound **9a**: A solution of pyrone **5a** (100 mg, 0.21 mmol) in toluene (10 mL) was heated under reflux for 10 h. The solvent was evaporated and the crude purified by flash chomatography (25–50% EtOAc/hexanes) to afford a 91:9 ratio of diastereoisomers **9a** and **10a** as colorless oils [98%, $R_f$ (50% EtOAc/hexanes): **9a** = 0.54, **10a** = 0.70].

**(1*R*,5*S*,6*R*,7*R*,$R_S$)-9-*tert*-Butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-8-ene-3,3-dicarbonitrile (9a)**: $[\alpha]_D = +108$ ($c = 0.65$); $^1$H NMR: $\delta = 7.61$ (d, $J = 8.1$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 6.63 (d, $J = 5.0$ Hz, 1H), 5.32 (t, $J = 4.9$ Hz, 1H), 3.73 (m, 1H), 3.13 (d, $J =$ 14.5 Hz, 1H), 2.63 (d, $J = 14.7$ Hz, 1H), 2.50 (s, 3H), 2.49 (m, 1H), 2.08 (m, 1H), 1.68 (m, 1H), 0.98 (s, 9H), 0.25 (s, 6H); $^{13}$C NMR: $\delta = 189.3$ (C), 147.5 (C), 143.7 (C), 138.8 (C), 130.8 (CH), 124.5 (CH), 123.8 (CH), 114.6 (CN), 114.3 (CN), 96.7 (C), 77.7 (CH), 76.5 (CH), 44.9 (CH), 41.3 ($CH_2$), 40.4 ($CH_2$), 34.3 (C), 25.4 ($CH_3$), 22.6 ($CH_3$), 18.3 (C), −4.7 ($CH_3$); LRMS/FAB: *m/z*: 483 (95) $[M+H]^+$, 426 (16), 425 (56), 371 (100), 281 (29), 257 (16), 239 (23); HRMS: calcd for $C_{25}H_{31}O_4SiSN_2$: 483.1773, found 483.1751.

**(1*S*,5*R*,6*S*,7*S*,$R_S$)-9-*tert*-Butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxa-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-8-en-3,3-dicarbonitrile (10a)**: $[\alpha]_D = +15.7$ ($c = 0.37$); $^1$H NMR: $\delta = 7.48$ (d, $J = 8.1$ Hz, 2H), 7.39 (d, $J = 8.1$ Hz, 2H), 6.27 (d, $J = 5.0$ Hz, 1H), 5.07 (t, $J = 5.3$ Hz, 1H), 3.48 (dd, $J = 5.8$, 6.6 Hz, 1H), 3.29 (m, 1H), 3.03 (d, $J = 14.6$ Hz, 1H), 2.62 (d, $J = 14.6$ Hz, 1H), 2.47 (s, 3H), 2.34 (dd, $J = 9.9$, 14.4 Hz, 1H), 1.75 (m, 1H), 0.97 (s, 9H), 0.22 (s, 6H); $^{13}$C NMR: $\delta = 189.5$ (C), 147.2 (C), 142.8 (C), 138.6 (C), 130.6 (CH), 123.5 (CH), 123.0 (CH), 115.2 (CN), 114.5 (CN), 96.2 (C), 76.1 (CH), 74.0 (CH), 41.9 ($CH_2$), 41.6 (CH), 40.2 ($CH_2$), 34.1 (C), 25.5 ($CH_3$), 21.5 ($CH_3$), 18.3 (C), −4.7 ($CH_3$); LRMS: *m/z*: 425 (34) $[M - C_4H_9]^+$, 335 (4), 285 (58), 182 (71), 139 (100); HRMS: calcd for $C_{25}H_{30}O_4SiSN_2$: 425.0991, found: 425.0974.

**Diethyl (1*R*,5*S*,6*R*,7*R*,$R_S$)-9-*tert*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-8-ene-3,3-dicarboxylate (9b)** and **(1*S*,5*R*,6*S*,7*S*,$R_S$)-9-*tert*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-10-oxo-11-oxatricyclo[5.3.1.0$^{1,5}$]-undec-8-ene-3,3-dicarboxylate (10b)**: The cycloaddition of **5b** gave a 97:3 mixture of diastereoisomers **9b** and **10b** as colorless oils [99%, $R_f$ (20% EtOAc/hexanes): **9b** = 0.20, **10b** = 0.30].

Compund **9b**: $[\alpha]_D = +90$ ($c = 0.6$); $^1$H NMR: $\delta = 7.61$ (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 6.60 (d, $J = 4.9$ Hz, 1H), 5.10 (t, $J = 5.3$ Hz, 1H), 4.13 (m, 4H), 3.87 (t, $J = 5.9$ Hz, 1H), 3.0 (d, $J = 14.8$ Hz, 1H), 2.51 (d, $J =$ 14.8 Hz, 1H), 2.43 (s, 3H), 2.33 (m, 1H), 1.68 (m, 2H), 1.19 (m, 6H), 0.97 (s, 9H), 0.21 (s, 6H); $^{13}$C NMR: $\delta = 191.4$ (C), 170.4 (C), 170.1 (C), 147.7 (C), 142.7 (C), 139.1 (C), 130.4 (CH), 124.8 (CH), 124.3 (CH), 97.5 (C), 76.9 (CH), 76.3 (CH), 61.9 ($CH_2$), 61.7 ($CH_2$), 61.2 (C), 44.3 (CH), 37.1 ($CH_2$), 36.3 ($CH_2$), 25.5 ($CH_3$), 21.5 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), 13.9 ($CH_3$), −4.7 ($CH_3$); LRMS: *m/z*: 519 (8) $[M - C_4H_9]^+$, 380 (21), 333 (11), 233 (25), 173 (46), 139 (40); HRMS: calcd for $C_{29}H_{40}O_8SiS - C_4H_9$: 519.1509, found: 519.1523.

Compound **10b**: $[\alpha]_D = +41$ ($c = 0.2$); $^1$H NMR: $\delta = 7.52$ (d, $J = 7.9$ Hz, 2H), 7.36 (d, $J = 7.9$ Hz, 2H), 6.23 (d, $J = 5$ Hz, 1H), 4.80 (t, $J = 5.4$ Hz, 1H), 4.13 (m, 4H), 3.74 (t, $J = 6.0$ Hz, 1H), 3.1 (m, 1H), 3.08 (d, $J = 14.85$ Hz, 1H), 2.48 (d, $J = 14.85$ Hz, 1H), 2.43 (s, 3H), 1.92 (m, 2H), 1.21 (m, 6H), 0.96 (s, 9H), 0.22 (s, 6H); $^{13}$C NMR: $\delta = 192.2$ (C), 171.0 (C), 169.5 (C), 147.2 (C), 142.0 (C), 139.2 (C), 130.3 (CH), 123.7 (CH), 123.5 (CH), 97.2 (C), 75.4 (CH), 73.9 (CH), 61.8 ($CH_2$), 61.7 ($CH_2$), 61.2 (C), 41.7 (CH), 37.5 ($CH_2$), 37.3 ($CH_2$), 25.9 ($CH_3$), 21.8 ($CH_3$), 18.7 (C), 14.3 ($CH_3$), 14.3 ($CH_3$), −4.2 ($CH_3$); LRMS/FAB: *m/z*: 577 (79) $[M+H]^+$, 421 (30), 363 (34), 281 (50), 233 (24), 221(66), 173 (100); HRMS: calcd for $C_{29}H_{41}O_8SiS$ 577.2291, found 577.2291.

**(1*R*,5*R*,6*R*,7*R*,$R_S$)-9-*tert*-Butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.0$^{1,5}$]undec-8-en-10-one (9c)** and **(1*S*,5*S*,6*S*,7*S*,$R_S$)-9-*tert*-butyldimethylsilyloxy-6-[*p*-tolylsulfinyl-11-oxa-3-thiatricyclo[5.3.1.0$^{1,5}$]undec-8-en-10-one (10c)**: The cycloaddition of **5c** gave a 93:7 mixture of diastereoisomers **9c** and **10c** as colorless oils [95%, $R_f$ (30% EtOAc/hexanes): **9c** = 0.55, **10c** = 0.70]. The diastereomeric ratio was determined by integrating the signals of the H-7 (t) of the two isomers in the $^1$H NMR of the crude reaction mixture.

Compound **9c**: $[\alpha]_D = +73$ ($c = 1.9$); $^1$H NMR: $\delta = 7.60$ (d, $J = 7.9$ Hz, 2H), 7.37 (d, $J = 7.9$ Hz, 2H), 6.63 (d, $J = 4.8$ Hz, 1H), 5.26 (t, $J = 5.03$ Hz, 1H), 3.51 (m, 1H), 3.45 (m, 1H), 2.78 (d, $J = 12$ Hz, 1H), 2.5 (m, 1H), 2.45 (s, 3H), 2.38 (m, 1H), 1.77 (dd, $J = 3.2$, 8.9 Hz, 1H), 1. 0 (s, 9H), 0.24 (s, 6H); $^{13}$C NMR: $\delta = 191.6$ (C), 147.7 (C), 143.2 (C), 139.1 (C), 130.4 (CH), 124.8 (CH), 124.2 (CH), 100.2 (C), 77.3 (CH), 75.8 (CH), 49.8 (CH), 35.7 ($CH_2$), 35.2 ($CH_2$), 25.2 ($CH_3$), 23.1 ($CH_3$), 18.4 (C), −4.6 ($CH_3$); LRMS FAB: *m/z*: 451 (54) $[M+H]^+$, 393 (13), 255 (11), 179 (100), 163 (97); HRMS: calcd for $C_{22}H_{31}O_4S_2Si$: 451.1433, found: 451.1421.

Compound **10c**: $[\alpha]_D = +11.5$ ($c = 0.23$); $^1$H NMR: $\delta = 7.52$ (d, $J = 7.9$ Hz, 2H), 7.37 (d, $J = 7.9$ Hz, 2H), 6.23 (d, $J = 4.9$ Hz, 1H), 4.84 (t, $J = 5.16$ Hz, 1H), 3.46 (d, $J = 13.3$ Hz, 1H), 3.36 (m, 1H), 3.26 (m, 1H), 2.88 (dd, $J = 7.9$, 12.5 Hz, 1H), 2.76 (d, $J = 13.3$ Hz, 1H), 2.43 (s, 3H), 2.11 (d, $J = 12.5$ Hz, 1H), 0.97 (s, 9H), 0.22 (s, 6H); $^{13}$C NMR: $\delta = 192.3$ (C), 148.0 (C), 143.1 (C), 139.6 (C), 130.8 (CH), 124.4 (CH), 123.7 (CH), 100.5 (C), 76.1 (CH), 74.1 (CH), 48.2 (CH), 36.7 ($CH_2$), 36.2 ($CH_2$), 26.0 ($CH_3$), 22.0 ($CH_3$), 18.8 (C), −4.3 ($CH_3$); LRMS/FAB: *m/z*: 451 (61) $[M+H]^+$, 312 (38), 255 (31), 237 (57), 221 (38), 179 (100) 163 (54); HRMS: calcd for $C_{22}H_{31}O_4S_2Si$: 451.1433, found: 451.1413.

**Diethyl (1*R*,5*R*,7*S*)-9-*tert*-butyldimethylsilyloxy-10-oxo-11-oxatricyclo-[5.3.1.0$^{1,5}$]undec-8-ene-3,3-dicarboxylate [(+)-(11)]**: A solution of compound **9b** (35 mg, 0.06 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (300 mg) in THF (4 mL). The reaction mixture was heated under reflux for 25 min, allowed to cool to RT, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by flash chromatography (5% EtOAc/hexanes) to afford **11** as a colorless oil (23 mg, 85%, 97% *ee*, $R_f = 0.33$ (10% EtOAc/hexanes). Enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$ (0.3 equiv) by comparison of the split signals of the vinylic proton with those of racemic **11**. $[\alpha]_D = +43$ ($c = 1$); $^1$H NMR: $\delta = 6.21$ (d, $J =$ 4.9 Hz, 1H), 4.81 (dt, $J = 4.8$, 1.8 Hz, 1H), 4.17 (m, 4H), 3.13 (d, $J =$ 14.7 Hz, 1H), 2.60 (m, 1H), 2.54 (m, 1H), 2.45 (m, 1H), 2.33 (m, 1H), 2.14 (m, 2H), 1.24 (m, 6H), 0.91 (s, 9H), 0.13 (s, 6H); $^{13}$C NMR: $\delta = 193.4$ (C), 170.9 (C), 145.6 (C), 128.7 (CH), 97.1 (C), 75.6 (CH), 61.9 (C), 61.7 ($CH_2$), 61.5 ($CH_2$), 43.4 (CH), 38.9 ($CH_2$), 37.7 ($CH_2$), 37.0 ($CH_2$), 25.5 ($CH_3$), 18.4 (C), 14.0 ($CH_3$), −4.321 ($CH_3$); LRMS/FAB: *m/z*: 439 (100) $[M+H]^+$, 381 (52), 307 (79), 289 (44); HRMS: calcd for $C_{22}H_{35}O_7Si$: 439.2152, found: 439.2133.

**Diethyl (1*R*,5*R*,7*S*,10*S*)-10-*tert*-butyldimethylsilyloxy-9-oxo-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-3,3-dicarboxylate (−)-12**: A solution of compound **9b** (200 mg, 0.10 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (1.0 g) in THF (12 mL). The reaction mixture was heated under reflux for 1 h under atmosphere of $H_2$ (balloon), allowed to cool to RT, filtered, and poured into water. Extraction with $Et_2O$, drying and concentration gave a residue which was purified by flash chromatography (3–20% EtOAc/hexanes) to afford **12** as a colorless oil (107 mg, 66%, 97% *ee*). $[\alpha]_D = -19$ ($c = 1.2$); $R_f = 0.23$ (15% EtOAc/hexanes). Enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$ (0.3 equiv) by comparison of the split signals of the TBS methyl protons with those of racemic **12**. $[\alpha]_D = -19$ ($c = 1.1$); $^1$H NMR: $\delta = 4.39$ (d, $J =$ 6.1 Hz, 1H), 4.02 (m, 5H), 2.63 (d, $J = 14.0$ Hz, 1H), 2.51 (m, 3H), 2.28 (d, $J = 13.7$ Hz, 1H), 2.12 (d, $J = 15.2$ Hz, 1H), 2.01 (m, 2H), 1.84 (m, 1H), 1.12 (m, 6H), 0.80 (s, 9H), 0.00 (s, 3H), −0.11 (s, 3H); $^{13}$C NMR: $\delta = 205.1$ (C), 171.1 (C), 95.7 (C), 78.0 (CH), 76.0 (CH), 61.4 ($CH_2$), 61.2 ($CH_2$), 48.2 ($CH_2$), 41.0 ($CH_2$), 40.6 (CH), 39.5 ($CH_2$), 39.3 ($CH_2$), 25.6 ($CH_3$), 18.3 (C), 13.8 ($CH_3$), −4.4 ($CH_3$), −5.8 ($CH_3$); LRMS: *m/z*: 383 (100) $[M - C_4H_9]^+$, 365 (21), 355 (14), 339 (12), 337 (14), 291 (30), 263 (14), 235 (6), 155 (16), 129 (6), 139 (88), 57 (4); HRMS: calcd for $C_{18}H_{27}O_7Si$: 383.1526, found: 383.1535.

**(1*R*,5*S*,7*R*)-3-*tert*-Butyldimethylsilyloxy-1,7-dimethyl-8-oxabicyclo[3.2.1]-octan-3-en-2-one [(+)-13]**: Raney nickel (300 mg) was washed with THF (3x5 mL) and heated in THF (4 mL). The compound **9c** (30 mg, 0.07 mmol) in THF (2 mL) was added onto the hot suspension and the reaction mixture was heated under reflux for 2 h. The resulting suspension was allowed to cool to RT, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by



0947-6539/02/0804-0892 $ 17.50+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 4

flash chromatography (5% EtOAc/hexanes) to afford **13**[8] (23 mg, 69%, 97% *ee*) as a colorless oil. $R_f = 0.38$ (6% EtOAc/hexanes); $[\alpha]_D = +103$ ($c = 1$).

**(1*R*,2*S*,5*S*,7*R*)-2-*tert*-Butyldimethylsilyloxy-1,7-dimethyl-8-oxabicyclo-[3.2.1]octan-3-one [(−)-(14)]**: A solution of compound **9c** (350 mg, 0.7 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (5.0 g) in THF (6 mL) under hydrogen atmosphere (balloon). The reaction mixture was heated under reflux for 60 min, allowed to cool to room temperature, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by flash chromatography (2–7% EtOAc/hexanes) to afford **14**[7b] (124 mg, 65%, 97% *ee*) as a colorless oil. $R_f = 0.30$ (6% EtOAc/hexanes); $[\alpha]_D = -44$ ($c = 0.25$). Enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$ (0.35 equiv) by comparison of the split signals of H-5 with those of racemic **14**. $^1$H NMR: $\delta = 4.5$ (t, $J = 6.1$ Hz, 1H), 3.9 (s, 1H), 2.75 (dd, $J =$ 5.5, 14.7 Hz, 1H), 2.23 (m, 2H), 1.97 (dd, $J = 9.1$, 12.8 Hz, 1H), 1.59 (m, 1H), 1.32 (s, 3H), 0.92 (d, 3H), 0.9 (s, 9H), 0.14 (s, 3H), 0.01 (s, 3H).

**Diethyl 2-[(5-*tert*-Butyldimethylsilyloxy-4-oxo-4*H*-2-pyranyl)methyl]-2-[(2*E*,*R*$_s$)-3-*p*-tolylsulfinyl-2-propenyl]malonate (16)**: Diethylmalonate (2.3 g, 14.6 mmol) was added to a −78 °C cooled suspension of NaH (0.483 g, 60% mineral oil, 14.6 mmol) in THF (20 mL). After stirring for 15 min at RT, the reaction mixture was cooled at −78 °C, and chloride **15**[7b] (2 g, 7.30 mmol) and NaI (1.1 g, 7.3 mmol) were added. The mixture was stirred for 4 h at RT, poured into brine, extracted with $Et_2O$, dried, filtered, and concentrated. The crude was purified by flash chromatography (5–40% EtOAc/hexanes) to afford the coupling product as a colorless viscous oil (2.2 g, 75%). $R_f = 0.10$ (10% EtOAc/hexanes); $^1$H NMR: $\delta = 7.51$ (s, 1H), 6.12 (s, 1H), 4.12 (q, $J = 7.15$ Hz, 4H), 3.63 (t, $J = 7.7$ Hz, 1H), 3.01 (d, $J = 7.7$ Hz, 2H), 1.16 (t, $J = 7.15$ Hz, 6H), 0.85 (s, 9H), 0.13 (s, 6H); $^{13}$C NMR: $\delta = 174.8$ (C), 168.2 (C), 163.6 (C), 144.9 (C), 143.7 (CH), 114.1 (CH), 61.6 ($CH_2$), 49.0 (CH), 31.9 ($CH_2$), 25.1 ($CH_3$), 18.1 (C), 13.8 ($CH_3$), −4.9 ($CH_3$); LRMS: $m/z$: 383 (3) $[M - CH_3]^+$, 341 (100), 269 (18), 239 (25), 195 (74), 151 (7); HRMS: calcd for $C_{19}H_{30}O_7Si - CH_3$: 383.1526, found: 383.1508. The conversion of this product into **16** was carried out following the same procedure than for the transformation of **2b** into **5b**. [70%, $R_f =$ 0.35 (50% EtOAc/hexanes), viscous oil]. **16**: $[\alpha]_D = +75$ ($c = 0.45$); $^1$H NMR: $\delta = 7.50$ (s, 1H), 7.47 (d, $J = 8.2$ Hz, 2H), 7.30 (d, $J = 8.2$ Hz, 2H), 6.42 (m, 1H), 6.28 (d, $J = 15.0$ Hz, 1H), 6.10 (s, 1H), 4.15 (m, 4H), 3.12 (s, 2H), 2.76 (d, $J = 7.3$ Hz, 2H), 2.39 (s, 3H), 1.21 (m, 6H), 0.93 (s, 9H), 0.20 (s, 6H); $^{13}$C NMR: $\delta = 174.9$ (C), 168.8 (C), 162.5 (C), 145.3 (C), 143.8 (CH), 141.8 (C), 140.1 (C), 139.8 (CH), 131.2 (CH), 130.0 (CH), 124.5 (CH), 116.1 (CH), 62.1 ($CH_2$), 56.6 (C), 36.2 $CH_2$), 34.9 ($CH_2$), 25.4 ($CH_3$), 21.3 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), −4.5 ($CH_3$); LRMS/FAB: $m/z$: 577 (100) $[M+H]^+$, 520 (11), 519 (34), 307 (19), 277 (13), 204 (10), 154 (54); HRMS: calcd for $C_{29}H_{41}O_8SiS$: 577.2291, found: 577.2263.

**Diethyl (1*R*,5*R*,6*S*,7*S*,*R*$_S$)-9-*tert*-butyldimethylsilyloxy-8-oxo-6-(*p*-tolylsulfinyl)-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-9-ene-3,3-dicarboxylate (17)** and **diethyl (1*S*,5*S*,6*R*,7*R*,*R*$_S$)-9-*tert*-butyldimethylsilyloxy-8-oxo-6-(*p*-tolylsulfinyl)-11-oxatricyclo[5.3.1.0$^{1,5}$]undec-9-ene-3,3-dicarboxylate (18)**: A solution of compound **16** (124 mg, 0.215 mmol) in toluene (20 mL) was heated at 160 °C for 48 h. The solvent was evaporated and the crude purified by flash chomatography (15–25% EtOAc/hexanes) to afford a 89:11 mixture of diastereoisomers **17** and **18** as colorless oils [51%, $R_f =$ (20% EtOAc/hexanes): **17** = 0.45, **18** = 0.18]. The diastereomeric ratio is based on isolated products. **17**: $^1$H NMR: $\delta = 7.53$ (d, $J = 8.1$ Hz, 2H), 7.33 (d, $J =$ 8.1 Hz, 2H), 6.44 (s, 1H), 4.70 (d, $J = 7.2$ Hz, 1H), 4.13 (m, 4H), 3.61 (dd, $J = 5.0$, 7.42 Hz, 1H), 3.2 (m, 1H), 2.72 (d, $J = 14.4$ Hz, 1H), 2.54 (d, $J =$ 14.4 Hz, 1H), 2.41 (s, 3H), 2.1–1.85 (m, 2H), 1.22 (m, 6H), 0.95 (s, 9H), 0.22 (s, 6H); $^{13}$C NMR: $\delta = 190.8$ (C), 170.6 (C), 170.5 (C), 148.4 (C), 141.6 (C), 139.5 (C), 130.0 (CH), 129.8 (CH), 123.8 (CH), 91.8 (C), 83.8 (CH), 71.6 (CH), 61.9 ($CH_2$), 61.7 (C), 61.7 ($CH_2$), 45.2 (CH), 42.1 ($CH_2$), 38.5 ($CH_2$), 25.6 ($CH_3$), 21.4 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), 13.8 ($CH_3$), −4.6 ($CH_3$); LRMS/FAB: $m/z$: 577 (100) $[M+H]^+$, 519 (70), 277 (24), 205 (149), 173 (11); HRMS: calcd for $C_{29}H_{41}O_8SiS$: 577.2291, found: 577.2264.

Compound **18**: $[\alpha]_D = +18$ ($c = 0.23$); $^1$H NMR: $\delta = 7.59$ (d, $J = 8.0$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 6.43 (s, 1H), 4.88 (d, $J = 7.2$ Hz, 1H), 4.14 (m, 4H), 3.75 (dd, $J = 5.5$, 7.1 Hz, 1H), 2.69 (d, $J = 14.5$ Hz, 1H), 2.50 (d, $J =$ 14.5 Hz, 1H), 2.42 (m, 1H), 2.41 (s, 3H), 2.05 (dd, $J = 4.9$, 13.7 Hz, 1H), 1.68 (dd, $J = 9.8$, 13.7 Hz, 1H), 1.21 (m, 6H), 0.95 (s, 9H), 0.23 (s, 6H); $^{13}$C NMR: $\delta = 190.0$ (C), 170.8 (C), 170.1 (C), 148.2 (C), 142.6 (C), 139.2 (C), 130.3 (CH), 129.9 (CH), 125.2 (CH), 91.7 (C), 84.6 (CH), 71.9 (CH), 62.0 ($CH_2$), 61.9 (C), 61.8 ($CH_2$), 50.7 (CH), 42.3 ($CH_2$), 37.9 ($CH_2$), 25.6 ($CH_3$), 21.5 ($CH_3$), 18.4 (C), 13.9 ($CH_3$), 13.8 ($CH_3$), −4.5 ($CH_3$); LRMS: $m/z$: 519 (49) $[M - C_4H_9]^+$, 395 (0.2), 277 (38), 204 (38), 139 (29), 73 (100). HRMS: calcd for $C_{29}H_{41}O_8SiS$ 577.2291, found 577.2264.

**Diethyl (1*S*,5*S*,7*R*)-9-*tert*-butyldimethylsilyloxy-8-oxo-11-oxatricyclo-[5.3.1.0$^{1,5}$]-undec-9-ene-3,3-dicarboxylate (20)**: A solution of compound **17** (36 mg, 0.06 mmol) in THF (1 mL) was added to a suspension of activated Raney nickel (250 mg) in THF (6 mL). The reaction mixture was heated under reflux for 35 min, allowed to cool to RT, filtered, and poured into water. Extraction with EtOAc, drying and concentration gave a residue which was purified by flash chromatography (2–10% EtOAc/hexanes) to afford **20** (19 mg, 68%, 97% *ee*) as a colorless oil. $R_f = 0.40$ (10% EtOAc/hexanes). Enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$ (0.40 equiv) by comparison of the split signals of the C-2 methylenic protons with those of racemic **20**. $[\alpha]_D = +64$ ($c = 0.5$); $^1$H NMR: $\delta = 6.39$ (s, 1H), 4.63 (d, $J = 7.9$ Hz, 1H), 4.17 (m, 4H), 2.66 (s, 2H), 2.60 (m, 1H), 2.37 (m, 2H), 2.20 (m, 1H), 1.87 (m, 1H), 1.22 (m, 6H), 0.90 (s, 9H), 0.12 (s, 6H); $^{13}$C NMR: $\delta = 194.0$ (C), 171.7 (C), 170.5 (C), 146.9 (C), 131.0 (CH), 91.5 (C), 83.6 (CH), 62.0 ($CH_2$), 61.8 ($CH_2$), 61.5 (C), 47.8 (CH), 42.0 ($CH_2$), 40.1 ($CH_2$), 33.1 ($CH_2$), 25.5 ($CH_3$), 18.3 (C), 14.1 ($CH_3$), −4.6 ($CH_3$); LRMS: $m/z$: 381 (58) $[M - C_4H_9]^+$, 307 (19), 255 (14), 205 (25), 182 (30), 73 (100); HRMS: calcd for $C_{22}H_{34}O_7Si - C_4H_9$: 381.1369, found: 381.1357.

**Diethyl 2-[(5-*tert*-Butyldimethylsilyloxy-4-oxo-4*H*-2-pyranyl)methyl]-2-[(*R*$_s$)-2-*p*-tolylsulfinyl-2-propenyl]malonate (23)**: Methanesulfonyl chloride (0.09 mL, 1.18 mmol) was added dropwise to a solution of (*S*$_s$)-2-(*p*-tolylsulfinyl)prop-2en-1-ol (**21**)[27] [58 mg, 0.296 mmol, 97% *ee*; $[\alpha]_D =$ +102.0 ($c = 0.55$, EtOH); lit.: $[\alpha]_D = +103.0$ ($c = 0.55$, *ee* = 97%)] and $Et_3N$ (0.16 mL, 1.18 mmol) in $CH_2Cl_2$ (8 mL) at 0 °C. After the addition, the reaction mixture was warmed to RT and stirred for 2 h. The mixture was poured into water, extracted with $CH_2Cl_2$, dried, filtered, and concentrated to afford a residue with **22** as the major product. $^1$H NMR: $\delta = 7.55$ (d, $J =$ 8.0 Hz, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 6.41 (s, 1H), 6.08 (s, 1H), 4.8 (d, 1H), 4.6 (d, 1H), 3.0 (s, 3H), 2.41 (s, 3H). This crude residue was dissolved in THF (2 mL) and added to diethyl-2-[(5-*tert*-butyldimethylsilyloxy-4-oxo-4*H*-2-pyranyl)methyl]malonate (130 mg, 0.33 mmol) and NaH (13 mg, 0.33 mmol) in THF (5 mL). The mixture was stirred at RT for 30 min, poured into brine, extracted with $Et_2O$, dried, filtered, and concentrated. The crude was purified by flash chromatography (20–60% EtOAc/hexanes) to afford **23** as a colorless oil (136 mg, 82% from **21**). $R_f = 0.15$ (40% EtOAc/hexanes); $[\alpha]_D = +61$ ($c = 0.71$); $^1$H NMR: $\delta = 7.28$ (d, $J =$ 8.0 Hz, 2H), 7.06 (d, $J = 8.0$ Hz, 2H), 6.09 (s, 1H), 5.95 (s, 1H), 5.53 (s, 1H), 3.96 (m, 4H), 3.00 (s, 2H), 2.53 (d, $J = 16.4$ Hz, 1H), 2.24 (d, $J = 16.4$ Hz, 1H), 2.18 (s, 3H), 1.04 (m, 6H), 0.72 (s, 9H), 0.00 (s, 6H); $^{13}$C NMR: $\delta =$ 174.8 (C), 170.0 (C), 169.9 (C), 162.4 (C), 149.3 (C) 145.2 (C), 143.7 (CH), 142.3 (C), 138.7 (C), 129.9 (CH), 125.8 (CH), 118.7 ($CH_2$), 116.1 (CH), 62.2 ($CH_2$), 62.1 ($CH_2$), 56.2 (C), 35.9 ($CH_2$), 31.1 ($CH_2$), 25.4 ($CH_3$), 21.3 ($CH_3$), 18.3 (C), 13.7 ($CH_3$), −4.7 ($CH_3$); LRMS: $m/z$: 519 (100) $[M - C_4H_9]^+$, 419 (14), 339 (20), 277 (42), 204 (69), 73 (80); HRMS: calcd for $C_{29}H_{40}O_8SiS - C_4H_9$: 519.1509, found: 519.1533.

**Cycloaddition of 23**: A solution of compound **23** (45 mg, 0.11 mmol) in toluene (10 mL) was heated at 110 °C for 4 h. The solvent was evaporated and the crude purified by flash chomatography (2–20% EtOAc/hexanes) to give **24** [42 mg, 93%, $R_f = 0.18$ (5% EtOAc/hexanes)].

Compound **24**: $[\alpha]_D = +92$ ($c = 1.35$); $^1$H NMR: $\delta = 7.47$ (d, $J = 8.1$ Hz, 2H), 7.29 (d, $J = 8.1$ Hz, 2H), 6.59 (s, 1H), 4.57 (d, $J = 7.7$ Hz, 1H), 4.19 (m, 4H), 2.91 (d, $J = 14.0$ Hz, 1H), 2.74 (d, $J = 14.4$ Hz, 1H), 2.67 (d, $J =$ 14.0 Hz, 1H), 2.41 (s, 3H), 2.37–2.26 (m, 2H), 1.97 (d, $J = 14$ Hz, 1H), 1.25 (m, 6H), 0.97 (s, 9H), 0.24 (s, 6H); $^{13}$C NMR: $\delta = 192.9$ (C), 170.6 (C), 169.9 (C), 149.7 (C), 142.3 (C), 136.7 (C), 129.8 (CH), 126.2 (CH), 125.4 (CH), 93.8 (C), 81.9 (CH), 78.0 (C), 61.9 ($CH_2$), 61.7 ($CH_2$), 59.9 (C), 41.7 ($CH_2$), 36.8 ($CH_2$), 35.4 ($CH_2$), 25.5 ($CH_3$), 21.4 ($CH_3$), 18.3 (C), 14.0 ($CH_3$), 13.9 ($CH_3$), −4.53 ($CH_3$), −4.61 ($CH_3$); LRMS: $m/z$: 519 (55) $[M - C_4H_9]^+$, 437 (3), 233 (25), 179 (72), 139 (25), 73 (100); HRMS: calcd for $C_{29}H_{40}O_8SiS - C_4H_9$: 519.1508, found: 577.1490.

**Diethyl (1*S*,7*R*)-9-*tert*-butyldimethylsilyloxy-8-oxo-11-oxatricyclo[5.3.1.0$^{1,5}$]-undec-4,9-diene-3,3-dicarboxylate (25)**: Heating of compound **23** (97 mg, 0.17 mmol) in toluene at 110 °C in presence of P(OEt)$_3$ (56 mg, 0.34 mmol) for 52 h gave **25** (58 mg, 78%, 97% *ee*). $R_f = 0.48$ (5% EtOAc/hexanes). Enantiomeric excess was determined by $^1$H NMR in presence of Pr(hfc)$_3$

(0.3 equiv) by comparison of the split signals of H-7 with those of racemic **25** prepared from racemic **23**.

Compound **25**: $[\alpha]_D = +60$ ($c = 0.5$); $^1$H NMR: $\delta = 6.56$ (s, 1H), 5.74 (s, 1H), 4.88 (d, $J = 7.6$ Hz, 1H), 4.22 (m, 4H), 3.05 (d, $J = 13.5$ Hz, 1H), 2.96 (m, 1H), 2.34 (d, $J = 13.5$ Hz, 1H), 2.23 (m, 1H), 1.25 (m, 6H), 0.94 (s, 9H), 0.17 (s, 6H); $^{13}$C NMR: $\delta = 193.0$ (C), 170.0 (C), 169.8 (C), 149.8 (C), 146.6 (C), 129.7 (CH), 119.3 (CH), 93.2 (C), 86.0 (CH), 71.5 (C), 62.0 ($CH_2$), 61.8 ($CH_2$), 42.4 ($CH_2$), 26.4 ($CH_2$), 25.5 ($CH_3$), 18.4 (C), 14.0 ($CH_3$), $-4.63$ ($CH_3$), $-4.71$ ($CH_3$); LRMS: $m/z$: 379 (34) $[M - C_4H_9]^+$, 333 (14), 233 (18), 204 (100), 131 (6), 73 (54); HRMS: calcd for $C_{22}H_{32}O_7Si - C_4H_9$ 379.1213, found: 379.1205.

**Diethyl (2*E*,$R_S$)-3-*p*-tolylsulfinyl-2-propenylmalonate (27)**: KI (0.33 g, 2.01 mmol) was added to a solution of mesylate **4** (0.55 g, 2.01 mmol) in acetone (40 mL). After stirring for 3 h at RT the reaction mixture was poured into water, extracted with $Et_2O$, dried, filtered and concentrated. The crude residue was used without further purification in the next reaction. $^1$H NMR: $\delta = 7.42$ (d, $J = 8.1$ Hz, 2H), 7.25 (d, $J = 8.1$ Hz, 2H), 6.64 (m, 1H), 6.29 (d, $J = 14.8$ Hz, 1H), 3.85 (d, $J = 8.1$ Hz, 2H), 2.33 (s, 3H).

Diethylmalonate (0.65 g, 4.03 mmol) was added to a cooled ($-78\,^\circ$C) suspension of NaH (0.16 g, 60% mineral oil, 4.03 mmol) in THF (25 mL). After being stirred for 20 min at RT, a solution of the above crude iodide (2.01 mmol) in THF (3 mL) was added. The reaction mixture was stirred for 20 min at RT, poured into brine, extracted with $Et_2O$, dried, filtered and concentrated. The crude residue was purified by flash chromatography (30–40% EtOAc/hexanes) to afford **27** as a colorless oil (537 mg, 79%). $R_f = 0.65$ (40% EtOAc/hexanes); $[\alpha]_D = +112$ ($c = 0.77$); $^1$H NMR: $\delta =$ 7.31 (d, $J = 7.9$ Hz, 2H), 7.11 (d, $J = 7.9$ Hz, 2H), 6.31 (m, 1H), 6.09 (d, $J =$ 15.1 Hz, 1H), 3.92 (m, 4H), 3.27 (t, $J = 7.3$ Hz, 1H), 2.58 (m, 2H), 2.16 (s, 3H), 0.99 (m, 6H); $^{13}$C NMR: $\delta = 168.5$ (C), 141.9 (C), 140.8 (C), 138.0 (CH), 134.6 (CH), 130.4 (CH), 125.0 (CH), 62.0 ($CH_2$), 51.0 (CH), 31.1 ($CH_2$), 21.7 ($CH_3$), 14.3 ($CH_3$); LRMS: $m/z$: 338 (2.42) $[M]^+$, 321 (15), 293 (9), 290 (31), 216 (56), 143 (100); HRMS: calcd for $C_{17}H_{22}O_5S$: 338.1188, found: 338.1193.

**Amination of alkenylsulfoxide 27 with *O*-mesitylsulfonyl hydroxylamine (MSH)**: MSH (412 mg, 1.92 mmol) was added to a 0 °C cooled solution of alkenylsulfoxide **27** (405 mg, 1.20 mmol) in $CH_3CN$ (7 mL). After being stirred at 0 °C for 2 h the reaction mixture was slowly allowed to reach RT and stirred further for 18 h. The mixture was diluted in $CH_2Cl_2$ (5 mL), poured into a cold (0 °C) aqueous solution of NaOH (10%, 10 mL), stirred for 15 min, and extracted with $CH_2Cl_2$. The organic phases were dried, filtered, and concentrated. The resulting crude sulfoximine **28a** was used for the next step without further purification. $^1$H NMR: $\delta = 7.83$ (d, $J =$ 8.3 Hz, 2H), 7.32 (d, $J = 8.0$ Hz, 2H), 6.85 (m, 1H), 6.50 (d, $J = 14.9$ Hz, 1H), 4.15 (m, 4H), 3.47 (t, $J = 7.3$ Hz, 1H), 2.80 (m, 2H), 2.40 (s, 3H), 2.29 (s, 1H), 1.18 (m, 6H).

**Preparation of *N*-substituted sulfoximine derivatives 28b–i: 28b**: Acetyl chloride (44 mg, 0.57 mmol) was added dropwise to a stirred solution of the crude alkenylsulfoximine **28a** (0.28 mmol) and $Et_3N$ (57 mg, 0.57 mmol) in $CH_2Cl_2$ (5 mL) cooled at 0 °C. After being stirred for 30 min at 0 °C the mixture was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The residue was purified by flash chromatography (30–40% EtOAc/hexanes) to afford **28b** as a colorless oil (93 mg, 82% for two steps). $R_f = 0.15$ (40% EtOAc/hexanes); $[\alpha]_D = +15$ ($c = 0.85$); $^1$H NMR: $\delta = 7.77$ (d, $J = 8.3$ Hz, 2H), 7.31 (d, $J = 8.2$ Hz, 2H), 6.90 (m, 1H), 6.51 (d, $J =$ 15.0 Hz, 1H), 4.13 (m, 4H), 3.49 (t, $J = 7.3$ Hz, 1H), 2.83 (m, 2H), 2.43 (s, 3H), 2.14 (s, 3H), 1.23 (m, 6H); $^{13}$C NMR: $\delta = 179.6$ (C), 167.8 (C), 144.5 (C), 142.2 (CH), 134.9 (C), 131.1 (CH), 130.0 (CH), 127.3 (CH), 61.8 ($CH_2$), 50.0 (CH), 30.2 ($CH_2$), 26.7 ($CH_3$), 21.5 ($CH_3$), 13.8 ($CH_3$); LRMS: $m/z$: 350 (8.1) $[M - C_2H_5O]^+$, 308 (5), 247 (39), 215 (10), 201 (14), 139 (100); HRMS: calcd for $C_{17}H_{20}NO_5S$: 350.1062, found: 350.1066.

Compound **28c**: Trifluoroacetic anhydride (196 mg, 0.93 mmol) was added dropwise to a stirred solution of the crude alkenylsulfoximine **28a** (0.47 mmol) and $Et_3N$ (95 mg, 0.93 mmol) in $CH_2Cl_2$ (8 mL) at 0 °C. After being stirred for 30 min at 0 °C the mixture was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (20–40% EtOAc/hexanes) to afford **28c** as a colorless oil (151 mg, 72% for two steps). $R_f = 0.56$ (40% EtOAc/hexanes); $[\alpha]_D = +14$ ($c = 1.6$); $^1$H NMR: $\delta = 7.79$ (d, $J = 8.4$ Hz, 2H), 7.40 (d, $J =$ 8.1 Hz, 2H), 7.06 (m, 1H), 6.52 (d, $J = 14.0$ Hz, 1H), 4.15 (m, 4H), 3.53 (t, $J = 7.2$ Hz, 1H), 2.89 (m, 2H), 2.46 (s, 3H), 1.22 (m, 6H); $^{13}$C NMR: $\delta =$ 167.7 (C), 145.9 (C), 144.8 (CH), 133.0 (C), 130.5 (CH), 129.3 (CH), 127.4 (CH), 62.0 ($CH_2$), 49.9 (CH), 30.4 ($CH_3$), 21.6 ($CH_3$), 13.9 ($CH_3$); LRMS: $m/z$: 404 (9.1) $[M - C_2H_5O]^+$, 380 (40), 262 (4), 247 (18), 201 (16), 139 (100); HRMS: calcd for $C_{17}H_{17}NO_5F_3S$: 404.0780, found: 404.0789.

Compound **28d**: Benzoyl chloride (160 mg, 1.13 mmol) was added dropwise to a stirred solution of the crude alkenylsulfoximine **28a** (0.57 mmol), $Et_3N$ (115 mg, 1.13 mmol) and DMAP (14 mg, 0.2 mmol) in $CH_2Cl_2$ (10 mL) at 0 °C. After being stirred for 10 h at RT the mixture was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (20–35% EtOAc/hexanes) to afford **28d** as a colorless oil (155 mg, 60% for two steps). $R_f = 0.15$ (30% EtOAc/hexanes); $[\alpha]_D = +6$ ($c = 2.1$); $^1$H NMR: $\delta = 8.20$ (m, 2H), 7.81 (m, 2H), 7.45 (m, 5H), 7.12 (m, 1H), 6.65 (d, $J = 15.0$ Hz, 1H), 4.15 (m, 4H), 3.52 (t, $J = 7.4$ Hz, 1H), 2.87 (m, 2H), 2.44 (s, 3H), 1.15 (m, 6H); $^{13}$C NMR: $\delta = 192.5$ (C), 175 (C), 167.6 (C), 145 (C), 143.6 (CH), 136 (C), 134.3 (CH), 133.1 (CH), 131.0 (CH), 134.3 (CH), 129.3 (CH), 127.2 (CH), 61.7 ($CH_2$), 49.8 (CH), 30.2 ($CH_2$), 21.3 ($CH_3$), 13.7 ($CH_3$); LRMS: $m/z$: 412 (16) $[M - C_2H_5O]^+$, 380 (2), 351 (8), 258 (6), 247 (100), 201 (17), 173 (19), 139 (62); HRMS: calcd for $C_{22}H_{22}NO_5S$: 412.1218, found: 412.1229.

**Procedure for the synthesis of 28e and 28i**

Compound **28e**: A solution of the crude alkenylsulfoximine **28a** (0.620 mmol) in $CH_2Cl_2$ (5 mL) was added to a stirred solution of *p*-nitrobenzoic acid (130 mg, 0.78 mmol), EDC (179 mg, 0.94 mmol) and DMAP (15 mg, 0.12 mmol) in $CH_2Cl_2$ (10 mL) at RT. After being stirred for 12 h the reaction was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (20% EtOAc/hexanes) to afford **28e** as a colorless oil (252 mg, 81% for two steps). $R_f = 0.15$ (30% EtOAc/hexanes); $[\alpha]_D = +11$ ($c = 1.6$); $^1$H NMR: $\delta = 8.20$ (d, $J = 8.7$ Hz, 2H), 8.12 (d, $J = 8.6$ Hz, 2H), 7.75 (d, $J = 8.4$ Hz, 2H), 7.29 (d, $J = 8.4$ Hz, 2H), 6.97 (m, 1H), 6.57 (d, $J = 15.0$ Hz, 1H), 4.05 (m, 4H), 3.48 (t, $J = 7.4$ Hz, 1H), 2.82 (m, 2H), 2.34 (s, 3H), 1.12 (m, 6H); $^{13}$C NMR: $\delta = 171.3$ (C), 167.6 (C), 149.6 (C), 144.9 (C), 143.1 (CH), 141.0 (C), 134.3 (C), 130.7 (CH), 130.5 (CH), 130.1 (CH), 127.2 (CH), 122.9 (CH), 61.7 ($CH_2$), 49.8 (CH), 30.2 ($CH_2$), 21.3 ($CH_3$), 13.7 ($CH_3$); LRMS: $m/z$: 457 (6.2) $[M - C_2H_5O]^+$, 380 (2), 288 (3), 247 (55), 201 (18), 139 (100); HRMS: calcd for $C_{22}H_{21}N_2O_7S$: 457.1069, found: 457.1080.

Compound **28i**: 74% for two steps, colorless oil; $R_f = 0.10$ (35% EtOAc/hexanes); $^1$H NMR: $\delta = 7.52 - 7.08$ (m, 9H), 6.76 (m, 1H), 6.31 (s, 1H), 4.73 (s, 1H), 4.09 (m, 4H), 3.42 (s, 3H), 3.38 (m, 1H), 2.73 (m, 2H), 2.31 (s, 3H), 1.18 (m, 6H); $^{13}$C NMR: $\delta = 178.7$ (C), 167.8 (C), 144.6 (C), 142.7 (C), 138.0 (CH), 134.7 (CH), 130.7 (CH), 130.0 (CH), 128.3 (CH), 128.1 (C), 127.2 (CH), 125.0 (CH), 85.9 (CH), 61.9 ($CH_2$), 57.4 ($CH_3$), 50.0 (CH), 30.3 ($CH_2$), 21.5 ($CH_3$), 13.9 ($CH_3$); LRMS: $m/z$: 456 (1.2) $[M - C_2H_5O]^+$, 380 (100), 290 (1), 234 (5), 121 (32); HRMS: calcd for $C_{26}H_{31}NO_7S$: 501.1821, found: 501.1826.

Compound **28f**: Methanesulfonyl chloride (122 mg, 0.1.08 mmol) was added dropwise to an ice-water cooled solution of the crude alkenylsulfoximine **28a** (0.71 mmol) and $Et_3N$ (110 mg, 1.08 mmol) in $CH_2Cl_2$ (10 mL) at 0 °C. After being stirred for 30 min at 0 °C the mixture was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (30–70% EtOAc/hexanes) to afford **28f** as a colorless oil (230 mg, 75% for two steps). $R_f = 0.56$ (60% EtOAc/hexanes); $[\alpha]_D = +17$ ($c = 1.5$); $^1$H NMR: $\delta = 7.79$ (d, $J = 8.3$ Hz, 2H), 7.35 (d, $J = 8.3$ Hz, 2H), 6.92 (m, 1H), 6.50 (d, $J = 14.9$ Hz, 1H), 4.14 (m, 4H), 3.48 (t, $J = 7.2$ Hz, 1H), 3.10 (s, 3H), 2.82 (m, 2H), 2.42 (s, 3H), 1.19 (m, 6H); $^{13}$C NMR: $\delta = 167.7$ (C), 145.4 (C), 143.2 (CH), 134.4 (C), 131.5 (CH), 130.2 (CH), 127.6 (CH), 61.8 ($CH_2$), 49.8 (CH), 45.2 ($CH_3$), 30.2 ($CH_2$), 21.5 ($CH_3$), 13.8 ($CH_3$); LRMS: $m/z$: 386 (27) $[M - C_2H_5O]^+$, 337 (3), 247 (50), 215 (100), 201 (19), 139 (98).

Compound **28g**: Trifluoromethanesulfonic anhydride (450 mg, 1.60 mmol) was added dropwise to a stirred solution of the crude alkenylsulfoximine **28a** (1.06 mmol) and pyridine (241 mg, 3.05 mmol) in $CH_2Cl_2$ (12 mL) at 0 °C. The resulting bright yellow solution was stirred for 10 min at 0 °C and poured into water (10 mL). The organic layer was extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (25–40% EtOAc/hexanes) to afford **28g** as a colorless oil (230 mg, 65% two steps). $R_f = 0.76$ (40% EtOAc/hexanes); $[\alpha]_D = +16$ ($c = 1.6$); $^1$H NMR: $\delta = 7.79$ (d, $J = 8.3$ Hz, 2H), 7.39 (d, $J = 8.3$ Hz, 2H), 7.05 (m, 1H), 6.57 (d, $J = 14.9$ Hz, 1H), 4.10 (m, 4H), 3.52 (t, $J = 7.2$ Hz,



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1H), 2.86 (m, 2H), 2.43 (s, 3H), 1.18 (m, 6H); $^{13}$C NMR: $\delta$ = 168.1 (C), 147.1 (C), 146.0 (CH), 134.0 (C), 131.0 (CH), 130.7 (CH), 127.9 (CH), 62.4 ($CH_2$), 50.2 (CH), 30.7 ($CH_2$), 22.0 ($CH_3$), 14.2 ($CH_3$); LRMS: *m*/*z*: 486 (100) $[M+H]^+$, 470 (22), 440 (37), 339 (74), 215 (72), 199 (94); HRMS: calcd for $C_{18}H_{23}NO_7S_2$ 486.0868, found 486.0876.

Compound **28h**: *p*-Tolylsulfonyl chloride (78 mg, 0.41 mmol) was added to a stirred solution of the crude alkenylsulfoximine **28a** (0.34 mmol) in dry pyridine at 0 °C. After being stirred at RT for 12 h the mixture was concentrated. The crude residue was purified by flash chromatography (15–30% EtOAc/hexanes) to afford **28h** as a colorless oil (123 mg, 71% for two steps). $R_f$ = 0.55 (35% EtOAc/hexanes); $[\alpha]_D$ = +1 (*c* = 1.6); $^1$H NMR: $\delta$ = 7.68 (m, 4H), 7.21 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 6.78 (m, 1H), 6.39 (d, *J* = 14.9 Hz, 1H), 4.02 (m, 4H), 3.36 (t, *J* = 7.3 Hz, 1H), 2.70 (m, 2H), 2.31 (s, 3H), 2.27 (s, 3H), 1.09 (m, 6H); $^{13}$C NMR: $\delta$ = 168.2 (C), 145.8 (C), 143.6 (CH), 143.1 (C), 142.2 (C), 135.2 (C), 132.1 (CH), 130.6 (CH), 129.6 (CH), 128.2 (CH), 127.0 (CH), 62.3 ($CH_2$), 50.3 (CH), 30.7 ($CH_2$), 22.0 ($CH_3$), 21.9 ($CH_3$), 14.3 ($CH_3$); LRMS: *m*/*z*: 462 (2.08) $[M-C_2H_5O]^+$, 434 (0.5), 352 (0.5), 292 (9), 247 (19), 139 (100); HRMS: calcd for $C_{24}H_{29}O_7S_2N-C_2H_5O$: 462.1045, found: 462.1040.

**Procedure for the synthesis of pyrones 29a–h**

Compound **29h**: A solution of compound **28h** (105 mg, 0.21 mmol) in THF (2 mL) was added to an ice-cooled suspension of NaH (8.5 mg, 60% mineral oil, 0.21 mmol) in THF (5 mL). After stirring for 20 min at RT a solution of bromide **1** (167 mg, 0.52 mmol) in THF (2 mL) was added. The reaction mixture was stirred at RT for 1 h and quenched by adding water (3 mL). The mixture was poured into brine, extracted with $Et_2O$, dried, filtered and concentrated. The crude was purified by flash chromatography (30–50% EtOAc/hexanes) to afford pyrone **29h** as a colorless oil (142 mg, 91%). $R_f$ = 0.10 (30% EtOAc/hexanes); $[\alpha]_D$ = −9 (*c* = 1.6); $^1$H NMR: $\delta$ = 7.81 (m, 4H), 7.53 (d, *J* = 5.5 Hz, 1H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.23 (d, *J* = 8.3 Hz, 2H), 6.93 (m, 1H), 6.57 (d, *J* = 14.8 Hz, 1H), 6.28 (d, *J* = 5.5 Hz, 1H), 4.07 (m, 4H), 3.44 (s, 2H), 2.75 (d, *J* = 7.5 Hz, 2H), 2.43 (s, 3H), 2.38 (s, 3H), 1.16 (m, 6H), 0.97 (s, 9H), 0.26 (s, 6H); $^{13}$C NMR: $\delta$ = 173.7 (C), 169.0 (C), 152.9 (CH), 151.8 (C), 145.2 (C), 144.3 (C), 142.6 (C), 142.0 (CH), 140.7 (C), 134.9 (C), 132.6 (CH), 130.1 (CH), 129.1 (CH), 127.7 (CH), 126.5 (CH), 115.6 (CH), 62.1 ($CH_2$), 56.2 (C), 35.2 ($CH_2$), 31.5 ($CH_2$), 25.9 ($CH_3$), 21.5 ($CH_3$), 21.4 ($CH_3$), 18.7 (C), 13.8 ($CH_3$), −3.8 ($CH_3$); LRMS: *m*/*z*: 688 (20.3) $[M-C_4H_9]^+$, 550 (2), 460 (1), 379 (18), 305 (11), 233 (29), 173 (19), 139 (58), 91 (100); HRMS: calcd for $C_{32}H_{38}NO_{10}S_2Si$: 688.1706, found: 688.1728.

Compound **29a**: 70%, colorless oil; $R_f$ = 0.15 (55% EtOAc/hexanes); $[\alpha]_D$ = +9 (*c* = 1.0); $^1$H NMR: $\delta$ = 7.53 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 5.5 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.58 (m, 1H), 6.13 (d, *J* = 14.8 Hz, 1H), 6.03 (d, *J* = 5.5 Hz, 1H), 3.85 (m, 4H), 3.17 (s, 2H), 2.45 (d, *J* = 7.6 Hz, 2H), 2.22 (s, 3H), 0.96 (m, 6H), 0.90 (s, 9H), 0.06 (s, 6H); $^{13}$C NMR: $\delta$ = 173.3 (C), 169.1 (C), 152.8 (C), 152.0 (CH), 144.2 (C), 143.5 (C), 139.2 (C), 138.6 (CH), 136.2 (CH), 129.6 (CH), 127.8 (CH), 115.5 (CH), 61.9 ($CH_2$), 56.3 (C), 36.3 ($CH_2$), 31.2 ($CH_2$), 25.9 ($CH_3$), 21.3 ($CH_3$), 18.7 (C), 13.8 ($CH_3$), −3.8 ($CH_3$); LRMS: *m*/*z*: 534 (100) $[M-C_4H_9]^+$, 379 (10), 339 (36), 277 (13), 182 (59), 139 (53), 107 (31); HRMS: calcd for $C_{25}H_{32}NO_8SiS$: 534.1618, found: 534.1650.

Compound **29b**: 77%, colorless oil: $R_f$ = 0.23 (40% EtOAc/hexanes); $[\alpha]_D$ = +5 (*c* = 1.3); $^1$H NMR: $\delta$ = 7.75 (d, *J* = 8.3 Hz, 2H), 7.53 (d, *J* = 5.6 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 6.90 (m, 1H), 6.45 (d, *J* = 14.9 Hz, 1H), 6.29 (d, *J* = 5.6 Hz, 1H), 4.12 (m, 4H), 3.43 (s, 2H), 2.76 (d, *J* = 7.6 Hz, 2H), 2.42 (s, 3H), 2.12 (s, 3H), 1.20 (m, 6H), 0.97 (s, 9H), 0.26 (s, 6H); $^{13}$C NMR: $\delta$ = 179.6 (C), 173.8 (C), 169.1 (C), 169.0 (C), 152.9 (CH), 151.9 (C), 144.3 (C), 141.2 (CH), 135.1 (C), 132.1 (CH), 130.1 (CH), 127.3 (CH), 115.6 (CH), 62.1 ($CH_2$), 56.3 (C), 35.3 ($CH_2$), 31.6 ($CH_2$), 26.7 ($CH_3$), 25.9 ($CH_3$), 21.5 ($CH_3$), 18.7 (C), 13.8 ($CH_3$), −3.8 ($CH_3$); LRMS: *m*/*z*: 576 (100) $[M-C_4H_9]^+$, 534 (19), 428 (2), 379 (12), 339 (36), 277 (13), 233 (37), 182 (59), 139 (57), 107 (31); HRMS: calcd for $C_{27}H_{34}NO_9SiS$: 576.1723, found: 576.1701.

Compound **29c**: 93%, colorless oil; $R_f$ = 0.31 (40% EtOAc/hexanes); $[\alpha]_D$ = −14 (*c* = 0.5); $^1$H NMR: $\delta$ = 7.80 (d, *J* = 8.4 Hz, 2H), 7.55 (d, *J* = 5.5 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.15 (m, 1H), 6.49 (d, *J* = 14.9 Hz, 1H), 6.32 (d, *J* = 5.5 Hz, 1H), 4.17 (m, 4H), 3.48 (s, 2H), 2.81 (d, *J* = 7.5 Hz, 2H), 2.47 (s, 3H), 1.25 (m, 6H), 0.99 (s, 9H), 0.28 (s, 6H); $^{13}$C NMR: $\delta$ = 173.8 (C), 169.1 (C), 152.9 (CH), 151.9 (C), 145.8 (C), 144.4 (CH), 144.1 (C), 133.1 (C), 130.5 (CH), 130.1 (CH), 129.0 (C), 128.2 (C), 127.4 (CH), 115.7 (CH), 62.3 ($CH_2$), 56.4 (C), 35.4 ($CH_2$), 31.9 ($CH_2$), 26.0 ($CH_3$), 21.6 ($CH_3$), 18.8 (C), 13.9 ($CH_3$), −3.7 ($CH_3$); LRMS: *m*/*z*: 630 (85) $[M-C_4H_9]^+$, 573 (4), 492 (4), 379 (26), 305 (23), 278 (6), 233 (51), 182 (100), 139 (72), 91 (38); HRMS: calcd for $C_{27}H_{31}NO_9F_3SiS$: 630.1441, found: 630.1463.

Compound **29d**: 78%, colorless oil; $R_f$ = 0.21 (40% EtOAc/hexanes); $[\alpha]_D$ = +5 (*c* = 1.5); $^1$H NMR: $\delta$ = 8.17 (d, *J* = 8.1 Hz, 2H), 7.86 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 5.5 Hz, 1H), 7.35–7.45 (m, 5H), 7.05 (m, 1H), 6.58 (d, *J* = 14.9 Hz, 1H), 6.31 (d, *J* = 5.5 Hz, 1H), 4.15 (m, 4H), 3.45 (s, 2H), 2.82 (d, *J* = 7.6 Hz, 2H), 2.42 (s, 3H), 1.23 (m, 6H), 0.99 (s, 9H), 0.28 (s, 6H); $^{13}$C NMR: $\delta$ = 173.8 (C), 173.6 (C), 169.2 (C), 152.9 (CH), 152.0 (C), 144.0 (C), 141.5 (CH), 135.7 (C), 135.3 (C), 132.3 (CH), 132.0 (CH), 130.2 (CH), 129.4 (CH), 127.9 (CH), 127.5 (CH), 115.7 (CH), 62.2 ($CH_2$), 56.5 (C), 35.5 ($CH_2$), 31.7 ($CH_2$), 26.0 ($CH_3$), 21.5 ($CH_3$), 18.8 (C), 13.9 ($CH_3$), −3.7 ($CH_3$); LRMS: *m*/*z*: 695 (3.5) $[M]^+$, 650 (10), 639 (42), 638 (100), 379 (28), 316 (29), 278 (10), 233 (60), 182 (98), 139 (56), 105 (99), 77 (16); HRMS: calcd for $C_{36}H_{45}NO_9SiS$: 695.2539, found: 695.2563.

Compound **29e**: 77%, colorless oil; $R_f$ = 0.27 (40% EtOAc/hexanes); $[\alpha]_D$ = +5 (*c* = 0.9); $^1$H NMR: $\delta$ = 8.27 (m, 4H), 7.84 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 5.5 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.15 (m, 1H), 6.60 (d, *J* = 14.9 Hz, 1H), 6.32 (d, *J* = 5.5 Hz, 1H), 4.17 (m, 4H), 3.50 (s, 2H), 2.84 (d, *J* = 7.6 Hz, 2H), 2.46 (s, 3H), 1.23 (m, 6H), 0.99 (s, 9H), 0.28 (s, 6H); $^{13}$C NMR: $\delta$ = 173.7 (C), 171.4 (C), 169.1 (C), 152.9 (CH), 151.9 (C), 149.8 (C), 145.0 (C), 144.3 (C), 142.4 (CH), 141.1 (C), 134.6 (C), 131.5 (CH), 130.3 (CH), 128.9 (CH), 127.3 (CH), 123.1 (CH), 115.7 (CH), 62.1 ($CH_2$), 56.3 (C), 35.4 ($CH_2$), 31.7 ($CH_2$), 25.9 ($CH_3$), 21.5 ($CH_3$), 18.7 (C), 13.8 ($CH_3$), −3.8 ($CH_3$); LRMS: *m*/*z*: 683 (33) $[M-C_4H_9]^+$, 575 (1), 428 (4), 379 (17), 305 (26), 278 (10), 233 (64), 182 (74), 139 (85), 73 (100); HRMS: calcd for $C_{32}H_{35}N_2O_{11}SiS$: 683.1730, found: 683.1729.

Compound **29f**: 80%, colorless oil; $R_f$ = 0.23 (40% EtOAc/hexanes); $[\alpha]_D$ = −5 (*c* = 2.2); $^1$H NMR: $\delta$ = 7.78 (d, *J* = 8.3 Hz, 2H), 7.51 (d, *J* = 5.6 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 2H), 6.93 (m, 1H), 6.45 (d, *J* = 14.9 Hz, 1H), 6.27 (d, *J* = 5.5 Hz, 1H), 4.12 (m, 4H), 3.41 (s, 2H), 3.08 (s, 3H), 2.75 (d, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 1.21 (m, 6H), 0.95 (s, 9H), 0.24 (s, 6H); $^{13}$C NMR: $\delta$ = 173.7 (C), 168.9 (C), 152.9 (C), 151.8 (CH), 145.4 (C), 144.3 (C), 142.1 (CH), 134.6 (C), 132.5 (CH), 130.2 (CH), 127.7 (CH), 115.6 (CH), 62.1 ($CH_2$), 56.2 (C), 35.2 ($CH_2$), 31.4 ($CH_2$), 25.9 ($CH_3$), 21.5 ($CH_3$), 18.7 (C), 14.1 ($CH_3$), 13.8 ($CH_3$), −3.8 ($CH_3$); LRMS: *m*/*z*: 612 (96) $[M-C_4H_9]^+$, 520 (3), 474 (15), 379 (39), 339 (7), 288 (27), 233 (76), 182 (100), 139 (85), 57 (68).

Compound **29g**: 76%, colorless oil; $R_f$ = 0.40 (50% EtOAc/hexanes); $[\alpha]_D$ = −8 (*c* = 2.2); $^1$H NMR: $\delta$ = 7.81 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 5.5 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.10 (m, 1H), 6.48 (d, *J* = 14.9 Hz, 1H), 6.29 (d, *J* = 5.5 Hz, 1H), 4.17 (m, 4H), 3.47 (s, 2H), 2.79 (d, *J* = 6.5 Hz, 2H), 2.46 (s, 3H), 1.22 (m, 6H), 0.98 (s, 9H), 0.26 (s, 6H); $^{13}$C NMR: $\delta$ = 174.2 (C), 169.4 (C), 153.5 (CH), 152.2 (C), 147.0 (C), 144.9 (CH), 144.8 (C), 134.2 (C), 131.4 (CH), 131.1 (CH), 128.0 (CH), 120.1 ($CF_3$), 116.1 (CH), 62.8 ($CH_2$), 56.7 (C), 35.7 ($CH_2$), 32.2 ($CH_2$), 26.4 ($CH_3$), 22.4 ($CH_3$), 19.2 (C), 14.2 ($CH_3$), −3.3 ($CH_3$); LRMS: *m*/*z*: 666 (9.6) $[M-C_4H_9]^+$, 577 (1), 528 (2), 379 (11), 305 (11), 278 (79), 231 (21), 182 (59), 139 (100), 91 (74); HRMS: calcd for $C_{26}H_{31}NO_{10}F_3SiS_2$: 666.1111, found: 666.1131.

**Procedure for the thermal cycloadditions of the sulfoximines**

Substrate **29h**: A solution of pyrone **29h** (130 mg, 0.17 mmol) in toluene (7 mL) was heated under reflux for 1 h. The solvent was evaporated and the crude purified by flash chromatography (20–30% EtOAc/hexanes) to afford a 90:10 ratio of an inseparable mixture of diastereoisomers **30h** and **31h** as a colorless oil (88%). $R_f$ = 0.62 (30% EtOAc/hexanes); $[\alpha]_D$ = −170 (*c* = 0.6). The diastereomeric ratio was determined by integrating the signals of the H-7 (t) of the two isomers in the $^1$H NMR spectrum of the crude reaction mixture.

Compounds **30h**+**31h**: $^1$H NMR: $\delta$ = 7.87 (d, *J* = 8.2 Hz, 4H), 7.79 (d, *J* = 8.2 Hz, 4H), 7.43 (d, *J* = 8.2 Hz, 4H), 7.24 (d, *J* = 8.1 Hz, 4H), 5.98 (d, *J* = 4.8 Hz, 2H), 5.16 (t, *J* = 5.2 Hz, 2H), 4.65 (t, *J* = 6.1 Hz, 1H), 4.44 (t, *J* = 6.1 Hz, 1H), 4.11 (m, 8H), 3.09 (d, *J* = 14.9 Hz, 1H), 2.97 (d, *J* = 14.9 Hz, 1H), 2.73 (m, 1H), 2.48 (s, 6H), 2.45 (m, 1H), 2.40 (s, 6H), 1.69 (m, 4H), 1.18 (m, 12H), 0.91 (s, 18H), 0.07 (s, 6H), 0.06 (s, 6H); $^{13}$C NMR: $\delta$ = 191.0 (C), 170.7 (C), 169.7 (C), 147.1 (C), 146.0 (C), 142.8 (C), 140.7 (C), 134.2 (C), 130.8 (CH), 129.3 (CH), 128.1 (CH), 126.5 (CH), 122.5 (CH), 97.9 (C), 75.4 (CH), 73.1 (CH), 62.0 ($CH_2$), 61.0 (C), 44.0 (CH), 36.8 ($CH_2$), 35.7 ($CH_2$), 25.4 ($CH_3$), 21.7 ($CH_3$), 21.5 ($CH_3$), 18.1 (C), 13.9 ($CH_3$), 1.0 ($CH_3$), −4.9 ($CH_3$); LRMS: *m*/*z*: 688 (30.4) $[M-C_4H_9]^+$, 379 (30), 333 (12), 305

(19), 233 (38), 205 (27), 182 (36), 173 (14), 139 (64), 91 (100); HRMS: calcd for $C_{32}H_{38}NO_{10}S_2Si$: 688.1706, found: 688.1720.

The cycloaddition of **29a** afforded a 50:50 mixture of diastereoisomers **30a** and **31a** as colorless oils (86%). $R_f$ (40% EtOAc/hexanes): **30a** = 0.48, **31a** = 0.54].

Compound **30a**: $[\alpha]_D = -67$ ($c = 0.45$); $^1$H NMR: $\delta = 7.81$ (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.3$ Hz, 2H), 6.50 (d, $J = 4.9$ Hz, 1H), 5.13 (m, 1H), 4.23 (m, 1H), 4.13 (m, 4H), 3.01 (d, $J = 14.9$ Hz, 1H), 2.89 (m, 1H), 2.49 (m, 1H), 2.43 (s, 3H), 2.25 (m, 1H), 1.81 (m, 1H), 1.23 (m, 6H), 0.97 (s, 9H), 0.23 (s, 6H); LRMS: *m/z*: 591 (33.0) $[M]^+$, 534 (76), 381 (7), 339 (85), 204 (54), 139 (100), 91 (27); HRMS: calcd for $C_{29}H_{41}NO_8SiS$: 591.2322, found: 591.2329.

Compound **31a**: $[\alpha]_D = 38$ ($c = 0.35$); $^1$H NMR: $\delta = 7.85$ (d, $J = 8.3$ Hz, 2H), 7.37 (d, $J = 8.3$ Hz, 2H), 6.40 (d, $J = 4.9$ Hz, 1H), 4.93 (m, 1H), 4.25 (m, 1H), 4.15 (m, 4H), 3.09 (d, $J = 14.9$ Hz, 1H), 3.04 (m, 1H), 2.51 (m, 1H), 2.47 (s, 3H), 2.15 (m, 1H), 2.03 (m, 1H), 1.23 (m, 6H), 0.97 (s, 9H), 0.23 (s, 6H).

The cycloaddition of **29b** afforded a 65:35 mixture of diastereoisomers **30b** and **31b** as a colorless oil (86%). $R_f = 0.23$ (30% EtOAc/hexanes); $[\alpha]_D = -31$ ($c = 1.1$).

Compound **30b**+**31b**: $^1$H NMR: $\delta = 7.76$ (d, $J = 8.3$ Hz, 4H), 7.39 (d, $J = 8.1$ Hz, 4H), 6.49 (d, $J = 4.9$ Hz, 1H), 6.18 (d, $J = 4.9$ Hz, 1H), 5.22 (m, 1H), 4.62 (m, 1H), 4.32 (m, 2H), 4.06 (m, 8H), 3.30 (m, 1H), 3.17 (d, $J = 15.0$ Hz, 1H), 3.02 (d, $J = 15.0$ Hz, 1H), 2.85 (m, 1H), 2.62 (m, 1H), 2.51 (m, 1H), 2.48 (s, 3H), 2.46 (s, 3H), 2.17 (s, 3H), 2.04 (s, 3H), 1.65 (m, 4H), 1.23 (m, 12H), 0.94 (s, 18H), 0.19 (s, 12H); $^{13}$C NMR: $\delta = 191.3$ (C), 179.8 (C), 179.1 (C), 171.1 (C), 171.0 (C), 146.9 (C), 145.0 (C), 134.9 (C), 134.1 (C), 130.7 (CH), 127.5 (CH), 124.0 (CH), 123.6 (CH), 97.8 (C), 97.6 (C), 75.9 (CH), 75.0 (CH), 72.8 (CH), 72.5 (CH), 62.0 ($CH_2$), 61.0 (C), 45.1 (CH), 44.5 (CH), 36.8 ($CH_2$), 35.8 ($CH_2$), 26.6 ($CH_3$), 25.5 ($CH_3$), 21.6 ($CH_3$), 18.3 (C), 13.8 ($CH_3$), −4.7 ($CH_3$); LRMS: *m/z*: 576 (100) $[M - C_4H_9]^+$, 534 (39), 516 (7), 428 (3), 379 (16), 339 (39), 305 (30), 277 (25), 233 (76), 182 (68), 139 (88), 107 (45); HRMS: calcd for $C_{27}H_{34}NO_9SiS$: 576.1723, found: 576.1729.

The cycloaddition of **29c** afforded a 86:14 mixture of diastereoisomers **30c** and **31c** as colorless oils (85%). $R_f$ (30% EtOAc/hexanes): **30c** = 0.60, **31c** = 0.54]. The diastereomeric ratio was determined integrating the signals of the the H-7 (t) of the two isomers in the $^1$H NMR spectrum of the crude reaction mixture.

Compound **30c**: $[\alpha]_D = -115$ ($c = 2.5$); $^1$H NMR: $\delta = 7.78$ (d, $J = 8.3$ Hz, 2H), 7.47 (d, $J = 8.2$ Hz, 2H), 6.42 (d, $J = 4.9$ Hz, 1H), 5.27 (t, $J = 5.2$ Hz, 1H), 4.42 (t, $J = 6.3$ Hz, 1H), 4.12 (m, 4H), 3.05 (d, $J = 15.0$ Hz, 1H), 2.87 (m, 1H), 2.49 (m, 1H), 2.48 (s, 3H), 1.77 (m, 2H), 1.26 (m, 6H), 0.96 (s, 9H), 0.20 (s, 3H); $^{13}$C NMR: $\delta = 190.9$ (C), 171.1 (C), 169.7 (C), 164.1 (C), 147.3 (C), 146.5 (C), 131.8 (C), 131.2 (CH), 127.4 (CH), 122.8 (CH), 117.1 (C), 97.9 (C), 75.8 (CH), 72.8 (CH), 62.1 ($CH_2$), 61.1 (C), 44.1 (CH), 36.9 ($CH_2$), 35.8 ($CH_2$), 25.5 ($CH_3$), 21.8 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), −4.8 ($CH_3$); LRMS: *m/z*: 630 (91) $[M - C_4H_9]^+$, 612 (7), 492 (13), 399 (3), 379 (51), 305 (48), 277 (26), 259 (15), 233 (99), 182 (89), 139 (92), 91 (48), 73 (100); HRMS: calcd for $C_{27}H_{31}NO_9F_3SiS$: 630.1441, found: 630.1434.

Compound **31c**: $[\alpha]_D = +65$ ($c = 0.50$); $^1$H NMR: $\delta = 7.78$ (d, $J = 8.3$ Hz, 2H), 7.47 (d, $J = 8.2$ Hz, 2H), 6.07 (d, $J = 4.9$ Hz, 1H), 4.59 (t, $J = 5.2$ Hz, 1H), 4.44 (m, 1H), 4.12 (m, 4H), 3.27 (m, 1H), 3.11 (d, $J = 15.0$ Hz, 1H), 2.57 (m, 1H), 2.48 (s, 3H), 2.18 (m, 2H), 1.26 (m, 6H), 0.96 (s, 9H), 0.20 (s, 3H).

The cycloaddition of **29d** afforded a 76:24 mixture of diastereoisomers **30d** and **31d** as colorless oils (95%). $R_f$ (30% EtOAc/hexanes): **30d** = 0.62, **31d** = 0.58. The diastereomeric ratio was determined integrating the signals of the the H-7 (t) of the two isomers in the $^1$H NMR spectrum of the crude reaction mixture.

Compound **30d**: $[\alpha]_D = -106$ ($c = 1.5$); $^1$H NMR: $\delta = 8.15$ (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 8.1$ Hz, 2H), 7.47 (m, 5H), 6.56 (d, $J = 4.9$ Hz, 1H), 5.38 (t, $J = 5.3$ Hz, 1H), 4.41 (t, $J = 6.3$ Hz, 1H), 4.15 (m, 4H), 3.07 (d, $J = 15.0$ Hz, 1H), 2.93 (m, 1H), 2.51 (d, $J = 15.0$ Hz, 1H), 2.45 (s, 3H), 1.79 (m, 2H), 1.24 (m, 6H), 0.95 (s, 9H), 0.20 (s, 3H); $^{13}$C NMR: $\delta = 191.4$ (C), 173.8 (C), 171.1 (C), 169.9 (C), 147.0 (C), 145.1 (C), 135.3 (C), 134.1 (C), 132.3 (CH), 130.8 (CH), 129.4 (CH), 128.1 (CH), 127.5 (CH), 123.8 (CH), 97.8 (C), 76.0 (CH), 72.8 (CH), 62.0 ($CH_2$), 61.1 (C), 44.4 (CH), 36.9 ($CH_2$), 36.0 ($CH_2$), 25.5 ($CH_3$), 21.7 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), −4.7 ($CH_3$); LRMS: *m/z*: 638 (84) $[M - C_4H_9]^+$, 379 (20), 316 (53), 278 (12), 233 (68), 182 (59), 139 (51), 105 (100), 77 (11); HRMS: calcd for $C_{32}H_{36}NO_9SiS$: 638.1880, found: 638.1870.

Compound **31d**: $[\alpha]_D = +94$ ($c = 0.5$); $^1$H NMR: $\delta = 8.06$ (d, $J = 8.3$ Hz, 2H), 7.80 (d, $J = 8.2$ Hz, 2H), 7.42 (m, 5H), 6.28 (d, $J = 4.9$ Hz, 1H), 4.79 (t, $J = 5.3$ Hz, 1H), 4.41 (t, $J = 6.3$ Hz, 1H), 4.15 (m, 4H), 3.32 (m, 1H), 3.17 (d, $J = 15.0$ Hz, 1H), 2.48 (d, $J = 14.7$ Hz, 1H), 2.46 (s, 3H), 2.25 (m, 2H), 1.26 (m, 6H), 0.95 (s, 9H), 0.23 (s, 3H).

The cycloaddition of **29e** afforded a 58:42 mixture of diastereoisomers **30e** and **31e** as colorless oils (91%). $R_f$ (40% EtOAc/hexanes): **30e** = 0.70, **31e** = 0.65.

Compound **30e**: $[\alpha]_D = -108$ ($c = 3.5$); $^1$H NMR: $\delta = 8.23$ (m, 4H), 7.79 (d, $J = 8.3$ Hz, 2H), 7.43 (d, $J = 8.2$ Hz, 2H), 6.50 (d, $J = 4.9$ Hz, 1H), 5.36 (t, $J = 5.3$ Hz, 1H), 4.47 (t, $J = 6.5$ Hz, 1H), 4.16 (m, 4H), 3.06 (d, $J = 15.0$ Hz, 1H), 2.91 (m, 1H), 2.50 (d, $J = 15.2$ Hz, 1H), 2.46 (s, 3H), 1.78 (m, 2H), 1.22 (m, 6H), 0.94 (s, 9H), 0.19 (s, 3H); $^{13}$C NMR: $\delta = 191.1$ (C), 171.7 (C), 171.1 (C), 169.7 (C), 150.1 (C), 147.2 (C), 145.6 (C), 140.7 (C), 133.4 (C), 130.9 (CH), 130.4 (CH), 127.4 (CH), 123.4 (CH), 123.3 (CH), 97.7 (C), 76.0 (CH), 72.8 (CH), 62.0 ($CH_2$), 61.1 (C), 44.5 (CH), 36.9 ($CH_2$), 35.9 ($CH_2$), 25.5 ($CH_3$), 21.7 ($CH_3$), 18.3 (C), 13.9 ($CH_3$), −4.7 ($CH_3$); LRMS: *m/z*: 683 (98) $[M - C_4H_9]^+$, 525 (1), 428 (6), 396 (11), 380 (17), 379 (31), 305 (46), 277 (28), 233 (80), 182 (67), 150 (70), 57 (100); HRMS: calcd for $C_{32}H_{35}N_2O_{11}SiS$: 683.1730, found: 683.1737.

Compound **31e**: $[\alpha]_D = +82$ ($c = 3.2$); $^1$H NMR: $\delta = 8.27$ (s, 4H), 7.81 (d, $J = 8.3$ Hz, 2H), 7.44 (d, $J = 8.2$ Hz, 2H), 6.23 (d, $J = 5.0$ Hz, 1H), 4.80 (t, $J = 5.2$ Hz, 1H), 4.46 (t, $J = 6.1$ Hz, 1H), 4.25 (m, 4H), 3.35 (m, 1H), 3.17 (d, $J = 15.0$ Hz, 1H), 2.54 (d, $J = 16.1$ Hz, 1H), 2.47 (s, 3H), 2.26 (m, 2H), 1.26 (m, 6H), 0.94 (s, 9H), 0.24 (s, 3H).

The cycloaddition of **29f** afforded a 77:23 mixture of diastereoisomers **30f** and **31f** as a colorless oil (88%). $R_f = 0.41$ (40% EtOAc/hexanes); $[\alpha]_D = -95$ ($c = 1.1$).

Compound **30f**+**31f**: $^1$H NMR: $\delta = 7.86$ (d, $J = 8.3$ Hz, 4H), 7.43 (d, $J = 8.2$ Hz, 4H), 6.38 (d, $J = 4.9$ Hz, 1H), 6.08 (d, $J = 4.9$ Hz, 1H), 5.23 (t, $J = 5.2$ Hz, 1H), 4.71 (t, $J = 5.2$ Hz, 1H), 4.45 (m, 2H), 4.14 (m, 8H), 3.08 (s, 6H), 3.05 (m, 2H), 2.78 (m, 2H), 2.47 (s, 6H), 2.44 (m, 2H), 1.72 (m, 4H), 1.20 (m, 12H), 0.95 (s, 18H), 0.19 (s, 6H), 0.18 (s, 6H); $^{13}$C NMR: $\delta = 191.4$ (C), 171.3 (C), 170.2 (C), 147.8 (C), 146.7 (C), 134.1 (C), 131.3 (CH), 128.7 (CH), 122.9 (CH), 98.4 (C), 75.7 (CH), 74.9 (CH), 62.5 ($CH_2$), 61.6 (C), 45.5 (CH), 37.2 ($CH_2$), 36.2 ($CH_2$), 25.9 ($CH_3$), 22.2 ($CH_3$), 18.7 (C), 14.4 ($CH_3$), 14.1 ($CH_3$), −4.4 ($CH_3$), −4.9 ($CH_3$); LRMS: *m/z*: 612 (100) $[M - C_4H_9]^+$, 520 (7), 474 (26), 379 (79), 339 (8), 288 (38), 233 (97), 182 (46), 139 (60), 57 (99).

The cycloaddition of **29g** afforded a 87:13 mixture of diastereoisomers **30g** and **31g** as colorless oils (80%). $R_f$ (30% EtOAc/hexanes): **30g** = 0.65, **31g** = 0.58].

Compound **30g**: $[\alpha]_D = -123$ ($c = 1.0$); $^1$H NMR: $\delta = 7.90$ (d, $J = 8.4$ Hz, 2H), 7.52 (d, $J = 8.2$ Hz, 2H), 6.35 (d, $J = 4.9$ Hz, 1H), 5.24 (t, $J = 5.2$ Hz, 1H), 4.57 (m, 1H), 4.12 (m, 4H), 3.03 (d, $J = 15.0$ Hz, 1H), 2.83 (m, 1H), 2.52 (s, 3H), 2.46 (m, 1H), 1.75 (m, 2H), 1.21 (m, 6H), 0.97 (s, 9H), 0.24 (s, 3H), 0.20 (s, 3H); $^{13}$C NMR: $\delta = 190.7$ (C), 170.9 (C), 169.5 (C), 147.6 (C), 147.4 (C), 133.1 (C), 131.2 (CH), 127.8 (CH), 121.5 (CH), 98.2 (C), 75.4 (CH), 73.7 (CH), 62.2 ($CH_2$), 61.0 (C), 44.0 (CH), 36.8 ($CH_2$), 35.6 ($CH_2$), 25.4 ($CH_3$), 21.9 ($CH_3$), 18.2 (C), 13.8 ($CH_3$), −4.8 ($CH_3$), −4.9 ($CH_3$); LRMS: *m/z*: 666 (44.9) $[M - C_4H_9]^+$, 648 (1), 528 (8), 380 (12) 379 (31), 305 (25), 278 (6), 233 (65), 182 (78), 139 (67), 73 (100); HRMS: calcd for $C_{26}H_{31}NO_{10}F_3SiS_2$: 666.1111, found: 666.1117.

Compound **31g**: $[\alpha]_D = +80$ ($c = 0.50$); $^1$H NMR: $\delta = 7.90$ (d, $J = 8.4$ Hz, 2H), 7.52 (d, $J = 8.2$ Hz, 2H), 6.07 (d, $J = 4.9$ Hz, 1H), 4.67 (t, $J = 5.2$ Hz, 1H), 4.57 (m, 1H), 4.12 (m, 4H), 3.20 (m, 1H), 3.12 (d, $J = 15.0$ Hz, 1H), 2.59 (m, 1H), 2.52 (s, 3H), 2.20 (m, 2H), 1.21 (m, 6H), 0.97 (s, 9H), 0.24 (s, 3H), 0.20 (s, 3H).

**Procedure for the desulfuration of cycloadducts 30**

Compound **30c**: A solution of compound **30c** (60 mg, 0.14 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (1.2 g) in THF (8 mL). The reaction mixture was heated under reflux for 2 h, allowed to cool to RT, filtered, and poured into water. Extraction with $Et_2O$, drying and concentration gave a residue which was purified by flash chromatography (3–20% EtOAc/hexanes) to afford (+)-**12** as a colorless oil (29 mg, 76%, 96% *ee*). $R_f = 0.23$ (15% EtOAc/hexanes); $[\alpha]_D = +19$ ($c = 1.1$). Enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$



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(0.3 equiv) by comparison of the split signals of the TBS methyl protons with those of racemic **12**. $^1$H NMR: $\delta = 4.39$ (d, $J = 6.1$ Hz, 1H), 4.02 (m, 5H), 2.63 (d, $J = 14.0$ Hz, 1H), 2.51 (m, 3H), 2.28 (d, $J = 13.7$ Hz, 1H), 2.12 (d, $J = 15.2$ Hz, 1H), 2.01 (m, 2H), 1.84 (m, 1H), 1.12 (m, 6H), 0.80 (s, 9H), 0.00 (s, 3H), −0.11 (s, 3H); $^{13}$C NMR: $\delta = 205.1$ (C), 171.1 (C), 95.7 (C), 78.0 (CH), 76.0 (CH), 61.4 ($CH_2$), 61.2 ($CH_2$), 48.2 ($CH_2$), 41.0 ($CH_2$), 40.6 (CH), 39.5 ($CH_2$), 39.3 ($CH_2$), 25.6 ($CH_3$), 18.3 (C), 13.8 ($CH_3$), −4.4 ($CH_3$), −5.8 ($CH_3$); LRMS: *m/z*: 383 (100) $[M - C_4H_9]^+$, 365 (21), 355 (14), 339 (12), 337 (14), 291 (30), 263 (14), 235 (6), 155 (16), 129 (6), 139 (88), 57 (4); HRMS: calcd for $C_{18}H_{27}O_7Si$: 383.1526, found: 383.1535.

The desulfuration of the other sulfoximines **30** was achieved in similar yields (71–83%) using the same conditions. In the case of the *N*-acetyl, mesyl and tosyl derivatives the desulfurization was carried out with the mixture of diastereoisomers thereby yielding **12** with smaller optical rotation.

**Procedure for opening the oxa-bridge of 20 and 13**

Compound **20**: MeLi (0.2 mL, 1.5 M) was added to a solution of **20** (110 mg, 0.251 mmol) in THF (10 mL) cooled at −78 °C. The reaction mixture was stirred at that temperature for 10 min, $BF_3 \cdot OEt_2$ (0.16 mL, 1.26 mmol) was added and the resulting solution stirred for 30 min. The mixture was poured into a saturated ammonium chloride solution, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (5–30% EtOAc/hexanes) to afford **35** as a viscous oil (86 mg, 79%). $R_f = 0.20$ (10% EtOAc/hexanes); $[\alpha]_D = +35.3$ ($c = 0.34$); $^1$H NMR: $\delta = 5.91$ (s, 1H), 4.18 (m, 4H), 3.76 (dd, $J = 3.3$, 10.8 Hz), 3.15 (s, 2H), 2.83 (m, 2H), 2.68 (m, 1H), 2.17 (dd, $J = 2.8$, 11.1 Hz, 1H), 1.88 (m, 2H), 1.35 (s, 3H), 1.24 (s, 6H), 26.2 (s, 9H), −2.48 (s, 3H), −2.68 (s, 3H); $^{13}$C NMR: $\delta = 200.9$ (C), 170.8 (C), 170.8 (C), 158.6 (C), 121.8 (CH), 85.5 (C), 74.0 (CH),61.8 ($CH_2$), 57.8 (C), 42.5 ($CH_2$), 41.3 ($CH_2$), 40.4 (CH), 35.3 ($CH_2$), 26.3 ($CH_2$), 20.5 ($CH_3$), 18.8 (C), 14.0 ($CH_3$), −2.5 ($CH_3$), −2.7 ($CH_3$); HRMS: calcd for $C_{23}H_{38}O_7Si$: 454.2387, found: 454.2380.

Compound **33**: 72%, colorless oil; $R_f = 0.45$ (15% EtOAc/hexanes); $[\alpha]_D = -14$ ($c = 1.0$); $^1$H NMR: $\delta = 6.38$ (dt, $J = 5.2$, 12.2 Hz, 1H), 5.94 (dt, $J = 12.2$, 1.5 Hz, 1H), 2.38 (m, 2H), 2.15 (m, 1H), 2.00 (br s, 1H), 1.40 (s, 3H), 1.20 (s, 3H), 1.06 (d, $J = 7.1$ Hz, 3H), 0.84 (s, 9H), 0.12 (s, 3H), 0.06 (s, 3H); $^{13}$C NMR: $\delta = 203.8$ (C), 142.5 (CH), 129.8 (CH), 88.0 (C), 77.6 (C), 40.0 (CH), 34.6 ($CH_2$), 26.2 ($CH_3$), 25.5 ($CH_3$), 23.2 ($CH_3$), 18.8 (C), 17.9 ($CH_3$), −2.5 ($CH_3$), −2.9 ($CH_3$); LRMS: *m/z*: 298 (1) $[M+H]^+$, 241 (16) $[M - C_4H_9]^+$, 170 (14), 169 (100), 159 (32), 115 (17), 103 (17), 73 (97); HRMS: calcd for $C_{16}H_{30}O_3Si$: 298.1964, found: 298.1963.

**Synthesis of nemorensic acid [(+)-(36)]**: Pyrone **37**[9b] (500 mg, 3.20 mmol) was added to a solution of KOH (200 mg, 3.53 mmol) in $H_2O$ (10 mL). After being stirred for 5 min the mixture was concentrated and stored under vacuum (with $P_2O_5$) for 12 h. The residue was dissolved in acetone, KI (750 mg, 4.81 mmol) and PMBCl (800 mg, 4.81 mmol) were added and the mixture was heated under reflux for 4 h. After cooling at RT the mixture was poured into water, extracted with $Et_2O$, dried, filtered and concentrated. The crude residue was purified by flash chromatography (50–75% EtOAc/hexanes) to afford the expected PMB protected derivative as a white solid (726 mg, 82%). $R_f = 0.22$ (65% EtOAc/hexanes); $^1$H NMR: $\delta = 7.27$ (d, $J = 8.7$ Hz, 2H), 6.86 (d, $J = 8.5$ Hz, 2H), 6.17 (s, 1H), 5.12 (s, 2H), 4.27 (s, 2H), 3.78 (s, 3H), 2.24 (s, 3H); $^{13}$C NMR: $\delta = 176.6$(C), 165.5 (C), 160,3 (C), 158.9 (C), 142.3 (C),131.3 (CH), 128.9 (C), 115.2 (CH), 114.3 (CH), 73.7 ($CH_2$), 58.0 ($CH_2$), 55.6 ($CH_3$), 20.0 ($CH_3$); LRMS: *m/z*: 276 (0.6) $[M]^+$, 121 (100), 101 (4), 78 (6); HRMS: calcd for $C_{15}H_{16}O_5$: 276.0997, found: 276.0995.

$CBr_4$ (2.60 g, 7.75 mmol) was added to a solution of above alcohol (1.72 g, 6.2 mmol) and $PPh_3$ (2.30 g, 2.90 mmol) in THF (20 mL) at 0 °C. After stirring for 10 min at room temperature, the resulting mixture was poured into water, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude residue was purified by flash chromatography on alumina (5–20% EtOAc/hexanes) to afford bromide **38** as a white solid (1.76 g, 84%). $R_f = 0.68$ (50% EtOAc/hexanes); $^1$H NMR: $\delta = 7.31$ (d, $J = 8.6$ Hz, 2H), 6.85 (d, $J = 8.6$ Hz, 2H), 6.15 (s, 1H), 5.17 (s, 2H), 4.14 (s, 2H), 3.78 (s, 3H), 2.24 (s, 3H); $^{13}$C NMR: $\delta = 175.6$(C), 164.6 (C), 159,7 (C), 154.9 (C), 142.5 (C),130.6 (CH), 128.4 (C), 114.9 (CH), 113.8 (CH), 73.3 ($CH_2$), 55.1 ($CH_3$), 22.5 ($CH_2$), 19.5 ($CH_3$); LRMS: *m/z*: 259 (0.20) $[M - Br]^+$, 202 (1), 199 (2), 121 (100), 78 (10), 51 (4); HRMS: calcd for $C_{15}H_{15}O_4$: 259.0970, found: 259.0976.

The conversion of **38** to **39** was carried out following the same procedure used for the transformation of **1** into **5c**. **39**: (95%); $R_f = 0.15$ (50% EtOAc/hexanes); $[\alpha]_D = +113$ ($c = 0.8$); $^1$H NMR: $\delta = 7.38$ (d, $J = 8.2$ Hz, 2H), 7.23 (d, $J = 8.1$ Hz, 2H), 7.15 (d, $J = 6.6$ Hz, 2H), 6.78 (d, $J = 6.6$ Hz, 2H), 6.40 (m, 1H), 6.28 (d, $J = 15.0$ Hz, 1H), 6.08 (s, 1H), 5.01 (m, 2H) 3.72 (s, 3H), 3.22 (s, 2H), 3.10 (d, $J = 6.79$ Hz, 2H), 2.32 (s, 3H), 2.16 (s, 3H); $^{13}$C NMR: $\delta = 175.2$ (C), 164.3 (C), 159.4 (C), 157.1 (C), 141.5 (C), 141.3 (C), 140.1 (C), 137.4 (CH), 132.6 (CH), 130.5 (CH), 129.7 (CH), 128.0 (C), 124.2 (CH), 114.3 (CH), 113.5 (CH), 73.0 ($CH_2$), 54.8 ($CH_3$), 31.6 ($CH_2$), 26.8 ($CH_2$), 21.0 ($CH_3$), 19.2 ($CH_3$); LRMS: *m/z*: 349 (0.1) $[M - C_8H_9O]^+$, 333 (32), 259 (4), 244 (3), 163 (26), 121 (100), 111 (10); HRMS: calcd for $C_{17}H_{17}O_4S_2$: 349.0568, found: 349.0579.

To a solution of compound **39** (550 mg, 1,17 mmol) in $CH_2Cl_2$ (12 mL) was added trifluoroacetic acid (0.4 mL). After stirring for 30 min at RT the mixture was poured into water, extracted with $CH_2Cl_2$, dried, filtered, and concentrated. The crude residue, without further purification, was disolved in $CH_2Cl_2$ (15 mL), and imidazole (125 mg, 1.83 mmol) and TBSCl (250 mg, 1.65 mmol) were added. After stirring for 2 h at RT, the mixture was poured into brine, extracted with $CH_2Cl_2$, dried, filtered and concentrated. The crude was purified by flash chromatography (50–80% EtOAc/hexanes) to afford **40** as a viscous oil (422 mg, 78%). $R_f = 0.33$ (60% EtOAc/hexanes); $[\alpha]_D = +132$ ($c = 0.65$); $^1$H NMR: $\delta = 7.55$ (d, $J = 7.9$ Hz, 2H), 7.37 (d, $J = 7.9$ Hz, 2H), 6.70 (m, 1H), 6.40 (d, $J = 14.9$ Hz, 1H), 6.10 (s, 1H), 3.72 (s, 2H), 3.41 (d, $J = 6.85$ Hz, 2H), 2.45 (s, 3H), 2.20 (s, 3H), 0.95 (s, 9H), 0.15 (s, 6H); $^{13}$C NMR: $\delta = 174.3$ (C), 163.4 (C), 152.2 (C), 141.4 (C), 141.1 (C), 140.1 (C), 137.5 (CH), 133.0 (CH), 129.8 (CH), 124.6 (CH), 112.9 (CH), 32.7 ($CH_2$), 27.7 ($CH_2$), 25.8 ($CH_3$), 21.1 ($CH_3$), 19.3 ($CH_3$), 18.5 (C), −3.9 ($CH_3$); LRMS: *m/z*: 407 (68) $[M - C_4H_9]^+$, 391 (1), 269 (5), 227 (100), 196 (62); HRMS: calcd for $C_{19}H_{23}O_4S_2Si$: 407.0807, found: 407.0806.

**Cycloaddition of 40**: A solution of pyrone **40** (345 mg, 0.743 mmol) in toluene (35 mL) was heated at 160 °C for 48 h. The solvent was evaporated and the crude purified by flash chomatography (10–15% EtOAc/hexanes) to afford a 93:7 ratio of diastereoisomeric adducts as colorless oils (82%; $R_f$ (20% EtOAc/hexanes): 0.64 and 0.77]. The diastereoisomeric ratio was determined by integrating the signals of the $C_2$ methylenic protons of the two isomers in the $^1$H NMR spectrum of the crude reaction mixture.

Major isomer: $[\alpha]_D = +143$ ($c = 1.4$); $^1$H NMR: $\delta = 7.58$ (d, $J = 8.1$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 6.49 (s, 1H), 3.44 (d, $J = 12.9$ Hz, 1H), 3.00 (d, $J = 6.5$ Hz, 1H), 2.74 (d, $J = 13.0$ Hz, 1H), 2.42 (s, 3H), 2.34 (m, 1H), 2.22 (m, 1H), 1.77 (s, 3H), 1.71 (m, 1H), 0.98 (s, 9H), 0.23 (s, 6H); $^{13}$C NMR: $\delta = 193.1$ (C), 147.3 (C), 143.2 (C), 139.5 (C), 130.4 (CH), 128.5 (CH), 125.0 (CH), 98.1 (C), 85.2 (C), 79.5 (CH), 52.2 (CH), 35.6 ($CH_2$), 35.6 ($CH_2$), 25.5 ($CH_3$), 25.0 ($CH_3$), 21.5 ($CH_3$), 18.4 (C), −4.6 ($CH_3$); LRMS: *m/z*: 407 (40) $[M - C_4H_9]^+$, 268 (38), 193 (78), 179 (65), 139 (29); HRMS: calcd for $C_{19}H_{23}O_4S_2Si$: 407.0807, found: 407.0814.

Minor isomer: $[\alpha]_D = +117.7$ ($c = 0.70$); $^1$H NMR: $\delta = 7.45$ (d, $J = 8.1$ Hz, 2H), 7.34 (d, $J = 8.1$ Hz, 2H), 6.14 (s, 1H), 3.43 (d, $J = 13.3$ Hz, 1H), 3.23 (m, 1H), 2.80 (d, $J = 7.0$ Hz, 1H),2.71 (d, $J = 13.3$ Hz, 1H), 2.62 (m, 1H), 2.42 (s, 3H), 1.67 (m, 1H), 1.64 (s, 3H), 0.97 (s, 9H), 0.23 (s, 6H); $^{13}$C NMR: $\delta = 191.8$ (C), 146.9 (C), 142.1 (C), 138.7 (C), 130.3 (CH), 127.7 (CH), 123.7 (CH), 98.0 (C), 82.3 (C), 78.1 (CH), 47.5 (CH), 36.08 ($CH_2$) 35.7 ($CH_2$), 25.6 ($CH_3$), 23.5 ($CH_3$), 21.4 ($CH_3$), 18.3 (C), −4.7 ($CH_3$); LRMS: *m/z*: 407 (18) $[M - C_4H_9]^+$, 268 (39), 239 (28), 193 (100), 179 (53), 139 (22); HRMS: calcd for $C_{19}H_{23}O_4S_2Si$: 407.0807, found: 407.0814.

A solution of the above major cycloadduct (100 mg, 0.22 mmol) in THF (2 mL) was added to a suspension of activated Raney nickel (2.70 g) in THF (20 mL). The reaction mixture was heated under reflux for 2 h, allowed to cool to RT, filtered, and poured into water. Extraction with $Et_2O$, drying and concentration gave a residue which was purified by flash chromatography (1–5% EtOAc/hexanes) to afford **41** (46 mg, 71%, 97% *ee*) as a colorless oil. $R_f = 0.52$ (5% EtOAc/hexanes). The enantiomeric excess was determined by $^1$H NMR in presence of Eu(hfc)$_3$ (0.3 equiv) by comparation of the split signals of the TBS methyl protons with those of racemic **41**. $[\alpha]_D = -50.4$ ($c = 1.70$); $^1$H NMR: $\delta = 3.87$ (s, 1H), 2.47 (d, $J = 14.5$ Hz, 1H), 2.21 (m, 2H), 2.12 (m, 1H), 1.33 (s, 3H), 1.25 (s, 3H) 1.21 (m, 1H), 0.90 (d, $J = 7.5$ Hz, 1H), 0.84 (s, 9H), 0.10 (s, 3H), −0.06 (s, 3H); $^{13}$C NMR: $\delta = 206.3$ (C), 86.7 (C), 83.0 (CH), 80.0 (C), 53.5 ($CH_2$), 46.7 ($CH_2$), 35.2 (CH), 26.1 ($CH_3$), 25.7 ($CH_3$), 19.5 ($CH_3$), 18.9 ($CH_3$), 18.3 (C), −4.3 ($CH_3$), −5.2 ($CH_3$); HRMS: calcd for $C_{16}H_{30}O_3Si$: 298.1964, found: 298.1968.

The transformation of compound **41** into natural nemorensic acid was accomplished in two steps as previously described. (+)-**36** [white solid, m.p. 143–145 °C, $[\alpha]_D = +87$ ($c = 0.35$, EtOH), {lit.: $[\alpha]_D = +87$ ($c = 0.84$, EtOH)}].

## Acknowledgement

We are grateful to the Spanish M.E.C. (PB97-0524) for financial support. F.L. thanks the Spanish M.E.C. for a predoctoral fellowship.

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Received: August 24, 2001 [F3507]