DOI: 10.1002/ejoc.201100868

Asymmetric Synthesis of Functionalized Bicyclic β-Amino Alcohols by Cascade Hydrometallation–Cyclization–Reduction of Glycinyl-Substituted Alkenylsulfoximines – Application to the Synthesis of an Aggrecanase Inhibitor Mimic

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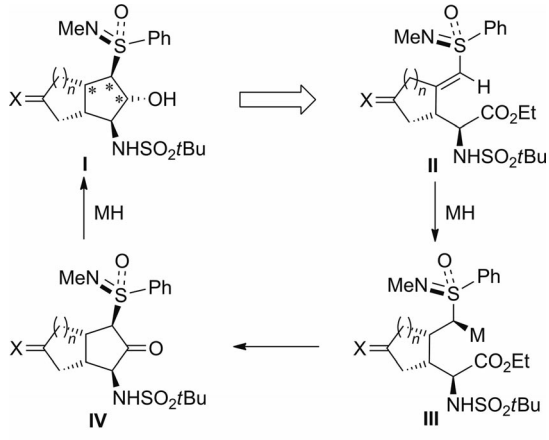
Keywords: Asymmetric synthesis / Cascade reactions / Cyclization / Hydrometallation / Enzyme inhibitors / β-Amino alcohols / Sulfoximines / Aggrecanase inhibitor mimic

The treatment of exocyclic alkenylsulfoximines, which carry an α-glycinyl group at the allylic position, with $HAliBu_2$ caused cascade hydroalumination–cyclization–reduction and delivered the corresponding enantio- and diastereopure sulfoximine-substituted bicyclic β-amino alcohols with a bicyclo[3.3.0]octane and bicyclo[4.3.0]nonane skeleton in high yields. Three consecutive stereogenic C atoms of the bicyclic β-amino alcohols were generated in the cascade reactions with high diastereoselectivities. Application of the hydroalumination–cyclization–reduction to a ketal-substituted six-membered exocyclic alkenylsulfoximine afforded the corresponding sulfoximine-substituted β-amino alcohol with a ketal-functionalized bicyclo[4.3.0]nonane skeleton. Reduction of a sulfoximine-substituted β-amino alcohol gave the parent β-amino alcohol, whereas its oxidative deamination afforded the corresponding sulfonyl-substituted β-amino alcohol. The treatment of a sulfoximine-substituted β-amino alcohol with chloro- and iodoformates stereoselectively furnished the corresponding chloro- and iodo-substituted β-amino alcohols. Finally, the feasibility of a dehydration and elimination of sulfoximine-substituted β-amino alcohols with formation of the corresponding amino-substituted alkenylsulfoximine and allylic amine was demonstrated. An enantio- and diastereopure protected aggrecanase inhibitor mimic was synthesized in high yield starting from the sulfoximine-substituted bicyclic β-amino alcohol with a bicyclo[4.3.0]nonane skeleton and (*R*)-2-(3-benzyloxy)benzyl-4-*tert*-butoxy-4-oxobutanoic acid. Coupling of both building blocks gave the corresponding succinamide, the *tert*-butoxycarbonyl group of which was converted into the corresponding *O*-benzyl-hydroxycarbamoyl group.

Introduction

Carbocyclic β-amino alcohols are of considerable importance as chiral auxiliaries and catalysts[1] and building blocks of enzyme inhibitors.[2] For example, bicyclic β-amino alcohols serve as key components of potent aggrecanase[3] and HIV-1 protease[4] inhibitors. We envisioned a stereoselective synthesis of the sulfoximine-substituted bicyclic β-amino alcohols **I** through metal hydride mediated cascade hydrometallation–cyclization–reduction of the glycinyl-substituted alkenylsulfoximines **II** through the metallated sulfoximines **III** and keto sulfoximines **IV** with the generation of three stereogenic centres (C*, Scheme 1). We have previously described an asymmetric synthesis of glycinyl-substituted alkenylsulfoximines **II** through γ-aminoalkylation of the allylic sulfoximines **V** with the imino ester **VI** (Scheme 2).[5,6] Although several methods have been developed for the asymmetric synthesis of carbocyclic β-amino alcohols including the ring opening of bicyclic epoxides,[7] reductive cyclization of C=O and C=N group-containing



Scheme 1. Bicyclic β-amino alcohols from cascade hydrometallation–cyclization–reduction of glycinyl-substituted alkenylsulfoximines.

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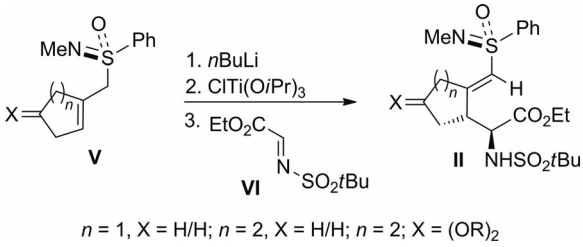
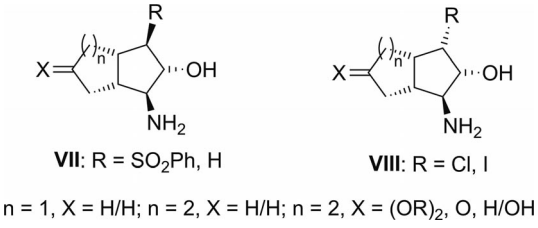
precursors[8,9] and hydrogenation of amino cycloalkanones,[10] a cascade hydrometallation–cyclization–reduction has rarely been applied.[11,12]



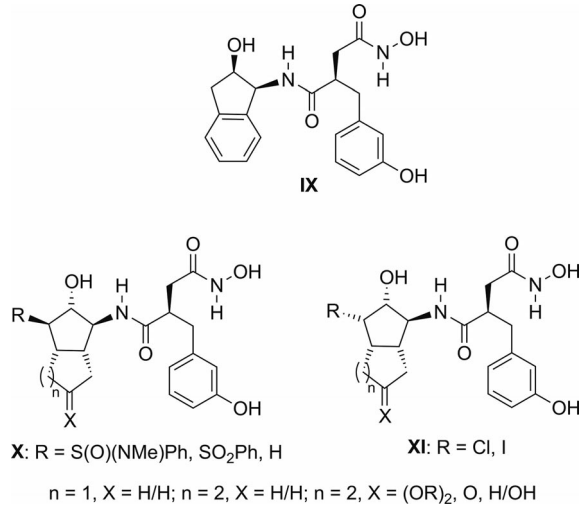
Scheme 2. Asymmetric synthesis of glycinyl-substituted alkenylsulfoximines.

Because of the particular reactivity of the sulfoximine group,[13,14] the β-amino alcohols **I** should also allow the synthesis of substituted bicyclic β-amino alcohols of type **VII** and **VIII** carrying a sulfonyl group, H, Cl and I atom instead of the sulfoximine group (Scheme 3).



Scheme 3. Substituted bicyclic β-amino alcohols.

Here we report on the asymmetric synthesis of sulfoximine-substituted bicyclic β-amino alcohols of type **I** featuring stereoselective cascade hydroalumination–cyclization–reduction of **II** using diisobutylaluminumhydride as the metal hydride. Also reported are the syntheses of β-amino alcohols of type **VII** and **VIII** through chemo- and stereoselective transformations of the sulfoximine group of **I**. Finally, we describe the asymmetric synthesis of a protected aggrecanase inhibitor mimic of type **X** [R = S(O)(NMe)Ph] using the corresponding sulfoximine-substituted β-amino alcohol **I** as the starting material (Scheme 4). The metalloprotease aggrecanase (ADAMTS5)[15a,15b,15d] plays an important role in cartilage aggrecan degradation, a process believed to be a leading cause of osteoarthritis and rheumatoid arthritis.[15] The quest for better arthritis therapy led to an intensive study of aggrecanase inhibitors.[3,15c,15e] It was recently found that the hydroxamic acid derivative **IX** containing a bicyclic β-amino alcohol moiety is an efficient but unspecific aggrecanase inhibitor.[3] Crucial to the activity of **IX** is the structure of the β-amino alcohol. Therefore, we became interested in the synthesis of hydroxamic acid derivatives **X** and **XI**, which carry a bicyclic β-amino alcohol component of type **I**, **VII** and **VIII**, as potential aggrecanase inhibitors. The structural variation provided by the β-amino alcohols **I**, **VII** and **VIII** could perhaps serve to find new potent inhibitors of aggrecanase. Of particular interest are the sulfoximine-substituted derivatives **X** [R = S(O)(NMe)Ph] because of the possibility of a specific inhibitory coordination of the Lewis basic sulfoximine group[13] to the Zn atom in the active site of aggrecanase.[3]

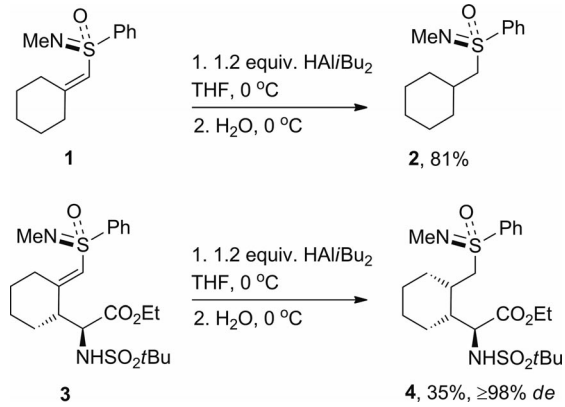


Scheme 4. Aggrecanase inhibitor **IX** and aggrecanase inhibitor mimics **X** and **XI**.

Results and Discussion

Hydroalumination–Cyclization–Reduction

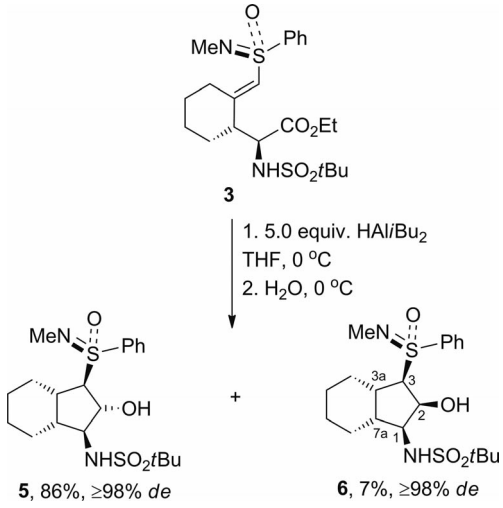
According to Scheme 1 the synthesis of the bicyclic amino alcohols **I** from the alkenylsulfoximines **II** require chemo- and stereoselective hydrometallations in the first and third steps. Diisobutylaluminumhydride was selected as the reagent because of its ability to perform hydroaluminations of both C=C and C=O double bonds.[16] Model experiments with alkenylsulfoximines **1**[17] and **3**[5] (Scheme 5) were performed in order to seek answers to the following questions: 1) do the double bonds of alkenylsulfoximines react with $HAliBu_2$? 2) is hydroalumination of the C=C double bond with $HAliBu_2$ faster than that of the C=O double bond? and 3) is the hydroalumination stereoselective?



Scheme 5. Hydroalumination of exocyclic alkenylsulfoximines **1** and **3**.

The treatment of alkenylsulfoximine **1** with 1.2 equiv. of HAl*i*Bu$_2$ gave alkylsulfoximine **2** in 81% yield. A similar treatment of glycinyl-substituted alkenylsulfoximine **3** with 2.0 equiv. of HAl*i*Bu$_2$ afforded glycinyl-substituted alkylsulfoximine **4** with ≥ 98% *de* in 35% yield. The low yield of **4** was in part due to isolation problems. The *cis* configuration of **4** was determined by NOE experiments, which revealed a strong correlation between the H atoms at the stereogenic C atoms of the cyclohexane ring. Although the diastereoselectivity of the hydroalumination of **3** was high, not much can be said about the competition between the hydroalumination of the C=C and C=O double bonds because of the low yield of **4**.

Having obtained favourable results concerning the diastereoselectivity of the hydroalumination of **II**, the next steps following the hydroalumination, the cyclization of the putative α-diisobutylaluminosulfoximine **III** and the reduction of ketone **IV** were studied. After some experimentation it was found that the treatment of the alkenylsulfoximine **3** with 5.0 equiv. of HAl*i*Bu$_2$ resulted in the envisioned cascade hydroalumination–cyclization–reduction to give β-amino alcohol **5** with ≥ 98% *de* (NMR) in 86% yield and the diastereomeric β-amino alcohol **6** with ≥ 98% *de* (NMR) in 7% yield (Scheme 6). The application of 3.0 equiv. of HAl*i*Bu$_2$ afforded **5** in only 50% yield. The configuration of β-amino alcohol **5** was determined by X-ray crystal structure analysis (Figure 1)[18] and that of diastereomeric alcohol **6** was secured by NOE experiments. Strong NOEs were recorded not only between H-3a and H-7a but also between H-1 and H-2, H-1 and H-3, and H-2 and H-3. No NOEs were observed between H-2 and H-3a or H-2 and H-7a.



Scheme 6. Hydroalumination–cyclization–reduction of the cyclohexanoid alkenylsulfoximine **3**.

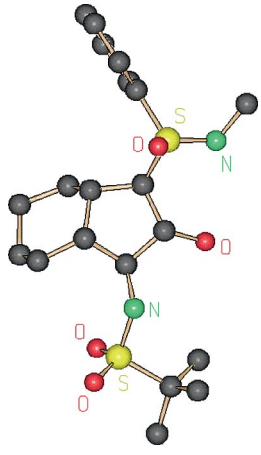
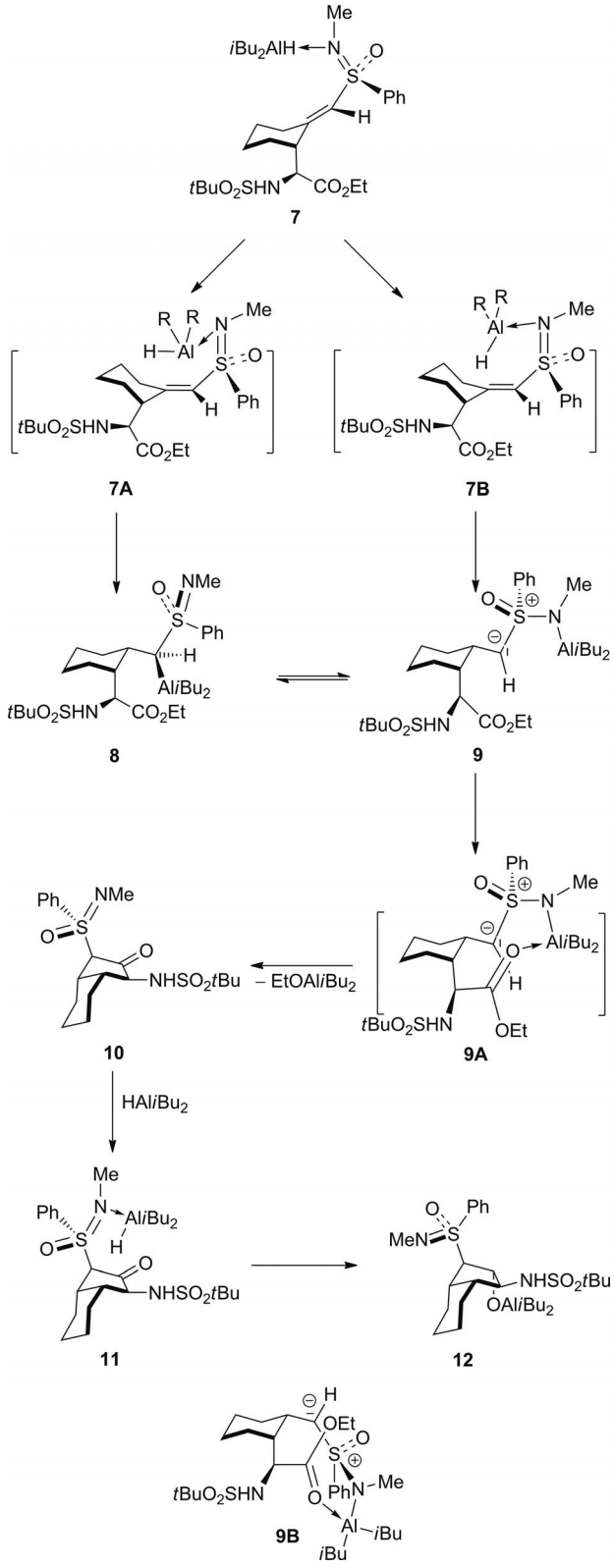


Figure 1. Crystal structure of β-amino alcohol **5**. Color code: C black, S yellow, O red, N green.

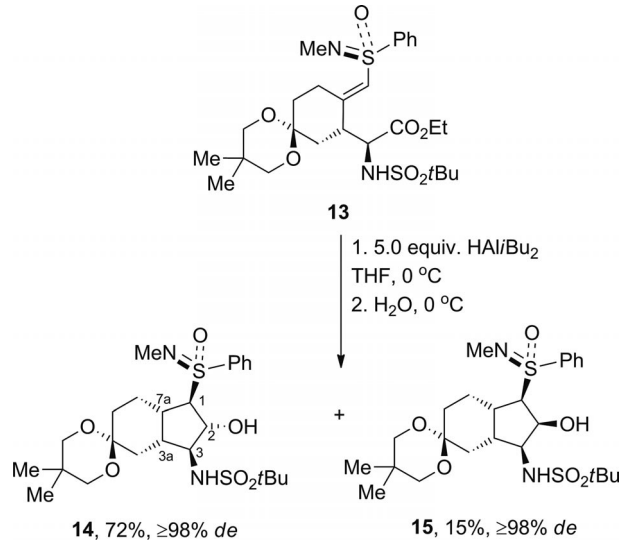
The three new stereogenic centres of **5** were formed in the cascade reactions of **3** with high diastereoselectivities. This is rationalized as follows: according to X-ray crystal structure analysis and NMR spectroscopy the cyclohexane ring of **3**[5] preferentially adopts a chair-like conformation in which the glycinyl group occupies a pseudoaxial position (Scheme 7). Because of the Lewis basicity of *N*-methylsulfoximines,[13] sulfoximine **3** and HAl*i*Bu$_2$ perhaps engaged in the formation of complex **7**, which underwent a HAl*i*Bu$_2$ addition[16] by the four-membered cyclic transition state **7A** to the C=C double bond from the *Si*–*Re* side and stereoselectively gave *R*-configured C$_\alpha$-metallated sulfoximine **8**. Sulfoximine **8** is perhaps configurationally unstable and suffers a migration of the diisobutylaluminum group to the N atom (or O atom) with formation of aminosulfoxonium ylide **9**. Both the ylide and organoaluminum species are perhaps in equilibrium. C$_\alpha$-Titanated sulfoximines show a dynamic C,N-migratory behaviour of this type.[19] Alternatively, **7** may have undergone a HAl*i*Bu$_2$ addition to the C and N atoms through the six-membered cyclic transition state **7B** and directly delivered ylide **9**. The stereoselective cyclization of **9** by transition state **9A** involving an attack of the carbonyl group at the *Si* side of the C$_\alpha$ atom afforded ketone **10**. The attack of the carbonyl group at the *Re* side of the C$_\alpha$ atom, as depicted in transition state **9B**, seems to be unfavoured because of steric reasons. Subsequently, ketone **10** perhaps reacted with a second equivalent of HAl*i*Bu$_2$ with coordination to the sulfoximine group and formed **11**, which underwent an intramolecular H–Al bond addition to the carbonyl group at the *Si* side and stereoselectively afforded alcoholate **12**.

The highly selective cascade reactions of alkenylsulfoximine **3** prompted a study of the analogous ketal-substituted alkenylsulfoximine **13** (Scheme 8), which was obtained from the corresponding cyclic allylic sulfoximine and *N*-*tert*-butylsulfonyl imino ester in 75% yield with ≥ 98% *de*.[20] Gratifyingly, treatment of **13** with 5.0 equiv. of HAl*i*Bu$_2$ afforded β-amino alcohol **14** with ≥ 98% *de* (NMR) in 72% yield and the diastereomeric alcohol **15** with ≥ 98% *de* (NMR) in 15% yield. The configurations of **14** and **15** were determined by NOE experiments. In the case of **14** a medium NOE was observed between H-7a and H-2, and strong NOEs were recorded between H-3a and H-7a, and H-2 and H-3a. In addition, a strong NOE was observed between H-1 and H-3 and a NOE between H-3 and H-3a



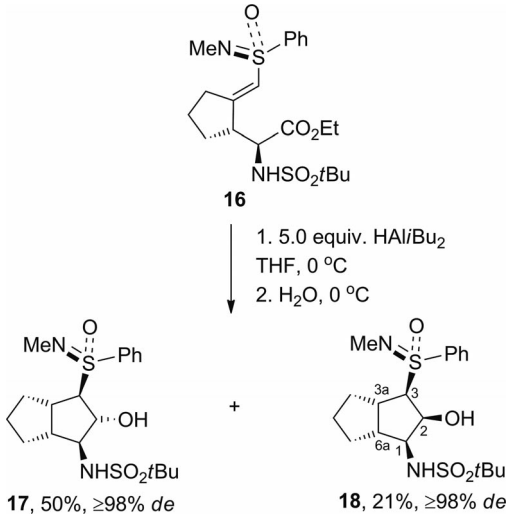
Scheme 7. Rationalization of the stereochemical course of cascade hydroalumination–cyclization–reduction.

was not observed. For **15** strong NOEs were observed between H-1 and H-2, H-2 and H-3, and H-3a and H-7a. No NOEs were recorded between H-2 and H-3a or H-2 and H-7a.



Scheme 8. Hydroalumination–cyclization–reduction of the cyclohexanoid alkenylsulfoximine **13**.

Because of the ready formation of β-amino alcohols **5**, **6**, **14** and **15**, which have a bicyclo[4.3.0]nonane skeleton, it was of interest to see whether β-amino alcohols of this type with a bicyclo[3.3.0]octane skeleton were also accessible by this route. The similar treatment of cyclopentanoid alkenylsulfoximine **16**[5] with 5.0 equiv. of HAl*i*Bu$_2$ afforded β-amino alcohol **17** with ≥ 98% *de* (NMR) in 50% yield and the diastereomeric alcohol **18** with ≥ 98% *de* (NMR) in 21% yield (Scheme 9). The configuration of β-amino alcohol **17** was determined by X-ray crystal structure analysis (Figure 2),[18] and that of diastereomeric alcohol **18** was secured by NOE experiments. Strong NOEs were observed not only between H-3a and H-6a but also between H-1 and H-2, H-1 and H-3, and H-2 and H-3. No NOEs were recorded between H-3 and H-3a or H-1 and H-6a.



Scheme 9. Hydroalumination–cyclization–reduction of the cyclopentanoid alkenylsulfoximine **16**.

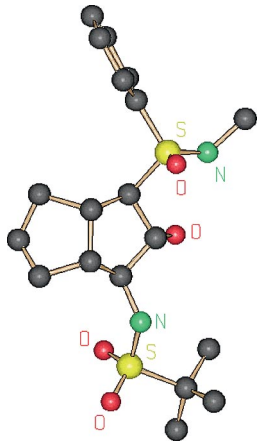
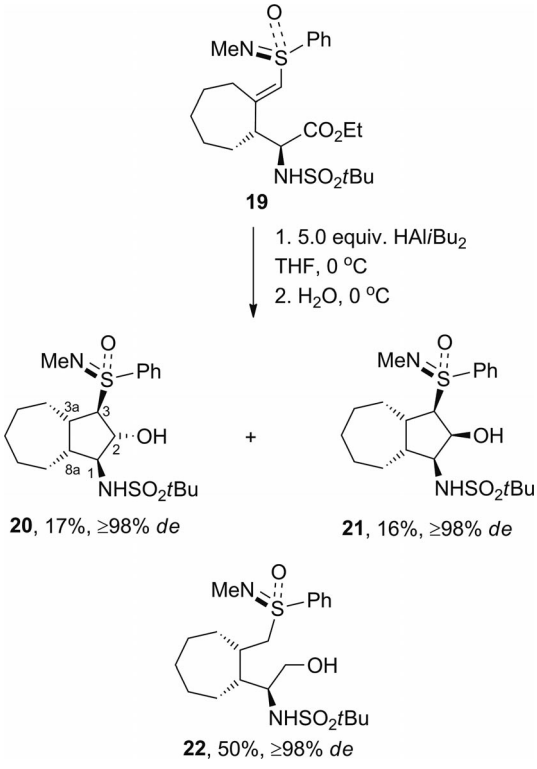


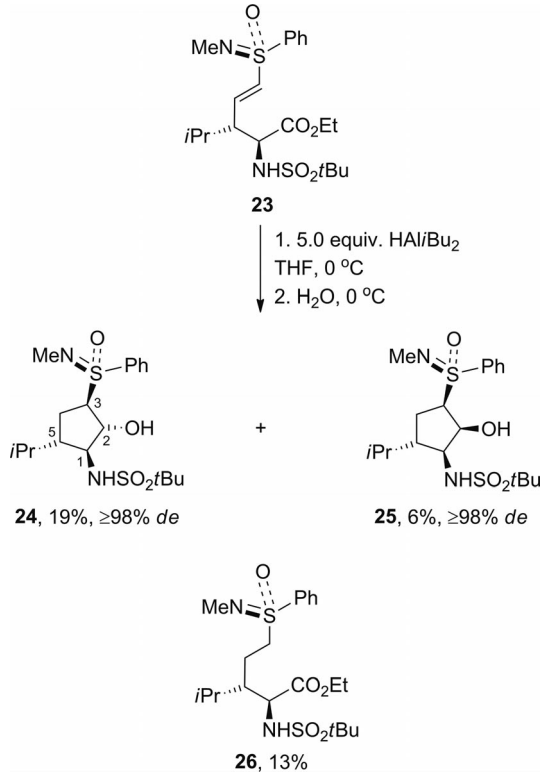
Figure 2. Crystal structure of β-amino alcohol **17**. Color code: C black, S yellow, O red, N green.

Finally, the feasibility of the hydroalumination–cyclization–reduction of cycloheptanoid alkenylsulfoximine **19** was probed. The similar treatment of alkenylsulfoximine **19**[5] with 5.0 equiv. of HAl*i*Bu$_2$ afforded β-amino alcohol **20** with ≥ 98% *de* (NMR) in 17% yield and the diastereomeric alcohol **21** with ≥ 98% *de* (NMR) in 16% yield (Scheme 10). However, the major product was hydroxymethyl-substituted alkylsulfoximine **22**, which was isolated with ≥ 98% *de* (NMR) in 50% yield. The configurations of the diastereomeric alcohols **20** and **21** and of the primary alcohol **22** were determined by NOE experiments. For **20** strong NOEs were observed between H-1 and H-3, and H-3a and H-8a. No NOEs were observed between H-1 and H-8a or H-3 and H-3a. In the case of diastereomer **21** strong NOEs were not only recorded between H-3a and H-8a but also between H-1 and H-2, H-2 and H-3, and H-1 and H-3. In the case of **22** strong NOEs between the H-atoms at the stereogenic ring C atoms gave proof of *cis* configuration. Although the hydroalumination and cyclization occurred in the case of **19** with high diastereoselectivities, the low yields of **20** and **21** show that the attainment of bicyclic amino alcohols of type **I** with a bicyclo[5.3.0]decane skeleton by the cascade reactions is less feasible.

So far only the hydroalumination–cyclization–reduction of cyclic alkenylsulfoximines has been studied. This led to the question of whether the cascade reactions are also applicable to acyclic alkenylsulfoximines. The treatment of the alkenylsulfoximine **23**[5] with 5.0 equiv. of HAl*i*Bu$_2$ afforded cyclopentanoid β-amino alcohol **24** with ≥ 98% *de* (NMR) in 19% yield and diastereomeric alcohol **25** with ≥ 98% *de* (NMR) in 6% yield (Scheme 11). In addition, alkylsulfoximine **26** was obtained in 13% yield. The configurations of diastereomeric alcohols **24** and **25** were determined by NOE experiments. For **24** strong NOEs were recorded between H-1 and H-3, and H-2 and H-5, and weak NOEs between H-1 and H-2, H-2 and H-3, and H-1 and H-5. In the case of **25** strong NOEs were observed between H-1 and H-2, H-1 and H-3, and H-2 and H-3. The low yields of **24**, **25** and **26** were in part due to isolation problems. Optimization experiments were, however, not carried out. An indication that the hydroalumination of **23** might have occurred with



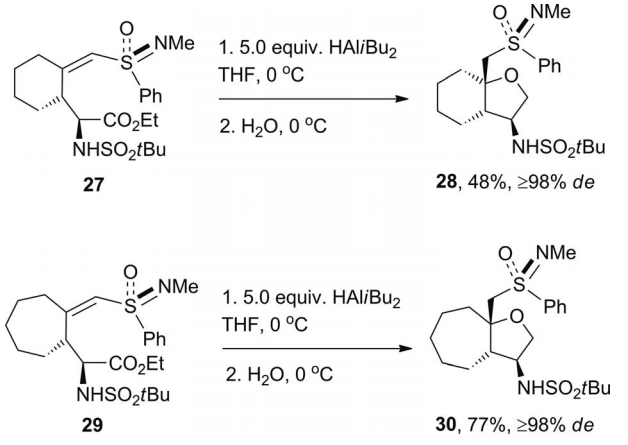
Scheme 10. Hydroalumination–cyclization–reduction of cycloheptanoid alkenylsulfoximine **19**.



Scheme 11. Hydroalumination–cyclization–reduction of the acyclic alkenylsulfoximine **23**.

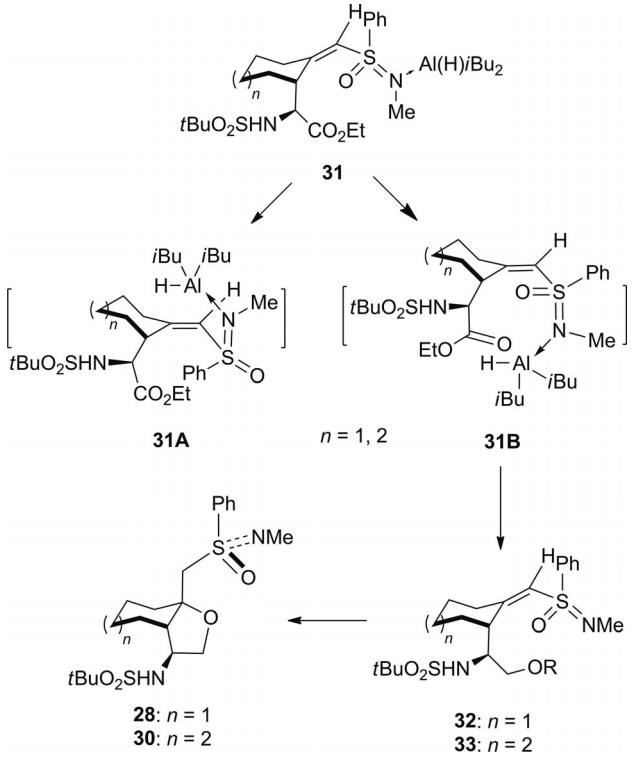
high chemoselectivity at the C=C double bond was provided by the reaction of the *N*-allyl derivative of **23** with 2 equiv. of HAl*i*Bu$_2$, which gave the corresponding alkylsulfoximine ester in 91% yield.[21] Interestingly, the cyclizations of the intermediate acyclic aminosulfoxonium ylides (not shown) leading to **24** and **25** occurred with similarly high diastereoselectivities as those of the ylides derived from the exocyclic alkenylsulfoximines (cf. Scheme 7).

The synthesis of the *E*-configured alkenylsulfoximines **3** and **19** from the corresponding sulfoximine-substituted allyltitanium complexes and *N*-*tert*-butylsulfonyl imino ester was accompanied by the formation of the corresponding diastereomeric *Z*-configured alkenylsulfoximines **27** and **29** (Scheme 12).[5] Having the isomers **27** and **29** in hand, it was of interest to study their reactivity towards HAl*i*Bu$_2$. Surprisingly, the treatment of **27** with 5.0 equiv. of HAl*i*Bu$_2$ did not give **5** or a diastereomer thereof but the aminofuran derivative **28** with ≥ 98% *de* (NMR) in 48% yield. The relatively low yield was in part due to isolation problems. Similarly, cycloheptanoid alkenylsulfoximine **29** afforded after treatment with 5.0 equiv. of HAl*i*Bu$_2$ the amino furan derivative **30** with ≥ 98% *de* (NMR) in 77% yield. The configurations of **28** and **30** were assigned based on NOE experiments, which revealed strong NOEs between the H atom at the bridgehead positions and the H atoms at the α-position to the sulfoximine group.



Scheme 12. Reduction–cyclization of the *Z*-configured cyclic alkenylsulfoximines **27** and **29**.

In order to rationalize the diastereoselective hydroalumination of alkenylsulfoximine **3**, the prior formation of complex **7** was proposed, which underwent an intramolecular C,C/C,N addition of the hydride through transition states **7A** and **7B**, respectively (cf. Scheme 7). The *Z*-configured alkenylsulfoximines **27** and **29** are also expected to form complexes of type **31** with HAl*i*Bu$_2$ (Scheme 13). Because of the *Z*-configuration of complexes **31**, they can, unlike the *E*-configured **7**, undergo both an intramolecular C,C/C,N hydroalumination through transition states **31A** and a C,O hydroalumination by transition state **31B** leading to a reduction of the ester group with formation of the corresponding alcohols **32** and **33**. Transition state **31A** is perhaps unfavoured because of a steric interaction between the phenyl group and the glycinyl group at the allylic position. Finally, alcohols **32** and **33** experienced a diastereoselective cyclization[22,23e] as such or at the stage of the corresponding aluminum alcoholates with formation of the furan derivatives **28** and **30**, respectively.

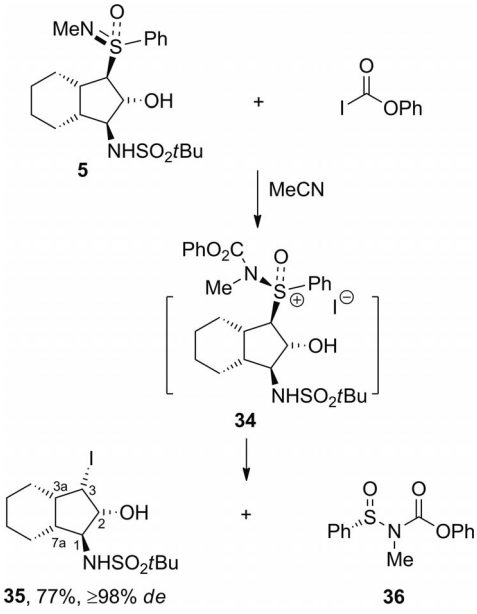


Scheme 13. Rationalization of the formation of furans **28** and **30**.

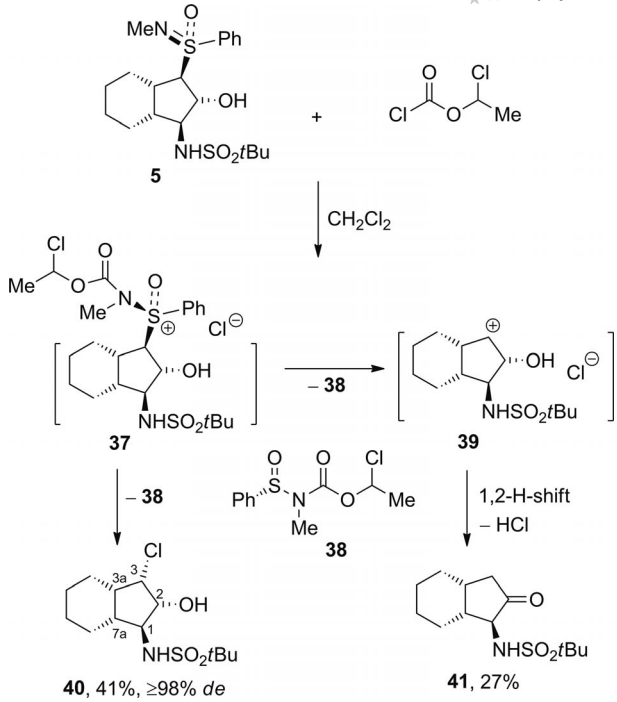
Selective Transformations of Sulfoximine-Substituted β-Amino Alcohols

The transformation of the sulfoximine group of the bicyclic β-amino alcohols to other functional groups would significantly enhance their versatility as building blocks for the synthesis of drug candidates and as chiral auxiliaries and catalysts. Thus, sulfoximine-substituted β-amino alcohol **5** was subjected to a number of transformations, which we and others have developed for sulfoximines. The treatment of sulfoximine **5** with iodophenylformate led to the formation of iodo-substituted β-amino alcohol **35**, which was isolated with ≥ 98% *de* (NMR) in 77% yield (Scheme 14).

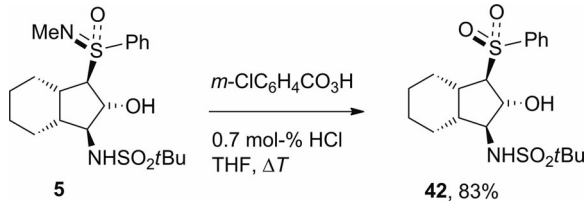
We have previously shown that this type of substitution of the sulfoximine group commences with an acylation at the N atom of the sulfoximine group,[23] which should have afforded in the present case the aminosulfoxonium salt **34**. Salt **34** then underwent a S_N2 reaction and delivered under inversion of configuration the iodide **35**. It is noteworthy that the substitution of the aminosulfoxonium group of **34** by iodide was not accompanied by an intramolecular substitution by the hydroxyl group under epoxide formation. The sulfinamide **36**[23e,23f] was isolated in 75% yield. We



Scheme 14. Substitution of the sulfoximine group of **5** by an I atom.



Scheme 15. Substitution of the sulfoximine group of **5** by a Cl atom.



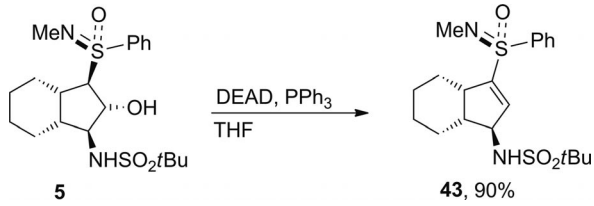
Scheme 16. Oxidative deamination of sulfoximine **5**.

have previously shown that the substitution of the *N*-methylsulfoximine group with iodoformate proceeds with complete retention of the configuration at the S atom.[23e,23f] The configuration of iodide **35** was determined by NOE experiments, which showed strong correlations between H-2 and H-3, H-3 and H-3a, and H-3a and H-7a.

Generally, the reaction of an alkylsulfoximine with a chloroformate gives the corresponding chloride.[23] Therefore, sulfoximine **5** was treated with 1-chloroethyl chloroformate, which afforded chloride **40** with ≥ 98% *de* (NMR) in 41% yield (Scheme 15). Sulfoximine **5** was most likely converted by the formate to the *N*-(acylamino)sulfoxonium chloride **37**, which underwent a S_N2 reaction with the chloride ion and gave **40**. The configuration of chloride **40** was determined by NOE experiments, which revealed strong correlations between H-2 and H-3, H-3 and H-3a, and H-3a and H-7a. Surprisingly, ketone **41** was also isolated in 27% yield. Because of the lower nucleopilicity of the chloride compared to the iodide ion, salt **37** presumably lost in a competing reaction sulfinamide **38** with formation of the carbenium ion **39**, which underwent a 1,2-H shift[24] and, after deprotonation, gave ketone **41**. The sulfinamide **38**, whose formation has been demonstrated in similar cases,[23] was not isolated.

The sulfoximine group conveys additional basicity to the cyclic β-amino alcohols, which can perhaps be detrimental in some synthetic application of the β-amino alcohols. Therefore, sulfoximine **5** was submitted to an oxidative deamination with *m*-chloroperbenzoic acid,[25] which afforded sulfone **42** in 83% yield (Scheme 16). The sulfonyl group is considerably less basic than the sulfoximine group and provides further possibilities for the synthetic application of the β-amino alcohols.[26]

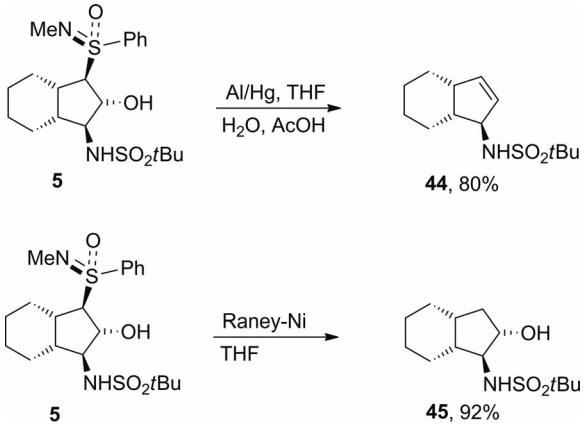
Alkenylsulfoximines offer a considerable synthetic potential through the application of, for example, Michael[5] and cross-coupling reactions.[27] Therefore, the dehydration of the alcohol **5** was studied. The treatment of **5** with ethyl azodicarboxylate and triphenylphosphane[28] gave alkenylsulfoximine **43** in 90% yield (Scheme 17).



Scheme 17. Dehydration of the hydroxy sulfoximine **5**.

Finally, the reduction of the sulfoximine group[29,30] of **5** was probed. The treatment of sulfoximine **5** with aluminum amalgam caused, however, a reductive elimination[31] and gave alkene **44** in 80% yield (Scheme 18). The alkene can perhaps serve as a versatile starting material for the synthesis of the corresponding dihydroxy- and hydroxyamino-sub-

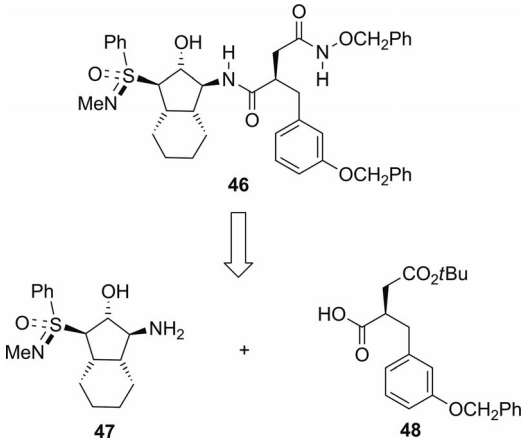
stituted bicyclic β-amino alcohols. A clean reduction of sulfoximine **5** was achieved upon treatment with Raney nickel, which furnished β-amino alcohol **45** in 92% yield.



Scheme 18. Elimination and reduction of the hydroxy sulfoximine **5**.

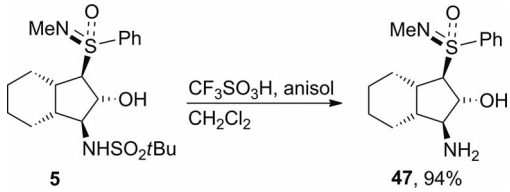
Synthesis of a Protected Aggrecanase Inhibitor Mimic

The hydroxamic acid derivative **IX** (cf. Scheme 4) is a potent aggrecanase inhibitor,[3] the activity of which crucially depends on the β-amino alcohol moiety. The cyclic β-amino alcohols **5**, **6**, **14**, **15**, **17**, **18**, **20**, **21**, **24**, **25**, **35**, **40**, **42** and **45** should serve to further probe the relevance of this structural unit for the activity of aggrecanase inhibitors of type **IX**. In the first step, we envisioned the synthesis of the protected aggrecanase inhibitor mimic **46** with a sulfoximine group through coupling of β-amino alcohol **47** with succinic acid derivative **48** (Scheme 19). The amide coupling would ensure a high degree of structural flexibility in regard to both key components of **X** and **XI**, the amine and acid. In the case of **IX** an elegant and efficient, but less flexible, synthetic strategy in regard to the two components was followed featuring the establishment of the stereogenic centre in α-position to the carbonyl group as the last step.[13]



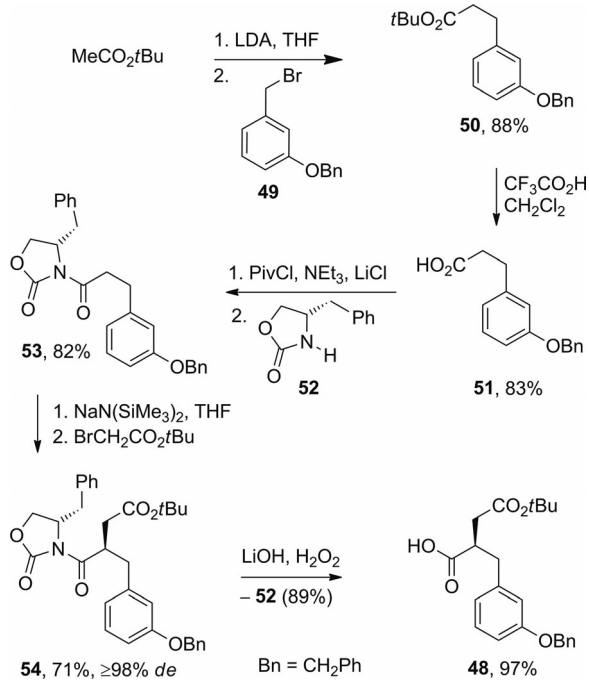
Scheme 19. Retrosynthesis of the aggrecanase inhibitor mimic **46**.

Cleavage of sulfonamide **5** with CF_3SO_3H in the presence of anisol in dry CH_2Cl_2[32] gave amine **47** containing 0.5 equiv. of CF_3SO_3H in 94% yield (Scheme 20).



Scheme 20. Deprotection of sulfonamide **5**.

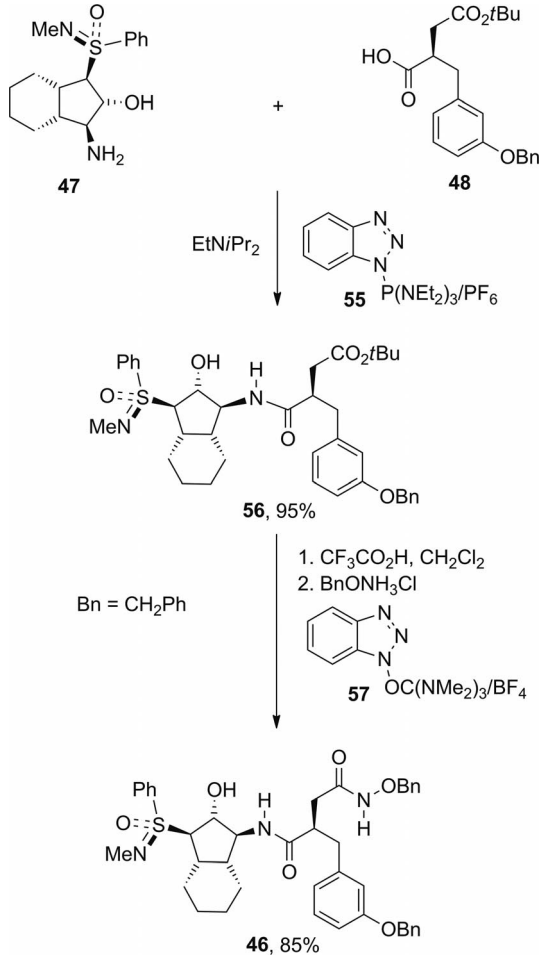
The acid **51**, which was required as the starting material for the synthesis of succinic acid **48**, was obtained in 72% overall yield through alkylation of the lithium enolate of *tert*-butylacetate with bromide **49**[33] and hydrolysis of the thus formed ester **50** (Scheme 21). The asymmetric synthesis of succinic acid **48** was carried out by the oxazolidinone method,[34] which has already been successfully applied to the synthesis of structurally related acids.[35,36] Coupling of acid **51** with chiral auxiliary **52** gave oxazolidinone **53** in 82% yield. The successive treatment of **53** with sodium hexamethyldisilazide and *tert*-butylbromoacetate afforded substituted amide **54** with ≥ 98% *de* (NMR) in 71% yield. Amide **54** was assigned as the *R*-configuration on the basis of literature precedent.[34–36] Hydrolysis of amide **54** with $LiOH/H_2O_2$ furnished the *R*-configured succinic acid **48** in 97% yield.



Scheme 21. Asymmetric synthesis of the succinic acid **48**.

The crucial coupling of the two building blocks, the enantio- and diastereopure amine **47** containing 0.5 equiv. of CF_3SO_3H and acid **48**, proceeded readily using the phosphonium salt **55**[37] and gave the amide **56** in 95% yield (Scheme 22). According to NMR spectroscopy, amide **56** was diasteromerically pure (≥ 98% *de*). Thus, the hydrolysis of amide **54** occurred without racemization. It has been shown previously that the cleavage of amides of type **54**

with $LiOH/H_2O_2$ is free of racemization.[34] Hydrolysis of ester group of **56** furnished the corresponding acid, which was coupled without isolation with *O*-benzylhydroxyamine by applying uronium salt **57**.[38] This afforded the *O*,*O*-dibenzylhydroxamic acid derivative **46** in 85% yield. The ^1H and ^{13}C NMR spectra of **46** at room temperature in $CDCl_3$ showed the presence of two species in a ratio of approximately 4:1. At 55 °C reversible coalescence phenomena of the signals of the two species were observed. On the basis of these observations we ascribe the two species of **46** to conformers in respect to the C,N bond of the *O*-benzyl-hydroxycarbamoyl group.[39]



Scheme 22. Synthesis of the protected aggrecanase inhibitor mimic **46**.

Conclusions

Cascade hydroalumination–cyclization–reduction of the glycinyl-substituted *E*-configured exocyclic alkenylsulfoximines provided an efficient access to enantio- and diastereopure sulfoximine-substituted bicyclic β-amino alcohols. Although the hydroalumination and cyclization proceeded with high diastereoselectivities, the selectivities of the reduction were lower depending on the structure of the bicyclic ring system. Chemo- and stereoselective transformations of the sulfoximine group of the β-amino alcohols including substitution, oxidative deamination, and reduction gave access to synthetically interesting enantio- and diastereopure substituted β-amino alcohols. Elimination of either both the sulfoximine and hydroxy groups or only the hydroxy group afforded the allylic amine and amino-substituted alkenylsulfoximine, respectively. Because of the ready coupling of the bicyclic β-amino alcohol with the chiral succinic acid derivative, a large number of enantio- and diastereopure aggrecanase inhibitor mimics with different bicyclic β-amino alcohol moieties should be accessible.

Experimental Section

General Methods: All reactions involving oxygen- and water-sensitive compounds were carried out under argon using standard Schlenk and syringe techniques in oven-dried glassware. THF and toluene were distilled with sodium benzophenone ketyl. CH_2Cl_2, $HNiPr_2$, NEt_3, $EtNiPr_2$, DMF and MeCN were distilled from CaH_2. Unless otherwise specified, all reagents were purchased from commercial suppliers and used without further purification. The enantiopure alkenylsulfoximine **1**[16] was prepared from enantiopure (*S*)-*N*,*S*-dimethylphenylsulfoximine[40,41] and cyclohexanone according to the literature. The enantio- and diastereopure glycinyl-substituted alkenylsulfoximines **3**,[5] **13**,[21] **16**,[5] **19**,[5] **23**,[5] **27**[5] and **29**[5] were synthesized starting from the corresponding enantiopure allylic sulfoximines and ethyl 2-(*tert*-butylsulfonylimino)acetate[6] according to the literature. The benzylic bromide **49** was prepared from the corresponding benzylic alcohol according to literature.[33] Solutions of $HAliBu_2$ in THF were prepared from neat $HAliBu_2$ and absolute THF. The concentration of *n*BuLi in THF was determined by titration with diphenylacetic acid.[42] ^1H NMR spectra were recorded with Varian VXR 300 (300 MHz), Varian Gemini 300 (300 MHz), Inova 400 (400 MHz) and Unity 500 (500 MHz) spectrometers. Chemical shifts are given in ppm using Me_3Si (δ = 0.00 ppm) as internal standard. The following abbreviations are used in order to describe the signals observed in the ^1H NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br, broad signal and combinations thereof. Assignments in ^1H NMR spectra were made by GMQCOSY, GNOE and GTOCSY experiments. ^{13}C NMR spectra were ^1H broad band-decoupled and measured with Varian VXR 300 (75 MHz), Varian Gemini 300 (75 MHz), Inova 400 (100 MHz) and Unity 500 (125 MHz) spectrometers. The chemical shifts are given in ppm using Me_3Si (δ = 0.00 ppm) as internal standard. Peaks in the ^{13}C NMR spectra are assigned as u for carbons with zero or two attached protons and d for carbons with one or three attached protons, as determined from APT experiment. Assignments in ^{13}C NMR spectra were made by DEPT, HETCOR or GHMQC experiments. Mass spectra were recorded with a Finnigan MAT 95 spectrometer using either electron ionization (EI, 70 eV) or chemical ionization (CI, CH_4 and isobutane). HRMS were recorded with a Varian MAT 95 using electron ionization (EI, 70 eV). FTMS analysis was performed with a LTQ Orbitrap XL™ instrument (Thermo Scientific, Bremen, Germany). Infrared spectra were recorded with a Perkin–Elmer FTIR 1760 S instrument. Only bands with intensities ≥ 10% were listed and the following abbreviations were used: w = weak, m = middle, s = strong and vs. = very strong. Optical rotations were measured with a Perkin–Elmer Polarimeter PE 241 and given in grad × mL/dm × g, and the concentration *c* in g/100 mL. The measurements were run at approximately 22 °C. TLC

was performed using precoated aluminum sheets (Merck silica gel 60 F_{254}). Column and flash chromatography were conducted using silica gel 60 (Merck, 40–63 μm). HPLC separations were performed with a Varian SD-1 Pump with built-in UV detector (Prostar 320) and RI detector (Knauer) using a Kromasil Si 100 (100 mm × 30 mm) column.

[{(*S*)-*N*-Methylphenylsulfonimidoyl}methyl]cyclohexane (2): To a solution of **1** (487 mg, 1.95 mmol) in THF (20 mL) was added HAl*i*Bu_2 (2.01 mL of 1.12 M in THF, 2.25 mmol) dropwise whilst stirring at 0 °C. After the mixture was warmed to room temperature over 4 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was further stirred for 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 300 mL) and the filtrate was concentrated in vacuo. Purification by column chromatography (pentane/Et_2O, 1:4) furnished **2** (395 mg, 81%) as pale yellow oil. R_f = 0.27 (pentane/Et_2O, 1:4). $[a]_D$ = +86.7 (c = 1.02, in CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85–1.37 (m, 5 H), 1.56–1.78 (m, 4 H), 1.87–1.92 (m, 1 H), 2.01–2.06 (m, 1 H, SCH_2CH), 2.64 (s, 3 H, NCH_3), 2.96 (dd, J = 6.5, J = 14.3 Hz, 1 H, SC*H*H), 3.12 (dd, J = 5.7, J = 14.3 Hz, 1 H, SCH*H*), 7.53–7.64 (m, 3 H, Ph), 7.84–7.88 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.7 (u), 25.76 (u), 25.82 (u), 29.5 (d), 32.8 (d), 33.1 (u), 33.3 (u), 63.2 (u), 129.1 (d), 129.4 (d), 132.6 (d), 138.8 (u) ppm. MS (EI, 70 eV): m/z (%) = 251 (4) $[M]^+$, 173 (11), 172 (20), 171 (8), 156 (27), 155 (15), 154 (5), 140 (28), 127 (5), 126 (20), 125 (77), 109 (5), 108 (9), 107 (100), 106 (14), 105 (14), 97 (15), 95 (8), 94 (7), 91 (20), 81 (9), 79 (5), 78 (22), 77 (18), 67 (6), 55 (49), 54 (6), 53 (7). IR (capillary): $\tilde{\nu}$ = 3061 (w), 2924 (vs), 2855 (s), 2801 (m), 2362 (w), 1448 (m), 1401 (w), 1242 (vs), 1147 (s), 1105 (m), 1080 (m), 915 (w), 863 (w), 779 (m), 740 (s) (m) cm^{-1}. HRMS: calcd. for $C_{14}H_{21}NOS$ $[M]^+$ 251.134387; found 251.134370.

(*S*)-Ethyl 2-(1,1-Dimethylethylsulfonamido)-2-[(1*R*,2*S*)-2-({(*S*)-*N*-methylphenyl-sulfonimidoyl}methyl)cyclohexyl]acetate (4): To a solution of **3** (468 mg, 0.99 mmol) in THF (40 mL) was added HAl*i*Bu_2 (1.78 mL of 1.12 M in THF, 1.99 mmol) dropwise whilst stirring at 0 °C. After the mixture was warmed to room temperature over 4 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was further stirred for 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 300 mL) and the filtrate was concentrated in vacuo. Purification by flash chromatography (EtOAc/cyclohexane, increasing polarity from 1:9 to 4:1) furnished **4** (165 mg, 35%) as white solid; m.p. 55–57 °C. $[a]_D$ = +65.4 (c = 1.0, in CH_2Cl_2). R_f = 0.48 (EtOAc/cyclohexane, 4:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88–0.94 (m, 1 H), 1.26–1.60 (m, 4 H), 1.71–1.92 (m, 3 H), 1.31 (t, J = 7.1 Hz, 3 H, CH_2CH_3), 1.40 [s, 9 H, $C(CH_3)_3$], 1.98–2.08 (m, 1 H, NCHC*H*), 2.63 (s, 3 H, NCH_3), 2.93 (dd, J = 8.4, J = 14.1 Hz, 1 H, SC*H*H), 3.04–3.11 (m, 1 H, SCH_2CH), 3.75–3.80 (m, 1 H, SCH*H*), 4.12 (dd, J = 9.1, J = 10.4 Hz, 1 H, NCH), 4.21 (dt, J = 7.1, J = 12.6 Hz, 2 H, OCH_2), 7.38 (d, J = 10.4 Hz, 1 H, NH), 7.55–7.63 (m, 3 H, Ph), 7.94–7.98 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.3 (d), 20.4 (u), 24.3 (d), 25.3 (u), 25.9 (u), 29.0 (d), 29.2 (d), 31.4 (u), 44.4 (d), 53.9 (u), 59.7 (u), 59.8 (d), 61.6 (u), 129.3 (d), 129.4 (d), 132.8 (d), 138.6 (u), 173.0 (u) ppm. MS (EI, 70 eV): m/z (%) = 473 (3) $[M + 1]^+$, 399 (18), 352 (7), 351 (34), 275 (7), 274 (40), 250 (5), 202 (9), 198 (19), 197 (18), 196 (100), 173 (6), 172 (9), 170 (13), 169 (5), 168 (6), 157 (6), 156 (60), 155 (7), 140 (33), 126 (6), 125 (47), 124 (72), 108 (6), 107 (57), 106 (5), 105 (7), 102 (28), 95 (19), 91 (11), 81 (7), 79 (5), 77 (7), 67 (6), 57 (46). IR (capillary): $\tilde{\nu}$ = 3986 (w), 3957 (w), 3876 (m), 3841 (w), 3768 (w), 3722 (w), 3697 (w), 3604 (w), 3571 (m), 3520 (m), 3413 (m), 3375 (m), 3331 (w), 3279 (m), 3204 (w), 3113 (w), 3070 (w), 2928 (vs), 2865 (s), 2769 (w), 2694 (w), 2639 (w), 2588 (w), 2508 (w), 2238 (w), 1735 (m), 1580 (w), 1445 (vs), 1314 (m), 1245 (w), 1120 (s), 1025 (m), 912 (w), 874 (w), 750 (w) cm^{-1}. HRMS: calcd. for $C_{19}H_{31}N_2O_3S_2$ $[M - C_3H_5O_2]^+$ 399.177613; found 399.177727.

***N*-[(1*S*,2*R*,3*R*,3a*S*,7a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octa-hydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (5) and *N*-[(1*S*,2*S*,3*R*,3a*S*,7a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (6):** To a solution of **3** (400 mg, 0.85 mmol) in THF (40 mL) was added HAl*i*Bu_2 (3.79 mL of 1.12 M in THF, 4.25 mmol) dropwise whilst stirring at 0 °C. After the reaction mixture was warmed to room temperature over 3 h, pieces of ice were added until hydrogen gas evolution ceased. The mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 300 mL) and the filtrate was concentrated in vacuo. Purification and separation by flash chromatography (EtOAc/cyclohexane, increasing polarity from 1:9 to 1:1) furnished **5** (313 mg, 86%) and **6** (26 mg, 7%) as white solids. For **5**: M.p. 213 °C. $[a]_D$ = +32.2 (c = 1.0, in CH_2Cl_2). R_f = 0.35 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.01–1.11 (m, 3 H), 1.34–1.60 (m, 4 H), 1.87–1.90 (m, 1 H), 1.47 [s, 9 H, $C(CH_3)_3$], 1.96–1.99 (m, 1 H, $NCHCHCH_2$), 2.16–2.21 (m, 1 H, $SCHCHCH_2$), 2.62 (s, 3 H, NCH_3), 3.08 (dd, J = 3.8, J = 6.6 Hz, 1 H, SCH), 3.74 (ddd, J = 7.7, J = 10.1, J = 11.5 Hz, 1 H, NCH), 4.35 (d, J = 10.1 Hz, 1 H, NH), 4.59 (dd, J = 6.6, J = 7.7 Hz, 1 H, O-CH), 7.57–7.66 (m, 3 H, Ph), 7.85–7.87 (m, 2 H, Ph) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.9 (u), 23.5 (u), 24.3 (d), 24.4 (u), 29.2 (d), 30.1 (u), 35.2 (d), 41.7 (d), 60.2 (u), 61.7 (d), 73.2 (d), 76.8 (d), 129.6 (d), 129.6 (d), 133.2 (d), 136.5 (u) ppm. MS (EI, 70 eV): m/z (%) = 429 (1) $[M + 1]^+$, 355 (1), 292 (8), 260 (2), 198 (4), 156 (100), 152 (24), 136 (55), 125 (48), 77 (4), 57 (24). IR (KBr): $\tilde{\nu}$ = 3984 (w), 3911 (w), 3856 (w), 3450 (w), 3271 (vs), 3065 (w), 2971 (m), 2930 (s), 2864 (m), 2803 (w), 1453 (s), 1398 (w), 1305 (vs), 1235 (vs), 1178 (w), 1125 (vs), 1082 (s), 1013 (m), 962 (w), 916 (m), 870 (m), 828 (m), 804 (m), 760 (m) cm^{-1}. $C_{20}H_{32}N_2O_4S_2$ (428.61): calcd. C 56.05, H 7.53, N 6.54; found C 56.28, H 7.62, N 6.56. For **6**: M.p. 148 °C. $[a]_D$ = +12.3 (c = 1.0, in CH_2Cl_2). R_f = 0.19 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28–1.92 (m, 7 H), 1.85–1.92 (m, 1 H), 1.43 [s, 9 H, $C(CH_3)_3$], 2.23–2.33 (m, 1 H, $NCHCHCH_2$), 2.66 (s, 3 H, NCH_3), 2.78–2.89 (m, 1 H, $SCHCHCH_2$), 2.95 (dd, J = 5.0, J = 5.3 Hz, 1 H, SCH), 3.50 (ddd, J = 4.0, J = 10.1, J = 11.1 Hz, 1 H, NCH), 4.15 (dd, J = 4.0, J = 5.0 Hz, 1 H, OCH), 4.64 (d, J = 10.1 Hz, 1 H, NH), 7.57–7.66 (m, 3 H, Ph), 7.91–7.94 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (u), 23.6 (u), 23.7 (u), 24.3 (d), 28.7 (d), 31.2 (u), 35.0 (d), 40.4 (d), 59.7 (u), 60.4 (d), 69.2 (d), 69.9 (d), 129.3 (d), 129.8 (d), 133.5 (d), 137.7 (u) ppm. MS (EI, 70 eV): m/z (%) = 429 (1) $[M + 1]^+$, 307 (8), 292 (17), 198 (9), 156 (36), 152 (100), 136 (20), 125 (25), 107 (13), 78 (4), 57 (23). IR (KBr): $\tilde{\nu}$ = 3602 (w), 3281 (s), 3056 (w), 2932 (s), 2808 (m), 1735 (w), 1446 (s), 1366 (w), 1315 (s), 1246 (s), 1125 (vs), 1082 (m), 1025 (w), 986 (m), 927 (m), 900 (m), 850 (m), 805 (m), 754 (m) cm^{-1}. $C_{20}H_{32}N_2O_4S_2$ (428.61): calcd. C 56.05, H 7.53, N 6.54; found C 56.14, H 7.64, N 6.45.

***N*-[(1′*R*,2′*R*,3′*S*,3a′*R*,7a′*S*)-2′-Hydroxy-5,5-dimethyl-1′-{(*S*)-*N*-methylphenyl-sulfonimidoyl}octahydrospiro[1,3-dioxane-2,5′-indene]-3′-yl]-2-methylpropane-2-sulfonamide (14) and *N*-[(1′*R*,2′*S*,3′*S*,3a′*R*,7a′*S*)-2′-Hydroxy-5,5-dimethyl-1′-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydrospiro[1,3-dioxane-2,5′-indene]-3′-yl]-2-methylpropane-2-sulfonamide (15):** To a solution of **13** (260 mg, 0.46 mmol) in THF (20 mL) was added HAl*i*Bu_2 (2.03 mL of 1.12 M in THF, 2.28 mmol) dropwise whilst stirring at 0 °C. After

the mixture was warmed to room temperature over 3 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was further stirred for 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 300 mL), and the filtrate was concentrated in vacuo. Purification and separation by flash chromatography (EtOAc/cyclohexane, increasing polarity from 1:9 to 1:1) furnished **14** (174 mg, 72%) and **15** (36 mg, 15%) as white solids. For **14**: M.p. 121 °C. $[a]_D$ = –12.8 (c = 1.0, in CH_2Cl_2). R_f = 0.21 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (s, 3 H, CH_2CCH_3), 0.99 (s, 3 H, CH_2CCH_3), 1.21–1.33 (m, 3 H), 1.95–2.08 (m, 2 H, NCHCHC*H*H, SCHCHCH_2, SCHCHCH$_2$CH_2), 1.47 [s, 9 H, C(CH_3)$_3$], 1.80 (dd, J = 5.0, J = 14.3 Hz, 1 H, NCHCHCH*H*), 2.18–2.27 (m, 1 H, NCHC*H*CH$_2$), 2.40–2.48 (m, 1 H, SCHC*H*CH$_2$), 2.63 (s, 3 H, NCH_3), 3.16 (t, J = 5.8 Hz, 1 H, SCH), 3.36–3.41 (m, 3 H, OCH_2, OC*H*H), 3.50 (d, J = 11.5 Hz, 1 H, OCH*H*), 3.79–3.86 (m, 1 H, NCH), 4.48 (s, 1 H, OH), 4.55–4.58 (m, 1 H, OCH), 4.63 (d, J = 9.6 Hz, 1 H, NH), 7.55–7.65 (m, 3 H, Ph), 7.85–7.89 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.4 (d), 22.7 (d_3), 24.3 (d), 25.2 (u), 28.2 (u), 29.2 (d), 29.9 (u), 32.5 (u), 35.4 (d), 41.4 (d), 60.2 (u), 65.0 (d), 69.7 (u), 69.9 (u), 72.1 (d), 78.6 (d), 97.0 (u), 129.4 (d), 129.5 (d), 133.0 (d), 136.7 (u) ppm. MS (EI, 70 eV): m/z (%) = 529 (1) [M + 1]$^+$, 392 (8), 373 (7), 253 (18), 252 (100), 237 (6), 236 (32), 197 (8), 167 (19), 166 (29), 156 (27), 150 (12), 141 (7), 125 (19), 107 (6), 69 (11). IR (KBr): $\tilde{\nu}$ = 3248 (m), 3062 (w), 2952 (s), 2871 (m), 2810 (w), 1738 (w), 1638 (w), 1450 (m), 1396 (w), 1364 (m), 1309 (s), 1241 (s), 1189 (w), 1125 (vs), 1015 (w), 972 (w), 901 (m), 834 (w), 794 (m), 753 (m) cm^{-1}. HRMS: calcd. for $C_{25}H_{40}N_2O_6S_2$ [M]$^+$ 528.232782; found 528.232902. For **15**: M.p. 104 °C. $[a]_D$ = +20.7 (c = 1.0, in CH_2Cl_2). R_f = 0.37 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (300 MHz, CD_3OD): δ = 0.86 (s, 3 H, CH_2CCH_3), 0.98 (s, 3 H, CH_2CCH_3), 1.36–1.47 (m, 2 H, SCHCHC*H*H, SCHCHCH$_2$C*H*H), 1.39 [s, 9 H, C(CH_3)$_3$], 1.55–1.59 (m, 1 H, SCHCHCH*H*), 1.81 (dd, J = 6.6, J = 14.0 Hz, 1 H, NCHCHC*H*H), 2.05 (dd, J = 6.6, J = 14.0 Hz, 1 H, NCHCHCH*H*), 2.11–2.15 (m, 1 H, SCHCHCH$_2$CH*H*), 2.40–2.46 (m, 1 H, NCHC*H*CH$_2$), 2.64 (s, 3 H, NCH_3), 2.67–2.71 (m, 1 H, SCHC*H*CH$_2$), 3.36 (dd, J = 4.0, J = 6.3 Hz, 1 H, SC*H*), 3.40–3.47 (m, 3 H), 3.55–3.58 (m, 1 H, OCH_2, OCH_2), 3.54–3.57 (m, 1 H, NCH), 4.22 (t, J = 4.0 Hz, 1 H, OCH), 7.64–7.74 (m, 3 H, Ph), 7.88–7.92 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 21.2 (d), 21.7 (d), 23.3 (d), 26.3 (u), 27.6 (u), 29.44 (d), 29.44 (u), 31.6 (u), 34.1 (d), 38.7 (d), 59.3 (u), 61.8 (d), 69.1 (d), 69.60 (u), 69.60 (u), 71.3 (d), 98.0 (u), 129.2 (d), 129.5 (d), 133.4 (d), 137.3 (u) ppm. MS (EI, 70 eV): m/z (%) = 529 (2) [M + 1]$^+$, 392 (20), 373 (7), 254 (5), 253 (18), 252 (100), 237 (6), 236 (14), 235 (6), 234 (22), 198 (10), 196 (28), 168 (8), 166 (29), 156 (18), 148 (6), 141 (6), 125 (12), 57 (15). IR (CH_2Cl_2): $\tilde{\nu}$ = 3482 (w), 3364 (w), 3272 (w), 3061 (m), 2956 (s), 2871 (m), 2806 (w), 1472 (m), 1449 (m), 1397 (w), 1366 (w), 1308 (s), 1278 (m), 1242 (s), 1126 (vs), 1015 (w), 968 (w), 900 (w), 811 (w), 778 (w), 707 (m) cm^{-1}. HRMS: calcd. for $C_{21}H_{30}NO_4S$ [M – $C_4H_{10}NO_2S$]$^+$ 392.189556; found 392.189601.

***N*-[(1*S*,2*R*,3*R*,3a*S*,6a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydropentalen-1-yl]-2-methylpropane-2-sulfonamide (17) and *N*-[(1*S*,2*S*,3*R*,3a*S*,6a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydropentalen-1-yl]-2-methylpropane-2-sulfonamide (18):** To a solution of **16** (260 mg, 0.57 mmol) in THF (20 mL) was added HAl*i*Bu$_2$ (2.85 mL of 1.0 M in THF, 2.85 mmol) dropwise whilst stirring at 0 °C. After the mixture was warmed to room temperature over 3 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 300 mL) and the filtrate was concentrated in vacuo. Purification and separation by HPLC (Kromasil Si 100, 30 mm, EtOAc/cyclohexane, 3:7, 254 nm + RI, 20 mL/min) furnished **17** (120 mg, 51%) and **18** (52 mg, 20%) as white solids [R_f (**18**) > R_f (**17**)]. For **17**: M.p. 221 °C. $[a]_D$ = +101.7 (c = 1.0, in CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.42–0.46 (m, 1 H), 1.05–1.15 (m, 1 H), 1.25–1.35 (m, 1 H), 1.40–1.53 (m, 2 H), 1.94–1.99 (m, 1 H), 1.47 [s, 9 H, C(CH_3)$_3$], 2.24–2.32 (m, 1 H, NCHC*H*), 2.63 (s, 3 H, NCH_3), 2.65–2.73 (m, 1 H, SCHC*H*), 2.93 (t, J = 9.4 Hz, 1 H, SCH), 3.28–3.38 (m, 1 H, NCH), 4.16 (d, J = 9.7 Hz, 1 H, NH), 4.30 (t, J = 9.4 Hz, 1 H, OCH), 7.57–7.68 (m, 3 H, Ph), 7.82–7.85 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.3 (d), 25.1 (u), 28.9 (d), 29.9 (u), 32.4 (u), 37.6 (d), 47.6 (d), 60.3 (u), 65.0 (d), 71.3 (d), 74.8 (d), 129.6 (d), 129.8 (d), 133.6 (d), 136.5 (u) ppm. MS (EI, 70 eV): m/z (%) = 414 (1) [M]$^+$, 293 (21), 198 (6), 156 (53), 140 (15), 139 (17), 138 (100), 125 (34), 122 (19), 110 (15), 107 (14), 106 (5), 96 (10), 78 (7), 77 (8), 69 (8), 57 (58), 56 (17). IR (KBr): $\tilde{\nu}$ = 3282 (vs), 3066 (w), 2939 (m), 2871 (m), 2803 (w), 2370 (w), 2344 (w), 1627 (w), 1455 (m), 1384 (w), 1359 (w), 1305 (s), 1229 (s), 1122 (vs), 1026 (w), 1001 (w), 917 (m), 878 (m), 830 (m), 765 (m) cm^{-1}. $C_{19}H_{30}N_2O_4S_2$ (414.58): calcd. C 55.04, H 7.29, N 6.76; found C 55.14, H 7.04, N 6.62. For **18**: M.p. 169 °C. $[a]_D$ = +14.3 (c = 1.0, in CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 [s, 9 H, C(CH_3)$_3$], 1.42–1.49 (m, 1 H), 1.59–1.82 (m, 5 H), 2.63–2.70 (m, 1 H, NCHC*H*), 2.69 (s, 3 H, NCH_3), 2.71–2.74 (m, 1 H, SCH), 3.17 (dt, J = 2.9, J = 9.9 Hz, 1 H, NCH), 3.36–3.44 (m, 1 H, SCHC*H*), 4.03 (t, J = 2.9 Hz, 1 H, OCH), 4.63 (d, J = 9.9 Hz, 1 H, NH), 7.58–7.68 (m, 3 H, Ph), 7.85–7.88 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.3 (d), 25.2 (u), 28.5 (d), 30.4 (u), 33.1 (u), 40.5 (d), 49.1 (d), 59.6 (u), 64.4 (d), 69.0 (d), 73.1 (d), 129.3 (d), 129.9 (d), 133.6 (d), 137.8 (u) ppm. IR (KBr): $\tilde{\nu}$ = 3056 (w), 2960 (m), 2872 (m), 2810 (w), 1446 (s), 1310 (s), 1247 (s), 1129 (vs), 1018 (w), 984 (w), 915 (m), 850 (m), 819 (w), 788 (w), 760 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 415 (1) [M + 1]$^+$, 293 (7), 157 (9), 156 (100), 140 (16), 139 (26), 138 (42), 126 (6), 125 (55), 122 (28), 110 (7), 107 (11), 96 (8), 81 (5), 78 (6), 77 (7), 58 (48), 57 (11). HRMS: calcd. for $C_{19}H_{30}N_2O_4S_2$ [M]$^+$ 414.164703; found 414.164641.

***N*-[(1*S*,2*R*,3*R*,3a*S*,8a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}decahydroazulen-1-yl]-2-methylpropane-2-sulfonamide (20), *N*-[(1*S*,2*S*,3*R*,3a*S*,8a*R*)-2-Hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}decahydroazulen-1-yl]-2-methylpropane-2-sulfonamide (21) and *N*-[(1*S*)-2-Hydroxy-1-{(1*R*,2*S*)-2-({(*S*)-*N*-methylphenylsulfonimidoyl}methyl)cycloheptyl}ethyl]-2-methylpropane-2-sulfonamide (22):** To a solution of **19** (320 mg, 0.66 mmol) in THF (10 mL) was added HAl*i*Bu$_2$ (2.95 mL of 1.12 M in THF, 3.30 mmol) dropwise whilst stirring at 0 °C. After the mixture was warmed to room temperature over 4 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper and the residue was washed with hot EtOAc (ca. 50 °C, 400 mL). The filtrate was concentrated in vacuo. Purification by column chromatography (EtOAc/cyclohexane, 1:1) afforded **22** (144 mg, 50%) as white solid and a mixture of the alcohols **20** and **21** (R_f = 0.54, EtOAc/cyclohexane, 1:1). Separation by HPLC (Kromasil Si 100, 30 mm, Et_2O/cyclohexane, 1:2, 254 nm + RI, 30 mL/min) gave **20** (49 mg, 17%) and **21** (46 mg, 16%) as white solids [R_f (**20**) > R_f (**21**)]. For **20**: M.p. 228 °C. $[a]_D$ = +51.4 (c = 1.0, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.39–0.44 (m, 1 H), 0.83–0.89 (m, 1 H), 1.01–1.43 (m, 4 H), 1.61–1.67 (m, 2 H), 1.81–1.87 (m, 1 H), 2.11–2.19 (m, 1 H), 1.47 [s, 9 H, C(CH_3)$_3$], 1.88–1.97 (m, 1 H, NCHC*H*CH$_2$), 2.35–2.43 (m, 1 H, SCHC*H*CH$_2$), 2.61 (s, 3 H, NCH_3), 3.00 (dd, J = 8.0, J = 9.1 Hz, 1 H, SCH), 3.37–3.45 (m, 1 H, NCH), 4.04 (d, J = 9.9 Hz, 1 H, NH), 4.32–4.36 (m, 1 H, OCH),

5.20 (s, 1 H, OH), 7.56–7.66 (m, 3 H, Ph), 7.82–7.85 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3 (d), 27.1 (u), 28.7 (u), 28.9 (d), 29.8 (u), 30.8 (u), 31.8 (u), 38.6 (d), 46.4 (d), 60.2 (u), 64.3 (d), 72.1 (d), 74.1 (d), 129.4 (d), 129.5 (d), 133.3 (d), 136.4 (u) ppm. MS (EI, 70 eV): *m*/*z* (%) = 443 (2) $[M + 1]^+$, 306 (10), 168 (12), 167 (25), 166 (65), 157 (9), 156 (100), 150 (59), 149 (16), 148 (10), 126 (5), 125 (53), 124 (6), 107 (16), 106 (7), 81 (5), 78 (7), 77 (8), 67 (6), 58 (57), 57 (24), 56 (10). MS (CI, CH_4): *m*/*z* (%) = 471 (6) $[M + C_2H_5]^+$, 445 (11), 444 (25), 443 (100), 441 (13), 168 (5), 166 (9), 156 (19), 150 (8), 125 (10). IR ($CHCl_3$): $\tilde{\nu}$ = 3957 (w), 3872 (w), 3831 (w), 3789 (w), 3727 (w), 3698 (w), 3578 (w), 3512 (w), 3458 (w), 3283 (s), 3063 (w), 3017 (m), 2925 (s), 2857 (m), 2809 (w), 1452 (s), 1365 (m), 1308 (s), 1234 (s), 1124 (vs), 1081 (s), 1026 (m), 918 (m), 865 (m), 812 (w), 757 (vs) cm^{-1}. HRMS: calcd. for $C_{21}H_{35}N_2O_4S_2$ $[M + H]^+$ 443.203828; found 443.204662. For **21**: M.p. 119 °C. $[\alpha]_D$ = –7.8 (*c* = 1.0, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.90 (m, 1 H), 1.19–1.49 (m, 4 H), 1.81–1.92 (m, 3 H), 2.02–2.08 (m, 1 H), 2.15–2.20 (m, 1 H), 1.37 [s, 9 H, $C(CH_3)_3$], 2.39–2.48 (m, 1 H, NCHC*H*CH_2), 2.70 (s, 3 H, NCH_3), 2.80 (dd, *J* = 3.3, *J* = 9.3 Hz, 1 H, SCH), 3.03–3.12 (m, 1 H, SCHC*H*CH_2), 3.16 (dt, *J* = 3.3, *J* = 10.2 Hz, 1 H, NCH), 3.94 (t, *J* = 3.3 Hz, 1 H, OCH), 4.45 (d, *J* = 10.2 Hz, 1 H, NH), 7.42 (s, 1 H, OH), 7.57–7.65 (m, 3 H, Ph), 7.86–7.89 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3 (d), 28.0 (u), 28.5 (d), 29.5 (uH_2), 29.7 (u), 31.2 (u), 32.4 (u), 40.3 (d), 47.1 (d), 59.6 (u), 64.1 (d), 68.5 (d), 70.8 (d), 129.0 (d), 129.6 (d), 133.3 (d), 137.7 (u) ppm. MS (EI, 70 eV): *m*/*z* (%) = 443 (11) $[M + 1]^+$, 321 (8), 306 (18), 303 (6), 198 (13), 168 (17), 167 (32), 166 (100), 157 (8), 156 (73), 151 (7), 150 (32), 149 (19), 148 (31), 138 (14), 137 (8), 136 (8), 132 (5), 126 (6), 125 (54), 124 (11), 123 (6), 109 (7), 108 (5), 107 (28), 106 (13), 105 (7), 97 (8), 96 (5), 95 (6), 94 (5), 91 (6), 82 (5), 81 (9), 80 (5), 79 (5), 78 (10), 77 (11), 72 (6), 71 (5), 69 (5), 67 (9), 58 (64), 57 (53), 56 (16). MS (CI, CH_4): *m*/*z* (%) = 471 (1) $[M + C_2H_5]^+$, 443 (12), 125 (5), 101 (7), 87 (12), 85 (65), 83 (100). IR ($CHCl_3$): $\tilde{\nu}$ = 3521 (w), 3271 (m), 3020 (m), 2924 (s), 2855 (m), 1448 (m), 1311 (m), 1237 (m), 1128 (s), 1082 (m), 1023 (w), 921 (w), 864 (w), 820 (w), 756 (vs) cm^{-1}. HRMS: calcd. for $C_{21}H_{35}N_2O_4S_2$ $[M + 1]^+$ 443.203828; found 443.204473. For **22**: M.p. 109 °C. $[\alpha]_D$ = +48.5 (*c* = 1.0, in CH_2Cl_2). R_f = 0.20 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.42–1.61 (m, 9 H), 1.86–1.94 (m, 1 H), 1.45 [s, 9 H, $C(CH_3)_3$], 2.15–2.22 (m, 1 H, NCHC*H*), 2.61 (s, 3 H, NCH_3), 2.96 (dd, *J* = 7.7, *J* = 14.0 Hz, 1 H, SC*H*H), 3.05–3.09 (m, 1 H, SCH_2CH), 3.51–3.55 (m, 2 H, SCH*H*, NCH), 3.85 (dd, *J* = 3.0, *J* = 11.8 Hz, 1 H, OC*H*H), 3.93 (dd, *J* = 3.0, *J* = 11.8 Hz, 1 H, OCH*H*), 5.74 (d, *J* = 9.6 Hz, 1 H, NH), 7.57–7.67 (m, 3 H, Ph), 7.84–7.89 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.5 (d), 24.7 (u), 26.4 (u), 26.6 (u_2), 28.5 (u), 29.1 (d), 31.3 (d), 34.0 (u), 46.3 (d), 56.2 (u), 59.6 (d), 59.8 (u), 63.3 (u), 129.0 (d), 129.6 (d), 133.2 (d), 138.1 (u) ppm. MS (EI, 70 eV): *m*/*z* (%) = 445 (7) $[M + 1]^+$, 413 (19), 323 (6), 308 (6), 293 (10), 258 (10), 246 (12), 216 (7), 180 (7), 170 (12), 169 (11), 168 (56), 157 (5), 156 (49), 152 (8), 140 (13), 139 (12), 138 (100), 126 (6), 125 (41), 124 (10), 108 (6), 107 (42), 105 (9), 97 (5), 95 (6), 81 (6), 78 (10), 77 (8), 69 (5), 67 (11), 60 (30), 59 (15), 57 (52), 56 (8), 55 (8). IR (KBr): $\tilde{\nu}$ = 3965 (w), 3896 (w), 38.42 (w), 3749 (w), 3469 (s), 2928 (vs), 2807 (m), 2370 (w), 2344 (w), 2323 (w), 2250 (w), 1629 (m), 1520 (m), 1455 (s), 1303 (s), 1235 (s), 1123 (vs), 912 (m), 865 (m), 737 (s) cm^{-1}. HRMS: calcd. for $C_{20}H_{33}N_2O_3S_2$ $[M – CH_3O]^+$ 413.193263; found 413.193663.

Ethyl (2*S*,3*S*)-2-(1,1-Dimethylethylsulfonamido)-3-isopropyl-5-[(*S*)-*N*-methylphenylsulfonimidoyl]pentanoate (26): To a solution of **23** (300 mg, 0.65 mmol) in THF (20 mL) was added $HAliBu_2$ (3.27 mL of 1.0 M in THF, 3.27 mmol) dropwise whilst stirring at 0 °C. After the mixture was warmed to room temperature over 4 h, pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper and the residue was washed with hot EtOAc (ca. 50 °C, 300 mL). The filtrate was concentrated in vacuo. Purification by column chromatography (EtOAc/cyclohexane, 1:1) afforded **26** (39 mg, 13%) as a white solid and a mixture of **24** and **25** (R_f: 0.43, EtOAc/cyclohexane, 1:1). Separation of the mixture by HPLC (Kromasil Si 100, 30 mm, EtOAc/cyclohexane, 35:65, 254 nm + RI, 25 mL/min) gave **24** (51 mg, 19%) and **25** (16 mg, 6%) as white solids [R_f (14) > R_f(15)]. For **24**: M.p. 76 °C. $[\alpha]_D$ = +15.7 (*c* = 1.0, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.80 (d, *J* = 7.1 Hz, 3 H, CHC*H*$_3$), 0.86 (d, *J* = 7.1 Hz, 3 H, CHC*H*$_3$), 1.39–1.44 (m, 1 H, CHC*H*H), 1.47 [s, 9 H, $C(CH_3)_3$], 1.79–1.87 (m, 1 H, CH_3CHC*H*), 1.95 (ddd, *J* = 7.4, *J* = 10.4, *J* = 14.0 Hz, 1 H, CHCH*H*), 2.08–2.15 (m, 1 H, CH_3C*H*), 2.62 (s, 3 H, NCH_3), 3.30 (dt, *J* = 8.6, *J* = 10.4 Hz, 1 H, SCH), 3.52–3.57 (m, 1 H, NCH), 4.20 (d, *J* = 9.9 Hz, 1 H, NH), 4.40–4.44 (t, *J* = 8.6 Hz, 1 H, OCH), 7.57–7.68 (m, 3 H, Ph), 7.81–7.85 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.8 (d), 20.1 (u), 21.7 (d), 24.4 (d), 26.3 (d), 29.2 (d), 47.9 (d), 60.3 (u), 62.8 (d), 65.6 (d), 75.8 (d), 129.5 (d), 129.7 (d), 133.4 (d), 136.4 (u) ppm. MS (CI, CH_4): *m*/*z* (%) = 445 (6) $[M + C_2H_5]^+$, 419 (11), 418 (22), 417 (100), 415 (7), 206 (6), 156 (21), 125 (10). IR (capillary): $\tilde{\nu}$ = 3062 (w), 3028 (w), 2955 (vs), 2802 (m), 1463 (s), 1370 (m), 1250 (vs), 1198 (w), 1145 (s), 1090 (s), 979 (m), 922 (w), 864 (s), 838 (s), 777 (m) cm^{-1}. HRMS: calcd. for $C_{15}H_{23}N_2O_3S_2$ $[M – C_4H_9O]^+$ 343.115013; found 343.114980. For **25**: M.p. 89–90 °C. $[\alpha]_D$ = –12.8 (*c* = 1.0, in CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (d, *J* = 6.6 Hz, 3 H, CHC*H*$_3$), 0.97 (d, *J* = 6.6 Hz, 3 H, CHC*H*$_3$) 1.38 [s, 9 H, $C(CH_3)_3$], 1.85–2.01 (m, 2 H, CH_3C*H*, CHC*H*H), 2.17–2.25 (m, 1 H, CH_3CHC*H*), 2.53 (ddd, *J* = 9.9, *J* = 11.3, *J* = 13.7 Hz, 1 H, CHCH*H*), 2.68 (s, 3 H, NCH_3), 3.08 (dt, *J* = 3.3, *J* = 9.9 Hz, 1 H, SCH), 3.37 (dt, *J* = 3.3, *J* = 10.2 Hz, 1 H, NCH), 4.04 (t, *J* = 3.3 Hz, 1 H, OCH), 4.54 (d, *J* = 10.2 Hz, 1 H, NH), 7.21 (s, 1 H, OH) 7.57–7.65 (m, 3 H, Ph), 7.85–7.88 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.2 (d), 21.2 (u), 22.0 (d), 24.2 (d), 27.1 (d), 28.5 (d), 47.6 (d), 59.5 (u), 61.2 (d), 62.5 (d), 71.1 (d), 129.1 (d), 129.7 (d), 133.5 (d), 137.2 (u) ppm. MS (EI, 70 eV): *m*/*z* (%) = 416 (1) $[M]^+$, 295 (14), 280 (13), 210 (33), 156 (50), 154 (5), 142 (12), 141 (14), 140 (100), 126 (8), 125 (39), 124 (7), 123 (7), 122 (35), 107 (14), 98 (10), 86 (11), 85 (17), 77 (8), 70 (17), 69 (8), 57 (69), 55 (12). IR (KBr): $\tilde{\nu}$ = 3238 (m), 3058 (w), 2955 (m), 2875 (m), 2810 (w), 1451 (s), 1385 (m), 1308 (s), 1239 (s), 1126 (vs), 1081 (s), 1014 (m), 997 (w), 905 (s), 847 (m), 789 (w) cm^{-1}. HRMS: calcd. for $C_{15}H_{23}N_2O_2S$ $[M – C_4H_9SO_2]^+$ 295.148026; found 295.147926. For **26**: M.p. 137 °C. $[\alpha]_D$ = +23.8 (*c* = 1.0, in CH_2Cl_2). R_f = 0.15 (EtOAc/cyclohexane, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (d, *J* = 6.9 Hz, 3 H, CHC*H*$_3$), 0.91 (d, *J* = 6.9 Hz, 3 H, CHC*H*$_3$), 1.20 (t, *J* = 7.1 Hz, 3 H, CH_2C*H*$_3$), 1.30 [s, 9 H, $C(CH_3)_3$], 1.56–1.68 (m, 2 H, CHC*H*$_2$), 1.86–1.96 (m, 2 H, CH_3C*H*, CH_2C*H*), 2.58 (s, 3 H, NCH_3), 3.13–3.19 (m, 1 H, SC*H*H), 3.34–3.41 (m, 1 H, SCH*H*), 4.09–4.15 (m, 3 H, NC*H*, CH_3C*H*$_2$), 5.91 (d, *J* = 8.2 Hz, 1 H, NH), 7.48–7.57 (m, 3 H, Ph), 7.78–7.81 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3 (d), 19.7 (d), 21.0 (u), 21.9 (d), 24.4 (d), 29.5 (d), 29.7 (d), 47.4 (d), 54.9 (u), 58.6 (d), 60.2 (u), 61.8 (u), 129.3 (dH), 129.5 (d), 132.9 (dH), 137.5 (u), 172.2 (u) ppm. MS (EI, 70 eV): *m*/*z* (%) = 460 (5) $[M]^+$, 387 (12), 339 (7), 325 (8), 324 (44), 238 (14), 232 (5), 186 (28), 185 (5), 184 (35), 182

***N*-(1*S*,2*R*,3*R*,5*S*)-2-Hydroxy-5-isopropyl-3-[(*S*)-*N*-methylphenylsulfonimidoyl]cyclopentyl-2-methylpropane-2-sulfonamide (24), *N*-(1*S*,2*S*,3*R*,5*S*)-2-Hydroxy-5-isopropyl-3-[(*S*)-*N*-methylphenylsulfonimidoyl]cyclopentyl-2-methylpropane-2-sulfonamide (25) and**

(6), 170 (6), 169 (27), 157 (6), 156 (38), 155 (18), 141 (6), 140 (21), 126 (7), 125 (43), 113 (8), 112 (76), 111 (8), 110 (6), 108 (8), 107 (93), 106 (8), 105 (8), 102 (15), 97 (7), 96 (9), 95 (9), 91 (6), 83 (18), 78 (13), 77 (12), 70 (11), 69 (8), 68 (6), 57 (100), 57 (12), 56 (23), 46 (7). IR ($CHCl_3$): $\tilde{\nu}$ = 3685 (w), 3622 (w), 3021 (vs), 2976 (m), 2934 (w), 2900 (w), 2736 (w), 2582 (w), 2402 (m), 2268 (w), 2115 (w), 1733 (m), 1524 (w), 1477 (w), 1426 (w), 1322 (w), 1230 (s), 1203 (m), 1131 (w), 1041 (m), 929 (w), 793 (vs) cm^{-1}. HRMS: calcd. for $C_{21}H_{36}N_2O_5S_2$ $[M]^+$ 460.206567; found 460.206441.

2-Methyl-*N*-[(3*S*,3a*S*,7a*S*)-7a-({(*S*)-*N*-methylphenylsulfonimidoyl}methyl)octa-hydrobenzofuran-3-yl]propane-2-sulfonamide (28): To a solution of **27** (497 mg, 1.06 mmol) in THF (35 mL) was added HAl*i*Bu_2 (5.5 mL of 1.0 M in THF, 5.49 mmol) dropwise whilst stirring at 0 °C. After the mixture was stirred at 0 °C for 2 h, it was warmed to room temperature over 3 h. Pieces of ice were added until hydrogen gas evolution ceased. Then the mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper, the residue was washed with hot EtOAc (ca. 50 °C, 400 mL) and the filtrate was concentrated in vacuo. Purification by flash chromatography (EtOAc/cyclohexane, increasing polarity from 1:9 to 1:1) furnished **28** (215 mg, 48%) as white solid; m.p. 117 °C. $[a]_D$ = +168.7 (c = 1.0, in CH_2Cl_2). R_f = 0.35 (cyclohexane/EtOAc, 1:1). ^1H NMR (500 MHz, CD_3OD, H_2O): δ = 1.26 [s, 9 H, $C(CH_3)_3$], 1.30–1.57 (m, 7 H), 2.05–2.11 (m, 1 H), 2.34–2.38 (m, 1 H, NCHC*H*), 2.47 (s, 3 H, NCH_3), 3.34 (d, J = 15.3 Hz, 1 H, SC*H*H), 3.37 (dd, J = 6.7, J = 9.0 Hz, 1 H, OC*H*H), 3.64 (d, J = 15.3 Hz, 1 H, SCH*H*), 3.83–3.87 (m, 1 H, NCH), 3.96 (dd, J = 6.7, J = 8.0 Hz, 1 H, OCH*H*), 4.87 (br. s, H_2O), 7.51–7.60 (m, 3 H, Ph), 7.77–7.80 (m, 2 H, Ph) ppm. ^{13}C NMR (125 MHz, CD_3OD): δ = 20.6 (u), 21.7 (u), 23.3 (d), 23.7 (u), 28.1 (d), 32.7 (u), 46.9 (d), 57.1 (d), 59.1 (u), 60.7 (u), 71.5 (u), 81.4 (u), 128.8 (d), 129.2 (d), 132.9 (d), 138.7 (u) ppm. MS (EI, 70 eV): m/z (%) = 428 (5) $[M]^+$, 371 (11), 293 (8), 292 (47), 277 (15), 213 (6), 171 (10), 170 (100), 169 (11), 156 (55), 154 (10), 152 (13), 151 (8), 140 (52), 138 (15), 137 (14), 136 (37), 125 (42), 124 (31), 123 (25), 122 (19), 107 (34), 95 (13), 91 (12), 77 (12), 57 (58), 55 (14). IR (KBr): $\tilde{\nu}$ = 3447 (w), 3076 (m), 2932 (s), 2864 (m), 1636 (w), 1477 (m), 1446 (m), 1404 (w), 1366 (w), 1312 (vs), 1232 (s), 1189 (w), 1155 (s), 1129 (vs), 1104 (s), 1077 (m), 1048 (m), 1020 (w), 991 (m), 947 (w), 909 (w), 888 (w), 856 (w), 835 (w), 802 (w), 784 (w) cm^{-1}. $C_{20}H_{32}N_2O_4S_2 \cdot 1/2H_2O$ (428.61+1/2H_2O): calcd. C 55.31, H 7.81, N 6.29; found C 55.42, H 7.41, N 6.39.

2-Methyl-*N*-[(3*S*,3a*S*,8a*S*)-8a-({(*S*)-*N*-methylphenylsulfonimidoyl}methyl)octahydro-2*H*-cyclohepta[*b*]furan-3-yl]propane-2-sulfonamide (30): To a solution of **29** (200 mg, 0.41 mmol) in THF (20 mL) was added HAl*i*Bu_2 (1.8 mL of 1.12 M in THF, 2.05 mmol) dropwise whilst stirring at 0 °C. The reaction mixture was allowed to stir at 0 °C for 1 h and warmed to room temperature over 6 h. Afterwards pieces of ice were added until hydrogen gas evolution ceased. The mixture was stirred for a further 30 min. The gel-like mixture was suction filtered through filter paper and the residue was washed with hot EtOAc (ca. 50 °C, 300 mL). The filtrate was concentrated in vacuo. Purification by flash chromatography (EtOAc/Et_2O, 6:4) furnished **30** (140 mg, 77%) as a white solid; m.p. 51 °C. $[a]_D$ = +63.6 (c = 1.0, in CH_2Cl_2). R_f = 0.53 (EtOAc/Et_2O, 6:4). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.43 [s, 9 H, $C(CH_3)_3$], 1.36–1.47 (m, 2 H), 1.56 (br. s, H_2O), 1.57–1.70 (m, 3 H), 1.76–1.86 (m, 4 H), 1.96–2.03 (m, 1 H), 2.67 (s, 3 H, NCH_3), 2.98–3.03 (m, 1 H, NCHC*H*), 3.48 (d, J = 14.6 Hz, 1 H, SC*H*H), 3.64 (d, J = 14.6 Hz, 1 H, SCH*H*), 3.66–3.71 (m, 1 H, NCH), 3.72 (dd, J = 3.9, J = 9.1 Hz, 1 H, OC*H*H), 3.97 (dd, J = 5.0, J = 9.1 Hz, 1 H, OCH*H*), 7.01 (d, J = 8.5 Hz, 1 H, NH), 7.56–7.61 (m, 3 H, Ph), 7.88–7.91 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.2 (u), 24.5 (d), 27.0 (u), 29.6 (d), 30.4 (u), 30.6 (u), 38.1 (u), 53.1 (d), 59.6 (u), 62.9 (d), 66.0 (u), 72.5 (u), 86.3 (u), 129.1 (d), 129.3 (d), 133.0 (d), 139.3 (u) ppm. MS (EI, 70 eV): m/z (%) = 443 (1) $[M + 1]^+$, 385 (7), 321 (9), 307 (8), 306 (32), 287 (5), 227 (7), 180 (10), 171 (15), 170 (100), 169 (10), 166 (25), 165 (13), 156 (59), 152 (47), 151 (24), 150 (62), 141 (12), 140 (84), 138 (23), 137 (30), 136 (18), 135 (6), 125 (57), 109 (13), 108 (10), 107 (33), 106 (18), 105 (8), 97 (6), 96 (7), 95 (9), 94 (11), 93 (8), 91 (21), 82 (6), 85 (11), 80 (8), 79 (9), 78 (11), 77 (17), 67 (19), 60 (14), 59 (7), 57.4 (99), 56.6 (11), 56 (22), 55 (6). IR ($CHCl_3$): $\tilde{\nu}$ = 3281 (w), 3057 (w), 2927 (s), 2685 (m), 2806 (w), 1398 (w), 1367 (w), 1306 (s), 1127 (vs), 1086 (s), 1052 (s), 996 (w), 962 (w), 921 (w), 862 (w), 803 (w) cm^{-1}. $C_{21}H_{34}N_2O_4S_2 \cdot 1/2H_2O$ (442.64 + 1/2H_2O): calcd. C 55.85, H 7.81, N 6.20; found C 55.90, H 7.54, N, 6.25.

***N*-[(1*S*,2*R*,3*S*,3a*S*,7a*R*)-2-Hydroxy-3-iodooctahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (35) and (*S*)-Phenylmethyl(phenylsulfinyl)carbamate (36):** To a solution of NaI (669 mg, 4.5 mmol) in CH_3CN (7 mL) was added $ClCO_2Ph$ (0.25 mL, 1.9 mmol) and the resulting mixture was stirred at 70 °C for 1.5 h. Formation of a colourless precipitate was observed. After the mixture was cooled to room temperature, **5** (200 mg, 0.47 mmol) was added. After the mixture was stirred for 2 h, the volatiles were removed in vacuo. Purification by column chromatography (pentane/Et_2O, 9:1) gave **36** (95 mg, 75%) as a viscous oil and **35** (145 mg, 77%) of ≥ 98% *de* as a white solid. For **35**: M.p. 163 °C. $[a]_D$ = –20.8 (c = 1.0, in CH_2Cl_2). R_f = 0.32 (pentane/Et_2O, 9:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.36 (m, 3 H), 1.50–1.60 (m, 2 H), 1.69–1.85 (m, 3 H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.90–1.94 (m, 1 H, NCHC*H*), 2.01–2.08 (m, 1 H, ICHC*H*), 2.91 (d, J = 2.2 Hz, 1 H, OH), 3.78 (dt, J = 3.3, J = 9.6 Hz, 1 H, NCH), 3.92–3.96 (m, 1 H, OCH), 4.26 (d, J = 9.6 Hz, 1 H, NH), 4.53 (t, J = 7.1 Hz, 1 H, ICH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.0 (u), 24.1 (u), 24.3 (d), 25.3 (u), 28.9 (u_2), 38.7 (d), 43.4 (d), 44.9 (d), 60.1 (u), 62.8 (d), 78.7 (d) ppm. MS (CI, CH_4): m/z (%) = 402 (10) $[M + 1]^+$, 328 (81), 282 (60), 264 (45), 247 (27), 202 (16), 154 (100). IR (KBr): $\tilde{\nu}$ = 3731 (w), 3676 (w), 3505 (s), 3285 (s), 3070 (w), 2936 (s), 2861 (s), 2373 (w), 2345 (w), 1606 (m), 1448 (m), 1372 (m), 1311 (s), 1266 (s), 1181 (m), 1120 (s), 1052 (w), 981 (m), 917 (m), 728 (m) cm^{-1}. $C_{13}H_{24}INO_3S$ (401.30): calcd. C 38.91, H 6.03, N 3.49; found C 39.21, H 6.24, N 3.45.

***N*-[(1*S*,2*R*,3*S*,3a*S*,7a*R*)-3-Chloro-2-hydroxyoctahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (40) and 2-Methyl-*N*-[(1*S*,3a*R*,7a*R*)-2-oxooctahydro-1*H*-inden-1-yl]propane-2-sulfonamide (41):** To a solution of **5** (300 mg, 0.70 mmol) in CH_2Cl_2 (10 mL) was added $ClCO_2CH(Cl)Me$ (97 μL, 0.91 mmol) and the mixture was stirred at room temperature for 3 h. Concentration in vacuo and purification by column chromatography (pentane/Et_2O, 2:3) gave **40** (90 mg, 41%) of ≥ 98% *de* and **41** (51 mg, 27%) as white solids. For **40**: M.p. 144 °C. $[a]_D$ = –12.9 (c = 1.0, in CH_2Cl_2). R_f = 0.51 (pentane/Et_2O, 2:3). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.12–1.23 (m, 1 H), 1.33–1.48 (m, 2 H), 1.55–1.64 (m, 2 H), 1.73–1.83 (m, 3 H), 1.85–1.90 (m, 1 H), 1.44 [s, 9 H, $C(CH_3)_3$], 2.17–2.25 (m, 1 H, ClCHC*H*), 2.81 (d, J = 2.5 Hz, 1 H, OH), 3.76 (dt, J = 4.1, J = 9.6 Hz, 1 H, NCH), 4.07–4.10 (m, 1 H, OCH), 4.19 (d, J = 9.6 Hz, 1 H, NH), 4.35 (t, J = 6.5 Hz, 1 H, ClCH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.7 (u), 23.8 (u), 24.0 (u), 24.2 (u), 24.3 (d) 42.3 (d), 42.7 (d) 60.0 (u), 63.9 (d), 64.1 (d), 78.2 (d) ppm. MS (CI, CH_4): m/z (%) = 310 (15) $[M + 1]^+$, 238 (36), 236 (100), 190 (31), 154 (47), 136 (12), 119 (15), 82 (10). IR (KBr): $\tilde{\nu}$ = 3504 (s), 3293 (s), 2930 (s), 2863 (m), 1453 (m), 1371 (w), 1295 (s), 1241 (m), 1212 (w), 1120 (s), 1063 (m), 989 (m), 923 (m), 886 (m), 758 (m) cm^{-1}. $C_{13}H_{24}ClNO_3S$ (309.85): calcd. C 50.39, H 7.81, N 4.52; found C 50.48, H 7.88, N 4.40. For **41**; m.p. 142 °C. $[a]_D$ = +40.5

(c = 1.0, in CH_2Cl_2). R_f = 0.35 (pentane/Et_2O, 2:3). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.11–1.21 (m, 2 H), 1.24–1.32 (m, 1 H), 1.48–1.67 (m, 3 H), 1.73–1.77 (m, 2 H), 1.47 [s, 9 H, $C(CH_3)_3$], 1.96–2.00 (m, 1 H, NCHC*H*), 2.08–2.15 (m, 1 H, COC*H*H), 2.19–2.25 (m, 1 H, CH_2CHCH_2), 2.39 (dd, J = 8.4, J = 19.3 Hz, 1 H, COCH*H*), 3.99 (d, J = 8.8 Hz, 1 H, NH), 4.13 (dd, J = 8.8, J = 12.9 Hz, 1 H, NCH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.6 (u), 24.1 (u), 24.2 (d), 25.0 (u), 29.5 (u), 31.2 (d), 42.7 (d), 43.1 (u), 60.57 (u), 60.63 (d), 215.3 (u) ppm. MS (EI, 70 eV): m/z (%) = 273.1 (5) $[M]^+$, 189 (4), 164 (14), 163 (33), 153 (15), 152 (38), 125 (21), 124 (18), 82 (17), 57 (100), 56 (41). IR (KBr): $\tilde{\nu}$ = 3889 (w), 3314 (s), 2925 (vs), 1752 (s), 1450 (m), 1304 (vs), 1234 (w), 1126 (vs), 1071 (m), 983 (w), 899 (m), 870 (m) cm^{-1}. HRMS: cacld. for $C_{13}H_{23}NO_3S$ $[M]^+$ 273.139866; found 273.139783.

***N*-[(1*S*,2*R*,3*R*,3a*S*,7a*R*)-2-Hydroxy-3-(phenylsulfonyl)octahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (42):** Sulfoximine **5** (107 mg, 0.25 mmol), *m*-$ClC_6H_4CO_3H$ (60 mg, 0.35 mmol) and HCl (0.1 M, 18 μL) were dissolved in THF (2 mL) and the mixture was heated to reflux for 7 h. After the mixture was cooled to room temperature, it was treated with NaOH (1 M, 1.2 mL), and the mixture was extracted into Et_2O (3× 15 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (Et_2O) afforded **42** (86 mg, 83%) as a white solid; m.p. 87 °C. $[\alpha]_D$ = –54.5 (c = 1.0, in CH_2Cl_2). R_f = 0.59 (Et_2O). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.21–1.68 (m, 7 H), 1.83–1.87 (m, 1 H), 1.43 [s, 9 H, $C(CH_3)_3$], 2.19–2.27 (m, 1 H, NCHC*H*CH_2), 2.45–2.52 (m, 1 H, SCHC*H*CH_2), 3.08 (dd, J = 1.7, J = 4.7 Hz, 1 H, SCH), 3.61 (d, J = 2.2 Hz, 1 H, OH), 3.67–3.76 (m, 1 H, NCH), 4.38–4.44 (m, 1 H, OCH), 4.47 (d, J = 9.4 Hz, 1 H, NH), 7.56–7.71 (m, 3 H, Ph), 7.92–7.95 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (u), 23.5 (u), 24.3 (d), 25.1 (u), 30.0 (u), 36.8 (d), 41.5 (d), 60.3 (u), 64.0 (d), 74.3 (d), 78.7 (d), 128.5 (d), 129.4 (d), 134.0 (d), 137.8 (u) ppm. MS (CI, CH_4): m/z (%) = 444 (4) $[M + C_2H_5]^+$, 416 (11), 342 (6), 298 (6), 297 (15), 296 (100), 274 (70), 154 (16), 74 (7). IR (KBr): $\tilde{\nu}$ = 3955 (w), 3482 (s), 3284 (s), 2930 (s), 2863 (m), 1627 (w), 1454 (s), 1298 (vs), 1130 (vs) 1005 (m), 911 (m), 826 (w) cm^{-1}. $C_{19}H_{29}NO_5S_2$ (415.57): calcd. C 54.91, H 7.03, N 3.37; found C 54.73, H 7.32, N 3.17.

2-Methyl-*N*-[(1*S*,3a*S*,7a*R*)-3-(*N*-methylphenylsulfonimidoyl)-3a,4,5,6,7,7a-hexahydro-1*H*-inden-1-yl]propane-2-sulfonamide (43): To a solution of **5** (203 mg, 0.47 mmol) and PPh_3 (128 mg, 0.49 mmol) in THF (10 mL) was added diethyl azodicarboxylate (85 μL, 0.54 mmol) at room temperature. After the mixture was stirred for 16 h at room temperature, the volatiles were removed in vacuo. Purification by chromatography (EtOAc/cyclohexane, 4:1) gave **43** (172 mg, 90%) as a white solid; m.p. 109 °C. $[\alpha]_D$ = –62.2 (c = 1.0, in CH_2Cl_2). R_f = 0.39 (EtOAc/cyclohexane, 4:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.78–0.89 (m, 1 H), 1.02–1.12 (m, 1 H), 1.17–1.28 (m, 1 H), 1.37–1.49 (m, 1 H), 1.53–1.62 (m, 2 H), 1.77–1.84 (m, 1 H), 1.93–2.00 (m, 1 H), 1.42 [s, 9 H, $C(CH_3)_3$], 2.11–2.17 (m, 1 H, NCHC*H*), 2.68–2.72 (m, 1 H, SCHC*H*), 2.70 (s, 3 H, NCH_3), 4.48 (t, J = 10.2 Hz, 1 H, NCH), 4.83 (d, J = 10.2 Hz, 1 H, NH), 6.69 (d, J = 1.1 Hz, 1 H, NCHC*H*C), 7.52–7.67 (m, 3 H, Ph), 7.88–7.92 (m, 2 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5 (u), 24.0 (u), 24.0 (u), 24.4 (d), 29.5 (d), 29.6 (u), 42.3 (d), 48.7 (d), 60.0 (u), 60.8 (d), 129.0 (d), 129.3 (d), 132.9 (d), 138.0 (u), 142.1 (d), 151.0 (u) ppm. MS (EI, 70 eV): m/z (%) = 410 (3) $[M]^+$, 291 (8), 290 (32), 289 (74), 276 (6), 275 (13), 274 (72), 260 (6), 244 (6), 226 (17), 165 (13), 156 (21), 152 (5), 148 (6), 139 (5), 136 (19), 135 (37), 134 (100), 125 (39), 119 (7), 117 (11), 110 (7), 109 (10), 107 (15), 106 (19), 97 (7), 94 (6), 91 (15), 83 (10), 79 (11), 77 (12), 57.4 (82), 56.6 (14), 56 (11). IR (KBr): $\tilde{\nu}$ = 3458 (w), 3263 (w), 3076 (m), 2927 (s), 2807 (m), 2745 (w), 2253 (w), 1611 (w), 1454 (s), 1384 (w), 1309 (vs), 1236 (s), 1123 (vs), 1022 (m), 999 (m), 893 (s), 756 (w) cm^{-1}. MS (CI, CH_4): m/z (%) = 439 (13) $[M + C_2H_5]^+$, 429 (8), 413 (11), 412 (23), 411 (100), 410 (6), 409 (12), 289 (7), 274 (5). HRMS: cacld. for $C_{16}H_{21}N_2OS$ $[M - C_4H_9SO_2]^+$ 289.137461; found 289.137707.

***N*-[(1*R*,3a*R*,7a*R*)-3a,4,5,6,7,7a-Hexahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (44):** $HgCl_2$ (1.0 g) was dissolved in H_2O (50 mL) and small pieces of aluminum (1.5 g) were added. After the mixture was stirred for 2 min, it was filtered and the residue suspended in THF/H_2O/AcOH (2:1:1, 40 mL). Then the slurry was added to a solution of **5** (200 mg, 0.47 mmol) in THF (10 mL). After the mixture was stirred for 3 h at room temperature, it was filtered and the filtrate was concentrated in vacuo. Purification by column chromatography (pentane/Et_2O, 4:1) gave **44** (97 mg, 80%) as a viscous colourless oil. $[\alpha]_D$ = –90.9 (c = 1.0, in CH_2Cl_2). R_f = 0.26 (pentane/Et_2O, 4:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.03–1.12 (m, 1 H), 1.16–1.45 (m, 2 H), 1.47–1.63 (m, 3 H), 1.67–1.85 (m, 2 H), 1.41 [s, 9 H, $C(CH_3)_3$], 1.93–1.99 (m, 1 H, NCHC*H*CH_2), 2.58–2.65 (m, 1 H, CH=CHC*H*CH_2), 4.06 (d, J = 9.9 Hz, 1 H, NH), 4.17–4.23 (m, 1 H, NCH), 5.75 (dt, J = 1.6, J = 5.8 Hz, 1 H, NCHC*H*=CH), 5.94 (dt, J = 2.2, J = 5.8 Hz, 1 H, NCHCH=C*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5 (u), 23.7 (u), 24.5 (d), 24.9 (u), 29.5 (u), 42.2 (d), 46.6 (d), 59.7 (u), 63.4 (d), 131.7 (d), 139.9 (d) ppm. MS (EI, 70 eV): m/z (%) = 257 (3) $[M]^+$, 200 (7), 137 (93), 136 (100), 120 (44), 108 (16), 94 (19), 82 (15), 57 (92). IR (KBr): $\tilde{\nu}$ = 3273 (s), 3052 (w), 2926 (s), 2857 (s), 2256 (w), 1447 (m), 1212 (w), 1126 (s), 1076 (m), 1018 (w), 977 (w), 914 (s), 732 (s) cm^{-1}. HMRS: calcd. for $C_{13}H_{23}NO_2S$ $[M]^+$ 257.144952; found 257.144917.

***N*-[(1*S*,2*S*,3a*R*,7a*R*)-2-Hydroxyoctahydro-1*H*-inden-1-yl]-2-methylpropane-2-sulfonamide (45):** To a solution of **5** (80 mg, 0.19 mmol) in THF (5 mL) was added Raney nickel (50%-slurry in H_2O, 880 mg, 7.47 mmol) and the mixture was stirred at room temperature for 10 h. Then mixture was filtered through celite and the filtrate was concentrated in vacuo. Purification by column chromatography (pentane/Et_2O, 1:2) yielded **45** (47 mg, 92%) as a white solid; m.p. 121 °C. $[\alpha]_D$ = –82.4 (c = 1.0, in CH_2Cl_2). R_f = 0.48 (pentane/Et_2O, 1:4). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.17–1.39 (m, 2 H), 1.48–1.73 (m, 6 H), 1.44 [s, 9 H, $C(CH_3)_3$], 1.79–1.85 (m, 1 H, NCHC*H*CH_2), 1.89–1.97 (m, 1 H, CH_2CHCH_2), 2.15–2.23 (m, 2 H, OCHCH_2), 3.40 (d, J = 1.9 Hz, 1 H, OH), 3.55 (dt, J = 5.0, J = 9.9 Hz, 1 H, NCH), 4.10 (ddd, J = 1.7, J = 5.0, J = 9.2 Hz, 1 H, OCH), 4.28 (d, J = 9.9 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (u), 24.3 (d), 24.7 (u), 24.9 (u), 29.6 (u), 36.3 (d), 37.9 (u), 44.3 (d), 60.1 (u), 66.3 (d), 80.4 (d) ppm. MS (EI, 70 eV): m/z (%) = 276 (2) $[M + 1]^+$, 155 (27), 154 (100), 138 (9), 137 (8), 136 (17), 111 (12), 110 (89), 109 (20), 95 (15), 94 (6), 93 (11), 82 (8), 81 (7), 79 (6), 72 (18), 69 (6), 67 (13), 59 (6), 58 (10), 57 (98), 56 (31), 55 (18), 54 (6), 53 (5). IR ($CHCl_3$): $\tilde{\nu}$ = 3501 (s), 3272 (s), 2926 (vs), 28.59 (vs), 2663 (w), 1728 (w), 1586 (w), 1453 (s), 1396 (w), 1366 (w), 1297 (s), 1216 (m), 1121 (s), 1000 (m), 917 (m), 892 (m), 833 (w), 757 (vs) cm^{-1}. HRMS: calcd. for $C_9H_{16}NO$ $[M - C_4H_9SO_2]^+$ 154.123189; found 154.123076.

(1*S*,2*R*,3*R*,3a*S*,7a*R*)-1-Amino-3-[(*S*)-*N*-methylphenylsulfonimidoyl]octahydro-1*H*-inden-2-ol (47): To a solution of **5** (300 mg, 0.70 mmol) and anisole (0.1 mL, 0.70 mmol) in CH_2Cl_2 (30 mL) was added CF_3SO_3H (60 mL, 0.12 M solution in CH_2Cl_2) at 0 °C. The mixture was warmed to room temperature over 2 h and its pH value was adjusted to 8 by the addition of saturated aqueous $NaHCO_3$. The aqueous phase was extracted into CH_2Cl_2 (3× 100 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography

(Et_2O/MeOH, 9:1) gave **47**·1/2CF_3SO_3H (202 mg, 94%) as a white solid; m.p. 51 °C. $[\alpha]_D$ = +48.9 (c = 1.0, in CH_2Cl_2). R_f = 0.33 (Et_2O/MeOH, 1:4). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.93–1.08 (m, 3 H), 1.16–1.30 (m, 1 H), 1.35–1.54 (m, 3 H), 1.71–1.80 (m, 2 H), 2.11–2.18 (m, 1 H, SCHC*H*CH_2), 2.63 (s, 3 H, NCH_3), 2.86 (br. s, 2 H, NH_2), 3.04–3.08 (m, 1 H, SCH), 3.11–3.15 (m, 1 H, NCH), 4.31 (t, J = 7.7 Hz, 1 H, OCH), 7.55–7.65 (m, 3 H, Ph), 7.85–7.89 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 (u), 23.6 (u), 24.6 (u), 29.2 (d), 30.6 (u), 35.6 (d), 41.3 (d), 57.9 (d), 73.7 (d), 78.8 (d), 129.5 (d), 129.6 (d), 133.0 (d), 136.8 (u) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –78.3 (s) ppm. MS (EI, 70 eV): m/z (%) = 309 (17) $[M + 1]^+$, 156 (12), 155 (11), 154 (83), 153 (55), 137 (16), 13 (80), 125 (89), 110 (39), 110 (17), 109 (18), 108 (15), 107 (25), 106 (22), 97 (40), 95 (14), 94 (13), 93 (16), 91 (17), 82 (13), 81 (15), 80 (11), 79 (15), 78 (18), 77 (55), 67 (24), 56 (100), 55 (13), 53 (15), 51 (18), 51 (14). IR ($CHCl_3$): $\tilde{\nu}$ = 3062 (w), 3011 (w), 2928 (s), 28.58 (m), 2804 (w), 1589 (w), 1448 (m), 1348 (w), 1236 (s), 1145 (m), 1107 (m), 1079 (m), 993 (w), 869 (w), 827 (w), 795 (w), 754 (vs) cm^{-1}. $C_{16}H_{24}N_2O_2S$·1/2 (CF_3SO_3H) (383.48): calcd. C 51.68, H 6.44, N 7.31; found C 51.88, H 6.40, N 7.24. HRMS: calcd. for $C_{16}H_{25}N_2O_2S$ $[M + H]^+$ 309.163676; found 309.163596.

***tert*-Butyl 3-[3-(Benzyloxy)phenyl]propanoate (50):** To a solution of HN*i*Pr_2 (2.0 mL, 14.3 mmol) in THF (15 mL) at 0 °C was added *n*BuLi (6.86 mL, 1.6 M in THF, 10.98 mmol) and the mixture was stirred for 15 min. After the mixture was cooled to –78 °C, *tert*-butyl acetate (1.48 mL, 10.98 mmol) was added dropwise and the mixture was warmed to –30 °C over 1 h and then cooled to –78 °C. Then a solution of **49** (2.49 g, 9.0 mmol) in THF (8 mL) was added. After the mixture was stirred for 1 h, saturated aqueous NH_4Cl was added and the mixture was extracted into Et_2O (4 × 100 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash column chromatography (pentane/Et_2O, increasing polarity from 19:1 to 1:1) furnished **50** (2.46 g, 88%) as a white solid; m.p. 47 °C. R_f = 0.53 (pentane/Et_2O, 9:1). ^1H NMR (400 MHz, $CDCl_3$): δ = 1.42 [s, 9 H, $C(CH_3)_3$], 2.53 (t, J = 7.9 Hz, 2 H, COC*H*$_2$), 2.88 (t, J = 7.9 Hz, 2 H, $COCH_2CH_2$), 5.04 (s, 2 H, $PhCH_2O$), 7.17–7.21 (m, 3 H, Ph), 7.30–7.34 (m, 1 H, Ph), 7.36–7.44 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.1 (d), 31.1 (u), 36.9 (u), 69.8 (u), 80.2 (u), 112.2 (d), 114.8 (d), 120.8 (d), 127.3 (d), 127.7 (d), 128.4 (d), 129.2 (d), 136.9 (u), 142.3 (u), 158.7 (u), 172.0 (u) ppm. MS (EI, 70 eV): m/z (%) = 312 (15) $[M]^+$, 256 (19), 239 (8), 196 (7), 165 (7), 123 (7), 92 (9), 91 (100), 57 (8). IR (KBr): $\tilde{\nu}$ = 2969 (m), 2934 (m), 2881 (m), 1724 (vs), 1608 (s), 1580 (s), 1486 (s), 1452 (s), 1371 (s), 1305 (s), 1281 (s), 1228 (m), 1149 (vs), 1026 (s), 933 (w), 905 (m), 850 (m), 786 (m), 752 (s) cm^{-1}. $C_{20}H_{24}O_3$ (312.40): calcd. C 76.89, H 7.74; found C 76.99, H 7.48.

3-[3-(Benzyloxy)phenyl]propanoic Acid (51): To a solution of **50** (4.37 g, 14 mmol) in CH_2Cl_2 (90 mL) was added CF_3CO_2H (10.8 mL, 140 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 10 h. The volatiles were removed in vacuo and the residue dissolved in EtOAc (100 mL). The mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (EtOAc/cyclohexane, 3:2) furnished **51** (2.98 g, 83%) as a white solid; m.p. 74–76 °C. R_f = 0.35 (EtOAc/cyclohexane, 2:3). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.61 (t, J = 8.0 Hz, 2 H, COC*H*$_2$), 2.89 (t, J = 8.0 Hz, 2 H, $COCH_2CH_2$), 4.98 (s, 2 H, $PhCH_2O$), 6.76–6.81 (m, 3 H, Ph), 7.29–7.40 (m, 6 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.9 (u), 36.1 (u), 69.8 (u), 112.3 (d), 114.8 (d), 120.7 (d), 127.3 (d), 127.7 (d), 128.3 (d), 129.3 (d), 136.8 (u), 141.9 (u), 158.7 (u), 178.6 (u) ppm. MS (EI, 70 eV): m/z (%) = 256 (25) $[M]^+$, 91 (100), 65 (7). IR (KBr): $\tilde{\nu}$ = 3032 (w), 2973 (w), 2936 (w), 1703 (vs), 1594 (m), 1493 (w), 1444 (m), 1381 (w), 1315 (m), 1256 (s), 1165 (m), 1082 (w), 1017 (m), 915 (w), 853 (w), 793 (m) cm^{-1}. $C_{16}H_{16}O_3$ (256.30): calcd. C 74.98, H 6.29; found C 75.24, H 5.99.

(4*S*)-4-Benzyl-3-[3-{3-(benzyloxy)phenyl}propanoyl]oxazolidin-2-one (53): Carboxylic acid **51** (1.56 g, 6.09 mmol) was dissolved in THF (30 mL) and the solution was cooled to –30 °C. NEt_3 (2.1 mL, 15.2 mmol) and *t*BuC(O)Cl (0.75 mL, 6.09 mmol) were added and the mixture was stirred at –30 °C for 2 h. Then LiCl (284 mg, 6.7 mmol) and **52** (1.03 g, 5.79 mmol) were added at once and the mixture was allowed to stir for 1 d whereby the temperature of the mixture slowly rose to room temperature. The mixture was diluted with Et_2O (200 mL) and washed successively with saturated aqueous NH_4Cl, NaOH (1.0 M) and brine. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (EtOAc/cyclohexane, 2:3) afforded **53** (1.97 g, 82%) as a colourless oil. $[\alpha]_D$ = +53.6 (c = 1.0, in CH_2Cl_2). R_f = 0.51 (EtOAc/cyclohexane, 2:3). ^1H NMR (400 MHz, $CDCl_3$): δ = 2.73 (dd, J = 9.4, J = 13.5 Hz, 1 H, OC*H*HCH), 2.93–3.04 (m, 2 H, $COCH_2CH_2$), 3.17–3.34 (m, 3 H, OCH*H*CH, COC*H*$_2$), 4.10 (d, J = 5.2 Hz, 2 H, $PhCH_2CH$), 4.60 (m, 1 H, NCH), 5.00 (s, 2 H, $PhCH_2O$), 6.79–6.92 (m, 3 H, Ph), 7.12–7.43 (m, 11 H, Ph) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.2 (u), 36.9 (u), 37.7 (u), 54.9 (d), 66.0 (u), 69.7 (u), 112.3 (d), 115.0 (d), 120.9 (d), 127.0 (d), 127.3 (d), 127.7 (d), 128.3 (d), 128.7 (d), 129.2 (d), 129.3 (d), 135.0 (u), 136.8 (u), 141.9 (u), 153.1 (u), 158.7 (u), 172.0 (u) ppm. MS (EI, 70 eV): m/z (%) = 416 (15) $[M + 1]^+$, 415 (56), 324 (11), 239 (7), 238 (23), 147 (7), 92 (11), 90 (100), 65 (6). IR ($CHCl_3$): $\tilde{\nu}$ = 3062 (w), 3028 (w), 2920 (w), 2868 (w), 1781 (vs), 1700 (s), 1586 (m), 1490 (m), 1450 (m), 1385 (s), 1353 (m), 1256 (s), 1214 (s), 1159 (m), 1109 (m), 1077 (w), 1046 (m), 920 (w), 875 (w), 847 (w), 755 (vs) cm^{-1}. HRMS: calcd. for $C_{26}H_{25}NO_4$ $[M]^+$ 415.178358; found 415.178285.

***tert*-Butyl (3*R*)-4-[(*S*)-4-Benzyl-2-oxooxazolidin-3-yl]-3-[3-(benzyloxy)benzyl]-4-oxobutanoate (54):** To a solution of **53** (1.38 g, 3.33 mmol) in THF (40 mL) at –65 °C was added $NaN(SiMe_3)_2$ (3.66 mL of 1.0 M in THF, 3.66 mmol) dropwise over 10 min. After the mixture was stirred for 45 min at –65 °C, *tert*-butyl-2-bromoacetate (0.63 mL, 4.33 mmol) was added dropwise over 12 min. After the mixture was stirred for 3 h at –70 °C, saturated aqueous NH_4Cl was added and the mixture was stirred for 12 h. The volatiles were removed in vacuo and the remaining aqueous phase was extracted into EtOAc (3 × 250 mL). The combined organic phases were successively washed with HCl (1.0 M), saturated aqueous $NaHCO_3$ and brine. The organic phase was dried ($MgSO_4$) and concentrated in vacuo. Purification by flash column chromatography (EtOAc/cyclohexane, increasing polarity from 1:9 to 2:3) furnished **54** (1.26 g, 71%) of ≥ 98% *de* as a colourless oil. $[\alpha]_D$ = +94.9 (c = 1.0, in CH_2Cl_2). R_f = 0.59 (EtOAc/cyclohexane, 2:3). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 2.36 (dd, J = 4.2, J = 17.0 Hz, 1 H, COC*H*H), 2.60 (dd, J = 9.2, J = 13.1 Hz, 1 H, CC*H*HCHCO), 2.73 (dd, J = 9.9, J = 13.4 Hz, 1 H, OC*H*HCH), 2.82 (dd, J = 10.9, J = 17.0 Hz, 1 H, COCH*H*), 2.99 (dd, J = 6.2, J = 13.1 Hz, 1 H, CCH*H*CHCO), 3.30 (dd, J = 3.2, J = 13.4 Hz, 1 H, OCH*H*CH), 3.91 (m, 1 H, PhC*H*HCHN), 4.06 (dd, J = 2.5, J = 8.9 Hz, 1 H, PhCH*H*CHN), 4.42–4.56 (m, 2 H, NCH, NCOCH), 5.05 (s, 2 H, $PhCH_2O$), 6.80–6.93 (m, 3 H, Ph), 7.16–7.44 (m, 11 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1 (d), 36.7 (u), 37.6 (u), 38.3 (u), 41.2 (d), 55.6 (d), 65.9 (u), 69.9 (u), 80.8 (u), 113.3 (d), 115.6 (d), 121.9 (d), 127.2 (d), 127.6 (dH), 127.9 (d), 128.5 (d), 128.9 (d), 129.45 (d), 129.53 (d), 135.7 (u), 137.0 (u), 139.6 (u), 153.0 (u), 158.8 (u), 171.2 (u), 175.3 (u) ppm. MS (EI, 70 eV): m/z (%) = 529 (3) $[M]^+$, 474 (10), 473 (31), 456 (8),

382 (7), 187 (6), 178 (32), 117 (9), 92 (9), 91 (100), 57 (13). IR ($CHCl_3$): $\tilde{\nu}$ = 2928 (w), 1780 (vs), 1723 (s), 1700 (s), 1597 (m), 1488 (w), 1451 (m), 1389 (m), 1356 (m), 1289 (w), 1255 (m), 1217 (m), 1154 (s), 1110 (w), 1022 (m), 955 (w), 843 (w), 757 (vs) cm^{-1}. $C_{32}H_{35}NO_6$ (529.62): calcd. C 72.57, H 6.66, N 2.64; found C 72.80, H 6.63, N 2.57.

(3*R*)-2-[3-(Benzyloxy)benzyl]-4-*tert*-butoxy-4-oxobutanoic Acid (48): To a solution of **54** (2.83 g, 5.34 mmol) in THF/H_2O (4:1, 12.5 mL) at 0 °C were added H_2O_2 (1.84 mL, 35% solution in H_2O, 21.4 mmol) and LiOH (205 mg, 8.55 mmol) and the resulting mixture was stirred for 3 h. The mixture was diluted with H_2O and the volatiles were removed in vacuo. The mixture was cooled to 0 °C and EtOAc (50 mL) was added. The pH of the mixture was adjusted to 4–5 upon addition of 10% aqueous citric acid under intensive stirring. The organic phase was separated and the aqueous phase was extracted into EtOAc (3× 150 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography (pentane/Et_2O/AcOH, 1:4:0.1) gave **48** (1.92 g, 97%) as a colourless oil and **52** (843 mg, 89%) (R_f = 0.15, pentane/Et_2O/AcOH, 1:4:0.1) as a white solid. For **48**: $[\alpha]_D$ = +7.9 (c = 1.0, in CH_2Cl_2). R_f = 0.76 (pentane/Et_2O/AcOH, 1:4:0.1). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.41 [s, 9 H, $C(CH_3)_3$], 2.33 (dd, J = 4.5, J = 16.8 Hz, 1 H, HOOCCHC*H*H), 2.54 (dd, J = 8.7, J = 16.8 Hz, 1 H, HOOCCHCH*H*), 2.71 (dd, J = 10.5, J = 15.2 Hz, 1 H, CC*H*HCHCO), 3.03–3.13 (m, 2 H, CCH*H*CHCO, HOOCC*H*), 5.03 (s, 2 H, $PhCH_2O$), 6.75–6.86 (m, 3 H, Ph), 7.17–7.22 (m, 1 H, Ph), 7.30–7.44 (m, 5 H, Ph), 11.35 (br. s, 1 H, COO*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.1 (d), 36.1 (u), 37.5 (u), 43.2 (d), 70.0 (u), 81.2 (u), 113.1 (d), 115.7 (d), 121.7 (d), 127.5 (d), 128.0 (d), 128.6 (d), 129.6 (d), 136.9 (u), 139.7 (u), 158.9 (u), 170.9 (u), 180.6 (u) ppm. MS (EI, 70 eV): m/z (%) = 370 (8) $[M]^+$, 314 (29), 205.0 (11), 91 (100), 57 (11). IR (capillary): $\tilde{\nu}$ = 2976 (s), 2931 (m), 2874 (m), 1725 (vs), 1593 (m), 1489 (m), 1450 (m), 1371 (m), 1259 (s), 1155 (vs), 1030 (m), 951 (w), 847 (w), 781 (w), 740 (m) cm^{-1}. $C_{22}H_{26}O_5$ (370.44): calcd. C 71.33, H 7.07; found C 71.38, H 7.08.

***tert*-Butyl (3*R*)-3-[3-(Benzyloxy)benzyl]-4-[(1*S*,2*R*,3*R*,3a*S*,7a*R*)-2-hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydro-1*H*-inden-1-ylamino]-4-oxobutanoate (56):** To a mixture of **47** (591 mg, 1.92 mmol) and **48** (591 mg, 1.60 mmol) in DMF (20 mL) at 0 °C was added **55** (708 mg, 1.60 mmol) followed by Et*N*iPr_2 (0.74 mL, 4.48 mmol). The mixture was warmed to room temperature and stirred for 5 h. The mixture was quenched with 10% aqueous citric acid and extracted into EtOAc (3× 100 mL). The combined organic phases were successively washed with H_2O, aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography ($CHCl_3$/Et_2O, 1:1) furnished **56** (1.0 g, 95%) as a white solid; m.p. 71 °C. $[\alpha]_D$ = +13.8 (c = 1.0, in MeOH). R_f = 0.51 ($CHCl_3$/Et_2O, 1:1). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98–1.52 (m, 8 H), 1.40 [s, 9 H, $C(CH_3)_3$], 1.92–2.00 (m, 1 H, NCHC*H*CH_2), 2.17–2.27 (m, 1 H, SCHC*H*CH_2), 2.36 (dd, J = 4.0, J = 17.1 Hz, 1 H, COCHC*H*HCO), 2.61 (dd, J = 9.9, J = 17.1 Hz, 1 H, COCHCH*H*CO), 2.63 (s, 3 H, NCH_3), 2.69 (dd, J = 7.2, J = 13.0 Hz, 1 H, $COCH_2$CHC*H*H), 2.77–2.87 (m, 1 H, NCOCH), 2.97 (dd, J = 7.4, J = 13.0 Hz, 1 H, $COCH_2$CHCH*H*), 3.05–3.08 (m, 1 H, SCH), 4.11–4.19 (m, 1 H, NCH), 4.30 (s, 1 H, OH), 4.35–4.40 (m, 1 H, OCH), 5.08 (s, 2 H, $PhCH_2O$), 5.79 (d, J = 6.4 Hz, 1 H, NH), 6.81–6.89 (m, 3 H, Ph), 7.22–7.59 (m, 9 H, Ph), 7.81–7.85 (m, 2 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.7 (u), 23.6 (u), 24.8 (u), 28.0 (d), 29.4 (d), 30.1 (u), 36.7 (d), 37.3 (u), 38.1 (u), 40.1 (d), 44.5 (d), 57.9 (d), 70.0 (u), 74.3 (d), 77.9 (d), 81.0 (u), 113.1 (d), 115.7 (d), 121.8 (d), 127.6 (d), 127.9 (d), 128.6 (d), 129.4 (d), 129.7 (d), 132.9 (d), 137.1 (u), 140.5 (u), 159.0 (u), 171.7 (u), 175.9 (u) ppm. MS (EI, 70 eV): m/z (%) = 660 (4) $[M]^+$, 449 (14), 315 (15), 314 (85), 279 (10), 154 (26), 152 (18), 137 (19), 136 (98), 135 (16), 125 (38), 107 (45), 97 (10), 91 (100), 79 (16), 78 (15), 58 (24), 57 (29), 55 (18), 52 (12). IR (KBr): $\tilde{\nu}$ = 3331 (m), 3249 (w), 3061 (m), 2932 (vs), 2863 (m), 2343 (w), 2330 (w), 2249 (w), 1727 (vs), 1643 (m), 1588 (w), 1544 (m), 1491 (w), 1450 (m), 1369 (m), 1316 (w), 1254 (s), 1151 (s), 1083 (w), 1028 (m), 953 (w), 911 (w), 846 (w), 795 (w), 735 (s) cm^{-1}. $C_{38}H_{48}N_2O_6S$ (570.74): calcd. C 69.06, H 7.32, N 4.24; found C 68.96, H 7.05, N 4.15.

(2*R*)-N^4-Benzyloxy-2-[3-(benzyloxy)benzyl]-N^1-[(1*S*,2*R*,3*R*,3a*S*,7a*R*)-2-hydroxy-3-{(*S*)-*N*-methylphenylsulfonimidoyl}octahydro-1*H*-inden-1-yl]succinamide (46): To a solution of **56** (208 mg, 0.31 mmol) in CH_2Cl_2 (6 mL) and H_2O (0.55 mL) was added CF_3CO_2H (5.5 mL, 71 mmol) dropwise and the resulting mixture was stirred at room temperature for 3 h. The mixture was concentrated to half of its original volume in vacuo. Then the residue was dried by coevaporation with toluene (3× 15 mL). The resulting crude acid, $PhCH_2ONH_3Cl$ (99 mg, 0.62 mmol) and **57** (100 mg, 0.31 mmol) were dissolved in DMF (10 mL) and the solution was cooled to 0 °C followed by the addition of Et*N*iPr_2 (0.26 mL, 1.55 mmol). The mixture was stirred at 0 °C for 15 min and then warmed to room temperature. After the mixture was stirred for 2 h, it was poured into a mixture of EtOAc (20 mL) and 5% aqueous citric acid (20 mL). The mixture was extracted into EtOAc (3× 25 mL). The combined organic phases were successively washed with 5% aqueous citric acid, H_2O, saturated aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated in vacuo. Purification by HPLC (Kromasil Si 100, 30 mm, EtOAc, 254 nm + RI, 25 mL/min) afforded **46** (188 mg, 85%) as a white solid; m.p. 84 °C. $[\alpha]_D$ = +16.4 (c = 1.0, in CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$, room temperature): δ = 0.85–1.46 (m, 8 H), 1.81–1.84 (m, 1 H, NCHC*H*CH_2), 2.07–2.15 (m, 2 H, NCOC*H*$_2$) 2.26–2.32 (m, 1 H, SCHC*H*CH_2), 2.50 (s, 3 H, NCH_3), 2.63 (dd, J = 6.9, J = 13.5 Hz, 1 H, $NCOCH_2$CHC*H*H), 2.81–2.86 (m, 1 H, $NCOCH_2$CHCH*H*), 2.93–2.98 (m, 1 H, NCOCH), 3.01 (dd, J = 6.0, J = 9.3 Hz, 1 H, SCH), 4.12 (dt, J = 6.0, J = 11.0 Hz, 1 H, NCH), 4.33 (t, J = 6.0 Hz, 1 H, OCH), 4.72 (s), 4.75 (s, 2 H, $NOCH_2Ph$), 4.95 (s, 2 H, $COCH_2Ph$), 6.51 (br. s, 1 H, CHN*H*), 6.70–6.77 (m, 3 H, Ph), 7.10–7.51 (m, 14 H, Ph), 7.72–7.77 (m, 2 H, Ph), 9.01 (br. s), 9.20 (br. s), (1 H, ON*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, room temperature): δ = 21.1 (u, CH_2), 23.8 (u, CH_2), 24.7 (u, CH_2), 29.5 (d, CH_3), 29.9 (u, CH_2), 33.6 (u, CH_2), 35.2 (u, CH_2), 36.6 (d, CH), 38.7 (u, CH_2), 40.1 (d, CH), 43.5 (d, CH), 45.0 (d, CH), 57.6 (d, CH), 69.9 (u, CH_2), 74.0 (d, CH), 76.8 (d, CH), 78.2, 79.3 (u, CH_2), 113.1 (d, CH), 115.7 (d, CH), 121.8 (d, CH), 127.6 (d, CH), 127.8 (d, CH), 128.5 (d, CH), 129.0 (d, CH), 129.4 (d, CH), 129.6 (d, CH), 132.9 (d, CH), 135.4 (u, C), 136.7 (u, C), 137.0 (u, C), 140.1 (u, C), 140.7 (u, C), 158.8 (u, C), 169.1 (u, C), 175.2, 175.9 (u, C) ppm. ^1H NMR (400 MHz, $CDCl_3$, 55 °C): δ = 0.89–1.45 (m, 8 H), 1.91–1.87 (m, 1 H, NCHC*H*CH_2), 2.12–2.41 (m, 3 H, SCHC*H*CH_2, NCOC*H*$_2$), 2.51 (s, 3 H, NCH_3), 2.65 (dd, J = 6.9, J = 13.5 Hz, 1 H, $NCOCH_2$CHC*H*H), 2.83–2.88 (m, 1 H, $NCOCH_2$CHCH*H*), 2.93–2.95 (m, 1 H, NCOCH), 3.01 (dd, J = 5.8, J = 9.3 Hz, 1 H, SCH), 4.09 (dt, J = 5.8, J = 11.0 Hz, 1 H, NCH), 4.30 (t, J = 5.8 Hz, 1 H, OCH), 4.74 (s, 2 H, $NOCH_2Ph$), 4.96 (s, 2 H, $COCH_2Ph$), 6.23 (br. s, 1 H, CHN*H*), 6.71–6.77 (m, 3 H, Ph), 7.10–7.49 (m, 14 H, Ph), 7.71–7.74 (m, 2 H, Ph), 8.84 (br. s, 1 H, ON*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, 55 °C): δ = 21.1 (u, CH_2), 23.9 (u, CH_2), 24.6 (u, CH_2), 29.3 (d, CH_3), 29.8 (u, CH_2), 35.0 (u, CH_2), 36.6 (d, CH), 38.7 (u, CH_2), 40.2 (d, CH), 44.9 (d, CH), 57.9 (d, CH), 70.1 (u, CH_2), 74.2 (d, CH), 76.8 (d, CH), 78.4 (u, CH_2), 113.2 (d, CH), 115.9 (d, CH), 121.8 (d, CH), 127.4 (d, CH), 127.7

(d, CH), 128.4 (d, CH), 129.0 (d, CH), 129.3 (d, CH), 129.6 (d, CH), 132.7 (d, CH), 137.2 (u, C), 137.3 (u, C), 140.3 (u, C), 159.0 (u, C), 175.2 (u, C) ppm. MS (EI, 70 eV): *m/z* (%) = 709 (1) $[M]^+$, 156 (6), 136 (13), 125 (14), 108 (11), 107 (20), 106 (13), 105 (10), 97 (5), 91 (100), 79 (10), 78 (10), 77 (22), 65 (10), 52 (13). MS (CI, isobutane): *m/z* (%) = 710 (1) $[M + 1]^+$, 309 (10), 181 (5), 156 (24), 136 (5), 125 (41), 108 (10), 107 (68), 105 (7), 93 (10), 92 (8), 91 (100), 79 (39), 77 (6). IR ($CHCl_3$): $\tilde{\nu}$ = 3552 (w), 3276 (m), 3068 (w), 3012 (w), 2927 (s), 2860 (m), 2805 (w), 1652 (s), 1588 (w), 1548 (w), 1492 (w), 1448 (m), 1384 (w), 1240 (s), 1153 (m), 1108 (w), 1080 (w), 1030 (w), 908 (m), 877 (m), 755 (vs) cm^{-1}. HRMS (FTMS-ESI): calcd. for $C_{41}H_{47}N_3O_6S$ $[M + H]^+$ 710.32583; found 710.32585.

Acknowledgments

This work was supported by the Deutsche Forschungsgemeinschaft (DFG) (SFB 380 and GK 440). We thank Cornelia Vermeeren for the HPLC separations and Dr. Wolfgang Bettray for the MS analyses.

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Received: June 14, 2011
Published Online: August 24, 2011

