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The use of two optically active *N*-sulfinyl α-imino esters in the stereoselective aza-Diels–Alder reaction

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ABSTRACT

Diastereoselective aza-Diels–Alder (aza-DA) reactions of ethyl (*S*)-*N*-(*tert*-butanesulfinyl)iminoacetate (**2a**) and ethyl (*S*)-*N*-(*p*-toluenesulfinyl)iminoacetate (**2b**) with different dienes including activated, non-activated, cyclic, and acyclic dienes in the presence of Lewis acids are described. Reactions with **2a** were found to be more selective. Reactions of unactivated dienes (acyclic and cyclic) with stoichiometric amounts of TMSOTf as Lewis acid afforded the aza-DA adducts in modest yields and in diastereoselectivities up to 99%. A strong preference for *Re*-approach was observed for **2a**. Cyclic dienes gave the *exo* adducts as major products. For the aza-DA reaction with activated Danishefsky type dienes poor diastereoselectivities were observed. In these cases, the best results were obtained using stoichiometric amounts of $BF_3 \cdot Et_2O$ as Lewis acid (up to 69% de, 76% yield). The absolute configurations of six of the addition products were established by chemical correlation with known compounds. Acidic cleavage of the sulfinyl group occurred without racemization to optically active non-proteinogenic α-amino acid ethyl esters.

1. Introduction

The aza-Diels–Alder (aza-DA) reaction between dienes and imines is a powerful synthetic method for preparation of highly functionalized six-membered aza-cycles such as piperidines and tetrahydroquinolines.[1] In general, this reaction requires a highly activated (electron-rich) diene like the Danishefsky's diene and an electron-poor imine. The aza-DA reaction is usually slow due to the low reactivity of the imine functionality. The reactivity can often be increased by incorporation of an electron-withdrawing substituent on the imine and by addition of a Lewis acid to the reaction system. Several asymmetric protocols have appeared, involving either a diastereoselective aza-DA reaction applying chiral imines[2] or more recently, a catalytic enantioselective reaction.[3]

In 2000, Jørgensen et al. reported excellent results for the catalytic enantioselective aza-DA reaction by reacting the double activated *N*-tosyl α-imino ester **1** (see Fig. 1) with different dienes including activated, non-activated, cyclic, and acyclic dienes in the presence of chiral BINAP–copper(I) complexes.[3e] The described reaction provided an effective route to optically active non-proteinogenic α-amino acids of the piperidine type. A major drawback with this method is the removal of the *p*-toluenesulfonyl group (*p*-Ts), which requires harsh conditions.[4]

The chiral non-racemic *N*-sulfinylimino esters **2**, which are the sulfinyl analogs of **1** (see Fig. 1), have been described in the literature as 'chiral glycine cation equivalents' for the asymmetric synthesis of α-amino acids with excellent diastereoselectivities.[5] The chiral and electron-withdrawing sulfinyl group has been shown to activate the C=N bond for nucleophilic addition with high and predictable asymmetric induction, and is easily removed from the product.[6]

Since the known aza-DA chemistry of chiral *N*-sulfinyl imines (sulfinimines) as dienophiles was limited to only one report describing the reaction of 2-aryl substituted *N*-sulfinyl imines to the highly activated (electron-rich) Rawal diene,[7] an investigation of the aza-DA reaction of **2a** was initiated. We recently communicated that **2a** reacts with both activated and non-activated dienes in the presence of $BF_3 \cdot OEt_2$.[8] The aza-DA adducts were obtained in

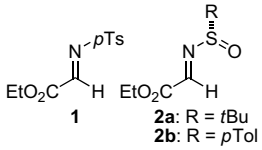

Figure 1. Activated dienophiles for the aza-Diels–Alder reaction.

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modest yields and in diastereoselectivities ranging from poor for the activated Danishefsky type dienes to excellent for the unactivated acyclic dienes (up to 99% de). Here, we present a more detailed report on this reaction with the α-imino ester dienophiles **2a** and **2b**. Assignment of the absolute configuration of the aza-DA adducts, a model explaining the stereochemical outcome of the reaction, and a study of the by-products in the reaction are addressed. Finally, hydrolysis of the aza-DA adducts for removal of the chiral sulfinyl auxiliary to afford optically active non-proteinogenic α-amino acid ethyl esters is presented.

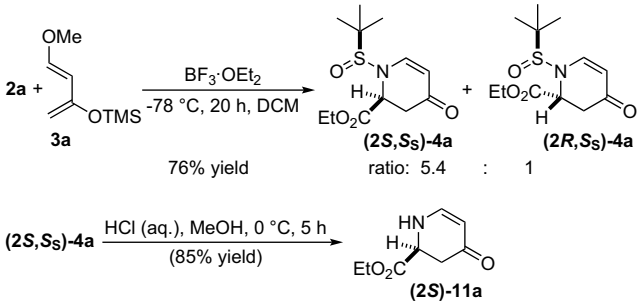
2. Results and discussion

2.1. The aza-Diels–Alder reaction

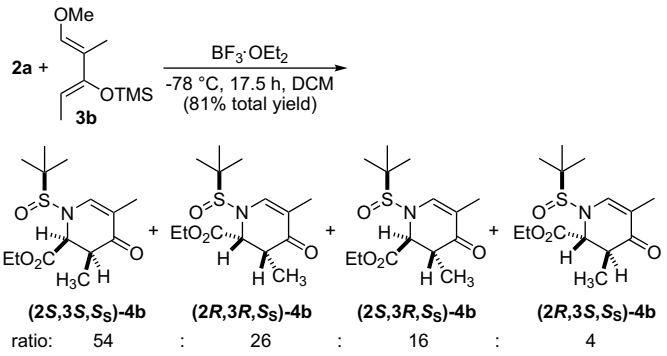
A series of Lewis acids (1 equiv) have previously been screened as promoters for the diastereoselective aza-DA test reaction of **2a** (1 equiv) with the activated Danishefsky's diene **3a** (2 equiv), shown in Scheme 1.[8] The best result was obtained with a stoichiometric amount of $BF_3\cdot OEt_2$ at −78 °C for 1.5 h in dry dichloromethane, yielding an epimeric mixture of **(2*S*,S_S)-4a** and **(2*R*,S_S)-4a** in ratio 5.4:1, and 76% combined yield. Using less than 1 equiv of the Lewis acid provided inferior results, indicating that it was consumed during the reaction. Recrystallization of the mixture from 10% isopropanol in *n*-hexane provided the major isomer in pure form, and an X-ray analysis established the relative configuration shown in **(2*S*,S_S)-4a**.[8]

Attempts to cleave off the sulfinyl group in **(2*S*,S_S)-4a** with concentrated HCl solution (aqueous) in methanol at room temperature failed, resulting in several decomposition products. However, repeating the experiment at 0 °C afforded the desired product **(2*S*)-11a** in 85% yield (see Scheme 1), and high purity (>99% ee) according to chiral GC analysis. Interestingly, when mixtures of **(2*S*,S_S)-4a** and **(2*R*,S_S)-4a** were treated with 1 M HCl solution (aqueous) in THF at 0 °C, a rate difference in cleavage of the sulfinyl group was observed for the two compounds. In general, the minor epimer **(2*R*,S_S)-4a** was cleaved at a faster rate, as exemplified in the experiment starting from an 81:19 mixture of **(2*S*,S_S)-4a** and **(2*R*,S_S)-4a** and 10 min reaction time, giving **11a**, **(2*S*,S_S)-4a**, and **(2*R*,S_S)-4a** in ratio 11:77:12, respectively.

The aza-DA reaction of **2a** with *trans*-1-methoxy-2-methyl-3-(trimethylsilyloxy)-1,3-pentadiene (**3b**), in the presence of stoichiometric amounts of $BF_3\cdot OEt_2$ (−78 °C, 17.5 h), afforded a mixture of four diastereomeric compounds as shown in Scheme 2. We were able to separate **(2*S*,3*S*,S_S)-4b**/**(2*R*,3*R*,S_S)-4b** from **(2*S*,3*R*,S_S)-4b**/**(2*R*,3*S*,S_S)-4b** by flash chromatography, and crystallization of the former fraction yielded pure **(2*S*,3*S*,S_S)-4b**. The absolute configuration was established by X-ray.[8] The relative configuration of **(2*R*,3*R*,S_S)-4b** was determined by ^{1}H NMR spectroscopy, showing a similar vicinal ^{1}H–^{1}H coupling constant (6.5 Hz) between H-2 and H-3 as for **(2*S*,3*S*,S_S)-4b** (6.0 Hz). The corresponding coupling constants for **(2*S*,3*R*,S_S)-4b** and **(2*R*,3*S*,S_S)-4b** were found to be 1.7 Hz and 2.3 Hz, respectively.



Scheme 1.



Scheme 2.

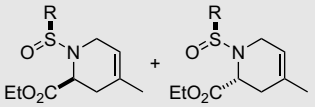
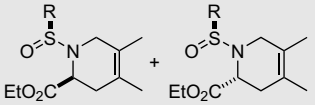
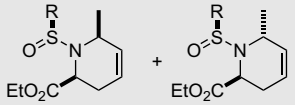
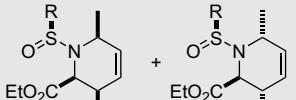
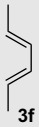
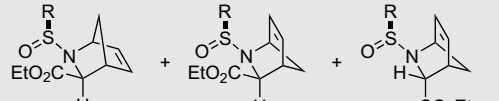
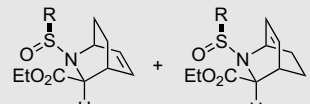
The absolute configurations of the latter two isomers could not be determined, and the proposed structures in Scheme 2 are based on the general preference for (*S*) configuration at the α-carbon (α to the ester group) in these reactions (see stereochemical model discussed below). The stereochemical result shown in Scheme 2 deviates from the results obtained by Jørgensen et al., where a chiral BINAP–copper(I) complex catalyzed the aza-DA reaction of tosyl imine **1** with **3b**, giving the trans adduct (corresponding to our minor **(2*S*,3*R*,S_S)-4b** and **(2*R*,3*S*,S_S)-4b**) as the major product.[3e] Their best result was a 10:1 ratio of the trans and cis adducts, and the former diastereomer was isolated in 83% yield and 94% ee. The cis adduct (corresponding to our **(2*S*,3*S*,S_S)-4b** and **(2*R*,3*R*,S_S)-4b**) was isolated in 8% yield (racemic).

A series of Lewis acids including $SnCl_4$, $Zn(OTf)_2$, $Cu(OTf)_2$, $Yb(OTf)_3$, trimethylsilyl trifluoromethanesulfonate (TMSOTf), $Mg(ClO_4)_2$, $AlBr_3$, and $BF_3\cdot Et_2O$ were screened as promoters (1 equiv) for the stereoselective aza-DA reaction of **2a** with non-activated dienes (acyclic and cyclic). The survey pointed out TMSOTf and $BF_3\cdot Et_2O$ to be the most selective and activating Lewis acids for the reaction. The more promising results are presented in Table 1. For comparison, results from reactions applying the *p*-toluenesulfinylimino ester **2b** as dienophile are included in Table 1. In the presence of Lewis acids, some of the dienes underwent polymerization at rates competitive to the preferred aza-DA reactions. For this reason, some excess diene (2 equiv) was generally used. Especially for isoprene (**3c**), a significant improvement of the yield was observed when using an even larger excess of **3c**. The yield of **(2*S*,S_S)-4c** was raised from 25% (Table 1, entry 2) to 48% (Table 1, entry 3) by increasing the amount of **3c** from 2 to 20 equiv.

Without exception, all reactions with **2a** were more selective than the reactions with **2b**, owing to the bulkiness of the *tert*-butyl group. In general, the best diastereoselectivities were obtained in reactions applying **2a** in combination with TMSOTf. The *tert*-butyl reactions of isoprene (**3c**, Table 1, entries 1–3) and 2,3-dimethylbutadiene (**3d**, Table 1, entries 5 and 6) provided only one observable diastereomer according to ^{1}H NMR (400 MHz) spectroscopy of respective crude products. Our results showed better selectivities (>99% de) versus the reported enantioselective aza-DA reaction of **1** with diene **3d** catalyzed by chiral BINAP–copper(I) complexes (up to 65% ee).[3e]

The aza-DA reaction of **2a** with (*E*)-1,3-pentadiene (**3e**, Table 1, entry 9) and (*E*,*E*)-2,4-hexadiene (**3f**, Table 1, entry 10) afforded mixtures of cis/trans adducts in 7 and 14% combined yields, respectively. The diastereomeric products in both reactions could be separated by flash chromatography. The proposed absolute configurations shown in Table 1 were not determined, but were based on NMR spectroscopy assigning the relative configuration between the Me/CO_2Et groups (see Fig. 2), and from the stereochemical model discussed below showing a preference for (*S*) configuration at the α-carbon (α to the ester group).

Table 1
Aza-DA reactions of **2a**,**b** (1 equiv) with non-activated dienes **3c**–**3h** (2 equiv) promoted by Lewis acid (1 equiv) in CH_2Cl_2 under argon atm

Entry	Imine	Diene	Lewis acid	Conditions	Aza-Diels–Alder adduct[a]	Yield[b] (%)
					 **(2*S*,S_S)-4c** **(2*R*,S_S)-4c**	
1	**2a** (R=*t*-Bu)	 **3c**	$BF_3\cdot Et_2O$	0 °C, 1 h	Ratio: >99:<1	19
2	**2a**		TMSOTf	−78 °C, 22 h	Ratio: >99:<1	25
3	**2a**		TMSOTf	−78 °C, 22 h	Ratio: >99:<1	48[c]
4	**2b** (R=*p*-Tol)		TMSOTf	−78 °C, 20 h	Ratio: 3:2	18
					 **(2*S*,S_S)-4d** **(2*R*,S_S)-4d**	
5	**2a** (R=*t*-Bu)	 **3d**	$BF_3\cdot Et_2O$	0 °C, 2 h	Ratio: >99:<1	42
6	**2a**		TMSOTf	−78 °C, 5 h	Ratio: >99:<1	64
7	**2b** (R=*p*-Tol)		$BF_3\cdot Et_2O$	0 °C, 3.5 h	Ratio: 4:1	35
8	**2b**		TMSOTf	−78 °C, 5.5 h	Ratio: 7:3	48
					 **(2*S*,6*S*,S_S)-4e** **(2*S*,6*R*,S_S)-4e**	
9	**2a** (R=*t*Bu)	 **3e**	TMSOTf	−78 °C, 20 h	Ratio: 2:1	7[d]
					 **(2*S*,3*R*,6*S*,S_S)-4f** **(2*S*,3*S*,6*R*,S_S)-4f**	
10	**2a** (R=*t*-Bu)	 **3f**	TMSOTf	−78 °C, 23 h	Ratio: 97:3	14[d]
					 **(1*S*,3*S*,4*R*,S_S)-4g** **(1*R*,3*S*,4*S*,S_S)-4g** **(1*R*,3*R*,4*S*,S_S)-4g**	
11	**2a** (R=*t*-Bu)	 **3g**	$BF_3\cdot Et_2O$	−50 °C, 25 h	Ratio: 88:12:0	52
12	**2a**		TMSOTf	−78 °C, 18 h	Ratio: >99:<1:0	49
13	**2b** (R=*p*-Tol)		$BF_3\cdot Et_2O$	−50 °C, 0.5 h	Ratio: 89:7:4	48
14	**2b**		TMSOTf	−78 °C, 17 h	Ratio: 89:7:4	63
					 **(1*S*,3*S*,4*R*,S_S)-4h** **(1*R*,3*S*,4*S*,S_S)-4h**	8[d]
15	**2a** (R=*t*-Bu)	 **3h**	TMSOTf	−78 °C, 16 h	Ratio: 87:13	

[a] The product ratio was determined by ^1H NMR (400 Hz) spectroscopy of the crude product.
[b] Total yield of isolated isomers.
[c] Compound **3c** (20 equiv) and 10 equiv of TMSOTf were added to 1 equiv **2a**.
[d] The proposed configurations were not determined, but rationalized by NOE experiments and from the stereochemical model discussed below.

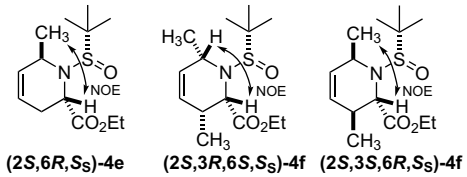
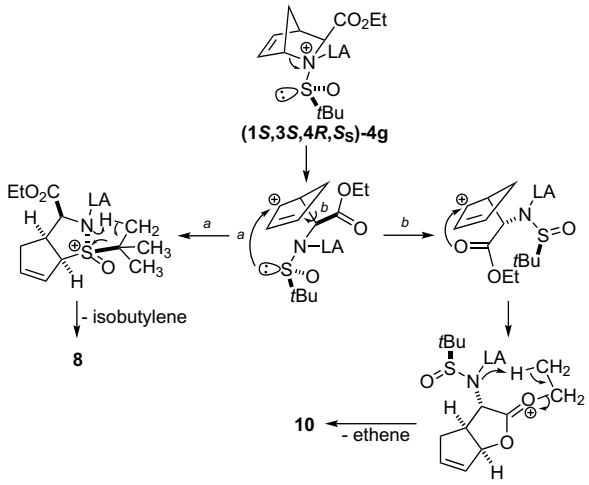


Figure 2. Relative configurations shown from NOE experiments.

An *exo* preference was found for **2a** in reactions with cyclopentadiene (**3g**, Table 1, entries 11 and 12) and cyclohexadiene (**3h**, Table 1, entry 15). The TMSOTf promoted reaction of **3g** at −78 °C afforded only one observable diastereomer **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*t*-Bu) in 49% yield (entry 12), while $BF_3{\cdot}Et_2O$ provided an 88:12 mixture of the *exo* **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*t*-Bu) and the *endo* **(1*R*,3*S*,4*S*,*S*$_S$)-4g** (*t*-Bu) in 52% combined yield (entry 11). The aza-DA reaction of **2b** with **3g** afforded an 89:7:4 mixture of **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*p*-Tol), **(1*R*,3*S*,4*S*,*S*$_S$)-4g** (*p*-Tol) and **(1*R*,3*R*,4*S*,*S*$_S$)-4g** (*p*-Tol), respectively (Table 1, entries 13 and 14). Recrystallization of the mixture from 10% isopropanol in *n*-hexane afforded the major isomer almost pure (97% de). The *exo* preference observed in reactions with unactivated cyclic dienes is in accordance with results reported for the enantioselective aza-DA reactions of **1** with **3g** and **3h**, catalyzed by chiral BINAP–copper(I) complexes.[3e] Yields and enantioselectivities of the major *exo* aza-DA adducts from **3g** and **3h** were reported up to 85% (83% ee) and 52% (95% ee), respectively.[3e]

2.2. By-products in the aza-Diels–Alder reaction

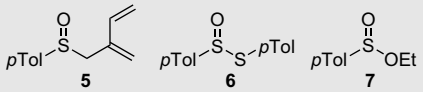
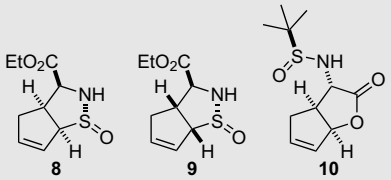
Several by-products were formed and identified during the course of this work. Although not always structurally interesting, attention to these products can provide new insight into the reaction. We did not observe any imine ene by-products in our reaction systems as reported for the chiral BINAP–copper(I) complex catalyzed aza-DA of tosyl imine **1**.[3e] Table 2 shows the most interesting by-products encountered and the reaction conditions under which they were formed. It should be pointed out that attempts to improve the yields of these products were not undertaken. Formation of products **5**, **6**,[9] and **7**[10] (Table 2, entries 1 and 2) must involve breaking of the sulfur–nitrogen bond of **2b** at some stage. It is obvious that a potential *p*-tolyl sulfoxide cation—or radical, would be more stabilized by resonance than the corresponding *tert*-butyl analog. Similar reactions with **2a** were not observed. Ene reactions with *p*-tolyl sulfoxide cation (formed in situ from *p*-toluenesulfinamide) have been reported,[11] which can explain the formation of the ene product **5**. Ene product **5** was observed in low yields (2–12%) when the reaction took place at −78 °C, but at higher temperature (0 °C) the yield improved (27%, Table 2, entry 2). Chiral HPLC analysis of **5** (Table 2, entry 1) showed that some degree of chiral induction took place in these reactions (40% ee), indicating that the sulfur–nitrogen bond could not have been completely broken during addition to the diene. Nucleophilic attack by an ethoxide rather than diene would provide **7**. This ethoxide would most likely come from the ethyl ester group of the sulfinimine, but details around the reaction remain unclear. The thiosulfinate **6** was observed in all aza-DA reactions with **2b** in various amounts. In most reactions, the yields were lower than 10%, but at higher temperatures (0 °C) more **6** was formed (28%, Table 2, entry 2). A decomposition of sulfinimine to sulfenic acid,[12] and a bimolecular dehydration of the sulfenic acid[13] can explain the formation of **6**.



Scheme 3.

The aza-DA adducts from cyclopentadiene reactions with **2a** were not particularly stable, and several by-products were identified (see Table 2, entries 3–5). Shortening the reaction time did not provide higher yields. A rationale for the formation of **8** and **10** from the *exo* aza-DA product **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*t*-Bu) is shown

Table 2
By-products from the aza-Diels–Alder reaction of sulfinimines **2a** and **2b**

Entry	Imine	Diene	Lewis acid	Conditions	By-products/yields[a] (%)	Aza-DA/yields[b] (%)
					 **5** **6** **7**	
1	**2b**	**3c**	TMSOTf	−78 °C, 20 h	12 (40% ee):6:8	18
2	**2b**	**3c**	TMSOTf	0 °C, 1 h	27:28:0	10
					 **8** **9** **10**	
3	**2a**	**3g**	TMSOTf	−78 °C, 15.5 h	17:0:11	44
4	**2a**	**3g**	$BF_3{\cdot}Et_2O$	−50 °C, 25 h	13:0:3	52
5	**2a**	**3g**	$BF_3{\cdot}Et_2O$	rt, 17.5 h	38[c]:4[c]:0	0

[a] Isolated yields.
[b] Combined yield of aza-DA adducts.
[c] Mixture of **8** and **9**.

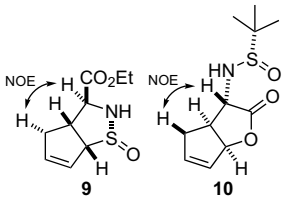


Figure 3. Structure determining NOE's for **9** and **10**.

in Scheme 3. Initiated by a Lewis acid (LA), the C–N bond breaks to form an allylic cation, which is attacked by either the ester or sulfinyl group. Rearrangement of a similar compound has been reported by Kobayashi et al., although the hydrolyzed ester was reported in this paper.[14] Since our reactions were carried out in anhydrous environment, we propose an alternative removal of the ethyl group. The proposed mechanism for the formation of **8** includes an attack by the sulfinyl-sulfur lone pair, explaining the inversion of the sulfinyl stereocentre. Similar nucleophilic attack by the sulfur in *tert*-butanesulfinyl compounds has been suggested by Davis et al., with the expulsion of isobutylene as an important driving force.[15] A similar rearrangement of the *endo* product **(1*R*,3*S*,4*S*,*S*$_S$)-4g** (*t*-Bu) would give **9**. The absolute configuration of **8** was determined by X-ray.[16] The relative configurations of **9** and **10** were found from NOE experiments. Structure determining NOE's are shown in Figure 3.

2.3. Stereochemical model

Although most aza-Diels–Alder reactions are concerted, there are many examples of stepwise Mannich–Michael type mechanisms.[1] Most of these examples involve electron-rich oxygenated dienes or use of Brønsted acids as catalysts, leading to relative stable intermediates. The absolute configurations of the major cycloadducts **(2*S*,*S*$_S$)-4a**, **(2*S*,3*S*,*S*$_S$)-4b**, **(2*S*,*S*$_S$)-4c** (*t*-Bu and *p*-Tol), **(2*S*,*S*$_S$)-4d** (*t*-Bu and *p*-Tol), and **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*t*-Bu and *p*-Tol) were determined (as described below). All major products had the (*S*)-configuration at the α-carbon atom (α to the ester group). A strong preference for *Re*-approach was observed for **2a** (*t*-Bu). In fact, for all unactivated dienes, *tert*-butyl products were apparently formed exclusively with (*S*)-configuration at the α-carbon, with the diastereomeric diversity originating from *endo*/*exo* approach. More evidently, *tert*-butyl reactions of isoprene (**3c**) and 2,3-dimethylbutadiene (**3d**) provided only one observable diastereomer, since *endo*/*exo* approaches lead to identical products in these cases. The expected *exo* preference was found for reactions with the cyclic dienes **3g** and **3h**,[3e] but the products deriving from acyclic dienes **3b**, **3e**, and **3f** showed the opposite *endo* preference. Products from the activated Danishefsky's dienes **3a** and **3b** are conspicuously less selective, forming diastereomers with both configurations at the α-carbon atom. This could result from a less selective, possibly stepwise, mechanism as suggested by Kawęcki.[7] However, we were not able to identify intermediate products in these reactions. The stereochemical outcome of the aza-DA reactions of **2a** and **2b** can be rationalized according to the model shown in Figure 4. The shown conformation has been

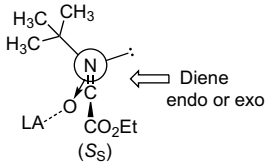
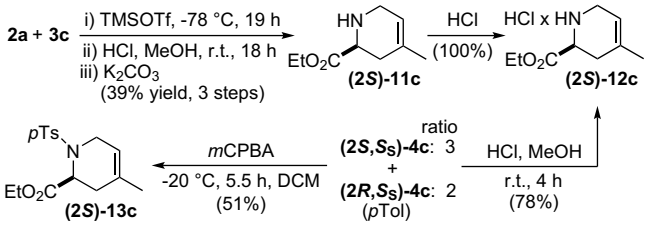


Figure 4. Stereochemical model.

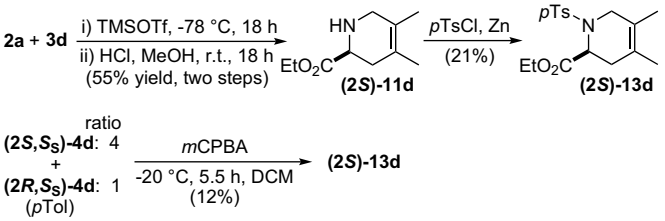
confirmed by calculations on different sulfinimines, both with and without Lewis acids (LA) present.[17] The model has earlier been used to explain the stereochemical outcome of Lewis acid promoted additions of both Grignard reagents[5a] and silyl nucleophiles[18] to sulfinimines.

2.4. Configuration of the aza-Diels–Alder products

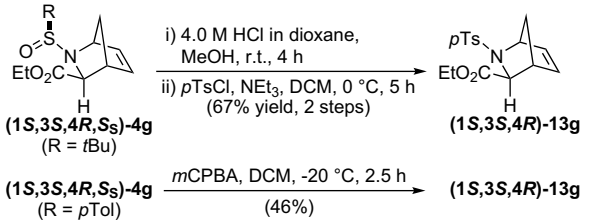
The determination of the absolute configuration of the aza-DA adducts **(2*S*,*S*$_S$)-4a** and **(2*S*,3*S*,*S*$_S$)-4b** has been described elsewhere.[8] Absolute configurations of the major aza-DA adducts **(2*S*,*S*$_S$)-4c** (*t*-Bu and *p*Tol), **(2*S*,*S*$_S$)-4d** (*t*-Bu and *p*-Tol) and **(1*S*,3*S*,4*R*,*S*$_S$)-4g** (*t*-Bu and *p*-Tol) were established by chemical correlation with the known HCl salt **(2*R*)-12c** (see Scheme 4),[19] **(2*S*)-13d** (Scheme 5),[3e] and **(1*S*,3*S*,4*R*)-13g** (Scheme 6),[3e] respectively.



Scheme 4.



Scheme 5.



Scheme 6.

The crude aza-DA adduct **(2*S*,*S*$_S$)-4c** (*t*-Bu), obtained by reacting **2a** with 20 equiv of **3c** in the presence of 10 equiv TMSOTf, was treated with concentrated aqueous HCl in methanol to afford the HCl salt **(2*S*)-12c** (see Scheme 4). By controlling the pH of the water phase, **(2*S*)-12c** was purified with extraction alone. Basic adjustment afforded enantiopure **(2*S*)-11c** (according to chiral GC analysis), and was then transformed back to **(2*S*)-12c** in concentrated aqueous HCl. Similarly, acidic removal of the tolylsulfinyl group in a 3:2 mixture of **(2*S*,*S*$_S$)-4c** (*p*-Tol) and **(2*R*,*S*$_S$)-4c** (*p*-Tol) afforded the enriched **(2*S*)-12c** in 78% yield. The tolylsulfinyl group in the aza-DA mixture was also oxidized with *m*-CPBA at −20 °C to the enantiomerically enriched tosyl analog **(2*S*)-13c** in 51% yield.

Crude **(2*S*,*S*$_S$)-4d** (*t*-Bu), obtained from the aza-DA reaction of **2a** with **3d** (see Scheme 5), was hydrolyzed in accordance with the method mentioned above for **(2*S*,*S*$_S$)-4c** (*t*-Bu) to **(2*S*)-11d**, and then tosylated under neutral conditions[20] to the known **(2*S*)-13d** (>99%

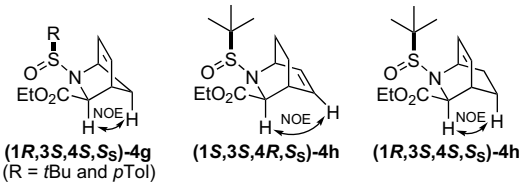


Figure 5. Proposed configurations for bicyclic aza-DA adducts.

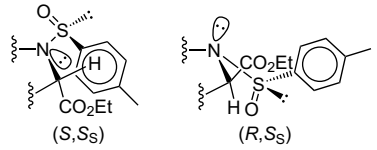


Figure 6. Model explaining observed shielding for (S,S_S)-isomers in ^{1}H NMR.

ee, HPLC).[3e] The configuration of a 4:1 mixture of **(2*S*,S_S)-4d** (*p*-Tol) and **(2*R*,S_S)-4d** (*p*-Tol) was established by an *m*-CPBA oxidation to the enantiomerically enriched **(2*S*)-13d**.

The absolute configuration of **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu) was determined by cleavage of the sulfinyl group[5e] and subsequent tosylation to the known *N*-tosyl compound **(1*S*,3*S*,4*R*)-13g**[3e] in 67% total yield (see Scheme 6). The configuration of **(1*S*,3*S*,4*R*,S_S)-4g** (*p*-Tol) was assigned by oxidation to **(1*S*,3*S*,4*R*)-13g**.

The relative configurations of the other isomers of **4g** and **4h**, disregarding the configuration at the α-carbon atom (α to the ester group), were found from NOE experiments. The structure determining NOE's are summarized in Figure 5. From the stereochemical model discussed above we assume (*S*)-configuration at the α-carbon, and with (*S*)-configuration fixed at sulfur, the following structures shown in Figure 5 are proposed.

The configurations of the *p*-toluene isomers **(1*R*,3*S*,4*S*,S_S)-4g** and **(1*R*,3*R*,4*S*,S_S)-4g** were deduced by the following reasoning: the aza-DA adducts are formally sulfinamides with the nitrogen taking part in a cyclic structure. Focusing only on the substituents from the parent sulfinimine, the sulfoxy group on nitrogen and the ester group on the neighboring carbon (α-C), some general observations can be rationalized for the aza-DA adducts of *p*-toluensulfinimine. To reduce van der Waals strain, the bulky sulfoxy group would preferably adopt an orientation trans to the ester group (see Fig. 6). Considering the rotation of the N–S bond, there is general preference for a staggered orientation of the sulfinamides, with the nitrogen lone pair *anti* to the sulfoxide oxygen.[21] This can be attributed to a stabilizing interaction between the nitrogen lone pair and the anti bonding σ-orbital of the S–O bond. In our work, compounds with (*S*)-configuration on sulfur were prepared, without any sign of racemization. This leads to two diastereomeric arrangements (ignoring the remaining part of the molecule), due to (*R*) or (*S*)-configuration of the carbon α to the ester group (see Fig. 6).

Table 3
Configuration at α-C versus OCH_2CH_3 proton shift

p-Tol aza-DA adducts	(*S*)/ppm	(*R*)/ppm
(2*S*,S_S)-4c+**(2*R*,S_S)-4c**	4.15	4.22
(2*S*,S_S)-4d+**(2*R*,S_S)-4d**	4.13	4.22
(1*S*,3*S*,4*R*,S_S)-4g	3.67, 3.62	
(1*R*,3*S*,4*S*,S_S)-4g	3.7–3.6	
(1*R*,3*R*,4*S*,S_S)-4g		4.29

As shown in Figure 6, the preferred conformer of the (S,S_S)-diastereomer puts the tolyl group in the vicinity of the ester group, leading to significant shielding of the ethyl (OCH_2CH_3) proton NMR signals. The (R,S_S)-diastereomer, however, does not show this effect. Table 3 shows the ethyl proton shifts for all tolyl aza-DA adducts described in this paper. A chemical shift at 3.6–3.7 for **(1*R*,3*S*,4*S*,S_S)-4g** supports (*S*)-configuration at C-3 (α-C), and a chemical shift at 4.29 for **(1*R*,3*R*,4*S*,S_S)-4** supports (*R*)-configuration at C-3.

3. Conclusion

In conclusion, diastereoselective aza-Diels–Alder (aza-DA) reactions of ethyl (*S*)-*N*-(*tert*-butanesulfinyl)iminoacetate (**2a**) and ethyl (*S*)-*N*-(*p*-toluenesulfinyl)iminoacetate (**2b**) in the presence of stoichiometric amounts of Lewis acids have been presented. A range of dienes have been applied. The reactions with **2a** were found to be the most selective. Reactions of unactivated dienes with TMSOTf as Lewis acid afforded aza-DA adducts in modest yield and diastereoselectivities up to 99%. A strong preference for the *Re*-approach was observed for **2a**. Cyclic dienes gave *exo* adducts as major products. For the aza-DA reactions with activated Danishefsky type dienes, poor diastereoselectivities were observed. In these cases the best results (up to 69% de, 76% yield) were obtained with $BF_3\cdot Et_2O$ as Lewis acid. Treatment of selected aza-DA adducts with HCl resulted in cleavage of the sulfinyl group without racemization, yielding optically active non-proteinogenic α-amino ethyl esters.

4. Experimental

4.1. General remarks

All reactions were performed under an argon or nitrogen atmosphere. Tetrahydrofuran (THF) was distilled under nitrogen from Na/benzophenone. Dichloromethane was distilled under nitrogen from calcium hydride. Sulfinimines **2a** and **2b** were prepared according to the literature.[5a] The racemic sulfinimines were also prepared to provide reference compounds for chiral GC and HPLC analysis. Melting points were determined on a Buchi 535 apparatus and are uncorrected. TLC was performed on Merck silica gel 60 F_{254} plates, using UV light at 312 nm and a 5% alcoholic molybdophosphoric acid for detection. Silica gel for flash chromatography was purchased from Merck. Optical rotations were measured with a Perkin–Elmer 241 Polarimeter. Enantiomeric excesses were determined by HPLC analysis, using Daicels columns Chiralcel OD-H and OJ and Chiralpak AD (250×4.6 mm), or by GC using CP Chirasil Dex CB column. ^{1}H and ^{13}C NMR spectra (Bruker Avance DPX instruments 300/75 MHz and 400/100 MHz) were obtained from solutions of $CDCl_3$, and chemical shifts are in parts per million and referenced to TMS via the lock signal of the solvent. ^{1}H and ^{13}C NMR signals were assigned by 2D correlation techniques (COSY, HSQC, HMBC, NOESY). IR spectra were run on a Thermo Nicolet FT-IR NEXUS instrument, and only the strongest/structurally most important peaks are listed. The mass spectra were recorded on a Finnigan MAT 95×L mass spectrometer. The electron-impact mass spectra, MS (EI), were recorded at 50 eV with a direct inlet, and the electron spray ionization mass spectra, MS (ESI), at 4.7 kV for low resolution spectra and 10 kV for high resolution spectra. The high resolution mass spectra, HRMS (EI) and (ESI), were obtained by using perfluorokerosene (PFK) and polyethyleneimine (PEI) as standards, respectively, to provide the reference masses. The elemental analyses were performed at the Mikroanalytisches labor Beller, Göttingen, Germany.

4.2. General procedure for aza-Diels–Alder reactions

Sulfinimine **2** (1.2–1.5 M in CH_2Cl_2, 0.25 mmol) was dissolved in dried CH_2Cl_2 (2 mL) and cooled down to the specified temperature (see Table 1) under an argon atmosphere. The diene **3** (1.4–2.0 equiv) and the Lewis acid (1.0–1.2 equiv) were added via syringe and the resultant mixture was stirred. After the appropriate reaction time (see Table 1), the reaction mixture was quenched by the addition of a phosphate buffer (pH=7, 3 mL), and allowed to warm to room temperature. The mixture was extracted with CH_2Cl_2 (4×4 mL) and the combined organics were dried ($MgSO_4$) and concentrated. The crude product was analyzed by ^{1}H NMR spectroscopy to determine the diastereomeric ratio and, thereafter, purified by flash chromatography.

4.2.1. Ethyl (2S,S$_S$)-1-(tert-butylsulfinyl)-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate, ***(2S,S$_S$)-4a****, and ethyl (2R,S$_S$)-1-(tert-butylsulfinyl)-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate,* ***(2R,S$_S$)-4a***

The asymmetric aza-DA reaction between sulfinimine **2a** (0.52 mmol) and the Danishefsky's diene **3a** (1.0 mmol) according to the general procedure (2×scale) at −78 °C for 20 h afforded a 5.4:1 mixture of **(2*S*,*S*$_S$)-4a** and **(2*R*,*S*$_S$)-4a**, which were not separable by flash chromatography (EtOAc/*n*-hexane, 1:1). The mixture was isolated as a pale yellow viscous oil (total yield: 108.3 mg, 76%). Crystallization of the mixture from 10% *i*-PrOH in *n*-hexane afforded the major isomer in pure form (white solid), and an X-ray analysis established the relative configuration to be that shown in **(2*S*,*S*$_S$)-4a**.[8] Anal. Calcd of the mixture $C_{12}H_{19}NO_4S$: C, 52.73; H, 7.01; N, 5.12; S, 11.73. Found: C, 52.69; H, 7.02; N, 5.05; S, 11.79. Data for **(2*S*,*S*$_S$)-4a**: R_f (EtOAc/*n*-hexane, 1:1)=0.1. Mp=127–128 °C (from 10% *i*-PrOH/*n*-hexane). $[\alpha]_D^{rt}$ −166 (*c* 0.30, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10:90, 1.0 ml min^{-1}, 230 nm): t_R 23.3 min. ^{1}H NMR (400 MHz): δ 7.52 (dd, 1H, *J*=8.2, 1.4 Hz, H-6), 5.42 (dd, 1H, *J*=8.2, 1.3 Hz, H-5), 4.37 (ddd, 1H, *J*=7.0, 2.1, 1.4 Hz, H-2), 4.25 (q, 2H, *J*=7.1 Hz, OC*H*$_2$), 3.05 (ddd, 1H, *J*=16.8, 2.1, 1.3 Hz, *trans*-H-3), 2.86 (dd, 1H, *J*=16.8, 7.0 Hz, *cis*-H-3), 1.28 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.26 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 190.10 (C-4), 169.0 (*C*O$_2$Et), 142.8 (C-6), 106.2 (C-5), 62.8 (O*C*H$_2$), 59.78 (*C*Me$_3$), 59.4 (C-2), 38.3 (C-3), 21.7 (C*Me*$_3$), 14.04 (OCH_2CH_3). IR (KBr tablet): 3050 (w), 3001 (m), 2979 (m), 2912 (m), 1740 (s), 1649 (s), 1577 (s), 1479 (m), 1421 (m), 1337 (m), 1295 (s), 1234 (s), 1194 (s), 1096 (s), 1042 (s), 1021 (m), 992 (s), 930 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 274 (M+1, 1), 217 (13), 169 (18), 144 (86), 96 (100), 95 (19), 78 (13), 68 (33), 67 (22), 57 (21), 41 (89), 39 (15). HRMS (EI) calcd for $C_{12}H_{19}NO_4S$ 273.1035 (M$^+$), found 273.1039. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10:90, 1.0 mL min^{-1}, 230 nm) of a racemic sample **(2*R**,*R*$_S^*$)-4a**: t_R 24.6 and 30.5 min. Data for **(2*R*,*S*$_S$)-4a**: R_f (EtOAc/*n*-hexane, 1:1)=0.1. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10:90, 1.0 ml min^{-1}, 230 nm): t_R 17.9 min. ^{1}H NMR (400 MHz): δ 7.29 (dd, 1H, *J*=8.0, 1.5 Hz, H-6), 5.31 (dd, 1H, *J*=8.0, 1.3 Hz, H-5), 4.70 (ddd, 1H, *J*=7.2, 2.1, 1.5 Hz, H-2), 4.20 (q, 2H, *J*=7.1 Hz, OC*H*$_2$), 3.04 (ddd, 1H, *J*=17.1, 2.1, 1.3 Hz, H-3A), 2.90 (dd, 1H, *J*=17.1, 7.2 Hz, H-3B), 1.26 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.26 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 190.12 (C-4), 168.9 (*C*O$_2$Et), 147.9 (C-6), 105.0 (C-5), 62.4 (O*C*H$_2$), 59.77 (*C*Me$_3$), 52.6 (C-2), 39.0 (C-3), 21.8 (C*Me*$_3$), 14.02 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10:90, 1.0 ml min^{-1}, 230 nm) of a racemic **(2*R**,*S*$_S^*$)-4a**: t_R 18.2 and 41.0 min.

4.2.2. Ethyl (2S,3S,S$_S$)-1-(tert-butylsulfinyl)-3,5-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate, ***(2S,3S,S$_S$)-4b****, ethyl (2R,3R,S$_S$)-1-(tert-butylsulfinyl)-3,5-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate,* ***(2R,3R,S$_S$)-4b****, ethyl (2S,3R,S$_S$)-1-(tert-butylsulfinyl)-3,5-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate,* ***(2S,3R,S$_S$)-4b****, and ethyl (2R,3S,S$_S$)-1-(tert-butylsulfinyl)-3,5-dimethyl-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate,* ***(2R,3S,S$_S$)-4b***

The asymmetric aza-DA reaction between sulfinimine **2a** (0.52 mmol) and the dimethyl substituted Danishefsky's diene **3b** (0.99 mmol) according to the general procedure (2×scale) at −78 °C for 17.5 h afforded a 54:26:16:4 mixture of **(2*S*,3*S*,*S*$_S$)-4b**, **(2*R*,3*R*,*S*$_S$)-4b**, **(2*S*,3*R*,*S*$_S$)-4b**, and **(2*R*,3*S*,*S*$_S$)-4b**, respectively. Flash chromatography (EtOAc/*n*-hexane, 1:2) separated **(2*S*,3*S*,*S*$_S$)-4b**/**(2*R*,3*R*,*S*$_S$)-4b** from **(2*S*,3*R*,*S*$_S$)-4b**/**(2*R*,3*S*,*S*$_S$)-4b** (total yield: 126.2 mg, 81%). Recrystallization of the main fraction from Et$_2$O/*n*-pentane yielded **(2*S*,3*S*,*S*$_S$)-4b** pure as white crystals (55.4 mg, 35%), and the absolute configuration was established by X-ray analysis.[8] Data for **(2*S*,3*S*,*S*$_S$)-4b**: R_f (EtOAc/*n*-hexane, 1:1)=0.3. Mp 87–88 °C (from Et$_2$O/*n*-pentane). $[\alpha]_D^{rt}$ −123 (*c* 1.0, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm): t_R 11.3 min. ^{1}H NMR (400 MHz): δ 7.24 (m, 1H, H-6), 4.24 (dd, 1H, *J*=6.0, 1.3 Hz, H-2), 4.20 (q, 2H, *J*=7.1 Hz, OC*H*$_2$), 2.94 (qd, 1H, *J*=7.1, 6.0 Hz, H-3), 1.74 (d, 3H, *J*=1.0 Hz, Me-5), 1.30 (d, 3H, *J*=7.1 Hz, Me-3), 1.26 (s, 9H, *t*-Bu), 1.25 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 193.3 (C-4), 168.0 (*C*O$_2$Et), 137.4 (C-6), 113.1 (C-5), 64.4 (C-2), 61.9 (O*C*H$_2$), 59.6 (*C*Me$_3$), 41.9 (C-3), 21.9 (C*Me*$_3$), 13.97 (OCH_2CH_3), 12.9 (Me-5), 11.3 (Me-3). IR (KBr tablet): 3037 (w), 2988 (m), 1737 (s), 1688 (s), 1606 (s), 1381 (m), 1366 (m), 1293 (m), 1194 (s), 1093 (s), 1027 (m), 941 (m), 914 (m), 879 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 301 (M$^+$, 1), 245 (63), 197 (87), 125 (22), 124 (100), 123 (32). HRMS (EI) calcd for $C_{14}H_{23}NO_4S$ 301.1348, found 301.1336. Anal. Calcd for $C_{14}H_{23}NO_4S$: C, 55.79; H, 7.69; N, 4.65; S, 10.64. Found: C, 55.68; H, 7.63, N, 4.64; S, 10.65. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,3*R**,*R*$_S^*$)-4b**: t_R 11.3 and 13.3 min. Data for **(2*R*,3*R*,*S*$_S$)-4b**: R_f (EtOAc/*n*-hexane, 1:1)=0.3. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm): t_R 13.9 min. ^{1}H NMR (400 MHz): δ 7.10 (m, 1H, H-6), 4.51 (dd, 1H, *J*=6.5, 1.3 Hz, H-2), 4.16 (m, 2H, OCH_2), 2.99 (qd, 1H, *J*=7.1, 6.5 Hz, H-3), 1.73 (d, 3H, *J*=1.0 Hz, Me-5), 1.27 (d, 3H, *J*=7.1 Hz, Me-3), 1.27 (s, 9H, *t*-Bu), 1.24 (t, 3H, *J*=7.2 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 193.1 (C-4), 168.5 (*C*O$_2$Et), 143.1 (C-6), 118.8 (C-5), 61.5 (O*C*H$_2$), 60.1 (*C*Me$_3$), 59.3 (C-2), 42.1 (C-3), 22.1 (C*Me*$_3$), 14.01 (OCH_2CH_3), 12.7 (Me-5), 11.1 (Me-3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,3*R**,*S*$_S^*$)-4b**: t_R 12.7 and 13.9 min. Data for **(2*S*,3*R*,*S*$_S$)-4b**: R_f (EtOAc/*n*-hexane, 1:1)=0.25. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm): t_R 17.8 min. ^{1}H NMR (400 MHz): δ 7.33 (m, 1H, H-6), 4.22 (q, 2H, *J*=7.1 Hz, OCH_2), 4.12 (app. t, 1H, *J*=1.6 Hz, H-2), 3.08 (qd, 1H, *J*=7.5, 1.7 Hz, H-3), 1.74 (d, 3H, *J*=1.0 Hz, Me-5), 1.31 (d, 3H, *J*=7.5 Hz, Me-3), 1.27 (s, 9H, *t*-Bu), 1.26 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 194.4 (C-4), 169.4 (*C*O$_2$Et), 139.1 (C-6), 111.8 (C-5), 65.2 (C-2), 62.5 (O*C*H$_2$), 60.1 (*C*Me$_3$), 43.1 (C-3), 22.1 (C*Me*$_3$), 17.5 (Me-3), 14.0 (OCH_2CH_3), 13.1 (Me-5). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,3*S**,*R*$_S^*$)-4b**: t_R 15.1 and 17.7 min. Data for **(2*R*,3*S*,*S*$_S$)-4b**: R_f (EtOAc/*n*-hexane, 1:1)=0.25. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 5:95, 1.0 ml min^{-1}, 230 nm): t_R 15.2 min. ^{1}H NMR (400 MHz): δ 7.12 (m, 1H, H-6), 4.32 (dd, 1H, *J*=2.3, 1.5 Hz, H-2), 4.18 (m, 1H, OC*H*H), 4.16 (m, 1H, OCH*H*), 2.98 (qd, 1H, *J*=7.4, 2.3 Hz, H-3), 1.72 (d, 3H, *J*=1.0 Hz, Me-5), 1.33 (d, 3H, *J*=7.4 Hz, Me-3), 1.27 (s, 9H, *t*-Bu), 1.25 (overlap, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, selected signals): δ 169.4 (*C*O$_2$Et), 144.3 (C-6), 62.1 (O*C*H$_2$), 60.2 (C-2), 60.2 (*C*Me$_3$), 43.7 (C-3), 21.9 (C*Me*$_3$), 17.5 (Me-3), 13.5 (Me-5).

4.2.3. Ethyl (2S,S$_S$)-1-(tert-butylsulfinyl)-4-methyl-1,2,3,6-tetrahydropyridine-2-carboxylate, ***(2S,S$_S$)-4c*** *(t-Bu)*

The asymmetric aza-DA reaction between sulfinimine **2a** and isoprene (**3c**) according to the general procedure (described above) afforded only **(2*S*,*S*$_S$)-4c** (*t*-Bu) as aza-DA adduct. The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:5). Data

for **(2*S*,S_S)-4c** (*t*-Bu): viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.35. $[\alpha]_D^{rt}$ −36 (*c* 1.59, CH_2Cl_2). GC [CP Chirasil Dex CB, 80 °C (0 min)–4 °C min^{-1}–190 °C (2 min)]: t_R 18.0 min. ^{1}H NMR (400 MHz): δ 5.34 (m, 1H, H-5), 4.39 (dd, 1H, *J*=6.5, 1.6 Hz, H-2), 4.20 (q, 2H, *J*=7.1, OCH_2), 3.82 (app. dp, 1H, *J*=18, 2.4 Hz, H-6), 3.60 (br d, 1H, *J*=18 Hz, H-6), 2.45 (br d, 1H, *J*=17 Hz, H-3), 2.36 (br d, 1H, *J*=17 Hz, H-3), 1.69 (s, 3H, Me-4), 1.27 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.17 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 172.0 (CO_2Et), 131.3 (C-4), 117.6 (C-5), 61.2 (OCH_2), 59.0 (CMe_3), 51.8 (C-2), 45.1 (C-6), 32.0 (C-3), 23.5 (Me-4), 22.3 (CMe_3), 14.0 (OCH_2CH_3). IR (thin film, NaCl): 2958 (m), 2928 (m), 1736 (s), 1448 (m), 1362 (m), 1194 (s), 1077 (s), 917 (m) cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_3S$: C, 57.11; H, 8.48; N, 5.12. Found: C, 57.21; H, 8.62, N, 5.10. GC [CP Chirasil Dex CB, 80 °C (0 min)–4 °C min^{-1}–190 °C (2 min)] of a racemic sample **(2*R**,R_S^*)-4c** (*t*-Bu): t_R 17.8 and 17.9 min.

4.2.4. *Ethyl (2S,S_S)-4-methyl-1-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine-2-carboxylate,* ***(2S,S_S)-4c*** *(p-Tol), ethyl (2R,S_S)-4-methyl-1-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine-2-carboxylate,* ***(2R,S_S)-4c*** *(p-Tol), and 2-(p-tolylsulfinylmethyl)-1,3-butadiene,* ***5***

The asymmetric aza-DA reaction between sulfinimine **2b** and isoprene (**3c**) according to the general procedure (described above) afforded an inseparable mixture of **(2*S*,S_S)-4c** (*p*-Tol) and **(2*R*,S_S)-4c** (*p*-Tol). In addition, various amounts of **5**, **6**,[9] and **7**[10] were formed dependent on the reaction conditions applied (see Table 2, entries 1 and 2). The mixture of **(2*S*,S_S)-4c** (*p*-Tol) and **(2*R*,S_S)-4c** (*p*-Tol) was purified by flash chromatography (EtOAc/*n*-hexane, 3:7) and obtained as a colorless oil. Anal. Calcd of the mixture $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56; S, 10.43. Found: C, 62.31; H, 6.75; N, 4.46; S, 10.28. IR of the mixture (thin film, NaCl): 2923 (m), 2852 (m), 1738 (s), 1446 (m), 1380 (m), 1338 (m), 1279 (m), 1197 (s), 1093 (s), 1072 (s) cm^{-1}. Data for **(2*S*,S_S)-4c** (*p*-Tol): R_f (EtOAc/*n*-hexane, 3:7)=0.2. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 35.8 min. ^{1}H NMR (300 MHz): δ 7.57 (app. d, 2H, *J*=8.2 Hz, tolyl), 7.29 (app. d, 2H, *J*=8.2 Hz, tolyl), 5.35 (app. s, 1H, H-5), 4.27 (dd, 1H, *J*=6.5, 2.2 Hz, H-2), 4.15 (q, 2H, *J*=7.1 Hz, OCH_2), 3.99 (d, 1H, *J*=17.1 Hz, H-6), 3.56 (d, 1H, *J*=17.1 Hz, H-6), 2.65–2.38 (m, 2H, H-3), 2.41 (s, 3H, ArCH_3), 1.70 (s, 3H, Me-4), 1.25 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 171.0 (CO_2Et), 141.2 (Ar), 140.4 (Ar), 131.1 (C-4), 129.7 (Ar), 126.5 (Ar), 118.0 (C-5), 61.2 (OCH_2), 55.5 (C-2), 42.8 (C-6), 32.7 (C-3), 23.4 (Me-4), 21.3 (ArCH_3), 14.1 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,R_S^*)-4c** (*p*-Tol): t_R 35.8 and 44.9 min. Data for **(2*R*,S_S)-4c** (*p*-Tol): R_f (EtOAc/*n*-hexane, 3:7)=0.2. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 47.5 min. ^{1}H NMR (300 MHz): δ 7.64 (app. d, 2H, *J*=8.2 Hz, tolyl), 7.32 (app. d, 2H, *J*=8.2 Hz, tolyl), 5.31 (app. s, 1H, H-5), 4.47 (dd, 1H, *J*=6.1, 2.4 Hz, H-2), 4.22 (q, 2H, *J*=7.1 Hz, OCH_2), 3.56 (d, 1H, *J*=17.1 Hz, H-6), 3.38 (d, 1H, *J*=17.1, H-6), 2.65–2.38 (m, 2H, H-3), 2.42 (s, 3H, ArCH_3), 1.70 (s, 3H, Me-4), 1.30 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 171.4 (CO_2Et), 141.22 (Ar), 140.7 (Ar), 130.6 (C-4), 129.7 (Ar), 126.5 (Ar), 118.1 (C-5), 61.3 (OCH_2), 57.9 (C-2), 39.4 (C-6), 32.8 (C-3), 23.4 (Me-4), 21.3 (ArCH_3), 14.2 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,S_S^*)-4c** (*p*-Tol): t_R 43.9 and 47.6 min. Data for **5**: R_f (EtOAc/*n*-hexane, 3:7)=0.12. $[\alpha]_D^{rt}$ −56.5 (*c* 0.4, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 10:90, 1.0 ml min^{-1}, 230 nm): 40% ee, t_R 8.9 (minor) and 10.5 (major) min. ^{1}H NMR (300 MHz): δ 7.51 (app. d, 2H, *J*=8.1 Hz, tolyl), 7.31 (app. d, 2H, *J*=8.1 Hz, tolyl), 6.37 (dd, 1H, *J*=17.6, 10.8 Hz, H-3), 5.33 (d, 1H, *J*=17.6 Hz, H-4), 5.23 (m, 1H, H-1), 5.19 (m, 1H, H-4), 5.00 (app. s, 1H, H-1), 3.79 (dd, 1H, *J*=12.5, 0.8 Hz, CH_2), 3.56 (dd, 1H, *J*=12.5, 0.6 Hz, CH_2), 2.41 (s, 3H, ArCH_3). ^{13}C NMR (100 MHz): δ 141.7 (Ar), 140.7 (Ar), 137.0 (C-3), 135.7 (C-2), 129.7 (Ar), 124.4 (Ar), 122.7 (C-1), 115.4 (C-4), 61.5 (CH_2), 21.4 (ArCH_3). IR (KBr tablet): 2932 (w), 1727 (m), 1445 (m), 1152 (m), 1085 (s), 1050 (s) cm^{-1}. HRMS (EI) calcd for $C_{12}H_{14}OS$ 206.0760 (M^+), found 206.0763.

4.2.5. *Ethyl (2S,S_S)-1-(tert-butylsulfinyl)-4,5-dimethyl-1,2,3,6-tetrahydropyridine-2-carboxylate,* ***(2S,S_S)-4d*** *(t-Bu)*

The asymmetric aza-DA reaction between sulfinimine **2a** and 2,3-dimethylbutadiene (**3d**) according to the general procedure (described above) afforded only **(2*S*,S_S)-4d** (*t*-Bu) as aza-DA adduct. The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:5). Data for **(2*S*,S_S)-4d** (*t*-Bu): viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.45. $[\alpha]_D^{rt}$ −23.7 (*c* 1.0, $CHCl_3$). GC [CP Chirasil Dex CB, 110 °C (0 min)–1 °C min^{-1}–150 °C (0 min)–15 °C min^{-1}–180 °C (5 min)]: t_R 32.0 min. ^{1}H NMR (400 MHz): δ 4.32 (dd, 1H, *J*=6.5, 0.9 Hz, H-2), 4.18 (q, 2H, *J*=7.1 Hz, OCH_2), 3.71 (br d, 1H, *J*=17 Hz, H-6), 3.40 (br d, 1H, *J*=17 Hz, H-6), 2.47 (br d, 1H, *J*=17 Hz, H-3), 2.32 (br d, 1H, *J*=17 Hz, H-3), 1.63 (s, 3H, Me-4), 1.57 (s, 3H, Me-5), 1.26 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.17 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 172.0 (CO_2Et), 123.1 (C-4), 122.5 (C-5), 61.1 (OCH_2), 58.9 (CMe_3), 52.4 (C-2), 49.4 (C-6), 33.0 (C-3), 22.4 (CMe_3), 18.9 (Me-4), 15.9 (Me-5), 14.2 (OCH_2CH_3). IR (thin film, NaCl): 2925 (m), 1736 (s), 1448 (m), 1362 (m), 1193 (s), 1135 (m), 1081 (s), 915 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 287 (M, 1), 231 (49), 183 (34), 182 (87), 158 (20), 157 (22), 110 (100), 108 (45), 57 (34). Anal. Calcd for $C_{14}H_{25}NO_3S$: C, 58.50; H, 8.77; N, 4.87; S, 11.16. Found: C, 58.42; H, 8.77; N, 4.94; S, 11.10. GC [CP Chirasil Dex CB, 110 °C (0 min)–1 °C min^{-1}–150 °C (0 min)–15 °C min^{-1}–180 °C (5 min)] of a racemic sample **(2*R**,R_S^*)-4d** (*t*-Bu): t_R 31.7 and 32.0 min.

4.2.6. *Ethyl (2S,S_S)-4,5-dimethyl-1-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine-2-carboxylate,* ***(2S,S_S)-4d*** *(p-Tol), and ethyl (2R,S_S)-4,5-dimethyl-1-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine-2-carboxylate,* ***(2R,S_S)-4d*** *(p-Tol)*

The asymmetric aza-DA reaction between sulfinimine **2b** and 2,3-dimethylbutadiene (**3d**) according to the general procedure (described above) afforded an inseparable mixture of **(2*S*,S_S)-4d** (*p*-Tol) and **(2*R*,S_S)-4d** (*p*-Tol). The mixture was purified by flash chromatography (EtOAc/*n*-hexane, 15:85): colorless oil. Anal. Calcd of the mixture $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.21; N, 4.36. Found: C, 63.51; H, 7.24; N, 4.16. IR of the mixture (thin film, NaCl): 2981 (m), 2917 (m), 2859 (m), 1738 (s), 1491 (m), 1446 (m), 1384 (m), 1285 (m), 1197 (s), 1135 (m), 1092 (s), 1071 (s), 1023 (s) cm^{-1}. Data for **(2*S*,S_S)-4d** (*p*-Tol): R_f (EtOAc/*n*-hexane, 1:1)=0.40. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}): t_R 33.2 min. ^{1}H NMR (300 MHz): δ 7.57 (app. d, 2H, *J*=8.2 Hz, tolyl), 7.29 (app. d, 2H, *J*=8.2 Hz, tolyl), 4.21 (d, 1H, *J*=7.2 Hz, H-2), 4.13 (q, 2H, *J*=7.2 Hz, OCH_2), 3.90 (app. d, 1H, *J*=16.9 Hz, H-6), 3.38 (app. d, 1H, *J*=16.9 Hz, H-6), 2.63–2.36 (m, 2H, H-3), 2.41 (s, 3H, ArCH_3), 1.64 (s, 3H, Me-4), 1.54 (s, 3H, Me-5), 1.23 (t, 3H, *J*=7.2 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 171.1 (CO_2Et), 141.1 (Ar), 140.6 (Ar), 129.6 (Ar), 126.5 (Ar), 122.9 (C-4), 122.8 (C-5), 61.0 (OCH_2), 55.5 (C-2), 47.0 (C-6), 33.9 (C-3), 21.3 (ArCH_3), 18.8 (Me-5), 15.8 (Me-4), 14.1 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}) of a racemic sample **(2*R**,R_S^*)-4d** (*p*-Tol): t_R 33.3 and 37.2 min. Data for **(2*R*,S_S)-4d** (*p*-Tol): R_f (EtOAc/*n*-hexane, 1:1)=0.40. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 31.5 min. ^{1}H NMR (300 MHz): δ 7.65 (app. d, 2H, *J*=8.4 Hz, tolyl), 7.32 (app. d, 2H, *J*=8.4 Hz, tolyl), 4.41 (dd, 1H, *J*=6.3, 2.5 Hz, H-2), 4.22 (q, 2H, *J*=7.2 Hz, OCH_2), 3.38 (app. d, 1H, *J*=17 Hz, H-6), 3.25 (app. d, 1H, *J*=17 Hz, H-6), 2.63–2.36 (m, 2H, H-3), 2.42 (s, 3H, ArCH_3), 1.64 (s, 3H, Me-4), 1.49 (s, 3H, Me-5), 1.29 (t, 3H, *J*=7.2 Hz, OCH_2CH_3). ^{13}C NMR: δ 171.6 (CO_2Et), 141.1 (Ar), 140.3 (Ar), 129.5 (Ar), 126.5 (Ar), 123.0 (C-4), 122.6 (C-5), 61.2 (OCH_2), 58.2 (C-2), 43.2 (C-6), 33.8 (C-3), 21.3 (ArCH_3), 18.8 (Me-4), 15.9 (Me-5), 14.1 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2*R**,S_S^*)-4d** (*p*-Tol): t_R 31.5 and 42.5 min.

4.2.7. Ethyl (2S,6S,S_S)-1-(tert-butylsulfinyl)-6-methyl-1,2,3,6-tetrahydropyridine-2-carboxylate, **(2S,6S,S_S)-4e**, and ethyl (2S,6R,S_S)-1-(tert-butylsulfinyl)-6-methyl-1,2,3,6-tetrahydropyridine-2-carboxylate, **(2S,6R,S_S)-4e**

The asymmetric aza-DA reaction between sulfinimine **2a** and (*E*)-1,3-pentadiene (**3e**) according to the general procedure afforded a mixture of **(2*S*,6*S*,S_S)-4e** and **(2*S*,6*R*,S_S)-4e**, which were separated by flash chromatography (two columns: first EtOAc/*n*-hexane, 1:1, and then Et_2O/*n*-pentane. 1:1). Data for **(2*S*,6*S*,S_S)-4e**: viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.4. $[\alpha]_D^{rt}$ −50 (*c* 0.77, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 12.0 min. ^1H NMR (400 MHz): δ 5.84 (app. ddt, 1H, *J*=10.4, 6.4, 3.4 Hz, H-4), 5.59 (app. dtd, 1H, *J*=10.4, 3.0, 0.8 Hz, H-5), 4.51 (dd, 1H, *J*=6.8, 1.3 Hz, H-2), 4.19 (dq, 1H, *J*=10.6, 7.2 Hz, OCH_2), 4.17 (dq, 1H, *J*=10.6, 7.2 Hz, OCH_2), 3.98 (m, 1H, H-6), 2.54 (app. dd, 1H, *J*=17.2, 6.4 Hz, H-3), 2.35 (app. ddtd, 1H, *J*=17.2, 6.8, 3.1, 2.4 Hz, H-3), 1.28 (t, 3H, *J*=7.2 Hz, OCH_2CH_3), 1.25 (s, 9H, *t*-Bu), 1.24 (d, 3H, *J*=7.2 Hz, Me-6). ^{13}C NMR (100 MHz): δ 173.0 (CO_2Et), 128.8 (C-5), 123.4 (C-4), 61.2 (OCH_2), 58.3 (CMe_3), 55.0 (C-6), 48.7 (C-2), 26.3 (C-3), 22.9 (CMe_3), 22.7 (Me-6), 14.1 (OCH_2CH_3). IR (thin film, NaCl): 3034 (w), 2979 (m), 2954 (m), 2931 (m), 1735 (s), 1456 (m), 1368 (m), 1283 (m), 1210 (m), 1189 (s), 1135 (m), 1103 (m), 1075 (s), 1040 (m), 970 (m) cm^{-1}. Anal. Calcd for $C_{13}H_{23}NO_3S$: C, 57.11; H, 8.48; N, 5.12; S, 11.73. Found: C, 57.05; H, 8.34; N, 5.06; S, 11.57. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 mL min^{-1}, 230 nm) of a racemic sample **(2R^*,6R^*,R_S^*)-4e**: t_R 10.2 and 12.1 min. Data for **(2*S*,6*R*,S_S)-4e**: viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.3. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 14.2 min. ^1H NMR (400 MHz): δ 5.78 (dddd, 1H, *J*=10.2, 4.3, 3.5, 2.0 Hz, H-4), 5.64 (app. ddt, 1H, *J*=10.2, 3.0, 2.0 Hz, H-5), 4.28 (m, 1H, H-2), 4.24 (dq, 1H, *J*=10.8, 7.1 Hz, OCH_2), 4.18 (m, 1H, H-6), 4.16 (dq, 1H, *J*=10.8, 7.1 Hz, OCH_2), 2.62 (m, 1H, H-3), 2.39 (m, 1H, H-3), 1.35 (d, 3H, *J*=7.1 Hz, Me-6), 1.28 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.23 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz, selected signals): δ 131.3 (C-5), 123.7 (C-4), 61.2 (OCH_2), 59.1 (CMe_3), 53.6 (C-2), 48.4 (C-6), 27.2 (C-3), 23.5 (CMe_3), 20.1 (Me-6), 14.2 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2R^*,6S^*,R_S^*)-4e**: t_R 14.4 and 17.2 min.

4.2.8. Ethyl (2S,3R,6S,S_S)-1-(tert-butylsulfinyl)-3,6-dimethyl-1,2,3,6-tetrahydropyridine-2-carboxylate, **(2S,3R,6S,S_S)-4f**, and ethyl (2S,3S,6R,S_S)-1-(tert-butylsulfinyl)-3,6-dimethyl-1,2,3,6-tetrahydropyridine-2-carboxylate, **(2S,3S,6R,S_S)-4f**

The asymmetric aza-DA reaction between sulfinimine **2a** and (*E*,*E*)-2,4-hexadiene (**3f**) according to the general procedure afforded a mixture of **(2*S*,3*R*,6*S*,S_S)-4f** and **(2*S*,3*S*,6*R*,S_S)-4f**, which were separated by flash chromatography (EtOAc/*n*-hexane, 1:5). Data for **(2*S*,3*R*,6*S*,S_S)-4f**: viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.4. $[\alpha]_D^{rt}$ −87 (*c* 1.35, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 10.6 min. ^1H NMR (400 MHz): δ 5.59 (m, 2H, H-4 and H-5), 4.38 (d, 1H, *J*=6.3 Hz, H-2), 4.17 (dq, 1H, *J*=10.8, 7.1 Hz, OCH_2), 4.14 (dq, 1H, *J*=10.8, 7.1 Hz, OCH_2), 4.03 (app. qd, 1H, *J*=7.1, 3.1 Hz, H-6), 2.58 (m, 1H, H-3), 1.30 (d, 3H, *J*=7.1 Hz, Me-6), 1.27 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.24 (s, 9H, *t*-Bu), 1.07 (d, 3H, *J*=7.5 Hz, Me-3). ^{13}C NMR (100 MHz): δ 170.9 (CO_2Et), 128.3 (C-4), 128.1 (C-5), 60.5 (OCH_2), 58.1 (CMe_3), 54.7 (C-6), 53.0 (C-2), 31.8 (C-3), 23.4 (CMe_3), 23.0 (Me-6), 17.3 (Me-3), 14.2 (OCH_2CH_3). IR (thin film, NaCl): 3029 (w), 2972 (m), 2933 (m), 1744 (s), 1458 (m), 1367 (m), 1156 (s), 1073 (s), 1029 (m), 979 (m) cm^{-1}. MS (ESI) *m*/*z* (% rel int): 310 (M^++Na, 16), 288 (M^++1, 2), 185 (10), 184 (100). HRMS (ESI) calcd for $C_{14}H_{25}NNaO_3S$ 310.1447 (M^++Na), found 310.1447. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2R^*,3S^*,6R^*,R_S^*)-4f**: t_R 8.7 and 10.6 min. Data for **(2*S*,3*S*,6*R*,S_S)-4f**: viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.3. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 11.2 min. ^1H NMR (400 MHz): δ 5.62 (m, 1H, H-4), 5.60 (m, 1H, H-5), 4.24 (m, 1H, H-6), 4.12 (app. q, 2H, *J*=7.1 Hz, OCH_2), 3.93 (br d, 1H, *J*=5.4 Hz, H-2), 2.79 (m, 1H, H-3), 1.37 (d, 3H, *J*=6.9 Hz, Me-6), 1.26 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.18 (s, 9H, *t*-Bu), 1.08 (t, 3H, *J*=6.9 Hz, Me-3). ^{13}C NMR (100 MHz): δ 171.2 (CO_2Et), 60.4 (OCH_2), 58.9 (C-2), 48.4 (C-6), 20.2 (Me-6), 19.2 (Me-3), 14.1 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(2R^*,3R^*,6S^*,R_S^*)-4f**: t_R 11.2 and 15.9 min.

4.2.9. Ethyl (1S,3S,4R,S_S)-2-(tert-butylsulfinyl)-2-azabicyclo[2.2.1]hept-5-ene-3-carboxylate, **(1S,3S,4R,S_S)-4g** (*t*-Bu), and ethyl (1R,3S,4S,S_S)-2-(tert-butylsulfinyl)-2-azabicyclo[2.2.1]-hept-5-ene-3-carboxylate, **(1R,3S,4S,S_S)-4g** (*t*-Bu)

The asymmetric aza-DA reaction between sulfinimine **2a** and cyclopentadiene (**3g**) according to the general procedure afforded either **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu) pure or as a mixture of **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu) and **(1*R*,3*S*,4*S*,S_S)-4g** (*t*-Bu). In addition various amounts of **8**, **9**, and **10** were formed dependent on the reaction conditions applied (see Table 2, entries 3–5). The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:5). The mixture of **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu) and **(1*R*,3*S*,4*S*,S_S)-4g** (*t*-Bu) was inseparable. Anal. Calcd of the mixture $C_{13}H_{21}NO_3S$: C, 57.54; H, 7.80; N, 5.16; S, 11.82. Found: C, 57.25; H, 7.64; N, 5.20; S, 12.10. Data for **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu): viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.35. $[\alpha]_D^{rt}$ −134 (*c* 1.17, $CHCl_3$). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 18.2 min. ^1H NMR (400 MHz): δ 6.50 (dd, 1H, *J*=5.6, 2.1 Hz, H-6), 6.35 (m, 1H, H-5), 4.28 (m, 1H, H-1), 4.21 (dq, 1H, *J*=10.9, 7.1 Hz, OCH_2), 4.18 (dq, 1H, *J*=10.9, 7.1 Hz, OCH_2), 3.62 (s, 1H, H-3), 3.32 (m, 1H, H-4), 2.10 (ddd, 1H, *J*=8.7, 1.9, 1.5 Hz, H-7*syn*), 1.35 (app. d, 1H, *J*=8.7 Hz, H-7*anti*), 1.28 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.14 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 173.0 (CO_2Et), 136.5 (C-5), 135.2 (C-6), 68.5 (C-1), 61.0 (OCH_2), 57.4 (CMe_3), 53.5 (C-3), 50.5 (C-4), 45.1 (C-7), 22.7 (CMe_3), 14.2 (OCH_2CH_3). IR (thin film, NaCl): 3067 (w), 2957 (m), 1743 (s), 1448 (m), 1362 (m), 1243 (m), 1188 (s), 1081 (m), 1061 (m), 963 (m), 875 (s) cm^{-1}. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(1R^*,3R^*,4S^*,R_S^*)-4g** (*t*-Bu): t_R 18.3 and 25.7 min. Data for **(1*R*,3*S*,4*S*,S_S)-4g** (*t*-Bu): viscous colorless oil. R_f (EtOAc/*n*-hexane, 1:1)=0.35. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 20.9 min. ^1H NMR (400 MHz): δ 6.45 (app. dd, 1H, *J*=5.6, 3.0 Hz, H-6), 6.20 (app. dd, 1H, *J*=5.6, 2.8 Hz, H-5), 4.47 (d, 1H, *J*=3.5 Hz, H-3), 4.43 (m, 1H, H-1), 4.13 (q, 2H, *J*=7.1 Hz, OCH_2), 3.49 (m, 1H, H-4), 1.90 (app. dt, 1H, *J*=8.5, 1.5 Hz, H-7*syn*), 1.55 (app. d, 1H, *J*=8.5 Hz, H-7*anti*), 1.25 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.17 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 172.1 (CO_2Et), 137.5 (C-5), 136.6 (C-6), 73.7 (C-1), 60.8 (OCH_2), 57.7 (CMe_3), 52.7 (C-3), 48.7 (C-7), 22.9 (CMe_3), 14.3 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(1R^*,3S^*,4S^*,S_S^*)-4g** (*t*Bu): t_R 16.7 and 21.0 min.

4.2.10. Ethyl (3S,3aS,6aS,R_S)-1-oxo-3,3a,4,6a-tetrahydro-2H-cyclopenta[d]isothiazole-3-carboxylate (**8**) and ethyl (3S,3aR,6aR,R_S)-1-oxo-3,3a,4,6a-tetrahydro-2H-cyclopenta[d]isothiazole-3-carboxylate (**9**)

The general procedure for the asymmetric aza-DA reaction was followed by reacting **2a** with **3g** using $BF_3{\cdot}OEt_2$ as the Lewis acid and 17.5 h reaction time at room temperature (Table 2, entry 5). Flash chromatography (EtOAc/*n*-hexane, 1:1) purification of the crude product, after work up, provided an inseparable mixture (viscous oil) of **8** and **9** (ratio 9.5:1, 22.4 mg, 42% total yield). Compound **8** was further purified by recrystallization from EtOAc/*n*-hexane, providing colorless crystals (9.3 mg, 17%). Data for **8**: R_f (acetone)=0.5. GC [CP Chirasil Dex CB, 80 °C (0 min)–4 °C min^{-1}–190 °C (2 min)]: t_R 24.2 min. ^1H NMR (400 MHz): δ 5.92 (app. dq, 1H, *J*=5.8, 2.0 Hz, H-5), 5.85 (app. dq, 1H, *J*=5.8, 2.3 Hz, H-6), 5.12

(dd, 1H, J=5.8, 1.0 Hz, H-3), 4.68 (br s, 1H, NH), 4.32 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 4.25 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 4.17 (m, 1H, H-6a), 3.57 (app. ddtd, 1H, J=9.1, 7.5, 5.7, 1.2 Hz, H-3a), 2.61 (app. ddtd, 1H, J=17.6, 9.1, 2.2, 0.9 Hz, H-4), 2.18 (app. dddt, 1H, J=17.6, 5.6, 3.3, 2.4 Hz, H-4′), 1.32 (t, 3H, J=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 170.0 (CO_2Et), 137.9 (C-5), 123.9 (C-6), 85.6 (C-6a), 64.5 (C-3), 61.7 (OCH_2), 41.8 (C-3a), 35.9 (C-4), 14.24 (OCH_2CH_3). IR (thin film, NaCl): 3447 (br), 3135 (br), 1733 (s), 1379 (m), 1265 (m), 1255 (m), 1243 (m), 1218 (m), 1107 (m), 1037 (s) cm^{-1}. MS (ESI) m/z (% rel int.): 238 (M^++Na, 100), 216 (M^++1, 26). HRMS (ESI) calcd for $C_9H_{14}NO_3S$ 216.0689 (M^++1), found 216.0684. HRMS (ESI) calcd for $C_9H_{13}NNaO_3S$ 238.0508 (M^++Na), found 238.0509. The absolute configuration of **8** was corroborated by X-ray crystallographic analysis.[16] GC [CP Chirasil Dex CB, 80 °C (0 min)–4 °C min^{-1}–190 °C (2 min)] of racemic **8**: t_R 23.6 and 24.4 min. Data for **9**: GC [CP Chirasil Dex CB, 80 °C (0 min)–4 °C min^{-1}–190 °C (2 min)]: t_R 23.4 min. ^{1}H NMR (400 MHz): δ 6.14 (app. dq, 1H, J=5.8, 1.9 Hz, H-5), 5.65 (app. dq, 1H, J=5.8, 2.3 Hz, H-6), 4.63 (m, 1H, H-6a), 4.60 (m, 1H, NH), 4.47 (dd, 1H, J=8.0, 1.8 Hz, H-3), 4.26 (overlap, 2H, OCH_2), 3.27 (dddd, 1H, J=9.6, 8.9, 8.0, 4.0 Hz, H-3a), 2.76 (app. ddtd, 1H, J=17.6, 8.9, 2.4, 1.6 Hz, H-4), 2.56 (overlap, 1H, H-4′), 1.32 (overlap, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 171.1 (CO_2Et), 137.6 (C-5), 123.4 (C-6), 78.7 (C-6a), 67.1 (C-3), 61.9 (OCH_2), 44.8 (C-3a), 37.3 (C-4), 14.17 (OCH_2CH_3).

4.2.11. *Ethyl (3S,3aS,6aS,R_S)-1-oxo-3,3a,4,6a-tetrahydro-2H-cyclopenta[d]isothiazole-3-carboxylate (**8**) and 2-methyl-N-(2-oxo-3,3a,4,6a-tetrahydro-2H-cyclopenta[b]-furan-3-yl) propane-2-sulfinamide (**10**)*

The asymmetric aza-DA reaction between sulfinimine **2a** and **3g** using TMSOTf as the Lewis acid at −78 °C for 15.5 h (Table 2, entry 3) afforded a mixture of **8** and **10** after flash chromatography (EtOAc/*n*-hexane, 1:1). Further purification by flash chromatography (acetone/pentane, 1:4) allowed separation of **8** (9.0 mg, 17%) and **10** (6.6 mg, 11%). For analytical data of **8** see Section 4.2.10. Data for **10**: colorless viscous oil, R_f (acetone)=0.6. GC [CP Chirasil Dex CB, 80 °C (0 min)–3 °C min^{-1}–190 °C (2 min)]: t_R 29.67 min. ^{1}H NMR (400 MHz): δ 6.10 (m, 1H, H-5), 5.91 (app. ddt, 1H, J=5.8, 2.6, 1.8 Hz, H-6), 5.59 (app. dp, 1H, J=7.8, 1.6 Hz, H-6a), 3.95 (dd, 1H, J=7.7, 2.0 Hz, H-3), 3.92 (br s, 1H, NH), 3.10 (app. qd, 1H, J=7.7, 1.5 Hz, H-3a), 2.81 (app. dddt, 1H, J=17.4, 7.1, 2.5, 2.1 Hz, H-4), 2.72 (m, 1H, H-4′), 1.27 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 175.2 (C-2), 136.5 (C-5), 129.2 (C-6), 88.0 (C-6a), 58.4 (C-3), 56.2 (CMe_3), 44.1 (C-3a), 37.3 (C-4), 22.4 (CMe_3). IR (thin film, NaCl): 3442 (br), 3279 (br), 1774 (s), 1641 (m), 1365 (m), 1134 (m), 1042 (s), 991 (m) cm^{-1}. MS (ESI) m/z (% rel int.): 266 (M^++Na, 18), 244 (M^++1, 100), HRMS (ESI) calcd for $C_{11}H_{18}NO_3S$ 244.1002 (M^++1), found 244.1001. HRMS (ESI) calcd for $C_{11}H_{17}NNaO_3S$ 266.0821 (M^++Na), found 266.0819. GC [CP Chirasil Dex CB, 80 °C (0 min)–3 °C min^{-1}–190 °C (2 min)] of racemic **10**: t_R 29.66 and 29.81 min.

4.2.12. *Ethyl (1S,3S,4R,S_S)-2-(p-tolylsulfinyl)-2-azabicyclo[2.2.1]hept-5-ene-3-carboxylate, **(1S,3S,4R,S_S)-4g** (p-Tol), ethyl (1R,3S,4S,S_S)-2-(p-tolylsulfinyl)-2-azabicyclo[2.2.1]hept-5-ene-3-carboxylate, **(1R,3S,4S,S_S)-4g** (p-Tol), and ethyl (1R,3R,4S,S_S)-2-(p-tolylsulfinyl)-2-azabicyclo[2.2.1]hept-5-ene-3-carboxylate, **(1R,3R,4S,S_S)-4g** (p-Tol)*

The asymmetric aza-DA reaction between sulfinimine **2b** and cyclopentadiene (**3g**) according to the general procedure yielded mixtures of **(1S,3S,4R,S_S)-4g** (*p*-Tol), **(1R,3S,4S,S_S)-4g** (*p*-Tol), and **(1R,3R,4S,S_S)-4g** (*p*-Tol) dependent on the reaction conditions applied (see Table 1, entries 13 and 14). Separation of the diastereomers by flash chromatography (EtOAc/*n*-hexane, 15:85 to 25:75) did not succeed, but recrystallization of the mixture from 10% *i*-PrOH in *n*-hexane afforded the major isomer **(1S,3S,4R,S_S)-4g** (*p*-Tol) as a white solid (97% de). Data for **(1S,3S,4R,S_S)-4g** (*p*-Tol): R_f (EtOAc/*n*-hexane, 25:75)=0.1. Mp=78–79 °C (from 10% *i*-PrOH in *n*-hexane). $[\alpha]_D^{rt}$ +20.7 (*c* 1.07, CH_2Cl_2). ^{1}H NMR (400 MHz): δ 7.53 (app. d, 2H, J=8 Hz, tolyl), 7.23 (app. d, 2H, J=8 Hz, tolyl), 6.53 (dd, 1H, J=5.2, 2.2 Hz, H-6), 6.35 (m, 1H, H-5), 4.62 (m, 1H, H-1), 3.69 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 3.62 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 3.42 (s, 1H, H-3), 3.13 (br s, 1H, H-4), 2.36 (s, 3H, ArCH_3), 2.22 (br d, 1H, J=8.6 Hz, H-7), 1.45 (br d, 1H, J=8.6 Hz, H-7), 0.94 (t, 3H, J=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 171.7 (CO_2Et), 141.1 (Ar), 140.7 (Ar), 135.5 (C-6), 135.3 (C-5), 129.03 (Ar), 125.77 (Ar), 67.2 (C-1), 60.6 (OCH_2), 53.0 (C-3), 49.7 (C-4), 46.2 (C-7), 21.2 (ArCH_3), 13.7 (OCH_2CH_3). IR (KBr tablet): 2990 (m), 2959 (m), 2929 (m), 1724 (s), 1474 (m), 1449 (m), 1370 (m), 1252 (m), 1234 (m), 1191 (s), 1167 (s), 1094 (s), 1069 (s), 1053 (s), 1024 (m), 964 (s) cm^{-1}. MS (EI) m/z (% rel int): 305 (M^+, 3), 257 (7), 240 (12), 232 (11), 166 (11), 141 (5), 140 (15), 139 (100), 138 (3), 123 (86), 120 (5), 94 (5), 93 (84), 92 (17), 91 (16), 77 (5), 67 (7), 66 (22), 65 (15). Anal. Calcd for $C_{16}H_{19}NO_3S$: C, 62.93; H, 6.27; N, 4.59; S, 10.50. Found: C, 62.97; H, 6.32, N, 4.35; S, 10.22. Data for **(1R,3S,4S,S_S)-4g** (*p*-Tol): ^{1}H NMR (400 MHz): δ 7.55 (app. d, 2H, J=8.3 Hz, tolyl), 7.21 (overlap, 2H, tolyl), 6.63 (dd, 1H, J=5.5, 3.0 Hz, H-6), 6.16 (dd, 1H, J=5.5, 2.6 Hz, H-5), 4.62 (overlap, 1H, H-1), 4.32 (d, 1H, J=3.2H, H-3), 3.7–3.6 (overlap, 2H, OCH_2), 3.42 (overlap, 1H, H-4), 2.35 (s, 3H, ArCH_3), 2.06 (br d, 1H, J=8.4 Hz, H-7), 1.63 (br d, 1H, J=8.4 Hz, H-7), 0.92 (overlap, 3H, OCH_2CH_3). ^{13}C NMR (100 MHz, selected signals): δ 137.8 (C-6), 137.1 (C-5), 129.01 (Ar), 125.82 (Ar), 69.8 (C-1), 60.3 (OCH_2), 52.3 (C-3), 49.0 (C-7), 47.3 (C-4), 14.2 (OCH_2CH_3). Data for **(1R,3R,4S,S_S)-4g** (*p*-Tol): ^{1}H NMR (400 MHz): δ 7.72 (app. d, 2H, J=8 Hz, tolyl), 7.33 (app. d, 2H, J=8 Hz, tolyl), 6.44 (dd, 1H, J=5.6, 2.4 Hz, H-6), 6.32 (m, 1H, H-5), 4.29 (q, 2H, J=7.1 Hz, OCH_2), 3.92 (m, 1H, H-1), 3.74 (s, 1H, H-3), 3.42 (overlap, 1H, H-4), 2.43 (s, 3H, ArCH_3), 1.75 (br d, 1H, J=8.9 Hz, H-7), 1.35 (t, 3H, J=7.1 Hz, OCH_2CH_3), 1.32 (overlap, 1H, H-7). ^{13}C NMR (100 MHz): δ 171.9 (CO_2Et), 141.2 (Ar), 141.0 (Ar), 138.0 (C-6), 133.8 (C-5), 129.5 (Ar), 126.2 (Ar), 62.0 (C-1), 61.5 (C-3), 61.3 (OCH_2), 49.2 (C-4), 45.8 (C-7), 21.3 (ArCH_3), 14.2 (OCH_2CH_3).

4.2.13. *Ethyl (1S,3S,4R,S_S)-2-(tert-butylsulfinyl)-2-azabicyclo[2.2.2]oct-5-ene-3-carboxylate, **(1S,3S,4R,S_S)-4h**, and ethyl (1R,3S,4S,S_S)-2-(tert-butylsulfinyl)-2-azabicyclo[2.2.2]oct-5-ene-3-carboxylate, **(1R,3S,4S,S_S)-4h***

The asymmetric aza-DA reaction between sulfinimine **2a** and 1,3-cyclohexadiene (**3h**) provided an inseparable mixture of **(1S,3S,4R,S_S)-4h** and **(1R,3S,4S,S_S)-4h**. The crude mixture was purified by flash chromatography (EtOAc/*n*-hexane, 1:5) yielding a viscous colorless oil. Analytical data of the mixture: IR (thin film, NaCl): 3053 (w), 2955 (m), 2929 (m), 1745 (s), 1461 (m), 1363 (m), 1258 (m), 1176 (s), 1085 (s), 1061 (m), 892 (m) cm^{-1}. MS (EI) m/z (% rel int.): 229 (32), 164 (22), 149 (58), 108 (22), 80 (100), 79 (40), 57 (32). MS (ESI) m/z (% rel int.): 308 (M^++Na, 50), 183 (10), 182 (100). HRMS (ESI) calcd for $C_{14}H_{23}NNaO_3S$ 308.1291 (M^++Na), found 308.1288. Anal. Calcd for $C_{14}H_{23}NO_3S$: C, 58.92; H, 8.12; N, 4.91; S, 11.24. Found: C, 59.02; H, 8.12; N, 4.79; S, 11.06. Data for **(1S,3S,4R,S_S)-4h**: R_f (EtOAc/*n*-hexane, 1:1)=0.35. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 18.3 min. ^{1}H NMR (400 MHz): δ 6.52 (ddd, 1H, J=8.2, 5.1, 1.5 Hz, H-6), 6.47 (ddd, 1H, J=8.2, 6.7, 1.6 Hz, H-5), 4.20 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 4.18 (dq, 1H, J=10.8, 7.1 Hz, OCH_2), 4.03 (dd, 1H, J=3.3, 1.6 Hz, H-3), 3.92 (m, 1H, H-1), 3.02 (m, 1H, H-4), 2.20 (dddd, 1H, J=12.9, 9.6, 5.6, 2.7 Hz, H-7*syn*), 1.63 (app. ddt, 1H, J=12.6, 9.6, 2.9 Hz, H-8*syn*), 1.38 (m, 1H, H-7*anti*), 1.28 (t, 3H, J=7.1 Hz, OCH_2CH_3), 1.12 (s, 9H, *t*-Bu), 1.09 (m, 1H, H-8*anti*). ^{13}C NMR (100 MHz): δ 127.2 (CO_2Et), 134.6 (C-5), 133.0 (C-6), 60.8 (OCH_2), 57.5 (CMe_3), 54.8 (C-1), 52.7 (C-3), 33.8 (C-4), 24.3 (C-7), 22.4 (CMe_3), 20.5 (C-8), 14.3 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of

a racemic sample **(1*R**,3*R**,4*S**,*R*S*)-4h**: t_R 18.3 and 20.2 min. Data for **(1*R*,3*S*,4*S*,*S*S)-4h**: R_f (EtOAc/*n*-hexane, 1:1)=0.35. HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): t_R 15.5 min. ^{1}H NMR (400 MHz): δ 6.56 (ddd, 1H, *J*=8.1, 6.7, 1.9 Hz, H-6), 6.19 (app. t, 1H, *J*=7 Hz, H-5), 4.26 (d, 1H, *J*=2.9 Hz, H-3), 4.11 (q, 2H, *J*=7.1 Hz, OCH_2), 4.06 (m, 1H, H-1), 3.10 (m, 1H, H-4), 2.28 (dddd, 1H, *J*=13, 9, 4, 3 Hz, H-7*syn*), 1.74 (dddd, 1H, *J*=13, 9, 5, 2 Hz, H-8*syn*), 1.39 (m, 1H, H-8*anti*), 1.26 (m, 1H, H-7*anti*), 1.23 (t, 3H, *J*=7.1 Hz, OCH_2CH_3), 1.14 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz): δ 172.3 (CO_2Et), 134.3 (C-6), 131.6 (C-5), 60.7 (OCH_2), 57.3 (CMe_3), 54.3 (C-1), 53.1 (C-3), 34.4 (C-4), 26.0 (C-7), 22.8 (CMe_3), 20.4 (C-8), 14.2 (OCH_2CH_3). HPLC (Chiralpak AD, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of a racemic sample **(1*R**,3*S**,4*S**,*S*S*)-4h**: t_R 14.0 and 15.5 min.

4.3. Chemical derivatization of the aza-DA products

4.3.1. Ethyl (2S)-4-oxo-1,2,3,4-tetrahydropyridine-2-carboxylate, ***(2S)-11a***

Diastereomerically pure **(2*S*,*S*S)-4a** (7.4 mg, 0.027 mmol) was dissolved in MeOH (2 mL) and cooled to 0 °C. Aqueous HCl (concd, ~20 equiv) was added and the resultant solution stirred at 0 °C for 5 h before neutralization with phosphate buffer (pH 7, 1.5 mL). The mixture was extracted with CH_2Cl_2 (4×4 mL) and the combined organic layer was dried ($MgSO_4$). The solution was filtered, concentrated, and the residue purified by flash chromatography (EtOAc), providing **(2*S*)-11a** (3.9 mg, 85%) as a white solid. Data for **(2*S*)-11a**: $[\alpha]_D^{rt}$ +276 (*c* 0.39, $CHCl_3$). GC [CP Chirasil Dex CB, 110 °C (0 min)–2 °C min^{-1}–180 °C (2 min)]: >99% ee, t_R 18.1. ^{1}H NMR (400 MHz): δ 7.22 (ddd, 1H, *J*=7.5, 6.3, 0.5 Hz, H-6), 5.41 (br s, 1H, NH), 5.09 (app. d, 1H, *J*=7.5 Hz, H-5), 4.34 (ddd, 1H, *J*=12.8, 6.0, 1.4 Hz, H-2), 4.28 (dq, 1H, *J*=10.7, 7.1 Hz, OCH_2), 4.26 (dq, 1H, *J*=10.7, 7.1 Hz, OCH_2), 2.78 (app. ddt, 1H, *J*=16.4, 6.0, 0.9 Hz, H-3), 2.71 (dd, 1H, *J*=16.4, 12.8 Hz, H-3), 1.31 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). The ^{1}H NMR data is compatible with data reported for the racemic **(2*R**)-11a**.[22] GC [CP Chirasil Dex CB, 110 °C (0 min)–2 °C min^{-1}–180 °C (2 min)] of racemic **(2*R**)-11a**: t_R 18.1 and 18.7 min.

4.3.2. Ethyl (S)-4-methyl-1,2,3,6-tetrahydropyridine-2-carboxylate, ***(2S)-11c***

The aza-DA product **(2*S*,*S*S)-4c** (*t*-Bu) was prepared according to the general procedure (Section 4.2) using TMSOTf (10 equiv) as the Lewis acid and a large excess of isoprene (**3c**, 20 equiv.) at −78 °C for 19 h. The crude product was dissolved in MeOH (3 mL), added aqueous HCl (concd, ~5 mmol), and stirred at room temperature for 18 h. The solution was concentrated, added water (5 mL) and aqueous HCl (concd, one drop), and washed with diethyl ether (9×5 mL) to remove impurities. The aqueous phase was basified with K_2CO_3 and extracted with diethyl ether (6×5 mL). The combined organic phases from the latter extractions were dried ($MgSO_4$), filtered, and concentrated to provide **(2*S*)-11c** (16.7 mg, 39% yield from sulfinimine **1a**) as a colorless viscous oil. Data for **(2*S*)-11c**: $[\alpha]_D^{rt}$ −83 (*c* 0.2, $CHCl_3$). GC [CP Chirasil Dex CB, 80 °C (0 min)–1 °C min^{-1}–110 °C (0 min)–20 °C min^{-1}–180 °C (3 min)]: >99% ee, t_R 13.1 min. ^{1}H NMR (400 MHz): δ 5.43 (m, 1H, H-5), 4.20 (q, 2H, *J*=7.2 Hz, OCH_2), 3.56 (dd, 1H, *J*=8.2, 6.1 Hz, H-2), 3.42 (m, 1H, H-6), 3.38 (m, 1H, H-6), 2.22 (m, 1H, H-3), 2.20 (m, 1H, H-3), 1.70 (m, 3H, Me-4), 1.29 (t, 3H, *J*=7.2 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 173.4 (CO_2Et), 131.5 (C-4), 120.1 (C-5), 60.9 (OCH_2), 55.3 (C-2), 44.2 (C-6), 32.7 (C-3), 23.3 (Me-4), 14.2 (OCH_2CH_3). IR (thin film, NaCl): 3346 (br), 2925 (m), 1736 (s), 1448 (m), 1376 (m), 1181 (s), 1035 (m) cm^{-1}. MS (EI) *m*/*z* (rel int.): 169 (M^+, 8), 148 (20), 96 (100), 94 (24). MS (ESI) *m*/*z* (% rel int.): 170 (M^++1, 100). HRMS (ESI) calcd for $C_9H_{16}NO_2$ 170.1176 (M^++1), found 170.1178. GC [CP Chirasil Dex CB, 80 °C (0 min)–1 °C min^{-1}–110 °C (0 min)–20 °C min^{-1}–180 °C (3 min)] of racemic **(2*R**)-11c**: t_R 12.7 and 13.1 min.

4.3.3. The HCl salt of ethyl (S)-4-methyl-1,2,3,6-tetrahydropyridine-2-carboxylate, ***(2S)-12c***

(a) Enantiopure **(2*S*)-11c** (12.5 mg, 0.0739 mmol) was added to aqueous HCl (concd, ~0.5 mmol) and dried under high vacuum overnight to give **(2*S*)-12c** (15.2 mg, 100%) as a white solid. Data for **(2*S*)-12c**: $[\alpha]_D^{rt}$ −79 (*c* 0.76, EtOH) {lit. data for the (*R*)-enantiomer: $[\alpha]_D^{25}$ +113.7 (*c* 1.0, EtOH)}.[19] ^{1}H NMR (300 MHz): δ 10.2 (br s, 1H, NH), 9.98 (br s, 1H, NH), 5.42 (app. s, 1H, H-5), 4.31 (app. q, 2H, *J*=7.0 Hz, OCH_2), 4.16 (br s, 1H, H-2), 3.96 (app. d, 1H, *J*=15.9 Hz, H-6), 3.38 (m, 1H, H-6), 2.65 (m, 2H, H-3), 1.78 (s, 3H, H-5), 1.32 (t, 3H, *J*=7.0 Hz, OCH_2CH_3). The ^{1}H NMR data are compatible with data reported for the racemic **(2*R**)-12c**.[23]

(b) A mixture of **(2*S*,*S*S)-4c** (*p*-Tol) and **(2*R*,*S*S)-4c** (*p*-Tol, in ratio 3:2, 14.2 mg, 0.046 mmol) was dissolved in MeOH (3 mL), added aqueous HCl (concd, 12 drops), and stirred at room temperature for 4 h. The reaction mixture was concentrated in vacuo to afford a colorless oil, which precipitated by addition of diethyl ether to provide **(2*S*)-12c** (7.4 mg, 78%) as a white salt. $[\alpha]_D^{rt}$ −68.3 (*c* 0.74, EtOH) {lit. data for the (*R*)-enantiomer: $[\alpha]_D^{25}$ +113.7 (*c* 1.0, EtOH)}.[19]

4.3.4. Ethyl (2S)-4-methyl-1-(p-tosyl)-1,2,3,6-tetrahydropyridine-2-carboxylate, ***(2S)-13c***

A mixture of **(2*S*,*S*S)-4c** (*p*-Tol) and **(2*R*,*S*S)-4c** (*p*-Tol, in ratio 3:2, 19.7 mg, 0.064 mmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to −20 °C under argon atmosphere. A solution of *m*-CPBA (32.1 mg, 0.186 mmol) in CH_2Cl_2 (3 mL) was cannulated into the mixture. The resultant mixture was stirred for 5.5 h, and then water (2 mL) and an aqueous saturated solution of K_2CO_3 (3 mL) was added. The mixture was extracted with CH_2Cl_2 (3×5 mL). The combined organic layer was washed with brine (3 mL), dried ($MgSO_4$), filtered, and concentrated. The residue was purified by flash chromatography (EtOAc/*n*-hexane, 18:85) yielding **(2*S*)-13c** (10.6 mg, 51%) as a colorless oil. Data for **(2*S*)-13c**: $[\alpha]_D^{rt}$ +18.7 (*c* 0.33, $CHCl_3$), HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 10:90, 1.0 ml min^{-1}, 230 nm): 42% ee, t_R 23.2 (*R*) and 33.4 (*S*) min. ^{1}H NMR (300 MHz): δ 7.69 (app. d, 2H, *J*=8.3 Hz, tolyl), 7.28 (app. d, 2H, *J*=8.3 Hz, tolyl), 5.33 (s, 1H, H-5), 4.87 (dd, 1H, *J*=6.6, 1.7 Hz, H-2), 4.04–3.88 (m, 3H, H-6/OCH_2), 3.78 (d, 1H, *J*=17.5 Hz, H-6), 2.51–2.35 (m, 2H, H-3), 2.42 (s, 3H, $ArCH_3$), 1.66 (s, 3H, Me-4), 1.08 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 170.4 (CO_2Et), 143.2 (Ar), 136.6 (Ar), 130.3 (C-4), 129.4 (Ar), 127.3 (Ar), 116.9 (C-5), 61.2 (OCH_2), 53.1 (C-2), 42.1 (C-6), 32.3 (C-3), 23.2 (Me-4), 21.5 ($ArCH_3$), 13.9 (OCH_2CH_3). IR (thin film, NaCl): 2976 (w), 1742 (s), 1343 (s), 1197 (s), 1155 (s), 1099 (s) cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO_4S$: C, 59.42; H, 6.54; N, 4.33; S, 9.91. Found: C, 59.20; H, 6.57, N, 4.29; S, 9.93.

4.3.5. Ethyl (S)-4,5-dimethyl-1,2,3,6-tetrahydropyridine-2-carboxylate, ***(2S)-11d***

The aza-DA adduct **(2*S*,*S*S)-4d** (*t*-Bu) was prepared according to the general procedure (Section 4.2) using TMSOTf as the Lewis acid at −78 °C for 18 h. The crude product was hydrolyzed according to the procedure described in Section 4.3.2, afforded **(2*S*)-11d** (25.4 mg, 55% yield from sulfinimine **1a**) as a colorless viscous oil. Data for **(2*S*)-11d**: ^{1}H NMR (400 MHz): δ 4.19 (app. q, 2H, *J*=7.1 Hz, OCH_2), 3.53 (app. t, 1H, *J*=7.1 Hz, H-2), 3.35–3.20 (m, 2H, H-6), 2.25–2.15 (m, 2H, H-3), 1.97 (br s, 1H, NH), 1.64 (m, 3H, Me-4), 1.57 (m, 3H, Me-5), 1.28 (t, 3H, *J*=7.1 Hz, OCH_2CH_3). ^{13}C NMR (100 MHz): δ 173.6 (CO_2Et), 125.2 (C-5), 123.3 (C-4), 60.8 (OCH_2), 55.8 (C-2), 49.4 (C-6), 33.8 (C-3), 18.7 (Me-4), 16.0 (Me-5), 14.2 (OCH_2CH_3). IR (thin film, NaCl): 3438 (br), 2985 (m), 2917 (m), 1736 (s), 1638 (s), 1447 (m), 1373 (m), 1303 (m), 1182 (s), 1131 (m), 1031 (m) cm^{-1}. MS (EI) *m*/*z* (% rel int.): 183 (M^+, 15), 124 (29), 110 (100), 108 (45), 107 (68), 94 (20). HRMS (EI) calcd for $C_{10}H_{17}NO_2$ 183.1259 (M^+), found 183.1253.

4.3.6. Ethyl (2S)-4,5-dimethyl-1-(p-tosyl)-1,2,3,6-tetrahydropyridine-2-carboxylate, **(2S)-13d**

(a) The amine **(2*S*)-11d** (22.4 mg, 0.12 mmol) was tosylated by following the general procedure described by Murty et al.[20] The crude product was purified by flash chromatography (EtOAc/*n*-hexane, 1:10) providing **(2*S*)-13d** (8.4 mg, 21%) as a light yellow, viscous oil. Data for **(2*S*)-13d**: R_f (EtOAc/*n*-hexane, 1:10)=0.1. $[\alpha]_D^{rt}$ +16.6 (*c* 0.15, $CHCl_3$) {lit. 65% ee, $[\alpha]_D^{rt}$ +17.4 (*c* 0.4, $CHCl_3$)}.[3e] HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): >99% ee, t_R 36.6 min. HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm) of racemic **(2R^*)-13d**: t_R 27.8 and 37.0 min.

(b) A mixture of **(2*S*,S_S)-4d** (*p*-Tol) and **(2*R*,S_S)-4d** (*p*-Tol, in ratio 4:1, 27.5 mg, 0.086 mmol) was oxidized according to the procedure shown in Section 4.3.4. Flash chromatography (EtOAc/*n*-hexane, 1:10) of the crude product afforded **(2*S*)-13d** (3.6 mg, 12%) as a colorless oil. Data for **(2*S*)-13d**: $[\alpha]_D^{rt}$ +13.4 (*c* 0.36, $CHCl_3$), {lit. 65% ee, $[\alpha]_D^{rt}$ +17.4 (*c* 0.40, $CHCl_3$)}.[3e] HPLC (Chiralcel OJ, *i*-PrOH/*n*-hexane, 2:98, 1.0 ml min^{-1}, 230 nm): 72% ee, t_R 30.8 (*R*) and 40.6 (*S*) min.

4.3.7. Ethyl (1S,3S,4R)-2-(p-tosyl)-2-azabicyclo[2.2.1]hept-5-ene-3-carboxylate, **(1*S*,3*S*,4*R*,S_S)-13g**

(a) Pure **(1*S*,3*S*,4*R*,S_S)-4g** (*t*-Bu, 0.130 g, 0.48 mmol) was dissolved with stirring in MeOH (4 mL) and treated with 4.0 M HCl in dioxane (0.610 mL, 2.44 mmol) at room temperature for 4 h.[5e] The reaction mixture was concentrated under reduced pressure. The residue was dissolved with stirring by addition of dry CH_2Cl_2 (2 mL) and triethylamine (0.214 mL, 1.54 mmol), and then cooled to 0 °C. A solution of *p*-TsCl (92.7 mg, 0.486 mmol) in dry CH_2Cl_2 (3 mL) was cannulated into the mixture. The resultant mixture was stirred for 5 h at 0 °C and then warmed to room temperature. The reaction mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography (EtOAc/*n*-hexane, 15:85 to 20:80) affording **(1*S*,3*S*,4*R*,S_S)-13g** (0.103 g, 67%) as a white solid. Data for **(1*S*,3*S*,4*R*,S_S)-13g**: R_f (EtOAc/*n*-hexane, 1:5)=0.1.$[\alpha]_D^{rt}$ −241.1 (*c* 1.0, $CHCl_3$), {lit. 83% ee, $[\alpha]_D^{rt}$ −195.7 (*c* 1.0, $CHCl_3$)}.[3e] ^{1}H NMR (400 MHz): δ 7.77 (app. d, 2H, *J*=8.3 Hz, Ts), 7.28 (m, 2H, Ts), 6.26 (m, 1H, H-5 or H-6), 6.21 (app. dd, 1H, *J*=5.6, 2.1 Hz, H-5 or H-6), 4.59 (m, 1H, H-1), 4.18 (app. q, 2H, *J*=7.1 Hz, OCH_2), 3.50 (m, 1H, H-3), 3.32 (m, 1H, H-4), 2.43 (s, 3H, Ts), 2.06 (app. dt, 1H, *J*=8.7, 1.7 Hz, H-7*syn*), 1.47 (app. d, 1H, *J*=8.7 Hz, H-7*anti*), 1.26 (t, 3H, *J*=7.1 Hz, OCH_2CH_3).

(b) The *p*-tolylsulfinyl aza-DA adduct **(1*S*,3*S*,4*R*,S_S)-4g** (*p*-Tol, 0.068 mmol, 97% de) was oxidized according to the procedure shown in Section 4.3.4. Flash chromatography (EtOAc/*n*-hexane, 15:85) of the crude product afforded **(1*S*,3*S*,4*R*,S_S)-13g** in 46% yield as a white solid. Data for **(1*S*,3*S*,4*R*,S_S)-13g**: $[\alpha]_D^{rt}$ −244 (*c* 0.5, $CHCl_3$) {lit. 83% ee, $[\alpha]_D^{rt}$ −195.7 (*c* 1.0, $CHCl_3$)}.[3e] HPLC (Chiralcel OD-H, *i*-PrOH/*n*-hexane, 5:95, 0.5 mL min^{-1}, 230 nm): 97% ee, t_R 27.2 (major) and 35.4 min (minor).

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