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New approach to exclusive formation of both enantiomers of β-amino acid derivatives

Teresa M.V.D. Pinho e Melo [a,*], Ana Lúcia Cardoso [a], Francisco Palacios [b], Jesús M. de los Santos [b], Alberto A.C.C. Pais [a], Paulo E. Abreu [a], José A. Paixão [c], Ana Matos Beja [c], Manuela Ramos Silva [c]

[a] Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal
[b] Department of Organic Chemistry I, Faculty of Pharmacy, University of the Basque Country, Apartado 450, 01080 Vitoria, Spain
[c] Department of Physics, University of Coimbra, 3004-516 Coimbra, Portugal

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ABSTRACT

A highly selective two-step approach to chiral β-amino esters via the hydride reductive amination of chiral allenes is reported. β-Enamino esters were obtained from the nucleophilic addition of amines to 2,3-allenoates bearing a chiral auxiliary. The reduction of the (1*R*)-(−)-10-phenylsulfonylisobornyl β-enamino esters gave the corresponding β-amino esters with *S* configuration whereas the reduction of the (1*S*)-(+)-10-phenylsulfonylisobornyl β-enamino esters led to β-amino esters with *R* configuration. The rationalization of the observed selectivity was supported by semi-empirical molecular orbital calculations (PM3).

1. Introduction

The design of new synthetic methodologies for the asymmetric synthesis of β-amino acids is a research area of considerable current interest.[1] The importance of this class of compounds lies in their unique biological properties, their occurrence in natural products, and their use as precursors of biologically and medicinally important molecules. β-Amino acids are precursors of β-lactams and are present in a variety of bioactive molecules such as taxol, one of the most active antitumor agents. Furthermore, β-amino acids, although not as abundant as their α-analogues, are also segments in peptide natural products with various biological activities. There is also considerable interest in the synthesis of unnatural β-amino acids for the construction of β-peptides, which are a class of unnatural biopolymers that present interesting secondary structures, as well as increased potency and enzymatic stability.[2–7]

Asymmetric hydrogenation of β-enamino esters has been used to prepare β-enamino acids either by the use of chiral auxiliaries or by the use of chiral catalysts.[8] Stereoselective reduction of fluorinated β-enamino esters obtained from fluorinated imidoyl chlorides and chiral ester enolates has been reported.[9] However, in the reported Lewis acid/$NaBH_4$ reduction of β-enamino esters bearing a chiral auxiliary in the ester moiety, the higher diastereoselectivity was obtained by the use of (−)-8-phenylmenthol group (de 60%).[9] On the other hand, the stereoselective reduction of β-enamino esters using sodium triacetoxyborohydride in acetic acid has also been reported.[10] In this case, the β-enamino esters were prepared from the condensation of chiral amines with β-keto esters or by acylation of lithium imines with carbonates or chloroformates. Moderate asymmetric induction was observed, ranging from de 30% to 69% and the stereochemistry outcome was determined by the bulkiness of the substituent at the β-position. Therefore, the trend of asymmetric induction was not modulated by the nature of the chiral auxiliary.[10]

In connection with our interest in the chemistry of amino ester derivatives,[11] in this paper an alternative and highly selective two-step approach to chiral β-amino esters with control of the stereochemistry outcome via the hydride reductive amination of chiral allenes is reported.

2. Results and discussion

Functionalized hydrazones,[12] oximes,[13] and β-enamines[14] can be obtained from the nucleophilic addition of hydrazines, hydroxylamines, or amines, respectively, to allenes.[15] If allenes bearing a chiral auxiliary are used chiral β-amino esters could be obtained. We have previously described a new asymmetric Wittig reaction that allows the synthesis of allenic esters with axial chirality.[16] The

* Corresponding author. Tel.: +351 239 854475.
E-mail address: tmelo@ci.uc.pt (T.M.V.D. Pinho e Melo).

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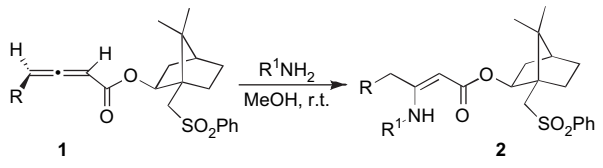
reaction between 10-phenylsulfonylisobornyl (triphenylphosphoranylidene)acetates and ketenes results in asymmetric induction: the use of (1*R*)-(−)-10-phenylsulfonylisoborneol unit allows the synthesis of allenes with *S* configuration, whereas use of the (1*S*)-(+)-10-phenylsulfonylisoborneol unit produces allenes with *R* configuration. Having available these allene derivatives we set out to explore their reactivity toward amines and to study the reduction of the corresponding β-enamino esters in order to find a route to chiral β-amino esters.

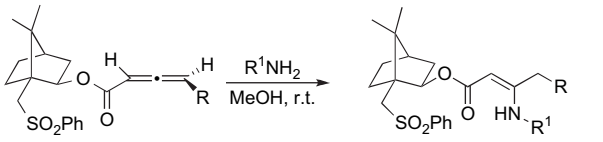
The synthesis of (1*R*)-(−)-10-phenylsulfonylisobornyl β-enamino esters (**2**) was achieved by carrying the reaction at room temperature of the corresponding allenic esters (**1**) with the selected amines (benzylamine, 4-methoxyaniline, and prop-2-en-1-amine) (Table 1). The reaction works smoothly giving the desired products in good to high yields (50–85%). However, the synthesis of β-enamino ester **2c** was carried out by heating the reaction mixture at 45 °C resulting in an improvement of the yield from 38% to 74%. Using the same synthetic methodology (1*S*)-(+)-10-phenylsulfonylisobornyl β-enamino esters (**4**), bearing a chiral auxiliary enantiomeric to the one of β-enamino esters **2**, were also obtained in yields ranging from 61% to 90% (Scheme 1 and Supplementary data).

Table 1
Synthesis of β-enamino esters **2**



Entry	Product	R	R^1	Yield (%)	$[\alpha]_D^{25}$
1	**2a**	H	Bn	75	+30
2	**2b**	Me	Bn	50	+35
3	**2c**	*i*-Pr	Bn	74[a]	+20
4	**2d**	*t*-Bu	Bn	82	+30
5	**2e**	Bn	Bn	84	+35
6	**2f**	H	*p*-$MeOC_6H_4$	85	+20
7	**2g**	H	$CH_2CH{=}CH_2$	76	+30

[a] Reaction mixture heated at 45 °C.



3a R = H
3b R = Me
3c R = *i*-Pr
3d R = *t*-Bu
3e R = Bn

4a R = H; R^1 = Bn
4b R = Me; R^1 = Bn
4c R = *i*-Pr;R^1 = Bn
4d R = *t*-Bu;R^1 = Bn
4e R = R^1= Bn
4f R = H; R^1 = C_6H_4OMe-*p*
4g R = H; R^1 = $CH_2CH{=}CH_2$

Scheme 1.

The downfield chemical shift observed for the N–H proton (8.87–10.11 ppm) of the β-enamino esters (**2** and **4**) is typical of a hydrogen bond with the carbonyl group oxygen, which indicates *Z* configuration.[9] In fact, the structure of β-enamino ester **4d** determined by X-ray crystallography confirms the *Z* enamine geometry (Fig. 1a). It was also observed that in the solid state the compound is stabilized by the intramolecular hydrogen bond between the β-enamino proton and the carbonyl group.

We observed that carrying out the reduction of (1*R*)-(−)-10-phenylsulfonylisobornyl β-enamino esters **2a**–**2g** with sodium triacetoxyborohydride in acetic acid, the corresponding chiral β-amino esters **5** are obtained in good yields (Table 2, entries 1–3, 5–7, 9, and 10). The ^{1}H NMR spectra of β-amino esters **5** showed signals for single diastereoisomer. However, two rotamers are observed in the ^{1}H NMR and ^{13}C NMR spectra of these compounds recorded at ambient temperature but the spectra are simpler at higher temperature. In fact, we found that the ^{1}H NMR spectrum of (1*R*)-(−)-10-phenylsulfonylisobornyl (*S*)-3-(benzylamino)butanoate **5a** recorded at room temperature, showed two sets of signals corresponding to the AB system of the 10-phenylsulfonylisobornyl group but when recorded at 70 °C, showed a single set of signals. The chiral β-amino esters **5** showed positive values for the optical rotation.

Interestingly, the reduction of (1*S*)-(+)-10-phenylsulfonylisobornyl β-enamino esters **4** with sodium triacetoxyborohydride in acetic acid led to the efficient and stereoselective synthesis of β-amino esters **6a**–**6g** (Scheme 2 and Supplementary data), which are enantiomers of the corresponding β-amino esters **5a**–**5g**. In fact, both series of chiral β-amino esters show the same physical properties and values for the optical rotation with opposite sign. The reduction of **4d** led to β-amino ester **6d** in 55% yield together with the recovery of the starting material (45%). However, increasing the reaction time to 18 h compound **6d** could be obtained in 91% yield.

The structure of (1*S*)-(−)-10-phenylsulfonylisobornyl (*R*)-3-(benzylamino)-5,5-dimethylhexanoate **6d** was determined by X-ray crystallography (Fig. 1b). This allowed us to establish the *R* configuration to the new chiral center of β-amino esters **6** and to conclude that the enantiomeric series of β-amino esters **5** must have *S* configuration.

The stereochemical outcome of the β-enamino esters reduction with sodium triacetoxyborohydride in acetic acid can be rationalized as follows (Scheme 3). Ligand exchange between β-enamino esters **2** and one of the acetoxy ligands of $NaHB(OAc)_3$ leads to enol ester-diacetoxyborohydrides **7**. These intermediates undergo intramolecular hydride reduction affording **8**. The chiral auxiliary shields one of the diastereofaces of the protonated imines **7** thus allowing for the observed selectivity. Intermediates **8** are converted into β-amino esters **5** by action of acetic acid.

Semi-empirical molecular orbital calculations using the PM3 Hamiltonian were carried in order to further corroborate the rationalization of the observed selectivity. We concentrated on the reduction of β-enamino ester **2b** with sodium triacetoxyborohydride leading to β-amino ester **5b** (Table 2). Therefore, we have examined the intramolecular hydride transfer in the case of **7b** (R=Me and R^1=Bn) bearing the (1*R*)-(−)-10-phenylsulfonylisobornyl chiral auxiliary.

We have conducted a very thorough search for the transition states corresponding to the two possibilities depicted in Scheme 3, the hydride attack to the two diastereofaces of the immonium function. For the calculation of the transition state (**TS I**), the Hessian (matrix of the second derivatives of the energy in order to the nuclear coordinates) was calculated at every point as to provide a suitable guide for finding the transition state and, also a small enough trust radius (0.01 Å) in order not to overshoot the saddle point. After the localization of this point, its character was confirmed by inspecting the corresponding Hessian matrix, in which only one imaginary frequency should be present. The normal mode associated to the imaginary frequency (i997.78 cm^{-1}) corresponds to the motion of the hydrogen atom between the carbon and boron atoms. In the transition state, this hydrogen is at a distance of 1.407 Å from the boron atom, and 1.529 Å from the carbon atom, with a boron–hydrogen–carbon angle of 129.42° (Fig. 2). The MOPAC charges of the atoms involved directly in this hydrogen transit are q(B)=0.035, q(C)=0.249, and q(H)=−0.026*e*. The corresponding Mulliken charges are q(B)=0.184, q(C)=0.234, and

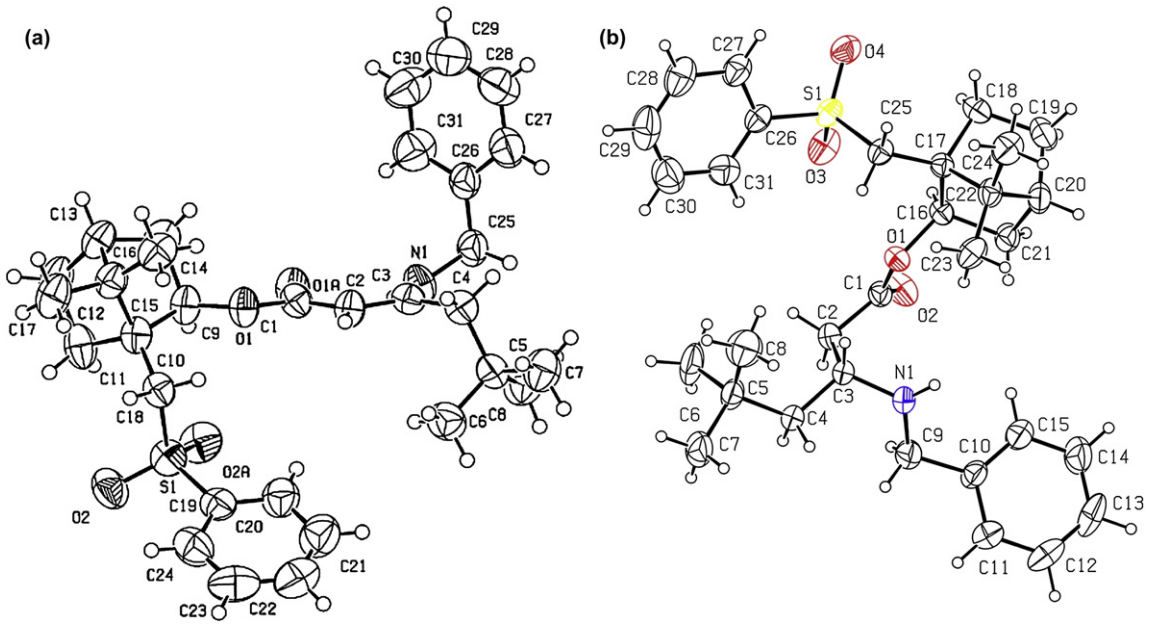


Figure 1. X-ray structures: (a) (1*S*)-(+)-10-phenylsulfonylisobornyl (*Z*)-3-(benzylamino)-5,5-dimethylhex-2-enoate **4d**; (b) (1*S*)-(−)-10-phenylsulfonylisobornyl (*R*)-3-(benzylamino)-5,5-dimethylhexanoate **6d**.

q(H)=−0.047*e*. The bond orders for the two transition state bonds are B.O.(C–H)=0.364 and B.O.(B–H)=0.524. The calculated heat of formation is −318.7 kcal/mol.

For the other transition state (**TS II**), which corresponds to the attack to the more hindered face of the imine, we started from the previous geometry and changed the position of the groups attached to the carbon atom, so as to provide an initial geometry. This search used the same criteria as above, and only one transition state was located with a single imaginary frequency. Inspection of the mode corresponding to this imaginary frequency (i972.20 cm^{-1}) showed that the motion again corresponds to hydrogen atom moving between the carbon and the boron atoms. In the transition state, distance B–H is 1.330 Å, with 1.611 Å for C–H. The B–H–C angle is 133.22°. The MOPAC charges of the atoms involved directly in the hydrogen transit were q(B)=0.062, q(C)=0.268, and q(H)=−0.034*e*, while the Mulliken values are q(B)=0.155, q(C)=0.255, and q(H)=−0.056*e*. In what concerns bond orders, we have B.O.(C–H)=0.294 and B.O.(B–H)=0.597. The heat of formation calculated is −310.6 kcal/mol, i.e., 8.1 kcal/mol above the other one.

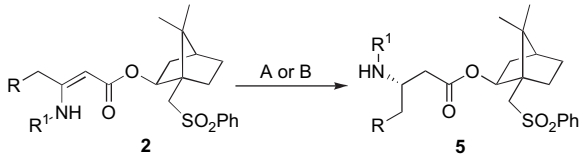
Therefore, the calculated difference in energy between the transition state that leads to the synthesis of β-amino ester **5b** (**TS I**) and the one leading to the corresponding diastereoisomer **9** (**TS II**) justifies the observed exclusive formation of the former.

In a similar way, the stereoselective formation of β-amino esters **6** with *R* configuration from β-enamino esters **4** can be explained considering the intramolecular selective reduction of intermediates **10** (Scheme 4).

The reduction of β-enamino esters **2c** and **2e** was also performed using ZnI_2 and $NaBH_4$,[9] affording the corresponding β-amino esters (**5c** and **5e**) as single diastereoisomers (Table 2, entries 4 and 8). On the other hand, β-amino esters with *R* configuration at the new chiral center were obtained carrying out the reduction of β-enamino esters **4a**, **4b**, and **4d** with ZnI_2 and $NaBH_4$ (see Supplementary data). However, using these reduction conditions, compound **4a** gave a mixture of the expected **6a** together with the *N*-unprotected derivative.

The stereoselectivity observed in the reduction of the β-enamino esters with $ZnI_2/NaBH_4$ can be explained as outlined in Scheme 5. Starting from β-enamino esters **2** the initially formed Zn(II)-complex **11** undergoes the hydride attack by the *re*-face since the chiral auxiliary shields the *si*-face. Therefore, β-amino esters with *S*

Table 2
Reduction of β-enamino esters **2** to β-amino esters **5**

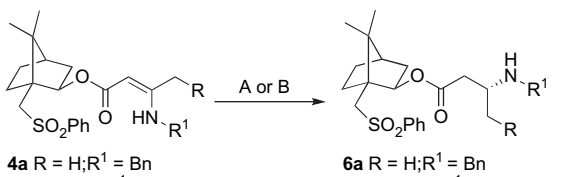


2 **5**

Procedure A: $NaBH(OAc)_3$/AcOH, 0 °C, 4h
Procedure B: $NaBH_4/ZnI_2$, r.t.

Entry	Product	R	R^1		Yield (%)	$[\alpha]_D^{25}$
1	**5a**	H	Bn	A	94	+40
2	**5b**	Me	Bn	A	90	+25
3	**5c**	*i*-Pr	Bn	A	88	+30
4	**5c**	*i*-Pr	Bn	B	85	+30
5	**5d**	*t*-Bu	Bn	A	52[a]	+45
6	**5d**	*t*-Bu	Bn	A	93[b]	+45
7	**5e**	Bn	Bn	A	91	+35
8	**5e**	Bn	Bn	B	68	+35
9	**5f**	H	*p*-$MeOC_6H_4$	A	68	+35
10	**5g**	H	$CH_2CH{=}CH_2$	A	91	+35

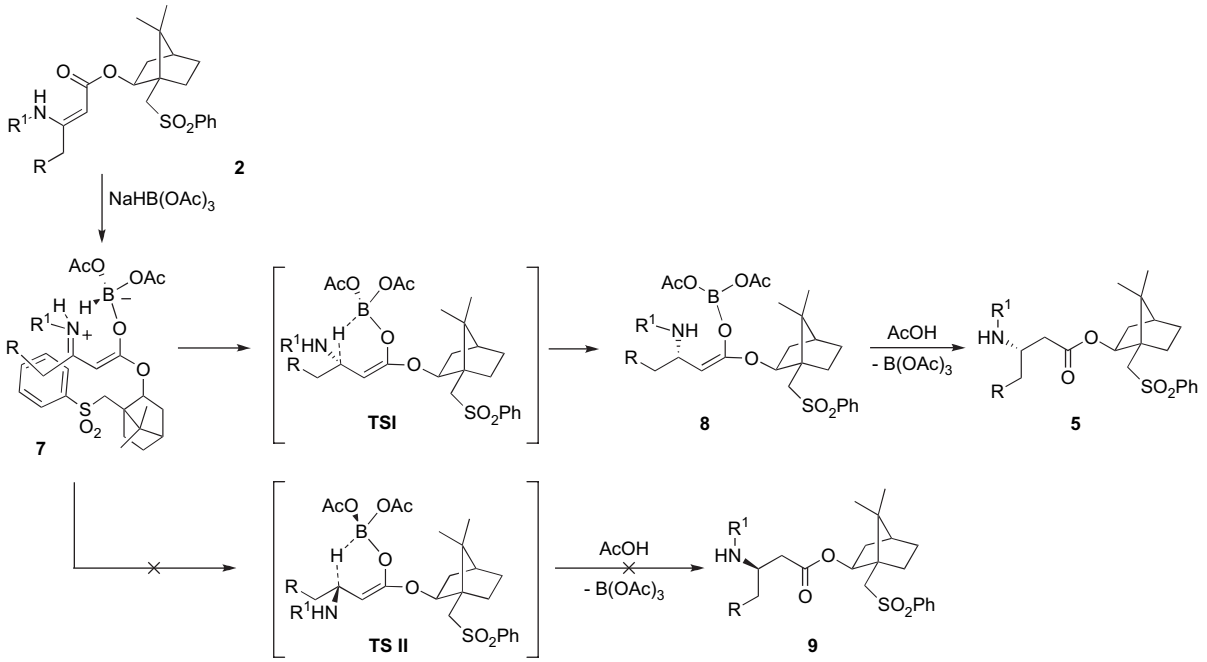
[a] Starting material (**2d**) recovered (46%).
[b] Reaction time: 18 h.



4a R = H;R^1 = Bn
4b R = Me; R^1 = Bn
4c R = *i*-Pr;R^1 = Bn
4d R = *t*-Bu;R^1 = Bn
4e R = R^1= Bn
4f R = H;R^1 = C_6H_4OMe-*p*
4g R = H; R^1 = $CH_2CH{=}CH_2$

6a R = H;R^1 = Bn
6b R = Me; R^1= Bn
6c R = *i*-Pr; R^1= Bn
6d R = *t*-Bu;R^1= Bn
6e R = R^1 = Bn
6f R = H; R^1 = C_6H_4OMe-*p*
6g R = H; R^1 = $CH_2CH{=}CH_2$

Scheme 2.



Scheme 3.

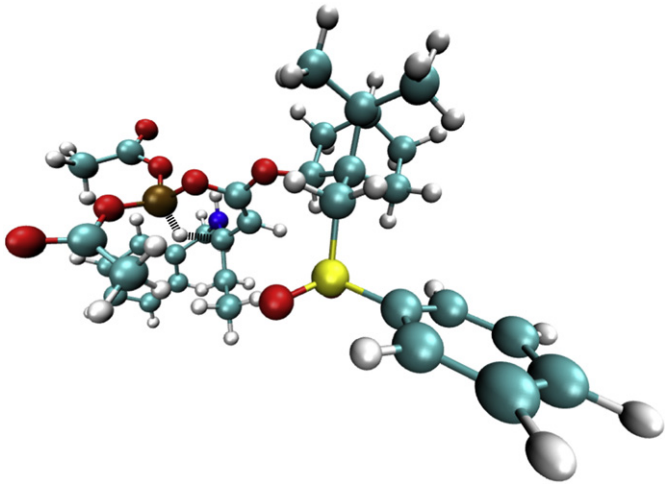
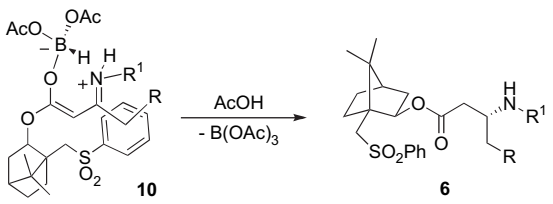
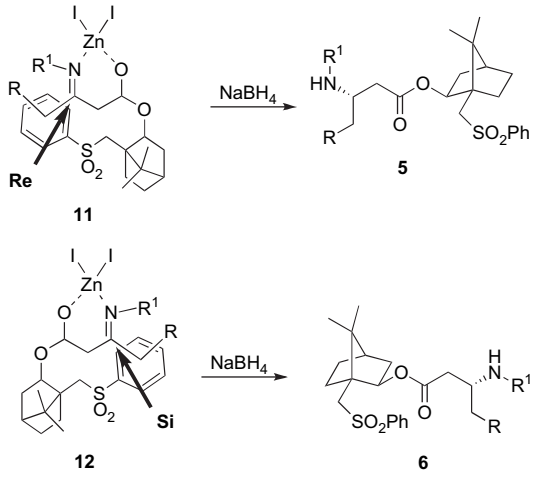


Figure 2. Reduction of β-enamino ester **2b** into β-amino ester **5b** with sodium triacetoxyborohydride: geometry of the PM3 transition state **I** (**TS I**) for the intramolecular hydride transfer in the case of intermediate **7b** (R=Me and R^1=Bn). The brown atom is boron, light blue carbon, light gray hydrogen, red oxygen, dark blue nitrogen, and yellow sulfur. Image produced using VMD.[17]



Scheme 4.

configuration are obtained. On the other hand, starting from β-enamino esters **4** the hydride attack occurs at the *si*-face of Zn(II)-complex **12** giving β-amino esters with *R* configuration (**6**).



Scheme 5.

3. Conclusion

Herein, we reported an approach to chiral β-amino esters involving the stereoselective reduction of β-enamino esters bearing a chiral auxiliary in the ester moiety, obtained from the nucleophilic addition of amines to chiral 2,3-allenoates. The nature of the chiral auxiliary of these β-enamino esters determines the chirality of the β-amino esters, which are obtained exclusively: (1*R*)-(−)-10-phenylsulfonylisobornyl β-enamino esters gave β-amino esters with *S* configuration whereas the (1*S*)-(+)-10-phenylsulfonylisobornyl β-enamino esters led to β-amino esters with *R* configuration. Therefore, it has been shown that this route to chiral β-amino esters is very versatile, high stereoselective and allows the control of the stereochemistry outcome by the selection of the chiral auxiliary. Computational studies corroborated the rationalization of the observed selectivity.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded on a Bruker Avance 300 instrument operating at 300 MHz. ^{13}C NMR spectra were recorded on a Bruker Avance 300 instrument operating at 75.5 MHz. The solvent is deuteriochloroform except where indicated otherwise. IR spectra were recorded on a Perkin Elmer 1720X FTIR spectrometer. Mass spectra were recorded on a HP GC 6890/MSD5973 instrument under electron impact (EI) except where indicated otherwise. Optical rotations were measured on an Optical Activity AA-5 electrical polarimeter. Microanalyses were performed using an EA 1108-HNS-O Fisons instrument. Mps were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase.

4.2. General procedure for the synthesis of β-enamino esters

The appropriate allene (5 mmol) was dissolved in dry methanol (50 mL) followed by the dropwise addition of the amine (5 mmol). The reaction mixture was stirred overnight at room temperature. The solvent was evaporated off and the product crystallized.

*4.2.1. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)but-2-enoate **2a** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)but-2-enoate **4a***

IR (KBr) 1598, 1643, 2953 cm^{-1}; ^{1}H NMR 0.86 (3H, s), 0.95 (3H, s), 1.17–1.27 (1H, m), 1.56–1.91 (6H, m), 1.94 (3H, s), 2.98 (1H, d, *J*=14.1 Hz), 3.69 (1H, d, *J*=14.1 Hz), 4.41–4.44 (3H, m), 4.49–4.53 (1H, m), 7.26–7.39 (5H, m, Ar–H), 7.44–7.55 (3H, m, Ar–H), 7.88–7.92 (2H, m, Ar–H), 8.88 (NH, br t, *J*=6.2 Hz); ^{13}C NMR 19.8, 20.4, 20.8, 27.6, 29.9, 40.4, 44.6, 47.3, 49.6, 50.3, 55.6, 75.9, 83.8, 127.3, 127.8, 128.3, 129.2, 129.4, 133.6, 139.1, 141.6, 161.9, 169.4.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)but-2-enoate **2a*** was obtained as a white solid (75%), mp 132.0–133.2 °C (from ethanol). MS (CI) *m*/*z* 468 (MH^+, 34), 277 (13), 174 (100); HRMS (CI) *m*/*z* 467.2130 ($C_{27}H_{33}NO_4S$ [M^+], 467.2119); HRMS (ESI-TOF) *m*/*z* 468.2203 ($C_{27}H_{34}NO_4S$ [MH^+], 468.2203). $[\alpha]_D^{25}$ +30 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)but-2-enoate **4a*** was obtained as a white solid (90%), mp 132.3–132.8 °C (from ethanol). MS (CI) *m*/*z* 468 (MH^+, 45), 277 (10), 174 (100); HRMS (ESI-TOF) *m*/*z* 490.2023 ($C_{27}H_{33}NNaO_4S$ [MNa^+], 490.2024). $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

*4.2.2. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)pent-2-enoate **2b** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)pent-2-enoate **4b***

IR (KBr) 1600, 1645, 2953 cm^{-1}; ^{1}H NMR 0.87 (3H, s), 0.96 (3H, s), 1.16 (3H, t, *J*=7.5 Hz), 1.14–1.21 (1H, m), 1.57–1.98 (6H, m), 2.26 (2H, q, *J*=7.5 Hz), 2.99 (1H, d, *J*=14.1 Hz), 3.71 (1H, d, *J*=14.1 Hz), 4.41–4.44 (3H, m), 4.50 (1H, dd, *J*=3.0 and 7.7 Hz), 7.28–7.54 (8H, m, Ar–H), 7.89–7.93 (2H, m, Ar–H), 8.88 (NH, br t, *J*=6.0 Hz); ^{13}C NMR 12.3, 20.0, 20.4, 25.2, 27.2, 29.4, 39.9, 44.1, 46.4, 49.1, 49.8, 55.1, 75.4, 81.4, 126.9, 127.4, 127.8, 128.8, 129.0, 133.2, 138.7, 141.1, 166.5, 169.4.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)pent-2-enoate **2b*** was obtained as a white solid (50%), mp 135.1–136.4 °C (from ethanol). MS (APCI) *m*/*z* 482 (MH^+, 100), 277 (33), 135 (55); HRMS (CI) *m*/*z* 481.2286 ($C_{28}H_{35}NO_4S$ [M^+], 481.2282). $[\alpha]_D^{25}$ +35 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)pent-2-enoate **4b*** was obtained as a white solid (68%), mp 135.3–136.6 °C (from ethanol). MS (APCI) *m*/*z* 482 (MH^+, 100), 277 (20), 135 (38); HRMS (CI) *m*/*z* 481.2286 ($C_{28}H_{35}NO_4S$ [M^+], 481.2278). $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

*4.2.3. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-methylhex-2-enoate **2c** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-methylhex-2-enoate **4c***

IR (KBr) 1597, 1651, 2950 cm^{-1}; ^{1}H NMR 0.87 (3H, s), 0.95 (3H, s), 1.00 (3H, d, *J*=6.6 Hz), 1.03 (3H, d, *J*=6.6 Hz), 1.14–1.21 (1H, m), 1.61–2.17 (9H, m), 2.97 (1H, d, *J*=14.1 Hz), 3.69 (1H, d, *J*=14.1 Hz), 4.40–4.43 (3H, m), 4.51 (1H, dd, *J*=3.0 and 7.7 Hz), 7.26–7.51 (8H, m, Ar–H), 7.88–7.91 (2H, m, Ar–H), 8.87 (NH, br t, *J*=6.0 Hz); ^{13}C NMR 20.0, 20.4, 22.5, 27.2, 27.4, 29.3, 39.9, 41.5, 44.1, 46.7, 49.0, 49.8, 54.9, 75.3, 83.7, 126.9, 127.4, 127.8, 128.7, 129.0, 133.2, 138.7, 141.1, 164.1, 169.1.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-methylhex-2-enoate **2c*** was obtained as a white solid (74%), mp 112.3–113.4 °C (from ethanol). MS (CI) *m*/*z* 510 (MH^+, 81), 467 (19), 277 (28), 216 (100); HRMS (CI) *m*/*z* 509.2599 ($C_{30}H_{39}NO_4S$ [M^+], 509.2592). $[\alpha]_D^{25}$ +20 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-methylhex-2-enoate **4c*** was obtained as a white solid (77%), mp 111.9–113.2 °C. MS (CI) *m*/*z* 510 (MH^+, 74), 277 (33), 216 (100); HRMS (CI) *m*/*z* 509.2599 ($C_{30}H_{39}NO_4S$ [M^+], 509.2583). $[\alpha]_D^{25}$ −20 (*c* 1, CH_2Cl_2).

*4.2.4. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5,5-dimethylhex-2-enoate **2d** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)-5,5-dimethylhex-2-enoate **4d***

IR (KBr) 1598, 1648, 2952 cm^{-1}; ^{1}H NMR 0.87 (3H, s), 0.95 (3H, s), 1.09 (9H, s), 1.15–1.21 (1H, m), 1.58–2.03 (6H, m), 2.15 (1H, d, *J*=13.4 Hz), 2.20 (1H, d, *J*=13.4 Hz), 2.96 (1H, d, *J*=14.0 Hz), 3.70 (1H, d, *J*=14.0 Hz), 4.37 (1H, s), 4.43–4.51 (3H, m), 7.26–7.52 (8H, m, Ar–H), 7.87–7.91 (2H, m, Ar–H), 9.02 (NH, br t, *J*=6.2 Hz); ^{13}C NMR 20.0, 20.4, 27.2, 29.3, 30.2, 32.3, 39.9, 44.1, 47.5, 49.1, 49.8, 54.9, 75.3, 85.6, 127.0, 127.4, 127.8, 128.8, 129.0, 133.2, 138.7, 141.1, 163.1, 168.9.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5,5-dimethylhex-2-enoate **2d*** was obtained as a white solid (82%), mp 134.0–134.9 °C (from ethanol). MS (CI) *m*/*z* 524 (MH^+, 60), 467 (72), 277 (21); HRMS (ESI-TOF) *m*/*z* 524.2829 ($C_{31}H_{42}NO_4S$ [MH^+], 524.2830). Calcd for $C_{31}H_{41}NO_4S$: C, 71.09; H, 7.89; N, 2.67; S, 6.12. Found: C, 70.70; H, 8.05; N, 2.79; S, 6.24. $[\alpha]_D^{25}$ +30 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5,5-dimethylhex-2-enoate **4d*** was obtained as a white solid (88%), mp 134.1–135.5 °C. MS (CI) *m*/*z* 524 (MH^+, 62), 467 (74), 277 (20); HRMS (ESI-TOF) *m*/*z* 524.2829 ($C_{31}H_{42}NO_4S$ [MH^+], 524.2829). Calcd for $C_{31}H_{41}NO_4S$: C, 71.09; H, 7.89; N, 2.67; S, 6.12. Found: C, 70.69; H, 7.79; N, 2.79; S, 5.94. $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

*4.2.5. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-phenylpent-2-enoate **2e** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-phenylpent-2-enoate **4e***

IR (KBr) 1603, 1649, 2948 cm^{-1}; ^{1}H NMR 0.87 (3H, s), 0.96 (3H, s), 1.14–1.21 (1H, m), 1.56–2.00 (6H, m), 2.48–2.54 (2H, m), 2.81–2.87 (2H, m), 2.99 (1H, d, *J*=14.1 Hz), 3.70 (1H, d, *J*=14.1 Hz), 4.39–4.42 (2H, m), 4.49 (1H, s), 4.51–4.54 (1H, m), 7.16–7.53 (13H, m, Ar–H), 7.87–7.92 (2H, m, Ar–H), 8.92 (NH, br t, *J*=6.2 Hz); ^{13}C NMR 20.0, 20.4, 27.2, 29.4, 34.1, 34.7, 39.9, 44.1, 46.6, 49.1, 49.8, 55.1, 75.5, 82.7, 126.4, 126.9, 127.5, 127.8, 128.2, 128.6, 128.8, 129.0, 133.2, 138.6, 140.4, 141.2, 164.4, 169.2.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-phenylpent-2-enoate **2e*** was obtained as a white solid (84%), mp 144.9–146.0 °C (from ethanol). MS (CI) *m*/*z* 558 (MH^+, 33), 277 (19), 264 (100); HRMS (CI) *m*/*z* 557.2599 ($C_{34}H_{39}NO_4S$ [M^+], 557.2599). $[\alpha]_D^{25}$ +35 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(benzylamino)-5-phenylpent-2-enoate **4e*** was obtained as a white solid (71%), mp 145.4–146.6 °C. MS (CI) *m*/*z* 558 (MH^+, 30), 277 (40), 264 (100); HRMS (CI) *m*/*z* 558.2678 ($C_{34}H_{40}NO_4S$ [MH^+], 558.2674). $[\alpha]_D^{25}$ −35 (*c* 1, CH_2Cl_2).

*4.2.6. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(4-methoxyphenylamino)but-2-enoate **2f** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(4-methoxyphenylamino)but-2-enoate **4f***

IR (film) 1582, 1647, 2946 cm^{-1}; ^1H NMR 0.87 (3H, s), 0.98 (3H, s), 1.17–1.27 (1H, m), 1.59–1.87 (6H, m), 1.91 (3H, s), 3.01 (1H, d, *J*=14.1 Hz), 3.70 (1H, d, *J*=14.1 Hz), 3.81 (3H, s), 4.54 (1H, s), 4.62–4.65 (1H, m), 6.86–6.88 (2H, m, Ar–H), 7.02–7.06 (2H, m, Ar–H), 7.49–7.60 (3H, m, Ar–H), 7.92–7.94 (2H, m, Ar–H), 10.11 (NH, s); ^{13}C NMR 19.8, 19.9, 20.2, 27.1, 29.4, 39.8, 44.0, 49.0, 49.7, 55.0, 55.3, 75.6, 84.7, 114.1, 126.5, 127.6, 129.0, 131.9, 133.1, 141.1, 157.2, 159.6, 168.8.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(4-methoxyphenylamino)but-2-enoate **2f*** was obtained as an oil (85%). MS (CI) *m*/*z* 484 (MH^+, 91), 277 (36), 190 (100); HRMS (CI) *m*/*z* 484.2157 ($C_{27}H_{34}NO_5S$ [M^+], 484.2144). $[\alpha]_D^{25}$ +20 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(4-methoxyphenylamino)but-2-enoate **4f*** was obtained as an oil (61%). $[\alpha]_D^{25}$ −20 (*c* 1, CH_2Cl_2).

*4.2.7. (1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(but-3-enylamino)but-2-enoate **2g** and (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(but-3-enylamino)but-2-enoate **4g***

IR (KBr) 1457, 1477, 1739, 2987 cm^{-1}; ^1H NMR 0.86 (3H, s), 0.95 (3H, s), 1.14–1.21 (1H, m), 1.56–2.00 (6H, m), 1.93 (3H, s), 2.98 (1H, d, *J*=14.1 Hz), 3.69 (1H, d, *J*=14.1 Hz), 3.82–3.86 (2H, m), 4.38 (1H, s), 4.54 (1H, dd, *J*=3.0 and 7.8 Hz), 5.16–5.28 (2H, m), 5.82–5.95 (1H, m), 7.46–7.51 (2H, m, Ar–H), 7.55–7.61 (1H, m, Ar–H), 7.89–7.93 (2H, m, Ar–H), 8.61 (NH, br t, *J*=6.1 Hz); ^{13}C NMR 19.5, 20.4, 20.8, 27.6, 29.9, 40.4, 44.6, 45.6, 49.6, 50.2, 55.5, 75.8, 83.4, 116.4, 128.3, 129.4, 133.6, 135.2, 141.7, 162.0, 169.4.

*(1R)-(−)-10-Phenylsulfonylisobornyl (Z)-3-(but-3-enylamino)but-2-enoate **2g*** was obtained as a white solid (76%), mp 147.2–149.0 °C (from ethanol); MS (CI) *m*/*z* 418 (MH^+, 94), 277 (57), 124 (100); HRMS (CI) *m*/*z* 418.2052 ($C_{23}H_{32}NO_4S$ [MH^+], 418.2053). $[\alpha]_D^{25}$ +30 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (Z)-3-(but-3-enylamino)but-2-enoate **4g*** was obtained as a white solid (80%), mp 148.3–150.2 °C (from ethanol); MS (CI) *m*/*z* 418 (MH^+, 90), 277 (16), 124 (100); HRMS (CI) *m*/*z* 417.1970 ($C_{23}H_{31}NO_4S$ [M^+], 417.1974). $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

4.3. General procedure for the reduction of β-enamino esters

Procedure A.[10c] A solution of $NaBH(OAc)_3$ was prepared by adding $NaBH_4$ (0.34 g, 9.0 mmol) in glacial acetic acid (5 mL) while keeping the temperature between 10 °C and 20 °C. After the H_2 evolution ceased (1 h), acetonitrile (5 mL) was added and the solution was cooled to 0 °C. The β-enamino ester (3.0 mmol) was added in one portion and the reaction mixture stirred for 4 h at 0 °C. Acetic acid and acetonitrile were evaporated off and the residue dissolved in CH_2Cl_2 and the combined organic layers were washed with saturated aqueous solution of Na_2CO_3 and dried over magnesium sulfate affording the β-amino ester after removal of the solvent.

Procedure B.[9] To a solution of anhydrous zinc iodide (1.91 g, 6.0 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added the β-enamino ester (2.0 mmol). The resulting mixture was stirred at the same temperature for 1 h after which $NaBH_4$ (0.375 g, 10 mmol) was added, also at 0 °C. The solution was allowed to reach room temperature and left overnight. The reaction was then quenched with saturated ammonium chloride solution. The reaction mixture was extracted with CH_2Cl_2 and the combined organic layers were washed with brine and dried over magnesium sulfate affording the β-amino ester after removal of the solvent.

The ^1H NMR and ^{13}C NMR spectra of β-amino ester recorded at ambient temperature showed the existence of two rotamers but the spectra are simpler at higher temperature. In fact, we found that the ^1H NMR spectrum of (1*R*)-(−)-10-phenylsulfonylisobornyl (*R*)-3-(benzylamino)butanoate **5a** recorded at room temperature showed two sets of signals corresponding to the AB system of the 10-phenylsulfonylisobornyl group but when recorded at 70 °C showed a single set of signals. The ^{13}C NMR spectra were described considering only the main conformer. On the other hand, the ^1H NMR spectrum of (1*S*)-(+)-10-phenylsulfonylisobornyl (*R*)-3-[(2*S*)-2-(2-methoxycarbonylpyrrolid-1-yl)ethyl]butanoate (**16e**) recorded at room temperature, showed two sets of signals corresponding to the proton at C-1 of the 10-phenylsulfonylisobornyl group but when recorded at 100 °C, showed a single set of signals.

*4.3.1. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-butanoate **5a** and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)butanoate **6a***

IR (film) 1447, 1636, 1729, 2953 cm^{-1}; ^1H NMR 0.84 (3H, br s), 0.90 and 0.92 (3H, s), 1.16–1.19 (4H, m), 1.63–1.81 (6H, m), 1.93–2.00 (1H, m), 2.26–2.35 (1H, m), 2.41–2.51 (1H, m), 2.96 and 2.98 (1H, d, *J*=14.0 Hz), 3.13–3.19 (1H, m), 3.50 and 3.51 (1H, d, *J*=14.0 Hz), 3.72–3.87 (2H, m), 4.86–4.90 (1H, m), 7.24–7.32 (5H, m, Ar–H), 7.52–7.63 (3H, m, Ar–H), 7.87–7.91 (2H, m, Ar–H); ^{13}C NMR 19.8, 20.2, 20.4, 27.1, 29.8, 39.6, 41.5, 41.9, 43.9, 49.2, 49.6, 51.1, 55.0, 77.7, 126.8, 127.6, 128.1, 128.3, 129.2, 133.5, 140.2, 141.2, 170.8.

*(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)butanoate **5a*** was obtained as a colorless oil. MS (CI) *m*/*z* 470 (MH^+, 77), 277 (20), 134 (100); HRMS (ESI-TOF) *m*/*z* 470.2360 ($C_{27}H_{36}NO_4S$ [MH^+], 470.2355). $[\alpha]_D^{25}$ +40 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(benzylamino)butanoate **6a*** was obtained as a colorless oil. MS (CI) *m*/*z* 470 (MH^+, 100), 277 (21), 134 (83); HRMS (ESI-TOF) *m*/*z* 470.2360 ($C_{27}H_{36}NO_4S$ [MH^+], 470.2353). $[\alpha]_D^{25}$ −40 (*c* 1, CH_2Cl_2).

*4.3.2. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-pentanoate **5b** and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)pentanoate **6b***

IR (KBr) 1450, 1727, 2945 cm^{-1}; ^1H NMR 0.84–0.96 (9H, m), 1.16–1.19 (1H, m), 1.49–1.99 (8H, m), 2.38–2.41 (2H, m), 2.95–3.00 (2H, m), 3.51 (1H, d, *J*=14.0 Hz), 3.74–3.79 (2H, m), 4.86–4.89 (1H, m), 7.21–7.34 (5H, m, Ar–H), 7.51–7.63 (3H, m, Ar–H), 7.88–7.91 (2H, m, Ar–H); ^{13}C NMR 9.7, 19.9, 20.2, 26.4, 27.1, 29.8, 39.0, 39.6, 44.0, 49.3, 49.8, 50.8, 55.0, 55.3, 77.7, 126.8, 127.6, 128.1, 128.3, 129.2, 133.5, 140.4, 171.1.

*(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)pentanoate **5b*** was obtained as an oil. MS (APCI) *m*/*z* 484 (MH^+, 100), 277 (34), 135 (29); HRMS (CI) *m*/*z* 484.2521 ($C_{28}H_{38}NO_4S$ [MH^+], 484.2522). $[\alpha]_D^{25}$ +25 (*c* 1, CH_2Cl_2).

*(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(benzylamino)pentanoate **6b*** was obtained as an oil. MS (APCI) *m*/*z* 484 (MH^+, 100), 277 (87), 135 (81); HRMS (CI) *m*/*z* 484.2521 ($C_{28}H_{38}NO_4S$ [MH^+], 484.2511). $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

*4.3.3. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5-methylhexanoate **5c** and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)-5-methylhexanoate **6c***

IR (film) 1451, 1732, 2947 cm^{-1}; ^1H NMR 0.84–0.92 (12H, m), 1.18–1.30 (2H, m), 1.44–1.50 (1H, m), 1.61–1.84 (5H, m), 1.94–1.99 (1H, m), 2.39–2.42 (2H, m), 2.96 and 2.98 (1H, d, *J*=14.0 Hz), 3.05–3.08 (1H, m), 3.52 (1H, d, *J*=14.0 Hz), 3.73–3.81 (2H, m), 4.89 (1H, dd, *J*=3 and 8 Hz), 7.21–7.34 (5H, m, Ar–H), 7.51–7.64 (3H, m, Ar–H), 7.88–7.92 (2H, m, Ar–H); ^{13}C NMR 19.9, 20.3, 22.5, 22.8, 23.0, 24.9, 27.1, 29.9, 39.3, 39.6, 44.0, 49.3, 49.9, 50.7, 52.3, 55.1, 77.8, 126.9, 127.7, 128.3, 129.2, 133.5, 140.4, 141.3, 171.0.

*(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5-methylhexanoate **5c*** was obtained as an oil (88%). MS (CI) *m*/*z* 512 (MH^+, 100), 454 (21), 277 (79); HRMS (CI) *m*/*z* 511.2756 ($C_{30}H_{41}NO_5S$ [M^+], 511.2741). $[\alpha]_D^{25}$ +30 (*c* 1, CH_2Cl_2).

(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(benzylamino)-5-methylhexanoate **6c** was obtained as an oil. MS (CI) *m/z* 512 (MH^+, 100), 454 (21), 277 (82); HRMS (CI) *m/z* 512.2834 ($C_{30}H_{42}NO_5S$ [MH^+], 512.2824). $[\alpha]_D^{25}$ −30 (*c* 1, CH_2Cl_2).

4.3.4. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5,5-dimethylhexanoate **5d** *and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)-5,5-dimethylhexanoate* **6d**

IR (film) 1448, 1729, 2955 cm^{-1}; ^1H NMR 0.84 (3H, s), 0.92 (3H, s), 0.95 (9H, s), 1.19–1.98 (7H, m), 2.42–2.45 (2H, m), 2.97 and 2.98 (1H, d, *J*=14.0 Hz), 3.06–3.12 (1H, m), 3.51 and 3.52 (1H, d, *J*=14.0 Hz), 3.71–3.82 (2H, m), 4.89–4.93 (1H, m), 7.21–7.34 (5H, m, Ar–H), 7.52–7.64 (3H, m, Ar–H), 7.87–7.92 (2H, m, Ar–H); ^{13}C NMR 19.9, 20.3, 27.1, 29.9, 30.0, 30.1, 30.5, 39.6, 41.0, 41.6, 44.0, 48.5, 49.3, 49.9, 51.1, 51.9, 55.2, 77.8, 126.8, 127.7, 128.3, 129.2, 133.5, 140.4, 141.3, 170.9.

(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5,5-dimethylhexanoate **5d** was obtained as an oil. MS (CI) *m/z* 526 (MH^+, 100), 454 (17), 277 (27); HRMS (ESI-TOF) *m/z* 526.2986 ($C_{31}H_{44}NO_4S$ [MH^+], 526.2980). $[\alpha]_D^{25}$ +45 (*c* 1, CH_2Cl_2).

(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(benzylamino)-5,5-dimethylhexanoate **6d** was obtained as a solid, mp 48.6–50.1 °C. MS (CI) *m/z* 526 (MH^+, 67), 454 (17), 277 (24); HRMS (ESI-TOF) *m/z* 526.2986 ($C_{31}H_{44}NO_4S$ [MH^+], 526.2981). $[\alpha]_D^{25}$ −45 (*c* 1, CH_2Cl_2).

4.3.5. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5-phenylpentanoate **5e** *and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)-5-phenylpentanoate* **6e**

IR (film) 1448, 1724, 2957 cm^{-1}; ^1H NMR 0.83 (3H, s), 0.88 and 0.90 (3H, s), 1.16–1.20 (1H, m), 1.59–1.99 (8H, m), 2.44–2.47 (2H, m), 2.66–2.75 (2H, m), 2.97 and 2.98 (1H, d, *J*=14.0 Hz), 3.07–3.11 (1H, m), 3.50 (1H, d, *J*=14.0 Hz), 3.74–3.83 (2H, m), 4.87–4.92 (1H, m), 7.15–7.33 (10H, m, Ar–H), 7.50–7.63 (3H, m, Ar–H), 7.87–7.91 (2H, m, Ar–H); ^{13}C NMR 19.9, 20.3, 27.1, 29.9, 31.9, 35.7, 39.3, 39.6, 44.0, 49.3, 49.9, 50.7, 53.6, 55.1, 77.7, 125.8, 126.9, 127.7, 128.3, 128.4, 129.3, 133.5, 140.4, 141.3, 142.0, 171.1.

(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(benzylamino)-5-phenylpentanoate **5e** was obtained as an oil. MS (CI) *m/z* 560 (MH^+, 100), 277 (55), 224 (77); HRMS (CI) *m/z* 560.2834 ($C_{34}H_{42}NO_5S$ [MH^+], 560.2830). $[\alpha]_D^{25}$ +35 (*c* 1, CH_2Cl_2).

(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(benzylamino)-5-phenylpentanoate **6e** was obtained as an oil. MS (CI) *m/z* 560 (MH^+, 100), 277 (83), 224 (81); HRMS (CI) *m/z* 559.2756 ($C_{34}H_{41}NO_5S$ [M^+], 559.2741). $[\alpha]_D^{25}$ −35 (*c* 1, CH_2Cl_2).

4.3.6. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(4-methoxyphenylamino)butanoate **5f** *and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(4-methoxyphenylamino)butanoate* **6f**

IR (film) 1727, 2942 cm^{-1}; ^1H NMR 0.84 (3H, s), 0.89–0.95 (3H, m), 1.18–1.31 (4H, m), 1.58–1.97 (6H, m), 2.32–2.39 (1H, m), 2.54–2.64 (1H, m), 2.98 and 2.99 (1H, d, *J*=14.0 Hz), 3.51 and 3.53 (1H, d, *J*=14.0 Hz), 3.73 and 3.74 (3H, s), 3.81–3.85 (1H, m), 4.90–4.93 (1H, m), 6.58–6.62 (2H, m, Ar–H), 6.74–6.78 (2H, m, Ar–H), 7.49–7.54 (2H, m, Ar–H), 7.59–7.63 (1H, m, Ar–H), 7.85–7.88 (2H, m, Ar–H); ^{13}C NMR 19.8, 20.2, 27.0, 29.8, 39.6, 40.8, 41.0, 43.9, 46.8, 49.3, 49.8, 55.1, 55.7, 77.8, 114.9, 115.1, 127.5, 129.2, 133.5, 140.8, 141.2, 152.2, 170.3.

(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(4-methoxyphenylamino)butanoate **5f** was obtained as a colorless oil. MS (CI) *m/z* 485 (M^+, 100), 277 (12), 150 (74); HRMS (ESI-TOF) *m/z* 486.2309 ($C_{27}H_{36}NO_5S$ [MH^+], 486.2305). $[\alpha]_D^{25}$ +35 (*c* 1, CH_2Cl_2).

(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(4-methoxyphenylamino)butanoate **6f** wasobtained as a colorless oil. MS (CI) *m/z* 485 (M^+, 100), 277 (29), 150 (69); HRMS (ESI-TOF) *m/z* 486.2309 ($C_{27}H_{36}NO_5S$ [MH^+], 486.2306). $[\alpha]_D^{25}$ −35 (*c* 1, CH_2Cl_2).

4.3.7. (1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(but-3-enylamino)butanoate **5g** *and (1S)-(+)-10-phenylsulfonylisobornyl (R)-3-(but-3-enylamino)butanoate* **6g**

IR (film) 1479, 1730, 2961 cm^{-1}; ^1H NMR 0.85 (3H, s), 0.96 (3H, s), 1.14 and 1.16 (3H, d, *J*=2.7 Hz), 1.14–1.21 (1H, m), 1.56–2.01 (6H, m), 2.25–2.33 (1H, m), 2.39–2.49 (1H, m), 2.98 (1H, d, *J*=13.9 Hz) and 2.99 (1H, d, *J*=14.0 Hz), 3.14–3.30 (3H, m), 3.52 and 3.53 (1H, d, *J*=14.0 Hz), 4.89–4.92 (1H, m), 5.05–5.09 (1H, m), 5.14–5.21 (1H, m), 5.82–5.95 (1H, m), 7.54–7.65 (3H, m, Ar–H), 7.89–7.94 (2H, m, Ar–H); ^{13}C NMR 19.9, 20.2, 20.3, 27.1, 29.8, 32.6, 39.6, 41.6, 41.8, 44.0, 49.3, 49.8, 55.0, 77.7, 115.9, 127.6, 129.4, 133.5, 136.7, 141.3, 170.8.

(1R)-(−)-10-Phenylsulfonylisobornyl (S)-3-(but-3-enylamino)butanoate **5g** was obtained as an oil. MS (CI) *m/z* 420 (MH^+, 100), 277 (50), 135 (76); HRMS (CI) *m/z* 420.2209 ($C_{23}H_{34}NO_4S$ [MH^+], 420.2193). $[\alpha]_D^{25}$ +35 (*c* 1, CH_2Cl_2).

(1S)-(+)-10-Phenylsulfonylisobornyl (R)-3-(but-3-enylamino)butanoate **6g** was obtained as an oil. MS (CI) *m/z* 420 (MH^+, 100), 277 (17), 135 (28); HRMS (CI) *m/z* 420.2209 ($C_{23}H_{34}NO_4S$ [MH^+], 420.2199). $[\alpha]_D^{25}$ −35 (*c* 1, CH_2Cl_2).

4.4. Crystallographic data

The X-ray data were collected on an Enraf-nonius Mach-3 single crystal diffractometer, at 298(3) K, using graphite-monochromated Cu Kα radiation (λ=1.5418 Å). Intensities were recorded as full profiles of ω–θ scans. The structures were solved by direct methods and refined by full-matrix least-squares using SHELXL97[a]. Examination of the structure with PLATON confirmed the absence of voids in the crystal structures, which might be occupied by solvent molecules.

4.4.1. Crystal data for (1S)-(+)-10-phenylsulfonylisobornyl (Z)-3-(benzylamino)-5,5-dimethylhex-2-enoate **4d**

$C_{31}H_{43}NO_4S$, *M*=525.72, monoclinic, $P2_1$ with unit cell, *a*=9.293(4) Å, *b*=14.5697(8) Å, *c*=11.5070(14) Å, α=90°, β=104.120(18)°, γ=90°, *V*=1510.9(6) $Å^3$. It contains two molecules/unit cell. ρ_{calcd}=1.156 g cm^{-3}, *Z*=2, μ=1.214 mm^{-1}. $R(I>2\sigma(I))$=0.0793 and R_w=0.2197 for 5931 independent reflections. H atoms were placed at calculated positions and refined as riding on their parent atoms.

4.4.2. Crystal data for (1S)-(−)-10-phenylsulfonylisobornyl (R)-3-(benzylamino)-5,5-dimethylhexanoate **6d**

The X-ray data were collected on a Bruker Apex II single crystal diffractometer at room temperature. The structure of this compound was determined using a transparent very thin rectangular plate single crystal with dimensions 0.37×0.12×0.02 mm ($P2_12_12_1$) with unit cell, *a*=10.5297(7) Å, *b*=13.4361(9) Å, *c*=21.1730(14) Å, and *V*=2995.5(5) $Å^3$. It contains four molecules/unit cell. ρ_{calcd}=1.1616 g/cm^3, μ=0.142 mm^{-1}. Mo Kα radiation was used (0.71073 Å). A total of 2747 reflections with $I>2\sigma(I)$ were used. *R*=0.0549.

4.5. Computational methods

The calculations were carried out on Intel-based computers, running Linux, using MOPAC2007.[18] The geometry of the transition state was optimized first with MOPAC2007, and a subsequent Hessian calculation was performed to assess the rank of the critical point obtained. All the calculations in MOPAC2007 used the PM3 Hamiltonian,[19–22] and the localization of the transition state geometry was performed until the gradient was less than 0.01 kcal/Å.

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Supplementary data

Data regarding the synthesis of β-enamino esters **4** and the reduction of β-enamino esters **4** to β-Amino Esters **6**. Crystallographic data for compounds **4d**, **6d**, and computational study data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.053.

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