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Indium-mediated diastereoselective allylation of *N-tert*-butanesulfinyl imines derived from α-ketoesters

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Dedicated to Professor Gary Posner on occasion of his retirement

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ABSTRACT

The indium-mediated allylation of α-aldimino and -ketimino esters **3** with allylic bromides proceeds with high diastereoselectivity to yield homoallylic α-amino ester derivatives **5**, in both THF and water as solvents. The reactions are diastereospecific, the stereochemical outcome depending on the configuration of both the sulfur atom of the sulfinyl group and the C=N double bond. Of particular interest are the reaction products using ethyl bromomethylacrylate as allylating reagent because amino diesters are obtained, which can be easily transformed into enantiomerically pure α-methylidene-γ-butyrolactams **6** with an alkoxycarbonyl group on the ring bearing the nitrogen atom.

1. Introduction

The addition of an allylic organometallic compound to an imine or imine derivative is of great synthetic interest because a homoallyl amine is formed. Importantly, if the allylation is carried out in a stereoselective fashion, enantioenriched homoallylic amines would be produced.[1] These compounds are valuable building blocks, because along with the carbon stereogenic centre bonded to the nitrogen atom, the double bond of the allylic moiety can participate in a number of further synthetically useful transformations.[2] Although catalytic enantioselective allylations[3] using Lewis acids or bases as chiral inductors are the ideal method of choice for performing these transformations, more efficient and practical protocols have been developed when the stereoselective allylations are carried out with stoichiometric amounts of chiral reagents,[4] such as imines bearing a chiral auxiliary. In this context, it is worth mentioning that *N-tert*-butanesulfinyl derivatives[5] have found high applicability in synthesis as electrophiles because both enantiomers are accessible in large-scale processes[6] and because the chiral auxiliary is easily removed under acidic conditions. In addition, practical processes for recycling the *tert*-butanesulfinyl group upon deprotection of *N-tert*-butanesulfinyl amines have also been reported.[7] With regards to this, we have described the stereoselective allylation of *N-tert*-butanesulfinyl aldimines[8] and ketimines[9] with allylindium species and the first one-pot α-aminoallylation of aldehydes with chiral *tert*-butanesulfinamide, allyl bromides, and indium, which provides homoallylic amines with high chemo- and stereo-selectivity.[10] Continuing our interest in this topic, we herein report our first approach to the indium-mediated addition of allylic bromides to *N-tert*-butanesulfinyl imines derived from α-ketoesters and alkyl glyoxylate esters. These imines are precursors of α-amino esters upon reaction with nucleophiles: The addition of arylboronic acids,[11] trimethylsilane pronucleophiles,[12] organozinc,[13] and organomagnesium compounds[14] to these imines has been already reported, the diastereoselective reduction of *N-tert*-butanesulfinyl imines derived from α-ketoesters leading to α-amino acid derivatives being also known.[15] To the best of our knowledge, the first example of allylindium intermediate additions to the *N-tert*-butanesulfinyl imine derived from ethyl glyoxylate was provided by Grigg and co-workers in their study of three-component palladium–indium-mediated diastereoselective cascade allylation using allenes and aryl iodides as precursors of the allylindium

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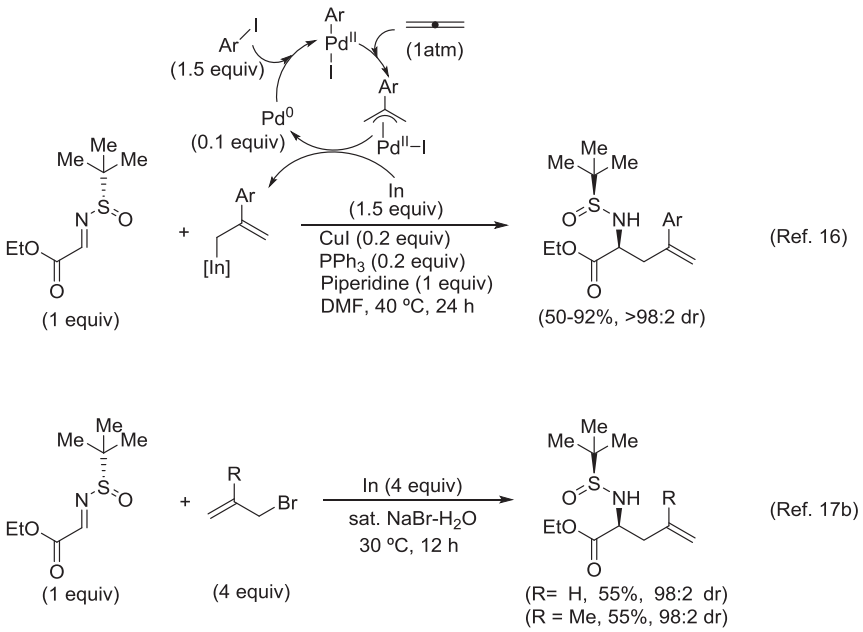
0040-4020/

intermediate (Scheme 1).[16] More recently, the indium-mediated allylation of the same imino ester with allylic bromides was also performed in a saturated sodium bromide aqueous solution to give the expected α-amino ester derivatives in a highly diastereoselective manner (Scheme 1).[17]

solution. Compound **3b** was also accessible in almost quantitative yield when the condensation was performed in the presence of 10 mol% of pyrrolidine and 4 Å MS.[19] The previously mentioned reaction conditions for the formation of aldimines **3a** and **3b** failed to provide condensation products when ketoesters **2c**–**e** were used as

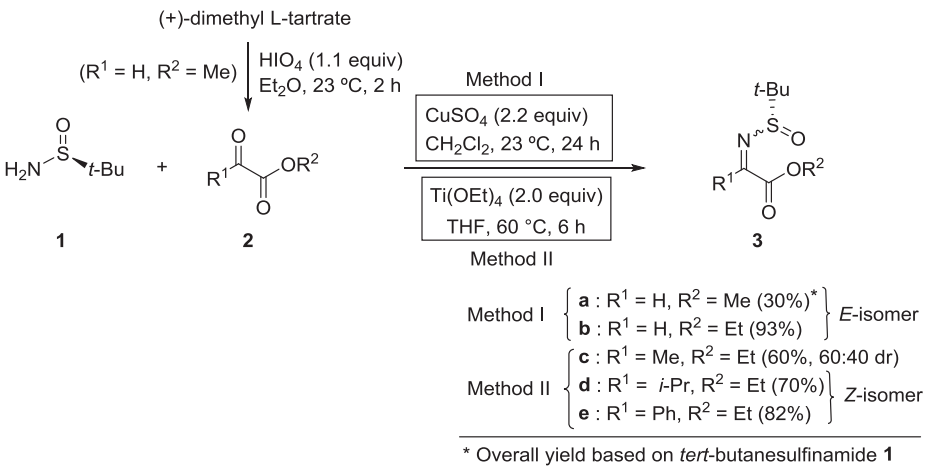


Scheme 1. Previous work on indium-mediated allylation of *N*-*tert*-butanesulfinyl imines derived from ethyl glyoxylate.

2. Results and discussion

Starting sulfinyl imino esters **3** were prepared according to the standard procedures described in the literature by reaction of commercially available (*S*)-*tert*-butanesulfinamide **1** with aldehydes **2a**,**b** or ketones **2c**–**e**. Thus, direct condensation of methyl (**2a**) or ethyl glyoxylate (**2b**) and (*S*)-*tert*-butanesulfinamide (**1**), in the presence of $CuSO_4$ in dichloromethane led to iminoesters **3a** and **3b**, respectively (Scheme 2).[18] Methyl glyoxylate (**2a**) was prepared in situ by oxidative cleavage of (+)-dimethyl L-tartrate and used in the condensation step without further purification, yielding methyl iminoester **3a** in a moderate overall 30% yield. On the other hand, ethyl imino ester **3b** was prepared in high yield from freshly distilled ethyl glyoxylate (**2b**) from a commercially available 50% toluene

the reactant. Fortunately, the use of 2 equiv of $Ti(OEt)_4$ in THF at 60 °C provided relatively high yields of imino esters **3c**–**e** (Scheme 2). The configuration of the C=N bond of imines **3** is very important in the study of the diastereoselective addition of allylic nucleophiles to the imine group. This matter has not been commented on in detail in previous publications. We assumed that aldimines **3a** and **3b** exhibit *E*-configuration, and ketimines **3d** and **3e** *Z*-configuration, according to their NMR spectra. However, the imine **3c** derived from ethyl pyruvate (**2c**) was isolated as a 6:4 mixture of *E*:*Z* diastereoisomers which could not be separated by column chromatography. The ^1H NMR chemical shift for the *t*-Bu group of the minor diastereoisomer is 1.25 ppm (1.31 ppm for the major diastereoisomer with *E* configuration) and is coincident with the *t*-Bu group of **3d** which exhibited an exclusively *Z* configuration.



Scheme 2. Synthesis of *N*-*tert*-butanesulfinyl iminoesters **3**.

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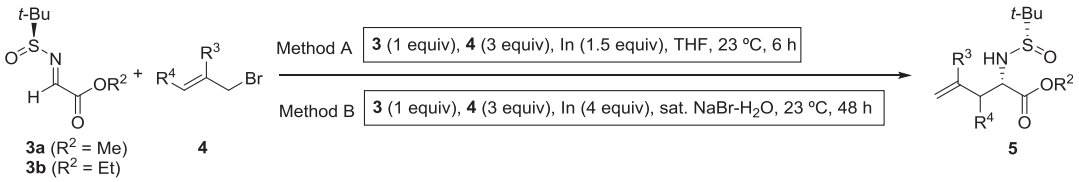
The reaction of *N-tert*-butanesulfinyl imino ester **3a** derived from methyl glyoxylate (**2a**) with allyl bromide (**4a**, 3 equiv), in the presence of indium metal (1.5 equiv), in THF for 6 h at room temperature (Method A), led to the formation of the homoallyl amino ester derivative **5aa** as a single diastereoisomer (Table 1, entry 1). Those are typical reaction conditions developed in our group for the allylation of *N-tert*-butanesulfinyl imines.[8,9] Under the same reaction conditions, the ethyl imino ester **3b** gave compound **5ba** in 61% yield (Table 1, entry 4) and, when methallyl bromide (**4b**) was used as the allylating reagent for **3b**, compound **5bd** was obtained in 82% yield (Table 1, entry 5). Crotylation of **3a** is a more challenging process, because of the regiochemistry of the addition at the most substituted γ-position of the crotyl indium intermediate took place through a six-membered cyclic transition state, leading to an almost 2:1 mixture of *syn* an *anti*-diastereoisomers **5ac** (Table 1, entry 2). Unfortunately, allylation of **3a** and **3b** with ethyl 2-bromomethylacrylate (**4d**) did not proceed in THF at room temperature (Method A) or at higher temperatures. Based on our previous experience with this allylating reagent (**4d**),[20] we found that total conversion occurred when the reaction was carried out in a saturated aqueous solution of sodium bromide in the presence of 4 equiv of indium at room temperature for 48 h (Method B), leading to amino diester derivatives **5ad** and **5bd** in excellent yields (Table 1, entries 3 and 6). Those were the reaction conditions developed by Xu and Lin,[17a] and applied previously to the allylation of imino ester **3b** by both the groups of Xu and Lin, and Babu.[17b] A major drawback of this methodology is the use of a large excess of indium (4 equiv instead of 1.5 equiv as in Method A) which is the most expensive component of the reaction mixture. Regarding the configuration of the newly created stereogenic centres, **5ba** was assigned after comparison of the NMR spectra with those reported in literature for the same compound[17b] and its enantiomer.[17a] *ent*-**5ba** was unambiguously characterized after transformation into the known compound D-allylglycine. Thus, we assumed that the indium mediated allylation proceeded through the same stereochemical pathway in imines **3a** and **3b**, with (E,S_S) configuration, the addition of the allyl moiety taking always place at the *Si* face of these systems (Table 1).

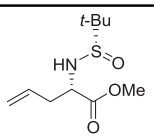
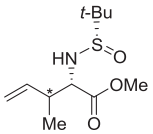
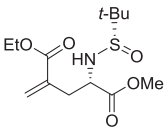
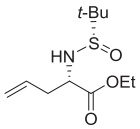
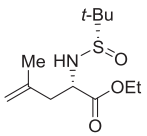
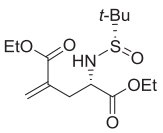
Table 1
Allylation of *N-tert*-butanesulfinyl imines **3a**,**b** derived from glyoxylate esters **2a**,**b**



3a (R^2 = Me)
3b (R^2 = Et)

4

5

Entry	Imino ester **3**	Allylic bromide **4**	Method	α-Amino ester **5**		
				No.	Structure	Yield (%)[a,b]
1	**3a**	**4a** (R^3=H, R^4=H)	A	**5aa**		41
2	**3a**	**4c** (R^3=H, R^4=Me)	A	**5ac**		53 (66:34)[c]
3	**3a**	**4d** (R^3=CO_2Et, R^4=H)	B	**5ad**		79
4	**3b**	**4a** (R^3=H, R^4=H)	A	**5ba**		61
5	**3b**	**4b** (R^3=Me, R^4=H)	A	**5bb**		82
6	**3b**	**4d** (R^3=CO_2Et, R^4=H)	B	**5bd**		93

[a] Yield was determined after column chromatography purification and is based on the starting sulfinimide **3**.
[b] In all cases the allylation proceeded with high face diastereoselectivities (>95:5) that were determined after ^{1}H NMR analysis of the reaction crude.
[c] Diastereomeric *syn*/*anti* ratio is given in parenthesis.

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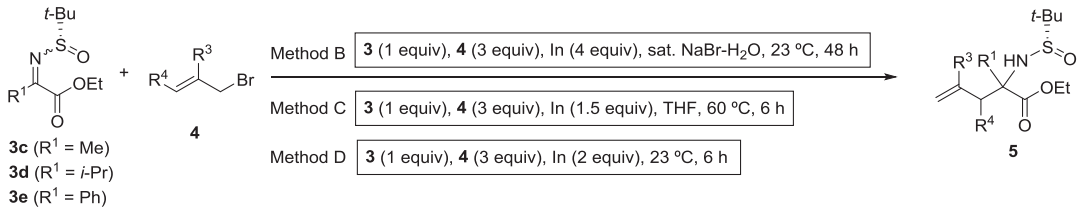
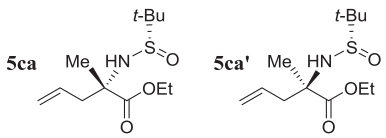
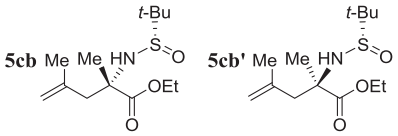
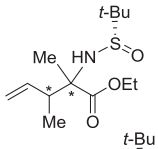
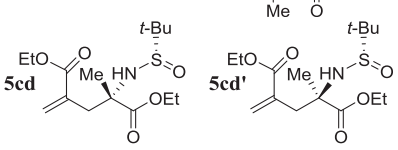
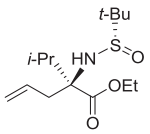
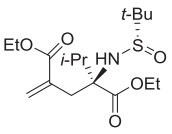
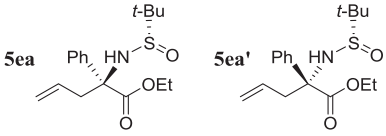
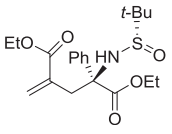
The allylation of ketimines **3c**–**e** did not take place with allylic bromides **4a**–**c** in the presence of 1.5 equiv of indium in THF at room temperature (Method A). However, it proceeded effectively to yield the expected allylated products at a higher temperature (Method C). The indium-mediated allylation of ketimine **3c**, derived from ethyl pyruvate (**2c**) (isolated as a 6:4 mixture of *E*:*Z* stereoisomers) was performed either in a saturated aqueous solution of sodium bromide at room temperature (Method B) or in THF at 60 °C (Method C), to give a mixture of diastereoisomers **5ca** and **5ca′**, in 75 and 62% yield, respectively (Table 2, entries 1 and 2). Importantly, there is a correlation between the *E*:*Z* isomeric ratio of the starting ketimines **3c** (6:4) and the diastereomeric mixture of the reaction products (58:42, and 60:40). It indicates that the allylation is stereospecific. The same correlation was observed in the reaction of **3c** with methallyl bromide (**4b**) and ethyl-bromomethylacrylate (**4d**) (Table 2, entries 3 and 5). Taking into

Table 2
Allylation of *N*-*tert*-butanesulfinyl imines **3c**–**e** derived from α-keto esters **2c**–**e**



Entry	Imino ester **3**	Allylic bromide **4**	Method	α-Amino ester **5**		
				No.	Structure	Yield (%)[a]
1	**3c**	**4a** (R^3=H, R^4=H)	B	**5ca** / **5ca′**		75 (58:42)[b]
2	**3c**	**4a** (R^3=H, R^4=H)	C			62 (60:40)[b]
3	**3c**	**4b** (R^3=Me, R^4=H)	C	**5cb** / **5cb′**		58 (60:40)[b]
4	**3c**	**4c** (R^3=H, R^4=Me)	C	**5cc**		59 (46:26:14:14)[b]
5	**3c**	**4d** (R^3=CO_2Et, R^4=H)	B	**5cd** / **5cd′**		65 (60:40)[b]
6	**3d**	**4a** (R^3=H, R^4=H)	C	**5da**		60
7	**3d**	**4d** (R^3=CO_2Et, R^4=H)	D	**5dd**		67
8	**3e**	**4a** (R^3=H, R^4=H)	C	**5ea** / **5ea′**		45 (63:33)[b]
9	**3e**	**4d** (R^3=CO_2Et, R^4=H)	D	**5ed**		58

[a] Yield was determined after column chromatography purification and is based on the starting sulfinimide **3**.
[b] Combined yield. Diastereomeric ratios are given in parenthesis and were determined after ^{1}H NMR analysis of the reaction crude.

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account the stereochemical outcome for aldimines **3a** and **3b** (Table 1), which exhibit exclusively *E* configuration, we postulate that the allylation would proceed also through the *Si*-face on the (E,S_S) major isomer of the imine **3c**, leading to the major diastereoisomers **5ca-cd** with *S* configuration at the 2-position (Table 2, entries 1–3 and 4). On the other hand, a complex mixture of 4 diastereoisomers was obtained with crotyl bromide (**4c**). In this case, along with the stereospecific face selectivity, a second stereogenic centre is formed with low stereocontrol, leading in addition to *syn*:*anti* isomers (Table 2, entry 4). In contrast, ketimines **3d** and **3e** were isolated as single *Z* geometrical isomers, and we expected that the allylation with allyl bromide (**4a**) would proceed with total face diastereoselectivity. That was the case for the isopropyl derivative **3d** (Table 2, entry 6). Surprisingly, the ethyl phenylglyoxylate derivative **3e** led to an almost 2:1 mixture of diastereoisomers **5ea** and **5ea′** when it was submitted to the same reaction conditions (Table 2, entry 8). Finally, we found the highest yields in the allylation of **3d** and **3e** with ethyl 2-bromomethylacrylate (**4d**) when the process was carried out under solvent free reaction conditions at room temperature (Method D), to give the expected amino diesters **5dd** and **5ed**, respectively, as single diastereoisomers (Table 2, entries 7 and 9). The allylation in a saturated aqueous solution of sodium bromide (Method B) was far less effective for these transformations.

We have observed that these indium-promoted allylations are diastereospecific and the stereochemical pathways are governed by the configuration of both the sulfur atom of the sulfinyl group and the configuration of the C=N double bond. For that reason, two different transition states have been proposed in order to rationalize the observed diastereoselectivities, depending on the configuration of the C=N double bond, since all the sulfinyl imines exhibit S_S configuration. Thus, for imines **3a**, **3b** and the major isomer of **3c** with (E,S_S) configuration, the allylation would proceed through a six-membered Zimmerman–Traxler like ring model **I**, with an attached five-membered metallacycle, in which indium is chelated both by the ester carbonyl oxygen and the nitrogen atoms of the imine moiety, which locates the *tert*-butanesulfinyl and the ester groups axially. For these imines, the addition of the allyl moiety takes place at the less hindered *Si* face (Fig. 1). The rest of the imines (minor isomer of **3c**, **3d** and **3e**) exhibit (E,S_S) configuration, and allylation should take place through a necessarily different pathway, because of the opposite stereochemical outcome (a total correlation was observed between the *E*:*Z* isomeric ratio of starting ketimines **3c**, and the diastereomeric mixture of reaction products **5ca**–**cd**). The nucleophilic addition to the *Re*-face of imines with (Z,S_S) configuration could be explained by considering a six-membered chair-like transition state **II**, where the indium is coordinated by the nitrogen atom of the imine, and the *tert*-butanesulfinyl group and R^1 are located at axial positions. In the proposed **I** and **II** models, we also consider that the imine and sulfinyl units adopt the most stable *s-cis* conformation[21] (Fig. 1).

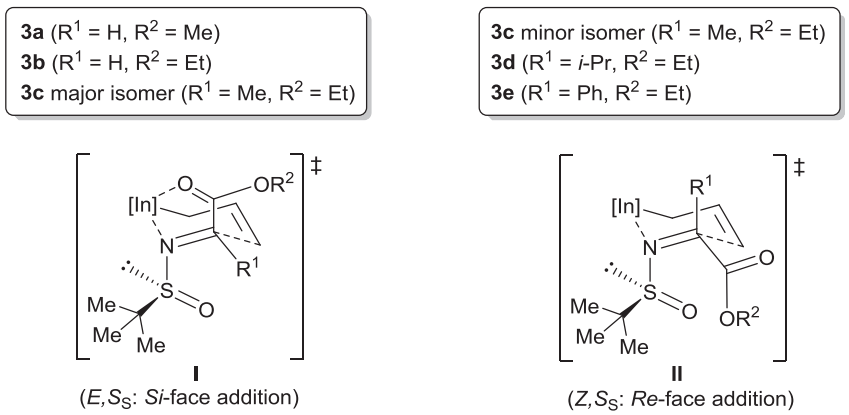
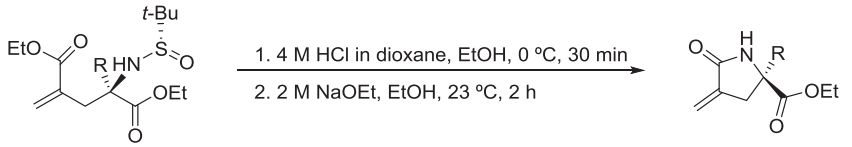


Fig. 1. Proposed stereochemical models for the diastereoselective allylation of *N*-*tert*-butanesulfinyl iminoesters **3**.

Amino diesters **5dd** and **5ed**, derived from the allylation of imino esters **3d** and **3e**, respectively, with ethyl bromomethylacrylate (**4d**), can be easily transformed into α-methylene-γ-butyrolactams **6d** and **6e** in a one-pot, two-step process. First, the *tert*-butanesulfinyl unit was removed under acidic conditions to produce the ammonium salt, and after that, treatment with sodium ethoxide promoted the intramolecular cyclization of the free amine. These reactions were carried out in ethanol as solvent in order to avoid the formation of mixtures of esters by transesterification (Scheme 3). Compounds **5** are of interest not only because they can be transformed into the corresponding α-amino acid derivatives, some of them with the nitrogen bonded to a quaternary stereocentre, but also because the allylic moiety can participate in a number of further synthetically useful transformations, such as cross-metathesis, epoxidation, oxidative cleavage, Heck type reaction, cycloaddition, hydroboration, hydroformylation, hydrogenation, hydration, ozonolysis, etc.[2] In addition, the α,β-unsaturated lactam moiety in compounds **6** allows further structural modifications by reaction with nucleophiles and electrophiles, leading to more complex molecules (Fig. 2).



5dd (R = *i*-Pr)
5ed (R = Ph)

6d (R = *i*-Pr, 71%)
6e (R = Ph, 74%)

Scheme 3. Synthesis of α-methylene-γ-butyrolactams **6** from amino diesters **5dd** and **5ed**.

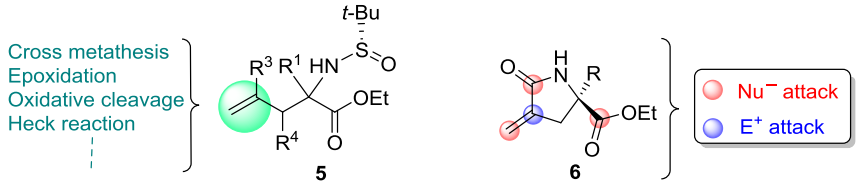


Fig. 2. Potential applications as synthetic intermediates of compounds **5** and **6**.

3. Conclusions

From the results shown here we conclude that the indium-mediated allylation of *N*-*tert*-butanesulfinyl imines derived from α-keto esters takes place with high diastereoselectivity. Interestingly, the configuration of the newly created stereogenic centre is determined by the configuration of both the sulfur atom of the *tert*-butanesulfinyl unit and the C=N double bond of the imine. Enantioenriched homoallylic α-amino esters can be prepared following this methodology, these compounds being synthetic intermediates of wide applicability.

4. Experimental

4.1. General

(R_S)-*tert*-Butanesulfinamide was a gift of Medalchemy (>99% ee by chiral HPLC on a Chiracel AS column, 90:10 *n*-hexane/*i*-PrOH, 1.2 mL/min, λ=222 nm). TLC was performed on silica gel 60 F_{254}, using aluminum plates and visualized with phosphomolybdic acid (PMA) stain. Flash chromatography was carried out on handpacked columns of silica gel 60 (230–400 mesh). Melting points are uncorrected. Optical rotations were measured using a Jasco P-1030 polarimeter with a thermally jacketted 5 cm cell at approximately 23 °C and concentrations (*c*) are given in g/100 mL. Infrared analyses were performed with an ATR Jasco FT/IR-4100 spectrophotometer; wave numbers are given in cm^{-1}. Low-resolution mass spectra (EI) were obtained with an Agilent GC/MS5973N spectrometer at 70 eV; and fragment ions in *m*/*z* with relative intensities (%) in parentheses. High-resolution mass spectra (HRMS) were also carried out in the electron impact mode (EI) at 70 eV and on a Finnigan MAT95S spectrometer equipped with a time of flight (TOF) analyzer and the samples were ionized by ESI techniques and introduced through an ultra-high pressure liquid chromatography (UPLC) model. ^{1}H NMR spectra were recorded at 300 or 400 MHz for ^{1}H NMR and 75 or 100 MHz for ^{13}C NMR with a Bruker AV300 Oxford or a Bruker AV400 spectrometers, respectively, using $CDCl_3$ as the solvent and TMS as internal standard (0.00 ppm). The data is being reported as: s=singlet, d=doublet, t=triplet, q=quartet, sept=septet, m=multiplet or unresolved, br s=broad signal, coupling constant(s) in Hz, integration. ^{13}C NMR spectra were recorded with ^{1}H-decoupling at 100 MHz and referenced to $CDCl_3$ at 77.16 ppm. DEPT-135 experiments were performed to assign CH, CH_2 and CH_3. All reactions requiring anhydrous conditions were performed in oven dried glassware under argon. Otherwise indicated, all commercially available chemicals were purchased from Acros or Sigma–Aldrich and used without purification.

4.2. Preparation of (S_S,*E*)-methyl 2-[(*tert*-butanesulfinyl)imino]acetate (3a)

To a (+)-dimethyl L-tartrate (0.890 g, 5.0 mmol) solution in diethyl ether (10 mL) was slowly added periodic acid (1.254 g, 5.5 mmol). The reaction mixture is stirred at room temperature for 2 h and after that, the solid was filtered off and washed with ethyl acetate (3×10 mL). The organic layer was dried over anhydrous magnesium sulfate for 30 min, and after filtration, the solvent was evaporated (15 Torr) to give methyl glyoxylate (**2a**) as a colorless oil (0.720 g), which was used in the next step without further purification. To a solution of the crude methyl glyoxylate (**2a**, 0.720 g, 8.1 mmol), and (S_S)-*tert*-butanesulfinamide (**1**, 0.787 g, 6.5 mmol) in dry dichloromethane (15 mL) under argon was added anhydrous copper(II) sulfate (1.760 g, 11.0 mmol) and the reaction mixture was stirred at room temperature for 24 h. The solid was filtered off, washed with ethyl acetate (3×10 mL) and the organic layer was evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 6/1) to yield pure (S_S,*E*)-methyl 2-[(*tert*-butanesulfinyl)imino]acetate (**3a**) as a colorless oil (0.372 g, 30%). R_f=0.60 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +173 (*c* 0.88, CH_2Cl_2); ν (film) 2957, 1750, 1735, 1609, 1457, 1291, 1092 cm^{-1}; δ_H 1.28 [9H, s, $(CH_3)_3$], 3.94 (3H, s, CH_3), 8.02 (1H, s, CH); δ_C 22.7, 53.1 (CH_3), 59.0 (C), 155.2 (CH), 161.6 (C); LRMS (EI) *m*/*z* 135 (M^+−56, 29%), 106 (9), 103 (8), 75 (7), 59 (10), 57 (100); HRMS (ESI): calculated for $C_3H_5NO_3S$ (M^+−C_4H_8) 134.9990, found 134.9985.

4.3. Preparation of (*E*,S_S)-ethyl 2-[(*tert*-butanesulfinyl)imino]acetate (3b)[16]

To a solution of the freshly distilled from a 50% solution in toluene of ethyl glyoxylate (**2b**, 0.510 g, 5.0 mmol), and (S_S)-*tert*-butanesulfinamide (**1**, 0.665 g, 5.5 mmol) in dry dichloromethane (15 mL) under argon was added anhydrous copper(II) sulfate (1.760 g, 11.0 mmol) and the reaction mixture was stirred at room temperature for 24 h. The solid was filtered off, washed with ethyl acetate (3×10 mL) and the organic layer was evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/ethyl acetate, 6/1) to yield pure (*E*,S_S)-ethyl 2-[(*tert*-butanesulfinyl)imino]acetate (**3b**) as a colorless oil (0.953 g, 93%). R_f=0.72 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +183 (*c* 0.92, CH_2Cl_2); ν (film) 2967, 2955, 1753, 1735, 1609, 1456, 1285, 1110 cm^{-1}; δ_H 1.28 [9H, s, $(CH_3)_3$], 1.39 (3H, t, *J*=7.2 Hz, CH_2CH_3), 4.39 (2H, q, *J*=7.2 Hz, OCH_2), 8.02 (1H, s, CH); δ_C 14.5, 22.7 (CH_3), 58.9 (C), 62.4 (CH_2), 155.9 (CH), 161.1 (C); LRMS (EI) *m*/*z* 149 (M^+−56, 20%), 120 (12), 117 (7), 89 (10), 73 (10), 57 (100).

4.4. General procedure for the preparation of ketimines 3c–e

To a solution of the corresponding ketoester **2c**–**d** (5.5 mmol) in dry THF (15 mL) was added (S_S)-*tert*-butanesulfinamide (**1**, 0.605 g, 5.0 mmol) and titanium tetraethoxide (2.280 g, 2.095 mL, 10.0 mmol). The resulting mixture was stirred at 60 °C for 6 h, and after that quenched with brine (4.0 mL), and diluted with ethyl acetate (3×10 mL). The resulting suspension was filtered through a short plug of Celite® and concentrated (15 Torr). The residue was purified by column chromatography (hexane/ethyl acetate) to yield pure compounds **3c**–**e**. Yields for these compounds **3** are given on Scheme 2. Physical and spectroscopic data follow.

*4.4.1. (S_S)-Ethyl 2-[(tert-butanesulfinyl)imino]propanoate (**3c**).*[15a] (60:40 *E*:*Z* diastereomeric mixture) yellow oil; R_f=0.56 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +151 (*c* 0.65, CH_2Cl_2); ν (film) 2980, 1725, 1629, 1458, 1365,

1275, 1087 cm^{-1}; δ_H 1.25 [3.6H, s, $(CH_3)_3$], 1.31 [5.4H, s, $(CH_3)_3$], 1.33–1.40 (3H, m, CH_2CH_3), 2.34 (1.2H, s, CH_3), 2.58 (1.8H, s, CH_3), 4.27–4.34 (2H, m, OCH_2); δ_C 14.0, 18.4, 22.8, 25.2 (CH_3), 59.2 (C), 62.3 (CH_2), 163.4, 167.3, 167.6 (C); LRMS (EI) *m/z* 163 (M^+–56, 95%), 145 (8), 117 (46), 89 (73), 57 (100).

*4.4.2. (Z,S_S)-Ethyl 2-[(tert-butanesulfinyl)imino]-3-methylbutanoate (**3d**).*[15a] yellow oil; R_f=0.78 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +262 (*c* 0.60, CH_2Cl_2); *ν* (film) 2975, 1735, 1625, 1459, 1364, 1251, 1089 cm^{-1}; δ_H 1.19 [3H, d, *J*=6.9 Hz, $CH(CH_3)(CH_3)$], 1.20 [3H, d, *J*=6.9 Hz, $CH(CH_3)(CH_3)$], 1.25 [9H, s, $(CH_3)_3$], 1.35 (3H, t, *J*=7.2 Hz, CH_2CH_3), 2.85 [1H, sept, *J*=6.6 Hz, $CH(CH_3)_2$], 4.29–4.34 (2H, m, OCH_2); δ_C 14.0, 18.9, 19.3, 22.5, 37.1 (CH_3), 58.1 (C), 61.8 (CH_2), 166.6, 174.2 (C); LRMS (EI) *m/z* 191 (M^+–56, 56%), 146 (12), 143 (13), 117 (100), 70 (26), 57 (59).

*4.4.3. (Z,S_S)-Ethyl 2-[(tert-butanesulfinyl)imino]-2-phenylacetate (**3e**).*[15a] Yellow oil; R_f=0.85 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +108 (*c* 0.80, CH_2Cl_2); *ν* (film) 2979, 2867, 1735, 1590, 1571, 1447, 1290, 1205 cm^{-1}; δ_H 1.37 [9H, s, $(CH_3)_3$], 1.43 (3H, t, *J*=7.2 Hz, CH_2CH_3), 4.43–4.52 (2H, m, OCH_2), 7.28–7.55 (3H, m, ArH), 7.78–7.81 (2H, m, ArH); δ_C 14.0, 23.0 (CH_3), 59.5 (C), 62.3 (CH_2), 127.9, 128.9, 132.6 (CH), 133.1, 163.3, 165.8 (C); LRMS (EI) *m/z* 207 (M^+–74, 9%), 153 (37), 152 (30), 132 (6), 104 (100), 103 (77), 77 (39), 51 (27).

4.5. General procedure for the allylation of imines 3 in THF at 23 °C (Method A)

To a solution of the corresponding imine **3** (0.5 mmol) in THF (2 mL) was added the corresponding allylic bromide **4** (1.5 mmol) and indium (0.086 g, 0.75 mmol). The resulting suspension was stirred at 23 °C for 6 h and after that quenched with brine (4.0 mL), extracted with ethyl acetate (3×10 mL) and the organic layer was dried over anhydrous magnesium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure compounds **5**. Yields for these compounds **5** are given on Table 1. Physical and spectroscopic data follow.

*4.5.1. (2S,S_S)-Methyl 2-[N-(tert-butanesulfinyl)amino]pent-4-enoate (**5aa**).* Yellow oil; R_f=0.30 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +64 (*c* 0.58, CH_2Cl_2); *ν* (film) 2980, 2953, 1735, 1363, 1272, 1221, 1095, 1060 cm^{-1}; δ_H 1.25 [9H, s, $(CH_3)_3$], 2.50–2.55 (2H, m, CH_2), 3.75 (1H, d, *J*=5.2 Hz, NH), 3.77 (3H, s, CH_3), 4.04–4.09 (1H, m, CHN), 5.08–5.15 (2H, m, CH=CH_2), 5.66–5.74 (1H, m, CH=CH_2); δ_C 22.6 (CH_3), 38.1 (CH_2), 52.5 (CH_3), 56.2 (C), 57.1 (CH), 118.8 (CH_2), 132.4 (CH), 173.0 (C); LRMS (EI) *m/z* 177 (M^+–56, 43%), 159 (20), 135 (39), 118 (54), 100 (55), 88 (26), 57 (100); HRMS (ESI): calculated for $C_8H_{16}NOS$ (M^+–CO_2CH_3) 174.0953, found 174.0955.

*4.5.2. (2S,S_S)-Methyl 2-[N-(tert-butanesulfinyl)amino]-3-methylpent-4-enoate (**5ac**).* (Major isomer) yellow oil; R_f=0.36 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +55 (*c* 0.77, CH_2Cl_2); *ν* (film) 2957, 2870, 1735, 1638, 1437, 1207, 1070 cm^{-1}; δ_H 1.02 (3H, d, *J*=5.7 Hz, CH_3), 1.24 [9H, s, $(CH_3)_3$], 2.56–2.64 (1H, m, CHCH$_3$), 3.50 (1H, d, *J*=5.2 Hz, NH), 3.74 (3H, s, CH_3), 3.85 (1H, dd, *J*=6.5, 4.0 Hz, CHN), 5.00–5.10 (2H, m, CH=CH_2), 5.60–5.80 (1H, m, CH=CH_2); δ_C 15.1, 22.7 (CH_3), 42.0, 52.3 (CH), 56.4 (C), 62.2 (CH_3), 116.1 (CH_2), 138.9 (CH), 172.9 (C); LRMS (EI) *m/z* 191 (M^+–56, 46%), 173 (14), 135 (76), 114 (30), 88 (50), 57 (100); HRMS (ESI): calculated for $C_9H_{18}NOS$ (M^+–CO_2CH_3) 188.1109, found 188.1110.

*4.5.3. (2S,S_S)-Ethyl 2-[N-(tert-butanesulfinyl)amino]pent-4-enoate (**5ba**).*[17b] Yellow oil; R_f=0.27 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +77 (*c* 1.96, CH_2Cl_2); *ν* (film) 2952, 2928, 1735, 1642, 1465, 1365, 1185, 1075 cm^{-1}; δ_H 1.25 [9H, s, $(CH_3)_3$], 1.29 (3H, t, *J*=6.9 Hz, CH_2CH_3), 2.51–2.53 (2H, m, CH_2), 4.04 (1H, q, *J*=5.7 Hz, CH), 4.14 (1H, d, *J*=6.3 Hz, NH), 4.22 (2H, q, *J*=7.2 Hz, OCH_2), 5.09–5.14 (2H, m, CH=CH_2), 5.70–5.77 (1H, m, CH=CH_2); δ_C 14.2, 22.6 (CH_3), 38.1 (CH_2), 56.1 (C), 56.9 (CH), 61.8 (CH_2), 118.8 (CH_2), 132.4 (CH), 172.4 (C); LRMS (EI) *m/z* 191 (M^+–56, 15%), 167 (17), 149 (74), 100 (18), 97 (39), 95 (27), 85 (39), 83 (37), 81 (27), 71 (55), 69 (49), 57 (100), 55 (48).

*4.5.4. (2S,S_S)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-4-methylpent-4-enoate (**5bb**).*[17b] Yellow oil; R_f=0.22 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +47 (*c* 0.88, CH_2Cl_2); *ν* (film) 2952, 2922, 1736, 1649, 1455, 1366, 1264, 1179, 1060 cm^{-1}; δ_H 1.23 [9H, s, $(CH_3)_3$], 1.29 (3H, t, *J*=6.9 Hz, CH_2CH_3), 1.75 (3H, s, CH_3), 2.35–2.53 (2H, m, CH_2), 4.01–4.11 (2H, m, CH, NH), 4.22 (2H, q, *J*=7.2 Hz, OCH_2), 4.75 (1H, br s, C=C*H*H), 4.83 (1H, br s, C=CH*H*); δ_C 14.1, 22.1, 29.7 (CH_3), 42.4 (CH_2), 56.2 (C and CH), 61.7 (CH_2), 114.5 (CH_2), 140.3, 173.2 (C); LRMS (EI) *m/z* 205 (M^+–56, 8%), 167 (15), 149 (63), 141 (30), 111 (21), 97 (30), 85 (34), 83 (38), 81 (20), 71 (46), 57 (100).

4.6. General procedure for the allylation of imines 3 in H_2O at 23 °C (Method B)

To a suspension of the corresponding imine **3** (0.5 mmol) in a saturated sodium bromide aqueous solution (5 mL) was added the corresponding allylic bromide **4** (1.5 mmol) and indium (0.232 g, 2.0 mmol). The resulting reaction mixture was stirred at 23 °C for 48 h and after that, extracted with ethyl acetate (3×10 mL) and the organic layer was dried over anhydrous magnesium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure compounds **5**. Yields are given on Tables 1 and 2. Physical and spectroscopic data follow.

*4.6.1. (2S,S_S)-5Ethyl 1-methyl 2-[N-(tert-butanesulfinyl)amino]-4-methylenepentanedioate (**5ad**).* Orange oil; R_f=0.26 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +36 (*c* 0.70, CH_2Cl_2); *ν* (film) 2956, 2871, 1710, 1630, 1518, 1457, 1368, 1214, 1147, 1059 cm^{-1}; δ_H 1.21 [9H, s, $(CH_3)_3$], 1.31 (3H, t, *J*=6.9 Hz, CH_2CH_3), 2.68 (1H, dd, *J*=13.8, 1.2 Hz, C*H*H), 2.78 (1H, dd, *J*=13.8, 1.2 Hz, CH*H*), 3.76 (3H, s, CH_3), 4.10–4.26 (4H, m, NH, CHN, OCH_2), 5.62 (1H, br s, C=C*H*H), 6.27 (1H, br s, C=CH*H*); δ_C 14.2, 22.6 (CH_3), 36.8 (CH_2), 52.5 (CH_3), 56.3 (C), 57.1 (CH), 61.0 (CH_2), 128.5 (CH_2) 135.8, 166.4, 173.2 (C); LRMS (EI) *m/z* 249 (M^+–56, 7%), 190 (17), 158 (20), 135 (32), 115 (96), 87 (81), 69 (100); HRMS (ESI): calculated for $C_{11}H_{20}NO_3S$ (M^+–CO_2CH_3) 246.1164, found 246.1158.

*4.6.2. (2S,S_S)-Diethyl 2-[N-(tert-butanesulfinyl)amino]-4-methylenepentanedioate (**5bd**).* Yellow oil; R_f=0.24 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +32 (*c* 1.24, CH_2Cl_2); *ν* (film) 2979, 2943, 1713, 1631, 1474, 1301, 1268, 1182, 1060 cm^{-1}; δ_H 1.21 [9H, s, $(CH_3)_3$], 1.26–1.34 (6H, m, 2 CH_2CH_3), 2.64–2.82 (2H, m, CH_2), 4.11–4.26 (6H, m, 2 OCH_2, CH, NH), 5.62 (1H, br s, C=C*H*H), 6.27 (1H, br s, C=CH*H*); δ_C 14.0, 14.2, 22.6 (CH_3), 36.9 (CH_2), 56.3 (C), 57.0 (CH), 61.0, 61.8 (CH_2), 128.4 (CH_2) 135.9, 166.4, 172.8 (C); LRMS (EI) *m/z* 263 (M^+–56, 37%), 217 (80), 172 (39), 143 (85), 141 (100), 96 (25), 57 (67); HRMS (ESI): calculated for $C_{10}H_{17}NO_5S$ (M^+–C_4H_8) 263.0827, found 263.0837.

*4.6.3. (2S,S_S)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2-methylpent-4-enoate (**5ca**).* (Major diastereoisomer) yellow oil; R_f=0.31 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +31 (*c* 0.72, CH_2Cl_2); *ν* (film) 2980, 1734, 1633, 1457, 1364, 1218, 1069 cm^{-1}; δ_H 1.16 [9H, s, $(CH_3)_3$], 1.22 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.47 (3H, s, CH_3), 2.55–2.61 (2H, m, CH_2), 4.08–4.16 (3H, m, OCH_2, NH), 5.05–5.09 (2H, m, CH=CH_2), 5.68–5.82 (1H, m, CH=CH_2); δ_C 13.2, 21.6, 23.1 (CH_3), 44.1 (CH_2), 55.1 (C), 60.6 (CH_2), 60.8 (C), 118.8 (CH_2), 131.1 (CH), 172.3 (C); LRMS

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(EI) *m/z* 205 (M^+-56, 18%), 187 (13), 163 (10), 132 (100), 114 (45), 89 (19); HRMS (ESI): calculated for $C_9H_{18}NOS$ ($M^+-CO_2CH_2CH_3$) 188.1109, found 188.1110.

*4.6.4. (2R,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2-methylpent-4-enoate (**5ca′**).* (Minor diastereoisomer) yellow oil; R_f=0.36 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +46 (*c* 0.79, CH_2Cl_2); *ν* (film) 2981, 2870, 1732, 1640, 1457, 1364, 1220, 1071 cm^{-1}; δ_H 1.16 [9H, s, $(CH_3)_3$], 1.22 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.52 (3H, s, CH_3), 2.43–2.49 (2H, m, CH_2), 4.10–4.17 (3H, m, OCH_2, NH), 5.01–5.06 (2H, m, CH=C*H*$_2$), 5.55–5.69 (1H, m, C*H*=CH_2); δ_C 13.1, 21.7, 23.2 (CH_3), 43.5 (CH_2), 55.0, 60.1 (C), 60.7 (CH_2), 118.3 (CH_2), 131.1 (CH), 173.0 (C); LRMS (EI) *m/z* 205 (M^+-56, 18%), 187 (13), 163 (6), 132 (100), 114 (37), 89 (19), 57 (25); HRMS (ESI): calculated for $C_9H_{18}NO_2S$ ($M^+-CO_2CH_2CH_3$) 188.1109, found 188.1110.

*4.6.5. (2S,S$_S$)-Diethyl 2-[N-(tert-butanesulfinyl)amino]-2-methyl-4-methylenepentanedioate (**5cd**).* (Major diastereoisomer) orange oil; R_f=0.34 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +16 (*c* 0.57, CH_2Cl_2); *ν* (film) 2981, 1718, 1626, 1531, 1457, 1368, 1214, 1197, 1024 cm^{-1}; δ_H 1.20 [9H, s, $(CH_3)_3$], 1.23–1.31 (6H, m, 2 CH_2CH_3), 1.62 (3H, s, CH_3), 2.79 (1H, d, *J*=13.8 Hz, C*H*H), 2.92 (1H, d, *J*=13.8 Hz, *CH*H), 4.00–4.18 (4H, m, 2 OCH_2), 4.54 (1H, s, NH), 5.81 (1H, br s, C=C*H*H), 6.31 (1H, br s, C=CH*H*); δ_C 14.0, 22.5, 22.6, 24.1 (CH_3), 42.6 (CH_2), 55.3, 57.4 (C), 61.2, 61.7, 130.3 (CH_2) 135.3, 167.4, 172.9 (C); LRMS (EI) *m/z* 277 (M^+-56, 2%), 227 (12), 204 (87), 186 (20), 163 (95), 140 (27), 114 (41), 87 (50), 69 (100); HRMS (ESI): calculated for $C_{11}H_{19}NO_5S$ ($M^+-C_4H_8$) 277.0984, found 277.0986.

*4.6.6. (2R,S$_S$)-Diethyl 2-[N-(tert-butanesulfinyl)amino]-2-methyl-4-methylenepentanedioate (**5cd′**).* (Minor diastereoisomer) orange oil; R_f=0.30 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +25 (*c* 1.24, CH_2Cl_2); *ν* (film) 2981, 1720, 1630, 1530, 1457, 1368, 1214, 1200, 1024 cm^{-1}; δ_H 1.17 [9H, s, $(CH_3)_3$], 1.23–1.31 (6H, m, 2 CH_2CH_3), 1.53 (3H, s, CH_3), 2.58 (1H, d, *J*=13.8 Hz, C*H*H), 2.98 (1H, d, *J*=13.8 Hz, *CH*H), 4.13–4.32 (4H, m, 2 OCH_2), 4.30 (1H, s, NH), 5.60 (1H, br s, C=C*H*H), 6.28 (1H, br s, C=CH*H*); δ_C 14.0, 22.0, 22.6, 24.1 (CH_3), 42.6 (CH_2), 55.3, 56.4 (C), 61.2, 61.8, 130.3 (CH_2) 135.3, 167.2, 174.0 (C); LRMS (EI) *m/z* 277 (M^+-56, 3%), 232 (7), 204 (87), 186 (20), 163 (94), 140 (25), 114 (41), 87 (50), 69 (100); HRMS (ESI): calculated for $C_{11}H_{19}NO_5S$ ($M^+-C_4H_8$) 277.0984, found 277.0983.

4.7. General procedure for the allylation of imines 3 in THF at 60 °C (Method C)

To a solution of the corresponding imine **3** (0.5 mmol) in THF (2 mL) was added the corresponding allylic bromide **4** (1.5 mmol) and indium (0.086 g, 0.75 mmol). The resulting suspension was stirred at 60 °C for 6 h and after that, the reaction mixture was cooled down, quenched with brine (4.0 mL), extracted with ethyl acetate (3×10 mL) and the organic layer was dried over anhydrous magnesium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure compounds **5**. Yields are given on Table 2. Physical and spectroscopic data follow.

*4.7.1. (2S,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2,4-dimethylpent-4-enoate (**5cb**).* (major diastereoisomer) yellow oil; R_f=0.40 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +25 (*c* 0.60, CH_2Cl_2); *ν* (film) 2921, 1719, 1644, 1421, 1360, 1221, 1063, 736 cm^{-1}; δ_H 1.22 [9H, s, $(CH_3)_3$], 1.30 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.60 (3H, s, CH_3), 1.67 (3H, br s, CH_3), 2.50–2.62 (2H, m, CH_2), 4.02 (1H, s, NH), 4.16–4.26 (2H, m, OCH_2), 4.74 (1H, br s, C=C*H*H), 4.86 (1H, br s, C=CH*H*); δ_C 14.0, 22.7, 23.5, 25.0 (CH_3), 31.9 (C), 47.8 (CH_2), 56.0 (C), 61.8, 115.6 (CH_2), 140.2, 174.6 (C); LRMS (EI) *m/z* 219 (M^+-56, 18%), 191 (9), 163 (80), 157 (20), 146 (100), 130 (90), 117 (41), 109 (18), 89 (92), 55 (17); HRMS (ESI): calculated for $C_{10}H_{20}NOS$ ($M^+-CO_2CH_2CH_3$) 202.1266, found 202.1267.

*4.7.2. (2R,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2,4-dimethylpent-4-enoate (**5cb′**).* (Minor diastereoisomer) yellow oil; R_f=0.44 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +18 (*c* 1.00, CH_2Cl_2); *ν* (film) 2924, 1732, 1644, 1457, 1375, 1204, 1073, 895 cm^{-1}; δ_H 1.24 [9H, s, $(CH_3)_3$], 1.29 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.63 (3H, s, CH_3), 1.70 (3H, br s, CH_3), 2.70–2.58 (2H, m, CH_2), 4.09 (1H, s, NH), 4.14–4.25 (2H, m, OCH_2), 4.80 (1H, br s, C=C*H*H), 4.96 (1H, br s, C=CH*H*); δ_C 14.1, 22.7, 23.5, 24.6 (CH_3), 31.9 (C), 49.4 (CH_2), 56.3 (C), 61.5 (CH_2), 116.6 (CH_2), 140.4, 175.3 (C); LRMS (EI) *m/z* 219 (M^+-56, 18%), 191 (9), 163 (100), 157 (50), 146 (95), 130 (97), 117 (41), 109 (18), 89 (92), 55 (37); HRMS (ESI): calculated for $C_{10}H_{20}NOS$ ($M^+-CO_2CH_2CH_3$) 202.1266, found 202.1266.

*4.7.3. (2S,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2,3-dimethylpent-4-enoate (**5cc**).* (Major diastereoisomer) yellow oil; R_f=0.44 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +55 (*c* 0.61, CH_2Cl_2); *ν* (film) 2924, 1730, 1642, 1458, 1368, 1201, 1068, 894 cm^{-1}; δ_H 0.99 (3H, d, *J*=6.9 Hz, CH_3), 1.25 [9H, s, $(CH_3)_3$], 1.29 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.55 (3H, s, CH_3), 2.40–2.55 (1H, m, CH), 4.17–4.25 (2H, m, OCH_2), 4.33 (1H, br s, NH), 5.06–5.13 (2H, m, CH=C*H*$_2$), 5.60–5.74 (1H, m, *CH*=CH_2); δ_C 14.1, 19.2, 22.8 (CH_3), 47.4 (CH), 56.1 (C), 61.7 (CH_2), 63.1 (C) 117.4 (CH_2), 137.8 (CH), 174.5 (C); LRMS (EI) *m/z* 219 (M^+-56, 5%) 203 (6), 164 (8), 146 (100), 128 (19), 98 (20), 73 (5), 55 (9);; HRMS (ESI): calculated for $C_{10}H_{20}NOS$ ($M^+-CO_2CH_2CH_3$) 202.1266, found 202.1262.

*4.7.4. (2S,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2-isopropylpent-4-enoate (**5da**).* Yellow oil; R_f=0.48 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +26 (*c* 0.61, CH_2Cl_2); *ν* (film) 2961, 2923, 1725, 1366, 1220, 1072 cm^{-1}; δ_H 0.98 [3H, d, *J*=6.8 Hz, $CH(CH_3)(CH_3)$], 1.04 [3H, d, *J*=6.8 Hz, $CH(CH_3)(CH_3)$], 1.26 [9H, s, $(CH_3)_3$], 1.27–132 (3H, m, CH_2CH_3), 2.23–2.32 [1H, m, $CH(CH_3)_2$], 2.74–2.77 (2H, m, CH_2), 4.17–4.25 (2H, m, OCH_2), 4.41 (1H, s, NH), 5.05–5.14 (2H, m, CH=C*H*$_2$), 5.63–5.72 (1H, m, C*H*=CH_2); δ_C 14.2, 16.7, 17.8, 22.6 (CH_3), 36.9 (CH), 38.5 (CH_2), 57.0 (C), 61.5 (CH_2), 69.1 (C), 118.8 (CH_2), 133.1 (CH), 172.6 (C); LRMS (EI) *m/z* 233 (M^+-56, 2%) 190 (22), 161 (15), 160 (100), 144 (23), 126 (62), 117 (40), 100 (27), 72 (8), 70 (15); HRMS (ESI): calculated for $C_{10}H_{19}NO_3S$ ($M^+-C_4H_8$) 233.1086, found 233.1090.

*4.7.5. (2S,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2-phenylpent-4-enoate (**5ea**).* (Major diastereoisomer) yellow oil; R_f=0.50 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +44 (*c* 0.50, CH_2Cl_2); *ν* (film) 3011, 2933, 1728, 1638, 1366, 1225, 1117, 1072 cm^{-1}; δ_H 1.20 [9H, s, $(CH_3)_3$], 1.19–1.22 (3H, m, CH_2CH_3), 3.23 (2H, d, *J*=7.2 Hz, CH_2), 4.05–4.25 (2H, m, OCH_2), 4.68 (1H, s, NH), 5.14–5.20 (2H, m, CH=C*H*$_2$), 5.74–5.83 (1H, m, C*H*=CH_2), 7.26–7.38 (5H, m, ArH); δ_C 14.0, 22.7 (CH_3), 40.9 (CH_2), 56.4 (C), 62.0 (CH_2), 67.0 (C), 120.3 (CH_2), 126.7, 128.1, 128.4, 131.7 (CH), 140.0, 172.7 (C); LRMS (EI) *m/z* 267 (M^+-56, 20%), 204 (57), 203 (100), 175 (24), 157 (25), 135 (35), 131 (75), 129 (55), 91 (23), 57 (47); HRMS (ESI): calculated for $C_{13}H_{17}NO_3S$ ($M^+-C_4H_8$) 267.0929, found 267.0945.

*4.7.6. (2R,S$_S$)-Ethyl 2-[N-(tert-butanesulfinyl)amino]-2-phenylpent-4-enoate (**5ea′**).* (Minor diastereoisomer) yellow oil; R_f=0.42 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ +52 (*c* 0.58, CH_2Cl_2); *ν* (film) 3010, 3002, 2934, 1726, 1638, 1362, 1225, 1117, 1070 cm^{-1}; δ_H 1.20 (3H, t, *J*=7.2 Hz, CH_2CH_3), 1.23 [9H, s, $(CH_3)_3$], 3.13 (2H, d, *J*=7.2 Hz, CH_2), 4.13–4.22 (2H, m, OCH_2), 4.68 (1H, s, NH), 5.18–5.24 (2H, m, CH=C*H*$_2$), 5.70–5.80 (1H, m, C*H*=CH_2), 7.26–7.42 (5H, m, ArH); δ_C 14.1, 22.7 (CH_3), 41.2 (CH_2), 56.7 (C), 62.2 (CH_2), 67.3 (C), 120.0 (CH_2), 126.7, 128.3, 128.5, 132.2 (CH), 139.8, 172.4 (C); LRMS (EI) *m/z* 267 (M^+-56, 30%), 204 (40), 203 (100), 175 (45), 157 (25), 135 (35), 131

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(75), 129 (50), 91 (30), 57 (40); HRMS (ESI): calculated for $C_{13}H_{17}NO_3S$ ($M^+-C_4H_8$) 267.0929, found 267.0932.

4.8. General procedure for the allylation of imines 3 under solvent free reaction conditions (Method D)

A mixture of the corresponding imine **3** (0.5 mmol), ethyl bromomethylacrylate (**4d**, 0.290 g, 0.210 mL, 1.5 mmol) and indium (0.116 g, 1.0 mmol) was stirred at 23 °C for 6 h. After that, the reaction mixture was quenched with water (50 mL), extracted with ethyl acetate (3×10 mL) and the organic layer was dried over anhydrous magnesium sulfate and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure compounds **5**. Yields are given on Table 2. Physical and spectroscopic data follow.

*4.8.1. (2S,S_S)-Diethyl 2-[N-(tert-butanesulfinyl)amino]-2-isopropyl-4-methylenepentanedioate (**5dd**).* Orange oil; R_f=0.45 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ −8.5 (*c* 0.50, CH_2Cl_2); *ν* (film) 2959, 2928, 1716, 1625, 1456, 1366, 1260, 1155, 1026 cm^{-1}; δ_H 1.07 [3H, d, *J*=6.9 Hz, CH(C*H*$_3$)(CH$_3$)], 1.08 [3H, d, *J*=6.8 Hz, CH(CH$_3$)(C*H*$_3$)], 1.24 [9H, s, (CH$_3$)$_3$], 1.26–1.32 (6H, m, 2 CH$_2$C*H*$_3$), 2.36 [1H, sept, *J*=6.9 Hz, C*H*(CH)$_3$], 2.88–2.94 (2H, m, CH$_2$), 4.05–4.24 (4H, m, 2 OCH$_2$), 4.34 (1H, s, NH), 5.83 (1H, br s, C=C*H*H), 6.31 (1H, br s, C=CH*H*); δ_C 14.0, 14.1, 16.6, 18.0, 22.9 (CH$_3$), 35.4 (CH), 38.0 (CH$_2$), 57.3 (C), 61.0, 61.4 (CH$_2$), 69.3 (C), 129.1 (CH$_2$), 135.8 (C), 167.6 (C), 172.6 (C); LRMS (EI) *m*/*z* 305 (M^+−56, 39%), 287 (29), 259 (60), 214 (27), 185 (71), 183 (92), 174 (52), 168 (36), 145 (100), 144 (73), 138 (36), 137 (27), 117 (28), 57 (64); HRMS (ESI): calculated for $C_{13}H_{23}NO_5S$ ($M^+-C_4H_8$) 305.1297, found 305.1301.

*4.8.2. (2S,S_S)-Diethyl 2-[N-(tert-butanesulfinyl)amino]-4-methylene-2-phenylpentanedioate (**5ed**).* Orange oil; R_f=0.43 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ −6.0 (*c* 0.70, CH_2Cl_2); *ν* (film) 3008, 2931, 1719, 1620, 1455, 1366, 1250, 1155, 1014 cm^{-1}; δ_H 1.16–1.28 (6H, m, 2 CH$_2$C*H*$_3$), 1.23 [9H, s, (CH$_3$)$_3$], 3.45 (1H, d, *J*=14.0 Hz, C*H*H), 3.54 (1H, d, *J*=14.0 Hz, CH*H*), 4.02–4.22 (4H, m, 2 OCH$_2$), 4.80 (1H, s, NH), 6.03 (1H, d, *J*=1.5 Hz, C=C*H*H), 6.36 (1H, d, *J*=1.5 Hz, C=CH*H*), 7.33–7.39 (5H, m, ArH); δ_C 13.8, 14.1, 22.8 (CH$_3$), 37.5 (CH$_2$), 56.6 (C), 60.9 (CH$_2$), 61.9 (CH$_2$), 66.8 (C), 127.2, 128.2, 128.3 (CH), 131.3 (CH$_2$), 135.0, 139.4, 167.2, 172.5 (C); LRMS (EI) *m*/*z* 339 (M^+−56, 30%), 294 (10), 266 (30), 221 (37), 185 (71), 179 (100), 168 (36), 144 (43), 136 (38), 117 (28), 77 (24); HRMS (ESI): calculated for $C_{16}H_{21}NO_5S$ ($M^+-C_4H_8$) 339.1140, found 339.1157.

4.9. General procedure for the preparation of α-methylene-γ-butyrolactams 6

To a solution of the corresponding amino diester derivative **5** (0.2 mmol) in ethanol (0.5 mL) was added a 4 M HCl dioxane solution (0.1 mL, 0.4 mmol) at 0 °C. After 30 min of stirring at the same temperature, a 2 M sodium ethoxide ethanol solution (0.25 mL, 0.5 mmol) was added, and the resulting mixture was stirred for 2 h at 23 °C. After that, it was diluted with water (10 mL), extracted with EtOAc (3×10 mL), dried over anhydrous magnesium sulfate, and evaporated (15 Torr). The resulting residue was then purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure compounds **6**. Yields are given on Scheme 3. Physical and spectroscopic data follow.

*4.9.1. (S)-5-Ethoxycarbonyl-5-isopropyl-3-methylenepyrrolidin-2-one (**6d**).* yellow oil; R_f=0.25 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ −9.5 (*c* 1.50, CH_2Cl_2); *ν* (film) 2965, 2926, 1733, 1702, 1660, 1463, 1370, 1252, 1041, 928 cm^{-1}; δ_H 0.89 [3H, d, *J*=6.9 Hz, CH(C*H*$_3$)(CH$_3$)], 1.20–1.33 [6H, m, CH$_2$C*H*$_3$, CH(CH$_3$)(C*H*$_3$)$_2$], 2.14 [1H, sept, *J*=6.9 Hz, C*H*(CH)$_3$], 2.83 (1H, dt, *J*=17.7, 2.4 Hz, C*H*H), 3.14 (1H, dt, *J*=17.7, 2.4 Hz, C*H*H), 4.22 (2H, q, *J*=7.2 Hz, OCH$_2$), 5.38 (1H, br s, C=C*H*H), 6.01 (1H, t, *J*=2.7 Hz, C=CH*H*), 6.25 (1H, br s, NH); δ_C 14.2, 16.0, 17.0 (CH$_3$), 29.7 (CH$_2$), 35.8 (CH), 61.8 (CH$_2$), 65.8 (C), 116.8 (CH$_2$), 138.0, 169.2, 172.9 (C); LRMS (EI) *m*/*z* 183 (M^+−28, 100%), 175 (20), 144 (60), 131(30), 102 (25), 58 (67); HRMS (ESI): calculated for $C_8H_{10}NO_3$ ($M^+-C_3H_7$) 168.0661, found 168.0667.

*4.9.2. (S)-5-Ethoxycarbonyl-3-methylene-5-phenylpyrrolidin-2-one (**6e**).* Orange oil; R_f=0.22 (hexane/AcOEt 2:1); $[\alpha]_D^{30}$ −2.7 (*c* 0.80, CH_2Cl_2); *ν* (film) 3014, 2924, 1710, 1670, 1437, 1360, 1220, 1090, 734, 701 cm^{-1}; δ_H 1.20–1.30 (3H, m, CH$_2$C*H*$_3$), 3.01 (1H, dt, *J*=17.1, 2.4 Hz, C*H*H), 3.81 (1H, dt, *J*=17.1, 2.3 Hz, C*H*H), 4.19–4.25 (2H, m, OCH$_2$), 5.41 (1H, br s, C=C*H*H), 6.07 (1H, br s, C=CH*H*), 6.81 (1H, br s, NH), 7.37–7.40 (5H, m, ArH); δ_C 14.0, 39.6, 62.4 (CH$_2$), 65.2 (C), 117.9 (CH$_2$), 124.4, 128.4, 129.0 (CH), 137.1, 141.0, 169.2, 171.5 (C); LRMS (EI) *m*/*z* 218 (M^+−28, 100%), 172 (80), 159 (8), 144 (10), 129 (11), 104 (12), 91 (5), 77 (7); HRMS (ESI): calculated for $C_{11}H_{10}NO$ ($M^+-CO_2CH_2CH_3$) 172.0762, found 172.0768.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2016.07.020.

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