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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b01178 • Publication Date (Web): 29 Jun 2017

Stereoselective Coupling of *N-tert*-Butanesulfinyl Aldimines and β-Keto Acids: Access to β-Amino Ketones

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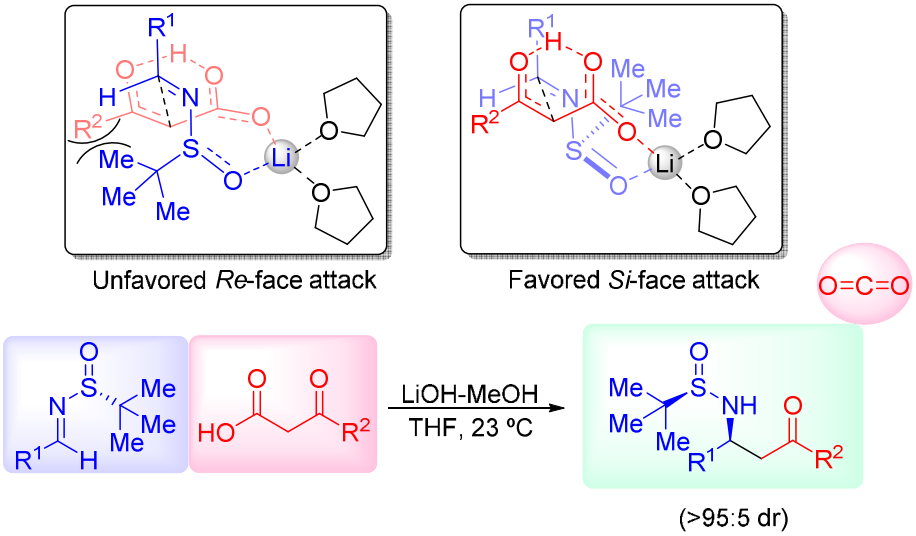


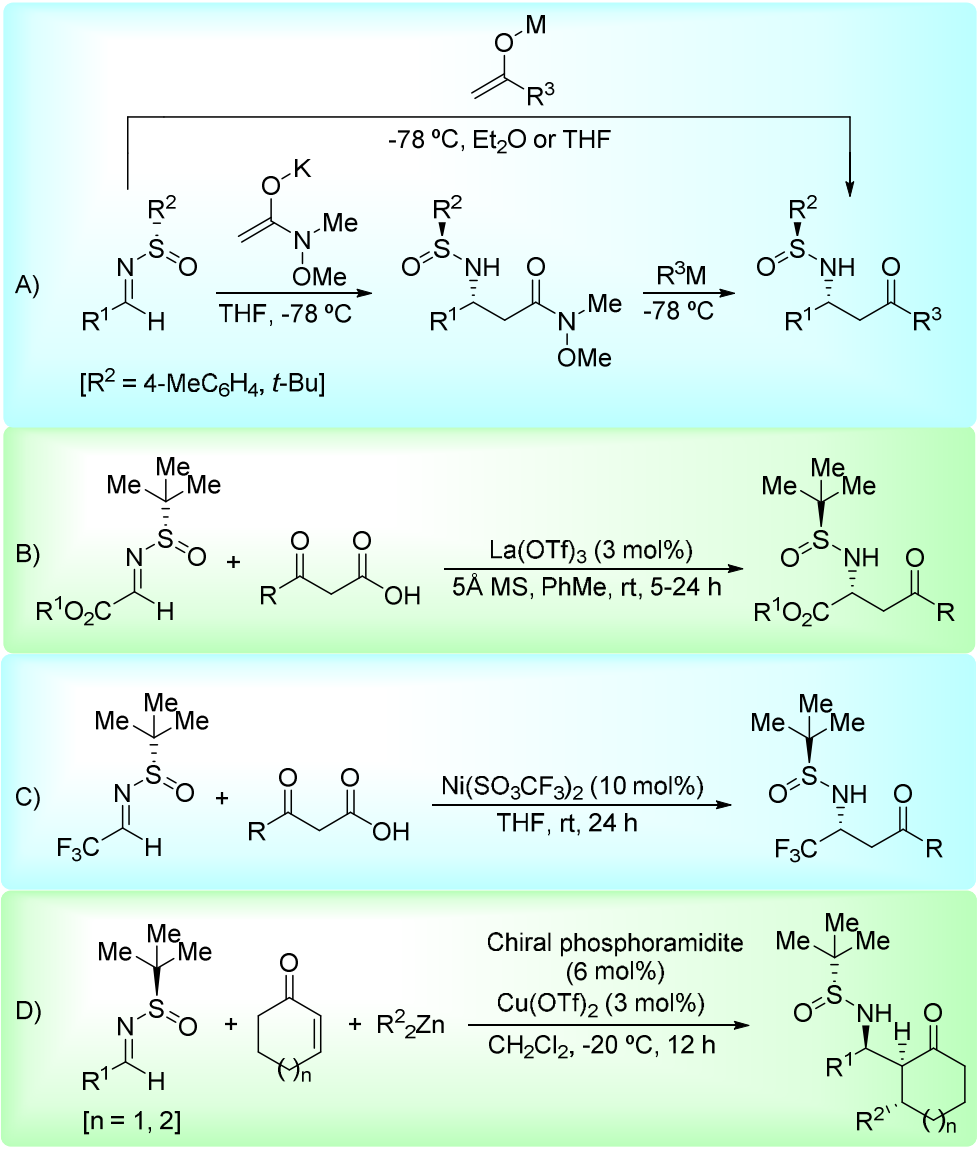
ABSTRACT. The reaction of chiral *N-tert*-butanesulfinyl aldimines with β-keto acids under basic conditions at room temperature proceeds with high levels of diastereocontrol, leading to β-amino ketones in high yields. Based on DFT calculations, an eight-membered cyclic transition state involving coordination of the lithium atom to the oxygens of carboxylate and sulfinyl units was proposed, being in agreement with the observed experimental diastereomeric ratios. The synthesis of the piperidine alkaloid (–)-pelletierine was successfully undertaken in order to demonstrate the utility of this methodology.

KEYWORDS. Chiral sulfinyl imines, β-keto acids, β-amino ketones, diastereoselective Mannich reaction, DFT calculations.

INTRODUCTION

Coupling of enolizable carbonyl compounds with imines, the so-called Mannich reaction, render β-amino carbonyl compounds.[1] These are interesting molecular systems because they can be converted into polyfunctionalized molecules and act as versatile building-blocks.[2] Highly efficient methodologies to perform the stereoselective version of these transformations have been developed in recent years by means of chiral organic and organometallic catalytic systems.[3] The stereoselective Mannich reactions are also performed with stoichiometric amounts of chiral reagents. In these reactions, the stereochemical information could be provided by a chiral imine,[4] in which most commonly a chiral auxiliary is a substituent of the iminic nitrogen, or by a chiral nucleophile derived from aldehydes, ketones, esters or enol ethers.[5] Among chiral imines, those derived from *tert*-butanesulfinamide have been extensively used as electrophiles over the past decade in many synthetic transformations,[6] due mainly to the ready availability of both enantiomers of *tert*-butanesulfinamide at reasonable prices, the easy deprotection of the resulting amine under mild acidic conditions and the possibility of recycling the chiral auxiliary.[7] Davis reported the synthesis of β-amino carbonyl compounds in a two-step process by reaction of the corresponding sulfinyl imine (both, *p*-toluene and *tert*-butane derivatives) with the potassium enolate of *N*-methoxy *N*-methylacetamide at low temperature, and subsequent addition of an organometallic reagent to the resulting β-amino Weinreb amide.[8] The same reaction products were also obtained by direct addition of the corresponding methyl ketone enolate to the sulfinyl imine at low temperature (Scheme 1A).[9] Enolates of methyl ketones should be prepared with stoichiometric amounts of strong bases at low temperature in order to avoid autocondensation, that representing a limitation of this methodology. On the other hand, β-keto acids have been used as surrogate enolates in different processes,[10] among then decarboxylative Mannich-reactions by reacting with different imines. Considering these transformations, as far as we know, there are only two examples of nucleophilic additions of β-keto acids to activated *N*-*tert*-butanesulfinyl imines: the $La(OTf)_3$ catalyzed addition to *N*-*tert*-butanesulfinyl α-imino esters (Scheme 1B)[11] and the nickel catalyzed addition to a trifluoroacetaldehyde derivative (Scheme 1C).[12] Based on our experience on nucleophilic additions to *N*-*tert*-butanesulfinyl imines of homochiral enolates resulting from the diastereoselective addition of dialkylzinc reagents to cyclic α,β-unsaturated enones (Scheme 1D)[13] and of diethyl malonate under basis conditions,[14] we herein report our approach to the stereoselective synthesis of β-amino carbonyl compound derivatives from dicarbonyl compounds as pronucleophiles.

Scheme 1. Examples of *N-tert*-butanosulfinyl imines in Mannich-type reactions.

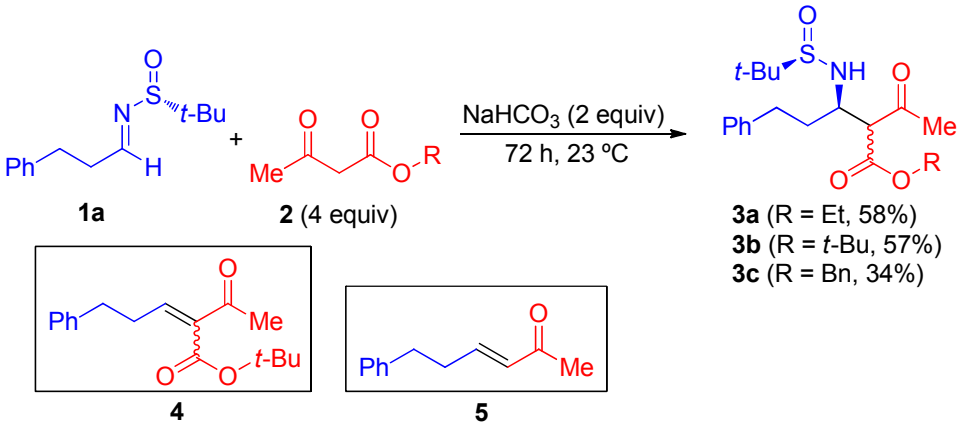


RESULTS AND DISCUSSION

The coupling of the *N-tert*-butanesulfinyl imine derived from 3-phenylpropanal **1a** and different acetoacetate esters **2** under basic conditions was first studied. The applied reaction conditions were identical to those we found to work well in the case of this type of imines and dimethyl malonate.[14] The expected compounds **3** were obtained in variable yields, the nucleophilic addition taking place in an almost total diastereoselective fashion. With regard to the second stereogenic center, an equimolecular amount of both possible epimers was obtained, due to the presence of an acidic proton at that center, so epimerization occurs very fast under the basic reaction conditions (Scheme 2). Unfortunately, all the attempts to carry out the decarboxylation of compounds **3** in order to produce a β-amino carbonyl compound lead to a complex mixture of reaction products. For

instance, α,β-unsaturated compounds **4** and **5** were the major components of these mixtures when the *tert*-butyl ester derivative **3b** was the starting material (Scheme 2).

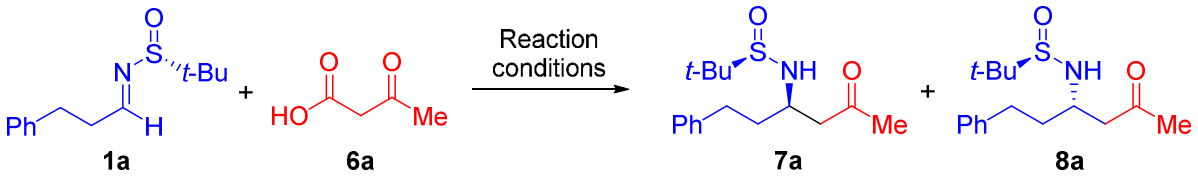
Scheme 2. Base-promoted coupling of sulfinyl imine **1a** and different acetoacetate esters **2**.



Considering the previously commented results and that β-keto acids have been successfully used as surrogate enolates,[10] we decided to study the decarboxylative Mannich-reaction using these compounds. For that reason, we took the imine derived from (*R*)-*tert*-butanesulfinamide and 3-phenylpropanal **1a**, along with the most challenging acetyl acetic acid (**6a**) among β-keto acids, as model compounds for the optimization of the reaction conditions. It is worth to mention that acetyl acetic acid (**6a**) is especially unstable and undergoes decarboxylation very easily at room temperature, and this could be the reason why it has not been used in the reactions with *N*-*tert*-butanesulfinyl α-imino esters (Scheme 1B)[11] and the trifluoroacetaldehyde derivative (Scheme 1C).[12] Although many assays were undertaken, only the most significant ones are compiled in Table 1. Thus, the reaction of imine **1a** with 3 equivalents of keto acid **6a** at room temperature for 12 hours under solvent-free conditions led to an almost 1:5 mixture of both expected diastereoisomers **7a** and **8a**. Unfortunately, starting imine **1a** was not consumed completely in spite of working with an excess of keto acid **6a**, and a significant amount of *tert*-butanesulfinamide was also formed, presumably through a β-elimination process from the expected Mannich adducts **7a** and **8a** (Table 1, entry 1). Decomposition by decarboxylation at room temperature of **6a** could explain that the reaction did not go to completion after 12 hours. Compounds **7a** and **8a** were not found working in a THF solution with the same reaction mixture (Table 1, entry 2) and low conversion was also observed in ethyl acetate in the presence of 1.5 equivalents of sodium bicarbonate (Table 1, entry 3). When the reaction was carried out in the presence of a stronger base such as potassium *tert*-butoxide, total conversion occurred and *tert*-butanesulfinamide was found to be the only reaction product that we could identified from the crude reaction mixture (Table 1, entry 4). The reaction did

not proceed in methanol with 3 equivalents of triethylamine (Table 1, entry 5), but total conversion occurred when 6 equivalents of sodium methoxide in methanol were used. Importantly, β-amino ketone derivatives **7a** (48%) and **8a** (29%) were now the major reaction products, and by contrary to what we found in the previous entries, the one resulting from the nucleophilic attack to the *Si*-face of imine **7a** is now predominant (Table 1, entry 6). Deprotonation of keto acid **6a** with strong bases prevents its decomposition. The diastereoselectivity was highly improved when keto acid **6a** was deprotonated first with *n*-BuLi in dry THF at low temperature and after that, the resulting system reacted with the imine **1a** at room temperature (Table 1, entry 7). However, no reaction took place when lithium hydroxide was used as a base in THF (Table 1, entry 8). The reaction working with 6 equivalents of a 2M lithium hydroxide solution in methanol led to total conversion but also to a lower diastereoselectivity (Table 1, entry 9). The diastereoselectivity was improved again when imine **1a** reacted for 12 h at room temperature with a solution of 1.5 equivalents of keto acid **6a** in THF and 1.5 equivalents of a 2M lithium hydroxide methanol solution. However, almost half of the starting imine **1a** remained unreactive (Table 1, entry 10). The best result was obtained working in THF at room temperature with 1.5 equivalents of keto acid **6a** and 2.0 equivalents of lithium hydroxide from a 2M solution in methanol. After just 30 minutes, compound **7a** was produced in a highly diastereoselective fashion (97:3 dr) in quantitative yields (Table 1, entry 13). When the deprotonation step was performed with a 1M THF solution of lithium ethoxide, the results were rather similar but in a slightly lower diastereoselectivity (Table 1, entry 14). Finally, lithium hydroxide in methanol seemed to be superior to sodium methoxide in methanol in the deprotonation step of keto acid **6a** (Table 1, compare entries 11 and 12), and prolonged reaction times are not beneficial for this reaction, since yield and diastereoselectivity were higher after 30 minutes than after 16 hours (Table 1, compare entries 12 and 13).

Table 1. Optimization of the reaction of imine **1a** and β-keto acid **6a**



1a **6a** **7a** **8a**

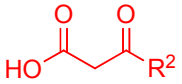
Entry	Reaction conditions	**1a**/**7a**/**8a**/*t*-BuSONH$_2$[a]
1	**1a** (0.2 mmol), **6a** (0.6 mmol), 23 ºC, 12 h	31/6/33/30
2	**1a** (0.2 mmol), **6a** (0.6 mmol), THF (0.2 mL), 23 ºC, 12 h	77/--/--/23
3	**1a** (0.2 mmol), **6a** (0.6 mmol), $NaHCO_3$ (0.3 mmol), AcOEt (1 mL), 23 ºC, 12 h	79/3/5/13
4	**1a** (0.2 mmol), **6a** (0.6 mmol), KO*t*-Bu (0.3 mmol), THF (0.4 mL), 23 ºC, 12 h	--/--/--/100
5	**1a** (0.2 mmol), **6a** (0.6 mmol), Et_3N (0.6 mmol), MeOH (0.2 mL), 23 ºC, 12 h	100/--/--/--
6	**1a** (0.2 mmol), **6a** (0.6 mmol), NaOMe/MeOH (2M, 1.2 mmol), 0 to 23 ºC, 12 h	--/48/29/23
7	1) **6a** (0.4 mmol), *n*-BuLi (2M, 0.6 mmol), THF (2 mL), -78 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 12 h	11/84/5/--
8	1) **6a** (0.3 mmol), LiOH (0.3 mmol), THF (2 mL), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 12 h	100/--/--/--
9	**1a** (0.2 mmol), **6a** (0.6 mmol), LiOH/MeOH (2M, 1.2 mmol), 0 to 23 ºC, 16 h	--/44/34/22
10	1) **6a** (0.3 mmol), LiOH/MeOH (2M, 0.3 mmol), THF (2 mL), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 12 h	45/53/2/--
11	1) **6a** (0.3 mmol), NaOMe/MeOH (2M, 0.4 mmol), THF (2 mL), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 16 h	--/45/10/45
12	1) **6a** (0.3 mmol), LiOH/MeOH (2M, 0.45 mmol), THF (2 mL), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 16 h	10/58/9/23
13	1) **6a** (0.3 mmol), LiOH/MeOH (2M, 0.4 mmol), THF (2 mL), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 0.5 h	--/97/3/--
14	1) **6a** (0.3 mmol), LiOEt/THF (1M, 0.4 mmol), 0 to 23 ºC 2) **1a** (0.2 mmol), 23 ºC, 0.5 h	--/95/5/--

[a] Reaction products ratio was determined by ^{1}H-NMR analysis of the crude reaction mixtures.

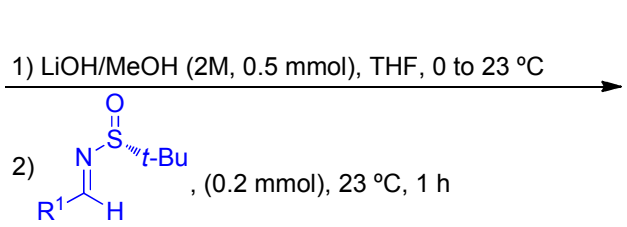
We studied next the scope of the reaction of *N*-*tert*-butanesulfinyl imines **1** with different β-keto acids **6**, by applying the optimized conditions shown in Table 1, entry 13. Two different sets of reaction times were applied, depending of the type of imine **1**: the reaction time was 1 hour for aliphatic imines (although most of the reactions were over after 30 minutes) and 5 hours in the case of the sterically hindered imine derived from isobutyraldehyde and also for aromatic imines (Table 2). The expected β-amino ketone derivatives **7** were obtained in high yields (quantitative yields in most of the cases) with excellent diastereoselectivities (trace amounts of minor diastereoisomers **8** were detected but not isolated). The reaction was also performed on a gram-scale for the imine

derived from decanal **1c** (4.0 mmol) and β-keto acid **6a**, giving rise to amino ketone derivative **7c** in 82% isolated yield (Table 2). The poorest yields were found working with the β-keto acid **6d** (R^2 = *t*-Bu), with values ranging from 80 to 94% (Table 2, compounds **7q-t**). The configuration of the newly created stereogenic centre in compounds **7** was primary assigned by comparing the specific rotation and the NMR data of **7g** with those provided in the literature for its enantiomer,[8b] and later confirmed by crystal X-ray analysis (see the Supporting Information) of the solid compounds **7h**[15] and **7u**.[16] We assume that the nucleophilic attack took always place to the *Si*-face of the imines with R_S configuration in compounds **7** (Table 2).

Table 2. Scope of the Mannich-type coupling of imines **1** and keto acids **6**[a]

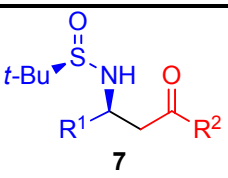


(0.4 mmol)
6a (R^2 = Me)
6b (R^2 = Et)
6c (R^2 = *i*-Pr)
6d (R^2 = *t*-Bu)
6e (R^2 = Ph)

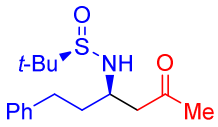


1) LiOH/MeOH (2M, 0.5 mmol), THF, 0 to 23 ºC
2) , (0.2 mmol), 23 ºC, 1 h

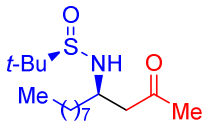
1a [R^1 = $Ph(CH_2)_2$], **1b** [R^1 = $CH_3(CH_2)_7$]
1c [R^1 = $CH_3(CH_2)_8$], **1d** [R^1 = *i*-Pr], **1e** [R^1 = *i*-$PrCH_2$]
1f [R^1 = $Br(CH_2)_4$], **1g** [R^1 = Ph], **1h** [R^1 = 4-BrC_6H_4]



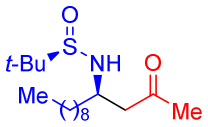
7



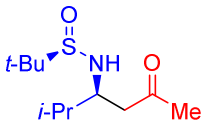
7a (98%, >95:5 dr)



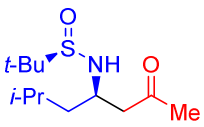
7b (98%, >95:5 dr)



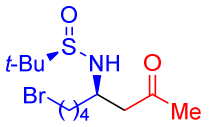
7c (82%, >95:5 dr)[b]



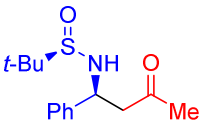
7d (62%, >95:5 dr)[c]



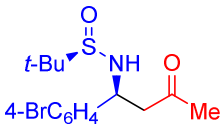
7e (98%, >95:5 dr)



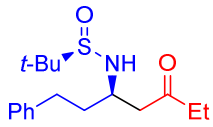
7f (98%, >95:5 dr)



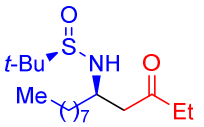
7g (86%, >95:5 dr)[c]



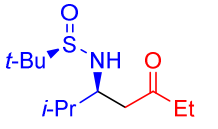
7h (98%, >95:5 dr)[c]



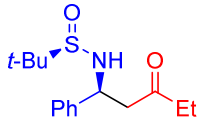
7i (96%, >95:5 dr)



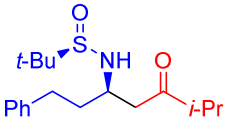
7j (89%, >95:5 dr)



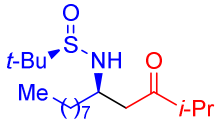
7k (97%, >95:5 dr)[c]



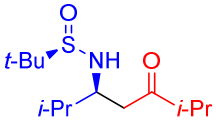
7l (98%, >95:5 dr)[c]



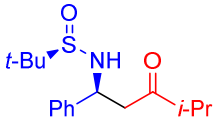
7m (98%, >95:5 dr)



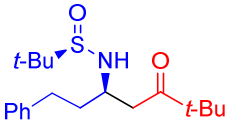
7n (97%, >95:5 dr)



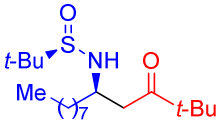
7o (95%, >95:5 dr)[c]



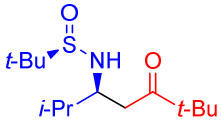
7p (98%, >95:5 dr)[c]



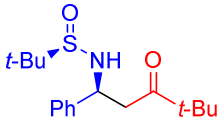
7q (94%, >95:5 dr)



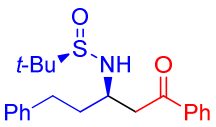
7r (81%, >95:5 dr)



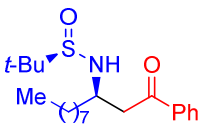
7s (87%, >95:5 dr)[c]



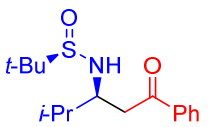
7t (80%, >95:5 dr)[c]



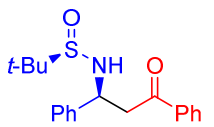
7u (86%, >95:5 dr)



7v (98%, >95:5 dr)



7w (54%, >95:5 dr)[c]



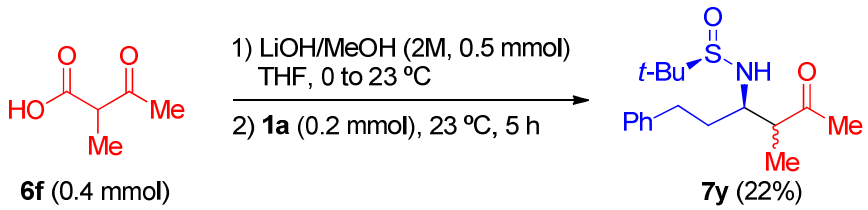
7x (69%, >95:5 dr)[c]

[a] Reactions were carried out starting from 0.2 mmol of the corresponding imine **1**. Isolated yields after column

chromatography purification are given in parenthesis. [b] This reaction was carried out starting from 4.0 mmol of the imine derived from decanal **1c**. [c] Reaction time: 5 h.

Unfortunately, the coupling reactions did not worked well with β-keto acids bearing substituents at 2-position. For instance, the reaction of imine **1a** with 2-methyl-3-oxobutanoic acid (**6f**) under the optimized reaction conditions led after 5 hours to the expected compound **7y**, which was isolated as mixture of epimers in 22% yield (Scheme 3).

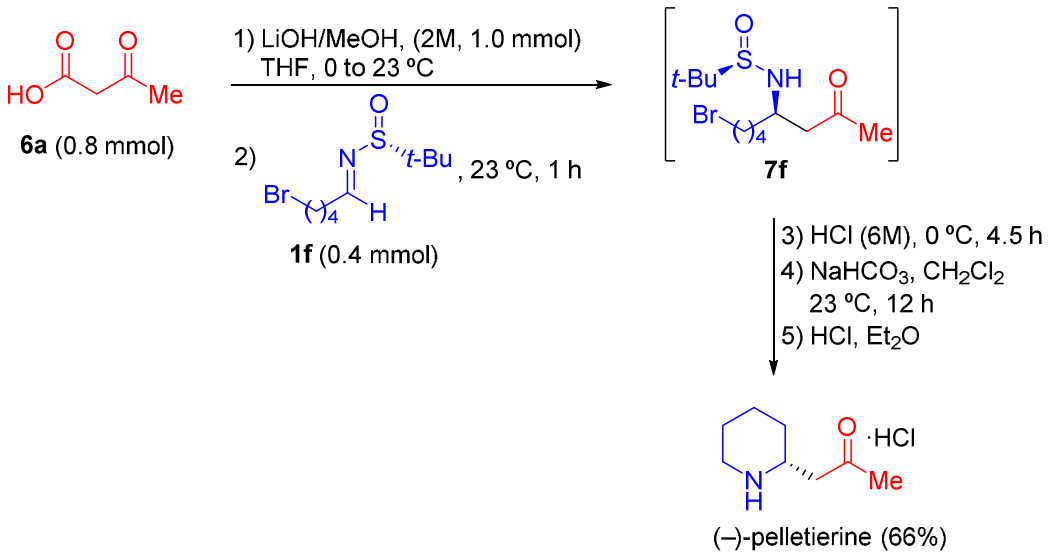
Scheme 3. Reaction of sulfinyl imine **1a** with 2-methyl-3-oxobutanoic acid (**6f**).



6f (0.4 mmol) **7y** (22%)

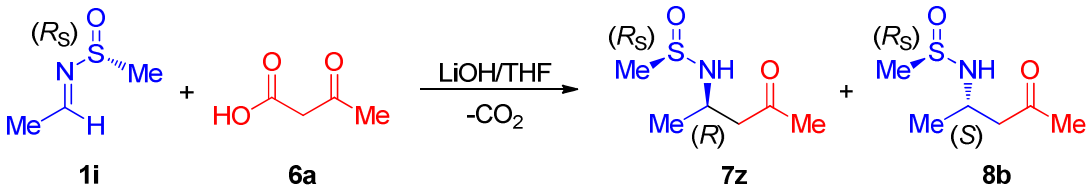
Enantiomerically pure β-amino ketone derivatives are interesting building blocks in the synthesis of alkaloids and other compounds with potential biological activity. The utility of the here presented methodology is demonstrated in the straightforward synthesis of piperidine alkaloid (–)-pelletierine, using 3-oxobutanoic acid (**6a**) and the *N*-*tert*-butanesulfinyl imine derived from 4-bromopentanal (**1f**)[17] as starting materials. Thus, the base-promoted decarboxylative-Mannich coupling of these reagents led to β-amino ketone derivative **7f**, which was not isolated and treated with a 6M hydrochloric acid solution at 0 ºC for 4.5 hours. The resulting acidic aqueous phase containing the ammonium salt was basified to produce the free amine and further extracted with dichloromethane. To the new organic phase was added a saturated aqueous sodium bicarbonate solution, and the reaction mixture was vigorously stirred at room temperature overnight. Combined GC/MS showed the formation of (–)-pelletierine, which was finally isolated as its hydrochloride derivative (see Supporting Information for NMR spectra of the crude material) upon addition of a solution of hydrogen chloride in diethyl ether solution and further removal of volatile solvents, in 66% overall yield. All these transformations were easily followed by TLC and no column chromatography purification was necessary at any moment (Scheme 4).

Scheme 4. Synthesis of (-)-pelletierine from sulfinyl imine **1e** and 3-oxobutanoic acid (**6a**).



We performed density-functional theory (DFT) calculations in order to understand the origins of the stereocontrol of this reaction, as well as the features of each elementary step associated with the Mannich-like/decarboxylation sequence. We focused our calculations on a model reaction in the presence of lithium hydroxide and tetrahydrofuran as solvent, and took imine **1i** as the model (*E*)-imine (Scheme 5). After reaction with 3-oxobutanoic acid **6a**, under the above-indicated conditions, imine **1i** can yield diastereomeric β-aminoketones **7z** and **8b**, in which the (*R*) configuration of the sulfur atom is the source of chiral induction to the new C-C bond. This model reaction captures the essential features that control the stereochemical outcome of the process studied experimentally in detail, namely the **1a**+**6a**→**7a**+**8a** reaction (Table 1).

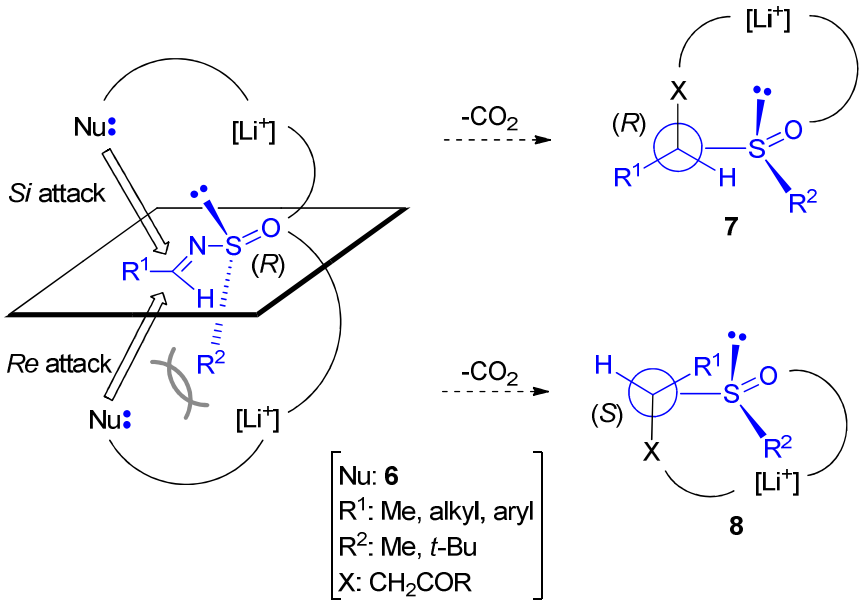
Scheme 5. Model reaction considered in the DFT studies.



As far as the stereochemistry of the new C-C bond is concerned, since the decarboxylation step destroys the chiral information of the α-carbon atom of 3-oxobutiric acid, only the two prochiral faces of (*E*)-imines **1** determine the final stereochemical outcome (Figure 1). In principle, the *Si* attack of the nucleophiles **6** (actually, their carboxylate lithium salts) should result in the formation of **7**, in which the new chiral carbon atom has (*R)* configuration, whereas the *Re* attack would lead to (*S*)-diastereomers **8**. In this latter case, coordination of the sulfoxamide moiety to the lithium cation should generate a significant steric congestion between the R^2 group (*tert*-butyl in the

experimental system, methyl in the computational model reaction) and the nucleophile. Therefore, preferential formation of (*R*) diastereomers **7** should be expected according to this preliminary analysis.

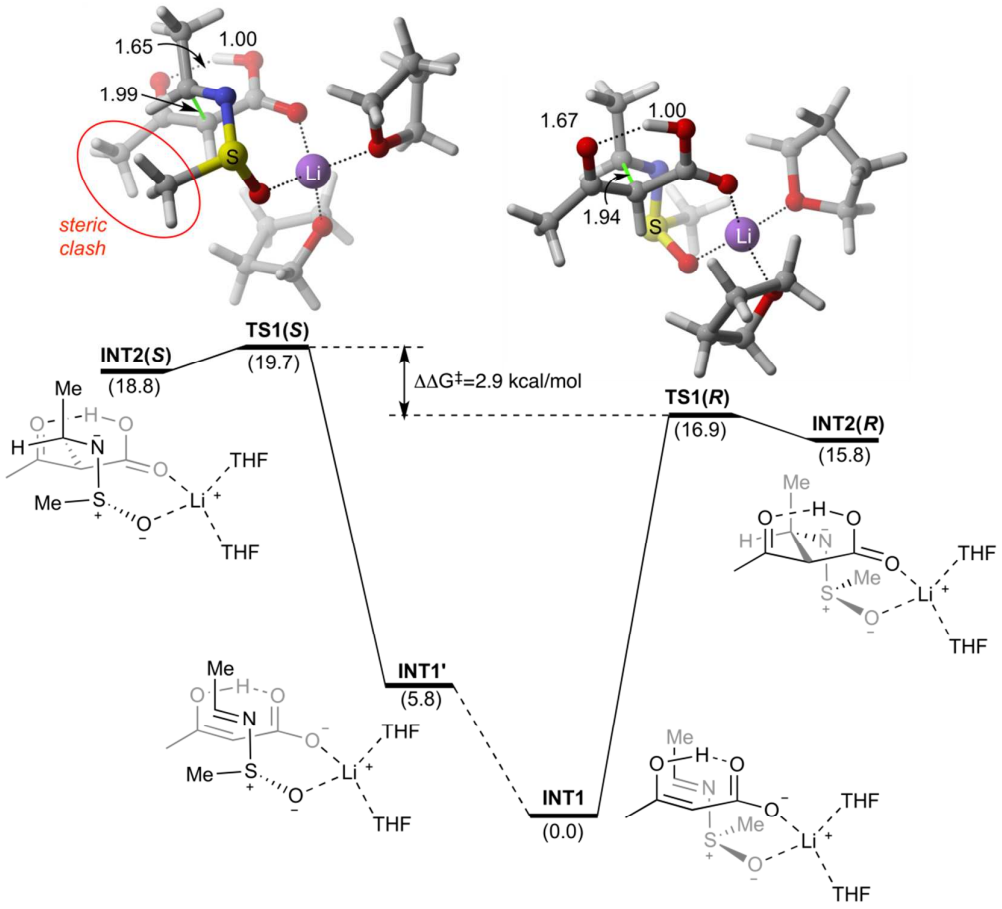
Figure 1. Model trajectories for the nucleophilic attacks on the *Si* and *Re* prochiral faces of (*E*)-imines **1**.



DFT calculations[18] at the B3LYP/6-31+G(d) level[19] including Grimme's D3 correction for the dispersion energy[20] and polarization continuum model (PCM)[21] for unspecific solvent effects (THF was used in the continuum dielectric approach) yielded the reaction profiles gathered in Figure 2. Two discrete molecules of THF were included in the calculations in order to saturate the tetrahedral coordination ability of lithium (I). Interestingly, when the nitrogen atom of the imine was installed close to the Li(I) center and one molecule of THF was pushed away, the nitrogen was not able to coordinate to the cationic center during the optimization. Instead, the second molecule of THF interacted more efficiently thus providing a tetrahedral all-oxygen environment around the metal. This coordination pattern was kept along the reaction coordinates leading to C-C adducts **INT2(*R*)** and **INT2(*S*)**.

Figure 2. Computational profiles [B3LYP-D3(PCM=THF)/6-31+G(d) level of theory] associated with the nucleophilic attack of lithium 2-oxobutyrate on model (*E*)-imine **1i**. Two discrete molecules of THF were considered along the reaction coordinates leading to diastereomeric intermediates **INT2**. Numbers in parenthesis correspond to the relative Gibbs energies (in kcal/mol)

with respect to starting complex **INT1**. Bond distances are given in Å. The steric clash associated with the proximity between the acetyl and S-methyl groups in **TS1(*S*)** is highlighted in red.



In these simulations the cyclic geometries of transition structures are determined by the preferential coordination of two molecules of solvent, the oxygen of the sulfinamide moiety and the carboxylate group to the lithium cation. In addition, the (*E*)-configuration of the starting imine folds the cyclic array thus yielding an extended boat structure, which is completely different to the six-membered chair conformation associated with the Zimmerman-Traxler[22] arrangement. In the case of **TS1(*R*)** (Figure 2), the S-Me group (S-*t*-Bu in the experiments) lies away of the cyclic structure and the proton migration from the starting enol to the carboxy moiety has been completed. The critical C···C bond distance is close to 2 Å, an expected value for aldol-like reactions involving complex lithium enolates.[23] The chief geometric features of **TS1(*S*)** are similar to those of its (*R*)-congener, with the exception of the steric clash generated by the S-Me group and the acetyl group coming from the 2-oxobutirate. As a consequence, **TS1(*S*)** lies 2.9 kcal/mol above **TS1(*R*)**. This difference in Gibbs energy corresponds to a **INT2(*R*)**:**INT(*S*)** kinetic ratio of 99.3:0.7, a result in qualitative agreement with the **7a**:**8a** ratio of 97:3 obtained in the experimental studies (Table 1, entry 13).

In summary, β-amino ketone derivatives were prepared from *N*-*tert*-butanesulfinyl aldimines and β-keto acids with high diastereoselectivity in excellent yields, working under basic conditions in THF at room temperature. The robustness of this method was proved working in a gram-scale with the same levels of stereoselectivity and chemical yield, and a straightforward synthesis of piperidine alkaloid (-)-pelletierine demonstrated also the potential utility in synthesis of this procedure. In addition, and in order to explain the stereochemical outcome of these processes, an eight-membered cyclic transition state, which is in agreement with the experimental results, has been proposed based on DFT calculations. Since these reactions are stereospecific, the configuration of newly created stereogenic centre bearing the nitrogen atom is determined by the configuration of the sulphur atom of the starting sulfinyl imine.

EXPERIMENTAL SECTION

General Remarks: (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 polarimeter with a thermally jacketted 5 cm cell at approximately 20 ºC and concentrations (*c*) are given in g/100 mL. Infrared analyses were performed with a spectrophotometer equipped with an ATR component; wavenumbers are given in cm^{-1}. Low-resolution mass spectra (EI) were obtained 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 using a quadrupole mass analyzer or in the electrospray ionization mode (ESI) using a TOF analyzer. ^{1}H NMR spectra were recorded at 300 or 400 MHz for ^{1}H NMR and 75 or 100 MHz for ^{13}C NMR, using $CDCl_3$ as the solvent and TMS as internal standard (0.00 ppm). The data are being reported as: s = singlet, d = doublet, t = triplet, q = quadruplet, h = septuplet, 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. Compounds **1a**,[24] **1b**,[25] **1c**,[26] **1d**,[27] **1e**,[28] **1f**,[29] **1g**[27] and **1h**[30] were prepared from the corresponding aldehyde and (R_S)-*tert*-butanesulfinamide in THF in the presence of two equivalents of titanium tetraethoxide. Compounds **6a-e** were prepared by hydrolysis of the corresponding β-ketoester **2**.

General Procedure for the Reaction of β-Keto Esters 2 with *N*-*tert*-Butanesulfinyl Imine 1a. Synthesis of Compounds 3: A heterogeneous mixture of the corresponding β-keto ester **2** (4.0 mmol), $NaHCO_3$ (118 mg, 2.0 mmol), and sulfinyl imine **1a** (237 mg, 1.0 mmol) was stirred at rt for 72 h. The resulting mixture was hydrolyzed with H_2O (10 mL), acidified with 2M HCl (2 mL), and extracted with AcOEt (3 × 15 mL). The organic phase was dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **3**. Yields, physical and spectroscopic data follow.

(3*R*,*R*$_S$)-Ethyl 2-Acetyl-3-amino-*N*-(*tert*-butanesulfinyl)-5-phenylpentanoate (3a): The representative procedure was followed by using β-keto ester **2a** (520 mg, 0.51 mL, 4.0 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **3a** (213 mg, 0.58 mmol, 58%) as a yellow oil (1:1 mixture of diastereoisomers); R_f 0.27 (hexane/EtOAc, 1:1); IR ν (film) 2959, 2927, 1732, 1713, 1455, 1363, 1235, 1157, 1062, 732, 700 cm^{-1}; δ_H 7.33–7.10 (m, 10H), 4.45 (d, J = 9.9 Hz, 1H), 4.38 (d, J = 9.9 Hz, 1H), 4.32–4.08 (m,4H), 4.08 (d, J = 4.3 Hz, 1H), 4.00 (d, J = 4.7 Hz, 1H), 3.87–3.67 (m, 2H), 2.93–2.75 (m, 2H), 2.72–2.53 (m, 2H), 2.26 (s, 3H), 2.19 (s, 3H), 2.33–2.04 (m, 2H), 1.98–1.69 (m, 2H) 1.34–1.18 (m, 6H), 1.26 (s, 9H), 1.25 (s, 9H); δ_C 203.5, 202.8, 169.0, 168.7, 141.2, 141.2 (C), 128.6, 128.55, 126.2 (CH), 63.4, 63.2 (CH), 61.9, 61.7 (CH_2), 56.4 (C), 56.3, 55.9 (CH), 35.5, 35.4, 32.7, 32.7 (CH_2), 30.7 (CH_3), 30.6, 22.9, 14.2, 14.1 (CH_3); LRMS (EI) m/z 246 (M^+–t-$BuSONH_2$, 3%), 204 (10), 201 (14), 200 (29), 158 (17), 157 (13), 129 (25), 128 (12), 117 (10), 91 (100), 65 (10); HRMS (EI): Calculated for $C_{13}H_{13}O_2$ [M^+–(t-$BuSONH_2$+EtO)] 201.0916; found 201.0918.

(3*R*,*R*$_S$)-*tert*-Butyl 2-Acetyl-3-amino-*N*-(*tert*-butanesulfinyl)-5-phenylpentanoate (3b): The representative procedure was followed by using β-keto ester **2b** (632 mg, 0.672 mL, 4.0 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **3b** (225 mg, 0.57 mmol, 57%) as a yellow oil (1:1 mixture of diastereoisomers); R_f 0.42 and 0.33 (hexane/EtOAc, 1:1); IR ν (film) 2976, 2931, 1712, 1454, 1367, 1252, 1144, 1026, 843, 748, 696 cm^{-1}; δ_H 7.34–7.10 (m, 10H), 4.43 (d, J = 9.9 Hz, 1H), 4.28 (d, J = 9.6 Hz, 1H), 4.03 (d, J = 4.5 Hz, 1H), 3.95 (d, J = 4.5 Hz, 1H), 3.83–3.62 (m, 2H), 2.91–2.74 (m, 2H), 2.74–2.54 (m, 2H), 2.25 (s, 3H), 2.19 (s, 3H), 2.20–1.86 (m, 2H), 1.88–1.69 (m, 2H), 1.48 (s, 9H), 1.42 (s, 9H), 1.26 (s, 9H), 1.25 (s, 9H); δ_C 204.1, 202.6, 168.1, 168.0, 141.4, 141.3 (C), 128.6, 128.55, 126.2, 126.1 (CH), 83.3, 82.8 (C), 64.65, 63.8 (CH), 56.35 (C), 56.3, 55.5 (CH), 35.1, 34.8, 32.75, 32.5 (CH_2), 30.7, 30.35, 28.1, 28.0, 22.9 (CH_3); LRMS (EI) m/z 218 [M^+–(C_4H_9+t-BuSONH), 25%], 201 (25), 200 (47), 174 (17), 129 (15), 117 (20), 104 (15), 91 (100), 57 (28), 56 (27); HRMS (EI): Calculated for $C_{13}H_{14}O_3$ [M^+–(C_4H_9+t-BuSONH)] 218.0943; found 218.0938.

(3*R*,*R*$_S$)-Benzyl 2-Acetyl-3-amino-*N*-(*tert*-butanesulfinyl)-5-phenylpentanoate (3c): The representative procedure was followed by using β-keto ester **2c** (769 mg, 0.692 mL, 4.0 mmol).

Purification by column chromatography (hexane/AcOEt, 4:1) yielded **3c** (146 mg, 0.34 mmol, 34%) as a yellow oil (1:1 mixture of diastereoisomers); R_f 0.44 and 0.33 (hexane/EtOAc, 1:1); IR ν (film) 2962, 1718, 1622, 1454, 1363, 1213, 1161, 1076, 895, 746, 696 cm^{-1}; δ_H 7.42-7.03 (m, 20H), 5.28–5.14 (m, 4H), 4.42 (d, J = 9.9 Hz, 1H), 4.33 (d, J = 10.1 Hz, 1H), 4.11 (d, J = 4.1 Hz, 1H), 4.05 (d, J = 4.7 Hz, 1H), 3.88–3.68 (m, 2H), 2.90–2.70 (m, 2H), 2.68–2.46 (m, 2H), 2.23 (s, 3H), 2.17 (s, 3H), 2.16–1.79 (m, 2H), 1.79–1.63 (m, 2H), 1.22 (s, 9H), 1.21 (s, 9H); δ_C 203.2, 202.6, 168.7, 168.4, 141.1, 141.0, 135.0, 134.9 (C), 128.8, 128.7, 128.5, 128.4, 126.1 (CH), 67.7, 67.5 (CH_2), 63.3, 63.1 (CH), 56.4 (C), 56.4, 56.0 (CH), 35.5, 32.7, 32.6 (CH_2), 30.7, 30.6, 22.8 (CH_3); LRMS (EI) m/z 218 [M^+–(C_7H_7+*t*-BuSONH), 3%], 217 (22), 200 (8), 199 (50), 157 (20), 92 (9), 91 (100), 77 (9), 65 (11); HRMS (EI): Calculated for $C_{13}H_{13}O_3$ [M^+–(C_7H_7+*t*-BuSONH_2)] 217.0865; found 217.0865.

Reaction of β-Keto Acid 6a with *N*-*tert*-Butanesulfinyl Imine 1a in NaOMe/MeOH. Synthesis of Compounds 7a and 8a: To a mixture of 3-oxobutanoic acid (**6a**, 61.2 mg, 0.6 mmol), and sulfinyl imine **1a** (48 mg, 0.2 mmol) was added a 2M solution of NaOMe in MeOH (1.2 mL, 2.4 mmol) at 0 ºC. The resulting mixture was stirred at rt for 12 h. After that, it was hydrolyzed with a mixture of H_2O (5 mL) and brine (5 mL), and extracted with AcOEt (3 × 15 mL). The organic phase was dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc, 5:1) to yield products **7a** (28.3 mg, 0.096 mmol, 48%) and **8a** (17.1 mg, 0.058 mmol, 29%). Physical and spectroscopic data follow.

(4*R*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-6-phenylhexan-2-one (7a): Yellow oild; $[\alpha]_D^{20}$ –30.7 (c = 1.04, CH_2Cl_2); R_f 0.14 (hexane/EtOAc, 1:3); IR ν (film) 2954, 2867, 1710, 1603, 1497, 1454, 1410, 1362, 1161, 1050, 746, 699 cm^{-1}; δ_H 7.34–7.11 (m, 5H), 4.15 (d, J = 9.3 Hz, 1H), 3.62–3.44 (m, 1H), 2.95 (dd, J = 17.8, 5.5 Hz, 1H), 2.85–2.70 (m, 2H), 2.70–2.53 (m, 1H), 2.12 (s, 3H), 2.08–1.89 (m, 1H), 1.86-1.71 (m, 1H), 1.23 (s, 9H); δ_C 208.3, 141.5 (C), 128.5, 128.45, 126.1 (CH), 56.1 (C), 53.4 (CH), 49.0, 37.4, 32.5 (CH_2), 31.1, 22.8 (CH_3); LRMS (EI) m/z 239 (M^+–C_4H_8, 27%), 181 (37), 118 (12), 117 (100), 91 (49), 57 (30), 43 (26), 41 (9); HRMS (ESI): Calculated for $C_{16}H_{26}NO_2S$ (M^++H) 296.1684, found 296.1681.

(4*S*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-6-phenylhexan-2-one (8a): Yellow oild; $[\alpha]_D^{20}$ –75.8 (c = 1.06, CH_2Cl_2); R_f 0.26 (hexane/EtOAc, 1:3); IR ν (film) 2952, 2867, 1710, 1603, 1496, 1454, 1408, 1363, 1176, 1046, 749, 700 cm^{-1}; δ_H 7.32–7.16 (m, 5H), 3.96 (d, J = 5.5 Hz, 1H), 3.71–3.59 (m, 1H), 2.99 (dd, J = 17.7, 9.3 Hz, 1H), 2.84–2.62 (m, 2H), 2.56 (dd, J = 17.7, 4.0 Hz, 1H), 2.19–2.06 (m, 1H), 2.13 (s, 3H), 1.91–1.76 (m, 1H), 1.20 (s, 9H); δ_C 207.9, 141.3 (C), 128.6, 128.5, 126.1 (CH), 55.9 (C), 52.0 (CH), 49.8, 36.1, 32.35 (CH_2), 30.75, 22.7 (CH_3); LRMS (EI) m/z 239

(M^+–C_4H_8, 27%), 181 (37), 118 (12), 117 (100), 91 (49), 57 (30), 43 (26), 41 (9); HRMS (ESI): Calculated for $C_{16}H_{26}NO_2S$ (M^++H) 296.1684, found 296.1676.

General Procedure for the Reaction of β-Keto Acids 6 with *N*-*tert*-Butanesulfinyl Imines 1. Synthesis of Compounds 7: To a solution of the corresponding β-keto acid **6** (0.3 mmol) in THF (2 mL) was added a 2M solution of LiOH in MeOH (0.2 mL, 0.4 mmol) at 0 ºC. The reaction mixture was allowed to reach rt and then the corresponding imine **1** (0.2 mmol) was added and stirring was continued for 1 or 5 h (see Table 2). The resulting mixture was hydrolyzed with H_2O (10 mL), and extracted with AcOEt (3 × 15 mL). The organic phase was dried with anhydrous $MgSO_4$, and the solvent evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield products **7**. Yields, physical and spectroscopic data follow.

(4*R*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-6-phenylhexan-2-one (7a): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7a** (57.9 mg, 0.196 mmol, 98%) as a yellow oil; physical and spectroscopic data have been given above.

(4*R*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)dodecan-2-one (7b): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1b** (49 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7b** (59.5 mg, 0.196 mmol, 98%) as a yellow oil; $[\alpha]_D^{20}$ –45.5 (c = 1.05, CH_2Cl_2); R_f 0.22 (hexane/EtOAc, 1:3); IR ν (film) 2922, 2855, 1712, 1458, 1411, 1362, 1165, 1048, 889 cm^{-1}; δ_H 3.98 (d, J = 8.9 Hz, 1H), 3.57–3.44 (m, 1H), 2.87 (dd, J = 17.4, 5.5 Hz, 1H), 2.76 (dd, J = 17.8, 4.9 Hz, 1H), 2.14 (s, 3H), 1.73–1.21 (m, 14H), 1.18 (s, 9H), 0.85 (t, J = 5.8 Hz, 3H); δ_C 208.3, 55.9 (C), 53.7 (CH), 49.1, 35.7, 31.9 (CH_2), 31.1 (CH_3), 29.55, 29.3, 26.2 (CH_2), 22.7, 14.2 (CH_3); LRMS (EI) m/z 247 (M^+–C_4H_8, 13%), 190 (11), 189 (100), 84 (9), 70 (14), 57 (28), 43 (29), 41 (12); HRMS (ESI): Calculated for $C_{16}H_{34}NO_2S$ (M^++H) 304.2310, found 304.2305.

(4*R*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)tridecan-2-one (7c): The representative procedure was followed by using β-keto acid **6a** (612 mg, 6.0 mmol) and imine **1c** (1.0378 g, 4.0 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7c** (1.0415 g, 3.28 mmol, 82%) as a yellow oil; $[\alpha]_D^{20}$ –45.3 (c = 1.19, CH_2Cl_2); R_f 0.20 (hexane/EtOAc, 1:3); IR ν (film) 2924, 2854, 1711, 1462, 1412, 1363, 1169, 1049, 897 cm^{-1}; δ_H 3.99 (d, J = 9.0 Hz, 1H), 3.59–3.44 (m, 1H), 2.89 (dd, J = 17.7, 5.5 Hz, 1H), 2.78 (dd, J = 17.7, 4.9 Hz, 1H), 2.16 (s, 3H), 1.66-1.23 (m, 16H), 1.20 (s, 9H), 0.88 (t, J = 6.7 Hz, 3H); δ_C 208.25, 55.9 (C), 53.7 (CH), 49.2, 35.7, 31.95 (CH_2), 31.1 (CH_3), 29.6, 29.35, 29.3, 26.25 (CH_2), 22.75, 14.2 (CH_3); LRMS (EI) m/z 261 (M^+–C_4H_8, 13%), 204 (12), 203 (100), 84 (9), 70 (15), 57 (27), 43 (37), 41 (11); HRMS (EI): Calculated for $C_{13}H_{27}NO_2S$ (M^+–C_4H_8) 261.1762, found 261.1761.

(4*S*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-5-methylhexan-2-one (7d): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1d** (35 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7d** (28.9 mg, 0.124 mmol, 62%) as a yellow oil; $[\alpha]_D^{20}$ –67.0 (*c* = 1.01, CH_2Cl_2); R_f 0.15 (hexane/EtOAc, 1:3); IR ν (film) 2960, 2873, 1716, 1625, 1521, 1468, 1411, 1363, 1166, 1029, 904, 690 cm^{-1}; δ_H 3.91 (d, *J* = 8.9 Hz, 1H), 3.38–3.30 (m, 1H), 2.83 (d, *J* = 5.3 Hz, 2H), 2.18 (s, 3H), 1.98-1.88 (m, 1H), 1.21 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); δ_C 208.4 (C), 59.1 (CH), 56.2 (C), 46.4 (CH_2), 32.1 (CH), 31.1, 22.9, 19.4 (CH_3), 18.82(CH_3); LRMS (EI) *m*/*z* 177 (M^+–C_4H_8, 21%), 119 (100), 113 (20), 86 (16), 71 (10), 70 (12), 57 (61), 56 (22), 55 (13), 44 (19), 43 (94), 41 (26); HRMS (ESI): Calculated for $C_{11}H_{24}NO_2S$ (M^++H) 234.1528, found 234.1520.

(4*R*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-6-methylheptan-2-one (7e): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1e** (37.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7e** (48.5 mg, 0.196 mmol, 98%) as a yellow wax; $[\alpha]_D^{20}$ –46.8 (*c* = 1.02, CH_2Cl_2); R_f 0.15 (hexane/EtOAc, 1:3); IR ν (film) 3222, 2958, 1710, 1458, 1417, 1390, 1364, 1168, 1142, 1039, 900 cm^{-1}; δ_H 3.98 (d, *J* = 9.8 Hz, 1H), 3.66–3.51 (m, 1H), 2.92 (dd, *J* = 17.9, 5.6 Hz, 1H), 2.79 (dd, *J* = 17.8, 4.3 Hz, 1H), 2.15 (s, 3H), 1.81–1.65 (m, 1H), 1.69–1.54 (m, 1H), 1.28–1.14 (m, 1H), 1.20 (s, 9H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H); δ_C 208.4, 56.0 (C), 52.1 (CH), 49.5, 44.85 (CH_2), 31.2 (CH_3), 24.8 (CH), 23.2, 22.7, 21.5 (CH_3); LRMS (EI) *m*/*z* 191 (M^+–C_4H_8, 18%), 191 (18), 133 (100), 91 (10), 86 (13), 77 (11), 71 (14), 70 (10), 69 (13), 57 (51), 44 (11), 43 (81), 41 (21); HRMS (ESI): Calculated for $C_{12}H_{26}NO_2S$ (M^++H) 248.1684, found 248.1680.

(4*R*,*R*$_S$)-4-Amino-8-bromo-*N*-(*tert*-butanesulfinyl)octan-2-one (7f): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1f** (53.6 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7f** (64.0 mg, 0.196 mmol, 98%) as a yellow oil; $[\alpha]_D^{20}$ –38.0 (*c* = 1.01, CH_2Cl_2); R_f 0.12 (hexane/EtOAc, 1:3); IR ν (film) 2946, 1710, 1459, 1362, 1254, 1168, 1051, 907, 731 cm^{-1}; δ_H 4.02 (d, *J* = 9.1 Hz, 1H), 3.58–3.45 (m, 1H), 3.41 (t, *J* = 6.6 Hz, 2H), 2.92 (dd, *J* = 17.9, 5.6 Hz, 1H), 2.81 (dd, *J* = 17.9, 4.6 Hz, 1H), 2.16 (s, 3H), 1.93–1.79 (m, 2H), 1.70–1.42 (m, 4H), 1.21 (s, 9H); δ_C 208.2, 56.01 (C), 53.5 (CH), 49.1, 34.65, 33.7, 32.2 (CH_2), 31.1 (CH_3), 24.8 (CH_2), 22.7 (CH_3); LRMS (EI) *m*/*z* 271 (M^+–C_4H_9, 13%), 269 (13%), 213 (100), 211 (99), 172 (13), 84 (14), 57 (62), 43 (54), 41 (20); HRMS (EI): Calculated for $C_8H_{16}{}^{79}BrNO_2S$ (M^+–C_4H_8) 269.0085, found 269.0083.

(4*S*,*R*$_S$)-4-Amino-*N*-(*tert*-butanesulfinyl)-4-phenylbutan-2-one (7g): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1g** (41.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7g** (46.0 mg, 0.172

mmol, 86%) as a yellow solid; mp 73–74 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –96.3 (c = 1.06, CH_2Cl_2); R_f 0.17 (hexane/EtOAc, 1:3); IR ν (film) 3205, 2957, 1704, 1455, 1421, 1362, 1277, 1159, 1046, 890, 774, 704 cm^{-1}; δ_H 7.33 (m, 5H), 4.83–4.74 (m, 1H), 4.66 (d, J = 4.6 Hz, 1H), 3.08–2.96 (m, 2H), 2.13 (s, 3H), 1.20 (s, 9H); δ_C 207.5, 140.9 (C), 128.7, 127.95, 127.4 (CH), 55.7 (C), 55.3 (CH), 50.65 (CH_2), 30.9, 22.7 (CH_3); LRMS (EI) m/z 211 (M^+–C_4H_8, 15%), 153 (47), 148 (11), 147 (87), 105 (13), 104 (21), 77 (11), 59 (12), 57 (42), 43 (100), 41 (14); HRMS (ESI): Calculated for $C_{14}H_{22}NO_2S$ (M^++H) 268.1371, found 268.1362.

(4*S*,*R*$_S$)-4-Amino-4-(4-bromophenyl)-*N*-(*tert*-butanesulfinyl)butan-2-one (7h): The representative procedure was followed by using β-keto acid **6a** (30.6 mg, 0.3 mmol) and imine **1h** (57.6 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7h** (67.8 mg, 0.196 mmol, 98%) as a yellow solid; mp 89–90 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –73.4 (c = 1.03, CH_2Cl_2); R_f 0.17 (hexane/EtOAc, 1:3); IR ν (film) 3203, 2954, 1715, 1592, 1485, 1412, 1362, 1288, 1161, 1045, 1011, 902, 815 cm^{-1}; δ_H 7.51–7.42 (m, 2H), 7.25–7.17 (m, 2H), 4.79–4.70 (m, 1H), 4.68 (d, J = 4.5 Hz, 1H), 3.07–2.93 (m, 2H), 2.14 (s, 3H), 1.20 (s, 9H); δ_C 207.2, 140.0 (C), 131.9, 129.2 (CH), 121.85, 55.8 (C), 54.7 (CH), 50.4 (CH_2), 30.9, 22.7 (CH_3); LRMS (EI) m/z 291 (M^+–C_4H_9, 7%), 289 (6%), 233 (16), 231 (15), 227 (44), 225 (45), 184 (14), 182 (11), 57 (60), 43 (100), 41 (15); HRMS (ESI): Calculated for $C_{14}H_{21}{}^{79}BrNO_2S$ (M^++H) 346.0476, found 346.0472.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-7-phenylheptan-3-one (7i): The representative procedure was followed by using β-keto acid **6b** (34.8 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7i** (59.3 mg, 0.192 mmol, 96%) as a yellow solid; mp 52–53 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –31.8 (c = 1.02, CH_2Cl_2); R_f 0.34 (hexane/EtOAc, 1:3); IR ν (film) 3265, 2937, 1699, 1454, 1361, 1116, 1064, 942, 748, 703 cm^{-1}; δ_H 7.33–7.11 (m, 5H), 4.25 (d, J = 9.2 Hz, 1H), 3.63–3.45 (m, 1H), 2.92 (dd, J = 17.6, 5.5 Hz, 1H), 2.86–2.69 (m, 2H), 2.68–2.54 (m, 1H), 2.48–2.33 (m, 2H), 2.07–1.90 (m, 1H), 1.87–1.71 (m, 1H), 1.24 (s, 9H), 1.02 (t, J = 7.3 Hz, 3H); δ_C 211.2, 141.5 (C), 128.5, 128.5, 126.1 (CH), 56.1 (C), 53.6 (CH), 47.75, 37.5, 37.05, 32.6 (CH_2), 22.8, 7.5 (CH_3); LRMS (EI) m/z 253 (M^+–C_4H_8, 28%), 181 (33), 118 (12), 117 (100), 91 (47), 57 (63), 41 (9); HRMS (ESI): Calculated for $C_{17}H_{28}NO_2S$ (M^++H) 310.1841, found 310.1831.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)tridecan-3-one (7j): The representative procedure was followed by using β-keto acid **6b** (34.8 mg, 0.3 mmol) and imine **1b** (49 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7j** (56.5 mg, 0.178 mmol, 89%) as a yellow oil; $[\alpha]_D^{20}$ –41.0 (c = 1.05, CH_2Cl_2); R_f 0.46 (hexane/EtOAc, 1:3); IR ν (film) 2925, 2855, 1710, 1458, 1411, 1363, 1051, 897, 671 cm^{-1}; δ_H 4.06 (d, J = 8.9 Hz, 1H), 3.57–3.43 (m, 1H), 2.84 (dd, J = 17.4, 5.4 Hz, 1H), 2.73 (dd, J = 17.4, 4.9 Hz, 1H), 2.41 (q, J = 7.3 Hz, 2H),

1.65–1.20 (m, 14H), 1.18 (s, 9H), 1.01 (t, J = 7.3 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); δ_C 211.1, 55.9 (C), 53.85 (CH), 47.8, 37.1, 35.7, 31.9, 29.55, 29.3, 26.2 (CH_2), 22.75 (CH_3), 22.7 (CH_2), 14.2, 7.55 (CH_3); LRMS (EI) m/z 247 (M^+–C_4H_8, 13%), 190 (11), 189 (100), 84 (9), 70 (14), 57 (28), 43 (29), 41 (12); HRMS (ESI): Calculated for $C_{16}H_{34}NO_2S$ (M^++H) 304.2310, found 304.2305.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-6-methylheptan-3-one (7k): The representative procedure was followed by using β-keto acid **6b** (34.8 mg, 0.3 mmol) and imine **1d** (35 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7k** (28.9 mg, 0.194 mmol, 97%) as a yellow oil; $[\alpha]_D^{20}$ –67.0 (c = 1.01, CH_2Cl_2); R_f 0.15 (hexane/EtOAc, 1:3); IR ν (film) 2960, 2873, 1716, 1625, 1521, 1468, 1411, 1363, 1166, 1029, 904, 690 cm^{-1}; δ_H 3.91 (d, J = 8.9 Hz, 1H), 3.38–3.30 (m, 1H), 2.83 (d, J = 5.3 Hz, 2H), 2.18 (s, 3H), 1.98-1.88 (m, 1H), 1.21 (s, 9H), 0.92 (d, J = 6.7 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H); δ_C 208.4 (C), 59.1 (CH), 56.2 (C), 46.4 (CH_2), 32.1 (CH), 31.1, 22.9, 19.4 (CH_3), 18.82(CH_3); LRMS (EI) m/z 261 (M^+–C_4H_8, 13%), 197 (9), 190 (12), 189 (100), 142 (10), 84 (9), 70 (14), 57 (63), 41 (11); HRMS (ESI): Calculated for $C_{17}H_{36}NO_2S$ (M^++H) 318.2467, found 318.2467.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-5-phenylpentan-3-one (7l): The representative procedure was followed by using β-keto acid **6b** (34.8 mg, 0.3 mmol) and imine **1g** (41.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7l** (46.0 mg, 0.196 mmol, 98%) as a yellow solid; mp 57–58 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –92.2 (c = 1.03, CH_2Cl_2); R_f 0.36 (hexane/EtOAc, 1:3); IR ν (film) 3218, 2979, 1707, 1455, 1354, 1278, 1048, 888, 762, 702 cm^{-1}; δ_H 7.40–7.24 (m, 5H), 4.83–4.74 (m, 2H), 3.06–2.89 (m, 2H), 2.41 (dd, J = 7.3, 1.8 Hz, 1H), 2.38 (dd, J = 7.3, 1.7 Hz, 1H), 1.21 (s, 9H), 1.00 (t, J = 7.3 Hz, 3H); δ_C 210.4, 141.1 (C), 128.7, 127.9, 127.4 (CH), 55.7 (C), 55.4 (CH), 49.4, 37.0 (CH_2), 22.7, 7.5 (CH_3); LRMS (EI) m/z 225 (M^+–C_4H_8, 8%), 161 (37), 153 (27), 121 (7), 105 (7), 104 (13), 57 (100), 41 (7); HRMS (ESI): Calculated for $C_{15}H_{24}NO_2S$ (M^++H) 282.1528, found 282.1515.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2-methyl-7-phenylheptan-3-one (7m): The representative procedure was followed by using β-keto acid **6c** (39 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7m** (63.4 mg, 0.196 mmol, 98%) as a yellow oil; $[\alpha]_D^{20}$ –33.0 (c = 1.07, CH_2Cl_2); R_f 0.50 (hexane/EtOAc, 1:3); IR ν (film) 2966, 1705, 1496, 1455, 1363, 1173, 1054, 736, 697 cm^{-1}; δ_H 7.33–7.13 (m, 5H), 4.32 (d, J = 9.2 Hz, 1H), 3.62–3.47 (m, 1H), 2.97 (dd, J = 17.8, 5.6 Hz, 1H), 2.89–2.71 (m, 2H), 2.70–2.46 (m, 2H), 2.03 – 1.86 (m, 1H), 1.85–1.68 (m, 1H), 1.24 (s, 9H), 1.07 (d, J = 6.9 Hz, 3H), 1.07 (d, J = 6.8 Hz, 3H); δ_C 214.5, 141.5 (C), 128.5, 128.5, 126.0 (CH), 56.0 (C), 53.6 (CH), 45.8 (CH_2), 41.6 (CH), 37.4, 32.6 (CH_2), 22.8, 18.0 (CH_3); LRMS (EI) m/z 267 (M^+–C_4H_8, 23%), 249 (12), 203 (9),

181 (27), 134 (11), 118 (11), 117 (100), 91 (51), 71 (31), 57 (27), 43 (29), 41 (11); HRMS (ESI): Calculated for $C_{18}H_{30}NO_2S$ (M^++H) 324.1997, found 324.1993.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2-methyltridecan-3-one (7n): The representative procedure was followed by using β-keto acid **6c** (39 mg, 0.3 mmol) and imine **1b** (49 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7n** (64.3 mg, 0.194 mmol, 97%) as a yellow oil; $[\alpha]_D^{20}$ –37.8 (*c* = 1.04, CH_2Cl_2); R_f 0.57 (hexane/EtOAc, 1:3); IR ν (film) 2925, 2855, 1707, 1466, 1363, 1176, 1051, 912, 731 cm^{-1}; δ_H 4.14 (d, *J* = 8.9 Hz, 1H), 3.58–3.48 (m, 1H), 2.91 (dd, *J* = 17.6, 5.6 Hz, 1H), 2.81 (dd, *J* = 17.6, 4.6 Hz, 1H), 2.57 (h, *J* = 6.9 Hz, 1H), 1.65–1.23 (m, 14H), 1.21 (s, 9H), 1.10 (s, 3H), 1.08 (s, 3H), 0.88 (t, *J* = 6.8 Hz, 3H); δ_C 214.5, 55.9 (C), 53.9 (CH), 45.9 (CH_2), 41.7 (CH), 35.6, 31.9, 29.6, 29.3, 26.3 (CH_2), 22.8 (CH_3), 22.7 (CH_2), 18.0, 14.2 (CH_3); LRMS (EI) *m*/*z* 275 (M^+–C_4H_8, 15%), 211 (14), 190 (12), 189 (100), 142 (18), 84 (10), 71 (39), 70 (16), 57 (29), 43 (36), 41 (14); HRMS (ESI): Calculated for $C_{18}H_{38}NO_2S$ (M^++H) 332.2623, found 332.2620.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2,6-dimethylheptan-3-one (7o): The representative procedure was followed by using β-keto acid **6c** (39 mg, 0.3 mmol) and imine **1d** (35 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7o** (50.3 mg, 0.190 mmol, 95%) as a yellow oil; $[\alpha]_D^{20}$ –62.8 (*c* = 1.04, CH_2Cl_2); R_f 0.48 (hexane/EtOAc, 1:3); IR ν (film) 2961, 2873, 1705, 1467, 1385, 1364, 1175, 1056, 904, 733 cm^{-1}; δ_H 4.10 (d, *J* = 8.8 Hz, 1H), 3.42–3.27 (m, 1H), 2.98–2.76 (m, 2H), 2.60 (h, *J* = 7.0 Hz, 1H), 2.00–1.86 (m, 1H), 1.22 (s, 9H), 1.12 (s, 3H), 1.09 (s, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); δ_C 214.5 (C), 59.2 (CH), 56.1 (C), 43.0 (CH_2), 41.6, 31.8 (CH), 22.8, 19.4, 18.8, 18.15, 18.1 (CH_3); LRMS (EI) *m*/*z* 205 (M^+–C_4H_8, 24%), 144 (29), 141 (23), 119 (100), 114 (10), 72 (19), 71 (63), 70 (15), 69 (11), 57 (48), 56 (22), 55 (16), 43 (98), 41 (30); HRMS (ESI): Calculated for $C_{13}H_{28}NO_2S$ (M^++H) 262.1841, found 262.1836.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2-methyl-5-phenylpentan-3-one (7p): The representative procedure was followed by using β-keto acid **6c** (39 mg, 0.3 mmol) and imine **1g** (41.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7p** (63.4 mg, 0.196 mmol, 98%) as a yellow solid; mp 50–51 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –93.4 (*c* = 1.02, CH_2Cl_2); R_f 0.50 (hexane/EtOAc, 1:3); IR ν (film) 3210, 2970, 1708, 1456, 1352, 1278, 1046, 896, 758, 698 cm^{-1}; δ_H 7.41–7.22 (m, 5H), 4.86 (d, *J* = 4.4 Hz, 1H), 4.84–4.72 (m, 1H), 3.07 (dd, *J* = 17.1, 4.7 Hz, 1H), 2.96 (dd, *J* = 17.1, 7.5 Hz, 1H), 2.52 (h, *J* = 6.9 Hz, 1H), 1.21 (s, 9H), 1.04 (s, 3H), 1.02 (s, 3H); δ_C 213.6, 141.15 (C), 128.6, 127.8 (CH), 127.35 (CH), 55.6 (C), 55.45 (CH), 47.45 (CH_2), 41.7 (CH), 22.7, 17.8 (CH_3); LRMS (EI) *m*/*z* 239 (M^+–C_4H_8, 9%), 175 (30), 153 (28),

135 (10), 105 (9), 104 (15), 71 (100), 57 (24), 43 (36), 41 (12); HRMS (ESI): Calculated for $C_{16}H_{26}NO_2S$ (M^++H) 296.1684, found 296.1682.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2,2-dimethyl-7-phenylheptan-3-one (7q): The representative procedure was followed by using β-keto acid **6d** (43.2 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7q** (63.4 mg, 0.188 mmol, 94%) as a yellow wax; $[\alpha]_D^{20}$ –30.4 (c = 1.00, CH_2Cl_2); R_f 0.55 (hexane/EtOAc, 1:3); IR ν (film) 2954, 2865, 1703, 1477, 1455, 1364, 1054, 946, 747, 699 cm^{-1}; δ_H 7.33–7.12 (m, 5H), 4.42 (d, J = 9.3 Hz, 1H), 3.64–3.47 (m, 1H), 2.99 (dd, J = 18.0, 5.6 Hz, 1H), 2.87 (dd, J = 17.9, 4.1 Hz, 1H), 2.85–2.71 (m, 1H), 2.69–2.53 (m, 1H), 2.05–1.84 (m, 1H), 1.82–1.64 (m, 1H), 1.25 (s, 9H), 1.11 (s, 9H); δ_C 216.1, 141.6 (C), 128.5, 128.5, 126.0 (CH), 56.0 (C), 53.9 (CH), 44.5 (C), 42.3, 37.3, 32.7 (CH_2), 26.3, 22.9 (CH_3); LRMS (EI) m/z 281 (M^+–C_4H_8, 33%), 217 (12), 206 (11), 181 (30), 134 (14), 118 (11), 117 (100), 91 (52), 85 (14), 57 (88), 41 (15); HRMS (ESI): Calculated for $C_{19}H_{32}NO_2S$ (M^++H) 338.2154, found 338.2155.

(5*R*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2,2-dimethyltridecan-3-one (7r): The representative procedure was followed by using β-keto acid **6d** (43.2 mg, 0.3 mmol) and imine **1b** (49 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7r** (56.0 mg, 0.162 mmol, 81%) as a yellow oil; $[\alpha]_D^{20}$ –36.2 (c = 1.08, CH_2Cl_2); R_f 0.66 (hexane/EtOAc, 1:3); IR ν (film) 2925, 2855, 1702, 1465, 1364, 1176, 1052, 905 cm^{-1}; δ_H 4.23 (d, J = 9.0 Hz, 1H), 3.62–3.43 (m, 1H), 2.94 (dd, J = 17.8, 5.5 Hz, 1H), 2.85 (dd, J = 17.8, 4.5 Hz, 1H), 1.63–1.22 (m, 14H), 1.21 (s, 9H), 1.13 (s, 9H), 0.88 (t, J = 6.9 Hz, 3H); δ_C 216.0, 55.9 (C), 54.2 (CH), 44.5 (C), 42.4, 35.5, 31.9, 29.6, 29.3 (CH_2), 26.3, 22.8 (CH_3), 22.75 (CH_2), 14.2 (CH_3); LRMS (EI) m/z 289 (M^+–C_4H_8, 17%), 225 (19), 214 (10), 190 (12), 189 (100), 142 (22), 85 (19), 70 (16), 57 (96), 43 (19), 41 (19); HRMS (ESI): Calculated for $C_{19}H_{40}NO_2S$ (M^++H) 346.2780, found 346.2780.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2,2,6-trimethylheptan-3-one (7s): The representative procedure was followed by using β-keto acid **6d** (43.2 mg, 0.3 mmol) and imine **1d** (35 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7s** (48 mg, 0.174 mmol, 87%) as a yellow oil; $[\alpha]_D^{20}$ –61.7 (c = 1.05, CH_2Cl_2); R_f 0.55 (hexane/EtOAc, 1:3); IR ν (film) 3172, 2963, 1703, 1478, 1465, 1364, 1006, 916, 715 cm^{-1}; δ_H 4.11 (d, J = 8.8 Hz, 1H), 3.40–3.29 (m, 1H), 2.96 (dd, J = 17.9, 5.4 Hz, 1H), 2.85 (dd, J = 17.9, 5.0 Hz, 1H), 2.01–1.88 (m, 1H), 1.22 (s, 9H), 1.15 (s, 9H), 0.91 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.8 Hz, 3H); δ_C 215.8 (C), 59.3 (CH), 56.1 (C), 44.6 (C), 39.4 (CH_2), 31.5 (CH), 26.45, 22.9, 19.4, 18.8 (CH_3); LRMS (EI) m/z 219 (M^+–C_4H_8, 15%), 155 (13), 144 (17), 128 (13), 119 (56), 85 (21), 72 (14), 71 (11), 70 (12), 69 (13), 57 (100), 56 (13), 55 (13), 43 (45), 41 (25); HRMS (ESI): Calculated for $C_{14}H_{30}NO_2S$ (M^++H) 276.1997, found 276.1990.

(5*S*,*R*$_S$)-5-Amino-*N*-(*tert*-butanesulfinyl)-2,2-dimethyl-5-phenylpentan-3-one (7t): The representative procedure was followed by using β-keto acid **6d** (43.2 mg, 0.3 mmol) and imine **1g** (41.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7t** (49.5 mg, 0.160 mmol, 80%) as a yellow solid; mp 75–76 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –88.9 (c = 1.06, CH_2Cl_2); R_f 0.55 (hexane/EtOAc, 1:3); IR ν (film) 3089, 2979, 1700, 1476, 1459, 1363, 1177, 1043, 916, 764, 701 cm^{-1}; δ_H 7.41–7.24 (m, 5H), 4.91 (d, J = 4.3 Hz, 1H), 4.82–4.70 (m, 1H), 3.12 (dd, J = 17.2, 4.4 Hz, 1H), 2.94 (dd, J = 17.2, 7.8 Hz, 1H), 1.22 (s, 9H), 1.06 (s, 9H); δ_C 215.1, 141.3 (C), 128.65, 127.9, 127.5 (CH), 55.7 (C), 55.6 (CH), 44.6 (C), 44.1 (CH_2), 26.0, 22.8 (CH_3); LRMS (EI) m/z 253 (M^+–C_4H_8, 7%), 189 (18), 153 (18), 104 (13), 85 (46), 57 (100), 41 (12); HRMS (ESI): Calculated for $C_{17}H_{28}NO_2S$ (M^++H) 310.1841, found 310.1833.

(3*R*,*R*$_S$)-3-Amino-*N*-(*tert*-butanesulfinyl)-1,5-diphenylpentan-1-one (7u): The representative procedure was followed by using β-keto acid **6e** (49.2 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7u** (61.5 mg, 0.172 mmol, 86%) as a yellow solid; mp 40–41 ºC (hexane/CH_2Cl_2); $[\alpha]_D^{20}$ –39.1 (c = 1.01, CH_2Cl_2); R_f 0.40 (hexane/EtOAc, 1:2); IR ν (film) 3191, 2962, 1680, 1449, 1355, 1211, 1057, 1005, 959, 895, 753, 727, 687 cm^{-1}; δ_H 7.96–7.86 (m, 2H), 7.61–7.49 (m, 1H), 7.50–7.37 (m, 2H), 7.33–7.21 (m, 2H), 7.23–7.12 (m, 3H), 4.35 (d, J = 9.0 Hz, 1H), 3.86–3.68 (m, 1H), 3.41 (d, J = 5.5 Hz, 2H), 2.91–2.75 (m, 1H), 2.75–2.59 (m, 1H), 2.15–1.96 (m, 1H), 1.99–1.81 (m, 1H), 1.25 (s, 9H); δ_C 199.5, 141.55, 137.05 (C), 133.5, 128.7, 128.55, 128.5, 128.2, 126.1 (CH), 56.2 (C), 53.9 (CH), 44.4, 37.5, 32.6 (CH_2), 22.9 (CH_3); LRMS (EI) m/z 301 (M^+–C_4H_8, 15%), 181 (43), 134 (12), 133 (12), 121 (12), 118 (12), 117 (100), 116 (11), 105 (99), 91 (86), 78 (11), 77 (40), 57 (41), 43 (16), 41 (14); HRMS (ESI): Calculated for $C_{21}H_{28}NO_2S$ (M^++H) 358.1841, found 358.1834.

(3*R*,*R*$_S$)-3-Amino-*N*-(*tert*-butanesulfinyl)-1-phenylundecan-1-one (7v): The representative procedure was followed by using β-keto acid **6e** (49.2 mg, 0.3 mmol) and imine **1b** (49 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7v** (71.6 mg, 0.196 mmol, 98%) as a yellow oil; $[\alpha]_D^{20}$ –46.0 (c = 1.08, CH_2Cl_2); R_f 0.51 (hexane/EtOAc, 1:2); IR ν (film) 2924, 1685, 1448, 1363, 1212, 1050, 900, 752, 688 cm^{-1}; δ_H 7.98–7.91 (m, 2H), 7.61–7.51 (m, 1H), 7.50–7.41 (m, 2H), 4.16 (d, J = 8.8 Hz, 1H), 3.81–3.67 (m, 1H), 3.41 (dd, J = 17.3, 4.8 Hz, 1H), 3.34 (dd, J = 17.3, 5.9 Hz, 1H), 1.75–1.53 (m, 2H), 1.49–1.23 (m, 12H), 1.22 (s, 9H), 0.86 (t, J = 7.0 Hz, 3H); δ_C 199.5, 137.1 (C), 133.4, 128.7, 128.2 (CH), 56.0 (C), 54.2 (CH), 44.5, 35.7, 31.9, 29.6, 29.4, 29.3, 26.3 (CH_2), 22.8 (CH_3), 22.8 (CH_2), 14.21 (CH_3); LRMS (EI) m/z 309 (M^+–C_4H_8, 8%), 190 (12), 189 (100), 142 (18), 121 (27), 120 (10), 105 (99), 84 (10), 77 (32), 70 (17), 57 (37), 43 (9), 41 (14); HRMS (ESI): Calculated for $C_{21}H_{36}NO_2S$ (M^++H) 366.2467, found 366.2465.

(3*S*,R_S)-3-Amino-*N*-(*tert*-butanesulfinyl)-4-methyl-1-phenylpentan-1-one (7w): The representative procedure was followed by using β-keto acid **6e** (49.2 mg, 0.3 mmol) and imine **1d** (35 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7w** (31.9 mg, 0.108 mmol, 54%) as a yellow wax; $[\alpha]_D^{20}$ –67.8 (c = 0.99, CH_2Cl_2); R_f 0.40 (hexane/EtOAc, 1:2); IR ν (film) 2959, 1681, 1597, 1448, 1364, 1211, 1053, 896, 749, 689 cm^{-1}; δ_H 8.00–7.90 (m, 2H), 7.61–7.52 (m, 1H), 7.50–7.42 (m, 2H), 4.12 (d, J = 8.7 Hz, 1H), 3.62–3.47 (m, 1H), 3.43 (dd, J = 17.2, 5.0 Hz, 1H), 3.34 (dd, J = 17.2, 5.8 Hz, 1H), 2.14–1.96 (m, 1H), 1.23 (s, 9H), 0.97 (d, J = 6.8 Hz, 3H), 0.92 (d, J = 6.8 Hz, 3H); δ_C 199.6 (C), 137.1 (C), 133.45 (CH), 128.8 (CH), 128.2 (CH), 59.6 (CH), 56.3 (C), 41.5 (CH_2), 31.8 (CH), 22.9 (CH_3), 19.5 (CH_3), 18.7 (CH_3); LRMS (EI) m/z 239 (M^+–C_4H_8, 10%), 221 (11), 188 (18), 175 (11), 121 (28), 119 (100), 105 (99), 77 (33), 72 (13), 57 (28), 56 (18), 43 (10), 41 (12); HRMS (EI): Calculated for $C_{12}H_{17}NO_2S$ (M^+–C_4H_8) 239.0980, found 239.0970.

(3*S*,R_S)-3-Amino-*N*-(*tert*-butanesulfinyl)-1,3-diphenylpropan-1-one (7x): The representative procedure was followed by using β-keto acid **6e** (49.2 mg, 0.3 mmol) and imine **1g** (41.8 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7x** (45.5 mg, 0.138 mmol, 69%) as a yellow wax; $[\alpha]_D^{20}$ –69.1 (c = 1.03, CH_2Cl_2); R_f 0.42 (hexane/EtOAc, 1:2); IR ν (film) 2958, 1681, 1597, 1449, 1363, 1258, 1205, 1026, 919, 749 cm^{-1}; δ_H 7.97–7.86 (m, 2H), 7.62–7.51 (m, 1H), 7.50–7.23 (m, 7H), 4.97 (dt, J = 8.1, 4.2 Hz, 1H), 4.86 (d, J = 4.1 Hz, 1H), 3.60 (dd, J = 17.4, 4.4 Hz, 1H), 3.49 (dd, J = 17.4, 7.9 Hz, 1H), 1.22 (s, 9H); δ_C 198.65, 141.1, 136.6 (C), 133.7, 128.8, 128.2, 128.0, 127.6 (CH), 55.7 (C) 55.45 (CH), 46.0 (CH_2), 22.75 (CH_3); LRMS (EI) m/z 273 (M^+–C_4H_8, 3%), 209 (11), 153 (49), 106 (15), 105 (100), 104 (9), 77 (24), 57 (14); HRMS (ESI): Calculated for $C_{19}H_{24}NO_2S$ (M^++H) 330.1528, found 330.1522.

(4*R*,R_S)-4-Amino-*N*-(*tert*-butanesulfinyl)-6-phenylhexan-2-one (7y): The representative procedure was followed by using β-keto acid **6f** (34.8 mg, 0.3 mmol) and imine **1a** (48 mg, 0.2 mmol). Purification by column chromatography (hexane/AcOEt, 1:2) yielded **7y** (13.6 mg, 0.044 mmol, 22%) as a yellow wax; R_f 0.27 (hexane/EtOAc, 1:3); IR ν (film) 2925, 1705, 1495, 1454, 1362, 1174, 1047, 951, 733, 698 cm^{-1}; Major isomer δ_H 7.34–7.10 (m, 5H), 4.26 (d, J = 8.8 Hz, 1H), 3.46–3.26 (m, 1H), 3.14–2.72 (m, 2H), 2.66–2.51 (m, 1H), 2.11 (s, 3H), 2.08–1.89 (m, 1H), 1.82–1.69 (m, 1H), 1.28 (s, 9H), 1.23 (d, J = 7.3 Hz, 3H); δ_C 212.3, 141.5 (C), 128.6, 128.5, 126.2, 58.8 (CH), 56.5 (C), 51.0 (CH), 36.5, 32.6 (CH_2), 29.85, 23.0, 13.5 (CH_3); Minor isomer δ_H 7.32–7.10 (m, 5H), 4.12 (d, J = 8.1 Hz, 1H), 3.46–3.26 (m, 1H), 3.11–2.73 (m, 1H), 2.67–2.50 (m, 2H), 2.15 (s, 3H), 2.07–1.92 (m, 1H), 1.84–1.65 (m, 1H), 1.25 (s, 9H), 1.17 (d, J = 7.4 Hz, 3H); δ_C 212.4, 141.6 (C), 128.6, 128.5, 126.1, 58.5 (CH), 56.25 (C), 50.8 (CH), 33.4, 32.9 (CH_2), 29.5, 22.9, 13.4 (CH_3); LRMS (EI) m/z 253 (M^+–C_4H_8, 14%), 181 (45), 134 (12), 133 (8), 118 (11), 117

(100), 91 (50), 57 (27), 43 (25), 41 (8); HRMS (EI): Calculated for $C_{13}H_{19}NO_2S$ (M^+–C_4H_8) 253.1136, found 253.1133.

Synthesis of (–)-Pelletierine Hydrochloride from β-Keto Acid 6a and Imine 1f: To a solution of β-keto acid **6a** (82.0 mg, 0.8 mmol) in THF (4 mL) was added a 2M solution of LiOH in MeOH (0.5 mL, 1.0 mmol) at 0 ºC. The reaction mixture was allowed to reach rt and then the imine **1f** (107.2 g, 0.4 mmol) was added and stirring was continued for 1 h. Complete formation of the β-keto amine derivative **7f** was followed by TLC. After that, 6M HCl (0.5 mL, 3.0 mmol) was added to the resulting mixture at 0 ºC and it was stirred for 4.5 h at the same temperature. Removal of the *tert*-butanesulfinyl group with concomitant formation of the free amine hydrochloride was also followed by TLC. Then, a mixture of H_2O (5 mL) and AcOEt (5 mL) was added. The resulting aqueous phase was basified with a 2M NaOH aqueous solution (12 mL) and extracted with CH_2Cl_2 (4 × 3 mL). To this new organic phase containing exclusively the free amine was added a saturated aqueous solution of $NaHCO_3$ (8 mL) and this heterogeneous mixture was stirred 12 h at room temperature. The organic phase containing (–)-pelletierine [GC-MS.- single peak, *m*/*z* 141 (M^+, 14%)] was treated with a 2M HCl solution in Et_2O (0.5 mL, 1.0 mmol) for 15 min and after that the solvents were evaporated (15 Torr) to yield (–)-pelletierine hydrochloride as a white solid (46.9 mg, 0.26 mmol, 66%); $[\alpha]_D^{20}$ –16.1 (*c* = 0.61, EtOH) [lit.[31] for (–)-pelletierine hydrochloride $[\alpha]_D^{20}$ –18.0 (*c* = 0.5, EtOH)], *ca.* 92% ee (from the dr of the intermediate **7f**); δ_H 9.44 (s, 1H), 9.17 (s, 1H), 3.58–3.44 (m, 2H), 3.32 (dd, *J* = 18.2, 4.1 Hz, 1H), 2.99 (dd, *J* = 18.2, 8.0 Hz, 1H), 2.95–2.86 (m, 1H), 2.22 (s, 3H), 2.03–1.82 (m, 4H), 1.79–1.67 (m, 1H), 1.62–1.47 (m, 1H); δ_C 205.1 (C), 53.1 (CH), 46.0 (CH_2), 45.1 (CH_2), 30.6 (CH_3), 28.4, 22.3, 22.15 (CH_2).

ASSOCIATED CONTENT

Supporting Information. Copies of ^1H, ^{13}C NMR and DEPT spectra for all the reported compounds, X-ray structures of compounds **7h** (Figure S1) and **7u** (Figure S2), as well as Cartesian coordinates, number of imaginary frequencies (NIMAG), and energy data of stationary points gathered in Figure 2 (Tables S1-S6).

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ACKNOWLEDGMENT

We thank the continued financial support from our Ministerio de Ciencia e Innovación (MCINN; projects CTQ2010-20387, CONSOLIDER INGENIO 2010-CDS2007-00006, CTQ2011-24165), the Ministerio de Economía y Competitividad (MINECO; projects CTQ2014-53695-P, CTQ2016-80375-P, CTQ2014-51912-REDC, CTQ2016-81797-REDC), FEDER, the Generalitat Valenciana (PROMETEO 2009/039, PROMETEOII/2014/017), Gobierno Vasco/Eusko Jaurlaritza (Grant IT-324-07), and the University of Alicante.

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