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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/jo402759v • Publication Date (Web): 21 Jan 2014

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Stereoselective Synthesis of Indoline, Tetrahydroquinoline and Tetrahydrobenzazepine Derivatives from *ortho*-Bromophenyl *N*-*tert*-Butylsulfinyl Aldimines

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ABSTRACT. The diastereoselective addition of an allylic indium intermediate to chiral *ortho*-bromophenyl sulfinyl imine **4** proceeds with good levels of diastereoselectivity. The resulting homoallylic amine derivatives were transformed into lactams **7** and **12**, which upon copper-mediated intramolecular *N*-arylation leads to the formation of benzo-fused 1-azabicyclo[*m,n,o*]alkanes **8** and **13**. Benzo-fused 2-allyl substituted heterocycles **14** could also be prepared by means of a palladium-catalyzed *N*-arylation of the corresponding free amine. The synthesis of alkaloid (-)-angustureine was easily accomplished from (*S*)-2-allyltetrahydroquinoline **14b**.

KEYWORDS. Chiral sulfinyl imines, diastereoselective addition, intramolecular *N*-arylation, indolizidine, quinolizidine, indoline, tetrahydroquinoline, benzazepine, (-)-angustureine.

INTRODUCTION

Substituted benzo-fused 1-azabicyclo[m,n.o]alkanes with general structures **I-VI** (Figure 1) are embedded in numerous natural products and other biologically active compounds. Because of that, a rapid assembly of such molecules, in addition to the search for new molecular scaffolds represents a constant challenge to synthetic organic and medicinal chemists. Thus, the development of new methodologies to access to these systems is of great interest. Related to the benzo-fused pyrrolizidine **I** is, for instance, (-)-isatisine A (**1**), a complex alkaloid isolated from the leaves of *Isatis indigotica* Fort,¹ a herbaceous plant species used in Chinese folk medicine. One acetone of (-)-isatisine A exhibits cytotoxicity against C8166 cells and anti-HIV activity. On the other hand, 14,15-didehydro-10,11-dimethoxy-16-epivincamine (**2**),² an alkaloid isolated from *E. officinalis*, *E. divaricata*, and *E. divaricata* Gouyahua plants of the Apocynaceae family, which have been applied in China as folklore herbs for the treatment of hypertension and sore throat, is an example of the benzo-fused indolizidine **II** (Figure 1). Structurally related to azabicycloalkane **III** is the pyridoacridine marine alkaloid arnoamine C (**3**),³ isolated from ascidians of the genus *Cystodytes*, which displays strong cytotoxic activity in different cell lines at low concentration (Figure 1). In addition, compounds bearing the 1-benzazepine moiety, a structural motif common to heterocycles of type **V** and **VI**, have achieved significant relevance as drugs, especially as antidepressants, for the treatment of neurodegenerative disorders and also in cardiovascular diseases. This class of compounds exhibit biological activity toward different targets, such as enzymes, ion channels and G-protein-coupled receptors (GPCRs).⁴ Different synthetic methodologies have been used to access to benzo-fused 1-azabicyclo[m,n.o]alkanes **I-VI** in both, a racemic or a enantioselective manner. For instance, the Schmidt reaction involving benzocycloalkyl carbocations and alkyl azides has been applied to the synthesis of heterocycles of the type **I**, **III-V**.⁵ The benzo-pyrrolizidine and -indolizidine units, **I** and **II**, respectively, were also synthesized through a palladium(II)-catalyzed⁶ or copper-promoted⁷ oxidative tandem cyclization using *N*-acryloyl- or -benzoyl *o*-allyl aromatic amines as substrates. The same type of heterocycles were prepared by means of a general catalytic protocol of non-carbonyl-stabilized rhodium carbenoid C-H insertions starting from *N*-aziridinyl imines⁸ and also using a selenium-based approach for a solid-phase synthesis.⁹ Tricycles of general structure **I** and **III** were obtained under palladium catalysis from chiral unsaturated amines taking place an intramolecular *N*-arylation reaction followed by an intermolecular alkene carboamination reaction.¹⁰ A recent reported methodology combining a regio- and stereoselective allylation and crotylation of indoles with potassium organotrifluoroborate salts with ring-closing metathesis allowed the synthesis in this case of compounds of type **II**.¹¹ Iridium-catalyzed enantioselective hydrogenation of 2-substituted quinolines was used as the key step in the stereoselective synthesis of heterocyclic compounds **III** and **IV**.¹² Enantioenriched benzo-fused indolizidines and

quinolizidines of type **III** and **IV** were also accessed via a catalytic asymmetric hydrogenation cascade using Hantzsch dihydropyridine as hydride donor and catalytic amounts of a chiral BINOL-based phosphoric acid¹³ as well as through 7-*endo-trig*/ring contraction cascades involving phenonium ions, but in this last case in a racemic form.¹⁴ Regarding 1-benzazepines derivatives **V** and **VI**, many methodologies to synthesized these compounds are based on the expansion of smaller rings involving cationic and radical intermediates.¹⁵ More recently, palladium-catalyzed C-C and C-N bond forming reactions have also been employed for the preparation of these compounds.¹⁶ On the other hand, we described the stereoselective allylation of *N*-*tert*-butylsulfinyl aldimines¹⁷ and ketimines¹⁸ 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 stereoselectivities.¹⁹ It is worth mentioning that *N*-*tert*-butylsulfinyl derivatives²⁰ have found high applicability in synthesis as electrophiles because both enantiomers are accessible in large-scale processes²¹ 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*-butylsulfinyl amines have also been reported.²² Being aware of the importance of heterocycles of general structures **I-VI** with regard to biological activity and organic synthesis, we decided to applied the indium-promoted diastereoselective addition of allylic bromides to *N*-*tert*-butylsulfinyl aldimines bearing an *o*-bromophenyl unit, in combination with an intramolecular *N*-arylation, to develop new and flexible synthetic pathways to the target compounds of type **I-VI**.

Figure 1. Basic Structures of Benzo-fused 1-Azabicyclo[m,n,o]alkanes and Representative Natural Products

RESULTS AND DISCUSSION

We have already reported that the reaction of ethyl 2-(bromomethyl)acrylate (**5**) with different chiral *N*-sulfinyl aldimines in a saturated aqueous sodium bromide solution in the presence of 4 equivalents of indium at room temperature for 48 hours proceeded with high diastereoselectivity to give rise to the corresponding amino ester derivative which could be easily transformed into an α -methylene- γ -butyrolactam.²⁴ When we applied these reaction conditions to chiral imines **4**, amino esters **6** were obtained in reasonable yields and diastereoselectivities (Scheme 1). Diastereomeric ratio for compounds bearing the *tert*-butylsulfinyl unit was easily determined by ¹H-NMR analysis of the crude reaction mixture through the comparison of the integrals of the *t*-Bu and the N–H groups for each diastereoisomer. On the other hand, yields given on Scheme 1 refer to isolated yield of the major diastereomer after column chromatography purification. The stereochemical pathway of the process is well known,²⁴ the attack of the allylic indium intermediate occurring preferentially on the *Re* face of these imines with the *S* configuration at the sulfur atom.

Scheme 1. Diastereoselective synthesis of amino ester derivatives **6**

Aminoester derivatives **6** were converted into butyrolactams **7** upon removal of the *tert*-butylsulfinyl group by treatment first with a 4M HCl dioxane solution in methanol and then with sodium methoxide in methanol until basic pH. Good to excellent yields were achieved for compounds **7**, the corresponding α -methylene- γ -butyrolactams being isolated in an almost enantiopure form (Scheme 2).

Scheme 2. Synthesis of α -methylene- γ -butyrolactams **7** from amino ester derivatives **6**

Then, we carried out an intramolecular *N*-arylation under Ullmann-type reaction conditions in compounds **7**. For a model reaction, we optimized the cyclization of compound **7b** using a simple catalyst system developed by Buchwald and co-workers: CuI, a diamine ligand and K₂CO₃ as base.²⁵ All the reactions were performed at 100 °C in the presence of 2 equivalents of K₂CO₃. Regarding the solvent, a higher conversion was achieved using dioxane instead of toluene (Table 1, compare entries 1 and 2). In all cases, copper(I) salt (CuI) and diamine [*N,N'*-dimethylethylenediamine (DMEDA)] were in a 1:2 molar ratio, and 8 mol% was the optimal amount of copper(I) salt which led to a complete conversion (Table 1, entry 3).

Table 1. Optimization of the intramolecular *N*-arylation of compound **7b**

Entry	Reaction conditions	Conversion (%) ^a
1	CuI (5 mol%), DMEDA (10 mol%), K ₂ CO ₃ (2 equiv), PhMe, 110 °C, 20 h	28
2	CuI (5 mol%), DMEDA (10 mol%), K ₂ CO ₃ (2 equiv), 1,4-dioxane, 100 °C, 20 h	50
3	CuI (8 mol%), DMEDA (16 mol%), K ₂ CO ₃ (2 equiv), 1,4-dioxane, 100 °C, 20 h	100

^a Conversion is given based on the disappearance of the starting compound **7b** by ¹H-NMR.

When we applied the optimized conditions depicted in Table 1, entry 3, to enantioenriched butyrolactams **7**, pyrrolo-indoline (**8a**), -tetrahydroquinoline (**8b**) and tetrahydrobenzazepine (**8c**)

derivatives were obtained, although in the case of compound **8c**, in a modest yield (Scheme 3). These compounds possess the pattern hydrocarbon skeleton of type **I**, **III** and **V** (Figure 1) and exhibit (*S*)-configuration at the stereogenic center. The corresponding enantiomers could be produced starting from the chiral aldimines **4** with (*R*)-configuration at the sulphur atom through the same synthetic pathway.

Scheme 3. Synthesis of tricyclic compounds **8** from α -methylene- γ -butyrolactams **7**

In order to access to compounds with the pattern hydrocarbon skeleton of type **II**, **IV** and **VI** (Figure 1) we envisioned a different protocol where the allylation of chiral *tert*-butylsulfinyl imines **1** was the first step of the synthesis. The allylation on imines **4** under standard conditions developed in our group, that is, treatment with allyl bromide in the presence of indium metal at 60 °C produced the homoallyl amine derivatives **9** in excellent yields and diastereoselectivities (Scheme 4).²³ The same reaction products were prepared in slightly lower yields and with almost identical diastereoselectivity performing an one-pot α -aminoallylation of the corresponding aldehyde with (*S*)-*tert*-butanesulfinamide and allyl bromide in the presence of indium metal and titanium tetraethoxide (Scheme 4).¹⁹ Column chromatography purification allowed access to compounds **9** with high optical purity, the attack of allyl indium taking here also place on the *Re* face of these imines with the *S* configuration at the sulfur atom.

Scheme 4. Diastereoselective synthesis of homoallyl amine derivatives **9**

Removal of the *tert*-butylsulfinyl unit in homoallylamine derivatives **9** took place under acidic conditions giving rise to the free amines **10** in almost quantitative yields (Scheme 5). Treatment of amines **10** under Shotten-Baumann reaction conditions with acryloyl chloride at 0 °C in a two-phase solvent system, consisting of 4M aqueous sodium hydroxide and dichloromethane, led to the formation of the targets acrylamide derivatives **11** in good yields (Scheme 5). It is important to perform the acylation at 0 °C, because at higher temperatures, the 3-chloropropanamide derivative resulting from the conjugate addition of the anion chloride to the acrylamide is formed in a significant amount. In addition, column chromatography separation of acrylamides and 3-chloropropanamides is not an easy task. Although these undesired reaction products do not interfere in the next step of the synthesis, this side reaction could be an important drawback by affecting the yield of the whole process.

Scheme 5. Synthesis of acrylamides **11** from homoallyl amine derivatives **9**

Ring-closing metathesis (RCM) of acrylamides **11** by means a Hoveyda-Grubbs second generation ruthenium catalyst produced dihydropyridin-2-ones **12** in high yields in all cases (Scheme 6). Then, compounds **12** were treated under the optimized conditions depicted in Table 1, entry 3, to perform an intramolecular *N*-arylation, leading to the expected tricyclic compounds **13a** and **13b** in excellent yields. However, the reaction failed in the case of the pyrido-tetrahydrobenzazepine derivative **13c**, the starting lactam **12c** being recovered at the end of the reaction (Scheme 6). Pyrido-indoline (**13a**) and -tetrahydroquinoline (**13b**) derivatives possess the pattern hydrocarbon skeleton of type **II** and **IV** (Figure 1), but we could not access through this synthetic strategy to a member of the family type **VI**, like compound **13c**.

Scheme 6. Synthesis of tricyclic compounds **13** from dihydropyridin-2-ones **12**

Since the formation of the seven-membered ring through an Ullmann-intramolecular *N*-arylation from bromophenyl dihydropyridin-2-one derivative **12c** failed, we planned to perform first an intramolecular *N*-arylation of the free amine **10c** to synthesize the seven-membered ring of the benzazepine unit and after that the lactam ring. In order to find out the best reaction conditions for the intramolecular *N*-arylation, we took homoallyl amine derivative **10b** as a model compound. As we expected, cyclization did not take place under the Ullmann-type reaction conditions depicted on Table 1, entry 3, which were found to be optimal for the lactam derivatives **7** and **12** (Table 2, entry 1). We were pleased to find that 100% of conversion was achieved under palladium catalysis using 5 mol% of $\text{Pd}(\text{OAc})_2$ and 7.5 mol% of ($\pm$)-BINAP, 2 equivalents of Cs_2CO_3 as base, in toluene at 100°C

°C for 15 hours (Table 2, entry 2).²⁶ Total conversion was also achieved under very similar reaction conditions, but using 15 mol% of PPh₃ instead of the more expensive ligand (±)-BINAP (Table 2, entry 3). Unfortunately, decreasing the loading of Pd(OAc)₂ from 5 mol% to 2 mol% led to a lower conversion (Table 2, entry 4).

Table 2. Optimization of the intramolecular *N*-arylation of homoallylamine **10b**

Entry	Reaction conditions	Conversion (%) ^a
1	CuI (8 mol%), DMEDA (16 mol%), K ₂ CO ₃ (2 equiv), 1,4-dioxane, 100 °C, 20 h	0
2	Pd(OAc) ₂ (5 mol%), (±)-BINAP (7.5 mol%), Cs ₂ CO ₃ (2 equiv), PhMe, 110 °C, 15 h	100
3	Pd(OAc) ₂ (5 mol%), PPh ₃ (15 mol%), Cs ₂ CO ₃ (2 equiv), PhMe, 110 °C, 21 h	100
4	Pd(OAc) ₂ (2 mol%), PPh ₃ (6 mol%), Cs ₂ CO ₃ (2 equiv), PhMe, 110 °C, 24 h	68

^a Conversion is given based on the disappearance of the starting **10b** by ¹H-NMR.

Bicyclic compounds **14** were obtained when homoallylamine derivatives **10** were submitted to the reaction conditions shown in Table 2, entry 3. Purification of the reaction products was very easy by performing an acidic-basic work-up. Concerning the chemical efficiency of the cyclization regarding the size of the ring, 2-allylindoline (**14a**) was formed in lower yield than the tetrahydroquinoline (**14b**) and tetrahydrobenzazepine (**14c**) derivatives (Scheme 7).

Scheme 7. Synthesis of 2-allylindoline **14a**, -tetrahydroquinoline **14b** and -tetrahydrobenzazepine **14c** from homoallylamines **10**

Fortunately, pyrido-tetrahydrobenzazepine derivative **13c** was prepared in two steps from tetrahydrobenzazepine (**14c**): first *N*-acylation with acryloyl chloride in dichloromethane under anhydrous reaction conditions and subsequent RCM of the resulting acrylamide **15c** using the Hoveyda-Grubbs second generation ruthenium catalyst (Scheme 8). Just for a comparative study regarding the effectiveness of both synthetic strategies to access to compounds **13**, pyrido-tetrahydroquinoline derivative **13b** was also synthesized from 2-allyltetrahydroquinoline (**14b**) in two steps, being the yields a little bit higher than for **13c** (Scheme 8). Thus, starting from common intermediate **10b**, the overall yield is 52.3% in the process from **10b** → **11b** → **12b** → **13b** (lactam formation first followed by *N*-arylation), meanwhile the route **10b** → **14b** → **15b** → **13b** (first palladium catalyzed *N*-arylation and then formation of the lactam) was carried out in a 45.5% overall yield. The first strategy seems to be superior, although benzazepine derivative **13c** could only be prepared following the second route.

Scheme 8. Synthesis of tricyclic compounds **13b** and **13c** from **14b** and **14c**

Compounds **8** and **13** are of interest not only because of their basic molecular architecture but also because the α,β -unsaturated lactam moiety allows further structural modifications, leading to more complex systems (Figure 2). In addition, the double bond of the allylic moiety in compounds **14** can participate in a number of further synthetically useful transformations: cross metathesis, epoxidation, oxidative cleavage, Heck type reaction, cycloaddition, hydroboration, hydroformylation, hydrogenation, hydration, ozonolysis, etc.²⁷

Figure 2. Potential Application in Synthesis of Compounds **8**, **13** and **14**

For instance, the synthetic utility of (*S*)-2-allyltetrahydroquinoline (**14b**) was exemplified in the synthesis of natural alkaloid (-)-angustureine (**18**) isolated from *Galipea officinalis*,²⁸ a Venezuelan shrubby tree used in folk medicine as tonic in dyspepsia, dysentery, chronic diarrhea and also as antipyretic (Scheme 9).²⁹ Tetrahydroquinoline derivative **14b** was treated first with paraformaldehyde and NaBH_3CN to give the 2-allyl-*N*-methyltetrahydroquinoline (**16**) in 95% yield, followed by a cross-metathesis with (*Z*)-hex-3-ene and final *in situ* hydrogenation of the resulting olefin **17** (Scheme 9). From compound **16**, it was also possible to synthesize dehydrohomocuspareine **19**, a compound related to tetrahydroquinoline alkaloid cuspareine, by performing a Heck-type reaction with 4-bromoveratrol (Scheme 9).

Scheme 9. Synthesis of (-)-angustureine (**18**) from (*S*)-2-allyltetrahydroquinoline **14b**

In summary, benzo-fused 1-azabicyclo[m,n.o]alkanes **8** and **13**, with general structures **I-VI**, and 2-allylindoline, -tetrahydroquinoline and -tetrahydrobenzazepine **14**, were easily accessible in high

optical purity from the imines derived from aliphatic aldehydes with a 2-bromophenyl substituent and (*S*)-*tert*-butanesulfinamide. The methodology presented here comprised as key steps a diastereoselective addition of an allylic indium intermediate to the chiral sulfinyl imine **4**, and an intramolecular *N*-arylation, under Ullmann-type reaction conditions for lactams **7** and **12**, or a palladium-mediated process in the case of the free amines **10**. Functionalized tricyclic compounds **8** and **13**, as well as 2-allyl substituted heterocycles **14** could be used as building blocks for the synthesis of more complex molecules. As an example, natural alkaloid (-)-angustureine (**18**) was synthesized starting from (*S*)-2-allyltetrahydroquinoline **14b**.

EXPERIMENTAL SECTION

General Remarks: (*S*)-*tert*-Butanesulfinamide and its enantiomer were a gift of Medalchemistry (> 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 F₂₅₄, 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 °C 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 and on an apparatus equipped with a time of flight (TOF) analyzer and the samples were ionized by ESI techniques and introduced through an ultra-high pressure liquid chromatograph (UPLC) model. ¹H NMR spectra were recorded at 300 or 400 MHz for ¹H NMR and 75 or 100 MHz for ¹³C NMR, using CDCl₃ as the solvent and TMS as internal standard (0.00 ppm). The data is being reported as: s = singlet, d = doublet, t = triplet, q = quatriplet, h = heptet, m = multiplet or unresolved, br s = broad signal, coupling constant(s) in Hz, integration. ¹³C NMR spectra were recorded with ¹H-decoupling at 100 MHz and referenced to CDCl₃ at 77.16 ppm. DEPT-135 experiments were performed to assign CH, CH₂ and CH₃. Compound **2a**,¹⁰ **4b**¹⁰ and **4c**²³ were prepared from the corresponding *o*-bromophenyl aldehyde and (*S*)-*tert*-butanesulfinamide in THF in the presence of two equivalents of titanium tetraethoxide.

General procedure for the synthesis of amino ester derivatives 6:

A mixture of the corresponding aldimine **4** (0.5 mmol), ethyl 2-(bromomethyl)acrylate (**5**, 0.128 g, 0.65 mmol) and indium powder (0.226 g, 2.0 mmol) in a saturated aqueous NaBr solution (5 mL) was stirred for 48 h at 23 °C. Then, the resulting mixture was hydrolyzed with water (10 mL), extrated with EtOAc (3 × 10 mL), dried over anhydrous MgSO₄ and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure products **6**. Yields, physical and spectroscopic data follow.

(4*R*,*Ss*)-Ethyl *N*-(*tert*-butylsulfinyl)-4-amino-5-(2-bromophenyl)-2-methylenepentanoate (6a**):**

The representative procedure was followed by using imine **4a** (302 mg, 1 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **6a** (272 mg, 65%) as a colorless oil; $[\alpha]_{\text{D}}^{23} +2$ (*c* 1.01, CH₂Cl₂); *R*_f 0.45 (AcOEt); IR ν (film) 3220, 1714, 1472, 1045 cm⁻¹; δ_{H} 7.52 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.25 (d, *J* = 7.6, 2.2 Hz, 1H), 7.22 (d, *J* = 7.6, 1.2 Hz, 1H), 7.07 (ddd, *J* = 8.0, 6.9, 2.3 Hz, 1H), 6.35 (d, *J* = 1.3 Hz, 1H), 5.74 (d, *J* = 1.1 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.89-3.78 (m, 1H), 3.60 (br d, *J* = 7.0 Hz, 1H), 2.96 (dd, *J* = 13.8, 5.7 Hz, 1H), 2.89 (dd, *J* = 13.8, 8.8 Hz, 1H), 2.83 (dd, *J* = 14.0, 7.1 Hz, 1H), 2.64 (ddd, *J* = 14.1, 5.8, 0.6 Hz, 1H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.04 (s, 9H); δ_{C} 167.4 (C), 138.2 (C), 137.0 (C), 133.0 (CH), 132.0 (CH), 128.9 (CH₂), 128.3 (CH), 127.4 (CH), 125.2 (C), 61.2 (CH₂), 56.7 (CH), 56.0 (C), 42.2 (CH₂), 38.9 (CH₂), 22.6 (CH₃), 14.3 (CH₃); LRMS (EI) *m/z* 361 [*M*⁺ (⁸¹Br)-C₄H₈, 2%], 281 (16), 270 (21), 268 (18), 262 (15), 247 (73), 245 (70), 208 (14), 207 (62), 191 (15), 190 (100), 184 (40), 182 (38), 174 (89), 172 (18), 171 (43), 169 (45), 166 (27), 144 (22), 143 (15), 142 (96), 129 (11), 128 (35), 118 (31), 117 (24), 116 (21), 115 (25), 112 (11), 100 (37), 96 (19), 91 (37), 90 (33), 89 (31), 87 (20), 69 (33), 63 (10), 59 (10); HRMS (EI): Calculated for C₁₄H₁₈⁸¹BrNO₃S (*M*⁺-C₄H₈) 361.0170, found 361.0161.

(4*S*,*Ss*)-Ethyl *N*-(*tert*-butylsulfinyl)-4-amino-6-(2-bromophenyl)-2-methylenehexanoate (6b**):**

The representative procedure was followed by using imine **4b** (316 mg, 1 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **6b** (324 mg, 75%) as a colorless oil; $[\alpha]_{\text{D}}^{23} +40$ (*c* 1.01, CH₂Cl₂); *R*_f 0.66 (AcOEt); IR ν (film) 3276, 1714, 1471, 1370, 1046 cm⁻¹; δ_{H} 7.52 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.19-7.26 (m, 2H), 7.06 (ddd, *J* = 8.1, 6.7, 2.4 Hz, 1H), 6.32 (d, *J* = 1.3 Hz, 1H), 5.72 (d, *J* = 1.0 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.71 (br d, *J* = 6.4 Hz, 1H), 3.45-3.61 (m, 1H), 2.91 (ddd, *J* = 13.5, 11.1, 5.0 Hz, 1H), 2.69-2.78 (m, 2H), 2.65 (dd, *J* = 14.2, 5.6 Hz, 1H), 1.84 (ddd, *J* = 13.9, 10.8, 5.4 Hz, 1H), 1.66-1.77 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.25 (s, 9H); δ_{C} 167.5 (C), 141.2 (C), 137.1 (C), 132.9 (CH), 130.4 (CH), 128.6 (CH₂), 127.8 (CH), 127.7 (CH), 124.4 (C), 61.2 (CH₂), 56.1 (C), 55.5 (CH), 38.7 (CH₂), 35.9 (CH₂), 32.6 (CH₂), 22.9 (CH₃), 14.27 (CH₃); LRMS (EI) *m/z* 375 [*M*⁺ (⁸¹Br)-C₄H₈, 2%], 294 (13), 261 (81), 260 (10), 259 (78), 197 (57), 195 (57), 191 (13), 171 (100), 170 (10), 169 (100), 142 (11), 132 (43), 130 (11), 117 (53), 116 (12),

115 (28), 104 (10), 103 (11), 91 (14), 90 (20), 89 (13), 87 (25), 77 (16), 69 (13); HRMS (ESI): Calculated for $C_{19}H_{29}^{79}BrNO_3S$ ($M^+ + H$) 430.1052, found 430.1054.

(4*S*,*Ss*)-Ethyl *N*-(*tert*-butylsulfinyl)-4-amino-7-(2-bromophenyl)-2-methyleneheptanoate (6c**):**

The representative procedure was followed by using imine **4c** (304 mg, 0.92 mmol). Purification by column chromatography (hexane/AcOEt, 2:1) yielded **6c** (306 mg, 74%) as a colorless oil; $[\alpha]_D^{23} +39$ (*c* 1.01, CH_2Cl_2); R_f 0.67 (AcOEt); IR ν (film) 3228, 2978, 1712, 1174, 1049, 751 cm^{-1} ; δ_H 7.52 (dd, $J = 7.9, 1.1$ Hz, 1H), 7.24-7.16 (m, 2H), 7.05 (ddd, $J = 8.0, 6.9, 2.3$ Hz, 1H), 6.30 (d, $J = 1.3$ Hz, 1H), 5.69 (d, $J = 1.1$ Hz, 1H), 4.21 (q, $J = 7.1$ Hz, 2H), 3.60 (d, $J = 5.9$ Hz, 1H), 3.54-3.42 (m, 1H), 2.72 (t, $J = 7.6$ Hz, 2H), 2.61 (br d, $J = 6.2$ Hz, 2H), 1.82-1.48 (m, 4H), 1.31 (t, $J = 7.1$ Hz, 3H), 1.19 (s, 9H); δ_C 167.6 (C), 141.5 (C), 137.2 (C), 132.9 (CH), 130.4 (CH), 128.5 (CH₂), 127.7 (CH), 127.5 (CH), 124.5 (C), 61.2 (CH₂), 55.9 (C), 55.2 (CH), 38.3 (CH₂), 36.1 (CH₂), 35.1 (CH₂), 25.9 (CH₂), 22.9 (CH₃), 14.3 (CH₃); LRMS (EI) m/z 389 [M^+ (^{81}Br)- C_4H_8 , 4%], 275 (35), 273 (36), 211 (43), 209 (48), 207 (10), 187 (10), 174 (11), 171 (22), 169 (24), 146 (11), 132 (11), 131 (100), 130 (16), 115 (23), 104 (19), 103 (11), 91 (21), 90 (12), 87 (18), 77 (12), 69 (13); HRMS (EI): Calculated for $C_{16}H_{22}^{81}BrNO_3S$ ($M^+ - C_4H_8$) 387.0504, found 387.0490.

General procedure for the synthesis of α -methylene- γ -butyrolactams **7:**

To a solution of the corresponding aminoester **6** (0.2 mmol) in MeOH (1 mL) was added a 4M HCl dioxane solution (0.5 mL) at 0 °C. After 2 h stirring at the same temperature, a 2M NaOMe MeOH solution (2 mL) was added and the resulting mixture was stirred for 1 at 0 °C. After that, it was hydrolyzed with water (10 mL), extrated with EtOAc (3 $\times$ 10 mL), dried over anhydrous $MgSO_4$ and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure products **7**. Yields, physical and spectroscopic data follow.

(*R*)-5-(2-Bromobenzyl)-3-methylenepyrrolidin-2-one (7a**):** The representative procedure was followed by using amino ester derivative **6a** (129 mg, 0.31 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **7a** (62 mg, 75%) as a colorless oil; $[\alpha]_D^{23} -60$ (*c* 0.85, CH_2Cl_2); R_f 0.57 (AcOEt); IR ν (film) 3210, 1694, 1658, 1439 cm^{-1} ; δ_H 7.58 (dd, $J = 7.9, 1.2$ Hz, 1H), 7.28 (dd, $J = 7.3, 1.3$ Hz, 1H), 7.21 (dd, $J = 7.6, 2.0$ Hz, 1H), 7.13 (ddd, $J = 7.9, 7.2, 2.0$ Hz, 1H), 6.42 (br s, 1H), 6.01 (t, $J = 2.7$ Hz, 1H), 5.37 (t, $J = 2.3$ Hz, 1H), 4.08-3.99 (m, 1H), 3.04 (dd, $J = 13.5, 5.8$ Hz, 1H), 2.99 (ddt, $J = 17.1, 7.8, 2.6$ Hz, 1H), 2.86 (dd, $J = 13.5, 8.0$ Hz, 1H), 2.61 (ddt, $J = 17.1, 4.0, 2.6$ Hz, 1H); δ_C 170.2 (C), 138.9 (C), 136.7 (C), 133.4 (CH), 131.5 (CH), 128.9 (CH), 127.9 (CH), 124.8 (C), 116.7 (CH₂), 50.8 (CH), 43.5 (CH₂), 32.9 (CH₂); LRMS (EI) m/z 267 [M^+ (^{81}Br), 1%], 96 (100), 53 (14); HRMS (ESI): Calculated for $C_{12}H_{13}^{79}BrNO$ ($M^+ + H$) 266.0181, found 266.0192.

(S)-5-(2-Bromophenylethyl)-3-methylenepyrrolidin-2-one (7b): The representative procedure was followed by using amino ester derivative **6b** (202 mg, 0.47 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **7b** (124 mg, 94%) as a colorless oil; $[\alpha]_D^{23}$ -25 (*c* 0.91, CH₂Cl₂); *R*_f 0.46 (AcOEt); IR ν (film) 3203, 1693, 1658, 1299, 1022, 924 cm⁻¹; δ_H 7.53 (d, *J* = 7.8 Hz, 1H), 7.42 (br s, 1H), 7.26-7.21 (m, 1H), 7.12-7.03 (m, 1H), 5.99 (q, *J* = 2.4 Hz, 1H), 5.36 (t, *J* = 2.3 Hz, 1H), 3.77-3.66 (m, 1H), 3.02 (ddt, *J* = 17.1, 7.8, 2.5 Hz, 1H), 2.80 (t, *J* = 8.0 Hz, 2H), 2.54 (ddt, *J* = 17.2, 4.3, 2.7 Hz, 1H), 1.92-1.79 (m, 2H); δ_C 170.9 (C), 140.4 (C), 139.5 (C), 133.0 (CH), 130.5 (CH), 128.1 (CH), 127.8 (CH), 124.4 (C), 116.2 (CH₂), 51.0 (CH), 37.5 (CH₂), 33.1 (CH₂), 32.4 (CH₂); LRMS (EI) *m/z* 200 (M⁺-Br, 81%), 201 (14), 97 (10), 96 (100), 53 (15); HRMS (ESI): Calculated for C₁₃H₁₅⁷⁹BrNO (M⁺+H) 280.0337, found 280.0333.

(S)-5-(3-Bromophenylpropyl)-3-methylenepyrrolidin-2-one (7c): The representative procedure was followed by using amino ester derivative **6c** (115 mg, 0.26 mmol). Purification by column chromatography (hexane/AcOEt, 1:1) yielded **7c** (71 mg, 93%) as a white solid; mp 59-61 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ -17 (*c* 0.91, CH₂Cl₂); *R*_f 0.51 (AcOEt); IR ν (KBr) 3199, 1694, 1658, 1439, 1291, 749 cm⁻¹; δ_H 7.53 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.25-7.18 (m, 2H), 7.06 (ddd, *J* = 8.0, 6.9, 2.2 Hz, 1H), 6.94 (br s, 1H), 5.97 (t, *J* = 2.8 Hz, 1H), 5.34 (s, 1H), 3.73-3.64 (m, 1H), 2.98 (dd, *J* = 17.1, 7.8 Hz, 1H), 2.76 (t, *J* = 7.5 Hz, 2H), 2.45 (ddt, *J* = 17.1, 4.3, 2.7 Hz, 1H), 1.73-1.50 (m, 4H); δ_C 170.6 (C), 141.1 (C), 139.4 (C), 133.0 (CH), 130.5 (CH), 127.9 (CH), 127.6 (CH), 124.5 (C), 116.2 (CH₂), 51.2 (CH), 37.0 (CH₂), 36.0 (CH₂), 33.2 (CH₂), 26.0 (CH₂); LRMS (EI) *m/z* 295 [M⁺ (⁸¹Br), 1%], 214 (59), 171 (5), 169 (5), 96 (100), 53 (12); HRMS (EI): Calculated for C₁₄H₁₆⁸¹BrNO 295.0395, found 295.0390.

General procedure for the synthesis of tricyclic compounds **8** from α -methylene- γ -butyrolactams **7**:

A mixture of the corresponding α -methylene- γ -butyrolactams **7** (0.3 mmol), CuI (4.6 mg, 0.024 mmol), K₂CO₃ (83 mg, 0.6 mmol) and *N,N,N',N'*-tetrametiletilendiamina (5.6 mg, 7 μ L, 0.048 mmol) in dry dioxane (0.75 mL) was stirred at 100 °C under Ar for 20 h in a high-pressure tube. Then, the resulting mixture was cooled down to room temperature and hydrolyzed with H₂O (5 mL), extracted with AcOEt (3 $\times$ 10 mL), dried over anhydrous MgSO₄ and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure products **8**. Yields, physical and spectroscopic data follow.

(S)-2-Methylene-9,9a-dihydro-1*H*-pyrrolo[1,2-*a*]indol-3(2*H*)-one (8a):³⁰ The representative procedure was followed by using lactam **7a** (42 mg, 0.16 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **8a** (15 mg, 52%) as a white solid; mp 76-78 °C

(hexane/CH₂Cl₂); $[\alpha]_D^{23} +285$ (*c* 1.09, CH₂Cl₂); *R*_f 0.24 (hexane/AcOEt: 3/1); IR ν (KBr) 1686, 1657, 1602, 1480, 1410, 757 cm⁻¹; δ_H 7.68 (d, *J* = 7.8 Hz, 1H), 7.26-7.19 (m, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.07 (dd, *J* = 3.4, 1.6 Hz, 1H), 5.42 (dd, *J* = 2.9, 1.4 Hz, 1H), 4.65-4.55 (m, 1H), 3.21 (dd, 15.7, 8.2 Hz, 1H), 3.17 (dd, 16.0, 6.8, 1.5 Hz, 2H), 2.90 (dd, *J* = 15.4, 10.7 Hz, 1H), 2.78-2.68 (m, 1H); δ_C 164.4 (C), 143.7 (C), 139.7 (C), 134.1 (C), 128.0 (CH), 125.4 (CH), 124.8 (CH), 117.1 (CH₂), 115.2 (CH), 60.2 (CH), 36.3 (CH₂), 34.2 (CH₂); LRMS (EI) *m/z* 185 (M⁺, 100%), 186 (14), 184 (18), 157 (16), 156 (32), 117 (42), 90 (14), 89 (16), 68 (14); HRMS (ESI): Calculated for C₁₂H₁₂NO (M⁺+H) 186.0919, found 186.0915.

(S)-2-Methylene-3,3a,4,5-tetrahydropyrrolo[1,2-a]quinolin-1(2H)-one (8b): The representative procedure was followed by using lactam **7b** (89 mg, 0.318 mmol). Purification by column chromatography (hexane/AcOEt, 4:1) yielded **8b** (34 mg, 54%) as a white solid; mp 88-92 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23} +150$ (*c* 1.11, CH₂Cl₂); *R*_f 0.33 (hexane/AcOEt: 3/1); IR ν (KBr) 3062, 2843, 1681, 1655, 1390, 905, 745 cm⁻¹; δ_H 8.71 (d, *J* = 8.3 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 7.05 (td, *J* = 7.5, 1.1 Hz, 1H), 6.10 (t, *J* = 2.8 Hz, 1H), 5.40 (t, *J* = 2.4 Hz, 1H), 3.93-3.84 (m, 1H), 3.06 (ddt, *J* = 16.8, 7.6, 2.1 Hz, 1H), 3.01-2.94 (m, 1H), 2.93-2.85 (m, 1H), 2.49 (ddt, *J* = 16.9, 6.3, 3.1 Hz, 1H), 2.23-2.16 (m, 1H), 1.75 (ddd, *J* = 25.0, 12.7, 5.6 Hz, 1H); δ_C 166.3 (C), 139.6 (C), 136.8 (C), 129.3 (CH), 126.9 (CH), 126.3 (C), 124.1 (CH), 120.0 (CH), 116.5 (CH₂), 54.7 (CH), 31.4 (CH₂), 29.6 (CH₂), 27.7 (CH₂); LRMS (EI) *m/z* 199 (M⁺, 100%), 200 (14), 198 (43), 170 (39), 131 (24), 130 (26); HRMS (EI): Calculated for C₁₃H₁₃NO 199.0997, found 199.0983.

(S)-2-Methylene-2,3,3a,4,5,6-hexahydro-1H-benzo[*f*]pyrrolo[1,2-a]azepin-1-one (8c): The representative procedure was followed by using lactam **7c** (67 mg, 0.228 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **8c** (13 mg, 27%) as a white solid; mp 101-103 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23} -31$ (*c* 1.03, CH₂Cl₂); *R*_f 0.17 (hexane/AcOEt: 3/1); IR ν (KBr) 2931, 1689, 1659, 1494, 1402 cm⁻¹; δ_H 7.35 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.29-7.14 (m, 3H), 6.13 (t, *J* = 2.8 Hz, 1H), 5.45 (ddd, *J* = 2.6, 1.7, 0.7 Hz, 1H), 3.63-3.53 (m, 1H), 3.16 (ddt, *J* = 16.7, 8.7, 3.3 Hz, 1H), 2.83-2.66 (m, 2H), 2.51 (ddd, *J* = 16.8, 3.6, 1.8 Hz, 1H), 2.08-1.94 (m, 2H), 1.74-1.55 (m, 1H), 1.54-1.36 (m, 1H); δ_C 167.5 (C), 139.4 (C), 139.3 (C), 138.7 (C), 130.3 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 117.0 (CH₂), 58.3 (CH), 39.5 (CH₂), 35.2 (CH₂), 33.8 (CH₂), 25.8 (CH₂); LRMS (EI) *m/z* 213 (M⁺, 100%), 214 (15), 212 (45), 198 (14), 185 (11), 184 (33), 156 (15), 145 (10), 144 (18), 117 (23), 68 (10); HRMS (EI): Calculated for C₁₄H₁₆NO 214.1232, found 214.1223.

General procedure for the synthesis of homoallyl amine derivatives **9** from imines **4**:

A mixture of the corresponding *N*-*tert*-butylsulfinyl imine **4** (1.0 mmol), allyl bromide (166 mg, 0.132 mL, 1.5 mmol), and indium (144 mg, 1.25 mmol) in dry THF (3 mL) was stirred for 6 h at 60

°C. Then, the resulting mixture was hydrolyzed with H₂O (5 mL), and the solution was extracted with AcOEt (3 × 5 mL). The combined organic phases were washed with brine (3 × 10 mL), dried with anhydrous MgSO₄, and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **9**. Yields, physical and spectroscopic data follow.

(2*R*,*S*_S)-1-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)pent-4-en-2-amine (9a):²³ The representative procedure was followed by using imine **4a** (453 mg, 1.5 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9a** (378 mg, 73%) as a yellow solid; mp 42-45 °C (hexane/CH₂Cl₂); [α]_D²³ +9 (*c* 1.08, CH₂Cl₂); *R*_f 0.32 (hexane/AcOEt: 1/1); IR ν(KBr) 3216, 1736, 1472, 1045, 1024, 912, 749 cm⁻¹; δ_H 7.53 (d, *J* = 8.5 Hz, 1H), 7.21-7.25 (m, 2H), 7.03-7.11 (m, 1H), 5.79-5.93 (m, 1H), 5.18-5.25 (m, 2H), 3.63-3.72 (m, 1H), 3.34 (br d, *J* = 6.9 Hz, 1H), 2.95 (dd, *J* = 7.2, 5.5 Hz, 2H), 2.48 (t, *J* = 6.7 Hz, 2H), 1.06 (s, 9H); δ_C 138.3 (C), 133.9 (CH), 133.0 (CH), 132.0 (CH), 128.3 (CH), 127.4 (CH), 125.2 (C), 119.5 (CH₂), 56.2 (CH), 56.0 (C), 41.8 (CH₂), 40.7 (CH₂), 22.6 (CH₃); LRMS (EI) *m/z* 247 (3), 245 (3), 208 (9), 184 (8), 182 (8), 171 (11), 169 (11), 118 (100), 91 (11), 90 (11), 89 (10).

(3*S*,*S*_S)-1-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)hex-5-en-3-amine (9b):²³ The representative procedure was followed by using imine **4b** (221 mg, 0.70 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9b** (202 mg, 81%) as a colorless oil; [α]_D²³ +43 (*c* 0.95, CH₂Cl₂); *R*_f 0.34 (hexane/AcOEt: 1/1); IR ν(film) 3215, 1471, 1439, 1052, 1022, 749 cm⁻¹; δ_H 7.52 (d, *J* = 7.9 Hz, 1H), 7.19-7.26 (m, 2H), 7.03-7.09 (m, 1H), 5.75-5.87 (m, 1H), 5.15-5.22 (m, 2H), 3.37-3.46 (m, 1H), 3.33 (br d, *J* = 6.6 Hz, 1H), 2.89 (ddd, *J* = 13.5, 11.1, 5.1 Hz, 1H), 2.73 (ddd, *J* = 13.5, 11.1, 5.7 Hz, 1H), 2.39-2.55 (m, 2H), 1.70-1.91 (m, 2H), 1.25 (s, 9H); δ_C 141.3 (ArC), 134.0 (CH), 133.0 (CH), 130.4 (CH), 127.9 (CH), 127.7 (CH), 124.5 (ArC), 119.4 (CH₂), 56.1 (C), 55.1 (CH), 40.7 (CH₂), 35.5 (CH₂), 32.7 (CH₂), 22.9 (CH₃); LRMS (EI) *m/z* 261 (29), 259 (29), 222 (46), 197 (37), 195 (37), 172 (16), 171 (97), 169 (100), 132 (39), 118 (23), 117 (49), 115 (10), 104 (12), 103 (14), 102 (15), 91 (24), 90 (28), 89 (17), 77 (26), 70 (21).

(4*S*,*S*_S)-7-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)hept-1-en-4-amine (9c):²³ The representative procedure was followed by using imine **4c** (300 mg, 0.91 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9c** (318 mg, 94%) as a colorless oil; [α]_D²³ +40 (*c* 1.06, CH₂Cl₂); *R*_f 0.44 (hexane/AcOEt: 1/1); IR ν(film) 3217, 1471, 913, 750 cm⁻¹; δ_H 7.50-7.56 (m, 1H), 7.16-7.26 (m, 2H), 7.01-7.10 (m, 1H), 5.70-5.86 (m, 1H), 5.11-5.20 (m, 2H), 3.31-3.41 (m, 1H), 3.22 (br d, *J* = 6.0 Hz, 1H), 2.72 (t, *J* = 7.6 Hz, 2H), 2.38-2.46 (m, 1H), 2.27-2.37 (m, 1H), 1.51-1.8 (m, 4H), 1.20 (s, 9H); δ_C 141.5 (C), 134.2 (CH), 132.9 (CH), 130.4 (CH), 127.7 (CH), 127.5 (CH), 124.5 (C), 119.1 (CH₂), 55.9 (C), 54.7 (CH), 40.5 (CH₂), 36.2 (CH₂), 34.7 (CH₂), 25.9

(CH₂), 22.8 (CH₃); LRMS (EI) *m/z* 317 (20), 315 (19), 275 (11), 273 (11), 224 (10), 211 (29), 209 (30), 171 (25), 169 (25), 146 (12), 132 (11), 131 (100), 130 (18), 118 (24), 115 (16), 104 (29), 103 (18), 102 (15), 91 (40), 90 (21), 89 (16), 77 (25), 70 (14), 56 (15), 55 (10).

General procedure for the synthesis of homoallyl amine derivatives **9 from 2-bromophenyl aldehydes:**

A mixture of indium powder (173 mg, 1.50 mmol), (*S*)-*tert*-butanesulfinamide (121 mg, 1.00 mmol), the corresponding 2-bromophenyl aldehyde (1.15 mmol), and Ti(OEt)₄ (456 mg, 0.450 mL, 2.00 mmol) in THF (2 mL) was stirred under Ar for 1 h at 23 °C. At this time, allyl bromide (166 mg, 0.132 mL, 1.5 mmol) was added and the reaction mixture heated for 5 h at 60 °C. The mixture was allowed to cool to room temperature, quenched with brine (2 mL), and diluted with EtOAc. The resulting suspension was filtered through a short pad of Celite and concentrated in vacuo (15 Torr). The residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **9**. Yields follow.

(2*R*,*S*_S)-1-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)pent-4-en-2-amine (9a):²³ The representative procedure was followed by using imine (2-bromophenyl)acetaldehyde (995 mg, 5.0 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9a** (1.07 g, 62%) as a yellow solid.

(3*S*,*S*_S)-1-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)hex-5-en-3-amine (9b):²³ The representative procedure was followed by using 3-(2-bromophenyl)propanal (782 mg, 3.67 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9b** (1.04 g, 80%) as a colorless oil.

(4*S*,*S*_S)-7-(2-Bromophenyl)-*N*-(*tert*-butylsulfinyl)hept-1-en-4-amine (9c):²³ The representative procedure was followed by using 4-(2-bromophenyl)butanal (1.16 g, 5.11 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **9c** (1.51 g, 80%) as a colorless oil.

General procedure for the synthesis of homoallyl amines **10 from homoallyl amine derivatives **9**:**

To a solution of the corresponding homoallyl amide derivative **9** (0.5 mmol) in dry THF (1 mL) at 0 °C was added HCl (6M solution, 0.25 mL, 1.5 mmol). The reaction mixture was stirred at room temperature for 1 h. Then, it was cooled down to 0 °C and NaOH (4M solution, 1 mL, 4 mmol) was added. The mixture was diluted with AcOEt (10 mL). The aqueous phase was extracted with AcOEt (2 × 10 mL). Then, the organic phases were washed with H₂O (10 mL), dried with anhydrous MgSO₄ and evaporated (15 Torr) to yield free amines **10**. Yields, physical and spectroscopic data follow.

(R)-1-(2-Bromophenyl)pent-4-en-2-amine (10a): The representative procedure was followed by using sulfinamide **9a** (688 mg, 2.0 mmol). Removal of the solvents at low pressure yielded **10a** (475 mg, 97%) as a yellow oil; $[\alpha]_D^{23}$ -10 (*c* 1.11, CH₂Cl₂); *R_f* 0.41 (CH₂Cl₂/MeOH: 9/1); IR ν (film) 2923, 2856, 1470, 1438 cm⁻¹; δ_H 7.55 (d, *J* = 7.8 Hz, 1H), 7.26-7.22 (m, 2H), 7.12-7.05 (m, 1H), 5.84 (dddd, *J* = 16.8, 10.2, 7.9, 6.4 Hz, 1H), 5.20-5.08 (m, 2H), 3.19 (tt, *J* = 8.2, 4.9 Hz, 1H), 2.95 (dd, *J* = 13.4, 5.0 Hz, 1H), 2.64 (dd, *J* = 13.4, 8.4 Hz, 1H), 2.31 (dddt, *J* = 13.8, 6.3, 4.7, 1.4 Hz, 1H), 2.18-2.05 (m, 1H), 1.47 (br s, 2H); δ_C 139.1 (C), 135.6 (CH), 133.1 (CH), 131.7 (CH), 128.1 (CH), 127.4 (CH), 125.0 (C), 117.9 (CH₂), 50.6 (CH), 44.3 (CH₂), 42.1 (CH₂); LRMS (EI) *m/z* 200 [*M*⁺ (⁸¹Br)-C₃H₅, 22%], 198 (22), 119 (16), 118 (11), 91 (11), 70 (100); HRMS (ESI): Calculated for C₁₁H₁₅⁷⁹BrN (*M*⁺+H) 240.0388, found 240.0379.

(S)-1-(2-Bromophenyl)hex-5-en-3-amine (10b): The representative procedure was followed by using sulfinamide **9b** (573 mg, 1.50 mmol). Removal of the solvents at low pressure yielded **10b** (380 mg, 100%) as a colorless oil; $[\alpha]_D^{23}$ -7 (*c* 1.16, CH₂Cl₂); *R_f* 0.37 (CH₂Cl₂/MeOH: 9/1); IR ν (film) 2917, 1470, 1438, 1022, 913, 747 cm⁻¹; δ_H 7.52 (d, *J* = 7.8 Hz, 1H), 7.24-7.21 (m, 2H), 7.11-7.00 (m, 1H), 5.89-5.73 (m, 1H), 5.16-5.11 (m, 1H), 5.10-5.08 (m, 1H), 2.93-2.71 (m, 3H), 2.36-2.25 (m, 1H), 2.12-1.97 (m, 1H), 1.75 (dddd, *J* = 13.5, 10.8, 5.9, 5.0 Hz, 1H), 1.66-1.53 (m, 1H), 1.46 (br d, *J* = 0.8 Hz, 2H); δ_C 141.7 (C), 135.7 (CH), 132.9 (CH), 130.4 (CH), 127.7 (CH), 127.6 (CH), 124.5 (C), 117.7 (CH₂), 50.5 (CH), 42.7 (CH₂), 38.0 (CH₂), 33.1 (CH₂); LRMS (EI) *m/z* 214 [*M*⁺ (⁸¹Br)-C₃H₅, 98%], 213 (12), 212 (100), 197 (8), 195 (8), 171 (77), 169 (78), 90 (13), 70 (19); HRMS (ESI): Calculated for C₁₂H₁₇⁷⁹BrN (*M*⁺+H) 254.0544, found 254.0537.

(S)-7-(2-Bromophenyl)hept-1-en-4-amine (10c): The representative procedure was followed by using sulfinamide **9c** (502 mg, 1.35 mmol). Removal of the solvents at low pressure yielded **10c** (357 mg, 99%) as a colorless oil; $[\alpha]_D^{23}$ -4 (*c* 1.01, CH₂Cl₂); *R_f* 0.34 (CH₂Cl₂/MeOH: 9/1); IR ν (film) 2925, 1470, 1437, 1022, 913 cm⁻¹; δ_H 7.53-7.50 (m, 1H), 7.23-7.20 (m, 2H), 7.08-7.01 (m, 1H), 5.85-5.73 (m, 1H), 5.12-5.06 (m, 2H), 2.88-2.79 (m, 1H), 2.79-2.67 (m, 2H), 2.30-2.20 (m, 1H), 2.06-1.94 (m, 1H), 1.79-1.58 (m, 2H), 1.57-1.34 (m, 4H); δ_C 141.8 (C), 135.8 (CH), 132.9 (CH), 130.4 (CH), 127.6 (CH), 127.5 (CH), 124.5 (C), 117.5 (CH₂), 50.5 (CH), 42.6 (CH₂), 37.3 (CH₂), 36.3 (CH₂), 26.7 (CH₂); LRMS (EI) *m/z* 214 [*M*⁺ (⁸¹Br)-C₃H₅, 99%], 227 (12), 226 (100), 169 (11), 130 (39), 129 (12), 104 (14), 70 (23), 56 (12); HRMS (ESI): Calculated for C₁₃H₁₉⁷⁹BrN (*M*⁺+H) 268.0701, found 268.0691.

General procedure for the synthesis of acrylamides **11** from homoallyl amine derivatives **9**:

To a solution of the corresponding homoallyl amide derivative **9** (0.5 mmol) in dry THF (1 mL) at 0 °C was added HCl (6M solution, 0.25 mL, 1.5 mmol). The reaction mixture was stirred at room

temperature for 1 h. Then, it was cooled down to 0 °C and NaOH (4M solution, 1 mL, 4 mmol) was added, and after 5 min, CH₂Cl₂ (1.5 mL) and acryloyl chloride (54 mg, 51 μL, 0.6 mmol) were also added. The resulting reaction mixture was stirred for 30 minutes at room temperature and after that it was diluted with AcOEt (15 mL). The aqueous phase was extracted with AcOEt (2 × 15 mL). Then, the organic phases were washed with H₂O (10 mL), dried with anhydrous MgSO₄ and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **11**. Yields, physical and spectroscopic data follow.

(R)-N-Acryloyl-1-(2-bromophenyl)pent-4-en-2-amine (11a): The representative procedure was followed by using sulfinamide **9a** (473 mg, 1.38 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **11a** (281 mg, 69%) as a white solid; mp 81-83 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ -18 (*c* 1.04, CH₂Cl₂); *R*_f 0.56 (hexane/AcOEt: 1/1); IR ν (KBr) 3215, 1471, 1439, 1052, 1022, 749 cm⁻¹; δ_H 7.52 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.29-7.19 (m, 2H), 7.06 (ddd, *J* = 8.0, 6.9, 2.2 Hz, 1H), 6.19 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.02 (dd, *J* = 17.0, 10.1 Hz, 1H), 5.92-5.73 (m, 1H), 5.76 (br d, *J* = 6.7 Hz, 1H), 5.57 (dd, *J* = 10.1, 1.6 Hz, 1H), 5.17-5.07 (m, 2H), 4.47-4.33 (m, 1H), 2.99 (d, *J* = 7.2 Hz, 1H), 2.45-2.26 (m, 2H); δ_C 165.2 (C), 137.9 (C), 134.2 (CH), 132.9 (CH), 131.3 (CH), 131.1 (CH), 128.3 (CH), 127.7 (CH), 126.3 (CH₂), 125.0 (C), 118.4 (CH₂), 49.9 (CH), 39.9 (CH₂), 38.8 (CH₂); LRMS (EI) *m/z* 295 [*M*⁺ (⁸¹Br), 2%], 254 (29), 252 (29), 214 (10), 200 (33), 198 (34), 124 (100), 91 (10), 90 (11), 89 (10), 70 (53), 55 (46); HRMS (ESI): Calculated for C₁₄H₁₇⁷⁹BrNO (*M*⁺+H) 294.0494, found 294.0485.

(S)-N-Acryloyl-1-(2-bromophenyl)hex-5-en-3-amine (11b): The representative procedure was followed by using sulfinamide **9b** (179 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **11b** (230 mg, 84%) as a white solid; mp 50-53 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ +17 (*c* 1.05, CH₂Cl₂); *R*_f 0.56 (hexane/AcOEt: 1/1); IR ν (KBr) 3271, 1654, 1626, 1543, 1438 cm⁻¹; δ_H 7.51 (d, *J* = 7.8 Hz, 1H), 7.25-7.20 (m, 2H), 7.10-7.00 (m, 1H), 6.29 (dd, *J* = 17.0, 1.6 Hz, 1H), 6.11 (dd, *J* = 17.0, 10.1 Hz, 1H), 5.88-5.71 (m, 1H), 5.64 (dd, *J* = 10.1, 1.6 Hz, 1H), 5.59 (br d, *J* = 8.8 Hz, 1H), 5.15-5.04 (m, 2H), 4.19 (m, 1H), 2.88-2.67 (m, 2H), 2.42-2.22 (m, 2H), 1.87 (dddd, *J* = 10.4, 6.2, 5.5, 3.7 Hz, 1H), 1.79-1.62 (m, 1H); δ_C 165.3 (C), 141.0 (C), 134.1 (CH), 132.9 (CH), 131.2 (CH), 130.6 (CH), 127.9 (CH), 127.7 (CH), 126.5 (CH₂), 124.3 (C), 118.3 (CH₂), 48.7 (CH), 39.3 (CH₂), 34.8 (CH₂), 33.0 (CH₂); LRMS (EI) *m/z* 309 [*M*⁺ (⁸¹Br), 2%], 307 (2), 269 (11), 268 (85), 267 (12), 266 (86), 215 (10), 214 (97), 213 (11), 212 (100), 197 (24), 195 (25), 171 (43), 169 (45), 132 (16), 125 (13), 116 (12), 115 (11), 90 (14), 89 (10), 84 (10), 77 (13), 72 (28), 7 (16), 55 (69); HRMS (ESI): Calculated for C₁₅H₁₉⁷⁹BrNO (*M*⁺+H) 308.0650, found 308.0638.

(S)-N-Acryloyl-7-(2-bromophenyl)hept-1-en-4-amine (11c): The representative procedure was followed by using sulfinamide **9c** (155 mg, 0.42 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **11c** (111 mg, 83%) as a white solid; mp 73-75 °C (hexane/CH₂Cl₂);

$[\alpha]_D^{23}$ -2.5 (*c* 1.02, CH₂Cl₂); *R*_f 0.57 (hexane/AcOEt: 1/1); IR ν (KBr) 3273, 2941, 1653, 1625, 1545, 748 cm⁻¹; δ_H 7.51 (d, *J* = 8.0 Hz, 1H), 7.23-7.16 (m, 2H), 7.04 (ddd, *J* = 8.0, 6.4, 2.7 Hz, 1H), 6.26 (dd, *J* = 16.9, 1.6 Hz, 1H), 6.07 (dd, *J* = 16.9, 10.2 Hz, 1H), 5.85-5.68 (m, 1H), 5.62 (dd, *J* = 10.2, 1.6 Hz, 1H), 5.45 (br d, *J* = 9.0 Hz, 1H), 5.13-5.02 (m, 2H), 4.22-4.07 (m, 1H), 2.82-2.65 (m, 2H), 2.37-2.16 (m, 2H), 1.75-1.39 (m, 4H); δ_C 165.2 (C), 141.5 (C), 134.2 (CH), 132.9 (CH), 131.2 (CH), 130.5 (CH), 127.7 (CH), 127.5 (CH), 126.4 (CH₂), 124.5 (C), 118.2 (CH₂), 48.5 (CH), 39.2 (CH₂), 36.0 (CH₂), 34.1 (CH₂), 26.4 (CH₂); LRMS (EI) *m/z* 323 [*M*⁺ (⁸¹Br), 1%], 282 (32), 280 (32), 228 (77), 226 (79), 211 (40), 209 (41), 171 (20), 169 (15), 152 (13), 130 (19), 129 (11), 124 (10), 91 (11), 90 (12), 72 (52), 70 (26), 56 (13), 55 (100); HRMS (ESI): Calculated for C₁₆H₂₁⁷⁹BrNO (*M*⁺+H) 322.0807, found 322.0811.

General procedure for the synthesis of pyridine-2-ones **12** from acrylamides **11**:

A mixture of the corresponding acrylamide **11** (0.75 mmol), ruthenium Hoveyda-Grubbs catalyst (19 mg, 0.0225 mmol) in dry CH₂Cl₂ (7.5 mL) was stirred at 40 °C under Ar for 3 h. Then the solvent was evaporated (15 Torr) and the resulting residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **12**. Yields, physical and spectroscopic data follow.

(*R*)-6-(2-Bromobenzyl)-5,6-dihydropyridin-2(1*H*)-one (12a): The representative procedure was followed by using acrylamide **11a** (221 mg, 0.75 mmol). Purification by column chromatography (hexane/AcOEt, 3:2) yielded **12a** (164 mg, 82%) as a white solid; mp 69-72 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ -13 (*c* 1.02, CH₂Cl₂); *R*_f 0.47 (AcOEt); IR ν (KBr) 3220, 1672, 1609, 1470, 1426 cm⁻¹; δ_H 7.57 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.28 (td, *J* = 7.4, 1.2 Hz, 1H), 7.21 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.14 (td, *J* = 7.9, 1.8 Hz, 1H), 6.61 (ddd, *J* = 9.9, 4.9, 3.5 Hz, 1H), 5.94 (ddd, *J* = 9.9, 3.6, 2.0 Hz, 1H), 5.68 (br s, 1H), 4.00-3.91 (m, 1H), 3.06 (dd, *J* = 13.5, 6.0 Hz, 1H), 2.95 (dd, *J* = 13.5, 8.2 Hz, 1H), 2.45 (dt, *J* = 17.7, 5.3 Hz, 1H), 2.28 (dddd, *J* = 17.7, 9.5, 3.4, 2.3 Hz, 1H); δ_C 166.3 (C), 140.4 (CH), 136.3 (C), 133.5 (CH), 131.6 (CH), 129.0 (CH), 127.9 (CH), 124.9 (C), 124.7 (CH), 50.5 (CH), 41.7 (CH₂), 29.6 (CH₂); LRMS (EI) *m/z* 171 [*M*⁺ (⁸¹Br)-C₅H₆NO, 3%], 169 (3), 97 (6), 96 (100), 95 (12), 78 (12), 68 (10); HRMS (ESI): Calculated for C₁₂H₁₃⁷⁹BrNO (*M*⁺+H) 266.0181, found 266.0177.

(*S*)-6-(2-Bromophenethyl)-5,6-dihydropyridin-2(1*H*)-one (12b): The representative procedure was followed by using acrylamide **11b** (90 mg, 0.29 mmol). Purification by column chromatography (hexane/AcOEt, 3:2) yielded **12b** (61 mg, 75%) as a white solid; mp 80-83 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ +26 (*c* 0.70, CH₂Cl₂); *R*_f 0.38 (AcOEt); IR ν (KBr) 3220, 1672, 1610, 1470, 1422 cm⁻¹; δ_H 7.53 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 4.1 Hz, 2H), 7.08 (dt, *J* = 8.0, 4.4 Hz, 1H), 6.61 (ddd, *J* = 9.9, 5.2, 3.3 Hz, 1H), 6.44 (br s, 1H), 5.93 (ddd, *J* = 9.9, 3.5, 2.1 Hz, 1H), 3.72-3.60 (m, 1H), 2.81 (ddd, *J* = 9.1, 6.9, 2.4 Hz, 2H), 2.46 (tt, *J* = 9.7, 4.9 Hz, 1H), 2.31-2.18 (m, 1H),

1.97-1.80 (m, 2H); δ_{C} 166.6 (C), 140.6 (CH), 140.3 (C), 133.0 (CH), 130.4 (CH), 128.1 (CH), 127.8 (CH), 124.6 (CH), 124.4 (C), 50.6 (CH), 35.6 (CH₂), 32.1 (CH₂), 29.8 (CH₂); LRMS (EI) m/z 200 (M^+ -Br, 54%), 132 (10), 96 (100), 78 (10), 68 (11); HRMS (ESI): Calculated for C₁₃H₁₅⁷⁹BrNO (M^+ +H) 280.0337, found 280.0330.

(S)-6-[3-(2-Bromophenyl)propyl]-5,6-dihydropyridin-2(1H)-one (12c): The representative procedure was followed by using acrylamide **11c** (129 mg, 0.40 mmol). Purification by column chromatography (hexane/AcOEt, 3:2) yielded **12c** (96 mg, 81%) as a colorless oil; $[\alpha]_{\text{D}}^{23} +33$ (c 0.77, CH₂Cl₂); R_{f} 0.47 (AcOEt); IR ν (film) 3221, 2933, 1672, 1610, 749 cm⁻¹; δ_{H} 7.52 (dd, J = 8.0, 1.0 Hz, 1H), 7.26-7.18 (m, 2H), 7.06 (ddd, J = 7.9, 7.1, 2.1 Hz, 1H), 6.59 (ddd, J = 9.9, 5.3, 3.1 Hz, 1H), 6.04 (br s, 1H), 5.93-5.87 (m, 1H), 3.67-3.58 (m, 1H), 2.80-2.72 (m, 2H), 2.40 (dt, J = 17.7, 5.4 Hz, 1H), 2.20-2.10 (m, 1H), 1.74-1.55 (m, 4H); δ_{C} 166.6 (C), 141.0 (C), 140.7 (CH), 133.0 (CH), 130.4 (CH), 127.9 (CH), 127.6 (CH), 124.6 (CH), 124.4 (C), 50.9 (CH), 35.9 (CH₂), 35.0 (CH₂), 29.9 (CH₂), 25.8 (CH₂); LRMS (EI) m/z 294 (M^+ (⁸¹Br)-1, 2%), 292 (2), 267 (5), 265 (5), 214 (26), 96 (100); HRMS (ESI): Calculated for C₁₄H₁₇⁷⁹BrNO (M^+ +H) 294.0473, found 294.0482.

General procedure for the synthesis of tricyclic compounds **13** from pyridine-2-ones **12**:

A mixture of the corresponding pyridine-2-one **12** (0.3 mmol), CuI (4.6 mg, 0.024 mmol), K₂CO₃ (83 mg, 0.6 mmol) and *N,N,N',N'*-tetramethylethylenediamine (5.6 mg, 7 μ L, 0.048 mmol) in dry dioxane (0.75 mL) was stirred at 100 °C under Ar for 20 h in a high-pressure tube. Then, the resulting mixture was cooled down to room temperature and hydrolyzed with H₂O (5 mL), extracted with AcOEt (3 $\times$ 10 mL), dried over anhydrous MgSO₄ and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure products **13**. Yields, physical and spectroscopic data follow.

(R)-9a,10-Dihydropyrido[1,2-*a*]indol-6(9H)-one (13a): The representative procedure was followed by using pyridine-2-one **12a** (112 mg, 0.42 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **13a** (70 mg, 90%) as a white solid; mp 93-96 °C (hexane/CH₂Cl₂); $[\alpha]_{\text{D}}^{23} +89$ (c 1.00, CH₂Cl₂); R_{f} 0.41 (hexane/AcOEt, 1:1); IR ν (KBr) 1650, 1587, 1478, 1416 cm⁻¹; δ_{H} 8.22 (d, J = 7.9 Hz, 1H), 7.26-7.19 (m, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.68 (ddd, J = 9.8, 6.4, 2.0 Hz, 1H), 6.10 (dd, J = 9.9, 3.0 Hz, 1H), 4.26-4.16 (m, 1H), 3.29 (dd, J = 15.5, 8.3 Hz, 1H), 2.88 (dd, J = 15.5, 10.9 Hz, 1H), 2.70 (dt, J = 17.63, 5.18 Hz, 1H), 2.45-2.34 (m, 1H); δ_{C} 162.3 (C), 142.4 (C), 139.1 (CH), 129.7 (C), 127.8 (CH), 126.8 (CH), 124.6 (CH), 123.7 (CH), 116.1 (CH), 57.8 (CH), 36.0 (CH₂), 31.1 (CH₂); LRMS (EI) m/z 185 (M^+ , 100%), 186 (13), 156 (16), 118 (97), 117 (56), 90 (26), 89 (28), 68 (61), 63 (10); HRMS (ESI): Calculated for C₁₂H₁₂NO (M^+ +H) 186.0919, found 186.0912.

(S)-4,4a,5,6-Tetrahydro-1H-pyrido[1,2-a]quinolin-1-one (13b): The representative procedure was followed by using pyridine-2-one **12b** (49 mg, 0.175 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **13b** (29 mg, 83%) as a white solid; mp 58-60 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23} +83$ (*c* 0.81, CH₂Cl₂); *R*_f 0.44 (hexane/AcOEt, 1:1); IR ν (KBr) 3045, 2942, 1665, 1488, 1397, 1316 cm⁻¹; δ_H 8.06 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.22-7.16 (m, 1H), 7.10-7.06 (m, 1H), 6.99 (td, *J* = 7.4, 1.2 Hz, 1H), 6.70-6.65 (m, 1H), 6.08 (ddd, *J* = 9.7, 2.2, 1.4 Hz, 1H), 4.00-3.92 (m, 1H), 2.82-2.68 (m, 2H), 2.49-2.36 (m, 2H), 2.05 (dq, *J* = 13.7, 4.6 Hz, 1H), 1.84 (dtd, *J* = 13.1, 10.1, 4.9 Hz, 1H); δ_C 164.63 (C), 140.27 (CH), 136.91 (C), 130.20 (C), 128.27 (CH), 126.98 (CH), 126.34 (CH), 124.06 (CH), 123.61 (CH), 56.48 (CH), 31.66 (CH₂), 29.77 (CH₂), 27.63 (CH₂); LRMS (EI) *m/z* 199 (M⁺, 100%), 200 (15), 170 (12), 132 (87), 131 (74), 130 (97), 103 (10), 77 (14), 68 (12); HRMS (ESI): Calculated for C₁₃H₁₄NO (M⁺+H) 200.1075, found 200.1066.

General procedure for the synthesis of 2-allylbenzo-fused heterocycles 14 from homoallyl amines 10:

A mixture of the homoallyl amine **10** (0.5 mmol), Cs₂CO₃ (326 mg, 1.0 mmol), PPh₃ (20 mg, 0.075 mmol) and Pd(OAc)₂ (5.6 mg, 0.025 mmol) in dry toluene (5 mL) was stirred at 110 °C under Ar for 21 h in a high-pressure tube. Then, the resulting mixture was cooled down to room temperature, hydrolyzed with 3M HCl (5 mL, 15 mmol) and diluted with AcOEt (10 mL). The organic phase was extracted with 3M HCl (4 × 10 mL) and then all the aqueous phases were basified with NaOH until pH 13 and extracted with AcOEt (4 × 15 mL). The resulting organic phase was dried over anhydrous MgSO₄ and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/EtOAc) to yield pure products **14**. Yields, physical and spectroscopic data follow.

(R)-2-Allylindoline (14a): The representative procedure was followed by homoallyl amine **10a** (96 mg, 0.40 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **14a** (43 mg, 68%) as a yellow oil; $[\alpha]_D^{23} +14$ (*c* 0.75, CH₂Cl₂); *R*_f 0.43 (hexane/AcOEt, 10:1); IR ν (film) 3375, 2926, 1608, 1484, 1466, 1246, 914, 744 cm⁻¹; δ_H 7.07 (d, *J* = 7.3 Hz, 1H), 7.00 (t, *J* = 7.6 Hz, 1H), 6.68 (td, *J* = 7.4, 1.0 Hz, 1H), 6.60 (d, *J* = 7.7 Hz, 1H), 5.90-5.75 (m, 1H), 5.17-5.06 (m, 2H), 3.89 (dtd, *J* = 8.7, 7.2, 6.0 Hz, 1H), 3.14 (dd, *J* = 15.6, 8.7 Hz, 1H), 2.73 (dd, *J* = 15.6, 7.1 Hz, 1H), 2.36-2.28 (m, 2H); δ_C 150.7 (C), 135.3 (CH), 128.6 (C), 127.4 (CH), 124.9 (CH), 118.7 (CH), 117.6 (CH₂), 109.3 (CH), 58.8 (CH), 41.1 (CH₂), 35.8 (CH₂); LRMS (EI) *m/z* 159 (M⁺, 12%), 118 (100), 117 (17), 91 (14); HRMS (ESI): Calculated for C₁₁H₁₄N (M⁺+H) 160.1126, found 160.1126.

(S)-2-Allyl-1,2,3,4-tetrahydroquinoline (14b): The representative procedure was followed by homoallyl amine **10b** (127 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **14b** (77 mg, 89%) as a yellow oil; $[\alpha]_D^{23} +48$ (*c* 1.07, CH₂Cl₂); *R*_f

0.55 (hexane/AcOEt, 9:1); IR ν (film) 3398, 2921, 1483, 1309, 913 cm^{-1} ; δ_{H} 6.97-6.91 (m, 2H), 6.59 (td, $J = 7.4, 1.1$ Hz, 1H), 6.47-6.43 (m, 1H), 5.88-5.76 (m, 1H), 5.19-5.12 (m, 2H), 3.84 (br s, 1H), 3.28 (dddd, $J = 9.8, 8.0, 5.0, 2.9$ Hz, 1H), 2.87-2.68 (m, 2H), 2.36-2.28 (m, 1H), 2.21-2.12 (m, 1H), 1.95 (dddd, $J = 12.5, 5.7, 3.7, 3.0$ Hz, 1H), 1.63 (dddd, $J = 12.8, 11.2, 9.8, 5.5$ Hz, 1H); δ_{C} 144.61 (C), 135.1 (CH), 129.3 (CH), 126.8 (CH), 121.3 (C), 118.0 (CH_2), 117.1 (CH), 114.2 (CH), 50.6 (CH), 41.3 (CH_2), 28.3 (CH_2), 26.5 (CH_2); LRMS (EI) m/z . 173 (M^+ , 16%), 133 (12), 132 (100), 130 (17), 117 (17); HRMS (ESI): Calculated for $\text{C}_{12}\text{H}_{16}\text{N}$ ($\text{M}^+\text{+H}$) 174.1283, found 174.1280.

(S)-2-Allyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (14c): The representative procedure was followed by homoallyl amine **10c** (134 mg, 0.50 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **14c** (79 mg, 84%) as a yellow oil; $[\alpha]_{\text{D}}^{23}$ -19 (c 1.07, CH_2Cl_2); R_{f} 0.61 (hexane/AcOEt, 9:1); IR ν (film) 3341, 2924, 1476, 1258, 737 cm^{-1} ; δ_{H} 7.11-6.99 (m, 2H), 6.83 (td, $J = 7.4, 1.2$ Hz, 1H), 6.70 (dd, $J = 7.7, 1.1$ Hz, 1H), 5.83 (dddd, $J = 16.2, 11.0, 8.8, 5.3$ Hz, 1H), 5.27-5.12 (m, 2H), 3.70 (br s, 1H), 2.86-2.64 (m, 3H), 2.40-2.13 (m, 2H), 2.02-1.81 (m, 2H), 1.66-1.42 (m, 2H); δ_{C} 148.9 (C), 135.9 (CH), 134.2 (C), 130.6 (CH), 126.7 (CH), 121.2 (CH), 119.9 (CH), 118.4 (CH_2), 57.0 (CH), 42.1 (CH_2), 38.1 (CH_2), 35.6 (CH_2), 26.4 (CH_2); LRMS (EI) m/z 187 (M^+ , 9%), 147 (11), 146 (100), 131 (12), 130 (13), 118 (18); HRMS (ESI): Calculated for $\text{C}_{13}\text{H}_{18}\text{N}$ ($\text{M}^+\text{+H}$) 188.1439, found 188.1433.

General procedure for the synthesis of acrylamides **15** from heterocycles **14**:

To a solution of the corresponding heterocycle **14** (1.25 mmol) and Et_3N (171 mg, 0.24 mL, 1.7 mmol) in dry CH_2Cl_2 (3 mL) was added dropwise acryloyl chloride (159 g, 0.15 mL, 1.76 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and after that it was hydrolyzed with H_2O (5 mL) and diluted with AcOEt (15 mL). The aqueous phase was extracted with AcOEt (3 $\times$ 10 mL). Then, the organic phases were dried with anhydrous MgSO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **15**. Yields, physical and spectroscopic data follow.

(S)-N-Acryloyl-2-allyl-1,2,3,4-tetrahydroquinoline (15b): The representative procedure was followed by heterocycle **14b** (77 mg, 0.44 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **15b** (63 mg, 63%) as a colorless oil; $[\alpha]_{\text{D}}^{23}$ -389 (c 1.03, CH_2Cl_2); R_{f} 0.30 (hexane/AcOEt, 6:1); IR ν (film) 2947, 1651, 1651, 1614, 1489, 1404, 1323, 1241, 914, 750 cm^{-1} ; δ_{H} 7.22-7.13 (m, 3H), 7.02 (d, $J = 7.1$ Hz, 1H), 6.42 (s, 1H), 6.41 (d, $J = 0.8$ Hz, 1H), 5.81-5.69 (m, 1H), 5.65-5.59 (m, 1H), 5.00 (s, $J = 1.1$ Hz, 1H), 4.98-4.94 (m, 1H), 4.93-4.84 (m, 1H), 2.66 (dt, $J = 15.1, 5.4$ Hz, 1H), 2.56 (ddd, $J = 15.2, 10.1, 5.5$ Hz, 1H), 2.42-2.25 (m, 2H), 2.20-2.11 (m, 1H), 1.54 (dddd, $J = 12.8, 10.1, 6.9, 5.6$ Hz, 1H); δ_{C} 165.4 (C), 137.2 (C), 134.4 (CH), 129.8

(CH), 127.8 (CH), 127.7 (CH₂), 126.4 (CH), 126.3 (CH), 125.9 (CH), 117.4 (CH₂), 51.7 (CH), 38.9 (CH₂), 29.7 (CH₂), 25.7 (CH₂); LRMS (EI) m/z 186 (M^+ -C₃H₅, 46%), 133 (11), 132 (100), 130 (10), 55 (16); HRMS (ESI): Calculated for C₁₅H₁₈NO (M^+ +H) 228.1388, found 228.1383.

(S)-N-Acryloyl-2-allyl-2,3,4,5-tetrahydro-1H-benzo[b]azepine (15c): The representative procedure was followed by homoallyl amine **14c** (180 mg, 0.96 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **15c** (122 mg, 52%) as a yellow oil; $[\alpha]_D^{23}$ -179 (c 1.09, CH₂Cl₂); R_f 0.28 (hexane/AcOEt, 6:1); IR ν (film) 2928, 1653, 1490, 1405, 1254 cm⁻¹; δ_H 7.31-7.18 (m, 3H), 7.02 (d, J = 6.8 Hz, 1H), 6.36 (dd, J = 16.8, 2.1 Hz, 1H), 5.94 (dd, J = 16.8, 10.3 Hz, 1H), 5.74 (ddt, J = 17.1, 10.3, 6.8 Hz, 1H), 5.48 (dd, J = 10.3, 2.1 Hz, 1H), 5.06-4.93 (m, 3H), 2.81-2.72 (m, 1H), 2.65 (dt, J = 14.2, 4.5 Hz, 1H), 2.15-2.03 (m, 1H), 1.99-1.86 (m, 2H), 1.84-1.72 (m, 1H), 1.65-1.51 (m, 2H); δ_C 165.3 (C), 140.4 (C), 138.3 (C), 135.2 (CH), 130.4 (CH), 129.8 (CH), 129.1 (CH), 128.4 (CH), 127.5 (CH₂), 126.8 (CH), 117.0 (CH₂), 51.3 (CH), 36.1 (CH₂), 33.3 (CH₂), 31.1 (CH₂), 21.2 (CH₂); LRMS (EI) m/z 241 (M^+ , 3%), 201 (10), 200 (66), 147 (13), 146 (100), 55 (14); HRMS (ESI): Calculated for C₁₆H₂₀NO (M^+ +H) 242.1545, found 242.1544.

General procedure for the synthesis of tricyclic compounds **13** from acrylamides **15**:

A mixture of the corresponding acrylamide **15** (0.50 mmol), ruthenium Hoveyda-Grubbs catalyst (12.6 mg, 0.015 mmol) in dry CH₂Cl₂ (5 mL) was stirred under Ar at 40 °C for 3 h. Then the solvent was evaporated (15 Torr) and the resulting residue was purified by column chromatography (silica gel, hexane/AcOEt) to yield products **13**. Yields, physical and spectroscopic data follow.

(S)-4,4a,5,6-Tetrahydro-1H-pyrido[1,2-a]quinolin-1-one (13b): The representative procedure was followed by using acrylamide **15b** (58 mg, 0.25 mmol). Purification by column chromatography (hexane/AcOEt, 3:1) yielded **13b** (42 mg, 83%) as a white solid.

(S)-4a,5,6,7-Tetrahydrobenzo[f]pyrido[1,2-a]azepin-1(4H)-one (13c): The representative procedure was followed by homoallyl amine **15c** (87 mg, 0.36 mmol). Purification by column chromatography (hexane/AcOEt, 10:1) yielded **13c** (60 mg, 79%) as a white solid; mp 130-132 °C (hexane/CH₂Cl₂); $[\alpha]_D^{23}$ -118 (c 1.03, CH₂Cl₂); R_f 0.30 (hexane/AcOEt, 1:2); IR ν (KBr) 1657, 1614, 1595, 1434, 1426 cm⁻¹; δ_H 7.28-7.17 (m, 4H), 6.59 (dddd, J = 9.8, 6.2, 2.4, 1.3 Hz, 1H), 6.06 (ddd, J = 9.9, 3.0, 0.6 Hz, 1H), 3.63-3.54 (m, 1H), 2.92 (ddt, J = 18.0, 7.2, 2.7 Hz, 1H), 2.80 (ddd, J = 14.2, 11.9, 2.3 Hz, 1H), 2.69 (ddd, J = 14.2, 6.2, 2.2 Hz, 1H), 2.34-2.16 (m, 2H), 2.08-1.95 (m, 1H), 1.68-1.58 (m, 1H), 1.58-1.41 (m, 1H); δ_C 163.0 (C), 142.0 (C), 139.7 (C), 138.6 (CH), 130.1 (CH), 128.5 (CH), 127.7 (CH), 127.1 (CH), 125.0 (CH), 57.9 (CH), 34.9 (CH₂), 33.8 (CH₂), 31.0 (CH₂), 26.1 (CH₂); LRMS (EI) m/z 213 (M^+ , 85%), 214 (13), 212 (25), 196 (10), 184 (11), 146 (21), 145 (100), 144 (28), 130 (17), 118 (30), 117 (46), 115 (10), 91 (11), 90 (18), 89 (15), 68 (15); HRMS (ESI): Calculated for C₁₄H₁₆NO (M^+ +H) 214.1232, found 214.1225.

Synthesis of (S)-2-allyl-N-methyl-1,2,3,4-tetrahydroquinoline (16): A mixture of the 2-allyltetrahydroquinoline **14b** (123 mg, 0.71 mmol), paraformaldehyde (95 mg, 3.2 mmol), NaBH₃CN (133 mg, 2.1 mmol) and acetic acid (126 mg, 0.120 mL, 2.1 mmol) in acetonitrile (6 mL) was stirred at 23 °C for 16 h. Then, the resulting mixture was hydrolyzed with 3M HCl (5 mL, 15 mmol) and diluted with AcOEt (10 mL). The organic phase was extracted with 3M HCl (4 × 10 mL) and then all the aqueous phases were basified with NaOH until pH 13 and extracted with AcOEt (4 × 15 mL). The resulting organic phase was dried over anhydrous MgSO₄ and evaporated (15 Torr) to give 126 mg (0.67 mmol, 95%) of pure compound **16**. Physical and spectroscopic data follow: Yellow wax; $[\alpha]_D^{23}$ -9 (*c* 1.27, CH₂Cl₂); *R*_f 0.72 (hexane/AcOEt, 9:1); IR ν (film) 2929, 1602, 1497, 1332, 1213, 911 cm⁻¹; δ_H 7.08 (t, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 7.3 Hz, 1H), 6.59 (td, *J* = 7.3, 1.1 Hz, 1H), 6.53 (d, *J* = 8.2 Hz, 1H), 5.79 (dddd, *J* = 16.8, 10.3, 8.1, 6.4 Hz, 1H), 5.12-5.03 (m, 2H), 3.37-3.27 (m, 1H), 2.93 (s, 3H), 2.89-2.74 (m, 1H), 2.70-2.60 (m, 1H), 2.47-2.36 (m, 1H), 2.21-2.08 (m, 1H), 1.97-1.79 (m, 2H); δ_C 145.3 (C), 135.6 (CH), 128.8 (CH), 127.2 (CH), 121.9 (C), 117.2 (CH₂), 115.6 (CH), 110.6 (CH), 58.8 (CH), 38.0 (CH₃), 36.0 (CH₂), 24.4 (CH₂), 23.5 (CH₂); LRMS (EI) *m/z* 187 (M⁺, 12%), 147 (11), 146 (100), 144 (11), 131 (17), 130 (15); HRMS (ESI): Calculated for C₁₃H₁₈N (M⁺+H) 188.1439, found 188.1445.

Synthesis of (-)-angustureine (18) from (S)-2-allyl-N-methyl-1,2,3,4-tetrahydroquinoline (16): A mixture of 2-allyl-N-methyltetrahydroquinoline **16** (93 mg, 0.50 mmol), *cis*-3-hexene (86 mg, 0.127 mL, 1.0 mmol) and ruthenium Hoveyda-Grubbs catalyst (12.7 mg, 0.015 mmol) in dry CH₂Cl₂ (6 mL) was stirred under Ar at 40 °C for 3 h. Then the solvent was evaporated (15 Torr), the resulting residue was dissolved in MeOH (9 mL) and Pd/C 10% (27 mg, 0.015 mmol) was added. The resulting reaction mixture was stirred for 12 h at 23 °C under H₂ (1 atm), then filtered through celite and evaporated (15 Torr). The resulting residue was purified by column chromatography (silica gel, hexane/AcOEt: 20/1) to yield 59 mg (0.27 mmol, 54%) of pure (-)-angustureine (**18**).³¹ Physical and spectroscopic data follow: colorless oil; $[\alpha]_D^{23}$ -6.8 (*c* 1.00, CH₂Cl₂); *R*_f 0.18 (hexane/AcOEt, 20:1); IR ν (film) 2926, 1602, 1498, 741 cm⁻¹; δ_H 7.06 (t, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 7.3 Hz, 1H), 6.57 (td, *J* = 7.3, 1.0 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 3.21 (dq, *J* = 8.5, 4.2 Hz, 1H), 2.91 (s, 3H), 2.84-2.73 (m, 1H), 2.64 (dt, *J* = 16.2, 4.2 Hz, 1H), 1.92-1.83 (m, 2H), 1.64-1.53 (m, 1H), 1.45-1.20 (m, 8H), 0.89 (t, *J* = 6.9 Hz, 3H); δ_C 145.5 (C), 128.7 (CH), 127.2 (CH), 122.0 (C), 115.3 (CH), 110.5 (CH), 59.1 (CH), 38.1 (CH₃), 32.2 (CH₂), 31.4 (CH₂), 25.9 (CH₂), 24.6 (CH₂), 23.7 (CH₂), 22.8 (CH₂), 14.2 (CH₃); LRMS (EI) *m/z* 217 (M⁺, 14%), 147 (11), 146 (100), 144 (8).

Synthesis of (*S,E*)-2-[3-(3,4-Dimethoxyphenyl)allyl]-1-methyl-1,2,3,4-tetrahydroquinoline (19**):**

A mixture of 2-allyl-*N*-methyltetrahydroquinoline **16** (51 mg, 0.27 mmol), 4-bromoveratrol (148 mg, 0.100 mL, 0.68 mmol), K₂CO₃ (75 mg, 0.54 mmol) and Pd(PPh₃)₄ (15.6 mg, 0.0135 mmol) in dry dioxane (1 mL) was stirred at 100 °C under Ar for 24 h in a high-pressure tube. Then, the resulting mixture was cooled down to room temperature, diluted with AcOEt (10 mL), filtered through a short pad of Celite and concentrated in vacuo (15 Torr). The residue was purified by column chromatography (silica gel, hexane/AcOEt: 17/1) to yield 35 mg (0.11 mmol, 40%) of pure compound **19**. Physical and spectroscopic data follow: yellow oil; $[\alpha]_D^{23}$ -29 (*c* 1.10, CH₂Cl₂); *R*_f 0.53 (hexane/AcOEt, 3:1); IR ν (film) 2931, 1601, 1511, 1498, 1260 cm⁻¹; δ_H 7.09 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.1 Hz, 1H), 6.90-6.85 (m, 2H), 6.81 (d, *J* = 8.8 Hz, 1H), 6.61 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.05 (ddd, *J* = 15.0, 8.0, 6.8 Hz, 1H), 3.90 (s, 3H), 3.87 (s, 3H), 3.41 (td, *J* = 8.4, 4.3 Hz, 1H), 2.97 (s, 3H), 2.93-2.81 (m, 1H), 2.73-2.63 (m, 1H), 2.59-2.49 (m, 1H), 2.29 (dt, *J* = 14.0, 8.6 Hz, 1H), 2.02-1.86 (m, 2H); δ_C 149.2 (C), 148.6 (C), 145.3 (C), 132.0 (CH), 130.8 (C), 128.9 (CH), 127.3 (CH), 125.3 (CH), 121.9 (C), 119.0 (CH), 115.7 (CH), 111.3 (CH), 110.6 (CH), 108.7 (CH), 59.2 (CH₃), 56.1 (CH₃), 56.0 (CH₃), 38.1 (CH), 35.2 (CH₂), 24.7 (CH₂), 23.6 (CH₂); LRMS (EI) *m/z* 323 (M⁺, 39%), 203 (10), 172 (25), 147 (12), 146 (100), 144 (19), 131 (16), 130 (15), 120 (29), 91 (10); HRMS (ESI): Calculated for C₂₁H₂₆NO₂ (M⁺+H) 324.1964, found 324.1974.

ASSOCIATED CONTENT

Supporting Information. Copies of ¹H, ¹³C NMR and DEPT spectra for all the reported compounds. This material is available free of charge via the Internet at <http://pubs.acs.org/>.

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ACKNOWLEDGMENT

We thank the Spanish Ministerio de Ciencia e Innovación (Grant No. CTQ2007-65218, Consolider Ingenio 2010-CSD-2007-00006 and CTQ2011-24165), the Generalitat Valenciana (Grant No. PROMETEO/2009/039 and FEDER) and the University of Alicante for generous and continuous financial support.

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