DOI: 10.1002/ejoc.201301174

A Short Asymmetric Synthesis of Octahydroindole Derivatives by Application of Catalytic C(sp^3)–H Amination Reaction

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Keywords: Synthetic methods / Medicinal chemistry / Nitrogen heterocycles / Amination / Diastereoselectivity / Cycloaddition

The stereoselective synthesis of octahydroindole derivatives is reported according to 3–4-step sequences. The strategy relies on our previously developed catalytic asymmetric C(sp^3)–H amination reaction. Its application to cyclic enol triflates affords allylic amines in good yields and stereoselectivity. The C–H functionalization step, then, is followed by a Heck coupling reaction, a Mitsunobu reaction and a final intramolecular cycloaddition reaction thereby leading to the isolation of the expected heterocyclic compounds with an overall yield of up to 69 %. In addition, the chirality introduced in the intermolecular C(sp^3)–H amination reaction allows controlling the configuration of the three other stereocenters created in the intramolecular cycloaddition reaction. A second sequence starts from benzocyclobutene and affords fused benzo-octahydroindole derivatives over three steps.

Introduction

Classical medicinal chemistry mainly relies on the coupling and functionalization of aromatic compounds, as mirrored by the structure of the 33 new molecular entities approved by the US Food and Drug Administration in 2012.[1] Recent trends in medicinal chemistry, however, encourage medicinal chemists to "escape from flatland"[2] and explore a new chemical space with the preparation of complex saturated molecules. In addition to providing new molecular scaffolds with improved chances of patentability, it has been recently proposed that molecular topology has a long neglected influence on the pharmacokinetics of bioactive compounds. Reducing the aromatic character of a molecule as well as the introduction of chiral centers are likely to improve these properties.[3] The search for efficient stereoselective methodology giving a rapid access to a collection of natural product-like molecules, thus, should offer invaluable opportunities as emphasized in the reviews on diversity-oriented synthesis.[4]

Indole is one of the most investigated privileged scaffolds.[5] It has been the purpose of many methodological developments because of its ubiquity in nature and medicinal chemistry.[6] The saturated hydroindole analogs are no less important and are receiving increasing attention. These heterocycles are found in several natural products such as lycorine, pancracine, and mesembrine that belong to the families of Amaryllidaceae and Sceletium alkaloids,[7] as well as aeruginosins of marine origin (Figure 1).[8] The motif is also present in the angiotensin-converting-enzyme (ACE) inhibitor Perindorpil® that has been approved for the treatment of hypertension.[9] These compounds illustrate the capacity to access new bioactive compounds by derivatization of polyhydroindole scaffolds.

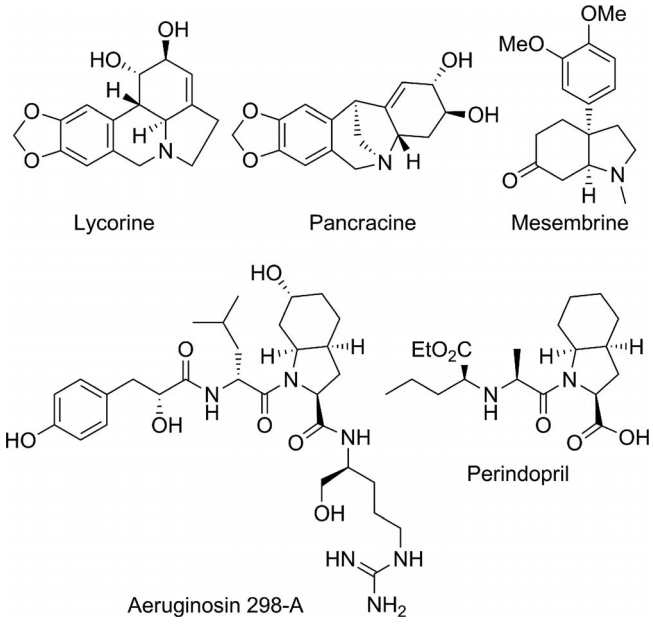

Figure 1. Naturally occurring polyhydroindole derivatives.

The growing importance of perhydroindole analogs has driven the design of stereoselective methods for their prepa-

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201301174.

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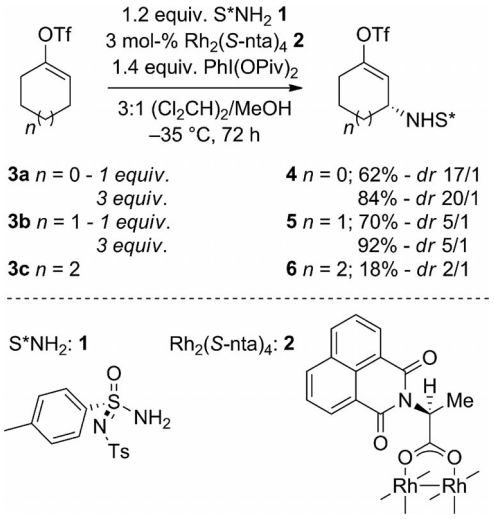
ration. These rely, for example, on catalytic hydrogenation of indolic substrates,[10] stereospecific reactions from tyrosine derivatives,[11] cycloaddition,[12] or palladium-catalyzed allylic alkylation.[13] It was with the aim to develop an alternative rapid access to the octahydroindole scaffold that we have envisaged the application of catalytic C–H functionalization reactions. This new class of transformation has received considerable attention in the last decade.[14] Several natural product and drug syntheses,[15] such as, the recent application of C(sp^3)–H alkenylation reaction to the preparation of hexahydroindoles,[15h] highlight the opportunities offered by the selective functionalization of C(sp^3)–H bonds. We therefore wish to report that the application of catalytic intermolecular C(sp^3)–H amination provides an efficient stereoselective route to chiral octahydroindole scaffolds. Short sequences involving Heck couplings, Mitsunobu reactions and intramolecular [4+2] cycloaddition reactions, then, lead to the sequential introduction of structural elements that could be further derivatized to create libraries for biological screening. In addition, the chirality introduced in the C–H functionalization step generally allows control of the configuration of the other stereogenic centers in the final octahydroindole products.

Results and Discussion

Catalytic C(sp^3)–H and C(sp^2)–H amination has been extensively investigated in the last decade.[16] The most spectacular results, to date, have been obtained with the application of oxidative conditions for the formation of metallanitrenes and their subsequent insertion into different C(sp^3)–H bonds. Several metal complexes have been shown to catalyze efficiently the overall process with dinuclear rhodium(II) species remaining the catalyst of choice to this end.[17–19] In this domain, our group has demonstrated that highly stereo- and chemoselective C(sp^3)–H amination can be performed in very good yields by using a chiral nitrene generated from the combination of the (*S*)-sulfonimidamide **1** and the chiral rhodium(II) complex Rh_2(*S*-nta)$_4$ **2**.[20] The reaction particularly applies to benzylic and allylic methylene sites as well as to the tertiary C(sp^3)–H bonds of simple alkanes. The scope has recently been extended to more functionalized substrates such as terpenes and enol carbonates.[20d] The rapid stereoselective access to perhydroindole derivatives, as a first application of this method, capitalizes on these results.

The first route relies on vinyl triflates which have been previously shown to be relevant substrates for this reaction in a single example.[20d] Catalytic asymmetric C–H amination reaction of cyclic triflates **3**, that were prepared from corresponding ketones under standard conditions,[21] leads to the expected products with various results according to the ring size (Scheme 1). The reaction with cyclopentenyl derivative **3a** used as the limiting agent gave the best diastereomeric ratio of 17:1, whereas the highest yield was obtained starting from cyclohexenyl analog **3b**. It should be mentioned that, in both cases, the conversion could be improved by carrying out the reaction in the presence of 3 equiv. of triflates **3**. This allowed isolating compounds **4** and **5** in 84% and 92% yields, respectively. Moreover, we have found that C–H aminated product **5** could be obtained with a higher diatereomeric ratio of > 20:1 after recrystallization in diisopropyl ether. Seven-membered product **6** was isolated with a low yield of 18% and a *dr* of 2:1, which were not optimized.[22]



Scheme 1. Catalytic stereoselective C–H amination reaction of vinyl triflates **3**.

Aminated triflates **4** and **5** were then engaged in a Heck coupling reaction with various alkenes. Optimization of the reaction conditions were carried out with six-membered derivative **5** in the presence of methyl acrylate as the coupling partner. The screening of either the solvent or the catalyst led us to find that use of Pd(dppf)Cl_2 in dimethylformamide (DMF) affords the best conversion, the corresponding product **7a** being isolated in 90% yield after 12 h of reaction (Scheme 2).[23] These conditions allowed us to introduce efficiently various alkenes with different electron-withdrawing groups such as an ester, a ketone, a nitrile or a sulfone. However, the introduction of a styrenyl unit required the use of Pd(PPh_3)$_2Cl_2$.[24] This was also necessary in the case of the five-membered derivative **4** that was converted into the corresponding product **8** with a lower yield of 42%.

With dienes **7** and **8** in hand, we then investigated the introduction of an alkenyl side chain with the aim to perform the subsequent intramolecular Diels–Alder cycloaddition reaction. Surprisingly, the alkylation of the sulfonimidamides with simple allyl halides did not afford the expected tertiary derivatives thereby confirming the non-classical behavior of the terminal nitrogen of these functional groups. We thus took inspiration from a previous study of Fensterbank, Lacôte, and Malacria that describes the functionalization of primary sulfonimidamides through a Mitsunobu reaction.[25] Application of the reported conditions with allyl alcohol, however, led to the corresponding product always being contaminated by traces of diisopropyl azodicarboxylate (DIAD). Accordingly, replacement of the latter by its *tert*-butyl analog combined with the use of PPh_3

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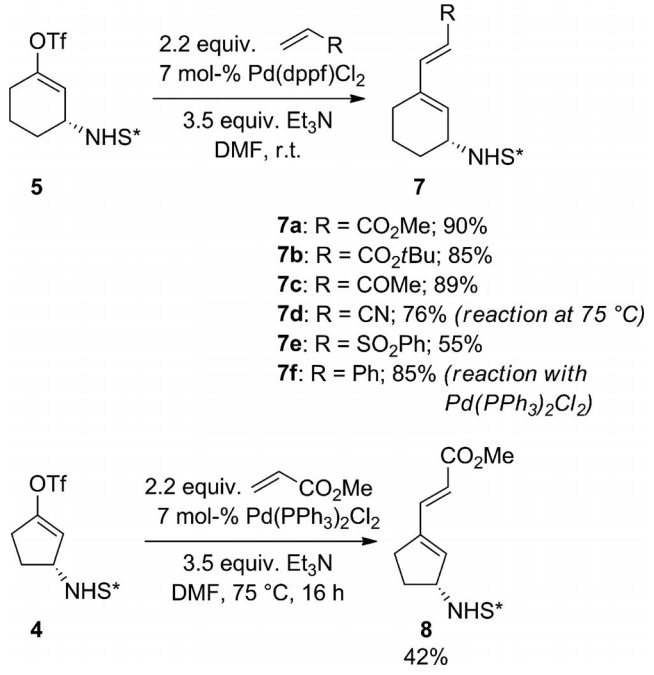
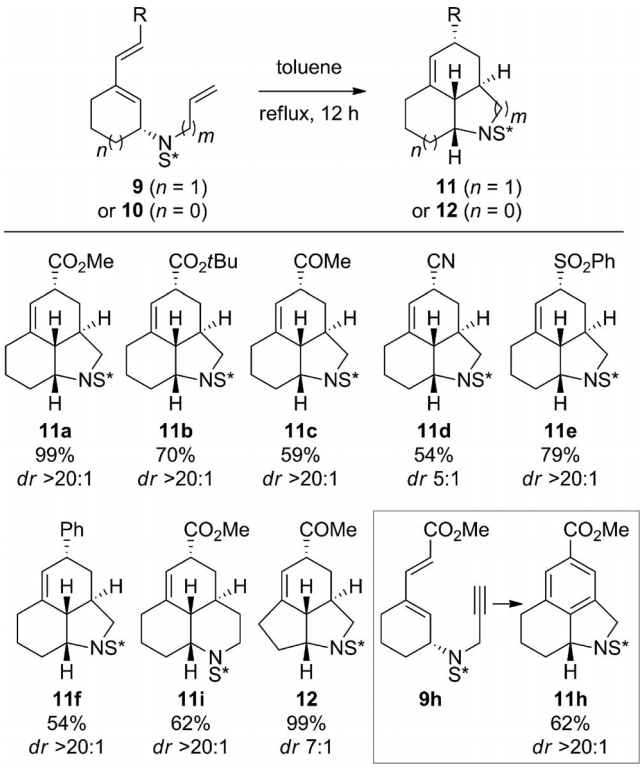


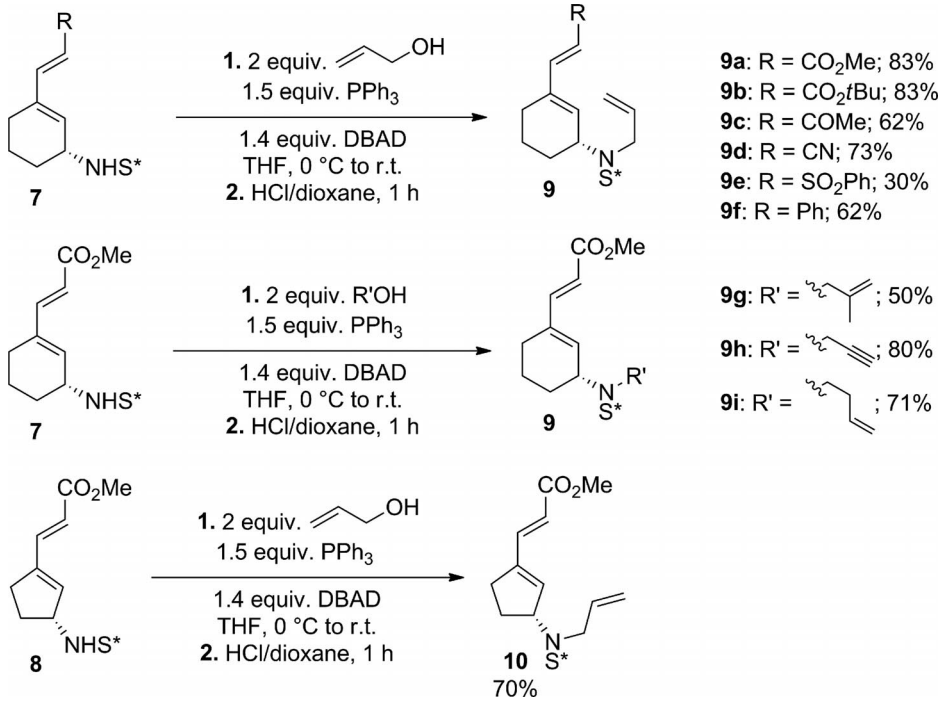
Scheme 2. Heck coupling reactions with aminated vinyl triflates **4** and **5**.

allowed ready access to tertiary allyl sulfonimidamides after an acidic treatment, with yields generally in the 62–83% range (Scheme 3). These conditions also revealed appropriate for the allylation of the five-membered analog **8** as well as for the introduction of a methallyl, a propargyl, and a but-3-en-1-yl side chain on compound **7a**. Unexpectedly, the application of these conditions did not allow the introduction of a but-2-en-1-yl and a but-3-yn-1-yl side chain.

The intramolecular Diels–Alder reaction,[26] pleasingly, has been found to proceed smoothly in toluene heated to reflux for 12h (Scheme 4). The corresponding cycloadduct **11a** is isolated from compound **9a** as a single stereoisomer after flash chromatography on SiO_2. The product is sup-



Scheme 4. Intramolecular Diels–Alder reaction.



Scheme 3. Mitsunobu reaction for introduction of unsaturated side chains.

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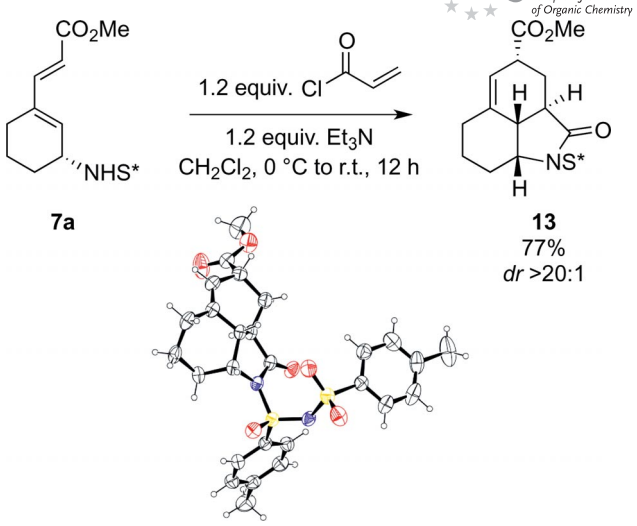
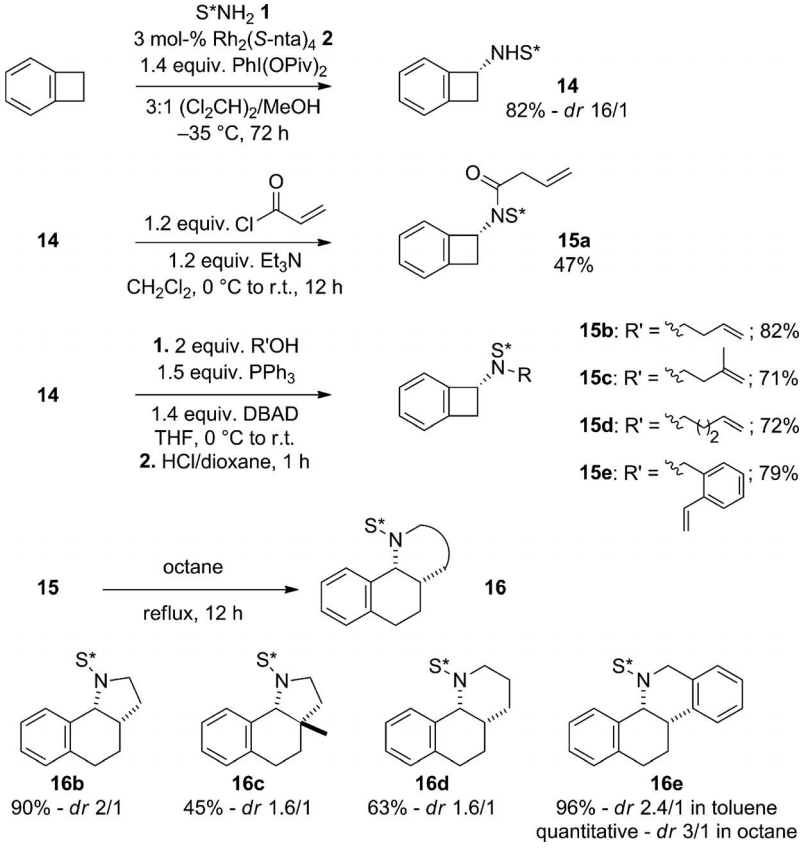
posed to arise from an *exo*-transition state.[27,28] Application of the reaction conditions to **9b**–**9f** has then allowed isolating the expected tricyclic compounds **11b**–**11f** with yields in the 54–79% range.[28] However, while the more substituted methallyl substrate **9g** did not undergo cyclization, propargyl analog **9h** gave a diene that spontaneously aromatized to afford benzofused product **11h** in 62% yield.

It was also possible to form efficiently higher or lower analogs of octahydroindole derivatives starting from, respectively, but-2-en-1-yl substrate **9i** and cyclopentenyl motif **10**. However, in the latter case, corresponding cycloadduct **12** has been isolated with a diastereomeric ratio of 7:1. Such erosion of diastereoselectivity appears to result from the epimerization of the stereocenter prior to the cycloaddition reaction because heating resulting cycloadduct **12** in toluene for several hours does not change the *dr*. More interestingly, during attempts to introduce an acryloyl side chain final onto compound **7a** prior to the intramolecular cycloaddition, we were very pleased to observe the clean one-pot formation of cycloadduct **13** at room temperature. This was isolated as a diastereoisomerically pure crystalline solid in 77% yield, and the X-ray crystal structure leads us to secure the formerly supposed absolute stereochemistry of the octahydroindole derivatives (Scheme 5).



Scheme 5. Formation of compound **13** from **7a**.

These results obtained for the stereoselective formation of octahydroindole analogues prompted us to design a second straightforward strategy based on the catalytic C(sp^3)–H amination of benzylic substrates. We had previously demonstrated that indane and tetrahydronaphthalene can be efficiently converted under these conditions to the corresponding benzylic amines with excellent yields and diastereoselectivities.[20] Application of the reaction to benzocyclobutene was envisaged because the latter is a useful precursor to perform intramolecular [4+2] cycloaddition reactions.[29,30] However, contrary to the sequence designed from vinyl triflates, we recognized that the stereochemical



Scheme 6. Synthesis of perhydroindole derivatives from benzocyclobutene.

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information introduced in the C(sp^3)–H amination step should be lost after the thermally-induced benzocyclobutene ring opening. Nevertheless, it was conjectured that the remaining stereochemistry on the sulfur center could secure good diastereocontrol in the cycloaddition reaction.

Catalytic C(sp^3)–H amination reaction of benzocyclobutene was found to proceed efficiently on a millimolar scale to afford expected aminated product **14** with a yield of 82% and a *dr* of 16:1, thereby confirming that secondary benzylic positions are highly reactive towards nitrene insertion (Scheme 6). The precursors of the intramolecular [4+2] cycloaddition reaction, then, were directly obtained through application of the previous condition reactions reported in Scheme 3 for the Mitsunobu reaction, or by simple acylation in the case of **15a**. Various alkenyl side chains likely to react with the in situ generated *ortho*-quinodimethane, were thus introduced leading to compounds **15a**–**15e** with yields ranging from 47 to 82%. The last step of the strategy, finally, occurred with complete conversion in octane heated to reflux except, not surprisingly, in the case of vinylacetyl derivative **15a**. The 5,6-bicyclic products and the 6,6 analogs were isolated in yields of up to 96%, and as *cis* isomers, as corroborated by the coupling constant of approximately 8 Hz for the benzylic proton in the ^{1}H NMR spectra.[30a,30b] Pleasingly, the substitution on the alkene unit was tolerated as **15c** could be converted into corresponding cycloadduct **16c**, contrary to the case of compound **9g**. However, the results in terms of diastereoselectivity proved to be below our expectations, as the chirality transfer did not proceed efficiently. Screening of the conditions in the case of compound **16e** revealed that the best *dr* of 3:1, obtained by running the reaction in octane, was slightly lower (around 2:1) in other solvents such as toluene. It should be nevertheless mentioned that optically pure heterocycles are accessible through this sequence as we have been able to separate the two diastereoisomers of compound **16b** by column chromatography over SiO_2.

Conclusions

In conclusion, the catalytic intermolecular C(sp^3)–H amination of cycloalken-1-yl triflates as well as of benzocyclobutene affords chiral amines, which are versatile building blocks for the stereoselective formation of natural-product-like compounds. The octahydroindole derivatives are produced in only 3 to 4 steps with overall yields of up to 69% and excellent diastereomeric ratios generally $> 20:1$.[31,32] These privileged heterocyclic scaffolds should be further derivatized following either cleavage of the double bond, reduction of the ester, keto, or cyano groups, or deprotection of the amine.[20] It should be also emphasized that the use of the enantiomeric matched pair of reagents, i.e. sulfonimidamide (*R*)-**1** with rhodium complex Rh_2(*R*-nta)$_4$, gives access to the other enantiomer of allylic amines.[20] The chirality transfer observed during the intramolecular cycloaddition reaction gives an opportunity to isolate the enantiomers of these heterocyclic structures. Work is now in progress to produce chemical libraries of nitrogen-containing molecules by application of the catalytic selective C(sp^3)–H amination reaction.[33]

Experimental Section

General Remarks: Melting points were measured in capillary tubes and recorded with a Büchi B-540 melting point apparatus. Infrared spectra were recorded with a Perkin–Elmer Spectrum BX FT-IR spectrometer. Optical rotations were determined with a JASCO P-1010 polarimeter. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded with Bruker spectrometers: Avance 300 NMR (300 MHz). Chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as internal standard. NMR spectroscopic experiments were carried out in deuteriochloroform ($CDCl_3$). The following abbreviations are used for the proton spectra multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet. Coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were obtained with an LCT (Micromass) instrument by using electrospray ionization and Time of Flight analyzer (ESI-MS) for high-resolution mass spectra (HRMS). Thin-layer chromatography was performed on silica gel 60 plates with a fluorescent indicator and visualized under a UVP Mineralight UVGL-58 lamp (254 nm) and with a solution of ninhydrin in ethanol. Flash chromatography was performed with silica gel 60 (40–63 μm, 230–400 mesh ASTM) at medium pressure (200 mbar). All solvents were distilled and stored over 4 Å molecular sieves before use. All reagents were obtained from commercial suppliers unless otherwise stated. Organic extracts were, in general, dried with magnesium sulfate ($MgSO_4$).

Typical C–H Amination Procedure (4–6): In an oven-dried tube were introduced activated 4 Å molecular sieves (100 mg), Rh_2[(*S*)-nta]$_4$ **2** (7.70 mg, 0.006 mmol) and (–)-*N*-(*p*-tolylsulfonyl)-*p*-toluenesulfonimidamide (–)-(*S*)-**1** (78.0 mg, 0.240 mmol). The tube was capped with a rubber septum and purged with argon. Anhydrous and degassed 1,1,2,2-tetrachloroethane (0.75 mL) and methanol (0.25 mL) were added under argon, and the mixture was stirred for 5 min before addition of the substrate (0.200 mmol). The tube was cooled to –78 °C, and bis(*tert*-butylcarbonyloxy)iodobenzene (115 mg, 0.280 mmol) was added. The mixture was stored in the freezer (–35 °C) for 3 days. After dilution with dichloromethane (3 mL), the molecular sieves were removed by filtration and the filtrate was evaporated to dryness under reduced pressure. The oily residue was purified by flash chromatography on silica gel, affording the following C–H amination products.

Compound 4: Prepared following the typical amination procedure from cyclopenten-1-yl trifluoromethanesulfonate **3a**. Corresponding amination product was obtained (dichloromethane/ethyl acetate, 20:1) as an orange solid in 62% yield (67.0 mg) and 17:1 *dr* (^{1}H NMR evaluation), m.p. 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 17/*diastereoisomer B 1* δ = 1.75–1.88 (m, 1 H), 2.20–2.31 (m, 1 H), 2.44–2.50 (m, 1 H), 2.42 (s, 3 H), 2.44 (s, 3 H), 2.57–2.69 (m, 1 H), 4.33–4.44 (m, 1 H), *5.26–5.30 (m, 1 H)*, 5.53–5.55 (m, 1 H), *5.84–5.88 (m, 1 H)*, *6.33–6.36 (d, J = 9.1, 1 H, NH)*, 6.40–6.46 (d, *J* = 9.1, 1 H NH), 7.24–7.34 (m, 4 H), 7.80–7.87 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 17/*diastereoisomer B 1* δ = 21.5 (CH_3), 21.6 (CH_3), 29.0 (CH_2), 29.7 (CH_2), *30.9 (CH_2)*, 55.6 (CH), 116.3 (Cq), 117.0 (CH), 126.7 (2× CH), 127.7 (2× CH), 129.3 (2× CH), 130.0 (2× CH), 135.6 (Cq), 140.2 (Cq), 143.1 (Cq), 145.1 (Cq), 152.4 (Cq) ppm. IR: $\tilde{\nu}$ = 3235, 1667, 1596, 1424, 1299, 1264, 1250, 1204, 1139, 1080, 1090, 1016, 1000, 922, 813, 760, 658 cm^{-1}. HRMS

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(ESI): calcd. for $C_{20}H_{20}F_3N_2O_6S_3$ [M – H]$^-$ 537.0436; found 537.0458.

Compound 5: Prepared following the typical amination procedure from cyclohexen-1-yl trifluoromethanesulfonate **3b**. Corresponding amination product was obtained (heptane/ethyl acetate, 70:30) as a white solid in 70% yield (77.5 mg) and 5:1 *dr* (^{1}H NMR evaluation), m.p. 114–115 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 1.35–1.49 (m, 1 H), 1.60–1.81 (m, 3 H), 2.21–2.33 (m, 2 H), 2.40 (s, 3 H), 2.42 (s, 3 H), 3.94–4.04 (m, 1 H), *5.30–5.35 (m, 1 H)*, 5.63–5.67 (m, 1 H), 6.01 (d, *J* = 8.9 Hz, 1 H), 7.24–7.34 (m, 4 H), 7.74–7.86 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 19.4, 21.57, 21.63, 27.1, 28.1, 48.7, 118.8, 120.6, *126.7*, 126.8, *127.6*, 127.7, *129.3*, 129.4, 130.0, *130.1*, 135.7, 140.2, 143.2, 145.2, 152.0 ppm. IR: $\tilde{\nu}$ = 3208, 2925, 1686, 1597, 1417, 1303, 1210, 1143, 1109, 1061, 1017, 897, 815 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{24}F_3N_2O_6S_3$ [M + H]$^+$ 553.0749; found 553.0757. Compound **5** can be recrystallized from diisopropyl oxide affording white needles with > 20:1 *dr*. $[\alpha]_D^{20}$ = +93.5 (*c* = 1.04, $CHCl_3$).

Compound 6: Prepared following the typical amination procedure from cyclohepten-1-yl trifluoromethanesulfonate **3c** (0.600 mmol, 3 equiv.). Corresponding amination product was obtained (dichloromethane/ethyl acetate, 20:1) as an orange oil in 18% yield (20.0 mg) and 2:1 *dr* (^{1}H NMR evaluation). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 2/*diastereoisomer B 1* δ = 1.45–1.78 (m, 6 H), 2.34 (s, 3 H), 2.35 (s, 3 H), 2.37–2.44 (m, 2 H), *3.32–3.44 (m, 1 H)*, 3.86–3.98 (m, 1 H), *5.31–5.33 (d, J = 4.7* Hz, *1 H)*, 5.66–5.70 (d, *J* = 4.7 Hz, 1 H), 6.21–6.26 (d, *J* = 8.3 Hz, 1 H NH), *6.30–6.32 (d, J = 8.3* Hz, *1 H, NH)*, 7.14–7.26 (m, 4 H), 7.69–7.80 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 2/*diastereoisomer B 1* δ = 21.5 (CH_3), 21.6 (CH_3), 24.1 (CH_2), *24.2 (CH_2)*, 5.0 (CH_2), *25.1 (CH_2)*, *30.7 (CH_2)*, 32.6 (CH_2), 32.8 (CH_2), *33.8 (CH_2)*, *50.2 (CH)*, 50.4 (CH), 123.8 (Cq), 125.0 (CH), 126.7 (2× CH), *126.7 (2× CH)*, 127.6 (2× CH), *127.6 (2× CH)*, 129.3 (2× CH), *129.3 (2× CH)*, 129.9 (2× CH), 135.6 (Cq), 140.2 (Cq), 143.1 (Cq), 145.1 (Cq), 153.2 (Cq) ppm. IR: $\tilde{\nu}$ = 2927, 1597, 1413, 1303, 1246, 1206, 1107, 1089, 1017, 988, 869, 813 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{26}F_3N_2O_6S_3$ [M + H]$^+$ 567.0905; found 567.0904.

Compound 7a: To a solution of Pd(dppf)Cl_2 (32.3 mg, 44.0 μmol) in dry DMF (15 mL) under argon, were introduced C–H amination product of cyclohexen-1-yl trifluoromethanesulfonate **5** (347 mg, 0.630 mmol) in dry DMF (6 mL), methyl acrylate (125 μL, 1.38 mmol) and triethylamine (296 μL, 2.20 mmol). The reaction mixture was stirred at room temperature for 12 h. Dichloromethane was added (30 mL) and the solution was washed with a saturated solution of ammonium chloride (1× 30 mL), water (1× 30 mL) and brine (1× 30 mL). After drying, filtration and concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 70:30 to 65:35) to afford a white solid in 90% yield (276 mg), m.p. 63–64 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 8/*diastereoisomer B 1* δ = 1.35–1.53 (m, 2 H), 1.56–1.76 (m, 2 H), 1.98–2.06 (m, 2 H), 2.38 (s, 3 H), 2.40 (s, 3 H), *3.70 (s, 3 H)*, 3.73 (s, 3 H), 3.86–3.99 (m, 1 H), *5.62–5.65 (m, 1 H)*, *5.76–5.82 (d, J = 15.8* Hz, *1 H)*, 5.78–5.83 (d, *J* = 15.8 Hz, 1 H), 5.87–5.92 (m, 1 H), 6.40–6.43 (d, *J* = 8.6 Hz, 1 H NH), *7.03–7.09 (d, J = 15.7* Hz, *1 H)*, 7.14–7.29 (m, 5 H), 7.76–7.87 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 8/*diastereoisomer B 1* δ = *19.2 (CH_2)*, 19.6 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.4 (CH_2), *23.5 (CH_2)* 28.9 (CH_2), *30.0 (CH_2)*, *49.9 (CH)*, 50.0 (CH), 51.7 (CH_3), 117.4 (CH), 126.8 (2× CH), 127.7 (2× CH), 129.2 (2× CH), 129.8 (2× CH), *134.6 (CH)*, 136.1 (CH), 136.2 (Cq), 137.7 (Cq), *138.2 (Cq)*, 140.3 (Cq), 142.8 (Cq), 144.7 (Cq), *146.4 (CH)* 146.5 (CH), 167.4 (Cq) ppm. IR: $\tilde{\nu}$ = 2945, 1715, 1631, 1433, 1303, 1284, 1248, 1124, 1106, 1090, 1062, 1035, 1016, 977, 930, 813, 752, 702, 658 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{29}N_2O_5S_2$ [M + H]$^+$ 589.1518; found 589.1539.

Compound 7b: To a solution of Pd(dppf)Cl_2 (9.20 mg, 13.0 μmol) in dry DMF (0.5 mL) under argon, were introduced a solution of C–H amination product of cyclohexen-1-yl trifluoromethanesulfonate **5** (100 mg, 0.181 mmol) in dry DMF (1.5 mL), *tert*-butyl acrylate (58.0 μL, 0.398 mmol) and triethylamine (86.0 μL, 0.634 mmol). The reaction mixture was stirred at room temperature for 12 h. Dichloromethane was added (2 mL) and the organic layer was washed with a saturated solution of ammonium chloride (2 mL), water (2 mL) and brine (2 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 70:30) to afford a colorless gum in 85% yield (81 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 9/*diastereoisomer B 1* δ = 1.36–1.46 (m, 1 H), *1.48 (s, 9 H)*, 1.49–1.54 (m, 10 H), 1.62–1.75 (m, 2 H), 2.01–2.10 (m, 2 H), 2.41 (s, 3 H), 2.43 (s, 3 H), 3.88–4.01 (m, 1 H), *5.56–5.50 (m, 1 H)*, 5.75–5.80 (d, *J* = 15.8 Hz, 1 H), 5.86–5.92 (m, 1 H), 6.19–6.21 (d, *J* = 8.8 Hz, NH), *6.97–7.02 (d, J = 15.8* Hz, *1 H)*, 7.08–7.13 (d, *J* = 15.8 Hz, 1 H), 7.17–7.26 (m, 4 H), 7.73–7.79 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 9/*diastereoisomer B 1* δ = 19.5 (CH_2), 21.55 (CH_3), 21.62 (CH_3), 23.6 (CH_2), *23.8 (CH_2)*, 28.2 (3× CH_3), 29.2 (CH_2), *29.7 (CH_2)*, 50.0 (CH), 80.5 (Cq), 120.2 (CH), 126.8 (2× CH), 127.8 (2× CH), 129.3 (2× CH), 129.9 (2× CH), 134.5 (CH), 136.2 (Cq), 138.2 (Cq), 140.3 (Cq), 143.0 (Cq), 144.92 (Cq), 144.93 (CH), 166.2 (Cq) ppm. IR: $\tilde{\nu}$ = 3587, 2255, 1750, 1640, 1392, 1039, 919 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{33}N_2O_5S_2$ [M – H]$^-$ 529.1831; found 529.1828.

Compound 7c: To a solution of Pd(dppf)Cl_2 (9.20 mg, 12.6 μmol) in dry DMF (0.5 mL) under argon, were introduced a solution of C–H amination product of cyclohexen-1-yl trifluoromethanesulfonate **5** (100 mg, 0.181 mmol) in dry DMF (1.5 mL), but-3-en-2-one (34.0 μL, 0.398 mmol) and triethylamine (86.0 μL, 0.634 mmol). The reaction mixture was stirred at room temperature for 12 h. Dichloromethane was added (2 mL) and the organic layer was washed with a saturated solution of ammonium chloride (2 mL), water (2 mL) and brine (2 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 50:50) affording a yellow oil in 89% yield (76.0 mg). $[\alpha]_D^{20}$ = +218.3 (*c* = 1.03, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.35–1.48 (m, 1 H), 1.50–1.61 (m, 1 H), 1.67–1.77 (m, 2 H), 2.08–2.17 (m, 2 H), 2.32 (s, 3 H), 2.43 (s, 3 H), 2.46 (s, 3 H), 3.91–4.03 (m, 1 H), 6.02–6.05 (d, *J* = 8.8 Hz, 1 H NH), 6.06–6.09 (m, 1 H), 6.10–6.16 (d, *J* = 16.4 Hz, 1 H), 7.05–7.10 (d, *J* = 16.2 Hz, 1 H), 7.25–7.37 (m, 4 H), 7.81–7.87 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 19.6 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.5 (CH_2), 27.2 (CH_3), 29.1 (CH_2), 50.1 (CH), 126.7 (2× CH), 127.0 (CH), 127.8 (2× CH), 129.2 (2× CH), 129.9 (2× CH), 136.0 (Cq), 136.5 (CH), 138.3 (Cq), 140.3 (Cq), 142.9 (Cq), 144.9 (Cq), 145.1 (CH), 198.8 (Cq) ppm. IR: $\tilde{\nu}$ = 2320, 1737, 1375, 1039, 919 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{27}N_2O_4S_2$ [M – H]$^-$ 471.1412; found 471.1413.

Compound 7d: To a solution of Pd(dppf)Cl_2 (9.20 mg, 13.0 μmol) in dry DMF (0.5 mL) under argon, were introduced a solution of C–H amination product **5** (100 mg, 0.181 mmol) in dry DMF (1.5 mL), acrylonitrile (26.0 μL, 0.396 mmol) and triethylamine (86.0 μL, 0.634 mmol). The reaction mixture was stirred at 75 °C

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for 1 h. Dichloromethane was added (2 mL) and the organic layer was washed with a saturated solution of ammonium chloride (2 mL), water (2 mL), and brine (2 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (dichloromethane/ethyl acetate, 95:5 to 90:10) affording a colorless gum in 80% yield (66.0 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 1.38–1.57 (m, 2 H), 1.63–1.81 (m, 2 H), 1.97–2.05 (m, 2 H), *2.43 (s, 3 H)*, 2.44 (s, 3 H), 2.46 (s, 3 H), 3.93–4.01 (m, 1 H), *5.23–5.26 (d, J = 16.4* Hz, *1 H)*, 5.31–5.34 (d, *J* = 16.4 Hz, 1 H), *5.66–5.69 (m, 1 H)*, 5.98–6.00 (m, 1 H), 6.04–6.05 (d, *J* = 8.6 Hz, 1 H, NH), *6.60–6.63 (d, J = 16.4* Hz, *1 H)*, 6.93–6.97 (d, *J* = 16.4 Hz, 1 H), 7.26–7.36 (m, 4 H), 7.83–7.87 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 19.4 (CH_2), 21. 6 (CH_3), 21.7 (CH_3), 22.8 (CH_2), *28.5 (CH_2)*, 28.8 (CH_2), 49.9 (CH), *94.4 (CH)*, 96.1 (CH), 118.1 (CN), 126.7 (2× CH), 127.8 (2× CH), 129.3 (2× CH), 129.9 (2× CH), 136.0 (Cq), 137.0 (CH), 137.2 (Cq), 140.3 (Cq), 143.0 (Cq), 145.0 (Cq), 151.9 (CH) ppm. IR: $\tilde{\nu}$ = 2928, 2217, 1735, 1598, 1374, 1302, 1244, 1150, 1090, 1016, 968, 926, 813, 753, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{26}N_3O_3S_2$ $[M + H]^+$ 456.1416; found 456.1415.

Compound 7e: To a solution of $Pd(PPh_3)_2Cl_2$ (17.5 mg, 25.3 μmol) in dry DMF (1 mL) under argon, were introduced a solution of C–H amination product **5** (200 mg, 0.362 mmol) in dry DMF (3 mL), (vinylsulfonyl)benzene (135 mg, 0.796 mmol) and triethylamine (171 μL, 1.27 mmol). The reaction mixture was stirred at 75 °C for 2 h. Dichloromethane was added (4 mL) and the organic layer was washed with a saturated solution of ammonium chloride (4 mL), water (4 mL) and brine (1× 4 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 80:20 to 60:40) affording a yellow solid in 63% yield (130 mg), m.p. 71–72 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 1.38–1.45 (m, 1 H), 1.46–1.54 (m, 1 H), 1.66–1.73 (m, 2 H), 1.97–2.03 (m, 2 H), 2.43 (s, 3 H), 2.44 (s, 3 H), 3.91–4.00 (m, 1 H), *5.65–5.68 (m, 1 H)*, *5.88–5.90 (m, 1 H)*, *5.92–5.93 (d, J = 8.8* Hz, *1 H, NH)*, 6.08–6.10 (m, 1 H), 6.24–6.26 (d, *J* = 8.8 Hz, 1 H NH), 6.31–6.34 (d, *J* = 15.3 Hz, 1 H), 7.20–7.23 (d, *J* = 15.3 Hz, 1 H), 7.26–7.33 (m, 4 H), 7.53–7.58 (m, 2 H), 7.62–7.65 (t, *J* = 7.2 Hz, 1 H), 7.79–7.87 (m, 4 H), 7.89–7.94 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 19.4 (CH_2), *19.8 (CH_2)*, 21.57 (CH_3), 21.62 (CH_3), 23.6 (CH_2), *24.8 (CH_2)*, 28.8 (CH_2), *29.1 (CH_2)*, 50.0 (CH), *50.1 (CH)*, 126.7 (2× CH), *127.2 (2× CH)*, *127.4 (2× CH)*, 127.6 (2× CH), 127.8 (2× CH), 129.2 (CH), 129.3 (2× CH), 129.4 (2× CH), *129.8 (2× CH)*, 129.9 (2× CH), 133.4 (CH), 135.8 (Cq), 136.3 (Cq), 138.1 (CH), 140.1 (Cq), 140.2 (Cq), 142.9 (Cq), 144.0 (CH), 144.8 (Cq) ppm. IR: $\tilde{\nu}$ = 3211, 2927, 1596, 1495, 1447, 1302, 1253, 1145, 1105, 1062, 1016, 972, 928, 836, 812 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{34}N_3O_5S_3$ $[M + NH_4]^+$ 588.1661; found 588.1631.

Compound 7f: To a solution of $Pd(PPh_3)_2Cl_2$ (5.00 mg, 7.21 μmol) in dry DMF (1 mL) under argon, were introduced a solution of C–H amination product **5** (57.0 mg, 0.103 mmol) in dry DMF (2 mL), styrene (25.3 μL, 0.227 mmol) and triethylamine (49.3 μL, 0.361 mmol). The reaction mixture was stirred at 75 °C for 12 h. Dichloromethane was added (10 mL) and the organic layer was washed with a saturated solution of ammonium chloride (10 mL), water (10 mL) and brine (10 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 70:30) to afford a colorless gum in 20% yield (11.0 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 10/*diastereoisomer B 1* δ = 1.38–1.46 (m, 1 H), 1.64–1.77 (m, 3 H), 2.22–2.27 (m, 2 H), 2.43 (s, 3 H), 2.46 (s, 3 H), 3.94–4.04 (m, 1 H), *5.11–5.15 (m, 1 H)*, 5.73–5.78 (m, 1 H), 6.02–6.05 (d, *J* = 8.5 Hz, 1 H NH), *6.20–6.22 (d, J = 8.5* Hz, *1 H)*, *6.34–6.40 (d, J = 16.1* Hz, *1 H)*, 6.51–6.56 (d, *J* = 16.1 Hz, 1 H), 6.69–6.75 (d, *J* = 16.1 Hz, 1 H), 7.22–7.27 (m, 2 H), 7.31–7.36 (m, 4 H), 7.40–7.44 (m, 2 H), 7.83–7.89 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 10/*diastereoisomer B 1* δ = *19.2 (CH_2)*, 19.5 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.9 (CH_2), 29.4 (CH_2), 50.1 (CH), 126.4 (2× CH), 126.7 (2× CH), 127.6 (CH), 127.8 (2× CH), 128.1 (CH), 128.3 (CH), 128.6 (2× CH), 129.2 (2× CH), 129.8 (2× CH), 130.8 (CH), 136.4 (Cq), 137.1 (Cq), 139.6 (Cq), 140.5 (Cq), 142.8 (Cq), 144.7 (Cq) ppm. IR: $\tilde{\nu}$ = 2927, 1709, 1597, 1494, 1448, 1302, 1256, 1152, 1100, 1091, 1064, 1017, 965, 814, 751, 694, 658 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{29}N_2O_3S_2$ $[M - H]^-$ 505.1620; found 505.1650.

Compound 8: To a solution of $Pd(PPh_3)_2Cl_2$ (8.35 mg, 11.9 μmol) in dry DMF (1 mL) under argon, were introduced a solution of C–H amination product of **4** (44.0 mg, 79.6 μmol) in dry DMF (0.7 mL), methyl acrylate (16.3 μL, 0.175 mmol) and triethylamine (39.2 μL, 0.279 mmol). The reaction mixture was stirred at 75 °C for 3 h. Dichloromethane was added (2 mL) and the organic layer was washed with a saturated solution of ammonium chloride (2 mL), water (2 mL) and brine (2 mL). After concentration under reduced pressure, the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 70:30) affording a colorless gum in 37% yield (14.0 mg). $[\alpha]_D^{20}$ = +147.2 (*c* = 1.02, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.53–1.64 (m, 1 H), 2.05–2.15 (m, 1 H), 2.17–2.26 (m, 1 H), 2.33 (s, 3 H), 2.37 (s, 3 H), 2.38–2.51 (m, 1 H), 3.69 (s, 3 H), 4.29–4.40 (m, 1 H), 5.72–5.77 (d, *J* = 15.8 Hz, 1 H), 5.85–5.88 (m, 1 H), 5.91–5.94 (d, *J* = 9.0 Hz, 1 H NH), 7.15–7.26 (m, 4 H), 7.29–7.34 (d, *J* = 15.8 Hz, 1 H), 7.72–7.78 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.5 (CH_3), 21.6 (CH_3), 29.2 (CH_2), 31.0 (CH_2), 51.7 (CH), 59.5 (CH), 121.1 (CH), 126.7 (2× CH), 127.8 (2× CH), 129.2 (2× CH), 129.9 (2× CH), 135.8 (Cq), 136.7 (CH), 139.3 (CH), 140.3 (Cq), 142.9 (Cq), 143.7 (Cq), 144.9 (Cq), 167.1 (Cq) ppm. IR: $\tilde{\nu}$ = 2254, 1717, 1709, 1449, 1388, 1305, 1201, 1163, 1124, 1050, 908 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{30}N_3O_5S_2$ $[M + NH_4]^+$ 492.1627; found 492.1610.

Typical Mitsunobu Procedure (for 9a–10): Secondary sulfonimidamide **7** or **8** (0.150 mmol) was dissolved in tetrahydrofuran (0.7 mL) at room temperature, under an argon atmosphere. Triphenylphosphine (0.225 mmol), the alcohol (0.300 mmol) and di-*tert*-butyl azodicarboxylate (0.210 mmol) were then added at room temperature and the reaction mixture was stirred overnight. A 4 M solution of hydrochloric acid in dioxane (0.6 mL) was then added and the mixture was stirred for 1 h at room temperature. The solvents were removed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2 (2 mL). The organic phase was washed successively with a solution of HCl 4 M (2 mL), and HCl 1 M (2 mL), before being dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.

Compound 9a: Prepared following the typical Mitsunobu procedure from **7a** and allylic alcohol. Corresponding product **9a** was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless gum in 83% yield (66 mg), m.p. 63–65 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 12/*diastereoisomer B 1* δ = 1.51–1.74 (m, 3 H), 1.90–2.00 (m, 1 H), 2.11–2.17 (m, 1 H), 2.17–2.25 (m, 1 H), 2.39 (s, 3 H), 2.45 (s, 3 H), 3.75 (s, 3 H), *3.76 (s, 3 H)*, 3.79–3.84 (m, 1 H), 3.87–3.97 (m, 1 H), 4.74–4.84 (m, 1 H), 5.07–5.13 (m, 1 H), 5.16–5.25 (m, 1 H), *5.37–5.42 (m, 1 H)*, 5.53–5.59 (m, 1 H), 5.72–5.87 (m, 1 H), 5.80–5.85 (d, *J* = 15.9 Hz, 1 H), *6.01–6.04 (m, 1 H)*, 7.08–7.13 (d, *J* = 15.9 Hz, 1 H), 7.22–7.35 (m, 4 H), 7.77–

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7.83 (m, 2 H), 7.85–7.90 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 12/*diastereoisomer B 1* δ = 21.3 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.6 (CH_2), 27.6 (CH_2), 47.4 (CH_2), 51.7 (CH_3), 56.7 (CH), 117.2 (CH), 117.9 (CH_2), 126.7 (2× CH), 127.3 (2× CH), 129.2 (2× CH), 129.9 (2× CH), 134.9 (CH), 136.1 (CH), 137.2 (Cq), 139.3 (Cq), 141.0 (Cq), 142.6 (Cq), 144.6 (Cq), 146.1 (CH), 167.5 (Cq) ppm. IR: $\tilde{\nu}$ = 2947, 1712, 1597, 1435, 1362, 1303, 1247, 1153, 1101, 1062, 1014, 813, 749, 703, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{33}N_2O_5S_2$ $[M + H]^+$ 529.1857; found 529.1831.

Compound 9b: Prepared following the typical Mitsunobu procedure from **7b** and allylic alcohol. Corresponding product **9b** was obtained (dichloromethane 100%) as a white solid in 83% yield (71 mg), m.p. 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 1.49 (s, 9 H), 1.61–1.67 (m, 2 H), 1.88–1.97 (m, 1 H), 2.00–2.09 (m, 1 H), 2.10–2.15 (m, 1 H), 2.16–2.28 (m, 1 H), 2.39 (s, 3 H), *2.42 (s, 3 H)*, 2.44 (s, 3 H), 3.73–3.79 (dd, *J* = 16.9, 6.2 Hz, 1 H), 3.89–3.95 (dd, *J* = 16.9, 5.6 Hz, 1 H), *4.01–4.10 (m, 1 H)*, *4.26–4.37 (m, 1 H)*, 4.73–4.82 (m, 1 H), 5.08–5.11 (dd, *J* = 10.4 Hz, 1.2 Hz, 1 H), 5.18–5.24 (dd, *J* = 17.0 Hz, 1.2 Hz, 1 H), *5.33–5.38 (m, 1 H)*, 5.45–5.49 (m, 1 H), 5.72–5.78 (d, *J* = 15.8 Hz, 1 H), 5.72–5.87 (m, 1 H), 6.96–7.02 (d, *J* = 15.8 Hz, 1 H), 7.22–7.33 (m, 4 H), 7.76–7.89 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 21.3 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.7 (CH_2), *26.4 (CH_2)*, *26.8 (CH_2)*, 27.7 (CH_2), 28.1 (3× CH_3), *38.2 (CH)*, *42.4 (CH)*, *45.5 (CH)*, 47.3 (CH_2), *53.0 (CH_2)*, 56.8 (CH), *59.8 (CH)*, 80.5 (Cq), 117.8 (CH_2), *118.5 (CH)*, 119.5 (CH), *126.6 (2× CH)*, 126.7 (2× CH), 127.3 (2× CH), *127.5 (2× CH)*, 129.1 (2× CH), *129.7 (2× CH)*, 129.9 (2× CH), 135.0 (CH), 135.1 (CH), 136.5 (Cq), 139.5 (Cq), 141.0 (Cq), 142.6 (Cq), 144.6 (Cq), 144.8 (CH), 166.4 (Cq) ppm. IR: $\tilde{\nu}$ = 2937, 1724, 1368, 1315, 1249, 1165, 1064, 1015, 845, 813, 734, 702, 657 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{42}N_3O_5S_2$ $[M + NH_4]^+$ 588.2566; found 588.2596.

Compound 9c: Prepared following the typical Mitsunobu procedure from **7c** and allylic alcohol. Corresponding product **9c** was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless gum in 62% yield (48 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 1.59–1.71 (m, 2 H), 1.84–2.03 (m, 1 H), 2.05–2.10 (m, 1 H), 2.11–2.14 (m, 1 H), 2.20–2.24 (m, 1 H), 2.29 (s, 3 H), 2.40 (s, 3 H), *2.43 (s, 3 H)*, 2.45 (s, 3 H), *3.08–3.25 (m, 2 H)*, *3.31–3.39 (m, 1 H)*, 3.79–3.85 (dd, *J* = 16.7, 6.2 Hz, 1 H), 3.94–3.99 (dd, *J* = 16.7, 6.2 Hz, 1 H), 4.76–4.86 (m, 1 H), 5.07–5.11 (d, *J* = 9.9 Hz, 1 H), 5.16–5.22 (d, *J* = 17.1 Hz, 1 H), *5.40–5.44 (m, 1 H)*, 5.70–5.75 (m, 1 H), 5.75–5.85 (m, 1 H), 6.08–6.13 (d, *J* = 15.9 Hz, 1 H), *6.21–6.26 (m, 2 H)*, 6.95–7.00 (d, *J* = 15.9 Hz, 1 H), *7.08–7.14 (d, J = 15.9* Hz, *1 H)*, 7.12–7.27 (m, 4 H), 7.67–7.83 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 21.3 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.7 (CH_2), 27.67 (CH_2), 27.75 (CH_3), *28.4 (CH_3)*, *45.6 (CH_2)*, 47.5 (CH_2), 56.7 (CH), *59.6 (CH)*, *117.0 (CH_2)*, 118.0 (CH_2), 126.3 (CH), 126.6 (2× CH), *126.7 (2× CH)*, 127.4 (2× CH), *127.5 (2× CH)*, 129.2 (2× CH), *129.7 (2× CH)*, 130.0 (2× CH), 134.8 (CH), 136.5 (Cq), 137.1 (CH), 139.5 (Cq), 140.9 (Cq), 142.6 (Cq), 144.6 (CH), 144.7 (Cq), 198.7 (Cq) ppm. IR: $\tilde{\nu}$ = 3405, 2891, 1726, 1672, 1366, 1245, 1150, 1089, 1012, 815, 723, 650 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{33}N_2O_4S_2$ $[M + H]^+$ 513.1882; found 513.1893.

Compound 9d: Prepared following the typical Mitsunobu procedure from **7d** and allylic alcohol. Corresponding product **9d** was obtained (petroleum ether/ethyl acetate, 80:20) as a pasty white solid in 73% yield (54 mg), m.p. 62–63 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 4/*diastereoisomer B 1* δ = 1.56–1.74 (m, 2 H), 1.95–2.03 (m, 2 H), 2.07–2.14 (m, 1 H), 2.17–2.29 (m, 1 H), 2.41 (s, 3 H), *2.44 (s, 3 H)*, 2.46 (s, 3 H), *3.10–3.17 (m, 1 H)*, *3.26–3.35 (m, 1 H)*, *3.46–3.54 (m, 1 H)*, 3.77–3.83 (dd, *J* = 16.4, 6.1 Hz, 1 H), 3.90–3.96 (dd, *J* = 16.4, 6.1 Hz, 1 H), *4.34–4.46 (m, 1 H)*, 4.73–4.87 (m, 1 H), 5.07–5.14 (m, 1 H), 5.14–5.33 (m, 2 H), 5.62–5.66 (m, 1 H), 5.71–5.83 (m, 1 H), *6.50–6.54 (d, J = 16.5* Hz, *1 H)*, 6.83–6.86 (d, *J* = 16.5 Hz, 1 H), 7.23–7.35 (m, 4 H), 7.77–7.90 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 4/*diastereoisomer B 1* δ = 21.1 (CH_2), *21.48 (CH_3)*, 21.53 (CH_3), 21.6 (CH_3), 22.9 (CH_2), *25.1 (CH_2)*, *27.2 (CH_2)*, 27.4 (CH_2), 47.6 (CH_2), *47.7 (CH_2)*, *56.2 (CH)*, 56.5 (CH), *94.1 (CH)*, 95.6 (CH), 118.1 (CH_2), *118.2 (CH_2)*, 118.3 (CN), 126.6 (2× CH), 127.4 (2× CH), 129.2 (2× CH), 130.0 (2× CH), *134.56 (CH)*, 134.64 (CH), 137.5 (CH), *138.0 (CH)*, 138.5 (Cq), 139.5 (Cq), 140.9 (Cq), 142.8 (Cq), 144.8 (Cq), *150.1 (CH)*, 151.7 (CH) ppm. IR: $\tilde{\nu}$ = 3480, 2953, 2292, 1761, 1374, 1198, 1153, 1094, 815, 754, 658 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{33}N_4O_3S_2$ $[M + NH_4]^+$ 513.1994; found 513.2011.

Compound 9e: Prepared following the typical Mitsunobu procedure from **7e** and allylic alcohol. Corresponding product **9e** was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless gum in 30% yield (28 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 1.49–1.73 (m, 2 H), 180–1.97 (m, 3 H), 2.11–2.23 (m, 1 H), 2.31 (s, 3 H), *2.37 (s, 3 H)*, 2.39 (s, 3 H), *2.90–2.97 (m, 1 H)*, *3.03–3.12 (m, 1 H)*, 3.67–3.73 (dd, *J* = 16.9, 6.2 Hz, 1 H), 3.82–3.87 (dd, *J* = 16.9, 5.6 Hz, 1 H), *4.18–4.30 (m, 1 H)*, 4.66–4.77 (m, 1 H), 5.00–5.04 (m, 1 H), 5.09–5.15 (m, 1 H), *5.40–5.45 (m, 1 H)*, 5.60–5.65 (m, 1 H), 5.65–5.78 (m, 1 H), 6.16–6.21 (d, *J* = 15.0 Hz, 1 H), 7.00–7.05 (d, *J* = 15.0 Hz, 1 H), 7.19–7.29 (m, 4 H), 7.42–7.51 (m, 2 H), 7.51–7.59 (m, 1 H), 7.67–7.75 (m, 2 H), 7.76–7.86 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 6/*diastereoisomer B 1* δ = 21.1 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.7 (CH_2), 27.4 (CH_2), *29.7 (CH_2)*, *47.49 (CH_2)*, 47.53 (CH_2), 56.7 (CH), 118.0 (CH_2), 126.6 (2× CH), 126.8 (CH), 127.3 (2× CH), 127.6 (2× CH), 129.2 (2× CH), 129.3 (2× CH), 130.0 (2× CH), 133.4 (CH), 134.7 (CH), 136.4 (Cq), 137.6 (Cq), 138.8 (CH), 140.6 (Cq), 140.9 (Cq), 142.7 (Cq), 143.4 (CH), 144.8 (Cq) ppm. IR: $\tilde{\nu}$ = 3578, 2981, 2254, 1727, 1441, 1380, 1209, 1039, 917, 750 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{35}N_2O_5S_3$ $[M + H]^+$ 611.1708; found 611.1708.

Compound 9f: Prepared following the typical Mitsunobu procedure from **7f** and allylic alcohol. Corresponding product **9f** was obtained (petroleum ether/ethyl acetate, 80:20) as a colorless gum in 62% yield (51 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 1.58–1.67 (m, 2 H), 1.90–2.02 (m, 1 H), 2.14–2.24 (m, 2 H), 2.28–2.33 (m, 1 H), 2.40 (s, 3 H), 2.46 (s, 3 H), 3.83–3.88 (dd, *J* = 16.7, 6.2 Hz, 1 H), 3.95–4.01 (dd, *J* = 16.7, 6.2 Hz, 1 H), *4.09–4.20 (dd, J = 16.7, 6.2* Hz, *1 H)*, *4.62–7.71 (m, 1 H)*, 4.73–4.83 (m, 1 H), 5.06–5.14 (m, 1 H), 5.17–5.26 (m, 1 H), 5.34–5.39 (m, 1 H), *5.47–5.51 (m, 1 H)*, 5.76–5.92 (m, 1 H), 6.48–6.53 (d, *J* = 16.1 Hz, 1 H), 6.60–6.65 (d, *J* = 16.1 Hz, 1 H), *6.74–6.79 (d, J = 16.1* Hz, *1 H)*, 7.22–7.42 (m, 9 H), 7.79–7.93 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 21.51 (CH_2), 21.53 (CH_3), 21.6 (CH_3), 24.0 (CH_2), 28.0 (CH_2), 47.1 (CH_2), *53.0 (CH_2)*, *55.3 (CH)*, 56.8 (CH), 117.7 (CH_2), *117.8 (CH_2)*, *126.2 (2× CH)*, 126.4 (2× CH), *126.6 (2× CH)*, 126.7 (2× CH), *127.49 (2× CH)*, 127.55 (2× CH), 127.6 (CH), 127.7 (CH), 128.4 (CH), 128.6 (2× CH), 129.1 (2× CH), *129.2 (2× CH)*, *129.7 (2× CH)*, 129.9 (2× CH), 130.7 (CH), *130.9 (CH)*, 135.2 (CH), 136.7 (Cq), 137.1 (Cq), 141.0 (Cq), 141.1 (Cq), 142.5 (Cq), 144.4 (Cq) ppm. IR: $\tilde{\nu}$ = 2934, 1732, 1597, 1493, 1448, 1316, 1248, 1153, 1102, 1069, 1015, 962, 910, 812, 729,

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691 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{35}N_2O_3S_2$ $[M + H]^+$ 547.2089; found 547.2066.

Compound 9g: Prepared following the typical Mitsunobu procedure from **7a** and 2-methylprop-2-en-1-ol. Corresponding product **9g** was obtained (dichloromethane 100%) as a colorless gum in 50% yield (41 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 8/*diastereoisomer B 1* δ = 1.60–1.68 (m, 2 H), 1.73 (s, 3 H), 1.89–1.99 (m, 1 H), 2.00–2.09 (m, 1 H), 2.11–2.22 (m, 1 H), 2.25–2.35 (m, 1 H), 2.40 (s, 3 H), *2.46 (s, 3 H)*, 2.48 (s, 3 H), 3.50–3.56 (d, *J* = 16.8 Hz, 1 H), 3.76 (s, 3 H), *3.78 (s, 3 H)*, 3.85–3.90 (d, *J* = 16.8 Hz, 1 H), *4.83–4.86 (m, 1 H)*, 4.87–4.97 (m, 2 H), 5.07–5.11 (m, 1 H), 5.37–5.41 (m, 1 H), 5.80–5.85 (d, *J* = 15.9 Hz, 1 H), *6.03–6.09 (m, 1 H)*, 7.02–7.08 (d, *J* = 15.9 Hz, 1 H), 7.22–7.38 (m, 4 H), 7.78–7.92 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 8/*diastereoisomer B 1* δ (ppm) 20.2 (CH_3), 21.4 (CH_2), 21.5 (CH_3), 21.6 (CH_3), *23.5 (CH_2)*, 23.7 (CH_2), 27.6 (CH_2), *28.2 (CH_2)*, 50.5 (CH_2), 51.7 (CH_3), *56.4 (CH)*, 57.6 (CH), 113.7 (CH_2), 117.1 (CH), 126.6 (2× CH), 127.2 (2× CH), *127.7 (2× CH)*, 129.2 (2× CH), *129.9 (2× CH)*, 130.0 (2× CH), 135.6 (CH), 136.4 (Cq), 139.5 (Cq), 141.0 (Cq), 141.6 (Cq), 142.6 (Cq), 144.7 (Cq), 146.2 (CH), 167.6 (Cq) ppm. IR: ṽ = 2947, 1713, 1631, 1597, 1435, 1364, 1304, 1250, 1219, 1154, 1104, 1089, 1015, 905, 814, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{38}N_3O_5S_2$ $[M + NH_4]^+$ 560.2253; found 560.2280.

Compound 9i: Prepared following the typical Mitsunobu procedure from **7a** and but-3-en-1-ol. Corresponding product **9i** was obtained (petroleum ether/ethyl acetate, 75:25) as a colorless oil in 71% yield (58 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 12/*diastereoisomer B 1* δ = 1.54–1.69 (m, 2 H), 1.93–2.02 (m, 1 H), 2.06–2.18 (m, 2 H), 2.25–2.36 (m, 1 H), 2.36–2.53 (m, 2 H), 2.39 (s, 3 H), 2.45 (s, 3 H), 3.05–3.16 (m, 1 H), 3.22–3.34 (m, 1 H), 3.74 (s, 3 H), *3.76 (s, 3 H)*, 4.62–4.71 (m, 1 H), 5.00–5.02 (m, 1 H), 5.04–5.07 (m, 1 H), 5.38–5.42 (m, 1 H), 5.63–5.77 (m, 1 H), 5.79–5.85 (d, *J* = 15.8 Hz, 1 H), *6.07–6.11 (m, 1 H)*, 6.95–7.01 (d, *J* = 15.8 Hz, 1 H), 7.14–7.27 (m, 4 H), 7.70–7.83 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 12/*diastereoisomer B 1* δ = 21.3 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 23.6 (CH_2), 27.6 (CH_2), *35.7 (CH_2)*, 35.9 (CH_2), 44.7 (CH_2), 51.7 (CH_3), *56.1 (CH)*, 56.6 (CH), 117.1 (CH_2), 117.2 (CH), 126.7 (2× CH), 127.3 (2× CH), 129.2 (2× CH), 130.0 (2× CH), 134.7 (CH), 136.1 (CH), 136.3 (Cq), 139.4 (Cq), 141.1 (Cq), 142.6 (Cq), 144.7 (Cq), 146.1 (CH), 167.5 (Cq) ppm. IR: ṽ = 2947, 1717, 1631, 1435, 1303, 1249, 1153, 1102, 1088, 1085, 1015, 911, 813, 728, 655 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{35}N_2O_5S_2$ $[M + H]^+$ 543.1987; found 543.1996.

Compound 10: Prepared following the typical Mitsunobu procedure from **8** (33 mg, 69.5 μmol) and allylic alcohol (9.45 μL, 0.139 μmol). Corresponding product **10** was obtained by preparative chromatography (dichloromethane/ethyl acetate, 80:20) as a colorless oil in 70% yield (25 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 18/*diastereoisomer B 1* δ = 1.89–2.04 (m, 1 H), 2.23–2.46 (m, 3 H), 2.31 (s, 3 H), 2.36 (s, 3 H), 3.68 (s, 3 H), 3.69–3.76 (m, 2 H), 4.96–5.02 (m, 1 H), 5.02–5.10 (m, 1 H), 5.10–5.19 (m, 1 H), 5.51–5.55 (m, 1 H), 5.62–5.75 (m, 1 H), 5.72–5.78 (d, *J* = 15.8 Hz, 1 H), *5.98–6.02 (m, 1 H)*, 7.14–7.25 (m, 4 H), 7.26–7.31 (d, *J* = 15.8 Hz, 1 H), 7.67–7.74 (m, 2 H), 7.76–7.83 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.5 (CH_3), 21.6 (CH_3), 27.9 (CH_2), 29.5 (CH_2), 47.0 (CH_2), 51.7 (CH), 64.7 (CH), 117.7 (CH_2), 120.9 (CH), 126.7 (2× CH), 127.4 (2× CH), 129.2 (2× CH), 129.9 (2× CH), 134.8 (CH), 135.6 (CH), 136.2 (Cq), 139.2 (CH), 141.0 (Cq), 142.6 (Cq), 144.6 (CH), 144.7 (Cq), 167.1 (Cq) ppm. IR: ṽ = 2913, 1726, 1601, 1443, 1310, 1195, 1090, 820, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{34}N_3O_5S_2$ $[M + NH_4]^+$ 532.1940; found 532.1931.

Typical Diels–Alder Reaction Procedure (for 11a–12): The Mitsunobu product was dissolved in toluene at room temperature under an argon atmosphere. The resulting mixture was then stirred at 110 °C overnight. After cooling to room temperature, the solvent was removed under reduced pressure and the resulting residue was purified by column chromatography on silica gel.

Compound 11a: Following the procedure for the intramolecular Diels–Alder reaction starting from **9a** (188 mg, 0.356 mmol), **11a** was obtained (petroleum ether/ethyl acetate, 80:20) as a colorless oil in 99% yield (187 mg). $[\alpha]_D^{20}$ = +146.0 (*c* = 0.98, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.66–1.78 (m, 3 H), 1.99–2.09 (m, 2 H), 2.14–2.26 (m, 2 H), 2.28–2.34 (m, 1 H), 2.38–2.51 (m, 2 H), 2.40 (s, 3 H), 2.43 (s, 3 H), 3.12–3.17 (m, 1 H), 3.19–3.23 (m, 1 H), 3.27–3.32 (m, 1 H), 3.69 (s, 3 H), 4.28–4.35 (m, 1 H), 5.37–5.42 (m, 1 H), 7.25–7.32 (m, 4 H), 7.79–7.83 (m, 2 H), 7.90–7.94 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.4 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 26.4 (CH_2), 26.9 (CH_2), 27.3 (CH_2), 38.2 (CH), 41.5 (CH), 45.5 (CH), 52.1 (CH_3), 53.0 (CH_2), 59.8 (CH), 117.9 (CH) 126.6 (2× CH), 127.5 (2× CH), 129.2 (2× CH), 129.8 (2× CH), 135.8 (Cq), 141.0 (Cq), 141.1 (Cq), 142.5 (Cq), 144.5 (Cq), 174.8 (Cq) ppm. IR: ṽ = 2947, 1714, 1631, 1596, 1435, 1350, 1304, 1250, 1154, 1107, 1089, 1015, 814, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{33}N_2O_5S_2$ $[M + H]^+$ 529.1831; found 529.1842.

Compound 11b: Following the procedure for the intramolecular Diels–Alder reaction starting from **9b** (75.0 mg, 0.130 mmol), **11b** was obtained (petroleum ether/ethyl acetate, 75:25) as a colorless oil in 70% yield (53 mg). $[\alpha]_D^{20}$ = +96.5 (*c* = 0.77, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.17–1.31 (m, 2 H), 1.44 (s, 9 H), 1.59–1.77 (m, 3 H), 1.95–2.02 (m, 1 H), 2.19–2.26 (m, 3 H), 2.38–2.47 (m, 1 H), 2.40 (s, 3 H), 2.43 (s, 3 H), 3.10–3.23 (m, 3 H), 4.27–4.37 (m, 1 H), 5.33–5.40 (m, 1 H), 7.20–7.35 (m, 4 H), 7.75–7.85 (m, 2 H), 7.87–7.96 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.4 (CH_2), 21.50 (CH_3), 21.54 (CH_3), 26.4 (CH_2), 26.8 (CH_2), 27.3 (CH_2), 28.1 (3× CH_3), 38.2 (CH), 42.4 (CH), 45.5 (CH), 53.1 (CH_2), 59.8 (CH), 80.7 (Cq), 118.5 (CH), 126.6 (2× CH), 127.5 (2× CH), 129.1 (2× CH), 129.7 (2× CH), 135.8 (Cq), 140.6 (Cq), 141.2 (Cq), 142.4 (Cq), 144.5 (Cq), 173.8 (Cq) ppm. IR: ṽ = 2932, 1723, 1368, 1303, 1249, 1152, 1028, 1015, 813, 753, 657 cm^{-1}. HRMS (ESI): calcd. for $C_{30}H_{39}N_2O_5S_2$ $[M + H]^+$ 571.2300; found 571.2330.

Compound 11c: Following the procedure for the intramolecular Diels–Alder reaction starting from **9c** (23.0 mg, 37.7 μmol), **11c** was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless oil in 59% yield (14.0 mg). $[\alpha]_D^{20}$ = +36.7 (*c* = 0.54, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.51–1.61 (m, 1 H), 1.70–1.87 (m, 3 H), 1.88–1.98 (m, 2 H), 2.17–2.27 (m, 2 H), 2.32 (s, 3 H), 2.37–2.45 (m, 2 H), 2.40 (s, 3 H), 2.43 (s, 3 H), 2.68–2.73 (dd, *J* = 17.1, 4.8 Hz, 1 H), 3.09–3.16 (m, 1 H), 3.32–3.39 (m, 1 H), 4.46–4.54 (m, 1 H), 6.58–6.62 (m, 1 H), 7.23–7.34 (m, 4 H), 7.78–7.84 (m, 2 H), 7.85–7.90 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 18.3 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 25.8 (CH_3), 27.1 (CH_2), 30.1 (CH_2), 33.4 (CH_2), 36.0 (CH), 49.5 (CH), 52.8 (CH_2), 58.5 (CH), 71.8 (CH), 126.6 (2× CH), 127.5 (2× CH), 129.2 (2× CH), 129.9 (2× CH), 135.2 (Cq), 137.4 (Cq), 142.6 (Cq), 144.7 (Cq), 145.0 (Cq), 145.1 (CH), 199.2 (Cq) ppm. IR: ṽ = 2901, 1669, 1244, 1151, 1082, 1025, 814, 733, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{33}N_2O_4S_2$ $[M + H]^+$ 513.1882; found 513.1918.

Compound 11d: Following the procedure for the intramolecular Diels–Alder reaction starting from **9d** (26.0 mg, 52.4 μmol), **11d** was obtained (petroleum ether/ethyl acetate, 75:25) as a yellow oil

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in 54% yield (14 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 1.73–1.83 (m, 2 H), 1.91–1.99 (m, 1 H), 2.07–2.12 (m, 1 H), 2.14–2.20 (m, 1 H), 2.21–2.29 (m, 3 H), 2.37–2.46 (m, 1 H), 2.41 (s, 3 H), 2.44 (s, 3 H), 2.52–2.59 (m, 1 H), 3.13–3.20 (m, 1 H), 3.28–3.32 (m, 1 H), 3.47–3.52 (m, 1 H), *4.23–4.31 (m, 1 H)*, 4.36–4.43 (m, 1 H), *5.24–5.27 (m, 1 H)*, 5.27–5.31 (m, 1 H), 7.22–7.36 (m, 4 H), 7.74–7.96 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 5/*diastereoisomer B 1* δ = 20.1 (CH_2), 21.55 (CH_3), 21.60 (CH_3), 26.8 (CH_2), 27.3 (CH_2), 27.7 (CH), *28.1 (CH)*, 28.7 (CH_2), *28.9 (CH_2)*, 37.9 (CH), *39.3 (CH)*, *44.8 (CH)*, 45.0 (CH), *52.3 (CH_2)*, 52.4 (CH_2), 59.4 (CH), *59.5 (CH)*, *114.4 (CH)*, 114.5 (CH), 121.5 (Cq), 126.6 (2× CH), 127.4 (2× CH), 129.3 (2× CH), 129.9 (2× CH), 135.6 (Cq), 140.9 (Cq), 142.7 (Cq), 143.4 (Cq), 144.9 (Cq) ppm. IR: $\tilde{\nu}$ = 2945, 1597, 1302, 1248, 1152, 1038, 1014, 911, 813, 728, 657 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{33}N_4O_3S_2$ [M + NH_4]$^+$ 513.1994; found 513.1982.

Compound 11e: Following the procedure for the intramolecular Diels–Alder reaction starting from **9e** (23.0 mg, 37.7 μmol), **11e** was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless oil in 78% yield (18 mg). $[\alpha]_D^{20}$ = +144.7 (*c* = 0.93, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.96–1.09 (m, 1 H), 1.69–1.80 (m, 2 H), 1.81–1.91 (m, 2 H), 1.96–2.05 (m, 1 H), 2.23–2.31 (m, 2 H), 2.38–2.52 (m, 2 H), 2.40 (s, 3 H), 2.46 (s, 3 H), 2.99–3.04 (m, 1 H), 3.12–3.20 (m, 1 H), 3.85–3.92 (m, 1 H), 4.28–4.38 (m, 1 H), 5.49–5.53 (m, 1 H), 7.22–7.34 (m, 4 H), 7.51–7.60 (m, 2 H), 7.62–7.70 (m, 1 H), 7.73–7.80 (m, 2 H), 7.83–7.93 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.2 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 24.6 (CH_2), 27.1 (CH_2), 27.2 (CH_2), 36.2 (CH), 45.3 (CH), 52.5 (CH_2), 59.3 (CH), 62.0 (CH), 112.3 (CH), 126.5 (2× CH), 127.4 (2× CH), 129.0 (2× CH), 129.1 (2× CH), 129.2 (2× CH), 129.8 (2× CH), 133.8 (CH), 135.5 (Cq), 137.5 (Cq), 141.0 (Cq), 142.6 (Cq), 144.7 (Cq), 146.9 (Cq) ppm. IR: $\tilde{\nu}$ = 2927, 1596, 1445, 1299, 1248, 1147, 1105, 1079, 1018, 1015, 998, 938, 807, 757, 723, 698, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{35}N_2O_5S_3$ [M + H]$^+$ 611.1708; found 611.1704.

Compound 11f: Following the general procedure for the intramolecular Diels–Alder reaction starting from **9f** (37.0 mg, 67.7 μmol), **11f** was obtained (dichloromethane 100%) as a colorless oil in 54% yield (20 mg). $[\alpha]_D^{20}$ = +55.9 (*c* = 1.08, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.31–1.38 (m, 1 H), 1.83–1.90 (m, 2 H), 2.02–2.12 (m, 2 H), 2.12–2.18 (m, 1 H), 2.26–2.34 (m, 2 H), 2.42 (s, 3 H), 2.43 (s, 3 H), 2.45–2.48 (m, 1 H), 2.50–2.60 (m, 1 H), 3.00–3.07 (m, 1 H), 3.12–3.20 (m, 1 H), 3.67–3.74 (m, 1 H), 4.29–4.41 (m, 1 H), 5.36–5.40 (m, 1 H), 7.17–7.22 (m, 2 H), 7.23–7.26 (m, 1 H), 7.27–7.33 (m, 6 H), 7.81–7.84 (m, 2 H), 7.93–7.96 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.7 (CH_2), 21.53 (CH_3), 21.54 (CH_3), 27.0 (CH_2), 27.7 (CH_2), 33.1 (CH_2), 36.2 (CH), 41.4 (CH), 45.8 (CH), 53.0 (CH_2), 60.0 (CH), 123.2 (CH), 126.2 (CH), 126.6 (2× CH), 127.5 (2× CH), 127.8 (2× CH), 128.4 (2× CH), 129.2 (2× CH), 129.7 (2× CH), 135.8 (Cq), 138.7 (Cq), 141.2 (Cq), 142.5 (Cq), 144.5 (Cq), 147.0 (Cq) ppm. IR: $\tilde{\nu}$ = 2925, 1597, 1449, 1302, 1247, 1151, 1063, 1015, 813, 757, 701, 654 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{35}N_2O_3S_2$ [M + H]$^+$ 547.2089; found 547.2100.

Compound 11h: Prepared following the typical Mitsunobu procedure from **7a** and propargylic alcohol. Corresponding product **9h**, which was obtained (petroleum ether/ethyl acetate, 70:30) as a colorless oil in 80% yield (63.0 mg), was directly engaged in the intramolecular Diels–Alder reaction because of its low stability. Following the general procedure starting from **9h** (60.0 mg, 0.114 mmol), **11h** was obtained (dichloromethane/ethyl acetate, 20:1) as a colorless oil in 62% yield (37 mg). $[\alpha]_D^{20}$ = +21.5 (*c* = 0.99, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.78–1.90 (m, 1 H), 2.08–2.16 (m, 1 H), 2.39–2.49 (m, 1 H), 2.41 (s, 3 H), 2.45 (s, 3 H), 2.63–2.72 (m, 1 H), 2.74–2.81 (m, 1 H), 2.85–2.93 (dd, *J* = 17.7, 7.1 Hz, 1 H), 3.90 (s, 3 H), 4.30–4.35 (m, 1 H), 4.74–4.80 (m, 2 H), 7.25–7.30 (m, 2 H), 7.32–7.39 (m, 2 H), 7.64–7.67 (m, 1 H), 7.74–7.77 (m, 1 H), 7.87–7.94 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.0 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 25.3 (CH_2), 29.6 (CH_2), 52.2 (CH_3), 54.8 (CH_2), 63.0 (CH), 120.8 (CH), 126.7 (2× CH), 128.0 (2× CH), 128.7 (CH), 129.2 (2× CH), 129.9 (2× CH), 130.6 (Cq), 133.9 (Cq), 134.0 (Cq), 134.7 (Cq), 141.0 (Cq), 142.4 (Cq), 142.7 (Cq), 145.1 (Cq), 166.2 (Cq) ppm. IR: $\tilde{\nu}$ = 2925, 1717, 1436, 1302, 1216, 1153, 1063, 1015, 814, 769, 657 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{29}N_2O_5S_2$ [M + H]$^+$ 525.1518; found 525.1527.

Compound 11i: Following the procedure for the intramolecular Diels–Alder reaction starting from **9i** (46.0 mg, 85.0 μmol), **11i** was obtained (dichloromethane/ethyl acetate, 90:10) as a colorless oil in 62% yield (29 mg). $[\alpha]_D^{20}$ = +69.0 (*c* = 0.52, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.33–1.38 (m, 1 H), 1.42–1.67 (m, 6 H), 1.73–1.82 (m, 1 H), 1.95–2.01 (m, 1 H), 2.08–2.13 (m, 1 H), 2.14–2.21 (m, 1 H), 2.21–2.29 (m, 1 H), 2.39 (s, 3 H), 2.42 (s, 3 H), 2.81–2.89 (m, 1 H), 3.10–3.15 (m, 1 H), 3.69 (s, 3 H), 3.78–3.83 (m, 1 H), 4.46–4.53 (m, 1 H), 5.41–5.44 (m, 1 H), 7.19–7.32 (m, 4 H), 7.71–7.78 (m, 2 H), 7.81–7.87 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.7 (CH_2), 21.2 (CH_2), 21.5 (CH_3), 21.6 (CH_3), 27.4 (CH_2), 30.0 (CH_2), 30.2 (CH), 30.9 (CH_2), 40.2 (CH), 41.8 (CH_2), 42.4 (CH), 52.0 (CH_3), 52.1 (CH), 118.2 (CH), 126.6 (2× CH), 127.3 (2× CH), 129.1 (2× CH), 129.8 (2× CH), 136.3 (Cq), 141.1 (Cq), 141.9 (Cq), 142.5 (Cq), 144.3 (Cq), 174.9 (Cq) ppm. IR: $\tilde{\nu}$ = 2948, 1730, 1597, 1436, 1315, 1303, 1251, 1197, 1152, 1102, 1088, 1071, 1016, 959, 913, 813, 705, 702, 655 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{35}N_2O_5S_2$ [M + H]$^+$ 543.1987; found 543.1981.

Compound 12: Following the procedure for the intramolecular Diels–Alder reaction starting from **10** (18.0 mg, 35.0 μmol), **12** was obtained (dichloromethane/ethyl acetate, 98:2) as a colorless oil in 99% yield (18 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 7/*diastereoisomer B 1* δ = 1.72–1.82 (m, 2 H), 2.01–2.09 (m, 1 H), 2.21–2.37 (m, 3 H), 2.40 (s, 3 H), 2.43 (s, 3 H), 2.66–2.72 (m, 1 H), 2.74–2.80 (m, 1 H), 2.81–2.86 (m, 1 H), 3.01–3.07 (m, 1 H), 3.59–3.64 (m, 1 H), 3.68 (s, 3 H), *4.49–4.57 (m, 1 H)*, 4.69–4.74 (m, 1 H), *5.40–5.43 (m, 1 H)*, 5.72–5.75 (m, 1 H), 7.22–7.32 (m, 4 H), 7.74–7.76 (m, 2 H), 7.87–7.89 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 7/*diastereoisomer B 1* δ = 21.5 (CH_3), 21.6 (CH_3), 24.0 (CH_2), *24.8 (CH_2)*, 31.9 (CH_2), 32.1 (CH_2), 33.6 (CH), 38.7 (CH), *41.4 (CH)*, 46.4 (CH), 51.5 (CH_2), 52.1 (CH_3), 65.6 (CH), 116.3 (CH), 126.6 (2× CH), 127.3 (2× CH), 129.1 (2× CH), 129.8 (2× CH), 136.0 (Cq), 141.1 (Cq), 142.2 (Cq), 142.5 (Cq), 144.4 (Cq), 174.8 (Cq) ppm. IR: $\tilde{\nu}$ = 2953, 1732, 1597, 1436, 1315, 1250, 1152, 1053, 1015, 911, 814, 728, 656 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{34}N_3O_5S_2$ [M + NH_4]$^+$ 532.1940; found 532.1932.

Compound 13: A solution of **7a** (235 mg, 0.481 mmol) in dichloromethane (3.4 mL) was added dropwise at 0 °C to a solution of acryloyl chloride (47.0 μL, 0.577 mmol) in dichloromethane (2 mL). Triethylamine (78.3 μL, 0.577 mmol) was then added and the reaction mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 70:30) affording a colorless oil in 77% yield (201 mg), m.p. 167–168 °C. $[\alpha]_D^{20}$ = +258.8 (*c* = 0.84, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.32–1.46 (m, 1 H), 1.76–

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1.89 (m, 3 H), 2.15–2.25 (m, 1 H), 2.26–2.33 (m, 2 H), 2.39–2.43 (m, 1 H), 2.41 (s, 6 H), 2.44–2.47 (m, 1 H), 2.77–2.88 (m, 1 H), 3.25–3.36 (m, 1 H), 3.66 (s, 3 H), 4.62–4.73 (m, 1 H), 5.41–5.45 (m, 1 H), 7.25–7.34 (m, 4 H), 7.87–7.95 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 19.8 (CH_2), 21.5 (CH_3), 21.7 (CH_3), 23.6 (CH_2), 23.7 (CH_2), 26.2 (CH_2), 40.0 (CH), 41.4 (CH), 41.7 (CH), 52.1 (CH_3), 59.1 (CH), 119.3 (CH), 126.7 (2× CH), 128.3 (2× CH), 129.3 (2× CH), 129.6 (2× CH), 134.2 (Cq), 140.2 (Cq), 141.2 (Cq), 143.1 (Cq), 145.8 (Cq), 172.1 (Cq), 174.2 (Cq) ppm. IR: $\tilde{\nu}$ = 2952, 1750, 1733, 1596, 1323, 1263, 1156, 1101, 1091, 1067, 1016, 658 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_6S_2$ $[M + H]^+$ 543.1624; found 543.1620.

Compound 14: Prepared following the typical amination procedure from benzocyclobutene. Corresponding amination product was obtained (dichloromethane/ethyl acetate, 20:1) as a white solid in 82% yield and 16:1 *dr* (^{1}H NMR evaluation), m.p. 158–159 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 16/*diastereoisomer B 1* δ = 2.34 (s, 3 H), 2.38 (s, 3 H), 2.83–2.88 (dd, *J* = 14.7, 2.6 Hz, 1 H), *3.04–3.11 (dd, J = 14.7, 2.6* Hz, *1 H)*, 3.29–3.34 (dd, *J* = 14.6, 5.1 Hz, 1 H), *3.51–3.56 (dd, J = 14.6, 5.1* Hz, *1 H)*, 4.71–4.79 (m, 1 H), 6.20–6.23 (d, *J* = 9.4 Hz, 1 H), 6.51–6.54 (d, *J* = 9.4 Hz, 1 H), 6.91–6.98 (dd, *J* = 12.4, 7.1 Hz, 1 H), 7.10–7.20 (m, 4 H), 7.25–7.28 (d, *J* = 8.4 Hz, 1 H), 7.74–7.83 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 16/*diastereoisomer B 1* δ = 21.56 (CH_3), 21.64 (CH_3), 39.7 (CH_2), 52.5 (CH), 123.0 (CH), 123.2 (CH), 126.8 (2× CH), 127.7 (CH), 127.9 (2× CH), 129.2 (2× CH), 129.8 (CH), 130.0 (2× CH), 135.6 (Cq), 140.4 (Cq), 142.2 (Cq), 142.9 (Cq), 144.0 (Cq), 145.0 (Cq) ppm. IR: $\tilde{\nu}$ = 3201, 1595, 1423, 1313, 1303, 1249, 1205, 1184, 1156, 1105, 1090, 1015, 997, 949, 927, 881, 813, 752, 681 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{21}N_2O_3S_2$ $[M - H]^-$ 425.0994; found 425.1010.

Compound 15a: Compound **14** (60.0 mg, 0.141 mmol) was added at room temperature to a solution of but-3-enoyl chloride (29.3 mg, 0.280 mmol) in dichloromethane (1.5 mL). Triethylamine (22.7 µL, 0.168 mmol) was then added and the reaction mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the resulting residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 75:25) affording a pale yellow oil in 47% yield (33 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 17/*diastereoisomer B 1* δ = 2.39 (s, 3 H), 2.42 (s, 3 H), 3.26–3.31 (m, 2 H), 3.58–3.66 (dd, *J* = 14.4, 3.2 Hz, 1 H), *3.51–3.55 (dd, J = 13.9, 5.4* Hz, *1 H)*, 3.69–3.76 (dd, *J* = 13.9, 5.4 Hz, 1 H), 4.86–4.96 (m, 1 H), 5.03–5.09 (m, 1 H), 5.69–5.81 (m, 1 H), 5.81–5.86 (m, 1 H), *6.01–6.09 (m, 1 H)* , 6.96–7.01 (m, 1 H), 7.06–7.12 (m, 1 H), 7.14–7.21 (m, 1 H), 7.22–7.34 (m, 5 H), 7.82–7.94 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 17/*diastereoisomer B 1* δ = 21.8 (CH_3), 21.9 (CH_3), 39.7 (CH_2), *39.9 (CH_2)*, 42.6 (CH_2), *42.8 (CH_2)*, 56.3 (CH), 119.1 (CH_2), 122.7 (CH), 123.4 (CH), 126.9 (2× CH), 127.8 (CH), 128.1 (2× CH), 129.3 (CH), 129.6 (2× CH), 130.0 (2× CH), 130.2 (CH), 135.6 (Cq), 140.4 (Cq), 141.0 (Cq), 143.5 (Cq), 145.1 (Cq), 145.9 (Cq), 172.1 (Cq) ppm. IR: $\tilde{\nu}$ = 2932, 1708, 1596, 1400, 1324, 1267, 1211, 1155, 1107, 1088, 1070, 1015, 927, 814, 754, 685, 658 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{27}N_2O_4S_2$ $[M + H]^+$ 495.1412; found 495.1391.

Compound 15b: Prepared following the typical Mitsunobu procedure from **14** (304 mg, 0.713 mmol) and 3-buten-1-ol (113 µL, 1.32 mmol). Corresponding product **15b** was obtained (dichloromethane) as a yellow oil in 82% yield (281 mg). $[\alpha]_D^{20}$ = +88.4 (*c* = 0.70, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.26–2.35 (m, 2 H), 2.38 (s, 3 H), 2.44 (s, 3 H), 3.07–3.27 (m, 2 H), 3.23–3.31 (dd, *J* = 15.2, 2.5 Hz, 1 H), 3.52–3.60 (dd, *J* = 15.0, 4.9 Hz, 1 H), 4.85–4.96 (m, 2 H), 5.37–5.43 (m, 1 H), 5.50–5.64 (ddt, *J* = 17.0, 10.5, 6.6 Hz, 1 H), 6.50–6.52 (d, *J* = 7.4 Hz, 1 H), 7.04–7.13 (m, 2 H), 7.20–7.28 (m, 3 H), 7.30–7.36 (m, 2 H), 7.85–7.92 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.7 (CH_3), 21.8 (CH_3), 35.8 (CH_2), 38.3 (CH_2), 44.6 (CH_2), 57.6 (CH), 117.2 (CH_2), 123.42 (CH), 123.48 (CH), 126.9 (2× CH), 127.6 (CH), 127.7 (2× CH), 129.4 (2× CH), 129.8 (CH), 130.2 (2× CH), 134.9 (CH), 136.1 (Cq), 141.2 (Cq), 142.7 (Cq), 142.9 (Cq), 143.4 (Cq), 144.9 (Cq) ppm. IR: $\tilde{\nu}$ = 2930, 1597, 1456, 1317, 1257, 1207, 1153, 1068, 1015, 961, 914, 855, 813, 747, 704 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{29}N_2O_3S_2$ $[M + H]^+$ 481.1620; found 481.1622.

Compound 15c: Prepared following the typical Mitsunobu procedure from **14** (100 mg, 0.234 mmol) and 3-methylbut-3-en-1-ol (46.5 µL, 0.469 mmol). Corresponding product **15c** was obtained (dichloromethane) as a yellow oil in 70% yield (80 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 10/*diastereoisomer B 1* δ = 1.48 (s, 3 H), 2.18–2.29 (m, 2 H), 2.38 (s, 3 H), 2.44 (s, 3 H), *2.45 (s, 3 H)*, 3.08–3.32 (m, 3 H), 3.51–3.60 (dd, *J* = 15.0, 5.1 Hz, 1 H), 4.42–4.47 (m, 1 H), 4.59–4.64 (m, 1 H), *4.70–4.72 (m, 1 H)*, 5.39–5.44 (m, 1 H), *5.53–5.58 (m, 1 H)*, *6.42–6.45 (d, J = 7.7* Hz, *1 H)*, 6.55–6.58 (d, *J* = 7.7 Hz, 1 H), 7.04–7.14 (m, 2 H), 7.20–7.28 (m, 3 H), 7.30–7.36 (m, 2 H), 7.83–7.93 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 10/*diastereoisomer B 1* δ = 21.75 (CH_3), 21.83 (CH_3), 22.5 (CH_3), *32.2 (CH_2), 32.8 (CH_2)*, 38.4 (CH_2), 39.5 (CH_2), 44.0 (CH_2), 57.6 (CH), 112.2 (CH_2), 123.5 (2× CH), 126.9 (2× CH), 127.6 (CH), 127.7 (2× CH), 129.4 (2× CH), 129.8 (CH), 130.2 (2× CH), 136.3 (Cq), 141.2 (Cq), 142.6 (Cq), 142.8 (Cq), 142.9 (Cq), 143.4 (Cq), 144.9 (Cq) ppm. IR: $\tilde{\nu}$ = 2928, 1597, 1493, 1455, 1374, 1317, 1303, 1259, 1153, 1088, 1064, 1015, 962, 892, 812, 759, 746, 700 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_3S_2$ $[M + H]^+$ 495.1776; found 495.1775.

Compound 15d: Prepared following the typical Mitsunobu procedure from **14** (125 mg, 0.293 mmol) and 4-pentenol (55.8 µL, 0.545 mmol). Corresponding product **15d** was obtained (dichloromethane) as a yellow oil in 72% yield (103 mg). $[\alpha]_D^{20}$ = +83.4 (*c* = 0.74, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.59–1.69 (m, 2 H), 1.82–1.92 (m, 2 H), 2.38 (s, 3 H), 2.44 (s, 3 H), 3.02–3.17 (m, 2 H), 3.20–3.28 (dd, *J* = 15.0, 2.5 Hz, 1 H), 3.51–3.60 (dd, *J* = 15.0, 5.1 Hz, 1 H), 4.80–4.83 (m, 1 H), 4.84–4.88 (m, 1 H), 5.40–5.44 (m, 1 H), 5.48–5.62 (ddt, *J* = 17.6, 9.7, 6.4 Hz, 1 H), 6.48–6.52 (d, *J* = 7.3 Hz, 1 H), 7.03–7.13 (m, 2 H), 7.20–7.28 (m, 3 H), 7.30–7.37 (m, 2 H), 7.83–7.92 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.7 (CH_3), 21.8 (CH_3), 30.3 (CH_2), 31.0 (CH_2), 38.4 (CH_2), 44.8 (CH_2), 57.6 (CH), 115.3 (CH_2), 123.41 (CH), 123.44 (CH), 126.9 (2× CH), 127.6 (CH), 127.7 (2× CH), 129.4 (2× CH), 129.8 (CH), 130.2 (2× CH), 136.2 (Cq), 137.4 (CH), 141.2 (Cq), 142.7 (Cq), 142.8 (Cq), 143.5 (Cq), 144.8 (Cq) ppm. IR: $\tilde{\nu}$ = 2931, 1597, 1457, 1318, 1258, 1153, 1068, 1015, 970, 913, 812, 752, 707 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_3S_2$ $[M + H]^+$ 495.1776; found 495.1770.

Compound 15e: Prepared following the typical Mitsunobu procedure from **14** (217 mg, 0.469 mmol) and (2-vinylphenyl)methanol (126 mg, 0.939 mmol). Corresponding product **15e** was obtained (dichloromethane) as a yellow oil in 79% yield (202 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 13/*diastereoisomer B 1* δ = 2.38 (s, 3 H), *2.44 (s, 3 H)*, 2.46 (s, 3 H), 2.93–3.02 (dd, *J* = 15.0, 2.6 Hz, 1 H), *3.09–3.17 (dd, J = 14.9, 5.3* Hz, *1 H)*, 3.34–3.42 (dd, *J* = 14.9, 5.3 Hz, 1 H), 4.28–4.34 (d, *J* = 16.1 Hz, 1 H), *4.35–4.41 (d, J = 16.1* Hz, *1 H)*, 4.52–4.57 (d, *J* = 16.1 Hz, 1 H), *4.58–4.63 (d, J = 16.1* Hz, *1 H)*, 5.07–5.13 (dd, *J* = 10.9, 1.5 Hz, 1 H),

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5.35–5.44 (dd, *J* = 17.3, 1.5 Hz, 1 H), *5.56–5.60 (m, 1 H)*, 5.60–5.66 (m, 1 H), 6.13–6.18 (d, *J* = 7.5 Hz, 1 H), 6.48–6.59 (dd, *J* = 17.3, 11.0 Hz, 1 H), 6.89–7.0 (m, 2 H), 7.11–7.19 (m, 3 H), 7.21–7.25 (m, 2 H), 7.26–7.31 (m, 1 H), 7.32–7.38 (m, 3 H), 7.87–7.93 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 13/*diastereoisomer B 1* δ = 21.7 (CH_3), 21.8 (CH_3), *37.1 (CH_2)*, 37.8 (CH_2), 45.7 (CH_2), *57.9 (CH)*, 58.4 (CH), 116.8 (CH), 123.3 (CH), 123.5 (CH), 126.1 (CH), 127.0 (2× CH), 127.4 (CH), 127.7 (CH), 127.86 (2× CH), 127.91 (CH), 128.8 (CH), 129.4 (2× CH), 129.7 (CH), 130.3 (2× CH), 133.9 (CH), 134.5 (Cq), 135.7 (Cq), 136.7 (Cq), 141.2 (Cq), 142.86 (Cq), 142.89 (Cq), 142.94 (Cq), 145.0 (Cq) ppm. IR: ṽ = 2925, 1596, 1491, 1455, 1318, 1259, 1207, 1154, 1105, 1099, 1078, 1015, 977, 911, 838, 812, 751, 728 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{31}N_2O_3S_2$ [M + H]$^+$ 543.1776; found 543.1741.

Compound 16b: Following the procedure for the intramolecular Diels–Alder reaction starting from **15b** (85.0 mg, 0.177 mmol) in octane, **16b** was obtained (petroleum ether/ethyl acetate, 75:25) as a pale yellow oil in 90% yield (77 mg) with two diastereoisomers (2:1).

Diastereoisomer A (29%): $[\alpha]_D^{20}$ = –3.9 (*c* = 0.62, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.66–1.81 (m, 2 H), 1.99–2.12 (m, 2 H), 2.37 (s, 3 H), 2.39 (s, 3 H), 2.56–2.67 (m, 1 H), 2.69–2.80 (m, 1 H), 2.82–2.90 (m, 1 H), 2.91–3.00 (m, 1 H), 3.54–3.63 (m, 1 H), 5.36–5.39 (d, *J* = 8.1 Hz, 1 H), 7.02–7.07 (m, 1 H), 7.13–7.18 (m, 2 H), 7.21–7.30 (m, 4 H), 7.69–7.72 (m, 1 H), 7.82–7.91 (m, 4 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.76 (CH_3), 21.81 (CH_3), 24.5 (CH_2), 25.9 (CH_2), 29.4 (CH_2), 37.5 (CH), 48.8 (CH_2), 61.2 (CH), 126.7 (CH), 126.9 (2× CH), 127.2 (CH), 128.3 (2× CH), 128.4 (CH), 129.4 (2× CH), 130.0 (CH), 130.1 (2× CH), 135.7 (Cq), 136.0 (Cq), 137.4 (Cq), 141.3 (Cq), 142.7 (Cq), 145.0 (Cq) ppm. IR: ṽ = 2924, 1597, 1492, 1453, 1316, 1245, 1151, 1062, 1014, 812, 745, 703 cm^{-1}. HRMS (ESI): calcd. for $C_{26}H_{29}N_2O_3S_2$ [M + H]$^+$ 481.1620; found 481.1621.

Diastereoisomer B (61%): $[\alpha]_D^{20}$ = +94.8 (*c* = 1.03, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.48–1.56 (m, 1 H), 1.60–1.68 (m, 2 H), 1.75–1.81 (m, 1 H), 1.87–1.99 (m, 1 H), 2.04–2.14 (m, 1 H), 2.37 (s, 3 H), 2.41 (s, 3 H), 2.48–2.59 (m, 1 H), 2.62–2.75 (m, 1 H), 3.41–3.48 (m, 1 H), 4.84–4.87 (d, *J* = 7.9 Hz, 1 H), 6.98–7.02 (m, 1 H), 7.11–7.18 (m, 1 H), 7.18–7.23 (m, 3 H), 7.26–7.29 (m, 2 H), 7.77–7.80 (m, 3 H), 7.85–7.88 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.76 (CH_3), 21.80 (CH_3), 24.5 (CH_2), 26.0 (CH_2), 29.2 (CH_2), 37.5 (CH), 49.1 (CH_2), 61.2 (CH), 126.88 (CH), 126.92 (2× CH), 127.4 (CH), 127.8 (2× CH), 127.9 (CH), 129.3 (2× CH), 130.0 (CH), 130.1 (2× CH), 134.5 (Cq), 134.7 (Cq), 137.1 (Cq), 141.1 (Cq), 142.8 (Cq), 144.7 (Cq) ppm. IR: ṽ = 2928, 1602, 1492, 1460, 1312, 1288, 1154, 1065, 1062, 1008, 812, 754, 658 cm^{-1}. HRMS (ESI): $C_{26}H_{29}N_2O_3S_2$ [M + H]$^+$ 481.1620; found 481.1631.

Compound 16c: Following the procedure for the intramolecular Diels–Alder reaction starting from **15c** (57.0 mg, 0.115 mmol) in octane, **16c** was obtained (petroleum ether/ethyl acetate, 50:50) as a pale yellow oil in 47% yield (27 mg) with two diastereoisomers (1.6:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 1.6/*diastereoisomer B 1* δ = 0.65 (s, 3 H), *1.08 (s, 3 H)*, 1.52–1.70 (m, 3 H), 1.77–1.87 (m, 1 H), *2.34 (s, 3 H)*, 2.36 (s, 6 H), 2.50–2.75 (m, 2 H), *3.02–3.12 (m, 1 H)*, 3.41–3.50 (m, 1 H), 3.51–3.67 (m, 1 H), 4.46 (s, 1 H), *4.67 (s, 1 H)*, 6.95–7.02 (m, 1 H), 7.05–7.23 (m, 6 H), 7.61–7.73 (m, 2 H), 7.81–7.93 (m, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 1.6/*diastereoisomer B 1* δ = 21.7 (CH_3), 21.8 (CH_3), 26.0 (CH_3), *26.7 (CH_3)*, 27.0 (CH_2), *27.2 (CH_2)*, 33.9 (CH_2), *34.2 (CH_2)*, 36.4 (CH_2), *37.2 (CH_2)*, 42.3 (Cq), *42.4 (Cq)*, 48.1 (CH_2), *48.3 (CH_2)*, *68.0 (CH)*, 68.1 (CH), *126.3 (CH)*, 126.6 (CH), *126.9 (2× CH)*, 127.0 (2× CH), 127.49 (CH), *127.54 (CH)*, 127.6 (CH), *127.8 (CH)*, 127.9 (2× CH), *128.2 (2× CH)*, 129.29 (2× CH), *129.31 (2× CH)*, 129.8 (2× CH), *129.82 (2× CH)*, 130.8 (CH), *131.0 (CH)*, 134.8 (Cq), 135.2 (Cq), *135.4 (Cq)*, 137.5 (Cq), *137.9 (Cq)*, 142.7 (Cq), 144.5 (Cq), 144.6 (Cq) ppm. IR: ṽ = 2927, 1597, 1494, 1456, 1316, 1254, 1153, 1103, 1067, 1014, 989, 813, 733, 655 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_3S_2$ [M + H]$^+$ 495.1776; found 495.1785.

Compound 16d: Following the procedure for the intramolecular Diels–Alder reaction starting from **15d** (48.0 mg, 0.088 mmol) in octane, **16d** was obtained (dichloromethane/ethyl acetate, 90:10) as a pale yellow oil in 96% yield (46 mg) with two diastereoisomers (1.6:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 1.6/*diastereoisomer B 1* δ = 1.33–1.41 (m, 3 H), 1.51–1.62 (m, 1 H), 1.62–2.04 (m, 3 H), *2.36 (s, 3 H)*, 2.37 (s, 3 H), 2.42 (s, 3 H), 2.59–2.79 (m, 2 H), 2.80–2.97 (m, 1 H), *3.67–3.71 (d, J = 14.5* Hz, *1 H)*, 4.04–4.09 (d, *J* = 14.5 Hz, 1 H), 5.21–5.22 (d, *J* = 4.4 Hz, 1 H), *5.37–5.39 (d, J = 4.5* Hz, *1 H)*, 7.00–7.23 (m, 5 H), 7.27–7.33 (m, 2 H), 7.65–7.93 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 1.6/*diastereoisomer B 1* δ = 21.5 (CH_3), 21.6 (CH_3), 23.3 (CH_2), *23.4 (CH_2)*, 23.8 (CH_2), *24.1 (CH_2)*, 24.27 (CH_2), *24.34 (CH_2)*, *23.25 (CH_2)*, 27.32 (CH_2), 32.2 (CH), *32.9 (CH)*, *40.2 (CH_2)*, 42.6 (CH_2), 56.7 (CH), *57.1 (CH)*, *126.5 (CH)*, 126.6 (CH), 126.7 (2× CH), *126.9 (2× CH)*, 127.0 (2× CH), *127.1 (2× CH)*, *127.6 (CH)*, 128.0 (CH), 128.8 (CH), *129.0 (CH)*, *129.1 (2× CH)*, 129.2 (2× CH), 129.9 (CH), 130.0 (2× CH), 132.9 (Cq), *130.0 (Cq)*, 136.8 (Cq), *137.1 (Cq)*, 138.1 (Cq), 141.1 (Cq), 142.3 (Cq), *142.5 (Cq)*, 144.2 (Cq), *144.4* (Cq) ppm. IR: ṽ = 2925, 1598, 1501, 1472, 1317, 1252, 1154, 1067, 1062, 1016, 954, 933, 813, 746 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{31}N_2O_3S_2$ [M + H]$^+$ 495.1776; found 495.1782.

Compound 16e: Following the procedure for the intramolecular Diels–Alder reaction starting from **15e** (48.0 mg, 0.088 mmol), **16e** was obtained (dichloromethane/ethyl acetate, 90:10) as a pale yellow oil in 96% yield (46 mg) with two diastereoisomers (2.4:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): diastereoisomer A 2.4/*diastereoisomer B 1* δ = 1.91–2.04 (m, 1 H), 2.29 (s, 3 H), *2.29 (s, 3 H)*, 2.34–2.41 (m, 1 H), *2.35 (s, 3 H)*, 2.38 (s, 3 H), 2.41–2.50 (m, 2 H), 2.96–3.03 (m, 1 H), *3.39–3.46 (m, 1 H)*, 3.99–4.05 (d, *J* = 17.1 Hz, 1 H), *4.26–4.32 (d, J = 17.8* Hz, *1 H)*, 4.55–4.60 (d, *J* = 17.4 Hz, 1 H), *4.94–5.00 (d, J = 17.8* Hz, *1 H)*, 5.47–5.49 (d, *J* = 6.4 Hz, 1 H), *5.75–5.77 (d, J = 6.3* Hz, *1 H)*, 6.74–6.92 (m, 2 H), 7.01–7.27 (m, 10 H), 7.63–7.65 (m, 1 H), 7.71–7.80 (m, 1 H), *7.83–7.86 (m, 2 H)*, 7.88–7.91 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): diastereoisomer A 2.4/*diastereoisomer B 1* δ = 21.65 (CH_3), *21.68 (CH_3)*, 21.70 (CH_3), *21.73 (CH_3)*, 24.1 (CH_2), *24.3 (CH_2)*, *25.57 (CH_2)*, 25.64 (CH_2), 33.4 (CH), *34.4 (CH)*, *42.9 (CH_2)*, 45.1 (CH_2), 55.5 (CH), *56.4 (CH)*, *125.9 (CH)*, 126.0 (CH), *126.3 (CH)*, 126.4 (CH), 126.6 (CH), *126.79 (2× CH)*, *126.83 (CH)*, 127.0 (2× CH), 127.1 (2× CH), *127.2 (2× CH)*, 127.3 (CH), *127.38 (CH)*, *127.43 (CH)*, 127.5 (CH), 127.8 (CH), *128.0 (CH)*, 128.5 (CH), 128.9 (CH), *129.1 (CH)*, *129.3 (2× CH)*, 129.4 (2× CH), 129.8 (2× CH), *129.9 (2× CH)*, *131.7 (Cq)*, 132.2 (Cq), 132.5 (Cq), *132.7 (Cq)*, 133.9 (Cq), *134.3 (Cq)*, *136.6 (Cq)*, 137.0 (Cq), 138.0 (Cq), *138.2 (Cq)*, 141.2 (Cq), *142.6 (Cq)*, 142.8 (Cq), 144.5 (Cq), *144.6 (Cq) ppm*. IR: ṽ = 2900, 1598, 1495, 1450, 1320, 1249, 1153, 1103, 1062, 1015, 954, 932, 900, 864, 811, 769, 743, 703, 688, 673 cm^{-1}. HRMS (ESI): calcd. for $C_{31}H_{31}N_2O_3S_2$ [M + H]$^+$ 543.1776; found 543.1802.

Supporting Information (see footnote on the first page of this article): Copies of the ^{1}H NMR and ^{13}C NMR spectra of all compounds, and crystallographic data for compound **13**.

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Acknowledgments

The authors thank the Institut de Chimie des Substances Naturelles, the LabEx CHARM3AT (CHimie des ARchitectures Moléculaires Multifonctionnelles et des MATériaux), the European Union (EU) (COST Action D40, Innovative Catalysis: New Processes and Selectivities), and the Agence Nationale de la Recherche (ANR-08-BLAN-0013-01, grant to C. L.) for financial support. The Ministère de l'Enseignement Supérieur et de la Recherche (MESR) is kindly acknowledged for a fellowship to M. M.

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[23] On the one hand, DMF proved to give better conversions than acetonitrile, dimethyl sulfoxide or *N*-methyl-2-pyrrolidone. On the other hand, use of $Pd(PPh_3)_2Cl_2$ in DMF allows isolation of **7a** in 72% yield after 45 h at room temp. whereas $Pd(PPh_3)_4$ only leads to 49% of **7a**. Other palladium catalysts such as $PdCl_2$, $Pd(MeCN)_2Cl_2$ did not prove successful. It should be also mentioned that products resulting from the palladium-catalyzed Heck coupling reaction, as well as those obtained after the subsequent Mitsunobu reaction, are isolated with slightly variable diastereomeric ratios.

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Received: August 2, 2013
Published Online: October 15, 2013

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