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Intermolecular C−H Amination of Complex Molecules: Insights into the Factors Governing the Selectivity

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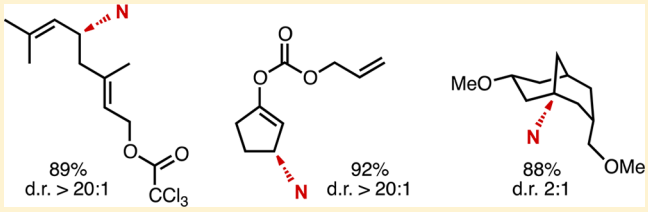
Supporting Information

ABSTRACT: Transition-metal-catalyzed C−H amination via nitrene insertion allows the direct transformation of a C−H into a C−N bond. Given the ubiquity of C−H bonds in organic compounds, such a process raises the problem of regio- and chemoselectivity, a challenging goal even more difficult to tackle as the complexity of the substrate increases. Whereas excellent regiocontrol can be achieved by the use of an appropriate tether securing intramolecular addition of the nitrene, the intermolecular C−H amination remains much less predictable. This study aims at addressing this issue by capitalizing on an efficient stereoselective nitrene transfer involving the combination of a chiral aminating agent **1** with a chiral rhodium catalyst **2**. Allylic C−H amination of terpenes and enol ethers occurs with excellent yields as well as with high regio-, chemo-, and diastereoselectivity as a result of the combination of steric and electronic factors. Conjugation of allylic C−H bonds with the π-bond would explain the chemoselectivity observed for cyclic substrates. Alkanes used in stoichiometric amounts are also efficiently functionalized with a net preference for tertiary equatorial C−H bonds. The selectivity, in this case, can be rationalized by steric and hyperconjugative effects. This study, therefore, provides useful information to better predict the site of C−H amination of complex molecules.



INTRODUCTION

The past decade has witnessed considerable interest in the area of catalytic C−H functionalization, a new class of reactions that provides unprecedented bond disconnections.[1] Recent examples of natural product syntheses perfectly showcase the unique opportunities offered by these transformations.[2] In addition, site-selective C−H functionalization affords the possibility to tailor "a façon" drugs or materials with the aim of modifying their properties or tackle the issue of diversity-oriented synthesis.[3,4] Application of this strategy to incorporate a nitrogen group into a molecule is thus of fundamental importance.

Catalytic C−H amination has been extensively investigated in the past decade as shown by the growing number of reviews devoted to the field.[5] The direct introduction of a nitrogen functionality can be efficiently achieved by catalytic C−H activation[6,7] or, more frequently, by C−H insertion of a metallanitrene that has led to great achievements in synthesis.[5] The efficiency and scope of the latter process have recently been improved by the design of several transition metal complexes,[8−12] among which dirhodium(II) catalysts hold a prominent position,[13] or sustainable metal-free conditions.[14] However, although catalytic C−H amination is a method of choice to prepare amines, an efficient chemoselective intermolecular process remains to be developed. Whereas catalytic intramolecular nitrene C−H insertion occurs with very good levels of regio-, chemo-, and stereocontrol, the intermolecular reaction, by comparison, appears less predictable. The selective amination of a specific C−H bond in compounds displaying several functional groups, especially alkenes, remains a challenge to tackle.[1d,15]

Notwithstanding foreseeable difficulties, it was decided to capitalize on our previous studies with sulfonimidamides[16,17] to address the issue of chemoselectivity in intermolecular C−H amination. The purpose was to gain helpful information to better predict the site of functionalization of complex molecules. This was inspired by the observation that, contrary to C−H hydroxylation mediated by oxidases,[18] a chemoselective intermolecular C−H amination is not known in nature. Whereas a lot of studies have focused on the search for new efficient catalysts to perform nitrene transfers, we have recently documented the conception of new types of reagents for a more practical synthetic nitrene chemistry. This led us to report the use of sulfonimidamides together with chiral rhodium(II) complexes in the presence of the soluble iodine oxidant PhI(OCO-*t*-Bu)$_2$ in stereoselective intermolecular C−H amination of various simple hydrocarbons.[16] The excellent results obtained by combining the amide **1** with the chiral catalyst Rh$_2$(*S*-nta)$_4$ **2** (Figure 1) then persuaded us to explore the chemoselective functionalization of more complex molecules with the aim to better predict the selectivity of intermolecular C−H amination. We therefore describe in this paper the site-selective catalytic C−H amination of substrates

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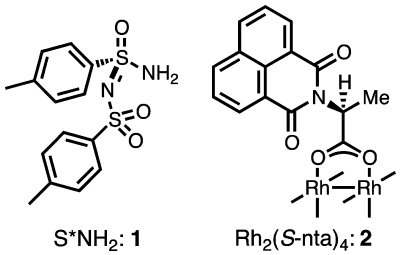


Figure 1. Sulfonimidamide **1** and the rhodium catalyst $Rh_2(S\text{-nta})_4$ **2**.

of increasing complexity that relies on the influence of several factors.

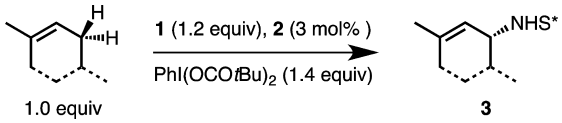
RESULTS AND DISCUSSION

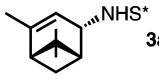
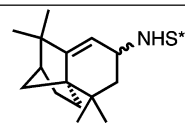
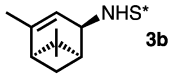
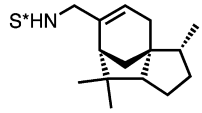
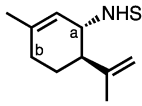
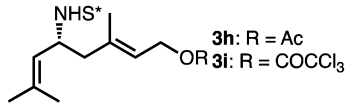
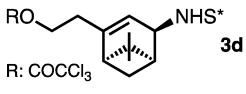
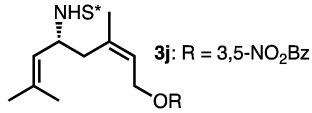
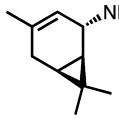
C–H Amination of Terpenes. Attention was first paid to terpenes with initial experiments carried out on both enantiomers of α-pinene.[19] Catalytic C–H amination of substrates used as the limiting reagents proved highly efficient since the expected C–H aminated products **3a** and **3b** were isolated in 91% and 71% yields, respectively (Table 1, entries 1 and 2). A single compound is formed in each case as a consequence of steric and electronic factors. Secondary allylic C–H bonds are thus selectively functionalized in the presence of primary and tertiary positions. This preference matches that reported for carbenes, resulting from the best compromise in terms of steric and electronic effects provided by a methylene group.[5a] The *trans* stereochemistry, in addition, was deduced from NOESY experiments run on compounds **3a** and **3b** and then corroborated by the X-ray crystal structure of **3a** obtained from (*R*)-α-pinene (see the Supporting Information). Interestingly, our previous studies[16] have shown that the combination of (*S*)-**1** with the (*S*)-catalyst **2** induces the formation of optically active amine derivatives with the (*R*)-configuration. Because either (*R*)- or (*S*)-amides are here isolated with the same matched pair of (*S*)-reagents, these results suggest that the stereoselectivity of the nitrene C–H insertion is controlled by the substrate. Steric factors are also responsible for the selective introduction of the amino group at the less hindered secondary site ("a" vs "b") of (*S*)-limonene, *trans* to the isopropenyl chain (entry 3). In this case, the bulky chiral metallanitrene allows the discrimination of only one out of 11 available allylic C–H bonds of limonene, affording enantiopure compound **3c** in 73% yield.

Pleasingly, comparable high levels of regio-, chemo-, and stereoselectivity were observed with nopol trichloroacetate that affords exclusively the product **3d** in 98% yield (entry 4). In this case, unfavorable inductive effects from the trichloroacetyl ester deactivate the exocyclic secondary allylic position. A similar inhibiting effect was observed when the reaction was applied to (*R*)-(−)-carvone (data not shown). The presence of a carbonyl deactivates the vinylogous allylic position, thereby leading to the complete recovery of the starting material. Carene also proved to give a major isomer though with a lower yield of 27% (entry 5).[20] By contrast, both (−)-isolongifolene and (−)-α-cedrene provided unexpected results (entries 6 and 7). Whereas the former afforded a 60:40 mixture of allylic amines **3f** with a good yield of 85%, the latter led to a rare example of C–H amination at a primary allylic position, as indicated by the X-ray crystal structure of **3g** (see the Supporting Information). This switch in regiochemistry can be rationalized by the steric hindrance induced by the neopentyl position.

An important feature of the amination is the chemoselective formation of compounds **3a–g**; the potentially reactive alkene

Table 1. Allylic Amination of Terpenes[a]



Entry	Product	Yield	d.r.[b]	Entry	Product	Yield	d.r.[b]
1	 **3a**	91	39:1	6	 **3f**	85	1.5:1
2	 **3b**	71	49:1	7	 **3g**	34 (63)[c]	-
3	 **3c**	73	49:1	8	 **3h**: R = Ac **3i**: R = $COCCl_3$	90 89	19:1 >20:1
4	 **3d**	98	>20:1	9	 **3j**: R = 3,5-NO_2Bz	81	5:1
5	 **3e**	27	10:1				

[a]Reaction conditions: terpene (0.2 mmol) in a 3:1 mixture of 1,1,2,2-tetrachloroethane/MeOH at −35 °C. [b]The diastereomeric ratios have been determined by ^{1}H NMR or HPLC. [c]Yield in parentheses obtained using 5 equiv of substrate.

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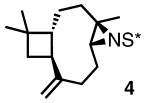
units proved inert under these conditions since the corresponding aziridines were not isolated. Based on the X-ray structure obtained for the amino derivatives **3a** and **3e** (see the Supporting Information), we propose to rationalize this observation by the involvement of stereoelectronic factors resulting from the dihedral angle of 60° between the plane of the olefin and each allylic C−H bonds. This allows their hyperconjugation with the π-bond, thereby increasing their reactivity. This hypothesis, interestingly, is corroborated by the result observed in the case of β-(−)-caryophyllene that led us to isolate the aziridine **4** as a single isomer in 28% yield (79% using 5 equiv of caryophyllene). The structure of compound **4** was confirmed by X-ray crystallography (see the Supporting Information). A closer inspection of the product then revealed that allylic C−H bonds, in this case, nearly lie in the plane of the alkene. Such a conformation would deactivate these bonds toward C−H amination. Electron density of the olefin, moreover, would be substantially increased by the hyperconjugation of allylic σ_{C-C} orbitals, which are perpendicular to its plane.[21]



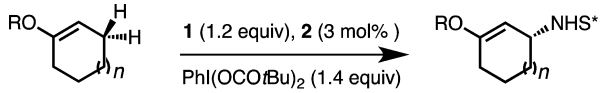
4

High efficiency and selectivity, finally, have been observed in the case of geranyl derivatives (entry 8). A single aminated product was isolated in each case despite the presence of 15 allylic C−H bonds. A screening of various protecting groups (see the Supporting Information) then led to the finding that a trichloroacetyl substituent was suitable to grow single crystals. This allowed us to confirm unambiguously the structure of the resulting product **3i** (see the Supporting Information). Once again, the combination of (*S*)-**1** with the (*S*)-catalyst **2** induces the formation of optically active (*R*)-amine derivatives. Such a high level of regio- and stereoselectivity can be rationalized by a reactive allylic position that is less hindered and electronically deactivated than both others allylic methylene groups. A comparable result was obtained starting from neryl 3,5-dinitrobenzoate though with lower yield and diastereoselectivity (entry 9). From a synthetic point of view, the regioselective C−H amination of terpenes, ultimately, affords synthetic products displaying structures complementary to those previously reported by application of different oxidizing conditions.[22]

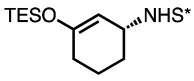
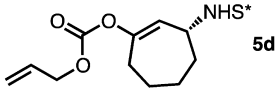
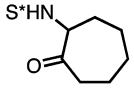
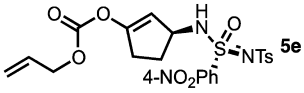
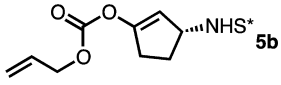
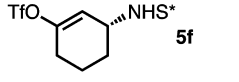
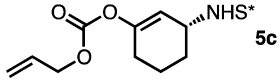
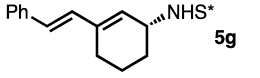
C−H Amination of Enol Ethers. We next turned our attention to cyclic enol ethers likely to produce useful intermediates, which could be further functionalized. Fundamentally, these substrates possess an electron-rich alkene even more prone to react with nitrenes.[23] Nevertheless, inspired by the studies of Hashimoto that describe the enantioselective C−H amination of cyclohexanone-derived enol ethers with ees of up to 72%,[24] we initially investigated the reactivity of silyl enol ethers. We first confirmed that a triethylsilyl protecting group is the most compatible with the reaction conditions. However, whereas the 6-membered silyl enol ether afforded the expected product **5a** though in low yield and moderate stereoselectivity (Table 2, entry 1), C−H amination of the cyclopentanone-derived analogue did not prove successful (data not shown). In addition, the 7-membered derivative gave a single isomer of a compound **6** that turned out to be the product of α-amination arising from initial alkene aziridination followed by hydrolytic ring-opening of the resulting aziridine (entry 2). All these disappointing results then convinced us to screen other enol ethers and led us to concentrate on allyl enol carbonates.[25]

In our hands, these allyl carbonates proved highly useful since we were able to perform C−H amination with high levels of regio-, chemo-, and stereoselectivity comparable to those recorded with terpenes despite six available secondary allylic C−H bonds. Thus, the 5-, 6-, and 7-membered cyclic enol ethers undergo amination at a single methylene group to afford a sole isomer with yields ranging from 52% to 98% (entries 3−6). Based on the previous results, the hypothesis of steric hindrance and unfavorable inductive effects allows predicting that the reaction occurs at the β-position. This, and the absolute configuration of the newly created stereocenter, were confirmed by X-ray crystallography of compound (*S*)-**5e** obtained by using the opposite matched pair of reagent, i.e.,

Table 2. Allylic C−H Amination of Enol Ethers[a]



1.0 equiv **5**

Entry	Product	Yield	d.r.[b]	Entry	Product	Yield	d.r.[b]
1	 **5a**	20 (63)[c]	4:1	5	 **5d**	52	>20:1
2	 **6**	30	199:1	6[d]	 **5e**	98	>20:1
3	 **5b**	92	>20:1	7	 **5f**	70	5:1
4	 **5c**	80	9:1	8	 **5g**	58	5:1

[a]Reaction conditions: enol ether (0.2 mmol) in a 3:1 mixture of 1,1,2,2-tetrachloroethane/MeOH at −35 °C. [b]The diastereomeric ratios have been determined by ^{1}H NMR or HPLC. [c]Yield in parentheses obtained using 5 equiv of substrate. [d]Reaction performed with the (*R*)-enantiomer of the *p*-nitro analogue of **1** in the presence of catalyst (*R*)-**2**.

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the (*R*)-enantiomer of the (*p*-nitrobenzene)sulfonimidamide with the (*R*)-Rh(II) catalyst **2** (Supporting Information).

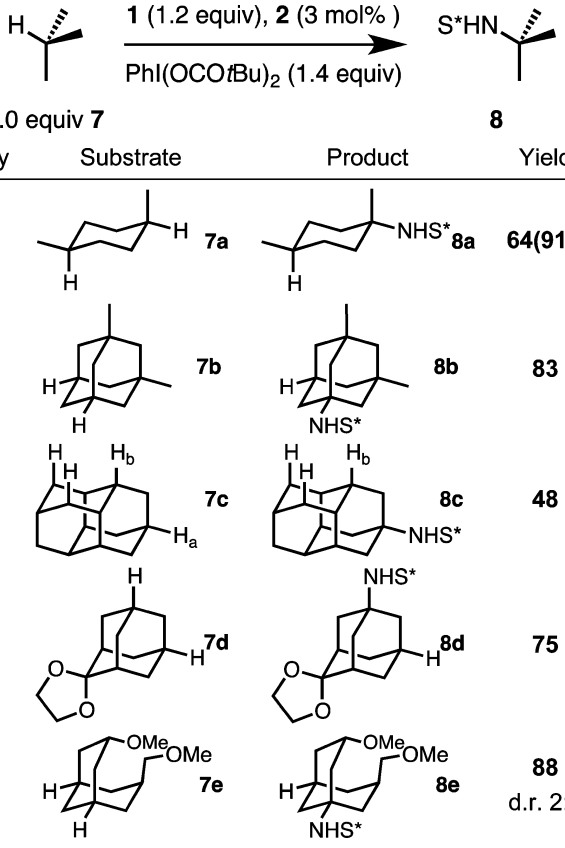
A vinyl triflate also efficiently reacts under these conditions as nicely demonstrated by the isolation of product **5f** in 70% yield and with a dr of 5:1 (entry 7).[26] Application of palladium-cross coupling to the latter then affords a variety of more complex enantioenriched amino derivatives.[27] We have demonstrated, on the other hand, that this sequence of reactions can be performed in reversed order with equal success as shown by entry 8. The formation of compound **5g**, resulting from the application of C−H amination to the coupling product with styrene, thus showcases again the high chemoselectivity of the reaction since aziridination of the electron-rich styrene moiety is not observed. To the best of our knowledge, this is the first example of a selective C−H amination of a 1,3-diene.

C−H Amination of Alkanes. We finally focused on the selective C−H amination of alkanes. Despite recent significant achievements in catalytic C−H hydroxylation,[18] examples of efficient selective functionalization of unactivated Csp^3−H bonds are scarce. In the case of amination, they still remain confined to hydrocarbons used in excessive amount. Our matched pair of reagents, by comparison, allows the efficient selective functionalization of several cyclic substrates used as the limiting agents (Table 3).

Both isomers of 1,4-dimethylcyclohexane, first, were textbook cases to document the higher reactivity of tertiary equatorial C−H bonds as a consequence of combined steric and hyperconjugative effects.[28] Whereas the *trans*-isomer with two axial tertiary C−H bonds proved to give minute amounts of a C−H aminated compound (data not shown), the equatorial C−H bond of the *cis*-isomer **7a** was efficiently transformed (entry 1). This trend was corroborated by the reaction with dimethyladamantane **7b** that affords a direct precursor of memantine[13k] in 83% yield (entry 2). That the selective functionalization of a methine group can be achieved by the introduction of additional steric factors, was then demonstrated by the C−H amination of diamantane **7c**. The latter displays six equivalent "internal" tertiary C−H_b bonds and two external identical sites (H_a). Despite an adverse statistical distribution, one of the latter was exclusively aminated in 48% yield (entry 3) as indicated by the X-ray crystal structure (Supporting Information). This selectivity can be rationalized by 1,3-diaxial interactions disfavoring the amination of the C−H_b bonds, which are axial with respect to one cyclohexyl ring (contrary to the purely equatorial C−H_a bonds).[29]

Discriminating a tertiary position among several ones can also be envisaged through inductive effects.[30] Whereas 2-adamantanone did not undergo amination either at the α- or γ-tertiary center, it was found that the inhibiting effect of the ketone is suppressed by its protection as a ketal. Compound **7d** thus reacts selectively at the less deactivated tertiary position to afford product **8d** in 75% yield (entry 4). Last but not least, another type of tertiary bridgehead position can be efficiently functionalized with sulfonimidamide-derived nitrenes. The adamantanone-derived bicyclo[3.3.1]nonane derivative **7e** afforded the expected amine **8e** in 88% yield and, more fundamentally, with a diastereomeric ratio of 2:1 (entry 5). Though modest, this diastereoselectivity suggests that desymmetrization of *meso* substrates could be achieved using catalytic nitrene transfers.

Table 3. Catalytic C−H Amination of Alkanes[a]



[a]Reaction conditions: alkane (0.2 mmol) in a 3:1 mixture of 1,1,2,2-tetrachloroethane/MeOH at −35 °C. [b]Yield in parentheses obtained using 5 equiv of substrate. [c]Reaction performed in a 3:3:1 mixture of 1,1,2,2-tetrachloroethane/benzene/MeOH.

CONCLUSION

In conclusion, the use of a sulfonimidoylnitrene species allows the intermolecular chemoselective C−H amination of various complex molecules used in stoichiometric amounts. This reaction gives access to enantiopure aminated derivatives, which are not easily accessible by "classical" organic synthesis.[31] Allylic methylene units of terpenes and enol ethers have been efficiently aminated with yields of up to 98% and very high diastereomeric ratios (of up to 199/1). More importantly, the combination of steric, inductive, and conformational factors leads to the chemoselective functionalization of allylic positions vs adjacent π-bonds. The site-selective amination of alkanes also proves possible under these conditions with yields of up to 88%. Steric and stereoelectronic effects, in this case, favor the amination of tertiary equatorial C−H bonds. This efficient catalytic C−H functionalization therefore provides information on the inherent reactivity of various substrates. These should serve as a guide to incorporate this transformation into retrosynthetic analysis. Work is now in progress to apply catalytic C−H amination in total synthesis as well as to investigate the desymmetrization of *meso* compounds by C−H oxidation.

EXPERIMENTAL SECTION

General Information. Melting points were measured in capillary tubes and are uncorrected. Infrared spectra were recorded on a FT-IR spectrometer. Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on 300 and 500 MHz spectrometers. Carbon NMR (^{13}C) spectra were recorded at 125 or 75 MHz, using a broadband

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decoupled mode with the multiplicities obtained using a JMOD or DEPT sequence. NMR experiments were carried out in deuterochloroform ($CDCl_3$), methanol (CD_3OD), benzene (C_6D_6), and dimethyl sulfoxide (DMSO). Chemical shifts (δ) are reported in parts per million (ppm) with reference to tetramethylsilane (TMS) or residual solvent peaks as internal standards. Coupling constants (J) are reported in hertz (Hz). Values in italics refer to the minor diastereomer, where applicable. Mass spectra were obtained either with a LCT instrument using electrospray ionization (ES) or from a time of flight analyzer (ESI-MS) for the high-resolution mass spectra (HRMS). Elemental analyses were performed on an analyzer with a detection by catharometry. All reagents were obtained from commercial suppliers unless otherwise stated. The rhodium catalyst **2** is prepared from rhodium(II) acetate which was purchased either from a commercial supplier. Where necessary, organic solvents were routinely dried and/or distilled prior to use and stored over molecular sieves under argon. Organic extracts were dried over magnesium sulfate ($MgSO_4$) or sodium sulfate (Na_2SO_4).

General Procedure for Catalytic C−H Amination. In an oven-dried tube were introduced activated 4 Å molecular sieves (100 mg), $Rh_2[(S)\text{-nta}]_4$ **2** (7.7 mg, 0.006 mmol), and (−)-*N*-(*p*-toluenesulfonyl)-*p*-toluenesulfonimidamide (−)-(*S*)-**1** (78 mg, 0.24 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 (0.2 mmol). The tube was cooled to −78 °C, and bis(*tert*-butylcarbonyloxy)iodobenzene (115 mg, 0.28 mmol) was added. The mixture was stirred at −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 insertion products.

1R,2S,5R)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-amine ***3a***. Prepared following the typical amination procedure from (*R*)-α-pinene, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a white crystalline solid (83 mg, 91%): 39:1 dr (HPLC, Hypercarb column, 100 × 4.6 mm, 5 μm, MeCN + 0.1% $HCOOH/H_2O$ + 0.1% HCOOH:80/20, 1 mL min^{-1}, t_{maj} = 17.25 min); R_f = 0.60 (heptane/ethyl acetate 50/50); mp 55−57 °C; $[\alpha]^{20}_D$ = −10.6 (*c* 1.00 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.85−7.75 (m, 4H), 7.30−7.22 (m, 4H), 5.86 (d, *J* = 8.6 Hz, 1H), 5.21 (qd, *J* = 1.6, 3.1 Hz, 1H), 3.92−3.84 (m, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.20 (td, *J* = 5.5, 9.5 Hz, 1H), 1.98 (td, *J* = 1.3, 5.5 Hz, 1H), 1.83−1.76 (m, 1H), 1.70 (t, *J* = 1.7 Hz, 3H), 1.19 (s, 3H), 1.25−1.17 (m, 1H), 0.76 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ= 150.5, 144.6, 142.8, 140.6, 136.5, 129.9, 129.2, 127.8, 126.9, 115.0, 54.2, 47.1, 46.6, 44.5, 28.7, 26.4, 22.8, 21.7, 21.6, 20.5; IR (neat, cm^{-1}) ν = 3218, 2925, 1596, 1403, 1301, 1258, 1150, 1105, 1089, 1074, 1016, 1002, 810; HRMS (ESI) calcd for $C_{24}H_{30}N_2O_3S_2Na$ 481.1596, found 481.1588.

(1S,2R,5S)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-amine ***3b***. Prepared following the typical amination procedure from (*S*)-α-pinene, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a white crystalline solid (65 mg, 71%): 49:1 dr (HPLC, Hypercarb column, 100 × 4.6 mm, 5 μm, MeCN + 0.1% $HCOOH/H_2O$ + 0.1% HCOOH:90/10, 1 mL min^{-1}, t_{maj} = 13.08 min); R_f = 0.55 (heptane/ethyl acetate 50/50); mp 123−125 °C; $[\alpha]^{20}_D$ = +142 (c 1.00 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.80 (t, *J* = 7.7 Hz, 4H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 5.91 (br s, 1H), 4.85−4.80 (m, 1H), 3.79 (br s, 1H), 2.44 (s, 3H), 2.40 (s, 3H), 2.34 (td, *J* = 5.5, 9.5 Hz, 1H), 2.25−2.19 (m, 1H), 2.00 (t, *J* = 5.5 Hz, 1H), 1.63 (s, 3H), 1.28 (s, 3H), 1.28−1.23 (m, 1H), 0.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 150.7, 144.8, 143.0, 140.6, 136.6, 130.0, 129.3, 127.9, 127.0, 115.0, 54.3, 47.2, 46.7, 44.6, 28.8, 26.4, 22.9, 21.82, 21.76, 20.6; IR (neat, cm^{-1}) ν = 3236, 2920, 1596, 1420, 1300, 1245, 1150, 1104, 1088, 1016, 1000, 811; HRMS (ESI) calcd for $C_{24}H_{30}N_2O_3S_2$ Na 481.1596, found 481.1575.

(1S,6R)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-3-methyl-6-(prop-1-en-2-yl)cyclohex-2-enamine ***3c***. Prepared following the typical amination procedure from (*S*)-limonene, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a white crystalline solid (67 mg, 73%): 49:1 dr (HPLC, Hypercarb column, 100 × 4.6 mm, 5 μm, MeCN + 0.1% $HCOOH/H_2O$ + 0.1% HCOOH: 80/20, 1 mL min^{-1}, t_{maj} = 46.38 min); R_f = 0.54 (heptane/ethyl acetate 50/50); mp 83−85 °C; $[\alpha]^{20}_D$ = +105.5 (c 1.00 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.84−7.79 (m, 2H), 7.77−7.71 (m, 2H), 7.26−7.20 (m, 4H), 5.72 (d, *J* = 8.0 Hz, 1H), 5.46 (br s, 1H), 4.59 (s, 1H), 4.56−4.52 (m, 1H), 3.62−3.51 (m, 1H), 2.39 (s, 3H), 2.38 (s, 3H), 2.05−1.93 (m, 2H), 1.90−1.78 (m, 1H), 1.65 (s, 3H), 1.62−1.42 (m, 2H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.1, 144.8, 143.0, 140.7, 138.2, 135.6, 129.6, 129.4, 128.6, 127.0, 122.9, 113.6, 53.1, 48.4, 29.6, 27.1, 23.4, 21.79, 21.76, 18.6; IR (neat, cm^{-1}) ν = 3190, 1597, 1424, 1299, 1283, 1146, 1109, 1030, 1014, 806; HRMS (ESI) calcd for $C_{24}H_{30}N_2O_3S_2Na$ 481.1596, found 481.1608.

2-((1R,4R,5S)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-4-amino-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethyl 2,2,2-trichloroacetate ***3d***. Prepared following the typical amination procedure from (1*R*)-(−)-nopol trichloroacetate, the corresponding amination product was obtained (heptane/ethyl acetate: 80/20 to 70/30) as a white foam (124 mg, 98%): >20:1 dr (^1H NMR evaluation); R_f = 0.30 (heptane/ethyl acetate 70/30); $[\alpha]^{20}_D$ = −60.6 (*c* 1.00 in acetone); ^1H NMR (300 MHz, $CDCl_3$) δ = 7.84−7.76 (m, 4H), 7.34−7.20 (m, 4H), 5.96 (d, *J* = 9.2 Hz, 1H), 4.99−4.93 (m, 2H), 4.38−4.22 (m, 1H), 3.88−3.80 (m, 1H), 2.44 (s, 3H), 2.44−2.34 (m, 3H), 2.40 (s, 3H), 2.28−2.20 (m, 1H), 2.18−2.12 (m, 1H), 1.30 (s, 3H), 1.28 (d, *J* = 9.7 Hz, 1H), 0.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.0, 152.4, 148.8, 145.0, 143.1, 140.5, 136.5, 130.1, 129.4, 127.9, 127.0, 118.4, 66.8, 54.0, 46.7, 46.0, 44.9, 35.1, 29.1, 26.4, 21.83, 21.75, 20.9; IR (neat, cm^{-1}) ν = 3225, 2925, 1764, 1597, 1303, 1241, 1153, 1108, 1092, 1017, 815, 755, 680; HRMS (ESI) calcd for $C_{27}H_{32}Cl_3N_2O_5S_2$ 633.0818, found 633.0804.

(1R,2S,6S)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-4,7,7-trimethylbicyclo[4.1.0]hept-3-en-2-amine ***3e***. Prepared following the typical amination procedure from (*S*)-3-carene, the corresponding amination product was obtained (dichloromethane/ethyl acetate 100/0 to 95/5) as a white crystalline solid (25 mg, 27%): 10:1 dr (^1H NMR evaluation): R_f = 0.40 (dichloromethane/ethyl acetate 98/2); mp 105−109 °C; $[\alpha]^{20}_D$ = +32.6 (c 1.00 in acetone); ^1H NMR (500 MHz, $CDCl_3$) δ = 7.88−7.80 (m, 4H), 7.34−7.21 (m, 4H), 5.87 (d, *J* = 9.2 Hz, 1H), 5.24−5.17 (m, 1H), 3.75−3.64 (m, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.29−2.15 (m, 1H), 1.83−1.70 (m, 1H), 1.60 (s, 3H), 0.76 (s, 3H), 0.75−0.63 (m, 1H), 0.66 (s, 3H), 0.29 (d, *J* = 8.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.7, 142.9, 140.7, 137.6, 136.7, 129.9, 129.3, 128.0, 127.0, 120.1, 46.9, 28.0, 25.1, 23.6, 23.3, 21.7, 18.6, 16.1, 13.4; IR (neat, cm^{-1}) ν = 3171, 2943, 1598, 1446, 1427, 1283, 1260, 1300, 1146, 1112, 1016, 995, 806, 766, 743, 704, 666; HRMS (ESI) calcd for $C_{24}H_{31}N_2O_3S_2$ 459.1776, found 459.1754.

(2R,4aR)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-1,1,5,5-tetramethyl-2,3,4,5,6,7-hexahydro-1H-2,4a-methanonaphthalen-7-amine ***3f***. Prepared following the typical amination procedure from (-)-isolongifolene, the corresponding amination product was obtained (heptane/ethyl acetate 90/10 to 80/20) as a white foam (89 mg, 85%): 1.5:1 dr (^1H NMR evaluation); R_f = 0.35 (heptane/ethyl acetate 80/20); diastereomer A 1.5/*diastereomer B 1*
^1H NMR (500 MHz, $CDCl_3$) δ = 7.86−7.78 (m, 4H), 7.34−7.22 (m, 4H), 5.79 (d, *J* = 8.6 Hz, 1H), *5.60 (d, J = 9.1 Hz, 1H), 5.05 (s, 1H),* 4.76 (d, *J* = 4.0 Hz, 1H), *3.83−3.76 (m, 1H),* 3.76−3.70 (m, 1H), 2.44 (s, 3H), *2.404 (s, 3H),* 2.400 (s, 3H), 1.82−1.76 (m, 1H), 1.74−1.54 (m, 4H), 1.51−1.35 (m, 2H), 1.29−1.22 (m, 2H), *1.21−1.16 (m, 2H), 1.06 (s, 3H),* 1.04 (s, 3H), *0.94 (s, 3H),* 0.93 (s, 6H), 0.91 (s, 3H), *0.82 (s, 3H), 0.72 (s, 3H);* ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.0, 161.2, 144.80, *144.77, 142.92,* 142.87, 140.75, *140.66, 136.6,* 136.1, 130.0, *129.9,* 129.4, 128.2, *128.0, 127.0,* 126.9, 112.0, 109.5, 56.4, *56.2, 50.6,* 49.0, *46.8,* 46.5, 42.7, *42.6, 41.7,* 41.0, 37.0, *36.7, 32.9,* 31.1, *29.0, 28.8,* 28.4, 28.2, 26.6, 26.4, 25.5, *24.8,* 24.7, *24.5, 21.79,* 21.78, 21.7; IR (neat,

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cm^{-1}) ν = 3224, 2960, 1596, 1403, 1302, 1257, 1150, 1105, 811, 734 ; HRMS (ESI) calcd for $C_{29}H_{37}N_2O_3S_2$ 525.2246, found 525.2257.

(3R,3aS,7R,8aS)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-(3,8,8-trimethyl-2,3,4,7,8,8a-hexahydro-1H-3a,7-methanoazulen-6-yl)methanamine ***3g***. Prepared following the typical amination procedure from (−)-cedrene, the corresponding amination product was obtained (dichloromethane 100%) as an orange oil recrystallized in MeOH to afford white crystals (36 mg, 34%): R_f = 0.30 (dichloromethane); mp 159−160 °C ; $[\alpha]^{20}_D$ = −37.0 (c 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.88−7.80 (m, 4H), 7.31 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 7.9 Hz, 2H), 5.68 (dd, J = 4.7, 7.9 Hz, 1H), 5.49−5.44 (m, 1H), 3.52 (ddd, J = 0.8, 4.7, 14.2 Hz, 1H), 3.32 (qdd, J = 2.0, 7.9, 14.2 Hz, 1H), 2.43 (s, 3H), 2.40 (s, 3H), 2.20−2.10 (m, 1H), 1.89−1.47 (m, 9H), 1.41−1.27 (m, 2H), 1.23 (d, J = 10.5 Hz, 1H), 0.82 (d, J = 7.0 Hz, 1H), 0.79 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.1, 143.0, 140.7, 138.6, 134.9, 130.0, 129.4, 128.3, 126.9, 124.2, 59.1, 54.2, 50.9, 48.7, 48.5, 41.5, 40.5, 38.8, 36.2, 27.5, 25.4, 24.9, 21.79, 21.76, 15.6; IR (neat, cm^{-1}) ν = 3224, 2929, 1595, 1458, 1312, 1238, 1149, 1110, 1091, 1052, 870, 812, 754, 668; HRMS (ESI) calcd for $C_{29}H_{39}N_2O_3S_2$ 527.2402; found 527.2394.

(R,E)-5-[N-(S)-(p-toluenesulfonyl)-p-toluenesulfonimidoyl]amino-3,7-dimethylocta-2,6-dien-1-yl Acetate ***3h***. Prepared following the typical amination procedure from geranyl acetate, the corresponding amination product was obtained (dichloromethane/ethyl acetate: 20/1) as a clear oil (93 mg, 90%); 19:1 dr (^{1}H NMR evaluation). R_f = 0.36 (heptane/ethyl acetate 60/40); $[\alpha]^{20}_D$ = +25.4 (c 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.80 (d, J = 8.5 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.28−7.18 (m, 4H), 5.55 (d, J = 5.0 Hz, 1H), 5.29 (t, J = 6.8 Hz, 1H), 4.86 (d, J = 9.0 Hz, 1H), 4.46 (d, J = 7.0 Hz, 2H), 4.05−4.12 (m, 1H), 2.40 (s, 3H), 2.37 (s, 3H), 2.13−2.07 (m, 1H), 2.04 (s, 3H), 2.03−1.98 (m, 1H), 1.56 (s, 3H), 1.51 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.3, 144.7, 142.9, 140.7, 137.1, 136.6, 136.0, 129.7, 129.4, 128.1, 126.9, 124.3, 123.3, 61.1, 51.0, 46.1, 25.8, 21.8, 21.7, 21.2, 18.3, 16.4; IR (neat, cm^{-1}) ν = 3229, 1732, 1596, 1443, 1232, 1151, 1105, 1089, 1016, 812; HRMS (ESI) calcd for $C_{26}H_{34}N_2O_5S_2Na$ 541.1807, found 541.1779.

(R,E)-5-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-amino-3,7-dimethylocta-2,6-dien-1-yl 2,2,2-Trichloroacetate ***3i***. Prepared following the typical amination procedure from geranyl trichloroacetate, the corresponding amination product was obtained (heptane/ethyl acetate 80/20 to 70/30) as a white crystalline solid (110 mg, 89%): >20:1 dr (^{1}H NMR evaluation); R_f = 0.50 (heptane/ethyl acetate 70/30); mp 103−106 °C; $[\alpha]^{20}_D$ = −18.6 (*c* 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.86−7.75 (m, 4H), 7.31−7.21 (m, 4H), 5.67 (d, J = 5.3 Hz, 1H), 5.36 (td, J = 1.1, 7.0 Hz, 1H), 4.89−4.82 (m, 1H), 4.77 (dd, J = 7.2, 12.1 Hz, 1H), 4.71 (dd, J = 6.6, 12.1 Hz, 1H), 4.24−4.13 (m, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.19 (dd, J = 7.1, 13.4 Hz, 1H), 2.06 (dd, J = 7.1, 13.5 Hz, 1H), 1.58 (s, 3H), 1.57 (d, J = 1.1 Hz, 3H), 1.54 (d, J = 1.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 162.1, 144.8, 143.0, 140.7, 140.5, 136.7, 136.6, 129.7, 129.4, 128.0, 126.9, 123.90, 123.86, 120.6, 65.7, 51.2, 46.1, 25.7, 21.78, 21.75, 18.4, 16.7; IR (neat, cm^{-1}) ν = 3166, 2974, 2918, 1764, 1597, 1444, 1419, 1378, 1304, 1285, 1221, 1157, 1102, 1065, 1050, 1019, 951, 883, 810, 747, 679; HRMS (ESI) calcd for $C_{26}H_{31}Cl_3N_2O_5S_2Na$ 643.0638, found 643.0618.

(R,Z)-5-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-amino-3,7-dimethylocta-2,6-dien-1-yl 3,5-Dinitrobenzoate ***3j***. Prepared following the typical amination procedure from neryl 3,5-dinitrobenzoate, the corresponding amination product was obtained (dichloromethane/ethyl acetate 98/2) as a pasty solid (108 mg, 81%): 5:1 dr (^{1}H NMR evaluation); R_f = 0.30 (dichloromethane/ethyl acetate 98/2); diastereomer A 5/*diastereomer B 1* ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.22−9.11 (m, 3H), 7.80−7.64 (m, 4H), 7.32−7.15 (m, 4H), *6.19 (d, J = 5.9 Hz, 1H),* 5.78 (d, J = 5.7 Hz, 1H), *5.70 (t, J = 7.8 Hz, 1H),* 5.54 (t, J = 7.4 Hz, 1H), *5.14 (dd, J = 8.7, 12.2 Hz, 1H),* 5.02−4.87 (m, 2H), 4.80 (dd, J = 6.6, 12.3 Hz, 1H), *4.67−4.60 (m, 1H),* 4.32−4.19 (m, 1H), *2.73 (dd, J = 8.6, 13.8 Hz, 1H),* 2.50 (dd, J = 7.1, 13.4 Hz, 1H), *2.45−2.35 (m, 1H),* 2.42 (s, 3H), *2.40 (s, 3H),* 2.38 (s, 3H), *2.37 (s, 3H),* 2.17 (dd, J = 7.5, 13.4 Hz, 1H), *1.87 (s, 3H),* 1.67 (s, 3H), 1.56 (s, 3H), 1.55 (s, 3H), *1.38 (d, J = 1.1 Hz, 3H), 1.32 (d, J = 1.1 Hz, 3H);* ^{13}C NMR (75 MHz, $CDCl_3$) δ = *163.3,* 162.8, 148.80, *148.75,* 144.8, *144.4,* 142.94, *142.86,* 140.64, *140.59,* 139.8, *139.6, 136.8,* 136.6, 136.5, *136.1,* 134.1, *129.9,* 129.74, 129.70, *129.4,* 129.32, *129.25,* 128.0, 126.8, *126.7,* 124.1, *124.0,* 122.5, *122.1,* 121.7, 63.3, *63.1,* 51.5, *50.4,* 38.5, *38.3,* 25.7, *25.5,* 24.0, *23.6,* 21.75, 21.69, 18.4, *18.0*; IR (neat, cm^{-1}) ν = 3243, 3102, 2924, 1729, 1544, 1344, 1270, 1152, 1090, 813, 720; HRMS (ESI) calcd for $C_{31}H_{34}N_4O_9S_2Na$ 693.1665, found 693.1685.

(1R,4R,6R,10S)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-4,12,12-trimethyl-9-methylene-5-azatricyclo[8.2.0.0^{4,6}]dodecane ***4***. Prepared following the typical amination procedure from *β*-(−)-caryophyllene, the aziridine **4** was obtained (dichloromethane/ethyl acetate: 100/0 to 98/2) as a white crystalline solid (29 mg, 28%): >20:1 dr (^{1}H NMR evaluation); R_f = 0.30 (dichloromethane); mp 125−128 °C; $[\alpha]^{20}_D$ = −80.1 (c 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.79−7.73 (m, 2H), 7.71−7.64 (m, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 4.93 (d, J = 1.4 Hz, 1H), 4.76 (d, J = 1.4 Hz, 1H), 3.03 (dd, J = 4.0, 11.1 Hz, 1H), 2.58 (dd, J = 9.5, 10.5 Hz, 1H), 2.41 (s, 3H), 2.36 (s, 3H), 2.27−2.17 (m, 2H), 2.06−1.95 (m, 1H), 1.93−1.82 (m, 1H), 1.81−1.52 (m, 4H), 1.51−1.35 (m, 1H), 1.30 (s, 3H), 1.31−1.18 (m, 1H), 0.99 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 151.1, 144.5, 142.3, 140.9, 137.6, 129.6, 129.0, 127.8, 126.9, 113.4, 57.7, 51.6, 49.8, 48.9, 39.7, 34.6, 34.3, 30.0, 29.8, 29.7, 27.4, 21.8, 21.6, 18.8; IR (neat, cm^{-1}) ν = 2926, 2868, 1596, 1456, 1384, 1316, 1232, 1151, 1090, 1067, 1048, 1014, 974, 915, 890, 811, 763, 709, 650; HRMS (ESI) calcd for $C_{29}H_{39}N_2O_3S_2$ 527.2402, found 527.2401.

(R)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-3-((triethylsilyl)oxy)cyclohex-2-enamine ***5a***. Prepared following the typical amination procedure from (cyclohex-1-en-1-yloxy)-triethylsilane, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a pasty solid (21 mg, 20%): 4:1 dr (^{1}H NMR evaluation); R_f = 0.22 (heptane/ethyl acetate 50/50) diastereomer A 4/*diastereomer B 1* ^{1}H NMR (300 MHz, C_6D_6) δ = 8.22 (d, J = 8.3 Hz, 2H), *7.93 (d, J = 8.3 Hz, 2H),* 7.90 (d, J = 8.3 Hz, 2H), 6.86−6.81 (m, 2H), 6.75 (d, J = 8.3 Hz, 2H), 6.47 (d, J = 8.1 Hz, 1H), *6.43 (d, J = 8.1 Hz, 1H),* 5.07 (d, J = 4.1 Hz, 1H), *4.66 (d, J = 4.1 Hz, 1H),* 4.20−4.14 (m, 1H), 4.08-*4.03 (m, 1H),* 1.89 (s, 3H), *1.88 (s, 3H), 1.85 (s, 3H),* 1.84 (s, 3H), 1.81−1.46 (m, 2H), 1.44−1.23 (m, 2H), 1.22−1.06 (m, 1H), 1.00 (t, J = 7.9 Hz, 9H), *0.90 (t, J = 7.9 Hz, 9H),* 0.67 (q, J = 7.5 Hz, 15.6 Hz, 6H), *0.54 (q, J = 7.5 Hz, 15.6 Hz, 6H)*; ^{13}C NMR (75 MHz, C_6D_6) δ = *156.0,* 155.8, 144.3, *144.2,* 142.8, *142.7,* 142.60, *142.56,* 138.7, *138.6,* 130.1, 129.7, *127.74,* 127.69, 104.5, *103.5,* 50.7, *50.4, 30.6, 30.1,* 30.0, 29.5, *21.49,* 21.46, 19.7, *19.6,* 7.4, *7.3,* 5.7, *5.6*; IR (neat, cm^{-1}) ν = 3233, 2953, 2876, 1660, 1597, 1495, 1457, 1414, 1369, 1314, 1302, 1250, 1199, 1151, 1106, 1090, 1062, 1016, 927, 897, 812, 744, 703, 657; HRMS (ESI) calcd for $C_{26}H_{37}N_2O_4S_2Si$ 533.1964, found 533.1959.

2-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-aminocycloheptanone ***6***. Prepared following the typical amination procedure from (cyclohept-1-en-1-yloxy)triethylsilane, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a pasty solid (26 mg, 30%): 199:1 dr (HPLC, Hypercarb column, 100 × 4.6 mm, 5 μm, MeCN + 0.1% HCOOH/H_2O + 0.1% HCOOH: 80/20, 1 mL min^{-1}, t_{maj} = 13.52 min); R_f = 0.37 (heptane/ethyl acetate 50/50); ^{1}H NMR (300 MHz, C_6D_6) δ = 8.21 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.5 Hz, 2H), 7.08−6.94 (m, 1H), 6.80 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 7.9 Hz, 2H), 4.40−4.35 (m, 1H), 2.09−2.04 (m, 2H), 1.85 (s, 3H), 1.81 (s, 3H), 1.77−1.70 (m, 1H), 1.43−1.36 (m, 1H), 1.24−1.14 (m, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ = 207.8, 144.7, 142.7, 142.6, 138.1, 130.2, 129.7, 128.1, 127.7, 62.5, 41.0, 32.8, 29.0, 27.1, 23.5, 21.5; IR (neat, cm^{-1}) ν = 3357, 3260, 1597, 1448, 1300, 1154, 1097, 1035, 1009, 902, 812; HRMS (ESI) calcd for $C_{21}H_{26}N_2O_4S_2Na$ 457.1232, found 457.1229.

(R)-Allyl (3-[N-(S)-(p-toluenesulfonyl)-p-toluenesulfonimidoyl]-aminocyclopent-1-en-1-yl) carbonate ***5b***. Prepared following the typical amination procedure from allyl cyclopent-1-en-1-yl carbonate, the corresponding amination product was obtained (heptane/ethyl acetate 70/30) as a pasty solid (90 mg, 92%): >20:1 dr (^{1}H NMR evaluation); R_f = 0.47 (heptane/ethyl acetate 50/50); ^{1}H NMR (500

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MHz, C_6D_6) δ = 8.23 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H), 6.82 (d, J = 8.2 Hz, 2H), 6.69 (d, J = 8.2 Hz, 2H), 5.94−5.79 (m, 1H), 5.63−5.53 (m, 2H), 5.06 (d, J = 17.4 Hz, 1H), 4.91 (d, J = 10.4 Hz, 1H), 4.28 (d, J = 5.8 Hz, 2H), 4.27−4.22 (m, 1H), 2.23−2.15 (m, 1H), 1.99−1.90 (m, 1H), 1.86 (s, 3H), 1.81 (s, 3H), 1.66−1.57 (m, 1H), 1.27−1.18 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.3, 145.1, 143.1, 136.2, 131.1, 130.1, 129.5, 128.0, 127.0, 119.9, 111.8, 69.4, 57.0, 29.7, 29.3, 21.83, 21.78; IR (neat, cm^{-1}) ν = 3224, 2925, 2856, 1766, 1645, 1596, 1437, 1383, 1313, 1304, 1284, 1220, 1211, 1152, 1108, 1087, 1014, 976, 922, 885, 813, 779, 732, 682; HRMS (ESI) calcd for $C_{23}H_{26}N_2O_6S_2Na$ 513.1130, found 513.1124.

(R)-Allyl (3-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-aminocyclohex-1-en-1-yl) carbonate ***5c***. Prepared following the typical amination procedure from allyl cyclohex-1-en-1-yl carbonate, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a pasty solid (81 mg, 80%): 9:1 dr (^{1}H NMR evaluation); R_f = 0.40 (heptane/ethyl acetate 50/50); diastereomer A 9/*diastereomer B 1* ^{1}H NMR (500 MHz, C_6D_6) δ = 8.23−8.16 (m, 2H), 7.91−7.84 (m, 2H), 6.88−6.82 (m, 2H), 6.79 (d, J = 8.2 Hz, 1H), 6.75 (d, J = 8.5 Hz, 2H), 5.73−5.69 (m,1H), 5.69−5.55 (m, 1H), *5.35−5.32 (m, 1H),* 5.14−5.05 (m, 1H), 4.98−4.91 (m, 1H), 4.35 (dd, J = 1.2 Hz, 5.5 Hz, 2H), *4.29 (dd, J = 1.2 Hz, 5.5 Hz, 2H),* 4.09−4.00 (m, 1H), *3.98−3.91 (m, 1H), 3.46−3.44 (m, 1H),* 2.02−1.92 (m, 2H), 1.90 (s, 3H), 1.89−1.85 (m, 1H), 1.84 (s, 3H), 1.42−1.27 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 152.8, 152.5, 145.1, 143.1, 140.6, 136.3, 131.3, 130.1, 129.5, 128.0, 127.0, 119.7, 114.8, 69.2, 49.0, 27.3, 26.2, 21.83, 21.76, 19.3; IR (neat, cm^{-1}) ν = 3232, 2949, 1755, 1596, 1447, 1363, 1210, 1149, 1088, 1056, 1015, 924, 882, 812, 752, 700, 655, 612; HRMS (ESI) calcd for $C_{24}H_{28}N_2O_6S_2Na$ 527.1287, found 527.1296.

(R)-Allyl (3-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-aminocyclohept-1-en-1-yl) Carbonate ***5d***. Prepared following the typical amination procedure from allyl cyclohex-1-en-1-yl carbonate, the corresponding amination product was obtained (dichloromethane/ethyl acetate 20/1) as a pasty solid (54 mg, 52%): >20:1 dr (^{1}H NMR evaluation); R_f = 0.43 (heptane/ethyl acetate 50/50); ^{1}H NMR (300 MHz, C_6D_6) δ = 8.25−8.19 (m, 2H), 7.81−7.75 (m, 2H), 6.81 (d, J = 8.1 Hz, 2H), 6.68 (d, J = 8.1 Hz, 2H), 6.26 (d, J = 8.3 Hz, 1H), 5.71 (d, J = 4.9 Hz, 1H), 5.69−5.57 (m, 1H), 5.14−5.05 (m, 1H), 4.97−4.90 (m, 1H), 4.36−4.32 (m, 2H), 4.06−3.95 (m, 1H), 2.16−2.07 (m, 2H), 1.85 (s, 3H), 1.78 (s, 3H), 1.49−1.20 (m, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ = 153.8, 153.5, 144.1, 142.1, 141.6, 137.5, 131.8, 129.8, 129.4, 127.9, 127.3, 120.8, 118.5, 68.6, 51.4, 33.2, 32.1, 27.0, 24.7, 21.1; IR (neat, cm^{-1}) ν = 3237, 2932, 1749, 1687, 1596, 1440, 1316, 1278, 1237, 1212, 1152, 1150, 1086, 1014, 993, 919, 811, 734, 684, 654; HRMS (ESI) calcd for $C_{25}H_{30}N_2O_6S_2Na$ 541.1443, found 541.1469.

(S)-Allyl (3-[N-(R)-(p-Toluenesulfonyl)-p-nitrobenzenesulfonimidoyl]aminocyclopent-1-en-1-yl) Carbonate ***5e***. Prepared following the typical amination procedure from allyl cyclopent-1-en-1-yl carbonate using (*R*)-*p*-NO$_2$-**1** and (*R*)-**2**, the corresponding amination product was obtained (heptane/ethyl acetate: 50/50) as white needles (102 mg, 98%): >20:1 dr (^{1}H NMR evaluation); R_f = 0.47 (heptane/ethyl acetate 50/50); mp 124−126 °C; $[\alpha]^{20}_D$ = −30.3 (*c* 0.53 in acetone); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.35−8.29 (m, 2H), 8.15−8.09 (m, 2H), 7.84−7.77 (m, 2H), 7.30−7.22 (m, 2H), 6.06 (d, J = 8.8 Hz, 1H), 6.00−5.85 (m, 1H), 5.49−5.44 (m, 1H), 5.42−5.34 (m, 1H), 5.33−5.28 (m, 1H), 4.65 (dt, J = 1.3, 5.9 Hz, 2H), 4.51−4.40 (m, 1H), 2.65−2.51 (m, 1H), 2.44−2.31 (m, 1H), 2.40 (s, 3H), 2.25−2.11 (m, 1H), 1.72−1.57 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 154.7, 151.7, 150.7, 145.8, 143.7, 140.0, 131.0, 129.6, 129.2, 126.9, 124.6, 120.0, 111.0, 69.4, 57.5, 29.8, 28.9, 21.8; IR (neat, cm^{-1}) ν = 3211, 2924, 1767, 1650, 1607, 1531, 1349, 1219, 1154, 1115, 1091, 1039, 1012, 945, 855, 817, 723, 682; HRMS (ESI) calcd for $C_{22}H_{22}N_3O_8S_2$ 520.0848, found 520.0855.

(R)-3-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-aminocyclohex-1-en-1-yl Trifluoromethanesulfonate ***5f***. Prepared following the typical amination procedure from cyclohexen-1-yl trifluoromethanesulfonate, the corresponding amination product was obtained (heptane/ethyl acetate 70/30) as a white solid in 70% yield and 5:1 dr (^{1}H NMR evaluation), which can be recrystallized from diisopropyl oxide leading to white needles and a 13:1 dr: R_f = 0.30 (heptane/ethyl acetate 70/30); mp 114−115 °C; diastereomer A 5/*diastereomer B 1* ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35−1.49 (m, 1H), 1.60−1.81 (m, 3H), 2.21−2.33 (m, 2H), 2.40 (s, 3H), 2.42 (s, 3H),, 3.94−4.04 (m, 1H), *5.30−5.35 (m, 1H),* 5.63−5.67 (m, 1H), 6.01 (d, J = 8.9 Hz, 1H), 7.24−7.34 (m, 4H), 7.74−7.86 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) 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; IR (neat, cm^{-1}) ν 3208, 2925, 1686, 1597, 1417, 1303, 1210, 1143, 1109, 1061, 1017, 897, 815; HRMS (ESI) calcd for $C_{21}H_{24}F_3N_2O_6S_3$ 553.0749, found 553.0757.

(R,E)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-3-styryl-cyclohex-2-enamine ***5g***. Prepared following the typical amination procedure from (2-(cyclohex-1-en-1-yl)vinyl)benzene, the corresponding amination product was obtained (heptane/ethyl acetate 90/10) as a yellow oil in 58% yield and 5:1 dr (^{1}H NMR evaluation): R_f = 0.51 (heptane/ethyl acetate 50/50); diastereomer A 5/*diastereomer B 1* ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33−1.43 (m, 1H), 1.58−1.75 (m, 3H), 2.15−2.27 (m, 2H), *2.34 (s, 3H)*, 2.39 (s, 3H), *2.41 (s, 3H)*, 2.42 (s, 3H), *3.85−3.93 (m, 1H),* 3.93−4.00 (m, 1H), *5.38−5.41 (m, 1H),* 5.71−5.74 (m, 1H), 5.85 (d, J = 8.2 Hz, 1H), *6.02 (d, J = 8.2 Hz, 1H), 6.34 (d, J = 16.2 Hz, 1H),* 6.52 (d, J = 16.2 Hz, 1H), 6.69 (d, J = 16.2 Hz, 1H),7.18−7.23 (m, 2H), 7.27−7.33 (m, 5H), 7.35−7.40 (m, 2H), 7.79−7.85 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.5, 21.56, 21.61, 23.9, 29.5, 50.1, 126.5, 126.6, 126.8, 127.6, 127.8, 128.1, 128.2, *128.3*, *128.4*, 128.7, *129.0*, 129.2, *129.7*, 129.8, 130.7, 139.7, 144.8; IR (neat, cm^{-1}) ν 3242, 2930, 1709, 1597, 1494, 1449, 1302, 1151, 1106, 1064, 910, 813; MS m/z 505 [(M − H)$^-$], HRMS (ESI) calcd for $C_{28}H_{29}N_2O_3S_2$ 505.1620, found 505.1633.

(1r,4r)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-1,4-dimethylcyclohexanamine ***8a***. Prepared following the typical amination procedure from *cis*-1,4-dimethylcyclohexane, the corresponding product was obtained (dichloromethane/ethyl acetate 20/1) as a pasty solid (56 mg, 64%): R_f = 0.53 (heptane/ethyl acetate 50/50); ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.79 (d, J = 7.9 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.25−7.20 (m, 4H), 6.17 (s, 1H), 2.39 (s, 3H), 2.38 (s, 3H), 1.77−1.70 (m, 1H), 1.67−1.60 (m, 2H), 1.57−1.44 (m, 2H), 1.39 (td, J = 4.1, 12.8 Hz, 1H), 1.35−1.25 (m, 1H), 1.16 (s, 3H), 1.01−0.93 (m, 2H), 0.82 (d, J = 6.4 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.4, 143.0, 140.6, 139.3, 129.8, 129.4, 127.8, 127.0, 60.0, 38.6, 37.9, 31.6, 31.0, 30.95, 27.9, 23.3, 21.78, 21.75; IR (neat, cm^{-1}) ν = 3235, 2925, 2861, 1597, 1495, 1447, 1380, 1312, 1301, 1277, 1245, 1148, 1089, 1060, 1015, 976, 861, 811, 755, 702, 656.; HRMS (ESI) calcd for $C_{22}H_{30}N_2O_3S_2Na$ 457.1596, found 457.1611.

(1r,3R,5S,7r)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-3,5-dimethyladamantan-1-amine ***8b***. Prepared following the typical amination procedure from dimethyladamantane, the corresponding product was obtained (dichloromethane 100%) as a white crystalline solid (81 mg, 83%): R_f = 0.30 (dichloromethane); mp 124−126 °C; $[\alpha]^{20}_D$ = +14.7 (*c* 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.85−7.74 (m, 4H), 7.30−7.21 (m, 4H), 6.09 (s, 1H), 2.42 (s, 3H), 2.40 (s, 3H), 2.05 (quint, J = 3.1 Hz, 1H), 1.67 (td, J = 2.5, 11.7 Hz, 1H), 1.55−1.15 (m, 9H), 1.06 (s, 3H), 0.772 (s, 3H), 0.767 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.4, 143.0, 140.6, 139.3, 129.7, 129.4, 127.8, 127.0, 59.2, 50.2, 49.3, 49.2, 42.3, 42.2, 41.3, 32.94, 32.88, 30.3, 30.0, 21.79, 21.77; IR (neat, cm^{-1}) ν = 3278, 2902, 1650, 1454, 1317, 1233, 1152, 1107, 1090, 1019, 815, 655; HRMS (ESI) calcd for $C_{26}H_{35}N_2O_3S_2$ 487.2089, found 487.2089.

(4r,4ar,8r,8ar,9r,10r)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-decahydro-2,8,4,6-(epibutane[1,2,3,4]tetrayl)naphthalen-2-amine ***8c***. Prepared following the typical amination procedure from diamantane, the corresponding product was obtained (dichloromethane 100%) as a white crystalline solid (49 mg, 48%): R_f = 0.35 (dichloromethane); mp 210−213 °C; $[\alpha]^{20}_D$ = +27.0 (*c* 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.86−7.74 (m, 4H), 7.29−7.20 (m, 4H), 6.10 (s, 1H), 2.41 (s, 3H), 2.40 (s, 3H), 1.86−1.56 (m, 19H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.4, 142.9, 140.6, 139.3, 129.7, 129.4, 127.9, 127.0, 56.7, 43.6, 38.7, 37.2, 36.1, 25.5, 21.8; IR (neat, cm^{-1}) ν = 3564, 3135, 2917, 1629, 1455, 1297, 1285, 1239,

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1150, 1107, 1055, 1043, 1014, 884, 814, 688, 662; HRMS (ESI) calcd for $C_{28}H_{34}N_2O_3S_2Na$ 533.1909, found 533.1907.

(1R,3S,5s,7s)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-spiro[adamantane-2,2′-[1,3]dioxolan]-5-amine **8d**. Prepared following the typical amination procedure from dioxolane adamantane, the corresponding product was obtained (dichloromethane/ethyl acetate 100/0 to 90/10) as a white foam (77 mg, 75%): R_f = 0.50 (dichloromethane/ethyl acetate 90/10); $[\alpha]^{20}_D$ = +16.9 (c 1.00 in acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ =7.84−7.75 (m, 4H), 7.29−7.21 (m, 4H), 6.14 (s, 1H), 3.88 (s, 6H), 2.41 (s, 3H), 2.40 (s, 3H), 2.16−2.08 (m, 1H), 2.03−1.65 (m, 10H), 1.55−1.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.5, 143.0, 140.6, 139.1, 129.8, 129.4, 127.9, 127.0, 109.6, 64.6, 64.5, 56.8, 42.5, 40.5, 40.0, 37.6, 37.5, 33.21, 33.19, 28.2, 21.80, 21.78; IR (neat, cm^{-1}) ν = 3238, 2921, 2858, 1596, 1448, 1300, 1285, 1258, 1148, 1088, 1055, 1014, 927, 812, 755, 725, 650; HRMS (ESI) calcd for $C_{26}H_{34}N_2O_5S_2$ 517.1831, found 517.1843.

(1R,3S,5S,7R)-[N-(S)-(p-Toluenesulfonyl)-p-toluenesulfonimidoyl]-3-methoxy-7-(methoxymethyl)bicyclo[3.3.1]nonan-1-amine **8e**. Prepared following the typical amination procedure from 3-methoxy-7-(methoxymethyl)bicyclo[3.3.1]nonane, the corresponding product was obtained (heptane/ethyl acetate 70/30 to 50/50) as a colorless pasty solid (87 mg, 88%): 2:1 dr (^{1}H NMR evaluation); R_f = 0.35 (heptane/ethyl acetate 60/40); diastereomer A 2/ *diastereomer B 1:* ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.85−7.72 (m, 4H), 7.30−7.19 (m, 4H), *6.18 (s, 1H),* 6.16 (s, 1H), 3.55−3.46 (m, 1H), 3.27 (s, 3H), *3.23 (s, 3H), 3.20 (s, 3H),* 3.19 (s, 3H), 3.09−2.96 (m, 2H), 2.40 (s, 6H), 2.27−2.09 (m, 2H), 2.07−1.56 (m, 7H), 1.42−1.15 (m, 3H), *1.06 (dd, J = 2.7, 12.0 Hz, 1H)*; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.3, *144.2,* 142.9, *142.8,* 140.6, *139.38,* 139.35, 129.70, *129.68,* 129.3, 127.64, *127.57, 126.94,* 126.92, 78.3, *78.2,* 77.4, 77.2, *77.1,* 58.8, *58.7,* 57.9, *57.8, 56.03,* 56.00, *42.7,* 42.6, 37.7, *37.6, 35.04,* 35.00, 34.90, *34.88,* 30.9, *30.7, 28.4,* 28.3, 25.79, *25.76,* 21.7; IR (neat, cm^{-1}) ν = 3232, 2928, 1597, 1450, 1301, 1286, 1254, 1149, 1102, 1072, 1051, 1016, 1006, 909, 812, 727, 702, 656; HRMS (ESI) calcd for $C_{26}H_{35}N_2O_5S_2$ 519.1988, found 519.1978.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra of all compounds. Crystallographic data and X-ray structures of **3a**,**e**,**g**,**i**, **4**, **5e**, and **8c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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†C.L. and B.D. contributed equally to this work.

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(27) Heck-type couplings with styrene or methyl acrylate have been performed using $Pd(PPh_3)_2Cl_2$.

(28) Orbital overlap of the C−C σ bonding orbital with the C−H σ antibonding orbital is allowed by their *trans* antiperiplanar disposition, thereby leading to activation of the C−H bond.

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