Asymmetric Synthesis of Amines through Rhodium-Catalyzed C–H Amination with Sulfonimidoylnitrenes

Benjamin Darses,[1,a] Amanda G. Jarvis,[1,a] Abdel-Kader Mafroud,[a,b] Geneviève Estenne-Bouhtou,[b] Gihad Dargazanli,[b] Philippe Dauban*[a]

[a] Institut de Chimie des Substances Naturelles, UPR 2301 CNRS, Centre de Recherche de Gif, Avenue de la Terrasse, 91198 Gif-sur-Yvette, France
Fax +33(1)69077247; E-mail: philippe.dauban@cnrs.fr

[b] Sanofi-Aventis Recherche et Développement, Unité Exploratoire, 1 Avenue Pierre Brossolette, 91385 Chilly-Mazarin, France

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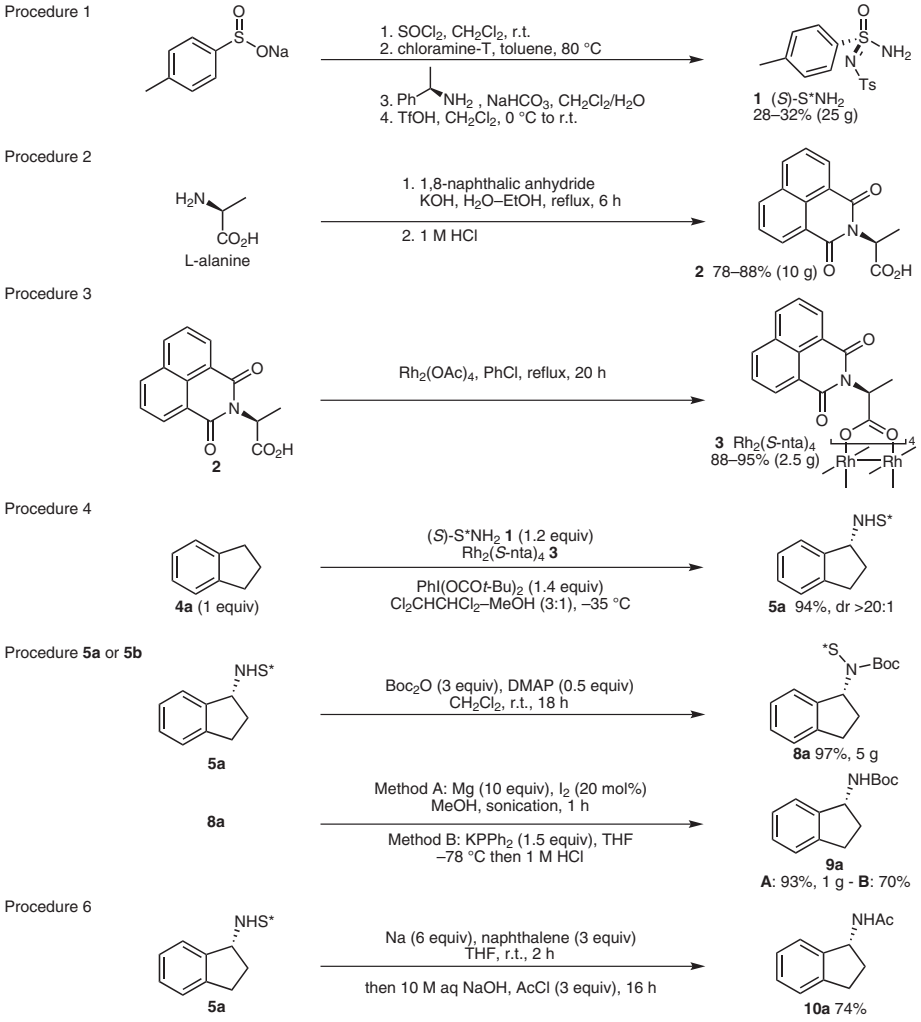
Abstract: An efficient asymmetric C–H amination of benzylic and allylic substrates, as well as of adamantane derivatives, through catalytic C–H insertion of a chiral nitrene is reported. The reaction involves a chiral rhodium(II) complex, an iodine(III) oxidant, and a sulfonimidamide as a nitrene precursor. Experimental protocols for the preparation of the reagents and the catalytic nitrene are provided. The C–H amination can provide the corresponding amino derivatives on a gram scale. Various methods for the cleavage of the sulfonimidoyl group to give the corresponding *tert*-butoxycarbonyl- or acetyl-protected optically pure amines are also described.

Key words: rhodium, amines, nitrene, asymmetric catalysis, C–H amination



Scheme 1 Procedures for the practical preparation of optically pure protected amines through catalytic C–H amination

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Introduction

The development of C–N bond-forming reactions is a research area of longstanding interest that has fundamental applications in natural-product synthesis, the life sciences, and materials science.[2] The field has been revolutionized by the recent discovery of efficient protocols for the direct conversion of C–H bonds into C–N bonds, which has streamlined the preparation of nitrogen-containing compounds. The most significant achievements, exemplified by a total synthesis of tetrodotoxin,[3] involve the use of metal-catalyzed nitrene transfers.[4] These reactions have been improved through the design of a wide range of transition-metal-complex catalysts, of which dirhodium(II) compounds are the most efficient.[5] The use of iodine(III) oxidants permits the generation of nitrenes from various nitrogen functionalities.[6] In this context, we recently reported a catalytic stereoselective intermolecular C–H amination based on a chiral nitrene generated from a matched combination of a sulfonimidamide **1** and a chiral rhodium(II) catalyst **3** (Scheme 1).[7] Starting from a substrates used as the limiting agent, benzylic or allylic C–H aminations can be performed in high yields and with excellent levels of regio-, chemo-, and stereoselectivity to give optically pure amines. Alkanes can also be functionalized efficiently under these conditions. Here, we describe some practical protocols for the preparation of the necessary reagents on a gram scale, for the subsequent catalytic C–H amination reaction, and for the removal of the sulfonimidoyl moiety (Scheme 1).

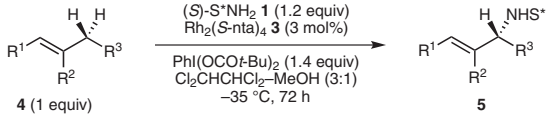
Scope and Limitation

The optically pure (*S*)-sulfonimidamide **1** can be prepared on a multigram scale in four steps, starting from 50 grams of commercially available sodium 4-toluenesulfinate (Scheme 1, procedure 1), according to a strategy adapted from a previously published procedure.[8] The overall yield of 28–32% includes the resolution of the diastereomeric mixture obtained by condensation of *N*-tosyl-4-toluenesulfonimidoyl chloride with [(1*R*)-1-phenylethyl]amine, which involves precipitation in a mixture of dichloromethane and methyl *tert*-butyl ether, followed by recrystallization from ethanol. Treatment with 1.5 equivalents of triflic acid in dichloromethane then results in the cleavage of the chiral auxiliary with a 93% yield.

The chiral rhodium(II) complex **3** can be obtained on a multigram scale from commercially available dirhodium tetraacetate by simple ligand exchange with the protected L-alanine derivative **2** in refluxing chlorobenzene (Scheme 1, procedure 3).[9] The large-scale preparation of L-alanine derivative **2**, however, proved troublesome, because application of the classical conditions for its formation (heating L-alanine in the presence of 1,8-naphthalic anhydride in *N*,*N*-dimethylformamide or dimethyl sulfoxide)[10] induced partial racemization of the chiral center. Fortunately, the use of potassium hydroxide in a refluxing mixture of ethanol and water[11] allowed the isolation of the optically pure protected alanine derivative **2** in 88% yield on a 50 mmol scale (Scheme 1, procedure 2).

Rhodium-catalyzed C–H amination proceeded efficiently at low temperature in a 3:1 mixture of 1,1,2,2-tetrachloroethane and methanol with a hydrocarbon as the limiting agent, as exemplified in Scheme 1, procedure 4.[12] Secondary benzylic and allylic positions were functionalized under these conditions in very good yields and excellent diastereomeric ratios (Table 1).[13] With regard to the absolute configuration of the product, a combination of (*S*)-**1** and (*S*)-**3** generally gives the (*R*)-benzylic or (*R*)-allylic amine, whereas the *S*-isomer is isolated with the corresponding enantiomeric pair of matched *R*-configured reagents; this has been confirmed by various X-ray crystal-structure determinations.[7] The amination of indan (**4a**; Scheme 1, procedure 4 and Table 1, entry 1) illustrates the efficiency of the process, which gives a yield of 90% and a dr of >20:1 when the reaction is carried out on a 20 mmol scale in the presence of only 0.3 mol% of rhodium catalyst **3**. The results obtained with various indan derivatives **4b–d** (entries 2–4) show that the nitrene addition process tolerates a range of useful functional groups. The moderate to good regioselectivities observed with the nonsymmetrical 1,2-diphenylethanes **4e** and **4f** demonstrate that electron-deficient nitrenes react preferentially with electron-rich C–H bonds (entries 5 and 6).

Table 1 Benzylic and Allylic C–H Aminations in the Presence of (*S*)-S*NH$_2$ (**1**)



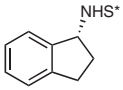
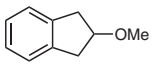
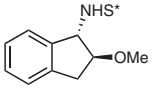
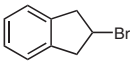
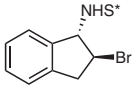
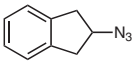
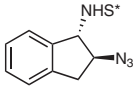
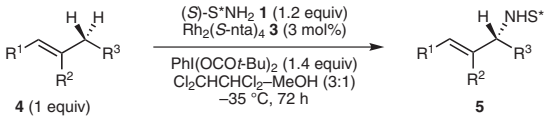
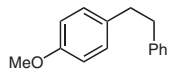
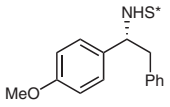
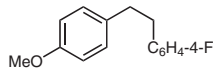
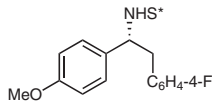
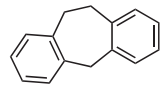
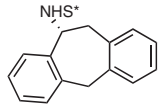
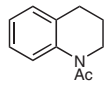
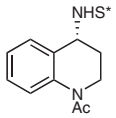
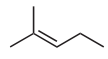
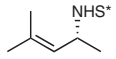
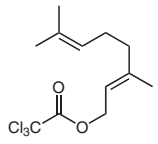
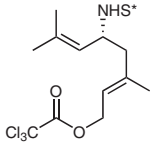
Entry[a]	Substrate	Product[b]	Yield[c] (%)	dr[d] (%)
1[e]	 **4a**	 **5a**	90	>20:1
2	 **4b**	 **6b**	94	>20:1
3[f]	 **5c**	 **5c**	70	>20:1
4	 **4d**	 **5d**	97	>20:1

Table 1 Benzylic and Allylic C–H Aminations in the Presence of (*S*)-S*NH$_2$ (**1**) (continued)



Entry[a]	Substrate	Product[b]	Yield[c] (%)	dr[d] (%)
5	 **4e**	 **5e**	83[g]	>20:1 (6.5:1)[h]
6[i]	 **4f**	 **5f**	96[g]	>20:1 (9:1)[h]
7	 **4g**	 **5g**	99	>20:1
8	 **4h**	 **5h**	70	>20:1
9	 **4i**	 **5i**	97	14:1
10	 **4j**	 **5j**	89	13:1
11	 **4k**	 **5k**	95	12:1
12	 **4l**	 **5l**	88 87[j] 65[k]	>20:1 >20:1 >20:1

[a] The reaction was performed on a 2 mmol scale unless otherwise stated.
[b] S* = (*S*)-NHS(=O)(=NTs)4-Tol
[c] Isolated yield.
[d] Determined by ^{1}H NMR spectroscopy.
[e] Reaction performed on a 20 mmol scale using 0.3 mol% of Rh catalyst **3**.
[f] Reaction performed on a 1.8 mmol scale.
[g] The regioisomers were not separated.
[h] Regioisomer ratio determined by ^{1}H NMR spectroscopy.
[i] Reaction performed on a 0.75 mmol scale.
[j] Reaction performed with 0.3 mol% of Rh catalyst **3**.
[k] Reaction performed with 0.03 mol% of Rh catalyst **3**.

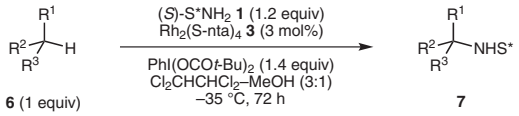
Steric factors might be responsible for discrimination between various benzylic sites within a substrate, as illustrated by the regioselective amination of 10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulene (**4g**; entry 7). The amination of 1-acetyl-1,2,3,4-tetrahydroquinoline (**4h**; entry 8) proves that the reaction can be efficiently applied to nitrogen heterocycles; however, the ring size and the position of the nitrogen atom are critical, because neither N-protected indolines nor tetrahydroisoquinolines gave satisfactory yields of the expected amines (data not shown).

In the case of allylic substrates (entries 9–12), the reaction proceeds successfully with either linear or cyclic alkenes, although lower diastereoselectivities are observed in some cases. More importantly, the absence of products arising from classical alkene aziridination[6] emphasizes the excellent chemoselectivity observed in the catalytic C–H insertion of sulfonimidoylnitrenes. Interestingly, the reaction with (+)-α-pinene (**4j**) allowed us to recover and recycle the rhodium catalyst **3**; the recycled catalyst gave compound **5j** with comparable yield and dr. In addition, C–H amination of geranyl trichloroacetate (**4l**) clearly demonstrated that the amount of rhodium complex catalyst can be reduced by an order of magnitude without diminishing the yield. Indeed, the use of as little as 0.03 mol% of catalyst **3** led to clean formation of the expected product **5l** in 65% yield.

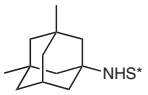
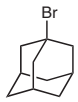
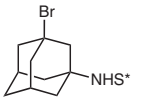
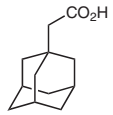
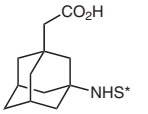
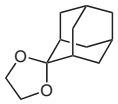
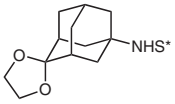
The reaction conditions reported in procedure 4 also permit efficient C–H functionalization of nonactivated alkanes selectively at tertiary positions. The reaction of adamantyl derivatives (Table 2) illustrates the high reactivity of cyclic substrates with sulfonimidoylnitrenes.[14] 1,3-Dimethyladamantane (**6a**) was efficiently converted into a protected analogue of the NMDA antagonist memantine, useful for the treatment of moderate to severe Alzheimer's disease (Table 2, entry 1). Once again, the transformation tolerates the presence of an electron-withdrawing group such as a bromo or carboxylic acid group (entries 2 and 3), whereas the result observed for ketal **6d** (entry 4) demonstrates the possibility of overriding the lack of reactivity of the corresponding ketone.

Finally, the sulfonimidoyl moiety can be cleaved without loss of enantioselectivity. Three methods have been shown to be effective in this transformation of benzylic substrates. The first two strategies rely on the activation of the N–S bond by the addition of a *tert*-butyloxycarbonyl group onto the nitrogen atom. With product **5a** this can be achieved in high yields (97%) for 10 mmol amounts of substrate. Once activated, the N–S bond can be cleaved by either the magnesium, methanol and catalytic iodine system under sonication (Scheme 1, procedure 5, method A) or by nucleophilic displacement by the diphenyl phosphide anion followed by acid workup[15] (procedure 5, method B). These methods allowed us to isolate the protected amine **9a** in 93% and 70% yield, respectively, starting from 2.5 grams of sulfonimidamide **8a**. The overall yield for the conversion of **5a** into **9a** was 68–90%, depending on the method used.[16]

Table 2 Catalytic C–H Amination Reactions of Adamantyl Derivatives



6 (1 equiv) **7**

Entry[a]	Substrate	Product	Yield[b] (%)
1			94
	6a	**7a**	
2			76
	6b	**7b**	
3			84
	6c	**7c**	
4			54
	6d	**7d**	

[a] Reaction performed on a 2 mmol scale.
[b] Isolated yield.

On moving to the allylic or adamantyl derivatives, protection of the nitrogen with the *tert*-butyloxycarbonyl group failed to give the desired product or gave it in low yield, possibly due to steric hindrance. This led us to revisit an earlier removal method based on reduction with sodium naphthalenide.[7a] Treatment of **5a** (2.5 mmol) with sodium naphthalenide followed by addition of 10 M sodium hydroxide and acetyl chloride to aid isolation of the product gave the *N*-acetyl amine **10a** in one step and 74% yield. We assume that the protection of the free amine is quantitative and, therefore, the yield that was obtained corresponds to the yield for the removal of the sulfonimidoyl moiety.

In summary, the use of sulfonimidamides as nitrene precursors in combination with a chiral dirhodium(II) catalyst permits the direct C–H amination of hydrocarbons on a gram scale with high efficiency and selectivity. The reaction provides access to optically pure protected amines, the protecting groups of which can be replaced by a simple *tert*-butoxycarbonyl or acetyl group.

Melting points were measured in capillary tubes on a Büchi B-540 apparatus and are uncorrected. IR spectra were recorded with a PerkinElmer Spectrum BX FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz or 75 MHz, respectively, on a Bruker Aspect 3000 (300 MHz) instrument. High-resolution mass spectra were obtained by using a Kratos MS-80 spectrometer. Optical rotations were determined with a JASCO P-1010 polarimeter. Chiral HPLC was performed by using a ChiralPack IA column (5 μm, 250 × 4.6 mm) in a Waters 2695 Separations Module coupled to a Waters 996 Photodiode Array Detector. All solvents were stored over 3 Å MS and purged with argon. All commercial reagents were purchased from the Aldrich Chemical Co. or Alfa Aesar, and were used without further purification.

N-[(1*S*)-Amino(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (1); Procedure 1

Sodium *p*-toluenesulfinate (50.0 g, 0.281 mol) was dried by heating under vacuum and then suspended in anhyd toluene (500 mL) at 0 °C under argon. Freshly distilled $SOCl_2$ (102 mL, 1.40 mol) was added over 5 min from an equilibrating addition funnel. After 10 min, the ice bath was removed and the mixture was stirred for 16 h at r.t. It was then concentrated under vacuum at 40 °C to give the crude 4-toluenesulfinyl chloride as a yellow slurry that was used in the next step without further purification.

Chloramine-T trihydrate was freshly dried by heating in a drying pistol at 80 °C under vacuum for 8 h. [***Caution!*** *This is liable to explode if heated to a higher temperature.*] The dried chloramine-T (64.0 g, 0.281 mol) was added to a solution of the crude 4-toluenesulfinyl chloride in anhyd toluene (600 mL). The mixture was heated at 80 °C for 4 h then concentrated under vacuum at 40 °C to afford the crude 4-toluenesulfonimidoyl chloride as a yellow slurry, which was used in the next step without further purification.

A solution of the crude 4-toluenesulfonimidoyl chloride in CH_2Cl_2 (300 mL) at 0 °C was treated with [(1*R*)-1-phenylethyl]amine (42.9 mL, 0.337 mol), followed immediately by a solution of $NaHCO_3$ (28.3 g, 0.337 mol) in H_2O (300 mL). The mixture was stirred vigorously overnight while slowly warming to r.t. After 16 h, the mixture was diluted with H_2O (200 mL) and the organic phase was decanted. The aqueous phase was extracted with CH_2Cl_2 (2 × 150 mL) and the organic layers were combined, washed with 0.1 M aq HCl (250 mL), dried (Na_2SO_4), and filtered. The filtrate was concentrated under vacuum at 40 °C to give a yellow viscous oil that was directly dissolved in CH_2Cl_2 (50 mL). *t*-BuOMe (400 mL) was immediately added and white needles began to form rapidly. After 2 h, the mixture was cooled to 0 °C for 2 h and then to –30 °C for 15 h. The white needles were collected by filtration to give the required protected sulfonimidamide; yield: 49.5 g (17:1 mixture of diastereoisomers). Recrystallization from boiling EtOH (225 mL) gave the diastereoisomerically pure protected sulfonimidamide as white needles; yield: 43.4 g (36%); mp 160–161 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.33 (dd, *J* = 6.6, 0.9 Hz, 3 H), 2.39 (s, 3 H), 2.37 (s, 3 H), 4.48 (q, *J* = 6.6 Hz, 1 H), 6.26 (s, 1 H), 7.31–7.10 (m, 9 H), 7.85–7.68 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.74, 21.77, 23.1, 54.1, 126.5, 127.0, 127.9, 128.0, 128.8, 129.4, 129.9, 136.2, 140.5, 141.8, 143.0, 144.8.

From an equilibrating funnel with a greased glass tap, TfOH (5.33 mL, 60.2 mmol) was added dropwise over 1 min to a solution of the protected sulfonimidamide (17.2 g, 40.1 mmol) in CH_2Cl_2 (55 mL) at 0 °C. After 5 min, the ice bath was removed and the orange solution was stirred at r.t. After 1 h a precipitate began to form. When the starting material had been consumed [2 h; TLC (EtOAc–CH_2Cl_2, 1:9)], the mixture was poured into PE (250 mL) to precipitate a product. The orange solid was collected by filtration and washed with H_2O (250 mL). The resulting white solid was dried under vacuum for 20 h then dissolved in boiling MeOH (100 mL). The vigorously stirred refluxing solution was treated with H_2O (300 mL) previously heated at 65 °C. The mixture was then cooled to r.t. and the resulting precipitate was collected by filtration and dried under vacuum to afford the pure sulfonimidamide **1** as an off-white solid; yield: 12.1 g (93%); mp 159–160 °C; $[\alpha]_D^{22}$ –106 (*c* 0.19, acetone).

IR (ATR, neat): 3270, 3182, 3071, 1597, 1560, 1495, 1451, 1405, 1384, 1303, 1288, 1265, 1138, 1098, 1059, 1018, 937, 811, 739, 670, 658 cm^{-1}.

^1H NMR (300 MHz, acetone-d_6): δ = 2.37 (s, 3 H), 2.41 (s, 3 H), 7.10 (br s, 2 H), 7.20–7.29 (m, 2 H), 7.30–7.37 (m, 2 H), 7.61–7.71 (m, 2 H), 7.73–7.83 (m, 2 H).

^{13}C NMR (75 MHz, acetone-d_6): δ = 21.4, 21.5, 127.3, 127.8, 129.8, 130.3, 140.2, 142.5, 143.0, 144.8.

HRMS [ESI(+)]: *m/z* $[M + H]^+$ calcd for $C_{14}H_{17}N_2O_3S_2$: 325.0675; found: 325.0691.

(2*S*)-2-(1,3-Dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)propanoic Acid [(*S*)-nta]; Procedure 2

Lightly crushed pellets of KOH (2.8 g, 50 mmol) were added to a solution of L-alanine (4.9 g, 55 mmol) in H_2O (63 mL), and the mixture was stirred at r.t. for 20 min. EtOH (188 mL) and 1,8-naphthalic anhydride (9.9 g, 50 mmol) were added to give a cream-colored suspension. The mixture was refluxed for 6.5 h, and then cooled slightly to about 80 °C. 1 M aq HCl (50 mL) was added and the mixture was stirred for 10 s and then left to stand for 16–48 h. The beige needle crystals were collected by filtration, washed sequentially with H_2O (4 × 120 mL) and ice-cold EtOH (120 mL), and dried in vacuo; yield: 11.7 g [88%, >99% ee (HPLC)]; mp 262–264 °C; $[\alpha]_D^{20}$ –25 (*c* 0.30, MeOH).

HPLC: IA column (250 × 4.6 mm, 5 μm), heptane–EtOH (60:40) + 0.1% HCO_2H, 35 °C, 0.9 mL/min; R_t = 15.1 min.

IR (ATR, neat): 1715, 1670, 1664, 1623, 1587, 1437, 1367, 1328, 1231, 1189, 1103, 1035, 966, 891, 852, 783, 676, 657 cm^{-1}.

^1H NMR (300 MHz, DMSO-d_6): δ = 1.56 (d, *J* = 7.0 Hz, 3 H), 5.60 (q, *J* = 7.0 Hz, 1 H), 7.82 (dd, *J* = 7.8, 7.6 Hz, 2 H), 8.40 (d, *J* = 7.8 Hz, 2 H), 8.45 (d, *J* = 7.6 Hz, 2 H), 12.73 (s, 1 H).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 14.6, 48.5, 121.7, 127.26, 127.29, 131.1, 131.2, 134.7, 162.9, 171.5.

HRMS [ESI(–)]: *m/z* $[M - H]^-$ calcd for $C_{15}H_{10}NO_4$: 268.0610; found: 268.0621.

Dirhodium Tetrakis{(2*S*)-2-(1,3-dioxo-1*H*-benzo[*de*]isoquinolin-2(3*H*)-yl)propanoic acid} {Rh_2[(*S*)-nta]$_4$}; Procedure 3

$Rh_2(OAc)_4$ (1.00 g, 2.26 mmol) and (*S*)-nta (2.92 g, 10.8 mmol) were placed in a 500 mL round-bottomed flask fitted with a condenser and a Soxhlet extractor filled with one-third sand and two-thirds anhyd Na_2CO_3 by weight (55 g total). PhCl (250 mL) was added, ensuring that the contents of the Soxhlet extractor were thoroughly wetted. The mixture was then heated at 165 °C for 23 h. The solvent was removed and the product was eluted through a short column of alumina (200 g) with MeOH–CH_2Cl_2 (1:20, 500 mL) followed by MeOH–CH_2Cl_2 (1:9, 100 mL). The solvent was removed and the dark-green solid was washed with CH_2Cl_2 (20 mL) to remove any grease, then dried in vacuo at 150 °C overnight to give an olive-green solid; yield: 2.55 g (88%); mp 330–331 °C; $[\alpha]_D^{26}$ +127.0 [*c* 0.10, MeOH–$CHCl_3$ (1:9)].

IR (ATR, neat): 2937, 1702, 1660, 1587, 1411, 1377, 1339, 1295, 1239, 1193, 1097, 1034, 969, 889, 845, 777, 683 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$ + 1 drop CD_3OD): δ = 1.71 (d, *J* = 6.9 Hz, 12 H), 5.89 (q, *J* = 6.9 Hz, 4 H), 7.73 (dd, *J* = 8.2, 7.3 Hz, 8 H), 8.12 (d, *J* = 8.2 Hz, 8 H), 8.60 (d, *J* = 7.3 Hz, 8 H).

^{13}C NMR (75 MHz, $CDCl_3$ + 1 drop CD_3OD): δ = 15.2, 50.7, 122.6, 127.0, 128.1, 131.48, 131.53, 133.9, 163.5, 188.5.

HRMS [ESI(–)]: *m/z* $[M + HCO_2]^-$ calcd for $C_{61}H_{41}N_4O_{18}Rh_2$: 1323.0531; found: 1323.0549.

Anal. Calcd for $C_{60}H_{40}N_4O_{16}Rh_2 \cdot CH_2Cl_2$: C, 53.72; H, 3.10; N, 4.11. Found: C, 53.80; H, 3.43; N, 4.16.

***N*-[(Substituted Amino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamides; General Procedure (Procedure 4)**

The sulfonimidamide **1** (1.2 equiv, 2.4 mmol), Rh_2[(*S*)-nta]$_4$ (**3**; 3 mol%, 0.06 mmol), 4 Å MS (1 g), and the substrate (1 equiv, 2 mmol, introduced either as a solid or as a solution in the reaction solvent) were placed in a carousel tube (Radleys Discovery Technologies) under argon. $Cl_2CHCHCl_2$ (7.5 mL) and MeOH (2.5 mL) were added and the mixture was stirred until everything dissolved. The mixture was then cooled to –78 °C, and $PhI(OPiv)_2$ (1.4 equiv, 2.8 mmol) was added as a solid. The reaction vessels were placed in the carousel and stirred at –35 °C for 3 d. The solvent was removed in vacuo and the products were isolated by column chromatography (silica gel). Diastereoisomeric ratios of the products were determined by ^1H NMR spectroscopic analysis.

***N*-[(2,3-Dihydro-1*H*-inden-1-ylamino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5a)**

Prepared by the general procedure from indan (2.45 mL, 20 mmol). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (1:20)] as a white solid; yield: 7.89 g (90%; dr >20:1); mp 168–169 °C; $[\alpha]_D^{22}$ +82.5 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3227, 1593, 1478, 1425, 1316, 1304, 1242, 1213, 1183, 1155, 1105, 1066, 1014, 989, 941, 906, 814, 752, 740, 703, 679, 656 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.76–1.60 (m, 1 H), 2.20–2.08 (m, 1 H), 2.41 (s, 3 H), 2.43 (s, 3 H), 2.74–2.64 (m, 1 H), 2.90–2.80 (m, 1 H), 4.80 (app q, *J* = 7.9 Hz, 1 H), 6.06 (br d, *J* = 8.7 Hz, 1 H), 7.37–7.12 (m, 8 H), 7.85 (dd, *J* = 8.5, 8.2 Hz, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.78, 21.84, 30.2, 33.8, 58.6, 124.8, 124.9, 127.0, 127.3, 128.1, 128.7, 129.4, 130.1, 136.3, 140.6, 141.3, 142.9, 143.1, 145.0.

HRMS [ESI(+)]: *m/z* $[M + H]^+$ calcd for $C_{23}H_{25}N_2O_3S_2$: 441.1307; found: 441.1322.

***N*-[(2-Methoxy-2,3-dihydro-1*H*-inden-1-ylamino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5b)**

Prepared by the general procedure from 2-methoxyindan (296 mg). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (1:20)] as a light-brown solid; yield: 881 mg (94%; dr >20:1); mp 115–116 °C; $[\alpha]_D^{26}$ +105.0 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3179, 1594, 1447, 1301, 1256, 1186, 1149, 1124, 1102, 1056, 991, 947, 807, 764, 747, 700, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 3 H), 2.43 (s, 3 H), 2.65 (dd, *J* = 15.8, 6.4 Hz, 1 H), 3.00 (s, 3 H), 3.18 (dd, *J* = 15.8, 6.9 Hz, 1 H), 3.81 (app q, *J* = 6.4 Hz, 1 H), 4.72 (dd, *J* = 8.1, 5.9 Hz, 1 H), 6.50 (d, *J* = 8.3 Hz, 1 H), 7.17–7.10 (m, 1 H), 7.28–7.21 (m, 4 H), 7.30 (d, *J* = 8.4 Hz, 2 H), 7.46–7.39 (m, 1 H), 7.83 (d, *J* = 8.4 Hz, 2 H), 7.88 (d, *J* = 8.5 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.78, 21.82, 36.0, 57.3, 63.2, 87.7, 125.2, 125.3, 127.0, 127.8, 128.3, 129.2, 129.5, 129.7, 136.7, 138.6, 139.5, 140.6, 143.1, 144.8.

HRMS [ESI(+)]: *m/z* $[M + H]^+$ calcd for $C_{24}H_{27}N_2O_4S_2$: 471.1412; found: 471.1397.

HRMS [ESI(–)]: *m/z* $[M - H]^-$ calcd for $C_{24}H_{25}N_2O_4S_2$: 469.1256; found: 469.1245.

***N*-[(2-Bromo-2,3-dihydro-1*H*-inden-1-ylamino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5c)**

Prepared by the general procedure from 2-bromoindan (353 mg, 1.8 mmol). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (1:20)] as an off-white solid; yield: 730 mg, (70%; dr >20:1); mp 152–154 °C (dec.); $[\alpha]_D^{26}$ +157.4 (*c* 0.98, $CHCl_3$).

IR (ATR, neat): 3228, 1598, 1439, 1426, 1324, 1254, 1156, 1126, 1094, 1061, 1017, 939, 878, 805, 756, 741, 699, 657 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 2.44 (s, 3 H), 3.10 (dd, *J* = 16.5, 7.0 Hz, 1 H), 3.48 (dd, *J* = 16.5, 7.3 Hz, 1 H), 4.12 (app q, *J* = 6.8 Hz, 1 H), 4.93 (dd, *J* = 8.5, 6.2 Hz, 1 H), 6.66 (d, *J* = 8.5 Hz, 1 H), 7.20–7.13 (m, 1 H), 7.28–7.23 (m, 4 H), 7.31 (d, *J* = 8.4 Hz, 2 H), 7.54–7.42 (m, 1 H), 7.82 (d, *J* = 8.3 Hz, 2 H), 7.91 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 21.9, 41.4, 50.7, 67.2, 124.6, 125.4, 127.0, 128.3, 128.6, 129.5 (2 C), 130.0, 136.0, 139.1, 140.1, 140.5, 143.3, 145.4.

HRMS [ESI(–)]: *m/z* [M – H]$^-$ calcd for $C_{23}H_{22}BrN_2O_3S_2$: 517.0255 (100), 519.0235 (97); found: 517.0276 (90), 519.0260 (100).

_N_-[(2-Azido-2,3-dihydro-1_H_-inden-1-ylamino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5d)

Prepared by the general procedure from 2-azidoindan (318 mg). The product was obtained by column chromatography [heptane–EtOAc (70:30)] as a white foamy solid; yield: 932 mg (97%, dr >20:1); mp 140–142 °C; $[\alpha]_D^{26}$ + 91.5 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3213, 3028, 2922, 2102, 1596, 1444, 1257, 1148, 1104, 1050, 812, 748 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3 H), 2.44 (s, 3 H), 2.76 (dd, *J* = 15.8, 7.6 Hz, 1 H), 3.23 (dd, *J* = 15.8, 7.5 Hz, 1 H), 3.84–3.96 (m, 1 H), 4.58–4.68 (m, 1 H), 6.70 (d, *J* = 9.0 Hz, 1 H), 7.12–7.19 (m, 1 H), 7.21–7.37 (m, 6 H), 7.44–7.51 (m, 1 H), 7.78–7.86 (m, 2 H), 7.88–7.96 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 21.9, 36.1, 63.4, 68.0, 124.9, 125.3, 127.0, 128.23, 128.25, 129.45, 129.50, 130.0, 136.0, 138.4, 138.7, 140.4, 143.3, 145.4.

HRMS [ESI(+)]: *m/z* [M + H]$^+$ calcd for $C_{23}H_{24}N_5O_3S_2$: 481.1315; found: 481.1316.

_N_-[{[1-(4-Methoxyphenyl)-2-phenylethyl]amino}(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5e)

Prepared by the general procedure from 1-methoxy-4-(2-phenylethyl)benzene (425 mg). The product was obtained by column chromatography [heptane–EtOAc (80:20 to 70:30)] as a white foamy solid; yield: 1.03 g (96%, dr >20:1, 6.5:1 regioisomeric ratio).

IR (ATR, neat): 3235, 3025, 2925, 1612, 1514, 1301, 1247, 1149, 1106, 1090, 1033, 811, 747 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 2.36 (s, 3 H), 2.87–2.96 (m, 2 H), 3.77 (s, 3 H),* 3.78 (s, 3 H), 4.34–4.44 (m, 1 H), 6.37 (d, *J* = 7.1 Hz, 1 H), 6.41 (d, *J* = 7.4 Hz, 1 H),* 6.60–6.68 (m, 2 H),* 6.73–6.82 (m, 2 H), 6.83–6.93 (m, 2 H), 7.01–7.22 (m, 9 H), 7.41–7.49 (m, 2 H), 7.64–7.73 (m, 2 H). * Independent peaks for the minor regioisomer.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (2 C), *43.2*,* 44.1, *55.36*, 55.44, 59.4, *60.1*,* 113.98, *114.04*,* 126.89, 126.92, 127.8, 128.2, *128.6*,* 128.7, 129.3, 129.5, *129.6*,* 129.7, *130.4*,* 132.7, 135.5, 136.6, 140.4, 142.9, 144.4, 159.2. * Independent peaks for the minor regioisomer.

HRMS [ESI(+)]: *m/z* [M + H]$^+$ calcd for $C_{29}H_{31}N_2O_4S_2$: 535.1720; found: 535.1723.

_N_-[({1-(4-Methoxyphenyl)-2-[4-(trifluoromethyl)phenyl]ethyl}amino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5f)

Prepared by the general procedure from 1-methoxy-4-{2-[4-(trifluoromethyl)phenyl]ethyl}benzene (210 mg, 0.75 mmol). The product was obtained by column chromatography [EtOAc–heptane (2:8 then 3:7)] as a white solid; yield: 436 mg (96%, dr >20:1, 9:1 regioisomeric ratio); mp 67–68 °C; $[\alpha]_D^{26}$ + 108.5 (*c* 1.00, $CHCl_3$)

IR (ATR, neat): 3213, 2934, 1612, 1514, 1419, 1323, 1301, 1247, 1149, 1106, 1066, 1038, 1016, 810, 760, 702, 669 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 6 H), 3.09–2.87 (m, 2 H), 3.76 (s, 3 H),* 3.79 (s, 3 H), 4.49–4.35 (m, 1 H), 6.47 (d, *J* = 7.2 Hz, 1 H),* 6.66 (d, *J* = 8.0 Hz, 2 H),* 6.71 (d, *J* = 8.0 Hz, 1 H), 6.79 (d, *J* = 8.5 Hz, 2 H), 7.06–6.97 (m, 4 H), 7.19–7.09 (m, 4 H), 7.30 (d, *J* = 8.2 Hz, 2 H), 7.45 (d, *J* = 8.3 Hz, 2 H), 7.67 (d, *J* = 8.3 Hz, 2 H), 7.74 (d, *J* = 6.9 Hz, 2 H).* * Independent peaks for the minor regioisomer.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6, 21.7, 43.7, 55.5, 59.6, 114.2, 124.4 (q, *J* = 271 Hz), 125.4 (q, *J* = 4 Hz), 126.9, 127.7, 128.2, 129.0 (q, *J* = 33 Hz), 129.4, 129.6, 129.8, 132.6, 135.7, 140.4, 141.2, 143.0, 144.6, 159.4.

HRMS [ESI(–)]: *m/z* [M – H]$^-$ calcd for $C_{30}H_{28}F_3N_2O_4S_2$: 601.1443; found: 601.1451.

_N_-[(10,11-Dihydro-5_H_-dibenzo[_a_,_d_][7]annulen-10-ylamino)(4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5g)

Prepared by the general procedure from 10,11-dihydro-5*H*-dibenzo[*a*,*d*][7]annulene (389 mg). The product was obtained by column chromatography [heptane–EtOAc (70:30)] as an off-white foamy solid; yield: 1.02 g (99%, dr >20:1); mp 71–73 °C; $[\alpha]_D^{26}$ + 33.9 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3227, 3024, 2925, 1596, 1493, 1446, 1302, 1259, 1151, 1107, 1089, 1026, 814, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H), 2.47 (s, 3 H), 2.72 (dd, *J* = 14.4, 7.5, Hz, 1 H), 3.14 (dd, *J* = 14.4, 3.5 Hz, 1 H), 3.86 (d, *J* = 15.4 Hz, 1 H), 4.14 (d, *J* = 15.5 Hz, 1 H), 4.94–5.03 (m, 1 H), 5.63 (d, *J* = 8.9 Hz, 1 H), 6.67–6.73 (m, 1 H), 7.06–7.23 (m, 8 H), 7.33–7.47 (m, 3 H), 7.70–7.78 (m, 2 H), 7.86–7.94 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 21.9, 37.7, 41.2, 54.4, 126.9, 127.1, 127.4, 127.5, 128.0, 128.2, 128.6, 129.4, 130.0, 130.2 (2 C), 132.3, 134.6, 136.4, 137.3, 137.7, 140.6, 140.7, 143.0, 145.1.

HRMS [ESI(+)]: *m/z* [M + H]$^+$ calcd for $C_{29}H_{29}N_2O_3S_2$: 517.1614; found: 517.1636.

_N_-[[(1-Acetyl-1,2,3,4-tetrahydroquinolin-4-yl)amino](4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5h)

Prepared by the general procedure from 1-acetyl-1,2,3,4-tetrahydroquinoline (351 mg). The product was obtained by a modified work-up procedure to remove residual Rh. After removal of the solvent, the residue was dissolved in CH_2Cl_2 (25 mL) and stirred with sat. aq thiourea (15 mL) for 1 h. The organic layer washed with phosphate buffer (pH 7, 0.1 M aq $Na_2HPO_4{\cdot}KH_2PO_4$, 15 mL), and the resulting aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The organic layers were combined, washed with phosphate buffer (pH 7, 100 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by column chromatography [silica gel, EtOAc–CH_2Cl_2 (1:9 to 3:9)] to give an off-white solid; yield: 691 mg (70%; dr >1:20);[17] mp 173–174 °C; $[\alpha]_D^{26}$ +110.2 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3167, 1626, 1580, 1493, 1401, 1304, 1254, 1207, 1153, 1108, 1075, 1042, 1017, 966, 929, 886, 812, 798, 764, 750, 701, 659 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.90–1.72 (m, 2 H), 2.19 (s, 3 H), 2.41 (s, 3 H), 2.44 (s, 3 H), 3.66–3.48 (m, 1 H), 3.83–3.66 (m, 1 H), 4.55–4.43 (m, 1 H), 6.42 (br s, 1 H), 7.41–7.07 (m, 7 H), 7.52 (d, *J* = 7.1 Hz, 1 H), 7.96–7.67 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7, 21.8, 23.4, 30.9, 40.8, 50.3, 124.6, 125.8, 126.9, 127.8, 128.2, 128.3, 129.4, 130.1, 136.6, 138.4, 140.6, 143.1, 145.0, 170.4; 1 C not observed.

HRMS [ESI(–)]: *m/z* [M – H]$^-$ calcd for $C_{25}H_{26}N_3O_4S_2$: 496.1365; found: 496.1368.

_N_-[[(3-Methylcyclohex-2-en-1-yl)amino](4-tolyl)oxido-λ^4-sulfanylidene]tosylamide (5i)

Prepared by the general procedure from 1-methylcyclohexene (0.24 mL). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (2:98 to 1:20)] as an off-white solid; yield: 780 mg (97%; dr 14:1); mp 145–148 °C; $[\alpha]_D^{26}$ +113.0 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3251, 2946, 1597, 1445, 1421, 1377, 1316, 1303, 1286, 1240, 1156, 1103, 1085, 1071, 1043, 1017, 998, 924, 905, 847, 819, 811, 735, 703, 679, 655 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.61–1.28 (m, 4 H), 1.67 (s, 3 H), 1.95–1.78 (m, 2 H), 2.41 (s, 3 H), 2.43 (s, 3 H), 3.70 (s, 1 H),* 3.82 (br s, 1 H), 5.05–4.99 (m, 1 H),* 5.38–5.33 (m, 1 H), 5.84 (d, *J* = 8.2 Hz, 1 H), 7.33–7.18 (m, 4 H), 7.88–7.76 (m, 4 H). * Independent peaks for the minor diastereomer.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.6, 21.7, 21.8, 23.8, 29.1, 29.6, 49.8, 121.4, 126.9, 128.0, 129.3, 129.9, 136.7, 140.1, 140.7, 142.9, 144.7.

HRMS [ESI(–)]: *m/z* $[M - H]^-$ calcd for $C_{21}H_{25}O_3N_2S_2$: 417.1307; found: 417.1331.

_N_-{(4-Tolyl)(oxido)[(4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-yl)amino]-λ⁴-sulfanylidene}tosylamide (5j)

Prepared by the general procedure from (*S*)-α-pinene (319 μL). The product was isolated by chromatography [CH_2Cl_2–EtOAc (100:0 to 98:2)] as a white foamy solid; yield: 812 mg (89%, dr 13:1); mp 55–57 °C; $[\alpha]_D^{20}$ –69.5 (*c* 1.00, acetone).

IR (ATR, neat): 3236, 2920, 1596, 1420, 1300, 1245, 1150, 1104, 1088, 1016, 1000, 811 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.76 (s, 3 H), 1.23–1.28 (m, 1 H), 1.28 (s, 3 H), 1.63 (s, 3 H), 1.95–2.02 (m, 1 H), 2.16–2.25 (m, 1 H), 2.32 (td, *J* = 9.5, 5.5 Hz, 1 H), 2.38 (s, 3 H), 2.42 (s, 3 H), 3.74–3.84 (m, 1 H), 4.80–4.85 (m, 1 H), 6.03 (d, *J* = 9.01 Hz, 1 H), 7.17–7.32 (m, 4 H), 7.73–7.85 (m, 4 H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.5, 21.6, 21.7, 22.8, 26.4, 28.7, 44.5, 46.6, 47.1, 54.2, 115.0, 126.9, 127.8, 129.2, 129.9, 136.5, 140.6, 142.8, 144.6, 150.5.

HRMS [ESI(+)]: *m/z* $[M + Na]^+$ calcd for $C_{24}H_{30}N_2NaO_3S_2$: 481.1596; found: 481.1588.

_N_-[[(1,3-Dimethylbut-2-en-1-yl)amino](4-tolyl)oxido-λ⁴-sulfanylidene]tosylamide (5k)

Prepared by the general procedure from 2-methylpent-2-ene (0.244 mL). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (2:98 to 1:20)] as an off-white oil; yield: 774 mg (95%; dr 12:1); $[\alpha]_D^{26}$ +23.5 (*c* 0.97, $CHCl_3$).

IR (ATR, neat): 3239, 2930, 1735, 1596, 1495, 1448, 1375, 1302, 1250, 1149, 1106, 1088, 1059, 1016, 980, 916, 811, 752, 702, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.6 Hz, 3 H), 1.55 (d, *J* = 1.1 Hz, 3 H), 1.59 (d, *J* = 1.2 Hz, 3 H), 2.39 (s, 3 H), 2.41 (s, 3 H), 4.25–4.05 (m, 1 H), 4.72–4.63 (m, 1 H),* 5.00–4.88 (m, 1 H), 5.76 (d, *J* = 5.6 Hz, 1 H), 5.98–5.91 (m, 1 H),* 7.23 (d, *J* = 7.9 Hz, 2 H), 7.26 (d, *J* = 7.9 Hz, 2 H), 7.87–7.70 (m, 4 H). * Independent peaks for the minor diastereomer.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.3, 21.7, 21.8, 22.1, 25.7, 48.9, 125.6, 127.0, 128.0, 129.4, 129.8, 135.7, 136.9, 140.7, 142.9, 144.7.

HRMS [ESI(–)]: *m/z* $[M - H]^-$ calcd for $C_{20}H_{25}N_2O_3S_2$: 405.1307; found: 405.1299.

(2*E*)-3,7-Dimethyl-5-{[*S*-(4-tolyl)-*N*-tosylsulfonimidoyl}amino]octa-2,6-dien-1-yl Trichloroacetate (5l)

Prepared by the general procedure from geranyl trichloroacetate (599 mg). The product was isolated by column chromatography [heptane–EtOAc (80:20 to 60:40)] as a white crystalline solid; yield: 1.09 g (88%, dr >20:1); mp 103–106 °C; $[\alpha]_D^{20}$ –18.5 (*c* 1.00, acetone).

IR (ATR, neat): 3166, 2974, 2918, 1764, 1597, 1444, 1419, 1378, 1304, 1285, 1221, 1157, 1102, 1065, 1050, 1019, 951, 883, 810, 747, 679 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.53 (d, *J* = 1.1 Hz, 3 H), 1.56 (d, *J* = 1.1 Hz, 3 H), 1.58 (s, 3 H), 2.06 (dd, *J* = 13.5, 7.1 Hz, 1 H), 2.19 (dd, *J* = 13.4, 7.1 Hz, 1 H), 2.39 (s, 3 H), 2.42 (s, 3 H), 4.13–4.24 (m, 1 H), 4.67–481 (m, 2 H), 4.82–4.89 (m, 1 H), 5.36 (td, *J* = 7.0, 1.1 Hz, 1 H), 5.67 (d, *J* = 5.3 Hz, 1 H), 7.21–7.31 (m, 4 H), 7.75–7.86 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.7, 18.4, 21.75, 21.78, 25.7, 46.1, 51.2, 65.7, 120.6, 123.86, 123.90, 126.9, 128.0, 129.4, 129.7, 136.6, 136.7, 140.5, 140.7, 143.0, 144.8, 162.1.

HRMS [ESI(+)]: *m/z* $[M + Na]^+$ calcd for $C_{26}H_{31}Cl_3N_2NaO_5S_2$: 643.0638; found: 643.0618.

_N_-[[(3,5-Dimethyl-1-adamantyl)amino](4-tolyl)oxido-λ⁴-sulfanylidene]tosylamide (7a)

Prepared by the general procedure from 1,3-dimethyladamantane (371 μL). The product was isolated by column chromatography (CH_2Cl_2) as a white solid; yield: 864 mg (94%); mp 124–126 °C; $[\alpha]_D^{20}$ +14.7 (*c* 1.00, acetone).

IR (ATR, neat): 3278, 2902, 1650, 1454, 1317, 1233, 1152, 1107, 1090, 1019, 815, 655 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.767 (s, 3 H), 0.772 (s, 3 H), 1.06 (s, 2 H), 1.15–1.55 (m, 9 H), 1.67 (td, *J* = 11.7, 2.5 Hz, 1 H), 2.05 (quint, *J* = 3.1 Hz, 1 H), 2.40 (s, 3 H), 2.42 (s, 3 H), 6.09 (s, 1 H), 7.21–7.30 (m, 4 H), 7.74–7.85 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.77, 21.79, 30.0 (2 C), 30.3, 32.88, 32.94, 41.3, 42.2, 42.3, 49.2, 49.3, 50.2, 59.2, 127.0, 127.8, 129.4, 129.7, 139.3, 140.6, 143.0, 144.4.

HRMS [ESI(+)]: *m/z* $[M + H]^+$ calcd for $C_{26}H_{35}N_2O_3S_2$: 487.2089; found: 487.2089.

_N_-[[(3-Bromo-1-adamantyl)amino](4-tolyl)oxido-λ⁴-sulfanylidene]tosylamide (7b)

Prepared by the general procedure from 1-bromoadamantane (430 mg). The product was obtained by column chromatography [heptane–EtOAc (80:20 to 70:30)] as an off-white foam; yield: 820 mg (76%); mp 68–71 °C; $[\alpha]_D^{26}$ +70.4 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3224, 2916, 2860, 1596, 1452, 1300, 1285, 1148, 1102, 1056, 973, 812, 749 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.45–1.64 (m, 2 H), 1.66–1.77 (m, 2 H), 1.79–1.89 (m, 2 H), 2.07–2.24 (m, 6 H), 2.34–2.47 (m, 8 H), 6.33 (s, 1 H), 7.21–7.32 (m, 4 H), 7.74–7.86 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (2 C), 32.4 (2 C), 33.9, 40.7, 41.1, 47.36, 47.43, 53.9, 59.1, 62.0, 127.0, 127.7, 129.3, 129.8, 138.9, 140.4, 143.0, 144.5.

HRMS [ESI(+)]: *m/z* $[M + H]^+$ calcd for $C_{24}H_{30}BrN_2O_3S_2$: 537.0876 (100), 539.0856 (97); found: 537.0880 (90), 539.0872 (100).

(3-{[*S*-(4-Tolyl)-*N*-(tosyl)sulfonimidoyl]amino}-1-adamantyl)acetic Acid (7c)

Prepared by the general procedure from 1-adamantanylacetic acid (389 mg). The product was isolated by using a modified workup. Purification by column chromatography [silica gel EtOAc–CH_2Cl_2 (1:9) + 1% HCO_2H] gave an off-white solid; 917 mg (89%; 84% corrected for contamination with the sulfonimidamide). An analytical sample was obtained by crystallization (*i*-PrOH–PE); mp 139–141 °C; $[\alpha]_D^{26}$ +55.9 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3239, 2909, 2850, 1701, 1598, 1450, 1284, 1237, 1149, 1103, 1083, 1052, 976, 815, 761, 744, 700, 668, 654 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.52 (br m, 6 H), 1.65–1.56 (m, 1 H), 1.88–1.68 (m, 5 H), 2.14–1.99 (m, 4 H), 2.40 (s, 3 H), 2.41 (s, 3 H), 6.38 (s, 1 H), 7.25 (app d, *J* = 8.5 Hz, 4 H), 7.79 (app t, *J* = 7.8 Hz, 4 H); the acid proton was not observed.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.77, 21.79, 29.66, 29.69, 34.9, 35.0, 40.6, 40.8, 42.0, 42.1, 47.4, 47.7, 58.1, 127.0, 127.8, 129.4, 129.8, 139.2, 140.5, 143.0, 144.5, 179.4.

HRMS [ESI(–)]: *m/z* $[M - H]^-$ calcd for $C_{26}H_{31}N_2O_5S_2$: 515.1674; found: 515.1678.

HRMS [ESI(+)]: *m/z* [M + NH_4]$^+$ calcd for $C_{26}H_{36}N_3O_5S_2$: 534.2096; found: 534.2102.

_N_-[(4-Tolyl)(oxido)(5′*H*-spiro[1,3-dioxolane-2,2′-tricyclo[3.3.1.1^{3,7}]decan]-5′-ylamino)-λ^4-sulfanylidene]tosylamide (7d)

Prepared by the general procedure from spiro[2,2′-adamantane-1,3-dioxolane] (388 mg). The product was isolated by column chromatography [CH_2Cl_2 then EtOAc–CH_2Cl_2 (1:20)] as a white solid; yield 557 mg (54%) + 116 mg of recovered starting material (30%); mp 74–75 °C; $[\alpha]_D^{26}$ +72.9 (*c* 0.91, $CHCl_3$).

IR (ATR, neat): 3229, 2910, 1567, 1447, 1386, 1300, 1286, 1247, 1148, 1089, 1054, 1015, 984, 927, 875, 812, 755, 721, 702, 656 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.55–1.42 (m, 2 H), 1.89–1.65 (m, 8 H), 2.04–1.90 (m, 2 H), 2.17–2.09 (m, 1 H), 2.41 (s, 3 H), 2.42 (s, 3 H), 3.89 (s, 4 H), 6.15 (s, 1 H), 7.33–7.18 (m, 4 H), 7.79 (d, *J* = 8.4 Hz, 2 H), 7.82 (d, *J* = 8.3 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.57, 21.58, 28.0, 33.0 (2 C), 37.3, 37.4, 39.8, 40.3, 42.2, 56.5, 64.3, 64.4, 109.4, 126.8, 127.7, 129.2, 129.6, 138.9, 140.4, 142.8, 144.3.

HRMS [ESI(+)]: *m/z* [M + H]$^+$ calcd for $C_{26}H_{33}N_2O_5S_2$: 517.1831; found: 517.1829.

HRMS [ESI(–)]: *m/z* [M – H]$^-$ calcd for $C_{26}H_{31}N_2O_5S_2$: 515.1674; found: 515.1678.

***tert*-Butyl 2,3-Dihydro-1*H*-inden-1-yl[*S*-(4-tolyl)-*N*-(tosyl)sulfonimidoyl]carbamate (8a); Procedure 5 (Part 1)**

Anhyd N_2-purged CH_2Cl_2 (100 mL) and Boc_2O (6.55 g, 30 mmol) were added sequentially to a round-bottomed flask containing the substrate **5a** (4.41 g, 10 mmol) and DMAP (0.61 g, 5 mmol) under argon, and the mixture was stirred for 18 h at r.t. The solvent was removed in vacuo and the crude product was purified by column chromatography [silica gel, CH_2Cl_2 then EtOAc–CH_2Cl_2 (2:98)] to give a white solid; yield: 5.23 g (97%); mp 61–63 °C; $[\alpha]_D^{26}$ +101.2 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 2980, 1730, 1596, 1460, 1369, 1323, 1247, 1151, 1106, 1078, 1016, 870, 812, 750, 700, 674, 655 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 9 H), 2.39 (s, 3 H), 2.44 (s, 3 H), 2.78–2.63 (m, 1 H), 3.00–2.85 (m, 1 H), 3.08 (ddd, *J* = 15.8, 10.3, 3.0 Hz, 1 H), 6.21 (dd, *J* = 9.0, 7.9 Hz, 1 H), 7.39–7.05 [m with two underlying d; 7.31 (d, *J* = 8.2 Hz) and 7.26 (d, *J* = 8.2 Hz), 8 H], 7.92 (d, *J* = 8.3 Hz, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8, 21.9, 27.6, 30.5, 31.0, 64.6, 84.9, 123.9, 124.9, 126.8, 126.96, 127.01, 127.8, 128.3, 129.7, 136.7, 141.1, 141.5, 142.3, 143.1, 145.2, 149.9.

HRMS [ESI(+)]: *m/z* [M + K]$^+$ calcd for $C_{28}H_{32}KN_2O_5S_2$: 579.1390; found: 579.1390.

***tert*-Butyl (1*R*)-2,3-Dihydro-1*H*-inden-1-ylcarbamate (9a); Procedure 5 (Part 2)**

Method A. Mg (1.12 mg, 46.2 mmol) and I_2 (243 mg, 20 mol%, 0.92 mmol) were added to a solution of carbamate **8a** (2.50 g, 4.62 mmol) in MeOH (46 mL), and the resulting suspension was sonicated. After 1 h, the mixture was filtered through Celite (~24 g), which was washed with MeOH (100 mL). Silica gel (20 g) was immediately added to the mixture for dry loading onto a column. Automatic column chromatography [silica gel (160 g), EtOAc–heptane (1:9)] gave a white solid; yield: 1.01 g (93%).

Method B. A 0.5 M solution of $KPPh_2$ in THF (13.9 mL, 6.93 mmol) was added to a solution of carbamate **8a** (2.50 g, 4.62 mmol) in degassed anhyd THF (46 mL) at –78 °C under argon. While the mixture was stirred for 2.5 h at –78 °C, its color changed from orange to yellow. 1 M aq HCl (23 mL) was then added dropwise at –78 °C and the mixture was stirred for a further 45 min at r.t. Sat. aq $NaHCO_3$ solution (100 mL) was added and the mixture was extracted with EtOAc (3 × 100 mL). The organic extracts were combined, dried (Na_2SO_4), filtered, and concentrated in vacuo. Automatic column chromatography [silica gel (120 g, dry loading), heptane then EtOAc–heptane (1:9)] gave a white solid; yield: 0.74 g (70%); mp 82–83 °C; $[\alpha]_D^{26}$ +40.4 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3379, 2969, 2931, 1684, 1506, 1484, 1459, 1387, 1360, 1319, 1275, 1237, 1161, 1053, 1028, 942, 895, 870, 837, 780, 766, 753 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.50 (s, 9 H), 1.79 (dddd, *J* = 12.8, 8.6, 8.3, 8.1 Hz, 1 H), 2.58 (dddd, *J* = 12.8, 8.2, 8.1, 4.1 Hz, 1 H), 3.04–2.75 (m, 2 H), 4.83–4.40 (br m, 1 H), 5.20 (td, *J* = 7.4, 7.4 Hz, 1 H), 7.26–7.17 (m, 3 H), 7.37–7.28 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.7, 30.3, 34.6, 56.2, 79.6, 124.2, 124.9, 126.9, 128.0, 143.4, 143.8, 155.9.

HRMS [ESI(+)]: *m/z* [2M + H]$^+$ calcd for $C_{28}H_{39}N_2O_4$: 467.2910; found: 467.2902.

***N*-[(1*R*)-2,3-Dihydro-1*H*-inden-1-yl]acetamide (10a); Procedure 6**

A flame-dried round-bottomed flask was charged with Na (345 mg, 15 mmol) and naphthalene (961 mg, 7.5 mmol) under argon. Degassed anhyd THF (10 mL) was added and the mixture was stirred at r.t. for 4 h to give a dark-green solution. A solution of substrate **5a** (1.10 g, 2.5 mmol) in degassed anhyd THF (15 mL) was added dropwise, and the color changed from dark-green to dark-brown. The mixture was stirred for 2 h at r.t. then cooled to 0 °C. H_2O (2–3 drops) was added to give a white suspension, followed by 10 M aq NaOH (12.5 mL) and AcCl (0.54 mL, 7.5 mmol). The mixture was allowed to warm to r.t. and after 18 h it was filtered through Celite. Sat. aq NaCl (10 mL) was added, and the aqueous layer was extracted with EtOAc (3 × 25 mL). The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated. Automatic column chromatography [silica gel (120 g, wet loaded with CH_2Cl_2) gradient EtOAc–heptane (4:6 to 6:4)] gave a white solid; yield: 324 mg (74%); mp 153–154 °C; $[\alpha]_D^{26}$ +73.3 (*c* 1.00, $CHCl_3$).

IR (ATR, neat): 3283, 2961, 2930, 1631, 1545, 1480, 1458, 1436, 1370, 1289, 1211, 1151, 1123, 1052, 1039, 1023, 993, 929, 770, 749, 730, 717 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.80 (dddd, *J* = 12.9, 8.8, 8.0, 7.1 Hz, 1 H), 2.02 (s, 3 H), 2.58 (dtd, *J* = 12.9, 7.8, 4.3 Hz, 1 H), 3.05–2.75 (m, 2 H), 5.46 (dt, *J* = 8.4, 7.4 Hz, 1 H), 5.78 (br s, 1 H), 7.36–7.12 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.6, 30.4, 34.3, 55.0, 124.2, 125.0, 127.0, 128.2, 143.4, 143.6, 170.0.

HRMS [ESI(+)]: *m/z* [M + H]$^+$ calcd for $C_{11}H_{14}NO$: 176.1075; found: 176.1075.

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(12) Replacement of $(CHCl_2)_2$ by CH_2Cl_2 led to a slight decrease in the yields.

(13) Whereas primary benzylic positions can be aminated, albeit with lower yields (see ref. 7b), tertiary benzylic sites do not generally react under these conditions as a consequence of steric hindrance.

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(16) Both the addition of the Boc group and the cleavage of the N–S bond by Mg/MeOH are substrate dependent. For example, on replacing **5a** with **5g**, the desired product is only obtained (0.2 mmol, 60%) on changing the solvent from MeOH to NH_4Cl/MeOH.

(17) In cases where Rh contamination was still observed after column chromatography, the product could be dissolved in CH_2Cl_2 and filtered through a pad of activated charcoal on Celite, without loss of material (0.2 mmol scale). Filtration before and after column chromatography without the use of the thiourea solution was not sufficient to completely remove Rh contamination.

