New Initiation Modes for Directed Carbonylative C-C Bond Activation: Rhodium-Catalyzed (3+1+2) Cycloadditions of Aminomethylcyclopropanes

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Supporting Information

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**General Experimental Details.** Starting materials sourced from commercial suppliers were used as received unless otherwise stated. Dry solvents, where necessary, were obtained by distillation using standard procedures or by passage through a column of anhydrous alumina using equipment from Anhydrous Engineering based on the Grubb’s design.\(^1\) Petrol refers to the fraction of petroleum ether boiling in the range of 40-60 °C. The removal of solvents *in vacuo* was achieved using both a Büchi rotary evaporator (bath temperatures up to 45 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at r.t.. Reactions requiring anhydrous conditions were run under an atmosphere of dry nitrogen or argon; glassware, syringes and needles were either flame dried immediately prior to use or placed in an oven (200 °C) for at least 2 h and allowed to cool either in a desiccator or under an atmosphere of nitrogen or argon; liquid reagents, solutions or solvents were added *via* syringe through rubber septa; solid reagents were added *via* Schlenk type adapters. Commerically available Merck Kieselgel 60F\(_{254}\) aluminium backed plates were used for TLC analysis. Visualisation was achieved by either UV fluorescence, basic KMnO\(_4\) solution and heat. Flash column chromatography (FCC) was performed using silica gel (Aldrich 40-63 µm, 230-400 mesh). The crude material was applied to the column as a solution in CH\(_2\)Cl\(_2\) or by pre-adsorption onto silica, as appropriate. Melting points were determined using a Reichert melting point table and temperature controller and are uncorrected. Infra-red spectra were recorded in the range 4000-600 cm\(^{-1}\) on a Perkin Elmer Spectrum either as neat films or solids compressed onto a diamond window. Abbreviations used are: w (weak), m (medium) or s (strong). NMR spectra were recorded using either a Varian 400 MHz or Varian 500 MHz spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm), coupling constants (\(J\)) are given in Hz to the nearest 0.5 Hz. Other abbreviations used are s (singlet), d (doublet), t (triplet), m (multiplet) and br. (broad). \(^1\)H and \(^{13}\)C NMR spectra were referenced to the appropriate residual solvent peak. \(^{19}\)F spectra were referenced to CCl\(_3\)F as an external standard, \(^{31}\)P spectra were referenced to H\(_3\)PO\(_4\) as external standards. Assignments of \(^1\)H NMR and \(^{13}\)C NMR signals were made, where possible, using COSY, HMQC, HMBC, NOE and TOCSY experiments. Where mixtures of isomers (e.g. diastereomers and/or rotamers) have been characterized together, they are referred to as A and B. *Numbering systems for NMR signal assignments are specified on the structure and are not related to those used for the compound names.* Mass spectra were determined by the University of Bristol mass spectrometry service by either electron impact (ESI\(^+\)) or chemical ionization (CI\(^+\)) using a Fisons VG Analytical Autospec spectrometer.
Experimental Procedures and Data

**General Procedure A for protection of cyclopropylmethanamines**

To a stirred solution of cyclopropylamine (100 mol%) and triethylamine (120 mol%) in dichloromethane (0.2 M) was added the corresponding acid chloride/sulfonyl chloride (120 mol%) dropwise over 10 minutes at 0 °C under an atmosphere of nitrogen. The mixture was warmed to r.t. and stirred overnight. The mixture was diluted with water (10 mL/mmol) and extracted with dichloromethane (3 × 10 mL/mmol). Organic extracts were combined, washed with brine (10 mL/mmol), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography under the conditions noted to yield the desired product.

**General Procedure B for alkylation of protected cyclopropylmethanamines**

To a solution of NaH (500 mol%, 60 % dispersion in mineral oil) in THF (0.3 M) was added a solution of protected aminocyclopropane (100 mol%) in THF (2.0 M) and the reaction was stirred at r.t. for 1 h. Allyl bromide (500 mol%) or (bromomethyl)cyclopropane (200 mol%) was added dropwise over 5 minutes at 0 °C and the reaction was stirred at r.t. for 18 h. Water (5 mL/mmol) was added and the mixture was extracted with Et₂O (3 × 2 mL/mmol). Then the organic extracts were combined, washed with brine (5 mL/mmol), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography under the conditions noted to yield the desired product.

**General Procedure C for preparation of substituted cyclopropylcarboxamides from substituted cyclopropanecarboxylic acid**

To an ice-cold stirring solution of allylamine (100 mol%), EDCI (110 mol%) and DMAP (100 mol%) in anhydrous CH₂Cl₂ (0.5 M) under an atmosphere of nitrogen was added substituted cyclopropanecarboxylic acid (110 mol%) in CH₂Cl₂ (2.0 M) dropwise over 5 minutes. The mixture was warmed to r.t. and stirred overnight. Then the mixture was concentrated in vacuo and suspended in aq. 1M NaOH (5 mL/mmol) and extracted with EtOAc (3 × 5 mL/mmol). The organic extracts were combined and washed with 1M HCl (5 mL/mmol), brine (5 mL/mmol), dried over Na₂SO₄ and concentrated in vacuo to yield the desired product which was pure enough to be used without further purification.

**General Procedure D for reduction of substituted cyclopropylcarboxamides**
Substituted cyclopropylcarboxamides (100 mol%) in anhydrous THF (0.2 M) was added dropwise to an ice-cold suspension of LiAlH₄ (150 mol%) in THF (2.0 M) over 5 minutes. The solution was warmed to r.t. and then heated at reflux for 18 h. The reaction was cooled to r.t. and carefully added H₂O (0.5 mL/mmol), aq. 4M NaOH (0.5 mL/mmol), and H₂O (2 mL/mmol), and stirred for 0.5 h. Then the crude mixture was filtered through a pad of Celite®, the filtrate was extracted with Et₂O (3 × 5 mL/mmol) and the organic extracts combined and washed with brine (5 mL/mmol), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography under the conditions noted to yield desired product.

**General Procedure E for protection of substituted cyclopropylmethanamines**

To a solution of cyclopropylmethanamine (100 mol%) in anhydrous toluene (0.2 M) was added potassium carbonate (200 mol%) and benzyl chloroformate/ sulfonyl chloride (200 mol%). The reaction mixture was heated to 50 °C and stirred overnight. The suspension was cooled to r.t. and water (10 mL/mmol) was added, the aqueous layer was extracted with EtOAc (3 × 10 mL/mmol) and the organic extracts combined, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography under the conditions noted to yield the desired product.

**General Procedure F for addition of Grignard reagent to imines**

To a solution of imine (100 mol%) in THF (0.2 M) at -78 °C was added BF₃·Et₂O (110 mol%) over 5 minutes, and the solution was stirred for 15 mins at -78 °C. Then the corresponding Grignard reagent (120 mol%) was added dropwise over 10 minutes. The solution was stirred at -78 °C for 6 h and then quenched with acetic acid (0.5 mL/mmol). The solution was warmed to r.t. and sat. aq. NaHCO₃ solution (15 mL/mmol) was added. The mixture was extracted with Et₂O (3 × 15 mL/mmol) and the organic extracts were combined, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography to yield the desired compound.

**General Procedure G (‘Conditions A’)**:

An oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(cod)Cl]₂ (3.75 mol%) and AsPh₃ (7.5 mol%), the tube was fitted with a rubber septum and purged with argon. Then cyclopropylmethanamine substrates (100 mol%) in anhydrous mesitylene (0.18
M) was added by syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated in vacuo and purified by flash column chromatography under the conditions noted to afford the desired product.

**General Procedure H (‘Conditions B’):**

An oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(CO)$_2$Cl]$_2$ (5.0 mol%), Na$_2$SO$_4$ (20.0 mol%), the tube was fitted with a rubber septum and purged with argon. Cyclopropylmethanamine substrates (100 mol%) in anhydrous mesitylene (0.3 M) was added by syringe, then 1,4-oxathiane (30 mol%) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated in vacuo and purified by flash column chromatography under the conditions noted to afford the desired product.

**Ethyl (cyclopropylmethyl)carbamate**

![Chemical Structure](attachment:image.png)

**General procedure A:** Cyclopropylmethylamine (0.82 g, 11.5 mmol) and ethyl carbonochloridate (1.21 mL, 12.7 mmol) were employed, the crude mixture was purified by flash column chromatography (0-30 % EtOAc/hexane) to afford the title compound (1.60 g, 97 %) as a colourless oil; $\nu_{\text{max}}$ / cm$^{-1}$: 3330 (m), 1691 (s), 1525 (s), 1242 (s), 1136 (m), 1030 (s); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 4.85 (1H, br. m), 4.07 (2H, q, $J = 7.0$ Hz), 3.07 (2H, br. t, $J = 6.5$ Hz), 1.20 (3H, t, $J = 7.0$ Hz), 0.91 (1H, m), 0.47 – 0.43 (2H, m), 0.16 – 0.13 (2H, m); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 156.7, 60.1, 45.9, 14.7, 11.1, 3.3; $m/z$ (CI$^+$) HRMS: Calculated for C$_7$H$_{14}$NO$_2$: 144.1025. Found [M+H]$^+$: 144.1021.

**Ethyl butyl(cyclopropylmethyl)carbamate (4a)**
To a solution of ethyl (cyclopropylmethyl)carbamate (1.30 g, 9.1 mmol), NaOH (2.72 g, 68.2 mmol), K$_2$CO$_3$ (2.82 mg, 20.5 mmol) and NBu$_4$HSO$_4$ (308 mg, 0.9 mmol) in toluene (45 mL) was added 1-bromobutane (2.93 mL, 27.3 mmol). The reaction mixture was heated at reflux for 18 h and then cooled to r.t. Water (100 mL) was added and the solution was extracted with Et$_2$O (3 × 30 mL). The organic extracts were combined, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (5-10 % EtOAc/hexane) to afford the title compound 4a (975 mg, 54 %) as a colourless oil; $\nu_{\text{max}}$/ cm$^{-1}$: 1693 (s), 1470 (m), 1421 (m), 1250 (m), 1169 (s), 1018 (m); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 4.11 (2H, q, $J$ = 7.0 Hz), 3.28 (2H, br. $t$, $J$ = 7.5 Hz), 3.17 – 3.06 (2H, br. $m$), 1.56 – 1.48 (2H, m), 1.34 – 1.23 (5H, m), 1.00-0.89 (4H, m), 0.50 – 0.45 (2H, m), 0.23 – 0.16 (2H, br. m); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 156.6, 61.0, 51.4, 47.2, 46.6*, 30.7, 30.4*, 20.2, 14.9, 14.0, 10.4, 3.6. *Doubling of some peaks due to two different conformers in solution. m/z (Cl$^+$) HRMS: Calculated for C$_{11}$H$_{22}$NO$_2$: 200.1651. Found [M+H$^+$]: 200.1648.

(E)-Ethyl but-2-en-1-yl(butyl)carbamate and (E)-ethyl but-1-en-1-yl(butyl)carbamate (10a)

To a sealed tube containing [Rh(cod)$_2$]BF$_4$ (10.2 mg, 0.025 mmol) and triphenylphosphine (19.8 mg, 0.076 mmol) under an argon atmosphere was added carbamate 4a (100 mg, 0.503 mmol) in anhydrous toluene (5.0 mL). The tube was sealed and heated to 140 °C for 4 h. The reaction was cooled to r.t. and concentrated in vacuo. An in situ yield of alkene 10a-A (11%) and vinyl carbamate 10a-B (74%) was obtained by $^1$H NMR against 1,4-dinitrobenzene as an
The residue was purified by flash column chromatography (0-3 % EtOAc/toluene) to afford vinyl carbamate 10a-B (73 mg, 73 %) as a colourless oil and alkene 10a-A (8 mg, 8 %, mixture of stereoisomers in a 3:1 (A:B) ratio) as colourless oils.

Data for alkene 10a-A: $\nu_{\text{max}}$ / cm$^{-1}$: 2959 (m), 1696 (s), 1467 (m), 1420 (m), 1380 (m), 1223 (s), 1149 (m), 1095 (m); $^1$H NMR (CD$_3$CN, 400 MHz): $\delta$ 5.67-5.60 (2H, m, 1 × C2-H, A+B), 5.49 – 5.40 (2H, m, 1 × C3-H, A+B), 4.08 (4H, q, $J = 7.0$ Hz, 2 × C6-H$_2$, A+B), 3.91 (1H, br. d, $J = 6.5$ Hz, 1 × C4-H$_2$, B), 3.78 (2H, br. d, $J = 6.0$ Hz, 1 × C4-H$_2$, A), 3.20 (4H, t, $J = 7.5$ Hz, 2 × C8-H$_2$, A+B), 1.70 (6H, dd, $J = 6.5$, 1.5 Hz, 3 × C1-H$_3$, A+B), 1.54 – 1.48 (4H, m, 2 × C9-H$_2$, A+B), 1.34 – 1.27 (4H, m, 2 × C10-H$_2$, A+B), 1.23 (6H, t, $J = 7.0$ Hz, 3 × C7-H$_3$, A+B), 0.96 – 0.93 (6H, m, 3 × C11-H$_3$, A+B); $^{13}$C NMR (CD$_3$CN, 100 MHz): $\delta$ 157.1 (C5, A+B), 126.3 (C4), 111.2 (C3), 62.1 (C6), 44.0 (C4, B), 31.1 (C9), 23.9 (C1), 19.6 (C7), 14.9, 14.4, 13.7 (C1, C7 and C11); m/z HRMS: (Cl$^+$) Calculated for C$_{11}$H$_{22}$NO$_2$: 200.1651. Found [M+H]$^+$: 200.1656.

Data for vinyl carbamate 10a-B: $\nu_{\text{max}}$ / cm$^{-1}$: 2960 (m), 1703 (s), 1661 (m), 1464 (m), 1411 (s), 1320 (m), 1245 (m), 1152 (s), 1030 (m); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 6.82 (1H, br. m, 1 × C4-H), 5.02 (1H, dt, $J = 14.5$, 6.5 Hz, 1 × C3-H), 4.17 (2H, q, $J = 7.0$ Hz, 2 × C6-H$_2$), 3.51 (2H, t, $J = 7.5$ Hz, 2 × C8-H$_2$), 2.11-2.06 (2H, m, 2 × C2-H$_2$), 1.54 (2H, tt, $J = 7.5$, 6.5 Hz, 2 × C9-H$_2$), 1.38-1.31 (2H, m, 2 × C10-H$_2$), 1.28 (3H, t, $J = 7.0$ Hz, 3 × C7-H$_3$), 1.02 (3H, t, $J = 7.5$ Hz, 3 × C11-H$_3$), 0.96 (3H, t, $J = 7.5$ Hz, 3 × C11-H$_3$); $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 126.3 (C4), 111.2 (C3), 62.1 (C6), 43.9 (C8), 29.7 (C9), 23.9 (C2), 20.3 (C10), 14.9, 14.4, 13.7 (C1, C7 and C11); m/z HRMS: (Cl$^+$) Calculated for C$_{11}$H$_{22}$NO$_2$: 200.1651. Found [M+H]$^+$: 200.1645.

Ethyl butyl(2-methylallyl)carbamate (10a’)}
To a sealed tube containing [Rh(cod)Cl]$_2$ (6.2 mg, 0.012 mmol) and PPh$_3$ (19.8 mg, 0.076 mmol) under an argon atmosphere was added carbamate 4a (100 mg, 0.503 mmol) in anhydrous toluene (5.0 mL). The tube was sealed and heated to 140 °C for 4 h. The reaction was cooled to r.t. and concentrated in vacuo. An in situ yield was obtained by $^1$H NMR against 1,4-dinitrobenzene as an internal standard; a 3% yield of alkene 10a' and 93% of remaining starting material 4a were observed. Extending the reaction time to 60 h resulted in a 26% in situ yield of alkene 10a', however, the product could not be readily separated from the starting material, the structure of alkene 10a' was determined by analysis of the $^1$H NMR of the reaction mixture.

Data for alkene 10a': Characteristic peaks only: $^1$H NMR (CDCl$_3$, 400 MHz): δ 4.83-4.76 (2H, m, 2 × C$_2$-H$_2$), 3.80 (2H, br. m, 2 × C$_4$-H$_2$), 1.67 (3H, s, 3 × C$_1$-H$_3$).

**Benzyl cyclopropyl(cyclopropylmethyl)carbamate (4b)**

To a solution of NaH (0.20 g, 5.0 mmol, 60% dispersion in mineral oil) in THF (5.0 mL) was added a solution of benzyl cyclopropylcarbamate (0.38 g, 2.5 mmol) (prepared according to literature procedure$^2$) in THF (10 mL) and the reaction was stirred at r.t. for 1 h. (Bromomethyl)cyclopropane (0.65 g 5.0 mmol) was added dropwise over 5 mintues at r.t. and the reaction was heated to 50 °C and stirred for 12 h. Water (10 mL) was added and the mixture was extracted with Et$_2$O (3 × 5 mL), the organic extracts were combined, washed with brine (10 mL), dried over Na$_2$SO$_4$ and concentrated in vacuo. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 4b (0.44
g, 90 %) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 3081 (m), 1698 (s), 1453 (m), 1408 (s), 1277 (s), 1151 (m); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.46 – 7.17 (5H, m), 5.15 (2H, s), 3.15 (2H, d, \( J = 6.9 \) Hz), 2.70 (1H, tt, \( J = 7.2, 3.9 \) Hz), 1.11 – 0.94 (1H, m), 0.82 – 0.73 (2H, m), 0.66 – 0.56 (2H, m), 0.50 – 0.42 (2H, m), 0.26 – 0.15 (2H, m); \(^1^3\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 157.5, 137.0, 128.4, 127.8, 127.7, 66.9, 52.4, 29.1-28.8(m), 10.0, 8.3, 3.4; \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{15}\)H\(_{19}\)NO\(_2\)Na: 268.1308. Found [M+Na\(^+\)]: 268.1302.

Benzyl \((E)-(\text{cyclopropylmethyl})\text{ (prop-1-en-1-yl)carbamate} \text{ and Benzyl } (((E)-\text{but-2-en-1-yl} \text{)) (\((E)-\text{prop-1-en-1-yl})\text{carbamate} \ (11a \text{ and } 11b)\n
Two oven dried reaction tubes (tube I and tube II), fitted with a magnetic stirrer, was charged with [Rh(cod)\(_2\)]BF\(_4\) (4.10 mg, 0.01 mmol) and PPh\(_3\) (7.86 mg, 0.03mmol). The tubes were fitted with a rubber septum and purged with argon. Benzyl cyclopropyl(cyclopropylmethyl)carbamate 4b (49.20 mg, 0.20 mmol) in anhydrous toluene (2 mL) was added via syringe to each tube. The mixtures then were heated at 140 °C for 1h for tube I, and 3h for tube II. Then the reactions were cooled to r.t., concentrated in vacuo and purified by flash column chromatography (10 % EtOAc/Hex), respectively, the desired products were obtained as a mixture (for tube I, 92 %, 11a/11b=13/1, for tube II, 90 %, 11a/11b =7/3). The products 11a and 11b could not be readily separated by column chromatography. The structure of the 11a and 11b were determined by analysis of the \(^1\)H NMR of the mixture and corroborated by COSY data.

Data for 11a: Characteristic peaks only: \(^1\)H NMR (400 MHz, CD\(_3\)CN, 65 °C): \( \delta \) 5.21 (2H, s, 2 × C5-H\(_2\)), 5.14 (1H, dq, \( J = 14.4, 6.6 \) Hz, 1 × C7-H), 3.48 (2H, d, \( J = 6.7 \) Hz, 2 × C3-H\(_2\)), 1.14 (1H, tt, \( J = 8.1, 6.6, 5.0 \) Hz, 1 × C2-H), 0.50 – 0.40 (2H, m, 2 × C1-H\(_2\)), 0.34 – 0.18 (2H, m, 2 × C1-H\(_2\)); \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{15}\)H\(_{19}\)NO\(_2\)Na: 268.1308. Found [M+Na\(^+\)]: 268.1295.
Data for 11b: Characteristic peaks only: $^1$H NMR (400 MHz, CD$_3$CN, 65 °C): $\delta$ 5.68 – 5.56 (1H, m, 1 $\times$ C2-H), 5.53 – 5.42 (1H, m, 1 $\times$ C3-H), 5.21 (2H, s, 1 $\times$ C6-H$_2$), 5.05 (2H, dq, $J$ = 13.2, 6.5 Hz, 1 $\times$ C8-H), 4.15 – 4.06 (2H, m, 2 $\times$ C4-H$_2$). $m/z$ (ESI$^+$) HRMS: Calculated for C$_{15}$H$_{19}$NO$_2$Na: 268.1308. Found [M+Na]$^+$: 268.1312.

**N-(Cyclopropylmethyl)pyridin-2-amine**

To a solution of cyclopropylmethanamine (1.42 g, 20 mmol) in DMSO (60 mL) at r.t. was added K$_2$CO$_3$ (5.52 g, 40 mmol) and 2-fluoropyridine (2.91 g, 30 mmol). The solution was stirred at 120 °C for 24 h and were cooled to r.t., then quenched with H$_2$O (60 mL) and extracted with EtOAc (2 $\times$ 60 mL), the organic extracts were combined, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash column chromatography (10 % EtOAc/Hex) to yield the title compound (0.70 g, 24 %) as a colorless solid; m.p.: 43 – 45 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 3270 (m), 3006 (m), 1600 (s), 1501 (m), 1444 (m), 1285 (m), 904 (s); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.11 – 7.98 (1H, m), 7.45 – 7.34 (1H, m), 6.54 (1H, ddd, $J$ = 7.2, 5.0, 1.1 Hz), 6.40 – 6.32 (1H, m), 4.64 (1H, br. s), 3.11 (2H, dd, $J$ = 6.9, 5.7 Hz), 1.15 – 1.00 (1H, m), 0.56 – 0.50 (2H, m), 0.29 – 0.16 (2H, m); $^{13}$C NMR: (100 MHz, CDCl$_3$): $\delta$ 158.8, 148.2, 137.3, 112.7, 106.6, 47.2, 10.8, 3.4; $m/z$ (ESI$^+$) HRMS: Calculated for C$_9$H$_{13}$N$_2$: 149.1073. Found [M+H]$^+$: 149.1077.

**N-Allyl-N-(cyclopropylmethyl)pyridin-2-amine (6a)**

General procedure B: N-(Cyclopropylmethyl)pyridin-2-amine (0.32 g, 2.1 mmol) and allyl bromide (1.26 g, 10.5 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6a (0.33 g, 85 %) as a colorless oil; $\nu_{\text{max}}$ / cm$^{-1}$: 3076 (m), 3004 (m), 1592 (s), 1485 (s), 1435 (m), 1244 (m), 977 (m); $^1$H NMR (500 MHz, CDCl$_3$, 50 °C): $\delta$ 8.22 – 8.02 (1H, m), 7.46 – 7.31 (1H, m), 6.62 –
6.41 (2H, m), 5.86 (1H, ddt, $J = 17.2, 10.2, 5.1$ Hz), 5.21 – 5.04 (2H, m), 4.17 (2H, dd, $J = 5.2, 1.8$ Hz), 3.42 (2H, d, $J = 6.5$ Hz), 1.14 – 1.01 (1H, m), 0.58 – 0.39 (2H, m), 0.32 – 0.19 (2H, m); $^{13}$C NMR: (127 MHz, CDCl$_3$, 50 °C): δ 158.3, 147.9, 136.9, 134.5, 115.7, 111.4, 106.0, 52.1, 50.7, 9.7, 3.6; m/z (ESI$^+$) HRMS: Calculated for C$_{12}$H$_{17}$N$_2$: 189.1386. Found [M+H]$^+$: 189.1393.

3-(Cyclopropylmethyl)-1,1-dimethylurea

![Diagram of 3-(Cyclopropylmethyl)-1,1-dimethylurea]

**General procedure A:** Cyclopropylmethylamine (3.00 g, 42.0 mmol) and dimethylcarbamyl chloride (4.64 mL, 50.4 mmol) were employed, the crude mixture was recrystallized from Et$_2$O/Hex to yield the title compound (5.89 g, 80%) as a colorless solid; m.p.: 62 – 64 °C (EtOAc/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 3309 (s), 2919 (s), 1616 (s), 1532 (s), 1363 (s), 1223 (s); $^1$H NMR (400 MHz, CDCl$_3$): δ 4.53 (1H, br.s), 3.00 – 2.97 (2H, m), 2.83 (6H, s), 0.88 (1H, m), 0.41 – 0.37 (2H, m), 0.12 – 0.08 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 158.5, 45.8, 36.1, 11.3, 3.2; m/z (ESI$^+$) HRMS: Calculated for C$_7$H$_{14}$N$_2$: 165.1001. Found [M + Na]$^+$: 165.0998.

1-Allyl-1-(cyclopropylmethyl)-3,3-dimethylurea (6b)

![Diagram of 1-Allyl-1-(cyclopropylmethyl)-3,3-dimethylurea (6b)]

**General procedure B:** 3-(Cyclopropylmethyl)-1,1-dimethylurea (0.86 g, 6.0 mmol) allyl bromide (1.44 g, 12.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6b (0.95 g, 87 %) as a pale yellow oil; $\nu_{\text{max}}$ / cm$^{-1}$: 2920 (m), 1639 (s), 1488 (m), 1383 (m), 1198 (m), 1142 (m); $^1$H NMR (400 MHz, CDCl$_3$, 50 °C): δ 5.87 – 5.68 (1H, m), 5.27 – 4.82 (2H, m), 3.95 – 3.79 (2H, m), 2.96 (2H, d, $J = 6.7$ Hz), 2.83 – 2.72 (6H, m), 1.01 – 0.88 (1H, m), 0.50 – 0.41 (2H, m), 0.16 – 0.05 (2H, m); $^{13}$C NMR: (100 MHz, CDCl$_3$, 50 °C): δ 165.3, 134.9, 116.4, 52.2, 50.9, 38.6, 9.4, 3.5; m/z (ESI$^+$) HRMS: Calculated for C$_{10}$H$_{19}$N$_2$O: 183.1492. Found [M+H]$^+$: 183.1497.
(3aR*, 7aR*)-N,N-Dimethyl-5-oxooctahydro-2H-isindoile-2-carboxamide (8b)

General procedure G: Compound 3b (27.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (80 % EtOAc/Hex) to yield the title compound 8b (16.7 mg, 53 %, > 15:1 d.r.) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 2938 (m), 1711 (s), 1624 (s) 1500 (m), 1395 (s), 1369 (m); \(^1\text{H} \text{NMR} \) (400 MHz, C\(_6\)D\(_6\)): \( \delta \) 3.09 (1H, dd, \( J = 9.8, 6.6 \text{ Hz} \), 1 \times C8-H2), 2.97 (1H, dd, \( J = 9.7, 6.6 \text{ Hz} \), 1 \times C1-H2), 2.81 – 2.64 (2H, m, 1 \times C8-H2, 1 \times C1-H2), 2.49 (6H, s, 6 \times C10-H3), 2.18 (1H, ddd, \( J = 14.0, 3.8, 1.9 \text{ Hz} \), 1 \times C5-H2), 2.15 – 2.08 (1H, m, 1 \times C3-H2), 1.68 – 1.59 (1H, m, 1 \times C3-H2), 1.48 (1H, ddd, \( J = 13.9, 13.1, 0.9 \text{ Hz} \), 1 \times C5-H2), 1.33 (1H, dddd, \( J = 12.4, 6.7, 3.4, 2.1 \text{ Hz} \), 1 \times C6-H2), 1.15 – 1.04 (1H, m, 1 \times C2-H), 1.03 – 0.94 (1H, m, 1 \times C7-H), 0.86 – 0.70 (1H, m, 1 \times C6-H2); \(^{13}\text{C} \text{NMR} \) (100 MHz, C\(_6\)D\(_6\)): \( \delta \) 206.6 (C4), 162.6 (C9), 53.4 (C1), 52.5 (C8), 43.8 (C5), 43.4 (C2), 41.7 (C7), 39.7 (C3), 37.7 (C10), 26.4 (C6); m/z (ESI\(^+\)) HRMS: Calculated for C\(_{11}\)H\(_{19}\)N\(_2\)O\(_2\): 211.1441. Found [M+H]\(^+\): 211.1443. The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed from C3a-H to C2-H, and from C3b-H to C7-H.

Benzyl (cyclopropylmethyl)carbamate

General procedure A: Cyclopropylmethylamine (3.00 g, 42.0 mmol) and benzyl chloroformate (8.57 g, 50.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound (7.90 g, 92 %) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 3332 (s), 1694 (s), 1516 (s), 1456 (m), 1240 (s), 1131 (m); \(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)): \( \delta \) 7.37 – 7.26 (5H, m), 5.10 (2H, s), 4.88 (1H, br. s), 3.06 (2H, t, \( J = 6.5 \text{ Hz} \)), 0.95 (1H, m), 0.51 – 0.47 (2H, m), 0.21 – 0.16 (2H, m); \(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \)
156.3, 136.6, 128.5, 128.0, 66.6, 46.0, 11.0, 3.2; \textit{m/z} (ESI\textsuperscript{+}) HRMS: Calculated for C\textsubscript{12}H\textsubscript{15}NO\textsubscript{2}Na: 228.0995. Found [M+Na]\textsuperscript{+}: 228.1004. The spectroscopic properties of this compound consistent with the data available in the literature.\textsuperscript{3}

**Benzyllallyl(cyclopropylmethyl)carbamate (6c)**

\[
\text{N} \quad \text{O} \quad \text{O} \quad \text{N} \quad \text{O} \quad \text{O}
\]

**General procedure B:** Benzyl (cyclopropylmethyl)carbamate (4.49 g, 21.9 mmol) and allyl bromide (7.88 g, 65.7 mmol) were employed, the crude mixture which was purified by column chromatography (10\% EtOAc/Hex) to yield the title compound 6c (4.57 g, 85\%) as a colorless oil; \(\nu_{\text{max}}/\text{cm}^{-1}\): 1697 (s), 1514 (s), 1239 (s), 1132 (m), 1020 (m); \(\text{\textsuperscript{1}H NMR}\) (500 MHz, CD\textsubscript{3}CN, 65 °C): \(\delta\) 7.7 – 7.0 (5H, m), 6.2 – 5.7 (1H, m), 5.4 – 4.9 (4H, m), 4.0 (2H, ddd, \(J = 5.7, 2.6, 1.5\) Hz), 3.5 – 2.8 (2H, m), 1.2 – 0.9 (1H, m), 0.7 – 0.4 (2H, m), 0.2 (2H, m); \(\text{\textsuperscript{13}C NMR}\) (126 MHz, CD\textsubscript{3}CN, 65 °C) \(\delta\) 155.9, 137.6, 134.5, 128.4, 127.8, 127.6, 116.9, 66.5, 51.1, 49.4, 9.9, 3.0, 2.8; HRMS: (CI\textsuperscript{+}) Calculated for C\textsubscript{15}H\textsubscript{20}NO\textsubscript{2}: 246.1494. Found [M + H]\textsuperscript{+}: 246.1503.

**General procedure G:** Compound 6c (36.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33\% EtOAc/Hex) to yield the title compound 8c (34.4 mg, 84\%, > 15:1 d.r. 1:1 mixture of rotamers A:B) as an off white solid; m.p.: 79 – 81 °C (EtOAc/Hex); \(\nu_{\text{max}}/\text{cm}^{-1}\): 1699 (s), 1419 (s), 1358 (s), 1170 (m), 1079 (m); \(\text{\textsuperscript{1}H NMR}\) (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.36 – 7.28 (5H, m, 2 × C\textsubscript{12}-H, A+B, 2 × C\textsubscript{13}-H, A+B, 1 ×C\textsubscript{14}-H, A+B), 5.20 – 5.10 (2H, m, 2 ×C\textsubscript{10}-H\textsubscript{2}, A+B), 3.81 – 3.67 (2H, m, 1 ×C\textsubscript{8}-H, A+B, 1 ×C\textsubscript{1}-H, A+B), 3.07 – 2.96 (2H, m, 1 ×C\textsubscript{8}-H, A+B, 1 ×C\textsubscript{1}-H, A+B), 2.66 – 2.56 (1H, m, 1
× C3-H2, A+B), 2.53 – 2.47 (1H, m, 1 × C5-H2, A+B), 2.40 – 2.30 (1H, m 1 × C5-H2, A+B), 2.22 – 2.11 (2H, m, 1 × C3-H2, A+B, 1 × C6-H2, A+B), 2.10 – 1.91 (2H, m, 1 × C2-H, A+B, 1 × C7-H, A+B), 1.78 – 1.30 (1H, m, 1 × C6-H2, A+B), 2.22 – 2.11 (2H, m, 1 × C3-H2, A+B, 1 × C6-H2, A+B), 2.10 – 1.91 (2H, m, 1 × C2-H, A+B, 1 × C7-H, A+B), 1.78 – 1.30 (1H, m, 1 × C6-H2, A+B), 15.7 (C9, A), 154.7 (C9, B), 136.8 (C11, A), 136.7 (C11, B), 128.5, 128.0, 127.9 (C12, A+B, C13, A+B, C14, A+B), 66.8 (C10, A+B), 51.2 (C1, A), 51.0 (C1, B), 50.4 (C8, A), 50.2 (C8, B), 44.4 (C2, A), 44.2 (C3, A), 44.2 (C3, B), 43.7 (C2, B), 43.0 (C7, A), 42.3 (C7, B), 40.1 (C5, A), 40.0 (C5, B), 26.8 (C6, A+B); HRMS: (CI+) Calculated for C16H19NO3: 274.1443. Found [M + H]+: 274.1445. The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.

N-(Cyclopropylmethyl)benzamide

General procedure A: Cyclopropylmethylamine (3.00 g, 42.0 mmol) and benzoyl chloride (7.06 g, 50.4 mmol) were employed, the crude mixture was recrystallized from Et2O/Hex to yield the title compound (5.89 g, 80 %) as a colorless solid; m.p.: 78 – 80 °C (EtOAc/Hex); νmax / cm⁻¹: 3306 (s), 2988 (s), 1631 (s), 1542 (s), 1492 (s), 1295 (s); ¹H NMR (400 MHz, CDCl3): δ 7.78 – 7.76 (2H, m), 7.47 (1H, m), 7.42 – 7.37 (2H, m), 6.40 (1H, br. s), 3.31 – 3.27 (2H, m), 1.04 (1H, m), 0.55 – 0.50 (2H, m), 0.27 – 0.23 (2H, m); ¹³C NMR (100 MHz, CDCl3): δ 167.4, 134.8, 131.3, 128.5, 126.9, 44.9, 10.7, 3.5; m/z (ESI⁺) HRMS: Calculated for C11H13NONa: 198.0893. Found [M + Na]+: 198.0889.
N-Allyl-N-(cyclopropylmethyl)benzamide (6d)

\[ \text{6d} \]

**General procedure B:** N-Allyl-N-(cyclopropylmethyl)benzamide (2.30 g, 13.1 mmol) was employed, the crude mixture was purified by column chromatography (66 % EtOAc/Hex) to yield the title compound 6d (2.53 g, 90 %) as a yellow oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 2988 (m), 1629 (s), 1388 (m), 1414 (s), 1262 (s), 1075 (s); \(^1\)H NMR (500 MHz, CD\(_3\)CN, 65 °C): \( \delta \) 7.45 – 7.38 (5H, m), 5.87 (1H, br. s), 5.23 – 5.18 (2H, m), 4.10 (2H, br. s), 3.26 (2H, br. s), 1.03 (1H, br. s), 0.51 (2H, br. d, \( J = 7.8 \text{ Hz} \)), 0.18 (2H, br. m); \(^1^3\)C NMR (126 MHz, CD\(_3\)CN, 65 °C): \( \delta \) 171.1, 137.6, 134.2, 129.0, 128.3, 126.4, 116.9, 51.6-48.8 (br), 9.6, 3.2, 3.1. \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{14}\)H\(_{18}\)N\(_2\): 216.1383. Found [M + H]\(^+\): 216.1386.

(3a\(^R\), 7a\(^R\))-2-Benzoyloctahydro-5H-isooindol-5-one (8d)

\[ \text{6d} \rightarrow \text{8d} \]

**General procedure G:** Compound 6d (32.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (80 % EtOAc/Hex) to yield the title compound 8d (29.9 mg, 82 %, > 15:1 d.r., 1:1 mixture of rotamers A:B) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 2870 (m), 1710 (s), 1623 (s), 1575 (s), 1417 (s), 1028 (m); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.52 – 7.48 (2H, m, 2 \( \times \) C\(_{12}\)-H\(_2\), A+B), 7.43 – 7.36 (3H, m, 2 \( \times \) C\(_{11}\)-H\(_2\), A+B, C\(_{13}\)-H\(_2\), A+B), 3.96 (0.5H, dd, \( J = 12.0, 7.5 \text{ Hz} \), 1 \( \times \) C\(_1\)-H\(_2\), A), 3.90 (0.5H, dd, \( J = 12.0, 6.5 \text{ Hz} \), 1 \( \times \) C\(_8\)-H\(_2\), A), 3.63 (0.5H, dd, \( J = 10.0, 6.0 \text{ Hz} \), 1 \( \times \) C\(_{11}\)-H\(_2\), B), 3.57 (0.5H, dd, \( J = 10.1, 6.5 \text{ Hz} \), 1 \( \times \) C\(_8\)-H\(_2\), B), 3.32 – 3.15 (2H, m, 1 \( \times \) C\(_1\)-H\(_2\), A+B, 1 \( \times \) C\(_8\)-H\(_2\), A+B), 2.69 (0.50H, dt, \( J = 14.5, 3.0, 3.0 \text{ Hz} \), 1 \( \times \) C\(_3\)-H\(_2\), A), 2.55 – 2.45 (1.50H, m, 1 \( \times \) C\(_3\)-H\(_2\), B, 1 \( \times \) C\(_5\)-H\(_2\), A+B), 2.41 – 1.93 (5H, m, C\(_2\)-H\(_2\), A+B, 1 \( \times \) C\(_3\)-H\(_2\), A+B, 1 \( \times \) C\(_5\)-H\(_2\), A+B, 1 \( \times \) C\(_6\)-H\(_2\), A+B, C\(_7\)-H\(_2\), A+B),
1.65 – 1.47 (1H, m, 1 × C6-H₂, A+B); ¹³C NMR (100 MHz, CDCl₃): δ 208.7 (C₄, A), 208.6 (C₄, B), 169.9 (C₉, A+B), 136.5 (C₁₀, A), 136.4 (C₁₀, B), 130.1 (C₄, A+B), 128.3 (C₁₁, A), 128.3 (C₁₁, B), 127.2 (C₁₂, A), 127.1 (C₁₂, B), 55.0 (C₈, A), 53.9 (C₁, A), 51.3 (C₈, B), 50.5 (C₁, B), 44.8 (C₂, A), 44.3 (C₃, A), 44.0 (C₃, B), 43.3, 43.2 (C₂, B, C₇, A), 41.8 (C₇, B), 40.2 (C₅, A), 39.9 (C₅, B), 26.9 (C₆, A), 26.6 (C₆, B); m/z (ESI⁺) HRMS: Calculated for C₁₅H₁₇N₂O₂Na: 266.1151. Found, [M + Na]⁺: 266.1143. The relative stereochemistry of this compound was assigned by analogy to that of 8c.

N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide

![N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide](image)

**General procedure A:** Cyclopropylmethylamine (1.01 g, 14.1 mmol) and p-toluenesulfonyl chloride (3.22 g, 16.9 mmol) were employed, the crude mixture was purified by column chromatography (25 % EtOAc/Hex) to yield title sulfonamide (2.70 g, 85 %) as a colorless solid; m.p. 58 – 60 °C (CH₂Cl₂/Hex); νmax / cm⁻¹: 3258 (m), 3004 (m), 2868 (m), 1595 (m), 1154 (s), 1091 (s); ¹H NMR (400 MHz, CDCl₃): δ 7.91 – 7.66 (2H, m), 7.48 – 7.13 (2H, m), 4.71 (1H, br. s), 2.80 (2H, dd, J = 7.1, 5.9 Hz), 2.42 (3H, s), 0.86 (1H, dddd, J = 12.2, 8.1, 7.2, 2.8 Hz), 0.63 – 0.22 (2H, m), 0.13 – 0.02 (2H, m); ¹³C NMR (100 MHz, CDCl₃): δ 143.3, 137.1, 129.6, 127.1, 48.3, 21.5, 10.7, 3.5; m/z (ESI⁺) HRMS: Calculated for C₁₁H₁₅NO₂SNa: 248.0716. Found [M+Na]⁺: 248.0714.

N-Allyl-N-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6e)

![N-Allyl-N-(cyclopropylmethyl)-4-methylbenzenesulfonamide](image)

**General procedure B:** N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.68 g, 3.0 mmol) and allyl bromide (1.80 g, 15.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6e (0.70 g, 88 %) as a colorless oil. νmax / cm⁻¹: 1341 (s), 1305 (m), 1154 (s), 1091 (s), 1019 (m); ¹H NMR (400 MHz, CDCl₃): δ 7.67 (2H, d, J = 8.5 Hz), 7.26 (2H, d, J = 8.5 Hz), 5.64 (1H, ddt, J = 17.5, 10.7, 3.5; m/z (ESI⁺) HRMS: Calculated for C₁₅H₂₁N₂O₂Na: 284.1342. Found [M+Na]⁺: 284.1343.
10.0, 6.0 Hz), 5.16 (1H, dd, \( J = 17.0, 1.5 \) Hz), 5.10 (1H, dd, \( J = 10.0, 1.5 \) Hz), 3.90 (2H, d, \( J = 6.0 \) Hz), 3.01 (2H, d, \( J = 7.0 \) Hz), 2.39 (3H, s), 0.85 (1H, m), 0.47 – 0.43 (2H, m), 0.13 (2H, dt, \( J = 6.0, 4.5 \) Hz); \(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)): \( \delta \) 143.0, 137.6, 133.5, 129.6, 127.1, 188.3, 51.6, 50.0, 21.5, 9.6, 4.0; \( \text{HRMS} \): (CI\(^+\)) Calculated for C\(_{14}\)H\(_{20}\)NO\(_2\)S: 266.1215. Found [M + H]\(^+\): 266.1209.

(3\( aR^*\), 7\( aR^*\))-2-Tosylhexahydro-1\( H\)-isoindol-5(6\( H\))-one (8e)

\[
\begin{align*}
\text{6e} & \quad \rightarrow \quad \text{8e}
\end{align*}
\]

**General procedure G:** Compound 6e (39.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8e (38.7 mg, 88 %, > 15:1 d.r.) as an off white solid; m.p.: 172 – 173 \(^\circ\)C (CH\(_2\)Cl\(_2\)/Hex); \( \nu_{\text{max}} \) / cm\(^{-1}\): 1703 (m), 1338 (m), 1194 (m), 1156 (s), 1087 (m); \(^1\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)): \( \delta \) 7.71 (2H, d, \( J = 8.5 \) Hz, 2 \( \times \) C\(_{10}\)-H), 7.32 (2H, d, \( J = 8.5 \) Hz, 2 \( \times \) C\(_{11}\)-H), 3.66 (1H, dd, \( J = 9.5, 7.0 \) Hz, 1 \( \times \) C\(_{8}\)-H\(_2\)), 3.57 (1H, dd, \( J = 9.5, 7.0 \) Hz, 1 \( \times \) C\(_{1}\)-H\(_2\)), 2.94 (1H, dd, \( J = 10.5, 9.5 \) Hz, 1 \( \times \) C\(_{1}\)-H\(_2\)), 2.84 (1H, dd, \( J = 10.5, 9.5 \) Hz, 1 \( \times \) C\(_{8}\)-H\(_2\)), 2.51 (1H, ddd, \( J = 14.5, 4.0, 2.0 \) Hz, 1 \( \times \) C\(_{3}\)-H\(_2\)), 2.45 – 2.40 (4H, m, 1 \( \times \) C\(_{5}\)-H\(_2\), 3 \( \times \) C\(_{13}\)-H\(_3\)), 2.31 (1H, ddd, \( J = 15.5, 13.0, 6.5 \) Hz, 1 \( \times \) C\(_{5}\)-H\(_2\)), 2.15 – 2.07 (2H, m, 1 \( \times \) C\(_{3}\)-H\(_2\), 1 \( \times \) C\(_{6}\)-H\(_3\)), 1.91 – 1.83 (1H, m, C\(_2\)-H), 1.79 – 1.67 (1H, m, C\(_{7}\)-H), 1.42 (1H, ddt, \( J = 13.0, 12.0, 5.0 \) Hz, 1 \( \times \) C\(_{6}\)-H\(_2\)); \(^{13}\text{C} \text{NMR} \) (100 MHz, CDCl\(_3\)): \( \delta \) 208.3 (C4), 143.6 (C12), 134.4 (C9), 129.8 (C11), 12.8 (C10), 52.6 (C1), 51.9 (C8), 44.2 (C7), 43.9 (C3), 42.7 (C2), 39.8 (C5), 26.5 (C6), 21.5 (C13); \( \text{HRMS} \): (CI\(^+\)) Calculated for C\(_{15}\)H\(_{20}\)NO\(_3\)S: 294.1164. Found [M + H]\(^+\): 294.1157. The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.
**N-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide**

**General procedure A:** Cyclopropylmethylamine (1.42 g, 20.0 mmol) and 4-(trifluoromethyl)benzoyl chloride (3.56 mL, 24.0 mmol) were employed, the crude mixture was recrystallized from Et₂O/Hex to yield the title compound (4.10 g, 84 %) as a colourless solid; m.p.: 127 – 128 °C (EtOAc/Hex); νₘₚₓ / cm⁻¹: 3245 (s), 1642 (m), 1625 (s), 1557 (s), 1323 (s), 1154 (s), 1113 (s); ¹H NMR (400 MHz, CDCl₃): δ 7.88 (2H, d, J = 8.0 Hz), 7.67 (2H, d, J = 8.0 Hz), 6.42 (1H, br. s), 3.31 (2H, dd, J = 7.0, 5.5 Hz), 1.05 (1H, m, C₂-H), 0.57 – 0.53 (2H, m), 0.29 – 0.25 (2H, m); ¹³C NMR (100 MHz, CDCl₃): δ 166.2, 138.0, 133.0 (q, J = 32.5 Hz), 127.4, 125.5 (q, J = 4.0 Hz), 123.7 (q, J = 272.5 Hz), 45.1, 10.6, 3.5; m/z (ESI⁺) HRMS: Calculated for C₁₂H₁₂F₃NOna: 266.0763. Found [M + Na⁺]: 266.0764.

**N-Allyl-N-(cyclopropylmethyl)-4-(trifluoromethyl)benzamide (6f)**

**General procedure B:** N-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide (2.43 g, 10.0 mmol) and allyl bromide (4.33 mL, 50.0 mmol) were employed, the crude mixture was
purified by flash column chromatography (30 % EtOAc/Hex) to yield the compound 6f (2.63 g, 93%) as a yellow oil; $\nu_{\text{max}}/\text{cm}^{-1}$: 1686 (s), 1455 (m), 1169 (s), 1201 (s), 1137 (s); $^1$H NMR (500 MHz, CD$_3$CN, 65 °C): 7.76 (2H, d, $J = 8.0$ Hz), 7.58 (2H, d, $J = 7.7$ Hz), 5.87 (1H, br., s), 5.48 – 4.97 (2H, m), 4.10 (2H, br., s), 3.28 (2H, br., s), 1.05 (1H, br., s), 0.63 – 0.40 (2H, br., m), 0.20 (2H, br., s); $^{13}$C NMR (126 MHz, CD$_3$CN, 65 °C): δ 169.8, 141.4, 133.8, 130.5 (q, $J = 32.7$, 32.0 Hz), 127.2, 125.3 (q, $J = 3.9$ Hz), 124.2 (q, $J = 271.4$ Hz), 116.4, 47.7-53.3 (br., m), 9.5, 3.2; $^{19}$F NMR (377 MHz, CDCl$_3$): δ -62.8 (s, CF$_3$); $m/z$ (ESI$^+$) HRMS: Calculated for C$_{15}$H$_7$F$_3$NO: 284.1257. Found [M + H]$^+$: 284.1252.

(3a$R^*$, 7a$R^*$)-2-(4-(Trifluoromethyl)benzoyl)octahydro-5H-isoinodol-5-one (8f)

![Diagram of 6f and 8f](image)

**General procedure G:** Compound 6f (42.5 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound 8f (33.7 mg, 72 %, > 15:1 d.r., 1:1 mixture of rotamers A:B) as a colorless oil; $\nu_{\text{max}}/\text{cm}^{-1}$: 2967 (m), 1713 (s), 1627 (s), 1428 (s), 1322 (s), 1165 (s), 1123 (s); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.68 – 7.60 (4H, m, 2 × C11-H, A+B, 2 × C12-H, A+B), 4.06 – 3.81 (1H, 1 × C8-H$_2$, A, 1 × C1-H$_2$, A), 3.68 – 3.40 (1H, m, 1 × C8-H$_2$, B, 1 × C1-H$_2$, B), 3.38 – 3.01 (2H, m, 1 × C1-H$_2$, A+B, 1 × C8-H$_2$, A+B), 2.69 (0.5H, dd, $J = 14.5$, 3.1 Hz, 0.50 × C3-H$_2$, A), 2.59 – 2.43 (1.50H, m, 0.50 × C3-H$_2$, B, 1 × C5-H$_2$, A+B), 2.42 – 1.95 (5H, m, 1 × C3-H$_2$, A+B, 1 × C5-H$_2$, A+B, 1 × C6-H$_2$, A+B, C2-H, A+B, C7-H, A+B), 1.60 (1H, m, 1 × C6-H$_2$, A+B); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 208.5 (C4, B), 208.4 (C4, A), 168.5 (C9, A+B), 139.9 (C10, A+B), 132.1 (q, $J = 32.5$ Hz, C13, A+B), 127.6 (C11, B), 127.6 (C11, A), 125.5 (q, $J = 5.0$ Hz, C12, A+B), 123.8 (q, $J = 272.5$ Hz, C14, A+B), 54.6 (C1, A), 53.9 (C8, B), 51.4 (C1, B), 50.6 (C8, A), 44.9 (C2, A), 44.4 (C3, A), 44.0 (C3, B), 43.5, 43.3 (C2, B, C7, B), 41.9 (C7, A), 40.2 (C5, A), 40.0 (C5, B), 26.9 (C6, A), 26.6 (C6, B); $^{19}$F NMR (470 MHz, CDCl$_3$): δ -62.9 (s, CF$_3$, A), -63.0 (s, CF$_3$, B); $m/z$ (ESI$^+$) HRMS: Calculated for C$_{16}$H$_7$F$_3$NO$_2$: 312.1206. Found [M + H]$^+$: 312.1221. *The relative stereochemistry of this compound was assigned by analogy to that of 8c and 8d.*
**N-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide**

![Chemical Structure](image)

**General procedure A:** Cyclopropylmethylamine (1.07 g, 15.0 mmol) and p-toluenesulfonyl chloride (3.65 g, 16.5 mmol) were employed, the crude mixture was purified by column chromatography (25 % EtOAc/Hex) to yield title sulfonamide (3.34 g, 87 %) as an off-white solid; m.p. 114 – 116 °C (CH₂Cl₂/Hex); νₘₐₓ / cm⁻¹: 3285 (m), 1522 (s), 1431 (m), 1334 (s), 1157 (s) 1048 (s); ¹H NMR (400 MHz, CDCl₃): 8.47 – 8.21 (2H, m), 8.13 – 7.87 (2H, m), 5.23 (1H, t, J = 5.9 Hz), 2.88 (2H, dd, J = 7.2, 5.8 Hz), 0.97 – 0.76 (1H, m), 0.55 – 0.32 (2H, m), 0.11 (2H, t, J = 5.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 150.0, 146.2, 128.3, 124.4, 48.5, 10.8, 3.7; m/z (ESI⁺) HRMS: Calculated for C₁₀H₁₂N₂O₄SNa: 279.0410. Found [M+Na]⁺: 279.0397.

**N-Allyl-N-(cyclopropylmethyl)-4-nitrobenzenesulfonamide (6g)**

![Chemical Structure](image)

**General procedure B:** N-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide (1.40 g, 5.5 mmol) and allyl bromide (3.30 g, 27.5 mmol) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound 6g (1.48g, 91 %) as an off-white solid; m.p. 67 – 69 °C (CH₂Cl₂/Hex); νₘₐₓ / cm⁻¹: 1524 (s), 1346 (s), 1313 (m), 1150 (s), 1088 (m) 906 (m); ¹H NMR (400 MHz, CDCl₃): 8.45 – 8.19 (2H, m), 8.08 – 7.87 (2H, m), 5.62 (1H, ddt, J = 16.5, 10.2, 6.2 Hz), 5.30 – 4.96 (2H, m), 3.98 (2H, dd, J=6.3, 1.5 Hz), 3.10 (2H, d, J = 6.9 Hz), 0.95 – 0.72 (1H, m), 0.55 – 0.40 (2H, m), 0.17 (2H, dd, J = 4.9, 1.4 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 149.8, 146.6, 132.5, 128.2, 124.3, 119.1, 51.8, 50.0, 9.5, 4.1; m/z (ESI⁺) HRMS: Calculated for C₁₃H₁₆N₂O₄SNa: 319.0723. Found [M+Na]⁺: 319.0724.

**(3aR*, 7aR*)-2-((4-Nitrophenyl)sulfonyl)octahydro-5H-isoinodol-5-one (8g)**
General procedure G: Compound 6g (44.4 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8g (18.1 mg, 37 %, > 15:1 d.r.) as an off white solid; m.p.: above 200 °C (CH₂Cl₂/Hex); ν max / cm⁻¹: 2955 (m), 1706 (m), 1528 (m), 1348 (s), 1159 (s), 1033 (s); ¹H NMR (500 MHz, DMSO-d₆, 80 °C): δ 8.40 (1H, d, J = 8.9 Hz, 2 × C11-H), 8.07 (1H, d, J = 9.6, 7.1 Hz, 1 × C10-H), 3.59 (1H, dd, J = 9.6, 7.1 Hz, 1 × C8-H₂), 3.52 (1H, dd, J = 9.5, 6.9 Hz, 1 × C8-H₂), 2.88 (1H, dd, J = 10.8, 9.4 Hz, 1 × C8-H₂), 2.81 (1H, dd, J = 10.7, 9.6 Hz, 1 × C1-H₂), 2.34 – 2.21 (3H, m, 2 × C3-H₂, 1 × C5-H₂), 2.19 – 2.11 (1H, m, 1 × C5-H₂), 2.00 – 1.91 (1H, m, 1 × C6-H₂), 1.91 – 1.82 (1H, m, 1 × C2-H), 1.81 – 1.70 (1H, m, 1 × C7-H), 1.45 – 1.29 (1H, m, 1 × C6-H₂); ¹³C NMR (126 MHz, DMSO-d₆, 80 °C): δ 209.0 (C₄), 150.3 (C₁₂), 142.8 (C₉), 129.1 (C₁₀), 125.2 (C₁₁), 52.9 (C₈), 52.2 (C₁), 43.6 (C₇), 43.4 (C₃), 41.9 (C₂), 39.7 (C₅), 25.9 (C₆); HRMS: (CI⁺) Calculated for C₁₄H₁₆N₂O₅SNa: 347.0672. Found [M + H]⁺: 347.0663. The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C₈α-H and C₂-H, C₈β-H and C₇-H, no significant nOe was observed between C₂-H and C7-H. The stereochemical assignment of this compound is consistent with that of 8e.

N-(Cyclopropylmethyl)hex-1-en-3-amine

![Chemical structure]

General procedure F: (E)-N-(cyclopropylmethyl)butan-1-imine (0.82 g, 6.6 mmol) (prepared according to literature procedure⁴) and vinylmagnesium bromide (6.6 mL, 13.2 mmol, 2.0 M in THF) were employed, the crude mixture was purified by column chromatography (66 % EtOAc/Hex) to yield the title compound (0.27 g, 27 %) as a red oil; ν max / cm⁻¹: 3203 (m), 2958 (m), 1590 (m), 1428 (m), 1054 (s), 992 (s), 938 (s); ¹H NMR (400 MHz, CDCl₃): δ 6.51 (1H, br. s), 5.84 – 5.63 (1H, m), 5.51 (1H, dd, J = 10.2, 1.0 Hz), 5.42 (1H, dd, J = 16.9, 0.9 Hz), 3.63 (1H, td, J = 10.0, 4.1 Hz), 2.90 (2H, dd, J = 7.5, 1.8 Hz), 1.93
- 1.79 (1H, m), 1.79 – 1.62 (1H, m), 1.47 – 1.21 (2H, m), 1.19 – 1.11 (1H, m), 0.92 (3H, t, \( J = 7.3 \) Hz), 0.74 – 0.57 (2H, m), 0.44 – 0.24 (2H, m); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 131.5, 124.3, 62.4, 51.4, 33.4, 18.5, 13.3, 6.9, 4.5, 3.8; \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{10}\)H\(_{20}\)N: 154.1590. Found \([M+H]^+\): 154.1589.

**Benzyl (cyclopropylmethyl)(hex-1-en-3-yl)carbamate (6h)**

![Diagram of 6h]

**General Procedure E:** \( N \)-(Cyclopropylmethyl)hex-1-en-3-amine (0.33 g, 2.2 mmol) and benzyl chloroformate (0.70 ml, 4.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6h (0.59 g, 92 %) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 2958 (m), 1692 (s), 1412 (m), 1255 (m), 1145 (m), 1087 (m), 696 (s); \(^1\)H NMR (400 MHz, CD\(_3\)CN, 65 \(^{\circ}\)C): \( \delta \) 7.66 – 7.04 (5H, m), 5.97 (1H, ddd, \( J = 17.1, 10.5, 6.3 \) Hz), 5.36 – 4.90 (4H, m), 4.40 (1H, dtt, \( J = 8.1, 6.5, 1.5 \) Hz), 3.19 – 3.11 (1H, m), 3.10 – 3.03 (1H, m), 1.84 – 1.58 (2H, m), 1.52 – 1.24 (2H, m), 1.15 – 1.00 (1H, m), 0.94 (3H, t, \( J = 7.4 \) Hz), 0.59 – 0.35 (2H, m), 0.35 – 0.14 (2H, m); \(^{13}\)C NMR (126 MHz, CD\(_3\)CN, 65 \(^{\circ}\)C): \( \delta \) 156.1, 138.5, 137.6, 128.3, 127.7, 127.6, 116.9, 66.4, 59.1, 49.3, 34.3, 19.3, 13.0, 11.0, 3.8, 3.6; \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{18}\)H\(_{25}\)NO\(_2\)Na: 310.1778. Found \([M+Na]^+\): 310.1763.

**Benzyl-(1S*, 3aR*, 7aR*) and (1R*, 3aR*, 7aR*)-6-oxo-1-propylhexahydro-1H-isindole-2(3H)-carboxylate (8h)**

![Diagram of 8h and A, B]

**General procedure G:** Compound 6h (43.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title
compound 8h (32.6 mg, 69 %, 1:1 mixture of rotomers A:B ) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. Under general procedure H, title compound 8h was obtained in 60 % yield (28.4 mg, 1:1 mixture of rotomers A:B ) as a colorless oil. A mixture of diastereomers A and B were obtained in a 2:1 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOes was observed from C1-H to C9-H, and no significant nOe was observed between C5-H and C10-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of 8I. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8I.

$\nu_{\text{max}}$ / cm$^{-1}$: 2957 (m), 1698 (s), 1411 (m), 1356 (m), 1265 (m), 1075 (m); m/z (ESI$^+$) HRMS: Calculated for C$_{19}$H$_{23}$NO$_{3}$Na: 338.1727. Found [M+Na]$^+$: 338.1736

Data for mixture of diastereomers A and B: $^1$H NMR (400 MHz, CD$_3$CN, 65 °C): δ 8.47 – 6.45 (10H, m, 2 × C15-H, A+B, 2 × C16-H, A+B, 1 × C17-H, A+B), 5.23 – 5.02 (4H, m, 2 × C13-H$_2$, A+B), 3.94 – 3.84 (2H, m, 1 × C11-H$_2$, A, 1 × C1-H, B), 3.70 – 3.57 (1H, br. m, 1 × C11-H$_2$, B), 3.51 (1H, dt, J = 9.6, 4.8 Hz, 1 × C1-H, A), 2.98 (1H, dd, J = 10.5, 10.5 Hz, 1 × C11-H$_2$, B) 2.94 – 2.79 (1H, m, 1 × C11-H$_2$, A), 2.53 (1H, dd, $J = 14.5$, 4.0 Hz, 1 × C6-H$_2$, A), 2.45 – 2.25 (8H, m, 1 × C6-H$_2$, A, 2 × C8-H$_2$, A, 2 × CH$_2$, B, 2 × CH$_2$, B, 1 × CH$_2$ B), 2.22 – 2.16 (1H, br. m, 1 × CH$_2$, B), 2.17 – 2.09 (1H, m, 1 × C9-H$_2$, A), 2.04 – 2.03 (1H, m, 1 × CH$_3$, A), 2.02 – 1.98 (1H, m, 1 × C10-H, A), 1.89 – 1.72 (3H, m, 1 × C5-H, A, 2 × C2-H$_2$, A), 1.63 – 1.44 (4H, m, 1 × C9-H$_2$, A, 1 × CH$_2$, B, 1 × CH$_2$, B, 1 × CH$_2$, B), 1.33 – 1.28 (4H, m, 2 × C3-H$_2$, A, 1 × CH$_2$, B, 1 × CH$_2$, B), 0.98-0.84 (6H, m, 3 × C4-H$_3$, A, 3 × C4-H$_3$, B); $^{13}$C NMR (126 MHz, CD$_3$CN): δ 209.2 (C7, B, A+B), 209.0 (C7, B, A+B), 155.1 (C12, A, A), 154.9 (C12, B, A), 154.8 (C12, B, B), 154.4 (C12, A, B), 137.7 (C14, A, A+B), 137.4 (C14, B, A+B), 128.4, 127.9, 127.8, 127.6, 127.5 (C15, A, A+B, C16, A, A+B, C17, A, A+B, C15, B, A+B, C16, B, A+B, C17, B, A+B), 66.3 (C13, A, A), 66.2 (C13, B, A), 66.0 (C13, B, B), 65.9 (C13, A, B), 62.5 (C1, A, A), 62.0 (C1, A, B), 59.5 (C1, B, A), 59.2 (C1, B, B), 51.2 (C11, A, A), 50.9 (C11, A, B), 50.5 (C11, B, A), 50.3 (C11, B, B), 49.5 (C5, A, A), 49.5 (C5, A, B), 47.5 (B, A), 46.8 (B, B), 44.5 (C6, A, A+B), 42.0 (B, A+B), 41.6 (C10, A, A), 41.6 (C10, A, B), 39.7 (B, A), 39.7 (B, B), 39.6 (C8, A, A+B), 39.0 (B, A), 38.1 (B, B), 34.4 (C2, A, A), 35.0 (C2, A, B), 33.1 (B, A), 32.9 (B, B), 27.4 (B, A), 27.3 (B, B), 25.8 (C9, A, A+B), 19.9 (B, A), 19.8 (B, B), 17.2 (C3, A, A), 17.0 (C3, A, B), 13.7 (C4, A, A), 13.6 (C4, A, B),
13.6 (C4, B, A), 13.5 (C4, B, B). Minor diastereomer B could not be fully assigned based on the 1D and 2D NMR data.

**N-(Cyclopropylmethyl)-N-(hex-1-en-3-yl)-4-methylbenzenesulfonamide (6i)**

**General Procedure E:** N-(cyclopropylmethyl)hex-1-en-3-amine (0.15 g, 1.0 mmol) and p-toluenesulfonyl (0.39 g, 2.0 mmol) were employed, the crude mixture was purified by column chromatography (100 % Toluene) to yield the title compound 6i (0.28 g, 90 %, > 15:1) as a yellow oil; $\nu_{\text{max}}$ / cm$^{-1}$: 2959 (m), 1458 (m), 1331 (s), 1154 (s), 1090 (s), 670 (s); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.71 (2H, d, $J = 8.3$ Hz), 7.25 (2H, d, $J = 8.0$ Hz), 5.57 (1H, ddd, $J = 16.9, 10.6, 6.0$ Hz), 5.40 – 4.76 (2H, m), 4.31 (1H, dt, $J = 8.0, 6.5$ Hz), 3.08 (1H, ddd, $J = 15.1, 6.4$ Hz), 2.84 (1H, dd, $J = 15.1, 7.1$ Hz), 2.40 (3H, s), 1.97 – 1.15 (2H, m), 1.07 – 0.97 (1H, m), 0.88 (3H, t, $J = 7.3$ Hz), 0.63 – 0.40 (2H, m), 0.41 – 0.11 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.7, 138.5, 136.8, 129.4, 127.2, 117.3, 59.2, 48.9, 34.5, 21.5, 19.5, 13.8, 12.0, 5.5, 4.8; m/z (ESI$^+$) HRMS: Calculated for C$_{17}$H$_{25}$NO$_2$SNa: 330.1498. Found [M+Na]$^+$: 330.1500.

(3$S^*$, 3a$R^*$, 7a$R^*$) and (3$R^*$, 3a$R^*$, 7a$R^*$)-3-Propyl-2-tosylhexahydro-1H-isooindol-5(6$H$)-one (8i)

**General procedure G:** Compound 6i (46.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title
compound 8i (32.2 mg, 64 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 8:1 (A:B) ratio. Under general procedure H, title compound 8i was obtained in 61 % yield (30.7 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOe was observed between C1-H and C10-H, and no significant nOe was observed between C5-H and C10-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of 8i. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8i.

νmax / cm⁻¹: 2957 (m), 1712 (s), 1457 (m), 1341 (s), 1124 (s), 1089 (s); m/z (ESI⁺) HRMS: Calculated for C₁₈H₂₅NO₃Sn: 358.1447. Found [M+Na]⁺: 358.1455;

Data for major diastereomer A: ¹H NMR (500 MHz, CDCl₃): δ 7.72 (2H, d, J = 8.3 Hz, 2 × C13-H), 7.32 (2H, d, J = 8.1 Hz, 2 × C14-H), 3.71 (1H, dd, J = 11.4, 6.4 Hz, 1 × C11-H₂), 3.38 – 3.24 (1H, m, 1 × C1-H), 2.90 (1H, dd, J = 11.2 Hz, 11.2 Hz, 1 × C11-H₂), 2.53 (1H, ddd, J = 14.3, 3.9, 1.9 Hz, 1 × C6-H₂), 2.43 (3H, s, 3 × C16-H₃), 2.41 – 2.31 (1H, m, 1 × C8-H₂), 2.18 – 2.07 (1H, m, 1 × C8-H₂), 2.05 – 1.90 (2H, m, 1 × C6-H₂, 1 × C9-H₂), 1.85 – 1.62 (3H, m, 2 × C2-H₂, 1 × C5-H), 1.49 – 1.40 (1H, m, 1 × C3-H₂), 1.39 – 1.19 (3H, m, 1 × C3-H₂, 1 × C9-H₂, 1 × C10-H), 0.97 – 0.84 (3H, m, 1 × C4-H₃); ¹³C NMR (126 MHz, CDCl₃): δ 208.6 (C7), 143.5 (C15), 135.5 (C12), 129.8 (C14), 127.3 (C13), 65.1 (C1), 53.0 (C11), 49.4 (C5), 45.0 (C6), 42.0 (C10), 39.5 (C8), 35.9 (C2), 25.9 (C9), 21.5 (C16), 17.6 (C3), 14.2 (C4).

Data for minor diastereomer B: Characteristic peaks only: ¹H NMR (500 MHz, CDCl₃): δ 3.68 – 3.58 (2H, m, 1 × C11-H₂, 1 × C1-H), 2.64 (1H, dd, J = 11.2 Hz, 11.2 Hz, 1 × C11-H₂).

4-Methyl-N-(1-phenylbut-3-en-2-yl)benzenesulfonamide

General procedure F: (E)-4-Methyl-N-(2-phenylethylidene)benzenesulfonamide (2.44 g, 8.5 mmol) (prepared according to literature procedure) and vinylmagnesium bromide (17.0
mL, 17.0 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (2.14 g, 76 %) as a colorless oil; $\nu_{\max}$ / cm$^{-1}$: 3274 (m), 2923 (m), 1413 (m), 1324 (s), 1153 (s), 1093 (s), 923 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.61 (2H, d, $J = 8.3$ Hz), 7.33 – 6.98 (5H, m), 7.13 – 6.74 (2H, m), 5.85 – 5.42 (1H, m), 5.23 – 4.88 (2H, m), 4.68 (1H, d, $J = 7.5$ Hz), 4.31 – 3.79 (1H, m), 3.08 – 2.61 (2H, m), 2.40 (3H, s); $^1$H NMR (100 MHz, CDCl$_3$): $\delta$ 143.1, 137.5, 137.2, 136.3, 129.5, 129.4, 128.5, 127.1, 126.8, 116.2, 56.9, 41.9, 21.5; $m/z$ (ESI$^+$) HRMS: Calculated for C$_{17}$H$_{19}$NO$_2$SNa: 324.1029. Found [M+Na]$^+$: 324.1034;

N-(Cyclopropylmethyl)-4-methyl-N-(1-phenylbut-3-en-2-yl)benzenesulfonamide (6j)

![Chemical Structure](image)

**General procedure E:** 4-Methyl-N-(1-phenylbut-3-en-2-yl)benzenesulfonamide (1.26 g, 4.0 mmol) and (bromomethyl)cyclopropane (1.08 g, 8.0 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound 6j (0.79 g, 56 %) as a colorless oil; $\nu_{\max}$ / cm$^{-1}$: 2924 (m), 1454 (m), 1330 (s), 1152 (s), 1090 (s), 1018 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.62 (2H, d, $J = 8.0$ Hz), 7.33 – 6.78 (7H, m), 5.77 (1H, ddd, $J = 17.1$, 10.5, 6.3 Hz), 5.08 (1H, d, $J = 10.5$ Hz), 4.99 (1H, d, $J = 17.3$ Hz), 4.70 – 4.54 (1H, m), 3.15 (1H, dd, $J = 15.1$, 6.6 Hz), 3.10 – 2.93 (3H, m), 2.39 (3H, s), 1.24 – 0.83 (1H, m), 0.67 – 0.42 (2H, m), 0.35 – 0.06 (2H, m); $^1$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.8, 138.4, 138.1, 135.7, 129.4, 129.3, 128.4, 127.2, 126.4, 118.4, 61.3, 49.5, 39.9, 21.5, 11.9, 5.5, 5.2; $m/z$ (ESI$^+$) HRMS: Calculated for C$_{21}$H$_{25}$NO$_2$SNa: 378.1498. Found [M+Na]$^+$: 378.1507;

(3$^S$, 3a$^R$, 7a$^R$) and (3$^R$, 3a$^R$, 7a$^R$)-3-benzyl-2-tosylhexahydro-1H-isoindol-5(6$H$)-one (8j)
General procedure G: Compound 6j (53.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8j (37.4 mg, 65 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 5:1 (A:B) ratio. Under general procedure H, title compound 8j was obtained in 67 % yield (38.6 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). A nOe between C2b-H and C7-H was observed, and no significant nOe was observed between C7-H and C12-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of 8l. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8l.

νmax / cm⁻¹: 2925 (m), 1711 (s), 1339 (s), 1155 (s), 1089 (m), 1028 (m); m/z (ESI⁺) HRMS: Calculated for C₂₂H₂₅NO₃SNa: 406.1447. Found [M+Na]⁺: 406.1431;

Data for major diastereomer A: ¹H NMR (400 MHz, CDCl₃): δ 7.80 (2H, d, J = 8.2 Hz, 2 × C15-H), 7.45 – 7.05 (7H, m, 2 × C16-H, 2 × C5-H, 2 × C4-H, 1 × C6-H), 3.68 (1H, dd, J = 11.4, 6.1 Hz, 1 × C13-H₂), 3.50 (1H, ddd, J = 9.2, 7.7, 3.4 Hz, 1 × C1-H), 3.27 (1H, dd, J = 13.7, 3.4 Hz, 1 × C2-H₂), 3.07 (1H, dd, J = 13.7, 7.8 Hz, 1 × C2-H₂), 2.76 (1H, dd, J = 11.2, 11.2 Hz, 1 × C13-H₂), 2.45 (3H, s, 3 × C18-H₃), 2.38 – 2.25 (1H, m, 1 × C10-H₂), 2.09 – 1.96 (1H, m, 1 × C10-H₂), 1.97 – 1.82 (2H, m, 1 × C8-H₂, 1 × C11-H₂), 1.73 (1H, dd, J = 13.8, 13.8 Hz, 1 × C8-H₂), 1.68 – 1.56 (1H, m, 1 × C7-H), 1.33 – 1.11 (2H, m, 1 × C11-H₂, 1 × C12-H); ¹³C NMR (100 MHz, CDCl₃): δ 208.3 (C9), 143.7 (C17), 136.7 (C3), 135.1 (C14), 129.9, 129.8, 128.5, 127.4, 126.8 (C15, C16, C4, C5, C6), 66.0 (C1), 52.8 (C13), 49.2 (C7), 44.6 (C8), 41.7 (C12), 40.4 (C2), 39.3 (C10), 25.6 (C11), 21.6 (C18).
Data for minor diastereomer B: Characteristic peaks only: $^1$H NMR (400 MHz, CDCl$_3$): δ 4.06 (1H, ddd, $J = 9.4, 7.7, 3.2$ Hz, 1 × C1-H), 3.17 (1H, dd, $J = 14.5, 3.3$ Hz, 1 × C2-H$_2$), 2.96 (1H, dd, $J = 14.6, 9.5$ Hz, 1 × C2-H$_2$), 2.62 (1H, dd, $J = 10.6, 9.1$ Hz, 1 × C13-H$_2$), 2.25 – 2.16 (1H, m, 1 × C7-H), 1.50 – 1.42 (1H, m, 1 × C12-H);

4-Methyl-N-(4-methylpent-1-en-3-yl)benzenesulfonamide

General procedure F: (E)-4-Methyl-N-(2-methylpropylidene)benzenesulfonamide (1.40 g, 6.2 mmol) (prepared according to literature procedure$^6$) and vinylmagnesium bromide (12.4 mL, 12.4 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15% EtOAc/Hex) to yield the title compound (1.44 g, 92%) as a colorless solid; m.p.: 76 – 78 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 3279 (m), 2962 (m), 1434 (m), 1323 (s), 1155 (s), 919 (m); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.73 (2H, d, $J = 8.3$ Hz), 7.26 (2H, d, $J = 8.5$ Hz), 5.53 (1H, ddd, $J = 17.1, 10.5, 6.7$ Hz), 5.21 – 4.81 (2H, m), 4.59 – 4.56 (1H, br. m), 3.91 – 3.34 (1H, m), 2.41 (3H, s), 1.78 – 1.70 (1H, m), 0.83 (6H, dd, $J = 6.8, 1.5$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 143.1, 138.1, 135.7, 129.4, 127.2, 116.6, 61.6, 32.7, 21.5, 18.2, 18.0; m/z (ESI$^+$) HRMS: Calculated for C$_{13}$H$_{19}$NO$_2$SNa: 276.1029. Found [M+Na]$^+$: 276.1039;

N-(Cyclopropylmethyl)-4-methyl-N-(4-methylpent-1-en-3-yl)benzenesulfonamide (6k)

General procedure E: 4-Methyl-N-(4-methylpent-1-en-3-yl)benzenesulfonamide (0.51 g, 2.0 mmol) and (bromomethyl)cyclopropane (0.54 g, 4.0 mmol) were employed, the crude mixture was purified by column chromatography (10% EtOAc/Hex) to yield the title compound 6k (0.63 g, 92%) as a colorless oil; $\nu_{\text{max}}$ / cm$^{-1}$: 2962 (m), 1333 (s), 1156 (s), 1090 (m), 1018 (m), 925 (m); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.70 (2H, d, $J = 8.3$ Hz), 7.23 (2H, d,
\( J = 8.0 \text{ Hz} \), 5.65 (1H, ddd, \( J = 17.1, 10.4, 8.7 \text{ Hz} \)), 5.09 – 5.03 (1H, m), 4.95 (1H, ddd, \( J = 17.2, 1.7, 0.9 \text{ Hz} \)), 3.86 (1H, dd, \( J = 10.6, 8.7 \text{ Hz} \)), 3.07 (1H, dd, \( J = 15.1, 6.4 \text{ Hz} \)), 2.91 (1H, dd, \( J = 15.1, 7.0 \text{ Hz} \)), 2.39 (3H, s), 2.06 – 1.75 (1H, m), 1.14 – 0.93 (4H, m), 0.87 (3H, d, \( J = 6.5 \text{ Hz} \)), 0.52 – 0.45 (2H, m), 0.35 – 0.07 (2H, m); 1\(^3\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 142.6, 138.5, 135.1, 129.2, 127.4, 119.0, 67.5, 49.5, 30.4, 21.5, 20.5, 20.3, 11.6, 5.8, 4.7; m/z (ESI\(^+\)) \) HRMS: Calculated for C\(_{17}\)H\(_{25}\)NO\(_2\)SNa: 330.1498. Found [M+Na\(^+\)]: 330.1501.

(3S*, 3aR*, 7aR*) and (3R*, 3aR*, 7aR*)-3-Isopropyl-2-tosylhexahydro-1H-isindol-5(6H)-one (8k)

**General procedure H:** Compound 6k (46.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8k (33.8 mg, 67 %) as an off-white solid. A mixture of diastereomers A and B were obtained in a 10:1 (A:B) ratio. **Under general procedure G, title compound 8k was obtained in 45 % yield (22.7 mg) as an off-white solid. A mixture of diastereomers A, B and C were obtained in a 14:2:1 (A:B:C) ratio.

Major diastereomer A could be recrystallized from the mixture (EtOAc/Hex), its structure and relative stereochemistry were determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8l.

\( \nu_{\text{max}} / \text{cm}^{-1} \): 2961 (m), 1709 (s), 1335 (s), 1156 (s), 1090 (m), 1002 (m); m/z (ESI\(^+\)) HRMS: Calculated for C\(_{18}\)H\(_{25}\)NO\(_3\)SNa: 358.1447. Found [M+Na\(^+\)]: 358.1452.

Data for major diastereomer A: m.p.: 100-102 °C (CH\(_2\)Cl\(_2\)/Hex); \(^1\)H NMR (400 MHz, CD\(_3\)CN): \( \delta 7.85 – 7.75 (2H, m, 2 \times C13-H), 7.53 – 7.39 (2H, m, 2 \times C14-H), 3.72 (1H, dd, \( J = 11.8, 6.5 \text{ Hz}, 1 \times C11-H2), 3.34 (1H, dd, \( J = 9.1, 4.0 \text{ Hz}, 1 \times C1-H), 2.84 (1H, dd, \( J = 11.8 \text{ Hz}, 11.8 \text{ Hz}, 1 \times C11-H2), 2.50 – 2.42 (4H, m, 1 \times C6-H2, 3 \times C16-H3), 2.41 – 2.34 (1H, m, 1

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× C2-H), 2.28 – 2.19 (1H, m, 1 × C8-H2), 2.13 – 2.00 (2H, m, 1 × C8-H2, 1 × C6-H3), 1.94 – 1.81 (2H, m, 1 × C5-H1 × C9-H2), 1.48 – 1.30 (1H, m, 1 × C9-H2), 1.20 – 1.09 (1H, m, 1 × C10-H), 0.97 – 0.94 (6H, m, 3 × C3-H3, 3 × C4-H3); 13C NMR (100 MHz, CD3CN): δ 207.1 (C7), 142.5 (C15), 134.2 (C12), 128.5 (C14), 126.1 (C13), 68.5 (C1), 51.9 (C11), 45.1 (C6), 43.2 (C5), 40.9 (C10), 37.6 (C8), 30.6 (C2), 23.5 (C9), 19.3 (C16), 17.4 (C3), 14.2 (C4);

Data for minor diastereomer B: Characteristic peaks only: 1H NMR (400 MHz, CD3CN): δ 7.73 – 7.70 (1H, m, 2 × C13-H), 3.60 – 3.51 (2H, m, 1 × C11-H2, 1 × C1-H), 2.68 (1H, dd, J = 10.1 Hz, 10.1 Hz, 1 × C11-H2).

N-(1-(Benzyl oxy)but-3-en-2-yl)-4-methylbenzenesulfonamide

General procedure F: (E)-N-(2-(Benzyl oxy)ethyldene)-4-methylbenzenesulfonamide (2.99 g, 9.5 mmol) (prepared according to literature procedure7) and vinylmagnesium bromide (19.0 mL, 19.0 mmol, 1.0 M in THF) were employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (2.24 g, 73 %) as a colorless oil; νmax / cm⁻¹: 3274 (m), 2901 (m), 1325 (m), 1160 (s), 1091 (s), 698 (s); 1H NMR (400 MHz, CDCl3): δ 7.71 (2H, d, J = 8.3 Hz), 7.45 – 7.26 (3H, m), 7.27 – 7.10 (4H, m), 5.69 (1H, ddd, J = 17.0, 10.4, 6.3 Hz), 5.16 (1H, dd, J = 17.2, 1.5 Hz), 5.09 (1H, dd, J = 10.5, 1.4 Hz), 4.98 (1H, br. s), 4.41 (2H, s), 3.96 – 3.88 (1H, m), 3.75 – 3.03 (2H, m), 2.41 (3H, s); 13C
NMR (100 MHz, CDCl$_3$): $\delta$ 143.3, 137.6, 137.4, 135.1, 129.5, 128.4, 127.9, 127.7, 127.2, 117.5, 73.2, 71.8, 55.7, 21.5; $m/z$ (ESI$^+$) HRMS: Calculated for C$_{18}$H$_{21}$NO$_3$SNa: 354.1134. Found [M+Na]$^+$: 354.1141.

1-(Benzylxy)-N-(cyclopropylmethyl)but-3-en-2-amine (6l)

![Structural diagram of 6l]

**General procedure E:** N-(1-(Benzylxy)but-3-en-2-yl)-4-methylbenzenesulfonamide (0.46 g, 1.3 mmol) and (bromomethyl)cyclopropane (0.36 g, 2.6 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound 6l (0.36 g, 71 %) as a colorless oil; $\nu_{\text{max}}$ / cm$^{-1}$: 3311 (w), 2858 (m), 1642 (m), 1240 (m), 1153 (m), 1090 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.73 (2H, d, $J = 8.3$ Hz), 7.49 – 7.21 (5H, m), 7.18 (2H, d, $J = 8.6$ Hz), 6.12 – 5.54 (1H, m), 5.38 – 4.98 (2H, m), 4.75 – 4.57 (1H, m), 4.46 (2H, d, $J = 3.0$ Hz), 3.70 (2H, d, $J = 6.9$ Hz), 3.11 (1H, dd, $J = 15.1, 6.8$ Hz), 2.37 (3H, s), 1.04 – 0.85 (1H, m), 0.55 – 0.34 (2H, m), 0.30 – 0.06 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.7, 138.4, 137.8, 134.4, 129.3, 128.3, 127.7, 127.6, 127.3, 118.6, 73.0, 70.7, 58.7, 49.6, 21.5, 11.8, 5.1, 5.0; $m/z$ (ESI$^+$) HRMS: Calculated for C$_{22}$H$_{27}$NO$_3$SNa: 408.1604. Found [M+Na]$^+$: 408.1617.

(3$R^*$, 3a$R^*$, 7a$R^*$) and (3$S^*$, 3a$R^*$, 7a$R^*$)-3-((Benzylxy)methyl)-2-tosylhexahydro-1H-isoindol-5(6H)-one (8l)

![Structural diagrams of 6l and 8l]
**General procedure H:** Compound 6l (57.8 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8l (42.2 mg, 68 %) as an off-white solid. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. Under general procedure G, title compound 8l was obtained in 61 % yield (37.9 mg) as an off-white solid. A mixture of diastereomers A and B were obtained in a 2:1 (A:B) ratio.

Diastereomer A and B could be separated by flash column chromatography (20 % EtOAc/hexane) using 60H silica. The structure and relative stereochemistry of major diastereomer A was determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C14–H and C13–H, C14b and C8, these results indicated a trans ring junction for diastereomer B (same as diastereomer A), which suggests that the stereochemistry at C1 for diastereomer B is opposite to that of diastereomer A.

\[ \nu_{\text{max}} / \text{cm}^{-1}: 2885 (\text{m}), 1711 (\text{s}), 1343 (\text{m}), 1157 (\text{s}), 1088 (\text{s}), 662 (\text{s}); m/z (ESI\^+) HRMS: \text{Calculated for C}_{23}\text{H}_{27}\text{NO}_{3}\text{SNa}: 436.1553. \text{Found [M+Na]}^{\text{+}}: 436.1544. \]

Data for major diastereomer A: m.p.: 132 – 135 °C (CH2Cl2/Hex); \(^1\)H NMR (400 MHz, C6D6): δ 7.70 (2H, d, J = 8.1 Hz, 2 × C16–H), 7.36 – 7.08 (4H, m, 2 × C6–H, 2 × C5–H), 7.11 – 6.91 (1H, m, 1 × C7–H), 6.78 (2H, dd, J = 8.2, 2.0 Hz, 2 × C17–H), 4.27 (2H, s, 2 × C3–H), 3.89 (1H, dd, J = 9.6, 3.2 Hz, 1 × C2–H2), 3.62 (1H, dd, J = 9.6, 6.7 Hz1 × C2–H2), 3.49 (1H, dd, J = 11.0, 6.8 Hz, 1 × C14–H2), 3.30 (1H, ddd, J = 9.6, 6.7, 3.2 Hz, 1 × C1–H), 2.63 (1H, ddd, J = 13.9, 3.7, 1.8 Hz, 1 × C9–H2), 2.49 (1H, dd, J = 11.2, 1.4 Hz, 1 × C14–H2), 2.01 – 1.88 (1H, m, 1 × C11–H2), 1.86 (3H, s, 3 × C19–H3), 1.68 – 1.53 (1H, m, 1 × C8–H), 1.52 – 1.39 (1H, m, 1 × C9–H2), 1.27 (1H, td, J = 14.2, 6.8 Hz, 1 × C11–H2), 1.13 – 0.94 (1H, m, 1 × C12–H2), 0.94 – 0.72 (1H, m, 1 × C13–H), 0.62 – 0.40 (1H, m, 1 × C12–H2); \(^{13}\)C NMR (100 MHz, C6D6): δ 205.9 (C10), 142.7 (C18), 138.3 (C4), 136.5 (C15), 129.3 (C16), 128.3, 127.8, 127.5, 127.4 (C5, C6, C7, C17), 73.3 (C3), 72.0 (C2), 64.1 (C1), 52.9 (C14), 48.4 (C8), 44.5 (C9), 41.2 (C13), 38.8 (C11), 25.1 (C12), 20.7 (C19).
Data for minor diastereomer B: m.p.: 131 – 133 °C (CH₂Cl₂/Hex); ¹H NMR (400 MHz, C₆D₆): δ 7.68 (2H, d, J = 8.2 Hz, 2 × C16-H), 7.19 – 7.15 (4H, m, 2 × C6-H, 2 × C5-H), 7.08 – 6.99 (1H, m, 1 × C7-H), 6.78 (2H, d, J = 8.3 Hz, 2 × C17-H), 4.25 (2H, s, 2 × C3-H₂), 3.57 (3H, dt, J = 16.5, 6.7 Hz, 2 × C2-H₂, 1 × C1-H), 3.40 (1H, dd, J = 8.5, 6.6 Hz, 1 × C14-H₂), 2.38 – 2.17 (2H, m, 1 × C14-H₂, 1 × C9-H₂), 2.07 (1H, dd, J = 14.1, 14.1 Hz, 1 × C9-H₂), 1.99 – 1.88 (1H, m, 1 × C11-H₂), 1.87 (3H, s, 3 × C19-H₃), 1.82 – 1.70 (1H, m, 1 × C13-H), 1.52 (1H, td, J = 14.2, 6.3 Hz, 1 × C11-H₂), 1.19 – 1.09 (1H, m, 1 × C12-H₂), 1.04 – 0.89 (1H, m, 1 × C8-H), 0.37 – 0.25 (1H, m, 1 × C12-H₂). ¹³C NMR (100 MHz, C₆D₆): δ 206.3 (C10), 142.8 (C18), 138.2 (C4), 134.9 (C15), 128.3 (C16), 127.6, 127.5, 127.5 (C5, C6, C7, C17), 73.4 (C3), 70.6 (C2), 60.5 (C1), 52.4 (C14), 46.3 (C8), 41.9 (C9), 39.3 (C11), 39.1 (C13), 26.1 (C12), 20.7 (C19).

**N-(2-(Benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide**

![Chemical structure of N-(2-(Benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide]

**General procedure F:** (E)-N-(2-(Benzyloxy)ethylidene)-4-methylbenzenesulfonamide (0.91 g, 3.0 mmol) and cyclopropylmagnesium bromide (0.86 g, 6.0 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound (0.68 g, 66 %) as a colorless oil; νmax / cm⁻¹: 3276 (m), 2900 (m), 1321 (m), 1157 (m), 1084 (s), 1026 (s); ¹H NMR (400 MHz, CDCl₃): δ 7.74 (2H, d, J = 8.3 Hz), 7.40 – 7.04 (7H, m), 5.27 – 5.22 (1H, br. m), 4.40 (2H, s), 3.46 (1H, dd, J = 9.5, 4.4 Hz), 3.37 (1H, dd, J = 9.5, 4.2 Hz), 2.71 (1H, ddd, J = 8.6, 7.1, 4.3 Hz), 2.39 (3H, s), 0.96 (1H, ddt, J = 8.4, 4.9,
4.9 Hz), 0.52 – 0.40 (1H, m), 0.39 – 0.29 (1H, m), 0.24 – 0.14 (2H, m); 13C NMR (100 MHz, CDCl3): δ 143.0, 138.4, 137.9 129.4, 128.4, 127.7, 127.6, 127.1, 73.2, 72.0, 58.4, 21.5, 13.9, 3.9, 3.4; m/z (ESI+) HRMS: Calculated for C19H23NO3SNa: 368.1291. Found [M+Na]+: 368.1289.

N-allyl-N-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (6m)

**General procedure B:** N-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (0.65 g, 1.9 mmol) were employed, the mixture was purified by column chromatography (10% EtOAc/Hex) to yield title amide 6m (0.64 g, 88%) as a colorless oil; ν max / cm−1: 2921 (m), 1698 (m), 1327 (m), 1154 (s), 1089 (m), 883 (m); 1H NMR (400 MHz, CDCl3): δ 7.71 (2H, d, J = 8.3 Hz), 7.38 – 7.27 (3H, m), 7.23 – 7.18 (2H, m), 7.15 (2H, d, J = 7.9 Hz), 5.83 (1H, ddt, J = 17.2, 10.1, 6.3 Hz), 5.11 (1H, dd, J = 17.2, 1.5 Hz), 5.02 (1H, dd, J = 10.2, 1.4 Hz), 4.43 (1H, d, J = 11.9 Hz), 4.36 (1H, d, J = 11.9 Hz), 3.94 (2H, ddt, J = 6.3, 3.1, 1.5 Hz), 3.66 – 3.56 (2H, m), 3.26 (1H, ddd, J = 9.9, 7.6, 4.9 Hz), 2.37 (3H, s), 0.99 (1H, ddt, J = 9.8, 8.0, 4.9 Hz), 0.68 – 0.52 (1H, m), 0.45 – 0.39 (1H, m), 0.36 – 0.23 (2H, m); 13C NMR (100 MHz, CDCl3): δ 142.6, 138.4, 138.0, 136.4, 129.1, 128.3, 127.8, 127.5, 116.7, 72.9, 71.4, 63.3, 47.7, 21.5, 12.5, 6.2, 3.9; m/z (ESI+) HRMS: Calculated for C23H27NO4SNa: 408.1604. Found [M+Na]+: 408.1596.

(1S*, 3aR*, 7aR*) and (1R*, 3aR*, 7aR*)-1-((benzyloxy)methyl)-2-tosylhexahydro-1H-isoindol-5(6H)-one (8m)
**General procedure H:** Compound 6m was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8m (31.7 mg, 51 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 9:1 (A:B) ratio. Under general procedure G, title compound 8m was obtained in 26 % yield (16.2 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 4:1 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure). nOes were observed between C7-H and C8-H, from C9-H to C2-H, and no significant nOe was observed between C7-H and C2-H. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of 8n. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8o.

\[
\nu_{max} / \text{cm}^{-1}: 2900 (\text{m}), 1712 (\text{s}), 1341 (\text{m}), 1161 (\text{s}), 1090 (\text{s}), 733 (\text{s}); m/z (\text{ESI}^+) \text{ HRMS: } \text{Calculated for } C_{23}H_{27}NO_{3}SNa: 436.1553. \text{ Found } [\text{M+Na}]^+: 436.1546.
\]

\(^1\text{H NMR (400 MHz, CDCl₃): } \delta 7.73 (2\text{H}, d, J = 8.2 \text{ Hz}, 2 \times \text{C16-H}), 7.55 – 6.98 (7\text{H}, m, 2 \times \text{C17-H}, 2 \times \text{C12-H}, 2 \times \text{C13-H}, 1 \times \text{C14-H}), 4.48 (2\text{H}, s, 2 \times \text{C10-H2}), 3.87 (1\text{H}, dt, J = 7.6, 4.5 \text{ Hz}, 1 \times \text{C8-H}), 3.65 (2\text{H}, d, J = 4.6 \text{ Hz}, 2 \times \text{C9-H2}), 3.59 (1\text{H}, dd, J = 8.6, 6.6 \text{ Hz}, 1 \times \text{C1-H2}), 2.68 (1\text{H}, dd, J = 10.6, 8.7 \text{ Hz}, 1 \times \text{C1-H}), 2.54 (1\text{H}, ddd, J = 14.1, 4.2, 1.9 \text{ Hz}, 1 \times \text{C3-H2}), 2.48 – 2.31 (5\text{H}, m, 3 \times \text{C19-H3}, 1 \times \text{C5-H2}, 1 \times \text{C2}), 2.19 – 2.02 (2\text{H}, m, 1 \times \text{C5-H2}, 1 \times \text{C6-H2}), 1.96 (1\text{H}, dd, J = 13.7, 13.7 \text{ Hz}, 1 \times \text{C3-H2}), 1.80 – 1.65 (1\text{H}, m, 1 \times \text{C6-H2}), 1.64 – 1.57 (1\text{H}, m, 1 \times \text{C7-H}); ^{13}\text{C NMR (100 MHz, CDCl₃): } \delta 208.6 (\text{C4}), 143.6 (\text{C18}), 138.7 (\text{C11}), 134.1 (\text{C15}), 129.8 (\text{C17}), 128.4, 127.7, 127.7, 127.5 (\text{C16, C12, C13, C14}), 73.6 (\text{C10}), 70.7 (\text{C9}), 60.4 (\text{C8}), 53.0 (\text{C1}), 45.5 (\text{C7}), 44.4 (\text{C3}), 40.9 (\text{C2}), 40.1 (\text{C5}), 24.2 (\text{C6}), 21.6 (\text{C19}).\]
Data for minor diastereomer B: Characteristic peaks only: $^1$H NMR (400 MHz, CDCl$_3$): δ 3.30 (1H, ddd, $J = 9.5$, 6.4, 3.2 Hz, 1 × C8-H), 3.03 (1H, dd, $J = 11.4$ Hz, 1 × C1-H$_2$).

**N-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide**

![Chemical structure of N-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide](image)

**General procedure A:** 1-Cyclopropylethanamine (0.30 g, 3.5 mmol) and p-toluenesulfonyl chloride (0.83 g, 4.2 mmol) were employed, the crude mixture was purified by column chromatography (20% EtOAc/Hex) to yield title sulfonamide (0.61 g, 71%) as a colorless oil; $\nu_{max}$ / cm$^{-1}$: 3273 (m), 2972 (m), 1423 (m), 1320 (s), 1154 (s), 1089 (s), 970 (m); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.75 (2H, d, $J = 8.3$ Hz), 7.28 (2H, d, $J = 8.0$ Hz), 4.59 (1H, d, $J = 6.4$ Hz), 2.69 – 2.61 (1H, m), 2.42 (3H, s), 1.14 (3H, d, $J = 6.6$ Hz), 0.79 – 0.70 (1H, m), 0.44 (1H, dddd, $J = 9.1$, 8.3, 5.7, 4.5 Hz), 0.32 (1H, dddd, $J = 9.1$, 7.9, 5.6, 4.6 Hz), 0.12 (1H, dddd, $J = 9.4$, 5.6, 4.7, 4.7 Hz), 0.01 (1H, dddd, $J = 9.6$, 5.7, 4.8, 4.8 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 143.1, 138.1, 129.5, 127.1, 54.7, 21.5, 21.2, 17.9, 3.6, 3.3; m/z (ESI$^+$) HRMS: Calculated for C$_{12}$H$_{17}$NO$_2$SNa: 262.0872. Found [M+Na]$^+$: 262.0869.

**N-allyl-N-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6n)**

![Chemical structure of N-allyl-N-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6n)](image)

**General procedure B:** N-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide (0.52 g, 2.1 mmol) and allyl bromide (1.26 g, 10.5 mmol) were employed, the crude mixture was purified by column chromatography (10% EtOAc/Hex) to yield the title compound 6n (0.53 g, 91%) as a colorless oil; $\nu_{max}$ / cm$^{-1}$: 2974 (m), 1332 (s), 1151 (s), 1090 (s), 1038 (s), 879 (m); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.67 (2H, d, $J = 8.1$ Hz), 7.25 (2H, d, $J = 8.0$ Hz), 5.90 (1H, ddt, $J = 16.9$, 10.2, 6.2 Hz), 5.21 (1H, dd, $J = 17.2$, 1.7 Hz), 5.09 (1H, dd, $J = 10.2$, 1.3 Hz), 4.01 – 3.95 (1H, m), 3.90 – 3.84 (1H, m), 3.13 (1H, dq, $J = 9.2$, 6.8 Hz), 2.40 (3H, s), 1.13 (3H, dd, $J = 6.8$, 0.7 Hz), 0.86 (1H, qt, $J = 8.5$, 4.9 Hz), 0.53 (1H, tdd, $J = 8.6$, 7.0, 5.2 Hz).
(1R*, 3aR*, 7aR*) and (1S*, 3aR*, 7aR*)-1-Methyl-2-tosylhexahydro-1H-isindol-5(6H)-one (8n)

**General procedure H:** Compound 6n (41.9 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33% EtOAc/Hex) to yield the title compound 8n (27.6 mg, 60%) as a colorless solid. A mixture of diastereomers A and B were obtained in a 6:1 (A:B) ratio. Under general procedure G, title compound 8n was obtained in 44% yield (20.3 mg) as a colorless solid. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio.

Major diastereomers A was recrystallized from the mixture of A and B (EtOAc/Hex). The structure and relative stereochemistry of major diastereomers A was determined unambiguously by X-ray crystallography. At the same time, the relative stereochemistry of major diastereomers A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C7-H and C8-H, from Clα-H to C2-H, between C7-H and Clβ-H were observed. The relative stereochemistry of minor diastereomer B was tentatively assigned by analogy to that of minor diastereomer B of 8o.

$\nu_{\text{max}} / \text{cm}^{-1}$: 2971 (m), 1713 (s), 1338 (m), 1162 (m), 1043 (m), 816 (m); m/z (ESI⁺) HRMS: Calculated for C₁₆H₂₁NO₃SNa: 330.1134. Found [M+Na]⁺: 330.1147.

Data for major diastereomer A: m.p.: 159 – 160 °C (CH₂Cl₂/Hex); ¹H NMR (400 MHz, CD₂Cl₂): $\delta$ 7.74 (2H, d, $J = 7.8$ Hz, $2 \times C11$-H), 6.85 (2H, d, $J = 8.1$ Hz, $2 \times C12$-H), 3.91 (1H, td, $J = 6.7$, 6.7 Hz, $1 \times C8$-H), 3.22 (1H, dd, $J = 8.7$, 6.4 Hz, $1 \times C1$-H₂), 2.31 (1H, dd, $J = 10.6$, 8.7, Hz, $1 \times C1$-H₂), 2.06 (1H, dddd, $J = 14.0$, 4.1, 1.9 Hz, $1 \times C3$-H₂), 2.00 – 1.84 (4H, Hz), 0.34 (1H, ddt, $J = 9.6$, 8.4, 5.1 Hz), 0.17 (1H, dddd, $J = 9.7$, 4.9 Hz), 0.07 (1H, dddd, $J = 9.9$, 5.1 Hz); ¹³C NMR (100 MHz, CDCl₃): $\delta$ 142.8, 138.6, 136.6, 129.4, 127.0, 116.6, 59.4, 46.5, 21.5, 18.9, 16.2, 5.5, 4.3; m/z (ESI⁺) HRMS: Calculated for C₁₅H₂₁NO₂SNa: 302.1185. Found [M+Na]⁺: 302.1178.
m, 1 × C5-H2, 3 × C14-H3), 1.38 – 1.24 (2H, m, 1 × C5-H2, 1 × C2-H), 1.13 (1H, dd, J = 13.6, 13.6 Hz, 1 × C3-H2), 0.97 – 0.88 (4H, m, 1 × C6-H2, 3 × C9-H3), 0.86 – 0.76 (1H, m, 1 × C7-H), 0.76 – 0.62 (1H, m, 1 × C6-H2); 13C NMR (100 MHz, C6D6): δ 205.6 (C4), 142.6 (C13), 135.9 (C10), 129.3 (C12), 127.6 (C11), 56.9 (C8), 52.9 (C1), 45.0 (C7), 43.4 (C3), 39.5 (C2), 39.2 (C5), 23.5 (C6), 20.7 (C14), 17.7 (C9).

Data for minor diastereomer B: Characteristic peaks only: 1H NMR (400 MHz, C6D6): δ 7.68 (2H, d, J = 8.2 Hz, 2 × C11-H2), 6.80 (2H, d, J = 8.0 Hz, 2 × C12-H2), 3.39 (1H, dd, J = 10.9, 6.5 Hz, × C1-H2), 2.84 (1H, dt, J = 8.7, 6.1 Hz, 1 × C8-H), 2.58 (1H, dd, J = 10.7, 10.7 Hz, 1 × C1-H2), 0.50 – 0.39 (1H, m, 1 × C6-H2).

Benzyl (1-cyclopropylethyl)carbamate

General procedure A: 1-Cyclopropylethanamine (0.40 g, 4.7 mmol) and benzyl chloroformate (0.85 g, 5.6 mmol) were employed, the crude mixture was purified by column chromatography (20 % EtOAc/Hex) to yield title carbamate (0.42 g, 41 %) as a colorless oil; νmax / cm⁻¹: 3329 (s), 2975 (m), 1679 (s), 1532 (s), 1362 (m), 1252 (s), 1058 (s); 1H NMR (400 MHz, CDCl3): δ 7.45 – 7.26 (5H, m), 5.09 (2H, s), 4.76 (1H, s), 3.23 – 3.04 (1H, m), 1.21 (3H, d, J = 6.6 Hz), 0.81 – 0.78 (1H, m), 0.54 – 0.38 (2H, m), 0.38 – 0.30 (1H, m), 0.23 – 0.19 (1H, m); 13C NMR (100 MHz, CDCl3): δ 155.8, 136.7, 128.5, 128.1, 128.0, 66.5, 51.4,
20.6, 17.5, 3.1, 2.9; m/z (ESI+) HRMS: Calculated for C_{13}H_{17}NO_{2}Na: 242.1151. Found [M+Na]+: 242.1157.

Benzyl allyl (1-cyclopropylethyl)carbamate (6o)

General procedure B: Benzyl (1-cyclopropylethyl)carbamate (0.40 g, 1.8 mmol) and allyl bromide (1.11 g, 9.2 mmol) were employed was employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6o (0.40 g, 85 %) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 3079 (m), 1690 (s), 1408 (s), 1253 (s), 1136 (m), 1028 (m), 918 (m); \( ^1H \) NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.41 – 7.31 (5H, m), 5.91 (1H, ddt, \( J = 16.1, 10.4, 5.6 \) Hz), 5.24 – 5.02 (4H, m), 3.92 (2H, d, \( J = 5.8, \) Hz), 3.36 – 3.27 (1H, br. m), 1.23 (3H, dd, \( J = 6.8, 0.9 \) Hz), 1.10 – 0.90 (1H, m), 0.60 – 0.50 (1H, m), 0.40 (1H, tdd, \( J = 7.9, 2.5, 1.3 \) Hz), 0.25 (2H, br. s); \( ^13C \) NMR (100 MHz, CDCl\textsubscript{3}): \( \delta \) 155.7, 137.6, 136.4, 128.3, 127.7, 127.6, 115.1, 66.3, 57.7, 46.0, 17.8, 15.4, 4.1, 3.3; m/z (ESI+) HRMS: Calculated for C_{16}H_{21}NO_{2}Na: 282.1464. Found [M+Na]+: 282.1470.

Benzyl (1R*, 3aR*, 7aR*) and (1S*, 3aR*, 7aR*)-1-methyl-5-oxohexahydro-1H-isoindole-2(3H)-carboxylate (8o)

General procedure H: Compound 6o (38.9 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8o (29.8 mg, 69 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 3:1 (A:B) ratio. Under general procedure G, title compound 8o was obtained in
52 % yield (22.5 mg) as a colorless oil. A mixture of diastereomers A and B were obtained in a 1:1 (A:B) ratio.

Diastereomer A and B could be separated by flash column chromatography (20 % EtOAc/hexane). The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C7-H and C8-H, and from C9-H to C2-H were observed. The stereochemical assignment of major diastereomer A is consistent with that of major diastereomer A of 8n. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure B). nOes between C2-H and C8-H, from C9-H to C7-H were observed.

v<sub>max</sub> / cm<sup>-1</sup>: 2935 (m), 1696 (s), 1410 (s), 1351 (m), 1090 (m), 770 (m); m/z (ESI<sup>+</sup>) HRMS: Calculated for C<sub>17</sub>H<sub>21</sub>NO<sub>3</sub>Na: 310.1414. Found [M+Na]<sup>+</sup>: 310.1418.

Data for major diastereomer A: 'H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.38 – 7.28 (5H, m, 2 × C<sub>13</sub>H<sub>3</sub>, A+B, 2 × C14-H, A+B, 1 × C15-H, A+B), 5.19 – 5.06 (2H, m, 2 × C11-H<sub>2</sub>, A+B), 4.19 – 4.02 (1H, m, 1 × C8-H, A+B), 3.67 (1H, ddd, J = 10.3, 6.3, 6.3 Hz, 1 × C1-H<sub>2</sub>, A+B), 3.03 (1H, ddd, J = 13.6, 10.1, 10.1 Hz, 1 × C1-H<sub>2</sub>, A+B), 2.63 (1H, ddd, J = 26.6, 10.2, 2.0 Hz, 1 × C3-H<sub>2</sub>, A+B), 2.54 – 2.47 (1H, m, 1 × C5-H<sub>2</sub>, A+B), 2.36 – 2.27 (1H, m, 1 × C7-H<sub>2</sub>, A+B), 2.24 – 2.14 (2H, m, 1 × C3-H<sub>2</sub>, A+B, 1 × C2-H, A+B), 2.14 – 2.04 (1H, m, 1 × C7-H<sub>2</sub>, A+B), 2.03 – 1.96 (1H, m, 1 × C6-H<sub>2</sub>, A+B), 1.66 – 1.55 (1H, m, 1 × C6-H<sub>2</sub>, A+B), 1.08 (3H, dd, J = 23.7, 6.6 Hz, 3 × C9-H<sub>3</sub>, A+B); 13C NMR (126 MHz, CDCl<sub>3</sub>): δ 209.1 (C4, A), 209.0 (C4, B), 154.8 (C10, A), 154.5 (C10, B), 136.8 (C12, A), 136.8 (C12, B), 128.5, 128.5, 127.9, 127.9 (C13, A+B, C14, A+B, C15, A+B), 66.8 (C11, A), 66.6 (C11, B), 55.2 (C8, A), 54.8 (C8, B), 51.3 (C1, A), 51.0 (C1, B), 46.0 (C7, A), 45.3 (C7, B), 44.8 (C3, A), 44.7 (C3, B), 40.4 (C5, A), 40.2 (C5, B), 40.2 (C2, A), 39.5 (C2, B), 24.5 (C6, A), 24.4 (C6, B), 15.8 (C9, A), 15.1 (C9, B).

Data for minor diastereomer B: 'H NMR (500 MHz, CDCl<sub>3</sub>): δ 7.41 – 7.27 (5H, m, 2 × C13-H<sub>3</sub>, A+B, 2 × C14-H, A+B, 1 × C15-H, A+B), 5.21 – 5.04 (2H, m, 2 × C11-H<sub>2</sub>, A+B), 3.96 – 3.76 (1H, m, 1 × C1-H<sub>2</sub>, A+B), 3.49 – 3.33 (1H, m, 1 × C8-H, A+B), 3.03 (1H, dd, J = 10.7, 10.7 Hz, 1 × C1-H<sub>2</sub>, A+B), 2.64 – 2.47 (2H, m, 1 × C3-H<sub>2</sub>, A+B, 1 × C5-H<sub>2</sub>, A+B), 2.33 (1H, ddd, J=15.2, 12.7, 6.6 Hz, 1 × C5-H<sub>2</sub>, A+B), 2.22 – 2.05 (2H, m, 1 × C3-H<sub>2</sub>, A+B, 1 × C6-H<sub>2</sub>, A+B), 1.96 – 1.81 (1H, m, 1 × C2-H, A+B), 1.73 – 1.63 (1H, m, 1 × C7-H, A+B), 1.54 (1H,
ddd, J = 12.6, 4.7, 4.7 Hz, 1 × C6-H₂, A+B), 1.40 (3H, dd, J = 42.0, 6.0 Hz, 3 × C9-H₃, A+B); ¹³C NMR (126 MHz, CDCl₃): δ 209.1 (C₄, A+B), 155.5 (C₁₀, A), 154.9 (C₁₀, B), 136.8 (C₁₂, A), 136.7 (C₁₂, B), 128.5 , 128.0 , 127.9 (C₁₃, A+B, C₁₄, A+B, C₁₅, A+B), 67.1 (C₁₁, A), 66.6 (C₁₁, B), 58.2 (C₈, A), 57.7 (C₈, B), 51.8 (C₇, A), 51.7 (C₁, A), 51.5 (C₁, B), 51.1 (C₇, B), 44.1 (C₃, A+B), 42.8 (C₂, A), 42.7 (C₂, B), 40.3 (C₅, A+B), 26.6 (C⁶, A), 26.5 (C⁶, B), 19.8 (C⁹, A), 18.6 (C⁹, B).

(1S*, 2S*)-N- Allyl-2-butylcyclopropane-1-carboxamide

![Diagram](attachment:image.png)

**General procedure C**: (1S*, 2S*)-2-Butylcyclopropanecarboxylic acid (1.50 g, 10.5 mmol, > 15:1 d.r.) (prepared according to literature procedure) was employed and afforded the title compound (1.86 g, 98 %, > 15:1 d.r.) as an off-white solid which was pure enough to be used without further purification; m.p.: 48 – 50 °C (CH₂Cl₂/Hex); νmax / cm⁻¹: 3283 (m), 2921 (m), 1638 (s), 1547 (s), 1235 (s), 916 (s); ¹H NMR (400 MHz, CDCl₃): δ 5.85 (1H, dddd, J = 17.6, 7.4, 5.6, 1.8 Hz), 5.68 – 5.61 (1H, br. m), 5.22 – 5.10 (2H, m), 3.91 – 3.88 (2H, br. m), 1.38 – 1.24 (7H, m), 1.16 – 1.06 (2H, m), 0.90 – 0.86 (3H, m), 0.60 – 0.55 (1H, m); ¹³C NMR (100 MHz, CDCl₃): δ 173.2, 134.5, 116.2, 42.1, 32.8, 31.4, 22.4, 22.3, 21.5, 14.4, 14.0; m/z (ESI⁺) HRMS: Calculated for C₁₁H₁₉NONa: 204.1359. Found [M+Na]⁺: 204.1363.

(1S*, 2S*)-N-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine

![Diagram](attachment:image.png)

**General procedure D**: (1S*, 2S*)-N- Allyl-2-butylcyclopropane-1-carboxamide (1.10 g, 6.1 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.88 g, 87 %, > 15:1 d.r. 1:1 mixture of two rotamers) as a colorless oil; νmax / cm⁻¹: 2919 (s), 2852 (m), 1455 (m), 992 (m), 915 (s), 727 (m); ¹H NMR (400 MHz CD₃CN) δ 5.88 (1H, ddt, J = 17.2, 10.2, 5.8 Hz), 5.19 – 5.17 (0.5H, m), 5.14 – 5.13 (0.5H, m), 5.06 – 5.05 (0.5H, m), 5.03 – 5.02 (0.5H, m), 3.21 (2H, dt, J = 5.8, 1.5 Hz), 2.47 (1H, dd, J = 12.0, 6.5 Hz), 2.36 (1H, dd, J = 12.1, 7.1 Hz), 1.43 – 1.15 (7H, m), 0.93 – 0.89 (3H, m), 0.68 – 0.61 (1H, m), 0.55 – 0.47 (1H, m), 0.28 – 0.19 (2H, m); ¹³C NMR (100 MHz, CDCl₃): δ 155.5 (C₁₀, A), 154.9 (C₁₀, B), 136.8 (C₁₂, A), 136.7 (C₁₂, B), 128.5 , 128.0 , 124.0 (C₁₃, A+B, C₁₄, A+B, C₁₅, A+B), 58.2 (C₈, A), 57.7 (C₈, B), 51.8 (C₇, A), 51.7 (C₁, A), 51.5 (C₁, B), 51.1 (C₇, B), 44.1 (C₃, A+B), 42.8 (C₂, A), 42.7 (C₂, B), 40.3 (C₅, A+B), 26.6 (C₆, A), 26.5 (C₆, B), 19.8 (C₉, A), 18.6 (C₉, B).
MHz, CD$_3$CN): $\delta$ 138.0, 117.3, 53.5, 51.8, 33.3, 31.6, 22.2, 18.8, 17.4, 13.4, 9.9; m/z (ESI$^+$) HRMS: Calculated for C$_{11}$H$_{22}$N: 168.1747. Found [M+H]$^+$: 168.1749;

Benzyl (1S*, 2S*)-allyl((-2-butylcyclopropyl)methyl)carbamate (6p)

General procedure E: (1S*, 2S*)-N-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine (0.68 g, 5.3 mmol) and benzyl chloroformate (1.08 g, 6.4 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6p (1.24 g, 78 %, > 15:1 d.r.) as a colorless oil; $v_{\text{max}} / \text{cm}^{-1}$: 2921 (m), 1694 (s), 1455 (s), 1404 (s), 1220 (s), 1158 (s); $^1$H NMR (500 MHz, CD$_3$CN, 65 $^\circ$C): $\delta$ 7.38 – 7.31 (5H, m), 5.88 – 5.80 (1H, m), 5.17 – 2.12 (4H, m), 4.01 – 3.93 (2H, m), 3.22 (1H, dd, $J = 14.5, 6.4$ Hz), 3.11 (1H, dd, $J = 14.5, 7.3$ Hz), 1.39 – 1.15 (6H, m), 0.91 – 0.89 (3H, m), 0.79 – 0.73 (1H, m), 0.67 – 0.61 (1H, m), 0.35 (1H, dt, $J = 8.8, 4.7$ Hz), 0.25 (1H, dt, $J = 8.2, 4.8$ Hz); $^{13}$C NMR (126 MHz, CD$_3$CN, 65 $^\circ$C): $\delta$ 155.8, 134.5, 128.3, 127.7, 127.6, 116.9, 115.6, 66.5, 50.6, 49.4, 33.0, 31.4, 22.1, 17.6, 17.5, 13.3, 10.1; m/z (ESI$^+$) HRMS: Calculated for C$_{19}$H$_{27}$NO$_2$Na: 324.1934. Found [M+Na]$^+$: 324.1943.

Benzyl (3aR*, 4S*, 7aR*)-4-butyl-6-oxooctahydro-2H-isooindole-2-carboxylate (8p)

General procedure H: Compound 6p (45.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8p (39.1 mg, 79 %, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil; Under general procedure G, title compound 8p was obtained in 54 % yield (26.8 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil.
$\nu_{\text{max}} / \text{cm}^{-1}$: 2925 (m), 1690 (s), 1402 (s), 1357 (s), 1112 (s), 697 (s); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.40 – 7.30 (5H, m, 2 × C16-H, A+B, 2 × C17-H, A+B, 1 × C18-H, A+B), 5.18 – 5.11 (2H, m, 2 × C14-H, A+B), 3.86 (0.5H, dd, $J = 10.4, 6.9$ Hz, 0.5 × C1-H, B), 3.80 – 3.67 (1.5H, m, 1 × C12-H, A+B, 0.5 × C1-H, A), 3.06 – 2.97 (2H, m, 1 × C12-H, A+B, 1 × C1-H, A+B), 2.63 – 2.54 (2H, m, 1 × C3-H, A+B, 1 × C5-H, A+B), 2.24 – 2.15 (1H, m, 1 × C3-H, A+B), 2.05 – 1.92 (2H, m, 1 × C5-H, A+B, 1 × C6-H, A+B), 1.87 – 1.76 (1H, m, 1 × C2-H, A+B), 1.75 – 1.65 (1H, m, 1 × C11-H, A+B), 1.52 – 1.41 (1H, m, 1 × C7-H, A+B), 1.35 – 1.17 (5H, m, 1 × C7-H, A+B, 2 × C8-H, A+B, 2 × C9-H, A+B), 0.89 (3H, t, $J = 6.9$ Hz, 3 × C10-H, A+B). $^{13}$C NMR (100 MHz, CDCl$_3$): 209.1 (C4, A), 209.1 (C4, B), 154.8 (C13, A+B), 136.8 (C15, A), 136.8 (C15, B), 128.5 (1 × CAr, A+B), 128.1, 128.0, 128.0, 127.9 (2 × CAr, A+B), 66.9 (C14, A+B), 51.1 (C12, A), 50.8 (C12, B), 49.7 (C1, A), 49.4 (C1, B), 48.5 (C2, A), 47.8 (C2, B), 46.1(C5, A), 46.0(C5, B), 44.0(C3, A+B), 43.4 (C6, A), 42.7 (C6, B), 39.6 (C11, A), 39.5 (C11, B), 34.7 (C7, A), 28.1, 28.1, 22.7, (C7, B, C8, A+B, C9, A+B), 14.0(C10, A), 13.9 (C10, B); $m/z$ (ESI$^+$) HRMS: Calculated for C$_{20}$H$_{27}$NO$_3$Na: 352.1883. Found [M+Na]$^+$: 352.1895; The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes from C2-H to C6-H, and from C11-H to C7-9-H were observed. The stereochemical assignment of this compound is consistent with that of 8q and 8s.

$(1R^*, 2S^*)$-N-allyl-2-cyclohexylcyclopropanecarboxamide

**General procedure C:** $(1R^*, 2S^*)$-2-Cyclohexylcyclopropanecarboxylic acid (0.98 g, 86 %, > 15:1 d.r.) (prepared according to literature procedure$^2$) was employed and afforded the title compound (0.98 g, 86 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification. m.p.: 93 – 95 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}} / \text{cm}^{-1}$: 2920 (m), 2849 (m), 1697 (s), 1414 (m), 1228 (m), 1244 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 5.85 (1H, ddt, $J = 17.1, 10.2, 5.7$ Hz), 5.57 (1H, br. s), 5.30 – 4.87 (2H, m), 4.12 – 3.63 (2H, m), 1.80 – 1.66 (5H, m), 1.65 – 1.53 (3H, m), 1.29 – 1.01 (5H, m), 0.80 – 0.53 (2H, m); $^{13}$C NMR (100 MHz, CD$_3$CN): $\delta$ 173.2, 134.5, 116.2, 42.1, 41.7, 32.7, 32.5, 28.0, 26.4, 26.1, 21.1, 13.1; $m/z$ (ESI$^+$) HRMS: Calculated for C$_{13}$H$_{21}$NO$_3$Na: 230.1515. Found [M+Na]$^+$: 230.1519.
(1R*, 2S*)-N-((2-Cyclohexylcyclopropyl)methyl)prop-2-en-1-amine

\[ \text{General procedure D: } (1R*, 2S*)-N-\text{Allyl-2-cyclohexylcyclopropanecarboxamide} (0.57 \text{ g,} \ 2.8 \text{ mmol}) \text{ was employed, the crude mixture was purified by column chromatography (100 \% EtOAc) to yield the title compound (0.49 g, 90 \%, > 15:1 d.r.) as a colorless oil; } \nu_{\text{max}} / \text{cm}^{-1}: 2920 (\text{m}), 2849 (\text{m}), 1698 (\text{m}), 1414 (\text{m}), 1244 (\text{m}), 1228 (\text{m}); \ ^1\text{H NMR (400 MHz, CDCl}_3): \delta 5.96 (1H, ddt, \ J = 16.8, 10.2, 6.3 \text{ Hz}), 5.53 – 4.91 (2H, m), 4.46 (1H, br. s), 3.39 (2H, d, \ J = 6.3 \text{ Hz}), 2.99 – 2.22 (2H, m), 2.00 – 1.47 (5H, m), 1.18 – 0.92 (5H, m), 0.91 – 0.73 (1H, m), 0.67 – 0.51 (1H, m), 0.47 – 0.20 (3H, m); \ ^{13}\text{C NMR (100 MHz, CDCl}_3): \delta 134.0, 118.4, 52.8, 51.0, 42.0, 33.1, 32.7, 26.5, 26.2, 24.8, 15.9, 9.7; \ m/z \ (\text{ESI}^+) \text{ HRMS: Calculated for C}_{13}\text{H}_{24}\text{N: 194.1903. Found [M+H]^+: 194.1908.}

Benzyl (1R*, 2S*)-allyl-((2-cyclohexylcyclopropyl)methyl)carbamate (6q)

\[ \text{General procedure E: } (1R*, 2S*)-N-(\text{2-Cyclohexylcyclopropyl)methyl})\text{prop-2-en-1-amine (0.48 g, 2.5 mmol) and benzyl chloroformate (0.85 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 \% EtOAc/Hex) to yield the title compound 6q (0.54 g, 67 \%, > 15:1 d.r.) as a colorless oil; } \nu_{\text{max}} / \text{cm}^{-1}: 2920 (\text{m}), 1697 (\text{s}), 1244 (\text{m}), 1229 (\text{m}), 1076 (\text{s}), 697 (\text{s}); \ ^1\text{H NMR (500 MHz, CD}_3\text{CN, 65^\circ C): } \delta 7.80 – 6.97 (5\text{H, m), 6.07 – 5.61 (1H, m), 5.51 – 4.65 (4H, m), 4.18 – 3.79 (2H, m), 3.24 (1H, dd, } \ J = 14.5, 6.3 \text{ Hz), 3.09 (1H, dd, } \ J = 14.6, 7.4 \text{ Hz), 1.80 – 1.47 (5H, br. m), 1.31 – 1.15 (3H, br. m), 1.13 – 0.94 (2H, br. m), 0.92 – 0.75 (1H, m), 0.71 – 0.57 (1H, m), 0.57 – 0.43 (1H, m), 0.46 – 0.11 (2H, m); \ ^{13}\text{C NMR (126 MHz, CD}_3\text{CN, 65^\circ C): } \delta 155.8, 134.5, 128.3, 127.7, 127.7, 116.9, 66.5, 50.5, 49.4, 41.9, 32.7, 32.4, 26.3, 26.0, 24.2, 16.1, 8.7; \ m/z \ (\text{ESI}^+) \text{ HRMS: Calculated for C}_{21}\text{H}_{29}\text{NO}_2\text{Na: 350.2096. Found [M+Na]^+: 350.2091.}} \]
Benzyl (3aR*, 4S*, 7aR*)-4-cyclohexyl-6-oxohexahydro-1H-isoindole-2(3H)-carboxylate (8q)

\[
\begin{align*}
\text{6q} & \quad \text{8q}
\end{align*}
\]

**General procedure H:** Compound 6q (49.1 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (30% EtOAc/Hex) to yield the title compound 8q (37.9 mg, 71%, >15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid; Under general procedure G, title compound 8q was obtained in 38% yield (20.3 mg, >15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid.

m.p.: 112 – 114 °C (CH\textsubscript{2}Cl\textsubscript{2}/Hex); \(\nu_{\text{max}}\) / cm\(^{-1}\): 2922 (m), 2851 (m), 1693 (s), 1417 (s), 1357 (m), 1076 (m); \(^1\text{H NMR}\) (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.68 – 7.26 (5H, m), 5.42 – 4.72 (2H, m), 3.85 (0.5H, dd, \(J = 10.4, 6.8\) Hz), 3.82 – 3.56 (1.5H, m), 3.24 – 2.78 (2H, m), 2.70 – 2.48 (1H, m), 2.45 – 2.30 (1H, m), 2.25 – 2.09 (2H, m), 2.08 – 1.86 (2H, m), 1.84 – 1.57 (6H, m), 1.47 (1H, dd, \(J = 12.9, 12.9\) Hz), 1.41 – 1.26 (1H, m), 1.27 – 0.89 (4H, m); \(^{13}\text{C NMR}\) (100 MHz, CDCl\textsubscript{3}): \(\delta\) 209.9 (C\textsubscript{4}, A), 209.9 (C\textsubscript{4}, B), 154.8 (C\textsubscript{13}, B), 154.7(C\textsubscript{13}, B), 136.7, 128.5, 128.5, 128.1, 128.1, 128.0, 127.9 (CAr, A+B), 66.9, 66.8*, 51.0, 50.7*, 49.6, 49.2*, 45.4, 44.9*, 44.8, 44.7*, 44.0, 44.0*, 43.6, 42.9*, 42.2, 41.9*, 40.8, 40.5*, 30.7, 30.5*, 27.5, 27.1*, 26.7, 26.7*, 26.5, 26.4*. Doubling of some peaks due to two different conformers in solution. This compound could not be fully assigned based on the 1D and 2D NMR data, the structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography. \(m/z\) (ESI\(^+\)) HRMS: Calculated for C\textsubscript{22}H\textsubscript{29}NO\textsubscript{3}Na: 378.2040. Found [M+Na]\(^+\): 378.2053.
(1S*, 2S*)-N-Allyl-2-phenylcyclopropanecarboxamide

\[ \text{[Representation of the molecule]} \]

**General procedure C:** (1S*, 2S*)-2-Phenylcyclopropanecarboxylic acid (1.0 g, 6.2 mmol, > 15:1 d.r.) was employed and afforded the title compound (1.20 g, 92 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification; m.p.: 91 – 93 °C (CH\(_2\)Cl\(_2\)/Hex); \( \nu_{\text{max}} / \text{cm}^{-1} \): 3250 (m), 1697 (s), 1632 (s), 1406 (s), 1239 (s), 696 (s); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.29 – 7.25 (2H, m), 7.22 – 7.14 (1H, m), 7.09 – 7.07 (2H, m), 6.02 – 5.67 (2H, m), 5.37 – 5.04 (2H, m), 3.93 – 3.90 (2H, m), 2.66 – 2.33 (1H, m), 1.70 – 1.50 (2H, m), 1.24 – 1.20 (1H, m); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 171.7, 140.8, 134.2, 128.4, 126.2, 126.0, 116.5, 42.3, 26.7, 25.1, 15.9; \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{13}\)H\(_{15}\)NONa: 224.1046. Found [M+Na\(^+\)]: 224.1049.

(1S*, 2S*)-N-((2-Phenylcyclopropyl)methyl)prop-2-en-1-amine

\[ \text{[Representation of the molecule]} \]

**General procedure D:** (1S*, 2S*)-N-Allyl-2-phenylcyclopropanecarboxamide (1.13 g, 5.6 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.90 g, 86 %, > 15:1 d.r. 1:1 mixture of two rotamers) as a colorless oil; \( \nu_{\text{max}} / \text{cm}^{-1} \): 2821 (m), 1702 (s), 1452 (m), 1417 (s), 697 (s); \(^1\)H NMR (400
(1S*, 2S*)-N-((2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (6r)

![Chemical Structure of 6r]

**General procedure E:** (1S*, 2S*)-N-((2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (0.73 g, 3.9 mmol) and benzyl chloroformate (1.33 g, 7.8 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6r (1.19 g, 95 %, > 15:1 d.r.) as a colorless oil; ν\text{max} / cm\(^{-1}\): 3028 (m), 1696 (s), 1455 (s), 1413 (s), 1240 (s), 697 (s); \(^1\)H NMR (500 MHz, CD\(_3\)CN, 65 °C): δ 7.43 – 7.31 (5H, m), 7.30 – 7.23 (2H, m), 7.21 – 7.13 (1H, m), 7.11 – 7.02 (2H, m), 5.99 – 5.71 (1H, m), 5.36 – 4.89 (4H, m), 4.01 (2H, dt, J = 5.5, 1.6 Hz), 3.59 – 3.38 (1H, m), 3.34 – 3.27 (1H, m), 1.92 – 1.86 (1H, m), 1.43 – 1.29 (1H, m), 1.03 – 0.86 (2H, m); \(^13\)C NMR (126 MHz, CD\(_3\)CN, 65 °C): δ 155.9, 142.8, 137.5, 134.4, 128.4, 128.2, 127.8, 127.7, 125.7, 125.4, 119.8, 118.9, 107.3, 66.6, 50.4, 49.6, 22.1, 21.9, 13.8; \(m/z\) (ESI\(^+\)) HRMS: Calculated for C\(_{21}\)H\(_{23}\)NO\(_2\)Na: 344.1621. Found [M+Na]\(^+\): 344.1620.

Benzyl (3aR*, 4S*, 7aR*)-6-oxo-4-phenylhexahydro-1H-isoindole-2(3H)-carboxylate (8r)
General procedure H: Compound 6r (48.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33% EtOAc/Hex) to yield the title compound 8r (26.5 mg, 51%, >15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil; Under general procedure G, title compound 8r was obtained in 27% yield (14.1 mg, >15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil.

ν_max / cm⁻¹: 2884 (m), 1697 (s), 1417 (s), 1357 (s), 1135 (s), 699 (s); ¹H NMR (400 MHz, CDCl₃): δ 7.70 – 6.69 (10H, m, 2 × C₈-H, A+B, 2 × C₉-H, A+B, C₁₀-H, A+B, 2 × C₁₆-H, A+B, 2 × C₁₇-H, A+B, C₁₈-H, A+B), 5.42 – 4.71 (2H, m, 2 × C₁₄-H₂, A+B), 3.73 (1H, ddd, J = 21.3, 10.3, 7.0 Hz, 1 × C₁-H₂, A+B), 3.41 (1H, ddd, J = 27.8, 10.6, 7.1 Hz, 1 × C₁₂-H₂, A+B), 3.07 (1H, td, J = 10.5, 1.6 Hz, 1 × C₁₁-H₂, A+B), 3.00 – 2.72 (2H, m, 1 × C₁₂-H₂, A+B, 1 × C₆-H, A+B), 2.70 – 2.54 (2H, m, 1 × C₃-H₂, A+B, 1 × C₅-H₂, A+B), 2.55 – 2.43 (1H, m, 1 × C₅-H₂, A+B), 2.36 – 2.19 (2H, m, 1 × C₁₁-H, A+B, 1 × C₅-H₂, A+B), 2.16 – 1.99 (1H, m, 1 × C₂-H, A+B) ¹³C NMR (100 MHz, CDCl₃): 208.0 (C₄, A), 207.9 (C₄, B), 154.7 (C₁₃, A+B), 141.6, 141.5, 136.7, 129.1, 129.0, 128.5, 128.4, 128.1, 128.0, 127.9, 127.4, 127.4, 126.6, 126.5 (C₇, A+B, C₈, A+B, C₉, A+B, C₁₀, A+B, C₁₅, A+B, C₁₆, A+B, C₁₇, A+B, C₁₈, A+B), 66.9 (C₁₄, A+B), 51.3 (C₁, A), 51.1 (C₁, B), 49.7 (C₁₂, A), 49.3 (C₁₂, B), 48.8 (C₅, A), 48.5 (C₅, B), 48.4 (C₁₁, A), 48.1 (C₁₁, B), 45.9 (C₆, A), 45.8 (C₆, B), 44.0 (C₃, A+B), 43.5 (C₂, A), 42.8 (C₂, B); m/z (ESI⁺) HRMS: Calculated for C₂₂H₂₃NO₃Na: 372.1570. Found [M+Na]⁺: 372.1574; The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure) A nOe was observed between C₂-H and C₆-H, and no significant nOe was observed between C₂-H and C₁₁-H. The stereochemical assignment of this compound is consistent with that of 8q and 8s.

(1R*, 2S*)-N-allyl-2-benzylcyclopropanecarboxamide
**General procedure C:** (1R*, 2S*)-2-Benzylcyclopropanecarboxylic acid (0.85 g, 4.8 mmol, > 15:1 d.r.) (prepared according to literature procedure) was employed and afforded the title compound (0.92 g, 88 %, > 15:1 d.r.) as a colorless solid which was pure enough to be used without further purification. m.p.: 60 – 62 °C (CH₂Cl₂/Hex); ν<sub>max</sub> / cm<sup>-1</sup>: 3285 (m), 2912 (m), 1637 (m), 1546 (s), 1238 (s), 697 (s); <sup>1</sup>H NMR (400 MHz, CDCl₃) δ 7.33 – 7.25 (2H, m), 7.25 – 7.16 (3H, m), 5.83 (1H, ddt, J = 17.2, 10.2, 5.6 Hz), 5.70 (1H, s), 5.32 – 4.88 (2H, m), 4.07 – 3.69 (2H, m), 2.67 (2H, d, J = 6.9 Hz), 1.85 – 1.59 (1H, m), 1.39 – 1.08 (2H, m), 0.86 – 0.59 (1H, m); <sup>13</sup>C NMR (100 MHz, CDCl₃): 172.7, 140.4, 134.4, 128.4, 128.3, 126.1, 116.2, 42.1, 38.4, 22.2, 21.5, 14.2; m/z (ESI<sup>+</sup>) HRMS: Calculated for C₁₄H₁₇NONa: 238.1202. Found [M+Na]<sup>+</sup>: 238.1207.

(1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine

**General procedure D:** (1R*, 2S*)-N-2-Allyl-2-benzylcyclopropanecarboxamide (0.61 g, 2.8 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.53 g, 92 %, > 15:1 d.r.) as a colorless oil; ν<sub>max</sub> / cm<sup>-1</sup>: 2915 (m), 1642 (m), 1452 (m), 1239 (m), 915 (s), 736 (s); <sup>1</sup>H NMR (400 MHz, CD₃CN): 7.37 – 7.25 (4H, m), 7.25 – 7.15 (1H, m), 5.87 (1H, ddt, J = 17.1, 10.2, 5.9 Hz), 5.24 – 5.07 (1H, m), 5.09 – 4.87 (1H, m), 3.16 (2H, dt, J = 5.8, 1.5 Hz), 2.58 (2H, d, J = 6.6 Hz), 2.51 (1H, dd, J = 12.1, 6.1 Hz), 2.38 (1H, dd, J = 12.2, 6.7 Hz), 1.65 (1H, br. s) 0.99 – 0.70 (2H, m), 0.56 – 0.25 (2H, m); <sup>13</sup>C NMR (100 MHz, CD₃CN): 142.3, 137.7, 128.3, 128.2, 125.8, 117.3, 53.1, 51.6, 39.1, 18.9, 18.7, 10.0; m/z (ESI<sup>+</sup>) HRMS: Calculated for C₁₄H₂₀N: 202.1590. Found [M+H]<sup>+</sup>: 202.1597.

Benzyl (1R*, 2S*)-allyl((2-benzylcyclopropyl)methyl)carbamate (6s)
General procedure E: (1R*, 25*)-N-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine (0.50 g, 2.5 mmol) and benzyl chloroformate (0.84 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6s (0.62 g, 75 %, > 15:1 d.r.) as a colorless oil; $\nu_{\text{max}}$ / cm$^{-1}$: 2917 (m), 1688 (s), 1455 (m), 1414 (s), 1226 (s), 737 (s); $^1$H NMR (500 MHz, CD$_3$CN, 65 °C): $\delta$ 7.44 – 7.32 (5H, m), 7.32 – 7.27 (2H, m), 7.27 – 7.18 (3H, m), 5.89 – 5.70 (1H, m), 5.23 – 4.98 (4H, m), 4.11 – 3.72 (2H, m), 3.29 (1H, dd, $J = 14.6$, 5.5 Hz), 3.09 (1H, dd, $J = 14.5$, 7.1 Hz), 2.63 (1H, dd, $J = 14.5$, 5.8 Hz), 2.51 (1H, dd, $J = 14.5$, 6.6 Hz), 1.10 – 0.88 (2H, m), 0.63 – 0.30 (2H, m); $^{13}$C NMR (126 MHz, CD$_3$CN, 65 °C): $\delta$ 155.8, 141.9, 137.5, 134.5, 128.4, 128.3, 128.2, 127.7, 127.6, 125.8, 116.9, 66.5, 50.3, 49.3, 39.0, 18.8, 17.6, 10.1; m/z (ESI+) HRMS: Calculated for C$_{22}$H$_{25}$NO$_2$Na: 358.1778. Found [M+Na]$^+$: 358.1778.

Benzyl (3aR*, 4S*, 7aR*)-4-benzyl-6-oxohexahydro-1H-isoindole-2(3H)-carboxylate (8s)

General procedure H: Compound 6s (50.2 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8s (46.8 mg, 86 %, > 15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid; Under general procedure G, title compound 8s was obtained in 58 % yield (31.6 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as an off-white solid.

m.p.: 126 – 127 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 2970 (m), 1696 (s), 1396 (s), 1357 (s), 1138 (m), 1059 (s); $^1$H NMR (400 MHz, CD$_3$CN): $\delta$ 7.42 – 7.17 (8H, m, 8 $\times$ CAr-H, A+B), 7.15 – 7.04 (2H, m, 2 $\times$ CAr-H, A+B), 5.14 (2H, s, 2 $\times$ C15-H$_2$, A+B), 3.92 (0.5H, dd, $J = 10.5$, 7.1
Hz, $1 \times \text{C13-H}, A), 3.84 – 3.63 (1.5H, $1 \times \text{C13-H}, B, 1 \times \text{C1-H}, A+B), 3.14 – 2.91 (2H, m, 1 \times \text{C1-H}, A+B, 1 \times \text{C13-H}, A+B), 2.90 – 2.73 (1H, m, 1 \times \text{C7-H}, A+B), 2.70 – 2.47 (2H, m, 1 \times \text{C7-H}, A+B, 1 \times \text{C3-H}, A+B), 2.45 – 2.31 (1H, m, 1 \times \text{C5-H}, A+B), 2.28 – 2.11 (1H, m, 1 \times \text{C3-H}, A+B), 2.10 – 1.94 (3H, m, 1 \times \text{C5-H}, A+B, 1 \times \text{C6-H}, A+B, 1 \times \text{C2-H}, A+B), 1.95 – 1.77 (1H, m, 1 \times \text{C12-H}, A+B); ^{13}\text{C NMR} (100 \text{ MHz, CD}_{3}\text{CN}): \delta \ 208.6 (\text{C4, A}), 208.5 (\text{C4, B}), 154.8 (\text{C14, A}), 154.7 (\text{C14, B}), 138.0, 137.8 (\text{C15, B}), 136.7 , 129.1 , 129.1 , 128.5 , 128.5 , 128.0, 127.9 , 127.9 , 126.6 (\text{CAr, A+B}), 66.9 (\text{C15, A+B}), 50.9 (\text{C1, A}), 50.7 (\text{C1, B}), 49.7 (\text{C13, A}), 49.4 (\text{C13, B}), 48.2 (\text{C12, A}), 47.2 (\text{C12, B}), 45.9 (\text{C5, A}), 45.8 (\text{C5, B}), 43.8 (\text{C3, A+B}), 43.4 (\text{C2, A}), 42.7 (\text{C2, B}), 41.5 (\text{C7, A} , 41.3 (\text{C7, B}), 41.2 (\text{C6, A+B}); m/z (\text{ESI}^{+}) \text{ HRMS: Calculated for C}_{23}\text{H}_{23}\text{NO}_{3}\text{Na: 386.1727. Found [M+Na]}^{+}: 386.1744; The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.}

(1S*, 2S*)-N-Allyl-N-((2-butylcyclopropyl)methyl)-4-methylbenzenesulfonamide (6t)

![Chemical Structure](image.png)

**General procedure E:** (1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine (0.50 g, 2.5 mmol) and p-toluenesulfonyl chloride (0.95 g, 5.0 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title...
compound 6t (0.52 g, 61 %, > 15:1 d.r.) as a colorless oil; \( \nu_{\text{max}} \) / cm\(^{-1}\): 2918 (m), 1453 (m), 1340 (s), 1154 (s), 1090 (m), 911 (m), 754 (s); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.82 – 7.57 (2H, m), 7.39 – 7.24 (4H, m), 7.23 – 7.17 (1H, m), 7.17 – 7.11 (2H, m), 5.56 (1H, ddt, \( J = 17.7, 9.5, 6.2 \) Hz), 5.24 – 4.79 (2H, m), 3.82 (1H, dd, \( J = 15.8, 6.0 \) Hz), 3.70 (1H, dd, \( J = 15.8, 6.2 \) Hz), 3.18 (1H, dd, \( J = 14.5, 6.2 \) Hz), 2.93 (1H, dd, \( J = 14.5, 7.2 \) Hz), 2.56 – 2.45 (2H, m), 2.42 (3H, s), 0.97 – 0.64 (2H, m), 0.58 – 0.22 (2H, m); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 143.0, 137.6, 133.4, 129.6, 128.3, 127.1, 126.0, 118.3, 50.6, 49.6, 39.2, 21.5, 19.4, 16.9, 11.0; \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{21}\)H\(_{25}\)NO\(_2\)SNa: 378.1498. Found [M+Na]\(^+\): 378.1508.

(3aR\(^*\), 7S\(^*\), 7aR\(^*\)) -7-Butyl-2-tosylhexahydro-1H-isindol-5(6H)-one (8t)

![Diagram of compound 6t to 8t conversion](image)

**General procedure H**: Compound 6t (53.3 mg, 0.15 mmol) was employed, the crude mixture was purified by column chromatography (30 % EtOAc/Hex) to yield the title compound 8t (49.3 mg, 86 %, > 15:1 d.r.) as an off-white solid; **Under general procedure G**, the title compound 8t was obtained in 66 % yield (37.8 mg, > 15:1 d.r.) as an off-white solid.

m.p.: 160 – 162 °C (CH\(_2\)Cl\(_2\)/Hex); \( \nu_{\text{max}} \) / cm\(^{-1}\): 2940 (m), 1702 (m), 1337 (s), 1158 (s), 1087 (m), 1026 (m), 817 (m); \(^1\)H NMR (400 MHz, C\(_6\)D\(_6\)): \( \delta \) 7.84 (2H, d, \( J = 8.2 \) Hz, 2 × C\(_{15}\)-H), 7.19 – 7.04 (3H, m, 2 × C10-\( H\), 1 × C11-\( H\), 6.96 (2H, d, \( J = 7.9 \) Hz, 2 × C15-\( H\)), 6.84 – 6.71 (2H, m, 2 × C9-\( H\)), 3.58 (1H, dd, \( J = 9.5, 7.0 \) Hz, 1 × C13-\( H\)), 3.31 (1H, dd, \( J = 8.2, 7.1 \) Hz, 1 × C1-\( H\)), 2.74 – 2.44 (2H, m, 1 × C1-\( H\), 1 × C13-\( H\)), 2.20 (1H, dd, \( J = 13.5, 4.8 \) Hz, 1 × C7-\( H\)), 2.13 – 1.96 (5H, m, 1 × C3-\( H\), 1 × C5-\( H\), 3 × C18-\( H\)), 1.91 (1H, dd, \( J = 13.5, 8.0 \) Hz, 1 × C7-\( H\)), 1.44 – 1.17 (3H, m, 1 × C3-\( H\), 1 × C5-\( H\), 1 × C6-\( H\)), 1.16 – 0.98 (1H, m, 1 × C2-\( H\)), 1.00 – 0.79 (1H, m, 1 × C12-\( H\)); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)): \( \delta \) 205.4 (C4), 142.8 (C17), 138.0 (C8), 135.9 (C14), 129.5 (C16), 129.1 (C9), 128.3 (C10), 127.6 (C15), 126.5 (C11), 52.1 (C1), 51.0 (C13), 46.7 (C12), 45.0 (C5), 42.7 (C3), 42.4 (C2), 40.8 (C7), 40.1 (C6), 20.8 (C18); \( m/z \) (ESI\(^+\)) HRMS: Calculated for C\(_{22}\)H\(_{23}\)NO\(_2\)SNa: 406.1447. Found [M+Na]\(^+\):
The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). nOes between C12-H and C7α-H, C12-H and C13β-H, C2-H and C13α-H were observed. The stereochemical assignment of this compound is consistent with that of 8q and 8s.

\((1S^*, 2R^*)\)-N- Allyl-2- butylcyclopropanecarboxamide

**General procedure C:** \((1S^*, 2R^*)\)-2-Butylcyclopropanecarboxylic acid (1.00 g, 7.0 mmol, > 15:1 d.r.) (prepared according to literature procedure) was employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound (1.07 g, 84 %, > 15:1 d.r.) as an colorless oil. \(\nu_{\text{max}} / \text{cm}^{-1}\): 3300 (m), 2921 (m), 1641 (m), 1537 (m), 1240 (m), 1154 (m); \(^1\)H NMR (400 MHz, CDCl₃): \(\delta \) 5.84 (1H, ddt, J = 17.2, 10.2, 5.7 Hz), 5.75 – 5.55 (1H, br. s), 5.31 – 4.85 (2H, m), 4.16 – 3.65 (2H, m), 1.53 – 1.40 (3H, m), 1.39 – 1.22 (4H, m), 1.16 – 1.04 (1H, m), 1.00 – 0.92 (1H, m), 0.91 – 0.82 (4H, m); \(^13\)C NMR (100 MHz, CDCl₃): \(\delta \) 171.4, 134.7, 116.1, 42.1, 32.0, 26.7, 22.4, 20.9 20.1, 14.1, 11.5; \(m/z\) (ESI⁺) HRMS: Calculated for C₁₁H₁₉NONa: 204.1359. Found [M+Na]⁺: 204.1357.

\((1S^*, 2R^*)\)-N-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine

**General procedure D:** \((1S^*, 2R^*)\)-N- Allyl-2-butylcyclopropanecarboxamide (0.70 g, 3.9 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (0.56 g, 86 %, > 15:1 d.r.) as a colorless oil; \(\nu_{\text{max}} / \text{cm}^{-1}\): 1696 (s), 1413 (m), 1240 (s), 1078 (m), 697 (s); \(^1\)H NMR (400 MHz, CDCl₃): \(\delta \) 5.93 (1H, ddt, J = 16.9, 10.2, 6.0 Hz), 5.55 – 4.16 (2H, m), 3.64 – 2.98 (2H, m), 2.67 (1H, dd, J = 12.1, 6.9 Hz), 2.54 (1H, dd, J = 12.1, 7.4 Hz), 1.55 (1H, br. s), 1.47 – 1.26 (5H, m), 1.21 – 1.14 (1H, m), 1.03 – 0.93 (1H, m), 0.94 – 0.87 (3H, m), 0.85 – 0.72 (1H, m), 0.67 (1H, td, J = 8.3, 4.4 Hz), 0.01 (1H, q, J = 5.2 Hz); \(^13\)C NMR (100 MHz, CDCl₃): \(\delta \) 136.9, 115.8, 52.4, 49.1, 32.4, 28.3, 22.6, 15.8, 15.6, 14.1, 10.1; \(m/z\) (ESI⁺) HRMS: Calculated for C₁₁H₂₂N: 168.1747. Found [M+H]⁺: 168.1749.
Benzyl (1S*, 2R*)-allyl ((-2-butylicyclopropyl)methyl)carbamate (6u)

![Chemical Structure of 6u]

**General procedure E:** (1S*, 2R*)-N-(2-Butylicyclopropyl)methyl)prop-2-en-1-amine (0.27 g, 1.6 mmol) and p-toluenesulfonyl chloride (0.61 g, 3.2 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6u (0.33 g, 66 %, > 15:1 d.r.) as a colorless oil; $\nu_{\text{max}} / \text{cm}^{-1}$: 2922 (m), 1697 (m), 1343 (m), 1154 (s), 1091 (s), 755 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.70 (2H, d, $J = 8.3$ Hz), 7.44 – 6.93 (2H, m), 5.65 (1H, ddt, $J = 17.2$, 10.1, 6.2 Hz), 5.50 – 4.81 (2H, m), 4.21 – 3.71 (2H, m), 3.43 (1H, dd, $J = 14.3$, 5.5 Hz), 2.96 (1H, dd, $J = 14.3$, 8.5 Hz), 2.41 (3H, s), 1.47 – 1.24 (5H, m), 1.18 – 0.99 (1H, m), 0.93 – 0.82 (4H, m), 0.81 – 0.70 (1H, m), 0.66 (1H, td, $J = 8.3$, 4.5 Hz), 0.01 (1H, td, $J = 5.4$, 5.4 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.9, 137.6, 133.5, 129.6, 127.1, 118.2, 49.7, 47.0, 32.3, 28.3, 22.5, 21.5, 16.1, 14.1, 13.9, 11.2; m/z (ESI$^+$) HRMS: Calculated for C$_{18}$H$_{27}$NO$_2$SNa: 344.1655. Found [M+Na$^+$]: 344.1659;

(3aR*, 6S*, 7aR*) and (3aR*, 6R*, 7aR*)-6-Butyl-2-tosylhexahydro-1H-isoindol-5(6H)-one and (3aR*, 7R*, 7aR*)-7-butyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8u)

![Chemical Structures of 6u and 8u]

**General procedure G:** Compound 6u (48.2 mg, 0.15 mmol) was employed, the reaction was heated at 130 °C. The crude mixture was purified by column chromatography (33 %...
EtOAc/Hex) to yield the title compound **8u** (46.1 mg, 88 %) as a colorless oil. A mixture of diastereomers A and B and regioisomer C were obtained in a 5:1:1 (A:B:C) ratio; *Under general procedure H*, title compound **8u** was obtained in 85 % yield (44.5 mg) as a colorless oil. A mixture of diastereomers A and B and regioisomer C were obtained in a 4:1:2 (A:B:C) ratio.

Regioisomer C was separated from diastereomers A and B by flash column chromatography (20 % EtOAc/hexane). The regiochemistry of regioisomer C was confirmed by HMBC analysis (as indicated on the compound structure). The relative stereochemistry of regioisomer C was corroborated by nOe experiments (as indicated on the compound structure). A nOe between C7-e-H and C2-H was observed, and no significant nOe was observed between C2-H and C11-H. Diastereomer A was recrystallized from the mixture of A and B (EtOAc/Hex), its structure and relative stereochemistry were determined unambiguously by X-ray crystallography. Diastereomer B could not be isolated in a pure form, and the proton signals for diastereomer B overlapped significantly with diastereomer A. Diastereomers A and B have the same chemical shift at C12-H2 (for A: 3.64 ppm and 2.81 ppm; for B: 3.63 ppm and 2.80 ppm), which indicates that C12 must be in a similar chemical environment, therefore ruling out the possibility of that B is a regioisomer of A. A TOCSY experiment irradiating C2-H of diastereomer B was utilized to enable coupling constant analysis of C1-H and C12-H of diastereomer B: 3.63 (1H, dd, J = 9.8, 6.8 Hz, 1 × C12-H2), 3.55 (1H, dd, J = 9.4, 7.5 Hz, 1 × C1-H2), 2.94 (1H, dd, J = 10.2, 10.2 Hz, 1 × C1-H2), 2.80 (1H, dd, J = 10.7, 9.2 Hz, 1 × C12-H2); the coupling constant of C1-H and C12-H observed for diastereomer A: 3.64 (1H, dd, J = 9.5, 7.0 Hz, 1 × C12-H2), 3.54 (1H, dd, J = 9.7, 7.0 Hz, 1 × C1-H2), 2.94 (1H, dd, J = 10.8, 9.7 Hz, 1 × C1-H2), 2.81 (1H, dd, J = 10.9, 9.5 Hz, 1 × C12-H2), these similar coupling constants indicated a trans ring junction for diastereomer B (same with diastereomer A) which suggesting that the stereochemistry at C5 was the opposite to that of diastereomer A.

ν<sub>max</sub> / cm<sup>-1</sup>: 2927 (m), 1712 (s), 1340 (m), 1202 (m), 1157 (s), 1097 (m); m/z (ESI<sup>+</sup>) HRMS: Calculated for C<sub>19</sub>H<sub>27</sub>N0<sub>3</sub>SNa: 372.1604. Found [M+Na]<sup>+</sup>: 372.1604.

Data for major diastereomer A: m.p.: 108 – 110 °C (CH<sub>2</sub>Cl<sub>2</sub>/Hex); ¹H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.70 (2H, d, J = 8.2 Hz, 2 × C14-H), 7.31 (2H, d, J = 8.0 Hz, 2 × C15-H), 3.64 (1H, dd, J = 9.5, 7.0 Hz, 1 × C12-H2), 3.54 (1H, dd, J = 9.7, 7.0 Hz, 1 × C1-H2), 2.94 (1H,
dd, $J = 10.8, 9.7$ Hz, 1 × C1-H$_2$), 2.81 (1H, dd, $J = 10.9, 9.5$ Hz, 1 × C12-H$_2$), 2.49 (1H, dd, $J = 13.4, 3.9$ Hz, 1 × C3-H$_2$), 2.43 (3H, s, 3 × C17-H$_3$), 2.27 – 2.08 (3H, m, 1 × C10-H$_2$), 1 × C5-H, 1 × C3-H$_2$), 2.04 – 1.86 (1H, m, 1 × C11-H), 1.83 – 1.72 (1H, m, 1 × C6-H$_2$), 1.72 – 1.51 (1H, m, 1 × C2-H), 1.41 – 0.95 (6H, m, 2 × C8-H$_2$, 2 × C7-H$_2$, 1 × C10-H$_2$, 1 × C6-H$_2$), 0.85 (3H, t, $J = 7.0$ Hz, 3 × C9-H$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 209.5 (C4), 143.5 (C16), 134.4 (C13), 129.8 (C15), 127.2 (C14), 52.6 (C1), 51.9 (C12), 48.7 (C5), 45.0 (C2), 44.1 (C3), 43.2 (C11), 33.1 (C10), 29.1 (C7), 28.5 (C6), 22.7 (C8), 21.5 (C17), 13.9 (C9). (N.B. C7 and C8 could not be assigned confidently).

Data for minor diastereomer B: Characteristic peaks only: 7.71 (2H, d, $J = 8.2$ Hz, 2 × C14-H$_2$), 7.32 (2H, d, $J = 8.0$ Hz, 2 × C13-H) 3.63 (1H, dd, $J = 9.8, 6.8$ Hz, 1 × C12-H$_2$), 3.55 (1H, dd, $J = 9.4, 7.5$ Hz, 1 × C1-H$_2$), 2.94 (1H, dd, $J = 10.2, 10.2$ Hz, 1 × C1-H$_2$), 2.80 (1H, dd, $J = 10.7, 9.2$ Hz, 1 × C12-H$_2$), 2.42 – 2.34 (1H, m, 1 × C2-H).

Data for regioisomer C: m.p.: 129 – 132 °C (CH$_2$Cl$_2$/Hex); $^1$H NMR (400 MHz, CD$_3$CN): δ 7.74 (2H, d, $J = 8.3$ Hz, 2 × C14-H$_2$), 7.43 (2H, d, $J = 7.9$ Hz, 2 × C13-H$_2$), 3.58 (1H, dd, $J = 9.8, 6.9$ Hz, 1 × C1-H$_2$), 3.45 (1H, dd, $J = 9.8, 7.6$ Hz, 1 × C12-H$_2$), 3.05 (1H, dd, $J = 11.1, 9.8$ Hz, 1 × C12-H$_2$), 2.88 (1H, dd, $J = 10.5, 9.8$ Hz, 1 × C1-H$_2$), 2.44 (3H, s, 3 × C17-H$_3$), 2.41 – 2.23 (3H, m, 1 × C3-H$_2$, 2 × C5-H$_2$), 2.17 (1H, m, 2 × C11-H$_2$), 2.17 – 2.06 (2H, m, 1 × C3-H$_2$, 1 × C6-H$_2$), 1.94 – 1.80 (1H, m, C2-H), 1.42 – 1.01 (5H, m, 2 × C8-H$_2$, 2 × C9-H$_2$, 1 × C7-H$_2$), 0.86 (3H, t, $J = 7.1$ Hz, 3 × C10-H$_3$), 0.84 – 0.73 (1H, m, 1 × C7-H$_2$); $^{13}$C NMR (100 MHz, CD$_3$CN): δ 209.0 (C4), 143.8 (C16), 134.3 (C13), 129.8 (C15), 127.3 (C14), 52.9 (C1), 48.6 (C12), 45.9 (C11), 44.6 (C5), 43.6 (C3), 37.9 (C2), 34.1 (C6), 29.6 (C8), 26.3 (C9), 22.4 (C7), 20.5 (C17), 13.2 (C10). (N.B. C8 and C9 could not be assigned confidently).
(1\(R^*\), 5\(S^*\), 6\(R^*\))-\(N\)-Allylbicyclo[3.1.0]hexane-6-carboxamide

**General procedure C:** (1\(R^*\), 5\(S^*\), 6\(R^*\))-Bicyclo[3.1.0]hexane-6-carboxylic acid (3.20 g, 25.4 mmol, 5:1 d.r.) (prepared according to literature procedure\(^2\)) was employed and afforded the title compound (3.74 g, 88 %, 10:1 d.r.) as a off-white solid which can be recrystallized in Hex/EA to separate two diastereomers. Major diastereomer was obtained as a colorless solid and minor diastereomer was obtained as a colorless oil.

\(\nu_{\text{max}} / \text{cm}^{-1}\): 3287 (s), 2959 (m), 1632 (s), 1544 (s), 1410 (m), 1212 (m), 906 (s);

\(m/z\) (ESI\(^+\))

HRMS: Calculated for C\(_{10}\)H\(_{15}\)NONa: 188.1046. Found [M+Na]\(^+\): 188.1049.

Data for major diastereomer:

\(\delta\) 5.83 (1H, ddt, \(J = 17.2, 10.2, 5.7\) Hz), 5.64 (1H, s), 5.32 – 4.84 (2H, m), 3.91 – 3.82 (2H, m), 1.88 – 1.65 (6H, m), 1.66 – 1.46 (1H, m), 1.14 (1H, t, \(J = 2.9\) Hz), 1.12 – 0.93 (1H, m);

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 172.9, 134.6, 116.2, 42.0, 27.4, 27.3, 23.4, 20.5.

Data for minor diastereomer:

\(\delta\) 5.82 (1H, ddt, \(J = 17.3, 10.2, 5.8\) Hz), 5.64 (1H, br. s), 5.26 – 4.96 (2H, m), 3.90 – 3.77 (2H, m), 2.01 – 1.90 (2H, m), 1.88 – 1.76 (2H, m), 1.69 – 1.39 (4H, m), 1.15 – 0.90 (1H, m);

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 170.2, 134.3, 116.5, 41.9, 26.2, 24.2, 22.8, 22.3.

(1\(R^*\), 5\(S^*\), 6\(R^*\))-\(N\)-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine

**General procedure D:** (1\(R^*\), 5\(S^*\), 6\(R^*\))-\(N\)-Allylbicyclo[3.1.0]hexane-6-carboxamide (2.60 g, 15.8 mmol) was employed, the crude mixture was purified by column chromatography (100 % EtOAc) to yield the title compound (2.29 g, 96 %, > 15:1 d.r.) as a colorless oil; \(\nu_{\text{max}} / \text{cm}^{-1}\): 3307 (m), 2859 (s), 1643 (m), 1449 (s), 1157 (m), 915 (s); \(^1\)H NMR (400 MHz,
CD₃CN): δ 5.90 (1H, ddt, J = 17.2, 10.3, 5.9 Hz), 5.17 (1H, m), 5.05 (1H, m), 3.20 (2H, dt, J = 5.9, 1.5 Hz), 2.39 (2H, d, J = 6.9 Hz), 2.05 – 1.86 (1H, m), 1.82 – 1.60 (4H, m), 1.54 (1H, dt, J = 12.8, 8.0 Hz), 1.25 – 1.10 (1H, m), 1.10 – 1.05 (2H, m), 0.72 (1H, tt, J = 6.7, 3.1 Hz);

13C NMR (100 MHz): δ 137.6, 117.3, 51.9, 51.6, 27.1, 23.0, 21.1, 19.0; m/z (ESI⁺) HRMS: Calculated for C₁₀H₁₈N: 152.1434. Found [M+H⁺]: 152.1434.

Benzyl (1R*, 5S*, 6R*)-allyl((-bicyclo[3.1.0]hexan-6-yl)methyl)carbamate (6v)

General procedure E: (1R*, 5S*, 6R*)-N-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine (2.40 g, 15.6 mmol) and benzyl chloroformate (5.30 g, 31.2 mmol) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6v (4.12 g, 97 %, > 15:1 d.r.) as a colorless oil; νmax / cm⁻¹: 2951 (m), 1696 (s), 1412 (s), 1239 (s), 917 (m); ¹H NMR (400 MHz, CD₃CN, 65 °C): δ 7.69 – 7.07 (5H, m), 6.13 – 5.58 (1H, m), 5.36 – 4.72 (4H, m), 3.97 (2H, dt, J = 5.5, 1.5 Hz), 3.16 (2H, dd, J = 6.9, 1.1 Hz), 1.84 – 1.61 (4H, m), 1.63 – 1.37 (1H, m), 1.25 – 0.97 (3H, m), 0.81 (1H, tt, J = 6.7, 3.1 Hz); ¹³C NMR (100 MHz, CD₃CN, 65 °C): 155.8, 134.6, 128.4, 128.3, 127.7, 127.6, 116.9, 66.5, 49.3, 49.2, 27.0, 23.2, 21.0, 18.2; m/z (ESI⁺) HRMS: Calculated for C₁₈H₂₃NO₂Na: 308.1621. Found [M+Na⁺]: 308.1624.

Benzyl (3aR*, 5aR*, 8aR*, 8bR*)-5-oxodecahydrocyclopenta[e]isoindole-2(3H)-carboxylate (8v)

In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(CH₂CH₂)₂Cl]₂ (2.92 mg, 0.0075 mmol). Then took the reaction tube out of the glove box,
compound 6v (42.80 mg, 0.15 mmol) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added via syringe, then (7-t-BuO)-norbornadiene (2.6 uL, 0.015 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated in vacuo. The crude mixture was purified by column chromatography (30 % EtOAc/Hex) to yield the title compound 8v (28.7 mg, 61 %, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil;

**Under general procedure G, title compound 8v was obtained in 20 % yield (9.4 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil; Under general procedure H, title compound 8v was obtained in 52 % yield (24.5 mg, > 15:1 d.r. 1:1 mixture of rotamers A:B) as a colorless oil;**

νmax / cm⁻¹: 2945 (m), 1695 (s), 1416 (s), 1356 (s), 1122 (m), 1075 (s), 698 (m); ¹H NMR (400 MHz, CDCl₃): δ 7.57 – 7.25 (5H, m, 2 × C¹⁵-H, A+B, 2 × C¹⁶-H, A+B, 1 × C¹⁷-H, A+B), 5.12 (2H, s, 2 × C¹³-H₂, A+B), 3.96 – 3.66 (2H, m, 1 × C¹-H, A+B, 1 × C¹¹-H, A+B), 3.13 – 2.87 (2H, m, 1 × C¹-H, A+B, 1 × C¹¹-H, A+B), 2.76 – 2.47 (2H, m, 1 × C³-H, A+B, 1 × C⁵-H, A+B), 2.34 – 2.08 (3H, m, 1 × C²-H, A+B, 1 × C¹⁰-H, A+B, 1 × C³-H, A+B), 1.96 – 1.51 (6H, m, 2 × C⁶-H, A+B, 1 × C⁸-H, A+B, 2 × C⁷-H, A+B, 1 × C⁹-H, A+B), 1.50 – 1.29 (1H, m, 1 × C⁸-H, A+B); ¹³C NMR (100 MHz, CDCl₃): δ 212.7 (C⁴, A), 212.6 (C⁴, B), 154.7 (C¹², A), 154.6 (C¹², B), 136.8 (C¹⁴, A), 136.8 (C¹⁴, B), 128.5, 128.0, 127.9 (C¹⁵, A+B, C¹⁶, A+B, C¹⁷, A+B), 66.8 (C¹³, A), 66.8 (C¹³, B), 52.0 (C⁵, A), 52.0 (C⁵, B), 51.6 (C¹, A), 51.3 (C¹, B), 50.8 (C¹¹, A), 50.6 (C¹¹, B), 45.7 (C⁹, A) 44.9 (C⁹, B) 43.6 (C¹⁰, A), 43.5 (C¹⁰, B), 41.7 (C³, A), 41.6 (C³, B), 40.9 (C², A+B), 31.9 (C⁸, A+B), 28.1, 28.0, 24.3, 24.2. (C⁶, A+B, C⁷, A+B) (N.B. C⁶ and C⁷ could not be assigned confidently). m/z (ESI⁺) HRMS: Calculated for C₁₉H₂₃NO₃Na: 336.1570. Found [M+Na]⁺: 336.1565; The relative stereochemistry of this compound was assigned by analogy to that of 8q and 8s.

(E)-N-(But-2-en-1-yl)-N-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6w)
General procedure B: \(N\)-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (1.72 g, 7.2 mmol) and \((E)\)-1-bromobut-2-ene (1.92 g 14.4 mmol, \(E/Z = 17/1\)) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound \(6w\) (1.89 g, 90 %, mixed with \((Z)\)-isomer, \(E/Z = 14:1\)) as a colorless oil;

\[ \nu_{\text{max}} / \text{cm}^{-1}: 2918 \text{ (m)}, 1336 \text{ (s)}, 1154 \text{ (s)}, 1090 \text{ (m)}, 967 \text{ (m)}, 734 \text{ (s)}; m/z \text{ (ESI+ HRMS):} \] Calculated for \(\text{C}_{15}\text{H}_{21}\text{NO}_{2}\text{SNa}: 302.1185\). Found [M+Na]+: 302.1190.

Data for major \(E\)-isomer: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 7.68 (2\text{H}, d, J = 8.3 \text{ Hz}), 7.29 – 7.24 \text{ (2H, m)}, 5.64 – 5.52 (1\text{H, m}), 5.32 – 5.22 (1\text{H, m}), 3.85 (2\text{H, ddd}, \(J = 6.6, 1.3, 1.3 \text{ Hz}), 3.01 \text{ (2H, d, } J = 6.8 \text{ Hz)}, 2.41 (3\text{H, s}), 1.70 – 1.56 (3\text{H, m}), 0.95 – 0.77 (1\text{H, m}), 0.52 – 0.38 \text{ (2H, m), 0.14 (2H, dt, } J = 5.9, 4.7 \text{ Hz}); ^{13}\text{C NMR (100 MHz, CDCl3):} \delta 142.8, 137.7, 129.8, 129.5, 127.1, 126.0, 51.3, 49.3, 21.5, 17.6, 9.7, 4.0. \]

Data for minor \(Z\)-isomer: Characteristic peaks only: \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta 3.98 \text{ (2H, d, } J = 6.9 \text{ Hz)}\) (3\(aS\)\(^*, \ 4R\(^*, \ 7aR\(^*)\)-4-Methyl-2-tosylhexahydro-1\(H\)-isoindol-5(6\(H\))-one (8\(w\))

In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with \([\text{Rh(CH}_2\text{CH}_2\text{)}_2\text{Cl}]_2\) (2.92 mg, 0.0075 mmol). Then took the reaction tube out of the glove box, compound \(6w\) (41.90 mg, 0.15 mmol, mixed with \((Z)\)-isomer, \(E/Z = 14:1\)) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added \text{via} syringe, and 1,4-oxathiane (4.2 uL, 0.045 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds. Then the reaction heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated \textit{in vacuo}. The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound \(8w\) (29.5 mg, 64 %, > 15:1 d.r.) as a colorless solid; \textit{Under general procedure G}, title compound \(8w\) was obtained in 56 % yield (25.8 mg, > 15:1 d.r.) as a
colorless solid; Under general procedure H, title compound 8w was obtained in 59 % yield (27.2 mg, > 15:1 d.r.) as a colorless solid.

m.p.: 102 – 104 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 2954 (m), 1702 (s), 1393 (s), 1157 (s), 1110 (m), 1029 (m), 811 (m); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.71 (2H, d, $J = 8.3$ Hz, 2 $\times$ C11-H), 7.33 (2H, d, $J = 8.5$ Hz, 2 $\times$ C12-H), 3.65 (1H, dd, $J = 9.5, 7.1$ Hz, 1 $\times$ C9-H$_2$), 3.59 (1H, dd, $J = 9.6, 7.1$ Hz, 1 $\times$ C1-H$_2$), 3.00 (1H, dd, $J = 10.8, 9.6$ Hz, 1 $\times$ C1-H$_2$), 2.85 (1H, dd, $J = 10.9, 9.5$ Hz, 1 $\times$ C9-H$_2$), 2.47 – 2.39 (4H, m, 3 $\times$ C14-H$_3$, 1 $\times$ C6-H$_2$), 2.34 – 2.16 (2H, m, 1 $\times$ C6-H$_2$, 1 $\times$ C3-H), 2.09 (1H, dddd, $J = 12.3, 6.4, 3.5, 2.0$ Hz, 1 $\times$ C7-H$_2$), 2.04 – 1.95 (1H, m, 1 $\times$ C8-H), 1.54 – 1.35 (2H, m, 1 $\times$ C7-H$_2$, 1 $\times$ C2-H), 0.96 (3H, d, $J = 6.5$ Hz, 3 $\times$ C4-H$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 209.7 (C5), 143.5 (C13), 134.4 (C10), 129.8 (C12), 127.2 (C11), 52.3 (C9), 52.1 (C1), 51.0 (C2), 47.9 (C3), 42.9 (C8), 40.0 (C6), 27.1 (C7), 21.5 (C14), 12.4 (C4); m/z (ESI$^+$) HRMS: Calculated for C$_{16}$H$_{21}$NO$_3$SNa: 330.1134. Found [M+Na]$^+$: 330.1148. The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.

(E) –N-(Cyclopropylmethyl)-4-methyl-N-(pent-2-en-1-yl)benzenesulfonamide (6x)

\[ \text{N} \quad \text{O} \quad \text{S} \quad \text{O} \]

\[ \text{N} \quad \text{O} \quad \text{S} \quad \text{O} \]

\[ \text{6x} \]
General procedure B: N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.27 g, 1.2 mmol) and (E)-1-bromopent-2-ene (0.21 g, 1.4 mmol, E/Z = 12:1) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6x (0.33 g, 79 %, mixed with (Z)-isomer, E/Z = 9:1) as a colorless oil.

\[ \nu_{\text{max}} / \text{cm}^{-1}: 2965 (\text{m}), 1598 (\text{m}), 1338 (\text{m}), 1154 (\text{s}), 905 (\text{s}), 727 (\text{s}); m/z (\text{ESI}^+) \text{ HRMS:} \]

Calculated for C_{16}H_{23}NO_{2}SNa: 316.1342. Found [M+Na]^+: 316.1345.

Data for major E isomer: \[^1\text{H NMR (400 MHz, CDCl}_3): \delta 7.68 (2H, d, J = 10.3 \text{ Hz}), 7.27 (2H, d, J = 9.9 \text{ Hz}), 5.68 – 5.52 (1H, m), 5.29 – 5.12 (1H, m), 3.85 (2H, d, J = 6.6 \text{ Hz}), 3.01 (2H, dd, J = 6.9, 2.0 \text{ Hz}), 2.40 (3H, s), 2.05 – 1.90 (2H, m), 0.98 – 0.82 (4H, m), 0.49 – 0.42 (2H, m), 0.19 – 0.08 (2H, m); \text{^13C NMR (100 MHz, CDCl}_3): \delta 142.8, 137.7, 136.7, 129.5, 127.1, 123.6, 51.3, 49.4, 25.1, 21.5, 13.2, 9.7, 4.0.\]

Data for minor isomer: Characteristic peaks only: 5.52 – 5.42 (1H, m), 3.96 (3H, d, J = 6.8 Hz).

(3aS*, 4R*, 7aR*)-4-Ethyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8x)

In a glove box, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(CH_2CH_2)_2Cl]_2 (2.92 mg, 0.0075 mmol) and Na_2SO_4 (4.26 mg, 0.03 mmol). Then took the reaction tube out of the glove box, compound 6x (44.00 mg, 0.15 mmol, E/Z = 9:1) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added via syringe, and 1,4-oxathiane (4.2 uL, 0.045 mmol) was added by microlitre syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated in vacuo. The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8x (25.2 mg, 52 %, > 15:1 d.r.) as a colorless solid;
Under general procedure G, title compound 8x was obtained in 49 % yield (23.8 mg, > 15:1 d.r.) as a colorless solid; Under general procedure H, title compound 8x was obtained in 47 % yield (22.8 mg, > 15:1 d.r.) as a colorless solid.

m.p.: 100 – 102 °C (CH₂Cl₂/Hex); ν_{max} / cm\(^{-1}\): 1712 (m), 1343 (m), 1160 (m), 903 (s), 723 (s); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.71 (2H, d, J = 8.2 Hz, 2 × C₁₂-H), 7.32 (2H, d, J = 7.8 Hz, 2 × C₁₃-H), 3.67 – 3.55 (2H, m, 1 × C₁₀-H₂, 1 × C₁-H₂), 3.00 (1H, dd, J = 10.8, 9.6 Hz, 1 × C₁-H₂), 2.84 (1H, dd, J = 10.9, 9.5 Hz, 1 × C₁₀-H₂), 2.46 – 2.34 (4H, m, 1 × C₇-H₂, 3 × C₁₅-H₃), 2.34 – 2.18 (1H, m, 1 × C₇-H₂), 2.15 – 1.91 (3H, m, 1 × C₈-H₂, 1 × C₉-H, 1 × C₃-H), 1.63 – 1.47 (2H, m, 1 × C₄-H₂, 1 × C₂-H), 1.48 – 1.31 (2H, m, 1 × C₈-H₂, 1 × C₄-H₂), 0.83 (3H, t, J = 7.4 Hz, 3 × C₅-H₃); \(^1^3\)C NMR (100 MHz, CDCl₃): δ 209.4 (C₆), 143.6 (C₁₄), 134.4 (C₁₁), 129.8 (C₁₃), 127.2 (C₁₂), 54.4 (C₃), 52.1, 52.0 (C₁, C₁₀), 48.9 (C₂), 43.2 (C₉), 40.4 (C₇), 27.2 (C₈), 21.5 (C₁₅), 20.2 (C₄), 11.5 (C₅). (N.B. C₁ and C₁₀ could not be assigned confidently). m/z (ESI\(^+\)) HRMS: Calculated for C₁₇H₂₃NO₃Na: 344.1291. Found [M+Na\(^+\)]: 344.1291; The relative stereochemistry of this compound was assigned by analogy to that of 8w.

(Z)-N-(Cyclopropylmethyl)-4-methyl-N-(pent-2-en-1-yl)benzenesulfonamide (6x\(^+\))

\[ \text{NMR spectrum} \]

\[ \text{General procedure B:} \]

\(N\)-(Cyclopropylmethyl)-4-methylbenzenesulfonamide (0.64 g, 3 mmol) and (Z)-1-bromopent-2-ene (1.33 g, 9 mmol) (prepared according to literature procedure\(^8\)) were employed, the crude mixture was purified by column chromatography (10% EtOAc/Hex) to yield the title compound 6x\(^+\) (0.66 g, 80 %) as a colorless oil; ν_{max} / cm\(^{-1}\): 2965 (m), 1341 (m), 1153 (s), 1090 (m), 909 (m), 813 (m); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.68 (2H, d, J = 8.3 Hz), 7.26 (2H, d, J = 8.1 Hz), 5.54 – 5.36 (1H, m), 5.23 – 5.10 (1H, m), 3.96 (2H, dd, J = 6.7, 1.7 Hz), 3.01 (2H, dd, J = 6.9, 1.2 Hz), 2.40 (3H, s), 2.03 (2H, ddd, J = 7.5, 1.5, 1.5 Hz), 0.94 (3H, t, J = 7.5 Hz), 0.91 – 0.83 (1H, m), 0.49 – 0.44 (2H, m), 0.17 – 0.12 (2H, m); \(^1^3\)C NMR (100 MHz, CDCl₃): δ 142.9, 137.6, 135.3, 129.5, 127.1, 123.9, 51.6,
44.1, 21.5, 20.6, 14.0, 9.7, 4.0; m/z (ESI+) HRMS: Calculated for C_{16}H_{23}NO_{2}SNa: 316.1342. Found [M+Na]^+: 316.1360.

(3aS*, 4S*, 7aR*) and (3aS*, 4R*, 7aR*)-4-Ethyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8x')

An oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(cod)Cl]_{2} (2.77 mg, 0.0056 mmol) and AsPh_{3} (3.45 mg, 0.011 mmol) and Na_{2}SO_{4} (4.26 mg, 0.03 mmol). The tube was fitted with a rubber septum and purged with argon. Compound 6x' (44.00 mg, 0.15 mmol) in anhydrous 1, 2-dichlorobenzene (0.82 mL, 0.18 M) was added via syringe. The reaction mixture was purged with CO for 10 minutes and subsequently sparged with CO for ca. 10 seconds, then heated at 140 °C under a CO atmosphere (1 atm) for 72 h. The mixture was cooled to r.t., concentrated in vacuo, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8x' (24.3 mg, 50 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 7:1 (A:B) ratio. (There was a trace amount of unidentified impurity mixed in product). Under general procedure G, title compound 8x' was obtained in 46 % yield (22.4 mg) as a colorless oil, A mixture of diastereomers A and B were obtained in a 7:1 (A:B) ratio; Under general procedure H, title compound 8x' was obtained in 57 % yield (27.7 mg) as a colorless oil, A mixture of diastereomers A and B were obtained in a 8:3 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C9-H and C4-H, C10β-H and C9-H, from C10α-H to C2-H, from C2-H to C3-H were observed. Analysis of relative stereochemistry of minor diastereomer B see 8x.

ν_{max} / cm\(^{-1}\): 2963 (m), 1707 (s), 1339 (m), 1157 (s), 1092 (m), 815 (m); m/z (ESI+) HRMS: Calculated for C_{17}H_{23}NO_{3}SNa: 344.1291. Found [M+Na]^+: 344.1307.
Data for major diastereomer A: $^1$H NMR (400 MHz, CDCl$_3$): δ 7.70 (2H, d, $J = 8.3$ Hz, 2 × C12-H), 7.32 (2H, d, $J = 8.1$ Hz, 2 × C12-H), 3.65 (1H, dd, $J = 9.4$, 7.0 Hz, 1 × C10-H$_2$), 3.36 (1H, dd, $J = 9.7$, 7.5 Hz, 1 × C1-H$_2$), 3.22 (1H, dd, $J = 11.2$, 9.8 Hz, 1 × C1-H$_2$), 2.73 (1H, dd, $J = 10.6$, 9.5 Hz, 1 × C10-H$_2$), 2.45 – 2.31 (5H, m, 1 × C7-H$_3$, 3 × C15-H$_3$, 1 × C3-H$_1$), 2.27 – 2.15 (1H, m, 1 × C7-H$_2$), 2.21 – 2.11 (1H, m, 1 × C9-H$_1$), 2.07 (1H, dddd, $J = 12.6$, 6.2, 3.9, 2.1 Hz, 1 × C8-H$_2$), 1.89 – 1.77 (1H, m, 1 × C2-H$_1$), 1.59 – 1.40 (2H, m, 2 × C4-H$_2$), 1.33 (1H, dddd, $J = 13.3$, 11.9, 4.7 4.7 Hz, 1 × C8-H$_2$), 0.81 (3H, t, $J = 7.4$ Hz, 3 × C5-H$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 211.9 (C6), 143.6 (C14), 134.3 (C11), 129.8 (C13), 127.3 (C12), 52.8 (C3), 52.2 (C10), 48.5 (C1), 47.6 (C2), 36.6, 36.6 (C7, C9), 27.5 (C8), 21.5 (C15), 18.8 (C4), 11.8 (C5). (N.B. C7 and C9 could not be assigned confidently).

See compound 8x for minor diastereomer

($1R^*$, $2S^*$)-2-Benzyl-N-tosylcyclopropane-1-carboxamide

![Chemical structure]

To an ice-cold stirring solution of ($1R^*$, $2S^*$)-2-Benzylcyclopropane-1-carboxylic acid (1.76 g, 10.0 mmol), EDCI (2.48 g, 13.0 mmol) and DMAP (1.71 g, 14.0 mmol) in anhydrous CH$_2$Cl$_2$ (25 mL) under an atmosphere of nitrogen was added $p$-methylbenzenesulfonamide (2.05 g, 12.0 mmol) in CH$_2$Cl$_2$ (2 mL). The mixture was heated to 50 °C and stirred for 24 h. Then the mixture was concentrated in vacuo and suspended in 1M NaOH (50 mL) and extracted with EtOAc (3 × 50 mL), the organic layers were combined and washed with 1M HCl (50 mL), brine (50 mL), dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by column chromatography (20 % EtOAc/Hex) to yield the title compound (1.99 g, 61 %, > 15:1 d.r.) as a colorless solid; m.p.: 135 – 137 °C (CH$_2$Cl$_2$/Hex); $\nu_{\text{max}}$ / cm$^{-1}$: 3231 (m), 2921 (m), 1686 (m), 1453 (s), 1341 (m), 1175 (s), 1087 (s), 805 (m); $^1$H NMR (400 MHz, CDCl$_3$): δ 8.97 (1H, s), 7.91 (2H, d, $J = 8.4$ Hz), 7.36 – 7.29 (2H, m), 7.28 – 7.15 (3H, m), 7.14 – 7.04 (2H, m), 2.68 (1H, dd, $J = 14.8$, 6.4 Hz), 2.56 (1H, dd, $J = 14.8$, 7.0 Hz), 2.44 (3H, s), 1.77 – 1.61 (1H, m), 1.46 – 1.36 (1H, m), 1.26 (1H, ddd, $J = 8.8$, 4.4, 4.4 Hz), 0.84 (1H, ddd, $J = 7.9$, 6.6, 4.3 Hz); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 171.1, 145.0, 139.4, 135.6,
129.6, 128.4, 128.3, 128.2, 126.4, 37.9, 24.6, 21.7, 21.7, 16.3; m/z (ESI+) HRMS: Calculated for C_{18}H_{19}NO_{3}Na: 352.0978. Found [M+Na]⁺: 352.0974.

(1R*, 2S*)-N-((2-Benzycyclopropyl)methyl)-4-methylbenzenesulfonamide

General procedure D: (1R*, 2S*)-2-Benzyl-N-tosylcyclopropane-1-carboxamide (0.99 g, 3.0 mmol) was employed, the crude mixture was purified by column chromatography (15 % EtOAc/Hex) to yield the title compound (0.69 g, 74%, > 15:1 d.r.) as a colorless oil; νmax / cm⁻¹: 3277 (m), 2921 (m), 1425 (m), 1321 (s), 1154 (s), 1054 (s), 813 (m); ¹H NMR (400 MHz, CDCl₃): δ 7.73 – 7.67 (2H, m), 7.31 – 7.26 (4H, m), 7.24 – 7.18 (1H, m), 7.17 – 7.11 (2H, m), 4.64 (1H, br. s), 2.96 – 2.71 (2H, m), 2.48 (2H, d, J = 6.4 Hz), 2.42 (3H, s), 0.83 – 0.72 (2H, m), 0.45 – 0.40 (1H, m), 0.39 – 0.33 (1H, m); ¹³C NMR (100 MHz, CDCl₃): δ 143.3, 141.3, 137.0, 129.7, 128.4, 128.2, 127.1, 126.1, 47.6, 38.9, 21.5, 19.0, 18.0, 10.8; m/z (ESI⁺) HRMS: Calculated for C_{18}H_{21}NO_{2}Na: 338.1185. Found [M+Na]⁺: 338.1194.

(1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide (6y)

General procedure E: (1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide (0.57 g, 1.8 mmol) and (E)-1-bromobut-2-ene (0.37 g, 2.7 mmol, E/Z = 17/1) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 6y (0.59 g, 89 %, > 15:1 d.r. mixed with (Z)-isomer, E/Z = 10:1) as a colorless oil;

νmax / cm⁻¹: 2916 (m), 1452 (m), 1335 (s), 1154 (s), 1090 (s), 932 (m); m/z (ESI⁺) HRMS: Calculated for C_{22}H_{27}NO_{2}Na: 392.1655. Found [M+Na]⁺: 392.1649.
Data for major E-isomer A: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ $^1$H NMR (400 MHz, CDCl$_3$): $\delta$
7.67 (2H, d, $J = 8.3$ Hz), 7.30 – 7.22 (4H, m), 7.23 – 7.09 (3H, m), 5.60 – 5.37 (1H, m), 5.20 (1H, dddd, $J = 16.9$, 8.3, 5.8, 1.7 Hz), 3.75 (1H, dd, $J = 15.3$, 6.5 Hz), 3.65 (1H, dd, $J = 15.3$, 6.8 Hz), 3.14 (1H, dd, $J = 14.5$, 6.1 Hz), 2.93 (1H, dd, $J = 14.5$, 7.0 Hz), 2.51 (2H, d, $J = 6.5$ Hz), 1.61 (3H, dd, $J = 6.5$, 1.4 Hz), 0.91 – 0.72 (2H, m), 0.47 – 0.34 (2H, m);
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 142.9, 141.3, 137.8, 129.8, 129.5, 128.3, 128.3, 127.1, 126.0, 125.9, 50.4, 49.0, 39.2, 21.5, 19.3, 17.6, 17.0, 11.1.

Data for minor Z-isomer B: Characteristic peaks only: $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 3.93 – 3.80 (2H, m).

(3a$^S^*$, 4$^R^*$, 7$^S^*$, 7a$^R^*$) and (3a$^S^*$, 4$^S^*$, 7$^S^*$, 7a$^R^*$)-7-Benzyl-4-methyl-2-tosyloctahydro-5H-isoindol-5-one (8y)

General procedure H: Compound 6y (55.4 mg, 0.15 mmol, $E/Z = 10:1$) was employed, and the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8y (32.2 mg, 54 %) as an off-white solid. A mixture of diastereomers A and B were obtained in an 11:1 (A:B) ratio. Under general procedure G, title compound 8y was obtained in 19 % yield (11.3 mg) as an off-white solid, A mixture of diastereomers A and B were obtained in a 9:1 (A:B) ratio.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A). nOes between C13-H and C3-H, C2-H and C4-H, from C2-H to C7-H were observed. For minor diastereomer B, the coupling constants observed for C1-H and C14-H for diastereomer A and diastereomer B are similar with each other (for diastereomer A: (dd, $J = 9.5$, 7.1 Hz, 1 × C1-H$_2$), (dd, $J = 10.2$, 10.2 Hz, 1 × C14-H$_2$) for diastereomer B: characteristic peaks only: (dd, $J = 9.8$, 7.1 Hz, 1 × C1-H$_2$), 3.14 (dd,
$J = 10.1, 10.1$ Hz, 1 × C14-H2), these results indicated a trans ring junction for diastereomer B (same with diastereomer A). Combined with the stereochemical analysis results from 8t, which was obtained as a single diasteromer, minor diastereomer B should have same stereochemistry with major diastereomer A at C7. The relative stereochemistry of C3 of diastereomer B was assigned by comparison to 8x and is believed to be formed from the 10 % Z-isomer of 6y.

$\nu_{\text{max}} / \text{cm}^{-1}$: 2953 (m), 1695 (s), 1418 (s), 1357 (m), 1136 (m), 911 (m); m/z (ESI+) HRMS: Calculated for C23H27NO3SNa: 420.1604. Found [M+Na]+: 420.1621.

Data for major diastereomer A: $^1$H NMR (500 MHz, CDCl3): $\delta$ 7.75 – 7.61 (2H, m, 2 × C16-H), 7.35 (2H, d, $J = 8.0$ Hz, 2 × C17-H), 7.32 – 7.16 (3H, m, 2 × C11-H, 1 × C12-H), 7.03 (2H, dd, $J = 6.9, 1.6$ Hz, 2 × C10-H), 3.70 (1H, dd, $J = 9.7, 7.0$ Hz, 1 × C14-H2), 3.58 (1H, dd, $J = 9.5, 7.1$ Hz, 1 × C1-H2), 2.97 (1H, dd, $J = 10.8, 9.6$ Hz, 1 × C1-H2), 2.86 (1H, dd, $J = 10.2, 10.2$ Hz, 1 × C14-H2), 2.71 (1H, dd, $J = 13.6, 4.6$ Hz, 1 × C8-H2), 2.49 – 2.39 (4H, m, 1 × C8-H2, 3 × C19-H3), 2.31 (1H, dd, $J = 13.8, 3.4$ Hz, 1 × C6-H2), 2.15 (1H, dq, $J = 13.0, 6.4$ Hz, 1 × C3-H), 1.97 (1H, dd, $J = 13.8, 12.7$ Hz, 1 × C6-H2), 1.93 – 1.85 (1H, m, 1 × C7-H), 1.84 – 1.74 (1H, m, 1 × C13-H), 1.56 – 1.45 (1H, m, 1 × C2-H), 0.94 (3H, d, $J = 6.5$ Hz, 3 × C4-H3); $^{13}$C NMR (126 MHz, CDCl3): $\delta$ 209.3 (C5), 143.6 (C18), 137.7 (C9), 134.4 (C15), 129.8 (C17), 129.0 (C10), 128.5 (C12), 127.3 (C16), 126.7 (C11), 51.8 (C1), 51.5 (C14), 49.9 (C2), 47.8 (C13), 47.4 (C3), 45.7 (C6), 41.5 (C7), 41.2 (C8), 21.6 (C19), 12.3 (C4).

Data for minor diastereomer B: Characteristic peaks only: $^1$H NMR (500 MHz, CDCl3): $\delta$ 3.36 (1H, dd, $J = 9.8, 7.1$ Hz, 1 × C1-H2), 3.14 (1H, dd, $J = 10.1, 10.1$ Hz, 1 × C14-H2), 2.58 – 2.53 (1H, m, 1 × C3-H). 0.97 (1H, d, $J = 7.4$ Hz, 3 × C4-H3).

(E)-N-(But-2-en-1-yl)-N-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6z)

![Chemical Structure](attachment:image.png)
**General procedure E:** \(N-(1\text{-Cyclopropylethyl})-4\text{-methylbenzenesulfonamide} \) (0.48 g, 2 mmol) and \((E)-1\text{-bromobut-2-ene} \) (0.41 g, 3.0 mmol, \(E/Z = 17:1\)) were employed, the crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound \(6z\) (0.49 g, 85 %, mixed with \((Z)\)-isomer, \(E/Z = 9:1\)) as a colorless oil.

\[ \nu_{\text{max}} / \text{cm}^{-1}: 2972 \text{ (s)}, 1450 \text{ (m)}, 1332 \text{ (s)}, 1150 \text{ (s)}, 876 \text{ (m)}; m/z \text{ (ESI\textsuperscript{+}) HRMS:} \]

Calculated for \(C_{16}H_{23}NO_2Na\): 316.1342. Found \([M+Na]^+\): 316.1346.

Data for major isomer: \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)): \(\delta\) 7.66 (2H, d, \(J = 8.2 \text{ Hz}\)), 7.25 (2H, d, \(J = 8.7 \text{ Hz}\)), 5.68 – 5.54 (1H, m), 5.54 – 5.40 (1H, m), 3.95 – 3.87 (1H, m), 3.86 – 3.78 (1H, m), 3.11 (1H, dq, \(J = 9.1, 6.8 \text{ Hz}\)), 2.40 (3H, s), 1.65 (3H, dd, \(J = 6.3, 1.4 \text{ Hz}\)), 1.13 (3H, d, \(J = 6.8 \text{ Hz}\)), 0.88 (1H, dt, \(J = 9.7, 8.1, 4.9 \text{ Hz}\)), 0.53 (1H, dddd, \(J = 8.8, 8.0, 5.8, 4.3 \text{ Hz}\)), 0.34 (1H, dddd, \(J = 8.9, 7.9, 5.5, 4.5 \text{ Hz}\)), 0.17 (1H, dddd, \(J = 9.0, 5.4, 4.5, 4.5 \text{ Hz}\)), 0.10 – 0.03 (1H, m); \(^{13}\text{C NMR} \) (100 MHz, CDCl\(_3\)): \(\delta\) 142.6, 138.8, 129.3, 129.0, 128.0, 127.0, 59.3, 45.9, 21.5, 19.1, 17.6, 16.2, 5.5, 4.2.

Data for minor isomer: *Characteristic peaks only*: \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)): \(\delta\) 4.04 (1H, dd, \(J = 16.9, 4.8 \text{ Hz}\)).

\((1R^*, 3aS^*, 4R^*, 7aR^*) \) and \((1S^*, 3aS^*, 4R^*, 7aR^*) \) and \((1R^*, 3aS^*, 4S^*, 7aR^*)-1, 4-Dimethyl-2-tosyloctahydro-5H-isooindol-5-one \((8z)\)
General procedure H: Compound 6z (44.0 mg, 0.15 mmol, mixed with (Z)-conformation isomer, E/Z = 9:1) was employed, the crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8z (22.4 mg, 46 %) as a colorless oil. A mixture of diastereomers A, B and C were obtained in a 13:3:1 (A:B:C) ratio; Under general procedure G, title compound 8z was obtained in 21 % yield (10.3 mg) as a colorless oil, A mixture of diastereomers A, B and C were obtained in a 10:3:1 (A:B:C) ratio.

The relative stereochemistry of diastereomers A was corroborated by nOe experiments (as indicated on the compound structure A). nOes from C1σ-H to C2-H, from C1α-H to C4-H, from C1β-H to C8-H, and between C4-H to C10-H were observed. For minor diastereomer B, the coupling constants of C9-H (dt, J = 9.4, 6.0 Hz) are different from those of major diastereomer A (dt, J = 6.6, 6.6 Hz), and similar to coupling constants of C8-H for minor diastereomer B of product 8n (dt, J = 8.7, 6.1 Hz). This indicates that diastereomer B and diastereomer B of 8n have the same stereochemistry at ring junction and the CH position. At the same time, the coupling constants observed for C4-H of diastereomer A and diastereomer B are similar to each other (for diastereomer A: dd, J = 6.5, 0.8 Hz; for diastereomer B: dd, J = 6.6, 0.8 Hz), this indicates the same stereochemistry at C3 for diastereomer A and diastereomer B. Based on these results, minor diastereomer B was assigned with the stereochemistry indicated on compound structure B. For minor diastereomer C: the coupling constants observed for C9-H of diastereomer A and diastereomer C are similar to each other (for diastereomer A: dt, J = 6.8, 6.8 Hz; for diastereomer B dt, J = 6.6, 6.6 Hz), indicating diastereomer C and diastereomer A have same stereochemistry at C9 and the ring junction, which suggests that the stereochemistry at C3 for diastereomer C is opposite to that of diastereomer A.

ν_max / cm⁻¹: 2970 (m), 1711 (s), 1339 (s), 1159 (m), 1037 (m), 816 (m); m/z (ESI⁺) HRMS: Calculated for C₁₇H₂₃NO₃Na: 344.1291. Found [M+Na]⁺: 344.1297.

Data for major diastereomer A: ¹H NMR (500 MHz, C₆D₆): δ 7.77 (2H, d, J = 8.0 Hz, 2 × C12-H), 6.92 – 6.81 (2H, m, 2 × C13-H), 3.69 (1H, dt, J = 6.8, 6.8 Hz, 1 × C9-H), 3.47 – 3.42 (1H, m, 1 × C1-H₂), 2.50 (1H, dd, J = 10.2, 8.6 Hz, 1 × C1-H₂), 2.06 – 1.96 (1H, m, 1 × C6-H₂), 1.90 (3H, s, 1 × C15-H₂), 1.44 – 1.36 (1H, m, 1 × C6-H₂), 1.33 – 1.24 (1H, m, 1 × C2-H), 1.23 – 1.15 (1H, m, 1 × C3-H), 1.06 – 0.98 (2H, m, 1 × C7-H, 1 × C8-H), 0.96 – 0.93 (3H, m), 1.02 – 0.96 (1H, m, 1 × C7-H); 0.76 (3H, dd, J = 6.5, 0.8 Hz, 3 × C4-H); ¹³C NMR
(126 MHz, C₆D₆): δ 207.2 (C5), 142.6 (C14), 136.0 (C11), 129.3 (C13), 127.5 (C12), 57.4 (C9), 52.4 (C1), 47.5 (C3), 46.6 (C2), 45.4 (C8), 39.4 (C6), 24.2 (C7), 20.7 (C15), 17.8 (C10), 12.2 (C4).

Data for minor diastereomer B: Characteristic peaks only: ¹H NMR (500 MHz, C₆D₆): δ 3.58 (1H, dd, J = 10.9, 7.0 Hz, 1 × C1-H₂), 2.89 (1H, dt, J = 9.4, 6.0 Hz, 1 × C9-H), 2.75 – 2.68 (1H, m, 1 × C1-H₂), 0.72 (3H, dd, J = 6.6, 0.8 Hz, 3 × C4-H₃).

Data for minor diastereomer C: Characteristic peaks only: ¹H NMR (500 MHz, C₆D₆): δ 3.30 (1H, dt, J = 6.6, 6.6 Hz, 1 × C9-H), 3.25 – 3.18 (1H, m, 1 × C1-H₂), 3.01 (1H, dd, J = 10.8, 4.6 Hz, 1 × C1-H₂).

**Binding Competition Studies.**

[Rh(CO)₂Cl]₂ (1.94 mg, 0.005 mmol), and P(3,5-(CF₃)₂C₆H₃)₃ (13.4 mg, 0.020 mmol) and DCM (50 uL) were added to three NMR tubes (tube I, tube II, tube III), evolution of CO was noted on addition of CH₂Cl₂. After 10 minutes, AsPh₃ (6.12 mg, 0.020 mmol) was added to tube II, and 1,4-oxathiane (1.90 uL, 0.020 mmol) was added to tube III. These NMR tubes were left standing at r.t. for 15 minutes before the ³¹P NMR analysis. ³¹P NMR analysis of the three NMR tubes showed that trans-Rh[P(3,5-(CF₃)₂C₆H₃)₃]₂(CO)Cl has formed in all three tubes ((³¹P NMR (CH₂Cl₂, 162 MHz, 25 °C) tube I: δ 29.24 (d, J = 130.7 Hz), tube II: δ 29.18 (d, J = 130.0 Hz) and tube III: δ 29.23 (d, J = 128.9 Hz)), indicating that neither AsPh₃ nor 1,4-oxathiane undergo ligand exchange significantly with Rh[P(3,5-(CF₃)₂C₆H₃)₃]₂(CO)Cl.

³¹P spectra for binding competition studies:
$P(3,5-(CF_3)_2C_6H_3)_3$

$(C_6H_3(F_3C)_{2-5,3})_3P$-$Rh$-$P(3,5-(CF_3)_2C_6H_3)_3$

$CO$

$(C_6H_3(F_3C)_{2-5,3})_3P$-$Rh$-$P(3,5-(CF_3)_2C_6H_3)_3 + AsPh$_3$

$(C_6H_3(F_3C)_{2-5,3})_3P$-$Rh$-$P(3,5-(CF_3)_2C_6H_3)_3 + }

S72
(3a\textsuperscript{R*}, 5\textsuperscript{R*}, 7a\textsuperscript{R*})-2-Tosyloctahydro-1\textit{H}-isoindol-5-ol and (3a\textsuperscript{R*}, 5\textsuperscript{S*}, 7a\textsuperscript{R*})-2-tosyloctahydro-1\textit{H}-isoindol-5-ol (12e)

To a solution of cyclohexanone 8e (73.3 mg, 0.25 mmol) in anhydrous Et\textsubscript{2}O (1 mL) at 0 °C was added NaBH\textsubscript{4} (18.9 mg, 0.50 mmol) in two aliquots. Two drops of MeOH were added to facilitate the reaction, the mixture was warmed to r.t. and stirred overnight. Then the mixture was diluted with water (5 mL) and extracted with EtOAc (3 × 5 mL), the organic layers were
combined, washed with brine (5 mL), dried over Na$_2$SO$_4$ and concentrated in vacuo. The crude mixture was purified by column chromatography (50 % EtOAc/Hex) to yield the title compound 12e (65.9 mg, 90 %) as an off-white solid. A mixture of diastereomers A and B were obtained in a 10:1 (A:B:C) ratio.

**Major diastereomer A** was recrystallized from the mixture, and its structure and relative stereochemistry was determined unambiguously by X-ray crystallography. The relative stereochemistry of minor diastereomer B was assigned as the opposite diastereomer of major diastereomer A on position C4.

$\nu_{\text{max}}$ / cm$^{-1}$: 3408 (m), 2928 (m), 1335 (s), 1159 (s), 1092 (s), 1016 (s); $m/z$ (ESI$^+$) HRMS: Calculated for C$_{15}$H$_{21}$NO$_3$SNa: 318.1134. Found [M+Na$^+$]: 318.1141.

Data for major diastereomer A: m.p.: 148 – 151 °C (CH$_2$Cl$_2$/Hex); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.67 (2H, d, $J = 7.9$ Hz, 2 $\times$ C$_{10}$-H), 7.30 (2H, d, $J = 7.9$ Hz, 2 $\times$ C$_{11}$-H), 3.62 – 3.54 (1H, m, 1 $\times$ C$_4$-H), 3.52 – 3.41 (2H, m, 1 $\times$ C$_1$-H$_2$, 1 $\times$ C$_8$-H$_2$), 2.83 – 2.69 (2H, m, 1 $\times$ C$_1$-H$_2$, 1 $\times$ C$_8$-H$_2$), 2.41 (3H, s, 3 $\times$ C$_{13}$-H), 2.09 – 2.01 (1H, br. m, 1 $\times$ C$_3$-H$_2$), 2.01 – 1.93 (1H, br. m, 1 $\times$ C$_5$-H$_2$), 1.89 (1H, br. d, $J = 12.6$ Hz, (OH)), 1.83 – 1.77 (1H, br. m, 1 $\times$ C$_6$-H$_2$), 1.43 – 1.14 (3H, m, 1 $\times$ C$_5$-H$_2$, 1 $\times$ C$_2$-H, 1 $\times$ C$_7$-H), 1.09 – 0.95 (2H, m, 1 $\times$ C$_3$-H$_2$, 1 $\times$ C$_6$-H$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 143.3 (C$_{12}$), 134.6 (C$_9$), 129.7 (C$_{11}$), 127.2 (C$_{10}$), 70.0 (C$_4$), 52.4, 52.3 (C$_1$, C$_8$), 43.8, 42.9 (C$_2$, C$_7$), 37.1 (C$_3$), 34.6 (C$_5$), 25.7 (C$_6$), 21.5 (C$_{13}$). *(N.B. C1 and C8, C2 and C7 could not be assigned confidently).*

Data for minor diastereomer B: Characteristic peaks only: $^1$H NMR (400 MHz, CDCl$_3$): 4.09 (1H, br. m, 1 $\times$ C$_4$-H).
(3aR*, 5R*, 7aR*) and (3aR*, 5S*, 7aR*)-5-Phenyl-2-tosyloctahydro-1H-isoinod-5-ol (13e)

To a stirring solution of 8e (73.3 mg, 0.25 mmol) in anhydrous THF (1 mL) at -78 °C was added phenylmagnesium chloride (0.25 mL, 0.50 mmol, 2.0 M in THF) dropwise and the mixture was stirred at -78 °C for 6 h. Then the reaction mixture was quenched with sat. aq. NH₄Cl (1 mL), warmed to r.t., diluted with water (2 mL) and extracted with EtOAc (3 × 5 mL), the organic extracts were combined, washed with water (5 mL), brine (5 mL), dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography (33 % EtOAc/Hex) to yield the title compounds 13e-A (64.8 mg, 69%) as a colorless solid and the title compound 13e-B (19.8 mg, 21%) as a colorless oil.

The relative stereochemistry of major diastereomer A was corroborated by nOe experiments (as indicated on the compound structure A) nOes between OH and C9α-H, C9α-H and C10α-H, C10α-H and C12-H were observed. No significant nOe was observed between C2-H and C11-H. The relative stereochemistry of minor diastereomer B was corroborated by nOe experiments (as indicated on the compound structure B). A nOe from C2-H to OH was observed. No significant nOe was observed between C2-H and C11-H.

ν max / cm⁻¹: 3236 (m), 2971 (m), 1340 (s), 1150 (s), 1014 (m), 765 (s); m/z (ESI⁺)

Data for major diastereomer A: m.p.: 79 – 81 °C (CH₂Cl₂/Hex); ¹H NMR (400 MHz, CDCl₃): 7.65 (2H, d, J = 8.3 Hz, 2 × C14-H), 7.47 – 7.43 (2H, m, 2 × C6-H), 7.39 – 7.31 (2H, m, 2 × C7-H), 7.30 – 7.23 (3H, m, 2 × C15-H, 1 × C8-H), 3.50 – 3.40 (2H, m, 1 × C1-H₂, 1 × C12-H₂), 2.57 – 2.51 (2H, m, 1 × C3-H₂, 1 × C9-H₂), 2.40 (3H, s, 3 × C17-H₃), 2.01 (1H, br. s, OH), 1.86 – 1.82 (1H, m, 1 × C10-H₂), 1.71 (1H, td, J = 13.7, 4.1 Hz, 1 × C9-H₂), 1.56 – 1.37 (2H,
m, 1 × C3-H2, 1 × C2-H), 1.37 – 1.22 (1H, m, 1 × C11-H), 1.19 – 1.08 (1H, m, 1 × C10-H2);
13C NMR (100 MHz, CDCl3): δ 144.0 (C5), 143.2 (C16), 134.8 (C13), 129.6 (C15), 128.7 (C7), 127.8 (C8), 127.2 (C14), 126.1 (C6), 73.7 (C4), 52.2, 52.1 (C1, C12), 44.5 (C2), 41.7 (C11), 40.7 (C3), 37.6 (C9), 25.7 (C10), 21.5 (C17).

Data for minor diastereomer B: 1H NMR (400 MHz, CDCl3): 7.72 (2H, d, J = 8.2 Hz, 2 × C14-H), 7.45 – 7.40 (2H, m, 2 × C6-H), 7.36 – 7.29 (4H, m, 2 × C15-H, 2 × C7-H), 7.28 – 7.22 (1H, m, 1 × C8-H), 3.60 (1H, dd, J = 9.2, 6.7 Hz, 1 × C12-H2), 3.52 (1H, dd, J = 9.2, 7.2 Hz, 1 × C1-H2), 2.87 (2H, dd, J = 10.9, 9.3 Hz, 1 × C1-H2, 1 × C12-H2), 2.44 (3H, s, 3 × C17-H3), 2.07 – 1.95 (1H, m, 1 × C2-H), 1.95 – 1.90 (1H, m, 1 × C3-H2), 1.88 – 1.72 (3H, m, 2 × C9-H2, 1 × C10-H2), 1.63 (1H, br. s, OH), 1.60 – 1.49 (2H, m, 1 × C10-H2, 1 × C3-H2), 1.49 – 1.38 (1H, m, 1 × C11-H2); 13C NMR (100 MHz, CDCl3): δ 148.4 (C5), 143.2 (C16), 134.7 (C13), 129.7 (C15), 128.4 (C7), 127.3 (C14), 127.1 (C8), 124.2 (C6), 73.5 (C4), 52.6 (C12), 52.5 (C1), 43.9 (C11), 40.9 (C3), 39.9 (C2), 38.5 (C9), 24.0 (C10), 21.5 (C17).

(3aR*, 7aR*)-2-Tosyl-2,3,3a,4,7,7a-hexahydro-1H-isooindol-5-yl trifluoromethanesulfonate and (3aS*, 7aR*)-2-tosyl-2,3,3a,6,7,7a-hexahydro-1H-isooindol-5-yl trifluoromethanesulfonate (14e)

To a solution of 8e (105.0 mg, 0.36 mmol) in anhydrous THF (1.8 mL) at -78 °C was added potassium hexamethyldisilazide (KHMDs) (1 M in THF, 0.43 ml, 0.43 mmol) dropwise. Then the reaction was stirred at -78 °C for 10 minutes, and N-(5-chloro-2-pyridyl)bis(trifluoromethanesulfonylimide) (Comin’s reagent) (169.0 mg, 0.43 mmol) was added and the reaction was warmed slowly to r.t. over 3 h. The reaction was diluted with EtOAc (10 mL), washed with citric acid (10% w/v, 2 x 4 mL), H2O (4 mL), and brine (4 mL), then dried over Na2SO4, filtered and concentrated in vacuo. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 14e (82.3 mg, 68
% as an off-white solid. A mixture of regioisomers A and B were obtained in a 8:1 (A:B) ratio.

The configuration of the enol triflate for major regioisomer A was determined by COSY data. Correlation between C6-H and C7-Hα, C8-H and C7-Hβ were observed.

νmax / cm⁻¹: 2935 (m), 1420 (s), 1342 (s), 1210 (s), 859 (s); m/z (ESI⁺) HRMS: Calculated for C₁₆H₁₈NO₅S₂F₃Na: 448.0471. Found [M+Na]⁺: 448.0453

Data for major regioisomer A: ¹H NMR (400 MHz, CDCl₃): δ 7.70 (2H, d, J = 8.3 Hz, 2 × C11-H), 7.32 (2H, d, J = 8.2 Hz, 2 × C12-H), 5.77 – 5.73 (1H, m, 1 × C6-H), 3.73 – 3.59 (2H, m, 1 × C1-H₂, 1 × C9-H₂), 2.96 – 2.79 (2H, m, 1 × C1-H₂, 1 × C9-H₂), 2.47 – 2.40 (4H, m, 3 × C14-H₃, 1 × C8-H₂, 1 × C3-H₂), 2.39 – 2.31 (1H, m, 1 × C7-H₂), 2.25 – 2.16 (1H, m, 1 × C8-H), 1.99 – 1.84 (2H, m, 1 × C7-H₂, 1 × C2-H), 1.80 – 1.70 (1H, m, 1 × C8-H); ¹³C NMR (100 MHz, CDCl₃): δ 148.1 (C₄), 143.6 (C₁₃), 134.2 (C₁₀), 129.8 (C₁₂), 127.3 (C₁₁), 118.4 (q, J = 320.2 Hz) (C₅), 118.2 (C₆), 52.2, 52.0 (C₁, C₉), 40.5 (C₈), 39.1 (C₂), 31.1 (C₃), 26.1 (C₇), 21.5 (C₁₄). (N.B. C₁ and C₉ could not be assigned confidently)

Data for minor regioisomer B: Characteristic peaks only: ¹H NMR (400 MHz, CDCl₃): δ 3.58 – 3.55 (2H, m, 1 × C1-H₂, 1 × C9-H₂).

(3aR*, 7aR*)-5-(p-Tolyl)-2-tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoinde and (3aR*, 7aR*)-6-(p-tolyl)-2-tosyl-2,3,3a,4,5,7a-hexahydro-1H-isoinde (15e)
An oven dried reaction tube, fitted with a magnetic stirrer, was charged compound 14e (33.6 mg, 0.1 mmol), p-tolyboronic acid (16.2 mg, 0.12 mmol), [Pd(dtbpf)Cl]$_2$ (dtbpf = 1,1′-Bis(di-tertbutylphosphino)ferrocene) (6.6 mg, 0.01 mmol), and K$_2$CO$_3$ (20.7 mg, 0.15 mmol). Then MeCN/H$_2$O(1:1, 1 mL) was added and the reaction tube was sealed under an argon atmosphere and heated to 80 °C for 2 h. The reaction mixture was cooled to r.t. and diluted with H$_2$O (5 mL). The aqueous phase was extracted with EtOAc (3 x 5 mL), the combined organic layers were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The crude mixture was purified by column chromatography (10 % EtOAc/Hex) to yield the title compound 15e (25.8 mg, 71 %) as an off-white solid. A mixture of regioisomer A and B were obtained in a 9:1 (A:B) ratio.

$v_{max}$ / cm$^{-1}$: 2921 (m), 1340 (s), 1158 (s), 1093 (m), 1040 (m), 917 (m), 971 (m); $m/z$ (ESI$^+$) HRMS: Calculated for C$_{22}$H$_{25}$NO$_2$SNa: 390.1498. Found [M+Na]$^+$: 390.1508.

Data for major regioisomer A: $^1$H NMR (400 MHz, CDCl$_3$): δ 7.74 (2H, d, $J = 8.3$ Hz, 2 × C15-H), 7.32 (2H, d, $J = 8.1$ Hz, 2 × C16-H), 7.20 (2H, d, $J = 8.3$ Hz, 2 × C6-H), 7.10 (2H, d, $J = 7.9$ Hz, 2 × C7-H), 6.01 – 5.98 (1H, m, 1 × C10-H), 3.79 – 3.63 (2H, m, 1 × C1-H$_2$, 1 × C13-H$_2$), 3.01 – 2.81 (2H, m, 1 × C1-H$_2$, 1 × C13-H$_2$), 2.61 – 2.55 (1H, m, 1 × C3-H$_2$), 2.43 (3H, s, 3 × C18-H$_3$), 2.41 – 2.33 (1H, m, 1 × C11-H$_2$), 2.32 (3H, s, 3 × C9-H$_3$), 2.22 – 2.11 (1H, m, 1 × C3-H$_2$), 2.00 – 1.90 (1H, m, 1 × C11-H$_2$), 1.85 – 1.69 (2H, m, 1 × C2-H, 1 × C12-H$_2$); $^{13}$C NMR (100 MHz, CDCl$_3$): δ 143.3 (C17), 138.7 (C5), 136.8 (C8), 136.1 (C4), 134.6 (C14), 129.7 (C16), 129.0 (C7), 127.3 (C15), 125.0 (C6), 122.6 (C10), 53.3, 53.2 (C1, C13), 40.9 (C2), 40.0 (C12), 31.0 (C3), 29.0 (C11), 21.5 (C18), 21.0 (C9). (N.B. CI and C13 could not be assigned confidently).

Data for minor regioisomer B: Characteristic peaks only: $^1$H NMR (400 MHz, CDCl$_3$): δ 3.62 – 3.58 (2H, dd, $J = 9.5, 6.9$ Hz, 1 × C1-H$_2$, 1 × C13-H$_2$).

(3a$^R$, 7a$^R$)-2-Tosyloctahydro-1H-isooindole (16e)
A stirred solution of 8e (146.0 mg, 0.5 mmol) and hydrazinemonohydrate (0.25 ml, 5.0 mmol) in ethylene glycol (6 mL) was heated at 130 °C for 3 h. After removal of excess hydrazine hydrate under reduced pressure, KOH (330.0 mg, 5.0 mmol) was added to the mixture, and the reaction was heated at 170 °C for 16 h. The resulting solution was cooled to r.t., treated with saturated aq. NH₄Cl and extracted with diethyl ether (3 × 10 mL). The organic extracts were combined, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (10 % EtOAc/hexane) to afford the title compound 16e (124.6 mg, 90 %) as a off-white solid; m.p.: 105 - 107 °C (CHCl₃/Hex); νmax / cm⁻¹: 2932 (m), 1341 (s), 1159 (s), 1092 (s), 1028 (s), 816 (m); ¹H NMR (CDCl₃, 400 MHz): δ 7.71 (2H, d, J = 8.3 Hz, 2 × C₆-H), 7.31 (2H, d, J = 7.9 Hz, 2 × C₇-H), 3.50 (2H, dd, J = 9.4, 6.5 Hz, 2 × C₁-H₂), 2.77 (2H, dd, J = 10.8, 9.3 Hz, 2 × C₁-H₂), 1.85 – 1.76 (2H, m, 2 × C₄-H₂), 1.76 – 1.66 (2H, m, 2 × C₃-H₂), 1.37 – 1.20 (2H, m, 2 × C₂-H), 1.21 – 1.07 (2H, m, 2 × C₃-H₂), 1.04 – 0.84 (2H, m, 2 × C₄-H₂); ¹³C NMR (CDCl₃, 100 MHz): δ 143.0 (C₈), 134.9 (C₅), 129.6 (C₇), 127.3 (C₆), 53.0 (C₁), 44.4 (C₂), 28.3 (C₄), 25.3, 21.5 (C₃); m/z (ESI⁺) HRMS: Calculated for C₁₅H₂₂NO₂S: 280.1366. Found [M+H]⁺: 280.1365.

Deprotection of Catalytic Products

To a solution of 8h (48.0 mg, 0.15 mmol, d.r.=3:1) in MeOH (5.0 mL) was added 10 wt. % palladium hydroxide on carbon ( 2.1 mg, 0.015 mmol) under the H₂ atmosphere (1 atm). Then evacuated and back-fill the flask with hydrogen three times. The reaction was stirred at 40 °C for 18 hours. The reaction mixture was then filtered through a short plug of silica, washed with MeOH, and concentrated in vacuo to afford 8h’ as a colorless oil which was directly dissolved in anhydrous toluene (2.0 ml), and then potassium carbonate (41.4 mg, 0.3 mmol) and sulfonyl chloride (57.0 mg, 0.3 mmol) were added to the solution. The reaction mixture was heated to 50 °C and stirred overnight. The suspension was cooled to r.t. and water (5 mL) was added, the aqueous layer was extracted with EtOAc (3 × 5 mL) and the
organic extracts combined, dried over Na₂SO₄ and concentrated in vacuo. The crude mixture was purified by column chromatography (33 % EtOAc/Hex) to yield the title compound 8i (24.7 mg, 51 %) as a colorless oil. A mixture of diastereomers A and B were obtained in a 9:1 ratio.

(3aR*, 7aR*)-2-Tosyloctahydrospiro[isoindole-5,2'-[1,3]dioxolane] (17e)

To a flask equipped with a Dean–Stark apparatus under argon, was added 8e (0.44g, 1.5 mmol), p-toluenesulfonic acid (15.0 mg, 0.09 mmol), ethylene glycol (0.9 mL, 15.0 mmol), and toluene (10 mL). The reaction solution was stirred under reflux for 5 h and water was removed through the Dean-Stark apparatus. The solution was cooled to 25 ºC, diluted with aq. NaHCO₃, and extracted with diethyl ether (3 × 10 mL). The organic extracts were combined, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (50 % EtOAc/hexane) to afford the title compound 17e (0.50 g, 99 %) as a colorless solid; m.p.: 102 - 104 ºC (CH₂Cl₂/Hex); ν max / cm⁻¹: 2944 (m), 2880 (m), 1338 (s), 1157 (s), 1085 (s), 1035 (m); ¹H NMR (CDCl₃, 400 MHz): δ 7.69 (2H, d, J = 8.2 Hz, 2 × C12-H), 7.30 (2H, d, J = 7.8 Hz, 2 × C13-H), 3.94 – 3.84 (4H, m, 2 × C5-H₂, 2 × C6-H₂), 3.54 (1H, dd, J = 9.3, 6.8 Hz, 1 × C1-H₂), 3.48 (1H, dd, J = 9.3, 7.2 Hz, 1 × C9-H₂), 2.84 (1H, dd, J = 11.1, 9.3 Hz, 1 × C9-H₂), 2.77 (1H, dd, J = 10.9, 9.3 Hz, 1 × C1-H₂), 2.43 (3H, s, 3 × C15-H₃), 1.86 – 1.72 (3H, m, 1 × C3-H₂, 1 × C7-H₂, 1 × C8-H₂), 1.71 – 1.65 (1H, m, 1 × C9-H), 1.47 (1H, td, J = 13.6, 4.7 Hz, 1 × C7-H₂), 1.43 – 1.33 (1H, m, 1 × C2-H), 1.33 – 1.18 (2H, m, 1 × C3-H₂, 1 × C8-H₂); ¹³C NMR (CDCl₃, 100 MHz): δ 143.2 (C14), 134.7 (C11), 129.7 (C13), 127.2 (C12), 108.8 (C4), 64.4, 66.3(C5, C6), 52.3, 52.2 (C1, C10), 43.5 (C2), 42.2 (C9), 37.4 (C8), 34.3 (C7), 24.8 (C3), 21.5 (C15); m/z (ESI⁺) HRMS: Calculated for C17H24NO₄S: 338.1421. Found [M+H]⁺: 338.1425.
Mg turnings (96.0 mg, 4.0 mmol) was added to a solution of 17e (134.8 mg, 0.40 mmol) in dry MeOH (4 mL), and the mixture was refluxed for 24 hours. The suspension was cooled to r.t. and then was filtered through a short plug of silica, washed with MeOH, and concentrated in vacuo. The residue was purified by flash column chromatography (from 10 % MeOH/DCM to MeOH/DCM/NH₄OH = 8:1:0.1) to afford the title compound 18e (67.9 mg, 93 %) as a red oil; $\nu_{\text{max}}$ / cm$^{-1}$: 3411 (s), 2928 (s), 2717 (m), 1361 (m), 1144 (s), 1069 (s), 948 (m); $^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 4.05 – 3.75 (4H, m, 2 × C$_5$-H$_2$, 2 × C$_6$-H$_2$), 3.36 (1H, s, br. NH), 3.03 (2H, dd, $J_1 = 9.8$, 7.0 Hz, 1 × C$_1$-H$_2$, 1 × C$_{10}$-H$_2$), 2.46 (2H, dd, $J_2 = 10.4$, 10.4 Hz, 1 × C$_1$-H$_2$, 1 × C$_{10}$-H$_2$), 1.92 – 1.85 (1H, m, 1 × C$_8$-H$_2$), 1.84 – 1.73 (2H, m, 1 × C$_3$-H$_2$, 1 × C$_7$-H$_2$), 1.73 – 1.66 (1H, m, 1 × C$_9$-H), 1.52 (1H, td, $J_3 = 13.2$, 4.4 Hz, 1 × C$_7$-H$_2$), 1.44 – 1.36 (1H, m, 1 × C$_2$-H), 1.35 – 1.23 (2H, m, 1 × C$_3$-H$_2$, 1 × C$_8$-H$_2$); $^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 109.6 (C$_4$), 64.4, 64.3 (C$_5$, C$_6$), 50.5, 50.3 (C$_1$, C$_{10}$), 45.0 (C$_2$), 43.7 (C$_9$), 38.0 (C$_8$), 34.9 (C$_7$), 25.4 (C$_3$); m/z (ESI$^+$) HRMS: Calculated for C$_{10}$H$_{17}$NO$_2$: 184.1332. Found [M+H]$^+$: 184.1333.
Copies of $^1\text{H}$ and $^{13}\text{C}$ NMR for Novel Compounds

Ethyl (cyclopropylmethyl)carbamate
Ethyl butyl(cyclopropylmethyl)carbamate (4a)
(E)-Ethyl but-2-en-1-yl(butyl)carbamate and (Z)-Ethyl but-2-en-1-yl(butyl)carbamate (10a-A)

\[ \text{E/Z}=3:1 \]
Ethyl (E)-but-1-en-1-yl(butyl)carbamate (10a-B)
Benzyl cyclopropyl(cyclopropylmethyl)carbamate (4b)
Benzyl \((E)-(cyclopropylmethyl)\) (prop-1-en-1-yl)carbamate (11a) and Benzyl \(((E)-\text{but-2-en-1-yl})((E)-\text{prop-1-en-1-yl})\)carbamate (11b)

1h ○ : ● = 13:1

3h ○ : ● = 7:3
$N$-(Cyclopropylmethyl)pyridin-2-amine
$N$-Allyl-$N$-(cyclopropylmethyl)pyridin-2-amine (6a)
3-(Cyclopropylmethyl)-1,1-dimethylurea
1- Allyl-1-(cyclopropylmethyl)-3,3-dimethylurea (6b)
(3aR*, 7aR*)-N,N-Dimethyl-5-oxooctahydro-2H-isoindole-2-carboxamide (8b)
Benzylallyl(cyclopropylmethyl)carbamate (6c)
(3aR*, 7aR*)-Benzyloxohexahydro-1H-isoindole-2(3H)-carboxylate (8c)
N-(Cyclopropylmethyl)benzamide
$N$-Allyl-$N$-(cyclopropylmethyl)benzamide (6d)
(3aR*, 7aR*)-2-Benzoyloctahydro-5H-isoindol-5-one (8d)
N-(Cyclopropylmethyl)-4-methylbenzenesulfonamide
$N$-Ally-$N$-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6e)
(3aR*, 7aR*)-2-Tosylhexahydro-1H-isoindol-5(6H)-one (8e)
$N$-(Cyclopropylmethyl)-4-(trifluoromethyl)benzamide
$N$-Allyl-$N$-(cyclopropylmethyl)-4-(trifluoromethyl)benzamide (6f)
(3aR*, 7aR*)-2-(4-(Trifluoromethyl)benzoyl)octahydro-5H-isoindol-5-one (8f)
N-(Cyclopropylmethyl)-4-nitrobenzenesulfonamide
N- Allyl-N-(cyclopropylmethyl)-4-nitrobenzenesulfonamide (6g)
(3aR*, 7aR*)-2-((4-Nitrophenyl)sulfonyl)octahydro-5H-isoindol-5-one (8g)
$N$-(Cyclopropylmethyl)hex-1-en-3-amine
Benzyl (cyclopropylmethyl)(hex-1-en-3-yl)carbamate (6h)
(1S*, 3aR*, 7aR*) and (1R*, 3aR*, 7aR*)-Benzy 6-oxo-1-propylhexahydro-1H-isoindole-2(3H)-carboxylate (8h)
$N$-($\text{Cyclopropylmethyl}$)-$N$-($\text{hex-1-en-3-yl}$)-4-$\text{methylbenzenesulfonamide}$ (6i)
(3S*,3aR*,7aR*) and (3R*,3aR*,7aR*)-3-Propyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8i)
4-Methyl-N-(1-phenylbut-3-en-2-yl)benzenesulfonamide
$N$-(Cyclopropylmethyl)-4-methyl-$N$-(1-phenylbut-3-en-2-yl)benzenesulfonamide (6j)
(3$S^*$, 3$aR^*$, 7$aR^*$) and (3$R^*$, 3$aR^*$, 7$aR^*$)-3-Benzyl-2-tosylhexahydro-1$H$-isoindol-5(6$H$)-one (8j)
4-Methyl-N-(4-methylpent-1-en-3-yl)benzenesulfonamide
$N$-(Cyclopropylmethyl)-4-methyl-$N$-(4-methylpent-1-en-3-yl)benzenesulfonamide (6k)
(3S*, 3aR*, 7aR*) and (3R*, 3aR*, 7aR*) -3-Isopropyl-2-tosylhexahydro-1H-isooindol-5(6H)-one (8k)
\[ N-(1-\text{(Benzyloxy)but-3-en-2-yl})-4\text{-methylbenzenesulfonamide} \]
1-(Benzyloxy)-N-(cyclopropylmethyl)but-3-en-2-amine (6l)
(3R*,3aR*,7aR*)-3-((Benzoyloxy)methyl)-2-tosylhexahydro-1H-isoindol-5(6H)-one (8l-A)
(3S*,3aR*,7aR*) -3-((Benzyloxy)methyl)-2-toslyhexahydro-1H-isooindol-5(6H)-one (8l-B)
N-(2-(Benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide
N-Allyl-N-(2-(benzyloxy)-1-cyclopropylethyl)-4-methylbenzenesulfonamide (6m)
(1S*, 3aR*, 7aR*) and (1R*,3aR*,7aR*)-1-((Benzyloxy)methyl)-2-tosylhexahydro-1H-
isoindol-5(6H)-one (8m)
N-(1-Cyclopropylethyl)-4-methylbenzenesulfonamide
N-Allyl-N-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6n)
(1R*, 3aR*, 7aR*) and (1S*, 3aR*, 7aR*)-1-Methyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8n)
Benzyl (1-cyclopropylethyl)carbamate
Benzyl allyl(1-cyclopropylethyl)carbamate (60)
(1R*, 3aR*, 7aR*)-Benzyl 1-methyl-5-oxohexahydro-1H-isooindole-2(3H)-carboxylate (8o-A)
(15\(^*\), 3a\(^R\)*, 7a\(^R\)*)-Benzyl 1-methyl-5-oxohexahydro-1H-isoindole-2(3\(H\))-carboxylate (8o-B)
(1S*, 2S*)-N-Allyl-2-butylocyclopropane-1-carboxamide
(1S*, 2S*)-N-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine
(1S*, 2S*)-Benzyl allyl(-2-butylcyclopropyl)methylcarbamate (6p)
(3aR*, 4S*, 7aR*)-Benzy1-4-buty1-6-oxooctahydro-2H-isoindole-2-carboxylate (8p)
(1R*, 2S*)-N-allyl-2-cyclohexylcyclopropanecarboxamide
(1R*, 2S*)-N-((-2-Cyclohexylcyclopropyl)methyl)prop-2-en-1-amine
(1\textit{R}*, 2\textit{S}*)-Benzyl allyl((2-cyclohexylcyclopropyl)methyl)carbamate (6q)
(3R*, 4S*, 7aR*)-Benzyl 4-cyclohexyl-6-oxohexahydro-1H-isooindole-2(3H)-carboxylate (8q)
(1S*, 25*)-N-allyl-2-phenylcyclopropanecarboxamide
(1S*, 2S*)-N-((-2-Phenylcyclopropyl)methyl)prop-2-en-1-amine
(1S*, 2S*)-N-((2-Phenylcyclopropyl)methyl)prop-2-en-1-amine (6r)
(3aR*, 4S*, 7aR*)-Benzyl 6-oxo-4-phenylhexahydro-1H-isoindole-2(3H)-carboxylate (8r)
(1R*, 2S*)-N-Allyl-2-benzylcyclopropanecarboxamide
(1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)prop-2-en-1-amine
(1R*, 2S*)-Benzyl allyl((2-benzylcyclopropyl)methyl)carbamate (6s)
(3aR*, 4S*, 7aR*)-Benzy1 4-benzy1-6-oxohexahydro-1H-isooindole-2(3H)-carboxylate (8s)
(1S*, 2S*)-N-allyl-N-((2-butylicyclopropyl)methyl)-4-methylbenzenesulfonamide (6t)
(3a\text{R}^*, 7S^*, 7a\text{R}^*) - 7-Butyl-2-tosylhexahydro-1H-isoindol-5(6\text{H})-one (8t)
(1S*, 2R*)-N-Allyl-2-butylcyclopropanecarboxamide
(1S*, 2R*)-N-(2-Butylcyclopropyl)methyl)prop-2-en-1-amine
(1S*, 2R*)-Benzyl allyl(-2-butylcyclopropyl)methylcarbamate (6u)
(3aR*, 6S*, 7aR*) and (3aR*, 6R*, 7aR*) -6-Butyl-2-tosylhexahydro-1H-isoindol-5(6H)-one and (3aR*, 7R*, 7aR*)-7-butyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8u)
(1R*, 5S*, 6R*)-N-Allylbicyclo[3.1.0]hexane-6-carboxamide
(1R*, 5S*, 6R*)-N-((Bicyclo[3.1.0]hexan-6-ylmethyl)prop-2-en-1-amine

\[
\begin{align*}
\text{H} & \quad \text{N} \\
\text{H} & \quad \text{H} \\
\end{align*}
\]
(1R*, 5S*, 6R*)-Benzyl allyl((-bicyclo[3.1.0]hexan-6-yl)methyl)carbamate (6v)
(3aR*, 5aR*, 8aR*, 8bR*)-Benzyl 5-oxodecahydrocyclopenta[e]isoindole-2(3H)-carboxylate (8v)
(E)-N-(But-2-en-1-yl)-N-(cyclopropylmethyl)-4-methylbenzenesulfonamide (6w)
(3aS*, 4R*, 7aR*)-4-Methyl-2-tosylethoxyhexahydro-1H-isoindol-5(6H)-one (8w)
(E) –N-(Cyclopropylmethyl)-4-methyl-N-(pent-2-en-1-yl)benzenesulfonamide (6x)
(3aS*, 4R*, 7aR*)-4-Ethyl-2-tosylhexahydro-1H-isooindol-5(6H)-one (8x)
(Z)-N-(Cyclopropylmethyl)-4-methyl-N-(pent-2-en-1-yl)benzenesulfonamide (6x')
(3aS*, 4S*, 7aR*) and (3aS*, 4R*, 7aR*)-4-Ethyl-2-tosylhexahydro-1H-isoindol-5(6H)-one (8x')
(1R*, 2S*)-2-Benzyl-N-tosylcyclopropane-1-carboxamide
(1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)-4-methylbenzenesulfonamide
(1R*, 2S*)-N-((2-Benzylcyclopropyl)methyl)-N-(E-but-2-en-1-yl)-4-methylbenzenesulfon amide (6y)
(3aS*, 4R*, 7S*, 7aR*) and (3aS*, 4S*, 7S*, 7aR*)-7-Benzyl-4-methyl-2-tosyloctahydro-5H-isooindol-5-one (8y)
(E)-N-(But-2-en-1-yl)-N-(1-cyclopropylethyl)-4-methylbenzenesulfonamide (6z)
(1$R^*$, 3$aS^*$, 4$R^*$, 7$aR^*$) and (1$S^*$, 3$aS^*$, 4$R^*$, 7$aR^*$) and (1$R^*$, 3$aS^*$, 4$S^*$, 7$aR^*$)-1,4-Dimethyl-2-tosyloctahydro-5$H$-isoindol-5-one (8z)
(3aR*, 5R*, 7aR*)-2-Tosyloctahydro-1H-isoindol-5-ol and (3aR*, 5S*, 7aR*)-2-tosyloctahydro-1H-isoindol-5-ol (12e)
(3aR*, 5R*, 7aR*) -5-Phenyl-2-tosyloctahydro-1H-isoindol-5-ol (13e-A)
(3aR*, 5S*, 7aR*)-5-Phenyl-2-tosyloctahydro-1H-isoindol-5-ol (13e-B)
(3aR*, 7aR*)-2-Tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoindol-5-yl trifluoromethanesulfonate and (3aS*, 7aR*)-2-tosyl-2,3,3a,6,7,7a-hexahydro-1H-isoindol-5-yl trifluoromethanesulfonate (14e)
(3aR*, 7aR*)-5-(p-Tolyl)-2-tosyl-2,3,3a,4,7a-hexahydro-1H-isoindole and (3aR*, 7aR*)-
6-(p-tolyl)-2-tosyl-2,3,3a,4,5,7a-hexahydro-1H-isoindole (15e)
(3aR*, 7aR*)-2-Tosyloctahydro-1H-isoindole (16e)
(3a$R^*$, 7a$R^*$)-2-Tosyloctahydrospiro[isoindole-5,2'-[1,3]dioxolane] (17e)
(3aR*, 7aR*)-Octahydropyrrolo[isoindole-5,2'-[1,3]dioxolane] (18e)
Selected Reaction Optimization Results

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Rh catalyst (5 mol%)</th>
<th>Ligand (mol%)</th>
<th>Solvent (M)</th>
<th>Yield a</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Rh(cod)Cl]_2</td>
<td>AsPh_3 (10)</td>
<td>1,2-DCB (0.18)</td>
<td>39 %</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>None</td>
<td>1,2-DCB (0.18)</td>
<td>44 %</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>DMSO (30)</td>
<td>1,2-DCB (0.18)</td>
<td>52 %</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand A (15)</td>
<td>1,2-DCB (0.18)</td>
<td>31 %</td>
</tr>
<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand B (15)</td>
<td>1,2-DCB (0.18)</td>
<td>(9 %)</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand C (15)</td>
<td>1,2-DCB (0.18)</td>
<td>(36 %)</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand D (30)</td>
<td>1,2-DCB (0.18)</td>
<td>54 %</td>
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<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand E (30)</td>
<td>1,2-DCB (0.18)</td>
<td>45 %</td>
</tr>
<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand F (30)</td>
<td>1,2-DCB (0.18)</td>
<td>49 %</td>
</tr>
<tr>
<td>[Rh(CH_2CH_2)_2Cl]_2</td>
<td>Ligand G (30)</td>
<td>1,2-DCB (0.18)</td>
<td>63 %</td>
</tr>
<tr>
<td>[Rh(CO)_2Cl]_2</td>
<td>Ligand G (30)</td>
<td>Mesitylene (0.3)</td>
<td>71 % b</td>
</tr>
</tbody>
</table>

a In situ yields are given in parentheses, in all case d.r >15:1; b Na_2SO_4 (20 mol%) was used as additive.

**References**