Palladium(II) Catalyst Systems for the Addition of Boronic Acids to Bicyclic Alkenes: New Scope and Reactivity

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1. Methods

Unless otherwise noted, all reactions were carried out under nitrogen atmosphere with magnetic stirring. Boronic acids were obtained from Aldrich, Maybridge, or TCI and used without further purification. Methanol (ACS grade) was used undistilled. Oxabicyclic **1a**¹ and azabicyclic **3a**² were synthesized according to literature procedures. Analytical thin layer chromatography was performed with Silicycle™ normal phase 0.25 mm aluminum-backed TLC plates. Visualization was accomplished with 254 nm UV light and ethanolic anisaldehyde or aqueous potassium permanganate solutions. Purification of reaction products was done by flash chromatography with Silicycle™ Ultra-Pure 230-400 mesh silica gel. ¹H NMR spectra were recorded at 300, 400, or 500 MHz, and ¹³C NMR spectra (proton-decoupled but not fluorine decoupled) were recorded at 75, 100, or 126 MHz, using Varian spectrometers and TMS as the internal standard. ¹⁹F NMR spectra were recorded with chemical shifts relative to CFC1₃ (external standard). Spectral features are tabulated in the following order: chemical shift (δ, ppm); number of protons; multiplicity (s-singlet, d-doublet, t-triplet, q-quartet, m-complex multiplet); coupling constants (*J*, Hz). IR spectra were obtained using a Perkin-Elmer Spectrum 1000 FT-IR spectrometer as a neat film on a NaCl plate. High resolution mass spectra were obtained from a Micromass 70S-250 mass spectrometer (EI) or an ABI/Sciex Qstar mass spectrometer (ESI). Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. HPLC analysis was performed with an Agilent 1100 series HPLC with photodiode array and Chiracel chiral columns with Uniguard pre-column filters. Optical rotations were measured in a 10 cm cell

¹ Stiles, M.; Miller, R. G. *Can J. Chem.* **1965**, *43*, 1599.

² Lautens, M.; Fagnou, K.; Zunic, V. *Org. Lett.* **2002**, *4*, 3465.

with a Perkin-Elmer 243 B polarimeter with sodium lamp and are reported as follows: $[\alpha]_D^{T^\circ}$
 C (c = g/100 mL, solvent).

2. Experimental Procedures

a) Synthesis of azabicycle **3b**:

2-Amino-4,5-dimethoxy-benzoic acid (2.5 g, 12.7 mmol) and trichloroacetic acid (15 mg) were added to a 200 mL beaker with stir bar. THF (30 mL) was added and the reaction was stirred while heating in an oil bath at 50°C. After all solids had dissolved, isoamyl nitrite (2.75 mL, 20.5 mmol) was added dropwise, forming a dark red precipitate after several minutes. The mixture was stirred for 2 h before the resulting tan-colored precipitate was cooled on ice and filtered. The filter cake was not allowed to dry fully (diazo salts are known to be potentially explosive!), and it was rinsed with a small amount of THF. The filter cake was transferred to a 250 mL round-bottom flask with diglyme (50 mL) and N-Boc pyrrole (2.5 mL, 15.0 mmol). A reflux condenser was attached and the reaction was placed in the oil bath at 50°C. The heat was increased to 120°C, at which temperature the elimination of CO₂ and N₂ was vigorous. After bubbling had ceased (~15 min.) the diglyme was removed by rotary evaporator and the crude was purified by flash chromatography (5 cm x 6 cm silica gel, eluted with 20% EtOAc/hexanes). **3b** was obtained as an orange, glassy solid. Yield = 61%. Spectral data matches that recently reported in the literature.³

b) Synthesis of azabicycle **3c**:

³ Hodgson, D. M.; Willis, P.; Bebbington, M. W. P. *Org. Lett.* **2002**, 4, 4353.

1,2-Dibromo-4,5-difluorobenzene (0.75 g, 2.78 mmol) and N-Boc pyrrole (0.56 g, 3.36 mmol) were added to a flame-dried 100 mL round-bottom flask with stir bar. The flask was sealed under nitrogen and distilled toluene (10 mL) was added. The solution was cooled to -78°C before *n*-BuLi (1.6 M in hexanes, 1.72 mL) was added dropwise. The reaction was removed from the cooling bath and stirred for ~18 h at room temperature. The reaction was then quenched by adding water (10 mL). The layers were separated and the aqueous portion was extracted with EtOAc (4 x 10 mL). The organics were dried over MgSO₄, filtered, and evaporated down to a brown oil. The crude was purified by flash chromatography (4 cm x 12 cm silica gel, eluted with 5% EtOAc/hexanes) to give a pale yellow solid. Yield = 42%. Spectral data matches that recently reported in the literature.³

c) General procedure for the ring opening of oxabicyclic alkenes: preparation of compound **2ab**.

Oxabicycle **1a** (50 mg, 0.347 mmol), 4-bromophenylboronic acid (84 mg, 0.418 mmol, 1.2 eq.), and (bis-1,3-diphenylphosphinopropane)palladium (II) dichloride (2.0 mg, 0.0034 mmol, 0.01 eq.) were added to a 1-dram vial with stir bar. The vial was sealed with a septum and flushed with nitrogen. Methanol (2 mL) was added by syringe, followed by the addition of a saturated aqueous solution of Cs₂CO₃ (~5M, 0.069 mL, 1 eq.). The flask was stirred at room temperature for 4 h. TLC analysis (25% EtOAc/hexanes) indicated that reaction was complete. The reaction was adsorbed onto a minimum amount of silica gel (neutralized with NEt₃) and purified by flash column (~3/4" x 6" silica gel, eluted with 2-15% EtOAc/hexanes + 0.5% NEt₃). Yield = 83%.

d) General procedure for the ring opening of azabicyclic alkenes: preparation of compound **4aa**.

Azabicyclic **3a** (5 g, 20.55 mmol), phenylboronic acid (3.76 g, 30.84 mmol, 1.5 eq.), and (bis-1,3-diphenylphosphinopropane)palladium(II)dichloride (0.121 g, 0.205 mmol, 0.01 eq.) were added to a 250 mL round-bottom flask with stir bar. The flask was sealed with a septum and evacuated/flushed with nitrogen three times. Methanol (75 mL) was added by syringe, followed by saturated aqueous solution of Cs_2CO_3 (~5M, 4.1 mL, 1 eq.). The flask was put in an oil bath at 60°C and the reaction was heated for 1.5 h. NMR analysis indicated that reaction was complete. The reaction was adsorbed onto a minimum amount of silica gel and purified by flash column (~4" x 6" silica gel, eluted with 2-10% EtOAc/hexanes). Yield = 98%.

e) Screening of solvents and ligands in the asymmetric ring opening of oxabicyclic **1a** with PhB(OH)_2 (Table 1 of paper).

Reactions were performed in parallel in 1-dram vials with 25 mg of **1a**. The reactions were worked up by transferring the reaction solutions (usually 0.5 mL) onto small glass columns (~1" diameter) packed with silica gel (~2"). The columns were rapidly eluted with 20% EtOAc/hexanes to remove any catalyst and elute all starting material and products. The resulting solutions were evaporated and redissolved with 5% isopropanol/hexanes for HPLC analysis. Conditions: Chiracel OD, 1 mL/min., 5% isopropanol/hexanes. Enantiomers of **2aa** at 10.6, 17.9 minutes, starting material **1a** at 11.2 minutes. Conversion was measured at $\lambda = 205$ nm by taking the ratio of areas of products to starting material, and multiplying by 0.96 (correction factor calculated from a known mixture of product and starting material).

3. Additional Experimental Data

Table 1. Initial Ligand Screening. Pd(II)-catalyzed asymmetric ring opening of **1a** with PhB(OH)₂

entry	ligand	<i>ee</i> (%) ^b	conversion (%) ^b
1	none	-	-
2	PPh ₃ (0.11 eq.) ^d	-	-
3	PPF-P(t-Bu) ₂	13	>95
4	PPF-P(t-Bu) ₂ (no base) ^e	6	5
5	MOP	42	27
6	Chiraphos	17	39
7	Me-DuPhos	74	59
8	t-Bu-POX	70	25
9	i-Pr-DIPOF	40	30
10	BINAP	63	87
11	Tol-BINAP	67	>95

^a Protocol: Pd(CH₃CN)₂Cl₂ (2.2 mg, 0.05 eq.) and ligand (0.055 eq.) were added to a 1-dram vial with stir bar. The vial was sealed with a 14mm septum and flushed with N₂ before THF (0.5 mL) was added. The resulting solution/suspension was stirred for ~40 min. before a solution of oxabicyclic **1** (25 mg, 1 eq.) and PhB(OH)₂ (26 mg, 1.2 eq.) was added by syringe from a sealed vial with THF (0.5 mL total). Finally, Cs₂CO₃ solution (5M in H₂O, 35 μL, 1 eq.) was added.^b Measured by chiral HPLC. ^c As measured by chiral HPLC^a MeOH was used as solvent. ^d Water was added to this reaction (35 μL).

Table 2. Ligand Screening: Racemic ring opening of azabicycle **3a**.

entry	ligand	conversion (%) ^b
1	DPPE ^c	0
2	DPPP ^d	39 (100 after 24 h)
3	DPPB ^e	trace
4	BIPHEP ^f	8
5	DPPF ^g	0
6	PPh ₃ ^h	0 (24 after 27 h at 60°C)

^a Protocol: Same as Table 1. ^b As measured by NMR. ^c 1,2-bis(diphenylphosphino)ethane. ^d 1,2-bis(diphenylphosphino)propane. ^e 1,2-bis(diphenylphosphino)butane. ^f 2,2'-bis(diphenylphosphino)-1,1'-biphenyl. ^g 1,1'-bis(diphenylphosphino)ferrocene. ^h Pre-formed Pd(PPh₃)₂Cl₂ was used

4. Characterization of new products

Relative configurations of the products in this paper have been assigned by analogy to similar compounds for which x-ray structures have been obtained.⁴

All of the following products were isolated from reactions with 50 mg of oxabicyclic starting material.

(1S*, 2R*)-1,2-Dihydro-2-(4-bromophenyl)-1-naphthol (2ab):

Purified by flash column chromatography (~3/4" x 6" silica gel, pre-adsorbed crude on silica gel (neutralized w/ NEt₃), eluted with 2-15 % EtOAc/hexanes + 0.5% NEt₃). Yield = 83%. White solid, m.p. = 113-114°C. *R_f* = 0.36 (25% EtOAc/hexanes); IR (film) ν = 3543, 3419 (br), 3032, 2893, 1485, 1452, 1407, 1189, 1074, 1011, 837, 300 (d), 765 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40 (2H, dm, *J* = 8.4 Hz), 7.33-7.21 (3H, m), 7.11 (2H, dm, *J* = 8.4 Hz), 6.69 (1H, dd, *J* = 9.5, 1.8 Hz), 6.05 (1H, dd, *J* = 9.5, 4.0 Hz), 4.88 (1H, s), 3.78 (1H, ddd, *J* = 6.0, 4.0, 2.2 Hz), 1.51 (1H, s); ¹³C (100 MHz, CDCl₃) δ 137.0, 136.0, 132.5, 131.7, 131.1, 129.3, 128.6, 128.5, 128.3, 126.7, 126.6, 121.4, 71.3, 46.9; HRMS calc. for C₁₆H₁₃BrO: 300.0150, found 300.0155.

(1S*, 2R*)-1,2-Dihydro-2-(2-methoxyphenyl)-1-naphthol (2ac):

Purified by flash column chromatography (~3/4" x 4" silica gel, pre-adsorbed crude on silica gel (neutralized w/ NEt₃), eluted with 2-12 % EtOAc/hexanes + 0.5% NEt₃). Yield = 74%. White solid, m.p. = 91-92°C. *R_f* = 0.25 (25% EtOAc/hexanes); IR (film) ν = 3531, 3447 (br), 3031, 2936, 2835, 1599, 1585, 1492, 1461, 1437, 1290, 1242, 1109, 1072, 1052, 1028, 988, 836, 817, 789, 754, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35 (1H, dm, *J* = 7.3 Hz), 7.30-7.20 (4H, m), 7.16 (1H, dm, *J* = 7.3 Hz), 6.92 (1H, dm, *J* = 7.2 Hz), 6.90 (1H, dm, *J* = 8.1 Hz), 6.70 (1H, dd, *J* = 9.9, 2.6 Hz), 6.04 (1H, dd, *J* = 9.9, 3.3 Hz), 4.90 (1H, d, *J* = 5.5 Hz), 4.41 (1H, ddd, *J* = 5.5, 2.9, 2.9 Hz), 3.84 (3H, s); ¹³C (100 MHz, CDCl₃) δ 157.4, 135.9, 132.5, 130.2, 129.9, 128.40, 128.36,

⁴ a) Cheng, C.-H.; Duan, J.-P. *Organometallics* **1995**, *14*, 1608.

b) Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, *4*, 1311.

128.2, 127.9, 127.6, 126.9, 126.5, 121.0, 110.6, 70.1, 55.6, 40.4 ; HRMS calc. for C₁₇H₁₆O₂: 252.1150, found 252.1161.

(1S*, 2R*)-1,2-Dihydro-2-(3-methoxyphenyl)-1-naphthol

(2ad): Purified by flash column chromatography (~3/4" x 4" silica gel, pre-adsorbed crude on silica gel (neutralized w/ NEt₃), eluted with 2-20% EtOAc/hexanes + 0.5% NEt₃). Yield = 86%.

Colourless oil. R_f = 0.27 (25% EtOAc/hexanes); IR (film) ν = 3441 (br), 3031, 2936, 2833, 1600, 1583, 1486, 1452, 1465, 1436, 1379, 1315, 1256, 1153, 1073, 1049, 992, 860.5 (d), 818, 777 (d), 708 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.35 (1H, dm, J = 7.3 Hz), 7.30-7.20 (4H, m), 7.16 (1H, dm, J = 7.3 Hz), 6.92 (1H, dm, J = 7.2 Hz), 6.90 (1H, dm, J = 8.1 Hz), 6.70 (1H, dd, J = 9.9, 2.6 Hz), 6.04 (1H, dd, J = 9.9, 3.3 Hz), 4.90 (1H, d, J = 5.5 Hz), 4.41 (1H, ddd, J = 5.5, 2.9, 2.9 Hz), 3.84 (3H, s); ¹³C (75 MHz, CDCl₃) δ 159.9, 139.5, 136.2, 132.7, 129.7, 128.4, 128.3, 128.1, 126.8, 126.4, 121.6, 114.9, 112.9, 71.3, 55.2, 47.5; HRMS calc. for C₁₇H₁₆O₂: 252.1150, found 252.1148.

(1R*, 2R*)-1,2-Dihydro-2-(2-acetylphenyl)-1-naphthol (2ae):

Note: This compound was isolated as hemiketal 2ae2. Purified by flash column chromatography (~3/4" x 5" silica gel, pre-adsorbed crude on silica gel (neutralized w/ NEt₃), eluted with 2-25 %

EtOAc/hexanes + 0.5% NEt₃). Yield = 83%. Colourless oil. R_f = 0.24

(25% EtOAc/hexanes); IR (film) ν = 3382 (br), 3031, 1603, 1490, 1454, 1377, 1206, 1159, 1125, 1106, 1082, 1036, 994, 961, 922, 910,

838, 772, 723 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.35 (1H, dm, J = 7.3 Hz), 7.30-7.20 (4H, m), 7.16 (1H, dm, J = 7.3 Hz), 6.92 (1H, dm, J = 7.2 Hz), 6.90 (1H, dm, J = 8.1 Hz), 6.70 (1H, dd, J = 9.9, 2.6 Hz), 6.04 (1H, dd, J = 9.9, 3.3 Hz), 4.90 (1H, d, J = 5.5 Hz), 4.41 (1H, ddd, J = 5.5, 2.9, 2.9 Hz), 3.84 (3H, s), 2.90 (1H, s, br); ¹³C (75 MHz, CDCl₃) δ 137.7, 134.7, 133.6, 132.3, 130.6, 130.0, 129.4, 128.8, 128.7, 127.9, 127.3, 126.9, 126.42, 126.35, 96.1, 66.8, 38.8, 30.2; HRMS calc. for C₁₈H₁₆O₂: 264.1150, found 264.1148.

(1S, 2R)-1,2-Dihydro-2-(3-furanyl)-1-naphthol (2af): Note:

compound is light-sensitive, especially in non-polar solvents. Purified

by flash column chromatography (~3/4" x 5" silica gel, pre-adsorbed

crude on silica gel (neutralized w/ NEt₃), eluted with 2-15 % EtOAc/hexanes + 0.5% NEt₃).

Yield = 82%. Pale yellow oil. R_f = 0.29 (25% EtOAc/hexanes); IR (film) ν = 3423 (br),

3033, 2905, 1499, 1484, 1452, 1380, 1189, 1157, 1065, 1027, 993, 873, 824, 787, 700 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.35 (1H, dm, J = 7.3 Hz), 7.30-7.20 (4H, m), 7.16 (1H, dm, J = 7.3 Hz), 6.92 (1H, dm, J = 7.2 Hz), 6.90 (1H, dm, J = 8.1 Hz), 6.70 (1H, dd, J = 9.9, 2.6 Hz), 6.04 (1H, dd, J = 9.9, 3.3 Hz), 4.90 (1H, d, J = 5.5 Hz), 4.41 (1H, ddd, J = 5.5, 2.9, 2.9 Hz), 3.84 (3H, s); ¹³C (100 MHz, CDCl₃) δ 143.4, 140.9, 136.7, 132.6, 129.3, 128.3, 128.1, 128.0, 126.4, 126.3, 121.3, 111.0, 70.6, 38.2; HRMS calc. for C₁₄H₁₂O₂: 212.0837, found 212.0842.

Assay of enantiomeric excess: chiral HPLC (Chiracel OD, 5% isopropanol/hexanes, 1

mL/min, λ = 254 nm; t_r (major) = 14.8 min., t_r (minor) = 10.3 min.), 71% ee. $[\alpha]_D^{20}$ = +120 (c = 1.03, CHCl₃, measured with a sample of 68% ee.)⁵

Note: The carbamates listed below usually show minor peaks corresponding to minor rotamers in solution- the peaks coalesce at elevated temperatures. Unless otherwise noted, all products were isolated from reactions with 100 mg of azabicyclo starting material.

(1S*, 2R*)-[1,2-Dihydro-2-phenyl-naphthalen-1-yl]-carbamic acid

tert-butyl ester (4aa): Reaction was performed with 5 g of substrate.

Purified by flash column chromatography (~4" x 6" silica gel,

adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes).

Yield = 98%. White solid, m.p. = 84-86°C. R_f = 0.29 (10% EtOAc/hexanes); IR (film) ν =

3427, 2976, 1717, 1493, 1451, 1365, 1237, 1167, 1055, 755, 702 cm⁻¹; ¹H NMR (300 MHz,

CDCl₃) δ 7.27-7.05 (9H, m), 6.67 (1H, dd, J = 9.9, 1.6 Hz), 6.12 (1H, dd, J = 9.6, 4.9 Hz),

5.30 (1H, dd, J = 10.5, 7.7 Hz), 4.53 (1H, d, J = 10.1 Hz), 3.85 (1H, dd, 7.5, 5.8 Hz), 1.39

(9H, s); ¹³C (75 MHz, CDCl₃) δ 155.5, 137.7, 134.9, 133.5, 130.5, 129.2, 128.5, 128.4,

⁵ The absolute configuration of **2af** is assumed based on a comparison with the same product obtained from a Rh-catalyzed reaction, for which an analogous product has been characterized by x-ray. Lautens, M.; Dockendorff, C.; Fagnou, K.; Malicki, A. *Org. Lett.* **2002**, 4, 1311.

128.2, 127.8, 127.3, 126.5, 125.6, 79.5, 52.4, 44.9, 28.5; HRMS calc. for $C_{21}H_{23}NO_2Na$ (ESI): 344.1621, found 344.1629.

(1S*, 2R*)-[(1,2-Dihydro-6,7-dimethoxy-2-phenyl-naphthalen-1-yl)]-carbamic acid *tert*-butyl ester (4ba): Purified by flash column chromatography (~3/4" x 7" silica gel, adsorbed crude on silica gel, eluted with 2-20 % EtOAc/hexanes). Yield = 79%.

White solid, m.p.= 148-149°C. R_f = 0.25 (25% EtOAc/hexanes); IR (film) ν = 3440, 2932, 1714, 1604, 1513 (d), 1367, 1274, 1235, 1166, 1118, 1055, 867 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.30-7.20 (3H, m), 7.18-7.11 (2H, m), 6.76 (1H, s), 6.70 (1H, s), 6.58 (1H, dd, J = 9.7, 1.5 Hz), 6.03 (1H, dd, J = 9.7, 4.7 Hz), 5.18 (1H, dd, J = 9.7, 7.0 Hz), 4.56 (1H, d, J = 10.3 Hz), 3.90 (3H, s), 3.85 (3H, s), 1.37 (9H, s); ^{13}C (75 MHz, $CDCl_3$) δ 155.4, 148.7, 148.3, 138.3, 129.2, 128.5, 127.9, 127.6, 127.2, 126.1, 110.1, 109.8, 79.4, 56.1, 52.3, 45.0, 28.4; HRMS calc. for $C_{23}H_{27}NO_4$: 381.1940, found 381.1949.

(1S*, 2R*)-[(6,7-Difluoro-1,2-dihydro-2-phenyl-naphthalen-1-yl)]-carbamic acid *tert*-butyl ester (4ca): Purified by flash column chromatography (~3/4" x 5" silica gel, adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes). Yield = 91%. White solid,

m.p.= 93-94°C. R_f = 0.19 (10% Et_2O /hexanes); IR (film) ν = 3435, 2978, 1713, 1600, 1505, 1367, 1310, 1241, 1166, 1053, 882, 785, 762, 702 cm^{-1} ; 1H NMR (300 MHz, $CDCl_3$) δ 7.28-7.20 (3H, m), 7.10-6.90 (4H, m), 6.57 (1H, d, J = 9.9 Hz), 6.16 (1H, dd, J = 9.6, 5.2 Hz), 5.29 (1H, dd, J = 10.2, 8.5 Hz), 4.47 (1H, d, J = 10.2 Hz), 3.80 (1H, dd, 7.5, 6.0 Hz), 1.42 (9H, s); ^{13}C (75 MHz, $CDCl_3$) δ 151.6, 151.4, 148.25, 148.08, 136.5, 131.34, 131.31, 129.1, 128.7, 127.7, 126.61, 126.59, 126.56, 115.3, 115.1, 80.0, 51.8, 44.2, 28.4; ^{19}F (376 MHz, $CDCl_3$) δ -138.2 (1F, m), -140.6 (1F, m); HRMS calc. for $C_{21}H_{21}F_2NO_2$: 357.1540, found 357.1540.

(1S*, 2R*)-[1,2-Dihydro-2-(2-methylphenyl)-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4ab): Purified by flash column chromatography (~3/4" x 4" silica gel, adsorbed crude on silica gel,

eluted with 2-10 % EtOAc/hexanes). Yield = 92%. White solid, m.p.= 149-153°C. R_f = 0.24 (10% EtOAc/hexanes); IR (film) ν = 3435, 2975, 1717, 1495, 1366, 1245, 1229, 1168, 1055, 861, 778, 764, 752, 728 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.30-7.00 (8H, m), 6.67 (1H, dd, J = 9.9, 1.9 Hz), 6.08 (1H, dd, J = 9.6, 4.1 Hz), 5.27 (1H, dd, J = 10.2, 7.1 Hz), 4.64 (1H, d, J = 9.9 Hz), 4.20 (1H, m), 2.42 (3H, s), 1.31 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 155.2, 136.85, 136.82, 134.9, 133.1, 131.1, 130.5, 128.7, 128.3, 128.2, 128.0, 127.1, 126.5, 126.2, 79.4, 51.0, 40.8, 28.4, 19.9; HRMS calc. for $\text{C}_{22}\text{H}_{25}\text{NO}_2$: 335.1885, found 335.1894.

(1S*, 2R*)-[2-(2-Chlorophenyl)-1,2-dihydro-naphthalen-1-yl]-

carbamic acid *tert*-butyl ester (4ac): Purified by flash column

chromatography (~2/3" x 7" silica gel, adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes). Yield = 84%. Colourless oil/white foam. R_f = 0.35 (15% EtOAc/hexanes); IR (film) ν = 3413, 2970, 2918, 1717, 1700, 1558, 1540, 1490, 1364, 1244 (br), 1165, 1051 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.42-7.35 (1H, m), 7.34-7.07 (7H, m), 6.70 (1H, dd, J = 9.6, 2.2 Hz), 6.05 (1H, dd, J = 9.6, 3.8 Hz), 5.30 (1H, dd, J = 10.2, 6.6 Hz), 4.64 (1H, d, J = 10.4 Hz), 4.54 (1H, m), 1.28 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 154.9, 136.6, 134.9, 134.6, 132.7, 130.2, 129.6, 129.6, 128.9, 128.4, 128.2, 127.1, 126.8, 126.6, 79.3, 50.5, 41.9, 28.4; HRMS calc. for $\text{C}_{21}\text{H}_{22}\text{O}_2\text{NCl}$: 299.0713, found 299.0721.

(1S*, 2R*)-[1,2-Dihydro-2-(2-methoxyphenyl)-naphthalen-1-yl]-

carbamic acid *tert*-butyl ester (4ad): Purified by flash column

chromatography (~3/4" x 5" silica gel, adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes). Yield = 93%. White solid, m.p.= 139-141°C. IR (film) ν = 3432, 2975, 1716, 1494, 1366, 1244, 1167, 1054, 1030, 754 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.32-7.00 (6H, m), 6.90-6.76 (2H, m), 6.65 (1H, dd, J = 9.9, 2.2 Hz), 6.06 (1H, dd, J = 9.6, 3.9 Hz), 5.22 (1H, dd, J = 9.9, 6.9 Hz), 4.76 (1H, d, J = 10.2 Hz), 4.47 (1H, m), 3.83 (3H, s), 1.29 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 157.6, 155.2, 135.3, 133.0, 130.7, 129.6, 128.3, 128.2, 128.0, 127.8, 127.0, 126.9, 126.3, 120.5, 110.4, 78.9, 55.6, 51.0, 38.0, 28.4; HRMS calc. for $\text{C}_{22}\text{H}_{25}\text{NO}_3$: 351.1834, found 351.1825.

(1S*, 2R*)-[2-(4-Chlorophenyl)-1,2-dihydro-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4ae): Purified by flash column chromatography (~3/4" x 5" silica gel, adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes). Yield = 93%. White

solid, m.p.= 111-115°C. R_f = 0.22 (10% EtOAc/hexanes); IR (film) ν = 3427, 2976, 1717, 1488, 1366, 1238, 1167, 1092, 1055, 1015, 838, 795, 773 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.30-7.10 (6H, m), 7.09-6.97 (2H, d, J = 8.2), 6.68 (1H, d, J = 9.6 Hz), 6.09 (1H, dd, J = 9.6, 4.9 Hz), 5.28 (1H, dd, J = 9.9, 7.4 Hz), 4.50 (1H, d, J = 10.2 Hz), 3.85 (1H, dd, 7.5, 5.5 Hz), 1.40 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 155.4, 136.2, 134.4, 133.3, 133.2, 130.6, 130.0, 128.7, 128.6, 128.4, 128.0, 126.6, 125.6, 79.7, 52.3, 44.3, 28.5 ; HRMS calc. for $\text{C}_{17}\text{H}_{14}\text{NO}_2\text{Cl}$ (loss of C_4H_8): 299.0713, found 299.0704.

(1S*, 2R*)-[2-(4-Acetylphenyl)-1,2-dihydro-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4af): Purified by flash column chromatography (~3/4" x 6" silica gel, adsorbed crude on silica gel, eluted with 2-15 % EtOAc/hexanes). Yield = 92%.

White solid, m.p.= 134-135°C. R_f = 0.31 (25% EtOAc/hexanes); IR (film) ν = 3345, 2977, 1710, 1682, 1606, 1494, 1364, 1268, 1166, 1055, 1016, 776 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 7.82 (2H, d, J = 8.1 Hz), 7.30-7.18 (5H, m), 7.15 (1H, d, J = 7.0 Hz), 6.71 (1H, dd, J = 9.9, 1.5 Hz), 6.10 (1H, dd, J = 9.5, 4.8 Hz), 5.30 (1H, dd, J = 10.3, 7.3 Hz), 4.59 (1H, d, J = 10.3 Hz), 3.95 (1H, dd, 7.0, 5.5 Hz), 2.52 (3H, s), 1.38 (9H, s); ^{13}C (100 MHz, CDCl_3) δ 197.7, 155.3, 143.7, 136.2, 134.4, 133.1, 129.5, 129.4, 128.9, 128.5, 128.4, 128.0, 126.6, 125.7, 79.6, 52.3, 44.9, 28.3, 26.6 ; HRMS calc. for $\text{C}_{23}\text{H}_{25}\text{NO}_3\text{Na}$ (ESI): 386.1726, found 386.1716.

(1S*, 2R*)-[1,2-dihydro-2-(4-(N, N-dimethylaminophenyl)-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4ag): Purified by flash column chromatography (~3/4" x 7" silica gel, adsorbed crude on silica gel, eluted with 2-10 %

EtOAc/hexanes). Yield = 71%. Colourless oil/white foam. R_f = 0.36 (25% EtOAc/hexanes); IR (film) ν = 3434, 2976, 1716, 1612, 1520, 1494, 1365, 1232, 1167, 1054, 946, 778 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 7.25-7.07 (4H, m), 6.91 (2H, dm, J = 8.8 Hz), 6.61 (1H, d, J = 9.5 Hz), 6.57 (2H, dm, J = 8.8 Hz), 6.11 (1H, dd, J = 9.5, 5.5 Hz), 5.30 (1H, dd, J = 10.2, 7.5 Hz), 4.55 (1H, d, J = 9.9 Hz), 3.71 (1H, dd, 7.6, 6.2 Hz), 2.86 (6H, s), 1.44 (9H, s); ^{13}C (100 MHz, CDCl_3) δ 155.8, 150.0, 135.1, 133.8, 131.4, 129.9, 128.0, 127.6, 127.5, 126.2, 125.1, 124.5, 112.7, 79.4, 52.5, 43.8, 40.6, 28.5, 22.7; HRMS calc. for $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}_2$ ($M+1$): 365.2223, found 365.2211.

(1S*, 2R*)-[1,2-Dihydro-2-(3-furanyl)-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4ah): Purified by flash column chromatography (~3/4" x 5" silica gel, adsorbed crude on silica gel, eluted with 2-10 % EtOAc/hexanes). Yield = 94%. Colourless oil. R_f = 0.40 (10%

Et_2O /hexanes); IR (film) ν = 3423, 2977, 1715, 1497, 1366, 1244, 1167, 1056, 1028, 873, 787 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.28-7.19 (5H, m), 7.14-7.08 (1H, m), 6.58 (1H, dd, J = 9.6, 1.1 Hz), 6.07 (1H, dd, J = 9.6, 5.2 Hz), 6.01 (1H, m), 5.22 (1H, dd, J = 10.1, 6.9 Hz), 4.73 (1H, d, J = 9.9 Hz), 3.72 (1H, dd, 7.2, 5.5 Hz), 1.45 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 155.7, 143.2, 140.5, 135.2, 133.3, 129.9, 128.2, 128.1, 127.8, 126.5, 125.4, 121.6, 110.8, 79.7, 51.7, 35.8, 28.5; HRMS calc. for $\text{C}_{19}\text{H}_{21}\text{NO}_3$: 311.1521, found 311.1530.

(1S*, 2R*)-[1,2-Dihydro-2-(thiophen-3-yl)-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4ai): Reaction was performed with 5 g of substrate. Purified by flash column chromatography (~4" x 6" silica gel, adsorbed crude on silica gel, eluted with 2-10 %

EtOAc/hexanes). Yield = 99%. Colourless oil. R_f = 0.22 (10% Et_2O /hexanes); IR (film) ν = 3429, 2976, 1715, 1496, 1366, 1232, 1168, 1055, 854, 780 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.27-7.10 (5H, m), 6.97 (1H, ddd, J = 3.0, 1.4, 0.6 Hz), 6.74 (1H, dd, J = 4.9, 1.4 Hz), 6.61 (1H, dd, J = 9.6, 1.4 Hz), 6.14 (1H, dd, J = 9.6, 5.2 Hz), 5.28 (1H, dd, J = 10.1, 7.4 Hz), 4.62 (1H, d, J = 9.9 Hz), 3.95 (1H, dd, 7.2, 5.5 Hz), 1.44 (9H, s); ^{13}C (75 MHz, CDCl_3) δ 155.7, 138.3, 135.1, 133.4, 130.4, 128.21, 128.18, 128.0, 127.8, 126.5, 125.8, 125.4, 122.9, 79.7, 52.1, 40.3, 28.5; HRMS calc. for $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{S}$: 327.1293, found 327.1309.

(1S*, 2R*)-[2-(1-Benzenesulfonyl-1H-indol-3-yl)-1,2-dihydro-2-naphthalen-1-yl]-carbamic acid *tert*-butyl ester (4aj):

Purified by flash column chromatography (~3/4" x 7" silica gel, adsorbed crude on silica gel, eluted with 2-10 %

EtOAc/hexanes). Yield = 99%. White solid, m.p.= 80-83°C. IR (film) ν = 3432, 2977, 2362, 1710, 1498, 1448, 1367, 1175, 1122, 1095, 1055, 985, 910, 728 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.98 (1H, d, J = 8.1 Hz), 7.70 (2H, d, J = 7.8 Hz), 7.53 (2H, m), 7.44-7.18 (9H, m), 6.75 (1H, d, J = 9.5 Hz), 6.17 (1H, dd, J = 9.5, 5.1 Hz), 5.44 (1H, dd, J = 9.8, 6.8 Hz), 4.62 (1H, d, J = 10.3 Hz), 4.19 (1H, dd, 7.1, 5.4 Hz), 1.42 (9H, s); ^{13}C (126 MHz, CDCl_3) δ 155.3, 137.9, 135.3, 134.6, 133.7, 133.1, 130.9, 129.4, 129.2, 128.5, 128.1, 127.9, 126.7, 126.6, 125.31, 125.25, 124.9, 123.3, 120.1, 119.0, 113.7, 79.7, 52.4, 35.9, 28.4 ; HRMS calc. for $\text{C}_{25}\text{H}_{20}\text{N}_2\text{O}_4\text{S}$ (loss of C_4H_8): 444.1144, found 444.1146.