Catalytic Asymmetric Hydroboration/Amination and Alkylamination with Rhodium Complexes of 1,1′-(2-Diarylphosphino-1-naphthyl)isoquinoline

Elena Fernandez, Kenji Maeda, Mark W. Hooper, and John M. Brown*[a]

Abstract: Catecholboronate esters formed by asymmetric hydroboration of arylalkenes are not directly converted to amines by reaction with hydroxylamine-*O*-sulfonic acid. Prior conversion to a trialkylborane by reaction with $ZnEt_2$ or MeMgCl permits a subsequent amination reaction to occur with essentially complete retention of configuration, leading to a range of primary α-arylalkylamines in up to 97% enantiomeric excess (*ee*). Secondary, but not tertiary amines may be formed by a related pathway when in situ generated alkylchloramines are employed as the aminating agent. The catalytic asymmetric hydroboration, β-alkylation and amination steps may be combined in a single stage. Overall, this provides a practical procedure for the synthesis of enantiomerically enriched arylamines, exemplified inter alia by the synthesis of (*S*)-1,2,3,4-tetrahydro-1-naphthylamine in 95–97% *ee* and of (*R*)-*N*-(cyclohexyl)-1′-(4-methoxyphenyl)ethylamine in 93% *ee*.

Keywords: aminations · homogeneous catalysts · hydroborations · rhodium · vinylarenes

Introduction

The catalytic asymmetric synthesis of amines may be accomplished in several ways.[1] In defining methods for the synthesis of simple monofunctional amines[2] in which the C–N bond is created in the enantioselective step, the reduction of imines has proved to be the most widely employed approach. This can be accomplished by hydrogenation, for which iridium catalysts have proved superior; a large-scale herbicide synthesis is carried out in this way.[3] Transfer hydrogenation is an equally promising alternative, and the ruthenium catalysts developed by Noyori and colleagues provide excellent examples.[4] Although the hydrosilylation and other reductive reactions of imines are less intensively developed, they offer potentially viable alternatives.[5] Several recent studies have been concerned with the catalysis of the allylation of imines, which may be achieved in up to 99% *ee*.[6]

By contrast, the direct catalytic addition of ammonia or an amine to alkenes is more difficult to achieve,[7] and efforts to effect this in an enantioselective reaction are only just beginning.[8] The same goal may, however, be achieved by a two-step reaction in which catalytic asymmetric hydroboration[9] is followed by an amination step such that the stereogenic carbon atom is transferred from boron to nitrogen. This procedure has good precedent in stoichiometric asymmetric hydroborations.[10] The stoichiometric reaction has been developed to the point where the chiral auxiliary may be recovered through its selective transfer in the reduction of acetaldehyde. This requires a multistep procedure; low-temperature recrystallisation of the hydroboration product is required for optimum *ee* (Scheme 1). A distinction from the stoichiometric reaction is that effective Rh-catalysed hydroborations of alkenes are limited to the addition of catecholborane,[11] whilst most stoichiometric asymmetric hydroboration reactions involve a dialkylborane.[12] The reactivity of alkylboranes in electrophilic aliphatic substitution is very dependent on the other substituents on the boron, with deactivation is the rule for O or N groups.

In a recent paper[13] we described attempts to optimise the direct amination of catecholboronate esters. Even under the best conditions with $ClMgN(Me)OSiMe_3$, the chemoselectivity was no better than 60% with respect to amine formation. This led to the appraisal of alternative approaches which bypassed the problem, and a simple solution was found when it was discovered that catechol could be cleanly displaced from the catecholboronate ester by nucleophilic alkylating agents, notably diethylzinc[14] or methylmagnesium chloride. The resulting trialkylborane could be converted into the desired benzylic amine with complete retention of configuration in the amination step.[15] Herein we provide a more detailed discussion of these earlier results as well as the extension to the asymmetric synthesis of secondary amines; tertiary amines still remain elusive.

[a] J. M. Brown, E. Fernandez, K. Maeda, M. W. Hooper
The Dyson Perrins Laboratory
South Parks Rd, Oxford OX1 3QY (UK)
Fax: (+44) 1865-275674
E-mail: john.brown§chemistry.oxford.ac.uk

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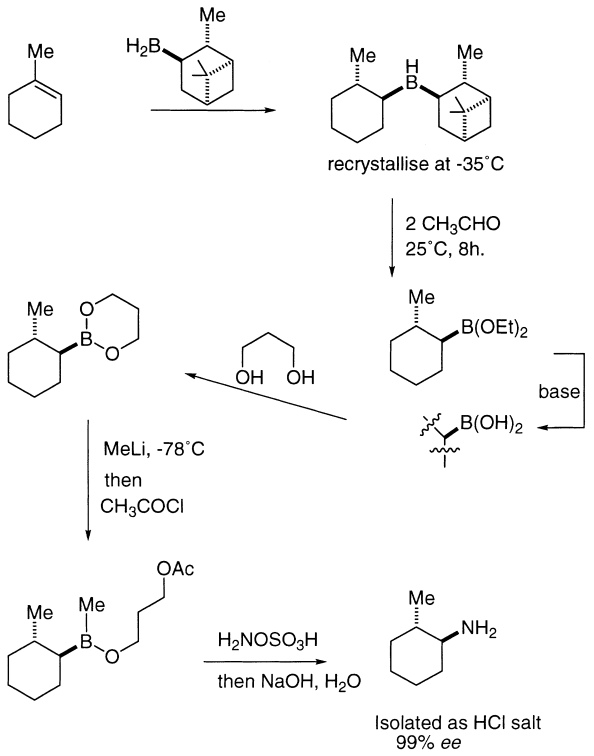


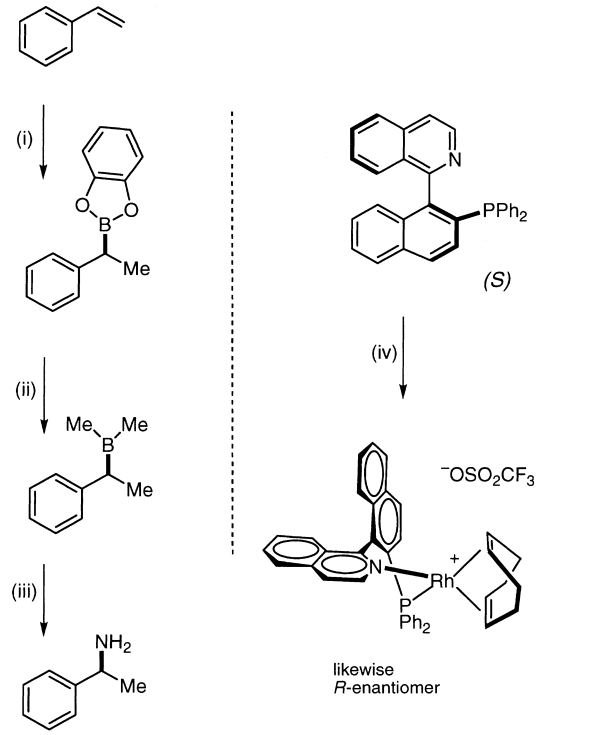
Scheme 1. Two-step enantioselective asymmetric synthesis of amines in which catalytic asymmetric hydroboration is followed by an amination reaction.

Results and Discussion

Primary amines: Given the very wide variety of transformations which can be achieved through alkene hydroboration, it is surprising that the vast majority of catalytic hydroborations have been applied to the formal synthesis of alcohols by means of oxidation of the initial adduct with hydroperoxide. The reason is not hard to find; compared to trialkylboranes, boronate esters are poor electrophiles and they cannot be made directly by catalytic routes. In an effort to extend the synthetic scope of our hydroboration procedure that employs Rh complexes of the P–N atropisomerically chiral QUINAP, we attempted a transmetallation from boron to zinc in the hope that the stereogenic centre would not be compromised in the process. That problem has now been addressed by Knochel and co-workers who have shown that the configuration of chiral organozinc compounds can be maintained under carefully defined conditions.[16] In our case, initial reaction of the catecholboronate ester in toluene with one equivalent of Et_2Zn led to the complete formation of the corresponding alkyldiethylborane, with concurrent formation of a dense white precipitate of zinc catecholate. No transmetallation was observed, and after this initial observation a precedent was found in Cabbidu's work where the reaction of primary alkyl catecholboronate esters with alkylmagnesium halides gave rise to good yields of alkylboranes (Scheme 2).[17]

The reaction pathway was monitored by ^{11}B NMR spectroscopy in THF. For the catecholboronate ester derived from 4-methoxystyrene in THF, a broad line was observed at $\delta =$ 35. On addition of an equivalent quantity of Et_2Zn and agitation, the spectrum changed to give a new broad line at $\delta = 80$. This is in agreement with expected literature values of $\delta = 32 \pm 3$ for $RB(OR')_2$ and 80 ± 3 for RBR'_2.[18] When the reaction was incomplete a peak at $\delta = 53$ was observed which could also be seen transiently in the course of successful reactions.

Having demonstrated a viable route from catecholboronate esters to trialkylboranes, a further point in favour of the stated objectives is the chemoselectivity of hydroboration/amination, a reaction which operates for only two of the three alkyl residues. Methyl or primary alkyl groups migrate with greater reluctance than more substituted alkyl groups.[19] Hence the substituted benzyl group was expected to be transformed into the corresponding amine on treatment with hydroxylamine-*O*-sulfonic acid. In preliminary experiments in which an isolated boronate ester was employed, this was indeed realised, and it was verified that the enantiomeric purity of the amine was identical, within experimental error, to that of the secondary alcohol produced by hydroperoxide oxidation (Scheme 2). Subsequent work involved the development of a one-pot reaction in which the catalytic hydroboration of the alkene, the B-alkylation step and the amination were all performed without isolation of the intermediate products. The results of these reactions are given in Table 1. For the most part, the reactions reported here were carried out on a 0.5 millimolar scale with 1 mol% catalyst. On a larger scale, the chemoselectivity towards the primary amine could be lower, and it was found for the case of 1,2-dihydronaphthalene that an improved yield could be achieved with NH_2Cl prepared in situ,[20] albeit with a slight lowering of the *ee* value (95%). The procedure affords access to the potentially



Scheme 2. Synthesis of primary amines. i) Catecholborane, 0.2–1% catalyst, 20°C, THF, 1 h; ii) MeMgCl (2 equiv, 3M in THF), 20°C, 30 min; iii) H_2NOSO_3H (3 equiv), THF, 10 h; iv) [(cod)Rh(acac)], $Me_3SiOSO_2CF_3$, THF then pentane.

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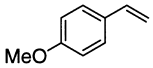
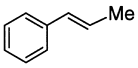
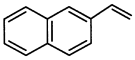
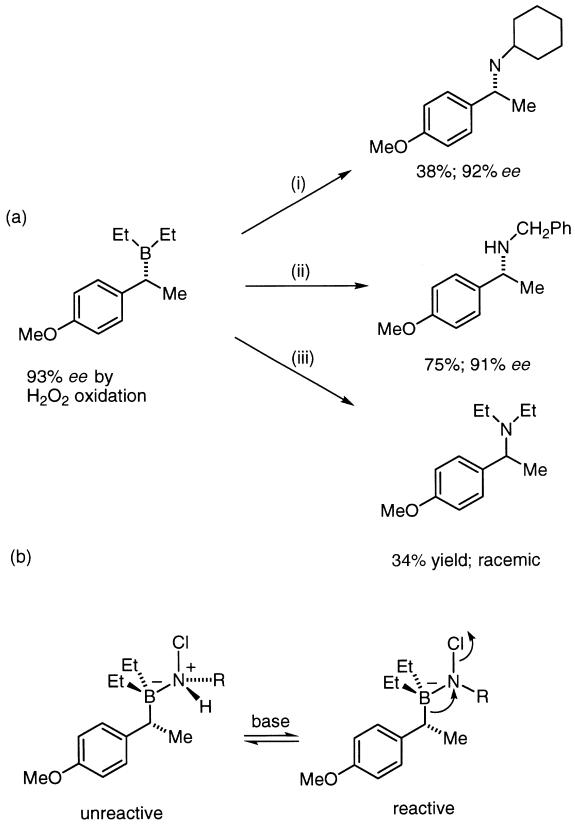
Table 1. Hydroboration/amination of vinylarenes.[a]

Entry	Reactant	Benzylic amine[b]	*ee* [%][c]	Configuration	Yield [%]
1		> 98	98[c]	*S*	56
2		> 98	87[c]	*S*	54
3		> 98	90[c]	*S*	50
4		> 98	77[c]	*S*	61
5		96	97[c]	*S*	51
6		98	89[c]	*S*	64
7		92	90[d]	*S*	62
8		75	68[d]	*S*	51
9		–	84[d]	*S*	54

[a] Reaction conditions: 2 h, ambient temperature, 1 mol% catalyst. [b] Remainder regioisomeric amine. [c] GC or NMR determination, see the Experimental Section. [d] Determination of *ee* by ^{1}H NMR spectroscopy with [Eu(hfc)$_3$].



Scheme 3. a) Synthesis of secondary amines from catecholboronate esters (i) $C_6H_{11}NHOSO_3H$, diglyme, 24 H; 20 °C; (ii) $PhCH_2NHCl$ (generated in situ from $PhCH_2NH_2$ and aq. NaOCl,), 0 °C, 5 min then 20 °C, 1 h; (iii) Et_2NHCl (generated in situ from Et_2NH and aq. NaOCl)). b) A simple mechanism which explains the lower effectiveness of chloroamines from secondary amines.

useful (*S*)-1-amino-1,2,3,4-tetrahydronaphthalene and related compounds.[21]

The reaction represents a simple and direct route from vinylarenes to the corresponding enantiomerically enriched α-alkylbenzylamines. The reaction is limited to alkenes of modest steric bulk as delineated in the previous paper.[11] It is apparent that 1-vinylnaphthalene approaches the limit in this respect since the *ee* is considerably reduced. Although (*S*)-QUINAP is used in the examples given in Table 1, both enantiomers of the ligand are available. Provided that the Et_2Zn or MeMgCl transmetallation procedure is compatible with substituents on the alkene, the range of reactants and the ensuing *ee* values are comparable with those obtained for secondary alcohols in the corresponding peroxide oxidations of catecholboronate esters.

Secondary amines: Following the successful demonstration of amination with hydroxylamine-*O*-sulfonic acid as the electrophile, extension of the reaction to the synthesis of secondary amines was considered. The simple expedient of direct reaction with the corresponding alkylhydroxylamine derivative (Scheme 3) was successful to some extent; however, the yield was modest, although the enantioselectivity was encouraging. Given the difficulty of preparing a pure sulfonic acid reagent[22] this approach was not developed further.

A more successful method involved the reaction with monochloralkylamines. These can be generated in situ by reaction of a solution of a primary or secondary amine in an organic solvent with commercial sodium hypochlorite solution[23] and used directly (c.f. the chloramine preparation above). A specific difference between monoalkyl and dialkyl chloramines was discovered. The reaction of trialkylboranes with $ClNEt_2$, verified as being formed cleanly by NMR spectroscopy, gave a range of products and more significantly the tertiary amine was formed with complete racemisation. This is in line with the radical reaction pathway first proposed by Davies, Roberts and co-workers; some of the side products may be formed by competing cationic routes.[24] In contrast, the chloramines formed from primary amines reacted cleanly and with retention of configuration to thus provide a viable synthetic route to enantiomerically enriched benzylic secondary amines. The implication is clear; in the alkyl migration step of Scheme 3 deprotonation of the N–H either precedes or is concurrent with C–N bond formation making the pathway impossible for a secondary chloramine. The successful method was demonstrated for the examples shown in Table 2; both the amine and the borane can be varied without detriment. Two alternative protocols were adapted. In the first of these (Method A1), hydroboration was carried out in toluene with 1 mol% catalyst followed by the direct addition of $ZnEt_2$ in C_7H_8 and subsequent reaction with preformed RNHCl in Et_2O. A fivefold scale-up procedure employed 0.2 mol% catalyst (Method A2). Alternatively, a similar sequence was followed in which the catecholboronate ester isolated first (Method B). Table 2 demonstrates that the nature of the primary amine can be varied without detriment.

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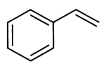
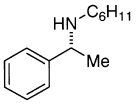
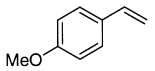
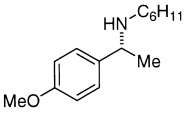
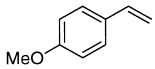
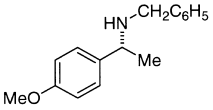
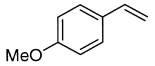
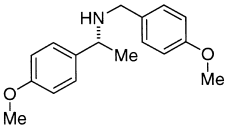
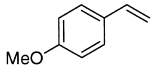
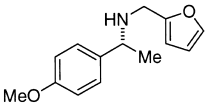
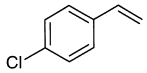
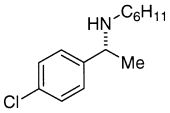
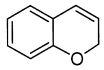
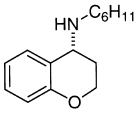
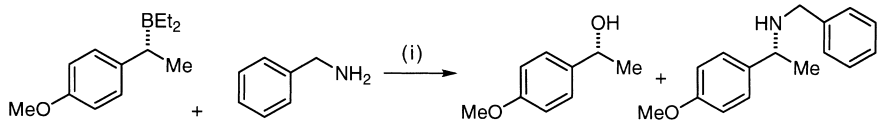
Table 2. Alkylaminations according to Scheme 2.

Entry	Reactant	Product	*ee* [%][a]	Yield [%]	Method[b]
1			87	71	A1
2			93 92	73 82	A2 B
3			91	75	B
4[c]			90 87	77 81	A2 B
5			91	76	B
6			78	50	A1
7			87	48	A1

[a] The enantiomeric purity of the (*R*)-product amine was determined by ^{1}H NMR spectroscopy ([D$_6$]acetone) in the presence of enantiomerically pure mandelic acid. [b] Method A1 (1 mol% catalyst) and Method A2 (0.2 mol% catalyst) refer to one-pot reactions. Method B refers to reactions of the pre-isolated catecholboronate according to the Experimental Section. [c] A small amount of the Schiff's base of *p*-methoxybenzaldehyde, formed in the amine chlorination step, was detected as a by-product.[26]

In the examples shown the chloramine was synthesised first and then reacted with the borane. It was of interest to determine whether chlorination could be performed in the presence of the borane—with the possibility of competing direct oxidation—thereby broadening the synthetic scope. It was found that both reactions occurred to give either the alcohol or the secondary amine, depending on the pathway. The chemoselectivity was strongly dependent on pH, and selective in favour of the amine only in acidic media (Scheme 4). This is in agreement with previous results which probe the pH stability of aqueous chloramine solutions.[25]



Scheme 4. i) Bleach solution added, buffered to the specified pH and precooled to 0 °C to the mixture of borane and amine in C_7H_8.

Experimental Section

General: Reactions were conducted under a dry argon atmosphere with standard vacuum line and Schlenk techniques. Reactions were carried out in solvents distilled from standard drying agents. Catecholborane (Aldrich) was distilled under reduced pressure before use. The complex [Rh(cod)-(QUINAP)]OSO_2CF_3,[11a, 27] was prepared in a similar manner to the reported procedure. All amines and alkenes except for 3,4-chromene were commercially available from Aldrich; 3,4-chromene was prepared by a literature procedure.[28] Enantiomerically pure (*R*)-1-(4-methoxyphenyl)-ethylamine was obtained from Lancaster Chemicals. Commercial bleach was used as the source of sodium hypochlorite after determination of its concentration by iodometric titration which was generally ≈2 M. All alkenes, except for 4-methoxystyrene, were distilled before use; all amines and 4-methoxystyrene were used without further purification. NMR Spectra were recorded on a Varian Gemini 200 and Bruker AM250 or AMX500 spectrometers. GC analyses were performed on a Fison 8000 chromatograph equipped with a Chrompack WCOT Fused Silica column, CP-Chirasil-DEX CB, 25 m, injector temperature 250 °C, detector temperature 275 °C, inlet pressure 2.90 psi.

Catalytic hydroboration/amination with catecholborane: **general procedure**: The freshly prepared complex (*S*)-[1-(2-diphenylphosphino-1-naphthyl)isoquinoline](cyclooctadiene)rhodium(I) trifluoromethanesulfonate (4.0 mg, 0.005 mmol, 1.0 mol%), THF (0.5 mL) and the alkene (0.5 mmol) were placed in a vial under argon. Freshly distilled catecholborane (53 μL, 59 mg, 0.5 mmol) was added with stirring and then left for 1 h. MeMgCl (3 M in THF, 333 μL, 1.0 mmol) was added and the solution stirred for 30 min. The reactant solution was added to pre-dried hydroxylamine-*O*-sulfonic acid (169 mg, 1.5 mmol) with THF (0.7 mL), and stirred under argon overnight. Hydrochloric acid (1 M, 2 mL) was added, and the mixture poured into water (4 mL). The aqueous layer was extracted with ether (3 × 20 mL), and then made strongly alkaline with sodium hydroxide (1 M, 3 mL). The mixture was extracted with diethyl ether (3 × 20 mL). The diethyl ether extracts were combined, dried ($MgSO_4$) and the solvent removed in vacuo.

In those cases in which GC analysis was employed, the amines were converted into their acetamides: primary amines (0.5 mmol) were dissolved in toluene (2 mL) and acetic acid (0.6 mmol) was added by syringe with an equivalent of 1,1′-carbonyl-diimidazole. The mixture was stirred vigorously overnight and then extracted with toluene. The organic extracts were washed with sodium hydroxide (1 M, 3 × 20 mL), dried ($MgSO_4$) and the solvent removed in vacuo.

***N*-Acetyl-1-phenylethylamine**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.21-7.39$ (m, 5H; Ar), 6.01 (brs, 1H; N–H), 5.13 (q, $^3J(H,H) = 7.4$ Hz, 1H), 1.97 (s, 3H; $COCH_3$), 1.49 (d, $^3J(H,H) = 7.4$ Hz, 3H).

***N*-Acetyl-1(-4-methoxy)phenylethylamine**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.27$ (d, $^3J(H,H) = 8$ Hz, 2H; Ar), 6.88 (d, $^3J(H,H) = 8$ Hz, 2H; Ar), 5.70 (brs, 1H; N–H), 5.12 (q, $^3J(H,H) = 7.4$ Hz, 1H), 3.84 (s, 3H; OCH_3), 1.98 (s, 3H; $COCH_3$), 1.48 (d, $^3J(H,H) = 7.4$ Hz, 3H).

***N*-Acetyl-1-phenylpropylamine**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.23-7.47$ (m, 5H; Ar), 5.66 (brs, 1H; N–H), 4.90 (q, $^3J(H,H) = 7.5$ Hz, 1H), 2.01 (s, 3H; $COCH_3$), 1.84 (dq, $^3J(H,H) = 7.5$ Hz, $^3J(H,H) = 2.6$ Hz, 2H), 0.91 (t, $^3J(H,H) = 7.5$ Hz, 3H).

***N*-Acetyl-1-aminoindane**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.19-7.31$ (m, 4H; Ar), 5.88 (brs, 1H; N–H), 5.46 (q, $^3J(H,H) = 8$ Hz, 1H), 2.94 (m, 2H), 2.58 (m, 1H), 2.02 (s, 3H; $COCH_3$), 1.81 (m, 1H).

***N*-Acetyl-1-(1,2,3,4-tetrahydro-1-naphthyl)amine**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.08-7.32$ (m, 4H; Ar), 5.73 (brs, 1H; N–H), 5.23 (q, $^3J(H,H) = 6$ Hz, 1H), 2.80 (m, 2H), 2.03 (s, 3H; $COCH_3$), 1.87 (m, 4H).

***N*-Acetyl-1-amino-4-chroman**: ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.24$ (m, 2H; Ar), 6.91 (m, 2H; Ar), 5.77 (brs, 1H; N–H), 5.16 (q, $^3J(H,H) = 5.5$ Hz, 1H), 4.26 (ddd, $^2J(H,H) = 11.3$ Hz, $^3J(H,H) = 3.4$ Hz, $^3J(H,H) = 3.3$ Hz, 1H), 4.16 (ddd, 1H; $^2J(H,H) = 11.7$ Hz, $^3J(H,H) = 9.3$ Hz,

^3J(H,H) = 2.6 Hz, 1H), 2.21 (m, 2H), 2.07 (m, 2H), 2.03 (s, 3H; $COCH_3$); ^{13}C NMR ($CDCl_3$): δ = 23.33, 28.87, 43.62, 63.19, 117.35, 120.95, 129.52. Not previously obtained in enantiomerically enriched form; $[\alpha]_D^{23} = -55.2$, (c = 0.36, $CHCl_3$). Configuration assigned by comparison with 4-chromanol.

1-(2-Naphthyl)ethylamine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.9 – 7.6 (m, 4H), 7.5 – 7.3 (m, 3H), 5.20 (br s, 1H; N–H), 4.25 (q, ^3J(H,H) = 6.8 Hz, 1H), 1.40 (d, ^3J(H,H) = 6.8 Hz, 3H).

1-(1-Naphthyl)ethylamine: δ = 8.12 (d, ^3J(H,H) = 8.6 Hz, 1H), 7.80 (d, ^3J(H,H) = 8.2 Hz, 1H), 7.78 (d, ^3J(H,H) = 9.0 Hz, 1H), 7.49 (t, ^3J(H,H) = 8.3 Hz, 1H), 7.36 (t, ^3J(H,H) = 8.4 Hz, 1H), 7.27 (d, ^3J(H,H) = 9.0 Hz, 1H), 5.60 (br s, 1H; N–H), 4.87 (q, ^3J(H,H) = 6.8 Hz, 1H), 1.53 (d, ^3J(H,H) = 6.8 Hz, 3H).

1-Acenaphthylamine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.8-7.3 (m, 6H), 4.64 (dd, ^3J(H,H) = 7.1 and 2.5 Hz, 1H), 3.65 (dd, ^2J(H,H) = 17.8 and ^3J(H,H) = 7.1 Hz, 1H), 3.02 (dd, ^2J(H,H) = 17.8 and ^3J(H,H) = 2.5 Hz, 1H).

Determination of the enantiomeric excess and absolute configuration:

Method A: By gas chromatography on a Chrompack WCOT Fused Silica column, CP-Chirasil-DEX CB, 25 m, inlet pressure 2.90 psi (Table 3).

Method B: By NMR spectroscopy with [Eu(tfc)$_3$] as the chiral shift reagent. Absolute configuration determined by comparison of the sign of optical rotation with the literature: 1-(2-naphthyl)ethylamine: *ee* calculated with CH*Me* shifted to δ = 9 – 10; 1-(1-naphthyl)ethylamine: *ee* calculated with CH*Me* shifted to δ = 9 – 10; 1-acenaphthylamine: *ee* calculated on *CH*CH_2 shifted to δ = 9 – 10.

Amination of 1,2-dihydronaphthalene with NH_2Cl (in situ): To a solution of [Rh(cod)(acac)] (0.01 mmol, 3.2 mg, 0.2 mol %) and (*S*)-QUINAP (0.01 mmol, 4.4 mg, 0.2 mol %) in dry THF (2 mL) under argon, was added trimethylsilyl triflate (0.03 mmol, 5 μL) with stirring. The volume was reduced to 0.5 mL in vacuo and pentane (2 × 10 mL) was added to precipitate the catalyst. The pentane was removed by means of a syringe and the catalyst was placed in vacuo, then under argon. THF (5 mL) was added, followed by 1,2-dihydronaphthalene (1 mmol, 0.13 mL) and then freshly distilled catecholborane (1.1 mmol, 0.12 mL) was added slowly by means of a syringe. After the mixture had been stirred for 3 h, $ZnMe_2$ (1 mmol, 2 M in THF, 0.5 mL) was added and the solution was stirred for 2 h. Chloramine was generated by the addition of sodium hypochlorite (5 mmol, ≈2 M in H_2O) to a solution of NH_3 (5 mmol, 0.5 M in dioxane) at 0 °C, stirred for 30 min with THF (3 mL). The alkylborane solution was then added to the chloramine solution and the reaction mixture was stirred at room temperature overnight. The mixture was extracted with ether (3 × 20 mL), washed with NaOH (0.5 M, 10 mL), dried ($MgSO_4$), filtered and evaporated in vacuo to give the crude product with ≈90 % conversion to RNH_2. This was dissolved in Et_2O (20 mL) and extracted with HCl (2 M in H_2O, 2 × 10 mL). The combined aqueous portions were made basic with solid NaOH (0.75 g) and extracted with Et_2O (3 × 20 mL). The combined organic fractions were dried ($MgSO_4$), filtered and evaporated to give the amine, pure by NMR spectroscopy, (112 mg, 77 %). The method for the determination of *ee* as described above gave a value of 95 % (*S*).

Catalytic hydroboration alkylamination reactions: general procedure

Method A1 (One-pot reaction, 1 mol % catalyst): To a solution of [(cod)Rh(acac)] (0.01 mmol, 3.2 mg, 0.2 mol %) and (*R*)-QUINAP (0.01 mmol, 4.4 mg, 0.2 mol %) in dry THF (2 mL) under argon, was added trimethylsilyl triflate (0.03 mmol, 5 μL) with stirring. The volume was reduced to 0.5 mL in vacuo, and pentane (2 × 10 mL) was added to precipitate the catalyst. The pentane was removed with a syringe and the catalyst was placed in vacuo, then under argon. Toluene (1 mL) was added, followed by the alkene (1.0 mmol), and then catecholborane (106.6 μL, 119.9 mg, 1.0 mmol) was added slowly with a syringe. The mixture was stirred for 2 h and $ZnEt_2$ (1.1 M in toluene, 1.1 mmol, 1.0 mL) was added slowly with a syringe. The mixture was stirred for 2 h, and a white precipitate formed. The alkylchloramine was generated by the addition of sodium hypochlorite (1.2 mmol, 2 M in H_2O) to the amine solution (1.2 mmol) in diethyl ether (6 mL) at 0 °C. The alkylborane solution, precooled to 0 °C, was added to the chloramine solution. The borane residue was dissolved with further ether (2 mL), which was also added to the chloramine solution. The reaction mixture was stirred at 0 °C for 5 min, allowed to warm to room temperature, and then stirred for 60 min. Aqueous HCl (1.0 M, 5 mL) was added and the mixture was stirred for 10 min and then washed with diethyl ether (3 × 10 mL). Aqueous NaOH (2.0 M, 5 mL) was added to the aqueous layer, which was then extracted with diethyl ether (3 × 10 mL), dried ($MgSO_4$), filtered and evaporated to give the product amine. Although almost pure, it was further purified by column chromatography (silica gel, diethyl ether:pentane 1:5). The enantiomeric purity of the product amine was determined directly by ^{1}H NMR spectroscopy ([D$_6$]acetone) with (+)- or (–)-mandelic acid as the NMR shift reagent. Isolated yields of the product amine are based on the starting alkene.

Method A2 (One-pot reaction, 0.2 mol % catalyst): The procedure was the same as Method A1 except the quantities of reagents and solvents were scaled up by a factor of five while the weight of catalyst remained constant.

Method B (Multistep reaction): The procedure of catalytic hydroboration was carried out as in Method A1, pentane (10 mL) then being added to the reaction mixture to precipitate the catalyst. The pentane solution was transferred to another Schlenk with a syringe and the solvent was removed in vacuo to give a sample of catecholboronate ester which was manipulated under argon. Toluene (1 mL) was added, and the transmetallation reaction, amination reaction, and work-up were carried out as in Method A1. The isolated yield of the product amine quoted in Table 2 was based on the isolated catecholboronate ester.

(*R*)-(+)-*N*-Cyclohexyl-1-phenylethylamine: Method A1; yield: 71 % (87 % *ee*); clear colourless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.37 – 7.23 (m, 5H), 3.97 (q, J = 6.6 Hz, 1H), 2.32 – 2.24 (m, 1H), 1.99 (d, J = 10.0 Hz, 1H), 1.80 – 1.57 (m, 3H), 1.56 (s, 1H), 1.33 (d, J = 6.6 Hz, 3H), 1.27 – 0.99 (m, 6H); ^{13}C NMR (200 MHz, $CDCl_3$): δ = 146.5, 128.6, 126.9, 126.6, 54.3, 53.5, 34.5, 33.1, 26.1, 25.1, 24.9, 24.8; IR (neat): $\tilde{\nu}$ = 3325, 3061, 3023, 2926, 2852, 1491, 1448, 1128, 760, 700 cm^{-1}; GC – MS (CI$^+$): m/z (%): 204 ([M^++1], 100), 188 (32), 105 (19); $[\alpha]_D^{22} = +64.6$ (c = 0.71, $CHCl_3$); lit.:[29] $[\alpha]_D^{25} = +66.7$ (c = 1.53, $CHCl_3$).

(*R*)-(+)-*N*-Cyclohexyl-1-(4-chlorophenyl)ethylamine: Method A1; yield: 50 %, (78 % *ee*); clear colourless oil; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.33 – 7.22 (m, 4H), 3.96 (q, J = 6.6 Hz, 1H), 2.25 – 2.18 (m, 1H), 1.96 (d, J = 9.7 Hz, 1H), 1.80 – 1.57 (m, 3H), 1.57 (s, 1H), 1.31 (d, J = 6.7 Hz, 3H), 1.56 – 0.96 (m, 6H); ^{13}C NMR (200 MHz, $CDCl_3$): δ = 145.0, 132.4, 128.7, 128.1, 53.8, 53.6, 34.4, 33.0, 26.0, 25.1, 24.9, 24.8; IR (neat): $\tilde{\nu}$ = 3310, 2926, 2852, 1491, 1449, 1126, 1091, 1013, 829 cm^{-1}; GC – MS (CI$^+$): m/z (%): 238 ([M^++1], 100), 240 (25), 222 (25), 139 (18); $[\alpha]_D^{22} = +63.3$ (c = 0.41, $CHCl_3$); ref.:[30] (*S* enantiomer) $[\alpha]_D^{25} = -28.0$ (neat).

(*R*)-(+)-*N*-Cyclohexyl-1-(4-methoxyphenyl)ethylamine: Method A2: yield: 73 % (93 % *ee*); Method B: yield: 82 % (92 % *ee*); clear colourless

Table 3. GC retention times in the separation of amine enantiomers as acetamides.

Acetamide	Temp. of oven [°C]	Retention time [min]	
		Enantiomer 1	Enantiomer 2
N-acetyl-1-phenylethylamine	140	27.69 (*S*)-(–)[a]	30.02 (*R*)-(+)
N-acetyl-1(4-methoxy)phenylethylamine	150	63.54 (*S*)-(–)[b]	65.69 (*R*)-(+)
N-acetyl-1-phenylpropylamine	140	35.06 (*S*)-(–)[b]	37.00 (*R*)-(+)
N-acetyl-1-aminoindane	150	47.81 (*S*)-(+)[a]	52.11 (*R*)-(–)
N-acetyl-1-(1,2,3,4-tetrahydro-1-naphthyl)amine	150	71.47 (*S*)-(–)[b]	84.62 (*R*)-(+)
N-acetyl-1-amino-4-chroman	150	70.44 (*S*)-(–)[b]	78.28 (*R*)-(+)

[a] Absolute configuration determined by comparison with an authentic sample (Aldrich). [b] Absolute configuration assigned by similarity in elution order in the GC analysis of 1-(4-methoxy)phenylethanol, 1-phenylpropanol, 1,2,3,4-tetrahydro-1-naphthol, 4-chromanol.

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oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.22$ (d, $J = 8.6$ Hz, 2H), 6.87(d, $J = 8.7$ Hz, 2H), 3.93 (q, $J = 6.6$ Hz, 1H), 3.81 (s, 3H), 2.29–2.24 (m, 1H), 1.98 (d, $J = 12$ Hz, 1H), 1.72–1.56 (m, 3H), 1.55 (s, 1H), 1.32 (d, $J = 6.6$ Hz, 3H), 1.19–0.99 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 158.3$, 138.1, 127.4, 113.7, 55.2, 53.7, 53.5, 34.4, 33.1, 26.1, 25.2, 24.9; IR (neat): $\tilde{\nu} = 3316$, 3099, 3061, 2925, 2850, 1610, 1585, 1511, 1449, 1245, 1174, 1126, 1038, 830 cm^{-1}; GC–MS (CI$^+$): m/z (%): 234 ([M^++1], 61), 218 (48), 135 (100); HRMS: m/z: calcd for $C_{15}H_{24}NO$ [M^++1] 234.1858, found 234.1857; $[\alpha]_D = +58.5$ ($c = 0.47$, methanol).

(+)-*N*-Chroman-4-yl-cyclohexylamine: Method A1; yield: 48% (87% *ee*); clear colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.25$ (d, $J = 7.6$ Hz, 1H), 7.14 (t, $J = 8.0$ Hz, 1H), 6.88 (t, $J = 7.4$ Hz, 1H), 6.81 (d, $J = 8.2$ Hz, 1H), 4.32 (t, $J = 10.8$ Hz, 1H), 4.24–4.12 (m, 1H), 3.90 (t, $J = 4.0$ Hz, 1H), 2.70–2.63 (m, 1H), 2.06–1.98 (m, 2H), 1.92–1.73 (m, 3H), 1.66–1.62 (m, 1H), 1.37–1.09 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 154.7$, 129.6, 128.3, 125.5, 120.2, 116.8, 62.5, 54.0, 47.7, 34.9, 33.6, 28.6, 26.1, 25.2, 25.0; IR (neat): $\tilde{\nu} = 3329$, 3069, 3036, 2921, 2852, 1608, 1582, 1488, 1451, 1180, 733 cm^{-1}; MS (CI$^+$): m/z (%): 232 ([M^++1], 100), 203 (26), 133 (59), 100 (24); HRMS: m/z: calcd for $C_{15}H_{22}NO$ [M^++1]: 232.1701, found 232.1698; $[\alpha]_D = +29.2$ ($c = 0.16$, methanol).

(*R*)-(+)-*N*-Benzyl-1-(4-methoxyphenyl)ethylamine: Method B; yield: 75% (91% *ee*); clear colourless oil; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.39–7.23$ (m, 7H), 6.92 (d, $J = 8.7$ Hz, 2H), 3.84 (s, 3H), 3.80 (q, $J = 6.5$ Hz, 1H), 3.69 (d, $J = 13.1$ Hz, 1H) 3.60 (d, $J = 13.2$ Hz, 1H), 1.71 (s, 1H), 1.38 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (200 MHz, $CDCl_3$): $\delta = 158.8$, 140.8, 137.7, 128.5, 128.3, 127.9, 127.0, 113.9, 56.7, 55.2, 51.5, 24.4; IR (neat): $\tilde{\nu} = 3324$, 3061, 3026, 2999, 2959, 2929, 2834, 1610, 1585, 1513, 1245, 1176, 1114, 1037, 832 cm^{-1}; GC–MS (CI$^+$): m/z (%): 242 ([M^++1], 16), 226 (27), 135 (100), 108 (39), 91 (28); $[\alpha]_D^{22} = +46.9$ ($c = 1.31$, $CHCl_3$); ref.:[31] $[\alpha]_D^{22} = +40.3$ ($c = 0.77$, $CHCl_3$).

(*R*)-(+)-*N*-4-Methoxybenzyl-1-(4-methoxyphenyl)ethylamine: Method A2: yield: 77% (90% *ee*); Method B: yield: 81% (87% *ee*); clear colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.29$ (d, $J = 8.6$ Hz, 2H), 7.21 (d, $J = 8.6$ Hz, 2H), 6.91 (d, $J = 8.7$ Hz, 2H), 6.87 (d, $J = 8.6$ Hz, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 3.77 (q, $J = 6.6$ Hz, 1H), 3.60 (d, $J = 12.9$ Hz, 1H), 3.56 (d, $J = 12.9$ Hz, 1H), 1.74 (s, 1H), 1.35 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 158.5$, 158.5, 137.6, 132.7, 129.3, 127.7, 113.8, 113.7, 56.6, 55.2, 55.2, 50.9, 24.4; IR (neat): $\tilde{\nu} = 3325$, 3061, 3029, 2957, 2931, 2908, 2834, 1610, 1584, 1509, 1250, 1174, 1108, 1036, 832 cm^{-1}; MS (CI$^+$): m/z (%): 272 ([M^++1], 63), 256 (36), 135 (100), 121 (58); HRMS: m/z: calcd for $C_{17}H_{22}NO_2$ [M^++1] 272.1651, found 272.1652; $[\alpha]_D = +37.8$ ($c = 0.10$, methanol).

(*R*)-(+)-*N*-Furfuryl-1-(4-methoxyphenyl)ethylamine: Method B; yield: 76% (91% *ee*); clear colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.37–7.36$ (m, 1H), 7.27 (d, $J = 8.6$ Hz, 2H), 6.89 (d, $J = 8.7$ Hz, 2H), 6.31–6.30 (m, 1H), 6.11 (d, $J = 3.1$ Hz, 1H), 3.82 (s, 3H), 3.75 (q, $J = 6.6$ Hz, 1H), 3.66 (d, $J = 14.4$ Hz, 1H) 3.57 (d, $J = 14.4$ Hz, 1H), 1.72 (s, 1H), 1.35 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 158.6$, 154.0, 137.6, 141.7, 137.1, 127.8, 113.8, 110.0,106.8,, 56.3, 55.2, 43.9, 24.3; IR (neat): $\tilde{\nu} = 3332$, 3114, 3061, 2997, 2960, 2929, 2834, 1611, 1585, 1511, 1244, 1178, 1112, 1036, 833 cm^{-1}; MS (CI$^+$): m/z (%): 232 [M^++1], 45), 216 (48), 135 (100), 81 (33); HRMS: m/z: calcd for $C_{14}H_{18}NO_2$ [M^++1]: 232.1338, found 232.1330; $[\alpha]_D = +80.1$ ($c = 0.32$, methanol).

Absolute configuration of alkylamines: (*R*)-*N*-cyclohexyl-1-(4-methoxyphenyl)ethylamine was synthesised from cyclohexanone and the enantiomerically pure primary amine by reductive amination,[32] confirming the *R* configuration for the product of hydroboration. Other alkylamines were assigned by analogy. In particular by comparison of CD spectra in MeOH the UV/CD spectra consistently showed a positive band at $\lambda = 225–235$ nm; the band at 260–285 nm varied in sign.

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