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Catalytic asymmetric synthesis of secondary alcohols using chiral *cis*-1-amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene as chiral ligand

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Abstract: The synthesis and resolution of *cis*-1-amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene **5** by a simple and straightforward methodology has been achieved. The homochiral aminoalcohol has been used in the catalytic reduction of ketones by means of $BH_3 \cdot SMe_2$ affording secondary alcohols in high enantiomeric excesses. On the contrary low enantiomeric excesses have been obtained when (1S,2R)-N,N-dibutyl-1-amino-2-hydroxytetrahydronaphthalene **11** has been used to catalyze the enantioselective addition of Et_2Zn to benzaldehyde. © 1997 Elsevier Science Ltd. All rights reserved.

Enantiomerically pure *cis*-1,2-aminols and their N-alkyl derivatives have found extensive application as chiral ligands for catalytic asymmetric organic synthesis.[1] The most important applications for these ligands are the enantioselective addition of Et_2Zn to aldehydes[2] and the enantioselective reduction of ketones with $BH_3 \cdot SMe_2$.[3] We have recently introduced the use of optically active *cis*-1-amino-2-indanols as effective ligands to promote both these kinds of reaction.[4]

The potential of (1S,2R)- and (1R,2S)-amino indanols[5] has been extended by the Merck group, which achieved a practical, large scale asymmetric synthesis, based on the enantioselective epoxidation of indene in the presence of the Jacobsen's salen chiral catalyst,[6] followed by a Ritter type acid catalyzed opening of the optically active indene epoxide.[7] This methodology has been further applied to the asymmetric synthesis of other *cis*-aminoalcohols.[7b] The use of amino indanols or other sterically constrained aminoalcohols in catalysis follows the idea that more rigid catalysts can enhance the enantioselectivity in catalytic reactions.[8]

We wish now to describe an alternative and convenient route to enantiopure *cis*-1-amino-2-hydroxy tetrahydronaphthalene **5** and the results obtained from its use as chiral ligand. Our synthesis started from the commercially available 3,4-dihydronaphthalene which was brominated and treated with water and magnesium carbonate to give in good yield the racemic *trans*-1-hydroxy-2-bromo-naphthalene **1**. Reaction of **1** with ammonia afforded the corresponding *trans*-1-amino-2-hydroxy-tetrahydronaphthalene **2**. Benzoylation of **2**, followed by the treatment with $SOCl_2$ gave the oxazoline **4** which was hydrolysed to the *cis*-aminoalcohol **5**. The resolution of **5** was achieved by chromatographic separation of the diastereoisomeric amides **6** and **7**, formed by the treatment of **5** with N-BOC-L-phenylalanine (Scheme 1).

The final hydrolysis of **6** and **7** with NaOH afforded the enantiomerically pure aminoalcohols (+)- and (−)-**5** (Scheme 2).[9] The absolute configuration of (+)-**5** was assigned by comparison of the sign of its specific rotation which was opposite to that of (1R,2S)-1-amino-2-hydroxy tetrahydronaphthalene prepared using the Merck methodology.[7] Thus, the dihydronaphthalene was epoxidised using the Jacobsen's (R,R)-salen manganese catalyst to give (1R,2S)-epoxy-3,4-dihydronaphthalene **8**, which was opened in CH_2Cl_2 in the presence of H_2SO_4 to give the corresponding mixture of *cis*- and *trans*-dihydroxy-naphthalene **9** and **10**. The mixture was treated in the Ritter conditions,[7] to give,

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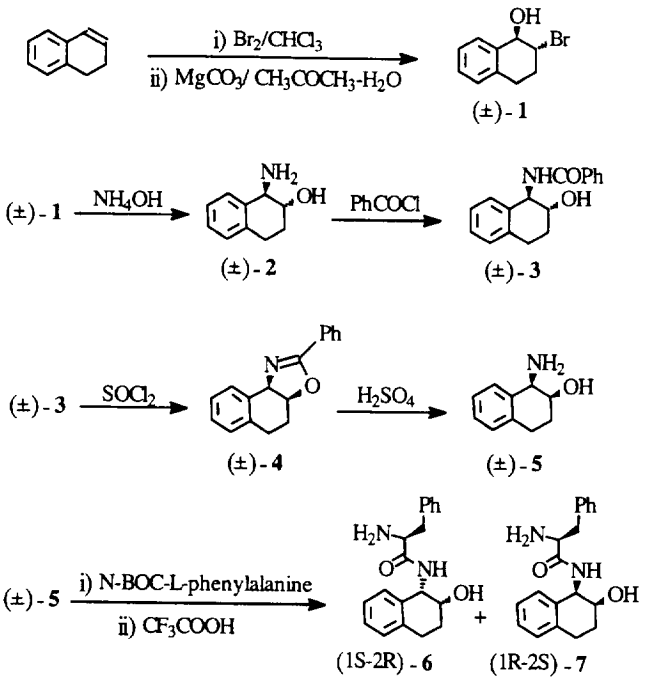
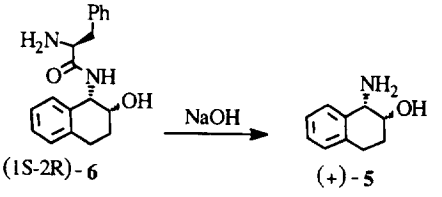
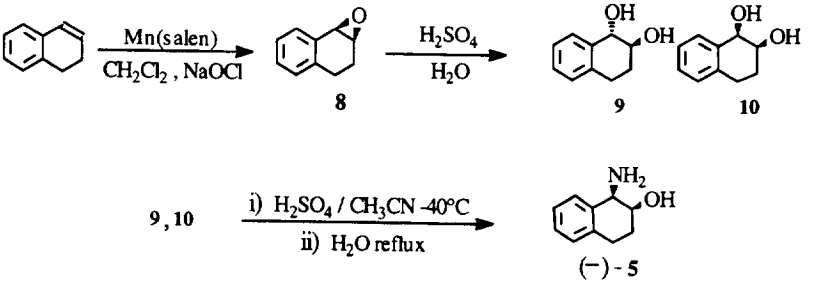


Scheme 1.

after sublimation, (1R,2S)-(−)-**5** (Scheme 2). The highly polar aminoalcohol **5** is difficult to purify by column chromatography, but we found that sublimation is an effective methodology.

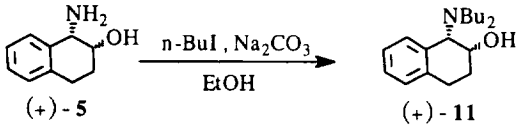




Scheme 2.

In our previous work, we have shown that the rigid cyclic framework of *cis*-1,2-aminoindanol makes it a very enantioselective ligand for the reduction of prochiral ketones by BH_3, however poor enantiocontrol is achieved when the addition of Et_2Zn to aldehydes is catalyzed by the corresponding

N,N-dialkyl derivatives, although good chemical yields are obtained. We planned to check the newly prepared *cis*-1-amino-2-hydroxytetrahydronaphthalene (+)-**5** and (−)-**5** with the aim of enhancing the enantioselectivity of the latter reaction. This expectation was supported by greater conformational bias of the six-membered ring of the tetrahydronaphthalene moiety, with respect to the indane moiety. Thus we synthetised the N,N-dialkyl ligand (+)-**11** (Scheme 3) which effectively catalyzed the addition of Et_2Zn to benzaldehyde.



(+)-**5** (+)-**11**

Scheme 3.

In Table 1 we report the results obtained from the addition of Et_2Zn to benzaldehyde (Scheme 4) in the presence of the chiral ligand (+)-**11**.

The ligand **11** promotes the addition of Et_2Zn to benzaldehyde with moderate enantioselectivity. All attempts to improve the enantiomeric excess based on different order of addition, different solvent and reaction temperature, failed. Although in other reactions stereochemically controlled by chiral auxiliary prepared from *cis*-1-amino-2-indanol and *cis*-1-amino-2-hydroxytetrahydronaphthalene higher diastereoselection is obtained with the former,[10] in our case, the enantiomeric excess of the reaction is not influenced by the increased steric bias of the latter. In fact, we obtained the same enantiomeric excess in the catalyzed addition of Et_2Zn to benzaldehyde promoted by *cis*-1-amino-2-indanol and by **11**. In the light of these results we were not surprised to find that in the case of the catalytic reduction of ketones in the presence of BH_3, the ligand **5** (Scheme 5) gives high enantiomeric excess as was the case when the *cis*-1-amino-2-indanol was employed for promoting the same reaction. The results obtained with different ketones are collected in Table 2.

The observed trend prompts us to propose a rationalization on the basis of the known models for the two catalytic reactions. The mechanism of the R_2Zn addition to aldehydes promoted by aminoalcohols has been clarified by Noyori[2a] and Soai:[2b] the actual catalyst is a 2-alkyl-1,3,2-oxazazincolidine which coordinates firstly a R_2Zn molecule at the oxygen atom, then the aldehyde at zinc atom complexed by the amino alcohol. The secondary alcohol derives from an attack to the *Re* face of the coordinated aldehyde.

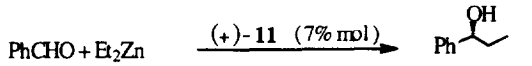
On the contrary, according to the mechanism proposed by Corey,[11] the borane reduction of ketones catalyzed by (+) and (−)-**5**, requires the formation of the 2-alkyl-1,3,2-oxazaborolidine, then the coordination of the second molecules of BH_3 which occurs to the nitrogen atom.[12] In this case the attack of the hydride occurs to the *Si* face of the coordinated ketone. High enantiomeric excess is obtained when the R^1 and R^2 of the ketones are sterically well differentiated.

In summary we have described the easily prepared *cis*-1-amino-2-hydroxytetrahydronaphthalene as a new efficient ligand for the the catalytic reduction of aryl ketones. Further effort of this laboratory

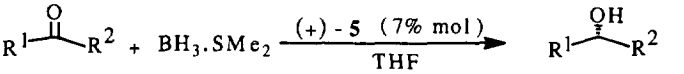
Table 1. Enantioselective addition of Et_2Zn to benzaldehyde catalyzed by the ligand (+)-(**11**)

Entry[a]	Aldehyde	T (°C)	E.e.%[b,c]	Yield %[d]
1	PhCHO	0	44	84
2	PhCHO	25	31	90

a)The reactions were carried out in toluene by adding diethylzinc to a solution of the aldehyde and the catalyst (0.07 mol equiv.). b)Determined by GC analysis on chiral MEGADEX 5 column. c)The (R) absolute configuration of the product was determined by comparison of the sign of the specific rotation with the literature data: see ref. 4. d)Isolated yield.



Scheme 4.



Scheme 5.

Table 2. Catalytic asymmetric reduction of ketones promoted by the ligands (+)- and (−)-(5)

Entry	Ketone	Ligand[a]	Product[b]	Yield %[c]	E.e. %[d,e]
1		(+)-**5**		90	84[e]
2		(+)-**5**		95	92
3		(+)-**5**		95	85
4		(+)-**5**		90	84[e]
5		(-)-**5**		90	90[e]
6		(-)-**5**		93	92

a) All the reactions were carried out in THF using 0.07 mol. equiv. of the ligand (**5**) b) The absolute configuration was determined by comparison of the specific rotation with that of the commercially available compound or with the literature values: see ref. 4. c) Isolated yield. d) Determined by GC analysis on a chiral MEGADEX 5 column. e) Determined by GC analysis of the corresponding TMS ethers on a chiral MEGADEX 5 column.

will be directed to synthesize other rigid amino alcohols as chiral ligands to improve the enantiomeric excesses of these and other reactions.

Experimental section

General

^{1}H-NMR spectra have been recorded at 200 and 300 MHz by means of Varian Gemini instruments. Chemical shifts are given in δ units with respect to TMS and coupling costant J are measured in Hz. IR spectra have been measured with a Nicolet 205 FT spectrometer and are given in cm^{-1}. MS spectra have been taken by EI ionization at 70 eV on a Hewlett–Packard 5971 with GC injection. They are reported as follows: m/z (rel. intens.). Enantiomeric excess were determinated by gas chromatography with a Fison CG 8000 instrument equipped with a MEGADEX 5 (dimethylpentyl-β-cyclodextrin) column (25 m length, 0.25 mm i.d., 0.15 μm film thickness, H_2 carrier gas 0.7 Kpa). Column flash chromatographies were run over 270–400 mesh silica gel. All the reactions were carried out in oven dried glassware under nitrogen atmosphere. Hexane, toluene and THF were freshly distilled from benzophenone ketyl. CH_2Cl_2 was distilled from P_2O_5. DMF was distilled from molecular sieves

and stored under nitrogen on activated molecular sieves. All the other chemicals were commercially available and used as received. GC–MS analysis effected on the chromatographed samples showed that the purity of 99% was achieved.

(±)-trans-*1-Hydroxy-2-bromo-1,2,3,4-tetrahydronaphthalene 1*

To a stirred solution of the commercially available dihydronaphthalene (3.61 g, 27.8 mmol) in $CHCl_3$ (60 mL) at 0°C, was added a $CHCl_3$ solution (40 mL) of Br_2 (1.44 mL, 56 mmol) in a dropwise manner. The reaction was allowed to warm to room temperature and was stirred overnight. The solvent was removed under low pressure to give a brown solid. The solid was transferred in a flask and $MgCO_3$ (3.7 g, 43.8 mmol), acetone (56 mL) and water (9 mL) were added. The mixture was refluxed for 6 hours then cooled to room temperature. The mixture was filtered and the residue washed with Et_2O. The organic phase was separated, washed with brine, dried and the solvent was eliminated under reduced pressure. The solid obtained was purified by flash chromatography (cyclohexane:Et_2O 8:2) (94%). ^{1}H-NMR (200 MHz, $CDCl_3$) 7.53 (m, 1H); 7.28–7.10 (m, 3H); 4.92 (d, 1H, J=7.0, C*H*OH); 4.37 (ddd, 1H, J=9.8, 7.0, 3.3, C*H*Br); 2.97 (m, 2H); 2.53 (m, 1H); 2.31 (m, 2H) MS, m/e: 226 (m+, 4); 147 (36); 129 (100); 120 (18); 119 (32); 115 (16); 91 (23). IR (nujol): 3250, 3100–3000, 1450, 1380, 1310, 1060, 920, 750. M.p.=110°C $C_{10}H_{11}BrO$ (FW 227.11).

(±)-trans-*1-Amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene 2*

To 30% solution of NH_4OH (1000 mL) **1** (4 g, 17.84 mmol) was added at 0°C and the mixture was stirred in a stopped flask for 72 hours at the same temperature. The flask was opened and NH_3 was eliminated by vacuum. The water was eliminated under reduced pressure and the residue was dried under vacuum at 60°C (93%). ^{1}H-NMR (300 MHz, CD_3OD) 7.44–7.40 (m, 1H); 7.30–7.26 (m, 2H); 7.22–7.19 (m, 1H); 4.80 (d, 1H, J=8.04); 4.5 (ddd, 1H, J=10.37, 8.04, 3.38); 3.00–2.90 (m, 2H); 2.20–2.10 (m, 1H); 1.95–1.80 (m, 1H). IR (nujol): 3340, 2900, 1510, 1490, 1380, 1310, 1060, 780, 750. $C_{10}H_{11}NO$ (FW 163.23).

(±)-Oxazoline 4

To a stirred solution of **3** (2.7 g, 16.54 mmol) in CH_2Cl_2 (100 mL) i-Pr_2NEt (5 mL, 45.57 mmol) was added and the mixture was cooled at −40°C. To the mixture, benzoyl chloride (1.9 mL, 17.7 mmol) was added dropwise and the reaction was allowed to warm to room temperature and stirred for 1 hour. The reaction was quenched with a saturated solution of $NaHCO_3$ then the organic phase was separated and dried over Na_2SO_4. The organic phase was partially evaporated and Et_2O was added to precipitate the amide. The solid was filtered and washed with Et_2O. The collected solid was suspended in CH_2Cl_2 (40 mL) and the mixture was cooled at −10°C, then $SOCl_2$ (3.8 mL, 52.10 mmol) was added. The mixture was warmed to room temperature and stirred for 16 hours. The reaction was quenched with a saturated solution of $NaHCO_3$ and extracted with $CHCl_3$ (3×60 mL). The organic phases were combined, dried and decolorated with activated carbon and filtered over celite. The organic phase was evaporated under reduced pressure to give a foamy solid (75%). ^{1}H-NMR (300 MHz, CD_3OD) 7.98–7.11 (m, 9H); 5.41 (d, 1H, J=9.6); 5.23 (dt, 1H, J=9.6, 4.4); 2.80 (ddd, 1H, J=15.3, 11.7, 3.6); 2.61 (dt, 1H, J=15.3, 4.5); 2.29 (m, 1H); 1.94 (m, 1H). MS: 249 (m+, 75); 221 (48); 193 (20); 145 (19); 128 (100); 117 (65); 115 (51); 105 (43); 91 (24); 77 (40). IR (nujol): 3100–3000, 1650, 1100, 1050, 750. $C_{17}H_{15}NO$ (FW 249.31).

(±)-cis-*1-Amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene 5*

The oxazoline **4** (1.9 g, 7.6 mmol) was suspended in H_2O (35 mL) and H_2SO_4 (7 mL) was added. The mixture was refluxed for 16 hours, then the mixture was cooled to 0°C. The mixture was filtered and to the aqueous phase was added NaOH 12N until the pH of the mixture was 12. The mixture was extracted with $CHCl_3$ (3×30 mL) and the organic phases were combined, dried and evaporated under reduced pressure to give a grey solid which was dried under vacuum at 40°C overnight (90%). ^{1}H-NMR (300 MHz, CD_3OD) 7.35 (m, 1H); 7.15–7.05 (m, 3H); 4.85 (brs, 3H); 4.00–3.88 (m, 1H);

2.97 (m, 2H); 2.82 (m, 1H); 2.00 (m, 1H); 1.84 (m, 1H). MS: 163 (m+, 3); 146 (43); 119 (100); 118 (32); 117 (11); 106 (12); 92 (22); 91 (16). IR (nujol): 3330–3260, 3100, 1600, 1470, 1380–1370, 1330, 1080. M.p.=104–105°C $C_{10}H_{13}NO$ (FW 163.23).

*Preparation of the amides **6** and **7***

To a solution of the (±)-1-amino-2-hydroxy-dihydronaphthalene **5** (2 g, 12.3 mmol) in anhydrous DMF (40 mL), hydroxybenzotriazole hydrate (1.8 g, 15 mmol), N-ethyl-N′[3-(dimethylamino)propyl]carbodiimide (WSC) (2.6 g, 15 mmol), N-BOC-phenylalanine (3.9 g, 15 mmol) and triethylamine (1.9 mL, 15 mmol) were added. The mixture was stirred at room temperature for 24 hours, then was quenched with a 10% solution of citric acid (50 mL). The mixture was extracted with AcOEt (2×25 mL) and the organic phases were combined, washed with H_2O (50 mL) and then with a saturated solution of $NaHCO_3$ (2×25 mL). The organic phase was dried and concentrated under reduced pressure to give a viscous oil (80%). The oil was dissolved in $CHCl_3$ (30 mL) and CF_3COOH (8 mL) was added at room temperature. After 3 hours the solution was diluted CH_2Cl_2 and partially evaporated. The residue was diluted with $CHCl_3$ (30 mL) and the organic phase was washed with a 15% solution of NH_4OH. The organic phase was dried and the solvent was eliminated under reduce pressure to afford a grey solid (60%). The two diastereoisomers were separated by flash chromatography (AcOEt:MeOH 9:1).

First eluted diastereoisomer **6**: ^{1}H-NMR (300 MHz, $CDCl_3$) 7.57 (d, 1H, J=8.2); 7.39–7.03 (m, 9H); 5.20 (dd, 1H, J=8.2, 4.0); 4.15 (dt, 1H, J=7.6, 4.0); 3.76 (dd, 1H, J=8.6, 4.6); 3.27 (dd, 1H, J=13.6, 4.6); 2.91 (m, 3H); 1.92 (m, 5H). MS: 310 (m+, 3); 220 (6); 219 (45); 147 (14); 130 (11); 129 (14); 121 (20); 120 (100); 119 (17); 117 (14); 103 (13); 91 (19); 73 (22) 51 (3). IR (nujol): 3380–3340, 3300, 3100, 2920–2860, 1650, 1550, 1460, 1070, 970, 750, 730. M.p.=178°C $C_{19}H_{22}N_2O_2$ (FW 310.42).

Second eluted diastereoisomer **7**: ^{1}H-NMR (300 MHz, $CDCl_3$) 7.53 (d, 1H, J=8.0); 7.37–7.07 (m, 9H); 5.19 (dd, 1H, J=8.0, 3.9); 4.16 (dt, 1H, J=7.2, 3.9); 3.71 (dd, 1H, J=8.7, 4.5); 3.27 (dd, 1H, J=13.6, 4.6); 2.88 (m, 3H); 1.94 (m, 5H). MS: 310 (m+, 3); 275 (5); 220 (6); 219 (45); 147 (14); 162 (5); 147 (14); 130 (10); 129 (14); 121 (20); 120 (100); 119 (17) 118 (8); 117 (14); 103 (13); 91 (19); 73 (22). IR (nujol): 3380–3340, 3300, 3100, 2920–2860, 1650, 1550, 1460, 1070, 970, 750, 730, 710. M.p.=152°C $C_{19}H_{22}N_2O_2$ (FW 310.42).

*(1S,2R)-(+)-*cis*-1-Amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene (+)-**5***

To a solution of **6** (0.9 g, 2.9 mmol) in EtOH (30 mL) a 20% aqueous solution of NaOH (7.5 mL) was added and the mixture was refluxed overnight. The mixture was cooled to room temperature, then extracted with $CHCl_3$ (2×25 mL). The organic phases were combined, dried and concentrated under reduced pressure to give a brown solid which was purified by sublimation (90%) (75°C, 0.15 mmHg). ^{1}H-NMR (200 MHz, CD_3OD) 7.35 (m, 1H); 7.20–7.07 (m, 3H); 4.85 (brs, 3H,); 4.02–3.89 (m, 2H,); 3.03–2.71 (m, 2H); 2.03 (m, 1H); 1.84 (m, 1H). M.p.=95°C Anal. Calcd for $C_{11}H_{13}ON$: (FW 161.23). $[\alpha]_D^{25}$=+68 (c 0.92, MeOH).

*(1R,2S)-(−)-*cis*-1-Amino-2-hydroxytetrahydronaphthalene (−)-**5***

The compound (−)-**5** was prepared from **7** according to the procedure above described. $[\alpha]_D^{25}$=−68 (c 0.88, MeOH).

*(1R,2S)-1,2-Oxy-1,2,3,4-tetrahydronaphthalene **8***

The pH of a commercial bleach solution (50 mL) was adjusted to 11.3 by adding Na_2HPO_4 0.6M and NaOH 1M. This solution was transferred in a flask with a mechanical stirrer and cooled with an ice-bath. To the mixture were added 3,4-dihydronaphthalene (1.63 g, 12.5 mmol), 4-phenylpyridine-N-oxide (0.17 g, 1 mmol) and [(R,R)-N,N′-bis(3,5-di-t-butylsalicylidene)-1,2-cyclohexadiamminato]manganese(III) chloride (Jacobsen's catalyst) (0.16 g, 0.25 mmol) dissolved in CH_2Cl_2 (13 mL). The mixture was vigorously stirred for 5 hours, then the reaction was diluted with CH_2Cl_2 (20 mL). The organic phase was separated, dried and evaporated under *vacuo* to give a

solid brown residue which was purified by flash chromatography (0.7 g, 44%). ^{1}H-NMR (300 MHz, $CDCl_3$) 7.43 (dd, 1H, J=6.9, 1.5); 7.31–7.20 (m, 2H); 7.11 (d, 1H, J=6.9); 3.87 (d, 1H, J=4.2); 3.75 (m, 1H); 2.77 (ddd, 1H, J=13.2, 13.2, 6.3); 2.55 (dd, 1H, J=13.2, 5.7); 1.81 (ddd, 1H, J=13.2, 13.2, 5.7) $[\alpha]_D^{25}$=+88 (c 0.392, $CHCl_3$). The enantiomeric excess of **8** was evaluated 60% by comparison of the known specific rotation value $[\alpha]_D^{25}$=+145.[13]

*(1R,2S)-(−)-*cis*-1-Amino-2-hydroxy-tetrahydronaphthalene (−)-5*

To a solution of the mixture of **9** and **10** (0.066 g, 0.402 mmol) in CH_3CN (0.7 mL) at −40°C CF_3SO_3H (0.071 mL) was added, then the mixture was warmed to room temperature and stirred for 1 hour. Water (1 mL) was added and CH_3CN was evaporated under reduced pressure. The mixture was heated to reflux for 5 hours, then the reaction was quenched by adding solid NaOH until pH 12 was reached. The mixture was extracted with CH_2Cl_2 (2×1 mL) and the organic phases were combined dried and concentrated under reduced presure to give a solid purified by sublimation. (0.030 g 46%). $[\alpha]_D^{25}$=−38 (c 0.792, MeOH).

*(1S,2R)-1-Dibutylamino-2-hydroxy-1,2,3,4-tetrahydronaphthalene (+)-**11***

1-Iodobutane (2.5 mL, 20 mmol) was added to a suspension of (+)-**5** (1.5 g, 9.2 mmol) in EtOH (10 mL). The reaction mixture was heated to reflux for 12 hours, then cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash chromatography (cyclohexane:AcOEt 50:50) to afford a brown oil (1.6 g, 63%). ^{1}H-NMR (300 MHz, $CDCl_3$) 7.30–7.13 (m, 4H); 4.06 (d, 1H, J=5.7); 3.78 (m, 1H); 2.84 (m, 2H); 2.48 (m, 3H); 1.98 (m, 1H); 1.56 (m, 6H); 1.28 (m, 5H); 0.91 (t, 6H, J=7.2). MS: 310 (m+, 3); 220 (6); 219 (45); 147 (14); 130 (11); 129 (14); 121 (20); 120 (100); 119 (17); 117 (14); 103 (13); 91 (19); 73 (22). IR (nujol, cm^{-1}):3350, 3040, 3000, 2930, 2900, 1480, 1100. $[\alpha]_D^{25}$=+127 (c 1, $CHCl_3$).

*Enantioselective addition of Et_2Zn to benzaldehyde catalyzed by **11**. General procedure*

A 1M solution of Et_2Zn in hexane (2.2 mL) was added to a solution of (**11**) (0.011 g, 0.07 mmol) in toluene (1 mL) and the mixture was stirred at room temperature for 1 hour, then the solution was cooled to 0°C and a solution of benzaldehyde (0.1 mL, 1 mmol) in toluene (1 mL) was added in 1 hour. The mixture was stirred at 0°C for 16 hours then quenched by adding a solution of HCl 1M (1 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×10 mL). The organic phases were combined, dried and concentrated under reduce pressure to afford an oil which was purified by flash chromatography (cyclohexane:Et_2O 8:2) and identified by comparison with the spectroscopic data reported in the literature.

*Enantioselective reduction of prochiral ketones catalyzed by **5**. General procedure*

To a solution of enantiomerically pure 1-amino-2-hydroxy-tetrahydronaphthalene **5** (0.008 g, 0.05 mmol) in THF (3 mL), a 2M solution of $BH_3 \cdot Me_2S$ (0.35 mL, 0.7 mmol) was added and the resulting solution was stirred at room temperature for 12 hours. To this mixture a solution of the ketone (1 mmol) in THF (5 mL) was added during 2 hours. The reaction was quenched by adding CH_3OH at 0°C (2 mL). Water was added and THF and MeOH were evaporated under reduced pressure. The aqueous phase was extracted with CH_2Cl_2 (3×10 mL), then the organic phases were combined, dried and evaporated under reduced pressure to afford the crude alcohol, which was purified by flash chromatography (cyclohexane:AcOEt 90:10–70:30) and identified by comparison with the analytical data reported in literature.

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