Monatshefte für Chemie 133, 115–126 (2002)

**Monatshefte für Chemie**
**Chemical Monthly**


# Enantioselective Catalysis CXLI [1]. Tridentate Ligands with 1-(Pyridin-2-yl)ethylamine as Chiral Building Block in the Enantioselective Transfer Hydrogenation of Acetophenone

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**Summary.** A series of novel tridentate ligands with nitrogen and oxygen donor sites was synthesized starting from enantiomerically pure (*S*)- and (*R*)-1-(pyridin-2-yl)ethylamine, the preparation and resolution of which was developed. The new optically active ligands were tested as *in situ* catalysts together with $Ru(PPh_3)_3Cl_2$ in the enantioselective transfer hydrogenation of acetophenone with isopropanol. The secondary amine ligand (*S*)-2,4-di-*tert*-butyl-6-(1-(pyridin-2-yl)ethylamino)-methylphenol gave the best results with almost quantitative conversion and 47% *ee*.

**Keywords.** Catalysis; Chirality; Transfer hydrogenation; Tridentate ligands.

## Introduction

Enantioselective catalysis is a useful tool in organic syntheses for a wide range of reactions [2–4]. Most of the catalysts contain bidentate ligands with phosphorus atoms as donors. Chiral ligands with other donor atoms, like nitrogen or oxygen, are of raising importance [5, 6]. Some of them are very good ligands for transfer hydrogenation reactions, a research area of current interest [7, 8]. For the transfer of the hydride from an alcohol such as isopropanol to a prochiral ketone such as acetophenone different mechanisms are discussed. Metal-ligand bifunctional catalysis has been proven for ligands containing N–H bonds in (arene)ruthenium half-sandwich complexes [8]. A six-membered transition state has been postulated for the simultaneous transfer of two hydrogens from a metal complex to the ketone.

Optically active tridentate ligands should be able to form selective chiral pockets around metal centers more easily than comparable bidentate ligands. Our approach to develop effective chiral tridentate ligands for asymmetric catalysis involved the replacement of 1-phenylethylamine by 1-(pyridin-2-yl)ethylamine [9].

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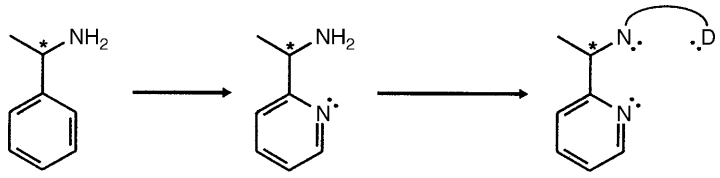



**Scheme 1.** 1-Phenylethylamine, 1-(pyridin-2-yl)ethylamine, and its tridentate derivatives

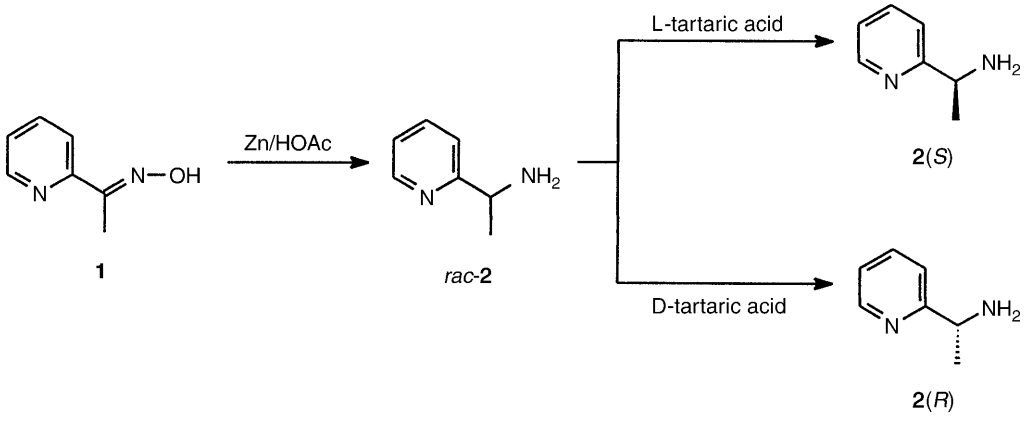
1-Phenylethylamine, used since decades in *Schiff* base condensations, is the most simple chiral primary amine with a phenyl, a methyl, and a hydrogen substituent at the chiral center. Replacing the phenyl group by pyridine converts 1-phenylethylamine into 1-(pyridin-2-yl)ethylamine, rendering bidentate ligands tridentate due to the additional pyridine coordination site (Scheme 1). Complexes with this class of ligands have not been tested in enantioselective catalysis extensively [10–12].

## Results and Discussion

### *Synthesis of (S)- and (R)-1-(pyridin-2-yl)ethylamine*

Although the enantioselective synthesis of 1-(pyridin-2-yl)ethylamine [13] has been described, preparative amounts of this optically active amine are most easily obtained *via* a route starting from 2-acetylpyridine, which first is converted to the corresponding oxime **1** with $NH_3OH \cdot HCl$ in almost quantitative yield (Scheme 2) [14]. **1** is reduced to 1-(pyridin-2-yl)ethylamine *rac*-**2** with an excess of zinc dust and glacial acetic acid in a mixture of ethanol and water [15, 16]. After work-up, distillation at reduced pressure gives an 80–95% yield of the almost colorless liquid *rac*-**2**. It can be stored provided light and air are excluded.

Resolution of *rac*-**2** was carried out with tartaric acid. Several recrystallizations of *rac*-**2** combined with an equimolar amount of *L*-tartaric acid from a mixture of water/ethanol gave the pure salt **2**(*S*)/L-tartaric acid from which enantiomerically pure **2**(*S*) was liberated in 28% yield. Similarly, the amine **2** liberated from the mother liquors was treated with D-tartaric acid to give 25% of enantiomerically pure **2**(*R*) (Scheme 2).

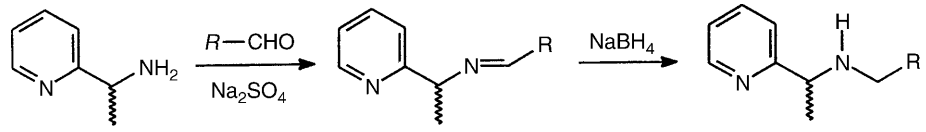



**Scheme 2.** Synthesis and resolution of 1-(pyridin-2-yl)ethylamine

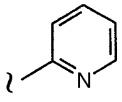
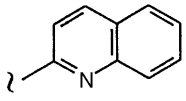
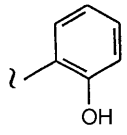
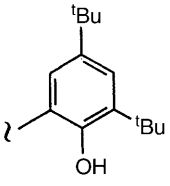
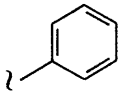
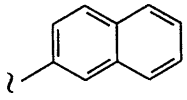
*Synthesis of the tridentate ligands*

1-(Pyridin-2-yl)ethylamine was derivatized by condensation with aldehydes to afford the imines **3**–**6**. From the imines, the corresponding secondary amines **7**–**13** were obtained by reduction with $NaBH_4$. The ligands **3**–**13** are shown in Scheme 3.

To synthesize the imine type ligands **3**–**6**, the corresponding amine and the required aldehyde were reacted in non-aqueous solvents, the more volatile component being used in slight excess. In order to shift the equilibrium to the *Schiff* base side, $Na_2SO_4$ was added to remove the water formed in the condensation. The crude oily products were worked up as described for the individual compounds which were yellow oils (**3**, **6**) or solids (**4**, **5**).




**2**(*S*), **2**(*R*)

| *R*: | | |
|---|---|---|
|  | **3**(*S*), **3**(*R*) | **7**(*S*), **7**(*R*) |
|  | **4**(*S*), **4**(*R*) | **8**(*S*), **8**(*R*) |
|  | **5**(*S*), **5**(*R*) | **9**(*S*), **9**(*R*) |
|  | **6**(*S*), **6**(*R*) | **10**(*S*), **10**(*R*) |
|  | | **11**(*S*), **11**(*R*) |
|  | | **12**(*S*), **12**(*R*) |
|  | | **13**(*S*), **13**(*R*) |

**Scheme 3.** Imines and secondary amines obtained from (*S*)- and (*R*)-1-(pyridin-2-yl)ethylamine

The secondary amines **7**–**13** were synthesized by reduction of the corresponding imines produced *in situ*. Therefore, the non-polar solvents of the imine formation had to be removed before the reduction was carried out in methanolic solution. The reagent $NaBH_4$ was used in excess and added in small portions. For work-up of the ligands without phenolic OH group (**7**, **8**, **11**–**13**), the reaction mixtures were made alkaline with a few drops of KOH solution (50%) and extracted with $CH_2Cl_2$. The phenolic ligands **9** and **10** were isolated by extraction with $CH_2Cl_2$ after careful neutralization with acetic acid. The ligands **11**–**13** could be purified by bulb-to-bulb distillation *in vacuo*. For the other ligands, distillation was accompanied by decomposition.

*Ru-catalyzed transfer hydrogenation of acetophenone*

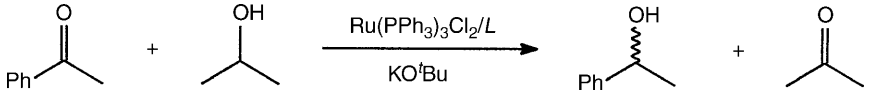
Catalysts generated *in situ* from the half-sandwich precursor $[(p\text{-cymene})RuCl_2]_2$ and the ligands **11** and **12** gave poor results in the asymmetric transfer hydrogenation of acetophenone with isopropanol [9]. The results were improved by using ligands **3**–**12** and $Ru(PPh_3)_3Cl_2$ as the metal component as shown in Table 1 (Scheme 4).

Surprisingly, increased steric hindrance (quinolyl *vs.* pyridinyl and 4,6-di-*tert*-butylphenolyl *vs.* phenolyl) in the imines **4/3** and **6/5** and in the amines **8/7** and **10/9**

**Table 1.** Screening of the catalysts $Ru(PPh_3)_3Cl_2$/ligand **3**–**12** in the enantioselective transfer hydrogenation of acetophenone with isopropanol under standard conditions[a]

| Entry | *L* | Conversion[b] | *ee*[b] |
|---|---|---|---|
| | | % | % |
| 1 | **3**(*S*) | 6 | 0 |
| 2 | **4**(*S*) | 55 | 0 |
| 3 | **5**(*S*) | 58 | 15(*S*) |
| 4 | **6**(*S*) | 80 | 25(*S*) |
| 5 | **7**(*S*) | 6 | 0 |
| 6 | **8**(*S*) | 50 | 0 |
| 7 | **9**(*S*) | 20 | 30(*S*) |
| 8 | **10**(*S*) | 80 | 23(*S*) |
| 9 | **11**(*S*) | 17 | 23(*R*) |
| 10 | **12**(*S*) | 9 | 16(*R*) |

[a] Reactions were carried out with 0.1 *M* acetophenone solution in isopropanol (substrate:Ru:*L*:base = 200:1:1.1:2) for 16 h at 28°C; the catalysts were generated by stirring *L* and $Ru(PPh_3)_3Cl_2$ for 1 h at room temperature; [b] %conversion and %*ee* were determined by GC analysis with a CP-Chirasil-Dex-CB capillary column




**Scheme 4.** Enantioselective transfer hydrogenation of acetophenone with isopropanol using *in situ* catalysts $Ru(PPh_3)_3Cl_2$/**3**–**12**

**Table 2.** Optimization of the catalysts $Ru(PPh_3)_3Cl_2$/ligand **5**, **10**–**12** in the enantioselective transfer hydrogenation of acetophenone with isopropanol (variation of ligand and base concentration)[a]

| Entry | *L* | Ligand[b] | $NaO^tBu$[b] | Conversion[c] | *ee*[c] |
|---|---|---|---|---|---|
| | | | | % | % |
| 1 | **5**(*S*) | 2.2 | 2 | 7 | 6(*S*) |
| 2 | **10**(*S*) | 2.2 | 2 | 90 | 42(*S*) |
| 3 | **10**(*S*) | 5.5 | 2 | 80 | 43(*S*) |
| 4 | **10**(*S*) | 1.1 | 1 | 98 | 47(*S*) |
| 5 | **10**(*S*) | 1.1 | 5 | 88 | 10(*S*) |
| 6 | **10**(*S*) | 1.1 | 10 | 60 | 7(*S*) |
| 7 | **11**(*S*) | 2.2 | 2 | 47 | 27(*R*) |
| 8 | **12**(*S*) | 2.2 | 2 | 6 | 7(*R*) |

[a] Reactions were carried out with 0.1 *M* acetophenone solution in isopropanol (substrate:Ru = 200:1) for 16 h at 28°C; the catalysts were generated by stirring *L* and $Ru(PPh_3)_3Cl_2$ for 1 h at room temperature; [b] equivalents with respect to Ru; [c] %conversion and %*ee* were determined by GC analysis with a CP-Chirasil-Dex-CB capillary column

afforded higher conversions (Table 1, entries 2/1, 4/3, 6/5, 8/7). The pyridinyl and quinolyl ligands **3**(*S*) and **4**(*S*) and their reduced forms **7**(*S*) and **8**(*S*) produced racemic products only. The catalyst systems with the bidentate ligands **11**(*S*) and **12**(*S*) showed low conversions (Table 1, entries 9, 10), but matched those of the phenolic ligands **5**(*S*), **6**(*S*) and **9**(*S*), **10**(*S*) with respect to enantioselectivity (Table 1, entries 3, 4, 7, 8). The fact that the secondary amines and the corresponding imines yielded almost the same enantioselectivities does not support the idea of metal-ligand bifunctional catalysis of the N–H containing amines [8].

For some of the new ligands the ligand/precursor and ligand/base ratio was varied, focussing on ligands **5**(*S*) and **10**(*S*) which were solids (Table 2). Doubling the amount of the imine **5**(*S*) almost stopped the conversion (Table 2, entry 1; compared to Table 1, entry 3). Obviously, the complex with two ligands **5**(*S*) no longer is a good catalyst. For **10**(*S*), overstoichiometric ligand concentration did not affect conversion and enantioselectivity (Table 2, entries 2, 3; compared to Table 1, entry 8), whereas increasing amounts of base lowered the stereoselectivity appreciably (Table 2, entries 5, 6). The best result was obtained for ligand **10**(*S*) with one equivalent of base: the conversion was almost quantitative with 47% *ee* of (*S*) product (Table 2, entry 4). Conversion increased for ligand **11**(*S*) when the amount of ligand and base was doubled (Table 2, entry 7), but not for ligand **12**(*S*) (Table 2, entry 8).

## Experimental

The ligands were prepared under an atmosphere of dry $N_2$. $^1H$ and $^{13}C$ NMR spectra: Bruker AC 250 (250 MHz ($^1H$), 63 MHz ($^{13}C$)), chemical shifts in ppm downfield from *TMS*. DCI mass spectra: Finnigan MAT 95. EI mass spectra: Finnigan MAT 311A. Optical rotations: Perkin-Elmer polarimeter 241. The syntheses of the (*R*)-enantiomers is analogous to that of the corresponding (*S*)-enantiomers. The complete analytical data are given for the (*S*)-enantiomers only. Correct elemental analyses were obtained for all compounds.

*1-(Pyridin-2-yl)methyl ketoxime* (**1**; $C_7H_8N_2$)

2-Acetylpyridine (23 $cm^3$, 25 g, 0.2 mol) and hydroxylamine hydrochloride (21.7 g, 0.3 mol) were dissolved in a mixture of 75 $cm^3$ EtOH and 15 $cm^3$ $H_2O$. To the clear solution NaOH (41.5 g, about 1 mol) was added in small portions. A white precipitate was formed. The hot solution was refluxed for 5 min. After cooling to room temperature it was poured into 130 $cm^3$ of concentrated HCl. The precipitated white hydrochloride was dissolved in 250 $cm^3$ of $H_2O$. Addition of a solution of $K_2CO_3$ (50%) afforded a white powder at *pH* 5–7. After recrystallization from EtOH and drying *in vacuo*, **1** was obtained as a white crystalline powder.

Yield: 24.5 g (90%); m.p.: 118.5°C; $^1$H NMR ($CDCl_3$): $\delta = 2.42$ (s, 3H, $CH_3$), 7.28 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.4$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.70 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.4$ Hz, $^3J(H^4\text{-}H^3) = 8.0$ Hz, $pyH^4$), 7.85 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 8.0$ Hz, $pyH^3$), 8.66 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$), 9.19 (bs, 1H, OH) ppm; MS (EI): $m/z = 136$ ($M^+$).

*1-(Pyridin-2-yl)ethylamine* (*rac*-**2**; $C_7H_{10}N_2$)

**1** (10 g, 73 mmol) was dissolved in a mixture of 135 $cm^3$ EtOH and 15 $cm^3$ $H_2O$. To the solution, zinc dust (80 g) and glacial acetic acid (80 g) were added in small portions over a period of 6 h. After 3 d of stirring at room temperature the solution was filtered, and the residue was washed with EtOH. The combined filtrates were evaporated, and the oily residue was acidified with a small amount of concentrated HCl. The free acetic acid was removed by repeated addition of $H_2O$ followed by evaporation. The amine was liberated with a solution of 50% KOH and extracted five times with diethyl ether. The organic layers were combined, dried ($Na_2SO_4$), and the solvent was removed *in vacuo*. Distillation of the crude product under reduced pressure yielded *rac*-**2** as an almost colorless liquid of characteristic odour.

Yield: 7.1–8.5 g (80–95%); b.p.: 77°C (16 hPa); $^1$H NMR ($CDCl_3$): $\delta = 1.43$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 1.75 (s, 2H, $NH_2$), 4.15 (q, 1H, $^3J = 6.7$ Hz, CH), 7.14 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.7$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.30 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.64 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.9$ Hz, $^3J(H^4\text{-}H^5) = 7.7$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 8.55 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.9$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$) ppm; MS (EI): $m/z = 122$ ($M^+$).

*(S)-1-(Pyridin-2-yl)ethylamine* (**2**(*S*); $C_7H_{10}N_2$) and (*R*)-1-(Pyridin-2-yl)ethylamine (**2**(*R*); $C_7H_{10}N_2$)

*rac*-**2** (20 g, 164 mmol) and L-tartaric acid (24.6 g, 164 mmol) were dissolved in 28 $cm^3$ of $H_2O$ with heating. After adding 100 $cm^3$ of EtOH, the solution was allowed to cool to room temperature. After standing for 4 h, the white precipitate was collected and washed with EtOH and diethyl ether. Recrystallization from a mixture of $H_2O$/EtOH was repeated until the optical rotation did not change any more. The pure amine was liberated by addition of KOH solution. Extraction with diethyl ether and removal of the solvent yielded **2**(*S*).

Yield: 5.6 g (28%); b.p.: 77°C (16 hPa); $^1$H NMR ($CDCl_3$): $\delta = 1.43$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 1.92 (s, 2H, $NH_2$), 4.15 (q, 1H, $^3J = 6.7$ Hz, CH), 7.14 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.7$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.30 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.64 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.9$ Hz, $^3J(H^4\text{-}H^5) = 7.7$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 8.55 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.9$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$) ppm; $[\alpha]_\lambda$ ($c = 1.7$ mg/100 $cm^3$, EtOH): −21.9° ($Na_D$), −23.1° (578 nm), −25.5° (546 nm); MS (EI): $m/z = 122$ ($M^+$).

14 g amine (115 mmol, residue obtained from the mother liquors of the resolution of **2**(*S*)) and D-tartaric acid (17.2 g, 115 mmol) were dissolved in 20 $cm^3$ $H_2O$ with heating. **2**(*R*) was obtained by using the same procedure as for the resolution of **2**(*S*).

Yield: 5.0 g (25%); $[\alpha]_\lambda$ ($c = 1.8$ mg/100 cm$^3$, EtOH): $+20.2°$ ($Na_D$), $+21.7°$ (578 nm), $+23.3°$ (546 nm).

*(S)-2-(1-(Pyridin-2-yl)ethylimino)methylpyridine* (**3**(*S*); $C_{13}H_{13}N_3$)

**2**(*S*) (500 mg, 4.1 mmol) and pyridine-2-carbaldehyde (0.39 cm$^3$, 0.44 g, 4.1 mmol) were dissolved in 30 cm$^3$ diethyl ether. After addition of $Na_2SO_4$, the mixture was stirred for 4 h at room temperature. The solvent was removed *in vacuo* after filtration. To the oily residue, pentane and as much diethyl ether as necessary to dissolve the oil were added. After filtration the solvent was removed. The yellow liquid was dried *in vacuo*.

Yield: 0.8 g (95%); $^1$H NMR ($CDCl_3$): $\delta = 1.66$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 4.78 (q, 1H, $^3J = 6.7$ Hz, CH), 7.17 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.7$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, pyH$^5$), 7.32 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.9$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, py′H$^5$), 7.54 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.9$ Hz, pyH$^3$), 7.68 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.7$ Hz, $^3J(H^4\text{-}H^3) = 7.9$ Hz, pyH$^4$), 7.76 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.7$ Hz, $^3J(H^4\text{-}H^5) = 7.9$ Hz, $^3J(H^4\text{-}H^3) = 7.9$ Hz, py′H$^4$), 8.11 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.9$ Hz, py′H$^3$), 8.54 (s, 1H, =CH), 8.58 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, pyH$^6$), 8.66 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.7$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, py′H$^6$) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta = 23.4$ ($CH_3$), 71.2 (CH), 121.2 (pyC$^5$), 121.6 (pyC$^3$); 122.1 (py′C$^3$), 124.8 (py′C$^5$), 136.5, 136.6 (pyC$^4$, py′C$^4$), 149.1, 149.4 (pyC$^6$, py′C$^6$), 154.6 (py′C$^2$), 161.5 (pyC$^2$), 163.4 (=CH) ppm; $[\alpha]_\lambda$ ($c = 2.4$ mg/100 cm$^3$, MeOH): $+39.9°$ ($Na_D$), $+42.4°$ (578 nm), $+49.5°$ (546 nm); MS (EI): $m/z = 211$ ($M^+$).

*(R)-2-(1-(Pyridin-2-yl)ethylimino)methylpyridine* (**3**(*R*); $C_{13}H_{13}N_3$)

Yield: 0.8 g (96%); $[\alpha]_\lambda$ ($c = 0.85$ mg/100 cm$^3$, *THF*): $-45.8°$ ($Na_D$), $-48.2°$ (578 nm), $-57.6°$ (546 nm).

*(S)-2-(1-(Pyridin-2-yl)ethylimino)methylquinoline* (**4**(*S*); $C_{17}H_{15}N_3$)

**2**(*S*) (1.0 g, 8.2 mmol) and quinoline-2-carbaldehyde (1.27 g, 8.1 mmol) were dissolved in 40 cm$^3$ diethyl ether. After addition of $Na_2SO_4$, the yellow solution was stirred for 16 h at room temperature. Filtration and removal of the solvent yielded a brownish oil which was extracted 5 times with pentane. The combined organic phases were dried ($Na_2SO_4$), and the solvent was removed *in vacuo*. **4**(*S*) remained as a yellow solid which was dried *in vacuo*.

Yield: 1.9 g (89%); m.p.: 58–60°C; $^1$H NMR ($CDCl_3$): $\delta = 1.70$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 4.86 (q, 1H, $^3J = 6.7$ Hz, CH), 7.16 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.4$ Hz, $^4J(H^5\text{-}H^3) = 1.4$ Hz, pyH$^5$), 7.52–7.75 (m, 5H, pyH$^4$, pyH$^3$, quiH$^5$, quiH$^6$, quiH$^7$), 8.13 (m, 1H, quiH$^8$), 8.19 (d, 1H, $^3J(H^3\text{-}H^4) = 8.5$ Hz, quiH$^3$), 8.29 (d, 1H, $^3J(H^4\text{-}H^3) = 8.5$ Hz, quiH$^4$), 8.60 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, pyH$^6$), 8.71 (s, 1H, =CH) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta = 23.6$ ($CH_3$), 71.2 (CH), 118.6 (pyC$^5$), 121.2, 122.1 (pyC$^3$, quiC$^3$), 127.5, 127.7 (quiC$^5$, quiC$^6$), 128.8 (quiC$^{10}$), 129.7, 129.8 (quiC$^7$, quiC$^8$), 136.5, 136.7 (pyC$^4$, quiC$^4$), 147.8 (quiC$^9$), 149.1 (pyC$^6$), 154.9 (quiC$^2$), 162.1 (=CH), 163.4 (pyC$^2$) ppm; $[\alpha]_\lambda$ ($c = 1.0$ mg/100 cm$^3$, $CH_2Cl_2$): $-40.1°$ ($Na_D$), $-42.1°$ (578 nm), $-50.1°$ (546 nm); MS (EI): $m/z = 261$ ($M^+$).

*(R)-2-(1-(Pyridin-2-yl)ethylimino)methylquinoline* (**4**(*R*); $C_{17}H_{15}N_3$)

Yield: 1.8 g (87%); m.p.: 59–61°C; $[\alpha]_\lambda$ ($c = 0.5$ mg/100 cm$^3$, *THF*): $+36.0°$ ($Na_D$), $+40.0°$ (578 nm), $+44.0°$ (546 nm).

*(S)-2-(1-(Pyridin-2-yl)ethylimino)methylphenol* (**5**(*S*); $C_{14}H_{14}N_2O$)

**2**(*S*) (0.73 g, 6.0 mmol) was dissolved in 30 $cm^3$ of acetone, and $Na_2SO_4$ was added. To the stirred mixture, 2-hydroxybenzaldehyde (0.7 $cm^3$, 6.5 mmol) was added dropwise. After stirring for 4 h at room temperature, the yellow solution was filtered and the solvent was removed. The oily residue was washed once with petroleum ether and then dissolved in 5 $cm^3$ diethyl ether. To this solution, petroleum ether was added until it was muddy. After crystallization at −16°C for 10 h the resulting crystals were filtered and washed with petroleum ether. Drying *in vacuo* yielded orange crystals of **5**(*S*).

Yield: 0.8 g (60%); m.p.: 60–62°C; $^1$H NMR ($CDCl_3$): $\delta = 1.69$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 4.71 (q, 1H, $^3J = 6.7$ Hz, CH), 6.89 (ddd, 1H, $^4J(H^5\text{-}H^3) = 1.1$ Hz, $^3J(H^5\text{-}H^4) = 7.2$ Hz, $^3J(H^5\text{-}H^6) = 7.7$ Hz, $PhH^5$), 6.97 (ddd, 1H, $^3J(H^3\text{-}H^4) = 8.3$ Hz, $^4J(H^3\text{-}H^5) = 1.1$ Hz, $^5J(H^3\text{-}H^6) = 0.4$ Hz, $PhH^3$), 7.19 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.5$ Hz, $^4J(H^5\text{-}H^3) = 1.3$ Hz, $pyH^5$), 7.28 (ddd, 1H, $^5J(H^6\text{-}H^3) = 0.4$ Hz, $^4J(H^6\text{-}H^4) = 1.7$ Hz, $^3J(H^6\text{-}H^5) = 7.7$ Hz, $PhH^6$), 7.32 (ddd, 1H, $^3J(H^4\text{-}H^3) = 8.3$ Hz, $^3J(H^4\text{-}H^5) = 7.2$ Hz, $^4J(H^4\text{-}H^6) = 1.7$ Hz, $PhH^4$), 7.44 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.3$ Hz, $^3J(H^3\text{-}H^4) = 7.9$ Hz, $pyH^3$), 7.70 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.5$ Hz, $^3J(H^4\text{-}H^3) = 7.9$ Hz, $pyH^4$), 8.52 (s, 1H, =CH), 8.56 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$), 13.40 (s, 1H, OH) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 23.5$ ($CH_3$), 70.3 (CH ), 117.0 ($PhC^6$), 118.8 ($pyC^5$), 118.9 ($PhC^2$), 120.7 ($PhC^4$), 122.4 ($pyC^3$), 131.6 ($PhC^3$), 132.5 ($PhC^5$), 137.0 ($pyC^4$), 149.1 ($pyC^6$), 161.0 ($PhC^1$), 162.5 ($pyC^2$), 164.6 (=CH) ppm; $[\alpha]_\lambda$ ($c = 0.6$ mg /100 $cm^3$, EtOH): +142.6° ($Na_D$), +155.4° (578 nm), +190.6° (546 nm); MS (EI): $m/z = 226$ ($M^+$).

*(R)-2-(1-(Pyridin-2-yl)ethylimino)methylphenol* (**5**(*R*); $C_{14}H_{14}N_2O$)

Yield: 0.8 g (58%); m.p.: 61–63°C; $[\alpha]_\lambda$ ($c = 0.7$ mg /100 $cm^3$, EtOH): −153.1° ($Na_D$), −160.4° (578 nm), −196.60° (546 nm).

*(S)-2,4-Di-tert-butyl-6-(1-(pyridin-2-yl)ethylimino)methylphenol* (**6**(*S*); $C_{22}H_{30}N_2O$)

**2**(*S*) (0.55 g, 4.5 mmol) was dissolved in 25 $cm^3$ MeOH, and $Na_2SO_4$ was added. To the stirred mixture, 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (1.0 g, 4.4 mmol) was added. After stirring for 4 h at room temperature, the dark yellow solution was filtered, and the solvent was removed. The oily residue was taken up in ethyl acetate /petroleum ether (1:2) and chromatographed on a $SiO_2$ column. The yellow zone was collected, and the solvent was removed. **6**(*S*) remained as a yellow oil.

Yield: 1.0 g (66%); $^1$H NMR ($CDCl_3$): $\delta = 1.30$ (s, 9H, $^t$Bu), 1.46 (s, 9H, $^t$Bu), 1.69 (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 4.70 (q, 1H, $^3J = 6.7$ Hz, CH), 7.12 (d, 1H, $^4J(H^3\text{-}H^5) = 2.4$ Hz, $PhH^3$), 7.18 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.6$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.39 (d, 1H, $^4J(H^5\text{-}H^3) = 2.4$ Hz, $PhH^5$), 7.47 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.1$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.69 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.6$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 8.53 (s, 1H, =CH), 8.55 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.1$ Hz, $pyH^6$), 13.71 (s, 1H, OH) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 23.6$ ($CH_3$), 29.5, 31.5 ($CH_3^{tert\text{-}Bu}$), 34.2, 35.1 ($C^{tert\text{-}Bu}$), 70.4 (CH), 118.0 ($PhC^6$), 120.8 ($pyC^5$), 121.2 ($pyC^3$), 126.2 ($PhC^5$), 127.2 ($PhC^3$), 136.7 ($PhC^2$), 137.0 ($pyC^4$), 140.3 ($PhC^4$), 149.0 ($pyC^6$), 158.0 ($PhC^1$), 162.9 ($pyC^2$), 165.7 (=CH) ppm; $[\alpha]_\lambda$ ($c = 0.55$ mg /100 $cm^3$, EtOH): +90.8° ($Na_D$), +96.3° (578 nm), +121.7° (546 nm); MS (EI): $m/z = 338$ ($M^+$).

*(R)-2,4-Di-tert-butyl-6-(1-(pyridin-2-yl)ethylimino)methylphenol* (**6**(*R*); $C_{22}H_{30}N_2O$)

Yield: 1.0 g (67%); $[\alpha]_\lambda$ ($c = 0.7$ mg /100 $cm^3$, EtOH): −88.3° ($Na_D$), −94.1° (578 nm), −114.4° (546 nm).

*(S)-(1-(Pyridin-2-yl)ethyl)(pyridin-2-yl)methylamine* (**7**(*S*); $C_{13}H_{15}N_3$)

**2**(*S*) (0.5 g, 4.1 mmol) and pyridine-2-carbaldehyde (0.4 $cm^3$, 4.1 mmol) were dissolved in 25 $cm^3$ diethyl ether. $Na_2SO_4$ was added, and the mixture was stirred for 4 h. After filtration and removal of the solvent, the residue was dissolved in 20 $cm^3$ MeOH and reduced with $NaBH_4$ (220 mg, 5.8 mmol) which was added in small portions. After stirring for 12 h at room temperature, the solvent was removed *in vacuo*, and the residue was hydrolized with 30 $cm^3$ of $H_2O$. The mixture was made alkaline with a KOH solution (50%). After extraction (3 ×) with diethyl ether and drying of the organic layers, the solvent was removed and the product **7**(*S*) was dried *in vacuo*.

Yield: 0.8 g (87%); $^1$H NMR ($CDCl_3$): $\delta = 1.48$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 3.23 (bs, 1H, NH), 3.79 (d, 1H, $^2J = 14.1$ Hz, $CH_2$), 3.86 (d, 1H, $^2J = 14.1$ Hz, $CH_2$), 4.00 (q, 1H, $^3J = 6.7$ Hz, CH), 7.12–7.19 (m, 2H, pyH$^5$, py′H$^5$), 7.28, 7.39 (m, 2H, pyH$^3$, py′H$^3$), 7.58–7.67 (m, 2H, pyH$^4$, py′H$^4$), 8.56 (m, 2H, pyH$^6$, py′H$^6$) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta = 22.9$ ($CH_3$), 53.2 ($CH_2$), 59.2 (CH), 121.0 (pyC$^5$), 121.8, 121.9 (pyC$^3$, py′C$^5$), 122.2 (py′C$^3$), 136.3, 136.5 (pyC$^4$, py′C$^4$), 149.2, 149.3 (pyC$^6$, py′C$^6$), 158.9 (py′C$^2$), 164.5 (pyC$^2$) ppm; $[\alpha]_\lambda$ ($c = 0.9$ mg /100 $cm^3$, EtOH): −42.9° ($Na_D$), −43.9° (578 nm), −49.5° (546 nm); MS (DCI): $m/z = 214$ ($MH^+$).

*(R)-(1-(Pyridin-2-yl)ethyl)(pyridin-2-yl)methylamine* (**7**(*R*); $C_{13}H_{15}N_3$)

Yield: 0.7 g (83%); $[\alpha]_\lambda$ ($c = 0.9$ mg /100 $cm^3$, EtOH): +43.5° ($Na_D$), +44.6° (578 nm), +52.2° (546 nm).

*(S)-(1-(Pyridin-2-yl)ethyl)(quinolin-2-yl)methylamine* (**8**(*S*); $C_{17}H_{17}N_3$)

**2**(*S*) (0.4 g, 3.6 mmol) and quinoline-2-carbaldehyde (0.5 g, 3.5 mmol) were dissolved in 25 $cm^3$ diethyl ether. $Na_2SO_4$ was added, and the mixture was stirred for 16 h. After filtration and removal of the solvent the residue was extracted 5 times with pentane. The organic layers were combined and the solvent was removed. The resulting yellow powder was dissolved in 30 $cm^3$ MeOH and reduced with $NaBH_4$ (264 mg, 7.0 mmol) to give **8**(*S*). Further procedure: as described for **7**(*S*).

Yield: 0.8 g (82%); $^1$H NMR ($CDCl_3$): $\delta = 1.53$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 3.53 (bs, 1H, NH), 4.00 (d, 1H, $^2J = 14.7$ Hz, $CH_2$), 4.07 (d, 1H, $^2J = 14.7$ Hz, $CH_2$), 4.08 (q, 1H, $^3J = 6.7$ Hz, CH), 7.16 (ddd, 1H, $^3J$(H$^5$-H$^6$) = 4.9 Hz, $^3J$(H$^5$-H$^4$) = 7.5 Hz, $^4J$(H$^5$-H$^3$) = 1.2 Hz, pyH$^5$), 7.41, 7.43 (m, 2H, quiH$^3$, quiH$^6$), 7.50 (ddd, 1H, $^5J$(H$^3$-H$^6$) = 1.0 Hz, $^4J$(H$^3$-H$^5$) = 1.2 Hz, $^4J$(H$^3$-H$^4$) = 7.6 Hz, pyH$^3$), 7.63–7.72 (m, 2H, quiH$^5$, quiH$^7$), 7.78 (ddd, 1H, $^4J$(H$^4$-H$^6$) = 1.7 Hz, $^3J$(H$^4$-H$^5$) = 7.5 Hz, $^3J$(H$^4$-H$^3$) = 7.6 Hz, pyH$^4$), 8.04–8.10 (m, 2H, quiH$^4$, quiH$^8$), 8.58 (ddd, 1H, $^3J$(H$^6$-H$^5$) = 4.9 Hz, $^4J$(H$^6$-H$^4$) = 1.7 Hz, $^5J$(H$^6$-H$^3$) = 1.0 Hz, pyH$^6$) ppm; $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta = 23.0$ ($CH_3$), 53.8 ($CH_2$), 59.5 (CH), 120.6 (pyC$^5$), 121.2 (pyC$^3$), 121.9 (quiC$^3$), 126.0 (quiC$^6$), 127.3 (quiC$^{10}$), 127.5 (quiC$^5$), 129.1, 129.3 (quiC$^7$, quiC$^8$), 136.3, 136.6 (pyC$^4$, quiC$^4$), 147.7 (quiC$^9$), 149.3 (pyC$^6$), 164.6 (pyC$^2$) ppm; $[\alpha]_\lambda$ ($c = 1.4$ mg /100 $cm^3$, EtOH): −27.2° ($Na_D$), −27.9° (578 nm), −30.8° (546 nm); MS (DCI): $m/z = 264$ ($MH^+$).

*(R)-(1-(Pyridin-2-yl)ethyl)(quinolin-2-yl)methylamine* (**8**(*R*); $C_{17}H_{17}N_3$)

Yield: 0.7 g (79%); $[\alpha]_\lambda$ ($c = 0.7$ mg /100 $cm^3$, EtOH): +27.3° ($Na_D$), +28.7° (578 nm), +31.6° (546 nm).

*(S)-2-(1-(Pyridin-2-yl)ethylamino)methylphenol* (**9**(*S*); $C_{14}H_{16}N_2O$)

**2**(*S*) (0.5 g, 4.3 mmol) and 2-hydroxybenzaldehyde (0.45 $cm^3$, 4.3 mmol) were dissolved in 30 $cm^3$ MeOH. $Na_2SO_4$ was added, and the mixture was stirred for 2 h. After filtration, the residue was

reduced with $NaBH_4$ (190 mg, 5.0 mmol) by stirring for 16 h followed by removal of the solvent. To the residue, 30 $cm^3$ $H_2O$ were added. The mixture was carefully neutralized with acetic acid and extracted 3 times with $CH_2Cl_2$. The organic layers were combined, dried ($Na_2SO_4$), and the solvent was removed. The residue **9**(*S*) was washed 3 times with petroleum ether and dried.

Yield: 0.8 g (82%); b.p.: 170–180°C (decomp.); $^1$H NMR ($CDCl_3$): $\delta = 1.43$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 3.65 (d, 1H, $^2J = 13.9$ Hz, $CH_2$), 3.89 (q, 1H, $^3J = 6.7$ Hz, CH), 3.93 (d, 1H, $^2J = 13.9$ Hz, $CH_2$), 6.25 (bs, NH, OH), 6.74 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.0$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^4J(H^3\text{-}H^4) = 7.6$ Hz, $pyH^3$), 6.84, 6.87 (m, 2H, $PhH^4$, $PhH^6$), 7.13, 7.16 (m, 2H, $PhH^3$, $PhH^5$), 7.21 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.8$ Hz, $^3J(H^5\text{-}H^4) = 7.6$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.66 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.7$ Hz, $^3J(H^4\text{-}H^5) = 7.6$ Hz, $^3J(H^4\text{-}H^3) = 7.5$ Hz, $pyH^4$), 8.61 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.8$ Hz, $^4J(H^6\text{-}H^4) = 1.7$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 22.6$ ($CH_3$), 50.3 ($CH_2$), 57.2 (CH), 116.4 ($PhC^6$), 119.0 ($pyC^5$), 122.2, 122.4 ($pyC^3$, $PhC^4$), 122.7 ($PhC^2$), 128.5, 128.7 ($PhC^3$, $PhC^5$), 136.7, ($pyC^4$), 149.7 ($pyC^6$), 158.4 ($PhC^1$), 162.2 ($pyC^2$) ppm; $[\alpha]_\lambda$ ($c = 0.5$ mg / 100 $cm^3$, EtOH): −61.2° ($Na_D$), −63.2° (578 nm), −71.4° (546 nm); MS (DCI): $m/z = 229$ ($MH^+$).

*(R)-2-(1-(Pyridin-2-yl)ethylamino)methylphenol* (**9**(*R*); $C_{14}H_{16}N_2O$)

Yield: 0.9 g (96%); $[\alpha]_\lambda$ ($c = 1.1$ mg /100 $cm^3$, EtOH): +67.7° ($Na_D$), +69.6° (578 nm), +79.8° (546 nm).

*(S)-2,4-Di-tert-butyl-6-(1-(pyridin-2-yl)ethylamino)methylphenol* (**10**(*S*); $C_{22}H_{32}N_2O$)

**2**(*S*) (0.9 g, 7.5 mmol) and 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (1.7 g, 7.2 mmol) were dissolved in 30 $cm^3$ MeOH. $Na_2SO_4$ was added, and the mixture was stirred for 4 h. After filtration, reduction with $NaBH_4$ (420 mg, 11 mmol), and work-up as described for **9**(*S*), **10**(*S*) was obtained as a fine white powder.

Yield: 0.8 g (82%); m.p.: 78–80°C; $^1$H NMR ($CDCl_3$): $\delta = 1.25$ (s, 9H, $^t$Bu), 1.43 (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 1.44 (s, 9H, $^t$Bu), 3.66 (d, 1H, $^2J = 13.5$ Hz, $CH_2$), 3.87 (d, 1H, $^2J = 13.5$ Hz, $CH_2$), 3.90 (q, 1H, $^3J = 6.7$ Hz, CH), 6.71 (d, 1H, $^4J(H^5\text{-}H^3) = 2.5$ Hz, $PhH^5$), 7.21 (d, 1H, $^4J(H^3\text{-}H^5) = 2.5$ Hz, $PhH^3$), 7.15–7.23 (m, 2H, $pyH^3$, $pyH^5$), 7.66 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.6$ Hz, $^3J(H^4\text{-}H^3) = 7.6$ Hz, $pyH^4$), 8.60 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.8$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.0$ Hz, $pyH^6$) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 22.5$ ($CH_3$), 29.7, 31.7 ($CH_3^{tert\text{-}Bu}$), 34.1, 35.0 ($C^{tert\text{-}Bu}$), 51.3 ($CH_2$), 57.4 (CH), 122.0, 122.3, 122.9 ($PhC^4$, $pyC^5$, $pyC^3$), 122.1 ($PhC^2$), 123.4 ($PhC^3$), 135.9 ($PhC^5$), 136.6 ($pyC^4$), 140.3 ($PhC^4$), 149.7 ($pyC^6$), 154.8 ($PhC^1$), 162.5 ($pyC^2$) ppm; $[\alpha]_\lambda$ ($c = 0.3$ mg /100 $cm^3$, EtOH): −43.2° ($Na_D$), −48.5° (578 nm), −51.3° (546 nm); MS (DCI): $m/z = 341$ ($MH^+$).

*(R)-2,4-Di-tert-butyl-6-(1-(pyridin-2-yl)ethylamino)methylphenol* (**10**(*R*); $C_{22}H_{32}N_2O$)

Yield: 2.0 g (84%); m.p.: 79–81°C; $[\alpha]_\lambda$ ($c = 0.65$ mg /100 $cm^3$, EtOH): +47.9° ($Na_D$), +49.4° (578 nm), +58.7° (546 nm).

*(S)-Isobutyl(1-(pyridin-2-yl)ethyl)amine* (**11**(*S*); $C_{11}H_{18}N_2$)

**2**(*S*) (1.0 g, 8.2 mmol) was dissolved in 25 $cm^3$ $CH_2Cl_2$, isobutyraldehyde (0.76 $cm^3$, 8.3 mmol) and $Na_2SO_4$ were added, and the mixture was stirred for 24 h at room temperature. After heating to reflux for 1 h, the solution was filtered. 5 $cm^3$ of MeOH were added, and the mixture was reduced with $NaBH_4$ (0.65 g, 2 equiv.). The solvent was removed, and the residue was hydrolized with 30 $cm^3$ $H_2O$. The latter was made alkaline with 50% KOH solution and extracted 3 times with ether. The

organic layers were combined, dried, and the solvent was removed. The oily residue gave **11**(*S*) as a colorless liquid by bulb-to-bulb distillation *in vacuo*.

Yield: 0.7 g (48%); b.p.: 95°C (4 hPa); $^1$H NMR ($CDCl_3$): $\delta = 0.88$ (d, 3H, $^3J = 6.7$ Hz, $CH_3^{i\text{-Pr}}$), 0.89 (d, 3H, $^3J = 6.7$ Hz, $CH_3^{i\text{-Pr}}$), 1.38 (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 1.72 (m, 1H, $CH^{i\text{-Pr}}$), 1.82 (bs, 1H, NH), 2.18 (dd, 1H, $^2J = 11.3$ Hz, $^3J = 6.3$ Hz, $CH_2$), 2.37 (dd, 1H, $^2J = 11.3$ Hz, $^3J = 6.3$ Hz, $CH_2$), 3.84 (q, 1H, $^3J = 6.7$ Hz, CH), 7.14 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.6$ Hz, $^4J(H^5\text{-}H^3) = 1.3$ Hz, $pyH^5$), 7.33 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.2$ Hz, $^4J(H^3\text{-}H^5) = 1.3$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.64 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.6$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 8.55 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.2$ Hz, $pyH^6$) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 20.6$, 20.8 ($CH_3^{i\text{-Pr}}$), 22.9 ($CH_3$), 28.6 ($CH^{i\text{-Pr}}$), 55.9 ($CH_2$), 59.6 (CH), 120.9 ($pyC^5$), 121.7 ($pyC^3$), 136.4 ($pyC^4$), 149.2 ($pyC^6$), 165.1 ($pyC^2$) ppm; $[\alpha]_\lambda$ ($c = 1.0$ mg/100 cm$^3$, MeOH): −49.3° ($Na_D$), −54.2° (578 nm), −62.1° (546 nm); MS (DCI): $m/z = 179$ ($MH^+$).

*(R)-Isobutyl(1-(pyridin-2-yl)ethyl)amine* (**11**(*R*); $C_{11}H_{18}N_2$)

Yield: 0.8 g (57%); $[\alpha]_\lambda$ ($c = 1.3$ mg/100 cm$^3$, $CH_2Cl_2$): +29.8° ($Na_D$), +32.2° (578 nm), +35.2° (546 nm).

*(S)-Benzyl(1-(pyridin-2-yl)ethyl)amine* (**12**(*S*); $C_{14}H_{16}N_2$)

**2**(*S*) (2.15 g, 17.6 mmol) was dissolved in 50 cm$^3$ MeOH, benzaldehyde (1.7 cm$^3$, 17.1 mmol) and $Na_2SO_4$ were added, and the mixture was stirred for 24 h at room temperature. The deep red solution was filtered and reduced with $NaBH_4$ (1.3 g, 2 equiv.). Further procedure: as described for **11**(*S*). The oily residue was purified to the pale yellow liquid **12**(*S*) by bulb-to-bulb distillation in high vacuum.

Yield: 2.2 g (61%); b.p.: 90°C (0.03 hPa); $^1$H NMR ($CDCl_3$): $\delta = 1.40$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 2.22 (bs, 1H, NH), 3.62 (d, 1H, $^2J = 13.1$ Hz, $CH_2$), 3.68 (d, 1H, $^2J = 13.1$ Hz, $CH_2$), 3.92 (q, 1H, $^3J = 6.7$ Hz, CH), 7.15 (ddd, 1H, $^3J(H^5\text{-}H^6) = 5.1$ Hz, $^3J(H^5\text{-}H^4) = 7.5$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.25–7.35 (m, 5H, Ph), 7.33 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.2$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.64 (ddd, 1H, $^4J(H^4\text{-}H^6) = 2.0$ Hz, $^3J(H^4\text{-}H^5) = 7.5$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 8.58 (ddd, 1H, $^3J(H^6\text{-}H^5) = 5.1$ Hz, $^4J(H^6\text{-}H^4) = 2.0$ Hz, $^5J(H^6\text{-}H^3) = 1.2$ Hz, $pyH^6$) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 22.9$ ($CH_3$), 51.8 ($CH_2$), 58.7 (CH), 121.3 ($pyC^5$), 121.9 ($pyC^3$), 126.9 ($PhC^4$), 128.2 ($PhC^2$, $PhC^6$), 128.4 ($PhC^3$, $PhC^5$), 136.5 ($pyC^4$), 140.5 ($PhC^1$), 149.4 ($pyC^6$), 164.6 ($pyC^2$) ppm; $[\alpha]_\lambda$ ($c = 0.75$ mg/100 cm$^3$, EtOH): −27.5° ($Na_D$), −29.3° (578 nm), −34.6° (546 nm); MS (DCI): $m/z = 213$ ($MH^+$).

*(R)-Benzyl(1-(pyridin-2-yl)ethyl)amine* (**12**(*R*); $C_{14}H_{16}N_2$)

Yield: 2.4 g (66%); $[\alpha]_\lambda$ ($c = 1.9$ mg/100 cm$^3$, MeOH): +43.2° ($Na_D$), +44.3° (578 nm), +50.2° (546 nm).

*(S)-(Naphthalen-2-yl)methyl(1-(pyridin-2-yl)ethyl)amine* (**13**(*S*); $C_{18}H_{18}N_2$)

**2**(*S*) (1.8 g, 15 mmol) was dissolved in 50 cm$^3$ $CH_2Cl_2$, naphthalene-2-carbaldehyde (2.3 g, 14.9 mmol) and $Na_2SO_4$ were added, and the mixture was stirred for 24 h at room temperature. The yellow solution was filtered, and the solvent was removed. The residue was taken up in 25 cm$^3$ MeOH, and $CH_2Cl_2$ was added until the solid was dissolved. The solution was reduced with $NaBH_4$ (1.1 g, 2 equiv.). Work-up: as described for **11**(*S*). The oily brown residue was purified to give the yellow oil **13**(*S*) by bulb-to-bulb distillation *in vacuo*.

Yield: 2.5 g (64%); b.p.: 160–170°C (0.04 hPa); $^1$H NMR ($CDCl_3$): $\delta = 1.43$ (d, 3H, $^3J = 6.7$ Hz, $CH_3$), 2.22 (bs, 1H, NH), 3.77 (d, 1H, $^2J = 13.5$ Hz, $CH_2$), 3.83 (d, 1H, $^2J = 13.5$ Hz, $CH_2$), 3.96

(q, 1H, $^3J = 6.7$ Hz, CH), 7.14 (ddd, 1H, $^3J(H^5\text{-}H^6) = 4.9$ Hz, $^3J(H^5\text{-}H^4) = 7.6$ Hz, $^4J(H^5\text{-}H^3) = 1.2$ Hz, $pyH^5$), 7.33 (ddd, 1H, $^5J(H^3\text{-}H^6) = 1.1$ Hz, $^4J(H^3\text{-}H^5) = 1.2$ Hz, $^3J(H^3\text{-}H^4) = 7.8$ Hz, $pyH^3$), 7.38–7.48 (m, 3H, $NpH^3$, $NpH^6$, $NpH^7$), 7.63 (ddd, 1H, $^4J(H^4\text{-}H^6) = 1.8$ Hz, $^3J(H^4\text{-}H^5) = 7.6$ Hz, $^3J(H^4\text{-}H^3) = 7.8$ Hz, $pyH^4$), 7.75–7.82 (m, 4H, $NpH^1$, $NpH^4$, $NpH^5$, $NpH^8$), 8.59 (ddd, 1H, $^3J(H^6\text{-}H^5) = 4.9$ Hz, $^4J(H^6\text{-}H^4) = 1.8$ Hz, $^5J(H^6\text{-}H^3) = 1.1$ Hz, $pyH^6$) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 23.0$ ($CH_3$), 51.9 ($CH_2$), 58.8 (CH), 121.4 ($pyC^5$), 122.0 ($pyC^3$), 125.5, 125.9, 126.4, 126.7, 127.7, 127.8, 128.0 ($NpC^1$, $NpC^3$, $NpC^4$, $NpC^5$, $NpC^6$, $NpC^7$, $NpC^8$), 132.7 ($NpC^{10}$), 133.5 ($NpC^9$), 136.5 ($pyC^4$), 138.0 ($NpC^2$), 149.4 ($pyC^6$), 164.6 ($pyC^2$) ppm; $[\alpha]_\lambda$ ($c = 1.3$ mg/100 cm$^3$, $CH_2Cl_2$): $-31.5°$ ($Na_D$), $-39.2°$ (578 nm), $-43.8°$ (546 nm); MS (DCI): $m/z = 263$ ($MH^+$).

*(R)-(Naphthalen-2-yl)methyl(1-(pyridin-2-yl)ethyl)amine* (**13**(*R*); $C_{18}H_{18}N_2$)

Yield: 2.9 g (75%); $[\alpha]_\lambda$ ($c = 0.8$ mg/100 cm$^3$, $CH_2Cl_2$): $+24.9°$ ($Na_D$), $+27.2°$ (578 nm), $+29.6°$ (546 nm).

*Transfer hydrogenation (general procedure)*

The precursor $Ru(PPh_3)_3Cl_2$ (8.2 mg, 8.6 μmol) and ligand *L* (9.4 μmol) were dissolved in 17.15 cm$^3$ of isopropanol under $N_2$. After 1 h, KO$^t$Bu (1.9 mg) was added, followed by the substrate acetophenone (0.2 cm$^3$, 1.7 mmol).

After stirring for 16 h at 28°C, a 0.1 *M* solution of acetic acid in isopropanol was added to stop the reaction. The solvent was removed at reduced pressure in a *Kugelrohr* apparatus. The product 1-phenylethanol distilled at 50–60°C/5 hPa. The colorless liquid was weighed, dissolved in $CH_2Cl_2$, and quantitatively analyzed by gas chromatography as indicated in Tables 1 and 2.

## Acknowledgment

We thank the *Fonds der Chemischen Industrie* and the *Deutsche Forschungsgemeinschaft* for financial support.

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*Received August 17, 2001. Accepted August 27, 2001*