DOI: 10.1002/ejoc.200900524

1,1′-Binaphthyldiamine-Based Lewis Bases as Readily Available and Efficient Organocatalysts for the Reduction of *N*-Aryl and *N*-Alkyl Ketimines

Stefania Guizzetti,[a] Maurizio Benaglia,*[a] and Giuseppe Celentano[b]

Keywords: Reduction / Lewis bases / Organocatalysis / Binaphthyldiamines / Enantioselectivity

The development of simple, low-cost, efficient, and sustainable routes to enantiomerically pure amines is a topic of extraordinary interest, specially in view of future industrial applications. In this context, we wish to report a chemical and stereochemical efficient synthesis of chiral amines through the Lewis base activated trichlorosilane reduction of ketimines. An organocatalyst, easily prepared in a single step through the condensation of picolinic acid and commercially available 1,1′-binaphthyldiamine, is the key element of this metal-free methodology, that allowed the synthesis of chiral secondary and primary amines in high yields and stereoselectivity. Noteworthy, such catalysts are able to promote the reduction of *N*-alkyl ketimines, often in quantitative yield and up to 87 % enantioselectivity; it is worth mentioning that for such transformations only one other organocatalytic system has been reported so far.

The demand for enantiomerically pure primary and secondary amines has called for a considerable effort to be placed in the development of efficient stereoselective catalytic processes;[1] among the different approaches, the reduction of ketimines represents a powerful and widely used transformation that allows the generation of a new nitrogen-bearing stereocenter. Although hydrosilylation of imines[2] and enantioselective hydrogenation[3] have been widely studied over the last few years, it must be said that only a few efficient chiral catalytic organometallic systems are currently available for C=N bond reduction.[4] Moreover, they suffer from some drawbacks: they are generally quite expensive species, typically composed of an enantiomerically pure ligand (whose synthesis may be costly, long, and difficult) and a metal species, in many cases a precious element. Since chiral amines are finding applications in an always increasing number of fields, such as pharmaceuticals, agrochemicals, and fragrances, the possibility of developing an organocatalytic approach has attracted much attention because it might present a solution to the problems related to the presence of toxic metals, whose leaching could contaminate the product.[5]

Basically, two metal-free catalytic methodologies have recently been employed in the stereoselective reduction of ketimines; in one case, binaphthol-derived phosphoric acids were successfully employed in a process that involves the use of a dihydropyridine-based compound as the reducing agent.[6] In the other case, the reducing agent is trichlorosilane, which is activated by coordination with Lewis bases, such as *N*,*N*-dimethylformamide, acetonitrile, and trialkylamines, to generate a hexacoordinate hydridosilicate, which, under mild conditions, operates as the actual reducing agent.[7] The use of chiral Lewis bases has been widely explored in the last few years and has led to the development of some stereochemical efficient catalysts.[8] However, both methodologies have been shown to be efficient with *N*-aryl ketimines but unable to control the stereochemical outcome for the reduction of *N*-alkyl imines. Only very recently, the organocatalyzed enantioselective reduction of *N*-alkyl imines was reported.[9] Here, we wish to report the results of our studies on the use of 1,1′-binaphthyldiamine-based chiral Lewis bases as efficient organocatalysts for the reduction of *both N*-aryl and *N-alkyl ketimines*.

Our approach is based on the idea that the metal-free catalyst should easily be obtained by modification of an inexpensive, commercially available, enantiopure material whose manipulation must be kept to minimum. In this context, a very short route to chiral Lewis bases was envisaged in the reaction between 2-pyridinecarboxylic acid and enantiomerically pure, commercially available diamines.[10] This straightforward approach was extended to binaphthyl-diamine derivatives, commercialized in both the enantiomeric forms. Picolinic acid was condensed with (*R*)-*N*,*N*′-dimethylamino binaphthyl diamine[11] to afford product **1** in 73% yield after chromatographic purification. (Figure 1) Analogously, starting from the same chiral diamine, other C_1-symmetric picolinamide derivatives **2**–**5** were prepared by a simple two-step sequence in order to better investigate the

[a] Dipartimento di Chimica Organica e Industriale,
Università degli Studi di Milano,
Via Golgi 19, 20133 Milano, Italy
Fax: +39-0250314159
E-mail: maurizio.benaglia@unimi.it
[b] Istituto di Chimica Organica della Facolta' di Farmacia,
Università degli Studi di Milano,
Via Golgi 19, 20133 Milano, Italy
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.200900524.

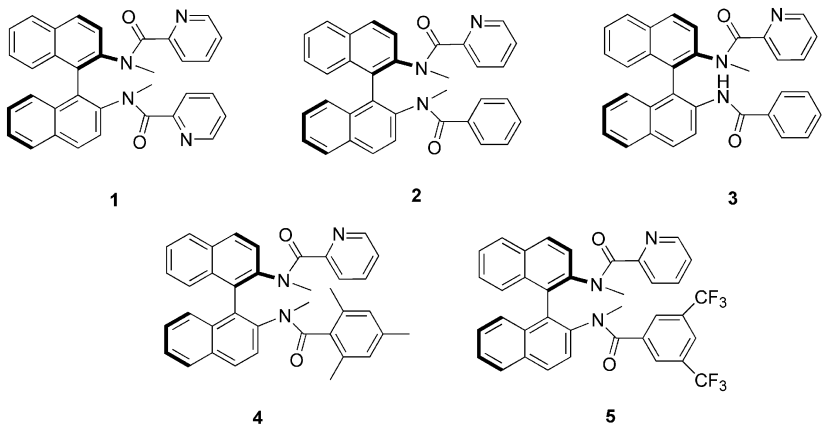
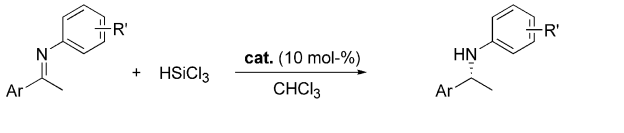


Figure 1. Structures of compounds **1**–**5**.

structure–activity relationship of the catalyst in the ketimine reduction (see Supporting Information).[12]

First, the addition of trichlorosilane to *N*-aryl imines derived from aryl/alkyl ketones was investigated (Scheme 1). The results are collected in Table 1. It was observed that bis(picolinoylamide) **1** was able to promote the reduction of the *N*-phenyl imine of acetophenone in quantitative yield after 12 h at 0 °C in dichloromethane and 75% *ee*.[12] Interestingly, the catalyst maintained a similar level of stereoselectivity also when employed in small amounts, 1 mol-% (Entry 3, Table 1). Catalyst **2**, in which one picolinoyl group is substituted with a benzoyl residue, still showed an excellent chemical activity as an organocatalyst for ketimine reduction (Entry 4, Table 1); the same level of enantioselectivity was observed.[13] However, the presence of a hydrogen atom, which is able to interfere with the coordination mode of trichlorosilane to the picolinamide group, was deleterious for the efficiency of the catalyst (catalyst **3**, Entry 5, Table 1). Based on this observation, we decided to investigate the role of the aryl group as a steric and/or electronic shield of the catalytic site made up by the pyridine nitrogen atom and the amide CO group. Binaphthyldiamine-derived picolinamide **4**, featuring a 2,4,6 trimethylphenyl ring, proved to be an excellent catalyst, but the product was afforded in lower enantioselectivity, while Lewis base **5**, bearing an electron deficient aromatic ring, showed only a modest catalytic ability (Entries 6 and 7).



6 Ar = Ph, R' = H
7 Ar = β–naphthyl, R' = H
8 Ar = 4-CF_3-C_6H_4, R' = H
9 Ar = Ph, R' = 2-OMe
10 Ar = Ph, R' = 4-OMe

11 Ar = Ph, R' = H
12 Ar = β–naphthyl, R' = H
13 Ar = 4-CF_3-C_6H_4, R' = H
14 Ar = Ph, R' = 2-OMe
15 Ar = Ph, R' = 4-OMe

Scheme 1.

The catalyst of choice, C_2-symmetric bis(picolinamide) **1**,[14] was employed in the reduction of other differently substituted imines. It was able to efficiently promote the synthesis of chiral *N*-phenylamines derived from 2-acetonaphtone and methyl-4-trifluoromethylphenyl ketone with an enantioselectivity that is higher than 80% (Entries 8 and 9).

Table 1. Enantioselective catalytic reduction in DCM at 0 °C of *N*-aryl imines **6**–**10**.

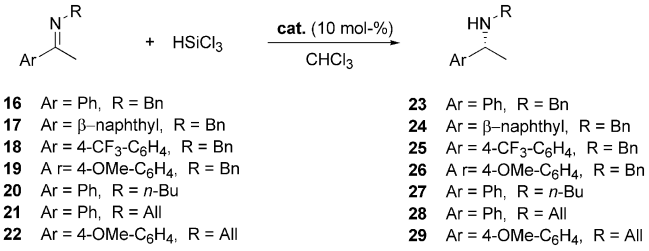
Entry	Catalyst	Imine	Yield[a] [%]	*ee*[b] [%]
1	**1**	**6**	99	75
2[c]	**1**	**6**	99	67
3[d]	**1**	**6**	93	70
4	**2**	**6**	99	75
5	**3**	**6**	99	<5
6	**4**	**6**	95	55
7	**5**	**6**	25	45
8	**1**	**7**	99	81
9	**1**	**8**	98	80
10	**1**	**9**	99	83
11	**1**	**10**	99	81

[a] Yields determined after chromatographic purification, reaction time 12 h. [b] Enantiomeric excess determined by HPLC on chiral stationary phase. [c] Reaction run in chloroform. [d] Reaction run with 1 mol-% catalyst.

More importantly, catalyst **1** also reduced *N*-2-methoxyphenyl and *N*-4-methoxyphenyl imines **9** and **10** in quantitative yields and up to 83% enantioselectivity, which led to products that are immediate precursors of the corresponding primary amine (Entries 10 and 11).

On the basis of these positive results, catalyst **1** was tested in the more challenging reduction of *N*-benzyl and *N*-alkyl ketimines (Scheme 2). The results obtained in the trichlorosilane addition to *N*-benzyl imines of methyl aryl ketones are collected in Table 2. The reduction of the *N*-benzyl imine of acetophenone **16** was selected as the reaction model in order to find the best experimental conditions. By performing the trichlorosilane addition in chloroform at 0 °C in the presence of 10 mol-% of catalyst **1**, the product was isolated in 70% yield and 83% enantioselectivity (Entry 1, Table 2). The enantiomeric excess was further increased to 87% by working in dichloromethane (Entry 2, Table 2). The result is extremely interesting in view of the possibility of removing the benzyl group by selective

hydrogenation, which opens the route for the preparation of enantiomerically enriched primary amines.[15] By lowering the reaction temperature, the stereoselectivity did not improve. It must also be noted that catalyst **2**, which features one pyridinecarboxyamide group only, was able to promote the reaction in 90% yield and 83% *ee* (Table 2, Entry 5).



16 Ar = Ph, R = Bn
17 Ar = β–naphthyl, R = Bn
18 Ar = 4-CF_3-C_6H_4, R = Bn
19 A r= 4-OMe-C_6H_4, R = Bn
20 Ar = Ph, R = *n*-Bu
21 Ar = Ph, R = All
22 Ar = 4-OMe-C_6H_4, R = All

23 Ar = Ph, R = Bn
24 Ar = β–naphthyl, R = Bn
25 Ar = 4-CF_3-C_6H_4, R = Bn
26 A r= 4-OMe-C_6H_4, R = Bn
27 Ar = Ph, R = *n*-Bu
28 Ar = Ph, R = All
29 Ar = 4-OMe-C_6H_4, R = All

Scheme 2.

Table 2. Enantioselective reduction of *N*-benzyl imines **16**–**19** promoted by catalyst **1**.

Entry	Solvent	*T* [°C]	Imine	Yield[a] [%]	*ee*[b] [%]
1	$CHCl_3$	0	**16**	70	82
2	DCM	0	**16**	**99**	**87**
3	$CHCl_3$	–20	**16**	43	77
4	DCM	–20	**16**	98	78
5[c]	DCM	0	**16**	90	83
6[d]	DCM	0	**16**	90	80
7	DCM	0	**17**	99	77
8	DCM	0	**18**	99	81
9	DCM	0	**19**	**99**	**87**

[a] Yields determined after chromatographic purification, reaction time 12 h. [b] Enantiomeric excess determined by HPLC on chiral stationary phase. [c] Reaction run with catalyst **2**. [d] Reaction run with 1 mol-% catalyst.

It is worth noting that it was possible to further decrease the catalyst loading. By performing the reduction in the presence of only 1 mol-% of catalyst **1**, it was possible to isolate the product in 90% yield and 80% *ee*.

The reduction of *N*-benzyl imine derived from methyl aryl ketones bearing either electron-withdrawing or electron-donating groups was accomplished; for example, the reaction of trichlorosilane reaction with imine **17** obtained from 2-acetonaphthone afforded the product in quantitative yield and 77% *ee*. With catalyst **1**, chiral amine **25** derived from the imine of 4-trifluoromethyl acetophenone **18** was formed in 99% yield and 81% enantioselectivity, while it performed even better in the reduction of the imine of 4-methoxyacetophenone **19** to give amine **26** in 99% yield and 87% *ee* (Entries 7–9, Table 2).

Finally, the methodology was further extended to *N*-alkyl and *N*-allyl derivatives (see Table 3). The reaction of the *N*-butyl imine of acetophenone **20** at 0 °C was investigated; as in the previous case of *N*-benzyl imine **16**, catalyst **1** performed better in dichloromethane than in chloroform, which led to the chiral amine **27** in quantitative yield and 85% enantioselectivity (Entries 1 and 2, Table 3). Lower temperatures did not help the reaction. Further, with this substrate, C_1-symmetric catalyst **2** promoted the reaction, but in lower yield and stereoselectivity (Table 3, Entry 5).

Table 3. Enantioselective reduction of *N*-alkyl imines **20**–**22** promoted by catalyst **1**.

Entry	Solvent	*T* [°C]	Imine	Yield[a] [%]	*ee*[b] [%]
1	$CHCl_3$	0	**20**	98	73
2	DCM	0	**20**	**99**	**85**
3	$CHCl_3$	–20	**20**	98	66
4	DCM	–20	**20**	98	71
5[c]	DCM	0	**20**	45	75
6	DCM	0	**21**	97	71
7	DCM	0	**22**	**99**	**83**

[a] Yields determined after chromatographic purification, reaction time 12 h. [b] Enantiomeric excess determined by HPLC on chiral stationary phase. [c] Reaction run with catalyst **2**.

The reduction of *N*-allyl imines was also successfully accomplished at 0 °C in dichloromethane; the results were found to be dependent on the electronic features of the ketimine: while the *N*-allyl imine of acetophenone **21** reacted to afford the corresponding amine in 71% *ee*, imine **22** derived from 4-methoxyacetophenone was reduced to the chiral amine **29** in quantitative yield and 83% *ee*.

In conclusion, we have developed a very convenient and efficient methodology for the synthesis of chiral primary and secondary amines by trichlorosilane addition to ketimines; the low cost of the metal-free catalyst, which is easily prepared in one step only from commercially available compounds, the mild reaction conditions, and the general applicability of the catalyst to a wide variety of substrates are all positive features of this new family of organocatalysts. It is worth noting that the binaphthyldiamine-derived bis(picolinamide)s showed a remarkable and almost unprecedented activity in performing the reduction of *N*-aryl and *N*-benzyl and *N*-alkyl ketimines with up to 87%*ee*. Even if the level of stereoselection is slightly inferior to that obtained with the only other catalytic system reported for *N*-alkyl imine reduction so far,[9] the easier and straightforward preparation of bis(picolinoylamide) **1**, its availability in both enantiomeric forms, the low catalyst loading, the fact that the best performance was obtained at 0 °C without the need for lower temperatures are all characteristics that favorably compare with those of already known catalysts. Further studies aimed to explore the variation in the catalyst structure and to increase the enantioselectivity are currently underway and will be reported in due course.

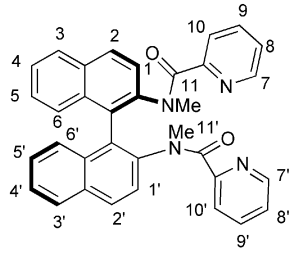
Experimental Section

All reactions were carried out in oven-dried glassware with magnetic stirring under a nitrogen atmosphere, unless otherwise stated. Dry solvents were purchased by Fluka and stored under nitrogen over molecular sieves (bottles with crown cap). Reactions were monitored by analytical thin-layer chromatography (TLC) by using silica gel 60 F_{254} pre-coated glass plates (0.25-mm thickness) and visualized by using UV light or phosphomolybdic acid. Proton NMR spectra were recorded on spectrometers operating at 200, 300 or 500 MHz, respectively. Proton chemical shifts are reported

in ppm (δ) with the solvent reference relative to tetramethylsilane (TMS) employed as the internal standard ($CDCl_3$ δ = 7.26 ppm). ^{13}C NMR spectra were recorded on 300 or 500 MHz spectrometers operating at 75 and 125 MHz, respectively, with complete proton decoupling. Carbon chemical shifts are reported in ppm (δ) relative to TMS with the respective solvent resonance as the internal standard ($CDCl_3$, δ = 77.0 ppm). Optical rotations were obtained on a polarimeter at 589 nm by using a 5-mL cell with a length of 1 dm. HPLC for *ee* determination was performed on Agilent 1100 instruments under the conditions reported below. Mass spectra (MS) were obtained with a hybrid quadrupole time-of-flight mass spectrometer equipped with an ESI ion source. Microwave-accelerated reactions were performed in a CEM Discover class S instrument.

Synthesis of the Catalysts – General Procedure: A stirred solution of the picolinic acid or its derivatives (1 mol equiv.) in thionyl chloride (1 mL/mmol substrate) was heated at reflux for 2 h. The solvent was then evaporated under vacuum, and the residue, dissolved in THF (2 mL) with a few drops of DMF, was added to a solution of chiral amino alcohol (1 mol equiv.) and TEA (3 mol equiv.) in THF. The reaction mixture was stirred for 12 h at reflux. The organic phase was quenched with an aqueous saturated solution of $NaHCO_3$ and brine. The organic phase was then dried with Na_2SO_4, filtered, and concentrated under vacuum to give the crude product. Purification by flash chromatography afforded the products.

Synthesis of Catalyst 1



***N*,*N*′-Dimethyl-(*R*)-1,1′-binaphthyldiamine-bis-2-pyridinecarboxyamide (1):** This catalyst was obtained (73% yield, 0.35 g) by the condensation of binaphthyldiamine (1 mmol, 0.28 g) with picolinoyl chloride (2 mmol, 0.28 g).

Rotamer 1: ^1H NMR (500 MHz, $CDCl_3$): δ = 8.57 (d, J = 2.7 Hz, 2 H, **7**, **7**′), 8.05 (d, J = 8.8 Hz, 2 H, **2**, **2**′), 7.95 (d, J = 8 Hz, 2 H, **3**, **3**′), 7.87 (d, J = 9, 2 Hz, **1**, **1**′), 7.72 (d, J = 7.8 Hz, 2 H, **10**, **10**′), 7.7 (t, 2 H, **9**, **9**′), 7.48 (t, J = 8.1 Hz, 2 H, **4**, **4**′), 7.29 (t, J = 6.8 Hz, 2 H, **5**, **5**′), 7.25 (t, 2 H, **8**, **8**′), 7.2 (d, 2 H, **6**, **6**′), 2.98 (s, 6 H, **11**′, **11**) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169 (2 C), 155.2 (2 C), 148.2 (2 C), 141.2 (2 C), 137.2 (2 C), 133.8 (2 C), 132.4 (2 C), 130.1 (2 C), 128.4 (2 C), 127.9 (2 C), 126.7 (2 C), 126.4 (2 C), 125.7 (2 C), 124.2 (2 C), 124 (2 C), 123.9 (2 C), 39.1 (2 C) ppm.

Rotamer 2: ^1H NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, J = 4.4 Hz, 2 H, **7**, **7**′), 7.83 (d, J = 8.8 Hz, 2 H, **3**, **3**′), 7.72 (d, J = 7.8 Hz, 2 H, **10**, **10**′), 7.60 (d, J = 8.7 Hz, 2 H, **2**, **2**′), 7.59 (t, 2 H, **9**, **9**′), 7.45 (t, J = 7.5 Hz, 2 H, **4**, **4**′), 7.29 (t, J = 6.8 Hz, 2 H, **5**, **5**′), 7.1 (t, 4 H, **8**, **8**′, **6**, **6**′), 6.93 (d, J = 8.8 Hz, 2 H, **1**, **1**′), 2.64 (s, 6 H, **11**, **11**′) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171 (2 C), 153.4 (2 C), 148.2 (2 C), 143.4 (2 C), 136 (2 C), 134.6 (2 C), 131.4 (2 C), 129.6 (2 C), 128.6 (2 C), 128.2 (2 C), 126.9 (2 C), 126.7 (2 C), 126.1 (2 C), 124.4 (2 C), 124 (2 C), 123.9 (2 C), 37.3 (2 C) ppm. IR (DCM): $\nu_{C=O}$ = 1650, 1458, 1380 cm^{-1}. $[\alpha]_D^{25}$ = +353.6 (solvent: DCM; c = 0.1 g/100 mL; λ = 589 nm). MS (ESI+): m/z = 523.6. $C_{34}H_{26}N_4O_2$ (522.21): calcd. C 78.14, H 5.01, N 10.72; found C 78.19, H 5.07, N 10.68.

Synthesis of Imines: In a typical experiment, the amine (1 equiv.) reacted in toluene with ketone (1 equiv.) in the presence of montmorillonite (250 mg for 5 mmol of reagent) in a microwave reactor (PW = 200 W; T = 130 °C; t = 4 h 30 min). The product was purified by fractional distillation.

Imine Reduction – General Procedure: The imine (1 mmol/equiv.) was added to a stirred solution of catalyst (0.1–0.01 mol-%/equiv. mmol) in the chosen solvent (2 mL). The mixture was then cooled to the chosen temperature, and trichlorosilane (3.5 mmol/equiv.) was added dropwise by means of a syringe. After stirring at the appropriate temperature, the reaction was quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (1 mL). The mixture was warmed to room temperature, and water (2 mL) and dichloromethane (5 mL) were added. The organic phase was separated, and the combined organic phases were dried with Na_2SO_4, filtered, and concentrated under vacuum at room temperature to afford the crude product. If necessary, the amine was purified by flash chromatography. Selected examples are given.

***N*-Benzyl-1-phenylethanamine (23):** The product was purified with a hexane/ethyl acetate mixture (8:2) as eluent. The ^1H NMR spectroscopic data are in agreement with those reported in the literature. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.24 (m, 10 H, Ar), 3.82 (q, J = 11.5 Hz, 1 H CH–N), 3.67, 3.60 (AB, J = 12.0 Hz, 2 H, N–CH_2), 1.57 (br. s, 1 H, NH), 1.37 (d, J = 11.5 Hz, 3 H, CH_3) ppm. The enantiomeric excess was determined by HPLC on a Chiralcel OD-H column (99:1 hexane/2-propanol; flow rate: 0.8 mL/min; λ = 210 nm): t_R = 7.8 min, t_S = 8.4 min.

***N*-(1-Phenylethyl)butan-1-amine (27):** The product was purified with a hexane/ethyl acetate mixture (8:2) as eluent. The ^1H NMR spectroscopic data are in agreement with those reported in the literature. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.3–7.1 (m, 5 H, Ph), 3.73 (q, J = 11.0 Hz, 1 H CH–N), 2.40 (m, 2 H, N–CH_2), 1.36 (m, 2 H, N–CH_2CH_2), 1.32 (d, J = 11.0 Hz, 3 H, CH_3), 1.19 (m, 2 H, CH_2CH_2), 0.79 (t, J = 9.0 Hz, 3 H, CH_3) ppm. The enantiomeric excess was determined by analysis of the acetamide obtained by reaction of the isolated amine with acetic anhydride at 25 °C for 12 h. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.4 (m, 5 H, Ph), 6.0 (q, J = 12.0 Hz, 1 H CH–N), 5.0* (q, J = 10.0 Hz, 1 H CH–N), 3.3–2.8 (m, 2 H, N–CH_2), 2.2 (s, 3 H, N-Ac), 2.1* (s, 3 H, N-Ac), 1.6 (d, J = 12.0 Hz, 3 H), 1.5* (d, J = 10.0 Hz 3 H), 1.4 (m, 2 H, N–CH_2CH_2), 1.2 (m, 2 H, CH_2CH_2), 0.8 (t, J = 12.0 Hz, 3 H) ppm. The enantiomeric excess was determined by HPLC on a Chiralcel IB column (9:1 hexane/2-propanol; flow rate: 0.8 mL/min; λ 210 nm): t_R = 8.5 min, t_S = 9.4 min.

***N*-{1-[4-(Methoxy)phenyl]ethyl}prop-2-en-1-amine (29):** The product was purified with a hexane/ethyl acetate mixture (9:1) as eluent. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.2 (d, J = 14.0 Hz, 2 H, H *meta* to OMe), 6.8 (d, J = 14.0 Hz, 2 H, H *ortho* to OMe), 5.9 (m, 1 H, $CH$$CH_2$), 5.1 (m, $CH$$CH_2$), 3.9 (m, 4 H, OMe and CHN), 3.1 (m, 2 H, NCH_2), 1.4 (d, J = 11.0 Hz, 3 H) ppm. The enantiomers of *N*–CF_3CO-**29** were analyzed by HPLC by using a chiral OD-H column (99:1 hexane/2-propanol; flow rate: 0.8 mL/min; λ = 254 nm); t_R = 10.6 min, t_S = 11.1 min.

Supporting Information (see footnote on the first page of this article): Synthesis and characterization of catalysts **2**–**5**, characterization of all the amines obtained by ketimine reduction, selected ^1H NMR and HPLC chromatograms of the chiral amines are presented.

Acknowledgments

Financial support by the Ministero dell' Istruzione, Università e ricerca (MIUR) – (Nuovi metodi catalitici stereoselettivi e sintesi stereoselettiva di molecole funzionali) is gratefully acknowledged.

[1] T. Okhuma, R. Noyori in *Comprehensive Asymmetric Catalysis, Suppl. 1* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, New York, **2004**.
[2] X. Verdaguer, U. E. W. Lange, S. L. Buchwald, *Angew. Chem. Int. Ed.* **1998**, *37*, 1103.
[3] For a special issue on hydrogenation and transfer hydrogenation see: M. J. Krische, Y. Sun (Editors), *Acc. Chem. Res.* **2007**, *40*, Issue 12.
[4] H.-U. Blaser, B. Pugin, F. Spindler, M. Thommen, *Acc. Chem. Res.* **2007**, *40*, 1240 and references cited therein. See also R. Kadyrov, T. H. Riermeier, *Angew. Chem. Int. Ed.* **2003**, *42*, 5472.
[5] Reviews: a) P. I. Dalko, L. Moisan, *Angew. Chem. Int. Ed.* **2004**, *43*, 5138; b) A. Dondoni, A. Massi, *Angew. Chem. Int. Ed.* **2008**, *47*, 4638. For reviews on supported organic catalysts see: c) A. Puglisi, F. Cozzi, M. Benaglia, *Chem. Rev.* **2003**, *103*, 3401–3430; d) F. Cozzi, *Adv. Synth. Catal.* **2006**, *348*, 1367–1390; e) M. Benaglia, *New J. Chem.* **2006**, *30*, 1525–1533.
[6] Reviews: a) S. J. Connon, *Org. Biomol. Chem.* **2007**, *5*, 3407; b) T. Akiyama, *Chem. Rev.* **2007**, *107*, 5744; c) M. Terada, *Chem. Commun.* **2008**, 4098.
[7] Reviews: a) M. Benaglia, S. Guizzetti, L. Pignataro, *Coord. Chem. Rev.* **2008**, *252*, 492; b) S. E. Denmark, G. L. Beutner, *Angew. Chem. Int. Ed.* **2008**, *47*, 1560.
[8] Selected references: a) A. V. Malkov, A. Mariani, K. N. MacDougal, P. Kočovský, *Org. Lett.* **2004**, *6*, 2253; b) A. V. Malkov, S. Stončius, P. Kočovský, *Angew. Chem. Int. Ed.* **2007**, *46*, 3722; c) A. V. Malkov, M. Figlus, P. Kočovský, *J. Org. Chem.* **2008**, *73*, 3985; d) Y. Matsumura, K. Ogura, Y. Kouchi, F. Iwasaki, O. Onomura, *Org. Lett.* **2006**, *8*, 3789; e) Z. Wang, X. Ye, S. Wei, P. Wu, A. Zhang, J. Sun, *Org. Lett.* **2006**, *8*, 999; f) D. Pei, Z. Wang, S. Wei, Y. Zhang, J. Sun, *Org. Lett.* **2006**, *8*, 5913; g) D. Pei, Y. Zhang, S. Wei, M. Wang, J. Sun, *Adv. Synth. Catal.* **2008**, *350*, 619; h) P. Wu, Z. Wang, M. Cheng, L. Zhou, J. Sun, *Tetrahedron* **2008**, *64*, 11304; i) H. Zheng, J. Deng, W. Lin, X. Zhang, *Tetrahedron Lett.* **2007**, *48*, 7934; j) F.-M. Gautier, S. Jones, S. J. Martin, *Org. Biomol. Chem.* **2009**, *7*, 229; k) A. V. Malkov, M. Figlus, S. Stoncius, P. Kocovský, *J. Org. Chem.* **2007**, *72*, 1315–1325; l) C. Baudequin, D. Chaturvedi, S. B. Tsogoeva, *Eur. J. Org. Chem.* **2007**, 2623–2629; m) L. Zhou, Z. Wang, S. Wei, J. Sun, *Chem. Commun.* **2007**, 2977–2979. For the first report where picolinamides were used as catalysts see: n) F. Iwasaki, O. Onomura, K. Mishima, T. Kanematsu, T. Maki, Y. Matsumura, *Tetrahedron Lett.* **2001**, *42*, 2525.
[9] C. Wang, X. Wu, L. Zhou, J. Sun, *Chem. Eur. J.* **2008**, *14*, 8789.
[10] For a preliminary report on chiral diamine-derived Lewis bases in ketimine reductions see: S. Guizzetti, M. Benaglia, F. Cozzi, S. Rossi, G. Celentano, *Chirality* **2009**, *21*, 233.
[11] The compound was easily prepared in a two steps, one purification only procedure in 90% yield, see: M. C. Mimmi, M. Gullotti, L. Santagostini, R. Pagliarin, L. De Gioia, E. Monzani, L. Casella, *Eur. J. Inorg. Chem.* **2003**, 3934.
[12] S.Guizzetti, M. Benaglia, European Patent Application No. EP07023240.0, September 22, **2008**.
[13] The use of the bisbenzamide of the 1,1′-binaphthyl diamine as organocatalyst led to the formation of the chiral amine in only 20% yield and with no stereoselectivity, as clear demonstration of the fundamental role of the picolinamide moiety to guarantee high chemical and stereochemical efficiency of the catalyst.
[14] The introduction of a substituent in the 3 or 6 position of the pyridine ring decreased the stereochemical efficiency of the catalyst, while substitution in the 4 position seems not to have any remarkable effect.
[15] For selective debenzylation reactions see: M. Kanai, M. Yasumoto, Y. Kuriyama, K. Inomiya, Y. Katsuhara, K. Higashiyama, A. Ishii, *Org. Lett.* **2003**, *5*, 1007.

Received: May 11, 2009
Published Online: June 24, 2009

