DOI: 10.1002/adsc.200600304

Enantioselective Hydrogenation of *N*-Acetyldehydroamino Acids over Supported Palladium Catalysts

György Szöllősi,[a,*] Emese Szabó,[b] and Mihály Bartók[a,b]

[a] Organic Catalysis Research Group of the Hungarian Academy of Sciences, University of Szeged, Department of Organic Chemistry, 6720 Szeged, Dóm tér 8, Hungary
Fax: (+36)-62-544-200; e-mail: szollosi@chem.u-szeged.hu
[b] University of Szeged, Department of Organic Chemistry, Dóm tér 8, 6720 Szeged, Hungary

Received: June 26, 2006

Abstract: The enantioselective hydrogenation of two *N*-acetyldehydroamino acids over *Cinchona* alkaloid-modified, supported palladium catalysts has been studied. Moderate enantioselectivities, up to 36%, were obtained in the hydrogenation of 2-acetamidocinnamic acid over cinchonidine-modified Pd/TiO_2 under low hydrogen pressure. Increase in the pressure or use of benzylamine as additive led to a gradual decrease in the enantiomeric excess and eventually inversion of the sense of the enantioselectivity. On the contrary, the optical purity of the product resulting from the hydrogenation of 2-acetamidoacrylic acid was significantly increased by addition of benzylamine to the reaction mixture. Enantiomeric excess values up to 58% and 60% were obtained over Pd/Al_2O_3 modified by cinchonidine and cinchonine, respectively. These optical purities are the best obtained in the hydrogenation of dehydroamino acid derivatives over chirally modified heterogeneous metal catalysts.

Keywords: *N*-acetyldehydroamino acid; *Cinchona* alkaloids; enantioselectivity; heterogeneous catalysis; hydrogenation; palladium catalyst

Introduction

The enantioselective catalytic hydrogenations of prochiral unsaturated carboxylic acids are among the simplest methods for the production of optically enriched chiral carboxylic acids and their derivatives.[1] Although, for these purposes the most widely used catalysts are chiral homogeneous metal complexes,[1,2] the recent developments published on the heterogeneous enantioselective hydrogenation of some substituted α-phenylcinnamic acids over *Cinchona* alkaloid-modified, supported palladium catalysts makes this latter method an attractive potential alternative.[3,4] Over 90% enantiomeric excess (*ee*) could be obtained by a proper choice of the catalyst and use of benzylamine (**1**) as additive.[4] However, both the *ee*[5,6] and the effect of **1** were found to be highly dependent on the substrate structure, the largest increase in the *ee* induced by the use of **1** was observed in the hydrogenation of itaconic acid.[7]

Following the early results obtained in the hydrogenation of α,β-unsaturated acids, several attempts were published on the extension of the scope of the *Cinchona*-modified, supported palladium catalytic system.[8,9] These attempts also included hydrogenations of the C=N group leading to amino acid derivatives, however, only low *ee* could be obtained.[10] Recently, special attention has been paid to the enantioselective hydrogenation of the C=C group in dehydroamino acid derivatives, due to the high importance of the production of optically pure amino acids.[11–14] The hydrogenation of 2-acetylaminocinnamic acid and 2-benzoylaminocinnamic acid led to nearly racemic product over cinchonidine-modified, supported Pd catalysts,[11] and only low *ee*, up to 24%, were obtained in the hydrogenation of dehydroamino acid esters.[12,13]

In a recent report the enantioselective hydrogenation of several *N*-benzoyldehydroamino acids has been attempted and for the first time the effect of equivalent amounts of an achiral base additive such as triethylamine has been studied.[14] Although, in most of these reactions low substrate/modifier molar ratios were used, an *ee* of 26% has been reached only in the hydrogenation of *N*-benzoyl-2-cyclohexylideneglycine, in the case of the other substrates lower values were obtained.[14] The successful use of **1** as additive in the enantioselective hydrogenation of α-phenylcinnamic acid,[15] several aliphatic α,β-unsaturated acids and itaconic acid,[7] encouraged us to attempt the application of this method of increasing the enantioselectivity in the hydrogenation of two *N*-acetyldehydroamino acids, that is, 2-acetamidocinnamic acid (**2**) and 2-acetamidoacrylic acid (**3**). The results of

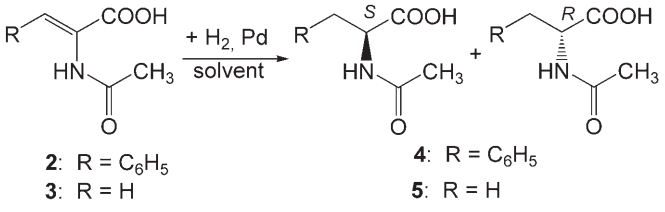
these hydrogenations are summarized in the present report.

Results and Discussion

The hydrogenation of **2** has already been studied over Pd catalysts in presence of *Cinchona* alkaloids, however, only without basic additives.[11] As a second test molecule we used the α-substituted acrylic acid **3**, which has not yet been studied in this catalytic system and has a terminal olefinic bond, similar to itaconic acid. The hydrogenation of **2** and **3** results in the formation of the corresponding *N*-acetyl-α-amino acids: *N*-acetylphenylalanine (**4**) and *N*-acetylalanine (**5**), as shown in Scheme 1.

The *ee* values obtained in the hydrogenation of **2** over cinchonidine (**6**)-modified Pd/Al_2O_3 under different pressures in the absence and in presence of an equivalent amount of **1** are presented in Figure 1. In contrast to the published results,[11] we have obtained enantioselection even in the absence of **1**, yet the highest *ee* value under atmospheric H_2 pressure was only 13% in favour of the *R* enantiomer. By increasing the pressure the *ee* decreased and interestingly under higher pressure (5 MPa) a small, but reproducible excess of the *S* enantiomer was obtained. An even more striking effect of the H_2 pressure was observed when the hydrogenations were carried out in the presence of one equivalent of **1**. Thus, in the hydrogenation under 0.1 MPa the *ee* was slightly increased by the presence of **1**, while under higher pressures again the opposite enantiomer was formed in excess, reaching an *ee* of 8% in favour of (*S*)-**4**. As shown by the values in Figure 1, the initial rates decreased as an effect of the addition of **1**.

Several examples of inversion of the enantioselectivity have been reported in the hydrogenation of activated ketones over *Cinchona*-modified Pt catalysts. These reports showed that the extent of the hydrogenation,[16] a change in the substituents on the C-9 of the modifier[17] or a simple change in the solvent[18] may cause changes in the direction of the enantioselection. Inversion was also observed over palladium catalysts in the hydrogenation of pyruvic acid esters.[19] Recently, the first report on inversion of the



Scheme 1. Hydrogenation of *N*-acetyldehydroamino acids over palladium catalyst.

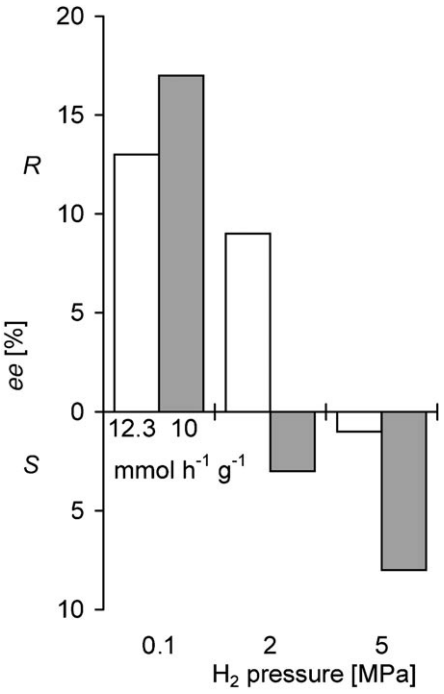


Figure 1. Enantiomeric excesses in the hydrogenation of 2-acetamidocinnamic acid (**2**) over Pd/Al_2O_3. *Reaction conditions*: 25 mg catalyst, 3 mL methanol, 0.05 mmol modifier **6**, 0.5 mmol **2**, 295 K; white columns: without addition of **1**; dark columns: using 0.5 mmol **1** (initial rates under the columns).

enantioselectivity in the heterogeneous catalytic hydrogenation of the C=C bond has been described.[13] In the hydrogenation of the methyl ester of **2** over *Cinchona*-modified Pd/Al_2O_3 an increase in the concentration of the modifier led to an inversion of the enantioselectivity.

Our present study is the first that reports such inversion in the hydrogenation of an α,β-unsaturated carboxylic acid. Furthermore, it has never been reported that changes in the H_2 pressure may lead to inversion of the enantioselectivity, which may be even more amplified by the presence of an equivalent amount of an achiral additive such as **1**. One should not neglect that this phenomenon was observed only in the case of α-acetamidocinnamic acid (present work) and its methyl ester,[13] although the H_2 pressure dependence has been studied for α,β-unsaturated carboxylic acids of various structures.[6,20,21] In a first approach, this shows that the α-acetamido group of the unsaturated acid is necessary to observe this effect.

Using a 5% Pd/TiO_2 catalyst successfully applied in the hydrogenation of α-phenylcinnamic acid,[22] we have obtained the results presented in Table 1.

The hydrogenation under 0.1 MPa H_2 pressure using **6** as modifier led to the highest *ee* (36%) in the hydrogenation of an α-acetamido-α,β-unsaturated car-

Table 1. Hydrogenation of **2** over 5% Pd/TiO_2 catalyst.[a]

Entry	Modifier	Additive	p H_2 [MPa]	Ri[b] [mmol h^{-1} g^{-1}]	*ee*[c] [%]
1	-	-	0.1	36.0	-
2	**6**	-	0.1	2.1	36 (*R*)
3	**6**	-	5	5.3	5 (*S*)
4	**6**	**1**	0.1	1.5	5 (*R*)
5	**6**	**1**	5	4.4	6 (*S*)
6[d]	**6**	-	0.1	5.9	5 (*R*)
7	**7**	-	0.1	2.8	10 (*S*)
8	**7**	**1**	0.1	1.1	4 (*R*)
9	**8**	-	0.1	4.3	2 (*R*)
10	**9**	-	0.1	4.9	0
11[e]	**6**	-	0.1	2.2	35 (*R*)

[a] *Reaction conditions:* 50 mg catalyst, 3 mL methanol, 0.05 mmol modifier, 0.5 mmol **2**, 0.5 mmol **1**.
[b] Initial rate (see Experimental Section).
[c] Configuration of the excess enantiomer in parenthesis.
[d] DMF (2.5 vol% water) was used as solvent.
[e] 100 mg catalyst, 5 mL methanol, 0.1 mmol **6**, 2 mmol **2**, 95% conversion.

Table 2. Hydrogenation of **3** over **6**-modified Pd/Al_2O_3.[a]

Entry	Additive	pH_2 [MPa]	Ri[b] [mol h^{-1} g^{-1}]	*ee*[c] [%]
1	-	0.1	0.26	2 (*S*)
2	-	2	1.61	6 (*S*)
3	-	5	3.45	9 (*S*)
4[d]	-	5	4.21	-
5	**1**	0.1	0.19	29 (*S*)
6	**1**	2	1.23	54 (*S*)
7	**1**	5	2.70	56, 58[e] (*S*)

[a] *Reaction conditions:* 25 mg catalyst, 3 mL methanol, 0.05 mmol **6**, 0.5 mmol **3**, 0.5 mmol **1**.
[b] Initial rate (see Experimental Section).
[c] Configuration of the excess enantiomer in parenthesis.
[d] Hydrogenation without modifier.
[e] Hydrogenation at 275 K.

boxylic acid over a supported metal catalyst, and a more than one magnitude decrease in the initial rate. The *ee* value decreased significantly on changing the solvent from methanol to *N*,*N*-dimethylformamide (DMF) or by using **1** as additive. A lower *ee* value was also obtained with cinchonine (**7**) as modifier, in accordance with the results usually obtained in the enantioselective hydrogenations over *Cinchona*-modified catalysts.[23,24] As expected the major enantiomer formed in presence of **7** had the opposite absolute configuration as obtained in presence of **6**, and the addition of **1** also resulted in inversion of the enantioselectivity. Significantly decreased values were obtained when the C-6′-methoxy-substituted *Cinchona* alkaloids quinine (**8**) or quinidine (**9**) were used; in the presence of the latter the racemic product was obtained. Decreased *ee* values were also obtained in the hydrogenation of α-phenylcinnamic acid using **8** or **9** as chiral source,[24] possibly due to the steric hindrance of the C-6′-methoxy group.

To sum up, the highest *ee* value in the hydrogenation of **2** was obtained in methanol over Pd/TiO_2 under low (0.1 MPa) H_2 pressure using **6** as modifier and without addition of **1**. We have also carried out the reaction by increasing four times the substrate amount and the results were similar with that obtained on the smaller scale (see Entry 11, Table 1). Refluxing this product overnight in methanol in presence of concentrated H_2SO_4 resulted in the formation of (*R*)-phenylalanine methyl ester isolated in 90% yield and 35% optical purity.

Intrigued by the still open question as to whether solely the α-acetylamino group is responsible for the interesting inversion of the enantioselectivity experienced in the hydrogenation of **2** we then chose **3** (see Scheme 1) as the next substrate.

Hydrogenation of **3** over **6**-modified Pd/Al_2O_3 in the absence of **1** led to poor *ee* values, a small increase in the *ee* was obtained by increasing the H_2 pressure, however, even under 5 MPa H_2 only 9% *ee* was obtained in favour of (*S*)-**5** (see Table 2). As expected the initial hydrogenation rate of **3** was three orders of magnitude larger than that of **2**, due mainly to the bulky β-substituent of the latter. Only a small decrease in the initial rate was observed as an effect of the modification with **6**, contrary to the high decrease of more than one magnitude detected in the hydrogenation of **2**. Thus, the lack of substituents in the β position of α-acetamido-α,β-unsaturated acids leads to only a small decrease in the hydrogenation rate in the presence of *Cinchona* alkaloids and to poor *ee* values. Using molar amounts of **1** as achiral additive led to a surprisingly high increase in the *ee*, up to 58% under 5 MPa H_2 at 275 K. The use of **1** was also accompanied by a moderate decrease in the initial rate. Even more intriguing were the results obtained in the hydrogenation of **3** over **7**-modified catalysts, shown in Table 3.

The presence of **7** reduced even less the rate of hydrogenation than **6** (see Entries 1 and 2, Table 3) and the obtained *ee* was very low even under 5 MPa H_2 pressure. As expected, the opposite enantiomer was formed in excess compared to the reaction over the **6**-modified catalyst. In presence of **1** the *ee* was even slightly higher when modifier **6** was replaced with **7**. Thus, it was possible to obtain the unnatural *R* enantiomer of **5** in 60% *ee*, a value which exceeds any result published on the enantioselective hydrogenation of dehydroamino acid derivatives over chirally modified heterogeneous metal catalysts. A similar *ee* (55%) result from the hydrogenation over Pd/TiO_2 under otherwise identical reaction conditions, while

Table 3. Hydrogenation of **3** over **7**-, **8**- or **9**-modified catalysts.[a]

Entry	Modifier	Additive	Ri[b] [mol $h^{-1} g^{-1}$]	*ee*[c] [%]
1	-	-	4.21	-
2	**7**	-	4.08	3 (*R*)
3	**7**	**1**	3.34	60 (*R*)
4[d]	**7**	**1**	2.03	55 (*R*)
5[e]	**7**	**1**	n.d.	35 (*R*)
6[f]	**7**	-	0.79	12 (*R*)
7[f]	**7**	**1**	n.d.	8 (*R*)
8	**8**	**1**	2.31	12 (*S*)
9	**9**	**1**	2.51	5 (*R*)
10[g]	**7**	**1**	n.d.	56 (*R*)

[a] *Reaction conditions:* 25 mg Pd/Al_2O_3, 3 mL methanol, 0.05 mmol modifier, 0.5 mmol **3**, 0.5 mmol **1**, pH_2 5 MPa.
[b] Initial rate (see Experimental Section), n.d. = not determined.
[c] Configuration of the excess enantiomer in parenthesis.
[d] Hydrogenation over Pd/TiO_2.
[e] Reaction under 10 MPa H_2 pressure.
[f] DMF (2.5 vol% water) was used as solvent.
[g] 50 mg catalyst, 5 mL methanol, 0.2 mmol **7**, 2 mmol **3**, 2 mmol **1**.

increase in the H_2 pressure to 10 MPa brought down the *ee* to 35%. Although, in the absence of **1** a promising increase in the *ee* was obtained by changing the solvent to DMF (2.5 vol% H_2O), the use of the additive **1** had an opposite effect as in methanol, decreasing the *ee* to 8%. The good enantioselectivity was also maintained at the 2 mmol scale, proving that the method may be used on a larger scale (see Entry 10, Table 3). This product was transformed in (*R*)-*N*-acetylalanine methyl ester using $SOCl_2$ in methanol,[10b] the ester isolated in 94% yield and 55% optical purity.

In the hydrogenations of **3** over **6-** or **7**-modified catalysts, no inversion in the enantioselectivity occurred as an effect of changes in the H_2 pressure, this phenomenon seems to be a special case, characteristic of α-acetamido-β-phenyl-α,β-unsaturated carboxylic acids and esters. Obviously the inversion is related with the presence of the α-acetamido group complemented with the steric effect of the β-phenyl substituent. Interestingly the configurations of the products obtained in excess in the hydrogenation of **2** and **3** using the same modifier under low H_2 pressures were opposite. This observation is in accordance with our suggestion on the role of the β-substituents in determining the sense of the chiral induction in the hydrogenation of α,β-unsaturated acids over *Cinchona*-modified palladium.[6] Modifiers **8** and **9** gave low *ee* in the presence of **1** and the initial hydrogenation rate of **3** decreased as compared with the rates obtained over **6**- and **7**-modified catalysts.

The role of **1** in the enantioselective hydrogenation of unsaturated α,β-unsaturated carboxylic acids over *Cinchona*-modified palladium is still unclear. The only substrate for which hydrogenation in presence of **1** has been studied in more detail was α-phenylcinnamic acid.[15] Thus, the results obtained in our present work complement the few observations published until now. The results of our present study showed that the effect of **1** on the hydrogenation of α-acetamido-α,β-unsaturated acids was different as compared with that on the hydrogenation of α-phenylcinnamic acid. Furthermore, though increase in the *ee* was found in the hydrogenation of several aliphatic α,β-unsaturated carboxylic acids,[7] up to now this increase was high only in the reaction of two compounds bearing a terminal C=C group, that is, itaconic acid[7] and 2-acetamidoacrylic acid (present work).

Conclusions

The first example of the heterogeneous catalytic hydrogenation of an *N*-acylated dehydroamino acid with good enantioselectivity over a chirally modified metal catalyst has been described. The hydrogenation of 2-acetamidocinnamic acid resulted in (*R*)-*N*-acetylphenylalanine of 36% optical purity over cinchonidine-modified Pd/TiO_2 under low H_2 pressure. Increasing the pressure led to an interesting inversion in the sense of the enantioselectivity which was more pronounced if benzylamine was used as additive. In the hydrogenation of 2-acetamidoacrylic acid the enantioselectivities were significantly increased by using benzylamine as achiral base under elevated H_2 pressures. Thus, it was possible to obtain (*R*)-*N*-acetylalanine in 60% optical purity using cinchonine as chiral modifier and 5 MPa H_2 pressure. The results presented in this report broaden the range of unsaturated carboxylic acid derivatives which can be hydrogenated enantioselectively with the *Cinchona*-modified palladium catalytic system.

Experimental Section

Materials

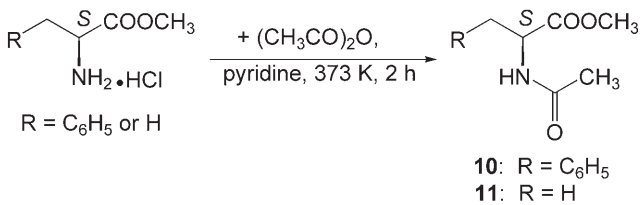
Benzylamine (**1**, ≥99.5%), 2-acetamidocinnamic acid (**2**, ≥99%), 2-acetamidoacrylic acid (**3**, ≥99%), cinchonidine (**6**, ≥98%), cinchonine (**7**, ≥98%), quinine (**8**, ≥98%) and quinidine (**9**, ≥98%) were commercial products (Fluka) and were used as received. The catalysts used were: commercial alumina-supported Pd catalyst (5% Pd/Al_2O_3, Engelhard 40692, 0.21 Pd dispersion[25]) and 5% Pd/TiO_2 (TiO_2, Degussa P-25) prepared by a deposition-precipitation method according to a described procedure.[26] Commercial high purity solvents were used without purification.

Catalytic Hydrogenations and Product Analysis

Hydrogenations were carried out using a conventional glass hydrogenation apparatus or a stainless steel autoclave equipped with a glass liner and an automatic pressure recorder. In a typical run the catalyst was pretreated by stirring the given amount of catalyst in the solvent for 0.5 h under H_2 at 297 K followed by addition of the modifier, benzylamine (when used) and the substrate. The reactor was flushed and filled with H_2 to the specified pressure and the reaction was started by stirring (1000 rpm) the slurry. The H_2 consumption was monitored and recorded, after the gas uptake ceased the catalyst was filtered and the solution was prepared for analysis.

The *N*-acetylamino acids resulting from the hydrogenations were identified by GC-MS (Agilent Techn. 6890N GC-5973 MSD) analysis. The initial rates were calculated at $15\pm2\%$ conversions from the H_2 uptake curves. For determination of the conversions and selectivities including the *ee*, the products were transformed in methyl esters using diazomethane ethereal solution. Unless otherwise mentioned complete conversion and no significant side-products were obtained. The corresponding methyl esters were identified by GC-MS analysis and by comparison with products obtained from commercial amino acid derivatives. Conversions and *ee*s were determined by GC analysis using HP-5890 II GC-FID and Permabond®-L-Chirasil-Val (25 m × 0.25 mm, Macherey–Nagel) chiral capillary column. The enantiomeric excess (*ee*%) was calculated with the formula $ee\% = 100 \times |E_1 - E_2|/(E_1 + E_2)$, where E_1 and E_2 are the concentrations of the corresponding product enantiomers. The absolute configurations of the excess products were determined by comparison of the retention times of the products with the retention times of compounds prepared from commercially available optically pure substances. The optically pure methyl esters (**10** and **11**) were prepared by acylation of L-phenylalanine methyl ester hydrochloride (≥99%, Fluka) and L-alanine methyl ester hydrochloride (≥99%, Fluka) using acetic anhydride/pyridine as shown in Scheme 2.

The isolated products (see Entry 11, Table 1 and Entry 10, Table 3) were identified by ^{1}H NMR analysis (Bruker AVANCE DRX-500 spectrometer), their spectra were identical with those previously published.[27] Their optical purity was determined by optical rotation measurements (Polamat A polarimeter) and using literature values.[27]



Scheme 2. Preparation of product methyl esters with known absolute configurations.

Acknowledgements

Financial support by the Hungarian National Science Foundation (OTKA Grants TS 044690 and T 048764) is highly appreciated. Gy. Sz. is grateful for the financial support of HAS through Bolyai János Research grant.

References

[1] a) H.-U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103–151; b) H.-U. Blaser, B. Pugin, F. Spindler, *J. Mol. Catal. A: Chem.* **2005**, *231*, 1–20.
[2] W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029–3069.
[3] T. Sugimura, J. Watanabe, T. Okuyama, Y. Nitta, *Tetrahedron: Asymmetry* **2005**, *16*, 1573–1575.
[4] Y. Nitta, J. Watanabe, T. Okuyama, T. Sugimura, *J. Catal.* **2005**, *236*, 164–167.
[5] K. Borszeky, T. Mallat, A. Baiker, *Tetrahedron: Asymmetry* **1997**, *8*, 3745–3753.
[6] Gy. Szöllősi, S. Niwa, T. Hanaoka, F. Mizukami, *J. Mol. Catal. A: Chem.* **2005**, *230*, 91–95.
[7] Gy. Szöllősi, T. Hanaoka, S. Niwa, F. Mizukami, M. Bartók, *J. Catal.* **2005**, *231*, 480–483.
[8] a) K. Borszeky, T. Mallat, A. Baiker, *Tetrahedron: Asymmetry* **1999**, *10*, 4781–4789; b) W.-R. Huck, T. Mallat, A. Baiker, *New J. Chem.* **2002**, 26, 6–8; c) M. Maris, W.-R. Huck, T. Mallat, A. Baiker, *J. Catal.* **2003**, *219*, 52–58; d) G. Fogassy, A. Tungler, A. Lévai, *J. Mol. Catal. A: Chem.* **2003**, *192*, 189–194; e) K. Szőri, Gy. Szöllősi, K. Felföldi, M. Bartók, *React. Kinet. Catal. Lett.* **2005**, *84*, 151–156.
[9] a) M. Studer, H.-U. Blaser, C. Exner, *Adv. Synth. Catal.* **2003**, *345*, 45–65; b) A. Tungler, É. Sípos, V. Háda, *Current Org. Chem.* **2006**, *10*, 1569–1583.
[10] a) K. Borszeky, T. Mallat, R. Aeschiman, W. B. Schweizer, A. Baiker, *J. Catal.* **1996**, *161*, 451–458; b) Gy. Szöllősi, I. Kun, M. Bartók, *Chirality* **2001**, *13*, 619–624.
[11] A. Tungler, Á. Fürcht, Zs. P. Karancsi, G. Tóth, T. Máthé, L. Hegedűs, Á. Sándi, *J. Mol. Catal. A: Chem.* **1999**, *139*, 239–244.
[12] H.-U. Blaser, H. Hönig, M. Studer, C. Wedemeyer-Exl, *J. Mol. Catal. A: Chem.* **1999**, *139*, 253–257.
[13] N. J. Colston, R. P. K. Wells, P. B. Wells, G. J. Hutchings, *Catal. Lett.* **2005**, *103*, 117–120.
[14] M. Gomes Jr., R. Hernández-Valdés, C. E. S. J. Marques, M. L. Bastos, D. A. G. Aranda, O. A. C. Antunes, *React. Kinet. Catal. Lett.* **2006**, *87*, 19–24.
[15] a) Y. Nitta, *Chem. Lett.* **1999**, 635–636; b) Y. Nitta, *Top. Catal.* **2000**, *13*, 179–185.
[16] M. von Arx, T. Mallat, A. Baiker, *Angew. Chem.* **2001**, *113*, 2369–2372; *Angew. Chem. Int. Ed.* **2001**, *40*, 2302–2305.
[17] a) H. U. Blaser, H. P. Jalett, W. Lottenbach, M. Studer, *J. Am. Chem. Soc.* **2000**, *122*, 12675–12682; b) S. Diezi, A. Szabo, T. Mallat, A. Baiker, *Tetrahedron: Asymmetry* **2003**, *14*, 2573–2577; c) R. Hess, A. Vargas, T. Mallat, T. Bürgi, A. Baiker, *J. Catal.* **2004**, *222*, 117–128; d) E. Toukoniitty, I. Busygin, R. Leino, D. Y. Murzin, *J. Catal.* **2004**, *227*, 210–216; e) S. Diezi, T.

Mallat, A. Szabó, A. Baiker, *J. Catal.* **2004**, *228*, 162–173; f) Sz. Cserényi, K. Felföldi, K. Balázsik, Gy. Szöllősi, I. Bucsi, M. Bartók, *J. Mol. Catal. A: Chem.* **2006**, *247*, 108–115.

[18] a) Gy. Szöllősi, Cs. Somlai, P. T. Szabó, M. Bartók, *J. Mol. Catal. A: Chem.* **2001**, *170*, 165–173; b) M. Bartók, M. Sutyinszki, K. Felföldi, Gy. Szöllősi, *Chem. Commun.* **2002**, 1130–1131; c) K. Felföldi, T. Varga, P. Forgó, M. Bartók, *Catal. Letters* **2004**, *97*, 65–70; d) M. Bartók, M. Sutyinszki, I. Bucsi, K. Felföldi, Gy. Szöllősi, F. Bartha, T. Bartók, *J. Catal.* **2005**, *231*, 33–40; e) M. Bartók, K. Balázsik, I. Bucsi, Gy. Szöllősi, *J. Catal.* **2006**, *239*, 74–82; f) K. Szőri, K. Balázsik, K. Felföldi, M. Bartók, *J. Catal.* **2006**, *241*, 149–154.

[19] P. J. Collier, T. J. Hall, J. A. Iggo, P. Johnston, J. A. Slipszenko, P. B. Wells, R. Whyman, *Chem. Commun.* **1998**, 1451–1452.

[20] K. Borszeky, T. Mallat, A. Baiker, *Catal. Lett.* **1996**, *41*, 199–202.

[21] Y. Nitta, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1971–1972.

[22] Y. Nitta, K. Kobiro, Y. Okamoto, *Stud. Surf. Sci. Catal.* **1997**, *108*, 191–198.

[23] M. Bartók, M. Sutyinszki, K. Balázsik, Gy. Szöllősi, *Catal. Lett.* **2005**, *100*, 161–167.

[24] Y. Nitta, A. Shibata, *Chem. Lett.* **1998**, 161–162.

[25] K. Borszeky, T. Bürgi, Z. Zhaohui, T. Mallat, A. Baiker, *J. Catal.* **1999**, *187*, 160–166.

[26] W.-J. Shen, M. Okumura, Y. Matsumura, M. Haruta, *Appl. Catal. A: Gen.* **2001**, *213*, 225–232.

[27] a) N. W. Fadnavis, N. Prabhakar Reddy, U. T. Bhalerao, *J. Org. Chem.* **1989**, *54*, 3218–3221; b) M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125–10138; c) I. A. Rivero, S. Heredia, A. Ochoa, *Synth. Commun.* **2001**, *31*, 2169–2175; d) K. Omata, S. Aoyagi, K. Kabuto, *Tetrahedron: Asymmetry* **2004**, *15*, 2351–2356.

