Tetrahedron: *Asymmetry* 20 (2009) 2403–2406

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Asymmetric organocatalyzed Michael addition of aldehydes to β-nitrostyrene in ionic liquids

Mária Mečiarová, Štefan Toma, Radovan Šebesta *

Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University in Bratislava, Mlynská dolina CH2, 84215 Bratislava, Slovakia

ARTICLE INFO

Article history:
Received 8 September 2009
Accepted 25 September 2009
Available online 28 October 2009

ABSTRACT

The addition of aliphatic aldehydes to β-nitrostyrene, catalyzed by proline-derived organocatalysts, proceeded well in various ionic liquids. Products were obtained in high yields and *syn*/*anti* diastereoselectivity. However, the enantioselectivity was only mediocre, even though some analogous reactions in organic solvents were highly enantioselective. We also evaluated the temperature effect on the diastereoselectivity as well as on the enantioselectivity of the Michael addition.

1. Introduction

The Michael addition of enolizable aldehydes to nitro olefins is an important carbon–carbon bond forming reaction. Its asymmetric variant, performed via enamine activation, is particularly appealing because enantiomerically enriched nitrocarbonyl compounds are valuable building blocks. A broad range of highly efficient organocatalyzed 1,4-additions of various types of carbonyl compounds have been described.[1–3] However, the use of aldehydes in this reaction is more challenging. The first report of a catalytic asymmetric Michael reaction of aliphatic aldehydes with nitro olefins was published by Barbas.[4,5] The addition of isovaleraldehyde to *trans*-β-nitrostyrene proceeded with high yields and diastereoselectivities, but with only moderate enantioselectivities when different diamines were used as catalysts. In THF, the most effective catalyst was (*S*)-2-(morpholinomethyl)pyrrolidine (78% yield, *syn*/*anti* 92/8, 72% ee). In contrast, reactions with L-proline and its analogues provided only trace amounts of the product. Later, several other diamine organocatalysts were reported. Alexakis used *N*-isopropyl-2,2′-bipyrrolidine (up to 99% yields, dr 95:5, and enantioselectivities up to 85% ee).[6,7] Chiral rigid 6-pyrrolidine-1-yl-1-aza-spiro[4,4]nonane was tested in the Michael addition of isovaleraldehyde to β-nitrostyrene. The reaction proceeded smoothly to give the adduct in 93% yield, but with poor diastereoselectivity (*syn*/*anti* 58:42) and moderate enantioselectivity [47% ee (*syn*) and 62% ee (*anti*)].[8] The utility of C2-symmetric bipiperidine and bimorpholine derivatives as organocatalysts for Michael addition of aldehydes to β-nitrostyrene was recently described. *N*-Isopropylbipiperidine was found to be the most efficient catalyst, affording products in high diastereo- (up to 94:6) as well as enantioselectivities (up to 96%).[9]

Recently, also other types of organocatalysts have been introduced for the Michael addition of aldehydes to nitroalkenes. Palomo described highly enantioselective *trans*-4-hydroxyprolylamides.[10] The optimum results (yields up to 90%, *syn*/*anti* ⩾99:1, and ee ⩾99%) were achieved when the reactions were carried out in CH_2Cl_2 at 0 °C to rt with 5–10 mol % of the catalysts. Jacobsen et al.[11] proved that chiral primary amine–thiourea catalysts were highly effective in the Michael addition of α,α-disubstituted aldehydes to nitro olefins in CH_2Cl_2/H_2O reaction system. Additions proceeded with 78–94% yields, *syn*/*anti* >50:1, and ee up to 99%.

Hayashi[12] described a highly enantioselective Michael addition of aldehydes to nitroolefins using diphenylprolinol silyl ethers as the catalysts. The reaction in hexane afforded products in yields of up to 85% with excellent diastereoselectivities (*syn*/*anti* up to 96:4) and enantioselectivities (99% ee). Silylation of prolinol dramatically improved the catalytic activity. On the other hand, the use of proline as a catalyst again led to low yield and enantioselectivity. Diphenylprolinol silyl ether and its derivatives were found to be effective for the Michael addition of acetaldehyde to nitroalkenes as well as in other solvents, such as hexane, toluene, water, THF, and acetonitrile.[13,14] Recyclable dendritic catalysts derived from diphenylprolinol were successfully used in the Michael addition of aldehydes to various nitrostyrenes in CCl_4 (up to 81% yields, *syn*/*anti* up to 95:5, up to 99% ee). The recovered catalysts could be re-used at least five times with only a slight loss of activity.[15]

Ionic liquids often serve as convenient media for many organocatalytic reactions.[16] In our laboratory, we have recently demonstrated that ionic liquid, [bmim]PF_6, was a suitable solvent for the organocatalyzed Michael addition of carbonyl compounds to nitroalkenes.[17] L-Proline was found to be the best catalyst and the reaction products were isolated in good yields (up to 91%) and with medium to high diastereoselectivities (*syn*/*anti* up to 95:5), although enantioselectivities were only mediocre (up to 58% ee). On the other hand, an ionic liquid with dissolved organocatalyst can be re-used several times with only small adverse

* Corresponding author. Tel.: +421 2 60296603; fax: +421 2 60296337.
E-mail address: sebesta@fns.uniba.sk (R. Šebesta).

0957-4166/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2009.09.025

effects on the reaction. L-Proline-derived *N*-toluenesulfonylcarboxamides also proved to be viable organocatalysts in the enantioselective Michael addition of isovaleraldehyde to nitrostyrene in various ionic liquids. The reaction rate and enantioselectivity were strongly dependent on the ionic liquid. Changes in enantioselectivity were attributed to both the cation and the anion of the ionic liquid.[18]

Several research groups have recently described an interesting thermal effect in organocatalyzed reactions. Hayashi et al.[19] observed that L-proline-catalyzed α-aminoxylation of cyclohexanone in CH_3CN proceeded with the same enantioselectivity both at −20 °C and rt. Similarly, Bräse[20] determined that L-proline-catalyzed α-amination of disubstituted aldehydes with azodicarboxylates in CH_3CN proceeded with high enantioselectivities both at 60 °C (84% ee) as well as at 80 °C (82% ee). Bolm[21] studied a three-component L-proline-catalyzed Mannich reaction in DMSO under microwave irradiation and found that the temperature increase from 45 to 75 °C did not affect the enantioselectivity of the reaction (98% ee). Similar observations were made by Kappe[22] for a two-component microwave Mannich reaction in DMSO. Alexakis[23] studied microwave organocatalytic aldol reactions in DMSO catalyzed by L-proline and observed that temperature between rt and 35 °C did not change the ee of the product. Cordova[24] described the organocatalyzed-Michael addition of diarylphosphines to cinnamic aldehyde in $CHCl_3$, in which the ee of the product went through a maximum at 4 °C and decreased when the temperature increased and decreased from this point. Brimble[25] made an extensive study of the aldol reaction in DMSO catalyzed by (*S*)-5-(2-pyrrolidinyl)-1*H*-tetrazole and found that increasing the temperature from rt to 35 °C or even to 50 °C led to only a small decrease in the enantioselectivity (90% ee via 85% ee to 78% ee), but yields raised considerably. Recently, Gong[26] described organocatalytic three-component domino reaction in $CHCl_3$ leading to enantiomerically enriched dihydropyridines which can be conveniently performed at elevated temperatures. Raising temperature from 25 °C to 50 °C resulted in higher enantioselectivity of the reaction from 19% to 82% ee. During our study of enantioselective aldol reactions catalyzed by *N*-toluenesulfonyl-L-proline amides in ionic liquids, we also noticed a non-typical temperature effect. Raising the reaction temperature from 20 to 50 °C led to increased chemical yields and acceleration of the reactions, but without significant effect on enantioselectivity.[27]

In this context, we decided to study the Michael addition of aliphatic aldehydes to β-nitrostyrene catalyzed by various easily accessible organocatalysts in ionic liquids. Furthermore, we evaluated the effect of temperature on diastereoselectivity and enantioselectivity of this reaction.

2. Results and discussion

We started our investigation with six common, commercially available or easily accessible, organocatalysts (Fig. 1).

To evaluate the influence of the reaction medium, we used five common ionic liquids with different cations and anions. The results of the Michael addition of isovaleraldehyde to β-nitrostyrene (Scheme 1) are shown in Table 1. Based on our previous studies,[18] 1.5 equiv of aldehyde was enough for appropriate course of the reaction. Additions catalyzed by L-proline **1**, *N*-toluenesulfonyl-L-proline amide **2**, *N*-(4-nitrophenyl)sulfonyl-L-proline amide **3**, and (*S*)-5-(2-pyrrolidinyl)-1*H*-tetrazole **4** proceeded well while adduct **9a** was isolated in moderate to excellent yields after 20–48 h at rt. High *syn*/*anti* selectivities (up to 98:2) were observed, but enantioselectivities were only moderate (up to 54% ee). Catalyst **2** afforded product **9a** with the opposite sense of asymmetric induction compared to other catalysts, when used in [emim]SO_4Et and

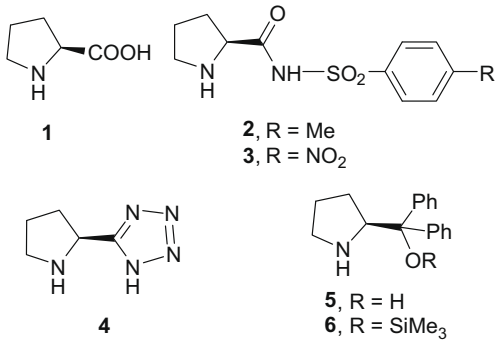
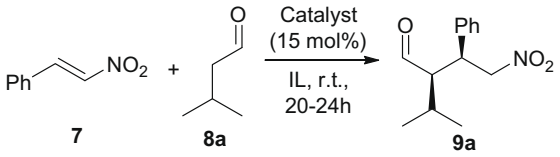


Figure 1.



Scheme 1.

Table 1
Michael addition of isovaleraldehyde **8a** to nitrostyrene **7**

Entry	Cat.	Ionic liquid	Yield[a] (%)	dr[b] (*syn*/*anti*)	ee[c] (%)
1	**1**	[bmim]BF_4	85	98:2	38
2	**1**	[bmim]BF_4[d]	51	94:6	33
3	**1**	[emim]SO_4Et	68	95:5	32
4	**1**	[bmim]CF_3SO_3	60	96:4	35
5	**1**	[bmim]$SO_4C_8H_{17}$	72	97:3	47
6	**1**	[bmpyr]$N(CN)_2$[g]	81	95:5	35
7	**2**	[emim]SO_4Et	80	92:8	38 (−)
8	**2**	[bmim]CF_3SO_3	68	95:5	36 (−)
9	**2**	[bmim]$SO_4C_8H_{17}$	98	95:5	45
10	**2**	[bmpyr]$N(CN)_2$[g]	96	94:6	42
11	**3**	[bmim]BF_4	38	96:4	14
12	**3**	[emim]SO_4Et	45	98:2	28
13	**3**	[bmim]CF_3SO_3	72	95:5	46
14	**3**	[bmim]$C_8H_{17}SO_4$	51	88:12	46
15	**3**	[bmpyr]$N(CN)_2$[g]	64	95:5	54
16	**4**	[bmim]BF_4	68	95:5	32
17	**4**	[bmim]BF_4[d]	36	97:3	45
18	**4**	[bmim]BF_4[e]	47[f]	97:3	36
19	**4**	[emim]SO_4Et	74	95:5	12
20	**4**	[emim]SO_4Et[d]	45	96:4	8
21	**4**	[bmim]CF_3SO_3	64	86:14	40
22	**4**	[bmim]$SO_4C_8H_{17}$	51	93:7	34
23	**4**	[bmpyr]$N(CN)_2$[g]	70	93:7	34
24	**5**	[bmim]BF_4	<5	60:40	nd
25	**5**	[bmim]CF_3SO_3	10[f]	94:6	nd
26	**6**	[bmim]BF_4	47	71:29	8
27	**6**	[emim]SO_4Et	21	75:25	53

[a] Isolated yields.
[b] Determined by ^{1}H NMR spectra.
[c] Reported values refer to the *syn* isomer and were determined by chiral HPLC.
[d] Reactions were performed with 5 mol % of the catalyst.
[e] Reactions were performed with 2.5 mol % of the catalyst.
[f] Reactions proceeded for 48 h.
[g] 1-Butyl-1-methylpyrrolidinium dicyanamide.

[bmim]CF_3SO_3 (Table 1, entries 7 and 8). This observation is probably due to an interaction of reaction intermediate with the cation and anion of the ionic liquid.[18,28]

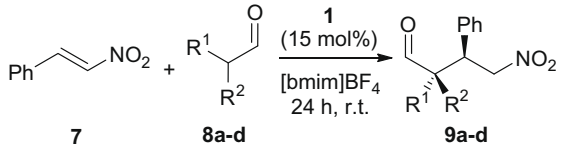
In organic solvents, such as THF, L-proline is ineffective in the Michael addition of isovaleraldehyde to nitrostyrene[4] as well as in aziridination of α,β-unsaturated aldehydes in $CHCl_3$.[29] On the other hand, in ionic liquids, L-proline is an active catalyst of the

reaction. The likely reason is the better solubility of L-proline in ionic liquids than in less polar organic solvents.

All reactions proceeded with 15 mol % of the catalyst. Lower catalyst loading did not affect the diastereoselectivity of the reaction (Table 1, entries 2, 17, and 20). Interestingly, with catalyst **4** in [bmim]BF_4 the reaction proceeded more selectively when 5 mol % catalyst loading was used. Product **9a** was isolated with 45% ee instead of 32% (15 mol % of **4**). Decreasing the catalyst loading further to 2.5 mol % led to lower enantioselectivities (36% ee, Table 1, entries 16, 17, and 18). Concentration of the reaction mixture had no influence on the reaction course.

(*S*)-α,α-Diphenyl-2-pyrrolidinemethanol **5** and (*S*)-α,α-diphenyl-2-pyrrolidinemethanol trimethylsilyl ether **6** are efficient catalysts for the Michael addition of aldehydes to nitroalkanes in organic solvents, such as hexane,[12] dioxane,[13] and CH_3CN.[14] We found that catalysts **5** and **6** are considerably less effective in ionic liquids. Catalyst **5** was inactive in [bmim]BF_4 as well as in [bmim]CF_3SO_3 when only small amounts of the adduct **9a** were isolated or detected by ^{1}H NMR (Table 1, entries 24 and 25). Somewhat better results were achieved with catalyst **6** (Table 1, entries 26 and 27), which afforded product **9a** in 47% yield in [bmim]BF_4 and 21% yield in [emim]SO_4Et, respectively. Diastereoselectivities were very similar 71:29 ([bmim]BF_4), and 75:25 ([emim]SO_4Et), although considerably lower than those of other catalysts. The reaction medium had a strong influence on enantioselectivities with this catalyst. Whilst in [bmim]BF_4, product **9a** was isolated with 8% ee, in [emim]SO_4Et it was isolated with 53% ee. Even more interesting is the comparison with apolar organic solvents, such as hexane, in which 99% ee was observed.[12] A possible explanation for this difference is the presence of trace amounts of imidazole in these ionic liquids, which can serve as achiral catalyst thus decreasing the enantioselectivity of the reaction.

L-Proline-catalyzed Michael additions of several other aliphatic aldehydes **8b**–**d** to β-nitrostyrene **7** in [bmim]BF_4 (Scheme 2) behaved similarly to the reaction of isovaleraldehyde **8a**. Products **9b**–**d** were isolated in high yields (77–85%), excellent *syn*/*anti* ratio from 94:6 to 96:4 and moderate ee (19–38%). Results are given in Table 2.



7 8a-d 9a-d

Scheme 2.

Table 2
Michael addition of various aldehydes to nitrostyrene

R^1	R^2	Product	Yield[a] (%)	dr[b] (*syn*/*anti*)	ee[c] (%)
H	*i*Pr	**9a**	85	96:4	38
H	Me	**9b**	77	95:5	19
H	Et	**9c**	80	94:6	20
Me	Me	**9d**	78	—	30

[a] Isolated yields.
[b] Determined by ^{1}H NMR spectra.
[c] Reported values refer to the *syn* isomer and were determined by chiral HPLC.

In the second part of our work, we studied the effect of temperature on the organocatalyzed Michael addition of isovaleraldehyde **8a** to β-nitrostyrene in ionic liquids. For comparison, experiments were performed in DMSO. Results are shown in Table 3. Increasing reaction temperature from 5 to 80 °C generally resulted in a decrease in diastereoselectivity of the reaction in ionic liquids as well as in DMSO. While the *syn*/*anti* ratio was from 93:7 to 95:5 at 5 °C and rt, it decreased to 67:33–80:20 at 80 °C. Similar observations were made when the organocatalyzed Michael addition of aldehydes to nitrostyrene was performed in $CHCl_3$,[6,9] CH_2Cl_2,[10] THF,[7] hexane,[12] and CCl_4,[15] respectively. On the other hand, enantioselectivity of the addition was not reduced when the temperature increased from 5 to 80 °C. Interestingly, the enantioselectivity of the reaction went through a maximum at 60 °C. When 5-(2-pyrrolidinyl)-1*H*-tetrazole **4** was used as the catalyst, the ee decreased from 42% (5 °C) to 32% (20 °C) and rose again to 40% ee at 60 and 80 °C. Slight increase in the enantioselectivity was observed in all the studied reactions when the reaction temperature was increased from 20 to 80 °C.

3. Conclusion

In conclusion, we have confirmed that (a) the organocatalyzed Michael addition of aldehydes to β-nitrostyrene in ionic liquids proceeds at rt with high yields, excellent diastereoselectivities, and moderate enantioselectivities; (b) L-proline is a more effective catalyst in ionic liquids than in non-polar organic solvents; (c) (*S*)-α,α-diphenyl-2-pyrrolidinemethanol **5** and its trimethylsilyl ether **6**, which have been described as more effective L-proline catalysts than in molecular organic solvents, were found to be less effective in ionic liquids; (d) enantioselectivity of the Michael addition did not decrease at higher temperatures. Studies toward deeper understanding of these effects are underway in our laboratory.

4. Experimental

4.1. General

Catalysts **2** and **3** were prepared according to the literature procedures.[30] Ionic liquids were purchased from Merck and Solvent Innovation. ^{1}H NMR spectra were recorded at 300 MHz on a Varian Gemini spectrometer in $CDCl_3$ with TMS as an internal standard. Optical rotations were measured on Perkin–Elmer 241 instrument. Enantiomeric excesses were determined by HPLC on chiral columns Daicel Chiralpak AD-H or Chiralcel OD-H, using hexane/*i*PrOH as mobile phase and UV detection at 254 nm.

4.2. General experimental procedure for the Michael addition of carbonyl compounds to nitrostyrene

Catalyst (0.15 mmol) was added to a solution of β-nitrostyrene (1.00 mmol, 150 mg) in ionic liquid (1 mL). This mixture was stirred at rt for 10 min, then aldehyde (1.5 mmol) was added and the reaction mixture was stirred at specified temperatures for the time given in Tables 1–3 and monitored by TLC. The solution was then extracted with *t*BuOMe (20 × 3 mL). The combined organic extracts were concentrated and the residue was purified by column chromatography (SiO_2, hexane/EtOAc 7:1). The enantiomeric excess was determined by HPLC.

4.2.1. (2*R*,3*S*)-2-Isopropyl-4-nitro-3-phenylbutanal 9a[4,15,27]

$[\alpha]_D$ = +16.5 (*c* 0.77, $CHCl_3$, 30% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9,93 (d, *J* = 2.7 Hz, 1H), 7.38–7.27 (m, 3H), 7.21–7.18 (m, 2H), 4.67 (dd, *J* = 12.5, 4.5 Hz, 1H), 4.58 (dd, *J* = 12.5, 10.0 Hz, 1H), 3.90 (ddd, *J* = 10.0, 10.0, 4.20 Hz, 1H), 2.80–2.75 (m, 1H), 1.75–1.69 (m, 1H), 1.10 (d, *J* = 7.2 Hz, 3H), 0,89 (d, *J* = 7.2 Hz, 3H). Enantiomeric excess was determined by HPLC (Chiralpak AD-H, *i*PrOH/hexane 70:30, 0.75 mL/min) t_R(major) 7.1 min, t_R(minor) 8.2 min.

4.2.2. (2*R*,3*S*)-2-Methyl-4-nitro-3-phenylbutanal 9b[4]

$[\alpha]_D$ = +8.2 (*c* 1.0, $CHCl_3$, 19% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9,72 (d, *J* = 1.5 Hz, 1H), 7.38–7.29 (m, 3H), 7.18–7.15 (m, 2H), 4.80 (dd, *J* = 12.6, 5.0 Hz, 1H), 4.69 (dd, *J* = 12.6, 9.2 Hz, 1H), 3.81 (ddd, *J* = 9.2, 9.2, 5.0 Hz, 1H), 2.82–2.72 (m, 1H), 1.01 (d,

Table 3
Temperature effect on the Michael addition

Entry	Catalyst	Ionic liquid	Temp. (°C)	Yield[a] (%)	dr[b] (*syn*/*anti*)	ee[c] (%)
1	**1**	[bmim]BF_4	5	64	96:4	40
2	**1**	[bmim]BF_4	20	85	96:4	38
3	**1**	[bmim]BF_4	30	90	95:5	40
4	**1**	[bmim]BF_4	40	94	86:14	42
5	**1**	[bmim]BF_4	50	96	83:17	40
6	**1**	[bmim]BF_4	60	94	67:33	54
7	**1**	[bmim]BF_4	70[d]	78	75:25	50
8	**1**	[bmim]BF_4	80[d]	64	67:33	46
9	**4**	[bmim]BF_4	5	55	94:6	42
10	**4**	[bmim]BF_4	20	68	95:5	32
11	**4**	[bmim]BF_4	40	85	91:9	34
12	**4**	[bmim]BF_4	60	89	80:20	40
13	**4**	[bmim]BF_4	80[d]	68	67:33	40
14	**1**	[emim]$EtSO_4$	5	47	95:5	33
15	**1**	[emim]$EtSO_4$	20	61	95:5	32
16	**1**	[emim]$EtSO_4$	40	68	83:17	34
17	**1**	[emim]$EtSO_4$	60	80	75:25	38
18	**1**	[emim]$EtSO_4$	80[d]	62	75:25	38
19	**1**	DMSO	5	34	95:5	36
20	**1**	DMSO	20	55	93:7	36
21	**1**	DMSO	40	47	86:14	38
22	**1**	DMSO	60	36	80:20	40
23	**1**	DMSO	80[d]	51	80:20	40

[a] Isolated yields.
[b] Determined by ^{1}H NMR spectra.
[c] Reported values refer to the *syn* isomer and were determined by chiral HPLC.
[d] Reactions proceeded for 2 h.

J = 7.2 Hz, 3H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane/*i*PrOH 80:20, 1.0 mL/min) t_R(major) 16.4 min, t_R(minor) 17.4 min.

4.2.3. (2*R*,3*S*)-2-Ethyl-4-nitro-3-phenylbutanal 9c[4,15]

$[\alpha]_D$ = +6.8 (*c* 1.1, $CHCl_3$, 20% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9,75 (d, *J* = 2.7 Hz, 1H), 7.38–7.29 (m, 3H), 7.20–7.17 (m, 2H), 4.73 (dd, *J* = 12.8, 5.0 Hz, 1H), 4.63 (dd, *J* = 12.8, 9.5 Hz, 1H), 3.79 (ddd, *J* = 9.7, 9.7, 5.0 Hz, 1H), 2.72–2.64 (m, 1H), 1.53–1.49 (m 2H), 0.83 (t, *J* = 7.8 Hz, 3H). Enantiomeric excess was determined by HPLC (Daicel Chiralpak AD-H, hexane/*i*PrOH 90:10, 1.0 mL/min), t_R(major) 8.4 min, t_R(minor) 9.1 min.

4.2.4. (*R*)-2,2-Dimethyl-4-nitro-3-phenylbutanal 9d[15]

$[\alpha]_D$ = +3.2 (*c* 1.0, $CHCl_3$, 30% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1H), 7.34–7.29 (m, 3H), 7.21–7.18 (m, 2H), 4.86 (dd, *J* = 13.2, 11.4 Hz, 1H), 4.71 (dd, *J* = 13.2, 4.5 Hz, 1H), 3.78 (dd, *J* = 11.4, 4.5 Hz, 1H), 1.14 (s, 3H), 1.01 (s, 3H). Enantiomeric excess was determined by HPLC (Chiralcel OD-H, hexane/*i*PrOH 80:20, 1.0 mL/min), t_R(major) 12.6 min, t_R(minor) 17.3 min.

Acknowledgments

NMR measurements were performed on the equipment supported by the Slovak State Program Project No. 2003SP200280203. The European Commission is gratefully acknowledged for financial support; project FP7-201431 (CATAFLU.OR). We thank Mr. Filip Bilčík for performing HPLC analyses and Ms. Melinda Mojzesová for performing some preliminary experiments.

References

1. Tsogoeva, S. B. *Eur. J. Org. Chem.* **2007**, 1701–1716.
2. Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471–5569.
3. Pellissier, H. *Tetrahedron* **2007**, *63*, 9267–9331.
4. Betancort, J. M.; Barbas, C. F. *Org. Lett.* **2001**, *3*, 3737–3740.
5. Mase, N.; Thayumanavan, R.; Tanaka, F.; Barbas, C. F. *Org. Lett.* **2004**, *6*, 2527–2530.
6. Alexakis, A.; Andrey, O. *Org. Lett.* **2002**, *4*, 3611–3614.
7. Andrey, O.; Alexakis, A.; Tomassini, A.; Bernardinelli, G. *Adv. Synth. Catal.* **2004**, *346*, 1147–1168.
8. Planas, L.; Pérard-Viret, J.; Royer, J. *Tetrahedron: Asymmetry* **2004**, *15*, 2399–2403.
9. Laars, M.; Ausmees, K.; Uudsemaa, M.; Tamm, T.; Kanger, T.; Lopp, M. *J. Org. Chem.* **2009**, *74*, 3772–3775.
10. Palomo, C.; Vera, S.; Mielgo, A.; Gómez-Bengoa, E. *Angew. Chem., Int. Ed.* **2006**, *45*, 5984–5987.
11. Lalonde, M. P.; Chen, Y.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2006**, *45*, 6366–6370.
12. Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 4212–4215.
13. Hayashi, Y.; Itoh, T.; Ohkubo, M.; Ishikawa, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 4722–4724.
14. García-García, P.; Ladépęche, A.; Halder, R.; List, B. *Angew. Chem., Int. Ed.* **2008**, *47*, 4719–4721.
15. Li, Y.; Liu, X.-Y.; Zhao, G. *Tetrahedron: Asymmetry* **2006**, *17*, 2034–2039.
16. Toma, Š.; Mečiarová, M.; Šebesta, R. *Eur. J. Org. Chem.* **2009**, *74*, 321–327.
17. Kotrusz, P.; Toma, Š.; Schmalz, H. G.; Adler, A. *Eur. J. Org. Chem.* **2004**, 1577–1583.
18. Mečiarová, M.; Hubinská, K.; Toma, Š.; Koch, B.; Berkessel, A. *Monatsh. Chem.* **2007**, *138*, 1181–1186.
19. Hayashi, Y.; Yamaguchi, J.; Hibino, K.; Shoji, M. *Tetrahedron Lett.* **2003**, *44*, 8293–8296.
20. Baumann, T.; Bächle, M.; Hartmann, C.; Bräse, S. *Eur. J. Org. Chem.* **2008**, 2207–2212.
21. Rodriguez, B.; Bolm, C. *J. Org. Chem.* **2006**, *71*, 2888–2891.
22. Hosseini, M.; Stiasni, N.; Barbieri, V.; Kappe, C. O. *J. Org. Chem.* **2007**, *72*, 1417–1424.
23. Mosse, S.; Alexakis, A. *Org. Lett.* **2006**, *8*, 3577–3580.
24. Ibrahem, I.; Rios, R.; Vesely, J.; Hammar, P.; Eriksson, L.; Himo, F.; Córdova, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 4507–4510.
25. Tong, S.-T.; Harris, P. W. R.; Barker, D.; Brimble, M. A. *Eur. J. Org. Chem.* **2008**, 164–170.
26. Jiang, J.; Yu, J.; Sun, X.-X.; Rao, Q.-Q.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2008**, *47*, 2458–2462.
27. Mečiarová, M.; Toma, Š.; Berkessel, A.; Koch, B. *Lett. Org. Chem.* **2006**, *3*, 437–441.
28. Dere, R. T.; Pal, R. R.; Patil, P. S.; Salunkhe, M. M. *Tetrahedron Lett.* **2003**, *44*, 5351–5353.
29. Vesely, J.; Ibrahem, I.; Zhao, G.-L.; Rios, R.; Córdova, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 778–781.
30. Berkessel, A.; Koch, B.; Lex, J. *Adv. Synth. Catal.* **2004**, *346*, 1141–1146.