Pergamon

SCIENCE DIRECT®

Tetrahedron: *Asymmetry* 14 (2003) 3291–3295

TETRAHEDRON: *ASYMMETRY*

The facile synthesis of chiral oxazoline catalysts for the diethylzinc addition to aldehydes

Antonio L. Braga,[a,*] Rodrigo M. Rubim,[a] Henri S. Schrekker,[b] Ludger A. Wessjohann,[b] Martin W. G. de Bolster,[c] Gilson Zeni[a] and Jasquer A. Sehnem[a]

[a]*Departamento de Quimica, Universidade Federal de Santa Maria, 97105-900, Santa Maria, RS, Brazil*
[b]*Institute of Plant Biochemistry, Weinberg 3, D-06120 Halle (Saale), Germany*
[c]*Faculty of Sciences Chemistry Division, Department of Organic and Inorganic Chemistry, Vrije Universiteit Amsterdam, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands*

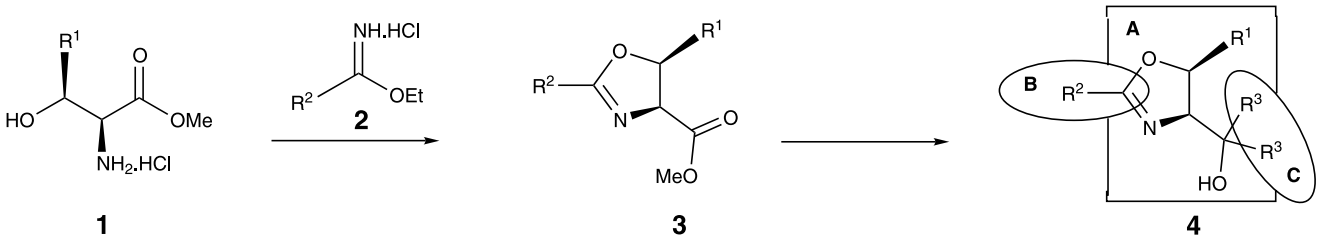
Received 29 May 2003; accepted 7 August 2003

Abstract—A range of chiral 4-(1′-hydroxyalkyl)oxazoline catalysts can be obtained in a straightforward two step synthesis, starting from β-hydroxy amino acids like L-serine or L-threonine. Catalyst **4c** forms a complex with diethylzinc, effective for the enantioselective addition to aldehydes resulting in high yields and enantiomeric excesses up to >99% even with aliphatic aldehydes. In the latter case the enantiomeric excess showed a marked dependence of the aldehyde's chain length.

1. Introduction

The synthesis of chiral ligands for the application in transition metal catalyzed asymmetric reactions is an area of intensive research.[1] The success of a ligand depends on many factors and is not only based on the efficiency in the asymmetric catalytic reaction. Other important factors are: (1) the availability and price of the starting materials, e.g. from the chiral pool; (2) the simplicity of the synthesis; (3) the possibility to obtain structural diversity.

Natural amino acids are readily available from the chiral pool and are proven to be very attractive for the synthesis of chiral compounds, including oxazoline catalysts which are easy to synthesize and have been applied successfully in various asymmetric catalytic reactions.[2] In our ongoing research on amino acid based chiral catalysts for asymmetric catalysis[3] and screening of biological activity[4] we decided to synthesize a set of 4-(1′-hydroxyalkyl)oxazolines **4** (Scheme 1) via a route which could be extended to obtain a focused library if required.



Scheme 1. Synthetic strategy for the synthesis of hydroxymethyl oxazoline ligands, with the combinatorial variables R from three building blocks/reagents (A–C).

* Corresponding author. Tel.: +11-55-55-220-8761; fax: +11-55-55-220-8031; e-mail: albraga@quimica.ufsm.br

0957-4166/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2003.08.029

The hydroxymethyl oxazolines **4a–b**, and **6a–c** have already been tested in the diethylzinc addition to benzaldehyde by Williams et al. (Fig. 1).[5]

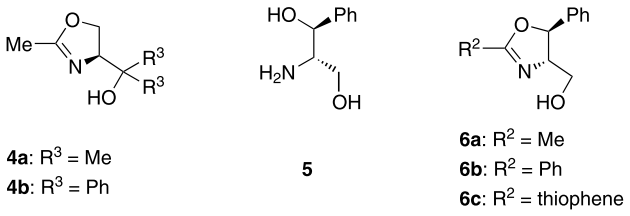
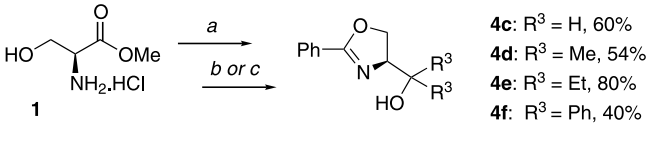


Figure 1. Hydroxymethyl oxazolines previously applied as catalysts in the diethylzinc addition.[5]

The 2-methyl oxazolines **4a–b** were prepared by the synthetic strategy depicted in Scheme 1 and resulted in poor enantioselectivities and yields (**4b**, e.e. = 30% (*R*), 27% yield, 4 h) and lacked stability because they are prone to hydrolysis. Hydroxymethyl oxazolines **6a–c** derived from (1*S*,2*S*)-(+)-2-amino-1-phenyl-1,3-propanediol **5** proved to be more successful resulting in an e.e. of 57% (*S*) and a 65% yield after 18 h for **6b**. A disadvantage of the synthetic strategy used for **6** is the limitation in being able to vary other substituents than R^2.

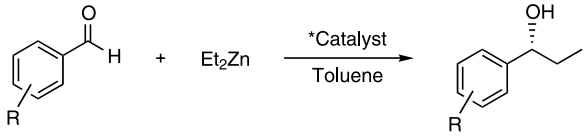
2. Results and discussion

The above results prompted us to synthesize the 2-phenyl oxazolines **4c–f** (Scheme 2) from the natural amino acid L-serine. An attractive synthetic strategy for **4** in which a high structural diversity can be obtained in a straightforward two step sequence is depicted in Scheme 1. The commercially available methyl-ester **1** of the natural amino acid L-serine or optionally L-threonine will form the framework (A, R^1, in Scheme 1) of the final hydroxymethyl oxazoline **4**. Oxazoline ester **3** can be synthesized by reaction of **1** with a nitrile or imidate ester hydrochloride **2**.[6] This transformation, which offers the possibility to introduce many different substituents in the 2-oxazoline position (B, R^2, in Scheme 1) contributes an important part in obtaining structural diversity. However, most important is the opportunity to increase the diversity in the sidechain at position 4 (at C-1′) in the last step. The desired hydroxyalkyl oxazolines **4** can be obtained by reduction of **3** or by reaction with carbon nucleophiles, thus introducing different substituents at the C^4-hydroxymethyl group (C, R^3, in Scheme 1). Application of existing methodologies or small variations thereof resulted in good overall yields for **4c** (54%),[7] **4d** (31%),[8] **4e** (72%), and **4f** (36%). To the best of our knowledge the oxazolines **4e–f** have not been described in the literature previously.



Scheme 2. 2-Phenyl oxazolines. *Reagents and conditions*: (a) **2**, CH_2Cl_2, NEt_3, reflux, 24 h, 90% yield; (b) $LiBHEt_3$, THF, reflux, 24 h, or (c) R^3MgX, THF, reflux, 24 h.

Our first goal was to test the 4-(1′-hydroxyalkyl)oxazolines **4c–f** in enantioselective organozinc additions to aldehydes.[9] The diethylzinc addition to benzaldehyde (Scheme 3) was chosen as the standard reaction to evaluate the catalyst derivatives.



Scheme 3. Diethylzinc addition to aromatic aldehydes.

With the oxazoline catalysts **4c–f** (Table 1) we could evaluate the influence of the 5-oxazoline subtituent (R^1, in Scheme 1, cf. compounds **4a**,**b**), the 2-oxazoline substituent (R^2) as well as the influence of substituents near the hydroxyl moiety (R^3). We conclude that the absence of the 5-phenyl substituent of **6b**[5] (A, R^1, in Scheme 1) has a dramatic effect on the stereochemical outcome of the reaction: With **4c** the enantiomeric excess increased to 95% (Table 1, entry 1) after 24 h at room temperature.

Table 1. The diethylzinc addition to benzaldehyde with oxazolines **4c–f**[a]

Entry	Cat.	Mol% **4**	Yield (%)[b]	E.e. (%)[c,d]
1	**4c**	10	91	95 (*R*)
2	**4c**	5	52	95 (*R*)
3	**4c**	2	41	95 (*R*)
4[e]	**4c**	10	63	95 (*R*)
5	**4d**	10	86	86 (*R*)
6	**4e**	10	85	77 (*R*)
7	**4f**	10	78	55 (*R*)

[a] The reactions were run for 24 h at 20°C, except entry 4.
[b] Yields are calculated based on GC analysis using naphthalene as the internal standard.[10]
[c] Enantiomeric excesses were determined by chiral GC using a hydrodex-β-3P column.
[d] The absolute configuration was determined by specific rotation and related to literature data.[3a,11]
[e] Reaction at 0°C.

The first condition tested seemed to be optimal for catalyst **4c**, because variations in catalyst concentration or a lower temperature decreased the conversion without effecting the enantioselectivity (Table 1, entries 2–4). Under the best reaction conditions for **4c** (10 mol%, rt, 24 h) we studied the influence of substituents at the hydroxymethyl group (C, R^3, in Scheme 1). Oxazolines **4d–f** with a more crowded sterical environment around the hydroxyl functionality suffered from a decrease in the reactivity and enantioselectivity (Table 1, entries 5–7). A Newman-projection can give more insight into the role of the increased steric bulk around C-1′ (Fig. 2). A comparison of the catalysts **4a–b** and **4d**/**f** reveals that the 2-phenyl substituent (B, R^2, in

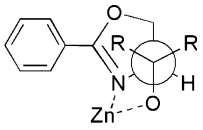


Figure 2. Newman projection of catalyst **4**.

Scheme 1) is more effective than the 2-methyl substituent.

Since **4c** combined sufficient activity as a catalyst with good enantioselectivity, its potential in the reaction of diethylzinc with substituted aromatic aldehydes was tested (Table 2).

Table 2. The enantioselective addition of diethylzinc to substituted aromatic aldehydes employing 10 mol% of catalyst **4c**[a]

Entry	Aldehyde	Yield (%)[b]	E.e. (%)[c,d]
1	R = H	91	95 (*R*)
2	R = *p*-OMe	94	70 (*R*)
3	R = *o*-OMe	65	40 (*R*)
4	R = *p*-Me	65	89 (*R*)
5	R = *o*-Me	57	72 (*R*)
6	R = *p*-Cl	75	>99 (*R*)
7	R = *o*-Cl	90	>99 (*R*)

[a] The reactions were run for 24 h at 20°C.
[b] Yields are calculated based on GC analysis using naphthalene as the internal standard.[10]
[c] Enantiomeric excesses were determined by chiral GC using a hydrodex-β-3P column.
[d] The absolute configuration was determined by specific rotation and related to literature data.[3a,11]

A general trend with respect to yield was not observed when electron donating and withdrawing substituents were compared. Otherwise, the effect on the enantioselectivity was clear; electron donating substituents led to a decrease in enantiomeric excess while electron withdrawing substituents led to an increase. This resulted in an e.e. value of more than 99% when a chloro substituent was present (Table 2, entries 6 and 7).

With the less reactive, electron-rich benzaldehydes, the steric effect obviously also gains some importance. In this case *ortho*-substitution resulted in a slight decrease in yield and enantiomeric excess (Table 2, entry 2 versus 3, and 4 versus 5). The disfavored interaction between the *ortho*-substituent and the ethyl groups attached to the zinc atom no. 2 in the transition state (Fig. 3) may account for the loss in enantioselectivity.

The diethylzinc additions to the less reactive and more often problematic aliphatic aldehydes gave clear results (Table 3). The tail-length of linear aliphatic aldehydes had a dramatic effect on the observed enantioselectivity (Table 3, entries 2–6). Addition of diethylzinc to pentanal gave the secondary alcohol in a low yield and e.e. (25%). However, the reaction with hexanal resulted in an excellent e.e. of more than 99%. A one-, two- and

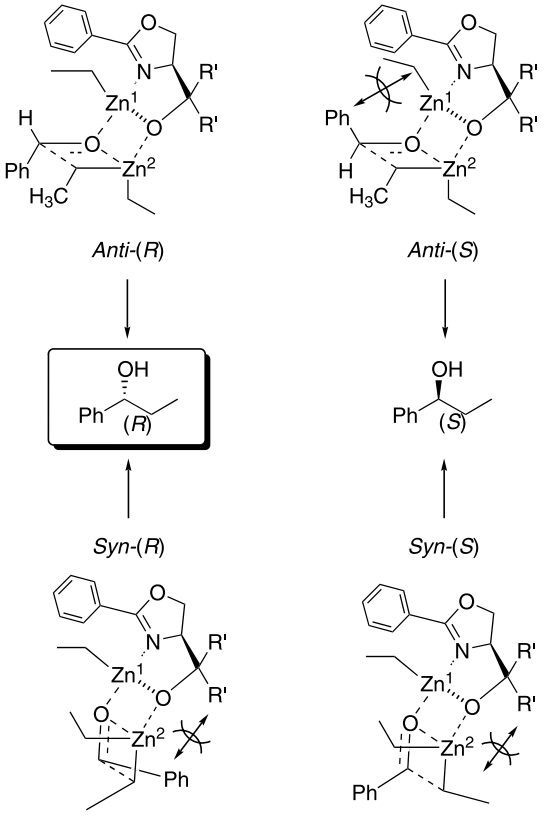


Figure 3. Transition state models to explain the stereochemical outcome of the diethylzinc additions to aldehydes.

Table 3. The enantioselective addition of diethylzinc to aliphatic aldehydes employing 10 mol% of catalyst **4c**[a]

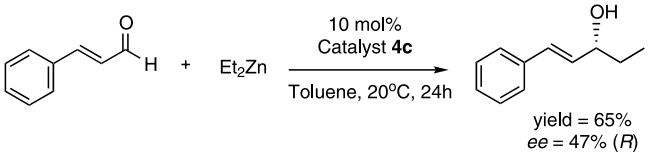
Entry	Aldehyde	Yield (%)[b]	E.e. (%)[c,d]
1	Isobutyraldehyde	14	15 (*R*)
2	Pentanal	35	25 (*R*)
3	Hexanal	67	>99 (*R*)
4	Heptanal	73	81 (*R*)
5	Octanal	65	53 (*R*)
6	Decanal	58	42 (*R*)

[a] The reactions were run for 24 h at 20°C.
[b] Yields are calculated based on GC analysis using naphthalene as the internal standard.[10]
[c] Enantiomeric excesses were determined by chiral GC using a hydrodex-β-3P column.
[d] The absolute configuration was determined by specific rotation and related to literature data.[3a,11]

four-carbon extension decreased the enantiomeric excess continuously to 81, 53, and 42% respectively. This unexpected dependence on the length of the aliphatic chain was also observed previously with a disulfide catalyst in our research group,[3a,b] which demonstrated once again the difficulty in developing a catalyst with broad applicability. With some of these catalysts other chain lengths were prefered. We believe that the study of the correlation of the chain length and the enantiomeric excess is mandatory for each ligand type in order to obtain good results with aliphatic aldehydes.

Interestingly, not only the e.e. values depended on the chain length; the yields showed an almost identical relationship. The oxazoline catalytic system seemed to fail with even the most simplest α-branched aliphatic aldehyde, isobutyraldehyde, leading to a sluggish reaction and a strongly diminished enantiomeric excess (Table 3, entry 1). This most likely originates from the smaller chain length, but additionally may be effected by the increased bulk.

The efficiency of catalyst **4c** was diminished in the reaction of diethylzinc with cinnamaldehyde (Scheme 4).



Scheme 4. Diethylzinc addition to cinnamaldehyde. The absolute configuration was determined by specific rotation and related to literature data.[11]

The stereochemical outcome of these diethylzinc additions to aldehydes is in agreement with the two possible *anti*-transition state structures depicted in Figure 3, based on the dinuclear zinc complexes proposed by Noyori et al.[10,12] The *anti*-(*R*) transition state which leads to the preferential formation of the (*R*)-enantiomer appears to be favored because it avoids axial positioning of the aldehyde alkyl or aryl-group and thus avoids any destabilizing interactions with the ethyl-substituent of zinc Zn^1 and the oxazoline phenyl.

The *syn*-transition states with all major substituents around the Zn_2O_2 four-membered ring being on the same side does not appear to be favourable. However, the unexpected substrate specificity of aliphatic aldehydes can not easily be explained by any of these transition states. Here secondary interactions depending on the lipophilicity in combination with size seem to play an important role, and may allow the system to switch from one preference to another one.

In conclusion, we have successfully applied a flexible synthetic strategy for the synthesis of 4-hydroxyalkyl oxazolines. Application of catalyst **4c** in the diethylzinc addition to aldehydes resulted in clearly improved enantioselectivities compared to previous results. It can be shown that there is a distinct substrate specificity for aliphatic aldehydes. Our results clearly demonstrate the importance of a versatile synthetic approach like the one presented here, to allow the individual adaption of ligands to a desired substrate aldehyde, e.g. by the construction of focused libraries based on these results.

3. Experimental

3.1. General

All aldehydes used are commercially available and were distilled before use. The diethylzinc was used as purchased. Optical rotations were measured on a Perkin–Elmer 341 polarimeter. The NMR spectra were recorded on a Bruker DPX 400 spectrometer using $CDCl_3$ as the solvent and TMS as the internal standard. Chemical shifts δ are quoted in parts per million (ppm), and coupling constants J are given in hertz (Hz). Infrared spectra were recorded in the range of 4000–600 cm^{-1} using a Nicolet Magna 550 spectrometer. Gaschromatography (GC) was performed using a Varian 3800 gaschromatograph with a hydrodex-β-3P column. HPLC analyses were carried out on a Shimadzu SCL-10 AVP chromatograph using a Diacel Chiralcel OD-column; solvent: 99:1 hexane:isopropanol; flow rate = 0.5 ml min^{-1}; UV-detection: 254 nm. Elemental analysis was performed on a Leco CHNS-932 analyzer. High resolution mass spectra were recorded on a Bruker BioApex 70e FT-ICR (Bruker Daltonics, Billerica, USA) instrument in ESI-mode.

3.2. Procedure for the preparation of (*R*)-4-hydroxymethyl-2-phenyl-1,3-oxazoline 4c

A solution of $LiHBEt_3$ in THF (1 M, 9 mmol) was added dropwise to a stirred solution of ester **3** (615 mg, 3.0 mmol) in THF under argon at room temperature. The mixture was refluxed for 24 h. Subsequently, the mixture was quenched by the addition of aq. NH_4Cl (10 mL). The water layer was extracted with CH_2Cl_2 (2×10 mL). The collected organic phase was dried over $MgSO_4$ and concentrated in vacuo to give a crude colourless oil. Flash chromatography (silica gel, hexane:ethyl acetate = 60:40) provided alcohol **4c** in 60% yield. $[\alpha]_D^{20} = +35$ (c 0.42, CH_2Cl_2). IR (CCl_4) (cm^{-1}): 3302 (br); 2934 (w); 1649 (s); 1455 (m). HRMS-ESI m/z calcd for $C_{10}H_{11}O_2NNa$ ($M+Na^+$) 200.0682, found 200.0683. ^1H NMR ($CDCl_3$, 400 MHz), δ: 7.81–7.79 (m, 2H); 7.43–7.26 (m, 3H); 4.44–4.30 (m, 3H); 3.93 (dd, $J' = 11.6$ Hz, $J'' = 4$ Hz, 1H); 3.63 (dd, $J' = 11.6$ Hz, $J'' = 4$ Hz, 1H); 2.89(s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 165.45; 131.38; 128.24; 128.14; 126.95; 69.17; 68.00; 63.60.

3.3. General procedure for the preparation of C-1′-disubstituted (*S*)-4-hydroxymethyl-2-phenyl-1,3-oxazolines 4d–f

A solution of RMgX in THF (3 equiv.) was added dropwise to a stirred solution of ester **3** (615 mg, 3.0 mmol) in THF (5 mL) under argon at room temperature. The mixture was then refluxed for 24 h. Subsequently, the mixture was quenched by the addition of aq. NH_4Cl (15 mL). The water layer was extracted with CH_2Cl_2 (3×15 mL). The collected organic phase was dried over $MgSO_4$ and concentrated in vacuo to give the crude colourless oil. Flash chromatography (silica gel, hexane:ethylacetate = 64:36) provided alcohol **4d–f** in 54–80% yield.

3.3.1. (*S*)-4-(1′-Methyl-1′-hydroxyethyl)-2-phenyl-1,3-oxazoline 4d. Yield = 54%. $[\alpha]_D^{20} = +62$ (c 0.73, CH_2Cl_2). IR (CCl_4) (cm^{-1}): 3196 (br); 2971 (s); 1644 (s); 1450 (m). HRMS-ESI m/z calcd for $C_{12}H_{15}NNaO_2$ ($M+Na^+$)

228.0995, found 228.0990. Anal. calcd for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82. Found: C, 69.87; H, 7.20; N, 6.53. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.96–7.93 (m, 2H); 7.47–7.26 (m, 3H); 4.42–4.31 (m, 2H); 4.21 (dd, $J'=8$ Hz; $J''=2.4$ Hz; 1H); 2.42 (s, 1H); 1.31 (s, 3H); 1.17 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 164.87; 131.40; 128.29; 128.21; 127.44; 75.62; 71.50; 68.75; 26.52; 25.15.

3.3.2. (*S*)-4-(1′-Ethyl-1′-hydroxypropyl)-2-phenyl-1,3-oxazoline 4e. Yield = 80%. $[\alpha]_D^{20}=+41$ (c 0.55, CH_2Cl_2). IR (CCl_4) (cm^{-1}): 3418 (br); 2956 (s); 1645 (s); 1450 (m). HRMS-ESI m/z calcd for $C_{14}H_{19}NNaO_2$ ($M+Na^+$) 256.1308, found 256.1301. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.95–7.93 (m, 2H); 7.47–7.35 (m, 3H); 4.37–4.28 (m, 3H); 1.78–1.74 (m, 3H); 1.51–1.48 (m, 1H); 1.37–1.36 (m, 1H); 0.94 (t, $J=7.6$ Hz, 3H); 0.89 (t, $J=7.6$ Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 164.66; 131.25; 128.22; 128.14; 127.60; 75.16; 72.53; 68.14; 28.38; 26.58; 7.71; 7.50.

3.3.3. (*S*)-4-(Hydroxydiphenylmethyl)-2-phenyl-1,3-oxazoline 4f. Yield = 80%. $[\alpha]_D^{20}=-41$ (c 0.79, CH_2Cl_2). IR (CCl_4) (cm^{-1}): 3541 (s); 2959 (m); 1644 (s); 1495 (s); 1455 (s); 1355 (s). HRMS-ESI m/z calcd for $C_{22}H_{20}O_2N$ ($M+H^+$) 330.1489, found 330.1482. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 7.92–7.26 (m, 15H); 5.45 (t, $J=9.4$ Hz, 1H); 4.22 (m, 2H); 2.64 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 166.58; 145.97; 144.17; 131.57; 128.27; 128.21; 127.90; 127.41; 127.22; 127.12; 127.02; 126.87; 125.76; 78.22; 73.18; 69.24.

3.4. General procedure for the diethylzinc addition to aldehydes

In a 25 mL flask, a solution of toluene (7 mL), aldehyde (1.0 mmol), and catalyst (0.25 mmol) was stirred for 30 min at room temperature. Diethylzinc (1 M in hexane, 2.5 mmol) was slowly injected under constant stirring. Stirring was continued for 24 h at room temperature. Cooling (0°C) of the reaction mixture was followed by the slow addition of HCl solution (aq., 1 M, 5 mL). The organic layer was separated and washed with HCl solution (aq., 1 M, 2×8 mL). Drying over sodium sulfate, filtration, and evaporation of the solvent in vacuo yielded the crude alcohol, which was analysed by GC.

Acknowledgements

The authors wish to thank CAPES and DAAD (German Academic Exchange Service) for travel grants as part of PROBRAL, and CNPq, FAPERGS for financial support.

References

1. (a) Gawley, R. E.; Aube, J. *Principles of Asymmetric Synthesis*; Pergamon: London, 1996; (b) Noyori, R. *Asymmetric Catalysis in Organic Synthesis*; Wiley: New York, 1994; (c) Seyden-Penne, J. *Chiral Auxiliaries and Ligands in Asymmetric Synthesis*; Wiley: New York, 1995; (d) Bolm, C.; Hildebrand, J. P.; Muñiz, K.; Hermanns, N. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 3284–3308.
2. (a) Bolm, C. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 542–543; (b) Pfaltz, A. *Acc. Chem. Res.* **1993**, *26*, 339–345; (c) Togni, A.; Venanzi, L. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 497–526; (d) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron: Asymmetry* **1998**, *9*, 1–45; (e) Imai, Y.; Matsuo, S.; Zhang, W.; Nakatsuji, Y.; Ikeda, I. *Synlett* **2000**, 239–241; (f) Schinnerl, M.; Seitz, M.; Kaiser, A.; Reiser, O. *Org. Lett.* **2001**, *3*, 4259–4262; (g) Gómez, M.; Jansat, S.; Muller, G.; Maestro, M. A.; Mahía, J. *Organometallics* **2002**, *21*, 1077–1087; (h) Halland, N.; Velgaard, T.; Jørgensen, K. A. *J. Org. Chem.* **2003**, *68*, 5067–5074; (i) Zhang, X.-M.; Zhang, H.-L.; Lin, W.-Q.; Gong, L.-Z.; Mi, A.-Q.; Cui, X.; Jiang, Y.-Z.; Yu, K.-B. *J. Org. Chem.* **2003**, *68*, 4322–4329.
3. (a) Braga, A. L.; Appelt, H. R.; Schneider, P. H.; Silveira, C. C.; Wessjohann, L. A. *Tetrahedron: Asymmetry* **1999**, *10*, 1733–1738; (b) Braga, A. L.; Appelt, H. R.; Schneider, P. H.; Rodrigues, O. E. D.; Silveira, C. C.; Wessjohann, L. A. *Tetrahedron* **2001**, *57*, 3291–3295; (c) Braga, A. L.; Vargas, F.; Silveira, C. C.; de Andrade, L. H. *Tetrahedron Lett.* **2002**, *43*, 2335–2337; (d) Braga, A. L.; Rodrigues, O. E. D.; Paixão, M. W.; Appelt, H. R.; Silveira, C. C.; Bottega, D. P. *Synthesis* **2002**, 2338–2340; (e) Braga, A. L.; Appelt, H. R.; Silveira, C. C.; Wessjohann, L. A.; Schneider, P. H. *Tetrahedron* **2002**, *58*, 10413–10416.
4. Rossato, J. I.; Ketzer, L. A.; Centurião, F. B.; Silva, S. J. N.; Lüdtke, D. S.; Zeni, G.; Braga, A. L.; Rubin, M. A.; Rocha, J. B. T. *Neurochem Res.* **2002**, *4*, 297–303.
5. (a) Allen, J. V.; Frost, C. G.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1993**, *4*, 649–650; (b) Allen, J. V.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1994**, *5*, 277–282.
6. Huang, Y.; Dalton, D. R.; Carroll, P. J. *J. Org. Chem.* **1997**, *62*, 372.
7. Dondoni, A.; Perrone, D.; Turturici, E. *J. Org. Chem.* **1999**, *64*, 5557–5564.
8. Novachek, K. A.; Meyers, A. I. *Tetrahedron Lett.* **1996**, *37*, 1743–1746.
9. Pu, L.; Yu, H.-B. *Chem. Rev.* **2001**, *101*, 757–824.
10. Wolf, C.; Francis, C. J.; Hawes, P. A.; Shah, M. *Tetrahedron: Asymmetry* **2002**, *13*, 1733–1744 and references cited therein.
11. (a) Cho, B. T.; Chun, Y. S. *Tetrtahedron: Asymmetry* **1998**, *9*, 1489–1492; (b) Huang, W.-S.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **1998**, *63*, 1364–1365 (see also suporting information).
12. (a) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69; (b) Yamakawa, M.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 6327–6335; (c) Goldfuss, B.; Houk, K. N. *J. Org. Chem.* **1998**, *63*, 8998–9006 and references cited therein; (d) Vázquez, J.; Pericàs, M. A.; Maseras, F.; Lledós, A. *J. Org. Chem.* **2000**, *65*, 7303–7309; (e) Jimeno, C.; Pastó, M.; Riera, A.; Pericàs, M. A. *J. Org. Chem.* **2003**, *68*, 3130–3138; (f) Goldfuss, B.; Steigelmann, M.; Rominger, F. *Eur. J. Org. Chem.* **2000**, 1785–1792 and references cited therein.