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Enantioselective addition of dimethylzinc to aldehydes catalyzed by *N*-substituted mandelamide-Ti(IV) complexes

Gonzalo Blay, Isabel Fernández, Víctor Hernández-Olmos, Alícia Marco-Aleixandre and José R. Pedro*

Departament de Química Orgànica, Facultat de Química, Universitat de València, Dr. Moliner 50, E-46100 Burjassot, Spain

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Abstract—Amides derived from (*S*)-(+)-mandelic acid in the presence of titanium isopropoxide catalyze the enantioselective addition of dimethylzinc to aromatic aldehydes with good yields and ee up to 90%.

1. Introduction

The formation of C–C bonds is one of the most challenging goals in organic synthesis. Among the existing methods, the addition of dialkylzinc to aldehydes or ketones to give alcohols is one of the most convenient because these organometallic reagents can be easily prepared, stored and are compatible with many functional groups.[1] This reaction can be carried out in an enantioselective fashion to provide enantioenriched chiral alcohols, and hence, a multitude of chiral ligands have been used alone or in the presence of Lewis acids for this purpose.[2]

Since the introduction of DAIB (Fig. 1) by Noyori,[3] a large variety of amino alcohols have been employed in this reaction. 1,2-Amino alcohols[4] have been mostly used, but the class includes 1,3-,[5] and 1,4-amino alcohols,[6] and hydroxypyridines.[7] Furthermore, the reaction has been carried out in the presence of some of their derivatives such as imino alcohols[8] and hydroxysulfonamides,[9] these last usually in combination with titanium isopropoxide. In the case of the hydroxy sulfonamides, the different acidity between the alcohol ($pK_a \sim 16.5$) and sulfonamide ($pK_a \sim 8$) is considered important for the activity and enantioselectivity of the reaction.

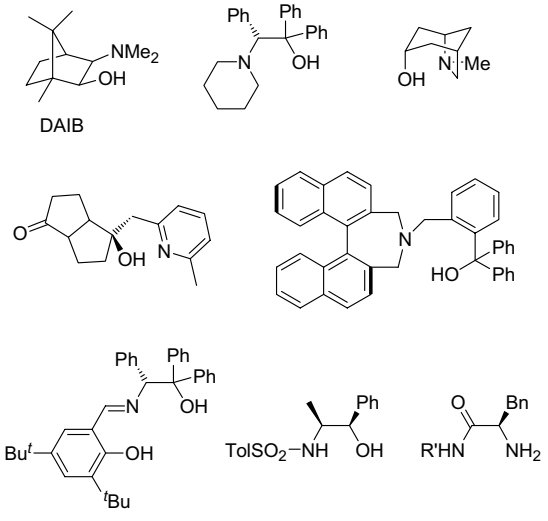

Figure 1. Amino alcohols and related compounds used as ligands in the enantioselective addition of dialkylzinc to aldehydes.

Recently, the use of nickel complexes from α-amino amides as catalysts in the enantioselective Et_2Zn addition to benzaldehyde has been reported.[10] Again, the presence of two atoms with different acidity and coordinating capabilities was considered important for the outcome of the reaction.

Finally, the use of hydroxy carboxylic acids, obtained by diazotization of amino acids, as ligands for enantioselective addition of diethylzinc to aldehydes has recently been reported.[11]

* Corresponding author. Tel.: +34 96 3544329; fax: +34 96 3544328; e-mail: jose.r.pedro@uv.es

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According to these antecedents, we considered α-hydroxy amides as possible candidates to be used as ligands in the enantioselective addition of dialkylzinc reagents to aldehydes, and we have recently reported the use of C_2 symmetric chiral bis(amino alcohol)oxalamides of type I (Fig. 2) for this purpose.[12] The presence of C_2 symmetry is generally considered an advantageous structural feature,[13] but recent examples show the potential of C_1 symmetric ligands that, in some cases, can be more efficient than related C_2 systems.[14] Herein, we report the use of C_1 symmetric hydroxy amides II derived from (*S*)-mandelic acid (mandelamides) as chiral inducers in the enantioselective dialkylzinc addition to aldehydes. This kind of compounds has hardly been used as ligands in asymmetric catalysis although they are readily prepared from inexpensive and readily available sources, stable and storable, and present some structural features that make them very attractive in this respect. Thus, the presence of two groups with different coordinating capabilities, the hydroxyl and the N–H amide functionalities, which can be both deprotonated, may favor the formation of strong metal complexes with a defined steric and electronic environment, which can be optimized through the appropriate selection of R.

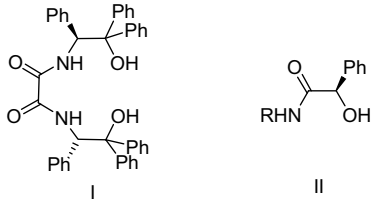


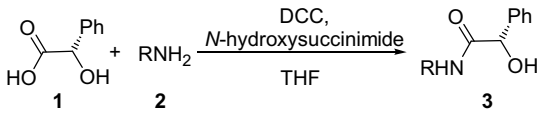
Figure 2.

Herein, we have centered our attention to the addition of dimethylzinc to aldehydes. Because of its lower reactivity, asymmetric addition of Me_2Zn has attracted less attention than the corresponding Et_2Zn additions. However, the chiral 1-hydroxyethyl moiety resulting from the addition of a methyl group to an aldehyde is found widespread in nature, and makes this reaction very interesting from a synthetic point of view.[15] *N*,*N*-Di-*n*-butylnorephedrine has been used for the addition of dimethylzinc to aliphatic aldehydes with good selectivity,[16] and *N*,*N*-dialkyltriphenylaminoethanol derivatives have provided good enantioselectivity in the addition of this reagent to benzaldehyde and heptanal.[17]

2. Results and discussion

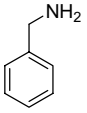
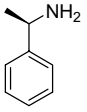
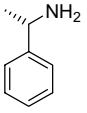
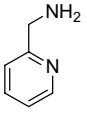
2.1. Synthesis of *N*-substituted mandelamides

Unlike α-amino amides, whose syntheses require protection of the amino group, α-hydroxy amides can be prepared in just one step by treatment of commercially available (*S*)-(+)-mandelic acid **1** with primary amines RNH_2 **2** in the presence of dicyclohexylcarbodiimide (DCC) and *N*-hydroxysuccinimide.[18] The *N*-substituted mandelamides **3** are generally obtained with excellent yields (Scheme 1, Table 1).



Scheme 1.

Table 1. Synthesis of ligands **3**

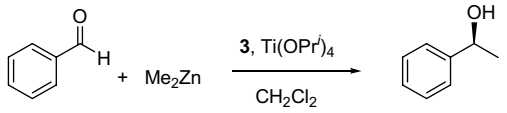
Ligand **3**	RNH_2	Yield (%)[a]
a		80
b		94
c		80
d		74
e		94

[a] Yields refer to isolated products.

2.2. Enantioselective addition of dimethylzinc to aldehydes

The addition of dimethylzinc to benzaldehyde was chosen as the test reaction. The reaction was carried out using 0.2 equiv of ligand **3** and 6 equiv of Me_2Zn (2 M in toluene) in dichloromethane solution at 0 °C (Table 2). When ligand **3a** was used alone in the absence of other Lewis acids, no catalytic activity was observed (entry 1). Therefore, we performed the reaction in the presence of titanium isopropoxide since it is known that this reaction tends to be more efficient and selective in the presence of this particular Lewis acid.[19] Under these conditions, the reaction took place with good yield and acceptable enantioselectivity (entry 2). The effect of the amine substituent was studied with ligands **3b**–**e**. Thus, ligands **3b** and **3c** introduce an additional stereogenic center on the amine, while in ligand **3d** the benzene ring was substituted by an electron deficient pyridine ring with a potentially coordinating nitrogen atom. Finally, ligand **3e** was derived from a bulky aliphatic *tert*-butyl amine. In all the cases (entries 3–6), both the yield and ee of the reaction were lower than those obtained with ligand **3a**. The effect of other metal salts was also studied. However, the use of $Cu(OAc)_2$ or $Ni(OAc)_2$ in a 1:1 ratio (entries 7 and 8) gave disappointing results. Copper acetate was completely inactive after 24 h while nickel acetate gave an almost racemic mixture with low yield after 48 h. These results contrast with the results found for these metal salts using amino amides as ligands.[10]

Table 2. Addition of Me_2Zn to benzaldehyde in the presence of metal complexes of **3**



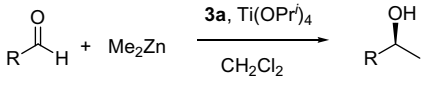
Entry	Ligand	Additive	Yield (%)[a]	ee (%)[b]
1	**3a**	—	—	—
2	**3a**	$Ti(O^iPr)_4$	85	78
3	**3b**	$Ti(O^iPr)_4$	47	49
4	**3c**	$Ti(O^iPr)_4$	57	57
5	**3d**	$Ti(O^iPr)_4$	65	19
6	**3e**	$Ti(O^iPr)_4$	69	35
7	**3a**	$Cu(OAc)_2$	—	—
8	**3a**	$Ni(OAc)_2$	59	4[c]
9	**3a**[d]	$Ti(O^iPr)_4$	70	51

[a] Yields refer to isolated products.
[b] (*S*)-(−)-1-Phenylethanol.
[c] (*R*)-(+)-1-Phenylethanol.
[d] Et_2Zn was used. (*S*)-(−)-1-Phenylpropanol.

The influence of the dialkylzinc reagent was also tested. Surprisingly, the reaction with diethylzinc (entry 9) gave a lower ee than the corresponding dimethylzinc reagent. It is noteworthy that this tendency is the opposite of that found with aminoalcohols[20] and hydroxy sulfonamide ligands.[9g,21]

The catalytic system formed by **3a** and $Ti(O^iPr)_4$ was applied to other aromatic aldehydes. The results are shown in Table 3. Reasonable to good yields and enantioselectivities are obtained with most of the aromatic aldehydes (entries 1–12). In general, we observed little dependence of the enantioselectivity with the electronic character of the substituent in the *ortho*- (entries 9–12) and *meta*- (entries 6–8) substituted benzaldehydes. However, there was a dramatic decrease in the ee in the case of *p*-nitrobenzaldehyde (entry 3) with respect to other *p*-substituted benzaldehydes. In these cases, it appears that electron-donating substituents increase the ee. On the other hand, *ortho*-substituted benzaldehydes give higher ee than *meta*-substituted, and those higher than *para*-substituted ones, clearly indicating a dependence between the ee and the steric environment of the aldehyde carbonyl group.

Table 3. Addition of Me_2Zn to aldehydes catalyzed by **3a** and titanium isopropoxide



Entry	Aldehyde	Yield (%)[a]	ee (%)[b]
1	Benzaldehyde	85	78
2	*p*-Chlorobenzaldehyde	94	74
3	*p*-Nitrobenzaldehyde	92	49
4	*p*-Methylbenzaldehyde	83	82
5	*p*-Methoxybenzaldehyde	91	80
6	*m*-Nitrobenzaldehyde	97	82
7	*m*-Methylbenzaldehyde	96	85
8	*m*-Methoxybenzaldehyde	90	78
9	*o*-Nitrobenzaldehyde	82	85
10	*o*-Methylbenzaldehyde	75	89
11	*o*-Ethylbenzaldehyde	45	90
12	*o*-Methoxybenzaldehyde	95	85
13	Decanal	75	63
14	Dihydrocinnamaldehyde	70	61
15	Cyclohexanecarboxyaldehyde	33	55

[a] Yields refer to isolated products.
[b] *S* configuration in all the cases.

2.3. Mechanistic considerations

In all of the cases, the reaction led to an alcohol with an (*S*)-configuration resulting from the attack of the alkyl group to the *Si* face of the aldehyde carbonyl. The stereochemical course of the reaction can be rationalized in terms of a transition state related to that proposed for the addition of dialkylzinc to carbonyl compounds using hydroxy sulfonamides as ligands in the presence of titanium isopropoxide (Fig. 3).[9c] In these cases, the transition state is considered to be a bimetallic alkyltitanium species, bearing two titanium atoms, one being the coordination center for the aldehyde and the other carrying a methyl group transferred from dimethylzinc.[22,23] Coordination of the aldehyde to the titanium atom takes place *anti* to the apical isopropoxy group,[22,23] which is directed toward the less hindered face of the five-membered ring described by the octahedral titanium and the ligand, opposite to the mandelic acid phenyl group. Alternatively, a pentacoordinated cationic titanium atom may be considered, with the benzaldehyde being coordinated in the same way.[9c,24] The aldehyde is arranged in such a way that the *Si* face of the carbonyl group is exposed to the methyl group, which is transferred from the second titanium atom. This arrangement might be stabilized by a hydrogen bond between the ligand oxygen and the aldehyde hydrogen in a similar way as described by Corey and Lee for other enantioselective reactions,[25] and by a π-stacking effect between the aldehyde aryl group and the benzyl substituent on the amido group of **3a**.[9c]

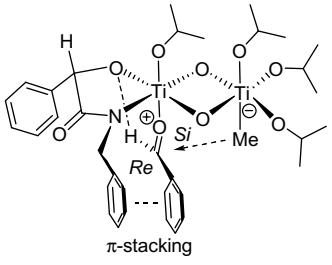


Figure 3. Proposed TS for the addition of dimethylzinc to benzaldehyde catalyzed by ligand **3a** and $Ti(OPr^i)_4$.

This last effect could explain the low ee obtained with aliphatic aldehydes, as well as the low ee obtained with benzaldehyde and ligand **3e**.

3. Conclusions

In conclusion, we have shown that α-hydroxy amides, such as *N*-substituted mandelamides, which are easily prepared from chiral mandelic acid and amines, can be successfully used as ligands in the enantioselective addition of dialkylzinc reagents to aldehydes in the presence of titanium isopropoxide. The outcome of the reaction is largely dependent on the amino substituent of the ligand, therefore the catalytic activity and enantioselectivity can be tuned by a proper selection of the amine. Of all the tested amides, *N*-benzylmandelamide was shown to be superior. Better results have been obtained with dimethylzinc than with the corresponding diethylzinc reagent, this behavior being unusual for this type of reaction. The enantioselection is higher for aromatic aldehydes ($o > m > p$) than for aliphatic ones. The stereochemical course of the reaction may be explained in the terms of a bimetallic TS similar to that proposed for analogous reactions catalyzed by hydroxy sulfonamides. Further design and applications of α-hydroxy amides as ligands for enantioselective reactions are under investigation and will be reported in due time.

4. Experimental

4.1. General

Commercial reagents were used as purchased. Dichloromethane was distilled from CaH_2 and stored over 4 Å molecular sieves. All asymmetric reactions were carried out in dry glassware under an argon atmosphere. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040–0.063 mm. Specific optical rotations were measured using sodium light (D line 589 nm). IR were recorded as liquid films in NaCl for oils and as KBr discs for solids. ^{1}H NMR were run at 299.95 MHz for ^{1}H and at 50.3 MHz for ^{13}C NMR, and referenced to the solvent as internal standard. The carbon type was determined by DEPT experiments. MS(EI) were run at 70 eV. Chiral GLC analyses were carried out in a Thermo Quest Trace GC 2000 series instrument equipped with a flame ionization detector using nitrogen (1 mL/min) as carrier gas, $T_{injector}$ = 220 °C, $T_{detector}$ = 220 °C. Chiral HPLC analyses were performed in an Agilent 1100 series instrument equipped with a refraction index detector. Retention times for GLC and HPLC are given in min.

4.2. General procedure for the synthesis of mandelamides 3a–e

N,*N*′-Dicyclohexylcarbodiimide (7.5 g, 36.1 mmol) was added to a stirred solution of (*S*)-(+)-mandelic acid (5 g, 32.9 mmol), amine (32.9 mmol) and *N*-hydroxysuccinimide (4.2 g, 36.1 mmol) in anhydrous tetrahydrofuran (140 mL) at 0 °C under an argon atmosphere. The cooling bath was removed and reaction mixture stirred overnight, filtered and the cake of dicyclohexylurea washed with THF (2 × 10 mL). The solvent was removed under reduced pressure, and the residue dissolved with ethyl acetate. The solution was washed successively with saturated sodium carbonate, water, 1 M HCl (except in the case of **3d**), water and brine and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude product purified by flash chromatography on silica gel eluting with hexane–ethyl acetate mixtures (Yields are reported in Table 1).

4.2.1. *N*-Benzyl-(*S*)-mandelamide 3a. Mp 134–135 °C (CH_3OH) $[\alpha]_D^{25} = +83.2$ (c 0.54, $CHCl_3$), $[\alpha]_D^{25} = +45.7$ (c 0.52, CH_3OH), {lit[26] $[\alpha]_D^{25} = +82.2$ (c 1.09, $CHCl_3$)}; spectral data identical to those reported in the literature.[26a]

4.2.2. *N*-[(*R*)-1-Phenylethyl]-(*S*)-mandelamide 3b. Mp 57–58 °C (CH_3OH) $[\alpha]_D^{25} = +115.2$ (c 0.52, $CHCl_3$), $[\alpha]_D^{25} = +143.2$ (c 0.52, CH_3OH), {lit[27] $[\alpha]_D^{25} = +111.4$ (c 1.2, $CHCl_3$)}; spectral data identical to those reported in the literature.[27]

4.2.3. *N*-[(*S*)-1-Phenylethyl]-(*S*)-mandelamide 3c. Mp 108–110 °C (CH_3OH) $[\alpha]_D^{25} = +11.1$ (c 0.50, $CHCl_3$), $[\alpha]_D^{25} = -49.1$ (c 0.50, CH_3OH), {lit[27] $[\alpha]_D^{25} = +11.1$ (c 0.64, $CHCl_3$), lit[28] $[\alpha]_D^{25} = -52.4$ (c 0.50, CH_3OH)}; spectral data identical to those reported in the literature.[27]

4.2.4. *N*-(Pyridin-2-ylmethyl)-(*S*)-mandelamide 3d. Mp 132–133 °C (CH_3OH); $[\alpha]_D^{25} = +46.8$ (c 0.52, $CHCl_3$), $[\alpha]_D^{25} = +33.3$ (c 0.52, CH_3OH); IR ν 3300, 3131, 1656 cm^{-1}; MS(EI) 243 (M^++1, 1), 136 (16), 135 (100), 93 (21), 92 (37); HRMS 243.1086 $C_{14}H_{15}N_2O_2$ required 243.1134; ^{1}H NMR ($CDCl_3$) δ 8.13 (1H, d, J = 5.0 Hz), 7.81 (1H, unresolved t), 7.52 (1H, t, J = 7.8 Hz), 7.37 (2H, dd, J = 7.0, 1.5 Hz), 7.30–7.15 (3H, m), 7.10 (1H, d, J = 7.8 Hz), 7.03 (1H, dd, J = 7.8, 5.0 Hz), 5.65 (1H, br s), 5.07 (1H, s), 4.42 (2H, d, J = 5.4 Hz); ^{13}C NMR ($CDCl_3$) δ 172.6 (s), 156.4 (s), 148.7 (d), 139.9 (s), 137.1 (d), 128.6 (d), 128.2 (d), 126.8 (d), 122.5 (d), 122.4 (d), 74.3 (d), 44.0 (t).

4.2.5. (*N*)-(*tert*-Butyl)-(*S*)-mandelamide 3e. Mp 74–76 °C (CH_3OH) $[\alpha]_D^{25} = +63.4$ (c 0.53, $CHCl_3$), $[\alpha]_D^{25} = +28.1$ (c 0.54, CH_3OH), {lit[29] $[\alpha]_D^{24} = +28.8$ (c 0.54, CH_3OH)}; spectral data identical to those reported in the literature.[29]

4.3. Enantioselective addition of dimethylzinc to aldehydes

To a solution of ligand **3a** (48 mg, 0.2 mmol) in dry CH_2Cl_2 (5 mL) under Ar was added $Ti(OPr^i)_4$ (0.42 mL, 1.4 mmol). After 1 h, the reaction mixture was cooled to 0 °C and a 2 M solution of dimethylzinc in toluene (3 mL, 6 mmol) was added. After 30 min, the aldehyde (1 mmol) was added and stirring continued at this temperature for 24 h. Then, the reaction was quenched with 1 M HCl (20 mL) (CAUTION! Exother-

mic reaction, gas evolution), filtered and extracted with diethyl ether (3 × 15 mL). The organic layer was washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Flash chromatography on silica gel eluting with hexane–diethyl ether mixtures gave the corresponding alcohol. Yields and ee are included in Table 3.

4.3.1. (*S*)-(−)-1-Phenyl-1-ethanol. GC (Supelco β-dex-225): t_R = 24.2, t_S = 26.4 (T_{column} = 100 °C).

4.3.2. (*S*)-(−)-1-(4-Clorophenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 44.8, t_S = 47.4 (T_{column} = 120 °C).

4.3.3. (*S*)-(−)-1-(4-Nitrophenyl)-1-ethanol. HPLC (Chiralcel OD-H): t_R = 30.1, t_S = 31.8 (hexane/^{i}PrOH 98:2, flow 1 mL/min).

4.3.4. (*S*)-(−)-1-(4-Methylphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 36.9, t_S = 43.1 (T_{column} = 100 °C).

4.3.5. (*S*)-(−)-1-(4-Methoxyphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 34.1, t_S = 36.7 (T_{column} = 125 °C).

4.3.6. (*S*)-(−)-1-(3-Nitrophenyl)-1-ethanol. HPLC (Chiralpack AD-H): t_R = 23.6, t_S = 28.38 (hexane/^{i}PrOH 98:2, flow 1 mL/min).

4.3.7. (*S*)-(−)-1-(3-Methylphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 28.3, t_S = 31.3 (T_{column} = 105 °C).

4.3.8. (*S*)-(−)-1-(3-Methoxyphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 75.2, t_S = 75.6 (T_{column} = 90 °C (60 min) to 200 °C at 5 °C/min).

4.3.9. (*S*)-(+)-1-(2-Nitrophenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 28.8, t_S = 29.3 (T_{column} = 100 °C (5 min) to 200 °C at 3 °C/min).

4.3.10. (*S*)-(−)-1-(2-Methylphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 62.8, t_S = 63.7 (T_{column} = 85 °C).

4.3.11. (*S*)-(−)-1-(2-Ethylphenyl)-1-ethanol. GC (Supelco β-dex-225): t_R = 87.2, t_S = 88.3 (T_{column} = 85 °C).

4.3.12. (*S*)-(−)-1-(2-Methoxyphenyl)-1-ethanol. GC (Mega DETTBSIL β): t_R = 43.6, t_S = 41.2 (T_{column} = 95 °C (30 min) to 200 °C at 3 °C/min).

4.3.13. (*S*)-(+)-2-Undecanol. HPLC (Chiralpack AD-H): t_R = 23.4, t_S = 22.9 (hexane/^{i}PrOH 98:2, flow 0.25 mL/min).

4.3.14. (*S*)-(+)-4-Phenyl-2-butanol. GC (Supelco β-dex-225): t_R = 57.9, t_S = 58.9 (T_{column} = 105 °C).

4.3.15. (*S*)-(+)-1-Cyclohexylethanol. HPLC (Chiralpack AD-H): t_R = 27.0, t_S = 24.6 (hexane/^{i}PrOH 98:2, flow 0.5 mL/min).

Acknowledgements

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References

1. Knochel, P. In *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 1998, p 467.
2. Pu, L.; Yu, H.-B. *Chem. Rev.* **2001**, *101*, 757–824.
3. (a) Kitamura, M.; Suga, S.; Kawai, K.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 6071–6072; (b) Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M.; Oguni, N.; Hayashi, M.; Kaneko, T.; Matsoda, Y. *J. Organomet. Chem.* **1990**, *382*, 19–37; (c) Noyori, R.; Kitamura, M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 49–69.
4. (a) Superchi, S.; Meca, T.; Giorgio, E.; Rosini, C. *Tetrahedron: Asymmetry* **2001**, *12*, 1235–1239; (b) Lu, G.; Li, X.; Zhou, Z.; Chan, W. L.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2147–2152; (c) Superchi, S.; Giorgio, E.; Scafato, P.; Rosini, C. *Tetrahedron: Asymmetry* **2002**, *13*, 1385–1391; (d) Steiner, D.; Sethofer, S. G.; Goralski, C. T.; Singaram, B. *Tetrahedron: Asymmetry* **2002**, *13*, 1477–1483; (e) Solà, L.; Reddy, K. S.; Vidal-Ferran, A.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvárez-Larena, A.; Piniella, J. F. *J. Org. Chem.* **1998**, *63*, 7078–7082; (f) Fontes, M.; Verdaguer, X.; Solà, L.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **2004**, *69*, 2532–2543.
5. (a) Cimarelli, C.; Palmieri, G.; Volpini, E. *Tetrahedron: Asymmetry* **2002**, *13*, 2417–2426; (b) Lu, J.; Xu, X.; Wang, S.; Wang, C.; Hu, Y.; Hu, H. *J. Chem. Soc., Perkin 1* **2002**, 2900–2903; (c) Panda, M.; Phuan, P.; Kozlowski, M. C. *J. Org. Chem.* **2003**, *68*, 564–571.
6. (a) Scarpi, D.; Lo Galbo, F.; Occhiato, E. G.; Guarna, A. *Tetrahedron: Asymmetry* **2004**, *15*, 1319–1324; (b) Martínez, A. G.; Vilar, E. T.; Fraile, A. G.; de la Moya Cerero, S.; Maroto, B. L. *Tetrahedron: Asymmetry* **2003**, *14*, 1959–1963; (c) Trabocchi, A.; Menchi, G.; Rolla, M.; Machetti, F.; Bucelli, I.; Guarna, A. *Tetrahedron* **2003**, *59*, 5251–5258; (d) Hanyu, N.; Aoki, T.; Mino, T.; Sakamoto, T.; Fujita, T. *Tetrahedron: Asymmetry* **2000**, *11*, 2971–2979.
7. (a) Zhong, Y.; Lei, X.; Lin, G. *Tetrahedron: Asymmetry* **2002**, *13*, 2251–2255; (b) Huang, H.; Chen, H.; Hu, X.; Bai, C.; Zheng, Z. *Tetrahedron: Asymmetry* **2003**, *14*, 297–304; (c) Goanvic, D. L.; Holler, M.; Pale, P. *Tetrahedron: Asymmetry* **2002**, *13*, 119–121.
8. (a) Mino, T.; Oishi, K.; Yamashita, M. *Synlett* **1998**, 965–966; (b) Fleischer, R.; Braun, M. *Synlett* **1998**, 1441–1443.
9. (a) Ito, K.; Kimura, Y.; Okamura, H.; Katsuki, T. *Synlett* **1992**, 573–574; (b) Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **1997**, *8*, 2479–2496; (c) Ramón, D. J.; Yus, M. *Tetrahedron* **1998**, *54*, 5651–5666; (d) Zhang, X.; Guo, C. *Tetrahedron Lett.* **1995**, *36*, 4947–4950; (e) Verdugo, D.; Larter, M. L.; Christie, R.; Kenney, P.; Walsh, P. J. *Tetrahedron* **1997**, *53*, 4145–4158; (f) Qiu, J.; Gho, C.; Zhang, X. *J. Org. Chem.* **1997**, *62*, 2665–2668; (g) Yus, M.; Ramón, D. J.; Prieto, O. *Tetrahedron: Asymmetry* **2002**, *13*, 1573–1579; (h) Prieto, O.; Ramón, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2000**, *11*, 1629–1644.
10. Burguete, M. I.; Collado, M.; Escorihuela, J.; Galindo, F.; García-Verdugo, E.; Luis, S. V.; Vicent, M. J. *Tetrahedron Lett.* **2003**, *44*, 6891–6894.
11. (a) Bauer, T.; Tarasiuk, J. *Tetrahedron Lett.* **2002**, *43*, 687–689; (b) Bauer, T.; Gajewiak, J. *Tetrahedron* **2004**, *60*, 9163–9170.

12. Blay, G.; Fernández, I.; Marco-Aleixandre, A.; Pedro, J. R. *Tetrahedron: Asymmetry* **2005**, *16*, 1207–1213.
13. (a) Whitesell, J. *Chem. Rev.* **1989**, *89*, 1581–1590; (b) Halm, C.; Kurth, M. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 510–512.
14. (a) Shi, M.; Sui, W. S. *Tetrahedron: Asymmetry* **2000**, *11*, 835–841; (b) Malkov, A. V.; Spoor, P.; Vinader, V.; Kocovsky, P. *Tetrahedron Lett.* **2001**, *42*, 509–512; (c) Sibi, M. P.; Venkatraman, L.; Liu, M.; Jasperse, C. P. *J. Am. Chem. Soc.* **2001**, *123*, 8444–8445; (d) Nugent, W. A. *Org. Lett.* **2002**, *4*, 2133–2136; (e) Cohn, A. J. A.; Marson, C. M. *Tetrahedron: Asymmetry* **2001**, *12*, 1547–1550; (f) Wipf, P.; Wang, X. *Org. Lett.* **2002**, *4*, 1197–1200; (g) Preigo, J.; Mancheno, O. G.; Cabrera, S.; Carretero, J. C. *J. Org. Chem.* **2002**, *67*, 1346–1353.
15. (a) Jones, G. B.; Heaton, S. B. *Tetrahedron: Asymmetry* **1993**, *4*, 247–259; (b) Jones, G. B.; Huber, R. S.; Chapman, B. J. *Tetrahedron: Asymmetry* **1997**, *8*, 1797–1809.
16. Soai, K.; Yokoyama, S.; Hayasaka, T. *J. Org. Chem.* **1991**, *56*, 4264–4268.
17. García-Delgado, N.; Fontes, M.; Pericàs, M. A.; Riera, A.; Verdaguer, X. *Tetrahedron: Asymmetry* **2004**, *15*, 2085–2090.
18. (a) Cobb, A. J. A.; Marson, C. M. *Tetrahedron: Asymmetry* **2001**, *12*, 1547–1550; (b) Tanaka, K.; Hiratsuka, T.; Urbanczyk-Lipkowska, Z. *Eur. J. Org. Chem.* **2003**, 3043–3046.
19. (a) Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807–832; (b) Lake, F.; Moberg, C. *Tetrahedron: Asymmetry* **2001**, *12*, 755–760; (c) Xu, Q.; Wang, H.; Pan, X.; Chan, A. S. C.; Yang, T. *Tetrahedron Lett.* **2001**, *42*, 6171–6173.
20. Kell, R. G.; Hodge, P.; Nisar, M.; Watson, D. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1803–1807.
21. (a) Nowotny, S.; Vettet, S.; Knochel, P. *Tetrahedron Lett.* **1994**, *35*, 4539–4540; (b) Lütjents, H.; Nowotny, S.; Knochel, P. *Tetrahedron: Asymmetry* **1995**, *6*, 2675–2678.
22. Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, 2171–2209.
23. (a) Wu, K.-H.; Gau, H.-M. *Organometallics* **2004**, *23*, 580–588; (b) You, J.-S.; Shao, M.-Y.; Gau, H.-M. *Organometallics* **2000**, *19*, 3368–3373.
24. Seebach, D.; Marti, R. E.; Hintermann, T. *Helv. Chim. Acta* **1996**, *79*, 1710–1740.
25. (a) Corey, E. J.; Lee, T. *Chem. Commun.* **2001**, 1321–1329; (b) Corey, E. J.; Barnes-Seeman, D.; Lee, T.; Goodman, S. N. *Tetrahedron Lett.* **1997**, *38*, 6513–6516; (c) Mackey, M. D.; Goodman, J. M. *J. Chem. Soc., Chem. Commun.* **1997**, 2383–2384.
26. (a) Carpentier, J.-F.; Mortreux, A. *Tetrahedron: Asymmetry* **1997**, *8*, 1083–1099; (b) Roucoux, A.; Thieffry, L.; Carpentier, J.-F.; Devocelle, M.; Méliet, C.; Agbossou, F.; Mortreux, A. *Organometallics* **1996**, *15*, 2440–2449.
27. Garry, S. W.; Neilson, D. G. *J. Chem. Soc., Perkin 1* **1987**, 601–605.
28. Jourdain, F.; Hirokawa, T.; Kogane, T. *Tetrahedron Lett.* **1999**, *40*, 2509–2512.
29. Denmark, S. E.; Fan, Y. *J. Am. Chem. Soc.* **2003**, *125*, 7825–7827.