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Enantioselective nucleophilic addition to *N*-(2-pyridylsulfonyl)imines by use of dynamically induced chirality

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Abstract—Enantioselective nucleophilic addition of Grignard reagents to *N*-(2-pyridylsulfonyl)imines in the presence of bis(oxazoline) afforded products with good enantioselectivity. Dynamically induced chirality on the sulfur by coordination of a chiral Lewis acid to a pyridyl nitrogen and one of the sulfonyl oxygens fixes the conformation of the complex and induces enantioselectivity. Since the 2-pyridylsulfonyl group can be easily removed after the addition reaction, it acts not only as a protecting group but also as an efficient stereocontroller.

1. Introduction

The stereoselective nucleophilic addition reaction of organometallic reagents to C=N bonds is one of the most efficient methods for the preparation of chiral amines. For the preparation of chiral amines, diastereoselective reactions of imines having various chiral auxiliaries with organometallic reagents have been extensively studied.[1] Enantioselective addition of organometallic reagents to imines has also been developed[2] in the reaction of *N*-substituted imines,[3] diphenylphosphinoylimines,[4] *N*-acylimines,[5] and sulfonyl imines[6] since the first report of chiral ligand-mediated addition of organolithium reagents to a C=N bond.[7] In these reactions, various Lewis acids and chiral ligands have been examined to coordinate to the imino nitrogen in a monodentate manner for the stereoselective intermolecular alkylation of imines. Exceptionally, there are only a few reports for asymmetric nucleophilic addition reaction to imines through bidentate fixation with a chiral Lewis acid;[8] however, it is often found difficult in these reactions to remove the protecting group from the products. Enantioselective reactions of imines described above have been performed by alkylation with organolithium or organozinc reagents, but there are no reports of the enantioselective reaction using Grignard reagents. It is important to develop an easily removable protecting group, which also has sufficient activating property for imines to react with Grignard reagents. Thus, we designed the 2-pyridylsulfonyl group as a new coordinative protecting and activating group as well as a stereocontroller:[9] The 2-pyridylsulfonyl group may have the following advantages: (1) the electron-withdrawing property increases the reactivity of imines for the nucleophilic addition, (2) coordination of a Lewis acid to the pyridyl nitrogen and one of the sulfonyl oxygens controls the stereoselectivity and stereochemistry, and (3) the 2-pyridylsulfonyl group is easily removable from the products (Fig. 1). We now report a new enantioselective nucleophilic addition to 2-pyridylsulfonylimines with Grignard reagents and conversion to chiral amines.[10,11]

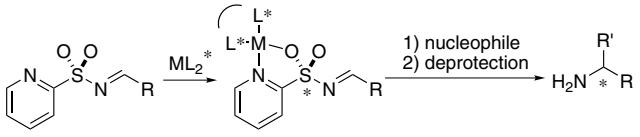

Figure 1. 2-Pyridylsulfonyl group as a new coordinative protecting and activating group as well as a stereocontroller.

Keywords: 2-Pyridylsulfonyl group; Grignard reagents; Stereocontroller; Imine.
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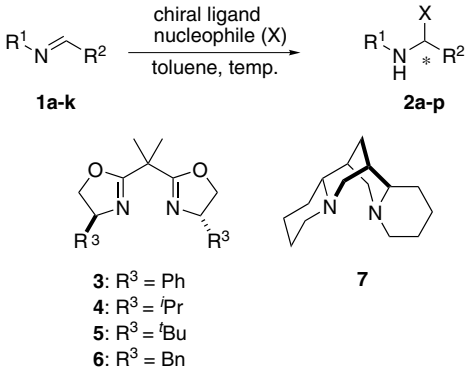
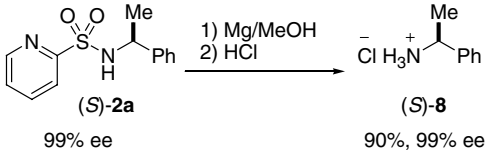
2. Results and discussion

We examined the reaction of *N*-benzylidene-2-pyridinesulfonamide **1a** with CH_3MgI (2 equiv) using various chiral ligands (1.5 equiv) such as bis(oxazoline)s **3**–**6** and (−)-sparteine **7** (Scheme 1). As a result, bis(oxazoline)-Ph **3** was found to be an efficient ligand for this reaction (entries 1–5).[12] Performing the reaction at −95 °C increased enantioselectivity (entry 6). Reaction of **1a** with CH_3MgBr gave better results in comparison with CH_3MgI and CH_3MgCl to give the *S*-isomer with 83% ee in 79% yield (entry 7).[13] The reactions of various



Scheme 1.

2-pyridylsulfonylimines **1b**–**f** (R^2 = *p*-tolyl, 4-chlorophenyl, 1-naphthyl, cinnamyl, 2-furyl) with CH_3MgBr were examined and it was found that the corresponding sulfonamides **2b**–**f** were formed in good yields with good enantioselectivities (entries 9–13). To our knowledge, this reaction is the first highly enantioselective addition of Grignard reagents to imines.[14] Efficiency of 2-pyridylsulfonyl group in the reaction with Grignard reagents is shown by the following results. *N*-(2-Pyridylmethyl)aldimine **1g** did not show enough reactivity toward CH_3MgBr because of the lack of a sulfonyl group (entry 14). In addition, *N*-benzylidene-*p*-methoxyaniline **1h**, which is often used in the enantioselective addition of organolithium reagents was not a good substrate for the addition with CH_3MgI (entry 15).[15] Furthermore, *N*-benzylidene-*p*-toluenesulfonamide **1i** and *N*-benzylidene-2,4,6-triisopropylbenzenesulfonamide **1j** were also not proper choice as substrates and their reaction with CH_3MgI at −78 °C in the presence of bis(oxazoline)-



Scheme 2.

Table 1. Enantioselective addition of organometallic reagents to aldimines **1a**–**k**

Entry	Imine	R^1	R^2	Nucleophile	Ligand	Temperature (°C)	Product	Yield (%)	ee[a] (%)
1	**1a**	2-$PySO_2$	Ph	CH_3MgI	**3**	−78	**2a**	75	59
2	**1a**	2-$PySO_2$	Ph	CH_3MgI	**4**	−78	**2a**	31	7
3	**1a**	2-$PySO_2$	Ph	CH_3MgI	**5**	−78	**2a**	56	40
4	**1a**	2-$PySO_2$	Ph	CH_3MgI	**6**	−78	**2a**	77	0
5	**1a**	2-$PySO_2$	Ph	CH_3MgI	**7**	−78	**2a**	90	0
6	**1a**	2-$PySO_2$	Ph	CH_3MgI	**3**	−95	**2a**	27	72
7	**1a**	2-$PySO_2$	Ph	CH_3MgBr	**3**	−95	**2a**	79	83 (>99)[b]
8	**1a**	2-$PySO_2$	Ph	CH_3MgCl	**3**	−95	**2a**	53	86
9	**1b**	2-$PySO_2$	*p*-Tol	CH_3MgBr	**3**	−95	**2b**	67	83
10	**1c**	2-$PySO_2$	*p*-ClC_6H_4	CH_3MgBr	**3**	−95	**2c**	77	76
11[c]	**1d**	2-$PySO_2$	1-Naphthyl	CH_3MgBr	**3**	−95	**2d**	74	76 (95)[b]
12	**1e**	2-$PySO_2$	Cinnamyl	CH_3MgBr	**3**	−95	**2e**	98	82
13[c]	**1f**	2-$PySO_2$	2-Furyl	CH_3MgBr	**3**	−95	**2f**	38	87
14	**1g**	2-$PyCH_2$	Ph	CH_3MgI	**3**	−95	**2g**	0	—
15	**1h**	*p*-$MeOC_6H_4$	Ph	CH_3MgI	**3**	−95	**2h**	0	—
16	**1i**	*p*-$TolSO_2$	Ph	CH_3MgI	**3**	−78	**2i**	92	11
17	**1j**	$TipSO_2$[d]	Ph	CH_3MgI	**3**	−78	**2j**	69	20
18	**1k**	8-$QnSO_2$[e]	Ph	CH_3MgI	**3**	−78	**2k**	52	0
19	**1a**	2-$PySO_2$	Ph	EtMgBr	**3**	−95	**2l**	74	50
20	**1a**	2-$PySO_2$	Ph	BuMgBr	**3**	−95	**2m**	69	51
21	**1a**	2-$PySO_2$	Ph	^{i}PrMgBr	**3**	−95	**2n**	87	6
22[c,f]	**1a**	2-$PySO_2$	Ph	^{t}BuMgBr	**3**	−78	**2o**	15	6
23	**1b**	2-$PySO_2$	Ph	PhMgI	**3**	−95	**2p**	41	66
24	**1b**	2-$PySO_2$	*p*-Tol	PhMgBr	**3**	−95	**2p**	72	61
25[g]	**1a**	2-$PySO_2$	*p*-Tol	Et_2Zn	**3**	−40	**2l**	49	46
26	**1a**	2-$PySO_2$	Ph	MeLi	**3**	−78	**2a**	35	35[g]

[a] ee was determined by the HPLC analysis.
[b] ee in parentheses is that obtained after single recrystallization.
[c] Bis(oxazoline) **3** (2 equiv) was used.
[d] $TipSO_2$ = (2,4,6-triisopropylphenyl)sulfonyl.
[e] 8-$QnSO_2$ = (8-quinolyl)sulfonyl.
[f] *N*-(2-Pyridylsulfonyl)benzylamine was obtained in 35% yield.
[g] The *R*-isomer was obtained.

Ph **3** afforded the products **2i** and **2j**, respectively, in poor yields with low enantioselectivities (entries 16 and 17). The reaction of *N*-benzylidene-8-quinolinesulfonamide **1k** afforded the racemic product **2k** (entry 18). The reaction of **1a** with EtMgBr, BuMgBr, and ^{i}PrMgBr gave products **2l–n** in good yields but with enantioselectivity lower than that with CH_3MgBr (entries 19–21 vs entry 7). The reaction using ^{t}BuMgBr resulted in a low yield of the product **2o** besides the formation of an abnormal Grignard product[16] (entry 22). The reaction of **1a** with PhMgI and PhMgBr gave products **2p** in good yields and enantioselectivity (entries 23 and 24). The nucleophilic addition of Et_2Zn to *N*-benzylidene-2-pyridinesulfonamide **1a** did not proceed with high enantioselectivity (entry 25), whereas the nucleophilic addition of MeLi mainly gave the *R*-isomer (entry 26).

Since most of the products were crystalline, enantiomerically pure sulfonamides were easily obtainable by recrystallization. For example, recrystallization of **2a** (83% ee) from hexane/CH_2Cl_2 afforded enantiomerically pure (*S*)-**2a**. To realize the synthetic potential of this stereoselective preparation of chiral amines, we confirmed the easy removal of the 2-pyridylsulfonyl group. Although removal of arylsulfonyl groups generally needs drastic reaction conditions,[17] the pyridylsulfonyl group could be removed from the optically active (*S*)-**2a** on treatment with magnesium in MeOH at 0 °C[18] and chiral amine (*S*)-**8** was found to be formed without loss of optical purity (Scheme 2).[19]

The reaction of *p*-tolylsulfonylimine **1i** and 2,4,6-triisopropylphenylsulfonylimine **1j** with CH_3MgI afforded products **2i** and **2j** with low enantioselectivities, whereas the reaction of 2-pyridylsulfonylimine **1a** showed high enantioselectivity (Table 1, entries 16 and 17 vs entry 1), showing that 2-pyridylsulfonyl group acts not only as an activating group but also as an efficient stereocontroller. Assuming that Mg(II) forms a tetrahedral bidentate-coordinating complex with the substrate **1a**,[20] there would be two types of coordination for the complex to be considered:[21] One is the *N*,*N*-type complex, in which Mg(II) coordinates to the imino and pyridyl nitrogens and the other is the *N*,*O*-type complex, in which Mg(II) coordinates to a pyridyl nitrogen and one of the sulfonyl oxygens. Energies of the Mg(II) complexes of 2-pyridylsulfonylimine **1a** and bis(oxazoline)-Ph **3**, were calculated by the MOPAC 93/PM3 method,[22] showing the stable complex in which Mg(II) coordinates to a pyridyl nitrogen and a *pro*-*S* sulfonyl oxygen (Fig. 2). CH_3MgX approaches the *Si*-face of this imine complex to form (*S*)-**2a**. Dynamically induced chirality on the sulfur indeed plays a definitive role in induction of enantioselectivity: It can be categorized as a new type of chiral relay.[23]

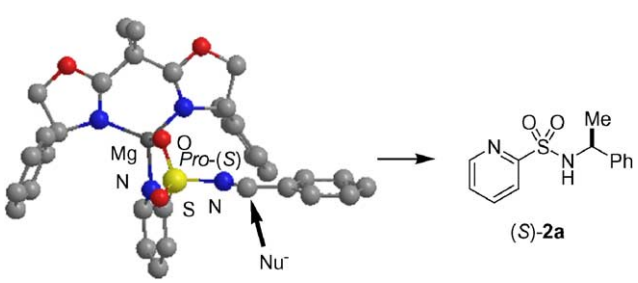


Figure 2. Geometry optimization of **1a**–**3** complex by MOPAC 93/PM3.

3. Conclusion

The first highly enantioselective reaction of imines with Grignard reagents was achieved in the presence of bis(oxazoline)s by using a pyridylsulfonyl group as a protective group. The reaction was suggested by the MOPAC 93/PM3 calculation to proceed through a complex in which one of the sulfonyl oxygens is preferably coordinated to Mg(II). The 2-pyridylsulfonyl group was shown to be an easily removable, efficient protective group, which has notable properties of high chiral inducibility and activation of the imino group toward the addition of Grignard reagents.[24]

Acknowledgment

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References and notes

1. For reviews, see: (a) Enders, E.; Reinhold, U. *Tetrahedron: Asymmetry* **1997**, *8*, 1895–1946, and references cited therein; (b) Alvaro, G.; Savoia, D. *Synlett* **2002**, 651–673; (c) Bloch, R. *Chem. Rev.* **1998**, *98*, 1407–1438.
2. For reviews, see: (a) Denmark, S. E.; Nicaise, O. J.-C. *J. Chem. Soc., Chem. Commun.* **1996**, 999–1004; (b) Kobayashi, S.; Ishitani, H. *Chem. Rev.* **1999**, *99*, 1069–1094.
3. (a) Tomioka, K.; Inoue, I.; Shindo, M.; Koga, K. *Tetrahedron Lett.* **1991**, *32*, 3095–3098; (b) Inoue, I.; Shindo, M.; Koga, K.; Tomioka, K. *Tetrahedron: Asymmetry* **1993**, *4*, 1603–1606; (c) Denmark, S. E.; Nakajima, N.; Nicaise, O. J.-C. *J. Am. Chem. Soc.* **1994**, *116*, 8797–8798; (d) Inoue, I.; Shindo, M.; Koga, K.; Kanai, M.; Tomioka, K. *Tetrahedron: Asymmetry* **1995**, *6*, 2527–2533; (e) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 8489–8490; (f) Itsuno, S.; Watanabe, K.; Ito, K.; El-Shehawy, A. A.; Sarhan, A. A. *Angew. Chem., Int. Ed.* **1997**, *36*, 109–110; (g) Chen, G. M.; Ramachandran, P. V.; Brown, H. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 825–826; (h) Motoyama, Y.; Mikami, Y.; Kawakami, H.; Aoki, K.; Nishiyama, H. *Organometallics* **1999**, *18*, 3584–3588; (i) Denmark, S. E.; Stiff, C. M. *J. Org. Chem.* **2000**, *65*, 5875–5878; (j) Porter, J. R.; Traverse, J. F.; Hoveyda, A. H.; Snapper, M. L. *J. Am. Chem. Soc.* **2001**, *123*, 984–985; (k) Cabello, N.; Kizirian, J.-C.; Alexakis, A. *Tetrahedron Lett.* **2004**, *45*, 4639–4642.
4. For enantioselective reactions of phosphinoylimines with dialkylzinc reagents, see: (a) Soai, K.; Hatanaka, T.; Miyazawa, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1097–1098; (b) Guijarro, D.; Pinho, P.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 2530–2535; (c) Kodaka, R.; Sato, I.; Soai, K. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2912–2914; (d) 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.

5. Dahmen, S.; Bräse, S. *J. Am. Chem. Soc.* **2002**, *124*, 5940–5941.
6. (a) Fang, X.; Johannsen, M.; Yao, S.; Gathergood, N.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1999**, *64*, 4844–4849; (b) Hayashi, T.; Ishigedani, M. *J. Am. Chem. Soc.* **2000**, *122*, 976–977; (c) Fujihara, H.; Nagai, K.; Tomioka, K. *J. Am. Chem. Soc.* **2000**, *122*, 12055–12056; (d) Soeta, T.; Nagai, K.; Fujihara, H.; Kuriyama, M.; Tomioka, K. *J. Org. Chem.* **2003**, *68*, 9723–9727; (e) Wang, C. J.; Shi, M. *J. Org. Chem.* **2003**, *68*, 6229–6237; (f) Otomaru, Y.; Tokunaga, N.; Shintani, R.; Hayashi, T. *Org. Lett.* **2005**, *7*, 307–310, and reference cited therein.
7. Tomioka, K.; Inoue, I.; Shindo, M.; Koga, K. *Tetrahedron Lett.* **1990**, *31*, 6681–6684.
8. For the enantioselective allylation reaction of acylhydrazones, see: (a) Hirabayashi, R.; Ogawa, C.; Sugiura, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 9493–9499; (b) Berger, R.; Rabbat, P. M. A.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 9596–9597; For the reaction of *N*-(2-hydroxyphenyl)imines, see: (c) Ishitani, H.; Kobayashi, S. *Tetrahedron Lett.* **1996**, *37*, 7357–7360; (d) Ishitani, H.; Ueno, M.; Kobayashi, S. *J. Am. Chem. Soc.* **1997**, *119*, 7153–7154; (e) Kobayashi, S.; Komiyama, S.; Ishitani, H. *Angew. Chem., Int. Ed.* **1998**, *37*, 979–981; (f) Gastner, T.; Ishitani, H.; Akiyama, R.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 1896–1898.
9. We have reported highly enantioselective radical addition to vinylsulfones, in which a chiral Lewis acid selectively coordinates one of the enantiotopic sulfonyl oxygens and nitrogen in the heteroarylsulfonyl group: (a) Sugimoto, H.; Nakamura, S.; Watanabe, Y.; Toru, T. *Tetrahedron: Asymmetry* **2003**, *14*, 3045–3055; (b) Sugimoto, H.; Kobayashi, K.; Nakamura, S.; Toru, T. *Tetrahedron Lett.* **2004**, *45*, 4213–4216; (c) Watanabe, Y.; Mase, N.; Furue, R.; Toru, T. *Tetrahedron Lett.* **2001**, *42*, 2981–2984.
10. The 2-pyridylsulfonyl group has been used for the synthesis of sulfonamides: (a) Han, H.; Bae, I.; Yoo, E. J.; Lee, J.; Do, Y.; Chang, S. *Org. Lett.* **2004**, *6*, 4109–4112; (b) Arrayâs, R. G.; Cabrera, S.; Carretero, J. C. *Org. Lett.* **2005**, *7*, 219–221.
11. Recently, chiral 2-pyridinesulfonamide derivatives have been reported to have an inhibitory activity to the osteoclast-specific cysteine protease cathepsin K: (a) Marquis, R. W.; Ru, Y.; LoCastro, S. M.; Zeng, J.; Yamashita, D. S.; Oh, H.-J.; Erhard, K. F.; Davis, L. D.; Tomaszek, T. A.; Tew, D.; Salyers, K.; Proksch, J.; Ward, K.; Smith, B.; Levy, M.; Cummings, M. D.; Haltiwanger, R. C.; Trescher, G.; Wang, B.; Hemling, M. E.; Quinn, C. J.; Cheng, H.-Y.; Lin, F.; Smith, W. W.; Janson, C. A.; Zhao, B.; McQueney, M. S.; D'Alessio, K.; Lee, C.-P.; Marzulli, A.; Dodds, R. A.; Blake, S.; Hwang, S.-M.; James, I. E.; Gress, C. J.; Bradley, B. R.; Lark, M. W.; Gowen, M.; Veber, D. F. *J. Med. Chem.* **2001**, *44*, 1380–1395; (b) Trout, R. E. L.; Marquis, R. W. *Tetrahedron Lett.* **2005**, *46*, 2799–2801.
12. The reaction of **1a** with a catalytic amount (0.3 equiv) of bis(oxazoline) **3** and MeMgBr gave **2a** with 29% ee.
13. Typical procedure for enantioselective addition of Grignard reagents to **1a**: Preparation of *N*-(1-phenylethyl)-2-pyridinesulfonamide (*S*)-**2a**. To a solution of bis(oxazoline)-Ph (244 mg, 0.731 mmol) and imine **1a** (120 mg, 0.487 mmol) in toluene (10 mL) was added MeMgBr (1.04 mol L^{-1} in Et_2O, 0.937 mL, 0.974 mmol) at −95 °C and the reaction mixture was stirred for 1 h. The reaction was quenched with 1 N HCl and extracted with Et_2O. The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure to leave a residue, which was purified by column chromatography (SiO_2 20 g, benzene/ethyl acetate = 90/10) to afford (*S*)-**2a** (101 mg, 79%, 83% ee). Recrystallization from hexane/CH_2Cl_2 afforded (*S*)-**2a** with 99% ee.
14. There are some examples for the enantioselective reaction of nitrones with Grignard reagents: (a) Ukaji, Y.; Hatanaka, T.; Ahmed, A.; Inomata, K. *Chem. Lett.* **1993**, 1313–1316; (b) Merchan, F. L.; Merino, P.; Rojo, I.; Tejero, T.; Dondoni, A. *Tetrahedron: Asymmetry* **1996**, *7*, 667–670.
15. Generally, the reactivity of Grignard reagents to imines is low: Saito, S.; Hatanaka, K.; Yamamoto, H. *Synlett* **2001**, 1859–1861.
16. (a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392–4398; (b) Swain, C. G.; Boyles, H. B. *J. Am. Chem. Soc.* **1951**, *73*, 870–872.
17. (a) Kovacs, J.; Ghatak, U. R. *J. Org. Chem.* **1966**, *31*, 119–121; (b) Ji, S.; Gortler, L. B.; Waring, A.; Battisti, A.; Bank, S.; Closson, W. D.; Wriede, P. *J. Am. Chem. Soc.* **1967**, *89*, 5311–5312; (c) D'Souza, L.; Day, R. A. *Science* **1968**, *160*, 882–883; Conversion to *N*-alkyl-*N*-sulfonyl compounds or *N*-Boc-*N*-sulfonyl compounds prior to the cleavage is needed for removal of a tosyl group from the primary amines, see: (d) Nyasse, B.; Grehn, L.; Ragnarsson, U. *Chem. Commun.* **1997**, 1017–1018, and references cited therein; (e) Juhl, K.; Gathergood, N.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 2995–2997.
18. (a) Goulaouic-Dubois, C.; Guggisberg, A.; Hesse, M. *J. Org. Chem.* **1995**, *60*, 5969–5972; (b) Pak, C. S.; Lim, D. S. *Synth. Commun.* **2001**, *31*, 2209–2214.
19. Preparation of (*S*)-1-phenylethylamine hydrochloride (*S*)-**8**: A mixture of (*S*)-**2a** (20.2 mg, 0.077 mmol) and Mg powder (9.3 mg, 0.385 mmol) in MeOH (2 mL) and THF (0.5 mL) was stirred for 2 h at 0 °C. Then, diethyl ether (3 mL) and saturated aq NH_4Cl (3 mL) were added and the reaction mixture was stirred for 2 h at room temperature. The aqueous layer was extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to leave the oil, which was purified by column chromatography (CH_2Cl_2/MeOH/aq NH_3 = 90/10/0.5) to afford the amine. The amine was dissolved in THF (2 mL) and to the resultant solution was added a 2 N HCl solution. After stirring for 30 min at room temperature, the solution was concentrated under reduced pressure to give (*S*)-**8** (10.9 mg, 90%). In order to determine the enantiopurity, (*S*)-**8** was transformed to *N*-benzoyl-1-phenylethylamine on treatment with benzoyl chloride and triethylamine in CH_2Cl_2 at room temperature. This amide was found to be 99% ee by HPLC analysis using CHIRALCEL OD-H.
20. Tetrahedral Mg(II) complex has been proposed: (a) Corey, E. J.; Ishihara, K. *Tetrahedron Lett.* **1992**, *33*, 6807–6810; (b) Sibi, M. P.; Sausker, J. B. *J. Am. Chem. Soc.* **2002**, *124*, 984–991; The octahedral structure has been also proposed: (c) Sibi, M. P.; Petrovic, G.; Zimmerman, J. *J. Am. Chem. Soc.* **2005**, *127*, 2390–2391; (d) Gothelf, K. V.; Hazell, R. G.; Jørgensen, K. A. *J. Org. Chem.* **1998**, *63*, 5483–5488.
21. Yao, S.; Saddy, S.; Hazell, R. G.; Jørgensn, K. A. *Chem. Eur. J.* **2000**, *6*, 2435–2448.
22. Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209–220.
23. For chiral relay in enantioselective reactions, see: Corminboeuf, O.; Quaranta, L.; Renaud, P.; Liu, M.; Jasperse, C. P.; Sibi, M. P. *Chem. Eur. J.* **2003**, *9*, 28–35.
24. Just before the submission of this manuscript, Carretero and co-workers have reported the enantioselective conjugate addition of Me_2Zn to *N*-(2-pyridyl)sulfonyl-α,β-unsaturated ketimines derived from chalcone, see: Esquivias, J.; Arrayás, R. G.; Carretero, J. C. *J. Org. Chem.* **2005**, *70*, 7451–7454.