Pergamon

Tetrahedron, Vol. 52, No. 38, pp. 12571-12586, 1996

0040-4020/96 $15.00 + 0.00

PII: S0040-4020(96)00746-6

Diastereoselective Addition of Methyllithium and Dimethylcuprate-Boron Trifluoride to Imines Derived from (*S*)-1-Phenylethylamine

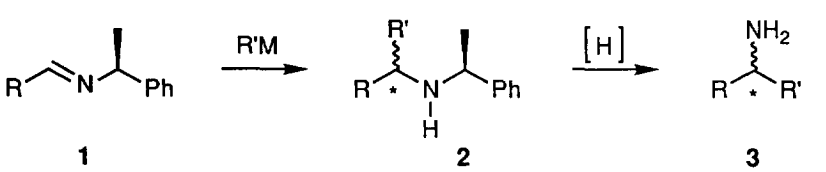
Giuseppe Alvaro, Diego Savoia * and Maria R. Valentinetti §

Dipartimento di Chimica "G. Ciamician", Università degli Studi di Bologna, via Selmi 2, 40126 Bologna, Italy

Abstract: The reactions of dimethylcuprate-boron trifluoride reagents with the imines derived from (*S*)-1-phenylethylamine afforded the secondary amines by addition to the *Si* face of the imines. (*S,S*)-bis(1-phenylethyl)amine and (*S*)-1-cyclohexylethanamine were prepared with high stereoselectivity, in the latter case by a two step sequence involving the final cleavage of the auxiliary. Methyllithium attacked mainly the *Si* face of the imines derived from 4-pyridine carboxaldehyde and 2-methoxybenzaldehyde, but the *Re* face of the imines derived from 2-pyridine and 2-furan carboxaldehyde.

The addition of organometallic reagents to imines **1** derived from homochiral 1-phenylethanamine is an appealing route to optically active secondary and primary amines **2** and **3**, respectively (Scheme 1), owing to the availability and low cost of both enantiomers of this amine. However, the reactions of Grignard and organolithium reagents are often plagued by the poor yields due to the low electrophilicity of the C=N double bond, the competing α-metalation of enolizable imines and the formation of byproducts coming from SET processes of aromatic imines.[1] The organometallic reaction is most successful with imines activated by electron withdrawing substituents as substrates, e.g. α-imino esters[2] or 1,2-diimines,[3] and/or by using benzylic and allylic organometallic reagents.[2-4] The auxiliary can be removed from **2** when R is an alkyl group, or a phenyl group with two alkoxy substituents,[5] to obtain the primary amines **3**.

Prompted by the report of the efficient addition of organocopper-boron trifluoride reagents to imines,[6] and by the lack of general methods for the diastereoselective addition of alkylmetal compounds to imines **1**,[7] we undertook a research program, whose preliminary results have been reported.[8] Here we describe the full experimental study of the reactions of methylmetal reagents with imines derived from (*S*)-1-phenylethylamine.



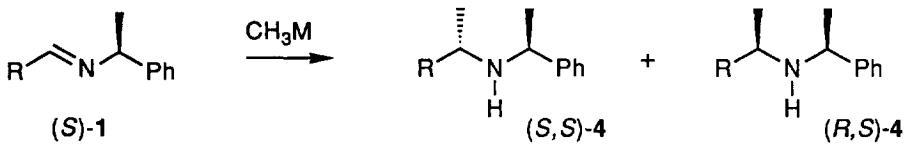
1 **2** **3**

Scheme 1

§ Present address: Agip Petroli, via Laurentina 449, 00142 Roma, Italy

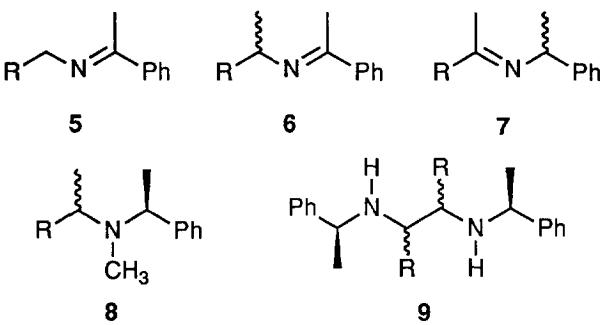
RESULTS AND DISCUSSION

The addition of methylmetal reagents to the imines **1a-i** afforded mixtures of diastereomeric secondary amines **4** (Scheme 2). The best results were obtained by using methyllithium and methylcopper- and dimethylcuprate-boron trifluoride reagents in tetrahydrofuran (Table 1). The formation of byproducts **5-9** was affected by the nature of the group R of the imine and the organometallic reagent and was more relevant working in diethyl ether.



a: R = Ph
b: R = 2-Pyridyl
c: R = 4- Pyridyl
d: R = 2-CH_3O-C_6H_4
e: R = 4-CH_3O-C_6H_4
f: R = 2,5-$(CH_3O)_2C_6H_3$
g: R = 2-Furyl
h: R = n-C_5H_{11}
i: R = Cyclohexyl

Byproducts:



Scheme 2

The reactivity of the aromatic imines towards CH_3Li was affected by the electronic effects of the aryl substituents: the reaction with the pyridine imines **1b,c** was particularly rapid at -78 °C, but with the methoxy-substituted benzaldimines **1d-f** and the 2-furan imine started only by raising the temperature and gave more amounts of byproducts. The progress of the reactions was highlighted by the appearance of an intense red colour of the solution.

The preparation of methylcopper- and dimethylcuprates-BF_3 reagents from CH_3Li or CH_3MgCl and their reaction with the imines were performed according to the reported procedure.[6] Working on **1a** it was found that dimethylcuprates prepared from CH_3MgCl were more reactive, although slightly less diastereoselective, than the dimethylcuprate prepared from CH_3Li and the methylcopper reagents, so this reagent (2-5 equivalents) was successively used with the other imines. Surprisingly, **1b,c** were almost unreactive even in the absence of BF_3. Less satisfactory results (not reported in Table 1) were also obtained with **1a** and cuprate-BF_3 reagents prepared from CuCN and $CuBr\text{-}S(CH_3)_2$, as well by adding PBu_3 (1 equivalent) to $CH_3Cu\text{-}MgICl\text{-}BF_3$. Moreover, CH_3MgCl and the cerium and titanium reagents prepared from CH_3Li and stoicheiometric amounts of $CeCl_3$ and $TiCl_4$, respectively, were unreactive or worked unsatisfactorily with **1a** and/or **1b**.

Table 1. Addition of Methyllithium and Methylcopper Reagents to the Imines **1a-i**.[a]

Imine	R	CH_3M (equivalents)	Amine	Yield (%)[b]	*S,S*/*R,S*[b]
1a	Ph	CH_3Li (2.2)	**4a**	88[c]	70:30
		CH_3Cu-LiI-BF_3 (2)		43[c]	94:6
		$(CH_3)_2CuLi$-LiI-BF_3 (5)		47[c]	93:7
		CH_3Cu-MgICl-BF_3 (2)		70[c]	90:10
		$(CH_3)_2CuMgCl$-MgICl-BF_3 (2)		87[c] (75)[d]	86:14
1b	2-pyridyl	CH_3Li (1.5)	**4b**	100 (96)[d]	18:82[d]
1c	4-pyridyl	CH_3Li (1.1)	**4c**	87[e] (76)[d]	90:10
1d	2-CH_3O-C_6H_4	CH_3Li (1.1)	**4d**	83[f,g]	69:31
		$(CH_3)_2CuMgCl$-MgICl-BF_3 (5)		70	70:30
1e	4-CH_3O-C_6H_4	CH_3Li (1.2)	**4e**	81[f,h]	70:30
		$(CH_3)_2CuMgCl$-MgICl-BF_3-$S(CH_3)_2$ (5)		38[i]	88:12
1f	2,5-$(CH_3O)_2C_6H_3$	CH_3Li (1,2)	**4f**	92[j]	70:30
1g	2-furyl	CH_3Li (1.2)	**4g**	100[f]	30:70
		$(CH_3)_2CuMgCl$-MgICl-BF_3 (4)		97	73:27
1h	n-C_5H_{11}	CH_3Cu-MgICl-BF_3 (5)	**4h**	55[k]	84:16
1i	cyclohexyl	CH_3Li (1.1)	**4i**	44[l]	74:26
		$(CH_3)_2CuMgCl$-MgICl-BF_3 (2)		93[m] (91[d]	93:7

(a) The imine (1 mmol) was added slowly to the solution of CH_3Li (1.6 M in Et_2O) or the methylcopper species in anhydrous THF cooled to -78 or -40 °C, respectively. (b) Determined by GC-MS analysis; for the dibenzylic amines **4a-g** the *S,S* diastereomer was eluted first, but for **4h,i** the inverse order of elution was observed. (c) The product **4a** was accompanied mainly by the starting imine **1a**, although some byproducts were present. (d) Yield of isolated crude product. (e) **7c**, 13%. (f) The reaction starts only allowing the temperature to raise to -10 °C. (g) **8d**, 12%; other byproducts, 5%. (h) **6e**, 9%; **7e**, 5%; **8e**, 3%. (i) **1e**, 58%; **9**, 4% (j) **6f**, 8%. (k) Higher boiling products, probably coming from the autocondensation of the starting imine were produced. (l) **1h** (44%) and other unidentified products were present. (m) Unidentified higher boiling products were formed (7%).

The reaction of CH_3Li with **1a,b** was studied thoroughly by varying several factors: temperature, solvent, procedure of addition, and commercial solutions of CH_3Li (Table 2). The addition of CH_3Li to **1a** did not proceed at -90 °C (no colour), then the temperature was allowed to increase gradually to 0 °C during 3 h, meanwhile a dark red colour was observed, and the reaction mixture was quenched to give **4a** with moderate yield and diastereoselectivity, accompanied by the starting imine and byproducts. Comparable results were obtained at 0 °C. By performing the addition of CH_3Li (Et_2O solution) to **1b** in Et_2O the yield of **4b** was lower, owing to the presence of byproducts **5b**, **6b** and **8b**, with respect to the corresponding reaction performed in THF (Table 1). Moreover, the reaction in THF with CH_3Li as a THF-cumene solution gave a poor yield of **4b** and the main product was acetophenone coming from the hydrolysis of the ketimine **6b** (Scheme 2). By using the CH_3Li-LiBr or by adding preliminarily ZnI_2 to **1b** in THF the yield of **4b** was very high, but the diastereomeric ratios were again lower than that obtained in THF. The inverse addition of the imine to CH_3Li in either THF and Et_2O gave similar results. No improvement in either the yield and the diastereoselectivity of **4b** was obtained by working with CH_3Li in 1,2-dimethoxyethane.

Table 2. Addition of Methyllithium to **1a,b** in Different Experimental Conditions.[a]

Imine	CH_3Li	Solvent	Procedure[b]	Temp.(°C)	**4**, Yield (%)[c]	$(S,S)/(R,S)$[c]
1a	1.6 M, Et_2O[d]	Et_2O	A	-30 to 0	**4a**, 85[e]	69:31
"	1.6 M, Et_2O	"	B	-78 to 0	", 54[f]	65:35
"	"	"	"	0	", 65[f]	61:39
1b	"	"	"	-78	**4b**, 72[g]	20:80
"	"	"	A	"	", 77[g]	25:75
"	"	THF	C	"	", 96	20:80
"	1 M, THF-cumene (1:9)	cumene-THF (1:2)	"	"	", 12[h]	21:79
"	-LiBr, 1.5 M, THF	THF	A or B	"	", 96[i]	24:76

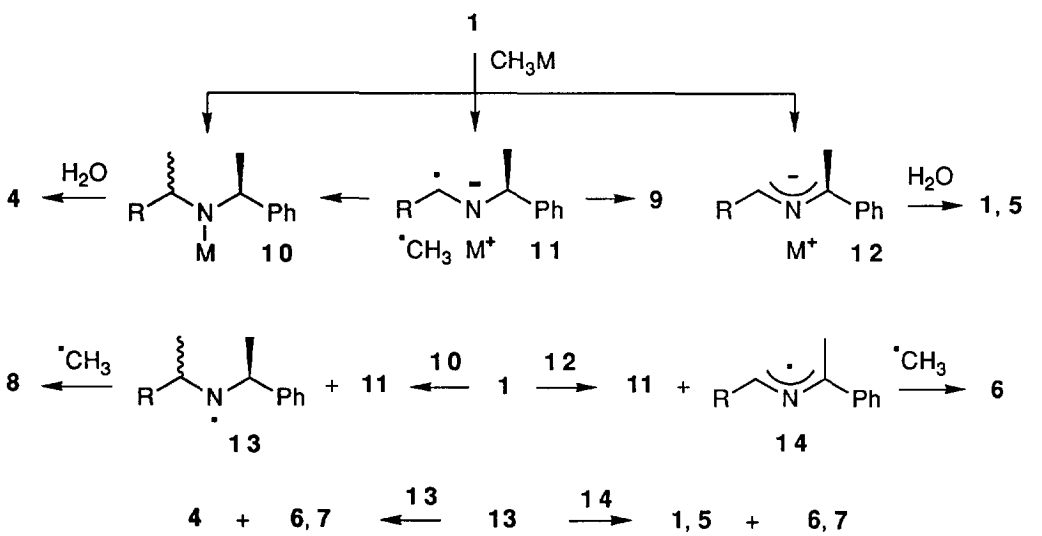
(a) Unless otherwise specified, the reactions were performed on 1 mmol of **1a,b** by using 1,5 molar equivalents of CH_3Li and quenching with H_2O after 3 h. (b) A: the imine was added to the 0.5 M solution of CH_3Li; B: CH_3Li was added to the 0.5 M solution of the imine; C: dried ZnI_2 (1 equiv.) was added to the solution of the imine, followed by CH_3Li (4 equiv.). (c) The yields and ratios were determined by GC-MS analysis. (d) 3 Equivalents of CH_3Li were used. (e) **1a**, 12%. (f) **1a**, 7-12%; **5a**, 16-19%; **6a = 7a**, 4-6%. (g) **1b**, 4-8%; **5b**, 14-21%; **6b-7b**, 2-4%. (h) $PhCOCH_3$ (67%); **5b** (9%); **9b** (8%). (i) Three minor byproducts, presumably including **6b-7b**, 4%.

Unidentified high-boiling products were obtained from the aliphatic imine **1g** probably by autocondensation of the imine, through its metalation in the α position (CH-C=N). On the other hand, the structures of the byproducts **5-9** coming from the aromatic imines were generally determined only on the basis of the molecular ion and fragmentation pattern observed in their mass spectra,[9] as we made no effort to isolate them. For example the structure of **8e** was inferred by the presence of the molecular ion (m/z 269, 3%) and of the fragments coming from α-scission at either the benzylic positions (m/z 135, 100%; 105, 10%) and β-scission of the methyl group (m/z 254, 87%). Isomeric ketimines **1/5** and **6/7** could be similarly recognized by the m/z values of the benzylic fragments present in their mass spectra, but **6a** (**7a**) was unambiguosly identified by comparison of the GC retention times and mass spectrum with those of an authentic sample prepared from acetophenone and 1-phenylethylamine.

Mechanisms

The side products **5-9** were formed especially in the reactions of CH_3Li with aromatic imines through pathways alternative to the polar addition leading to the adduct amide **10**, when the latter was disfavoured by electronic effects, i.e. the presence of methoxy substituents on the aryl group, or the use of diethyl ether as the solvent (Scheme 3). The purple colour observed for the reaction mixtures can be attributed to the formation of a charge transfer complex,[10] or an imine radical-anion coming from a SET process.[11] The SET process would lead to the expected product **4** through radical anion (**11**)-radical cation ($\cdot CH_3$ Li^+) coupling; the presence of little amounts of 1,2-diamines **9** in some reaction mixtures (**1d**-CH_3Li-THF, **1e**-cuprate-THF, **1a**-CH_3Li-Et_2O, **1b**-CH_3Li-THF-cumene) supports the occurrence, at least partially, of the SET mechanism. A third reaction pathway involves metalation of the imine at the benzylic position (H-C*) to give the coloured 2-azaallylanion **12**,[12] whose protonation on quenching leads to either the starting imine **1** and/or the isomeric ketimine **5**.

The ketimines **6/7** and tertiary amines **8** were unexpected in these reactions and any mechanism able to explain their formation can be only speculative at the moment. We propose that the intermediate amide **10** reacts by a SET mechanism with the starting imine **1**, to give the radical anion **11** and the aminyl radical **13**, from which the tertiary amine **8** can be produced by coupling with a methyl radical (Scheme 3). We also envisaged that the 2-azaallyl anion **12** reacts similarly (SET) with **1**, giving **11** and the 2-azaallyl radical **14**, which is converted to **6** by coupling with a methyl radical. The disproportionation reaction (hydrogen atom transfer) of two aminyl radicals **14**, as well as of the radicals **14** and **15**, can account for the formation of the imines **1/5** and **6/7**. Notably, the products of aromatic substitution reactions were never formed from the methoxy-substituted benzaldimines **1d-f**, contrary to the observation of such pathway in the reaction of methyllithium with analogous imines carrying a very bulky alkyl substituent at nitrogen.[13]

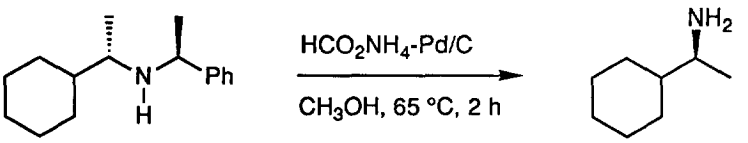


Scheme 3

Configuration of the Secondary Amines 4 and Synthesis of (S)-1-Cyclohexylethylamine (S)-15i

The configuration of the prevalent diastereomers of **4a**, **4b** and **4d** was unambiguously determined on the isolated products by measurements of their optical activity and ^{1}H-NMR spectra, and by comparison with the authentic (*S,S*)-**4a**,[14] (*S,S*)**4b**,[14-16] and (*S,S*)-**4d**.[14] Since all these *S,S* diastereomers were eluted first, the configuration of the diastereomers of the other dibenzylic amines **4c,e-g** could be assigned simply on the basis of the relative GC-MS retention times. The ^{1}H NMR analysis of the diastereomeric mixtures was also usefully applied to determine the configuration of **4a-d,g**, the *S,S* diastereomers gave signals for the benzylic and methyl protons at higher fields than the *R,S* diastereomers.[4b]

Moreover, removal of the auxiliary group of **4i** lead to (*S*)-(+)-**15i**, as evidenced by comparison with the commercially available authentic compound (Scheme 4). The *S,S*-configuration of the prevalent diastereomer of **4h** was assumed by analogy. Notably, the order of elution (GC) of the diastereoisomers of the N-(1-phenylethyl) N-(sec-alkyl) amines **4h,i** was inverted with respect to the dibenzylic amines **4a-g**.



(*S,S*)-**4l**, d.r. 93:7 (*S*)-**15i**

Scheme 4

Asymmetric Induction

The sense of asymmetric induction in the reactions with methyllithium was affected by the capability of the imine to form chelate complexes with lithium, as the bidentate 2-pyridineimine **1b** and 2-furylimine **1g** underwent addition mainly to the *Re* face, contrary to the other aliphatic and aromatic imines, including the potentially bidentate imines **2d,f**. Notably, mesomeric electronic effects had no relevance on the asymmetric induction, since the additions to either electron poor and electron rich aromatic imines, e.g.**1c** and **1e**, respectively, followed the same sense of asymmetric induction (Table 1).

We assume that they proceed through the preliminary formation of a complex between the σ-donor imine and methyllithium, followed by the carbon-carbon bond forming step. Depending on the nature of the R group of the imine and the ML_n fragment (the size and the capability of chelation), the complex takes the preferred conformation by rotation of the R-C and N-C* bonds. Since the reaction is exothermic, the early transition state will resemble the complex and the diastereoselectivity will be dictated by the orientation of the auxiliary group, the nucleophile attacking preferably the less hindered π face of the imine. The situation is made even more complex by the possibility for the imine to undergo *E* to *Z* isomerization;[17] however, we believe that this occurs only when the steric interactions in the *E* imine-ML_n complex or in the consequent transition state are excessive.

Hence, we examined the ^{1}H-NMR spectra of several imines and their complexes with suitable Lewis acids (Figure 1), considering these complexes as models for imine-methyllithium complexes. In particular, we performed n.O.e. experiments irradiating the azomethyne proton of the solutions in $CDCl_3$ or in THF-d_8 (when specified). These studies allowed us to determine the different chelation capability of the imines, as well as the different conformation assumed by the auxiliary according to the steric bulkiness of the ML_n fragment.[18]

The imines having an heteroatom in the ortho position, e.g. **1f**, and the 2-pyridine imine **1b** assume preferably the planar conformation in which the heteroatom is oriented anti to the imine nitrogen, as indicated by the absence of n.O.e. on the aryl hydrogen atoms. However, a small positive response was observed on the ortho hydrogen Ha of the 2-furan imine **1g**, suggesting that it exists at least partially in the conformation having eclipsed Ha and H-C=N hydrogens. The n.O.e. experiments showed that in all the imines the orientation of the auxiliary is that having Hb eclipsed with H-C=N.

The heterocyclic imines **1b** and **1g** were capable to coordinate at least partially lithium perchlorate even in THF-d_8, as indicated by the complete dissolution of $LiClO_4$ (1 equiv.) in the $CDCl_3$ solutions of these imines and by the nO.e. experiments, although the chemical shift of the complexes did not differ significantly from those of the free imines. Conversely, $LiClO_4$ did not dissolve completely in the $CDCl_3$ solutions of the 2-methoxy-substituted aromatic imines **1d,f**, and in THF-d_8 the monodentae complex **1f**-$LiClO_4$ was exclusively formed, owing to the lack of n.O.e. on Ha Bidentate chelation was also observed for the complex **1b**-$Zn(CH_3)_2$ and **1d**-$ZnBr_2$ in $CDCl_3$.

It could be also demonstrated by the same experiments that in all these complexes the auxiliary maintains the orientation observed in the free imines, i.e. H-C* and H-C=N hydrogens were eclipsed. Conversely, the auxiliary assumed a different disposition in the complexes of **1a** and **1b** with $SnCl_4$, as a very weak or no response in the n.O.e. experiments was determined on H-C*, but a significant one on the phenyl hydrogens of the auxiliary in **1a**-$SnCl_4$. Hence we assume that, following coordination of the imine with the bulkier $SnCl_4$, the auxiliary undergoes a rotation of approximatively 180 °C, in order to reduce steric interactions of the substituents at C* with the metal ligands. This hypothesis, previously advanced by us for analogous complexes of imines derived from (*S*)-methyl valinate,[18] was supported by the consistent shift of the absorption of H-C* to lower fields (about 1.3 ppm). Moreover, very similar results were obtained by performing n.O.e. experiments on the imine **1a** complexed with a borate derived from 1,1'-bi-2-naphthol and the same orientation of the auxiliary group was consequently deduced.[28]

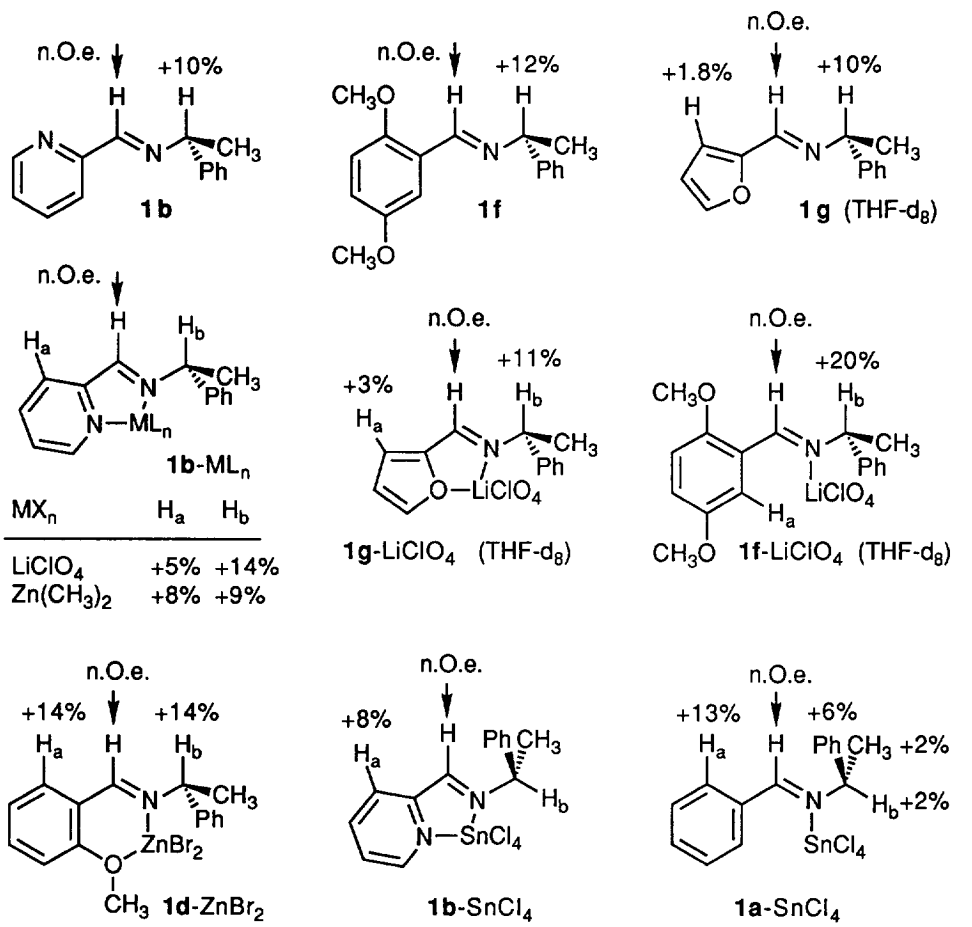


Figure 1. Structure/Conformation of Imine Complexes by N.O.E. Intensity (%) Experiments

In our opinion, these observations can be used to deduce the preferred conformation of the imine-$(LiCH_3)_n$ complexes intermediate in the corresponding reactions with methyllithium. Following the complexation of the non-chelating imines with tetrameric methyllithium,[19] the auxiliary group should assume the conformation shown in Figure 2, similar to that proposed for **1a**-$SnCl_4$ (Figure 1). The complex **1**-$(LiCH_3)_4$ can be in equilibrium with the more reactive complex **1**-$(CH_3Li)_2$,[20] where lithium can be further coordinated by a THF molecule, preserving the tetracoordination and the conformation of the auxiliary. The amine **4** is then likely produced by attack to the less hindered *Si* face, i.e. from the side of the methyl group of the auxiliary.

Conversely, the imines **1b** and **1g**, capable of acting as bidentate ligands towards lithium, presumably disaggregate $(LiCH_3)_4$ to form reactive imine-$(CH_3Li)_2$ complexes, e.g. **1b**-$(LiCH_3)_2$-**A** (Figure 2), in which the non-bonding interactions of the organometallic moiety with the group R (e.g. Ph) and the auxiliary are replaced by a bonding interaction or greatly reduced, respectively. It is reasonable to assume that the auxiliary maintains the orientation existing in the free imine and in the structurally similar complex **1b**-$Zn(CH_3)_2$ (Figure 1). Successively, the open dimer complex should convert to the open dimer **1b**-$(LiCH_3)_2$-**B**, which will then deliver the amine (*R*,*S*)-**4b** through a six-membered cyclic transition state.

This view is in agreement with recent theoretic studies that have given support to the importance of solvated methyllithium open dimer reacting with formaldehyde through a six-centered transition state.[21] However, semiempirical calculations[22] and experimental results[23] have demonstrated the higher reactivity of monomers *vs* dimers of σ-organolithiums chelated intra- or intermolecularly by polydentate bases, so that the involvement of a solvated monomeric complex **1b**-$LiCH_3$ can not be ruled out. It may be also envisaged that the bidentate ligand is able to promote the ionic dissociation of the C-Li bond in **1b**-$(LiCH_3)_2$-**B** affording the ionic pairs [**1b**-Li]+$[Li(CH_3)_2]^-$,[11a,24] analogous to known "triple ions" or "ion triplets" $[Li(solv)_n]^+[LiR_2]^-$.[25,26]

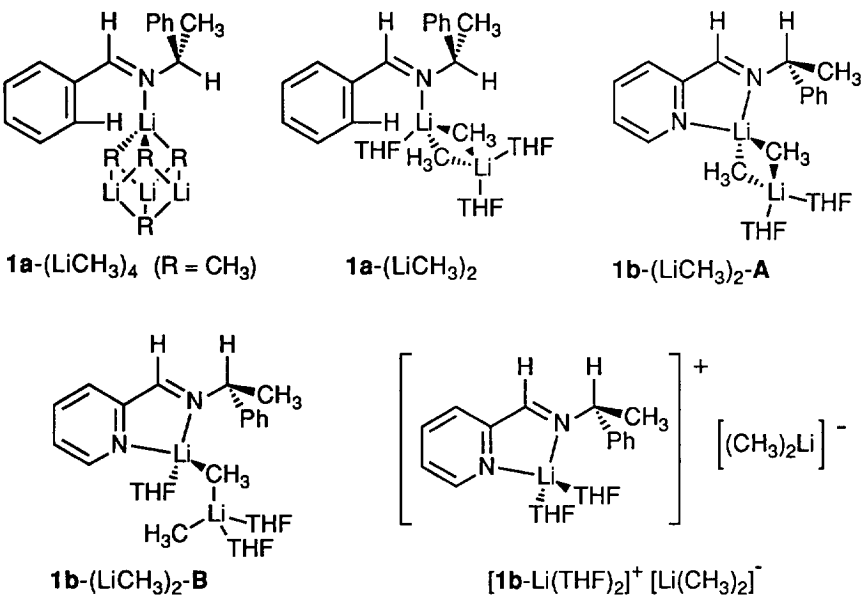


Figure 2. Conformation of imines and intermediate complexes in organometallic reactions

The *Si* face diastereoselectivity observed in the addition of methyllithium to the *ortho*-methoxy-substituted benzaldimines **1d,f** is probably a consequence of the reduced ability of lithium to form six-membered chelate complexes, as previously observed in the addition to β-alkoxycarbonyl compounds.[27] We believe that the planar six-membered chelated complex **1d,f**-$LiCH_3$ would suffer from angular constraint with respect to the stable tetrahedral geometry.

The reactions of methylcopper- or dimethylcuprate-BF_3 reagents reasonably take place through the preliminary coordination of BF_3 to the imine nitrogen, and we postulate that in the intermediate **1**-BF_3 complex the auxiliary takes the conformation shown in **I**, where the H-C* bond is approximately eclipsed with BF_3 (Figure 3).[28] Then, the attack of nucleophilic copper would occur to the less hindered *Si* face to give an intermediate **d**-π* complex **II**,[29] precursor of the σ complex **III**, or directly **III**.[30] Then the amine (*S,S*)-**4** would be formed from **III** with retention of configuration.

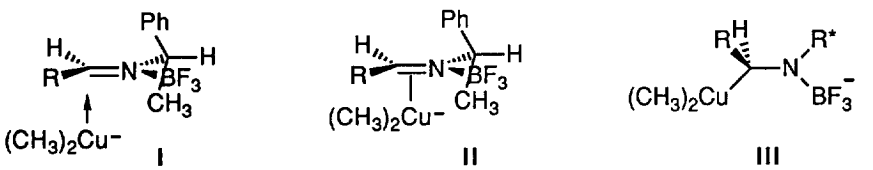


Figure 3. Stereochemical Model and Intermediates for the Addition of $(CH_3)_2CuM$-BF_3 to **1**

Conclusions

We have demonstrated that the asymmetric induction in the addition of dimethylcuprate-boron trifluoride and methyllithium to monodentate imines derived from (*S*)-1-phenylethylamine is opposite to that observed in the corresponding addition of methyllithium to strongly chelating bidentate imines such as those prepared from 2-pyridine and 2-furan carboxaldehyde.

The rationalization of these results takes into account the spatial disposition of the auxiliary in the reactive imine-ML_n complexes involved in the step determining the diastereoselectivity. This view is supported by n.O.e. experiments performed on several imine-Lewis acid complexes in which different orientations of the auxiliary were observed depending on the nature/steric hindrance of the Lewis acid.

From the synthetic point of view, the addition of dimethylcuprate-BF_3 reagents to the chiral imines derived from phenylethylamine is useful for the diastereoselective preparation of secondary dibenzylic amines, and primary benzylic and sec-alkylamines when the selective removal of the auxiliary group is possible.[4b,5] The good overall yield and optical purity of the secondary amines, e.g. (*S,S*)-**4a**, having C_2-symmetry, and (*R,S*)-**4b**, and the primary amine (*R*)-**10i** make the present method competitive with the auxiliary induced reduction of the corresponding ketimines.[5,14-16,31] Moreover, at our knowledge the preparation of (*R,S*)-**4b** has never been reported.

Preliminary experiments performed on **1a,b** with other alkyl-, vinyl- and benzyl organometallic reagents gave comparable diastereoselectivities: **1a**, BuLi, d.r. 72:28; **1a**, BuCu-LiI-BF_3, d.r. 80:20; **1a**, CH_2=CHLi, d.r. 65:35; **1b**, BuLi, d.r. 10:90; **1b**, $PhCH_2MgCl$, d.r. 26:74.

EXPERIMENTAL SECTION

General Information.

Instruments and general methods[32] and the preparation of the imines[4b] **1a-e** were previously reported. The imine **1g,h** were similarly prepared, but **1g** could be obtained pure (>95%) after repeated distillation.

(*S*)-N-2-Furylmethylidene-1-phenylethylamine 1g: $[\alpha]_D^{25}$ +76.4 (c 1.1, $CHCl_3$); GC-MS m/z (relative intensity) 199 (M+, 65), 105 (100), 184 (35), 77 (25), 51 (10); ^{1}H-NMR (300 MHz), THF-d_8, TMS) δ 8.14 (s, 1 H, CH=N), 7.54 (m, 1 H, furyl), 7.40-7.05 (m, 5 H, Ph), 6.78 (m, 1 H, furyl), 6.43 (m, 1 H, furyl), 4.37 (q, 1 H, C*H*CH_3), 1.43 (d, *J* 6.6 Hz, CHC*H*$_3$) ppm.

(*S*)-N-Hexylidene-1-phenylethylamine 1h: GC-MS m/z (relative intensity) 105 (100), 147 (31), 77 (18), 104 (17), 79 (15), 132 (12), 188 (5); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) δ 7.70 (t, 1 H, CH=N), 7.35-7.15 (m, R H, Ph), 4.24 (q, 1 H, C*H*CH_3), 2.23 (m, 2 H, C*H*$_2$CH=N), 1.47 (d, 3H, CHC*H*$_3$), 1.55-1.20 (m, 6 H, $(CH_2)_3$), 0.85 (t, 3 H, CH_2CH_3) ppm.

(*S*)-N-Cyclohexylmethylidene-1-phenylethylamine 1i:[33] GC-MS m/z (relative intensity) 105 (100), 147 (43), 77 (17), 79 (16), 56 (15), 106 (15), 104 (13), 200 (10); ^{1}H-NMR (300 MHz), $CDCl_3$, TMS) δ 7.59 (d, 1 H, CH=N), 7.40-7.20 (m, 5 H, Ph), 4.26 (q, 1 H, C*H*CH_3), 2.25 (m, 1 H, C*H*-CH=N), 1.49 (d, 3 H, CHC*H*$_3$), 1.95-1.60 (m, 6 H, cyclohexyl) 1.45-1.10 (m, 4 H, cyclohexyl) ppm; IR (neat) 1680 cm^{-1}.

Preparation, ^{1}H-NMR and N.O.E. Experiments of Imine-ML_n Complexes. To the solution of 1 mmol of the imine in $CDCl_3$ was added one equivalent of $LiClO_4$, $ZnBr_2$, $SnCl_4$, and the mixture was stirred a few minutes until complete dissolution. Similarly, one equivalent of the imine was added to the solution of $Zn(CH_3)_2$ in toluene, then the solvent was removed under vacuum, and the residue was redissolved in $CDCl_3$. The solutions were analyzed by ^{1}H-NMR (300 MHz) using tetramethylsilane as the internal standard.

1a-$SnCl_4$: δ 8.55 (s, 1 H, HC=N), 7.99 (m, 2 H, *Ph*CH=N), 7.8-7.4 (m, 8 H, Ph), 5.85 (q, 1 H, C*H*CH_3), 2.03 (d, *J* 6.9 Hz, 3 H, CHC*H*$_3$) ppm; positive n.O.e.: 7.99 (+13%), 7.65 (+6%), 5.85 (+1.9%), and 2.03 (+1.6%) ppm.

1b-$LiClO_4$: δ 8.60 (m, 1 H, pyridyl), 8.51 (s, 1 H, HC=N), 8.05 (m, 1 H, pyridyl), 7.84 (m, 1 H, pyridyl), 7.48-7.17 (m, 6 H, aryl), 4.68 (q, 1 H, C*H*CH_3), 1.58 (d, *J* 6.6 Hz, CHC*H*$_3$), ppm; n.O.e.: 8.05 (+5%) and 4.68 (+14%) ppm

1b-$Zn(CH_3)_2$: δ 8.68 (m, 1 H, pyridyl), 8.29 (s, 1 H, HC=N), 7.88 (m, 1 H, pyridyl), 7.65 m, 1 H, pyridyl), 7.50-7.15 (m, 6 H, aryl), 4.90 (q, 1 H, C*H*CH_3), 1.80 (d, *J* 6.7 Hz, CHC*H*$_3$), -1.0 (s, 6 H, $ZnCH_3$) ppm; n.O.e. effects: 7.65 (+8%) and 4.90 (+9%) ppm.

1b-$SnCl_4$: δ 9.62 (m, 1 H, pyridyl), 8.36 (m, 1 H, pyridyl), 8.22 (s, 1 H, HC=N), 8.04 m, 1 H, pyridyl), 7.93 (m, 1 H, pyridyl), 7.65-7.45 (m, 5 H, Ph), 6.20 (q, 1 H, C*H*CH_3), 2.08 (d, *J* 6.8 Hz, CHC*H*$_3$) ppm; n.O.e.: 7.93 (+8%) ppm.

1d-$ZnBr_2$: δ 8.40 (s, 1 H, HC=N), 7.70-7.10 (m, 9 H, aryl), 5.12 (q, 1 H, C*H*CH_3), 4.21 (s, 3 H, OCH_3), 1.95 (d, *J* 6.7 Hz, CHC*H*$_3$); ppm; n.O.e.: 7.6 (+14%) and 5.12 (+14%) ppm.

1f-$LiClO_4$ (THF-d_8): δ 8.78 (s, 1 H, HC=N), 7.60 (m, 1 H, aryl), 7.40 (m, 2 H, aryl), 7.25 (m, 2 H, aryl), 7.15 (m, 1 H, aryl), 6.93 (m, 2 H, aryl), 4.49 (q, 1 H, C*H*CH_3), 3.77 and 3.72 (2 s, 6 H, OCH_3), 1.49 (d, *J* 6.6 Hz, CHC*H*$_3$) ppm; n.O.e.: 4.49 (+20%) ppm.

1g-$LiClO_4$: (THF-d_8) δ 8.18 (s, 1 H, CH=N), 7.57 (m, 1 H, furyl), 7.40-7.10 (m, 5 H, Ph), 6.82 (m, 1 H, furyl), 6.46 (m, 1 H, furyl), 4.42 (q, 1 H, C*H*CH_3), 1.46 (d, *J* 6.6 Hz, CHC*H*$_3$) ppm; n.O.e.: 6.82 (+3%), 4.42 (+11%) ppm.

Addition of $(CH_3)_2CuMgCl$-$MgICl$-BF_3 to Chiral Imines. General Procedure:
(*S,S*)-bis(1-Phenylethyl)amine (*S,S*)-4a: The stirred suspension of CuI (Aldrich, 99.999%, 0.95 g, 5 mmol) in anhydrous THF (20 ml) in N_2 atmosphere was cooled to -40 °C and the solution of CH_3MgCl (3 M in THF, 3.34 ml, 10 mmol) in THF (3 ml) was slowly added. After stirring for 20 min at -40 °C the mixture is cooled to -78 °C and BF_3-Et_2O (0.80 ml, 5 mmol) was added, the mixture was stirred during 5 min, then the solution of the imine **1a** (0.523 g, 2.5 mmol) in THF (2 ml) was added, the temperature of the bath was raised to -40 °C and the mixture was stirred 3 h, while allowing the temperature to slowly rise to -30 °C. An aqueous solution of NH_4OH and NH_4Cl (1:1, 20 ml) was added and the organic phase was extracted with Et_2O (3 X 20 ml). The collected organic layers were dried (Na_2SO_4), and concentrated to leave an oil. Flash-chromatography on SiO_2 eluting with cyclohexane-Et_2O (95:5) afforded 0.422 g (75%) of **4a**, which was a mixture of the *S,S*- and *R,S* diastereomers and an unidentified impurity (90:8:2 respectively, by GC-MS analysis): m/z (relative intensity) 106 (100), 210 (72), 105 (69), 77 (26), 79 (25), 211 (14); $[\alpha]_D^{20}$ -162 (c 2.1, C_2H_5OH); lit.[14] -157 (c 2.4, C_2H_5OH); ^{1}H-NMR (60 MHz, $CDCl_3$,TMS) of (*S,S*)-**4a**: δ 7.20 (m, 10 H, Ph), 3.47 (q, 2 H, C*H*CH_3), 1.60 (br, 1 H, NH), 1.24 (d, 6 H, CHC*H*$_3$) ppm. (*R,S*)-**4a** had different ^{1}H-NMR absorptions at δ 7.20 (m, 10 H, Ph), 3.70 (q, 2 H, C*H*CH_3), 1.50 (br, 1 H, NH), 1.34 (d, 6 H, CHC*H*$_3$) ppm.

Addition of Methyllithium to Chiral Imines. General Procedure.
Preparation of N-[1(*R*)-(2-Pyridyl)ethyl]-1(*S*)-phenylethylamine (*R,S*)-4b: To the solution of CH_3Li (1.6 M in Et_2O, 3.75 ml, 26 mmol) in anhydrous THF (15 ml) in N_2 atmosphere to was added the solution of the imine **1b** (4.20 g, 20 mmol) in THF 15 ml) at -78 °C with stirring during 30 min. After stirring for further 30 min the reaction mixture was quenched with H_2O (20 ml), and the organic phase was extracted with Et_2O (3 X 20 ml). The collected Et_2O layers were dried (Na_2SO_4) and concentrated to leave an oil: 4.34 g (96%); GC-MS indicated a complete conversion and a 18:82 ratio of diastereomers. 1.9 g of the crude product was chromatographed on a SiO_2 column eluting with cyclohexane-ethyl acetate mixture (50:50): from the first fractions was obtained a mixture of the diastereomers (0.600 g), then 1.02 g (50% yield) of (*R,S*)-**4b** was isolated >99% pure by GC-MS analysis: m/z (relative intensity) 107 (100), 106 (69), 120 (38), 105 (37), 79 (19), 78 (19), 77 (18), 51 (9), 211 (7); $[\alpha]_D^{20}$ +9.96 (c 1.1, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) 8.51 (m, 1 H, pyridyl), 7.56 (m, 1 H, pyridyl), 7.32-7.08 (m, 7 H, aryl), 3.84 (m, 2 H, C*H*CH_3), 2.1 (br, 1 H, NH), 1.39 and 1.38 (2 d, *J* 9.9 Hz, 6 H, CHC*H*$_3$) ppm.

Another aliquot of the crude product (2.29 g, ca 10 mmol) was added to a solution of D-tartaric acid (1.48 g, 10 mmol) in CH_3OH (5 ml), the solvent was evaporated at reduced pressure, and the residue was dissolved in $CHCl_3$ by heating. After the night white crystals of the tartrate were 0.448 g (12%); m.p. 160-160.5 °C; the tartrate of (*S,S*)-**4b** described in the literature[14] had m.p. 159.2-160.4 °C. Basic treatment of the white solid and extraction with Et_2O (3 X 10 ml) afforded (*S,S*)-**4b**, corresponding to the first eluted minor diastereoisomer in the GC-MS analysis (dr 90:10): $[\alpha]_D^{20}$ -170 (c 1, $CHCl_3$); lit.[14] $[\alpha]_D^{20}$ -189 (c 9.6, $CHCl_3$); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) δ 8.60 (m, 1 H, pyridine), 7.60 (m, 1 H, pyridyl), 7.40-7.04 (m, 7 H, aryl), 3.59 (q, 1 H, PyC*H*CH_3), 3.45 (q, 1 H, PhC*H*CH_3), 2.2 (br, 1 H, NH), 1.31 and 1.28 (2 d, *J* 10 Hz, 6 H, CHC*H*$_3$) ppm.

The mother liquor of the tartrate salt were concentrated and the residue was treated with 10% aq NaOH (10 ml) and the organic material was extracted with Et_2O (3 X 10 ml), the organic phase was dried (Na_2SO_4) and concentrated to leave (*R,S*)-**4b** as an oil: 1.50 g (66%); d.r. 7:93; $[\alpha]_D^{20}$ +8.25 (c 1.1, $CDCl_3$).

By the one and/or the other procedure were prepared the following amines (Table 1):

N-[1(*S*)-(4-Pyridyl)ethyl]-1-(*S*)-phenylethylamine (*S,S*)-**4c**: GC-MS m/z (relative intensity) 106 (100), 211 (90), 105 (81), 107 (27), 77 (25), 51 (16), 78 (13), 212 (15), 79 (9); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) δ 8.55 (m, 2 H, pyridyl), 7.40-7.15 (m, 7 H, aryl), 3.48 (m, 2 H, C*H*CH_3), 1.80 (broad, 1 H, NH), 1.29 and 1.26 (2 d, *J* 11.6 Hz, CHC*H*$_3$) ppm. The minor diastereomer (*R,S*)-**4c** had different ^{1}H-NMR absorptions at δ 8.50 (m, 2 H, pyridyl), 3.75 (m, 2 H, C*H*CH_3), and 1.36 (m, 6 H, CHC*H*$_3$) ppm.

N-[1(*S*)-(2-Methoxyphenyl)ethyl]-1-(*S*)-phenylethylamine (*S,S*)-**4d**: Flash-chromatography of the crude product coming from the reaction of **1d** (5 mmol) with 5 equiv. of $(CH_3)_2CuMgCl$-BF_3 (1.95 g, containing mainly unreacted imine and a 70:30 mixture of diastereomeric amines) on SiO_2 eluting with cyclohexane-Et_2O (70:30) afforded a first fraction containing 0.18 g (*S,S*)-**4d** (96% pure, >98% de): $[\alpha]_D^{25}$ -108 (c 1.8, $CHCl_3$); lit:[14] $[\alpha]_D^{25}$ -110 (c 2.5, $CHCl_3$); GC-MS m/z (relative intensity) 240 (100), 136 (90), 135 (82), 105 (78), 77 (35), 79 (28), 106 (15), 241 (15), 91 (12), 120 (11), 103 (10); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) δ 7.37-6.75 (m, 9 H, aryl), 3.76 (s, 3 H, OCH_3), 3.74 and 3.52 (2 q, 2 H, C*H*CH_3), 2.05 (s, 1 H, NH), 1.29 and 1.27 (2 d, *J* 10 Hz, CHC*H*$_3$) ppm. The chromatographic fractions eluted successively contained increasing amounts of the minor diastereomer (*R,S*)-**4d**, which could not be isolated pure; characteristic ^{1}H-NMR absorptions were observed at δ 4.24 and 3.81 (2 q, 2 H, C*H*CH_3), 3.78 (s, 3 H, OCH_3), 1.46 and 1.45 (2 d, *J* 10 Hz, CHC*H*$_3$) ppm.

N-[1-(4-Methoxyphenyl)ethyl]-1-(*S*)-phenylethylamine (*S,S*)- **and** (*R,S*)-**4e**: the product was not isolated from the reaction mixtures: GC-MS m/z (relative intensity) 136 (100), 240 (95), 135 (90), 105 (75), 77 (26), 79 (20), 241 (15), 91 (14), 103 (12).

N-[1-(2,5-Dimethoxyphenyl)ethyl]-1-(*S*)-phenylethylamine (*S,S*)- **and** (*R,S*)-**4f**: the product was not isolated from the reaction mixtures: GC-MS m/z (relative intensity) 270 (100), 166 (89), 165 (61), 105 (45), 150 (17), 271 (17), 135 (15), 77 (15), 106 (11), 107 (11), 285 (5).

N-[1(*S*)-(2-Furylethyl)]-1-(*S*)-phenylethylamine (*S,S*)-**4g**: GC-MS m/e (relative intensity) 95 (100), 200 (60), 105 (56), 96 (47), 106 (22), 77 (14), 79 (11), 67 (9), 201 (8); ^{1}H-NMR (300 MHz), $CDCl_3$, TMS) δ 7.40–7.10 (m, 5 H, aryl), 6.32 (m, 1 H, furyl), 6.02 (m, 1 H, furyl), 3.65 and 3.56 (2 q, 2 H, C*H*CH_3), 1.34 and 1.29 (2 d, *J* 7 Hz, 6 H, C*H*CH_3) ppm. (*R,S*)-**4g** had different ^{1}H-NMR absorptions at δ 6.20 and 5.96 (2 m, 2 H, furyl), 3.85-3.77 (m, 2 H, C*H*CH_3), 1.65 and 1.57 (2 d, *J* 7 Hz, 6 H, CHC*H*$_3$) ppm.

N-[2(*S*)-Heptyl]-1-(*S*)-phenylethylamine (*S,S*)-**4h**: GC-MS m/e (relative intensity) 105 (100), 44 (65), 148 (56), 106 (21), 79 (14), 77 (12), 204 (12); ^{1}H-NMR (300 MHz), $CDCl_3$, TMS) δ 7.40–7.20 (m, 5 H, Ph), 3.90 (q, 1 H, PhC*H*CH_3), 2,50 (m, 1 H, C_5H_{11}C*H*CH_3), 1.55-1.05 (m, 9 H, $(CH_2)_4$ and NH), 1.35 (d, *J* 9.8 Hz, PhCHC*H*$_3$), 0.95 (d, J 9.8 Hz, 3 H, C_5H_{11}CHC*H*$_3$), 0.85 (t, 3 H, CH_2C*H*$_3$) ppm. The minor diastereomer (*R,S*)-**4h** had different ^{1}H-NMR absorptions at δ 2.40 (m, 1 H, C_5H_{11}C*H*CH_3), and 1.00 (d, *J* 9.8 Hz, 3 H, C_5H_{11}CHC*H*$_3$) ppm.

N-[1(*R*)-Cyclohexylethyl)]-1(*S*)-phenylethylamine (*S,S*)-**4i**: by following the same procedure on 3 mmol (0.645 g) of **1i**, the crude product (0.700 g) was obtained and chromatographed on a SiO_2 column eluting with cyclohexane-ether 90:10. The eluted fractions were analyzed by GC-MS and the first fractions containing

almost pure(*S,S*)-**4i** were collected and concentrated to leave an oil: 231mg (33%). The fractions eluted after and containing both diastereoisomers were collected and concentrated to leave an oil: 400 mg (58%); (*S,S*)/(*R,S*) = 90:10. (*S,S*)-**4i**: GC-MS m/e (relative intensity) 105 (100), 148 (74), 79 (19), 77 (19),106 (12), 55 (10), 149 (8), 78 (6), 216 (2); ^{1}H-NMR (300 MHz, $CDCl_3$, TMS) δ 7.40–7.20 (m, 5 H, Ph), 3.86 (q, 1 H, PhC*H*CH_3), 2.41 (m, 1 H, C_6H_{11}C*H*CH_3), 1.85-0.90 (m, 12 H, C_6H_{11} and NH), 1.31 (d, *J* 9.8 Hz, 3 H, PhCHC*H*$_3$), 0.87 (d, *J* 9.8 Hz 3 H, C_6H_{11}CHC*H*$_3$) ppm. (*R,S*)-**4i** had different ^{1}H-NMR absorptions at δ 3.91 (q, 1 H, PhC*H*CH_3), 2.19 (m, 1 H, cyclohexylC*H*CH_3), 1.33 (d, *J* 9.8 Hz, 3 H, PhCHC*H*$_3$), 0.96 (d, *J* 9.8 Hz 3 H, C_6H_{11}CHC*H*$_3$) ppm.

(*S*)-1-Cyclohexylethylamine (*S*)-15i from (*S,S*)-4i:

To the solution of the diastereomerically pure (d.r. 99:1) secondary amine **4i** (0.231 g, 1 mmol) in dry methanol (20 ml) was added Pd/C (0.025 g) and ammonium formate (0.19 g, 3 mmol). The mixture was magnetically stirred at the reflux temperature during 1.5 h. After cooling, the reaction mixture was filtered, and the solvent evaporated at reduced pressure to leave the primary amine (*S,S*)-**4i** as an oil (0.13 g), which contained some ethyl benzene. To the mixture, 6N HCl was added until pH 4 was reached. Toluene (5 ml) and methanol (5 ml) were added, then the solvents were removed at reduced pressure. The residue was recrystallized from dichloromethane/petroleum ether to give 0.149 g (92% yield) of the hydrochloride of (*S*)-**15i**: mp 232 °C; $[\alpha]_D^{25}$ +5.8 (c 0.77, $CHCl_3$); the hydrochloride similarly prepared from commercial (*S*)-(+)-1-cyclohexylethylamine had mp 232-234 °C and $[\alpha]_D^{25}$ +6.1 (c 0.75, $CHCl_3$). The ^{1}H-NMR spectra (300 MHz, $CDCl_3$, TMS) of the two samples were identical: δ 8.35 (broad s, 3 H, NH_3+), 3.15 (m, 1 H, C*H*CH_3), 1.0-2.0 (m, 11 H, C_6H_{11}), 1.39 (d, *J* = 9.9 Hz, 3 H, CHC*H*$_3$) ppm.

"Research supported by University of Bologna (Funds for selected research topics)"

REFERENCES AND NOTES

1. (a) Volkmann, R. A. in *Comprehensive Organic Synthesis*, Trost, B. M. Ed.; Pergamon Press, New York. 1991; Vol. 1, pp. 356-. (b) Harada, K. in "*The Chemistry of Carbon-Nitrogen Bond*", Patai, S. Ed., Interscience, New York. 1970; Vol. 6, p. 266. (c) Thies, H.; Schoenenberger, H. *Arch. Pharm. (Weinheim, Ger.)* **1956**, *289*, 408.
2. (a) Yamamoto,Y.; Nishii, S.; Maruyama, K.; Komatsu, T.; Ito, W. *J. Am. Chem. Soc.* **1986**, *108*, 7777; (b) Yamamoto, Y.; Ito, W. *Tetrahedron* **1988**, *44*, 5415. (c) Hallet, D. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1995**, 657. The addition of methylmagnesium iodide to the imines derived from (*S*)- and (*R*)-1-phenylethanamine and (-)-menthyl glyoxylate (double asymmetric induction, principally dictated by the menthyl group) was reported: (d) Fiaud, J.-C.; Kagan, H. B. *Tetrahedron Lett.* **1970**, 1813.
3. Neumann, W. L.; Rogic, M. R.; Dunn, T. J. *Tetrahedron Lett.* **1991**, *32*, 5865.
4. (a) Bocoum. A.; Boga, C.; Savoia, D.; Umani-Ronchi, A. *Tetrahedron Lett.* **1991**, *32*, 1367. (b) Alvaro, G.; Boga, C.; Savoia, D.; Umani-Ronchi, A. *J. Chem. Soc. Perkin Trans. 1* **1996**, 875.
5. Bringmann, G.; Geisler, J.-P. Geuder, T.; Kuenkel,.G.; Kinzinger, L. *Liebigs Ann. Chem.* **1990**, 795.

6. Wada, M.; Sakurai, Y.; Akiba, K. *Tetrahedron Lett.* **1984**, *25*, 1079.
7. The addition of RLi (a)-(g) or R_2Zn (h)-(i) to achiral imines catalyzed by chiral ligand gave rarely high e.e.: (a) Ukaji, Y.; Hatanaka, T.; Ahmed, A.; Inomata, K. *Chem. Lett.* **1993**, 1313. (b) Inoue, I.; Shindo, M.; Koga, K.; Tomioka, K. Tetrahedron **1994**, *50*, 4429. (c) Denmark, S. E.; Nakajima, N.; Nicaise, J.-C. *J. Am. Chem. Soc.* **1994**, *116*, 8797. (d) Itsuno, S.; Sasaki, M.; Kuroda, S.; Ito, K. *Tetrahedron: Asymmetry* **1995**, *6*, 1507. (e) Inoue, I.; Shindo, M.; Koga, K.; Kanai, M.; Tomioka, K. *Tetrahedron: Asymmetry* **1995**, *6*, 2527. (f) Jones, C. A.; Jones, I. G.; North, M.; Pool, C. R. *Tetrahedron Lett.* **1995**, *36*, 7885. (g) Huffman, M. A.; Yasuda, N.; DeCamp, A. E.; Grabowski, E. J. J. *J. Org. Chem.* **1995**, *60*, 1590. (h) Katritzky, A. R. ; Harris, P. A. *Tetrahedron: Asymmetry* **1992**, *3*, 437.
8. Boga, C.; Savoia, D.; Umani-Ronchi, A. *Tetrahedron: Asymmetry* **1990**, *1*, 291. In this preliminary communication the configuration of the amine **4h** was erroneously assigned.
9. MS m/z (relative intensity) of the main byproducts are the following. **5a**: 91 (100, $PhCH_2^+$), 208 (41, M+ -H), 209 (25, M+), 65 (20). **5b**: 92 (100, $PyCH_2^+$), 195 (46, M+-CH_3), 91 (33), 77 (31), 65 (27), 78 (22), 118 (21),.103 (20), 209 (15, M+-H), 210 (12, M+). **6a** = **7a**: 105 (100, $PhCHCH_3^+$), 222 (49, M+-H), 223 (33, M+), 77 (28), 208 (25, M+-CH_3), 104 (25), 103 (20), 79 (18), 78 (12), 167 (10). **7b**: 105 (100, $PhCHCH_3^+$), 209 (70 (M+-CH_3), 77 (48), 106 (45), 79 (42), 78 (35), 104 (35), 103 (25), 51 (20),.223 (2, M+-H). **7c**: 105 (100, $PhCHCH_3^+$), 224 (23, M+), 79 (23), 77 (17), 209 (15, M+-CH_3), 223 (12, M+-H), 51 (10). **6e**: 135 (100, 4-$CH_3OC_6H_4CHCH_3^+$), 253 (12, M+), 136 (11), 105 (10), 103 (8), 77 (8). **7e**: 105 (100, $PhCHCH_3^+$), 252 (85, M -H), 238 (50, M+-CH_3), 253 (46, M+), 135 (38), 119 (25), 134 (24), 91 (22), 103 (17), 79 (15). **6f**: 165 (100, 2,5-$(CH_3O)_2C_6H_3CHCH_3^+$), 150 (35), 207 (27), 77 (13), 283 (12, M+), 135 (12), 105 (11), 252 (11), 120 (9), 268 (5, M+-CH_3). **8d**: 135 (100, 2-$CH_3OC_6H_4CHCH_3^+$), 105 (50, $PhCHCH_3^+$), 77 (22), 91 (18), 254 (14, M+-CH_3), 79 (16), 134 (16), 224 (12), 51 (10), 238 (8). **8e**: 135 (100, 4-$CH_3OC_6H_4CHCH_3^+$), 254 (87, M+-CH_3), 136 (67), 91 (23), 119 (20), 255 (17), 120 (12), 77 (10), 105 (10), 269 (3, M+). The mass spectra of all the observed 1,2-diamines **9** had generally the most abundant ions at m/z = $(M/2)^+$. Two unidentified isomeric compounds produced in low yield from **1i** had m/z 105 (100), 72 (56), 216 (53), 112 (50), 176 (34), 79 (20), 106 (15), 55 (14), 77 (12).
10. The complex **1b**-CH_3Li is apparently analogous to the coloured charge transfer complexes of lithium (a) and zinc (b) reagents with mono- and bidentate heteroaromatic ligands: (a) Watson, S. C.; Eastham, J. F. *J. Organometal. Chem.* **1967**, *9*, 168. (b) Noltes, J. G.; Boersma, J. *J. Organomet. Chem.* **1967**, *7*, 1.
11. (a) Kaim., W. *Chem. Ber.* **1981**, *114*, 3789. (b) Kaim, W. *Acc. Chem. Res.* **1983**, *18*, 160. (c) Klerks, J. M.; Jastrzebski, J. T. B. H.; van Koten, G.; Vreeze, K. *J. Organomet. Chem.* **1982**, *224*, 107. (d) van Koten, G.; Jastrzebski, J. T. B. H.; Vrieze, K. *J. Organomet. Chem.* **1983**, *250*, 49. (e) Stamp, L.; tom Dieck, H. *J. Organomet. Chem.* **1984**, *277*, 297. (f) Wissing, E.; Kleijn, H.; Boersma, J.; van Koten, G. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 618. (g) Wissing, E.; Kaupp, M.; Boersma, J.; Spek, A. L.; van Koten, G. *Organometallics* **1994**, *13*, 2349.
12. Duhamel, L.; Plaqueuent, J. C. *J. Organometal. Chem.* **1993**, *448*, 1.
13. Filippin, L. A.; Carter, D. S.; Bubree, N. J. P. *Tetrahedron Lett.* **1993**, *34*, 3255.
14. Eleveld, M. B.; Hogeven, H.; Schudde, E. P. *J. Org. Chem.* **1986**, *51*, 3635.
15. Brunner, H.; Reiter, B.; Riepl, G. *Chem. Ber.* **1984**, *117*, 1330.

16. Fuller, J. C.; Belisle, C. M.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett.* **1994**, *35*, 5389.
17. The *E/Z* isomerization of imines was previously proposed to explain the diastereoselective addition of (a) crotylboranes, (b) boron enolates, (c) silyl ketene acetals-$TiCl_4$, and 9-allyl-9-BBN[4b] to imines: (a) Roush, W. R. in *Comprehensive Organic Synthesis*, Trost, B. M. Ed., Pergamon Press, London and New York, 1991, Vol. 2, p. 1. (b) Corey, E. C.; Decicco, C. P.; Newbold, R. C. *Tetrahedron Lett.* **1991**, *32*, 5287.(c) Ojima, I.; Inaba, S.-i. *Tetarahedron Lett.* **1980**, *21*, 2081. *E/Z* isomerization of an iminium ion: (d) Waldmann, H.; Schmidt, G.; Jansen, M.; Geb, J. *Tetrahedron* **1994**, *50*, 11865.
18. The same approach was used by us to explain the opposite diastereoselectivity exhibited by allyltin trihalides with respect to allylzinc bromide and allyllead bromide in the addition to methyl (*S*)-N-(2-pyridinemethylidene) valinate: Alvaro, G; Savoia, D.; *Tetrahedron: Asymmetry* **1996**, *7*, 2083.
19. (a) Weiss, E. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1501. (b) Kaufmann, E.; Raghavachari, K.; Reed, A. E.; von Ragué Schleyer, P. *Organometallics* **1988**, *7*, 1597. (c) Lewis, H. L.; Brown, T. L. *J. Am. Chem. Soc.* **1970**, *92*, 4664.
20. In THF solutions of butyllithium an equilibrium is established between the tetramer and the more reactive dimer: (a) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 1805. (b) McGarrity J. F.; Ogle, C..; Brich, Z.; Loosli, H.-R. *J. Am. Chem. Soc.* **1985**, *107*, 1810.
21. Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1993**, *115*, 11016.
22. Pratt, M. P.; Khan, I. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2165.
23. (a) Luitjes, H.; de Kanter, F. J. J.; Schakel, R. F.; Scmitz, R. F.; Klumpp, G. W. *J. Am. Chem. Soc.* **1995**, *117*, 4179. (b) Pratt, L. M.; Khan, I. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2165.
24. 2,2'-Bipyridine and $LiB(C_2H_5)_3H$ form an ionic pair [2,2'-bipyridine-Li]+ $[B(C_2H_5)_3H]^-$, from which the radical [2,2'-bipyridine-Li]• and $B(C_2H_5)_3$ are then produced by a SET process involving loss of hydrogen: Kaim, W.; Lubitz, W. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 892.
25. The crystal structure of triple ions derived from organolithium and magnesium compounds has been reported. $[Li(THF)_4]^+[Li(C(TMS)_3)]^-$ and $[Li(TMEDA)_2]^+[Li(C(TMS)_3)]^-$: (a) Eaborn, C.; Hitchcock, P. B.; Smith,, J. D.; Sullivan, A. C. *J. Chem. Soc., Chem. Commun.* **1983**, 827. (b) Eaborn, C.; Hitchcock, P. B.; Smith, J. D.; Sullivan, A. C. *J. Organometal Chem.* **1984**, *263*, C23. (c) Buttrus, N. *Commun.* **1986**, 969. $[Na(TMEDA)]_3^+[LiPh_4]^-$: (d) Schuemann, U.; Weiss, E. *Angew. Chem., Int. Ed; Engl.* **1988**, *27*, 584. $[[Cp^*(C_2B_9H_{11})ScCH(TMS)_2]_2Li]^-[Li(THF)_3]^+$: (e) Bazan, G. C.; Schaefer, W. P.; Bercaw, J. E. *Organometallics*, **1993**, *12*, 2126. $[(CH_3)_3CMg(2,1,1\text{-cryptand})]^+[(CH_3)_3C)_3Mg)]^-$ and $[C_2H_5Mg(2,1,1\text{-cryptand})]^+[(C_2H_5)_6Mg_2]^-$: (f) Squiller, E. P.; Whittle, R. R.; Richey, H. G., Jr. *J. Am. Chem. Soc.***1985**, *107*, 432. $[CH_3Mg(15\text{-crown-}5)]^+[(CH_3)_5Mg_2]^-$: (g) Pajerski, A. D.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2660. The formation of an organometallic rotaxanes from Ph_2Mg and crown ethers was explained by the intermediacy of the ionic couples $[PhMg(crown)]^+$ $[Ph_3Mg]^-$: (h) Markies, P. R.; Nomoto, T.; Akkerman, O.S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 4845. (i) Markies, P. R.; Schat, G.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. Organometallics 1991, 10, 3538. $[Zn(pyridine)_2]^+$ $[Zn(CN)_4]^-$: (j) Pickard, J.; Staub, B. *Z. Naturforsch.* **1995**, *50b*, 1517.
26. Triple ions $[Li(solvent)]^+[LiX_2]^-$ where X is a resonance stabilized carbanion or a heteroatomic group were structurally characterized or proven intermediates in organic reactions. X^- = enolate: (a) Raban, M.; Noe, E. A.; Yamamoto, G. *J. Am. Chem. Soc.***1977**, *99*, 6529. (b) Raban, M.; Haritos, D. P. *J. Am.*

Chem. Soc. **1979**, **101**, 5178. (c) Cambillau, C.; Ourevitch, M. *J. Chem. Soc., Chem. Commun.* **1981**,996. (d) Teixidor, F.; Llobet, A.; Casabo, J.; Solans, X.; Font-Altaba, M.; Aguilo, M. *Inorg. Chem.* **1985**, *24*, 2315. (e) Dotcheva, D.; Tsvetanov, Ch.; Lochmann, L. *J. Polym. Sci.* , *Polym. Chem. Ed.* **1987**, *25*, 3005. X^- = azaenolate and porphyrinate: (f) Hogen-Esch, T. E.; Jenkins, W. L. *J. Am. Chem. Soc.* **1981**, *103*, 3666. (g) Tsvetanov, Ch. B.; Dotcheva, D. T. *J. Polym Sci., Polym. Chem. Ed.* **1986**, *24*, 2253. (h) Jhan, I. M.; Hogen,-Esch, T. E. *J. Polym Sci., Polym. Chem. Ed.* **1988**, *26*, 2553. (i) Galiano-Roth, A. S.; Collum, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 3546. (j) Arnold, J.; Dawson, D. Y.; Hoffman, C. G. *J. Am. Chem. Soc.* **1993**, *115*, 2707. (k) Gornitzka, H.; Stalke, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 693. X^- = cycloalkadienyl anion: (l) Fraenkel, G.; Hallden-Abberton, M. P. *J. Am. Chem. Soc* **1981**, *103*, 657. (m) Fraenkel, G.; Pramanik, *J. Org. Chem.* **1984**, *49*, 1314. (n) Hertkorn, N.; Koehler, F. H. Z. *Naturforsch.* **1990**, *45b*, 848. (o) Paquette, L. A.; Bauer, W.; Sivik, M. R.; Buehl, M. Feigel, M.; von Ragué Schleyer, P.*J. Am. Chem. Soc.* **1990**, *112*, 8776. (q) Bauer, W.; O'Doherty, G. A.; von Ragué Schleyer, P.; Paquette, L. A. *J. Am. Chem. Soc.* **1991**, *113*, 7094. (r) Eiermann, M.; Hafner, K. *J. Am. Chem. Soc.* **1992**, *114*, 135. $X^- = R_2N^-$: (s) DePue, J. S.; Collum, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 5518, 5524. (t) Romesberg, F. E.; Gilchrist, J. H.; Harrison, A. H.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1991**, *113*, 5751. (u) Romesberg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1992**, *114*, 2112. (v) Romesberg, F. E.; Bernstein, M. P.; Gilchrist, J. H.; Harrison, A. T.; Fuller, D. J.; Collum, D. B. *J. Am. Chem. Soc.* **1993**, *115*, 3475. (w) Romesberg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1994**, *116*, 9187, 9198. (x) Romesberg, F. E.; Collum, D. B. *J. Am. Chem. Soc.* **1995**, *117*, 2166. $Li(12\text{-crown-}4)_2]^+[Li(N(TMS)_2SPh)_2]^-$: (y) Pauer, F.; Rocha, J.; Stalke, D. *J. Chem. Soc., Chem. Commun.* **1991**, 1477.

27. (a) Leitereg, T. J.; Cram, D. J. *J. Am. Chem. Soc.* **1968**, *90*, 4019. (b) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035. (c) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556. (d) Kauffmann, T. *Synthesis* **1995**, 745. A β- or γ-heterosubstituent stabilizes organolithium compounds by intramolecular chelation: (e) Gschwend, H. W.; Rodriguez, H. R. *Organic Reactions (N. Y.)* **1979**, *26*, 1. (f) Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356. $(CH_3)_2Mg$ forms a more stable chelate with 4-methoxy-2-butanone than with methoxyacetone: (g) Mori, S.; Nakamura, M.; Nakamura, E.; Koga, N.; Morokuma, K. *J. Am. Chem. Soc.* **1995**, *117*, 5055.
28. Ishihara, K.; Miyata, M.; Hattori, K.; Tada, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1994**, *116*, 10520.
29. (a) Lipshutz, B. H.; Sengupta, S. *Org. React.* **1992**, *41*, 135. (b) Vellekoop, A. S.; Smith, R. A. J. *J. Am. Chem. Soc.* **1994**, *116*, 2902. (c) Snyder, J. P. *J. Am. Chem. Soc.* **1995**, *117*, 11025.
30. The alkylation of N-benzylideneaniline by lithium trimethylferrate has been assumed to proceed through the attack of the nucleophilic iron to the C=N bond, followed by a reductive elimination step, and/or a SET process: Kauffmann, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 386.
31. (a) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 2436. (b) Marx, E.; El Bouz, M.; Célérier, J. P.; Lhommet, G. *Tetrahedron Lett.* **1992**, *33*, 4307. (c) Moss, N.; Gauthier, J.; Ferland, J.-M. *Synlett* **1995**, 142.
32. Basile, T.; Bocoum, A.; Savoia, D.; Umani-Ronchi, A. *J. Org. Chem.* **1994**, *59*, 7766.
33. Hattori, K. Yamamoto, K. *Tetrahedron* **1993**, *49*, 1749.

(*Received in UK* 6 *June* 1996; *revised* 12 *August* 1996; *accepted* 15 *August* 1996)