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Addition of Allylmetal Reagents to the Imine Derived from 2-Pyridine Carboxaldehyde and Methyl (*S*)-Valinate. Synthesis of (*S*)- and (*R*)-1-(2-Pyridyl)-3-butenamine

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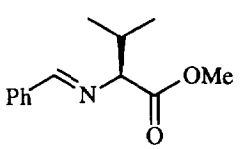
Abstract: Allylmetal reagents add to the imine derived from 2-pyridine carboxaldehyde and methyl (*S*)-valinate or to preformed imine-metal salt complexes to give mainly the *S,S*- or the *R,S*-secondary homoallylic amine, depending on the nature of the allylmetal reagent. Both the (*S*)- and (*R*)-1-(2-pyridyl)-3-butenamine were prepared with high enantiomeric purity by removal of the auxiliary group. Copyright © 1996 Elsevier Science Ltd

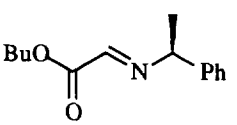
INTRODUCTION

High levels of diastereoselectivity are often obtained in the addition of organometallic compounds to chiral bidentate imines which have a heteroatom either in the carbon skeleton coming from the parent aldehyde or in the auxiliary group attached to nitrogen, owing to the formation of rigid chelation intermediates.[1] We recently reported the preparation of homoallylic amines with excellent or perfect diastereoselectivity by the addition of allylmetal or allylmetal-metal salt mixtures to aliphatic and aromatic imines derived from valine esters, e.g. (*S*)-**1**. Comparable levels of stereocontrol were obtained in reactions proceeding through a rigid N,O-bidentate complex between the imine and the allylmetal reagent or a proper metal salt, and in reactions with less polar allylmetal species that required activation of the imine by boron trifluoride, which coordinates only the nitrogen atom and allows the free rotation of the auxiliary group around the N-C* axis.[2]

Notably, the diastereoselectivity of the allylation of imine (*S*)-**2** derived from butyl glyoxylate and (*S*)-1-phenylethanamine was dependent on the allylmetal reagent: 9-allyl-9-BBN and other allylmetal reagents attacked the *Si* face,[3] but allyltrichlorotin added the *Re* face.[4] On the other hand, we recently found that the same boron[5] and tin[6] reagents both attacked the *Re* face of the imine (*S*)-**3**. Since the factors controlling the mechanism and the diastereoselectivity of the reactions of the bidentate imines **1-3** with allylmetal reagents were not elucidated, we examined the behaviour of the imine (*S*)- which contains an heteroatom in either the auxiliary or in the aromatic ring coming from the parent aldehyde.



(*S*)-**1**



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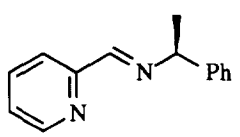
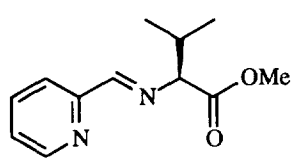
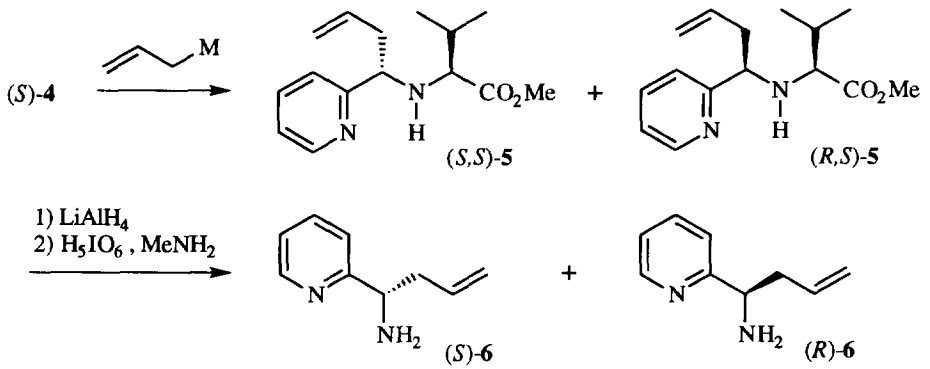


(*S*)-**3**



(*S*)-**4**

We performed the addition of several allylmetal reagents to the imine (*S*)-**4** and its metal salt complexes (*S*)-**4**-M'X_n (Scheme 1). Since the imine can act as a bidentate (N,N or N,O) or tridentate (N,N,O) ligand towards the allylmetal or metal salt species, we envisaged that a different stereochemical outcome of the allylmetallation reaction might be achieved by varying the reagents, affording either the *S,S* or *R,S* homoallylic amine **5**. Moreover, the removal of the auxiliary group would allow the preparation of the primary homoallylic amines (*S*)- and (*R*)-**6**, which are potentially useful as bidentate ligands or catalysts in asymmetric synthesis, by analogy with other α-substituted (2-pyridyl)methanamines,[7] and can be converted to more complex molecules by functionalization of the C=C double bond.



Scheme 1

RESULTS AND DISCUSSION

Selected results obtained by following Grignard (THF, -78 °C) and Barbier (THF, 25 °C) procedures for the allylation of (*S*)-**4** are reported in Table 1. The diastereoisomeric ratio (d.r.) was readily determined by GC-MS analysis, as the (*S,S*)-homoallylic amines derived from aromatic imines are eluted prior to the (*R,S*)-diastereoisomers.[2] In the addition of allylcopper and cuprate species generated from allylmagnesium chloride (entry 1, 2) and allylzinc bromide (entry 3) the prevalent formation of the (*S,S*)-**5** was observed, although the diastereoselectivity was lower than that obtained with (*S*)-**1**.[2] As expected, the Barbier reaction employing allyl bromide and zinc powder (entry 4), being performed at higher temperature, gave a slightly lower d.r., which further decreased with time due to the reversibility of the reaction. Moreover, the partial attack to the pyridine ring and ester group could not be avoided. Anhydrous $CeCl_3$ or $SnCl_2$ (one equivalent), preliminarly added to the imine, increased the reaction rate with allylzinc bromide but not the d.r. (entries 5, 6).

Allyllead bromide, prepared by transmetallation of allylmagnesium chloride and $PbBr_2$, although being unreactive towards (*S*)-**1** in the absence of BF_3 or $AlCl_3$,[2] reacted readily with (*S*)-**4** with a high level of diastereoselectivity, favoring the formation of (*S,S*)-**5** (92% d.e., entry 7). Surprisingly, the Barbier procedure that exploited the bimetal redox system Al-$PbBr_2$ gave almost the same d.r. (entry 8).

The opposite sense of asymmetric induction was observed with allyltin trihalides. Allyltin trichloride, prepared by ligand exchange of allyltributyltin with $SnCl_4$ in CH_2Cl_2, afforded (*R,S*)-**5** with high diastereoselectivity (entry 9), that could be enhanced (94% d.e.) by using allyldichloroiodotin, prepared by

oxidative addition of $SnCl_2$ to allyl iodide in THF (entry 10). The reaction performed by following the Barbier procedure gave initially almost the same d.r., but was affected by the progressive epimerization with increasing the reaction time (entry 11). Notably, the reaction of allyldichloroiodotin to the imine-$SnCl_2$ complex (entry 12) and gave predominantly the same diastereomer (*R*, *S*)-**5** that was produced in the absence of the salt.

Allylmagnesium chloride in THF added the imine to give mainly (*S*, *S*)-**5**. However, further addition of the organometallic reagent to the ester and/or pyridine group occurred in part, as observed by GC-MS analysis of the reaction mixture (entry 13), so that the lower diastereoselectivity (with respect to Zn, Cu, and Pb reagents) may be attributed to the overreaction being faster on (*R*, *S*)-**5** than on (*S*, *S*)-**5**. The even lower d.r. obtained in the corresponding reaction of the imine-$SnCl_4$ complex (entry 14) may be due to the partial transmetallation producing *in situ* the allyltin reagent which gives mainly (*R*, *S*)-**5**.

Table 1. Preparation of Secondary Homoallylic Amines 5 from (*S*)-4. [a]

Entry	Reagents (equiv.)	T (°C)	Time (h)	Yield (%) of **5** [b]	(*S*, *S*/*R*, *S*) [b]
1	allylCu-MgICl (1.5) [c]	-78	1.5	92 (99) [d]	90:10
2	$(allyl)_2CuMgCl$-MgICl (1.5) [c]	-78	0.5	98	93:7
3	allylZnBr (2) [c]	-78	0.16	90	86:14
4	allylBr (1.1), Zn (1.5) [e]	25	0.5	75 [f]	80:20 [g]
5	allylZnBr (1.5), $CeCl_3$ (1) [h]	-78	0.08	99	78:22
6	allylZnBr (1.5), $SnCl_2$ (1) [h]	-78	0.08	98	80:20
7	allylPbBr$_2$·MgBrCl (1.1) [c]	-78	0.16	98 (80) [i]	96:4
8	allylBr (1.1), Al (1.5), $PbBr_2$ (1.1) [e]	25	2.5	98	95:5 [j]
9	allylSnCl$_3$ (1) [c, k]	-78	0.16	100	13:87
10	allylSnICl$_2$ (1.5) [c]	-78	0.08	90 (85) [i]	3:97
11	allylI (1.5), $SnCl_2$ (1.1) [e]	25	0.16	100	4:96 [g]
12	allylSnICl$_2$ (1.1), $SnCl_2$ (1.1) [h]	-78	0.08	98	7:93
13	allylMgCl (1.1)	-78	0.5	70 [f]	83:17
14	allylMgCl (1), $SnCl_4$ (1) [h]	-78	0.08	80	65:35

(a) All the reactions were performed in THF on 1 mmol of the imine. (b) The yields and the diastereomeric ratios were determined by GC/MS analysis. (c) The imine was added to the allylmetal. (d) By quenching the reaction mixture after 1 d at 25 °C. (e) The allyl halide was added dropwise to the mixture of the imine and the other reagent(s). (f) Allylation of the pyridine and ester groups was observed. (g) Avoiding quenching of the reaction mixture, partial epimerization increasing with time occurred. (h) The salt was added to the imine at 25 °C and the mixture was stirred for 10 min, then cooled to -78 °C, and the allylmetal was added. (i) Yield of isolated pure compound. (j) When the imine was added to the mixture of allyl bromide (1.1 equiv.), Al (1.5 equiv.) and $PbBr_2$ (0.1 equiv.) the ratio was 81:19. (k) The reaction was performed in CH_2Cl_2.

The absolute configuration of the homoallylic amines (*S*, *S*)- and (*R*, *S*)-**5**, coming from the complementary procedures, was confirmed by the preparation of the primary amines (*S*)-(-)- and (*R*)-(+)-(**6**) in good yield and enantiomeric purity (ee >86%), as determined by comparison of the specific rotation with the value reported in literature for the *R* enantiomer.[6] This was accomplished by the usual procedure to remove the

valine auxiliary group,[2] i.e. reduction of the ester with lithium aluminium hydride, followed by oxidative cleavage of the intermediate β-amino alcohol[9] (Scheme 1).

Spectroscopic Studies of the Imines (S-1) and (S-4) and their Complexes with Metal Salts

We reasoned that the opposite stereochemical outcome obtained with tin(IV) reagent compared to the other organometallic reagents might be due to the different chelating ability of tin with the imine. In fact, if the carbonyl oxygen of the auxiliary group is not bound to the metal, the nitrogen substituent can rotate along the N-C* bond and assume several possible spatial orientation differently affecting the sense of asymmetric induction. Therefore, we examined the spectroscopic properties of (*S*)-**4** and its complexes with $ZnCl_2$, $SnCl_2$, and $SnCl_4$[10] (Figure 1), assuming that these complexes are satisfactory models for the imine-allylmetal complexes. The benzaldimine (*S*)-**1** and its complexes with $ZnBr_2$ were also examined for comparison.

The IR spectra of (*S*)-**4** and (*S*)-**1** and their complexes with the metal salts (Table 2) gave information on chelation capability of the two imines towards the metal salts, particularly on the involvement of the ester group. The spectra were taken for the THF solutions, because this solvent, that we used in the organometallic reactions, can act as a ligand for the metal in competition with the ester function.

Table 2. Selected IR Absorptions of (*S*)-4, (*S*)-1 and their Complexes with $ZnBr_2$.

Compound [a,b]	C=O, C=N and pyridyl absorptions (cm^{-1})
(*S*)-**4**	1743s, 1735s, 1651m, 1582m, 1558m
(*S*)-**4**-$ZnBr_2$	1750s, 1689w, 1642m, 1599s, 1576w
(*S*)-**4**-$SnCl_2$	1738s, 1692m, 1646m, 1599s, 1570w
(*S*)-**4**-$SnCl_4$	1747s, 1644m, 1600s, 1570w
(*S*)-**1** [c]	1745s, 1733s, 1643s, 1583m
(*S*)-**1**-$ZnBr_2$	1745s, 1733s, 1705m,[d] 1671m,[d] 1642s, 1601w,[d] 1581m

(a) 0.5M solutions in anhydrous THF. (b) The solutions of the imine-metal salt complexes were obtained *in situ* by adding one molar equivalent of salt to the THF solution of the imine. (c) R = C_2H_5. (d) The intensity of the absorption increased after addition of another equivalent of salt.

A strong absorption band at 1750 cm^{-1} was present in the solution of (*S*)-**4**-$ZnBr_2$, and we attributed it to the free carbonyl group, although it did not fit exactly to that observed in the imine. Only a weak band was present at a lower frequency (1689 cm^{-1}), that could be attributed to the coordinated carbonyl group.[11] Similarly, the spectrum of (*S*)-**4**-$SnCl_2$ solution showed the absorptions of both the free (prevalent) and complexed carbonyl groups (1738 and 1692 cm^{-1}, respectively), although it could be argued from the intensity of the band at 1692 cm^{-1} that the ester group was bound more strongly than in (*S*)-**4**-$ZnBr_2$. Conversely, in (*S*)-**4**-$SnCl_4$ only the absorption of the free ester group was present.[12] In all the three complexes the coordination of the azomethine and pyridine groups was evidenced by the appearance of new bands approximately at 1644 and 1600 cm^{-1}, that can be compared to the absorptions measured for several complexes of imines and dipyridine with metal salts.[13] On the other hand, the IR spectrum of the benzaldimine complex (*S*)-**1**-$ZnBr_2$ in THF

showed the presence of the free (prevalent) and complexed imine, which acted apparently as a bidentate N,O-ligand: both the absorptions due to the coordinated C=O (1705 cm^{-1}) and C=N (1671 cm^{-1}) groups had low intensity, which increased after the addition of one more equivalent of $ZnBr_2$, showing that an equilibrium is established in THF between the free and complexed imines

The ^{13}C-NMR spectra of the complexes of the imine (*S*)-**4** with the metal salts (Table 3) showed in every case a weak absorption of the carbonyl group with a chemical shift identical or very close to that determined in the free imine, the maximum shift being observed for $SnCl_2$ (+2 ppm). Comparable shifts (2.5-4.1 ppm) of the carbonyl carbons to lower fields have been previously reported for 2-ethoxycarbonyl-2-alkenylzinc bromides[11] and analogous organo(IV) halides[14] with respect to the parent halides. We observed also shifts to higher fields of the ring C_1 and stereogenic (C*) carbons, more conspicuous in the $SnCl_4$ complex, and of the azomethine carbon only with $SnCl_4$. On the other hand, in the case of (*S*)-**1**-$ZnBr_2$ the chemical shift of the carbonyl group was definetely shifted downfield (8 ppm) with respect to the imine, clearly indicating the N,O-chelation mode.

Table 3. ^{13}C-NMR Absorptions of (*S*)-4 and (*S*)-1 and their Metal Salt Complexes.[a]

Compound	C_2-C_5 [b]	C_1 [b]	C=O	CH=N	C*	OR	$CH(CH_3)_2$	$CH(CH_3)_2$
(*S*)-**4**	121-149	153	171	164	79	51 [c]	31	18-19
(*S*)-**4**-$ZnBr_2$	128-149	145	172	163	73	53 [c]	34	18-19
(*S*)-**4**-$SnCl_2$	128-149	149	173	164	76	53 [c]	33	18-19
(*S*)-**4**-$SnCl_4$	131-146	139	170	157	68	53 [c]	33	18-19
(*S*)-**1**	128-131 [d]	136	172	163	80	61 [e]	32	18-19
(*S*)-**1**-$ZnBr_2$	129-135 [d]	131	180	173	75	66 [e]	35	19

(a) The spectra were taken at 300 MHz in $CDCl_3$ (TMS as the internal standard) and the absorptions are given as δ (ppm). (b) See Figure 1 for numbering. (c) R = CH_3. (d) C_2-C_6. (e) R = CH_2CH_3 (CH_2CH_3 at 14 ppm).

In the ^1H-NMR spectra (Table 4) the coordination of the metal salts to (*S*)-**4** produced a definite shift of the pyridine (apart H_3), azomethine, and H-C* protons to low fields, most markedly with $SnCl_4$. Most importantly, n.O.e. experiments performed either in $CDCl_3$ and THF-d_8 (Figure 1) gave information on the preferred conformations of the imines and their metal salt complexes, concerning the rotation of the auxiliary group along the N-C* bond. Irradiation of the azomethine proton of (*S*)-**4** had a remarkable positive effect on the H-C* proton, but not on the pyridine hydrogen H_2, indicating the coplanar *anti* disposition of the pyridine and azomethyne groups. Analogous results were obtained by performing the same experiment on the imine (*S*)-**1**, apart the lack of response by the isopropyl group. Essentially the same n.O.e. effect was then observed on (*S*)-**4**-$ZnBr_2$ and (*S*)-**4**-$SnCl_2$. It is evident that the auxiliary group has the same spatial disposition regardless the ester is coordinated or not to the metal ($ZnCl_2$ or $SnCl_2$). Conversely, in (*S*)-**4**-$SnCl_4$ the same n.O.e. experiment gave a positive effect only on the pyridine hydrogen H_2, confirming the N,N-chelation mode. Moreover, the H-C* hydrogen had a chemical shift at very low field (5.57 ppm), indicating that it was probably eclipsed with a chlorine atom. It can be reasonably assumed that the auxiliary takes this conformation in order to avoid the more severe steric interactions of isopropyl and ester groups with $SnCl_4$.

Table 4. ^{1}H-NMR Absorptions of (*S*)-4 and (*S*)-1 and their Metal Salt Complexes. [a]

Compound	H_5 [b]	H_4 [b]	H_3 [b]	H_2 [b]	CH=N	H-C*	OR	$CH(CH_3)_2$	$CH(CH_3)_2$
(*S*)-4	8.67	7.34	7.76	8.13	8.35	3.78	3.76 [c]	2.41	0.97
(*S*)-4-$ZnBr_2$	8.76	7.82	8.17	8.17	8.97	4.45	3.86 [c]	2.51	1.05
(*S*)-4-$SnCl_2$	9.35	7.67	8.12	8.24	8.91	4.35	3.80 [c]	2.39	0.98
(*S*)-4-$SnCl_4$	9.57	8.10	8.45	8.26	9.30	5.57	3.84 [c]	2.58	1.17
(*S*)-1		7.43 [d]	-	7.82 [e]	8.27	3.65	4.24 [f]	2.40	0.97
(*S*)-1-$ZnBr_2$		7.60 [d]	-	8.05 [e]	8.59	4.27	4.55 [g]	2.50	1.11

(a) The spectra were taken at 300 MHz in $CDCl_3$ (TMS as the internal standard and absorptions are given as δ (ppm). (b) See Figure 1 for numbering. (c) R = CH_3. (d) H_3-H_5. (e) H_6 = H_2. (f) R = CH_2CH_3 (CH_2CH_3 at 1.30 ppm). (g) R = CH_2CH_3 (CH_2CH_3 at 1.43 ppm).

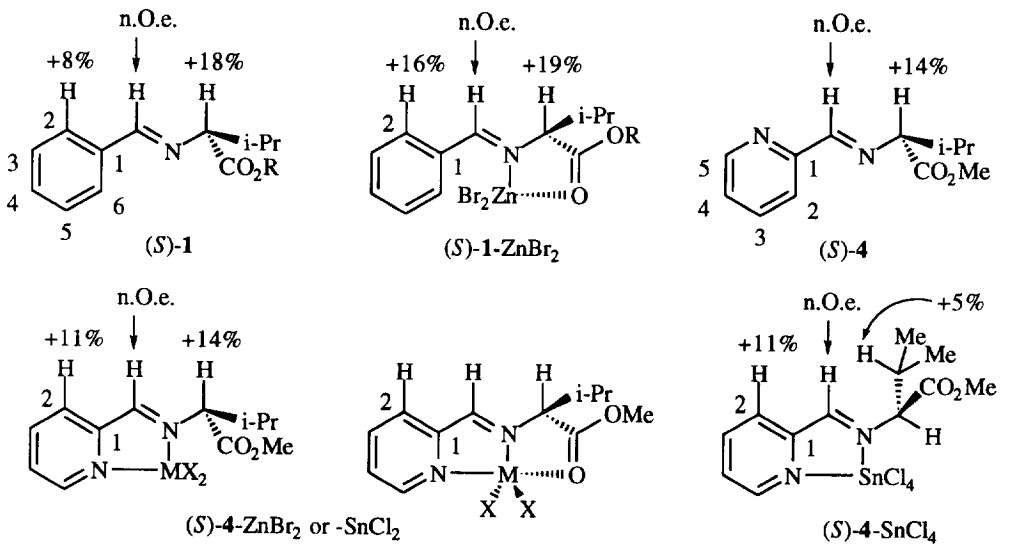


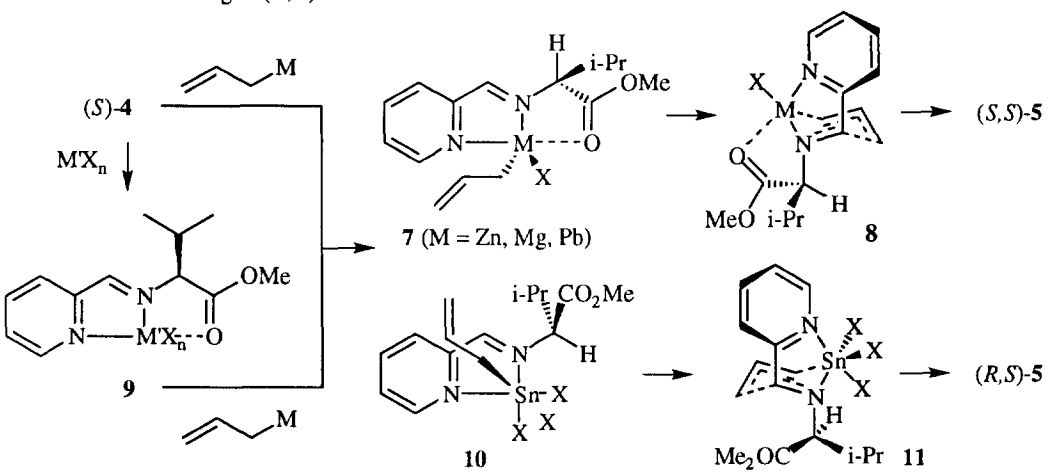
Figure 1. Structures, Conformations and N.O.E. Experiments of (*S*)-1, (*S*)-4 and their Metal Salt Complexes

Mechanism of the Addition of Allylmetal Reagents to (S)-4 and (S)-4-Metal Salt Complexes

We assume that the addition of allylmetal reagents to the imine (*S*)-4 occurs largely by a polar mechanism and through cyclic transition states. The same assumption was made by different authors who described the addition of allylmagnesium chloride to a chiral 1,2-diimine,[15] and a zinc dienolate (behaving as an α-substituted allylzinc chloride when reacting at the γ-position) with (*S*)-4.[16] A SET process could be envisaged, as 2-pyridine imines are good π-acceptors,[17] like 1,2-diimines, which react with organometallic compounds (RLi, R_2Mg, RMgX, R_2Zn and R_3Al) to give N- and/or C-alkylated products at least in part through a radical (SET) mechanism.[18] However, alkylzinc halides do not react with the same 1,2-diimines.[18f] The reaction of

diethylzinc with a 2-pyridine imine occurred only above 40 °C and afforded mainly the dimer of the imine through a radical mechanism.[18d] Moreover, ethymagnesium bromide reacted with 1,2-diimines to give mainly the N-alkylation products (SET), but with a 2-pyridineimine gave exclusively the C-alkylation product,[18e] perhaps through a polar mechanism, as it was initially proposed to explain the alkylation at carbon in the addition of organoaluminium compounds to 1,2-diimines.[18a,b]

Since we have never observed N-alkylation products or dimers of the imine in our reaction mixtures, we believe that a polar mechanism is largely or exclusively operating, involving the intermediate complexes and the cyclic transition states reported in Scheme 2. The allylmetal compounds in which the metal is capable of tricoordination, e.g. zinc and magnesium, would form the most rigid association complexes **7** with the imine, from which the amine (*S*,*S*)-**5** is produced through the cyclic transition state **8**. However, even if the ester has no bonding interaction with the metal, the auxiliary would not change conformation significatively, by analogy with the most stable conformation of (*S*)-**4**-$ZnBr_2$ and -$SnCl_2$ (Figure 1) and the same facial diastereoselectivity should be obtained. In the case of the allyltin(IV) reagents the intermediate complex displays probably a different orientation of the auxiliary group with respect to **7**, as shown in **10** (Scheme 2), due to the lack of Sn-O coordination and the necessity to avoid non bonding interaction, by analogy with the preferred conformation of the complex (*S*)-**4**-$SnCl_4$ (Figure 1). The allyl group in **10** should be preferably in the axial position *anti* to the bulky isopropyl group of the auxiliary, and the attack to the *Re* face of the imine should then occur through the transition state **11** leading to (*R*,*S*)-**5**.



Scheme 2

It should be emphasized that allyltin trihalides, in the absence of a strong Lewis acid, react exclusively with activated bidentate imines, such as (*S*)-**4**[6] and (*S*)-**3**.[4] Similarly, boron trifluoride is required for the successful reaction of allyllead bromide with (*S*)-**1**,[2] but not with (*S*)-**4**. For both the allylmetal reagents, chelation by the 1,2-diimine moiety increases the electron density on the metal and consequently the nucleophilicity of the allyl group, which is then transferred to the azomethine carbon by a cyclic transition state.

The asymmetric induction observed in the organometallic reactions of the imine-metal salt complexes can not be explained by a mechanism involving an acyclic transition state. In fact, the preferred conformation of the auxiliary in the imine-$ZnCl_2$ and -$SnCl_2$ complexes (Figure 1) would dictate the nucleophilic addition to the *Si* face, whereas allyltin trihalides attacked the *Re* face of (*S*)-**4**-$SnCl_2$ (Table 1, entry 12). Similarly, the addtition

to the *Re* face of (*S*)-**4**-$SnCl_4$ (Figure 1) would be expected in reactions proceeding through an acyclic transition state, but allylmagnesium chloride added the *Si* face with moderate diastereoselectivity (entry 14). Hence, we propose a mechanism in which the allylmetal reagent replaces the chelated metal salt in **9** to form the reactive complexes **7** or **10**, depending on the allylmetal species, which display a different orientation of the auxiliary and consequently the opposite diastereoselectivity (Scheme 2).

EXPERIMENTAL SECTION

General methods and procedures for the preparation of the imines and the organometallic reactions were described previously.[2]

Methyl N-(2-Pyridylmethylidene)-(*S*)-valinate (*S*)-4: the crude material had $[\alpha]^{25}_D$ -101.65 (c 2.1, $CHCl_3$); GC-MS *m/z* (relative intensity) 161 (100), 92 (72), 119 (47), 177 (39), 145 (35), 118 (35), 78 (16), 65 (15).

Reaction of (*S*)-4 with Allyllead Bromide. Synthesis of Methyl N-[(4*S*)-4-(2-Pyridyl)but-1-en-4-yl)]-(*S*)-valinate (*S*, *S*)-5. To the stirred suspension of $PbBr_2$ (4.40 g, 12 mmol) in anhydrous THF (15 mL) at -78 °C in N_2 atmosphere was added allylmagnesium chloride (2.0 M in THF, 6 mL, 12 mmol) and the mixture was stirred for 30 minutes, then the solution of imine (*S*)-**4** (2,20 g, 10 mmol) in THF (5 mL) was added during 5 min. After 30 min the reaction was quenched with 1M KOH (10 mL), the cooling bath was removed, the mixture was filtered, the solid phase washed thoroughly with Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 X 25 mL). The collected organic layers were dried (Na_2SO_4) and concentrated at reduced pressure to leave an oil. Flash chromatography on a short column of SiO_2 (cyclohexane-ethyl acetate 80:20) gave crude (*S*, *S*)-**5** as an oil (2.10 g, 80 %); ^{1}H-NMR δ 8.50 (m, 1), 7.65 (m, 1), 7.49 (m, 1), 7.14 (m, 1) 5.84-5.68 (m, 1), 5.16-5.0 (m, 2), 3.75 (m, 1), 3.69 (s, 3), 2.80 (d, *J* = 6 Hz, 1), 2.40-2.20 (m, 2), 2.3 (br, 1), 1.95-1.78 (m, 1), 0.91 and 0.85 (2 d, *J* = 6.8 Hz, 6) ppm; GC-MS *m/z* (relative intensity) 221 (100), 161 (57), 119 (56), 117 (48), 132 (45), 92 (40), 130 (35), 133 (27), 107 (24), 203 (24). Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.67%; H 8.45%; N, 10.68%. Found: C, 68.52%; H, 8.46%; N, 10.70%.

Reaction of (*S*)-4 with $AllylSnICl_2$. Synthesis of Methyl N-[(4*R*)-4-(2-Pyridyl)but-1-en-4-yl)]-(*S*)-valinate (*R*, *S*)-5. To the stirred solution of $SnCl_2$ (2.27 g, 12 mmol) in anhydrous THF (15 mL) in N_2 atmosphere was added allyl iodide (2.016 g, 12 mmol) and the mixture was stirred for 15 min, then cooled to -78 °C. After 10 min the imine (*S*)-**4** (2.20 g, 10 mmol) dissolved in THF (5 ml) was added during 5 min, and the mixture was stirred for further 30 min. After quenching and workup as above described, crude (*R*, *S*)-**5** was obtained as an oil (2.227 g, 85 %): ^{1}H-NMR δ 8.57 (m, 1), 7.71 (m, 1), 7.68 (m, 1), 7.29 (m, 1), 5.86-5.70 (m, 1), 5.20-5.04 (m, 2), 3.75 (m, 1 H), 3.73 (s, 3), 2.91 (d, *J* = 6 Hz, 1), 2.70-2.40 (m, 2H), 2.3 (broad, 1), 2.10-1.95 (m, 1), 0.97 and 0.90 (2 d, *J* = 6.8 Hz, 6) ppm.

Preparation of (*S*)- and (*R*)-1-(2-Pyridyl)-3-butenamine (6): To the stirred solution of (*R*, *S*)- or (*S*, *S*)-**5** (2.0 g, 7.6 mmol) in THF (10 mL). at -5 °C in N_2 atmosphere was added portionwise $LiAlH_4$ (0.288 g, 7.6 mmol). After stirring for 30 min at -5-0 °C, the mixture was quenched with 1M KOH (10 mL), stirred for 15 min at 20 °C, and filtered. The solid was washed with Et_2O, the organic layer separated, and the aqueous layer extracted with Et_2O (3 X 25 mL). The collected organic layers were dried (Na_2SO_4) and concentrated at reduced pressure to leave an oil: 1.7 g (95%). The ^{1}H-NMR spectra were consistent with the expected β-amino alcohol: *S*, *S* diastereomer, δ 8.60 (m, 1), 7.65 (m, 1), 7.20 (m, 2), 5.82-5.70 (m, 1), 5.15-5.0 (M, 2), 3.80

(m, 1), 3.65 and 3.45 (dd, 2), 2.50 (m, 2), 2.6-2.0 (broad, 2), 1.65 (m, 1), 0.87 and 0.80 (2d, 6); *R,S* diastereomer, δ 8.55 (m, 1), 7.55 (m, 1), 7.30 (m, 1), 7.15 (m, 1), 5.85-5.70 (m, 1), 5.20-5.05 (m, 2), 3.95 (m, 1), 3.42-3.25 (m, 2), 2.55-2.30 (m, 2), 1.85 (m, 1), 2.6-2.0 (broad, 2), 0.95 and 0.90 (2d, 6). GC-MS *m/z* (relative intensity) 192 (100), 131 (50), 91 (50), 202 (20). To the solution of the β-amino alcohol (1.62 g, 6.9 mmol) in MeOH (25 mL) was added 40 % aq $MeNH_2$ (4.4 mL), then H_5IO_6 (5.79 g, 25.4 mmol) dissolved in H_2O (10 mL) during 5 min. The mixture was stirred magnetically over 1 h, then H_2O (10 mL) was added, the mixture was filtered, and the filtered solution was extracted with Et_2O (20 mL X 3). After usual workup the crude amine (*S*)- or (*R*)-**6** was obtained: 1.02 g, 100 %, >90% pure by GC-MS and ^{1}H-NMR analysis. The pure compound was obtained by bulb to bulb distillation: 0.750-0.810 g (70-75% based on **5**); $[\alpha]_D^{25}$ -32 (c 1.17, $CHCl_3$) for (*S*)-**6**; $[\alpha]_D^{25}$ +32.2 (c 1.20, $CHCl_3$) for (*R*)-**6**; lit.[8] +36.50 (EtOH) for the *R* enantiomer; ^{1}H-NMR δ 8.55 (m, 1), 7.64 (m, 1), 7.30 (m, 1), 7.16 (m, 1), 5.75 (m, 1), 5.09 (m, 2), 4.01 (m, 1), 2.60 (m, 1), 2.40 (m, 1), 8.15 (broad) and 2.81 (d, 2) ppm; GC-MS *m/z* (relative intensity) 107 (100), 80 (20), 78 (10), 108 (8), 53 (7), 105 (5).

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