Diastereoselectivity in the Allylation of *N*-Trialkylsilylimines of *O*-Protected (2*S*)-Lactal − Some Unexpected Results

Gianfranco Cainelli,*[a] Daria Giacomini,[a] Paola Galletti,*[a] and Arianna Quintavalla[a]

Keywords: Allylation / Diastereoselectivity / Imines / Inversion temperature / Temperature effect

A comparison of the diastereoselective addition of allylMgCl to differently *O*-protected *N*-trialkylsilyllactaldimine and to *N*-benzyllactaldimines is reported. The stereoselectivity strongly depends on the *O*- and *N*-protecting groups, on the metal cation, and on the reaction temperature, and varies from predominance of the *anti* diastereoisomer to predominance of the *syn* one. *O*-TBS- and *O*-TIPS-silyl imines displayed better *anti* diastereoselectivity than their *O*-alkyl counterparts. The *N*-protection produced unexpected results: in particular, the bulky, achiral, *N*-TIPS group favoured the predominance of the *syn* diastereoisomer. The temperature dependence of the stereochemical outcome provides evidence of the important role of differential entropies of activation ($\Delta\Delta S^{\neq}$), and the presence of inversion temperatures (T_{inv}) related to dynamic solvation phenomena.

Introduction

Great efforts have been devoted in recent years to studies of the stereoselective synthesis of enantiopure amines by nucleophilic addition.[1] As an example, the addition of organometallic reagents to azomethine moieties, involving C−C bond formation with establishment of a new stereogenic centre, is of considerable interest in asymmetric synthesis.[2] The products of this reaction are optically active amines, the characteristic structural features of which are present both in natural products and in pharmacologically active compounds.[3]

Diastereofacial selectivity in allyl organometallic additions to aldimines containing one or more stereogenic centres has been extensively studied in recent years, and many research groups have been involved in studies of allyl- and crotylmetal reagents for the construction of homoallylic amines.[4] Yamamoto et al. have examined *N*-propylaldimines derived from 2-phenylpropanal and observed that allylstannane (in the presence of $TiCl_4$), allylGrignard and allyl-9-BBN additions provided predominantly or exclusively *anti* products.[5] In the case of an α-alkoxyaldimine obtained from (*S*)-2-(methoxymethyl)propanal, the same authors obtained predominantly *syn*-homoallylamines when using allylmagnesium, -aluminium and -zinc reagents, whereas the *anti* isomer was obtained with allylboron and -titanium reagents.[6] Jäger et al. investigated the *O*,*N*-dibenzyllactaldimine, which predominantly provided the *syn* isomer with allyl Grignard reagents.[7] The stereochemical outcomes of these reactions have been discussed mainly in terms of chelation or nonchelation control[8] in the nucleophilic addition, modulated by the metal cation and by the protecting group of the α-alkoxy group, thus limiting analysis to enthalpic contributions.

In this chemistry, the important goal of obtaining primary amines directly could be achievable by use of particular nitrogen substituents on the parent imine, and in this regard *N*-metallated imines can be really considered the reagent of choice, due to their hydrolytically cleavable metal−nitrogen bonds. In this context we report our work and results on the diastereofacial selectivity of *N*-silylimines of *O*-protected (2*S*)-lactal in nucleophilic additions of allylmagnesium chloride.

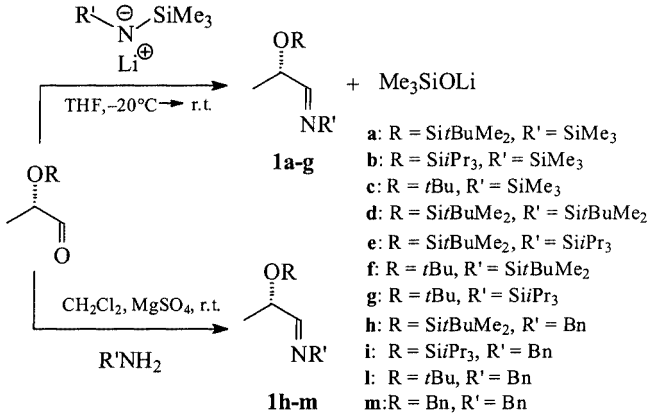
A previous paper reports the initial employment of *N*-trimethylsilylimines of (2*S*)-*O*-(*tert*-butyldimethylsilyl)lactal, showing the predominance of *anti*-aminols with the use of copper reagents, derived either from allylmagnesium chloride or from allyl Grignard reagents, in the presence of boron trifluoride−diethyl ether.[9] In this paper we describe the stereoselective allylation with allylMgCl of differently *O*-protected *N*-trialkylsilyllactaldimine in comparison with *N*-benzyllactaldimines, and the dependence of the stereoselectivity of this process on the *O*- and *N*-protecting groups, on the metal cation and on the reaction temperature.

Results and Discussion

The imines were synthesized from the corresponding aldehydes by the methodology reported in Scheme 1. In par-

[a] Department of Chemistry "G. Ciamician", University of Bologna
Via Selmi 2, 40126 Bologna, Italy
Fax: (internat.) + 39-051/209-9456
E-mail: cainelli@ciam.unibo.it
paolag@ciam.unibo.it

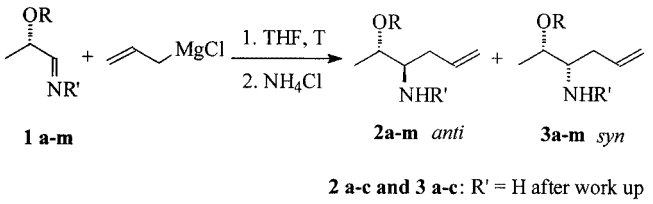
ticular, *N*-trialkylsilylimines were obtained from the corresponding secondary alkylamines by our previously developed procedure.[10]



Scheme 1

All imines could easily be obtained in a salt-free state: *N*-trialkylsilylimines **1a**–**g** can be purified by distillation and thus separated from Me_3SiOLi, the other reaction product, whereas *N*-benzylimines **1h**–**m** can be obtained pure by filtering off the magnesium salts.

Allylation was performed by treating 1 equiv. of imines **1a**–**m** with 1.2 equiv. of a 2 M solution of allylmagnesium chloride in THF at the desired reaction temperature (Scheme 2). Conversion into the products was complete within a few minutes, and the crude reaction mixture was analysed at different reaction times for the determination of the diastereomeric ratio by GC.



Scheme 2

In the case of *N*-trialkylsilylimines **1a**–**g**, the addition of allylmagnesium chloride was performed both on distilled imines and on imines prepared "in situ" (that is to say, still in the presence of 1 equiv. of Me_3SiOLi).

The absolute configurations of the newly formed stereogenic centres in the homoallylic amines were determined by NMR analysis, by comparison with or by chemical conversion into known products (see Exp. Sect.).

The results of our experiments performed at room temperature are collected in Table 1.

The phenomenon of reversibility, depending on the nature of the metal and on the basicity of the nitrogen atom, has to be fully taken into account in allylic organometallic aldimine reactions.[11] As reported above, reactions between imines **1a**–**m** and allylMgCl at 25 °C are complete in a few minutes, and so, to test for the presence of those equilibration phenomena, we measured the diastereomeric ratios at longer reaction times (Table 1). Our data clearly show that reversibility is greater for *O*-alkyl-protected imines and also depends on the presence of lithium cations, so that only **1c** and **1c*** (Entries 5 and 6 Table 1) significantly equilibrate. In the other cases the equilibration phenomenon is not detected.

Table 1. Diastereomeric *anti*/*syn* ratio in the addition of allylMgCl to imines **1a**–**m** at T = 25 °C detected at different reaction times

Entry	Substrate	R	R′	**2** (*anti*)/**3** (*syn*) (%) [reaction times < 30 min]	**2** (*anti*)/**3** (*syn*) (%) [reaction times > 240 min]
1	**1a**	Si*t*BuMe$_2$	SiMe$_3$	92:8	90:10
2	**1a***[a]	Si*t*BuMe$_2$	SiMe$_3$	70:30	70:30
3	**1b**	Si*i*Pr$_3$	SiMe$_3$	94:6	94:6
4	**1b***	Si*i*Pr$_3$	SiMe$_3$	83:17	85:15
5	**1c**	*t*Bu	SiMe$_3$	78:22	74:26
6	**1c***	*t*Bu	SiMe$_3$	64:36	50:50
7	**1d**	Si*t*BuMe$_2$	Si*t*BuMe$_2$	93:7	93:7
8	**1d***	Si*t*BuMe$_2$	Si*t*BuMe$_2$	77:23	77:23
9	**1e**	Si*t*BuMe$_2$	Si*i*Pr$_3$	73:27	75:25
10	**1e***	Si*t*BuMe$_2$	Si*i*Pr$_3$	49:51	33:67
11	**1f**	*t*Bu	Si*t*BuMe$_2$	55:45	54:46
12	**1f***	*t*Bu	Si*t*BuMe$_2$	34:66	35:65
13	**1g**	*t*Bu	Si*i*Pr$_3$	19:81	19:81
14	**1g***	*t*Bu	Si*i*Pr$_3$	10:90	11:89
15	**1h**	Si*t*BuMe$_2$	Bn	81:19	81:19
16	**1i**	Si*i*Pr$_3$	Bn	90:10	89:11
17	**1l**	*t*Bu	Bn	58:42	57:43
18	**1m**	Bn	Bn	27:73	27:73

[a] * = Imines prepared and used in situ, still in the presence of 1 equiv. of Me_3SiOLi.

Further evidence was obtained with imine **1a**: we performed the addition reaction at −78 °C, obtaining a 95:5 *anti*/*syn* ratio, after which the reaction system was slowly warmed to reach room temperature, and hence possibly to equilibrate. The final *anti*/*syn* ratio remained unaltered.

It should be underlined that the absence of equilibration phenomena ensures that the reaction proceeds under kinetic control.

Effects of *N*- and *O*-Protecting Groups and of Me_3SiOLi

The effect of protecting groups on the nitrogen atom and on the hydroxy positions is impressive, and the presence of Me_3SiOLi in the reaction medium also has great influence, the diastereoselection varying from predominance of the *anti* diastereoisomer (Entries 1−9, Table 1) to predominance of the *syn* form (Entries 10, 12, 13, 14 and 18, Table 1).

On comparison of imines with the same *N*-protection, it is seen that silyl ethers are more *anti*-diastereoselective than alkyl ethers and that better *anti* diastereoselection is obtained with the bulky *O*-TIPS group (cf. imines **1a** and **1b**, **1h** and **1i**). In particular, the highest *anti* diastereoselectivity is obtained from *O*-TBS and *O*-TIPS silyl imines (Entries 1, 3 and 7) whereas the highest *syn* diastereoselection is provided by the *O*-*t*Bu and *O*-Bn groups (Entries 13, 14 and 18).

On comparison of imines with the same *O*-protection, the influence of *N*-protection was quite unexpected. In fact, the presence of the *N*-TIPS group always produced a great increase in the *syn* diastereoisomer amount, and in the cases of imine **1g** and **1g*** (distilled and prepared in situ) and of imines **1e*** and **1f*** (prepared in situ) we obtained predominance of the *syn* isomers (cf. Entries 10, 12, 13 and 14).

Although the observed reversal in diastereoselectivity (cf. Entries 2−10 and 5−13) could be explained by invoking a "classic" chelation or nonchelation control[8] in the nucleophilic addition, such a prospect is hardly tenable in our case. Nor can a chelate intermediate explain the increase in *syn* isomer with *N*-TIPS imines, it being in fact quite unbelievable that *N*-TIPS imines would favour chelation better than *N*-TMS or *N*-TBS imines.[12]

Our results show that, even in the case of achiral *N*-substitution, imines possess a further element of stereocontrol: the protecting group on the nitrogen atom. It is hard to explain this result in term of conformational models because the *N*-protecting group lies in the C=N plane, losing any steric effect in the transition state.

As far as the effect of Me_3SiOLi is concerned, the *anti* percentage was higher for all distilled imines (absence of Me_3SiOLi) than for nondistilled ones (presence of Me_3SiOLi), even in cases of *syn* dominance. That is to say, the effect of Me_3SiOLi is an increase in *syn* diastereoselectivity (cf. Entries 1−14). With the aim of clarifying the effect of Me_3SiOLi, we also carried out the addition of allylmagnesium chloride to the distilled imine in the presence of 1 equiv. of anhydrous $LiClO_4$. This procedure was repeated at two different temperatures (25 °C and −4 °C). In both cases the diastereomeric ratio was close to the value obtained with the imine prepared in situ, thus suggesting that the effect of Me_3SiOLi was simply to furnish Li^+ ions.

Table 2. *anti*/*syn* ratio in the addition of allylMgCl to imines **1a**, **1a*** and **1e**, **1e*** at selected temperatures

Imine	*T* [°C]	*anti* (%)	*syn* (%)	Imine	*T* [°C]	*anti* (%)	*syn* (%)	Imine	*T* [°C]	*anti* (%)	*syn* (%)
1a	61	89.8	10.2	**1a***	23	67.2	32.8	**1e**	−30	92.9	7.1
"	53	90.3	9.7	"	9.5	66.7	33.3	"	−41	95.5	4.5
"	45	90.7	9.3	"	−4	71.4	28.6	"	−50	96.6	3.4
"	35	91.9	8.1	"	−12.5	75.1	24.9	"	−55	96.5	3.5
"	30	91.6	8.4	"	−20	74.6	25.4	"	−59.5	97.3	2.7
"	25	92	8	"	−30	80.3	19.7	"	−64.5	97.3	2.7
"	15	91.5	8.5	"	−31	77.7	22.3	"	−70	97.8	2.2
"	10	92.4	7.6	"	−40	79.3	20.7	"	−75	97.9	2.1
"	5.5	91.6	8.4	"	−44	80.7	19.3	"	−80	98.1	1.9
"	0.5	93.6	6.4	"	−49	86.5	13.5	"	−90	98.0	2.0
"	−10.5	92.9	7.1	"	−51	87.9	12.1	**1e***	40	31.6	68.4
"	−20	93.9	6.1	"	−60	91.9	8.1	"	35	28.5	71.5
"	−29	94.5	5.5	"	−70	94.2	5.8	"	30	32.2	67.8
"	−30	94.0	6.0	"	−78	96	4	"	20	32.9	67.1
"	−36.5	95.2	4.8	**1e**	55	61.8	38.2	"	10	34.7	65.3
"	−40	95.1	4.9	"	50	64.7	35.3	"	0	39.7	60.3
"	−53	95.6	4.4	"	45	65.5	34.5	"	−10	43.1	56.9
"	−63	95.4	4.6	"	40	63.6	36.4	"	−20	47.3	52.7
"	−69	95.4	4.6	"	35	67.7	32.3	"	−40	51.5	48.5
"	−81.5	95.7	4.3	"	30	70.5	29.5	"	−46.5	94.7	5.3
"	−84.5	96.2	3.8	"	25	74.7	25.3	"	−52.5	95.2	4.8
"	−94	96.2	3.8	"	20	73.4	26.6	"	−62.5	96.1	3.9
1a*[a]	51	60.2	39.8	"	10	78.7	21.3	"	−73	97.4	2.6
"	42	65.6	34.4	"	0	83.7	16.3	"	−83	97.3	2.7
"	31	63.8	36.2	"	−10	86.9	13.1	"	−92.5	97.5	2.5
"	25	68	32	"	−20	91.1	8.9	"			

[a] * = Imines prepared in situ, still in the presence of 1 equiv. of Me_3SiOLi.

Once again, this fact could be explained by assuming that the lithium cation favours chelation and thus the *syn* isomer, but, once more, this cannot occur with *N*-TIPS imines, in which the effect of the TIPS group should prevent a chelation control.

Effect of Reaction Temperature

We decided to take a deeper look in the reaction stereocontrol by studying the temperature dependence of the stereochemical outcome. Temperature is a very important parameter in control and analysis of stereoselection; temperature-dependent measurements, indeed, allow the evaluation of reaction thermodynamic parameters through the modified Eyring equation [Equation (1)],[13] where S is the selectivity, the *anti*/*syn* ratio can be calculated from the chromatographic areas of the two diastereoisomers, and $\Delta\Delta H^{\neq}$ and $\Delta\Delta S^{\neq}$ represent the differences in activation enthalpy and entropy of the two diastereomeric reaction paths, respectively ($\Delta\Delta H^{\neq} = \Delta H^{\neq}_{anti} - \Delta H^{\neq}_{syn}$ and $\Delta\Delta S^{\neq} = \Delta S^{\neq}_{anti} - \Delta S^{\neq}_{syn}$).

$$\ln S = \ln (anti/syn) = -\Delta\Delta H^{\neq}/RT + \Delta\Delta S^{\neq}/R \quad (1)$$

The reaction depicted in Scheme 2 was therefore performed for imines **1a**, **1a***, and **1e**, **1e*** (distilled and prepared in situ) at different temperatures ranging from −94 to +61 °C. The obtained data are reported in Table 2 and plotted in Figures 1 and 2.

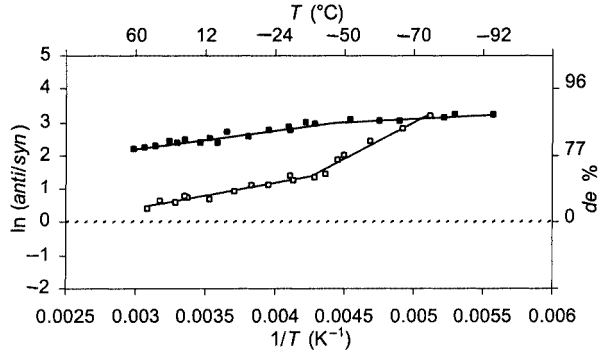


Figure 1. Eyring plots for addition of allylMgCl in THF to imines **1a** (black square: distilled), **1a*** (open square: prepared in situ)

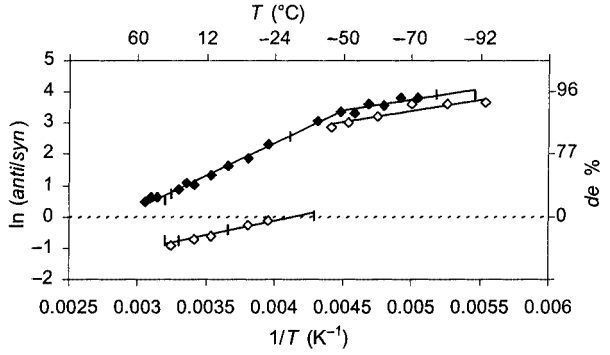


Figure 2. Eyring plots for addition of allylMgCl in THF to imines **1e** (black diamond: distilled), **1e*** (open diamond:, prepared in situ)

The data have been treated by least-squares analysis to fit Equation (1). For each data set we applied a residual analysis to evaluate the presence of linear trends. The values for $\Delta\Delta H^{\neq}$ and $\Delta\Delta S^{\neq}$ have been obtained from slopes and intercepts of linear plots.

In all Eyring plots of Figures 1 and 2, the existence of two linear relationships and of two different sets of thermodynamic parameters appears evident (Table 3). The temperature at the intersection is called the *inversion temperature* (T_{inv}) and its significance has been a matter of debate.[14] Our previous studies demonstrated that the presence of an inversion temperature represents a particular effect of the reaction solvent on the stereoselectivity. We have proposed that T_{inv} constitutes a transition temperature between two different solute-solvent clusters, which act as two distinct supramolecules with different thermodynamic properties, reactivity and, therefore, stereoselectivity.[15]

The distilled imines **1a** and **1e** show better *anti* diastereoselectivity than those prepared in situ through the whole temperature range, but the diastereoselection trends with temperature are quite different. For imine **1a** in particular, the observed diastereoselection is less dependent on temperature than that of the nondistilled imine **1a***, this behaviour originating directly from a lower value of $\Delta\Delta H^{\neq}$ (imine **1a**, $T < T_{inv}$). The behaviour of imine **1e** with temperature is quite peculiar: the distilled imine shows *anti* diastereoselectivity (from 62 to 98%) over the whole T range whereas the nondistilled imine **1e*** shows a reversal of diastereoselectivity with temperature, going from 97% of the *anti* isomer at −90 °C to 65% of the *syn* isomer at 60 °C. Moreover in the temperature range −40 to −46 °C we have an abrupt jump in diastereoselectivity, from 51.5% to 94% of the *anti* isomer. This unusual phenomenon is due to the fact that the enthalpic term in the two temperature regions is quite similar (−1.8 and −1.5 kcal/mol) whereas the entropic term is quite different (−7.4 and −0.5 cal/mol K respectively).

It is useful to remember that a reversal of diastereoselectivity occurs whenever $\Delta\Delta H^{\neq}$ and $\Delta\Delta S^{\neq}$ have the same sign: a negative $\Delta\Delta H^{\neq}$ derives from $\Delta H^{\neq}_{syn} > \Delta H^{\neq}_{anti}$, a lower activation barrier in the formation of the *anti* isomer (that is to say, the *anti* isomer is preferred by enthalpy); the opposite for $\Delta\Delta H^{\neq} > 0$ (the enthalpy now favouring the *syn* isomer). Regarding the entropy, assuming that an addition reaction is accompanied by a loss of activation entropy, a $\Delta\Delta S^{\neq}$ value < 0 derives from $|\Delta S^{\neq}_{anti}| > |\Delta S^{\neq}_{syn}|$: this means that the entropic loss in the formation of the *anti* isomer is larger than that of the *syn* one, so a negative entropic term favours the formation of the *syn* stereoisomer. The opposite applies for $\Delta\Delta S^{\neq} > 0$: the entropy now favours the *anti* isomer.[17] For imine **1e***, the same signs of enthalpy and entropy dictate a reversal of diastereoselectivity with temperature and for imine **1e** a strong decrease in diastereoselectivity at high temperatures.

The value of $\Delta\Delta H^{\neq}$ is negative in all cases that we studied (Table 3, Entries 1−4), and since $\Delta\Delta H^{\neq} = \Delta H^{\neq}_{anti} - \Delta H^{\neq}_{syn}$

Table 3. Values of $\Delta\Delta H^{\neq}$ and $\Delta\Delta S^{\neq}$ and T_{inv} for imines **1a**, **1a*** and **1e**, **1e***

Entry	Imine	T_{inv} [°C]	$T > T_{inv}$		$T < T_{inv}$	
			$\Delta\Delta H^{\neq}$ [kcal/mol]	$\Delta\Delta S^{\neq}$ [cal/mol K]	$\Delta\Delta H^{\neq}$ [kcal/mol]	$\Delta\Delta S^{\neq}$ [cal/mol K]
1	**1a**	−47	−1.1 ± 0.1	1.0 ± 0.4	−0.38 ± 0.08	4.3 ± 0.4
2	**1a***[a]	−38	−1.5 ± 0.1	−3.7 ± 0.4	−4.3 ± 0.4	−15 ± 2
3	**1e**	−58	−4.0 ± 0.3	−11.3 ± 0.3	−1.0 ± 0.3	2.7 ± 1.3
4	**1e***	−40 to −46	−1.8 ± 0.1	−7.4 ± 0.5	−1.5 ± 0.3	−0.5 ± 1.5

[a] * = Imines prepared in situ, still in the presence of 1 equiv. of Me_3SiOLi.

this means that the *anti* isomer is always enthalpically favoured. The entropic term $\Delta\Delta S^{\neq}$ is positive or negative depending on the imine and on the presence of Me_3SiOLi. By analysis of the sign of the experimentally determined $\Delta\Delta S^{\neq}$ we can formulate a hypothesis concerning the transition state order: $\Delta\Delta S^{\neq} < 0$ requires $|\Delta S^{\neq}_{anti}| > |\Delta S^{\neq}_{syn}|$: the entropic loss in the formation of *anti* is larger than that of *syn*, so, if $\Delta\Delta S^{\ddagger}$ is negative (as for imine **1a*** and **1e*** prepared in situ), the transition state giving rise to the *anti* isomer is more ordered than the *syn* one. This fact definitively rules out the hypothesis that the lithium cation and the *N*-TIPS group favour *syn* formation through a chelated transition state.[16] When $\Delta\Delta S^{\neq} > 0$ (as for distilled imine **1a** and for distilled imine **1e** at $T < T_{inv}$), the *syn* transition state is more ordered.[17]

The thermodynamic data in Table 3 show that the main difference between the imines is in the sign of the entropic term $\Delta\Delta S^{\neq}$: in the case of the distilled imine **1a** the *anti* isomer is always favoured by entropy, while the presence of the Me_3SiOLi entropically favours the *syn* isomer and, in fact, the diastereomeric ratio in this case is lower or, in other terms, the amount of the *syn* diastereoisomer becomes higher with increasing reaction temperature.

We have already demonstrated the fundamental importance of the entropic term in determining diastereoselectivity in previous papers in which we had found reversals of diastereoselectivity with temperature for the addition of *n*BuLi to differently *O*-protected (2*S*)-lactal[18] and its silylimines.[15]

The influence of the entropic term and the presence of a T_{invs} due to dynamic solvation phenomena are therefore critical for control of stereoselectivity.

VT NMR Experiment

Moreover, we have recently shown[19] that, in nucleophilic addition to aldehydes, T_{inv} depends mainly on the aldehyde-solvent couple and its value may be determined by ^{13}C NMR analysis by variable-temperature (VT) experiments. The variation of the C=N chemical shift with temperature presents two linear trends, the intersection of which (referred to as T_{NMR}) lies near the T_{inv} of the same substrate-solvent system, within experimental error. We therefore speculated that T_{NMR} and T_{inv} might have a common origin, and could in fact represent two independent experimental observations concerning the solvation-clustering phenomenon. The nature of T_{NMR} is related to the solvation of the substrate in the fundamental state (absence of the nucleophile) whereas T_{inv} is related to the reaction transition state, so their closeness confirms that the nature of T_{inv} is directly linked to dynamic solvation phenomena of the sole substrate.

We performed VT ^{13}C NMR analysis of distilled **1a** in [D_4]THF. The δ value of the imine C=N chemical shift decreases with increasing temperature between −80 and +20 °C, and two linear regions can clearly be recognized (Figure 3). T_{NMR} occurs at $T = -42.7$ °C and, as expected, once again corresponds to T_{inv} within experimental error.

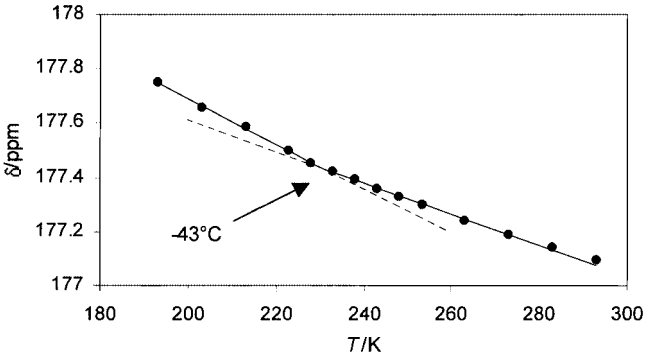
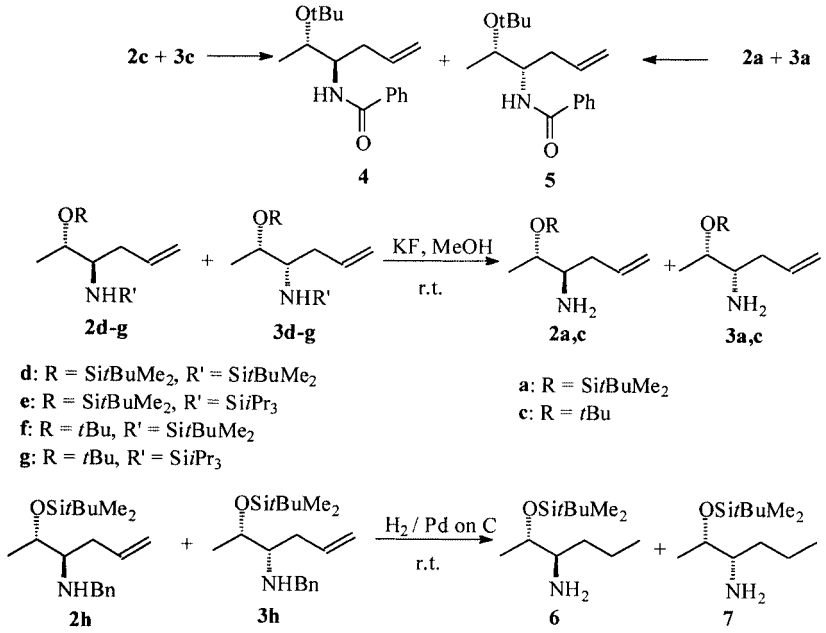


Figure 3. ^{13}C=O chemical shifts vs. temperature in [D_8]THF for distilled imine **1a**

Conclusion

By analysis of the experimental data obtained in the diastereoselective addition of allylMgCl to differently *O*-protected lactaldimines, we found that diastereoselection varies from predominance of the *anti* isomer towards predominance of the *syn* one, depending on the reaction temperature, on the *O*- and *N*-protecting groups and on the presence of lithium cations. The predominance of one isomer over the other is hard to interpret by "classical" conformational models, whereas an analysis of diastereoselectivity against temperature by the Eyring equation provided evidence of the presence of inversion temperatures, directly connected to solvation phenomena, and disclosed the determining role of the entropic term in modulating stereoselectivity.



Scheme 3

Experimental Section

General Remarks: All reactions were performed in flame-dried glassware under argon. ^{1}H and ^{13}C NMR were recorded with a Varian Gemini 300 instrument using a 5-mm probe. All chemical shifts are relative to deuterated solvent signals, δ in ppm, *J* in Hz. The temperature was controlled by a VT unit with a flow of temperature-regulated nitrogen gas. The temperature was calibrated with the aid of chemical shift differences in a methanol sample.[20] FT-IR: Nicolet 205 FT measured as films between NaCl plates and reported in cm^{-1}. GC-MS: HP5980, capillary column HP-1 or HP-5 connected to HP5970 (70 eV). GC: FISONS G8000, column: HP-5 M.S. crosslinked 5% PhMeSilicone, 30 m × 0.25 mm × 0.25μm, chiral column OV 1701 H. TLC: Merck 60F$_{254}$. Column chromatography: Merck silica gel 200−300 mesh. Liquid N_2/acetone baths in Dewar containers or oil baths with water cooling were used during reactions to set and maintain the temperature in a range of ± 1 °C. Temperatures refer to the interior of the reaction apparatus.

Starting Materials: THF was distilled from sodium benzophenone ketyl and stored over molecular sieves (4 Å), allylmagnesium chloride was a commercial 2 M solution in THF purchased from Aldrich. Imines **1a**−**g** were prepared from the corresponding aldehydes by the procedure reported in the literature[21] and purified when necessary by distillation in high vacuum (1.2 10^{-5} mbar). In a typical experiment, the imine (**1a**−**m**, 1 mmol) was dissolved in anhydrous THF (7 mL) under an inert gas, and the solution was cooled or warmed to the desired temperature. Allylmagnesium chloride (1.2 mmol, 0.6 mL of a 2 M solution in THF) was then added dropwise. After the starting material had disappeared (GC monitoring), the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl, extracted with CH_2Cl_2 (3 × 50 mL), and dried with Na_2SO_4. Chromatography of the residue on a silica gel column gave mixtures of the aminols **2a**−**m** and **3a**−**m**, so that the chemical yields, which ranged from 80 to 90%, could be calculated. The *anti*/*syn* ratio and the % *de* value were obtained from GC analysis of the crude products. The average standard deviation for the % *de* measurements was less than 1%. The aminol configurations were determined by NMR analysis of the corresponding oxazolidinones or by chemical conversion into known products: aminols **2a**−**3a** are known products,[14] the configurations of which were assigned by chemical conversion into the corresponding 1,3-oxazolidin-2-ones,[22] **2b**−**3b** were attributed by comparison with **2a**−**3a**, the aminol mixture **2d**−**3d** was converted into **2a**−**3a** by removal of the *N*-silyl group, **2e**−**3e** were attributed by comparison with **2d**−**3d**, aminols **2f**−**3f** and **2g**−**3g** were converted into **2c**−**3c**, which in turn were transformed into compounds **4**−**5** and compared with the same products prepared from **2a**−**3a**. Aminols **2m**−**3m** are known products,[7] **2h**−**3h** were hydrogenated, converted into **6**−**7** and compared with the homologues (2*S*,3*R*)- and (2*S*,3*S*)-3-amino-2-(*tert*-butyldimethylsilyloxy)heptane, which are known compounds,[16] and **2i**−**3i** were attributed by comparison with **2h**−**3h**.

***anti* Isomer 2a:** IR (film): ṽ = 3380 cm^{-1}, 3280, 1640, 1250, 1100. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 (s, 6 H, CH_3Si), 0.92 [s, 9 H, $SiC(CH_3)_3$,], 1.10 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.60 (br. s, 2 H, NH_2), 1.90−2.40 (m, 2 H, CH_2), 2.75 (m, 1 H, C*H*NH_2), 3.73 (dq, *J* = 6.2 Hz, 1 H, *J* = 4.5 Hz CHOSi), 4.95−5.10 (m, 2 H, $CH_2CH=CH_2$), 5.60−5.85 (m, 1 H, $CH_2CH=CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.9, −4.5, 17.9, 18.0, 25.7, 37.6, 56.3 (C−N), 71.5 (C−O), 116.8, 136.1 ppm. MS (70 eV): *m*/*z* (%) = 214 (1) [M$^+$ − CH_3], 188 (11), 172 (21) [M$^+$ − *t*Bu], 159 (3), 130 (17), 115 (5), 74 (39), 70 (100). $C_{12}H_{27}NOSi$ (229.44).

***syn* Isomer 3a:** IR (film): ṽ = 3380 cm^{-1}, 3280, 1640, 1250, 1100. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.04 (s, 6 H, CH_3Si), 0.85 [s, 9 H, $SiC(CH_3)_3$,], 1.16 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.60 (br. s, 2 H, NH_2), 1.90−2.40 (m, 2 H, CH_2), 2.58 (m, 1 H, C*H*NH_2), 3.65 (dq, *J* = 6.2 Hz, 1 H, *J* = 4.5 Hz CHOSi), 5.07−5.18 (m, 2 H, $CH_2CH=CH_2$), 5.70−5.90 (m, 1 H, $CH_2CH=CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.1, −4.4, 18.0, 20.2, 25.6, 38.7,

56.8 (C−N), 71.5 (C−O), 117.0, 136.4 ppm. MS (70 eV): *m*/*z* (%) = 214 (1) [$M^+ - CH_3$], 188 (11), 172 (21) [$M^+ - t$Bu], 159 (3), 130 (17), 115 (5), 74 (39), 70 (100). $C_{12}H_{27}NOSi$ (229.44).

***anti* Isomer 2b:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (m, 21 H), 1.10 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.60 (br. s, 2 H, NH_2), 1.96−2.18 (m, 2 H, CH_2), 2.88 (m, 1 H, C*H*NH_2), 3.90 (dq, *J* = 6.2, *J* = 4.5, 1 H, CHOSi), 5.03−5.13 (m, 2 H, $CH_2CH{=}CH_2$), 5.72−5.90 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.5, 17.7, 18.1, 37.8, 56.4 (C−N), 71.2 (C−O), 116.9, 136.0 ppm.

***syn* Isomer 3b:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05(m, 21 H), 1.18 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.60 (br. s, 2 H, NH_2), 1.96−2.18 (m, 2 H, CH_2), 2.65 (m, 1 H, C*H*NH_2), 3.61 (dq, *J* = 6.2 Hz, 1 H, *J* = 4.5 Hz CHOSi), 5.05−5.13 (m, 2 H, $CH_2CH{=}CH_2$), 5.70−5.90 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 16.9, 18.1, 38.2, 57.0 (C−N), 71.8 (C−O), 116.9, 136.0 ppm.

***anti* Isomer 2c:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.18 (s, 9 H, *t*Bu), 1.64 (br. s, 2 H, NH_2), 1.90−2.28 (m, 2 H, CH_2), 2.81 (m, 1 H, C*H*NH_2), 3.56 (m, 1 H, CHOSi), 5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.7, 28.6, 38.0, 55.8 (C−N), 69.6 (C−O), 73.5, 117.0, 136.0 ppm.

***syn* Isomer 3c:** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.18 (s, 9 H, *t*Bu), 1.64 (br. s, 2 H, NH_2), 1.90−2.28 (m, 2 H, CH_2), 2.64 (m, 1 H, C*H*NH_2), 3.46 (m, 1 H, CHOSi), 5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.7, 28.9, 38.2, 56.1 (C−N), 70.7 (C−O), 73.5, 117.2, 136.1 ppm.

***anti* Isomer 2d:** IR (film): $\tilde{\nu}$ = 3380 cm^{-1}, 3080, 1640, 1250, 1100. ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.05−0.10 (m, 12 H, Me_2SiO, Me_2SiN), 0.80−0.95 (s, 18 H, NSi*t*Bu, OSi*t*Bu), 1.12 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.52 (br. s, 1 H, NH), 1.90−2.40 (m, 2 H, CH_2), 2.55 (m, 1 H, C*H*NH_{Si}), 3.62 (m, 1 H, CHOSi), 4.90−5.25 (m, 2 H, $CH_2CH{=}CH_2$), 5.70−6.00 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.1, −4.0, −3.7, 18.1, 21.0, 25.9, 26.5, 38.0, 56.6 (C−N), 73.8 (C−O), 116.1, 137.1 ppm. MS (70 eV): *m*/*z* (%) = 328 (1) [$M^+ - CH_3$], 302 (7), 184 (100), 147 (12), 115 (5), 73 (50). $C_{18}H_{41}NOSi_2$ (343.70).

***syn* Isomer 3d:** IR (film): $\tilde{\nu}$ = 3380 cm^{-1}; 3080, 1640, 1250, 1100. ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.05−0.10 (m, 12 H, Me_2SiO, Me_2SiN), 0.80−0.95 (s, 18 H, NSi*t*Bu, OSi*t*Bu), 1.06 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.52 (br. s, 1 H, NH), 1.90−2.40 (m, 2 H, CH_2), 2.85 (m, 1 H, C*H*NH_{Si}), 3.76 (m, 1 H, CHOSi), 4.90−5.25 (m, 2 H, $CH_2CH{=}CH_2$), 5.70−6.00 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.4, −4.3, −4.1, 18.0, 19.6, 25.9, 26.5, 40.2, 57.3 (C−N), 70.7 (C−O), 115.7, 137.6 ppm. MS (70 eV): *m*/*z* (%) = 328 (1) [$M^+ - CH_3$], 302 (23), 184 (100), 147 (13), 73 (57). $C_{18}H_{41}NOSi_2$ (343.70).

***anti* Isomer 2e:** IR (film): $\tilde{\nu}$ = 3350 cm^{-1}; 3080, 1640, 1250, 1200. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 3 H, Me_2SiN), 0.10 (m, 3 H, Me_2SiO), 0.90 (m, 9 H, Si*t*Bu), 1.16 (m, 21 H, Si*i*Pr_3), 1.15 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.58 (br. s, 1 H, NH), 2.20−2.40 (m, 2 H, CH_2), 2.72 (m, 1 H, C*H*NH_{Si}), 3.80 (m, 1 H, CHOSi), 4.90−5.15 (m, 2 H, $CH_2CH{=}CH_2$), 5.70−6.10 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.6, −3.9, 12.8, 18.1, 18.4, 21.0, 26.0, 38.5, 57.1 (C−N), 74.2 (C−O), 115.9, 137.1 ppm. MS (70 eV): *m*/*z* (%) = 370 (1) [$M^+ - CH_3$], 344 (14), 226 (100), 157 (5), 115 (14), 87 (6), 73 (12), 59 (16). $C_{22}H_{47}NOSi_2$ (385.32).

***syn* Isomer 3e:** IR (film): $\tilde{\nu}$ = 3350 cm^{-1}; 3080, 1640, 1250, 1200. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.07 (s, 3 H, Me_2SiN), 0.10 (m, 3 H, Me_2SiO), 0.90 (m, 9 H, Si*t*Bu), 1.06 (m, 21 H, Si*i*Pr_3), 1.13 (d, *J* = 6.0 Hz, 3 H, CH_3), 1.58 (br. s, 1 H, NH), 1.90−2.30 (m, 2 H, CH_2), 2.72 (m, 1 H, C*H*NH_{Si}), 3.80 (m, 1 H, CHOSi), 4.90−5.15 (m, 2 H, $CH_2CH{=}CH_2$), 5.70−6.10 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.7, −4.1, 12.4, 18.2, 18.6, 19.6, 25.9, 40.3, 57.1 (C−N), 70.4 (C−O), 115.9, 137.4 ppm. MS (70 eV): *m*/*z* (%) = 370 (1) [$M^+ - CH_3$], 344 (40), 226 (100), 157 (4), 115 (15), 87 (6), 73 (18), 59 (15). $C_{22}H_{47}NOSi_2$ (385.32).

***anti* Isomer 2f:** IR (film): $\tilde{\nu}$ = 3400 cm^{-1}; 3085, 1637, 1250. ^{1}H NMR (300 MHz, $CDCl_3$): δ = +0.01 (s, 6 H, Me_2SiN), 0.89 (s, 18 H, Si*t*Bu), 1.08 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.19 (s, 9 H, *t*Bu), 1.80−2.40 (m, 2 H, CH_2), 2.45 (br. s, 1 H, NH), 2.66 (m, 1 H, C*H*NH_{Si}), 3.46 (dq, *J* = 6.3 Hz, 1 H, *J* = 4.2 Hz CHOSi), 4.90−5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80−5.90 (m, 1 H, $CH_2CH{=}CH_2$) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.2, −3.9, 17.9, 18.9, 26.4, 28.8, 39.6, 57.3, 71.7, 73.0, 116.0, 137.2 ppm. MS (70 eV): *m*/*z* (%) = 270 (1) [$M^+ - CH_3$], 244 (4), 184 (100), 172 (6), 73 (55), 57 (25). $C_{16}H_{35}NOSi$ (285.55).

***syn* Isomer 3f:** IR (film): $\tilde{\nu}$ = 3400 cm^{-1}; 3085, 1637, 1250. ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 6 H, Me_2SiN), 0.89 (s, 18 H, Si*t*Bu), 1.05 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.18 (s, 9 H, *t*Bu), 1.80−2.40 (m, 2 H, CH_2), 2.66 (m, 1 H, C*H*NH_{Si}), 2.45 (br. s, 1 H, NH), 3.52 (dq, *J* = 6.3 Hz, 1 H, *J* = 3.8 Hz CHOSi), 4.80−5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80−5.90 (m, 1 H, $CH_2CH{=}CH_2$) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −4.0, −3.7, 17.4, 17.8, 26.4, 28.8, 38.3, 56.8, 70.6, 73.0, 115.5, 137.9 ppm. MS (70 eV): *m*/*z* (%) = 270 (1) [$M^+ - CH_3$], 244 (4), 184 (100), 172 (6), 73 (55), 57 (25). $C_{16}H_{35}NOSi$ (285.55).

***anti* Isomer 2g:** IR (film): $\tilde{\nu}$ = 3380 cm^{-1}; 3085, 1638, 1250, 1050. ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.96−1.10 (m, 24 H, CH_3, Si-*i*Pr_3), 1.19 (s, 9 H, O*t*Bu), 1.90−2.10 (m, 2 H, CH_2), 2.25 (m, 1 H, C*H*NH_{Si}), 2.82 (br. s, 1 H, NH), 3.60 (m, 1 H, CHOSi), 4.90−5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80−6.05 (m, 1 H, $CH_2CH{=}CH_2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.7, 18.1, 18.6, 28.8, 40.5, 57.0, 71.3, 72.9, 115.9, 137.0 ppm. MS (70 eV): *m*/*z* (%) = 286 (4), 226 (100), 186 (5), 157 (5), 140 (4), 115 (22), 57 (45). $C_{19}H_{41}NOSi$ (327.63).

***syn* Isomer 3g:** IR (film): $\tilde{\nu}$ = 3380 cm^{-1}; 3085, 1638, 1250, 1050. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96−1.10 (m, 24 H, CH_3, Si-*i*Pr_3), 1.17 (s, 9 H, O*t*Bu), 1.90−2.10 (m, 2 H, CH_2), 2.45 (m, 1 H, C*H*NH_{Si}), 2.82 (br. s, 1 H, NH), 3.60 (m, 1 H, CHOSi), 4.90−5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.80−6.05 (m, 1 H, $CH_2CH{=}CH_2$) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.3, 16.8, 18.5, 28.7, 38.2, 56.4, 70.7, 72.9, 115.6, 137.9 ppm. MS (70 eV): *m*/*z* (%) = 286 (4), 226 (100), 186 (5), 157 (5), 140 (4), 115 (22), 57 (45). $C_{19}H_{41}NOSi$ (327.63).

***anti* Isomer 2h:** IR (film): $\tilde{\nu}$ = 3340 cm^{-1}; 3070, 1650, 1252, 1108−^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 3 H, CH_3Si), 0.06 (s, 3 H, CH_3Si), 0.90 (s, 9 H, Si*t*Bu), 1.18(d, *J* = 6.2 Hz, 3 H, CH_3), 1.65 (br. s, 1 H, NH), 2.10−2.33 (m, 2 H, CH_2), 2.60 (m, 1 H, C*H*NH), 3.85 (d, 2 H, CH_2Ph), 3.91 (m, 1 H, CHOSi), 5.04−5.06 (m, 2 H, $CH_2CH{=}CH_2$), 5.75−5.91 (m, 1 H, $CH_2CH{=}CH_2$), 7.35 (m, 5 H) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.1, −4.8, 17.7, 18.5, 25.6, 34.8, 51.7 (C−N), 61.8, 69.5 (C−O), 116.3, 126.4, 127.8, 127.9, 135.9, 140.5 ppm. MS (70 eV): *m*/*z* (%) = 305 (1) [M^+], 278 (10), 160 (100), 91 (68), 73 (6). $C_{19}H_{33}NOSi$ (319.56).

***syn* Isomer 3h:** IR (film): $\tilde{\nu}$ = 3340 cm^{-1}; 3070, 1650, 1252, 1108. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 (s, 3 H, CH_3Si), 0.06 (s, 3

H, CH_3Si), 0.92 (s, 9 H, Si*t*Bu), 1.17 (d, J = 6.2 Hz, 3 H, CH_3), 1.65 (br. s, 1 H, NH), 2.10−2.42 (m, 2 H, CH_2), 2.53 (m, 1 H, C*H*NH), 3.85 (d, 2 H, CH_2Ph), 3.91 (m, 1 H, CHOSi), 5.08−5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.75−5.91 (m, 1 H, $CH_2CH{=}CH_2$), 7.35 (m, 5 H) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = −5.0, −4.5, 17.7, 18.9, 25.6, 33.8, 51.8 (C−N), 62.1, 69.1 (C−O), 116.2, 126.4, 127.8, 127.9, 136.2, 140.6 ppm. MS (70 eV): *m*/*z* (%) = 305 (1) [M^+], 278 (5), 160 (100), 91 (68), 73 (6). $C_{19}H_{33}NOSi$ (319.56).

***anti* Isomer 2i:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05−1.08 (m, 21 H), 1.18 (d, J = 6.2 Hz, 3 H, CH_3), 2.35 (br. s, 1 H, NH), 2.39−2.42 (m, 2 H, CH_2), 2.82 (m, 1 H, C*H*NH), 3.85 (d, 2 H, CH_2Ph), 3.91 (dq, J = 6.2 Hz, 1 H, J = 4.5 Hz CHOSi), 4.86−5.26 (m, 2 H, $CH_2CH{=}CH_2$), 5.61−5.97 (m, 1 H, $CH_2CH{=}CH_2$), 7.52 (m, 5 H, Ph) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 12.4, 17.7, 18.1, 35.3, 52.0 (C−N), 62.5, 69.7 (C−O), 116.8, 126.9, 127.9, 128.3, 135.6, 139.9 ppm.

***syn* Isomer 3i:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05−1.08 (m, 21 H), 1.18 (d, J = 6.2 Hz, 3 H, CH_3), 2.35 (br. s, 1 H, NH), 2.39−2.42 (m, 2 H, CH_2), 2.63−2.69 (m, 1 H, C*H*NH), 3.85 (d, 2 H, CH_2Ph), 3.91 (dq, J = 6.2 Hz, 1 H, J = 4.5 Hz CHOSi), 4.86−5.26 (m, 2 H, $CH_2CH{=}CH_2$), 5.61−5.97 (m, 1 H, $CH_2CH{=}CH_2$), 7.52 (m, 5 H, Ph) − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 12.4, 17.7, 18.1, 35.3, 52.0 (C−N), 62.5, 68.9 (C−O), 116.8, 126.9, 127.9, 128.3, 135.6, 139.9 ppm.

***anti* Isomer 2l:** IR (film): $\tilde{\nu}$ = 3330 cm^{-1}; 3065, 1645. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13−1.18 (m, 12 H, CH_3, *t*Bu), 2.24 (br. s, 1 H, NH), 2.35−2.43 (m, 2 H, CH_2), 2.82−2.91 (m, 1 H, C*H*NH_2), 3.91 (m, 1 H, CHOSi), 4.10 (m, 2 H, CH_2Ph), 5.30 (m, 2 H, $CH_2CH{=}CH_2$), 6.09 (m, 1 H, $CH_2CH{=}CH_2$), 7.65 (m, 5 H, Ph) − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.0, 28.3, 35.9, 51.7 (C−N), 61.0, 68.3 (C−O), 73.3, 116.4, 126.5, 127.8, 128.0, 136.0, 140.7 ppm.

***syn* Isomer 3l:** IR (film): $\tilde{\nu}$ = 3330 cm^{-1}; 3065, 1645. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, J = 6.0 Hz, 3 H, CH_3), 1.18 (s, 9 H, *t*Bu), 2.24 (br. s, 1 H, NH), 2.35−2.43 (m, 2 H, CH_2), 2.69−2.82 (m, 1 H, C*H*NH_2), 3.91 (m, 1 H, CHOSi), 4.20 (d, 2 H, CH_2Ph), 5.30 (m, 2 H, $CH_2CH{=}CH_2$), 6.04−6.13 (m, 1 H, $CH_2CH{=}CH_2$), 7.50 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.1, 28.5, 35.6, 52.1 (C−N), 61.7, 68.0 (C−O), 73.3, 116.4, 126.5, 127.8, 128.0, 136.5, 140.7 ppm.

***anti* Isomer 2m:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, J = 6.0 Hz, 3 H, CH_3), 2.35−2.55 (m, 3 H, CH_2, NH), 2.80−2.85 (m, 1 H, C*H*NH_2), 3.91 (m, 1 H, CHOSi), 4.4−4.8 (d, 4 H, CH_2Ph), 5.09−5.20 (m, 2 H, $CH_2CH{=}CH_2$), 5.75−5.92 (m, 1 H, $CH_2CH{=}CH_2$), 7.35 (m, 10 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 33.5, 51.5 (C−N), 60.0, 70.7 (C−O), 117.2, 127.0−128.0, 135.6, 138.7 ppm.

***syn* Isomer 3m:** ^1H NMR (300 MHz, $CDCl_3$): δ = 1.25 (d, J = 6.0 Hz, 3 H, CH_3), 2.35−2.55 (m, 3 H, CH_2, NH), 2.69−2.75 (m, 1 H, C*H*NH_2), 3.91 (m, 1 H, CHOSi), 4.4−4.8 (d, 4 H, CH_2Ph), 5.09−5.20 (m, 2 H, $CH_2CH{=}CH_2$), 5.75−5.92 (m, 1 H, $CH_2CH{=}CH_2$), 7.35 (m, 10 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.5, 34.1, 51.6 (C−N), 60.5, 70.9 (C−O), 117.2, 127.0−128.0, 135.6, 138.7 ppm.

***anti* Isomer 4:** ^1H NMR (200 MHz, $CDCl_3$): δ = 1.05−1.03 (m, 12 H, CH_3, *t*Bu), 2.20−2.45 (m, 2 H, CH_2), 3.93 (m, 1 H, C*H*NH), 4.09 (m, 1 H, C*H*OH*t*Bu), 5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.85 (m, 1 H, $CH_2CH{=}CH_2$), 6.20 (d, J = 7.0 Hz, 1 H, NH), 7.5 (m, 5 H, aromatic), ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.9, 28.5, 33.0, 55.6 (C−N), 68.4 (C−O), 73.2, 116.8, 126.5, 128.6, 130.2, 134.3, 135.1, 166.7 ppm.

***syn* Isomer 5:** ^1H NMR (200 MHz, $CDCl_3$): δ = 1.05−1.03 (m, 12 H, CH_3, *t*Bu), 2.20−2.45 (m, 2 H, CH_2), 3.60 (m, 1 H, C*H*NH), 4.25 (m, 1 H, C*H*OH*t*Bu), 5.10 (m, 2 H, $CH_2CH{=}CH_2$), 5.85 (m, 1 H, $CH_2CH{=}CH_2$), 6.20 (d, J = 7.0 Hz, 1 H, NH), 7.5 (m, 5 H, aromatic). ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.9, 28.6, 36.4, 53.2 (C−N), 67.1 (C−O), 73.1, 116.8, 126.5, 128.2, 128.6, 134.6, 135.1, 166.8 ppm.

Acknowledgments

This work was supported by the MURST (ex 60%), COFIN 2000 (ex 40%) and the University of Bologna (fund for selected topics).

[1] For reviews see: [1a] E. F. Kleinman, R. A. Volkmann in *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming, G. H. Heathcock), Pergamon Press, Oxford, **1991**, vol. II, p. 475. [1b] R. Bloch, *Chem. Rev.* **1998**, *98*, 1407. [1c] D. Enders, U. Reinhold, *Tetrahedron: Asymmetry* **1997**, *8*, 1895.

[2] E. L. Eliel, S. H. Wilen, L. N. Mander, *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, p. 875.

[3] [3a] D. H. Rich in *Protease Inhibitors* (Eds.: A. J. Barrett, G. Salvesen), Elsevier, New York, **1986**, p. 179. [3b] K. Nakanishi, T. Goto, S. Ito, S. Natori, S. Nozoe, *Natural Product Chemistry*, Oxford, University Press, **1983**, vol. 3.

[4] [4a] S. Kobayashi, R. Hirabayashi, *J. Am. Chem. Soc.* **1999**, *121*, 6942. [4b] G. Alvaro, C. Boga, D. Savoia, A. Umani-Ronchi, *J. Chem. Soc., Perkin Trans. 1* **1996**, 875. [4c] Y. Yamamoto, T. Komatsu, K. Maruyama, *J. Chem. Soc., Chem. Commun.* **1985**, 815.

[5] Y. Yamamoto, S. Nishii, K. Maruyama, T. Komatsu, W. Ito, *J. Am. Chem. Soc.* **1986**, *108*, 7778.

[6] A. Yanagisawa, K. Ogasawara, K. Yasue, H. Yamamoto, *Chem. Commun.* **1996**, 367.

[7] T. Franz, M. Hein, U. Veith, V. Jäger, E.-M. Peters, K. Peters, H. G. von Schnering, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1298.

[8] For a recent review, see: A. Mengel, O. Reiser, *Chem. Rev.* **1999**, *99*, 1191−1223. See also ref.[17]

[9] G. Cainelli, D. Giacomini, E. Mezzina, M. Panunzio, P. Zarantonello, *Tetrahedron Lett.* **1991**, *32*, 2967.

[10] [10a] G. Cainelli, D. Giacomini, P. Galletti, A. Gaiba, *Synlett* **1996**, *7*, 657. [10b] G. Cainelli, D. Giacomini, P. Galletti, *Synthesis* **1997**, *8*, 886−890.

[11] Reversibility in the reactions of γ-monosubstituted allyllithium, -magnesium and -zinc reagents with aldimines has been observed at room temperature: [11a] L. Miginiac, B. Mauzé, *Bull. Soc. Chim. Fr.* **1968**, 4674. [11b] B. Mauzé, L. Miginiac, *Bull. Soc. Chim. Fr.* **1973**, 1082. [11c] B. Mauzé, L. Miginiac, *Bull. Soc. Chim. Fr.* **1973**, 1832. [11d] B. Mauzé, L. Miginiac, *Bull. Soc. Chim. Fr.* **1973**, 1838.

[12] [12a] X. Chen, E. R. Hortelano, E. L. Eliel, S. V. Frye, *J. Am. Chem. Soc.* **1992**, *114*, 1778. [12b] X. Chen, E. R. Hortelano, E. L. Eliel, *J. Am. Chem. Soc.* **1990**, *112*, 6130. [12c] C. Rucker, *Chem. Rev.* **1995**, *95*, 1009.

[13] [13a] H. Eyring, *J. Phys. Chem.* **1935**, *3*, 107. [13b] S. Glasstone, K.J. Laidler, H. Eyring, *The Theory of Rate Processes*, McGraw-Hill, New York, **1941**, chapter 4.

[14] [14a] H. Buschmann, H.-D. Scharf, N. Hoffmann, P. Esser, *Angew. Chem.* **1991**, *103*, 480; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 477. [14b] K. J. Hale, J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2* **1995**, 1601. [14c] K. J. Hale, J. H. Ridd, *J. Chem. Soc., Chem. Commun.* **1995**, 357.

[15] G. Cainelli, D. Giacomini, P. Galletti, *Chem. Commun.* **1999**, 567.

[16] Predominant formation of *syn* isomers is generally attributed to a chelated transition state (chelation control), while the *anti* isomer should arise from an open-chain transition state (non-chelation control). See for instance: M. T. Reetz, *Acc. Chem. Res.* **1993**, *26*, 462. M. T. Reetz, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 556. However, the chelated transition state should be more rigid and more ordered than the open-chain one.
[17] G. Cainelli, D. Giacomini, P. Galletti, *Eur. J. Org. Chem.* **1999**, 61.
[18] G. Cainelli, D. Giacomini, P. Galletti, P. Orioli, F. Paradisi, *Eur. J. of Org. Chem.* **2000**, 3619−3626.
[19] G. Cainelli, P. Galletti, D. Giacomini, P. Orioli, *Angew. Chem. Int. Ed.* **2000**, *39*, 523−527.
[20] H. Friebolin, G. Schilling, L. Pohl, *Org. Magn. Reson.* **1979**, *12*, 569.
[21] G. Cainelli, D. Giacomini, P. Galletti, *Synthesis* **1997**, *8*, 886−890.
[22] G. Cainelli, M. Panunzio, M. Contento, D. Giacomini, E. Mezzina, D. Giovagnoli, *Tetrahedron* **1993**, *49*, 3809−3826.

Received April 19, 2002
[O02218]