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2-(*p*-Tolylsulfinyl)benzyl Halides as Efficient Precursors of Optically Pure *trans*-2,3-Disubstituted Aziridines

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Dedicated to Professor José Barluenga on the occasion of his 70th birthday

Abstract: Aziridination of (*R*)-*N*-sulfinylaldimines (aryl, heteroaryl and alkenyl derivatives) with 2-(*p*-tolyl sulfinyl)benzyl iodide in the presence of sodium hexamethyl disilazide takes place with almost complete control of the stereoselectivity (facial and *anti*/*syn*) and with very high yields affording optically pure *N*-sulfinyl *trans*-2,3-disubstituted aziridines **7**. Simultaneous removal of both C- and *N*-*p*-tolylsulfinyl groups with *t*BuLi provides the corresponding *trans*-NH aziridines **8** without affecting their optical purity. Some experimental results suggest these processes evolve through benzyl halocarbenoids as intermediates, whereas theoretical calculations support the formation of benzyl carbanions. These results have served for revising the mechanistic aspects of the reactions of substituted 2-*p*-tolylsulfinyl benzylcarbanions with electrophiles.

Keywords: asymmetric synthesis · aziridination · chiral aziridines · diastereoselectivity · sulfinylimines

Introduction

α-Haloorganolithium (or organosodium) compounds, also called halocarbenoids, belong to the synthetically most useful reactive intermediates in organic synthesis because they have both nucleophilic and electrophilic reactivities.[1] Additionally, the tetravalent nature of carbenoids may confer a high level of stereoselectivity to their reactions, which is difficult to attain by using divalent free carbenes. α-Haloalkyl-,[2] α-halocyclopropyl,[3] α-haloalkylidene[4] and α-haloallyllithium[5] carbenoids have been used as versatile reagents in organic synthesis and extensively analyzed by spectroscopic methods and theoretical calculations.[1b,6] In contrast, (α-halobenzyl)lithium carbenoids have received much less attention due to their extremely strong tendency to give eliminative dimerization.[1] The electrophilic character of α-bromobenzylcarbenoids was first detected by Closs and Moss[7] in the preparation of arylcyclopropanes from $ArCHBr_2$, alkyllithiums and alkenes. Later on, the reaction of (benzylchloromethyl)lithium with alkenes was reported.[8] With respect to the reactions with electrophiles other than benzyl halides the only example in the literature is the trimethylsilylation of (benzylchloromethyl)lithium and (benzylbromomethyl)lithium.[9] More recently, Florio et al. reported that (3-pyridylchloromethyl)lithium behaved like a benzylic α-chloroorganolithium and reacts with carbonyl compounds and Schiff's bases.[10]

We have recently reported the almost completely stereoselective transfer of chiral benzyl groups to different electrophiles by starting from 2-(*p*-tolylsulfinyl)benzyl carbanions bearing alkyl,[11] trimethylsilyloxy,[12] and methylthio[13] substituents at the benzylic carbon atom. In all these reactions, the stereochemical results were explained by assuming the formation of chelated species, with the lithium intramolecularly stabilized by the sulfinyl oxygen atom. According to

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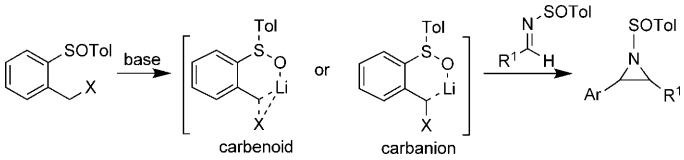
theoretical calculations, these carbanion–Li^+ complexes adopt a quasi-boat conformation with the metal restricting the access of the electrophile to one of the faces of the nucleophile,[13c,14] which justifies the complete stereoselectivity observed in the transfer of the prochiral benzylcarbanions, mainly controlled by a remote sulfinyl group. At this point, we reasoned that if the *ortho* sulfinyl group was able to stabilize the (α-halobenzyl)lithium carbenoids it would reduce their tendency to the eliminative dimerization and highly stereoselective reactions with electrophiles could be carried out. As potential precursors of the stabilized carbenoids we chose the 2-*p*-tolylsulfinylbenzyl halides (Scheme 1), and *N*-

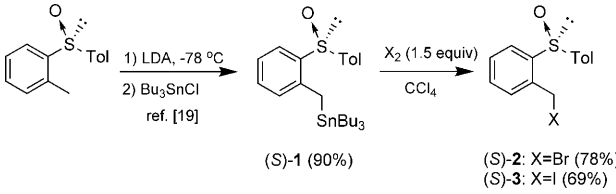


Scheme 1. Possible intermediates for the reaction of 2-*p*-tolylsulfinylbenzyl halides and *N*-sulfinylimines to give aziridines.

sulfinylimines were selected as electrophiles for obtaining aziridines, prevalent structures in biologically active molecules[15] and versatile building blocks for selective organic transformations by ring-opening processes.[16] Here we describe the results obtained in this study which have provided one of the most efficient methods for obtaining *trans*-aziridines in a highly stereoselective manner (Scheme 1). The stereochemical results obtained in these reactions are different to those observed from other *ortho*-sulfinylbenzyl carbanions previously studied, which suggests a different structure for the involved intermediates (maybe carbenoids). However, theoretical calculations concerning the structure of the possible intermediates support the carbanionic structures as the most stable ones, putting in question the existence of carbenoid intermediates. Finally, a good explanation of the experimental results is provided by the theoretical study of the transition states corresponding to the different approaches of the reagents.

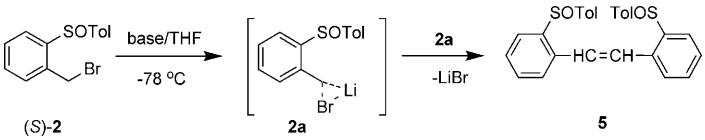
Results and Discussion

To apply the new strategy, presumably involving carbenoid structures stabilized by the sulfinyl oxygen atom, the use of the 2-*p*-tolylsulfinyl benzyl bromide or iodide as precursors are required. We performed the synthesis of the haloderivatives (*S*)-**2**[17] and (*S*)-**3**[18] by reaction of bromine or iodine with the tin derivative (*S*)-**1**, which in its turn was obtained from enantiomerically enriched (*S*)-2-(*p*-tolylsulfinyl)toluene according to the procedure previously reported by us[19] (Scheme 2).



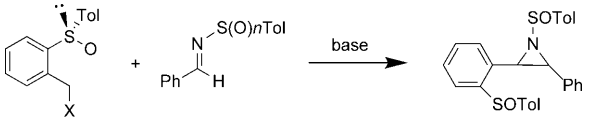
Scheme 2. Synthesis of α-halo-2-(*p*-tolylsulfinyl)toluenes (*S*)-**2** and (*S*)-**3**.

Optically pure *N*-*p*-tolyl and *N*-*tert*-butylsulfinylimines (**4a**–**m**) were prepared from the corresponding aldehydes according to the procedures reported by Davis[20] and Ellman, respectively.[21] To find the optimal conditions for the aziridination procedure, the influence of different bases and halobenzyl derivatives as well as the addition sequence were investigated (Scheme 3 and Table 1). The experiences carried out by adding bromobenzyl derivative (*S*)-**2** (1 equiv) to strong bases, such as lithium diisopropylamide (LDA) or lithium hexamethyl disilazide (LHMDS; 1.5 equiv), and soon after the imine (*R*)-**4a**, were found to



Scheme 3. Homocoupling reaction from (*S*)-**2**.

Table 1. Influence of the base, the halogen and the substituent on the nitrogen atom on the aziridination process.



(*S*)-**2**: X=Br
(*S*)-**3**: X=I

(*R*)-**4a**: *n*=1
(*S*)-**4a**: *n*=1
4a': *n*=2

cis-**6a**, *trans*-**7a**

Entry	X	Base	Imine	Yield [%][a]	d.r.[b]	*de* [%][b] *trans*-**7a**/*cis*-**6a**
1	Br	phosphacene	(*R*)-**4a**	–[c]	–	–
2	Br	LDA	(*R*)-**4a**	40[d]	43:57	>98:>98
3	Br	LHMDS	(*R*)-**4a**	90	75:25	>98:>98
4	Br	NaHMDS	(*R*)-**4a**	87	80:20	>98:>98
5	Br	LHMDS	(*S*)-**4a**	28[e]	50:50	5:5
6	Br	LHMDS	**4'a**	–[f]	–	–
7	I	LHMDS	(*R*)-**4a**	90	89:11	>98:>98
8	I	NaHMDS	(*R*)-**4a**	89[g]	96:4	>98:>98

[a] Combined isolated yield for both *cis*-**6a** and *trans*-**7a** isomers. [b] Determined by ^{1}H NMR spectroscopy from the crude reaction. [c] Starting materials were recovered unaltered. [d] 50% of (*S*)-**2** was recovered unaltered. [e] 65% of (*S*)-**2** was recovered unaltered. [f] Complex mixture. [g] Isolated yield for the *trans*-**7a** isomer.

be inefficient for preparing aziridines because, under these conditions, alkene **5** is almost quantitatively formed. This behaviour is compatible with the conversion of (*S*)-**2** into the carbenoid **2a**, which subsequently would suffer a quick homocoupling reaction followed by 1,2-elimination of LiBr[22] to afford **5** (Scheme 3). Nevertheless, the formation of **5** from a carbene intermediate cannot be excluded.

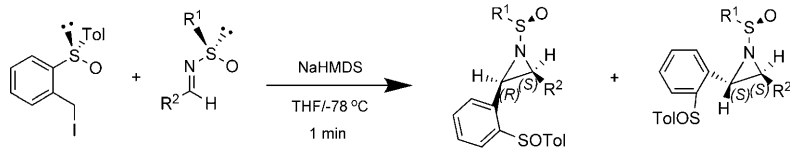
When **2a** was generated from (*S*)-**2** in the presence of the imine (*R*)-**4a** (Barbier conditions),[23] the homocoupling reaction is prevented. As summarized in Table 1, under these conditions, a mixture of two aziridines, *cis*-**6a** and *trans*-**7a**, were observed in all cases except when phosphacene was used as a base. (Table 1, entry 1). LDA leads to an almost equimolecular mixture of two diastereisomers, *cis*-**6a** and *trans*-**7a**, in rather modest yield but with complete facial selectivity for both diastereoisomers (entry 2). A dramatic improvement of the yield was observed when using LHMDS as a base (90%, entry 3), which also enhanced the *trans*/*cis* relationship to 75:25 maintaining the excellent facial selectivity (diastereomeric excess (*de*) >98%). We achieved a further increase in *trans* selectivity by employing lithium hexamethyl disilazide (NaHMDS), which yielded an 80:20 mixture of *trans*-**7a** and *cis*-**6a** without modifying the yield and the facial selectivity (entry 4).

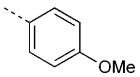
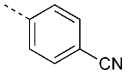
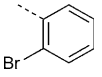
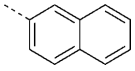
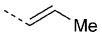
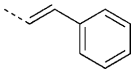
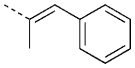
At this point, we investigated the influence of a change of the configuration of the imine. The reaction of (*S*)-**2** with (*S*)-**4a** in the presence of LHMDS yielded an almost equimolecular mixture of the four possible aziridines in low yield (Table 1, entry 5), which contrasts with the good results obtained from (*R*)-**4a** (entry 3). It proves that the matched pair for this double asymmetric induction process is formed by the reagents with a different configuration at the sulfur atom (see later). Otherwise, we have also checked the reaction of (*S*)-**2** with the sulfonamide **4′a**, which afforded a complex mixture of compounds the complete analysis of which was not possible in our hands (entry 6).

Finally, the influence of the halogen atom at the benzylic position on the course of the reaction was also studied. Reactions carried out by starting from ioderivative (*S*)-**3** and (*R*)-**4a** produced a higher *trans* selectivity than those with (*S*)-**2** (Table 1, cf. entries 7 and 8 with 3 and 4, respectively). Once again, the best base was NaHMDS, which yielded a 96:4 mixture of *trans*-**7a** and *cis*-**6a**, with the isolation of optically pure *trans*-**7a** in 89% yield achieved after chromatography (entry 8). The *trans/cis* ratio dropped to 89:11 when we used LHMDS as a base (entry 7). These results proved that the diastereoselectivity is clearly dependent on the metal (Li or Na) and the halogen atom (Br or I), thus allowing the possibility of excluding the carbenes as intermediates in these reactions.

Once the optimal reaction conditions for the aziridination process had been established, we studied the behaviour of different (*R*)-*N*-sulfinylimines (**4a–m**) with (*S*)-**3** to determine the scope of the reaction (Table 2). In all the experiences, aziridination reactions were completed within one

Table 2. Stereoselective aziridination of *N*-sulfinylimines (*R*)-**4a–m** with α-iodo-2-(*p*-tolylsulfinyl)toluene (*S*)-**3**.



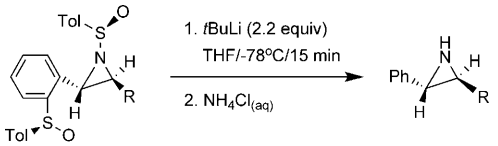
Entry	(*R*)-Imine/R^1	R^2	Yield [%][a] *trans*-**7**	*trans*-**7**/*cis*-**6**[b]	*de* [%][b] *trans*-**7**/*cis*-**6**
1	**4a**/*p*-Tol		89	96:4	>98	–
2	**4b**/*p*-Tol		88	>98:2	>98	–
3	**4c**/*p*-Tol		61[c]	65:35	33	>98
4	**4d**/*p*-Tol		83	87:13	>98	>98
5	**4e**/*p*-Tol		94	97:3	>98	–
6	**4f**/*p*-Tol		88	96:4	>98	–
7	**4g**/*p*-Tol		90	>98:2	>98	–
8	**4h**/*p*-Tol		90	>98:2	>98	–
9	**4i**/*p*-Tol		82	97:3	>98	–
10	**4j**/*p*-Tol		59	72:28	>98	42
11	**4k**/*p*-Tol		67	80:20	>98	10
12	**4l**/*t*Bu		72	85:15	>98	>98
13	**4m**/*t*Bu		79	90:10	>98	>98

[a] Determined by ^{1}H NMR spectroscopy from the crude reaction. [b] Yield of isolated product. [c] Calculated from the ratios (2*S*,3*S*)-**7**/*trans*-(2*R*,3*R*)-**7** or *cis*-(2*R*,3*R*)-**6**/*cis*-(2*R*,3*S*)-**6**, measured by ^{1}H NMR spectroscopy. The second isomer is not detected in the crude reactions for those cases for which the *de* is higher than 98%.

minute, at −78 °C, and aziridines *trans*-**7** were obtained as major or exclusive compounds in high yields and with total facial selectivity over a range of substrates. The only exception was the reaction starting from the imine **4c**, containing a strong electron-withdrawing group, which was produced with a low diastereomeric *trans*/*cis* ratio and with 33 % *de* for the *trans* isomer (Table 2, entry 3). The reactions with arylimines **4a**, **4b**, and **4e** (containing neutral, electron-donating or bulky groups) and heteroarylimine **4f** evolved with an almost complete *trans* selectivity (*trans*/*cis* ratio ranges from 96:4 to >98:2) in excellent isolated yields (88–94 %) (entries 1, 2, 5 and 6). For arylimine **4d**, bearing the bulkier 2-bromophenyl group, the *trans*/*cis* ratio slightly decreased to 87:13, although a high isolated yield in the optically pure *trans*-**7d** could be achieved (entry 4). The aziridination procedure was also found to be successful for alkenylaldimines **4g–i**, furnishing the corresponding *trans*-aziridines **7g–i** as the exclusive (*trans*/*cis* >98:2; entries 7 and 8) or major (*trans*/*cis* 97:3; entry 9) diastereoisomers. The reactions with *N*-*p*-toluensulfinyl alkylimines **4j** and **4k** evolved in moderate *trans* selectivity and with low *de* for the *cis* isomers (entries 10 and 11). Fortunately, the use of the *N*-*tert*-butylsulfinylimines[24] **4l** and **4m** improved the *trans* selectivity and a complete facial selectivity was achieved for both isomers (entries 12 and 13). These results allow us to conclude that reactions of (*S*)-**3** with *N*-sulfinylaldimines provide one of the best so far reported methods to obtain optically pure *trans*-2,3-disubstituted aziridines.

The *cis* or *trans* stereochemistry assigned to aziridines **6** and **7**, respectively, was deduced from the vicinal coupling constants of the protons joined to C-2 and C-3. $^3J_{2,3}$ values for the *cis* isomers ranged between 6.8 and 7.8 Hz (dihedral angle ≈0°), whereas those for the *trans* isomers are much lower (3.6–4.4 Hz, dihedral angle ≈120°). The absolute configurations for compounds *cis*-**6a** and *trans*-**7a** were unequivocally established by X-ray diffraction studies. They allowed us to assign the *S* configuration to both ring carbon atoms at *trans*-**7a** and 2*R*,3*S* for *cis*-**6a**[25] (see the scheme in Table 2). The similar behaviour observed in all the aziridination reactions summarized in Table 2, all of them evolving with complete facial selectivity and excellent *trans*/*cis* diastereoselectivity, suggests that the absolute configuration for *trans*-aziridines **4b–m** is also 2*S*,3*S*.

Deprotection of the obtained disulfinylated compounds is required to provide NH-aziridines, which are valuable intermediates to a range of synthetically useful compounds.[26] At this point, it is important to note that there is not any one-step protocol able to synthesize NH-aziridines and most of the methods for the asymmetric synthesis of aziridines provide N-protected aziridines for which the substituents at the nitrogen atom are usually difficult to remove. In our case, simultaneous C- and N-desulfinylation of the disulfinylated aziridines **7** can be performed by reaction with 2.2 equivalents of *t*BuLi in good yields. We have checked the efficiency of this procedure in the case of compounds **7a**, **7b**, **7e** and **7h** (Scheme 4). The optical purity of the NH-aziridine **8h** was determined by HPLC with a Chiralcel OD-H column (98.5 % enantiomeric excess (*ee*)), which indicates that reaction conditions do not produce significant epimerisation at the starting material.



7a: R = Ph
7b: R = *p*-MeOC$_6$H$_4$
7e: R = 2-naphthyl
7h: R = (*E*)-PhCH=CH

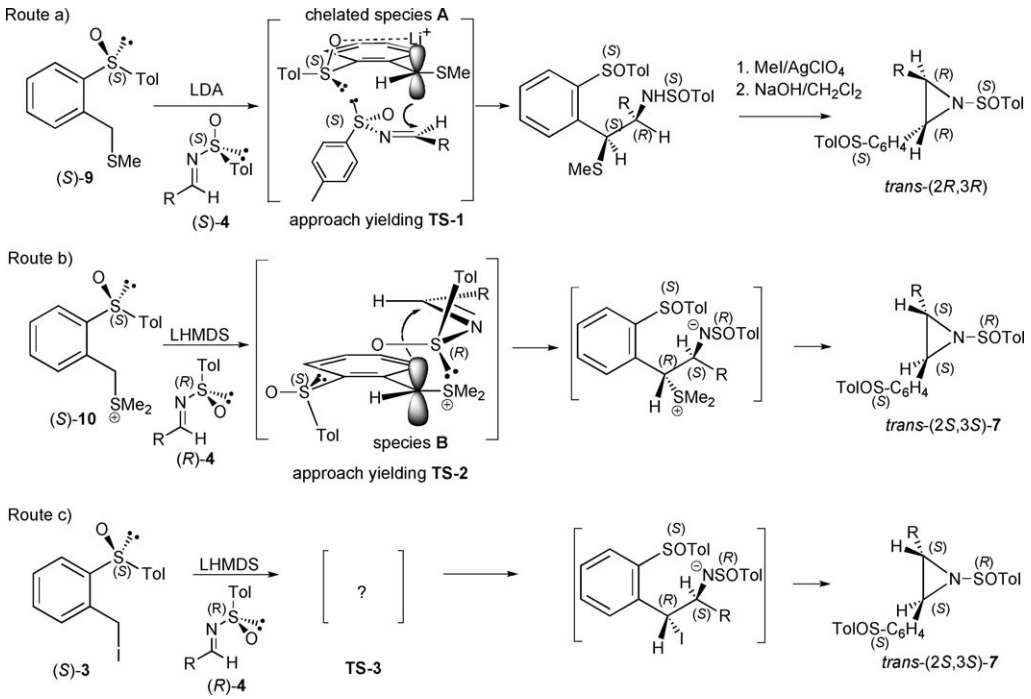
8a (75 %)
8b (67 %)
8e (75 %)
8h (70 %)

Scheme 4. C- and N-desulfinylation of aziridines *trans*-**7**.

To get a deeper understanding of the stereochemical results described herein it is necessary to compare them with those observed in previously studied reactions starting from α-methylsulfenyl- and α-dimethyl sulfonium benzyl carbanions, Li-(*S*)-**9** and Li-(*S*)-**10**, respectively (Scheme 5). In the first case, the matched pair is formed by the reagents with the same configuration at sulfur, (*S*)-**9** and (*S*)-**4**, and the obtained β-sulfanylamines[13a] were subsequently transformed into (2*R*,3*R*)-aziridines,[27] by following the synthetic sequence showed in Scheme 5, route a. These results could be explained by assuming the reaction proceeded through the chelated species **A**, with the lithium intramolecularly stabilized by the sulfinyl oxygen atom, and with the sulfinyl oxygen atom at the sulfinylimine adopting its most stable (s)-*cis* conformation around the C=N bond (both hypothesis were supported by theoretical calculations).[13c] Accordingly, **TS-1** must be the presumably most stable transition state, because it would result from the *transoid* approach of both reagents in which electronic repulsion between N and S atoms is minimized, to their respectively less-hindered faces.

The second strategy previously used for synthesizing aziridines involves the reaction of the ylide derived from (*S*)-**10** with (*R*)-**4**[28] (Scheme 5, route b). In this case, the matched pair is formed by reagents of the opposite configuration at their sulfinyl centres and (2*S*,3*S*)-aziridines are obtained as the major products. The stereochemical model so far proposed to explain these results is based on the assumption that the ylide reacts through the planar free carbanion **B**, stabilized by the electron-withdrawing $[SMe_2]^+$ group and displaying the sulfinyl oxygen atom far from the carbanionic carbon atom. According to theoretical calculations,[28] **TS-2** is now the most stable transition state because it would result from the *cisoid* approach of both reagents (strongly favoured by electrostatic attractions between N and S^+) to their respectively less-hindered faces.

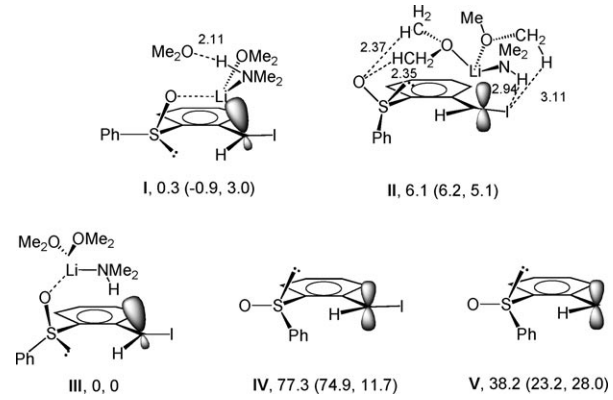
The results obtained in this paper (Scheme 5, route c) starting from iododerivative (*S*)-**3** are very similar to those observed from sulfonium ylides, because the matched pair is formed by reagents with different configurations at their sulfur atoms and reactions afford almost exclusively (2*S*,3*S*)-**7** aziridines. However, it is not easy to assume a similar mechanism for both transformations because the halogen would not be able to stabilize a free carbanion similar to



Scheme 5. Conversion of Li-(*S*)-**9**, Li-(*S*)-**10**, (*S*)-**3** into the corresponding (2*R*,3*R*) or (2*S*,3*S*)-aziridines via TSs **TS-1**, **TS-2** and **TS-3**.

that of **B** (due to electronic repulsion of the lone electron pairs at the halogen and carbanionic carbon atoms) nor the *cisoid* approach of the reagents yielding a transition state similar to **TS-2** (presumably unstabilized by the dipolar repulsion of the C-I and C=N bonds). Thus, the formation of intermediates different to both **A** and **B** species, maybe carbenoids, emerged as one possible explanation of the observed stereochemical results.

To understand the nature of the intermediates involved in these reactions, the possible structures of the species resulting in the reaction of (*S*)-**3** with LHMDS were studied theoretically at the DFT (B3LYP)[29] level by using the Gaussian 03 program.[30,31] The most stable structures found for model carbanion–Li^+ complexes and free carbanions are shown in Scheme 6. Dimethyl ether and dimethylamine were used as simplified models for solvent and base, respectively, and have been included as ligands for the lithium atom. The tolyl group has also been simplified as a phenyl one. Two stable structures have been found for carbanion–Li^+ complexes. Chelated species **I**, with the sulfinyl oxygen and carbanionic carbon atoms coordinated to the lithium atom, is more stable than **II**, for which the sulfinyl oxygen atom has been shifted by a molecule of ether (Scheme 6).[32] Structure **I** is identical to chelated species **A** depicted in Scheme 5, and considered as the most reactive intermediate in the case of benzylcarbanions joined to SMe, OMe or alkyl groups. The lower stability of **II** could be a consequence of the higher association ability of the sulfinyl oxygen atom to the metal. Considering the question about the "carbenoid character" of **II**, there is only a slight elongation[1b] of the C–I bond (2.24 Å) relative to the nonlithiated species (2.22 Å), which suggests that the carbanion character

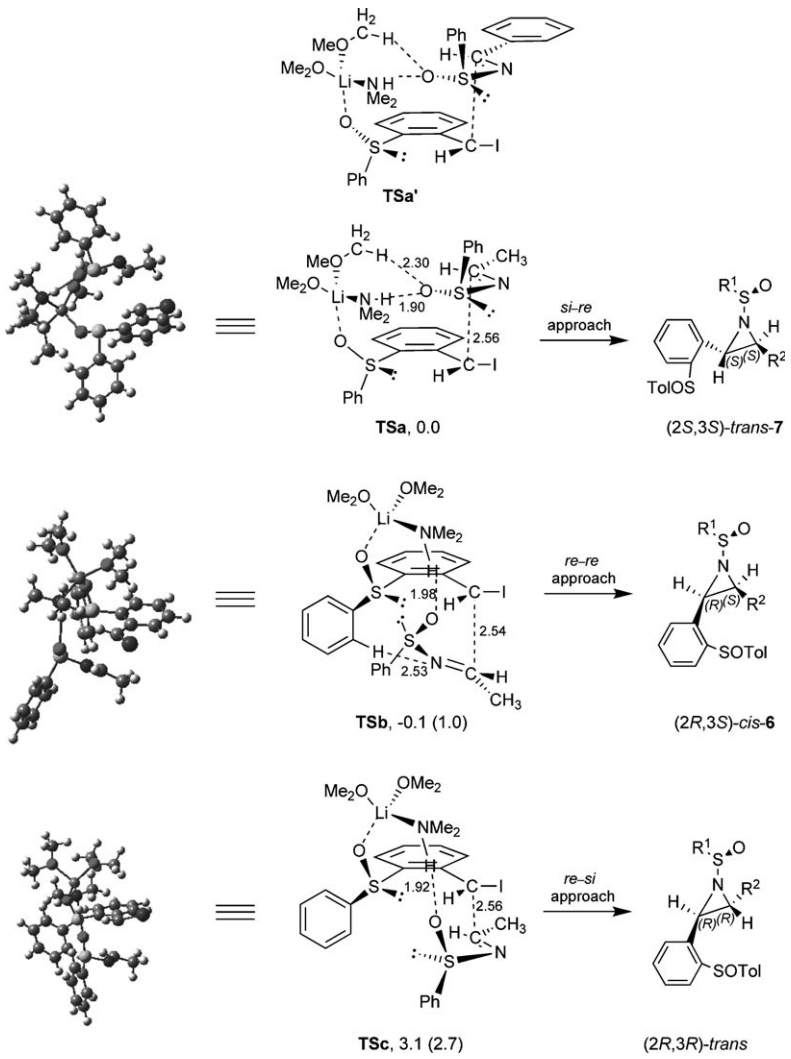


Scheme 6. Molecular structures, representative distances of the hydrogen bonds [Å], and energies [kcal mol^{-1}] of possible carbanionic species. The first value indicates the relative energy, with ZPE correction included, of I, II, IV (+Li(NHMe$_2$)(OMe$_2$)$_3$–OMe$_2$) and V (+Li(NHMe$_2$)(OMe$_2$)$_2$I) with respect to III, which is considered as the most stable. Free-energy correction is indicated in brackets, first in vacuo and second in THF (mimicked by IEFPCM).

seems to be preferred probably due to the high delocalization of the charge into the benzyl system. The search of other structures exhibiting a clear carbenoid character has been unsuccessful.

Another two structures have been considered in which the carbanionic carbon atom is not directly joined to the metal. The first one, **III**, is a free carbanion stabilized by a hydrogen bond with the dimethylamine ligand. This type of complex would probably be the first formed after the deprotonation step and, therefore, it could be considered as a precursor of the species **I**, in which the carbanion acts as a

ligand of the metal, shifting one molecule of Me_2O. The comparison of the calculated energy values for **I** and **III** indicates that the former is slightly more stable in a vacuum, but the latter one is the most stable (by 3 kcal mol^{-1}) when considering the effect of the solvent. We have also studied the free carbanion structure **IV**, for which the Li^+ is not stabilizing the carbanion, because a similar structure was invoked to satisfactorily explain the selectivity observed in the reaction of sulfinylimines (*R*)-**4** with the dimethylsulfonium analogue.[28] However in the present case, free carbanion **IV** is considerably less stable than the most favoured structures (**I** or **III**), even when solvent effects are considered (11.7 kcal mol^{-1}), thus contrasting with the small difference existing (2.8 kcal mol^{-1}) for similar species in the case of the dimethylsulfonium analogue.[28] Finally, we have also studied the energy corresponding to a carbene structure **V**, but it is also much less stable than all the Li^+-stabilized complexes previously considered.



Scheme 7. Molecular structures, representative distances [Å] and energies [kcal mol^{-1}] of possible transition states between model anion III and model (*E*)-*N*-phenylsulfinylimine derived from acetaldehyde that would yield *trans*-**7** (**TSa**) and *cis*-**6** (**TSb**). The first value indicates the relative energy, with ZPE correction included. Free-energy correction is indicated in brackets

Looking at the two most stable structures, **I** and **III**, the metal with its ligands are oriented toward the *si* face of the benzylic carbanion, thus imposing serious steric interactions in the approach of the electrophiles to that face. However, the experimental results indicate that the major *trans*-aziridines **7** result in the approach of the electrophile to that face. This fact suggests a complex situation also involving another type of interaction that is different from the steric ones, which would be only understandable by studying the relative stability of the transition states leading to the four possible diastereoisomers, that is, *re–re*, *re–si*, *si–re* and *si–si* approaches of the carbanion and imine reagents. We have been unsuccessful in the search of the transitions states starting from **I**, but some of them could be localized by starting from **III**. Scheme 7 shows the TSs found in the reaction of the complex **III** with the (*E*)-*N*-phenylsulfinylimine derived from acetaldehyde[33] (as the simplest imine).[34]

In all these TSs the presence of stabilizing interactions (hydrogen bonds) between the model imine and the ligands of the metal is essential. TSs without these interactions or with sulfinyl imine coordinated to the metal were not found. The three TSs found (see Scheme 7) seem to derive from the initial formation of a hydrogen bond between the sulfinyl oxygen atom at sulfinamide and the aminic hydrogen atom that was bonded to the carbanionic centre in **III**. After this interchange of acceptor in the hydrogen bond of the N–H (not unexpected on the basis of the high ability of the sulfinyl oxygen atom to form this type of bond) the approach of the imine to the upper face of the carbanion (*si–re* approach, Scheme 7) produces **TSa** that will evolve into *trans*-(2*S*,3*S*)-**7**. In this transition state, there are no significant steric restrictions, the sulfinyl oxygen atom in the imine adopts its most stable (s)-*cis* conformation and the groups around the incipient C–C bond show a slightly distorted *gauche* conformation (N-C-C-I = −68.3°). When the attack of the imine bonded to the aminic hydrogen atom takes place to the bottom face of the carbanion, two transition states, **TSb** and **TSc** (resulting from the *re–re* and *re–si* ap-

proaches, respectively, Scheme 7), were found. In **TSb**, which evolves into the *cis*-(2*R*,3*S*)-**6**, the imine also adopts the (s)-*cis* conformation and the groups around the newly formed C–C bond show an almost antiperiplanar arrangement (N-C-C-I = +161.3°), which will probably be favoured with respect to the *gauche* one by the low dipolar repulsion of the C–N and C–I bonds. Additionally, it is stabilized by a hydrogen bond between the iminic nitrogen atom and one of the protons of the aryl group (d = 2.53 Å). These two factors would be able to explain the small difference in energy between **TSa** and **TSb** calculated for *N*-phenyl methylideneimine, despite the twisted arrangement adopted by the reagents to reach **TSb**. The low *trans*/*cis* selectivity experimentally observed for alkyl imines (72:28 ratio; Table 2, entry 10) agrees with the similar energy calculated for **TSa** and **TSb**. When the PhSO group at the imines is substituted by the *t*BuSO one, it is expected that the stability of **TSa** would be scarcely affected, whereas that of **TSb** would decrease on steric grounds (*t*Bu/Ph interaction would affect the hydrogen bond N···H–Ar, see Scheme 7), thus explaining the higher selectivity observed for *tert*-butylsulfinylimines (Table 2, entries 12 and 13). On the other hand, the angles formed by the planes containing the imine group ($N–C_{iminic}–Me$) and the carbanion ($C_{Bn}–C_{ipso}–C_{ortho}$) are different for **TSa** (17.7°) and **TSb** (44.8°). These differences could explain the complete facial selectivity observed in reactions of the arylimines (Table 2), by assuming that **TSa′** (Scheme 7) is stabilized by π-stacking interactions (these interactions also explained the results found in reactions with *N*-aryl derivatives of arylimines[4]), whereas it would not possible for **TSb** because the relative arrangement of both aryl groups is not appropriated. Finally, the *re–si* approach of the imine to the bottom face of the carbanion generates **TSc**, precursor of the *trans*-(2*R*,3*R*)-aziridines. This lack of the stabilizing hydrogen bond of the iminic nitrogen with the aromatic hydrogen atom in the transition state determines that the sulfinyl oxygen atom at the imine does not adopt the most stable (S)-*cis* arrangement and the groups around the incipient C–C bond show a slightly distorted *gauche* conformation (N-C-C-I = +68.0°). All these facts could be responsible for the lower stability of **TSc** with respect to **TSa** or **TSb** (Scheme 7) determining the absence of the (2*R*,3*R*)-aziridines in the reaction mixtures. Finally, we were unable to find the transition state corresponding to the *si–si* approach of the imine to the upper face of the carbanion, affording the *cis*-(2*S*,3*R*)-aziridines. These compounds were only experimentally observed in the case of alkyl imines (Table 2, entries 10 and 11).

Conclusion

2-(*p*-Tolylsulfinyl)benzyl iodide (*S*)-**3** is an efficient precursor of enantiomerically pure *trans*-2-substituted-3-phenyl aziridines, with aromatic, heteroaromatic, α,β-unsaturated and alkyl *N*-sulfinylimines acting as eletrophiles at these aziridination processes. The excellent facial selectivity, high *trans* selectivity and good isolated yields, make this reaction potentially useful in organic synthesis. Theoretical calculations support the carbanionic structure of the intermediates despite some experimental results that suggested that carbenoid species could be involved. It has been possible to find the transition states providing aziridines *trans*-(2*S*,3*S*)-**7**, obtained as the major or exclusive isomers in these reactions, and aziridines *cis*-(2*R*,3*S*)-**6**, obtained as the minor ones in some reactions. The structural differences between these transition states allow us to rationalize their energetic differences, which in their turn justify the observed stereoselectivity in these reactions.

Experimental Section

General methods: Dry solvents and liquid reagents were distilled under argon just prior to use. THF was distilled from Na/benzophenone ketyl, CH_2Cl_2 and diisopropylamine were dried over P_2O_5 and KOH, respectively. NaHMDS (1.0 M solution in THF), *n*BuLi and *t*BuLi (2.5 and 1.5 M solution in hexanes, respectively) were purchased from commercial suppliers and used as received. All reactions were carried out in flame- or oven-dried glassware under an inert Ar atmosphere. Reactions were monitored by TLC on commercially available precoated plates (Silica Gel 60 F_{254}). Flash column chromatography was performed by using by Silica Gel 60 (230–400 mesh) and a SCX column. NMR spectra were obtained in $CDCl_3$ solutions at 300 and 75 MHz for ^1H and ^{13}C NMR spectroscopy, respectively, (chemical shifts (δ) are given in ppm), and all coupling constants, *J*, are given in Hz. Diastereoisomeric ratios were determined from the integration of well-separated signals in the ^1H NMR spectra of the crude reaction mixtures (H-C2 and H-C3 for *cis*/*trans* compounds). Mass spectra were measured by electron impact (EI, 70 eV) or FAB. Melting points were measured in open capillary tubes and they are uncorrected. Characterization data of compounds **6a**, **6c–f**, **6i–m**, **7b-f** and **7j** and NMR spectra of compounds **6a**, **6c–f**, **6i–m**, **7g–i**, **7k–m**, **8b**, **8e** and **8h** as well X-ray structure and refinement details of compounds **6a** and **7a** can be found in the Supporting Information.

General procedure for the reactions summarized in Table 2: NaHMDS (1.2 equiv) at −78 °C was added dropwise to a stirred solution of (*S*)-α-iodo-2-(*p*-tolylsulfinyl)toluene (0.15 mmol, 1.0 equiv) and *N*-sulfinylimine ((*R*)-**4a–m**, 0.15 mmol, 1.0 equiv) in THF (3 mL). When the reaction was completed (one minute), the mixture was hydrolyzed at that temperature with saturated aqueous NH_4Cl solution (1 mL) and extracted with CH_2Cl_2 (3 × 5 mL,). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography.

trans-*(2*S,3*S)-2-Phenyl-3-[(*S)-2-(*p-*toluenesulfinyl)phenyl]-1-[(*R)-(*p-*toluene sulfinyl)]aziridine (**7a**)*: Eluent for chromatography: hexane/Et_2O 1:4; yield: 89 %; white solid; m.p. 118–119 °C (hexane/Et_2O); $[\alpha]_D^{20}$ = −145.4 (c = 0.9 in $CHCl_3$) (lit.[28] = −145.5 (c = 0.6 in $CHCl_3$)); spectroscopic data of compound **7a** are coincident with those previously reported: ^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (dd, 1H, J = 7.8, 1.1 Hz), 7.56, 7.41, 7.24, 7.10 (two AA′BB′ systems, 8H), 7.51 (dd, 1H, J = 7.8, 1.1 Hz), 7.38–7.28 (m, 7H), 4.35, 3.75 (2d, 2H, J = 4.3 Hz), 2.37, 2.29 ppm (2s, 6H).

trans-*(2*S,3*S)-2-Propenyl-3-[(*S)-2-(*p-*toluenesulfinyl)phenyl]-1-[(*R)-(*p-*toluene sulfinyl)]aziridine (**7g**)*: Eluent for chromatography: hexane/Et_2O 1:3; yield: 90 %; yellow syrup; $[\alpha]_D^{20}$ = −236.0 (c = 0.3 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (dd, 1H, J = 7.9, 1.2 Hz), 7.59, 7.42, 7.23, 7.17 (two AA′BB′ systems, 8H), 7.44–7.42 (m, 1H), 7.27–7.20 (m, 1H), 6.90 (d, 1H, J = 7.7 Hz), 4.67–4.63 (m, 2H), 4.12 (d, 2H, J = 3.8 Hz), 2.66 (dd, 1H, J = 3.8, 1.3 Hz), 2.36, 2.34 (2s, 6H), 1.77 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.5, 142.4, 141.8, 141.7, 141.5, 134.4, 134.2, 130.9, 129.9, 129.5, 128.4, 126.3, 125.6, 124.6, 124.5, 123.8, 52.8, 33.4, 21.4,

18.1 ppm; HRMS: *m/z*: calcd for $C_{18}H_{18}NOS$: 296.1109 [M^+−SOTol]; found: 296.1112.

trans-*(2S,3S)-2-Cinnamyl-3-[(S)-2-(*p*-toluenesulfinyl)phenyl]-1-[(R)-(*p*-toluene sulfinyl)]aziridine (**7h**)*: Eluent for chromatography: hexane/Et_2O 1:3; yield: 90%; yellow solid; m.p. 68–69°C (hexane/Et_2O); $[\alpha]_D^{20}$ = −570.0 (*c* = 0.1 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (dd, 1H, *J* = 7.0, 0.8 Hz), 7.63, 7.38, 7.25, 7.01 (two AA′BB′ systems, 8H), 7.48–7.24 (m, 7H), 6.32 (dd, 1H, *J* = 15.7, 8.8 Hz), 6.31 (d, 1H, *J* = 8.8 Hz), 4.18 (d, 2H, *J* = 3.7 Hz), 2.75 (dd, 1H, *J* = 8.8, 3.7, 1.3 Hz), 2.37, 2.07 ppm (2s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.0, 142.3, 142.2, 141.8, 141.1, 135.7, 133.9, 136.8, 130.9, 130.1, 129.6, 128.6, 128.4, 126.7, 126.5, 125.4, 124.6, 123.8, 122.3, 53.4, 34.0, 21.4, 21.1 ppm; HRMS: *m/z*: calcd for $C_{23}H_{20}NOS$: 358.1266 [M^+−SOTol]; found: 358.1259.

trans-*(2S,3S)-2-(1-Methylcinnamyl)-3-[(S)-2-(*p*-toluenesulfinyl)phenyl]-1-[(R)-(*p*-toluenesulfinyl)]aziridine (**7i**)*: Eluent for chromatography: hexane/Et_2O 1:3; yield: 82%; yellow syrup (compound **7i** is particularly unstable in solution); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (dd, 1H, *J* = 7.9, 1.2 Hz), 7.61, 7.53, 7.30, 7.25 (two AA′BB′ systems), 7.52–7.40 (m, 3H), 7.35–6.90 (m, 5H), 6.53 (s, 1H), 4.04, 3.67 (2d, 2H, *J* = 4.5 Hz), 2.39, 2.34 (2s, 6H), 1.83 ppm (s, 3H).

trans-*(2S,3S)-2-Isopropyl-3-[(S)-2-(*p*-toluenesulfinyl)phenyl]-1-[(R)-(*p*-toluene sulfinyl)]aziridine (**7k**)*: Eluent for chromatography: hexane/Et_2O 1:2; yield: 67%; white syrup; $[\alpha]_D^{20}$ = −200.2 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.89 (dd, 1H, *J* = 7.7, 0.8 Hz), 7.54, 7.47, 7.24, 7.19 (two AA′BB′ systems, 8H), 7.42, 7.32 (2dt, 2H, *J* = 7.6, 1.0 Hz), 7.06 (d, 1H, *J* = 7.5 Hz), 3.82 (d, 1H, *J* = 3.8 Hz), 2.36, 2.34 (2s, 6H), 2.61 (dd, 1H, *J* = 8.8, 3.8 Hz), 2.17–1.90 (m, 1H), 1.08, 0.74 ppm (2d, 6H, *J* = 6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.0, 142.6, 141.7, 141.6, 141.4, 134.9, 131.1, 130.0, 129.5, 129.4, 128.7, 126.1, 125.1, 124.7, 49.4, 30.3, 28.3, 21.3, 21.1, 20.4 ppm; HRMS: *m/z*: calcd for $C_{18}H_{20}NO_2S_2$: 346.0935 [M^+ −SOTol]; found: 346.0942.

trans-*(2S,3S)-2-Butyl-3-[(S)-2-(*p*-toluenesulfinyl)phenyl]-1-[(R)-(*tert*-butane sulfinyl)]aziridine (**7l**)*: Eluent for chromatography: hexane/Et_2O 1:2.5; yield: 72%; colourless oil; $[\alpha]_D^{20}$ = −182.5 (*c* = 0.2 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.55–7.42 (m, 2H), 7.49, 7.23 (AA′BB′ system, 4H), 7.15 (d, 1H, *J* = 7.5 Hz), 3.66 (d, 1H, *J* = 3.9 Hz), 2.35 (s, 3H), 2.21–2.19 (m, 1H), 1.74–0.87 (3m, 6H), 1.13 (s, 9H), 0.81 ppm (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.3, 142.1, 142.0, 135.7, 131.1, 130.1, 128.4, 126.6, 125.4, 124.1, 57.3, 49.6, 32.1, 29.8, 27.5, 22.4, 22.6, 21.4, 13.8 ppm; HRMS: *m/z*: calcd for $C_{19}H_{22}NO_2S_2$: 360.1092 [M^+−*t*Bu]; found: 360.1093.

trans-*(2S,3S)-2-Isopropyl-3-[(S)-2-(*p*-toluenesulfinyl)phenyl]-1-[(R)-(*tert*-butane sulfinyl)]aziridine (**7m**)*: Eluent for chromatography: hexane/Et_2O 1:2.5; yield: 79%; white syrup; $[\alpha]_D^{20}$ = −198.8 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.05 (d, 1H, *J* = 7.3 Hz), 7.54–7.44 (m, 2H), 7.49, 7.23 (AA′BB′ system, 4H), 7.12 (d, 1H, *J* = 7.0 Hz), 3.74 (d, 1H, *J* = 3.6 Hz), 2.34 (s, 3H), 2.17 (dd, 1H, *J* = 9.7, 3.7 Hz), 1.90–1.83 (m, 1H), 1.14, 0.46 (2d, 6H, *J* = 6.5 Hz), 1.10 ppm (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.4, 142.0, 141.8, 136.3, 131.3, 130.2, 128.5, 126.6, 125.7, 124.8, 57.5, 56.0, 31.4, 27.7, 21.3, 21.1, 20.6 ppm; HRMS: *m/z*: calcd for $C_{18}H_{20}NO_2S_2$: 346.0935 [M^+−*t*Bu]; found: 346.0942.

Representative procedure for total desulfinylation of *N*-sulfinyl aziridines: *t*BuLi (0.18 mL, 0.27 mmol, 1.5 M in hexane, 2.2 equiv) was added to a stirred solution of **7a**, **7b**, **7e** and **7h** (0.12 mmol) in THF (2 mL). When the reaction was completed (15 min), the mixture was hydrolyzed with saturated aqueous NH_4Cl (1 mL) and extracted with CH_2Cl_2 (3× 3 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography.

*(−)-(2S,3S)-2,3-Diphenylaziridine (**8a**)*: Eluent for SCX column chromatography NH_3/methanol (7M); yield: 75%; colourless syrup; $[\alpha]_D^{20}$ = −320.0 (*c* = 0.5 in $CHCl_3$) (lit.[35] = −328.8 (*c* = 1.25 in $CHCl_3$)); spectroscopic data of compound **8a** are coincident with those previously reported: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.29 (m, 10H), 3.12 (s, 2H), 1.70 ppm (br s, 1H).

*(+)-(2S,3S)-2-(*p*-Methoxyphenyl)-3-phenylaziridine (**8b**)*: Eluent for chromatography hexane/Et_2O 1:3; yield: 67%; white solid; m.p. 79–80°C; $[\alpha]_D^{20}$ = +251.2 (*c* = 0.2 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.27 (m, 5H), 7.21, 6.89 (AA′BB′ system, 4H), 3.82 (s, 3H), 3.07 (br s, 2H), 1.50 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 139.7, 131.7, 128.6, 127.2, 126.6, 125.4, 114.0, 55.3, 43.3 ppm; HRMS: *m/z*: calcd for $C_{15}H_{15}NO$: 225.1154; found: 225.1145.

*(−)-(2S,3S)-2-(2-Naphthyl)-3-phenylaziridine (**8e**)*: Eluent for chromatography hexane/Et_2O 1:1; yield: 75%; white solid; m.p. 74–75°C; $[\alpha]_D^{20}$ = −160.3 (*c* = 0.3 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.78 (m, 4H), 7.52, 7.27 (m, 8H), 3.30, 3.20 (2s, 2H), 1.61 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6, 137.0, 133.3, 132.8, 128.7, 128.4, 127.7, 127.6, 127.4, 126.3, 125.7 125.5, 124.4, 123.4 ppm (C-2 and C-3 are missing); HRMS: *m/z*: calcd for $C_{18}H_{15}N$: 245.1205; found: 245.1193; HPLC (98.5 *ee*, Daicel Chiralcel OD-H, hexane/IPA 90:10, 0.7 mL min^{-1}, 254 nm, 25°C): t_R = 39 min (2*S*,3*S*).

*(−)-(2S,3S)-2-Cinnamyl-3-phenylaziridine (**8h**)*: Eluent for chromatography hexane/Et_2O 1:2.5; yield: 70%; white syrup; $[\alpha]_D^{20}$ = −104.7 (*c* = 0.6 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 10H, 6.70 (d, 1H, *J* = 15.8 Hz), 5.92 (dd, 1H, *J* = 15.8, 7.7 Hz), 3.08 (s, 1H), 2.71 (d, 1H, *J* = 7.7 Hz), 1.60 ppm (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.3, 136.5, 131.8, 129.5, 128.6, 128.5, 127.6, 127.2, 126.1, 125.6 ppm (C-2 and C-3 are missing); HRMS: *m/z*: calcd for $C_{16}H_{15}N$: 221.1205; found: 221.1199.

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[1] For reviews, see: a) M. Braun, *Angew. Chem.* **1998**, *110*, 444–465; *Angew. Chem. Int. Ed.* **1998**, *37*, 430–451; b) G. Boche, C. W. Lohrenz, *Chem. Rev.* **2001**, *101*, 697–756; c) A. Basu, S. Thayumanavan, *Angew. Chem.* **2002**, *114*, 740–763; *Angew. Chem. Int. Ed.* **2002**, *41*, 716–738; d) M. Braun in *The Chemistry of Organolithium Compounds* (Eds.: Z. Rappoport, I. Marek), Wiley, New York, **2004**, Chapter 13, pp. 829–898.

[2] For leading and recent references, see: a) H. C. Stiasny, R. W. Hoffmann, *Chem. Eur. J.* **1995**, *1*, 619- 624; b) R. W. Hoffmann, H.-C. Stiasny, J. Krüger, *Tetrahedron* **1996**, *52*, 7421–7434; c) M. Shimizu, T. Hata, T. Hiyama, *Heterocycles* **2000**, *52*, 707–717; d) M. Shimizu, T. Fujimoto, X. Y. Liu, H. Minezaki, T. Hata, T. Hiyama, *Tetrahedron* **2003**, *59*, 9811–9823; e) P. R. Blakemore, S. P. Marsden, H. D. Vater, *Org. Lett.* **2006**, *8*, 773–776; f) B. A. Pearlman, S. R. Putt, J. A. Fleming, *J. Org. Chem.* **2006**, *71*, 5646–5677.

[3] For a review, see: A. De Meijere, M. Vonseebach, S. Zollner, S. I. Kozhushkov, V. N. Belov, R. Boese, T. Haumann, J. Benetbuchholz, D. S. Yufit, J. A. K. Howard, *Chem. Eur. J.* **2001**, *7*, 4021–4034, and references therein.

[4] For recent references, see: a) J. Kvícala, A. Pelter, *Collect. Czech. Chem. Commun.* **2001**, *66*, 1508–1520; b) H. Yanagisawa, K. Miura, M. Kitamura, K. Narasaka, K. Ando, *Helv. Chim. Acta* **2002**, *85*, 3130–3135; c) H. Yanagisawa, K. Miura, M. Kitamura, K. Narasaka, K. Ando, *Bull. Soc. Chim.* **2003**, *76*, 2009–2026; d) Y. H. Li, L. Lu, X. M. Zhao, *Org. Lett.* **2004**, *6*, 4467–4470; e) M. Braun, A. Hohmann, J. Rahematpura, C. Buhne, S. Grimme, *Chem. Eur. J.* **2004**, *10*, 4584–4593.

[5] For recent references, see: a) G. J. Gordon, T. Luker, M. W. Tuckett, R. J. Whitby, *Tetrahedron* **2000**, *56*, 2113–2129; b) S. Dixon, S. M. Fillery, A. Kasatkin, D. T. E. Norton, R. J. Whitby, *Tetrahedron* **2004**, *60*, 1401–1416.

[6] For recent references, see: a) H. Hermann, J. C. W. Lohrenz, A. Kuhn, G. Boche, *Tetrahedron* **2000**, *56*, 4109–4115; b) J. Kvicala, J. Stambasky, S. Bohm, O. Paleta, *J. Fluorine Chem.* **2002**, *113*, 147–

154; c) L. M. Pratt, B. Ramachandran, J. D. Xidos, C. J. Cramer, D. G. Truhlar, *J. Org. Chem.* **2002**, *67*, 7607–7612; d) L. M. Pratt, N. Van Nguyen, L. T. Le, *J. Org. Chem.* **2005**, *70*, 2294–2298; e) L. M. Pratt, L. T. Le, T. N. Truong, *J. Org. Chem.* **2005**, *70*, 8298–8302; f) F. M. Bickelhaupt, H. L. Hermann, G. Boche, *Angew. Chem.* **2006**, *118*, 838–841; *Angew. Chem. Int. Ed.* **2006**, *45*, 823–826; g) K. Ando, *J. Org. Chem.* **2006**, *71*, 1837–1850.

[7] G. L. Closs, R. A. Moss, *J. Am. Chem. Soc.* **1964**, *86*, 4042–4053.

[8] R. A. Olofson, C. M. Dougherty, *J. Am. Chem. Soc.* **1973**, *95*, 581–582.

[9] H. Andringa, Y. A. Heus-Kloos, L. Brandsma, *J. Organomet. Chem.* **1987**, *336*, C41-C43.

[10] a) S. Florio, L. Troisi, *J. Org. Chem.* **1996**, *61*, 4148–4150; b) V. Capriati, S. Florio, R. Luisi, *Synlett* **2005**, 1359–1369; c) V. Capriati, S. Florio, F. M. Perna, *Chem. Eur. J.* **2009**, *15*, 7958–7979.

[11] a) J. L. García Ruano, M. C. Carreño, M. A. Toledo, J. M. Aguirre, M. T. Aranda, J. Fischer, *Angew. Chem.* **2000**, *112*, 2848–2849; *Angew. Chem. Int. Ed.* **2000**, *39*, 2736–2737; b) J. L. García Ruano, J. Alemán, J. F. Soriano, *Org. Lett.* **2003**, *5*, 677–680; c) J. L. García Ruano, M. T. Aranda, J. M. Aguirre, *Tetrahedron* **2004**, *60*, 5383–5392; d) J. L. García Ruano, J. Alemán, J. A. Parra, *J. Am. Chem. Soc.* **2005**, *127*, 13048–13054; e) J. L. García Ruano, J. Aleman, B. Cid, *Synthesis* **2006**, 687–686; f) J. L. Garcia Ruano, V. Marcos, J. Alemán, *Angew. Chem.* **2008**, *120*, 6942–6945; *Angew. Chem. Int. Ed.* **2008**, *47*, 6836–6839; g) J. L. García Ruano, J. Alemán, S. Catalán, V. Marcos, S. Monteagudo, A. Parra, C. Pozo, S. Fustero, *Angew. Chem.* **2008**, *120*, 8059–8062; *Angew. Chem. Int. Ed.* **2008**, *47*, 7941–7944; h) J. L. García Ruano, A. Parra, V. Marcos, C. del Pozo, S. Catalán, S. Monteagudo, S. Fustero, *J. Am. Chem. Soc.* **2009**, *131*, 9432–9441; i) J. L. García Ruano, V. Marcos, J. Alemán, *Synthesis* **2009**, 3339–3349.

[12] J. L. García Ruano, J. Alemán, *Org. Lett.* **2003**, *5*, 4513–4516.

[13] a) Y. Arroyo, A. Meana, J. F. Rodríguez, M. Santos, M. A. Sanz-Tejedor, J. L. García Ruano, *J. Org. Chem.* **2005**, *70*, 3914–3920; b) Y. Arroyo, A. Meana, J. F. Rodríguez, M. Santos, M. A. Sanz-Tejedor, J. L. García Ruano, *J. Org. Chem.* **2007**, *72*, 1035–1038; c) Y. Arroyo, A. Meana, J. F. Rodríguez, M. A. Sanz-Tejedor, I. Alonso, J. L. García Ruano, *J. Org. Chem.* **2009**, *74*, 764–772.

[14] J. L. García Ruano J. Alemán, I. Alonso, A. Parra, V. Marcos, J. Aguirre, *Chem. Eur. J.* **2007**, *13*, 6179–6195.

[15] a) S. R. Rajski, R. M. Williams, *Chem. Rev.* **1998**, *98*, 2723–2796; b) T. J. Hodgkinson, T. J. M. Shipman, *Tetrahedron* **2001**, *57*, 4467–4488; c) S. Fürmeier, J. O. Metzger, *Eur. J. Org. Chem.* **2003**, 649–659.

[16] For reviews on this subject, see: a) D. Tanner, *Angew. Chem.* **1994**, *106*, 625–646; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 599–619; b) H. M. I. Osborn, J. Sweeney, *Tetrahedron: Asymmetry* **1997**, *8*, 1693–1715; c) A-H. Li, L.-X. Dai, V. K. Aggarwal, *Chem. Rev.* **1997**, *97*, 2341–2372; d) T. Ibuka, *Chem. Soc. Rev.* **1998**, *27*, 145–154; e) W. McCoull, F. A. Davis, *Synthesis* **2000**, 1347–1365; f) J. B. Sweeney, *Chem. Soc. Rev.* **2002**, *31*, 247–258; g) P. Müller, C. Fruit, *Chem. Rev.* **2003**, *103*, 2905–2919; h) X. E. Hu, *Tetrahedron* **2004**, *60*, 2701–2743; i) X. L. Hou, J. Wu, R. H. Fan, C. H. Ding, Z. B. Luo, X. L. Dai, *Synlett* **2006**, 181–193.

[17] J. L. García Ruano, J. Alemán, A. Parra, A. Alcudia, C. Maya, *J. Org. Chem.* **2009**, *74*, 2145–2152.

[18] Y. Arroyo, A. Meana, M. A. Sanz-Tejedor, J. L. Garcia Ruano, *Org. Lett.* **2008**, *10*, 2151–2154.

[19] J. L. García Ruano, J. Alemán, A. Padwa, *Org. Lett.* **2004**, *6*, 1757–1760.

[20] F. K. Davis, R. E. Reddy, J. M. Szewczyk, G. V. Reddy, P. S. Portonovo, H. Zhang, D. Fanelli, R. T. Reddy, P. Zhou, P. J. Carrol, *J. Org. Chem.* **1997**, *62*, 2555–2563.

[21] J. A. Ellman, D. A. Cogan, T. P. Tang, G. Liu, T. D. Owens, *J. Org. Chem.* **1999**, *64*, 1278–1284.

[22] The eliminative dimerization of lithium carbenoids to give alkenes has been extensively studied. In these processes, the 1,2-elimination of LiBr is very fast, see: a) B. J. Wakefield in *Organolithium Methods*, Academic Press, London, **1988**; b) V. Capriati, S. Florio, R. Luisi, M. T. Rochetti, *J. Org. Chem.* **2002**, *67*, 759–763; see also reference [1d].

[23] M. Julia, J. N. Verpaux, T. Zahneisen, *Synlett* **1990**, 769–770.

[24] It is noteworthy that reactions of *N*-*tert*-butylsulfinylimines derived from aromatic aldehydes with (*S*)-**3** afforded complex mixtures of compounds the complete analysis of which was not possible in our hands.

[25] CCDC-719589 contains the supplementary crystallographic data for this compound. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See also the Supporting Information.

[26] Recent reviews: a) Z. Zhijun, I. D. G. Watson, A. K. Yudin, *J. Am. Chem. Soc.* **2005**, *127*, 17516–17529; b) I. D. G. Watson, A. K. Yudin, *Acc. Chem. Res.* **2006**, *39*, 194–206. Others references, see: c) L. Gentilucci, Y. Grijzen, L. Thijs, B. Zwanenburg, *Tetrahedron Lett.* **1995**, *36*, 4665–4668; d) F. A. Davis, Y. Zhang, A. Rao, Z. Zhang, *Tetrahedron* **2001**, *57*, 6345–6352; e) F. A. Davis, J. Deng, Y. Zhang, R. C. Haltiwanger, *Tetrahedron* **2002**, *58*, 7135–7143; f) F. A. Davis, Y. Wu, H. Yan, W. McCoull, K. R. Prasad, *J. Org. Chem.* **2003**, *68*, 2410–2419.

[27] Y. Arroyo, A. Meana, J. F. Rodríguez, M. Santos, M. A. Sanz-Tejedor, J. L. García Ruano, *Tetrahedron* **2006**, *62*, 8525–8532.

[28] Y. Arroyo, A. Meana, J. F. Rodríguez, M. A. Sanz-Tejedor, I. Alonso, J. L. García Ruano, *J. Org. Chem.* **2009**, *74*, 4217–4224.

[29] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372–1377.

[30] Gaussian 03, Revision E.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Wallingford CT, **2004**.

[31] Geometries have been fully optimized by using the standard 6-31G(d) basis set for all the atoms except I: a) R. Ditchfield, W. J. Hehre, J. A. Pople, *J. Chem. Phys.* **1971**, *54*, 724–728; b) M. M. Francl, W. J. Petro, W. J. Hehre, J. S. Binkley, M. S. Gordon, D. J. DeFrees, J. A. Pople, *J. Chem. Phys.* **1982**, *77*, 3654–3665; the LANL2DZ basis set supplemented with an ad function of exponent 0.289 was used for iodine; c) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299–310; d) A. Höllwarth, M. Böhme, S. Dapprich, A. W. Ehlers, A. Gobbi, V. Jonas, K. F. Köhler, R. Stegmann, A. Veldkamp, G. Frenking, *Chem. Phys. Lett.* **1993**, *208*, 237–240; frequencies and zero-point energy (ZPE) were also computed at the same level of theory. Final energies have been obtained by using the more extended 6-311+G** basis set for all atoms except iodine: e) A. D. McLean, G. S. Chandler, *J. Chem. Phys.* **1980**, *72*, 5639–5648; f) R. Krishnan, J. S. Binkley, R. Seeger, J. A. Pople, *J. Chem. Phys.* **1980**, *72*, 650–654; For I, a basis set of similar quality (SDB-aug-cc-pVTZ) was used: g) J. M. L. Martin, A. Sundermann, *J. Chem. Phys.* **2001**, *114*, 3408–3420; relative free energies (in kcal mol^{-1}) were evaluated at the B3LYP/6-311+G** level with ZPE and entropy corrections evaluated at 298 K by using the frequencies previously calculated at the B3LYP/6-31G(d) level. Because of the importance of solvent effects, especially when charged species are involved, model structures **I**–**V** have also been optimized in a dielectric medium mimicking THF, by using the IEF-PCM model: h) E. Cancès, B. Mennucci, J. J. Tomasi, *J. Chem. Phys.* **1997**, *107*, 3032–

3041; i) M. Cossi, V. Barone, B. Mennucci, J. Tomasi, *Chem. Phys. Lett.* **1998**, *286*, 253–260; in the case of model transition states, this optimization including solvent effects was not possible.

[32] Complexes of type **I** and **II**, varying the N-Li-C-I dihedral angle, and type **III**, varying the C-S-O-Li dihedral angle, turned out to be less stable (see the Supporting Information for complexes **Ib**, **IIb** and **IIIb**).

[33] This imine was used as a model in our previous study of the reaction of dimethylsulfonium derivatives (see reference [28]). The rotamer with the sulfinyl oxygen atom in a (s)-*cis* arrangement with respect to the C=N bond was the most stable. However, solvent effects and stabilizing interactions within the transition states can dramatically modify the conformation around the N–S bond.

[34] Due to the complexity expected for the TSs formed from complex **III**, a preliminary study by starting from different relative orientations of model carbanion **IV** (Scheme 6) and the (*E*)-*N*-phenylsulfinylimine derived from acetaldehyde was carried out (see the Supporting Information for the corresponding structures of transition states **TS′a**–**d**). The difference in energy between **TS′a** and **TS′b** (2.0 kcal mol^{-1}) predicts a *trans*/*cis* ratio of 97:3, much higher than the 72:28 ratio experimentally observed with alkyl imines (Table 2, entry 10).

[35] B. B. Lohray, J. R. Ahujas, *J. Chem. Soc. Chem. Commun.* **1991**, 95–97.

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