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Nitrogen Stereodynamics and Complexation Phenomena as Key Factors in the Deprotonative Dynamic Resolution of Alkylideneaziridines: A Spectroscopic and Computational Study

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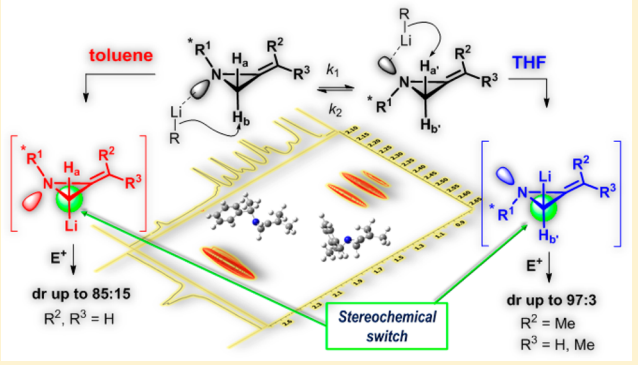
Supporting Information

ABSTRACT: The present work is aimed at shedding light on the origin of the stereoselectivity observed in the reactions of chiral heterosubstituted organolithiums, generated by lithiation of alkylideneaziridines. Factors such as the nitrogen inversion barrier, the stereochemistry at the nitrogen atom, the substitution pattern of the alkylideneaziridines, and the reaction conditions are taken into consideration. The interplay between nitrogen stereodynamics and complexation phenomena seems to be crucial in determining the stereochemical outcome of the lithiation/trapping sequence. The findings were rationalized by a synergistic use of NMR experiments, run on the lithiated intermediates, alongside computational data. It has been demonstrated that, in such systems, the stereochemistry-determining step is the deprotonation reaction, and a model based on a deprotonative dynamic resolution has been proposed. Such findings could find application in dynamic systems other than aziridines.



INTRODUCTION

Chiral organolithiums are well-established reactive intermediates that enable the creation of new C−C and C−X bonds with a high level of stereocontrol.[1] Most strategies for the generation of chiral organolithiums rely on deprotonation reactions of chiral starting materials using achiral lithiating agents.[2−4] If the generated organolithiums retain their stereochemical integrity, for the time scale of the reaction, enantioenriched products are formed upon subsequent reaction with electrophiles. A second approach uses racemic or prochiral substrates that are deprotonated stereoselectively with chiral bases or alkyllithiums in the presence of chiral ligands.[5] In this latter case, where an asymmetric deprotonation (AD) occurs, the enantioselectivity is dependent on the configurational stability of the chiral organolithium. In the presence of configurationally unstable chiral organolithiums, several strategies have been developed to induce stereocontrol in the reaction with electrophiles. In particular, dynamic resolutions under thermodynamic or kinetic control, reported, respectively, as dynamic thermodynamic resolution and as dynamic kinetic resolution, have proven to be effective.[6] More recently, new synthetic protocols, based on AD and dynamic kinetic resolution using a catalytic amount of precious chiral ligands, have been introduced.[7] Such modern approaches to chiral organolithiums, based on the seminal works by Gawley, Coldham, and O'Brien provide new ways of performing asymmetric synthesis by exploiting highly reactive intermediates. However, success requires a deep understanding of the structure−reactivity relationships. Our interest in molecular dynamics/reactivity relationships in nitrogenated small heterocycles[8,9] led us to observe that stereodifferentiation based on a stereoselective deprotonation of slowly equilibrating neutral substrates would complement the well-documented kinetic resolution of configurationally labile organolithiums.

In previous work, we demonstrated that, in aziridines, control of the pyramidal inversion affected the regioselectivity of the deprotonation (Scheme 1). In fact, two different lithiated intermediates could be regioselectively generated and, upon electrophilic quench, different products obtained (Scheme 1).[8d,10] It has been proposed that this regioselectivity switch depends on both nitrogen stereodynamics and complexation phenomena as well as on the reaction temperature.[11] In particular, higher temperatures favored the α-lithiation (removal of H_α), and lower temperatures favor remote lithiation (removal of H_r).

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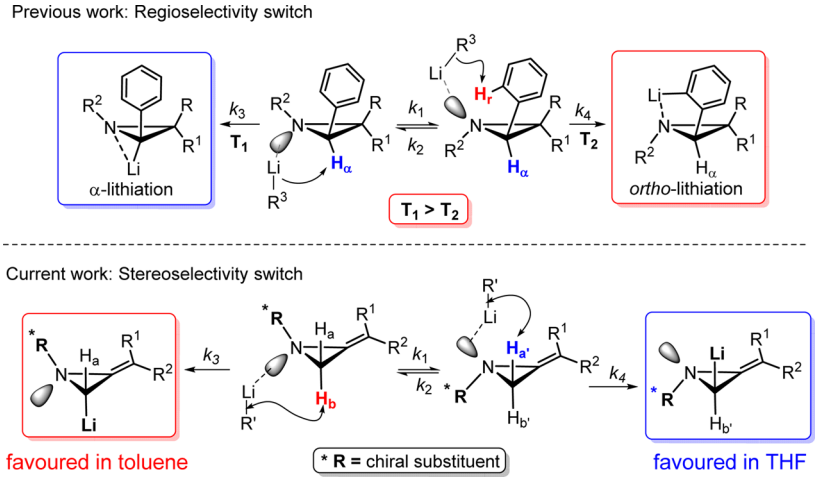
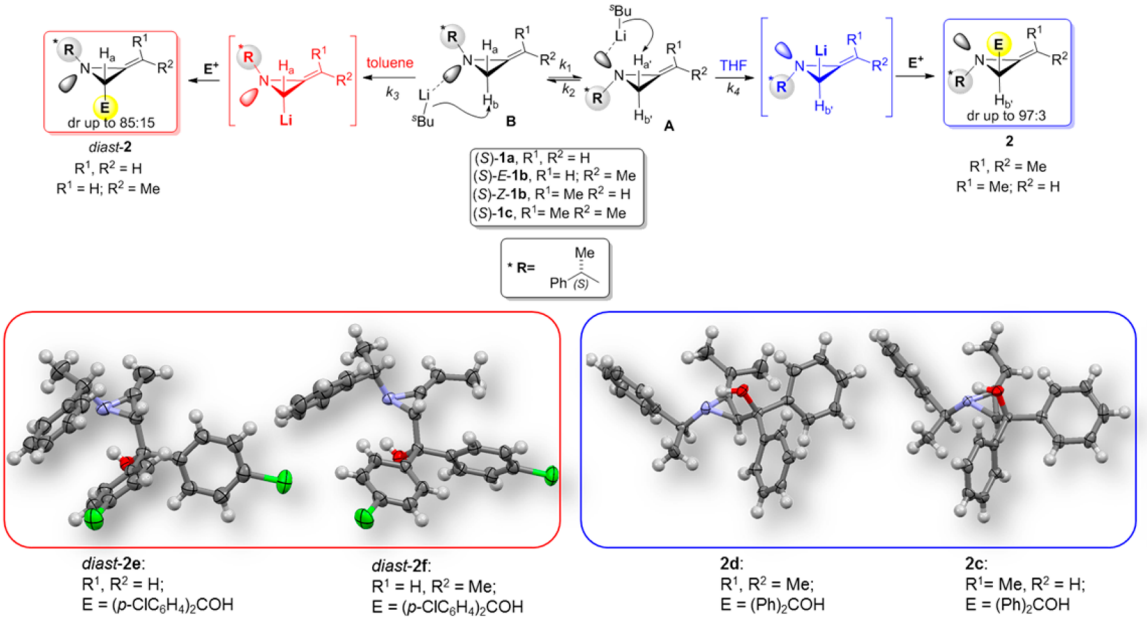
Scheme 1. Reactivity Switch Based on Nitrogen Stereodynamics



Scheme 2. Reactivity Switch Based on Nitrogen Stereodynamics (X-ray Structures at 50% Ellipsoid Probability)



In the case of alkylideneaziridines, which are considered useful synthons in organic synthesis,[12] a stereoselectivity switch has been observed as a consequence of a preference for removal of $H_{a'}$ over H_b (or vice versa) in the deprotonation step (Scheme 1).[13] Again, nitrogen stereodynamics and good lone pair availability for complexation are thought to account for the observed stereoselectivities. Here, we disclose additional structural and computational investigations on this system that support the proposed model and demonstrate that the stereoselectivity switch, observed in the deprotonation/electrophilic quench of alkylideneaziridines, represents an example of what we term deprotonative dynamic resolution (D-DR).

RESULTS AND DISCUSSION

Recently, we reported the lithiation/electrophilic trapping sequence of aziridines **1a−c** bearing a chiral alkyl group as the nitrogen substituent (Scheme 2).[13] These systems seemed to fit the model proposed in Scheme 1, and we invoked nitrogen stereodynamics and complexation phenomena to explain the stereochemical course of the reaction. As reported in Scheme 2, and according to reactivity and variable-temperature (VT) NMR evidence, two slowly equilibrating nitrogen invertomers (A and B) and configurationally stable lithiated intermediates are involved.[14] Assuming that, under the reaction conditions, k_1, $k_2 \gg k_3$ (or k_4) > k_4 (or k_3), the preferential removal of $H_{a'}$ or H_b followed by electrophilic quench leads, respectively, to adducts **2** or *diast*-**2** with some level of stereoselectivity. In particular, it has been found that the alkene substitution and the solvent of the reaction affected the stereoselectivity. High stereoselectivity was observed using THF as the solvent with aziridines (*S*)-*Z*-**1b** and (*S*)-**1c**, whereas (*S*)-**1a** and (*S*)-*E*-**1b** react with opposite stereoselectively in toluene and low to poor stereoselectivity in THF. Since our initial report, we have obtained further evidence confirming the stereochemical assignments. Through additional X-ray crystal structures for *diast*-**2e** and *diast*-**2f**, which were obtained by carrying out the reactions of lithiated (*S*)-**1a** and (*S*)-*E*-**1b** in toluene,[15] we confirmed the stereochemistry that was predicted by the model based on nitrogen stereodynamics. Interestingly, all of the available X-ray structures, including **2c**

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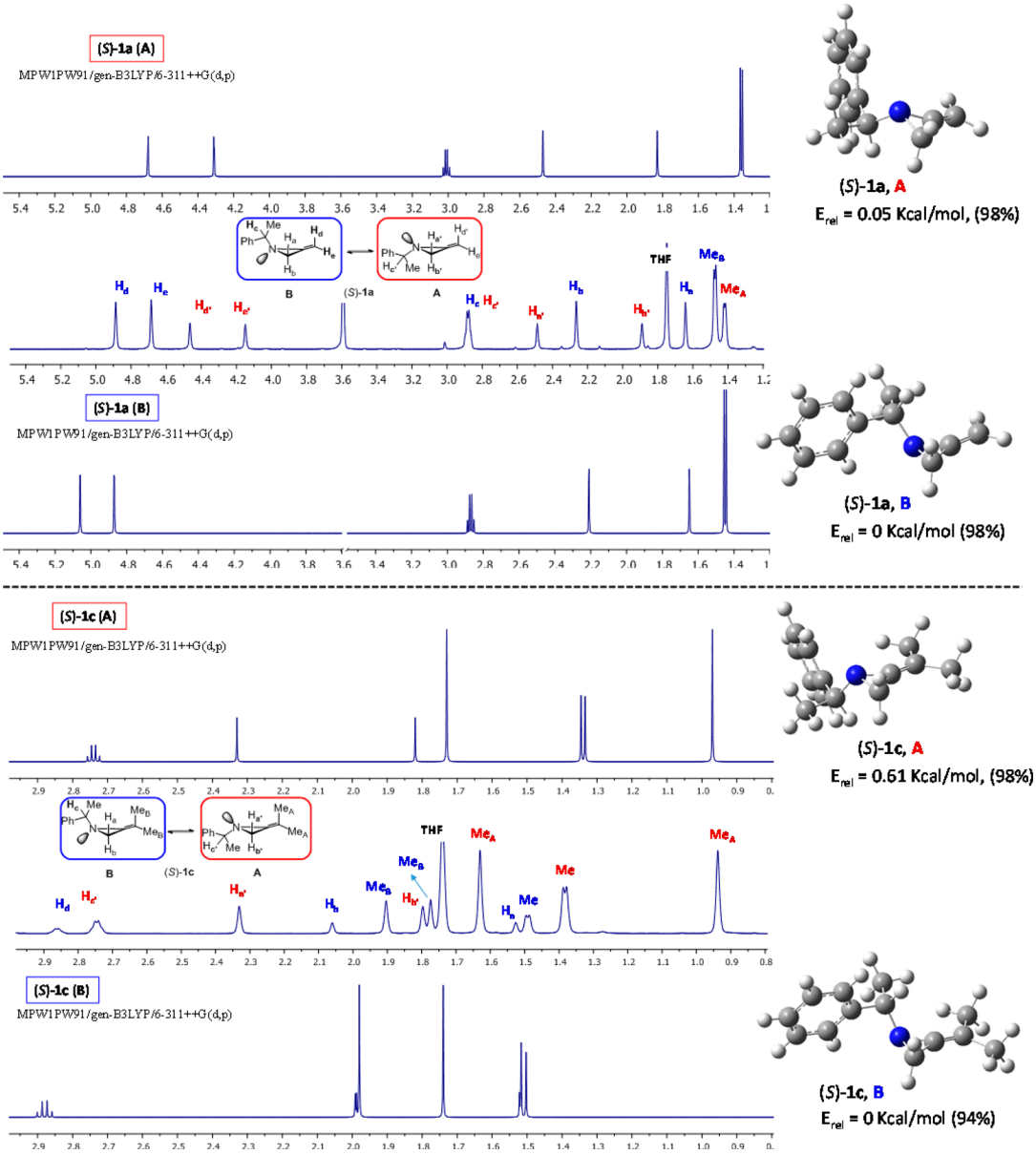

Figure 1. Comparison between calculated and experimental ^{1}H NMR spectra for N-invertomers of aziridines (*S*)-**1a** and (*S*)-**1c**. Simulated spectra for invertomer A are reported in the top part, and simulated spectra for invertomer B are reported in the bottom part. Measured spectra of aziridines (*S*)-**1a** and (*S*)-**1c**, recorded under slow exchange conditions (200 K, THF-d_8), are reported between them. On the left side, equilibrium geometries at the SMD-DFT-B3LYP/6-311++G(2d,p) level of theory for each invertomer of aziridines **1a** and **1c**, the relative total energy of the N-invertomers A and B, and the Boltzmann weighting factor of the lowest-energy conformers (c_i; see Supporting Information).

and **2d** reported previously,[16] reveal a cis arrangement between the nitrogen lone pair and the introduced electrophile. This is consistent with the idea that the proton syn to the nitrogen lone pair is preferentially removed in the lithiation step.[17]

Nevertheless, we were keen to gain further support for our model and learn more about the subtleties of the complex dynamic processes involved in this chemistry. Specifically, we sought to (a) determine how the invertomer distribution (A or B) is influenced by the substrate substitution pattern and reaction conditions and correlate it with the observed product distributions; (b) directly observe the lithiated intermediates and, in this way, gain evidence on the number of lithiated species in solution; and (c) understand more precisely how the aziridine nitrogen stereodynamics impacts the stereochemical course of the reaction.

First, we reasoned that it was very important to establish the N-configuration for invertomers A and B as well as the barrier to inversion. Attempts to assign the N-configuration by low-temperature NOESY experiments were not fruitful mainly because of exchange limits.[18,19] Since the NMR spectra of alkylideneaziridines, under slow exchange conditions (200 K), reveal differences in the ^{1}H chemical shifts of the equilibrating invertomers (see Supporting Information), we decided to explore an alternative method. High-level density functional theory (DFT) calculations of spectroscopic properties such as NMR chemical shifts and coupling constants have proven to be excellent tools for determining stereoisomeric structures with similar connectivity and magnetic environments such as heterocycles. Here, the ^{1}H NMR spectra of aziridines (*S*)-**1a−c** have been calculated by DFT methods in order to assign

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the structures to their slowly equilibrating N-invertomers. The computational work began with the conformational analysis for invertomers A and B of all aziridines (*S*)-**1a−c** using the hybrid DFT method B3LYP with the 6-31G(d,p) basis set (see Supporting Information).[20] The stable conformers were further minimized at the B3LYP/6-311++G(d,p) level and characterized with vibrational frequency calculations at the same level of theory. The optimized structures for aziridines (*S*)-**1a,c** are reported in Figure 1 (see also Supporting Information). The next step was the shielding constants' single-point calculation using the GIAO (gauge including atomic orbitals)[21] method, with the MPW1PW91 functional[22] and the pcS-2 basis set, specifically designed for NMR shielding constant calculations.[23] For the spin−spin coupling constant calculations on model systems, the hybrid B3LYP functional with the 6-311++G(d,p) basis set has been used for consistency with our previous studies.[24] All computational studies are carried out at the DFT level and take into account the long-range solvent effects using the SMD continuum solvation model (see Supporting Information).[25]

Comparisons between computed ^{1}H NMR spectra of each invertomer for aziridines (*S*)-**1a,c** and the experimental spectra of the slowly equilibrating mixture are reported in Figure 1.[26] The signals of the two slowly equilibrating invertomers could be readily assigned by matching with the calculated chemical shifts (respectively marked in red and blue in Figure 1). Marked differences for each invertomer were seen in both the calculated and real spectra of aziridines (*S*)-**1a**, (*S*)-*E*-**1b**, (*S*)-*Z*-**1b**, and (*S*)-**1c**, allowing the N-configurations for each invertomer to be confidently assigned (see Supporting Information). From this analysis, it was also deduced that invertomer B (Scheme 2) is predominant for aziridines (*S*)-**1a** and (*S*)-*E*-**1b**, whereas invertomer A is favored for (*S*)-*Z*-**1b** and (*S*)-**1c**.

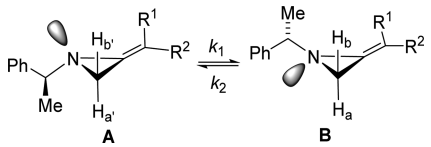
After the assignment of the N-configuration, the activation barriers for nitrogen inversion were calculated using VT NMR experiments and line shape analysis (see Supporting Information).[27] The values for the barriers to inversion are collected in Table 1.

The largest differences are seen between aziridines (*S*)-**1a** and (*S*)-**1c** ($\Delta\Delta G^{\ddagger} \approx 1.2$ kcal/mol), whereas similar barriers to inversion were derived for (*S*)-*Z*-**1b** and (*S*)-*E*-**1b**. The different invertomer distribution between the pairs of (*S*)-**1a** and (*S*)-*E*-**1b** (where B > A) and (*S*)-*Z*-**1b** and (*S*)-**1c** (where A > B) is ascribed to the alkene substituent. In particular, it seems that invertomer A is favored when $R^1 \neq H$. Next, we sought to establish if the presence of this non-equimolar mixture of slowly equilibrating invertomers actually affects the stereoselectivity of the lithiation/trapping sequence. Preferential deprotonation syn to the nitrogen lone pair of invertomers A and B would lead to diastereomeric lithiated intermediates whose ratio would depend on the relative rates k_3 and k_4 (Scheme 2). With this in mind, we performed multinuclear magnetic resonance investigations on lithiated aziridines (*S*)-**1a−c-Li** with a view to directly observing these intermediates, as has been achieved in other systems.[28] Thus, alkylideneaziridines (*S*)-**1a**, (*S*)-*E*-**1b**, (*S*)-*Z*-**1b**, and (*S*)-**1c** were separately lithiated in a NMR tube at 200 K in THF-d_8. Different outcomes were seen lithiating (*S*)-**1a** and (*S*)-*E*-**1b** compared to (*S*)-*Z*-**1b** and (*S*)-**1c**. When a THF-d_8 solution of (*S*)-**1a** was added to a precooled (200 K) THF-d_8 solution of *s*-BuLi (1.2 equiv), two set of signals emerged in both the ^{1}H and ^{13}C NMR spectra. The detected signals were assigned to two diastereomeric lithiated intermediates of (*S*)-**1a-Li** because trapping, in the NMR tube at 200 K, with CD_3OD or benzophenone gave the corresponding deuterated and hydroxyalkylated aziridines (*S*)-**1a-D** (98% D) and **2a**/*diast*-**2a** (80:20 dr). The signals for the α-lithiated carbon and the corresponding H_b proton were assigned by heteronuclear ^{1}H−^{13}C HSQC-DEPT experiments (correlation H_b−C_α in Figure 2). Strong shielding was observed for H_b linked to the lithiated carbon, with respect to the starting aziridines, as a result of increased charge density in the carbanionic species. Unfortunately, broad signals were observed for the lithiated carbon C_α and were not informative with regard to the aggregation state.[29] The possibility of assigning the two set of signals to slowly equilibrating nitrogen invertomers was ruled out by 2D NOESY experiments that did not provide evidence of exchange. Our findings suggest that at least two detectable lithiated species, likely diastereomeric at the lithiated carbon, are found in THF solution. The same experiments, conducted on aziridine (*S*)-*E*-**1b**, again led to a mixture of diastereoisomeric intermediates for (*S*)-*E*-**1b-Li** (Figure 2). In this case, the 2D heterocorrelation experiment revealed the presence of at least four detectable organolithium species (correlation H_b−C_α in Figure 2), likely resulting from aggregation phenomena.[30] In stark contrast, the multinuclear magnetic resonance investigations performed on aziridines (*S*)-*Z*-**1b** and (*S*)-**1c** revealed one predominant lithiated intermediate for both (*S*)-*Z*-**1b-Li** and (*S*)-**1c-Li** (Figure 2). Similarity in the structures of the lithiated aziridines (*S*)-**1a-c-Li** can be deduced from the chemical shift data. In all cases, H_b is upfield shifted (1.2−0.9 ppm) with respect to the parent neutral aziridines (2.5−1.5 ppm), whereas C_α-lithiated carbons are downfield shifted (52−54 ppm) with respect to the parent neutral aziridines (27−30 ppm).

The presence of several lithiated intermediates for (*S*)-*E*-**1b** and (*S*)-**1a** likely explains the low stereoselectivity observed in the reactions of these aziridines with electrophiles in THF.[13,16] Unfortunately, attempts to investigate by NMR the lithiated intermediates of aziridines (*S*)-**1a−c** generated in toluene-d_8 were unsuccessful. Only very broad signals were detected in all cases, perhaps due to aggregation phenomena.

Additional information on the structure of the lithiated aziridines came from a 2D NOESY experiment performed on (*S*)-**1c-Li**. In this case, the possibility to clearly identify the aziridine proton H_b allowed us to deduce a syn relationship between the C_α−Li bond and the nitrogen lone pair (Figure 3). Crucially, this piece of evidence lends strong support to the

Table 1. Barrier to Inversion in Aziridines (*S*)-1a−c Calculated in THF-d_8



aziridine	R^1	R^2	dr of **A**/**B**[a]	$\Delta G^{\ddagger}$ (kcal/mol)[b]
(*S*)-**1a**	H	H	38:62	10.4
(*S*)-*E*-**1b**	H	Me	38:62	11.3
(*S*)-*Z*-**1b**	Me	H	71:29	11.0
(*S*)-**1c**	Me	Me	71:29	11.6

[a]Diastereomeric ratio determined by ^{1}H NMR under slow exchange conditions (see Supporting Information). [b]Free energy of activation calculated by line shape analysis and Eyring plot at 213 K (see Supporting Information).

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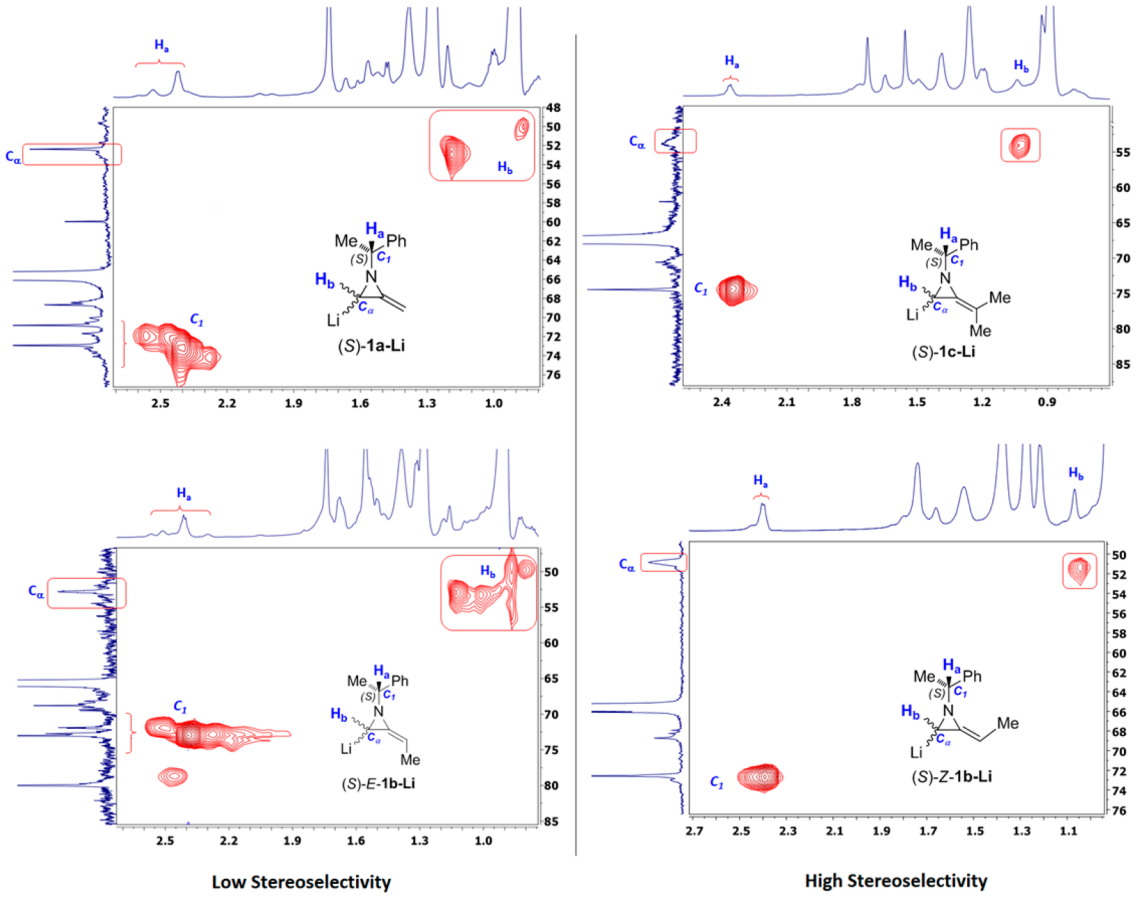

Figure 2. Comparison between heteronuclear $^{1}H-^{13}C$ HSQC-DEPT experiments for lithiated aziridines (*S*)-**1a–c** at 200 K in THF-d_8.

model proposed in Scheme 2, suggesting a role for the aziridine nitrogen (vide infra).

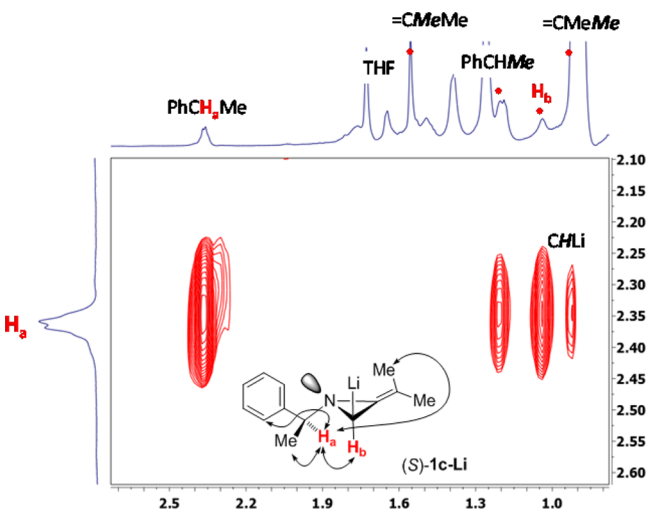

Figure 3. Two-dimensional NOESY spectra (600 MHz) of (*S*)-**1c-Li** [0.2 M] in THF-d_8 at 200 K.

All of the experimental evidence is in agreement with the proposed model (Scheme 2 and Table 2) and with a D-DR mechanism. In fact, our results prompt us to conclude that the stereoselectivity of the process is dependent on the relative amount of the two invertomers, the rates of nitrogen inversion (k_1, k_2), and the rates of deprotonation (k_3, k_4). For the sake of comparison, Table 2 collates the measured stereoselectivities observed in the reactions of aziridines (*S*)-**1a–c** with two diaryl ketones in both THF and toluene.[31] For reactions run in THF, stereoisomer **2** forms preferentially (Table 2, entries 1, 3, 5, and 7). The diastereomeric ratio observed confirms the importance on the relative amounts of invertomers A and B. Higher stereoselectivities are obtained in THF when A > B as seen for (*S*)-**1c** and (*S*)-*Z*-**1b** (Table 2, entries 5 and 7). The very high stereoselectivities seen with these two substrates infer that $k_4 > k_3$. Moreover, the NMR experiments confirm the presence of one predominant lithiated intermediate derived from (*S*)-**1c** and (*S*)-*Z*-**1b**, with the X-ray structures that are consistent with lithiation syn to the nitrogen lone pair (i.e., stereoselective removal of $H_{b'}$ from invertomer A, Table 2). For the lower levels of stereoselectivity observed with (*S*)-**1a** and (*S*)-*E*-**1b** in THF, these can be explained by the observation that B > A, leading to larger quantities of *diast*-**2** (assumes k_4 and k_3 are unchanged). In toluene, these substrates produce the opposite stereoselectivity, leading mainly to *diast*-**2**, presumably because B > A and $k_3 > k_4$ (Table 2, entries 2, 4, 9, and 10).[32]

The results suggest that the level of stereoselectivity is also influenced by the barrier to N-inversion in A and B. This is evident in the lithiation of (*S*)-*E*-**1b** and (*S*)-*Z*-**1b** in toluene (Table 2, entries 4, 6, and 10). For both aziridines, a similar barrier to inversion has been determined but with the opposite invertomers favored (Table 1). In the lithiation/trapping of (*S*)-*E*-**1b** in toluene, the A/B ratio is 38:62, suggesting that k_3 is slightly larger than k_4. In the case of (*S*)-*Z*-**1b**, where the A/B ratio is 70:30, the stereoselectivity observed in toluene closely reflects the invertomer ratio ($k_3 \approx k_4$). In the case of aziridine

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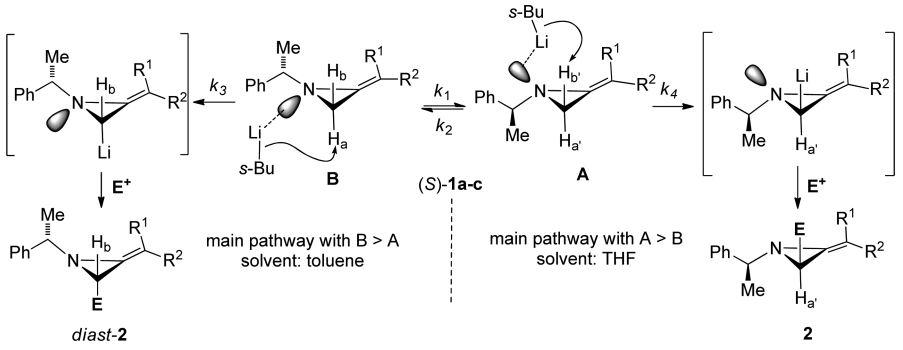
Table 2. Stereoselectivity with Aziridines (*S*)-1a−c



entry	R^1	R^2	solvent	adducts	dr of **2**/*diast*-**2b**[a]	yield[b] (%)	E^+
1	H	H	THF	**2a**/*diast*-**2a**	80:20	88	Ph_2CO
2	H	H	toluene	**2a**/*diast*-**2a**	15:85	80	Ph_2CO
3	H	Me	THF	**2b**/*diast*-**2b**	78:22	84	Ph_2CO
4	H	Me	toluene	**2b**/*diast*-**2b**	35:65	71	Ph_2CO
5	Me	H	THF	**2c**/*diast*-**2c**	98:2	80	Ph_2CO
6	Me	H	toluene	**2c**/*diast*-**2c**	70:30	76	Ph_2CO
7	Me	Me	THF	**2d**/*diast*-**2d**	94:6	80	Ph_2CO
8	Me	Me	toluene	**2d**/*diast*-**2d**	70:30	80	Ph_2CO
9	H	H	toluene	**2e**/*diast*-**2e**	15:85	85	$(4\text{-}ClC_6H_5)_2CO$
10	H	Me	toluene	**2f**/*diast*-**2f**	37:63	71	$(4\text{-}ClC_6H_5)_2CO$

[a]Diastereomeric ratio established by ^{1}H NMR of the crude reaction mixture. [b]Yield of isolated products.

(*S*)-**1a** with respect to (*S*)-*E*-**1b** (Table 2, entry 2 vs 4, and 9 vs 10), the higher stereoselectivity observed with (*S*)-**1a** can be explained by consideration of the different N-inversion barriers because the A/B ratios are identical.[33] More rapid conversion between invertomers A and B in (*S*)-**1a** would favor the formation of *diast*-**2** when $k_3 > k_4$ (Table 1). The conclusion drawn for the reactions of (*S*)-**1a** and (*S*)-*E*-**1b** in THF (where B > A) applies to the reaction of (*S*)-**1c** and (*S*)-*Z*-**1b** occurring in toluene with a lower level of stereoselectivity and without inversion of stereochemistry (Table 2, entries 6 and 8). However, in this latter case, it is worth noting that A > B.

CONCLUSIONS

The origin of the stereoselectivity in the reactions of lithiated alkylideneaziridines can be rationalized on the basis of additional NMR experiments performed on lithiated intermediates, DFT calculations that allowed us to assign the N-configuration of the slowly equilibrating invertomers, and the barriers to nitrogen inversion. With such details in hand and knowing that these lithiated aziridines are configurationally stable, it is possible to establish that the stereoselectivity-determining step is the deprotonation (lithiation). The proposed dynamic model based on a D-DR allows us to understand the stereochemistry of the final adducts **2**, which is further supported by X-ray analysis on adducts **2c**,**d** and *diast*-**2e**,**f** obtained, respectively, from reaction in THF and toluene (Scheme 2). This work highlights the subtle interplay between reaction conditions, nitrogen stereodynamics, and complexation phenomena when attempting to control the stereochemical outcome of reactions involving functionalized organolithiums. These D-DR concepts will be applied to other systems displaying dynamic phenomena related to a change of conformation or configuration, and the results will be reported in due course.

EXPERIMENTAL SECTION

General Procedure for the Lithiation/Electrophile Trapping of Alkylideneaziridines 1a−c. To a stirred solution of alkylideneaziridine (1.0 mmol) in 8 mL of THF (or toluene) at −78 °C was added dropwise *s*-BuLi (1.3 equiv). The reaction was stirred at −78 °C for 0.5 h, quenched with the electrophile (0.9−1.5 equiv), and stirred for 1 h at this temperature before being warmed to room temperature. Water was added, the layers were separated, and the aqueous phase was extracted with diethyl ether. The combined organic extracts were dried over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure. Purification by column chromatography provided adducts **2**/*diast*-**2**. For reactions using benzophenone, an additional reductive step was included in the workup to facilitate removal of excess electrophile. The spectroscopic data of functionalized alkylideneaziridines **2a−f**, *diast*-**2a**, and *diast*-**2c−f** have already been reported.[13,16] Spectroscopic data of the new compound *diast*-**2b** are reported here.

(2*R*,1′*S*)-(*E*)-3-Ethylidene-1-(1-phenylethyl)aziridin-2-yl)-diphenylmethanol, *diast*-2b: ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.42 (d, J = 6.5 Hz, 3 H), 1.90 (d, J = 6.5 Hz, 3 H), 2.80 (s, 1 H), 3.64 (q, J = 6.5 Hz, 1 H), 3.70 (br s, 1 H, OH), 5.12 (q, J = 6.5 Hz, 1 H), 6.98−7.31 (m, 15 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 13.9, 22.5, 47.9, 64.7, 74.6, 77.9, 96.5, 126.0, 126.2, 126.7, 126.9, 127.2, 127.7, 128.1, 130.1, 130.1, 135.8, 146.5; IR (film) ν_{max} 2250, 1448, 1030, 903, 1006, 726, 701 cm^{-1}; $[\alpha]_D^{20}$ (c = 1, $CHCl_3$) = −12; ESI-MS m/z 356.5 $[M + H]^+$.

NMR Experiments. All low-temperature multinuclear magnetic resonance experiments were conducted on a 600 MHz spectrometer equipped with a 5 mm auto switchable broad-band probe with gradient (*Z*) and on a triple resonance 5 mm probe with the gradient (*Z*) working at the following frequencies: 599.944 MHz (^{1}H), 150.856 MHz (^{13}C).

Typical Procedure for the NMR Study of Lithiated Aziridines 1a−c. In a 5 mm NMR tube equipped with an Omni-Fit valve, under Ar, a filtered (Celite) solution of commercial *s*-BuLi (0.06 mmol) was added, and the solvent was removed under vacuum. The resulting oil was then precooled to −78 °C and dissolved in 350 μL of THF-d_8. In a separate vial, under inert atmosphere (Ar), 0.04 mmol of aziridines **1a−c** was dissolved in 350 μL of dry THF-d_8. This solution was added to a precooled (−78 °C) 5 mm NMR tube containing the *s*-BuLi solution, and the resulting deep yellow mixture was quickly transferred

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into the NMR probe precooled to −78 °C. All of the experiments were run without spinning, and several preparations proved to be fully reproducible.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for new compounds and X-ray and calculation data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00848.

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Notes

The authors declare no competing financial interest.

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with the lithium bonded to the C_α carbon (see Supporting Information).
(30) Unfortunately, NMR experiments carried out in toluene-d_8 resulted in broad signals likely due to aggregation phenomena. However, trapping of the lithiated intermediates with Ph_2CO furnished the expected adducts **2** and *diast*-**2**.
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(33) We assume that the solvent does not significantly affect the barrier to N-inversion but only the kinetics of deprotonation.

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