Enantiotopos-Differentiating (−)-Sparteine-Mediated γ-Deprotonation of 1-Alkenyl Carbamates: DFT Calculations Verify the Observed Stereoselectivity

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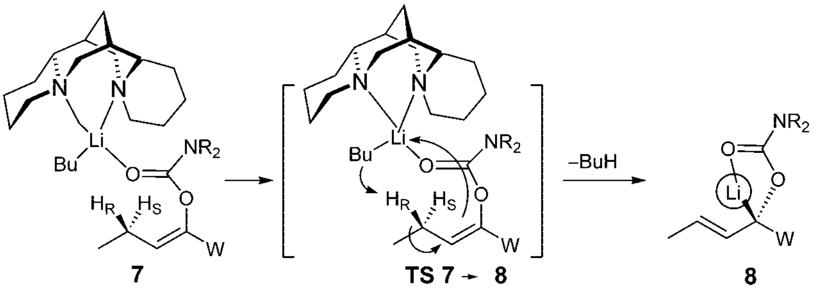

The enantioselective lithiation/γ-deprotonation of three 1-alkenyl *N*,*N*-diisopropylcarbamates **6** by alkyllithium/(−)-sparteine has been modeled by the DFT method B3LYP/6−31G(d). The results of these calculations predict the preferential removal of the γ-*pro-R* proton from the precomplexes **7** to give the (*S*)-lithio derivates **8**. The calculations also indicate the necessity of an anion-stabilizing substituent (Ph, -CC−Ph) in the α-position of the substrate. These data are in excellent concordance with the experimental results. It is demonstrated that the formation and the properties of lithium carbanions are predictable with high accuracy by standard quantum chemical calculations if these species are monomeric and rigidified to some extent by chelation.

Introduction

Eighteen years ago we introduced the enantioselective α-lithiation of *O*-alkyl carbamates **1** by means of *sec*-butyllithium/(−)-sparteine (**5**) (Scheme 1).[1,2] The chiral base removes in compounds **1** the *pro-S* proton with essentially perfect stereoselectivity leading to lithium compounds **3** which are configurationally stable below −40 °C and are trapped by electrophiles with retention of the configuration to form highly enantioenriched substitution products **4**. The ternary complex **2**, most likely, is the intermediate, permitting a kinetically controlled, intramolecular deprotonation. DFT calculations support this reaction course well and also predict the observed differences in activation energies by approximately 2 kcal/mol in favor for the *pro-S* proton.[3]

The method later has been extended by Beak et al. to *N*-Boc-pyrrolidine and to related *N*-carbamates.[4] Theoretical investigations by Wiberg, Bailey, and Beak substantiate an efficient selection between *pro-S* and *pro-R* protons.[5,6] Here, also, the

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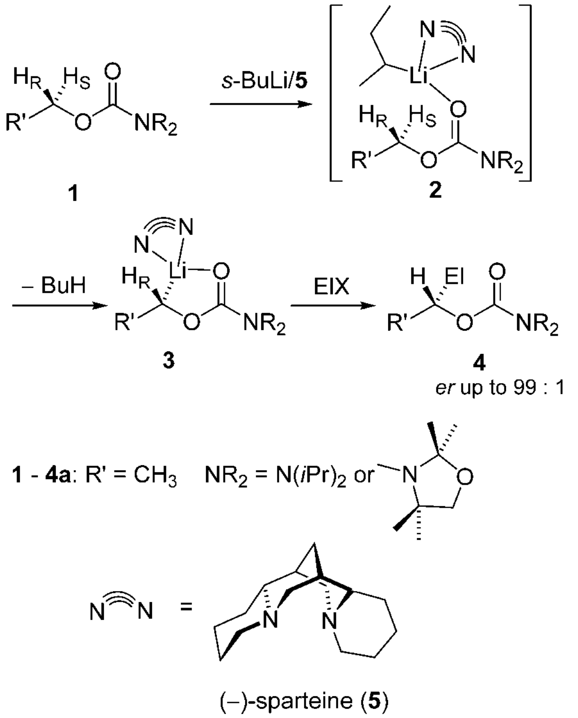
SCHEME 1. Enantioselective α-Lithiation of *O*-Alkyl Carbamates



good agreement between observed and calculated kinetic data supports strongly the absence of oligomeric products and transition states.[5,7−9] More recently, computational studies on ligand-assisted enantioselective deprotonation reactions have been published by Kozlowski et al.[10] and Metallinos, Dudding et al.[11]

As we discovered more recently by serendipity, (*Z*)-1-aryl-1-alkenyl *N*,*N*-diisopropylcarbamates **6a** (W = aryl), under similar conditions (*n*-butyllithium/(−)-sparteine (**5**), at −78 °C in toluene), undergo a highly stereoselective deprotonation in the γ-position, leading to configurationally stable lithium complexes **8a** (Scheme 2), which are trapped by electrophiles usually in the γ-position to form substitution products often with er'*s* > 99:1.[12] The selectivity for the removal of the *pro-R* proton over the *pro-S* proton is in the magnitude of 100:1. Similar selectivities are achieved with a moderately electron-withdrawing substituent such as W = trialkylsilyl,[13] 1-alkynyl,[14] or 1-alkenyl[15] in the 1-position.

From the *E*/*Z* mixture, only (*Z*)-**6** undergoes deprotonation under the reaction conditions.[12] Trapping the carbanionic species by addition of triphenyltin chloride (known for its preference to undergo antarafacial substitution reactions), the γ-stannane (*S*,*Z*)-**4a** (El = Ph_3Sn) is formed with high yield and er. Acetone, preferring a suprafacial reaction course with allylic nucleophiles, gave rise to homoallylic alcohol (*R*,*E*)-**10a** (El = CMe_2OH).[12]

It must be concluded from these results that the intermediate chelate complex **8** possesses the (1*S*,2*E*) configuration.

Quite surprisingly, the intramolecular proton transfer in the ternary complex **7** has to proceed via a cyclic nine-membered transition state **TS-7 → 8**. We investigated now this possibility and the resulting stereoselectivity by DFT calculations.

Methods

To investigate the mechanism and the stereochemical course of enantioselective (−)-sparteine-assisted γ-lithiodeprotonation reactions of vinyl carbamates, extensive DFT calculations using the B3LYP hybrid functional with the basis set 6−31G(d) were performed. We have chosen 1-substituted (*Z*)-but-1-enyl di-isopropylaminocarboxylates **6** as our model substrates, which have also been used in the experimental work. In our thorough study, we have included the starting materials (−)-sparteine **5**, isopropyllithium (as a symmetrical model for *sec*-butyllithium), the Lewis acid−base precomplex with carbamate **7** as a result of *O*-coordination at the carbamate carbonyl oxygen, the transition state for deprotonation **TS-7 → 8** and the resulting lithium compound **8** after loss of propane (Scheme 3).

(−)-Sparteine **5** (possessing C1 symmetry) allows two diastereomeric modes of coordination of the carbamate and the base, due to the stereogenic lithium cation (Li_R vs Li_S) produced. In principle, the (Z)-carbamate **6**, as used in the experiments, may adopt either sickle- or U-shaped conformations of the terminal ethyl group in the transition state. However, only in three cases were transition states resulting from the U-conformer competitive, although not being the energy lowest structural possibility. Furthermore, there are two different possibilities of interaction in the transition state with respect to the abstraction of the *pro-(R)* and of the *pro-(S)* protons, respectively. Consequently, eight stereochemically different reaction channels result. In our opinion, the bulkiness of the three components does not allow for the participation of coordinating solvent molecules and of oligomeric structures, which would make the modeling of the reaction sequence much more difficult.

Starting with PM3[16] reaction pathway calculations, which allow relatively easily the localization of the respective transition states after a thorough conformational analysis with respect to the isopropyllithium moiety and diisopropylamino group (see also ref 7a), the computations were continued using the Gaussian 03[17] package of programs with the (deprecated, but rather useful) option "mndofc" (opt = (ts, noeigentest, mndofc)), employing DFT functional B3LYP/6−31G(d).[3,18] We are aware that this basis set is not optimal, but it offers a relatively good compromise between precision and CPU costs. The B3LYP/6−31+G(d) method is not yet applicable for a systematic study with such a number of large molecules with 89−101 atoms. Comparing well-organized diastereomeric transition structures, possible inherent calculational errors are leveled out to a great extend. Consequently, even small calculated energy differences appear meaningful.[19]

Having obtained the transition state geometries **TS-7 → 8**, the respective minima **7** and **8** were localized by complete optimizations

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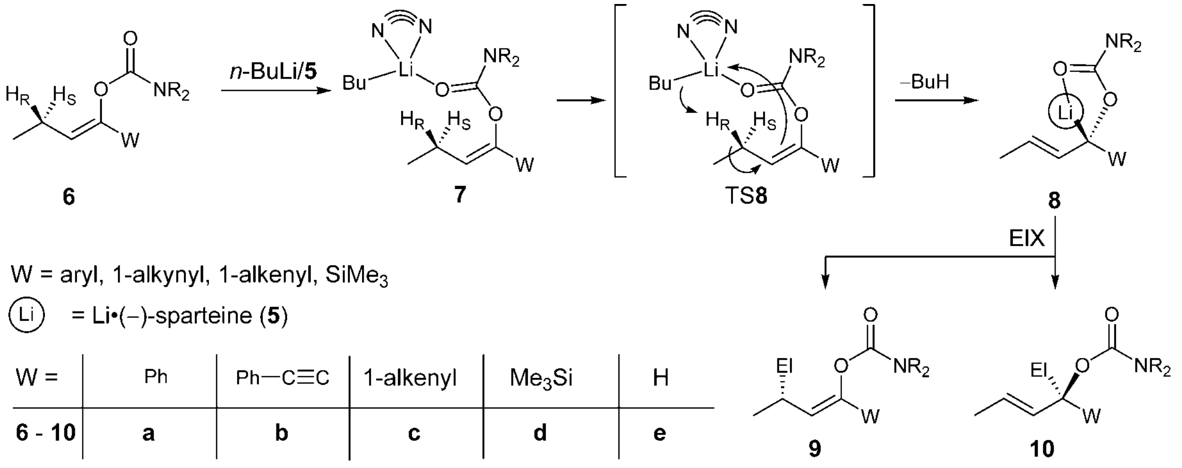
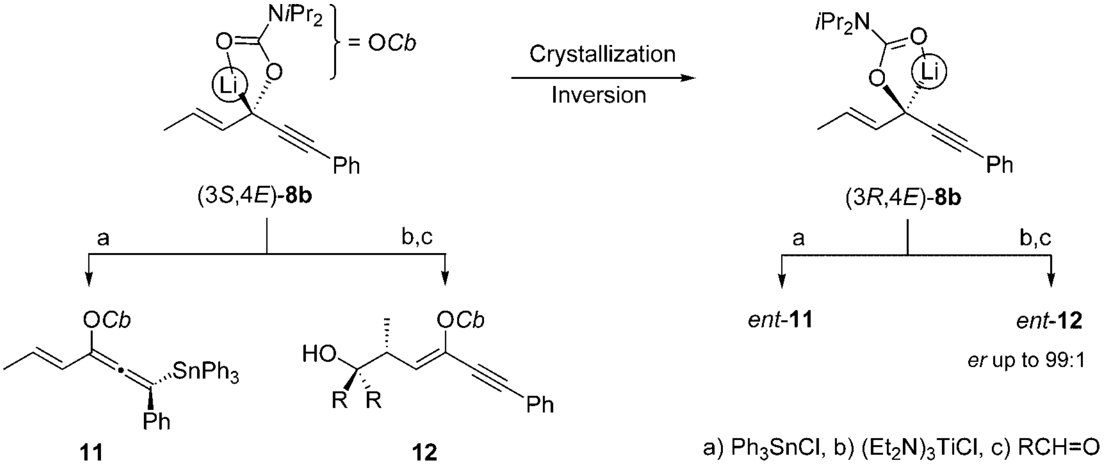
SCHEME 2. γ-Deprotonation and Electrophilic Substitution of 1-Alkenyl Carbamates



W =	Ph	Ph−C≡C	1-alkenyl	Me$_3$Si	H
6 - 10	**a**	**b**	**c**	**d**	**e**

SCHEME 3. Epimerisation and Electrophilic Substitution of Lithiated 1-Alkynylalkenyl Carbamates 8b



a) Ph_3SnCl, b) $(Et_2N)_3TiCl$, c) RCH=O

either after appropriate shifting of the migrating hydrogen atom into the direction of the precomplex and of the lithium compound, respectively or by IRC-calculations and subsequent optimizations. In contrast to the optimizations of the compact and rather rigid transition states these calculations were very CPU-time-consuming due to the very flat energy hyperfaces of the complexes and subject of conformational isomerism. The final lithioalkyl carbamates **8** were obtained as van der Waals complexes with propane. As a common energy of reference, in the tables the sum of the gas phase energies of (−)-sparteine, isopropyllithium and the respective carbamate, is given ($E_{\text{Precomplex}}$, E_{TS}, E_{Product}). Of course, in solution those species would be solvated.[8]

Results

First, we discuss the reaction course of the deprotonation of the 1-phenylalkenylcarbamate (*Z*)-**6a** using isopropyllithium in the presence of (−)-sparteine **5** (Scheme 2, Table 1). In the first step of the reaction, the three components form ternary precomplexes **7a** in an exothermic reaction. From a number of possible conformers (see above), two diastereoisomeric precomplexes (*Li$_R$*)-**7a** and (*Li$_S$*)-**7a**, lowest in energy, were identified (Figure 1 for a typical precomplex). These differ in enthalpy, according to the DFT calculations, by approximately 1.6 kcal/mol in favor for *(Li$_R$)*-**7** (E_{rel} = 0.00 kcal/mol) and, most likely, their formation is reversible. In these precomplexes, the distances from the lithium ion to the oxygen atom of the carbonyl group and to the central carbon atom of the isopropyl group are in most cases comparable (2.1−2.2 Å).

Subsequently, each of the two pairs of nine-membered transition states, **TS-*pro-R*-7a** → **8a** and **TS-*pro-S*-7a** → **8**, for the (*Z*,*R*$_{\text{Li}}$*)* on one hand and for the (*Z*,*S*$_{\text{Li}}$) diastereomer of **7a** on the other hand compete for lithiodeprotonation by intramolecular removal of the γ-*pro-R* or γ-*pro-S*-proton to form chelate complexes (*E,S*)-**8** and (*E,R*)-**8**, respectively (see Figure 2 for a typical example).

The calculations predict a preferred abstraction of the *pro-R* proton. The difference in activation energies ΔE_{act} of 0.96 kcal/mol between the two transition states TS-*pro-R*-**7a-8a** and *pro-S*-**7a-8a** (both with (*R$_{Li}$*)-configuration) lowest in energy out of

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TABLE 1. **(−)-Sparteine Assisted Deprotonation: Precomplexes 7a, Transition States TS-7a → 8a, and Lithiocarbamates 8a**[a]

precomplexes **7a** (W = Ph)			transition states **TS-7a** → **8a**				lithio carbamates **8a**	
stereonotation	$E_{\text{Precomplex}}$[b]	$E_{\text{rel Precomplex}}$[c]	stereonotation	E_{TS}[b]	E_{relTS}	E_{act}[c]	stereonotation	E_{Product}[b]
(Z,R_{Li})	−40.72	0.00	**(Z,R_{Li})-*pro-R***	**−32.28**	0.00	**8.44**	**(E,S_{Li},S)**	**−76.65**
			(Z,R_{Li})-*pro-S*	**−31.32**	0.96	**9.40**	**(E,S_{Li},R)**	**−76.29**
(Z,S_{Li})	−39.14	1.58	(Z,S_{Li})-*pro-R*	−29.29	2.98	11.43		
			(Z,S_{Li})-*pro-S*	−29.06	3.22	11.66		
			(Z,R_{Li})-*pro-S*[d]	−27.19	5.09	13.53	(Z,S_{Li},R)[d]	−72.06

[a] Including zero point energy (ZPE) [kcal/mol] (the best species of the *R*- and *S*-series are printed in bold). [b] Relative to (−)-sparteine + *i*PrLi + vinyl carbamate **6a**. [c] Relative to the best precomplex **(Z,R_{Li})-7a**. [d] U-conformation in the transition state, *Z*-configuration in the respective product **8a**.

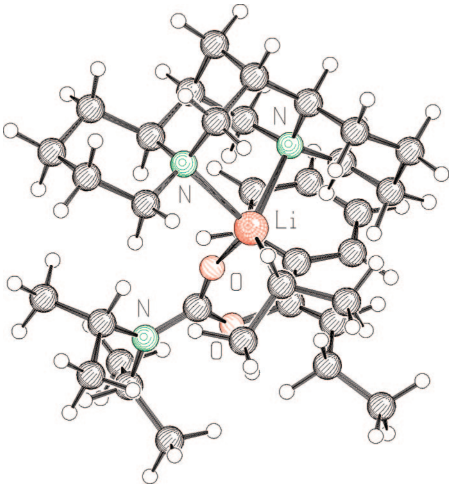

FIGURE 1. Molecular structure of precomplex (Z,R_{Li})-**8a** as obtained by quantum chemical geometry optimization (B3LYP/6−31G(d)//B3LYP/6−31G(d).

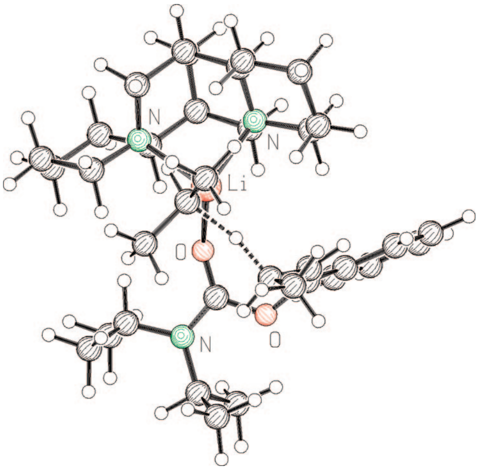

FIGURE 2. Molecular structure of transition state $(Z,R_{\text{Li}},$*pro-R*$)$-TS-**7a** → **8a** as obtained by quantum chemical geometry optimization (B3LYP/6−31G(d)//B3LYP/6−31G(d).

eight possible isomeric structures (see above) matches well with the average of enantiomer ratios of equal or greater than 97:3 at −78 °C (corresponding to a difference in the free enthalpy of activation of ca. 1.35 kcal/mol). From the structural point of view, the environment of the migrating hydrogen in the transition states is interesting: the distances to the carbamate carbon atom, where it was abstracted from, are calculated to amount to 1.33−1.36 Å, the distances to the carbon atom of the isopropyl base are 1.58−1.62 Å. This indicates an early transition state, more resembling the starting precomplexes than the lithiated carbamate.

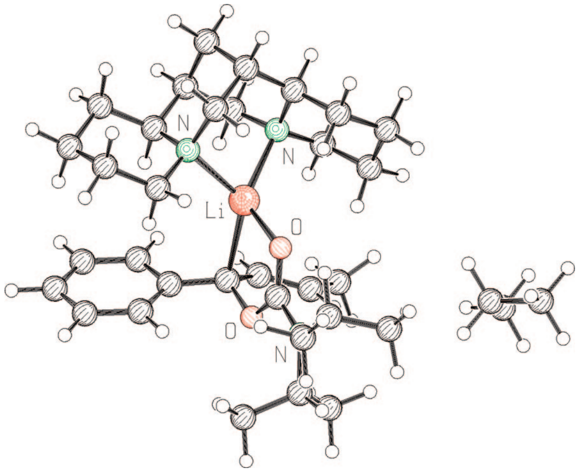

FIGURE 3. Molecular structure of lithio-carbamate (E,S_{Li},S)-**8a** as obtained by quantum chemical geometry optimization (B3LYP/6−31G(d)//B3LYP/6−31G(d).

Relaxing from these transition states to the products of the deprotonation, two diastereomeric lithio-carbamates **8a**, lowest in energy with (*R*) respectively (*S*) configuration at C1 (α-position of the alkenyl carbamate, the location of the lithium counterion) among a number of possible conformers were identified (see Figure 3 for an example). The diastereomer with (*S*)-configuration at C_{α}, produced via transition state **(Z,R_{Li})-*pro-R* TS-7a → 8a** was found as most favorable structure, whereas for the corresponding (*R*)-diastereomer (via **(Z,R_{Li})-*pro-S* TS-7a → 8a**) a relative energy of 0.26 kcal/mol was calculated. In these chelate complexes, the contacts of lithium to the carbonyl oxygen are quite strong (ca. 1.9 Å), whereas the lithium−carbon distances are significantly larger (ca. 2.3 Å). As expected, the transition states with sickle shape conformations of the (*Z*)-carbamates gave (*E*)-alkenylcarbamates, whereas the U-shaped transition states of the (*Z*)-carbamates led to (*Z*)-configurated products, which are substantially higher in energy (E_{rel} = 5.09 kcal/mol). Very interestingly, all the lithio-carbamates **8a** show (*S*)-configuration at the lithium ion. This epimerisation at lithium is a result of an intermediate three-coordinate-lithium structure, which was passed through during the relaxation from the transition state in the course of the geometry optimization. Obviously, these well-stabilized lithio-carbamates strongly prefer the (−)-sparteine-(*S*)-Li-diastereomers.

Experimentally; the mixture of complexes was trapped by appropriate electrophiles to achieve compounds **9 or 10** in high yield and excellent er.

To estimate the influence of the mesomerically stabilizing 1-phenyl residue in vinyl carbamate **6a**, we extended the calculations to the 1-unsubstituted (*Z*)-vinyl carbamate **6e** (Scheme 2 and Table 2) as the parent compound of this class

TABLE 2. (−)-Sparteine Induced Deprotonation: Precomplexes 7e, Transition States TS-7e → 8e, and Lithiocarbamates 8e[a]

precomplexes 7e (W=H)			transition states **TS-7e → 8e**				lithiocarbamates **8e**	
stereonotation	$E_{\mathrm{Precomplex}}$[b]	$E_{\mathrm{rel\ Precomplex}}$	stereo- notation	E_{TS}[b]	$E_{\mathrm{rel\ TS}}$	E_{act}[c]	stereonotation	E_{Product}[b]
(Z,R_{Li})	−42.35	0.00	**(Z,R_{Li})-*pro-R***	**−24.78**	0.00	**17.57**	(E,R_{Li},S)	−69.02
			(Z,R_{Li})-*pro-S*	**−23.19**	1.58	**19.15**	(E,R_{Li},R)	−65.46
(Z,S_{Li})	–42.32	0.03	(Z,S_{Li})-*pro-R*	−19.30	5.48	23.05	(E,S_{Li},R	−70.08
			(Z,S_{Li})-*pro-S*	−22.06	2.72	20.29	(E,S_{Li},S)	−69.96
			(Z,S_{Li})-*pro-R*[d]	−21.48	3.30	20.87	(Z,S_{Li},R)[d]	−66.62

[a] Including Zero Point Energy (ZPE) [kcal/mol](the best transition states of the *R*- and S-series are printed in bold). [b] Relative to (−)-sparteine + *i*PrLi + vinyl carbamate **6e**. [c] Relative to the best precomplex **(Z,R_{Li})-7e**. [d] U-conformation in the transition state, *Z*-configuration in the respective product **8e**.

TABLE 3. (−)-Sparteine Induced Deprotonation: Precomplexes 7b, Transition States TS-7b → 8b, and Lithiocarbamates 8b[a]

precomplexes **7b** W = CC−Ph			transition states **TS-7b → 8b**				lithiocarbamates **8b**	
stereonotation	$E_{\mathrm{Precomplex}}$[b]	$E_{\mathrm{rel\ Precomplex}}$	stereo- notation	E_{TS}[b]	$E_{\mathrm{rel\ TS}}$	E_{act}[c]	stereonotation	E_{Product}[b]
(Z,R_{Li})	−42.85	0.00	**(Z,R_{Li})-*pro-R***	**−35.72**	0.00	**7.13**	**(E,S_{Li},aS)**	**−84.97**
(Z,S_{Li})	−38.38	4.47	**(Z,R_{Li})-*pro-S***	**−34.28**	**1.44**	**8.57**	**(E,S_{Li},$R_{\mathrm{C\alpha}}$)**	**−82.46**
			(Z,S_{Li})-*pro-R*	−29.03	6.69	13.82		
			(Z,S_{Li})-*pro-S*	−31.82	3.90	11.03		
			(Z,S_{Li})-*pro-R*[d]	−31.24	4.48	11.61	(Z,S_{Li},$R_{\mathrm{C\alpha}}$)[d]	−79.76

[a] Including zero point energy (ZPE) [kcal/mol] (the best species of the *R*- and *S*-series are printed in bold). [b] Relative to (−)-sparteine + *i*PrLi + vinyl carbamate **6b**. [c] Relative to the best precomplex **(Z,R_{Li})-7b**. [d] U-conformation in the transition state, *Z*-configuration in the respective product **8b**.

of carbamates. Experimentally, 1-unsubstituted vinyl carbamates, such as **6e**, are rapidly deprotonated at the vinylic position and, thus, could not be incorporated into the experimental γ-deprotonation study.[20]

As expected, the enthalpy of formation for the precomplexes **7e** from **6e**, isopropyllithium, and (−)-sparteine (−42.4 and −41.9 kcal/mol) is in the same magnitude as found for **6a**. However, the activation energies of the deprotonation reactions via transition states *pro-R*-**TS-7e→8e** (17.6 kcal/mol) and via *pro-S*-**TS-7e→8e** (19.2 kcal/mol) are dramatically enhanced. The stereodifferentiation, resulting from the transition states lowest in energy, amounts to approximately 1.6 kcal/mol in favor for the abstraction of the *pro-R* proton, thus being significantly larger than for **6a**. Here we find distances of the migrating hydrogen to the carbamate carbon (1.39 − 1.41 Å) and to the base (1.50 −1.55 Å), which are located later on the reaction coordinate, thus resembling a little more the products than in the case of **TS-7a→8a.**

Further, a decreased stability of the lithiated intermediates **8e**—as predicted by intuition—is calculated: approximately −70 kcal/mol with respect to sum of the components, as compared to −76 kcal/mol for phenyl substituted chelate complexes **8a**. Similarly as for **8a**, the α-lithiated carbamate **(*E*,R_{Li},*S*)-8e** was generated via the preferred transition state **(*Z*,R_{Li})-*pro-R*-TS-7e → 8e**.

Furthermore, these results justify the conclusion that a successful γ-deprotonation of 1-alkylvinyl carbamates appears quite unlikely due to their diminished acidity. No change in configuration at lithium is observed for these less stabilized lithiocarbamates during relaxation from the transition states.

Experimentally, the use of *n*-butyllithium as base besides *s*-butyllithium has certain advantages as the reactions run more selectively but not as fast, probably due to the lower basicity of *n*-butyllithium. In order to study the influence of the base in more detail, the reaction sequence was also studied by means of calculations employing *n*-propyllithium as model for the experimentally used base *n*-butyllithium for the enantioselective deprotonation of **6e**. The calculated difference of the activation barriers leading to the diastereomeric transition states amounts to 1.36 versus 1.58 kcal/mol using isopropyllithium as base, favoring again the abstraction of the *pro-R* proton. We conclude from this rather similar data that the model base isopropyllithium matches well with the properties of experimentally used *n*-butyllithium.

When the phenyl group in carbamate **6a** is exchanged for 2-phenylethynyl (compound **6b**, Schemes 2 and 3) a further enhancement of the kinetic acidity and the thermodynamic stability of the resulting carbanionic species **8b** is expected to occur. Deprotonation of **6b** under standard conditions below −70 °C proceeds smoothly within 30 s to form chelate complex (3*S*,4*E*)-**8b** by removal of the *pro-R* proton. Keeping the solution at low temperature for 15 h at −78 °C, epimerization takes place to form (3*R*,4*E*)-**8b**—a conversion that is triggered by crystallization of the intermediate.[14] Chelate complexes **8b** exhibit propargylmetal reactivity and, as well, allylmetal reactivity, depending on the electrophile and the utilized counterion: Enantioenriched allene **11** was obtained with triphenyltin chloride, whereas aldehydes provide homoallylic alcohols **12** (er = >98:2) after lithium−titanium exchange.

DFT calculations result in activation energies E_{act} of 7.13 kcal/mol for the *pro-R* proton and 8.57 kcal for the *pro-S* proton (Table 3), leading to a stereodifferentiation of 1.44 kcal/mol. Due to the increased stability of the resulting lithium carbamate the distance of C_γ to the migrating hydrogen is comparably small (1.30−1.31 Å), whereas the distance to the carbon atom of the base is large (1.63−1.68 Å), indicating a rather early transition state.

In good agreement with the experimental results the generated lithiated carbamates **8b** show two types of structure, as some have the lithium counterion located at the α-position as **8a** and **8e**, whereas the energy lowest structure and others show an allenic (γ') position of lithium (Figure 4).

The energies of the carbanionic intermediates with respect to the sum of the reaction components are increased to approximately −80 to −85 kcal/mol, indicating the improved mesomeric stabilization of these intermediates in comparison

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(20) Kocienski, P.; Dixon, N. J. *Synlett* **1989**, 52–54.

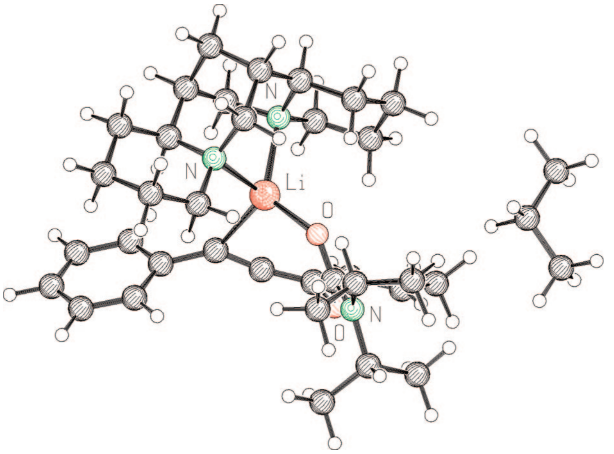

FIGURE 4. Molecular structure of lithio-carbamate ($E,S_{\mathrm{Li}},S,\gamma'$)-**8b** as obtained by quantum chemical geometry optimization (B3LYP/6−31G(d)//B3LYP/6−31G(d).

to **8a** and **8e**.[21] This is well in line with the picture of an early transition state. On the other hand, the good stabilization of the lithiated carbanions obviously facilitates their epimerization as indicated in the experiments.

As for **8a**, for **8b** we observed in most cases during the geometry optimizations (relaxation from the transition states) inversion at the chiral lithium ion via an intermediate three-coordinate-lithium structure. In all these cases, however, the relative stereochemistry of the carbanionic center was retained as formed in the transition state, independent of its position in α- or γ'-position. Thus, the γ'-lithiated carbamate **(E,S_{Li},aS)-8b** was generated via transition state **(Z,R_{Li})-*pro-R*-TS-7b → 8b,** whereas the α-lithio compound **($E,S_{\mathrm{Li}},R_{\mathrm{C\alpha}}$)-8b** was obtained by relaxation of **(Z,R_{Li})-*pro-S*-TS-7b → 8b**. The calculations indicate easy interconversion between α- and γ'-forms.

Conclusions

The DFT calculations, performed on the γ-deprotonation of (*Z*)-1-alkenyl *N*,*N*-diisopropylcarbamates by alkyllithium/(−)-sparteine, confirm excellently the experimental results. The kinetic discrimination between the γ-*pro-R*- and the γ-*pro-S* proton for **6a** (W = Ph) of 0.96 kcal/mol and for **6b** (*W* = CCPh) of 1.44 kcal/mol is in very good agreement with the observed diastereomeric ratios at −78 °C concluded from trapping experiments (Table 4). Such a high correspondence of calculated and observed results, which is quite unusual for the reactions of complex lithium compounds, is due to the monomeric nature of the involved compounds and transition states. Further, since well-organized diastereomeric structures are compared, possible inherent errors are leveled out. As a result, even small calculated energy differences appear meaningful. Moreover, the calculations reflect the stabilization of the different lithiated carbanions and, as well, the relative kinetic acidities of compounds **6a**, **6b**, and **6e**. The high activation energy for the 1-unsubstituted carbamate **6e** (17.6 versus 8.4 kcal/mol for the phenyl derivative **6a**) and the energies of the resulting lithium compounds (−70 versus −76 kcal/mol) indicate the importance of an electron-withdrawing substituent W for the γ deprotonation. Even the calculated distances between the migrating hydrogen atom and the carbamate on one side and the base on the other side in the transition states reflect the relative acidities of the precursors.

TABLE 4. Summarized Calculated Relative Transition State Energies for Substituted Carbamates[a]

stereonotation	**TS-7a → 8a** (W = Ph)	**TS-7b → 8b** (W = CC−Ph)	**TS-7e → 8e** (W = H)
(*Z*, R_{Li})-*pro-R*	0.00	0.00	0.00
(*Z*, R_{Li})-*pro-S*	0.96	1.44	1.58
(*Z*, S_{Li})-*pro*-R	2.98	6.69	5.48
(*Z*, S_{Li})-*pro-S*	3.22	3.90	2.72

[a] kcal/mol, with respect to the respective energy lowest transition state. Only sickle type structures are considered (see text).

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Supporting Information Available: Summaries of the quantum chemical calculations, that is, total energies (E_{tot}), Zero-point corrected energies (E(0K)), relative energies (E_{rel}), reaction energies (E_{R}), and activation energies (E_{act}), and GAUSSIAN ARCHIVE entries of the molecules studied. This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] Comparing the energies of both diastereoisomers for analysing the epimerization is not meaningful because the equilibrium is disturbed by a phase conversion.