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Solution structures of chiral lithium amides with internal sulfide coordination: sulfide versus ether coordination in chiral lithium amides

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Abstract—A series of chiral lithium amides with chelating sulfide groups has been investigated by NMR spectroscopy. These chiral lithium amides have previously been found to mediate higher enantioselectivity in the asymmetric addition of alkyllithium reagents to aldehydes than the corresponding lithium amides containing ether groups. The chiral lithium amido sulfide chelates form homodimers in both diethyl ether and tetrahydrofuran. In diethyl ether both sulfur atoms coordinate to the same lithium while the other lithium in the dimer is solvent coordinated. Tetrahydrofuran favours equivalently solvated homodimers. Mixed dimeric complexes are formed with excess *n*-butyllithium in both diethyl ether and tetrahydrofuran. The structural information was obtained from observed $^{6}Li,^{15}N$ couplings and cross peaks in the $^{6}Li,^{1}H$ HOESY spectrum. DFT calculations at B3LYP/6-31G(d) level of theory indicate that the Li–S chelate is much less stable than the Li–O chelate. However the calculations indicate that the stability of the dimeric chelates are in agreement with the NMR results of the diethyl ether and tetrahydrofuran solutions.
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1. Introduction

Chiral lithium amides are known to form mixed chiral dimers with alkyllithium reagents. The success of the asymmetric addition reaction has been rationalized based on chiral complex formation between one alkyllithium and a chiral lithium amide. The asymmetry of the complex is to a large extent dependent on the formation of a chelate. Recently we reported that the enantioselectivity of a chiral lithium amide mediated asymmetric butylation of benzaldehyde increases from 79% to 94% enantiomeric excess (ee) when the chelating ether is replaced by a sulfide.[1] This increase in enantioselectivity was surprising since the strength of the Li–S coordination, as part of the chelate, is expected to be much weaker than the corresponding Li–O coordination based on the simple HSAB principle. Thus the strength of the chelate does not correlate with the observed stereoselectivity in the addition reaction. The increase in enantioselectivity was also observed to be general among several investigated chiral lithium amides.

The increased stereoselectivity using the chiral sulfur amides, which should form much weaker chelates than the ethers, may indicate the presence of another structural motif or stereocontrol in the transition state. The Li–S chelate may be too weak to be formed in ether solvents, since the bulk of solvent, for example, tetrahydrofuran (THF) should compete with the intramolecular sulfide coordination. Is it possible that addition of THF breaks the sulfur coordination? A better understanding of these chelates and their stability, which may be obtained from NMR studies, is a prerequisite for a better understanding of the asymmetric induction using chiral lithium amides.

Our previous NMR spectroscopic studies have focused on a number of different chiral lithium amides with chelating ethers that form 1:1 mixed chiral complexes with *n*-butyllithium (*n*-BuLi). The structures of both homodimers and mixed complexes between chiral lithium amides and for example, *n*-BuLi have been extensively studied in solution by NMR spectroscopy.[2] These chiral mixed complexes have also been used successfully in the asymmetric addition of *n*-BuLi to aldehydes.[3] The five-membered chiral chelates formed have been widely employed both in the development of chiral inducers of asymmetric alkylation reactions and in the development

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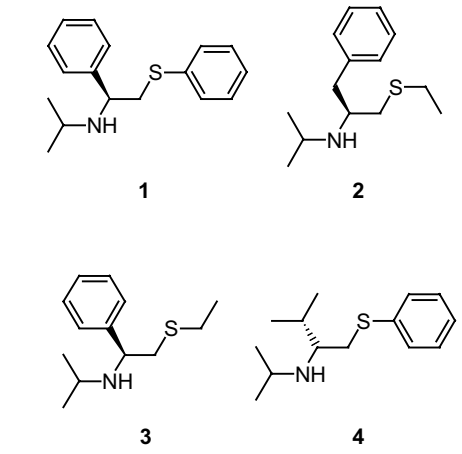
of chiral lithium amide bases for enantioselective deprotonation reactions.

Amino thiol and sulfide ligands have been used successfully in asymmetric synthesis with palladium and diethyl zinc.[4] In contrast to the extensive research on lithium amides with oxygen or nitrogen chelating groups, there has to our knowledge only been one report concerning lithium amides containing sulfide functions.[5] This is likely due to the higher thermodynamic acidity of the sulfides, which make them readily react with organolithium species at room temperature. An important class of such compounds is the α-stabilized sulfur carbanions, for example, lithio dithiane, which Boche et al. have studied in detail using low temperature NMR spectroscopy.[6] The only report on the strength of the Li–S coordination of organic molecules in comparison to that of Li–O is a computational study by Goldfuss et al., in which the Li–S interaction was found to be weaker than that of Li–O.[7]



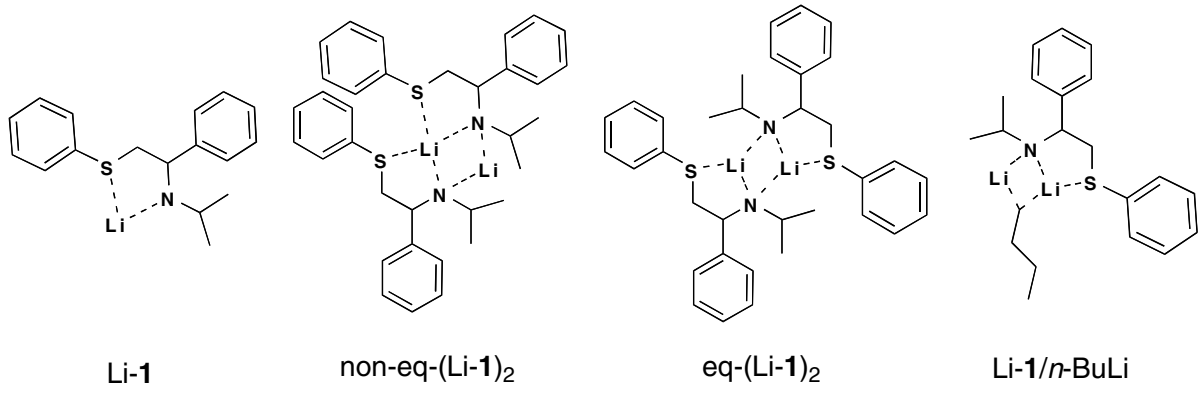
Herein, we report the results of multinuclear NMR spectroscopy and density functional theory calculations of the aggregation state and solution structure of the different complexes formed by the amines (*S*)-*N*-isopropyl-2-amino-2-phenyl-1-thiophenylethane **1**, (*S*)-*N*-isopropyl-2-amino-3-phenyl-1-thioethylpropane **2**, (*S*)-*N*-isopropyl-2-amino-2-phenyl-1-thioethylethane **3**, and (*S*)-*N*-isopropyl-2-amino-3-methyl-1-thiophenyl-butane **4** upon addition of [^{6}Li] *n*-BuLi in diethyl ether (Et_2O) and THF.

2. Results and discussion

2.1. NMR studies

To a Et_2O solution of *n*-BuLi (0.3 M) at −78 °C was added 1 equiv of amine **1**.[8] The ^{6}Li NMR spectrum of the mixture show two signals, in a 1:1 intensity ratio, at δ 2.3 and δ 4.1 and the ^{13}C NMR spectrum shows one set of resonances for the carbons of the lithiated amine. These NMR observations are consistent with the formation of chiral lithium amide dimers with non-equivalent lithiums (non-eq-(Li-**1**)$_2$) (see Scheme 1 and Table 1).

Further addition of *n*-BuLi to the solution of non-eq-(Li-**1**)$_2$ results in the formation of a new set of ^{13}C NMR signals. The ^{6}Li NMR spectrum shows two new signals, in a 1:1 intensity ratio at δ 3.0 and 3.5. The ^{6}Li NMR spectrum of a 2:1 mixture of *n*-BuLi and **1** dissolved in Et_2O-d_{10} at −78 °C shows only the two signals at δ 3.0 and 3.5 assigned to a mixed dimer complex Li-**1**/*n*-BuLi. The ^{13}C NMR spectrum shows only one set of resonances for each of the carbons in Li-**1**/*n*-BuLi. The α-carbon of the complexed *n*-BuLi is a quintet at δ 12.4 (J^{13}C, ^{6}Li = 8.9 Hz) due to coupling to two lithium-6 (I = 1) (see Table 1).



Scheme 1. Different complexes that may form upon addition of *n*-BuLi to **1**.

Table 1. Selected ^{13}C and ^{1}H NMR chemical shifts of the non-eq-(Li-**1**)$_2$ and the mixed complex formed by Li-**1** and *n*-BuLi in Et_2O at −78 °C

Complex	Nucleus	N*CH*	*CH*(CH$_3$)$_2$	*CH*$_2$S	CH(*CH*$_3$)$_2$	*CH*$_2$ (*n*-BuLi)
non-eq-(Li-**1**)$_2$	^{13}C	64.6	50.3	44.2	25, 28	
	^{1}H	3.9	2.6	3.3, 3.2	0.8, 1.1	
Li-**1**/*n*-BuLi	^{13}C	65.8	49.6	43.1	24, 27	12.4 (J = 8.9 Hz)
	^{1}H	4.3	2.6	3.0, 3.2	1.0, 1.3	−1.0

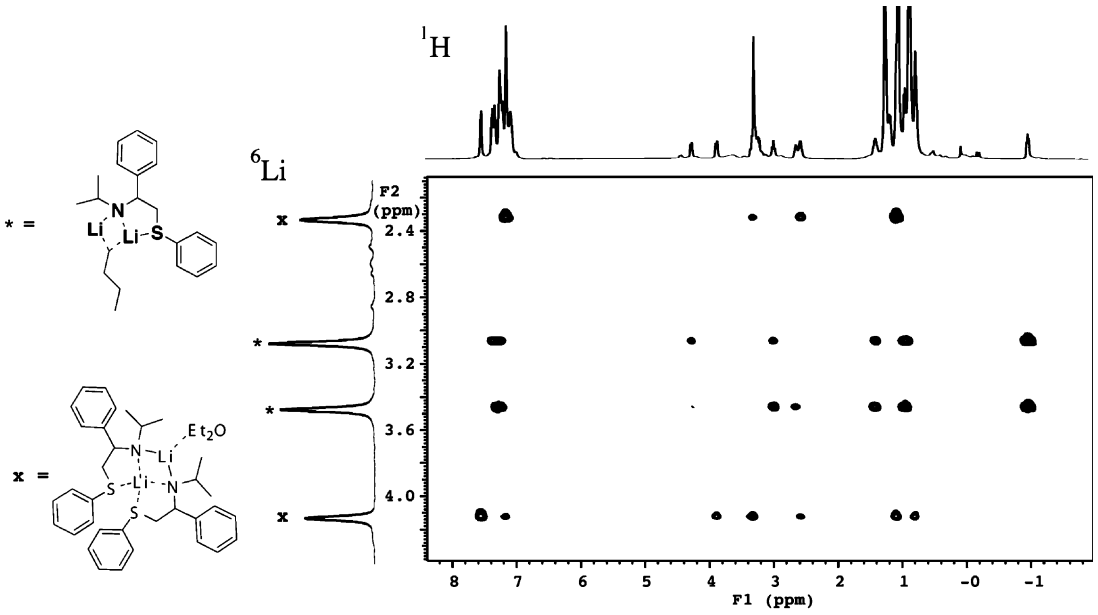


Figure 1. ^{6}Li,^{1}H HOESY spectrum of Li-**1**/*n*-BuLi and non-eq-(Li-**1**)$_2$ in Et$_2$O-d_{10} at −78 °C.

A ^{6}Li,^{1}H HOESY spectrum of the Et$_2$O solution containing a mixture of non-eq-(Li-**1**)$_2$ and Li-**1**/*n*-BuLi was obtained at −78 °C (see Fig. 1).[2e,9] It shows cross-peaks between the aliphatic protons of *n*-BuLi and the lithiums at δ 3.0 and 3.5 in the ^{6}Li NMR spectrum. The spectrum also reveals NOE's between the lithium signals at δ 3.0 and 3.5 and the aromatic protons at δ 7.2–7.3 of the mixed dimer, which confirm the formation of Li-**1**/*n*-BuLi. As for the non-eq-(Li-**1**)$_2$, the lithium signal at δ 4.1 shows NOE's to the resonances at δ 7.2 and δ 7.6 in the ^{1}H spectrum, while the more shielded lithium signal at δ 2.3 only shows cross-peaks to the aromatic protons at δ 7.0. The proton signals at δ 7.5 is assigned to protons of the thiophenyl, thus the lithium at δ 4.1, which shows strong NOE to the aromatic protons at δ 7.4, must be coordinated by the sulfide. However, the specific proton signals for the two aromatic groups of Li-**1** cannot be distinguished and it may also be argued that the bulk solvent Et$_2$O coordinates more strongly to lithium in the complex than does the internal chelating sulfide group. However, the non-equivalence of the two lithiums strongly argue that the internal chelation is favoured over a possible Et$_2$O coordination to lithium.

The ^{6}Li NMR spectrum upon addition of THF to the Et$_2$O solution of non-eq-(Li-**1**)$_2$ resulted in the appearance of a single signal at approximately δ 2.2. The presence of only one ^{6}Li resonance for Li-**1** in THF–Et$_2$O solutions indicates that the non-eq-dimer either breaks down into THF solvated monomers (Li-**1**) or equivalently solvated dimers (eq-(Li-**1**)$_2$) (see Scheme 1).

The aggregation state of lithium amides are generally obtained from the ^{6}Li,^{15}N couplings. However, ^{15}N labelled Li-**1** is not readily available. Instead we looked for analogous lithium amides. We observed that Li-**2** yields similar NMR spectrum as Li-**1** and the ^{15}N labelled amine **2** is easily available from [^{15}N]phenylalanine.

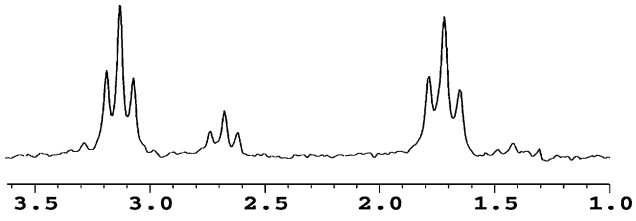


Figure 2. ^{6}Li NMR spectrum of Et$_2$O solvated nitrogen-15 labelled non-eq-(Li-**2**)$_2$ at −78 °C.

The mixed complex Li-**2**/*n*-BuLi in Et$_2$O gives rise to two doublets at δ 2.6 and 2.7 (J^6Li,^{15}N = 4.1 Hz and 4.9 Hz, respectively) while the non-eq-(Li-**2**)$_2$ appears as two triplets at δ 3.1 and 1.7 (J^6Li,^{15}N = 4.4 Hz and 5.2 Hz) in the ^{6}Li spectrum (see Fig. 2). A triplet at δ 1.6 (J^6Li,^{15}N = 4.3 Hz) appears in the ^{6}Li NMR spectrum upon addition of THF. This is consistent with an eq-(Li-**2**)$_2$ with one sulfide and one THF coordinated to each lithium.

In pure THF solution the triplet (J^6Li,^{15}N = 4.3 Hz) from eq-(Li-**2**)$_2$ appears at δ 1.3, while the two doublets (J^6Li,^{15}N = 3.8 Hz and 4.2 Hz, respectively) from the mixed complex appear at δ 1.5 and 2.1 in the ^{6}Li NMR spectrum at −78 °C (see Fig. 3). These results show that

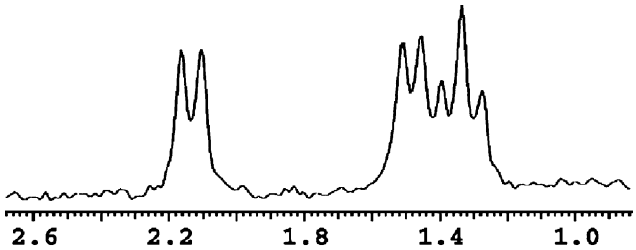


Figure 3. ^{6}Li NMR spectrum of ^{15}N-labelled (Li-**2**)$_2$ and *n*-BuLi/Li-**2** obtained in THF-d_8 solution at −78 °C.

Table 2. Selected ^{13}C and ^{1}H NMR chemical shifts of the eq-(Li-**1**)$_2$ and the mixed complex formed by Li-**1** and *n*-BuLi in a THF:Et_2O (1:3) mixture at −78 °C

Complex	Nucleus	N*CH*	*CH*$(CH_3)_2$	*CH*$_2$S	CH(*CH*$_3)_2$	*CH*$_2$ (*n*-BuLi)
eq-(Li-**1**)$_2$	^{13}C	64.2	50.0	41.7	26, 29	
	^{1}H	4.3	2.8	3.0, 3.3	0.7, 1.0	
Li-**1**/*n*-BuLi	^{13}C	65.4	49.8	44.7	26, 33	12.4 (J = 8.4 Hz)
	^{1}H	4.4	2.7	3.1, 3.2	0.9, 1.2	−1.1, −1.3

Li-**2** form eq-(Li-**2**)$_2$ and not monomers in THF. Based on this we propose that Li-**1** also forms equivalent dimers, eq-(Li-**1**)$_2$, in THF.

Addition of 0.5 equiv of *n*-BuLi to the sample of eq-(Li-**1**)$_2$ in 3:1 Et_2O/THF mixture at −78 °C, results in a ^{6}Li NMR signal at δ 1.9 for eq-(Li-**1**)$_2$ and two signals from the mixed complex at δ 2.1 and 2.9. The ^{13}C NMR spectrum shows a quintet at δ 12.4 ($J^{13}C,^{6}Li = 8.4$ Hz), consistent with the mixed dimeric complex Li-**1**/*n*-BuLi (Table 2).

$^{6}Li,^{1}H$ HOESY experiments performed on the mixture of Li-**1** and *n*-BuLi in THF at −70 °C, show strong cross-peaks between the lithium signal at δ 2.0 and the aliphatic protons of eq-(Li-**1**)$_2$ (Fig. 4). There are also strong NOE cross-peaks to the aromatic protons but unfortunately the proton signals of the phenylsulfide could not be assigned because of the overlapping phenyl protons. The mixed complex Li-**1**/*n*-BuLi shows NOE cross-peaks between the lithium signals at δ 2.1 and 2.9, the aliphatic protons of Li-**1** and the *n*-BuLi protons at δ −1.1 and −1.3.

The other amides studied herein, that is, Li-**3** and Li-**4** were observed to result in similar solvent dependent NMR signals, they are therefore suggested to form similar aggregates and mixed complexes with *n*-BuLi as those of Li-**1**.

The solution of non-eq-(Li-**1**)$_2$ in Et_2O-d_{10} was titrated with THF-d_8 in order to investigate the coordination competition between the sulfide and the strong donor solvent (Fig. 5). The ^{6}Li NMR signals at δ 4.1 and 2.3 disappear rapidly until 1 equiv of THF-d_8 per lithium had been added, resulting in one major signal at δ 2.2 from a dimer with equivalent lithiums, eq-(Li-**1**)$_2$. Since lithium is generally considered to be tetra-coordinated, the Et_2O coordinated dimer probably turns into a symmetric, THF solvated, dimeric complex rather than forming monomers, which would require 2 equiv of THF molecules per lithium.

To establish if the lithium is coordinated by the internal chelating sulfide groups in ether solvents, we studied the heteronuclear NOE between the lithiums and the protons of the sulfide groups of two different amides, Li-**3** and Li-**4** in solvent mixtures of THF and Et_2O. The dimeric aggregate of Li-**3** and its mixed aggregate were studied by $^{6}Li,^{1}H$ HOESY experiments in both Et_2O and THF. In these experiments the proton signals of the thiosulfide group overlap with other proton signals of the lithium amide. Consequently, the NOE's between the lithiums and these protons could not be separated from those of the other aliphatic protons. Li-**4** was studied as this amide only has one aromatic group and any hetero NOE's between one of the lithium signals and the aromatic protons must be due to specific Li-sulfide coordination. Thus, the *ortho*-protons of the

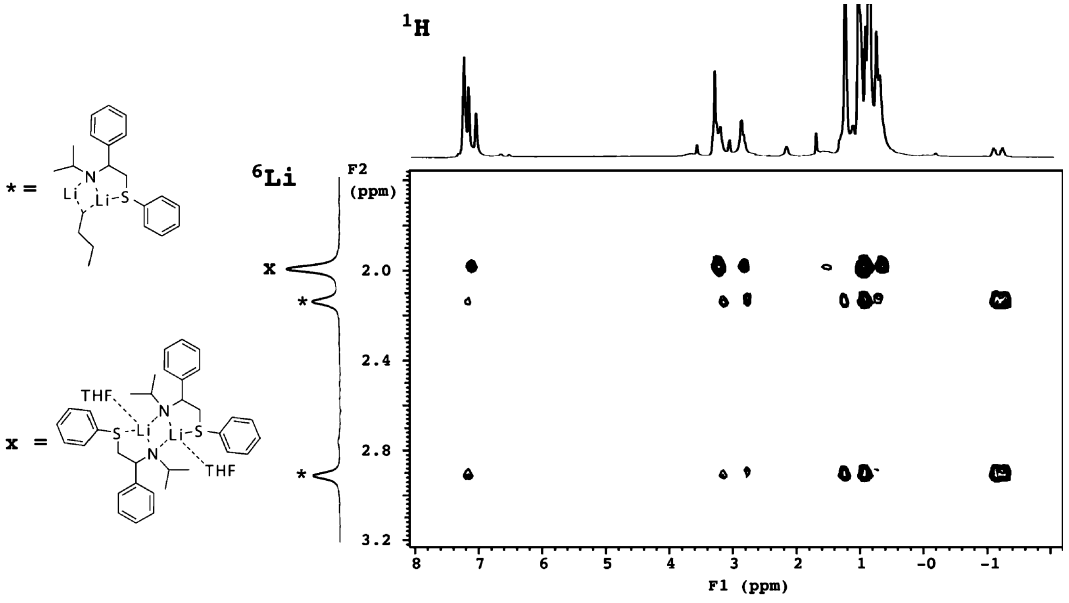


Figure 4. $^{6}Li,^{1}H$ HOESY spectrum of the mixture of (Li-**1**)$_2$ and Li-**1**/*n*-BuLi in 600 μL Et_2O-d_{10} and 200 μL THF-d_8 at −70 °C.

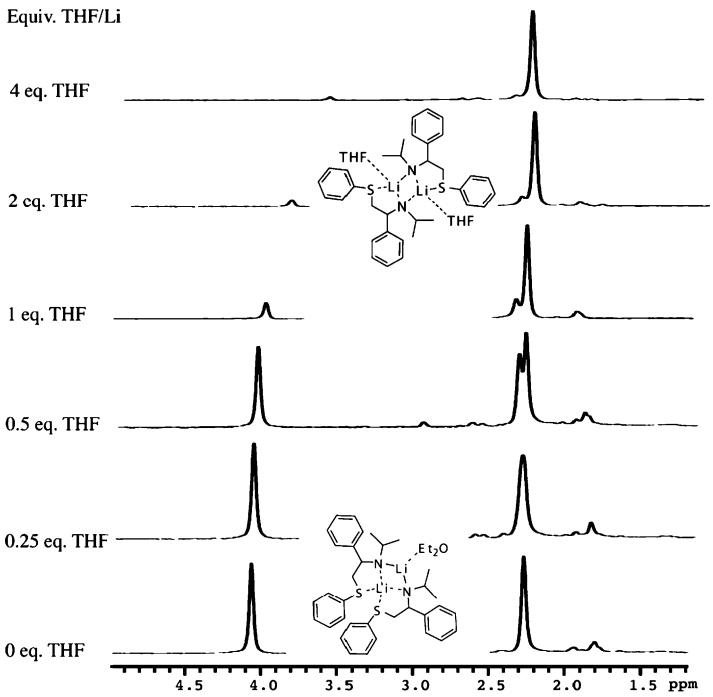


Figure 5. Titration of THF to non-eq-(Li-**1**)$_2$ in Et_2O at −78 °C.

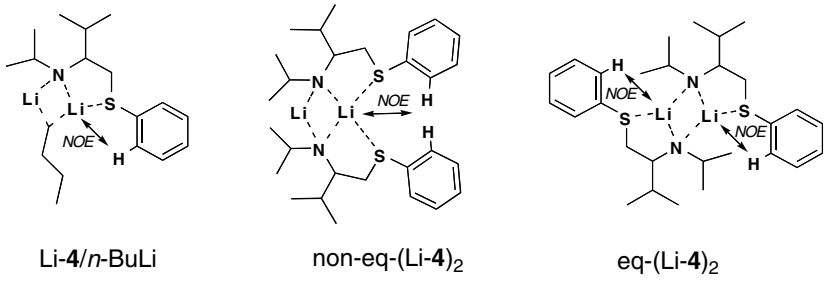
aromatic group should be in close proximity of the lithium. The ^{6}Li,^{1}H HOESY experiments of both Li-**4**/*n*-BuLi and (Li-**4**)$_2$, in Et_2O as well as in THF, successfully reveal strong NOE's between the deshielded lithium signal and the aromatic protons (see Scheme 2).

Thus, the deshielded lithium signal of non-eq-(Li-**4**)$_2$ must be from the lithium close to the sulfide. This shows that the mixed dimeric complex contains internal sulfide coordination of lithium in both Et_2O and THF at low temperatures, similar to that of lithiated amido ethers. In these complexes, the solvent exposed lithium appears more shielded in the ^{6}Li spectra while the more deshielded signal is assigned to the lithium coordinated by sulfide.

2.2. Computational studies

Different aggregates of the lithium amide Li-**3** have been investigated computationally at the B3LYP/6-31G(d) level of theory using G98 program.[10] The monomeric aggregate of Li-**3**, eq-(Li-**3**)$_2$ and non-eq-(Li-**3**)$_2$, with and without specific solvation by one or two solvent molecules (Et_2O or THF) were investigated. The calculations show that in the absence of specific solvation the eq-(Li-**3**)$_2$ is strongly favoured over the monomer by 41.7 kcal mol^{-1} and that the non-eq-(Li-**3**)$_2$ is 3.8 kcal mol^{-1} less stable than the eq-(Li-**3**)$_2$ (Table 3). When specific solvation of the lithiums in the different aggregates was included, the non-eq-(Li-**3**)$_2$ coordinated by one Et_2O molecule is favoured by 0.5 kcal mol^{-1} over the eq-(Li-**3**)$_2$ coordinated by two Et_2O molecules (Table 3 and Scheme 3). Attempts to find the non-eq-(Li-**3**)$_2$ solvated with two Et_2O molecules, only led to the dissociation of Et_2O from the lithium amide.

Upon solvation by THF instead of Et_2O, the most stable structure is eq-(Li-**3**)$_2$, each of the lithiums being solvated by one THF molecule and a sulfide, fully in agreement with the NMR results. The THF-solvated eq-(Li-**3**)$_2$ is lower in energy than the Et_2O-solvated non-eq-(Li-**3**)$_2$, which is in agreement with the experimental results that show that the lithium amide changes from the non-eq-(Li-**3**)$_2$ in Et_2O to the eq-(Li-**3**)$_2$ upon addition of THF (Scheme 3). Surprisingly, a THF



Scheme 2. NOE interactions between the lithium and the aromatic protons of Li-**4**/*n*-BuLi, non-eq-(Li-**4**)$_2$ and eq-(Li-**4**)$_2$.

Table 3. DFT calculated energies (B3LYP/6-31G(3)) of the monomers and the dimers of Li-**3**, both unsolvated and solvated by Et_2O and THF

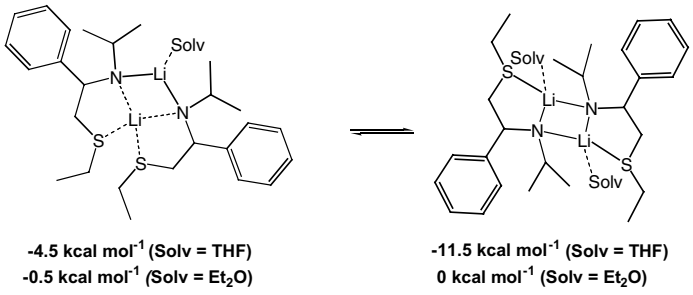
Aggregate	E/Hartree	Relative energy/ kcal mol^{-1}
Li-**3**	−967.9181618	57.7
Li-**3**·THF	−1200.399025	18.3
Li-**3**·$(THF)_2$	−1432.865199	−2.68
Li-**3**·(Et_2O)	−1201.608964	23.4
Li-**3**·$(Et_2O)_2$	−1435.280946	12.7
Eq-(Li-**3**)$_2$	−1935.902694	16.1
non-eq-(Li-**3**)$_2$	−1935.896708	19.8
eq-(Li-**3**)$_2$·THF	−2168.366229	7.25
eq-(Li-**3**)$_2$·$(THF)_2$	−2400.827228	0
eq-(Li-**3**)$_2$·Et_2O	−2169.572744	11.9
eq-(Li-**3**)$_2$·$(Et_2O)_2$	−2403.237091	11.4
non-eq-(Li-**3**)$_2$·THF	−2168.366742	6.9
non-eq-(Li-**3**)$_2$·$(THF)_2$	−2400.818797	5.29
non-eq-(Li-**3**)$_2$·Et_2O	−2169.574463	10.9

disolvated monomer is calculated to be of similar relative potential energy as the THF solvated dimer. This indicates that monomers and dimers are of similar energy and may coexist in solution even if the experiments did not detect any monomers. However, monomers of similar chiral lithium amides have previously been observed in THF solution.[11]

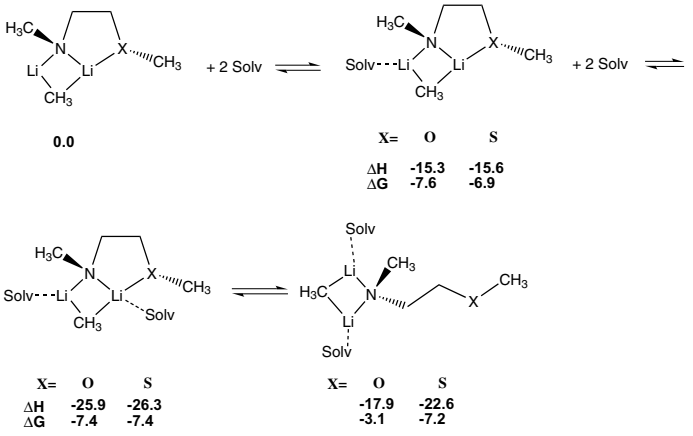
The difference in strength of the internal coordination between the amido sulfide mixed dimers and amido ether mixed dimers was investigated at the B3LYP/6-31G(d) level of theory (see Scheme 4). Both the enthalpic and the entropic contributions to the overall strength of the internal coordination were determined. Methyllithium was used as model for BuLi in the mixed dimers with the amido ethers and amido sulfides. Dimethyl ether was used as model for the coordinating solvent (THF and Et_2O).

The calculations show that both the relative enthalpy as well as the free energy of solvation, with one dimethyl ether molecule to the amido sulfide mixed dimers and amido ether mixed dimers, is favoured. The relative enthalpy for coordination of a second dimethyl ether is still somewhat exothermic for both the ether and the sulfide mixed dimers. However, the Gibbs free energy for the coordination of a second solvent molecule is positive for the ether but slightly negative for the sulfide complex. Apparently, there is a significant entropic cost associated with the coordination of the second ether to the mixed complexes at 298 K.

The relative Gibbs free energy cost for breaking the internal ether and sulfide coordination in the solvated mixed complexes, coordinated by two solvent molecules



Scheme 3. The most stable dimers of the amido sulfide non-eq-(Li-**3**)$_2$ and eq-(Li-**3**)$_2$ solvated by THF and Et_2O with the calculated potential energies.



Scheme 4. Calculated relative energies (ΔH and ΔG) for the mixed solvated complexes.

and the internal coordinating ether or sulfide, is 4.3 and 0.2 kcal mol^{-1}, respectively. This indicates that the intramolecular Li–S coordination is significantly weaker than the Li–O analogue. This result is in agreement with the HSAB principle.

3. Conclusion

In this structural investigation we chose to study the chiral lithium amide Li-**1**, which previously had been found to give the highest enantioselectivity, (98.5% ee) in the addition of *n*-BuLi to benzaldehyde, among a number of sulfur amides.[1] The other amides Li-**2**, Li-**3** and Li-**4** were also studied by NMR to aid the structural investigations of the lithium–sulfur coordination. However, all of these amides are known to give high enantioselectivity in the addition reaction.

We conclude that all these amides form mixed complexes with *n*-BuLi in Et_2O as well as THF, similar to those formed by lithium amides containing ether groups. Homodimeric lithium amides with one of the lithiums coordinated by the sulfides are formed in Et_2O, while eq-dimers are formed when THF is added. Sulfur is generally considered to be less electronegative than oxygen and it is therefore surprising that the sulfide–lithium chelate persists in the strongly coordinating solvent THF. In the addition of alkyllithium to aldehydes lithium amides with sulfide groups produce significantly higher ee's than their ether analogues. Although sulfide and ether chelates form similar mixed complexes with *n*-BuLi, the differences between the S–Li and O–Li interactions, such as bond lengths and electronegativity, affects both the geometry and reactivity of the mixed complex. This is illustrated by the computational studies, which clearly points out that although the internal S–Li interaction is strong enough to compete with the THF solvation in the initial state, it is a weak interaction compared to that of ether chelates. The transition state of the asymmetric alkylation may be favoured by weak internal coordination. The gained enantioselectivity from the development of ether chelates to sulfide chelates shows how important the coordinating groups are in chiral amides for asymmetric synthesis. Since the selectivity of the addition of alkyllithium to aldehydes is favoured by S–Li interactions, it is most probable that other metal ligands may be improved by changing ethers into sulfides without disrupting the structure of the aggregate. In a related reaction, the addition of Et_2Zn, Andersson et al. have reported that both the rate of addition and the stereoselectivity was increased using chiral thiols instead of chiral alcohols.[5]

4. Experimental

Glassware and syringes were dried at 50 °C in a vacuum oven before transfer into a glove box (Braun equipped with a gas purification system that removes oxygen and moisture) containing a nitrogen atmosphere. Typical moisture content was less than 1.5 ppm. Ether solvents, distilled under nitrogen from sodium and benzophenone, were kept over 4 Å molecular sieves in septum sealed flasks inside the glove box.

4.1. Preparation of amines 1, [^{15}N]-2, 3 and 4

The chiral amino sulfides **1**, **3** and **4** were prepared according to published methods.[1] The ^{15}N-labelled amine **2** was prepared from [^{15}N]-phenylalanine following the procedure for the preparation of **2**.[1]

4.2. In situ generation of the chiral lithium amido sulfides Li-1, Li-2, Li-3 and Li-4

The chiral lithium amido sulfides generated directly in the NMR tube from the chiral amines and *n*-BuLi. After the experiments the solutions containing the lithium amido sulfides were quenched with D_2O and analyzed by a gated decoupled ^{13}C NMR experiment. The obtained spectrum showed no sign of any deuterated carbons, indicating that the lithiation of the amine exclusively occurred on the nitrogens.

4.3. NMR instrumental

All NMR spectra were recorded using a Varian Unity 500 spectrometer equipped with three channels using a 5 mm ^{1}H, ^{13}C, ^{6}Li triple resonance probe head, built by the Nalorac Company. Measuring frequencies were 500 MHz (^{1}H), 125 MHz (^{13}C) and 73 MHz (^{6}Li). The ^{1}H and ^{13}C spectra were referenced to the solvent diethyl ether-d_{10} signals at δ 1.06 (^{1}H–CH_3) and δ 65.5 (^{13}C–CH_2), and the THF-d_8 signals at δ 1.72 (^{1}H–CH_2) and δ 67.6 (^{13}C–CH_2), respectively. Probe temperatures were measured after more than one hour of temperature equilibrium with the standard methanol thermometer supplied by Varian instruments. ^{6}Li,^{1}H HOESY experiments were performed with $\tau_M = 1.0$ s in both THF and Et_2O. For further data of the ^{6}Li,^{1}H HOESY experiments, see previous studies.[7]

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