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Studies of Complexes between Phenyllithium and (−)-Sparteine in Ether Solutions

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NMR studies and DFT chemical shift calculations of (−)-sparteine−phenyllithium (PhLi) complexes are reported. It is found that PhLi forms a tetrameric ladder complex in diethyl ether (Et_2O) solution complexed by (−)-sparteine. The tetrameric ladder core is terminated by (−)-sparteine ligands. Tetrahydrofuran (THF) coordinates more strongly to PhLi than (−)-sparteine; thus in THF solvent only the THF-solvated PhLi dimers are observed, while (−)-sparteine is free in solution. However, addition of substoichiometric quantities of THF to the Et_2O solution of the (−)-sparteine-solvated PhLi ladder tetramer results in PhLi dimers solvated by one (−)-sparteine and one THF molecule. GIAO DFT calculations on model systems at the B3LYP(6-311+G(d,p))//B3LYP(6-31+G(d) level of theory provide details regarding the solvation at lithium in these complexes, which supports the NMR results.

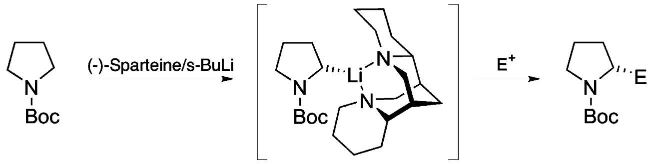
Introduction

The chiral diamine (−)-sparteine has been used extensively as chiral inducer together with various organometallic reagents by Hoppe and Beak in numerous stereoselective lithiation/substitution reactions.[1−4] In particular the mixture of *sec*-butyllithium (*s*-BuLi) and (−)-sparteine can be used for asymmetric substitution of, for example, Boc-pyrrolidine by a stereoselective deprotonation, Scheme 1.

Beak and co-workers have reported on a surprisingly large solvent dependence on the selectivity, a result that indicates that the equilibrium between different complexes of alkyllithium/(−)-sparteine is strongly solvent dependent.[3] It is commonly believed that the addition of a diamine such as (−)-sparteine to an alkyllithium reagent would deaggregate larger complexes such as tetramers or hexamers to, for example, (−)-sparteine-complexed dimers. Hoffman and Collum have reported that (−)-sparteine added to a toluene solution of *n*-butyllithium (BuLi) results in a dimeric complex i.e., [(BuLi)/(−)-sparteine]$_2$, with a (−)-sparteine diamine molecule coordinated to each of the two lithiums.[5]

Although mixtures of alkyllithiums and (−)-sparteine have been successful in asymmetric deprotonation reactions, the use of aryllithiums has not received much attention. In contrast (−)-sparteine-mediated addition of PhLi to various electrophiles generally procceds in similar or higher stereoselectivity than the corresponding addition of, for example, *n*-BuLi or methyllithium (MeLi). The first example of asymmetric addition of PhLi to aldehydes and ketones was reported by Nozaki and co-workers in 1970,[6] although the selectivity was low (1−4% ee). Later there have been numerous reports on asymmetric addition of PhLi/(−)-sparteine to, for example, imines,[7] prochiral arenes,[8] quinolines,[9] ferrocenes,[10] aminofulvenes,[11] and nitroalkenes.[12] There are also reports on the use of PhLi/(−)-sparteine in asymmetric substitution reaction with acetals.[13] Generally the addition reactions are conducted at −78 °C in toluene solution, but based on literature data the stereoselectivity is not lost in Et_2O solution, while in THF solution the selectivity is significantly lower.[3]

Scheme 1



A few NMR and X-ray studies of PhLi and its analogues have been reported. In the solid state PhLi has been found to exist as monomers, with the lithium solvated by a PMDTA,[14] as dimers with each lithium solvated by a TMEDA,[15] and as a cubic tetramer with each lithium solvated by either Et_2O[16] or Me_2S.[16] From solution NMR studies, mainly by Reich and co-workers, it has been verified that PhLi exists as monomers,

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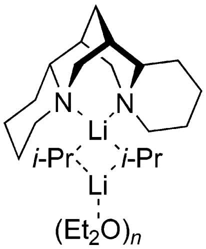

Figure 1. Structure of [(i-PrLi)$_2${(−)-sparteine}(Et_2O)$_n$] (**1**) as proposed by Beak and co-workers based on ^{6}Li and ^{13}C NMR spectroscopy at low temperatures.

dimers, and/or tetramers depending on solvent and/or additives.[17] Already in 1992 Beak and co-workers studied mixtures of (−)-sparteine and isopropyllithium (*i*-PrLi) by NMR at low temperature.[18,19] At that time they suggested, based on ^{13}C, ^{6}Li, and ^{6}Li,^{6}Li-COSY NMR experiments, that a mixed complex (i-PrLi)$_2$/(−)-sparteine/Et_2O is formed, consisting of two *i*-PrLi, one (−)-sparteine, and one or two Et_2O molecules; see Figure 1.

Previously we have reported that PhLi and (−)-sparteine form a mixed complex that precipitates from Et_2O solution.[20] The solid-state structure was determined to be [(PhLi)$_4${(−)-sparteine)}$_2$] (**2**). It has a “ladder-type” tetrameric core with one (−)-sparteine coordinated to each of the two terminal lithiums; see Figure 2. Strohmann and co-workers reported a few years ago on a tetrameric PhLi ladder structure, [(PhLi$_4${(+)-sparteine surrogate}$_2$)] (**3**), i.e., coordinated by two (+)-sparteine surrogate ligands; see Figure 2.[21] Interestingly, these structures differ in the arrangement of the PhLi core; in **2** the ladder forms the beginning of a helix, while in **3** the ladder is in a “zigzag” arrangement.

Strohmann and co-workers have reported on the solid-state structure of some alkyllithiums solvated by (−)-sparteine, i.e., [(isopropyllithium)$_2$/(−)-sparteine/Et_2O] and [(BuLi)/(−)-sparteine]$_2$.[22] Recently they also reported on the crystal structure of [(PhLi)$_2${(−)-sparteine}$_2$] (**4**).[23] They found that by mixing PhLi with (−)-sparteine two different crystals are formed, the dominating one being complex **2**, and the minor structure is the smaller complex **4**. There is much steric hindrance in complex **4**, which is suggested to be the reason for its lower amount in the solid.

Previously Kwon and co-workers have studied various unsolvated PhLi complexes by DFT methods;[3,24] however they did not take into account specific solvent coordination. Recently Maddaluno and co-workers employed DFT methods to study some PhLi dimers, particularly mixed complexes, although specific solvation was not studied in detail.[25] We recently reported that a solvation number of three and four at lithium is common among lithium amides in solution, as based on NMR studies.[26] On the basis of DFT energies alone it can be difficult to account for the correct number of solvent molecules coordinated to, for example, lithium cations, as recently discussed by Pratt.[27]

Intrigued by the crystal structures, we set out to investigate the solution structure of PhLi in the precence of (−)-sparteine. Herein we report on NMR studies (^{1}H, ^{6}Li, and ^{13}C NMR) and the results of DFT chemical shift calculations of the *ipso*-carbons of different PhLi solvates with TMEDA and dimethyl ether (Me_2O) respectively as models for (−)-sparteine and ethers (Et_2O and THF).

Experimental Section

Glassware and syringes were dried at 50 °C in a vacuum oven before transfer into a glovebox (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. All manipulations concerning the addition reactions were carried out using gastight syringes. Ethereal solvents, distilled under nitrogen from sodium and benzophenone, were kept over 4 Å molecular sieves in septum-sealed flasks inside the glovebox. (−)-Sparteine was distilled from CaH_2.

NMR Preparation and Studies. Ph[^{6}Li] was prepared according to the method of Reich and co-workers.[16] Crystals of pure Ph[^{6}Li] were dissolved in Et_2O. Typically 70 μL of a 1.5 M solution of Ph[^{6}Li] in protonated Et_2O was added to an NMR tube loaded with 700 μL of Et_2O-d_{10} (i.e., 0.15 M PhLi).

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 NMR spectra were referenced to the solvent Et_2O-d_{10} signals at δ 1.06 (^{1}H, $-CH_3$) and 65.5 (^{13}C, $-CH_2$) and the THF-d_8 signals at δ 1.72 (^{1}H, $-CH_2$) and 67.6 (^{13}C, $-CH_2$), respectively. For the ^{6}Li,^{1}H-HOESY spectrum the following parameters were used: spectral width of 2000 Hz ($f_2 = {}^6$Li) and 8000 Hz ($f_1 = {}^1$H); 96 increments and 32 scans per increment in t_1; mixing time 1.0 s; relaxation delay 8 s; sine-bell weighting in f_1 and f_2 for the phase-sensitive spectrum; 26 μs proton 90° decouple pulse. The ^{6}Li,^{6}Li-EXSY spectra were obtained and processed with the following parameters: spectral width of 1000 Hz (f_1 and f_2); 256 increments and 8 scans per increment in t_1; one time zero filling in f_1 and f_2; mixing time 3 s; no proton decoupling; absolute value data that were processed with exponential line broadening without symmetrization.

Computational Methods. The complexes of PhLi and (−)-sparteine in ether were also investigated using computational methods. All calculations were performed on a standard desktop computer with a P4 3200 MHz using the Gaussian program package.[28] NMR shielding tensors were calculated with the gauge-independent atomic orbital (GIAO) method within the Gaussian program package. Geometries were optimized without symmetry at the B3LYP/6-31+G level of theory and showed no negative frequencies. Energies and NMR shieldings were calculated at the B3LYP/6-311+G(d,p) level of theory using the B3LYP/6-31+G-optimized geometries.

Results and Discussion

NMR Studies of PhLi upon Addition of (−)-Sparteine in Et_2O-d_{10}. At −100 °C dimers and tetramers of PhLi are

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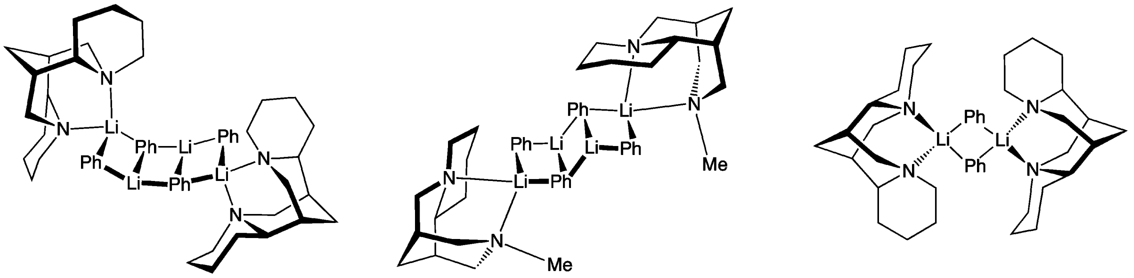
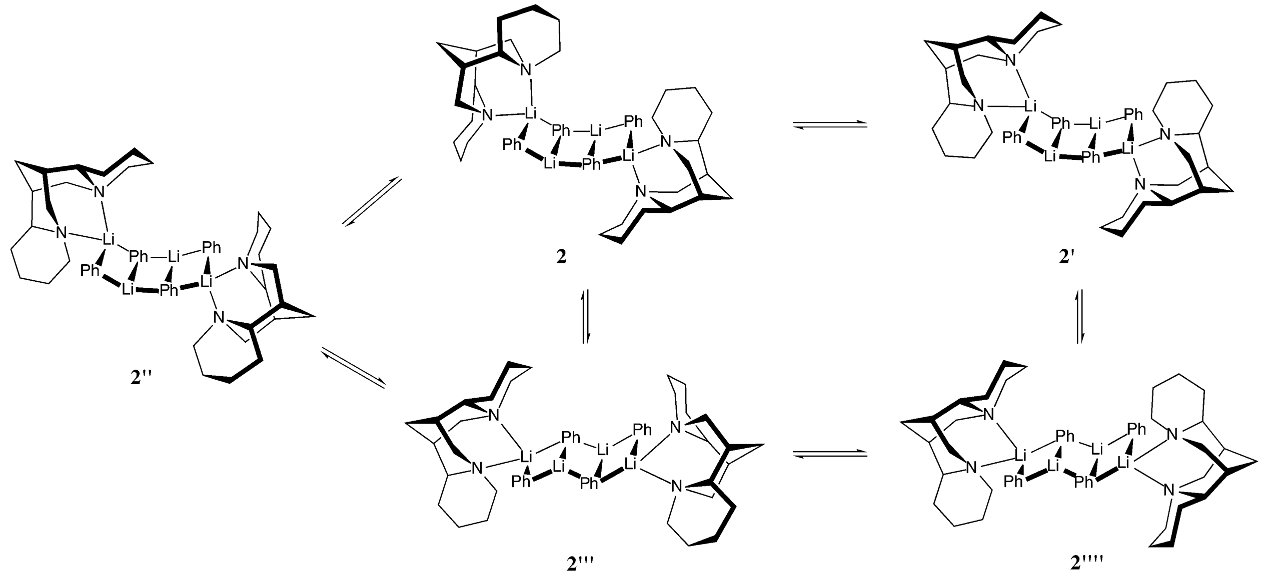


2 **3** **4**

Figure 2. Schematic representations of the crystal structures of [$(PhLi)_4$\{(−)-sparteine\}$_2$] (**2**), [$(PhLi)_4$\{(+)-sparteine surrogate\}$_2$] (**3**), and [$(PhLi)_2$\{(−)-sparteine\}$_2$] (**4**).

Scheme 2. Chemdraw Structures of the Five Possible Stereoisomers/Conformers of 2, 2′, 2″, 2‴, and 2⁗



observed for the 130 mM solution of PhLi in Et_2O, in agreement with other studies.[17] The ^{6}Li NMR signals for Et_2O-solvated dimeric PhLi and tetrameric PhLi are observed at δ 1.6 and 2.4.

New signals are observed in the ^{1}H, ^{13}C, and ^{6}Li NMR spectra upon addition of 10 μL or 0.5 equiv of (−)-sparteine (approximately 65 mM) per PhLi. The ^{6}Li NMR spectra at −90 °C show two signals in a 1:1 ratio at δ 1.99 and 2.30, from PhLi complexed by (−)-sparteine. The 1:1 ratio of these signals is temperature independent (±0 to −110 °C), but at higher temperatures the signals are significantly broadened, presumably due to intraaggregate exchange. The significantly different shifts of the two lithium signals indicate different solvation; that is, one lithium is solvated by (−)-sparteine while the other lithium is either unsolvated or solvated by Et_2O. In addition the ^{13}C NMR spectra at −90 °C reveal two PhLi *ipso*-carbon signals in a 1:1 ratio. There are no signals observed for free uncomplexed (−)-sparteine, indicating that all (−)-sparteine is complexed to PhLi or that there is a fast exchange between lithium-coordinated and free (−)-sparteine.

Upon further addition of (−)-sparteine in the range of 0.1 to 0.5 equiv per PhLi, the ^{13}C NMR signals from free (−)-sparteine increase without any observable shift change; thus they are not from time-averaged signals of coordinated and free (−)-sparteine. In addition the single set of signals for complexed (−)-sparteine establishes that there is only one dominating complex on the NMR time scale in solution for mixtures of (−)-sparteine and PhLi in Et_2O.

Altogether, this indicates the presence of a C_2-symmetric complex, which could either be [$(PhLi)_2$\{(−)-sparteine\}$(Et_2O)_n$] (**5**) analogous to the *i*-PrLi complex (**1**) reported by Beak and co-workers, or it could be a ladder-type tetrameric complex, similar to the solid-state structure **2**. Either the PhLi core could form the beginning of a helix as in the solid-state structure of **2**, or it could form a regular ladder as in the analogues solid-state structure of PhLi complexed with surrogate (+)-sparteine (**3**), reported by Strohmann and co-workers.[20,21] Considering the asymmetry of (−)-sparteine, there are in total four possible solvates (**2**, **2′**, **2″**, **2‴**, and **2⁗**) for five PhLi's complexed by two sparteine ligands, Scheme 2.

It has previously been established that the rotation of a diamine, such as TMEDA, complexed to a lithium cation is

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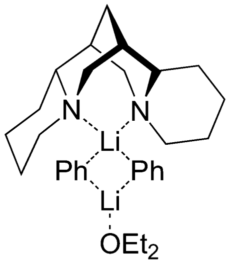

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Figure 3. Chemdraw representation of[$(PhLi)_2$\{(−)-sparteine\}-(Et_2O)] (**5**).

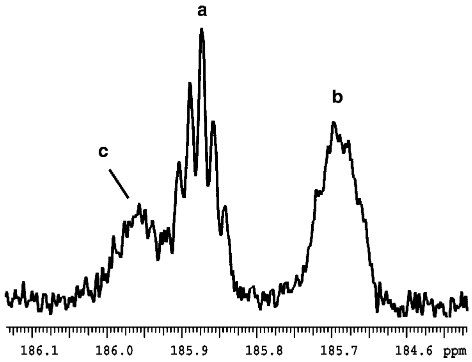

Figure 4. Downfield region of the ^{13}C NMR spectrum of a 100 mM Ph[^{6}Li] and 40 mM (−)-sparteine solution in Et_2O at −90 °C. The two signals a and b are from the two nonequivalent *ipso*-carbons of either **4** or **2**. The unresolved signal c at 185.95 is from the *ipso*-carbon of Et_2O-solvated dimeric PhLi.

slow at temperatures below −70 °C on the NMR time scale.[29] Thus the interconversion between the different stereoisomers/conformers of **2** (i.e., **2**, **2′**, **2″**, **2‴**, and **2⁗**) is likely to be slow on the NMR time scale. Furthermore, as PhLi and (−)-sparteine form the ladder-type complex **2** in the solid state, it is unlikely that a different isomer predominates in solution.

However, it is difficult to unambiguously determine the aggregation state of PhLi in Et_2O solution, Figure 3. The *ipso*-carbons of PhLi in the dimer should show coupling to two slightly different lithiums, and it may also give rise to two different *ipso*-carbon signals, due to the chiral (−)-sparteine. We anticipated that a ladder-type tetramer (of the type **2**) should give rise to a larger chemical shift difference between the two *ipso*-carbon signals. Furthermore, one of the *ipso*-carbon signals should show coupling to two different lithiums, while the other, on the central phenyl group, should couple to three lithiums, which should give rise to two significantly different ^{13}C,^{6}Li splitting patterns.

The ^{13}C NMR spectra of a 1:1 mixture of PhLi and (−)-sparteine in Et_2O-d_{10} obtained at −80, −90, and −100 °C show two major *ipso*-carbons for PhLi in a 1:1 intensity ratio, one 1:2:3:2:1 quintet at δ 185.9 ($^{1}J_{^{13}C,^{6}Li} = 8$ Hz) coupled to two lithiums and one unresolved multiplet at δ 185.7. In addition to the two larger *ipso*-carbon signals there is also a minor signal at δ 186.0 (Figure 4), which is assigned to the Et_2O-solvated PhLi dimer, since its intensity increases with addition of PhLi. At lower ratios of (−)-sparteine/Et_2O the Et_2O-solvated dimer of PhLi shows up as a well-resolved 1:2:3:2:1 quintet ($^{1}J_{^{13}C,^{6}Li} = 7.6$ Hz), in agreement with that reported by Reich and co-workers (Figure 4).[16]

Reich and co-workers have reported that the chemical shift of the *ipso*-carbon of PhLi is highly sensitive to aggregation. On the basis of the empirical relationship found by Reich, we could assign the chemical shift of these signals to the phenyl groups in dimeric aggregates. There are however also a number of other factors that can affect the chemical shift of the *ipso*-carbon of PhLi. Altogether, the large difference in splitting patterns of the *ipso*-carbon signals at δ 185.7 and 185.9 indicates a significant difference in their bonding to lithium. The ladder-type (−)-sparteine-solvated tetrameric PhLi core in Et_2O, as shown in Figure 2, can give rise to the observed signals.

The coordination number of lithium in organolithium complexes is generally three or four, the dimeric complex is expected to be solvated by one or two ether molecules, while such ether−lithium interactions may not be present in the tetrameric complex. One of the most powerful NMR spectroscopic techniques available for structure elucidation of organolithium compounds is the heteronuclear Overhauser effect experiment (^{6}Li,^{1}H-HOESY), introduced by Bauer et al.[30] We have extensively used HOESY experiments for the studies of various chiral mixed organolithium complexes.[31] A ^{6}Li,^{1}H-HOESY spectrum of the Et_2O-d_{10} solution containing PhLi and (−)-sparteine was collected at −100 °C; see Figure 5. The lithium signal at δ 1.99 shows strong NOEs to several proton signals of complexed (−)-sparteine, and the lithium signal at δ 2.30 shows strong heteronuclear NOEs only to the proton signals of the phenyl group. There is also a barely detectable NOE between the lithium at δ 2.30 and the protonated Et_2O protons at δ 3.4, not visible in Figure 5. This clearly indicates the formation of a tetrameric complex and not a dimeric complex. A dimeric complex should be expected to show a strong NOE between the lithium and the coordinating Et_2O ligand. Such coordination leads to a strong NOE between the lithium and protons.[31]

A small addition of THF to the ether solution of **2** results in a new, partially THF solvated mixed complex, [$(PhLi)_2$\{(−)-sparteine\}(THF)] (**6**), and THF-solvated dimeric PhLi, i.e., [$(PhLi)_2(THF)_2$] (**7**); see Scheme 3. Monomeric PhLi is obtained upon further additions of THF. Thus THF effectively competes with (−)-sparteine as ligand to lithium in these PhLi complexes, in contrast to the reports by Boche and co-workers in which TMEDA and (−)-sparteine coordinate to lithium in the presence of THF.[29,32] However, Boche and Hoppe with co-workers[33] have reported on (−)-sparteine-mediated asymmetric substitutions of C-lithiated substrates, which lost all stereoselectivity if performed in THF solution, indicating that (−)-sparteine is replaced by THF as ligand to lithium. Collum and co-workers have put much effort into clarifying the interplay between diamines and THF in the case of lithium amide solvation, and in most cases they find that THF solvation is dominating.[34] Previously we have also observed directly by NMR that THF coordinates more strongly than TMEDA.[35] Since there does not seem to be a general trend, it appears as if either THF or a diamine

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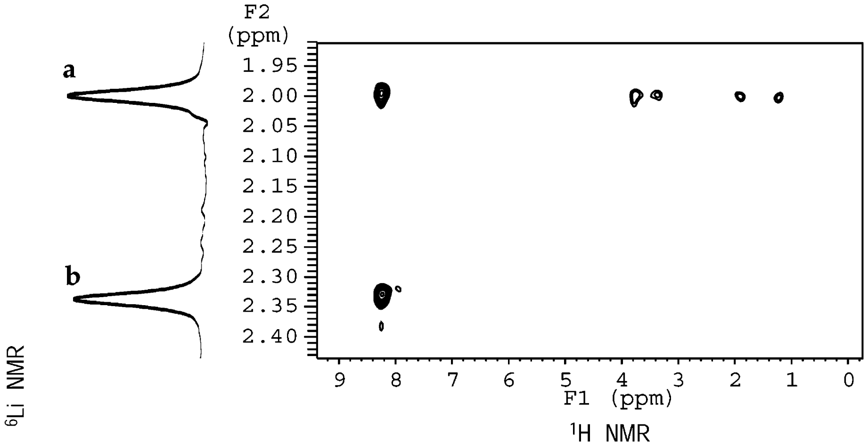
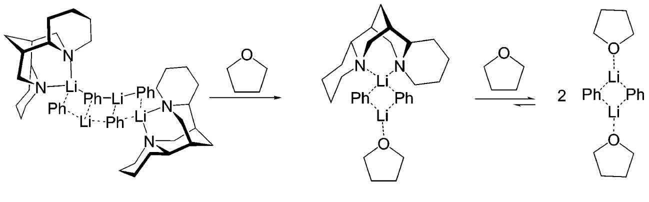


Figure 5. ^{6}Li,^{1}H-HOESY spectrum of a 100 mM PhLi and 40 mM (−)-sparteine solution in a mixture of Et$_2$O/Et$_2$O-d_{10} (1:12) at −90 °C. The two signals a and b are from the two nonequivalent lithiums of the [(PhLi)$_4${(−)-sparteine}$_2$] complex. Signal a is from the lithium coordinated to (−)-sparteine since it shows strong NOEs to the protons of the diamine.

Scheme 3. Small Addition of THF to the Solution of [(PhLi)$_4${(−)-sparteine)$_2$] (2) Results in the Mixed Complex of [(PhLi)$_2${(−)-sparteine}(THF)] (6); THF-Solvated Dimeric PhLi, i.e., [(PhLi)$_2$(THF)$_2$] (7), and Monomeric PhLi Are Obtained upon Further Additions of THF



2 **6** **7**

coordinates depending on the anion. With only 4 μL (0.48 mmol/61 mM or 0.5 equiv per PhLi) of THF added to the mixture of PhLi and (−)-sparteine in Et$_2$O three new ^{6}Li resonances, at δ 1.66, 1.87, and 2.15 with an approximately 1:1:1 ratio, were observed. The signal at δ 1.87 increased by further addition of THF, indicating that it is from a dimeric PhLi solvated only by THF.

The ^{6}Li,^{6}Li-EXSY experiment has previously been applied for the detection of intraaggregate ^{6}Li-exchange.[36] The ^{6}Li,^{6}Li-EXSY experiment also showed intraaggregate lithium exchange of the signals at δ 1.66 and 2.15 (Figure 6). The two lithium signals at δ 1.66 and 2.15 are assigned to the mixed complex **6**, in which one of the lithiums is solvated by (−)-sparteine and the other is solvated by one or two THF molecules.

A ^{6}Li,^{1}H-HOESY spectrum obtained for the solution of PhLi and (−)-sparteine in the presence of 6 μL of THF shows that the lithium signal at δ 2.15 corresponds to the (−)-sparteine-solvated lithium and that the lithium signal at δ 1.66 is from the THF-solvated lithium of the mixed complex **6** (Figure 7).

The ^{13}C NMR spectra display two overlapping but resolved quintets ($^{1}J_{^{13}\mathrm{C},^{6}\mathrm{Li}} \approx$ 8 Hz) at δ 187.6 and 187.7 from the nonequivalently solvated PhLi dimer, while the THF-solvated dimer appears as a quintet at δ 187.3 (Figure 8). Two different *ipso*-carbons of a nonequivalently solvated dimer of an organolithium compound with one coordinating (−)-sparteine have previously been observed. These carbon resonances differ in chemical shift by less than 0.1 ppm.[19]

Further addition of THF replaces (−)-sparteine completely (that is, THF competes readily with (−)-sparteine in coordinating to lithium). This explains the low selectivity generally observed with PhLi/(−)-sparteine in THF solution, since there can be no observable (−)-sparteine-solvated PhLi in a THF solution.

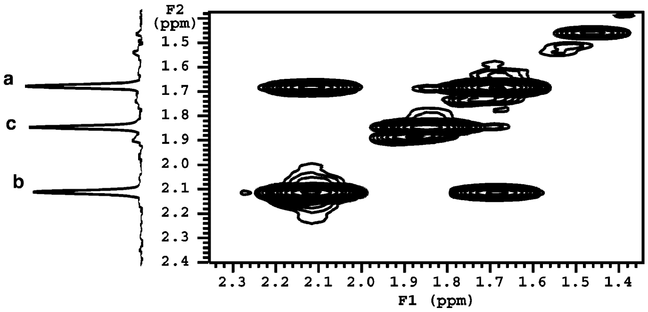


Figure 6. ^{6}Li,^{6}Li-EXSY (τ_m = 2.5 s) of the mixture of 100 mM PhLi and 40 mM (−)-sparteine with 4 μL of THF added to the Et$_2$O solution at −90 °C. The two exchanging signals a and b are from the two nonequivalent lithiums of [(PhLi)$_2${(−)-sparteine}(THF)] (**6**). The lithium signal c is from THF-solvated dimeric PhLi [(PhLi)$_2$(THF)$_2$] (**7**).

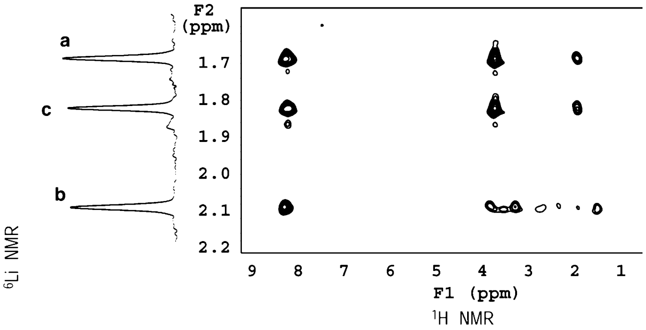


Figure 7. ^{6}Li,^{1}H-HOESY spectrum of 100 mM PhLi and 40 mM (−)-sparteine with 4 μL of THF added to the Et$_2$O solution at −90 °C. The two exchanging signals a and b are from the two nonequivalent lithiums of [(PhLi)$_2${(−)-sparteine}(THF)] (**6**). The lithium signal c is from THF-solvated dimeric PhLi [(PhLi)$_2$(THF)$_2$] (**7**).

DFT Calculations

The assignment of the structures in solution was strengthened using DFT computational methods. To validate the accuracy of the chemical shift calculations, we first set out to study simple PhLi solvates. Unsolvated (**8**), mono- (**9**), di- (**10**), and tri- (**11**) Me$_2$O-solvated PhLi monomers were all geometry optimized

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[36] (a) Bauer, W.; Fiegel, M.; Müller, G.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1988**, *110*, 6033. (b) Arvidsson, P. I.; Ahlberg, P.; Hilmersson, G. *Chem. Eur. J.* **1999**, *5*, 1348.

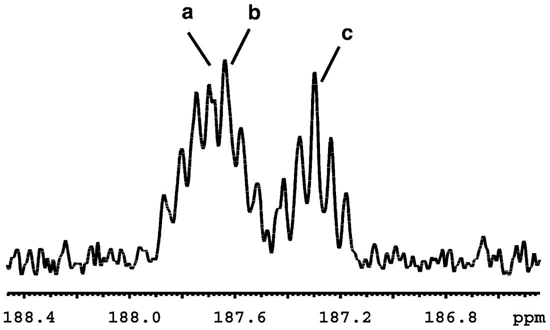
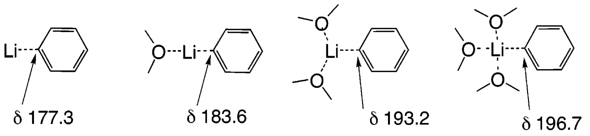
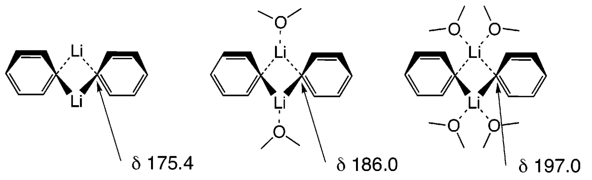


Figure 8. *ipso*-Carbon region of the ^{13}C NMR spectra for the mixture of 100 mM PhLi and 40 mM (−)-sparteine. The two exchanging signals a and b are from the two nonequivalent *ipso*-carbons of $[(PhLi)_2\{(-)\text{-sparteine}\}(THF)]$ (**6**). The *ipso*-carbon signal c at 187.3 is from the *ipso*-carbon of THF-solvated dimeric PhLi, i.e., $[(PhLi)_2(THF)_2]$ (**7**).



8 **9** **10** **11**

Figure 9. Calculated (B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d)) chemical shifts of the *ipso*-carbon of PhLi unsolvated and solvated by one, two, or three dimethyl ethers.



12 **13** **14**

Figure 10. Calculated (B3LYP/6-311+G(d,p)//B3LYP/6-31+G-(d)) chemical shifts of the *ipso*-carbon of PhLi dimers unsolvated and solvated by two and four Me_2O, respectively.

at the B3LYP(6-31+G(d)) level of theory, and the isotropic shifts of the *ipso*-carbon were calculated by B3LYP(6-311+G-(d,p)) and converted to chemical shifts using TMS as standard ($\delta = 0.0$). The calculated chemical shifts of the *ipso*-carbons of complex **8**, **9**, **10**, and **11** are given in Figure 9.

In addition we also optimized unsolvated (**12**), disolvated (**13**), and tetrasolvated PhLi dimers (**14**) and calculated the chemical shifts; the *ipso*-carbon chemical shifts are given in Figure 10. In the optimized structures the two lithiums are above and below the slightly distorted plane described by the phenyl rings.

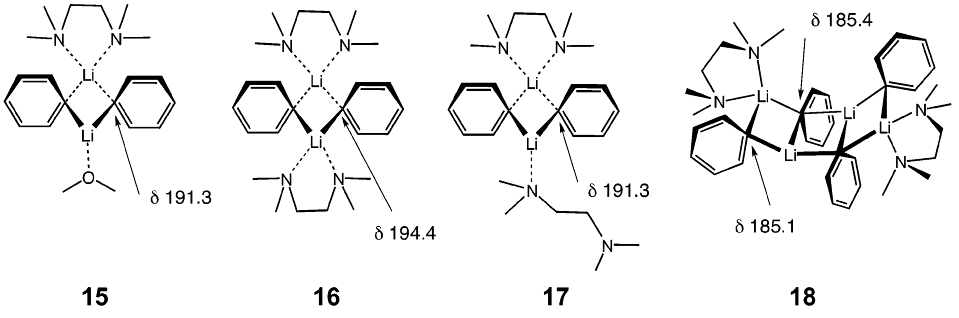
The calculated chemical shifts of the *ipso*-carbon appear to be sensitive to the solvation number at lithium, Figures 9 and 10. This indicates that the solvation number is at least as important for the chemical shift as the aggregation number reported by Reich.[16]

The reported chemical shift of the *ipso*-carbon for the THF-solvated PhLi monomer is 196 ppm, which is almost identical to 197 ppm, which we calculated for $[PhLi(Me_2O)_3]$ (**11**), Table 1.[16] This suggests that the PhLi monomer is mainly trisolvated in ether solution.

The two *ipso*-carbons of $[(PhLi)_2]$ (**12**) and $[(PhLi)_2(Me_2O)_2]$ (**13**) were calculated to have shifts of δ 175.4 and 186.0, respectively. For the PhLi dimer with each lithium solvated by two ethers, i.e., $[(PhLi)_2(Me_2O)_4]$ (**14**), we calculated the shifts as δ 197.0. Thus, the solvation number at lithium also strongly affects the chemical shift of the *ipso*-carbon, ranging about 11 ppm or from δ 186.0 to 197.0, by adding one solvent molecule to each lithium in $[PhLi(Me_2O)_2]$ (**10**). The experimentally observed chemical shifts of dimers of PhLi solvated by ethers are δ 188.0 and 187.2 respectively for Et_2O and THF.[16] The similarity between the observed and calculated chemical shifts suggests that PhLi dimers are solvated by only two molecules of THF or Et_2O; that is, the lithium is only tricoordinated.

The bidentate ligand TMEDA is known to form complexes with PhLi. Reich and co-workers report that dimers of PhLi are complexed with one TMEDA and one ether molecule, i.e., complex $(PhLi)_2/TMEDA/(THF)_n$ or $(PhLi)_2/TMEDA/(Et_2O)_n$ in solution.[17] The bis-TMEDA-solvated PhLi dimer, i.e., $(PhLi)_2/(TMEDA)_2$, has been crystallized by Thoennes and Weiss, and its structure was confirmed by X-ray analysis.[15] NMR studies by Reich and co-workers also indicate that the bis-TMEDA-solvated PhLi dimer exists in solution.[17] We calculated the carbon chemical shifts for model structures of various PhLi/TMEDA complexes to probe the accuracy of our computed chemical shifts (Figure 11). Both the mixed solvated dimer $[(PhLi)_2(Me_2O)(TMEDA)]$ (**15**) and the tetramer $[(PhLi)_4(TMEDA)_4]$ (**18**) were geometry optimized, and the chemical shifts of two *ipso*-carbons were calculated. The PhLi dimers complexed with two TMEDA ligands, i.e., complex **16** with two chelating TMEDA ligands (κ^2,κ^2) and complex **17** with one chelating TMEDA ligand (κ^2) and one TMEDA monocoordinated (κ^1 and κ^2) to lithium. The results are given in Table 2. Interestingly the *ipso*-carbon chemical shifts for these complexes are rather insensitive to solvation number, and they are all within 3 ppm. There is a very good agreement between the reported observed chemical shift of 190.7 ppm[17] and 191.8 ppm[17] for the dimers $(PhLi)_2/TMEDA/THF$ and $(PhLi)_2/TMEDA/Et_2O$ with the calculated chemical shift of 191.6 ppm for $[(PhLi)_2(Me_2O)(TMEDA)]$ (**15**), Table 1.

Furthermore, the chemical shifts for the *ipso*-carbons of PhLi/(−)-sparteine/Et_2O that we observed at 185.7 and 185.9 ppm are indeed almost identical to those calculated for $[(PhLi)_4(TMEDA)_2]$ (**18**) at 184.7 and 185.4 ppm. This strongly supports



15 **16** **17** **18**

Figure 11. Calculated (B3LYP/6-311+G(d,p)//B3LYP/6-31+G(d)) average chemical shifts of the *ipso*-carbon of PhLi dimers solvated by Me_2O and TMEDA (**15**) and two TMEDA (**16** and **17**) and PhLi tetramer solvated by two TMEDA (**18**), respectively.

Table 1. Reported and Calculated B3LYP(6-311+G(d,p)//6-31+G(d)) Chemical Shifts for the Various PhLi Solvates

entry	PhLi solvate	observed δ_{ipso} (^{13}C NMR)	calculated δ_{ipso} (^{13}C NMR)	energy (Hartree)
1	[PhLi] (**8**)		177.4	−239.203331004
2	[PhLi(Me_2O)] (**9**)		183.7	−394.312454568
3	[PhLi(Me_2O)$_2$] (**10**)		193.3	−549.411004168
4	[PhLi(Me_2O)$_3$] (**11**)		196.7	−704.499499011
5	PhLi/(THF)	196.4[a]		
6	PhLi/(PMDTA)	196.5[a]		
7	[(PhLi)$_2$] (**12**)		175.4	−478.478766526
8	[(PhLi)$_2$(Me_2O)$_2$] (**13**)		186.0	−788.685497974
9	[(PhLi)$_2$(Me_2O)$_4$] (**14**)		197.0	−1098.85602365
10	(PhLi)$_2$/(THF)	188.2		
11	(PhLi)$_2$/(Et_2O)	187.0		
12	[(PhLi)$_2$(Me_2O)(TMEDA)] (**15**)		191.3 191.8	−981.452385563
13	(PhLi)$_2$/TMEDA/Et_2O	191.8[a]		
14	(PhLi)$_2$/TMEDA/THF	190.7[a]		
15	PhLi/(−)-sparteine/Et_2O	185.7; 185.9		
16	PhLi/TMEDA (1:1)	187.3[b] 187.7[c]		
16	(PhLi)$_2$/TMEDA (1:1)	187.6[d]		
17	[(PhLi)$_2$(TMEDA)$_2$] (**16**)		194.4	−1174.23541080
18	[(PhLi)$_2$(κ^2-TMEDA)(κ^1-TMEDA)] (**17**)		190.2 192.4	−1174.22681765
19	[(PhLi)$_4$(TMEDA)$_2$] (**18**)		185.1 185.4	−1652.74965448
20	[(PhLi)$_4$(Me_2O)$_4$] (**19**)			
21	(PhLi)$_4$/Et_2O	174.0[a]		

[a] Reported by Reich and co-workers.[17] [b] Reported by Günther and co-workers.[30] [c] Reported by Fraenkel and co-workers.[31] [d] Reported by Collum and co-workers.[5b]

Table 2. Relative Energies for PhLi Solvates Computed at the DFT B3LYP(6-311+G(d,p)//6-31+G(d)) Level of Theory

entry	compound	electronic energy (Hartree)	relative energy (kcal mol^{-1})
1	Me_2O	−155.0770037	
2	TMEDA	−347.8466592	
3	[PhLi] (**8**)		0.0
4	[PhLi(Me_2O)] (**9**)		−40.3
5	[PhLi(Me_2O)$_2$] (**10**)		−67.4
6	[PhLi(Me_2O)$_3$] (**11**)		−81.8
7	[(PhLi)$_2$] (**12**)		−45.2
8	[(PhLi)$_2$(Me_2O)$_2$] (**13**)		−78.3
9	[(PhLi)$_2$(Me_2O)$_4$] (**14**)		−88.7
10	[(PhLi)$_2$(Me_2O)(TMEDA)] (**15**)		−76.6
11	[(PhLi)$_2$(TMEDA)$_2$] (**16**)		−85.0
12	[(PhLi)$_2$(κ^2-TMEDA)(κ^1-TMEDA)] (**17**)		−79.6
13	[(PhLi)$_4$(TMEDA)$_2$] (**18**)		−76.2

the conclusion that PhLi is a ladder-type tetramer not only when it is crystallized from a (−)-sparteine/Et_2O solution but also in Et_2O solution.

Interestingly the use of relative electronic DFT energies to predict the prevailing solvates does not give the same results as the chemical shifts do, Table 2. The electronic energies are inversely proportional to the number of ethers coordinated, indicating that the lithium cation is tetracoordinated in all structures. However, each specific coordination of a solvent molecule to a lithium cation is accompanied by a significant entropic cost. Thus, if free energies rather than electronic energies are considered, it is possible that the aggregates with a lower number of coordinated ethers may be energetically favored.

Conclusion

Addition of the bidentate ligand (−)-sparteine to an Et_2O solution of PhLi results in the formation of [(PhLi)$_4${(−)-sparteine}$_2$] (**2**), i.e., tetrameric ladder complexes of PhLi solvated by two (−)-sparteine molecules. The lithiums in the complex are not specifically solvated by Et_2O, since there are only weak heteronuclear NOEs observed between the lithium and the protons of Et_2O. Furthermore, the observed chemical shift of the *ipso*-carbon supports the formation of the ladder-type tetrameric PhLi. In addition, the calculated DFT chemical shifts of the *ipso*-carbons are almost identical to those observed by NMR for the mixture of PhLi and (−)-sparteine in Et_2O. Expected heteronuclear NOEs are also detected between protons and lithiums in the mixed complex. Altogether, the results strongly indicate that the tetrameric ladder-type complex of PhLi complexed by (−)-sparteine, previously observed in the crystal structure, is also present in solution. However in the presence of substoichiometric quantities of THF, which is a less sterically demanding ligand than Et_2O, complex **2** breaks down into mixed solvated dimeric PhLi, i.e., complex [(PhLi)$_2$(THF){(−)-sparteine}] (**6**). The observation that THF effectively replaces sparteine as ligand in aggregates of PhLi indicates that stereoselective PhLi/(−)-sparteine reactions can only be successful in Et_2O solution.

Supporting Information Available: Computational data (geometries, energies, and calculated GIAO nuclear magnetic shielding tensors (ppm) for complexes **8**−**18**). This information is available free of charge via the Internet at http://pubs.acs.org.

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