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Aggregation of Alkyllithiums in Tetrahydrofuran

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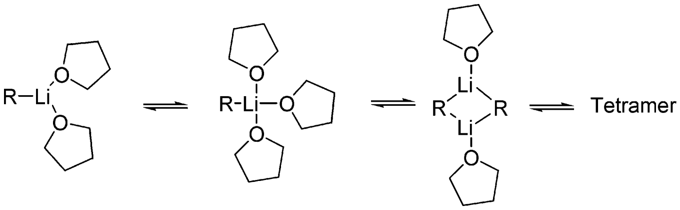

Density functional theory was used to examine the solvation number and aggregation state of several alkyllithium compounds in clusters with tetrahydrofuran molecules coordinated to each lithium atom. We then made the microsolvation approximation and approximated the bulk free energy of solvation by the free energy of clustering with solvent molecules in the gas phase. The trends in the computed results are in reasonable agreement with the available experimental data.

Introduction

Solvent effects are very important in organolithium chemistry. They dramatically influence the aggregation state and reactivity of alkyllithiums, lithium dialkylamides, and other organolithium compounds.[1−7] Hydrocarbon solvents involve little or no coordination to the lithium atoms, and the associated solvent effects consist primarily of dielectric polarization, dispersion interactions, and cavitation. Hexamethylphosphoramide (HMPA) is at the other extreme, coordinating so strongly to lithium that two-bond NMR spin coupling can be observed between lithium and phosphorus.[8,9] Ethereal solvents such as tetrahydrofuran (THF) are intermediate in their binding affinity for lithium. Rapid exchange of THF ligands prevents the observation of lithium−carbon spin coupling, although coordination of several ethers to lithium dialkylamides has been observed indirectly.[10,11]

A popular solvation model for lithium compounds is microsolvation by explicit coordinating ligands such as THF, oxetane, dimethyl ether, or trimethylamine.[4,5,12−15] The resulting "supermolecules" are presumed to serve as good models for the solution behavior of organolithium compounds. Although water has been occasionally used as a model ligand, it is a poor choice of model to represent ethers because of its higher dielectric constant and its propensity for hydrogen bonding. Dimethyl ether can also be considered as a model, but sterically (and perhaps electrostatically) it is a poor surrogate for THF. Another possible model would be an implicit solvation model employing a dielectric continuum,[16] but the use of such models with

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organolithium compounds is questionable because they may not reproduce the steric effects and specific interactions of coordinated ether ligands. Therefore the best choices appear to be the use of unsimplified explicit ethers, either alone (microsolvation) or combined with a continuum model to represent bulk solvent around the supermolecule (combined implicit−explicit model). The former choice is appealing because it is simpler, but a critical missing element in the use of the microsolvation models in organolithium chemistry to date is the systematic testing and validation against experiment. A key goal of the present study is to provide such validation for alkyllithiums in THF.

The aggregation states of several alkyllithiums have been determined experimentally,[17−19] and these results can be used to test the ability of theory to predict the extent of aggregation. Methyllithium has been found to be tetrameric in a 0.6 M solution in THF at 193 K.[17] In THF at 165−209 K, measurements and a paper by Bauer et al.[19] show that *n*-butyllithium is a dimer−tetramer mixture, *s*-butyllithium is a monomer−dimer equilibrium, and *t*-butyllithium is a monomer; typical concentrations for these measurements are 1.2−1.4 M. In cyclopentane, *n*-propyllithium is a mixture of hexamer, octamer, and nonamer.[18] Three lithium NMR signals have been observed for ethyllithium in a 1:1 mixture of THF and pentane at 158 K,[20] which presumably represent three different aggregates of yet undetermined structure. In cyclopentane, *s*-butyllithium is a mixture of diastereomeric tetramers and hexamers.[21] At 165 K, *t*-butyllithium is a dimer in diethyl ether and in a tetramer hydrocarbon solvents.[19]

We will compare the predictions of the microsolvation model to the experimental results in THF. Because most lithium NMR studies have been carried out at low temperatures, all calculations in this paper were carried out over a range of temperatures from 158 to 298.15 K. We seek to determine the number of coordinated THF ligands in each alkyllithium monomer and dimer and to determine the aggregation state of several alkyllithiums over this temperature range.

Computational Methods

All calculations were performed using Gaussian 98 or Gaussian 03.[22] The objective is to calculate the standard free energy of an alkyllithium solute, which is given by

$$G_T^{\mathrm{o}}\,(\mathrm{solute}) \rightarrow G_T^{\mathrm{o}}\,(\mathrm{gas}) + \Delta G_{\mathrm{S}}^{\mathrm{o}} \qquad (1)$$

where G_T^{o} (gas) is the standard gas-phase free energy at temperature T and $\Delta G_{\mathrm{S}}^{\mathrm{o}}$ is the standard free energy of solvation. The microsolvation model assumes that the latter is given by the free energy change when a gas-phase organolithium molecule $(\mathrm{RLi})_n$ is complexed by m explicit solvent ligands E (in this case THF)

$$(\mathrm{RLi})_n + m\mathrm{E} \rightarrow (\mathrm{RLi})_n\mathrm{E}_m \qquad (2)$$

In other words, the free energy of a gas-phase "supermolecule" $(\mathrm{RLi})_n\mathrm{E}_m$ relative to that of $(\mathrm{RLi})_n$ and m solvent molecules is assumed to yield the free energy of the solvated molecule $(\mathrm{RLi})_n$ in the condensed phase. The gas-phase free energies of the relevant species are calculated by

$$G_T^{\mathrm{o}}\,(\mathrm{gas}) = E_{\mathrm{EN}} + E_0^{\mathrm{vib}} + \Delta G_T^{\mathrm{o}} \qquad (3)$$

where the terms on the right-hand side as well as the procedure used for calculating them are described below.

The geometry of each molecule was first optimized using the B3LYP hybrid density functional method[23,24] with the MIDIX basis set.[25,26] A further refinement of the geometry and energy were done at the B3LYP/6-31+G(d)[27] level of theory. Then the terms in eq 3 are:

E_{EN} = the electronic energy plus nuclear repulsion of the equilibrium geometry, using B3LYP/6-31+G(d);

E_0^{vib} = unscaled B3LYP/MIDIX vibrational zero-point energy;

ΔG_T^{o} = B3LYP/MIDIX thermal corrections to the free energy for a standard state of 1 atm and specified temperature, which includes contributions from translational, rotational, and vibrational degrees of freedom;

ΔG^{o} = free energy changes for the "reactions" (dimerizations, tetramerizations, mixed aggregate formation, etc.) obtained as the sum of the G_T^{o} (gas) values of products minus those for reactants.

It is necessary to convert the usual gas-phase standard free energies, which correspond to a standard state 1 atm to the appropriate standard state for a solution, which is taken as 1 mol L^{-1}. The details of these conversions have been previously published.[28] These corrections amount to 0.80 kcal/mol at 158 K, 0.94 at 177 K, 1.06 at 193 K, 1.11 at 200 K, and 1.89 at 298 K. These conversion terms were included in all solution-phase reactions below.

Another conversion is required for proper treatment of the explicit solvent molecules used in microsolvation. The traditional approach is to set the standard state of a pure liquid to be the concentration of the pure liquid itself, which then allows one to drop the concentration of the pure liquid from equilibria expressions. In contrast, as an example, since we have decided to adopt the standard state of 1 mol L^{-1} for all species, the directly calculated free energy change for the process

$$2\mathrm{RLiE}_2 \rightarrow (\mathrm{RLiE})_2 + 2\mathrm{E} \qquad (4)$$

contains the concentration of E and is given by[29]

$$\Delta G^{\mathrm{o}} = -RT \ln \frac{[(\mathrm{RLiE})_2]}{[\mathrm{RLiE}_2]^2} - 2RT \ln[\mathrm{E}] \qquad (5)$$

where all concentrations are evaluated at equilibrium. (Recall that

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TABLE 1. Standard Third Solvation Energy (kcal/mol) of Alkyllithium Monomers (Eq 6)

RLi	158 K	177 K	193 K	200 K	298.15 K
MeLi	−4.35	−3.65	−3.06	−2.80	0.682
EtLi	−4.29	−3.60	−3.03	−2.78	0.607
s-BuLi	−1.81	−1.20	−0.695	−0.477	2.48
t-BuLi	−3.74	−3.20	−2.76	−2.57	−0.00534

TABLE 2. Standard Free Energy (kcal/mol) of Alkyllithium Dimer Tetrasolvate Formation (Eq 7)

RLi	158 K	177 K	193 K	200 K	298.15 K
MeLi	−6.31	−5.21	−4.32	−3.92	1.34
EtLi	−5.71	−4.68	−3.82	−3.44	1.52
s-BuLi	0.362	1.49	2.41	2.84	8.29
t-BuLi	5.27	6.50	7.51	7.95	13.9

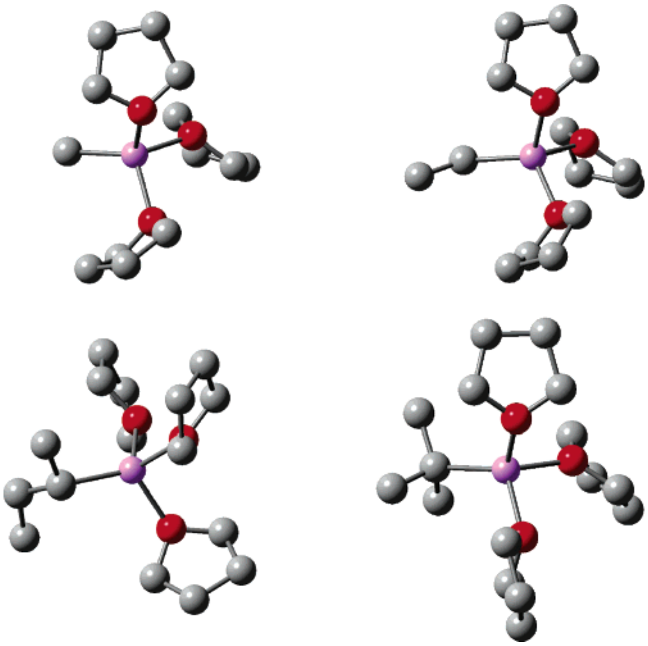

FIGURE 1. Optimized structures of THF trisolvated alkyllithium monomers. Top left, methyllithium; top right, ethyllithium; bottom left, *s*-butyllithium; bottom right, *t*-butyllithium. Note that hydrogen atoms are not depicted in the figures.

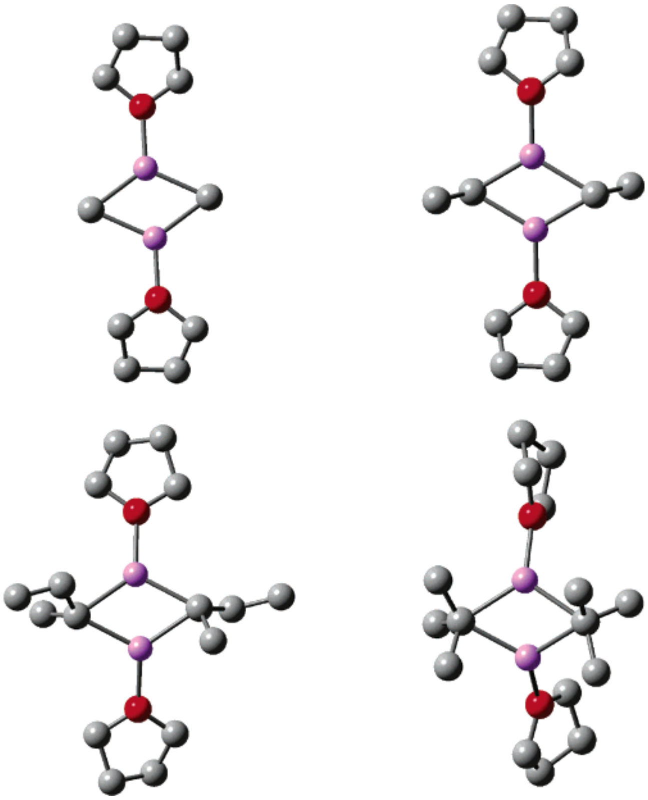

FIGURE 2. Optimized structures of THF disolvated alkyllithium dimers. Top left, methyllithium; top right, ethyllithium; bottom left, *s*-butyllithium; bottom right, *t*-butyllithium.

E is THF.) To evaluate the final term of eq 5, the molarity of the THF solvent was calculated at each temperature from its tabulated density.[30] The corrections due to the second term in the equation above are equal to −0.82, −0.91, −0.99, −1.03, and −1.49 kcal/mol per THF at 158, 177, 193, 200, and 298 K, respectively. These corrections were added to the directly calculated free energy changes for reactions in solution so that the standard free energy changes reported here correspond to the equilibrium constants as usually written, that is, without solvent concentrations. Thus, the $-2RT$ ln[THF] term in eq 5 will favor the disolvated monomer by 2.0546 kcal/mol at 200 K.

Basis set superposition errors (BSSE) can sometimes be significant when calculating aggregation energies. To try to correct for these errors counterpoise calculations were performed for each dimer and tetramer. The subunits were taken as the alkyllithium monomer units, each with its associated solvent ligands. Thus, the dimer was composed of two monomer units each with one THF ligand, and the tetramer contained 4 monomer units, each with one THF ligand.

Since free energies can be sensitive to the treatment of low-frequency vibrations, we repeated the dimerization energy calculations with the frequencies below 100 cm^{-1} raised to 100 cm^{-1} as a way to approximately account for anharmonieity. The difference was only a fraction of kcal/mol, so this correction was not included.

Each of the species examined can exist in numerous conformations, particularly the solvated systems. While it is not possible to examine every possible conformation, these often differ in energy from one another by only a fraction of a kcal/mol. The molecules were built in what appeared to be the lowest-energy conformation and optimized. Sometimes it was necessary to optimize more than one similar conformation and then choose the one that was lowest in energy, or to re-optimize a “transition structure” corresponding to a single bond rotation, thus locating a lower energy conformation.

Results and Discussion

Methyllithium, ethyllithium, *s*-butyllithium, and *t*-butyllithium were chosen for study because of the availability of experimental data for comparison. Because the alkyllithium monomers and dimers will be used in subsequent calculations to determine the aggregation states, it is necessary to know how many THF ligands are coordinated to those species. The monomer could accommodate up to 3 solvent ligands, and the dimer could

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TABLE 3. Standard Free Energies (kcal/mol) of Alkyllithium Dimerization from Disolvated Monomers (Eq 4)

RLi	158 K	177 K	193 K	200 K	298.15 K
MeLi	−7.26 [−5.55][a]	−7.50 [−5.80]	−7.70 [−6.00]	−7.79 [−6.08]	−8.89 [−7.18]
EtLi	−8.04 [−6.31]	−8.40 [−6.67]	−8.70 [−6.97]	−8.84 [−7.11]	−10.6 [−8.83]
s-BuLi	−1.76 [0.367]	−2.11 [0.0153]	−2.41 [−0.277]	−2.55 [−0.420]	−4.24 [−2.11]
t-BuLi	−1.23 [0.763]	−1.62 [0.372]	−1.95 [0.0462]	−2.09 [−0.0931]	−4.00 [−2.00]

[a] Values in brackets are counterpoise corrected.

TABLE 4. Standard Free Energies (kcal/mol) of Alkyllithium Dimerization from Trisolvated Monomer (Eq 8)

RLi	158 K	177 K	193 K	200 K	298.15 K
MeLi	1.45 [3.16][a]	−0.203 [1.50]	−1.58 [0.123]	−2.18 [−0.474]	−10.2 [−8.55]
EtLi	0.543 [2.27]	−1.19 [0.536]	−2.64 [−0.912]	−3.28 [−1.55]	−11.8 [−10.0]
s-BuLi	1.85 [3.98]	0.287 [2.42]	−1.01 [1.11]	−1.59 [0.534]	−9.21 [−7.08]
t-BuLi	6.24 [8.24]	4.78 [6.78]	3.57 [5.57]	3.04 [5.05]	−3.99 [−1.98]

[a] Values in brackets are counterpoise corrected.

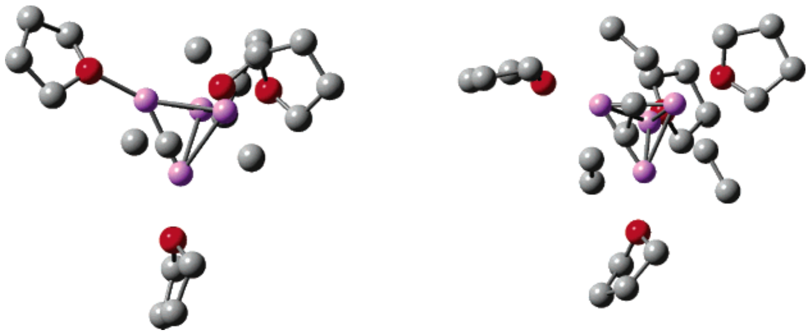

FIGURE 3. Optimized structures of THF tetrasolvated alkyllithium tetramers. Left, methyllithium; right, ethyllithium.

potentially have either one or two coordinated solvent molecules on each lithium atom. Geometry optimizations were therefore performed on the di- and trisolvated monomers and on the di- and tetrasolvated dimers. Methyllithium and ethyllithium tetrasolvated tetramers were also optimized, but no stable tetrasolvated tetramer could be located for *s*-butyllithium and *t*-butyllithium, in which one or more of the ligands dissociated when geometry optimizations were attempted.

The third solvation energies of the alkyllithium monomers were calculated according to

$$\mathrm{RLiE_2 + E \rightarrow RLiE_3} \qquad (6)$$

and the results are shown in Table 1. Likewise, formation of the tetrasolvated alkyllithium dimers were calculated according to

$$\mathrm{(RLiE)_2 + 2\,E \rightarrow (RLiE_2)_2} \qquad (7)$$

with the results presented in Table 2. The table shows that the standard free energy change for addition of the third THF to each alkyllithium monomer is negative at low temperature and positive at $T = 298$ K, except for *t*-butyllithium, for which it is 0.0 kcal/mol at 298 K. In the dimer, steric effects of the alkyl groups have a major effect on the solvation state, and even adding a second THF per Li to the disolvated dimers has a positive standard free energy for *s*-butyllithium and *t*-butyllithium over the entire temperature range. In contrast, methyllithium and ethyllithium are relatively more likely to exist as tetrasolvated dimers at low temperatures. The optimized geometries of the trisolvated alkyllithium monomers and disolvated dimers are shown in Figures 1and 2, respectively.

The free energies of alkyllithium dimerization were calculated via the disolvated and trisolvated monomers, according to eqs 4 and 8, respectively

$$\mathrm{2RLiE_3 \rightarrow (RLiE)_2 + 4E} \qquad (8)$$

The results are in Tables 3 and 4, which show that standard dimerization free energies become more negative with increasing temperature. At the higher temperatures, the disolvated monomer is found to be the dominant form, and the data in Table 3 show that little or no monomer is present for any of the alkyllithiums at the higher temperatures. At 158 K, the trisolvated form of the monomer dominates, and the dimerization free energies are given in Table 4. The data show a sharp temperature dependence on the dimerization free energies. Although the dimerization free energies of trisolvated methyllithium and ethyllithium to the disolvated dimer are predicted to be endergonic, those dimers exist primarily in the tetrasolvated form at 158 K, so the overall dimerization free energy is exergonic. This is consistent with the experimental evidence that methyllithium and ethyllithium form aggregates in THF. We find that *s*-butyllithium and *t*-butyllithium are primarily monomeric at 158 K, and the counterpoise-corrected dimerization free energy for *s*-butyllithium corresponds to

$$K_{\mathrm{eq}} = [\mathrm{E}]^4[(\mathrm{RLiE})_2]/[\mathrm{RLiE}]^2 = 3.12 \times 10^{-6} \qquad (9)$$

Furthermore, NMR studies have shown *s*-butyllithium to be a

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TABLE 5. Standard Free Energies (kcal/mol) of Tetrasolvated Alkyllithium Tetramer Formation from the Disolvated Dimer (Eq 10)

RLi	158 K	177 K	193 K	200 K	298.15 K
MeLi	−16.6 [−13.4]	−15.9 [−12.7]	−15.4 [−12.1]	−15.1 [−11.9]	−11.9 [−8.7]
EtLi	−4.3 [−0.7]	−3.4 [0.2]	−2.6 [1.0]	−2.2 [1.3]	2.2 [5.8]

[a] Values in brackets are counterpoise corrected.

monomer−dimer equilibrium at 165 K, so it appears that the microsolvation model at the B3LYP/ 6-31+G(d) level slightly overestimates the stability of the monomer.

The optimized geometries of the methyl- and ethyllithium tetramers are shown in Figure 3. The standard free energies of methyl- and ethyllithium tetramer formation were calculated according to

$$2(\mathrm{RLiE})_2 \rightarrow (\mathrm{RLiE})_4 \qquad (10)$$

and the results are shown in Table 5. Several attempts to optimize the tetrasolvated *s*- and *t*-butyllithium tetramers resulted in the dissociation of THF ligands, and this is consistent with the experimental aggregation state of those species. Formation of the methyllithium tetramer from the dimer was calculated to be quantitative over the entire temperature range. The calculated free energies of ethyllithium tetramer formation are consistent with an equilibrium of dimers and tetramers at 158 K. In an experimental study[20] performed in a 1:1 THF−pentane mixture (rather than in pure THF), a minor species was present in equilibrium with two major species, presumably the dimer and tetramer. The lower polarity of the solvent mixture is consistent with the formation of a small amount of higher aggregate, probably a hexamer.

Although the calculations predicted aggregation states that reproduce experimental trends, it is difficult to obtain quantitative predictions. PCM models are not well suited for lithium compounds, particularly in nonaqueous solvents, and were not used in this study. New continuum solvent models continue to be developed,[31] and these may be used in conjunction with the microsolvation model at a later date to include dielectric polarization of the bulk solvent beyond the first coordination shell. A slight improvement may be possible with larger basis sets and a density functional that provides a better representation of noncovalent interactions,[32] although the counterpoise calculations correct for most of the basis set effects. Finally, it would be interesting to estimate the entropic and averaging effects of the multiple conformations of the solvent, which is always a concern[16] in discrete models of solvation. In spite of these limitations, the microsolvation model proved useful in reproducing the experimental aggregation states of alkyllithium compounds.

Conclusions

The standard free energies of alkyllithium aggregate formation were calculated using a microsolvation model, in which the inner coordination sphere is represented by fully modeled explicit solvent ligands. The number of coordinated solvent molecules in the monomer and dimer show a significant temperature dependence, as does the aggregation state of the alkyllithiums. Overall the trends in the calculated results are in reasonable agreement with published experiments.

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Supporting Information Available: Tables of optimized geometries and energies of all alkyllithium structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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