

A Computational Study of Lithium Enolate Mixed Aggregates

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Ab initio calculations were performed to examine the formation of mixed dimer and trimer aggregates between the lithium enolate of acetaldehyde (lithium vinyloxyde, LiOV) and lithium chloride, lithium bromide, and lithium amides. Gas-phase calculations showed that in the absence of solvation effects, the mixed trimer 2LiOV·LiX is the most favored species. Solvation in ethereal solvents was modeled by a combination of specific coordination of dimethyl ether ligands on each lithium and “dielectric solvation” (DSE, dielectric solvation energies), immersion of each molecule in a cavity within a continuous dielectric having the dielectric constant of THF at room temperature. DSE is less important for aggregates (reduced dipoles or quadrupoles) than monomers (dipoles) and is also reduced for the coordinatively solvated species. Both solvation terms reduce the exothermicity of aggregation. In many cases, lithium salts that are three- rather than four-coordinate have significant populations at room temperature. The strongly basic lithium amides prefer mixed aggregates with weaker bases than homoaggregates. The computational results are consistent with the limited experimental data available.

Introduction

Many lithium enolates have long been known to exist primarily as tetrameric and dimeric aggregates at synthesis concentrations in ethereal solvents.^{1–6} Equilibrium constants for such aggregation have recently been determined experimentally for several lithium enolates in THF.^{7–13} Several structures have been determined by X-ray crystallography^{14–18} and the structures and ener-

getics of such aggregates have recently been interpreted with molecular orbital computations.^{19,20} Mixed aggregates between lithium enolates and other lithium salts are also known and have been characterized. Two different mixed aggregates of the lithium enolate of 3-pentanone with lithium tetramethylpiperidide (LiTMP) have been observed by Collum and co-workers, and have been considered to play a role in the *E/Z* stereoselectivity of deprotonation of 3-pentanone by lithium dialkylamides.^{21,22} A mixed aggregate of the lithium enolate of isobutyrophenone and LiCl has been characterized by NMR,¹ and the equilibrium constant for formation of a 1:1 dimer between a lithium enolate and LiBr has been determined.²³ Similarly, equilibrium constants have been determined between LiHMDS and two lithium enolates.²⁴ Several crystal structures of lithium enolate mixed aggregates have also been reported.^{25–27} Such mixed aggregates are considered to affect the regioselectivity and stereoselectivity of enolate reactions.^{28–31}

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Although it is often possible to determine the aggregation state of lithium enolates by spectroscopic methods, the structural details of the mixed aggregates in solution are more elusive. Computational methods have become increasingly important in recent years as tools for structure determination. Semiempirical methods, such as MNDO and PM3, can give useful geometries of some organolithium compounds^{20,32,33} but their aggregation energies of lithium enolates are seriously deficient.¹⁹ Recent advances in ab initio methods have permitted the study of relatively large systems that until recently could only be studied by semiempirical methods. The purpose of this work is to model the types and structures of mixed aggregates that can be formed from lithium enolates, determine their relative aggregation energies, and explore the role of solvation on such aggregates and their energies. The simplest enolate, lithium vinyloxy (LiOV), was used together with LiCl, LiBr, lithium amide (LiNH₂), and lithium dimethylamide (LiNMe₂). The scope of the present work was limited to dimers and trimers. Tetramers are important for some lithium enolates and we plan to consider their additional complexity in future work; nevertheless, the present work is the most detailed computational study of such mixed aggregates of which we are aware.

Computational Methods

The ab initio calculations were performed with Spartan (PC and Mac) and with Gaussian 94, Gaussian 98, and Gaussian 98W. Some of the calculations were run on a SGI Power Challenge Array and HP Convex exemplar at the National Center for Supercomputing Applications (NCSA) at the University of Illinois. All geometry optimizations were performed without symmetry constraints. Ab initio calculations were performed at the Hartree–Fock level with the standard 6-31G*³⁴ (6-31G(6d)) and 6-311+G* (6-311+G(d)) basis sets.³⁵ Some other basis sets were used as discussed in the text. The resulting coordinates and energies are summarized in the Supporting Information. Frequencies were computed at the HF/6-31G(6d) level and the computed reaction energies include the corresponding zero-point energies scaled by 0.9135.³⁶

As discussed below, solvation in ethereal solutions has two principal components: coordination of solvent oxygens to the metal cation and dielectric polarization effects in the bulk solvent. The former effect was modeled by explicit consideration of one or more solvent molecules in the computed structures. The latter effect is usually approximated by a cavity model in a continuous dielectric and results of this type are included for comparison. Both effects are expected to be most important for free lithium cation (charge), less so for ion pairs (dipoles), and still less for ion pair aggregates with reduced or zero dipole moments (quadrupoles). Moreover, the dielectric constants of ethers are relatively low and, accordingly, in the present work one objective was to determine how

well the mixed aggregates can be modeled in the absence of specific incorporation of dielectric effects. Structures without solvent were included to have a basis for comparison.

Results and Discussion

Unsolvated Mixed Aggregates. There is a strong electrostatic driving force for reaction of two ion pairs to form a cyclic dimer in which each ion now has two neighbors of opposite charge. The homodimer of LiOV, (LiOV)₂, forms a central ring with the lithiums and oxygens to which the vinyl groups are appended. At 6-31G* the minimum energy structure is C_s with the two vinyl groups trans and perpendicular to the four-membered ring. But the corresponding cis-structure is only 0.07 kcal mol⁻¹ higher in energy. The potential surface for rotating the vinyl groups is quite flat and different energy minima are found at different basis set levels. For example, at 6-311G* the two trans vinyl groups now have dihedral angles with the ring of 46° and -52° and at 6-311+G** the structure is almost planar with vinyl dihedral angles of 15° and -18°. The central four-membered ring is virtually planar and slightly distorted with Li–O bond distances of 1.78 and 1.81 Å. Lithium vinyloxy is known to form a tetramer in THF solution with a low barrier to rotation about the C–O bond.³⁷

A previous ab initio computation showed that the 1:1 mixed aggregate of **1** and LiBr is more stable than either homodimer by 3 kcal mol⁻¹;²⁷ that is, the equilibrium in eq 1 lies to the right. This result is in qualitative



agreement with the only reported experimental determination of such an equilibrium, $K = 13$, for formation of the mixed aggregate from the lithium enolate dimer of *p*-phenylsulfonylisobutyrophenone and (LiBr)₂ in THF.²³ The present work as summarized in Table 1 shows that this result is general for all of the mixed aggregates studied.

The dimerization energies in Table 1 show a significant basis set dependence; the exothermicity is greater with smaller basis sets. This effect is probably due in large part to basis set superposition error (BSSE) because the dimer has more basis functions for its description. The effect is shown by a more detailed study of basis set effects on the dimerization of LiNH₂ summarized in Table 2. These results show that addition of p-functions on hydrogen have only a small effect. The effect of a triple- ζ valence shell is more significant but still rather small. The biggest single effect is the addition of diffuse functions. Indeed, the relatively small 6-31+G* basis set gives results comparable to the 6-311+G* basis. The highest basis set level used, MP2/6-311+G**, is probably the most reliable of the methods used here, and gives a result similar to the RHF results with diffuse basis sets; in particular, it differs by only a few tenths of a kilocalorie per mole from the RHF/6-311+G* value. The B3LYP/6-311+G* result differs by only 1 kcal mol⁻¹ from MP2/6-311+G**. Two other density functional methods, as incorporated in Spartan, are included and bracket the MP2 result. As shown in Table 1, the incorporation of

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TABLE 1. Computed Energies (kcal mol⁻¹) for Formation of Dimers and Mixed Aggregates at HF/6-311+G* and 6-31G* (with ZPE Scaled by 0.9135) [with DSE]^a

LiX	dimerization energy ^b		formation of 1:1 mixed complex (LiOV·LiX) ^c		energy of eq 1 ^d	
	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*
LiOV	-56.37 (-54.73) [-45.82]	-63.17 (-61.54)				
LiCl	-48.55 (-47.39) [-37.58]	-50.01 (-48.85)	-53.03 (-51.56) [-30.17]	-57.60 (-56.13)	-1.14 (-0.99) [-3.27]	-2.01 (-1.86)
LiBr	-45.13 (-44.19) [-34.73]	-52.02 (-51.08)	-51.62 (-50.25) [-28.63]	-58.65 (-57.27)	-1.74 (-1.57) [-4.02]	-2.10 (-1.93)
LiNH ₂	-64.18 (-60.75) [-48.27]	-72.48 (-69.05)	-61.20 (-58.53) [-37.84]	-68.52 (-65.86)	-1.84 (-1.58) [-2.45]	-1.40 (-1.13)
LiNMe ₂	-56.94 (-54.99) [-44.92]	-61.78 (-59.84)	-57.32 (-55.39) [-35.12]	-63.00 (-61.07)	-1.33 (-1.06) [-2.48]	-1.04 (-0.77)

^a ZPE correction for 6-311+G(d) taken from 6-31G(d). The dielectric solvation energy (DSE) is taken from Table 4. ^b Energy for 2LiX = (LiX)₂. ^c Energy for LiX + LiOV = LiOV·LiX. ^d Energy for (LiX)₂ + (LiOV)₂ = 2LiX·LiOV.

TABLE 2. Basis Set Effect on the Dimerization of LiNH₂

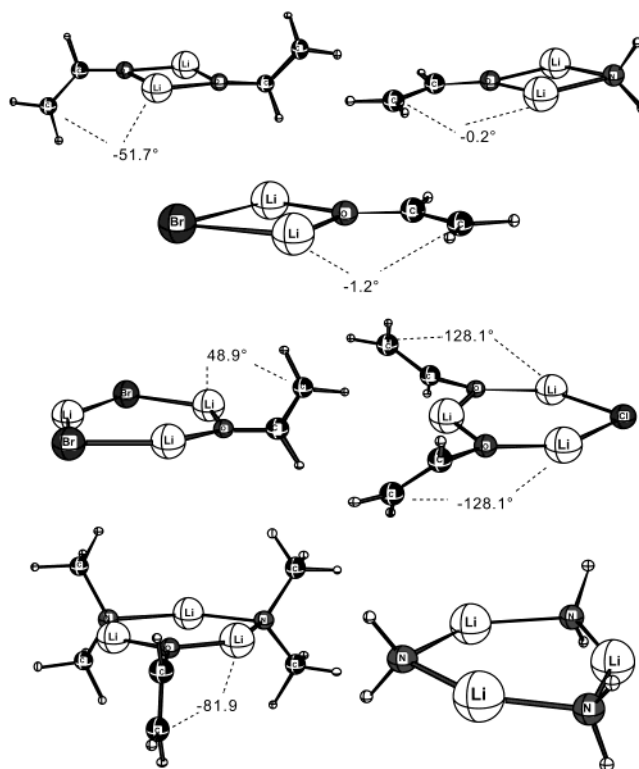
basis set	dimerization energy, kcal mol ⁻¹
RHF/631G*	-72.48
RHF/6-31G**	-72.18
RHF/631+G*	-65.00
RHF/6-311	-69.40
RHF/6-311+G*	-64.18
RHF/6-311+G**	-62.90
pBP86/DN* ^a	-61.31
VWN/DN* ^a	-67.87
B3LYP/6-311+G*	-62.71
MP2/6-311+G** ^b	-63.76

^a Density functional methods in Spartan. ^b Single point MP2(FC) at the 6-311+G** geometry.

vibrational zero-point energies (ZPE) has only a relatively small effect on the aggregation energies or the disproportionation energies of eq 1. On the basis of these comparisons we use RHF/6-31G*, because it is a popular basis with calibrated zero-point energies, and RHF/6-311+G*, as a larger reference that gives results comparable to MP2.

The dimers and 1:1 mixed aggregates form nearly planar central four-membered rings that are generally not square (Figure 1). The Li–X and Li–O bond distances in the aggregates generally differ by no more than about 0.01 Å from those of the homodimers. The location of the vinyl group in the mixed aggregates shows the same sensitivity to basis set as in the homodimer. For example, at 6-31G* the structure of LiOV·LiNH₂ is C_s with the vinyl group perpendicular to the ring; at 6-31+G*, the structure is almost coplanar with the dihedral angle of the vinyl group and adjacent O–Li only 2.0°; at 6-311+G** this dihedral angle is 22.7°. Calculations on nonplanar structures indicate essentially free rotation of the vinyl group with energy differences of only a few tenths of a kilocalorie per mole.

LiNMe₂ shows a significantly lower tendency to dimerize or form the mixed aggregate with the lithium enolate than does LiNH₂, perhaps because of steric hindrance effects with the bulkier NMe₂ group. With larger amides

**FIGURE 1.** Structures of some unsolvated aggregates at RHF/6-311+G*. Structures are CW from top left, (LiOV)₂, LiOV·LiNH₂, LiOV·LiCl, (LiOV)₂·LiCl, (LiNH₂)₃, LiOV·2LiNMe₂, LiOV·2LiCl.

and substituted enolates this tendency would be expected to increase.

The disproportionation reactions summarized in Table 1, eq 1, are all slightly exothermic and show little basis set dependence. For this type of reaction, in which there is little change in molecular size, size-related errors tend to cancel. The generalization is that the heterodimers are slightly more stable than the homodimers.

The energetics of trimer formation of the lithium salts are summarized in Table 3. In all cases, addition of a monomer to a dimer is less exothermic than the combi-

TABLE 3. Energetics of Formation (kcal mol⁻¹) of Various Trimers at 6-311+G* and 6-31G* (with ZPE Corrections Based on 6-31G* Frequencies and Scaled by 0.9135) [DSE Included from Table 4]

LiX	dimer + LiX = trimer		(2LiOV) + LiX = 2:1 mixed agg		(LiX) ₂ + LiOV = 1:2 mixed agg		(LiOV) ₃ + (LiX) ₃ = 2:1 + 1:2 mixed agg	
	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*
LiOV	-47.98 (-46.92) [-30.17]	-55.16 (-54.10)						
LiCl	-41.88 (-41.21) [-20.93]	-43.15 (-42.48)	-43.77 (-42.89) [-23.56]	-47.84 (-46.96)	-46.59 (-45.55)	-52.16 (-51.13)	-0.50 (-0.31)	-1.69 (-1.50)
LiBr	-37.99 (-37.35) [-16.20]	-48.13 (-47.50)	-41.54 (-40.65) [-20.73]	-51.28 (-50.39)	-46.40 (-45.23)	-56.11 (-54.94)	-1.97 (-1.61)	-4.09 (-3.73)
LiNH ₂	-53.18 (-52.81) [-36.76]	-59.85 (-59.49)	-52.98 (-50.98) [-34.65]	-60.52 (-58.52)	-48.97 (-47.91)	-55.62 (-54.57)	-0.79 (0.85)	-1.13 (0.51)
LiNMe ₂	-45.48 (-44.66) [-28.44]	-50.97 (-50.15)	-47.36 (-46.19) [-30.39]	-53.86 (-52.68)	-45.94 (-45.04)	-53.15 (-52.25)	0.17 (0.35)	-0.87 (-0.68)

nation of two monomers. Again, the 6-31G* results are more exothermic than the larger basis set undoubtedly because of the size effect. Computations were also made for the mixed trimers with one (1:2) and two (2:1) enolates. The energetics of these species are also summarized in Table 3.

The disproportionation of the homotrimers to the 2:1 and 1:2 mixed trimers is slightly exothermic except for the lithium amides which are both slightly endothermic at the higher basis set with ZPE correction. Even in these cases, however, the entropy of mixing will favor formation of the mixed aggregates. For the lithium halides there is a small preference for forming the 1:2 mixed trimers (LiOV·2LiX), but for the lithium amides the reverse is true. The generalization is not to have two strong bases in the same aggregate. The further aggregation of LiNMe₂ is again less exothermic than for LiNH₂ again probably because of steric hindrance effects. It is interesting to note that the 2:1 mixed aggregate is the only one not observed by Collum and co-workers with the more sterically hindered lithium tetramethylpiperidide.²²

The structures of these trimers are those of planar or near-planar six-membered rings with the amine substituents perpendicular to the ring and the vinyl groups at an angle (Figure 1). In particular, the lithium amide trimers do not form ladder structures; if such ladder structures were used as starting structures in the calculations the central Li–N bond lengthened to give the hexagonal optimized structure. For the rings with two vinyl groups the most stable conformation is sometimes cis and sometimes trans with the differences only a few tenths of a kilocalorie per mole.

Effect of Solvation. The computations discussed above refer to the ideal gas state in which the compounds are unsolvated. These results should be appropriate for solutions in hydrocarbons (for example, lithium diphenylamide is a cyclic dimer in toluene solution³⁸) but in the more commonly used ether solvents solvation is expected to be important. We approximate such solvation as the sum of two principal components: coordination of ether oxygens to the lithium cation (coordination solvation) and the electrostatic effect of the solvent dielectric (dielectric

solvation). The latter is usually approximated by enclosing the molecule in a cavity within a continuous dielectric. This effect is expected to be greatest for charged species such as free ions, less for dipoles such as our monomers, and still less for our aggregates that have zero or reduced dipole moments and are mostly quadrupoles. Computations of the dielectric solvation energy (DSE) were done with the unsolvated HF/6-311+G* structures, using the CPCM (also known as COSMO) option in Gaussian98.³⁹ Results for the monomers and some aggregates with the dielectric constant of THF at 295 K are summarized in Table 4. The method is calibrated to give total free energy of solvation as the sum of two terms, an electrostatic term (negative ΔG° derived from the interaction of the solute charges with the solvent) and a nonelectrostatic term (generally a positive ΔG° total summed from the ΔG° associated with the formation of the cavity in the continuum, a dispersion term (negative ΔG°), and a repulsion term (small positive ΔG°). A further correction that is not included in the results shown derives from the dipole moment in solution being slightly less than that in the gas phase. This correction, solute polarization is generally a positive contribution of a few tenths of a kilocalorie per mole. As expected from simple consideration of electrostatics, DSE for the monomeric ion pairs are significant, 11–17 kcal mol⁻¹. Those for the dimers and 1:1 mixed aggregates are substantially smaller at 2–10 kcal mol⁻¹, and the DSE for the trimers and 2:1 mixed aggregates are still less negative. Indeed, some of the net DSE for the trimers and mixed aggregates are positive: the energy required to create the cavity is greater than the resulting electrostatic stabilization. As a result, the dimerization energies in Table 1 corrected for DSE (6-311+G* including ZPE) and summarized in Table 1 become substantially less negative. Similarly, the energies for forming the trimer from dimer and monomer are smaller still (Table 3). The same trends are found for the mixed aggregates studied. Formation of the LiX·LiOV mixed aggregates is much less exothermic—by some 20 kcal mol⁻¹—with inclusion of DSE. The disproportionation energy, eq 1, is much less affected but inclusion of DSE does favor the mixed aggregates by 1–2 kcal mol⁻¹, probably because of their lower symmetry and

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TABLE 4. Dielectric Solvation Energies (DSE) for Monomers and Aggregates and Some Mixed Aggregates in THF (kcal mol⁻¹)

LiX	LiX			(LiX) ₂			(LiX) ₃		
	$\Delta G^\circ(\text{ES})^a$	$\Delta G^\circ(\text{non-ES})^b$	$\Delta G^\circ(\text{total})$	$\Delta G^\circ(\text{ES})^a$	$\Delta G^\circ(\text{non-ES})^b$	$\Delta G^\circ(\text{total})$	$\Delta G^\circ(\text{ES})^a$	$\Delta G^\circ(\text{non-ES})^b$	$\Delta G^\circ(\text{total})$
LiOV	-15.57	3.08	-12.49	-9.52	5.51	-4.01	-8.49	8.74	0.25
LiCl	-19.28	2.97	-16.31	-13.20	4.67	-8.53	-12.06	7.50	-4.56
LiBr	-19.74	2.61	-17.13	-13.81	4.27	-9.54	-12.59	7.07	-5.52
LiNH ₂	-14.14	2.23	-11.91	-5.72	3.18	-2.54	-3.45	5.05	1.60
LiNMe ₂	-12.93	1.60	-11.33	-5.77	4.10	-1.67	-4.28	7.50	3.22

LiX	LiX·LiOV			LiX·2LiOV		
	$\Delta G^\circ(\text{ES})^a$	$\Delta G^\circ(\text{non-ES})^b$	$\Delta G^\circ(\text{total})$	$\Delta G^\circ(\text{ES})^a$	$\Delta G^\circ(\text{non-ES})^b$	$\Delta G^\circ(\text{total})$
LiCl	-12.52	5.11	-7.41	-9.30	8.31	-0.99
LiBr	-12.90	4.90	-8.00	-9.56	8.34	-1.22
LiNH ₂	-8.02	4.31	-3.71	-6.95	7.36	0.41
LiNMe ₂	-8.23	4.68	-3.55	-8.01	8.47	0.46

^a Electrostatic term: polarized solute-solvent. ^b Nonelectrostatic term: sum of cavitation, dispersion, and repulsion energies.

higher dipole moments. Similarly, the formation of the 2:1 mixed aggregates from (LiOV)₂ and LiX becomes much less exothermic since the mixed aggregates have little net solvation energy.

The effects of coordinated solvent are substantially greater. An important question concerns the degree of such coordination. Lithium compounds generally crystallize from ethers, such as THF, with four-coordinate lithium except in cases of strong steric crowding,⁴⁰ but crystallization is a low entropy condition. The extent of solvation in ethereal solutions is more difficult to establish. In solution, four-coordinate lithium cations have clearly been recognized in NMR studies of solvent-separated ion pairs.^{41,42} For contact ion pairs, however, coordination is expected to be less important because of the electrostatic effect of the counterion. For ion pair dimers and trimers, in which the lithium is already coordinated to two or more anions, solvent coordination should be still less favorable. Four-coordination is nevertheless clearly involved for polydentate donors in which such coordination is achieved without much loss of entropy; examples are PhLi·pmdta,⁴³ neopentylithium·pmdta,⁴⁴ and LiHMDS solvated with diglyme.⁴⁵ The situation is not so clear-cut, however, for monodentate ethers where each coordination is accompanied by substantial loss of entropy. The effect of temperature on NMR spectra suggests that at least some ion pairs are not completely solvated at normal temperatures.⁴⁶ The same conclusion results from approximate models for quadrupole splitting constants.⁴⁷ The technique of titrating hydrocarbon solutions of lithium compounds with coordinating ethers to determine the stoichiometry of

coordination with the ethers can be quite useful but can also be complicated by the incorporation of ethers in a secondary solvent shell in addition to direct coordination to lithium.⁴⁵ Nevertheless, LDA dimers and trimers show only di- and tricoordinate lithiums even with the strongly coordinating ether oxetane;⁴⁸ the same conclusion appears to hold for the trimer of lithium diethylamide but is less clear for the dimer.⁴⁹ Studies of equilibria with THF in toluene suggest that the dimer of lithiated cyclohexanone phenylimine is disolvated and the monomer is trisolvated.⁵⁰ Similarly, infrared spectra of lithium thiocyanate in benzene-THF mixtures indicate that each lithium has 2-3 THF's in the monomer and two in the dimer.⁵¹ The CIP portion of diphenyl-*n*-hexyllithium in benzene with THF is of the form RLi·2THF.⁵² Titrating with HMPA, a strongly coordinating reagent for lithium cation, is another useful technique. For several lithium salts, it is suggestive (but not compelling) that several contact ion pairs are known of the type XLi_h and XLi_h₂ (h = HMPA) but not XLi₃. The use of >2 equiv of HMPA produces free HMPA in solution. A large excess yields the SSIP.^{41,53} Similar experiments with lithiated arylacetonitriles identified monomer CIP with one and two HMPAs and dimer with one HMPA but no trisolvated CIPs.⁴² Another type of argument comes from NMR studies of enolate aggregates. Lithium vinyloxy tetramer in THF shows species with two different degrees of solvation with the more highly solvated species having lower population;³⁷ thus, at least some significant population cannot be fully solvated. Similarly, NMR studies of the tetramer of lithioisobutyrophenone in dioxolane suggest different degrees of solvation.²

Dimethyl ether has been shown to be an effective model for ether solvation;⁵⁴ it has about the same basicity and steric effect as THF but is significantly smaller for

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TABLE 5. ΔE (kcal mol⁻¹) for Successive Coordination of Dimethyl Ether (E) at 6-311+G* and 6-31G* (+ZPE/6-31G* Scaled by 0.9135) [Addition of Dielectric Solvation Energies, DSE]

reaction	LiCl		LiBr		LiNH ₂		LiNMe ₂		LiOV	
	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*
LiY + E = LiY·E	-22.30 (-20.99) [-13.85]	-25.07 (-23.77) [-3.58]	-22.63 (-21.21) [-3.58]	-27.02 (-25.60) [-3.58]	-18.55 (-17.26) [-12.86]	-20.97 (-19.69) [-12.86]	-19.11 (-18.13) [-12.67]	-21.43 (-20.45) [-12.67]	-20.34 (-19.44) [-13.41]	-22.16 (-21.25) [-13.41]
LiY·E + E = LiY·2E	-15.22 (-14.03) [-9.57]	-16.70 (-15.52) [-9.57]	-15.42 (-14.24) [-9.56]	-16.96 (-15.79) [-9.56]	-11.15 (-10.11) [-5.59]	-12.89 (-11.85) [-5.59]	-12.62 (-11.62) [-6.99]	-13.37 (-12.36) [-6.99]	-14.78 (-13.49) [-8.63]	-16.19 (-14.90) [-8.63]
LiY·2E + E = LiY·3E	-9.50 (-8.49) [-5.32]	-11.09 (-10.09) [-5.32]	-9.42 (-8.50) [-5.42]	-11.66 (-10.74) [-5.42]	-7.30 (-6.04) [-2.37]	-7.88 (-6.62) [-2.37]	-6.04 (-5.17) [-0.38]	-7.75 (-6.88) [-0.38]	-9.07 (-8.03) [-3.13]	-10.86 (-9.82) [-3.13]

TABLE 6. Dielectric Solvation Energies (DSE, Kcal mol⁻¹) for Monomers and Aggregates Coordinatively Solvated by Dimethyl Ether (E) in THF at HF/6-311+G*

LiX	1E			2E			3E		
	elect	nonelect	total DSE	elect	nonelect	total DSE	elect	nonelect	total DSE
LiOV	-9.34	3.20	-6.14	-6.47	5.35	-1.12	-5.93	9.23	3.30
LiCl	-11.31	2.88	-8.43	-8.85	4.88	-3.97	-8.32	7.73	-0.59
LiBr	-11.20	2.57	-8.63	-8.94	4.94	-4.00	-8.65	7.93	-0.72
LiNH ₂	-9.17	2.04	-7.13	-6.45	4.00	-2.45	-5.98	7.32	1.34
LiNMe ₂	-7.45	1.92	-5.53	-5.63	4.88	-0.75	-4.61	8.70	4.09

LiX	(LiX)2·2E			(LiX)2·4E			LiX·LiOV·2E		
	elect	nonelect	total DSE	elect	nonelect	total DSE	elect	nonelect	total DSE
LiOV	-3.92	9.28	5.36						
LiCl	-7.06	6.84	-0.22	-6.46	13.58	7.12	-5.52	8.18	2.66
LiBr	-6.66	7.37	0.71				-5.64	8.20	2.56
LiNH ₂	-3.59	5.15	1.56				-3.54	7.32	3.78
LiNMe ₂	-2.59	9.19	6.60						

LiX	(LiX)3·3E			LiX·2LiOV·3E			LiOV·2LiX·3E		
	elect	nonelect	total DSE	elect	nonelect	total DSE	elect	nonelect	total DSE
LiOV	-5.60	17.79	12.19						
LiCl	-6.40	10.66	4.26	-4.88	15.17	10.29	-6.53	14.05	7.52
LiBr	-6.87	11.16	4.67	-5.81	16.41	10.60	-6.43	14.17	7.74
LiNH ₂	-4.66	10.72	6.06	-4.52	15.20	10.68	-4.27	12.50	8.23
LiNMe ₂	-3.37	16.40	13.03	-3.47	17.28	13.81			

computations. It was also shown that adding the third ether of solvation to lithium vinyloxy is only slightly exothermic. Water is significantly smaller for computations but is prone to give inappropriate hydrogen-bonded structures. In the present paper we use coordination by dimethyl ether (E) as our model for coordinative solvation. Lithium was coordinated with one or more dimethyl ether molecules and energy was minimized in the usual way at both the HF/6-31G* and HF/6-311+G* levels. The resulting structures and energies are summarized in the Supporting Information. The effect of successive coordinations of ether is summarized in Table 5 with the effects of DSE included in brackets.

Coordination of the first two ethers is highly exothermic but the addition of the third ether is far less so. As before, the higher basis set shows reduced exothermicity and the addition of zero-point energy changes reduces the exothermicities by another 1–2 kcal mol⁻¹. Each coordination of ether results in the loss of much of its translational entropy. The magnitude of this effect has been estimated by the entropy of fusion,⁵⁵ which for THF is 12.4 eu. For a reaction at room temperature with $\Delta H^\circ = -3.7$ kcal mol⁻¹ and $\Delta S^\circ = 12.4$ eu, $\Delta G^\circ = 0$; thus,

in Table 5 any reaction with ΔE of the order of 4–5 kcal mol⁻¹ will have equilibrium constants in the neighborhood of unity. For the amides, coordination of the third ether is in the neighborhood where the entropy loss is almost as great. The reduced coordination effectiveness of three ethers is also shown by structure. The normal O–Li bond distance in Me₂O-solvated lithium compounds is about 1.9 Å. In LiNMe₂·E this distance is a normal 1.93 Å. In LiNMe₂·2E it increases to 1.98 Å but in LiNMe₂·3E the three Li–O distances now range from 2.06 to 2.09 Å, a large increase.

The reduced solvation effectiveness of successive ether coordinations is exacerbated by consideration of dielectric solvation because the DSE is less exothermic with each such coordination. Representative coordinated structures were immersed as above in a continuous dielectric having the dielectric constant of THF at 295 K. The resulting DSE values are summarized in Table 6. As expected, the reduced dipole moments of the monomers coordinated to ethers result in somewhat lower electrostatic energies but the increased volume of the coordinated structures results in higher energies for forming the cavities in the continuum so that the resulting total DSE values become progressively more positive with additional coordinations.

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TABLE 7. Computed Energies (kcal mol⁻¹) for Formation of Solvated Dimers and Mixed Aggregates at HF/6-311+G* and 6-31G(6d) (with ZPE/6-31G* Scaled by 0.9135) [with DSE] According to Eqs 2 and 3

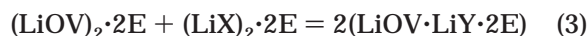
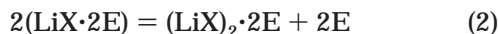
LiX·2E	dimerization energy (eq 2) ^a		formation of 1:1 mixed complex ^b		energy of eq 3	
	6-311+G*	6-31G*	6-311+G*	6-31G*	6-311+G*	6-31G*
LiOV	-20.15 (-20.98) [-13.17]	-23.26 (-24.09)				
LiCl	-11.22 (-12.85) [-4.41]	-8.37 (-9.99)	-16.10 (-17.15) [-9.07]	-16.72 (-17.77)	-0.83 (-0.49) [-0.58]	-1.80 (-1.45)
LiBr	-7.07 (-9.09) [0.01]	-8.85 (-10.87)	-14.42 (-15.65) [-7.60]	-17.13 (-18.36)	-1.62 (-1.24) [-2.05]	-2.14 (-1.76)
LiNH ₂	-29.18 (-28.80) [-22.08]	-32.14 (-31.76)	-25.64 (-25.79) [-18.23]	-28.95 (-29.11)	-1.94 (-1.81) [-1.22]	-2.50 (-2.37)
LiNMe ₂	-21.58 (-22.29) [-14.19]	-23.10 (-23.81)	-21.45 (-22.05)	-23.99 (-24.59)	-1.17 (-0.83)	-1.62 (-1.28)

^a Energy for 2(LiX·2E) = (LiX)₂·2E + 2E. ^b Energy for (LiX)₂·2E + (LiOV)₂·2E = 2(LiOV·LiX·2E).

For the fully coordinated lithium compounds, LiX·3E, the net DSE values are close to zero or are positive.

The values for DSE in Table 6 were used to correct the successive energies of solvent coordination in Table 5 and are summarized there in brackets. With the addition of the DSE values, the energies for successive solvent coordinations are 3–8 kcal mol⁻¹ less exothermic, primarily because of the successively reduced electrostatic stabilization of the reduced dipoles and the greater cavitation energy in the continuum. Indeed, coordination of the third ether is now not sufficiently exothermic to compensate for the entropy loss associated with localizing a solvent molecule. The results indicate that LiOV, LiCl, and LiBr have significant populations of disolvated molecules and that LiNH₂ and LiNMe₂ are dominantly only disolvated. Of course, these numbers do have approximations and could be in error by several kilocalories per mole, but the trends found do make sense chemically and do suggest that these monomers have significant populations of incompletely coordinated lithiums. Solvation of the lithium amides is substantially less exothermic than for the other lithium salts. The amide anions are the most basic moieties considered here and the electrostatic repulsion with the solvent dipoles is clearly a significant effect. For these reasons, in the following studies of the mixed aggregates, we consider mostly tricoordinated lithiums. This approach was further justified by a single calculation of a completely solvated dimer, (LiCl)₂·4E in Table 6. Addition of two dimethyl ethers to (LiCl)₂·2E to form (LiCl)₂·4E is exothermic by 18.27 kcal mol⁻¹ (6-311+G* with corrected ZPE) but is reduced to 10.93 kcal mol⁻¹ with inclusion of the DSE. Since the translational entropy of two solvent molecules is lost in this process, a significant amount of (LiCl)₂ remains incompletely solvated.

Solvated Mixed Aggregates. With inclusion of solvent up to tricoordination the equations for formation of dimers now become



The dimerization of unsolvated monomers is endo-entropic whereas eq 2 is entropically favorable. The

energies of formation of the solvated dimers and 1:1 mixed aggregates are shown in Table 7. For a number of cases, the DSE values were also computed (Table 8) and used to determine the values in brackets in Table 7.

The dimerization energies of the solvated monomers are much less exothermic than those of the unsolvated monomers because of the loss of solvation energy but are compensated in part by the translational entropy of the released solvent. This result is in agreement with the experimental observation that the aggregation of several lithium salts in ethereal solvents is primarily entropy-driven.⁵⁵

The computational results can be compared with some experimental data. Lithium bromide in THF is primarily dimeric with $K_{12} = 20 \text{ M}^{-1}$,⁵⁶ a value that corresponds to $\Delta G^\circ = 1.8 \text{ kcal mol}^{-1}$. The computational results in Table 7 suggest that this dimerization in THF is primarily entropy driven as in eq 2 and is of the right order of magnitude. The results do suggest, however, that some modest additional solvation of monomer and dimer could be involved. This is probably not the case, however, for lithium amides. The solvation energy of adding a third solvent to LiNH₂ is relatively small and the dimerization in Tables 5 and 7 is strongly exothermic. Lithium diethylamide, for example, was shown by NMR to be a cyclic dimer in THF.⁵⁷ The difference is probably largely a matter of basicity. The much more weakly basic lithium hexamethyldisilazide (LiHMDS) is monomeric in THF solution,⁵⁸ but does form mixed aggregates with some lithium enolates.²⁴ The disproportionation reactions of eq 3 are all just slightly exothermic. Comparison of Table 7 with Table 3 shows that solvation has almost no effect on disproportionation.

The same considerations were applied to the trimers and mixed trimers with LiOV. In all cases, a molecule of dimethyl ether was coordinated to each lithium such that each lithium is tricoordinated. The results are summarized in Table 8.

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TABLE 8. Energetics of Formation (kcal mol⁻¹) of Various Solvated Trimers at 6-311+G* and 6-31G* with the Dimethyl Ether Solvent Denoted by E (with ZPE Corrections Based on 6-31G* Frequencies and Scaled by 0.9135) [with DSE from Table 6]

LiX	dimer·2E + LiX·2E = trimer·3E + E		(LiOV) ₂ ·2E + LiX·2E = 2:1 mixed agg·3E + E		(LiX·E) ₂ + LiOV·2E = 1:2 mixed agg·3E + E		(LiOV·E) ₃ + (LiX·E) ₃ = 2:1.3E + 1:2.3E mixed agg	
	6-311+G* (+ZPE) [+DSE]	6-31G* (+ZPE)	6-311+G* (+ZPE)	6-31G* (+ZPE)	6-311+G* (+ZPE)	6-31G* (+ZPE)	6-311+G* (+ZPE)	6-31G* (+ZPE)
LiOV	-17.55 (-17.32) [-9.10]	-22.21 (-21.97)						
LiCl	-15.02 (-15.48) [-7.01]	-13.79 (-14.24)	-14.53 (-14.84) [-8.18]	-14.30 (-14.61)	-18.01 (-17.84)	-21.90 (-21.74)	0.04 (0.04)	-0.21 (-0.13)
LiBr	-9.76 (-10.20) [-2.19]	-16.12 (-16.55)	-10.54 (-10.64) [-3.65]	-17.49 (-17.59)	-17.24 (-16.99)	-25.60 (-25.35)	-0.47 (-0.47)	-4.77 (-4.40)
LiNH ₂	-21.79 (-21.53) [-14.30]	-25.09 (-24.84)	-22.87 (-22.16) [-16.51]	-26.89 (-26.18)	-18.63 (-18.73)	-22.15 (-22.26)	-2.16 (-2.16)	-1.74 (-1.62)
LiNMe ₂	-10.06 (-9.93) [-2.43]	-13.05 (-12.92)	-16.73 (-16.47) [-6.62]	-20.19 (-19.94)	-14.36 (-14.08)	-18.31 (-18.04)	-3.47 (-3.47)	-3.25 (-3.09)

By keeping all of the lithiums tricoordinate, all of the reactions in Table 8 are approximately isoentropic. The reactions of dimers with monomers to give homotrimers or mixed trimers are all about as exothermic as the comparable reactions of monomers to give homodimers or mixed dimers. The further aggregation of lithium amide is especially exothermic but that of lithium dimethylamide is much less so, probably because of steric hindrance. Correspondingly, the disproportionation reactions among the trimers are almost isoenergetic for the lithium halides but significantly more exothermic for the amides. Again, the generalization is that, although the lithium amides are prone to aggregate, they prefer mixed aggregates with less basic lithium salts. There are few experimental measurements for comparison, but LiHMDS, which is monomeric in THF, forms mixed dimers with the two lithium enolates studied. Similarly, LDA, which forms dimers in THF, appears to show a stronger tendency to form mixed aggregates with lithium enolates.²⁴

Structures of some solvated dimers and trimers are shown in Figure 2 corresponding to the unsolvated analogues of Figure 1. The dimer structures have essentially planar four-membered rings with the vinyl group now almost perpendicular to the ring plane. In the trimer structures the six-membered rings are puckered with the attached vinyl or ether groups extending away in various directions. The structures are clearly those of ionic aggregates with the substituents trying to get out of each other's way. This tendency is especially obvious with the lithium dimethylamide trimers in which the methyl groups cause much congestion. The congestion in such aggregates should be particularly marked in real cases with larger substituents on the nitrogen, in the enolate, and with larger ethers. Thus, small changes in the enolate and lithium amide structures are likely to have a significant effect on the distribution of the mixed aggregates.

Conclusions

The ab initio calculations model the strong tendency of lithium enolates to form mixed dimers and trimers

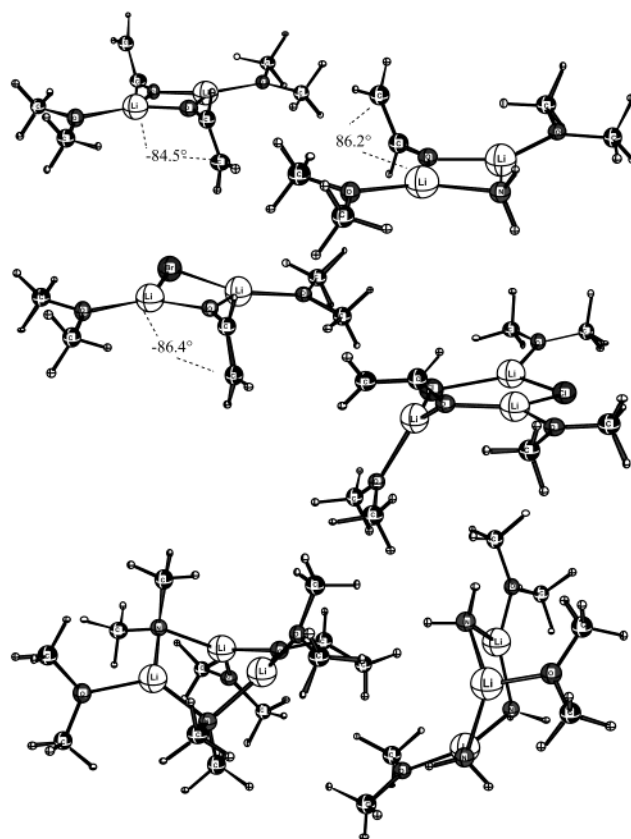


FIGURE 2. Structures of some aggregates solvated with dimethyl ether coordination to lithium at RHF/6-311+G*. The structures shown correspond to the unsolvated molecules in Figure 1.

with lithium halides and amides in the absence of coordinating solvents. This situation is approximated in hydrocarbon solvents, although lithium halides are generally not sufficiently soluble in hydrocarbons to be able to form mixed aggregates. The calculations do model the tendency of hydrocarbon-soluble lithium enolates to form mixed aggregates with lithium amides. With solvation modeled by coordination to dimethyl ether, the ap-

proximately isoentropic aggregation reactions are all strongly exothermic but this exothermicity is much reduced by incorporation of dielectric solvation. Inclusion of dielectric solvation also indicates that less than four-coordinate lithiums have significant populations at room temperature in many of the lithium salts. These models should be appropriate for dimers and trimers in THF. The calculated results appear to be consistent with the limited experimental data available.

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Supporting Information Available: Table of computational results, energies, and coordinates for RHF/6-31G*, RHF/6-311+G*, and ZPE at RHF/6-31G*. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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