# High-Field ¹H NMR Study of the Aggregation and Complexation of *n*-Butyllithium in Tetrahydrofuran[1]

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Abstract: Butyllithium exists in THF as a tetramer in equilibrium with a dimer. The species can be readily distinguished below –60 °C by ¹H (360 MHz) and ⁷Li (77.7 MHz) NMR. The equilibrium parameters $\Delta H° = -(6.3 \pm 0.4)$ kJ/mol and $\Delta S° = -(58 \pm 2)$ J/(mol·K) were established for the reaction $(BuLi)_4 \cdot 4THF + 4THF \rightleftharpoons 2((BuLi)_2 \cdot 4THF)$. The rates of exchange were measured by ⁷Li NMR at various temperatures and yielded the activation parameters for the dissociation, $\Delta H^{\ddagger} = 41 \pm 2$ kJ/mol and $\Delta S^{\ddagger} = -(30 \pm 10)$ J/(mol·K). In both aggregates the α-methylene ¹H resonances have a complexity typical of an AA'XX' system, indicating that rotation around the $C\alpha$–$C\beta$ bond is blocked (by the THF ligands). This conclusion is supported by the spectra of butyllithium-α-d_1 and butyllithium-β,β-d_2. No evidence could be obtained for monomeric butyllithium in THF even at concentrations of 10^{-4} M. In the presence of dioxygen, *n*-butyl alcohol, or *tert*-butyl alcohol, mixed alkyllithium–lithium alkoxide complexes $Bu_xLi_4(OBu)_{4-x}$ ($x = 1$–4) are formed. Equilibrium measurements indicate that incorporation of one or two alkoxy ligands stabilizes the tetrameric structures. The α-CH_2 resonances are progressively and regularly shifted to higher field with an increase in the number of oxygen ligands on lithium.

The influence of aggregation, complexation, and solvation on the reactivity of organometallic species is of paramount importance to synthetic organic chemists.[3] Our RINMR method,[4] now developed for a 360-MHz spectrometer,[5] is perfectly adapted to provide such information. Conventional NMR studies on organolithium species, most notably using ¹³C and ⁷Li nuclei, have in recent years revealed many details of aggregation and interaggregate exchange.[6] In particular, it is well established for *n*-butyllithium that the hexameric form **1**, preponderant in hydrocarbon solvents, is converted in coordinating solvents, e.g., THF to the solvated tetramer **2**. Very recently Seebach observed another form,[7] identified as the dimer **3** on the basis of the

$$R = n\text{-}C_4H_9 \qquad S = THF \qquad M = Li$$
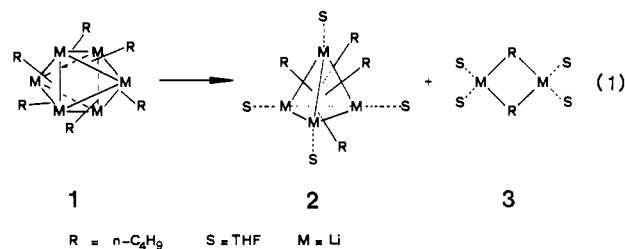
multiplicity of the α-¹³C resonance coupled with ⁶Li. Furthermore, it was established that the proportion of the dimeric structure increases with the addition of tetramethylethylenediamine (TMEDA) and with a decrease in temperature.

As a prelude to our systematic study of rapid organometallic reactions at low temperature, we report here on the great utility of ¹H NMR for the characterization and quantitative estimation of differing aggregates of BuLi in THF, including mixed alkoxide complexes.

Experimental Section

Instrumentation. The ¹H spectra were measured with a Bruker WH-360 instrument; chemical shifts (δ) expressed relative to Me₄Si were determined by using the residual α-H protons of the THF-d_8 solvent as an internal reference. Low temperatures were measured with a methanol tube previously calibrated against a Hewlett Packard 2802 A thermocouple. ⁷Li spectra were measured on a Bruker CXP-200 instrument operating at 77.7 MHz. Chemical shifts were measured relative to the solvent lock frequency and are quoted relative to LiCl 1 M in H₂O at 30

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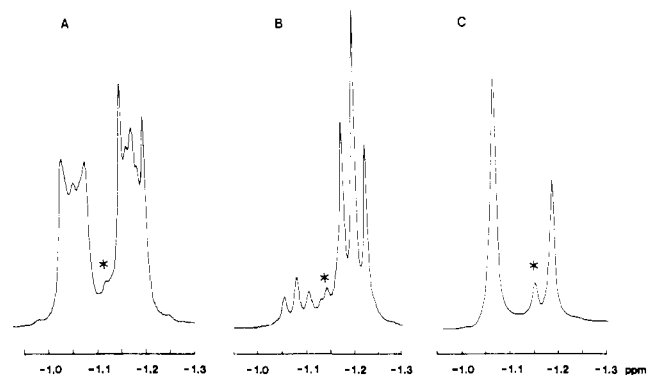
Figure 1. ^{1}H (360 MHz) spectra of (A) butyllithium, 27 mM, (B) butyllithium-α-d_1, 5.7 mM, and (C) butyllithium-β-d_2, 130 mM, in THF at -85 °C. An asterisk indicates an oxygen-derived impurity.

Table I. Concentration of Butyllithium in Species A ($\delta = -1.05$), B ($\delta = -1.17$), and C ($\delta = -1.14$) as a Function of Total Concentration and Temperature

T, K	[BuLi], mM	[A], mM	[B], mM	[C], mM
188	13	2	6	5
188	23	6	13	4
188	34	13	16	5
188	54	25	24	5
188	73	39	29	5
188	140	95	39	6
219	36.7	19.1	15.0	2.6
212	36.7	18.8	15.7	2.2
205	36.7	18.6	15.9	2.2
199	36.7	17.9	16.4	2.4
195	36.7	17.5	16.9	2.3
190	36.7	16.3	17.9	2.5
183	36.7	15.8	18.7	2.2
178	36.7	15.0	19.4	2.3

°C. Concentrations were determined wherever possible by comparison with an internal pentamethylbenzene reference—chosen for its ease of purification, mp = 54.3 °C, and weighing, convenient location of its aromatic ^{1}H resonance, and stability toward butyllithium. For dilute solutions peaks were cut out and weighed. A minor Lorentzian to Gaussian line shape transformation was applied on occasions, to provide base line separation of closely spaced broad CH_2-Li peaks for comparison among themselves; e.g., (Figure 2) LB = -2 Hz, GB = 0.4, $\Delta\nu_{1/2}$ = 5–6 Hz.

Sample Preparation. Hydrocarbon solvents were dried over 4A molecular seives and degassed prior to use. THF-d_8 was refluxed over sodium–potassium alloy and distilled under argon.[8] For samples prepared on the vacuum line, the THF (predried over sodium) was dried over methyllithium and the resultant methane was pumped off before transfer.

n-Butyllithium was obtained from Fluka AG (Buchs) as a solution in hexane. The hexane was removed on a Schlenk line at room temperature and replaced by the appropriate solvent, usually cyclohexane-d_{10} or toluene-d_8. These butyllithium solutions were titrated with dibenzyl ketone *p*-toluenesulfonylhydrazone in THF.[10]

(^{2}H$_1$)**Butyl bromide** was prepared by reduction of butanal by lithium aluminum deuteride and bromination of the resulting alcohol with phosphorus tribromide following standard procedures.[11]

(2-^{2}H$_2$)**Butyl bromide** was prepared by reduction of methyl propionate with lithium aluminum deuteride, bromination of the resultant alcohol with bromine and triphenylphosphine in DMF,[12] formation of the Grignard reagent and reaction with carbon dioxide, reduction of the resultant acid with lithium aluminum hydride, and bromination of the resultant alcohol.

Preparation of Deuterated Butyllithium Samples. The appropriate bromide (1 g, 7 mmol) was added to a stirred suspension of finely divided lithium wire (0.2 g, 28 mmol) in pentane (6 mL) at 0 °C under argon. The reaction was stirred at room temperature for 2 h and then the flask was capped with a rubber septum and its contents centrifuged. The supernatent was drawn off with a syringe from the blue precipitate and treated as described above for butyllithium.

Preparation of NMR Samples. Syringes and NMR tubes were oven dried at 80 °C overnight and cooled in a desiccator prior to use. NMR tubes containing a known amount of standard (typically 3 mg of pentamethylbenzene) were pumped out on a Schlenk line, charged with argon, and capped with a rubber septum. THF, typically 500 μL (10% contraction occurs on cooling to -78 °C), was added via a gas-tight syringe. Butyllithium solutions were introduced by syringe to the precooled (-78 °C) THF.

When desired, measured quantities of *n*-butyl alcohol, *tert*-butyl alcohol, and oxygen were added by syringe through the septum.

For the variable-temperature experiments butyllithium was short path distilled on a vacuum line (6.7 mPA at 80 °C) into an NMR tube

equipped with a B 14 ground glass joint. THF was distilled in, and the tube was sealed. After the NMR experiments the tube was opened and the butyllithium was titrated with HCl (phenolphtalein). For the high dilution experiments for which impurities including water had to be eliminated as much as possible, THF (550 μL) was distilled from methyllithium on a vacuum line into a NMR tube equipped with a ground glass joint. The tube was sealed, transported to an argon atmosphere, and then opened and capped with a rubber septum. NMR revealed a trace of water which was removed by addition of 100 nmol of BuLi, so its estimated concentration was 100 μM (2 ppm). No butyllithium peaks could be observed until another 5.0 nmol of BuLi was added.

Results and Discussion

Nature of Butyllithium Aggregates in THF. Figure 1A illustrates the α-CH$_2$ methylene resonances of butyllithium 60 mM in THF at -82 °C. The division into two complex resonances centered at δ -1.05 and -1.17 with ill-resolved fine structure is apparent. When the sample is heated the resonances broaden, coalesce at -40 °C, and sharpen to a well-resolved triplet at 0°, J = 8.5 Hz, ($\Delta\nu_{1/2}$ = 1.75 Hz). Hence equilibration of two different butyllithium species (or conceivably two geometrical isomers) present in THF occurs rapidly at 0 °C but is slow on the NMR time scale at -80 °C. The β-methylene protons also have distinct broad resonances at δ 1.44 and 1.35. Irradiation of the former resonance leads to the collapse of the multiplet at δ -1.17 to a broad singlet $\Delta\nu_{1/2}$ = 4.5 Hz. Similarly, irradiation at δ 1.35 collapses the other α-CH$_2$ resonance to a singlet $\Delta\nu_{1/2}$ = 6.25 Hz. The line broadening in the decoupled singlets is certainly due to nonresolved ^{7}Li-^{1}H coupling. The $^3J_{^7Li-^1H}$ coupling constant has been estimated to be less than 1 Hz in ethyllithium,[13] and quadrupolar relaxation of ^{7}Li, tending to remove the coupling and broaden the resonances, would be expected to be more significant at low temperatures. We conclude from the decoupling experiments that the hydrogens in the α-methylene groups are magnetically nonequivalent in each of the observed species. A resolution-enhanced spectrum indeed shows features of an AA'XX' system but could not be completely analyzed. Confirmation is provided by the spectra of butyllithium-α-d_1 and butyllithium-β,β-d_2 (Figure 1, parts B and C). In the former both resonances are apparent triplets: δ -1.08 (J = 9.2 Hz), -1.20 (J = 8.8 Hz). In the latter broad singlets are observed at δ -1.07 ($\Delta\nu_{1/2}$ = 6.5 Hz) and δ -1.19 ($\Delta\nu_{1/2}$ = 4.5 Hz). For each deuterium-substituted product a small isotope-induced chemical shift is noticeable.

The concentrations of butyllithium in the species with α-methylene ^{1}H chemical shifts at δ -1.05 (A) and -1.17 (B) and an oxygen-derived impurity at δ -1.14 (C) (see later) were measured at -85 °C for various total butyllithium concentrations (Table I). The first two concentrations were found to be correlated by the expression log A = 2.08 log B + 1.82 (r = 0.992). This result indicates that one species A is a dimer of the other B, but it does not indicate whether the equilibrium involves monomer–dimer, dimer–tetramer, etc. As it has been well established

(8) Lithium aluminum hydride was too inefficient as a desiccant for our requirements.[9] Reflux of THF-d_8 over sodium benzophenone ketyl dried it efficiently but resulted in deuterium–hydrogen exchange in the THF α position.

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up to now that butyllithium is predominently a tetramer in THF, and as Seebach has ascribed the dimer structure to his recently discovered species, we interpret our results in terms of a tetramer–dimer equilibrium. Addition of tetramethylethylenediamine (TMEDA) to a mixture of the species results in an increase of the (dimer) peak at δ −1.17. Hence the difference in the line widths of the decoupled resonances reflects the different multiplicities (nonresolved) of 10 and 7, due to coupling with ^{7}Li (I = $^3/_2$) in the tetramer and dimer, respectively.

From the data in Table I, we can evaluate the equilibrium constant $K = k_1/k_{-1}$ for eq 2. Dissociation of the tetramer

$$(BuLi)_4\cdot4THF + 4THF \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} 2(BuLi)_2\cdot4THF \qquad (2)$$
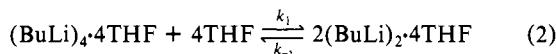
$$K = (0.021 \pm 0.004) \text{ M at } -85 \text{ °C}$$

becomes more important at lower temperatures as observed by Seebach. From the data in Table I we calculate $\Delta H° = -(6.3 \pm 0.4)$ kJ/mol and $\Delta S° = -(58 \pm 2)$ J/(mol·K).

The fact that the entropy change for the dissociation is negative is reasonably interpreted in terms of restriction of four extra solvent molecules in the solvated dimer, relative to the tetramer.[7] The enthalpy change for dissociation is rather small and negative. Theoretical calculations indicate that this dissociation in the gas phase is endothermic by 179.8 kJ mol^{-1} (PRDDO[14]) and by 144 kJ mol^{-1} (MNDO[15]). So the enthalpy of solvation by the second THF ligand to each lithium atom in the dimer is approximately −40 kJ/mol.

High Dilution Experiments. Non-integral (partial) order kinetics often have been found for butyllithium reactions in nonpolar solvents and have been interpreted in terms of reaction of the monomer in equilibrium with an oligomer. Reactions of butyllithium in THF have been less frequently studied, due to their rapidity or competing reactions with the solvent, but again kinetic orders varying between 0.25[16] (at −40 °C), 0.33 (at −22 °C),[17] up to 0.5[18] have been measured. A recent investigation of the reaction of butyllithium with THF itself has revealed a change in kinetic order from 0.33 to 1, as the concentration of butyllithium is diminished below 2 × 10^{-2} M.[19] The author reasonably concluded that at concentrations greater than this value, the prevalent species was the tetramer, whereas in more dilute solutions the monomer was preponderent. He furthermore deduced an approximate equilibrium constant $K \simeq 10^{-4}$ M^3 for the dissociation.

As a test for the presence of a monomer, several spectra were run of butyllithium in the concentration range 1 mM to 100 μM. For these experiments it was necessary to ensure that the solvent was as anhydrous and oxygen free as possible, to avoid interferences from mixed alkoxide complexes (see later). No new peaks could be systematically observed. In the highest dilution experiment with the butyllithium concentration less than 10^{-4} M only two signals could be observed in the α-methylene region. The major one was the dimer multiplet, and the other, of half the intensity, was an undefined broad resonance at δ −1.06. This resonance was not recognizable as the triplet which one would expect for the monomer, nor is its chemical shift appropriate for that of a butyllithium species with three oxygen ligands on the lithium (see later). As the tetramer (δ −1.05) should be of negligable importance at this concentration, we conclude that the new signal comprises several resonances. Hence we can neither prove nor exclude the presence of monomer in these conditions; however, we can evaluate an upper limit for the equilibrium constants K = [monomer]^2/[dimer] as $K < 3.3 \times 10^{-5}$ M and K_t = [monomer]^4/[tetramer] as $K_t < 2 \times 10^{-11}$ M^3. We note that not only do our high dilution results *not* support the interpretation of the

kinetic data in terms of a tetramer–monomer equilibrium but also based on our equilibrium data extrapolated to 25 °C the butyllithium tetramer will be 50% dissociated into *dimer* at a total concentration of 8.6 mM butyllithium. Consequently the observed change in kinetic order can be interpreted in terms of a change from tetramer to dimer. One may speculate that the much increased reactivity of butyllithium in THF compared to ether (for example) is due to the increased proportion of more reactive dimer present.[20] Indeed by use of our RINMR technique we have been able to directly confirm the much greater reactivity of dimer compared to tetramer.[21]

Structure of Butyllithium Aggregates. Complex NMR signals have previously been observed for the α-methylene protons of organolithium compounds. Fraenkel[22] examined the fine structure which in the spectrum of racemic 2-methylbutyllithium results from chemical shift differences in diastereomeric aggregates. Roberts[23] observed AA'XX' spin systems for a variety of 3,4-dimethylbutyl organometallic compounds in ether, where the bulky t-Bu group is blocked in a trans orientation relative to the metal atoms. Brown conjectured that in hexameric ethyllithium (in hexane), line broadening at low temperature for the ^{1}H resonances in both the ^{6}Li and ^{7}Li species might be caused by restricted rotation.[13] The importance of this effect in the tetramer and dimer was examined with molecular models based on recent crystallographic data. The models clearly indicate that in both aggregates the THF ligands block rotation around the C_1–C_2 bonds in the butyl groups. On the other hand, rotation around the C_1–Li bond is much less hindered. Hence the (C_1)-methylene protons can be chemically equivalent, but not magnetically equivalent, as they bear a different average angular relation to each of the β-methylene protons. The simplicity of the butyllithium-α-d_1 spectra (Figure 1) indicates that the propyl and lithium cluster substituents must be substantially in gauche as well as anti orientations.[24] We note a small difference in the $^3J_{H-C_1-C_2-H}$ coupling constants in the tetramer (9.2 Hz) and dimer (8.8 Hz). This difference could reflect a more electropositive nature of the Li$_3$ unit as a substituent compared to a Li$_2$ unit, provided that the substituent's orientation[25] is averaged by rotation around the C–Li^n bond.

Rate of Interconversion of Butyllithium Aggregates Measured by ^{7}Li NMR. The rate of interconversion of the dimer and tetramer cannot be correctly measured by line shape analysis of the α-methylene proton resonances, as the unresolved coupling to ^{7}Li makes the exchange a multi-site process and also masks the initial line broadening at the onset of exchange. Fortunately the exchange can be studied by ^{7}Li spectroscopy. Two signals were observed in the proton-decoupled spectrum at −86 °C, one broad ($\Delta\nu_{1/2}$ = 15.2 Hz) at δ −2.46 (relative to external aqueous LiCl 1 M at 30 °C) and the other narrow ($\Delta\nu_{1/2}$ = 4.7 Hz) at δ −2.05. The former signal is ascribed to the dimer as its relative intensity decreased as the temperature was raised. The difference in the ^{7}Li nuclear quadrupolar-induced relaxation times, as indicated by the different line widths, is striking. A likely explanation is that the electric field gradient around the Li nucleus is greater in the dimer, due to the replacement of a carbon ligand by another oxygen ligand. A difference in molecular correlation times is an improbable source of the line-width difference, as models show that both aggregates have approximately the same largest dimension and that the dimer is the smaller overall (with conse-

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(20) If the dimer were the only reactive species, then the kinetic order in the high-concentration limit should be 0.5; however, the variation in the observed orders from 0.25 to 0.5, depending on temperature and substrate, suggests that the magnitude of the fractional order should be interpreted with caution, at least for THF as solvent.

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(24) Otherwise, as *either* of the C_1 methylene protons could be substituted by deuterium, one should have two separate superposed AXX' spectra. Inevitably one of the HC$_1$C$_2$H dihedral angles would be close to 90°, giving an apparent doublet for the A part of one spectrum and a complicated pattern for the superposed spectra.

Table II. ^{7}Li NMR Data for the Exchange of Tetrameric and Dimeric Butyllithium in THF

T, K	dimer peak		tetramer peak		k_1,[a] s^{-1}	ln K[b]
	area[c]	width[d]	area[c]	width[d]		
168	50	22.4	50	5.1		−3.41
175	43	16.8	57	5.7		−3.82
187	42	15.2	58	4.7		−3.88
197	41	13.4	59	3.6		−4.00
208	39	12.5	61	3.8		−4.10
211	38	15.1	62	4.7	3.93	−4.20
216	37	28.0	63	6.2	8.30	−4.26
218	36		64		11.9	−4.31
224	36		64		23.3	−4.34
229	35		65		40.2	−4.40
234	33		67		60.1	−4.50
245	33		67		171	−4.56

[a] rate constant for conversion of tetramer into dimer. [b] Equilibrium constant = [dimer]^2/[tetramer]. [c] Expressed as % of the total. [d] At half-height ($\Delta\nu_{1/2}$).

quently a shorter correlation time leading to narrower signals).

As the temperature is raised to −66 °C both lines narrow and then broaden as exchange becomes important. The natural line widths in the exchange-broadened region were calculated by extrapolation of the relation of log (line width) against temperature^{-1} for the exchange-free region. These data were treated by an NMR line-fitting program to yield the relative populations and exchange rates for each temperature collected in Table II. There is a satisfying agreement between the equilibrium parameters calculated from the ^{7}Li population data, $\Delta H° = -(6.2 \pm 0.4)$ kJ/mol and $\Delta S° = -(66 \pm 2)$ J/(mol·K), and those established by ^{1}H experiments.

The activation parameters for the tetramer–dimer reaction can be evaluated as $\Delta H^\ddagger = 41 \pm 2$ kJ/mol and $\Delta S^\ddagger = -(30 \pm 10)$ J/(mol·K) or $E_a = 43 \pm 1$ kJ/mol and log $A = 11.5 \pm 0.2$.[26] These results support remarkably well Brown's analysis[27] of the exchange of methyllithium with lithium tetramethylborate, and lithium tetramethylaluminate in ether, in which the rate-determining step was proposed to be the dissociation of tetrameric methyllithium into dimer ($E_a = 47 \pm 4$ kJ/mol, log $A = 12$). For this latter reaction no equilibrium parameters are available as the tetrameric form is overwhelmingly favored. However, in the case of butyllithium in THF, comparison of equilibrium and activation parameters indicates very reasonably that solvation lags behind lithium–carbon bond cleavage in the transition state. One cannot hypothesize from these figures how many bonds are being broken in the transition state; however, examination of models suggests that there must be at least two, to allow sufficient flexibility for solvent approach.

Mixed Complexes of Alkyllithium and Lithium Alkoxides. In all of the proton spectra run of butyllithium samples, one could observe a (normally low intensity) multiplet, centered at δ −1.14 (e.g., Figure 1). The intensity of this resonance depended on the presence of traces of oxygen in the solvent, or on the history of the sample—for example, the temperature at which it had been prepared. Decoupling of this multiplet was possible by irradiation in the region of the methylene protons of the *tetramer*, not of the dimer. Hence it was concluded that the new butyllithium species had the Li$_4$ structural unit with one alkyl ligand replaced by an oxygen ligand, either butoxide or butylperoxide. Seebach has recently observed a similar mixed aggregate where one phenylacetylide ligand is substituted for a butyl group in tetrameric butyllithium.[28] Accordingly, when butyl alcohol was added to a mixture of tetrameric and dimeric butyllithium-β,β-d_2 (deuterated for spectral simplicity), the new peak (at δ −1.16 due to

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(26) Professor Seebach has informed us that he has also calculated these activation parameters by line shape analyses of his ^{13}C spectra. The two sets of results are in agreement within experimental error.

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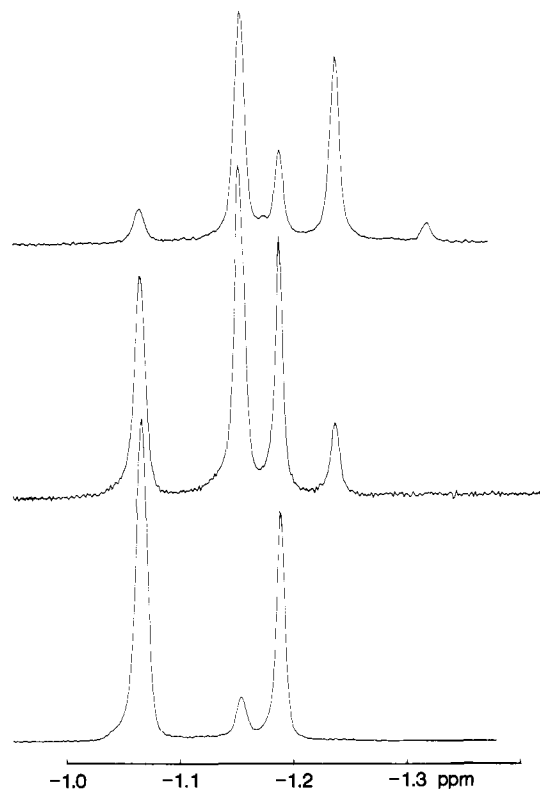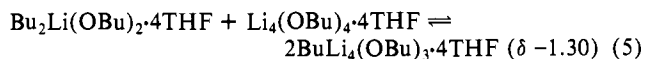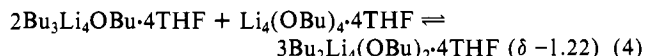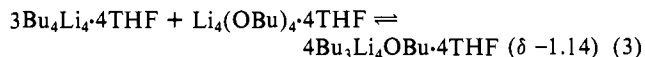(28) Hässig, R.; Seebach, D. *Helv. Chim. Acta* **1983**, *66*, 2269–2273.

Figure 2. ^{1}H (360 MHz) spectra of butyllithium–lithium butoxide mixtures: (A, bottom) [BuLi] = 91 mM, [LiOBu] = 2.3 mM; (B, middle) [BuLi] = 80 mM, [LiOBu] = 12 mM; (C, top) [BuLi] = 58 mM, [LiOBu] = 35 mM.

the isotope-induced shift) increased dramatically. Furthermore, two other broad ($\Delta\nu_{1/2} = 6.5$ Hz) resonances appeared at δ −1.24 and −1.32 (Figure 2). As further aliquots of butyl alcohol were added, the peaks at higher field increased in intensity at the expense of the others. Finally, when almost all the butyllithium had reacted, the only resonance visible was that at δ −1.32. When these experiments were carried out with nondeuterated butyllithium, all the new resonances had the same crude structure of an AA'XX' system, as observed for the dimer and tetramer. The fact that three *and only three* new peaks emerge as the concentration of lithium butoxide is increased, and as that of butyllithium is decreased, is consistent with successive replacement of alkyl groups by alkoxy groups in the tetrameric butyllithium structure. Furthermore, the line widths of 6.5 Hz indicate that there is nonresolved coupling to three lithium atoms, observed in the tetramer ($\Delta\nu_{1/2} = 6.5$ Hz), as opposed to the dimer ($\Delta\nu_{1/2} = 4.5$ Hz). This phenomenon is diminished in Figure 2 due to the Gaussian line shape. Therefore we conclude that none of the new peaks is due to a mixed BuLi$_2$OBu species.

$$3Bu_4Li_4\cdot4THF + Li_4(OBu)_4\cdot4THF \rightleftharpoons$$
$$4Bu_3Li_4OBu\cdot4THF \ (\delta\ -1.14) \quad (3)$$

$$2Bu_3Li_4OBu\cdot4THF + Li_4(OBu)_4\cdot4THF \rightleftharpoons$$
$$3Bu_2Li_4(OBu)_2\cdot4THF \ (\delta\ -1.22) \quad (4)$$

$$Bu_2Li(OBu)_2\cdot4THF + Li_4(OBu)_4\cdot4THF \rightleftharpoons$$
$$2BuLi_4(OBu)_3\cdot4THF \ (\delta\ -1.30) \quad (5)$$

As the number of butoxide ligands increases from 0 to 3, the methylene protons become more deshielded by δ 0.09, 0.08, and 0.08, respectively. It is tempting to correlate this variation with an increased polarization of the carbon lithium bonds. Such a polarization would be enhanced by a greater stabilization of positive charge on the lithium atom by electron-rich oxygen (especially oxyanion) ligands. One would then anticipate that butyllithium in a trialkoxy mixed complex would be more nucleophilic than in the tetramer or even dimer. Similarly new peaks appeared in the ^{7}Li spectra upfield of the resonances of the dimer

Aggregation and Complexation of BuLi and THF

J. Am. Chem. Soc., Vol. 107, No. 7, 1985 1809

Table III. Concentrations of Mixed Complexes $Bu_xLi_4(OBu)_{4-x}$ as a Function of Lithium Butoxide Concentration

[BuLi], mM	[LiOBu], mM	[Li_2Bu_2], mM	[$Bu_xLi_4(OBu)_{4-x}$], mM				[$Li_4(OBu)_4$], mM	K_3	K_2	K_1
			$x = 4$	$x = 3$	$x = 2$	$x = 1$				
91	2.3	14.5	13.7	2.3						
80	12.3	9.6	5.8	10.7	2.7					
69	24.3	6.6	2.6	10.9	5.9	0.8	0.05^a	11^a	8^a	6^a
63	30.3	4.8	1.5	9.9	8.4	1.1	0.10^a	13^a	22^a	6^a
58	35.3	4.2	0.9	8.4	9.4	2.0	0.52	11	14	3
51	42.3	3.0	0.5	6.6	10.0	3.2	1.5	10	12	3
47	46.3	2.3	0.3	4.8	11.2	4.6	1.3	11	19	5

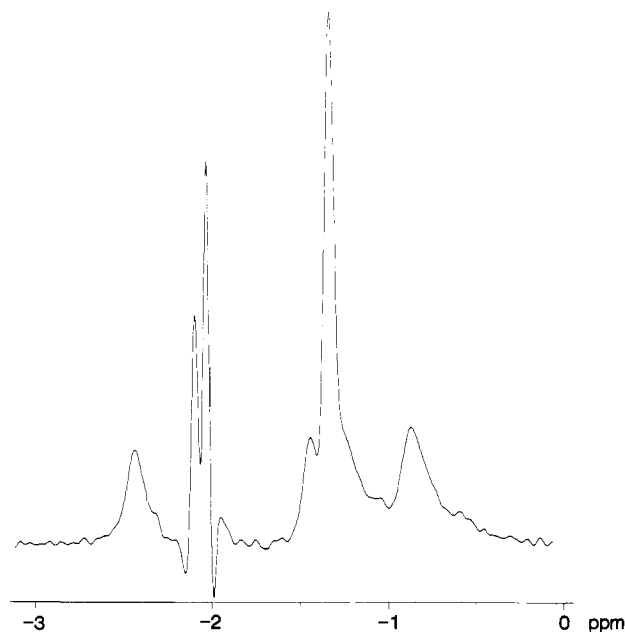^{a} The errors in these figures are certainly very great given the method of estimation.

Figure 3. ^7Li (77.7 MHz) spectrum of a butyllithium (66 mM)–lithium butoxide (36 mM) mixture in THF-d_8 at −80 °C.

and tetramer. As is often the case, Brown had previously made a similar observation by adding a low concentration of lithium ethoxide to ethyllithium in ether.[29] In the ^7Li spectrum of the mixture he observed one new peak upfield of the ethyllithium resonance; solubility limitations prevented the use of higher concentrations. However, in other experiments he could observe tetrahedral complexes of methyllithium and up to two units of lithium bromide in ether, but not in THF.[30] In these experiments the resonances of the mixed complexes were downfield of methyllithium in both the ^1H and ^7Li spectra. Our ^7Li spectra of the mixed alkyl–alkoxy lithium complexes $Bu_xLi_4(OBu)_{4-x}$ can be interpreted in terms of different local environments, as we recognize peaks for the lithium bonding partners: C, C, C for $x = 4$ at δ −2.05 (narrow); C, C, C for $x = 3$ at δ −2.11 (narrow); C, C, O for $x = 3$ and 2 at δ −1.34 (broad); C, O, O for $x = 2$ and 1 at δ −0.87 (broad); O, O, O for $x = 1$ and 0 at δ −0.56 (broad, indistinguishable in Figure 3). Again we notice an increase in ^7Li line width on changing the Li ligands from C, C, C, THF to C, C, O, THF, consistent with an increased electric field gradient at the lithium atom.

If one assumes that the stoichiometries expressed in 3–5 are correct, and if one can estimate the concentration of the free alkoxide, presumed to be a tetrameric aggregate, then an equilibrium constant K_x for the formation of each mixed complex $Bu_xLi_4(OBu)_{4-x}$ can be evaluated:

$$xBu_4Li_4 + (4 - x)Li_4(OBu)_4 \underset{}{\overset{K_x}{\rightleftharpoons}} 4Bu_xLi_4(OBu)_{4-x} \quad (6)$$
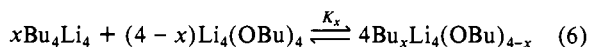
$$K_x = \frac{[Bu_xLi_4(OBu)_{4-x}]}{[Bu_4Li_4]^{x/4}[Li_4(OBu)_4]^{(1-x/4)}} \quad (7)$$

The values of K_x that could be calculated are included in Table III, and their internal consistancy supports the assumed stoichiometry. On the other hand, if one assumes that either the peak at δ −1.22 or −1.30 is that of a $BuLi_2OBu$ species, then the equilibrium constants calculated for its formation, from Bu_2Li_2 and Li_4OBu_4, increase regularly as the lithium butoxide concentration is increased.[31] On purely statistical grounds, the equilibrium constants K_1, K_2, K_3 would be 4, 6, 4. Hence we conclude that the tetrameric butyllithium structure is stabilized by substitution of one and two alkyl ligands by alkoxy groups. On the other hand, incorporation of three alkoxy groups results in destabilization.

Formation of Mixed Complexes with Other Oxygen Ligands. The addition of oxygen to butyllithium-β,β-d_2 leads to the formation of the lithium salt of butyl hydroperoxide, which can further react with butyllithium to form lithium butoxide.[32] The hydroperoxide salts can also be incorporated into mixed butyllithium complexes and give rise to α-methylene resonances (β-D_2) at δ −1.16, −1.30, and −1.43. The reaction of butyllithium with oxygen is also revealed by the appearance of a triplet at δ 3.67 due to the α-methylene group of the alkoxide or hydroperoxide salt. We wish to stress that in all of our investigations using solvents (THF) or reagents (*t*-BuOH) that had been distilled under argon and stored over molecular sieves which had not been very thoroughly degassed, we noticed extensive decomposition of the butyllithium *by oxygen*. In view of the incorporation of oxyanion ligands into the butyllithium oligomers, the unsuspected introduction of oxygen from molecular sieves could well lead to a troublesome interference in reactivity studies.

When *tert*-butyl alcohol is added to a solution of butyllithium in THF, the ^1H spectrum shows the same peaks as were observed for the *n*-butyl alcohol addition and a similar variation of these peaks with concentration. A crude estimation of the corresponding equilibrium constants $K_1 = 5.6$, $K_2 = 0.9$, $K_3 = 0.3$ indicates that for multiple incorporation, *tert*-butoxide ligands are less favored than the less bulky analogues. At higher *tert*-butoxide concentrations when the tetramer and dimer are no longer noticeable, a new peak appeared at δ −1.26. Due to overlap with its neighbors at δ −1.22 and −1.30, the line width of this peak could not be determined. We note that the resonance is upfield of the dimer resonance by the same shift as the increment for each alkoxy ligand in the complexes $Bu_xLi_4(OBu)_{4-x}$. Hence we speculate that this peak is due to a $BuLi_2O$-*t*-Bu·4THF complex, resulting from the lower propensity of *tert*-butoxide ligands to form mixed Li_4 species as noted above.

The related system formed by butyllithium–potassium *tert*-butoxide mixtures in THF is much more complex. At low ratios of BuLi/KO-*t*-Bu the α-methylene resonances of the (βD$_2$) butyl groups are at −0.25, −0.65, −0.70. As the butyllithium concentration is increased, these peaks disappear to be replaced by peaks at δ −0.87, −1.06, −1.10, −1.16 and principally a broad peak at δ −1.23. It appears likely that this latter peak corresponds to that observed with lithium *tert*-butoxide–butyllithium mixtures. Given the complexity of the medium, increased by apparent exchange between various species at low temperature, no further effort was invested to identify the newly observed species.

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Conclusion

Butyllithium in THF consists of a tetramer in equilibrium with a dimer; the proportion of dimer increases as the temperature is lowered. No evidence could be obtained for the presence of monomeric butyllithium in THF. Traces of alcohol or oxygen in the solvent lead to mixed alkyllithium–lithium alkoxide complexes with up to three alkoxide ligands. The dimer and the mixed complexes appear to have increased polarization of the carbon-lithium bond, relative to the tetramer, and may possess different reactivity. The testing of this latter expectation by use of our RINMR system is described in the following paper.

A Rapid-Injection NMR Study of the Reactivity of Butyllithium Aggregates in Tetrahydrofuran[1]

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Abstract: The influence of aggregation on the reactivity of butyllithium toward benzaldehyde and cyclopentadiene in THF was studied at –85 °C by the RINMR method. It was found that the dimer is more reactive than the tetramer toward each of the substrates; in the case of benzaldehyde the difference in rate is tenfold. When the aldehyde is injected into a stoichiometric excess of butyllithium dimer, the reaction is complete in 50 ms. In mixed butyllithium–lithium butoxide aggregates, the reactivity of the butyllithium increases with the number of alkoxy ligands. The aggregate $Bu_2Li_4(OBu)_2$ is of comparable reactivity to the dimer. When butyllithium adds to benzaldehyde, the product lithium 1-phenylpentanolate is formed in a nonequilibrated highly reactive state. It can compete with tetrameric butyllithium for benzaldehyde to reversibly form a hemiacetal salt. One can follow by RINMR the conversion of this reactive alcoholate into free alcoholate and then the complexation of this alcoholate onto the outside of the dimeric and tetrameric butyllithium aggregates. The rates of conversion of hexameric butyllithium into tetramer and dimer and of tetramer into dimer can be directly measured.

In the preceding paper[4] we have established that butyllithium exists in THF as a tetramer in equilibrium with a dimer and that the presence of lithium butoxide, due to oxygen contamination, leads to successive replacement of alkyl groups in the tetrameric structure by alkoxide ligands. It is obviously very desirable to determine the relative reactivity of these species, as the effects of concentration, temperature, and impurities on the reactions of organolithium compounds is of great synthetic importance.

Until now the high reactivity of butyllithium in THF, and toward THF, has limited the number of kinetic investigations on this system. Waack has established that the kinetic order with respect to butyllithium is 0.4 in its reaction with diphenylethylene[5] and is 0.25 in the reaction with triphenylmethane.[6] These partial orders and those for a variety of other organometallic reactions in various solvents[7] have been interpreted in terms of an initial rapid dissociation of aggregated butyllithium into monomer, which is considered to be the predominantly reactive species.[8] Such an interpretation has been supported by the observed change in reaction order in butyllithium, from approximately 0.33 to 1 in its reaction with the solvent THF, as the concentration is lowered from 100 to 1.5 mM.[9] We have, however, shown that *no* direct evidence for monomeric butyllithium in THF could be found at concentrations down to 100 μM and that at 25 °C the tetramer will be 50% dissociated into *dimer* at a total butyllithium concentration of 8.6 mM.[4]

Having at our disposal the rapid injection NMR (RINMR) technique[10,11] which allows us to follow several concurrent reactions that are complete in 1s at temperatures down to –90 °C, we chose to examine the reactions of butyllithium with cyclopentadiene (deprotonation) and with benzaldehyde (addition) with the goal of answering the following questions: (a) are the reactions too rapid to be followed, (b) do dimeric butyllithium and mixed butyllithium–lithium alkoxide complexes react more rapidly than the tetramer, (c) can the tetramer react, and (d) are the products incorporated into the aggregates?

Experimental Section

Instrumentation. NMR spectra were run on a Bruker WH-360 spectrometer. Chemical shifts (δ) were measured relative to the residual α-methylene protons in the THF solvent and are reported relative to Me$_4$Si. The rapid injection insert has been described.[11] The shortest acquistion time (AQT) used was 36 ms (corresponding to a sweep width of 14 000 Hz on 1 K data points, with digital resolution of 28 Hz). For most injections an AQT of 72 ms (SW = 14 000, SI = 2 K) was used. A delay of 30 ms was systematically imposed before the first acquistion, and normally a 30° pulse was used. Quantitative estimation of peak areas was carried out by weighing the cutouts. In some cases when differing butyllithium peaks were compared among themselves, a minor

(1) Presented in part at the Autumn Meeting of the Swiss Chemical Society, Bern, October 14, 1983.

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