Hydrolysis of the Diamide. An aqueous solution of the diamide and a small amount of ammonium sulfate was allowed to stand for 4 days at room temperature, during which time the water evaporated leaving a white solid which was recrystallized twice from hot water and after drying was washed with chloroform. This material (mp 163–167°) was very soluble in water and alcohols, but virtually insoluble in most organic solvents. *Anal.* Calcd for $C_{10}H_{17}N_2O_2P$: C, 52.63; H, 7.51; N, 12.27; P, 13.57; mol wt, 228. Found: C, 50.02; H, 7.74; N, 11.75; P, 13.14; mol wt, 218.

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Organometallic Exchange Reactions. I. Lithium-7 and Proton Nuclear Magnetic Resonance Spectra of Methyllithium and Ethyllithium in Ether[1]

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Abstract: The ^7Li and ^1H nmr spectra of ether solutions of methyllithium and ethyllithium have been observed in the temperature range from 30 to −80°. The data at lower temperatures provide evidence of association and can best be interpreted in terms of tetramer formation. The exchange process which causes collapse of the multiplet structure appears to be of the form $Li_4R_4 \rightarrow 2Li_2R_2$. It has also been established that lithium ethoxide, when present in concentrations which are low relative to the alkyllithium, is incorporated into the tetrameric structure to give a species of the form Li_4R_3OR.

The extents of association of several organolithium compounds in ether have been measured by ebulliometry. Wittig, *et al.*, report benzyl- and phenyllithium as being approximately dimeric, *n*-butyllithium pentameric, and methyllithium trimeric in boiling ether.[3] Talalaeva, *et al.*,[4] found phenyllithium and α-naphthyllithium to be dimeric, and *n*-butyllithium to be approximately hexameric in ether. The latter authors also report the association of lithium halides and mixtures of organolithium compounds with lithium halides; *e.g.*, methyllithium with lithium iodide is nearly tetrameric. However, ebulliometrically determined association numbers must be accepted with reservations since it is likely that there is some reaction with solvent, especially in the case of *n*-butyllithium and to a lesser extent phenyllithium. There is also danger of contamination from oxygen and water vapor in this type of experiment. In this respect, methyllithium should be the most favorable for the ebulliometric method.

In this paper we report the results of a study of the ^7Li and ^1H magnetic resonance spectra at low temperatures for ethereal solutions of methyl- and ethyllithium. The data have an important bearing on the question of the constitution of alkyllithium compounds and the mechanism of their reaction, in donor solvents.

Experimental Section

Materials and Procedures. All operations, except manipulations involving dimethylmercury, were performed in a glove box under argon atmosphere. Removal of traces of oxygen and water was effected by continuous circulation of the atmosphere through molecular sieve and manganese(II) oxide columns as described previously.[5] The concentrations of methyl- and ethyllithium solutions were determined by decomposing aliquot samples with water and titrating to a phenolphthalein end point with standard 0.1 *N* hydrochloric acid. Ethyllithium was obtained from Lithium Corp. of America, and dimethylmercury from Eastman Organic Chemicals. Mallinckrodt analytical reagent grade anhydrous ether was dried over sodium wire and used without further purification. Lithium-6 (96% isotopic purity) was purchased from Union Carbide Nuclear Co., Oak Ridge, Tenn.

Solutions of methyllithium in ether were prepared by adding dimethylmercury to a cooled lithium metal–ether mixture. Excess lithium was used to ensure complete reaction. The lithium–mercury amalgam and excess lithium were removed by filtration to produce a clear methyllithium solution. This method was chosen to eliminate contamination by lithium halides.

Ethyllithium was purified by sublimation under vacuum at 80–85° and then dissolved in cold ether (−10 to −15°) to give a clear, colorless solution. Low temperature is important to avoid reaction with ether, forming lithium ethoxide.

After the concentrations (usually about 1 *M*) of the separate methyl- and ethyllithium solutions were determined, the solutions were mixed in the appropriate volume proportions to form the methyllithium–ethyllithium mixtures. The solutions were degassed, sealed under vacuum in standard size nmr tubes, and stored in Dry Ice.

Samples containing lithium ethoxide were prepared by using an ethyllithium–ether solution containing lithium ethoxide (prepared by dissolving ethyllithium in ether at room temperature).

Nuclear Magnetic Resonance Spectra. Lithium-7 spectra were obtained at 23.3 Mc in a field of 14,092 gauss using a Varian Associates Model DP60 spectrometer. Aqueous lithium bromide solution (7 g of commercial grade LiBr/10 ml of solution) was employed as an external standard for the room temperature chemical shift measurements. A Varian Associates A-60 spectrometer was used to obtain the proton spectra.

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(1) The research was sponsored by a grant from the National Science Foundation.

(2) Alfred P. Sloan Research Fellow.

(3) G. Wittig, F. J. Meyer, and G. Lange, *Ann.*, **57**, 167 (1951).

(4) T. V. Talalaeva, A. N. Radinov, and K. A. Kocheshkov, *Dokl. Akad. Nauk SSSR*, **154**, 174 (1964).

(5) T. L. Brown, D. W. Dickerhoof, D. A. Bafus, and G. L. Morgan, *Rev. Sci. Instr.*, **33**, 491 (1962).

The low temperatures were obtained using the standard low-temperature accessories supplied by Varian Associates. After allowing the system to come to equilibrium at each temperature, a number of spectra were recorded, with temperature measurements before and after. In all cases, the line-width data represent an average of the data from more than one spectrum. The term line width, as used herein, refers to the width, in cps of the absorption line at half-height.

Results and Discussion

The chemical shift of the ^{7}Li resonance of ethereal methyllithium appears at -1.32 ppm relative to the aqueous LiBr external standard; it exhibits a negligible concentration dependence. The ^{7}Li chemical shift of ethyllithium is somewhat more concentration sensitive, appearing at -0.72 ppm in 1.35 *M* solution, at -0.58 ppm in 0.56 *M* solution. (All of these data apply to room temperature measurements.) The ^{7}Li absorptions consist in each case of a single, relatively sharp line (0.4 to 0.7 cps at room temperature). Upon lowering the temperature, the line broadens somewhat but the line remains single and symmetrical. The fact that a sizable chemical shift difference of about 16 cps occurs in the ^{7}Li resonances of methyl- and ethyllithium suggests that association of the organolithium species in ether might be detected from magnetic resonance spectra of mixed methyllithium–ethyllithium solutions at low temperatures. Presumably if mixed species are formed, the methyl and ethyl groups are randomly distributed among them; this presumption is in accord with a large body of data which indicates that only minor deviations from randomness are likely, in view of the close similarity of the methyl and ethyl groups.[6,7]

The ^{7}Li resonance spectra of mixed methyllithium–ethyllithium solutions consist at room temperature of a single line, with a chemical shift value approximately the weighted average of the methyllithium and ethyllithium values. The line broadens at lower temperatures, however, and appears as a distinct multiplet at about $-50°$. Satisfactory resolution of the spectra could be attained only at temperatures of about $-80°$. Figure 1 shows a number of representative spectra for varying ethyllithium/methyllithium ratio. It is apparent that four distinct absorptions are present in the ^{7}Li spectra of the mixtures, and that their relative intensities are sensitive to the ethyl/methyl ratio. The spectra are accounted for in terms of a general model which involves the disposition of two kinds of object, X and Y, in groups of three. There are in this case the four possibilities: 3X; 2X, 1Y; X, 2Y; 3Y. The relative abundances of each of these three types at a given X/Y ratio, assuming a random distribution, are easily computed. The calculated intensities of the four types can be matched to the spectra of the methyllithium–ethyllithium mixtures by assuming that the four ^{7}Li resonances are in the order of increasing ethyl group character with increasing field. The two end members of the quartet are separated by the same chemical shift differences as exists between methyllithium and ethyllithium at room temperature; any mixed species, as yet undefined, presumably will exhibit intermediate values of chemical shift. The calculated intensities of the four types of X–Y combination are shown in Figure 1 below the observed spectra. The resolution of the spectra is not good at this low temperature; furthermore, the inherent line widths of the partially resolved lines may not be the same, so a comparison of relative abundances based on apparent peak heights is not accurate; finally, the relative abundances of the various species may in some cases be a sensitive function of the ethyl/methyl ratio, and an error of perhaps 3%, which we estimate to be the uncertainty with which the ratio is known, can produce marked changes in the relative abundances of a pair of species. In spite of these limitations, however, the agreement between the calculated and observed spectra is remarkably good; no other assumption regarding the origin of the splitting in the spectra exhibits a reasonable agreement with experiments. We conclude, therefore, that the statistical model, and the assumption of a random distribution of methyl and ethyl groups, is consistent with the results.

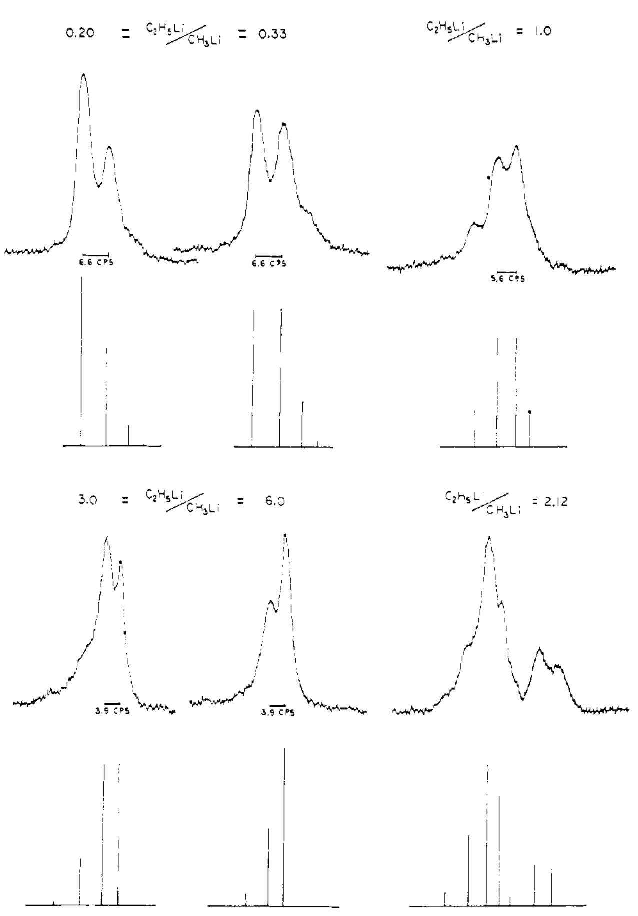

Figure 1. ^{7}Li resonance spectra of ethyllithium–methyllithium mixtures in ether at $-80°$. The lower right spectrum represents a solution containing lithium ethoxide. The calculated spectra, based on the "local environment" hypothesis, are shown beneath the observed spectra.

It remains to associate a molecular model with the statistical distribution. There are two models which are in accord with the results. The first is that of a trimer. A trimeric alkyllithium species would give rise to four distinct mixed species, Li_3X_3, Li_3X_2Y, Li_3XY_2, and Li_3Y_3. Since these four species would be present in the relative abundances given by the statistical analysis described above, it is necessary to further postulate for this model that there is rapid *intra*molecular exchange in the trimers such that all of the lithiums in each trimer are equivalent.

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(6) J. C. Lockhart, *Chem. Rev.*, **65**, 131 (1965).

(7) G. Calingaert and H. A. Beatty, *J. Am. Chem. Soc.*, **61**, 2748 (1939).

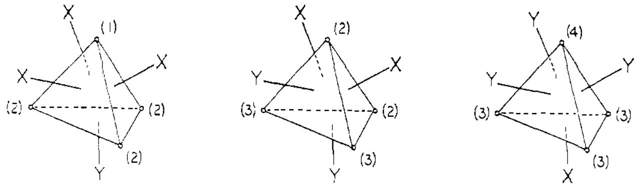

Figure 2. Schematic representations of the mixed tetrameric species resulting from random distribution of methyl and ethyl groups in alkyllithium tetramers. The apexes of the tetrahedra represent the locations of lithium atoms. The numbers in parentheses indicate the type of local environment experienced by each lithium (see Table I).

The second model which can be accommodated to the data is that of tetrameric species. There are, in fact, five possible tetrameric species, $\mathrm{Li_4X}_n\mathrm{Y}_{4-n}$. These tetramers would presumably possess the framework structure postulated earlier for solution and gaseous species,[8] and observed in the crystal structures of methyl-[9] and ethyllithium.[10] Three of the possible mixed tetrameric species are depicted schematically in Figure 2; the alkyl groups are bonded to faces of an $\mathrm{Li_4}$ tetrahedron, by what may be roughly described as four-center bonds. The observed spectra of the mixed systems can be accommodated to the tetramer model by what we term the *local environment hypothesis:* the chemical shift of a lithium in a mixed organolithium moiety is determined by the three neighboring alkyl groups only. On this basis, and assuming that there is *not* a rapid intramolecular exchange of lithiums, there are four distinct types of lithium environments. Assuming that there is a random distribution of methyl and ethyl groups in the tetramers, and accounting for the four kinds of local environments among the tetramers as in Table I, the statistical model described above is obtained. It should be emphasized that the distinct ^{7}Li resonances in the tetramer model correspond to different local environments rather than to distinct molecular species.

Table I. Number of Lithium Atoms in Each Type of Local Environment for All Possible Tetrameric Species in Methyllithium–Ethyllithium Mixtures (See Figure 2)

	(1) 3Me 0Et	(2) 2Me 1Et	(3) 1Me 2Et	(4) 0Me 3Et
$\mathrm{Li_4Me_4}$	4	0	0	0
$\mathrm{Li_4Me_3Et}$	1	3	0	0
$\mathrm{Li_4Me_2Et_2}$	0	2	2	0
$\mathrm{Li_4MeEt_3}$	0	0	3	1
$\mathrm{Li_4Et_4}$	0	0	0	4

The nuclear magnetic resonance spectra do not provide a means of deciding between the two models. On other grounds, however, the tetramer model is more attractive than the trimer model. The mass spectra of organolithium compounds consist largely of mass peaks derived from a tetrameric species.[11,12] There is no evidence of trimer in any of the compounds examined so far. Of course, the presence of a relatively polar donor solvent no doubt has important consequences for the relative stabilities of various organolithium polymeric species, but there is no physical evidence that a trimer species exists in solution. The data of Wittig and coworkers, reporting threefold association of methyllithium in boiling ether,[3] can be ascribed to the presence of an equilibrium of the form

$$\mathrm{Li_4R_4} \rightleftarrows 2\mathrm{Li_2R_2} \tag{1}$$

Indeed, it might be argued that if methyllithium were a trimer in boiling ether, it could hardly be expected to exhibit this same molecularity in quite concentrated ether solution at −80°. Various studies of the effect of ether and other donor solvents on the reactivity and other properties of alkyllithium compounds in hydrocarbon solution have been interpreted in terms of the formation of complex with dimer,[13,14] although in the light of the present results the possibility that a solvated tetramer is involved must be considered.[15] The tetrameric model is assumed, therefore, to be correct in the discussion which follows, although it is clear that very careful physical studies relating to the association of organolithium compounds in donor solvents are urgently needed.

The methyl group proton resonance signal in mixed methyllithium–ethyllithium solutions remains a single line at lower temperatures, and does not exhibit significant broadening over that observed in methyllithium solutions. The ethyl group proton resonance spectrum appears to be similarly insensitive to the effect of added methyllithium. The proton resonances of the alkyl groups are therefore insensitive to the identity of the other alkyl groups in a given tetrameric species. This result is not unexpected. Whereas the lithium atom interacts directly with the three alkyl groups which constitute its local environment, the alkyl groups interact with one another only through the intermediacy of the lithiums.

All of the low-temperature spectra for methyllithium–ethyllithium mixtures reported upon here were obtained for solutions free from lithium halide. The presence of halide appears to increase the complexity of the spectra. It seems clear that lithium halide is capable of forming mixed complexes with organolithium compounds. A limited study of the effect of lithium ethoxide was undertaken. The ethoxide is produced readily by permitting ethyllithium to react with the solvent. A typical spectrum of a mixed methyl–ethyl system containing some ethoxide is shown in Figure 1. Lithium ethoxide itself possesses a very low solubility in ether,[17] even at 25°, but is quite soluble in the presence

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[8] T. L. Brown, D. W. Dickerhoof, and D. A. Bafus, *J. Am. Chem. Soc.*, **84**, 1371 (1962).

[9] E. Weiss and E. A. C. Lucken, *J. Organometal. Chem.*, **2**, 197 (1964).

[10] H. Dietrich, *Acta Cryst.*, **16**, 681 (1963).

[11] J. Berkowitz, D. A. Bafus, and T. L. Brown, *J. Phys. Chem.*, **65**, 1380 (1961).

[12] G. E. Hartwell and T. L. Brown, unpublished mass spectral data for $\mathrm{(CH_3)_3SiCH_2Li}$ and $\mathrm{(CH_3)_3CLi}$. Only tetramers appear to be present in the vapor.

[13] Z. W. Cheema, G. W. Gibson, and J. F. Eastham, *J. Am. Chem. Soc.*, **85**, 3517 (1963).

[14] T. L. Brown, R. L. Gerteis, D. A. Bafus, and J. A. Ladd, *ibid.*, **86**, 2135 (1964).

[15] For example, the complex formed between *t*-butyllithium and triethylenediamine (TED),[16] $\mathrm{(LiC_4H_9)_4TED}$, can be formulated, in consonance with its very low solubility in organic solvents, as a linear polymer of tetrameric organolithium units joined by the difunctional bases.

[16] C. G. Screttas and J. F. Eastham, *J. Am. Chem. Soc.*, **87**, 3276 (1965).

[17] C. W. Kamienski and D. H. Lewis, *J. Org Chem.*, **30**, 3498 (1965).

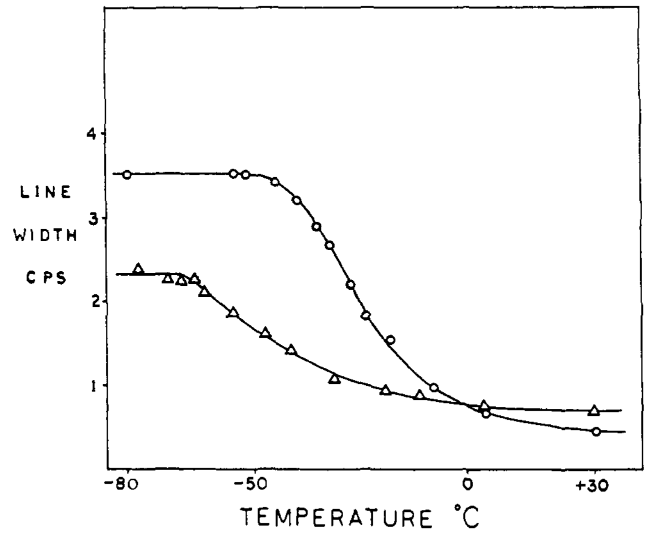

Figure 3. Temperature dependence of the ^{7}Li resonance half-intensity line width in ether solutions of methyllithium and ethyllithium (△, ethyllithium; ○, methyllithium).

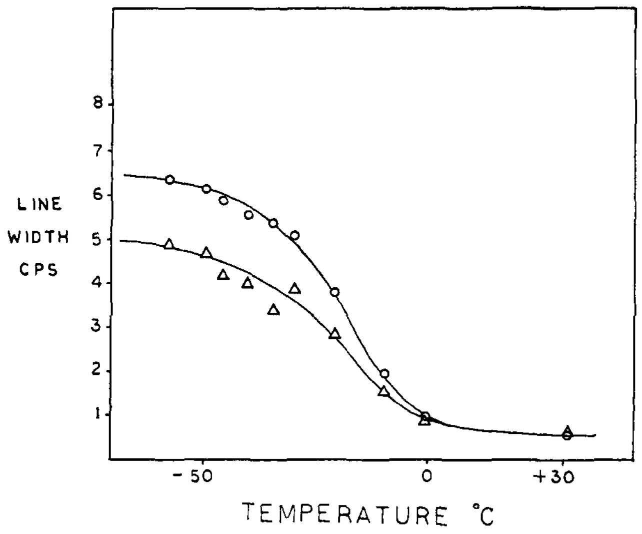

Figure 4. Temperature dependence of the methyllithium proton resonance line width in ether solution (○, ^{7}Li data; △, ^{6}Li data).

of alkyllithium. Ethyllithium solutions containing lithium ethoxide exhibit at low temperatures two ^{7}Li absorptions. The second absorption, characteristic of the presence of the ethoxide, appears upfield from the ethyllithium absorption. In terms of the tetramer model, and the local environment hypothesis, the second absorption is characteristic of lithium nuclei in a tetramer which experience a local environment of two ethyl and one ethoxide group. (This study has not been extended as yet to solutions containing more than a small percentage of ethoxide relative to ethyl, because of solubility limitations.) In solutions containing both methyllithium and ethyllithium, there are three possibilities for a local environment which contains at least one ethoxide group: two methyl; two ethyl; one methyl and one ethyl. These three possibilities are represented by the three highest upfield absorptions in the lower right spectrum of Figure 1. The agreement with the calculated relative intensities is reasonably good; these and other similar data provide strong indication that LiX species, where X might be halide, alkoxide, amide, etc., are incorporated into the organolithium tetrameric species in donor solvent.

This behavior is in sharp contrast with the result of adding lithium ethoxide to ethyllithium in hydrocarbon;[18] the ethoxide appears in the latter instance to coordinate to the outside of the hexamer. It may be that the rate of incorporation of a alkoxide into the alkyllithium polymer is slow in hydrocarbon solution.

Mixed organolithium species in hydrocarbon solution exhibit multiple ^{7}Li resonance spectra; a detailed study of certain of these systems will be reported upon soon, but it can simply be noted here that the multiplet structure is retained in these cases in some instances to temperatures of over 60°. The exchange processes which occur rapidly in the nmr time scale in ether at temperatures above $-50°$ are relatively much slower in hydrocarbon solutions. The tetramers are no doubt solvated by ether in a manner which promotes intermolecular exchange.

The four-line multiplet which appears at low temperatures in an ether solution containing roughly equal initial concentrations of methyllithium and ethyllithium exhibits a complex temperature dependence. The collapse of the structure with increasing temperature occurs first at the ethyl side of the multiplet, indicating that the exchange process, whatever its nature, is more facile for ethyl groups than for methyl. It is not feasible at present to obtain reliable information relating to the kinetics of exchange by observation of the temperature dependence of such a complex line shape. It is possible, however, to learn a good deal about the exchange process in methyllithium solutions alone.

The ^{7}Li line width in an ether solution of methyllithium changes rather markedly in the temperature range 0 to $-50°$ (Figure 3) but is rather insensitive to temperature variation both above and below this interval. This suggests that the interval 0 to $-50°$ represents the region of passage from a fast to a slow exchange in terms of the magnitude of the scalar coupling constant between ^{7}Li and the methyl group protons. Evidence for such an interaction in hydrocarbon solutions of ethyllithium has been presented.[19] In the case of a slow intramolecular *and* intermolecular exchange, each lithium nucleus interacts with the proton of three equivalent adjacent methyl groups, and with a fourth methyl group across the tetramer. Assuming that the scalar coupling for the latter interaction is negligible, the ^{7}Li line should then be split into a ten-line multiplet. However, if the coupling constant is small, on the order of perhaps 0.2 cps, the spin–spin interaction results in only a broadening. As the temperature is increased, and intermolecular exchange occurs, the ^{7}Li–^{1}H coupling disappears, and a sharpening of the ^{7}Li line is seen. Similar results are obtained for the ^{7}Li resonance of ethyllithium, but the temperature interval in which the line-width changes is shifted to lower temperature.

The proton resonance line width as a function of temperature for methyllithium solutions in ether is shown in Figure 4 for methyllithium prepared from ^{7}Li and ^{6}Li. These data provide excellent corrobora-

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[18] T. L. Brown, J. A. Ladd, and G. N. Newman, *J. Organometal. Chem.*, 3, 1 (1965).

[19] T. L. Brown and J. A. Ladd, *ibid.*, 2, 373 (1964).

tion of the interpretation placed upon the ^{7}Li line-width results. ^{6}Li possesses a smaller nuclear magnetic moment than ^{7}Li, and its nuclear spin is 1 as opposed to $^3/_2$ for ^{7}Li. The spin–spin coupling constant between proton and ^{7}Li is 2.6 times larger than for ^{6}Li. In the limit of fast exchange, above 0°, there is no difference in the proton line widths of the two samples. In the region from 0 to $-50°$, the line-width difference increases. Below $-50°$ the difference remains constant, indicating that the slow exchange limit has been reached.

There are two possible mechanisms for the exchange which deserve consideration. The first involves dissociation of the tetramer into dimers in the rate-determining process, as in eq 1. The second involves an ionic dissociation

$$\mathrm{Li_4R_4} \longrightarrow \mathrm{Li_4R_3^+} + \mathrm{R^-} \qquad (2)$$

Ions of the form $\mathrm{Li}_n\mathrm{R}_{n-1}^+$, particularly when $n = 4$, are the most important species seen in the mass spectra of alkyllithium compounds.[11,12] The ionic process would be facilitated by a polar, solvating medium. However, the Lewis acid character of the alkyllithium dimer is surely greater than that of the tetramer, since the number of alkyl groups bound to lithium is lower, so that a donor solvent would likewise assist in homolytic dissociation, as in eq 1. Optically active *sec*-alkyllithium compounds racemize much more rapidly in an ether-containing medium than in hydrocarbon solvent.[20,21] Since the racemization very probably proceeds through a carbanion intermediate, there is strong support for the argument that the ionic dissociation proceeds readily in ether. The observed rates of racemization do seem considerably slower than the rate of the exchange process being observed in the nmr, but it is difficult to draw relevant comparisons in view of the difference in the solvent conditions and the particular alkyllithium compounds involved. The recently reported results on the rate of inversion at the metal-bearing carbon of neohexyllithium in ether[22] afford a more direct comparison. Inversion, which presumably proceeds *via* eq 2, is considerably slower than the exchange process which we observe.

The results reported here do suggest how the presence of lithium halide or alkoxide might affect the reactivity of an alkyllithium reagent. In the species $\mathrm{Li_4R_3X}$, the ionic process depicted in eq 2 will occur to give $\mathrm{Li_4R_3^+} + \mathrm{X^-}$ when X is a more stable anionic species than the carbanion $\mathrm{R^-}$. Thus, in all $\mathrm{Li_4R_3X}$ species, the three R groups are partially or completely inactivated insofar as their appearance as carbanions is concerned. Furthermore, if $\mathrm{X^-}$ is a particularly stable carbanion, *e.g.*, a benzyl system, the same argument applies. On the other hand, the dissociation of $\mathrm{Li_4R_3X}$ into $\mathrm{Li_2R_2} + \mathrm{Li_2RX}$ should also be less facile than dissociation of $\mathrm{Li_4R_4}$. One expects, therefore, that the effect of LiX in low relative concentration will be to decrease the reactivity of an alkyllithium compound toward substances which behave as electrophiles. A strongly nucleophilic substrate, on the other hand, might compete with solvent for complex formation with $\mathrm{Li_4R_3^+}$, in which case it is possible that added LiX could enhance reactivity. It is not clear what effect larger relative concentrations of LiX (*i.e.*, greater than about 1LiX:3LiR) have on the structure of the species present in solution. In this connection, it is important to reemphasize that the studies reported here were conducted in the complete absence of lithium halide. Low-temperature ^{7}Li spectra obtained using methyllithium prepared from either methyl bromide or iodide are complex and do not provide sufficient resolution for interpretation at this time.

Acknowledgment. The authors are indebted to Dr. J. A. Ladd for assistance in the early stages of this work, and to Mr. O. W. Norton for assistance in obtaining the ^{7}Li spectra.

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(21) D. Y. Curtin and W. J. Koehl, Jr., *ibid.*, 84, 1967 (1962).

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