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Studies in Nuclear Resonance Spectroscopy. 14. Characterization and Structures of Lithioisobutyrophenone Aggregates in Ether Solvents[1]

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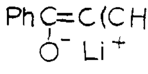
Abstract: Proton, ^{13}C, and ^{7}Li magnetic resonance spectroscopy, including studies of spin-lattice relaxation times, have been used to investigate the nature of ion pair aggregates of lithioisobutyrophenone (**1**) in several ether solvents. As previously observed for dioxolane solutions, **1** in tetrahydrofuran-d_8 and dioxane exists as two rapidly exchanging species, the relative concentrations of which are strongly temperature dependent. Two species also exist in dimethoxyethane but the equilibrium is much less temperature sensitive and the exchange is slow on the NMR time scale at −50 °C. The complex between **1** and LiCl in dioxolane has been shown to be $Li_4Cl(C_{10}H_{11}O)_3$. Carbon-13 chemical shifts indicate that in all species, except the major species in dimethoxyethane, the enolate ions have the same electron distribution. T_1 measurements for ^{13}C nuclei indicate that all species are tetramers except the major species in dimethoxyethane which appear to be a dimer. Quadrupole splitting constants for lithium-7 and the ^{13}C chemical shifts show trends expected for tetramer and dimer models. T_1 measurements for ^{13}C nuclei of solvent dimethoxyethane show that the dimer has one solvent molecule per lithium atom. Similar measurements for the other solvents indicate considerable internal rotation of solvent molecules bound to the aggregates. The above results are interpreted in terms of a cubic array of Li and O atoms in the tetramer and a planar square array for the dimer.

In part 11,[2] we reported proton NMR studies of solutions of lithioisobutyrophenone (**1**) in several ether solvents. Measurements of the chemical shifts of the two methyl groups in dioxolane at various temperatures revealed the occurrence of two species, one existing exclusively below −50 °C, the other exclusively above 50 °C. In the intermediate temperature range the two species coexist but are involved in a chemical exchange which is rapid on the NMR time scale. The position of equilibrium was shown to be independent of the concentration of lithium enolate and the thermodynamic parameters ($\Delta H = -10.3$ kcal mol^{-1}; $\Delta S = -38.7$ cal mol^{-1} deg^{-1}) are consistent with the two species being differently solvated ion pairs or ion pair aggregates.[3] It was also observed that the addition of lithium chloride or bromide to solutions of the enolate in dioxolane gives a new species which, at appropriate temperatures and concentration ratios, coexists with the two species referred to above. Exchange of the enolate ion between this new species and the other two is comparable with the proton NMR time scale. The empirical formula for the halide complex was found to be $Li_{4-5}X(enolate)_{3-4}$. The higher values appeared to fit better the data for the chloride complex although the lower value was more consistent with that for the bromide system. We have now considerably refined our techniques for sample preparation and analysis and it is clear (see below) that the formula of the chloride complex is $Li_4Cl(enolate)_3$.



$$\underset{O^{-}\ Li^{+}}{PhC}{=}C(CH_3)_2$$

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In this paper we report more extensive NMR studies, including ^{13}C and ^{7}Li resonances as well as measurements of spin-lattice relaxation times, which further delineate the various species existing in different ether solvents and in the presence of lithium chloride, and which permit the tentative formulation of the structure of these species as various ion pair aggregates.

Experimental Section

Materials. All compounds and solvents were prepared as previously described.[2]

Preparation of Lithium Isobutyrophenone Solutions. The vacuum line technique described earlier was modified to eliminate as many stopcocks as possible and is illustrated in Figure 1. *n*-Butyllithium was obtained by distillation of its solution (1.6 M) in *n*-hexane (Alfa) either directly into the reaction flask, A, through a short side arm heated (130 °C) by heating tape or into a break-seal storage bulb, B, which was subsequently attached to the neck of the reaction flask as illustrated. Diethyl ether stored over lithium aluminum hydride in the storage bulb, C, was degassed by several cycles of freezing, pumping, and thawing and then transferred to the reaction flask containing *n*-butyllithium (if the *n*-butyllithium was contained in the storage vial, the seal was broken at this stage and the contents were transferred to the flask by repeatedly condensing ether in the opened vial). The vial, D, containing degassed isobutyrophenone trimethylsilyl enol ether was opened, and the contents were vacuum transferred to the reaction flask. The mixture was then stirred at room temperature for 12 h. The diethyl ether was removed and replaced by degassed solvent stored over lithium aluminum hydride in the storage bulb E. This solvent was removed and the entire system was pumped down until the vacuum gauge F registered less than 2 μm. The storage bulb G was opened and the solvent was degassed and transferred to the reaction flask. If required, tetramethylsilane was introduced from a storage vial, H, at this stage. The reaction flask was then sealed and removed from the manifold. The contents of the reaction flask were drained through a medium porosity sintered glass septum J (Figure 2) into the flask of the "spider" K. Appropriate quantities were then transferred to the various attachments of the spider. Depending on the particular experiment, these consisted of 5 and 10 mm NMR tubes (the latter

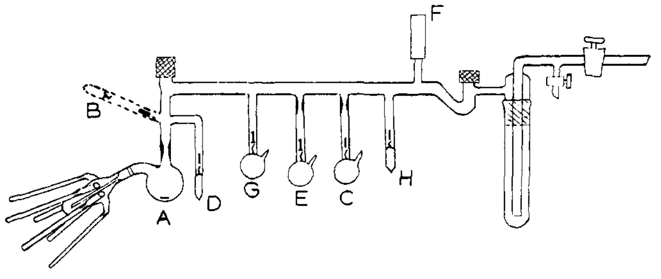


Figure 1. Apparatus for sample preparation.

containing a sealed capillary tube of acetone-d_6), a viscometer, and a calibrated density bulb.

The accurate dispensing of lithium chloride was effected by introducing an appropriate volume of a standardized solution of lithium chloride in anhydrous methanol to the NMR tubes. The methanol was carefully evaporated and the tubes were then attached to the spider. Removal of the last traces of solvent, together with any moisture introduced during the glass blowing operations, was achieved by heating the tubes at 110 °C (10^{-4} mm) for 12 h.

All solutions prepared by this technique were completely clear and virtually colorless. The concentrations of lithioisobutyrophenone were obtained at the completion of the experiments by opening the tubes and titrating the contents against 0.1 N HCl. The chloride ion concentrations were checked for several samples by adding aliquots to 0.2 M silver nitrate and back titration with 0.04 M potassium thiocyanate; the values agree within experimental error with the quantities of lithium chloride originally added to the tubes.

The viscosities were determined using a modified Cannon-Manning viscometer (L, Figure 2) thermostated to ±0.05 °C. The viscosity, η, is given by $\rho(ct - k/t)$ where ρ is the density of the liquid and t is the time of flow. The constants c and k were obtained by a least-squares fitting of data from liquids of known viscosity. Densities of solutions at various temperatures were determined by measuring the volume of liquid in the sealed, calibrated density bulb. The bulb was subsequently cut open, weighed, emptied, and reweighed.

NMR Spectroscopy. Proton spectra (100 MHz) were obtained with a Varian HA 100 spectrometer and the spectra were calibrated with a frequency counter (±0.1 Hz). Proton spectra (300 MHz) were obtained using the Varian 300 MHz superconducting magnet system at the Institute of Polymer Science, University of Akron, and operated by Mr. E. R. Santee, whose cooperation is gratefully acknowledged.

^{13}C (25 MHz) and ^7Li (39 MHz) were obtained using a Jeol spectrometer with a Nicolet 1080 data system. ^{35}Cl (9.8 MHz) spectra were obtained with a similar system in the Department of Chemistry, University of Colorado, through the courtesy of Dr. M. W. Hanna to whom we express our thanks. Spin-lattice relaxation times were determined using the 180°-τ-90° pulse sequence. For the short relaxation times (e.g., those of ^7Li) a 100-μs homospoil pulse was introduced immediately after the 180° pulse in order to remove phase imperfections associated with $T_2{}^*$.[4] Ten to fifteen randomly ordered τ values were used in each determination and the data were processed by the non-linear least-squares routine incorporated in the Nicolet software package. Generally, calculations based on peak heights gave lower standard deviations than those for areas although there was usually excellent agreement between the two determinations.

Measurements of NOE enhancements (η) were made by comparing the frequency domain signals in the noise decoupled ^{13}C spectrum with those of a similar spectrum in which the decoupler was gated off except during data acquisition.[5] Recovery times of $5 \times T_1$ (for carbon) were employed, these values being adequate for the expected values of $T_1(^{13}C)/T_1(^1H)$.[6] Approximately ten pairs of measurements were made for each value of η.

Sample temperatures were measured as described previously.[2] Care was taken to minimize rf heating by the decoupling radiation. The frequency of the decoupling radiation was set to coincide rather closely to the desired proton frequency(s) and the power was reduced to the minimum value for effective decoupling. In most experiments 100-Hz square-wave modulation of the decoupling radiation,[7] rather than noise modulation, was employed. Large volumes of liquid were used to eliminate possible contributions from efficient gas-phase spin-rotation relaxation to the observed relaxation times of the solvent ^{13}C nuclei.[8]

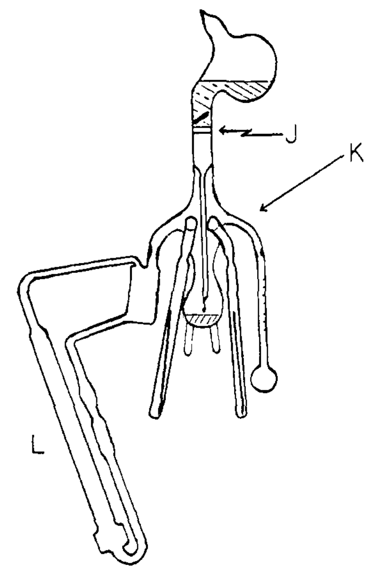


Figure 2. The "spider" for dispensing solutions under vacuum.

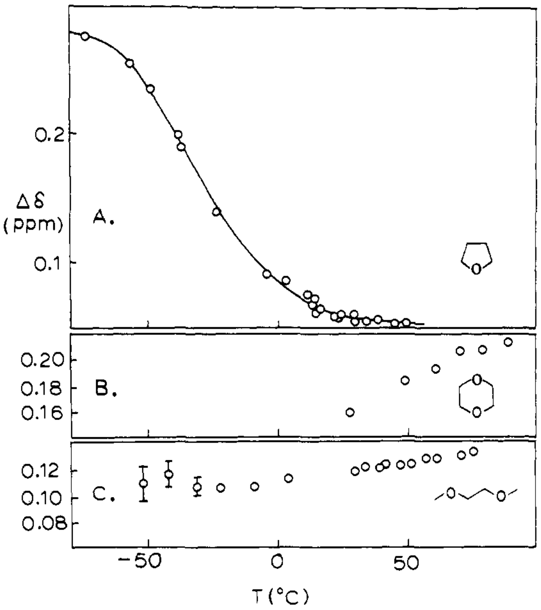


Figure 3. The temperature dependence of the proton chemical shift differences (Δδ) between the methyl groups of lithioisobutyrophenone in (A) tetrahydrofuran-d_8, (B) dioxane, and (C) dimethoxyethane.

Results

Coexisting Species in Various Solvents. As mentioned above, we have previously established the coexistence of two equilibrating species of lithioisobutyrophenone in dioxolane solution. Equilibration is rapid on the proton NMR time scale and the position of equilibrium is concentration independent. We have now extended our studies to include some other ether solvents. Figure 3 shows the temperature dependencies of the difference (Δδ) in proton chemical shifts of the two methyl groups in tetrahydrofuran-d_8, dioxane, and dimethoxyethane. The behavior in the former solvent is similar to that in dioxolane but corresponds to somewhat different thermodynamic parameters (Table I). It is probable that a similar phenomenon occurs in dioxane but the higher melting point of this solvent precluded determination of the thermodynamic parameters.

Our earlier studies of lithioisobutyrophenone in dimethoxyethane failed to reveal coexisting species. The chemical shift differences (Δδ) show only a small monotonic variation

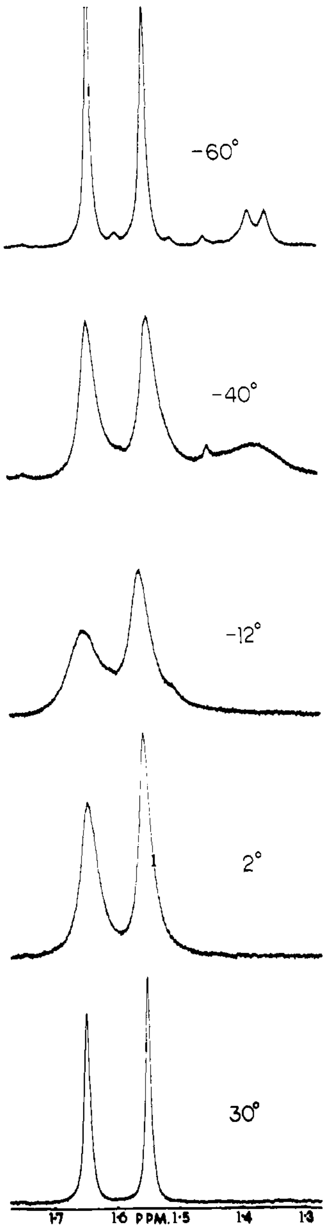


Figure 4. The temperature dependence of the methyl absorptions in the proton spectra of lithioisobutyrophenone at 300 MHz.

Table I. Thermodynamic Parameters for the Equilibrium between the High- and Low-Temperature Species of Lithioisobutyrophenone

Solvent	T, °C, for $K_e = 1$	ΔH,[a] kcal mol^{-1}	ΔS, cal mol^{-1} deg^{-1}
Dioxolane[2]	−8	−10.3 ± 0.3	−38.7 ± 1.0
Tetrahydro-furan-d_8	−31	−7.5 ± 0.2	−31.2 ± 0.7

[a] Low-temperature species ⇌ high-temperature species.

Table II. The Stoichiometry of the Lithium Chloride-Enolate Complex Li$_{n+1}$Cl(C$_{10}$H$_{11}$O)$_n$ in Dioxolane

[Li(enolate)], M	[LiCl], M	T, °C	n
0.40	0.088	−13	2.8
0.49	0.062	−13	2.9
0.45	0.041	−13	3.2
0.40	0.020	−13	2.8
0.45	0.041	−31	2.9
0.45	0.041	−4	3.2
0.45	0.041	33	3.2
0.45	0.041	46	2.9

Table III. ^{7}Li Chemical Shifts for Lithioisobutyrophenone (0.5 M) and Lithium Chloride in Various Solvents at 40 °C

Solvent	[LiCl], M	δ[a]
Dioxolane[b]	0.055	1.24
Dioxolane		1.05
Dioxolane	0.1	1.06
Dioxane		0.86
Dioxane	0.1	0.88
Dimethoxyethane		0.64
Dimethoxyethane	0.1	0.71
Dimethoxyethane	0.2	0.76

[a] Ppm upfield from external 0.31 M LiCl in methanol-*O-d*. [b] Lithioisobutyrophenone absent.

with temperature (Figure 3). In the region below −30 °C, however, some anomalous line broadening was apparent, an observation which has now led us to investigate the proton spectra at 300 MHz. The spectra are reproduced in Figure 4. At the lower temperatures, two species, which are exchanging slowly on the NMR time scale, are discernible. The major species constitutes approximately 85% of these low-temperature mixtures. The same information is available from low-temperature ^{13}C spectra (see below). Although it has not proved possible to carry out a quantitative study of the equilibrium between the two species, it is apparent from absolute chemical shifts and the chemical shift differences ($\Delta\delta$) for the methyl groups at high temperatures that the same species predominates.

Lithium Chloride Complexes. The improved techniques described in the Experimental Section afforded dioxolane solutions of lithioisobutyrophenone which, at low temperatures, exhibit no extraneous absorptions in the methyl region. Furthermore, the use of distilled butyllithium permitted accurate estimation of the lithium enolate concentration by acid-base titration. With these improvements we now find that the ratio of enolate ion to chloride ion in the complex is 3.0 ± 0.2 over a range of concentrations and temperatures (sample data are presented in Table II). The complex in dioxolane is thus assigned the empirical formula Li$_4$Cl(C$_{10}$H$_{11}$O)$_3$.

Examination of ^{7}Li spectra of solutions containing either excess lithium enolate or lithium chloride, in the temperature range −50 to 40 °C and at a ^{7}Li resonance frequency of 39 MHz, failed to reveal separate resonances characteristic of the complex. Although the chemical shift for lithium in the enolate salt and its lithium chloride complex appear to be similar (Table III), that for lithium chloride is sufficiently different to permit the conclusion that exchange of lithium between the complex and "free" lithium chloride is rapid on the NMR time scale ($\Delta\nu \sim 9$ Hz).[2]

The ^{35}Cl chemical shifts and spin-spin relaxation times (T_2) for lithium chloride and the chloride ion complex in dioxolane are reported in Table IV. These results indicate that there is no gross difference between the electrostatic environment of the chlorine nucleus in the complex and in lithium chloride. It has been shown for a wide concentration range of aqueous alkali metal chloride, bromide, and iodide solutions that the chemical shifts and T_2's vary linearly with each other, both for the cation and anion.[9] That neither vary appreciably in the system under discussion suggests that there is no appreciable difference in the correlation times, and hence molecular vol-

Table IV. ^{35}Cl Chemical Shifts and Spin–Spin Relaxation Times (T_2) for Lithium Chloride in Solutions of Lithioisobutyrophenone in Dioxolane at 23 °C

[Lithioisobutyrophenone], M	[LiCl], M	δ[a]	T_2, ms
	0.055	45	0.6
0.5	0.1	45	0.57
0.33	0.1	51	0.62
0.5	0.2	45	0.57
0.2	0.1	42	0.60

[a] Ppm upfield with respect to external 1.0 M NaCl in D_2O.

Table V. Proton Chemical Shifts of the Methyl Groups of Lithioisobutyrophenone in Various Solvents and in the Presence of Lithium Chloride

Solvent	[LiCl], M	T, °C	δ	δ
Dioxolane		20.5	1.388	1.484
Dioxolane	0.2	20.5	1.375	1.635
Dioxane		80	1.420	1.493
Dioxane	0.1	80	1.447	1.600
Tetrahydrofuran-d_8		35	1.441	1.500
Tetrahydrofuran-d_8	0.2	35	1.417	1.700
Dimethoxyethane		27	1.552	1.650
Dimethoxyethane	0.2	27	1.529	1.676

umes, of the complex and lithium chloride in dioxolane solution.

Lithium chloride also interacts with lithioisobutyrophenone in dioxane and tetrahydrofuran giving rise to characteristic shifts in the proton spectra (Table V), but we have not established the stoichiometry of the complexes in these solvents. Evidence for complex formation in dimethoxyethane is available from proton, ^{7}Li, and ^{13}C chemical shifts. The changes in $\delta(^7\text{Li})$[10] and $\Delta\delta(^{13}\text{C})$ (for the 1- and 2-carbon atoms) with lithium chloride concentration are strongly correlated [$\delta(^7\text{Li}) = -0.042\Delta\delta(^{13}\text{C}) + 3.29$; $r = 0.998$]. Figure 5 shows the dependence of the ^{13}C chemical shift with the mole fraction of lithium chloride. The data are consistent with the stoichiometry of the complex observed in dioxolane. Departure from the idealized curve for irreversible formation of $[\text{Li}_4\text{Cl}(\text{C}_{10}\text{H}_{11}\text{O})_3]_n$ may indicate incomplete complexation. Quantitative analysis of the data in terms of the stoichiometry of the complex and its formation constant is not feasible because of the complex nature of the equilibrium and because, as noted above, lithioisobutyrophenone is probably a mixture of two species. Further evidence in favor of the proposed stoichiometry is presented below. In contrast to the behavior in dioxolane, exchange of enolate ion and lithium chloride is rapid on the NMR time scale even at −70 °C.

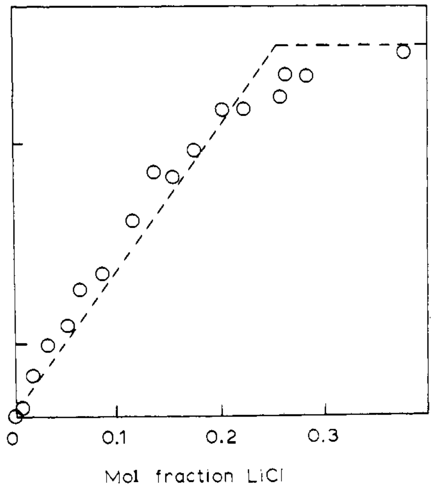


Figure 5. The dependence of ^{13}C chemical shift ($\Delta\delta$ ppm) between the 1- and 2-carbon atoms of lithioisobutyrophenone in dimethoxyethane on the mole fraction of lithium chloride. The broken line is the idealized curve for the irreversible formation of $\text{Li}_4\text{Cl}(\text{C}_{10}\text{H}_{11}\text{O})_3$.

It thus appears that, in all solvents studied, the addition of lithium chloride to the enolate salt leads to the formation of $[\text{Li}_4\text{Cl}(\text{C}_{10}\text{H}_{11}\text{O})_3]_n$. It should be noted that the solubility of lithium chloride in dioxolane is quite low which may preclude the observation of related complexes of higher chlorine content.

Carbon-13 Chemical Shifts. Although the proton spectra described above are useful for demonstrating the existence of various species of lithioisobutyrophenone in solution, it is difficult to derive structural information from the rather small differences in the proton chemical shifts. For this reason we have examined the carbon-13 spectra for some systems of interest. The assignments of the spectra are straightforward except for the ortho and meta carbon atoms, which generally have very similar chemical shifts, and those of the two nonequivalent methyl carbon atoms. The data are presented in Table VI.

It is expected that any substantial changes in the structures of ion pairs or their aggregates will cause a change in the electron distribution in the organic anion which will be reflected as changes in the ^{13}C shifts particularly that of the 2-carbon. Indeed, House, Prabhu, and Phillips[11] have recently observed such variations in a number of enolate ion systems. The data in Table VI allow the following conclusions to be drawn. The species which exist in dioxolane (both at −50 and 40 °C), dioxane, tetrahydrofuran, and tetrahydropyran are characterized by a chemical shift of the 2-carbon atom in the narrow range 96.1–96.4 ppm. The electron distribution in the enolate moieties in these solvents must, therefore, be essentially identical. House and his co-workers,[11] for instance, have ob-

Table VI. ^{13}C Chemical Shifts (δ ppm) for Lithioisobutyrophenone (0.5 M) in Various Solvents

Solvent	T, °C	Ipso	o, m	p	1	2	CH_3's
Dioxolane	40	146.8	128.7, 129.1	126.4	155.3	96.2	20.9, 18.9
Dioxolane	−46	147.0	128.5, 129.8	126.5	155.8	96.4	21.3, 19.6
Dioxolane (0.1 M LiCl)	40	146.7	128.7, 129.0	126.3	155.2	96.3	20.8, 18.8
Dioxane	40	146.7	128.8	126.5	155.1	96.1	21.3, 19.3
Tetrahydrofuran-d_8	40	147.1	128.4, 129.3	126.0	155.6	95.6	21.3, 19.1
Tetrahydropyran	40	146.7	128.3, 128.9	125.8	155.0	95.8	21.0, 19.0
Dimethoxyethane	40	147.6	127.6, 129.2	125.4	156.0	93.3	21.3, 18.9
Dimethoxyethane[a]	−50	147.4	127.2, 129.2	125.1	156.2	91.2	21.5, 18.9
Dimethoxyethane[b]	−50	146.1	128.9	126.5	154.6	95.8	21.5, 18.9
Dimethoxyethane (0.21 M LiCl)	40	147.0	128.3, 128.8	125.9	155.0	95.8	21.2, 18.9

[a] Major (85%) component. [b] Minor (15%) component.

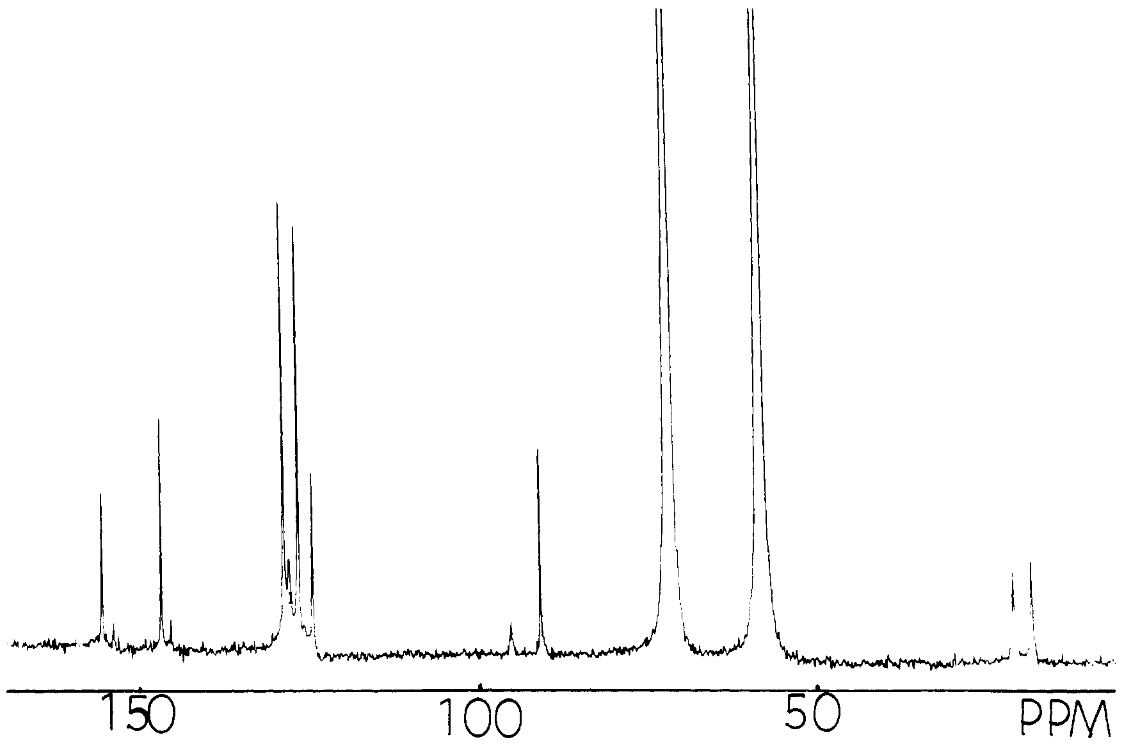


Figure 6. ^{13}C spectrum of lithioisobutyrophenone in dimethoxyethane at −52 °C.

served variations over a range of 6 ppm in the chemical shifts of the 2-carbon atom of the enolate ion of the phenylacetone with solvent and cation. In contrast, the major species in dimethoxyethane clearly is characterized by a different electron distribution in the enolate ion since at −50 °C the 2-carbon atom absorbs at some 5 ppm to higher field (Table VI and Figure 6). It is clear that House's systems exhibit similar effects but, in the absence of low-temperature spectra for them, quantitative comparisons are not possible.

The chemical shifts for the enolate ion in the minor species in dimethoxyethane closely resemble those in dioxolane. This is also true for the species generated by adding lithium chloride to the dimethoxyethane solutions.

Although attention has been focused on the 2-position, smaller but significant variations are observed between the chemical shifts of the 1-, para-, and ipso-carbon atoms for the major species in dimethoxyethane and the species in other ether solvents.

Carbon-13 Spin-Lattice Relaxation Times. The differences between the various species characterized above are likely to involve changes in the degree of aggregation and/or solvation. The delineation of their structures, therefore, requires the determination of molecular size over a wide temperature range and under conditions for which two or more species coexist. It appeared to us that an investigation of ^{13}C spin-lattice relaxation might offer advantages over the usual studies of colligative properties. Because the use of the spin-lattice relaxation time, T_1, in this context is less common and because it is important to appreciate the assumptions involved, some of the principles will now be briefly reviewed.

For all but small organic molecules,[12] the sole mechanism for relaxation of a ^{13}C nucleus bearing directly bonded protons involves the dipole-dipole interaction for which the corresponding relaxation time T_1^{DD}, in the extreme narrowing limit and assuming isotropic motion, is given by

$$1/T_1^{DD} = n\hbar^2\gamma_H^2\gamma_C^2r^{-6}\tau_c \qquad (1)$$

in which n is the number of protons attached to the carbon atom, r is the effective carbon-hydrogen internuclear separation, and τ_c is the correlation time for rotational reorientation. If the reorientation involves small-step rotational diffusion, τ_c may be related to the molecular volume through the Stokes-Einstein equation (eq 2), yielding

$$\begin{aligned} \tau_c &= V_m\eta/kT \\ \tau_c &= 4\pi r_s^3\eta/3kT \end{aligned} \qquad (2)$$

where V_m is the molecular volume and k is Boltzmann's constant. Equation 2 is valid for "large" spheres in a "continuum" fluid of viscosity η. This hydrodynamic equation has been extended to include prolate and oblate spheroids[13] and to the general case in which all three principal rotational diffusion constants are different.[14] In all cases a "stick" boundary condition has been assumed to prevail, i.e., that the fluid at the surface of the diffusing body rotates with the body.

It is known that eq 2 and its extensions satisfactorily describe rotational diffusion of large molecules but become increasingly less accurate with decreasing molecular size, so that eventually τ_c from eq 1 may be as much as ten times smaller than the value from the hydrodynamic equations. Another theoretical approach[15] using a "slip" boundary condition often removes this discrepancy.[16] Its application requires a knowledge of the macroscopic viscosity of the medium and the size and shape of the solute molecule.

An alternative approach is to introduce a microviscosity constant, f_r, into eq 2 which then becomes eq 3.

$$\tau_c = 4\pi r_s^3 f_r\eta/3kT \qquad (3)$$

The empirical eq 4 developed by Gierer and Wirtz[17] provides an approximate method of estimating f_r

$$1/f_r = 6r_o/r_s + (1 + r_o/r_s)^{-3} \qquad (4)$$

In this equation, r_o and r_s are the average radii of the solvent and solute molecules, respectively. We have employed eq 4 in the following way. Equations 1 (with an effective value of r = 1.107 Å[19]) and 3 are combined to give eq 5

$$r_s^3 = 1.68 \times 10^{-27} \times T/\eta f_r T_1^{DD} \qquad (5)$$

in which r_s is in centimeters and η is poise. The viscosity and

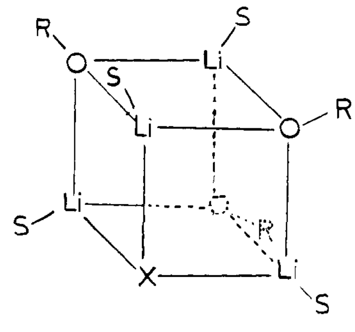
Table VII. Relaxation Times for the Para-Carbon Atom of Lithioisobutyrophenone and Viscosity Data for Various Solvent Systems

	T, °C	T_1, s	$10^2\eta$, P	r_s,[a] Å	f_r
Dioxolane	−45.0	0.08	2.280[b]	7.9	0.43
Dioxolane	−30.5	0.11	1.716[b]	7.9	0.44
Dioxolane	−24.5	0.13	1.540[b]	7.9	0.43
Dioxolane	−17.0	0.17	1.367[b]	7.6	0.42
Dioxolane	4.0	0.24	0.983	7.7	0.43
Dioxolane	20.0	0.37	0.794	7.4	0.41
Dioxolane	30.0	0.48	0.703	7.2	0.41
Dioxolane	40.0	0.58	0.627	7.1	0.40
Dioxolane	46.0	0.63	0.587	7.1	0.40
Dioxolane (0.22 M LiCl)	40.0	0.54	0.675	7.1	0.40
Dioxane	40.0	0.27	1.259	7.3	0.39
Tetrahydrofuran-d_8	40.0	0.68	0.51	7.3	0.39
Tetrahydropyran	40.0	0.37	1.101	7.1	0.39
Dimethoxyethane	40.0	1.27	0.480	6.4	0.34
Dimethoxyethane	17.5	0.78	0.749	6.4	0.34
Dimethoxyethane[c] (0.24 M LiCl)	40.0	1.07	0.42	6.9	0.36

[a] Computed using an effective p-C–H internuclear separation of 1.107 Å.[19] [b] Extrapolated from data in the range 0–50 °C. [c] 0.3 M lithioisobutyrophenone.

relaxation data for the para-carbon atom in Table VII were then used to evaluate r_s, assuming $f_r = 1$. This value of r_s and a value of r_0 based on empirical van der Waals volumes[20] were then used in eq 4 to yield an improved value of f_r. Iteration rapidly converged on the values of r_2 and f_r given in Table VII.

Although, at this stage, the absolute values of r_s must be regarded with considerable caution, certain conclusions may be drawn from their relative magnitudes. Thus the data strongly indicate that, at 40 °C, lithioisobutyrophenone in dioxolane, dioxane, tetrahydrofuran-d_8, and tetrahydropyran exists as aggregates which have approximately the same effective radii as the lithium chloride complex, $[Li_4Cl(C_{10}H_{11}O)_3]_n$. It is likely that $n = 1$ and that these species are tetramers and that they possess the general structure **2** in which each lithium cation is associated with at least one solvent molecule. We will, in fact, adopt structure **2** as a working hypothesis.

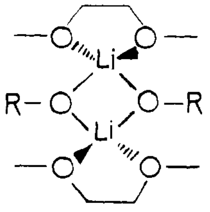


2

Structures **2** are approximately spherical and correspond to species of molecular weights in the range 900–1000 for which the extreme narrowing approximation should apply. Furthermore, as they are essentially ion pair aggregates, it is anticipated that there will be reasonably strong interactions between them and their surrounding sheaths of "free" solvent molecules. For these reasons we expect that a stick boundary condition for rotational diffusion will apply.[16] The enthalpy of activation for rotational reorientation for the aggregate in dioxolane in the temperature region 20–50 °C is approximately 2 kcal mol^{-1}, a value consistent with classical rotational diffusion. Finally, inspection of a molecular model of **2** (see below) indicates that rotation of the rather bulky enolate ion about its carbon-oxygen bond is substantially encumbered by the three adjacent solvent molecules so that rapid (relative to rotational diffusion) rotation is unlikely and the relaxation time of the para-carbon atoms will depend only on the motions of the aggregate as a whole. For these reasons we expect that the values of r_s calculated from eq 5 for systems involving structures **2** are reasonably accurate. A molecular model of **2** (S = dioxolane) was constructed using hydrogen van der Waals radii, normal carbon-carbon and carbon-oxygen bond lengths, and a value of 2.0 Å[21] for the Li-O ionic bonds. The maximum diameter was found to be 16 Å (through the corners of the Li-O cube) and the minimum 14 Å (through the faces of the cube), corresponding to an effective radius, r_s, of approximately 7 Å. In the light of this analysis we conclude that the absolute values of the radii derived from the relaxation times support the tetramer structure.

Decreasing the temperature of the dioxolane solution results in a progressive increase in the apparent size of the lithiisobutyrophenone species. The changes parallel the changes in the proton chemical shift difference between the two methyl groups.[2] As it is known that the equilibrium between the high- and low-temperature species is independent of the concentration of lithioisobutyrophenone,[2] the change in molecular volume cannot be due to increased aggregation. It could, however, arise from a change in the degree of solvation.

Although, as we showed above, dimethoxyethane solutions of lithioisobutyrophenone contain two species, some conclusions concerning the state of aggregation can be drawn. Figure 7 shows the aromatic carbon absorptions obtained under partially relaxed Fourier transform conditions using a 180°-τ-90° pulse sequence at −52 °C. The spectra are not sufficiently well resolved to permit quantitative evaluation of T_1's for both species, but it is clear that T_1 for the para-carbon atom of the minor component is significantly shorter than that of the major species. Analysis of both ^{13}C and proton chemical shift data at −50 and 40 °C indicates that the minor component constitutes 20–25% of the mixture at the higher temperature.[22] Relaxation data at 40 °C (Table VII) therefore indicate that the major species is smaller than the species which exist in the other ether solvents. The apparent molecular radius is, in fact, consistent with the formulation of the major species as the dimer **3**. A molecular model of **3**, using the internuclear distances referred to above, indicated that the most favorable conformation for this structure is approximately a prolate spheroid, with semiaxes of 8 and 5 Å, in which the carbon-hydrogen internuclear vector is coplanar with the major axis and with which it substends an angle of 30°. By employing these data in the treatment outlined in Woessner[23] we calculate that the relaxation time for the para-carbon atom in structure **3** would be 14% shorter than for a spherical structure with the same molecular volume. This leads to values of 8.4 and 5.2 Å for the major and minor semiaxes. Since at 40 °C the two lithioisobutyrophenone species are rapidly exchanging, the



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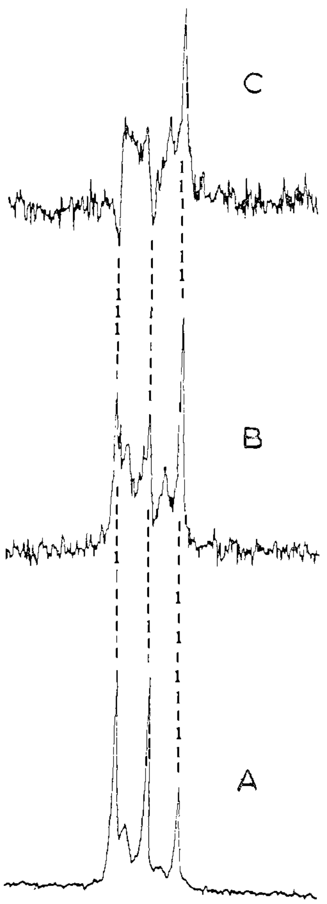

Figure 7. Partially relaxed FT spectra of the aromatic carbon atoms of lithioisobutyrophenone in dimethoxyethane at −52 °C: A, τ = 0.8 s; B, τ = 0.22 s; C, τ = 0.18 s.

relaxation time used in this calculation is a weighted average and the calculated values are therefore too high (probably by about 0.2–0.4 Å if the minor component is a tetramer; see below).

In contrast with the observations for the dioxolane solutions, addition of lithium chloride to lithioisobutyrophenone in dimethoxyethane leads to an increase in molecular volume which, at 0.24 M LiCl, appears to approach that of the high-temperature tetramer in dioxolane.

The effective molecular radii, r_s, strikingly parallel the carbon-13 chemical shifts of the 2-carbon atom. Thus all species having molecular radii in the range 7.0–7.4 Å have δ = 95.6–96.4 ppm for the 2-carbon atom. We, therefore, tentatively conclude that this chemical shift range is characteristic of tetramers and that a substantial increase in shielding (ca. 5 ppm) occurs in the dimer. These conclusions suggest that the minor species in dimethoxyethane is a tetramer and that, in this solvent, there is a fine balance between dimer and tetramer.

In considering the rotational diffusion of species **2** and **3**, we have considered their probable shapes, as well as their effective molecular volumes, in order to obtain the best available estimate of the relaxation times of the para-carbon atoms. It should not, however, be construed that the agreement found between the calculated and experimental values is evidence that the proposed shapes are correct. Too many assumptions are involved and, with only one meaningful relaxation time (that of the para-carbon atom) available for the system, no direct experimental evidence for isotropy or anisotropy of rotational diffusion is possible.

Table VIII. ^{7}Li Relaxation Times and Quadrupole Splitting Constants for Lithioisobutyrophenone in Various Solvents at 40 °C

Solvent	T_1^{DD},[a] s	T_1^Q, s	QSC, kHz
Dioxolane	0.58	0.18	133
Dioxane	0.27	0.081	135
Tetrahydrofuran-d_8	0.68	0.20	136
Dimethoxyethane	1.27	0.22	178

Lithium Quadrupole Relaxation. The conclusion that the carbon-13 chemical shift of the 2-carbon atom, and hence the charge density at that position, is related to the state of aggregation of the lithioisobutyrophenone suggests that a similar relation involving the electrostatic environment of the lithium cation should exist. An appropriate probe for this environment is provided by the ^{7}Li quadrupole splitting constant, QSC, which is given by eq 6

$$\mathrm{QSC} = (1 + \eta^2/3)^{1/2}(e^2Qq_{zz}/h) \qquad (6)$$

where $\eta = (q_{yy} - q_{xx})/q_{zz}$ is the asymmetry parameter and q_{zz} is the maximum electric field gradient at the ^{7}Li nucleus. An approximate estimate of QSC is available from a study of ^{7}Li spin-lattice relaxation. For a nucleus such as ^{7}Li, which has an electric quadrupole moment, spin-lattice relaxation is completely dominated by the quadrupole mechanism. The relaxation time, T_1^Q, is then given by eq 7 (for a spin number $I = 3/2$)

$$1/T_1^Q = \frac{2\pi^2}{5}(\mathrm{QSC})^2\tau_c \qquad (7)$$

T_1^{DD} for the para-carbon atom (eq 1; $n = 1$, $r = 1.107$ Å) can be used to evaluate τ_c leading to eq 8,

$$\mathrm{QSC} = 7.0(T_1^{DD}/T_1^Q)^{1/2} \times 10^4(\mathrm{Hz}) \qquad (8)$$

the assumption again being that the motions of the para CH internuclear vector are the same as motions of the aggregate as a whole.

It is seen (Table VIII) that QSC is the same for lithioisobutyrophenone in dioxolane, dioxane, and tetrahydrofuran, three solvents in which we believe that tetramers prevail. In contrast a substantially larger value is found for the dimethoxyethane system. The true value for the dimer must be even larger since only 75–80% of the salt exists as the dimer, the remainder being believed to be the tetramer. The value is raised an additional 20% by taking into account the effect of anisotropic rotational diffusion for the dimer. In the most favored conformation of **3**, q_{zz} subtends an angle of approximately 60° with the long axis compared with 30° for the para CH internuclear vector. QSC could be as high as 230 kHz for the dimer. In any event, the qualitative conclusion that the field gradient at lithium is appreciably higher in the dimer than the tetramer can be drawn. The quadrupole coupling constants in gaseous lithium halide, in which the asymmetry parameter is zero, range from 408 (LiF) to 172 (LiI) kHz.[24]

Solvation of Aggregates. In this section we outline attempts to establish the extent of solvation of the aggregates from a study of the relaxation times of solvent carbon atoms. The method depends on the expectation of a large difference between the dipole–dipole relaxation times for the solvent in the free and bound states. The observed values for the solution can then be used to determine the fraction of bound solvent. To do this it is necessary to estimate the relaxation times for the free and bound solvent molecules.

For the dimeric species in dimethoxyethane, in which we believe the solvent acts as a bidentate ligand, the methylene CH internuclear vectors for the bound solvent presumably follow the motions of the aggregate. The predicted relaxation

Table IX. Relaxation Times (s), Nuclear Overhauser Enhancements (NOE), Viscosities (cP), and Mole Fractions (*m*) Used in Calculations of Apparent Solvation Number (*n*) for Lithium in Lithioisobutyrophenone (0.5 M) in Various Solvents

	DME		Dioxolane		Dioxolane	
	-CH_2-	Dioxane	OCH_2O	CH_2CH_2	OCH_2O	CH_2CH_2
T, °C	40	40	40		−46	
T_1(ar)	1.27 ± 0.02	0.27 ± 0.01	0.58 ± 0.01		0.080 ± 0.005	
T_1(solv)	17.15 ± 0.25	12.9 ± 0.2	23.2 ± 0.6	24.3 ± 0.7	9.7 ± 0.2	9.0 ± 0.2
NOE(solv)	1.86 ± 0.02	1.89 ± 0.02	1.47 ± 0.05	1.65 ± 0.03	2.05 ± 0.05	2.08 ± 0.04
T_1(soln)	9.8 ± 0.1	6.03 ± 0.03	17.0 ± 0.2	18.0 ± 0.2	2.87 ± 0.05	2.89 ± 0.05
NOE(soln)	2.00 ± 0.03	2.00 ± 0.05	1.90 ± 0.05	1.85 ± 0.02		
η(solv)	0.374	0.921	0.521		1.249[a]	
η(soln)	0.466	1.259	0.628		1.732[a]	
T_1^{DD}(obsd)	9.8 ± 0.2	6.03 ± 0.03	17.7 ± 0.5	19.3 ± 0.3	2.87 ± 0.05	2.89 ± 0.05
T_1^{DD}(f)(stick)	14.7 ± 0.3	9.9 ± 0.2	25.9 ± 0.9	24.2 ± 0.8	7.00 ± 0.13	6.49 ± 0.17
T_1^{DD}(f)(slip)	18.3 ± 0.3	13.5 ± 0.2	31.2 ± 1.4	29.2 ± 1.0	9.7 ± 0.2	9.0 ± 0.2
T_1^{DD}(b)	0.71 ± 0.3	0.15 ± 0.005	0.32 ± 0.01		0.043 ± 0.003	
m^b	0.049 ± 0.005	0.040 ± 0.005	0.034 ± 0.003		0.034 ± 0.003	
n(stick)	0.55 ± 0.06	0.25 ± 0.03	0.17 ± 0.06	0.14 ± 0.15	0.28 ± 0.03	0.26 ± 0.03
n(slip)	0.75 ± 0.08	0.35 ± 0.04	0.23 ± 0.08	0.17 ± 0.06	0.32 ± 0.03	0.31 ± 0.03

[a] See footnote *a*, Table **VII**. [b] [Li]/[solvent].

time of the methylene carbon is then given by

$$T_1^{DD}(b) = T_1(ar) \cdot r_b^6/2r_{ar}^6 \qquad (9)$$

in which T_1(ar) is the relaxation time of the para-carbon atoms in aggregate and r_b and r_{ar} are the CH bond length for the methylene group of dimethoxyethane and the para position of the enolate, respectively. The factor 2 in the denominator occurs because the methylene carbon bears two protons.

An estimate of the relaxation time, T_1^{DD}(f), for the free solvent molecules can be made by correcting the value for the pure solvent to the viscosity of the solution. Ideally, the viscosity dependence can be determined experimentally.[16] In the present work we have considered the two extremes of viscosity dependence. The first corresponds to the "stick" boundary condition for which $T_1^{DD}(f) = T_1^{DD}(solvent) \cdot \eta(solution)$. The second is zero dependence on viscosity which would be true for spherical molecules with the "slip" boundary condition.

The number (n) of solvent molecules per lithium atom is given by eq 10

$$n = (1/T_1^{DD}(obsd) - 1/T_1^{DD}(f))/(1/T_1^{DD}(b) - 1/T_1^{DD}(obsd))/m \qquad (10)$$

in which m is the ratio of the total number of solvent molecules to the number of lithium atoms.

In order to evaluate T_1^{DD}(f) and T_1^{DD}(obsd) it is necessary to measure the nuclear Overhauser enhancements (NOE) for pure solvent and solution. These quantities, the viscosities, and all other raw data necessary for calculating n for the two boundary conditions are assembled in Table IX. In the absence of vibrationally averaged CH bond length for the solvents, the values of 1.08 and 1.1 Å were used in eq 9 for r_{ar} and r_b, respectively.

The range of values of n for dimethoxyethane (Table IX) is close to, but does not include, the expected value of unity. **3** indicates that these values will be little affected by correcting T_1^{DD}(b) for the anisotropy of rotational diffusion. It must be remembered, however, that the dimer only constitutes 80% of the total lithium enolate. It is expected that the value of n for the tetramer may be as low as 0.1-0.2 (see below) in which case the actual value of n for the dimer could be 15-20% higher. The agreement with model **3** is therefore reasonable. It should be noted that, in addition to the above source of error and the propagated random errors (Table IX), there is an uncertainty in the choice of values for r_{ar} and r_b. The appropriate values[25] corrected for anharmonicity and the mean squared vibrational displacements are unavailable for the latter. An error of 1% in r_{ar}/r_b will result in a 6% error in n!

Attempts to extend this method to a study of the tetramers in dioxane and dioxolane yield values of n (Table IX) which are clearly far too low. We conclude that, in these systems in which the solvent molecule is singly attached to the lithium cation, internal rotation of the bound solvent is significantly faster than rotational diffusion of the aggregate. It is true that the value of n for dioxolane at −46 °C is substantially greater than at 4 °C but we do not believe that this can be accepted as evidence of increased solvation at the lower temperature.

Discussion

The above findings that lithioisobutyrophenone in monodentate ether solvents exists as a tetramer and forms a mixed associated species $Li_4Cl(C_{10}H_{11}O)_3$ with lithium chloride suggests that there is a close resemblance between the lithium enolate and alkyllithium compounds which have been extensively studied by Brown and his co-workers.[25] Indeed, the rates of exchange of the enolate ion between $Li_4(C_{10}H_{11}O)_4$ and $Li_4X(C_{10}H_{11}O)_3$ (X = Cl or Br) are even of the same order of magnitude[26] as observed for the system $Li_4(CH_3)_4/Li_4Br(CH_3)_3$ in diethyl ether,[25] although in this latter system it was not possible to demonstrate that the kinetics of the reaction were consistent with a rate-controlling dissociation of the halide complex. The apparent similarities between these two systems, which incidentally involve anions with very different basicities, support the contention by Streitwieser and his co-workers[27] that the bonding in gaseous, monomeric methyllithium is predominantly ionic and thus the formation of ion pair aggregates is essentially a consequence of electrostatic interactions between the ions.

In solvents such as ethers which can only solvate anions by comparatively weak ion-dipole interactions, it is to be expected that aggregation will occur in such a way as to maximize the number of close (2 Å) interactions between anionic and cationic centers. Consideration of all possible tetrameric structures reveals that the average number of close interactions ranges from 7/4 to 5/2 per anion (and cation) in all except the cubic structure **2** in which the number is 3.

In addition to controlling the stabilities of the aggregates, the number of close interactions is expected to influence the ^{13}C chemical shift of the 2-carbon since such interactions will tend to localize the negative charge on oxygen and hence decrease the shielding at the 2-position. Acyclic and monocyclic structures for the tetramer have an average of two or fewer close interactions and should therefore be characterized by chemical shifts of the 2-carbon atom which would be smaller (more shielded) or equal to that observed for the dimer in dimethoxyethane. Bicyclic and tricyclic structures are consistent with the downfield shift observed in dioxolane but are inconsistent with the finding that this shift is unaltered by the addition of lithium chloride. In such structures, the four enolate ions are distributed between sites with different numbers of close interactions so that replacement of any one enolate ion by chloride ion must necessarily change the time averaged environments of the remaining ones. Only in **2** is the immediate environment of an enolate ion unaffected by replacement of another by a chloride ion.

Structure **2** for the chloride ion complex contains nonequivalent lithium nuclei, three of one type and one of another. The failure to observe two lithium resonances in this complex is not surprising, since this complex evidently exchanges lithium nuclei with "free" lithium chloride at a rate which is rapid on the NMR time scale. In all probability, structures such as **2** can also undergo rapid internal reorganization, for instance by rotation of opposite faces of the cube, or through the intermediacy of structures with fewer rings. Similar observations have been reported for $LiBr(CH_3)_3$[25,28,29] although two resonances with an intensity ratio of 1:3 were observed for $LiI(CH_3)_3$.[29] It is also noteworthy that the ^7Li chemical shift for $Li_4(CH_3)_4$ in diethyl ether is approximately 2 ppm downfield from the value for LiBr and LiI[29] in the same solvents in contrast to the much smaller chemical shift difference (Table III) between $Li_4(C_{10}H_{11}O)_4$ and LiCl. Since, at least in dimethoxyethane, the stabilities of the tetramer and dimer are very similar, we suggest that the exchange reaction may involve dissociations to dimers which may recombine with different partners or perhaps which could react with tetramers with the involvement of hexamers as either intermediates or transition states. There does not appear to be any compelling reason to postulate free ions or monomeric ion pairs in these exchange processes. Similar views have been expressed by Brown[25] concerning the methyllithium system.

The relation between the high- and low-temperature forms of the tetramer remains unclear. The fact that the ^{13}C chemical shifts are the same for both species strongly suggests that both have cubic arrays of ions of structure **2.** It does not appear then that, in agreement with the thermodynamic parameters for the equilibrium between these species, the relation between them is simply one of degree of solvation and does not involve a change in the numbers of close ion-ion interactions.

Preferential dimer formation in dimethoxyethane is doubtless due to the "chelation effect", although, as pointed out above, there appears to be only a small difference in the free energies of formation of dimer and tetramer in this solvent.

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