probably other distorted environments. In summary, DOR investigations of quadrupolar ^{27}Al nuclei, together with ^{31}P MAS experiments, yield a wealth of structural information on crystalline aluminophosphates.

Solution Structure and Dynamics of a Mixed Tetramer of Lithium 3,5-Dimethylphenolate and Lithium Perchlorate in Diethyl Ether and Some Related Systems

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Abstract: Lithium 3,5-dimethylphenolate forms a mixed tetramer $Li_4P_3(ClO_4)$ with lithium perchlorate. At temperatures below −20 °C, this tetramer exhibits only one type of phenolate ion in its ^{13}C spectrum but two resonances in the ratio of 1:3 in its ^7Li spectrum. It therefore has cubic tetramer structure 3. The ^7Li quadrupole splitting constants for the unique (Li$_U$) and three equivalent nuclei (Li$_E$) are 51 and 133 kHz, respectively, and correspond to a fully solvated tetrameric species. The tendency toward formation of this species depends on the solvent and decreases in the order Et$_2$O > dioxolane > THF, no mixed tetramer being observed in THF. In dioxolane, some mixed dimer is also formed. Lithium phenolate in dioxolane shows similar behavior. Lithium iodide also forms a mixed tetramer of type 3 in diethyl ether together with a minor amount of a tetramer containing two iodide ions. Contrary to an earlier report, methyllithium forms a mixed tetramer of type 3 with LiClO$_4$ in diethyl ether and this species may be important in reactions with ketones. The first-order rate constants for the intramolecular exchange of Li$_E$ and Li$_U$ and the intermolecular exchange between Li$_E$ and free LiClO$_4$ have been determined. These rate constants are of the order of 1 s^{-1}. The rates of exchange between free and bound ClO$_4$ and iodide ions are also of this order.

We have reported[1] that the regiochemistry of the methylation of the tetrameric lithium enolate of isobutyrophenone by methyl *p*-toluenesulfonate (methyl tosylate) in the weakly polar, aprotic solvent dioxolane is profoundly affected by both lithium tosylate, either formed during the reaction or initially added, and added lithium perchlorate. Similarly, we have observed that these salts strongly accelerate the O-methylation of lithium 3,5-dimethylphenolate under the same conditions.[2] Some observations made at the time indicated an interaction between the salts and the tetrameric lithium phenolate and we suggested that the resulting species may be responsible for the change in regiochemistry in the methylation of the enolate ion. The nature of this species was not, however, established but we suspected it might be mixed aggregate, in particular, a mixed tetramer.

Mixed tetramers involving organic lithium compounds have been identified in several systems. Not surprisingly, similarly constituted organolithium compounds, which are themselves prone to form tetramers in weakly polar solvents, form mixed tetramers (Li$_4$R$_n$R$'_{4-n}$, 1) when mixed together. Examples are MeLi/ETLi in diethyl ether,[3] [LiCH$_2$Si(CH$_3$)$_3$]/*t*-BuLi in hydrocarbons,[4] and the species 1 (R = BuLi, R' = PhCCLi, *n* = 3) in THF.[5] Organolithium compounds also afford mixed aggregates with lithium salts of stronger acids including lithium alkoxides[6,7] and, in particular, with LiBr and LiI. Thus Brown has demonstrated the

formation of Li$_4$(CH$_3$)$_3$I, Li$_4$(CH$_3$)$_3$Br, and Li$_4$(CH$_3$)$_2$Br$_2$ in diethyl ether[8] and has studied the dynamics of interaggregate exchange in the LiBr system.[9] X-ray structures of the mixed aggregates Li$_4$R$_2$Br$_2$(Et$_2$O)$_4$ (R = cyclopropyl)[10] and Li$_4$Ph$_3$Br-(Et$_2$O)$_3$[11] have been reported. We have shown that the lithium enolate of isobutyrophenone forms mixed aggregates of the type Li$_4$E$_3$X (X = Cl, Br) in dioxolane, dimethoxyethane, and THF.[12]

There is some evidence, in addition to that cited above, to indicate that the reactivity, regiochemistry, and even stereochemistry of the reaction of mixed tetramers may be significantly different from the parent homoaggregate. McGarrity[13] has convincingly shown that butyllithium/lithium butoxide mixed tetramers are appreciably more reactive than tetrameric butyllithium toward benzaldehyde in THF. Smith has similarly found that lithium ethoxide catalyzes the addition of *sec*-butyllithium to ethyl benzoate in cyclohexane.[14] In contrast, the lithium bromide and iodide mixed aggregates of methyllithium were found to be less reactive than methyllithium to 2,4-dimethyl-4'-(methylthio)benzophenone in diethyl ether.[15] Ashby and Noding[16]

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examined the effect of the addition of LiBr, LiI, LiO-*t*-Bu, and LiClO$_4$ on the stereochemistry of the addition of methyllithium to 4-*tert*-butylcyclohexanone and found that all three salts increased the rate of addition as well as the proportion of the axial alcohol produced in diethyl ether but not in THF. The effect was most striking in the case of the perchlorate although no NMR spectroscopic evidence could be found[17] for mixed aggregate formation with this salt (see below, however). Seebach[18] has reported excellent evidence for the role of a mixed aggregate controlling asymmetric induction in the aldol reaction and Michael addition of the lithium enolate of cyclohexanone in THF. In this system the mixed aggregates formed with a lithamide derived from a chiral secondary amine. There is little doubt that the parent enolate is tetrameric but it is not known whether the mixed species is also a tetramer, although Williard and Hintze[19] have established by X-ray diffraction a tricyclic (ladder) structure for a species Li$_4$E$_2$(N(*i*-Pr$_2$))$_2$. Finally, although as we have mentioned LiClO$_4$ catalyzes the O-methylation of lithium 3,5-dimethylphenolate, preliminary studies of the proton exchange between the phenol and the lithium phenolate reveal that the proton transfer occurs faster to the homotetramer than to its perchlorate mixed aggregate.[20]

The fragmentary evidence summarized above suggests that mixed tetramers are important in the chemistry of organic lithium compounds in general, and lithium enolates and phenolates in particular. We have already reported a detailed account of the solution structures of the mixed dimers of dimeric lithium 2,6-dimethylphenolate and of the factors influencing their formation.[21] We now present the results of a similar study of mixed tetramer formation by the 3,5-isomer.

Experimental Section

Materials. Solvents were purified as previously described.[21-23] All phenols were obtained from Aldrich Chemical Co. and were purified by either recrystallization from hexane or distillation immediately prior to use. Lithium perchlorate was obtained from J. T. Baker Chemical Co. Lithium iodide was obtained from Aldrich Chemical Co. All lithium salts were purified by recrystallization from distilled water. After purification, salts were heated to 160 °C under high vacuum for at least 8 h to remove water. Methyllithium was obtained from Aldrich Chemical Co. as a 1.4 M solution in diethyl ether (halide content ~0.05 M) and was used without further purification.

Sample Preparation. Lithium phenolate samples were prepared as previously described.[22,23] All salts were added to NMR tubes by syringing in a known amount of a dry methanol solution. After removal of the solvent the residue was heated at 160 °C for at least 8 h under high vacuum immediately prior to the addition of the phenolate solution, to ensure complete removal of water and/or solvent. Methyllithium solutions were prepared by syringing a known amount from a 1.4 M ether solution, degassing on the vacuum line, and removing the solvent. NMR solvent (90% diethyl ether, 10% C$_6$D$_{12}$) was then transferred under vacuum to the sample tube. After further degassing the sample was frozen and sealed under vacuum.

NMR Spectroscopy. NMR spectra were obtained with Bruker WM-360 and AM-500 instruments. ^{13}C chemical shifts are reported relative to internal C$_6$D$_{12}$ (26.40 ppm). ^{6}Li and ^{7}Li chemical shifts are reported relative to 0.3 M LiCl/MeOH (0.00 ppm) at 22 °C (see below). The temperatures were calibrated with use of a methanol standard.

The ^{6}Li, ^{7}Li, and ^{13}C relaxation times were measured with use of the inversion-recovery method. The relaxation times were determined with the Bruker three-parameter nonlinear least-squares program.

The ^{35}Cl (49.0 MHz) spectra were obtained with use of a 90° pulse width. The line widths of the signals were determined by using the Lorentzian fitting routine provided in the Bruker software.

The one-dimensional selective inversion-recovery experiment and the phase-sensitive EXSY 2D experiment were both carried out on a Bruker AM-500 spectrometer resonating at 73.6 MHz for ^{6}Li with a 10 mm VSP broadband probe. The temperature was maintained at 228 ± 1 K with the Bruker variable-temperature unit. The nonselective $\pi/2$ pulse width was 17.5 μs. For the selective inversion experiments, a Bruker selective excitation unit (SEU) was used to generate selective low-power 75-ms Gaussian pulses with a truncation level of 1%. The power output from the SEU was adjusted so that the 75-ms Gaussian pulses resulted in inversion for the selectively irradiated resonance. The selective inversion data were acquired in the difference mode as described by Freeman.[24] In this experiment, the time dependence of chemical or dipolar exchange is followed by obtaining the difference between the normal $(\pi/2)_{\text{nonselective}}$ FID and the FID obtained after a $\pi_{\text{selective}}$-τ-$(\pi/2)_{\text{nonselective}}$ inversion-recovery experiment. The phase-sensitive 2D EXSY(NOESY) experiment was performed with a mixing time of 0.1 s. Eight scans were acquired for each of 128 rows, and time proportional phase incrementation (TPPI) was used to yield absorption mode peaks in both dimensions.

Referencing of ^{7}Li and ^{6}Li Spectra. Nearly all lithium chemical shifts reported in the literature have been referenced to an *external* reference and several different standards have been used. This is necessary because an internal lithium reference is not feasible. With modern spectrometers which employ multifrequency probes and radiofrequency systems, a better procedure is to employ either a ^{1}H or ^{13}C internal reference for calibrating lithium spectra since it is independent of volume susceptibility and the choice of lock substance. In the studies presented here, TMS has been used as the primary ^{13}C internal reference, with perdeuteriocyclohexane as the secondary ^{13}C internal reference (and lock solvent). The choice of secondary ^{13}C internal reference is arbitrary and may be varied from sample to sample, as long as the relationship between the primary ^{13}C and the primary lithium reference is known. This is accomplished as follows.

First, the ^{13}C spectrum of a secondary ^{13}C reference in the standard lithium sample is obtained. The "absolute" frequency of the ^{13}C *primary* reference is then given by

$$\nu_{\text{ref}}(^{13}\text{C}) = \nu_{\text{tr}}(^{13}\text{C}) + \Delta\nu_{\text{off}}(^{13}\text{C}) - \Delta\nu_{\text{shift}} \qquad (1)$$

where ν_{tr} is the transmitter frequency in Hz, $\Delta\nu_{\text{off}}$ is the offset in Hz of the secondary reference from the transmitter frequency, and $\Delta\nu_{\text{shift}}$ is the shift in Hz of the secondary reference relative to the primary reference.

Next, the lithium (X nucleus) spectrum of the standard sample is obtained and the "absolute" frequency of the primary standard, $\nu_{\text{ref}}(\text{Li})$ = $\nu_{\text{tr}}(\text{Li}) + \Delta\nu_{\text{off}}(\text{Li})$.

With these values, it is possible to reference an arbitrary lithium sample by the following procedure. A ^{13}C spectrum of the sample is obtained, and a known ^{13}C resonance (such as a solvent peak) is used to find a new value $\nu'_{\text{ref}}(^{13}\text{C})$ for the absolute frequency of the ^{13}C primary reference as in eq 1. The new absolute frequency $\nu'_{\text{ref}}(\text{Li})$ of the primary lithium reference is *calculated* from the relationship

$$\nu'_{\text{ref}}(\text{Li}) = \nu_{\text{ref}}(\text{Li}) + [\nu'_{\text{ref}}(^{13}\text{C}) - \nu_{\text{ref}}(^{13}\text{C})]\gamma_{\text{Li}}/\gamma^{13}\text{C} \qquad (2)$$

where γ_{Li} and $\gamma^{13}\text{C}$ are the gyromagnetic ratios for ^{6}Li or ^{7}Li and ^{13}C, respectively. The difference between $\nu'_{\text{ref}}(\text{Li})$ and $\nu_{\text{tr}}(\text{Li})$ gives the offset in Hz required to reference the unknown lithium sample. Note that it *is not necessary to know* $\nu_{\text{tr}}(^{13}\text{C})$ and $\nu_{\text{tr}}(\text{Li})$ provided they are held constant in all experiments which is the usual operating procedure. The calibration must of course be performed for each spectrometer. The accuracy of the method involves the usual assumption regarding internal references, namely that their resonance frequencies are insensitive to their environment. For cyclohexane, as a secondary reference, the temperature sensitivity is 6 × 10^{-4} ppm/deg C. It clearly would be possible to use the ^{1}H resonance of TMS as the internal standard which presumably is a somewhat better internal reference. This, however, would have involved an extra step in the vacuum line procedures used for sample preparation in these studies, and in most cases we were interested in the ^{13}C, but not the ^{1}H, spectra. The ideal standard sample for the initial calibration procedure is 0.3 M LiCl in methanol-*d* containing 5% TMS.

In an actual example, using our Bruker WM-360, this reference sample was found to have $\Delta\nu_{\text{off}}$ equal to 65851.05 and 72007.81 Hz for the ^{13}C TMS reference ($\Delta\nu_{\text{shift}}$ = 0) and ^{7}Li, respectively, and these are then the values of $\nu_{\text{ref}}(^{13}\text{C})$ and $\nu_{\text{ref}}(\text{Li})$. The experimental sample containing cyclohexane-d_{12} as an internal ^{13}C reference ($\Delta\nu_{\text{shift}}$ = 26.40 ppm) × 90.56 = 2390.78 Hz) for which $\Delta\nu_{\text{off}}$ was found to be 68587.01 Hz giving $\Delta\nu'_{\text{ref}}(^{13}\text{C})$ = 66196.23 Hz and, from eq 2, $\nu'_{\text{ref}}(\text{Li})$ = 72541.26 Hz ($\gamma_{\text{Li}}/\gamma^{13}$C = 1.545). The zero-frequency reference was then set at this

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Solution Structure and Dynamics of Li₄P₃(ClO₄)

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Table I. [13]C Chemical Shifts for Lithium 3,5-Disubstituted Phenolates with and without Added Salts

substituent	solvent	temp,°C	species	δ^{13}C C(1)	C(2)	C(3)	C(4)
–CH₃	THF[a]	–70	Li₄P₄	168.1	118.1	138.3	116.4
–CH₃	ether	–57	Li₄P₄	167.7	118.4	138.1	116.6
		–50	Li₄P₃(ClO₄)	166.5	118.5	138.3	117.8
		–50	Li₄P₃I	166.5	118.5	138.3	117.7
		–40	Li₄P₂I₂	165.3	118.5	138.5	118.6
–CH₃	dioxolane[a]	–60	Li₄P₄	167.5	117.9	139.2	117.3
		–80	Li₆P₆	167.6	119.3	139.4	117.5
		–80	Li₄P₃(ClO₄)	166.6	118.0	139.5	118.5
		–80	Li₂P(ClO₄)	169.0	120.0	139.6	116.6
–H	dioxolane	–80	Li₄P₄	167.6	120.1	130.5	115.5
		–80	Li₆P₆	167.7	121.2	130.5	116.2
		–80	Li₄P₃(ClO₄)	166.7	120.5	130.6	116.8
		–80	Li₂P(ClO₄)	169.0	120.0	130.6	114.6

[a] Reference 23.

Table II. [7]Li and [13]C Spin–Lattice Relaxation Times and Quadrupolar Splitting Constants for Tetramer, Hexamer, and Mixed Tetramers of Lithium 3,5-Dimethylphenolate and Added Salts in Diethyl Ether

salt	temp, °C	equiv of salt	[7]Li T_1, s Li$_U$	Li$_E$	Li$_{pure}$	[13]C T_1, s	QSC, kHz
			Dioxolane				
	–57				0.28	0.19	57 (tet)
	–57				0.19	0.20	76 (hex)
			Diethyl Ether				
	–50				0.67	0.36	51 (tet)
LiClO₄	–50	0.25	0.67	0.10		0.36	51 (Li$_U$)
							133 (Li$_E$)
LiI	–60	0.25	0.70	0.08		0.33	48 (Li$_U$)
							142 (Li$_E$)

frequency (in Bruker software, SR = 72541.26). The listed frequencies and δ's for the lithium signals are then correctly referenced.

The use of an external reference could lead to significant errors. For example, contribution of volume susceptibility to measured δ's in dioxane and nitromethane differ by ~0.9 ppm which is about 10% of the usual range of Li chemical shifts.

Results

Structure of Lithium 3,5-Dimethylphenolate in Diethyl Ether and Dioxolane. The study of mixed aggregate formation presented below required us to extend our earlier observations of lithium 3,5-dimethylphenolate in solution. This salt in THF and dimethoxyethane has been established[22,23] as having structure **2**
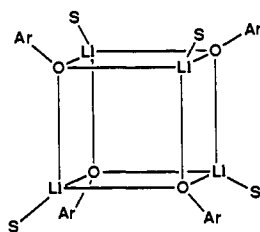
2

which is characterized by the ^{13}C chemical shifts of the phenolate moiety, particularly that of [13]C(4), and by the very low value of its [7]Li quadrupole splitting constant, QSC (a function of the quadrupole coupling constant and the asymmetry parameter).[25] We have now examined the species in diethyl ether and we conclude it is also a tetramer. Table I shows the close correspondence between the chemical shifts in THF and diethyl ether. The QSC values for fully solvated cubic tetramers are known[25,26] to lie in the range 40–65 kHz. The appropriate spin–lattice data and the value of QSC for the species in diethyl ether are given in Table II, and it is seen that the latter falls well within the range expected for structure **2**.

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(26) Jackman, L. M.; Bortiatynski, J. B. *Advances in Carbanion Chemistry*; Sniekus, V., Ed., Vol. I. In press.

Table III. Equilibrium Constants as a Function of Temperature and Thermodynamic Parameters for Tetramer ⇌ ²/₃Hexamer for Lithium 3,5-Dimethylphenolate in Dioxolane

| temp, K	% tet	I(h)/I(t)	K_{eq}, mol$^{-1/3}$
189	32.81	2.05	4.84
197	35.60	1.81	4.34
203	42.30	1.36	3.40
210	47.60	1.10	2.83
216	50.70	0.974	2.55
222	55.70	0.796	2.16

$\Delta H = -2.08$ kcal mol^{-1}; $\Delta S = -7.80$ cal mol^{-1} K^{-1}

We have also reinvestigated the species present in dioxolane, since it is now known that both hexamer and tetramer can coexist in this solvent. At low temperatures (–57 °C), the two species exchange slowly on the ^{13}C and ^{7}Li NMR time scales and both chemical shifts and QSC's can be determined. The chemical shifts for the tetramer are also included in Table I. The QSC data for the tetramer and hexamer are given in Table II. This is the first reported value of QSC for a hexamer, and its rather low value confirms our previous suggestion that the hexamer has an approximately hexagonal prismatic structure[23,27] in which each lithium is surrounded by three anions and one solvent. We has also taken this opportunity to determine the thermodynamic parameters for the tetramer/hexamer equilibrium (Table III).

Lithium 3,5-Dimethylphenolate/LiClO₄ in Diethyl Ether. Figure 1 shows the [7]Li spectra at –50 °C for lithium 3,5-dimethylphenolate with varying amounts of added LiClO₄. The most striking feature of these spectra is the appearance of a pair of signals at δ 0.91 and 0.30 ppm, the relative intensities of which are precisely 1:3 and independent of the amount of LiClO₄. This clearly indicates the formation of a mixed tetramer **3a** involving the incorporation of one perchlorate into the lithium 3,5-dimethylphenolate cubic tetramer **2**. Structure **3a** requires that the three phenolate residues are equivalent and the ^{13}C spectrum indicates that this is the case. The ^{13}C chemical shifts of this new

(27) Williard, P. G.; Carpenter, G. B. *J. Am. Chem. Soc.* **1986**, *108*, 462.

species are included in Table I.

3a X=OClO₃;Ar=3,5-(CH₃)₂C₆H₃
b X=OClO₃;Ar=C₆H₅
c X=I; Ar=3,5-(CH₃)₂C₆H₃
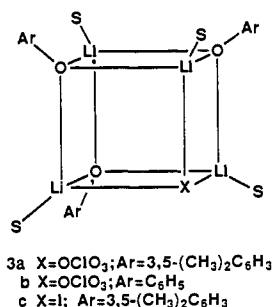
The rates of exchange of the two types of lithium nuclei in **3a** are sufficiently slow on the ^{13}C and ^{7}Li NMR time scales to allow accurate determinations of spin–lattice relaxations and hence ^{7}Li quadrupolar splitting constants (QSC) for the nonisochronous lithiums. Because of the near tetrahedral symmetry of **3a**, the assumption of isotropic rotational diffusion is valid and further-more, as pointed out elsewhere,[25] in phenolate systems the para CH internuclear vector, the reorientation of which is used for determining the correlation time τ_c, is colinear with the principal component of the electric field gradient, q_{zz}. We therefore believe that the values of the QSC's quoted in Table II are free from errors due to incorrect assumptions. This is, in fact, the first deter-mination of QSC values for two different ^{7}Li nuclei in the same molecule.

The QSC for the unique lithium nucleus is identical with the value for the pure tetramer indicating that this lithium is solvated by ether. A much higher value (135–160 kHz) is found for unsolvated lithium in tetramers.[25,26] The much larger value for the three lithiums which share the perchlorate ion indicates a considerable departure from tetrahedral symmetry of the effective negative charges of the four ligands of these lithium atoms. In-deed, an extreme explanation is tht the perchlorate ion is solvent separated from the rest of the aggregate.

To probe the environment of the perchlorate ion in **3a** we have determined ^{35}Cl line widths. Lithium perchlorate in diethyl ether at 0.1 M and room temperature is known to exist predominantly as contact ion pairs which characterized by a ^{35}Cl line width of 114 Hz.[28] For mixed tetramer **3a** we find a value of 305 Hz. An increase is expected because of a decreased rotational diffusion correlation time for the mixed tetramer. However, this value is clearly inconsistent with a solvent-separated perchlorate for which the symmetry of the charge distribution around the chlorine atom will be much closer to pure tetrahedral.

Careful integration of the spectrum in Figure 1c afforded the concentration of the three species in the equilibrium

$$Li_4P_4 + \tfrac{4}{3}LiX \rightleftharpoons \tfrac{4}{3}Li_4P_3X \tag{3}$$

from which an equilibrium constant of $\sim 10^3$ M^{-1} can be calcu-lated. The relative concentrations did not vary over the tem-perature range –55 to –90 °C and we therefore conclude that the process is isothermal and has $\Delta S \sim 13$ cal mol^{-1} deg^{-1}.

Solvent Effects on Mixed Aggregate Formation. The low-temperature ^{13}C spectra of lithium 3,5-dimethylphenolate in dioxolane are complicated by the fact that, in addition to exhibiting signals characteristic of coexisting hexamer and tetramer, the ortho and para resonances of both species have rather similar chemical shifts. For this reason we have studied lithium phenolate, itself, as well as its 3,5-dimethyl derivative. Relevant regions of a ^{13}C spectrum of lithium phenolate in the presence and absence of lithium perchlorate are shown in Figure 2. Clearly, two new species are produced by the addition of salt. One of these appears to be mixed tetramer **3b** (S = dioxolane) because the differences between its ^{13}C chemical shifts and those of the parent tetramer are the same as observed between lithium 3,5-dimethylphenolate mixed tetramer in diethyl ether. The second species is charac-terized by a $\delta(C4)$ of 114.6 ppm which is significantly lower than
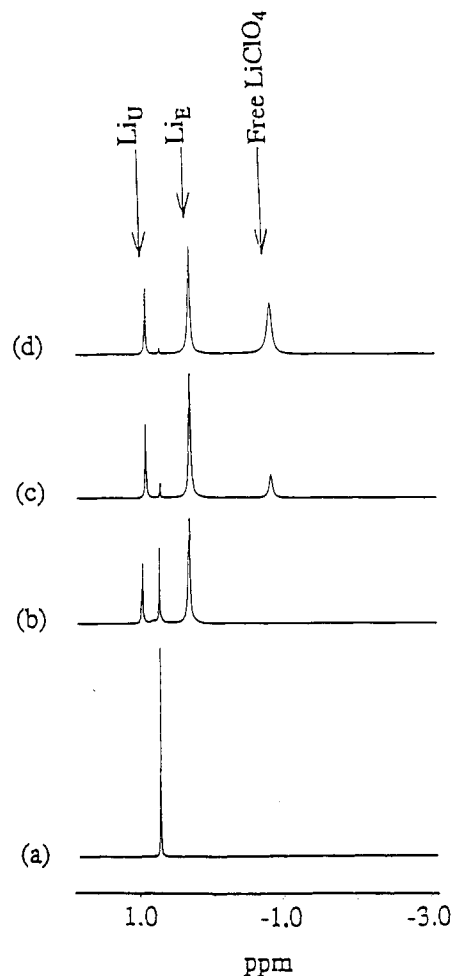
(28) James, D. W.; Mayes, R. E. *Aust. J. Chem.* **1982**, *35*, 1785.

Figure 1. The ^{7}Li (139.95 MHz) spectra of lithium 3,5-dimethyl-phenolate (0.2 M) in diethyl ether at –50 °C with (a) no added salt, (b) 0.25 equiv of LiClO₄, (c) 0.50 equiv of LiClO₄, and (d) 1.2 equiv of LiClO₄.
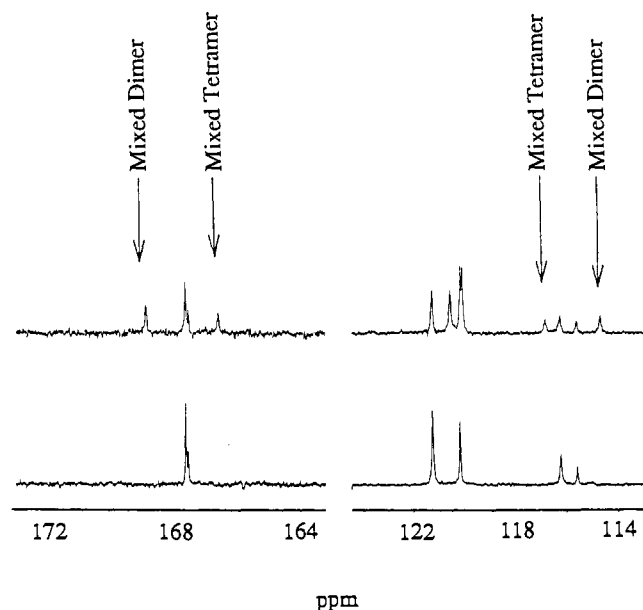

Figure 2. Partial ^{13}C (90.56 MHz) spectra of lithium phenolate (0.2 M) in dioxolane at –80 °C with (a, left) no added salt and (b, right) 1.0 equiv of LiClO₄.

either the hexamer or the tetrameric species. This we assign to a mixed dimer by the following argument. In general, $\delta C(1)$ and $\delta C(4)$ are shifted by ca. +2 and –3 ppm, respectively, in going from the tetramer to the dimer.[23] For lithium *p*-bromophenolate

Table IV. [13]C Chemical Shift δ and $\Delta\delta$ Values for Mixed Tetramers and Mixed Dimers of Lithium 3,5-Disubstituted Phenolates and Lithium Perchlorate in Dioxolane at -80 °C

| species	nuclei	phenolate		3,5-dimethyl-phenolate	
		δ	$\Delta\delta^a$	δ	$\Delta\delta$
Li₄P₃(ClO₄)	C(1)	166.7	0.9	166.6	1.0
	C(2)	120.0	0.1	117.8	0.2
	C(4)	116.8	-1.3	118.5	-1.1
Li₂P(ClO₄)	C(1)	169.0	-1.4	168.9	-1.3
	C(2)	120.5	-0.4	118.2	-0.2
	C(4)	114.6	0.9	116.6	0.8

$^a \Delta\delta = \delta(\text{tetramer}) - \delta(\text{mixed aggregate})$.

in dioxolane, for example, the differences are actually +2.1 and -3.1 ppm, respectively. Conversion of dimeric lithium 2,6-dimethylphenolate in dioxolane to its mixed dimer with lithium perchlorate shifts $\delta C(1)$ by -1 and $\delta C(4)$ by +1.9 ppm.[21] Applying these increments to the shifts for tetrameric lithium perchlorate in dioxolane leads to predicted values of $\delta C(1)$ = 168.8 ppm and $\delta C(4)$ = 114.3 ppm compared with the observed values of 169.0 and 114.6 ppm, respectively. The [7]Li spectrum is less clear (Figure 3). The resonances for the hexamer and tetramer are observed as discrete signals at δ 0.80 and 0.95 ppm, respectively, but the only other resonance, apart from free perchlorate, is a broad signal near δ 0.56 ppm. This is probably due to the mixed dimer and the Li$_E$ resonances of the mixed tetramer with the weak Li$_U$ signal under the tetramer or hexamer resonances. Alternatively, there may be rapid exchange between the two mixed aggregates on the [7]Li time scale with the line broadening being due to quadrupole relaxation since the QSC for both [7]Li$_E$ and [7]Li in the mixed dimer will be substantially greater than that for [7]Li in either the hexamer or pure tetramer. A sample of 0.2 M lithium phenolate in dioxolane with only 0.5 equiv of lithium perchlorate also exhibits the resonances characteristic of the mixed dimer and tetramer. A ^{13}C spectrum of the 3,5-dimethylphenolate (0.1 M) with 2.0 equiv of LiClO₄ exhibits a similar set of resonances (Tables I and IV), indicating coexistences of hexamer, tetramer, mixed tetramer, and mixed dimer. The spectrum for a solution at higher phenolate concentration (0.4 M) with 0.6 equiv of salt lacks the signals of the mixed dimer. There is, however, still a fourth species which we tentatively assign to a mixed hexamer having C(2) and C(4) resonances at 118.3 and ∼117.4 ppm, respectively.

What is clear for both the ^{13}C and [7]Li spectra is that mixed aggregate formation is considerably less favorable in dioxolane than in ether. In THF, there is no evidence for formation of mixed aggregate in either the ^{13}C or [7]Li spectra even at -100 °C.

Lithium 3,5-Dimethylphenolate/LiI in Diethyl Ether. The major species formed in this system is mixed tetramer **3c**. As with the perchlorate system, at temperatures below -20 °C, exchange between the various lithium sites is slow on the ^{7}Li and ^{13}C NMR time scales and it was therefore possible to determine T_1's and [7]Li QSC's; these results are included in Table II. The latter clearly indicate that it has the same structure as **3a**. A rough determination of the equilibrium constant from [7]Li integrals for 0.2 M phenolate/0.05 M lithium iodide solution gave a value of ∼10³ M⁻¹ at -60 °C on the assumption that eq 3 applies. This is probably valid since the concentration of free LiI is very low (<0.01 M) and colligative measurements[8] indicate that LiI is predominantly monomeric at low concentrations. Since the same
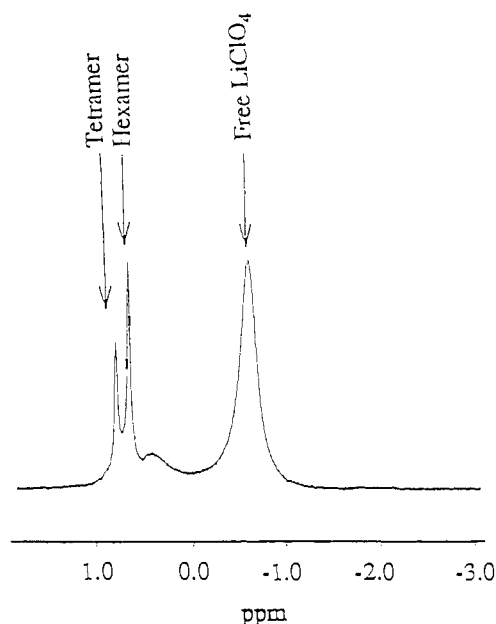
Figure 3. The [7]Li (139.95 MHz) spectrum of lithium phenolate (0.2 M) in dioxolane with 1.0 equiv of LiClO₄ at -80 °C.

value for the equilibrium constant was found at -90 °C, this equilibrium also appears to be isothermal.

In addition to species **3c**, small concentrations of diiodide **1** (R' = I, n = 2) are observed in the presence of 1 equiv of LiI at -4-°C. The ^{13}C chemical shifts are included in Table I. This species should exhibit two lithium resonances of equal intensity but only one (δ = 0.56 ppm) is observed; the other is presumably buried under one of the other resonances all of which are very intense. The formation of this new species is favored by higher temperatures and it is scarcely observable at -90 °C.

We have examined the [7]Li spectra of lithium 3,5-dimethylphenolate in diethyl ether containing 0.25 equiv of both LiClO₄ and LiI. At -90 °C, resonances with shifts corresponding to Li$_E$ in both mixed tetramers are observed indicating that exchange of the anions between the mixed tetramers is slow on the NMR time scale at this temperature. However, the interpretation of these spectra is not straightforward as additional resonances grow in as the temperature is lowered still further and the origins of these new peaks is not known.

[7]Li Chemical Shifts. The chemical shifts of [7]Li in the mixed tetramers are given in Table V. We note that in diethyl ether the shifts for Li$_U$ in the perchlorate and iodide are very similar and somewhat downfield from that in the pure tetramer. The Li$_E$ resonances, however, are dependent on the nature of the inorganic ion which may also be an argument in favor of contact ion pairing in structures **3**. For phenolate aggregates, however, interpretation of chemical shifts must be regarded with some skepticism since long-range shielding by the aromatic ring is probably of the same order of magnitude as the range of the shifts, and changes in the conformations of the aromatic rings arising from rotation about the C-O-Li axis could obscure the effects of changes in the local shielding produced by different ligands.

Methyllithium/LiClO₄ in Diethyl Ether. The [7]Li spectra of commercial methyllithium in diethyl ether with and without 1.5

Table V. [7]Li Chemical Shifts for Lithium 3,5-Disubstituted Phenolates with and without Added Salts

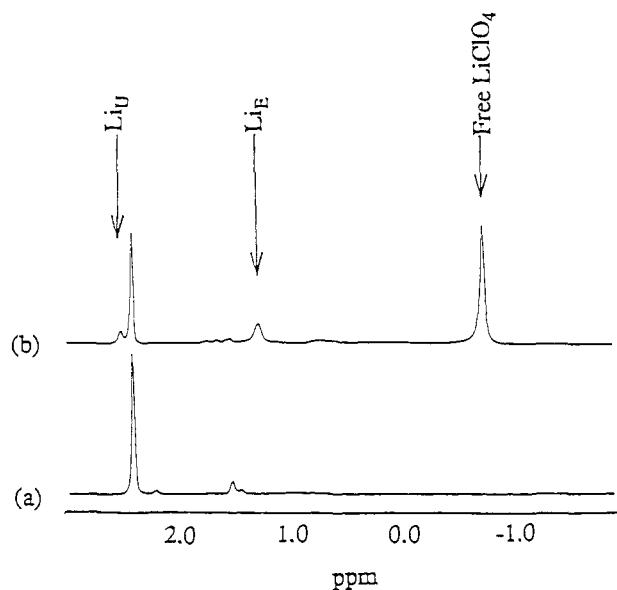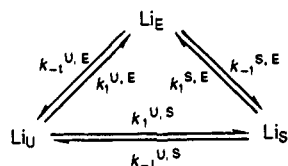| substituent	solvent	temp, °C	species	δ^7Li, ppm			
				Li$_U$	Li$_E$	Li$_S$	Li$_{PURE}$
-CH₃	ether	-50	Li₄P₄				0.72
		-50	Li₄P₃(ClO₄)	0.91	0.30	-0.81	
		-50	Li₄P₃I	0.86	0.68	0.51	
-CH₃	dioxolane	-50	Li₄P₄				0.87
		-50	Li₆P₆				0.68
-H	dioxolane	-50	Li₄P₄				0.95
		-50	Li₆P₆				0.80

Figure 4. The ^7Li (139.95 MHz) spectra of methyllithium 0.4 M in diethyl ether at −80 °C with (a) no added salt and (b) 1.5 equiv of $LiClO_4$.

Scheme I

Li_U = unique Li of $Li_4P_3(ClO_4)Li_E$ = equivalent Li of $Li_4P_3(ClO_4)$
Li_S = Li of free $LiClO_4$)

equiv of $LiClO_4$ at −80 °C are shown in Figure 4. It is clear from the appearance in the former of the two new peaks with a ratio of 1:3 that a mixed tetramer having structure 1 (R = CH_3, R′ = ClO_4, n = 3) is formed. The proton spectrum exhibits resonances at δ −2.0 [$(LiCH_3)_4$] and δ −1.9 ppm (mixed tetramer). The ^{13}C spectrum consists of two overlapping multiplets near δ −13 ppm. A rough estimate for the equilibrium constant for the formation of mixed tetramer, according to eq 3, is ~3 M^{-1} at −80 °C.

Dynamics of Lithium 3,5-Dimethylphenolate/$LiClO_4$ in Diethyl Ether. The rate constants of the exchange process implicit in the equilibria are shown in Scheme I. At room temperature they are of the order of the ^{13}C and ^7Li chemical shift differences and broad resonances are observed. These exchange processes are conveniently studied at a lower temperature (−45 °C) by saturation transfer[29] of ^6Li with enriched samples. The ^6Li chemical shift differences for the various species are large enough for this purpose provided highly selective excitation by Gaussian-shaped pulses are used. These experiments are greatly facilitated by the very long (~40 s) average spin–lattice relaxation times of ^6Li in these systems.

Figure 5 illustrates the effect of selective irradiations of the appropriate ^6Li resonances. The kinetic problem for this system is outlined in Scheme I. For the particular set of concentrations used we have, by integration, found $3[Li_U]$ = $[Li_E]$ = $[Li_S]$, whence $k_1^{S,E}/k_{-1}^{S,E}$ = 1 and, of course, $k_1^{U,E}/k_{-1}^{U,E}$ = 3. It is apparent from Figure 5, a and b, that the rate of transfer of magnetization between Li_U and Li_S is considerably slower than that between these sites and Li_E. This is also born out by a ^6Li 2-D chemical exchange (EXSY) spectrum obtained with a mixing time of 0.1 s (Figure 6) in which cross peaks are observed between ^6Li_E and ^6Li_U and between ^6Li_E and ^6Li_S but not between ^6Li_U and ^6Li_S. The formal analysis (Appendix) of the kinetic problem

(29) Forsén, S.; Hoffman, R. A. *J. Chem. Phys.* **1963**, *39*, 2892.
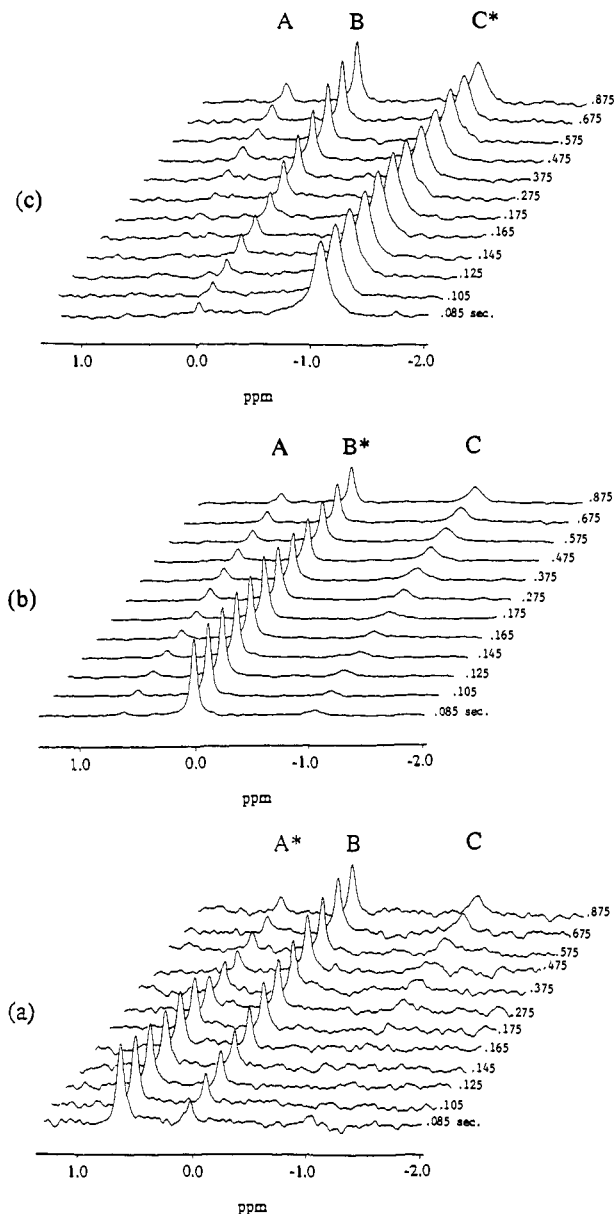

Figure 5. The results of the ^6Li selective excitation inversion-recovery experiment with lithium 3,5-dimethylphenolate (0.2 M) with 1.2 equiv of $LiClO_4$ in diethyl ether at −45 °C: (a) excitation of Li_U; (b) excitation of Li_E; (c) excitation of Li_S. A, B, and C are the resonances of Li_U, Li_E, and Li_S, respectively, and the asterisk designates the irradiated signal.

involves four independent parameters $k_1^{S,E}$, $k_1^{U,E}$, and $k_1^{U,S}$ together with the unperturbed magnetization of Li_U. Although spin–lattice relaxation can be included in the analysis, the time frame of the experiments in Figure 5 is short enought to justify neglecting T_1 contributions. Our purpose was to test the validity of Scheme I and obtain estimates of $k_1^{U,E}$ and $k_1^{S,E}$. We therefore reduced the problem to a three-parameter one by assuming $k_1^{U,S}$ ≪ $k_1^{U,E}$, $k_1^{S,E}$ and evaluating the remaining parameters by nonlinear least-squares fitting of the intensity vs time data from Figure 5. The data for the appearance of Li_E on irradiating Li_U (Figure 5a) affords $k_{-1}^{U,E}$ = 1.37 ± 0.03 s^{-1} and $k_{-1}^{S,E}$ = 0.81 ± 0.07 s^{-1}. These two rate constants were also obtained from the appearance of Li_U on irradiation of Li_E (Figure 5b) and the values of 1.32 ± 0.05 and 0.99 ± 0.11 s^{-1}, respectively, were obtained. The remaining experiment (Figure 5c) in which the appearance of Li_E on irradiation of Li_S is followed gave $k_{-1}^{S,E}$ = 1.07 ± 0.01 s^{-1} but, because of the small amount of Li_U produced, it did not allow a good determination of $k_1^{U,E}$. We also evaluated these rate constants from initial phases (0.0–0.275 s) of Figure 5, a and c, by assuming that the disappearance from the irradiated site is a simple first-order rate process, i.e. the subsequent transfer to the third
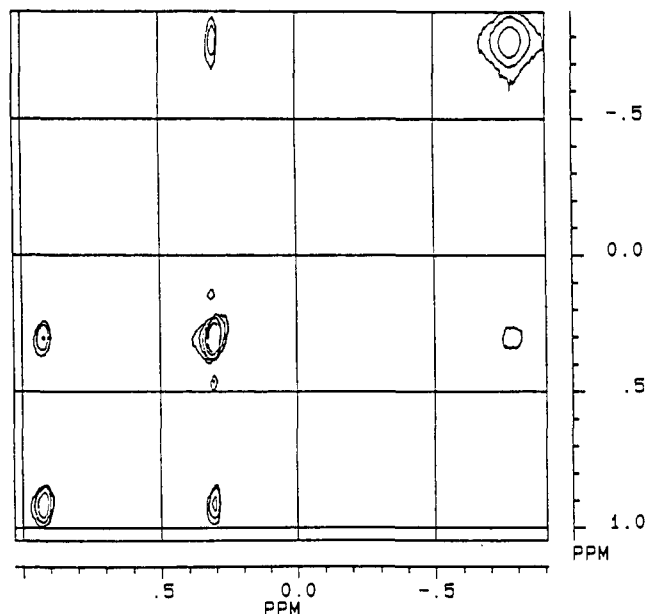
Figure 6. The ^{6}Li 2-D (EXSY) spectrum of lithium 3,5-dimethyl-phenolate (0.2 M) in diethyl ether with 1.2 equiv of LiClO$_4$ at −45 °C with a mixing time of 0.1 s.

site can be neglected to this point. This gives values of $k_{-1}^{U,E}$ = 1.47 ± 0.03 s^{-1} and $k_{-1}^{S,E}$ = 1.17 ± 0.03 s^{-1}. Although these values are in quite good agreement with those quoted above they are both somewhat larger indicating the neglect of the transfer to the third site does introduce errors.

Discussion

The observation of two magnetically distinct types of lithium nuclei in a ratio of 1:3 and of three equivalent phenolate residues for both the perchlorate and iodide mixed aggregates in diethyl ether is unequivocal proof of the existence of cubic tetramer structure 3. The question as to whether the inorganic anion forms a contact or solvent separated ion pair must, however, be addressed. Although the ^{13}C chemical shifts are essentially identical for the perchlorate and iodide mixed tetramers, there are significant differences in the chemical shifts of Li$_E$ in 3a and 3c, whereas those of Li$_U$ are the same (Table V). This evidence favors a contact ion pair structure; furthermore, the data presented above for the effect of mixed tetramer formation on the ^{35}Cl line width of the perchlorate ion are clearly consistent with contact ion pair formation. Experiments in which two inorganic lithium salts are added have shown[21] the anions exchange rapidly between the mixed dimers on the NMR time scale at temperatures at which exchange of lithium cations and phenolates is slow. Experiments designed to demonstrate similar differences in exchange rates for mixed tetramers formed from LiClO$_4$ and LiI indicate that anion exchange is not as rapid. However, both the solvents and the pairs of anions which could be studied were different from those used in the mixed dimer experiments.

The ^{7}Li QSC values for Li$_U$ in both the perchlorate and iodide mixed tetramers lie well within the range expected for fully solvated tetramers. This is noteworthy because it has been shown that, in the solid state, Li$_U$ in Li$_4$Ph$_3$Br(OEt$_2$)$_3$ is unsolvated.[11] This difference is presumably a result of steric crowding which is expected to be much more serious for phenyllithium since it is known to be partially dissociated to the dimer even in diethyl ether.[30] The much larger QSC of Li$_E$ in both mixed tetramers indicates a considerable departure from tetrahedral symmetry which is consistent with a rather weak interaction between the inorganic ions and the lithium cations, both salts being very much less basic than the phenolate ion.

The tetramer/mixed tetramer equilibrium is approximately isothermal as is also the case for the equilibrium between dimeric lithium 2,6-dimethylphenolate and its mixed dimer in dioxolane and THF. In both cases, the endothermicity of desolvation of lithium perchlorate, which accompanies mixed aggregate formation (eq 4), is therefore closely balanced by the electrostatic advantage of having all lithium cations in the system in close contact with the more basic phenolate ions.

$$\tfrac{3}{4}Li_4P_4S_4 + LiXS_3 \rightleftharpoons Li_4P_3XS_4 + 2S \qquad (4)$$

The degree of mixed aggregate formation is dependent on the nature of the solvent, the order being diethyl ether > dioxolane > THF. The most striking difference is for THF in which no evidence for mixed aggregation could be found. This parallels similar observations for LiCH$_3$/LiBr in diethyl ether and THF.[8,31] We have also found[21] that mixed dimer formation of lithium 2,6-dimethylphenolate is substantially less in THF than in dioxolane. These trends are expected because, as mentioned above, mixed aggregate formation involves an overall desolvation of the lithium cations. A further point of interest is the observable equilibrium between mixed tetramer 3a and a mixed dimer, presumably Li$_2$P(ClO$_4$)S$_4$ (S = solvent) in dioxolane, but not in diethyl ether. Formation of mixed dimer 4 involves no change in solvation (eq 5), whereas the production of mixed tetramer involves a formal release of two solvents per LiClO$_4$. Mixed dimer formation should, therefore, be more competitive in the better solvent.

$$Li_4P_4S_4 + 4LiXS_3 \rightleftharpoons 4LiPXS_4 \qquad (5)$$
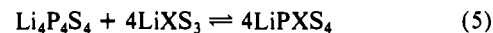
Lithium iodide is similar to LiClO$_4$ in its ability to form mixed tetramer 3b in diethyl ether and again the equilibrium is approximately isothermal. The structure of 3b is clearly very similar to the mixed tetramer formed with LiClO$_4$ since the QSC's for both Li$_E$ and Li$_U$ are nearly identical in the two systems. Unlike lithium perchlorate, lithium iodide exhibits some tendency to form the diiodide (1, R = 3,5-dimethylphenolate, R' = I, n = 2). Lithium halides also show a tendency to form mixed aggregates 1 with n < 3 with methyllithium[8,32] and phenyllithium.[11]

The formation of mixed tetramers 3, like that of mixed dimers, results in a deshielding of the C(4) of the phenolate (~1 ppm) relative to that of the parent aggregate. This is expected because of lithium cations associated with the weakly basic inorganic ion can form stronger bonds with the phenolate oxygens thereby increasing the localization of the negative charge on those atoms. This stronger interaction in the mixed tetramer is apparent in the observed bond length of the PhLi/LiBr mixed tetramer in which the appropriate C–Li bond lengths are 0.05 Å shorter than in the phenyllithium tetramer.[11] The introduction of a second iodide into the tetramer cube causes an additional 1 ppm deshielding of C(4).

The preliminary examination of MeLi/LiClO$_4$ in diethyl ether was undertaken because we believed that a mixed aggregate should be formed in spite of the evidence based on ^{13}C and ^{1}H spectra to the contrary. It is now clear that the differences in chemical shifts between tetramer and a mixed tetramer in these spectra are so small that the resonances would not have been resolvable at the field strengths available at the time of Ashby's investigation.[16] The ^{7}Li (Figure 4), however, provides unequivocal evidence for mixed-tetramer formation. Ashby demonstrated that the rate of reaction of methyllithium to 4-*tert*-butylcyclohexanone is dramatically increased by addition of lithium perchlorate as is the proportion of axial to equatorial alcohol produced. In the absence of evidence for mixed aggregate formation, he postulated that the mechanism involves coordination of the ketone to the lithium cation. It will now be necessary to consider the possible role of a mixed tetramer and a final answer will require a careful study of the reaction kinetics as well as a knowledge of the thermodynamics of mixed aggregate formation. It is interesting

(30) Jackman, L. M.; Scarmoutzos, L. M. *J. Am. Chem. Soc.* **1984**, *106*, 4627.

(31) Waack, R.; Doran, M. A.; Baker, E. B. *Chem. Commun.* **1967**, 1291.
(32) Eppers, O.; Günther, H. *Helv. Chim. Acta.* **1990**, *73*, 2071.

that $LiClO_4$ has no effect in THF. This is, of course, consistent with the explanation involving interaction of $LiClO_4$ with the ketone but, as we have already seen in the case of 3,5-dimethylphenolate, mixed tetramer formation is greatly, if not completely, suppressed in this solvent.

The fluxional behavior ($Li_U \rightleftharpoons Li_E$) of mixed tetramer **3a** is presumably a process similar to those observed with alkyllithium reagents[33] in hydrocarbon and ether solvents and which have recently been discussed by Thomas, Clarke, Jensen, and Young,[7] who point out that an understanding of the mechanism of fluxionality may have a bearing on the reactions of these reagents with other compounds. We concur with this opinion and we were therefore interested to obtain some rate data for both the intra- and intermolecular exchange processes. The results are significant in that, even in the presence of excess salt, they establish the integrity of mixed tetramer **3a**. The half-lives for the exchanges $Li_U \rightleftharpoons Li_E$ and $Li_E \rightleftharpoons Li_S$ are of the order of 1 s at -45 °C. If a similar situation prevails with lithium enolates, some reactions such as protonation and possibly even the aldol reaction could be faster than inter- and intraaggregate exchange. In this case, transient mixed aggregates formed during a reaction might live long enough to function as reactants.

Various mechanisms for the fluxional process in alkyllithium reagents have been discussed by Thomas and her co-workers. They conclude that no one mechanism can be accepted on the evidence currently available. Our rate studies on **3a** were undertaken simply to gain estimates of lifetimes. A much more detailed investigation, including the determination on the kinetic orders of all the processes in Scheme I, will be needed before any mechanistic conclusion can be drawn for our system. Fortunately the types of experiments described here are imminently suitable for such a study and will allow the examination of a wide range of pairs of weakly and strongly basic anions.

Summary

i. Lithium 3,5-dimethylphenolate forms mixed cubic tetramers Li_4P_3X in diethyl ether.

ii. The mixed tetramer is fully solvated (one Et_2O/Li).

iii. Mixed tetramer formation is favored by poor cation solvating power of the solvent.

iv. The anions X in Li_4P_3X form contact ion pairs.

v. Mixed dimers as well as tetramers can form in dioxolane.

vi. Methyllithium forms a mixed tetramer with $LiClO_4$ in Et_2O.

vii. The unique lithium in the mixed aggregate undergoes intramolecular exchange with the three equivalent lithium nuclei.

viii. The exchange between Li of free $LiClO_4$ with the unique Li is slow compared with the intramolecular exchange and the exchange between $LiClO_4$ and the three equivalent lithium nuclei.

Appendix. The Matrix Method for Solving Mechanisms Involving Only First-Order Kinetics

We start by identifying the species (resonances) involved in the chemical exchange and/or magnetization transfer (including relaxation and cross relaxation if appropriate). For convenience these are labeled A, B, C, ...

The differential equations that describe the time dependence of the concentration (or magnetization) of each species are given in (1). Note that each rate element on the right-hand side must be first order.

$$\frac{dA}{dt} = \left(\frac{-1}{T_{1A}} - k_{AB} - k_{AC} - ... \right)A + k_{BA}B + k_{CA}C + ...$$

$$\frac{dB}{dt} = k_{AB}A + \left(\frac{-1}{T_{1B}} - k_{BA} - k_{BC} - ... \right)B + k_{CB}C + ... \quad (1)$$

$$\cdot$$
$$\cdot$$
$$\cdot$$

The rate constants from the differential equations are assembled into a matrix $\mathbf{K}$

$$\mathbf{K} =$$

$$\begin{bmatrix} \left(\frac{-1}{T_{1A}} - k_{AB} - k_{AC} - ... \right) & k_{BA} & k_{CA} & \cdots \\ k_{AB} & \left(\frac{-1}{T_{1B}} - k_{BA} - k_{BC} ... \right) & k_{CB} & \cdots \\ \vdots & \vdots & \vdots & \vdots \end{bmatrix}$$

$$(2)$$

The set of differential equations can be written in matrix form as[34]

$$\frac{d|c\rangle}{dt} = \mathbf{K}|c\rangle$$

where

$$|c\rangle = \begin{bmatrix} A(t) \\ B(t) \\ C(t) \\ \cdot \\ \cdot \\ \cdot \end{bmatrix} \quad (3)$$

The eigenvalues λ_i of $\mathbf{K}$ are then found via the characteristic equation

$$\text{Det } (\mathbf{K} - \lambda_i \mathbf{I}) = 0 \quad (4)$$

where $\mathbf{I} \equiv$ identity or unit matrix.

The Lagrange–Sylvester formula gives the matrix projection operators $\mathbf{P}_i$ corresponding to each of the eigenvalues λ_i

$$\mathbf{P}_i = \prod_{\substack{j=1 \\ j \neq i}}^{N} (\mathbf{K} - \lambda_j \mathbf{I}) / \prod_{\substack{j=1 \\ j \neq i}}^{N} (\lambda_i - \lambda_j) \quad (5)$$

where the product in the numerator is obtained by matrix multiplication and that in the denominator by scalar multiplication.

The time dependence of the concentrations (magnetizations) is then given by

$$|c\rangle = \sum_i \exp(\lambda_i t) \mathbf{P}_i |c_0\rangle \quad (6)$$

where

$$|c_0\rangle = \begin{bmatrix} A_0 \\ B_0 \\ C_0 \\ \cdot \\ \cdot \\ \cdot \end{bmatrix}$$

i.e. the initial conditions. The first element of $|c\rangle$ obtained from eq 6 gives $A(t)$ given the initial conditions $|c_0\rangle$, the second gives $B(t)$, etc.

For the specific example considered above (Scheme I) it is only necessary to consider chemical exchange, since the T_1's of the ^6Li are large and negligible cross relaxation occurs between ^6Li nuclei due to weak dipolar coupling. It is further assumed that the rate

(33) Fraenkel, G.; Henrichs, M.; Hewitt, M.; Su, B. M. *J. Am. Chem. Soc.* **1984**, *106*, 255. Fraenkel, G.; Henrichs, M.; Hewitt, M.; Su, B. M. *J. Am. Chem. Soc.* **1980**, *102*, 3345. Witanowski, M.; Roberts, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 737. Fraenkel, G.; Beckenbaugh, W. E.; Yang, P. P. *J. Am. Chem. Soc.* **1976**, *98*, 6878. Fraenkel, G.; Hsu, H.; Su, B. M. *Lithium, Current Applications in Science, Medicine, and Technology*; Bach, R. O., Ed.; Wiley: New York, 1985; pp 273–289. Bywater, S.; Lachance, P.; Worsfold, d. J. *J. Phys. Chem.* **1975**, *79*, 2148. Seebach, D.; Amstutz, R.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2622.

(34) Starzak, M. E. *Mathematical Methods in Chemistry and Physics*; Plenum Press: New York, 1989; pp 186–191, 289–294.

of *direct* exchange between the U and S sites is negligible compared with those of the other exchange processes. The proposed mechanism is

$$U \xrightleftharpoons[k_u]{3k_u} E \xrightleftharpoons[k_s]{k_s} S$$
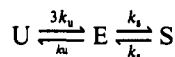
where $k_u \equiv k_{-1}^{U,E}$ and $k_S \equiv k_1^{S,E}$ in Scheme I and the rate constants refer to magnetization transfer by chemical exchange. The $3k_u$ to k_u ratio for the first step arises from the 3:1 ratio of integrated equilibrium magnetization observed (as it must be) for E:U. Similarly, the 1:1 $k_s:k_s$ ratio of rates for the second step reflects the 1:1 ratio of integrated equilibrium magnetization observed for E:S and is a consequence of the concentrations of phenolate and salt used in the experiment.

The differential equations are

$$\frac{dU}{dt} = -3k_u U + k_u E \qquad \frac{dE}{dt} = 3k_u U - (k_u + k_s)E + k_s S$$

$$\frac{dS}{dt} = k_s E - k_s S \qquad (7)$$

The matrix **K** is in this case

$$\mathbf{K} = \begin{bmatrix} -3k_u & k_u & 0 \\ 3k_u & -(k_u + k_s) & k_s \\ 0 & k_s & -k_s \end{bmatrix} \qquad (8)$$

The characteristic equation yields

$$-\lambda(7k_s k_u + 2k_s\lambda + 4k_u\lambda + \lambda^2) = 0$$

with eigenvalues

$$\lambda_1 = -2k_u - k_s - (4k_u^2 + k_s^2 - 3k_s k_u)^{1/2}$$
$$\lambda_2 = -2k_u - k_s + (4k_u^2 + k_s^2 - 3k_s k_u)^{1/2} \qquad \lambda_3 = 0 \qquad (9)$$

Equation 5 gives the projection operators $\mathbf{P}_1$, $\mathbf{P}_2$, and $\mathbf{P}_3$

$$\mathbf{P}_1 = \frac{(\mathbf{K} - \lambda_2\mathbf{I})(\mathbf{K} - \lambda_3\mathbf{I})}{(\lambda_1 - \lambda_2)(\lambda_1 - \lambda_3)} \qquad \mathbf{P}_2 = \frac{(\mathbf{K} - \lambda_1\mathbf{I})(\mathbf{K} - \lambda_3\mathbf{I})}{(\lambda_2 - \lambda_1)(\lambda_2 - \lambda_3)}$$
$$\mathbf{P}_3 = \frac{(\mathbf{K} - \lambda_1\mathbf{I})(\mathbf{K} - \lambda_2\mathbf{I})}{(\lambda_3 - \lambda_1)(\lambda_3 - \lambda_2)} \qquad (10)$$

Finally, eq 6 affords the time-dependent magnetization

$$\begin{bmatrix} U(t) \\ E(t) \\ S(t) \end{bmatrix} = \exp(\lambda_1 t)\mathbf{P}_1 \begin{bmatrix} U_o \\ E_o \\ S_o \end{bmatrix} + \exp(\lambda_2 t)\mathbf{P}_2 \begin{bmatrix} U_o \\ E_o \\ S_o \end{bmatrix} + \exp(\lambda_3 t)\mathbf{P}_3 \begin{bmatrix} U_o \\ E_o \\ S_o \end{bmatrix} \qquad (11)$$

An Analysis of Small-Molecule Binding to Functionalized Synthetic Polymers by ^{13}C CP/MAS NMR and FT-IR Spectroscopy

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Abstract: A spectroscopic investigation of the binding of mono- and diketones to template-functionalized network copolymers of styrene–*m*-diisopropenylbenzene is reported. Quantitative analysis of the binding modes of a substrate molecule (1,3-diacetylbenzene) to a difunctional polymer site was obtained by empirical calibration of FT-IR and ^{13}C CP/MAS NMR data. The two spectroscopic techniques provide a consistent representation of the manner in which 1,3-diacetylbenzene binds to the difunctionalized polymer site. The analysis also provides an opportunity to quantify site isolation within the polymer and the fidelity with which the functionalized site is maintained by the network polymer. Time-dependent binding studies yield information that aids in the analysis of the method by which template-functionalized polymers affect their recognition properties and calls attention to fundamental differences that exist in binding phenomena between naturally occurring macromolecules (proteins) and synthetic high polymers.

Introduction

Molecular imprinting has been found to be an effective means of encoding information in bulk material on a molecular scale.[1] The procedure involves incorporation of small amounts of an imprinting molecule in the polymerization medium. The imprinting molecule is removed after polymerization, leaving a functionalized cavity in the macromolecular network. The focus of past research has been to define the fidelity with which the network polymer maintains site integrity.

The introduction of organic functional groups at templated sites is achieved by the use of a polyfunctional imprinting or template molecule (A) (Scheme I). Sites prepared in this manner have

been evaluated for the ability of the imprinting (template) molecule to "control" the positioning of organic functional groups[2,3] (i.e., C) and influence the shape of the microenvironment.[4,5] In both cases, molecular recognition has been the diagnostic used to evaluate these phenomena, either in batch kinetic rebinding[6,7]

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