Structure of Lithium 2,2,6,6-Tetramethylpiperidide (LiTMP) and Lithium 2,2,4,6,6-Pentamethylpiperidide (LiPMP) in Hydrocarbon Solution: Assignment of Cyclic Trimer and Tetramer Conformational Isomers

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The explosive growth in organolithium structure determination stems from two complementary experimental approaches. X-ray crystallography provides detailed views of those structures that can form stable, diffracting single crystals,[1,2] while NMR spectroscopy offers a more global view of all stable structural forms, albeit at a substantially reduced atomic resolution.[2-4] However, a debate often emerges as to the extent to which one can rely upon the detailed pictures provided by crystallography to help fill in the spectroscopically elusive solution structure details. The correlation of solid and solution aggregation states can be straightforward. However, it is relatively rare that such comparisons include conformational preferences,[5] despite the central role that such spatial relationships often play in discussions of organolithium reactivity and selectivity.

We describe herein ^{6}Li and ^{15}N NMR spectroscopic studies of lithium 2,2,6,6-tetramethylpiperidide (LiTMP; **1**) and 2,2,4,6,6-pentamethylpiperidide (LiPMP; **2**) in hydrocarbon solution.[6-9] The conformationally mobile LiTMP and the conformationally anchored (yet otherwise analogous) LiPMP[6] allow us to uniquely assign the aggregation states and conformations of a complex ensemble of cyclic trimers and tetramers. These results are contrasted with the aggregation state and conformational preference of LiTMP in the solid state determined by Lappert and co-workers.[10]

^{6}Li and ^{15}N NMR spectroscopic studies of 0.10 M [^{6}Li,^{15}N]-LiTMP in pentane at −40 °C reveal the existence of two species (≈4:1), each displaying 1:2:1 ^{6}Li triplets and 1:2:3:2:1 ^{15}N quintets characteristic of cyclic oligomers (Figure 1A,B).[11] The predominant form was shown by concentration dependencies to be at a higher relative aggregation state. The inverse-detected ^{15}N homonuclear zero-quantum NMR spectrum[8] recorded at −50 °C reveals (supplementary material) that both oligomers are higher cyclic oligomers rather than cyclic dimers. Neither loss of coupling from *intermolecular* site exchanges nor an increase in multiplicity resulting from rapid *intramolecular* Li–Li site exchanges[12] was observed upon warming the probe to 20 °C.[13] Upon decreasing the probe temperature to −120 °C, the ^{6}Li resonance corresponding to the higher of the two oligomers decoalesces, affording a number of overlapping ^{6}Li triplets in the slow exchange limit (Figure 1C). The increased spectral complexity is fully consistent with a freezing out of the chair–chair conformational flip observed in previous studies of solvated LiTMP dimers and mixed aggregates.[6] In contrast, the ^{6}Li resonance corresponding to the lower of the two cyclic oligomers remains sharp over the entire temperature range (Figure D–F), suggestive of a single (symmetric) conformer.

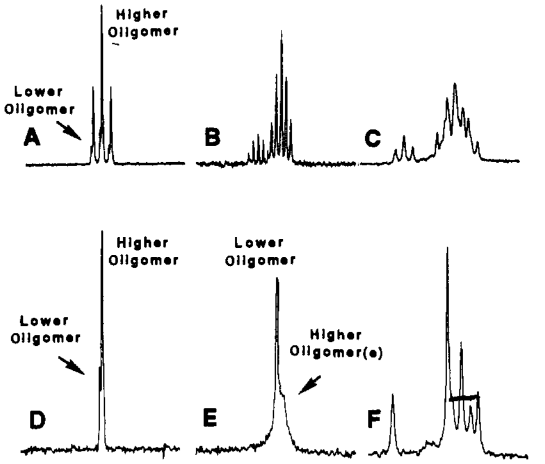

Figure 1. (A) ^{6}Li NMR spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP in pentane at −40 °C; (B) ^{15}N NMR spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP in pentane at −40 °C; (C) ^{6}Li NMR spectrum of 0.10 M [^{6}Li,^{15}N]LiTMP in pentane at −120 °C; (D) ^{6}Li NMR spectrum of 0.11 M [^{6}Li]LiTMP (^{14}N) in pentane at −50 °C; (E) ^{6}Li NMR spectrum of 0.11 M [^{6}Li]LiTMP in pentane at −75 °C; (F) ^{6}Li NMR spectrum of 0.11 M [^{6}Li]LiTMP in pentane at −100 °C.

We suspected that the two aggregation states correspond to cyclic trimers and tetramers. If so, there are six possible chemically distinct solution structures (**3**–**8**; methyls are omitted for clarity). Interestingly, the two trimers and the four tetramers are uniquely defined by their symmetries and consequent resonance numbers and atomic connectivities. However, since we could not be certain that we had fully attained the slow exchange limit, we turned to [^{6}Li,^{15}N]LiPMP. Previous studies[6] had shown that the remote 4-methyl substituent of LiPMP offers a conformational lock without measurably influencing aggregate morphology or distribution. Most importantly, stereoisomer interconversion in LiPMP requires a relatively slow N–Li bond rupture (eq 1). Indeed, the ^{6}Li and ^{15}N NMR spectra of [^{6}Li,^{15}N]LiPMP in pentane show high complexity that is invariant up to ambient temperature. A ^{6}Li–^{15}N heteronuclear multiple

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[11] Selected spectral data for [^{6}Li,^{15}N]LiTMP are as follows: ^{6}Li NMR (73.6 MHz, pentane, −40 °C) δ 2.71 (t, $^1J_{\text{Li-N}}$ = 6.2 Hz, major oligomer), 2.74 (t, $^1J_{\text{Li-N}}$ = 6.2 Hz, minor oligomer); ^{15}N NMR (50.7 MHz, pentane, −40 °C) δ 92.8 (t, $^1J_{\text{Li-N}}$ = 6.2 Hz, major oligomer), 93.6 (t, $^1J_{\text{Li-N}}$ = 6.2 Hz, minor oligomer).

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[13] Exchanges occur on laboratory time scales as shown by mixing independently prepared solutions of [^{6}Li]LiTMP and [^{6}Li,^{15}N]LiTMP, *heating to 70 °C*, and observing the appearance of ^{14}N–^{6}Li–^{15}N subunits by ^{6}Li NMR spectroscopy.

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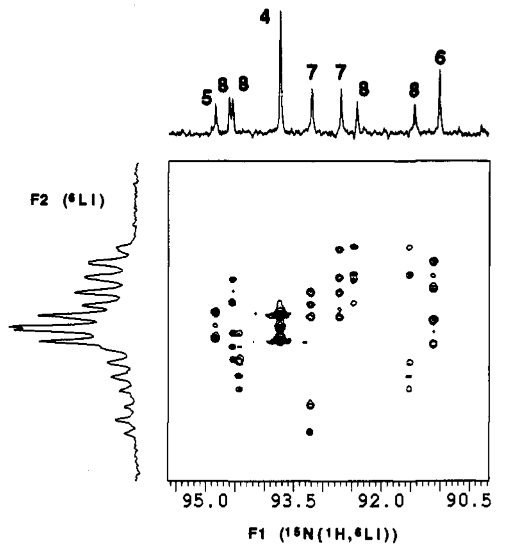
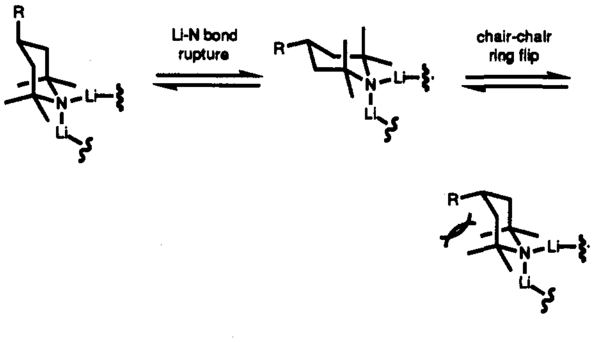


Figure 2. ^{6}Li–^{15}N HMQC spectrum of 0.1 M [^{6}Li,^{15}N]LiPMP in pentane at −100 °C; 256 t_1 increments were acquired with 32 transients/increment over 480 min. The left-hand and upper traces are the corresponding one-dimensional ^{6}Li and ^{15}N{^{1}H,^{6}Li}NMR spectra, respectively. The spectrum was recorded on a Varian Unity 500 spectrometer equipped with a custom-built three-channel probe designed to accommodate lithium and nitrogen pulses with concurrent proton decoupling. The spectrometer operates at 73.56 and 50.65 MHz for ^{6}Li and ^{15}N, respectively. Data were processed in the phase sensitive mode. Digital resolution in f_1 prior to zero filling is 2.0 Hz.



(1)

quantum correlation (HMQC) spectrum of [^{6}Li,^{15}N]LiPMP is illustrated in Figure 2.[9] The center lines of the triplets correspond to nonselected orders of coherence and are almost entirely canceled by the phase cycle.[14] The multiplicities, relative aggregation states, and resonance correlations allow us to detect and assign five of the structures depicted in Chart 1 (Table 1). The four tetramer isomers exist in nearly equal proportions. Only the unsymmetrical C_s trimer **3** is not detectable.

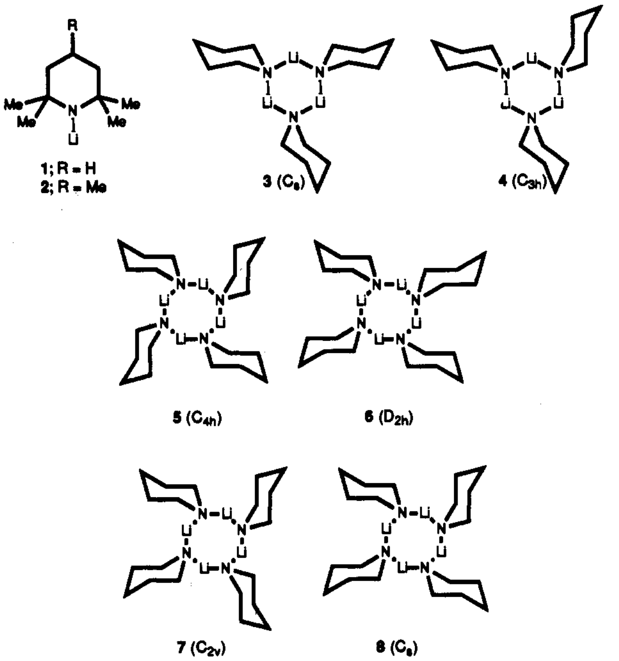
It is gratifying to unravel this level of structural complexity at such a high resolution using what are now relatively routine spectroscopic experiments. This reinforces our suspicion that the conformationally rich lithium piperidides might provide structural details generally not available from other lithium dialkylamides. The results also underscore important relationships between solution state and solid state structure determinations. The X-ray structure determination of unsolvated LiTMP by Lappert and co-workers revealed C_{4h} tetramer **5**.[10] While the crystal structure adequately foreshadows the existence of higher oligomers in hydrocarbon solution, the solid state conformational preference stems entirely from lattice packing effects. This suggests that inclusion of subtle conformational effects evident in solid state organolithium structures into discussions of solution structures and reactivities should be done with caution.

Table 1. ^{6}Li and ^{15}N NMR Spectroscopic Data of [^{6}Li,^{15}N]LiPMP[a]

structure	^{6}Li δ (m, $J_{\text{N-Li}}$)	^{15}N δ (m, $J_{\text{N-Li}}$)
4	2.74 (t, 6.2)	93.75 (quint, 6.2)
5	2.71 (t, 6.2)	95.35 (quint, 6.2)
6	2.41 (t, 6.7)	89.82 (quint, 6.3)
	2.77 (t, 6.0)	
7	2.32 (t, 7.0)	92.26 (quint, 6.6)
	2.60 (t, 6.1)	92.96 (quint, 6.3)
	3.33 (t, 6.6)	
8	2.31 (t, 7.0)	90.45 (quint, 6.4)
	2.51 (t, 5.8)	91.86 (quint, 6.0)
	2.87 (t, 6.3)	95.00 (quint, 6.3)
	3.05 (t, 6.2)	94.92 (quint, 6.6)

[a] Spectra were recorded on a Varian Unity 500 spectrometer equipped with a custom-built three-channel probe designed to accommodate lithium and nitrogen pulses with concurrent proton decoupling. The spectrometer operates at 73.56 and 50.65 MHz for ^{6}Li and ^{15}N, respectively. The chemical shifts are reported relative to 0.3 M ^{6}LiCl/MeOH at −100 °C (0.0 ppm) and [^{15}N]aniline (52 ppm).

Chart 1



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Supplementary Material Available: Inverse-detected ^{15}N homonuclear zero-quantum NMR spectrum of [^{6}Li,^{15}N]LiPMP (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(14) Slight differences in ^{6}Li–^{15}N coupling constants result in incomplete cancellation of the center lines of the triplets.