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, disintegrating 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,2 despite the central role that such spatial relationships often play in discussions of organolithium reactivity and selectivity.

We describe herein [6Li] and [15N] NMR spectroscopic studies of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) and LiPMP2,4 in hydrocarbon solution. The conformationally mobile LiTMP and the conformationally anchored (yet otherwise analogous) LiPMP 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

[6Li] and [15N] NMR spectroscopic studies of 0.10 M [6Li]LiTMP in pentane at -40 °C reveal the existence of two species (4:1), each displaying 1:2:1 [6Li] triplets and 1:2:3:2 [15N] quintets characteristic of cyclic oligomers (Figure 1A,B).11 The preponderant form was shown by concentration dependencies to be at a higher relative aggregation state. The inverse-detected [15N] NMR spectrum5 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 exchanges12 was observed upon warming the probe to 20 °C.13 Upon decreasing the probe temperature to -120 °C, the [6Li] resonance corresponding to the higher of the two oligomers decoalesces, affording a number of overlapping [6Li] 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.4 In contrast, the [6Li] 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.

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 [6Li,15N]LiPMP. Previous studies4 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 [6Li] and [15N] NMR spectra of [6Li,15N]LiPMP have sharp, well-defined [6Li] resonance corresponding to [6Li] quintets that are invariant up to ambient temperature. A [6Li,15N] heteronucleus multiple

11 Selected spectral data for [6Li,15N]LiTMP are as follows: [6Li] NMR (73.6 MHz, pentane, -40 °C) 2.71 (t, J6Li,15N = 6.2 Hz, major oligomer);15N NMR (50.7 MHz, pentane, -40 °C) 9.23 (t, J15N,13C = 6.2 Hz, major oligomer), 9.36 (t, J15N,13C = 6.2 Hz, minor oligomer).


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

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

<table>
<thead>
<tr>
<th>structure</th>
<th>$^6$Li $\delta$ (m, $J_{N-L}$)</th>
<th>$^15$N $\delta$ (m, $J_{N-L}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>2.74 (t, 6.2)</td>
<td>93.75 (quint, 6.2)</td>
</tr>
<tr>
<td>5</td>
<td>2.71 (t, 6.2)</td>
<td>95.35 (quint, 6.2)</td>
</tr>
<tr>
<td>6</td>
<td>2.41 (t, 6.7)</td>
<td>89.82 (quint, 6.3)</td>
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<tr>
<td>7</td>
<td>2.32 (t, 6.0)</td>
<td>92.26 (quint, 6.6)</td>
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<tr>
<td>8</td>
<td>2.31 (t, 7.0)</td>
<td>90.45 (quint, 6.4)</td>
</tr>
<tr>
<td>9</td>
<td>2.51 (t, 5.8)</td>
<td>91.86 (quint, 6.0)</td>
</tr>
<tr>
<td>10</td>
<td>2.87 (t, 6.3)</td>
<td>95.00 (quint, 6.3)</td>
</tr>
<tr>
<td>11</td>
<td>3.05 (t, 6.2)</td>
<td>94.92 (quint, 6.6)</td>
</tr>
</tbody>
</table>

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

1: $R = H$
2: $R = Me$
3 (C$_4$)
4 (C$_4$)
5 (C$_4$)
6 (D$_2$)
7 (C$_4$)
8 (C$_4$)