

## <sup>6</sup>Li/<sup>15</sup>N NMR-Based Solution Structural Determination of Et<sub>2</sub>O- and TMEDA-Solvated Lithiophenylacetonitrile and a LiHMDS Mixed Aggregate

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Deprotonated nitriles have proven to be useful reagents in organic synthesis.<sup>1</sup> However, in contrast to the enolates of ketones, esters, and amides, little information is available on the solution structures of the corresponding nitrile anions.<sup>1b</sup> Two central issues remain unresolved: the position of metalation and the degree of aggregation (Chart 1). In the solid state, both *N*-metalation and *C*-metalation have been observed.<sup>2,3</sup> Ab initio calculations indicate that a bridged structure 3 is favored for unsolvated lithioacetonitrile.<sup>4,5</sup> Solution state studies have been less conclusive.<sup>6</sup> On the basis of <sup>13</sup>C NMR spectroscopy, Bradamante and Pagani concluded that sodiated nitriles exist as solvent-separated or free ion pairs in DMSO, in which the negative charge is essentially localized on the α-carbon.<sup>7</sup> Therefore, in solvents of lower polarity/donicity, (α-cyanoalkyl)-metals such as 4 remain as another possibility. Aggregation state determinations have been attempted on the basis of colligative measurements, but varying results have been obtained.<sup>8,9</sup> In this communication we demonstrate the use of <sup>6</sup>Li/<sup>15</sup>N NMR spectroscopy<sup>10</sup> to unambiguously determine both the

Chart 1

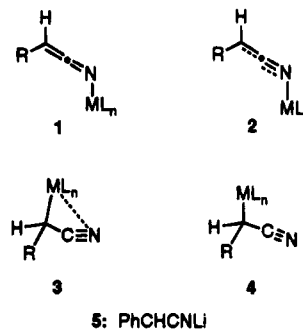
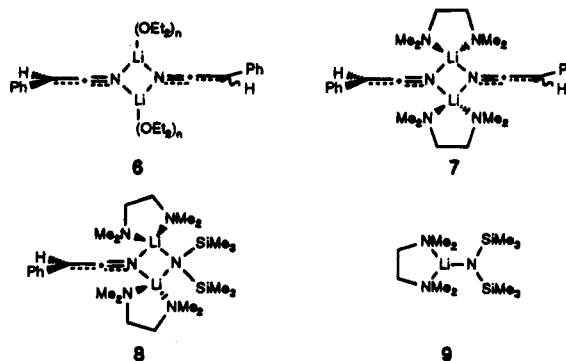


Chart 2



position of metalation and the aggregation state of Et<sub>2</sub>O- and TMEDA-solvated lithiophenylacetonitrile (5) in solution and to demonstrate the existence of a TMEDA-solvated 5/lithium hexamethyldisilazide (LiHMDS) mixed aggregate.

A 0.1 M solution of [<sup>6</sup>Li,<sup>15</sup>N]5 was prepared from [<sup>15</sup>N]phenylacetonitrile<sup>11</sup> and 1.0 equiv of [<sup>6</sup>Li]LiHMDS<sup>12</sup> in 2:1 toluene: diethyl ether at -78 °C. The <sup>6</sup>Li and <sup>15</sup>N NMR spectra recorded at -90 °C (<sup>6</sup>Li triplet, <sup>15</sup>N quintet, <sup>1</sup>J<sub>Li-N</sub> = 3.4 Hz) are consistent with a cyclic oligomer, characteristic of related *N*-lithiated species.<sup>13</sup> Inverse-detected <sup>15</sup>N homonuclear zero-quantum NMR spectroscopy<sup>14</sup> demonstrates that ether-solvated 5 has a cyclic dimer structure 6 (Chart 2) rather than that of a higher cyclic oligomer. Similarly, TMEDA-solvated 5 was demonstrated to be a dimer 7 in neat toluene, paralleling the structure observed in the solid state.<sup>3a</sup>

The observed <sup>6</sup>Li-<sup>15</sup>N coupling constants of 3.4 and 3.5 Hz in 6 and 7 are characteristic of dimeric *N*-lithiated species, suggesting little or no contribution from a *C*-lithiated tautomer such as 4. Furthermore, given the Li<sub>2</sub>N<sub>2</sub> core established by NMR spectroscopy, C-Li contact should be geometrically unfavorable. However, to further investigate this possibility, the <sup>13</sup>C NMR spectrum of [<sup>6</sup>Li,<sup>14</sup>N]7 was examined, and no <sup>6</sup>Li-<sup>13</sup>C coupling was observed at the α-cyano carbon (32.7 ppm) down to -90 °C. Fluxional behavior of the TMEDA ligands was also evident, exhibiting two methyl resonances and one methylene resonance at -90 °C. Coalescence of the methyls occurred at -70 °C, indicating Δ*G*<sup>‡</sup><sub>203K</sub> = 9.0 ± 0.3 kcal mol<sup>-1</sup> (Δ*ν* = 471 Hz).<sup>15,16</sup>

(11) Prepared from benzyl bromide and [<sup>15</sup>N]KCN in CH<sub>3</sub>CN in the presence of 18-crown-6.

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(3) Interestingly, the observed bond lengths in the *N*-metalated nitriles do not support the expected ketenimine structure 1; instead the structure is best formulated as the partially delocalized metalated nitrile 2. (a) {[PhCHCNLi(tmEDA)]<sub>2</sub>C<sub>6</sub>H<sub>6</sub>}: Boche, G.; Marsch, M.; Harms, K. *Angew. Chem., Int. Ed. Engl.* 1986, 25, 373. (b) {[PhCHCNLi(tmEDA)]<sub>2</sub>[Li(tmEDA)N(*i*-Pr)<sub>2</sub>]}: Zarges, W.; Marsch, M.; Harms, K.; Boche, G. *Angew. Chem., Int. Ed. Engl.* 1989, 28, 1392. (c) Barker, J.; Barnett, N. D. R.; Barr, D.; Clegg, W.; Mulvey, R. E.; O'Neil, P. A. *Angew. Chem., Int. Ed. Engl.* 1993, 32, 1366. (d) Hiller, W.; Frey, S.; Strähle, J.; Boche, G.; Zarges, W.; Harms, K.; Marsch, M.; Wollert, R.; Dehnicke, K. *Chem. Ber.* 1992, 125, 87. (e) Lambert, C.; Schleyer, P. v. R.; Pieper, U.; Stalke, D. *Angew. Chem., Int. Ed. Engl.* 1992, 31, 77.

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(5) Two metalated nitriles displaying intermolecular bridging have also been characterized by X-ray crystallography: (a) [Cp<sub>2</sub>La(η<sup>2</sup>-CH<sub>2</sub>CN)]<sub>2</sub>: Heeres, H. J.; Meetsma, A.; Teuben, J. H. *Angew. Chem., Int. Ed. Engl.* 1990, 29, 420. (b) A lithiated cyclopropyl nitrile: Boche, G.; Harms, K.; Marsch, M. *J. Am. Chem. Soc.* 1988, 110, 6925.

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(9) Moreover, the accuracy of colligative measurements is vulnerable to unseen impurities, and by their nature these methods can offer no direct information on the identity and population of the discrete aggregation states present. (a) Gregory, K.; Schleyer, P. v. R.; Snaith, R. *Adv. Inorg. Chem.* 1991, 37, 47. (b) Galiano-Roth, A. S.; Collum, D. B. *J. Am. Chem. Soc.* 1989, 111, 6772.

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**Table 1.** NMR Spectroscopic Data of 6–9<sup>a</sup>

compound	<sup>6</sup> Li δ (m, J <sub>N-Li</sub> )	<sup>15</sup> N δ (m, J <sub>N-Li</sub> )	solvent
[ <sup>15</sup> N]phenylacetonitrile		247.07	1:1 toluene:Et <sub>2</sub> O
[ <sup>6</sup> Li, <sup>15</sup> N]6	-0.28 (t, 3.4)	222.08 (q, 3.4)	2:1 toluene:Et <sub>2</sub> O
[ <sup>6</sup> Li, <sup>15</sup> N]7	0.26 (t, 3.5)	218.47 (q, 3.5)	toluene
[ <sup>6</sup> Li, <sup>14</sup> N, <sup>15</sup> N]8	-0.09 (d, 3.1)	223.54 (q, 3.1)	toluene
[ <sup>6</sup> Li, <sup>15</sup> N, <sup>15</sup> N]8	-0.09 (t, 3.1)	223.54 (q, 3.1)	toluene
		43.56 (q, 3.1)	
[ <sup>6</sup> Li, <sup>15</sup> N]9	0.75 (d, 6.1)	47.49 (t, 6.1)	toluene

<sup>a</sup>Spectra were recorded at [Li]<sub>total</sub> = 0.1 M at -90 °C in the designated solvent. The chemical shifts are reported relative to 0.3 M <sup>6</sup>LiCl/MeOH (0.0 ppm) and [<sup>15</sup>N]dimethylethylamine (25.7 ppm), both at -90 °C (external reference). All *J* values are reported in Hz: d, doublet; t, triplet; q, quintet.

<sup>6</sup>Li/<sup>15</sup>N NMR spectroscopy has been an effective tool for uncovering the stereochemical diversity present in lithium amides.<sup>10,17</sup> Interestingly, the *anti* and *syn* diastereomers of 6 and 7 cannot be resolved under these conditions, although we cannot rigorously exclude formation of a single isomer. Also of note is the complete loss of <sup>6</sup>Li-<sup>15</sup>N scalar coupling in [<sup>6</sup>Li,<sup>15</sup>N]5 in THF-pentane or THF-toluene solvent mixtures at temperatures down to -110 °C.<sup>18</sup> <sup>13</sup>C NMR spectroscopy in toluene-*d*<sub>8</sub>-THF-*d*<sub>8</sub> mixtures at temperatures down to -125 °C failed to demonstrate <sup>6</sup>Li-<sup>13</sup>C coupling. Apparently THF facilitates rapid chemical exchange, and we are thus unable to confirm the monomeric aggregation state of 5 at low concentrations in THF proposed by Bauer and Seebach<sup>8a</sup> and Streitwieser.<sup>19</sup> The possibility that 5 exists as a solvent-separated ion pair in THF also cannot be ruled out.

Finally, addition of 0.5 equiv of [<sup>15</sup>N]phenylacetonitrile to 0.1 M [<sup>6</sup>Li]LiHMDS in toluene containing 1 equiv of TMEDA gave a 1:2:2 mixture of 7, mixed aggregate [<sup>6</sup>Li,<sup>14</sup>N,<sup>15</sup>N]8, and TMEDA-solvated LiHMDS 9.<sup>20</sup> <sup>6</sup>Li-<sup>15</sup>N HMQC<sup>21</sup> of [<sup>6</sup>Li,<sup>15</sup>N,<sup>15</sup>N]8 prepared from [<sup>6</sup>Li,<sup>15</sup>N]LiHMDS confirmed the structural assignment (Figure 1). Mixed aggregates of lithiated nitriles with alkylolithiums have been proposed as intermediates in solution,<sup>3b,22</sup> and a mixed aggregate of 5 and lithium diisopropylamide has been characterized in the solid state.<sup>3b</sup> In contrast to a previous <sup>13</sup>C NMR study,<sup>22</sup> we find no evidence for mixed aggregation of 5 and LiHMDS in THF.<sup>23</sup>

(16) Methyl site exchange has also been observed by Schleyer and Weiss in TMEDA-solvated lithioindole dimer ( $\Delta\nu = 693$  Hz,  $T_c = -65$  °C,  $\Delta G_{298K}^\ddagger = 9.0$  kcal mol<sup>-1</sup>): Gregory, K.; Bremer, M.; Bauer, W.; Schleyer, P. v. R.; Lorenzen, N. P.; Kopf, J.; Weiss, E. *Organometallics* **1990**, *9*, 1485.

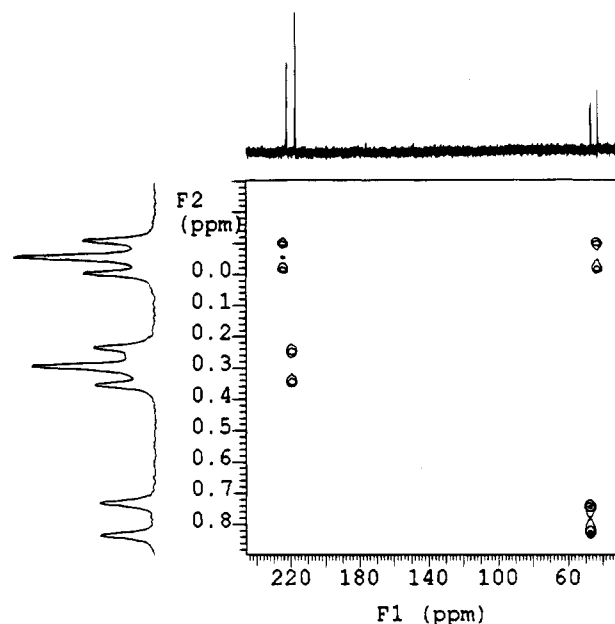
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(18) A sharp, single line is observed: in 1:2 pentane:THF, <sup>6</sup>Li δ -0.35 ppm,  $w_{1/2} = 1.3$  Hz; in 1:2 toluene:THF, <sup>6</sup>Li δ -0.52 ppm,  $w_{1/2} = 1.5$  Hz.

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**Figure 1.** <sup>6</sup>Li-<sup>15</sup>N HMQC spectrum of solution of 0.1 M [<sup>6</sup>Li,<sup>15</sup>N]-LiHMDS containing 0.5 equiv of [<sup>15</sup>N]phenylacetonitrile and 1.0 equiv of [<sup>14</sup>N<sub>2</sub>]TMEDA. The left and upper traces are the corresponding one-dimensional <sup>6</sup>Li and <sup>15</sup>N{<sup>1</sup>H,<sup>6</sup>Li} 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 <sup>6</sup>Li and <sup>15</sup>N, respectively. Data were processed in the phase sensitive mode. Digital resolution in *f*<sub>1</sub> prior to zero-filling is 188 Hz.

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**Supplementary Material Available:** <sup>6</sup>Li-, <sup>15</sup>N-, and <sup>6</sup>Li-detected <sup>15</sup>N zero-quantum NMR spectra for 6 and 7; <sup>6</sup>Li and <sup>15</sup>N spectra of mixtures of 7, 8, and 9; variable temperature <sup>13</sup>C NMR of [<sup>6</sup>Li,<sup>14</sup>N]7; synthetic procedure and analytical data for [<sup>15</sup>N]phenylacetonitrile (4 pages). 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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(23) The absence of mixed aggregation in THF may be an indication that 5 itself is monomeric in that solvent; under such conditions there may be little driving force for mixed aggregation with monomeric<sup>12a</sup> LiHMDS.