

$^6\text{Li}/^{15}\text{N}$ NMR-Based Solution Structural Determination of Et_2O - and TMEDA-Solvated Lithiophenylacetonitrile and a LiHMDS Mixed Aggregate

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Deprotonated nitriles have proven to be useful reagents in organic synthesis.¹ However, in contrast to the enolates of ketones, esters, and amides, little information is available on the solution structures of the corresponding nitrile anions.^{1b} 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.^{2,3} Ab initio calculations indicate that a bridged structure **3** is favored for unsolvated lithioacetonitrile.^{4,5} Solution state studies have been less conclusive.⁶ On the basis of ^{13}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.⁷ 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.^{8,9} In this communication we demonstrate the use of $^6\text{Li}/^{15}\text{N}$ NMR spectroscopy¹⁰ to unambiguously determine both the

Chart 1

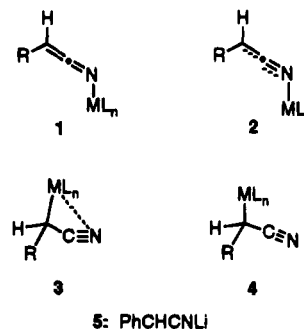
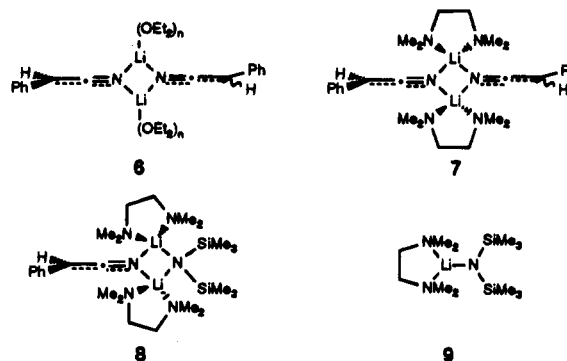


Chart 2



position of metalation and the aggregation state of Et_2O - 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 $[\text{}^6\text{Li},^{15}\text{N}]\text{5}$ was prepared from $[\text{}^{15}\text{N}]$ phenylacetonitrile¹¹ and 1.0 equiv of $[\text{}^6\text{Li}]\text{LiHMDS}$ ¹² in 2:1 toluene:diethyl ether at $-78\text{ }^\circ\text{C}$. The ^6Li and ^{15}N NMR spectra recorded at $-90\text{ }^\circ\text{C}$ (^6Li triplet, ^{15}N quintet, $^1J_{\text{Li-N}} = 3.4\text{ Hz}$) are consistent with a cyclic oligomer, characteristic of related *N*-lithiated species.¹³ Inverse-detected ^{15}N homonuclear zero-quantum NMR spectroscopy¹⁴ 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.^{3a}

The observed $^6\text{Li}-^{15}\text{N}$ 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_2N_2 core established by NMR spectroscopy, *C*-Li contact should be geometrically unfavorable. However, to further investigate this possibility, the ^{13}C NMR spectrum of $[\text{}^6\text{Li},^{14}\text{N}]\text{7}$ was examined, and no $^6\text{Li}-^{13}\text{C}$ coupling was observed at the α -cyano carbon (32.7 ppm) down to $-90\text{ }^\circ\text{C}$. Fluxional behavior of the TMEDA ligands was also evident, exhibiting two methyl resonances and one methylene resonance at $-90\text{ }^\circ\text{C}$. Coalescence of the methyls occurred at $-70\text{ }^\circ\text{C}$, indicating $\Delta G^\ddagger_{203\text{K}} = 9.0 \pm 0.3\text{ kcal mol}^{-1}$ ($\Delta\nu = 471\text{ Hz}$).^{15,16}

(11) Prepared from benzyl bromide and $[\text{}^{15}\text{N}]\text{KCN}$ in CH_3CN 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) $\{[\text{PhCHCNLi}(\text{tmeda})_2\text{C}_6\text{H}_6]\}$: Boche, G.; Marsch, M.; Harms, K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 373. (b) $\{[\text{PhCHCNLi}(\text{tmeda})\text{Li}(\text{tmeda})\text{N}(\text{i-Pr})_2]\}$: 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) $[\text{Cp}_2\text{La}(\eta^2\text{-CH}_2\text{CN})_2]$: 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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Table 1. NMR Spectroscopic Data of 6-9^a

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

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

⁶Li/¹⁵N NMR spectroscopy has been an effective tool for uncovering the stereochemical diversity present in lithium amides.^{10,17} 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 ⁶Li-¹⁵N scalar coupling in [⁶Li,¹⁵N]5 in THF-pentane or THF-toluene solvent mixtures at temperatures down to -110 °C.¹⁸ ¹³C NMR spectroscopy in toluene-*d*₈-THF-*d*₈ mixtures at temperatures down to -125 °C failed to demonstrate ⁶Li-¹³C 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^{8a} and Streitwieser.¹⁹ 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 [¹⁵N]phenylacetonitrile to 0.1 M [⁶Li]LiHMDS in toluene containing 1 equiv of TMEDA gave a 1:2:2 mixture of 7, mixed aggregate [⁶Li,¹⁴N,¹⁵N]8, and TMEDA-solvated LiHMDS 9.²⁰ ⁶Li-¹⁵N HMQC²¹ of [⁶Li,¹⁵N,¹⁵N]8 prepared from [⁶Li,¹⁵N]LiHMDS confirmed the structural assignment (Figure 1). Mixed aggregates of lithiated nitriles with alkylolithiums have been proposed as intermediates in solution,^{3b,22} and a mixed aggregate of 5 and lithium diisopropylamide has been characterized in the solid state.^{3b} In contrast to a previous ¹³C NMR study,²² we find no evidence for mixed aggregation of 5 and LiHMDS in THF.²³

(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, $\Delta G^\ddagger_{298K} = 9.0$ kcal mol⁻¹): 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, ⁶Li δ -0.35 ppm, $w_{1/2} = 1.3$ Hz; in 1:2 toluene:THF, ⁶Li δ -0.52 ppm, $w_{1/2} = 1.5$ Hz.

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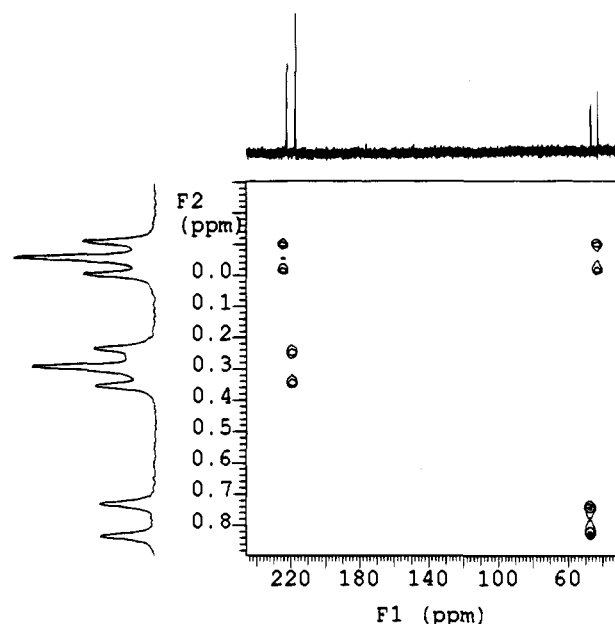


Figure 1. ⁶Li-¹⁵N HMQC spectrum of solution of 0.1 M [⁶Li,¹⁵N]-LiHMDS containing 0.5 equiv of [¹⁵N]phenylacetonitrile and 1.0 equiv of [¹⁴N₂]TMEDA. The left and upper traces are the corresponding one-dimensional ⁶Li and ¹⁵N{¹H,⁶Li} spectra, respectively. The spectrum was recorded on a Varian Unity 500 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 ⁶Li and ¹⁵N, respectively. Data were processed in the phase sensitive mode. Digital resolution in *f*₁ prior to zero-filling is 188 Hz.

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Supplementary Material Available: ⁶Li-, ¹⁵N-, and ⁶Li-detected ¹⁵N zero-quantum NMR spectra for 6 and 7; ⁶Li and ¹⁵N spectra of mixtures of 7, 8, and 9; variable temperature ¹³C NMR of [⁶Li,¹⁴N]7; synthetic procedure and analytical data for [¹⁵N]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^{12a} LiHMDS.